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New Iron-, Cobalt- and Nickel-Catalyzed Cross-Coupling Reactions.

Preparation and Application of Functionalized Aryllanthanum and Arylsamarium Reagents

von

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Erklärung

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Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

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(Andreas D. Benischke)

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Parts of this PhD Thesis have been published:

1) **Andreas D. Benischke**, Antoine J. A. Breuillac, Alban Moyeux, Gérard Cahiez, Paul Knochel, "Iron-Catalyzed Cross-Coupling of Benzylic Manganese Chlorides with Aryl and Heteroaryl Halides", *Synlett* **2016**, *27*, 471.

2) **Andreas D. Benischke**, Irina Knoll, Alice Rérat, Corinne Gosmini, Paul Knochel, "A Practical Cobalt-Catalyzed Cross-Coupling of Benzylic Zinc Reagents with Aryl and Heteroaryl Bromides or Chlorides", *Chem. Commun.* **2016**, *52*, 3171.

3) Zhi-Liang Shen[+], Vasudevan Dhayalan[+], **Andreas D. Benischke**[+], Robert Greiner, Konstantin Karaghiosoff, Peter Mayer, Paul Knochel, "Polyfunctional Lithium, Magnesium, and Zinc Alkenyl Reagents as Building Blocks for the Synthesis of Complex Heterocycles", *Angew. Chem. Int. Ed.* **2016**, *55*, 5332.

4) **Andreas D. Benischke**, Marcel Leroux, Irina Knoll, Paul Knochel, "Iron-Catalyzed Acylation of Polyfunctionalized Aryl- and Benzylzinc Halides with Acid Chlorides", *Org. Lett.* **2016**, *18*, 3626.

5) Yingxiao Cai, **Andreas D. Benischke**, Paul Knochel, Corinne Gosmini, "Cobalt-Catalyzed Reductive Cross-Coupling Between Styryl and Benzyl Halides", *Chem. Eur. J.* **2017**, *23*, 250.

6) **Andreas D. Benischke**, Grégoire Le Corre, Paul Knochel, "Preparation of Polyfunctional Organozinc Halides by an InX_3- and LiCl-Catalyzed Zinc Insertion to Aryl and Heteroaryl Iodides and Bromides", *Chem. Eur. J.* **2017**, *23*, 778.

7) **Andreas D. Benischke**, Alexandre Desaintjean, Thomas Juli, Gérard Cahiez, Paul Knochel, "Nickel-Catalyzed Cross-Coupling of Functionalized Organomanganese Reagents with Aryl and Heteroaryl Halides Promoted by 4-Fluorostyrene", *Synthesis* **2017**, *49*, 5396.

8) **Andreas D. Benischke**[+], Lucile Anthore-Dalion[+], Guillaume Berionni, Paul Knochel, "Preparation of Functionalized Diaryl- and Diheteroaryllanthanum Reagents by Fast Halogen-Lanthanum Exchange", *Angew. Chem. Int. Ed.* **2017**, *56*, 16390.

9) **Andreas D. Benischke**[+], Lucile Anthore-Dalion[+], Fabien Kohl, Paul Knochel, "Synthesis of Polyfunctionalized Triaryllanthanum Reagents Using Ph_3La and Related Species as Exchange Reagents", *Chem Eur. J.* **2018**, doi.org/10.1002/chem.201801527.

Reviews:

1) **Andreas D. Benischke**, Mario Ellwart, Matthias R. Becker, Paul Knochel, "Polyfunctional Zinc and Magnesium Organometallics for Organic Synthesis: Some Perspectives", *Synthesis* **2016**, *48*, 1101.

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List of Abbreviations:

Ac	acetyl
acac	acetylacetonate
aq.	aqueous
Ar	aryl
Bn	benzyl
Bu	butyl
calc.	calculated
conc.	concentrated
dba	trans,trans-dibenzylideneacetone
DBE	1,2-dibromoethane
DMA	*N*,*N*-dimethylacetamide
DMAP	4-(dimethylamino)pyridine
DMF	*N*,*N*-dimethylformamide
DMPU	*N*,*N′*-dimethylpropylenurea
dppe	1,2-bis(diphenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane
E	electrophile
EI	electron impact ionization
eq.	equation
equiv	equivalents
Et	ethyl
FG	functional group
GC	gas chromatography
h	hour
HRMS	high resolution mass spectrometry
*i*Pr	*iso*-propyl
IR	infra-red
J	coupling constant
M	molarity
m	meta
M.p.	melting point
Me	methyl
MeCN	acetonitrile
Met	metal
min	minute

mmol	millimole
MS	mass spectrometry
MTBE	methyl *tert*-butyl ether
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
o	ortho
p	para
Ph	phenyl
PMDETA	*N*,*N*,*N′*,*N″*,*N‴*-pentamethyldiethylenetriamine
QPhos	1,2,3,4,5-pentaphenyl-1′-(di-*tert*-butylphosphino)ferrocene
R	residue
r.t.	room temperature
SPhos	2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl
*t*Bu	*tert*-butyl
Tf	triflate
Tfp	tris-(2-furyl)phophine
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	*N*,*N*,*N′*,*N′*-tetramethylethane-1,2-diamine
TMP	2,2,6,6-tetramethylpiperidyl
TMS	trimethylsilyl
XPhos	2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl
XantPhos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

A. Introduction

A. Introduction

1. Overview

Organometallic compounds are still considered to be important tools in organic chemistry and are expedient intermediates for the formation of carbon–carbon bonds.[1] Almost 170 years ago, *Frankland* synthesized the first organometallic reagent, diethyl zinc, by the reaction of elemental zinc dust and ethyl iodide.[2] From that point on, the concept of "organometallic reagents and their application in organic synthesis" was born and was later on highlighted by the discovery of the first organomagnesium reagent by *Grignard* in 1900.[3] Those two breakthrough discoveries set the stage for other pioneering contributions of famous chemists like *Ziegler*,[4] *Wittig*,[5] *Gilman*,[6] and *Grubbs*[7] for instance. Today, we look back to more than 150 years of success, a variety of outstanding developments and several Nobel prizes which have been awarded. Among them, the Nobel prize awarded to *Negishi*, *Suzuki*, and *Heck* for "palladium-catalyzed cross-couplings in organic synthesis" in 2010 points out the high importance of this field for the synthetic community.[8] For synthetic chemists, organometallic chemistry is a versatile toolbox with a range of different metals and each has got its own reactivity and properties. In general, the unique reactivity of the used organometallic reagent is based on the nature of the carbon–metal bond. As a point of reference the difference in electronegativity of carbon and the metal directly attached to it can be used. Thus, the more polarized the carbon–metal bond, the more reactive it is, and only low functional group compatibility is reached. According to this general methodology a broad range of organometallic compounds with well differentiable and fine-tuned reactivity is available (Figure 1).

Li	La	Sm	Mg	Sc	Mn	Al	Zn	In	Ga	Cu	B
[0.98]	[1.10]	[1.17]	[1.30]	[1.36]	[1.55]	[1.61]	[1.65]	[1.78]	[1.81]	[1.90]	[2.04]

Electronegativity scale (Pauling)

C
[2.55]

Figure 1: Electronegativity scale of selected metals compared to carbon (Pauling scale).[9]

[1] a) *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **2004**; b) *Handbook of Functionalized Organometallics: Applications in Synthesis* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**.
[2] a) E. Frankland, *Liebigs Ann. Chem.* **1849**, *71*, 171; b) E. Frankland, *J. Chem. Soc.* **1849**, *2*, 263.
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[4] K. Ziegler, H. Colonius, *Liebigs Ann. Chem.* **1930**, *479*, 135.
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[6] H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106.
[7] *Handbook of Metathesis* (Eds.: R. H. Grubbs, A. G. Wenzel, D. J. O'Leary, E. Khosravi), Wiley-VCH, Weinheim, **2015**.
[8] a) E. Negishi, *Angew. Chem. Int. Ed.* **2011**, *50*, 6738; b) *The Nobel Prize in Chemistry 2010*, Nobelprize.org, 12.02.2018, www.nobelprize.org/nobel_prizes/chemistry/ laureates/2010.
[9] L. Pauling, *J. Am. Chem. Soc.* **1932**, *54*, 3570.

A. Introduction

Based on figure 1, organolithium reagents have got a highly polarized carbon–metal bond with a large difference in electronegativity (1.57). Therefore, they are considered to be the most reactive organometallic derivatives and show a low tolerance towards sensitive functional groups such as esters or nitriles. Some other candidates with a slightly improved functional group compatibility are lanthanide-derived organometallics such as organolanthanum or organosamarium reagents. With reference to their electronegativity, they still remain very reactive organometallics but sensitive functional groups like nitriles or esters can be tolerated under certain conditions.

In contrast to those highly reactive intermediates, organomagnesium and especially organomanganese reagents possess a less polarized carbon–metal bond (difference in electronegativity: 1.24, 1.00 respectively), show a middle-rate reactivity, and can be often used at appropriate low or even ambient temperatures including a range of different substituents. Furthermore, organoaluminum, -zinc and -indium derivatives have got an even more covalent carbon–metal bond, and a variety of sensitive functional groups like nitriles, ester, ketones and even aldehydes can be tolerated at room temperature. Nevertheless, due to the low difference in electronegativity of those metals and carbon, a significantly lower reactivity is observed, and higher temperatures for their preparation and subsequent transformations are needed. As a last point, organoboron compounds with the most covalent carbon–metal bond show the highest compatibility. As a drawback, either harsh conditions or well-designed catalysts are necessary for subsequent reactions with selected electrophiles.

Considering all this, the range of organometallic reagents displays a suitable and easy accessible toolbox of compounds which can be used for a variety of different reactions in organic synthesis. Their fine-tuned reactivities and often straightforward preparations can be applied to key steps for the preparation of complex molecules made by the agrochemical or pharmaceutical industry. Reactions such as 1,2-additions to aldehydes or ketones, 1,4-additions, acylations, allylic-substitutions and transition-metal-catalyzed cross-coupling reactions are the most common applications of such versatile intermediates. In the following, some synthetic routes towards selected pharmaceutical and agrochemical compounds are given, including the two medicinal products valsartan (**1**)[10] and efavirenz (**4**)[11] and the pesticides boscalid (**8**)[12] and ancymidol (**12**)[13].

Valsartan (**1**) belongs to the group of angiotensin II receptor antagonists, and is used for treatment of high blood pressure and congestive heart failure. One of the typical key steps for its preparation involves a *Negishi* cross-coupling of *N*-(4-bromobenzyl)-*N*-pentanoyl-L-valinate (**2**) with the *ortho*-metalated 5-phenyl-1-trityl-1*H*-tetrazole (**3**) using a catalytic system consisting of $Pd(OAc)_2$ and QPhos[14] leading to valsartan (**1**).[10]

[10] S. Ghosh, A. S. Kumar, G. N. Mehta, *Beilstein J. Org. Chem.* **2010**, *6*, 27.
[11] M. E. Pierce, R. L. Parsons, L. A. Radesca, Y. S. Lo, S. Silverman, J. R. Moore, Q. Islam, A. Choudhury, J. M. D. Fortunak, D. Nguyen, C. Luo, S. J. Morgan, W. P. Davis, P. N. Confalone, *J. Org. Chem.* **1998**, *63*, 8536.
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[13] R. Vince, A. P. Vartak, US20140121375, **2014**.
[14] G. D. Vo, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2008**, *47*, 2127.

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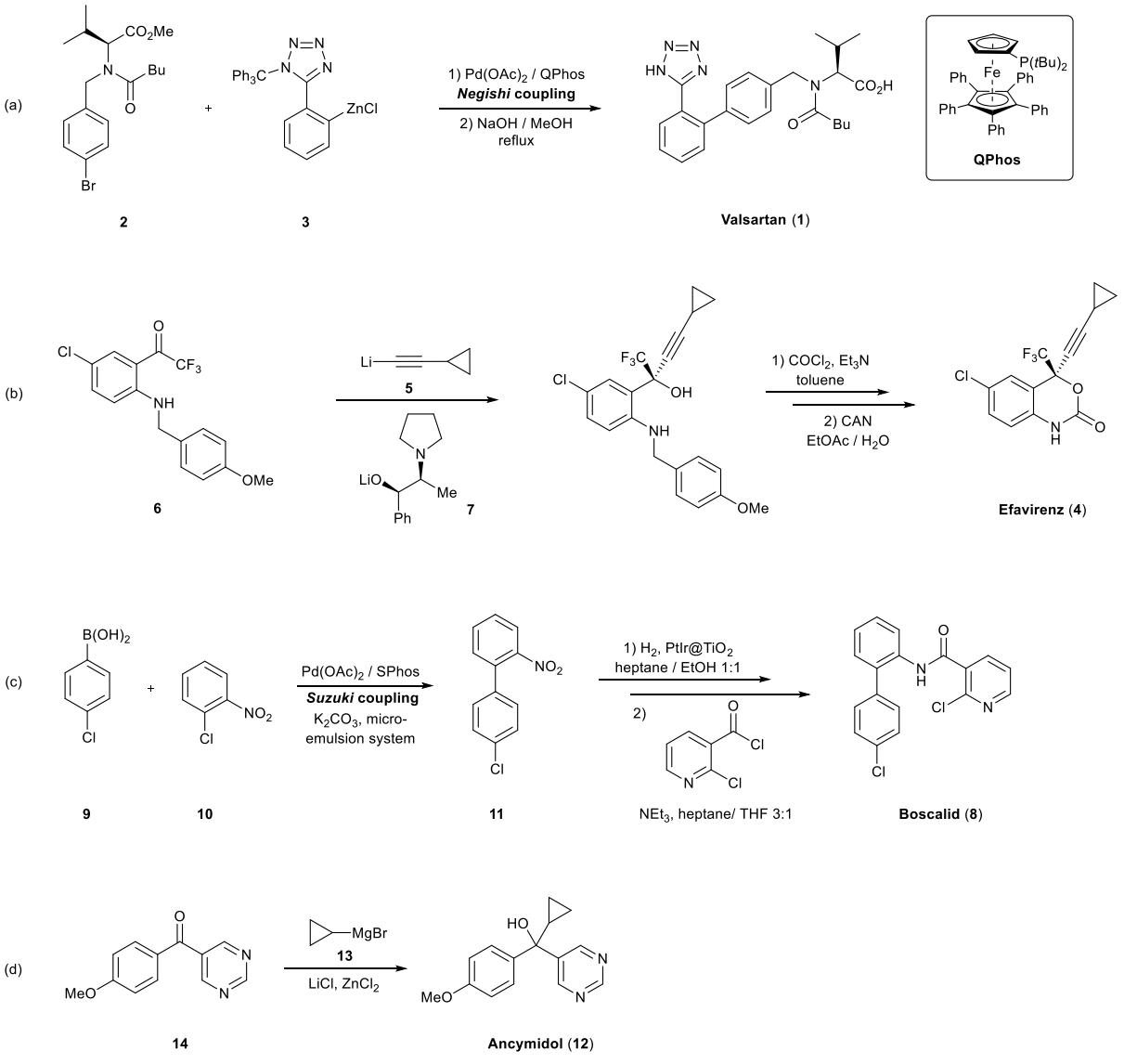
Efavirenz (**4**) is a HIV-1 reverse transcriptase inhibitor and used to treat and prevent AIDS. In the synthesis of *Confalone et al.*, an enantioselective addition of Li-cyclopropyl acetylide (**5**) to a *p*-methoxybenzyl-protected ketoaniline **6** mediated by the (1*R*,2*S*)-*N*-pyrrolidinylnorephedrine lithium alkoxide (**7**) is used to establish the stereogenic center.[11] Organometallic intermediates also play a crucial role in the typical syntheses of the two pesticides boscalid and ancymidol.[12,13] In the case of boscalid (**8**), a *Suzuki* cross-coupling of 4-chlorobenzeneboronic acid (**9**) and 1-chloro-2-nitrobenzene (**10**) is used to generate the desired biphenyl **11** which can be further modified. The last step for the preparation of ancymidol (**12**) is a 1,2-addition of an alkyl organometallic **13** to the prior formed ketone **14** (Scheme 1).



Scheme 1: Preparation of valsartan (**1**), efavirenz (**4**), boscalid (**8**) and ancymidol (**12**) using organometallic reagents in one of the key steps.

2. Preparation of Organomanganese Reagents

2.1. Introduction

In the recent years, the use of organometallic reagents in organic synthesis has attracted increased interest.[15] Intermediates derived from lithium,[16] magnesium,[17] and zinc[18] are still the most common ones, and the application of nickel or palladium catalysts is well established.[19] However, there is still a need for organometallic derivatives which display intermediate reactivity and possess unique properties. Nowadays, terms such as sustainability, atom-economy,[20] and eco-friendly synthesis play an important role in the strategies of the chemical industry.

By comparison with the above-mentioned metals, manganese can be an interesting alternative. Due to its slightly lower electronegativity (EN: 1.55) compared to zinc (EN: 1.65) and therefore more polarized carbon–metal bond, organomanganese reagents show a well-balanced and increased reactivity with still high tolerance towards sensitive functional groups. Moreover, manganese is relatively cheap and toxicologically benign.[21]

2.2. Oxidative Insertion of Manganese into Carbon–Halogen Bonds

Oxidative insertion reactions of metals into carbon–halogen bonds are very attractive, since the prior preparation of the corresponding organolithium or organomagnesium precursors and subsequent transmetalation are no longer necessary. This preparative pathway is a convenient way to obtain functionalized organomanganese derivatives, which can be often stored and used at room temperature. In 1983, *Hiyama* and co-workers described a new *Barbier-type* reaction, starting from commercially available manganese powder, an allyl bromide **15** as substrate and a carbonyl compound **16** as electrophile leading to secondary and tertiary alcohols **17**.[22] Later on, *Cahiez* developed a similar reaction pathway using massive coarse-ground manganese, allylic halides or α-halogenoesters **18** as starting material, $ZnCl_2$ as additive and different carbonyl compounds **19** as electrophiles generating the desired alcohols **20** (Scheme 2).[23]

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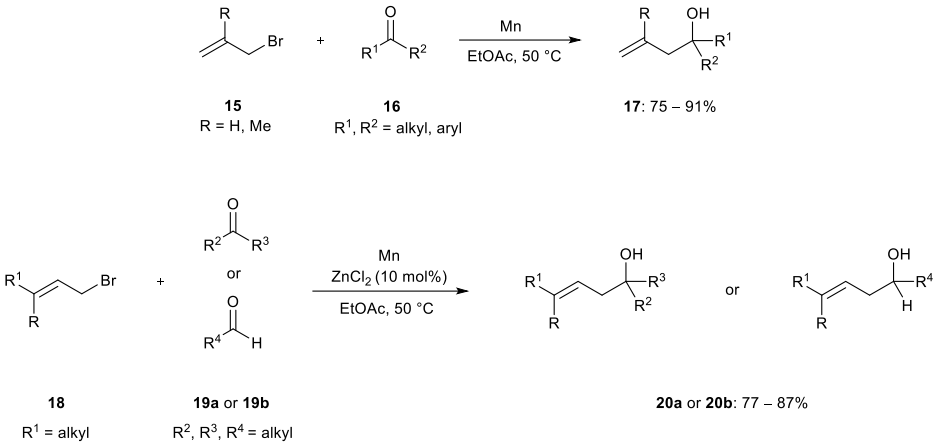
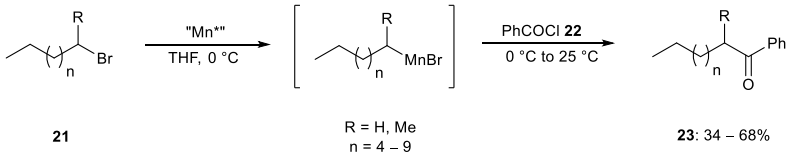
[15] *Comprehensive Organometallic Chemistry III: From Fundamentals to Applications* (Eds.: R. Crabtree, M. Mingos), Elsevier Ltd., Oxford, **2007**.
[16] *Organolithiums: Selectivity for Synthesis* (Ed.: J. Clayden), Elsevier Science Ltd., Oxford, **2002**.
[17] P. Knochel, A. Krasovskiy, I. Sapountzis, *Handbook of Functionalized Organometallics: Applications in Synthesis* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**, Vol 1, p. 109.
[18] *The Chemistry of Organozinc Compounds* (Eds.: Z. Rappoport, I. Marek), John Wiley & Sons Ltd., Chichester, **2006**.
[19] a) J. Corbet, G. Mignani, *Chem. Rev.* **2006**, *106*, 2651; b) J. Magano, J. R. Dunetz, *Chem. Rev.* **2011**, *111*, 2177; c) C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062.
[20] B. M. Trost, *Science* **1991**, *254*, 1471.
[21] C. Duplais, J. Buendia, G. Cahiez, *Chem. Rev.* **2009**, *109*, 1434.
[22] T. Hiyama, M. Sawahata, M. Obayashi, *Chem. Lett.* **1983**, *8*, 1237.
[23] G. Cahiez, P.-Y. Chavant, *Tetrahedron Lett.* **1989**, *30*, 7373.

Additionally, *Takai* found that manganese can be activated by the addition of catalytic amounts of $PbCl_2$ and TMSCl.[24]



Scheme 2: Oxidative addition of elemental manganese to allylic bromides **15** and **18** and *in situ* trapping with carbonyl compounds **16** and **19** (*Barbier-type* conditions).

In 1996, another approach was performed by *Rieke* who prepared highly reactive manganese by the reduction of anhydrous manganese halides with two equivalents of lithium, and a catalytic amount of naphthalene as electron carrier.[25] The corresponding alkyl bromide **21** was added to a solution of highly activated manganese in THF at 0 °C and subsequent addition of benzoyl chloride (**22**) gave the desired ketones **23** (Scheme 3).

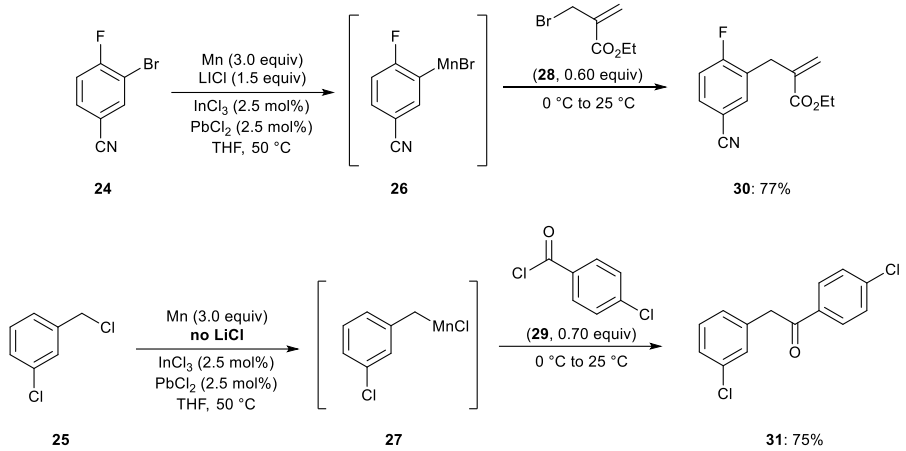


Scheme 3: *Rieke* manganese and its application towards alkyl bromides **21**.

Recently, also *Knochel* and co-workers demonstrated a new preparation of functionalized aryl and benzyl manganese reagents.[26] This pathway involves the use of commercially available manganese powder, LiCl as additive, and catalytic amounts of $InCl_3$ and $PbCl_2$. Prior reports on the activation of aluminum have shown that combinations of strong Lewis-acids like $InCl_3$, $PbCl_2$, $BiCl_3$ or $TiCl_4$ with LiCl are beneficial for the oxidative addition of metals into carbon–halogen bonds.[27] Thus, the oxidative insertion of manganese into an aryl or benzyl halide **24** and **25** proceeded under the above mentioned conditions, leading to the functionalized aryl or benzyl manganese halides **26** and **27**, and subsequent

[24] K. Takai, T. Ueda, T. Hayashi, T. Moriwake, *Tetrahedron Lett.* **1996**, *37*, 7049.
[25] a) R. D. Rieke, *Acc. Chem. Res.* **1977**, *10*, 301; b) S.-H. Kim, M. V. Hanson, R. D. Rieke, *Tetrahedron Lett.* **1996**, *37*, 2197; c) R. D. Rieke, S.-H. Kim, X. Wu, *J. Org. Chem.* **1997**, *62*, 6921; d) S.-H. Kim, R. D. Rieke, *Synth. Commun.* **1998**, *28*, 1065; e) S.-H. Kim, R. D. Rieke, *Tetrahedron Lett.* **1999**, *40*, 4931; f) R. D. Rieke, Y. S. Suh, S.-H. Kim, *Tetrahedron Lett.* **2005**, *46*, 5961.
[26] Z. Peng, P. Knochel, *Org. Lett.* **2011**, *13*, 3198.
[27] T. Blümke, Y.-H. Chen, Z. Peng, P. Knochel, *Nat. Chem.* **2010**, *2*, 313.

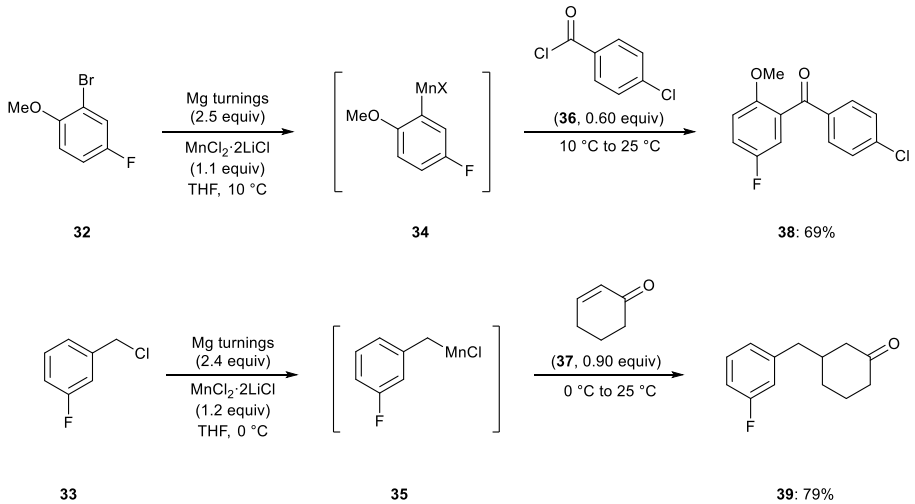
reaction with the electrophiles **28** and **29** gave the desired products **30** and **31**. In the case of benzyl halides the oxidative addition was performed in the absence of LiCl, since this salt favoured the formation of unwanted homocoupling (Scheme 4). An important and unique property of organo-manganese derivatives is that no transition-metal catalysts are needed for further transformations with selected electrophiles except cross-coupling reactions. Due to their exceptional reactivity, they selectively undergo acylation reactions with acid chlorides, allylic substitutions and 1,4-additions in the absence of any catalyst.



Scheme 4: Oxidative addition of manganese into carbon–halogen bonds promoted by $InCl_3$ and $PbCl_2$.

2.3. Magnesium Insertion in the Presence of $MnCl_2$

Besides the direct oxidative addition of elemental manganese into carbon–halogen bonds, another useful alternative for the preparation of functionalized organomanganese compounds exists. It relies on the oxidative insertion of magnesium in the presence of $MnCl_2 \cdot 2LiCl$, so called *in situ* transmetalation, and can be used for a variety of substrates and proceeds smoothly at appropriate low temperature in THF.[28]



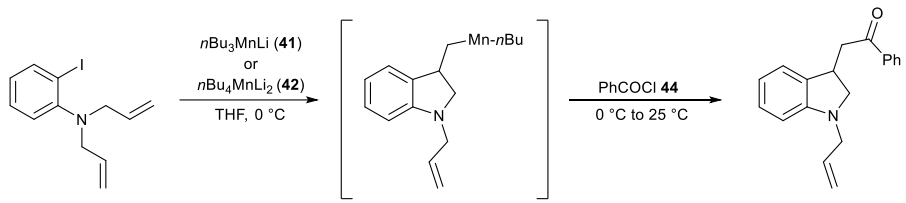
Scheme 5: Direct insertion of magnesium into aryl and benzyl halides in the presence of $MnCl_2 \cdot 2LiCl$.

[28] a) Z. Peng, N. Li, X. Sun, F. Wang, L. Xu, C. Jiang, L. Song, Z.-F. Yan, *Org. Biomol. Chem.* **2014**, *12*, 7800; b) P. Quinio, A. D. Benischke, A. Moyeux, G. Cahiez, P. Knochel, *Synlett* **2015**, *26*, 514.

This methodology involves magnesium turnings and a prior prepared $MnCl_2 \cdot 2LiCl$ solution in THF. Both components are mixed, cooled to an appropriate temperature, and the corresponding aryl or benzyl halide **32** or **33** is added. Once the LiCl-mediated direct insertion of magnesium is finished, the transmetalation by $MnCl_2$ takes place, and the desired aryl or benzyl manganese halides **34** or **35** are formed. Subsequent trapping reactions with either an acid chloride **36**, or an enone **37** can be performed without catalyst, yielding the desired products **38** and **39** (Scheme 5).

2.4. The Iodine-Manganese Exchange Reaction

Halogen-metal exchange reactions, such as halogen-lithium[29] or halogen-magnesium[30] exchange processes, are easy and straightforward synthetic pathways for the preparation of organometallic reagents. However, examples for a related halogen-manganese exchange are scarce, and only a few have been reported. *Hosomi*[31]and *Oshima*[32] described halogen-manganese exchange reactions by using an aryl iodide **40** and tri- or tetraalkylmanganates of type nBu$_3$MnLi (**41**) or nBu$_4$MnLi$_2$ (**42**). The reagents, such as the indoline-derivative **43**, prepared *via* these exchange reactions are often not long term stable, suffer from β-hydride elimation, and need to be trapped directly with reactive electrophiles such as benzoyl chloride (**44**) to form the desired ketone **45** (Scheme 6).

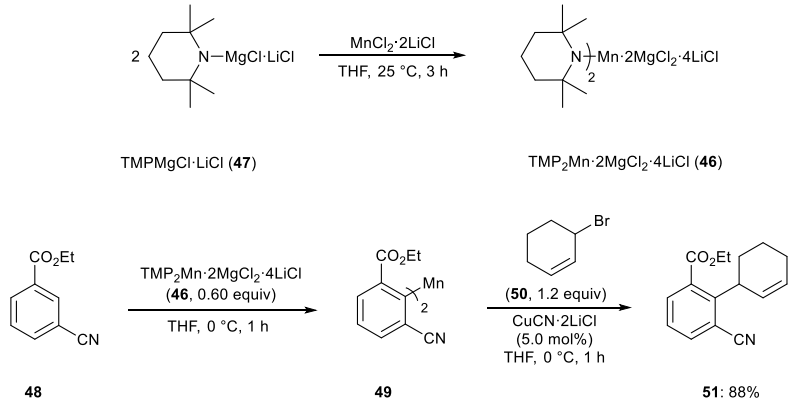


Scheme 6: Iodine-manganese exchange reaction.

[29] *Lithium Compounds in Organic Synthesis - From Fundamentals to Applications* (Eds.: R. Luisi, V. Capriati), Wiley-VCH, Weinheim, **2014**.
[30] *The Chemistry of Organomagnesium Compounds* (Eds.: Z. Rappoport, I. Marek), John Wiley & Sons Ltd, Chichester, **2008**.
[31] a) M. Hojo, H. Harada, H. Ito, A. Hosomi, *Chem. Commun.* **1997**, *21*, 2077; b) M. Hojo, H. Harada, H. Ito, A. Hosomi, *J. Am. Chem. Soc.* **1997**, *119*, 5459; c) M. Hojo, R. Sakuragi, Y. Murakami, Y. Baba, A. Hosomi, *Organometallics* **2000**, *19*, 4941.
[32] J. Nakao, R. Inoue, H. Shinokubo, K. Oshima, *J. Org. Chem.* **1997**, *62*, 1910.

2.5. Directed Deprotonation using Manganese Amide Bases

Another way to prepare polyfunctionalized organomanganese reagents relies on directed metalation *via* sterically hindered metal amide bases.[33] The convenient preparation of $TMP_2Mn{\cdot}2MgCl_2{\cdot}4LiCl$ (**46**) (TMP = 2,2,6,6-tetramethylpiperidyl) by transmetalation of TMPMgCl·LiCl (**47**) with $MnCl_2{\cdot}2LiCl$ at room temperature allows directed manganation reactions of a variety of functionalized arenes and heteroarenes.[34] Mild metalation conditions, unique chemoselectivity and better functional group tolerance, compared to the corresponding magnesium bases, make $TMP_2Mn{\cdot}2MgCl_2{\cdot}4LiCl$ (**46**) a very useful amide base for synthetic applications. As an example, ethyl 3-cyanobenzoate (**48**) proved to be a good substrate for such a directed metalation using **46** (0.60 equiv) at 0 °C. The resulting diaryl-manganese reagent **49** subsequently underwent an allylic substitution with 3-bromocyclohexene (**50**) affording product **51** (Scheme 7).



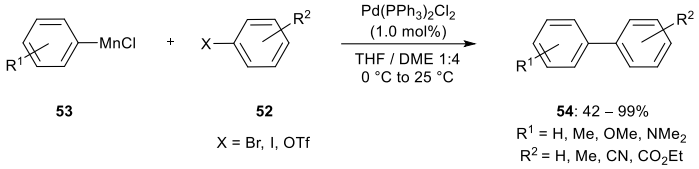
Scheme 7: Preparation of $TMP_2Mn{\cdot}2MgCl_2{\cdot}4LiCl$ (**46**) and its application in directed manganation.

2.6. Transition-Metal-Catalyzed Cross-Coupling Reactions of Organomanganese Reagents

For organometallic chemists, transition-metal-catalyzed cross-coupling reactions play an important role and are still of great interest.[35] Several metals have been applied to such transformations and a variety of catalysts have been developed. So far, *Kumada-Corriu* (organomagnesium),[36] *Negishi* (organozinc),[37]

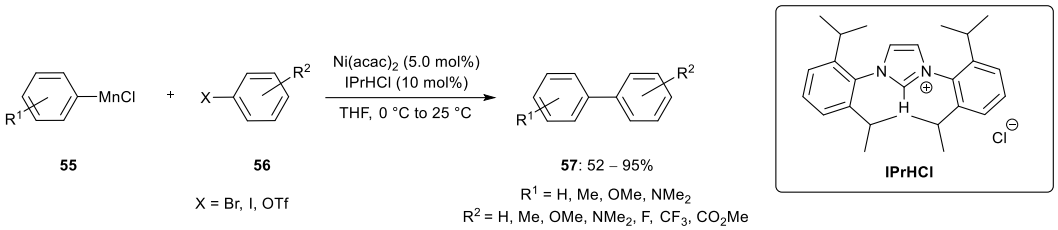
[33] B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794.
[34] S. H. Wunderlich, M. Kienle, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 7256.
[35] a) *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**; b) *Metal-Catalyzed Cross-Coupling Reactions and More* (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, **2014**.
[36] a) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374; b) C. E. I. Knappe, A. J. von Wangelin, *Chem. Soc. Rev.* **2011**, *40*, 4948.
[37] a) E. Negishi, S. Baba, *J. Am. Chem. Soc.* **1976**, *98*, 6729; b) D. Haas, J. M. Hammann, R. Greiner, P. Knochel, *ACS Catal.* **2016**, *6*, 1540.

S*tille* (organotin),[38] and *Suzuki-Miyaura* (organoboron)[39] cross-coupling reactions are well-established and found numerous applications. Recently, *Feringa* and co-workers described a practical Pd-catalyzed cross-coupling procedure of highly reactive organolithium reagents using $Pd_2(dba)_3$ and P(*t*Bu)$_3$ as catalytic system in toluene.[40] Regarding organomanganese reagents, the first palladium-catalyzed cross-coupling reaction was performed by *Cahiez et al.* in 1997.[41] In this report, they demonstrated a fast coupling of aryl halides and triflates **52** with functionalized arylmanganese chlorides **53** in the presence of $Pd(PPh_3)_2Cl_2$ leading to the unsymmetrical biaryls **54** (Scheme 8).



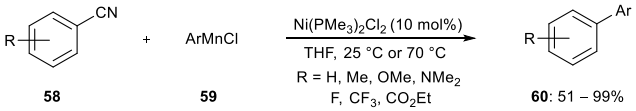
Scheme 8: Pd-catalyzed cross-couplings of arylmanganese chlorides **53** and aryl halides or triflates **52**.

Besides palladium catalyst, nickel-derived catalysts are considered to be powerful and cheap alternatives. In 2006, *Schneider* reported a catalytic system involving $Ni(acac)_2$ and a NHC ligand, which allows couplings of arylmanganese chlorides **55** and aryl halides **56** providing the biaryls **57** (Scheme 9).[42]



Scheme 9: Nickel-catalyzed, NHC ligand-promoted cross-coupling of organomanganese reagents.

Moreover, *Wang* and co-workers developed a nickel-catalyzed cross-coupling procedure of arene- or heteroarenecarbonitriles **58** with aryl- and heteroarylmanganese reagents **59** through a C–CN bond activation to obtain functionalized biaryls of type **60** (Scheme 10).[43]



Scheme 10: *Wang's* nickel-catalyzed cross-coupling procedure.

[38] a) J. K. Stille, *Angew. Chem. Int. Ed.* **1986**, *25*, 508; b) P. Espinet, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2004**, *43*, 4704.
[39] a) N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, *20*, 3437; b) A. Suzuki, *Angew. Chem. Int. Ed.* **2011**, *50*, 6722.
[40] M. Giannerini, M. Fananás-Mastral, B. L. Feringa, *Nat. Chem.* **2013**, *5*, 667.
[41] E. Riguet, M. Alami, G. Cahiez, *Tetrahedron Lett.* **1997**, *38*, 4397.
[42] A. Leleu, Y. Fort, R. Schneider, *Adv. Synth. Catal.* **2006**, *348*, 1086.
[43] N. Liu, Z.-X. Wang, *Adv. Synth. Catal.* **2012**, *354*, 1641.

In addition, several cross-coupling methodologies of organomanganese reagents involving iron,[44] cobalt,[45] and copper[46] catalysts are known. In this context, especially iron-catalyzed cross-coupling reactions are important, since it allows to replace palladium or nickel catalysts by inexpensive and nontoxic iron salts. In recent years, extensive studies were carried out on the catalytic activity of iron catalysts and their application in organometallic chemistry.[47]

[44] a) G. Cahiez, S. Marquais, *Tetrahedron Lett.* **1996**, *37*, 1773; b) G. Cahiez, S. Marquais, *Pure Appl. Chem.* **1996**, *68*, 53; c) M. S. Hofmayer, J. M. Hammann, G. Cahiez, P. Knochel, *Synlett* **2018**, *29*, 65.
[45] M. S. Hofmayer, J. M. Hammann, D. Haas, P. Knochel, *Org. Lett.* **2016**, *18*, 6456.
[46] a) J. G. Donkervoort, J. L. Vicario, J. T. B. H. Jastrzebski, R. A. Gossage, G. Cahiez, G. van Koten, *Recl. Trav. Chim. Pays-Bas Belg.* **1996**, *115*, 547; b) J. G. Donkervoort, J. L. Vicario, J. T. B. H. Jastrzebski, R. A. Gossage, G. Cahiez, G. van Koten, *J. Organomet. Chem.* **1998**, *558*, 61.
[47] a) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217; b) B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, *41*, 1500; c) W. M. Czaplik, M. Mayer, J. Cvengros, A. J. von Wangelin, *ChemSusChem* **2009**, *2*, 396.

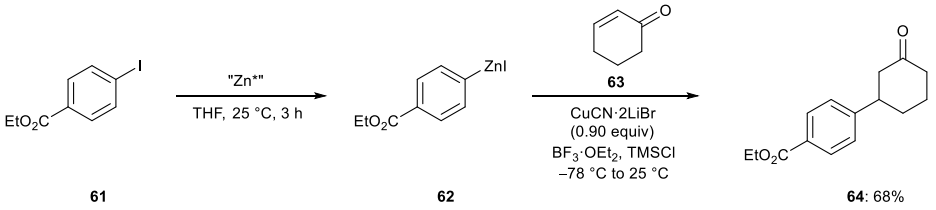
3. Preparation of Organozinc Reagents

3.1. Introduction

Organozinc reagents belong to the most frequently used organometallic intermediates, since they combine a high functional group compatibility with still appropriate reactivity.[48] Sensitive substituents like esters, nitriles or ketones can be tolerated at even high temperatures. Moreover, due to the more covalent character of the carbon–metal bond present in organozinc derivatives, it is also possible to tolerate electrophiles bearing acidic protons such as amides, amines or alcohols.[49] Taking this into account, organozinc compounds are versatile intermediates in organometallic chemistry, displaying a well-balanced reactivity, and an easy preparation through typical synthetic routes.

3.2. Oxidative Addition of Zinc into Carbon–Halogen Bonds

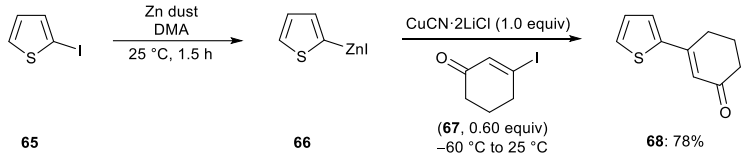
As already mentioned, the direct oxidative insertion of a metal into organic halides is a straightforward and atom-economical methodology for the preparation of organometallic reagents, and still one of the most used.[50] So far, several procedures have been described for such an oxidative addition. Already in 1989, *Rieke* reported the *in situ* reduction of zinc halides with metallic lithium in the presence of naphthalene to obtain highly reactive zinc, which then underwent insertion reactions to a variety of organic halides.[51] The addition of ethyl 4-iodobenzoate (**61**) to prior prepared active zinc led to the formation of the corresponding zinc reagent **62** within 3 h at 25 °C, subsequent copper-mediated 1,4-addition with enone **63** provided the desired product **64** (Scheme 11).



Scheme 11: *Rieke* zinc for the oxidative addition into ethyl 4-iodobenzoate (**61**).

[48] P. Knochel, H. Leuser, L.-Z. Cong, S. Perrone, F. F. Kneisel, *Handbook of Functionalized Organometallics: Applications in Synthesis* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**, Vol 1, p. 251.
[49] a) G. Manolikakes, C. Munoz Hernandez, M. A. Schade, P. Knochel, *J. Org. Chem.* **2008**, *7*3, 8422; b) G. Manolikakes, Z. Dong, H. Mayr, J. Li, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 1324.
[50] a) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Ed.* **2003**, *42*, 4302; b) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802; c) G. Dagousset, C. Francois, T. Léon, R. Blanc, E. Sansiaumme-Dagousset, P. Knochel, *Synthesis* **2014**, *46*, 3133; d) T. Klatt, J. T. Markiewicz, C. Sämann, P. Knochel, *J. Org. Chem*. **2014**, *79*, 4253; e) A. D. Benischke, M. Ellwart, M. R. Becker, *Synthesis* **2016**, *4*8, 1101.
[51] a) R. D. Rieke, *Science* **1989**, *246*, 1260; b) L. Zhu, R. M. Wehmeyer, R. D. Rieke, *J. Org. Chem.* **1991**, *56*, 1445; c) R. D. Rieke, M. V. Hanson, *Tetrahedron* **1997**, *53*, 1925; d) J. Lee, R. Velarde-Ortiz, A. Guijarro, J. R. Wurst, R. D. Rieke, *J. Org. Chem.* **2000**, *65*, 5428.

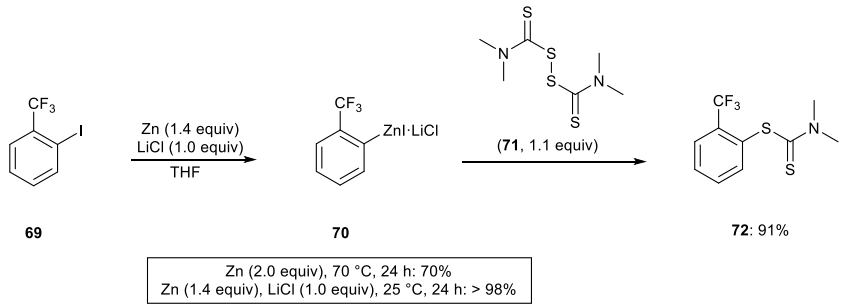
Later on, it was found that the addition of a polar co-solvent, such as *N*,*N*-dimethylacetamide (DMA), during the insertion reaction of commercial zinc dust to organic iodides enhanced the reaction rates.[52] Thus, the insertion of zinc to 2-iodothiophene (**65**) proceeded within 1.5 h at 25 °C, the resulting zinc reagent **66** was transmetalated to copper and further reacted with 3-iodo-cyclohexenone (**67**) yielding product **68** (Scheme 12).



Scheme 12: Oxidative insertion of elemental zinc dust in the presence of DMA.

In 2006, *Knochel* and co-workers reported that the addition of LiCl accelerates the rates of oxidative addition reactions to a large extent.[53] The insertion of zinc to 2-iodobenzotrifluoride (**69**) in the presence of LiCl took 24 h at 25 °C providing the desired zinc reagent **70** in above 98% yield, whereas without LiCl only 70% of reactive species **70** were obtained after 24 h at 70 °C. Subsequent trapping reaction with a thiocarbamoyl disulfide **71** led to the desired product **72** (Scheme 13).

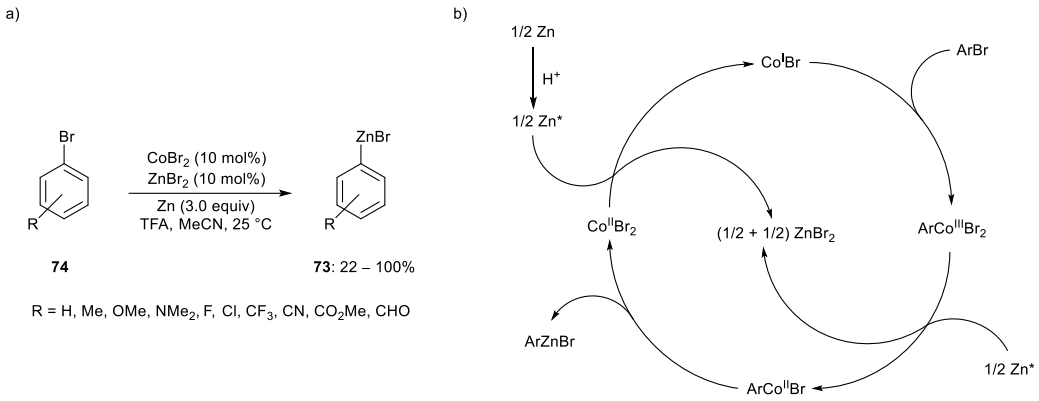
Quite recently, *Blum et al.* described the role of LiCl as additive during oxidative insertions by studying this process *via* fluorescence microscopy.[54] It was found that LiCl helps to solubilize the organozinc reagents generated at the surface of the zinc after oxidative addition.[55]



Scheme 13: LiCl-mediated zinc insertion into 2-iodobenzotrifluoride (**69**).

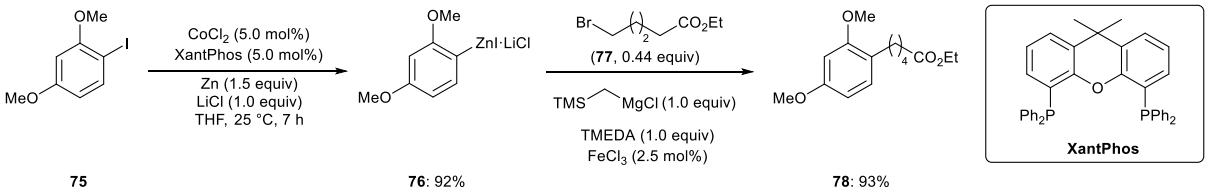
[52] T. N. Majid, P. Knochel, *Tetrahedron Lett.* **1990**, *31*, 4413; b) K. Takagi, *Chem. Lett.* **1993**, *22*, 469; c) K. Takagi, Y. Shimoishi, K. Sasaki, *Chem. Lett.* **1994**, *23*, 2055; d) M. Amano, A. Saiga, R. Ikegami, T. Ogata, K. Takagi, *Tetrahedron Lett.* **1998**, *39*, 8667; e) R. Ikegami, A. Koresawa, T. Shibata, K. Takagi, *J. Org. Chem.* **2003**, *68*, 2195, f) S. Huo, *Org. Lett.* **2003**, *5*, 423.
[53] A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040.
[54] C. Feng, D. W. Cunningham, Q. T. Easter, S. A. Blum, *J. Am. Chem. Soc.* **2016**, *138*, 11156.
[55] C. Feng, Q. T. Easter, S. A. Blum, *Organometallics* **2017**, *36*, 2389.

Another approach towards the preparation of organozinc bromides **73** by oxidative addition was developed by *Gosmini*.[56] In this report, a cobalt-catalyzed zinc insertion is described starting from aryl bromides **74**. The catalytic cycle is initiated by the reduction of $CoBr_2$ by zinc dust, which needs to be activated previously by traces of an acid. The resulting CoBr undergoes an oxidative addition with aryl halides to afford a trivalent cobalt complex $ArCoBr_2$. That latter species is reduced into ArCoBr by an excess of zinc dust. The cycle is completed by a transmetalation between ArCoBr and $ZnBr_2$ formed in the previous steps, leading to the arylzinc compound and regenerating divalent cobalt (Scheme 14).



Scheme 14: a) Cobalt-catalyzed zinc insertion into aryl bromides **74**; b) Mechanism for the oxidative addition using $CoBr_2$ and elemental zinc dust.

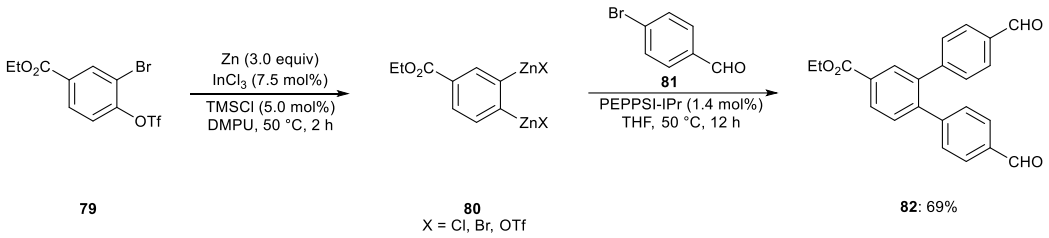
In 2011, *Yoshikai* and co-workers demonstrated a related cobalt-catalyzed procedure using a catalytic system involving $CoCl_2$ and the phosphine ligand XantPhos.[57,58] This cobalt-XantPhos-catalyzed, LiCl-mediated system allows the preparation of functionalized organozinc halides starting from the corresponding aryl halides (chloride, bromides or iodides) using THF as solvent. Thus, 1-iodo-2,4-dimethoxybenzene (**75**) underwent such a cobalt-catalyzed oxidative zinc insertion leading to the corresponding aryl zinc reagent **76** and after cross-coupling with ethyl 5-bromovalerate (**77**) the functionalized arene **78** was obtained (Scheme 15).



Scheme 15: Cobalt-XantPhos-catalyzed zinc addition into aryl halides.

[56] a) I. Kazmierski, C. Gosmini, J.-M. Paris, J. Périchon, *Tetrahedron Lett.* **2003**, *44*, 6417; b) H. Fillon, C. Gosmini, J. Périchon, *J. Am. Chem. Soc.* **2003**, *125*, 3867; c) C. Gosmini, M. Amatore, S. Claudel, J. Périchon, *Synlett* **2005**, 2171.
[57] a) M.-Y. Jin, N. Yoshikai, *J. Org. Chem.* **2011**, *76*, 1972; b) L. Adak, N. Yoshikai, *J. Org. Chem.* **2011**, *76*, 7563.
[58] a) J. Yin, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 6043; b) L. M. Klingensmith, E. R. Strieter, T. E. Barder, S. L. Buchwald, *Organometallics* **2006**, *25*, 82.

As a last point, *Knochel* developed a convenient preparation of 1,2-dimetallic compounds by the direct insertion of zinc using a combination of different activating reagents.[59] Therefore, commercially available zinc powder was treated with catalytic amounts of TMSCl[60] and $InCl_3$[61], and an aromatic *ortho*-bromotriflate (**79**) was used as substrate. The oxidative insertion proceeded smoothly at 50 °C in *N,N'*-dimethylpropylenurea (DMPU) as polar solvent providing the functionalized 1,2-dimetallic zinc reagent **80**, which underwent a PEPPSI-IPr-catalyzed[62] cross-coupling with 4-bromobenzaldehyde (**81**) leading to the desired product **82** (Scheme 16).



Scheme 16: $InCl_3$-catalyzed zinc insertion for the preparation 1,2-dimetallic compounds.

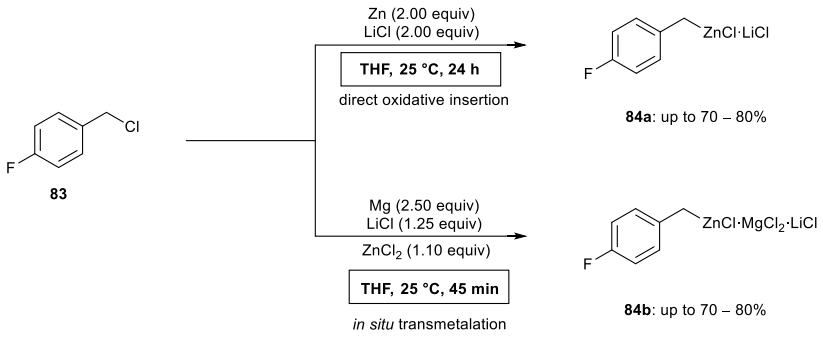
3.3. Magnesium Insertion in the Presence of $ZnCl_2$

The *in situ* transmetalation pathway is a good alternative compared to the classical oxidative addition of metals or the usual transmetalation of organolithium and organomagnesium compounds by zinc halides. Faster reaction rates and enhanced reactivity of the resulting organometallics, compared to the once without magnesium salt, are observed and no further activation of the metal surface is required. This synthetic route involves the direct insertion of magnesium to the corresponding organic halide followed by *in situ* transmetalation due to the presence of $ZnCl_2$.[63] This procedure is of high importance, since the prior preparation of especially polyfunctionalized organometallic reagents derived from lithium or magnesium is not possible or low temperatures are necessary to tolerate sensitive moieties like nitriles or esters. The *in situ* transmetalation often takes place at ambient temperature, and once the organomagnesium compound is formed, it is immediately transmetalated with zinc chloride without decomposition or generation of competitive side products.

[59] T. D. Blümke, T. Klatt, K. Koszinowski, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 9926.
[60] K. Takai, T. Ueda, T. Hayashi, T. Moriwake, *Tetrahedron Lett.* **1996**, *37*, 7049.
[61] K. Takai, Y. Ikawa, *Org. Lett.* **2002**, *4*, 1727.
[62] a) C. J. O'Brien, E. A. B. Kantchev, C. Valente, N. Hadei, G. A. Chass, A. Lough, A. C. Hopkinson, M. G. Organ, *Chem. Eur. J.* **2006**, *12*, 4743; b) M. G. Organ, S. Avola, I. Dubovyk, N.Hadei, E. A. B. Kantchev, C. J. O'Brien, C. Valente, *Chem. Eur. J.* **2006**, *12*, 4749.
[63] a) A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824; b) T. D. Blümke, F. M. Piller, P. Knochel, *Chem. Commun.* **2010**, *46*, 4082.

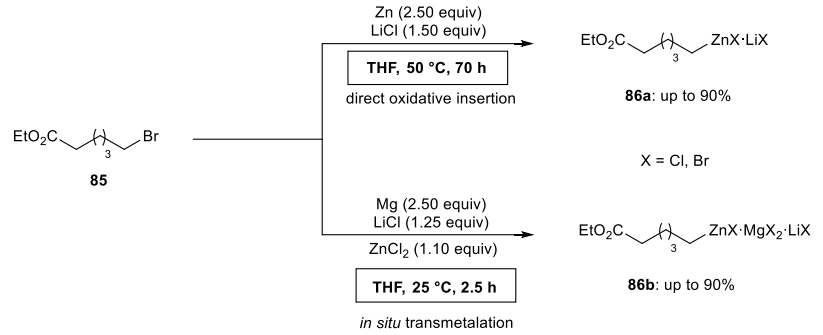
Based on this synthetic route, a range of functionalized organozinc reagents, including aryl, benzyl and alkyl, can be prepared starting from the corresponding organic halides. For the classical LiCl-promoted oxidative insertion of zinc into 4-fluorobenzyl chloride (**83**), 24 h at 25 °C are needed to obtain the desired benzylic zinc reagent **84a**. Using the *in situ* transmetalation *via* the direct insertion of magnesium turnings and LiCl in the presence of $ZnCl_2$, the formation of the benzylic zinc reagent **84b** is finished after 45 min at 25 °C (Scheme 17).[63a]

A classical transmetalation through a direct magnesium insertion and subsequent $ZnCl_2$ addition is not possible, since once the benzylic magnesium species is formed, huge amounts of competitive homocoupling of the benzyl moiety are produced.



Scheme 17: *In situ* transmetalation *versus* oxidative insertion for the preparation of (4-fluorobenzyl) zinc chloride (**84**).

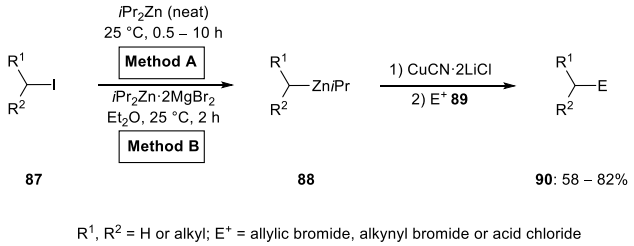
It is also possible to apply this procedure to the synthesis of functionalized alkyl zinc derivatives. Whereas the oxidative addition of zinc to ethyl 6-bromohexanoate (**85**) requires 70 h at 50 °C, the one pot *in situ* transmetalation using magnesium turnings, LiCl and $ZnCl_2$ is finished after 2.5 h at only 25 °C leading to the ester-bearing alkyl zinc species **86a** and **86b** (Scheme 18).[63b]



Scheme 18: *In situ* transmetalation *versus* oxidative insertion for the preparation of the functionalized alkyl zinc species **86**.

3.4. The Iodine-Zinc Exchange Reaction

The third major pathway to generate organometallic reagents is the halogen-metal exchange reaction. Besides halogen-metal exchange processes of lithium,[29] magnesium,[30] and manganese,[31,32] the first halogen-zinc exchange was described by *Knochel* in 1997.[64] In this report, secondary alkyl iodides **87** underwent an iodine-zinc exchange using *i*Pr_2Zn at room temperature leading to functionalized secondary dialkylzinc compounds **88**. After transmetalation to copper trapping reactions with acid chlorides, allylic bromides or alkynyl bromides (E^+; **89**) were performed to obtain the desired products of type **90**. Interestingly, the addition of two equivalents of $MgBr_2$ caused enhanced reaction rates and the exchange reactions proceeded almost 200 times faster than with iPr_2Zn itself (Scheme 19).

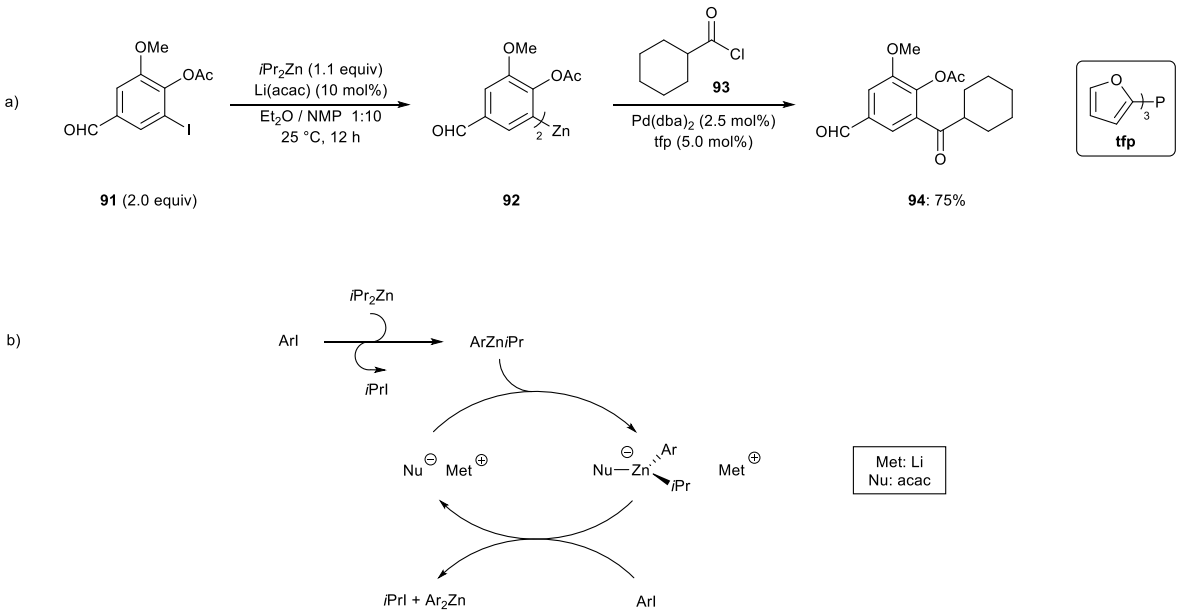


Scheme 19: Iodine-zinc exchange reaction using *i*Pr_2Zn.

It is worth mentioning, that also *Kondo* and *Sakamoto* reported a related halogen-zinc exchange reaction by using lithium zincates as reagents.[65] Nevertheless, those lithium zincates species, such as Me_3ZnLi or Me_4ZnLi_2 behave more or less like the corresponding lithium derivatives, and unsatisfying functional group compatibility is obtained.

Later on, *Knochel* and co-workers developed an improved iodine-zinc exchange process by using either *i*Pr_2Zn or *s*Bu_2Zn as exchange reagents, Li(acac) as additive and a polar solvent mixture of Et_2O and NMP in a 1:10 ratio (NMP = 1-methyl-2-pyrrolidone).[66] In the absence of a polar co-solvent, no reaction took place when an aryl iodide was treated with Et_2Zn or *i*Pr_2Zn in Et_2O or THF. Using NMP as solvent mixed diorganozinc reagents of type ArZn*i*Pr were formed. To promote the transfer of the second alkyl residue it was necessary to activate this mixed intermediate through the formation of an ate complex. This procedure allows efficient exchange reactions on polyfunctionalized aryl and heteroaryl iodides providing the corresponding diarylzinc compounds which undergo further transformations with electrophiles. Hence, the exchange on the functionalized aryl iodide **91** using *i*Pr_2Zn proceeded at 25 °C within 12 h generating the diarylzinc reagent **92**, and subsequent palladium-catalyzed acylation with cyclohexanecarbonyl chloride (**93**) gave the desired ketone **94** (Scheme 20).

[64] L. Micouin, P. Knochel, *Synlett* **199**7, 327.
[65] M. Uchiyama, M. Koike, M. Kameda, Y. Kondo, T. Sakamoto, *J. Am. Chem. Soc.* **1996**, *118*, 8733.
[66] F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 1017.



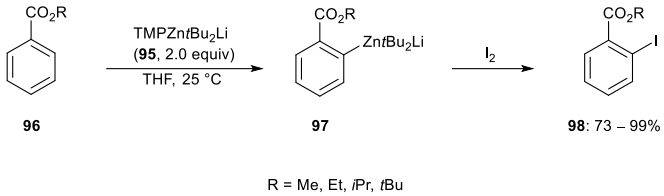
Scheme 20: a) Li(acac)-catalyzed iodine-zinc exchange using *i*Pr_2Zn; b) Proposed mechanism of the I/Zn-exchange through a zinc ate complex

3.5. Directed Deprotonation using Zinc Amide Bases

Besides the above mentioned synthetic routes for the preparation of organozinc derivaties, the functionalization of aromatics and heteroaromatics by directed metalation is a well-established procedure. In 1999, *Kondo* described a new TMP-zincate of type TMPZn*t*Bu_2Li (**95**), which allows chemoselective deprotonations of arenes.[67] This ate-complex **95** could be prepared by adding *t*Bu_2Zn, which was generated *via* transmetalation of *t*BuLi and $ZnCl_2$, to a solution of TMPLi[68] at −78 °C. TMPZn*t*Bu_2Li could be stored at room temperature and was used for efficient *ortho*-metalations of alkyl benzoates **96**.

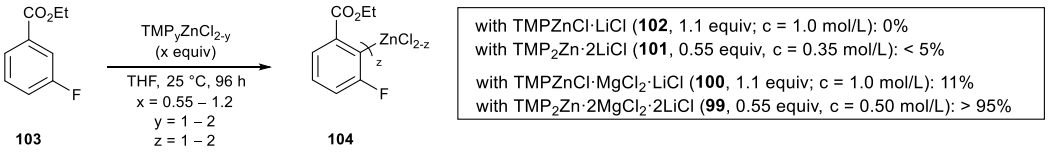
[67] a) Y. Kondo, H. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539; b) T. Imahori, M. Uchiyama, Y. Kondo, *Chem. Commun.* **2001**, 2450; c) P. F. H. Schwab, F. Fleischer, J. Michl, *J. Org. Chem.* **2002**, *67*, 443; d) M. Uchiyama, T. Miyoshi, Y. Kajihana, T. Sakamoto, Y. Otami, T. Ohwada, Y. Kondo, *J. Am. Chem. Soc.* **2002**, *124*, 8514; e) M. Uchiyama, Y. Kobayashi, T. Furuyama, S. Nakamura, Z. Kajihara, T. Miyoshi, T. Sakamoto, Y. Kondo, K. Morokuma, *J. Am. Chem. Soc*. **2008**, *130*, 472.
[68] I. E. Kopka, Z. A. Fataftah, M. W. Rathke, *J. Org. Chem*. **1987**, *52*, 448.

Thus, alkyl benzoates of type **96** were successfully metalated using TMP-zincate **95** leading to the corresponding arylzinc reagents **97** and further trapping with iodine gave the *ortho*-iodinated products **98** (Scheme 21). The structures of TMP-derived amide bases and metalated intermediates were extensively studied by *Mulvey* afterwards.[69]

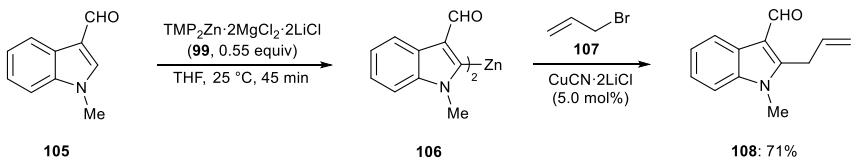


Scheme 21: *Ortho*-metalation using *Kondo's* TMP-zincate TMPZn*t*Bu$_2$Li (**95**).

In 2007, *Knochel* reported another TMP-zinc amide base of type TMP$_2$Zn·2MgCl$_2$·2LiCl (**99**), which could be prepared by transmetalation of the corresponding TMPMgCl·LiCl with ZnCl$_2$.[70] Due to the more covalent character of a carbon–zinc bond compared to carbon–magnesium or carbon–manganese, a broad range of sensitive functional groups, such as nitriles, esters, ketones or aldehydes, could be tolerated at ambient temperatures using this sterically hindered amide base. Remarkably, the addition of both salts LiCl and MgCl$_2$ seems to be essential for a good solubility, and high reactivity of the obtained TMP-zinc bases **99** and **100**. Moreover, bis-amide bases possess a higher kinetic reactivity than the related mono-amide bases (compare bases **99**-**102** for the metalation of ethyl 3-fluorobenzoate (**103**) leading to the zinc species **104**). As an example, the indole-derivative **105** could be metalated by using TMP$_2$Zn·2MgCl$_2$·2LiCl (**99**) at 25 °C affording the diarylzinc reagent **106** and copper-catalyzed allylic substitution with allyl bromide (**107**) gave the desired product **108** (Schemes 22 and 23).



Scheme 22: Comparison of different TMP-zinc bases regarding their reactivity towards arene **103**.[71]

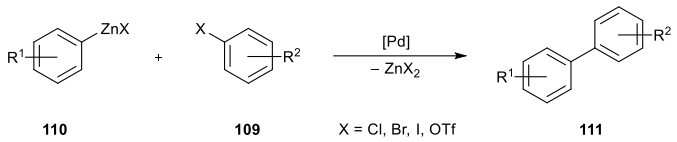


Scheme 23: Directed metalation using the bis-amide base TMP$_2$Zn·2MgCl$_2$·2LiCl (**99**).

[69] a) D. R. Armstrong, W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, *Angew. Chem. Int. Ed.* **2006**, *45*, 3775; b) R. E. Mulvey *Acc. Chem. Res.* **2009**, *42*, 743; c) W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, C. T. O'Hara, L. Russo, *Angew. Chem. Int. Ed.* **2008**, *47*, 731; d) W. Clegg, B. Conway, E. Hevia, M. D. McCall, L. Russo, R. E. Mulvey, *J. Am. Chem. Soc.* **2009**, *131*, 2375.
[70] S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685.
[71] S. H. Wunderlich, Dissertation, LMU München, **2010**.

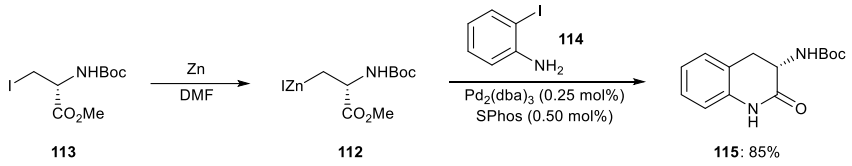
3.6. Transition-Metal-Catalyzed Cross-Coupling Reactions of Organozinc Reagents

Due to the broad applicability of organozinc reagents and the variety of synthetic routes for their preparation, organozinc derivatives have been extensively studied in the field of transition-metal-catalyzed cross-coupling reactions. Their excellent functional group tolerance combined with still high reactivity under mild reaction conditions make them the most used organometallics for such transformations.[72] The first step of this reaction is the oxidative insertion of palladium into the carbon–halogen bond of the organic halide **109**. Further transmetalation with an organozinc derivative of type **110** and subsequent reductive elimination leads to the desired coupling products **111**.



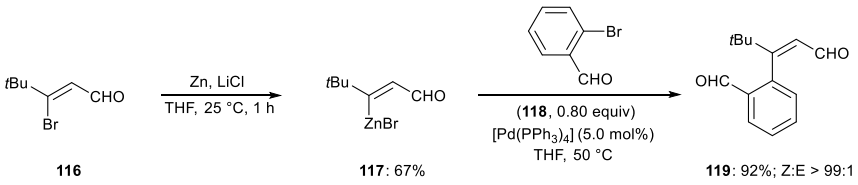
Scheme 24: General scheme of the *Negishi* cross-coupling reaction.[37]

In the following, a short summary of selected and recent Pd-catalyzed *Negishi* cross-couplings is presented which shows the versatility of such reactions. In 2010, *Jackson* described a *Negishi* coupling of an iodoalanine-derived zinc reagent **112**, prepared from the corresponding alkyl iodide **113**, with 2-iodoaniline (**114**) using a catalytic system consisting of $Pd_2(dba)_3$ and SPhos (Scheme 25).[73,74]



Scheme 25: *Jackson's* procedure for the preparation of lactam **115**.

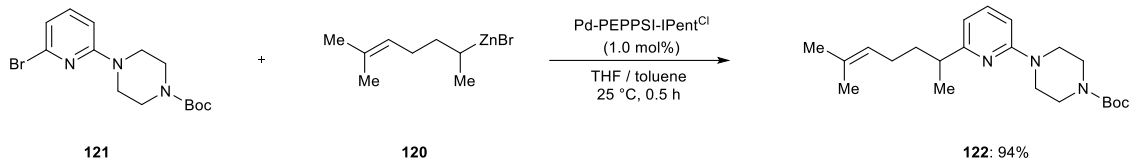
Another approach was developed by *Knochel* and co-workers, wherein an alkenyl bromide **116** was converted into zinc reagent **117** bearing a sensitive aldehyde moiety and cross-coupling with 2-bromo-benzaldehyde (**118**) at even 50 °C provided the polyfunctionalized arene **119** (Scheme 26).[75]



Scheme 26: Cross-coupling of alkenyl zinc reagent **117** with a carbonyl-substituted aryl bromide **118**.

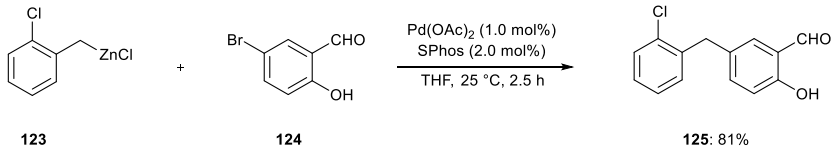
[72] a) *Organozinc Reagents* (Eds.: P. Knochel, P. Jones), Oxford University Press, New York, **1999**; b) P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117.
[73] A) T. E. Barder, S. D. Walker, J. R. Martinelli, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 4685; b) K. L. Billingsley, K. W. Anderson, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2006**, *45*, 3484.
[74] A. J. Ross, H. L. Lang, R. F. W. Jackson, *J. Org. Chem.* **2010**, *75*, 245.
[75] C. Sämann, M. A. Schade, S. Yamada, P. Knochel, *Angew. Chem. Int. Ed.* **2013**, *52*, 9495.

Also *Organ et al.* reported a *Negishi* cross-coupling of the secondary alkyl zinc reagent **120** with a substituted pyridine derivative **121** using the *N*-heterocyclic carbene-based catalyst Pd-PEPPSI-IPent^{Cl} leading to the alkyl-substituted pyridine **122** (Scheme 27).[76]



Scheme 27: Pd-PEPPSI-IPent^{Cl}-catalyzed cross-coupling reaction.

Another important advantage of these palladium-catalyzed cross-coupling reactions are the very fast reaction rates obtained by well-designed and highly reactive catalytic systems. Hence, it is possible to perform *Negishi* couplings of functionalized zinc reagents with aryl and heteroaryl halides bearing relatively acidic hydrogen atoms at ambient temperatures without protonation of the organometallic nucleophile. As an example, *Knochel* demonstrated such a reaction by adding (2-chlorobenzyl)zinc chloride (**123**) to an aryl bromide **124** bearing an aldehyde and an alcohol moiety using $Pd(OAc)_2$ and SPhos as catalytic system.[77] The crucial point of this cross-coupling is the very slow addition of the benzylic zinc compound **123** *via* a syringe pump, which ensures that, once the organometallic reagent is added, it is immediately cross-coupled without being protonated by the electrophile. Thus, functionalized intermediates such as **125** can be obtained in high yields through a very suitable carbon–carbon bond formation reaction (Scheme 28).

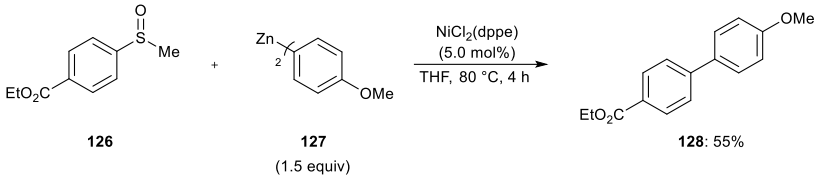


Scheme 28: *Negishi* cross-coupling of a phenol derivative **124** bearing relatively acidic hydrogen atoms with a benzylic zinc reagent **123**.

[76] a) S. Calimsiz, M. G. Organ, *Chem. Commun.* **2011**, *47*, 5181; b) M. Pompeo, R. D. J. Froese, N. Hadei, M. G. Organ, *Angew. Chem. Int. Ed.* **2012**, *51*, 11354.
[77] G. Manolikakes, M. A. Schade, C. Munoz Hernandez, H. Mayr, P. Knochel, *Org. Lett.* **2008**, *10*, 2765.

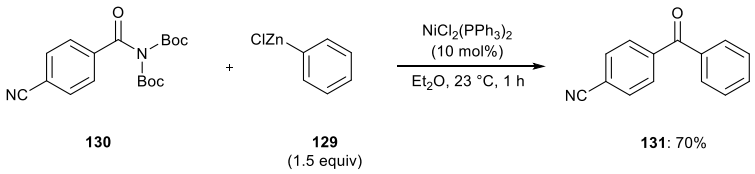
The major drawbacks of palladium-catalyzed cross-coupling reactions consist in the high costs of palladium and their phosphine ligands. As an alternative, nickel-catalyzed *Negishi* couplings found useful applications in recent years since they are a lot cheaper than palladium. Additionally, they display almost the same reaction scope as palladium-catalyzed cross-couplings due to their high catalytic activity.[78]

Quite recently, *Yorimitsu* and co-workers developed a nickel-catalyzed cross-coupling procedure of diarylzinc reagents with functionalized aryl sulfoxides. In this report, the ester-substituted sulfoxide **126** reacted with the diarylzinc reagent **127** using $NiCl_2$(dppe) as catalyst leading to the desired biphenyl derivative **128** (Scheme 29).[79]



Scheme 29: Nickel-catalyzed cross-coupling of diarylzinc species **127** and sulfoxide **126**.

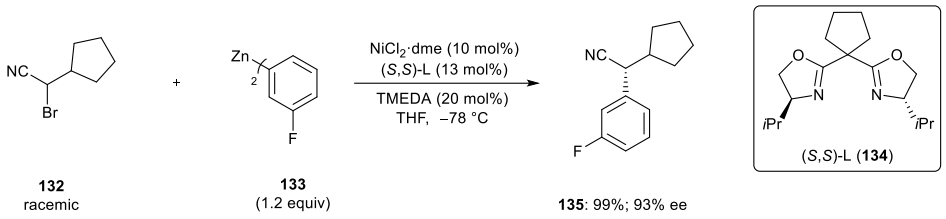
In addition to that, a direct *Negishi* cross-coupling of primary amides by *N*,*N*-di-Boc activation was reported by *Szostak* to synthesize functionalized diaryl ketones by N–C cleavage.[80] Therein, phenylzinc chloride (**129**) underwent an efficient coupling with the cyano-substituted amide **130** resulting in the ketone **131** (Scheme 30).



Scheme 30: Preparation of diaryl ketones *via* a *N*,*N*-di-Boc activation.

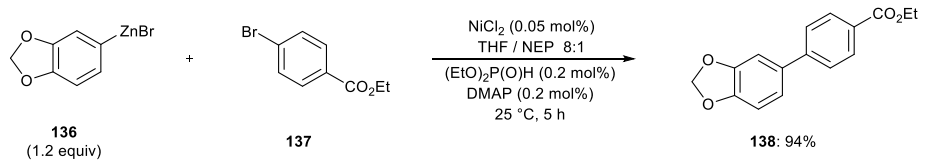
[78] For recent nickel-catalyzed *Negishi* cross-couplings, see: a) H.-Q. Do, E. R. R. Chandrashekar, G. C. Fu, *J. Am. Chem. Soc.* **2013**, *135*, 16288; b) J. Choi, P. Martin-Gago, G. C. Fu, *J. Am. Chem. Soc.* **2014**, *136*, 12161; c) A. Tarui, S. Shinohara, K. Sato, M. Omote, A. Ando, *Org. Lett.* **2016**, *18*, 1128; d) S. Shi, M. Szostak, *Chem. Eur. J.* **2016**, *22*, 10420; e) S. Shi, M. Szostak, *Synlett* **2017**, *49*, 3602.
[79] K. Yamamoto, S. Otsuka, K. Nogi, H. Yorimitsu, *ACS Catal.* **2017**, *7*, 7623.
[80] S. Shi, M. Szostak, *Org. Lett.* **2016**, *18*, 5872.

Moreover, *Fu et al.* described the first stereoconvergent cross-coupling of racemic α-halonitriles. A racemic alkyl bromide such as **132** was cross-coupled with the functionalized diarylzinc reagent **133** using the combination of $NiCl_2$·dme and a chiral bis(oxazoline)-derived ligand **134** providing an enantioenriched α-alkyl-α-aryl nitrile **135** (Scheme 31).[81]



Scheme 31: Stereocontrolled *Negishi* arylation of racemic α-halonitriles.

Already in 2005, *Knochel* and co-workers demonstrated, that even very small amounts of nickel-catalyst can be used to perform highly efficient cross-coupling reactions. In contrast to the three above mentioned procedures, a catalyst loading of only 0.05 mol% of $NiCl_2$ was enough to enable the expected aryl-aryl coupling reactions at mild conditions. Thus, the cross-coupling of the arylzinc bromide **136** with ethyl 4-bromobenzoate (**137**) proceeded in the presence of $NiCl_2$ as catalyst and DMAP plus $(EtO)_2P(O)H$ as additives at room temperature within 5 h leading to the desired biphenyl **138** in high yield (Scheme 32).[82]

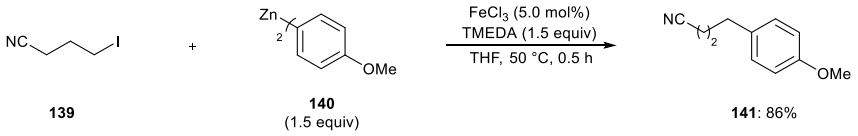


Scheme 32: *Knochel's* nickel-catalyzed aryl-aryl cross-coupling procedure.

Although palladium and nickel catalysts possess a high reactivity and show a very broad applicability in the field of *Negishi* cross-couplings, there is a need for less expensive and especially less toxic catalysts. The use of iron[47,83] and cobalt[84] catalysts has recently attracted increased interest in the synthetic organometallic community, and well-developed catalytic systems are currently used to enable such transformations.

[81] J. Choi, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 9102.
[82] A. Gavryushin, C. Kofink, G. Manolikakes, P. Knochel, *Org. Lett.* **2005**, *7*, 4871.
[83] For an overview on iron-catalyzed cross-couplings, see: a) A. Fürstner, A. Leitner, M. Méndez, H. Krause, *J. Am. Chem. Soc.* **2002**, *124*, 13856; b) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217; c) B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, *41*, 1500; d) W. M. Czaplik, M. Mayer, J. Cvengros, A. J. von Wangelin, *ChemSusChem* **2009**, *2*, 396; e) O. M. Kuzmina, A. K. Steib, A. Moyeux, G. Cahiez, P. Knochel, *Synthesis* **2015**, *47*, 1696; f) T. Parchomyk, K. Koszinowski, *Synthesis* **2017**, *49*, 3269.
[84] For an overview on cobalt-catalyzed cross-couplings, see: a) G. Cahiez, A. Moyeux, *Chem. Rev.* **2010**, *110*, 1435; b) J. M. Hammann, M. S. Hofmayer, F. H. Lutter, L. Thomas, *Synthesis* **2017**, *49*, 3887.

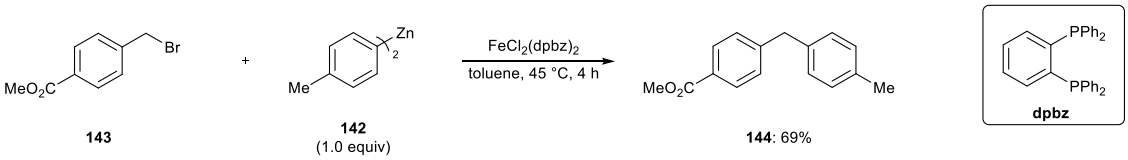
In 2005, *Nakamura* described one of the first iron-catalyzed *Negishi* cross-coupling reactions involving alkyl halides and diarylzinc reagents.[85] An alkyl halide such as 4-iodobutyronitrile (**139**) was treated with diarylzinc species **140** using $FeCl_3$ as catalyst and TMEDA as additive affording the alkyl-substituted methoxybenzene **141** (Scheme 33).



139 **140** (1.5 equiv) **141**: 86%

Scheme 33: Iron-catalyzed cross-coupling of diarylzinc reagent **140** and alkyliodide **139**.

In the following years, especially *Nakamura*[86] and *Bedford*[87] reported several iron-catalyzed *Negishi* couplings. One among them was *Bedford's* cross-coupling reaction of benzyl halides and phosphates with bis(*p*-tolyl)zinc (**142**) using $FeCl_2(dpbz)_2$ in toluene as solvent. In such a reaction, the ester-substituted benzyl bromide **143** reacted with **142** leading to the expected diarylmethane derivative **144** (Scheme 34).[88]

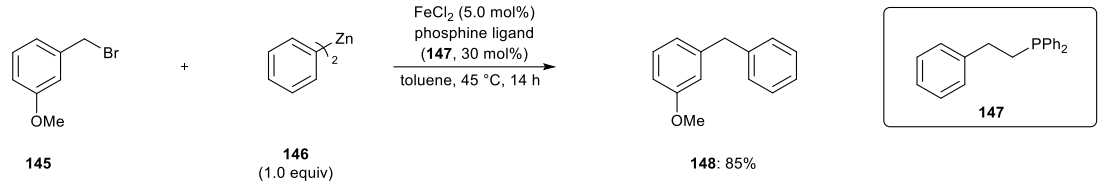


143 **142** (1.0 equiv) **144**: 69%

Scheme 34: Iron-catalyzed *Negishi* coupling of a benzyl bromide **143** and diarylzinc species **142**.

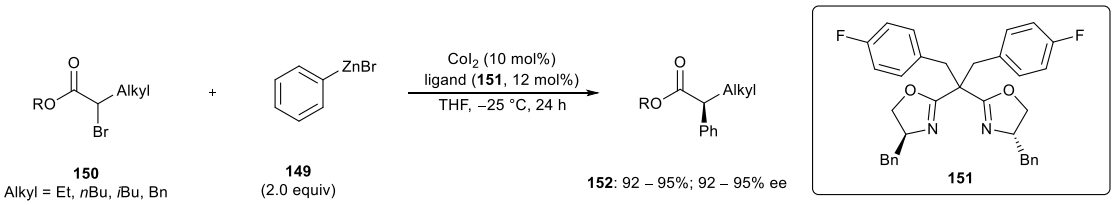
Later on, a related iron-catalyzed *Negishi* cross-coupling was developed by *Webster* and co-workers, who used the same combination of starting materials.[89] In contrast to *Bedford's* method, they were able to perform a similar reaction by using a simple diarylalkylphosphine as ligand and $FeCl_2$ as catalyst. Based on this protocol, the coupling of 3-methoxybenzyl bromide (**145**) with diphenylzinc (**146**) was promoted by phosphine **147** and furnished the expected diarylmethane compound **148** (Scheme 35).

[85] M. Nakamura, S. Ito, K. Matsuo, E. Nakamura, *Synlett* **2005**, 1794.
[86] a) T. Hatakeyama, Y. Kondo, Y. Fujiwara, H. Takaya, S. Ito, E. Nakamura, M. Nakamura, *Chem. Commun.* **2009**, 1216; b) S. Ito, Y. Fujiwara, E. Nakamura, M. Nakamura, *Org. Lett.* **2009**, *11*, 4306; c) T. Hatakeyama, N. Nakagawa, M. Nakamura, *Org. Lett.* **2009**, *11*, 4496.
[87] a) C. J. Adams, R. B. Bedford, E. Carter, N. J. Gower, M. F. Haddow, J. N. Harvey, M. Huwe, M. Á. Cartes, S. M. Mansell, C. Mendoza, D. M. Murphy, E. C. Neeve, J. Nunn, *J. Am. Chem. Soc.* **2012**, *134*, 10333; b) R. B. Bedford, E. Carter, P. M. Cogswell, N. J. Gower, M. F. Haddow, J. M. Harvey, D. M. Murphy, E. C. Neeve, J. Nunn, *Angew. Chem. Int. Ed.* **2013**, *52*, 1285.
[88] R. B. Bedford, M. Huwe, M. C. Wilkinson, *Chem. Commun.* **2009**, 600.
[89] C. A. Brown, T. A. Nile, M. F. Mahon, R. L. Webster, *Dalton Trans.* **2015**, *44*, 12189.



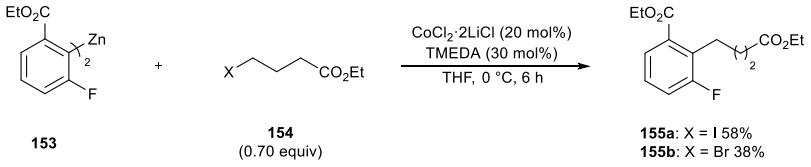
Scheme 35: *Webster's* route for iron-catalyzed aryl-benzyl *Negishi* cross-coupling reactions.

Recently, also cobalt-catalyzed *Negishi* cross-couplings found useful applications. As one of the latest examples, *Bian et al.* described the first enantionselective *Negishi* coupling employing a cobalt-bisoxazoline catalyst. Phenylzinc bromide (**149**) underwent a cobalt-catalyzed cross-coupling with α-haloesters of type **150** using CoI_2 and the oxazoline ligand **151** leading to the enantioenriched α-alkyl-α-aryl esters **152** (Scheme 36).[90]



Scheme 36: First cobalt-catalyzed enantionselective *Negishi* cross-coupling.

Additionally, *Knochel* and co-workers reported a cobalt-mediated cross-coupling of polyfunctionalized diarylzinc reagents with alkyl bromides or iodides. Diarylzinc compounds such as **153** reacted with alkyl halides **154** under mild conditions affording the alkyl-substituted arenes **155** (Scheme 37).[91] Later on, *Knochel* also demonstrated the feasibility of a cobalt-catalyzed *Negishi* coupling of aryl- and heteroarylzinc reagents with aromatic halides.[92]



Scheme 37: Cobalt-mediated aryl-alkyl cross-coupling procedure.

[90] F. Liu, J. Zhong, Y. Zhou, Z. Gao, P. J. Walsh, X. Wang, S. Ma, S. Hou, S. Liu, M. Wang, M. Wang, Q. Bian, *Chem. Eur. J.* **2018**, *24*, 2059.
[91] J. M. Hammann, D. Haas, P. Knochel, *Angew. Chem. Int. Ed.* **2015**, *54*, 4478.
[92] D. Haas, J. M. Hammann, F. H. Lutter, P. Knochel, *Angew. Chem. Int. Ed.* **2016**, *55*, 3809.

Besides those reports, also *Gosmini*[93] and *Hayashi*[94] developed several cobalt-catalyzed *Negishi* cross-coupling reactions in the recent years. Taking all this into account, transition-metal-catalyzed cross-coupling reactions, especially those catalyzed by iron and cobalt salts, display an important topic in organometallic chemistry and several different protocols have been published. Nevertheless, there is still a need for further investigations since the scope of all these new synthetic procedures is often limited and not all kind of transformations have been tested yet. Especially the use of organomanganese and organozinc derivatives in combinations with iron and cobalt catalysts is not extensively studied and therefore of great interest.

[93] a) M. Amatore, C. Gosmini, *Chem. Commun.* **2008**, 5019; b) J.-M. Bégouin, C. Gosmini, *J. Org. Chem.* **2009**, *74*, 3221; c) J.-M. Bégouin, S. Claudel, C. Gosmini, *Synlett* **2009**, 3192; d) J.-M. Béguin, M. Rivard, C. Gosmini, *Chem. Commun.* **2010**, *46*, 5972; e) M. Corpet, X.-Z. Bai, C. Gosmini, *Adv. Synth. Catal.* **2014**, *356*, 2937.
[94] a) T. Sawano, K. Ou, T. Nishimura, T. Hayashi, *Chem. Commun.* **2012**, *48*, 6106; b) T. Sawano, K. Ou, T. Nishimura, T. Hayashi, *J. Org. Chem.* **2013**, *78*, 8986.

4. Preparation of Organolanthanide Reagents

4.1. Introduction

Nowadays, there is still a need for metals which possess intermediate reactivity and unique properties. To the best of our knowledge, only manganese is known to be such a metal with well-balanced reactivity and specific qualities. In the series of reactivity of organometallic compounds (Figure 1), organo-manganese derivatives with an electronegativity of 1.55 are located between those of magnesium (EN: 1.31) and zinc (EN: 1.65). They possess a slightly lower reactivity compared to organomagnesium reagents, but therefore an optimized functional group tolerance due to the less polarized carbon–metal bond, which makes them a more reactive alternative compared to organozinc compounds.

Organolanthanide derivatives could also be useful alternatives to well-established organometallics such as those derived from lithium or magnesium. Due to their strong oxophilicity and highly polarized carbon–metal bond, organolanthanides could be good candidates to fill up the gap of reactivity between lithium and magnesium.[95] Although organolanthanides appear to be quite common in the field of inorganic chemistry and coordination chemistry,[96] their applications in organic chemistry are barely reported.

The majority of synthetic protocols regarding the preparation of organolanthanide reagents and their use in organic synthesis was reported by *Imamoto* and co-workers.[97] In 1984, they described a convenient preparation of organocerium reagents starting from the corresponding organolithiums and anhydrous $CeCl_3$ at −78 °C in THF.[98,99] Additionally, organocerium derivatives were found to be useful reagents for the nucleophilic addition to easily enolizable ketones due to their strong oxophilic character. In contrast, the addition of organomagnesium or organolithium reagents to such easily enolizable carbonyl compounds only results in the formation of enolates due the strong basicity of those reagents.[95e]

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[95] a) G. A. Molander, *Chem. Rev.* **1992**, *92*, 29; b) G. A. Molander, *Chem. Rev.* **1996**, *96*, 307; c) A. Knief, M. Laval, *Chem. Rev.* **1999**, *99*, 745; d) *Lanthanides: Chemistry and uses in Organic Synthesis* (Ed.: S. Kobayashi), Springer-Verlag, Berlin, **1999**; e) *Lanthanides: Chemistry and Use in Organic Synthesis* (Ed.: S. Kobayashi), Springer, Heidelberg, **1999**; f) S. Kobayashi, M. Sugiura, H. Kitagawa, W. W. L. Lam, *Chem. Rev.* **2002**, *102*, 2227; g) S. Kobayashi, K. Manabe, *Acc. Chem. Res.* **2002**, *35*, 209; h) F. T. Edelmann, D. M. M. Freckmann, H. Schumann, *Chem. Rev.* **2002**, *102*, 1851.

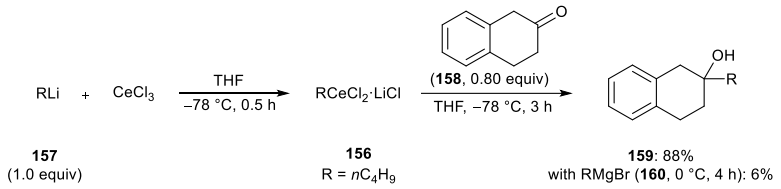
[96] A) G. Campari, F. A. Hart, *Inorg. Chim. Acta* **1982**, *65*, 217; b) P. B. Hitchcock, M. F. Lappert, R. G. Smith, R. A. Bartlett, P. P. Power, *J. Chem. Soc., Chem. Commun.* **1988**, 1007; c) J. L. Atwood, M. F. Lappert, R. G. Smith, H. Zhang, *J. Chem. Soc., Chem. Commun.* **1988**, 1308; d) C. J. Schaverien, N. Meijboom, A. G. Orpen, *J. Chem. Soc., Chem. Commun.* **1992**, 124; e) P. B. Hitchcock, Q.-G. Huang, M. F. Lappert, X.-H. Wie, *J. Mater. Chem.* **2004**, *14*, 3266; f) C. G. J. Tazelaar, S. Bambirra, D. van Leusen, A. Meetsma, B. Hessen, J. H. Teuben, *Organometallics* **2004**, *23*, 936; g) S. Bambirra, A. Meetsma, B. Hessen, *Organometallics* **2006**, *25*, 3454; h) M. Wiecko, G. B. Deacon, P. C. Junk, *Chem. Commun.* **2010**, *46*, 5076.

[97] a) T. Imamoto, T. Kusumoto, Y. Tawarayama, Y. Sugiura, T. Mita, Y. Hatanaka, M. Yokoyama, *J. Org. Chem.* **1984**, *49*, 3904; b) T. Imamoto, N. Takiyama, K. Nakamura, *Tetrahedron Lett.* **1985**, *26*, 4763; c) T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, Y. Kamiya, *J. Am. Chem. Soc.* **1989**, *111*, 4392; d) K. Asakura, K. Yamaguchi, T. Imamoto, *Chem. Lett.* **2000**, 424.

[98] T. Imamoto, Y. Sugiura, N. Takiyama, *Tetrahedron Lett.* **1984**, *25*, 4233.

[99] V. Dimitrov, K. Kostova, M. Genov, *Tetrahedron Lett.* **1996**, *37*, 6787.

Based on this report, the preparation of the alkylcerium reagent **156** succeeded *via* the transmetalation of the corresponding alkyllithium **157** with anhydrous $CeCl_3$ at −78 °C in THF and subsequent addition of β-tetralone **158** led to the expected alcohol **159**. The reaction of the *Grignard* reagent **160** with the same ketone **158** resulted in only traces of the desired tertiary alcohol **159**. (Scheme 38)

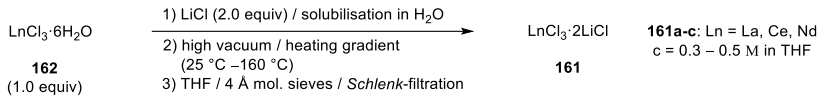


Scheme 38: Nucleophilic addition of the alkylcerium reagent **156** to an easy enolizable ketone **158**.

In the following years, also other research groups such as *Groth*[100] and *Molander*[101] published a few reports on the synthesis and application of organolanthanides in organic synthesis. However, protocols towards convenient preparations of organolanthanide reagents are still scarce, and so far these reagents can only be prepared by transmetalation reactions from the corresponding lithium species.[102]

4.2. Preparation and Application of Organolanthanum Reagents in Organic Synthesis

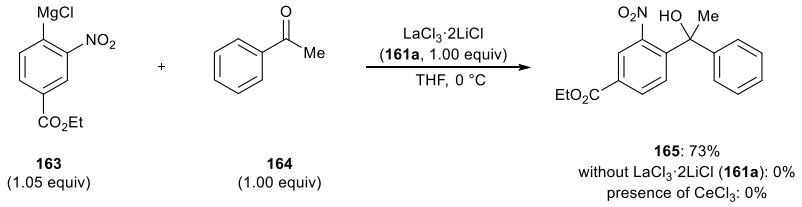
One significant drawback of the so far applied methods for the preparation of organolanthanide derivatives is the insufficient solubility of the lanthanide chlorides in THF. In 2006, *Knochel* described the preparation of THF-soluble lanthanide halides of type $LnCl_3 \cdot 2LiCl$ (**161**).[103] By mixing the lanthanide chlorides of type **162** with two equivalents of LiCl, solubilisation in water, submitted to a heating gradient under high vaccum and subsequent addition of THF, the desired THF-soluble lanthanide solutions could be obtained in satisfying concentrations of 0.3–0.5 M in THF (Scheme 39).



Scheme 39: Preparation of soluble lanthanide salts $LnCl_3 \cdot 2LiCl$ (**161a**–**c**).

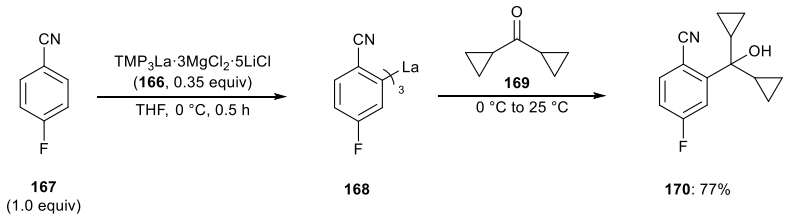
[100] A) C. Alcaraz, U. Groth, *Angew. Chem. Int. Ed.* **1997**, *36*, 2480; b) U. Groth, M. Jeske, *Angew. Chem. Int. Ed.* **2000**, *39*, 574; c) U. Groth, M. Jeske, *Synlett* **2001**, 129; d) S. Fischer, U. Groth, M. Jeske, T. Schütz, *Synlett* **2002**, 1922.
[101] A) M. Shenglof, D. Gelman, G. A. Molander, J. Blum, *Tetrahedron Lett.* **2003**, *44*, 8593; b) D. Tsvelikhovsky, D. Gelman, G. A. Molander, J. Blum, *Org. Lett.* **2004**, *6*, 1995.
[102] For an example starting from organomagnesium reagents, see: S. Matsubara, T. Ikeda, K. Oshima, K. Utimoto, *Chem. Lett.* **2001**, 1226.
[103] A. Krasovskiy, F. Kopp, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 497.

These THF-solutions of $LnCl_3 \cdot 2LiCl$ of type **161** were found to be efficient promoters for selective additions of organomagnesium reagents to sterically hindered and easy enolizable ketones. Especially $LaCl_3 \cdot 2LiCl$ (**161a**) was found to be a superior mediator for such reactions. Thus, the nitro-substituted *Grignard* reagent **163** reacted smoothly with acetophenone (**164**) using $LaCl_3 \cdot 2LiCl$ (**161a**) as promoter and the expected tertiary alcohol **165** was obtained. Performing this reaction without additive or in the presence of anhydrous $CeCl_3$ did not result in the desired product (Scheme 40).



Scheme 40: $LaCl_3 \cdot 2LiCl$-promoted addition of magnesium reagent **163** to acetophenone (**164**).

Later on, *Knochel* and co-workers found that these kind of selective additions of *Grignard* reagents to carbonyl compounds can also be performed in the presence of only catalytic amounts of $LaCl_3 \cdot 2LiCl$ (**161a**).[104] As examples for its applicability, *Nicolaou* used $LaCl_3 \cdot 2LiCl$ (**161a**) for one step of his synthesis of tryptamines,[105] and quite recently *Tius* applied **161a** in the total synthesis of rocaglamide.[106] In 2010, the concept of directed metalation with TMP-bases was extended to $TMP_3La \cdot 3MgCl_2 \cdot 5LiCl$ (**166**).[107] This amide base was prepared by the putative transmetalation of the mono TMP-magnesium base with $LaCl_3 \cdot 2LiCl$ at 0 °C and could be used for efficient directed *ortho*-metalations of different functionalized arenes and heteroarenes. According to this synthetic protocol, 4-fluorobenzonitrile (**167**) was easily metalated using $TMP_3La \cdot 3MgCl_2 \cdot 5LiCl$ (**166**) at 0 °C within 30 min generating the functionalized triaryllanthanum reagent **168** which further reacted with ketone **169** leading to the expected alcohol **170** (Scheme 41). Except the usual transmetalation pathway of organolithiums to organolanthanum reagents by lanthanum halides, this procedure displays the only preparative pathway to generate organolanthum derivatives up to now.

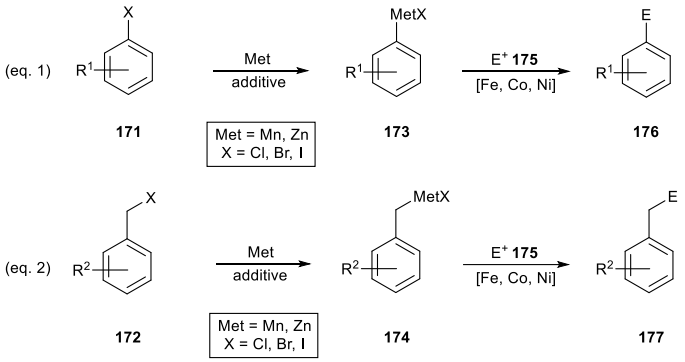


Scheme 41: Directed *ortho*-metalation using $TMP_3La \cdot 3MgCl_2 \cdot 5LiCl$ (**166**).

[104] A. Metzger, A. Gavryushin, P. Knochel, *Synlett* **2009**, 1433.
[105] a) K. C. Nicolaou, A. Krasovskiy, V. E. Trépanier, D. Y.-K. Chen, *Angew. Chem. Int. Ed.* **2008**, *47*, 4217; b) K. C. Nicolaou, A. Krasovskiy, U. Majumber, V. E. Trépanier, D. Y.-K. Chen, *J. Am. Chem. Soc.* **2009**, *131*, 3690.
[106] Z. Zhou, D. D. Dixon, A. Jolit, M. A. Tius, *Chem. Eur. J.* **2016**, *22*, 15929.
[107] S. H. Wunderlich, P. Knochel, *Chem. Eur. J.* **2010**, *16*, 3304.

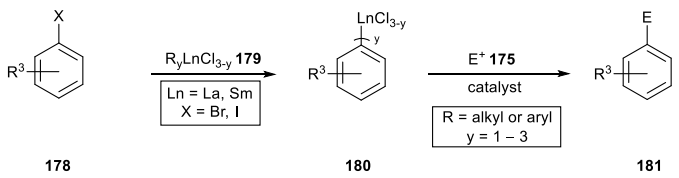
5. Objectives

The first major point of interest of this thesis was the preparation of functionalized aryl and benzylic organometallic reagents of manganese and zinc starting from the corresponding organic halides **171** or **172**. Those functionalized organomanganese or -zinc compounds **173** and **174** could be prepared *via* either already well-established synthetic routes or new and more efficient preparative pathways need to be developed. The resulting organometallics **173** and **174** were then supposed to undergo novel transition-metal-catalyzed cross-coupling reactions with different electrophiles (E^+; **175**) triggered by iron, cobalt or nickel catalysts leading to polyfunctionalized diaryl or diarylmethane derivatives **176** and **177** (Scheme 42).



Scheme 42: Preparation of aryl and benzyl organometallics of manganese and zinc and their transition-metal-catalyzed cross-coupling reactions.

The second topic of this thesis lay on the synthesis of functionalized organolanthanide compounds of lanthanum and samarium by halogen-metal exchange reactions. Starting from functionalized aryl halides of type **178**, a range of different alkyl or aryl derived exchange reagents **179** should be tested for a convenient and straightforward preparation of aryllanthanide reagents **180**. Subsequently, these novel aryllanthanide compounds **180** should further react with a variety of different electrophiles leading to polyfunctionalized products of type **181** (Scheme 43).



Scheme 43: Preparation of functionalized aryllanthanide reagents **180** by halogen-metal exchange reactions and subsequent trapping reactions.

B. Results and Discussion

1. Iron-Catalyzed Cross-Coupling of Benzylic Manganese Chlorides with Aryl and Heteroaryl Halides

1.1. Introduction

Iron-catalyzed cross-coupling reactions are an important method for the formation of carbon–carbon bonds, as it allows to replace palladium or nickel catalysts by inexpensive iron salts and in recent years the excellent catalytic activity of iron complexes has been extensively investigated.[108] In this context, an iron-catalyzed cross-coupling of benzylic organometallics with aryl and heteroaryl halides would be highly desirable since the resulting diarylmethane derivatives are present in many natural products and pharmacologically active compounds.[109] In general, benzylic organometallics of Mg,[110] In,[111] Al, [112] and Zn[113] are readily available. Among them, zinc reagents are especially attractive since they are compatible with numerous functional groups and can be easily prepared. However, benzylic zinc reagents display only moderate reactivity in iron-catalyzed cross-coupling reactions, and therefore compounds which show enhanced reactivity with a still appropriate functional group tolerance would be a useful alternative. From this point of view, benzylic manganese reagents would be a good choice, since they combine a high reactivity with still acceptable compatibility towards sensitive moieties. They can either be prepared by direct insertion of manganese metal into benzylic halides in the presence of catalytic amounts of $InCl_3$ and $PbCl_2$ or by the more practical *in situ* transmetalation using magnesium turnings in the presence of $MnCl_2 \cdot 2LiCl$ at 0 °C in THF.[28] Because functionalized benzylic magnesium reagents are difficult to prepare and benzylic zinc reagents do not readily transmetalate to iron, manganese with its intermediate electronegativity would be well suited for such iron-catalyzed cross-couplings.

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[108] For a recent cluster on iron-catalyzed reactions, see: a) A. K. Steib, T. Thaler, K. Komeyama, P. Mayer, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 3303; b) O. M. Kuzmina, A. K. Steib, D. Flubacher, P. Knochel, *Org. Lett.* **2012**, *14*, 4818; c) G. Cahiez, O. Gager, J. Buendia, C. Patinote, *Chem. Eur. J.* **2012**, *18*, 5860; d) O. M. Kuzmina, A. K. Steib, J. T. Markiewicz, D. Flubacher, P. Knochel, *Angew. Chem. Int. Ed.* **2013**, *52*, 4945; e) S. Malhotra, P. S. Seng, S. G. Koenig, A. J. Deese, K. A. Ford, *Org. Lett.* **2013**, *15*, 3698; f) G. Lefèvre, A. Justand, *Chem. Eur. J.* **2014**, *20*, 4796; g) G. Cahiez, A. Moyeux, J. Cossy, *Adv. Synth. Catal.* **2015**, *357*, 1983; h) O. M. Kuzmina, A. K. Steib, S. Fernandez, W. Boudot, J. T. Markiewicz, P. Knochel, *Chem. Eur. J.* **2015**, *21*, 8242; i) S. Toma, R. Sebesta, *Synthesis* **2015**, *47*, 1683.

[109] a) W. Hassan, R. Edrada, R. Ebel, V. Wray, A. Berg, R. van Soest, S. Wiryowidagdo, P. Proksch, *J. Nat. Prod.* **2004**, *67*, 817; b) Z. Jin, *Nat. Prod. Rep.* **2005**, *22*, 196; c) G. A. Molander, M. D. Elia, *J. Org. Chem.* **2006**, *71*, 9198; d) N. Kaila, K. Janz, A. Huang, A. Moretto, S. DeBernardo, P. W. Bedard, S. Tam, J. Clerin, J. C. Keith, D. H. H. Tsao, N. Sushkova, G. D. Shaw, R. T. Camphausen, R. G. Schraub, Q. Wang, *J. Med. Chem.* **2007**, *50*, 40; e) R. Ueoka, T. Fujita, S. Matsunaga, *J. Org. Chem.* **2009**, *74*, 4396.

[110] a) R. A. Benkeser, D. C. Snyder, *J. Org. Chem.* **1982**, *47*, 1243; b) T. P. Burns, R. D. Rieke, *J. Org. Chem.* **1987**, *52*, 3674; c) S. Harvey, P. C. Junk, C. L. Raston, G. Salem, *J. Org. Chem.* **1988**, *53*, 3134; d) K. V. Baker, J. M. Brown, N. Hughes, A. J. Skarnulis, A. Sexton, *J. Org. Chem.* **1991**, *56*, 698; e) A. Stoll, A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 606.

[111] Y.-H. Chen, M. Sun, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 2236.

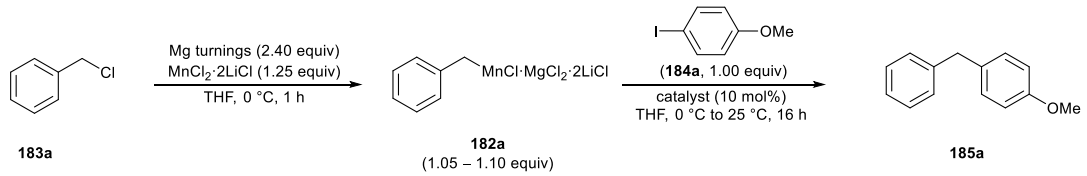
[112] T. D. Blümke, K. Groll, K. Karaghiosoff, P. Knochel, *Org. Lett.* **2011**, *13*, 6440.

[113] a) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107; b) A. Metzger, M. A. Schade, G. Manolikakes, P. Knochel, *Chem. Asian J.* **2008**, *3*, 1678.

1.2. Iron-Catalyzed Cross-Coupling Reactions of Benzylic Manganese Chlorides with Aryl or Heteroaryl Chlorides, Bromides and Iodides

First of all, a screening of different catalysts was carried out using benzylic manganese chloride (**182a**), prepared from benzyl chloride (**183a**) by *in situ* transmetalation, and 4-iodoanisole (**184a**) as electrophile. Neither an uncatalyzed, nor a $CrCl_2$-catalyzed reaction led to a detectable amount of the desired cross-coupling product **185a** (Table 1, entries 1 and 2). The use of cobalt(II) salts, such as $CoCl_2$ and $Co(acac)_2$, gave better but still only moderate yields (entries 3 and 4). Nevertheless, iron(II) and iron(III) salts displayed the best catalytic activity (entries 5–10) and especially $FeCl_2$ proved to be the most efficient catalyst within 16 h at 25 °C in THF (entry 10).

Table 1: Screening of metal catalysts for the palladium-free cross-coupling of benzylic manganese(II) chloride (**182a**) with 4-iodoanisole (**184a**).



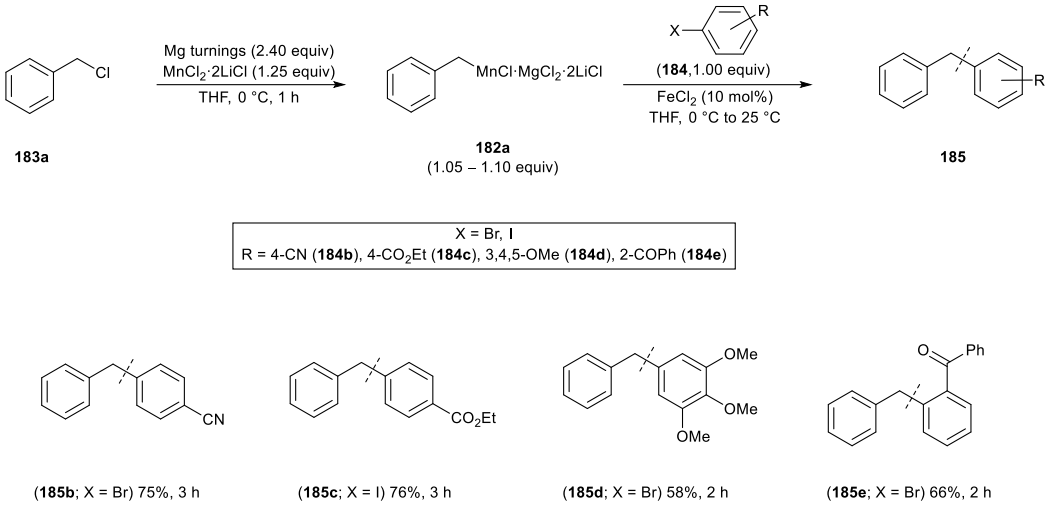
Entry	Catalyst[a]	Yield of **185a** (%)[b]
1	-	0
2	$CrCl_2$	0
3	$Co(acac)_2$	32
4	$CoCl_2$	36
5	$Fe(OTf)_3$	50
6	$FeBr_3$	53
7	$Fe(acac)_3$	69
8	$Fe(acac)_2$	72
9	$FeBr_2$	77
10	$FeCl_2$	84 (79)[c]

[a] Reducing the catalyst to 5.0 mol% led in some cases to decreased reaction yields; [b] Determined by GC-analysis using tetradecane ($C_{14}H_{30}$) as internal standard; [c] Isolated yield.

With these optimized conditions in hand, a short series of different cross-couplings was performed, using benzyl manganese(II) chloride (**182a**) and different aryl halides as electrophiles. It turned out, that it was possible to use either aryl bromides or aryl iodides as electrophiles and even sensitive substituents like a nitrile, an ester or a ketone moiety can be tolerated under these conditions (Scheme 44).

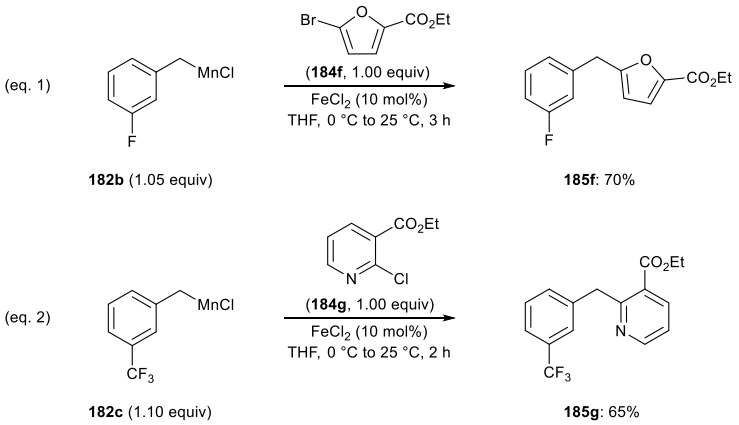
Thus, benzyl manganese reagent **182a** underwent efficient cross-coupling reactions with 4-bromo-benzonitrile (**184b**) and ethyl 4-iodobenzoate (**184c**) at 0 °C within 3 h leading to the expected

diarylmethane derivatives **185b** and **185c** in 75% and 76%, respectively. The reactions of **182a** with a relatively electron-rich aryl bromide **184d** and an aryl bromide bearing a sensitive ketone moiety **184e** also proceeded smoothly under these conditions, resulting in the desired products **185d** and **185e** in 58% and 66% yield, respectively (Scheme 44).



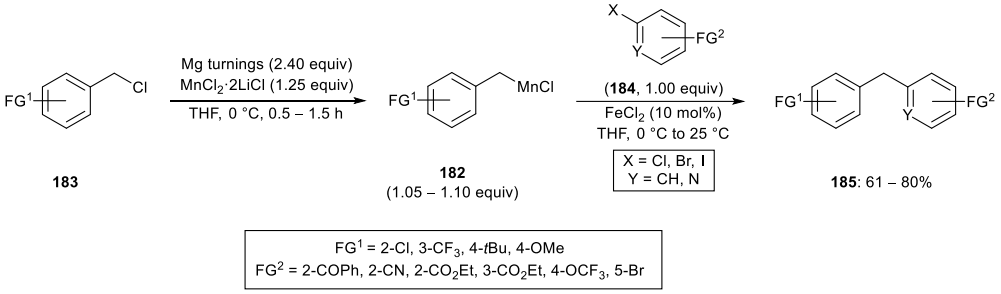
Scheme 44: Preliminary iron-catalyzed cross-couplings of benzyl manganese(II) chloride (**182a**) with different aryl halides of type **184**.

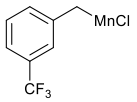
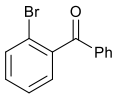
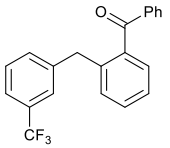
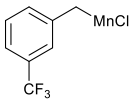
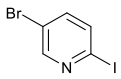
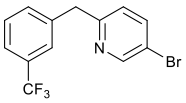
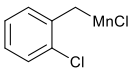
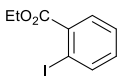
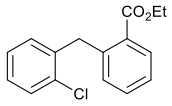
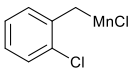
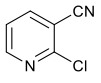
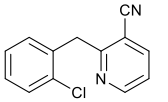
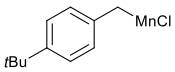
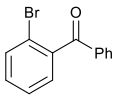
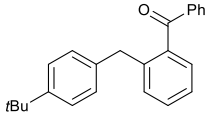
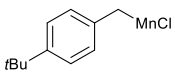
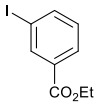
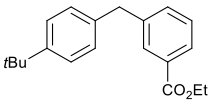
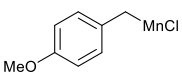
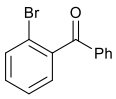
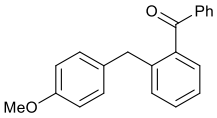
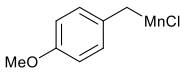
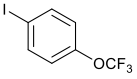
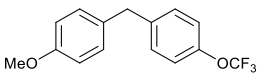
Apart from the unsubstituted benzyl manganese(II) chloride (**182a**), substituted functionalized benzylic manganese chlorides were also able to react with various aryl and heteroaryl halides. Hence, the fluoro-substituted benzylic manganese reagent **182b** reacted with ethyl 5-bromofuran-2-carboxylate (**184f**) at 0 °C within 3 h, leading to the arylheteroarylmethane derivative **185f** in 70% yield (Scheme 45, eq. 1). Furthermore, the CF_3-substituted benzylic manganese chloride **182c** underwent an iron-catalyzed cross-coupling with ethyl 2-chloronicotinate (**184g**) affording the benzylated pyridine **185g** within 2 h in 65% yield (eq. 2). However, under these conditions, unactivated aryl chlorides did not react.



Scheme 45: Further examples for iron-catalyzed cross-coupling reactions of benzylic manganese chlorides **182b** and **182c** with heteroaryl halides **184f** and **184g**.

Table 2: Iron-catalyzed cross-couplings of several benzylic manganese chlorides **182c–f** with aryl and heteroaryl halides.



Entry	Manganese Reagent	Aryl Halide	Product, Yield[a,b], Time
1	 **182c**	 **184e**	 **185h**: 80, 2 h
2	 **182c**	 **184h**	 **185i**: 70, 12 h
3	 **182d**	 **184i**	 **185j**: 68, 2 h
4	 **182d**	 **184j**	 **185k**: 70, 2 h
5	 **182e**	 **184e**	 **185l**: 79, 2 h
6	 **182e**	 **184k**	 **185m**: 79, 2 h
7	 **182f**	 **184e**	 **185n**: 75, 2 h
8	 **182f**	 **184l**	 **185o**: 61, 18 h

[a] Isolated yield; [b] Less than 15% of homocoupling of the manganese reagent was observed.

B. Results and Discussion

The scope of this iron-catalyzed cross-coupling procedure appeared to be quite broad. Further couplings of benzylic manganese reagent **182c** with either 2-bromobenzophenone (**184e**) or 5-bromo-2-iodo-pyridine (**184h**) proceeded at 0 °C within 2 h and 12 h respectively, and the desired polyfunctionalized diaryl- or arylheteroarylmethane derivatives **185h** and **185i** were obtained in 80% and 70% yield (Table 2, entries 1 and 2). Similarly, the *ortho*-chloro-substituted benzylic manganese chloride **182d** reacted with two different aryl halides. The coupling of **182d** with ethyl 2-iodobenzoate (**184i**) resulted in the ester-substituted diarylmethane compound **185j** in 68% yield, and the reaction with 2-chloronicotino-nitrile (**184j**) furnished the expected benzylated pyridine **185k** in 70% yield (entries 3 and 4). Finally, also more electron-rich benzylic manganese reagents were compatible with this synthetic procedure. Thus, the two benzylic manganese chlorides **182e** and **182f** underwent efficient couplings with selected aryl halides **184e**,**k**,**l** and the desired functionalized diarylmethane derivatives **185l–o** could be obtained in 61–79% yield (entries 5–8). In all these cross-couplings, less than 15% of homocoupling of benzylic manganese compounds was observed.

In summary, the use of $FeCl_2$ (10 mol%) allows a convenient iron-catalyzed cross-coupling reaction of benzylic manganese chlorides with various aryl and heteroaryl chlorides, bromides and iodides leading to polyfunctionalized diaryl- and arylheteroarylmethane derivatives. This method also tolerates a range of functional groups, such as esters, nitriles or ketones and proceeds smoothly at room temperature within 2–18 h.

As a second part in transition-metal-catalyzed cross-couplings of organomanganese reagents, a novel nickel-catalyzed, 4-fluorostyrene-promoted cross-coupling procedure of functionalized aryl, benzyl and alkyl manganese reagents with aryl and heteroaryl halides is described in the following.

2. Nickel-Catalyzed Cross-Coupling of Functionalized Organomanganese Reagents with Aryl and Heteroaryl Halides Promoted by 4-Fluorostyrene

2.1. Introduction

In recent years, nickel-catalyzed cross-coupling reactions have attracted much attention due to the high reactivity of nickel catalysts, the moderate price of the metal as well as the broad reaction scope of such couplings.[114,115] However, up to now, only a few nickel-catalyzed cross-coupling using organomanganese derivatives have been reported. *Schneider* developed a Ni(0)-imidazolium carbene catalyst, allowing the cross-coupling between arylmanganese reagents and aryl bromides or chlorides.[42] More recently, *Wang* and co-workers described a C–CN bond activation for cross-couplings with aryl- and heteroarylmanganese reagents.[43] To our knowledge, there was so far no nickel-catalyzed cross-coupling procedure reported, where one general catalytic system was applicable to all type of functionalized manganese reagents.

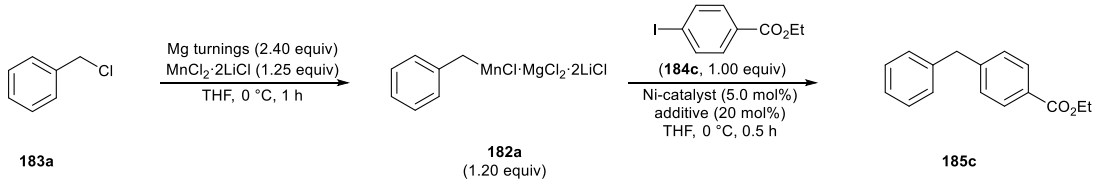
2.2. Nickel-Catalyzed, 4-Fluorostyrene-Promoted Cross-Couplings of Functionalized Organomanganese Reagents with Aryl and Heteroaryl Halides

In the search for such general conditions, an extensive screening of nickel-catalysts and additives was performed. Since benzylic manganese reagents already appeared to be suitable nucleophiles in iron-catalyzed cross-couplings (see paragraph 1.2), the preliminary screening was carried out using benzyl manganese chloride (**182a**, 1.20 equiv), freshly prepared from benzyl chloride (**183a**), magnesium turnings and $MnCl_2 \cdot 2LiCl$, and ethyl 4-iodobenzoate (**184c**, 1.00 equiv) as electrophile. Performing this coupling using nickel halides such as $NiCl_2$ (5.0 mol%) or $NiBr_2$ (5.0 mol%) resulted in already 42–55% isolated yield of the expected product ethyl 4-benzylbenzoate (**185c**) (Table 3, entries 1 and 2). Phosphine-derived nickel catalysts led to a drop-off of the yield to 33–49% (entries 3–6). In contrast, $NiCl_2 \cdot$dme and $Ni(acac)_2$ displayed a good activity affording **185c** in 52% and 57% yield, respectively (entries 7 and 8). As a consequence, $Ni(acac)_2$ was selected as catalytic source for further optimization experiments. Subsequently, the effect of *N*-based ligands was examined. Although *N*-heterocycles neither resulted in improved nor detrimental results (entries 9–15), it was found that especially 4-fluorostyrene[116] led to the best reaction outcome with 72% yield of the desired product **185c** (entry 18).

[114] For recent examples, see: a) C. K. Chu, Y. Liang, G. C. Fu, *J. Am. Chem. Soc.* **2016**, *138*, 6404; b) M. Tobisu, T. Takahira, T. Morioka, N. Chatani, *J. Am. Chem. Soc.* **2016**, *138*, 6711; c) K. M. M. Huihui, R. Shrestha, D. J. Weix, *Org. Lett.* **2017**, *19*, 340.
[115] For selected reviews, see: a) V. B. Phapale, D. J. Cardenas, *Chem. Soc. Rev.* **2009**, *38*, 1598; b) M. Tobisu, N. Chatani, *Acc. Chem. Res.* **2015**, *48*, 1717.
[116] R. Giovannini, T. Stüdemann, G. Dussin, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, **37**, 2387.

It should be noticed that also *N*,*N*,*N′*,*N′*-tetramethylethane-1,2-diamine (TMEDA) and *N*,*N*,*N′*,*N″*,*N″*-pentamethyldiethylenetriamine (PMDETA) gave good results of 67–70% yield (entries 16 and 17).[117] Interestingly, lowering the catalyst loading of $Ni(acac)_2$ from 5.0 mol% to 2.5 mol% or even 1.0 mol% only led to a slight decrease in isolated yield of **185c** (compare entry 18 (72%) with entries 19 and 20 with 68% and 60%, respesectively).

Table 3: Screening of catalysts for the nickel-catalyzed cross-coupling of benzylic manganese chloride (**182a**) with electrophile ethyl 4-iodobenzoate (**184c**).



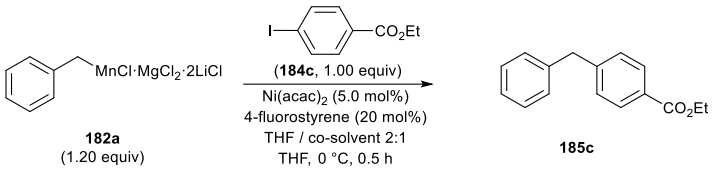
Entry	Catalyst	Additive	Yield of **185c** (%)[a]
1	$NiCl_2$	-	42
2	$NiBr_2$	-	55
3	$NiCl_2(PPh_3)_2$	-	33
4	$NiCl_2(PCy_3)_2$	-	35
5	$NiCl_2$(dppe)	-	38
6	$NiCl_2$(dppp)	-	49
7	$NiCl_2$·dme	-	52
8	$Ni(acac)_2$	-	57
9	$Ni(acac)_2$	pyridine	54
10	$Ni(acac)_2$	isoquinoline	50
11	$Ni(acac)_2$	2,2′-bipyridine	61
12	$Ni(acac)_2$	4-dimethylaminopyridine	65
13	$Ni(acac)_2$	1,10-phenanthroline	40
14	$Ni(acac)_2$	2,9-dimethyl-1,10-phenanthroline	53
15	$Ni(acac)_2$	2,9-di(*tert*-butyl)-1,10-phenanthroline	55
16	$Ni(acac)_2$	TMEDA	67
17	$Ni(acac)_2$	PMDETA	70
18	$Ni(acac)_2$	4-fluorostyrene	72
19	$Ni(acac)_2$	4-fluorostyrene	68[b]
20	$Ni(acac)_2$	4-fluorostyrene	60[c]

[a] Isolated yield. [b] A catalyst loading of 2.5 mol% was used; [c] A catalyst loading of 1.0 mol% was used.

[117] M. Guisan-Ceinos, R. Soler-Yanes, D. Collado-Sanz, V. B. Phapale, E. Bunuel, D. J. Cardenas, *Chem. Eur. J.* **2013**, *19*, 8405; b) S. E. Denmark, A. J. Cresswell, *J. Org. Chem.* **2013**, *78*, 12593; c) J. M. Hammann, A. K. Steib, P. Knochel, *Org. Lett.* **2014**, *16*, 6500; d) J. Magano, S. Monfette, *ACS Catal.* **2015**, *5*, 3120.

In addition, the influence of co-solvents was also examined. Thus, performing the reaction of benzyl manganese chloride (**182a**) with ethyl 4-iodobenzoate (**184c**) using a THF / 1,4-dioxane or THF / MTBE 2:1 mixture (MTBE = methyl *tert*-butyl ether) a similar outcome compared to THF as solvent was obtained (Table 4, entries 1–3). Remarkably, using a THF / Bu_2O 2:1 mixture gave the expected product **185c** in the highest yield of 82% with a slight decrease of homocoupling of the nucleophile (entry 4). Similarly, NMP (*N*-methyl-2-pyrrolidone) as polar co-solvent resulted in the desired diarylmethane derivative **185c** in 80% yield (entry 5).

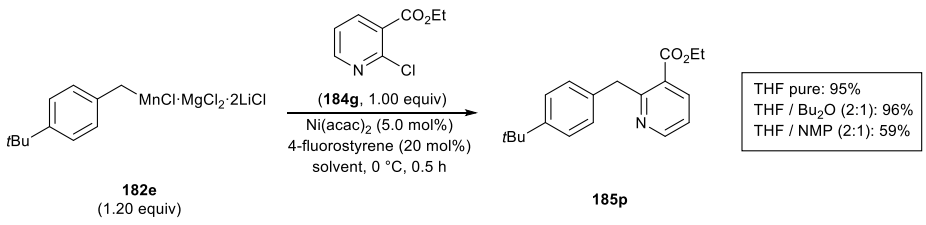
Table 4: Screening of selected co-solvents for the $Ni(acac)_2$-catalyzed cross-coupling of benzyl manganese chloride (**182a**) with ethyl 4-iodobenzoate (**184c**).



Entry	THF / Co-solvent	Yield of **185c** (%)[a]
1	THF	72
2	THF / 1,4-dioxane	67
3	THF / MTBE	72
4	THF / Bu_2O	82
5	THF / NMP	80

[a] Isolated yield; MTBE = methyl *tert*-butyl ether; NMP = *N*-methyl-2-pyrrolidone.

Based on these results, the three best performing conditions were tested on a second experiment. Starting from [4-(*tert*-butyl)benzyl]manganese chloride (**182e**), ethyl 2-chloronicotinate (**184g**) as electrophile and $Ni(acac)_2$ (5.0 mol%) as catalyst, the desired arylheteroarylmethane derivative **185p** was obtained in 95% yield in THF as solvent. In this case, using a THF / Bu_2O 2:1 mixture did not result in a better reaction outcome. Furthermore, a sluggish reaction was observed when performing the same cross-coupling in a more polar THF / NMP 2:1 mixture, and product **185p** was isolated in only 59% yield (Scheme 46).

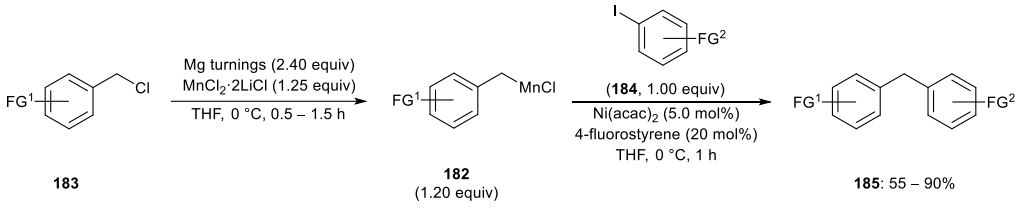


Scheme 46: Ni-catalyzed cross-coupling of benzylic manganese reagent **182e** with electrophile **184g**.

B. Results and Discussion

Since the addition of Bu_2O did not lead to significantly improved reaction yields in general, several benzylic manganese reagents **182b**–**h** underwent smooth Ni-catalyzed cross-couplings with a range of functionalized aryl and heteroaryl iodides or chlorides at 0 °C within 1 h in THF as solvent (Table 5).

Table 5: Ni-catalyzed, 4-fluorostyrene-mediated cross-coupling of benzylic manganese chlorides **182b**–**h** with several aryl iodides of type **184**.



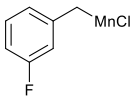
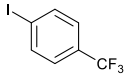
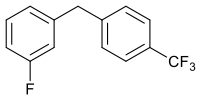
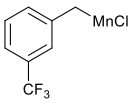
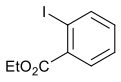
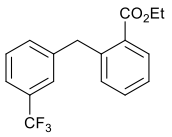
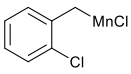
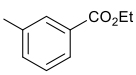
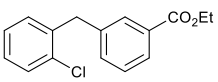
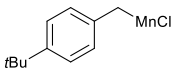
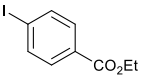
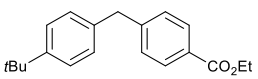
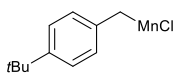
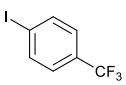
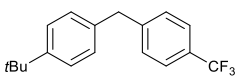
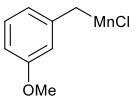
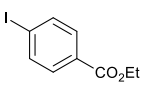
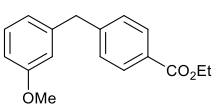
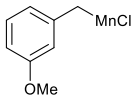
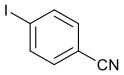
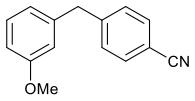
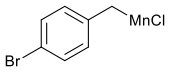
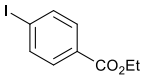
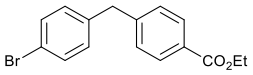
Entry	Manganese Reagent	Aryl Iodide	Product, Yield (%)[a]
			
1	**182b**	**184m**	**185q**: 74
			
2	**182c**	**184i**	**185r**: 90
			
3	**182d**	**184k**	**185s**: 71
			
4	**182e**	**184c**	**185t**: 71
			
5	**182e**	**184m**	**185u**: 62
			
6	**182g**	**184c**	**185v**: 72

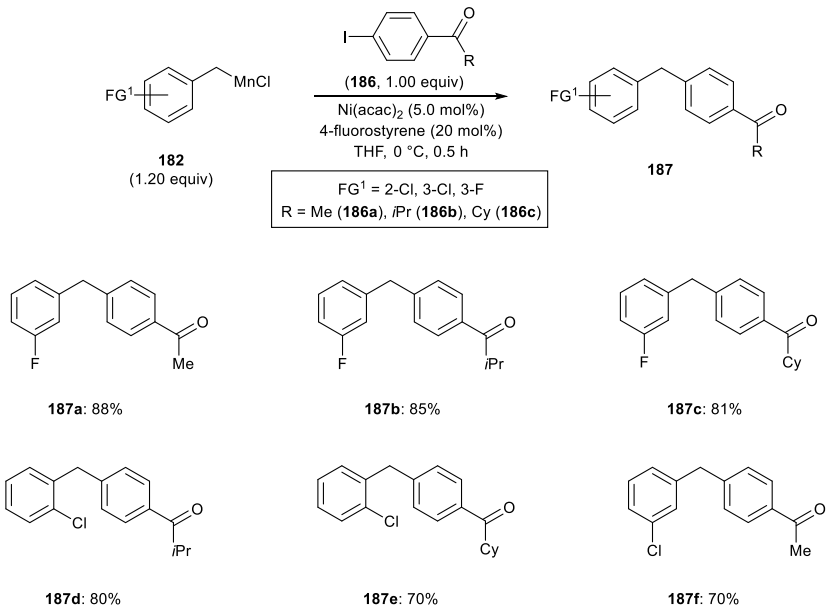
Table 5: (continued).

Entry	Manganese Reagent	Electrophile	Product, Yield (%)[a]
7	 **182g**	 **184n**	 **185w**: 55
8	 **182h**	 **184c**	 **185x**: 61

[a] Isolated yield.

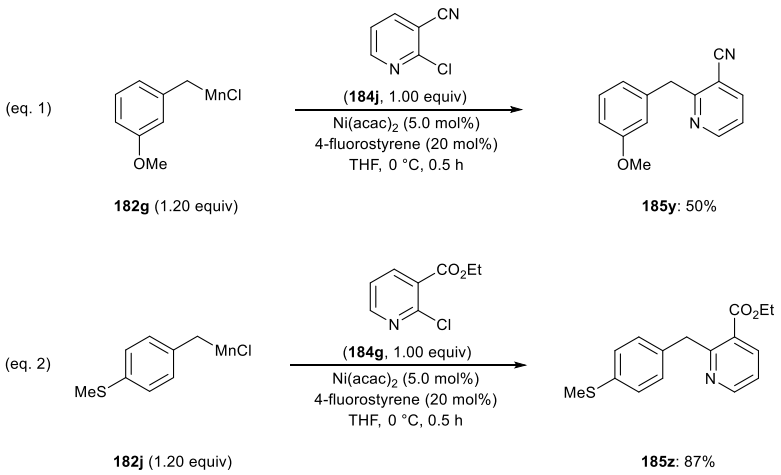
Thus, the cross-couplings of the two fluoro-substituted benzylic manganese reagents **182b** and **182c** with 4-iodobenzotrifluoride (**184m**) and ethyl 2-iodobenzoate (**184i**) proceeded at 0 °C within 1 h leading to the functionalized diarylmethane derivatives **185q** and **185r** in 74% and 90%, respectively (Table 5, entries 1 and 2). Subsequently, the *ortho*-chloro-substituted benzyl manganese chloride **182d** reacted with an ester-bearing aryl iodide **184k** affording the expected product **185s** in 71% yield (entry 3). Similarly, cross-couplings of electron-rich benzylic manganese reagents **182e** and **182g** with electrophiles **184c**,**m**,**n** resulted in the functionalized diarylmethane compounds **185t**–**w** in 55–72% yield (entries 4–7). Finally, a *para*-bromo-substituted benzyl manganese chloride **182h** underwent such a 4-fluorostyrene-promoted cross-coupling with ethyl 4-iodobenzoate (**184c**) producing the desired product **185x** in 61% yield (entry 8).

Since the scope of this Ni-catalyzed cross-coupling procedure appeared to be quite broad, more sensitive electrophiles such as keto- and 2-chloro-substituted aryl or heteroaryl halides were tested. Thus, (3-fluorobenzyl)manganese chloride (**182b**) reacted with three 4-iodoaryl ketones **186a**–**c** at 0 °C within 30 min leading to the keto-substituted diarylmethane derivatives **187a**–**c** in good yields of 81–88%. Additionally, the cross-couplings of the *ortho*- and *meta*-chloro-substituted benzylic manganese reagents **182d** and **182i** with **186a**–**c** furnished the expected products **187d**–**f** in 70–80% yield (Scheme 47).



Scheme 47: Ni-catalyzed cross-coupling of halogenated benzylic manganese chlorides **182** with 4-iodo-aryl ketones of type **186**.

As previously mentioned (Scheme 46), also the cross-coupling of 2-chloro-substituted pyridines as electrophiles proceeded smoothly under these optimized conditions. Thus, (3-methoxy)benzyl-manganese chloride (**182g**) underwent a coupling with 2-chloro-pyridine-3-carbonitrile (**184j**) leading to the desired arylheteroarylmethane derivative **185y** in 50% yield (Scheme 48, eq. 1). Also a sulfur-substituted benzyl manganese chloride **182j** reacted with ethyl 2-chloronicotinate (**184g**) to give the expected product **185z** in 87% yield (eq. 2).

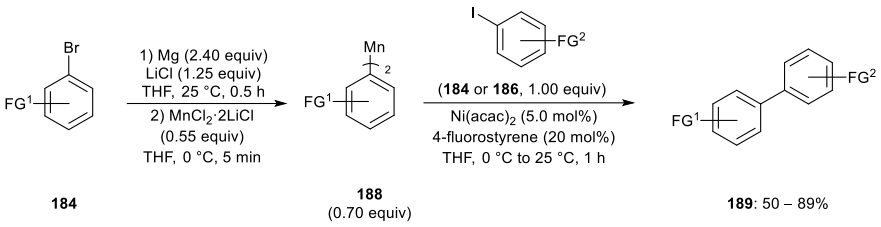


Scheme 48: Ni-catalyzed cross-coupling of benzyl manganese chlorides **182g** and **182j** with 2-chloro-substituted pyridines **184j** and **184g**.

More interestingly, it was possible to extend these Ni-catalyzed cross-couplings to aryl and alkyl manganese reagents. First of all, a variety of trapping reactions between functionalized bis-(aryl)manganese reagents **188a**–**h** and aryl or heteroaryl halides of type **184** was performed. Thus, bis-(4-methoxyphenyl)manganese (**188a**), prepared *via* the oxidative insertion of magnesium turnings (Mg (2.40 equiv), LiCl (1.25 equiv)) into 4-bromoanisole (**184o**) and subsequent transmetalation with $MnCl_2 \cdot 2LiCl$ (0.55 equiv), underwent an efficient cross-coupling with ethyl 4-iodobenzoate (**184c**) leading to the expected biphenyl **189a** in 89% yield (Table 6, entry 1). Similarly, the reaction of bis-(3,4,5-trimethoxyphenyl)manganese (**188b**) with ketone **186c** proceeded at 0 °C within 1 h to afford the polyfunctionalized biphenyl **189b** in 50% yield (entry 2). In addition, bis-[4-(trifluoromethoxy)phenyl]-manganese (**188c**) reacted under the same conditions with 4-iodoanisole (**184a**) and ethyl 4-iodo-benzoate (**184c**) to give the functionalized arenes **189c** and **189d** in 60% and 66%, respectively (entries 3 and 4). Subsequently, the cross-coupling of a TMS-substituted bis-(aryl)manganese reagent **188d** succeeded *via* these conditions with an aryl ester **184k** and the ketone **186b** resulting in the biphenyls **189e** and **189f** in 55% and 73% (entries 5 and 6). Also electron-deficient bis-(aryl)manganese reagents like **188e** and **188f** underwent such reactions with the aryl esters **184c** and **184k** and the ketone **186c** to afford the desired substituted arenes **189g**–**i** in 50–64% yield (entries 7–9). Furthermore, the cross-coupling of bis-[2-(trifluoromethyl)phenyl]manganese (**188g**) with ethyl 4-iodobenzoate (**184c**) and 1-(4-iodophenyl)-ethan-1-one (**186a**) proceeded smoothly at 0 °C leading to the polyfluoro-substituted biphenyls **189j** and **189k** in 61% and 80% yield (entries 10 and 11). Finally, bis-(benzo[*d*][1,3]dioxol-5-yl)manganese (**188h**) reacted with 4-iodobenzotrifluoride (**184n**) within 1 h to furnish the desired functionalized arene **189l** in 50% yield (entry 12).

Besides Ni-catalyzed cross-couplings of bis-(aryl)manganese reagents with aryl iodides, this procedure proved to be also useful for the coupling reactions with 2-chloro-substituted pyridines. Thus, bis-(3,4,5-trimethoxyphenyl)manganese (**188b**) underwent an efficient coupling with 2-chloro-5-(trifluoro-methyl)pyridine (**184p**) leading to the functionalized pyridine derivative **189m** in 72% yield. Similarly, the reaction of bis-(benzo[*d*][1,3]dioxol-5-yl)manganese (**188h**) with ethyl 2-chloronicotinate (**184g**) afforded the desired heteroarene **189n** in an excellent yield of 91%. As a last example, the coupling between bis-[4-(dimethylamino)phenyl]manganese (**188i**) and 2-chloro-3-pyridinecarbonitrile (**184j**) succeeded at 0 °C within 1 h resulting in the formation of the substituted pyridine **189o** in 53% yield (Scheme 49).

Table 6: 4-Fluorostyrene-mediated Ni-catalyzed cross-coupling of functionalized bis-(aryl)manganese reagents **188a–h** with various aryl halides of type **184** and keto-substituted aryl iodides of type **186**.



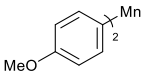
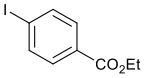
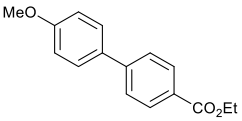
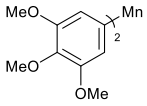
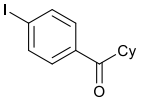
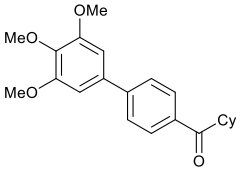
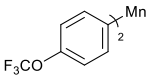
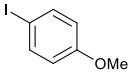
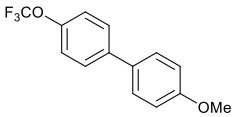
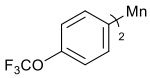
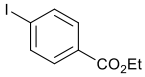
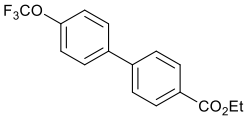
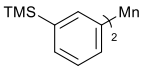
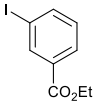
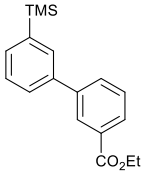
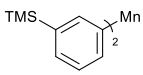
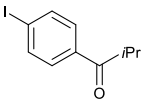
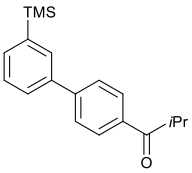
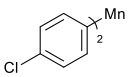
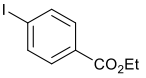
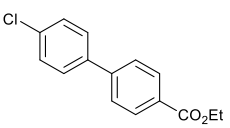
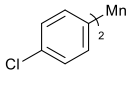
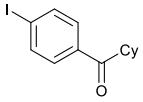
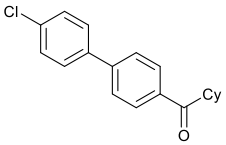
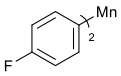
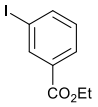
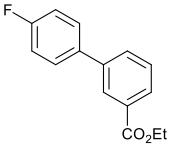
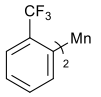
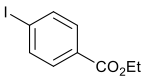
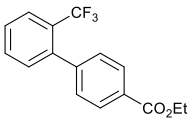
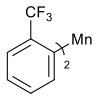
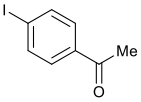
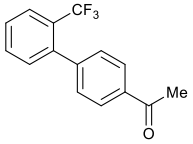
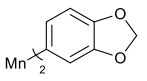
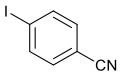
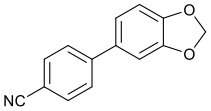
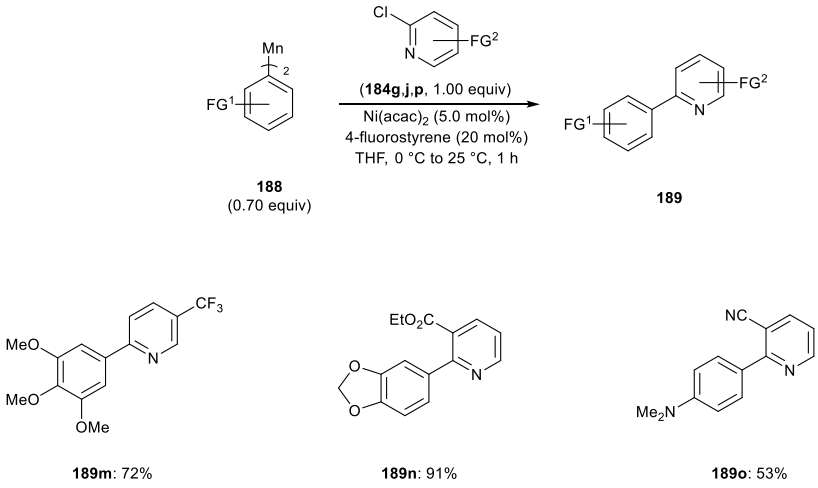
Entry	Manganese Reagent	Aryl Iodide	Product, Yield (%)[a]
1	 **188a**	 **184c**	 **189a**: 89
2	 **188b**	 **186c**	 **189b**: 50
3	 **188c**	 **184a**	 **189c**: 60
4	 **188c**	 **184c**	 **189d**: 66
5	 **188d**	 **184k**	 **189e**: 55
6	 **188d**	 **186b**	 **189f**: 73
7	 **188e**	 **184c**	 **189g**: 64

Table 6: (continued).

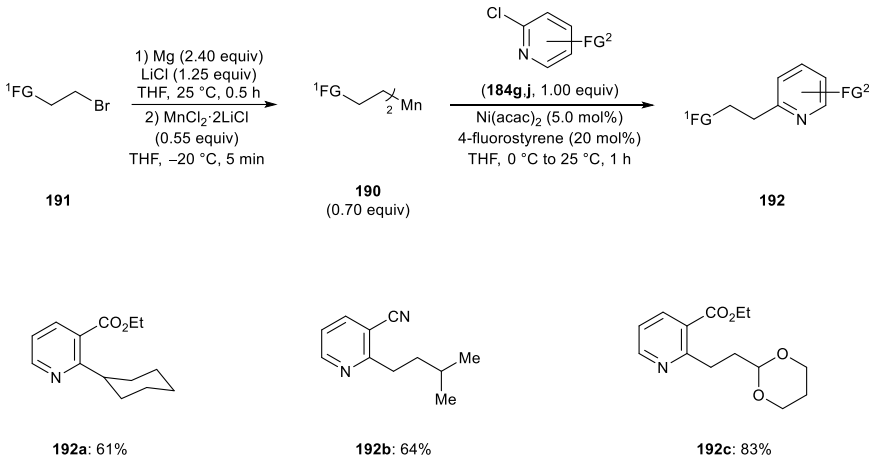
Entry	Manganese Reagent	Electrophile	Product, Yield (%)[a]
8	 **188e**	 **186c**	 **189h**: 50
9	 **188f**	 **184k**	 **189i**: 61
19	 **188g**	 **184c**	 **189j**: 80
11	 **188g**	 **186a**	 **189k**: 61
12	 **188h**	 **184n**	 **189l**: 50

[a] Isolated yield.



Scheme 49: Ni-catalyzed cross-coupling of bis-(aryl)manganese reagents **188** with 2-chloro-substituted pyridines **184g**,**j**,**p** as electrophiles.

As a last point, bis-(alkyl)manganese reagents proved to be useful cross-coupling partners in Ni-catalyzed reactions. Thus, bis-(cyclohexyl)manganese (**190a**), prepared *via* the oxidative insertion of magnesium turnings (Mg (2.40 equiv), LiCl (1.25 equiv)) into cyclohexylbromide (**191a**) and subsequent transmetalation with $MnCl_2 \cdot 2LiCl$ (0.55 equiv), underwent the cross-coupling with ethyl 2-chloronicotinate (**184g**) affording the alkyl-substituted pyridine **192a** in 61% yield. Subsequently, bis-(isopentyl)manganese (**190b**) reacted with 2-chloro-3-pyridinecarbonitrile (**184j**) leading to the desired product **192b** in 64% yield. Also the coupling of bis-[2-(1,3-dioxan-2-yl)ethyl]manganese (**190c**) with pyridine **184g** gave the *ortho*-substituted pyridine derivative **192c** in 83% yield (Scheme 50).



Scheme 50: Ni-catalyzed cross-coupling of bis-(alkyl)manganese reagents **190** with 2-chloro-substituted pyridines **184g**,**j** as electrophiles.

To sum it up, an efficient and general catalytic system consisting of $Ni(acac)_2$ (5.0 mol%) and 4-fluorostyrene (20 mol%) allows a convenient cross-coupling of functionalized benzylic manganese reagents with aryl and heteroaryl halides providing polyfunctionalized aryl- and heteroarylmethane derivatives. In addition, the scope of this reaction could be extended to aryl- and alkylmanganese reagents as well as electrophiles bearing sensitive ester or nitrile moieties. Remarkably, even keto-substituted 4-iodoarenes underwent such a smooth cross-coupling pathway at 0 °C within 30 min in good yields.

3. Iron-Catalyzed Acylation of Polyfunctionalized Aryl- and Benzylzinc Halides with Acid Chlorides

3.1. Introduction

Organozinc reagents belong to the most useful organometallics for organic synthesis since they show a high tolerance towards functional groups and undergo efficient transmetalations to various metallic salts leading to a broad reactivity pattern.[72a] The reaction of zinc reagents with acid chlorides is an important method for preparing a range of polyfunctionalized ketones.[72b] Although such acylations proceed without catalysts, the yields are usually low due to extensive side reactions.[118] A transmetalation of organozinc reagents to the corresponding copper reagents using CuCN·2LiCl[119] considerably extends the reaction scope of this acylation procedure and allows the preparation of various highly functionalized ketones.[50a] Although this acylation can be performed in many cases using substoichiometric amounts of copper, it generally results in lower yields. Alternatively, *Negishi* reported a palladium-catalyzed acylation method of organozinc halides,[120] and *Rieke* described a related nickel-catalyzed acylation for the preparation of aryl ketones.[121] Recently, *Gosmini* reported a cobalt-catalyzed acylation of arylzinc bromides.[122] Interestingly, organozinc reagents can also be acylated with thioesters as shown by *Fukuyama*[123] or with acyl cyanides.[124] Since iron salts are cheap, environmentally friendly and of moderate toxicity, their use as acylation catalysts would be especially attractive. *Marchese*[125] and *Fürstner*[126] already demonstrated that iron-catalyzed reactions of acid chlorides with organomagnesium reagents can be readily performed. In addition, *Cahiez* showed that organomanganese reagents prepared from the corresponding Grignard species undergo acylation reactions with excellent yields.[21]

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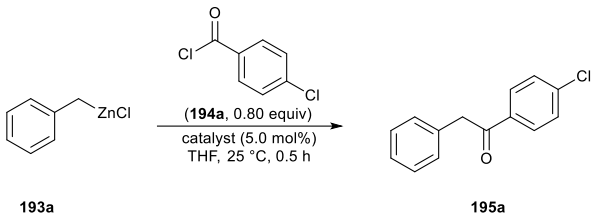
3.2. Iron-Catalyzed Acylation Reactions of Polyfunctionalized Aryl- and Benzylzinc Reagents with Acid Chlorides

In preliminary experiments, benzylzinc choride (**193a**, 1.0 equiv), prepared by the oxidative addition of Mg turnings in the presence of $ZnCl_2$ into the corresponding benzylic chloride,[63a] reacted with 4-chlorobenzoyl chloride (**194a**, 0.80 equiv) in THF at room temperature in the presence of various transition-metal salts (Table 7). This rapid screening indicated that iron salts and especially iron(II) chloride is an excellent catalyst (Table 7, entry 8). Other additives like 4-(dimethylamino)pyridine (DMAP),[127] $Sc(OTf)_3$[128] or $BF_3{\cdot}OEt_2$[129] did not lead to an improvement. In addition, testing various solvent mixtures, such as THF / NMP or THF / DMA in 2:1 ratio, showed that THF was the ideal solvent for this acylation reaction since the ketone **195a** was obtained after 30 min reaction time in 90% isolated yield. To ensure that $FeCl_2$ is the true catalyst, $FeCl_2$ of high purity (99.5%) was used for this acylation reaction. The coupling experiment with $FeCl_2$ of lower purity (98%) proceeded somewhat less cleanly and gave 70% yield of product **195a**.

Table 7: Screening of catalysts for the acylation of benzylzinc chloride (**193a**) with 4-chlorobenzoyl chloride (**194a**).



Entry	Catalyst	Yield of **196a** (%)[a]
1	-	74
2	$MnCl_2$	60
3	$CrCl_2$	65
4	$Fe(acac)_3$	60
5	$FeBr_3$[b]	85
6	$Fe(acac)_2$	73
7	$FeBr_2$[b]	82
8	$FeCl_2$	90[c] (70)[d]

[a] Isolated yield; [b] $FeBr_2$ and $FeBr_3$ of 98% purity; [c] $FeCl_2$ of 99.5% purity; [d] $FeCl_2$ of 98% purity.

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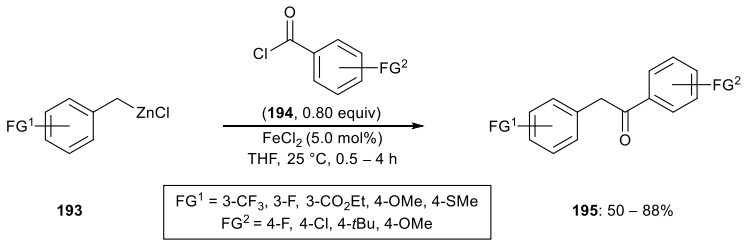
[129] a) M. Jaric, B. A. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 5451; b) M. Jaric, B. A. Haag, S. M. Manolikakes, P. Knochel, *Org. Lett.* **2011**, *13*, 2306; c) K. Groll, S. M. Manolikakes, X. Mollat du Jourdin, M. Jaric, A. Bredihhin, K. Karaghiosoff, T. Carell, P. Knochel, *Angew. Chem. Int. Ed.* **2013**, *52*, 6776.

B. Results and Discussion

The $FeCl_2$-catalyzed acylation procedure proved to be quite general. Thus, the reaction of of (3-trifluoromethylbenzyl)zinc chloride (**193b**) with 4-*tert*-butylbenzoyl chloride (**194b**) provides within 30 min at 25 °C the desired ketone **195b** in 65% yield (Table 7, entry 1). In the absence of an iron catalyst, the yield leveled at only 38% yield. Similarly, the acylation of **193b** with 4-chlorobenzoyl chloride (**194a**) gave the ketone **195c** in 71% yield (entry 2). Furthermore, (3-fluorobenzyl)zinc chloride (**193c**) reacted in the presence of $FeCl_2$ (5.0 mol%) with 4-*tert*-butylbenzoyl chloride (**194b**) within 30 min, furnishing the expected diaryl ketone **195d** in 88% yield (entry 3). The acylation of the benzylic zinc chloride **193c** with the electron-deficient 4-fluorobenzoyl chloride (**194c**) afforded the bisfluorinated ketone **195e** in 74% yield (entry 4). Similarly, the readily available benzylic zinc reagent **193d** bearing an ester moiety underwent an efficient acylation with 4-chlorobenzoyl chloride (**194a**) leading to the functionalized diaryl ketone **195f** in 50% yield (entry 5). Additionally, the electron-rich (4-methoxybenzyl)zinc chloride (**193e**) reacted with 4-*tert*-butylbenzoyl chloride (**194b**) to afford ketone **195g** in 58% yield (entry 6). Interestingly, the acylation of the sulfur-containing benzylic zinc chloride **193f** with 2-thiophenecarbonyl chloride (**194d**) succeeded within 4 h at 25 °C to give the desired aryl heteroaryl ketone **195h** in 60% yield (entry 7). Finally, the reaction of a secondary benzylzinc reagent **193g** with selected acid chlorides **194a**,**d** and **194e** provides the diaryl ketones **195i**–**k** in 65–79% yield (entries 8–10).

Table 8: Iron-catalyzed acylations of benzylic zinc halides **193** with acid chlorides **194**.



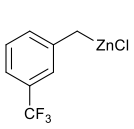
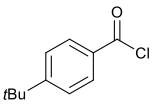
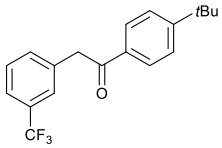
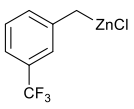
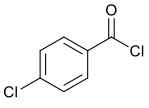
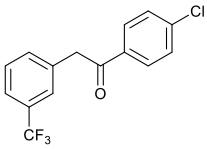
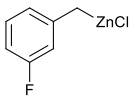
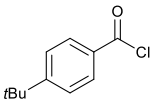
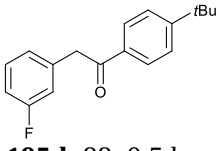
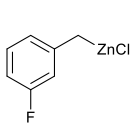
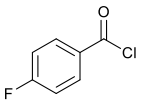
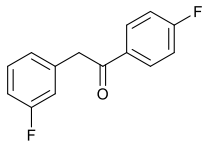
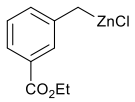
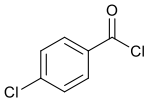
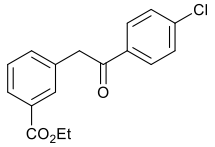
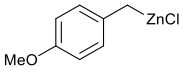
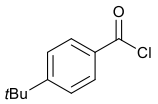
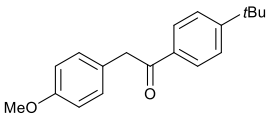
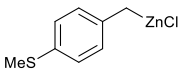
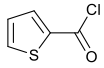
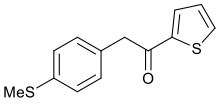
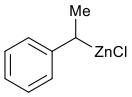
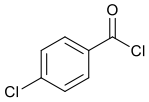
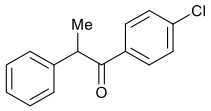
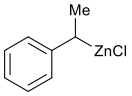
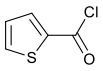
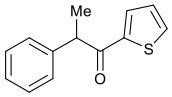
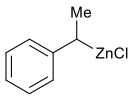
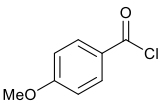
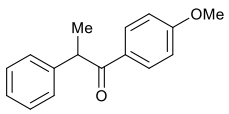
Entry	Benzylzinc Reagent	Acid Chloride	Product, Yield (%)[a,b], Time
1	 **193b**	 **194b**	 **195b**: 65 (38[c]), 0.5 h
2	 **193b**	 **194a**	 **195c**: 71, 0.5 h
3	 **193c**	 **194b**	 **195d**: 88, 0.5 h

Table 8: (continued).

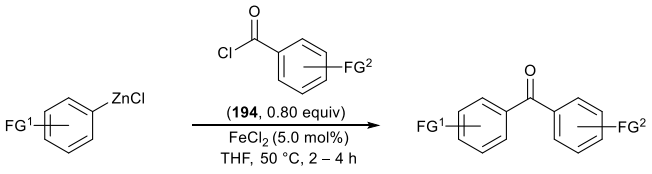
Entry	Benzylzinc Reagent	Acid Chloride	Product, Yield (%)[a,b], Time
			
4	**193c**	**194c**	**195e**: 74, 0.5 h
			
5	**193d**	**194a**	**195f**: 50, 4 h
			
6	**193e**	**194b**	**195g**: 58, 0.5 h
			
7	**193f**	**194d**	**195h**: 60, 4 h
			
8	**193g**	**194a**	**195i**: 78, 1 h
			
9	**193g**	**194d**	**195j**: 65, 1 h
			
10	**193g**	**194e**	**195k**: 79, 1 h

[a] Isolated yield; [b] Up to 20% of homocoupling of the benzylic residue was observed; [c] Isolated yield without catalyst.

Additionally, this cross-coupling has been extended to arylzinc chlorides. Compared to benzylic zinc reagents, the carbon–zinc bond of arylzinc halides has a much lower ionic character and, therefore, is significantly less reactive. Thus, the direct acylation of the electron-poor arylzinc halide **196a**, conveniently prepared *via* an I/Mg-exchange using *i*PrMgCl·LiCl followed by transmetalation with $ZnCl_2$,[30] proceeds only sluggishly with 4-chlorobenzoyl chloride (**194a**) at 50 °C in THF providing the ketone **197a** in 34% yield even after a prolonged reaction time of 12 h. In contrast, when $FeCl_2$ (5.0 mol%, 99.5% purity) was used, the acylation with **196a** was complete after 4 h at 50 °C, and the desired ketone **197a** was isolated in 62% yield (Table 9, entry 1).

Similarly, the arylzinc reagent **196a** underwent several acylations with the functionalized acid chlorides **194b**,**c** and **194f** leading to the diaryl ketones **197b−d** in 65–83% (entries 2−4). Furthermore, the related arylzinc reagent **196b**, bearing an ester moiety in *meta*-position, reacted rapidly with the acid chlorides **194a**,**b** and **194g** to afford the ketones **197e**–**g** within 4 h in 60−75% yield (entries 5−7). Performing such acylations using the *ortho*-substituted arylzinc chloride **196c** in combination with the two electron-poor acid chlorides 4-chlorobenzoyl chloride (**194a**) and 4-cyanobenzoyl chloride (**194h**) proceeded smoothly at 50 °C, yielding the functionalized diaryl ketones **197h** and **197i** in 62% and 74% yield, respectively (entries 8 and 9). The scope of this acylation procedure proved to be quite general for a range of other functionalized arylzinc reagents. Thus, the reaction of (4-(trifluoromethyl)phenyl)zinc chloride (**196d**) with acid chlorides bearing electron-donating substituents, like 4-*tert*-butylbenzoyl chloride (**194b**) and 4-methoxybenzoyl chloride (**194e**), gave the desired ketones **197j** and **197k** in 62% and 83% yield (entries 10 and 11). In addition, (4-fluoro-3-methylphenyl)zinc chloride (**196e**) underwent efficient acylations with the acid chlorides **194a**,**b** and **194e** to afford the functionalized diaryl ketones **197l**–**n** in 70–79% yield (entries 12–14). Finally, the electron-rich (4-methoxyphenyl)-zinc chloride (**196f**) reacted with selected acid chlorides bearing a chlorine **194a**, a *tert*-butyl **194b**, or a fluorine substituent **194c** in the *para*-position leading to the ketones **197o**–**q** within 3 h at 50 °C in 74–82% yield (entries 15−17).

Table 9: Iron-catalyzed acylations of arylzinc reagents **196** with acid chlorides **194**.



FG^1 = 2-CO_2Et; 3-CO_2Et; 4-CO_2Et; 4-CF_3, 3-Me; 4-F; 4-OMe
FG^2 = 4-F; 4-Cl; 4-Br; 4-CN; 4-*t*Bu; 4-OMe

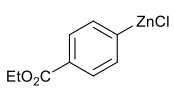
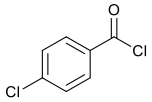
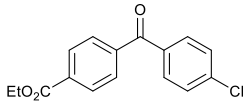
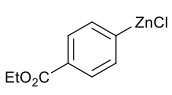
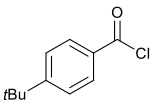
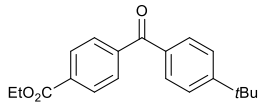
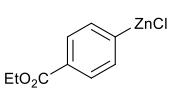
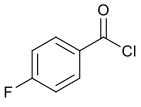
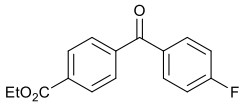
Entry	Arylzinc Reagent	Acid Chloride	Product, Yield (%)[a,b], Time
1	 **196a**	 **194a**	 **197a**: 62, (56[c], 34[d]), 4 h
2	 **196a**	 **194b**	 **197b**: 65, 4 h
3	 **196a**	 **194c**	 **197c**: 83 (21[d]), 4 h

Table 9: (continued).

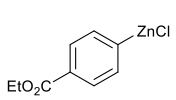
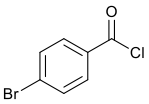
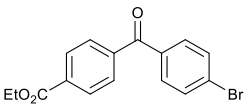
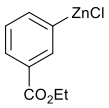
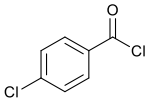
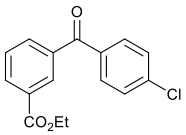
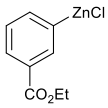
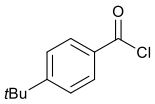
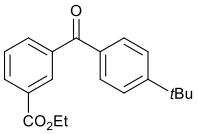
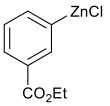
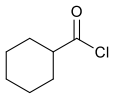
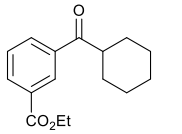
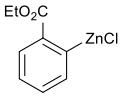
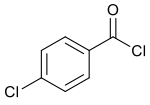
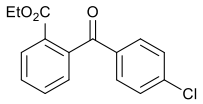
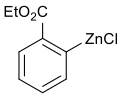
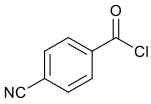
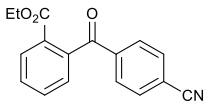
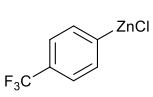
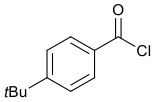
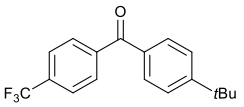
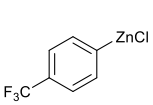
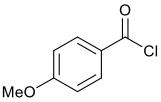
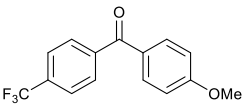
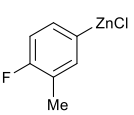
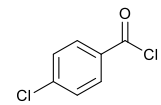
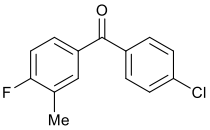
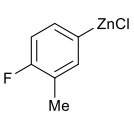
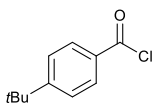
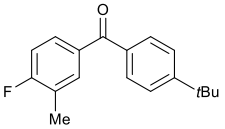
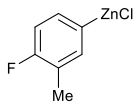
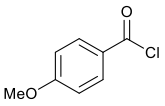
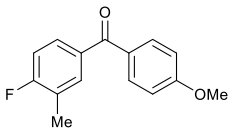
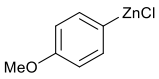
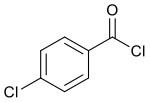
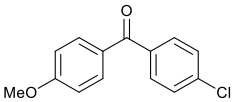
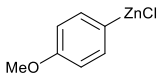
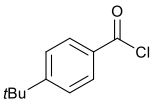
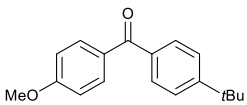
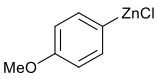
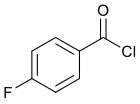
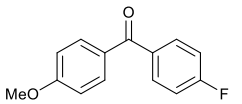
Entry	Arylzinc Reagent	Acid Chloride	Product, Yield (%)[a,b], Time
4	 **196a**	 **194f**	 **197d**: 68, 4 h
5	 **196b**	 **194a**	 **197e**: 75, 4 h
6	 **196b**	 **194b**	 **197f**: 72, 4 h
7	 **196b**	 **194g**	 **197g**: 60, 4 h
8	 **196c**	 **194a**	 **197h**: 74, 4 h
9	 **196c**	 **194h**	 **197i**: 62, 4 h
10	 **196d**	 **194b**	 **197j**: 83, 3 h
11	 **196d**	 **194e**	 **197k**: 62, 3 h
12	 **196e**	 **194a**	 **197l**: 76, 2 h
13	 **196e**	 **194b**	 **197m**: 70, 2 h

Table 9: (continued).

Entry	Arylzinc Reagent	Acid Chloride	Product, Yield (%)[a,b], Time
			
14	**196e**	**194e**	**197n**: 79, 2 h
			
15	**196f**	**194a**	**197o**: 74, 3 h
			
16	**196f**	**194b**	**197p**: 82, 3 h
			
17	**196f**	**194c**	**197q**: 82, 3 h

[a] Isolated yield; [b] Up to 10% of homocoupling of the arylzinc reagent was observed; [c] $FeCl_2$ with a purity of 99.99% was used; [d] Isolated yield without catalyst.

Taking all this into account, this Fe-catalyzed acylation procedure of functionalized aryl and benzylic zinc reagents with commercially available acid chlorides as electrophiles is a useful alternative towards the already established protocols by *Negishi*[120] or *Rieke*[121] and is able to replace expensive and toxic palladium or nickel catalysts by an environmentally friendly and cheap iron salt. This $FeCl_2$-catalyzed acylation proceeds furthermore under mild reaction conditions in THF leading to polyfunctionalized diaryl and arylheteroaryl ketones in only 0.5–4 h.

4. A Practical Cobalt-Catalyzed Cross-Coupling of Benzylic Zinc Reagents with Aryl and Heteroaryl Bromides or Chlorides

4.1. Introduction

Pd-catalyzed cross-couplings of organozinc reagents and various organic halides, called *Negishi* cross-couplings, constitute a key method to form C–C bonds.[37a] Due to the high price and toxicity of palladium, related transition-metal-catalyzed cross-couplings involving zinc organometallics and Ni-, Fe- or Co-catalysts have been examined.[83,84] Furthermore, the use of zinc organometallics is of special interest due to the high functional group compatibility of zinc reagents.[72] Recently, several preparation methods of benzylic zinc halides have been reported and demonstrated that these reagents undergo smooth *Negishi* cross-couplings.[77,113] *Bedford*[87] also reported that benzylic halides undergo useful Fe-catalyzed cross-couplings with arylzinc halides. *Gosmini* has shown in one-pot procedures that arylzinc reagents generated *in situ via* a cobalt-catalyzed zinc insertion undergo cross-couplings with benzyl halides.[93] Interestingly, *Ingleson* has described a transition-metal free coupling between relatively non-functionalized diarylzincs with benzylic bromides and chlorides performed in the absence of coordinating solvent.[130] In the following, a practical cobalt-catalyzed cross-coupling promoted by isoquinoline between various benzylic zinc reagents with aryl and heteroaryl bromides or chlorides resulting in the formation of valuable diaryl- and diheteroarylmethane derivatives is described.

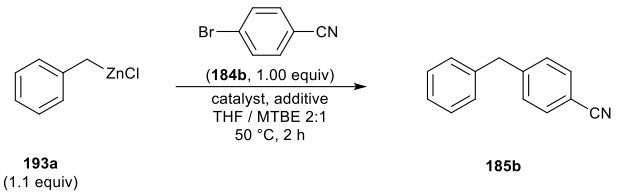
4.2. A Practical Cobalt-Catalyzed, Isoquinoline-Promoted Cross-Coupling of Benzylic Zinc Reagents with Aryl and Heteroaryl Bromides or Chlorides

Preliminary experiments performed with benzylzinc chloride (**193a**), prepared *via* the oxidative insertion of magnesium into the corresponding benzyl chloride in the presence of LiCl and $ZnCl_2$, and 4-bromobenzonitrile (**184b**) as electrophile in a THF / MTBE 2:1 mixture (MTBE = methyl *tert*-butyl ether)[108b,d,h] have shown that in the absence of transition-metal catalyst, no reaction is observed at 50 °C after 2 h (Table 10, entries 1 and 2). Fe-catalysts such as $Fe(acac)_3$, $Fe(acac)_2$ or $FeCl_2$ were also inefficient (entries 3–5). However, the use of 5.0 mol% of $CoBr_2$, $Co(acac)_2$ and $CoCl_2$ showed the formation of the desired cross-coupling product **185b** in 47–76% GC yield (entries 6–8). Previously reported additives like 4-fluorostyrene[116], TMEDA[117] or isoquinoline[108h] indicated a very positive effect (entries 9–11). By performing the reaction of **193a** with electrophile **184a** using 10 mol% of isoquinoline the desired diarylmethane derivative **185b** was obtained in 82% yield (entry 11). Decreasing the amount of isoquinoline to 5.0 mol% reduces somewhat the yield of product **185b** (entry 12). The use of the THF-soluble complex $CoCl_2 \cdot 2LiCl$ was also not advantageous (entries 13 and 14).

[130] J. J. Dunsford, E. R. Clark, M. J. Ingleson, *Angew. Chem. Int. Ed.* **2015**, *54*, 5688.

Additionally, the influence of the commercial origin of $CoCl_2$ as well as its purity were examined. Thus, $CoCl_2$ having a purity of 99.999% provided, under the same conditions (50 °C, 2 h), the desired diarylmethane **185b** in 72% yield (compared to 82%, Table 10, entry 11). The addition of MTBE as a co-solvent usually decreases the amount of homocoupling of the nucleophile and therefore enhances the product yield. However, large amounts of MTBE reduced the reaction rate, and a solvent mixture THF / MTBE of 2:1 was found to be optimal. Concerning the need of isoquinoline as ligand, an extensive screening of *N*-heterocycles, including simple pyridine, pyrimidine or 2,2′-biypridine and various phosphines, such as PPh_3, dppe or SPhos, was performed and isoquinoline proved to be the best.

Table 10: Screening of catalysts for the cross-coupling of benzylzinc chloride (**193a**) with 4-bromo-benzonitrile (**184b**).



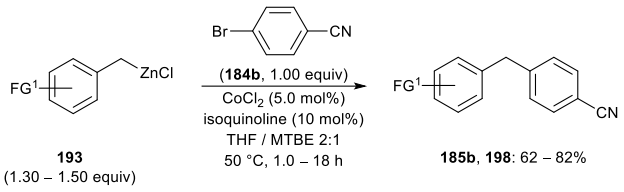
Entry	Catalyst (mol%)	Additive (mol%)	Yield of **185b** (%)[a]
1	-	-	0
2	-	isoquinoline (10)	0
3	$Fe(acac)_3$ (5.0)	-	0
4	$Fe(acac)_2$ (5.0)	-	traces
5	$FeCl_2$ (5.0)	-	traces
6	$CoBr_2$ (5.0)	-	47
7	$Co(acac)_2$ (5.0)	-	70
8	$CoCl_2$ (5.0)	-	76
9	$CoCl_2$ (5.0)	4-fluorostyrene (10)	66
10	$CoCl_2$ (5.0)	TMEDA (10)	68
11	$CoCl_2$ (5.0)	isoquinoline (10)	87 (82[b], 72[c])
12	$CoCl_2$ (5.0)	isoquinoline (5)	75
13	$CoCl_2 \cdot 2LiCl$ (5.0)	isoquinoline (10)	69
14	$CoCl_2 \cdot 2LiCl$ (5.0)	-	65

[a] Determined by GC-analysis using tetradecane ($C_{14}H_{30}$) as an internal standard; [b]Isolated yield; [c] $CoCl_2$ with a purity of 99.999% was used.

B. Results and Discussion

With these optimized conditions in hand, the reaction scope of the cross-coupling between various benzylic zinc chlorides **193** with a broad range of aryl and heteroaryl bromides or chlorides was studied. First, the treatment of benzylic zinc reagents **193a** and **193h** in the presence of $CoCl_2$ (5.0 mol%) and isoquinoline (10 mol%) with 4-bromobenzonitrile (**184b**) at 50 °C led to the diarylmethane derivatives **185b** and **198a** in 82% and 70% within 2 to 4 h (Table 11, entries 1 and 2). Furthermore, the cross-coupling of an *ortho*-substituted benzylzinc chloride **193i** with **184b** afforded the desired arene **198b** in 74% yield (entry 3). Similarly, the two functionalized benzylic zinc reagents **193b** and **193c** cross-coupled with **184b** giving the products **198c** and **198d** in 70–79% (entries 4 and 5). The ester-substituted benzylzinc chloride **193d** underwent a smooth cross-coupling with **184b** leading to the functionalized diarylmethane **198e** in 62% yield (entry 6). Additionally, the cross-couplings of the more electron-donating benzylic zinc reagents **193e** and **193f** with 4-bromobenzonitrile (**184b**) furnished the arenes **198f** and **198g** in 82% and 65% yield, respectively (entries 7 and 8).

Table 11: Isoquinoline-promoted Co-catalyzed cross-coupling of benzylic zinc reagents **193** with 4-bromobenzonitrile (**184b**)



FG[1] = 2-Cl; 3-F; 3-CF_3; 3-CO_2Et; 4-*t*Bu; 4-OMe; 4-SMe

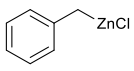
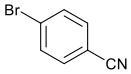
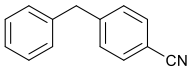
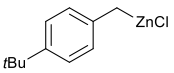
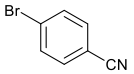
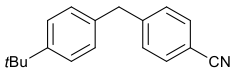
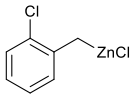
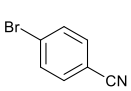
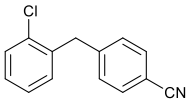
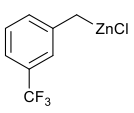
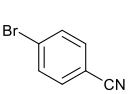
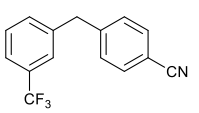
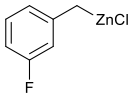
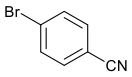
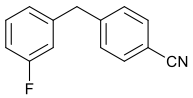
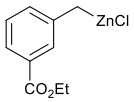
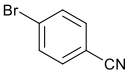
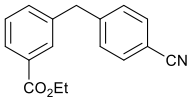
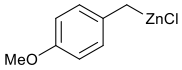
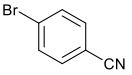
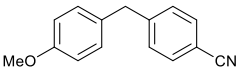
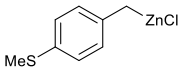
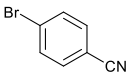
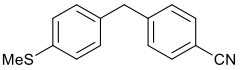
Entry	Benzylzinc Reagent	Aryl Bromide	Product, Yield (%)[a,b], Time
			
1	**193a**	**184b**	**185b**: 82, 2 h
			
2	**193h**	**184b**	**198a**: 77, 4 h
			
3	**193i**	**184b**	**198b**: 74, 18 h
			
4	**193b**	**184b**	**198c**: 70, 2 h

Table 11: (continued).

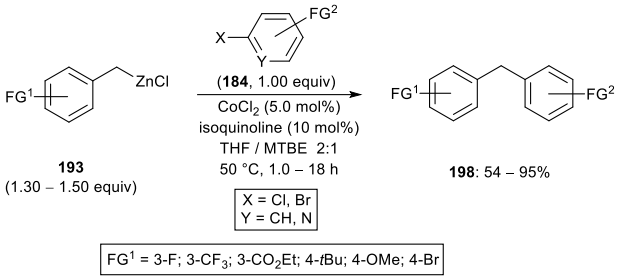
Entry	Benzylzinc Reagent	Aryl Bromide	Product, Yield (%)[a,b], Time
5	 **193c**	 **184b**	 **198d**: 79, 1 h
6	 **193d**	 **184b**	 **198e**: 62, 18 h
7	 **193e**	 **184b**	 **198f**: 82, 2 h
8	 **193f**	 **184b**	 **198g**: 65, 18 h

[a] Isolated yield; [b] Less than 15% of homocoupling of the zinc reagent was observed.

The reaction scope of this cross-coupling procedure proved to be quite broad. Thus, (3-(trifluoromethyl)benzyl)zinc chloride (**193b**) reacted with the two electrophiles ethyl 2-chloronicotinate (**184g**) and ethyl 4-bromobenzoate (**184q**) affording the desired diaryl- and arylheteroarylmethane derivatives **198h** and **198i** in 54% and 60% yield (Table 12, entries 1 and 2). Similarly, (3-fluorobenzyl)zinc chloride (**193c**) underwent two cross-couplings with **184f** and **184j** leading to the arylheteroarylmethanes **198j** and **198k** in 60% and 67% yield (entries 3 and 4). Furthermore, the cross-coupling of the benzylic zinc reagent bearing an ester moiety **193d** with the 2-chloro-substituted pyridine **184g** proceeded smoothly resulting in the pyridine derivative **198l** in 68% yield (entry 5). In the same way electron-rich benzylic zinc reagent such as **193e** and **193h** reacted with different electrophiles of type **184** providing the expected products **198m–p** in 64–95% yield (entries 6–9). Finally, the coupling of (4-bromobenzyl)zinc chloride (**193j**) with 2-chloronicotinonitrile (**184j**) succeeded under these conditions and the arylheteroarylmethane derivative **198q** was obtained in 68% yield (entry 10).

B. Results and Discussion

Table 12: Further Co-catalyzed cross-coupling reactions of benzylic zinc reagents of type **193** with aryl and heteroaryl halides **184**.



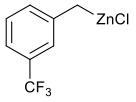
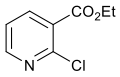
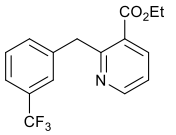
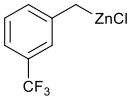
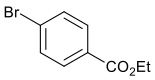
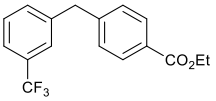
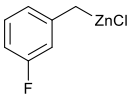
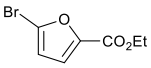
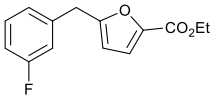
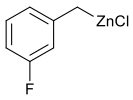
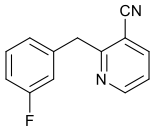
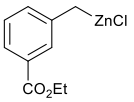
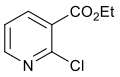
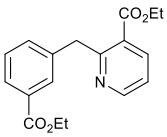
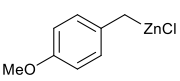
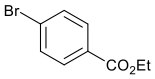
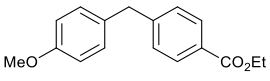
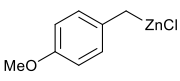
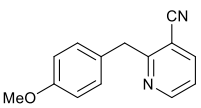
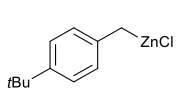
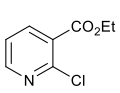
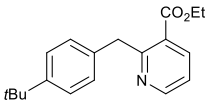
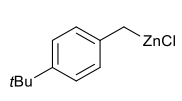
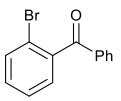
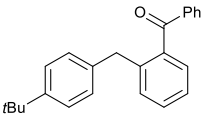
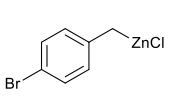
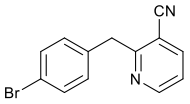
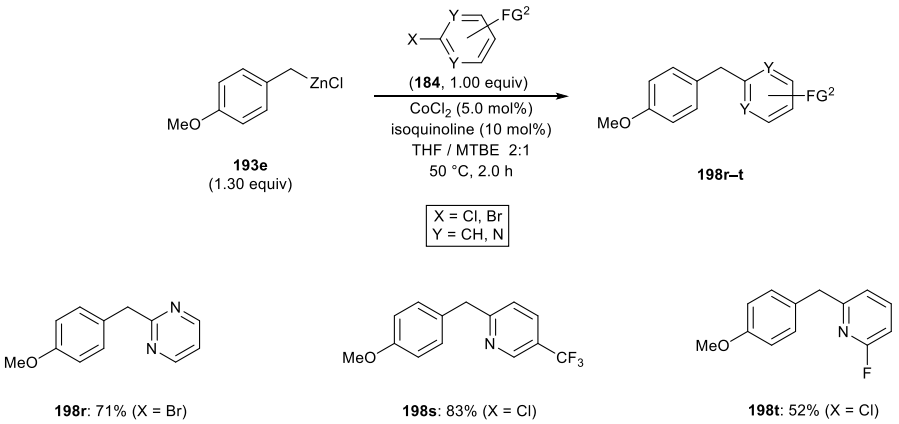
Entry	Benzylzinc Reagent	Aryl Halide	Product, Yield (%)[a,b], Time
1	 **193b**	 **184g**	 **198h**: 60, 2 h
2	 **193b**	 **184q**	 **198i**: 54, 18 h
3	 **193c**	 **184f**	 **198j**: 60, 3 h
4	 **193c**	 **184j**	 **198k**: 67, 3 h
5	 **193d**	 **184g**	 **198l**: 68, 18 h
6	 **193e**	 **184q**	 **198m**: 70, 1 h
7	 **193e**	 **184j**	 **198n**: 77, 2 h

Table 12: (continued).

Entry	Benzylzinc Reagent	Aryl Halide	Product, Yield (%)[a,b], Time
8	 **193h**	 **184g**	 **198o**: 77, 2 h
9	 **193h**	 **184e**	 **198p**: 64, 4 h
10	 **193j**	 **184j**	 **198q**: 68, 18 h

[a] Isolated yield; [b] Less than 15% of homocoupling of the zinc reagent was observed.

Moreover, this Co-catalyzed cross-coupling procedure was also suitable for couplings of other *N*-heterocycles. Thus, the reaction of (4-methoxybenzyl)zinc chloride (**193e**) with 2-bromopyrimidine (**184r**) and two 2-chloro-substituted pyridines **184p** and **184s** led rapidly to the functionalized arylheteroarylmethane derivatives **198r–t** in 52–83% yield (Scheme 51).



Scheme 51: Isoquinoline-promoted cross-couplings of the benzylic zinc reagent **193e** with electrophiles of type **184**.

5. Preparation of Polyfunctional Organozinc Halides by an InX_3- and LiCl-Catalyzed Zinc Insertion into Aryl and Heteroaryl Iodides and Bromides

5.1. Introduction

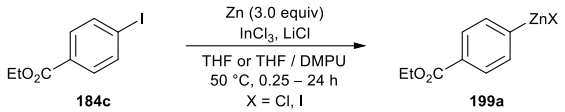
The direct insertion of metal powders into organic halides[50] is an atom-economical[20] method for the preparation of organometallic reagents. Pioneered by *Frankland*[2] in 1848 and *Grignard*[3] in 1900, this method is still one of the most widely used for preparing various Zn- and Mg-organometallics.[50d,e] This heterogeneous reaction requires a zinc insertion on the adsorbed organic halides at the metal surface. Several procedures have been developed to facilitate such an oxidative addition. Among them, the *Rieke* method[51] involving an *in situ* reduction of Zn- or Mg-halides with metallic lithium or the direct activation of Zn- or Mg-powders with LiCl[53] have found the broadest applications. The role of LiCl for the activation of zinc powder has been recently elucidated by *Blum*.[54,55] Also, the use of polar solvents (or co-solvents) such as DMA (*N*,*N*-dimethylacetamide)[52] or DMPU (*N*,*N*-dimethylpropylenurea)[59] has improved the reaction rates. More importantly, a metal salt catalysis was shown to considerably facilitate the metal insertion to organic halides. Thus, *Gosmini* has reported a $CoBr_2$-catalyzed oxidative zinc addition to aryl iodides and bromides in acetonitrile.[56] Later, *Yoshikai* showed that cobalt-Xantphos and LiCl allow the preparation of arylzinc derivatives in THF.[57] *Takai* has reported the exceptional activation of aluminum, gallium and manganese with $PbCl_2$ or $InCl_3$ for the preparation of allylic organometallics.[61] The use of $InCl_3$ as catalyst considerably facilitates the formation of 1,2-bis-zincated aromatics.[59] Despite the availability of these experimental procedures, there is still a need for more efficient catalyses allowing a faster metal insertion and a broader functional group tolerance. With these objectives in mind, the development of novel and improved insertion conditions of commercial zinc powder into organic halides would be highly desirable.

5.2. In-Catalyzed Oxidative Insertion of Zinc into Functionalized Aryl and Heteroaryl Halides

First of all, the influence of LiCl as additive for inserting commercial zinc powder into ethyl 4-iodobenzoate (**184c**) was examined. Whereas, in the absence of LiCl, no zinc insertion into **184c** was observed (Table 13, entry 1), the addition of LiCl (1.50 equiv) allowed to complete this oxidative addition within 24 h at 25 °C leading to the corresponding arylzinc reagent **199a** in 82% yield as indicated by iodometric titration (entry 2). Heating the reaction mixture to 50 °C shortens the reaction time to 4 h at the expense of a lower yield of 65%, due the increased formation of hydrolysis ($PhCO_2Et$) of the arylzinc species **199a** (entry 3). Thus, an additional metal salt catalysis was envisioned. After extensive experimentation testing various metallic salt additives such as $PbCl_2$, VCl_3, $LaCl_3{\cdot}2LiCl$, $Sc(OTf)_3$, $AlCl_3$, $TiCl_4$ and InX_3 (X = F, Cl, Br, OTf, OAc, acac), it became clear that only indium salts were effective. Hence, a complete conversion was reached after 12 h at 50 °C when performing the zinc

insertion in the presence of $InCl_3$ (10 mol%) (90%, entry 4). Using a catalytic system involving $InCl_3$ (3.0 mol%) and LiCl (30 mol%) allowed to further shorten the reaction time to 2 h at 50 °C with the highest yield of arylzinc reagent **199a** (92%, entry 5). Alternatively, a further rate acceleration was obtained by using DMPU as co-solvent (THF / DMPU 1:1) leading to a full conversion after only 15 min at 50 °C at the cost of a slightly lower yield (78%, entry 6). This small yield drop when changing from THF to a more polar solvent mixture has been observed in several optimization experiments and may be tentatively rationalized by side reactions of radical intermediates escaping the solvent-cage leading to the reduced product ($PhCO_2Et$). These side reactions become more important if more LiCl is added increasing the ionic force of the reaction medium (50–70%, entries 7 and 8).

Table 13: $InCl_3$-catalyzed oxidative insertion of zinc powder into ethyl 4-iodobenzoate (**184c**).

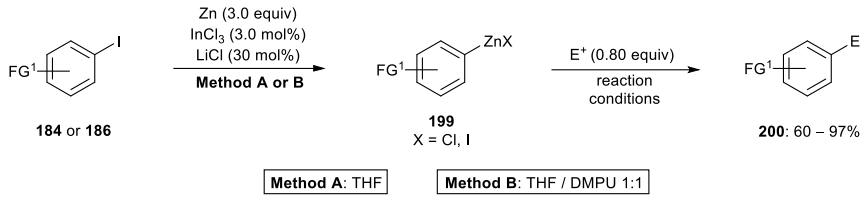


Entry	$InCl_3$ (mol%)	LiCl (equiv)	Time (h)	Solvent (50 °C)	Yield of **199a** (%)[a]
1	0	0	24	THF	< 5
2	0	1.50	24[b]	THF	82
3	0	1.50	4.0	THF	65
4	10	0	12	THF	90
5	3.0	0.30	2.0	THF	92
6	3.0	0.30	0.25	THF / DMPU 1:1	78
7	3.0	0.50	0.25	THF / DMPU 1:1	70
8	3.0	0.80	0.25	THF / DMPU 1:1	50

[a] Yield determined by iodometric titration; [b] Reaction performed at 25 °C.

The use of other co-solvents such as DMA, DMF, NMP, dioxane or MTBE led to only moderate metalation yields. Based on these preliminary optimization studies, two best perfoming reaction conditions, depending on the solvent used, have been defined. In both cases, $InCl_3$ (3.0 mol%) and LiCl (30 mol%) were used, but in Method A, the reaction was performed in pure THF, and in Method B, the reaction was performed in THF / DMPU 1:1. Generally, the highest yields were obtained with Method A, but the fastest oxidative insertions proceeded using Method B. As shown below, both methods allowed a broad range of trappings with electrophiles, such as aryl or heteroaryl halides (*Negishi* cross-coupling),[37] allylic bromides (allylic substitutions)[119] and acid chlorides (*Negishi* acylation).[120]

Table 14: $InCl_3$-catalyzed, LiCl-mediated insertion of zinc powder into organic iodides and further trapping reactions with electrophiles.



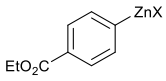
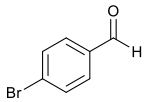
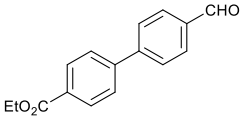
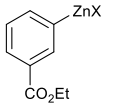
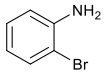
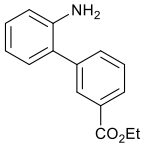
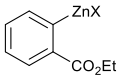
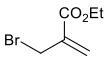
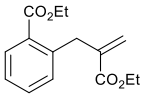
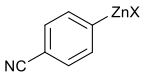
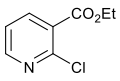
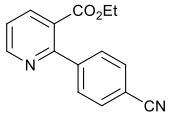
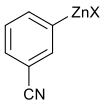
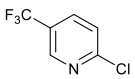
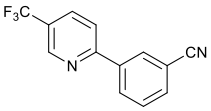
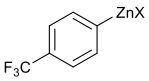
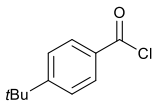
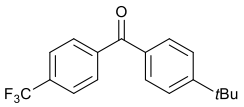
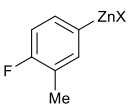
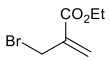
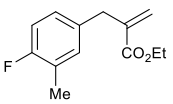
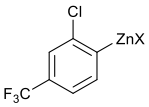
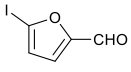
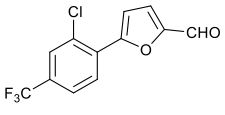
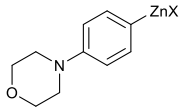
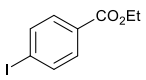
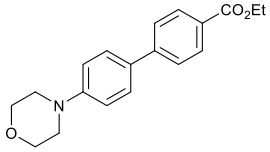
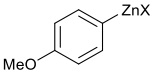
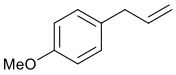
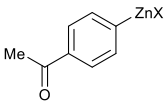
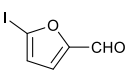
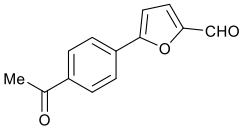
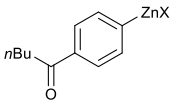
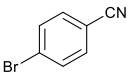
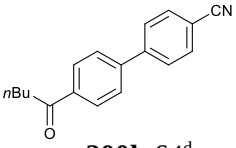
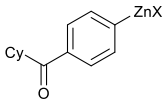
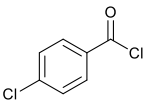
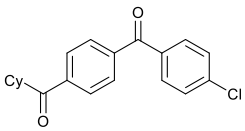
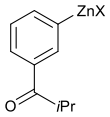
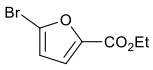
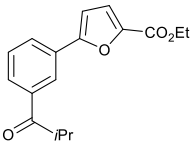
Entry	Arylzinc Reagent	Reaction Conditions[a,b]	Electrophile	Product, Yield (%)[c]
1	 **199a**	**A**: 50 °C; 2.0 h; 92% **B**: 50 °C; 0.25 h; 78%	 **201a**	 **200a**: 96[d]
2	 **199b**	**A**: 50 °C; 2.0 h; 90% **B**: 50 °C; 0.25 h; 78%	 **201b**	 **200b**: 97[d]
3	 **199c**	**A**: 25 °C; 0.25 h; 83% **B**: 25 °C; 0.25 h; 50%	 **201c**	 **200c**: 94[e]
4	 **199d**	**A**: 50 °C; 0.50 h; 95% **B**: 50 °C; 0.50 h; 60%	 **184g**	 **200d**: 94[d]
5	 **199e**	**A**: 50 °C; 0.50 h; 88% **B**: 50 °C; 0.50 h; 60%	 **184p**	 **200e**: 93[d]
6	 **199f**	**A**: 50 °C; 2.0 h; 80% **B**: 50 °C; 0.50 h; 68%	 **194b**	 **200f**: 85[f]
7	 **199g**	**A**: 50 °C; 4.0 h; 57% **B**: 50 °C; 0.50 h; 60%	 **201c**	 **200g**: 75e[e]
8	 **199h**	**A**: 25 °C; 0.25 h; 90% **B**: 25 °C; 0.25 h; 90%	 **201d**	 **200h**: 78[d]

Table 14: (continued).

Entry	Arylzinc Reagent	Reaction Conditions[a,b]	Electrophile	Product, Yield (%)[c]
9	 **199i**	**A**: 50 °C; 18 h; 93% **B**: 50 °C; 2.0 h; 50%	 **184c**	 **200i**: 88[d]
10	 **199j**	**A**: 50 °C; 6.0 h; 56% **B**: 50 °C; 3.0 h; 64%	 **201e**	 **200j**: 60[e]
11	 **199k**	**A**: 25 °C; 0.50 h; 45% **B**: 25 °C; 0.50 h; 62%	 **201d**	 **200k**: 87[d]
12	 **199l**	**A**: 25 °C; 0.25 h; 27% **B**: 25 °C; 0.25 h; 50%	 **184b**	 **200l**: 64[d]
13	 **199m**	**A**: 50 °C; 6.0 h; 62% **B**: 25 °C; 0.25 h; 50%	 **194a**	 **200m**: 77[f]
14	 **199n**	**A**: 25 °C; 0.50 h; 50% **B**: 25 °C; 0.50 h; 62%	 **184f**	 **200n**: 60[d]

[a] Reaction's completion was determined by GC-analysis of hydrolyzed aliquots; [b] Yield determined by iodometric titration; [c] Isolated yield; [d] $Pd(OAc)_2$ (4.0 mol%) and SPhos (8.0 mol%) were used; [e] CuCN·2LiCl (20 mol%) was used; [f] $[Pd(PPh_3)_4]$ (10 mol%) was used.

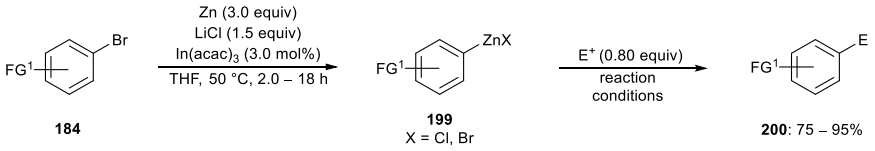
Thus, the treatment of ethyl 4-iodobenzoate (**184c**) with commercial zinc dust in the presence of $InCl_3$ (3.0 mol%) and LiCl (30 mol%) in THF led to the corresponding zinc reagent **199a** (X = Cl or I) within 2 h at 50 °C in 92% yield as indicated by iodometric titration (Method A). Alternatively, the same arylzinc species has been prepared in 15 min at 50 °C using a THF / DMPU 1:1 mixture in 78% yield (Method B). This trend in yield and reaction time difference between Methods A and B proved to be quite general. Trapping **199a** (obtained by Method B) with 4-bromobenzaldehyde (**201a**, 0.80 equiv) in the presence of $Pd(OAc)_2$ (4.0 mol%) and SPhos (8.0 mol%) provided the expected biphenyl derivative **200a** (25 °C, 2 h) in 96% yield (Table 14, entry 1). Similarly ethyl 3-iodobenzoate (**184k**) was converted

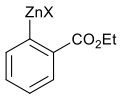
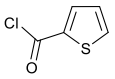
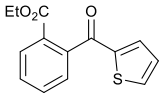
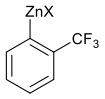
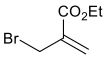
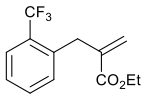
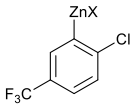
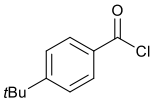
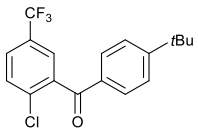
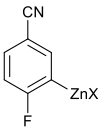
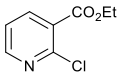
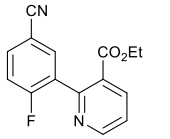
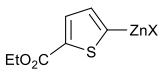
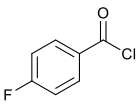
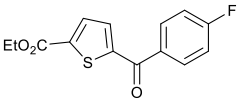
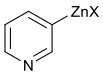
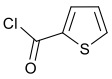
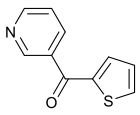
into the corresponding zinc reagent **199b** (Method A: 90% yield; Method B: 78% yield). Pd-catalyzed cross-coupling with 2-bromoaniline (**201b**; 0.80 equiv) gave the product **200b** in 97% yield. No protection of the free amino group was required (entry 2). The 2-carbethoxy-phenylzinc halide **199c** prepared in 83% yield according to Method A was allylated with the allylic bromide **201c** in the presence of CuCN·2LiCl (20 mol%) leading to the benzoate derivative **200c** in 94% yield. Cyano-substituted arylzinc species such as **199d** and **199e** were prepared in the same way in 88% and 95% yield (Method A). *Negishi* cross-coupling with 2-chloropyridines **184g** and **184p** furnished the pyridines **200d** and **200e** in 93% and 94% yield (entries 4 and 5). Various fluoro-substituted aryl iodides were converted to the zinc reagents **199f**–**h** in 57–90% yield (Method A) and trapped with different electrophiles leading to the products **200f**–**h** in 75–85% yield (entries 6–8). Interestingly, the acylation of **199f** with the acid chloride **194b** was best performed *via* a *Negishi* acylation using [$Pd(PPh_3)_4$] ((10 mol%), 50 °C, 18 h) leading to ketone **200f** in 85% yield (entry 6). Electron-donating substituted arylzinc halides such as **199i** and **199j** were prepared in the same way (Method A: 56% and 93% yield) and were arylated or allylated leading to the products **200i** and **200j** in 60% and 88% yield, respectively (entries 9 and 10). Remarkably, various iodoaryl ketones of type **186** including 4-iodoacetophenone (**186a**) led under these mild reaction conditions to the corresponding zinc reagents **199k–n** in 50–62% yield, using in this case Method B, and trapping with electrophiles afforded the polyfunctional ketones **200k–n** in 60–87% yield (entries 11–14).

In order to insert zinc into the less reactive aryl and heteroaryl bromides, a further optimization of the indium catalyst was performed. It was found that $In(acac)_3$ was a superior catalyst for such an insertion. Thus, the treatment of ethyl 2-bromobenzoate (**184t**) with zinc powder in the presence of $In(acac)_3$ (3.0 mol%) and LiCl (1.50 equiv) in THF led to the desired arylzinc reagent **199c** within 18 h at 50 °C in 70% yield. Subsequent *Negishi* acylation with 2-thiophenecarbonyl chloride (**194d**) gave the heteroaryl ketone **200o** in 86% yield (Table 15, entry 1). Using this $In(acac)_3$-promoted reaction procedure, several fluoro-substituted aryl bromides **184u**–**w** led to the corresponding functionalized arylzinc reagents **199o**–**q** within 2–6 h at 50 °C in 55–77% yield (entries 2–4). After further trapping reactions with an allylic bromide **201c**, 4-*tert*-butylbenzoyl chloride (**194b**) or ethyl 2-chloronicotinate (**184g**) the polyfunctionalized products **200p**–**r** were obtained in 75–92% yield (entries 2–4). Additionally, also heteroaryl bromides proved to be good substrates. Thus, ethyl 5-bromothiophene-2-carboxylate (**184x**) and 3-bromopyridine (**184y**) were converted to the heteroarylzinc reagents **199r** and **199s** within 2 h at 50 °C in 64–74% yield and underwent Pd-catalyzed acylations with acid chlorides **194c**,**d** leading to the desired ketones **200s** and **200t** in 82% and 95% yield (entries 5 and 6).

B. Results and Discussion

Table 15: $In(acac)_3$-catalyzed insertion of zinc powder to organic bromides and further trapping reactions with electrophiles.



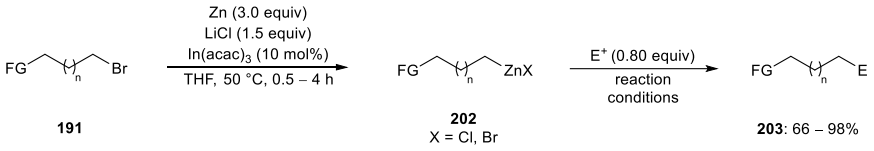
Entry	Arylzinc Reagent	Reaction Conditions[a,b]	Electrophile	Product, Yield (%)[c]
		50 °C; 18 h; 70%		
1	**199c**		**194d**	**200o**: 86[f]
		50 °C; 6.0 h; 55%		
2	**199o**		**201c**	**200p**: 75[e]
		50 °C; 2.0 h; 67%		
3	**199p**		**194b**	**200q**: 92[f]
		50 °C; 2.0 h; 77%		
4	**199q**		**184g**	**200r**: 83[d]
		50 °C; 2.0 h; 74%		
5	**199r**		**194c**	**200s**: 95[f]
		50 °C; 2.0 h; 64%		
6	**199s**		**194d**	**200t**: 82[f]

[a] Reaction's completion was determined by GC-analysis of hydrolyzed aliquots; [b] Yield determined by iodometric titration; [c] Isolated yield; [d] $Pd(OAc)_2$ (4.0 mol%) and SPhos (8.0 mol%) were used; [e] $CuCN{\cdot}2LiCl$ (20 mol%) was used; [f] $[Pd(PPh_3)_4]$ (10 mol%) was used.

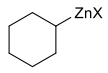
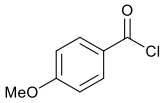
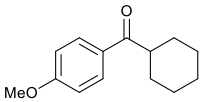
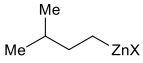
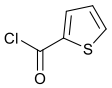
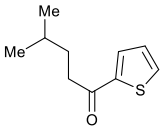
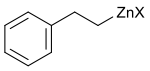
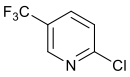
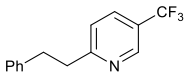
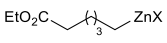
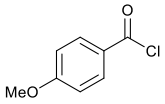
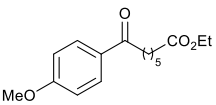
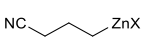
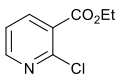
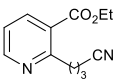
B. Results and Discussion

Finally, alkyl bromides also underwent such zinc insertions leading to the corresponding alkylzinc reagents using $In(acac)_3$ (10 mol%) and LiCl (1.50 equiv) within 0.5–4 h at 50 °C (Table 16). Thus, bromocyclohexane (**191a**) was converted to the zinc reagent **202a** within 3 h at 50 °C in 72% yield and subsequent *Negishi* acylation with 4-methoxybenzoyl chloride (**194e**) gave the ketone **203a** in 86% yield (Table 16, entry 1). Similarly, the zinc insertion into 1-bromo-3-methylbutane (**191b**) gave the alkylzinc reagent **202b** within 4 h in 73% yield. A Pd-catalyzed acylation with **194d** afforded the thiophene **203b** in 66% yield (entry 2). Also, alkyl bromide **191d** was converted to the corresponding alkylzinc species **202c** within 1 h at 50 °C in 70% yield. After further cross-coupling with the 2-chloro-substituted pyridine **184p** the product **203c** was obtained in 90% yield (entries 3).

Table 16: $In(acac)_3$-catalyzed insertion of zinc powder to alkyl bromides and further trapping reactions with electrophiles.



191 | **202** X = Cl, Br | **203**: 66 – 98%

Entry	Alkylzinc Reagent	Reaction Conditions[a,b]	Electrophile	Product, Yield (%)[c]
1	 **202a**	50 °C; 3.0 h; 72%	 **194e**	 **203a**: 86[e]
2	 **202b**	50 °C; 4.0 h; 73%	 **194d**	 **203b**: 66[e]
3	 **202c**	50 °C; 1.0 h; 70%	 **184p**	 **203c**: 90[d]
4	 **202d**	50 °C; 3.0 h; 68%	 **194e**	 **203d**: 90[e]
5	 **202e**	50 °C; 0.50 h; 79%	 **184g**	 **203e**: 98[d]

[a] Reaction's completion was determined by GC-analysis of hydrolyzed aliquots; [b] Yield determined by iodometric titration; [c] Isolated yield; [d] $Pd(OAc)_2$ (4.0 mol%) and SPhos (8.0 mol%) were used; [e] $[Pd(PPh_3)_4]$ (10 mol%) was used.

Finally, more functionalized alkyl bromides **191e** and **191f** underwent those kind of zinc insertions leading to the corresponding alkylzincs **202d** and **202e** in 68% and 79% yield. Subsequent trapping reactions with an acid chloride **194e** and a pyridine derivative **184g** resulted in the desired products **203d** **203e** in 90% and 98% yield, respectively (entries 4 and 5).

In summary, a catalytic system involving $InCl_3$ (3.0 mol%) and LiCl (30 mol%) allowed an efficient zinc insertion to a range of functionalized aryl iodides in THF at 50 °C in up to 95% yield. The use of THF / DMPU 1:1 as solvent mixture enabled the preparation of various keto-substituted arylzinc halides in 50–62% yield. A further optimization of the indium catalyst showed that $In(acac)_3$ (3.0–10 mol%) is a powerful catalyst for an efficient insertion into aryl and heteroaryl bromides, and the corresponding zinc reagents could be obtained in 70–80% yield. This catalyst could also be used to prepare functionalized primary and secondary alkylzinc derivatives from the corresponding alkyl bromides in up to 79%.

6. Preparation of Functionalized Diaryl- and Diheteroaryllanthanum Reagents by Fast Halogen-Lanthanum Exchange

6.1. Introduction

The halogen-lithium (Hal/Li) exchange reaction is one of the most powerful methods for preparing organolithium reagents.[29] However, because of the low tolerance of aryllithium reagents towards functional groups such as nitriles or esters, there is a need for other halogen-metal exchange processes. In this context, the Hal/Mg-exchange has found useful applications for the preparation of polyfunctional magnesium compounds.[30] In addition, I/Cu-[131] and I/Zn-exchange[64,66] processes have been reported. However, all of these exchange reactions are relatively slow compared to the Hal/Li-exchange. No other halogen-metal exchange reactions have been reported yet, but La^{III} organometallics could be good candidates for a halogen-metal exchange as the electronegativity of lanthanum (1.1) is very close to that of lithium (0.98), and therefore C–La bonds are expected to be highly reactive. Organolanthanide(III) reagents have found many applications in organic synthesis.[95] Of special interest is the strong Lewis acidity of La^{III} salts, leading to an exceptional reactivity towards carbonyl compounds.[97] These organometallic species are usually prepared by transmetalation[98] from organolithium derivatives or by directed metalation.[107] In the following, a new and very fast halogen-lanthanum exchange process is reported that enables the preparation of functionalized diaryl and diheteroaryllanthanum derivatives, which can then be trapped with a variety of electrophiles. As part of this study, an especially attractive acylation reaction using *N*,*N*-dimethylamides to generate ketones is described.[132]

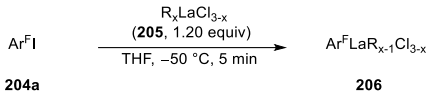
6.2. Preparation of Functionalized Diaryl- and Diheteroaryl(methyl)lanthanum Reagents via Halogen-Lanthanum Exchange Reactions

In preliminary experiments, the I/La-exchange with an electron-poor aryl iodide, namely 3,4-difluoro-1-iodobenzene (**204a**), and various alkyllanthanum compounds of type **205** was examined (Table 17). The alkyllanthanum reagents **205** were prepared from THF-soluble $LaCl_3 \cdot 2LiCl$[103] and organolithium reagents such as *t*BuLi, *s*BuLi, *n*BuLi, or MeLi. Whereas the *t*BuLi and *s*BuLi derived lanthanum reagents gave unsatisfactory results, combinations of *n*-butyl, methyl, and chloride residues provided the most promising results. Whereas nBuLaCl$_2$ (**205a**) was unreactive towards **204a**, nBu$_2$LaCl (**205b**) and nBu$_3$La (**205c**) exchanged one butyl group at −50 °C in THF within 5 min to provide the corresponding aryllanthanum species of type **206**, as indicated by protonation and iodolysis of reaction aliquots (entries 1–3). Similarly, Me$_3$La (**205d**) led to fast exchange, but again of only one methyl group (entry 4).

[131] X. Yang, T. Rotter, C. Piazza, P. Knochel, *Org. Lett.* **2003**, *5*, 1229.
[132] S. Collins, Y. Hong, *Tetrahedron Lett.* **1987**, *28*, 4391.

B. Results and Discussion

Table 17: Evaluation of alkyllanthanum(III) species as exchange reagents.

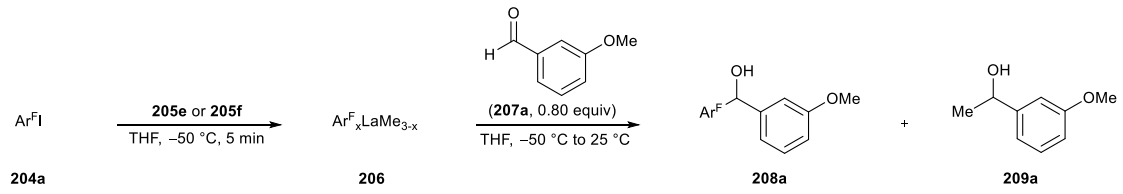


Entry	Exchange Reagent **205**	Product **206**	Conversion of **204a** (%)[a]
1	*n*BuLaCl$_2$·3LiCl (**205a**)	Ar^{F}LaCl$_2$ (**206a**)	0
2	*n*Bu$_2$LaCl·4LiCl (**205b**)	*n*BuAr^{F}LaCl (**206b**)	68
3	*n*Bu$_3$La·5LiCl (**205c**)	*n*Bu$_2$Ar^{F}La (**206c**)	100
4	Me$_3$La·5LiCl (**205d**)	Ar^{F}LaMe$_2$ (**206d**)	100

[a] Conversion of **204a** determined by GC-analysis; Ar^F = 3,4-difluorophenyl.

This partial transfer of alkyl groups, with unsatisfactory atom economy,[20] led us to examine mixed alkyllanthanum reagents prepared from various amounts of LaCl$_3$·2LiCl, MeLi, and *n*BuLi (Table 18). Thus, the use of *n*BuLaMe$_2$ (**205e**) led to a selective exchange of the butyl group, and quenching of the resulting aryllanthanum species **206e** with 3-methoxybenzaldehyde (**207a**) gave the desired alcohol **208a** in 72% yield (determined by GC-analysis). Unfortunately, alcohol **209a**, resulting from the competitive transfer of a methyl group present in **206e**, was also formed in 28% GC yield (entry 1). This side reaction was mostly avoided by switching to the mixed lanthanum reagent *n*Bu$_2$LaMe (**205f**). Addition of **204a** (1.0 equiv) to **205f** (0.70 equiv) led to the fast formation of **206f** (Ar$^F{}_2$LaMe; Ar^F = 3,4-difluorophenyl). Treatment of **206f** with **207a** (0.80 equiv) gave alcohol **208a** in 94% GC yield (63% isolated yield) and alcohol **209a** in less than 6% GC yield (entry 2). These experiments showed that *n*Bu$_2$LaMe (**205f**) is a promising exchange reagent in which both butyl groups undergo I/La-exchange whereas the methyl group plays the role of a non-transferable moiety when an electrophile is added.

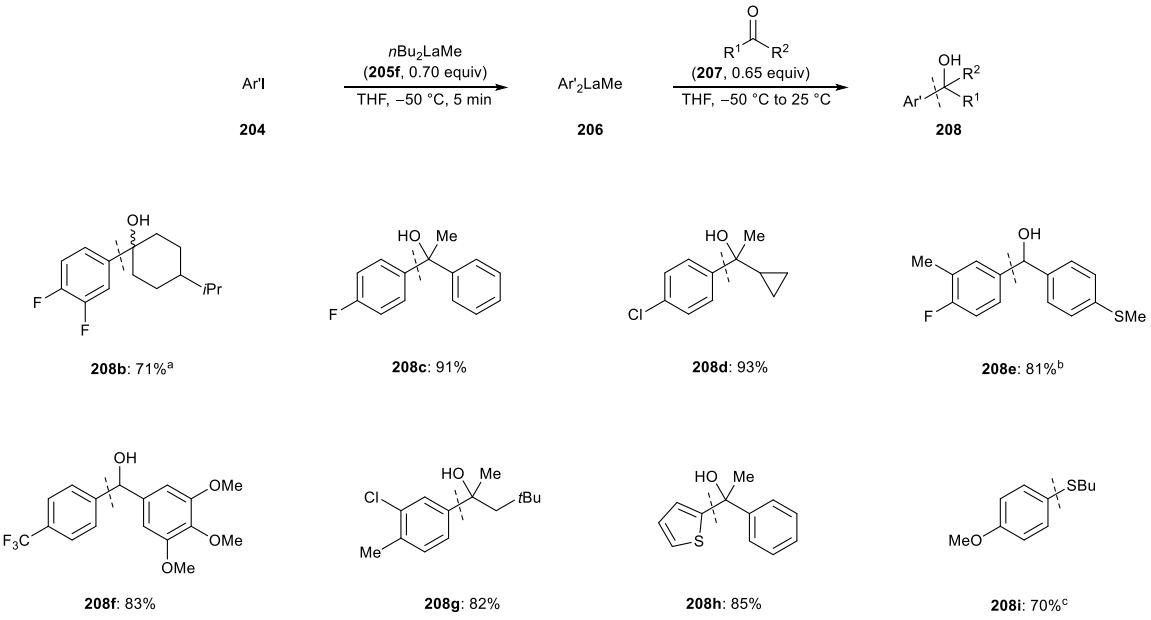
Table 18: Mixed alkyllanthanum(III) reagents and their reactivity towards **204a**.



Entry	Exchange Reagent **205**	Product **206**	Yield of **208a** (%)[a]	Yield of **209a** (%)[a]
1	*n*BuLaMe$_2$·5LiCl (**205e**, 1.2 equiv)	Ar^{F}LaMe$_2$ (**206e**)	72	28
2	*n*Bu$_2$LaMe·5LiCl (**205f**, 0.70 equiv)	Ar$^F{}_2$LaMe (**206f**)	94 (63)[b]	6

[a] The ratio of product **208a** and side product **209a** was determined by GC-analysis; [b] Yield of isolated product; Ar^F = 3,4-difluorophenyl.

Next, several aryl iodides of type **204** (1.0 equiv) were treated with **205f** (0.70 equiv) in THF at −50 °C for 5 min, producing the diaryl(methyl)lanthanum species **206** in yields of about 70–80% as shown by GC-analysis of reaction aliquots. Their trapping with a range of aldehydes and ketones of type **207** (0.65 equiv) led to secondary and tertiary alcohols **208b**–**h** in 70–93% yield. In addition, trapping with Bu_2S_2 at −50 °C provided the thioether **208i** in 70% yield (Scheme 52). In all of these reactions, the unwanted methyl transfer products of type **209** were only detected in trace amounts.

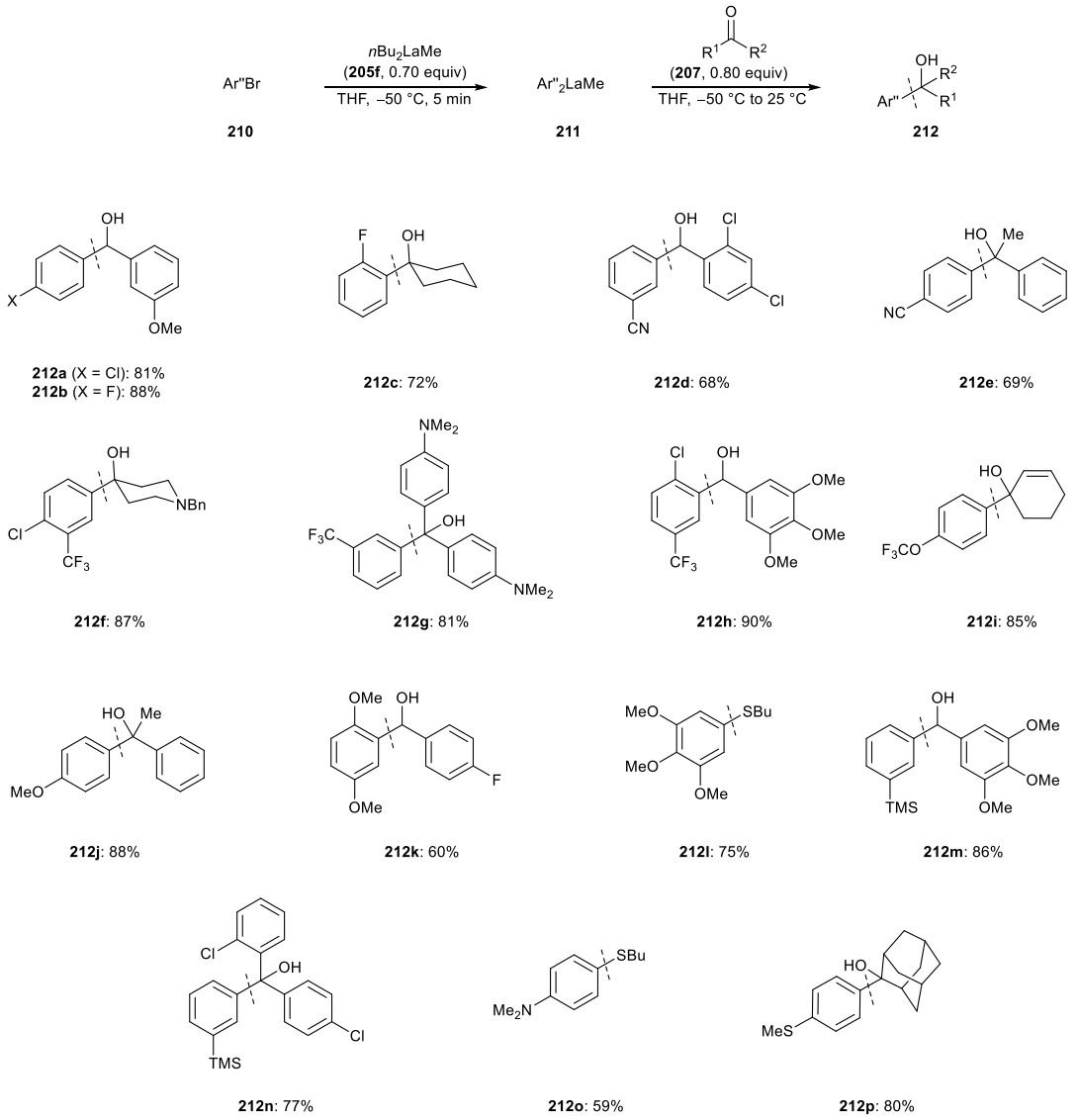


Scheme 52: I/La-exchange reactions of aryl iodides **204** with exchange reagent **205f** and subsequent trapping reactions with selected electrophiles: [a] dr = 4:6, 0.50 equiv of ketone were used; [b] 0.80 equiv of aldehyde were used; [c] 0.65 equiv of Bu_2S_2 were used.

These first promising results could be extended to the more important Br/La-exchange process because aryl bromides of type **210** are commercially available and less expensive than aryl iodides. Using the same exchange reagent **205f**, lanthanum derivatives of type **211** were obtained in about 90% yield. The higher reactivity of the aryl bromides compared to aryl iodides was ascribed to the detrimental presence of butyl iodide generated during the I/La-exchange.

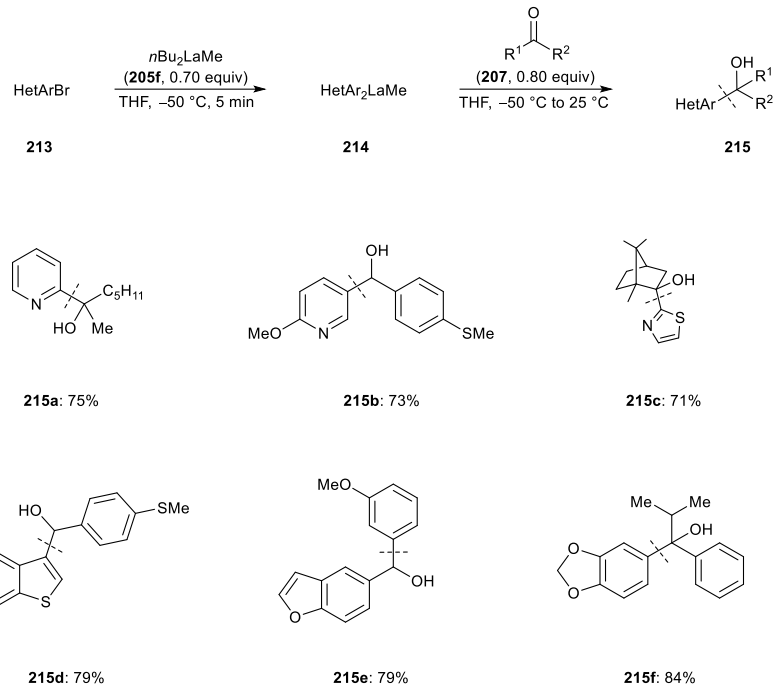
Functionalized aryl bromides bearing Cl, F, CN, CF_3, OCF_3, OMe, $SiMe_3$, and SMe substituents underwent this Br/La-exchange to afford diaryl(methyl)lanthanum reagents of type **211**. Trapping with aldehydes, ketones of type **207**, or a disulfide (0.80 equiv) gave products of type **212** in 57–90% yield (Scheme 53). Whereas 1-bromo-2-fluorobenzene (**210c**) is decomposed in the presence of *n*BuLi at −50 °C, the reaction of **210c** with *n*Bu_2LaMe (**205f**) proceeded smoothly, providing the tertiary alcohol **212c** in 72% yield upon cyclohexanone addition. Similarly, 3-bromo- and 4-bromobenzonitrile (**210d** and **210e**) decompose in the presence of *n*BuLi whereas they undergo clean Br/La-exchange with *n*Bu_2LaMe (**205f**), furnishing, after quenching with an aldehyde or a ketone, the alcohols **212d** and **212e** in 68% and 69% yield, respectively. Furthermore, the trifluoromethyl-substituted lanthanum reagents

211f–**h** were trapped with ketones and an aldehyde to give the corresponding products **212f**–**h** in 81–90% yield. The reaction of an enone with aryllanthanum reagent **211i** selectively provided the 1,2-addition product **212i** in 85% yield. Additionally, electron-rich aryl bromides **210j**–**l** also underwent the exchange at −50 °C within 5 min, and the resulting aryllanthanum reagents **211j**–**l** were trapped with acetophenone, 4-fluorobenzaldehyde, and Bu_2S_2, yielding **212j**–**l** in 75–88% yield. The silyl-substituted diaryllanthanum reagents **211m** and **211n** underwent an addition to 3,4,5-trimethoxybenzaldehyde (**207c**) and 2,4′-dichlorobenzophenone (**207b**) to give the alcohols **212m** and **212n** in 77–86% yield. The amino-substituted aryllanthanum reagent **211o** reacted with Bu_2S_2 to afford the thioether **212o** in 59% yield. Finally, a thiomethyl-substituted lanthanum reagent **211p** was prepared and added to a bulky ketone to generate the tertiary alcohol **212p** in 80% yield.



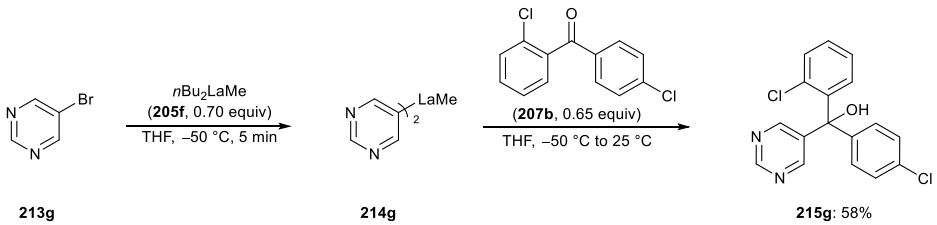
Scheme 53: Br/La-exchange processes of aryl bromides **210** with exchange reagent **205f** and subsequent trapping reactions with electrophiles.

The Br/La-exchange was also extended to a range of heterocyclic bromides of type **213**. Hence, bromopyridines **213a** and **213b** were converted into the corresponding diheteroaryl(methyl)lanthanum reagents **214a** and **214b**, and further additions to a ketone or aldehyde of type **207** gave alcohols **215a** and **215b** in 73% and 75% yield. Similarly, sulfur- and oxygen-containing heterocycles **213c**–**f** underwent the Br/La-exchange, and the resulting species added to selected ketones and aldehydes affording the desired products **215c-f** in 71–84% yield (Scheme 54).



Scheme 54: Br/La-exchange of heteroaryl bromides of type **213** with **205f** and subsequent trapping reactions.

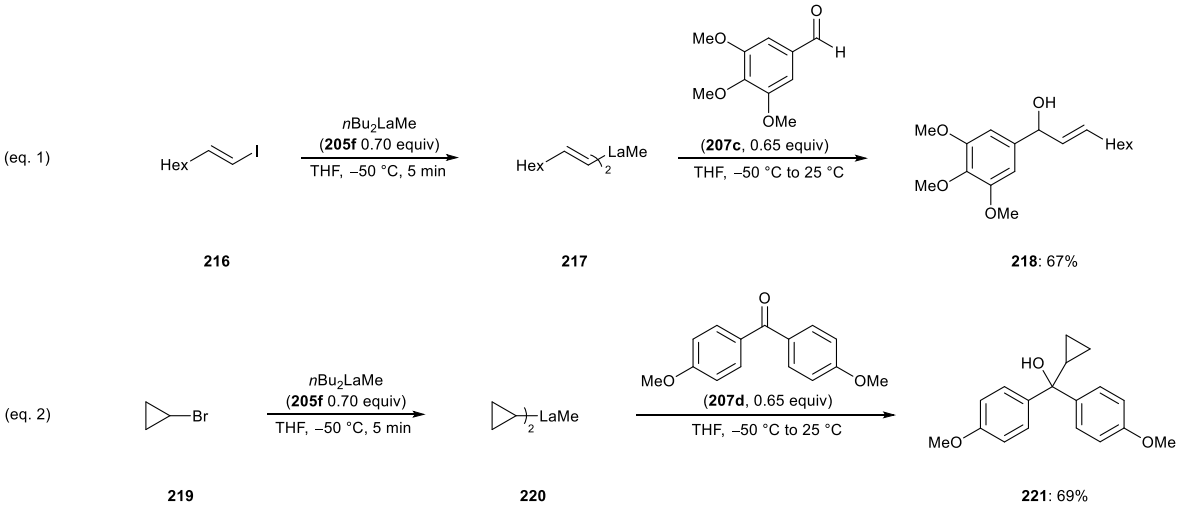
Interestingly, 5-bromopyrimidine (**213g**) was converted into lanthanum reagent **214g** and its addition to ketone **207b** furnished the fungicide fenarimol[133] (**215g**) in 58% yield (Scheme 55).



Scheme 55: Synthesis of fenarimol (**215g**).

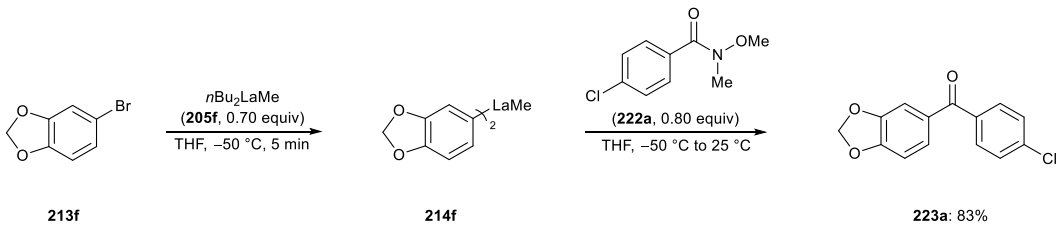
[133] J. D. Davenport, R. E. Hackler, H. M. Taylor, GB1218623, **1971**.

This halogen-lanthanum exchange was then further extended to alkenyl and cyclopropyl halides using *n*Bu$_2$LaMe (**205f**) as exchange reagent. The exchange on (*E*)-1-iodooctene (**216**) with **205f** (0.70 equiv) at −50 °C produced the alkenyllanthanum derivative **217** within 5 min. Subsequent trapping with 3,4,5-trimethoxybenzaldehyde (**207c**) led to the desired allylic alcohol **218** with retention of configuration. Additionally, cyclopropyl bromide (**219**) underwent a similar exchange with **205f** (0.70 equiv), furnishing cyclopropyl derivative **220**. Further reaction with 4,4′-dimethoxybenzophenone (**207d**) provided the tertiary alcohol **221** in 69% yield (Scheme 56).



Scheme 56: Halogen-lanthanum exchange of (*E*)-1-iodooctene (**216**) and cyclopropyl bromide (**219**) using **205f** and subsequent trapping reactions with **207c** and **207d**.

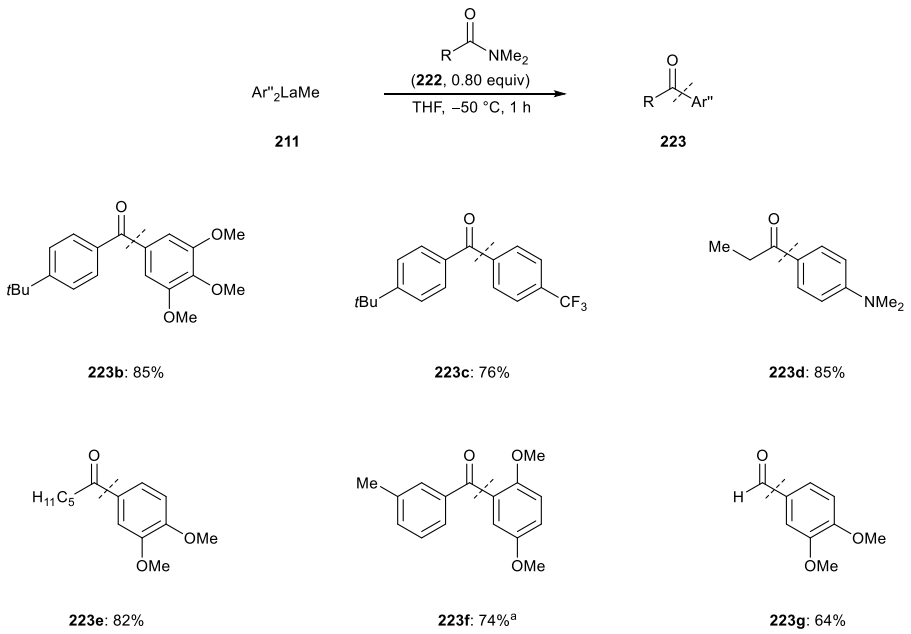
Remarkably, the lanthanum derivatives of type **211** and **214** underwent useful acylations with several amides **222**, leading selectively to ketones **223**. In a preliminary experiment, the Weinreb amide **222a** was used at −50 °C and the expected ketone **223a** was obtained in 83% yield (Scheme 57).



Scheme 57: Acylation reaction of diheteroaryllanthanum reagent **214f** using the Weinreb amide **222a**.

However, we soon realized that regular *N*,*N*-dimethylamides **222** could be employed to achieve the same transformation (Scheme 58). Thus, the reaction of the electron-rich diaryllanthanum reagent **211l** with 4-(*tert*-butyl)-*N*,*N*-dimethylbenzamide provided diaryl ketone **223b** in 85% yield. Similarly, the electron-deficient diaryllanthanum species **211q** reacted with the same amide to give ketone **223c** in 76% yield. In addition, alkyl-substituted *N*,*N*-dimethylamides underwent such efficient acylations with

the electron-donating lanthanum reagents **211o** and **211r** affording the desired ketones **223d** and **223e** in 85% and 82% yield, respectively. Based on this general procedure, acylations using *N*,*N*-diethyl-*m*-toluamide or *N*,*N*-dimethylformamide and dimethoxylanthanum reagents proceeded well, leading to the products **223f** and **223g** in 64–74% yield.



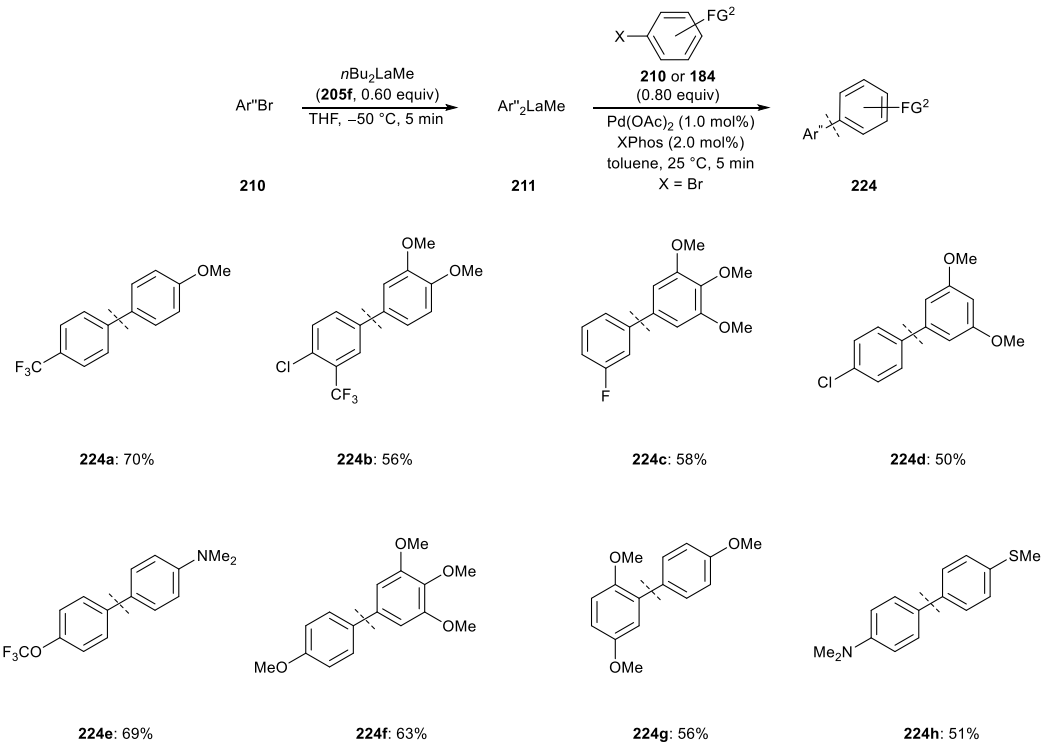
Scheme 58: Acylation reactions of aryllanthanum reagents **211** with amides of type **222**. [a] Prepared from the corresponding *N*,*N*-diethylamide.

In summary, a new alkyllanthanum reagent *n*Bu$_2$LaMe for fast and convenient halogen-lanthanum exchange reactions was developed. Starting from a variety of aryl and heteroaryl iodides or bromides, a range of funtionalized diaryl- and diheteroaryl(methyl)lanthanum derivatives were obtained at −50 °C within 5 min. Their strong oxophilicity enables efficient additions to various ketones, aldehydes and amides. Finally, this expedient halogen-lanthanum exchange could also be used for convenient syntheses of fenarimol (**215g**) and an analogue of penfluridol, **212f**.[134]

[134] P. A. Janssen, C. J. Niemegeers, K. H. Schellekens, F. M. Lenaerts, F. J. Verbruggen, J. M. Van Nueten, W. K. Schaper, *Eur. J. Pharmacol.* **1970**, *11*, 139.

Besides trapping reactions with ketones, aldehydes and amides, another approach towards transition-metal-catalyzed cross-couplings was developed. Although *Kumada-Corriu* (Mg),[36] *Negishi* (Zn),[37] *Stille* (Sn)[38] and *Suzuki-Miyaura* (B)[39] couplings are already known and well-established using typical Pd- or Ni-catalysts, the direct application of organolanthanides as coupling partner has not been reported yet. Recently, *Feringa* and co-workers also demonstrated the feasibility of a direct Pd- or Ni-catalyzed cross-coupling of highly reactive organolithium compounds.[40]

Due to their similar reactivity compared to organolithium reagents, it was envisaged that the cross-coupling of organolanthanum compounds will be challenging since the competitive formation of homocoupling products and fast halogen-lanthanum exchange on the electrophile need to be avoided. Since no reaction took place at low temperatures, the cross-coupling reactions were performed at room temperature. Additionally, very fast cross-coupling rates were necessary to achieve the desired products, because the prior generated diaryllanthanum derivatives were not long term stable at room temperature and decomposed within a few minutes. After a rapid screening of different catalysts and reaction conditions, it was found that cross-coupling reactions of diaryl(methyl)lanthanum reagents of type **211** can be performed with aryl bromides of type **184** and **210** using similar reaction conditions compared to *Feringa's* procedure. The catalytic system $Pd(OAc)_2$ (1.0 mol%) and XPhos (2.0 mol%)[135] proved to be the best performing one and toluene was used as solvent. Using this catalytic system a range of Pd-catalyzed cross-couplings were performed and the desired products of type **224** could be obtained in 50–70% yield (Scheme 59).



Scheme 59: Pd-catalyzed cross-coupling reactions of diaryllanthanum reagents of type **211** with aryl bromides **184** or **210**.

[135] J. Yin, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 6043.

Thus, the two CF_3-substituted diaryllanthanum derivatives **211f** and **211q** underwent efficient couplings with 4-bromoanisole and 4-bromoveratrole leading to the functionalized biphenyl compounds **224a** and **224b** within 5 min in 70% and 56%, respectively. Similarly, halogenated diaryllanthanum reagents **211a** and **211s** reacted with selected electrophiles 5-bromo-1,2,3-trimethoxybenzene and 1-bromo-3,5-dimethoxybenzene resulting in the desired products **224c** and **224d** in 50% and 58% yield. Furthermore, the reactions of more electron-rich diaryllanthanum reagents **211i–k** with aryl bromides succeeded under the above mentioned conditions affording the expected arenes **224e–g** in 58–69% yield. Finally, also the amino-substituted lanthanum reagent **211o** reacted in such a Pd-catalyzed cross-coupling with a sulfur-substituted aryl bromide leading product **224h** in 51% yield.

7. Preparation of Functionalized Triaryl- and Triheteroaryllanthanum Reagents by a Halogen-Lanthanum Exchange using Ph_3La as Exchange Reagent

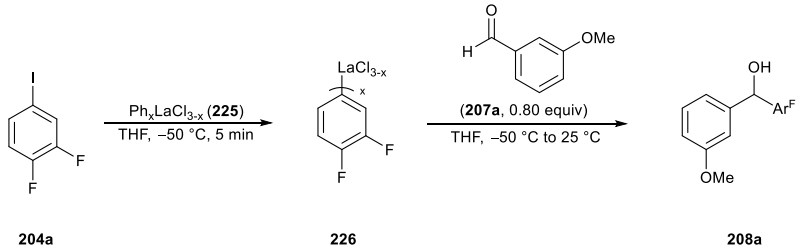
7.1. Introduction

The prior reported alkyllanthanum reagent *n*Bu_2LaMe (**205f**) gives access to a straightforward method to prepare functionalized diaryl- and diheteroaryllanthanum derivatives *via* a halogen-lanthanum exchange. This mixed alkyl species **205f** allows a fast and convenient halogen-lanthanum exchange on aryl and heteroaryl halides leading to the corresponding diaryl- or diheteroaryl(methyl)lanthanum reagents, which then undergo efficient trapping reactions with a variety of carbonyl compounds and amides. Nevertheless, *n*Bu_2LaMe (**205f**) needs to be freshly prepared at −30 °C, starting from the corresponding alkyllithium reagents and $LaCl_3 \cdot 2LiCl$. This reagent **205f** is not long-term stable and exchanges only its two butyl residues. Additionally, it fails in case of more sensitive substrates such as esters and selected heterocycles. In the following, a new and more practical exchange reagent Ph_3La (**225c**) with fine-tuned reactivity is described.

7.2. Preparation of Functionalized Triaryl- and Triheteroaryllanthanum Reagents using Ph_3La

In preliminary studies, it was found that aryl-derived lanthanum reagents can be used as exchange reagents. In a first experiment, 1,2-difluoro-4-iodobenzene (**204a**) was treated with various lanthanum reagents of type **225**. $PhLaCl_2$ (**225a**, 1.2 equiv) efficiently underwent such an exchange reaction with **204a** at −50 °C within 5 min, generating the corresponding Ar^FLaCl_2 (**226a**; Ar^F = 3,4-difluorophenyl) in 90% GC yield (Table 19, entry 1). Subsequent trapping with 3-methoxybenzaldehyde (**207a**, 0.80 equiv) led to the desired alcohol **208a** in 68% yield. Similarly, Ph_2LaCl (**225b**, 0.60 equiv) was able to exchange its two phenyl residues giving $Ar^F{}_2LaCl$ (**226b**), and the subsequent reaction with **207a** resulted in 83% yield of **208a** (entry 2). More interestingly, also Ph_3La (**225c**, 0.40 equiv) was reactive enough to exchange all three phenyl groups, leading to a triaryllanthanum derivative $Ar^F{}_3La$ (**226c**) in 95% GC yield, which then reacted with **207a** to produce the secondary alcohol **208a** in 81% isolated yield (entry 3).

Table 19: I/La-exchange reaction using phenyl-derived exchange reagents of type **225**.

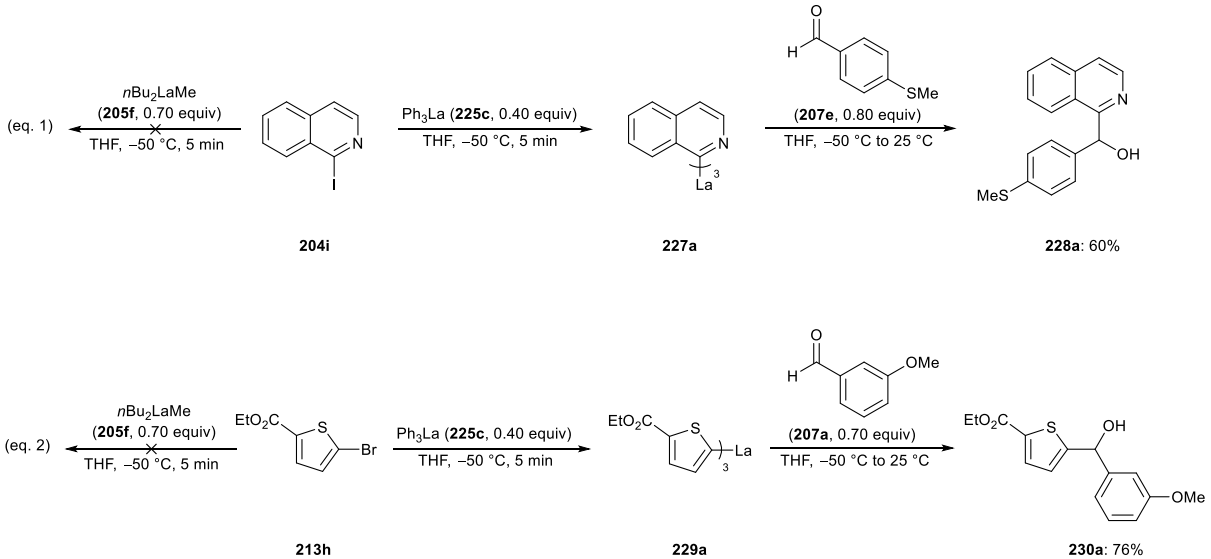


204a **226** **208a**

Entry	Exchange Reagent **225**	Amount of **225** (equiv)	Conversion of **204a** (%)[a]	Yield of **208a** (%)[b]
1	$PhLaCl_2 \cdot 3LiCl$ (**225a**)	1.2	100	68
2	$Ph_2LaCl \cdot 4LiCl$ (**225b**)	0.60	100	83
3	$Ph_3La \cdot 5LiCl$ (**225c**)	0.40	100	81

[a] Conversion of the aryl iodide **204a** determined by GC-analysis using $C_{14}H_{30}$ as internal standard; [b] Isolated yield; Ar^F = 3,4-difluorophenyl.

Moreover, it was found that several aryl or heteroaryl halides, which decomposed under the previous conditions using *n*Bu_2LaMe (**205f**), can now be converted to the desired triaryllanthanum derivatives. Whereas performing an exchange on 1-iodoisoquinoline (**204i**) with *n*Bu_2LaMe (**205f**) resulted in degradation, using Ph_3La (**225c**) the reaction proceeded smoothly at −50 °C within 5 min providing the triheteroaryllanthanum species **227a**, and subsequent trapping with aldehyde **207e** led to the desired alcohol **228a** in 60% yield (Scheme 60, eq. 1). Remarkably, even an ester moiety can be tolerated under those new conditions. Ethyl 5-bromothiophene-2-carboxylate (**213h**) was thus converted into the corresponding triheteroaryllanthanum derivative **229a** and reacted with **207a** yielding 76% of the secondary alcohol **230a** (Scheme 60, eq. 2).

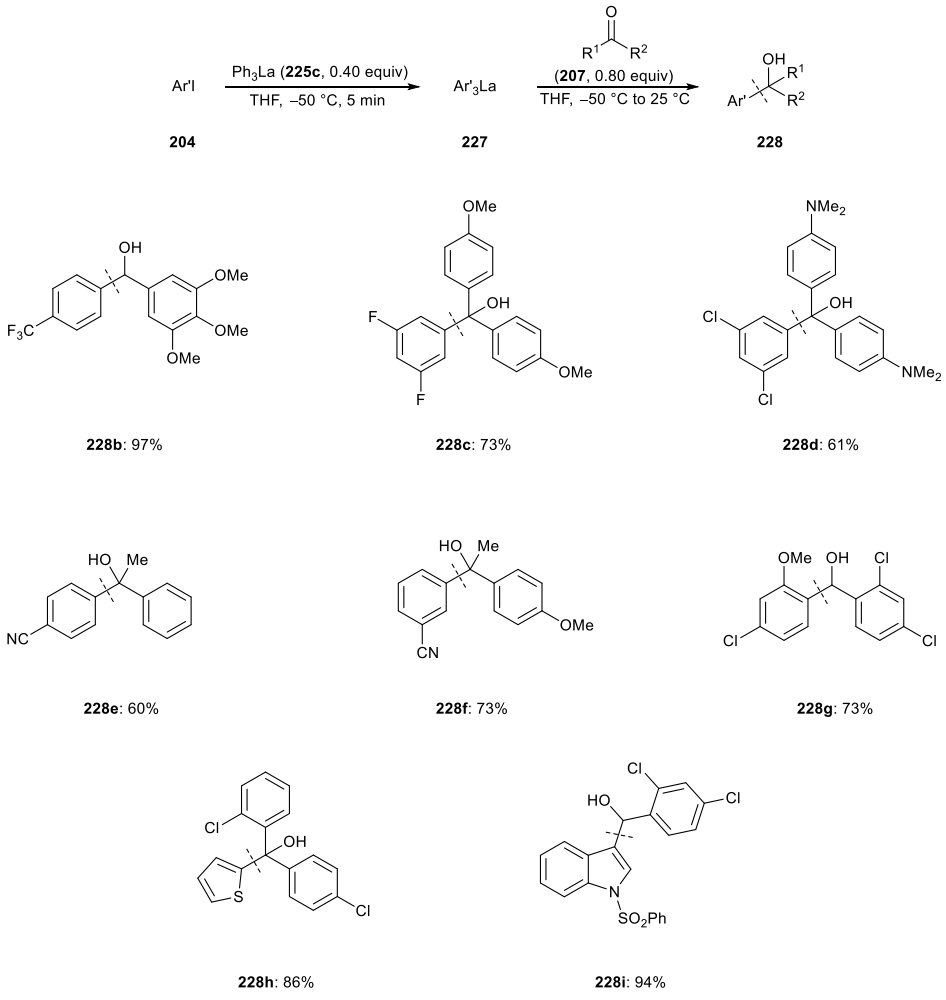


204i **227a** **228a**: 60%

213h **229a** **230a**: 76%

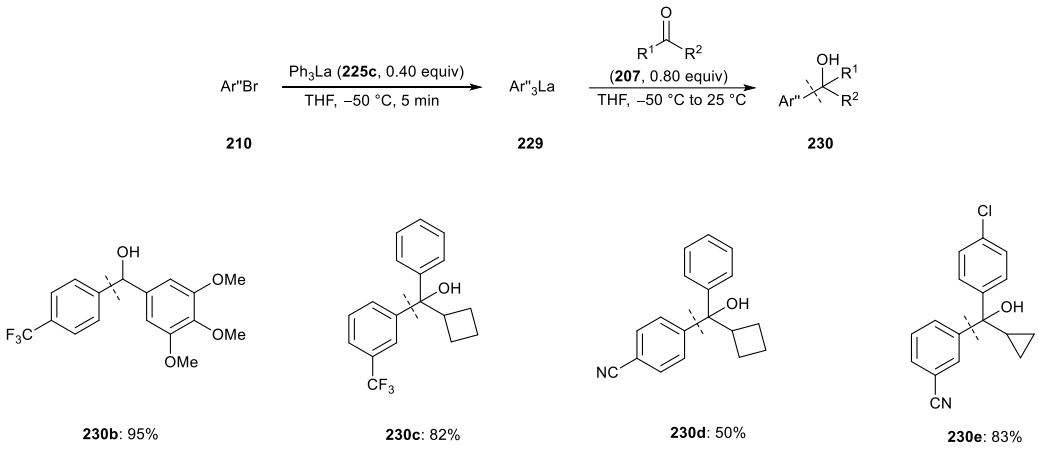
Scheme 60: Halogen-lanthanum exchanges using Ph_3La (**225c**) on 1-iodoisoquinoline (**204i**) and ethyl 5-bromo-thiophene-2-carboxylate (**213h**).

The scope of Ph_3La (**225c**) appeared to be quite promising. Thus, 4-iodobenzotrifluoride (1.0 equiv) underwent a fast exchange using Ph_3La (**225c**, 0.40 equiv) leading to the 4-CF_3-substituted triaryllanthanum reagent **227b**, and further reaction with 3,4,5-trimethoxybenzaldehyde (**207c**) led to the secondary alcohol **228b** in 97% yield. Similarly, two 3,5-dihalogenated aryl iodides **204j** and **204k** could be used for the same transformation, and subsequent trappings of **227c** and **227d** with bulky benzophenone derivatives resulted in the desired tertiary alcohols **228c** and **228d** in 73% and 61%, respectively. Additionally, also aryl iodides bearing sensitive nitrile moieties were compatible with these reaction conditions leading to the corresponding triaryllanthanum species **227e** and **227f**, and further addition to two different ketones gave the alcohols **228e** and **228f** in 60% and 74% yield. Even an electron-rich aryl iodide **204n** could be converted into the expected triaryllanthanum reagent **227g** by using Ph_3La (**225c**, 0.40 equiv) and was trapped with 2,4-dichlorobenzaldehyde (**207f**) to produce alcohol **228g** in 73% yield. Finally, 2-iodothiophene (**204e**) and a 3-iodoindole derivative **204o** underwent such exchanges, and the related lanthanum species **227h** and **227i** added to carbonyl compounds resulting in the alcohols **228h** and **228i** in 86% and 94% yield (Scheme 61).



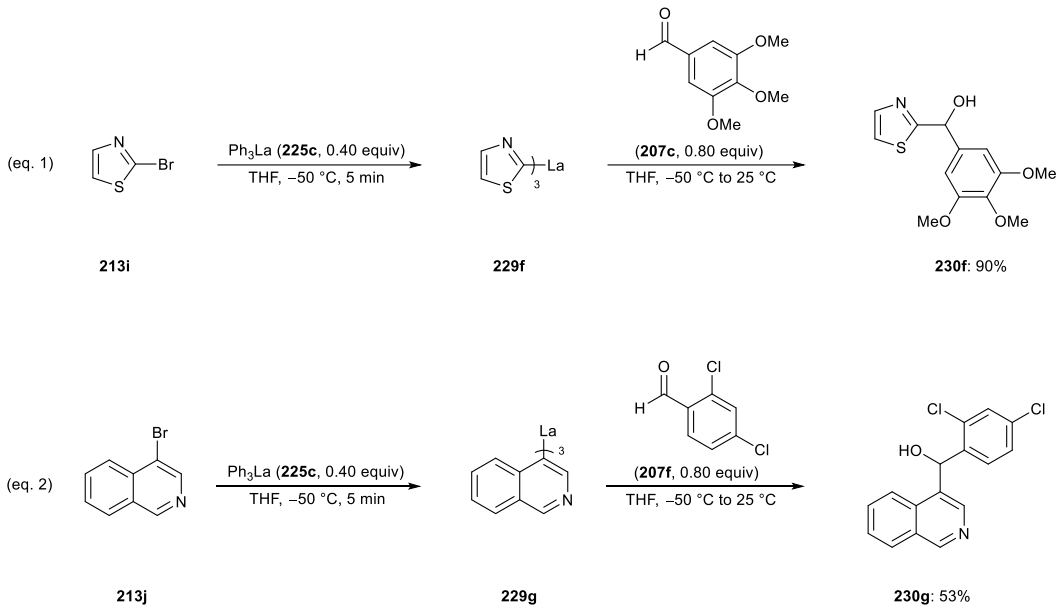
Scheme 61: I/La-exchange reactions of functionalized aryl iodides of type **204** using Ph_3La (**225c**).

This new exchange reagent Ph_3La (**225c**) was also suitable for performing the exchange on aryl bromides of type **210**. Thus, also the exchange using 4-bromobenzotrifluoride (1.0 equiv) and **225c** (0.40 equiv) succeeded at −50 °C within 5 min, affording the expected triaryllanthanum reagent **229b**, and subsequent trapping with 3,4,5-trimethoxybenzaldehyde (**207c**, 0.80 equiv) gave the desired alcohol **230b** in 95% yield. Similarly, the 3-CF_3-substituted aryllanthanum reagent **229c** could be prepared, and further addition to cyclobutyl phenyl ketone (**207g**) led to the tertiary alcohol **230c** in 82% yield. Furthermore, cyano-substituted aryl bromides underwent this exchange resulting in the corresponding triaryllanthanum reagents **229d** and **229e** and trapping reactions with two different ketones provided the expected alcohols **230d** and **230e** in 50% and 83% yield (Scheme 62).



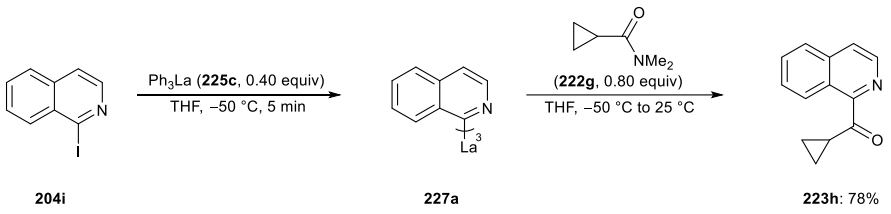
Scheme 62: Br/La-exchange of selected aryl bromides of type **210** using Ph_3La (**225c**).

In addition, the scope of exchange reagent **225c** was extended to heteroaryl bromides. Two selected examples involving 2-bromothiazole (**213i**) and 4-bromoisoquinoline (**213j**) reacted under the same conditions with Ph_3La (**225c**) at −50 °C within 5 min leading to the triheteroaryllanthanum derivatives **229f** and **229g**, which then further added to the aldehydes **207c** and **207f**, resulting in the desired secondary alcohols **230f** and **230g** in 90% and 53% yield, respectively (Scheme 63).



Scheme 63: Br/La-exchange on heteroarylbromides **213i** and **213j** using Ph_3La (**225c**).

Finally, we wanted to show that the acylation reaction with *N*,*N*-dimethylamides as electrophile could be applied to those triaryllanthanum reagents. As a proof of principle, the triheteroaryllanthanum reagent **227a**, which was prepared starting from 1-iodoisoquinoline (**204i**) and Ph_3La (**225c**), underwent the same acylation procedure as the prior synthesized diaryl- and diheteroaryl(methyl)lanthanum reagents of type Ar_2LaMe **211** or $HetAr_2LaMe$ **214** using a *N*,*N*-dimethylamide **222g** leading to the desired ketone **223h** in 78% yield (Scheme 64).



Scheme 64: Acylation reaction of triheteroaryllanthanum reagent **227a** with amide **222g**.

To sum it up, Ph_3La (**225c**) displays a useful alternative towards nBu_2LaMe (**205f**). All three phenyl residues can be transferred, it can be stored for at least two weeks at 0 °C and aryl or heteroaryl iodides as well as bromides can be converted into the desired triaryl- and triheteroaryllanthanum reagents at −50 °C within 5 min. Additionally, the scope of this reagent also includes several heterocycles, such as isoquinolines, and sensitive ester moieties were tolerated in some cases.

8. Preparation of Functionalized Diaryl- and Diheteroarylsamarium Reagents by a Halogen-Samarium Exchange

8.1. Introduction

Since the obtained results on the halogen-lanthanum exchange were quite encouraging, the development of another related halogen-lanthanide exchange procedure which displays a higher functional group tolerance was envisaged. In this context, a halogen-samarium exchange could be a good candidate, since samarium possesses a slightly higher electronegativity (EN.: 1.17) compared to lanthanum (EN.: 1.10) making the carbon–samarium bond less polarized, and therefore a better functional group compatibility with still fast reaction rates is expected. Up to now, especially samarium(II) found useful applications in the field of radical chemistry,[136] but reports concerning their application in organometallic chemistry are still scarce. In the early 1990's, *Kagan* and co-workers described the preparation of organo-samarium derivatives starting from organic iodides or bromides and SmI_2 in THF.[137,138] However, those organosamarium reagents were quite unstable and needed to be trapped as soon as possible with electrophiles. Later on, they found that the use of tetrahydropyran (THP) instead of THF has got a very positive effect on the stability of the generated organosamarium reagents, and according to this procedure even stable allyl- and benzylsamariums could be easily prepared at −15 to 0 °C.

There are two different ways to use organosamarium compounds prepared from SmI_2. The reaction is achieved by treating the organic halide with two equivalents of SmI_2 and is supposed to occur *via* stepwise one-electron transfer to the organic halide. The obtained organosamarium reagents can then be trapped with carbonyl compounds to produce the corresponding alcohols. This stepwise reaction is called *Samarium-Grignard* reaction. However, a one pot procedure, the so called *Samarium-Barbier* reaction, can also be used (Scheme 65).[139]

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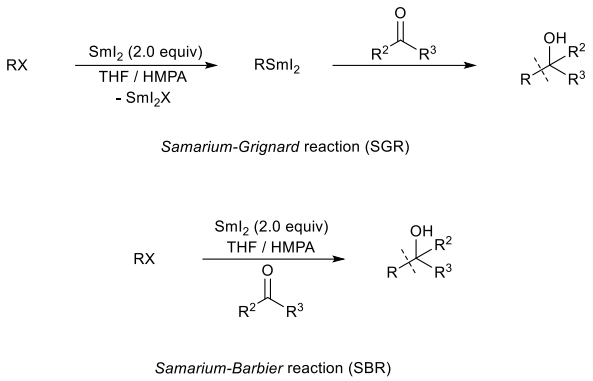
[136] a) A. Gansäuer, H. Blum, *Chem. Rev.* **2000**, *100*, 2771; b) P. G. Steel, *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727; c) A. Gansäuer, T. Lauterbach, S. Narayan, *Angew. Chem. Int. Ed.* **2003**, *42*, 5556; d) H. B. Kagan, *Tetrahedron* **2003**, *59*, 10351; e) J. Concéllon, H. Rodríguez-Solla, *Chem. Soc. Rev.* **2004**, *33*, 599; f) D. J. Edmonds, D. Johnston, D. J. Procter, *Chem. Rev.* **2004**, *104*, 3371; g) K. C. Nicolaou, S. P. Ellery, J. S. Chen, *Angew. Chem. Int. Ed.* **2009**, *48*, 7140; h) J. M. Concéllon, H. Rodríguez-Solla, C. Concéllon, V. del Amo, *Chem. Soc. Rev.* **2010**, *39*, 4103; i) M. Szostak, D. J. Procter, *Angew. Chem. Int. Ed.* **2011**, *50*, 7737; j) C. Beemelsmanns, H. U. Reissig, *Chem. Soc. Rev.* **2011**, *40*, 2199; k) B. Sautier, D. J. Procter, *Chimia* **2012**, *66*, 399; l) M. Szostak, D. J. Procter, *Angew. Chem. Int. Ed.* **2012**, *51*, 9238; m) H. Y. Harb, D. J. Procter, *Synlett* **2012**, 6; n) J. Streuff, *Synthesis* **2013**, 281; o) M. Szostak, M. Spain, D. J. Procter, *Chem. Soc. Rev.* **2013**, *42*, 9155; p) J. M. Concéllon, H. Rodríguez-Solla, *Eur. J. Org. Chem.* **2016**, 1613.

[137] a) J.-L. Namy, J. Collin, C. Bied, H. B. Kagan, *Synlett* **1992**, 733; b) C. Bied, J. Collin, H. B. Kagan, *Tetrahedron* **1992**, *48*, 3877; c) J.-L. Namy, M. Colomb, H. B. Kagan, *Tetrahedron Lett.* **1994**, *35*, 1723; d) B. Hamann, J.-L. Namy, H. B. Kagan, *Tetrahedron* **1996**, *52*, 14225; e) B. Hamann-Gaudinet, J.-L. Namy, H. B. Kagan, *Tetrahedron Lett.* **1997**, *38*, 6585; f) B. Hamann-Gaudinet, J.-L. Namy, H. B. Kagan, *J. Organometallic Chem.* **1998**, *567*, 39.

[138] P. Girard, J.-L. Namy, H. B. Kagan, *J. Am. Chem. Soc.* **1980**, *102*, 2693.

[139] A. Krief, A.-M. Laval, *Chem Rev.* **1999**, *99*, 745.



Scheme 65: General scheme for the use of organosamariums prepared *via* SGR or SBR procedures.

Additionally, extensive studies regarding the mechanisms and further preparations were also carried out by *Molander*[140] and *Curran*.[141] Nevertheless, alternative synthetic procedures for the preparation of functionalized organosamarium reagents are barely reported yet. Thus, a practical and convenient preparative pathway towards organosamariums *via* a halogen-samarium exchange would be useful. Moreover, such a transformation would be a suitable addition to the synthetic toolbox of organometallic chemistry having another metal with intermediate reactivity compared to the already well-established ones like lithium, magnesium or zinc.

8.2. Preparation of Diaryl- and Diheteroarylsamarium Reagents using *n*Bu_2SmCl and *n*Bu_2SmMe

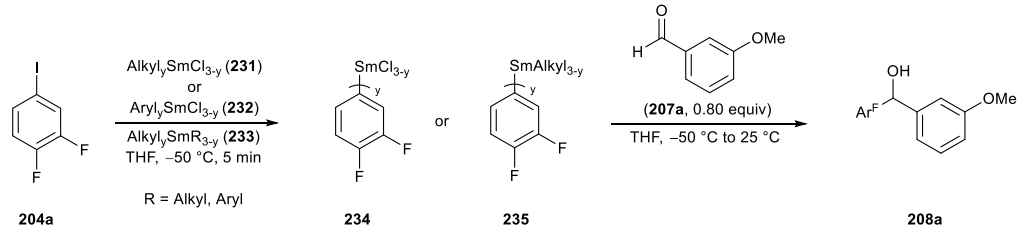
For a preliminary screening of exchange reagents the aryl iodide 1,2-difluoro-4-iodobenzene (**204a**) was used and treated with a broad range of different alkyl- and aryl-derived exchange reagents of types **231–233** at −50 °C in THF. With reference to Table 20, methyl-based exchange reagents such as $MeSmCl_2$ (**231a**) and Me_2SmCl (**232b**) neither underwent a sufficient exchange of **204a** nor resulted in an acceptable isolated yield of **208a** (Table 20, entries 1 and 2). Me_3Sm (**231c**) gave a full exchange of **204a**, but due to the formation of side-products, the desired alcohol **208a** could only be isolated in 47% (entry 3). Nevertheless, switching to *n*butyl-derived exchange reagents appeared to be promising. Thus, all three exchange reagents *n*$BuSmCl_2$ (**231d**), *n*Bu_2SmCl (**231e**) and *n*Bu_3Sm (**231f**) reacted smoothly with the aryl iodide **204a** at −50 °C, and subsequent trapping with aldehyde **207a** led to alcohol **208a** in satisfying yields of 73–93% (entries 4–6). Furthermore, secondary alkyl-derived exchange reagents, like *s*$BuSmCl_2$ (**231g**), *s*Bu_2SmCl (**231h**) and *s*Bu_3Sm (**231i**) were examined. Treating 1,2-difluoro-4-

[140] a) G. A. Molander, J. B. Etter, *J. Org. Chem.* **1986**, *51*, 1778; b) G. A. Molander, J. B. Etter, P. W. Zinke, *J. Am. Chem. Soc.* **1987**, *109*, 453; c) G. A. Molander, J. B. Etter, *J. Am. Chem. Soc.* **1987**, *109*, 6556; d) G. A. Molander, L. S. Harring, *J. Org. Chem.* **1990**, *55*, 6171; e) G. A. Molander, C. R. Harris, *J. Am. Chem. Soc.* **1995**, *117*, 3705; f) G. A. Molander, C. R. Harris, *Tetrahedron* **1998**, *54*, 3321; g) G. A. Molander, C. Alonso-Alija, *J. Org. Chem.* **1998**, *63*, 4366.

[141] a) D. P. Curran, T. L. Fevig, M. J. Totleben, *Synlett* **1990**, 773; b) D. P. Curran, R. L. Wolin, *Synlett* **1991**, 317; c) D. P. Curran, M. J. Totleben, *J. Am. Chem. Soc.* **1992**, *114*, 6050; d) D. P. Curran, B. Yoo, *Tetrahedron Lett.* **1992**, *33*, 6931; e) D. P. Curran, T. L. Fevig, C. P. Jasperse, M. J. Totleben, *Synlett* **1992**, 943.

iodobenzene (**204a**) with those three reagents gave only moderate conversions of 66–80%, and further addition to **207a** resulted in **208a** in 68–76% yield (entries 7–9). Besides alkyl-based exchange reagents, also aryl-derived reagents were investigated. Thus, the three different exchange reagents $PhSmCl_2$ (**232a**), Ph_2SmCl (**232b**) and Ph_3Sm (**232c**), prepared *via* transmetalation of PhLi and $SmCl_3 \cdot 2LiCl$ at −30 °C, proved to be very efficient reagents. Ph_3Sm (**232c**) even exchanged all three phenyl-residues leading to full conversion of the selected aryl iodide **204a**, and isolated yields of 85–98% of alcohol **208a** could be obtained (entries 10–12). Finally, different mixed species were tested. Performing the exchange on **204a** using *n*$BuSmMe_2$ (**233a**) resulted in full conversion of the aryl iodide, but gave the desired product **208a** in only 27% isolated yield due to the formation of significant amounts of competitive alkyl-transfer side products (entry 13). However, the other reagents *n*Bu_2SmMe (**233b**), *s*Bu_2SmMe (**233c**) and Ph_2SmMe (**233d**) proved to be quite powerful, furnished full conversion of aryl iodide **204a** and subsequent trapping with 3-methoxybenzaldehyde (**207a**) led to the expected secondary alcohol in 81–95% yield (entries 14–16). Taking all this into account, the most effective reagents regarding stability, atom-economy, reaction rates and obtained yields, were *n*Bu_2SmCl (**231e**) and the two mixed species *n*Bu_2SmMe (**233b**) or *s*Bu_2SmMe (**233c**).

Table 20: Evaluation of different alkyl- and aryl-derived exchange reagents for an efficient I/Sm-exchange of 1,2-difluoro-4-iodobenzene (**204a**).



Entry	Exchange Reagent	Amount (equiv)	Conversion of **204a** (%)[a]	Conversion of **207a** (%)[a]	Yield of **208a** (%)[b]
1	$MeSmCl_2 \cdot 3LiCl$ (**231a**)	1.2	48	28	0
2	$Me_2SmCl \cdot 4LiCl$ (**231b**)	0.60	70	33	6
3	$Me_3Sm \cdot 5LiCl$ (**231c**)	0.40	100	100	47
4	*n*$BuSmCl_2 \cdot 3LiCl$ (**231d**)	1.2	94	100	98
5	*n*$Bu_2SmCl \cdot 4LiCl$ (**231e**)	0.60	98	100	93
6	*n*$Bu_3Sm \cdot 5LiCl$ (**231f**)	0.40	91	84	73
7	*s*$BuSmCl_2 \cdot 3LiCl$ (**231g**)	1.2	66	85	68
8	*s*$Bu_2SmCl \cdot 4LiCl$ (**231h**)	0.60	70	86	74
9	*s*$Bu_3Sm \cdot 5LiCl$ (**231i**)	0.40	80	88	76

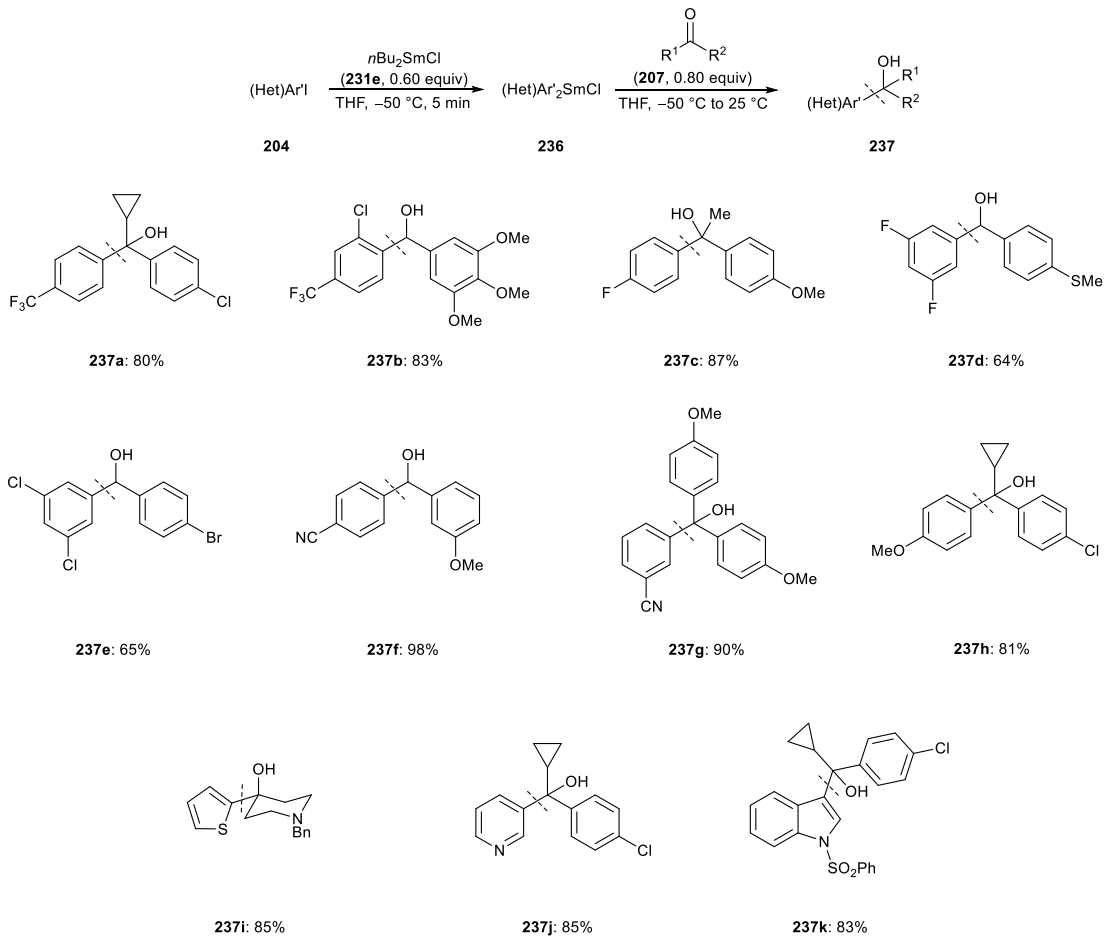
Table 20: (continued)

Entry	Exchange Reagent	Amount (equiv)	Conversion of **204a** (%)[a]	Conversion of **207a** (%)[a]	Yield of **208a** (%)[b]
10	$PhSmCl_2 \cdot 3LiCl$ (**232a**)	1.2	100	100	98
11	$Ph_2SmCl \cdot 4LiCl$ (**232b**)	0.60	100	100	86
12	$Ph_3Sm \cdot 5LiCl$ (**232c**)	0.40	100	100	85
13	nBuSm$Me_2 \cdot 5LiCl$ (**233a**)	1.2	100	85	27[c]
14	nBu$_2$SmMe·5LiCl (**233b**)	0.60	100	100	88
15	sBu$_2$SmMe·5LiCl (**233c**)	0.60	100	100	95
16	$Ph_2SmMe \cdot 5LiCl$ (**233d**)	0.60	100	100	81

[a] Conversion determined by GC-analysis; [b] Isolated yield; [c] alkyl-transfer side product was observed (1:1 ratio determined by GC-analysis).

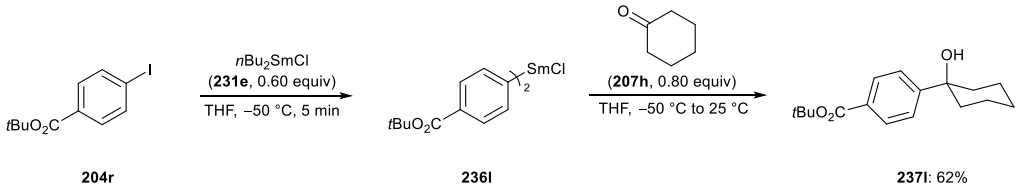
Since nBu$_2$SmCl (**231e**) proved to be a good candidate, it was tested as exchange reagent for a variety of functionalized aryl and heteroaryl iodides.

The scope of nBu$_2$SmCl (**231e**) appeared to be quite broad. Thus, the exchange of the two 4-CF_3-substituted aryl iodides using **231e** succeeded at −50 °C within 5 min generating the corresponding diarylsamarium chlorides **236a** and **236b** which further reacted with a ketone and an aldehyde, leading to the expected alcohols **237a** and **237b** in 80% and 83% yield, respectively. Similarly, halogenated aryl iodides underwent the same exchange, and the resulting diarylsamarium reagents **236c–e** added to three different carbonyl compounds affording the prodcuts **237c**–**e** in 64–87% yield. Furthermore, also cyano-substituted aryl iodides reacted smoothly with **231e** leading the diarylsamarium derivatives **236f** and **236g**, and subsequent trappings with an aldehyde or a ketone furnished the desired alcohols **237f** and **237g** in 98% and 90% yield. Also an electron-rich aryl iodide, 4-iodoanisole, underwent such an exchange and the corresponding diarylsamarium chloride **236h** reacted with a ketone yielding the tertiary alcohol **237h** in 81%. Finally, heteroaryl iodides could be converted into the diarylsamarium reagents **236i**–**k** and reacted with ketones to give the tertiary alcohols **237i**–**k** in 83–85% yield (Scheme 66).



Scheme 66: I/Sm-exchange reactions of functionalized aryl iodides using *n*Bu_2SmCl (**231e**).

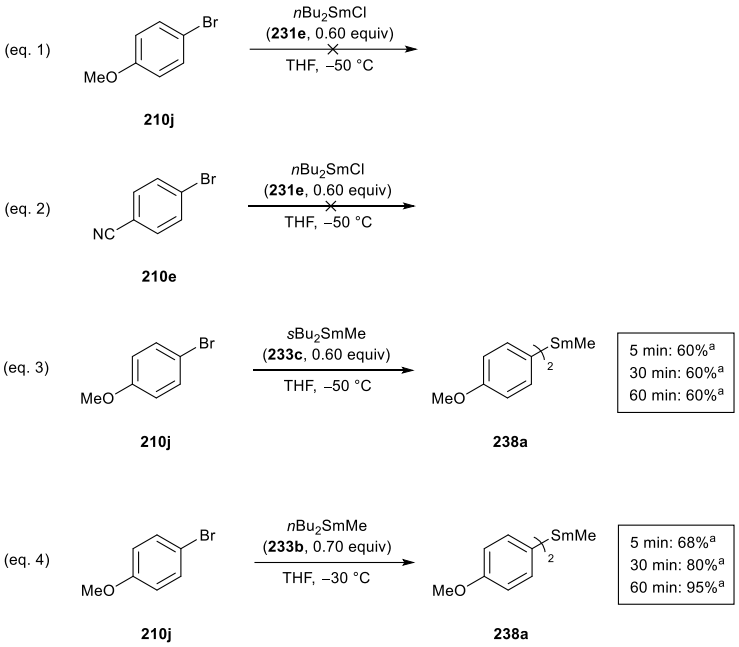
Since the carbon–samarium bond is slightly more covalent than the carbon–lanthanum bond, also more sensitive functional groups were tolerated. Hence, an aryl iodide bearing a bulky ester moiety **204r** could be used for this exchange and the resulting diarylsamarium reagent **236l** was immediately trapped with cyclohexanone (**207h**) leading to the desired alcohol **237l** in 62% yield (Scheme 67).



Scheme 67: I/Sm-exchange of *tert*-butyl 4-iodobenzoate (**204r**) using *n*Bu_2SmCl (**231e**).

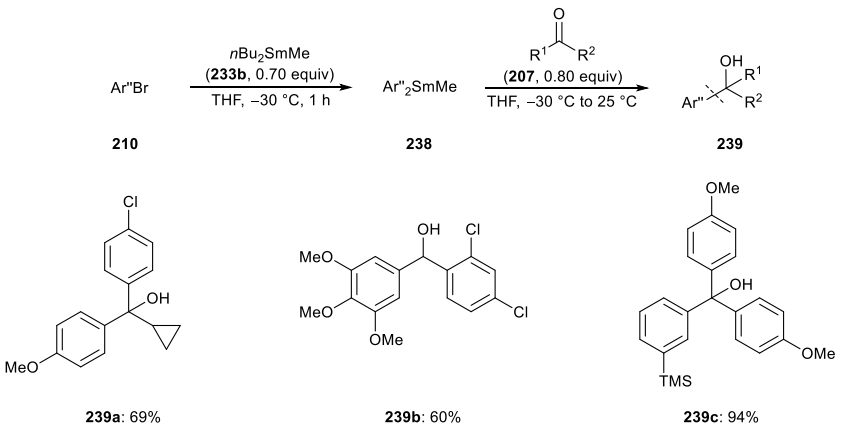
As a second step, the Br/Sm-exchange was examined. Preliminary experiments showed that *n*Bu_2SmCl (**231e**) was not reactive enough to perform an efficient exchange on functionalized aryl bromides at −50 °C. Even at higher temperatures and elongated reaction times, no exchange was detected on the two selected aryl bromides, 4-bromoanisole (**210j**) and 4-bromobenzonitrile (**210e**) (Scheme 68, eq. 1 and 2). Another attempt, using the more reactive mixed exchange reagent *s*Bu_2SmMe (**233c**) led to 60%

conversion of 4-bromoanisole at −50 °C within 5 min, but no more reaction progress was observed. It can be assumed that the secondary alkyl reagent **233c** is not long term stable under these conditions due to side reaction such as β-hydride elimination (Scheme 68, eq. 3). Nevertheless, performing the exchange of **210j** with *n*Bu_2SmMe (**233b**) succeeded at −30 °C within 1 h, and a continuous reaction progress was observed (eq. 4).



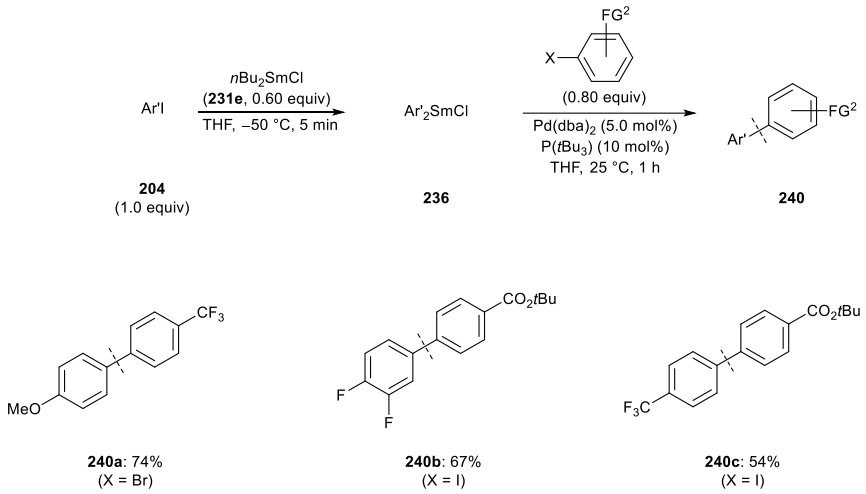
Scheme 68: Evaluation of the reagents for performing a Br/Sm-exchange reaction. [a] Conversion determined by GC-analysis.

Further experiments on the Br/Sm-exchange process using *n*Bu_2SmMe (**233b**) proved to be quite successful. Thus, besides 4-bromoanisole also two other relatively electron-rich aryl bromides of type **210**, 5-bromo-1,2,3-trimethoxybenzene and 1-bromo-3-(trimethylsilyl)benzene, could be converted into the diarylsamarium reagents **238a–c** at −30 °C within 1 h, and were subsequently trapped with two ketones and one aldehyde resulting in the desired alcohols **239a–c** in 60–94% yield (Scheme 69).



Scheme 69: Br/Sm-exchange using *n*Bu_2SmMe (**233b**).

After an extensive screening of different catalysts, it was also possible to perform Pd-catalyzed cross-couplings of diarylsamarium chlorides related to the procedure already mentioned in the case of diaryl(methyl)lanthanum reagents. A catalytic system involving $Pd(dba)_2$ (5.0 mol%) and $P(tBu)_3$ (10 mol%) proved to be the most efficient, and THF could be used as solvent. Thus, the three different aryl iodides 4-iodoanisole, 1,2-difluoro-4-iodobenzene and 4-iodobenzotrifluoride of type **204** were first converted into the corresponding diarylsamarium reagents **236** which then underwent cross-couplings at room temperature with 4-bromobenzotrifluoride and *tert*-butyl 4-iodobenzoate leading to the expected coupling products **240a–c** in 54–74% yield. Remarkably, almost no halogen-samarium exchange on the electrophile and no nucleophilic attack on the sensitive ester moiety was observed (Scheme 70).



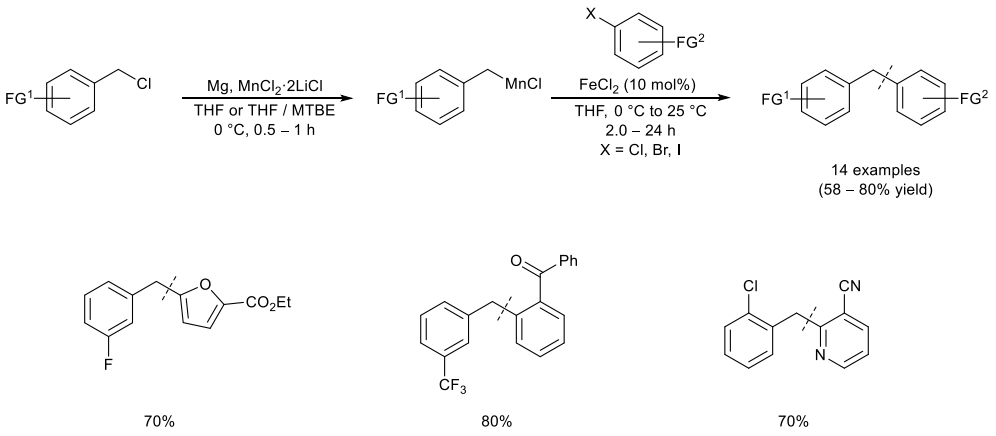
Scheme 70: Pd-catalyzed cross-couplings of diarylsamarium chlorides of type **236** with aryl halides.

In summary, the two different alkyl-derived exchange reagents nBu$_2$SmCl (**231e**) and nBu$_2$SmMe (**233b**) allowed efficient halogen-samarium exchange reactions of functionalized aryl and heteroaryl halides affording functionalized diaryl- and diheteroarylsamarium derivatives. The obtained samarium compounds could be trapped successfully with a range of different carbonyl compounds and additionally Pd-catalyzed cross-coupling reactions could be performed. Moreover still very fast exchange rates were achieved in case of the I/Sm-exchange at −50 °C using nBu$_2$SmCl (**231e**) and preliminary experiments on the Br/Sm-exchange proceeded smoothly at −30 °C using nBu$_2$SmMe (**233b**). Finally, due to the more covalent carbon–samarium bond, this exchange showed a slightly broader reaction scope compared to the already mentioned halogen-lanthanum exchange, and sensitive functional groups such as nitriles and esters could be tolerated at even −30 °C in some cases.

9. Summary

This thesis focused on the preparation of organometallic reagents of manganese, zinc, lanthanum and samarium and their applications in organic synthesis. Practical iron-, cobalt- and nickel-catalyzed cross-coupling procedures were developed and a novel, straightforward synthetic procedure towards functionalized organolanthanum and organosamarium derivatives was designed. As a conclusion, a short summary of each topic with their crucial reaction conditions and significant parameters is presented in the following. Additionally, selected examples are given to highlight the scope of each synthetic procedure and to show the utility of the different organometallic derivatives.

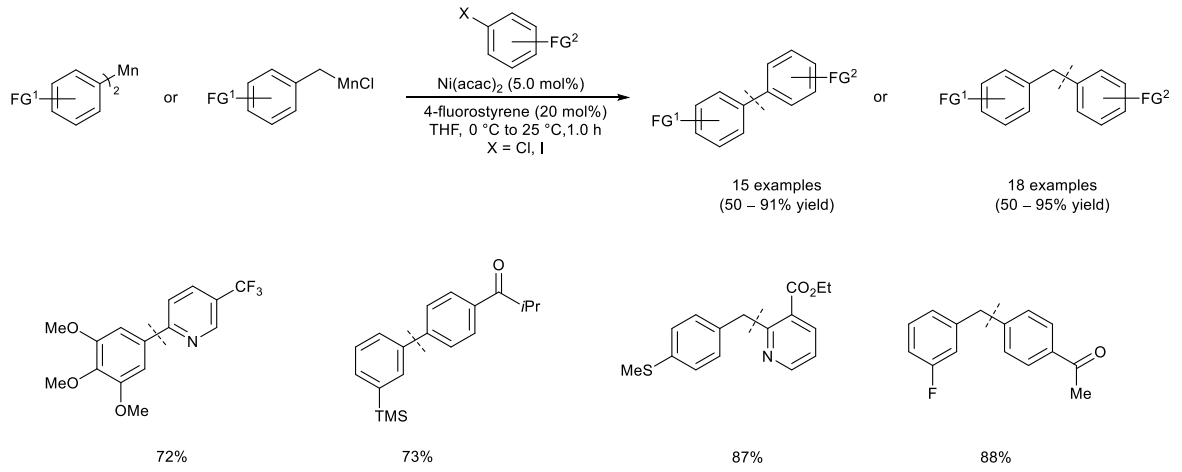
The first two topics of this thesis rely on the synthesis of functionalized aryl or benzylic manganese reagents and their transition-metal-catalyzed cross-couplings without the use of palladium. The preparation of the required benzylic manganese reagents succeeded *via* the *in situ* transmetalation pathway, employing magnesium turnings in the presence of $MnCl_2 \cdot 2LiCl$. By using the simple and practical iron catalyst $FeCl_2$ (10 mol%), a range of different benzylic manganese chlorides underwent efficient cross-couplings with a variety of aryl and heteroaryl halides at 0 °C in THF or a THF / MTBE mixture. Based on this procedure polyfunctionalized diaryl- and arylheteroarylmethane derivatives could be obtained in 58–80% yield (Scheme 71).



Scheme 71: Fe-catalyzed cross-couplings of benzylic manganese chlorides with aryl halides.

As a related topic, functionalized aryl and benzylic manganese reagents could be cross-coupled by the use of an effective catalytic system involving nickel catalysts. For the preparation of diarylmanganese reagents, the corresponding arylmagnesium compounds were prepared *via* a *Grignard* reaction, and subsequent transmetalation with $MnCl_2 \cdot 2LiCl$ led to the expected managanese reagents. The nickel-catalyzed cross-couplings of these reagents were achieved using a catalytic system consisting of the cheap and convenient $Ni(acac)_2$ (5.0 mol%) as catalyst and 4-fluorostyrene (20 mol%) as additive. The couplings proceeded smoothly at 0 °C within only 1 h, and a broad scope of electrophiles bearing

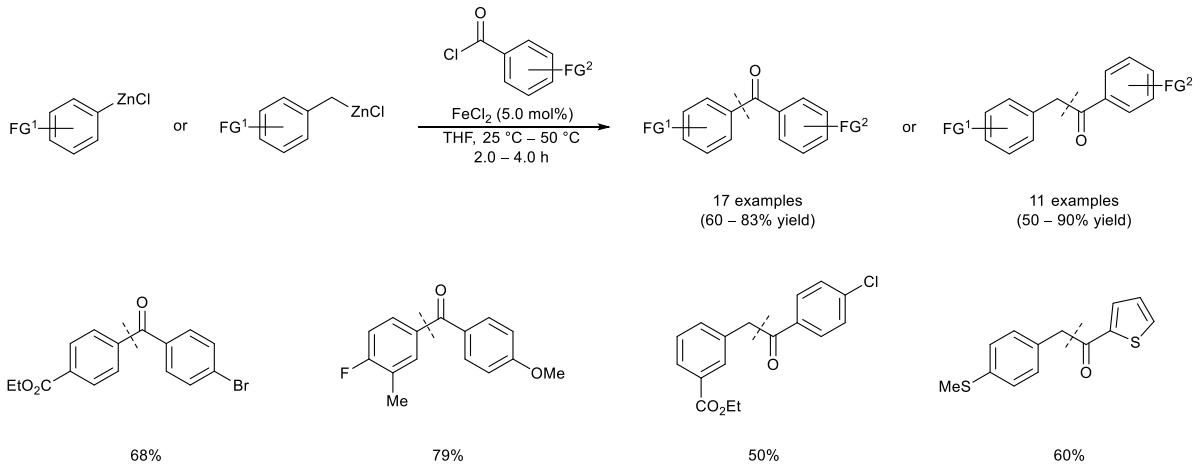
sensitive functional groups, such as esters, nitriles or even ketones, could be introduced. Thanks to this method, a variety of aryl- or arylheteroarylmethane derivatives and functionalized biphenyl compounds could be obtained in 50–90% yield (Scheme 72).



Scheme 72: Ni-catalyzed cross-couplings of diaryl and benzylic manganese reagents with aryl halides.

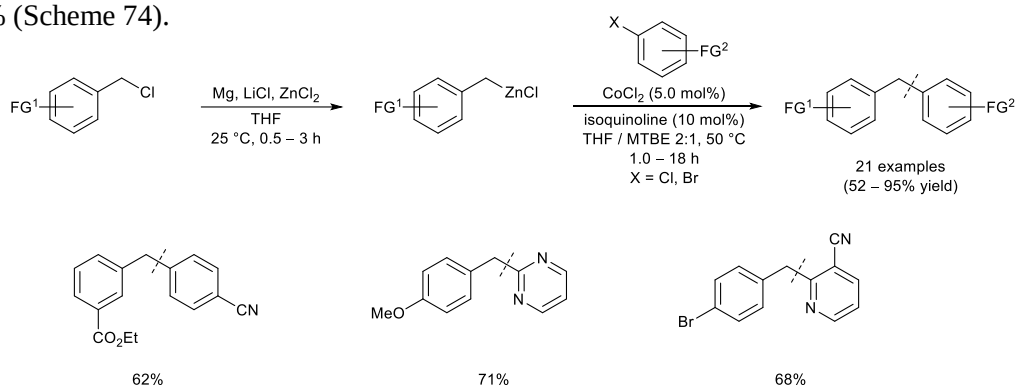
The second major topic was the preparation of functionalized aryl and benzylic zinc reagents and their palladium-free transition-metal-catalyzed transformations. Due to the less polarized and more covalent character of the carbon–zinc bond compared to the one present in organolithium, organomagnesium and organomanganese reagents, organozinc derivatives are known to display a much better functional group tolerance. This improved functional group compatibility makes the use of organozinc species for selective carbon–carbon bond formations highly interesting. Polyfunctionalized organozinc reagents, including compounds bearing sensitive substituents like esters, nitriles and ketones, are readily available and can be used for selective late stage functionalizations of electrophiles. Therefore, practical, less toxic and cheap cross-coupling methodologies with a broad applicability are of high importance.

In the following, a straightforward synthetic procedure for the preparation of diaryl and arylheteroaryl ketones, involving functionalized aryl or benzylic zinc regents and acid chlorides, is presented. This acylation pathway succeeded using $FeCl_2$ (5.0 mol%) as catalyst in THF at 25 °C or 50 °C within a few hours. Organozinc reagents bearing a variety of substituents underwent this transformation without the use of expensive or toxic palladium and nickel catalysts, and the desired ketones were obtained in 50–90% yield (Scheme 73).



Scheme 73: Fe-mediated acylations of functionalized organozinc reagents with acid chlorides.

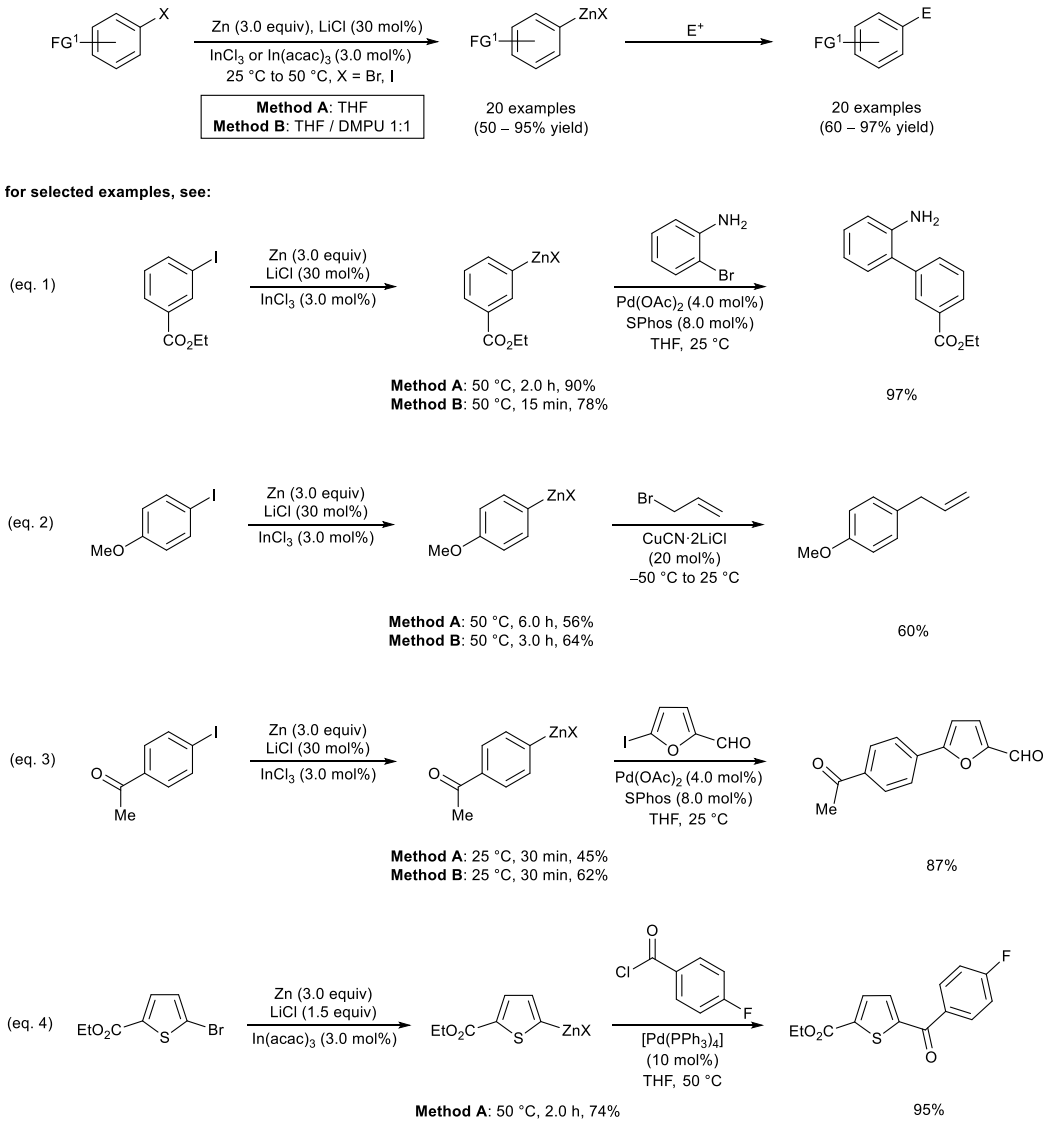
Additionally, a cobalt-catalyzed cross-coupling protocol using benzylic zinc chlorides and aryl bromides was performed. The benzylic zinc reagents were prepared starting from the corresponding benzylic chlorides *via* an *in situ* transmetalation pathway using magnesium turnings in the presence of LiCl and $ZnCl_2$. The resulting benzylic zinc compounds underwent subsequent cross-coupling reactions with selected aryl and heteroaryl bromides and chlorides using a catalytic system made out of $CoCl_2$ (5.0 mol%) and isoquinoline (10 mol%). The reactions were performed at 50 °C in a mixture of THF / MTBE 2:1, and functionalized aryl and arylheteroarylmethane derivatives could be obtained in 52–95% (Scheme 74).



Scheme 74: Co-catalyzed cross-couplings of benzylic zinc derivatives with aryl and heteroaryl halides.

Since organozinc reagents display such an important role in the field of organometallic chemistry, optimized preparative pathways towards functionalized organozincs are of high importance. Aside from the well-established synthetic routes such as transmetalation of organolithium or organomagnesium compounds with zinc halides or the directed metalation using zinc amide bases, the oxidative insertion of zinc powder is still one of the most broadly used protocols.Thus, the fifth topic of this thesis was the development of an optimized and very convenient synthesis towards functionalized organozinc reagents starting from organic halides and commercially available zinc powder. Since it is already known that the addition of LiCl facilitates the oxidative insertion of a metal to a carbon–halide bond, and metal salts like $TiCl_4$, $PbCl_2$, $BiCl_3$ and $InCl_3$ further promote this reaction, a combination of both was found to

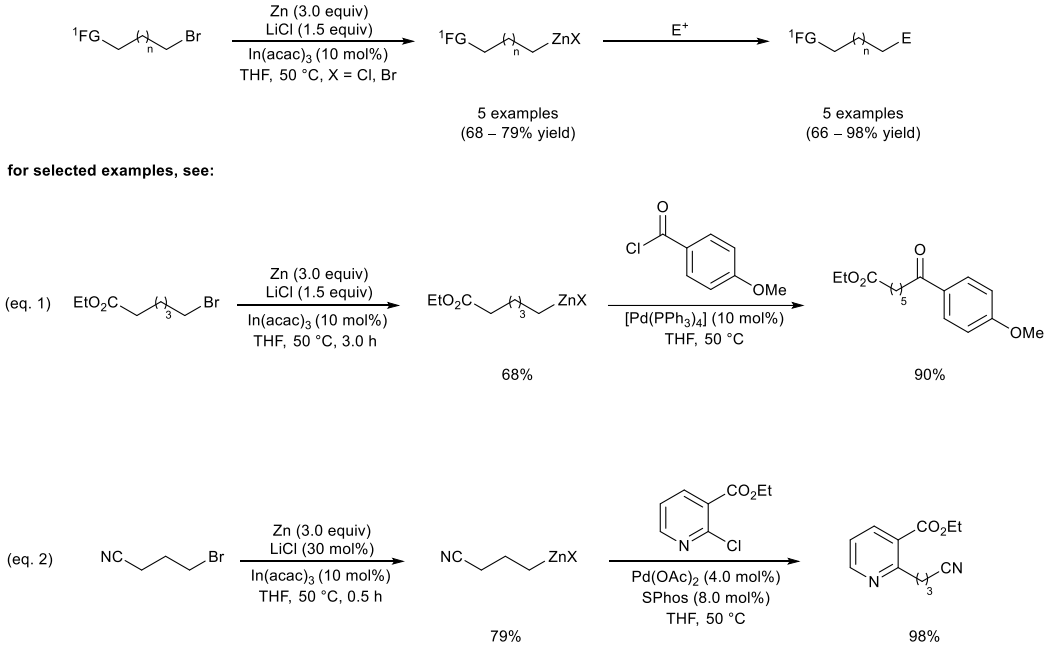
enhance this oxidative addition to a large extent. Additionally, the use of a more polar reaction medium using a mixture of THF / DMPU 1:1 allowed the preparation of functionalized organozinc reagents within only a few minutes in the case of aryl iodides and a few hours in the case of bromides. Usually, without the addition of a metal salt catalyst or of a polar co-solvent, several hours or even days are necessary to perform such transformations. Under these newly developed conditions, a fast and practical oxidative insertion of zinc into a variety of aryl and alkyl halides succeeded using LiCl as additive and $InCl_3$ or $In(acac)_3$ (3.0 mol%) as catalyst in either THF or THF / DMPU 1:1 as solvent. A range of substituted organozinc reagents could be prepared in up to 95% metalation yield, and even electron rich aryl halides underwent this reaction pathway. Additionally, various keto-substituted arylzinc compounds were prepared under these conditions in 50–62% yield. A further screening of the indium-catalyst showed that $In(acac)_3$ (3.0 mol%) enabled an efficient insertion of zinc into aryl and heteroaryl bromides in 70–80% yield (Scheme 75).



Scheme 75: $InCl_3$- or $In(acac)_3$-catalyzed insertions of zinc powder into aryl iodides and bromides.

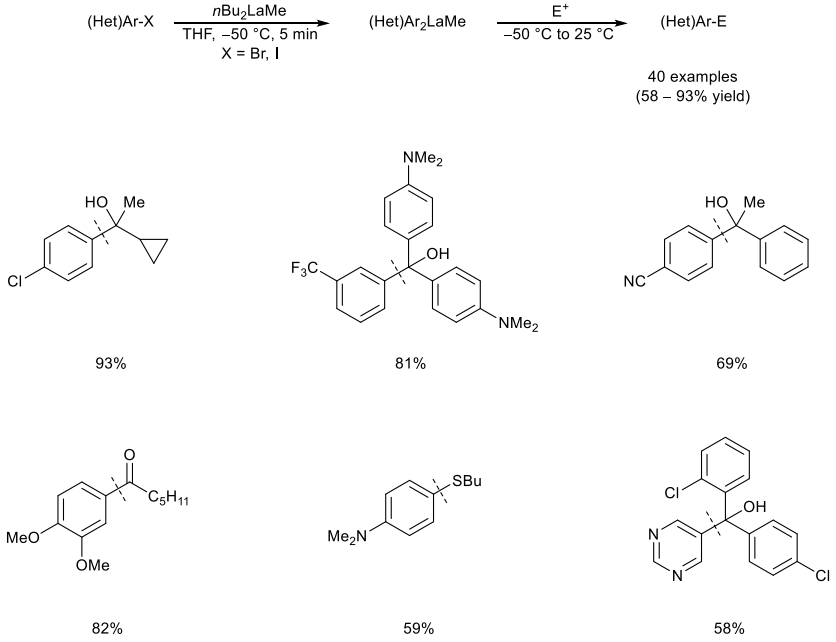
B. Results and Discussion

The scope of this reaction could also be extended to primary and secondary alkyl bromides using again $In(acac)_3$ (10 mol%) as catalyst and THF as solvent in the presence of an excess of LiCl. The corresponding alkyl zinc reagents could be obtained in 68–79% yield, and subsequent trapping reactions with selected electrophiles led to the desired products in 66–98% isolated yield (Scheme 76)



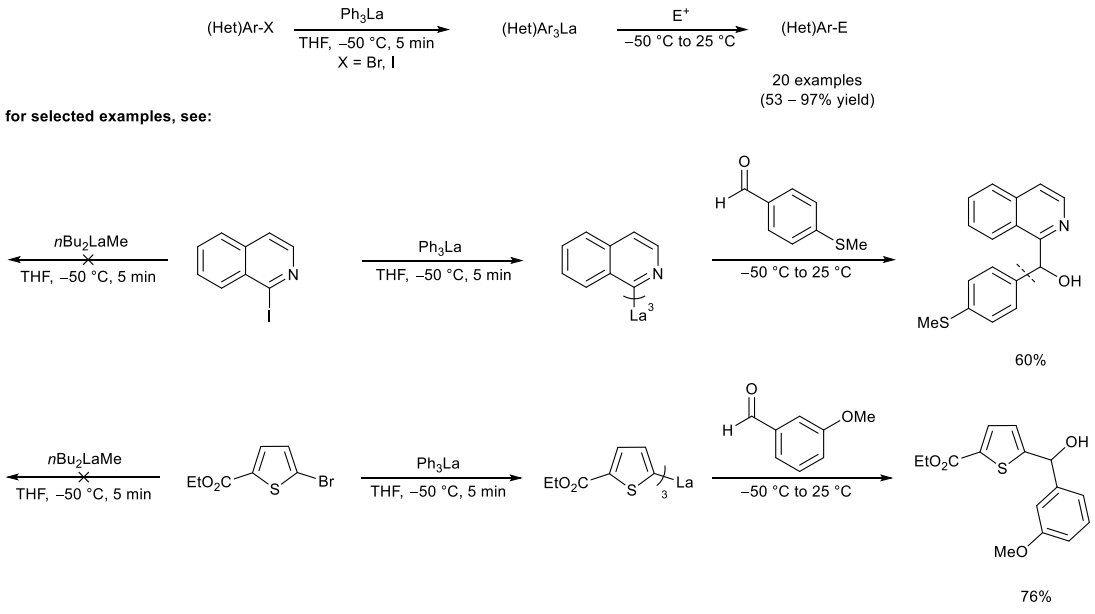
Scheme 76: $In(acac)_3$-catalyzed oxidative additions of zinc powder into alkyl bromides.

The last three subjects dealt with the preparation of organolanthanide reagents *via* a halogen-lanthanide exchange reaction. Since halogen-metal exchange reactions of lithium, magnesium, zinc and copper are already known, another exchange process involving metals with intermediate reactivity was of great interest. A halogen-lanthanum exchange process succeeded after extensive screening of different reagents by using either the mixed species nBu$_2$LaMe or the aryl-derived Ph$_3$La. Both reagents were able to perform the exchange on a broad range of aryl and heteroaryl halides, generating the corresponding lanthanum reagents in up to 90% yield, and further trapping reactions with carbonyl compounds, disulfides or amides led to the desired products in 53–97% yield (Scheme 77).



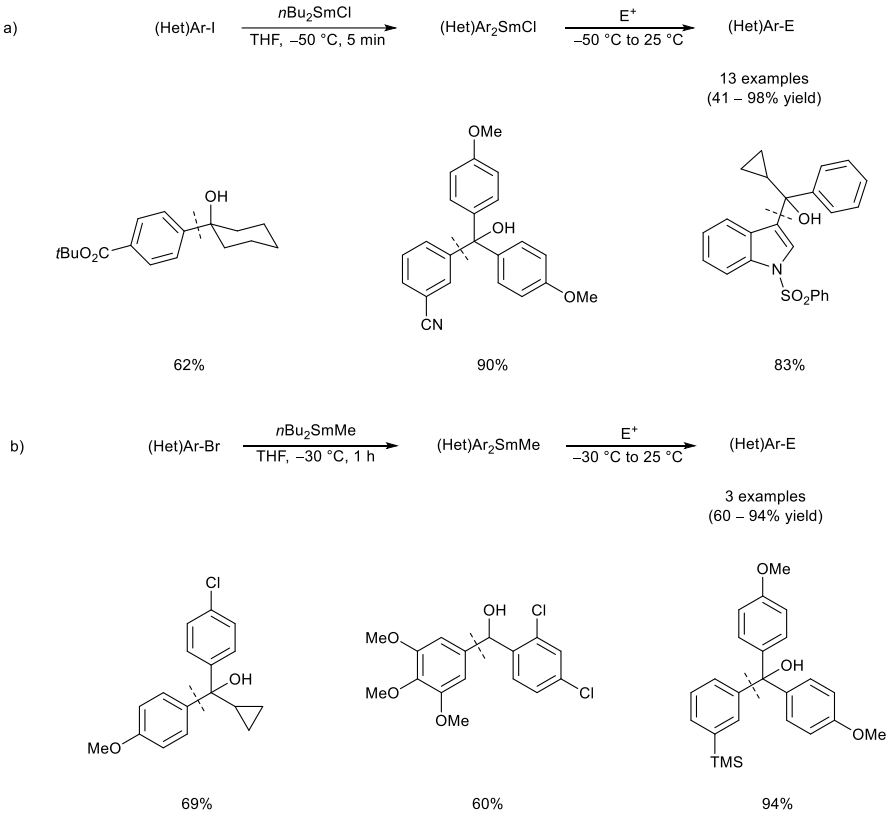
Scheme 77: Halogen-lanthanum exchanges of aryl or heteroaryl halides and subsequent trapping reactions with selected electrophiles.

In addition, the use of Ph_3La proved to be quite advantageous, since sensitive substituents or heterocycles could be tolerated without decomposition or competitive side reactions. The reactions proceeded smoothly at −50 °C within only 5 min. These key features make the halogen-lanthanum exchange a useful alternative to the well-established halogen-lithium exchange, since compared to the latter, a higher functional group compatibility is obtained (Scheme 78).



Scheme 78: Halogen-lanthanum exchanges using Ph_3La instead of nBu$_2$LaMe.

Furthermore, the related halogen-samarium exchange also succeeded using similar reagents of type nBu$_2$SmCl and nBu$_2$SmMe. Several aryl and heteroaryl iodides or bromides could be converted into the corresponding functionalized organosamarium reagents, and their trapping reactions with carbonyl compounds led to the expected alcohols in 41–98% yield. These reactions proceeded at −50 °C within 5 min using nBu$_2$SmCl in the case of aryl and heteroaryl iodides, and at −30 °C within 1 h using nBu$_2$SmMe in the case of aryl bromides. Due to the slightly less polarized carbon–samarium bond (EN.: 1.17) compared to the carbon–lanthanum bond (EN.: 1.10), even a *tert*-butyl ester and nitriles could be tolerated at −50 °C and −30 °C, respectively (Schemes 79)



Scheme 79: Hal/Sm-exchange reactions and subsequent trapping reactions with electrophiles.

This summary gave a short overview of recent topics in organometallic chemistry, wherein metals with intermediate reactivity and unique properties were of major interest. Whereas a variety of synthetic protocols towards organolithium, -magnesium and -zinc derivatives already exists, and their use in palladium- and nickel-catalyzed transformations is well-established, the preparation and application of other organometallics, such as the ones derived from manganese or especially lanthanides, are only barely reported. In this thesis, a range of new and very practical transformations of organomanganese and organozinc compounds involving less toxic and inexpensive iron and cobalt catalysts was developed. Furthermore, a novel and convenient preparative pathway towards organolanthanide derivatives was designed, which gives an initial access to a realtively untouched area of organometallic chemistry.

C. Experimental Section

C. Experimental Section

1. General Considerations

All reaction were carried out under magnetic stirring, in glassware previously dried with a heatgun under argon atmosphere, using standard *Schlenk* techniques, unless otherwise stated. Syringes were used to transfer solvents or reagents and purged three times with argon prior to use. Purified products were concentrated using a rotary evaporator and subsequently dried under high vacuum.

1.1. Procedure for Reaction Control

The reaction progress of all performed reactions was monitored by GC-analysis relative to an internal standard. Small amounts of the reaction mixture were hydrolyzed with a saturated aqueous solution of NH_4Cl, extracted with EtOAc and gas-chromatographically quantified. The process of halogen-metal exchange reactions and oxidative insertions was determined by iodolysis. Therefore, minor amounts of reaction mixture were iodolyzed with a solution of iodine in dry THF (1.0 mL) under argon, extracted with Et_2O or EtOAc after an addition of a saturated aqueous $Na_2S_2O_3$ solution, and gas-chromatographically measured.

1.2. Solvents

DMF was refluxed over CaH_2 (14 h) and distilled from CaH_2.

DMPU was pre-dried over CaH_2 (4 h) and distilled of.

1,4-Dioxane was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.

Et_2O was pre-dried over $CaCl_2$ and dried with the solvent purification system SPS-400-2 from *Innovative Technologies INC*.

MTBE was pre-dried over $CaCl_2$ and distilled from CaH_2.

NMP was refluxed over CaH_2 and distilled from CaH_2

THF was continuously refluxed and freshly distilled from sodium / benzophenone ketyl under nitrogen.

Toluene was pre-dried over $CaCl_2$ and distilled from CaH_2.

Solvents for column chromatography were distilled prior to use.

1.3. Reagents

All reagents obtained from commercial sources were used without any further purification unless otherwise stated.

***i*PrMgCl·LiCl** solution in THF was purchased from Chemetall.
MeLi solution in Et_2O was purchased from Sigma Aldrich.
***n*BuLi** solution in hexane was purchased from Albemarle.
***s*BuLi** solution in cyclohexane was purchased from Albemarle.
***t*BuLi** solution in pentane was purchased from Albemarle.
PhLi solution in Bu_2O was purchased from Sigma Aldrich.

$ZnCl_2$ (1.0 M in THF)

This solution was prepared by drying $ZnCl_2$ (34.1 g, 250 mmol) under high vacuum (1 mbar) for 24 h at 150 °C. After cooling to room temperature, freshly distilled THF (250 mL) was added, and stirring was continued until the salt was completely dissolved.

$MnCl_2$·2LiCl (1.0 M in THF)

A dry and argon-flushed 250 mL *Schlenk*-flask, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (6.78 g, 160 mmol) and heated up to 150 °C under high vacuum for 3 h. After cooling to room temperature under argon, $MnCl_2$ (10.1 g, 80.0 mmol, 99% purity) was added. The *Schlenk*-flask was further heated to 150 °C for 3 h under high vacuum, cooled to room temperature, and charged with freshly distilled THF (80 mL) under argon. The mixture was stirred for at least 24 h at 25 °C, and the resulting reagent $MnCl_2$·2LiCl (1.0 M in THF) appeared as a yellow solution.

CuCN·2LiCl (1.0 M in THF)

A dry and argon-flushed 250 mL *Schlenk*-flask, equipped with a magnetic stirring bar and a glass stopper, was charged with LiCl (6.78 g, 160 mmol) and heated up to 150 °C under high vacuum for 3 h. After cooling to room temperature under argon, CuCN (7.16 g, 80.0 mmol) was added, and the *Schlenk*-flask was further heated to 130 °C for 3 h under high vaccum, cooled to room temperature and charged with freshly distilled THF (80 mL) under vigorous stirring. The mixture was stirred for at least 24 h at 25 °C. The reagent CuCN·2LiCl (1.0 M in THF) appeared as a pale yellow solution.

$LaCl_3$·2LiCl (0.33 M in THF)

Commercially available $LaCl_3·6H_2O$ (35.3 g, 100 mmol) was mixed with LiCl (8.40 g, 200 mmol) in a 500 mL *Schlenk*-flask, and water (100 mL) was slowly added under vigorous stirring. The resulting slurry was stirred under high vacuum at room temperature for 4 h. Stirring was continued for 4 h at 40 °C, 4 h at 60 °C, 4 h at 80 °C, 4 h at 100 °C, 4 h at 120 °C, 4 h at 140 °C, and finally 4 h at 160 °C.

The slow increase of temperature and highly efficient stirring were essential. The resulting solid was cooled to room temperature, and freshly distilled THF (300 mL) was added. Then, molecular sieves (50 g, 4 Å) were added, and the resulting mixture was stirred for 24 h at room temperature. Finally, the insoluble material (mostly crushed molecular sieves) was removed by *Schlenk*-filtration under an argon atmosphere. By this procedure, a clear and colorless solution of $LaCl_3 \cdot 2LiCl$ (0.33 M in THF) was obtained, which was stored at room temperature under argon prior to use.

$SmCl_3 \cdot 2LiCl$ (0.33 M in THF)

Commercially available $SmCl_3 \cdot 6H_2O$ (36.5 g, 100 mmol) was mixed with LiCl (8.40 g, 200 mmol) in a 500 mL *Schlenk*-flask, and water (100 mL) was slowly added under vigorous stirring. The resulting slurry was stirred under high vacuum at room temperature for 4 h. Stirring was continued for 4 h at 40 °C, 4 h at 60 °C, 4 h at 80 °C, 4 h at 100 °C, 4 h at 120 °C, 4 h at 140 °C, and finally 4 h at 160 °C. The slow increase of temperature and highly efficient stirring were essential. The resulting solid was cooled to room temperature, and freshly distilled THF (300 mL) was added. Then, molecular sieves (50 g, 4 Å) were added, and the resulting mixture was stirred for 24 h at room temperature. Finally, the insoluble material (mostly crushed molecular sieves) was removed by *Schlenk*-filtration under an argon atmosphere. By this procedure, a clear and colorless solution of $SmCl_3 \cdot 2LiCl$ (0.33 M in THF) was obtained, which was stored at room temperature under argon prior to use.

1.4. Content Determination of Organometallic Reagents

Organomagnesium, **-manganese** and **-zinc** compounds were titrated against iodine in THF.[142]
Organolithium reagents, such as MeLi, *n*BuLi and *s*BuLi were titrated against isopropanol using 1,10-phenanthroline as indicator.[143]
Phenyllithium was titrated against *N*-benzylbenzamide in THF.[144]

[142] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, 890.
[143] H.-S. Lin, A. Paquette, *Synth. Commun*. **1994**, *24*, 2503.
[144] A. F. Burchat, J. M. Chong, N. Nielson, *J. Organometallic Chem.* **1997**, *542*, 281.

1.5. Chromatography

Thin layer chromatography (TLC) was performed using aluminum plates coated with SiO_2 (Merck 60, F-254). The spots were visualized by UV light (254 nm) or by staining of the TLC plate with one of the reagents below followed by heating if necessary.

- Phosphomolybdic acid (5.0 g), $Ce(SO_4)_2$ (2.0 g) and conc. H_2SO_4 (12.0 mL) in water (230 mL)

- Iodine absorbed on silica gel

- $KMnO_4$ (0.3 g), K_2CO_3 (20 g) and KOH (0.3 g) in water (300 mL)

Flash column chromatography was performed using SiO_2 (0.04–0.06 mm, 230–400 mesh) from Merck.

1.6. Analytical Data

NMR spectra were recorded on *Bruker* ARX 200, AC 300 WH 400 and AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the solvent peak. NMR spectra were recorded on solutions in $CDCl_3$ (residual chloroform: δ = 7.25 ppm for ^{1}H-NMR and δ = 77.0 ppm for ^{13}C-NMR). For the characterization of the observed signal multiplicities the following abbreviations were used: s (singulet), d (doublet), t (triplet), dd (doublet of doublet), ddd (doublet of doublet of doublet), dt (doublet of triplet), dq (doublet of quartet), q (quartet), qn (quintet), m (multiplet) as well as br (broad).

Melting points are uncorrected and were measured on a *Büchi* B. 540 apparatus.

Infrared spectra were recorded from 4000–600 cm^{-1} on a *PerkinElmer* 281 IR spectrometer. Samples were measured neat (ATR, Smiths Detection DuraSampl IR II Diamond ATR). The absorption bands were reported in wave numbers (cm^{-1}).

Gas chromatography was performed with machines of type *Agilent Technologies* 7890A GC-Systems with 6890 GC inlets, detectors and GC oven, using a column of type HP 5 (*Hewlett-Packard*, 5 % phenylmethylpolysiloxane; length: 10 m, diameter: 0.25 mm, film thickness: 0.25 μm). The detection was accomplished by the use of a flame ionization detector. The carrier gas was air, and alkanes like tetradecane ($C_{14}H_{30}$) were used as internal standards.

Gas chromatography-Mass spectra were performed with a *Hewlett-Packard* 6890/MSD 5973 GC/MS networking system, using a column of type HP 5 (*Hewlett-Packard*, 5 % phenylmethylpolysiloxane; length: 15 m, diameter: 0.25 mm, film thickness 0.25 μm).

Mass spectra were recorded on *Finnigan* MAT 95Q or *Finnigan* MAT 90 instruments for electron impact ionization (EI). High resolution mass spectra (HRMS) were recorded on the same instruments.

2. Iron-Catalyzed Cross-Coupling of Benzylic Manganese Chlorides with Aryl and Heteroaryl Halides

2.1. Typical Procedures

Typical procedure for the preparation of benzylic manganese(II) chlorides (182) (TP1)

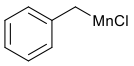
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with magnesium (0.18 g, 7.2 mmol, 2.4 equiv), followed by freshly distilled THF (3.0 mL) or MTBE (1.9 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv). The mixture was cooled to 0 °C, the benzyl chloride (3.0 mmol, 1.0 equiv) was added at once and maintained at 0 °C until complete conversion of the starting material was observed. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was completed, the solution of benzylic manganese(II) chloride was separated from the resulting salts *via* a syringe equipped with a filter and transferred to another pre-dried and argon-flushed *Schlenk*-tube, before being titrated against iodine.

Typical procedure for the iron-catalyzed cross-coupling of benzylic manganese(II) chlorides (182) with electrophiles (TP 2)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with $FeCl_2$ (10 mol%, 99.5% purity), the corresponding electrophile (1.00 equiv) and freshly distilled THF. Thereupon, the benzylic manganese(II) chloride solution (1.05–1.10 euqiv) was added dropwise at 0 °C. After the addition was completed, the reaction mixture was stirred for a given time at the prior adjusted temperature, and then allowed to warm to room temperature. The reaction completion was monitored by GC-analysis of quenched aliquots. A saturated aqueous solution of NH_4Cl was added, and the aqueous layer was extracted three times with Et_2O or EtOAc (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude products by flash column chromatography afforded the desired products.

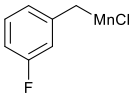
2.2. Preparation of the Benzylic Manganese(II) Chlorides (182a–f)

Preparation of benzylmanganese(II) chloride (182a)



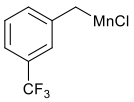
According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. Benzyl chloride (**183a**, 0.38 g, 0.35 mL, 3.0 mmol) was added at once at 0 °C, and the reaction mixture was stirred for 1 h at the given temperature. The concentration of benzylmanganese(II) chloride (**182a**) was determined by titration against iodine in THF (0.32 M, 73%).

Preparation of 3-fluorobenzylmanganese(II) chloride (182b)



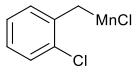
According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 3-Fluorobenzyl chloride (**183b**, 0.43 g, 0.36 mL, 3.0 mmol) was added at once at 0 °C, and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 3-fluorobenzylmanganese(II) chloride (**182b**) was determined by titration against iodine in THF (0.26 M , 59%).

Preparation of 3-(trifluoromethyl)benzylmanganese(II) chloride (182c)



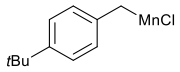
According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), MTBE (1.9 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 3-Trifluoromethylbenzyl chloride (**183c**, 0.58 g, 0.47 mL, 3.0 mmol) was added at once at 0 °C, and the reaction mixture was stirred for 1.5 h at the given temperature. The concentration of 3-(trifluoromethyl)benzylmanganese(II) chloride (**182c**) was determined by titration against iodine in THF (0.34 M , 65%).

Preparation of 2-chlorobenzylmanganese(II) chloride (182d)



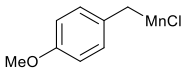
According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), MTBE (1.9 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 2-Chlorobenzyl chloride (**183d**, 0.48 g, 0.38 mL, 3.0 mmol) was added at once at 0 °C, and the reaction mixture was stirred for 1.5 h at the given temperature. The concentration of 2-chlorobenzylmanganese(II) chloride (**182d**) was determined by titration against iodine in THF (0.32 M, 61%).

Preparation of (4-(*tert*-butyl)benzyl)manganese(II) chloride (182e)



According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 4-*Tert*-butylbenzyl chloride (**183e**, 0.55 g, 0.57 mL, 3.0 mmol) was added at once at 0 °C, and the reaction mixture was stirred for 30 min at the given temperature. The concentration of (4-(*tert*-butyl)benzyl)manganese(II) chloride (**182e**) was determined by titration against iodine in THF (0.30 M , 68%).

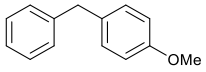
Preparation of 4-methoxybenzylmanganese(II) chloride (182f)



According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 4-Methoxybenzyl chloride (**183f**, 0.46 g, 0.39 mL, 3.0 mmol) was added at once at 0 °C, and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 4-methoxybenzyl manganese(II) chloride (**182f**) was determined by titration against iodine in THF (0.24 M, 54%).

2.3. Iron-Catalyzed Cross-coupling Reactions of Benzylic Manganese(II) Chlorides (182a–f) with Functionalized Electrophiles

Synthesis of 1-(4-methoxybenzyl)benzene (185a)



According to **TP2**, 4-iodoanisole (0.23 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Then, the benzylic manganese(II) chloride solution (**182a**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, the reaction mixture was allowed to warm to room temperature and stirred overnight. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 99 : 1, R_f = 0.33) yielding product **185a** (156 mg, 0.79 mmol, 79%) as a colorless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$, ppm) δ = 7.38 (td, *J* = 7.0, 1.9 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 3H), 7.21–7.18 (m, 2H), 6.93 (dd, *J* = 9.0, 2.3 Hz, 2H), 3.99 (s, 2H), 3.82 (s, 3H).

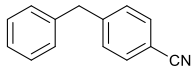
^{13}C-NMR (75 MHz, $CDCl_3$, ppm) δ = 158.1, 141.7, 133.3, 130.0, 128.9, 128.5, 126.1, 114.0, 55.3, 41.1.

IR (ATR, cm^{-1}) ṽ = 3061, 3027, 2906, 2834, 1610, 1584, 1509, 1493, 1452, 1439, 1300, 1243, 1174, 1106, 1073, 1033, 939, 836, 796, 768, 723, 696.

MS (EI, 70 eV, %) m/z = 199 (15), 198 (100), 197 (46), 183 (14), 167 (32), 165 (23), 153 (13), 125 (17), 111 (27), 109 (18), 97 (36), 91 (41), 83 (32), 69 (31), 58 (43).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{14}O$**: 198.1045; found: 198.1040.

Synthesis of 4-benzylbenzonitrile (185b)



Based on **TP2**, 4-bromobenzonitrile (0.18 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). The benzylic manganese(II) chloride solution (**182a**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 3 h at 0 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 99 : 1, R_f = 0.38) furnished product **185b** (145 mg, 0.75 mmol, 75%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50 (d, *J* = 8.4 Hz, 2H), 7.28–7.16 (m, 5H), 7.11 (d, *J* = 7.4 Hz, 2H), 3.98 (s, 2H).

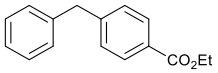
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 146.8, 139.4, 132.3, 129.7, 129.0, 128.8, 126.7, 119.0, 110.1, 42.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3064, 3029, 2926, 2228, 1734, 1507, 1496, 1454, 1414, 1373, 1242, 1178, 1113, 1074, 1046, 912, 854, 797, 761, 725, 698.

MS (EI, 70 eV, %) m/z = 194 (15), 193 (100), 192 (32), 190 (14), 165 (17), 91 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}N$**: 193.0891; found: 193.0885.

Synthesis of ethyl 4-benzylbenzoate (185c)



According to **TP2**, ethyl 4-iodobenzoate (0.28 g, 0.17 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Then, the benzylic manganese(II) chloride solution (**182a**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C. The reaction mixture was stirred for 3 h at 0 °C and then allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 99 : 1, R_f = 0.31) afforded product **185c** (183 mg, 0.76 mmol, 76%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.93 (d, *J* = 8.2 Hz, 2H), 7.27–7.16 (m, 5H), 7.12 (d, *J* = 8.3 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).

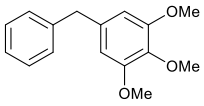
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.6, 146.5, 140.3, 129.9, 129.0 (2C), 128.7, 128.6, 126.5, 60.9, 42.0, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3063, 3028, 2982, 2934, 2361, 1713, 1611, 1602, 1496, 1454, 1415, 1367, 1272, 1245, 1177, 1099, 1046, 1021, 910, 855, 754, 733, 704, 696.

MS (EI, 70 eV, %) m/z = 241 (12), 240 (69), 212 (12), 196 (18), 195 (100), 168 (17), 167 (91), 166 (18), 165 (51), 152 (27), 91 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{16}O_2$**: 240.1150; found: 240.1144.

Synthesis of 5-benzyl-1,2,3-trimethoxybenzene (185d)



According to **TP2**, 5-bromo-1,2,3-trimethoxybenzene (0.25 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Thereupon, the benzylic manganese(II) chloride solution (**182a**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, the reaction mixture was allowed to warm to room temperature and stirred overnight. Finally, the crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.31) giving product **185d** (151 mg, 0.58 mmol, 58%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.26–7.22 (m, 2H), 7.17–7.13 (m, 3H), 6.35 (s, 2H), 3.87 (s, 2H), 3.77 (s, 3H), 3.75 (s, 6H).

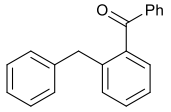
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.3, 141.0, 136.8, 136.5, 128.9, 128.6, 126.3, 106.1, 60.9, 56.1, 42.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3026, 2999, 2937, 2837, 2250, 1589, 1505, 1495, 1452, 1420, 1329, 1183, 1123, 1030, 1007, 970, 909, 844, 799, 781, 728, 700, 671.

MS (EI, 70 eV, %) m/z = 259 (21), 258 (100), 243 (34), 215 (13), 200 (15), 168 (15), 128 (14), 91 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{18}O_3$**: 258.1256; found: 258.1251.

Preparation of (2-benzylphenyl)(phenyl)methanone (185e)



Based on **TP2**, 2-bromo-benzophenone (0.26 g, 0.18 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Then, the benzylic manganese(II) chloride solution (**182a**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 99 : 1, R_f = 0.20) afforded product **185e** (179 mg, 0.66 mmol, 66%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.51–7.47 (m, 1H), 7.37–7.33 (m, 3H), 7.25–7.19 (m, 3H), 7.14–7.03 (m, 5H), 4.03 (s, 2H).

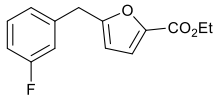
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.6, 140.6, 140.2, 138.9, 137.8, 133.2, 130.9, 130.4, 130.2, 129.3, 128.7, 128.4 (2C), 126.1, 125.7, 39.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3061, 3026, 1736, 1661, 1596, 1580, 1494, 1484, 1448, 1372, 1314, 1266, 1179, 1152, 1073, 1028, 1001, 924, 801, 764, 737, 731, 707, 694.

MS (EI, 70 eV, %) m/z = 273 (26), 272 (100), 271 (91), 257 (20), 255 (10), 254 (18), 253 (13), 195 (33), 194 (57), 166 (12), 165 (54), 152 (12), 105 (15), 91 (10), 77 (28).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{16}O$**: 272.1201; found: 272.1195.

Synthesis of ethyl 5-(3-fluorobenzyl)furan-2-carboxylate (185f)



According to **TP2**, ethyl 5-bromofuran-2-carboxylate (0.22 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Then, the benzylic manganese(II) chloride solution (**182b**, 4.0 mL, 0.26 M, 1.0 mmol, 1.0 equiv) was added dropwise to this solution at 0 °C. The reaction mixture was stirred for 2 h at 0 °C, and then allowed to warm to room temperature. Subsequent purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.11) afforded product **185f** (174 mg, 0.70 mmol, 70%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.24–7.20 (m, 1H), 7.05 (d, *J* = 3.4 Hz, 1H), 6.98 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.90 (m, 2H), 6.06 (dt, *J* = 3.4, 0.8 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (d, ^1J(C,F) = 245 Hz), 158.9, 158.6, 144.1, 139.3 (d, ^3J(C,F) = 7.0 Hz), 130.2 (d, ^3J(C,F) = 8.0 Hz), 124.6 (d, ^4J(C,F) = 3.0 Hz), 119.0, 115.9 (d, ^2J(C,F) = 22 Hz), 113.9 (d, ^2J(C,F) = 20 Hz), 109.2, 60.9, 34.5, 14.5.

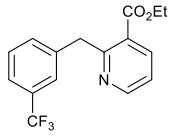
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −113.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3128, 2983, 2361, 1713, 1616, 1591, 1519, 1488, 1448, 1383, 1368, 1297, 1251, 1205, 1173, 1126, 1075, 1016, 970, 944, 912, 866, 789, 760, 731, 681.

MS (EI, 70 eV, %) m/z = 249 (10), 248 (67), 220 (10), 219 (23), 203 (42), 176 (17), 175 (100), 147 (16), 146 (40), 127 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}FO_3$**: 248.0849; found: 248.0845.

Synthesis of ethyl 2-(3-(trifluoromethyl)benzyl)nicotinate (185g)



Based on **TP2**, ethyl 2-chloronicotinate (0.19 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). The benzylic manganese(II) chloride solution (**182c**, 3.3 mL, 0.34 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 8 : 2, R_f = 0.17) leading to the desired product **185g** (200 mg, 0.65 mmol, 65%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.62 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.13 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.49 (s, 1H), 7.40–7.17 (m, 4H), 4.56 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.4, 160.4, 152.2, 140.7, 138.9, 132.6 (q, ^4J(C,F) = 2.4 Hz), 130.6 (q, ^2J(C,F)= 32 Hz), 128.7, 126.2, 125.9 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 271 Hz), 123.1 (q, ^3J(C,F) = 3.9 Hz), 121.7, 61.7, 42.2, 14.2.

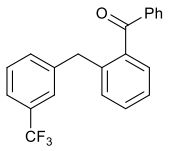
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3049, 2985, 2363, 1720, 1583, 1570, 1448, 1438, 1368, 1328, 1300, 1259, 1190, 1161, 1118, 1094, 1073, 1057, 1017, 917, 862, 822, 793, 782, 747, 734, 701, 676, 660.

MS (EI, 70 eV, %) m/z = 310 (18), 309 (83), 308 (92), 290 (12), 281 (11), 280 (54), 264 (52), 263 (59), 262 (13), 237 (16), 236 (100), 235 (59), 234 (65), 216 (18), 167 (31), 166 (23), 139 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}F_3NO$**: 309.0977; found: 309.0966.

Synthesis of phenyl(2-(3-(trifluoromethyl)benzyl)phenyl)methanone (185h)



Based on **TP2**, 2-bromo-benzophenone (0.26 g, 0.18 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). To this solution, the benzylic manganese(II) chloride solution (**182c**, 3.3 mL, 0.34 M, 1.1 mmol, 1.1 equiv) was added dropwise at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 19 : 1, R_f = 0.33) afforded product **185h** (271 mg, 0.80 mmol, 80%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.72–7.69 (m, 2H), 7.58–7.54 (m, 1H), 7.49–7.28 (m, 10H), 4.17 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.4, 141.5, 139.2, 138.9, 137.5, 133.4, 132.8 (q, ^4J(C,F) = 1.5 Hz), 131.1, 130.7, 130.6 (q, ^2J(C,F) = 27 Hz), 130.2, 129.0, 128.8, 128.5, 126.2, 125.9 (q, ^3J(C,F) = 3.8 Hz), 124.2 (q, ^1J(C,F) = 271 Hz), 123.0 (q, ^3J(C,F) = 3.9 Hz), 38.8.

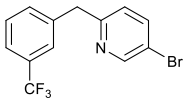
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3064, 3026, 2361, 1661, 1597, 1580, 1492, 1448, 1329, 1316, 1268, 1158, 1118, 1072, 1026, 1001, 939, 915, 880, 872, 790, 762, 736, 710, 698, 661.

MS (EI, 70 eV, %) m/z = 341 (24), 340 (100), 339 (99), 325 (18), 322 (19), 195 (18), 194 (38), 166 (16), 165 (70), 105 (26), 77 (55).

HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{15}F_3O$**: 340.1075; found: 340.1067.

Preparation of 5-bromo-2-(3-(trifluoromethyl)benzyl)pyridine (185i)



According to **TP2**, 5-bromo-2-iodopyridine (0.28 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). The benzylic manganese(II) chloride solution (**182c**, 3.3 mL, 0.34 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, the reaction mixture was then allowed to warm to room temperature and stirred overnight. Subsequently, the crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 19 : 1, R_f = 0.13) yielding product **185i** (220 mg, 0.70 mmol, 70%) as a yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.61 (d, *J* = 2.3 Hz, 1H), 7.71 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.51–7.39 (m, 4H), 7.02 (d, *J* = 8.3 Hz, 1H), 4.15 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.5, 150.8, 139.9, 139.4, 132.5 (q, ^4J(C,F) = 1.2 Hz), 131.1 (q, ^2J(C,F) = 32 Hz), 129.2, 125.8 (q, ^3J(C,F) = 3.8 Hz), 124.5, 124.2 (q, ^1J(C,F) = 271 Hz), 123.6 (q, ^3J(C,F) = 3.8 Hz), 118.8, 43.8.

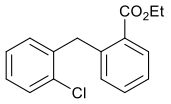
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3071, 2928, 1574, 1467, 1449, 1368, 1329, 1194, 1162, 1119, 1092, 1074, 1007, 907, 878, 849, 817, 794, 732, 700, 671, 658.

MS (EI, 70 eV, %) m/z = 317 (48), 316 (96), 315 (45), 314 (100), 296 (21), 294 (12), 247 (17), 245 (17), 236 (14), 235 (25), 167 (13), 166 (10), 159 (11), 109 (9), 43 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9BrF_3N$**: 314.9870; found: 314.9861.

Synthesis of ethyl 2-(2-chlorobenzyl)benzoate (185j)



Based on **TP2**, ethyl 2-iodobenzoate (0.28 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Thereupon, the benzylic manganese(II) chloride solution (**182d**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. The crude product was purified by flash column chromate-graphy (SiO_2, *i*-hexane : Et_2O = 9 : 1, R_f = 0.20) leading to product **185j** (188 mg, 0.68 mmol, 68%) as a pale yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.97 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.45–7.38 (m, 2H), 7.34–7.31 (m, 1H), 7.18–7.10 (m, 3H), 6.93 (dd, *J* = 6.4, 3.0 Hz, 1H), 4.49 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

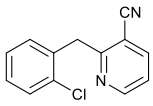
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 167.7, 140.5, 138.9, 134.3, 132.1, 131.3, 130.9, 130.7, 130.5, 129.4, 127.6, 126.9, 126.6, 61.1, 37.7, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3058, 2925, 2855, 2360, 2332, 2228, 1732, 1682, 1578, 1562, 1474, 1434, 1414, 1231, 1164, 1126, 1090, 1049, 1038, 986, 949, 805, 752, 716, 704, 678.

MS (EI, 70 eV, %) m/z = 274 (8), 245 (16), 231 (15), 230 (39), 229 (53), 228 (100), 211 (13), 194 (66), 166 (21), 165 (85), 164 (14), 163 (15), 133 (61), 105 (10), 82 (12), 81 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{15}ClO_2$**: 274.0761; found: 274.0751.

Synthesis of 2-(2-chlorobenzyl)nicotinonitrile (185k)



According to **TP2**, 2-chloronicotinonitrile (0.14 g, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). The benzylic manganese(II) chloride solution (**182d**, 3.4 mL, 0.32 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. Subsequent purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 8 : 2, R_f = 0.15) furnished product **185k** (159 mg, 0.70 mmol, 70%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.69 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.94 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.39–7.35 (m, 1H), 7.28–7.24 (m, 1H), 7.22–7.19 (m, 3H), 4.51 (s, 2H).

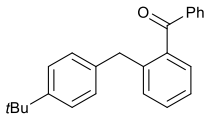
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.4, 152.8, 140.6, 135.6, 134.6, 131.6, 129.8, 128.6, 127.0, 121.4, 116.7, 109.9, 40.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3068, 2982, 2361, 1713, 1594, 1575, 1472, 1443, 1366, 1296, 1253, 1171, 1131, 1075, 1050, 1038, 1018, 908, 858, 803, 747, 728, 682, 666.

MS (EI, 70 eV, %) m/z = 228 (1), 194 (16), 191 (100), 190 (27).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9ClN_2$**: 228.0454; found: 228.0452.

Preparation of (2-(4-(*tert*-butyl)benzyl)phenyl)(phenyl)methanone (185l)



According to **TP2**, 2-bromo-benzophenone (0.26 g, 0.18 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Then, the benzylic manganese(II) chloride solution (**182e**, 3.7 mL, 0.30 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. Finally, the crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 99 : 1, R_f = 0.12) to obtain product **185l** (260 mg, 0.79 mmol, 79%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.48–7.44 (m, 1H), 7.37–7.29 (m, 3H), 7.24–7.18 (m, 3H), 7.14–7.08 (m, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 2H), 1.17 (s, 9H).

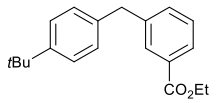
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.7, 148.8, 140.5, 139.1, 137.8, 137.5, 133.1, 130.9, 130.3 (2C), 129.0, 128.5, 128.3, 125.6, 125.2, 38.5, 34.4, 31.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3060, 3026, 2961, 2904, 2867, 2246, 1663, 1597, 1580, 1514, 1448, 1412, 1363, 1314, 1268, 1202, 1179, 1152, 1109, 1020, 1001, 936, 908, 842, 795, 763, 730, 709, 700, 668.

MS (EI, 70 eV, %) m/z = 329 (12), 328 (35), 327 (12), 313 (20), 272 (27), 271 (100), 255 (15), 254 (55), 195 (37), 194 (37), 178 (12), 177 (10), 165 (23), 105 (13), 104 (10), 77 (16), 57 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{24}H_{24}O$**: 328.1827; found: 328.1832.

Synthesis of ethyl 3-(4-(*tert*-butyl)benzyl)benzoate (185m)



According to **TP2**, ethyl 3-iodobenzoate (0.28 g, 0.17 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). The benzylic manganese(II) chloride solution (**182e**, 3.7 mL, 0.30 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 19 : 1, R_f = 0.27) afforded product **185m** (233 mg, 0.79 mmol, 79%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.88 (s, 1H), 7.85 (dt, *J* = 7.2, 1.7 Hz, 1H), 7.35–7.27 (m, 4H), 7.07 (d, *J* = 8.5 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.26 (s, 9H).

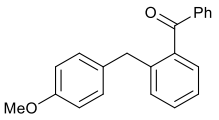
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.8, 149.2, 141.7, 137.6, 133.6, 130.2, 128.6 (2C), 127.4 (2C), 125.6, 61.6, 41.3, 34.5, 31.5, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2962, 2905, 2869, 2364, 1716, 1588, 1514, 1444, 1412, 1393, 1366, 1276, 1189, 1104, 1080, 1020, 930, 912, 840, 814, 800, 750, 740, 696.

MS (EI, 70 eV, %) m/z = 296 (17), 282 (36), 253 (20), 251 (12), 148 (29), 147 (17), 135 (19), 133 (39), 119 (14), 117 (17), 105 (21), 104 (11), 91 (29), 57 (80), 41 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{24}O_2$**: 296.1776; found: 296.1785.

Synthesis of (2-(4-methoxybenzyl)phenyl)(phenyl)methanone (185n)



According to **TP2**, 2-bromo-benzophenone (0.26 g, 0.18 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). Then, the benzylic manganese(II) chloride solution (**182f**, 4.6 mL, 0.24 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 19 : 1, R_f = 0.17) leading to product **185n** (226 mg, 0.75 mmol, 75%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.52–7.48 (m, 1H), 7.36 (t, *J* = 7.7 Hz, 3H), 7.26–7.20 (m, 3H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 8.7 Hz, 2H), 3.96 (s, 2H), 3.66 (s, 3H).

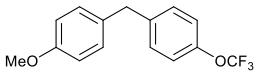
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.7, 158.0, 140.7, 138.9, 137.8, 133.2, 132.7, 130.7, 130.3, 130.2 (2C), 128.6, 128.4, 125.6, 113.8, 55.3, 38.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3061, 2854, 2933, 2835, 2251, 1661, 1611, 1597, 1581, 1510, 1464, 1448, 1315, 1266, 1243, 1176, 1152, 1108, 1073, 1000, 930, 906, 838, 808, 796, 763, 727, 703.

MS (EI, 70 eV, %) m/z = 303 (18), 302 (100), 301 (32), 287 (16), 285 (32), 284 (29), 225 (27), 195 (19), 194 (62), 193 (18), 181 (18), 165 (38), 153 (14), 152 (22), 121 (11), 112 (12), 105 (19), 77 (28).

HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{18}O_2$**: 302.1307; found: 302.1309.

Preparation of 1-methoxy-4-(4-(trifluoromethoxy)benzyl)benzene (185o)



Based on **TP2**, 1-iodo-4-(trifluoromethoxy)benzene (0.29 g, 0.16 mL, 1.0 mmol, 1.0 equiv) and $FeCl_2$ (13 mg, 0.10 mmol, 0.10 equiv) were dissolved in THF (1.0 mL). The benzylic manganese(II) chloride solution (**182f**, 4.6 mL, 0.24 M, 1.1 mmol, 1.1 equiv) was added dropwise to this solution at 0 °C, the reaction mixture was then allowed to warm to room temperature and stirred overnight. Subsequent purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 99 : 1, R_f = 0.26) generated product **185o** (173 mg, 0.61 mmol, 61%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.20 (d, *J* = 8.8 Hz, 2H), 7.15–7.10 (m, 4H), 6.87 (d, *J* = 8.7 Hz, 2H), 3.94 (s, 2H), 3.81 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.3, 147.7, 140.5, 132.7, 130.1, 130.0, 121.1, 120.7 (q, ^1J(C,F) = 255 Hz), 114.2, 55.4, 40.5.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −57.9.

IR (ATR, cm^{-1}) ṽ = 3006, 2956, 2936, 2911, 2838, 1612, 1585, 1508, 1465, 1441, 1300, 1245, 1219, 1155, 1108, 1036, 1020, 909, 860, 807, 774, 733, 670.

MS (EI, 70 eV, %) m/z = 283 (19), 282 (100), 281 (39), 267 (10), 251 (23), 197 (37), 165 (17), 153 (12), 152 (14), 121 (22).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}F_3O_2$**: 282.0868; found: 282.0866.

3. Nickel-Catalyzed Cross-Coupling of Functionalized Organomanganese Reagents with Aryl and Heteroaryl Halides Promoted by 4-Fluorostyrene

3.1. Typical Procedures

Typical procedure for the preparation of the benzylic manganese(II) chlorides (182g–j) (TP1)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), followed by freshly distilled THF (3.0 mL) or MTBE (1.9 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv). The mixture was cooled to 0 °C, the corresponding benzylic chloride (3.0 mmol, 1.0 equiv) was added at once and maintained at 0 °C until a complete conversion of starting material was observed. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was complete, the solution of benzylic manganese chloride was separated from the resulting salts *via* a syringe equipped with a filter and transferred to another pre-dried and argon-flushed *Schlenk*-tube, before being titrated with an iodine solution in THF.

Typical procedure for the preparation of bis-(aryl)manganese reagents of type 188 (TP2)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.42 g, 10 mmol, 1.2 equiv) and heated at 450 °C under high vacuum for 5 min. After cooling to room temperature under vigorous stirring, Mg turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were added. The mixture was cooled to 0 °C, the corresponding aryl bromide (8.0 mmol, 1.0 equiv) was added and the reaction mixture was allowed to warm to room temperature. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was complete, the solution was transferred to another predried and argon-flushed *Schlenk*-tube, before being titrated against iodine. The remaining arylmagnesium halide was cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The resulting bis-(aryl)-manganese reagent was titrated with an iodine solution one more time before being used.

Typical procedure for the preparation of bis-(alkyl)manganese reagents of type 190 (TP3)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.42 g, 10 mmol, 1.20 equiv) and heated at 450 °C under high vacuum for 5 min. After cooling to room temperature under vigorous stirring, Mg turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were added. The mixture was cooled to 0 °C, the corresponding alkyl bromide (8.0 mmol, 1.0 equiv) was added, and the reaction mixture was allowed to warm to room temperature. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was complete, the solution was transferred to

another predried and argon-flushed *Schlenk*-tube, before being titrated with iodine. The remaining alkylmagnesium reagent was cooled to –20 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The resulting bis-(alkyl)manganese reagent was titrated with iodine one more time before being used.

Typical procedure for the Ni-catalyzed 4-fluorostyrene-mediated cross-coupling of benzylic manganese chlorides of type 182 with several electrophiles (TP4)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum was charged with $Ni(acac)_2$ (13 mg, 0.05 mmol, 0.05 equiv) as catalyst, 4-fluorostyrene (24 mg, 0.20 mmol, 0.20 equiv), the aryl iodide or heteroaryl chloride as electrophile (1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL). The resulting suspension was cooled to 0 °C and the prior prepared benzylic manganese chloride solution (1.2 mmol, 1.2 equiv) was added dropwise at the prior adjusted temperature. The reaction conversion was monitored by GC-analysis of hydrolyzed aliquots. After full conversion of the selected electrophile, the reaction mixture was quenched with a sat. aqueous NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by flash column chromatography afforded the desired products.

Typical procedure for the Ni-catalyzed 4-fluorostyrene-mediated cross-coupling of bis-(aryl)manganese reagents of type 188 with several electrophiles (TP5)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum was charged with $Ni(acac)_2$ (13 mg, 0.05 mmol, 0.05 equiv) as catalyst, 4-fluorostyrene (24 mg, 0.20 mmol, 0.20 equiv), the aryl iodide or heteroaryl chloride as electrophile (1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL). The resulting suspension was cooled to 0 °C and the prior prepared bis-(aryl)manganese solution (0.70 mmol, 0.70 equiv) was added dropwise at the prior adjusted temperature. The reaction conversion was monitored by GC-analysis of hydrolyzed aliquots. After full conversion of the electrophile, the reaction mixture was quenched with a sat. aqueous NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by flash column chromatography afforded the desired products.

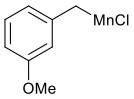
Typical procedure for the Ni-catalyzed 4-fluorostyrene-mediated cross-coupling of bis-(alkyl)manganese reagents of type 190 with 2-chloro-substituted pyridines (TP6)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum was charged with $Ni(acac)_2$ (13 mg, 0.05 mmol, 0.05 equiv) as catalyst, 4-fluorostyrene (24 mg, 0.20 mmol, 0.20 equiv), the selected 2-chloropyridine (1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL). The resulting suspension was cooled to 0 °C and the prior prepared bis-(alkyl)manganese solution

(0.70 mmol, 0.70 equiv) was added dropwise at the prior adjusted temperature. The reaction conversion was monitored by GC-analysis of hydrolyzed aliquots. After full conversion, the reaction mixture was quenched with sat. aqueous NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by flash column chromatography afforded the desired products.

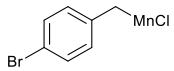
3.2. Preparation of the Benzylic Manganese(II) Chlorides (182g–j)

Preparation of (3-methoxybenzyl)manganese(II) chloride (182g)



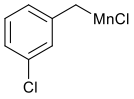
According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 1-(Chloromethyl)-3-methoxybenzene (**183g**, 0.47 g, 0.44 mL, 3.0 mmol, 1.0 equiv) was added at once at 0 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of (3-methoxybenzyl)manganese(II) chloride (**182g**) was determined by titration with iodine in THF (0.32 M, 73%).

Preparation (4-bromobenzyl)manganese(II) chloride (182h)



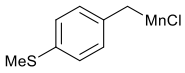
According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 1-Bromo-4-(chloromethyl)benzene (**183h**, 0.62 g, 3.0 mmol, 1.0 equiv) was added at once at 0 °C and the reaction mixture was stirred for 2 h at the given temperature. The concentration of (4-bromobenzyl)manganese(II) chloride (**182h**) was determined by titration with iodine in THF (0.22 M, 50%).

Preparation of (3-chlorobenzyl)manganese(II) chloride (182i)



According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), MTBE (1.8 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. 1-Chloro-3-(chloromethyl) benzene (**183i**, 0.48 g, 0.40 mL, 3.0 mmol, 1.0 equiv) was added at once at 0 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of (3-chlorobenzyl)manganese(II) chloride (**182i**) was determined by titration with iodine in THF (0.47 M, 88%).

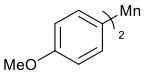
Preparation of (4-(methylthio)benzyl)manganese(II) chloride (182j)



According to **TP1**, magnesium turnings (0.18 g, 7.2 mmol, 2.4 equiv), THF (3.0 mL) and $MnCl_2 \cdot 2LiCl$ (3.8 mL, 3.8 mmol, 1.0 M in THF, 1.3 equiv) were used. (4-(Chloromethyl)phenyl)(methyl)sulfane (**183j**, 0.68 g, 0.58 mL, 3.0 mmol, 1.0 equiv) was added at once at 0 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of (4-(methylthio)-benzyl)manganese(II) chloride (**182j**) was determined by titration with iodine in THF (0.22 M, 50%).

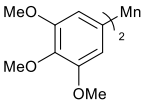
3.3. Preparation of the Bis-(Aryl)manganese Reagents of Type 188

Preparation of bis-(4-methoxyphenyl)manganese (188a)



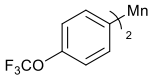
Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 4-bromoanisole (1.5 g, 1.0 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(4-methoxyphenyl)-manganese (**188a**) was determined by titration with iodine in THF (0.22 M).

Preparation of bis-(3,4,5-trimethoxyphenyl)manganese (188b)



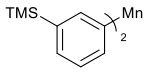
Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 5-bromo-1,2,3-trimethoxybenzene (2.0 g, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting (3,4,5-trimethoxyphenyl)manganese (**188b**) was determined by titration with iodine in THF (0.22 M).

Preparation of bis-(4-(trifluoromethoxy)phenyl)manganese (188c)



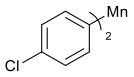
Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 1-bromo-4-(trifluoromethoxy)benzene (1.9 g, 1.2 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(4-(trifluoromethoxy)phenyl)manganese (**188c**) was determined by titration with iodine in THF (0.22 M).

Preparation of bis-(3-(trimethylsilyl)phenyl)manganese (188d)



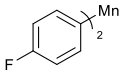
Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, (3-bromo-phenyl)trimethylsilane (1.8 g, 1.5 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF).The concentration of the resulting bis-(3-(trimethylsilyl)phenyl)manganese (**188d**) was determined by titration with iodine in THF (0.22 M).

Preparation of bis-(4-chlorophenyl)manganese (188e)



Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 1-bromo-4-chlorobenzene (1.5 g, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(4-chlorophenyl)manganese (**188e**) was determined by titration with iodine in THF (0.22 M).

Preparation of bis-(4-fluorophenyl)manganese (188f)

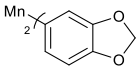


Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 1-bromo-4-fluorobenzene (1.4 g, 0.88 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(4-fluorophenyl)manganese (**188f**) was determined by titration with iodine in THF (0.26 M).

Preparation of bis-(2-(trifluoromethyl)phenyl)manganese (188g)

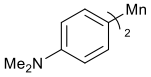
Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 1-bromo-2-(trifluoromethyl)benzene (1.8 g, 1.1 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(2-(trifluoromethyl)phenyl)manganese (**188g**) was determined by titration with iodine in THF (0.28 M).

Preparation of bis-benzo[*d*][1,3]dioxol-5-ylmanganese (188h)



Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 5-bromobenzo[*d*][1,3]dioxole (1.6 g, 1.0 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF).The concentration of the resulting bis-benzo[*d*][1,3]dioxol-5-ylmanganese (**188h**) was determined by titration with iodine in THF (0.28 M).

Preparation of bis-(4-(dimethylamino)phenyl)manganese (188i)



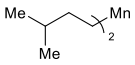
Based on **TP2**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 4-bromo-*N*,*N*-dimethylaniline (1.6 g, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained arylmagnesium halide was again cooled to 0 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(4-(dimethylamino)phenyl)manganese (**188i**) was determined by titration with iodine in THF (0.22 M).

3.4. Preparation of Bis-(Alkyl)manganese Reagents of Type 190

Preparation of bis-(cyclohexyl)manganese (190a)

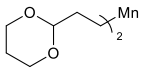
Based on **TP3**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8 mL) were used. The mixture was cooled to 0 °C, bromocyclohexane (1.3 g, 1.0 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained alkylmagnesium halide was cooled to −20 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(cyclohexyl)manganese (**190a**) was determined by titration with iodine in THF (0.17 M).

Preparation of bis-(isopentyl)manganese (190b)



Based on **TP3**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 1-bromo-3-methylbutane (1.2 g, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained alkylmagnesium halide was cooled to −20 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(isopentyl)manganese (**190b**) was determined by titration with iodine in THF (0.25 M).

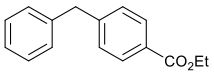
Preparation of bis-(2-(1,3-dioxan-2-yl)ethyl)manganese (190c)



Based on **TP3**, LiCl (0.42 g, 10 mmol, 1.2 equiv), magnesium turnings (0.47 g, 19 mmol, 2.4 equiv) and freshly distilled THF (8.0 mL) were used. The mixture was cooled to 0 °C, 2-(2-bromo-ethyl)-1,3-dioxane (1.6 g, 1.1 mL, 8.0 mmol, 1.0 equiv) was added and the reaction was allowed to warm to room temperature. The obtained alkylmagnesium halide was cooled to −20 °C and transmetalated with a solution of $MnCl_2 \cdot 2LiCl$ (0.55 equiv, 1.0 M in THF). The concentration of the resulting bis-(2-(1,3-dioxan-2-yl)ethyl)manganese (**190c**) was determined by titration with iodine in THF (0.24 M).

3.5 Nickel-Catalyzed, 4-Fluorostyrene-Mediated Cross-Couplings of Benzylic Manganese Chlorides of Type 182 with Electrophiles

Ethyl 4-benzylbenzoate (185c)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 ml) were used. The reaction mixture was cooled to 0 °C, benzylmanganese(II) chloride (**182a**, 3.9 mL, 1.2 mmol, 0.31 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 30 min. Purification by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.29) afforded the desired product **185c** (172 mg, 0.72 mmol, 72%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.93 (d, *J* = 8.2 Hz, 2H), 7.28–7.16 (m, 5H), 7.12 (d, *J* = 6.9 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).

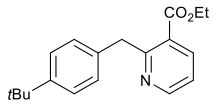
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.6, 146.5, 140.3, 129.9, 129.0 (2 C), 128.7, 128.6, 126.5, 60.9, 42.0, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1737, 1713, 1611, 1602, 1272, 1239, 1045, 937, 753, 740.

MS (EI, 70 eV, %) m/z = 241 (18), 240 (66), 196 (20), 195 (100), 168 (15), 167 (78), 166 (19), 165 (57), 151 (22), 91 (10).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{16}O_2$**: 240.1150; found: 240.1139.

Ethyl 2-[4-(*tert*-butyl)benzyl]nicotinate (185p)



Based on **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, [4-(*tert*-butyl)benzyl]manganese(II) chloride (**182e**, 3.3 mL, 1.2 mmol, 0.37 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 30 min. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9:1, R_f = 0.18) afforded **185p** (283 mg, 0.95 mmol, 95%) as a yellowish liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.71 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.17 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.33–7.19 (m, 5H), 4.58 (s, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3 H), 1.30 (s, 9H).

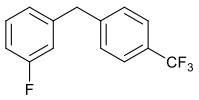
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.4, 161.2, 151.6, 148.6, 138.3, 136.4, 128.4, 126.1, 125.0, 121.0, 61.2, 41.6, 34.1, 31.2, 14.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2962, 1722, 1582, 1567, 1514, 1437, 1392, 1130, 1078, 807.

MS (EI, 70 eV, %) m/z = 298 (20), 297 (100), 296 (42), 283 (12), 282 (63), 236 (12), 195 (15), 194 (20), 166 (10), 57 (10).

HRMS (EI, 70 eV) m/z calc. for **$C_{19}H_{23}NO_2$**: 297.1729; found: 297.1724.

1-fluoro-3-[4-(trifluoromethyl)benzyl]benzene (185q)



With reference to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 4-iodobenzotrifluoride (272 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and a solution of (3-fluorobenzyl)manganese(II) chloride (**182b**, 4.0 mL, 1.2 mmol, 0.30 M in THF, 1.2 equiv) was added dropwise at the given temperature and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane, R_f = 0.45) afforded **185q** (187 mg, 0.74 mmol, 74%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.59 (d, *J* = 8.1 Hz, 2H), 7.32 (dd, *J* = 8.3, 2.2 Hz, 2H), 7.30–7.26 (m, 1H), 7.03–6.86 (m, 3H), 4.06 (s, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 162.9 (d, ^1J(C,F) = 246 Hz), 144.2 (q, ^4J(C,F) = 1.8 Hz), 142.3 (d, ^3J(C,F) = 7.2 Hz), 129.9 (d, ^3J(C,F) = 8.3 Hz), 129.0, 128.6 (q, ^2J(C,F) = 32 Hz), 125.4 (q, ^2J(C,F) = 3.8 Hz), 124.4 (d, ^4J(C,F) = 2.8 Hz), 124.1 (q, ^1J(C,F) = 270 Hz), 115.7 (d, ^2J(C,F) = 21 Hz), 113.3 (d, ^2J(C,F) = 21 Hz), 41.2 (d, ^4J(C,F) = 1.6 Hz).

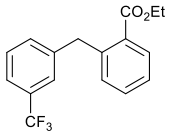
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –113.1, –62.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1613, 1589, 1509, 1486, 1449, 1417, 1321, 1250, 1160, 1018.

MS (EI, 70 eV, %) m/z = 255 (11), 254 (93), 253 (24), 186 (16), 185 (100), 184 (17), 183 (41), 165 (23), 109 (17), 82 (16), 57 (11), 43 (25), 41 (10), 40 (10).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_{10}F_4$**: 254.0719; found: 254.0718.

Ethyl 2-[(3-trifluoromethyl)benzyl]benzoate (185r)



Based on **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 2-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and [3-(trifluoromethyl)benzyl]manganese(II) chloride (**182c**, 3.9 mL, 1.2 mmol, 0.31 M in THF, 1.20 equiv) was added dropwise and the mixture was stirred for 1 h at the prior adjusted temperature. Subsequent purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.51) furnished **185r** (276 mg, 0.90 mmol, 90%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.96 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.49 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.47–7.44 (m, 2H), 7.42–7.31 (m, 3H), 7.24 (d, *J* =7.7 Hz, 1H), 4.47 (s, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 167.3, 141.8, 140.7, 130.0 (q, ^4J(C,F) = 1.8 Hz), 131.9, 131.4, 130.7, 130.4 (q, ^2J(C,F) = 32 Hz), 130.2, 128.5, 126.5, 125.3 (q, ^3J(C,F) = 3.8 Hz), 122.6 (q, ^3J(C,F) = 4.0 Hz), 60.8, 39.3, 14.0.

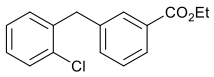
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1713, 1446, 1327, 1296, 1256, 1159, 1118, 1093, 1072, 789.

MS (EI, 70 eV, %) m/z = 308 (1), 279 (16), 263 (39), 262 (100), 165 (30), 159 (61), 133 (14), 109 (13).

HRMS (EI, 70 eV) m/z calc. for **$C_{17}H_{15}F_3O_2$**: 308.1024; found: 308.1018.

Ethyl 3-(2-chlorobenzyl)benzoate (185s)



With reference to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 3-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, (2-chlorobenzyl)manganese(II) chloride (**182d**, 5.5 mL, 1.2 mmol, 0.22 M in THF, 1.2 equiv) was added dropwise and the resulting reaction mixture was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.20) to afford **185s** (197 mg, 0.71 mmol, 71%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.94–7.89 (m, 2H), 7.40–7.34 (m, 3H), 7.21–7.13 (m, 3H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.16 (s, 2H), 1.39 (t, *J* = 7.1Hz, 3H).

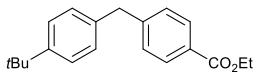
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.4, 139.6, 137.9, 134.0, 133.2, 130.8, 130.5, 129.9, 129.4, 128.3, 127.7, 127.4, 126.7, 60.8, 38.8, 14.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1714, 1588, 1472, 1442, 1392, 1366, 1304, 1276, 1184, 744.

MS (EI, 70 eV, %) m/z = 275 (16), 274 (66), 239 (13), 230 (15), 229 (100), 166 (21), 165 (74).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{15}ClO_2$**: 274.0761; found: 274.0751.

Ethyl 4-[4-(*tert*-butyl)benzyl]benzoate (185t)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, [4-(*tert*-butyl)benzyl]manganese(II) chloride (**182e**, 3.3 mL, 1.2 mmol, 0.37 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.34) led to the desired product **185t** (210 mg, 0.71 mmol, 71%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.92 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.26 (s, 9H).

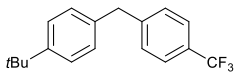
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 167.1, 149.6, 147.0, 137.6, 130.2, 129.4, 129.0, 128.9, 125.9, 61.2, 41.9, 34.9, 31.8, 14.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2961, 1714, 1609, 1576, 1269, 1176, 1098, 1020, 755, 739.

MS (EI, 70 eV, %) m/z = 296 (21), 282 (19), 281 (100).

HRMS (EI, 70 eV) m/z calc. for **$C_{20}H_{24}O_2$**: 296.1776; found: 296.1770.

1-(*tert*-butyl)-4-[(4-tifluoromethyl)benzyl]benzene (185u)



With reference to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 4-iodobenzotrifluoride (272 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, [4-(*tert*-butyl)benzyl]manganese(II) chloride (**182e**, 3.3 mL, 1.2 mmol, 0.37 M in THF, 1.2 equiv) was added dropwise, and the resulting solution was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane, R_f = 0.44) to obtain **185u** (181 mg, 0.62 mmol, 62%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.58 (d, *J* = 8.0 Hz, 2H), 7.38–7.34 (m, 4H), 7.15 (d, *J* = 8.5 Hz, 2H), 4.05 (s, 2H), 1.36 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 149.2, 145.2 (q, ^4J(C,F) = 1.8 Hz), 136.8, 129.0, 128.4, 128.3 (q, ^2J(C,F) = 32 Hz), 125.4, 125.2 (q, ^3J(C,F) = 3.8 Hz), 124.3 (q, ^1J(C,F) = 271 Hz), 41.1, 34.3, 31.2.

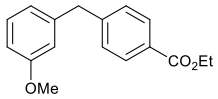
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –62.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2962, 1617, 1321, 1268, 1236, 1160, 1117, 1065, 1017, 816.

MS (EI, 70 eV, %) m/z = 292 (18), 278 (17), 277 (100), 158 (22).

HRMS (EI, 70 eV) m/z calc. for **$C_{18}H_{19}F_3$**: 292.1439; found: 292.1426.

Ethyl 4-(3-methoxybenzyl)benzoate (185v)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The mixture was cooled to 0 °C, (3-methoxybenzyl)manganese(II) chloride (**182g**, 3.8 mL, 1.2 mmol, 0.32 M in THF, 1.2 equiv) was added dropwise, and the resulting solution was stirred for 1 h at the given temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.40) to afford **185v** (194 mg, 0.72 mmol, 72%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.00 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.24 (t, *J* = 7.9 Hz, 1H), 6.80 (dd, *J* = 8.1, 2.6 Hz, 2H), 6.76–6.73 (m, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.03 (s, 2H), 3.80 (s, 3H), 1.41(t, *J* = 7.1 Hz, 3H).

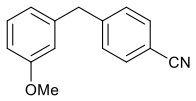
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.4, 159.6, 146.0, 141.5, 129.6, 129.4, 128.7, 128.3, 121.1, 114.6, 111.4, 60.6, 54.9, 41.7, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1712, 1597, 1584, 1488, 1271, 1256, 1176, 1148, 1100, 871.

MS (EI, 70 eV, %) m/z = 271 (18), 270 (100), 225 (49), 197 (27), 164 (18), 152 (14), 121 (18), 112 (10).

HRMS (EI, 70 eV) m/z calc. for **$C_{17}H_{18}O_3$**: 270.1256; found: 270.1251.

4-(3-methoxybenzyl)benzonitrile (185w)



Based on **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 4-iodobenzonitrile (229 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The mixture was cooled to 0 °C, (3-methoxybenzyl)manganese(II)chloride (**182g**, 3.8 mL, 1.2 mmol, 0.32 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 1 h at the prior adjusted temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.23) gave **185w** (123 mg, 0.55 mmol, 55%) as a pale yellow liquid.

^{1}H-NMR ($CDCl_3$, 600 MHz, ppm) δ = 7.57 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.25–7.21 (m, 1H), 6.79 (dd, *J* = 8.0, 2.2 Hz, 1H), 6.76 (d, *J* = 9.1 Hz, 1H), 6.72–6.69 (m, 1H), 4.00 (s, 2H), 3.78 (s, 3H).

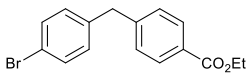
^{13}C-NMR ($CDCl_3$, 150 MHz, ppm) δ = 159.8, 146.4, 140.8, 132.2, 129.6, 129.5, 121.2, 118.9, 114.9, 111.6, 110.0, 55.1, 41.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2226, 1598, 1488, 1464, 1256, 1148, 1046, 1020, 840, 780.

MS (EI, 70 eV, %) m/z = 224 (17), 223 (100), 222 (19), 208 (41), 192 (20), 190 (31), 180 (42), 165 (15), 152 (11), 121 (14).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{13}NO$**: 223.0997; found: 223.0990.

Ethyl 4-(4-bromobenzyl)benzoate (185x)



Based on **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and (4-bromobenzyl)manganese(II) chloride (**182h**, 5.5 mL, 1.2 mmol, 0.22 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 1 h at the given temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.49) afforded the desired product **185x** (194 mg, 0.61 mmol, 61%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.00 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.00 (s, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

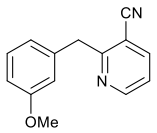
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.3, 145.4, 139.0, 131.5, 130.5, 129.7, 129.6, 128.6, 120.1, 60.7, 41.1, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1711, 1610, 1487, 1271, 1176, 1070, 1020, 921, 789, 753.

MS (EI, 70 eV, %) m/z = 321 (10), 320 (61), 319 (11), 318 (59), 275 (10), 274 (61), 273 (11), 272 (60), 246 (30), 244 (30), 240 (27), 239 (28), 211 (12), 195 (34), 167 (37), 166 (37), 165 (100), 152 (10).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{15}BrO_2$**: 318.0255; found: 318.0259.

2-(3-methoxybenzyl)nicotinonitrile (185y)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 2-chloro-3-pyridinecarbonitrile (139 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, (3-methoxybenzyl)manganese(II) chloride (**182g**, 3.8 mL, 1.2 mmol, 0.32 M in THF, 1.2 equiv) was added dropwise, and stirred for 1 h at the prior adjusted temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.15) to afford the desired product **185y** (111 mg, 0.50 mmol, 50%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 600 MHz, ppm) δ = 8.73 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.90 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.25 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.24–7.19 (m, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.94–6.92 (m, 1H), 6.77 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.35 (s, 2H), 3.78 (s, 3H).

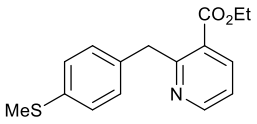
^{13}C-NMR ($CDCl_3$, 150 MHz, ppm) δ = 163.6, 159.8, 152.8, 140.7, 139.0, 129.7, 121.5, 121.4, 117.0, 114.8, 112.6, 109.2, 55.3, 43.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2936, 2228, 1734, 1580, 1488, 1432, 1404, 1256, 1148, 1044.

MS (EI, 70 eV, %) m/z = 224 (20), 223 (100), 208 (14), 192 (11), 181 (17), 179 (17).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_{12}N_2O$**: 224.0950; found: 224.0941.

2-[(4-methylthio)benzyl]nicotinonitrile (185z)



Based on **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and subsequently, [4-(methylthio)benzyl]manganese(II) chloride (**182j**, 5.5 mL, 1.2 mmol, 0.32 M in THF, 1.2 equiv) was added dropwise and the mixture was stirred for 1 h at the given temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.27) afforded **185z** (250 mg, 0.87 mmol, 87%) as an orange oil.

^{1}H-NMR ($CDCl_3$, 600 MHz, ppm) δ = 8.67 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.16 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.22 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 4.53 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 150 MHz, ppm) δ = 166.4, 161.1, 151.9, 138.6, 136.8, 135.7, 129.5, 126.9, 126.0, 121.3, 61.4, 41.8, 16.2, 14.2.

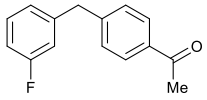
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 1718, 1568, 1492, 1436, 1404, 1254, 1130, 1078, 796.

MS (EI, 70 eV, %) m/z = 288 (13), 287 (77), 286 (37), 258 (22), 241 (22), 226 (11), 214 (52), 212 (11), 211 (69), 198 (17), 197 (12), 195 (19), 194 (100), 182 (12), 167 (71), 166 (51), 154 (16), 139 (21), 137 (11).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{17}NO_2S$**: 287.0980; found: 287.0974.

3.6. Nickel-Catalyzed Cross-Couplings of Benzylic Manganese Chlorides 182 with 4-Iodoaryl Ketones of Type 186

1-[4-(3-fluorobenzyl)phenyl]ethan-1-one (187a)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 1-(4-iodophenyl)ethan-1-one (246 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The mixture was cooled to 0 °C, (3-fluorobenzyl)manganese(II) chloride (**182b**, 4.0 mL, 1.2 mmol, 0.30 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 30 min. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.23) to yield **187a** (200 mg, 0.88 mmol, 88%) as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.92 (d, *J* = 8.3 Hz, 2H), 7.36–7.23 (m, 3H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.95 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.92–6.86 (m, 1H), 4.04 (s, 2H), 2.60 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 197.5, 162.8 (d, ^1J(C,F) = 246 Hz), 145.7, 142.3 (d, ^3J(C,F) = 7.2 Hz), 135.3, 129.9 (d, ^3J(C,F) = 8.3 Hz), 128.9, 128.5, 124.4 (d, ^4J(C,F) = 2.8 Hz), 115.6 (d, ^2J(C,F) = 21 Hz), 113.2 (d, ^2J(C,F) = 21 Hz), 41.3, 26.4.

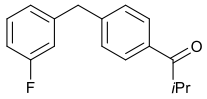
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –113.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 1679, 1605, 1588, 1485, 1448, 1412, 1357, 1265, 946.

MS (EI, 70 eV, %) m/z = 228 (35), 214 (16), 213 (100), 183 (25), 165 (31), 42 (10).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{13}FO$**: 228.0950; found: 228.0946.

1-[4-(3-fluorobenzyl)phenyl]-2-methylpropan-1-one (187b)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 1-(4-iodophenyl)-2-methylpropan-1-one (274 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of (3-fluorobenzyl)-manganese(II) chloride (**182b**, 4.0 mL, 1.2 mmol, 0.30 M in THF, 1.2 equiv) was added dropwise and the mixture was stirred for 30 min. Purification of the crude product by flash column chromato-graphy (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.40) afforded **187b** (219 mg, 0.85 mmol, 85%) as a yellowish liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.90 (d, *J* = 8.3 Hz, 2H), 7.30–7.23 (m, 3H), 6.97 (d, *J* = 6.7 Hz, 1H), 6.92 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.90–6.84 (m, 1H), 4.02 (s, 2H), 3.53 (hept, *J* = 6.9 Hz, 1H), 1.21 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.8, 162.8 (d, ^1J(C,F) = 246 Hz), 145.3, 142.4 (d, ^3J(C,F) = 7.3 Hz), 134.3, 129.9 (d, ^3J(C,F) = 8.3 Hz), 129.0, 128.6, 124.4 (d, ^4J(C,F) = 2.8 Hz), 115.7 (d, ^2J(C,F) = 21 Hz), 113.2 (d, ^2J(C,F) = 21 Hz), 41.4, 35.1, 19.0.

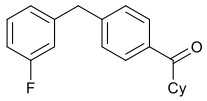
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –113.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2970, 1677, 1603, 1588, 1486, 1225, 1159, 1135, 947, 783.

MS (EI, 70 eV, %) m/z = 256 (1), 214 (15), 213 (100), 183 (17), 165 (16).

HRMS (EI, 70 eV) m/z calc. for **$C_{17}H_{17}FO$**: 256.1263; found: 256.1261.

Cyclohexyl[4-(3-fluorobenzyl)phenyl]methanone (187c)



With reference to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), cyclohexyl(4-iodophenyl)methanone (314 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, (3-fluoro-benzyl)manganese(II) chloride (**182b**, 4.0 mL, 1.2 mmol, 0.30 M in THF, 1.2 equiv) was added dropwise and the mixture was stirred for 30 min. After purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f =0.36), product **187c** (240 mg, 0.81 mmol, 81%) was obtained as a colorless liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.91 (d, *J* = 8.3 Hz, 2H), 7.32–7.26 (m, 3H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.95 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.89 (dd, *J* =10.0, 2.0 Hz, 1H), 4.04 (s, 2H), 3.26 (tt, *J* = 11.5, 3.2 Hz, 1H), 1.95–1.82 (m, 4H), 1.80–1.71 (m, 1H), 1.61–1.21 (m, 5H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.2, 162.8 (d, ^1J(C,F) = 246 Hz), 145.2, 142.4 (d, ^3J(C,F) = 7.2 Hz), 134.5, 129.8 (d, ^3J(C,F) = 8.3 Hz), 128.9, 128.5, 124.4 (d, ^4J(C,F) = 2.8 Hz), 115.6 (d, ^2J(C,F) = 21 Hz), 113.1 (d, ^2J(C,F) = 21 Hz), 45.4, 41.3, 29.3, 25.8, 25.7.

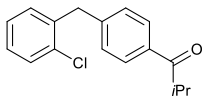
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –113.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2927, 2852, 1674, 1604, 1588, 1570, 1486, 1448, 1248, 1170.

MS (EI, 70 eV, %) m/z = 213 (16), 212 (100), 187 (24), 183 (13), 165 (14).

HRMS (EI, 70 eV) m/z calc. for **$C_{20}H_{21}FO$**: 296.1576; found: 296.1568.

1-[4-(2-chlorobenzyl)phenyl]-2-methylpropan-1-one (187d)



According to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 1-(4-iodophenyl)-2-methylpropan-1-one (274 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of (2-chlorobenzyl)-manganese(II) chloride (**182d**, 5.5 mL, 1.2 mmol, 0.22 M in THF, 1.2 equiv) was added dropwise and the mixture was stirred for 30 min. Purification of the crude product (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.26) led to the desired product **187d** (217 mg, 0.80 mmol, 80%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 100 MHz, ppm) δ = 7.92 (d, *J* = 8.3 Hz, 2H), 7.45–7.38 (m, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.25–7.16 (m, 3H), 4.18 (s, 2H), 3.55 (hept, *J* = 6.8 Hz, 1H), 1.23 (d, *J* = 6.8 Hz, 6H).

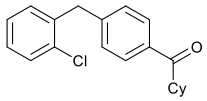
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.8, 144.6, 137.5, 134.2, 134.0, 130.9, 129.5, 128.9, 128.4, 127.8, 126.8, 39.0, 35.1, 19.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1678, 1644, 1606, 1470, 1444, 1414, 1226, 1160, 980, 748.

MS (EI, 70 eV, %) m/z = 272 (1), 231 (32), 230 (15), 229 (100), 166 (28), 165 (53).

HRMS (EI, 70 eV) m/z calc. for **$C_{17}H_{17}ClO$**: 272.0968; found: 272.0970.

[4-(2-chlorobenzyl)phenyl](cyclohexyl)methanone (187e)



With reference to **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), cyclohexyl(4-iodophenyl)methanone (314 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, (2-chlorobenzyl)-manganese(II) chloride (**182d**, 5.5 mL, 1.2 mmol, 0.22 M in THF, 1.2 equiv) was added dropwise and the reaction mixture was stirred for 30 min. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.20) leading to **187e** (219 mg, 0.70 mmol, 70%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.90 (d, *J* = 8.3 Hz, 2H), 7.45–7.37 (m, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.26–7.14 (m, 3H), 4.18 (s, 2H), 3.26 (tt, *J* = 11.5, 3.2 Hz, 1H), 1.96–1.79 (m, 4H), 1.79–1.70 (m, 1H), 1.60–1.23 (m, 5H).

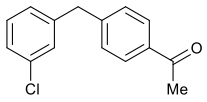
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.2, 144.6, 137.5, 134.3, 134.1, 130.9, 129.5, 128.9, 128.3, 127.8, 126.8, 45.4, 39.0, 29.3, 25.8, 25.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2928, 1676, 1606, 1444, 1414, 1250, 1210, 1184, 974, 946.

MS (EI, 70eV, %) m/z = 312 (1), 229 (13), 228 (100), 187 (23), 166 (13), 165 (24).

HRMS (EI, 70 eV) m/z calc. for **$C_{20}H_{21}ClO$**: 312.1281; found: 312.1283.

1-[4-(3-chlorobenzyl)phenyl]ethan-1-one (187f)



Based on **TP4**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 1-(4-iodophenyl)ethan-1-one (246 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of (3-chlorobenzyl)manganese(II) chloride (**182i**, 2.6 mL, 1.2 mmol, 0.47 M in THF, 1.2 equiv) was added dropwise and the mixture was stirred for 30 min at the given temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.29) led to the desired product **187f** (172 mg, 0.70 mmol, 70%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 600 MHz, ppm) δ = 7.90 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.23–7.18 (m, 2H), 7.16 (s, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 4.00 (s, 2H), 2.58 (s, 3H).

^{13}C-NMR ($CDCl_3$, 150 MHz, ppm) δ = 197.8, 145.9, 142.2, 135.6, 134.5, 130.0, 129.2, 129.1, 128.9, 127.2, 126.8, 41.6, 26.7.

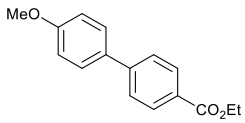
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1678, 1594, 1412, 1356, 1266, 1206, 1182, 1164, 1114, 1092.

MS (EI, 70 eV, %) m/z = 244 (4), 231 (32), 230 (15), 229 (100), 166 (41), 165 (63).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{13}ClO$**: 244.0655; found: 244.0647.

3.7. Ni-Catalyzed Cross-Coupling of Bis-(Aryl)manganese Reagents of Type 188 with Electrophiles

Ethyl 4′-methoxy[1,1′-biphenyl]-4-carboxylate (189a)



According to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The solution was cooled to 0 °C, bis-(4-methoxyphenyl)manganese (**188a**, 2.8 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the reaction mixture was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, i-hexane : EtOAc = 19:1, R_f = 0.27) leading to **189a** (228 mg, 0.89 mmol, 89%) as a white solid.

M.p. 107 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz) δ = 8.09 (d, *J* = 8.4 Hz, 2H), 7.60 (dd, *J* = 17.7, 8.6 Hz, 4H), 7.00 (d, *J* = 8.8 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H).

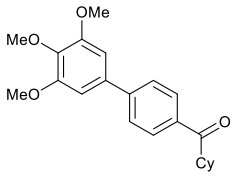
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.4, 159.6, 144.9, 132.3, 129.9, 128.4, 128.2, 126.2, 114.2, 60.7, 55.2, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2924, 1704, 1600, 1248, 1108, 1036, 828, 768, 718, 698.

MS (EI, 70 eV, %) m/z = 257 (14), 256 (79), 228 (51), 213 (19), 212 (16), 211 (100), 185 (17), 183 (24), 168 (30), 152 (20), 140 (22), 139 (48).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{16}O_3$**: 256.1099; found: 256.1093.

Cyclohexyl(3′,4′,5′-trimethoxy[1,1′-biphenyl]-4-yl)methanone (189b)



With reference to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), cyclohexyl(4-iodophenyl)methanone (314 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-(3,4,5-trimethoxyphenyl)manganese (**188b**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.42) afforded **189b** (169 mg, 0.50 mmol, 50%) as pale yellow solid.

M.p. 81 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz) δ = 8.02 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 6.83 (s, 2H), 3.96 (s, 6H), 3.92 (s, 3H), 3.31 (tt, *J* = 11.4, 3.2 Hz, 1H), 1.98–1.84 (m, 4H), 1.79–1.75 (m, 1H), 1.61–1.23 (m, 5H).

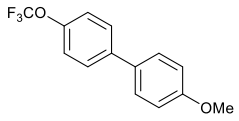
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.1, 153.4, 145.3, 138.2, 135.7, 134.8, 128.6, 127.0, 104.4, 60.8, 56.1, 45.5, 29.3, 25.8, 25.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2930, 1674, 1586, 1338, 1308, 1246, 1126, 1000, 974, 820.

MS (EI, 70 eV, %) m/z = 354 (23), 272 (17), 271 (100), 243 (16), 212 (11).

HRMS (EI, 70 eV) m/z calc. for **$C_{22}H_{26}O_4$**: 354.1831; found: 354.1824.

4-methoxy-4′-(trifluoromethoxy)-1,1′-biphenyl (189c)



Based on **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, bis-[4-(trifluoromethoxy)phenyl]manganese (**188c**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise, and the reaction mixture was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.44) leading to **189c** (160 mg, 0.60 mmol, 60%) as a pale yellow solid.

M. p. 100 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.58 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.29 (dd, *J* = 7.2, 1.5 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 159.3, 148.0 (q, ^4J(C,F) = 1.7 Hz), 139.5, 132.2, 128.0, 127.8, 121.1, 120.4 (q, ^1J(C,F) = 256 Hz), 114.2, 55.2.

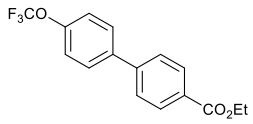
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –57.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2926, 1606, 1494, 1464, 1208, 1156, 1036, 828, 812, 796.

MS (EI, 70 eV, %) m/z = 269 (15), 268 (100), 254 (10), 253 (72), 226 (11), 225 (85), 159 (11), 139 (10), 133 (16), 128 (21).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_{11}F_3O_2$**: 268.0711; found: 268.0706.

Ethyl 4′-(trifluoromethoxy)[1,1′-biphenyl]-4-carboxylate (189d)



According to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution ofbis-[4-(trifluoromethoxy)phenyl]-manganese (**188c**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.15) afforded **189d** (205 mg, 0.66 mmol, 66%) as a white solid.

M.p. 64 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.12 (d, *J* = 8.6 Hz, 2H), 7.67–7.59 (m, 4H), 7.36–7.27 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.2, 149.1 (q, ^4J(C,F) = 1.9 Hz), 143.9, 138.6, 130.0, 129.5, 128.5, 126.8, 121.1, 120.3 (q, ^1J(C,F) = 256 Hz), 60.9, 14.2.

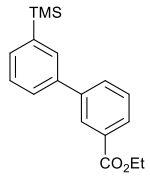
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –57.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2924, 1702, 1610, 1256, 1204, 1180, 1168, 1148, 1124, 1108.

MS (EI, 70 eV, %) m/z = 310 (56), 282 (24), 266 (16), 265 (100).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{13}F_3O_3$**: 310.0817; found: 310.0798.

Ethyl 3′-(trimethylsilyl)[1,1′-biphenyl]-3-carboxylate (189e)



Based on **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 3-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-(3-trimethylsilylphenyl)-manganese (**188d**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h at the given temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.40) gave **189e** (165 mg, 0.55 mmol, 55%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.30 (t, *J* = 1.7 Hz, 1H), 8.05 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.80 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.76 (s, 1H), 7.62 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.57 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.54–7.44 (m, 2H), 4.43 (t, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 0.34 (s, 9H).

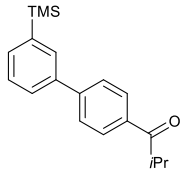
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.4, 141.7, 141.1, 139.4, 134.5, 132.5, 131.9, 131.4, 130.8, 128.6, 128.2, 128.0, 127.6, 60.9, 14.2, –1.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2956, 1718, 1300, 1238, 1170, 1108, 1082, 1054, 836, 794.

MS (EI, 70 eV, %) m/z = 298 (26), 284 (23), 283 (100).

HRMS (EI, 70 eV) m/z calc. for **$C_{18}H_{22}O_2Si$**: 298.1389; found: 298.1382.

2-methyl-1-[3′-(trimethylsilyl)[1,1′-biphenyl]-4-yl]propan-1-one (189f)



With reference to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 1-(4-iodophenyl)-2-methylpropan-1-one (274 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The solution was cooled to 0 °C, bis-(3-trimethylsilylphenyl)manganese (**188d**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.26) afforded **189f** (215 mg, 0.73 mmol, 73%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.06 (d, *J* = 8.5 Hz, 2H), 7.76 (s, 1H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.59 (ddt, *J* = 15.0, 7.3, 1.3 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 1H), 3.61 (hept, *J* = 6.8 Hz, 1H), 1.26 (d, *J* = 6.8 Hz, 6H), 0.33 (s, 9H).

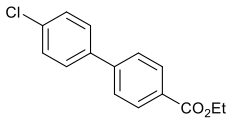
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.9, 145.7, 141.2, 139.1, 134.6, 133.0, 131.9, 128.7, 128.1, 127.6, 127.2, 35.2, 19.0, –1.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2958, 1740, 1680, 1604, 1382, 1248, 1224, 1120, 996, 836.

MS (EI, 70 eV, %) m/z = 296 (9), 281 (14), 254 (24), 253 (100), 210 (14).

HRMS (EI, 70 eV) m/z calc. for **$C_{19}H_{24}OSi$**: 296.1596; found: 296.1587.

Ethyl 4′-chloro[1,1′-biphenyl]-4-carboxylate (189g)



According to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-(4-chlorophenyl)manganese (**188e**; 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.21) to afford **189g** (168 mg, 0.64 mmol, 64%) as a white solid.

M.p. 70 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.11 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

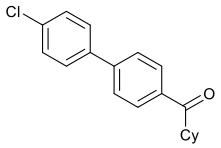
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.4, 144.2, 138.5, 134.3, 130.2, 129.6, 129.1, 128.5, 126.8, 61.1, 14.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1710, 1476, 1274, 1194, 1172, 1112, 1096, 1022, 1014, 1000.

MS (EI, 70 eV, %) m/z = 262 (12), 260 (38), 234 (13), 232 (41), 217 (32), 216 (13), 215 (99), 153 (13), 152 (100), 151 (17), 150 (15), 76 (13).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{13}ClO_2$**: 260.0604; found: 260.0601.

(4′-chloro[1,1′-biphenyl]-4-yl)(cyclohexyl)methanone (189h)



Based on **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), cyclohexyl(4-iodophenyl)methanone (314 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-(4-chlorophenyl)manganese (**188e**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.46) furnished **189h** (141 mg, 0.50 mmol, 50%) as a white solid.

M.p. 116 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.02 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 3.29 (tt, *J* = 11.4, 3.2 Hz, 1H), 1.96–1.83 (m, 4H), 1.81–1.68 (m, 1H), 1.65–1.18 (m, 5H).

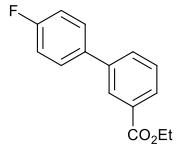
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 203.2, 143.9, 138.3, 135.1, 134.2, 129.0, 128.8, 128.3, 126.9, 45.6, 29.3, 25.8, 25.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2930, 2854, 1668, 1604, 1482, 1252, 978, 894, 820.

MS (EI, 70 eV, %) m/z = 298 (7), 230 (10), 217 (33), 216 (14), 215 (100), 152 (69).

HRMS (EI, 70 eV) m/z calc. for **$C_{19}H_{19}ClO$**: 298.1124; found: 298.1119.

Ethyl 4′-fluoro[1,1′-biphenyl]-3-carboxylate (189i)



With reference to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 3-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0mL) were used. The resulting solution was cooled to 0 °C, bis-(4-fluorophenyl)manganese (**188f**, 2.7 mL, 0.70 mmol, 0.26 M in THF, 0.70 equiv) was added dropwise, and the reaction mixture was stirred for 1 h at the given temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.45) to afford **189i** (150 mg, 0.61 mmol, 61%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.23 (t, *J* = 1.7 Hz, 1H), 8.02 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.72 (ddd, *J* = 7.7, 1.9, 1.2 Hz, 1H), 7.62–7.54 (m, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 8.7 Hz, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.3, 162.5 (d, ^1J(C,F) = 247 Hz), 140.3, 136.1 (d, ^4J(C,F) = 3.3 Hz), 131.1, 130.9, 128.7 (d, ^4J(C,F) = 4.0 Hz), 128.6, 128.1, 127.9, 115.6 (d, ^2J(C,F) = 21. Hz), 60.9, 14.2.

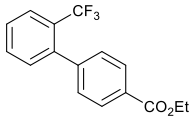
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –115.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 1714, 1598, 1514, 1368, 1304, 1268, 1236, 1172, 1158.

MS (EI, 70 eV, %) m/z = 244 (47), 216 (34), 200 (12), 199 (16), 171 (45), 170 (100), 85 (11).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{13}FO_2$**: 244.0900; found: 244.0895.

Ethyl 2′-(trifluoromethyl)[1,1′-biphenyl]-4-carboxylate (189j)



According to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-[2-(trifluoromethyl)phenyl]manganese (**188g**, 2.5 mL, 0.70 mmol, 0.28 M in THF, 0.70 equiv) was added dropwise, and the mixture was stirred for 1 h at the prior adjusted temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99:1, R_f = 0.17) gave the desired product **189j** (236 g, 0.80 mmol, 80%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.09 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.5, 144.5, 140.5 (q, ^4J(C,F) = 1.9 Hz), 131.7, 131.6, 130.0, 129.2, 128.5 (q, ^2J(C,F) = 30 Hz), 128.0, 126.3 (q, ^3J(C,F) = 5.3 Hz), 124.1 (q, ^1J(C,F) = 272 Hz), 61.2, 14.5.

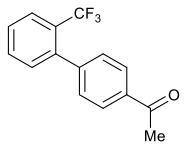
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –56.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2984, 1714, 1312, 1270, 1168, 1124, 1100, 1070, 1034, 1026.

MS (EI, 70 eV, %) m/z = 294 (14), 266 (57), 250 (15), 249 (100), 202 (11), 201 (80).

HRMS (EI, 70 eV) m/z calc. for **$C_{16}H_{13}F_3O_2$**: 294.0868; found: 294.0860.

1-[2′-(trifluoromethyl)[1,1′-biphenyl]-4-yl)ethan-1-one (189k)



Based on **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 1-(4-iodophenyl)ethan-1-one (246 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-[2-(trifluoromethyl)phenyl]manganese (**188g**, 2.5 mL, 0.70 mmol, 0.28 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.18) to afford **189k** (162 mg, 0.61 mmol, 61%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.00 (d, *J* = 8.6 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 1H), 2.65 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 197.9, 144.8, 140.3 (q, ^4J(C,F) = 1.9 Hz), 136.5, 131.7, 131.6, 129.4, 128.5 (q, ^2J(C,F) = 30 Hz), 128.1, 128.0, 126.3 (q, ^3J(C,F) = 5.3 Hz), 124.1 (q, ^1J(C,F) = 272 Hz), 26.8.

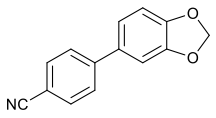
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –56.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1682, 1602, 1360, 1314, 1262, 1166, 1124, 1108, 1080, 1068.

MS (EI, 70 eV, %) m/z = 264 (10), 250 (15), 249 (100), 201 (64).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{11}F_3O$**: 264.0762; found: 264.0756.

4-(benzo[*d*][1,3]dioxol-5-yl)benzonitrile (189l)



According to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 4-iodobenzonitrile (229 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, bis-(benzo[*d*][1,3]dioxol-5-yl)manganese (**188h**, 2.5 mL, 0.70 mmol, 0.28 M in THF, 0.70 equiv) was added dropwise and the reaction mixture was stirred for 1 h at the given temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19:1, R_f = 0.15) furnished **189l** (112 mg, 0.50 mmol, 50%) as a pale yellow solid.

M.p. 130 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 7.68 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.11–7.02 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.02 (s, 2H).

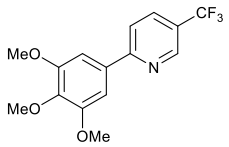
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 148.6, 148.4, 145.4, 133.5, 132.7, 127.4, 121.3, 119.1, 110.6, 109.0, 107.6, 101.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2220, 1600, 1480, 1440, 1414, 1236, 1106, 1036, 936, 886.

MS (EI, 70 eV, %) m/z = 224 (14), 223 (100), 222 (99), 166 (11), 164 (32).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_9NO_2$**: 223.0633; found: 223.0625.

5-(trifluoromethyl)-2-(3,4,5-trimethoxyphenyl)pyridine (189m)



According to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 2-chloro-5-(trifluoromethyl)pyridine (182 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, bis-(3,4,5-trimethoxyphenyl)-manganese (**188b**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.38) afforded **189m** (225 mg, 0.72 mmol, 72%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.92–8.89 (m, 1H), 7.95 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.28 (s, 2H), 3.96 (s, 6H), 3.91 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 153.5, 159.7 (q, ^4J(C,F) = 1.8 Hz), 146.2 (q, ^3J(C,F) = 4.1 Hz), 139.9, 133.7 (q, ^3J(C,F) = 3.5 Hz), 133.2, 124.4 (q, ^2J(C,F) = 32 Hz), 121.5 (q, ^1J(C,F) = 272 Hz), 119.5, 104.4, 60.8, 56.1.

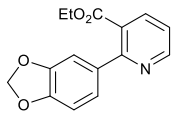
^{19}F-NMR ($CDCl_3$, 376 MHz, ppm) δ = –62.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1736, 1604, 1566, 1512, 1484, 1460, 1420, 1384, 1284, 1248.

MS (EI, 70 eV, %) m/z = 314 (24), 313 (100), 299 (11), 298 (37), 270 (23), 240 (45), 184 (15).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{14}F_3NO_3$**: 313.0926; found: 313.0920.

Ethyl 2-(benzo[*d*][1,3]dioxol-5-yl)nicotinate (189n)



Based on **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution bis-(benzo[*d*][1,3]dioxol-5-yl)manganese (**188h**, 2.5 mL, 0.70 mmol, 0.28 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h at the given temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.26) to afford **189n** (248 mg, 0.91 mmol, 91%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.71 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.03 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.28 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.08 (d, *J* = 1.7 Hz, 1H), 7.00 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.99 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.15 (t, *J* = 7.1 Hz, 3H).

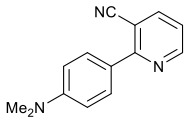
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 168.0, 157.8, 150.8, 148.0, 147.4, 137.5, 133.9, 127.0, 122.6, 121.1, 109.0, 107.8, 101.0, 61.3, 13.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2938, 1714, 1626, 1608, 1562, 1504, 1492, 1392, 1302, 1282.

MS (EI, 70 eV, %) m/z = 272 (16), 271 (100), 243 (14), 242 (90), 226 (17), 199 (15), 198 (13), 196 (13).

HRMS (EI, 70 eV) m/z calc. for **$C_{15}H_{13}NO_4$**: 271.0845; found: 271.0843.

2-[4-(dimethylamino)phenyl]nicotinonitrile (189o)



With reference to **TP5**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 2-chloro-3-pyridinecarbonitrile (139 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, bis-(4-dimethylaminophenyl)-manganese (**188i**, 3.2 mL, 0.70 mmol, 0.22 M in THF, 0.70 equiv) was added dropwise and the reaction mixture was stirred for 1 h at the prior adjusted temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.26) afforded **189o** (118 mg, 0.53 mmol, 53%) as a pale yellow solid.

M.p. 146 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.78 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.97 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 2H), 7.20 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 2H), 3.05 (s, 6H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 160.6, 152.3, 151.5, 141.8, 129.8, 124.4, 119.7, 118.4, 111.5, 105.4, 40.0.

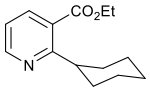
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2918, 2222, 1608, 1572, 1562, 1528, 1428, 1364, 1298, 1246.

MS (EI, 70 eV, %) m/z = 224 (12), 223 (100), 222 (89), 178 (12).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_{13}N_3$**: 223.1109; found: 223.1106.

3.8. Ni-Catalyzed Cross-Couplings of Bis-(Alkyl)manganese Reagents of Type 190 with 2-Chloro-substituted Pyridines

Ethyl 2-cyclohexylnicotinate (192a)



According to **TP6**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-(cyclohexyl)manganese (**190a**, 4.1 mL, 0.70 mmol, 0.17 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9:1, R_f = 0.44) to afford **192a** (143 mg, 0.61 mmol, 61%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.66 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.04 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.16 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.44 (tt, *J* = 11.7, 3.1 Hz, 1H), 1.88–1.78 (m, 4H), 1.76–1.64 (m, 3H), 1.47–1.27 (m, 3H), 1.39 (t, *J* = 7.1 Hz, 3H).

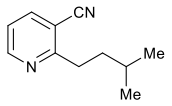
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.9, 165.9, 151.0, 138.0, 125.7, 120.2, 61.2, 42.6, 32.2, 26.4, 25.8, 14.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2924, 2852, 1722, 1584, 1566, 1448, 1434, 1390, 1366, 1350.

MS (EI, 70 eV, %) m/z = 234 (1), 205 (13), 204 (100), 160 (13), 150 (16).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_{19}NO_2$**: 233.1416; found: 233.1406.

2-isopentylnicotinonitrile (192b)



Based on **TP6**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), 2-chloro-3-pyridinecarbonitrile (139 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C, a solution of bis-(isopentyl)manganese (**190b**, 2.8 mL, 0.70 mmol, 0.25 M in THF, 0.70 equiv) was added dropwise and the mixture was stirred for 1 h at the given temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8:2, R_f = 0.40) afforded **192b** (112 mg, 0.64 mmol, 64%) as a yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.74 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.94 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.29 (dd, *J* = 7.8, 5.0 Hz, 1H), 3.13–3.02 (m, 2H), 1.84–1.56 (m, 3H), 1.00 (d, *J* = 6.4 Hz, 6H).

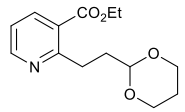
^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.2, 152.5, 141.1, 121.4, 117.1, 109.5, 38.8, 35.5, 28.5, 22.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2958, 2928, 2870, 2228, 1582, 1564, 1430, 1386, 1368, 1170.

MS (EI, 70 eV, %) m/z = 174 (2), 159 (23), 145 (10), 132 (13), 131 (75), 118 (100).

HRMS (EI, 70 eV) m/z calc. for **$C_{11}H_{14}N_2$**: 174.1157; found: 174.1104.

Ethyl 2-[2-(1,3-dioxan-2-yl)ethyl]nicotinate (192c)



With reference to **TP6**, $Ni(acac)_2$ (13 mg, 0.05 mmol, 5.0 mol%), 4-fluorostyrene (24 mg, 0.20 mmol, 20 mol%), ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), and freshly distilled THF (1.0 mL) were used. The resulting solution was cooled to 0 °C, bis-[2-(1,3-dioxan-2-yl)ethyl]manganese (**190c**, 2.9 mL, 0.70 mmol, 0.24 M in THF, 0.70 equiv) was added dropwise and the reaction mixture was stirred for 1 h at the prior adjusted temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 1:1, R_f = 0.35) gave 1**92c** (221 mg, 0.83 mmol, 83%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ = 8.62 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.11 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.17 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.57 (t, *J* = 5.2 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.07 (dd, *J* = 11.2, 5.6 Hz, 2H), 3.72 (td, *J* = 12.4, 2.5 Hz, 2H), 3.30–3.18 (m, 2H), 2.08–1.99 (m, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.29 (dtt, *J* = 13.4, 2.6, 1.4 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ = 166.7, 162.4, 151.7, 138.3, 126.0, 120.8, 101.8, 66.8, 61.4, 34.6, 31.3, 25.8, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2966, 2852, 1720, 1568, 1434, 1280, 1262, 1250, 1190, 1170.

MS (EI, 70 eV, %) m/z = 264 (5), 220 (10), 206 (34), 191 (10), 190 (17), 189 (14), 178 (18), 165 (23), 162 (10), 161 (14), 150 (69), 144 (13), 134 (11), 132 (20), 117 (16), 104 (18), 101 (44), 93 (34), 87 (100), 59 (11).

HRMS (EI, 70 eV) m/z calc. for **$C_{14}H_{19}NO_4$**: 265.1314; found: 264.1308.

4. Iron-Catalyzed Acylation of Polyfunctionalized Aryl- and Benzylzinc Halides with Acid Chlorides

4.1. Typical Procedures

Typical procedure for the preparation of benzylzinc(II) chlorides of type 193 (TP 1):
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.53 g, 13 mmol, 1.3 equiv) and heated to 450 °C for 5 min under high vacuum using a heat gun. After cooling to room temperature under vigorous stirring, $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv) was added under argon, the *Schlenk*-tube was heated to 320 °C for 5 min using a heatgun, cooled to room temperature and charged with magnesium turnings (0.58 g, 24 mmol, 2.4 equiv). Freshly distilled THF (10–15 mL) and the corresponding benzylic chloride (10 mmol, 1.0 equiv) were added and the reaction mixture was stirred at room temperature for a given time until full conversion of the starting material was observed. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was complete, the solution of the corresponding benzylzinc(II) chloride was separated from the resulting salts *via* a syringe equipped with a filter and transferred to another pre-dried and argon-flushed *Schlenk*-tube, before being titrated against iodine.

Typical procedure for the preparation of arylzinc(II) chlorides of type 196 (TP 2):
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with the corresponding aryl iodide (10 mmol, 1.0 equiv) and dissolved in freshly distilled THF (10 mL). The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for a given time at the prior adjusted temperature until full conversion of the starting material was observed. The completion of the exchange was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots, transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv) and finally titrated against iodine.

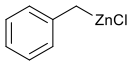
Typical procedure for the iron-catalyzed acylation of benzylic zinc chlorides (193) with acid chlorides of type 194 (TP 3):
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), the selected acid chloride (1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL). The corresponding prior prepared benzylic zinc chloride solution (1.3 mmol, 1.3 equiv) was added dropwise and the reaction mixture was stirred for a given time at room temperature. Subsequently, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude products by flash column chromatography afforded the desired products.

Typical procedure for the iron-catalyzed acylation of arylzinc chlorides (196) with acid chlorides of type 194 (TP 4):

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), the selected acid chloride (1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL). The corresponding prior prepared arylzinc chloride (1.3 mmol, 1.3 equiv) was added dropwise and the reaction mixture was stirred for a given time at 50 °C. Subsequently, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude products by flash column chromatography afforded the desired products.

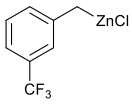
4.2. Preparation of the Benzylzinc(II) Chlorides (193a–g)

Preparation of benzylzinc(II) chloride (193a)



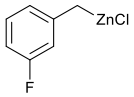
According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (10 mL) were used. Benzyl chloride (1.3 g, 1.2 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. The concentration of benzylzinc(II) chloride (**193a**) was determined by titration with iodine in THF (0.80 M, 80%).

Preparation of 3-(trifluoromethyl)benzylzinc(II) chloride (193b)



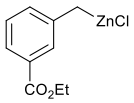
According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (10 mL) were used. 3-(trifluoromethyl)benzyl chloride (2.0 g, 1.6 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at room temperature. The concentration of 3-(trifluoromethyl)benzylzinc(II) chloride (**193b**) was determined by titration with iodine in THF (0.72 M, 72%).

Preparation of 3-fluorobenzylzinc(II) chloride (193c)



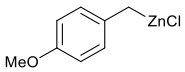
According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (10 mL) were used. 3-fluorobenzyl chloride (1.5 g, 1.2 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at room temperature. The concentration of 3-fluorobenzylzinc(II) chloride (**193c**) was determined by titration with iodine in THF (0.65 M, 65%).

Preparation of 3-(ethoxycarbonyl)benzylzinc(II) chloride (193d)



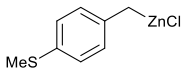
According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (15 mL) were used. Ethyl 3-(chloromethyl)-benzoate (2.0 g, 1.7 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 1.5 h at room temperature. The concentration of 3-(ethoxycarbonyl)benzylzinc(II) chloride (**193d**) was determined by titration with iodine in THF (0.38 M, 57%).

Preparation of 4-methoxybenzylzinc(II) chloride (193e)



According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (10 mL) were used. 4-Methoxybenzyl chloride (1.6 g, 1.4 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. The concentration of 4-methoxybenzylzinc(II) chloride (**193e**) was determined by titration with iodine in THF (0.60 M, 60%).

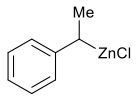
Preparation of 4-(methylthio)benzylzinc(II) chloride (193f)



According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (15 mL) were used. 4-(Methylthio)benzyl chloride (1.7 g, 1.5 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred

for 1 h at room temperature. The concentration of 4-(methylthio)benzylzinc(II) chloride (**193f**) was determined by titration with iodine in THF (0.35 M, 53%).

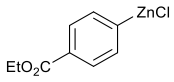
Preparation of (1-phenylethyl)zinc(II) chloride (193g)



According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (10 mL) were used. (1-Chloroethyl)benzene (1.41 g, 1.3 mL, 10 mmol, 1.0 equiv) was added drowise and the reaction mixture was stirred for 2 h at room temperature. The concentration of (1-phenylethyl)zinc(II) chloride (**193g**) was determined by titration with iodine in THF (0.56 M, 56%).

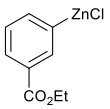
4.3. Preparation of the Arylzinc(II) Chlorides (196a–f)

Preparation of (4-(ethoxycarbonyl)phenyl)zinc(II) chloride (196a)



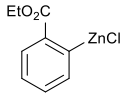
According to **TP2**, ethyl 4-iodobenzoate (2.8 g, 1.7 mL, 10 mmol, 1.0 equiv), tetradecane (0.5 mL) and freshly distilled THF (10 mL) were used. The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min at the prior adjusted temperature and subsequently transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv). The concentration of (4-(ethoxycarbonyl)phenyl)zinc(II) chloride (**196a**) was determined by titration with iodine in THF (0.32 M, >90%).

Preparation of (3-(ethoxycarbonyl)phenyl)zinc(II) chloride (196b)



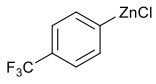
According to **TP2**, ethyl 3-iodobenzoate (2.8 g, 1.7 mL, 10 mmol, 1.0 equiv), tetradecane (0.5 mL) and freshly distilled THF (10 mL) were used. The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min at the prior adjusted temperature and subsequently transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv). The concentration of (3-(ethoxycarbonyl)phenyl)zinc(II) chloride (**196b**) was determined by titration with iodine in THF (0.31 M, >90%).

Preparation of (2-(ethoxycarbonyl)phenyl)zinc(II) chloride (196c)



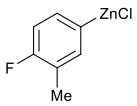
According to **TP2**, ethyl 2-iodobenzoate (2.8 g, 1.7 mL, 10 mmol, 1.0 equiv), tetradecane (0.5 μL) and freshly distilled THF (10 mL) were used. The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min at the prior adjusted temperature and subsequently transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv). The concentration of (2-(ethoxycarbonyl)phenyl)zinc(II) chloride (**196c**) was determined by titration with iodine in THF (0.34 M, >90%).

Preparation of (4-(trifluoromethyl)phenyl)zinc(II) chloride (196d)



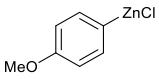
According to **TP2**, 4-iodobenzotrifluoride (2.7 g, 1.5 mL, 10 mmol, 1.0 equiv), tetradecane (0.25 mL) and freshly distilled THF (5.0 mL) were used. The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min at the prior adjusted temperature and subsequently transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv). The concentration of (4-(trifluoromethyl)-phenyl)zinc(II) chloride (**196d**) was determined by titration with iodine in THF (0.42 M, >90%).

Preparation of (4-fluoro-3-methylphenyl)zinc(II) chloride (196e)



According to **TP2**, 2-fluoro-5-iodotoluene (2.4 g, 10 mmol, 1.0 equiv), tetradecane (0.5 mL) and freshly distilled THF (10 mL) were used. The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min at the prior adjusted temperature and subsequently transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv). The concentration of (4-fluoro-3-methylphenyl)zinc(II) chloride (**196e**) was determined by titration with iodine in THF (0.33 M, >90%).

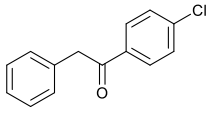
Preparation of (4-methoxyphenyl)zinc(II) chloride (196f)



According to **TP2**, 4-iodoanisole (2.3 g, 10 mmol, 1.0 equiv), tetradecane (0.5 mL) and freshly distilled THF (10 mL) were used. The solution was cooled to –20 °C and *i*PrMgCl·LiCl (10 mL, 12 mmol, 1.2 M in THF, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min at the prior adjusted temperature and subsequently transmetalated with $ZnCl_2$ (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv). The concentration of (4-methoxyphenyl)zinc(II) chloride (**196f**) was determined by titration with iodine in THF (0.36 M, >90%).

4.4. Iron-Catalyzed Acylation of Benzylic Zinc Chlorides (193a-g) with Acid Chlorides of Type 194

Preparation of 1-(4-chlorophenyl)-2-phenylethan-1-one (195a)



Based on **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The benzylzinc(II) chloride solution (**193a**, 1.6 mL, 1.3 mmol, 0.80 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.45) afforded the desired product **195a** (208 mg, 0.90 mmol, 90%) as a white solid.

M.p. 80 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.93 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.33-7.31 (m, 2H), 7.26–7.23 (m, 3H), 4.24 (s, 2H).

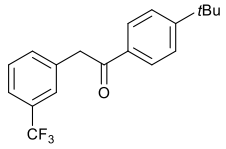
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 196.3, 139.6, 134.8, 134.1, 130.0, 129.3, 128.9, 128.7, 127.0, 45.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3028, 2901, 1723, 1686, 1588, 1571, 1496, 1485, 1452, 1395, 1336, 1320, 1271, 1217, 1201, 1169, 1104, 1088, 1072, 1004, 991, 961, 824, 795, 749, 711, 694, 661.

MS (EI, 70 eV, %) m/z = 230 (10), 141 (30), 139 (100), 111 (19), 91 (14), 57 (20), 43 (26), 41 (11)

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}ClO$**: 230.0498; found: 230.0484.

Preparation of 1-(4-(*tert*-butyl)phenyl)-2-(3-(trifluoromethyl)phenyl)ethan-1-one (195b)



According to **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 3-(trifluoromethyl)-benzylzinc(II) chloride solution (**193b**, 1.7 mL, 1.3 mmol, 0.72 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.15) leading to the desired product **195b** (208 mg, 0.65 mmol, 65%) (38% isolated yield without catalyst after prolonged reaction time of 2 h at room temperature) as a white solid.

M.p. 68 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.96 (d, *J* = 8.7 Hz, 2H), 7.56–7.43 (m, 6H), 4.33 (s, 2H), 1.35 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 196.1, 157.2, 135.4, 133.6, 132.9 (q, ^3J(C,F) = 4.0 Hz), 130.7 (q, ^2J(C,F) = 32 Hz), 128.8, 128.3, 126.2 (q, ^3J(C,F) = 3.8 Hz), 125.6, 123.9 (q, ^1J(C,F) = 271 Hz), 123.6 (q, ^3J(C,F) = 3.8 Hz), 44.7, 35.0, 30.9.

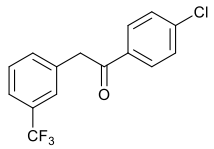
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2964, 1725, 1711, 1678, 1641, 1603, 1451, 1406, 1366, 1331, 1268, 1223, 1160, 1110, 1092, 1075, 1004, 992, 915, 880, 841, 829, 786, 720, 701, 658.

MS (EI, 70 eV, %) m/z = 320 (1), 305 (10), 162 (12), 161 (100), 118 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{19}F_3O$**: 320.1388; found: 320.1386.

Preparation of 1-(4-chlorophenyl)-2-(3-(trifluoromethyl)phenyl)ethan-1-one (195c)



According to **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 3-(trifluoromethyl)-benzylzinc(II) chloride solution (**193b**, 1.7 mL, 1.3 mmol, 0.72 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.22) furnished the product **195c** (212 mg, 0.71 mmol, 71%) as a white solid.

M.p. 54 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.95 (d, *J* = 8.7 Hz, 2H), 7.57–7.39 (m, 6H), 4.32 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.8, 140.5, 135.5, 135.1, 133.5 (q, ^4J(C,F) = 2.0 Hz), 131.4 (q, ^2J(C,F) = 32 Hz), 130.3, 129.6, 129.5, 126.8 (q, ^3J(C,F) = 3.8 Hz), 124.5 (q, ^1J(C,F) = 270 Hz), 124.4 (q, ^3J(C,F) = 3.8 Hz), 45.3.

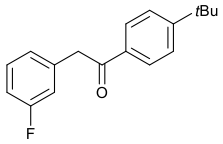
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2916, 1726, 1694, 1681, 1587, 1570, 1488, 1454, 1400, 1330, 1209, 1185, 1156, 1120, 1092, 1074, 1013, 1003, 990, 902, 878, 848, 812, 784, 700, 676, 657.

MS (EI, 70 eV, %) m/z = 298 (1), 141 (31), 140 (10), 139 (100), 111 (22), 75 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{10}ClF_3O$**: 298.0372; found: 298.0359.

Preparation of 1-(4-(*tert*-butyl)phenyl)-2-(3-fluorophenyl)ethan-1-one (195d)



Based on **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 3-fluorobenzylzinc(II) chloride (**193c**, 1.9 mL, 1.3 mmol, 0.65 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.50) leading to the desired product **195d** (237 mg, 0.88 mmol, 88%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.91 (d, *J* = 8.7 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.27–7.18 (m, 1H), 7.02–6.85 (m, 3H), 4.21 (s, 2H), 1.29 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 196.3, 162.7 (d, ^1J(C,F) = 245 Hz), 157.0, 137.0 (d, ^3J(C,F) = 7.7 Hz), 133.7, 129.8 (d, ^3J(C,F) = 8.4 Hz), 128.4, 125.5, 125.0 (d, ^4J(C,F) = 2.9 Hz), 116.3 (d, ^2J(C,F) = 22 Hz), 113.6 (d, ^2J(C,F) = 21 Hz), 44.8, 35.0, 30.9.

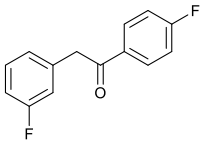
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –113.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3062, 2964, 2906, 2870, 1679, 1604, 1590, 1488, 1449, 1406, 1364, 1329, 1299, 1268, 1254, 1218, 1192, 1141, 1108, 994, 948, 850, 828, 774, 754, 711, 681.

MS (EI, 70 eV, %) m/z = 272 (1), 272 (3), 162 (10), 161 (55), 70 (11), 61 (16), 45 (15), 43 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}FO$**: 270.1420; found: 270.1413.

Preparation of 2-(3-fluorophenyl)-1-(4-fluorophenyl)ethan-1-one (195e)



According to **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-fluorobenzoyl chloride (**194c**, 159 mg, 0.12 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 3-fluorobenzylzinc(II) chloride (**193c**, 1.9 mL, 1.3 mmol, 0.65 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.38) afforded the product **195e** (172 mg, 0.74 mmol, 74%) as a white solid.

M.p. 48 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.96 (dd, *J* = 9.0, 5.4 Hz, 2H), 7.26–7.18 (m, 1H), 7.10–7.03 (m, 2H), 6.99–6.85 (m, 3H), 4.18 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.4, 166.0 (d, ^1J(C,F) = 254 Hz), 163.0 (d, ^1J(C,F) = 245 Hz), 136.8 (d, ^3J(C,F) = 7.7 Hz), 132.9 (d, ^4J(C,F) = 3.0 Hz), 131.3 (d, ^3J(C,F) = 9.4 Hz), 130.3 (d, ^3J(C,F) = 8.4 Hz), 125.3 (d, ^4J(C,F) = 2.9 Hz), 116.6 (d, ^2J(C,F) = 22 Hz), 116.0 (d, ^2J(C,F) = 22 Hz), 114.1 (d, ^2J(C,F) = 21 Hz), 45.1.

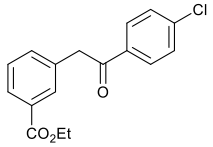
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –104.6, –112.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3061, 2927, 2854, 1680, 1591, 1507, 1488, 1448, 1412, 1327, 1298, 1250, 1236, 1207, 1156, 1144, 1100, 1008, 994, 954, 941, 886, 831, 815, 769, 738, 684.

MS (EI, 70 eV, %) m/z = 233 (8), 232 (1), 124 (10), 123 (100), 95 (28), 70 (10), 61 (13), 45 (11), 42 (79).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}F_2O$**: 232.0700; found: 232.0694.

Preparation of ethyl 3-(2-(4-chlorophenyl)-2-oxoethyl)benzoate (195f)



Based on **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 3-(ethoxycarbonyl)-benzylzinc(II) chloride (**193d**, 3.3 mL, 1.3 mmol, 0.38 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.21) leading to the product **195f** (151 mg, 0.50 mmol, 50%) as pale yellow solid.

M.p. 77 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.94–7.92 (m, 4H), 7.44–7.38 (m, 4H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.30 (s, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).

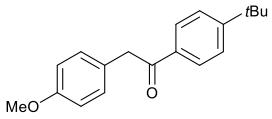
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 195.8, 166.3, 139.8, 134.7, 134.4, 133.9, 130.9, 129.9, 129.0, 128.7, 128.3, 61.0, 45.1, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 2915, 2853, 1703, 1693, 1606, 1587, 1570, 1483, 1444, 1396, 1365, 1332, 1280, 1170, 1106, 1087, 1029, 1000, 990, 831, 815, 796, 755, 721, 672.

MS (EI, 70 eV, %) m/z = 302 (5), 141 (30), 139 (100), 111 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{15}ClO_3$**: 302.0710; found: 302.0698.

Preparation of 1-(4-(*tert*-butyl)phenyl)-2-(4-methoxyphenyl)ethan-1-one (195g)



According to **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 4-methoxybenzylzinc(II) chloride (**193e**, 2.1 mL, 1.3 mmol, 0.60 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.28) gave the product **195g** (164 mg, 0.58 mmol, 58%) as a pale yellow solid.

M.p. 109 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.89 (d, *J* = 6.7 Hz, 2H), 7.40 (d, *J* = 6.7 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.13 (s, 2H), 3.71 (s, 3H), 1.27 (s, 9H).

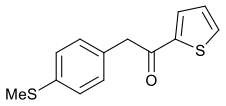
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 197.5, 158.5, 156.8, 134.0, 130.4, 128.6, 126.8, 125.6, 114.1, 55.3, 44.6, 35.1, 31.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2952, 2901, 2869, 2829, 1721, 1683, 1601, 1511, 1462, 1404, 1360, 1332 (w), 1300, 1268, 1241, 1174, 1104, 1040, 1022, 994, 860, 824, 794, 692.

MS (EI, 70 eV, %) m/z = 283 (1), 282 (5), 163 (12), 161 (100), 120 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{22}O_2$**: 282.1620; found: 282.1615.

Preparation of 2-(4-(methylthio)phenyl)-1-(thiophen-2-yl)ethan-1-one (195h)



Based on **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 2-thiophenecarbonyl chloride (**194d**, 147 mg, 0.11 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The 4-(methylthio)-benzylzinc(II) chloride (**193f**, 3.6 mL, 1.3 mmol, 0.35 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.35) leading to the product **195h** (149 mg, 0.60 mmol, 60%) as pale yellow solid.

M.p. 106 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.69 (d, *J* = 3.6 Hz, 1H), 7.56 (d, *J* = 4.8 Hz, 1H), 7.16 (s, 4H), 7.05 (t, *J* = 8.0 Hz, 1H), 4.08 (s, 2H), 2.39 (s, 3H).

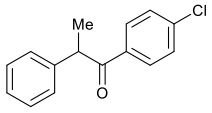
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 190.3, 143.8, 137.2, 134.1, 132.6, 131.1, 130.0, 128.2, 127.0, 45.8, 16.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3070, 2920, 1660, 1602, 1516, 1494, 1412, 1402, 1354, 1326, 1224, 1198, 1116, 1084, 1060, 956, 940, 916, 854, 796, 760, 744, 658.

MS (EI, 70 eV, %) m/z = 248 (14), 138 (12), 137 (100), 122 (12), 111 (48).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{12}OS_2$**: 248.0330; found: 248.0330.

Preparation of 1-(4-chlorophenyl)-2-phenylpropan-1-one (195i)



According to **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**195a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (1-phenylethyl)-zinc(II) chloride (**193g**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.34) afforded the product **195i** (192 mg, 0.78 mmol, 78%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.81 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.25–7.10 (m, 5H), 4.55 (q, *J* = 6.8 Hz, 1H), 1.47 (d, *J* = 6.8 Hz, 3H).

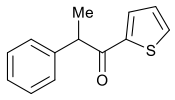
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 199.0, 141.2, 139.2, 134.8, 130.2, 129.1, 128.8, 127.7, 127.1, 48.1, 19.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3062, 3028, 2975, 2931, 2871, 1681, 1587, 1569, 1490, 1451, 1400, 1373, 1332, 1248, 1217, 1174, 1091, 1063, 1013, 1000, 950, 847, 786, 754, 731, 698.

MS (EI, 70 eV, %) m/z = 244 (2), 139 (100), 138 (48), 105 (24).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}ClO$**: 244.0655; found: 244.0652.

Preparation of 2-phenyl-1-(thiophen-2-yl)propan-1-one (195j)



According to **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 2-thiophenecarbonyl chloride (**194d**, 147 mg, 0.11 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (1-phenylethyl)-zinc(II) chloride (**193g**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.45) leading to the product **195j** (141 mg, 0.65 mmol, 65%) as pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.48 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.30–7.21 (m, 4H), 7.20–7.13 (m, 1H), 6.97 (dd, *J* = 4.9, 3.8 Hz, 1H), 4.45 (q, *J* = 6.9 Hz, 1H), 1.49 (d, *J* = 6.9 Hz, 3H).

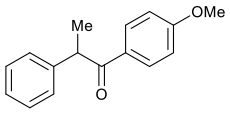
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 193.3, 143.8, 141.3, 133.6, 132.4, 128.9, 128.0, 127.8, 127.1, 49.4, 19.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3087, 3027, 2975, 2930, 2870, 1657, 1600, 1517, 1491, 1451, 1412, 1372, 1354, 1253, 1234, 1216, 1182, 1053, 1031, 942, 906, 854, 798, 719, 697.

MS (EI, 70 eV, %) m/z = 217 (3), 216 (5), 111 (100), 105 (28), 69 (12), 57 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{12}OS$**: 216.0609; found: 216.0598.

Preparation of 1-(4-methoxyphenyl)-2-phenylpropan-1-one (195k)



Based on **TP3**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-methoxybenzoyl chloride (**194e**, 171 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (1-phenylethyl)zinc(II) chloride (**193g**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.28) furnished the product **195k** (190 mg, 0.79 mmol, 79%) as a colourless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.89 (d, *J* = 9.0 Hz, 2H), 7.28–7.19 (m, 5H), 6.79 (d, *J* = 9.0 Hz, 2H), 4.58 (q, *J* = 6.9 Hz, 1H), 3.73 (s, 3H), 1.46 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.8, 163.2, 142.0, 131.1, 129.5, 128.9, 127.7, 126.8, 113.7, 55.4, 47.5, 19.6.

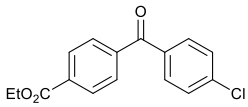
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2972, 2931, 2840, 1710, 1671, 1598, 1573, 1510, 1493, 1452, 1418, 1372, 1333, 1314, 1248, 1224, 1166, 1115, 1062, 1028, 951, 845, 795, 772, 751, 699.

MS (EI, 70 eV, %) m/z = 241 (1), 136 (10), 135 (100), 77 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{16}O_2$**: 240.1150; found: 241.1148.

4.5. Iron-Catalyzed Acylation of Arylzinc Chlorides (196a-f) with Acid Chlorides of Type 194

Preparation of ethyl 4-(4-chlorobenzoyl)benzoate (197a)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-(ethoxy-carbonyl)phenyl)zinc(II) chloride (**196a**, 3.9 mL, 1.3 mmol, 0.32 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.35) afforded the product **198a** (179 mg, 0.62 mmol, 62%) (34% isolated yield without catalyst after prolonged reaction time of 12 h at 50 °C) as a white solid.

M.p. 108 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.14 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.46 (d, *J* = 8.7 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

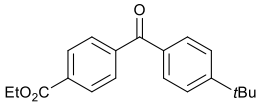
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 194.8, 165.7, 140.8, 139.5, 135.2, 133.8, 131.4, 129.5 (2C), 128.8, 61.5, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1714, 1648, 1586, 1568, 1401, 1368, 1301, 1268, 1144, 1105, 1091, 1010, 978, 931, 875, 853, 841, 783, 737, 708, 668.

MS (EI, 70 eV, %) m/z = 290 (19), 289 (11), 288 (56), 260 (14), 245 (18), 243 (51), 180 (11), 177 (59), 152 (11), 149 (17), 14 (34), 139 (100), 111 (25), 76 (11), 75 (10), 71 (34), 70 (14), 57 (46), 56 (28), 43 (82), 42 (47), 41 (40).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{13}ClO_3$**: 288.0553; found: 282.0549.

Preparation of ethyl 4-(4-(*tert*-butyl)benzoyl)benzoate (197b)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-(ethoxycarbonyl)phenyl)zinc(II) chloride (**196a**, 3.9 mL, 1.3 mmol, 0.32 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.29) leading to the desired product **197b** (203 mg, 0.65 mmol, 65%) as a pale yellow solid.

M.p. 88 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.07 (d, *J* = 8.6 Hz, 2H), 7.76 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.29 (s, 9H).

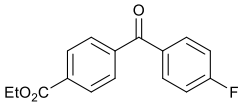
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.7, 165.9, 156.8, 141.6, 134.2, 133.4, 130.2, 129.6, 129.4, 125.4, 61.4, 35.2, 31.1, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2966, 2906, 2871, 1712, 1651, 1605, 1476, 1462, 1364, 1278, 1265, 1191, 1120, 1106, 1015, 932, 874, 843, 791, 759, 745, 715, 702, 673.

MS (EI, 70 eV, %) m/z = 311 (21), 310 (100), 297 (14), 296 (68), 266 (16), 265 (39), 178 (10), 177 (42), 145 (11), 125 (12), 121 (13), 118 (12), 115 (10), 111 (35), 104 (14), 76 (12), 65 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{22}O_3$**: 310.1569; found: 310.1558.

Preparation of ethyl 4-(4-fluorobenzoyl)benzoate (197c)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-fluorobenzoyl chloride (**194c**, 159 mg, 0.12 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-(ethoxycarbonyl)phenyl)zinc(II) chloride (**196a**, 3.9 mL, 1.3 mmol, 0.32 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.33) gave the product **197c** (227 mg, 0.83 mmol, 83%) (21% isolated yield without catalyst after prolonged reaction time of 12 h at 50 °C) as a white solid.

M.p. 76 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.14 (d, *J* = 8.6 Hz, 2H), 7.83 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.16 (t, *J* = 8.6 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 194.5, 165.7, 165.6 (d, ^1J(C,F) = 254 Hz), 141.1, 133.6, 132.7 (d, ^3J(C,F) = 9.1 Hz), 130.1, 129.5, 127.2, 115.7 (d, ^2J(C,F) = 22 Hz), 61.4, 14.3.

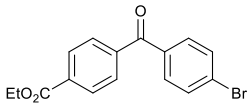
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –105.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3069, 2989, 1712, 1647, 1596, 1500, 1407, 1370, 1308, 1269, 1232, 1180, 1148, 1100, 1020, 1008, 978, 960, 934, 872, 856, 817, 787, 742, 718, 702, 672.

MS (EI, 70 eV, %) m/z = 273 (2), 272 (11), 253 (11), 226 (12), 123 (25), 70 (13), 61 (17), 45 (15), 42 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{13}FO_3$**: 272.0849; found: 272.0837.

Preparation of ethyl 4-(4-bromobenzoyl)benzoate (197d)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-bromobenzoyl chloride (**194f**, 220 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-(ethoxycarbonyl)-phenyl)zinc(II) chloride (**196a**, 3.9 mL, 1.3 mmol, 0.32 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.22) affording the product **197d** (227 mg, 0.68 mmol, 68%) as a white solid.

M.p. 108 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.15 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.73–7.58 (m, 4H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

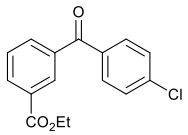
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 194.9, 165.7, 140.7, 135.7, 133.8, 131.8, 131.5, 129.6, 129.5, 128.1, 61.4, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2984, 2958, 2932, 1712, 1648, 1582, 1478, 1460, 1396, 1368, 1266, 1182, 1142, 1102, 1068, 1022, 978, 928, 838, 782, 732, 704, 664.

MS (EI, 70 eV, %) m/z = 335 (12), 334 (54), 333 (12), 332 (57), 289 (10), 287 (44), 185 (99), 183 (100), 178 (12), 177 (98), 157 (20), 149 (26), 76 (50), 75 (24).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{13}BrO_3$**: 332.0048; found: 332.0043.

Preparation of ethyl 3-(4-chlorobenzoyl)benzoate (197e)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (3-(ethoxy-carbonyl)phenyl)zinc(II) chloride (**196b**, 4.0 mL, 1.3 mmol, 0.31 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.36) furnished product **197e** (217 mg, 0.75 mmol, 75%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.33 (t, *J* = 1.7 Hz, 1H), 8.19 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.88 (dt, *J* = 7.7, 1.7 Hz, 1H), 7.68 (d, *J* = 8.7 Hz, 2H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

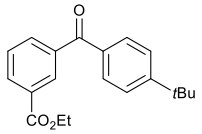
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 194.5, 165.7, 139.3, 137.6, 135.6, 133.8, 133.6, 131.4, 130.9, 130.8, 128.8, 128.7, 61.4, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 1716, 1660, 1601, 1584, 1486, 1399, 1367, 1302, 1287, 1239, 1170, 1150, 1088, 1014, 974, 960, 874, 844, 775, 734, 700.

MS (EI, 70 eV, %) m/z = 290 (16), 289 (10), 288 (40), 245 (13), 243 (36), 177 (40), 148 (12), 141 (33), 139 (100), 111 (259, 76 (12), 75 (10), 44 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{13}ClO_3$**: 288.0553; found: 288.0547.

Preparation of ethyl 3-(4-(*tert*-butyl)benzoyl)benzoate (197f)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol %), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (3-(ethoxy-carbonyl)phenyl)zinc(II) chloride (**196b**, 4.0 mL, 1.3 mmol, 0.31 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.16) gave the product **197f** (224 mg, 0.72 mmol, 72%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.38 (t, *J* = 1.5 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.90 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.29 (s, 9H).

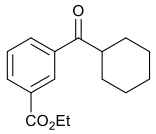
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.5, 165.9, 156.6, 138.3, 134.3, 133.9, 132.9, 130.8, 130.7, 130.1, 128.4, 125.4, 61.3, 35.1, 31.1, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2965, 2255, 1719, 1659, 1605, 1464, 1407, 1367, 1317, 1304, 1286, 1246, 1193, 1154, 1102, 1081, 1022, 975, 909, 876, 850, 781, 746, 730, 707, 675.

MS (EI, 70 eV, %) m/z = 312 (14), 311 (69), 310 (30), 298 (13), 296 (19), 295 (100), 267 (35), 265 (14), 253 (19), 176 (14), 161 (70), 148 (30), 146 (10), 145 (11), 118 (12), 111 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{22}O_3$**: 310.1569; found: 310.1563.

Preparation of ethyl 4-(cyclohexanecarbonyl)benzoate (197g)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), cyclohexanecarbonyl chloride (**194g**, 145 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (3-(ethoxy-carbonyl)phenyl)zinc(II) chloride (**196b**, 4.0 mL, 1.3 mmol, 0.31 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.50) leading to the product **197g** (155 mg, 0.60 mmol, 60%) as a colorless oil.

^{1}H-NMR (800 MHz, $CDCl_3$, ppm) δ = 8.59 (t, *J* = 1.6 Hz, 1H), 8.24 (dt, *J* = 7.7, 1.4 Hz, 1H), 8.14 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 3.32 (tt, *J* = 11.4, 3.3 Hz, 1H), 1.93–1.89 (m, 2H), 1.87 (dt, *J* = 13.4, 3.5 Hz, 2H), 1.79–1.73 (m, 1H), 1.64–1.60 (m, 1H), 1.52 (qd, *J* = 13.0, 3.2 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.30 (dtd, *J* = 12.9, 9.1, 4.6 Hz, 2H).

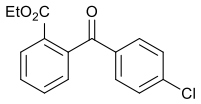
^{13}C-NMR (200 MHz, $CDCl_3$, ppm) δ = 203.3, 166.1, 136.8, 133.6, 132.5, 131.2, 129.4, 128.9, 61.5, 45.8, 29.5, 26.1, 25.9, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2929, 2853, 1719, 1681, 1601, 1447, 1367, 1295, 1276, 1238, 1198, 1172, 1135, 1100, 1077, 1022, 990, 981, 892, 864, 821, 760, 714, 693.

MS (EI, 70 eV, %) m/z = 260 (1), 215 (11), 187 (24), 178 (12), 177 (100), 149 (14), 83 (11), 55 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{20}O_3$**: 260.1412; found: 260.1407.

Preparation of ethyl 2-(4-chlorobenzoyl)benzoate (197h)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (2-(ethoxy-carbonyl)phenyl)zinc(II) chloride (**196c**, 3.7 mL, 1.3 mmol, 0.34 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.18) afforded product **197h** (213 mg, 0.74 mmol, 74%) as a white solid.

M.p. 78 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.07 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.67–7.52 (m, 2H), 7.42–7.34 (m, 3H), 4.11 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H).

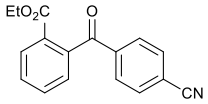
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.9, 165.8, 141.3, 139.6, 135.8, 132.6, 130.8, 130.4, 129.8, 129.4, 128.9, 127.6, 61.7, 13.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3070, 2988, 2938, 1710, 1676, 1584, 1576, 1486, 1474, 1446, 1398, 1364, 1282, 1260, 1166, 1140, 1086, 1016, 962, 928, 876, 848, 828, 768, 750, 708, 686.

MS (EI, 70 eV, %) m/z = 290 (11), 288 (37), 245 (17), 244 (15), 177 (44), 154 (33), 149 (100), 139 (76), 111 (27).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{13}ClO_3$**: 288.0553; found: 288.0551.

Preparation of ethyl 2-(4-cyanobenzoyl)benzoate (197i)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-cyanobenzoyl chloride (**194h**, 166 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (2-(ethoxycarbonyl)-phenyl)zinc(II) chloride (**196c**, 3.7 mL, 1.3 mmol, 0.34 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.13) yielding the product **197i** (173 mg, 0.62 mmol, 62%) as a pale yellow solid.

M.p. 149 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.09 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H), 7.67 (td, *J* = 7.5, 1.4 Hz, 1H), 7.61 (td, *J* = 7.6, 1.4 Hz, 1H), 7.38 (dd, *J* = 7.5, 1.3 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H).

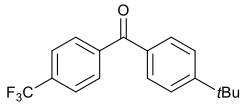
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.6, 165.6, 140.8, 140.5, 132.9, 132.5, 130.4, 130.2, 129.6, 129.4, 127.6, 118.1, 116.3, 61.8, 13.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3096, 2992, 2230, 1956, 1708, 1680, 1602, 1574, 1476, 1408, 1368, 1276, 1262, 1144, 1114, 1084, 1018, 932, 854, 760, 710, 690.

MS (EI, 70 eV, %) m/z = 279 (13), 235 (17), 234 (59), 177 (62), 149 (100), 130 (23), 102 (22).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{13}NO_3$**: 279.0895; found: 279.0890.

Preparation of (4-(*tert*-butyl)phenyl)(4-(trifluoromethyl)phenyl)methanone (197j)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-(trifluoromethyl)phenyl)zinc(II) chloride (**196d**, 3.0 mL, 1.3 mmol, 0.42 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.50) gave the product **197j** (255 mg, 0.83 mmol, 83%) as a white solid.

M.p. 76 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.82 (d, *J* = 8.0 Hz, 2H), 7.74–7.64 (m, 4H), 7.45 (d, *J* = 8.0 Hz, 2H), 1.31 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.2, 157.0, 141.0 (q, ^4J(C,F) = 2.0 Hz), 134.0, 133.5 (q, ^2J(C,F) = 32 Hz), 130.2, 130.0, 125.5, 125.3 (q, ^3J(C,F) = 3.8 Hz), 123.7 (q, ^1J(C,F) = 271 Hz), 35.2, 31.1.

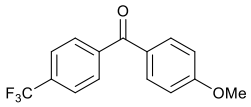
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –63.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2969, 1651, 1604, 1408, 1324, 1310, 1280, 1163, 1122, 1105, 1064, 1016, 972, 932, 860, 838, 774, 734, 698, 677.

MS (EI, 70 eV, %) m/z = 306 (2), 291 (15), 162 (13), 161 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}F_3O$**: 306.1231; found: 306.1233.

Preparation of (4-methoxyphenyl)(4-(trifluoromethyl)phenyl)methanone (197k)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol %), 4-methoxybenzoyl chloride (**194e**, 171 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-(trifluoromethyl)-phenyl)zinc(II) chloride (**196d**, 3.0 mL, 1.3 mmol, 0.42 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.25) leading to the product **197k** (173 mg, 0.62 mmol, 62%) as a white solid.

M.p. 124 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.78–7.74 (m, 4H), 7.67 (d, *J* = 8.2 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 194.3, 163.7, 141.5 (q, ^4J(C,F) = 2.0 Hz), 133.3 (q, ^2J(C,F) = 33 Hz), 132.6, 129.8, 129.4, 125.3 (q, ^3J(C,F) = 4.0 Hz), 123.7 (q, ^1J(C,F) = 271 Hz), 113.8, 55.6.

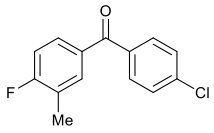
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –63.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1643, 1600, 1573, 1504, 1407, 1328, 1306, 1286, 1262, 1165, 1127, 1108, 1067, 1029, 1016, 972, 930, 861, 843, 770, 736, 700, 686.

MS (EI, 70 eV, %) m/z = 280 (26), 145 (14), 135 (100), 92 (13), 77 (16)

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{11}F_3O_2$**: 280.0711; found: 280.0707.

Preparation of (4-chlorophenyl)(4-fluoro-3-methylphenyl)methanone (197l)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-fluoro-3-methylphenyl)zinc(II) chloride (**196e**, 3.8 mL, 1.3 mmol, 0.33 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.40) afforded product **197l** (188 mg, 0.76 mmol, 76%) as a white solid.

M.p. 125 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.70 (d, *J* = 8.6 Hz, 2H), 7.66 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.58 (ddd, *J* = 7.4, 4.8, 2.1 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.08 (t, *J* = 8.8 Hz, 1H), 2.32 (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 194.3, 164.1 (d, ^1J(C,F) = 253 Hz), 138.8, 135.9, 133.6 (d, ^3J(C,F) = 6.0 Hz), 133.2, 131.2, 129.9 (d, ^3J(C,F) = 9.0 Hz), 128.6, 125.4 (d, ^2J(C,F) = 18 Hz), 115.0 (d, ^2J(C,F) = 23 Hz), 14.5.

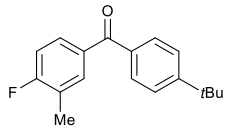
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –109.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2959, 2927, 2870, 1724, 1647, 1605, 1582, 1486, 1398, 1300, 1281, 1262, 1238, 1190, 1176, 1134, 1113, 1086, 1007, 972, 915, 858, 842, 828, 759, 751, 684.

MS (EI, 70 eV, %) m/z = 250 (24), 249 (12), 248 (76), 213 (13), 141 (13), 139 (42), 137 (100), 111 (14), 109 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}ClFO$**: 248.0404; found: 248.0396.

Preparation of (4-(*tert*-butyl)phenyl)(4-fluoro-3-methylphenyl)methanone (197m)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-fluoro-3-methylphenyl)zinc(II) chloride (**196e**, 3.8 mL, 1.3 mmol, 0.33 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.34) furnished product **197m** (189 mg, 0.70 mmol, 70%) as a colourless oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.73–7.70 (m, 2H), 7.65–7.59 (m, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.9 Hz, 2H), 2.34 (s, 3H), 1.37 (s, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 195.4, 164.0 (d, ^1J(C,F) = 252 Hz), 156.3, 135.0, 134.0, 133.8 (d, ^3J(C,F) = 5.4 Hz), 130.1, 125.4, 125.1, 115.0 (d, ^2J(C,F) = 23 Hz), 35.2, 31.3, 14.7.

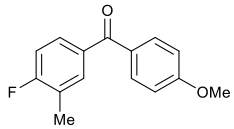
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –110.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2963, 2870, 1718, 1656, 1605, 1498, 1407, 1364, 1315, 1300, 1282, 1264, 1239, 1185, 1115, 1018, 968, 905, 850, 827, 772, 757, 726, 692.

MS (EI, 70 eV, %) m/z = 271 (7), 270 (35), 256 (25), 255 (100), 137 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}FO$**: 270.1420; found: 270.1419.

Preparation of (4-fluoro-3-methylphenyl)(4-methoxyphenyl)methanone (197n)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-methoxybenzoyl chloride (**194e**, 171 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-fluoro-3-methylphenyl)zinc(II) chloride (**196e**, 3.8 mL, 1.3 mmol, 0.33 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.26) yielding the product **197n** (194 mg, 0.79 mmol, 79%) as a white solid.

M.p. 76 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.77 (d, *J* = 9.0 Hz, 2H), 7.63 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.58–7.54 (m, 1H), 7.10–7.02 (m, 1H), 6.95 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.32 (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 194.4, 163.6 (d, ^1J(C,F) = 251 Hz), 163.1, 134.1, 133.4 (d, ^4J(C,F) = 3.6 Hz), 132.4, 130.2, 129.6 (d, ^3J(C,F) = 9.0 Hz), 125.1 (d, ^2J(C,F) = 18 Hz), 114.8 (d, ^2J(C,F)= 22.9 Hz), 113.6, 55.5, 14.5.

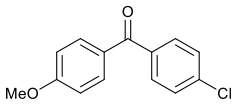
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –111.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3071, 2959, 2934, 2842, 1711, 1644, 1596, 1587, 1511, 1464, 1441, 1419, 1318, 1297, 1255, 1236, 1193, 1167, 1130, 1111, 1019, 964, 902, 873, 846, 818, 795, 766, 754, 685.

MS (EI, 70 eV, %) m/z = 245 (10), 244 (42), 137 (18), 136 (10), 135 (100), 109 (11), 77 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}FO_2$**: 244.0900; found: 244.0893.

Preparation of (4-chlorophenyl)(4-methoxyphenyl)methanone (197o)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-chlorobenzoyl chloride (**194a**, 175 mg, 0.13 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-methoxyphenyl)zinc(II) chloride (**196f**, 3.5 mL, 1.3 mmol, 0.36 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.30) afforded product **197o** (182 mg, 0.74 mmol, 74%) as a yellow solid.

M.p. 119 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.73 (d, *J* = 8.9 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H).

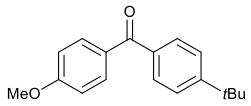
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 194.2, 163.4, 138.3, 136.6, 132.4, 131.2, 129.8, 128.5, 113.7, 55.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3014, 2934, 2841, 1722, 1637, 1600, 1588, 1509, 1461, 1414, 1397, 1299, 1283, 1245, 1170, 1147, 1086, 1062, 1028, 1013, 966, 950, 925, 853, 834, 759, 736, 722, 678.

MS (EI, 70 eV, %) m/z = 248 (32), 247 (14), 246 (99), 211 (16), 138 (26), 136 (22), 135 (100), 111 (22), 92 (18), 77 (22), 75 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}ClO_2$**: 246.0448; found: 246.0438.

Preparation of (4-(*tert*-butyl)phenyl)(4-methoxyphenyl)methanone (197p)



Based on **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol %), 4-*tert*-butylbenzoyl chloride (**194b**, 197 mg, 0.20 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-methoxyphenyl)zinc(II) chloride (**196f**, 3.5 mL, 1.3 mmol, 0.36 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.28) furnished product **197p** (219 mg, 0.82 mmol, 82%) as a colourless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.77 (d, *J* = 8.9 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 1.30 (s, 9H).

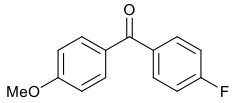
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.2, 163.1, 155.6, 135.5, 132.5, 130.5, 129.8, 127.0, 113.5, 55.5, 35.1, 31.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2962, 1649, 1600, 1574, 1509, 1462, 1442, 1418, 1364, 1314, 1305, 1281, 1252, 1172, 1151, 1104, 1028, 951, 929, 853, 836, 798, 772, 728, 687.

MS (EI, 70 eV, %) m/z = 269 (13), 268 (57), 254 (27), 253 (100), 161 (14), 135 (65), 77 (12), 44 (20).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{20}O_2$**: 268.1463; found: 268.1447.

Preparation of (4-fluorophenyl)(4-methoxyphenyl)methanone (197q)



According to **TP4**, $FeCl_2$ (6.3 mg, 0.05 mmol, 5.0 mol%), 4-fluorobenzoyl chloride (**194c**, 159 mg, 0.12 mL, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) were used. The (4-methoxyphenyl)zinc(II) chloride (**196f**, 3.5 mL, 1.3 mmol, 0.36 M in THF, 1.3 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The reaction was quenched with a saturated aqueous NH_4Cl solution and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.15) leading to the product **197q** (189 mg, 0.82 mmol, 82%) as a yellow solid.

M.p. 92 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.73 (dt, *J* = 9.0, 2.7 Hz, 4H), 7.08 (t, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 194.1, 165.1 (d, ^1J(C,F) = 252 Hz), 163.3, 134.5 (d, ^4J(C,F) = 3.1 Hz), 132.4, 132.3 (d, ^3J(C,F) = 9.0 Hz), 127.0, 115.3 (d, ^2J(C,F) = 22 Hz), 113.6, 55.5.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –107.0.

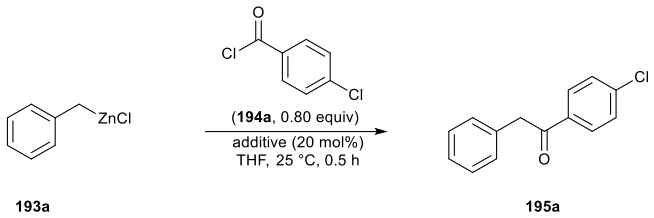
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2931, 2848, 1720, 1639, 1597, 1574, 1506, 1465, 1442, 1416, 1406, 1303, 1282, 1247, 1226, 1174, 1148, 1116, 1028, 1013, 967, 927, 856, 841, 789, 763, 681.

MS (EI, 70 eV, %) m/z = 230 (31), 135 (38), 123 (25), 95 (13), 85 (13), 83 (12), 71 (20), 57 (26), 55 (15), 44 (37), 43 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}FO_2$**: 230.0743; found: 230.0747.

4.6. Additional Screenings and Supporting Information

Table 21: Additional screening of additives for the acylation reaction of benzylic zinc chloride **193a** with 4-chlorobenzoyl chloride (**194a**).

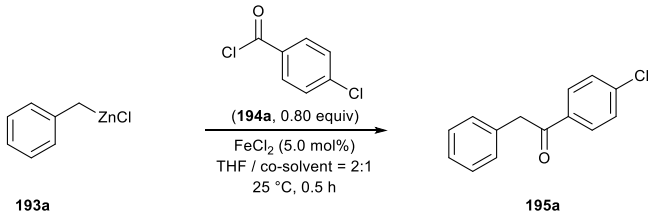


193a 195a

Entry	Additive	Yield (%)[a]
1	4-DMAP	55
2	$Sc(OTf)_3$	54
3	$InCl_3$	traces
4	$TiCl_4$	traces[b]
5	$BF_3{\cdot}OEt_2$	40
6	$LaCl_3{\cdot}2LiCl$	traces

[a] Isolated yield; [b] Almost quantitative amounts of homocoupling of the benzylic zincs reagent were observed.

Table 22: Additional screening of co-solvents for the acylation reaction of benzylic zinc chloride **193a** with 4-chlorobenzoyl chloride (**194a**).

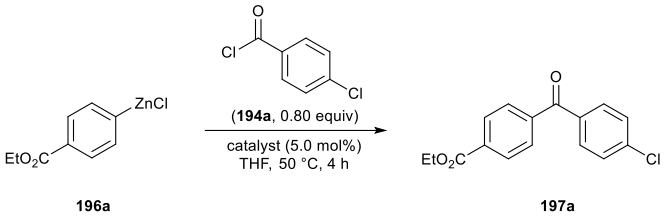


193a 195a

Entry	Solvent Ratio	Yield (%)[a]
1	THF : MeCN	87
2	THF : NMP	83
3	THF : DMPU	68
4	THF : dioxane	64
5	THF : DMF	29
6	THF : DMA	traces
7	THF	90

[a] Isolated yield.

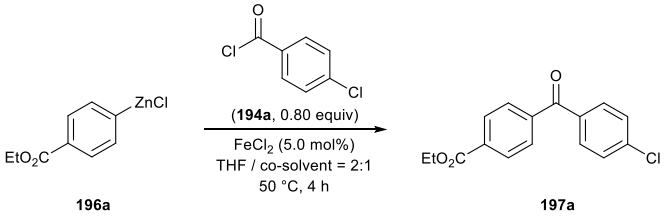
Table 23: Screening of iron catalysts for the acylation reaction of arylzinc reagent **196a** with 4-chlorobenzoyl chloride (**194a**)



Entry	Catalyst	Yield (%)[a]
1	-	34
2	$Fe(OTf)_3$	34
3	$Fe(acac)_3$	36
4	$FeBr_3$	53
5	$Fe(acac)_2$	60
6	$FeBr_2$	56
7	$FeCl_2$	62

[a] Isolated yield.

Table 24: Screening of co-solvents for the acylation reaction of arylzinc reagent **196a** with 4-chlorobenzoyl chloride (**194a**)



Entry	Solvent Ratio	Yield (%)[a]
1	THF : MeCN	60
2	THF : NMP	42
3	THF : DMPU	45
4	THF : dioxane	64
5	THF : DMF	38
6	THF : DMA	64
7	THF	62

[a] Isolated yield.

5. A Practical Cobalt-Catalyzed Cross-Coupling of Benzylic Zinc Reagents with Aryl and Heteroaryl Bromides or Chlorides

5.1. Typical Procedures

Typical procedure for the preparation of benzylzinc(II) chlorides (193a–j) (TP 1)

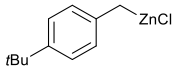
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.53 g, 13 mmol, 1.3 equiv) and heated up to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv) was added under argon, the *Schlenk*-tube was heated to 320 °C under high vacuum for 5 min, cooled to room temperature, charged with magnesium turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (10–15 mL) was added. The corresponding benzylic chloride (10 mmol, 1.0 equiv) was added and the reaction mixture was stirred at room temperature for a given time until full conversion of the starting material was observed. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was complete, the solution of the corresponding benzylzinc(II) chloride was separated from the resulting salts *via* a syringe equipped with a filter and transferred to another pre-dried and argon-flushed *Schlenk*-tube, before being titrated against iodine.

Typical procedure for the cobalt-catalyzed cross-coupling of benzylzinc((II) chlorides (193) with electrophiles of type 184 (TP 2)

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a rubber septum, was charged with $CoCl_2$ (5.0 mol%, $\geq$ 97% purity) and heated to 450 °C for 5 min under high vacuum. After cooling to room temperature, the corresponding electrophile (1.0 equiv), freshly distilled MTBE (methyl *tert*-butyl ether) and isoquinoline (10 mol%) were added. Thereupon, the benzylzinc(II) chloride solution (1.3–1.5 equiv) was added dropwise at room temperature and the reaction mixture was stirred for a given time at 50 °C. The reaction mixture was monitored by GC-analysis of quenched aliquots. A saturated aqueous solution of NH_4Cl was added and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude products by flash column chromatography afforded the desired products.

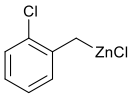
5.2. Preparation of the Benzylzinc(II) chlorides (193h–j)

Preparation of 4-(*tert*-butyl)benzylzinc(II) chloride (193h)



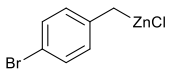
According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (15 mL) were used. The 4-*tert*-butylbenzyl chloride (1.8 g, 1.9 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 5 h at room temperature. The concentration of 4-(*tert*-butyl)benzylzinc(II) chloride (**193h**) was determined by titration with iodine in THF (0.44 M, 70%).

Preparation of 2-chlorobenzylzinc(II) chloride (193i)



According to **TP1**, LiCl (0.53 g, 13 mmol, 1.3 equiv), $ZnCl_2$ (1.5 g, 11 mmol, 1.1 equiv), Mg turnings (0.58 g, 24 mmol, 2.4 equiv) and freshly distilled THF (15 mL) were used. The 2-chlorobenzyl chloride (1.6 g, 1.3 mL, 10 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. The concentration of 2-chlorobenzylzinc(II) chloride (**193i**) was determined by titration with iodine in THF (0.54 M, 81%).

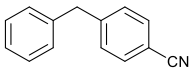
Preparation of 4-bromobenzylzinc(II) chloride (193j)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.64 g, 15 mmol, 1.5 equiv) and heated to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, zinc dust (2.0 g, 30 mmol, 3.0 equiv) was added under argon, the *Schlenk*-tube was heated to 450 °C for 5 min, cooled to room temperature and charged with freshly distilled THF (15 mL). Then, trimethylsilyl chloride (0.05 g, 0.06 mL, 0.45 mmol) and 1,2-dibromoethane (0.08 g, 0.04 mL, 0.45 mmol) were added dropwise. The reaction mixture was shortly heated to reflux, 4-bromobenzyl chloride (2.1 g, 10 mmol, 1.0 equiv) was added at once at room temperature and the reaction mixture was stirred for 2.5 h. After the zinc dust set down, the metalated species was transferred into another pre-dried and argon-flushed *Schlenk*-tube. The concentration of 4-bromobenzylzinc(II) chloride (**193j**) was determined by titration with iodine in THF (0.44 M, 66%).

5.3. Cobalt-Catalyzed Cross-Coupling of Benzylzinc(II) Chlorides 193 with 4-Bromobenzonitrile (184b) as Electrophile

Synthesis of 4-benzylbenzonitrile (185b)



Based on **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.5 mL). The benzylzinc(II) chloride solution (**193a**, 3.1 mL, 1.3 mmol, 0.43 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 19 : 1, R_f = 0.20) leading to the desired product **185b** (158 mg, 0.82 mmol, 82%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50 (d, *J* = 8.4 Hz, 2H), 7.28–7.16 (m, 5H), 7.11 (d, *J* = 7.4 Hz, 2H), 3.98 (s, 2H).

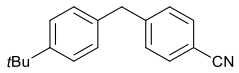
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 146.8, 139.4, 132.3, 129.7, 129.0, 128.8, 126.7, 119.0, 110.1, 42.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3064, 3029, 2926, 2228, 1734, 1507, 1496, 1454, 1414, 1373, 1242, 1178, 1113, 1074, 1046, 912, 854, 797, 761, 725, 698.

MS (EI, 70 eV, %) m/z = 194 (15), 193 (100), 192 (32), 190 (14), 165 (17), 91 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}N$**: 193.0891; found: 193.0885.

Synthesis of 4-(4-*tert*-butyl)benzyl)benzonitrile (198a)



According to **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 euqiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.5 mL). The 4-(*tert*-butyl)benzylzinc(II) chloride solution (**193h**, 3.0 mL, 1.30 mmol, 0.44 M in THF, 1.30 equiv) was added dropwise to this solution and the reaction mixture was stirred for 4 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.48) afforded the product **198a** (193 mg, 0.77 mmol, 77%) as a colorless liquid.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 4.01 (s, 2H), 1.32 (s, 9H).

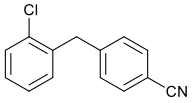
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 149.4, 146.8, 136.2, 132.1, 129.6, 128.5, 125.5, 118.9, 109.8, 41.4, 34.3, 31.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2961, 2868, 2223, 1691, 1605, 1510, 1502, 1478, 1407, 1362, 1270, 1108, 1019, 864, 819, 794, 754, 719, 669.

MS (EI, 70 eV, %) m/z = 249 (19), 235 (18), 234 (100), 116 (38), 102 (10), 57 (19), 43 (21), 42 (11), 41 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}N$**: 249.1517; found: 249.1511.

Synthesis of 4-(2-chlorobenzyl)benzonitrile (198b)



According to **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 euqiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.4 mL). The 2-chlorobenzylzinc(II) chloride solution (**193i**, 2.8 mL, 1.5 mmol, 0.54 M in THF, 1.50 equiv) was added dropwise to this solution and the reaction mixture was stirred for 18 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.30) yielding the product **198b** (168 mg, 0.74 mmol, 74%) as a pale yellow solid.

M.p. 55 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50 (d, *J* = 8.4 Hz, 2H), 7.35–7.30 (m, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.18–7.13 (m, 2H), 7.12–7.08 (m, 1H), 4.09 (s, 2H).

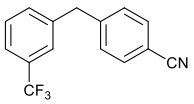
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 145.3, 137.1, 134.5, 132.4, 131.3, 130.0, 129.7, 128.5, 127.3, 119.1, 110.4, 39.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2924, 2853, 2225, 1741, 1607, 1470, 1443, 1413, 1115, 1102, 1049, 1033, 1020, 915, 843, 805, 758, 741, 673.

MS (EI, 70 eV, %) m/z = 229 (17), 227 (46), 192 (100), 191 (21), 190 (42), 165 (29), 82 (13), 71 (14), 57 (22), 56 (12), 44 (11), 43 (34), 42 (21), 41 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}ClN$**: 227.0502; found: 227.0498.

Synthesis of 4-(3-(trifluoromethyl)benzyl)benzonitrile (198c)



With reference to **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (0.90 mL). The 3-(trifluoromethyl)benzylzinc(II) chloride solution (**196b**, 1.8 mL, 1.3 mmol, 0.72 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.22) obtaining the product **198c** (184 mg, 0.70 mmol, 70%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.59 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.47–7.41 (m, 2H), 7.34 (d, *J* = 7.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.10 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 145.9, 140.7, 132.9, 132.7 (q, ^3J(C,F) = 3.8 Hz), 131.6 (q, ^2J(C,F) = 32 Hz), 130.1, 129.7, 126.0 (q, ^3J(C,F) = 3.8 Hz), 124.1 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 271 Hz), 119.2, 111.0, 42.1.

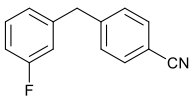
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.6.

IR (ATR, cm^{-1}) ṽ = 2928, 2228, 1607, 1508, 1449, 1414, 1326, 1160, 1117, 1093, 1072, 1021, 919, 877, 847, 795, 753, 739, 700, 659.

MS (EI, 70 eV, %) m/z = 263 (10), 262 (17), 261 (100), 260 (16), 242 (15), 241 (34), 240 (18), 221 (10), 193 (11), 192 (66), 191 (16), 190 (28), 165 (17), 159 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{10}F_3N$**: 261.0765; found: 261.0763.

Synthesis of 4-(3-fluorobenzyl)benzonitrile (198d)



Based on **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.0 mL). The 3-fluorobenzylzinc(II) chloride solution (**193c**, 2.0 mL, 1.3 mmol, 0.66 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 1 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.22) furnished the product **198d** (167 mg, 0.79 mmol, 79%) as a slightly yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.60 (d, *J* = 8.2 Hz, 2H), 7.33–7.27 (m, 3H), 6.99–6.81 (m, 3H), 4.04 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.1 (d, ^1J(C,F) = 246 Hz), 145.9, 141.9 (d, ^3J(C,F) = 7.2 Hz), 132.5, 130.3 (d, ^3J(C,F) = 8.3 Hz), 129.7, 124.7 (d, ^4J(C,F) = 3.0 Hz), 118.9, 116.0 (d, ^2J(C,F) = 21 Hz), 113.8 (d, ^2J(C,F) = 21 Hz), 110.5, 41.7.

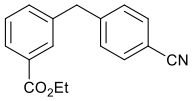
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −112.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3060, 2927, 2227, 1606, 1588, 1504, 1485, 1448, 1414, 1246, 1177, 1136, 1114, 1073, 1021, 947, 877, 842, 818, 783, 753, 731, 696, 682.

MS (EI, 70 eV, %) m/z = 212 (14), 211 (100), 210 (24), 208 (10), 183 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}FN$**: 211.0797; found: 211.0798.

Synthesis of ethyl 3-(4-cyanobenzyl)benzoate (198e)



According to **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (2.0 mL). The 3-(ethoxycarbonyl)benzylzinc(II) chloride solution (**193d**, 4.0 mL, 1.5 mmol, 0.38 M in THF, 1.5 equiv) was added dropwise to this solution and the reaction mixture was stirred for 18 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.12) gave the product **198e** (164 mg, 0.62 mmol, 62%) as a pale yellow liquid.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.92 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.89–7.85 (m, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.33 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.07 (s, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

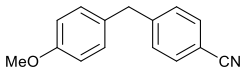
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 166.3, 145.9, 139.5, 133.3, 132.3, 130.9, 130.0, 129.5, 128.7, 127.8, 118.7, 110.2, 61.0, 41.6, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 2254, 2229, 1712, 1606, 1588, 1444, 1367, 1280, 1187, 1105, 1081, 1021, 906, 851, 812, 758, 725, 670.

MS (EI, 70 eV, %) m/z = 266 (14), 265 (61), 238 (10), 237 (54), 236 (11), 221 (22), 220 (100), 192 (29), 191 (15), 190 (31), 165 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{15}NO_2$**: 265.1103; found: 265.1090.

Synthesis of 4-(4-methoxybenzyl)benzonitrile (198f)



Based on **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.2 mL). The 4-methoxybenzylzinc(II) chloride solution (**193e**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.26) affording the product **198f** (182 mg, 0.82 mmol, 82%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.49 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.91 (s, 2H), 3.72 (s, 3H).

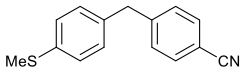
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.1, 147.0, 132.1, 131.2, 129.7, 129.3, 118.8, 113.9, 109.7, 55.0, 40.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3033, 3000, 2955, 2931, 2836, 2359, 2225, 1608, 1583, 1509, 1462, 1440, 1413, 1301, 1243, 1176, 1109, 1032, 917, 808, 761, 732.

MS (EI, 70 eV, %) m/z = 224 (15), 223 (100), 222 (27), 208 (20), 192 (14), 190 (13), 180 (13), 121 (37).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NO$**: 223.0997; found: 223.0993.

Synthesis of 4-(4-(methylthio)benzyl)benzonitrile (198g)



According to **TP2**, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.9 mL). The 4-(methylthio)benzylzinc(II) chloride solution (**193f**, 3.7 mL, 1.3 mmol, 0.35 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 18 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.27) leading to the product **198g** (156 mg, 0.65 mmol, 65%) as a white solid.

M.p. 73 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.49 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 3.92 (s, 2H), 2.40 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 146.7, 136.8, 136.3, 132.4, 129.7, 129.5, 127.2, 119.0, 110.2, 41.5, 16.1.

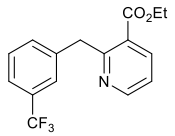
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2915, 2227, 1693, 1604, 1493, 1435, 1404, 1321, 1207, 1091, 1015, 968, 959, 917, 860, 848, 812, 791, 744, 654.

MS (EI, 70 eV, %) m/z = 240 (17), 239 (100), 192 (72), 191 (20), 190 (32), 165 (19), 137 (17), 57 (13), 43 (22), 42 (13), 41 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NS$**: 265.1103; found: 239.0766.

5.4. Cobalt-Catalyzed Cross-Coupling of Benzylzinc(II) Chlorides 193 with Several Aryl and Heteroaryl Halides of Type 184

Preparation of ethyl 2-(3-(trifluoromethyl)benzyl)nicotinate (198h)



With reference to **TP2**, ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (0.90 mL). The 3-(trifluoromethyl)benzylzinc(II) chloride solution (**193b**, 1.8 mL, 1.3 mmol, 0.72 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.21) led to the product **198h** (186 mg, 0.60 mmol, 60%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.62 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.13 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.49 (s, 1H), 7.40–7.17 (m, 4H), 4.56 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.4, 160.4, 152.2, 140.7, 138.9, 132.6 (q, ^4J(C,F) = 2.4 Hz), 130.6 (q, ^2J(C,F) = 32 Hz), 128.7, 126.2, 125.9 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 271 Hz), 123.1 (q, ^3J(C,F) = 3.9 Hz), 121.7, 61.7, 42.2, 14.2.

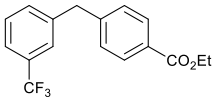
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3049, 2985, 2363, 1720, 1583, 1570, 1448, 1438, 1368, 1328, 1300, 1259, 1190, 1161, 1118, 1094, 1073, 1057, 1017, 917, 862, 822, 793, 782, 747, 734, 701, 676, 660.

MS (EI, 70 eV, %) m/z = 310 (18), 309 (83), 308 (92), 290 (12), 281 (11), 280 (54), 264 (52), 263 (59), 262 (13), 237 (16), 236 (100), 235 (59), 234 (65), 216 (18), 167 (31), 166 (23), 139 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}F_3NO_2$**: 309.0977; found: 309.0966.

Preparation of ethyl 4-(3-(trifluoromethyl)benzyl)benzoate (198i)



With reference to **TP2**, ethyl 4-bromobenzoate (229 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (0.90 mL). The 3-(trifluoromethyl)benzylzinc(II) chloride solution (**193b**, 1.8 mL, 1.3 mmol, 0.72 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 18 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.13) gave the desired product **198i** (166 mg, 0.54 mmol, 54%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.92 (d, *J* = 8.3 Hz, 2H), 7.42–7.26 (m, 4H), 7.17 (d, *J* = 9.2 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.6, 145.3, 141.2, 132.4 (q, ^4J(C,F) = 1.0 Hz), 131.1 (q, ^2J(C,F) = 32 Hz), 130.1, 129.2, 129.0, 125.7 (q, ^3J(C,F) = 3.7 Hz), 124.2 (q, ^1J(C,F) = 271 Hz), 123.5 (q, ^3J(C,F) = 3.8 Hz), 61.0, 41.8, 14.5.

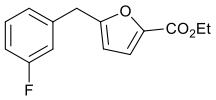
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 1713, 1610, 1449, 1415, 1367, 1329, 1273, 1161, 1119, 1101, 1073, 1021, 918, 905, 877, 851, 790, 769, 743, 699, 659.

MS (EI, 70 eV, %) m/z = 308 (22), 280 (20), 264 (19), 263 (100), 235 (39), 215 (12), 185 (20), 183 (20), 166 (20), 165 (37), 159 (29), 57 (10), 44 (10), 43 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{15}F_3O_2$**: 308.1024; found: 328.1017.

Preparation of ethyl 5-(3-fluorobenzyl)furan-2-carboxylate (198j)



According to **TP2**, ethyl 5-bromofuran-2-carboxylate (220 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.0 mL). The 3-fluorobenzylzinc(II) chloride solution (**193c**, 2.0 mL, 1.3 mmol, 0.66 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 3 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.26) obtaining the product **198j** (149 mg, 0.60 mmol, 60%) as pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.24–7.20 (m, 1H), 7.05 (d, *J* = 3.4 Hz, 1H), 6.98 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.90 (m, 2H), 6.06 (dt, *J* = 3.4, 0.8 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (d, ^1J(C,F) = 245 Hz), 158.9, 158.6, 144.1, 139.3 (d, ^3J(C,F) = 7.0 Hz), 130.2 (d, ^3J(C,F) = 8.0 Hz), 124.6 (d, ^4J(C,F) = 3.0 Hz), 119.0, 115.9 (d, ^2J(C,F) = 22 Hz), 113.9 (d, ^2J(C,F) = 20 Hz), 109.2, 60.9, 34.5, 14.5.

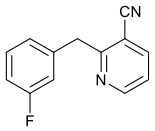
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −113.0.

IR (ATR, cm^{-1}) ṽ = 3128, 2983, 2361, 1713, 1616, 1591, 1519, 1488, 1448, 1383, 1368, 1297, 1251, 1205, 1173, 1126, 1075, 1016, 970, 944, 912, 866, 789, 760, 731, 681.

MS (EI, 70 eV, %) m/z = 249 (10), 248 (67), 220 (10), 219 (23), 203 (42), 176 (17), 175 (100), 147 (16), 146 (40), 127 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}FO_3$**: 248.0849; found: 248.0845.

Preparation of 2-(3-fluorobenzyl)nicotinonitrile (198k)



With reference to **TP2**, 2-chloronicotinonitrile (139 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.0 mL). The 3-fluorobenzylzinc(II) chloride solution (**193c**, 2.0 mL, 1.3 mmol, 0.66 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 3 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.20) led to the product **198k** (142 mg, 0.67 mmol, 67%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.75 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.32–7.22 (m, 2H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.07 (dt, *J* = 9.8, 1.9 Hz, 1H), 6.92 (td, *J* = 8.9, 3.5 Hz, 1H), 4.38 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (d, ^1J(C,F) = 245 Hz), 162.9, 152.8, 140.8, 139.8 (d, ^3J(C,F) = 7.5 Hz), 130.3 (d, ^3J(C,F) = 8.3 Hz), 124.9 (d, ^4J(C,F) = 2.9 Hz), 121.7, 116.8, 116.1 (d, ^2J(C,F) = 21 Hz), 114.1 (d, ^2J(C,F) = 22 Hz), 109.4, 42.8.

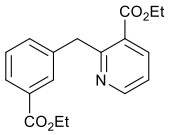
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −112.8.

IR (ATR, cm^{-1}) ṽ = 3062, 2961, 2930, 2856, 2228, 1614, 1589, 1580, 1564, 1486, 1447, 1431, 1247, 1160, 1137, 1093, 946, 880, 852, 800, 770, 735, 710, 685.

MS (EI, 70 eV, %) m/z = 212 (39), 211 (100), 210 (17), 190 (14), 129 (19), 109 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9FN_2$**: 212.0750; found: 212.0750.

Preparation of ethyl 2-(3-(ethoxycarbonyl)benzyl)nicotinate (198l)



According to **TP2**, ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (2.0 mL). The 3-(ethoxycarbonyl)benzylzinc(II) chloride solution (**193d**, 4.0 mL, 1.5 mmol, 0.38 M in THF, 1.5 equiv) was added dropwise to this solution and the reaction mixture was stirred for 18 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.15) yielding the product **198l** (212 mg, 0.68 mmol, 68%) as a pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.67 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.17 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.94 (t, *J* = 1.8 Hz, 1H), 7.87–7.83 (m, 1H), 7.42 (ddd, *J* = 7.1, 1.8, 1.2 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.23 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.62 (s, 2H), 4.33 (qd, *J* = 7.1, 0.8 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

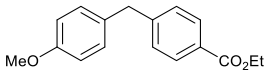
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.8, 166.5, 152.1, 140.1, 138.8, 133.6, 130.6, 130.2, 128.3, 127.5, 126.2, 121.5, 61.6, 60.9, 42.3, 14.4, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 2255, 1713, 1583, 1569, 1438, 1391, 1367, 1278, 1188, 1131, 1106, 1081, 1058, 1020, 906, 725, 694.

MS (EI, 70 eV, %) m/z = 314 (21), 313 (100), 312 (17), 268 (22), 256 (12), 240 (30), 239 (16), 238 (11), 221 (17), 212 (15), 211 (28), 194 (13), 167 (23), 166 (23).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}NO_4$**: 313.1314; found: 313.1322.

Preparation of ethyl 4-(4-methoxybenzyl)benzoate (198m)



According to **TP2**, ethyl 4-bromobenzoate (229 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.2 mL). The 4-methoxybenzylzinc(II) chloride solution (**193e**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 1 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.32) leading to the product **198m** (189 mg, 0.70 mmol, 70%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.90 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 2H), 3.71 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).

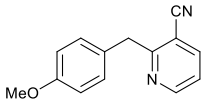
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.7, 158.3, 147.0, 132.4, 130.0, 129.9, 128.9, 128.5, 114.1, 60.9, 55.4, 41.2, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2981, 2835, 1711, 1610, 1584, 1510, 1463, 1441, 1414, 1391, 1366, 1301, 1271, 1243, 1175, 1104, 1033, 1020, 920, 869, 854, 831, 798, 772, 740, 698.

MS (EI, 70 eV, %) m/z = 271 (18), 270 (100), 241 (12), 225 (37), 197 (62), 165 (14), 153 (10), 121 (25), 113 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{18}O_3$**: 270.1256; found: 270.1240.

Preparation of 2-(4-methoxybenzyl)nicotinonitrile (198n)



According to **TP2**, 2-chloronicotinonitrile (139 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.2 mL). The 4-methoxybenzylzinc(II) chloride solution (**193e**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.17) obtaining the product **198n** (173 mg, 0.77 mmol, 77%) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.65 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 7.16 (dd, *J* = 7.8, 4.9 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.24 (s, 2H), 3.69 (s, 3H).

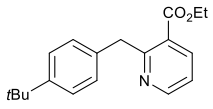
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 164.5, 158.9, 153.0, 141.0, 130.5, 130.0, 121.6, 117.4, 114.5, 109.3, 55.6, 42.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3051, 2999, 2956, 2932, 2836, 2227, 1610, 1581, 1563, 1509, 1431, 1301, 1276, 1245, 1176, 1109, 1088, 1031, 943, 806, 788, 742, 720, 696.

MS (EI, 70 eV, %) m/z = 225 (16), 224 (100), 223 (55), 209 (53), 192 (12), 179 (13), 121 (50), 43 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}N_2O$**: 224.0950; found: 224.0940.

Preparation of ethyl 2-(4-(*tert*-butyl)benzyl)nicotinate (198o)



According to **TP2**, ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.5 mL). The 4-(*tert*-butyl)benzylzinc(II) chloride solution (**193h**, 3.0 mL, 1.3 mmol, 0.44 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 4 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.15) affording the product **198o** (284 mg, 0.95 mmol, 95%) as a pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.68 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.15 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 7.24–7.18 (m, 3H), 4.56 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 t, *J* = 7.1 Hz, 3H), 1.28 (s, 9H).

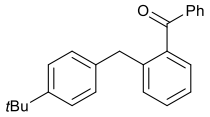
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 166.5, 161.3, 151.7, 148.6, 138.3, 136.5, 128.5, 126.1, 125.0, 121.0, 61.3, 41.7, 34.2, 31.3, 14.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2961, 2868, 1721, 1582, 1567, 1514, 1437, 1364, 1255, 1130, 1111, 1078, 1056, 1019, 860, 806, 762, 743, 663.

MS (EI, 70 eV, %) m/z = 298 (21), 297 (100), 296 (45), 283 (16), 282 (75), 254 (12), 236 (20), 224 (14), 196 (20), 195 (24), 167 (11), 57 (28), 43 (29), 42 (20), 41 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{23}NO_2$**: 297.1729; found: 297.1724.

Preparation of (2-(4-(*tert*-butyl)benzyl)phenyl)(phenyl)methanone (198p)



According to **TP2**, 2-bromo-benzophenone (261 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.5 mL). The 4-(*tert*-butyl)benzylzinc(II) chloride solution (**193h**, 3.0 mL, 1.3 mmol, 0.44 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 4 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.13) gave the desired product **198p** (210 mg, 0.64 mmol, 64%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.48–7.44 (m, 1H), 7.37–7.29 (m, 3H), 7.24–7.18 (m, 3H), 7.14–7.08 (m, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 2H), 1.17 (s, 9H).

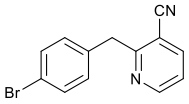
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.7, 148.8, 140.5, 139.1, 137.8, 137.5, 133.1, 130.9, 130.3 (2C), 129.0, 128.5, 128.3, 125.6, 125.2, 38.5, 34.4, 31.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3060, 3026, 2961, 2904, 2867, 2246, 1663, 1597, 1580, 1514, 1448, 1412, 1363, 1314, 1268, 1202, 1179, 1152, 1109, 1020, 1001, 936, 908, 842, 795, 763, 730, 709, 700, 668.

MS (EI, 70 eV, %) m/z = 329 (12), 328 (31), 327 (30), 313 (15), 272 (24), 271 (100), 255 (17), 254 (38), 195 (32), 194 (37), 193 (14), 165 (22), 147 (13), 105 (16), 91 (11), 77 (11), 57 (29), 43 (18), 42 (10), 41 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{24}H_{24}O$**: 328.1827; found: 328.1821.

Preparation of 2-(4-bromobenzyl)nicotinonitrile (198q)



With reference to **TP2**, 2-chloronicotinonitrile (139 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.5 mL). The 4-bromobenzylzinc(II) chloride solution (**193j**, 3.0 mL, 1.3 mmol, 0.44 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 18 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.24) furnished the product **198q** (186 mg, 0.68 mmol, 68%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.73 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.92 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.30–7.27 (m, 1H), 7.25 (d, *J* = 7.8 Hz, 2H), 4.33 (s, 2H).

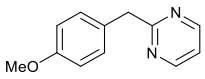
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.8, 152.4, 140.8, 136.2, 131.7, 130.8, 121.5, 121.0, 116.6, 109.1, 42.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3048, 2922, 2851, 2228, 1580, 1565, 1486, 1430, 1405, 1179, 1102, 1070, 1011, 842, 800, 767, 716, 701.

MS (EI, 70 eV, %) m/z = 274 (52), 273 (100), 272 (56), 271 (94), 248 (13), 246 (13), 192 (86), 171 (13), 167 (11), 166 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9BrN_2$**: 271.9949; found: 271.9949.

Preparation of 2-(4-methoxybenzyl)pyrimidine (198r)



With reference to **TP2**, 2-bromopyrimidine (159 g, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.2 mL). The 4-methoxybenzylzinc(II) chloride solution (**193e**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.10) leading to the desired product **198r** (142 mg, 0.71 mmol, 71%) as pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.58 (d, *J* = 4.9 Hz, 2H), 7.20 (d, 8.7 Hz, 2H), 7.01 (t, *J* = 4.9 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.16 (s, 2H), 3.68 (s, 3H).

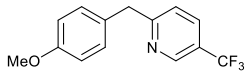
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 170.1, 158.1, 157.0 (2C), 130.1, 129.9, 118.3, 113.7, 54.9, 44.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3036, 2998, 2955, 2932, 2835, 2360, 2341, 1734, 1610, 1570, 1559, 1509, 1462, 1414, 1373, 1300, 1281, 1239, 1176, 1108, 1032, 993, 867, 847, 806, 732, 713, 668.

MS (EI, 70 eV, %) m/z = 200 (19), 199 (10), 185 (11), 70 (12), 61 (17), 45 (14), 43 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}N_2O$**: 200.0950; found: 200.0944.

Preparation of 2-(4-methoxybenzyl)-5-(trifluoromethyl)pyridine (198s)



According to **TP2**, 2-chloro-5-(trifluoromethyl)pyridine (182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.2 mL). The 4-methoxybenzylzinc(II) chloride solution (**193e**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.24) afforded the product **198s** (222 mg, 0.83 mmol, 83%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.81 (s, 1H), 7.79 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.23–7.17 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.17 (s, 2H), 3.79 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 165.3, 158.3, 146.1 (q, ^3J(C,F) = 4.1 Hz), 133.4 (q, ^3J(C,F) = 3.5 Hz), 130.3, 129.9, 124.1 (q, ^2J(C,F) = 33 Hz), 123.5 (q, ^1J(C,F) = 270 Hz), 122.4, 114.0, 55.1, 43.6.

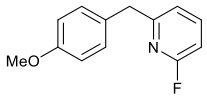
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2935, 2837, 1606, 1573, 1511, 1492, 1464, 1441, 1391, 1325, 1301, 1245, 1163, 1120, 1077, 1034, 1015, 941, 867, 829, 810, 785, 755, 727, 710.

MS (EI, 70 eV, %) m/z = 268 (15), 267 (100), 266 (78), 253 (10), 252 (64), 235 (13), 224 (27), 222 (14), 121 (45).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}F_3NO$**: 267.0871; found: 267.0867.

Preparation of 2-fluoro-6-(4-methoxybenzyl)pyridine (198t)



With reference to **TP2**, 2-chloro-6-fluoropyridine (132 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.2 mL). The 4-methoxybenzylzinc(II) chloride solution (**193e**, 2.3 mL, 1.3 mmol, 0.56 M in THF, 1.3 equiv) was added dropwise to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.20) leading to the desired product **198t** (113 mg, 0.52 mmol, 52%) as pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.69–7.59 (m, 1H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.95 (dd, *J* = 7.3, 2.3 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.73 (dd, *J* = 8.1, 2.3 Hz, 1H), 4.02 (s, 2H), 3.78 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.5 (d, ^1J(C,F) = 238 Hz), 161.1 (d, ^2J(C,F)= 13 Hz), 158.8, 141.8 (d, ^3J(C,F) = 7.7 Hz), 131.2, 130.6, 120.5 (d, ^4J(C,F) = 4.2 Hz), 114.5, 107.0 (d, ^2J(C,F) = 37 Hz), 55.7, 43.5.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −67.5.

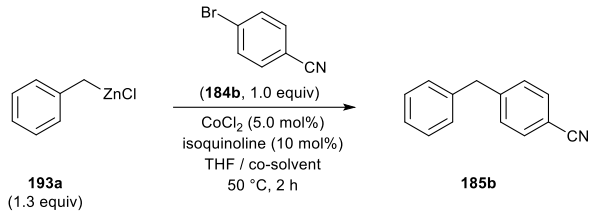
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3001, 2934, 2836, 1603, 1574, 1510, 1449, 1436, 1300, 1243, 1222, 1176, 1145, 1106, 1075, 1033, 995, 971, 848, 819, 797, 764, 746, 725, 704.

MS (EI, 70 eV, %) m/z = 218 (15), 217 (100), 216 (25), 202 (65), 185 (14), 174 (43), 172 (11), 121 (46).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{12}FNO$**: 217.0903; found: 217.0895.

5.5. Additional Screenings and Supporting Information

Table 25: Screening of co-solvents for the Co-catalyzed cross-coupling of benzylic zinc reagent **193a** with 4-bromobenzonitrile (**184b**).



Entry	THF / Co-solvent	Solvent Ratio	Yield (%)[a]
1	THF	-	77
2	THF / MTBE	1:1	60
3	THF / MTBE	1:2	57
4	THF / MTBE	2:1	82
5	THF / DMA	2:1	72
6	THF / NMP	2:1	69
7	THF / MeCN	2:1	68
8	THF / DMPU	2:1	66
9	THF / DMF	2:1	56

[a] Isolated yield.

6. Preparation of Polyfunctional Organozinc Halides by an InX_3- and LiCl-Catalyzed Zinc Insertion into Aryl and Heteroaryl Iodides and Bromides

6.1. Typical Procedures

Typical procedure for the direct insertion of zinc powder into aryl iodides using $InCl_3$ and LiCl as catalysts (Method A) (TP1)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.90 mmol, 30 mol%) and heated to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, $InCl_3$ (0.09 mmol, 3.0 mol%) was added and the *Schlenk*-tube was heated to 320 °C for 5 min under high vacuum. After cooling to room temperature, zinc powder (9.0 mmol, 3.0 equiv, zinc powder GR for analysis, particle size < 45 μm, commercially available from Merck KGaA) and freshly distilled THF (4.5 mL) were added. The resulting suspension was treated with a few drops of trimethylsilyl chloride and heated shortly to reflux. Subsequently, the corresponding aryl iodide (3.0 mmol, 1.0 equiv) was added and the reaction mixture was heated at a prior adjusted temperature for a given time. The reaction completion was determined by GC-analysis of water-quenched aliquots and the excess zinc dust was allowed to set down. The supernatant liquid was transferred *via* a syringe, equipped with a filter, into another pre-dried *Schlenk*-tube. Finally, the yield and concentration of the resulting arylzinc halide were determined by iodometric titration.

Typical procedure for the direct insertion of zinc powder into aryl iodides using $InCl_3$ and LiCl as catalysts and DMPU as polar co-solvent (Method B) (TP2)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.90 mmol, 30 mol%) and heated to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, $InCl_3$ (0.09 mmol, 3.0 mol%) was added and the *Schlenk*-tube was heated to 320 °C for 5 min under high vacuum. After cooling to room temperature, zinc powder (9.0 mmol, 3.0 equiv), freshly distilled THF (2.3 mL) and DMPU (*N*,*N'*-dimethylpropylen-urea) (2.3 mL) were added. The resulting suspension was treated with a few drops of trimethylsilyl chloride and heated shortly to reflux. Subsequently, the corresponding aryl iodide (3.0 mmol, 1.0 equiv) was added and the reaction mixture was heated at a prior adjusted temperature for a given time. The reaction completion was determined by GC-analysis of water-quenched aliquots. The excess zinc dust was allowed to set down and the supernatant liquid was transferred *via* a syringe, equipped with a filter, into another pre-dried *Schlenk*-tube. Finally, the yield and concentration of the resulting arylzinc halide were determined by iodometric titration.

Typical procedure for the direct insertion of zinc powder into aryl and heteroaryl bromides using $In(acac)_3$ as catalysts (TP3)

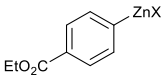
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (4.5 mmol, 1.5 equiv) and heated to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, $In(acac)_3$ (0.09 mmol, 3.0 mol%) was added and the *Schlenk*-tube was heated to 200 °C for 5 min under high vacuum. After cooling to room temperature, zinc powder (9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were added. The resulting suspension was treated with a few drops of trimethylsilyl chloride and 1,2-dibromoethane for activation and heated shortly to reflux. Subsequently, the corresponding aryl bromide (3.0 mmol, 1.0 equiv) was added and the reaction mixture was heated for a given time at 50 °C. The reaction completion was determined by GC-analysis of water-quenched aliquots and the excess zinc dust was allowed to set down. The supernatant liquid was transferred *via* a syringe, equipped with a filter, into another pre-dried *Schlenk*-tube. Finally, the yield and concentration of the resulting aryl- or heteroarylzinc halide were determined by iodometric titration.

Typical procedure for the direct insertion of zinc powder into alkyl bromides using $In(acac)_3$ as catalysts (TP4)

A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (4.5 mmol, 1.5 equiv) and heated to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, $In(acac)_3$ (0.3 mmol, 10 mol%) was added and the *Schlenk*-tube was heated to 200 °C for 5 min under high vacuum. After cooling to room temperature, zinc powder (9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were added. The resulting suspension was treated with a few drops of trimethylsilyl chloride and 1,2-dibromoethane for activation and heated shortly to reflux. Subsequently, the corresponding alkyl bromide (3.0 mmol, 1.0 equiv) was added and the reaction mixture was heated for a given time at 50 °C. The reaction completion was determined by GC-analysis of water-quenched aliquots. After the excess zinc dust was allowed to set down, the supernatant liquid was transferred *via* a syringe, equipped with a filter, into another pre-dried *Schlenk*-tube. Finally, the yield and concentration of the resulting alkylzinc halide was determined by iodometric titration.

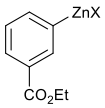
6.2. Preparation of the Functionalized Arylzinc Reagents (199a–n) via the Direct Insertion of Zinc using the Catalysis of $InCl_3$ and LiCl

Preparation of (4-(ethoxycarbonyl)phenyl)zinc(II) halide (199a)



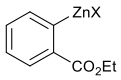
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Ethyl 4-iodobenzoate (828 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The concentration of (4-(ethoxycarbonyl)phenyl)zinc(II) halide (**199a**) was determined by the titration with iodine in THF (**Method A**: 2 h, 0.55 M, 92%; **Method B**: 15 min, 0.47 M, 78%).

Preparation of (3-(ethoxycarbonyl)phenyl)zinc(II) halide (199b)



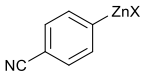
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Ethyl 3-iodobenzoate (828 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The concentration of (3-(ethoxycarbonyl)phenyl)zinc(II) halide (**199b**) was determined by the titration with iodine in THF (**Method A**: 2 h, 0.62 M, 90%; **Method B**: 15 min, 0.52 M, 78%).

Preparation of (2-(ethoxycarbonyl)phenyl)zinc(II) halide (199c)



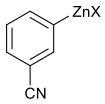
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Ethyl 2-iodobenzoate (828 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 15 min at 25 °C. The concentration of (2-(ethoxycarbonyl)phenyl)zinc(II) halide (**199c**) was determined by the titration with iodine in THF (**Method A**: 15 min, 0.55 M, 83%; **Method B**: 15 min, 0.33 M, 50%).

Preparation of (4-cyanophenyl)zinc(II) halide (199d)



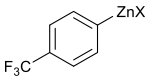
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 4-Iodobenzonitrile (687 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 30 min at 50 °C. The concentration of (4-cyanophenyl)zinc(II) halide (**199d**) was determined by the titration with iodine in THF (**Method A**: 30 min, 0.71 M, 95%; **Method B**: 30 min, 0.40 M, 60%).

Preparation of (3-cyanophenyl)zinc(II) halide (199e)



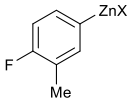
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 3-Iodobenzonitrile (687 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 30 min at 50 °C. The concentration of (3-cyanophenyl)zinc(II) halide (**199e**) was determined by the titration with iodine in THF (**Method A**: 30 min, 0.66 M, 88%; **Method B**: 30 min, 0.40 M, 60%).

Preparation of (4-(trifluoromethyl)phenyl)zinc(II) halide (199f)



According to **TP1**, LiCl (38 mg, 0.9 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 4-Iodobenzotrifluoride (816 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The concentration of (4-(trifluoromethyl)phenyl)zinc(II) halide (**199f**) was determined by the titration with iodine in THF (**Method A**: 2 h, 0.53 M, 80%, **Method B**: 30 min, 0.45 M, 68%).

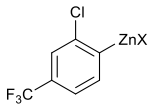
Preparation of (4-fluoro-3-methylphenyl)zinc(II) halide (199g)



According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 2-Fluoro-5-iodotoluene (708 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C.

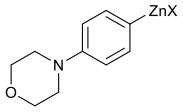
The concentration of (4-fluoro-3-methylphenyl)zinc(II) halide (**199g**) was determined by the titration with iodine in THF (**Method A**: 4 h, 0.38 M, 57%; **Method B**: 30 min, 0.40 M, 60%).

Preparation of (2-chloro-4-(trifluoromethyl)phenyl)zinc(II) halide (199h)



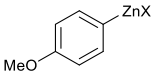
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 2-Chloro-1-iodo-4-(trifluoromethyl)benzene (919 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 15 min at 25 °C. The yield of (2-chloro-4-(trifluoromethyl)-phenyl)zinc(II) halide (**199h**) was determined by GC-analysis of water-quenched and iodolyzed aliquots using an internal standard (**Method A**: 15 min, 90%; **Method B**: 15 min, 90%).

Preparation of (4-morpholinophenyl)zinc(II) halide (199i)



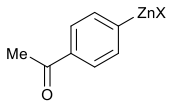
According to **TP1**, LiCl (38 mg, 0.9 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 4-(4-Iodophenyl)-morpholine (867 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 18 h at 50 °C. The concentration of (4-morpholinophenyl)zinc(II) halide (**199i**) was determined by the titration with iodine in THF (**Method A**: 18 h, 0.62 M, 93%; **Method B**: 2 h, 0.33 M, 50%).

Preparation of (4-methoxyphenyl)zinc(II) halide (199j)



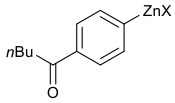
According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 4-Iodoanisole (702 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 6 h at 50 °C. The concentration of (4-methoxyphenyl)zinc(II) halide (**199j**) was determined by the titration with iodine in THF (**Method A**: 6 h, 0.37 M, 56%; **Method B**: 3 h, 0.43 M, 65%).

Preparation of (4-acetylphenyl)zinc(II) halide (199k)



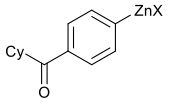
According to **TP2**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv), freshly distilled THF (2.3 mL) and DMPU (2.3 mL) were used. 4′-Iodoacetophenone (738 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 30 min at 25 °C. The concentration of (4-acetylphenyl)zinc(II) halide (**199k**) was determined by the titration with iodine in THF (**Method A**: 30 min, 0.30 M, 45%; **Method B**: 30 min, 0.41 M, 62%).

Preparation of (4-pentanoylphenyl)zinc(II) halide (199l)



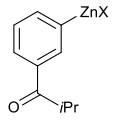
According to **TP2**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv), freshly distilled THF (2.3 mL) and DMPU (2.3 mL) were used. 1-(4-Iodophenyl)pentan-1-one (864 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 15 min at 25 °C. The concentration of (4-pentanoyl-phenyl)zinc(II) halide (**199l**) was determined by the titration with iodine in THF (**Method A**: 15 min, 0.18 M, 27%; **Method B**: 15 min, 0.33 M, 50%).

Preparation of (4-(cyclohexanecarbonyl)phenyl)zinc(II) halide (199m)



According to **TP1**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Cyclohexyl(4-iodo-phenyl)methanone (943 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 6 h at 50 °C. The concentration of (4-(cyclohexane-carbonyl)phenyl)zinc(II) halide (**199m**) was determined by the titration with iodine in THF (**Method A**: 6 h, 0.52 M, 62%; **Method B**: 15 min, 0.33 M, 50%).

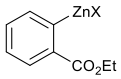
Preparation of (3-isobutyrylphenyl)zinc(II) halide (199n)



According to **TP2**, LiCl (38 mg, 0.90 mmol, 30 mol%), $InCl_3$ (20 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv), freshly distilled THF (2.3 mL) and DMPU (2.3 mL) were used. 1-(3-Iodophenyl)-2-methylpropan-1-one (822 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 30 min at 25 °C. The concentration of (3-isobutyrylphenyl)zinc(II) halide (**199n**) was determined by the titration with iodine in THF (**Method A**: 30 min, 0.33 M, 50%; **Method B**: 30 min, 0.41 M, 62%).

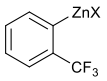
6.3. Preparation of the Functionalized Aryl- and Heteroarylzinc Reagents (199c, o–s) via the Direct Insertion of Zinc using $In(acac)_3$ as Catalyst

Preparation of (2-(ethoxycarbonyl)phenyl)zinc(II) halide (199c)



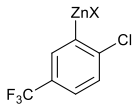
Based on **TP3**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (37 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Ethyl 2-bromobenzoate (687 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 18 h at 50 °C. The concentration of (2-(ethoxycarbonyl)phenyl)zinc(II) halide (**199c**) was determined by the titration with iodine in THF (0.60 M, 70%).

Preparation of (2-(trifluoromethyl)phenyl)zinc(II) halide (199o)



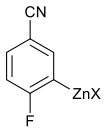
Based on **TP3**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (37 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 2-Bromobenzotrifluoride (675 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 6 h at 50 °C. The concentration of (2-(trifluoromethyl)phenyl)zinc(II) halide (**199o**) was determined by the titration with iodine in THF (0.41 M, 55%).

Preparation of (2-chloro-5-(trifluoromethyl)phenyl)zinc(II) halide (199p)



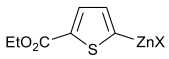
Based on **TP3**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (37 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 2-Bromo-1-chloro-4-(trifluoromethyl)benzene (778 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 2 h at 50 °C. The concentration of (2-chloro-5-(trifluoro-methyl)phenyl)zinc(II) halide (**199p**) was determined by the titration with iodine in THF (0.48 M, 67%).

Preparation of (2-chloro-5-cyanophenyl)zinc(II) halide (199q)



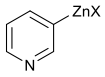
Based on **TP3**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (37 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 3-Bromo-4-chlorobenzonitrile (600 mg, 3.0 mmol, 1.0 equiv) was added at once and the reaction mixture was stirred for 2 h at 50 °C. The concentration of (2-chloro-5-cyanophenyl)zinc(II) halide (**199q**) was determined by the titration with iodine in THF (0.58 M, 77%).

Preparation of (5-(ethoxycarbonyl)thiophen-2-yl)zinc(II) halide (199r)



Based on **TP3**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (37 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Ethyl 5-bromothiophene-2-carboxylate (705 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The concentration of (5-(ethoxycarbonyl)-thiophen-2-yl)zinc(II) halide (**199r**) was determined by the titration with iodine in THF (0.53 M, 74%).

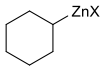
Preparation of pyridine-3-ylzinc(II) halide (199s)



Based on **TP3**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (37 mg, 0.09 mmol, 3.0 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 3-Bromopyridine (474 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 2 h at 50 °C. The concentration of pyridine-3-ylzinc(II) halide (**199s**) was determined by the titration with iodine in THF (0.53 M, 64%).

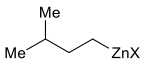
6.4. Preparation of the Alkylzinc Reagents (202a–e) via the Direct Insertion of Zinc using $In(acac)_3$ as Catalyst

Preparation of cyclohexylzinc(II) halide (202a)



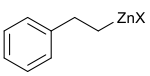
According to **TP4**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (124 mg, 0.30 mmol, 10 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Cyclohexyl bromide (489 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The concentration of cyclohexylzinc(II) halide (**202a**) was determined by the titration with iodine in THF (0.57 M, 72%).

Preparation of isopentylzinc(II) halide (202b)



According to **TP4**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (124 mg, 0.30 mmol, 10 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 1-Bromo-3-methylbutane (589 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 4 h at 50 °C. The concentration of isopentylzinc(II) halide (**202b**) was determined by the titration with iodine in THF (0.56 M, 73%).

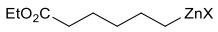
Preparation of phenethylzinc(II) halide (202c)



According to **TP4**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (124 mg, 0.30 mmol, 10 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. (2-Bromoethyl)-benzene (555 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 1 h

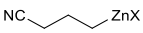
at 50 °C. The concentration of phenethylzinc(II) halide (**202c**) was determined by the titration with iodine in THF (0.49 M, 70%).

Preparation of (6-ethoxy-6-oxohexyl)zinc(II) halide (202d)



According to **TP4**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (124 mg, 0.30 mmol, 10 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. Ethyl 6-bromohexanoate (669 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 3 h at 50 °C. The concentration of (6-ethoxy-6-oxohexyl)-zinc(II) halide (**202d)** was determined by the titration with iodine in THF (0.52 M, 68%).

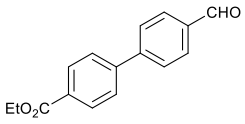
Preparation of (3-cyanopropyl)zinc(II) halide (202e)



According to **TP4**, LiCl (191 mg, 4.5 mmol, 1.5 equiv), $In(acac)_3$ (124 mg, 0.30 mmol, 10 mol%), zinc dust (589 mg, 9.0 mmol, 3.0 equiv) and freshly distilled THF (4.5 mL) were used. 4-Bromobutyronitrile (444 mg, 3.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred for 30 min at 50 °C. The concentration of (3-cyanopropyl)zinc(II) halide (**202e**) was determined by the titration with iodine in THF (0.59 M, 79%).

6.5. Trapping Reactions of the Functionalized Arylzinc Reagents (199a–n) with Electrophiles

Synthesis of ethyl 4'-formyl-[1,1'-biphenyl]-4-carboxylate (200a)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-bromobenzaldehyde (278 mg, 1.5 mmol, 1.0 equiv), $Pd(OAc)_2$ (14 mg, 0.06 mmol, 4.0 mol%), SPhos (49 mg, 0.12 mmol, 8.0 mol%) and freshly distilled THF (3.0 mL). The (4-(ethoxy-carbonyl)phenyl)zinc(II) halide (**199a**, 3.3 mL, 1.8 mmol, 0.55 M in THF, 1.2 equiv) was slowly added *via* a syringe pump at room temperature over 1 h. After further stirring for 1 h the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.34) leading to the product **200a** (366 mg, 1.44 mmol, 96%) as a yellow brown solid.

M.p. 68 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 10.07 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 2H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.70 (d, *J* = 8.6 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

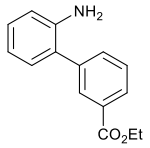
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 191.6, 166.0, 145.8, 143.7, 135.6, 130.6, 130.1, 130.0, 127.7, 127.1, 61.0, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2835, 1708, 1686, 1604, 1579, 1561, 1468, 1371, 1316, 1275, 1216, 1168, 1098, 1027, 1006, 871, 841, 824, 786, 767, 740, 724, 701, 665.

MS (EI, 70 eV, %) m/z = 255 (10), 254 (60), 226 (20), 225 (22), 210 (16), 209 (100), 153 (15), 152 (39), 151 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}O_3$**: 254.0943; found: 254.0933.

Synthesis of ethyl 2'-amino-[1,1'-biphenyl]-3-carboxylate (200b)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-bromoaniline (172 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (3-(ethoxycarbonyl)-phenyl)zinc(II) halide (**199b**, 1.9 mL, 1.2 mmol, 0.62 M in THF, 1.2 equiv) was slowly added *via* a syringe pump at room temperature over 1 h. After further stirring for 1 h the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.10) gave the product **200b** (234 mg, 0.97 mmol, 97%) as a brown yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.15 (t, *J* = 1.6 Hz, 1H), 8.04 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.66 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.18 (td, *J* = 7.9, 1.6 Hz, 1H), 7.13 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.84 (td, *J* = 7.5, 1.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

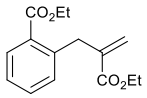
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.3, 143.3, 139.6, 133.3, 130.9, 130.2, 130.0, 128.7, 128.6, 128.1, 126.3, 118.5, 115.5, 60.9, 14.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3461, 3371, 2980, 2361, 1710, 1616, 1582, 1499, 1477, 1454, 1424, 1392, 1367, 1297, 1233, 1169, 1158, 1107, 1083, 1050, 1027, 998, 889, 820, 746, 735, 698.

MS (EI, 70 eV, %) m/z = 242 (19), 241 (100), 196 (13), 194 (29), 168 (48), 167 (84), 166 (20), 139 (11), 98 (11), 83 (14), 44 (22).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{15}NO_2$**: 241.1103; found: 241.1089.

Synthesis of ethyl 2-(2-(ethoxycarbonyl)allyl)benzoate (200c)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 2-(bromomethyl)acrylate (193 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) and cooled to –60 °C. To this solution, a pre-cooled mixture consisting of (2-(ethoxycarbonyl)phenyl)zinc(II) halide (**199c**, 2.2 mL, 1.2 mmol, 0.55 M in THF, 1.2 equiv) and CuCN·2LiCl (0.20 mL, 0.20 mmol, 1.0 M in THF, 0.20 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature, quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.29) afforded the product **200c** (247 mg, 0.94 mmol, 94%) as a colorless liquid.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.90–7.86 (m, 1H), 7.40 (td, *J* = 7.6, 1.4 Hz, 1H), 7.26 (td, *J* = 7.6, 1.2 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 1H), 6.16 (d, *J* = 1.3 Hz, 1H), 5.16 (d, *J* = 1.6 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.3 Hz, 3H).

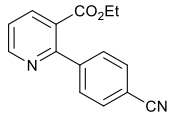
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 167.2, 166.8, 140.3, 139.7, 131.7, 131.4, 130.6, 130.4, 126.4, 125.2, 60.7, 60.6, 35.8, 14.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 2938, 2906, 2361, 1712, 1633, 1447, 1367, 1296, 1252, 1190, 1172, 1128, 1076, 1048, 1023, 947, 930, 857, 819, 751, 715, 659.

MS (EI, 70 eV, %) m/z = 262 (3), 217 (27), 216 (77), 189 (38), 188 (100), 161 (30), 160 (95), 145 (45), 144 (55), 143 (48), 142 (11), 133 (14), 132 (12), 131 (28), 117 (24), 116 (28), 115 (80), 91 (13), 89 (13), 77 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{18}O_4$**: 262.1205; found: 262.1201.

Synthesis of ethyl 2-(4-cyanophenyl)nicotinate (200d)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (4-cyanophenyl)zinc(II) halide (**199d**, 1.7 mL, 1.2 mmol, 0.71 M in THF, 1.2 equiv) was added dropwise and resulting solution was stirred for 2 h at 50 °C. The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.34) leading to the product **200d** (236 mg, 0.94 mmol, 94%) as a pale yellow solid.

M.p. 91 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.78 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.20 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.41 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H).

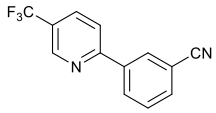
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.9, 157.3, 151.6, 144.8, 138.4, 133.8, 129.4, 127.1, 122.6, 118.7, 112.3, 61.8, 13.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2997, 2224, 1719, 1570, 1436, 1273, 1234, 1144, 1096, 1059, 1016, 858, 843, 824, 776, 741.

MS (EI, 70 eV, %) m/z = 253 (4), 252 (21), 224 (28), 223 (43), 207 (39), 180 (20), 179 (40), 152 (33).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{12}N_2O_2$**: 252.0899; found: 252.0893.

Synthesis of 3-(5-(trifluoromethyl)pyridin-2-yl)benzonitrile (200e)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-chloro-5-(trifluoromethyl)pyridine (182 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (3-cyanophenyl)zinc(II) halide (**199e**, 1.8 mL, 1.2 mmol, 0.66 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 14 h at 50 °C. The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.31) afforded the product **200e** (230 mg, 0.93 mmol, 93%) as a white solid.

M.p. 80 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.96 (d, *J* = 2.3 Hz, 1H), 8.40–8.32 (m, 1H), 8.27 (ddd, *J* = 8.0, 1.8, 1.2 Hz, 1H), 8.03 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.74 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.67–7.54 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 157.9 (q, ^4J(C,F) = 1.4 Hz), 146.8 (q, ^3J(C,F) = 4.0 Hz), 138.8, 134.2 (q, ^3J(C,F) = 3.5 Hz), 133.0, 131.1, 130.8, 129.7, 125.8 (q, ^2J(C,F) = 33 Hz), 123.3 (q, ^1J(C,F) = 270 Hz), 119.8, 118.2, 113.2.

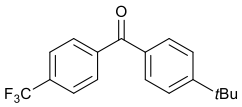
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 2854, 2225, 1600, 1588, 1566, 1385, 1323, 1244, 1169, 1131, 1080, 1010, 892, 847, 804, 765, 710, 681.

MS (EI, 70 eV, %) m/z = 249 (14), 248 (100), 247 (25), 179 (25).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_7F_3N_2$**: 248.0561; found: 248.0553.

Synthesis of (4-(*tert*-butyl)phenyl)(4-(trifluoromethyl)phenyl)methanone (200f)



A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-*tert*-butylbenzoyl chloride (197 mg, 1.0 mmol, 1.0 equiv), $[Pd(PPh_3)_4]$ (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The (4-(trifluoromethyl)phenyl)zinc(II) halide (**199f**, 2.3 mL, 1.2 mmol, 0.53 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 18 h at 50 °C. The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.30) gave the product **200f** (260 mg, 0.85 mmol, 85%) as a white solid.

M.p. 76 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.82 (d, *J* = 8.0 Hz, 2H), 7.74–7.64 (m, 4H), 7.45 (d, *J* = 8.0 Hz, 2H), 1.31 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.2, 157.0, 141.0 (q, ^4J(C,F) = 2.0 Hz), 134.0, 133.5 (q, ^2J(C,F) = 32 Hz), 130.2, 130.0, 125.5, 125.3 (q, ^3J(C,F) = 3.8 Hz), 123.7 (q, ^1J(C,F) = 271 Hz), 35.2, 31.1.

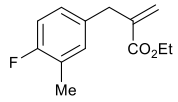
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –63.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2969, 1651, 1604, 1408, 1324, 1310, 1280, 1163, 1122, 1105, 1064, 1016, 972, 932, 860, 838, 774, 734, 698, 677.

MS (EI, 70 eV, %) m/z = 306 (2), 291 (15), 162 (13), 161 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}F_3O$**: 306.1231; found: 306.1233.

Synthesis of ethyl 2-(4-fluoro-3-methylbenzyl)acrylate (200g)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 2-(bromomethyl)acrylate (193 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) and cooled to –60 °C. To this solution a pre-cooled mixture consisting of (4-fluoro-3-methylphenyl)zinc(II) halide (**199g**, 3.2 mL, 1.2 mmol, 0.38 M in THF, 1.2 equiv) and CuCN·2LiCl (0.20 mL, 0.20 mmol, 1.0 M in THF, 0.20 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature, quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.40) furnished the product **200g** (167 mg, 0.75 mmol, 75%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.03 (dd, *J* = 7.5, 2.3 Hz, 1H), 7.00–6.97 (m, 1H), 6.96–6.90 (m, 1H), 6.25–6.24 (m, 1H), 5.48 (q, *J* = 1.4 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.58 (s, 2H), 2.26 (d, *J* = 1.9 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.8, 160.1 (d, ^1J(C,F) = 243 Hz), 146.4 (d, ^4J(C,F) = 1.0 Hz), 134.1 (d, ^3J(C,F) = 3.6 Hz), 132.0 (d, ^3J(C,F) = 5.0 Hz), 127.7 (d, ^3J(C,F) = 7.9 Hz), 125.9, 124.6 (d, ^2J(C,F) = 17 Hz), 114.8 (d, ^2J(C,F) = 22 Hz), 60.8, 37.3, 14.5 (d, ^3J(C,F) = 3.6 Hz), 14.1.

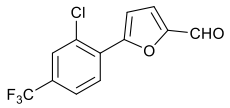
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –121.4.

IR (ATR, cm^{-1}) ṽ = 2983, 2930, 2361, 1714, 1632, 1597, 1501, 1368, 1301, 1248, 1208, 1194, 1132, 1118, 1026, 946, 872, 816, 775, 753, 671.

MS (EI, 70 eV, %) m/z = 222 (42), 221 (13), 177 (25), 176 (16), 161 (15), 149 (53), 148 (100), 147 (32), 134 (26), 133 (31), 123 (53), 109 (25), 97 (18), 85 (23), 73 (14), 71 (35), 70 (13), 69 (26), 57 (46), 55 (25), 44 (42).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}FO_2$**: 222.1056; found: 222.1051.

Synthesis of 5-(2-chloro-4-(trifluoromethyl)phenyl)furan-2-carbaldehyde (200h)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 5-iodo-2-furaldehyde (533 mg, 2.4 mmol, 0.80 equiv), $Pd(OAc)_2$ (23 mg, 0.10 mmol, 4.0 mol%), SPhos (82 mg, 0.20 mmol, 8.0 mol%) and freshly distilled THF (2.4 mL). The (2-chloro-4-(trifluoromethyl)phenyl)zinc(II) halide (**199h**, 4.5 mL, 3.0 mmol) was slowly added *via* a syringe pump at room temperature over 1 h. After further stirring for 1 h the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.38) leading to the product **200h** (514 mg, 1.87 mmol, 78%) as off white solid.

M.p. 86 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.73 (s, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.75 (s, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.43 (d, *J* = 3.8 Hz, 1H), 7.37 (d, *J* = 3.8 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 177.6, 153.6, 152.0, 131.8 (q, ^2J(C,F) = 33 Hz), 131.8, 130.7 (q, ^4J(C,F) = 2.0 Hz), 129.4, 128.1 (q, ^3J(C,F) = 3.9 Hz), 123.0 (q, ^1J(C,F) = 270 Hz), 124.0 (q, ^3J(C,F) = 3.7 Hz), 122.5, 114.6.

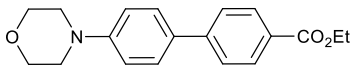
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –63.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3116, 2841, 1683, 1671, 1612, 1521, 1477, 1404, 1355, 1319, 1260, 1238, 1182, 1125, 1085, 1036, 974, 924, 890, 833, 808, 781, 768, 719, 675, 665.

MS (EI, 70 eV, %) m/z = 276 (28), 275 (23), 274 (100), 273 (44), 219 (12), 217 (40), 183 (10), 182 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_6ClF_3O_2$**: 274.0008; found: 274.0015.

Synthesis of ethyl 4'-morpholino-[1,1'-biphenyl]-4-carboxylate (200i)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 4-iodobenzoate (276 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (4-morpholinophenyl)zinc(II) halide (**199i**, 1.9 mL, 1.2 mmol, 0.62 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.30) afforded the product **200i** (273 mg, 0.88 mmol, 88%) as a yellow brown solid.

M.p. 205 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.01 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.87–3.77 (m, 4H), 3.21–3.11 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H).

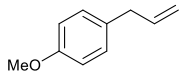
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.6, 151.2, 145.1, 131.1, 130.1, 128.4, 128.0, 126.1, 115.6, 66.8, 60.8, 48.9, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2968, 2839, 1702, 1600, 1532, 1497, 1446, 1402, 1381, 1368, 1310, 1273, 1238, 1218, 1182, 1121, 1105, 1012, 930, 856, 815, 771, 720, 696.

MS (EI, 70 eV, %) m/z = 312 (19), 311 (100), 253 (46), 208 (21), 152 (27), 104 (14), 103 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{21}NO_3$**: 311.1521; found: 311.1504.

Synthesis of 1-allyl-4-methoxybenzene (200j)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with allyl bromide (121 mg, 1.0 mmol, 1.00 equiv) and freshly distilled THF (1.0 mL) and cooled to –50 °C. To this solution a pre-cooled mixture consisting of (4-methoxyphenyl)zinc(II) halide (**199j**, 3.2 mL, 1.2 mmol, 0.37 M in THF, 1.2 euqiv) and CuCN·2LiCl (0.20 mL, 0.20 mmol, 1.0 M in THF, 0.20 equiv) was dropwise added. The reaction mixture was allowed to warm to room temperature, quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.49) leading to the product **200j** (89 mg, 0.60 mmol, 60%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.07 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 5.92 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.13–4.88 (m, 2H), 3.74 (s, 3H), 3.29 (d, *J* = 6.7 Hz, 2H)

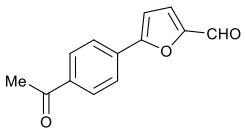
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.0, 137.9, 132.1, 129.5, 115.4, 113.9, 55.3, 39.4.

IR (ATR, cm^{-1}) ṽ = 3409, 2926, 2856, 2361, 1724, 1675, 1605, 1512, 1464, 1441, 1377, 1247, 1175, 1109, 1032, 825, 810.

MS (EI, 70 eV, %) m/z = 149 (15), 148 (100), 147 (40), 133 (15), 121 (27), 117 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}O$**: 148.0888; found: 148.0888.

Synthesis of 5-(4-acetylphenyl)furan-2-carbaldehyde (200k)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 5-iodo-2-furaldehyde (222 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (4-acetylphenyl)zinc(II) halide (**199k**, 2.9 mL, 1.2 mmol, 0.41 M in THF / DMPU 1:1, 1.2 equiv) was slowly added *via* a syringe pump at room temperature over 1 h. After further stirring for 1 h the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.30) afforded the product **200k** (187 mg, 0.87 mmol, 87%) as a yellow solid.

M.p. 134 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.70 (s, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 3.7 Hz, 1H), 6.97 (d, *J* = 3.7 Hz, 1H), 2.64 (s, 3H).

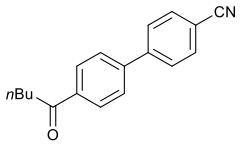
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 197.2, 177.5, 157.8, 152.6, 137.4, 132.9, 129.0, 127.5, 125.3, 109.5, 26.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3106, 1670, 1605, 1527, 1484, 1418, 1360, 1260, 1190, 1120, 1046, 1036, 966, 958, 924, 840, 820, 783, 769.

MS (EI, 70 eV, %) m/z = 214 (61), 200 (10), 199 (100), 115 (30), 114 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{10}O_3$**: 214.0630; found: 214.0624.

Synthesis of 4'-pentanoyl-[1,1'-biphenyl]-4-carbonitrile (200l)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (4-pentanoyl-phenyl)zinc(II) halide (**199l**, 3.6 mL, 1.2 mmol, 0.33 M in THF / DMPU 1:1, 1.2 equiv) was added dropwise and the resulting solution was stirred for 2 h at room temperature. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.16) gave the product **200l** (169 mg, 0.64 mmol, 64%) as a yellow orange solid.

M.p. 99 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.06 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 2H), 3.04–2.92 (m, 2H), 1.75 (q, *J* = 7.5 Hz, 2H), 1.43 (dq, *J* = 14.7, 7.4 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

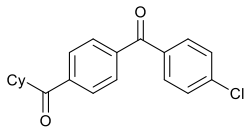
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 199.7, 144.2, 143.1, 136.7, 132.5, 128.7, 127.7, 127.2, 118.5, 111.7, 38.3, 26.3, 22.3, 13.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2931, 2869, 2224, 1736, 1673, 1603, 1466, 1411, 1396, 1270, 1201, 1112, 1004, 976, 861, 823, 794, 727.

MS (EI, 70 eV, %) m/z = 263 (5), 222 (11), 221 (75), 207 (13), 206 (100), 178 (17), 177 (17), 151 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}NO$**: 263.1310; found: 263.1309.

Synthesis of (4-(4-chlorobenzoyl)phenyl)(cyclohexyl)methanone (200m)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-chlorobenzoyl chloride (175 mg, 1.0 mmol, 1.0 equiv), [$Pd(PPh_3)_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The (4-(cyclohexanecarbonyl)-phenyl)zinc(II) halide (**199m**, 2.3 mL, 1.2 mmol, 0.52 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.28) leading to the product **200m** (252 mg, 0.77 mmol, 77%) as a white solid.

M.p. 114 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.05 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 3.30 (tt, *J* = 11.3, 3.3 Hz, 1H), 1.98–1.84 (m, 4H), 1.81–1.73 (m, 1H), 1.63–1.23 (m, 5H).

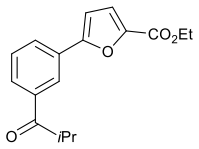
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 203.0, 194.5, 140.3, 139.3, 139.1, 135.1, 131.3, 129.8, 128.6, 128.0, 45.8, 29.1, 25.7, 25.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2930, 2853, 1680, 1648, 1588, 1448, 1402, 1300, 1282, 1246, 1206, 1089, 1010, 973, 932, 852, 814, 766, 746, 728, 677.

MS (EI, 70 eV, %) m/z = 328 (12), 326 (38), 291 (27), 245 (30), 244 (14), 243 (100), 180 (18), 152 (10), 139 (23), 55 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{19}ClO_2$**: 326.1074; found: 326.1074.

Synthesis of ethyl 5-(3-isobutyrylphenyl)furan-2-carboxylate (200n)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 5-bromofuran-2-carboxylate (219 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (3-isobutyrylphenyl)zinc(II) halide (**199n**, 2.9 mL, 1.2 mmol, 0.41 M in THF / DMPU 1:1, 1.2 equiv) was added dropwise and the resulting solution was stirred for 16 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.19) furnished the product **200n** (171 mg, 0.60 mmol, 60%) as a brown yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.29 (t, *J* = 1.5 Hz, 1H), 7.96 (dt, *J* = 7.8, 1.7 Hz, 1H), 7.89 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 4.0 Hz, 1H), 6.81 (d, *J* = 3.6 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.58 (hept, *J* = 6.8 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.22 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 204.0, 158.7, 156.3, 144.3, 136.9, 130.1, 129.2, 128.7, 128.4, 124.5, 119.7, 107.6, 61.0, 35.5, 19.1, 14.4.

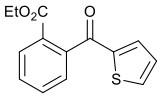
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2975, 2934, 1712, 1683, 1518, 1466, 1370, 1297, 1273, 1215, 1136, 1012, 992, 960, 929, 864, 799, 758, 742, 687.

MS (EI, 70 eV, %) m/z = 287 (15), 286 (100), 244 (68), 243 (33), 239 (30), 238 (15), 213 (12), 159 (11), 115 (16), 114 (32).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{18}O_4$**: 286.1205; found: 286.1197.

6.6. Trapping Reactions of the Functionalized Aryl- and Heteroarylzinc Reagents (199c, o–s) with Electrophiles

Synthesis of ethyl 2-(thiophene-2-carbonyl)benzoate (200o)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-thiophenecarbonyl chloride (147 mg, 1.0 mmol, 1.0 equiv), [$Pd(PPh_3)_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The (2-(ethoxycarbonyl)phenyl)zinc(II) halide (**199c**, 2.0 mL, 1.2 mmol, 0.60 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.29) afforded the product **200o** (224 mg, 0.86 mmol, 86%) as a pale yellow solid.

M.p. 66 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.07 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.71 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.68–7.54 (m, 2H), 7.49 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.33–7.24 (m, 1H), 7.08 (dd, *J* = 4.9, 3.8 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.14 (t, J = 7.1 Hz, 3H).

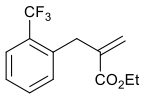
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 189.2, 166.0, 144.8, 141.0, 134.4 (2C), 132.2, 130.3, 129.9, 129.4, 128.1, 127.7, 61.6, 13.7.

IR (ATR, cm^{-1}) ṽ = 3100, 3085, 2983, 2927, 1715, 1654, 1644, 1576, 1519, 1477, 1442, 1415, 1363, 1282, 1264, 1237, 1142, 1092, 1080, 1052, 1016, 969, 897, 840, 768, 738, 711, 672.

MS (EI, 70 eV, %) m/z = 261 (16), 260 (100), 217 (11), 216 (40), 215 (90), 188 (12), 187 (13), 149 (44), 115 (24), 111 (87), 105 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}O_3S$**: 260.0507; found: 260.0504.

Synthesis of ethyl 2-(2-(trifluoromethyl)benzyl)acrylate (200p)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 2-(bromomethyl)acrylate (193 mg, 1.0 mmol, 1.0 equiv) and freshly distilled THF (1.0 mL) and cooled to –40 °C. To this solution, a pre-cooled mixture consisting of (2-(trifluoromethyl)-phenyl)zinc(II) halide (**199o**, 2.9 mL, 1.2 mmol, 0.41 M in THF, 1.2 equiv) and CuCN·2LiCl (0.20 mL, 0.20 mmol, 1.0 M in THF, 0.20 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature, quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.41) leading to the product **200p** (194 mg, 0.75 mmol, 75%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 6.33 (q, *J* = 1.1 Hz, 1H), 5.26 (q, *J* = 1.6 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 167.0, 139.5, 137.3, 131.7 (q, ^4J(C,F) = 1.0 Hz), 131.3, 129.0 (q, ^2J(C,F) = 30 Hz), 126.8, 126.6, 126.0 (q, ^3J(C,F) = 5.7 Hz), 124.4 (q, ^1J(C,F) = 272 Hz), 60.9, 34.3, 14.1.

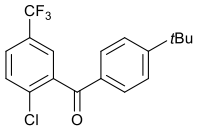
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –60.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2985, 1716, 1636, 1449, 1312, 1108, 1060, 1037, 950, 766.

MS (EI, 70 eV, %) m/z = 258 (21), 238 (31), 213 (40), 194 (29), 193 (22), 192 (10), 191 (19), 190 (100), 185 (26), 184 (30), 183 (14), 173 (19), 166 (13), 165 (69), 164 (51), 163 (11), 162 (43), 161 (18), 159 (12), 146 (14), 145 (14), 133 (17), 116 (22), 115 (42).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}F_3O_2$**: 258.0868; found: 258.0857.

Synthesis of (4-(*tert*-butyl)phenyl)(2-chloro-5-(trifluoromethyl)phenyl)methanone (200q)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-*tert*-butylbenzoyl chloride (197 mg, 1.0 mmol, 1.0 equiv), [$Pd(PPh_3)_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The (2-chloro-5-(trifluoromethyl)phenyl)-zinc(II) halide (**199p**, 2.5 mL, 1.2 mmol, 0.48 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.42) gave the product **200q** (224 mg, 0.92 mmol, 92%) as a orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.74 (d, *J* = 8.7 Hz, 2H), 7.71–7.66 (m, 1H), 7.64–7.57 (m, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 1.35 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 193.1, 158.2, 139.5, 134.9 (q, ^4J(C,F) = 1.0 Hz), 132.9, 130.5, 129.9, 129.2 (q, ^2J(C,F) = 34 Hz), 127.4 (q, ^3J(C,F) = 3.6 Hz), 125.7 (2C), 123.7 (q, ^1J(C,F) = 271 Hz), 35.2, 30.9.

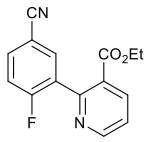
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2965, 1673, 1603, 1464, 1405, 1335, 1314, 1257, 1171, 1127, 1080, 1017, 953, 902, 851, 830, 815, 774, 740, 704.

MS (EI, 70 eV, %) m/z = 340 (17), 327 (31), 326 (17), 325 (100), 209 (10), 207 (31), 179 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{16}ClF_3O$**: 340.0842; found: 340.0840.

Synthesis of ethyl 2-(5-cyano-2-fluorophenyl)nicotinate (200r)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 2-chloronicotinate (149 mg, 0.80 mmol, 0.80 equiv), $Pd(OAc)_2$ (7.2 mg, 0.03 mmol, 4.0 mol%), SPhos (26 mg, 0.06 mmol, 8.0 mol%) and freshly distilled THF (0.8 mL). The (2-chloro-5-cyanophenyl)zinc(II) halide (**199q**, 2.1 mL, 1.2 mmol, 0.58 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 14 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.42) afforded the product **200r** (178 mg, 0.66 mmol, 83%) as a pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.83 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.33 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.93 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.72 (ddd, *J* = 8.5, 4.7, 2.2 Hz, 1H), 7.46 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.24–7.12 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 165.6, 162.0 (d, ^1J(C,F) = 257 Hz), 152.2, 151.6, 138.4, 135.3, 134.3 (d, ^3J(C,F) = 9.6 Hz), 130.4 (d, ^2J(C,F) = 17 Hz), 127.6, 123.2, 117.7, 116.3 (d, ^2J(C,F) = 24 Hz), 108.8, 61.6, 13.7.

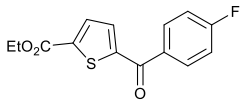
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –107.1.

IR (ATR, cm^{-1}) ṽ = 2984, 2231, 1719, 1612, 1588, 1567, 1494, 1440, 1394, 1367, 1279, 1264, 1239, 1208, 1176, 1136, 1089, 1058, 1015, 894, 827, 792, 746, 703, 668.

MS (EI, 70 eV, %) m/z = 271 (13), 270 (72), 255 (19), 242 (19), 241 (69), 226 (17), 225 (100), 224 (13), 222 (50), 198 (34), 197 (94), 196 (11), 177 (13), 171 (14), 170 (41), 169 (11), 150 (19), 43 (52).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{11}FN_2O_2$**: 270.0805; found: 270.0798.

Synthesis of ethyl 5-(4-fluorobenzoyl)thiophene-2-carboxylate (200s)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-fluorobenzoyl chloride (159 mg, 1.0 mmol, 1.0 equiv), [Pd(PPh$_3$)$_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The (5-(ethoxy-carbonyl)thiophen-2-yl)zinc(II) halide (**199r**, 2.3 mL, 1.2 mmol, 0.53 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.23) furnished the product **200s** (263 mg, 0.95 mmol, 95%) as a white solid.

M.p. 85 °C.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 7.93 (d, *J* = 5.3 Hz, 1H), 7.91 (d, *J* = 5.3 Hz, 1H), 7.79 (d, *J* = 4.0 Hz, 1H), 7.58 (d, *J* = 4.0 Hz, 1H), 7.24–7.14 (m, 2H), 4.39 (q, *J* = 7.0 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$, ppm) δ = 186.5, 165.6 (d, ^1J(C,F) = 255 Hz), 161.6, 147.4, 140.4, 133.6 (d, ^4J(C,F) = 3.1 Hz), 132.9, 131.9 (d, ^3J(C,F) = 9.2 Hz), 125.2, 115.8 (d, ^2J(C,F) = 22 Hz), 61.5, 14.3.

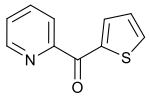
^{19}F-NMR (376 MHz, CDCl$_3$, ppm) δ = –105.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3119, 2986, 1705, 1626, 1597, 1526, 1504, 1452, 1405, 1366, 1274, 1224, 1154, 1098, 1050, 1010, 879, 860, 851, 748, 703, 688.

MS (EI, 70 eV, %) m/z = 279 (16), 278 (97), 250 (19), 234 (18), 233 (86), 206 (11), 205 (19), 183 (37), 123 (100), 95 (43).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}FO_3S$**: 278.0413; found: 278.0408.

Synthesis of pyridin-3-yl(thiophen-2-yl)methanone (200t)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-thiophenylcarbonyl chloride (147 mg, 1.0 mmol, 1.0 equiv), [$Pd(PPh_3)_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The pyridine-3-ylzinc(II) halide (**199s**, 2.3 mL, 1.2 mmol, 0.53 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 14 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.27) leading to the product **200t** (156 mg, 0.82 mmol, 82%) as a pale yellow solid.

M.p. 95 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.08 (s, 1H), 8.81 (d, *J* = 3.7 Hz, 1H), 8.15 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.78 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.65 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.46 (ddd, *J* = 7.9, 4.9, 0.7 Hz, 1H), 7.19 (dd, *J* = 4.9, 3.8 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 186.0, 152.6, 149.7, 142.8, 136.3, 135.0 (2C), 133.6, 128.1, 123.3.

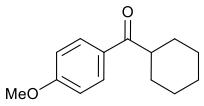
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 1630, 1585, 1518, 1477, 1414, 1356, 1300, 1247, 1192, 1072, 1026, 886, 878, 852, 818, 730, 715, 699, 662.

MS (EI, 70 eV, %) m/z = 190 (14), 189 (100), 188 (22), 111 (92), 78 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_7NOS$**: 189.0248; found: 189.0247.

6.7. Trapping Reactions of the Alkylzinc Reagents (202a–e) with Electrophiles

Synthesis of cyclohexyl(4-methoxyphenyl)methanone (203a)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-methoxybenzoyl chloride (171 mg, 1.0 mmol, 1.0 equiv), $[Pd(PPh_3)_4]$ (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The cyclohexylzinc(II) halide (**202a**, 2.1 mL, 1.2 mmol, 0.57 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.38) leading to the product **203a** (191 mg, 0.86 mmol, 86%) as a pale pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.93 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.21 (tt, *J* = 11.4, 3.2 Hz, 1H), 1.84 (td, *J* = 11.1, 10.4, 3.3 Hz, 4H), 1.76–1.67 (m, 1H), 1.58–1.18 (m, 5H).

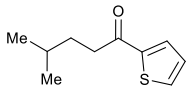
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 202.4, 163.2, 130.5, 129.3, 113.7, 55.4, 45.3, 29.6, 26.0, 25.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2929, 2853, 1668, 1598, 1575, 1509, 1450, 1419, 1372, 1312, 1247, 1208, 1163, 1027, 973, 893, 837, 819, 771, 682.

MS (EI, 70 eV, %) m/z = 218 (54), 163 (24), 150 (29), 136 (49), 135 (100), 107 (21), 92 (37), 77 (47), 64 (12), 55 (13), 41 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{18}O_2$**: 218.1307; found: 218.1300.

Synthesis of 4-methyl-1-(thiophen-2-yl)pentan-1-one (203b)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-thiophenecarbonyl chloride (147 mg, 1.0 mmol, 1.0 equiv), [$Pd(PPh_3)_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The isopentylzinc(II) halide (**202b**, 2.1 mL, 1.2 mmol, 0.56 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.48) gave the product **203b** (121 mg, 0.66 mmol, 66%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.70 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.60 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.11 (dd, *J* = 5.0, 3.8 Hz, 1H), 2.92–2.85 (m, 2H), 1.69–1.59 (m, 3H), 0.93 (d, J = 6.5 Hz, 6H).

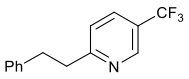
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 193.7, 144.5, 133.3, 131.6, 128.0, 37.5, 33.6, 27.8, 22.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2956, 2930, 2870, 1656, 1519, 1468, 1414, 1367, 1354, 1271, 1232, 1209, 1060, 927, 858, 848, 717.

MS (EI, 70 eV, %) m/z = 182 (3), 127 (10), 126 (34), 111 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{14}OS$**: 182.0765; found: 182.0765.

Synthesis of 2-phenethyl-5-(trifluoromethyl)pyridine (203c)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-chloro-5-(trifluoromethyl)pyridine (182 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The phenethylzinc(II) halide (**202c**, 2.5 mL, 1.2 mmol, 0.49 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.33) furnished the product **203c** (226 mg, 0.90 mmol, 90%) as a white solid.

M.p. 57 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.86 (s, 1H), 7.82 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.45–6.87 (m, 6H), 3.32-3.17 (m, 2H), 3.17–3.01 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 165.2, 146.2 (q, ^3J(C,F) = 4.1 Hz), 140.9, 133.4 (q, ^3J(C,F) = 3.4 Hz), 128.4 (2C), 126.2, 124.3 (q, ^2J(C,F) = 33 Hz), 123.7 (q, ^1J(C,F) = 270 Hz), 122.3, 40.0, 35.6.

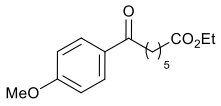
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2928, 1602, 1570, 1495, 1454, 1394, 1326, 1246, 1163, 1116, 1078, 1015, 943, 871, 841, 739, 702.

MS (EI, 70 eV, %) m/z = 252 (11), 251 (79), 250 (100), 174 (40), 91 (70).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}F_3N$**: 251.0922; found: 251.0912.

Synthesis of ethyl 7-(4-methoxyphenyl)-7-oxoheptanoate (203d)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 4-methoxybenzoyl chloride (171 mg, 1.0 mmol, 1.0 equiv), [$Pd(PPh_3)_4$] (116 mg, 0.10 mmol, 0.10 equiv) and freshly distilled THF (1.0 mL). The (6-ethoxy-6-oxohexyl)zinc(II) halide (**202d**, 2.3 mL, 1.2 mmol, 0.52 M in THF, 1.2 equiv) was added dropwise and the resulting suspension was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.63) afforded the product **203d** (250 mg, 0.90 mmol, 90%) as a yellow solid.

M.p. 43 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.92 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 2.94–2.87 (m, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.70 (ddt, *J* = 27.6, 15.2, 7.5 Hz, 4H), 1.49–1.35 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

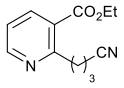
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.8, 173.7, 163.3, 130.3, 130.1, 113.7, 60.2, 55.4, 38.0, 34.2, 28.9, 24.8, 24.1, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2934, 1727, 1668, 1600, 1575, 1508, 1419, 1376, 1311, 1239, 1174, 1107, 1091, 1029, 1015, 973, 828, 818, 733.

MS (EI, 70 eV, %) m/z = 278 (2), 233 (11), 187 (12), 163 (13), 151 (16), 150 (25), 136 (24), 135 (40), 92 (14), 77 (20).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{22}O_4$**: 278.1518; found: 278.1506.

Synthesis of ethyl 2-(3-cyanopropyl)nicotinate (203e)



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with ethyl 2-chloronicotinate (186 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol, 4.0 mol%), SPhos (33 mg, 0.08 mmol, 8.0 mol%) and freshly distilled THF (1.0 mL). The (3-cyanopropyl)zinc(II) halide (**202e**, 2.0 mL, 1.2 mmol, 0.59 M in THF, 1.2 equiv) was added dropwise and the resulting solution was stirred for 2 h at 50 °C. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.17) gave the product **203e** (214 mg, 0.98 mmol, 98%) as a brown liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.63 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.18 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.23 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.34–3.16 (m, 2H), 2.44 (t, *J* = 7.3 Hz, 2H), 2.14 (q, *J* = 7.4 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.7, 161.1, 152.3, 139.1, 126.2, 121.8, 120.1, 62.0, 35.8, 25.3, 17.3, 14.7.

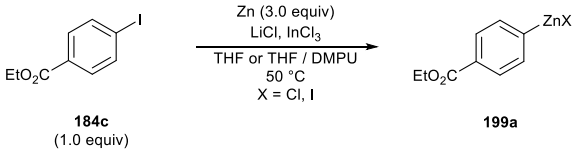
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 2938, 2246, 1717, 1624, 1584, 1570, 1536, 1442, 1367, 1273, 1250, 1133, 1082, 1019, 768.

MS (EI, 70 eV, %) m/z = 218 (4), 189 (32), 179 (15), 178 (96), 173 (45), 166 (12), 165 (100), 150 (52), 145 (18), 136 (33), 132 (19), 118 (12), 117 (13), 104 (16), 79 (19), 43 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{14}N_2O_2$**: 218.1055; found: 218.1050.

6.8. Additional Screenings and Supporting Information

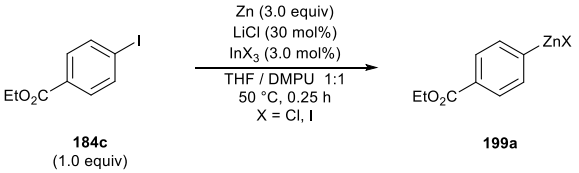
Table 26: Screening of reaction conditions for the oxidative insertion of zinc into ethyl 4-iodobenzoate (**184c**).



Entry	$InCl_3$ (mol%)	LiCl (mol%)	Time (h)	Yield (%)[a]
1	0	0	24	< 5
2	0	150	24[b]	82
3	0	150	4.0	65
4	10	0	12	90
5	10	0	0.50	87[c]
6	5.0	0	0.50	83[c]
7	3.0	0	0.50	83[c]
8	3.0	30	0.25	78[c]
9	3.0	50	0.25	70[c]
10	3.0	80	0.25	50[c]
11	3.0	30	1.0	70[d]
12	3.0	30	2.0	92

[a] Yield determined by iodometric titration; [b] Reaction temperature of 25 °C; [c] A mixture of THF / DMPU 1:1 was used; [d] A mixture of THF / DMPU 2:1 was used.

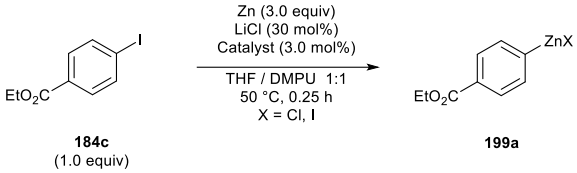
Table 27: Screening of In-catalysts for the oxidative addition of zinc into aryl iodide **184c**.



Entry	In-Catalyst	Yield (%)[a]
1	InF_3	60
2	$InCl_3$	78
3	$InBr_3$	60
4	$In(OTf)_3$	63
5	$In(OAc)_3$	53
6	$In(acac)_3$	53

[a] Yield determined by iodometric titration.

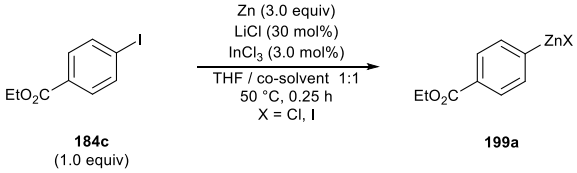
Table 28: Screening of other catalysts for the direct insertion of zinc into aryl iodide **184c**.



Entry	Catalyst	Yield (%)[a]
1	$PbCl_2$	52
2	VCl_3	40
3	$LaCl_3 \cdot 2LiCl$	24
4	$Sc(OTf)_3$	45
5	$AlCl_3$	27
6	$TiCl_4$	34
7	$InCl_3$	78

[a] Yield determined by iodometric titration.

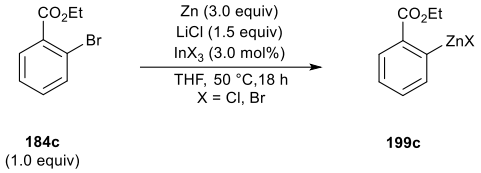
Table 29: Screening of co-solvents for the oxidative addition of zinc into aryl iodide **184c**.



Entry	THF / Co-Solvent	Yield (%)[a]
1	THF / DMA	43
2	THF / DMF	53
3	THF / MTBE	55
4	THF / dioxane	48
5	THF / NMP	63
6	THF / MeCN	87
7	THF / DMPU	78

[a] Yield determined by iodometric titration.

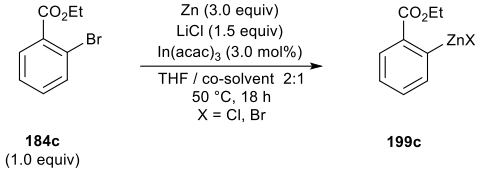
Table 30: Screening of In-catalysts for the direct insertion of zinc into ethyl 2-bromobenzoate (**184t**).



Entry	In-Catalyst	Yield (%)[a]
1	InF_3	45
2	$InCl_3$	51
3	$InBr_3$	traces
4	$In(OTf)_3$	26
5	$In(OAc)_3$	56
6	$In(acac)_3$	70

[a] Yield determined by iodometric titration.

Table 31: Screening of different co-solvents for the oxidative insertion of zinc into **184t**.



Entry	THF / Co-Solvent	Yield (%)[a]
1	THF / DMPU	56
2	THF / NMP	0[b]
3	THF / MeCN	0[b]
4	THF / toluene	57
5	THF / MTBE	57
6	THF / dioxane	67
7	THF	70

[a] Yield determined by iodometric titration; [b] Full hydrolysis of **184t** leading to $PhCO_2Et$.

7. Preparation of Functionalized Diaryl- and Diheteroaryllanthanum Reagents by Fast Halogen-Lanthanum Exchange

7.1. Typical Procedures

Preparation of *n*Bu$_2$LaMe·5LiCl (205f)

A dry and argon-flushed *Schlenk*-tube was charged with freshly prepared $LaCl_3$·2LiCl (4.2 mL, 1.4 mmol, 0.70 equiv, 0.33 M in THF) and cooled to –30 °C. Subsequently MeLi (0.60 mL, 1.4 mmol, 0.70 equiv, 2.35 M in Et_2O) and *n*BuLi (1.0 mL, 2.8 mmol, 1.4 equiv, 2.75 M in hexane) were added and the resulting solution was stirred at –30 °C for 30 min before being used.

Typical procedure for the iodine-lanthanum exchange using *n*Bu$_2$LaMe·5LiCl (205f) (TP1)

A dry and argon-flushed *Schlenk*-tube was charged with freshly prepared $LaCl_3$·2LiCl (4.2 mL, 1.4 mmol, 0.70 equiv, 0.33 M in THF) and cooled to –30 °C. Subsequently, MeLi (0.60 mL, 1.4 mmol, 0.70 equiv, 2.35 M in Et_2O) and *n*BuLi (1.0 mL, 2.8 mmol, 1.4 equiv, 2.75 M in hexane) were added and the resulting solution was stirred at –30 °C for 30 min before being used. This freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was further cooled to –50 °C and the corresponding aryl or heteroaryl iodide (2.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) as internal standard (50 µL) were added. The exchange progress was determined by GC-analysis of water quenched and iodolyzed reaction aliquots. Usually, all exchange reactions were completed after only 5 min and full conversion of aryl or heteroaryl iodide was observed. The resulting diaryl- or diheteroaryl(methyl)lanthanum reagents were immediately trapped by adding a selected electrophile (1.3 mmol, 0.65 equiv) neat at –50 °C. The reaction mixture was allowed to warm up to room temperature and the reaction progress was again checked by GC-analysis of water quenched aliquots. After full conversion of the selected electrophile, the reaction was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Finally, the crude product was purified by flash column chromatography leading to the desired products.

Typical procedure for the bromine-lanthanum exchange using *n*Bu$_2$LaMe·5LiCl (205f) (TP2)

A dry and argon-flushed *Schlenk*-tube was charged with freshly prepared $LaCl_3$·2LiCl (4.2 mL, 1.4 mmol, 0.70 equiv, 0.33 M in THF) and cooled to –30 °C. Subsequently, MeLi (0.60 mL, 1.4 mmol, 0.70 equiv, 2.35 M in Et_2O) and *n*BuLi (1.0 mL, 2.8 mmol, 1.4 equiv, 2.75 M in hexane) were added and the resulting solution was stirred at –30 °C for 30 min before being used. This freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was further cooled to –50 °C and the corresponding aryl or heteroaryl bromide (2.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) as internal standard (50 µL) were added. The exchange progress was determined by GC-analysis of water quenched and iodolyzed

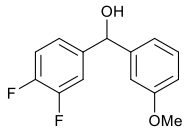
reaction aliquots. Usually, all exchange reactions were completed after only 5 min and full conversion of aryl or heteroaryl bromide was observed. The resulting diaryl- or diheteroaryl(methyl)lanthanum reagents were immediately trapped by adding a selected electrophile (1.6 mmol, 0.80 equiv) neat at –50 °C. The reaction mixture was allowed to warm up to room temperature and the reaction progress was again checked by GC-analysis of water quenched aliquots. After full conversion of the selected electrophile, the reaction was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Finally, the crude product was purified by flash column chromatography leading to the desired products.

Typical procedure for the Pd-catalyzed cross-couplings of diaryl(methyl)lanthanum reagents of type 211 with aryl bromides as electrophiles (TP3)

A pre-dried and argon-flushed *Schlenk*-tube was charged with $Pd(OAc)_2$ (1.8 mg, 8.0 μmol, 1.0 mol%), XPhos (7.6 mg, 16 μmol, 2.0 mol%) and a selected aryl bromide (0.80 mmol, 0.80 equiv) as electrophile. Freshly distilled toluene (2.4 mL) was added and the resulting solution was stirred for 2 min at room temperature. Subsequently, a diaryl(methyl)lanthanum reagent of type **211**, freshly prepared from the corresponding aryl or heteroaryl bromide (1.0 mmol, 1.0 equiv), was added within 2 min at room temperature. The reaction mixture was stirred for 5 min and the reaction progress was checked by GC-analysis of water quenched aliquots. After full conversion of the selected electrophile, the reaction was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Finally, the crude product was purified by flash column chromatography leading to the desired products.

7.2 Trapping Reactions of Diaryl- and Diheteroaryl(methyl)lanthanum Reagents (206a–h) with Electrophiles of Type 207

Preparation of (3,4-difluorophenyl)(3-methoxyphenyl)methanol (208a)



According to **TP1**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3,4-difluoroiodobenzene (480 mg, 0.24 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 3-methoxybenzaldehyde (184 mg, 0.16 mL, 1.3 mmol, 0.65 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.33) afforded the desired alcohol **208a** (205 mg, 0.82 mmol, 63%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.33–7.27 (m, 1H), 7.26–7.19 (m, 1H), 7.17–7.07 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 2H), 6.89–6.82 (m, 1H), 5.76 (s, 1H), 3.81 (s, 3H), 2.49 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.9, 150.4 (dd, ^1J(C,F) = 247 Hz, ^2J(C,F) = 12.8 Hz), 149.8 (dd, ^1J(C,F) = 247 Hz, ^2J(C,F) = 12.7 Hz), 144.8, 140.6 (dd, *J* = 4.8, 3.8 Hz), 129.8, 122.4 (dd, *J* = 6.3, 3.6 Hz), 118.8, 117.1 (d, ^2J(C,F) = 17 Hz), 115.5 (d, ^2J(C,F) = 17 Hz), 113.3, 112.2, 75.1, 55.3.

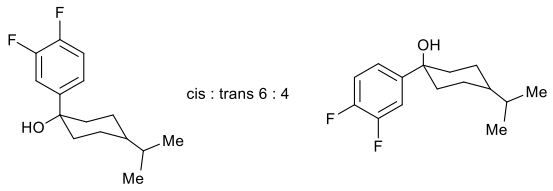
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –137.4, –139.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3390, 2942, 2838, 2514, 1608, 1600, 1586, 1514, 1486, 1466, 1454, 1434, 1320, 1276, 1258, 1208, 1154, 1138, 1112, 1090, 1036, 996, 960, 944, 874, 824, 794, 766, 748, 694, 656.

MS (EI, 70 eV, %) m/z = 250 (54), 217 (11), 201 (11), 189 (10), 188 (17), 141 (17), 135 (67), 115 (22), 109 (100), 108 (10), 94 (22), 78 (11), 77 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}F_2O_2$**: 250.0805; found: 250.0800.

Preparation of 1-(3,4-difluorophenyl)-4-isopropylcyclohexan-1-ol (208b)



According to **TP1**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3,4-difluoroiodobenzene (480 mg, 0.24 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 4-isopropylcyclo-hexan-1-one (140 mg, 1.0 mmol, 0.50 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.43 (*cis*) and 0.23 (*trans*)) afforded two separable isomers of alcohol **208b** in a 6:4 ratio (180 mg, 0.71 mmol, 71%) as white solids.

***Cis* isomer**

M.p. 82 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.33 (ddd, *J* = 12.2, 7.8, 2.3 Hz, 1H), 7.23–7.16 (m, 1H), 7.15–7.03 (m, 1H), 1.83–1.73 (m, 4H), 1.73–1.63 (m, 2H), 1.58 (s, 1H), 1.54–1.40 (m, 3H), 1.19–1.08 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 150.2 (dd, ^1J(C,F) = 247 Hz, ^2J(C,F) = 12.5 Hz), 149.2 (dd, ^1J(C,F) = 247 Hz, ^2J(C,F) = 12.7 Hz), 147.0 (dd, ^3J(C,F) = 4.3 Hz, ^4J(C,F) = 3.8 Hz), 120.6 (dd, ^3J(C,F) = 6.2 Hz, ^4J(C,F) = 3.5 Hz), 116.9 (d, ^2J(C,F) = 17.0 Hz), 114.2 (d, ^2J(C,F) = 18.1 Hz), 72.8 (d, ^4J(C,F) = 1.2 Hz), 43.4, 39.2, 32.9, 25.3, 20.0.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −138.1, −141.4.

IR (ATR, cm^{-1}) ṽ = 3371, 2920, 2869, 1607, 1517, 1504, 1443, 1417, 1367, 1272, 1220, 1162, 1117, 1050, 1018, 971, 879, 812, 772.

MS (EI, 70 eV, %) m/z = 254 (2), 236 (23), 193 (34), 179 (52), 169 (100), 166 (26), 165 (41), 164 (19), 156 (61), 151 (28), 146 (15), 141 (31), 140 (13), 127 (54).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{20}F_2O$:** 254.1482 found: 254.1478.

***trans* isomer**

M.p. 100 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.34 (ddd, *J* = 12.2, 7.7, 2.3 Hz, 1H), 7.25–7.21 (m, 1H), 7.13 (dt, *J* = 10.0, 8.4 Hz, 1H), 2.30–2.20 (m, 2H), 1.78 (ddd, *J* = 10.9, 6.5, 4.6 Hz, 2H), 1.49 (dq, *J* = 13.3, 6.7 Hz, 1H), 1.27–1.11 (m, 4H), 0.85 (d, *J* = 6.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 150.4 (dd, ^{1}J(C,F) = 247 Hz, ^{2}J(C,F) = 12.5 Hz), 149.5 (dd, ^{1}J(C,F) = 248 Hz, ^{2}J(C,F) = 12.7 Hz), 143.5–143.3 (m), 122.1 (dd, ^{3}J(C,F) = 6.2 Hz, ^{4}J(C,F) = 3.5 Hz), 117.1 (d, ^{2}J(C,F) = 16.7 Hz), 115.5 (d, ^{2}J(C,F) = 17.8 Hz), 73.1 (d, ^{4}J(C,F) = 1.2 Hz), 42.4, 37.4, 30.2, 26.3, 20.6.

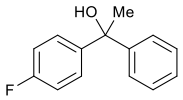
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −137.6, −140.2.

IR (ATR, cm^{-1}) ṽ = 3248, 2942, 2861, 1608, 1515, 1451, 1419, 1386, 1367, 1351, 1340, 1310, 1273, 1208, 1177, 1120, 1105, 1084, 1046, 1025, 978, 936, 877, 818, 772, 712.

MS (EI, 70 eV, %) m/z = 254 (1), 236 (38), 193 (58), 180 (10), 179 (91), 177 (11), 169 (100), 166 (47), 165 (75), 164 (30), 156 (68), 151 (48), 146 (26), 141 (34), 140 (23), 133 (12), 127 (90), 81 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{20}F_2O$:** 254.1482 found: 254.1479.

Preparation of 1-(4-fluorophenyl)-1-phenylethan-1-ol (208c)



With reference to **TP1**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-fluoroiodobenzene (444 mg, 0.23 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, acetophenone (156 mg, 1.3 mmol, 0.65 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.18) leading to the tertiary alcohol **208c** (257 mg, 1.19 mmol, 91%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.45–7.33 (m, 6H), 7.31–7.25 (m, 1H), 7.02 (t, *J* = 8.8 Hz, 2H), 2.26 (br. s, 1H), 1.97 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 161.6 (d, ^1J(C,F) = 245 Hz), 147.6, 143.7 (d, ^4J(C,F) = 3.2 Hz), 128.1, 127.4 (d, ^3J(C,F) = 8.0 Hz), 126.9, 125.6, 114.7 (d, ^2J(C,F) = 21 Hz), 75.7, 30.8.

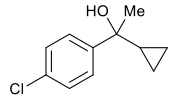
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –116.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3418, 3060, 3028, 2978, 2932, 1600, 1506, 1494, 1446, 1408, 1372, 1302, 1282, 1224, 1186, 1178, 1160, 1118, 1092, 1066, 1028, 1014, 940, 922, 908, 834, 798, 762, 722, 698, 678.

MS (EI, 70 eV, %) m/z = 216 (1), 201 (19), 199 (12), 198 (77), 197 (29), 196 (34), 184 (14), 183 (100), 177 (27), 176 (15), 123 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}FO$**: 216.0950; found: 216.0943.

Preparation of 1-(4-chlorophenyl)-1-cyclopropylethan-1-ol (208d)



According to **TP1**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-chloro-4-iodobenzene (477 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at once at this temperature. After 5 min reaction time, cyclopropyl methyl ketone (109 mg, 1.3 mmol, 0.65 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.17) obtaining the tertiary alcohol **208d** (238 mg, 1.21 mmol, 93%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.46 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 1.63 (br. s, 1H), 1.46 (s, 3H), 1.22 (ddd, *J* = 8.1, 5.4, 2.5 Hz, 1H), 0.60–0.49 (m, 2H), 0.48–0.36 (m, 2H).

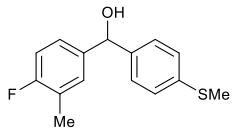
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 147.1, 133.1, 128.5, 127.1, 73.4, 29.0, 23.3, 2.5, 1.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3418, 3084, 3008, 2976, 2932, 2872, 1596, 1574, 1488, 1454, 1426, 1400, 1370, 1326, 1276, 1258, 1226, 1204, 1174, 1092, 1046, 1012, 952, 924, 898, 828, 730.

MS (EI, 70 eV, %) m/z = 196 (1), 178 (17), 168 (21), 155 (11), 144 (11), 143 (89), 142 (15), 141 (24), 138 (16), 137 (18), 129 (11), 128 (100), 127 (13), 125 (15), 115 (28), 102 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{13}ClO$**: 196.0655; found: 196.0647.

Preparation of 1-(4-fluoro-3-methylphenyl)-1-(4-(methylthio)phenyl)ethan-1-ol (208e)



Based on **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 2-fluoro-5-iodotoluene (472 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, acetophenone (244 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.38) gave the alcohol **208e** (340 mg, 1.30 mmol, 81%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.27 (q, *J* = 8.5 Hz, 4H), 7.19 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.14 (ddd, *J* = 7.5, 4.9, 2.3 Hz, 1H), 7.03–6.94 (m, 1H), 5.74 (s, 1H), 2.49 (s, 3H), 2.38 (br. s, 1H), 2.27 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 160.5 (d, ^1J(C,F) = 245 Hz), 140.5, 139.0 (d, ^4J(C,F) = 3.5 Hz), 137.6, 129.4 (d, ^3J(C,F) = 5.3 Hz), 126.8, 126.5, 125.2 (d, ^3J(C,F) = 8.1 Hz), 124.7 (d, ^2J(C,F) = 18 Hz), 114.7 (d, ^2J(C,F) = 23 Hz), 75.0, 15.6, 14.4.

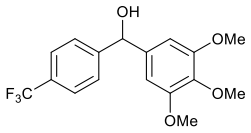
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –119.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3572, 3372, 3076, 3022, 2980, 2922, 1598, 1498, 1436, 1426, 1402, 1378, 1318, 1282, 1244, 1204, 1180, 1138, 1116, 1092, 1034, 1014, 968, 938, 930, 892, 812, 774, 756, 746, 730, 684.

MS (EI, 70 eV, %) m/z = 262 (38), 183 (14), 153 (12), 151 (56), 137 (100), 125 (49), 124 (33), 109 (23).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{15}FOS$**: 262.0828; found: 262.0820.

Prepararation of (4-(trifluoromethyl)phenyl)(3,4,5-trimethoxyphenyl)methanol (208f)



According to **TP1**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-iodobenzotrifluoride (544 mg, 2.0 mmol, 1.0 equiv) and C_{14} (50 µL) were added at this temperature. After 5 min reaction time, 3,4,5-trimethoxybenzaldehyde (255 mg, 1.3 mmol, 0.65 equiv) was added at once, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.25) furnished alcohol **208f** (370 mg, 1.08 mmol, 83%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 6.54 (s, 2H), 5.74 (s, 1H), 3.80–3.78 (m, 9H), 2.94 (br. s, 1H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 153.3, 147.5 (q, ^4J(C,F) = 1.3 Hz), 139.0, 137.3, 129.6 (q, ^2J(C,F) = 32 Hz), 126.6, 125.3 (q, ^3J(C,F) = 3.8 Hz), 124.1 (q, ^1J(C,F) = 272 Hz), 103.5, 75.7, 60.8, 56.0.

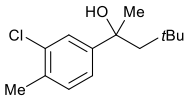
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3444, 2942, 2840, 1620, 1594, 1506, 1462, 1420, 1376, 1322, 1234, 1164, 1120, 1066, 1016, 1002, 970, 908, 868, 836, 818, 786, 766, 728, 704, 674.

MS (EI, 70 eV, %) m/z = 343 (10), 342 (54), 292 (15), 173 (100), 169 (66), 145 (22), 138 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}F_3O_4$**: 342.1079; found: 342.1065.

Preparation of 2-(3-chloro-4-methylphenyl)-4,4-dimethylpentan-2-ol (208g)



According to **TP1**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 2-chloro-4-iodo-1-methylbenzene (505 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 4,4-dimethyl-pentan-2-one (148 mg, 0.18 mL, 1.3 mmol, 0.65 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 98 : 2, R_f = 0.17) afforded the desired alcohol **208g** (256 mg, 1.06 mmol, 82%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.45 (d, *J* = 1.9 Hz, 1H), 7.21 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 2.35 (s, 3H), 1.90 (d, *J* = 14.8 Hz, 1H), 1.81 (d, *J* = 14.8 Hz, 1H), 1.75 (br. s, 1H), 1.54 (s, 3H), 0.83 (s, 9H).

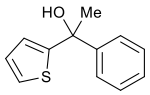
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 148.4, 134.1, 133.8, 130.5, 125.9, 123.5, 75.5, 56.0, 34.1, 31.8, 31.5, 19.7.

IR (ATR, cm^{-1}) ṽ = 346, 2951, 2869, 1560, 1492, 1477, 1466, 1446, 1385, 1364, 1238, 1200, 1120, 1084, 1048, 879, 860, 823, 710, 672.

MS (EI, 70 eV, %) m/z = 240 (1), 171 (35), 170 (11), 169 (100), 57 (12), 43 (29).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{21}ClO$:** 240.1281; found: 240.1270.

Preparation of 1-phenyl-1-(thiophen-2-yl)ethan-1-ol (208h)



According to **TP1**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 2-iodothiophene (420 mg, 0.22 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, acetophenone (156 mg, 0.15 mL, 1.3 mmol, 0.65 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 93 : 7, R_f = 0.20) afforded the desired alcohol **208h** (225 mg, 1.10 mmol, 85%) as a yellow solid.

M.p. 54 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.56–7.50 (m, 2H), 7.41–7.33 (m, 2H), 7.33–7.27 (m, 1H), 7.26 (dd, *J* = 5.0, 1.2 Hz, 1H), 6.96 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.92 (dd, *J* = 3.6, 1.2 Hz, 1H), 2.45 (br. s, 1H), 2.05 (s, 3H).

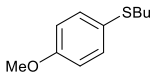
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.6, 147.4, 128.3, 127.4, 126.7, 125.4, 125.1, 124.3, 74.9, 32.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3538, 2972, 2928, 1492, 1445, 1367, 1335, 1235, 1165, 1120, 1083, 1059, 1024, 1014, 917, 903, 849, 838, 791, 760, 744, 108, 693, 672.

MS (EI, 70 eV, %) m/z = 204 (1), 189 (21), 187 (13), 186 (100), 185 (65), 184 (48), 152 (25), 111 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}OS$:** 204.0609; found: 204.0601.

Preparation of butyl(4-methoxyphenyl)sulfane (208i)



With reference to **TP1**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-iodoanisole (468 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added in one portion at this temperature. After 5 min reaction time, dibutyl disulfide (232 mg, 0.25 mL, 1.3 mmol, 0.65 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.50) leading to product **208i** (179 mg, 0.91 mmol, 70%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.36 (d, *J* = 8.9 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 2.91–2.78 (m, 2H), 1.60 (dt, *J* = 14.7, 7.3 Hz, 2H), 1.44 (dq, *J* = 14.2, 7.1 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.5, 132.7, 126.8, 114.3, 55.1, 35.3, 31.3, 21.6, 13.5.

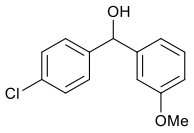
IR (ATR, cm^{-1}) ṽ = 3000, 2956, 2928, 2872, 2862, 2836, 1592, 1572, 1492, 1462, 1440, 1404, 1378, 1284, 1240, 1172, 1098, 1072, 1032, 1008, 914, 822, 798, 744, 730.

MS (EI, 70 eV, %) m/z = 197 (10), 196 (85), 153 (14), 140 (100), 139 (16), 125 (47).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{16}OS$**: 196.0922; found: 196.0911.

7.3. Trapping Reactions of Diaryl(methyl)lanthanum Reagents (211a–p) with Electrophiles of Type 207

Preparation of (4-chlorophenyl)(3-methoxyphenyl)methanol (212a)



According to **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-4-chlorobenzene (383 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at once at this temperature. After 5 min reaction time, 3-methoxybenzaldehyde (218 mg, 0.20 mL, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.16) leading to the desired alcohol **212a** (320 mg, 1.29 mmol, 81%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.31 (s, 4H), 7.28 (d, *J* = 8.1 Hz, 1H), 6.92 (dd, *J* = 4.1, 1.9 Hz, 2H), 6.84 (ddd, *J* = 8.2, 2.5, 0.9 Hz, 1H), 5.88–5.61 (m, 1H), 3.89–3.56 (m, 3H), 2.73–2.45 (m, 1H).

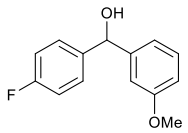
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.6, 144.9, 141.9, 133.0, 129.4, 128.3, 127.6, 118.6, 112.9, 111.9, 75.2, 55.0.

IR (ATR, cm^{-1}) ṽ = 3388, 3052, 3004, 2958, 2940, 2836, 2510, 1600, 1586, 1488, 1464, 1454, 1436, 1406, 1320, 1254, 1186, 1148, 1088, 1034, 1012, 908, 876, 836, 782, 764, 750, 734, 720, 698.

MS (EI, 70 eV, %) m/z = 250 (10), 248 (31), 152 (20), 141 (17), 139 (51), 135 (100), 109 (80), 108 (19), 105 (14), 94 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}ClO_2$**: 248.0604; found: 248.0599.

Preparation of (4-fluorophenyl)(3-methoxyphenyl)methanol (212b)



Based on **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-4-fluorobenzene (350 mg, 0.22 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 3-methoxybenzaldehyde (218 mg, 0.20 mL, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) gave the secondary alcohol **212b** (325 mg, 1.40 mmol, 88%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.35 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.31–7.27 (m, 1H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.97–6.92 (m, 2H), 6.84 (ddd, *J* = 8.2, 2.4, 1.1 Hz, 1H), 5.77 (s, 1H), 3.80 (s, 3H), 2.69 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 161.9 (d, ^1J(C,F) = 246 Hz), 159.5, 145.1, 139.3 (d, ^4J(C,F) = 3.1 Hz), 129.4, 128.0 (d, ^3J(C,F) = 8.1 Hz), 118.6, 115.0 (d, ^2J(C,F) = 21 Hz), 112.8, 111.9, 75.2, 55.0.

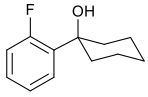
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –116.1.

IR (ATR, cm^{-1}) ṽ = 3400, 3004, 2942, 2838, 2524, 1602, 1586, 1506, 1486, 1466, 1454, 1436, 1320, 1256, 1220, 1186, 1156, 1098, 1034, 1014, 996, 910, 878, 838, 792, 770, 752, 694.

MS (EI, 70 eV, %) m/z = 232 (57), 199 (14), 183 (14), 171 (14), 170 (20), 135 (81), 123 (86), 109 (100), 108 (26), 97 (21), 94 (19), 77 (20).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}FO_2$**: 232.0900; found: 232.0893.

Preparation of 1-(2-fluorophenyl)cyclohexan-1-ol (212c)



According to **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.2 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-2-fluorobenzene (350 mg, 0.22 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, cyclohexanone (157 mg, 0.17 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 95 : 5, R_f = 0.28) afforded the desired alcohol **212c** (224 mg, 1.15 mmol, 72%) as a white solid.

M.p. 54 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.59–7.50 (m, 1H), 7.23 (dddd, *J* = 8.0, 6.9, 5.0, 1.9 Hz, 1H), 7.12 (td, *J* = 7.6, 1.3 Hz, 1H), 7.02 (ddd, *J* = 12.7, 8.1, 1.3 Hz, 1H), 2.12–2.02 (m, 2H), 1.98 (br. s, 1H), 1.84–1.75 (m, 4H), 1.75–1.69 (m, 1H), 1.69–1.58 (m, 2H), 1.38–1.30 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 160.6 (d, ^1J(C,F) = 245 Hz), 136.0 (d, ^2J(C,F) = 11 Hz), 128.6 (d, ^3J(C,F) = 8.9 Hz), 126.9 (d, ^3J(C,F) = 4.7 Hz), 124.2 (d, ^4J(C,F) = 3.3 Hz), 116.4 (d, ^2J(C,F)= 24 Hz), 72.8 (d, ^3J(C,F) = 3.5 Hz), 36.9, 36.8, 25.5, 22.0.

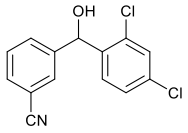
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −113.1.

IR (ATR, cm^{-1}) ṽ = 3369, 2925, 2858, 1612, 1581, 1481, 1446, 1373, 1260, 1213, 1194, 1096, 971, 905, 811, 757.

MS (EI, 70 eV, %) m/z = 194 (12), 176 (22), 261 (23), 151 (100), 148 (11), 146 (16), 138 (37), 133 (38), 123 (52), 109 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{15}FO$**: 194.1107; found: 194.1097.

Preparation of 3-((2,4-dichlorophenyl)(hydroxy)methyl)benzonitrile (212d)



Based on **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3-bromobenzonitrile (364 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added in one portion at this temperature. After 5 min reaction time, 2,4-dichlorobenzaldehyde (302 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.31) yielding **212d** (302 mg, 1.09 mmol, 68%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.66 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.54 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 2.1 Hz, 1H), 7.29 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.17 (s, 1H), 3.05 (br. s, 1H).

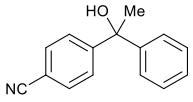
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 143.3, 138.6, 134.3, 132.7, 131.2, 131.1, 130.2, 129.2, 129.1, 128.7, 127.6, 118.4, 112.3, 70.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3414, 3070, 2964, 2928, 2872, 2232, 1662, 1588, 1562, 1468, 1434, 1380, 1322, 1298, 1260, 1230, 1188, 1172, 1142, 1102, 1058, 1036, 908, 866, 844, 824, 802, 768, 732, 702, 688, 668.

MS (EI, 70 eV, %) m/z = 279 (10), 277 (15), 242 (10), 190 (14), 177 (11), 176 (31), 174 (47), 173 (67), 149 (14), 146 (11), 131 (13), 130 (100), 111 (14), 104 (44), 103 (25), 75 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_9Cl_2NO$**: 277.0061; found: 277.0053.

Preparation of 4-(1-hydroxy-1-phenylethyl)benzonitrile (212e)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-bromobenzonitrile (364 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added neat at this temperature. After 5 min reaction time, acetophenone (192 mg, 1.6 mmol, 0.80 equiv) was added at once, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.38) gave the alcohol **212e** (245 mg, 1.10 mmol, 69%) as a yellow crystals.

M.p. 59 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.60 (d, *J* = 8.7 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.41 (dt, *J* = 8.3, 1.9 Hz, 2H), 7.36 (tt, *J* = 8.2, 1.6 Hz, 2H), 7.32–7.27 (m, 1H), 2.44 (br. s, 1H), 1.97 (s, 3H).

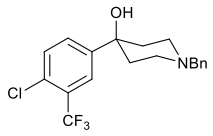
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.2, 146.4, 131.8, 128.3, 127.4, 126.3, 125.6, 118.6, 110.4, 75.7, 30.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3424, 3416, 3374, 2978, 2956, 2924, 2852, 2242, 2224, 1654, 1606, 1500, 1490, 1466, 1446, 1404, 1378, 1276, 1220, 1200, 1180, 1172, 1140, 1102, 1070, 1026, 1018, 932, 916, 846, 830, 822, 776, 760, 728, 700, 666.

MS (EI, 70 eV, %) m/z = 223 (12), 208 (40), 207 (100), 179 (19), 146 (15), 130 (10), 129 (37), 121 (24), 105 (23), 102 (41), 78 (16), 77 (31), 43 (65).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NO$**: 223.0997; found: 223.0982.

Preparation of 1-benzyl-4-(4-chloro-3-(trifluoromethyl)phenyl)piperidin-4-ol (212f)



According to **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 5-bromo-2-chlorobenzotrifluoride (518 mg, 0.30 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 1-benzylpiperidin-4-one (303 mg, 0.30 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.08) afforded the desired alcohol **212f** (513 mg, 1.39 mmol, 87%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.89 (d, *J* = 2.2 Hz, 1H), 7.64 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.40–7.28 (m, 5H), 3.61 (s, 2H), 2.89–2.81 (m, 2H), 2.47 (td, *J* = 12.1, 2.5 Hz, 2H), 2.16 (td, *J* = 13.4, 4.6 Hz, 2H), 1.88 (br. s, 1H), 1.72 (dd, *J* = 14.0, 2.6 Hz, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 147.8, 138.1, 131.3, 130.7 (q, ^3J(C,F) = 1.6 Hz), 129.3, 129.2, 128.3, 128.1 (q, ^2J(C,F) = 24 Hz), 127.2, 124.2 (q, ^3J(C,F) = 5.4 Hz), 123.0 (q, ^1J(C,F) = 273 Hz) 71.2, 63.2, 49.2, 38.5.

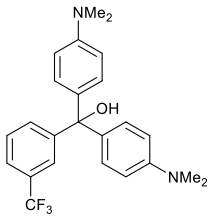
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.4.

IR (ATR, cm^{-1}) ṽ = 3030, 2922, 2816, 1606, 1576, 1481, 1468, 1454, 1408, 1366, 1343, 1315, 1260, 1212, 1174, 1125, 1111, 1077, 1046, 1032, 995, 939, 908, 831, 730, 698, 662.

MS (EI, 70 eV, %) m/z = 371 (27), 370 (30, 369 (76), 367 (43), 350 (18), 349 (12), 291 (22), 279 (12), 278 (33), 207 (11), 146 (28), 92 (19), 91 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{19}ClF_3NO$:** 369.1107; found: 369.1112.

Preparation of bis(4-(dimethylamino)phenyl)(3-(trifluoromethyl)phenyl)methanol (212g)



With reference to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3-bromobenzotrifluoride (450 mg, 0.28 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added neat at this temperature. After 5 min reaction time, 4,4′-bis(dimethylamino)benzophenone (429 mg, 1.6 mmol, 0.80 equiv) was added in one portion, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.36) yielding **212g** (539 mg, 1.30 mmol, 81%) as a pale yellow solid.

M.p. 157 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.77 (s, 1H), 7.60–7.47 (m, 2H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 4H), 6.69 (d, *J* = 9.0 Hz, 4H), 2.97 (s, 12H), 2.68 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 149.5, 148.7, 134.6, 131.1 (q, ^4J(C,F) = 1.8 Hz), 129.8 (q, ^2J(C,F) = 32 Hz), 128.6, 127.8, 126.2 (q, ^1J(C,F) = 271 Hz), 124.1 (q, ^3J(C,F) = 3.9 Hz), 123.3 (q, ^3J(C,F) = 3.8 Hz), 111.6, 81.1, 40.3.

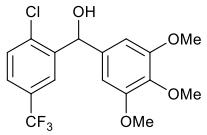
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.3.

IR (ATR, cm^{-1}) ṽ = 2924, 2900, 2886, 2854, 2810, 2360, 2338, 2324, 1610, 1560, 1520, 1484, 1446, 1358, 1320, 1306, 1296, 1284, 1230, 1208, 1190, 1162, 1148, 1114, 1098, 1070, 1010, 992, 948, 920, 892, 812, 798, 786, 758, 748, 728, 702, 678.

MS (EI, 70 eV, %) m/z = 415 (17), 414 (70), 398 (36), 397 (100), 381 (18), 294 (11), 270 (18), 269 (98), 253 (14), 173 (17), 148 (37).

HRMS (EI, 70 eV) m/z: calc. for **$C_{24}H_{25}F_3N_2O$**: 414.1919; found: 414.1911.

Preparation of (2-chloro-5-(trifluoromethyl)phenyl)(3,4,5-trimethoxyphenyl)methanol (212h)



With reference to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3-bromo-4-chlorobenzotrifluoride (519 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added in one portion at this temperature. After 5 min reaction time, 3,4,5-trimethoxybenzaldehyde (314 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) afforded the desired secondary alcohol **212h** (543 mg, 1.44 mmol, 90%) as a yellow solid.

M.p. 79 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.99 (d, *J* = 1.6 Hz, 1H), 7.46 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 6.56 (s, 2H), 6.10 (s, 1H), 3.78 (s, 3H), 3.78 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.0, 142.0, 137.2, 137.1, 135.7 (q, ^4J(C,F) = 1.4 Hz), 129.8, 129.3 (q, ^2J(C,F) = 32 Hz), 125.1 (q, ^3J(C,F) = 3.7 Hz), 124.6 (q, ^3J(C,F) = 3.8 Hz), 123.6 (q, ^1J(C,F) = 270 Hz), 103.7, 72.0, 60.5, 55.8.

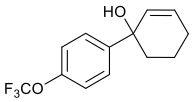
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) ṽ = 3474, 3430, 3372, 3348, 3328, 3310, 3302, 3286, 3274, 3006, 2956, 2936, 2842, 2360, 2338, 2324, 1592, 1502, 1464, 1418, 1324, 1274, 1234, 1168, 1122, 1080, 1040, 1034, 998, 970, 920, 898, 828, 770, 754, 734, 720, 700, 674.

MS (EI, 70 eV, %) m/z = 378 (17), 377 (10), 376 (50), 291 (16), 208 (32), 206 (100), 178 (16), 169 (75), 154 (12), 138 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{16}ClF_3O_4$**: 376.0689; found: 376.0687.

Preparation of 4'-(trifluoromethoxy)-3,4-dihydro-[1,1'-biphenyl]-1(2*H*)-ol (212i)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-4-(trifluoromethoxy)benzene (482 mg, 0.30 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, cyclohex-2-en-1-one (154 mg, 0.16 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.18) afforded the desired alcohol **212i** (349 mg, 1.35 mmol, 85%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.52–7.47 (m, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.04 (dt, *J* = 10.0, 3.8 Hz, 1H), 5.74 (d, *J* = 10.0 Hz, 1H), 2.28–2.18 (m, 1H), 2.18–2.01 (m, 2H), 1.99–1.89 (m, 1H), 1.85–1.72 (m, 2H), 1.68–1.55 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 148.1 (q, ^3J(C,F) = 1.7 Hz), 146.6, 131.7, 131.2, 127.0, 120.5 (q, ^1J(C,F) = 257 Hz), 120.4, 71.9, 39.6, 24.9, 19.1.

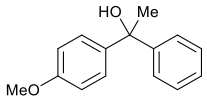
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −57.9.

IR (ATR, cm^{-1}) ṽ = 3256, 2941, 2867, 1608, 1514, 1450, 1419, 1386, 1367, 1351, 1310, 1258, 1207, 1158, 1081, 1046, 1020, 977, 937, 818, 772, 736.

MS (EI, 70 eV, %) m/z = 258 (5), 241 (13), 240 (100), 238 (38), 225 (25), 175 (57), 169 (12), 162 (10), 155 (49), 153 (33), 152 (36), 145 (21), 141 (24), 128 (15), 115 (32).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}F_3O_2$:** 258.0866; found: 258.0858.

Preparation of 1-(4-methoxyphenyl)-1-phenylethan-1-ol (212j)



Based on **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-bromoanisole (374 mg, 0.25 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, acetophenone (192 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.45) leading to **212j** (322 mg, 1.41 mmol, 88%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50–7.43 (m, 2H), 7.40–7.33 (m, 4H), 7.31–7.25 (m, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 2.33 (br. s, 1H), 1.97 (s, 3H).

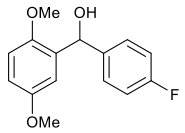
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.2, 148.1, 140.1, 127.9, 126.9, 126.6, 125.6, 113.2, 75.7, 55.0, 30.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3444, 3086, 3058, 3026, 2976, 2934, 2836, 1610, 1584, 1508, 1494, 1462, 1446, 1412, 1370, 1334, 1298, 1246, 1176, 1126, 1098, 1066, 1028, 906, 828, 786, 762, 728, 698, 678.

MS (EI, 70 eV, %) m/z = 228 (1), 213 (42), 211 (16), 210 (100), 209 (12), 196 (12), 195 (81), 194 (12), 180 (12), 179 (17), 178 (20), 167 (24), 166 (13), 165 (71), 152 (53), 135 (20), 115 (10), 105 (20), 77 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{16}O_2$**: 228.1150; found: 228.1145.

Preparation of (2,5-dimethoxyphenyl)(4-fluorophenyl)methanol (212k)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 2-bromo-1,4-dimethoxybenzene (434 mg, 0.30 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 4-fluorobenzaldehyde (198 mg, 0.70 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 85 : 15, R_f = 0.18) afforded the desired alcohol **212k** (252 mg, 0.96 mmol, 60%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.38–7.32 (m, 2H), 7.03–6.96 (m, 2H), 6.82 (dd, *J* = 5.9, 2.9 Hz, 2H), 6.78 (dd, *J* = 8.9, 3.0 Hz, 1H), 5.99 (d, *J* = 5.4 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.03 (dd, *J* = 5.4, 0.8 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.15 (d, ^1J(C,F) = 245 Hz), 153.9, 150.9, 139.0 (d, ^4J(C,F) = 3.1 Hz), 133.0, 128.3 (d, ^3J(C,F) = 8.1 Hz), 115.1 (d, ^2J(C,F) = 21 Hz), 114.1, 113.0, 112.0, 71.8, 56.1, 55.9.

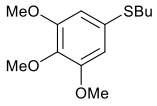
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −115.7.

IR (ATR, cm^{-1}) ṽ = 3419, 2941, 2835, 1602, 1493, 1463, 1428, 1275, 1212, 1177, 1154, 1026, 838, 804, 784, 733, 714, 697.

MS (EI, 70 eV, %) m/z = 263 (16), 262 (100), 244 (43), 243 (23), 186 (11), 183 (26), 170 (12), 165 (27), 159 (22), 151 (25), 139 (84), 133 (18), 124 (23), 123 (75), 109 (21), 97 (11), 95 (12), 77 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{15}FO_3$:** 262.1005; found: 262.0996.

Preparation of butyl(3,4,5-trimethoxyphenyl)sulfane (212l)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3,4,5-trimethoxybromobenzene (494 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added neat at this temperature. After 5 min reaction time, dibutyl disulfide (285 mg, 0.30 mL, 1.6 mmol, 0.80 equiv) was added at once, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.40) gave **212l** (308 mg, 1.20 mmol, 75%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.58 (s, 2H), 3.84 (s, 6H), 3.81 (s, 3H), 3.00–2.73 (m, 2H), 1.62 (q, *J* = 7.3 Hz, 2H), 1.44 (dq, *J* = 14.3, 7.3 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

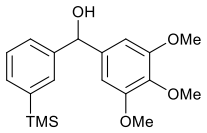
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.7, 137.2, 131.9, 107.6, 61.3, 56.6, 34.9, 31.8, 22.3, 14.1.

IR (ATR, cm^{-1}) ṽ = 2956, 2932, 2872, 2830, 1576, 1496, 1462, 1448, 1430, 1400, 1306, 1274, 1230, 1176, 1122, 1006, 924, 878, 808, 768, 734.

MS (EI, 70 eV, %) m/z = 257 (12), 256 (88), 242 (13), 241 (100), 213 (11), 200 (33), 199 (14), 185 (79), 142 (12), 125 (25), 124 (12), 97 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{20}O_3S$**: 256.1133; found: 256.1123.

Preparation of (3,4,5-trimethoxyphenyl)(3-(trimethylsilyl)phenyl)methanol (212m)



With reference to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, (3-bromophenyl)trimethylsilane (458 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 3,4,5-trimethoxybenzaldehyde (314 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.16) afforded **212m** (474 mg, 1.37 mmol, 86%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.59 (s, 1H), 7.49–7.41 (m, 1H), 7.32 (d, *J* = 4.6 Hz, 2H), 6.61 (s, 2H), 5.74 (s, 1H), 3.81 (s, 3H), 3.80 (s, 6H), 0.27 (s, 9H).

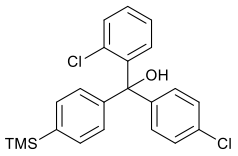
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 152.9, 142.5, 140.4, 139.3, 136.8, 132.4, 131.1, 127.6, 126.8, 103.3, 76.1, 60.5, 55.8, –1.4.

IR (ATR, cm^{-1}) ṽ = 3456, 3000, 2954, 2838, 1592, 1504, 1460, 1418, 1326, 1246, 1232, 1198, 1184, 1124, 1086, 1054, 1030, 1006, 972, 910, 888, 874, 834, 802, 782, 750, 726, 690, 664.

MS (EI, 70 eV, %) m/z = 346 (44), 177 (22), 169 (100), 154 (11), 138 (19), 119 (13), 73 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{26}O_4Si$**: 346.1600; found: 346.1594.

Preparation of (2-chlorophenyl)(4-chlorophenyl)(4-(trimethylsilyl)phenyl)methanol (212n)



With reference to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-4-(trimethylsilyl)benzene (458 mg, 0.37 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 2,4′-dichlorobenzophenone (402 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.44) led to the tertiary alcohol **212n** (493 mg, 1.23 mmol, 77%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.52 (d, *J* = 8.3 Hz, 2H), 7.43 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.36–7.28 (m, 3H), 7.25 (dd, *J* = 8.5, 3.8 Hz, 4H), 7.16 (td, *J* = 7.7, 1.4 Hz, 1H), 6.77 (dd, *J* = 7.9, 1.6 Hz, 1H), 4.44 (br. s, 1H), 0.31 (s, 9H).

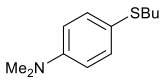
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 145.5, 144.3, 143.2, 139.8, 133.3, 133.2 (2C), 131.4 (2C), 129.3, 129.2, 128.1, 127.0, 126.5, 82.2, –1.1.

IR (ATR, cm^{-1}) ṽ = 3568, 3070, 2956, 2252, 1732, 1596, 1570, 1490, 1466, 1436, 1400, 1384, 1310, 1260, 1248, 1208, 1160, 1128, 1106, 1094, 1058, 1042, 1026, 1014, 948, 906, 838, 818, 758, 726, 688.

MS (EI, 70 eV, %) m/z = 403 (15), 402 (10), 400 (16), 389 (13), 388 (10), 387 (62), 386 (13), 385 (100), 383 (78), 382 (10), 381 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{22}H_{22}Cl_2OSi$**: 400.0817; found: 400.0807.

Preparation of 4-(butylthio)-*N*,*N*-dimethylaniline (212o)



According to **TP2**, freshly prepared nBu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-bromo-*N*,*N*-dimethylaniline (400 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, freshly distilled dibutyl disulfide (285 mg, 0.30 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane/Et_2O = 98:2, R_f = 0.29) afforded the desired sulfide **212o** (199 mg, 0.95 mmol, 59%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.36–7.28 (m, 2H), 6.72–6.62 (m, 2H), 2.95 (s, 6H), 2.80–2.74 (m, 2H), 1.60–1.50 (m, 2H), 1.48–1.36 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

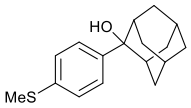
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 149.9, 133.9, 121.5, 113.0, 40.6, 36.5, 31.7, 22.0, 13.8.

IR (ATR, cm^{-1}) ṽ = 2955, 2926, 2871, 2802, 1594, 1502, 1442, 1349, 1222, 1192, 1166, 1129, 1101, 1060, 945, 810.

MS (EI, 70 eV, %) m/z = 209 (54), 152 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{19}NS$:** 209.1238; found: 209.1233.

Preparation of 2-(4-(methylthio)phenyl)adamantan-2-ol (212p)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. 4-Bromophenylthioanisole (406 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 2-adamantanone (240 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane/EtOAc = 93:7, R_f = 0.20) afforded the desired alcohol **212p** (350 mg, 1.28 mmol, 80%) as a white solid.

M.p. 102 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.46 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 2.52 (br. s, 2H), 2.49 (s, 3H), 2.39 (br. d, *J* = 12.2 Hz, 2H), 1.90 (s, *J* = 2.6 Hz, 1H), 1.78–1.63 (m, 9H), 1.49 (d, *J* = 1.8 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 142.3, 137.3, 126.8, 126.1, 75.4, 37.7, 35.7, 34.9, 32.9, 27.4, 26.9, 15.7.

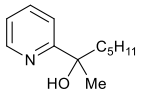
IR (ATR, cm^{-1}) ṽ = 3427, 2898, 2854, 1594, 1491, 1466, 1444, 1427, 1382, 1352, 1272, 1231, 1206, 1093, 1047, 999, 968, 909, 858, 834, 810, 727, 713.

MS (EI, 70 eV, %) m/z = 274 (20), 153 (24), 151 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{22}OS$:** 274.1391; found: 274.1383.

7.4. Trapping Reactions of Diheteroaryl-, Dialkenyl- and Dialkyllanthanum Reagents with Electrophiles of Type 207

Preparation of 2-(pyridin-2-yl)heptan-2-ol (215a)



According to **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 2-bromopyridine (316 mg, 0.19 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 2-heptanone (183 mg, 0.22 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 93 : 7, R_f = 0.17) afforded the desired alcohol **215a** (233 mg, 1.21 mmol, 75%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.53–8.44 (m, 1H), 7.81–7.50 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.18–7.13 (m, 1H), 5.17 (s, 1H), 1.87–1.67 (m, 2H), 1.41–1.29 (m, 1H), 1.26–1.09 (m, 4H), 0.98–0.86 (m, 1H), 0.79 (t, *J* = 6.8 Hz, 3H).

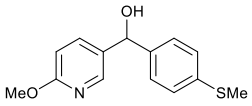
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 165.3, 147.3, 136.9, 121.8, 119.3, 73.8, 43.6, 32.2, 29.4, 23.5, 22.6, 14.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3402, 2955, 2931, 2860, 1592, 1570, 1468, 1432, 1388, 1293, 1169, 1047, 997, 960, 933, 903, 787, 749.

MS (EI, 70 eV, %) m/z = 146 (10), 132 (11), 123 (23), 122 (100), 117 (12), 104 (18), 80 (11), 79 (12), 78 (11).

HRMS (EI, 70 eV) m/z: calc. for [M−CH_3] **$C_{11}H_{16}NO$:** 178.1232; found: 178.1225.

Preparation of (6-methoxypyridin-3-yl)(4-(methylthio)phenyl)methanol (215b)



With reference to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 5-bromo-2-methoxypyridine (376 mg, 0.26 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 4-(methylthio)benzaldehyde (244 mg, 0.21 mL, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.35) led to **215b** (305 mg, 1.17 mmol, 73%) as white solid.

M.p. 79 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.08 (d, *J* = 2.4 Hz, 1H), 7.52 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.29–7.20 (m, 4H), 6.69 (d, *J* = 8.6 Hz, 1H), 5.74 (s, 1H), 3.91 (s, 3H), 3.01 (br. s, 1H), 2.47 (s, 3H).

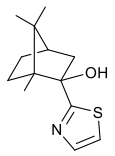
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.5, 144.8, 140.0, 137.7, 137.2, 132.0, 126.6, 126.5, 110.7, 73.1, 53.3, 15.6.

IR (ATR, cm^{-1}) ṽ = 3328, 3020, 2972, 2950, 2918, 2902, 2856, 1610, 1598, 1572, 1488, 1464, 1448, 1436, 1392, 1340, 1320, 1296, 1282, 1260, 1248, 1232, 1194, 1172, 1152, 1116, 1090, 1046, 1008, 974, 952, 940, 926, 872, 856, 834, 822, 810, 794, 768, 730, 712, 682.

MS (EI, 70 eV, %) m/z = 261 (35), 244 (11), 151 (16), 136 (100), 125 (30), 124 (28), 110 (22), 109 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{15}NO_2S$**: 261.0823; found: 261.0819.

Preparation of 1,7,7-trimethyl-2-(thiazol-2-yl)bicyclo[2.2.1]heptan-2-ol (215c)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 2-bromothiazole (328 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added neat at this temperature. After 5 min of reaction time, (+)-camphor (243 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9:1, R_f = 0.26) afforded the desired alcohol **215c** (268 mg, 1.13 mmol, 71%) as a yellow solid.

M.p. 60 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.76 (d, *J* = 3.3 Hz, 1H), 7.28 (d, *J* = 3.6 Hz, 2H), 3.01 (d, *J* = 0.9 Hz, 1H), 2.45–2.34 (m, 2H), 1.97–1.88 (m, 1H), 1.82–1.72 (m, 1H), 1.39–1.29 (m, 2H), 1.23 (s, 3H), 1.06 (s, 3H), 0.94 (s, 3H), 0.93–0.85 (m, 1H).

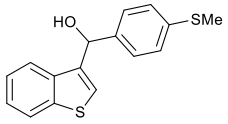
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 177.8, 142.2, 118.8, 83.6, 54.4, 50.2, 47.1, 45.5, 31.1, 26.9, 21.4, 21.2, 9.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3310, 2950, 2870, 1498, 1479, 1451, 1424, 1387, 1364, 1344, 1297, 1272, 1215, 1156, 1132, 1114, 1072, 1059, 1006, 966, 950, 913, 864, 798, 765, 719, 671.

MS (EI, 70 eV, %) m/z = 237 (8), 209 (14), 128 (100), 127 (74), 99 (62), 95 (53), 86 (50).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{19}NOS$:** 237.1187; found: 237.1184.

Preparation of benzo[*b*]thiophen-3-yl(4-(methylthio)phenyl)methanol (215d)



Based on **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 3-bromobenzo[*b*]thiophene (426 mg, 0.26 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 4-(methylthio)benzaldehyde (244 mg, 0.21 mL, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.40) afforded **215d** (364 mg, 1.27 mmol, 79%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.91–7.83 (m, 1H), 7.73–7.69 (m, 1H), 7.41–7.27 (m, 5H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.08 (s, 1H), 2.69 (br. s, 1H), 2.48 (s, 3H).

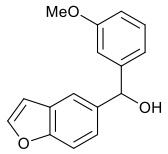
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 140.8, 138.9, 138.3, 138.0, 137.0, 127.2, 126.5, 124.2, 123.9, 123.6, 122.6, 122.4, 71.5, 15.5.

IR (ATR, cm^{-1}) ṽ = 3338, 3056, 3024, 2918, 2632, 1902, 1598, 1564, 1492, 1458, 1428, 1404, 1374, 1360, 1316, 1290, 1256, 1198, 1176, 1154, 1138, 1112, 1088, 1054, 1014, 996, 968, 942, 906, 870, 856, 836, 822, 798, 778, 760, 730, 692, 682, 670.

MS (EI, 70 eV, %) m/z = 287 (19), 286 (100), 222 (11), 221 (17), 161 (29), 150 (38), 134 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}OS_2$**: 286.0486; found: 286.0483.

Preparation of benzofuran-5-yl-(3-methoxyphenyl)methanol (215e)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-3,4-(methylenedioxy)-benzene (394 mg, 0.24 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min reaction time, 3-methoxybenzaldehyde (245 mg, 0.22 mL, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.44) producing **215e** (321 mg, 1.26 mmol, 79%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (d, *J* = 2.0 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.32 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.27 (t, *J* = 7.9 Hz, 1H), 7.04–6.97 (m, 2H), 6.84 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.75 (d, *J* = 1.4 Hz, 1H), 5.91 (s, 1H), 3.80 (s, 3H), 2.58 (br. s, 1H).

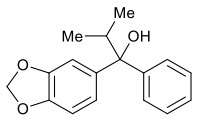
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.6, 154.2, 145.7, 145.2, 138.4, 129.2, 127.3, 123.1, 119.1, 118.7, 112.7, 111.9, 111.1, 106.5, 76.0, 55.0.

IR (ATR, cm^{-1}) ṽ = 3390, 3146, 3114, 3000, 2964, 2936, 2874, 2836, 1598, 1586, 1536, 1488, 1466, 1454, 1436, 1376, 1346, 1328, 1318, 1282, 1256, 1190, 1150, 1138, 1122, 1106, 1030, 996, 948, 940, 908, 880, 822, 786, 750, 732, 698, 676.

MS (EI, 70 eV, %) m/z = 254 (47), 165 (19), 147 (12), 145 (100), 135 (69), 119 (40), 118 (48), 109 (47), 108 (47), 107 (10), 94 (10), 91 (42), 89 (18), 77 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}O_3$**: 254.0943; found: 254.093.

Preparation of 1-(benzo[*d*][1,3]dioxol-5-yl)-2-methyl-1-phenylpropan-1-ol (215f)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 5-bromobenzo[*d*][1,3]dioxole (402 mg, 0.24 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 2-methyl-1-phenylpropan-1-one (237 mg, 0.24 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 96 : 4, R_f = 0.24) afforded the desired alcohol **215f** (365 mg, 1.35 mmol, 84%) as a white oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.51–7.44 (m, 2H), 7.31–7.25 (m, 2H), 7.20–7.15 (m, 1H), 7.01–6.96 (m, 2H), 5.90 (s, 2H), 2.82 (hept, *J* = 6.7 Hz, 1H), 2.01 (s, 1H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H).

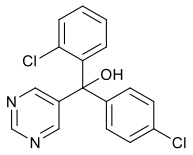
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 147.7, 146.9, 146.0, 141.2, 128.2, 126.5, 125.7, 118.9, 107.8, 107.0, 101.0, 80.5, 35.3, 17.4, 17.3.

IR (ATR, cm^{-1}) ṽ = 3557, 2969, 2876, 1600, 1501, 1485, 1446, 1433, 1385, 1343, 1296, 1234, 1167, 1112, 1084, 1037, 1014, 973, 932, 809, 754, 699, 655.

MS (EI, 70 eV, %) m/z = 253 (17), 252 (100), 237 (13), 227 (21), 207 (34), 178 (30), 152 (20), 129 (10), 115 (18), 105 (24).

HRMS (EI, 70 eV) m/z: calc. for [M−H_2O] **$C_{17}H_{16}O_2$:** 252.1150; found: 252.1143.

Preparation of (2-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (215g)



Based on **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 5-bromopyrimidine (318 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added neat at this temperature. After 5 min reaction time, 2,4′-dichlorobenzophenone (326 mg, 1.3 mmol, 0.65 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.15) leading to fenarimol **215g** (251 mg, 0.76 mmol, 58%) as a white solid.

M.p. 118 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.10 (s, 1H), 8.59 (s, 2H), 7.42 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.31 (td, *J* = 7.7, 1.6 Hz, 3H), 7.22–7.15 (m, 3H), 6.78 (dd, *J* = 7.9, 1.6 Hz, 1H), 4.74 (br. s, 1H).

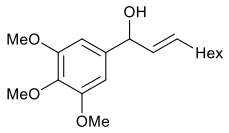
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 157.4, 156.0, 141.9, 140.9, 138.3, 134.0, 132.6, 131.7, 130.38, 130.0, 128.7, 128.5, 126.8, 79.4.

IR (ATR, cm^{-1}) ṽ = 3418, 3084, 3008, 2976, 2932, 2872, 1596, 1574, 1488, 1454, 1426, 1400, 1370, 1326, 1276, 1258, 1226, 1204, 1174, 1092, 1046, 1012, 952, 924, 898, 828, 730.

MS (EI, 70 eV, %) m/z = 330 (7), 253 (18), 251 (28), 221 (11), 219 (34), 207 (10), 191 (14), 183 (18), 141 (32), 139 (100), 112 (12), 107 (37).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{12}Cl_2N_2O$**: 330.0327; found: 330.0322.

Preparation of (*E*)-1-(3,4,5-trimethoxyphenyl)non-2-en-1-ol (218):



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, *trans*-1-iodo-1-octene (476 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added neat at this temperature. After 5 min reaction time, 3,4,5-trimethoxybenzaldehyde (255 mg, 1.3 mmol, 0.65 equiv) was added at once, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.38) afforded the desired alcohol **218** as a single isomer (268 mg, 0.87 mmol, 67%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.59 (s, 2H), 5.81–5.72 (m, 1H), 5.63 (ddt, *J* = 15.3, 6.8, 1.2 Hz, 1H), 5.08 (d, *J* = 6.8 Hz, 1H), 3.85 (s, 6H), 3.82 (s, 3H), 2.06 (q, *J* = 7.8, 7.4 Hz, 2H), 1.99 (s, 1H), 1.45–1.16 (m, 8H), 0.97 – 0.75 (m, 3H).

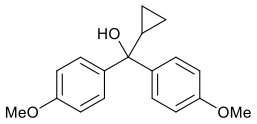
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.0, 139.0, 137.0, 132.8, 131.9, 102.8, 75.1, 60.6, 55.9, 32.0, 31.5, 28.8, 28.7, 22.4, 13.9

IR (ATR, cm^{-1}) ṽ = 3444, 2996, 2956, 2926, 2872, 2854, 1592, 1506, 1456, 1416, 1378, 1326, 1230, 1182, 1124, 1048, 1008, 964, 918, 840, 778, 724, 702, 676, 660.

MS (EI, 70 eV, %) m/z = 309 (20), 308 (100), 290 (19), 277 (23), 223 (28), 210 (11), 195 (15), 181 (16), 169 (51).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{28}O_4$**: 308.1988; found: 308.1984.

Preparation of cyclopropylbis(4-methoxyphenyl)methanol (221)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.2 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, bromocyclopropane (242 mg, 0.16 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, bis(4-methoxyphenyl)methanone (388 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.12) afforded the desired alcohol **221** (313 mg, 1.10 mmol, 69%) as a white glue.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.40–7.31 (m, 4H), 6.93–6.74 (m, 4H), 3.80 (s, 6H), 1.82 (br. s, 1H), 1.61–1.53 (m, 1H), 0.57 (ddd, *J* = 8.2, 6.1, 4.2 Hz, 2H), 0.45 (td, *J* = 5.8, 4.3 Hz, 2H).

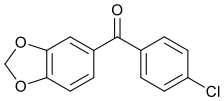
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.5, 139.7, 128.1, 113.2, 76.6, 55.2, 21.8, 1.8.

IR (ATR, cm^{-1}) ṽ = 3497, 3002, 2954, 2835, 1607, 1581, 1506, 1462, 1441, 1414, 1298, 1242, 1171, 1106, 1031, 983, 879, 824, 777.

MS (EI, 70 eV, %) m/z = 284 (4), 266 (14), 257 (11), 256 (66), 253 (12), 251 (10), 243 (40), 235 (12), 135 (100), 121 (21).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{20}O_3$:** 284.1412; found: 284.1407.

Preparation of benzo[*d*][1,3]dioxol-5-yl(4-chlorophenyl)methanone (223a)



According to **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 5-bromobenzo[*d*][1,3]dioxole (402 mg, 0.24 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 4-chloro-*N*-methoxy-*N*-methyl-benzamide (230 mg, 1.2 mmol, 0.60 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 95 : 5, R_f = 0.31) afforded the desired ketone **223a** (255 mg, 0.98 mmol, 83%) as a white solid.

M.p. 135 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.75–7.64 (m, 2H), 7.50–7.39 (m, 2H), 7.39–7.29 (m, 2H), 6.94–6.80 (m, 1H), 6.08 (s, 2H).

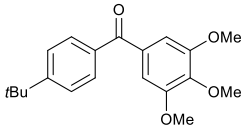
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 193.9, 151.7, 148.1, 138.4, 136.4, 131.6, 131.1, 128.6, 126.8, 109.8, 107.8, 101.9.

IR (ATR, cm^{-1}) ṽ = 1640, 1600, 1493, 1442, 1273, 1240, 1089, 1036, 1014, 969, 926, 882, 862, 844, 819, 808, 752, 696.

MS (EI, 70 eV, %) m/z = 262 (15), 260 (45), 225 (11), 149 (100), 139 (20), 121 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_9ClO_3$:** 260.0240; found: 260.0238.

Preparation of (4-(*tert*-butyl)phenyl)(3,4,5-trimethoxyphenyl)methanone (223b)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. 5-Bromo-1,2,3-trimethoxybenzene (494 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 4-(*tert*-butyl)-*N*,*N*-dimethylbenzamide (328 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to –20 °C and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) afforded the desired ketone **223b** (447 mg, 1.36 mmol, 85%) as a white solid.

M.p. 92 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.78–7.74 (m, 2H), 7.52–7.47 (m, 2H), 7.07 (s, 2H), 3.94 (s, 3H), 3.88 (s, 6H), 1.37 (s, 9H).

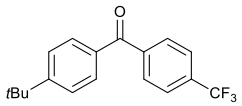
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.5, 156.2, 153.0, 142.0, 135.1, 133.1, 130.1, 125.4, 107.8, 61.1, 56.5, 35.2, 31.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 1643, 1604, 1581, 1498, 1454, 1413, 1331, 1232, 1120, 1016, 999, 865, 849, 832, 767, 725, 712, 668.

MS (EI, 70 eV, %) m/z = 329 (21), 328 (100), 314 (11), 313 (56), 285 (27), 195 (54), 161 (30), 145 (15), 142 (18), 118 (12), 115 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{24}O_4$:** 328.1675; found: 328.1668.

Preparation of (4-(*tert*-butyl)phenyl)(4-(trifluoromethyl)phenyl)methanone (223c)



According to **TP2**, freshly prepared nBu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-bromobenzotrifluoride (450 mg, 0.28 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, 4-(*tert*-butyl)-*N*,*N*-dimethyl-benzamide (328 mg, 1.6 mmol, 0.80 equiv) was added neat, the resulting reaction mixture was allowed to warm up to –20 °C and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 98 : 2, R_f = 0.31) afforded the desired ketone **223c** (374 mg, 1.22 mmol, 76%) as a white solid.

M.p. 67 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.89 (d, *J* = 8.0 Hz, 2H), 7.78–7.71 (m, 4H), 7.54–7.49 (m, 2H), 1.37 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 195.4, 157.2, 141.3 (q, ^4J(C,F) = 1.2 Hz), 134.1, 133.7 (q, ^2J(C,F) = 33 Hz), 130.3, 130.2, 125.7, 125.4 (q, ^4J(C,F) = 3.8 Hz), 123.9 (q, ^1J(C,F) = 269 Hz), 35.4, 31.2.

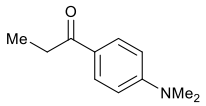
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −63.0.

IR (ATR, cm^{-1}) ṽ = 2966, 2871, 1651, 1603, 1507, 1463, 1407, 1362, 1323, 1310, 1279, 1163, 1122, 1105, 1063, 1015, 931, 859, 838, 774, 745, 733, 697, 676.

MS (EI, 70 eV, %) m/z = 306 (11), 292 (19), 291 (100), 263 (11), 235 (17), 173 (68), 145 (36).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}F_3O$:** 306.1231; found: 306.1224.

Preparation of 1-(4-(dimethylamino)phenyl)propan-1-one (223d)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. 4-Bromo-*N*,*N*-dimethylaniline (400 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, *N*,*N*-dimethylbutyramide (162 mg, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to –20 °C and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.26) afforded the desired ketone **223d** (241 mg, 1.36 mmol, 85%) as a yellowish solid.

M.p. 104 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.93–7.85 (m, 2H), 6.69–6.61 (m, 2H), 3.05 (s, 6H), 2.91 (q, *J* = 7.4 Hz, 2H), 1.20 (t, *J* = 7.3 Hz, 3H).

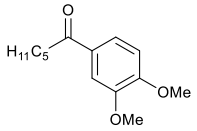
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 199.4, 153.4, 130.3, 125.2, 110.8, 40.2, 31.1, 9.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2969, 2929, 2894, 2870, 2656, 2594, 1519, 1446, 1411, 1348, 1230, 1185, 1126, 1079, 1068, 11009, 938, 830, 796, 773.

MS (EI, 70 eV, %) m/z = 177 (26), 100 (148), 134 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{15}NO$:** 177.1154; found: 177.1144.

Preparation of 1-(3,4-dimethoxyphenyl)hexan-1-one (223e)



According to **TP2**, freshly prepared *n*Bu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-bromoveratrole (434 mg, 0.29 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added dropwise at this temperature. After 5 min of reaction time, *N*,*N*-dimethylhexanamide (229 mg, 0.26 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to –20 °C and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) afforded the desired ketone **223e** (311 mg, 1.32 mmol, 82%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.58 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.53 (d, *J* = 2.0 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 3.94 (s, 3H), 3.94 (s, 3H), 2.95–2.85 (m, 2H), 1.82 – 1.66 (m, 2H), 1.36 (dq, *J* = 7.1, 3.6 Hz, 4H), 0.95–0.85 (m, 3H).

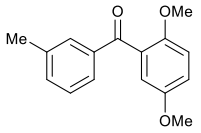
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 199.5, 153.3, 149.2, 130.5, 122.8, 110.4, 110.1, 56.2, 56.1, 38.3, 31.8, 24.6, 22.7, 14.1.

IR (ATR, cm^{-1}) ṽ = 2955, 2932, 2859, 1672, 1585, 1513, 1462, 1415, 1341, 1259, 1196, 1160, 1148, 1131, 1109, 1022, 880, 805, 765.

MS (EI, 70 eV, %) m/z = 236 (6), 180 (77), 165 (100), 137 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{20}O_3$:** 236.1412; found: 236.1403.

Preparation of (2,5-dimethoxyphenyl)(*m*-tolyl)methanone (223f)



According to **TP2**, freshly prepared nBu$_2$LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 1-bromo-2,5-dimethoxybenzene (434 mg, 0.30 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, *N*,*N*-diethyl-3-methyl-benzamide (306 mg, 0.31 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.40) afforded the desired ketone **223f** (304 mg, 1.19 mmol, 74%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.67 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.00 (dd, *J* = 9.0, 3.1 Hz, 1H), 6.94 (s, 1H), 6.93–6.89 (m, 1H), 3.79 (s, 3H), 3.67 (s, 3H), 2.39 (s, 3H).

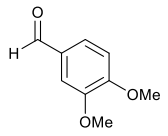
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 196.5, 153.6, 151.6, 138.2, 137.7, 134.0, 130.2, 129.9, 128.2, 127.5, 117.3, 114.5, 113.3, 56.5, 56.0, 21.4.

IR (ATR, cm^{-1}) ṽ = 3001, 2942, 2834, 1664, 1601, 1584, 1492, 1462, 1410, 1286, 1264, 1220, 1196, 1177, 1041, 1019, 814, 758, 710.

MS (EI, 70 eV, %) m/z = 256 (49), 239 (11), 198 (13), 165 (44), 151 (100), 119 (20), 91 (29).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{16}O_3$:** 256.1099; found: 256.1093.

Preparation of 3,4-dimethoxybenzaldehyde (223g)



According to **TP2**, freshly prepared *n*Bu_2LaMe·5LiCl (**205f**, 1.4 mmol, 0.70 equiv) was used and cooled to –50 °C. Thereupon, 4-bromoveratrole (434 mg, 0.29 mL, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added at this temperature. After 5 min of reaction time, *N*,*N*-dimethylformamide (117 mg, 0.12 mL, 1.6 mmol, 0.80 equiv) was added dropwise, the resulting reaction mixture was allowed to warm up to –20 °C and quenched with a saturated aqueous solution of NH_4Cl. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.37) afforded the desired aldehyde **223g** (171 mg, 1.03 mmol, 64%) as a white solid.

M.p. 46 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.84 (d, *J* = 0.9 Hz, 1H), 7.45 (ddd, *J* = 8.2, 1.8, 0.9 Hz, 1H), 7.40 (s, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 3.96 (d, *J* = 0.8 Hz, 3H), 3.93 (d, *J* = 0.8 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 190.9, 154.5, 149.7, 130.2, 126.9, 110.4, 109.0, 56.2, 56.0.

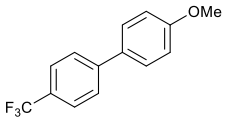
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2922, 2845, 1682, 1585, 1509, 1467, 1444, 1422, 1402, 1267, 1239, 1197, 1177, 1151, 1136, 1034, 1015, 963, 871, 801, 732.

MS (EI, 70 eV, %) m/z = 167 (10), 166 (100), 165 (78), 95 (15), 77 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{10}O_3$:** 166.0630; found: 166.0621.

7.5. Pd-Catalyzed Cross-Coupling Reactions of Diaryl(methyl)lanthanum Reagents of Type 211 with Aryl Bromides as Electrophiles

Preparation of 4-methoxy-4'-(trifluoromethyl)-1,1'-biphenyl (224a)



According to **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 4-bromoanisole (150 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211q,** freshly prepared from 4-bromobenzotrifluoride (225 mg, 1.0 mmol, 1.0 equiv) was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.58) gave the desired biphenyl **224a** (128 mg, 0.51 mmol, 64%) as a white solid.

M.p. 112 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 (s, 4H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.8, 144.3 (q, ^4J(C,F) = 1.0 Hz), 132.2, 128.7 (q, ^2J(C,F) = 33 Hz), 128.4, 126.9, 125.7 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 272 Hz), 114.4, 55.4.

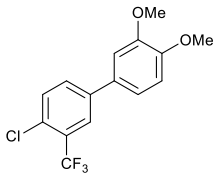
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.3.

IR (ATR, cm^{-1}) ṽ = 3030, 2846, 1602, 1582, 1532, 1500, 1460, 1442, 1402, 1320, 1294, 1276, 1256, 1200, 1180, 1166, 1110, 1072, 1034, 1010, 960, 850, 828, 812, 746, 720, 700.

MS (EI, 70 eV, %) m/z = 253 (18), 252 (100), 237 (42), 209 (59), 183 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}F_3O$:** 252.0762; found: 252.0756

Synthesis of 4-chloro-3',4'-dimethoxy-3-(trifluoromethyl)-1,1'-biphenyl (224b)



Based on **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 4-bromo-1,2-dimethoxybenzene (174 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211f**, freshly prepared from 4-bromo-1-chloro-2-(trifluoromethyl)benzene (259 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.54) led to the expected biphenyl **224b** (143 mg, 0.45 mmol, 56%) as a yellow solid.

M.p. 78 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.86 (d, *J* = 2.2 Hz, 1H), 7.66 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.07 (d, *J* = 2.1 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 3.99 (s, 3H), 3.96 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 149.4 (q, ^4J(C,F) = 1.0 Hz), 140.0, 131.8, 131.6, 130.9 (2C), 130.5 (q, ^4J(C,F) = 2.0 Hz), 128.6 (q, ^2J(C,F) = 31 Hz), 125.8 (q, ^3J(C,F) = 5.3 Hz), 122.9 (q, ^1J(C,F) = 273 Hz), 119.6, 111.6, 110.1, 56.1, 56.0.

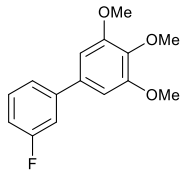
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.6.

IR (ATR, cm^{-1}) ṽ = 2935, 1604, 1593, 1519, 1477, 1468, 1427, 1337, 1316, 1248, 1213, 1166, 1134, 1110, 1058, 1027, 909, 855, 832, 805, 764, 725, 668.

MS (EI, 70 eV, %) m/z = 318 (33), 317 (16), 316 (100), 303 (10), 301 (31), 273 (28), 238 (28), 235 (12), 233 (22), 223 (14), 220 (17), 204 (11), 195 (17), 169 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{12}ClF_3O_2$:** 316.0478; found: 316.0470.

Synthesis of 3'-fluoro-3,4,5-trimethoxy-1,1'-biphenyl (224c)



With reference to **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 5-bromo-1,2,3-trimethoxybenzene (198 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211s**, freshly prepared from 1-bromo-3-fluorobenzene (175 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.21) resulting in the biphenyl **224c** (120 mg, 0.46 mmol, 58%) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.45–7.38 (m, 1H), 7.35 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.27 (dt, *J* = 10.2, 2.2 Hz, 1H), 7.06 (tdd, *J* = 8.4, 2.5, 1.1 Hz, 1H), 6.78 (s, 2H), 3.95 (s, 6H), 3.92 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.9 (d, ^1J(C,F) = 246 Hz), 153.3, 143.4 (d, ^3J(C,F) = 7.7 Hz), 137.9, 135.7 (d, ^4J(C,F) = 2.2 Hz), 130.1 (d, ^3J(C,F) = 8.5 Hz), 122.5 (d, ^4J(C,F) = 2.8 Hz), 113.9 (d, ^3J(C,F) = 6.1 Hz), 113.7 (d, ^3J(C,F) = 7.0 Hz), 104.2, 60.8, 56.1.

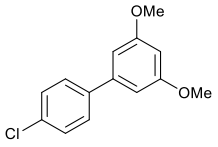
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –113.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2935, 1734, 1610, 1574, 1511, 1481, 1402, 1344, 1255, 1239, 1182, 1154, 1122, 1081, 1035, 1004, 946, 923, 874, 831, 813, 781, 765, 735, 679, 654.

MS (EI, 70 eV, %) m/z = 263 (16), 262 (100), 248 (11), 247 (79), 219 (32), 204 (27), 189 (12), 187 (36), 176 (13), 159 (24), 133 (38).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{15}FO_3$:** 262.1005; found: 262.1000.

Preparation of 4'-chloro-3,5-dimethoxy-1,1'-biphenyl (224d)



According to **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 1-bromo-3,5-dimethoxybenzene (174 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211a**, freshly prepared from 1-bromo-4-chlorobenzene (191 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.50) affording the desired product **224d** (99 mg, 0.40 mmol, 50%) as a white solid.

M.p. 64 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.53 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 6.71 (d, *J* = 2.2 Hz, 2H), 6.50 (t, *J* = 2.2 Hz, 1H), 3.87 (s, 6H).

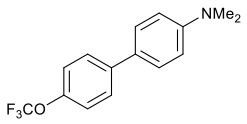
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 161.2, 142.2, 139.6, 133.6, 128.9, 128.4, 105.3, 99.5, 55.5.

IR (ATR, cm^{-1}) ṽ = 2991, 1593, 1565, 1496, 1454, 1424, 1390, 1351, 1331, 1307, 1297, 1217, 1207, 1192, 1152, 1090, 1060, 1032, 1011, 992, 951, 926, 839, 825, 810, 686.

MS (EI, 70 eV, %) m/z = 250 (30), 249 (15), 248 (100), 221 (13), 219 (41), 207 (13), 188 (10), 184 (28), 155 (10), 153 (12), 152 (11), 139 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}ClO_2$:** 248.0604; found: 248.0599.

Synthesis of *N*,*N*-dimethyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-4-amine (224e)



Based on **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 4-bromo-*N*,*N*-dimethylaniline (160 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211i**, freshly prepared from 1-bromo-4-(trifluoromethoxy)benzene (241 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.32) led to the biphenyl **224e** (155 mg, 0.55 mmol, 69%) as a white solid.

M.p. 173 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.9 Hz, 2H), 7.28–7.23 (m, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.03 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 150.2, 147.7 (q, ^4J(C,F) = 1.7 Hz), 140.0, 127.7, 127.4, 121.2, 120.6 (q, ^1J(C,F) = 257 Hz), 112.7, 40.5.

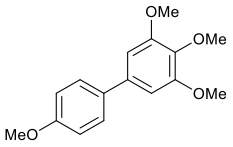
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –57.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2896, 1608, 1536, 1499, 1446, 1362, 1289, 1227, 1209, 1155, 1109, 1063, 1013, 946, 920, 849, 805, 769, 734, 715, 661.

MS (EI, 70 eV, %) m/z = 282 (16), 281 (100), 280 (86), 265 (16), 212 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{14}F_3NO$:** 281.1027; found: 281.1023.

Synthesis of 3,4,4',5-tetramethoxy-1,1'-biphenyl (224f)



With reference to **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 5-bromo-1,2,3-trimethoxybenzene (198 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211j**, freshly prepared from 4-bromoanisole (187 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.39) furnished the biphenyl **224f** (138 mg, 0.50 mmol, 63%) as an orange solid.

M.p. 63 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.49 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.74 (s, 2H), 3.92 (s, 6H), 3.89 (s, 3H), 3.85 (s, 3H).

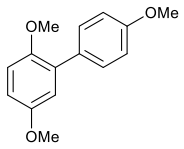
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.3, 153.5, 137.3, 137.0, 134.0, 128.2, 114.3, 104.2, 61.1, 56.3, 55.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2931, 1738, 1608, 1585, 1569, 1498, 1463, 1450, 1422, 1398, 1341, 1298, 1283, 1234, 1175, 1121, 1075, 1034, 993, 879, 852, 811, 766, 672.

MS (EI, 70 eV, %) m/z = 275 (16), 274 (98), 260 (15), 259 (100), 231 (17), 216 (14), 207 (13), 201 (11), 199 (26), 171 (14), 145 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{18}O_4$:** 274.1205; found: 274.1201.

Preparation of 2,4',5-trimethoxy-1,1'-biphenyl (224g)



According to **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 4-bromoanisole (150 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211k**, freshly prepared from 2-bromo-1,4-dimethoxybenzene (217 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.39) affording the biphenyl **224g** (113 mg, 0.46 mmol, 58%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.51 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.96–6.91 (m, 2H), 6.86 (dd, *J* = 8.8, 3.2 Hz, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 3.78 (s, 3H).

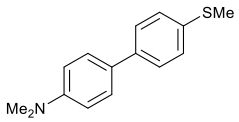
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.8, 153.8, 150.8, 131.4, 130.8, 130.6, 116.6, 113.5, 112.6 (2C), 56.3, 55.8, 55.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2935, 2831, 1608, 1586, 1572, 1515, 1492, 1461, 1439, 1399, 1293, 1260, 1229, 1243, 1214, 1206, 1173, 1144, 1108, 1048, 1038, 1021, 880, 829, 793, 736, 680.

MS (EI, 70 eV, %) m/z = 245 (16), 244 (100), 230 (12), 229 (80), 214 (43), 201 (14), 198 (33), 186 (17), 183 (12), 171 (11), 115 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{16}O_3$:** 244.1099; found: 244.1094.

Synthesis of *N*,*N*-dimethyl-4'-(methylthio)-[1,1'-biphenyl]-4-amine (224h)



With reference to **TP3**, $Pd(OAc)_2$ (1.8 mg, 8.0 µmol, 1.0 mol%), XPhos (7.6 mg, 16 µmol, 2.0 mol%), 4-bromothioanisole (163 mg, 0.80 mmol, 0.80 equiv) and freshly distilled toluene (2.4 mL) were used. To this solution, diaryl(methyl)lanthanum reagent **211o**, freshly prepared from 4-bromo-*N*,*N*-dimethyl-aniline (200 mg, 1.0 mmol, 1.0 equiv), was added dropwise within 2 min at room temperature and the reaction mixture was further stirred for 5 min. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.20) gave the desired biphenyl **224h** (100 mg, 0.41 mmol, 51%) as a pale yellow solid.

M.p. 170 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.49 (dd, *J* = 8.6, 2.1 Hz, 4H), 7.31 (d, *J* = 8.2 Hz, 2H), 6.80 (d, *J* = 7.7 Hz, 2H), 3.00 (s, 6H), 2.51 (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 150.3, 138.7, 136.0, 128.9, 127.8, 127.7, 127.0, 113.2, 41.0, 16.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2794, 1604, 1529, 1489, 1445, 1230, 1222, 1097, 1063, 1009, 948, 804, 781, 711.

MS (EI, 70 eV, %) m/z = 244 (15), 243 (100), 242 (10), 229 (11), 228 (76), 227 (18), 212 (12), 152 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{17}NS$:** 243.1082; found: 243.1077.

8. Preparation of Triaryl- and Triheteroaryllanthanum Reagents using Ph_3La and Related Reagents for Halogen-Lanthanum Exchange Reactions

8.1. Typical Procedures

Preparation of $Ph_3La \cdot 5LiCl$ (225c)

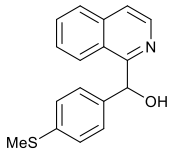
A pre-dried and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum was charged with freshly prepared $LaCl_3 \cdot 2LiCl$ (1.2 mL, 0.40 mmol, 0.40 equiv, 0.33 M in THF) and cooled to –30 °C. Subsequently, PhLi (0.63 mL, 1.2 mmol, 1.2 equiv, 1.9 M in Bu_2O) was added and the resulting solution was stirred at –30 °C for 30 min before being used.

Typical procedure for the halogen-lanthanum exchange using $Ph_3La \cdot 5LiCl$ (225c) (TP1)

A pre-dried and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum was charged with freshly prepared $Ph_3La \cdot 5LiCl$ (**225c**, 0.40 equiv) and cooled to –50 °C. Thereupon, the selected aryl or heteroaryl halide of type **204**, **210** or **213** (1.0 equiv) and tetradecane ($C_{14}H_{30}$) as internal standard were added dropwise, and the reaction mixture was further stirred at –50 °C. The exchange progress was determined by GC-analysis of water-quenched and iodolyzed reaction aliquots. Unless otherwise stated, all exchange reactions were completed after 5 min, and full conversion of the aryl or heteroaryl halide was observed. The resulting triaryl- or triheteroaryllanthanum derivatives of type **227** or **229** were immediately trapped by adding the corresponding electrophile of type **207** or **222** (0.80 equiv) neat at –50 °C. The reaction mixture was allowed to slowly warm up to room temperature, and the reaction progress was again checked by GC-analysis of water quenched aliquots. After full conversion of the electrophile, a saturated aqueous solution of NH_4Cl was added, and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Finally, the crude product was purified by flash column chromatography leading to the desired products of type **228**, **230** or **223**.

8.2. Preliminary Experiments using Ph_3La as exchange reagent

Preparation of isoquinolin-1-yl(4-(methylthio)phenyl)methanol (228a)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv), and cooled to –50 °C. Thereupon, 1-iodoisoquinoline (**204i**, 510 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 4-(methylthio)benzaldehyde (**207e**, 244 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.50) gave the desired secondary alcohol **228a** (270 mg, 0.96 mmol, 60%) as a yellow solid.

M.p. 112 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.51 (d, *J* = 5.7 Hz, 1H), 7.92 (dq, *J* = 8.5, 0.9 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.65–7.59 (m, 2H), 7.47 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.32 (s, 1H), 5.99 (br. s, 1H), 2.39 (s, 3H).

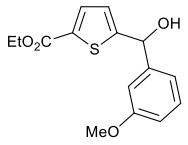
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.5, 140.7, 140.4, 138,6, 137.0, 130.7, 128.6, 127.9, 127.8, 127.2, 125.6, 125.2, 121.6, 72.5, 16.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3323, 1622, 1587, 1562, 1375, 1329, 1185, 1090, 1065, 1002, 993, 879, 830, 823, 750, 723, 699.

MS (EI, 70 eV, %) m/z = 281 (11), 279 (36), 278 (84), 264 (59), 263 (33), 251 (26), 250 (74), 232 (76), 217 (68), 207 (66), 204 (97), 151 (100), 123 (21), 79 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{15}NOS$:** 281.0874; found: 281.0880.

Preparation of ethyl 5-(hydroxy(3-methoxyphenyl)methyl)thiophene-2-carboxylate (230a)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.40 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, ethyl 5-bromothiophene-2-carboxylate (**213h**, 235 mg, 1.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 3-methoxybenzaldehyde (**207a**, 95 mg, 0.70 mmol, 0.70 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.50) affording the desired alcohol **230a** (154 mg, 0.53 mmol, 76%) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.59 (d, *J* = 3.8 Hz, 1H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.00–6.93 (m, 2H), 6.88–6.79 (m, 2H), 5.95 (s, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 3H), 2.84 (br. s, 1H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.3, 159.9, 155.4, 144.0, 133.2, 133.0, 129.8, 124.9, 118.6, 113.9, 111.8, 72.5, 61.1, 55.2, 14.3.

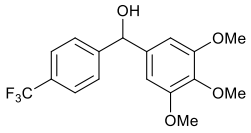
IR (ATR, cm^{-1}) ṽ = 3440, 2979, 1685, 1599, 1585, 1536, 1488, 1453, 1367, 1251, 1141, 1090, 1036, 907, 870, 825, 749, 728, 697.

MS (EI, 70 eV, %) m/z = 292 (22), 290 (16), 247 (14), 217 (16), 207 (12), 183 (14), 157 (87), 154 (34), 138 (12), 136 (41), 135 (100), 129 (58), 110 (58), 85 (19), 77 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{16}O_4S$:** 292.0769; found: 292.0764.

8.3. Iodine-Lanthanum Exchange Reactions of Functionalized Aryl and Heteroaryl Iodides using Ph_3La

Preparation of (4-(trifluoromethyl)phenyl)(3,4,5-trimethoxyphenyl)methanol (228b)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La{\cdot}5LiCl$ (**225c**, 1.2 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 4-iodobenzotrifluoride (816 mg, 3.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (150 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 3,4,5-trimethoxybenzaldehyde (471 mg, 2.4 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.43) furnished the expected alcohol **228b** (798 mg, 2.33 mmol, 97%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 6.54 (s, 2H), 5.75 (s, 1H), 3.80 (s, 9H), 2.86 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.1, 147.3 (q, ^4J(C,F) = 1.0 Hz), 138.7, 137.2, 129.4 (q, ^2J(C,F) = 32 Hz), 126.4, 125.1 (q, ^3J(C,F) = 3.8 Hz), 123.9 (q, ^1J(C,F) = 270 Hz), 103.4, 75.5, 60.6, 55.9.

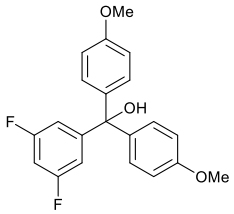
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3438, 2940, 1735, 1591, 1504, 1459, 1419, 1320, 1231, 1162, 1115, 1064, 1015, 1002, 968, 919, 866, 835, 816, 765, 702.

MS (EI, 70 eV, %) m/z = 343 (20), 342 (100), 325 (11), 278 (11), 172 (70), 145 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}F_3O_4$:** 342.1079; found: 342.1077.

Synthesis of (3,5-difluorophenyl)bis(4-methoxyphenyl)methanol (228c)



With reference to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 1,3-difluoro-5-iodobenzene (480 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 4,4′-dimethoxybenzophenone (388 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.48) led to the tertiary alcohol **228c** (414 mg, 1.16 mmol, 73%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.18 (d, *J* = 8.9 Hz, 4H), 6.94–6.83 (m, 6H), 6.78–6.67 (m, 1H), 3.83 (s, 6H), 2.82 (s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.5 (dd, ^1J(C,F) = 248 Hz, ^3J(C,F) = 13 Hz), 159.0, 151.5 (t, ^3J(C,F) = 8.0 Hz), 138.3, 129.0, 113.5, 111.1–110.7 (m), 102.4 (t, ^2J(C,F) = 26 Hz), 81.0 (t, ^4J(C,F) = 2.1 Hz), 55.3.

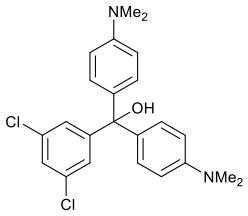
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –109.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3476, 1721, 1620, 1607, 1593, 1507, 1460, 1434, 1297, 1245, 1174, 1112, 1030, 992, 972, 914, 857, 829, 806, 771, 686.

MS (EI, 70 eV, %) m/z = 356 (25), 339 (13), 249 (16), 244 (13), 243 (100), 141 (42), 135 (78), 92 (12), 77 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{18}F_2O_3$:** 356.1224; found: 356.1221.

Synthesis of (3,5-dichlorophenyl)bis(4-(dimethylamino)phenyl)methanol (228d)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La{\cdot}5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 1,3-dichloro-5-iodobenzene (546 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 4,4′-bis(dimethylamino)benzophenone (429 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.36) resulting in the alcohol **228d** (401 mg, 0.97 mmol, 61%) as a pale blue solid.

M.p. 111 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.30 (d, *J* = 1.9 Hz, 2H), 7.25 (t, *J* = 1.9 Hz, 1H), 7.10 (d, *J* = 9.0 Hz, 4H), 6.69 (d, *J* = 9.0 Hz, 4H), 2.98 (s, 12H), 2.63 (s, 1H).

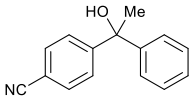
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 151.5, 149.7, 134.2, 134.1, 128.7, 126.8, 126.4, 111.8, 81.0, 40.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3450, 1609, 1511, 1446, 1349, 1164, 1028, 939, 856, 824, 793, 706, 686.

MS (EI, 70 eV, %) m/z = 416 (21), 414 (31), 400 (10), 399 (24), 398 (17), 397 (35), 270 (16), 269 (100), 253 (20), 148 (39).

HRMS (EI, 70 eV) m/z: calc. for **$C_{23}H_{24}Cl_2N_2O$:** 414.1266; found: 414.1260.

Synthesis of 4-(1-hydroxy-1-phenylethyl)benzonitrile (228e)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 1.2 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 4-iodobenzonitrile (687 mg, 3.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (150 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, acetophenone (288 mg, 2.4 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) afforded the expected alcohol **228e** (324 mg, 1.45 mmol, 60%) as a yellow solid.

M.p. 88 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.45–7.37 (m, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.32–7.27 (m, 1H), 2.35 (br. s, 1H), 1.98 (s, 3H).

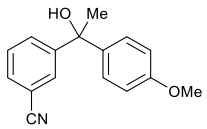
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.1, 146.4, 131.8, 128.3, 127.4, 126.3, 125.6, 118.7, 110.4, 75.8, 30.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3370, 2241, 2222, 1646, 1604, 1597, 1489, 1445, 1403, 1376, 1277, 1200, 1139, 1101, 1069, 1016, 932, 915, 846, 820, 775, 759, 726, 699, 666.

MS (EI, 70 eV, %) m/z = 223 (5), 209 (14), 208 (100), 130 (46), 121 (10), 105 (11), 102 (17), 77 (14), 43 (23).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NO$:** 223.0997; found: 223.0980.

Preparation of 3-(1-hydroxy-1-(4-methoxyphenyl)ethyl)benzonitrile (228f)



With reference to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 1-iodobenzonitrile (458 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 4-methoxyacetophenone (240 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.32) gave the desired alcohol **228f** (293 mg, 1.16 mmol, 73%) as a slightly yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.75 (t, *J* = 1.6 Hz, 1H), 7.65 (dt, *J* = 8.0, 1.3 Hz, 1H), 7.52 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 2.44 (br. s, 1H), 1.94 (s, 3H).

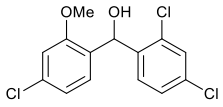
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.9, 150.0, 138.9, 130.4, 130.3, 129.5, 128.9, 127.2, 119.0, 113.8, 112.0, 75.4, 55.3, 30.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3471, 2227, 1609, 1581, 1508, 1371, 1297, 1246, 1176, 1089, 1028, 921, 832, 799, 752, 729, 693, 674.

MS (EI, 70 eV, %) m/z = 253 (17), 239 (17), 238 (100), 151 (32), 135 (17), 130 (73), 105 (11), 102 (30), 77 (22), 43 (70).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{15}NO_2$:** 253.1103; found: 253.1095.

Preparation of (4-chloro-2-methoxyphenyl)(2,4-dichlorophenyl)methanol (228g)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La{\cdot}5LiCl$ (**225c**, 0.40 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 4-chloro-1-iodo-2-methoxy-benzene (269 mg, 1.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 2,4-dichlorobenzaldehyde (140 mg, 0.80 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.21) affording the desired secondary alcohol **228g** (184 mg, 0.58 mmol, 73%) as a white solid.

M.p. 80 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.47 (d, *J* = 8.4 Hz, 1H), 7.41 (d, *J* = 2.1 Hz, 1H), 7.35–7.22 (m, 2H), 7.04 (d, *J* = 2.6 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.36 (s, 1H), 3.85 (s, 3H), 2.97 (br. s, 1H).

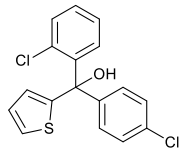
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 155.4, 138.0, 134.0, 133.5, 131.8, 129.4, 129.3, 128.8, 127.5, 125.9, 111.8, 67.5, 55.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3253, 1587, 1560, 1485, 1461, 1291, 1245, 1130, 1032, 1010, 902, 841, 811, 806, 729.

MS (EI, 70 eV, %) m/z = 318 (39), 302 (31), 300 (33), 281 (56), 263 (28), 249 (21), 228 (76), 199 (29), 174 (64), 173 (100), 155 (37), 143 (87), 125 (68), 75 (21).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}Cl_3O_2$:** 315.9825; found: 315.9817.

Preparation of (2-chlorophenyl)(4-chlorophenyl)(thiophen-2-yl)methanol (228h)



With reference to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 2-iodothiophene (420 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 2,4′-dichlorobenzophenone (402 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.32) led to the alcohol **228h** (460 mg, 1.37 mmol, 86%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.38 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.33 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.32–7.23 (m, 4H), 7.19–7.13 (m, 1H), 6.94 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.85 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.56 (dd, *J* = 3.6, 1.2 Hz, 1H), 4.58 (s, 1H).

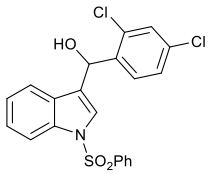
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 149.7, 143.8, 142.6, 133.4, 132.4, 131.2, 130.5, 129. 5, 128. 2, 128.1, 126.9, 126.5, 126. 2, 125.9, 80.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3549, 1588, 1568, 1487, 1464, 1433, 1399, 1328, 1266, 1233, 1131, 1090, 1056, 1038, 1011, 916, 906, 846, 815, 805, 755, 697, 655.

MS (EI, 70 eV, %) m/z = 333 (12), 303 (15), 301 (21), 225 (18), 223 (50), 197 (17), 196 (14), 195 (50), 194 (42), 160 (13), 141 (33), 139 (100), 111 (33).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{12}Cl_2OS$:** 333.9986; found: 333.9979.

Preparation of (2,4-dichlorophenyl)(1-(phenylsulfonyl)-1*H*-indol-3-yl)methanol (228i)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.40 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 3-iodo-1-(phenylsulfonyl)-1*H*-indole (383 mg, 1.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 2,4-dichlorobenzaldehyde (140 mg, 0.80 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.31) resulting in the desired secondary alcohol **228i** (332 mg, 0.77 mmol, 96%) as an orange solid.

M.p. 87 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.98 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 2H), 7.51 (dd, *J* = 8.0, 5.7 Hz, 3H), 7.46–7.38 (m, 4H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.26 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.33 (s, 1H), 2.97 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 138.0, 137.9, 135.6, 134.4, 134.0, 133.2, 129.5, 129.4, 129.3, 128.9, 127.7, 126.8, 125.2, 124.5, 124.0, 123.6, 120.4, 113.9, 66.4.

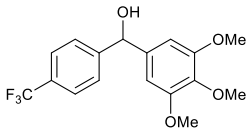
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3222, 1588, 1562, 1466, 1446, 1376, 1296, 1278, 1212, 1184, 1174, 1132, 1118, 1094, 1078, 1058, 1028, 1018, 970, 912, 844, 818, 798, 744, 724, 682.

MS (EI, 70 eV, %) m/z = 434 (14), 433 (45), 432 (24), 431 (79), 416 (13), 415 (15), 414 (25), 290 (21), 286 (27), 275 (24), 273 (44), 240 (15), 239 (15), 238 (54), 237 (14), 203 (24), 202 (14), 177 (20), 176 (16), 175 (84), 174 (16), 173 (100), 141 (13), 77 (29), 43 (23).

HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{15}Cl_2NO_3S$:** 431.0150; found: 431.0145.

8.4. Bromine-Lanthanum Exchange Reactions of Functionalized Aryl and Heteroaryl Bromides using Ph_3La

Preparation of (4-(trifluoromethyl)phenyl)(3,4,5-trimethoxyphenyl)methanol (230b)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 1.2 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 4-bromobenzotrifluoride (675 mg, 3.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (150 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 3,4,5-trimethoxybenzaldehyde (471 mg, 2.4 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.43) furnished the expected alcohol **230b** (779 mg, 2.28 mmol, 95%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 6.54 (s, 2H), 5.75 (s, 1H), 3.80 (s, 9H), 2.86 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.1, 147.3 (q, ^4J(C,F) = 1.0 Hz), 138.7, 137.2, 129.4 (q, ^2J(C,F) = 32 Hz), 126.4, 125.1 (q, ^3J(C,F) = 3.8 Hz), 123.9 (q, ^1J(C,F) = 270 Hz), 103.4, 75.5, 60.6, 55.9.

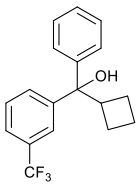
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3438, 2940, 1735, 1591, 1504, 1459, 1419, 1320, 1231, 1162, 1115, 1064, 1015, 1002, 968, 919, 866, 835, 816, 765, 702.

MS (EI, 70 eV, %) m/z = 343 (20), 342 (100), 325 (11), 278 (11), 172 (70), 145 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}F_3O_4$:** 342.1079; found: 342.1077.

Synthesis of cyclobutyl(phenyl)(3-(trifluoromethyl)phenyl)methanol (230c)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 3-bromobenzotrifluoride (450 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, cyclobutyl phenyl ketone (256 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.44) leading to the alcohol **230c** (401 mg, 1.31 mmol, 82%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.70 (dq, *J* = 1.8, 0.9 Hz, 1H), 7.51–7.43 (m, 2H), 7.40–7.20 (m, 6H), 3.49–3.34 (m, 1H), 2.20 (br. s, 1H), 2.11–1.66 (m, 7H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 147.1, 145.4, 130.2 (q, ^2J(C,F) = 32 Hz), 129.8 (q, ^4J(C,F) = 1.2 Hz), 128.4, 128.3, 128.0, 127.2, 126.3, 123.5 (q, ^3J(C,F) = 3.8 Hz), 122.8 (q, ^3J(C,F) = 3.9 Hz), 78.2, 43.9, 23.0, 22.5, 17.0.

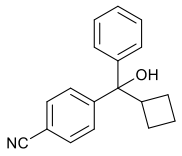
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 2942, 1490, 1444, 1326, 1250, 1216, 1160, 1120, 1096, 1074, 1048, 1032, 994, 964, 916, 800, 754, 700, 682, 660.

MS (EI, 70 eV, %) m/z = 306 (1), 252 (15), 251 (100), 183 (12), 173 (36), 145 (11), 105 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}OF_3$:** 306.1231; found: 306.1235.

Synthesis of 4-(cyclobutyl(hydroxy)(phenyl)methyl)benzonitrile (230d)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.40 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 4-bromobenzonitrile (182 mg, 1.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, cyclobutyl phenyl ketone (112 mg, 0.70 mmol, 0.70 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) leading to the expected alcohol **230d** (125 mg, 0.48 mmol, 69%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.57–7.51 (m, 2H), 7.48–7.43 (m, 2H), 7.35–7.19 (m, 5H), 3.43–3.30 (m, 1H), 2.16 (br. s, 1H), 2.08–1.93 (m, 3H), 1.93–1.79 (m, 1H), 1.78–1.62 (m, 2H).

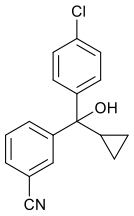
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 151.8, 145.5, 132.2, 128.9, 127.9, 127.4, 126.8, 119.4, 110.9, 78.8, 44.1, 23.6, 22.7, 17.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3490, 2980, 2228, 1604, 1496, 1446, 1406, 1352, 1318, 1280, 1248, 1216, 1186, 1158, 1074, 996, 964, 908, 882, 818, 770, 752, 730, 698.

MS (EI, 70 eV, %) m/z = 263 (1), 208 (100), 131 (30), 130 (29), 105 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}ON$:** 263.1310; found: 263.1306.

Preparation of 3-((4-chlorophenyl)(cyclopropyl)(hydroxy)methyl)benzonitrile (230e)



Based on **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 3-bromobenzonitrile (364 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 4-chlorophenyl cyclopropyl ketone (289 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.22) affording the alcohol **230e** (375 mg, 1.30 mmol, 83%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.78 (t, *J* = 1.6 Hz, 1H), 7.63 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.55 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.41–7.36 (m, 2H), 7.35–7.28 (m, 2H), 2.21 (br. s, 1H), 1.58 (tt, *J* = 8.2, 5.4 Hz, 1H), 0.75–0.55 (m, 2H), 0.54–0.42 (m, 2H).

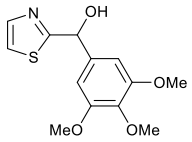
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 148.2, 144.3, 133.3, 131.1, 130.6, 130.0, 128.6, 128.2, 128.1, 118.7, 111.8, 76.1, 21.2, 2.0, 1.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3466, 2232, 1596, 1488, 1424, 1400, 1372, 1320, 1280, 1172, 1152, 1092, 1014, 996, 968, 906, 868, 830, 794, 728, 692.

MS (EI, 70 eV, %) m/z = 283 (1), 257 (20), 255 (100), 242 (16), 139 (16), 130 (40), 102 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{14}ONCl$:** 283.0764; found: 283.0758.

Synthesis of thiazol-2-yl(3,4,5-trimethoxyphenyl)methanol (230f)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 2-bromothiazole (328 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 3,4,5-trimethoxybenzaldehyde (314 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 4 : 6, R_f = 0.27) gave the expected alcohol **230f** (405 mg, 1.44 mmol, 90%) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.62 (d, *J* = 3.2 Hz, 1H), 7.27 (d, *J* = 3.2 Hz, 1H), 6.70 (s, 2H), 5.97 (s, 1H), 4.79 (br. s, 1H), 3.80 (s, 9H).

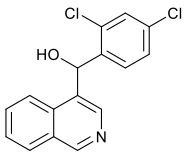
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 175.0, 153.3, 142.2, 137.7, 137.3, 119.5, 103.5, 73.7, 60.8, 56.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3188, 2935, 1591, 1503, 1459, 1416, 1326, 1229, 1180, 1119, 1051, 1000, 916, 841, 775, 725, 695.

MS (EI, 70 eV, %) m/z = 282 (13), 281 (91), 279 (44), 265 (54), 264 (17), 250 (100), 222 (16), 207 (27), 195 (30), 181 (79), 176 (11), 164 (10), 153 (17), 138 (19), 125 (15), 111 (30), 93 (11), 86 (13), 85 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}NO_4S$:** 281.0722; found: 281.0716.

Synthesis of (2,4-dichlorophenyl)(isoquinolin-4-yl)methanol (230g)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La \cdot 5LiCl$ (**225c**, 0.80 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 4-bromoisoquinoline (416 mg, 2.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (100 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, 2,4-dichlorobenzaldehyde (280 mg, 1.6 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 1 : 1, R_f = 0.27) gave the desired product **230g** (254 mg, 0.84 mmol, 53%) as a yellow-green solid.

M.p. 170 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.14 (s, 1H), 8.40 (s, 1H), 8.00 (t, *J* = 7.7 Hz, 2H), 7.80–7.70 (m, 1H), 7.70–7.58 (m, 1H), 7.42 (d, *J* = 2.1 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.24 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.81 (s, 1H), 3.30 (br. s, 1H).

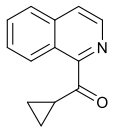
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 152.3, 140.2, 138.0, 134.4, 133.6, 133.4, 131.4, 131.0, 129.6, 129.4, 128.5, 128.0, 127.4 (2C), 122.7, 68.0.

IR (ATR, cm^{-1}) ṽ = 3090, 3056, 3042, 2360, 1624, 1588, 1562, 1502, 1464, 1378, 1244, 1196, 1138, 1068, 1048, 1018, 904, 890, 878, 856, 826, 806, 782, 746, 698, 664.

MS (EI, 70 eV, %) m/z = 303 (13), 268 (9), 139 (100), 129 (15), 128 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{11}ONCl_2$:** 303.0218; found: 303.0208.

Preparation of cyclopropyl(isoquinolin-1-yl)methanone (223h)



According to **TP1**, a pre-dried and argon flushed *Schlenk*-tube was charged with $Ph_3La{\cdot}5LiCl$ (**225c**, 0.40 mmol, 0.40 equiv) and cooled to –50 °C. Thereupon, 1-iodoisoquinoline (255 mg, 1.0 mmol, 1.0 equiv) and $C_{14}H_{30}$ (50 µL) were added dropwise, and the reaction mixture was stirred for additional 5 min. As electrophile, *N*,*N*-dimethylcyclopropanecarboxamide (91 mg, 0.80 mmol, 0.80 equiv) was used, and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.36) resulting in the desired ketone **223h** (122 mg, 0.62 mmol, 78%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.83 (d, *J* = 7.4 Hz, 1H), 8.64 (d, *J* = 5.5 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.82 (d, *J* = 5.6 Hz, 1H), 7.77–7.61 (m, 2H), 3.34 (tt, *J* = 7.9, 4.6 Hz, 1H), 1.47–1.29 (m, 2H), 1.17 (dq, *J* = 7.1, 3.4 Hz, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 203.5, 154.0, 141.2, 137.0, 130.4, 128.9, 126.9 (2C), 125.6, 124.1, 19.2, 13.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3051, 3005, 1674, 1621, 1578, 1554, 1497, 1446, 1395, 1364, 1330, 1270, 1233, 1206, 1086, 1068, 1026, 953, 882, 869, 829, 796, 752, 737, 716.

MS (EI, 70 eV, %) m/z = 196 (25), 182 (12), 169 (12), 168 (100), 167 (32), 129 (17), 128 (22), 44 (26).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{11}NO$:** 197.0841; found: 197.0836.

9. Preparation of Functionalized Diaryl- and Diheteroarylsamarium Reagents by a Halogen-Samarium Exchange

9.1. Typical Procedures

Preparation of *n*Bu_2SmCl·4LiCl (231e)

A pre-dried and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with $SmCl_3$·2LiCl (1.8 mL, 0.60 mmol, 0.60 equiv, 0.33 M in THF) and cooled to –30 °C. Subsequently, freshly titrated *n*BuLi (0.46 mL, 1.2 mmol, 1.2 equiv, 2.6 M in hexane) was added dropwise and the resulting solution was stirred for 30 min at –30 °C before being used.

Preparation of *n*Bu_2SmMe·5LiCl (233b)

A pre-dried and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with $SmCl_3$·2LiCl (2.1 mL, 0.70 mmol, 0.70 equiv, 0.33 M in THF) and cooled to –30 °C. Subsequently, freshly titrated MeLi (0.41 mL, 0.70 mmol, 0.70 equiv, 1.7 M in Et_2O) and *n*BuLi (0.54 mL, 1.4 mmol, 1.4 equiv, 2.6 M in hexane) were added dropwise and the resulting solution was stirred for 30 min at –30 °C before being used.

Typical procedure for the I/Sm exchange reaction using *n*Bu_2SmCl·4LiCl (231e) (TP1)

A pre-dried and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) and cooled to –50 °C. Thereupon, the selected aryl or heteroaryl iodide (1.0 mmol, 1.0 equiv) was added neat and the reaction mixture was further stirred for 5 min. Usually, all exchange processes were checked by GC-analysis of hydrolyzed and iodolyzed reaction aliquopts and finished after 5 min reaction time. Upon full conversion of the organic iodide, a selected electrophile (0.80 mmol, 0.80 equiv) was added neat to the generated diaryl- or diheteroarylsamarium reagent of type **236**, and the reaction mixture was allowed to warm to room temperature. The reaction progress was again checked by GC-analysis with water quenched aliquots. After full conversion of the electrophile was reached, the reaction was treated with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography led to the desired final product of type **237**.

Typical procedure for the Br/Sm exchange reaction using *n*Bu_2SmMe·5LiCl (233b) (TP2)

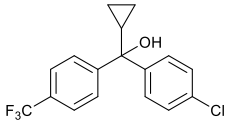
A pre-dried and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with freshly prepared *n*Bu_2SmMe·5LiCl (**233b**, 0.70 mmol, 0.70 equiv) and cooled to –30 °C. Thereupon, the selected aryl or heteroaryl bromide (1.0 mmol, 1.0 equiv) was added neat and the reaction mixture was further stirred for 5 min. Usually, all exchange processes were checked by GC-analysis of hydrolyzed and iodolyzed reaction aliquopts and finished after 1 h reaction time. Upon full conversion of the organic bromide, a selected electrophile (0.80 mmol, 0.80 equiv) was added neat to the generated diaryl- or diheteroaryl(methyl)samarium reagent of type **238**, and the reaction mixture was allowed to warm to room temperature. The reaction progress was again checked by GC-analysis with water quenched aliquots. After full conversion of the electrophile was reached, the reaction was treated with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography led to the desired final product of type **239**.

Typical procedure for the Pd-catalyzed cross-coupling reactions of diarylsamarium reagents of type 236 with selected aryl halides as electrophiles (TP3)

A pre-dried and argon-flushed *Schlenk*-tube was charged with $Pd(dba)_2$ (23 mg, 0.04 mmol, 5.0 mol%), P(*t*Bu)$_3$ (16 mg, 0.08 mmol, 10 mol%) and a selected aryl halide (0.80 mmol, 0.80 equiv) as electrophile. Freshly distilled THF (0.80 mL) was added and the resulting solution was stirred for 2 min at room temperature. Subsequently, a diarylsamarium reagent of type **236**, freshly prepared from the corresponding aryl iodide (1.0 mmol, 1.0 equiv), was added within 2 min at room temperature. The reaction mixture was stirred for 1 h and the reaction progress was checked by GC-analysis of water quenched aliquots. After full conversion of the selected electrophile, the reaction was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Finally, the crude product was purified by flash column chromatography leading to the desired product of type **240**.

9.2. Iodine-Samarium Exchange Reactions of Functionalized Aryl and Heteroaryl Iodides using *n*Bu_2SmCl

Preparation of (4-chlorophenyl)(cyclopropyl)(4-(trifluoromethyl)phenyl)methanol (237a)



According to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 4-iodobenzotrifluoride (272 mg, 1.0 mmol, 1.0 equiv) and tetradecane $C_{14}H_{30}$ (50 µL) were added and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-chlorophenyl cyclopropyl ketone (145 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.17) gave the desired tertiary alcohol **237a** (209 mg, 0.64 mmol, 81%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 1.98 (br. s, 1H), 1.59 (tt, *J* = 8.3, 5.4 Hz, 1H), 0.71–0.54 (m, 2H), 0.53–0.41 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 150.7 (q, ^4J(C,F) = 1.8 Hz), 144.9, 133.4, 129.4 (q, ^2J(C,F) = 32 Hz), 128.4, 128.3, 127.0, 125.0 (q, ^3J(C,F) = 4.0 Hz), 124.1 (q, ^1J(C,F) = 270 Hz), 76.6, 21.5, 2.1, 1.6.

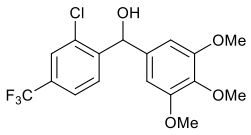
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) ṽ = 3474, 3005, 1722, 1617, 1488, 1409, 1322, 1255, 1162, 1121, 1067, 1013, 987, 874, 821, 772.

MS (EI, 70 eV, %) m/z = 326 (1), 300 (32), 299 (16), 298 (100), 285 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{14}ClF_3O$:** 326.0685; found: 326.0676.

Synthesis of (2-chloro-4-(trifluoromethyl)phenyl)(3,4,5-trimethoxyphenyl)methanol (237b)



Based on **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 2-chloro-1-iodo-4-(trifluoromethyl)benzene (307 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 3,4,5-trimethoxybenzaldehyde (157 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.36) afforded the expected secondary alcohol **237b** (247 mg, 0.66 mmol, 83%) as a white solid.

M.p. 112 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.79 (d, *J* = 8.2 Hz, 1H), 7.62–7.59 (m, 1H), 7.56 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.59 (s, 2H), 6.14 (s, 1H), 3.81 (s, 9H), 2.71 (br. s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.3, 144.8 (q, ^4J(C,F) = 1.1 Hz), 137.6, 137.1, 132.8, 131.0 (q, ^2J(C,F) = 33 Hz), 128.0, 126.6 (q, ^3J(C,F) = 3.9 Hz), 123.9 (q, ^{3}J(C,F) = 3.7 Hz), 123.2 (q, ^1J(C,F) = 272 Hz), 103.9, 72.3, 60.8, 56.1.

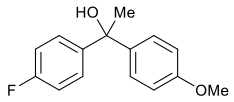
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3406, 2948, 2892, 2836, 1596, 1504, 1456, 1424, 1396, 1318, 1280, 1254, 1232, 1170, 1150, 1126, 1114, 1082, 1058, 1046, 1026, 1002, 964, 890, 866, 840, 796, 754, 734, 712, 700, 670.

MS (EI, 70 eV, %) m/z = 378 (20), 377 (12), 376 (66), 209 (31), 207 (100), 179 (14), 169 (71), 154 (11), 138 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{16}O_4ClF_3$:** 376.0689; found: 376.0682.

Preparation of 1-(4-fluorophenyl)-1-(4-methoxyphenyl)ethan-1-ol (237c)



Accroding to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 1-fluoro-4-iodobenzene (222 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-methoxyacetophenone (120 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.14) leading to the expected alcohol **237c** (171 mg, 0.70 mmol, 87%) as a colorless oil

^{1}H-NMR (400 MHz, DMSO, ppm) δ = 7.49–7.37 (m, 2H), 7.31 (dd, *J* = 8.8, 1.7 Hz, 2H), 7.08 (t, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 5.75–5.58 (m, 1H), 3.72 (s, 3H), 1.80 (s, 3H).

^{13}C-NMR (100 MHz, DMSO, ppm) δ = 161.1 (d, ^1J(C,F) = 242 Hz), 146.5 (d, ^4J(C,F) = 2.9 Hz), 141.8, 128.0 (d, ^3J(C,F) = 7.9 Hz), 127.2, 114.7 (d, ^2J(C,F) = 21 Hz), 113.5, 74.2, 55.5, 31.1.

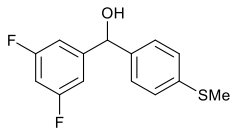
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −112.7.

IR (ATR, cm^{-1}) ṽ = 3473, 2933, 2836, 1651, 1600, 1504, 1462, 1407, 1371, 1326, 1303, 1246, 1222, 1177, 1157, 1108, 1084, 1030, 954, 928, 914, 831, 768, 732, 681, 652.

MS (EI, 70 eV, %) m/z = 246 (5), 232 (12), 231 (77), 229 (14), 228 (100), 214 (10), 213 (83), 198 (12), 197 (10), 183 (32), 170 (19), 165 (29), 135 (13), 123 (48).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{15}FO_2$:** 246.1056; found: 246.1048.

Preparation of (3,5-difluorophenyl)(4-(methylthio)phenyl)methanol (237d)



According to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 1,3-difluoro-5-iodobenzene (240 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-(methylthio)benzaldehyde (122 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.28) resulting in the alcohol **237d** (137 mg, 0.51 mmol, 64%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.29–7.22 (m, 4H), 6.96–6.87 (m, 2H), 6.71 (tt, *J* = 8.8, 2.4 Hz, 1H), 5.74 (s, 1H), 2.49 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (dd, ^1J(C,F) = 249 Hz, ^3J(C,F) = 13 Hz), 147.6 (t, ^3J(C,F) = 8.4 Hz), 139.5, 138.7, 127.1, 126.7, 109.0–109.0 (m), 102.8 (t, ^2J(C,F) = 25 Hz), 75.0, 15.7.

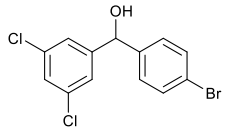
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –109.3.

IR (ATR, cm^{-1}) ṽ = 3384, 1624, 1596, 1494, 1454, 1438, 1404, 1310, 1116, 1092, 1042, 1014, 988, 960, 906, 872, 844, 818, 728, 666.

MS (EI, 70 eV, %) m/z = 266 (61), 250 (13), 219 (14), 202 (11), 201 (29), 183 (11), 153 (30), 151 (33), 141 (14), 125 (100), 109 (49).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}OF_2S$:** 266.0577; found: 266.0571.

Preparation of (4-bromophenyl)(3,5-dichlorophenyl)methanol (237e)



With reference to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 1,3-dichloro-5-iodobenzene (273 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-bromobenzaldehyde (148 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.14) leading to the desired product **237e** (168 mg, 0.52 mmol, 65%) as a colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.51 (d, *J* = 8.5 Hz, 2H), 7.28 (t, *J* = 1.9 Hz, 1H), 7.25 (d, *J* = 1.9 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 5.71 (s, 1H), 2.53 (br. s, 1H).

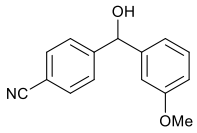
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 146.6, 141.6, 135.3, 132.1, 128.4, 128.0, 125.0, 122.3, 74.7.

IR (ATR, cm^{-1}) ṽ = 3314, 1590, 1568, 1486, 1430, 1400, 1298, 1186, 1098, 1072, 1036, 1010, 906, 862, 828, 792, 726, 668.

MS (EI, 70 eV, %) m/z = 332 (11), 330 (6), 253 (16), 251 (23), 199 (13), 187 (15), 185 (91), 183 (96), 177 (11), 175 (63), 173 (100), 163 (10), 159 (20), 158 (23), 157 (21), 77 (23), 75 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9OBrCl_2$:** 329.9214; found: 329.9206.

Preparation of 4-(hydroxy(3-methoxyphenyl)methyl)benzonitrile (237f)



According to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 4-iodobenzonitrile (229 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 3-methoxybenzaldehyde (109 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 7 : 3, R_f = 0.38) afforded the alcohol **237f** (186 mg, 0.78 mmol, 98%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.58 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.25 (t, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 9.7 Hz, 2H), 6.82 (ddd, *J* = 8.4, 2.5, 0.9 Hz, 1H), 5.78 (s, 1H), 3.76 (s, 3H), 2.77 (br. s, 1H).

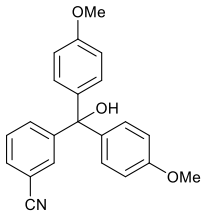
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.6, 148.6, 144.2, 132.0, 129.6, 126.8, 118.7, 118.6, 113.1, 112.1, 110.8, 75.2, 55.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3445, 2226, 1733, 1598, 1584, 1485, 1453, 1434, 1373, 1253, 1146, 1037, 1017, 994, 846, 828, 756, 695.

MS (EI, 70 eV, %) m/z = 240 (16), 239 (100), 137 (11), 135 (20), 130 (39), 109 (83), 104 (18), 102 (14), 77 (17)

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NO_2$:** 239.0946; found: 239.0940.

Preparation of 3-(hydroxybis(4-methoxyphenyl)methyl)benzonitrile (237g)



Based on **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 3-iodobenzonitrile (229 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4,4′-dimethoxybenzophenone (194 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.27) furnished the alcohol **237g** (249 mg, 0.72 mmol, 90%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.64 (t, *J* = 1.6 Hz, 1H), 7.58 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.54 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 8.9 Hz, 4H), 6.84 (d, *J* = 8.9 Hz, 4H), 3.80 (s, 6H), 2.99 (br. s, 1H).

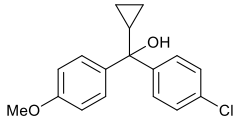
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.1, 149.0, 138.4, 132.3, 131.4, 130.8, 129.1, 128.7, 119.1, 113.6, 112.0, 81.0, 55.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3468, 2228, 1734, 1607, 1582, 1507, 1372, 1296, 1244, 1174, 1031, 890, 831, 801, 779, 694.

MS (EI, 70 eV, %) m/z = 345 (12), 244 (16), 243 (100), 135 (72), 130 (25).

HRMS (EI, 70 eV) m/z: calc. for **$C_{22}H_{19}NO_3$:** 345.1365; found: 345.1357.

Synthesis of (4-chlorophenyl)(cyclopropyl)(4-methoxyphenyl)methanol (237h)



According to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-chlorophenyl cyclopropyl ketone (145 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.22) resulting in the desired alcohol **237h** (188 mg, 0.65 mmol, 81%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.37–7.31 (m, 4H), 7.28–7.22 (m, 2H), 6.85–6.80 (m, 2H), 3.78 (s, 3H), 1.86 (br. s, 1H), 1.54 (tt, *J* = 8.3, 5.5 Hz, 1H), 0.66–0.58 (m, 1H), 0.55–0.37 (m, 3H).

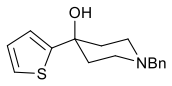
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.2, 146.5, 139.5, 133.1, 128.6, 128.4, 113.8, 77.0, 55.7, 22.1, 2.6, 1.9.

IR (ATR, cm^{-1}) ṽ = 3495, 1723, 1607, 1508, 1487, 1372, 1299, 1245, 1173, 1090, 1035, 1012, 985, 879, 871, 819, 789, 723.

MS (EI, 70 eV, %) m/z = 288 (1), 262 (31), 261 (17), 260 (100), 249 (11), 247 (35), 149 (11), 140 (30), 139 (92), 135 (58), 134 (17), 121 (67), 77 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}ClO_2$:** 288.0917; found: 288.0906.

Synthesis of 1-benzyl-4-(thiophen-2-yl)piperidin-4-ol (237i)



Based on **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 2-iodothiophene (210 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 1-benzylpiperidin-4-one (151 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.19) resulting in the desired tertiary alcohol **237i** (187 mg, 0.68 mmol, 85%) as a yellowish solid.

M.p. 95 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.42–7.32 (m, 4H), 7.33–7.24 (m, 1H), 7.24 (dd, *J* = 4.9, 1.3 Hz, 1H), 7.03–6.98 (m, 2H), 3.59 (s, 2H), 2.74 (dt, *J* = 8.6, 3.8 Hz, 2H), 2.52 (td, *J* = 11.6, 2.8 Hz, 2H), 2.21 (ddd, *J* = 13.3, 11.7, 4.4 Hz, 2H), 2.08–1.91 (m, 2H), 1.89 (br. s, 1H).

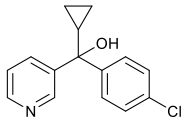
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.9, 138.5, 129.2, 128.3, 127.0, 126.8, 124.0, 122.0, 70.4, 63.1, 49.5, 39.7.

IR (ATR, cm^{-1}) ṽ = 3187, 2941, 2911, 2829, 1494, 1453, 1438, 1403, 1368, 1320, 1300, 1241, 1201, 1146, 1128, 1096, 1073, 1049, 1030, 997, 980, 962, 900, 842, 821, 799, 734, 693.

MS (EI, 70 eV, %) m/z = 273 (12), 255 (62), 254 (36), 189 (47), 188 (31), 182 (11), 172 (51), 164 (21), 146 (20), 137 (24), 135 (20), 109 (10), 97 (13), 91 (100).

HRMS (EI, 70 eV) m/z: calc. **$C_{16}H_{19}NOS$:** 273.1187; found: 273.1181.

Preparation of (4-chlorophenyl)(cyclopropyl)(pyridin-3-yl)methanol (237j)



With reference to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 3-iodopyridine (205 mg, 1.00 mmol, 1.00 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-chlorophenyl cyclopropyl ketone (145 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.18) gave the alcohol **237j** (175 mg, 0.68 mmol, 85%) as a white solid.

M.p. 111 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.41 (s, 1H), 8.24 (d, *J* = 4.8 Hz, 1H), 7.72 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.42–7.32 (m, 2H), 7.33–7.23 (m, 2H), 7.18 (dd, *J* = 8.0, 4.7 Hz, 1H), 4.36 (br. s, 1H), 1.63–1.36 (m, 1H), 0.76–0.41 (m, 4H).

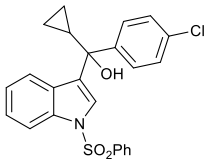
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 147.8, 147.5, 145.1, 143.0, 134.9, 133.1, 128.4, 128.2, 123.0, 75.2, 21.5, 1.9, 1.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3140, 1592, 1575, 1484, 1432, 1418, 1398, 1211, 1191, 1149, 1089, 1050, 1016, 986, 967, 948, 883, 823, 806, 734, 710, 687, 656.

MS (EI, 70 eV, %) m/z = 232 (15), 231 (100), 230 (46), 218 (23), 139 (26), 106 (27), 78 (17).

HRMS (EI, 70 eV) m/z: calc. for [*M*–C_2H_4] **$C_{13}H_{10}ClNO$:** 231.0451; found: 231.0445.

Preparation of (4-chlorophenyl)(cyclopropyl)(1-(phenylsulfonyl)-1*H*-indol-3-yl)methanol (237k)



Based on **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, 3-iodo-1-(phenylsulfonyl)-1*H*-indole (383 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, 4-chlorophenyl cyclopropyl ketone (145 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.18) gave the tertiary alcohol **237k** (268 mg, 0.66 mmol, 83%) as a white solid.

M.p. 62 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.94 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.85 (s, 1H), 7.63–7.56 (m, 1H), 7.50 (td, *J* = 7.1, 1.6 Hz, 2H), 7.34–7.21 (m, 5H), 7.18–7.00 (m, 2H), 1.99 (br. s, 1H), 1.63 (tt, *J* = 8.2, 5.5 Hz, 1H), 0.74–0.52 (m, 3H), 0.50–0.35 (m, 1H).

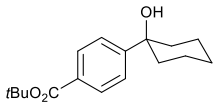
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 143.0, 138.1, 135.9, 134.0, 133.1, 129.3, 128.8, 128.6, 128.2, 127.7, 126.8, 124.9, 124.1, 123.3, 121.8, 113.7, 73.7, 21.7, 1.8, 1.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2360, 2338, 1488, 1446, 1400, 1366, 1336, 1312, 1294, 1270, 1174, 1122, 1088, 1040, 1014, 992, 964, 936, 874, 860, 810, 764, 746, 722, 684.

MS (EI, 70 eV, %) m/z = 439 (10), 437 (26), 411 (20), 410 (13), 409 (54), 398 (21), 397 (14), 396 (58), 298 (20), 270 (33), 269 (100), 255 (14), 233 (11), 141 (19), 139 (48), 77 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{24}H_{20}O_3NClS$:** 437.0852; found: 437.0846.

Synthesis of *tert*-butyl 4-(1-hydroxycyclohexyl)benzoate (237l)



According to **TP1**, freshly prepared *n*Bu_2SmCl·4LiCl (**231e**, 0.60 mmol, 0.60 equiv) was used and cooled to –50 °C. Thereupon, *tert*-butyl 4-iodobenzoate (304 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –50 °C. As electrophile, cyclohexanone (79 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.15) afforded the alcohol **237l** (136 mg, 0.49 mmol, 62%) as a white solid.

M.p. 124 °C.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.03–7.91 (m, 2H), 7.60–7.53 (m, 2H), 1.89–1.63 (m, 11H), 1.61 (s, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 165.7, 154.0, 130.4, 129.4, 124.5, 80.8, 73.3, 38.7, 28.2, 25.4, 22.0.

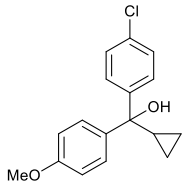
IR (ATR, cm^{-1}) ṽ = 3485, 2976, 2929, 2853, 1687, 1626, 1604, 1570, 1481, 1446, 1430, 1406, 1372, 1295, 1253, 1211, 1150, 1126, 1058, 1037, 1010, 971, 932, 907, 848, 835, 772, 720, 703, 669.

MS (EI, 70 eV, %) m/z = 276 (16), 258 (17), 233 (12), 220 (52), 219 (14), 203 (70), 202 (47), 192 (45), 187 (25), 185 (17), 177 (60), 175 (76), 164 (100), 159 (11), 157 (53), 149 (82), 133 (86), 131 (17), 129 (42), 128 (17), 115 (25), 91 (25), 57 (15), 55 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{24}O_3$:** 276.1725; found: 276.1715.

9.3. Bromine-Samarium Exchange Reactions of Functionalized Aryl Bromides using *n*Bu_2SmMe

Preparation of (4-chlorophenyl)(cyclopropyl)(4-methoxyphenyl)methanol (239a)



According to **TP2**, freshly prepared *n*Bu_2SmMe·5LiCl (**233b**, 0.70 mmol, 0.70 equiv) was used and cooled to –30 °C. Thereupon, 4-bromoanisole (187 mg, 1.0 mmol, 1.0 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –30 °C. As electrophile, 4-chlorophenyl cyclopropyl ketone (145 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.22) led to the desired alcohol **239a** (159 mg, 0.55 mmol, 69%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.37–7.31 (m, 4H), 7.28–7.22 (m, 2H), 6.85–6.80 (m, 2H), 3.78 (s, 3H), 1.86 (br. s, 1H), 1.54 (tt, *J* = 8.3, 5.5 Hz, 1H), 0.66–0.58 (m, 1H), 0.55–0.37 (m, 3H).

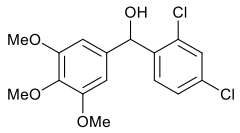
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.2, 146.5, 139.5, 133.1, 128.6 (2C), 128.4, 113.8, 77.0, 55.7, 22.1, 2.6, 1.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3495, 1723, 1607, 1508, 1487, 1372, 1299, 1245, 1173, 1090, 1035, 1012, 985, 879, 871, 819, 789, 723.

MS (EI, 70 eV, %) m/z = 288 (1), 262 (31), 261 (17), 260 (100), 249 (11), 247 (35), 149 (11), 140 (30), 139 (92), 135 (58), 134 (17), 121 (67), 77 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}ClO_2$:** 288.0917; found: 288.0906.

Synthesis of (2,4-dichlorophenyl)(3,4,5-trimethoxyphenyl)methanol (239b)



With reference to **TP2**, freshly prepared *n*Bu_2SmMe·5LiCl (**233b**, 0.70 mmol, 0.70 equiv) was used and cooled to –30 °C. Thereupon, 5-bromo-1,2,3-trimethoxybenzene (247 mg, 1.00 mmol, 1.00 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –30 °C. As electrophile, 2,4-dichlorobenzaldehyde (140 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 6 : 4, R_f = 0.49) resulting in alcohol **239b** (166 mg, 0.55 mmol, 60%) as a white solid.

M.p. 105 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.55 (d, *J* = 8.4 Hz, 1H), 7.39 (d, *J* = 2.1 Hz, 1H), 7.30 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.61 (s, 2H), 6.12 (s, 1H), 3.84 (s, 9H), 2.52 (br. s, 1H).

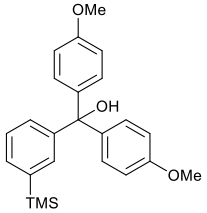
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 153.3, 139.6, 137.5, 133.9, 133.1, 129.3, 128.9, 127.5, 103.7, 72.2, 60.8, 56.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3418, 1595, 1505, 1460, 1422, 1324, 1229, 1127, 1026, 1002, 873, 832, 824, 775, 692.

MS (EI, 70 eV, %) m/z = 344 (30), 342 (46), 175 (42), 173 (65), 169 (100), 154 (11), 138 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{16}Cl_2O_4$:** 342.0426; found: 342.0420.

Preparation of bis(4-methoxyphenyl)(3-(trimethylsilyl)phenyl)methanol (239c)



According to **TP2**, freshly prepared *n*Bu_2SmMe·5LiCl (**233b**, 0.70 mmol, 0.70 equiv) was used and cooled to –30 °C. Thereupon, 1-bromo-3-(trimethylsilyl)benzene (229 mg, 1.00 mmol, 1.00 equiv) and tetradecane ($C_{14}H_{30}$) (50 µL) were added neat and the reaction mixture was stirred for further 5 min at –30 °C. As electrophile, 4,4′-dimethoxybenzophenone (194 mg, 0.80 mmol, 0.80 equiv) was added and the reaction was allowed to warm to room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.31) affording the expected tertiary alcohol **239c** (294 mg, 0.75 mmol, 94%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.57–7.53 (m, 1H), 7.46 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.26–7.17 (m, 5H), 6.87 (d, *J* = 8.9 Hz, 4H), 3.83 (s, 6H), 2.85 (br. s, 1H), 0.25 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.6, 146.3, 140.0, 139.6, 132.4, 132.1, 129.2, 128.6, 127.1, 113.1, 81.6, 55.3, –1.1.

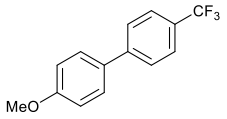
IR (ATR, cm^{-1}) ṽ = 3495, 2954, 1736, 1605, 1507, 1463, 1372, 1297, 1243, 1173, 1114, 1033, 926, 829, 797, 752, 691.

MS (EI, 70 eV, %) m/z = 392 (8), 376 (37), 375 (17), 362 (14), 361 (50), 345 (21), 303 (40), 285 (12), 244 (16), 243 (100), 242 (14), 227 (57), 195 (12), 165 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{24}H_{28}O_3Si$:** 392.1808; found: 392.1802.

9.4. Pd-Catalyzed Cross-Coupling Reactions of Diarylsamarium Reagents of Type 236 with selected Aryl Halides as Electrophiles

Preparation of 4-methoxy-4'-(trifluoromethyl)-1,1'-biphenyl (240a)



According to **TP3**, a dry and argon-flushed *Schlenk*-tube was charged with $Pd(dba)_2$ (23 mg, 0.04 mmol, 5.0 mol%), P(*t*Bu)$_3$ (16 mg, 0.08 mmol, 10 mol%) and 4-bromobenzotrifluoride (180 mg, 0.80 mmol, 0.80 equiv) as electrophile. Freshly distilled THF (0.80 mL) was added and the resulting solution was stirred for 2 min at room temperature. Subsequently, the diarylsamarium reagent of type **236**, freshly prepared from 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv), was added within 2 min at room temperature. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.26) resulting in the expected biphenyl **240a** (150 mg, 0.59 mmol, 74%) as a white solid.

M.p. 112 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 (s, 4H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 159.8, 144.3 (q, ^4J(C,F) = 1.0 Hz), 132.2, 128.7 (q, ^2J(C,F) = 33 Hz), 128.4, 126.9, 125.7 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 272 Hz), 114.4, 55.4.

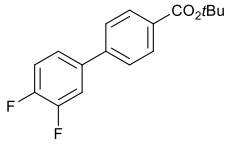
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3030, 2964, 2934, 2846, 1602, 1582, 1532, 1500, 1460, 1442, 1402, 1320, 1294, 1276, 1256, 1200, 1180, 1166, 1110, 1072, 1034, 1010, 960, 850, 828, 812, 746, 720, 700.

MS (EI, 70 eV, %) m/z = 253 (14), 252 (100), 237 (39), 183 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}OF_3$:** 252.0762; found: 252.0757.

Synthesis of *tert*-butyl 3',4'-difluoro-[1,1'-biphenyl]-4-carboxylate (240b)



Based on **TP3**, a dry and argon-flushed *Schlenk*-tube was charged with $Pd(dba)_2$ (23 mg, 0.04 mmol, 5.0 mol%), $P(tBu)_3$ (16 mg, 0.08 mmol, 10 mol%) and *tert*-butyl 4-iodobenzoate (243 mg, 0.80 mmol, 0.80 equiv) as electrophile. Freshly distilled THF (0.80 mL) was added and the resulting solution was stirred for 2 min at room temperature. Subsequently, the diarylsamarium reagent of type **236**, freshly prepared from 1,2-difluoro-4-iodobenzene (240 mg, 1.00 mmol, 1.0 equiv), was added within 2 min at room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.12) afforded the biphenyl **240b** (156 mg, 0.54 mmol, 67%) as a white solid.

M.p. 77 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.08 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.43 (ddd, *J* = 11.4, 7.5, 2.2 Hz, 1H), 7.35 (dddt, *J* = 7.8, 3.5, 2.2, 1.2 Hz, 1H), 7.27 (dt, *J* = 10.0, 8.3 Hz, 1H), 1.64 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 165.4, 151.1–148.9 (m, 2C), 142.9, 137.3 (dd, ^3J(C,F) = 5.9 Hz, ^4J(C,F) = 3.9 Hz), 131.4, 130.1, 126.7, 123.3 (dd, ^3J(C,F) = 6.3 Hz, ^4J(C,F) = 3.5 Hz), 117.7 (d, ^2J(C,F) = 18 Hz), 116.2 (d, ^2J(C,F) = 18.0 Hz), 81.2, 28.2.

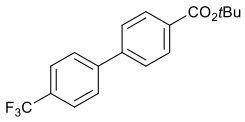
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –137.1, –139.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2980, 1696, 1604, 1528, 1500, 1476, 1430, 1396, 1370, 1296, 1262, 1234, 1182, 1158, 1118, 1104, 1030, 1014, 902, 858, 846, 822, 768, 700.

MS (EI, 70 eV, %) m/z = 290 (5), 235 (13), 234 (100), 217 (55), 188 (33).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{16}O_2F_2$:** 290.1118; found: 290.1111.

Preparation of *tert*-butyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate (240c)



With reference to **TP3**, a dry and argon-flushed *Schlenk*-tube was charged with $Pd(dba)_2$ (23 mg, 0.04 mmol, 5.0 mol%), $P(tBu)_3$ (16 mg, 0.08 mmol, 10 mol%) and *tert*-butyl 4-iodobenzoate (243 mg, 0.80 mmol, 0.80 equiv) as electrophile. Freshly distilled THF (0.80 mL) was added and the resulting solution was stirred for 2 min at room temperature. Subsequently, the diarylsamarium reagent of type **236**, freshly prepared from 4-iodobenzotrifluoride (272 mg, 1.0 mmol, 1.0 equiv), was added within 2 min at room temperature. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.13) furnished the desired cross-coupling product **240c** (138 mg, 0.43 mmol, 54%) as a white solid.

M.p. 117 °C.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.11 (d, *J* = 8.6 Hz, 2H), 7.74 (s, 4H), 7.67 (d, *J* = 8.6 Hz, 2H), 1.65 (s, 9H).

^{13}C-NMR (10 MHz, $CDCl_3$, ppm) δ = 165.4, 143.7 (q, ^4J(C,F) = 1.0 Hz), 143.6, 131.7, 130.4 (q, ^2J(C,F) = 33 Hz), 130.1, 127.6, 127.1, 125.8 (q, ^3J(C,F) = 3.8 Hz), 124.2 (q, ^1J(C,F) = 272 Hz), 81.3, 28.2

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2986, 1708, 1612, 1394, 1368, 1324, 1294, 1254, 1162, 1118, 1068, 1018, 1004, 868, 848, 834, 774, 734, 698, 666.

MS (EI, 70 eV, %) m/z = 322 (2), 267 (13), 266 (100), 249 (59), 201 (25), 152 (24).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}O_2F_3$:** 322.1182; found: 322.1175.