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**New Preparation of Organoaluminiums – Catalysed Metal
Insertion of Aluminium Powder and Synthetic Applications of
Organoalanes**

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**Preparation of 1,2-Bimetallics by Direct Insertion of Aluminium or
Zinc Powder**

von

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aus

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Erklärung

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BOOK CHAPTERS

1. Paul Knochel, Tobias Blümke, Klaus Groll, Yi-Hung Chen, "Preparation of Organoalanes for organic synthesis", Topics in Organometallic Chemistry – The Al volume (Ed. S. Woodward, S. Dagorne), Springer, **2012**, *submitted*.

POSTER PRESENTATIONS

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Da steh ich nun, ich armer Tor!

Und bin so klug als wie zuvor.

-Faust-

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LIST OF ABBREVIATIONS

Ac	acetyl
aq.	aqueous
Ar	aryl
ATR	attenuated total reflection (IR)
Boc	<i>tert</i> -butyloxycarbonyl
br	broad (NMR)
Bu	butyl
conc.	concentrated
d	doublet (NMR)
dba	<i>trans,trans</i> -dibenzylideneacetone
DIBAL	diisobutylaluminium hydride
dist.	Distilled
DCM	dichloromethane
DMAP	4-(dimethylamino)pyridine
DMF	<i>N,N</i> -dimethylformamide
dr	diastereomeric ratio
equiv	equivalent
E	electrophile
EI	electron ionization
ESI	electrospray ionization
Et	ethyl
FG	functional group
GC	gas chromatography
h	hour
HRMS	high resolution mass spectroscopy
<i>i</i> Pr	<i>iso</i> -propyl
IR	infrared
<i>J</i>	coupling constant (NMR)
M	mol/L
<i>m</i>	<i>meta</i>
Me	methyl
min	minute
mp.	melting point
MS	mass spectroscopy
NMR	nuclear magnetic resonance
NMP	<i>N</i> -methylpyrrolidin-2-one

o *ortho*

OPiv pivalate

p *para*

PEPPSI-*i*Pr [1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride

Ph phenyl

ppm parts per million

R organic substituent

sat. saturated

S-Phos 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl

t-Bu *tert*-butyl

TEA triethyl amine

THF tetrahydrofuran

TIPS triisopropylsilyl

TLC thin layer chromatography

TMP 2,2,6,6-tetramethylpiperidyl

TMS trimethylsilyl

ttmpp tris(trimethoxyphenyl)phosphine

TP typical procedure

A. INTRODUCTION

1 OVERVIEW

The 21st century is confronting humanity with unseen and unprecedented issues. According to the United States Census Bureau (USCB) it is estimated that the world population exceeded 7 billion people in March 2012.¹ More than 60% of the global population (4.2 billion) is located in Asia, a rapidly growing industrial market. This constant population expansion is of course accompanied by a series of environmental and social problems: Increased usage of resources (especially fossil fuels) is leading to higher pollution and rising levels of atmospheric greenhouse gases, proposing a serious threat to our global ecosystem and personal health.² Shrinking supplies of fresh water and limited area of cultivable acreage is threatening the global food supplies.³ Additionally, the uneven distribution of the *available* resources is destabilizing international relations and societies which may lead to future political or even military conflicts.⁴ It is of no doubt, that research and scientific progress are playing a major role in providing solutions to these new problems and threats.⁵ The chemical and pharmaceutical industry expends almost 20% of its annual turnover for research and development, investing second most in R&D among all other branches.⁶ In an incomparable way, chemistry and particularly organic chemistry has already provided, and is constantly developing, practical solutions to a variety of issues threatening our future. The development of fertilizers, herbicides and fungicides has led to more efficient cultivation of the available acreage, thus supplying more food on smaller space.⁷ Polymer chemistry has provided lighter and more functional materials leading for example to aircrafts and automobiles with lower weight, thus reducing fuel consumption and emission of greenhouse gases.⁸ Moreover, the invention of alternative energy supplies or more efficient energy saving processes, such as organic light emitting diodes (OLED)⁹ are necessary and helpful in dealing with the depletion of the worldwide available oil reserves on the market (peak oil).⁴ But of course chemistry itself has to fulfil many requirements nowadays and a change to sustainable chemistry is inevitable.¹⁰ Efficient, atom-economic syntheses and reaction sequences, preferably multistep or multicomponent reactions, with low waste production have to be developed.¹¹ Nontoxic alternatives to reagents and solvents have to be found. Great efforts are already done to avoid unnecessary protection/deprotection steps or interconversion of functional groups for example in the synthesis of natural products.¹² Like no other discipline, organometallic chemistry has revolutionized chemical thinking and has become one of the most important areas of chemical research. And like no other discipline,

¹ www.census.gov

² a) K. A. Miller, D. S. Siscovick, L. Sheppard, K. Shepherd, J. H. Sullivan, G. L. Anderson, J. D. Kaufman, *The New England Journal of Medicine* **2007**, *356*, 447; b) D. N. Cole, P. B. Landres, *Ecological Applications* **1996**, *6*, 168.

³ Z. W. Kundzewicz, L. J. Mata, N. W. Arnell, P. Döll, B. Jimenez, K. Miller, T. Oki, Z. Sen, I. Shiklomanov, *Hydrological Science J.* **2008**, *53*, 3.

⁴ Peak Oil – Sicherheitspolitische Implikationen knapper Ressourcen, Teilstudie 1, Zentrum für Transformation der Bundeswehr, Dezernat Zukunftsanalyse; www.zentrum-transformation.bundeswehr.de.

⁵ S. Kuznets, *Amer. Econ. Rev.* **1973**, *63*, 247.

⁶ a) M. A. Schade, Dissertation, LMU-München, **2011**; b) Verband der Chemischen Industrie (VCI), *Chemiewirtschaft in Zahlen* **2010**, 42.

⁷ [http://www.bayercropscience.com/besweb/cropprotection.nsf/id/DE_Zahlen_und_Fakten_2011/\\$file/BCS_Zahlen-Fakten-2011.pdf](http://www.bayercropscience.com/besweb/cropprotection.nsf/id/DE_Zahlen_und_Fakten_2011/$file/BCS_Zahlen-Fakten-2011.pdf)

⁸ G. Marsh, *Reinforced Plastics* **2007**, *51*, 26.

⁹ H. Burroughes, D. D. C. Bradley, A. R. Brown, R. N. Marks, K. Mackay, R. H. Friend, P. L. Burns, A. B. Holmes, *Nature* **1990**, *347*, 539.

¹⁰ a) T. Collins, *Science* **2001**, *291*, 48; b) C. Okkerse, H. van Bekkum, *Green Chemistry* **1999**, *1*, 107.

¹¹ a) B. M. Trost, *Science* **1991**, *254*, 1471; (b) B. M. Trost, *Angew. Chem. Int. Ed.* **1995**, *34*, 259; c) *Organic Synthesis* (Eds.: J.-H. Fuhrhop, G. Li) Wiley-VCH, Weinheim, **2003**.

¹² a) P. S. Baran, T. J. Maimone, J. M. Richter, *Nature* **2007**, *446*, 404; b) R. W. Hoffmann, *Synthesis* **2006**, 3551; c) V. Sofiyev, G. Navarro, D. Trauner, *Org. Lett.* **2008**, *10*, 149.

organometallic chemistry can cope with a lot of requirements which have to be met by modern organic chemistry. Organometallic chemistry today allows chemical transformations which have been unimaginable 20 years ago.

1.1 Organometallic Chemistry

The first organometallic compound was synthesized by *Louis Claude Cadet* in 1760, who isolated “*Cadet’s fuming liquid*” (cacodyl, Me_4As_2).¹³ This compound was later studied by *Frankland* and *Bunsen* and has opened a completely new field of chemistry. The central concept of organometallic chemistry is the formation of carbon-metal bonds and nowadays their use in synthetic chemistry. As all metals of the periodic system are less electronegative than carbon, the carbon atom in such compounds is negatively polarized. This results in a nucleophilic carbon atom, which allows new chemical transformations, unparalleled in history, for example new and easy ways of carbon-carbon bond formation. The reactivity of organometallic compounds is defined by the difference in electronegativity of the two bonding partners. The bigger the difference the more ionic bonds result and therefore more reactive organometallics arise. Thus, the most reactive organometallics are derived from alkali-metals (Li, Na, K) as these are the most electropositive metals available.¹⁴ Such reagents are excellent bases and provide highly nucleophilic carbon atoms. Of course this high reactivity is accompanied by a low functional group tolerance as these reagents attack nearly any group present in a molecule.¹⁵ This has led to development of organometallics with more covalent bond character, still owning a nucleophilic carbon atom but combined with a higher functional group tolerance.¹⁶ Such reagents derived from Mg, Zn, B, or Sn are nowadays widely employed in organic chemistry. A special role is attributed to transition metals: Because the d-orbitals can participate in the bonding to the carbon atom, very special reactivities are observed. These metals are widely used as catalysts for remarkable chemical transformations such as transition metal catalysed cross-coupling reactions¹⁷ (nowadays the most important C-C bond formation reaction) or olefin metathesis. Since the first observation of a carbon metal bond, organometallic chemistry has developed to a remarkably powerful synthetic tool. Nearly every metal available has been used in organic synthesis. The fine differences in various organometallics, depending on the properties of the metal employed, have led to a complex synthetic toolbox for the organic chemist, allowing fine-tuning of reactivities and numerous synthetic applications. In the course of these developments nine awarded Nobel-prizes in the field of organometallic chemistry speak its own language.¹⁸

¹³ a) D. Seyferth, *Organometallics* **2001**, *20*, 1488; b) J. J. Berzelius, *Jahresber.* **1839** *18*, 487.

¹⁴ a) E. Negishi, *Organometallics in Organic Synthesis*, Wiley, New York, **1980**; b) A. Boudier, L. O. Bromm, M. Lotz, P. Knochel, *Angew. Chem. Int. Ed.* **2003**, *39*, 4414.

¹⁵ G. Wu, M. Huang, *Chem. Rev.* **2006**, *106*, 2596.

¹⁶ *Handbook of Functionalized Organometallics* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**.

¹⁷ A. de Meijere, F. Diederich, *Metal-Catalyzed Cross Coupling Reactions*, 2nd ed., VCH, Weinheim, **2004**.

¹⁸ **1912**: Grignard, Sabatier, **1963**: Ziegler, Natta, **1973**: Wilkinson, Fischer, **1976**: Lipscomb; **1979**: Brown, Wittig; **1981**: Fukui, Hoffmann; **2001**: Knowles, Noyori, Sharpless; **2005**: Chauvin, Grubbs, Schrock, **2010**: Heck, Negishi, Suzuki.

1.2 Organoaluminium Chemistry

Organoaluminium compounds are known for more than 150 years. Following the groundbreaking experiments of *Frankland* (1849) on the preparation of dialkylzinc reagents by the reaction of zinc with alkyl iodides,¹⁹ the similar reaction of ethyl iodide and methyl iodide with aluminium were studied only 10 years later by *Hallwachs* and *Schaferik* (1859)²⁰ and *Cahours* (1860).²¹ After this discovery, organoaluminium reagents attracted little attention for almost a century. *Victor Grignard* investigated the formation of organomagnesium reagents and their invaluable synthetic use became apparent as a lot of organic halides could be converted easily to magnesium reagents in an ethereal solvent.²² In contrast, most organic halides were reluctant to undergo reaction with aluminium,²³ explaining why the focus of scientist lay on magnesium reagents. However, organoaluminium chemistry was revived by the discoveries of *Ziegler* in the 1950s when new ways to form carbon aluminium bonds were identified and moreover, the polymerization of olefins catalysed by aluminium compounds was introduced in organic chemistry.²⁴ These groundbreaking discoveries revolutionized polymer chemistry and *Ziegler* as well as *Natta* were honoured with the Nobel-prize in 1963 for their important work.²⁵ Since then the *Ziegler-Natta-Process* has become one of the most important industrial processes in the world and in 2007 more than 45 million tons of polypropylene and 20 million tons of polyethylene have been prepared by this process. Moreover, aluminium compounds have found numerous applications in organic synthesis. Compounds like LiAlH_4 or DIBAL are widely employed as reducing agents.²⁶ Me_3Al and Et_3Al have been used as alkylating reagents.²⁷ Because of the ambivalent properties of organoaluminiums,²³ pending between nucleophilicity and *Lewis* acidity they are also used in cyclization- or rearrangement reactions,²⁸ *Diels-Alder* reactions,²⁹ *Friedel-Crafts*-acylations³⁰ or carbonyl activations.³¹ The “*Tebbe*”-reagent³² is a commonly used alternative for the classical *Wittig*-reaction³³ and remarkably even enolizable carbonyls or esters can be transformed to alkenes (which is not possible with classical *Wittig* conditions) underlining the special reactivity often

¹⁹ E. Frankland, *Ann. Chem.* **1849**, *71*, 171.

²⁰ W. Hallwachs, A. Schaferik, *Ann. Chem.* **1859**, *109*, 206.

²¹ A. Cahours, *Ann. Chem.* **1860**, *114*, 227.

²² V. Grignard, *Ann. Chim.* **1901**, *24*, 433.

²³ T. Mole, E. A. Jeffery, *Organoaluminium Compounds*, Elsevier, Amsterdam, **1972**.

²⁴ K. Ziegler, *Organometallic Chemistry* (Ed.: H. H. Zeiss), Reinhold, New York, **1960**.

²⁵ a) K. Ziegler, E. Holzkamp, H. Breil, H. Martin, *Angew. Chem.* **1955**, *67*, 541; b) G. Natta, *Angew. Chem.* **1964**, *76*, 553; c) http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1963/.

²⁶ a) M. T. Reetz, M. W. Drewes, R. Schwickardi, *Org. Synth.* **1999**, *76*, 110; b) R. Oi, K. B. Sharpless, *Org. Synth.* **1996**, *73*, 1; c) H. Yamamoto, *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*, Georg Thieme Verlag, Stuttgart, **2004**; d) A. E. G. Miller, J. W. Bliss, L. H. Schwatzmann, *J. Org. Chem.* **1959**, *24*, 627; e) K. Ziegler, K. Schneider, J. Schneider, *Ann. Chem.* **1959**, *623*, 9; f) L. I. Zakharkin, I. M. Khorlina, *Tetrahedron Lett.* **1962**, *3*, 619; g) B. M. Frost, L. M. Jungheim, *J. Am. Chem. Soc.* **1980**, *102*, 7910; h) T. Sugimura, L. A. Paquette, *J. Am. Chem. Soc.* **1987**, *109*, 3017.

²⁷ a) T. Mole, J. R. Surtees, *Aust. J. Chem.* **1964**, *17*, 961; b) Y. Baba, *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2173; c) S. Sakane, K. Maruoka, H. Yamamoto, *J. Chem. Soc. Jpn.* **1985**, *324*; d) E. C. Ashby, J. T. Laemmle, *J. Org. Chem.* **1968**, *33*, 3398; e) H. M. Neumann, J. Laemmle, E. C. Ashby, *J. Am. Chem. Soc.* **1973**, *95*, 2597.

²⁸ a) H. Yamamoto, H. Nozaki, *Angew. Chem. Int. Ed.* **1978**, *17*, 169; b) K. Maruoka, H. Yamamoto, *Angew. Chem. Int. Ed.* **1985**, *24*, 668; c) K. Maruoka, H. Yamamoto, *Tetrahedron* **1988**, *44*, 5001.

²⁹ a) Y. Yates, P. Eaton, *J. Am. Chem. Soc.* **1960**, *82*, 4436; b) D. Nakashima, H. Yamamoto, *Org. Lett.* **2005**, *7*, 1251; c) S. Kobayashi, K. A. Jørgensen, *Cycloaddition Reactions in Organic Synthesis*; Wiley-VCH, Weinheim, **2002**; d) H. Yamamoto, *Lewis Acids in Organic Synthesis*; Wiley-VCH, Weinheim, **2000**; e) H. Yamamoto, *Lewis Acid Reagent: A Practical Approach*, Oxford University Press, Oxford, **1999**.

³⁰ a) A. R. Blazer, J. H. M. Lange, M. A. W. van der Neut, A. Mulder, F. S. den Boon, T. R. Werkman, C. F. Kruse, W. J. Wadman, *Eur. J. Med. Chem.* **2011**, *46*, 5086; d) T. Okauchi, M. Itonaga, T. Minami, T. Owa, K. Kitoh, H. Yoshino, *Org. Lett.* **2000**, *2*, 1485. e) J. H. Wynne, C. T. Lloyd, S. D. Jensen, S. Bosen, W. M. Stalick, *Synthesis* **2004**, 2277.

³¹ a) K. Maruoka, H. Yamamoto, *Pure Appl. Chem.* **1988**, *60*, 21; b) T. Ooi, E. Tayama, M. Takahashi, K. Maruoka, *Tetrahedron Lett.* **1997**, *38*, 7403.

³² F. N. Tebbe, G. W. Parshall, G. S. Reddy, *J. Am. Chem. Soc.* **1978**, *100*, 3611.

³³ G. Wittig, U. Schöllkopf, *Chem. Ber.* **1954**, *87*, 1318.

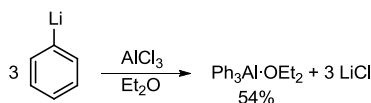
exhibited by organoalanes.³⁴ Using the right conditions or catalyst, organoaluminiums undergo a plethora of synthetic useful reactions providing a complex toolbox for the organic chemist and are finding more and more applications in material science.³⁵ Over only a few decades, organoaluminium compounds have developed to the most thoroughly investigated class of organometallics regarding to structure and reactivity. Notable 1600 scientific journal publications (not counting patents) within the last 10 years undoubtedly mark organoaluminium chemistry as a highly important research field.³⁶ It can be expected that the field of organoalanes will see substantial and continuous growth within the next years and many unforeseen reactivities, physical and biological properties as well as new functional materials will be uncovered.

1.3 Preparation methods of Organoaluminium Compounds

Organoaluminiums have received considerable attention in recent years³⁷ due to their unexpectedly high chemoselective reactivity, but also because of the attractive price of aluminium (less than one dollar per kilogram) and moderate toxicity. Their preparation has therefore been reexamined and several mild methods have been devised recently. This chapter summarizes the available preparation methods. Aryl-, alkynyl-, alkenyl-, allylic- and propargylic aluminium derivatives are readily available using the described methods.

1.3.1 Transmetallation

The most widely employed synthesis of organoaluminium compounds on laboratory scale is the transmetallation reaction (salt metathesis), using organometallics and an aluminium salt. The driving force of this reaction is the formation of a thermodynamically more stable carbon-metal bond, which is usually the more covalent bond. Thus, starting from lithium organometallics the reaction with AlCl_3 leads to triarylaluminium compounds (Scheme 1).³⁸ Organosodium compounds have also been used in an analogous way.³⁹



Scheme 1: Typical transmetallation using organolithium reagents and AlCl_3 .

Similarly, organolithium reagents have been used for the preparation of mixed aryl-dialkylaluminiums (Scheme 2).⁴⁰

³⁴ a) F. N. Tebbe, G. W. Parshall, D. W. Ovenall, *J. Am. Chem. Soc.* **1979**, *101*, 5074; b) L. Clawson, S. L. Buchwald, R. H. Grubbs, *Tetrahedron. Lett.* **1984**, *25*, 5733; c) S. H. Pine, G. Kim, V. Lee, *Org. Synth.* **1990**, *69*, 72; d) K. C. Nicolaou, A. E. Koumbis, S. A. Snyder, K. B. Simonsen, *Angew. Chem. Int. Ed.* **2000**, *39*, 2529.

³⁵ a) B. C. Lin, C. P. Cheng, Z.-Q. You, C.-P. Hsu, *J. Am. Chem. Soc.* **2005**, *127*, 66; b) J. Zhang, G. Frenking, *J. Phys. Chem. A* **2004**, *108*, 10296; c) M. D. Halls, H. B. Schlegel, *Chem. Mater.* **2001**, *13*, 2632; d) J. Ashenurst, L. Brancaloni, A. Hassan, W. Liu, H. Schmider, S. Wang, Q. Wu, *Organometallics* **1998**, *17*, 3186.

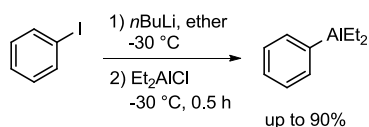
³⁶ Recently performed SciFinder search for „organoaluminium“, limited to results from 2000-2012.

³⁷ H. W. Roesky, *Inorg. Chem.* **2004**, *43*, 7284.

³⁸ G. Wittig, D. Wittenberg, *Ann.* **1957**, *606*, 1.

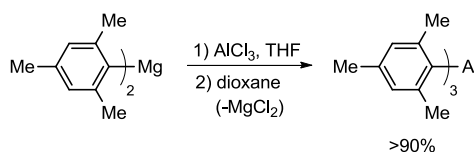
³⁹ a) J. F. Nobis, *U.S.2905126*, **1961**, *55*, 9346; b) K. Ziegler, *Brit.829628*, **1960**, *54*, 16020.

⁴⁰ C. Hawner, K. Li, V. Cirriez, A. Alexakis, *Angew. Chem. Int. Ed.* **2008**, *47*, 8211.



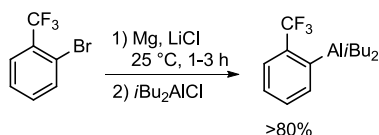
Scheme 2: Preparation of mixed aryl-dialkylaluminiums by transmetalation.

The reaction of organomagnesium reagents with AlCl_3 has been investigated thoroughly as well. Since early attempts⁴¹ this procedure has developed to a powerful synthetic methodology. Thus, for example starting from dimesitylmagnesium, sterically hindered organoaluminiums can be prepared easily (Scheme 3).^{42, 43}



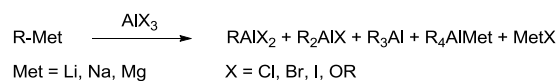
Scheme 3: Preparation of the sterically hindered trimesitylaluminium.

Even functionalized organoaluminiums have been prepared recently by the reaction of functionalized organomagnesium reagents with aluminium salts under *Barbier* conditions.^{44, 45}



Scheme 4: Preparation of functionalized aluminium reagents by *in situ* transmetalation using $i\text{Bu}_2\text{AlCl}$.

In general, the transmetalation reaction provides access to a variety of different aluminium organyls. Depending on the stoichiometry of the employed organometallic R-Met and the reaction conditions this methodology leads either to aluminium halides, alkoxides or in case of an excess of R-Met to triorganoalanes, or even aluminates (Scheme 5). Often mixtures of all organoalanes are formed because of a complex equilibrium,²³ similar to the *Schlenk*-equilibrium⁴⁶ known from *Grignard* reagents, which can be a major drawback.



Scheme 5: General transmetalation reaction for the preparation of various organoaluminiums.

Nowadays a huge variety of organolithium and functionalized organomagnesium reagents^{47, 48} can be prepared conveniently by different methods, allowing in principle the synthesis of a broad range of different organoalanes.

⁴¹ W. Menzel, *Z. Anorg. Allg. Chem.* **1952**, 52, 269.

⁴² a) W. Seidel, *Z. Anorg. Allg. Chem.* **1985**, 524, 101; b) M. S. Lalama, J. Kampf, D. G. Dick, J. P. Oliver, *Organometallics* **1995**, 14, 495.

⁴³ S. Zhou, D.-W. Chuang, S.-J. Chang, H.-M. Gau, *Tetrahedron: Asymmetry* **2009**, 20, 1407.

⁴⁴ J. Westermann, U. Imbery, A. T. Nguyen, K. Nickisch, *Eur. J. Inorg. Chem.* **1998**, 295.

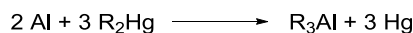
⁴⁵ H. Gao, P. Knochel, *Synlett* **2009**, 1321.

⁴⁶ W. Schlenk, J. Holtz, *Chem. Ber.* **1917**, 50, 262.

⁴⁷ a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, 37, 1701; b) M. Abarbri, F. Dehmel, P. Knochel, *Tetrahedron Lett.* **1999**, 40, 7449; c) A. E. Jensen, W. Dohle, I. Sapountzis, D. M. Lindsay, V. A. Vu, P. Knochel, *Synthesis* **2002**, 565.

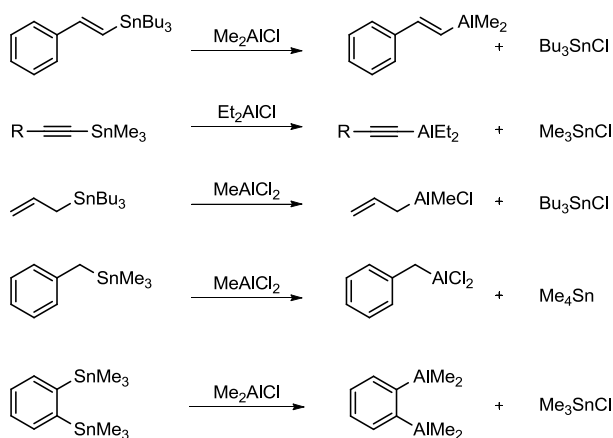
1.3.2 Metal-Exchange Reaction

The preparation of organoaluminium compounds has been achieved starting from mercury organyls (Scheme 6).⁴⁹ Of course, because of the use of toxic mercury this approach is not applicable nowadays anymore.



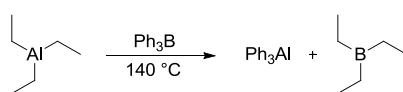
Scheme 6: Preparation of organoaluminium compounds from mercury organyls.

Such an exchange is not only occurring when the metal is used in its elemental state, but also between two organometallic compounds. Thus, several groups have demonstrated that organoaluminiums can be prepared by a Sn-Al exchange and alkenyl-, alkynyl-, allyl-, benzyl- and arylaluminiums have been synthesized using alkylaluminium chlorides (Scheme 7).⁵⁰



Scheme 7: Preparation of alkenyl-, alkynyl-, allyl-, benzyl- and arylaluminiums by Sn-Al exchange.

Organoboron reagents are relatively stable and most important, far less toxic than organomercury or organotin compounds. Of course, because of the similarity between boron and aluminium, exchange reactions between these two elements have been investigated.⁵¹ Thus, treatment of triethylaluminium with triphenylboron at 140 °C leads rapidly to an exchange of ligands (Scheme 8).^{49e}



Scheme 8: Typical example for a B-Al exchange reaction.

The exchange rate and the position of the equilibrium are strongly dependent on the electronic and steric nature of the substituents⁵² as well as stoichiometry and properties of the employed solvent.⁵³ Often the

⁴⁸ a) I. Sapountzis, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 1610; b) 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; c) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333; d) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; e) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802.

⁴⁹ a) G. B. Buckton, W. Odling, *Ann. (Supplement)* **1865**, *4*, 109; b) G. B. Buckton, *Proc. Roy. Soc. (London)* **1865**, *14*, 19; c) C. Friedel, J. M. Crafts, *Ann. Chim. et. Phys.* **1888**, *14*, 433; d) W. Strohmeier, K. Hümpfner, *Chem. Ber.* **1957**, *90*, 2339; e) J. R. Surtees, *Rev. Pure. Appl. Chem.* **1963**, *13*, 91.

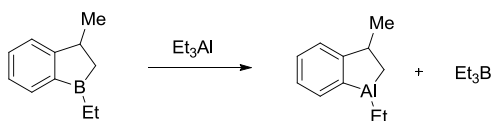
⁵⁰ a) W. P. Neumann, R. Scick, R. Köster, *Angew. Chem. Int. Ed.* **1964**, *3*, 385; b) J. J. Eisch, K. Mackenzie, H. Windisch, C. Krüger, *Eur. J. Inorg. Chem.* **1999**, 153; c) M. Tschinkl, R. E. Bachmann, F. P. Gabbai, *Chem. Commun.* **1999**, 1367.

⁵¹ K. Ziegler, *Organometallic Chemistry* (Ed.: H. H. Zeiss), Reinhold, New York, **1960**.

⁵² R. Köster, G. Bruno, *Ann.* **1960**, *629*, 89.

⁵³ J. Klosin, G. R. Roof, E. Y.-X. Chen, *Organometallics* **2000**, *19*, 4684.

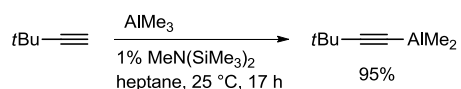
equilibrium has to be shifted by removal of volatile reaction products, such as Et_3B , to obtain high exchange rates.⁵⁴ Remarkably, this exchange has also been achieved using boracycles in which case aluminium heterocycles are generated (Scheme 9).⁵⁵



Scheme 9: Preparation of aluminacycles via a B-Al exchange.

1.3.3 Deprotonation (Metalation) Reactions

The use of strong metal bases to deprotonate (metalate) organic substances is a common way to generate organometallics of all kind. Thus, the use of BuLi for the generation of lithiated species is well known.¹⁶ Several other metal containing bases have been developed and have provided access to Li -,⁵⁶ Mg -,⁵⁷ Zn -,⁵⁸ Mn -,⁵⁹ Zr -,⁶⁰ Fe -⁶¹ or La -⁶² organyls.⁶³ In recent years also directed aluminations has been achieved. For example, alkynes undergo reaction with Me_3Al in the presence of a catalytic amount of amines, leading to alkynylaluminiums in hydrocarbon solvents (Scheme 10).⁶⁴



Scheme 10: Aluminations of terminal alkynes in the presence of catalytic amount of amines.

The deprotonation of aromatic systems has also been reported, but the use of a much stronger base is required. *Uchiyama* reported the use of an aluminate base for deprotonation of various aromatics. The base is readily prepared from $i\text{Bu}_3\text{Al}$ and TMPLi ($\text{TMP} = 2,2,6,6\text{-tetramethylpiperidyl}$) and is even strong enough for the deprotonation of electron rich aromatic rings such 1,3-dimethoxybenzene (Scheme 11).⁶⁵

⁵⁴ M. Bochmann, M. J. Sarfield, *Organometallics* **1998**, *17*, 5908.

⁵⁵ R. Köster, G. Benedikt, *Angew. Chem.* **1962**, *74*, 589.

⁵⁶ a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; b) R. Chinchilla, C. Nájera, M. Yus, *Chem. Rev.* **2004**, *104*, 2667; c) M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206; d) P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356.

⁵⁷ a) P. E. Eaton, R. M. Martin, *J. Org. Chem.* **1988**, *53*, 2728; b) P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016; c) Y. Kondo, Y. Akihiro, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **1996**, 2331; d) M. Shilai, Y. Kondo, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **2001**, 442; e) M.-X. Zhang, P. E. Eaton, *Angew. Chem. Int. Ed.* **2002**, *41*, 2169; f) P. E. Eaton, M.-X. Zhang, N. Komiyama, C. G. Yang, I. Steele, R. Gilardi, *Synlett* **2003**, *9*, 1275; g) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; h) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681; i) C. J. Rohbogner, G. C. Clososki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1503; j) C. J. Rohbogner, A. J. Wagner, G. C. Clososki, P. Knochel, *Org. Synth.* **2009**, *86*, 374.

⁵⁸ a) Y. Kondo, M. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539; b) T. Imahori, M. Uchiyama, T. Sakamoto, Y. Kondo, *Chem. Commun.* **2001**, 442; c) M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837; d) M. Mosrin, T. Bresser, P. Knochel, *Org. Lett.* **2009**, *11*, 3406; e) M. Mosrin, G. Monzon, T. Bresser, P. Knochel, *Chem. Commun.* **2009**, 5615; f) S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685; g) S. H. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705.

⁵⁹ S. H. Wunderlich, M. Kienle, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 7256.

⁶⁰ M. Jeganmohan, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 8520.

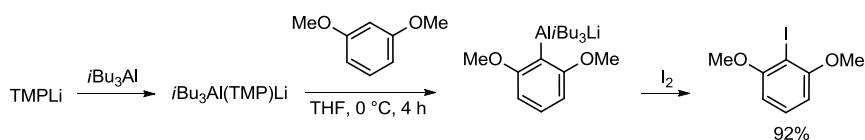
⁶¹ S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 9717.

⁶² S. H. Wunderlich, P. Knochel, *Chem. Eur. J.* **2010**, *16*, 3304.

⁶³ B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794.

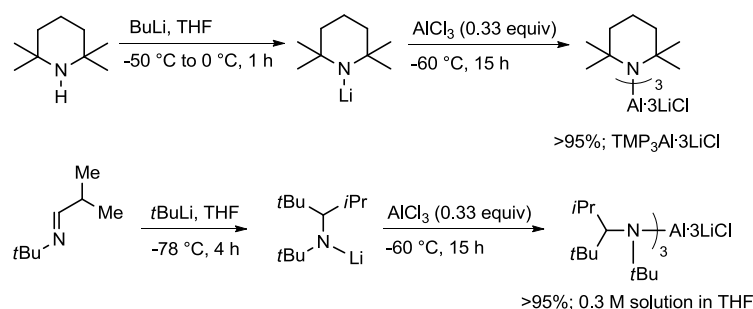
⁶⁴ a) Y. Zhou, T. Lecourt, L. Micouin, *Adv. Synth. Catal.* **2009**, *351*, 2595; b) J. J. Eisch, W. C. Kaska, *J. Organomet. Chem.* **1964**, *2*, 184.

⁶⁵ a) M. Uchiyama, H. Naka, Y. Masumoto, T. Ohwada, *J. Am. Chem. Soc.* **2004**, *126*, 10526; b) H. Naka, J. V. Morey, J. Haywood, D. J. Eisler, M. McPartlin, F. Garcia, H. Kudo, Y. Kondo, M. Uchiyama, A. E. H. Wheatley, *J. Am. Chem. Soc.* **2008**, *130*, 16193; c) H. Naka, M. Uchiyama, Y. Matsumoto, A. E. H. Wheatley, M. McPartlin, J. V. Morey, Y. Kondo, *J. Am. Chem. Soc.* **2004**, *129*, 1921.



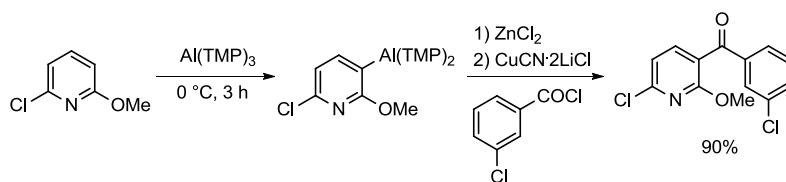
Scheme 11: Aluminations of 1,3-dimethoxybenzene using an aluminate base.

Knochel and coworkers have reported LiCl-monomerized aluminium bases (Scheme 12).⁶⁶ This new generation of bases is easily prepared and highly soluble in THF.



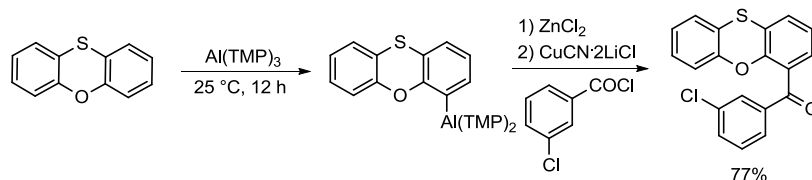
Scheme 12: LiCl monomerized highly active aluminium bases.

Using these bases a variety of aryl and heteroaryl-aluminium reagents have been prepared and used readily for several C-C bond formations (Scheme 13).^{66a}



Scheme 13: Directed aluminations of a methoxy-substituted pyridine using $\text{Al(TMP)}_3 \cdot 3\text{LiCl}$.

A further remarkable feature of these bases is their site-selective deprotonation in mixed heterocycles. In the case of mixed *S,O*- and *N,S*-heterocycles the metalation occurs in proximity of the best donor heteroatom. This heteroatom more readily forms a complex with the aluminium base and therefore directs the aluminations (Scheme 14).⁶⁶



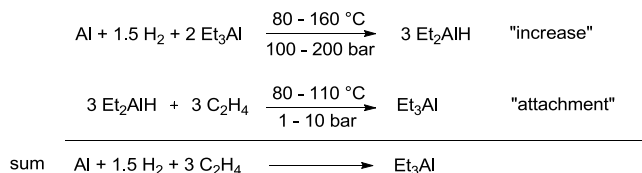
Scheme 14: Site-selective aluminations next to the strongest donor atom.

1.3.4 Hydrolaluminum

The addition of aluminium hydrogen bonds to unsaturated compounds such as alkenes and alkynes is referred to as hydroaluminum. The hydroaluminum reaction was recognized by *Ziegler*^{51, 67} and has

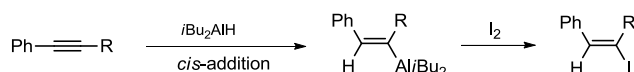
⁶⁶ a) S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 1501; b) M. Kienle, A. Unsinn, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 4751.

found application in one of the most important industrial syntheses of triorganoaluminiums: the “Ziegler direct process” (Scheme 15).⁶⁸ Two observations are combined in one process: First, Al reacts with hydrogen in the presence of AlR₃ leading to aluminium hydrides (increase) and secondly the Al-H bond can react with alkenes (attachment). In summary, R₃Al has been synthesized from Al, H₂ and alkene, the process therefore is referred to as “direct synthesis”.



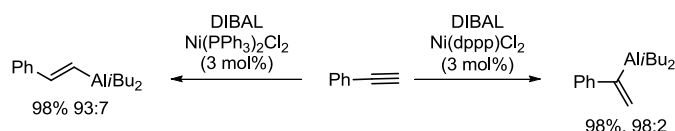
Scheme 15: Ziegler direct process.

Eisch and Wilke studied the regioselectivity of hydroalumination reactions of alkynes and noticed that the addition of the aluminium hydrogen bond usually occurs in a *cis*-manner, if the reaction is performed under kinetic control (Scheme 16).⁶⁹



Scheme 16: Hydroalumination using DIBAL yields *cis*-alkenylaluminiums.

The hydroalumination of alkynes and alkenes has developed to a general method for the preparation of various alkenylaluminium and alkylaluminium reagents.⁷⁰ Most recently it could be shown that the use of Ni-salts catalyses the hydroalumination. Remarkably, by changing the Ni-catalyst, regioselectivity of the hydroalumination can be achieved (Scheme 17).⁷¹



Scheme 17: The regioselectivity of the hydroalumination can be controlled by changing the Ni-catalyst.

1.3.5 Carboalumination

Not only hydrogen-aluminium bonds can undergo addition to unsaturated compounds, also carbon-aluminium bonds can be added to alkynes and alkenes. The reaction requires usually harsh conditions such as high pressure or temperature, if no catalyst is employed to facilitate the addition reaction (Scheme 18).^{26c, 72}

⁶⁷ a) K. Ziegler, H. Gellert, K. Zosel, W. Lehmkuhl, W. Pfohl, *Angew. Chem.* **1955**, *67*, 424; b) K. Ziegler, *Angew. Chem.* **1956**, *68*, 721.

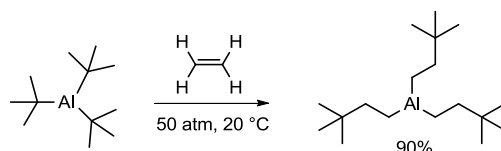
⁶⁸ C. Elschenbroich, *Organometallics*, Wiley-VCH, Weinheim, **2006**.

⁶⁹ a) G. Wilke, H. Müller, *Ann. Chem.* **1958**, *618*, 267; b) G. Wilke, H. Müller, *Chem. Ber.* **1956**, *89*, 444; c) G. Wilke, H. Müller, *Ann. Chem.* **1960**, *629*, 222; d) J. J. Eisch, M. W. Foxton, *J. Org. Chem.* **1971**, *36*, 3520; e) J. J. Eisch, W. C. Kaska, *J. Am. Chem. Soc.* **1971**, *88*, 2213; f) J. J. Eisch, W. C. Kaska, *J. Am. Chem. Soc.* **1963**, *85*, 2165.

⁷⁰ J. J. Eisch, *Comprehensive Organic Synthesis, Vol. 8* (Eds.: B. M. Trost, I. Fleming, S. L. Schreiber), Pergamon, Oxford, **1991**.

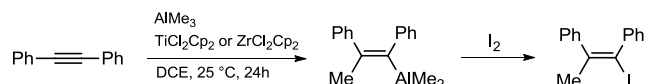
⁷¹ F. Gao, A. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 10961.

⁷² K. Ziegler, *Adv. Organomet. Chem.* **1968**, *6*, 1.



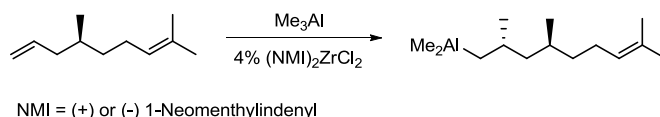
Scheme 18: The uncatalysed carboalumination requires harsh conditions.

In the presence of a suitable catalyst the carboalumination proceeds under much milder conditions. In the past mostly titanium and more effectively zirconium catalysts have been used for the carboalumination (Scheme 19).⁷³



Scheme 19: The catalysed carboalumination of a typical alkyne using Me_3Al proceeds in *cis*-fashion.

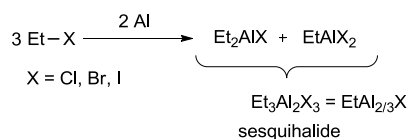
In recent years *Negishi* reported also an asymmetric version of a carboalumination (Scheme 20).⁷⁴ This Zr-catalysed asymmetric carboalumination (ZACA) has already found applications in the synthesis of natural products.⁷⁵



Scheme 20: Asymmetric carboalumination (ZACA) reaction.

1.3.6 Direct Insertion (Oxidative Addition) of Aluminium Powder

In 1859 *Hallwachs* and *Schaeferik* published their results on the reaction of ethyl iodide with elemental aluminium (Scheme 21).²⁰ They observed the formation of a liquid from which EtAlI_2 and Et_2AlI could be isolated by fractional distillation.^{20, 76}



Scheme 21: First preparation of an organoaluminium by *Hallwachs* and *Schaeferik*.

This mixture of halides which results from the insertion reaction is usually referred to as sesquihalide.²³ The reaction works extremely well for methyl- and ethyl halides. Extensions to allylic halides have also

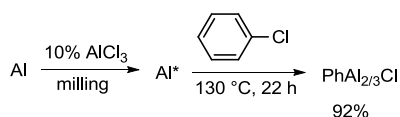
⁷³ a) E. Negishi, D. I. Kondakov, *Chem. Soc. Rev.* **1996**, 25, 417; b) D. E. van Horn, E. Negishi, *J. Am. Chem. Soc.* **1978**, 100, 225; c) E. Negishi, D. E. van Horn, T. Yoshida, *J. Am. Chem. Soc.* **1985**, 107, 6639; d) E. Negishi, D. I. Kondakov, D. Choueiry, K. Kasai, T. Takahashi, *J. Am. Chem. Soc.* **1996**, 118, 9577.

⁷⁴ a) D. Kondakov, E. Negishi, *J. Am. Chem. Soc.* **1995**, 117, 10771; b) D. Kondakov, E. Negishi, *J. Am. Chem. Soc.* **1996**, 118, 1577; c) S. Huo, J. Shi, E. Negishi, *Angew. Chem. Int. Ed.* **2002**, 41, 2141.

⁷⁵ Z. Tan, E. Negishi, *Angew. Chem. Int. Ed.* **2004**, 43, 2911; b) T. Novak, Z. Tan, B. Liang, E. Negishi, *J. Am. Chem. Soc.* **2005**, 127, 2838; c) B. Liang, E. Negishi, *Org. Lett.* **2008**, 10, 193; d) G. Zhu, B. Liang, E. Negishi, *Org. Lett.* **2008**, 10, 1099.

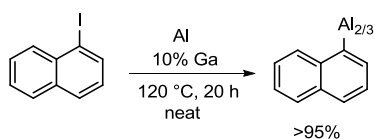
⁷⁶ a) V. Grignard, R. Jenkins, *Compt. Rend.* **1924**, 179, 98; b) H. Demarne, P. Cadiot, *Bull. Soc. Chim. France* **1968**, 205.

been reported.⁷⁷ Propyl- and butyl halides are already obtained in lower yields and higher alkyl halides cannot be conveniently subjected to this reaction.²³ Also, only a handful of aryl halides undergo this reaction.⁷⁸ The main drawback hampering a broad applicability of the reaction is the metal itself. Aluminium forms strong bonds to oxygen and the energy of the Al-O bond is estimated to be 138 kcal/mol.⁷⁹ Because of this highly oxophilic behaviour, aluminium is covered by an oxide and hydroxide layer by reaction with oxygen and water if exposed to air (passivation). This oxide layer hampers a smooth insertion reaction and the need for a clean metal surface has been pointed out by *Adkins* and *Scanley*.⁸⁰ Several metal activation methods have been reported.^{78, 81} Thus, it has been shown that the milling of aluminium powder with small amounts of aluminium chloride allows the insertion of aluminium powder to aryl iodides, bromides and chlorides (Scheme 22). In the case of chlorobenzene, a temperature of 130 °C is required for the formation of the aryl aluminium reagent in 92% yield.⁸²



Scheme 22: Activation of Al-powder by milling with catalytic amounts of AlCl₃.

Recently, it was reported that the addition of 10% Ga-metal to aluminium powder leads also to an activation and heating naphthyl iodide at high temperature with this metal mixture furnished the naphthyl sesquiodide (Scheme 23).⁸³



Scheme 23: Gallium as additive for activation of the aluminium surface.

Despite these attempts the direct insertion of aluminium into organic halides has never found the broad applicability as its magnesium counterpart, even 150 years after its discovery. Still, there is no convenient way of using aluminium powder for a direct insertion reaction into diverse organic substrates.

⁷⁷ a) S. Araki, S.-J. Jin, Y. Idou, Y. Butsugan, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1736; b) K. Takai, Y. Ikawa, *Org. Lett.* **2002**, *4*, 1727; c) J. Augé, N. Lubin-Germain, A. Thiaw-Woaye, *Tetrahedron Lett.* **1999**, *20*, 9245; d) H. Tanaka, M. Kuroboshi, *Current Organic Chemistry* **2004**, *8*, 1027; e) M. Gaudemar, *Bull. Soc. Chim. Fr.* **1958**, 1475; f) A. Stefani, P. Pino, *Hel. Chim. Acta* **1972**, *55*, 1110.

⁷⁸ a) J. F. Spencer, M. L. Wallace, *J. Chem. Soc.* **1908**, *93*, 1827; b) A. V. Grosse, J. M. Mavity, *J. Org. Chem.* **1940**, *5*, 106.

⁷⁹ H. Yamamoto, H. Nozaki, *Angew. Chem.* **1978**, *90*, 180.

⁸⁰ H. Adkins, C. Scanley, *J. Am. Chem. Soc.* **1951**, *73*, 2854.

⁸¹ a) H. Lehmkühl, R. Schäfer, *Tetrahedron Lett.* **1966**, 2315; b) G. P. van der Keelen, *Bull. Soc. Chim. Belges.* **1956**, *65*, 343; c) V. F. Hnizda, C. A. Kraus, *J. Am. Chem. Soc.* **1938**, *60*, 2276.

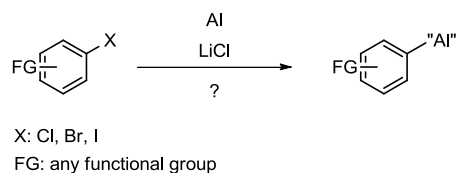
⁸² D. Wittenberg, *Ann. Chem.* **1962**, *654*, 23.

⁸³ X. Tang, D. Rawson, S. Woodward, *Synlett* **2010**, 636.

2 MOTIVATION AND OBJECTIVES

In recent years *Knochel et al.* introduced the use of LiCl in organometallic chemistry. This simple alkali salt has proven its beneficial effects on organometallic reactions several times. The preparation of $i\text{PrMgCl}\cdot\text{LiCl}$ (Turbo-Grignard) has led to development of a powerful exchange reagent and numerous aryl- and heteroaryl magnesium reagents have been prepared since then.⁸⁴ The addition of stoichiometric amounts of LiCl to TMP-bases has led to enormous increase in solubility of these formerly insoluble metal bases.⁸⁵ This effect seemed to be of a general nature and several metal bases have now found applications in organic synthesis and led to a variety of metal organic reagents.^{59-63, 66} Moreover, it could be shown that LiCl has a powerful effect on the insertion rate of several metals. Thus, the insertion of Zn and Mg is dramatically enhanced by LiCl and many functionalized organometallics have been prepared easily since this amazing discovery.⁸⁶ Even unreactive metals such as Mn and In undergo smooth insertion into various organic halides in the presence of LiCl.⁸⁷ It is supposed that LiCl helps in solubilizing the organometallic during its formation on the metal surface, thus leaving a fresh metal surface behind, on which a new insertion can occur much faster, leading overall to acceleration of the insertion and highly soluble metal reagents.⁸⁸

As there is no broad applicability of the insertion of aluminium to organic halides so far, a general method for the preparation of different organoaluminiums would be highly desirable, because of the low price of aluminium, the relatively low toxicity, the easy recyclability and the interesting properties and chemical reactivity of organoalanes. Inspired by the enormous beneficial effect of LiCl on the insertion of various metals we envisioned that LiCl may also be effective in accelerating the insertion of aluminium to organic halides. Thus, in this work we planned to develop a general method for the insertion of Al-powder to different organic halides in the presence of LiCl. First of all, the formation of aryl organoaluminiums should be investigated and a broad range of functionalities should be tolerated under the developed conditions (Scheme 24).



Scheme 24: LiCl-mediated insertion of Al into aryl halides.

⁸⁴ A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333.

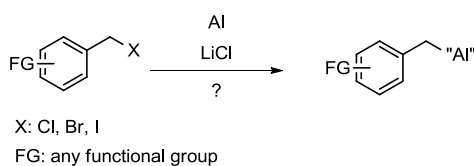
⁸⁵ a) C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295; b) C. R. Hauser, F. C. Frostick, *J. Am. Chem. Soc.* **1949**, *71*, 1350; c) P. E. Eaton, C.-H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016; d) P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc.* **1993**, *115*, 11370; e) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *Liebigs Ann.* **1995**, 1441; f) W. Schlecker, A. Huth, E. Ottow, *J. Org. Chem.* **1995**, *60*, 8414; g) K. W. Henderson, W. J. Kerr, *Chem. Eur. J.* **2001**, *7*, 3430; h) M.-X. Zhang, P. E. Eaton, *Angew. Chem. Int. Ed.* **2002**, *41*, 2169; i) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; j) G. C. Clososki, C. R. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681.

⁸⁶ A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040; b) N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358; c) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107; d) H. Ren, G. Dunet, P. Mayer, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 5376; e) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802.

⁸⁷ a) Y.-H. Chen, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 7648; b) Y.-H. Chen, M. Sun, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 2236; c) Z. Peng, P. Knochel, *Org. Lett.* **2011**, *13*, 3198.

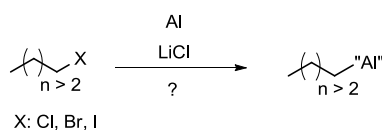
⁸⁸ A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 159.

Another project should be the extension of this methodology to benzylic halides as there are almost no reported reactions of benzylic halides with aluminium powder (Scheme 25).



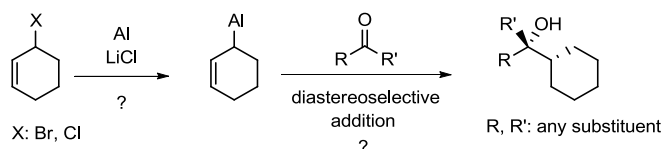
Scheme 25: LiCl-mediated insertion of Al into benzylic halides.

Furthermore, higher alkyl halides (longer carbon chain length than 4) cannot be conveniently prepared by the direct insertion of aluminium. In case LiCl allows the smooth insertion of Al-powder to organic halides, extensions of this method should be applied to higher alkyl substrates (Scheme 26).



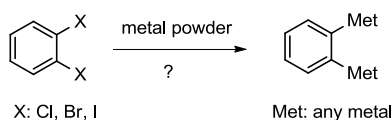
Scheme 26: LiCl-mediated insertion of Al into alkyl halides.

Also, we planned to develop a practical synthesis of allylic aluminium reagents. Their reactivity towards carbonyl groups should be investigated. As zinc reagents undergo highly diastereoselective addition to carbonyls a similar convenient synthetic procedure should be developed addition of allylic organoaluminiums to carbonyl functionalities (Scheme 27).



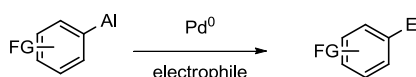
Scheme 27: Preparation of allylic aluminium reagents and diastereoselective addition to carbonyls.

Another project should be the preparation of 1,2-bimetallic species by direct insertion of metal powder. Little is known about such interesting species and a convenient procedure for the formation of such reagents had to be developed (Scheme 28).



Scheme 28: Preparation of 1,2-bimetallics by direct insertion of metal powder.

Moreover the potentially prepared organoaluminiums should be readily usable in different organic transformations. Special focus should be on the behaviour of organoaluminiums in cross-coupling reactions using common catalysts (Scheme 29).



Scheme 29: Direct cross-coupling of aluminium reagents.

B. RESULTS AND DISCUSSION

1 CATALYSED ALUMINIUM INSERTION INTO ARYL HALIDES

1.1 Abstract

Various aryl halides react with Al powder in the presence of a stoichiometric amount of LiCl and a suitable catalyst, leading for the first time to a broad range of functionalized aryl aluminium sesquihalides. The choice of the appropriate catalyst is dependent on the nature of the aryl halide. These new organometallics can be used in many organic transformations such as allylation reactions, Pd-catalysed cross-couplings, acylation reactions or conjugated addition after transmetallation with Zn-salts.

1.2 Introduction

The insertion of metals to unsaturated halides is the most straightforward method to prepare aromatic and heteroaromatic organometallics.⁸⁹ For example, the preparation of organomagnesium reagents (*Grignard* reagents) is conducted by adding an organic halide to a suspension of magnesium turnings in a polar, nonprotic solvent like THF or diethyl ether.⁹⁰ However, many unsaturated organometallic reagents (e.g. from zinc, indium, manganese or aluminium) are difficult to generate from commercial metal powders. The surface layer of the metal mostly consists of hydroxides and oxides (passivation), thus making the metal unreactive towards the organic halide. Especially the highly oxophilic aluminium is passivated very easily.⁹¹ The metal activation is therefore essential for the success of such direct insertions and several procedures including the use of *Rieke*-metals⁹² have been developed.⁹³ In fact, preparation methods of arylaluminium reagents are scarce.⁹⁴ A recently reported directed aluminatation⁹⁵ using an aluminium base allows the generation of arylaluminium compounds by a deprotonation reaction. Also, the transmetallation⁹⁶ of organolithium and organomagnesium reagents using aluminium salts provides a convenient route to arylaluminium derivatives. Although the reaction of metallic aluminium with organic halides is known since the pioneering work of *Hallwachs* and *Schaferik*⁹⁷ in 1859 only very few examples of aromatic halides undergo this reaction.^{98, 99} In recent years, it could be shown that several metals such as Zn,¹⁰⁰ In^{101, 102} and Mg^{103, 104} can be activated in the presence of stoichiometric amounts of LiCl, which

⁸⁹ P. Knochel, *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**.

⁹⁰ V. Grignard, *Ann. Chim.* **1901**, *24*, 433.

⁹¹ T. Mole, E. A. Jeffery, *Organoaluminium Compounds*, Elsevier, Amsterdam, **1972**.

⁹² a) R. D. Rieke, *Science* **1989**, *246*, 1260; b) R. D. Rieke, M. V. Hanson, *Tetrahedron*, **1997**, *53*, 1925; c) J. Lee, R. Velarde-Ortiz, A. Guijarro, J. R. Wurst, R. D. Rieke, *J. Org. Chem.* **2000**, *65*, 5428.

⁹³ a) U. Tilstam, H. Weinmann, *Org. Process Res. Dev.* **2002**, *6*, 906; b) K. V. Baker, J. M. Brown, N. Hughes, A. J. Skarnulis, A. Sexton, *J. Org. Chem.* **1991**, *56*, 698; c) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker in *Organic Reactions* (Ed. L. E. Overman), **2001**, Vol. 58, Wiley-VCH, New York.

⁹⁴ S. Saito in *Comprehensive Organometallic Chemistry III* (Ed. P. Knochel), **2007**, Vol. 9, Elsevier, Amsterdam.

⁹⁵ a) M. Uchiyama, H. Naka, Y. Matsumoto, T. Ohwada, *J. Am. Chem. Soc.* **2007**, *129*, 10526; b) H. Naka et al. *J. Am. Chem. Soc.* **2007**, *129*, 1921; c) H. Naka et al. *J. Am. Chem. Soc.* **2008**, *130*, 16193; d) S. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 1501.

⁹⁶ a) T. Ishikawa, A. Ogawa, T. Hirao, *J. Am. Chem. Soc.* **1998**, *120*, 5124; b) C. Hawner, K. Li, V. Cirriez, A. Alexakis, *Angew. Chem. Int. Ed.* **2008**, *47*, 8211; c) J. Westermann, U. Imbery, A. T. Nguyen, K. Nickisch, *Eur. J. Inorg. Chem.* **1998**, 295; d) H. Gao, P. Knochel, *Synlett*, **2009**, 1321.

⁹⁷ W. Hallwachs, A. Schaferik, *Ann.* **1859**, *109*, 206.

⁹⁸ J. F. Spencer, M. L. Wallace, *J. Chem. Soc.* **1908**, *93*, 1827.

⁹⁹ A. V. Grosse, J. M. Mavity, *J. Org. Chem.* **1940**, *5*, 106.

¹⁰⁰ a) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040; b) N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358; c) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107.

solubilizes and removes the resulting organometallic species from the metal surface, allowing therefore a further insertion to occur on the clean metal surface. Extensions of such an inexpensive activation to aluminium powder would be highly desirable due to the low toxicity, very low price and potentially high chemoselectivity of the organoaluminium reagents.¹⁰⁵

1.3 Preparation of Aryl Aluminium Sesquihalides

1.3.1 Preliminary Catalyst Screening

Preliminary results showed that aluminium powder did not insert to various organic halides in the presence of LiCl or other lithium salts. We envisioned that additional metallic salts may be beneficial since the preparation of allylic aluminium reagents is accelerated by the addition of InCl₃.¹⁰⁶ We have therefore screened the influence of several additives on the insertion rate of aluminium powder (3 equiv) in the presence of LiCl (3 equiv) to a typical substrate like 1-iodo-4-(trifluoromethyl)benzene (**1a**) in THF (Table 1). Whereas a number of metallic salts such as ZnCl₂, FeCl₃, MnCl₂, ZrCl₄, Cp₂ZrCl₂ or HfCl₄ have been proved to be ineffective affording less than 3% of the desired arylaluminium reagent **2a** (Table 1, Entries 1-6). To our delight, some metal chlorides dramatically accelerated the aluminium insertion (Table 1, Entries 7-22). The addition of PbCl₂ (5 mol%)¹⁰⁷ along with LiCl led to the desired aluminium reagent **2a** in 60% yield after 3 h at 30 °C whereas no product was obtained in the absence of LiCl. Additional activation of the aluminium suspension in THF with Me₃SiCl (3 mol%)¹⁰⁸ yielded **2a** in 77% (Table 1, Entry 7). In contrast the use of Pb(OAc)₂ led to formation of more than 70% of homodimer (Table 1, Entry 8). The addition of VCl₄ (5 mol%) afforded the desired aluminium reagent **2a** at 30 °C in 4 h in 47% yield, but the addition of NiCl₂ or CoCl₂ provided only homodimer (Table 1, Entries 9-11). Interestingly other chlorides such as InCl₃,¹⁰⁹ SnCl₂ or BiCl₃ were quite effective and provided **2a** in 85-87% yield (Table 1, Entries 12-14). Also, inexpensive TiCl₄ (5 mol%) led to the aluminium reagent **2a** in 62% yield within 30 min (Table 1, Entry 15). In this case again dimerization of **1a** leading to 4,4'-bistrifluoromethylbiphenyl was responsible for the lower yield. Iron salts, such as FeCl₂ or Fe(acac)₃, were also effective and provided the aluminium reagent **2a** in 47-66% yield (Table 1, Entries 16-17). Remarkably, even ferrocene was an effective catalyst and the aluminium reagent was formed in 77% yield after 19 h reaction time (Table 1, Entry 18). Simple MgCl₂ and several aluminium containing additives (AlCl₃, Al(O*i*Pr)₃ or AlMe₃) led also to the expected organometallic within 0.75 h and 4.5 h in 58-70% yield (Table 1, Entries 19-22).

¹⁰¹ Y.-H. Chen, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 7648.

¹⁰² Y.-H. Chen, M. Sun, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 2236.

¹⁰³ F. Piller, P. Appukkutan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6806.

¹⁰⁴ A. Metzger, F. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824.

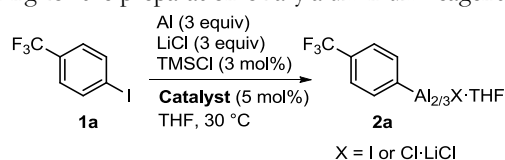
¹⁰⁵ a) E. Negishi, T. Takahashi, S. Baba, D. E. van Horn, N. Okukado, *J. Am. Chem. Soc.* **1987**, *109*, 2401; b) E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340; c) S.-L. Ku, X.-P. Hui, C.-A. Chen, Y.-Y. Kuo, H.-M. Gau, *Chem. Commun.* **2007**, 3847.

¹⁰⁶ a) S. Araki, S.-J. Jin, Y. Idou, Y. Butsugan, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1736; b) K. Takai, Y. Ikawa, *Org. Lett.* **2002**, *4*, 1727; c) J. Augé, N. Lubin-Germain, A. Thiaw-Woaye, *Tetrahedron Lett.* **1999**, *20*, 9245; d) H. Tanaka, M. Kuroboshi, *Current Organic Chemistry*, **2004**, *8*, 1027.

¹⁰⁷ K. Takai, T. Ueda, T. Hayashi, T. Moriwake, *Tetrahedron Lett.* **1996**, *37*, 7049.

¹⁰⁸ a) K. Takai, T. Kakiuchi, K. Utimoto, *J. Org. Chem.* **1994**, *59*, 2671; b) K. Takai, T. Ueda, N. Ikeda, T. Ishiyama, H. Matsushita, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 347; c) X.-L. Zhang, Y. Han, W.-T. Tao, Y.-Z. Huang, *J. Chem. Soc. Perkin. Trans. 1*, **1995**, 189.

¹⁰⁹ a) T.-P. Loh, G.-L. Chua, *Chem. Commun.* **2006**, 2739; b) S. Araki, T. Hirashita in *Comprehensive Organometallic Chemistry III* (ed. P. Knochel), Pergamon Press, Oxford, **2007**; c) J. Augé, N. Lubin-Germain, J. Uziel, *Synthesis*, **2007**, 1739.

Table 1: Catalyst screening for the preparation of arylaluminium reagents from the aryl iodide **1a**.

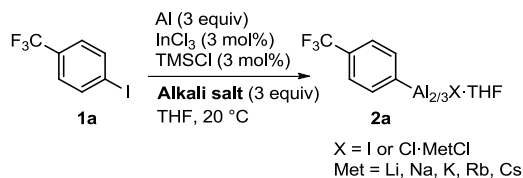
Entry	Catalyst	Reaction Time [h] ^a	Yield [%] ^b of 2a
1	ZnCl ₂	8	traces ^c
2	FeCl ₃	8	traces ^c
3	MnCl ₂	8	traces ^c
4	ZrCl ₄	8	traces ^c
5	Cp ₂ ZrCl ₂	8	traces ^c
6	HfCl ₄	8	traces ^c
7	PbCl ₂	3	77 ^d
8	Pb(OAc) ₄	4	- ^e
9	VCl ₄	4	47
10	NiCl ₂	5	- ^e
11	CoCl ₂	5	- ^{ef}
12	InCl ₃	2.5	87
13	SnCl ₂	8	85
14	BiCl ₃	4.5	85
15	TiCl ₄	0.5	62 ^g
16	FeCl ₂	5	66
17	Fe(acac) ₃	19	47
18	Cp ₂ Fe	19	77
19	MgCl ₂	4.5	69 ^h
20	AlCl ₃	3.5	58
21	Al(O <i>i</i> Pr) ₃	1.5	70
22	AlMe ₃	0.75	66 ⁱ

^a The amount of time the reaction was followed by GC analysis of hydrolyzed reaction aliquots. ^b Yield of organoaluminium reagent as determined by iodolysis in THF. ^c The amount of detectable iodolysed product remained below 5%. ^d Without TMS-Cl activation the yield dropped to 60%. ^e The reaction leads to almost quantitative formation of homodimer. ^f Xantphos (5 mol%) as was added. ^g Formation of homodimer is responsible for the lower yield. ^h MgCl₂ has been prepared anhydrous by insertion of Mg into dichloroethane in THF. ⁱ 2.5 mol% of catalyst were used.

Not only the additive (catalyst) is necessary for a smooth insertion of aluminium, also the alkali salt plays an important role. We screened the influence of several alkali chlorides (3 equiv) using the same typical aryl iodide **1a** and InCl₃ (3 mol%), as it proved to be a quite effective catalyst for the insertion into aryl iodides, in THF at 20 °C (Table 2). As mentioned before, without any alkali additive the reaction between the aryl iodide **1a** and aluminium powder proceeded rather sluggishly, if it appeared at all (Table 2, Entry 1), whereas the addition of LiCl led to a fast insertion rate (100% conversion, 5 h), providing the desired aluminium reagent **2a** in 75-85% yield (Table 2, Entry 2). Interestingly, other alkali salts had also tremendous influence on the reaction rate (Table 2, Entries 3-6). When the reaction was performed with

NaCl instead of LiCl, the overall reaction rate slowed down compared to the reaction with no alkali additive (Table 2, Entry 3), indicating that NaCl somehow inhibited a smooth insertion reaction. KCl instead showed a similar behaviour, being slow during the first 22 h, but then a sudden increase in turnover rate was recognized (Point A, Figure 1) leading to saturation after 44 h (Point B, Figure 1). This may be related to the solubility of the alkali salts in ethereal solvents such as THF.

Table 2: Influence of the alkali salt on the insertion rate of aluminium into a typical aryl iodide **1a**.



Entry	Alkali Salt	Reaction Time [h] ^a	Conversion [%] ^b
1	-	60	54
2	LiCl	5	100 ^c
3	NaCl	60	42
4	KCl	60	77
5	RbCl	47	60
6	CsCl	7	100 ^d

^a The amount of time the reaction was followed by GC analysis of hydrolyzed reaction aliquots. ^b Conversion of aryl iodide as indicated by GC analysis of hydrolyzed reaction aliquots using heptadecane as internal standard. ^c Yield of organoaluminium reagent: 75-85% as determined by iodolysis in THF. ^d Yield of organoaluminium reagent: 93% as determined by iodolysis in THF.

The use of RbCl led to acceleration in the beginning of the reaction but then again some inhibition occurred, leading to decrease in turnover and saturation after 22 h (Point C, Figure 1). This may again be attributed to a better solubility of RbCl in THF compared to KCl and NaCl. Finally, the largest of the alkali cations (Cs⁺) showed a dramatic acceleration effect similar to that of LiCl, leading to full conversion of the starting material after 7 h at 20 °C providing the aluminium reagent **2a** in 93% yield (Table 2, Entry 6). In conclusion, only the smallest and the largest alkali cation were beneficial leading to an accelerated insertion reaction with full conversion of the substrate. Both salts are quite soluble in THF, which may be the reason why the intermediate alkali sources (Na, K, Rb) cannot participate in the reaction, provided all the alkali salts have the same mode of action on the reaction course.

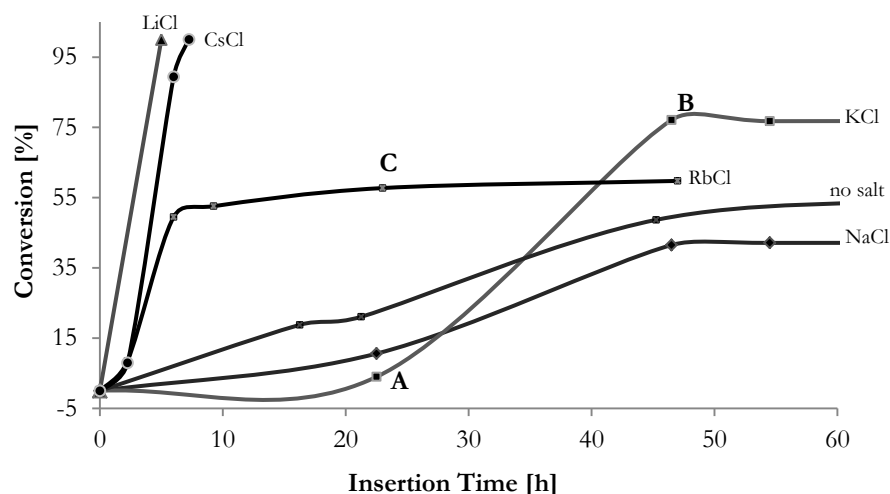
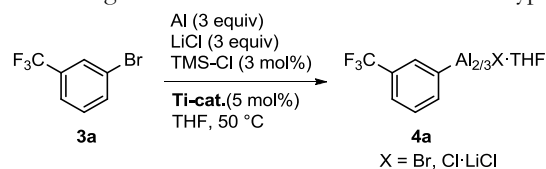


Figure 1: Alkali salt influence on the insertion of aluminium into aryl iodide **1a**.

1.3.2 Catalysed Aluminium Insertion into Aryl Bromides

Further experimentation has shown that the choice of the appropriate additive depends on the structure and the nature of the organic halide. Although PbCl_2 and InCl_3 can catalyse the insertion reaction into aryl bromides, usually long reaction times (>40 h) at 50 °C are required, leading to decreased yields of the obtained reagents. Thus, for the preparation of arylaluminium reagents starting from aryl bromides the addition of titanium catalysts was found to be the optimum and several Ti salts catalyse the reaction (Table 3).

Table 3: Ti-catalyst screening for the insertion of aluminium into a typical aryl bromide **3a**.



Entry	Ti-catalyst	Reaction Time [h] ^a	Yield of 4a [%] ^b
1	TiCl_2	n.r.	n.r.
2	TiF_4	16	26 % conversion
3	$\text{Ti}(\text{O}i\text{Pr})_4$	4	37
4	$\text{Ti}(\text{O}i\text{Pr})_3\text{Cl}$	3	48
5	$\text{Ti}(\text{O}i\text{Pr})_2\text{Cl}_2$	3	44
6	Cp_2TiCl_2	3.5	65
7	Cp_2TiCl	6	71
8	Cp^*TiCl_3	8	73
9	TiCl_4	2.5 - 4	78

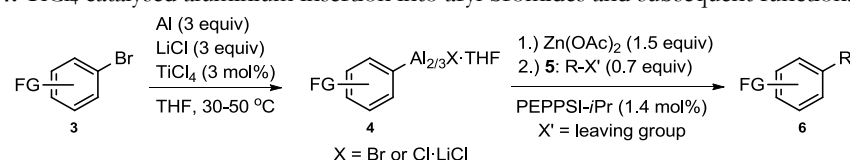
^a Reaction time until GC-analysis of hydrolysed reaction aliquots showed >95% conversion of the aryl bromide. ^b Yield of organometallic as determined by iodolysis in THF.

Titanium sources like TiCl_2 or TiF_4 did not afford the desired aluminium reagent, which is probably attributed to the low solubility in THF (Table 3, Entries 1-2). Titanium salts bearing isopropoxide substituents led to fast insertion reactions and full conversion of the aryl bromide, but resulted in low

yields of the organoaluminium reagent **4a** because more than 50% of the reagent got hydrolysed or reduced (Table 3, Entries 3-5). Several titanocene derivatives also provided the aluminium reagent **4a**. This class of catalysts was not as fast as the isopropoxide substituted catalysts, but the organometallic was obtained in much better yield (Table 3, Entries 6-8). Remarkably, the insertion is not only catalysed by Ti^{IV} salts, as Cp₂TiCl is also capable of catalysing the insertion reaction, being Ti^{III} (Table 3, Entry 7). Nevertheless, TiCl₄ proved to be the most reliable catalyst, combining a relatively fast insertion time (2-4 h) and good yield (78%) of the aluminium reagent **4a** (Table 3, Entry 9). With these conditions at hand several aryl bromides could be readily converted to the corresponding aluminium reagents.

The aluminium organometallic **4a** obtained by the insertion reaction into 3-bromobenzotrifluoride (**3a**) underwent a smooth Pd-catalysed cross-coupling reaction with 4-iodoacetophenone (**5a**) in the presence of Zn(OAc)₂ (1.5 equiv) and PEPPSI-*i*Pr (1.4 mol%).^{110, 111} The functionalized ketone **6a** was obtained in 82% yield (Table 4, Entry 1). Also, using the same conditions a cross-coupling with 4-bromobenzonitrile (**5b**, 0.7 equiv) on 20 mmol scale afforded the biphenyl **6b** in 86% yield, demonstrating the synthetic usefulness of the prepared reagents (Table 4, Entry 2). The treatment of 1-bromo-2-fluorobenzene (**3b**) with Al powder (3 equiv), LiCl (1.5 equiv) and TiCl₄ (3 mol%) at 30 °C for 3.5 h furnished the corresponding aluminium reagent (**4b**) which underwent a smooth Pd-catalysed cross-coupling in the presence of Zn(OAc)₂ (1.5 equiv) and PEPPSI-*i*Pr (1.4 mol%) with methyl 4-bromobenzoate (**5c**, 0.7 equiv) leading to the biphenyl ester **6c** in 93% yield (Table 4, Entry 3). Remarkably, the intermediate 2-fluoroarylaluminium reagent (**4b**) did not undergo elimination to an aryne under the preparation and cross-coupling conditions.

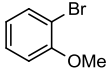
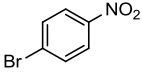
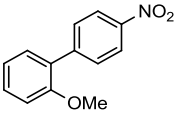
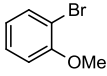
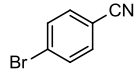
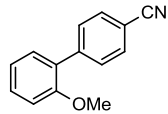
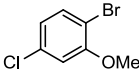
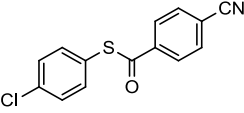
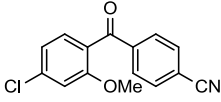
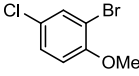
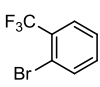
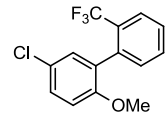
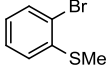
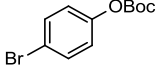

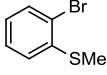

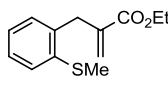
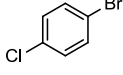
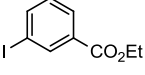
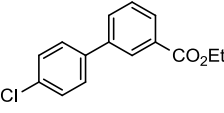
Table 4: TiCl₄ catalysed aluminium insertion into aryl bromides and subsequent functionalization.



Entry	Aryl Bromide	Conditions ^a	Electrophile ^b	Product ^c
1		50 °C 4 h		 6a : 82%
2		50 °C 4 h		 6b : 86%
3		30 °C 3.5 h		 6c : 93%

¹¹⁰ C. J. O'Brien et al., *Chem. Eur. J.* **2006**, *12*, 4743.

¹¹¹ M. G. Organ, S. Calimsiz, M. Sayah, K. H. Hoi, A. J. Lough, *Angew. Chem. Int. Ed.* **2009**, *121*, 2419.

4		50 °C 20 h			6d : 80%
5		50 °C 20 h			6e : 78%
6		50 °C 6 h			6f : 70%
7		50 °C 5 h			6g : 79% ^d
8		50 °C 16 h			6h : 68% ^d
9		50 °C 16 h			6i : 89%
10		50 °C 14 h			6j : 91% ^d

^a Time until a conversion of >95% according to GC-analysis was achieved. ^b 0.7 equiv of electrophile was used. ^c Isolated yields of analytically pure product estimated to be of >95% purity according to GC- and NMR analysis. ^d 0.6 equiv of electrophile was used.

Not only electron-poor arylaluminium reagents can be prepared, but also electron-rich aryl bromides reacted smoothly. Thus, aluminium inserted into 1-bromo-2-methoxybenzene (**3c**) at 50 °C within 20 h providing the aluminium reagent **4c** which was converted to the biphenyl derivatives **6d** and **6e** in 80% and 78% yield by cross-coupling reactions as described above (Table 4, Entries 4-5). Similarly, the 4-chloro-2-bromoanisole (**3d**) was converted to the corresponding organoaluminium reagent **4d** which after transmetalation with Zn(OAc)₂ (1.5 equiv) readily underwent a *Liebeskind-Srogl*^{112, 113} cross-coupling with the thioester **5e** to afford the functionalized benzophenone derivative **6f** in 70% yield (Table 4, Entry 6). Various substituted aryl bromides such as **3e-g** bearing substituents like a chloride, trifluoromethyl or a thiomethyl group were readily converted to the intermediate aluminium reagents at 50 °C within 5-16 h.

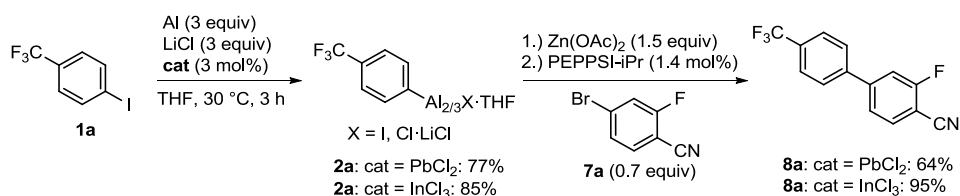
¹¹² J. Srogl, G. D. Allred, L. S. Liebeskind, *J. Am. Chem. Soc.* **1997**, *119*, 12376.

¹¹³ H. Prokopcov, C. O. Kappe, *Angew. Chem. Int. Ed.* **2009**, *48*, 2276.

Subsequent transmetalation and highly chemoselective Pd-catalysed cross-coupling with various aryl bromides or iodides bearing a carbonate, an acetyl or an ester group furnished the expected polyfunctional biphenyl adducts **6g-j** in 68-91% yield (Table 4, Entries 7-10).

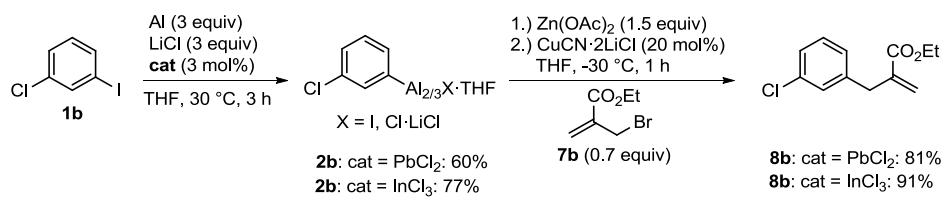
1.3.3 Catalysed Aluminium Insertion into Aryl Iodides

Among all the screened catalysts PbCl_2 , InCl_3 and BiCl_3 had been the most effective in catalysing the aluminium insertion into aryl iodides. The reaction between 4-iodobenzotrifluoride (**1a**), LiCl (3 equiv), Al powder (3 equiv) and PbCl_2 (3 mol%) afforded the aluminium reagent **2a** in 77% yield after 3 h at 30 °C. After transmetalation with Zn(OAc)_2 (1.5 equiv) a cross-coupling reaction (PEPPSI-*i*Pr, 1.4 mol%) with 4-bromo-2-fluorobenzonitrile (**7a**) afforded the biphenyl **8a** in 64% yield. Using the same conditions and InCl_3 as catalyst, the organoaluminium **2a** was obtained in 85% yield after 3 h at 30 °C. Similarly, the reagent prepared in this way smoothly underwent the same cross-coupling affording **8a** much more effectively in 95% yield (Scheme 30).



Scheme 30: Comparison of PbCl_2 - and InCl_3 -catalysed aluminium insertion into the aryl iodide **1a** and subsequent cross-coupling.

In the same way, 3-chloriodobenzene (**1b**) furnished the aluminium reagent **2b** in 60% yield using PbCl_2 as catalyst. Also in this case, the reagent **2b** is obtained in much better yield (77%) using InCl_3 as catalyst. In the presence of Zn(OAc)_2 both reagents underwent allylation ($\text{CuCN}\cdot 2\text{LiCl}$, -30 °C) using the acrylate **7b**, leading to the unsaturated ester **8b** in 81% and 91% yield (Scheme 31).

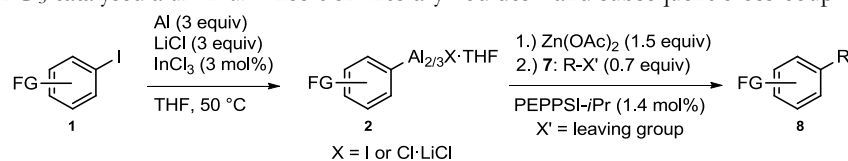


Scheme 31: Comparison of PbCl_2 - and InCl_3 -catalysed aluminium insertion into the aryl iodide **1b** and subsequent allylation.

These results clearly showed that InCl_3 is much more effective in catalyzing the aluminium insertion into aryl iodides than PbCl_2 . As a consequence the use of InCl_3 leads to higher yields in the subsequent functionalizations. Therefore we subjected several aryl iodides to the typical reaction conditions using InCl_3 as catalyst (Table 5). Thus, the reaction of 1-iodo-3,5-dimethylbenzene (**1c**) with Al powder (3 equiv) in the presence of LiCl (1.5 equiv) and InCl_3 (3 mol%) afforded the arylaluminium halide **2c** within 24 h reaction time at 50 °C. After treatment with Zn(OAc)_2 (1.5 equiv) a Pd-catalysed acylation with a bromo-substituted thioester (**7c**, 0.7 equiv)⁴⁸ provided the benzophenone **8c** in 89% yield with excellent chemoselectivity (Table 5, Entry 1). Remarkably, double bonds are also well tolerated under the reaction

conditions. The aryl iodide **1d** furnished the aluminium reagent **2d** which was converted to the substituted thiophene derivative **8d** in 75% yield after a typical cross-coupling reaction (Table 5, Entry 2).

Table 5: InCl₃ catalysed aluminium insertion into aryl iodides **1** and subsequent cross-coupling reaction.



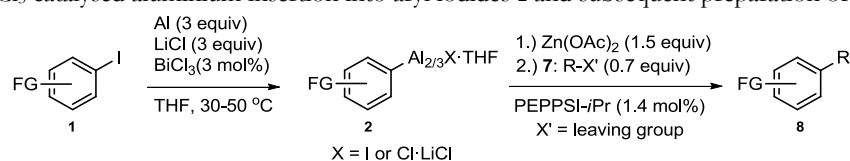
Entry	Aryl Iodide	Conditions ^d	Electrophile ^b	Product ^c
1		50 °C 24 h		 8c : 89%
2		50 °C 24 h		 8d : 75% ^d
3		50 °C 6 h		 8e : 92%
4		50 °C 3 h		 8f : 84%
5		50 °C 12 h		 8g : 74%
6		50 °C 24 h		 8h : 54% ^d

^a Time until a conversion of >95% according to GC-analysis was achieved. ^b 0.7 equiv of electrophile was used. ^c Isolated yields of analytically pure product estimated to be of >95% purity according to GC- and NMR analysis. ^d 0.6 equiv of electrophile was used.

Furthermore, *ortho*-, *meta*- and *para*-fluoro substituted aryl iodides (**1e-g**) were easily converted to the aluminium sesquihalides **2e-g** (50 °C, 3-12 h). Cross-coupling reactions of these reagents led to the fluorine substituted biphenyls **8e-g** in 74-92% yield (Table 5, Entries 3-5). Interestingly, not only aromatic sp²-carbon halide bonds undergo oxidative addition of aluminium, also a vinylic sp²-carbon iodine bond (**1h**) readily reacted under the reaction conditions and a cross-coupling with the benzylic bromide **7h** furnished the substituted alkene **8h** in 54% yield. (Table 5, Entry 6).

The preliminary catalyst screening had shown that BiCl₃ can also be used for the preparation of aryl sesquihalides (Table 1, Entry 12). Thus, using BiCl₃ (3 mol%) in the presence of Al (3 equiv) and LiCl (3 equiv), the typical aryl iodide **1a** furnished the reagent **2a** in 85% yield (4.5 h, 30 °C). Subsequent cross-coupling of this organometallic with the protected uracil derivative **7i** furnished the highly functionalized heterocycle **8i** in 73% yield (Table 6, Entry 1). Similarly, 3-fluoroiodobenzene (**1f**) or the trifluoromethoxy substituted iodide **1i** was converted to the aluminium reagents **2f** and **2g** within 3-12 h at 50 °C. Again, these reagents reacted smoothly with the heterocyclic electrophiles and the resulting uracil and nicotinic acid derivatives **8j-l** were isolated in 75-82% yield (Table 6, Entries 2-4).

Table 6: BiCl₃ catalysed aluminium insertion into aryl iodides **1** and subsequent preparation of heterocycles.

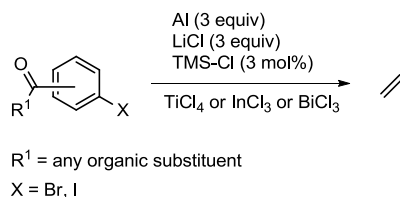


Entry	Aryl Iodide	Conditions ^a	Electrophile ^b	Product ^c
1		30 °C 4.5 h		 8i : 73%
2		50 °C 3 h		 8j : 76%
3		50 °C 3 h		 8k : 82%
4		50 °C 12 h		 8l : 75%

^a Time until a conversion of >95% according to GC-analysis was achieved. ^b 0.7 equiv of electrophile were used. ^c Isolated yields of analytically pure product estimated to be of >95% purity according to GC- and NMR analysis

1.3.4 Catalysed Aluminium Insertion into Functionalized Aryl- and Heteroaryl Halides Bearing Carbonyl Substituents

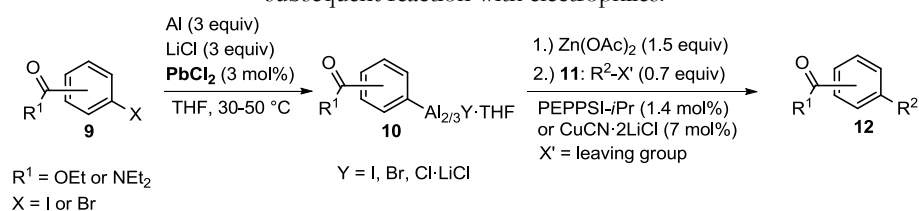
During the studies on the catalysed aluminium insertion into aryl bromides and aryl iodides it became apparent that neither TiCl_4 , nor BiCl_3 or InCl_3 were able to catalyse the insertion reaction whenever a carbonyl group was present in the corresponding substrate (Scheme 32). Either no reaction was observed at all, or the reaction stopped at ca. 10% conversion. Even prolonged heating or reflux conditions did not lead to a successful insertion of aluminium.



Scheme 32: Carbonyl functionalized aryl halides could not be converted to aluminium reagents in the presence of TiCl_4 , InCl_3 or BiCl_3 .

However, when the reaction was performed with PbCl_2 as additive instead, aluminium inserted readily into various carbonyl-substituted aromatics and heteroaromatics allowing for the first time the direct preparation of ester or amide functionalized aryl- and heteroarylaluminium halides (Table 7). Thus, ethyl 2-iodobenzoate (**9a**) furnished after treatment with Al-powder (3 equiv), LiCl (3 equiv) and PbCl_2 (3 mol%) after 4 h reaction time at 30 °C the functionalized aluminium halide **10a**. This reagent underwent an allylation reaction in the presence of $\text{Zn}(\text{OAc})_2$ (1.5 equiv) and $\text{CuCN}\cdot 2\text{LiCl}$ (7 mol%) with allyl bromide (**11a**, 0.7 equiv) affording the allylated ester **12a** in 80% yield (Table 7, Entry 1). Moreover, Pd-catalysed cross-couplings (1.4 mol% PEPPSI-*i*Pr) with substrates bearing acidic protons such as 1-(5-iodothiophen-2-yl)ethanone (**11b**, 0.7 equiv) or 1-(bromomethyl)-3-nitrobenzene (**11c**, 0.7 equiv) proceeded smoothly and the substituted thiophene **12b** as well as the functionalized diarylmethane **12c** were isolated in 63% and 81% yield (Table 7, Entries 2-3). Not only *ortho*-substituted ethyl esters leading to a “directed *ortho* insertion” (DOI)¹¹⁴ could be converted to aluminium organometallics, also *meta*-substituted ester derivatives such as **9b** worked seemingly well. However, the insertion time is dramatically increased to 25 h at 50 °C because of the missing directing ability of the ester functionality. After transmetallation with $\text{Zn}(\text{OAc})_2$ (1.5 equiv) an allylation with a catalytic amount of $\text{CuCN}\cdot 2\text{LiCl}$ (7 mol%) or a Pd-catalysed cross-coupling (1.4 mol% PEPPSI-*i*Pr) afforded the functionalized esters **12d** and **12e** in 88% and 78% yield (Table 7, Entries 4-5). Remarkably, also an amide functionality is perfectly compatible with the insertion conditions and **9c** was converted to the functionalized organoaluminium **10c** in 30 h at 50 °C. Cross-coupling using the standard conditions afforded the biphenyl **12f** in 91% (Table 7, Entry 5).

¹¹⁴ N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358.

Table 7: PbCl₂-catalysed insertion of aluminium to aryl and heteroaryl halides bearing carbonyl substituents and subsequent reaction with electrophiles.

Entry	Aryl Iodide	Conditions ^d	Electrophile ^b	Product ^c
1		30 °C 4 h		 12a: 80%
2		30 °C 4 h		 12b: 63%
3		30 °C 4 h		 12c: 81%
4		50 °C 25 h		 12d: 88%
5		50 °C 25 h		 12e: 78%
6		50 °C 30 h		 12f: 91%
7		50 °C 6 h		 12g: 92%
8		50 °C 6 h		 12h: 62%
9		50 °C 24 h		 12i: 83%

^d Time until a conversion of >95% according to GC-analysis was achieved. ^b 0.7 equiv of electrophile were used. ^c Isolated yields of analytically pure product estimated to be of >95% purity according to GC- and NMR analysis

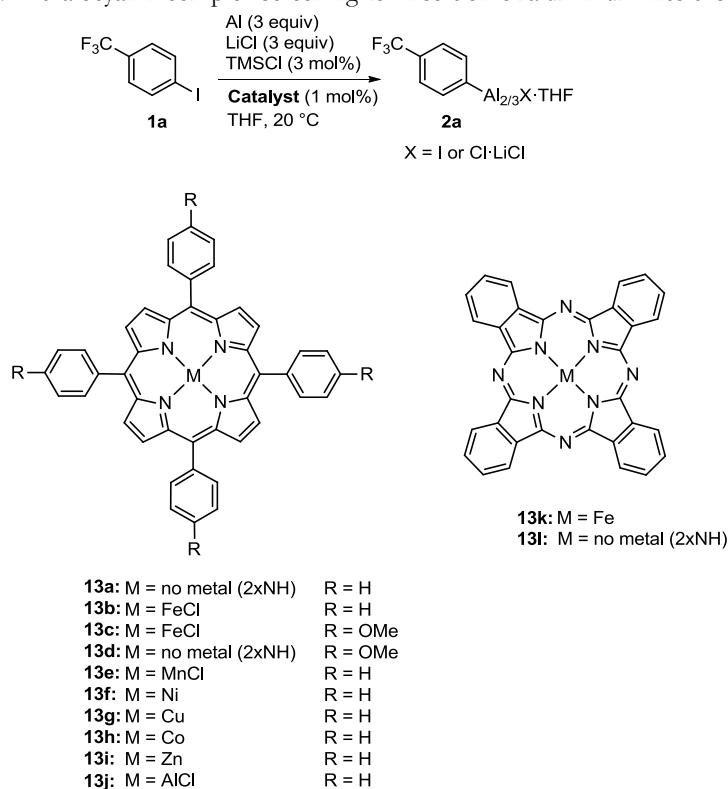
To our delight even heterocyclic esters could be converted to the corresponding aluminium reagents. Addition of 5-bromo-thiophene-2-carboxylic acid ethyl ester (**9d**) to Al powder in the presence of LiCl (1.5 equiv) and PbCl₂ (3 mol%) furnished after 6 h at 50 °C the *first functionalized heterocyclic aluminium sesquichloride* **10d**. A Pd-catalysed cross-coupling with 4-bromobenzaldehyde (**11g**, 0.7 equiv) produced the 2,5-disubstituted thiophene **12g** in 92% yield after prior transmetallation with Zn(OAc)₂ (1.5 equiv, Table 7, Entry 7). Remarkably, the sensitive formyl functionality was perfectly compatible with the cross-coupling conditions. Also, trapping the reagent with the functionalized allyl bromide **11h** led to the heterocyclic diester **12h** in 62% yield (Table 7, Entry 8). The corresponding furane derivative **9e** reacted equally well and after a cross-coupling with 2-bromobenzonitrile (**11i**, 0.7 equiv) the heterocyclic ester **12i** was isolated in 83 % yield. It is to note, that this is a remarkable transformation, as the thiophene- and furane rings do not undergo ring-opening during the insertion or cross-coupling reactions.

1.3.5 Extended Pi-Systems as Catalysts for the Direct Insertion of Aluminium to Aryl Halides

During the last decades several additives have been used for activation of different metals.¹¹⁵ Among these reports was a facilitated insertion of Mg to relatively unreactive aryl chlorides published by *Bogdanović* in 2000.¹¹⁶ He utilized different transition metals (FeCl₂ or MnCl₂) as well as porphin- or phthalocyanin complexes in combination with other additives for the activation of magnesium. We envisioned that these heterocyclic complexes may also be effective in catalyzing the aluminium insertion into aryl halides. We therefore screened the influence of porphin and phthalocyanin complexes on the reaction rate of the insertion of Al-powder into a typical aryl iodide **1a** (Table 8). Remarkably, any porphin- or phthalocyanin complex tested was able to accelerate the insertion of aluminium to the aryl iodide (Table 8, Entries 1-12) providing the aluminium reagent **2a** in 60-80% yield, nevertheless several differences could be noticed. The use of a “naked” (without a metal center) tetraphenylporphin (TPP) complex **13a** resulted in fast formation of the aluminium reagent **2a** (45 min, 20 °C) in 66% yield (Table 8, Entry 1). In contrast, the same porphin containing a Fe^{III}Cl metal center (**13b**) also generated the aluminium reagent in short time, but with higher yield (78%, Table 8, Entry 2). None of the other tested porphins (**13c-j**) could compete with this result, although all were effectively generating the aluminium reagent in similar yields (Table 8, Entries 3-10). Phthalocyanin derivatives (**3k-l**) also effectively catalysed the aluminium insertion into the iodide **1a**. Regardless of the metal center (Fe^{II}, or none) the aluminium reagent **2a** was obtained in 61% and 69% yield, although the metal center dramatically accelerated the reaction compared to the “naked” phthalocyanin (Table 8, Entries 11-12). As the porphins (TPP, TPP-OMe) and the phthalocyanin all were able to effectively catalyse the insertion reaction, even without a metal center, the question arose if the extended Pi-system is responsible for a smooth insertion. Thus, we tried the reaction with simple anthracen (**13m**). Remarkably, within 5 h at 20 °C even this simple Pi-system was able to catalyse the insertion reaction and the reagent **2a** was generated in 61% yield (Table 8, Entry 13).

¹¹⁵ U. Tilstam, H. Weinmann, *Org. Proc. Res. Dev.* **2002**, *6*, 906.

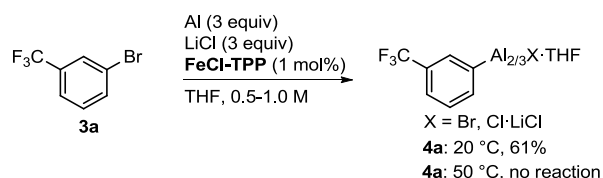
¹¹⁶ B. Bogdanović, M. Schwickardi, *Angew. Chem. Int. Ed.* **2000**, *39*, 4610.

Table 8: Porphin and Phthalocyanin complex screening for insertion of aluminium into the aryl iodide **1a**.

Entry	Catalyst ^a		Reaction Time [h] ^b	Yield (%) ^c
1	TPP	13a	0.75	66
2	FeCl-TPP	13b	0.75	78
3	FeCl-TPP-OMe	13c	20	72
4	TPP-OMe	13d	2.5	67
5	MnCl-TPP	13e	2	62 ^d
6	Ni-TPP	13f	3.5	73
7	Cu-TPP	13g	23	70
8	Co-TPP	13h	1	65
9	Zn-TPP	13i	23	71
10	AlCl-TPP	13j	1	71
11	Fe-Pc	13k	1	61
12	Pc	13l	16	69
13	Anthracen	13m	5	67

^a TPP = Tetraphenylporphyrin; Pc = Phthalocyanin. ^b Reaction time until GC-analysis of hydrolysed reaction aliquots showed >95% conversion of the aryl iodide. ^c Yield of organometallic as determined by iodolysis in THF. ^d Homodimer was obtained.

Interestingly, not only aryl iodides can be used, also an aryl bromide was readily converted to the corresponding aluminium reagents under mild conditions, with low catalyst loading. Thus, 3-bromobenzotrifluoride (**3a**) furnished the corresponding aluminium reagent **4a** in 61% yield after reaction with Al (3 equiv), LiCl (3 equiv) and a catalytic amount of FeCl-TPP (**13b**, 1 mol%) for 4 h at 20 °C (Scheme 33).



Scheme 33: Porphin-catalysed insertion of aluminium into the aryl bromide **3a** at 20 °C and 50 °C.

Interestingly, if the temperature was raised to 50 °C no reaction occurred at all, indicating that higher temperatures are leading to a deactivation of the catalyst somehow. Additionally, when the reaction was conducted in DMF instead of THF, also no reaction was observed. We speculated that CsCl may also lead to higher yields when used as alternative for LiCl, as the combination of $\text{InCl}_3/\text{CsCl}$ provided excellent yields in the case of aryl iodides. But again, no reaction occurred, indicating that LiCl is definitely needed for the porphins to act as catalyst.

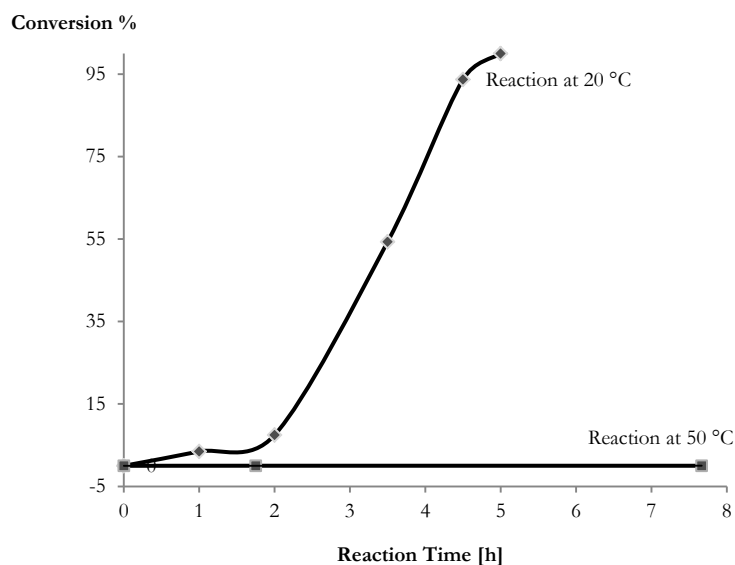
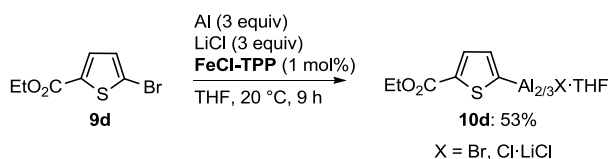


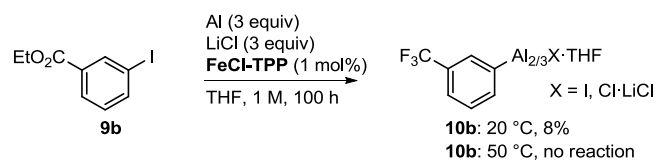
Figure 2: Conversion of the aryl bromide **3a** at 20 °C and 50 °C using FeCl-TPP (**13b**) as catalyst for the insertion of Al-powder.

Next, we tried if the porphin would also catalyse the insertion into substrates bearing carbonyl groups. Thus, the thiophene derivative **9d** was subjected to the same reaction conditions. Within 9 h full conversion of the starting material was achieved and the aluminium sesquihalide **10d** was obtained in 53% yield (Scheme 34). Remarkably, so far only PbCl_2 could be used for the generation of aluminium reagents bearing carbonyl functionalities and although the porphin catalyst is able to generate the organoalane the use of LiCl in combination with PbCl_2 is still the superior way to achieve this transformation (6h, ~80%).



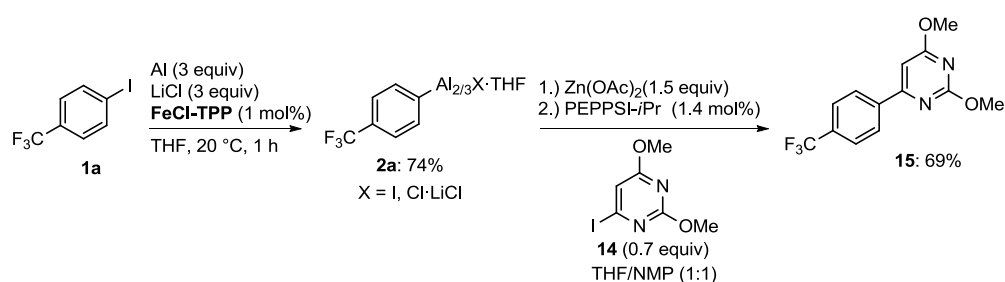
Scheme 34: Porphin-catalysed insertion of aluminium into the ester functionalized heteroaryl bromide **9d**.

Whereas the thiophene derivative **9d** could be converted to an organoalane, the use of ethyl 3-iodobenzoate (**9b**) proved to be problematic. The reaction of **9b** under the typical reaction conditions was very slow, achieving full conversion of the starting material after 100 h, but generating only 8% of reactive organoaluminium reagent **10b**, as shown by iodolysis in THF (Scheme 35). Again, when the reaction mixture was heated to 50 °C no reaction occurred at all.



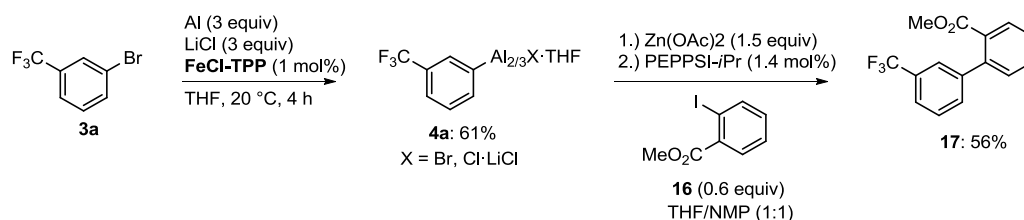
Scheme 35: Porphin-catalysed insertion of aluminium into the aryl iodide **9b** at 20 °C and 50 °C.

The next step was to test if the reagents prepared via the porphin catalysts would still undergo subsequent functionalization reactions, or if the macromolecules would hinder e.g. a cross-coupling reaction. Thus, the aluminium insertion catalysed by FeCl-TPP (**13b**) furnished the aluminium reagent **2a** in 74% yield within 1 h at room temperature (20 °C) starting from the aryl iodide **1a**. After transmetalation with Zn(OAc)₂ (1.5 equiv) a Pd-catalysed cross-coupling (PEPPSI-*i*Pr, 1.4 mol%) with **14** (0.7 equiv) furnished the functionalized uracil derivative **15** in 69% yield (Scheme 36).



Scheme 36: Porphin-catalysed insertion of aluminium into the aryl iodide **1a** at 20 °C and subsequent cross-coupling reaction.

In a similar way the trifluoromethyl substituted organoaluminium **3b**, prepared by the FeCl-TPP-catalysed aluminium insertion (20 °C, 4 h), underwent a cross-coupling reaction with methyl 2-iodobenzoate (**16**) furnishing the ester substituted biphenyl **17** in 56% yield (Scheme 37).



Scheme 37: Porphin-catalysed insertion of aluminium into the aryl bromide **3a** at 20 °C and subsequent cross-coupling reaction.

2 CATALYSED ALUMINIUM INSERTION INTO BENZYLIC HALIDES

2.1 Abstract

Various benzylic chlorides react with Al powder in the presence of catalytic amounts of InCl_3 (1-5 mol%) in an ethereal solvent, leading to benzylic aluminium sesquichlorides. These new organometallics can be used in many organic transformations such as allylation reactions, Pd-catalysed cross-couplings, acylation reactions or conjugated addition. Additionally, the preparation of *ortho*-, *meta*- and *para* bis-benzylic organometallics is possible using the presented methodology. NMR studies reveal a complex transmetallation equilibrium when benzylic aluminium sesquichlorides react with Zn sources like ZnCl_2 or $\text{Zn}(\text{OAc})_2$.

2.2 Introduction

Diarylmethanes are an important class of substances often showing pharmacological or biological activity.¹¹⁷ One of the most common ways to build up diarylmethanes is the addition of organometallics (such as PhLi) to aldehydes and subsequent reduction.¹¹⁸ Moreover cross-coupling reactions of organometallics with benzylic halides or other leaving groups such as acetates, carbonates and phosphates can be used to build up this important structural motif.¹¹⁹ The other way round, it is also possible to generate benzylic organometallics, which undergo cross-coupling with aromatic electrophiles. There are several methods for the preparation of benzylic organometallics.¹²⁰ Whereas benzylic lithium and magnesium organometallics do not tolerate functional groups, benzylic zinc organometallics are compatible with numerous functionalities and are readily prepared by direct insertion of zinc dust in the presence of LiCl .^{120i-k} Like zinc, aluminium is also a cheap metal with low toxicity. By comparing the electronegativities of the metals (Mg: 1.32, Al: 1.61, Zn: 1.65)¹²¹ we anticipated that benzylic aluminium

¹¹⁷ a) R. Ueoka, T. Fujita, S. Matsunaga, *J. Org. Chem.* **2009**, *74*, 4396. b) Z. Jin, *Nat. Prod. Rep.* **2005**, *22*, 196. c) W. Hassan, R. Edrada, E. Ebel, V. Wray, A. Berg, R. van Soest, S. Wiryo widagdo, P. Proksch, *J. Nat. Prod.* **2004**, *67*, 817. d) F. Horak, U. P. Zieglmayer, *Expert Rev. Clin. Immunol.* **2009**, *5*, 659. e) 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. Schaub, Q. Wang, *J. Med. Chem.* **2007**, *50*, 40.

¹¹⁸ a) D.A. Barda, Z.-Q. Wang, T. C. Britton, S. S. Henry, G. E. Jagdmann, D. S. Coleman, M. P. Johnson, S. L. Andis, D. D. Schoepp, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3099; b) Y.-Q. Long, X.-H. Jiang, R. Dayam, T. Sanchez, R. Shoemaker, S. Sei, N. Neamati, *J. Med. Chem.* **2004**, *47*, 2561; c) X. Wu, A. K. Mahalingam, M. Alterman, *Tetrahedron Lett.* **2005**, *46*, 1501; d) P. E. Gordon, A. J. Frey, *Tetrahedron Lett.* **2001**, *42*, 831; (e) N. L'Hermite, A. Giraud, O. Provot, J.-F. Peyrat, M. Alami, J.-D. Brion, *Tetrahedron* **2006**, *62*, 11994.

¹¹⁹ a) H. Juteau, Y. Gareau, M. Labelle, S. F. Sturino, N. Sawyer, N. Tremblay, S. Lamontagne, M.-C. Carriere, D. Denis, K. M. Metters, *Bioorg. Med. Chem.* **2001**, *9*, 1977; b) C. Klaner, A. Greiner, *Macromol. Rapid Commun.* **1998**, *19*, 605; c) N. Miyaura, T. Yano, A. Suzuki, *Tetrahedron Lett.* **1980**, *21*, 2865; d) M. J. Sharp, V. Snieckus, *Tetrahedron Lett.* **1985**, *26*, 5997; e) S. N. Nobre, A. L. Monteiro, *Tetrahedron Lett.* **2004**, *45*, 8225; f) R. Kuwano, M. Yokogi, *Org. Lett.* **2005**, *7*, 945; g) R. Kuwano, M. Yokogi, *Chem. Commun.* **2005**, 5899; h) M. McLaughlin, *Org. Lett.* **2005**, *7*, 4875; i) G. A. Molander, M. D. Elia, *J. Org. Chem.* **2006**, *71*, 9198.

¹²⁰ For lithium reagents: a) J. N. Reed in *Science of Synthesis*, (Ed.: V. Snieckus), Georg Thieme-Verlag KG, Stuttgart, **2006**, Vol. 8a, p 329; b) B. J. Wakefield, *Organolithium Methods*, Academic Press: New York, **1988**. c) S. L. Hargreaves, B. L. Pilkington, S. E. Russell, P. A. Worthington, *Tetrahedron Lett.* **2000**, *41*, 1653. For magnesium reagents: d) T. P. Burns, R. D. Rieke, *J. Org. Chem.* **1987**, *52*, 3674; e) R. A. Benkeser, D. C. Snyder, *J. Org. Chem.* **1982**, *47*, 1243; f) K. V. Baker, J. M. Brown, N. Hughes, A. J. Skarnulis, A. Sexton, *J. Org. Chem.* **1991**, *56*, 698; g) S. Harvey, P. C. Junk, C. L. Raston, G. Salem, *J. Org. Chem.* **1988**, *53*, 3134; h) A. H. Stoll, A. Krasovskiy, P. Knochel, *Angew. Chem., Int. Ed.* **2006**, *45*, 606. For zinc reagents: i) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107; j) A. Metzger, M. A. Schade, G. Manolikakes, P. Knochel, *Chem. Asian J.* **2008**, *3*, 1678; k) A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824.

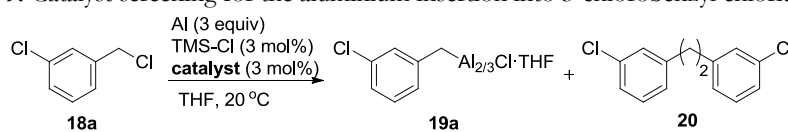
¹²¹ D. R. Lide, *CRC Handbook of Chemistry and Physics*: A ready reference book of chemical and physical data, Taylor & Francis, Boca Raton, FL, **2009**.

organometallics could also tolerate a number of functional groups.¹²² Reports on the reaction of aluminium with benzylic halides are scarce.^{122a} Inspired by the result obtained with aryl halides we envisioned that benzylic halides may be converted to aluminium reagents by proper activation of the metal surface, using the appropriate catalyst.

2.3 Preparation of Benzylic Aluminium Sesquichlorides

In preliminary experiments, 3-chlorobenzyl chloride (**18a**) was treated with Al-powder (3.0 equiv) and different metal salt additives (Table 9). The control experiment showed, that no reaction was observed in the absence of the metal salts, even in the presence of a stoichiometric amount of LiCl (Table 9, Entry 1). However, the addition of PbCl₂ (3 mol %) or BiCl₃ (3 mol %) lead to the formation of the 3-chlorobenzylaluminium reagent¹²³ **19a** in 20% and 64% yield along with the homodimer **20** (Table 9, Entries 2-3). InCl₃ proved to be the most effective catalyst and 3-chlorobenzyl chloride (**18a**) reacted with Al (3.0 equiv) in the presence of TMS-Cl (3 mol %)¹²⁴ and InCl₃ (3 mol %) within 3.5 h at 20 °C furnishing the aluminium reagent **19a** in 90% yield without the formation of **20** (Table 9, Entry 4). Interestingly, no reaction was observed when TiCl₄ or FeCl-TPP was used as catalyst although both are effective additives for the preparation of arylaluminiums (Table 9, Entries 5-6).

Table 9: Catalyst screening for the aluminium insertion into 3-chlorobenzyl chloride (**18a**).



Entry	Catalyst	Reaction Time	Yield (%) ^a of 19a	Yield (%) ^a of 20
1	-	24 h	n.r. ^b	n.r. ^b
2	PbCl ₂	22 h	20	5
3	BiCl ₃	12 h	64	36
4	InCl ₃	3.5 h	90	- ^c
5	TiCl ₄	12 h	n.r. ^b	n.r. ^b
6	FeCl-TPP	24 h	n.r. ^b	n.r. ^b

^a Yield was determined by iodolysis in THF. ^b No reaction was observed. ^c The detected amount of homodimer (by GC-analysis) was below 3%.

The insertion reaction worked best using THF as solvent with InCl₃ as catalyst, leading to the 3-chlorobenzyl aluminium reagent **19a** in 90% yield within 3.5 h at 20 °C. (Table 10, Entry 1). Other ethereal solvents such as diethyl- or dibutyl ether, as well as DME worked seemingly well, affording the expected organometallic in a similar yield, but slow down the reaction (Table 10, Entries 2-4). The use of MTBE as solvent did not lead to any detectable organometallic reagent, although no remaining 3-

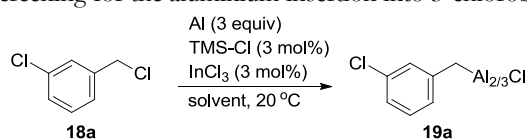
¹²² Organoaluminium compounds: a) T. Mole, E. A. Jeffery, *Organoaluminium Compounds*; Elsevier: Amsterdam, **1972**; b) E-i. Negishi, T. Takahashi, S. Baba, D. E. Horn, N. Okukado, *J. Am. Chem. Soc.* **1987**, *109*, 2393; c) G. Zweifel, J. A. Miller in *Organic Reactions* (Ed.: W. G. Dauben), Wiley, **1984**.

¹²³ An almost 1:1 mixture of RAlCl₂ and R₂AlCl is obtained as shown by NMR spectroscopy.

¹²⁴ For the metal surface activation with TMS-Cl see also: Takai, K.; Ueda, T.; Hayashi, T.; Moriwake, T. *Tetrahedron Lett.* **1996**, *37*, 7049.

chlorobenzyl chloride (**19a**) could be detected by GC-analysis of hydrolyzed reaction aliquots (Table 10, Entry 5). When hydrocarbon solvents were used for the reaction, no organometallic could be detected, but instead a precipitation was observed (Table 10, Entries 6-7). The use of aromatic solvents should be generally avoided as they are readily subjected to *Friedel-Crafts*-Alkylation (Table 10, Entries 8-9). In benzene the mixture violently reacted, producing diphenylmethane and chlorobenzene as identified by GC-MS analysis (Table 10, Entry 10). In more polar solvents like DMF or NMP the reaction mixture turned greenish, but no reaction with the benzylic chloride occurred (Table 10, Entries 11-12). The greenish color can probably be attributed to either some sort of complex formation or a reductive process. Finally, the reaction should not be performed in chlorinated solvents doing so will result in a violent exothermic reaction.

Table 10: Solvent screening for the aluminium insertion into 3-chlorobenzyl chloride (**18a**).



Entry	Solvent ^a	Reaction Time	Yield (%) of 19a ^b	Notes / Observations
1	THF	3.5 h	90	colorless solution
2	Et ₂ O	6 h	90	orange solution
3	Bu ₂ O	24 h	84	colorless solution
4	DME	7.5 h	86	colorless solution
5	MTBE	24 h	-	SM consumed ^f
6	Pentane	24 h	-	precipitation ^d
7	Cyclohexane	2.5 h	-	precipitation ^d
8	Toluene	2 min	-	<i>Friedel-Crafts</i> -Alkylation
9	Ph ₂ O	3 h	-	<i>Friedel-Crafts</i> -Alkylation
10	Benzene	2 min	-	Diphenylmethane + Chlorobenzene ^e
11	DMF	24 h	n.r.	greenish solution ^f
12	NMP	24 h	n.r.	greenish solution ^f
13	DCM	1.5 h	-	decomposition ^g

^a Solvents were dried according to the standard procedures and stored over molecular sieves prior to use. ^b GC-yield of organometallic as determined by iodolysis in THF. ^c No detectable organometallic was formed. ^d A brownish precipitate occurred; no detectable organometallic was formed. ^e The starting material decomposed and both products were identified by GC-MS analysis. ^f No reaction of the benzylic chloride was observed. ^g A violent explosive reaction occurred; no detectable organometallic was formed.

The resulting benzylic reagent **19a**, prepared in THF, underwent a smooth Pd-catalysed cross-coupling reaction¹²⁵ in the presence of Zn(OAc)₂ (1.5 equiv) and PEPPSI-*i*Pr (1.7 mol%)¹²⁶ with ethyl 3-iodobenzoate (**21a**, 0.7 equiv) furnishing the functionalized diarylmethane **22a** in 89% yield (Table 11, Entry 1).¹²⁷ Using the same conditions, 2-chlorobenzyl chloride (**18b**) and 2-bromobenzyl chloride (**18c**)

¹²⁵ (a) Mingxing, Q.; Negishi, E. *Tetrahedron Lett.* **2005**, *46*, 2927. (b) Metay, E.; Hu, Q.; Negishi, E. *Org. Lett.* **2006**, *8*, 5773. (c) Negishi, E.; Qian, M.; Zeng, F.; Anastasia, L.; Babinski, D. *Org. Lett.* **2003**, *5*, 1597.

¹²⁶ (a) Organ, M. G.; Calimsiz, S.; Sayah, M.; Hoi, K. H.; Lough, A. J. *Angew. Chem. Int. Ed.* **2009**, *48*, 2383. (b) O'Brien, C. J.; Kantchev, E. A. B.; Valente, C.; Hadei, N.; Chass, G. A.; Lough, A.; Hopkinson, A. C.; Organ, M. G. *Chem. Eur. J.* **2006**, *12*, 4743. (c) Nasielski, J.; Hadei, N.; Achonduh, G.; Kantchev, E. A. B.; O'Brien, C. J.; Lough, A.; Organ, M. G. *Chem. Eur. J.* **2010**, *16*, 10844.

¹²⁷ In the absence of stoichiometric amounts of Zn(OAc)₂ almost no cross-coupling was observed. Both, the acetate anion and the zinc cation seem to be important. We speculate that the acetate anion is reducing the Lewis-acidity of the aluminium species whereas the zinc cation favors the transfer of the aryl group to palladium.

afforded the corresponding aluminium reagents (3-12 h, 20 °C) which reacted well with allyl bromide (**21b**, 0.7 equiv) or 4-chlorobenzoyl chloride (**21c**, 0.7 equiv) after transmetalation with Zn(OAc)₂ (1.5 equiv) and addition of CuCN·2LiCl (20 mol%).¹²⁸ The expected products (**22b-c**) were obtained in 46% and 83% yield (Table 11, Entries 2-3). Several fluorine-substituted benzylic chlorides (**18d-g**) could be readily converted to the aluminium reagents (**19d-g**, 20 °C, 6-24 h) and reacted with various unsaturated halides in Pd-catalysed cross-couplings ((Zn(OAc)₂ (1.5 equiv); PEPPSI-*i*Pr (1.7 mol %)) affording the functionalized diarylmethanes **22d-g** in 71-98% yield (Table 11, Entries 4-7). Besides electron-deficient benzylic chlorides, also electron-rich chlorides could be readily used with this procedure. Thus, 4-methylbenzyl chloride (**18h**) furnished the benzylic sesquichloride **19h** which underwent an acylation reaction with 2-furoyl chloride (**21h**, 0.7 equiv) affording the heterocyclic ketone **22h** in 62% yield (Table 11, Entries 8). Similarly, *ortho*-, *meta*- and *para*-methoxybenzyl chloride (**18i-k**) reacted with Al-powder (3.0 equiv) in the presence of InCl₃ (3 mol%) within 5-20 h at 20 °C providing the expected intermediate aluminium reagents **19i-k**. Transmetalation with Zn(OAc)₂ (1.5 equiv) and subsequent cross-coupling reactions produced the diarylmethanes **22i-k** in 78-82% yield (Table 11, Entries 9-11).

Table 11: Aluminium insertion into benzylic chlorides **18** and subsequent functionalization.

Entry	Benzylic Chloride	Insertion Time ^a	Electrophile ^b	Product ^c
1		3.5 h		 22a : 89%
2		12 h		 22b : 46%
3		3 h		 22c : 83%
4		22 h		 22d : 98%
5		6 h		 22e : 71%

¹²⁸ Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J.; *J. Org. Chem.* **1988**, *53*, 2390.

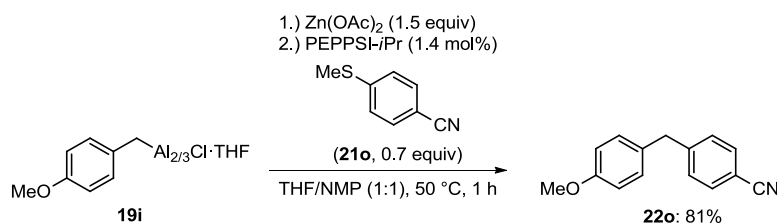
Entry	Benzyl Chloride	Insertion Time ^a	Electrophile ^b	Product ^c
6	 18f	6 h	 21f	 22f: 74%
7	 18g	24 h	 21g	 22g: 89%
8	 18h	3 h	 21h	 22h: 62%
9	 18i	5 h	 21i	 22i: 78%
10	 18j	12 h	 21j	 22j: 82%
11	 18k	20 h	 21j	 22k: 46%
12	 18l	7 h	 21l	 22l: 75%
13	 18m	3 h	 21m	 22m: 92%
14	 18m	3 h	 21n	 22n: 72%

^a Insertion time at 20 °C until GC-analysis of hydrolyzed reaction aliquots showed a conversion of the benzylic chloride of >95%. ^b 0.7 equiv of electrophile has been used. ^c Isolated yield of analytically pure product estimated to be of >95% purity as indicated by GC and NMR analysis.

Even 3,4,5-trimethoxybenzyl chloride (**18l**) or the thiomethyl substituted benzyl chloride **18m** could be readily used in this procedure and after a Cu(I)-mediated allylation reaction ($\text{Zn}(\text{OAc})_2$ (1.5 equiv),

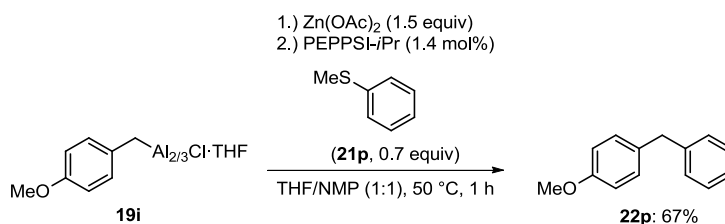
CuCN·2LiCl, -30 °C, 20 mol%) with ethyl (2-bromomethyl)acrylate¹²⁹ (**21l**, 0.7 equiv) or 3-bromocyclohexene (**21m**, 0.7 equiv) the functionalized alkenes **22l** and **22m** were isolated in 75% and 92% yield (Table 11, Entries 12-13). Similarly, the reaction of **18m** with the heterocyclic acid chloride **21n** (0.7 equiv) in the presence of Zn(OAc)₂ (1.5 equiv) and CuCN·2LiCl (10 mol%) furnished the expected ketone **22n** in 72% yield (Table 11, Entry 14).

During attempts to use the thiomethyl-substituted benzylic chloride **18m** in cross-coupling reactions we obtained side products, which indicated that the SMe-moiety underwent also oxidative addition of Pd. Cross-coupling reactions of zinc reagents in which a thioether can be used as electrophile are only known on electron poor heterocycles.¹³⁰ Thus, we tried a cross-coupling reaction of the *p*-methoxy-substituted aluminium reagent **19i** with the aryl thiomethyl ether (**21o**, 0.7 equiv) in the presence of Zn(OAc)₂ and PEPPSI-*i*Pr. Remarkably, the cross-coupling proceeded smoothly, furnishing the diarylmethane **22o** in 81% yield (Scheme 38).



Scheme 38: Thiomethyl cross-coupling of benzylic aluminium reagent **19i**.

In a similar way, the aluminium reagent **18i** also reacted with methyl(phenyl)sulfane (**21p**, 0.7 equiv) in a cross coupling reaction using the same conditions. The diarylmethane **22p** was isolated in 67% yield (Scheme 39).



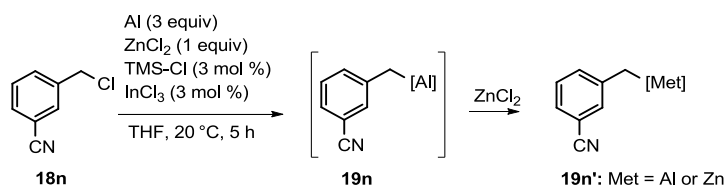
Scheme 39: Thiomethyl cross-coupling of benzylic aluminium reagent **19i**.

The fact that aromatic, non-activated SMe-groups can be used as alternative for halides in a cross-coupling reaction is not attributed to the released aluminium salts, as the benzylic reagent prepared by Zn-insertion in the presence of LiCl reacted equally well. It is highly likely that this reactivity can be attributed to the powerful catalytic system PEPPSI-*i*Pr. Further studies should be undertaken to explore the scope and generality of this method.

¹²⁹ (a) Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924. (b) Villieras, J.; Rambaud, M. *Org. Synth.* **1988**, 66, 220.

¹³⁰ A. Metzger, L. Melzig, C. Despotopoulou, P. Knochel, *Org. Lett.* **2009**, 11, 4228.

In the case of benzylic chlorides bearing an ester or nitrile functionality, as well as secondary benzylic systems the experimental procedure had to be modified. Although these benzylic chlorides reacted with Al-powder in the presence of InCl₃, the reaction resulted in low conversions, low yields of the aluminium reagent, or dimerization. Nevertheless, the addition of ZnCl₂ proved to be beneficial.¹³¹ Thus, 3-cyanobenzyl chloride (**18n**) reacted with Al-powder (3.0 equiv), InCl₃ (3 mol %) and ZnCl₂ (1.0 equiv) within 5 h, forming a mixture of the functionalized zinc and aluminium reagent **19n'** (Scheme 40). This has been verified by ¹H-, ¹³C- and ²⁷Al-NMR studies.



Scheme 40: *In situ* trapping strategy for insertion of Al into benzylic chlorides.

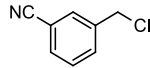

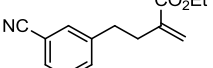
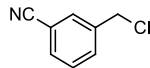
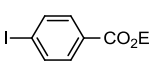
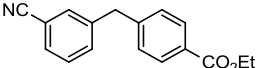
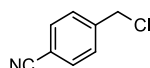
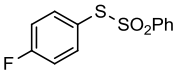
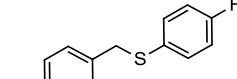
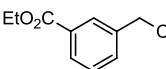
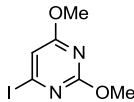
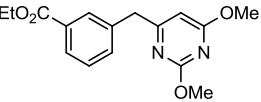
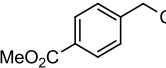

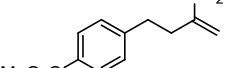
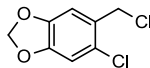

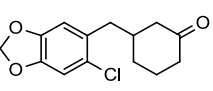
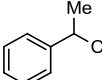

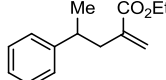
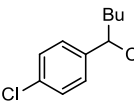
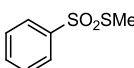
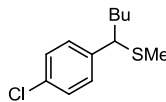
This benzylic organometallic was allylated with ethyl (2-bromomethyl)acrylate¹²⁹ (**21i**, 0.7 equiv) yielding the ester derivative **22q** in 93% yield (Table 12, Entry 1). A Pd-catalysed cross-coupling reaction with ethyl 4-iodobenzoate (**21q**, 0.7 equiv) furnished the functionalized diarylmethane **22r** in 56% yield (Table 12, Entry 2). Interestingly, a cyano group in *para*-position is also compatible with these reaction conditions and 4-cyanobenzyl chloride (**18o**) is converted to the expected organometallic which reacted with *S*-4-fluorophenyl benzenesulfonothioate (**21r**, 0.7 equiv) forming the thioether **22s** in 74% yield (Table 12, Entry 3). In the case of ester substituted benzylic chlorides (**18p-q**) the Al/ZnCl₂ method produced the expected benzylic organometallics which could be allylated in the presence of CuCN·2LiCl or underwent a cross-coupling reaction (PEPPSI-*i*Pr) affording the functionalized ester derivatives (**22t-u**) in 83% and 75% yield (Table 12, Entries 4-5). Piperonyl moieties are found in many pharmacologically active substances.¹³² Thus, the reaction of 5-chloro-6-(chloromethyl)benzo[d][1,3]dioxole (**18r**) with Al-powder and InCl₃ was performed (20 °C, 10 h). Without the presence of ZnCl₂ the *Wurtz*-coupling product is formed almost quantitatively. However, the use of a stoichiometric amount of ZnCl₂ allowed the formation of the intermediate organometallic within 8 h at 20 °C and after a Cu(I)-mediated 1,4-addition with cyclohexenone (**21t**) in the presence of TMS-Cl (2.5 equiv), the ketone **22v** was isolated in 68% yield (Table 12, Entry 6).¹³³ Secondary benzylic chlorides like **18s** or **18t** were also prone to dimerization during the insertion conditions but the use of ZnCl₂ prevented the dimerization and within 22 h full conversion to the benzylic reagents was readily achieved. Quenching with ethyl (2-bromomethyl)acrylate¹²⁹ (**21i**, 0.7 equiv) or *S*-methyl benzenesulfonothioate (**21u**, 0.7 equiv) afforded the ester **22w** and the thioether **22x** in 76% and 65% yield (Table 12, Entries 7-8).

¹³¹ a) Piller, F. M.; Appukkuttan, P.; Gavryushin, A.; Helm, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 6802. b) Piller, F. M.; Metzger, A.; Schade, M. A.; Haag, B. H.; Gavryushin, A.; Knochel, P. *Chem. Eur. J.* **2009**, *15*, 7192. c) Blümke, T. D.; Piller, F. M.; Knochel, P. *Chem. Commun.* **2010**, *46*, 4082.

¹³² a) Burton, W. H.; Budde, W. L.; Cheng, C.-C. *J. Med. Chem.* **1970**, *13*, 1009. b) Cahlikova, L.; Opletal, L.; Kurfurst, M.; Macakova, K.; Kulhankova, A.; Hostalkova, A. *Nat. Prod. Commun.* **2010**, *5*, 1751. c) Monge, A.; del Carmen Peña, M.; Palop, J. A.; Calderó, J. M.; Roca, J.; García, E.; Romero, G.; del Río, J.; Lasheras, B. *J. Med. Chem.* **1994**, *37*, 1320.

¹³³ Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *34*, 4029.

Table 12: InCl₃ catalysed aluminium insertion into functionalized benzyl chlorides and subsequent trapping with ZnCl₂ and various electrophiles.

Entry	Benzyl Chloride	Insertion Time ^a	Electrophile ^b	Product ^c
1	 18n	5 h	 21l	 22q: 93%
2	 18n	5 h	 21q	 22r: 56%
3	 18o	5 h	 21r	 22s: 74%
4	 18p	10 h	 21s	 22t: 83%
5	 18q	10 h	 21l	 22u: 75%
6	 18r	8 h	 21t	 22v: 68%
7	 18s	22 h	 21l	 22w: 76%
8	 18t	22 h	 21u	 22x: 65%

^a Insertion time at 20 °C until GC-analysis of hydrolyzed reaction aliquots showed a conversion of the benzylic chloride of >95%. ^b 0.7 equiv of electrophile have been used. ^c Isolated yield of analytically pure product estimated to be of >95% purity as indicated by GC and NMR analysis.

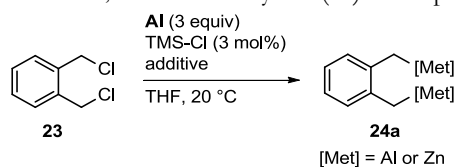
2.4 Preparation of Bis-Benzylic Organometallics

The preparation of allylic and benzylic organometallics by direct metal insertion is in general a difficult task, due to the stability of the intermediate allylic and benzylic radicals.¹³⁴ These stabilized radicals can leave the metal surface easily and are therefore – because of their longer lifetime – prone to *Wurtz*-coupling. The preparation of bis-benzylic organometallics makes the situation even worse. The results on the reaction of Al-powder with benzylic chlorides led us to a reinvestigation of the classical reaction between bis-benzylic chlorides and various metals in the presence of different additives. Starting with

¹³⁴ Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207.

aluminium, the control experiment showed that α,α' -dichloro-*o*-xylene (**23**) did not react with Al-powder within 24 h and even the addition of LiCl (3 equiv) did not lead to a sufficient activation of the metal surface (Table 13, Entries 1-2). Interestingly, the combination of Al-powder, LiCl (3 equiv) and 5% of InCl₃ did also not lead to any reaction, although this combination of additives leads to a reaction in the case of simple benzylic chlorides (Table 13, Entry 3).¹³⁵ Leaving out the LiCl suddenly results in the formation of the bimetallic **24a** in 15% yield within 10 h indicating that LiCl hampers the reaction, although InCl₃ is present as catalyst (Table 13, Entry 4). However, in the presence of ZnCl₂ (2 equiv) formation of the bimetallic was observed in 65% yield, showing that ZnCl₂ can overcome the deactivation by LiCl and additionally favors the formation of a bimetallic organometallic species (Table 13, Entry 5). This activation is clearly attributed to ZnCl₂ as the combination of Al, LiCl and ZnCl₂ also leads to the formation of the bimetallic in 52% yield (Table 13, Entry 6) but results in a lower yield and prolonged reaction time because of the absence of InCl₃ as catalyst. The deactivation by LiCl becomes clearly visible when the reaction is done without its presence. Thus, the combination of Al-powder and ZnCl₂ (2 equiv) results in fast formation of **24a** in 71% yield within 4.5 h at 20 °C even without the presence of InCl₃ as catalyst (Table 13, Entry 7). Nevertheless, InCl₃ still speeds up the reaction dramatically and the optimal combination of Al, ZnCl₂ and InCl₃ results in formation of **24a** in 70% yield within 1.75 h (Table 13, Entry 8). Remarkably, this combination allows for the first time the convenient preparation of bis-benzylic organometallics under mild conditions, without the need for dropwise addition of the starting material.

Table 13: Aluminium insertion into α,α' -dichloro-*o*-xylene (**23**) in the presence of different additives.



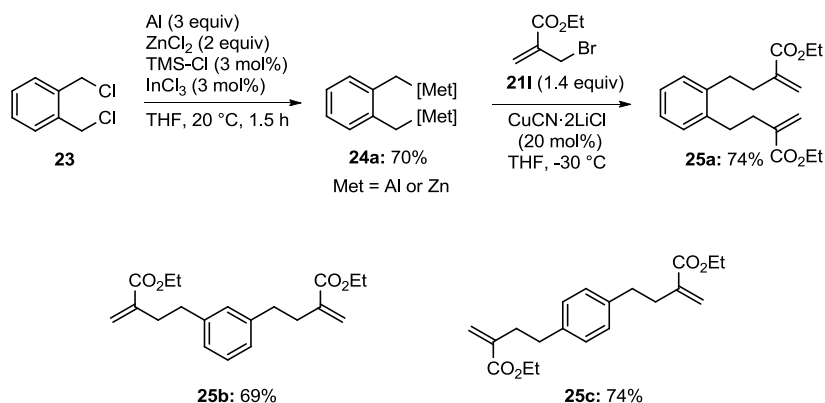
Entry	Additive ^a	Reaction Time ^b	Yield of 24a ^c
1	Al	24 h	n.r. ^d
2	Al, LiCl	24 h	n.r. ^d
3	Al, LiCl, InCl ₃	24 h	n.r. ^d
4	Al, InCl ₃	10 h	15%
5	Al, LiCl, ZnCl ₂ , InCl ₃	10 h	65%
6	Al, ZnCl ₂ , LiCl	23 h	52%
7	Al, ZnCl ₂	4.5h	71%
8	Al, ZnCl ₂ , InCl ₃	1.75 h	70%

^a LiCl (3 equiv); ZnCl₂ (2.2 equiv), InCl₃ (5 mol%). ^b Reaction time at 20 °C. ^c Yield of organometallic reagents determined by GC-analysis of reaction aliquots quenched with iodine in THF. ^d No reaction was observed.

The prepared bimetallic reagent **24a** underwent an allylation reaction with ethyl (2-bromomethyl)acrylate¹²⁹ (**211**, 0.7 equiv) furnishing the bis-functionalized benzene derivative **25a** in 74% yield (Scheme

¹³⁵ This combination of additives results usually in the formation of homo-coupling products.

41). The substitution pattern is not important as 1,3- and 1,4-bis-(chloromethyl)benzene reacted equally leading to **25b** and **25c** in 69% and 74% yield (Scheme 41).



Scheme 41: Preparation of bis-benzylic organometallics and subsequent allylation.

Inspired by the positive results with aluminium metal, we reinvestigated the reaction of **23** with Mg and various additives. As expected the reaction of **23** with Mg in THF rapidly lead to decomposition and the bimetallic **24b** was formed in approximately 8% yield (Table 14, Entry 1). The use of LiCl or InCl₃ as additive did not lead to any improvement (Table 14, Entries 2-3). The additional use of ZnCl₂ (2 equiv) again proved to be beneficial and although the reaction took much longer, the bimetallic was formed in 27% yield (Table 14, Entry 4). When InCl₃ was used in combination with ZnCl₂ the yield of the formed bimetallic rose to 34% (Table 14, Entry 5). Contrary to the results obtained with aluminium, LiCl did not hamper the reaction in the case of the Mg-insertion. The combination of Mg, LiCl and ZnCl₂ lead to formation of the expected bimetallic in 69% yield within 1 h at 20 °C, again without the need for dropwise addition of the xylene derivative (Table 14, Entry 6). Furthermore, InCl₃ speeds up the insertion reaction and the combination of all four additives afforded the bimetallic within 15 minutes in a similar yield (Table 14, Entry 7).

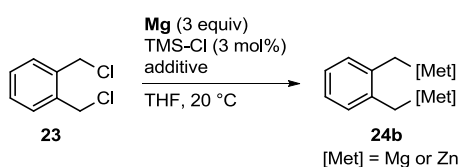
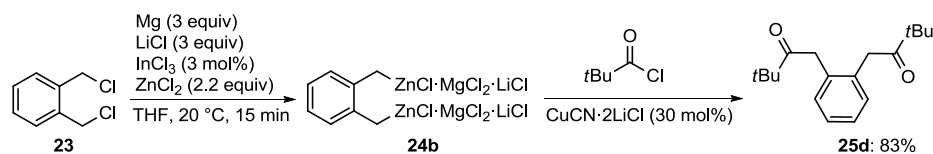


Table 14: Magnesium insertion into α,α' -dichloro-*o*-xylene (**23**) in the presence of different additives.

Entry	Additive ^a	Reaction Time ^b	Yield of 24b ^c
1	Mg	10 min	8%
2	Mg, LiCl	10 min	3%
3	Mg, InCl ₃	10 min	3%
4	Mg, ZnCl ₂	16 h	27%
5	Mg, ZnCl ₂ , InCl ₃	16 h	34%
6	Mg, ZnCl ₂ , LiCl	1 h	69%
7	Mg, ZnCl ₂ , LiCl, InCl ₃	15 min	71%

^a LiCl (3 equiv); ZnCl₂ (2.2 equiv), InCl₃ (5 mol%). ^b Reaction time at 20 °C. ^c Yield of organometallic reagents determined by GC-analysis of reaction aliquots quenched with iodine in THF.

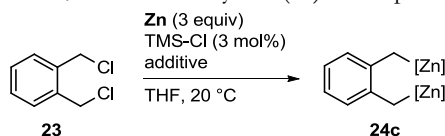
The so prepared reagent **24b** underwent a smooth acylation reaction in the presence of CuCN·2LiCl (30 mol%) with pivaloyl chloride (excess) leading to the diketone **25d** in 83% yield (Scheme 42).



Scheme 42: Preparation of bis-benzylic zinc-reagent **24b** and subsequent acylation.

Finally, we investigated the reaction of α,α' -dichloro-*o*-xylene (**23**) with Zn-powder. As expected no reaction took place between **23** and Zn-powder within 48 h (Table 15, Entry 1). Surprisingly, even in the presence of LiCl the benzylic chloride did not react (Table 15, Entry 2),¹³⁶ although the use of Zn and LiCl allows the preparation of a variety of benzylic zinc reagents.¹³⁷ This underlines the similarity of Al and Zn, as again the presence of LiCl hampers the reaction. The combination of Zn, LiCl and catalytic amounts of InCl₃ lead to complete decomposition of the starting material with no detectable organometallic reagent formed (Table 15, Entry 3). However, the simple combination of Zn-powder and InCl₃ (5 mol%) proved to be a successful preparation method for bis-benzylic zinc reagents and within 2.5 h at 20 °C the bimetallic was formed in 65% yield (Table 15, Entry 4).

Table 15: Zinc insertion into α,α' -dichloro-*o*-xylene (**23**) in the presence of different additives.



Entry	Additive ^a	Reaction Time ^b	Yield of 24c ^c
1	Zn	48 h	n.r. ^d
2	Zn, LiCl	48 h	n.r. ^d
3	Zn, LiCl, InCl ₃	24 h	decomposition ^e
4	Zn, InCl ₃	2.5 h	65%

^a LiCl (3 equiv); InCl₃ (5 mol%). ^b Reaction time at 20 °C. ^c Yield of organometallic reagents determined by GC analysis of reaction aliquots quenched with iodine in THF. ^d No reaction was observed. ^e No organometallic reagents was observed although starting material reacted.

Attempts to use In-powder for the insertion reaction did not lead to formation of an organometallic, regardless of the combination of additives.

In summary it could be shown, that Al, Zn and Mg metal can be used for the preparation of bis-benzylic organometallics. The combination of additives required for a successful insertion and formation of a bimetallic reagent is dependent on the nature of the metal. In the case of Al and Zn the use of LiCl prevents the formation of a bimetallic whereas it is needed in the case of Mg. The experiments have shown that InCl₃ is beneficial when Al and Mg are used for the reaction (leading to faster formation of the bimetallic reagent) and it is *required* for a smooth insertion of Zn. In all three cases no dropwise addition of

¹³⁶ Because of this unexpected result, the outcome of the reaction has been proved additionally by Dr. Albrecht Metzger and Andrej Angelowski.

¹³⁷ Metzger, A.; Schade, M. A.; Knochel, P. *Org. Lett.* **2008**, *10*, 1107.

the benzylic chloride is necessary and the reaction can be performed without cooling, at room temperature. This is a dramatic improvement of the former known preparation methods of bis-benzylic bimetallic reagents.

2.5 NMR Studies of the Transmetallation of Aluminium Reagents using Zn-Salts

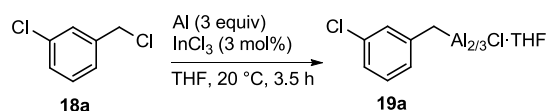
Several benzylic chlorides could not be successfully converted to the aluminium reagent by reaction with Al-powder in the presence of InCl_3 . Either the reaction was very slow, stopped, or dimerization of the benzylic reagents occurred. However, the additional use of a stoichiometric amount of ZnCl_2 proved to be beneficial and suddenly the insertion worked smoothly, leading readily to formation of benzylic organometallics. Of course it was not clear, whether ZnCl_2 is just additionally activating the aluminium surface, or *in situ* transmetallation is occurring leading to Zn reagents. We tried to clarify these questions by NMR studies. The strategy should be as follows:

1. Preparation of the organoaluminium reagent and measurement of the NMR spectra.
2. Preparation of the organozinc reagent by using Zn powder and measurement of the NMR spectra.
3. Analyse the NMR spectra of the *in situ* ZnCl_2 reaction and compare to 1 and 2.

As model system we chose 3-chlorobenzyl chloride (**18a**). This substrate can be converted relatively fast and in high yields to the pure organoaluminium compound, as well as to the pure Zn-reagent by using Zn-powder in the presence of LiCl. The high yield is important, as any side product formed will make analysis of the NMR spectra more difficult or even impossible.

2.5.1 NMR Spectra of the Benzylic Aluminium Reagent **19a**

It is generally accepted, that the insertion reaction of aluminium into any organic halide typically yields a mixture of R_2AlCl and RAlCl_2 .²³ That means, two sets of different protons and carbons can be expected in ^1H -NMR and ^{13}C -NMR spectroscopy resulting from the mixture. We prepared the aluminium reagent **19a** from 3-chlorobenzyl chloride (**18a**) by using the standard insertion conditions (Scheme 43). The remaining solution was separated from the Al-powder and the solvent removed completely under high vacuum. The remaining oil was dissolved in C_6D_6 and the resulting suspension filtrated through a syringe filter. ^1H -NMR, ^{13}C -NMR and ^{27}Al -NMR spectra were obtained from the filtrated solution.



Scheme 43: Preparation of benzylic aluminium reagent **19a** for subsequent NMR measurements.

As expected, the ^1H -NMR spectrum (Figure 3) showed the two relevant peaks of the benzylic protons resulting from the two aluminium compounds RAlCl_2 (1.81 ppm) and R_2AlCl (1.66 ppm). The integrals of the two signals correspond nearly to a ratio of 1:2 which shows that almost a 1:1 mixture of the two reagents is formed. A small amount of reagent was hydrolysed yielding 3-chlorotoluene (1.86 ppm). The

resulting methyl group signal can be seen next to the benzylic protons. As the NMR sample was dried under high vacuum prior to the measurement, it is remarkable, that the THF signal can also be seen, which proves that the reagents are obtained as THF-etherates and the THF is strongly coordinated to the aluminium centre and not easily removed.¹³⁸

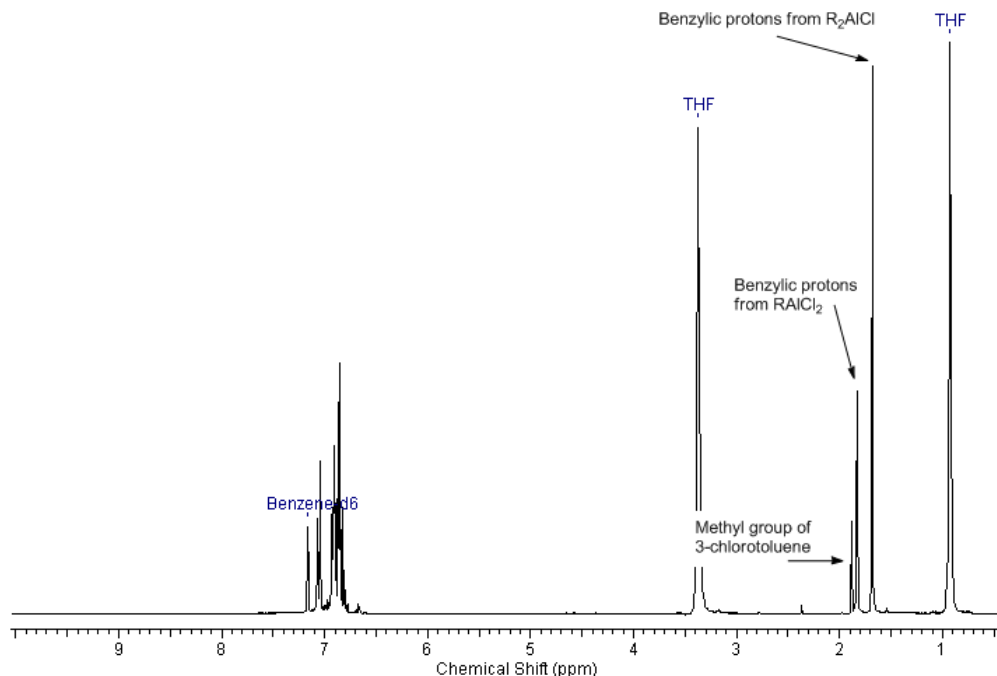


Figure 3: ¹H-NMR spectrum of the benzylic aluminium reagent **19a**.

Additionally, the ²⁷Al-NMR spectrum (Figure 4) shows clearly two intense signals (126.4 ppm and 53.5 ppm), which is consistent with the formation of a mixture of two compounds. A very sharp signal in between those compounds can be seen at 77 ppm. The sharpness of the signal is an indicator for a highly symmetric environment of the aluminium nucleus, which counteracts the quadrupole moment and therefore antagonizes the line broadening which is typically observed in ²⁷Al-NMR spectroscopy. This signal corresponds presumably to the AlCl₄ anion.

¹³⁸ Aluminium etherates have been thoroughly investigated and this is a typical phenomenon. Even prolonged heating times result rather in decomposition of the reagent, than in removal of the bound ether. For more information see reference 5.

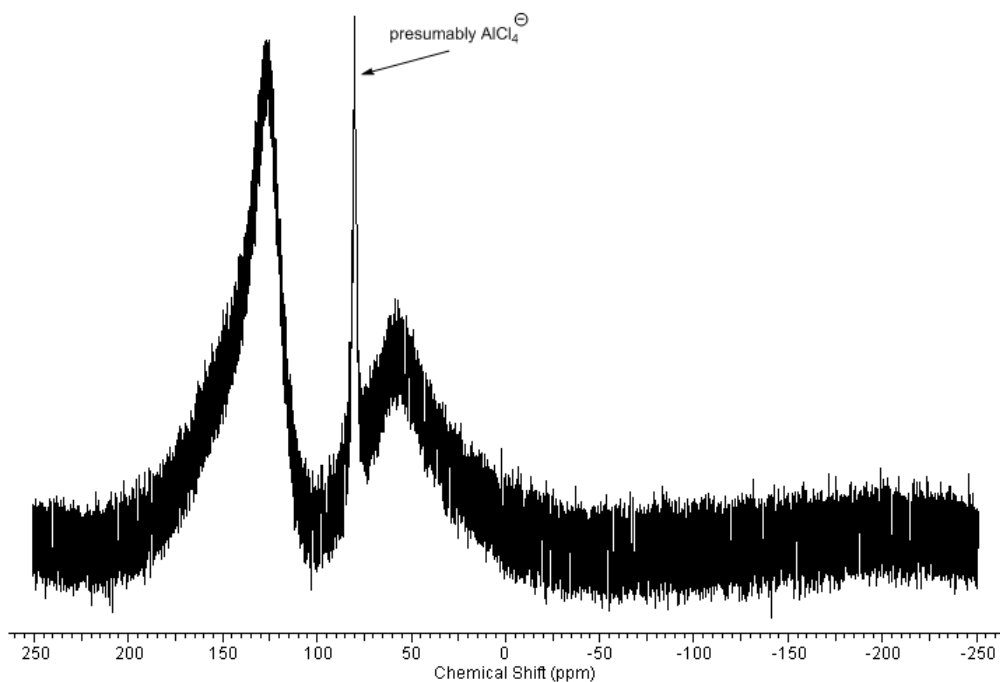


Figure 4: ^{27}Al -NMR spectrum of the benzylic aluminium reagent **19a**.

The ^{13}C -NMR spectrum (Figure 5) shows the benzylic carbon atom at 21 ppm. The broadening of the signals, due to the quadrupole moment of aluminium gives no resolution of the two organometallic species. Again, the methyl group signal resulting from hydrolysis can be seen next to the broad $\text{CH}_2\text{-Al}$ signal at 20.8 ppm. Also, an approximate 1:2 signal ration can be seen throughout the aromatic region and the carbon atoms of the two aluminium compounds have slightly different chemical shifts.

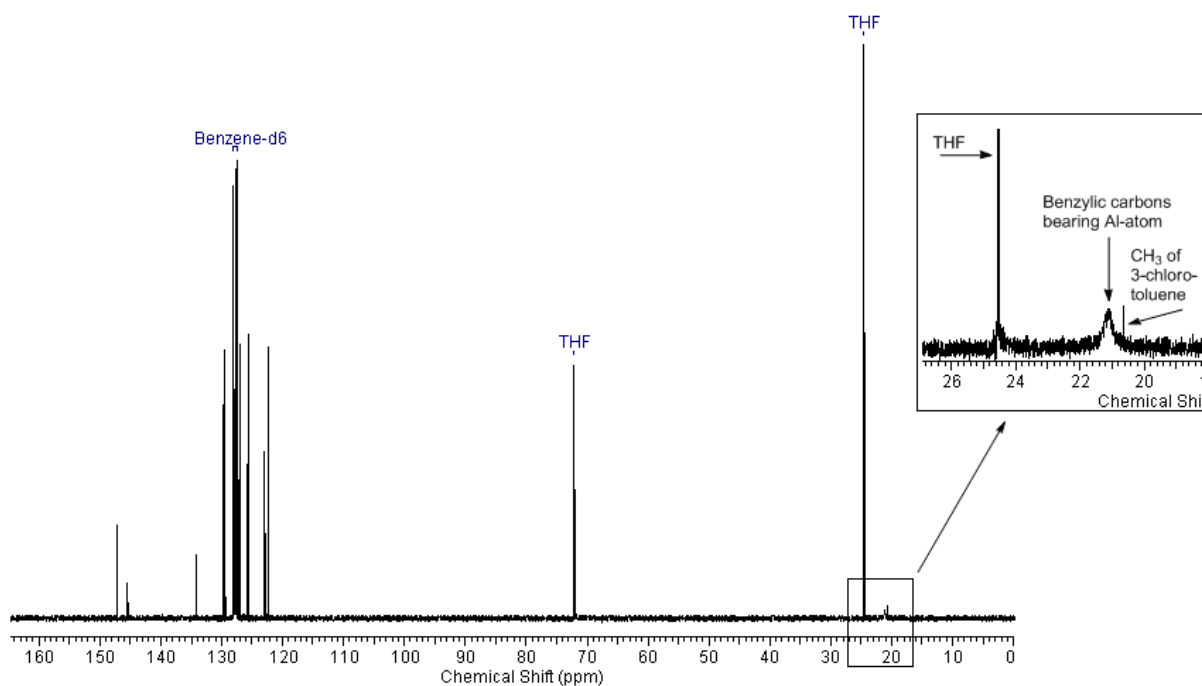
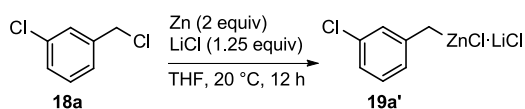


Figure 5: ^{13}C -NMR spectrum of the benzylic aluminium reagent **19a**.

2.5.2 NMR Spectra of the Benzylic Zinc Reagent **19a'**

The zinc reagent was prepared according to the known literature procedure.¹³⁹ The remaining solution was separated from the Zn-powder and the solvent removed completely under high vacuum. The remaining oil was dissolved in C₆D₆ and the resulting suspension filtrated through a syringe filter. NMR spectra were obtained from the filtrated solution.



Scheme 44: Preparation of benzylic zinc reagent **19a'** for subsequent NMR measurements.

The ¹H-NMR spectrum (Figure 6) shows the relevant CH₂-ZnCl peak at 2.15 ppm. A small amount of reagent was hydrolysed yielding 3-chlorotoluene. The resulting methyl group signal can be seen next to the benzylic protons at 1.89 ppm.

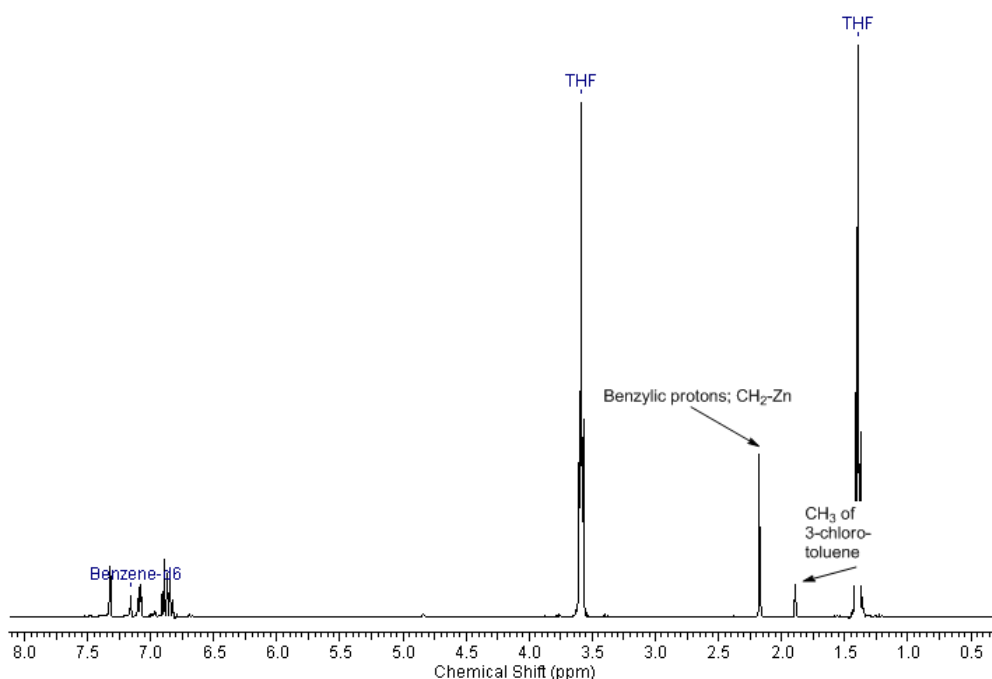


Figure 6: ¹H-NMR spectrum of the benzylic zinc reagent **19a'**.

The ¹³C-NMR spectrum (Figure 7) shows the benzylic carbon atom at 20.9 ppm. The chemical shift is almost the same as the corresponding aluminium reagent **19a**, showing the similar electronic nature of carbon-aluminium and carbon-zinc bonds. However, the signal is sharp and not broadened by a quadrupolar moment as in the case **19a** with aluminium. Again, the methyl group signal resulting from hydrolysis can be seen next to the CH₂-Zn signal (20.6 ppm).

¹³⁹ Metzger, A.; Schade, M. A.; Knochel, P. *Org. Lett.* **2008**, *10*, 1107.

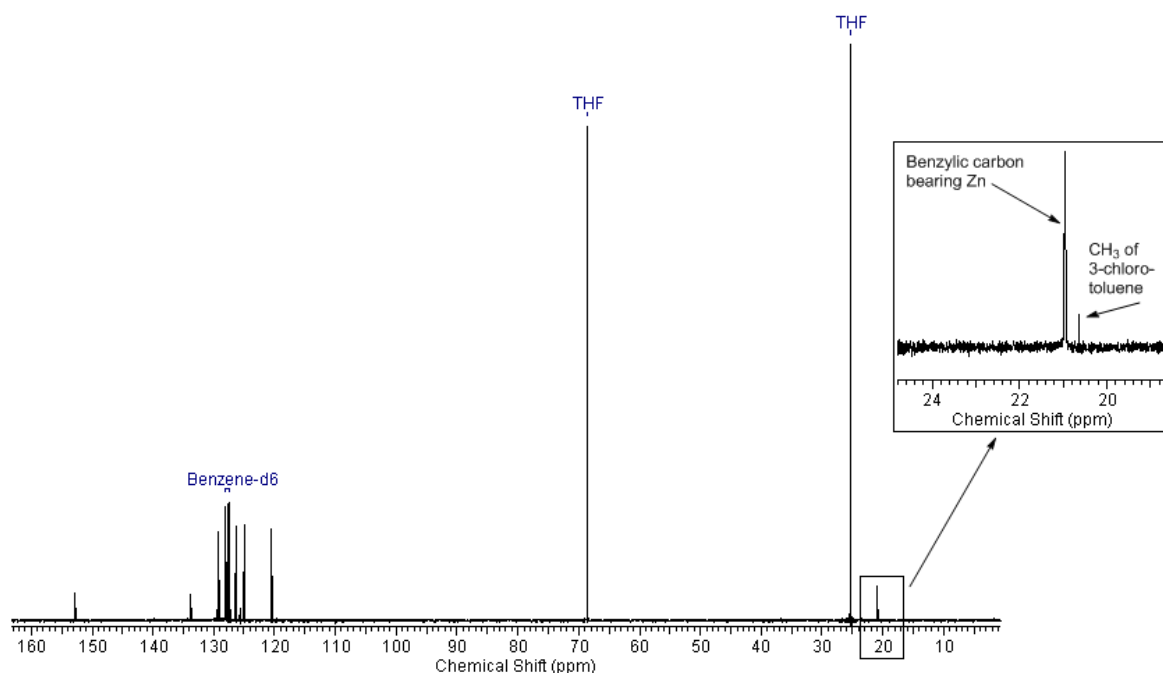
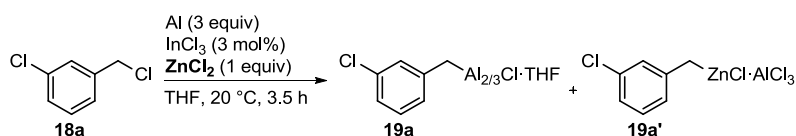


Figure 7: ^{13}C -NMR spectrum of the benzylic zinc reagent **19a'**.

2.5.3 NMR-Spectra of the Reagents Resulting From the *in situ* Experiments

With these spectra at hand we were able to investigate the NMR spectra from the *in situ* experiment. We treated 3-chlorobenzyl chloride (**18a**) with Al-powder (3 equiv), ZnCl_2 (1 equiv) and InCl_3 (3 mol%). Within 3.5 h full conversion of the starting material was achieved. The remaining solution was separated from the Al-powder and the solvent removed completely under high vacuum. The remaining oil was dissolved in C_6D_6 and the resulting suspension filtrated through a syringe filter. NMR spectra were obtained from the filtrated solution. From these spectra we can conclude that a mixture of aluminium reagent **19a** and zinc reagent **19a'** is obtained.



Scheme 45: InCl_3 -catalysed aluminium insertion in the presence of ZnCl_2 for subsequent NMR-measurements.

The ^1H -NMR spectrum shows several benzylic protons. From comparison with the previously obtained spectra of the pure organoaluminium and pure zinc reagent, we could make an assignment. The relevant $\text{CH}_2\text{-ZnCl}$ peak can be seen at 2.15 ppm. Additionally, the signals of the two aluminium compounds can also be seen again at 1.81 ppm (RAlCl_2) and 1.66 ppm (R_2AlCl). A small amount of reagent was hydrolysed yielding 3-chlorotoluene. The resulting methyl group signal can be seen next to the benzylic protons at 1.89 ppm. Integration of the signals let us conclude, that an almost 1:1 mixture of Zn an Al-reagent is obtained.

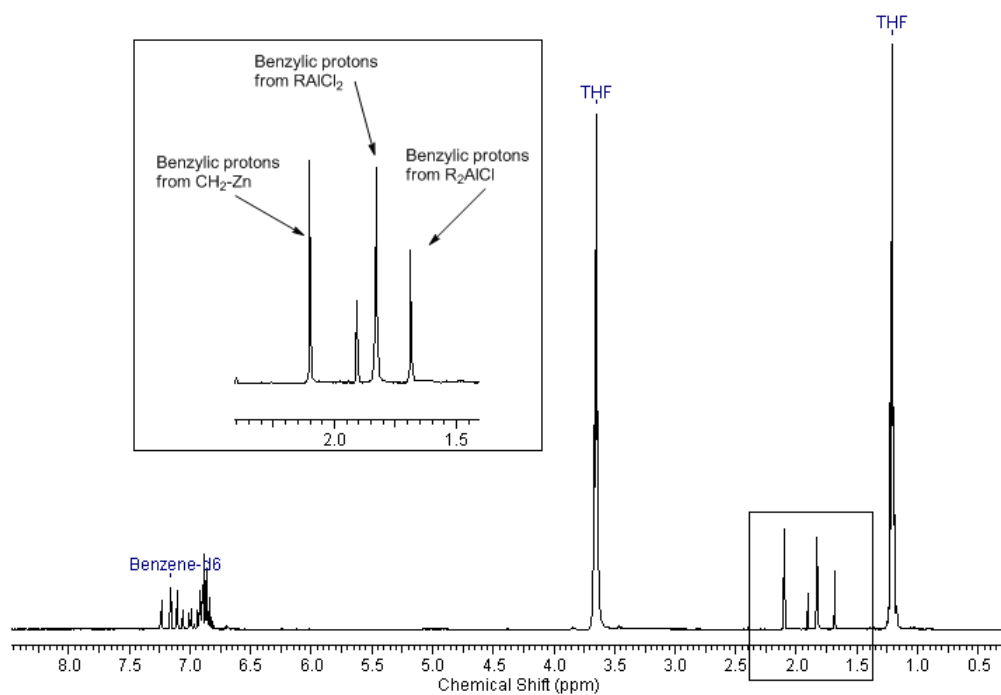


Figure 8: $^1\text{H-NMR}$ spectrum after *in situ* trapping of the aluminium reagent **19a**.

From the $^{13}\text{C-NMR}$ spectrum the mixture also becomes obvious. The benzylic carbon atom bearing the Zn atom can be seen as a sharp signal at 19.5 ppm as well as the broadened signal resulting from **19a** (21.1 ppm). Again, the methyl group signal resulting from hydrolysis can be seen at 20.7 ppm.

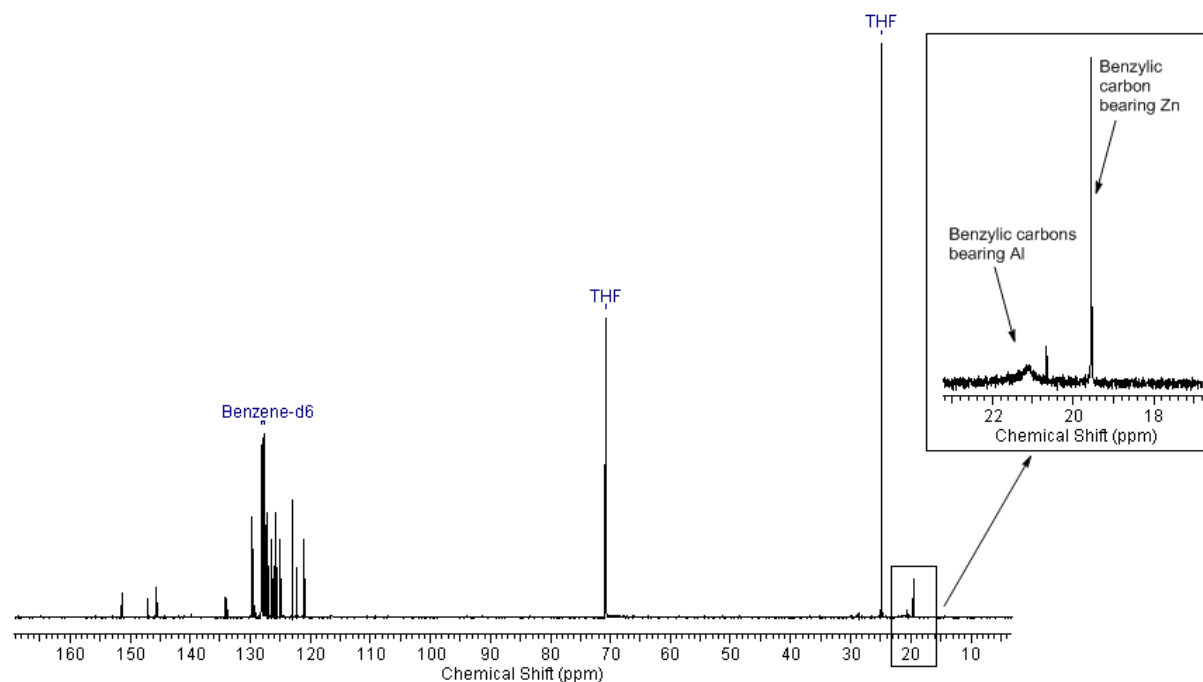


Figure 9: $^{13}\text{C-NMR}$ spectrum after *in situ* trapping of the aluminium reagent **19a**.

The $^{27}\text{Al-NMR}$ spectrum shows clearly the mixture of the two aluminium organometallics at 126 ppm and 56 ppm. The sharp peak in between corresponds presumably to the AlCl_4 anion.

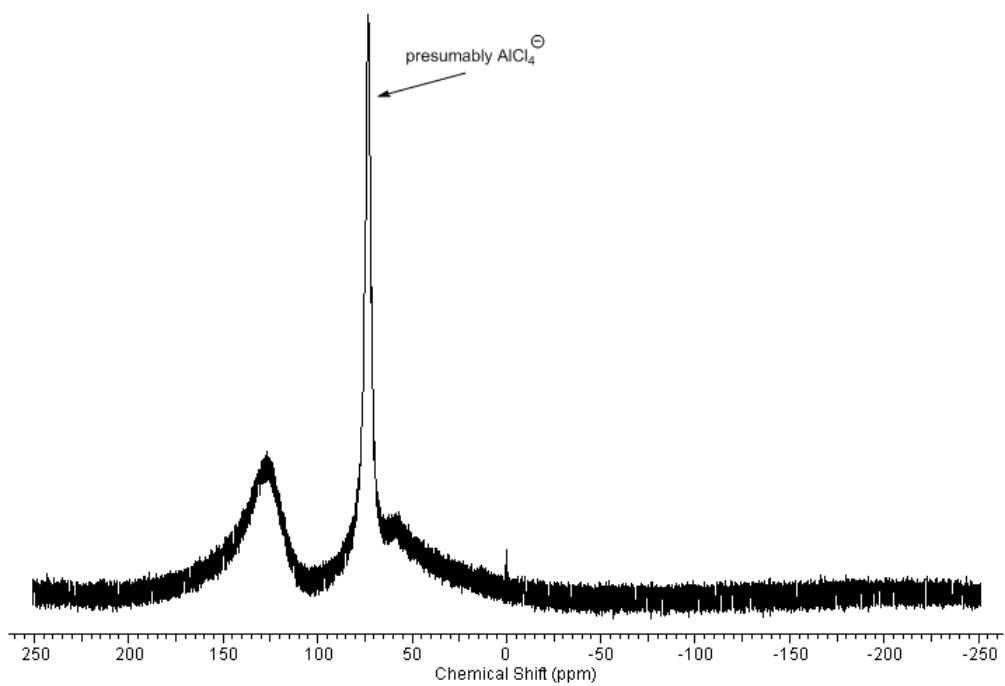


Figure 10: ^{27}Al -NMR spectrum after the *in situ* trapping of the aluminium reagent **19a**.

3 DIASTERESELECTIVE ADDITION OF ALLYLIC ALUMINIUM REAGENTS TO ALDEHYDES AND KETONES

3.1 Abstract

In the presence of catalytic amounts of InCl_3 various allylic bromides and even chlorides undergo reaction with aluminium powder in THF providing allylic aluminium sesquihalides. These aluminium organometallics undergo addition reaction to various functionalized aldehydes or ketones in a diastereoselective manner allowing the construction of two adjacent quaternary and tertiary centres. Remarkably, a broad range of functionalities is tolerated under the presented reaction conditions, including unprotected phenols.

3.2 Introduction

Allylic organometallics have been of interest to synthetic chemists since the early 1970's.¹⁴⁰ Whereas in the beginning people focused on the structural constitution of allyl metals and on the regioselectivity in reactions with electrophiles ($\text{S}_{\text{N}}2'$ vs. $\text{S}_{\text{N}}2$), the situation changed in the late 70's. Since more and more natural products and pharmacologically active substances were synthesized, which often require an exact control of the formation of one single diastereomer, or enantiomer, interest began to emerge whether stereo control of the C-C bond formation using allyl metals in the addition to aldehydes and ketones could be achieved. Since then a huge variety of allyl metals¹⁴⁰ has been prepared and subjected to addition reactions with several electrophiles including carbonyl compounds¹⁴¹ and imines.¹⁴² It could be shown that the addition proceeds in several cases with high diastereoselectivity.¹⁴³ Allylic boron and allylic zinc reagents have been, by far, the most studied allylic organometallics.¹⁴⁰ Allylic zinc reagents can nowadays be readily prepared by the reaction of allylic chlorides with Zn-powder in the presence of LiCl and their diastereoselective addition to carbonyl derivatives has been demonstrated.¹⁴⁴ Nevertheless, the preparation of allylic zinc reagents bearing sensitive functional groups (such as a cyano or an ester function) is limited due to the high reactivity of such allylic organometallics.¹⁴⁵ Besides zinc, aluminium is a metal which has many attractive features: it is of low toxicity, inexpensive and due to the low ionic character of the carbon-

¹⁴⁰ For an overview see: Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207.

¹⁴¹ S. R. Chemler, W. R. Roush in *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, Germany, **2000**, Chapter 10; b) S. E. Denmark, N. G. Almstead in *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, Germany, **2000**, Chapter 11; c) *Stereoselective Synthesis, Methods of Organic Chemistry (Houben-Weyl)*, (Eds.: G. Helmchen, R. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1996**, Vol. 3; d) S.-W. Li, R. A. Batey, *Chem. Commun.* **2004**, 1382; e) C. T. Buse, C. H. Heathcock, *Tetrahedron Lett.* **1978**, 1685; f) Y. Yamamoto, H. Yatagai, Y. Naruta, K. Maruyama, *J. Am. Chem. Soc.* **1980**, *102*, 7107; g) Y. Yatsumonji, T. Nishimura, A. Tsubouchi, K. Noguchi, T. Takeda, *Chem. Eur. J.* **2009**, *15*, 2680.

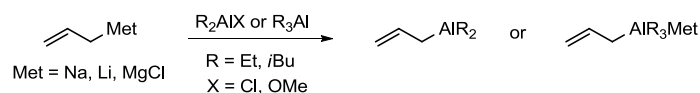
¹⁴² a) F. Barbot, L. Miginiac, *Synth. Commun.* **1997**, *27*, 2601; b) F. Barbot, *Tetrahedron Lett.* **1989**, *30*, 185.

¹⁴³ T. Basile, A. Bocoum, D. Savoia, A. Umani-Ronchi, *J. Org. Chem.* **1994**, *59*, 7766.

¹⁴⁴ a) H. Ren, G. Dunet, P. Mayer, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 5376; b) M. D. Helm, P. Mayer, P. Knochel, *Chem. Commun.* **2008**, 1916.

¹⁴⁵ a) N. E. Alami, C. Belaud, J. Villieras, *J. Organomet. Chem.* **1988**, *348*, 1-9; b) N. E. Alami, C. Belaud, J. Villieras, *J. Organomet. Chem.* **1988**, *353*, 157; c) M. Gaudemar, *Bull. Soc. Chim. Fr.* **1963**, *7*, 1475.

aluminium bond, it may tolerate a number of important functional groups.¹⁴⁶ Previously, allylic aluminium reagents were prepared by transmetallation using allylic sodium-, lithium- or magnesium reagents with dialkyl- or trialkylaluminium compounds, leading to mixed allyl-alkyl aluminium reagents or aluminates (Scheme 46).¹⁴⁷ Of course, the use of such reactive intermediates as lithium or sodium organyls precludes the presence of any functional group and is therefore not of much synthetic usefulness.



Scheme 46: Allylic aluminium reagents have previously been synthesized by transmetallation.

Additionally, allylic aluminium reagents have been prepared directly from aluminium powder according to *Gaudemar*¹⁴⁸ and *Miginiac*¹⁴⁹ using diethyl ether as solvent in the presence of a catalytic amount of HgCl₂.

Inspired by the results on the direct insertion of aluminium into aryl and benzylic halides, we envisaged a practical synthesis of functionalized allylic aluminium reagents using commercially available aluminium powder and a practical procedure for the preparation of homo-allylic alcohols in a diastereoselective fashion.

3.3 InCl₃-Catalysed Insertion of Aluminium to Allylic Halides

Preliminary studies have shown that an appropriate activation of aluminium is essential for achieving a smooth insertion to organic halides.^{150, 151} As InCl₃ proved to be quite efficient for the preparation of benzylic aluminium reagents we tested the reaction between simple allyl bromide (**26a**) and Al-powder (1.5 equiv) in the presence of a catalytic amount of InCl₃ (1 mol%) in THF. Within 2 h at 0 °C allyl bromide (**26a**) was converted to the sesquibromide **27a** which underwent a smooth addition to 2-bromobenzaldehyde (**28a**, 0.7 equiv, -78 °C, 1 h) furnishing the unsaturated alcohol **29a** in 87% yield (Scheme 47).

¹⁴⁶ Organoaluminium reagents: a) E.-i. Negishi, T. Takahashi, S. Baba, D. E. Van Horn, N. Okukado, *J. Am. Chem. Soc.* **1987**, *109*, 2393; b) E.-i. Negishi, *Acc. Chem. Res.* **1982**, *15*, 304; c) S.-L. Ku, X. Hui, C.-A. Chen, Y.-Y. Kuo, H.-M. Gau, *Chem. Commun.* **2007**, 3847; d) G. Zweifel, J. A. Miller in *Organic Reactions* (Ed.: W. G. Dauben), John Wiley & Sons, New York, **1984**.

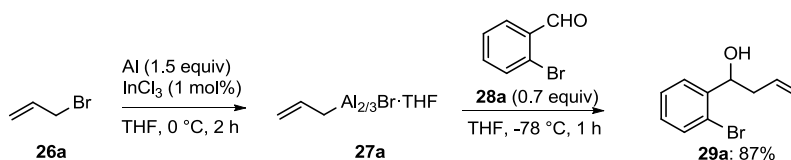
¹⁴⁷ a) D. B. Collum, J. H. McDonald, W. C. Still, *J. Am. Chem. Soc.* **1980**, *102*, 2118; b) M. Koreeda, Y. Tanaka, *J. Chem. Soc. Chem. Commun.* **1982**, 845; c) Y. Yamamoto, Y. Saito, K. Maruyama, *J. Organomet. Chem.* **1985**, *292*, 311; d) D. Hoppe, F. Lichtenberg, *Angew. Chem. Int. Ed.* **1982**, *21*, 372; e) D. Hoppe, F. Lichtenberg, *Angew. Chem. Int. Ed.* **1984**, *23*, 239. f) E. van Hiilsen, D. Hoppe, *Tetrahedron Lett.* **1985**, *26*, 411; g) Y. Yamamoto, H. Yatagai, K. Maruyama, *J. Am. Chem. Soc.* **1981**, *103*, 1969; *J. Chem. Soc. Chem. Commun.* **1980**, 1072.

¹⁴⁸ a) M. Gaudemar, *Bull. Soc. Chim. Fr.* **1958**, 1475; b) A. Stefani, P. Pino, *Hel. Chim. Acta*, **1972**, *55*, 1110.

¹⁴⁹ a) G. Picotin, P. Miginiac, *J. Org. Chem.* **1985**, *50*, 1299; b) L. Miginiac-Groizeleau, *Bull. Soc. Chim. Fr.* **1963**, 1449.

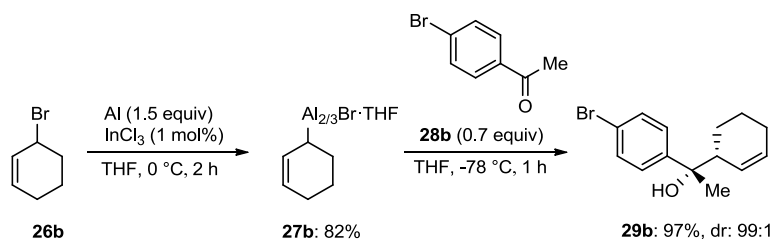
¹⁵⁰ Aluminium powder has been previously activated by PbCl₂, SnCl₂, TiCl₄ for insertion into allyl bromides and chlorides, see: a) K. Uneyama, N. Kamaki, A. Moriya, S. Torii, *J. Org. Chem.* **1985**, *50*, 5396; b) H. Tanaka, T. Nakahara, H. Dhimane, S. Torii, *Tetrahedron Lett.* **1989**, *30*, 4161; c) H. Tanaka, K. Inoue, U. Pokorski, M. Taniguchi, S. Torii, *Tetrahedron Lett.* **1990**, *31*, 3023.

¹⁵¹ For general activation of aluminium powder, see: S. Saito in *Science of Synthesis* (Ed.: H. Yamamoto), **2004**, vol. 7, p 5.



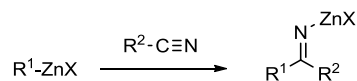
Scheme 47: Preparation of the allylic aluminium reagent **27a** and addition to 2-bromobenzaldehyde **28a**.

Similarly, as in the case of the benzylic halides, the additional use of LiCl led to almost quantitative dimerization. Additionally, the allyl bromide had to be added dropwise (syringe pump) to the reaction mixture, otherwise the reagent also underwent *Wurtz*-coupling immediately. In an analogous way we tested the reaction between a cyclic allylic bromide and Al-powder under the same conditions. Thus, 3-bromocyclohexene (**26b**) reacted with Al-powder (1.5 equiv) and InCl₃ (1 mol%) in THF at 0 °C within 2 h and provided the corresponding allylic aluminium reagent **27b** in 82% yield. Its reaction with 4'-bromoacetophenone (**28b**, 0.7 equiv, 1 h, -78 °C) led to the *syn*-homoallylic alcohol (**29b**) in 97% yield as single diastereoisomer (dr > 99:1)¹⁵² and surprisingly no enolization of the methyl ketone (and therefore protonation of the aluminium reagent) is observed (Scheme 48).



Scheme 48: Preparation of the allylic aluminium reagent **27b** and diastereoselective addition to 4'-bromoacetophenone (**28b**).

The reaction scope of such additions has been studied and we have found that the allylic aluminium reagent **27b** reacted well with variously substituted aromatic carbonyls. Thus, the addition to 4-chlorobenzaldehyde (**28c**, 0.7 equiv) furnished the homoallylic alcohol **29c** again as a single diastereoisomer in 91% yield (Table 16, Entry 1). Usually, cyano-substituents react rapidly with allylic organometallics such as zinc reagents (*Blaise* reaction, Scheme 49).¹⁵³



Scheme 49: Highly reactive organometallics usually attack cyano substituents (*Blaise* reaction).

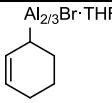
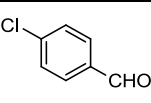
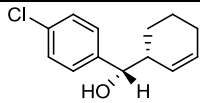
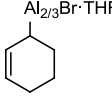
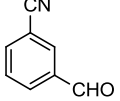
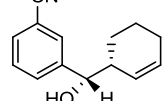
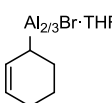
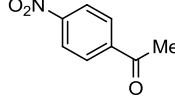
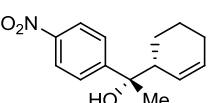
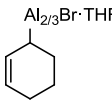
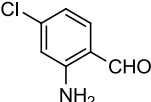
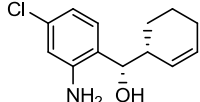
However, the addition of **27b** to the cyano substituted aldehyde (**28d**) proceeded well and the substituted alcohol **29d** was isolated in 98% yield (dr = 99:1), showing that no attack of the organometallic at the cyano-moiety occurred (Table 16, Entry 2). Moreover, nitro groups can be problematic in organometallic

¹⁵² The stereochemistry has been established by a comparison with the literature (¹H-NMR and ¹³C-NMR spectra): M. Yasuda, K. Hirata, M. Nishino, A. Yamamoto, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 13442.

¹⁵³ a) P. Knochel, J. F. Normant, *J. Organomet. Chem.* **1986**, *309*, 1; b) E. E. Blaise, *Compt. Rend.* **1901**, *132*, 478.

chemistry as they also readily react with organometallics.¹⁵⁴ Remarkably, despite the seemingly high nucleophilicity of the allylic aluminium reagents, the reagent **27b** added perfectly to 1-(4-nitrophenyl)ethanone (**28e**, 0.7 equiv) without reacting with the nitro group and the homoallylic alcohol **29e** (dr > 99:1) is isolated in 95% yield (Table 16, Entry 3). An unprotected amino group is also compatible with the aluminium reagent under these reaction conditions and the addition of **27** to 2-amino-5-chlorobenzaldehyde (**29f**, 0.7 equiv) affords the amino-alcohol **29f** (dr > 99:1) in 95% yield (Table 16, Entry 4).

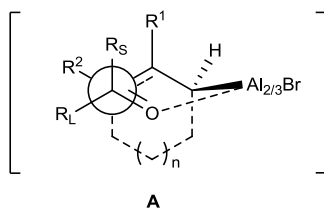
Table 16: Diastereoselective preparation of homoallylic alcohols of type **29** using allylic aluminium reagent **27b**.

Entry	Aluminium Reagent	Electrophile ^a	Product, Yield, dr ^b
1	 27b	 28c	 29c : 91%, 99:1
2	 27b	 28d	 29d : 98%, 99:1
3	 27b	 28e	 29e : 95%, 99:1
4	 27b	 28f	 29f : 95%, 99:1 ^c

^a 0.7 equiv of electrophile has been used. ^b Isolated yield of analytically pure product estimated to be of >95% purity as indicated by GC- and NMR analysis. ^c This experiment has been performed by Dr. Zhihua Peng is given here for the sake of completeness.

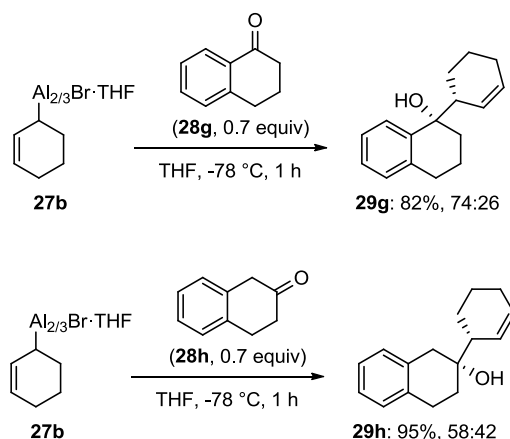
The stereochemical outcome of the reaction is best rationalized by a cyclic chair-like transition state **A** (Scheme 50). The oxophilic aluminium is coordinating to the carbonyl functionality, whereas the largest substituent of the carbonyl electrophile is oriented in the pseudo-equatorial position of the chair. In the case of aromatic aldehydes and ketones it can be clearly distinguished between the small (R_S) and the large (R_L) substituent and the aromatic ring system is located in the equatorial position leading to high diastereoselectivities (dr >99:1).

¹⁵⁴ a) T. Severin, *Angew. Chem.* **1958**, *70*, 164; b) T. Severin, M. Adam, *Chem. Ber.* **1964**, *97*, 186; c) G. Bartoli, *Acc. Chem. Res.* **1984**, *17*, 109; d) M. Makosza, J. Winiarski, *Acc. Chem. Res.* **1987**, *20*, 282; e) M. Makosza, *Synthesis* **1991**, 103; f) G. Bartoli, G. Palmieri, M. Bosco, R. Dalpozzo, *Tetrahedron Lett.* **1989**, *30*, 2129; g) A. Ricci, M. Fochi, *Angew. Chem. Int. Ed.* **2003**, *42*, 1444.



Scheme 50: Proposed cyclic chair-like transition state explaining the diastereoselective outcome of the addition of organoaluminium reagent to carbonyl derivatives.

In the case of α -tetralone (**28g**) and β -tetralone (**28h**) the situation is much more complex. Although the aluminium sesquibromide **27b** reacted with these aliphatic ketones, it is not easily possible to distinguish between the large and the small substituent because of the bicyclic structure, and therefore a decrease in diastereoselectivity is observed. Thus, the addition of **27b** to α -tetralone (**28g**, 0.7 equiv) furnished the *syn*-homoallylic alcohol **29g** in 82% yield, but with a diastereomeric ratio of 74:26 (Scheme 51). Remarkably, the organoaluminium reagent **27b** reacted also with β -tetralone (**28h**, 0.7 equiv) whereas the use of other organometallics derived from Li, Mg and even Zn led to enolization of the ketone and rapid decomposition. However, differentiation between R_L and R_S is not possible anymore leading to an almost 1:1 mixture of diastereoisomers of the alcohol **29h** (Scheme 51).



Scheme 51: Addition of aluminium reagent **27b** to easily enolizable ketones such as tetralones (**28g-h**).

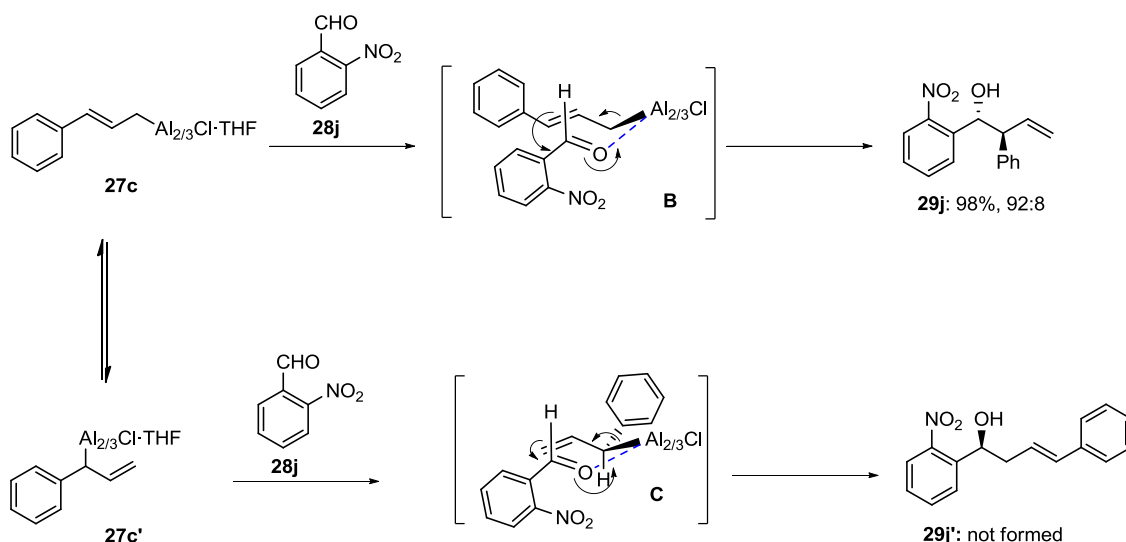
Similarly, the reaction of Al-powder (1.5 equiv) and InCl_3 (1 mol%) with cinnamyl chloride (**26c**) provided the aluminium reagent **27c** (73% yield) within 2 h at 25 °C. It reacted in an analogous way with aromatic ketones such 3,4-dichloroacetophenone (**28i**, 0.7 equiv) or aldehydes such as 2-nitrobenzaldehyde (**28j**, 0.7 equiv) furnishing the *anti*-homoallylic alcohols **29i** and **29j** in almost quantitative yield (92-98%) with good diastereoselectivity (Table 17, Entries 1-2).

Table 17: Diastereoselective preparation of homoallylic alcohols of type **29** using allylic aluminium reagent **27c**.

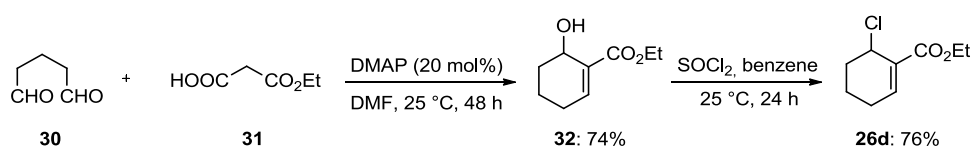
Entry	Aluminium Reagent	Electrophile ^a	Product, Yield, dr ^b
1			 29i : 92%, 92:8
2			 29j : 98%, 92:8

^a 0.7 equiv of electrophile have been used. ^b Isolated yield of analytically pure product estimated to be of >95% purity as indicated by GC- and NMR analysis.

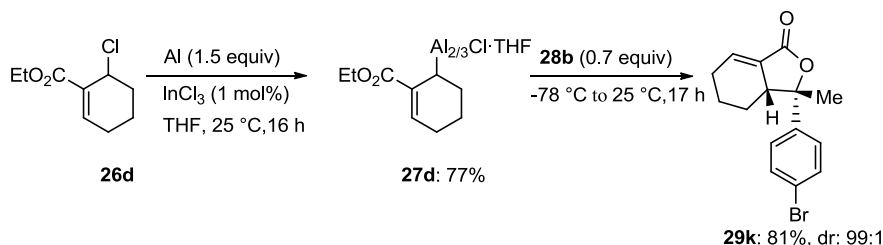
The stereoselectivity can again be rationalized by a cyclic chair-like transition state **B** (Scheme 52). The aluminium reagent **27c** could in principle isomerize leading to an organometallic **27c'**. The reaction would then proceed via the transition state **C**. However, the product **29j'** was not formed indicating that there is no significant isomerization (Scheme 52).

**Scheme 52:** Addition of the allylic aluminium reagent **27c** to 2-nitrobenzaldehyde (**28j**) and proposed cyclic chair-like transition state explaining the diastereoselective outcome of the reaction.

The next step was to investigate if functional groups like an ester can be tolerated during the insertion conditions. Thus, the cyclic allylic chloride bearing an ester moiety in *ortho*-position was readily prepared from simple glutaraldehyde (**30**) and ethyl malonic ester (**31**). Chlorination of the allylic alcohol **32** afforded the ester substituted cyclic allylic chloride **26d** in 76% yield (Scheme 53).

**Scheme 53:** Preparation of the cyclic allylic chloride **26d** bearing an ester group.

Remarkably, the ester functionality is well tolerated during the insertion conditions and the allylic chloride **26d** reacts with Al (1.5 equiv) in the presence of InCl₃ (1 mol%) furnishing the aluminium sesquichloride **27d** in 77% yield (25 °C, 16 h). It also reacted well with 4'-bromoacetophenone (**28b**, 0.7 equiv) and the diastereoselectively formed lactone **29k** (dr > 99:1) was isolated in 81% (Scheme 54).



Scheme 54: Preparation of the ester substituted allylic aluminium reagent **27d** and subsequent preparation of the lactone **29k**.

Interestingly, the reaction between the organoalane **27d** and 3-formylbenzonitrile **28d** did not lead to the formation of a lactone, instead, the uncyclized *syn*-alcohol **29l** was obtained in quantitative yield (dr = 95:5, Table 18, Entry 1). As most of the used electrophiles were electron deficient aldehydes or ketones, we wanted to test the reaction between the allylic aluminium reagent **27d** and an electron rich electrophile. Thus, we added **27d** to 4-dimethylaminobenzaldehyde (**28k**, 0.7 equiv) under the same reaction conditions. Although we expected prolonged reaction times, no significant change was noticed. The reagent underwent smooth addition to the electron rich carbonyl (1h, -78 °C) and the corresponding uncyclized *syn*-alcohol **29m** was formed with good diastereoselectivity (dr = 94:4) in 96% yield (Table 18, Entry 2).

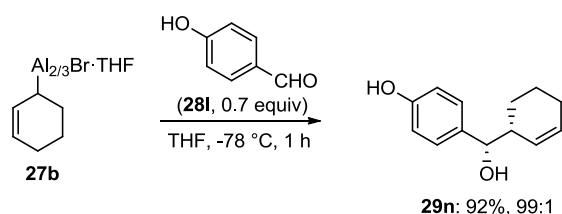
Table 18: Diastereoselective preparation of homoallylic alcohols of type **29** using allylic aluminium reagent **27d**.

Entry	Aluminium Reagent	Electrophile ^a	Product, Yield, dr ^b
1			 29l : 99%, 95:5
2			 29m : 96%, 94:6

^a 0.7 equiv of electrophile have been used. ^b Isolated yield of analytically pure product estimated to be of >95% purity as indicated by GC- and NMR analysis.

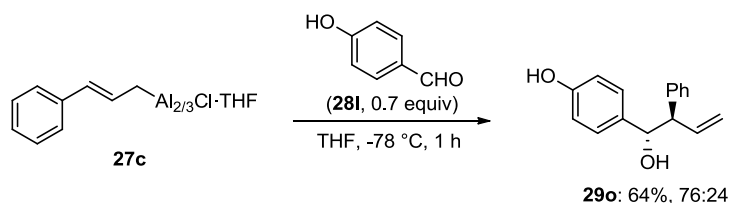
3.4 Tolerance of Acidic Protons – Addition to Carbonyls in the Presence of Unprotected Phenols

The results so far had shown that the allylaluminiums exhibit a great nucleophilicity towards carbonyl groups without attacking sensitive functionalities like ester, cyano or even nitro groups. Moreover, this seemingly high nucleophilicity was not accompanied by high basicity, as the reagents did not react with acidic protons in acetophenones. Even addition to α -tetralone or β -tetralone could be performed well, although both systems are easily enolized by other organometallics. These results tempted us to test addition to carbonyls in the presence of really acidic protons such as unprotected phenols (pKa \sim 10). Thus, we tried an addition reaction of the cyclic aluminium reagent **27b** to 4-hydroxybenzaldehyde (**28l**, 0.7 equiv). To our delight the addition proceeded smoothly without significant deprotonation of the free hydroxyl group and the corresponding *syn*-alcohol **29n** (dr > 99:1) was formed in 92% yield (Scheme 55).



Scheme 55: Addition of the allylic aluminium reagent **27b** to aldehyde **28l** bearing an acidic unprotected hydroxy group.

The cinnamyl reagent **27c** prepared from cinnamyl chloride (**26c**) reacted also with 4-hydroxybenzaldehyde (**28l**, 0.7 equiv) leading to the *anti*-homoallylic alcohol **29o** (dr = 76:24) in 64% yield (Scheme 56).



Scheme 56: Addition of the allylic aluminium reagent **27c** to aldehyde **28l** bearing acidic unprotected hydroxy group.

These preliminary results show clearly that allylic organoaluminiums exhibit high nucleophilicity to carbonyl functions, but are in contrast only weakly basic, allowing the tolerance of unprotected acidic protons. Further investigations should be undertaken, as this could lead to a powerful synthetic methodology in which unnecessary protection/deprotection steps could be avoided. This could be very important and may have a big influence e.g. in sugar chemistry.

4 CATALYSED ALUMINIUM INSERTION INTO ALKYL HALIDES

4.1 Abstract

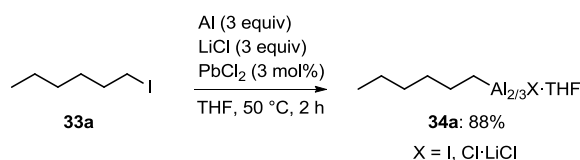
Preliminary results show that the additive catalysed insertion of aluminium powder can also be extended to alkyl halides.

4.2 Introduction

The reaction between ethyl iodide and aluminium was the first published preparation of an aluminium organometallic.²³ Since then this reaction has been studied and has even led to industrial processes (*Hüls-Process*).²³ Unfortunately this process suffers from several drawbacks, limiting the wide applicability. Typically high temperatures are needed. Additionally, only alkyl halides with a chain length of 1-4 can be conveniently converted to alkylaluminiums.²³ The longer the alkyl chain, Lewis-acid-catalysed elimination of hydrogen halide from the alkyl halide occurs more easily. This results in an overall autocatalytic formation of alkane, alkene, polymers, aluminium halide and hydrogen halide.¹⁵⁵ Extensions of a catalysed aluminium insertion into alkyl halides with longer chain lengths would be highly desirable, even more when the reaction can be performed under mild conditions. Inspired by the excellent results obtained with the catalysed insertion into aryl-, benzyl- and allylic halides we envisaged that this methodology may also be applied to higher alkyl chains.

4.3 Preliminary Results

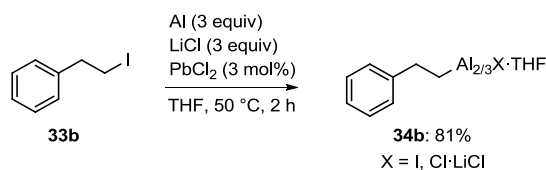
In preliminary studies we tried the reaction between a typical alkyl iodide, such as 1-iodohexane (**33a**), and aluminium powder (3 equiv) in the presence of LiCl (3 equiv) and catalytic amounts of an additive. So far, the aluminium insertion performed most efficiently when TiCl₄, InCl₃, BiCl₃ or FeCl-TPP was used as catalyst. But even in the presence of these salts, aluminium did not insert readily into the alkyl iodide. Interestingly, only the presence of PbCl₂ (3 mol%) led to formation of the alkyl aluminium sesquihalide **34a** in 88% yield within 2 h at 50 °C.



Scheme 57: Aluminium insertion into hexyl iodide (**33a**).

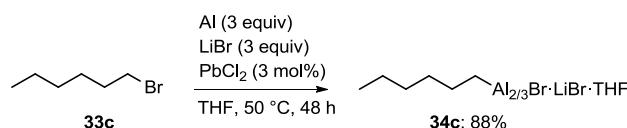
¹⁵⁵ a) S. Pasynkiewicz, W. Dahlig, M. Cieslak, *Roczniki Chem.* **1961**, *35*, 1283; b) A. G. Pozamantir, M. L. Genusov, *J. Gen. Chem. USSR Engl. Transl.* **1962**, *32*, 149.

Furthermore, with these reaction conditions at hand, the alkyl iodide **33b** could also be converted (2 h, 50 °C) to the corresponding alkyl aluminium reagent (**34b**, 81% yield).



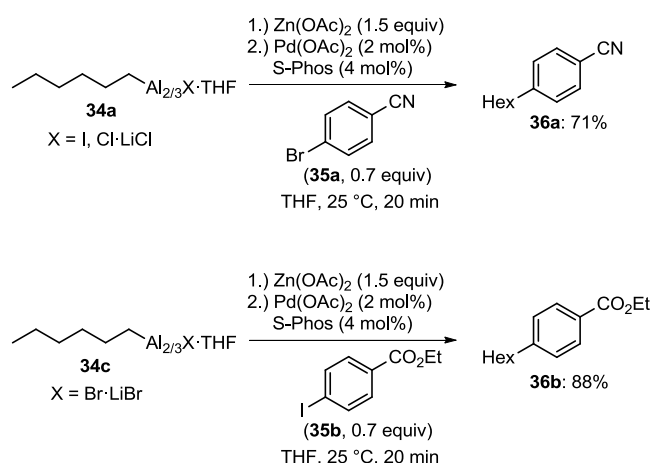
Scheme 58: Aluminium insertion into alkyl iodide **33b**.

In the case of alkyl bromides the use of LiCl proved to be unsatisfactory. The reaction conditions led only to substitution of the bromide, furnishing the corresponding alkyl chloride. To overcome this problem we utilized LiBr instead of LiCl. Thus, the reaction of 1-bromohexane (**33c**) with Al-powder (3 equiv), LiBr (3 equiv) and PbCl₂ (3 mol%) furnished the aluminium reagent **34c** in 88% yield after 48 h at 50 °C.



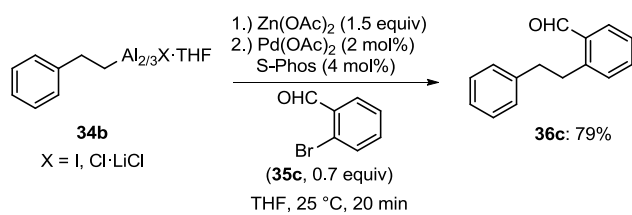
Scheme 59: Aluminium insertion into alkyl bromide **33c**.

The previously formed hexylaluminium reagent (**34a**) underwent a Pd-catalysed cross-coupling reaction with 4-bromobenzonitrile (**35a**, 0.7 equiv) or ethyl 4-iodobenzoate (**35b**, 0.7 equiv) in the presence of Zn(OAc)₂ (1.5 equiv) and Pd(OAc)₂ (2 mol%), in combination with S-Phos (4 mol%) as ligand. The alkylated nitrile **36a** and the alkylated benzoic acid ester **36b** were isolated in 71% and 88% yield (Scheme 60). The use of PEPPSI-*i*Pr (1.4 mol%) did not lead to a successful cross-coupling reaction, as *beta* hydride elimination occurred to a large extent and therefore lower yields of product were observed.



Scheme 60: Cross-coupling reaction of alkyl aluminium reagents **34a** and **34c** after transmetalation with Zn(OAc)₂.

In a similar way the alkyl aluminium reagent **34b** was converted to the alkylated aldehyde **36c** in 79% yield, by a successful cross-coupling reaction with 2-bromobenzaldehyde (**35c**, 0.7 equiv) using the same conditions.



Scheme 61: Cross-coupling of alkyl aluminium reagent **34b** in the presence of an aldehyde functionality.

5 InCl₃-MEDIATED PREPARATION OF 1,2-BIMETALLICS

5.1 Abstract

Catalytic amounts of indium additives allow the formation of 1,2-bimetallics from aromatic dibromides or *ortho*-bromo triflates by direct insertion of aluminium powder. These bimetallics can be bis-functionalized affording interesting compounds for pharmaceutical or material science. Moreover, InCl₃ also accelerates the insertion of Zn-powder into aryl halides. Thus, highly functionalized bimetallics derived from Zn can be obtained.

5.2 Introduction

Organometallics containing two carbon-metal bonds (bimetallics) often show unique reactivity patterns and have found several synthetic applications.¹⁵⁶ The chemical properties of such organometallics are dependent on the nature of the two metals and on the distance (number of carbon atoms) that separates them.¹⁵⁷ Whereas 1,*n*-bimetallic compounds (*n* = 1, 3-6)¹⁵⁸ have been prepared by several methods and efficiently employed as multicoupling reagents, the preparation of organometallics bearing two adjacent carbon-metal bonds (1,2-bimetallics) is in general difficult. Since the first synthesis of 1,2-dilithiobenzene from Hg-organometallics by Wittig and Bickelhaupt¹⁵⁹ only a few progresses have been made. The reduction of acetylenes with Li-metal at low temperatures (-78 °C) has led to 1,2-dilithio-alkenes.¹⁶⁰ Metal exchange reactions or transition metal catalysed trapping of arynes furnished 1,2-bimetallics from boron,¹⁶¹ aluminium,¹⁶² tin¹⁶³ and silicon¹⁶⁴. However, the direct insertion (oxidative addition) of a metal into a substrate such as 1,2-dibromobenzene would be the most straightforward method to generate a bimetallic, but all attempts so far have proved to be highly problematic.¹⁶⁵ Due to the thermal instability of the intermediately formed *ortho*-halo organometallic, side reactions are occurring, leading to low yield of the bimetallic.¹⁶⁶ The best results so far have been obtained using zinc powder, which can be rationalized by

¹⁵⁶ F. Bickelhaupt, *Angew. Chem.* **1987**, *99*, 1020.

¹⁵⁷ a) P. Knochel, J. F. Normant, *Tetrahedron Lett.* **1986**, *27*, 1039; b) C. E. Tucker, S. A. Rao, P. Knochel, *J. Org. Chem.* **1990**, *55*, 5446. c) J. J. Eisch, A. Piotrowski, *Tetrahedron Lett.* **1983**, *24*, 2043; d) F. N. Tebbe, G. W. Parshall, G. S. Reddy, *J. Am. Chem. Soc.* **1978**, *100*, 3611; e) S. H. Pine, R. Zahler, P. A. Evans, R. H. Grubbs, *J. Am. Chem. Soc.* **1980**, *102*, 3270; f) S. H. Pine, G. S. Shen, H. Hoang, *Synthesis*, **1991**, 165.

¹⁵⁷ a) M. S. Sell, M. V. Hanson, R. D. Rieke, *Synth. Commun.* **1994**, *24*, 2379; b) L. Zhu, R. M. Wehmer, R. D. Rieke, *J. Org. Chem.* **1991**, *56*, 1445; c) S. A. Rao, P. Knochel, *J. Org. Chem.* **1991**, *56*, 4591.

¹⁵⁸ a) L. Zhu, R. M. Wehmer, R. D. Rieke, *J. Org. Chem.* **1991**, *56*, 1445; b) S. A. Rao, P. Knochel, *J. Org. Chem.* **1991**, *56*, 4591.

¹⁵⁹ G. Wittig, F. Bickelhaupt, *Chem. Ber.* **1958**, *91*, 883.

¹⁶⁰ a) A. Maercker, U. Girreser, *Tetrahedron*, **1994**, *50*, 8019; b) A. Maercker, U. Girreser, *Angew. Chem.* **1990**, *102*, 718; c) A. Maercker, M. Kemmer, H. Wang, D.-H. Dong, M. Szwarc, *Angew. Chem.* **1998**, *37*, 2136.

¹⁶¹ H. Yoshida, K. Okada, S. Kawashima, K. Tanino, J. Ohshita, *Chem. Commun.* **2010**, *46*, 1763.

¹⁶² J. J. Eisch, K. Mackenzie, H. Windisch, C. Krüger, *Eur. J. Inorg. Chem.* **1999**, 153.

¹⁶³ a) H. Yoshida, K. Tanino, J. Ohshita, A. Kunai, *Angew. Chem. Int. Ed.* **2004**, *43*, 5042; b) H. Yoshida, K. Tanino, J. Ohshita, A. Kunai, *Chem. Commun.* **2005**, 5678; c) For another route to tin bimetallics see: T. N. Mitchell, K. Böttcher, P. Bleckmann, B. Costisella, C. Schwittek, C. Nettelbeck, *Eur. J. Org. Chem.* **1999**, 2413.

¹⁶⁴ H. Yoshida, J. Ikadai, M. Shudo, J. Ohshita, A. Kunai, *J. Am. Chem. Soc.* **2003**, *125*, 6638.

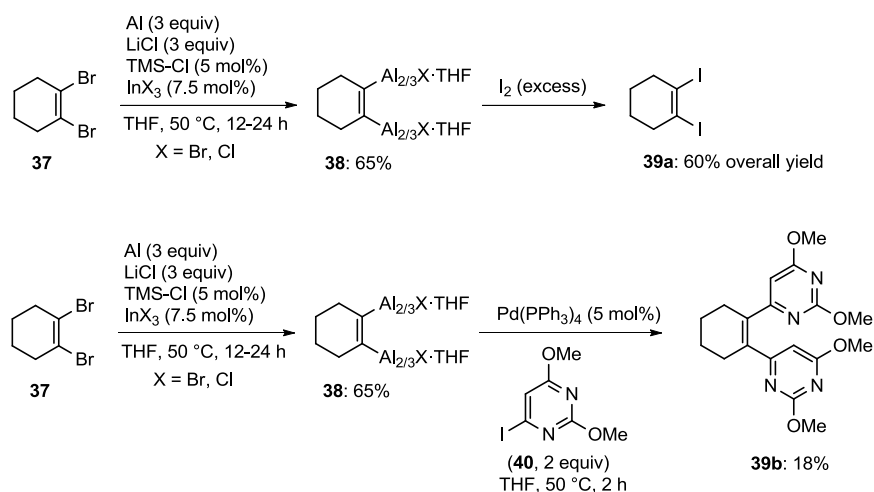
¹⁶⁵ a) M. A. G. M. Tinga, G. Schat, O. S. Akkerman, F. Bickelhaupt, E. Horn, H. Kooijman, W. J. J. Smeets, A. L. Smeets, A. L. Spek, *J. Am. Chem. Soc.* **1993**, *115*, 2808; b) G. Wittig, *Angew. Chem.* **1957**, *69*, 245; c) F. A. Hart, F. G. Mann, *J. Chem. Soc.* **1957**, 3939.

¹⁶⁶ a) L. S. Chen, C. J. Chen, C. Tamborski, *J. Organomet. Chem.* **1980**, *193*, 283; b) G. Wittig, *Angew. Chem. Int. Ed.* **1965**, *4*, 731.

the more covalent character of the carbon-metal bond compared to metals like Li or Mg.¹⁶⁷ Besides zinc, aluminium has proved to insert readily into various unsaturated halides after successful activation of the metal surface by various additives. Because of its similar electronegativity (Al: 1.66, Zn: 1.65)¹⁶⁸ we envisioned that Al could be used for the preparation of bimetallic species. Herein, we report the first synthesis of 1,2-aluminium bimetallics by direct insertion of Al powder into 1,2-substituted halides, in the presence of LiCl and a catalytic amount of InCl₃. Moreover we want to report that InCl₃ has also a dramatic accelerating effect on the insertion rate of Zn powder leading to highly functionalized 1,2-dizinc-organometallics.

5.3 InCl₃-Mediated Preparation of 1,2-Aluminium Bimetallics

In preliminary experiments we added 1,2-dibromocyclohexene (**37**) to Al powder (3 equiv), LiCl (3 equiv) and InCl₃ (7.5 mol%) in THF. Remarkably, no monometallic reagent was formed, but instead the reaction furnished directly the 1,2-bimetallic aluminium reagent **38** in ca. 65% yield within 24 h at 50 °C.¹⁶⁹ It reacted well with iodine and the resulting 1,2-diiodocyclohexene **39a** was isolated in 60% overall yield (Scheme 62). The bimetallic **38** also underwent a cross-coupling reaction with the iodo-uracil derivative **40** furnishing the bis-functionalized alkene **39b** in 18% yield (Scheme 62).



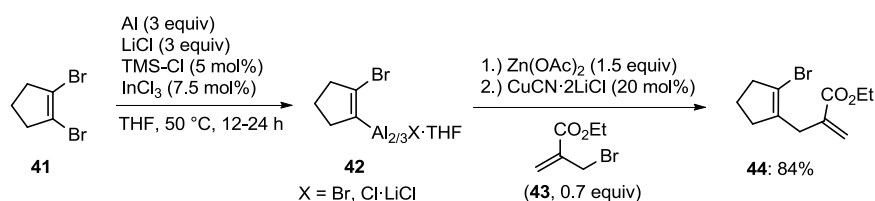
Scheme 62: Preparation of the cyclohexenyl 1,2-bimetallic **38** and subsequent functionalization.

In contrast, the reaction of the analogous five-membered ring **41** did not lead to a bimetallic reagent, but furnished exclusively the monometallic aluminium reagent **42**. It reacted well in a Cu-catalysed allylation reaction after transmetallation with Zn(OAc)₂ (1.5 equiv) using the acrylate **43**. The functionalized cyclic alkene was isolated in 84% yield (Scheme 63).

¹⁶⁷ a) H. Fillon, C. Gosmini, J.-Y. Nédélec, J. Périchon, *Tetrahedron Lett.* **2001**, *42*, 3843; b) K. Takagi, Y. Shimoishi, K. Sakaki, *Chem. Lett.* **1994**, 2055; c) M. Schreuder Goedheijt, T. Nijbacker, O. S. Akkerman, F. Bickelhaupt, N. Veldman, A. L. Spek, *Angew. Chem. Int. Ed.* **1996**, *35*, 1550.

¹⁶⁸ D. R. Lide, *CRC Handbook of Chemistry and Physics*: Taylor & Francis, Boca Raton, FL, **2009**.

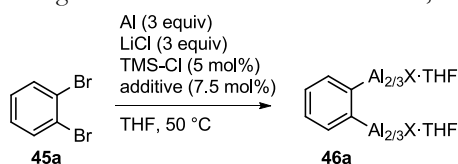
¹⁶⁹ a) Monitoring of the reaction by GC-analysis did not show any trace of a mono-bromide during the reaction. b) Using InBr₃ as catalyst, the reaction proceeded much faster, furnishing **38** within 12 h at 50 °C in the same yield.



Scheme 63: The 5-membered ring furnishes exclusively the mono-metallic reagent **42**.

Further experimentation had shown that also aromatic dibromides could be converted to aluminium bimetallics. A typical substrate like 1,2-dibromobenzene (**45a**) was treated with Al powder (3 equiv) and LiCl (3 equiv) in the presence of TMS-Cl (5 mol%) and several additives (Table 19). No reaction was observed between the dibromide and Al-powder in the absence of any catalyst, even in the presence of a stoichiometric amount of LiCl (Table 19, Entry 1).

Table 19: Catalyst screening for the aluminium insertion into 1,2-dibromobenzene (**45a**).




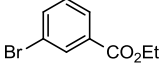
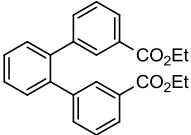

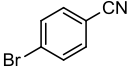
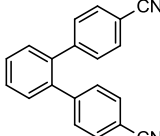
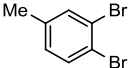

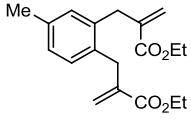
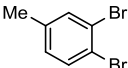
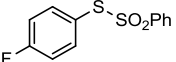
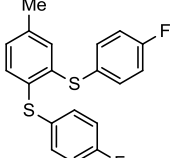
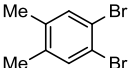
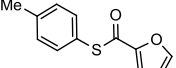
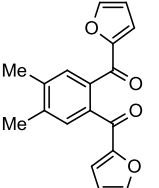
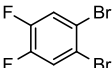
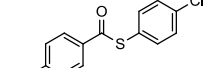
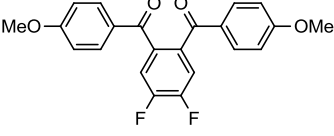
Entry	Additive	Reaction Time	Yield (%) ^a of 46a
1	-	24 h	n.r. ^b
2	TiCl ₄	1 h	decomp. ^c
3	FeCl-TPP	10 h	decomp. ^c
4	BiCl ₃	24 h	13% conv. ^d
5	PbCl ₂	24 h	20% conv. ^d
6	InCl ₃	4h	58%
7	InBr ₃	12h	54%
8	InF ₃	7h	54%
9	In(OTf) ₃	7h	55%

^a Yield of bimetallic reagent as indicated by GC-analysis of reaction aliquots quenched with iodine in THF, using an internal standard (heptadecane). ^b No reaction was observed. ^c Neither **45a** nor any bimetallic could be detected by GC-analysis. ^d The time for full conversion was not determined.

The addition of TiCl₄ (7.5 mol%) or FeCl-TPP (7.5 mol%) resulted in complete decomposition of the dibromide **45a** with no detectable organometallic formed (Table 19, Entries 2-3). However, the use of BiCl₃ or PbCl₂ led to formation of the bimetallic reagent **46a**, although the reaction proceeded only very slowly (Table 19, Entries 3-4). InCl₃ proved to be the most efficient additive, furnishing the bimetallic reagent **46a** in 58% yield within 4 h at 50 °C (Table 19, Entry 5). Other indium salts were also effective in catalyzing the insertion reaction into the dibromide **45a**, affording metal reagent **46a** in a similar yield (Table 19, Entries 7-9). After transmetalation with Zn(OAc)₂ (2 equiv) the aromatic bimetallic **46a** underwent Pd-catalysed cross-couplings with ethyl 3-bromobenzoate (**47a**) and 4-bromobenzonitrile (**47b**) in the presence of Zn(OAc)₂ (2 equiv) and PEPSI (2 mol%), leading to the terphenyls **48a** and **48b** in 63% and 59% yield (Table 20, Entries 1-2). We explored the reaction scope of this transformation and

tried the formation of aromatic bimetallics, starting from substituted 1,2-dibromides. Thus, the toluene derivative **45b** furnished a bimetallic reagent **46b** (50 °C, 12 h) in ca. 54% yield. An allylation reaction in the presence of Zn(OAc)₂ (2 equiv) and CuCN·2LiCl (10 mol%) with ethyl (2-bromomethyl)acrylate (**43**) afforded the bis-acrylate **48c** in 93% yield (Table 20, Entry 3). A reaction with the sulfonothioate **47c** led to the bis-sulfide **48d** in 37% yield after transmetalation with Zn(OAc)₂ (Table 20, Entry 4).

Table 20: Preparation of 1,2-bimetallics of type **46** and subsequent bis-functionalization.

Entry	Substrate	Conditions ^a	Electrophile ^b	Product ^c
1	 45a	50 °C, 4 h 58%	 47a	 48a : 63%
2	 45a	50 °C, 4 h 58%	 47b	 48b : 59%
3	 45b	50 °C, 12 h 54%	 43	 48c : 93%
4	 45b	50 °C, 12 h 54%	 47c	 48d : 37%
5	 45c	50 °C, 12 h 56%	 47d	 48e : 70%
6	 45d	50 °C, 48 h 51%	 47e	 48f : 35%


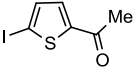
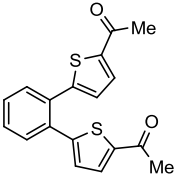
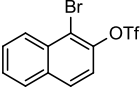

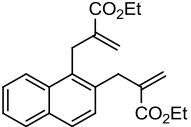
^a Insertion conditions: Temperature; time for full conversion, yield as indicated by GC-analysis of reaction aliquots quenched with iodine in THF using an internal standard (heptadecane). ^b 2 equiv of electrophile have been used based on the indicated yield of bimetallic. ^c Isolated product being of >95% purity as indicated by GC- and NMR analysis.

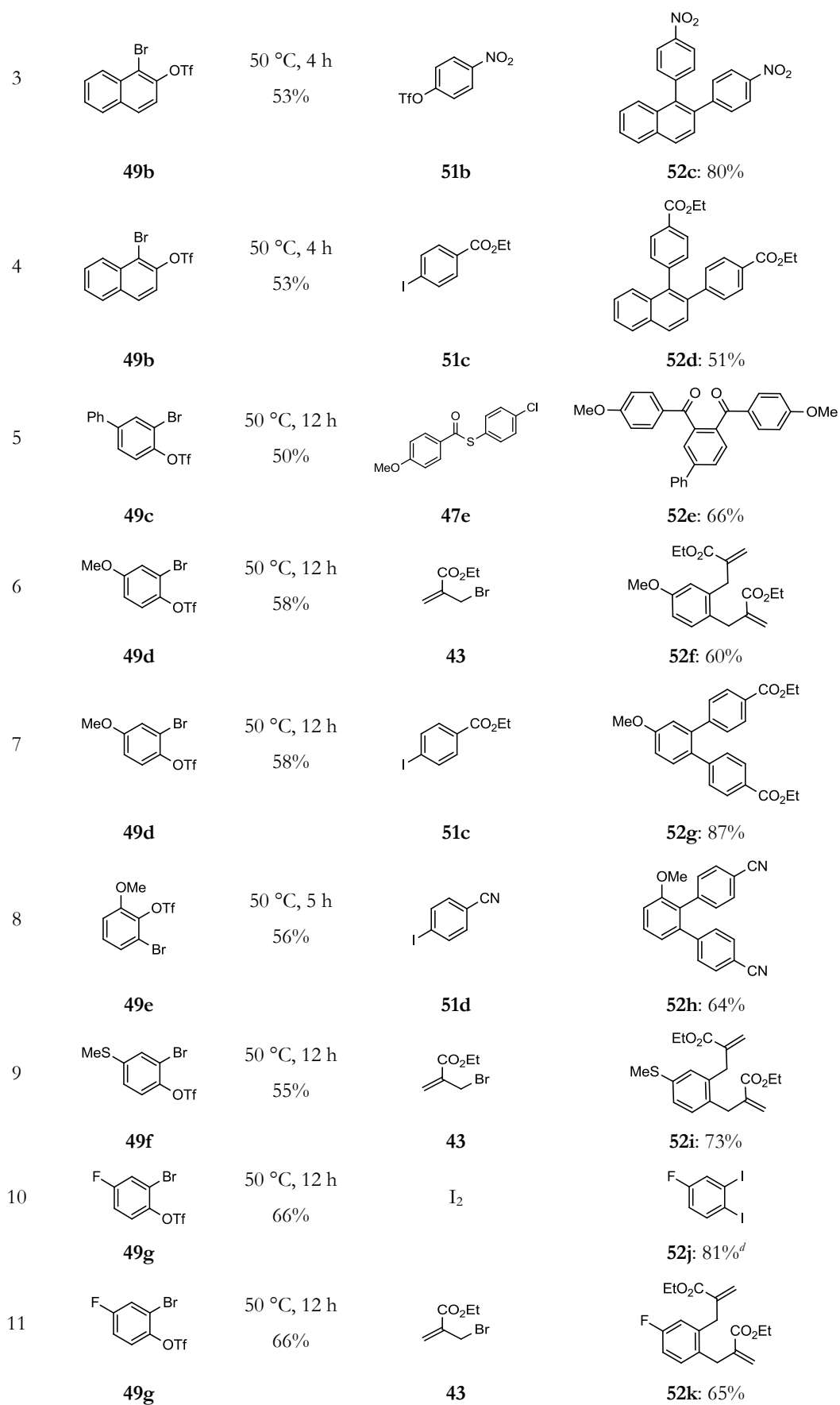
In an analogous way the xylene derivative **45c** also could be converted to the bimetallic **46c** in ca. 56% yield (50 °C, 12 h). It underwent a smooth *Liebeskind-Srogl* acylation in the presence of Zn(OAc)₂ and

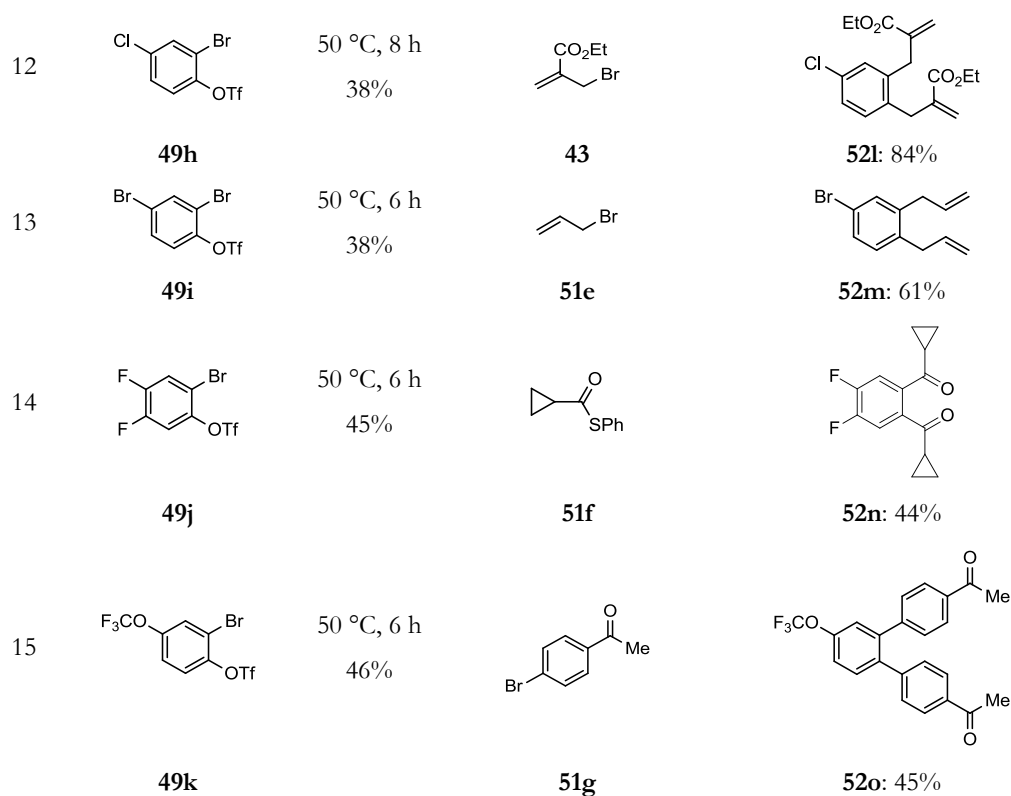
PEPPSI-*i*Pr with the heterocyclic thioester **47d** affording the bis-furyl ketone **48e** in 70% yield (Table 20, Entry 5). The difluoro-substituted dibromide **45d** furnished a bimetallic reagent after 48 h at 50 °C in ca. 50% yield. Again, *Liebeskind-Srogl* acylation using the electron rich thioester **47e** and PEPPSI-*i*Pr furnished the diketone **48f** in 35% yield (Table 20, Entry 6).

Remarkably, not only 1,2-dibromides could be used for the generation of bimetallic reagents, also *ortho*-bromo triflates reacted smoothly under the reaction conditions. Thus, the triflate **49a** furnished after 4 h at 50 °C a bimetallic reagent in ca. 50% yield after reaction with Al (3 equiv), LiCl (3 equiv) and InCl₃ (7.5 mol%). After transmetallation with Zn(OAc)₂ the reagent was bis-functionalized in a cross-coupling reaction using the thiophene derivative **51a**. The heterocyclic diketone **52a** was isolated in 34% yield (Table 21, Entry 1). Furthermore, the naphthyl-triflate **49b** or the biphenyl-triflate **49c** could be converted to bimetallic reagents (ca. 50-53% yield). Further functionalization in the presence of Zn(OAc)₂ afforded the products **52b-e** in 47-80% yield (Table 21, Entries 2-5). Moreover, even electron rich triflates bearing methoxy- or thiomethyl- substituents (**49d-f**) worked equally well. Subsequent cross-couplings (PEPPSI-*i*Pr) or allylations (CuCN·2 LiCl) furnished the products **52f-i** in 60-87% yield (Table 21, Entries 6-9). In the case of electron-deficient triflates, the situation proved to be more complex. In the presence of LiCl we observed complete decomposition under the reaction conditions. But, without the use of LiCl, even these triflates could be converted to bimetallic reagents, although in lower yield (typically around 40%). Thus, the halide substituted triflates (**49g-i**) furnished after treatment with Al-powder (3 equiv) and InCl₃ (7.5 mol%) the corresponding bimetallics. After transmetallation with Zn(OAc)₂ they reacted with iodine or in Cu^I-catalysed allylations leading to the unsaturated products (**52j-m**) in 61-84% yield (Table 21, Entries 10-13). Similarly, the fluoride containing triflates **49j** and **49k** afforded bimetallics in the absence of LiCl. Further functionalization proved to be difficult, as these reagents reacted only sluggishly. Nevertheless, a *Liebeskind-Srogl*-acylation and a cross-coupling afforded the bis-functionalized products **52n** and **52o** in 47% and 45% yield (Table 21, Entries 14-15).

Table 21: Preparation of 1,2-bimetallics of type **50** and subsequent bis-functionalization.

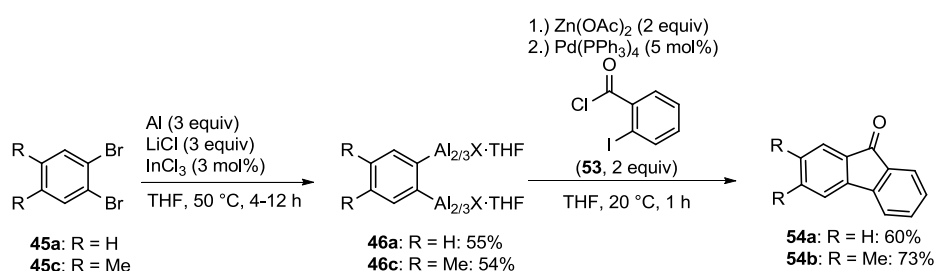
Entry	Substrate	Conditions ^a	Electrophile ^b	Product ^c
1		50 °C, 4 h 67%		
	49a		51a	52a: 34%
2		50 °C, 4 h 53%		
	49b		43	52b: 47%





^a Insertion conditions: Temperature; time for full conversion, yield as indicated by GC-analysis of reaction aliquots quenched with iodine in THF using an internal standard (heptadecane). ^b 2 equiv of electrophile have been used based on the indicated yield of bimetallic. ^c Isolated product being of >95% purity as indicated by GC- and NMR analysis. ^d Overall yield = 46%.

Moreover, bimetallics offer new synthetic strategies which are often difficult to achieve in another way. We envisioned that these reagents would be ideal for a simultaneous functionalization using substrates with two electrophilic centers. Thus, in the presence of Pd(PPh₃)₄ (5 mol%) the bimetallics **46a** and **46c** reacted smoothly with 2-iodobenzoylchloride (**53**) under mild conditions leading to fluorenone derivatives **54a-b** in 60% and 73% yield within 1 h at 20 °C (Scheme 64).



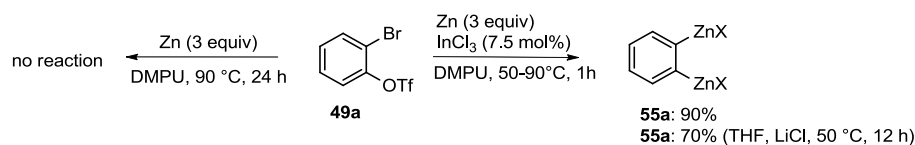
Scheme 64: Preparation of 1,2-bimetallics **46a** and **46c** and subsequent preparation of fluorenones **54a-b**.

5.4 InCl₃-Mediated Preparation of 1,2-Zinc Bimetallics

The reaction of aromatic *ortho*-iodo triflates has led to zinc bimetallics by reaction with Zn in DMPU at 90 °C.¹⁷⁰ Using the same conditions, the corresponding bromo-triflate **49a** is not reactive even after heating for one day. In contrast, the addition of a catalytic amount of InCl₃ (7.5 mol%) rapidly furnished

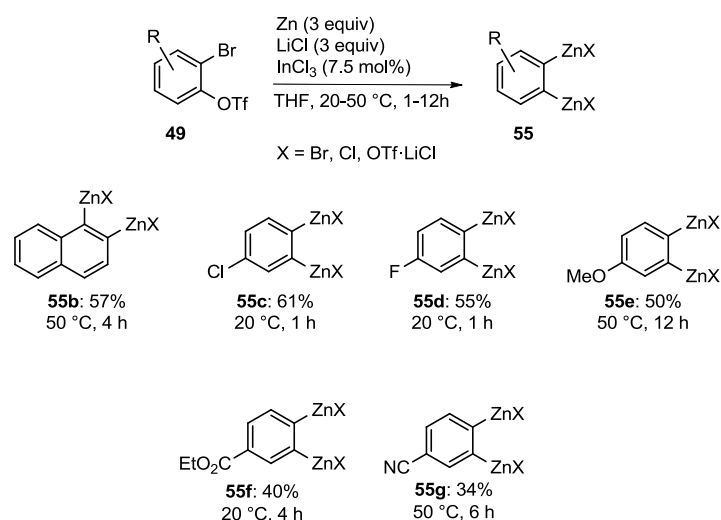
¹⁷⁰ M. Amano, A. Saiga, R. Ikegami, T. Ogata, K. Tagaki, *Tetrahedron Lett.* **1998**, *39*, 8667.

the bimetallic zinc reagent **55a** in 90% yield. The reaction can also be performed in THF in the presence of LiCl, leading also to **55a** in 70% yield.



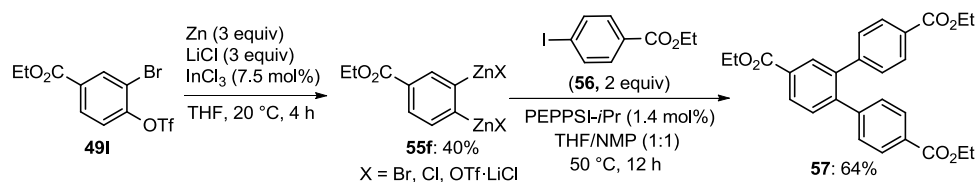
Scheme 65: Effect of InCl_3 on the insertion of Zn-powder into aromatic *ortho*-bromo-triflates.

This shows clearly the activating role of InCl_3 on metal insertion reactions. Also other substrates could be readily converted to zinc bimetallics by reaction of the corresponding aromatic bromo-triflate with Zn-powder (3 equiv), LiCl (3 equiv) and InCl_3 (7.5 mol%) in THF (Scheme 66). Usually the yields are higher and the reaction proceeds faster when DMPU is used. But the use of DMPU precludes the presence of LiCl, as the solution gets highly viscous making it almost impossible to use the prepared reagents.



Scheme 66: Preparation of various functionalized 1,2-bimetallics by direct insertion of Zn-powder.

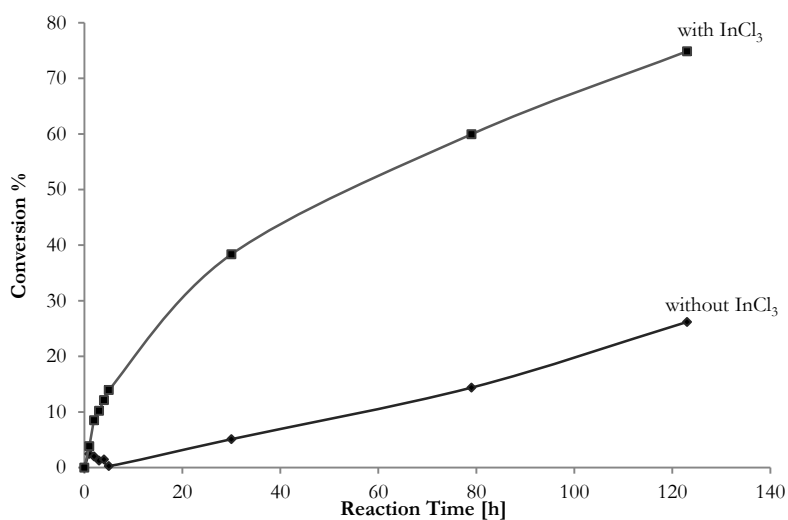
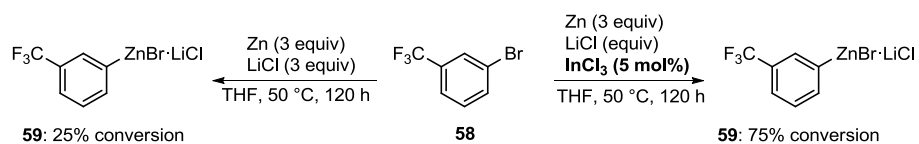
The 1,2-bimetallics obtained by the InCl_3 -catalysed insertion of Zn-powder could also be readily used in cross-coupling reactions. Thus, the functionalized bimetallic **55f** prepared from Zn insertion into **49f** underwent a smooth cross-coupling reaction with ethyl 4-iodobenzoate (**56**) furnishing the highly functionalized terphenyl **57** in 64% yield (Scheme 67).



Scheme 67: Zinc insertion into the triflate **49f** and subsequent cross-coupling of the resulting zinc reagent **55f**.

Aryl bromides are typically reluctant to undergo a Zn insertion and usually prolonged heating or refluxing is necessary to obtain aryl zinc reagents. Our results have shown that InCl_3 is a sufficient catalyst to accelerate the insertion of Zn powder dramatically. This acceleration is not only occurring in the case of

the aromatic *ortho*-bromo-triflates, but also in the case of other aryl bromides. We compared the insertion of Zn-powder (3 equiv) in the presence of LiCl (3 equiv) into 3-bromobenzotrifluoride (**58**) with and without a catalytic amount of InCl₃ in THF. Also in this case, the presence of InCl₃ dramatically accelerated the insertion of Zn-powder and within the same amount of time the reaction proceeded three times as fast.



Scheme 68: Effect of InCl₃ on the insertion of Zn-powder into the aryl bromide **58**.

5.5 ESI-Mass Spectrometry of 1,2-Aluminium Bimetallics

In order to analytically prove the formation of 1,2-bimetallic species we conducted ESI-mass spectrometry experiments. Electrospray-ionization (ESI) mass spectrometry allows the determination of stoichiometric information of dissolved charged organometallics in solution.¹⁷¹ This method has been applied several times for analysis of various organometallic species, including labile ones.¹⁷² As only a small amount of energy is transferred to the observed system it is commonly accepted that there's no significant alteration of the probed ions.¹⁷³ Thus, it can be assumed that the information obtained from gas-phase measurements is also representative for the ensemble of organometallics in solution. It has to be stated that only information about charged species is obtained. Neutral organometallics cannot be detected by ESI-mass spectrometry, thus the results in this chapter have to be seen in this context. Several charged aluminates could be detected, but it may well be that there are also several neutral organometallics in solution.

5.5.1 ESI-Mass Spectrometric Analysis of the Cyclohexenyl Bimetallic **38**

We added 1,2-dibromocyclohexene **37** to Al (3 equiv), LiCl (3 equiv), TMS-Cl (3 mol%) and InCl₃ (7.5 mol%) in THF. Full conversion to the aluminium reagent was achieved after 24 h at 50 °C. The remaining solution was separated from the Al-powder and subjected to the measurement after filtration through a syringe filter before subjected to ESI-mass spectrometric analysis. The main species (m/z 427, most abundant isotopologue) observed upon negative ion mode ESI is assigned to the bimetallic aluminate **A** (Figure 11). This complex contains one anionic aluminium center, whereas the second one is neutral and complexed by THF. Note that the experiments cannot determine whether the bromine atom binds to the neutral or the anionic aluminium center; most likely, the observed species corresponds to a mixture of both isomers.

¹⁷¹ M. Yamashita, J. B. Fenn, *J. Phys. Chem.* **1984**, *88*, 4451.

¹⁷² a) J. C. Traeger, *Int. J. Mass Spectrom.* **2000**, *200*, 387; b) D. A. Plattner, *Int. J. Mass Spectrom.* **2001**, *207*, 125; c) P. Chen, *Angew. Chem. Int. Ed.* **2003**, *42*, 2832; d) L. S. Santos, L. Knaack, J. O. Metzger, *Int. J. Mass Spectrom.* **2005**, *246*, 84; e) W. Henderson, J. S. McIndoe, *Mass Spectrometry of Inorganic, Coordination and Organometallic Compounds: Tools, Techniques, Tips*, Wiley, Chichester, **2005**; f) C. A. Müller, C. Markert, A. M. Teichert, A. Pfaltz, *Chem. Commun.* **2009**, 1607; g) A. Roglans, A. Pla-Quintana in *Reactive Intermediates: MS investigations in solution*, (Ed.: L. S. Santos), Wiley-VCH, Weinheim, **2009**; h) L. A. Hammad, D. Gerdes, P. Chen, *Organometallics* **2005**, *24*, 1907; h) M.-E. Moret, P. Chen, *Organometallics* **2007**, *26*, 1523.

¹⁷³ R. B. Cole, *J. Mass Spectrom.* **2000**, *35*, 763.

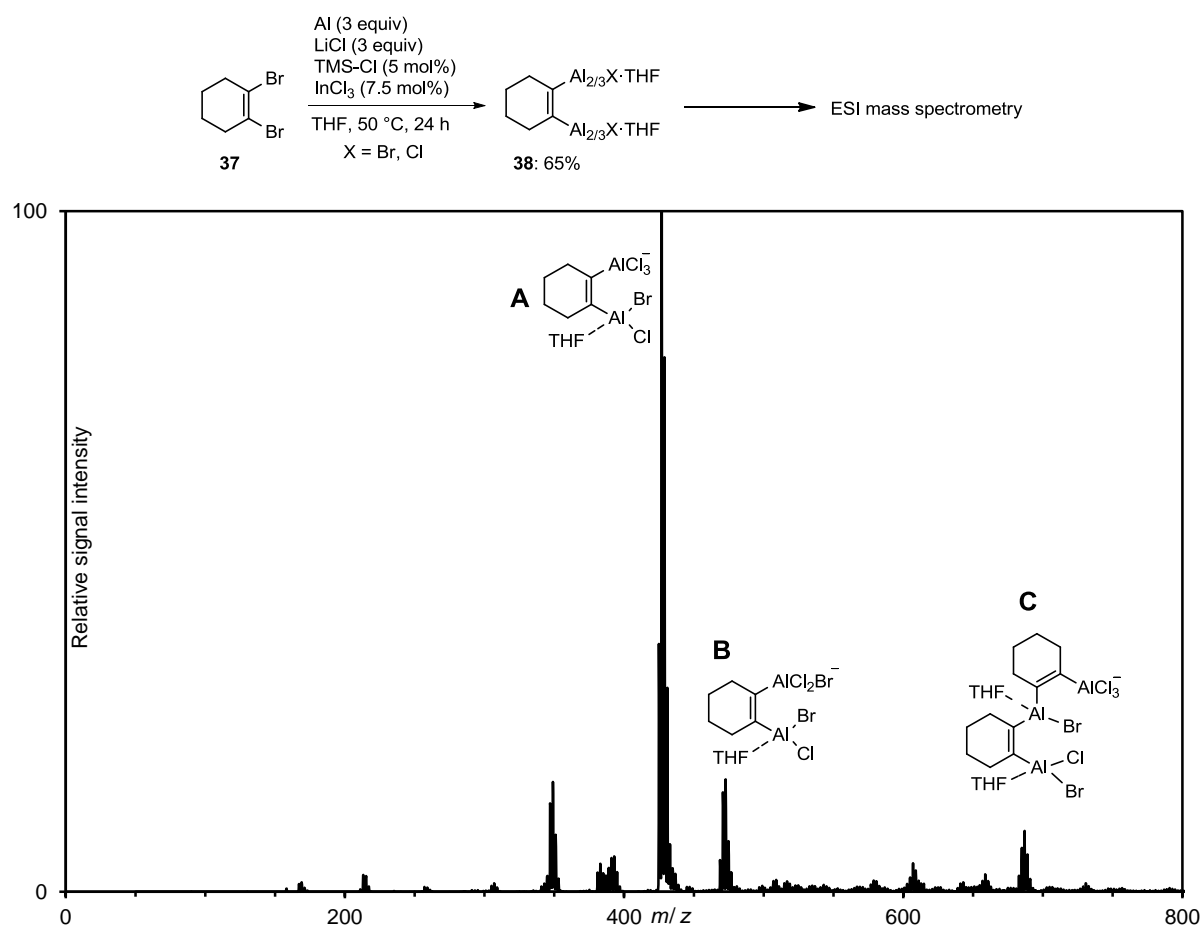


Figure 11: Negative ion mode ESI mass spectrum of an approx. 10 mM solution of the products obtained by the reaction of Al-powder with **37** under the typical insertion conditions. **A**, **B** and **C**: proposed structures of organoaluminates matching the detected m/z values.

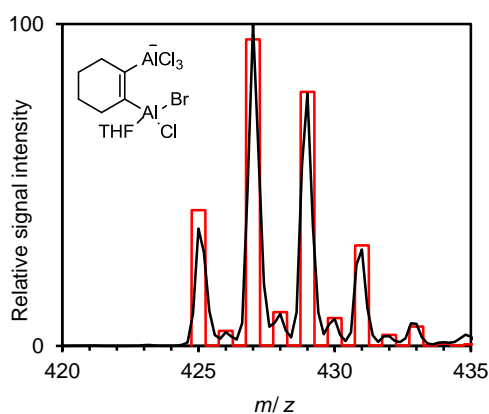


Figure 12: Measured isotope pattern of **A** (black) together with the calculated isotope pattern for $\text{C}_{10}\text{H}_{16}\text{Al}_2\text{BrCl}_4\text{O}$ (red).

The simulated isotope pattern is in excellent agreement with the measured one (Figure 12). Further evidence for the proposed structure comes from the CID experiments, which show losses of THF and, to a minor extent, of HBr (Figure 13).

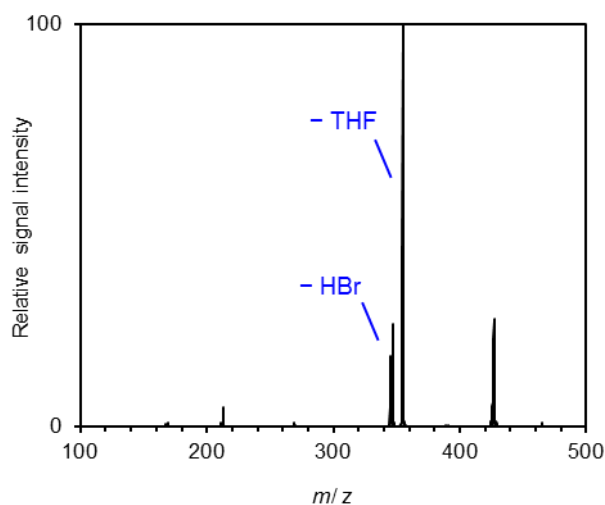
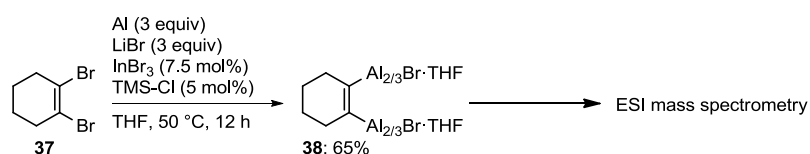


Figure 13: Mass spectrum of mass-selected **A** (m/z 427) and its fragment ions produced upon collision-induced dissociation ($V_{\text{exc}} = 0.20$ V).

Besides the main species **A**, two additional aluminate complexes were detected. The first one is similar to **A**, but contains a second bromine atom; again, the position of the chlorine and bromine atoms presumably is largely interchangeable (Figure 11, **B**). The other aluminate complex is remarkable in that it features three aluminium centers, one of which apparently bridges two organyl moieties (Figure 11, **C**). As shown above, the operation of halide exchange (bromide vs. chloride) reactions complicates the identification of aluminate species. To simplify the situation and provide further data in support of the given assignments, we performed an analogous experiment, in which we substituted LiCl for LiBr and InCl₃ for InBr₃.



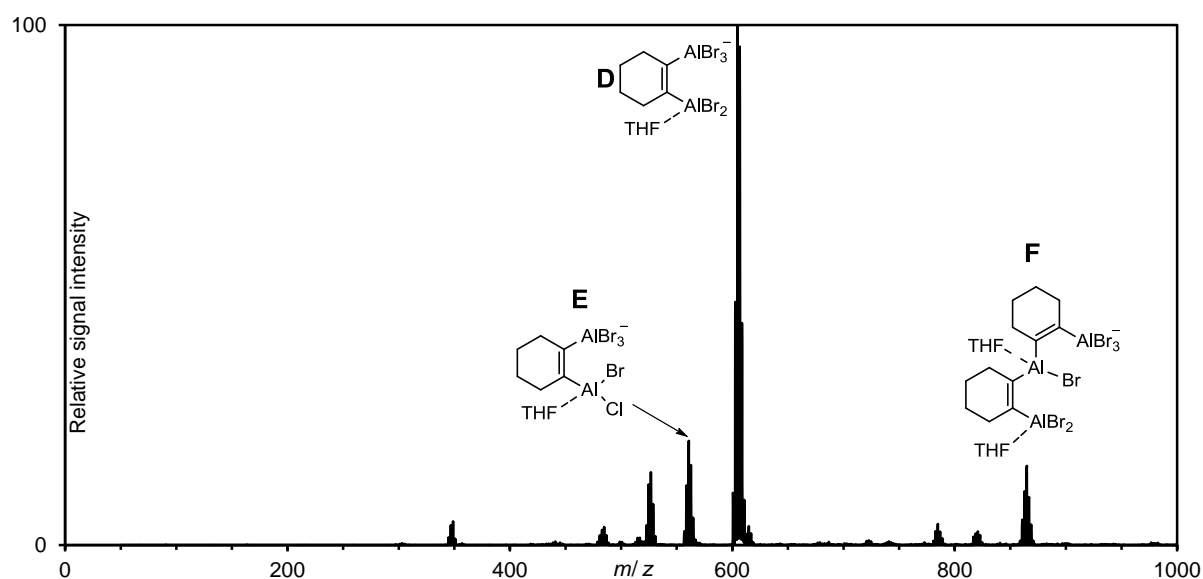


Figure 14: Negative ion mode ESI mass spectrum of an approx. 10 mM solution of the products obtained by the reaction of Al-powder with **37** under the typical insertion conditions using LiBr and InBr₃. **D**, **E** and **F**: proposed structures of organoaluminates matching the detected m/z values.

Indeed, the use of LiBr and InBr₃ depressed the formation of aluminates containing chlorides. Instead, the main species now corresponds to the bimetallic aluminate **D**, which constitutes the bromo counterpart of **A**. This assignment is corroborated both by a comparison of the measured and calculated isotope patterns (Figure 15) and by the loss of THF and HBr upon CID (Figure 16). Interestingly, complex **E** with one of the bromide ligands replaced by chloride was also detected, although no chloride source had been added to the reaction mixture except for TMS-Cl (5 mol%); this rather small amount apparently was sufficient to give rise to significant quantities of the singly chloride-exchanged complex **E** (Figure 14). With the trinuclear aluminate **F**, the bromo counterpart of **C** was also observed (Figure 14).

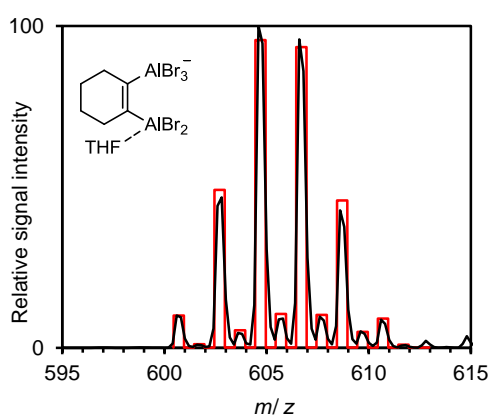


Figure 15: Measured isotope pattern of **D** (black) together with the calculated isotope pattern for C₁₀H₁₆Al₂Br₅O (red).

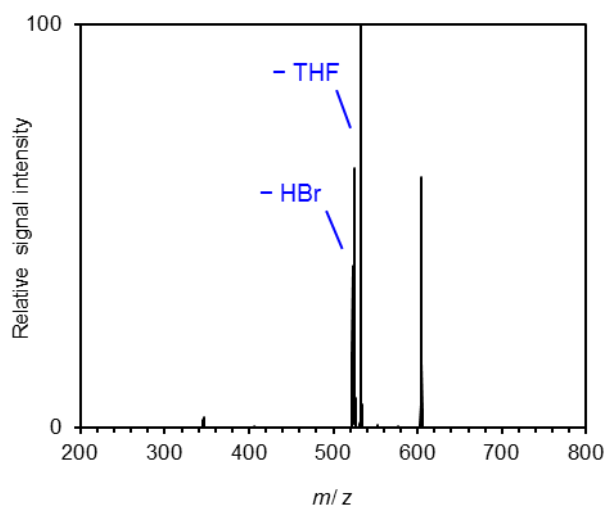
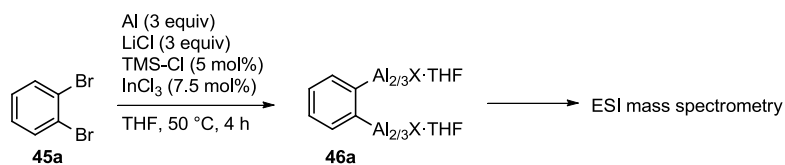


Figure 16: Mass spectrum of mass-selected **D** (m/z 605) and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V).

5.5.2 ESI-Mass Spectrometric Analysis of the Aryl Bimetallic **46a**

In the case of the aluminium insertion into aryl 1,2-dibromides, the situation is much more complex, as many charged species are generated under the reaction conditions. We performed the insertion into 1,2-dibromobenzene (**45a**) using Al-powder (3 equiv), LiCl (3 equiv), TMS-Cl (5 mol%) and InCl₃ (7.5 mol%) in THF.



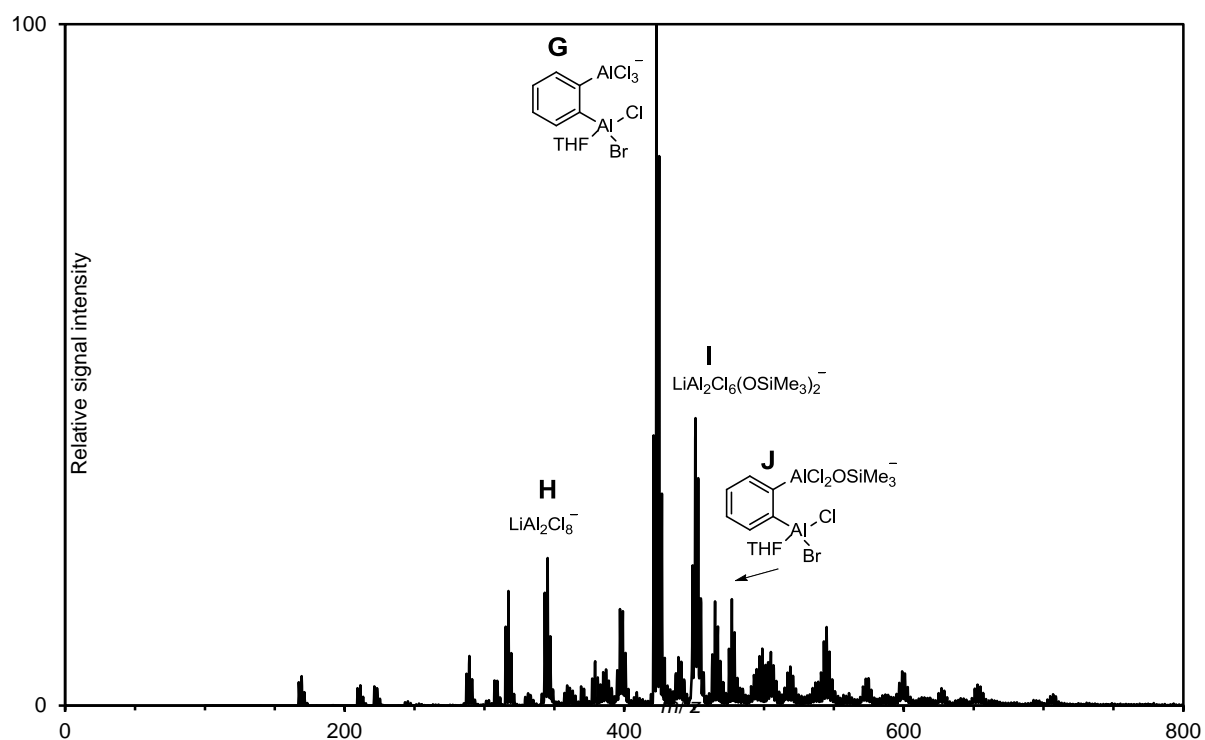


Figure 17: Negative ion mode ESI mass spectrum of an approx. 10 mM solution of the products obtained by the reaction of Al-powder with **4a** under the typical insertion conditions. **G, J**: proposed structures of organoaluminates matching the detected m/z values. **H, I**: other aluminates.

Negative-ion mode ESI mass spectrometric analysis of the diluted reaction mixture detected an ion as main species, whose m/z values (m/z 423 for the most abundant isotopologue) were shifted by 4 amu compared to complex **A** observed in the reaction of **37**. Accordingly, this ion is assigned an analogous structure with an aromatic ring (Figure 17, **G**). Comparison of the measured and calculated isotope pattern (Figure 18, left), deuterium labeling (using THF-*d*₈ as solvent for the reaction mixture, Figure 18, right), and CID experiments (see Experimental Section) fully confirm this assumption. In addition, simple inorganic lithium aluminates (Figure 17, **H, I**) and a bimetallic complex containing an OTMS ligand were detected (Figure 17, **J**).

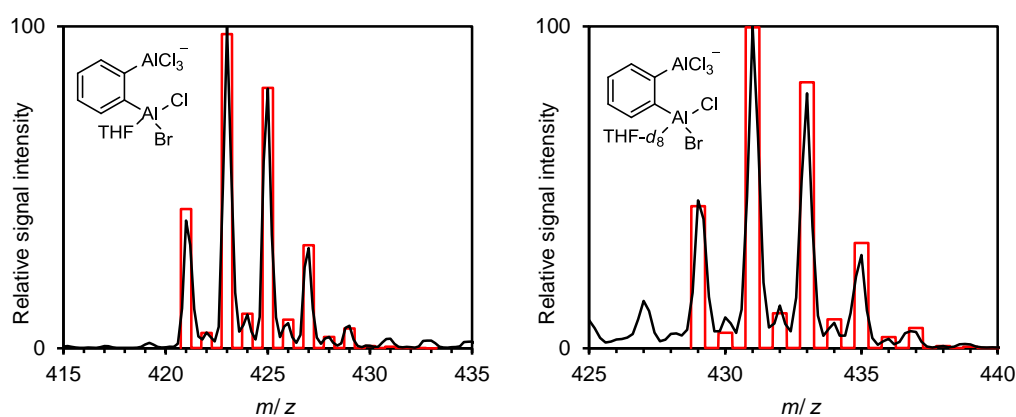
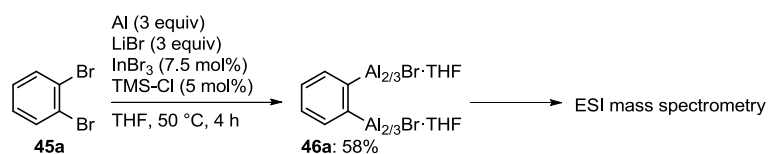


Figure 18: (left) Measured isotope pattern of **G** (black) together with the calculated isotope pattern for C₁₀H₁₂Al₂BrCl₄O (red). (right) Measured isotope pattern of **G**-THF-*d*₈ (black) together with the calculated isotope pattern for C₁₀H₄D₈Al₂BrCl₄O (red).



As in the case of **37**, we performed analogous experiments under similar reaction conditions, but with LiCl and InCl₃ replaced by LiBr and InBr₃. Again, the expected bimetallic aluminate containing only bromide was observed (Figure 19, **K**), whose identity was proven by comparison of the measured and calculated isotope pattern (Figure 20, the small deviation noticeable presumably results from the presence of an isobaric contaminant) and CID experiments (see Experimental Section). Furthermore, the presence of TMSCl again led to the formation of a chloride containing aluminate (Figure 19, **L**). In addition, a trinuclear complex comprising two aryl groups was detected (Figure 19, **M**).

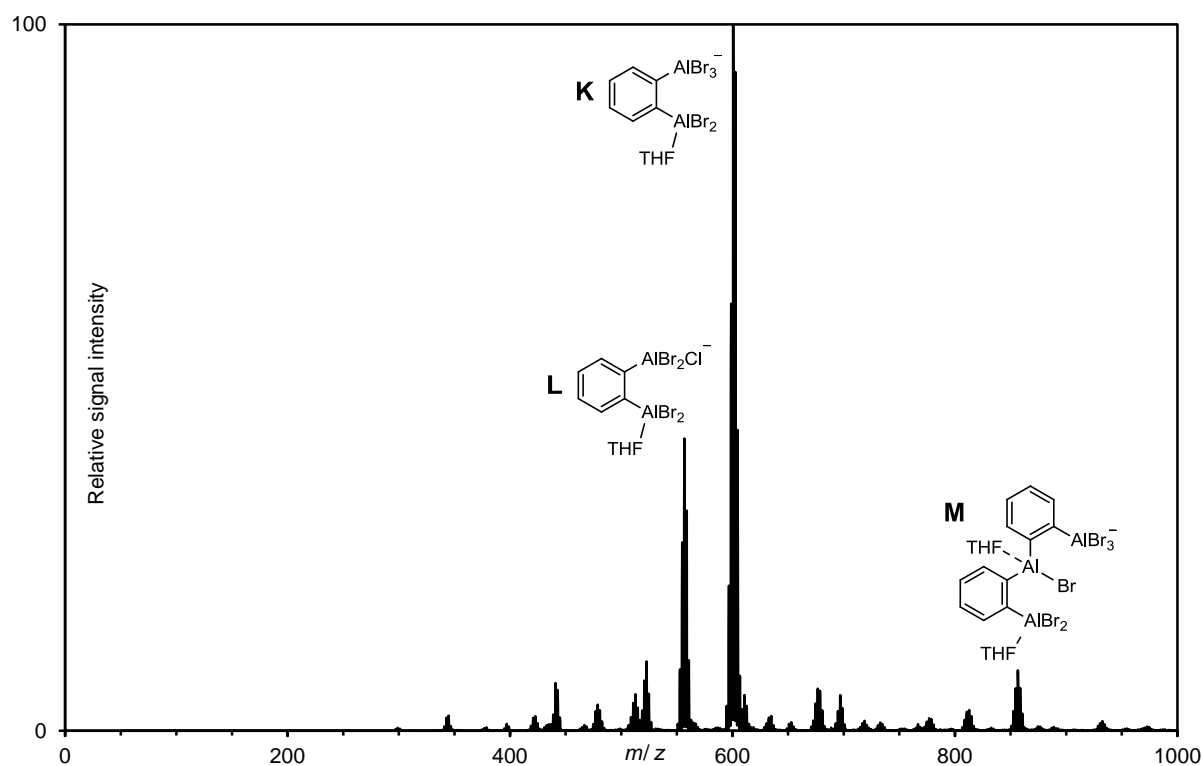


Figure 19: Negative ion mode ESI mass spectrum of an approx. 10 mM solution of the products obtained by the reaction of Al-powder with **45a** under the typical insertion conditions using LiBr and InBr₃. **K**, **L** and **M**: proposed structures of organoaluminates matching the detected m/z values.

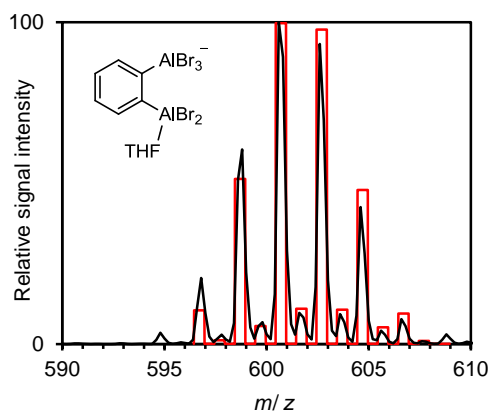


Figure 20: Measured isotope pattern of **K** (black) together with the calculated isotope pattern for $C_{10}H_{12}Al_2Br_5O$ (red).

5.5.3 ESI-Mass Spectrometric Analysis of the Aryl Bimetallic **50a**

We also prepared the bimetallic **50a** starting from the *ortho*-bromo triflate **49a**. To avoid overly complex ESI mass spectra due to exchange processes between chloride, bromide and triflate ligands, we avoided the use of LiCl and InCl₃. Thus, **49a** was treated with Al (3 equiv), LiBr (3 equiv), TMS-Cl (3 mol%) and InBr₃ (7.5 mol%) furnishing the bimetallic mixture within 4 h at 50 °C.

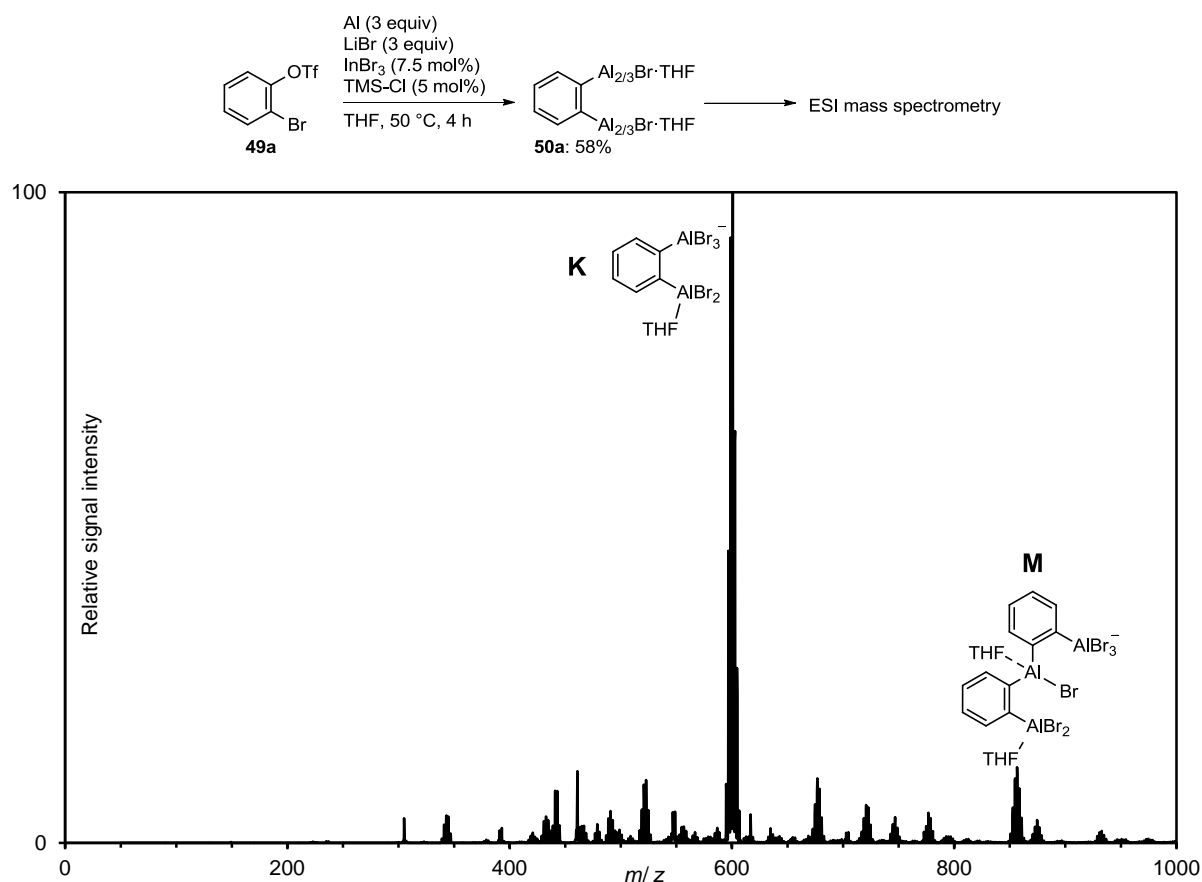
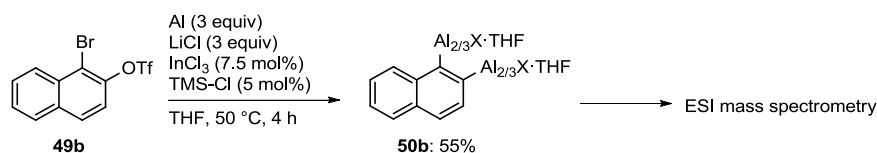


Figure 21: Negative ion mode ESI mass spectrum of an approx. 10 mM solution of the products obtained by the reaction of Al-powder with **49a** under the typical insertion conditions using LiBr and InBr₃. **K** and **M**: proposed structures of organoaluminates matching the detected m/z values.

Surprisingly, we did not obtain any evidence for aluminate ions containing a triflate ligand. Instead, the complexes **K** and **M** were observed (Figure 21) which are already known from the insertion into **45a**.

5.5.4 ESI-Mass Spectrometric Analysis of the Naphtyl Bimetallic **50b**

In order to prove the generality of this finding, we chose another triflate (**4d**) and allowed it to react with Al (3 equiv), LiCl (3 equiv), TMS-Cl (3 mol%) and InCl₃ (7.5 mol%) to furnish the bimetallic mixture in 4 h at 50 °C.



As expected, ESI mass spectrometry detected a bimetallic aluminate complex that contained both chloride and bromide, but no triflate (Figure 22, **N**). The identity of this species was corroborated by comparing the measured and calculated isotope pattern (Figure 23).

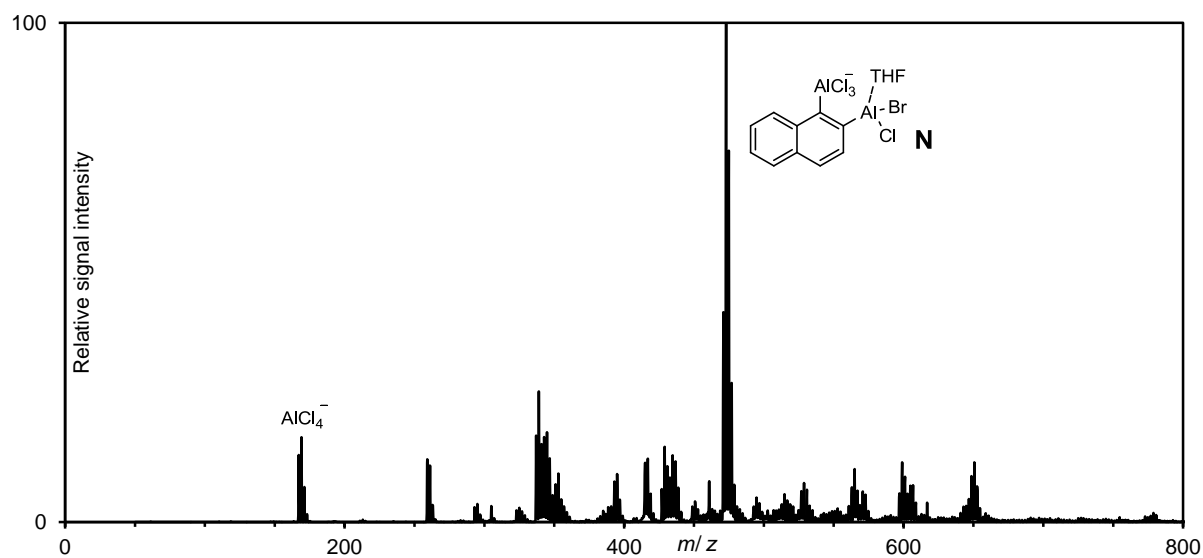


Figure 22: Negative ion mode ESI mass spectrum of an approx. 10 mM solution of the products obtained by the reaction of Al-powder with **4d** under the typical insertion conditions. **N**: proposed structure of organoaluminate matching the detected m/z value.

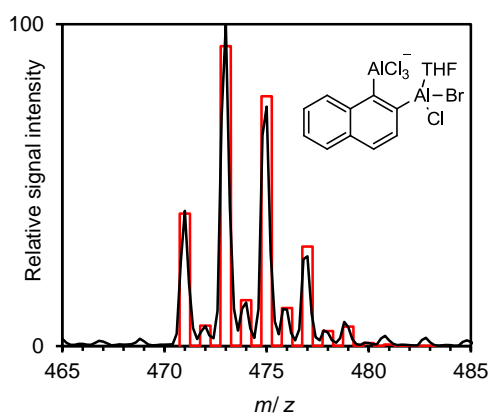
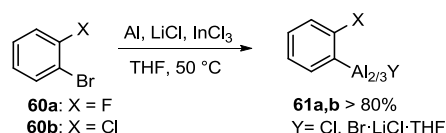


Figure 23: Measured isotope pattern of **N** (black) together with the calculated isotope pattern for $C_{14}H_{14}Al_2BrCl_4O$ (red).

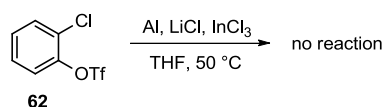
5.6 Mechanistical Considerations

The mechanism which leads to formation of the bimetallic species is certainly complex and several pathways may be present. That the formation of the bimetallic reagents proceeds cleanly via a stepwise double insertion of the metal, must be doubted. This may be, in the case of the dibromides, but probably not in the case of the triflates and for both classes of substrates different mechanisms may be active. Aluminium does not insert readily into aromatic carbon-chloride or carbon fluoride bonds. Thus using 1-bromo-2-fluorobenzene (**60a**) or 1-bromo-2-chlorobenzene (**60b**) the reaction furnished cleanly the mono-aluminium reagents (Scheme 69).



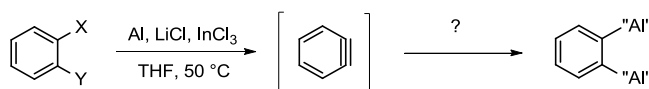
Scheme 69: Insertion into *ortho*-fluoro or *ortho*-chloro bromobenzene (**60a,b**) yields monometallic aluminium reagents (**61a,b**).

In contrast, insertion into the carbon-triflate bond using an *ortho*-chloro-substituted triflate **62** does not lead to any reaction (except deprotection over 48 h) showing that insertion into this bond is not occurring (Scheme 70). Other triflates showed the same behaviour.



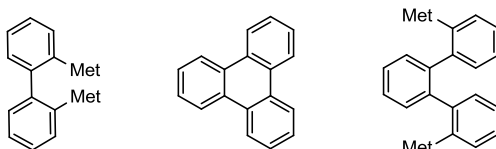
Scheme 70: Insertion of Al-powder does not occur into an aromatic triflates.

We speculated, that the formation of the bimetallic reagent could proceed over an aryne intermediate (Scheme 71).



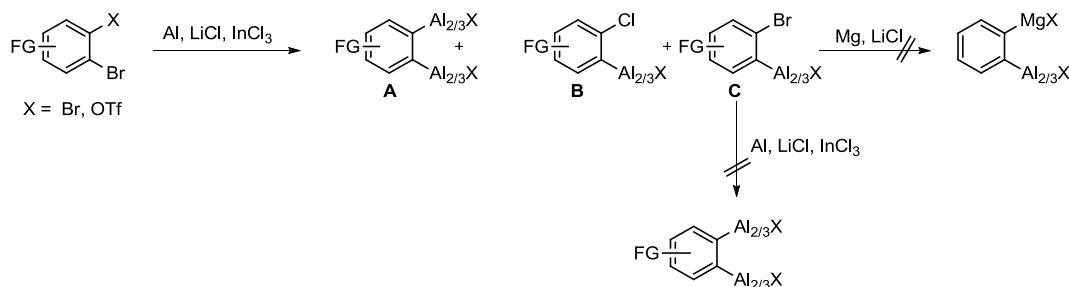
Scheme 71: Speculation that the bimetallic is formed via an aryne intermediate.

There are several evidences suggesting the formation of arynes during the insertion conditions. First of all, higher dimeric and trimeric structures which are typical for aryne formation could be identified using GC/MS analysis (Scheme 72). Some of them still contain active metal positions which could be identified in iodolysis experiments.



Scheme 72: Usually observed higher condensation products typical for aryne chemistry.

Moreover, in any experiment the reaction conditions led to formation of a mixture of products. Thus, next to the bimetallic **A**, monometallics are formed, containing either a chlorine (**B**) or bromine substituent (**C**, Scheme 73). The ratio between the three metallic species is dependent on the substituent on the ring, and all three are formed simultaneously from the beginning on, in this ratio. Then, this initial ratio stays constant and increases with time. No change of this ratio was observed by changing the amount of any of the reactants. The ratio did also not show significant concentration dependence. Under no circumstances could **C** be converted to the bimetallic **A**. Neither prolonged heating, nor addition of this mixture to a new batch of Al, LiCl and InCl₃ could convert this reagent to a bimetallic. Not even Mg did insert into this bond, showing that insertion into an anionic-carbon bearing aromatic system (highly electron rich), is not occurring easily, even when highly reactive metals are used.

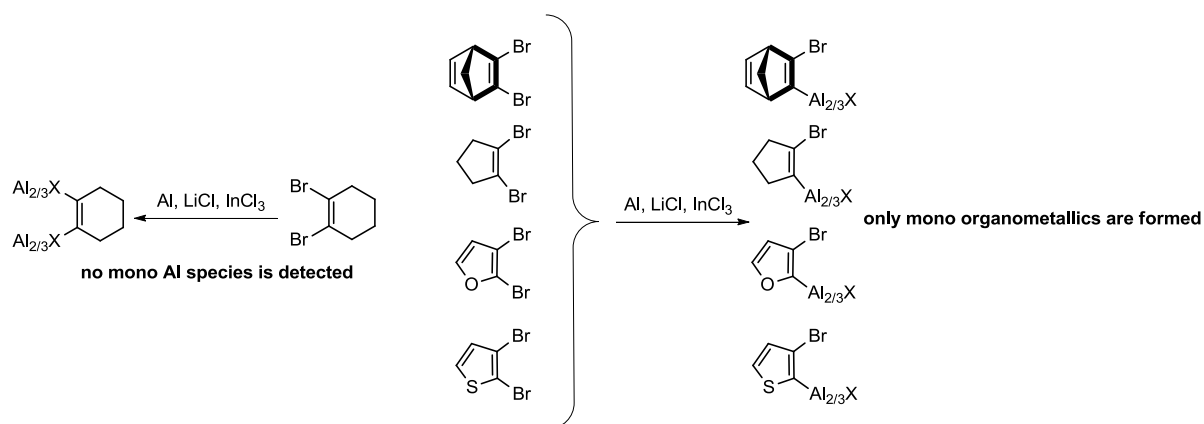


Scheme 73: Several products are generated during the formation of 1,2-bimetallic reagents.

The chlorine-substituted aluminium reagent (**B**) is not formed, when LiBr is used instead of LiCl, nevertheless **C** is formed in a higher quantity. This rules out, that the chlorine comes from the InCl₃ present, it definitely is provided by LiCl. Thus, one possibility for the generation this chloro-substituted mono-metallic reagent could be the reaction of the intermediately formed aryne with LiCl and subsequent transmetallation, or with AlCl₃ present in solution which would be a chloro-alumination similar to the addition of e.g. BBr₃ to unsaturated systems.

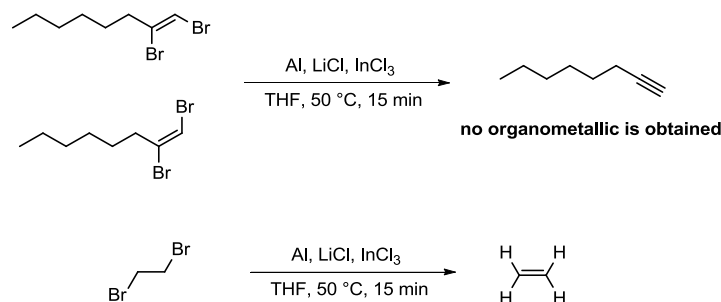
Furthermore, the 6-membered vinylic dibromide is converted easily to a bimetallic, whereas 5-membered ring systems exclusively form monometallics (Scheme 74). When the formation of the bimetallics is

occurring via elimination (cyclohexyne or aryne) this could explain why 5-membered ring systems do not undergo this reaction. Because of the higher ring-strain, which would result from elimination, this pathway is not favored.



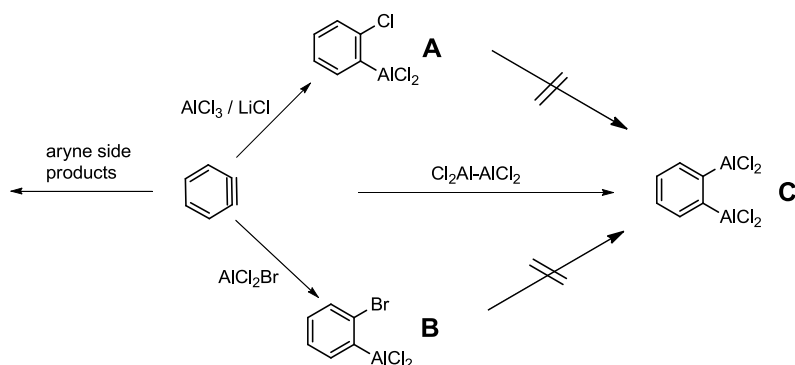
Scheme 74: 5-membered cyclic dibromides undergo exclusive mono insertion of aluminium.

In contrast, open chain systems undergo elimination immediately, forming alkynes without formation of bimetallics, showing that elimination is occurring easily under the reaction conditions (Scheme 75).



Scheme 75: Acyclic dibromides undergo elimination without formation of bimetallic reagents.

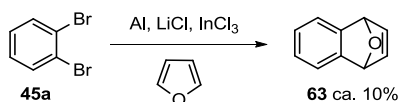
These results lead us to the following tentative proposal (Scheme 76): Once insertion is occurring, elimination slowly takes place under the reaction conditions. The triflate will eliminate more readily than a halide and the observed reaction times of the triflates are in accordance lower, leading faster and cleaner to bimetallic species. The intermediate aryne formed now can undergo several types of reaction. On the one hand it can decompose, leading to the typical aryne side products which are observed. Alternatively it can be trapped by aluminium salts present in solution. If it is reacting with aluminium salts bearing a chlorine (such as $AlCl_3$) it will lead to the typically observed chloro-monometallic **A**. Of course it can also react with $LiCl$ leading to an intermediate lithium reagent, which undergoes transmetalation immediately, leading also to **A**. If the aryne is trapped by an aluminium salt, bearing bromides it will result in formation of the bromo-substituted reagent **B**. Once this is formed, it is not reacting to the bimetallic, as experiments proved that no insertion is occurring anymore. This means, that the bimetallic is formed on a different pathway. We speculate here, that reaction with Al-Al salts may lead to the bimetallic **C**. Such salts may be formed when aluminium salts are reacting with reducing agents, such as sodium metal.²³ We also speculate here, that the presence of an excess of aluminium metal may lead to formation of such species, in which case the aluminium is acting as reducing agent providing the necessary electrons.



Scheme 76: Speculative mechanism for the formation of 1,2-bimetallic reagents.

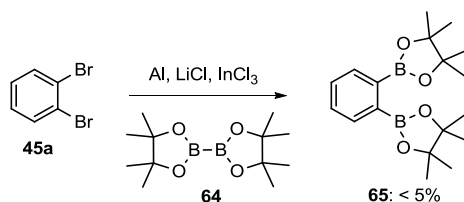
5.7 Critical Conclusion

We tried to prove the aryne formation by trapping it in a *Diels-Alder* reaction with furane. Thus, we performed the insertion in the presence of an excess of furane (Scheme 77). The *Diels-Alder* product **63** was obtained in approximately 10% yield as indicated by GC-analysis, showing that at least some aryne is formed during the insertion reaction. However, it may show that either the formation of the bimetallic is faster than the trapping with furane or that the bimetallic is formed in a different way.



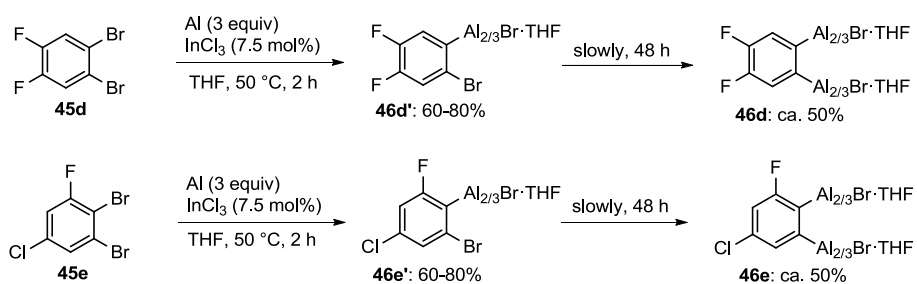
Scheme 77: Attempts to trap intermediately generated aryne with furane in a *Diels-Alder* reaction.

To test the hypothesis that Al-Al species may be present and react with the intermediately formed aryne we performed the insertion reaction in the presence of a similar compound containing a “metal-metal” bond, the bis-pinacol-borane **64** (Scheme 78). Although the product **65** could be detected by GC and GC-MS analysis, the low yield obtained (<5%) suggests either that the boron reagent cannot be trapped by an aryne, the concurrent reaction with the aluminium species is faster, or that there’s no Al-Al species present.



Scheme 78: Attempt to trap intermediately generated aryne with the bis-pinacolate **64**.

Moreover, two substrates showed an absolutely different behaviour. The insertion reaction into 1,2-dibromo-3,4-difluorobenzene (**45d**) and 1,2-dibromo-5-chloro-3-fluorobenzene (**45e**) cleanly proceeded stepwise, first forming a monometallic reagent **46d'-e'**, then slowly reacting to the bimetallics **46d-e**. None of the other tested substrates showed this behaviour and it may be speculated, that in these cases the bimetallic is formed via a stepwise double insertion.



Scheme 79: The aromatic dibromides **45d** and **45e** react stepwise to the bimetallics **64d** and **64e**.

In summary, we can conclude that the formation of bimetallics is an interesting phenomenon. The mechanistic pathway remains uncertain and speculative. There's a lot of evidence suggesting that the bimetallics may be formed via an intermediate aryne. There is also evidence that stepwise insertion may occur depending on the substrate. It may well be that several parallel mechanisms are acting together and neither one nor the other mechanism could be proved or disproved. Further mechanistical studies have certainly to be undertaken to shed more light into the dark.

6 DIRECT CROSS-COUPLING OF ALUMINIUM SESQUIHALIDES

6.1 Abstract

The aluminium reagents prepared by the direct insertion of Al-powder in the presence of an appropriate additive required transmetallation with Zn-salts for a successful cross-coupling. This problem can be overcome by the use of PdCl₂(ttmp)₂ as catalyst.

6.2 Introduction

Transition metal-catalysed cross-coupling of organic halides with organometallics is one of the most important C-C bond forming reactions in organic synthesis.¹⁷⁴ The great impact of these synthetic transformations has been culminating in 2010's Nobel Prize award to Heck,¹⁷⁵ Suzuki,¹⁷⁶ and Negishi.¹⁷⁷ Whereas the cross-coupling of B,¹⁷⁸ Zn,¹⁷⁹ Sn¹⁸⁰ and Mg¹⁸¹ organometallics has been thoroughly developed during the last decades, cross-coupling reactions of organoaluminiums are rare, although alkenylalanes were used early on in Pd- and Ni-catalysed cross-couplings.¹⁸² In general, the cross-coupling of aluminium compounds was restricted to triorganoalanes such as AlPh₃¹⁸³ or AlEt₃,¹⁸⁴ in which case only one organic rest was transferred. However, the coupling of mixed organoalanes like RAlEt₂ or RAl(*i*Bu)₂ (R = Ar, alkenyl or alkynyl) as well as organoaluminates e.g. RAl(*i*Bu)₃Li have been reported recently.^{182, 185} (The unsaturated R group was always transferred selectively.) The cross-coupling of alkyl, vinyl and allyl groups

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¹⁷⁵ a) R. F. Heck, *J. Am. Chem. Soc.* **1968**, *90*, 5518; b) R. F. Heck, *J. Am. Chem. Soc.* **1969**, *91*, 6707; c) R. F. Heck, J. P. Nolley, *J. Org. Chem.* **1972**, *37*, 2320.

¹⁷⁶ a) N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, *20*, 3437; b) N. Miyaura, A. Suzuki, *J. Chem. Soc. Chem. Commun.* **1979**, 866; c) A. Suzuki, *Angew. Chem.* **2011**, *123*, 6854; *Angew. Chem. Int. Ed.* **2011**, *50*, 6722.

¹⁷⁷ a) E. Negishi, S. Baba, *Chem. Commun.* **1976**, 596; b) S. Baba, E. Negishi, *J. Am. Chem. Soc.* **1976**, *98*, 6729; c) E. Negishi, A. O. King, N. Okukado, *J. Org. Chem.* **1977**, *42*, 1821; d) A. O. King, N. Okukado, E. Negishi, *J. Chem. Soc., Chem. Commun.* **1977**, 683; For reviews see: e) E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340; f) E. Negishi, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 233; g) E. Negishi, *Angew. Chem.* **2011**, *123*, 6870; *Angew. Chem. Int. Ed.* **2011**, *50*, 6738.

¹⁷⁸ a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; b) T. Ishiyama, H. Kizaki, T. Hayashi, A. Suzuki, N. Miyaura, *J. Org. Chem.* **1998**, *63*, 4726; c) A. Suzuki, *J. Organomet. Chem.* **1999**, *576*, 147; d) M. R. Rivero, G. A. Molander, *Org. Lett.* **2002**, *4*, 107.

¹⁷⁹ a) J. E. Milne, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 13028; b) S. Son, G. C. Fu, *J. Am. Chem. Soc.* **2008**, *130*, 2756; c) S. Sase, M. Jaric, A. Metzger, V. Malakhov, P. Knochel, *J. Org. Chem.* **2008**, *73*, 7380; d) C. Wang, T. Tobrman, Z. Xu, E. Negishi, *Org. Lett.* **2009**, *11*, 4092; e) A. Krasovskiy, C. Duplais, B. H. Lipshutz, *J. Am. Chem. Soc.* **2009**, *131*, 15592; f) C. Han, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 7532; g) L. Melzig, A. Metzger, P. Knochel, *Chem. Eur. J.* **2011**, *17*, 2948.

¹⁸⁰ a) F. K. Sheffy, J. P. Godschalx, J. K. Stille, *J. Am. Chem. Soc.* **1984**, *106*, 4833; b) J. K. Stille, *Angew. Chem.* **1986**, *98*, 504; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508; c) V. Farina, V. Krishnamurty, W. J. Scott, *Org. React.* **1997**, *50*, 1; d) D. A. Powell, T. Maki, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 510; e) J. R. Naber, S. L. Buchwald, *Adv. Synth. Catal.* **2008**, *350*, 957.

¹⁸¹ a) J. Terao, H. Watanabe, A. Ikumi, H. Kuniyasu, N. Kambe, *J. Am. Chem. Soc.* **2002**, *124*, 4222; b) N. Yoshikai, H. Mashima, E. Nakamura, *J. Am. Chem. Soc.* **2005**, *127*, 17978; c) R. Martin, S. L. Buchwald, *J. Am. Chem. Soc.* **2007**, *129*, 3844; d) S. Y. W. Lau, G. Hughes, P. D. O'Shea, I. W. Davies, *Org. Lett.* **2007**, *9*, 2239; e) N. Yoshikai, H. Yatsuda, E. Nakamura, *J. Am. Chem. Soc.* **2009**, *131*, 9590; f) A. López-Pérez, J. Adrio, J. C. Carretero, *Org. Lett.* **2009**, *11*, 5514; g) B.-T. Guan, X.-Y. Lu, Y. Zheng, D.-G. Yu, T. Wu, K.-L. Li, B.-J. Li, Z.-J. Shi, *Org. Lett.* **2010**, *12*, 396.

¹⁸² a) E. Negishi, S. Baba, *Chem. Commun.* **1976**, 596; b) S. Baba, E. Negishi, *J. Am. Chem. Soc.* **1976**, *98*, 6729.

¹⁸³ a) N. A. Bumagin, A. B. Ponomaryov, I. P. Beletskaya, *J. Organomet. Chem.* **1985**, *291*, 129; b) N. A. Bumagin, A. P. Ponomaryov, I. P. Beletskaya, *Tetrahedron Lett.* **1985**, *26*, 4819; c) E. Negishi, Y. Noda, F. Lamaty, E. Vawter, *Tetrahedron* **1990**, *31*, 4393; d) K.-H. Wu, H.-M. Gau, *J. Am. Chem. Soc.* **2006**, *128*, 14808; e) C.-A. Chen, K.-H. Wu, H.-M. Gau, *Angew. Chem.* **2007**, *119*, 5469; *Angew. Chem. Int. Ed.* **2007**, *46*, 5373; f) S.-L. Ku, X.-P. Hui, C.-A. Chen, Y.-Y. Kuo, H.-M. Gau, *Chem. Commun.* **2007**, 3847; For a Fe-catalysed version see: g) S. Kawamura, K. Ishizuka, H. Takaya, M. Nakamura, *Chem. Commun.* **2010**, *46*, 6054.

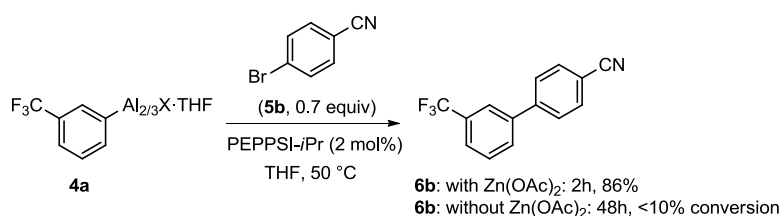
¹⁸⁴ a) E. Negishi, S. Gagneur in *Handbook of Organopalladium Chemistry for Organic Synthesis*, (Ed.: E. Negishi), John Wiley & Sons, New York, **2002**, pp. 597-618 and references therein; b) M. Shenglof, D. Gelman, G. A. Molander, J. Blum, *Tetrahedron Lett.* **2003**, *44*, 8593.

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is also possible by using appropriate amino and oxygen ligands.¹⁸⁶ Recently, we reported a new and general preparation of functionalized organoaluminiums by direct insertion of aluminium powder, leading to organoaluminium halides of the type R_2AlX and $RAlX_2$, abbreviated as $RAl_{2/3}X$. These aluminium reagents are reluctant to undergo directly C-C bond formation and a transmetallation to the corresponding zinc species was required for the performance of cross-couplings.

6.3 Direct Cross-Coupling of Aluminium Sesquihalides using $Pd(ttmpp)_2Cl_2$

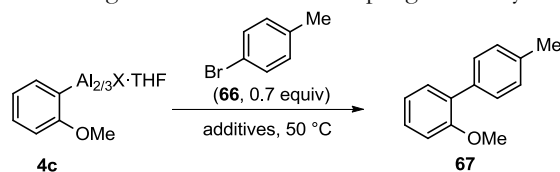
One of the major drawbacks of the catalysed aluminium insertion has been the necessity for transmetallation with Zn-salts prior to a successful cross-coupling of the aluminium sesquihalides. A comparison experiment showed clearly that the aryl aluminium sesquihalides did not undergo successful cross-coupling without the presence of Zn-salts (Scheme 80).



Scheme 80: Comparison of a PEPPSI-*i*Pr catalysed cross-coupling with and without the use of $Zn(OAc)_2$.

Even the more electron-rich aluminium reagent **4c** (which should undergo cross-coupling more easily) did not react under various conditions, whereas again the cross-coupling performed well using $Zn(OAc)_2$ and PEPPSI-*i*Pr leading to 100% conversion within 30 min (Table 22, Entry 1). It could be shown that it is not the acetate anion that facilitates the reaction, but the Zn-source, as the reaction with $Li(OAc)$ and PEPPSI-*i*Pr did not furnish the desired biphenyl **67** at all (Table 22, Entry 2). Additives like $EtAl_3$ (which should lead to disproportionation of the sesquihalide and therefore formation of $RAlEt_2$) did not lead to any cross-coupling although these reagents should at least transfer the aryl moiety (Table 22, Entries 3-4).¹⁸² Also, any attempt to displace the halides of the sesquihalide by addition of organometallics such as *n*BuLi, or MeMgCl and therefore formation of the mixed aryl-alkyl-aluminium reagent or aluminates did not lead to any useful results (Table 22, Entries 5-6). Iron or nickel catalysis using $Fe(acac)_3$ or $NiBr_2(PPh_3)_2$ was not successful (Table 22, Entries 7-8). The combination of $Pd(OAc)_2$ and PCy_3 has been reported to catalyse the cross-coupling of aryl-alkyl organoaluminiums,^{185c} but it is not capable to efficiently couple the aluminium halides (Table 22, Entry 9). Even the electron rich ligand $AsPh_3$ in combination with $Pd(dba)_2$ did not lead to a successful cross-coupling (Table 22, Entry 10).

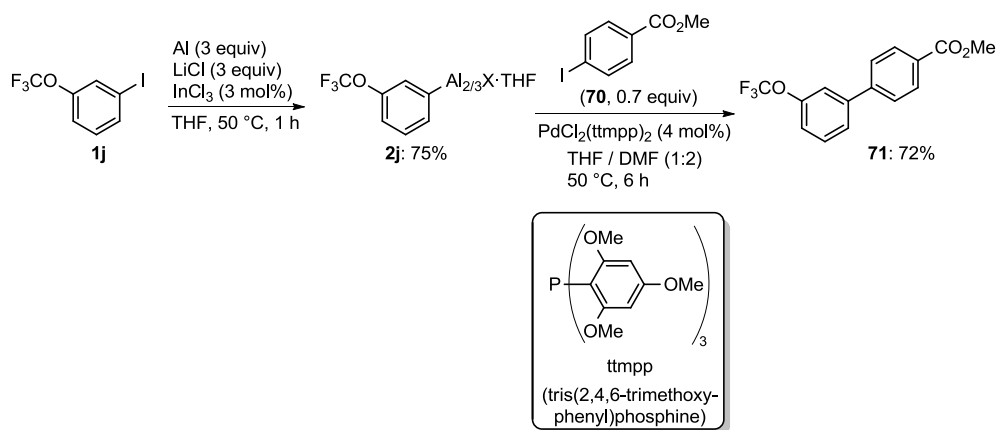
¹⁸⁶ a) J. Blum, D. Gelman, W. Baidossi, E. Shakh, A. Rosenfeld, Z. Aizenshtat, *J. Org. Chem.* **1997**, *62*, 8681; b) J. Blum, O. Berlin, D. Milstein, Y. Ben-David, B. Wassermann, S. Schutte, H. Schumann, *Synthesis* **2000**, 571; c) D. Gelman, S. Dechert, H. Schumann, J. Blum, *Inorg. Chim. Acta* **2002**, *334*, 149; d) M. Shenglof, G. A. Molander, J. Blum; *Synthesis* **2006**, 111; e) H. Schumann, J. Kaufmann, H.-G. Schmalz, A. Böttcher, B. Gotov, *Synlett* **2003**, 1783; f) E. Negishi, N. Okukado, A. O. King, D. E. Van Horn, B. I. Spiegel, *J. Am. Chem. Soc.* **1978**, *100*, 2254.

Table 22: Additive screening for the direct cross-coupling of the arylaluminium reagent **4c**.

Entry	Additives ^a	Reaction Time	Conversion ^b
1	PEPPSI, Zn(OAc) ₂ (1.5 equiv)	30 min	100%
2	PEPPSI, Li(OAc) (3.0 equiv)	24 h	- ^c
3	PEPPSI, Et ₃ Al (1.0 equiv)	24 h	- ^c
4	PEPPSI, Et ₃ Al (2.0 equiv)	24 h	- ^c
5	PEPPSI, <i>n</i> BuLi (1.5 equiv)	24 h	- ^c
6	PEPPSI, EtMgCl (1-2 equiv)	24 h	- ^c
7	Fe(acac) ₃	24 h	- ^c
8	NiBr ₂ (PPh ₃) ₂	24 h	- ^{c, d}
9	Pd(OAc) ₂ , PCy ₃	48 h	7%
10	Pd(dba) ₂ , AsPh ₃	48 h	4% ^e

^a PEPPSI-*n*Pr (2 mol%), Fe(acac)₃ (5 mol%), NiBr₂(PPh₃)₂ (5 mol%), Pd(OAc)₂ (2 mol%), PCy₃ (4 mol%), Pd(dba)₂ (2 mol%), AsPh₃ (4 mol%). ^b Conversion as indicated by GC-analysis of hydrolyzed reaction aliquots. ^c No conversion to product could be determined. ^d Ethyl 3-iodobenzoate was used as electrophile. ^e The reaction was tried with aluminium reagents **2a** and ethyl 3-bromobenzoate as electrophile.

However, the use of the electron-rich PdCl₂(ttmpp)₂ in combination with a polar co-solvent like NMP or DMF allowed for the first time the use of aluminium sesquihalides for a cross-coupling reaction. Thus, the aryl iodide **1j** was converted to the aluminium reagent **2j** in 75% yield by the reaction with Al-powder (3 equiv), LiCl (3 equiv) and InCl₃ (3 mol%) within 1 h at 50 °C. A successful cross-coupling with methyl 4-iodobenzoate (**70**) employing 4 mol% of PdCl₂(ttmpp)₂ furnished the ester substituted biphenyl **71** in 72% yield (Scheme 81).

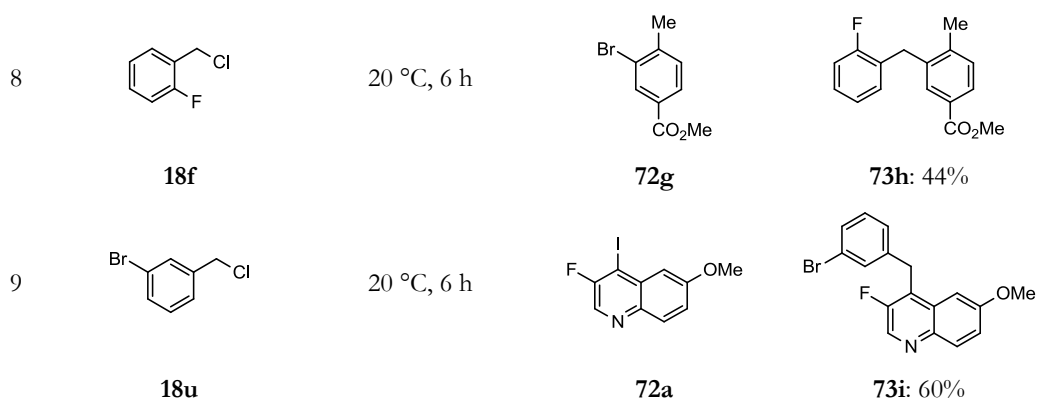
**Scheme 81:** Direct cross-coupling of the arylaluminium sesquichloride **69** using PdCl₂(ttmpp)₂.

This catalyst was not only effective in direct cross-couplings of aryl aluminiums, also benzylic aluminium halides could be coupled smoothly. Thus, 4-methyl benzyl chloride (**18h**) furnished after standard insertion conditions (12 h, 20 °C) the aluminium reagent **19h** which underwent a smooth cross-coupling

with the quinoline derivative **72a** in the presence of $\text{PdCl}_2(\text{ttmp})_2$. The functionalized heterocycle **73a** was isolated in 93% yield (Table 23, Entry 1). Also the electron-rich 4-methoxybenzyl chloride (**18i**) was converted to the aluminium reagent **19i** (20 °C, 5 h) using the typical conditions. Successful cross-couplings with ester bearing electrophiles (**72b-c**) led to the functionalized diarylmethanes **73b-c** in 36% and 69% yield (Table 23, Entries 2-3). Also, various other benzylic aluminium reagents could be readily functionalized using this new catalyst affording the functionalized diarylmethanes (**73d-i**) in moderate to good yields (42-78%, Table 23, Entries 4-9).

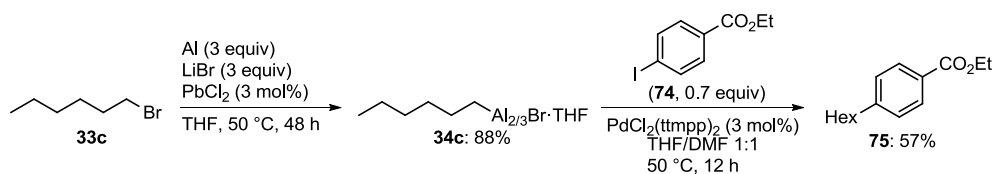
Table 23: Al-Insertion into benzylic chlorides and direct cross-coupling using $\text{PdCl}_2(\text{ttmp})_2$.

Entry	Benzylic Chloride	Insertion Conditions	Electrophile ^a	Product ^b
1		20 °C, 3 h		 73a: 93%
2		20 °C, 5 h		 73b: 36%
3		20 °C, 5 h		 73c: 69%
4		20 °C, 12 h		 73d: 78%
5		20 °C, 12 h		 73e: 70%
6		20 °C, 6 h		 73f: 68%
7		20 °C, 6 h		 73g: 42%



^a 0.7 equiv of electrophile has been used. ^b Isolated yield of analytically pure product.

Furthermore, also the alkylaluminium reagent **34c** reacted directly in a cross-coupling reaction. Thus, the reaction of **34c** with ethyl 4-iodobenzoate (**74**, 0.7 equiv) furnished after 4 h at 50 °C (THF/DMF = 1:2) the alkylated ester **75** in 57% yield. Unfortunately, in this case *beta*-hydride elimination is responsible for the lower yield.



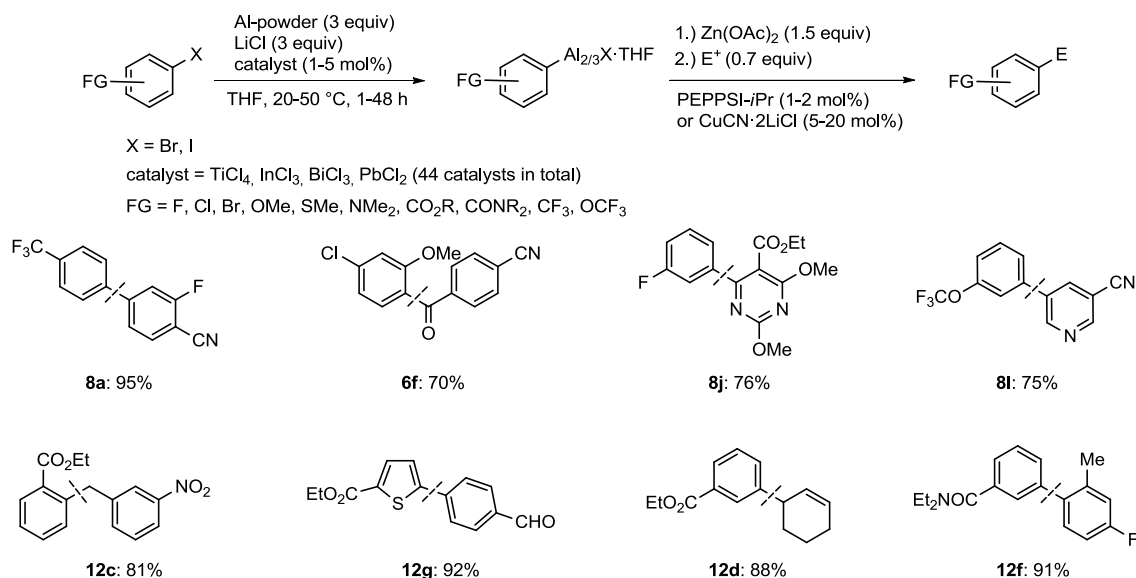
Scheme 82: Direct cross-coupling of an alkylaluminium sesquihalide using PdCl₂(tmpp)₂.

7 SUMMARY AND OUTLOOK

This work focused on the synthesis and applications of organoaluminium compounds. A new synthesis of aryl aluminium sesquihalides has been developed. Furthermore, the synthetic method could be applied to benzylic chlorides offering access to a new class of formerly not preparable aluminium reagents. Preliminary results show that this methodology is also applicable to alkyl halides. Moreover, allylic aluminium sesquihalides were prepared and their use in diastereoselective additions to carbonyls was demonstrated. A new synthesis of 1,2-bimetallic reagents has been developed. Finally, the synthetic value of organoaluminium sesquichlorides could be demonstrated in a newly developed cross-coupling reaction.

7.1 Catalysed Aluminium Insertion into Aryl Halides

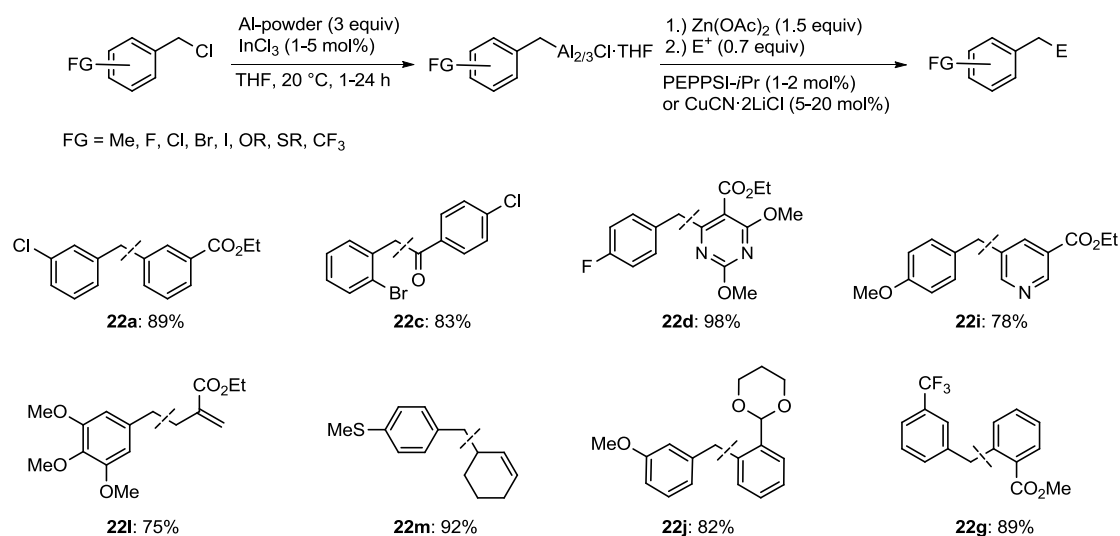
In summary, we have developed a new practical and convenient synthesis of aryl aluminium reagents by the direct insertion of Al-powder into various aryl halides in the presence of LiCl and catalytic amounts of certain additives. The choice of the additive depends on the nature of the aryl halide. We investigated the effect of 44 different additives on the reaction of aryl halides with Al-powder. For aryl bromides TiCl_4 proved to be the most effective catalyst. Aryl iodides are best converted to aluminium reagents using InCl_3 or BiCl_3 as catalyst. Aryl iodides and heterocyclic bromides bearing carbonyl functionalities are effectively converted to aryl aluminium reagents by utilizing PbCl_2 as additive. A broad range of functional groups is tolerated during the insertion and subsequent functionalization reactions leading to a variety of pharmaceutically interesting products (Scheme 83).



Scheme 83: Additive-catalysed insertion of Al-powder into aryl halides and subsequent functionalization.

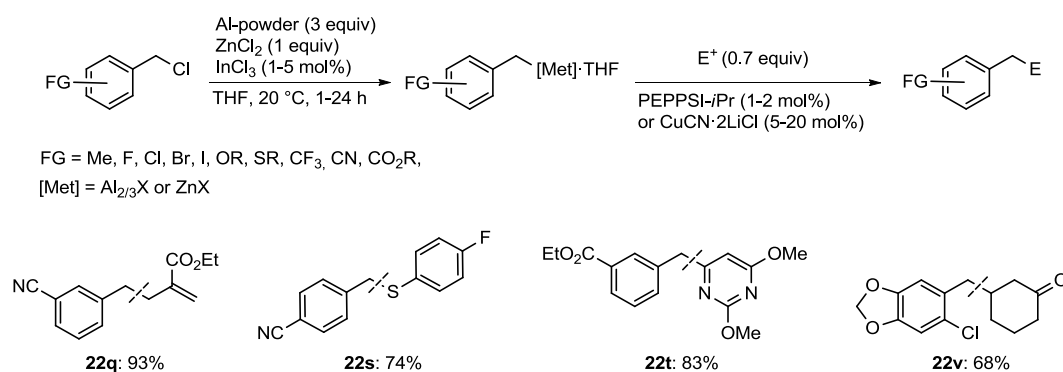
7.2 Catalysed Aluminium Insertion into Benzylic Halides

In summary, we have developed a new and general synthesis of benzylic aluminium sesquichlorides. These new reagents can be conveniently prepared under mild conditions and tolerate a broad range of functional groups during the insertion and functionalization reaction. Subsequent trapping with various electrophiles leads to a variety of pharmaceutically interesting compounds such as diarylmethanes (Scheme 84).



Scheme 84: InCl₃-mediated insertion of Al-powder into benzylic chlorides and subsequent functionalization.

Highly functionalized benzylic chlorides or secondary benzylic chlorides which are prone to undergo *Wurtz*-coupling can be conveniently converted to benzylic aluminium and zinc reagents in the presence of ZnCl₂ (Scheme 85).



Scheme 85: Aluminium insertion in the presence of ZnCl₂ and subsequent functionalization.

NMR-studies revealed that the aluminium insertion in the presence of ZnCl_2 leads to a mixture of benzylic aluminium and benzylic zinc reagents (Figure 24).

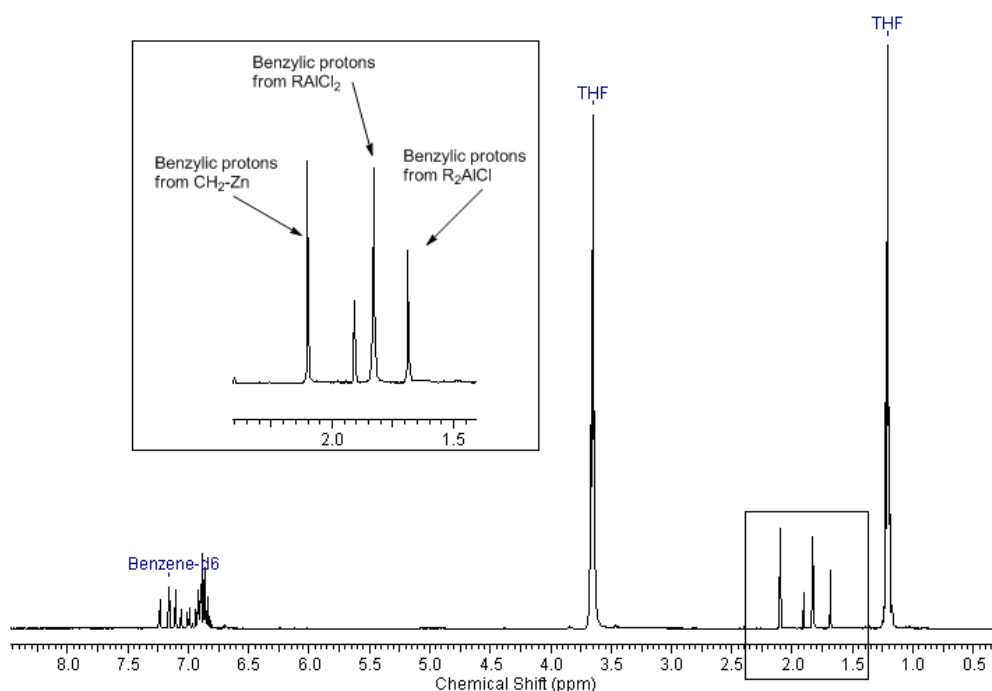
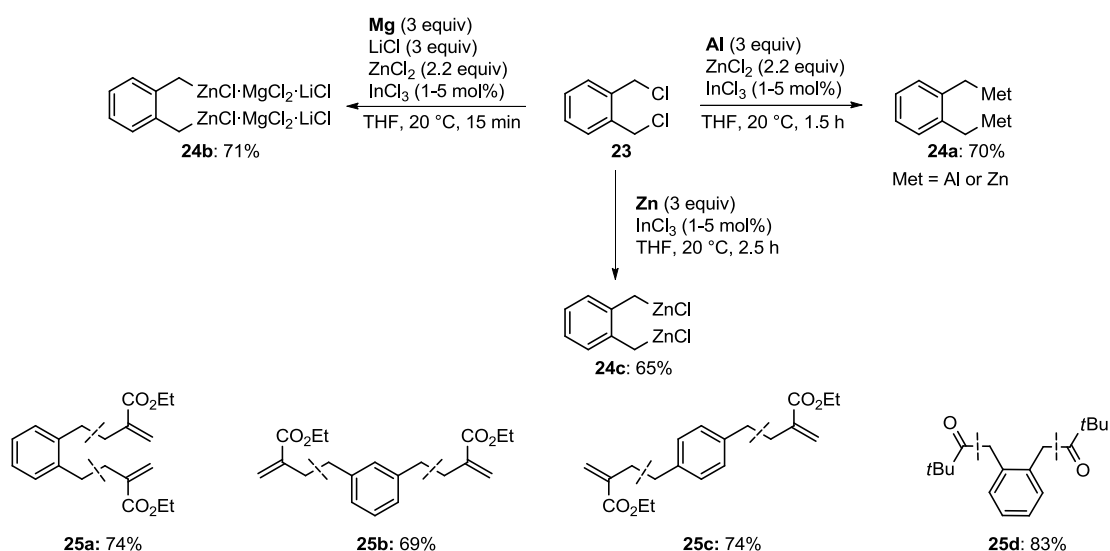


Figure 24: ^{13}C -NMR spectrum showing a mixture of benzylic aluminium and benzylic zinc reagent obtained by the insertion of Al-powder in the presence of ZnCl_2 .

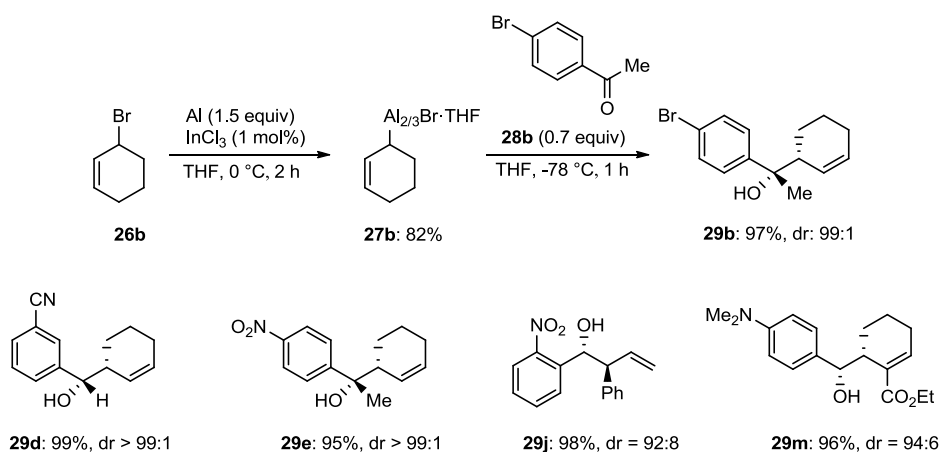
Moreover, efficient protocols for the preparation of bis-benzylic organometallics by direct insertion of Al, Mg and Zn have been developed. The reagents are obtained in good yields and can be prepared under mild conditions without the need for dropwise addition. It could be shown that catalytic amounts of InCl_3 dramatically accelerate the insertion of Al, Mg and Zn into benzylic chlorides (Scheme 86).



Scheme 86: Mg, Al and Zn can be readily inserted into benzylic chlorides under mild conditions in the presence of catalytic amounts of InCl_3 .

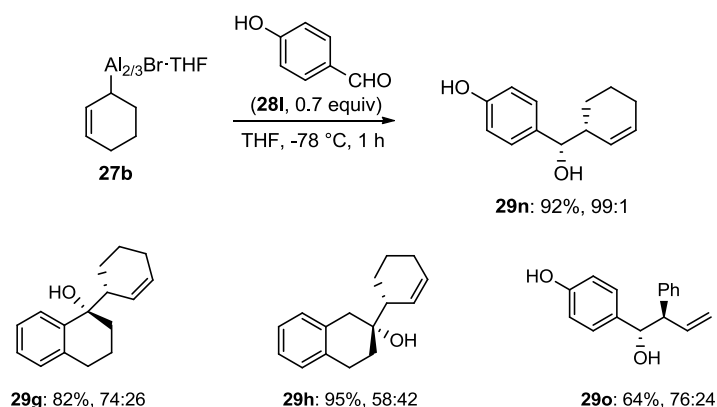
7.3 Diastereoselective Addition of Allylic Aluminium Reagents to Aldehydes and Ketones

An efficient protocol for the preparation of various allylic aluminium sesquichlorides has been developed. These allylic reagents undergo diastereoselective addition to carbonyl derivatives allowing the construction of two adjacent tertiary and quaternary centers. Remarkably, these reagents show a high nucleophilicity towards carbonyl groups, but do not attack other functionalities such as nitro-groups, nitriles or esters (Scheme 87).



Scheme 87: Allylic aluminium reagents add diastereoselectively to aldehydes and ketones.

Moreover, despite the high nucleophilicity the reagents do not display a high basicity, adding smoothly to enolizable ketones (which usually decompose in the presence of organometallic reagents) and tolerate even unprotected phenols (Scheme 88).

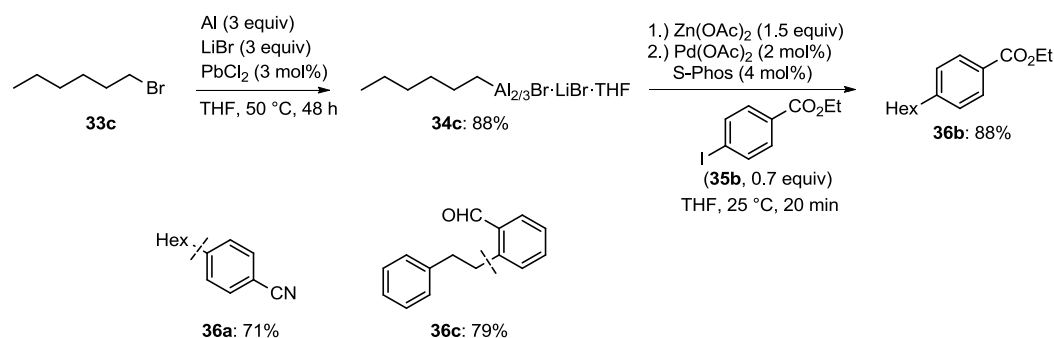


Scheme 88: Allylic aluminium reagents show an excellent tolerance towards acidic protons.

The tolerance of unprotected alcohols is a remarkable feature as non-economic protection/deprotection steps can be avoided. Future studies could include the use of these reagents in sugar-chemistry.

7.4 Catalysed Aluminium Insertion into Alkyl Halides

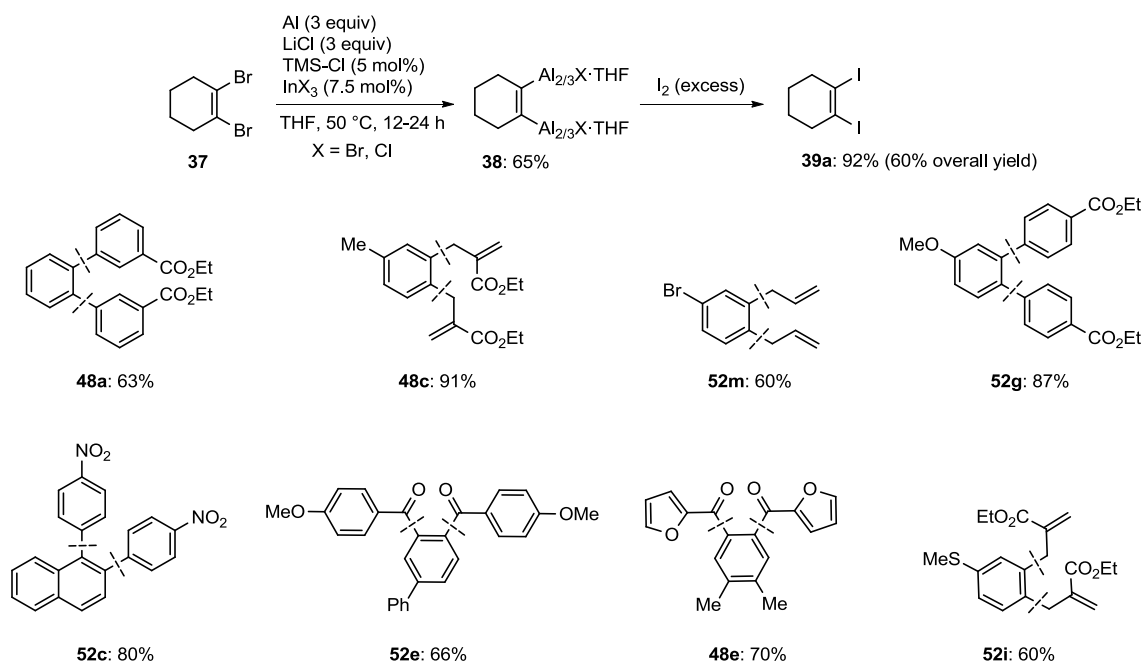
Preliminary studies have shown that the catalysed aluminium insertion can be extended to higher alkyl halides. This is a remarkable improvement as alkyl chains containing more than 4 carbon atoms could never be conveniently converted to aluminium sesquihalides by the direct insertion of aluminium powder (Scheme 89).



Scheme 89: Preparation of alkyl aluminium reagents and subsequent cross-coupling reaction.

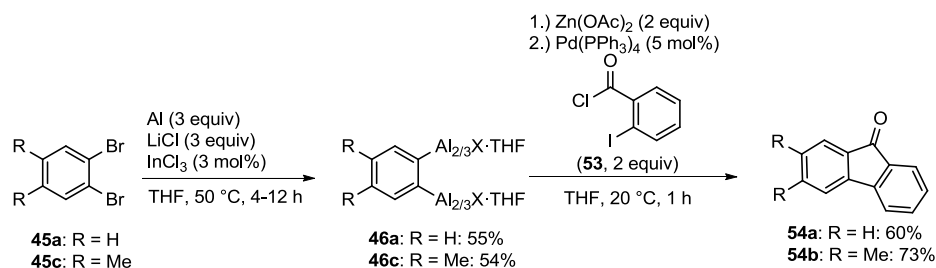
7.5 InCl₃-Mediated Preparation of 1,2-Bimetallics

A remarkable synthesis of 1,2-bimetallics has been achieved by direct insertion of aluminium powder to aryl and vinyl 1,2-dibromides as well as *ortho*-bromo triflates. These bimetallic reagents could be readily used for bis-functionalization in a one-step procedure affording interesting products for pharmaceutical or material science (Scheme 90).



Scheme 90: Preparation of vinylic and aromatic 1,2-bimetallics and subsequent bis-functionalizations.

Furthermore, these new organometallics can be used for cyclization reactions and allow for example the easy construction of fluorenones (Scheme 91).



Scheme 91: Preparation of 1,2-bimetallics and subsequent ring closure with 2-iodobenzoyl chloride.

The formation of 1,2-bimetallics has been proven additionally by ESI-mass spectrometry. The spectroscopic data reveals that several aluminates exist in solution (Figure 25).

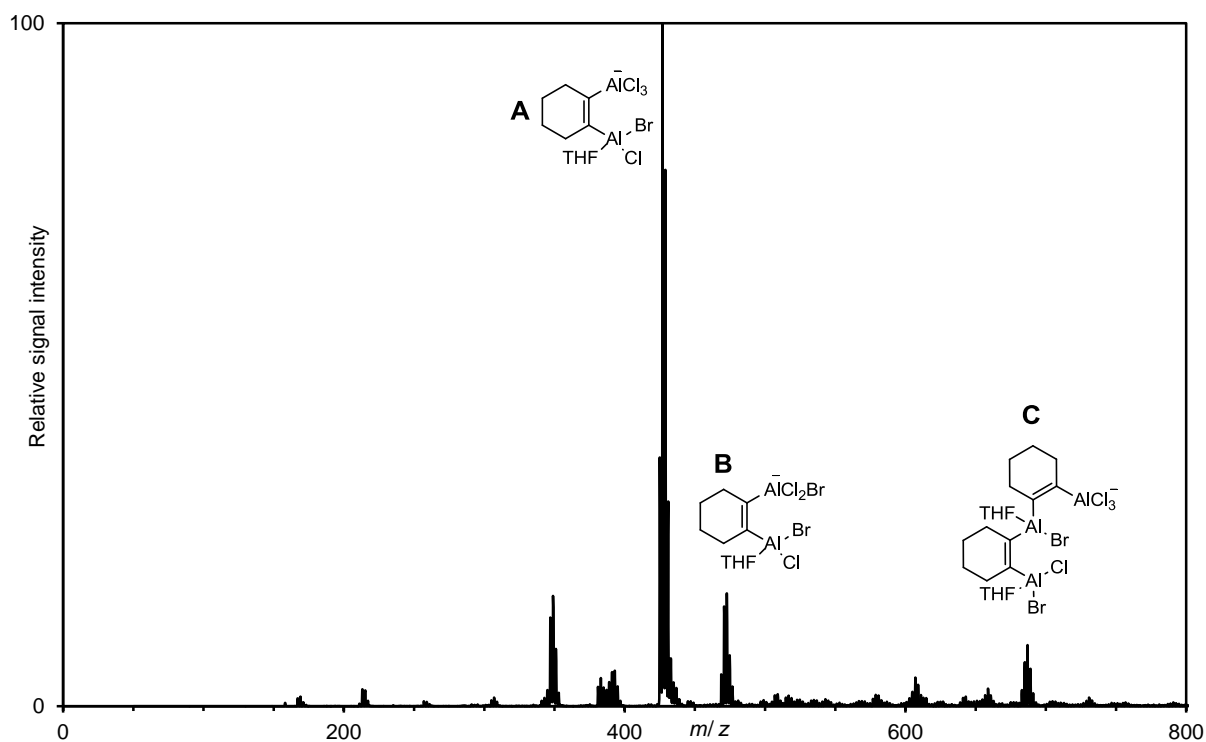
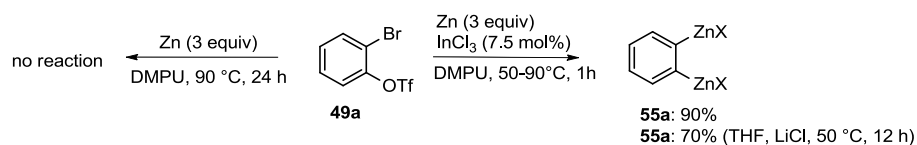


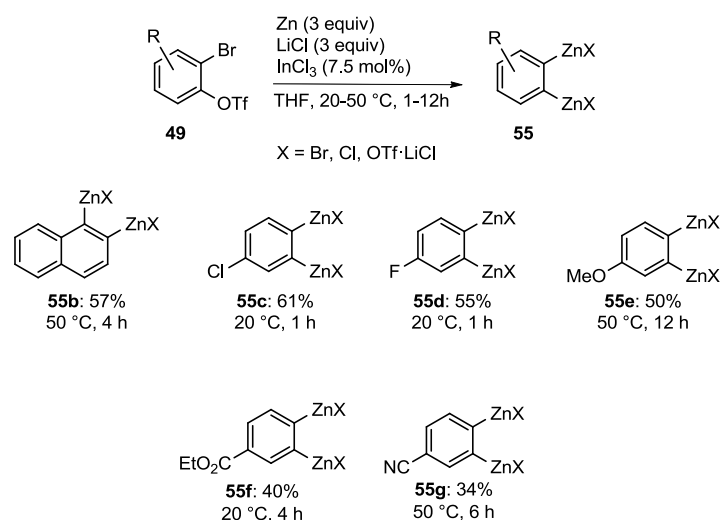
Figure 25: ESI-mass spectrometry reveals that several bimetallic aluminates are formed by the insertion of aluminium into 1,2-dihalides or *o*-bromo-triflates.

Moreover, our results have shown that InCl₃ also dramatically enhances the insertion of Zn-powder to aryl halides. 1,2-bimetallics can also be prepared conveniently from *ortho* bromo-triflates using Zn and a catalytic amount of InCl₃ whereas no reaction is occurring in the absence of the catalyst (Scheme 92).



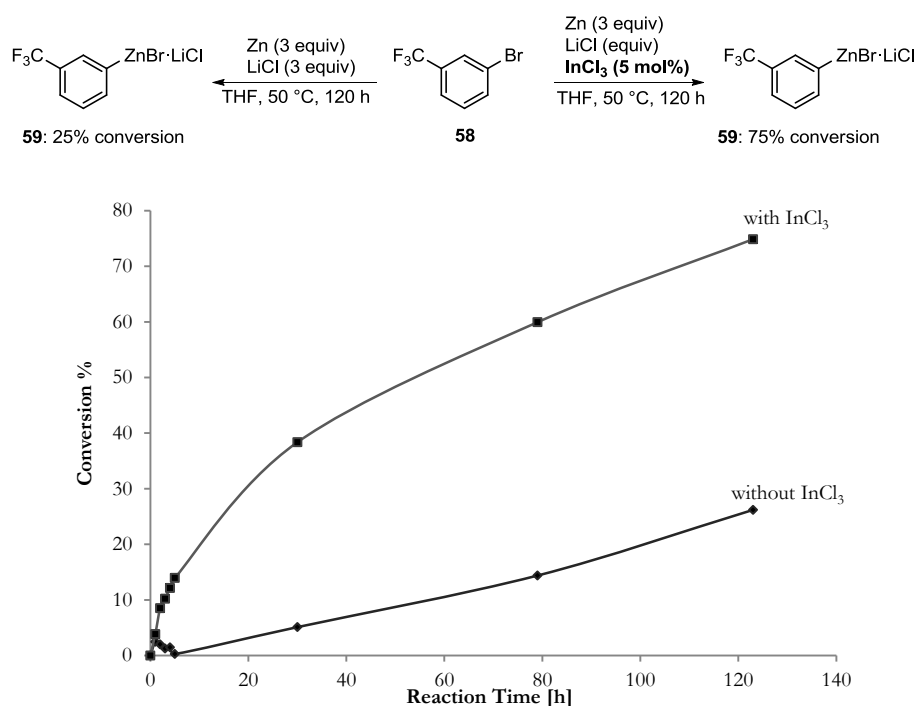
Scheme 92: InCl₃ promotes the insertion of Zn into aryl halides.

Several aromatic *ortho*-bromo triflates can be converted to 1,2-bimetallics by the insertion of Zn-powder in the presence of LiCl and InCl₃ (Scheme 93).



Scheme 93: Preparation of 1,2-bimetallics by direct insertion of Zn-powder.

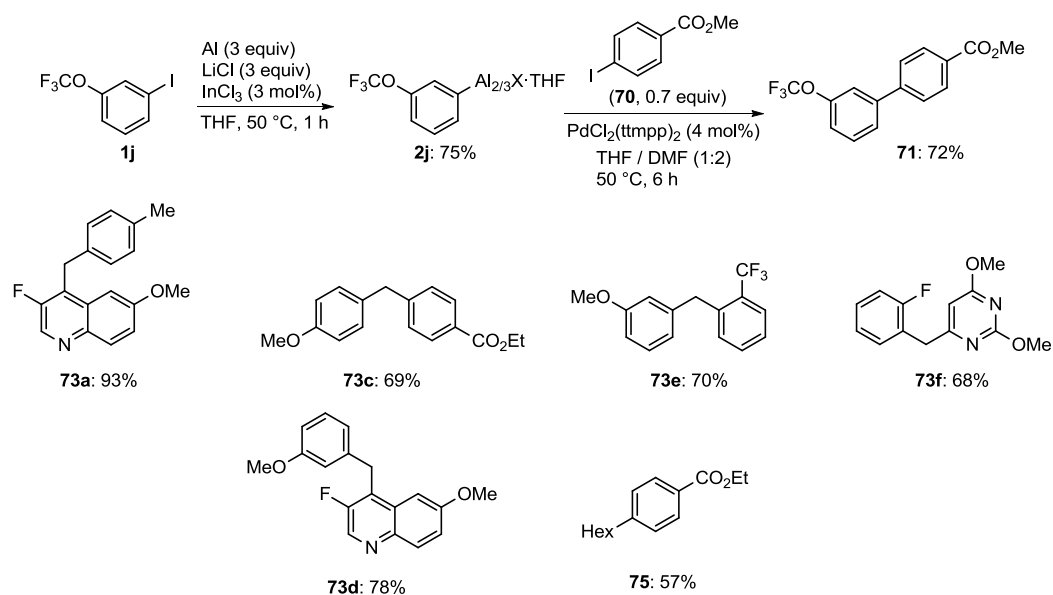
InCl₃ not only promotes the Zn-insertion into aromatic *ortho*-bromo-triflates, also other aromatic bromides can be converted to aryl zinc reagents in a faster way (Scheme 95). Further studies should be undertaken to investigate if a general preparation of aryl zinc reagents from aromatic bromides is possible.



Scheme 94: Effect of InCl₃ on the insertion of Zn-powder into the aryl bromide **58**.

7.6 Direct Cross-Coupling of Aluminium Sesquihalides

The aluminium sesquichlorides prepared by the direct insertion of aluminium were reluctant to react in cross-coupling reactions without the presence of Zn-salts. This drawback could be overcome by the use of the electron rich catalyst $\text{PdCl}_2(\text{ttmp})_2$. In summary, we have developed an atom-economical cross-coupling reaction of aluminium sesquichlorides. Aryl-, alkyl- and benzylic aluminium reagents could be readily used in the developed protocol (Scheme 95).



Scheme 95: Direct cross-coupling of aryl, benzyl and alkyl aluminium reagents using $\text{PdCl}_2(\text{ttmp})_2$.

C. EXPERIMENTAL SECTION

1 GENERAL CONSIDERATIONS

All reactions were carried out with magnetic stirring and, if air and moisture sensitive, under argon or nitrogen atmosphere in glassware dried with a heat gun. Syringes and needles which were used to transfer anhydrous solvents or reagents were purged three times with argon or nitrogen prior to use. High vacuum refers to a pressure of $9 \cdot 10^{-2}$ mbar. Indicated yields refer to isolated yields of compounds estimated to be of >95% purity as determined by $^1\text{H-NMR}$ spectroscopy or capillary GC, unless otherwise stated.

1.1 Solvents

Solvents were dried according to the standard procedures by distillation over drying agents and then stored under inert atmosphere (argon or nitrogen) over molecular sieves (4Å) purchased from ACROS.

CH_2Cl_2 was predried over CaCl_2 and distilled from CaH_2 .

DMF was heated to reflux for 14 h over CaH_2 and distilled from CaH_2 .

DMPU was heated to reflux for 14 h over CaH_2 and distilled from CaH_2 .

EtOH was treated with phthalic anhydride (25 g/L) and sodium, heated to reflux for 6 h and distilled.

Et₂O was predried over calcium hydride and dried with the solvent purification system SPS-400-2 from INNOVATIVE TECHNOLOGIES INC.

NMP was predried over CaCl_2 and distilled from CaH_2 .

Pyridine was dried over KOH and distilled.

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

Toluene was predried over CaCl_2 and distilled from CaH_2 .

NEt₃ was dried over KOH and distilled.

Solvents for column chromatography (pentane, isohexane, Et₂O, EtOAc and DCM) were distilled on a rotary evaporator prior to use.

1.2 Reagents

All reagents were obtained from commercial sources and used without further purification unless otherwise stated. Aluminium powder (99%, 200 mesh) was purchased from ALDRICH or CHEMPUR. Magnesium turnings (>99.5%) and zinc dust (>90%) were purchased from RIEDEL-DE HAËN. InCl_3 (99.99%, anhydrous), InBr_3 (99.99%, anhydrous) and PbCl_2 (99.999%, anhydrous) were purchased from CHEMPUR. BiCl_3 (98%+, anhydrous) and Zn(OAc)_2 (99%, anhydrous) were purchased from ACROS. TiCl_4 was purchased from ACROS and distilled prior to use. CuCN and ZnCl_2 were obtained from FLUKA. LiCl (99%) was obtained from GRÜSSING GmbH (Filsum, Germany).

***i*-PrMgCl·LiCl** solution in THF was purchased from CHEMETALL.

PhMgCl solution in THF was purchased from CHEMETALL.

***n*-BuLi** solution in hexane was purchased from CHEMETALL.

CuCN·2 LiCl solution (1.00 M) was prepared by drying CuCN (80.0 mmol, 7.17 g) and LiCl (160 mmol, 6.77 g) in a *Schlenk*-tube under vacuum at 140 °C for 5 h. After cooling, 80 mL dry THF were added and stirring was continued until the salt was dissolved.

ZnCl₂ solution (1.00 M) was prepared by drying ZnCl₂ (100 mmol, 136 g) in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, 100 mL dry THF were added and stirring was continued until the salt was dissolved.

1.3 Content Determination of Organometallic Reagents

Organozinc- and organomagnesium reagents were titrated against I₂ in THF or DCM.

The amount of organolithium reagent in solution was determined according to Parquette.¹⁸⁷

The amount of organoaluminium reagent in solution was determined by reacting an aliquot (0.5 – 1.0 mL) of the solution containing the aluminium reagent with an excess of I₂ in THF at 20 °C and subsequent back-titration of I₂ using a 0.1 N Na₂S₂O₃ stock solution.

1.4 Chromatography

Thin layer chromatography (TLC) was performed using aluminium plates coated with SiO₂ (MERCK 60, F-254). The spots were visualized either by UV light or by using one of the typical stains followed by heating with a heat gun if necessary.

- KMnO₄ (3.0 g), 5 drops of conc. H₂SO₄ in water (300 mL).
- Phosphomolybdic acid (5.0 g), Ce(SO₄)₂ (2.0 g) and conc. H₂SO₄ (12 mL) in water (230 mL).

Flash column chromatography was performed using silica gel 60 (0.040 – 0.063 mm, 230 – 400 mesh ASTM) from MERCK.

1.5 Analytical Data

¹H-NMR and **¹³C-NMR** spectra were recorded on VARIAN Mercury 200, BRUKER ARX 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments.

Mass spectroscopy: High resolution (HRMS) and low resolution (MS) spectra were recorded on a FINNIGAN MAT 95Q instrument. Electron impact ionization (EI) was conducted with an electron

¹⁸⁷ H.S. Lin, L. A. Paquette, *Synth. Commun.* **1994**, *24*, 2503.

energy of 70 eV. For the combination of gas chromatography with mass spectroscopic detection, a GC/MS from Hewlett-Packard HP 6890 / MSD 5973 was used.

Infrared spectra (IR) were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection a SMITHS DETECTION DuraSamplIR II Diamond ATR sensor was used. Wavenumbers are reported in cm^{-1} .

Melting points (mp) were determined on a BÜCHI B-540 apparatus and are uncorrected.

2 TYPICAL PROCEDURES

2.1 Typical Procedure for the TiCl_4 – Catalysed Aluminium Insertion into Aryl Bromides (TP1).

LiCl (1.5 – 3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with a solution of the catalyst (TiCl_4 , 1 M solution in toluene, 3 mol%) and internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH_4Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.2 Typical Procedure for the InCl_3 – Catalysed Aluminium Insertion into Aryl Iodides (TP2).

LiCl (1.5 – 3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. The catalyst (InCl_3 , 3 mol%) was added under argon and the drying process was repeated for 5 min. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH_4Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.3 Typical Procedure for the BiCl₃ – Catalysed Aluminium Insertion into Aryl Iodides (TP3).

LiCl (1.5 – 3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. The catalyst (BiCl₃, 3 mol%) was added under argon and the drying process was repeated for 5 min. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.4 Typical Procedure for the PbCl₂ – Catalysed Aluminium Insertion into Aryl- and Heteroaryl Halides (TP4).

LiCl (1.5 – 3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. PbCl₂ (3 mol%) was added under argon and the drying process was repeated for 5 min. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.5 Typical Procedure for the Catalysed Aluminium Insertion into Aryl Halides using extended Pi-Systems (TP5).

LiCl (1.5 – 3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl

(3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion followed by the catalyst (**13a-m**, 1-5 mol%) and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.6 Typical Procedure for Cross-Coupling Reactions of Aryl Aluminium Reagents (TP6)

The aluminium reagent prepared according to the typical procedures **TP1 – TP5** was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (1.5 equiv). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of the electrophile (0.6 – 0.7 equiv) and PEPPSI-*i*Pr (1 – 2 mol%) in THF or NMP was added. The reaction mixture was stirred at the indicated temperature until GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or sat. aqueous NH₄Cl solution showed completion of the reaction. After completion of the reaction HCl (2 M) or sat. aqueous NH₄Cl solution (approx. 1 mL / mmol) was added and the aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo* and the crude residue was purified by flash column chromatography.

2.7 Typical Procedure for Allylation Reactions of Aryl Aluminium Reagents (TP7)

The aluminium reagent prepared according to the typical procedures **TP1 – TP5** was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (1.5 equiv). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of CuCN·2 LiCl (1 M solution in THF, 5 – 20 mol%) was added at the indicated temperature, followed by the addition of the allylic electrophile (0.6 – 0.7 equiv). The reaction mixture was stirred at the indicated temperature until GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) (attention: HCN is formed!) or sat. aqueous NH₄Cl solution showed completion of the reaction. After completion of the reaction HCl (2 M) or sat. aqueous NH₄Cl solution (approx. 1 mL / mmol) was added and the aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo* and the crude residue was purified by flash column chromatography.

2.8 Typical Procedure for the InCl_3 – Catalysed Aluminium Insertion into Benzylic Chlorides (TP8)

InCl_3 (1 – 5 mol%) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the benzylic chloride (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M)¹⁸⁸ until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the benzylaluminium reagent was used for further reactions.

2.9 Typical Procedure for the InCl_3 – Catalysed Aluminium Insertion into Benzylic Chlorides in the Presence of ZnCl_2 (TP9)

InCl_3 (1 – 5 mol%) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 mL / mmol) and ZnCl_2 -solution (1 M in THF, 1 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the benzylic chloride (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M)¹⁸⁸ until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution was used for further reactions.

2.10 Typical Procedure for the InCl_3 – Catalysed Aluminium Insertion into Bis-Benzylic Chlorides in the Presence of ZnCl_2 (TP10)

InCl_3 (1 – 5 mol%) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was repeated for 5 min. The flask was evacuated and backfilled with argon three times before ZnCl_2 -solution (1 M in THF, 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until

¹⁸⁸ Quenching with sat. aqueous NH_4Cl solution results in several signals during GC-analysis and hinders the monitoring process.

ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the bis-benzylic chloride (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M)¹⁸⁸ until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution was used for further reactions.

2.11 Typical Procedure for the InCl₃ – Catalysed Aluminium Insertion into Allylic Bromides (TP11)

InCl₃ (1 – 5 mol%) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (1.5 equiv) was added under argon and the drying process was repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (2.5 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. After stirring for 5 min the reaction mixture was cooled down to 0 °C and a solution of the allylic bromide (1 equiv) in THF (2.5 mL / mmol) was added with a syringe pump over a period of 1 h. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the allylaluminium reagent was used for further reactions.

2.12 Typical Procedure for the InCl₃ – Catalysed Aluminium Insertion into Allylic Chlorides (TP12)

InCl₃ (1 – 5 mol%) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (1.5 equiv) was added under argon and the drying process was repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (2.5 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) a solution of the allylic chloride (1 equiv) in THF (2.5 mL / mmol) was added and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the allylaluminium reagent was used for further reactions.

2.13 Typical Procedure for the Addition Reaction of Allylic Aluminium Reagents to Aldehydes and Ketones (TP13)

The aluminium reagent prepared according to the typical procedures **TP11** and **TP12** was separated from the remaining aluminium powder and added dropwise to a new flask containing a solution of the corresponding aldehyde or ketone (0.7 equiv) in THF (1.5 mL / equiv) at -78 °C. The reaction mixture was stirred at -78 °C for 1-2 h and then slowly warmed to 20 °C before being quenched with water (2.5 mL / equiv). The aqueous layer was extracted with ethyl acetate and the combined organic extracts were concentrated *in vacuo*. The crude residue was purified by flash column chromatography.

2.14 Typical Procedure for the PbCl₂ – Catalysed Aluminium Insertion into Alkyl Halides (TP14)

LiCl (1.5 – 3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. PbCl₂ (3 mol%) was added under argon and the drying process was repeated for 5 min. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.15 Typical Procedure for Cross-Coupling Reactions of Alkyl Aluminium Reagents (TP15)

The aluminium reagent prepared according to the typical procedure **TP14** was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (1.5 equiv). The resulting suspension was stirred for 20 min at 20 °C before a solution of the electrophile (0.6 – 0.7 equiv), Pd(OAc)₂ (2 mol%) and S-Phos (4 mol%) in THF was added. The reaction mixture was stirred at the indicated temperature until GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) showed completion of the reaction. After completion of the reaction HCl (2 M) or sat. aqueous NH₄Cl solution (approx. 1 mL / mmol) was added and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were concentrated *in vacuo* and the crude residue was purified by flash column chromatography.

2.16 Typical Procedure for the Preparation of Vinylic Bimetallics (TP16)

LiCl (3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion followed by the InBr₃ (7.5 mol%) and the reaction mixture stirred at the indicated temperature. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.17 Typical Procedure for the Preparation of Aromatic Bimetallics from Dibromides (TP17)

LiCl (3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. InCl₃ (7.5 mol%) was added and the drying process was repeated for 2 min. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the starting material (1 equiv) was added in one portion and the reaction mixture stirred at 50 °C. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

2.18 Typical Procedure for the Preparation Aromatic Bimetallics from *o*-Bromo-Triflates (TP18)

Variant A: Preparation in the presence of LiCl: LiCl (3 equiv) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. Continue with variant **B**.

Variant B: InCl₃ (7.5 mol%) was placed in an argon flushed *Schlenk*-flask and dried 5 min by heating with a heat gun (450 °C) under high vacuum. Aluminium powder (3 equiv) was added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before THF (1 – 2 mL / mmol) was added, along with the internal standard (heptadecane). TMS-Cl

(3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) the triflate (1 equiv) was added in one portion and the reaction mixture stirred at 50 °C. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or saturated aqueous NH₄Cl solution until a conversion of >95% was reached. The aluminium powder was allowed to settle down and the remaining solution containing the aluminium reagent was used for further reactions.

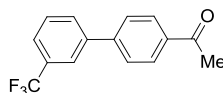
2.19 Typical Procedure for the Direct Cross-Coupling of Aluminium Reagents using PdCl₂(ttmpp)₂ (TP19)

The aluminium reagents prepared according to the typical procedures **TP1 – TP4, TP7, TP10** were separated from the remaining aluminium powder and transferred to a new flask containing a solution of the electrophile (0.6 – 0.7 equiv) and PdCl₂(ttmpp)₂ (2 – 4 mol%) in DMF (amount was varied to achieve an overall THF/DMF mixture of 1:1 or 1:2). The reaction mixture was stirred at the indicated temperature until GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M) or sat. aqueous NH₄Cl solution showed completion of the reaction. After completion of the reaction HCl (2 M) or sat. aqueous NH₄Cl solution (approx. 1 mL / mmol) was added and the aqueous layer was extracted with diethyl ether or ethyl acetate. The combined organic extracts were concentrated *in vacuo* and the crude residue was purified by flash column chromatography.

3 PRODUCT SYNTHESIS AND ANALYTICAL DATA

3.1 TiCl₄ – Catalysed Aluminium Insertion into Aryl Bromides

3.1.1 1-[3'-(Trifluoromethyl)biphenyl-4-yl]ethanone (**6a**)¹⁸⁹



The aluminium reagent **4a** was prepared according to **TP1** from 3-bromobenzotrifluoride (**3a**, 455 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 4 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-iodoacetophenone (**5a**, 350 mg, 1.4 mmol) and PEPSI-*i*Pr (19 mg, 0.028 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 0.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **6a** as yellowish liquid (302 mg, 82%).

¹H-NMR (400 MHz, CDCl₃) δ/ppm: 8.06 (d, *J* = 8.6 Hz, 2H), 7.86 (s, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 2.65 (s, 3H).

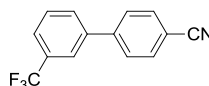
¹³C-NMR (100 MHz, CDCl₃) δ/ppm: 197.6, 144.1, 140.7, 136.4, 131.4 (q, *J* = 32 Hz), 130.5 (q, *J* = 1 Hz), 129.5, 129.1, 127.3, 124.8 (q, *J* = 4 Hz), 124.0 (q, *J* = 4 Hz), 123.9 (q, *J* = 273 Hz), 26.7.

MS (EI, 70 eV) *m/z* (%): 264 (22) [M⁺], 250 (15), 249 (100), 221 (16), 201 (31), 152 (25), 69 (11), 57 (13), 55 (12), 44 (23).

HRMS (EI) for C₁₅H₁₁F₃O: calculated: 264.0762, found: 264.0763.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3069 (VW), 2927 (VW), 1684 (S), 1607 (M), 1565 (VW), 1516 (VW), 1486 (VW), 1441 (W), 1400 (W), 1360 (W), 1335 (VS), 1310 (W), 1258 (VS), 1166 (S), 1124 (VS), 1098 (M), 1076 (M), 1035 (W), 1014 (VW), 1002 (VW), 958 (W), 904 (W), 844 (W), 825 (W), 801 (M), 694 (M), 656 (W).

3.1.2 3'-(Trifluoromethyl)-[1,1'-biphenyl]-4-carbonitrile (**6b**)



The aluminium reagent **4a** was prepared according to **TP1** from 3-bromobenzotrifluoride (**3a**, 4550 mg, 20 mmol), LiCl (1280 mg, 30 mmol), Al-powder (1620 mg, 60 mmol) and TiCl₄ (1 M solution in toluene, 0.6 mL, 0.6 mmol). The reaction was carried out in 40 mL THF at 50 °C for 12 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of

¹⁸⁹ This experiment has been performed partly by Dr. Y-H. Chen and is given here for the sake of completeness.

4-bromobenzonitrile (**5b**, 3500 mg, 14 mmol) and PEPPSI-*i*Pr (190 mg, 0.28 mmol) in THF (5 mL). The reaction mixture was stirred at 25 °C for 12 h and quenched with sat. aqueous NH₄Cl solution (10 mL) and HCl (2 M, 10 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **6b** as white solid (2907 mg, 84%).

mp: 79-81 °C.

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.83-7.80 (m, 1H), 7.79-7.76 (m, 1H), 7.76-7.69 (m, 4H), 7.68-7.65 (m, 1H), 7.64-7.57 (m, 1H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 144.1, 139.9, 132.8, 131.6 (q, $J = 32$ Hz), 130.5 (q, $J = 1$ Hz), 129.7, 127.8, 125.3 (q, $J = 4$ Hz), 124.0 (q, $J = 4$ Hz), 123.9 (q, $J = 272$ Hz), 118.6, 111.9.

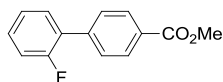
¹⁹F-NMR (282 MHz, CDCl₃) δ /ppm: -62.73.

MS (EI, 70 eV) m/z (%): 248 (16), 247 (100), 226 (11), 177 (12), 43 (22).

HRMS (EI) for C₁₄H₈F₃N: calculated: 247.0609, found: 247.0585.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3064 (VW), 2227 (W), 1848 (VW), 1732 (VW), 1608 (W), 1594 (VW), 1485 (W), 1438 (W), 1404 (W), 1332 (S), 1289 (W), 1274 (M), 1261 (M), 1218 (VW), 1199 (W), 1178 (M), 1162 (S), 1123 (VS), 1097 (S), 1076 (S), 1037 (M), 1019 (W), 970 (W), 954 (W), 925 (W), 846 (M), 835 (W), 828 (M), 805 (S), 731 (W), 702 (S), 658 (VW).

3.1.3 Methyl 2'-fluorobiphenyl-4-carboxylate (**6c**)¹⁸⁹



The aluminium reagent **4b** was prepared according to **TP1** from 1-bromo-2-fluorobenzene (**3b**, 354 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 4 mL THF at 30 °C for 3.5 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of methyl 4-bromobenzoate (**5c**, 304 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in THF (0.5 mL). The reaction mixture was stirred at 30 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 20:1) afforded **6c** as white solid (301 mg, 93%).

mp: 67-69 °C.

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 8.10 (d, $J = 8.5$ Hz, 2H), 7.61 (d, $J = 8.5$ Hz, 2H), 7.44 (td, $J = 7.7$ Hz, $J = 2.0$ Hz, 1H), 7.39-7.31 (m, 1H), 7.26-7.11 (m, 2H), 3.93 (s, 3H).

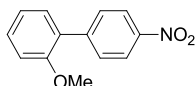
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 166.8, 159.7 (d, $J = 249$ Hz), 140.4 (d, $J = 1$ Hz), 130.6 (d, $J = 3$ Hz), 129.8 (d, $J = 8$ Hz), 129.7, 129.2, 129.0 (d, $J = 3$ Hz), 128.0 (d, $J = 13$ Hz), 124.5 (d, $J = 4$ Hz), 116.2 (d, $J = 23$ Hz), 52.1.

MS (EI, 70 eV) m/z (%): 230 (60) [M⁺], 200 (20), 199 (100), 171 (38), 170 (46), 111 (11), 97 (16), 85 (16), 83 (19), 82 (10), 71 (13), 69 (18), 57 (24), 55 (19), 44 (22).

HRMS (EI) for C₁₄H₁₁FO₂: calculated: 230.0743, found: 230.0718.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3064 (VW), 3003 (VW), 2952 (VW), 2903 (VW), 2847 (VW), 1934 (VW), 1806 (VW), 1720 (VS), 1612 (W), 1584 (VW), 1516 (VW), 1484 (M), 1453 (W), 1437 (M), 1403 (W), 1316 (W), 1280 (VS), 1252 (M), 1210 (W), 1190 (W), 1158 (VW), 1114 (M), 1102 (M), 1042 (VW), 1024 (VW), 1008 (W), 968 (VW), 868 (VW), 857 (VW), 832 (W), 818 (W), 778 (W), 756 (M), 727 (W), 703 (W).

3.1.4 2-Methoxy-4'-nitrobiphenyl (**6d**)



The aluminium reagent **4c** was prepared according to **TP1** from 2-bromoanisole (**3c**, 382 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 20 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-iodonitrobenzene (**5d**, 349 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in THF (2 mL). The reaction mixture was stirred at 0 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **6d** as orange solid (255 mg, 80%).

mp: 59-60 °C.

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 8.28 (d, *J* = 9.1 Hz, 2H), 7.72 (d, *J* = 9.1 Hz, 2H), 7.47-7.32 (m, 2H), 7.14-7.02 (m, 2H), 3.86 (s, 3H).

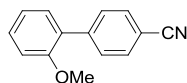
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 156.4, 146.7, 145.5, 130.7, 130.3, 130.2, 128.3, 123.2, 121.1, 111.5, 55.6.

MS (EI, 70 eV) *m/z* (%): 230 (13), 229 (100) [M⁺], 168 (39), 139 (20).

HRMS (EI) for C₁₃H₁₁NO₃: calculated: 229.0739, found: 229.0721.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3066 (W), 2925 (W), 2843 (W), 1598 (M), 1580 (W), 1517 (M), 1504 (S), 1480 (M), 1454 (M), 1435 (W), 1401 (W), 1347 (S), 1313 (M), 1303 (M), 1266 (S), 1237 (S), 1186 (M), 1165 (M), 1144 (W), 1124 (M), 1112 (M), 1100 (M), 1055 (M), 1022 (M), 1008 (M), 957 (W), 928 (W), 854 (S), 842 (M), 825 (M), 798 (M), 759 (M), 745 (S), 729 (VS), 695 (S), 645 (W), 630 (W).

3.1.5 2'-Methoxy-[1,1'-biphenyl]-4-carbonitrile (**6e**)



The aluminium reagent **4c** was prepared according to **TP1** from 2-bromoanisole (**3c**, 382 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 20 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-bromobenzonitrile (**5b**, 255 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in THF (2 mL). The reaction mixture was

stirred at 20 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **6e** as white solid (229 mg, 78%).

mp: 79-82 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.15-7.12 (m, 2H), 7.08-7.03 (m, 3H), 6.97-6.94 (m, 1H), 6.82-6.78 (m, 1H), 6.50-6.47 (m, 1H), 3.11 (s, 3H).

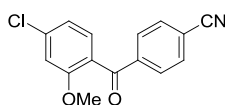
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 157.0, 143.6, 132.0, 131.2, 130.7, 130.3, 129.5, 121.5, 121.5, 119.4, 111.9, 111.4, 55.3.

MS (EI, 70 eV) m/z (%): 210 (13), 209 (100) [M⁺], 194 (34), 166 (14), 140 (11).

HRMS (EI) for C₁₄H₁₁NO: calculated: 209.0841, found: 209.0833.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3406 (VW), 3060 (VW), 3006 (W), 2960 (W), 2931 (W), 2834 (VW), 2230 (M), 2040 (VW), 1922 (VW), 1813 (VW), 1678 (VW), 1605 (M), 1582 (W), 1509 (W), 1484 (M), 1455 (M), 1434 (M), 1400 (W), 1362 (VW), 1304 (W), 1293 (W), 1266 (M), 1248 (M), 1230 (S), 1175 (M), 1167 (M), 1125 (M), 1108 (W), 1056 (M), 1022 (M), 1008 (M), 975 (W), 960 (W), 950 (W), 848 (M), 840 (M), 814 (W), 802 (W), 773 (M), 758 (VS), 727 (M), 674 (W), 648 (W).

3.1.6 4-(4-Chloro-2-methoxybenzoyl)benzotrile (**6f**)¹⁸⁹



The aluminium reagent **4d** was prepared according to **TP1** from 2-bromo-5-chloroanisole (**3d**, 452 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 6.5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The acylation reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of *S*-(4-chlorophenyl) 4-cyanobenzothioate (**5e**, 192 mg, 0.7 mmol) and PEPPSI-*i*Pr (10 mg, 0.014 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 6:1) afforded **6f** as yellowish solid (134 mg, 70%).

mp: 118-119 °C.

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.82 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.07 (dd, *J* = 8.2 Hz, *J* = 1.9 Hz, 1H), 6.98 (d, *J* = 1.9 Hz, 1H), 3.68 (s, 3H).

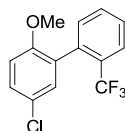
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 193.9, 158.2, 141.2, 139.0, 132.1, 131.3, 129.7, 125.8, 121.2, 118.1, 116.0, 112.3, 55.8.

MS (EI, 70 eV) m/z (%): 273 (11), 271 (40) [M⁺], 254 (29), 171 (25), 169 (100), 130 (14), 102 (17).

HRMS (EI) for C₁₅H₁₀ClNO₂: calculated: 271.0400, found: 271.0399.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2944 (VW), 2231 (W), 1664 (S), 1605 (M), 1590 (S), 1568 (M), 1485 (M), 1463 (M), 1404 (S), 1309 (M), 1292 (M), 1281 (S), 1249 (VS), 1182 (W), 1147 (W), 1120 (W), 1092 (M), 1024 (M), 928 (S), 908 (M), 870 (M), 855 (M), 845 (M), 818 (M), 768 (M), 729 (M), 698 (W), 680 (M), 648 (W), 628 (VW).

3.1.7 5-Chloro-2-methoxy-2'-(trifluoromethyl)biphenyl (**6g**)¹⁸⁹



The aluminium reagent **4e** was prepared according to **TP1** from 2-bromo-4-chloroanisole (**3e**, 452 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 5 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 2-bromobenzotrifluoride (**5f**, 273 mg, 1.2 mmol) and PEPPSI-*i*Pr (16 mg, 0.024 mmol) in THF (0.5 mL). The reaction mixture was stirred at 30 °C for 1.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 15:1) afforded **6g** as white solid (273 mg, 79%).

mp: 94-96 °C.

¹H-NMR (400 MHz, CDCl₃) δ/ppm : 7.74 (d, $J = 7.8$ Hz, 1H), 7.56 (t, $J = 7.6$ Hz, 1H), 7.48 (t, $J = 7.9$ Hz, 1H), 7.32 (dd, $J = 8.8$ Hz, $J = 2.6$ Hz, 1H), 7.27 (d, $J = 7.6$ Hz, 1H), 7.15 (d, $J = 2.6$ Hz, 1H), 6.87 (d, $J = 8.8$ Hz, 1H), 3.71 (s, 3H).

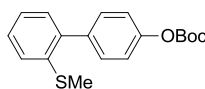
¹³C-NMR (100 MHz, CDCl₃) δ/ppm : 155.5 (q, $J = 1$ Hz), 136.1 (q, $J = 2$ Hz), 131.9, 131.2 (q, $J = 1$ Hz), 130.4 (q, $J = 1$ Hz), 130.1, 129.2 (q, $J = 30$ Hz), 128.9, 127.8, 126.1 (q, $J = 5$ Hz), 124.7, 124.0 (q, $J = 274$ Hz), 111.7, 55.8.

MS (EI, 70 eV) m/z (%): 288 (35) [M⁺], 287 (16), 286 (100), 251 (27), 249 (12), 236 (61), 235 (10), 202 (21), 188 (12), 42 (13), 40 (32).

HRMS (EI) for C₁₄H₁₀ClF₃O: calculated: 286.0372, found: 286.0372.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2942 (VW), 1608 (W), 1597 (VW), 1579 (VW), 1503 (M), 1479 (M), 1466 (M), 1441 (M), 1397 (W), 1313 (VS), 1288 (M), 1261 (S), 1234 (M), 1228 (M), 1170 (S), 1124 (VS), 1108 (VS), 1069 (S), 1034 (VS), 957 (VW), 907 (M), 890 (W), 839 (W), 810 (M), 767 (S), 730 (M), 656 (M).

3.1.8 *t*-Butyl 2'-(methylthio)biphenyl-4-yl carbonate (**6h**)¹⁸⁹



The aluminium reagent **4f** was prepared according to **TP1** from 2-bromothioanisole (**3f**, 406 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 16 h. The cross-coupling

reaction was carried out according to **TP6** using $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and a solution of *t*-butyl 4-bromophenyl carbonate (**5g**, 327 mg, 1.2 mmol) and PEPPSI-*i*Pr (16 mg, 0.024 mmol) in NMP (1.5 mL) and THF (0.5 mL). The reaction mixture was stirred at 30 °C for 1.5 h and quenched with sat. aqueous NH_4Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 20:1) afforded **6h** as yellowish solid (257 mg, 68%).

mp: 48-50 °C.

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ /ppm: 7.43 (d, $J = 8.6$ Hz, 2H), 7.36-7.31 (m, 2H), 7.30-7.26 (m, 2H), 7.25-7.17 (m, 2H), 2.36 (s, 3H), 1.58 (s, 9H).

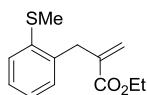
$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ /ppm: 151.9, 150.5, 140.0, 138.0, 137.2, 130.4, 130.1, 128.1, 125.3, 124.8, 120.9, 83.6, 27.7, 15.9.

MS (EI, 70 eV) m/z (%): 316 (6) [M^+], 217 (10), 216 (100), 201 (16), 183 (10), 57 (13).

HRMS (EI) for $\text{C}_{18}\text{H}_{20}\text{O}_3\text{S}$: calculated: 316.1133, found: 316.1132.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3056 (VW), 2981 (W), 2922 (VW), 1753 (S), 1586 (VW), 1512 (W), 1464 (M), 1436 (W), 1395 (W), 1370 (W), 1272 (S), 1255 (S), 1217 (M), 1141 (VS), 1102 (W), 1084 (W), 1044 (W), 1015 (W), 1006 (W), 954 (VW), 894 (M), 839 (M), 822 (W), 782 (W), 773 (W), 748 (M), 733 (M), 668 (W).

3.1.9 Ethyl 2-(2-(methylthio)benzyl)acrylate (**6i**)



The aluminium reagent **4f** was prepared according to **TP1** from 2-bromothioanisole (**3f**, 406 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl_4 (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. The allylation reaction was carried out according to **TP7** using $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol), $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M solution in THF, 0.15 mL, 0.15 mmol) and ethyl (2-bromomethyl)acrylate (**5h**, 270 mg, 1.4 mmol). The reaction mixture was stirred at -30 °C for 1.5 h and quenched with sat. aqueous NH_4Cl solution (1.0 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 20:1) afforded **6i** as colorless liquid (294 mg, 89%).

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 7.10-6.91 (m, 4H), 6.31 (d, $J = 1.5$ Hz, 1H), 5.22 (d, $J = 1.6$ Hz, 1H), 3.96 (q, $J = 7.1$ Hz, 2H), 3.95-3.92 (m, 2H), 3.14 (s, 3H), 0.91 (t, $J = 7.1$ Hz, 3H).

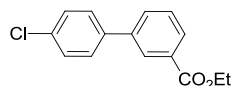
$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 166.2, 139.2, 138.3, 137.0, 129.9, 127.1, 126.2, 125.5, 124.9, 60.3, 35.7, 15.3, 13.7.

MS (EI, 70 eV) m/z (%): 236 (17) [M^+], 207 (13), 191 (15), 190 (13), 189 (100), 163 (37), 162 (10), 161 (67), 149 (18), 148 (34), 147 (83), 123 (11), 116 (20), 115 (29).

HRMS (EI) for $\text{C}_{13}\text{H}_{16}\text{O}_2\text{S}$: calculated: 236.0871, found: 236.0861.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3059 (VW), 2981 (W), 2922 (W), 1712 (VS), 1632 (W), 1589 (W), 1570 (VW), 1468 (M), 1438 (M), 1404 (W), 1392 (W), 1368 (W), 1300 (M), 1280 (M), 1264 (M), 1252 (M), 1185 (M), 1133 (VS), 1095 (M), 1067 (M), 1025 (S), 947 (M), 923 (W), 859 (W), 816 (M), 787 (W), 749 (S), 737 (S), 692 (W), 682 (M), 666 (M), 604 (W).

3.1.10 Ethyl 4'-chlorobiphenyl-3-carboxylate (**6j**)¹⁸⁹



The aluminium reagent **4g** was prepared according to **TP1** from 4-bromochlorobenzene (**3g**, 387 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and TiCl₄ (1 M solution in toluene, 0.06 mL, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 14 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of ethyl 3-iodobenzoate (**5i**, 338 mg, 1.2 mmol) and PEPPSI-*i*Pr (16 mg, 0.024 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 0.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 15:1) afforded **6j** as white solid (294 mg, 82%).

mp: 43-45 °C.

¹H-NMR (400 MHz, CDCl₃) δ/ppm : 8.23 (t, $J = 1.8$ Hz, 1H), 8.03 (ddd, 1H, $J = 7.8$ Hz, $J = 1.8$ Hz, $J = 1.2$ Hz), 7.72 (ddd, $J = 7.8$ Hz, $J = 2.0$ Hz, $J = 1.2$ Hz, 1H), 7.54 (d, $J = 8.6$ Hz, 2H), 7.50 (t, $J = 7.8$ Hz, 1H), 7.42 (d, $J = 8.6$ Hz, 2H), 4.41 (q, $J = 7.1$ Hz, 2H), 1.41 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (100 MHz, CDCl₃) δ/ppm : 166.4, 140.2, 138.6, 133.9, 131.2, 131.1, 129.0, 128.9, 128.6, 128.4, 128.0, 61.2, 14.4.

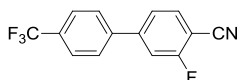
MS (EI, 70 eV) m/z (%): 262 (30), 261 (12), 260 (100) [M⁺], 232 (25), 217 (29), 216 (14), 215 (94), 187 (13), 152 (68), 151 (10), 76 (17).

HRMS (EI) for C₁₅H₁₃ClO₂: calculated: 260.0604, found: 260.0605.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2982 (W), 2905 (VW), 1719 (S), 1605 (VW), 1596 (VW), 1587 (VW), 1499 (W), 1476 (W), 1438 (W), 1392 (W), 1368 (W), 1305 (M), 1298 (M), 1262 (M), 1241 (VS), 1171 (W), 1108 (M), 1093 (M), 1043 (M), 1012 (W), 938 (VW), 916 (VW), 834 (W), 815 (W), 755 (M), 716 (VW), 693 (W).

3.2 InCl₃ – Catalysed Aluminium Insertion into Aryl Iodides

3.2.1 3-Fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbonitrile (**8a**)



The aluminium reagent **2a** was prepared according to **TP2** from 4-iodobenzotrifluoride (**1a**, 1088 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and InCl₃ (28 mg, 0.12 mmol). The reaction was carried out in 8 mL THF at 20 °C for 5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-bromo-2-fluorobenzonitrile (**7a**, 280 mg, 1.4 mmol) and PEPPSI-*t*Pr (20 mg, 0.028 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 2.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 7:1) afforded **8a** as white solid (354 mg, 95%).

mp: 117-118 °C.

¹H-NMR (600 MHz, CDCl₃) δ /ppm: 7.78-7.65 (m, 5H), 7.51-7.41 (m, 2H).

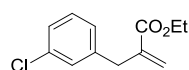
¹³C-NMR (150 MHz, CDCl₃) δ /ppm: 163.4 (d, $J = 260$ Hz), 146.9 (d, $J = 8$ Hz), 141.4 (dd, $J = 2$ Hz, $J = 1$ Hz), 134 (d, $J = 1$ Hz), 131.3 (q, $J = 33$ Hz), 127.6, 126.2 (q, $J = 4$ Hz), 123.8 (q, $J = 272$ Hz), 123.6 (d, $J = 4$ Hz), 115.2 (d, $J = 21$ Hz), 113.7, 100.9 (d, $J = 15$ Hz).

MS (EI, 70 eV) m/z (%): 265 (100) [M⁺], 246 (13).

HRMS (EI) for C₁₄H₇NF₄: calculated: 265.0515, found: 265.0512.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3072 (VW), 2920 (VW), 2849 (VW), 2647 (VW), 2390 (VW), 2303 (VW), 2236 (W), 2100 (VW), 1935 (VW), 1809 (VW), 1692 (VW), 1619 (M), 1585 (W), 1561 (M), 1494 (W), 1433 (W), 1396 (M), 1321 (S), 1272 (W), 1263 (W), 1200 (W), 1189 (W), 1162 (M), 1112 (VS), 1068 (S), 1030 (W), 1013 (M), 964 (W), 901 (M), 881 (M), 850 (M), 819 (S), 776 (M), 738 (M), 718 (W), 697 (W), 628 (W), 620 (W).

3.2.2 Ethyl 2-(3-chlorobenzyl)acrylate (**8b**)



The aluminium reagent **2b** was prepared according to **TP2** from 1-chloro-3-iodobenzene (**1b**, 492 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (14 mg, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 5 h. The allylation reaction was carried out according to **TP7** using Zn(OAc)₂ (556 mg, 3 mmol), CuCN·2 LiCl (1 M solution in THF, 0.14 mL, 0.14 mmol) and ethyl (2-bromomethyl)acrylate (**7b**, 270 mg, 1.4 mmol). The reaction mixture was stirred at 0 °C for 0.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 30:1) afforded **8b** as colorless liquid (286 mg, 91%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.26-7.15 (m, 3H), 7.08 (dt, $J = 7.0$ Hz, $J = 1.8$ Hz, 1H), 6.26 (s, 1H), 5.49 (s, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 3.60 (s, 2H), 1.26 (t, $J = 7.1$ Hz, 3H).

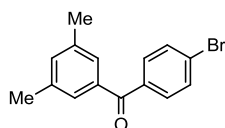
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 166.6, 140.9, 139.6, 134.1, 129.6, 129.1, 127.2, 126.5, 126.4, 60.9, 37.8, 14.1.

MS (EI, 70 eV) m/z (%): 224 (36) [M⁺], 179 (29), 178 (55), 152 (25), 151 (36), 150 (67), 149 (27), 125 (68), 116 (41), 115 (100), 111 (26), 97 (52), 89 (23), 83 (46), 82 (22), 77 (20), 71 (30), 70 (23), 69 (54), 57 (73), 56 (22), 55 (55), 44 (27), 43 (44), 41 (40).

HRMS (EI) for C₁₂H₁₃ClO₂: calculated: 224.0604, found: 224.0579.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2983 (W), 2936 (VW), 1714 (VS), 1632 (W), 1598 (W), 1574 (W), 1477 (M), 1431 (M), 1407 (W), 1369 (W), 1328 (W), 1300 (M), 1276 (M), 1254 (M), 1194 (S), 1136 (S), 1094 (M), 1079 (W), 1026 (M), 1000 (W), 950 (M), 908 (W), 865 (W), 854 (W), 818 (W), 782 (M), 728 (M), 685 (M).

3.2.3 (4-Bromophenyl)(3,5-dimethylphenyl)methanone (**8c**)¹⁸⁹



The aluminium reagent **2c** was prepared according to **TP2** from 5-iodo-*m*-xylene (**1c**, 492 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (14 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 24 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of *S*-(4-chlorophenyl) 4-bromobenzothioate (**7c**, 230 mg, 0.7 mmol) and PEPPSI-*t*Pr (10 mg, 0.014 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 30:1) afforded **8c** as white solid (182 mg, 89%).

mp: 90-91 °C.

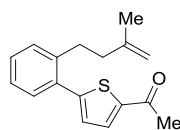
¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.66 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.36 (s, 2H), 7.23 (s, 1H), 2.37 (s, 6H).

¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 196.1, 138.1, 137.3, 136.6, 134.3, 131.5, 131.4, 127.7, 127.3, 21.2.

MS (EI, 70 eV) m/z (%): 290 (29), 288 (29), 209 (30), 184 (23), 182 (25), 165 (11), 156 (11), 133 (100), 105 (23), 77 (11), 57 (11), 43 (16), 42 (10).

HRMS (EI) for C₁₅H₁₃BrO: calculated: 288.0150, found: 288.0142.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2918 (VW), 2252 (VW), 1657 (M), 1604 (W), 1586 (M), 1565 (W), 1482 (W), 1441 (VW), 1394 (W), 1382 (W), 1316 (M), 1280 (VW), 1229 (M), 1176 (W), 1136 (W), 1103 (VW), 1070 (W), 1010 (W), 998 (VW), 969 (W), 944 (VW), 906 (S), 866 (W), 839 (W), 812 (M), 757 (M), 729 (VS), 672 (W), 649 (W), 627 (VW).

3.2.4 1-{5-[2-(3-Methylbut-3-en-1-yl)phenyl]-2-thienyl}ethanone (**8d**)¹⁸⁹

The aluminium reagent **2d** was prepared according to **TP2** from 1-iodo-2-(3-methylbut-3-en-1-yl)benzene (**1d**, 545 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (14 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 24 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 2-acetyl-5-bromothiophene (**7d**, 250 mg, 1.2 mmol) and PEPPSI-*i*Pr (16 mg, 0.024 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 15:1) afforded **8d** as yellow liquid (243 mg, 75%).

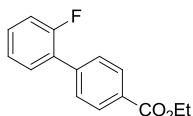
¹H-NMR (400 MHz, CDCl₃) δ/ppm: 7.67 (d, *J* = 3.8 Hz, 1H), 7.38-7.28 (m, 3H), 7.27-7.21 (m, 1H), 7.05 (d, *J* = 3.8 Hz, 1H), 4.69 (s, 1H), 4.62 (s, 1H), 2.90-2.81 (m, 2H), 2.58 (s, 3H), 2.26-2.18 (m, 2H), 1.67 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃) δ/ppm: 190.7, 151.8, 144.9, 143.9, 140.5, 132.9, 132.5, 130.8, 129.8, 129.0, 127.6, 126.1, 110.4, 39.4, 31.9, 26.7, 22.5.

MS (EI, 70 eV) *m/z* (%): 270 (37) [M⁺], 173 (31), 171 (17), 43 (100).

HRMS (EI) for C₁₇H₁₈OS: calculated: 270.1078, found: 270.1080.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3072 (VW), 3019 (VW), 2935 (W), 2253 (VW), 1657 (S), 1600 (VW), 1531 (W), 1488 (W), 1453 (M), 1435 (S), 1373 (W), 1359 (M), 1335 (W), 1274 (S), 1161 (VW), 1104 (VW), 1073 (W), 1034 (W), 1018 (W), 963 (W), 904 (S), 813 (M), 760 (S), 727 (VS), 649 (M), 609 (W).

3.2.5 Ethyl 2'-fluoro-[1,1'-biphenyl]-4-carboxylate (**8e**)

The aluminium reagent **2e** was prepared according to **TP2** from 2-fluoroiodobenzene (**1e**, 888 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and InCl₃ (28 mg, 0.12 mmol). The reaction was carried out in 8 mL THF at 50 °C for 6 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of ethyl 4-iodobenzoate (**7e**, 387 mg, 1.4 mmol) and PEPPSI-*i*Pr (20 mg, 0.028 mmol) in THF (4 mL). The reaction mixture was stirred at 25 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **8e** as white solid (315 mg, 92%).

mp: 75-77 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.21-8.15 (m, 2H), 7.43-7.37 (m, 2H), 7.07 (td, $J = 7.7$ Hz, $J = 1.8$ Hz, 1H), 6.93-6.78 (m, 3H), 4.15 (q, $J = 7.0$ Hz, 2H), 1.04 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.4, 160.5 (d, $J = 249$ Hz), 140.7 (d, $J = 1$ Hz), 131.4 (d, $J = 3$ Hz), 130.8, 130.4, 130.2 (d, $J = 8$ Hz), 129.7 (d, $J = 3$ Hz), 128.9 (d, $J = 13$ Hz), 124.9 (d, $J = 4$ Hz), 116.7 (d, $J = 23$ Hz), 61.2, 14.7.

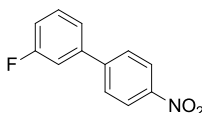
¹⁹F-NMR (376 MHz, C₆D₆) δ /ppm: -117.4.

MS (EI, 70 eV) m/z (%): 244 (38) [M⁺], 216 (23), 200 (14), 199 (100), 171 (26), 170 (30).

HRMS (EI) for C₁₅H₁₃O₂F: calculated: 244.0900, found: 244.0890.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3405 (VW), 3070 (VW), 2999 (VW), 2980 (W), 2905 (VW), 2409 (VW), 1934 (VW), 1823 (VW), 1716 (S), 1671 (W), 1609 (W), 1584 (W), 1514 (VW), 1484 (W), 1476 (W), 1454 (W), 1443 (W), 1401 (W), 1366 (W), 1315 (W), 1282 (S), 1268 (S), 1249 (S), 1228 (M), 1211 (M), 1186 (M), 1158 (W), 1130 (M), 1110 (M), 1101 (M), 1044 (W), 1026 (M), 1006 (M), 948 (W), 878 (W), 868 (M), 854 (W), 820 (M), 779 (W), 762 (VS), 734 (M), 724 (S), 701 (M), 632 (W).

3.2.6 3-Fluoro-4'-nitro-1,1'-biphenyl (**8f**)



The aluminium reagent **2f** was prepared according to **TP2** from 3-fluoriodobenzene (**1f**, 888 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and InCl₃ (28 mg, 0.12 mmol). The reaction was carried out in 8 mL THF at 50 °C for 3 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-iodonitrobenzene (**7f**, 349 mg, 1.4 mmol) and PEPPSI-*i*Pr (20 mg, 0.028 mmol) in THF (4 mL). The reaction mixture was stirred at 25 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 20:1) afforded **8f** as yellow solid (254 mg, 84%).

mp: 88-89 °C.

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.90-7.80 (m, 2H), 7.00-6.76 (m, 6H).

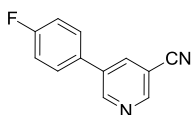
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 163.2 (d, $J = 242$ Hz), 147.3, 145.1 (d, $J = 2$ Hz), 140.8 (d, $J = 8$ Hz), 130.4 (d, $J = 9$ Hz), 127.3, 123.7, 122.8 (d, $J = 3$ Hz), 115.3 (d, $J = 21$ Hz), 114.1 (d, $J = 22$ Hz).

MS (EI, 70 eV) m/z (%): 218 (11), 217 (100) [M⁺], 187 (18), 171 (28), 170 (76), 169 (11), 159 (18).

HRMS (EI) for C₁₂H₈NO₂F: calculated: 217.0539, found: 217.0537.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3083 (W), 2937 (VW), 2846 (VW), 2700 (VW), 2604 (VW), 2449 (VW), 2302 (VW), 1933 (VW), 1877 (VW), 1802 (VW), 1694 (VW), 1602 (W), 1594 (M), 1582 (M), 1521 (M), 1506 (S), 1472 (M), 1446 (M), 1439 (M), 1398 (W), 1341 (S), 1320 (M), 1303 (M), 1288 (M), 1261 (M), 1182 (M), 1156 (M), 1115 (M), 1106 (M), 1078 (M), 1036 (W), 1014 (W), 1002 (W), 904 (W), 887 (W), 874 (M), 849 (VS), 791 (S), 753 (S), 728 (M), 698 (M), 687 (S), 651 (M), 631 (M).

3.2.7 5-(4-Fluorophenyl)nicotinonitrile (**8g**)



The aluminium reagent **2g** was prepared according to **TP2** from 4-fluoroiodobenzene (**1g**, 888 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and InCl₃ (28 mg, 0.12 mmol). The reaction was carried out in 8 mL THF at 50 °C for 12 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 5-bromonicotinonitrile (**7g**, 256 mg, 1.4 mmol) and PEPPSI-*i*Pr (20 mg, 0.028 mmol) in THF (4 mL). The reaction mixture was stirred at 25 °C for 0.5 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 5:1) afforded **8g** as off-white solid (205 mg, 74%).

mp: 166-168 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.50-8.30 (m, 2H), 7.04 (t, J = 2.1 Hz, 1H), 6.77-6.58 (m, 4H).

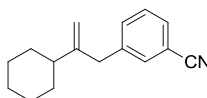
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 163.9 (d, J = 249 Hz), 151.2, 151.0, 136.8 (d, J = 0.5 Hz), 135.6, 132.1 (d, J = 3 Hz), 129.4 (d, J = 8 Hz), 117.0, 116.6 (d, J = 22 Hz), 110.6.

MS (EI, 70 eV) m/z (%): 199 (11), 198 (100) [M⁺], 197 (30).

HRMS (EI) for C₁₂H₇FN₂: calculated: 198.0593, found: 198.0591.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3056 (W), 2922 (W), 2233 (W), 1606 (M), 1568 (W), 1517 (M), 1447 (W), 1426 (M), 1399 (M), 1390 (M), 1343 (W), 1338 (W), 1316 (W), 1301 (W), 1225 (S), 1192 (M), 1165 (M), 1156 (M), 1057 (W), 1024 (W), 1018 (W), 964 (W), 951 (W), 926 (W), 898 (W), 873 (M), 831 (VS), 813 (M), 804 (M), 718 (W), 698 (S), 679 (S), 636 (W).

3.2.8 3-(2-Cyclohexylprop-2-en-1-yl)benzonitrile (**8h**)¹⁸⁹



The aluminium reagent **2h** was prepared according to **TP2** from (1-iodovinyl)cyclohexane (**1h**, 473 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (14 mg, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 24 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 3-(bromomethyl)benzonitrile (**7h**, 249 mg, 1.2 mmol) and PEPPSI-*i*Pr (16 mg, 0.024 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 0.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 20:1) afforded **8h** as colorless liquid (145 mg, 54%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.51-7.44 (m, 2H), 7.43-7.35 (m, 2H), 4.89 (s, 1H), 4.60 (s, 1H), 3.37 (s, 2H), 1.82-1.69 (m, 5H), 1.69-1.61 (m, 1H), 1.29-1.06 (m, 5H).

¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 153.1, 141.7, 133.7, 132.6, 129.8, 129.0, 119.1, 112.3, 110.7, 43.5, 41.2, 32.4, 26.6, 26.3.

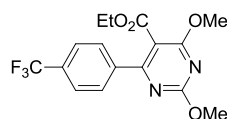
MS (EI, 70 eV) m/z (%): 225 (13) [M⁺], 199 (11), 168 (12), 154 (11), 143 (14), 142 (14), 140 (11), 130 (11), 127 (18), 123 (11), 116 (21), 110 (12), 109 (100), 97 (12), 83 (21), 82 (16), 81 (24), 69 (20), 67 (67), 57 (27), 55 (40), 44 (22), 43 (40), 41 (35).

HRMS (EI) for C₁₆H₁₉N: calculated: 225.1517, found: 225.1513.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2925 (M), 2852 (M), 2254 (VW), 2230 (W), 1641 (W), 1601 (VW), 1582 (VW), 1482 (W), 1448 (W), 1262 (VW), 1234 (VW), 1172 (VW), 1094 (VW), 1027 (VW), 949 (VW), 904 (S), 890 (S), 869 (W), 837 (VW), 798 (M), 730 (VS), 690 (S), 649 (M).

3.3 BiCl₃ – Catalysed Aluminium Insertion into Aryl Iodides

3.3.1 2,4-Dimethoxy-6-(4-trifluoromethyl-phenyl)-pyrimidine-5-carboxylic acid ethyl ester (**8i**)



The aluminium reagent **2a** was prepared according to **TP3** from 1-iodo-4-(trifluoromethyl)benzene (**1a**, 1088 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and BiCl₃ (40 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 5.5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-iodo-2,6-dimethoxy-pyrimidine-5-carboxylic acid ethyl ester (**7i**, 473 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (4 mL). The reaction mixture was stirred at 50 °C for 2.5 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 13:1) afforded **8i** as colorless liquid (366 mg, 73%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.61 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 3.91 (q, J = 7.1 Hz, 2H), 3.61 (s, 3H), 3.52 (s, 3H), 0.70 (t, J = 7.1 Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 169.2, 165.2, 164.8, 164.2, 141.3 (q, J = 1 Hz), 131.4 (q, J = 32 Hz), 128.8, 125.0 (q, J = 4 Hz), 124.3 (q, J = 272 Hz), 108.9, 61.1, 54.3, 53.9, 13.3.

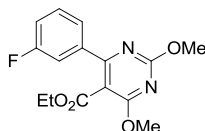
¹⁹F-NMR (376 MHz, C₆D₆) δ /ppm: -62.5.

MS (EI, 70 eV) m/z (%): 356 (20) [M⁺], 355 (10), 327 (26), 311 (33), 186 (23), 141 (11), 127 (14), 125 (11), 113 (15), 111 (12), 99 (25), 97 (27), 85 (57), 84 (11), 83 (30), 81 (11), 71 (76), 70 (18), 69 (34), 57 (100), 56 (19), 55 (39), 44 (57), 43 (30).

HRMS (EI) for C₁₆H₁₅F₃N₂O₄: calculated: 356.0984, found: 356.0982.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2986 (VW), 2959 (VW), 2904 (VW), 2878 (VW), 1728 (M), 1589 (M), 1571 (S), 1552 (S), 1520 (W), 1483 (M), 1460 (M), 1408 (W), 1376 (M), 1360 (S), 1322 (VS), 1262 (VS), 1243 (S), 1196 (M), 1166 (S), 1122 (S), 1110 (S), 1062 (VS), 1026 (M), 1013 (S), 946 (M), 853 (S), 809 (M), 793 (W), 770 (W), 757 (W), 736 (M), 702 (W), 692 (W), 680 (W), 667 (W), 656 (W), 639 (W), 623 (W).

3.3.2 Ethyl 4-(3-fluorophenyl)-2,6-dimethoxypyrimidine-5-carboxylate (**8j**)



The aluminium reagent **2f** was prepared according to **TP3** from 3-fluoriodobenzene (**1f**, 888 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and BiCl₃ (40 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 3 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of ethyl 4-iodo-2,6-dimethoxypyrimidine-5-carboxylate (**7i**, 473 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (4 mL). The reaction mixture was stirred at 25 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **8j** as colorless liquid (326 mg, 76%).

¹H-NMR (400 MHz, C₆D₆) δ/ppm : 7.66-7.62 (m, 1H), 7.54-7.50 (m, 1H), 6.89 (td, $J = 8.0$ Hz, $J = 5.9$ Hz, 1H), 6.82-6.76 (m, 1H), 4.03 (q, $J = 7.2$ Hz, 2H), 3.63 (s, 3H), 3.57 (s, 3H), 0.84 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ/ppm : 170.0, 166.3, 165.5, 164.6 (d, $J = 3$ Hz), 163.5 (d, $J = 249$ Hz), 140.8 (d, $J = 8$ Hz), 130.4 (d, $J = 8$ Hz), 124.8 (d, $J = 3$ Hz), 117.3 (d, $J = 21$ Hz), 116.3 (d, $J = 23$ Hz), 109.5, 61.9, 55.0, 54.6, 14.1.

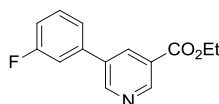
¹⁹F-NMR (376 MHz, C₆D₆) δ/ppm : -112.7.

MS (EI, 70 eV) m/z (%): 307 (13), 306 (80) [M⁺], 305 (24), 277 (60), 276 (15), 262 (18), 261 (100), 136 (32).

HRMS (EI) for C₁₅H₁₅FN₂O₄: calculated: 306.1016, found: 306.1015.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3075 (VW), 2985 (VW), 2958 (VW), 2903 (VW), 2876 (VW), 1727 (S), 1615 (W), 1572 (S), 1551 (VS), 1493 (M), 1481 (M), 1458 (M), 1373 (S), 1358 (S), 1263 (VS), 1244 (S), 1227 (VS), 1197 (S), 1114 (S), 1059 (VS), 1027 (S), 957 (W), 931 (S), 884 (M), 848 (W), 814 (M), 794 (S), 786 (S), 748 (W), 704 (M), 674 (M), 658 (M), 648 (W).

3.3.3 Ethyl 5-(3-fluorophenyl)nicotinate (**8k**)



The aluminium reagent **2f** was prepared according to **TP3** from 3-fluoriodobenzene (**1f**, 888 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and BiCl₃ (40 mg, 0.12 mmol). The

reaction was carried out in 4 mL THF at 50 °C for 3 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of ethyl 5-bromonicotinate (**7k**, 322 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (2 mL). The reaction mixture was stirred at 25 °C for 0.5 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **8k** as colorless liquid (282 mg, 82%).

¹H-NMR (400 MHz, C₆D₆) δ/ppm: 9.38 (d, *J* = 2.0 Hz, 1H), 8.71 (d, *J* = 2.3 Hz, 1H), 8.24 (dd, *J* = 2.3 Hz, *J* = 2.0 Hz, 1H), 6.89-6.65 (m, 4H), 4.04 (q, *J* = 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H).

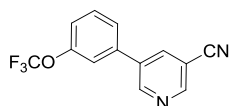
¹³C-NMR (100 MHz, C₆D₆) δ/ppm: 164.6, 163.2 (d, *J* = 245 Hz), 151.6, 149.9, 138.9 (d, *J* = 8 Hz), 134.7 (d, *J* = 2 Hz), 134.6, 130.4 (d, *J* = 8 Hz), 126.3, 122.6 (d, *J* = 3 Hz), 114.8 (d, *J* = 21 Hz), 114.0 (d, *J* = 23 Hz), 60.9, 13.8.

MS (EI, 70 eV) *m/z* (%): 246 (16), 245 (100) [M⁺], 217 (55), 201 (18), 200 (85), 173 (16), 172 (88), 171 (14), 145 (29), 144 (11), 125 (24), 97 (12), 86 (12), 83 (14), 71 (11), 69 (17), 57 (22), 55 (16), 44 (21), 43 (21), 41 (15).

HRMS (EI) for C₁₄H₁₂FN₂O₂: calculated: 245.0852, found: 245.0845.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3042 (W), 2989 (W), 1717 (VS), 1612 (W), 1587 (M), 1466 (M), 1442 (M), 1410 (W), 1388 (W), 1365 (W), 1337 (M), 1306 (M), 1258 (VS), 1189 (S), 1159 (M), 1129 (S), 1111 (M), 1083 (M), 1056 (M), 1021 (S), 976 (W), 968 (W), 954 (W), 936 (W), 919 (W), 880 (M), 868 (M), 846 (M), 790 (M), 784 (M), 766 (S), 748 (M), 707 (M), 696 (M), 689 (M), 674 (M), 625 (W), 618 (W).

3.3.4 5-(3-Trifluoromethoxy-phenyl)-nicotinonitrile (**8l**)



The aluminium reagent **2i** was prepared according to **TP3** from 1-iodo-3-trifluoromethoxy benzene (**1i**, 1152 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and BiCl₃ (40 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 8 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 5-bromo-nicotinonitrile (**7g**, 256 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (4 mL). The reaction mixture was stirred at 25 °C for 1.5 h and quenched with sat. aqueous NH₄Cl solution (3 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 3:1 + 1% NEt₃) afforded **8l** as white solid (270 mg, 73%).

mp: 50-51 °C.

¹H-NMR (400 MHz, C₆D₆) δ/ppm: 8.46 (d, *J* = 2.3 Hz, 1H), 8.38 (d, *J* = 1.8 Hz, 1H), 7.06 (t, *J* = 2.1 Hz, 1H), 6.95-6.90 (m, 1H), 6.88-6.82 (m, 2H), 6.68-6.62 (m, 1H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 150.9, 150.63, 149.5 (q, $J = 2$ Hz), 137.5, 136.4, 134.3, 130.3, 125.3, 120.8, 120.7 (q, $J = 257$ Hz), 119.7, 116.1, 109.9.

¹⁹F-NMR (376 MHz, C₆D₆) δ /ppm: -57.7.

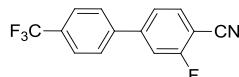
MS (EI, 70 eV) m/z (%): 265 (11), 264 (100) [M⁺].

HRMS (EI) for C₁₃H₇F₃N₂O: calculated: 264.0510, found: 264.0497.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3053 (VW), 2923 (VW), 2236 (W), 1611 (VW), 1588 (W), 1565 (VW), 1496 (VW), 1460 (VW), 1433 (W), 1406 (W), 1334 (W), 1278 (M), 1253 (S), 1206 (VS), 1152 (VS), 1142 (VS), 1110 (M), 1026 (W), 1000 (W), 967 (W), 942 (W), 908 (W), 890 (W), 882 (M), 804 (W), 790 (W), 781 (M), 717 (W), 704 (M), 691 (S), 637 (W), 619 (W).

3.4 PbCl₂ – Catalysed Aluminium Insertion

3.4.1 3-Fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbonitrile (**8a**)



The aluminium reagent **2a** was prepared according to **TP4** from 1-iodo-4-(trifluoromethyl)benzene (**1a**, 1088 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and PbCl₂ (34 mg, 0.12 mmol). The reaction was carried out in 8 mL THF at 20 °C for 3.5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-bromo-2-fluorobenzonitrile (**7a**, 280 mg, 1.4 mmol) and PEPPSI-*i*Pr (20 mg, 0.028 mmol) in THF (0.5 mL). The reaction mixture was stirred at 25 °C for 2.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 7:1) afforded **8a** as white solid (238 mg, 64%).

mp: 117-118 °C.

¹H-NMR (600 MHz, CDCl₃) δ /ppm: 7.78-7.65 (m, 5H), 7.51-7.41 (m, 2H).

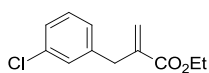
¹³C-NMR (150 MHz, CDCl₃) δ /ppm: 163.4 (d, $J = 260$ Hz), 146.9 (d, $J = 8$ Hz), 141.4 (dd, $J = 2$ Hz, $J = 1$ Hz), 134 (d, $J = 1$ Hz), 131.3 (q, $J = 33$ Hz), 127.6, 126.2 (q, $J = 4$ Hz), 123.8 (q, $J = 272$ Hz), 123.6 (d, $J = 4$ Hz), 115.2 (d, $J = 21$ Hz), 113.7, 100.9 (d, $J = 15$ Hz).

MS (EI, 70 eV) m/z (%): 265 (100) [M⁺], 246 (13).

HRMS (EI) for C₁₄H₇NF₄: calculated: 265.0515, found: 265.0512.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3072 (VW), 2920 (VW), 2849 (VW), 2647 (VW), 2390 (VW), 2303 (VW), 2236 (W), 2100 (VW), 1935 (VW), 1809 (VW), 1692 (VW), 1619 (M), 1585 (W), 1561 (M), 1494 (W), 1433 (W), 1396 (M), 1321 (S), 1272 (W), 1263 (W), 1200 (W), 1189 (W), 1162 (M), 1112 (VS), 1068 (S), 1030 (W), 1013 (M), 964 (W), 901 (M), 881 (M), 850 (M), 819 (S), 776 (M), 738 (M), 718 (W), 697 (W), 628 (W), 620 (W).

3.4.2 Ethyl 2-(3-chlorobenzyl)acrylate (**8b**)



The aluminium reagent **2b** was prepared according to **TP4** from 3-chloriodobenzene (**1b**, 954 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and PbCl₂ (34 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The allylation reaction was carried out according to **TP7** using Zn(OAc)₂ (556 mg, 3 mmol), CuCN·2 LiCl (1 M solution in THF, 0.14 mL, 0.14 mmol) and ethyl (2-bromomethyl)acrylate (**7b**, 270 mg, 1.4 mmol). The reaction mixture was stirred at -30 °C for 12 h and slowly warmed to 20 °C before being quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 25:1) afforded **8b** as yellow oil (256 mg, 81%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.26-7.15 (m, 3H), 7.08 (dt, $J = 7.0$ Hz, $J = 1.8$ Hz, 1H), 6.26 (s, 1H), 5.49 (s, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 3.60 (s, 2H), 1.26 (t, $J = 7.1$ Hz, 3H).

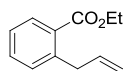
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 166.6, 140.9, 139.6, 134.1, 129.6, 129.1, 127.2, 126.5, 126.4, 60.9, 37.8, 14.1.

MS (EI, 70 eV) m/z (%): 224 (36) [M⁺], 179 (29), 178 (55), 152 (25), 151 (36), 150 (67), 149 (27), 125 (68), 116 (41), 115 (100), 111 (26), 97 (52), 89 (23), 83 (46), 82 (22), 77 (20), 71 (30), 70 (23), 69 (54), 57 (73), 56 (22), 55 (55), 44 (27), 43 (44), 41 (40).

HRMS (EI) for C₁₂H₁₃ClO₂: calculated: 224.0604, found: 224.0595.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2983 (W), 2936 (VW), 1714 (VS), 1632 (W), 1598 (W), 1574 (W), 1477 (M), 1431 (M), 1407 (W), 1369 (W), 1328 (W), 1300 (M), 1276 (M), 1254 (M), 1194 (S), 1136 (S), 1094 (M), 1079 (W), 1026 (M), 1000 (W), 950 (M), 908 (W), 865 (W), 854 (W), 818 (W), 782 (M), 728 (M), 685 (M).

3.4.3 Ethyl 2-allylbenzoate (**12a**)



The aluminium reagent **10a** was prepared according to **TP4** from ethyl 2-iodobenzoate (**9a**, 550 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 4 mL THF at 50 °C for 4 h. The allylation reaction was carried out according to **TP7** using Zn(OAc)₂ (556 mg, 3 mmol), CuCN·2 LiCl (1 M solution in THF, 0.14 mL, 0.14 mmol) and allyl bromide (**11a**, 171 mg, 1.4 mmol). The reaction mixture was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 20:1) afforded **12a** as yellowish liquid (210 mg, 80%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.87 (dd, $J = 8.0$ Hz, $J = 1.6$ Hz, 1H), 7.43 (td, $J = 7.6$ Hz, $J = 1.5$ Hz, 1H), 7.30-7.24 (m, 2H), 6.08-5.95 (m, 1H), 5.06-4.97 (m, 2H), 4.35 (q, 2H, $J = 7.2$ Hz), 3.75 (dt, $J = 6.4$ Hz, $J = 1.5$ Hz, 2H), 1.38 (t, $J = 7.2$ Hz, 3H).

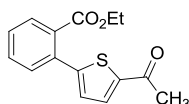
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 167.7, 141.3, 137.4, 131.9, 130.9, 130.5, 130.1, 126.1, 115.5, 60.8, 38.4, 14.3.

MS (EI, 70 eV) m/z (%): 190 (41) [M⁺], 175 (57), 147 (58), 146 (12), 145 (50), 144 (32), 117 (71), 116 (45), 115 (100), 91 (30), 89 (13), 77 (13), 65 (13), 63 (12), 59 (11), 43 (11).

HRMS (EI) for C₁₂H₁₄O₂: calculated: 190.0994, found: 190.0979.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3076 (VW), 2981 (W), 2906 (VW), 1715 (VS), 1638 (W), 1602 (W), 1577 (W), 1486 (W), 1478 (W), 1464 (W), 1447 (W), 1411 (VW), 1390 (W), 1366 (W), 1287 (M), 1254 (VS), 1204 (W), 1172 (W), 1132 (M), 1097 (M), 1072 (S), 1047 (W), 1020 (W), 996 (W), 915 (M), 855 (VW), 778 (VW), 748 (M), 712 (M), 670 (W).

3.4.4 Ethyl 2-(5-acetylthiophen-2-yl)benzoate (**12b**)



The aluminium reagent **10a** was prepared according to **TP4** from ethyl 2-iodobenzoate (**9a**, 1103 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and PbCl₂ (34 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 2.5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 1-(5-iodothiophen-2-yl)ethanone (**11b**, 353 mg, 1.4 mmol) and PEPPSI-*i*Pr (20 mg, 0.028 mmol) in NMP (2 mL) and THF (2 mL). The reaction mixture was stirred at 50 °C for 2.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **12b** as yellow oil (240 mg, 63%).

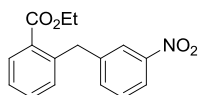
¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.73-7.68 (m, 1H), 7.18-7.14 (m, 1H), 7.05 (d, $J = 3.7$ Hz, 1H), 6.99-6.91 (m, 2H), 6.76 (d, $J = 3.9$ Hz, 1H), 3.98 (q, $J = 7.0$ Hz, 2H), 2.05 (s, 3H), 0.84 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 188.9, 167.3, 150.3, 144.7, 133.5, 132.3, 131.6, 130.8, 130.7, 129.7, 128.3, 127.3, 60.7, 25.8, 13.4.

MS (EI, 70 eV) m/z (%): 275 (11), 274 (61) [M⁺], 260 (15), 231 (32), 187 (14), 85 (13), 71 (17), 59 (12), 58 (24), 56 (10).

HRMS (EI) for C₁₅H₁₄O₃S: calculated: 274.0664, found: 274.0662.

3.4.5 Ethyl 2-(3-nitrobenzyl)benzoate (**12c**)



The aluminium reagent **10a** was prepared according to **TP4** from ethyl 2-iodobenzoate (**9a**, 1103 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and PbCl₂ (34 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 2.5 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 1-(bromomethyl)-3-nitrobenzene (**11c**, 303 mg, 1.4 mmol) and PEPPSI-*i*Pr (20 mg, 0.028 mmol) in NMP (4 mL). The reaction mixture was stirred at 50 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **12c** as yellow oil (324 mg, 81%).

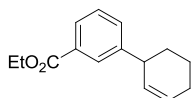
¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.07-8.00 (m, 2H), 7.98 (dd, $J = 7.9$ Hz, $J = 1.4$ Hz, 1H), 7.49 (td, $J = 7.5$ Hz, $J = 1.4$ Hz, 2H), 7.42 (t, $J = 7.8$ Hz, 1H), 7.36 (td, $J = 7.6$ Hz, $J = 1.3$ Hz, 1H), 7.28-7.24 (m, 1H), 4.49 (s, 2H), 4.29 (q, $J = 7.2$ Hz, 2H), 1.31 (t, $J = 7.2$ Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 167.2, 148.3, 143.2, 140.3, 135.0, 132.3, 131.7, 131.1, 130.1, 129.0, 127.0, 123.5, 121.1, 61.0, 39.3, 14.2.

MS (EI, 70 eV) m/z (%): 285 (11) [M⁺], 269 (15), 268 (100), 241 (12), 240 (75), 210 (42), 165 (35).

HRMS (EI) for C₁₆H₁₅NO₄: calculated: 285.1001, found: 285.0990.

3.4.6 Ethyl 3-cyclohex-2-en-1-ylbenzoate (**12d**)¹⁸⁹



The aluminium reagent **10b** was prepared according to **TP4** from ethyl 3-iodobenzoate (**9b**, 550 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 25 h. The allylation reaction was carried out according to **TP7** using Zn(OAc)₂ (556 mg, 3 mmol), CuCN·2 LiCl (1 M solution in THF, 0.14 mL, 0.14 mmol) and 3-bromocyclohexene (**11d**, 237 mg, 1.4 mmol). The reaction mixture was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 30:1) afforded **12d** as colorless liquid (282 mg, 88%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.92-7.84 (m, 2H), 7.40 (dt, $J = 7.5$ Hz, $J = 1.7$ Hz, 1H), 7.35 (td, $J = 7.5$ Hz, $J = 0.8$ Hz, 1H), 5.96-5.88 (m, 1H), 5.73-5.66 (m, 1H), 4.37 (q, $J = 7.2$ Hz, 2H), 3.50-3.42 (m, 1H), 2.15-2.06 (m, 2H), 2.06-1.98 (m, 1H), 1.80-1.69 (m, 1H), 1.68-1.49 (m, 2H), 1.39 (t, $J = 7.2$ Hz, 3H).

¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 166.8, 146.9, 132.3, 130.5, 129.5, 128.9, 128.8, 128.2, 127.2, 60.9, 41.7, 32.5, 24.9, 21.1, 14.4.

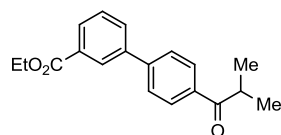
MS (EI, 70 eV) m/z (%): 246 (15), 245 (37), 244 (51), 230 (20) [M⁺], 229 (100), 228 (25), 217 (35), 216 (32), 215 (16), 201 (37), 200 (71), 199 (53), 198 (20), 193 (38), 177 (76), 173 (21), 172 (18), 171 (57), 170 (79),

163 (25), 155 (27), 149 (24), 145 (42), 144 (51), 143 (15), 141 (20), 131 (19), 129 (45), 128 (44), 127 (17), 117 (21), 116 (20), 115 (76), 91 (26), 77 (23), 76 (23), 55 (22).

HRMS (EI) for $C_{15}H_{18}O_2$: calculated: 230.1307, found: 230.1295.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2983 (W), 2937 (W), 1737 (S), 1719 (VS), 1445 (W), 1393 (W), 1372 (M), 1336 (W), 1287 (S), 1241 (VS), 1193 (M), 1170 (W), 1109 (M), 1084 (M), 1046 (M), 755 (M), 695 (W).

3.4.7 Ethyl 4'-isobutyrylbiphenyl-3-carboxylate (**12e**)¹⁸⁹



The aluminium reagent **10b** was prepared according to **TP4** from ethyl 3-iodobenzoate (**9b**, 550 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and $PbCl_2$ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 25 h. The cross-coupling reaction was carried out according to **TP6** using $Zn(OAc)_2$ (556 mg, 3 mmol) and a solution of 1-(4-iodophenyl)-2-methylpropan-1-one (**11e**, 384 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in THF (1 mL). The reaction mixture was stirred at 30 °C for 15 h and quenched with sat. aqueous NH_4Cl solution (1 mL) and HCl (1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **12e** as colorless liquid (324 mg, 78%).

¹H-NMR (400 MHz, $CDCl_3$) δ /ppm: 8.30 (t, $J = 1.9$ Hz, 1H), 8.09-8.07 (m, 1H), 8.05 (d, $J = 8.6$ Hz, 2H), 7.82-7.78 (m, 1H), 7.71 (d, $J = 8.6$ Hz, 2H), 7.54 (t, $J = 7.7$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 3.66-3.52 (m, 1H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.24 (d, $J = 6.8$ Hz, 6H).

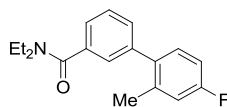
¹³C-NMR (100 MHz, $CDCl_3$) δ /ppm: 204.0, 166.3, 144.4, 140.2, 135.2, 131.5, 131.2, 129.1, 129.0, 128.9, 128.3, 127.3, 61.2, 35.4, 19.2, 14.4.

MS (EI, 70 eV) m/z (%): 296 (4) [M^+], 254 (13), 253 (100), 152 (11).

HRMS (EI) for $C_{19}H_{20}O_3$: calculated: 296.1412, found: 296.1411.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2975 (W), 2935 (W), 2874 (VW), 1718 (VS), 1682 (S), 1605 (M), 1587 (W), 1563 (VW), 1467 (W), 1439 (W), 1398 (W), 1384 (W), 1367 (W), 1306 (M), 1272 (M), 1242 (S), 1225 (VS), 1162 (W), 1110 (M), 1085 (W), 1045 (W), 1022 (W), 1000 (W), 981 (M), 869 (W), 851 (W), 818 (W), 769 (W), 747 (S), 717 (W), 692 (W).

3.4.8 *N,N*-Diethyl-4'-fluoro-2'-methylbiphenyl-3-carboxamide (**12f**)¹⁸⁹



The aluminium reagent **10c** was prepared according to **TP4** from *N,N*-diethyl-3-iodobenzamide (**9c**, 606 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and $PbCl_2$ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 30 h. The cross-coupling reaction was carried out according to **TP6** using $Zn(OAc)_2$ (556 mg, 3 mmol) and a solution of 2-bromo-5-fluorotoluene (**11f**,

267 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (2 mL). The reaction mixture was stirred at 50 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 4:1) afforded **12f** as colorless liquid (364 mg, 91%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.43 (t, J = 7.6 Hz, 1H), 7.36-7.32 (m, 1H), 7.32-7.26 (m, 2H), 7.19-7.13 (m, 1H), 6.99-6.88 (m, 2H), 3.52 (s, 2H), 3.33 (s, 2H), 2.24 (s, 3H), 1.17 (s, 6H).

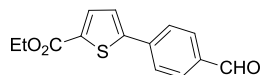
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 171.1, 162.1 (d, J = 246 Hz), 141.2, 137.7 (d, J = 8 Hz), 137.1 (d, J = 1 Hz), 137.0 (d, J = 3 Hz), 131.1 (d, J = 8 Hz), 130.0, 128.3, 127.0 (d, J = 1 Hz), 124.9, 116.8 (d, J = 21 Hz), 112.6 (d, J = 21 Hz), 43.4, 39.3, 20.6 (d, J = 2 Hz), 14.1, 13.0.

MS (EI, 70 eV) m/z (%): 285 (32) [M⁺], 284 (63), 214 (17), 213 (100), 185 (22), 183 (28), 170 (21), 165 (25), 44 (13).

HRMS (EI) for C₁₈H₂₀FNO: calculated: 285.1529, found: 285.1505.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2974 (W), 2935 (W), 2876 (VW), 1626 (VS), 1588 (M), 1500 (M), 1483 (M), 1470 (M), 1457 (M), 1433 (S), 1382 (M), 1364 (W), 1348 (W), 1316 (M), 1302 (M), 1274 (M), 1223 (S), 1184 (W), 1153 (M), 1100 (M), 1086 (M), 1070 (W), 1037 (W), 1004 (W), 951 (M), 909 (W), 882 (W), 864 (M), 808 (M), 792 (M), 766 (W), 727 (M), 710 (M), 683 (VW).

3.4.9 Ethyl 5-(4-formylphenyl)thiophene-2-carboxylate (**12g**)¹⁸⁹



The aluminium reagent **10d** was prepared according to **TP4** from ethyl 5-bromothiophene-2-carboxylate (**9d**, 470 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 1 mL THF at 50 °C for 6 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-bromobenzaldehyde (**11g**, 262 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in THF (1 mL). The reaction mixture was stirred at 30 °C for 2 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (1 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 5:1) afforded **12g** as yellowish solid (336 mg, 92%).

mp: 99-100 °C.

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 10.01 (s, 1H), 7.90 (d, J = 8.6 Hz, 2H), 7.77 (d, J = 8.6 Hz, 2H), 7.76 (d, J = 4.3 Hz, 1H), 7.40 (d, J = 4.3 Hz, 1H), 4.36 (q, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H).

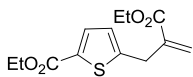
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 191.3, 161.9, 148.8, 139.0, 136.0, 134.4, 134.2, 130.5, 126.5, 125.3, 61.4, 14.3.

MS (EI, 70 eV) m/z (%): 387 (13), 276 (18), 261 (13), 260 (100) [M⁺], 259 (13), 248 (14), 233 (11), 232 (40), 231 (63), 216 (20), 215 (96), 188 (14), 187 (12), 159 (14), 158 (13), 143 (33), 115 (30), 114 (12), 43 (27).

HRMS (EI) for C₁₄H₁₂O₃S: calculated: 260.0507, found: 260.0503.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2988 (VW), 1695 (VS), 1666 (W), 1600 (M), 1566 (VW), 1478 (VW), 1451 (W), 1418 (VW), 1393 (VW), 1368 (W), 1315 (W), 1287 (S), 1274 (M), 1224 (W), 1214 (W), 1172 (W), 1100 (M), 1058 (W), 1013 (VW), 833 (W), 819 (W), 749 (W).

3.4.10 Ethyl 5-(2-(ethoxycarbonyl)allyl)thiophene-2-carboxylate (**12h**)



The aluminium reagent **10d** was prepared according to **TP4** from ethyl 5-bromothiophene-2-carboxylate (**9d**, 470 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 1 mL THF at 50 °C for 6 h. The allylation reaction was carried out according to **TP7** using Zn(OAc)₂ (556 mg, 3 mmol), CuCN·2 LiCl (1 M solution in THF, 0.14 mL, 0.14 mmol) and ethyl (2-bromomethyl)acrylate (**11h**, 270 mg, 1.4 mmol). The reaction mixture was stirred at -30 °C for 2 h before being quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (2 M, 5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **12h** as yellow oil (232 mg, 62%).

¹H-NMR (400 MHz, CDCl₃) δ/ppm : 7.64 (d, $J = 3.81$ Hz, 1H), 6.86-6.83 (m, 1H), 6.31-6.29 (m, 1H), 5.65-5.64 (m, 1H), 4.33 (q, $J = 7.15$ Hz, 2H), 4.22 (q, $J = 7.15$ Hz, 2H), 3.83 (s, 2H), 1.36 (t, $J = 7.15$ Hz, 3H), 1.29 (t, $J = 7.15$ Hz, 3H).

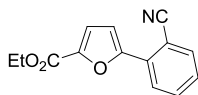
¹³C-NMR (100 MHz, CDCl₃) δ/ppm : 166.1, 162.2, 149.2, 138.8, 133.5, 132.3, 126.8, 126.5, 61.0, 61.0, 32.8, 14.3, 14.1.

MS (EI, 70 eV) m/z (%): 310 (18), 268 (28) [M⁺], 240 (21), 194 (42), 149 (25), 85 (40), 83 (36), 81 (30), 71 (66), 69 (58), 59 (37), 57 (100), 55 (61), 43 (70), 41 (54).

HRMS (EI) for C₁₃H₁₆O₄S: calculated: 268.0769, found: 268.0766.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2982 (W), 1705 (VS), 1654 (VW), 1633 (W), 1540 (W), 1457 (M), 1428 (W), 1368 (M), 1323 (W), 1279 (S), 1259 (S), 1231 (M), 1198 (M), 1171 (M), 1154 (M), 1087 (VS), 1023 (M), 951 (W), 924 (W), 859 (W), 816 (M), 749 (S), 670 (VW).

3.4.11 Ethyl 5-(2-cyanophenyl)-2-furoate (**12i**)¹⁸⁹



The aluminium reagent **10d** was prepared according to **TP4** from ethyl 5-bromo-2-furoate (**9d**, 447 mg, 2 mmol), LiCl (128 mg, 3 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 24 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 2-bromobenzonitrile (**11i**, 262 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in THF (1 mL). The reaction mixture was stirred at 30 °C for 3.5 h and quenched with sat. aqueous NH₄Cl solution (1 mL) and HCl (1 mL). Flash column

chromatographical purification on silica gel (pentane/diethyl ether = 6:1) afforded **12i** as brown solid (281 mg, 83%).

mp: 60-61 °C.

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 8.04 (t, J = 6.8 Hz, 1H), 7.74-7.68 (m, 1H), 7.68-7.60 (m, 1H), 7.44-7.35 (m, 2H), 7.28-7.21 (m, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H).

¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 158.4, 152.5, 144.8, 134.1, 133.1, 131.9, 128.5, 127.0, 119.5, 118.4, 111.8, 107.9, 61.2, 14.3.

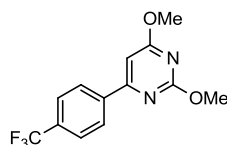
MS (EI, 70 eV) m/z (%): 242 (15), 241 (100) [M⁺], 213 (47), 197 (13), 196 (81), 169 (56), 141 (19), 140 (45), 113 (14).

HRMS (EI) for C₁₄H₁₁NO₃: calculated: 241.0739, found: 241.0740.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3128 (VW), 3076 (VW), 2984 (W), 2226 (W), 1714 (S), 1600 (W), 1584 (W), 1570 (W), 1526 (W), 1519 (W), 1482 (M), 1466 (W), 1437 (M), 1392 (W), 1375 (M), 1298 (VS), 1274 (M), 1259 (M), 1221 (M), 1171 (M), 1144 (S), 1113 (W), 1096 (W), 1061 (W), 1020 (M), 964 (W), 923 (W), 863 (W), 811 (W), 763 (S), 741 (W), 722 (VW), 714 (VW), 668 (W), 662 (W).

3.5 Catalysed Aluminium Insertion Using Extended Pi-Systems

3.5.1 2,4-Dimethoxy-6-(4-(trifluoromethyl)phenyl)pyrimidine (**15**)



The aluminium reagent **2a** was prepared according to **TP5** from 4-iodobenzotrifluoride (**1a**, 544 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and FeCl-TPP (**13b**, 28 mg, 0.04 mmol). The reaction was carried out in 4 mL THF at 20 °C for 1 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-iodo-2,6-dimethoxypyrimidine (**14**, 373 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (4 mL). The reaction mixture was stirred at 50 °C for 45 min and quenched with water (3 mL). Flash column chromatographical purification on silica gel (isohexane/ethyl acetate = 70:1) afforded **15** as brown solid (275 mg, 69%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.76 (d, J = 8.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 6.53 (s, 1H), 3.76 (s, 3H), 3.66 (s, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 173.0, 166.3, 164.4, 140.5 (q, J = 1 Hz), 131.7 (q, J = 32 Hz), 125.3 (q, J = 4 Hz), 127.7, 124.3 (q, J = 272 Hz), 97.6, 54.0, 53.3.

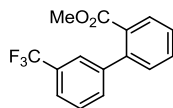
¹⁹F-NMR (376 MHz, C₆D₆) δ /ppm: -62.6.

MS (EI, 70 eV) m/z (%): 285 (11), 284 (100) [M⁺], 283 (64), 255 (14), 254 (42), 239 (14).

HRMS (EI) for C₁₃H₁₁F₃N₂O₂: calculated: 284.0773, found: 284.0769.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2951 (W), 1592 (S), 1577 (S), 1558 (S), 1515 (M), 1483 (S), 1452 (M), 1382 (M), 1358 (S), 1323 (S), 1310 (S), 1294 (S), 1217 (M), 1201 (M), 1165 (S), 1126 (S), 1117 (S), 1103 (VS), 1065 (VS), 1023 (M), 1012 (S), 984 (M), 964 (M), 868 (M), 852 (W), 837 (M), 822 (S), 781 (M), 768 (W), 673 (W).

3.5.2 Methyl 3'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate (**17**)



The aluminium reagent **3b** was prepared according to **TP5** from 3-bromobenzotrifluoride (**3a**, 450 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and FeCl-TPP (28 mg, 0.04 mmol). The reaction was carried out in 2 mL THF at 20 °C for 5 h. The cross-coupling reaction was carried out according to **TP6** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of methyl 2-iodobenzoate (**16**, 315 mg, 1.2 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (2 mL). The reaction mixture was stirred at 50 °C for 12 h and quenched with water (3 mL). Flash column chromatographical purification on silica gel (isohexane/ethyl acetate = 100:1) afforded **17** as brown liquid (187 mg, 56%).

¹H-NMR (400 MHz, C₆D₆) δ/ppm : 7.78-7.73 (m, 1H), 7.50-7.48 (m, 1H), 7.28-7.24 (m, 1H), 7.11-7.05 (m, 1H), 7.00-6.92 (m, 2H), 6.87 (t, $J = 7.7$ Hz, 1H), 6.84-6.81 (m, 1H), 3.16 (s, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ/ppm : 167.6, 142.3, 141.0, 131.7 (q, $J = 1$ Hz), 131.0, 130.9, 130.5, 130.1 (q, $J = 32$ Hz), 130.0, 128.1, 127.5, 124.5 (q, $J = 272$ Hz), 125.2 (q, $J = 4$ Hz), 123.6 (q, $J = 4$ Hz), 51.0.

¹⁹F-NMR (376 MHz, C₆D₆) δ/ppm : -62.3.

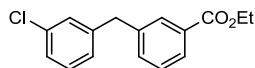
MS (EI, 70 eV) m/z (%): 280 (56), 250 (16), 249 (100), 201 (36), 152 (17).

HRMS (EI) for C₁₅H₁₁F₃O₂: calculated: 280.0711 [M⁺], found: 280.0709.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3068 (W), 2999 (W), 2954 (W), 1723 (S), 1600 (W), 1574 (W), 1478 (W), 1447 (W), 1433 (M), 1429 (M), 1333 (S), 1294 (S), 1279 (S), 1252 (S), 1243 (S), 1162 (S), 1119 (VS), 1092 (S), 1073 (S), 1050 (M), 1024 (M), 1002 (W), 964 (W), 905 (M), 840 (W), 804 (M), 759 (S), 737 (W), 702 (S), 670 (M), 654 (W).

3.6 InCl₃ – Catalysed Aluminium Insertion into Benzylic Chlorides

3.6.1 Ethyl 3-(3-chlorobenzyl)benzoate (**22a**)



The typical procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 3-chlorobenzyl chloride (**18a**, 322 mg, 2 mmol). The reaction was carried out at 25 °C for 3.5 h and provided the aluminium reagent **19a** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. Ethyl 3-iodobenzoate (**21a**, 386 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 2 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 30:1) afforded **22a** as colorless liquid (342 mg, 89%).

¹H-NMR (400 MHz, C₆D₆) δ/ppm: 8.04-7.99 (m, 2H), 7.01-6.90 (m, 4H), 6.75 (t, *J* = 8.0 Hz, 1H), 6.66-6.63 (m, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.48 (s, 2H), 1.01 (t, *J* = 7.1 Hz, 3H).

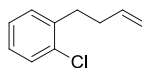
¹³C-NMR (100 MHz, C₆D₆) δ/ppm: 165.8, 142.6, 140.4, 134.3, 133.0, 131.2, 130.0, 129.6, 128.9, 128.4, 127.6, 126.8, 126.3, 60.5, 40.8, 13.9.

MS (EI, 70 eV) *m/z* (%): 276 (24), 275 (13), 274 (71), 246 (22), 245 (16), 239 (14), 231 (34), 230 (17), 229 (100), 211 (17), 203 (11), 210 (29), 167 (17), 166 (56), 165 (75), 97 (18), 83 (11), 82 (27), 57 (100).

HRMS (EI) for C₁₆H₁₅ClO₂: calculated: 274.0761, found 274.0756.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2981 (W), 2935 (VW), 2906 (VW), 1713 (VS), 1596 (W), 1588 (W), 1573 (W), 1475 (M), 1444 (M), 1430 (W), 1392 (W), 1366 (W), 1304 (M), 1276 (VS), 1189 (S), 1104 (S), 1080 (S), 1022 (M), 1001 (W), 944 (W), 919 (W), 896 (W), 858 (M), 821 (VW), 776 (M), 750 (S), 709 (S), 683 (S), 672 (W).

3.6.2 1-(But-3-en-1-yl)-2-chlorobenzene (**22b**)



The typical procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 2-chlorobenzyl chloride (**18b**, 281 mg, 2 mmol). The reaction was carried out at 25 °C for 20 h and provided the aluminium reagent **19b** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before allyl bromide (**21b**, 169 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 2 h before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were

concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22b** as colorless liquid (233 mg, 46%).

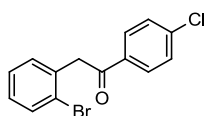
¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.37 (dd, $J = 7.8$ Hz, $J = 1.3$ Hz, 1H), 7.26-7.12 (m, 3H), 5.90 (ddt, $J = 17.1$ Hz, $J = 10.2$ Hz, $J = 6.6$ Hz, 1H), 5.13-5.05 (m, 1H), 5.03 (ddt, $J = 10.2$ Hz, $J = 1.9$ Hz, $J = 1.2$ Hz, 1H), 2.85 (dd, $J = 8.9$ Hz, $J = 6.8$ Hz, 2H), 2.41 (dtt, $J = 9.2$ Hz, $J = 6.5$ Hz, $J = 1.4$ Hz, 2H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 139.5, 137.8, 134.1, 130.5, 129.6, 127.4, 126.8, 115.3, 33.8, 33.2.

MS (EI, 70 eV) m/z (%): 166 (4) [M⁺], 131 (33), 127 (36), 125 (100), 89 (7), 63 (3).

HRMS (EI) for C₁₀H₁₁Cl: calculated: 166.0549, found 166.0545.

3.6.3 2-(2-Bromo-phenyl)-1-(4-chloro-phenyl)-ethanone (**22c**)



The typical procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 2-bromobenzyl chloride (**18c**, 411 mg, 2 mmol). The reaction was carried out at 25 °C for 3 h and provided the aluminium reagent **19c** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. CuCN·2 LiCl (1 M solution in THF, 0.4 mL, 0.4 mmol) was added at -30 °C and the reaction mixture stirred for 15 minutes at this temperature. 4-Chlorobenzoyl chloride (**21c**, 245 mg, 1.4 mmol) was added dropwise at -30 °C. The reaction mixture was stirred for 2 h and slowly warmed to 0 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 12:1) afforded **22c** as white solid (360 mg, 83%).

mp: 102-105 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.60-7.55 (m, 2H), 7.38-7.34 (m, 1H), 7.01-6.96 (m, 2H), 6.94-6.87 (m, 2H), 6.72-6.66 (m, 1H), 3.93 (s, 2H).

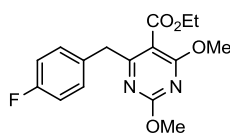
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 193.6, 139.0, 135.0, 134.9, 132.6, 131.6, 129.5, 128.6, 128.5, 127.1, 125.1, 45.3.

MS (EI, 70 eV) m/z (%): 229 (17), 140 (26), 138 (100), 111 (15).

HRMS (EI) for C₁₄H₁₀BrClO: calculated: 307.9604, found 307.9616.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 1688 (S), 1589 (M), 1400 (M), 1322 (M), 1217 (M), 1197 (M), 1174 (M), 1085 (S), 1021 (M), 1014 (M), 987 (S), 836 (M), 815 (S), 797 (M), 757 (VS), 730 (M).

3.6.4 Ethyl 4-(4-fluorobenzyl)-2,6-dimethoxypyrimidine-5-carboxylate (**22d**)



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 4-fluorobenzyl chloride (**18d**, 289 mg, 2 mmol). The reaction was carried out at 25 °C for 22 h and provided the aluminium reagent **19d** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. Ethyl 4-iodo-2,6-dimethoxypyrimidine-5-carboxylate (**21d**, 473 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 2 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 3:1) afforded **22d** as colorless oil (439 mg, 98%).

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 7.24-7.19 (m, 2H), 6.82-6.76 (m, 2H), 4.11 (q, $J = 7.1$ Hz, 2H), 4.00 (s, 2H), 3.58 (s, 3H), 3.52 (s, 3H), 0.99 (t, $J = 7.1$ Hz, 3H).

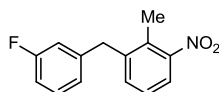
$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 169.1 (d, $J = 1$ Hz), 169.0, 165.5, 164.8, 161.8 (d, $J = 244$ Hz), 133.6 (d, $J = 3$ Hz), 130.9 (d, $J = 8$ Hz), 114.9 (d, $J = 21.4$ Hz), 108.5, 60.9, 54.1, 53.6, 40.3, 13.7.

MS (EI, 70 eV) m/z (%): 321 (15), 320 (88), 319 (28), 291 (20), 275 (50), 274 (100), 273 (27), 258 (11), 247 (44), 245 (17), 203 (11), 174 (10), 109 (15).

HRMS (EI) for $\text{C}_{16}\text{H}_{17}\text{FN}_2\text{O}_4$: calculated: 320.1172, found 320.1153.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2986 (W), 1721 (M), 1600 (M), 1577 (S), 1559 (S), 1508 (S), 1483 (S), 1459 (S), 1375 (S), 1360 (S), 1296 (M), 1259 (VS), 1220 (S), 1204 (M), 1176 (M), 1158 (M), 1116 (M), 1095 (M), 1057 (VS), 1016 (M), 937 (W), 858 (W), 838 (M), 812 (S), 772 (M), 738 (W), 718 (W), 679 (W).

3.6.5 1-(3-Fluorobenzyl)-2-methyl-3-nitrobenzene (**22e**).



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 3-fluorobenzyl chloride (**18e**, 289 mg, 2 mmol). The reaction was carried out at 25 °C for 6 h and provided the aluminium reagent **19e** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. 1-Bromo-2-methyl-3-nitrobenzene (**21e**, 302 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 2 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 70:1) afforded **22e** as colorless oil (243 mg, 71%).

¹H-NMR (400 MHz, CDCl₃) δ /ppm: 7.70 (dd, $J = 7.8$ Hz, $J = 1.4$ Hz, 1H), 7.42-7.23 (m, 3H), 7.01-6.87 (m, 2H), 6.80 (d, $J = 9.9$ Hz, 1H), 4.11 (s, 2H), 2.36 (s, 3H).

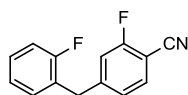
¹³C-NMR (100 MHz, CDCl₃) δ /ppm: 163.2 (d, $J = 246$ Hz), 151.8, 141.6 (d, $J = 7$ Hz), 141.1, 134.0, 130.9, 130.2 (d, $J = 8$ Hz), 126.5, 124.2 (d, $J = 3$ Hz), 122.5, 115.5 (d, $J = 21$ Hz), 113.5 (d, $J = 21$ Hz), 39.4 (d, $J = 1$ Hz), 15.1.

MS (EI, 70 eV) m/z (%): 245 (35), 228 (51), 211 (11), 198 (18), 197 (15), 196 (22), 184 (36), 183 (80), 133 (18), 132 (100), 109 (41).

HRMS (EI) for C₁₄H₁₂FNO₂: calculated: 245.0852, found 245.0844.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2931 (VW), 2870 (VW), 1615 (M), 1588 (M), 1522 (VS), 1487 (M), 1446 (M), 1383 (W), 1349 (S), 1302 (W), 1272 (W), 1252 (M), 1205 (W), 1160 (W), 1152 (W), 1134 (M), 1086 (W), 1074 (W), 1036 (VW), 944 (W), 885 (M), 869 (W), 834 (W), 806 (W), 781 (S), 752 (M), 731 (S), 710 (M), 685 (M), 660 (W).

3.6.6 2-Fluoro-4-(2-fluorobenzyl)benzonitrile (**22f**).



The general procedure was **TP8** followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 2-fluorobenzyl chloride (**18f**, 289 mg, 2 mmol). The reaction was carried out at 25 °C for 6 h and provided the aluminium reagent **19f** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. 4-Bromo-2-fluorobenzonitrile (**21f**, 280 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 2 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 8:1) afforded **22f** as colorless oil (321 mg, 74%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 6.86-6.66 (m, 4H), 6.60 (t, $J = 7.4$ Hz, 1H), 6.40 (d, $J = 9.4$ Hz, 1H), 6.30 (d, $J = 7.8$ Hz, 1H), 3.38 (s, 2H).

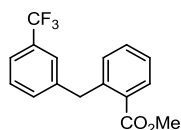
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 163.1 (d, $J = 215$ Hz), 160.6 (d, $J = 203$ Hz), 147.6 (d, $J = 8$ Hz), 132.9 (d, $J = 1$ Hz), 130.7 (d, $J = 4$ Hz), 128.7 (d, $J = 8$ Hz), 125.7 (d, $J = 16$ Hz), 124.5 (d, $J = 3$ Hz), 124.1 (d, $J = 3$ Hz), 116.1 (d, $J = 1$ Hz), 115.9 (d, $J = 1$ Hz), 113.6, 99.4 (d, $J = 15$ Hz), 34.3 (dd, $J = 3$ Hz, $J = 2$ Hz).

MS (EI, 70 eV) m/z (%): 230 (15), 229 (100), 228 (25), 208 (22).

HRMS (EI) for C₁₄H₉F₂N: calculated: 229.0703, found 229.0695.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3068 (VW), 2928 (VW), 2238 (W), 1621 (M), 1586 (W), 1570 (M), 1491 (S), 1456 (M), 1430 (S), 1282 (W), 1253 (W), 1230 (S), 1183 (W), 1112 (M), 1094 (W), 1033 (W), 960 (M), 925 (W), 883 (W), 865 (W), 846 (W), 826 (M), 752 (VS), 733 (M), 696 (W).

3.6.7 Methyl 2-(3-(trifluoromethyl)benzyl)benzoate (**22g**)



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 3-(trifluoromethyl)benzyl chloride (**18g**, 389 mg, 2 mmol). The reaction was carried out at 25 °C for 24 h and provided the aluminium reagent **19g** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. Methyl 2-iodobenzoate (**21g**, 367 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 2 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 40:1) afforded **22g** as colorless oil (367 mg, 89%).

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 7.87 (dd, $J = 7.6$ Hz, $J = 1.4$ Hz, 1H), 7.50 (s, 1H), 7.20 (d, $J = 7.8$ Hz, 1H), 7.06 (d, $J = 7.8$ Hz, 1H), 7.03-6.98 (m, 1H), 6.94-6.89 (m, 1H), 6.88-6.80 (m, 2H), 4.26 (s, 2H), 3.37 (s, 3H).

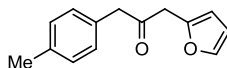
$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 167.0, 142.1, 141.4, 132.1 (q, $J = 1$ Hz), 131.8, 131.4, 130.8, 130.4 (q, $J = 32$ Hz), 129.8, 128.6, 126.3, 125.6 (q, $J = 3$ Hz), 124.7 (q, $J = 272$ Hz), 122.6 (q, $J = 3$ Hz), 51.0, 39.2.

MS (EI, 70 eV) m/z (%): 263 (22), 262 (100), 165 (16).

HRMS (EI) for $\text{C}_{16}\text{H}_{13}\text{F}_3\text{O}_2$: calculated: 294.0868, found 294.0862.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2954 (M), 1719 (S), 1600 (M), 1577 (M), 1490 (M), 1448 (S), 1435 (S), 1327 (S), 1296 (S), 1260 (S), 1160 (S), 1117 (VS), 1094 (S), 1072 (VS), 1049 (S), 1002 (M), 966 (M), 917 (S), 882 (M), 872 (M), 812 (M), 788 (S), 764 (S), 737 (S), 711 (S), 700 (S), 660 (M).

3.6.8 1-(Furan-2-yl)-2-(p-tolyl)ethanone (**22h**)



The typical procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 4-methylbenzyl chloride (**18h**, 281 mg, 2 mmol). The reaction was carried out at 25 °C for 3 h and provided the aluminium reagent **19h** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M solution in THF, 2 mL, 2 mmol) was added at -30 °C and the reaction mixture stirred for 15 minutes at this temperature. Furan-2-carbonyl chloride (**21h**, 183 mg, 1.4 mmol) was added dropwise at -30 °C. The reaction mixture was stirred for 1.5 h and slowly warmed to 20 °C within 15 h before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with ethyl acetate. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 5:1) afforded **22h** as orange solid (174 mg, 62%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.60-7.59 (m, 1H), 7.23-7.10 (m, 5H), 6.54-6.52 (m, 1H), 4.09 (s, 2H), 2.33 (s, 3H).

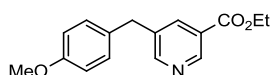
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 186.8, 152.4, 146.5, 136.6, 129.3, 129.3, 117.8, 112.3, 108.7, 45.1, 21.0.

MS (EI, 70 eV) m/z (%): 200 (40) [M⁺], 105 (83), 95 (100), 85 (12), 79 (11), 77 (13), 71 (15), 57 (21), 43 (13).

HRMS (EI) for C₁₃H₁₂O₂: calculated: 200.0837, found 200.0832.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3149 (VW), 3122 (W), 3026 (W), 2894 (W), 1735 (W), 1672 (S), 1604 (W), 1568 (M), 1516 (W), 1461 (S), 1390 (M), 1339 (M), 1316 (W), 1262 (W), 1248 (M), 1226 (W), 1215 (W), 1202 (W), 1184 (W), 1156 (M), 1118 (W), 1103 (VW), 1080 (W), 1029 (M), 995 (M), 913 (W), 902 (W), 882 (M), 855 (W), 846 (W), 824 (W), 809 (W), 770 (VS), 730 (S), 700 (W).

3.6.9 Ethyl 5-(4-methoxybenzyl)nicotinate (**22i**).



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 4-methoxybenzyl chloride (**18i**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h and provided the aluminium reagent **19i** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. Ethyl 5-bromonicotinate (**21i**, 322 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 2 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22i** as colorless oil (296 mg, 78%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 9.38 (d, J = 2.2 Hz, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.09 (t, J = 2.2 Hz, 1H), 6.80-6.76 (m, 2H), 6.71-6.66 (m, 2H), 4.03 (q, J = 7.1 Hz, 2H), 3.46 (s, 2H), 3.29 (s, 3H), 0.94 (t, J = 7.1 Hz, 3H).

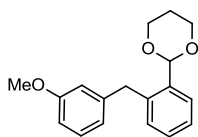
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 164.9, 158.5, 153.8, 148.8, 136.7, 136.5, 131.2, 129.6, 126.1, 114.1, 60.7, 54.3, 37.6, 13.7.

MS (EI, 70 eV) m/z (%): 272 (18), 271 (100), 270 (18), 242 (16), 226 (14), 198 (11), 121 (31).

HRMS (EI) for C₁₆H₁₇NO₃: calculated: 271.1208, found 271.1209.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2982 (W), 2935 (W), 2836 (VW), 1718 (S), 1611 (W), 1598 (W), 1584 (W), 1511 (S), 1456 (M), 1442 (M), 1428 (W), 1393 (W), 1368 (W), 1286 (S), 1245 (VS), 1205 (S), 1176 (S), 1105 (S), 1027 (S), 951 (W), 862 (W), 834 (M), 811 (M), 768 (M), 752 (M), 702 (M), 672 (W).

3.6.10 2-(2-(3-methoxybenzyl)phenyl)-1,3-dioxane (22j)



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 3-methoxybenzyl chloride (**18j**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 12 h and provided the aluminium reagent **19j** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. 2-(2-Bromophenyl)-1,3-dioxane (**21j**, 340 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 1 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22j** as colorless oil (326 mg, 82%).

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 7.97 (d, $J = 8.1$ Hz, 1H), 7.14-7.02 (m, 4H), 6.88 (s, 1H), 6.81 (d, $J = 7.5$ Hz, 1H), 6.70 (dd, $J = 8.1$ Hz, 2.5 Hz, 1H), 5.55 (s, 1H), 4.17 (s, 2H), 3.88 (dd, $J = 10.8$ Hz, $J = 5.0$ Hz, 2H), 3.43 (td, $J = 12.3$ Hz, $J = 2.3$ Hz, 2H), 3.29 (s, 3H), 1.87 (qt, $J = 12.7$ Hz, $J = 5.0$ Hz, 1H), 0.68-0.61 (m, 1H).

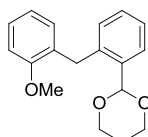
$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 160.4, 143.0, 138.9, 137.6, 130.6, 129.6, 128.9, 127.0, 126.4, 121.8, 115.1, 111.9, 100.5, 67.2, 54.6, 38.5, 25.9.

MS (EI, 70 eV) m/z (%): 209 (20), 208 (100), 175 (11).

HRMS (EI) for $\text{C}_{18}\text{H}_{20}\text{O}_3$: calculated: 284.1412, found 284.1403.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2960 (W), 2848 (W), 1598 (M), 1583 (M), 1488 (M), 1465 (M), 1454 (M), 1436 (M), 1393 (M), 1377 (M), 1348 (W), 1313 (W), 1297 (W), 1274 (M), 1256 (S), 1236 (M), 1145 (S), 1107 (VS), 1091 (VS), 1047 (S), 1007 (S), 986 (VS), 960 (M), 949 (M), 927 (M), 893 (W), 867 (M), 848 (W), 804 (VW), 776 (M), 750 (VS), 718 (M), 694 (S).

3.6.11 Diethyl 4,4'-(1,4-phenylene)bis(2-methylenebutanoate) (22k)



The typical procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 2-chlorobenzyl chloride (**18k**, 281 mg, 2 mmol). The reaction was carried out at 25 °C for 20 h and provided the aluminium reagent **19k** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before allyl bromide (**21k**, 169 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 2 h before being quenched with HCl (2 M,

2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22k** as colorless liquid (233 mg, 46%).

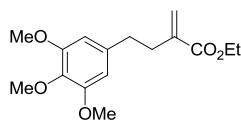
¹H-NMR (300 MHz, CDCl₃) δ /ppm: 8.03 (d, J = 7.4 Hz, 1H), 7.15-7.04 (m, 5H), 6.80 (td, J = 7.5 Hz, 1.0 Hz, 1H), 6.61 (d, J = 8.1 Hz, 1H), 5.67 (s, 1H), 4.36 (s, 2H), 3.88 (ddd, J = 11.8 Hz, J = 5.0 Hz, J = 1.3 Hz, 2H), 3.45 (td, J = 12.2 Hz, J = 2.5 Hz, 2H), 3.35 (s, 3H), 1.89 (qt, J = 12.5 Hz, J = 5.0 Hz, 1H), 0.66 (dt, J = 13.3 Hz, J = 2.3 Hz, J = 1.3 Hz, 1H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 157.8, 138.7, 138.0, 130.9, 130.2, 129.8, 128.9, 127.6, 126.9, 126.3, 121.0, 110.4, 100.4, 67.3, 54.9, 32.3, 26.0.

MS (EI, 70 eV) m/z (%): 226 (49), 210 (30), 209 (100), 195 (27), 179 (20), 176 (28), 118 (24), 91 (16), 56 (12).

HRMS (EI) for C₁₈H₂₀O₃: calculated: 284.1412, found 284.1399.

3.6.12 Ethyl 2-methylene-4-(3,4,5-trimethoxyphenyl)butanoate (**22l**)



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 3,4,5-trimethoxybenzyl chloride (**18l**, 433 mg, 2 mmol). The reaction was carried out at 25 °C for 7 h and provided the aluminium reagent **19l** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21l**, 270 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 3:1) afforded **22l** as colorless oil (309 mg, 75%).

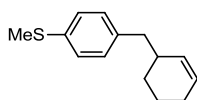
¹H-NMR (400 MHz, C₆D₆) δ /ppm: 6.36 (s, 2H), 6.20 (d, J = 1.6 Hz, 1H), 5.28 (q, J = 1.2 Hz, 1H), 4.01 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 3.43 (s, 6H), 2.77-2.65 (m, 4H), 0.97 (t, J = 7.2 Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.8, 154.1, 140.9, 137.9, 137.1, 124.7, 106.3, 60.6, 60.5, 55.8, 35.8, 34.7, 14.2.

MS (EI, 70 eV) m/z (%): 294 (22), 182 (11), 181 (100).

HRMS (EI) for C₁₆H₂₂O₅: calculated: 294.1467, found 294.1457.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2938 (W), 2838 (VW), 1711 (M), 1629 (W), 1589 (M), 1507 (M), 1457 (M), 1420 (M), 1369 (W), 1331 (M), 1236 (S), 1183 (S), 1121 (VS), 1008 (M), 975 (W), 944 (M), 860 (W), 820 (M), 778 (W), 693 (VW), 668 (VW).

3.6.13 (4-(Cyclohex-2-en-1-ylmethyl)phenyl)(methyl)sulfane (22m)

The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and (4-(chloromethyl)phenyl)(methyl)sulfane (**18m**, 345 mg, 2 mmol). The reaction was carried out at 25 °C for 3 h and provided the aluminium reagent **19m** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before 3-bromocyclohexene (**21m**, 225 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2.0, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane) afforded **22m** as colorless oil (281 mg, 92%).

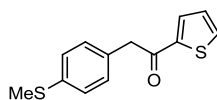
$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 7.16-6.86 (m, 4H), 5.75-5.55 (m, 2H), 2.53-2.35 (m, 2H), 2.33-2.21 (m, 1H), 2.05 (s, 3H), 1.92-1.83 (m, 2H), 1.67-1.53 (m, 2H), 1.47-1.34 (m, 1H), 1.24-1.11 (m, 1H).

$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 137.9, 136.2, 131.5, 129.9, 127.5, 127.3, 42.4, 37.5, 29.2, 25.7, 21.6, 15.9.

MS (EI, 70 eV) m/z (%): 218 (11), 137 (100).

HRMS (EI) for $\text{C}_{14}\text{H}_{18}\text{S}$: calculated: 218.1129, found 218.1114.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3402 (W), 3016 (M), 2919 (S), 2855 (M), 2836 (M), 1669 (M), 1627 (W), 1596 (W), 1562 (VW), 1493 (S), 1445 (M), 1435 (M), 1405 (S), 1088 (VS), 1048 (VS), 1015 (S), 954 (S), 834 (S), 810 (S), 785 (S), 720 (S), 700 (W), 674 (S).

3.6.14 2-(4-(Methylthio)phenyl)-1-(thiophen-2-yl)ethanone (22n)

The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and (4-(chloromethyl)phenyl)(methyl)sulfane (**18m**, 345 mg, 2 mmol). The reaction was carried out at 25 °C for 3 h and provided the aluminium reagent **19m** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 2 mL, 2 mmol) was added at -30 °C before thiophene carbonylchloride (**21n**, 205 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2.0, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 5:1) afforded **22n** as colorless oil (281 mg, 72%).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.26 (dd, $J = 3.8$ Hz, $J = 1.1$ Hz, 1H), 7.06-6.97 (m, 4H), 6.87 (dd, $J = 4.9$ Hz, $J = 1.2$ Hz, 1H), 6.53 (dd, $J = 4.9$ Hz, $J = 3.9$ Hz, 1H), 3.72 (s, 2H), 1.96 (s, 3H).

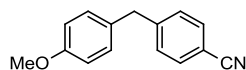
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 189.9, 144.9, 138.1, 134.0, 132.7, 132.0, 130.6, 128.3, 127.5, 46.1, 15.8.

MS (EI, 70 eV) m/z (%): 250 (11), 249 (19), 248 (100), 137 (63).

HRMS (EI) for C₁₃H₁₂S₂O: calculated: 248.0330, found 248.0334.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3069 (W), 1660 (S), 1601 (W), 1516 (W), 1494 (W), 1436 (VW), 1424 (VW), 1412 (M), 1402 (M), 1353 (W), 1324 (W), 1279 (W), 1223 (M), 1197 (M), 1115 (W), 1108 (W), 1094 (W), 1083 (W), 1059 (M), 1016 (W), 981 (W), 970 (W), 956 (W), 940 (M), 916 (W), 888 (W), 880 (VW), 875 (VW), 854 (M), 827 (W), 804 (W), 796 (W), 776 (W), 760 (S), 744 (VS), 724 (M), 699 (W).

3.6.15 4-(4-Methoxybenzyl)benzonitrile (22o)



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 4-methoxybenzyl chloride (**18i**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h and provided the aluminium reagent **19i** which was transferred to an argon flushed flask containing anhydrous Zn(OAc)₂ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. 4-(Methylthio)benzonitrile (**21o**, 209 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 1 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 6:1) afforded **22o** as colorless oil (253 mg, 81%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.51-7.46 (m, 2H), 7.21-7.16 (m, 2H), 7.03-6.94 (m, 2H), 6.80-6.74 (m, 2H), 3.89 (s, 2H), 3.71 (s, 3H).

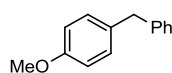
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 158.4, 147.2, 132.2, 131.4, 129.9, 129.5, 119.0, 114.1, 109.9, 55.3, 41.1.

MS (EI, 70 eV) m/z (%): 224 (12) [M⁺], 223 (100), 222 (18), 208 (11), 121 (15).

HRMS (EI) for C₁₅H₁₃NO: calculated: 223.0997 [M⁺], found: 223.0997.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3009 (W), 2955 (W), 2932 (W), 2907 (W), 2835 (W), 2226 (M), 1657 (W), 1650 (W), 1642 (W), 1607 (M), 1583 (M), 1510 (S), 1462 (M), 1451 (M), 1440 (M), 1420 (W), 1414 (M), 1335 (W), 1320 (W), 1301 (M), 1279 (M), 1247 (VS), 1208 (M), 1174 (S), 1150 (M), 1109 (M), 1034 (S), 1022 (M), 957 (W), 930 (W), 914 (W), 861 (M), 848 (M), 841 (M), 826 (M), 804 (VS), 760 (M), 736 (W), 708 (W), 683 (W).

3.6.16 1-Benzyl-4-methoxybenzene (22p)



The general procedure **TP8** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 4-methoxybenzyl chloride (**18i**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h and provided the aluminium reagent **19i** which was transferred to an argon flushed flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (556 mg, 3 mmol) and stirred for 20 min at 25 °C. 4-Methyl(phenyl)sulfane (**21p**, 174 mg, 1.4 mmol) and PEPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 1 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22p** as yellow oil (186 mg, 67%).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ /ppm: 7.32-7.25 (m, 2H), 7.22-7.15 (m, 3H), 7.13-7.08 (m, 2H), 6.87-6.80 (m, 2H), 3.93 (s, 2H), 3.78 (s, 3H).

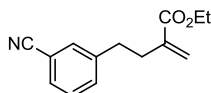
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ /ppm: 158.0, 141.6, 133.2, 129.8, 128.8, 128.4, 125.9, 113.9, 55.2, 41.0.

MS (EI, 70 eV) m/z (%): 199 (17), 198 (100) [M^+], 197 (66), 183 (13), 167 (24), 166 (11), 165 (22), 153 (15), 152 (19), 135 (144), 121 (68), 105 (11), 91 (20), 78 (13), 77 (23), 44 (30), 43 (67).

HRMS (EI) for $\text{C}_{14}\text{H}_{14}\text{O}$: calculated: 198.1045 [M^+], found: 198.1041.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3027 (W), 2907 (W), 2835 (W), 1655 (W), 1610 (M), 1584 (W), 1510 (S), 1494 (M), 1462 (M), 1453 (M), 1440 (M), 1316 (W), 1301 (M), 1280 (W), 1243 (VS), 1174 (S), 1150 (W), 1121 (W), 1106 (M), 1074 (W), 1031 (S), 938 (W), 837 (M), 797 (M), 769 (M), 724 (S), 696 (S).

3.6.17 Ethyl 4-(3-cyanophenyl)-2-methylenebutanoate (**22q**)



The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 2 mL, 2 mmol) and 3-cyanobenzyl chloride (**18n**, 303 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h and provided the reagent **19n** which was transferred to a new argon flushed flask. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21l**, 270 mg, 1.4 mmol) was added subsequently. The mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22q** as colorless oil (299 mg, 93%).

$^1\text{H-NMR}$ (300 MHz, C_6D_6) δ /ppm: 6.95-6.91 (m, 2H), 6.83-6.79 (m, 1H), 6.69-6.64 (m, 1H), 6.11-6.10 (m, 1H), 5.07-5.06 (m, 1H), 3.99 (q, $J = 7.2$ Hz, 2H), 2.43-2.28 (m, 4H), 0.96 (t, $J = 7.1$ Hz, 3H).

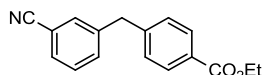
$^{13}\text{C-NMR}$ (75 MHz, C_6D_6) δ /ppm: 166.4, 142.7, 140.0, 132.6, 132.0, 129.7, 129.0, 125.0, 118.9, 113.0, 60.7, 34.4, 33.6, 14.1.

MS (EI, 70 eV) m/z (%): 184 (27), 183 (80), 182 (15), 158 (14), 156 (25), 155 (47), 154 (32), 130 (42), 129 (15), 117 (13), 116 (100), 89 (21).

HRMS (EI) for $C_{14}H_{15}NO_2$: calculated: 229.1103, found 229.1086.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3457 (VW), 2982 (W), 2938 (W), 2230 (M), 1716 (VS), 1631 (W), 1602 (W), 1583 (W), 1483 (W), 1445 (M), 1434 (M), 1370 (M), 1300 (M), 1254 (M), 1186 (VS), 1022 (S), 950 (W), 918 (W), 859 (W), 799 (S), 690 (VS).

3.6.18 Ethyl 4-(3-cyanophenyl)-2-methylenebutanoate (**22r**)



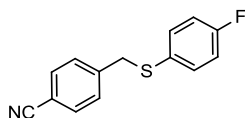
The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 2 mL, 2 mmol) and 3-cyanobenzyl chloride (**18n**, 303 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h and provided the reagent **19n** which was transferred to a new argon flushed flask. Ethyl 4-iodobenzoate (**21q**, 386 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 1 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 6:1) afforded **22r** as yellow liquid (241 mg, 56%).

¹H-NMR (400 MHz, C_6D_6) δ /ppm: 8.05-8.01 (m, 2H), 6.86-6.83 (m, 1H), 6.71-6.67 (m, 2H), 6.64-6.54 (m, 2H), 4.09 (q, $J = 7.2$ Hz), 3.24 (s, 2H), 0.98 (t, $J = 7.0$ Hz).

¹³C-NMR (100 MHz, C_6D_6) δ /ppm: 189.9, 144.9, 138.1, 134.0, 132.7, 132.0, 130.6, 128.3, 127.5, 46.1, 15.8.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3000 (VW), 2955 (VW), 2902 (VW), 2228 (W), 2206 (VW), 2196 (VW), 2191 (VW), 1708 (S), 1670 (W), 1606 (W), 1574 (W), 1506 (VW), 1474 (W), 1446 (W), 1436 (W), 1429 (W), 1414 (W), 1392 (W), 1364 (W), 1322 (VW), 1306 (W), 1276 (VS), 1257 (S), 1193 (W), 1176 (M), 1127 (W), 1108 (S), 1019 (M), 981 (W), 940 (W), 925 (W), 906 (W), 892 (W), 876 (W), 854 (W), 822 (VW), 788 (W), 765 (M), 727 (S), 699 (M), 689 (M).

3.6.19 4-(((4-Fluorophenyl)thio)methyl)benzonitrile (**22s**)



The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 2 mL, 2 mmol) and 4-cyanobenzyl chloride (**18o**, 303 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h and provided the reagent **19o** which was transferred to a new argon flushed flask. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before 5-(4-fluorophenyl) benzenesulfonothioate (**21r**, 376 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M,

2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 8:1) afforded **22s** as yellowish solid (252 mg, 74%).

mp: 53-54 °C.

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.58-7.50 (m, 2H), 7.31-7.18 (m, 4H), 7.01-6.89 (m, 2H), 4.02 (s, 2H).

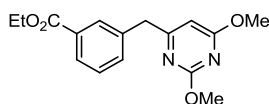
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 162.5 (d, *J* = 248 Hz), 143.4, 134.4, 132.2, 129.5, 129.3 (d, *J* = 3 Hz), 118.7, 116.2 (d, *J* = 22 Hz), 111.0, 40.5 (d, *J* = 1 Hz).

MS (EI, 70 eV) *m/z* (%): 243 (44), 117 (11), 116 (100), 89 (17).

HRMS (EI) for C₁₄H₁₀NFS: calculated: 243.0518, found 243.0501.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3058 (W), 2932 (W), 2856 (W), 2228 (M), 1862 (W), 1606 (M), 1588 (W), 1498 (W), 1488 (S), 1399 (M), 1298 (W), 1216 (S), 1158 (M), 1090 (M), 856 (S), 803 (S), 760 (S).

3.6.20 Ethyl 3-((2,6-dimethoxypyrimidin-4-yl)methyl)benzoate (**22t**)



The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol), ZnCl₂ (1 M in THF, 2 mL, 2 mmol) and ethyl 3-(chloromethyl)benzoate (**18p**, 397 mg, 2 mmol). The reaction was carried out at 25 °C for 10 h and provided the reagent **19p** which was transferred to a new argon flushed flask. 4-Iodo-2,6-dimethoxypyrimidine (**21s**, 373 mg, 1.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) dissolved in NMP (2 mL) were added subsequently. The reaction mixture was stirred at 50 °C for 1 h and quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 1:1) afforded **22t** as colorless oil (351 mg, 83%).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 8.22 (t, *J* = 1.5 Hz, 1H), 8.04 (dt, *J* = 7.6 Hz, 1.5 Hz, 1H), 7.21-7.18 (m, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.00 (s, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.72 (s, 3H), 3.65 (s, 2H), 3.56 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H).

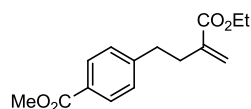
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 172.4, 170.7, 166.2, 166.1, 138.8, 133.8, 131.5, 130.8, 128.7, 128.2, 100.3, 60.8, 54.3, 53.3, 43.5, 14.2.

MS (EI, 70 eV) *m/z* (%): 302 (100), 287 (13), 273 (58), 257 (48), 255 (30), 240 (26), 230 (17), 229 (50), 227 (15), 199 (19), 157 (19), 156 (15), 128 (17), 106 (15).

HRMS (EI) for C₁₆H₁₈N₂O₄: calculated: 302.1267, found 302.1263.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2982 (W), 2957 (W), 1715 (S), 1582 (S), 1565 (S), 1478 (M), 1458 (M), 1446 (M), 1419 (W), 1381 (M), 1351 (VS), 1305 (M), 1273 (S), 1192 (S), 1155 (W), 1145 (W), 1098 (S), 1081 (M), 1056 (M), 1039 (M), 1024 (M), 1002 (W), 984 (W), 933 (W), 901 (W), 841 (W), 821 (W), 789 (W), 757 (M), 725 (M), 686 (W), 683 (W), 674 (VW).

3.6.21 Methyl 4-(3-(ethoxycarbonyl)but-3-en-1-yl)benzoate (22u)



The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 2 mL, 2 mmol) and methyl 4-(chloromethyl)benzoate (**18q**, 369 mg, 2 mmol). The reaction was carried out at 25 °C for 10 h and provided the reagent **19q** which was transferred to a new argon flushed flask. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21i**, 270 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentan/diethyl ether = 8:1) afforded **22u** as colorless oil (275 mg, 75%).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ/ppm : 8.10-8.07 (m, 2H), 6.97-6.93 (m, 2H), 6.13 (d, $J = 1.4$ Hz, 1H), 5.11 (q, $J = 1.4$ Hz, 1H), 3.99 (q, $J = 7.0$ Hz, 2H), 3.51 (s, 3H), 2.64-2.46 (m, 4H), 0.96 (t, $J = 7.1$ Hz, 3H).

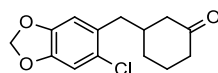
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ/ppm : 166.7, 166.5, 146.9, 140.3, 130.1, 128.8, 128.7, 124.9, 60.5, 51.5, 35.0, 33.8, 14.2.

MS (EI, 70 eV) m/z (%): 262 (11), 231 (18), 230 (19), 217 (13), 216 (15), 189 (16), 188 (42), 157 (30), 149 (100), 129 (21), 128 (11), 121 (26), 90 (11), 57 (12).

HRMS (EI) for $\text{C}_{15}\text{H}_{18}\text{O}_4$: calculated: 262.1205, found 262.1199.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2953 (W), 1715 (VS), 1611 (W), 1436 (M), 1415 (W), 1370 (W), 1276 (VS), 1179 (S), 1109 (S), 1100 (S), 1020 (M), 961 (W), 852 (W), 818 (W), 765 (M), 705 (M).

3.6.22 3-((6-Chlorobenzo[d][1,3]dioxol-5-yl)methyl)cyclohexanone (22v)



The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 2 mL, 2 mmol) and 5-chloro-6-(chloromethyl)benzo[d][1,3]dioxole (**18r**, 411 mg, 2 mmol). The reaction was carried out at 25 °C for 8 h and provided the reagent **19r** which was transferred to a new argon flushed flask. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 2.1 mL, 2.1 mmol) was added dropwise at -30 °C, before a mixture of cyclohex-2-enone (**21t**, 134 mg, 1.4 mmol) and TMSCl (380 mg, 3.5 mmol) in 2 mL THF was added subsequently. The reaction mixture was stirred at -30 °C for 12 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted

with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **22v** as colorless solid (254 mg, 68%).

mp: 62-63 °C.

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 6.70 (s, 1H), 6.32 (s, 1H), 5.19 (s, 2H), 2.38-2.24 (m, 3H), 2.18-2.10 (m, 1H), 1.83-1.71 (m, 2H), 1.69-1.60 (m, 1H), 1.50-1.34 (m, 2H), 1.17-1.03 (m, 1H), 0.89-0.78 (m, 1H).

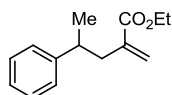
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 208.2, 147.1, 147.0, 130.6, 125.8, 110.6, 110.1, 101.5, 47.6, 41.2, 40.1, 39.6, 30.7, 25.0.

MS (EI, 70 eV) m/z (%): 268 (22), 267 (11), 266 (69), 208 (17), 170 (31), 169 (11), 168 (100).

HRMS (EI) for C₁₄H₁₅O₃Cl: calculated: 266.0710, found 266.0705.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2922 (W), 1699 (S), 1502 (S), 1479 (VS), 1414 (M), 1235 (S), 1118 (S), 1039 (VS), 980 (M), 939 (S), 879 (S), 867 (M), 834 (M), 691 (W).

3.6.23 Ethyl 2-methylene-4-phenylpentanoate (**22w**)



The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol), ZnCl₂ (1 M in THF, 2 mL, 2 mmol) and (1-chloroethyl)benzene (**18s**, 281 mg, 2 mmol). The reaction was carried out at 25 °C for 22 h and provided the reagent **19s** which was transferred to a new argon flushed flask. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21i**, 270 mg, 1.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 20:1) afforded **22w** as colorless oil (232 mg, 76%).

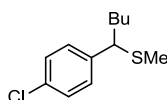
¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.37-7.19 (m, 5H), 6.14 (d, J = 1.4 Hz, 1H), 5.42-5.40 (m, 1H), 4.24 (q, J = 7.2 Hz, 2H), 3.10-2.97 (m, 1H), 2.72-2.53 (m, 2H), 1.38-1.28 (m, 6H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 167.2, 146.6, 139.2, 128.3, 127.0, 126.3, 126.0, 60.6, 40.9, 38.8, 21.3, 14.2.

MS (EI, 70 eV) m/z (%): 105 (100), 77 (12), 44 (21), 43 (10).

HRMS (EI) for C₁₄H₁₈O₂: calculated: 218.1307, found 218.1305.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3028 (VW), 2963 (W), 1713 (S), 1629 (W), 1603 (W), 1494 (W), 1452 (M), 1407 (W), 1369 (W), 1324 (W), 1302 (M), 1267 (W), 1255 (W), 1225 (M), 1195 (S), 1172 (M), 1147 (S), 1112 (W), 1094 (M), 1062 (W), 1026 (M), 1017 (M), 1000 (W), 944 (M), 908 (W), 871 (VW), 856 (W), 818 (W), 762 (M), 699 (VS).

3.6.24 (1-(4-Chlorophenyl)pentyl)(methyl)sulfane (**22x**)

The general procedure **TP9** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 2 mL, 2 mmol) and 1-chloro-4-(1-chloropentyl)benzene (**18t**, 434 mg, 2 mmol). The reaction was carried out at 25 °C for 22 h and provided the reagent **19t** which was transferred to a new argon flushed flask. *S*-Methyl benzenesulfonothioate (**21u**, 177 mg, 1.4 mmol) was added subsequently at 0 °C. The resulting suspension was stirred at 0 °C for 3 h and slowly warmed to 50 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane) afforded **22x** as colorless oil (208 mg, 65%).

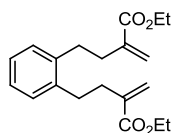
$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ /ppm: 7.30-7.19 (m, 4H), 3.61 (dd, $J = 8.7$ Hz, 6.4 Hz, 1H), 1.93-1.70 (m, 2H), 1.84 (s, 3H), 1.38-1.13 (m, 4H), 0.89-0.81 (m, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ /ppm: 141.2, 132.4, 129.1, 128.5, 50.8, 35.8, 29.8, 22.4, 14.3, 13.8.

MS (EI, 70 eV) m/z (%): 228 (16), 183 (10), 181 (39), 171 (11), 139 (11), 127 (36), 125 (100), 99 (10), 85 (21), 71 (50), 57 (36), 43 (10).

HRMS (EI) for $\text{C}_{12}\text{H}_{17}\text{SCl}$: calculated: 228.0739, found 228.0747.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2957 (M), 2929 (S), 2858 (M), 1490 (S), 1379 (W), 1190 (W), 1107 (M), 1091 (VS), 1014 (S), 958 (W), 936 (W), 836 (S), 827 (S), 815 (S), 758 (S).

3.6.25 Diethyl 4,4'-(1,2-phenylene)bis(2-methylenebutanoate) (**25a**)

The general procedure **TP10** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 4 mL, 4 mmol) and 1,2-bis(chloromethyl)benzene (**23**, 350 mg, 2 mmol). The reaction was carried out at 25 °C for 1.5 h and provided the reagent **24a** which was transferred to a new argon flushed flask. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21i**, 540 mg, 2.8 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 5 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **25a** as colorless oil (342 mg, 74%).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ /ppm: 7.13-7.05 (m, 4H), 6.20 (d, $J = 1.5$ Hz, 2H), 5.31 (q, 2H), 4.00 (q, $J = 7.1$ Hz, 4H), 2.89-2.83 (m, 4H), 2.66-2.60 (m, 4H), 0.96 (t, $J = 7.1$ Hz, 6H).

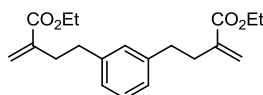
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 166.3, 140.5, 139.3, 129.4, 126.3, 124.5, 60.2, 34.1, 32.0, 13.8.

MS (EI, 70 eV) m/z (%): 285 (17), 256 (31), 238 (14), 210 (11), 183 (16), 182 (18), 171 (15), 145 (13), 144 (22), 143 (100), 142 (12), 141 (15), 129 (37), 128 (30), 115 (12), 104 (10), 91 (13), 57 (13).

HRMS (EI) for C₂₀H₂₆O₄: calculated: 330.1831, found 330.1838.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2981 (W), 2934 (W), 1711 (VS), 1630 (W), 1490 (W), 1464 (W), 1446 (W), 1409 (W), 1368 (W), 1323 (M), 1303 (M), 1270 (W), 1251 (M), 1239 (M), 1180 (VS), 1136 (S), 1093 (M), 1027 (M), 943 (M), 860 (W), 817 (M), 752 (M), 681 (W).

3.6.26 Diethyl 4,4'-(1,3-phenylene)bis(2-methylenebutanoate) (**25b**)



The general procedure **TP10** was followed using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol), ZnCl₂ (1 M in THF, 4 mL, 4 mmol) and 1,3-bis(chloromethyl)benzene (**23**, 350 mg, 2 mmol). The reaction was carried out at 25 °C for 1.5 h and provided the reagent **24a** which was transferred to a new argon flushed flask. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21i**, 540 mg, 2.8 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 5 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (pentane/diethyl ether = 10:1) afforded **25b** as colorless oil (319 mg, 69%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.11 (t, J = 7.5 Hz, 1H), 6.99 (s, 1H), 6.95 (dd, J = 7.3 Hz, 1.7 Hz, 2H), 6.17 (d, J = 1.5 Hz, 2H), 5.21 (q, J = 1.3 Hz, 2H), 4.00 (q, J = 7.1 Hz, 4H), 2.75-2.71 (m, 4H), 2.65-2.61 (m, 4H), 0.97 (t, J = 7.1 Hz, 6H).

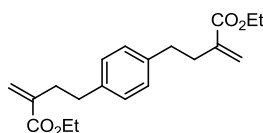
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 166.3, 141.5, 140.4, 128.7, 128.3, 126.1, 124.3, 60.1, 34.9, 34.1, 13.8.

MS (EI, 70 eV) m/z (%): 284 (26), 256 (26), 239 (53), 238 (44), 217 (17), 211 (24), 210 (40), 193 (20), 183 (32), 182 (15), 173 (72), 171 (54), 170 (32), 157 (33), 155 (19), 145 (70), 144 (16), 143 (100), 142 (21), 141 (28), 141 (28), 130 (17), 129 (42), 128 (56), 127 (11), 117 (17), 115 (21), 105 (48), 104 (31), 103 (21), 91 (19), 85 (12), 78 (16), 71 (16), 69 (11), 57 (25), 55 (13), 42 (21), 41 (15).

HRMS (EI) for C₂₀H₂₆O₄: calculated: 330.1831, found 330.1820.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2981 (W), 2931 (W), 1711 (VS), 1630 (W), 1445 (W), 1408 (W), 1369 (W), 1302 (M), 1270 (W), 1251 (M), 1182 (VS), 1136 (S), 1092 (M), 1028 (M), 942 (M), 860 (W), 817 (M), 791 (M), 703 (W).

3.6.27 Diethyl 4,4'-(1,4-phenylene)bis(2-methylenebutanoate) (**25c**)



The general procedure **TP10** was followed using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol), ZnCl_2 (1 M in THF, 4 mL, 4 mmol) and 1,4-bis(chloromethyl)benzene (**23**, 350 mg, 2 mmol). The reaction was carried out at 25 °C for 1.5 h and provided the reagent **24a** which was transferred to a new argon flushed flask. $\text{CuCN}\cdot 2\text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**21l**, 540 mg, 2.8 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 5 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). The aqueous layer was extracted with diethyl ether. The combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **25c** as colorless oil (341 mg, 74%).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ /ppm: 7.12 (s, 4H), 6.26 (d, $J = 1.4$ Hz, 2H), 5.28 (q, $J = 1.3$ Hz, 2H), 4.09 (q, $J = 7.1$ Hz, 4H), 2.86-2.78 (m, 4H), 2.75-2.66 (m, 4H), 1.05 (t, $J = 7.2$ Hz, 6H).

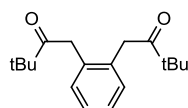
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ /ppm: 166.4, 140.5, 139.1, 128.6, 128.3, 124.4, 60.2, 34.7, 34.2, 13.9.

MS (EI, 70 eV) m/z (%): 284 (25), 239 (22), 238 (15), 217 (45), 210 (29), 171 (87), 143 (20), 129 (11), 128 (17), 117 (60), 107 (36), 105 (13), 104 (17), 91 (11), 85 (13), 71 (15), 70 (14), 61 (16), 57 (24), 55 (14), 45 (26), 44 (20), 43 (100), 41 (15).

HRMS (EI) for $\text{C}_{20}\text{H}_{26}\text{O}_4$: calculated: 330.1831, found 330.1816.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2982 (W), 2931 (W), 2865 (VW), 1712 (VS), 1631 (M), 1514 (W), 1477 (W), 1445 (W), 1409 (W), 1369 (W), 1303 (M), 1273 (M), 1251 (M), 1240 (M), 1180 (VS), 1131 (S), 1101 (M), 1028 (M), 942 (M), 862 (W), 816 (M), 680 (W).

3.6.28 1,1'-(1,2-phenylene)bis(3,3-dimethylbutan-2-one) (**25d**)



LiCl (254 mg, 6 mmol) was placed in an argon flushed *Schlenk*-flask and dried 5 – 10 min by heating with a heat gun (450 °C) under high vacuum. InCl_3 (13 mg, 0.06 mmol) was added and the drying process repeated for 5 min. Magnesium turnings (146 mg, 6 mmol) were added under argon and the drying process was again repeated for 5 min. The flask was evacuated and backfilled with argon three times before ZnCl_2 -solution (4.4 mL, 1M in THF, 4.4 mmol) was added, along with the internal standard (heptadecane). TMSCl (3 mol%) was added and the reaction mixture heated with a heat gun until ebullition occurred. When the reaction mixture had been cooled down to room temperature (20 °C) 1,2-bis(chloromethyl)benzene (**23**, 350 mg, 2 mmol) was added in one portion and the reaction mixture stirred at 20 °C for 15 min. The progress of the insertion reaction was monitored by GC analysis of hydrolysed reaction aliquots quenched with HCl (2 M)¹⁸⁸ until a conversion of >95% was reached. The magnesium turnings were allowed to settle down and the remaining solution was transferred to a new argon flushed flask. When the solution had been cooled down to -50 °C, $\text{CuCN}\cdot 2\text{LiCl}$ (0.6 mL, 1M in THF, 0.6 mmol) was added followed by pivaloyl chloride (531 mg, 4.4 mmol). The reaction mixture was allowed to warm to room temperature (20 °C) over night. The reaction was quenched with HCl (2 M, 5 mL) and extracted

three times with ethyl acetate. Flash column chromatographical purification (pentane/diethyl ether = 20:1) afforded **25d** as white solid (228 mg, 83%).

mp: 145-147 °C.

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.21-7.16 (m, 2H), 7.04 (dd, $J = 5.6$ Hz, 3.5 Hz, 2H), 3.80 (s, 4H), 1.21 (s, 18H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 213.1, 134.5, 130.7, 127.0, 44.5, 41.5, 26.6.

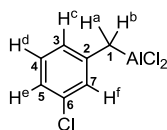
MS (EI, 70 eV) m/z (%): 274 (53) [M⁺], 104 (10), 85 (27), 57 (100).

HRMS (EI) for C₁₈H₂₆O₂: calculated: 274.1933 [M⁺], found: 274.1929.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3063 (VW), 3031 (VW), 2956 (M), 2905 (W), 2869 (W), 2363 (VW), 1950 (VW), 1701 (VS), 1662 (W), 1605 (VW), 1498 (W), 1478 (M), 1469 (M), 1456 (M), 1417 (W), 1405 (M), 1395 (W), 1365 (M), 1358 (M), 1329 (M), 1300 (W), 1229 (W), 1218 (W), 1207 (W), 1173 (VW), 1156 (VW), 1095 (VW), 1061 (VS), 1008 (M), 950 (W), 935 (W), 908 (VW), 857 (W), 844 (VW), 824 (VW), 784 (VW), 752 (M), 735 (S), 710 (W), 668 (VW).

3.7 ¹H-, ¹³C-, ²⁷Al-NMR Spectroscopy Experiments

3.7.1 Analytical data of 3-chlorobenzylaluminium dichloride (**19a**)



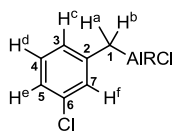
The aluminium reagent was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 3-chlorobenzyl chloride (**1a**, 322 mg, 2 mmol). The solution containing the aluminium reagent was separated from the remaining Al-powder and transferred to a new flask. The solvent was removed under high vacuum. The remaining residue was resuspended in C₆D₆ and the solution filtered through a syringe filter. NMR spectra were recorded from the filtrated solution. The chemical shifts could be completely assigned using 2D-NMR experiments and are given separately for R₂AlCl and RAlCl₂. Protons are labelled with letters (a-f) and carbon atoms with numerals (1-7). The chemical shifts have been estimated from the measured cross-peaks in COSY, HMQC and HMBC experiments.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.06 (H^f), 6.90 (H^e), 6.887 (H^c), 6.87 (H^d), 1.81 (H^a, H^b).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 145.5 (C2), 134.1 (C6), 129.7 (C5), 127.2 (C7), 125.8 (C3), 122.9 (C4), 21.3 (C1).

²⁷Al-NMR (376 MHz, C₆D₆) δ /ppm: 126.4.

3.7.2 Analytical data of bis-(3-chlorobenzyl)aluminium chloride (19a)



The aluminium reagent was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 3-chlorobenzyl chloride (**1a**, 322 mg, 2 mmol). The solution containing the aluminium reagent was separated from the remaining Al-powder and transferred to a new flask. The solvent was removed under high vacuum. The remaining residue was resuspended in C_6D_6 and the solution filtered through a syringe filter. NMR spectra were recorded from the filtrated solution. The chemical shifts could be completely assigned using 2D-NMR experiments and are given separately for R_2AlCl and RAlCl_2 . Protons are labelled with letters (a-f) and carbon atoms with numerals (1-7). The chemical shifts have been estimated from the measured cross-peaks in COSY, HMQC and HMBC experiments.

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ/ppm : 7.02 (H^f), 6.83 (H^e), 6.884 (H^c), 6.89 (H^d), 1.66 (H^a , H^b).

$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ/ppm : 147.1 (C2), 134.2 (C6), 129.6 (C5), 127.0 (C7), 125.6 (C3), 122.4 (C4), 21.1 (C1).

$^{27}\text{Al-NMR}$ (376 MHz, C_6D_6) δ/ppm : 56.5.

3.7.3 Analytical data of 3-chlorobenzylzinc chloride (19a')



The zinc reagent was prepared according to the known literature procedure.¹⁹⁰ The remaining solution was separated from the Zn-powder and the solvent removed completely under high vacuum. The remaining oil was dissolved in C_6D_6 and the resulting suspension filtrated through a syringe filter. NMR spectra were obtained from the filtrated solution. The chemical shifts could be completely assigned using 2D-NMR experiments. Protons are labelled with letters (a-f) and carbon atoms with numerals (1-7). The chemical shifts have been estimated from the measured cross-peaks in COSY, HMQC and HMBC experiments.

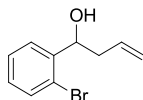
$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ/ppm : 7.30 (H^f), 7.07 (H^e), 6.87 (H^d), 6.82 (H^c), 2.15 (H^a , H^b).

$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ/ppm : 152.74 (C2), 133.7 (C6), 129.2 (C4), 126.3 (C7), 124.9 (C3), 120.47 (C5), 20.9 (C1).

¹⁹⁰ Metzger, A.; Schade, M. A.; Knochel, P. *Org. Lett.* **2008**, *10*, 1107.

3.8 Preparation of Homoallylic Alcohols

3.8.1 1-(2-Bromophenyl)but-3-en-1-ol (**29a**)



The aluminium reagent **27a** was prepared according to **TP11** from allyl bromide (**26a**, 242 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 2-bromobenzaldehyde (**28a**, 259 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 30:1) afforded **29a** as yellow oil (282 mg, 87%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.57 (dd, $J = 7.7$ Hz, $J = 1.4$ Hz, 1H), 7.53 (dd, $J = 8.0$ Hz, $J = 1.4$ Hz, 1H), 7.38-7.32 (m, 1H), 7.17-7.11 (m, 1H), 5.96-5.83 (m, 1H), 5.25-5.16 (m, 1H), 5.12 (dd, $J_{trans} = 8.3$ Hz, $J_{cis} = 3.9$ Hz, 1H), 2.70-2.61 (m, 1H), 2.43-2.31 (m, 2H), 2.19 (s, br, 1H).

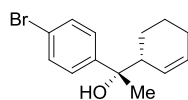
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 142.7, 134.2, 132.6, 128.8, 127.6, 127.3, 121.8, 118.7, 71.8, 42.1.

MS (EI, 70 eV) m/z (%): 226 (0.28) [M⁺], 187 (98), 185 (100), 159 (14), 157 (15), 78 (18), 77 (48).

HRMS (EI) for C₁₀H₁₁BrO: calculated: 225.9993, found 225.9991.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3373 (W), 3073 (W), 2979 (VW), 2910 (VW), 1735 (VW), 1640 (W), 1568 (W), 1467 (M), 1432 (M), 1352 (W), 1311 (W), 1216 (W), 1195 (W), 1126 (W), 1108 (W), 1044 (M), 1021 (S), 1001 (M), 986 (M), 945 (W), 915 (S), 872 (W), 827 (VW), 752 (VS), 723 (W), 681 (W), 666 (W).

3.8.2 1-(4-Bromophenyl)-1-(cyclohex-2-en-1-yl)ethanol (**29b**)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 4'-bromoacetophenone (**28b**, 279 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 1 h and then slowly warmed to 20 °C before being quenched with sat. aqueous NH₄Cl solution (7 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **29b** as colorless liquid (376 mg, 96%, dr > 99:1).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.44 (d, $J = 8.8$ Hz, 2H), 7.29 (d, $J = 8.8$ Hz, 2H), 5.98-5.89 (m, 1H), 5.76 (d, $J = 10.5$ Hz, 1H), 2.55-2.46 (m, 1H), 1.98-1.89 (m, 2H), 1.81 (s, 1H), 1.75-1.65 (m, 1H), 1.56 (s, 3H), 1.48 – 1.14 (m, 3H).

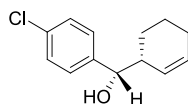
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 146.2, 132.2, 130.9, 127.2, 125.9, 120.3, 75.8, 46.4, 28.0, 25.1, 24.3, 21.8.

MS (EI, 70 eV) m/z (%): 281 (0.02) [M+H⁺], 201 (78), 200 (61), 199 (55), 198 (100), 43 (16).

HRMS (EI) for $C_{14}H_{17}BrO$: calculated: 281.0541 $[M+H^+]$, found 281.0515.

Spectral data matching those reported in the literature.^[191]

3.8.3 (4-Chlorophenyl)(cyclohex-2-en-1-yl)methanol (**29c**)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and $InCl_3$ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 4-chlorobenzaldehyde (**28c**, 197 mg, 1.4 mmol). The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **29c** as yellow oil (282 mg, 87%, dr > 99:1).

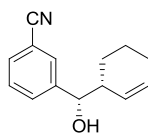
1H -NMR (300 MHz, $CDCl_3$) δ /ppm: 7.35-7.25 (m, 4H), 5.89-5.81 (m, 1H), 5.43-5.36 (m, 1H), 4.59 (d, $J = 6.4$ Hz, 1H), 2.53-2.42 (m, 1H), 2.03-1.96 (m, 2H), 1.94 (s, br, 1H), 1.81-1.60 (m, 2H), 1.57-1.46 (m, 2H).

^{13}C -NMR (75 MHz, $CDCl_3$) δ /ppm: 141.2, 133.0, 130.9, 128.3, 127.8, 127.6, 76.6, 43.0, 25.2, 23.6, 21.0.

MS (EI, 70 eV) m/z (%): 143 (35), 142 (10), 141 (100) $[M-H_2O]$, 115 (7), 113 (18), 81 (8), 79 (10), 77 (50), 67 (7), 51 (8).

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/cm^{-1}$: 3371 (W), 3023 (W), 2927 (M), 2861 (M), 2837 (W), 1490 (S), 1448 (M), 1432 (W), 1409 (M), 1344 (W), 1308 (W), 1265 (W), 1233 (W), 1218 (W), 1088 (VS), 1050 (M), 1024 (M), 1012 (VS), 960 (W), 932 (W), 885 (W), 836 (S), 814 (VS), 792 (W), 746 (W), 724 (S), 701 (W), 685 (M), 672 (S).

3.8.4 3-(Cyclohex-2-en-1-yl)(hydroxymethyl)benzonitrile (**29d**)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and $InCl_3$ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 3-formylbenzonitrile (**28d**, 184 mg, 1.4 mmol). The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 3:1) afforded **29d** as colorless oil (293 mg, 98%, dr > 99:1).

1H -NMR (300 MHz, $CDCl_3$) δ /ppm: 7.67-7.42 (m, 4H), 5.94-5.87 (m, 1H), 5.45-5.39 (m, 1H), 4.69 (d, $J = 5.5$ Hz, 1H), 2.55-2.44 (m, 1H), 2.09 (s, 1H), 2.04-1.95 (m, 2H), 1.81-1.69 (m, 1H), 1.61-1.44 (m, 3H).

¹⁹¹ M. Yasuda, K. Hirata, M. Nishino, A. Yamamoto, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 13442.

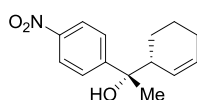
¹³C-NMR (75 MHz, CDCl₃) δ/ppm: 144.2, 131.7, 130.9, 130.8, 130.1, 128.9, 127.0, 118.9, 112.2, 76.0, 43.0, 25.1, 23.1, 21.0.

MS (EI, 70 eV) *m/z* (%): 213 (2) [M⁺], 133 (31), 132 (100), 130 (11), 104 (25), 82 (58), 81 (90), 79 (23), 77 (19), 53 (11), 43 (15), 41 (10).

HRMS (EI) for C₁₄H₁₅NO: calculated: 213.1154, found 213.1144.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3432 (M), 3022 (W), 2928 (S), 2861 (M), 2838 (M), 2230 (S), 1715 (M), 1685 (W), 1653 (W), 1481 (M), 1448 (M), 1433 (M), 1395 (M), 1344 (W), 1304 (M), 1261 (M), 1232 (M), 1218 (M), 1145 (M), 1139 (M), 1104 (W), 1087 (M), 1071 (M), 1050 (M), 1027 (S), 1001 (M), 988 (W), 962 (W), 921 (W), 903 (M), 882 (M), 802 (VS), 747 (M), 721 (VS), 697 (VS), 674 (M)

3.8.5 1-Cyclohex-2-enyl-1-(4-nitrophenyl)-ethanol (29e)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 1-(4-nitrophenyl)ethanone (**28e**, 231 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether =9:1) afforded **29e** as yellow oil (329 mg, 95%, dr > 99:1).

¹H-NMR (300 MHz, C₆D₆) δ/ppm: 7.85-7.80 (m, 2H), 7.07-7.02 (m, 2H), 5.75-5.68 (m, 1H), 5.54-5.48 (m, 1H), 2.17-2.08 (m, 1H), 1.76-1.60 (m, 1H), 1.50-1.42 (m, 1H), 1.26 (s, 1H), 1.24-1.15 (m, 1H), 1.12 (s, 3H), 1.09-1.04 (m, 2H).

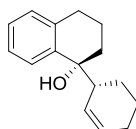
¹³C-NMR (75 MHz, C₆D₆) δ/ppm: 154.0, 146.5, 131.8, 125.9, 125.4, 122.7, 75.2, 46.0, 27.5, 24.9, 24.0, 21.6.

MS (EI, 70 eV) *m/z* (%): 248 (1) [M⁺], 167 (32), 166 (100), 150 (10), 120 (7), 43 (15).

HRMS (EI) for C₁₄H₁₇NO₃: calculated: 248.1287 [M+H⁺], found 248.1276.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3548 (W), 3028 (VW), 2974 (W), 2932 (W), 2860 (W), 2838 (W), 1600 (M), 1512 (VS), 1492 (M), 1448 (W), 1434 (W), 1408 (W), 1374(W), 1342 (VS), 1264 (W), 1232 (W), 1182 (W), 1142 (W), 1102 (M), 1078 (M), 1064 (M), 1046 (W), 1014 (W), 942 (W), 926 (VW), 906 (W), 894 (W), 880 (M), 852 (S), 770 (W), 756 (W), 740 (W), 724 (M), 704 (S), 678 (W).

3.8.6 1-(Cyclohex-2-en-1-yl)-1,2,3,4-tetrahydronaphthalen-1-ol (29g)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 3,4-dihydronaphthalen-1(2H)-one (**28g**, 205 mg, 1.4 mmol). The reaction

mixture was stirred at -78 °C for 1.5 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 5:1) afforded **29g** as colorless oil (261 mg, 82%, dr > 74:26).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.5 (dd, $J = 7.8$ Hz, $J = 1.6$ Hz, 1H), 7.13-7.08 (m, 1H), 7.06 (td, $J = 7.2$ Hz, $J = 1.6$ Hz, 1H), 6.97-6.92 (m, 1H), 5.59-5.53 (m, 1H), 5.17-5.12 (m, 1H), 2.96-2.87 (m, 1H), 2.54-2.36 (m, 2H), 2.18-2.08 (m, 1H), 1.90-1.47 (m, 9H), 1.40 (s, 1H).

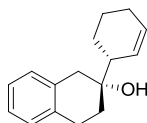
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 142.5, 138.4, 129.4, 129.3, 127.5, 127.4, 127.2, 127.1, 74.2, 47.5, 33.8, 31.1, 26.1, 24.2, 23.2, 20.0.

MS (EI, 70 eV) m/z (%): 210 (73) [M⁺-H₂O], 181 (56), 169 (40), 167 (100), 165 (94), 152 (52), 141 (67), 130 (76), 129 (96), 128 (71), 115 (56), 44 (85).

HRMS (EI) for C₁₆H₂₀O: calculated: 210.1409 [M⁺-H₂O], found 210.1369.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3414 (W), 3019 (W), 2928 (M), 2863 (M), 2835 (M), 1487 (W), 1448 (M), 1443 (M), 1393 (W), 1367 (W), 1340 (W), 1306 (W), 1277 (W), 1179 (W), 1157 (M), 1140 (W), 1082 (M), 1055 (W), 1005 (W), 978 (M), 962 (M), 942 (M), 930 (M), 917 (W), 902 (W), 880 (W), 858 (W), 841 (W), 788 (W), 762 (S), 735 (VS), 720 (S), 670 (W).

3.8.7 2-(Cyclohex-2-en-1-yl)-1,2,3,4-tetrahydronaphthalen-2-ol (**29h**)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 3,4-dihydronaphthalen-2(1*H*)-one (**28h**, 205 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 5:1) afforded **29h** as red solid (307 mg, 96%, dr > 58:42).

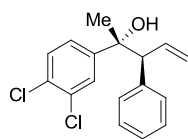
mp: 46-49 °C.

¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 136.7, 135.5, 135.5, 130.5, 130.4, 130.4, 130.1, 129.2, 128.0, 127.9, 126.5, 126.4, 126.4, 72.7, 46.2, 46.1, 40.3, 38.7, 32.6, 31.4, 26.6, 26.5, 25.9, 25.9, 24.5, 24.3, 23.0, 23.0. Due to the ratio of nearly 1:1, no allocation was possible.

MS (EI, 70 eV) m/z (%): 210 (40) [M⁺-H₂O], 181 (22), 167 (27), 147 (77), 146 (20), 129 (100), 128 (48), 117 (32), 115 (28), 104 (32), 91 (21), 77 (25).

HRMS (EI) for C₁₆H₂₀O: calculated: 210.1409 [M⁺-H₂O], found 210.1370.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3354 (M), 3059 (W), 3022 (W), 2924 (S), 2856 (M), 2836 (M), 1737 (W), 1718 (W), 1494 (W), 1452 (M), 1432 (M), 1418 (M), 1346 (M), 1317 (W), 1306 (M), 1278 (M), 1248 (M), 1228 (M), 1176 (M), 1156 (W), 1114 (M), 1092 (S), 1066 (M), 1039 (W), 1002 (W), 960 (S), 943 (M), 931 (M), 896 (W), 885 (M), 869 (W), 858 (W), 840 (W), 825 (W), 772 (M), 744 (VS), 731 (VS), 720 (VS), 692 (M)

3.8.8 2-(3,4-Dichlorophenyl)-3-phenylpent-4-en-2-ol (**29i**)

The aluminium reagent **27c** was prepared according to **TP12** from (*E*)-1-(3-chloroprop-1-enyl)benzene (**26c**, 305 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 1-(3,4-dichlorophenyl)ethanone (**28i**, 265 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 1.5 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 30:1) afforded **29i** as yellow oil (395 mg, 92%, dr > 92:8).

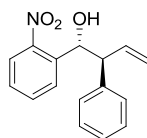
¹H-NMR (300 MHz, CDCl₃) δ/ppm: 7.50-7.47 (m, 1H), 7.38-7.27 (m, 4H), 7.17-7.12 (m, 3H), 6.19-6.07 (m, 1H), 5.13-4.94 (m, 2H), 3.57 (d, *J* = 8.8 Hz, 1H), 2.04 (s, 1H), 1.43 (s, 3H).

¹³C-NMR (75 MHz, CDCl₃) δ/ppm: 146.8, 139.5, 136.6, 131.9, 130.5, 129.6, 129.4, 128.3, 127.9, 127.1, 125.2, 118.7, 75.8, 61.7, 28.3.

MS (ESI) *m/z* (%): 367 (12), 365 (28), 353 (36), 351 (62), 343 (86), 341 (100) [M+Cl], 338 (8), 283 (4).

HRMS (ESI) for C₁₇H₁₆Cl₂O: calculated: 341.0272 [M+Cl], found 341.0274.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3550 (W), 3470 (W), 3064 (W), 3028 (W), 2977 (W), 1636 (W), 1558 (W), 1492 (W), 1471 (M), 1453 (M), 1418 (W), 1382 (M), 1345 (W), 1332 (W), 1277 (W), 1260 (W), 1199 (W), 1184 (W), 1134 (M), 1073 (M), 1028 (S), 996 (M), 969 (W), 922 (S), 896 (M), 818 (S), 759 (M), 716 (VS), 700 (VS), 675 (S).

3.8.9 1-(2-nitrophenyl)-2-phenylbut-3-en-1-ol (**29j**)

The aluminium reagent **27c** was prepared according to **TP12** from (*E*)-1-(3-chloroprop-1-enyl)benzene (**26c**, 305 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 2-nitrobenzaldehyde (**28j**, 265 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 2 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 5:1) afforded **29j** as red liquid (370 mg, 98%, dr > 92:8).

¹H-NMR (300 MHz, CDCl₃) δ/ppm: 7.85-7.73 (m, 2H), 7.61-7.56 (m, 1H), 7.40-7.19 (m, 6H), 6.38-6.25 (m, 1H), 5.64 (d, *J* = 5.5 Hz, 1H), 5.22-4.99 (m, 2H), 3.75 (d, *J* = 9.2 Hz, *J* = 5.5 Hz, 1H), 2.40 (s, br, 1H).

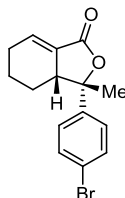
¹³C-NMR (75 MHz, CDCl₃) δ/ppm: 148.0, 140.8, 137.4, 135.7, 135.7, 132.7, 129.4, 128.7, 128.1, 126.9, 124.2, 119.0, 72.6, 56.7.

MS (ESI) *m/z* (%): 785 (14), 553 (21), 481 (42), 409 (38), 393 (13), 286 (50), 268 (100) [M-H], 252 (36).

HRMS (ESI) for C₁₆H₁₅NO₃: calculated: 268.0979 [M-H], found 268.0968.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3546 (W), 3442 (W), 3065 (VW), 3030 (VW), 1637 (VW), 1608 (W), 1601 (W), 1577 (W), 1558 (VW), 1520 (VS), 1496 (M), 1452 (W), 1419 (W), 1342 (S), 1300 (M), 1183 (W), 1164 (W), 1084 (W), 1058 (M), 1039 (M), 1000 (W), 975 (W), 921 (M), 857 (M), 787 (M), 758 (M), 748 (W), 717 (S), 700 (VS), 686 (M).

3.8.10 3-(4-Bromophenyl)-3-methyl-3a,4,5,6-tetrahydro-3H-isobenzofuran-1-one (29k).



The aluminium reagent **27d** was prepared according to **TP12** from ethyl 6-chlorocyclohex-1-enecarboxylate (**26d**, 378 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl_3 (5 mg, 0.02 mmol) in 16 h. The addition reaction was carried out according to **TP13** using 4'-bromoacetophenone (**28b**, 279 mg, 1.4 mmol). The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 3 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 3:1) afforded **29k** as colorless oil (328 mg, 76%, dr > 99:1).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ/ppm : 7.44 (d, $J = 8.8$ Hz, 2H), 7.00 (d, $J = 8.8$ Hz, 2H), 6.83 (q, $J = 3.3$ Hz, 1H), 2.96-2.85 (m, 1H), 2.32-2.17 (m, 1H), 2.08-1.88 (m, 1H), 1.86 (s, 3H), 1.85 -1.70 (m, 2H), 1.58 -1.39 (m, 1H), 0.51-0.34 (m, 1H).

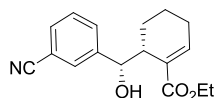
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ/ppm : 170.0, 140.2, 137.5, 131.4, 129.6, 126.9, 121.8, 87.5, 48.4, 27.8, 24.8, 24.5, 20.9.

MS (EI, 70 eV) m/z (%): 306 (2) [M^+], 108 (100), 80 (17), 79 (19).

HRMS (EI) for $\text{C}_{15}\text{H}_{15}\text{BrO}_2$: calculated: 306.0255 [M^+], found 306.0260.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2925 (W), 1755 (VS), 1239 (M), 1031 (S), 921 (M), 752 (M), 725 (W).

3.8.11 Ethyl 6-(3-cyanophenyl)(hydroxy)methyl)cyclohex-1-enecarboxylate (29l).



The aluminium reagent **27d** was prepared according to **TP12** from ethyl 6-chlorocyclohex-1-enecarboxylate (**26d**, 378 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl_3 (5 mg, 0.02 mmol) in 16 h. The addition reaction was carried out according to **TP13** using 3-formylbenzonitrile (**28d**, 184 mg, 1.4 mmol). The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 3 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 3:1) afforded **29l** as colorless oil (370 mg, 98%, dr > 95:5).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.57-7.56 (m, 1H), 7.35-7.32 (m, 1H), 7.04-6.97 (m, 2H), 6.77 (t, $J = 7.6$ Hz, 1H), 4.94 (d, $J = 3.9$ Hz, 1H), 3.99-3.87 (m, 2H), 2.86-2.81 (m, 1H), 1.88-1.55 (m, 5H), 1.19-0.94 (m, 5H).

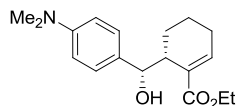
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 167.5, 145.9, 143.5, 131.4, 130.8, 130.7, 130.2, 129.1, 119.5, 113.0, 74.1, 60.7, 41.0, 26.1, 22.5, 19.4, 14.6.

MS (ESI) m/z (%): 475 (8), 344 (18), 330 (44), 320 (100) [M+Cl], 284 (6) [M-H].

HRMS (ESI) for C₁₇H₁₉NO₃: calculated: 320.1053 [M+Cl], found 320.1060.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3471 (W), 2937 (W), 2230 (W), 1696 (S), 1641 (W), 1479 (W), 1456 (W), 1447 (W), 1421 (W), 1375 (W), 1348 (W), 1240 (VS), 1172 (W), 1144 (W), 1096 (M), 1080 (M), 1054 (S), 1000 (W), 908 (W), 803 (M), 752 (M), 734 (M), 721 (W), 694 (M), 682 (W).

3.8.12 Ethyl 6-(4-(dimethylamino)phenyl)(hydroxy)methyl)cyclohex-1-enecarboxylate (29m)



The aluminium reagent **27d** was prepared according to **TP12** from ethyl 6-chlorocyclohex-1-enecarboxylate (**26d**, 378 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol) in 16 h. The addition reaction was carried out according to **TP13** using 4-(dimethylamino) benzaldehyde (**28k**, 209 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 3 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether = 3:1) afforded **29m** as orange oil (345 mg, 81%, dr > 94:6).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.47-7.43 (m, 2H), 7.10-7.07 (m, 1H), 6.67-6.64 (m, 2H), 5.20 (d, $J = 4.3$ Hz, 1H), 4.06-3.93 (m, 2H), 3.20-3.15 (m, 1H), 2.54 (s, 6H), 2.08-1.73 (m, 5H), 1.33-1.22 (m, 2H), 1.01 (t, $J = 7.2$ Hz, 3H).

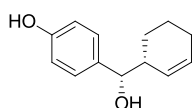
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 167.9, 150.5, 142.3, 132.8, 132.6, 127.7, 113.1, 75.3, 60.5, 41.6, 40.8, 26.3, 23.0, 19.6, 14.7.

MS (ESI) m/z (%): 630 (13), 629 (34), 607 (13), 367 (10), 326 (40), 304 (100) [M⁺+H], 286 (19).

HRMS (ESI) for C₁₈H₂₅NO₃: calculated: 304.1907 [M⁺+H], found 304.1906.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3494 (W), 2933 (W), 2870 (W), 2800 (W), 1700 (S), 1641 (W), 1614 (M), 1520 (S), 1477 (W), 1456 (W), 1445 (M), 1422 (W), 1344 (M), 1298 (W), 1235 (VS), 1183 (M), 1162 (M), 1142 (M), 1078 (M), 1054 (S), 967 (W), 946 (M), 910 (W), 887 (W), 816 (M), 752 (S), 724 (W), 702 (W).

3.8.13 4-(Cyclohex-2-en-1-yl)(hydroxy)methyl)phenol (29n)



The aluminium reagent **27b** was prepared according to **TP11** from 3-bromocyclohex-1-ene (**26b**, 322 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out

according to **TP13** using 4-hydroxybenzaldehyde (**28l**, 171 mg, 1.4 mmol). The reaction mixture was stirred at -78 °C for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether =1:1) afforded **29n** as colorless crystals (263 mg, 92%, dr > 99:1).

mp: 52-155 °C.

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 9.18 (s, 1H), 7.09-7.04 (m, 2H), 6.71-6.66 (m, 2H), 5.62-5.57 (m, 1H), 5.27-5.22 (m, 1H), 4.95 (s, br, 1H), 4.18 (d, $J = 7.4$ Hz, 1H), 2.29-2.21 (m, 1H), 1.92-1.85 (m, 2H), 1.75-1.62 (m, 2H), 1.46-1.37 (m, 2H).

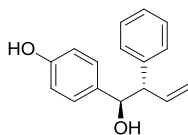
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 156.1, 134.8, 128.9, 127.8, 127.7, 114.5, 75.7, 42.8, 24.9, 24.8, 20.7.

MS (ESI) m/z (%): 425 (16), 408 (20), 407 (100), 249 (50), 239 (34), 203 (26) [M-H], 119 (10).

HRMS (ESI) for C₁₃H₁₆O₂: calculated: 203.1078 [M-H], found 203.1084.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3375 (M), 3132 (M), 3058 (M), 3021 (M), 2955 (M), 2906 (M), 2877 (M), 2834 (M), 1614 (W), 1600 (M), 1516 (M), 1468 (M), 1450 (M), 1398 (M), 1385 (M), 1306 (W), 1286 (W), 1250 (VS), 1244 (VS), 1202 (M), 1175 (M), 1080 (W), 1009 (M), 991 (S), 974 (M), 962 (M), 930 (M), 849 (M), 833 (S), 816 (VS), 790 (M), 752 (M), 724 (S), 695 (M), 672 (S).

3.8.14 4-(1-Hydroxy-2-phenylbut-3-en-1-yl)phenol (**29o**)



The aluminium reagent **27c** was prepared according to **TP12** from (*E*)-1-(3-chloroprop-1-enyl)benzene (**26c**, 305 mg, 2 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (5 mg, 0.02 mmol). The addition reaction was carried out according to **TP13** using 4-hydroxybenzaldehyde (**28l**, 147 mg, 1.2 mmol). The reaction mixture was stirred at -78 °C for 1 h. Flash column chromatographical purification on silica gel (pentane/diethyl ether =2:1) afforded **29o** as yellow oil (185 mg, 64%, dr > 76:24).

mp: 122-124 °C.

¹H-NMR (300 MHz, DMSO-*d*⁶) δ /ppm: 9.09 (s, 1H), 7.22-7.06 (m, 5H), 6.99-6.94 (m, 2H), 6.58-6.54 (m, 2H), 6.28-6.19 (m, 1H), 5.15 (d, $J = 4.7$ Hz, 1H), 5.03-4.99 (m, 1H), 4.89-4.83 (m, 1H), 4.70-4.67 (m, 1H), 3.50-3.45 (m, 1H).

¹³C-NMR (75 MHz, DMSO-*d*⁶) δ /ppm: 155.8, 142.3, 139.6, 134.7, 128.5, 127.8, 127.7, 125.8, 115.8, 114.2, 75.7, 57.8.

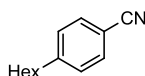
MS (ESI) m/z (%): 701 (11), 479 (12), 480 (43), 479 (100) [2M-H], 477 (18), 359 (20), 239 (31) [M-H], 237 (5).

HRMS (ESI) for C₁₆H₁₆O₂: calculated: 239.1078 [M-H], found 239.1079.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3367 (W), 3210 (W), 3028 (W), 2971 (W), 2360 (W), 1740 (M), 1615 (W), 1598 (W), 1580 (VW), 1514 (M), 1501 (W), 1451 (M), 1366 (M), 1216 (S), 1024 (M), 921 (W), 829 (S), 756 (M), 699 (VS), 672 (W).

3.9 PbCl₂ – Catalysed Aluminium Insertion into Alkyl Halides

3.9.1 4-Hexylbenzonitrile (36a)



The aluminium reagent **34a** was prepared according to **TP14** from 1-iodohexane (**33a**, 424 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 2 h. The cross-coupling reaction was carried out according to **TP15** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of 4-bromobenzonitrile (**35a**, 255 mg, 1.4 mmol), Pd(OAc)₂ (10 mg, 0.044 mmol) and S-Phos (33 mg, 0.080 mmol) in THF (3 mL). The reaction mixture was stirred at 20 °C for 15 min and quenched with HCl (5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 60:1) afforded **36a** as yellow oil (187 mg, 71%).

¹H-NMR (300 MHz, CDCl₃) δ/ppm: 7.63-7.54 (m, 2H), 7.34-7.24 (m, 2H), 2.69-2.64 (m, 4H), 1.68-1.57 (m, 6H), 0.92-0.85 (m, 3H).

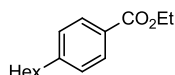
¹³C-NMR (75 MHz, CDCl₃) δ/ppm: 148.6, 132.1, 129.1, 119.2, 109.5, 36.1, 31.6, 30.9, 28.8, 22.5, 14.0.

MS (EI, 70 eV) *m/z* (%): 188 (4) [M+H], 187 (26) [M⁺], 118 (9), 117 (100), 116 (27), 89 (7), 43 (23), 41 (7).

HRMS (EI) for C₁₃H₁₇N: calculated: 187.1361, found 187.1353.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2955 (M), 2927 (VS), 2857 (S), 2227 (S), 1608 (M), 1504 (M), 1466 (M), 1458 (M), 1414 (W), 1378 (W), 1177 (W), 843 (S), 834 (S), 820 (VS), 725 (W).

3.9.2 Ethyl 4-hexylbenzoate (36b)



The aluminium reagent **34c** was prepared according to **TP14** from 1-bromohexane (**33c**, 330 mg, 2 mmol), LiBr (521 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 48 h. The cross-coupling reaction was carried out according to **TP15** using Zn(OAc)₂ (556 mg, 3 mmol) and a solution of ethyl 4-iodobenzoate (**35b**, 255 mg, 1.4 mmol), Pd(OAc)₂ (10 mg, 0.044 mmol) and S-Phos (33 mg, 0.080 mmol) in THF (3 mL). The reaction mixture was stirred at 20 °C for 15 min and quenched with HCl (5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 60:1) afforded **36a** as colorless liquid (187 mg, 88%).

¹H-NMR (300 MHz, C₆D₆) δ/ppm: 7.97-7.91 (m, 2H), 7.24-7.21 (m, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 2.68-2.61 (m, 2H), 1.67-1.55 (m, 2H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.34-1.24 (m, 6H), 0.91-0.84 (m, 3H).

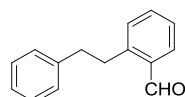
¹³C-NMR (75 MHz, C₆D₆) δ/ppm: 166.7, 148.4, 137.7, 131.0, 129.6, 128.4, 127.9, 60.7, 36.0, 31.7, 31.1, 28.9, 22.6, 14.4, 14.

MS (EI, 70 eV) m/z (%): 234 (22), 207 (13), 189 (55), 164 (13), 163 (25), 136 (21), 134 (15), 127 (12), 113 (13), 111 (13), 106 (13), 99 (21), 97 (22), 91 (11), 90 (53), 85 (51), 83 (22), 71 (76), 70 (17), 68 (25), 57 (100), 56 (25), 55 (41), 43 (80), 42 (46).

HRMS (EI) for $C_{15}H_{22}O_2$: calculated: 234.1620 $[M^+]$, found: 234.1617.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/cm^{-1}$: 2956 (W), 2929 (M), 2857 (W), 1715 (S), 1611 (W), 1464 (W), 1415 (W), 1392 (W), 1367 (W), 1309 (W), 1270 (VS), 1177 (M), 1104 (S), 1022 (M), 851 (W), 761 (M), 726 (W), 703 (M).

3.9.3 2-Phenethylbenzaldehyde (36c)



The aluminium reagent **34b** was prepared according to **TP14** from (2-iodoethyl)benzene (**33b**, 500 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and $PbCl_2$ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 2 h. The cross-coupling reaction was carried out according to **TP15** using $Zn(OAc)_2$ (556 mg, 3 mmol) and a solution of 2-bromobenzaldehyde (**35c**, 252 mg, 1.36 mmol), $Pd(OAc)_2$ (10 mg, 0.044 mmol) and S-Phos (33 mg, 0.080 mmol) in THF (3 mL). The reaction mixture was stirred at 20 °C for 45 min before being quenched with HCl (5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 80:1) afforded **36c** as yellow oil (227 mg, 79%).

1H -NMR (300 MHz, $CDCl_3$) δ/ppm : 10.26 (s, 1H), 7.89 (dd, $J = 7.46$ Hz, $J = 1.66$ Hz, 1H), 7.55 (td, $J = 7.5$ Hz, $J = 1.4$ Hz, 1H), 7.45 (td, $J = 7.7$ Hz, $J = 1.4$ Hz, 1H), 7.38-7.23 (m, 6H), 3.44-3.35 (m, 2H), 3.01-2.93 (m, 2H).

^{13}C -NMR (75 MHz, $CDCl_3$) δ/ppm : 192.3, 144.3, 141.1, 133.8, 133.7, 132.4, 131.2, 128.5, 128.4, 126.7, 126.1, 38.2, 34.9.

MS (EI, 70 eV): m/z (%) = 210 (17) $[M^+]$, 192 (12), 132 (14), 117 (12), 91 (100), 85 (11), 71 (23), 65 (12), 57 (32), 56 (11), 55 (11), 43 (39), 42 (14), 41 (19).

HRMS (EI) for $C_{15}H_{14}O$: calculated: 210.1045, found 210.1031.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/cm^{-1}$: 3062 (W), 3026 (W), 2924 (W), 2860 (W), 2736 (W), 1734 (VW), 1691 (VS), 1654 (W), 1599 (M), 1573 (M), 1495 (M), 1452 (M), 1403 (W), 1292 (W), 1204 (M), 1191 (M), 1160 (W), 1109 (W), 1072 (W), 1030 (W), 884 (W), 870 (W), 852 (W), 827 (W), 755 (VS), 724 (M), 698 (S), 663 (W).

3.10 InCl₃-Mediated Preparation of 1,2-Bimetallics

3.10.1 1,2-Diiodocyclohex-1-ene (39a)



The aluminium reagent **38** was prepared according to **TP16** from 1,2-dibromocyclohexene (**37**, 480 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InBr₃ (53 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 65% bimetallic (1.3 mmol). Iodine (10 mmol) was added at 0 °C and the reaction mixture stirred for 1 h. Excess iodine was quenched with sat. aqueous Na₂S₂O₃ solution. The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification (pentane) yielded **39a** as colorless oil (400 mg, 1.2 mmol, 92%, 60% overall).

¹H-NMR (400 MHz, C₆D₆) δ/ppm: 2.39-2.30 (m, 4H), 1.09-1.00 (m, 4H).

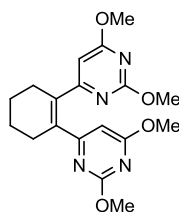
¹³C-NMR (100 MHz, C₆D₆) δ/ppm: 110.2, 42.5, 24.7.

MS (EI, 70 eV) *m/z* (%): 333 (38), 238 (11), 111 (11), 97 (18), 85 (21), 83 (19), 80 (27), 79 (24), 71 (32), 70 (14), 69 (27), 57 (68), 56 (18), 55 (27), 44 (100), 43 (30), 41 (32).

HRMS (EI) for C₆H₈I₂: calculated: 316.1675 [M⁺], found: 316.1669.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2928 (S), 2874 (M), 2855 (M), 2829 (M), 2652 (VW), 1735 (VW), 1685 (W), 1601 (M), 1444 (M), 1428 (M), 1349 (W), 1315 (M), 1260 (W), 1239 (W), 1170 (W), 1136 (W), 1114 (VW), 1092 (M), 1073 (W), 1001 (W), 978 (VS), 938 (M), 894 (W), 847 (W), 813 (W), 759 (W), 728 (VS).

3.10.2 1,2-bis(2,6-dimethoxypyrimidin-4-yl)cyclohex-1-ene (39b)



The aluminium reagent **38** was prepared according to **TP16** from 1,2-dibromocyclohexene (**37**, 480 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InBr₃ (53 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 65% bimetallic (1.3 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 4-iodo-2,6-dimethoxypyrimidine (1064 mg, 4 mmol) and Pd(PPh₃)₄ in THF (4 mL) was added. The reaction mixture was stirred at 50 °C for 12 h before being quenched with water (5 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 1:1) afforded **39b** as brown solid (84 mg, 0.23 mmol, 18%).

mp: 144-147 °C.

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 6.22 (s, 2H), 3.68 (s, 6H), 3.47 (s, 6H), 2.49-2.44 (m, 4H), 1.55-1.49 (m, 4H).

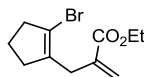
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 172.1, 170.5, 166.0, 137.2, 100.9, 54.3, 53.2, 29.5, 22.5.

MS (EI, 70 eV) m/z (%): 359 (20), 358 (100), 357 (30), 343 (25).

HRMS (EI) for C₁₈H₂₂N₄O₄: calculated: 358.1641 [M⁺], found: 358.1638.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2934 (W), 2861 (W), 1584 (S), 1559 (VS), 1475 (M), 1458 (M), 1432 (M), 1423 (W), 1384 (M), 1357 (S), 1340 (S), 1330 (S), 1274 (W), 1241 (W), 1199 (S), 1172 (M), 1139 (W), 1099 (S), 1064 (W), 1048 (M), 1012 (M), 1000 (M), 983 (W), 966 (W), 939 (W), 844 (W), 835 (M), 804 (W), 790 (W), 733 (W), 714 (W).

3.10.3 Ethyl 2-((2-bromocyclopent-1-en-1-yl)methyl)acrylate (**44**)



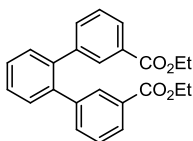
The aluminium reagent **42** was prepared according to **TP16** from 1,2-dibromocyclopentene (**41**, 224 mg, 1 mmol), LiCl (127 mg, 3 mmol), Al-powder (81 mg, 3 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 12 h. The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -30 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**43**, 135 mg, 0.7 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 60:1) afforded **44** as colorless liquid (152 mg, 84%).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 6.20-6.18 (m, 1H), 5.25-5.23 (m, 1H), 3.91 (q, J = 7.2 Hz, 2H), 3.21 (s, 2H), 2.46-2.30 (m, 2H), 2.05-1.90 (m, 2H), 1.58-1.38 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H).

¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 166.1, 137.8, 137.2, 124.9, 118.1, 60.3, 39.8, 33.6, 32.1, 21.4, 13.8.

HRMS (ESI) for C₁₁H₁₅BrO₂: calculated: 276.0599 [M⁺+NH₄], found: 276.0594.

3.10.4 Diethyl [1,1':2',1''-terphenyl]-3,3''-dicarboxylate (**48a**)



The aluminium reagent **46a** was prepared according to **TP17** from 1,2-dibromobenzene (**45a**, 472 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 4 h. Iodolysis indicated a yield of 58% bimetallic (1.16 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium

powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of ethyl 3-bromobenzoate (**47a**, 458 mg, 2 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (2 mL) was added. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 10:1) afforded **48a** as colorless oil (336 mg, 0.63 mmol, 63%).

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 8.19 (s, 2H), 7.97 (d, $J = 7.8$ Hz, 2H), 7.27-7.21 (m, 2H), 7.15-7.11 (m, 2H), 7.03 (d, $J = 7.7$ Hz, 2H), 6.85 (t, $J = 7.7$ Hz, 2H), 4.06 (q, $J = 7.1$ Hz, 4H), 0.97 (t, $J = 7.1$ Hz, 6H).

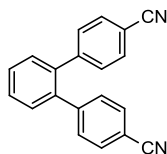
$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 165.6, 141.5, 139.7, 134.1, 130.9, 130.8, 130.4, 127.83, 127.80, 127.79, 60.4, 13.8.

MS (EI, 70 eV) m/z (%): 375 (23), 371 (100), 329 (26), 255 (20), 229 (39), 228 (36), 227 (25), 226 (31).

HRMS (EI) for $\text{C}_{24}\text{H}_{22}\text{O}_4$: calculated: 374.1518 [M^+], found: 374.1504.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3062 (VW), 2981 (W), 1714 (VS), 1605 (W), 1583 (W), 1472 (W), 1444 (W), 1425 (W), 1391 (W), 1366 (M), 1303 (S), 1285 (M), 1236 (S), 1225 (VS), 1169 (M), 1105 (S), 1082 (S), 1064 (M), 1033 (M), 1000 (M), 914 (W), 860 (W), 819 (W), 769 (M), 745 (VS), 700 (S), 673 (M), 666 (M).

3.10.5 [1,1':2',1''-Terphenyl]-4,4''-dicyanitrile (**48b**)



The aluminium reagent **46a** was prepared according to **TP17** from 1,2-dibromobenzene (**45a**, 472 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl_3 (33 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 4 h. Iodolysis indicated a yield of 54% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 4-bromobenzonitrile (**47b**, 364 mg, 2 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (3 mL) was added. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 7:1) afforded **48b** as white solid (165 mg, 0.59 mmol, 59%).

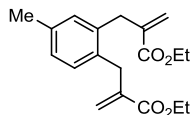
mp: 190-193 °C.

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 7.12-7.08 (m, 2H), 6.98-6.94 (m, 2H), 6.86-6.81 (m, 4H), 6.58-6.53 (m, 4H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 144.6, 138.5, 131.5, 130.3, 129.9, 128.4, 118.1, 111.1.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2228 (M), 1606 (W), 1595 (W), 1474 (M), 1440 (W), 1398 (M), 1274 (W), 1177 (M), 1156 (W), 1116 (W), 1103 (W), 1020 (W), 1006 (W), 1002 (W), 978 (W), 969 (W), 852 (S), 838 (S), 769 (VS), 736 (W), 709 (W).

3.10.6 Diethyl 2,2'-((4-methyl-1,2-phenylene)bis(methylene))diacrylate (48c)



The aluminium reagent **46b** was prepared according to **TP17** from 3,4-dibromotoluene (**45b**, 500 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 54% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -30 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**43**, 540 mg, 2.8 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **48c** as colorless oil (317 mg, 1.00 mmol, 93%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.01 (d, J = 7.6 Hz, 1H), 6.91 (s, 1H), 6.88 (d, J = 7.6 Hz, 1H), 6.28-6.25 (m, 2H), 5.18-5.15 (m, 2H), 3.97 (q, J = 7.1 Hz, 2H), 3.96 (q, J = 7.2 Hz, 2H), 3.71-3.68 (m, 4H), 2.10 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H).

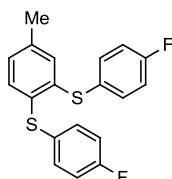
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.6, 166.6, 140.7, 140.6, 137.4, 136.3, 134.5, 131.3, 130.5, 127.8, 125.5, 125.5, 60.6, 60.6, 35.3, 35.0, 21.0, 14.1.

MS (EI, 70 eV) m/z (%): 316 (15), 271 (21), 270 (36), 243 (20), 242 (100), 225 (19), 224 (41), 213 (15), 197 (36), 196 (46), 170 (16), 169 (67), 167 (18), 157 (32), 155 (16), 154 (17), 153 (20), 143 (20), 142 (25), 141 (14), 129 (21), 128 (23), 115 (11).

HRMS (EI) for C₁₉H₂₄O₄: calculated: 316.1675 [M⁺], found: 316.1669.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2981 (W), 2929 (VW), 1711 (VS), 1631 (W), 1502 (W), 1477 (W), 1445 (W), 1428 (W), 1403 (W), 1390 (W), 1367 (W), 1298 (M), 1275 (M), 1249 (M), 1192 (M), 1177 (M), 1129 (VS), 1096 (M), 1025 (M), 946 (M), 914 (W), 831 (W), 816 (M), 662 (VW), 644 (W), 640 (W).

3.10.7 (4-Methyl-1,2-phenylene)bis((4-fluorophenyl)sulfane) (48d)



The aluminium reagent **46b** was prepared according to **TP17** from 3,4-dibromotoluene (**45b**, 500 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 54% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before *S*-4-fluorophenyl benzenesulfonothioate (**47c**, 751 mg, 2.8 mmol) was added subsequently. The reaction mixture was stirred at 20 °C for 16 h before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **48d** as yellow oil (140 mg, 0.41 mmol, 38%).

¹H-NMR (300 MHz, C₆D₆) δ/ppm: 7.14-7.05 (m, 5H), 6.92-6.90 (m, 1H), 6.67-6.58 (m, 5H), 1.85 (s, 3H).

¹³C-NMR (75 MHz, C₆D₆) δ/ppm: 162.8 (d, *J* = 248 Hz), 162.6 (d, *J* = 247 Hz), 139.1, 138.3, 134.8 (d, *J* = 8 Hz), 133.8, 133.6 (d, *J* = 8 Hz), 132.5, 131.6, 130.8 (d, *J* = 3 Hz), 129.9 (d, *J* = 3 Hz), 128.6, 116.7 (d, *J* = 22 Hz), 116.5 (d, *J* = 22 Hz), 20.7.

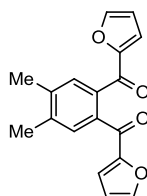
¹⁹F-NMR (282 MHz, C₆D₆) δ/ppm: -113.45-113.57 (m, 1F), -114.30-114.42 (m, 1F).

MS (EI, 70 eV) *m/z* (%): 346 (11), 345 (24), 344 (100), 216 (12), 215 (16), 202 (33).

HRMS (EI) for C₁₉H₁₄F₂S₂ calculated: 344.0505 [M⁺], found: 344.0503.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3047 (VW), 2920 (W), 2861 (VW), 1892 (VW), 1588 (M), 1487 (VS), 1458 (S), 1396 (W), 1381 (W), 1290 (W), 1255 (W), 1221 (VS), 1155 (S), 1111 (W), 1085 (M), 1035 (M), 1012 (M), 868 (W), 812 (VS), 714 (W), 686 (W).

3.10.8 (4,5-Dimethyl-1,2-phenylene)bis(furan-2-ylmethanone) (**48e**)



The aluminium reagent **46c** was prepared according to **TP17** from 3,4-dibromo-*o*-xylene (**45c**, 528 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 57% bimetallic (1.14 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of *S-p*-tolyl furan-2-carbothioate (**47d**, 873 mg, 4 mmol) and PEPPSI-*t*Pr (19 mg, 0.028 mmol) in DMPU (4 mL) was added. The reaction mixture was stirred at 50 °C for 2 h before being quenched with water (5 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 4:1 → 1:1) afforded **48e** as white solid (231 mg, 0.79 mmol, 70%).

mp: 131-132 °C.

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.39 (s, 2H), 6.88 (d, $J = 3$ Hz, 2H), 6.85 (s, 2H), 5.86-5.81 (m, 2H), 1.86 (s, 6H).

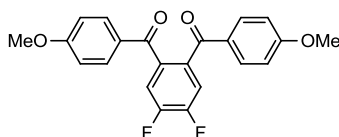
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 182.7, 153.5, 146.2, 139.7, 137.4, 130.8, 118.8, 112.2, 19.4.

MS (EI, 70 eV) m/z (%): 294 (37) [M⁺], 266 (60), 265 (100), 211 (20), 128 (14), 95 (15).

HRMS (EI) for C₁₈H₁₄O₄ calculated: 294.0892 [M⁺], found: 294.0882.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3145 (VW), 3121 (W), 2969 (VW), 2919 (W), 2854 (VW), 2363 (VW), 1740 (W), 1650 (S), 1637 (S), 1600 (M), 1559 (M), 1459 (S), 1391 (S), 1315 (M), 1301 (M), 1287 (M), 1275 (M), 1231 (W), 1222 (W), 1185 (W), 1156 (M), 1091 (W), 1082 (W), 1072 (W), 1014 (S), 974 (W), 955 (M), 933 (M), 906 (W), 897 (W), 882 (M), 838 (M), 814 (M), 778 (S), 766 (VS), 758 (S), 710 (W), 668 (VW).

3.10.9 (4,5-Difluoro-1,2-phenylene)bis((4-methoxyphenyl)methanone) (48f)



The aluminium reagent **46d** was prepared according to **TP17** from 1,2-dibromo-3,4-difluorobenzene (**45d**, 544 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 53% bimetallic (1.06 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of *S*-(4-chlorophenyl) 4-methoxybenzothioate (**47e**, 778 mg, 2.8 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in DMPU (4 mL) was added. The reaction mixture was stirred at 50 °C for 2 h before being quenched with water (5 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 4:1 → 1:1) afforded **48f** as white solid (140 mg, 0.37 mmol, 35%).

mp: 97-98 °C.

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.63-7.57 (m, 4H), 7.02 (t, $J = 8.9$ Hz, 2H), 6.55-6.49 (m, 4H), 3.14 (s, 6H).

¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 192.1, 163.9, 150.8 (dd, $J = 255$ Hz, $J = 14$ Hz), 137.9 (t, $J = 4$ Hz), 132.4, 130.2, 118.8-118.1 (m), 113.5, 54.5.

¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -134.1 (t, $J = 8.8$ Hz).

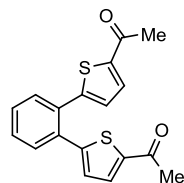
MS (EI, 70 eV) m/z (%): 383 (25), 382 (100) [M⁺], 275 (74), 259 (15), 135 (56).

HRMS (EI) for C₂₂H₁₆F₂O₄ calculated: 382.1017 [M⁺], found: 382.1010.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3045 (W), 3018 (VW), 2970 (VW), 2941 (W), 2846 (VW), 2362 (W), 2338 (W), 1739 (W), 1647 (M), 1597 (VS), 1576 (M), 1509 (M), 1457 (W), 1442 (W), 1424 (M), 1396 (VW), 1372 (W), 1366 (W), 1326 (M), 1315 (S), 1284 (S), 1259 (VS), 1218 (W), 1186 (M), 1171 (VS), 1113 (W),

1082 (M), 1015 (S), 968 (VW), 956 (VW), 939 (VW), 920 (W), 904 (VW), 883 (M), 847 (S), 824 (W), 812 (W), 790 (W), 784 (M), 769 (M), 736 (M), 703 (W), 696 (W), 687 (W), 667 (VW).

3.10.10 1,1'-(5,5'-(1,2-Phenylene)bis(thiophene-5,2-diyl))diethanone (52a)



The aluminium reagent **50a** was prepared according to **TP18A** from 2-bromophenyl trifluoromethanesulfonate (**49a**, 611 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 4 h. Iodolysis indicated a yield of 67% bimetallic (1.34 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 1-(5-iodothiophen-2-yl)ethanone (**51a**, 605 mg, 2.4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (3 mL) was added. The reaction mixture was stirred at 50 °C for 60 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether/DCM = 2:1:1) afforded **52a** as brown solid (146 mg, 0.45 mmol, 34%).

mp: 99-100 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.22-7.16 (m, 2H), 6.96-6.90 (m, 2H), 6.89-6.85 (m, 2H), 6.50-6.46 (m, 2H), 1.93 (s, 6H).

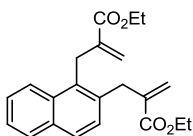
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 189.4, 150.3, 145.3, 133.3, 132.3, 131.3, 129.1, 128.5, 26.1.

MS (EI, 70 eV) m/z (%): 327 (16), 326 (95) [M⁺], 312 (20), 311 (100), 43 (24).

HRMS (EI) for C₁₈H₁₄O₂S₂ calculated: 326.0435 [M⁺], found: 326.0437.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2361 (W), 1652 (VS), 1527 (W), 1511 (W), 1457 (W), 1429 (S), 1356 (M), 1333 (W), 1300 (W), 1270 (S), 1237 (M), 1218 (M), 1160 (W), 1100 (W), 1087 (W), 1074 (W), 1053 (W), 1036 (M), 1016 (W), 967 (W), 954 (W), 924 (M), 897 (W), 881 (W), 831 (W), 816 (M), 790 (M), 768 (S), 754 (M), 726 (W), 720 (W), 670 (W).

3.10.11 Diethyl 2,2'-(naphthalene-1,2-diylbis(methylene))diacrylate (52b)



The aluminium reagent **50b** was prepared according to **TP18A** from 1-bromonaphthalen-2-yl trifluoromethanesulfonate (**49b**, 710 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 53% bimetallic (1.08 mmol). The solution containing the aluminium reagent was

separated from the remaining aluminium powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (552 mg, 3 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -78 °C. $\text{CuCN}\cdot 2\text{LiCl}$ (1 M in THF, 0.4 mL, 0.4 mmol) was added at -78 °C before ethyl 2-(bromomethyl)acrylate (**43**, 386 mg, 2 mmol) was added subsequently. The reaction mixture was allowed to slowly warm to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **52b** as yellow oil (164 mg, 0.47 mmol, 47%).

$^1\text{H-NMR}$ (300 MHz, C_6D_6) δ /ppm: 7.89-7.84 (m, 1H), 7.67-7.61 (m, 1H), 7.55 (d, $J = 8.6$ Hz, 1H), 7.28-7.19 (m, 3H), 6.25-6.14 (m, 2H), 5.10-4.84 (m, 2H), 4.27-4.24 (m, 1H), 4.06 (q, $J = 7.2$ Hz, 2H), 3.94 (q, $J = 7.0$ Hz), 3.81-3.77 (m, 2H), 0.98 (t, $J = 7.2$ Hz, 3H), 0.90 (t, $J = 7.2$ Hz, 3H).

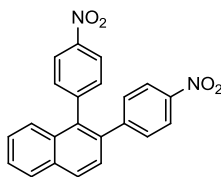
$^{13}\text{C-NMR}$ (75 MHz, C_6D_6) δ /ppm: 166.5, 166.1, 140.0, 139.1, 135.1, 133.1, 132.9, 132.4, 128.4, 128.3, 127.4, 126.2, 125.6, 125.1, 125.1, 124.3, 60.4, 60.3, 35.7, 30.2, 13.8, 13.7.

MS (EI, 70 eV) m/z (%): 306 (13), 279 (13), 278 (72), 261 (17), 260 (10), 239 (12), 233 (26), 232 (25), 206 (11), 205 (54), 204 (31), 203 (31), 202 (15), 193 (36), 191 (11), 190 (10), 189 (13), 179 (31), 178 (31), 178 (43), 167 (15), 166 (28), 165 (100), 141 (16).

HRMS (EI) for $\text{C}_{22}\text{H}_{24}\text{O}_4$ calculated: 352.1675 [M^+], found: 352.1659.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3050 (VW), 2980 (W), 1708 (VS), 1631 (M), 1598 (W), 1511 (W), 1463 (W), 1445 (W), 1428 (W), 1403 (W), 1389 (W), 1367 (M), 1337 (W), 1323 (W), 1277 (S), 1248 (S), 1218 (M), 1193 (M), 1172 (M), 1128 (VS), 1095 (M), 1063 (W), 1025 (M), 944 (M), 879 (W), 860 (W), 815 (S), 763 (M), 739 (M), 639 (W).

3.10.12 1,2-Bis(4-nitrophenyl)naphthalene (**52c**)



The aluminium reagent **50b** was prepared according to **TP18B** from 1-bromonaphthalen-2-yl trifluoromethanesulfonate (**49b**, 710 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl_3 (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 53% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 4-nitrophenyl trifluoromethanesulfonate (**51b**, 1085 mg, 4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in DMPU (3 mL) was added. The reaction mixture was stirred at 50 °C for 2 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 4:1) afforded **52c** as brown solid (305 mg, 0.82 mmol, 80%).

mp: 223-225 °C.

¹H-NMR (600 MHz, CDCl₃) δ /ppm: 8.22-8.06 (m, 4H), 8.04 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.61-7.46 (m, 4H), 7.41-7.27 (m, 4H).

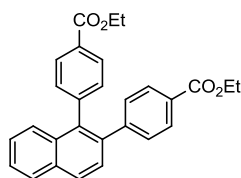
¹³C-NMR (150 MHz, C₆D₆) δ /ppm: 148.0, 147.1, 146.6, 145.5, 136.2, 135.6, 133.2, 132.3, 131.7, 130.8, 129.2, 128.3, 127.4, 127.1, 126.8, 126.0, 123.4, 123.2.

MS (EI, 70 eV) m/z (%): 371 (19), 370 (100), 277 (12), 276 (25), 265 (11), 44 (10).

HRMS (EI) for C₂₂H₁₄N₂O₄ calculated: 370.0954 [M⁺], found: 370.0948.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2847 (VW), 2361 (W), 2340 (W), 1934 (VW), 1595 (M), 1516 (S), 1509 (S), 1404 (W), 1342 (VS), 1314 (M), 1285 (M), 1249 (W), 1225 (W), 1212 (W), 1176 (W), 1163 (W), 1124 (W), 1105 (M), 1067 (W), 1026 (VW), 1013 (W), 973 (VW), 964 (W), 883 (W), 862 (W), 854 (M), 842 (M), 828 (S), 764 (M), 756 (M), 724 (W), 714 (W), 700 (M), 680 (W), 669 (VW).

3.10.13 Diethyl 4,4'-(naphthalene-1,2-diyl)dibenzoate (**52d**)



The aluminium reagent **50b** was prepared according to **TP18A** from 1-bromonaphthalen-2-yl trifluoromethanesulfonate (**49b**, 710 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 53% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of ethyl 4-iodobenzoate (**51c**, 552 mg, 2 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (3 mL) was added.. The reaction mixture was stirred at 50 °C for 4 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **52d** as white solid (216 mg, 0.45 mmol, 51%).

mp: 122-124 °C.

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 8.04-7.98 (m, 4H), 7.74-7.68 (m, 2H), 7.61 (d, J = 8.4 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.33-7.27 (m, 1H), 7.25-7.19 (m, 1H), 7.11-6.97 (m, 4H), 4.07 (q, J = 7.1 Hz, 2H), 4.04 (q, J = 7.2 Hz, 2H), 0.97 (t, J = 7.0 Hz, 3H), 0.94 (t, J = 7.1 Hz, 3H).

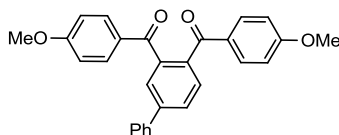
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 165.5 (2C), 146.2, 143.5, 137.3, 136.9, 133.1, 132.4, 131.3, 130.0, 129.5, 129.2, 129.1, 129.0, 128.1, 127.9, 127.7, 126.5, 126.5, 126.0, 60.4, 60.3, 13.8, 13.7.

MS (EI, 70 eV) m/z (%): 425 (35), 424 (100), 379 (13), 279 (10), 278 (16), 277 (15), 276 (17).

HRMS (EI) for C₂₈H₂₄O₄ calculated: 424.1675 [M⁺], found: 424.1671.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2363 (M), 2338 (M), 1738 (M), 1714 (S), 1703 (VS), 1366 (S), 1271 (VS), 1230 (M), 1218 (M), 1180 (M), 1114 (S), 1102 (S), 1022 (M), 843 (W), 826 (M), 773 (S), 752 (M), 708 (M).

3.10.14 [1,1'-Biphenyl]-3,4-diylbis((4-methoxyphenyl)methanone) (**52e**)



The aluminium reagent **50c** was prepared according to **TP18A** from 3-bromo-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (**49c**, 762 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 53% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of *S*-(4-chlorophenyl) 4-methoxybenzothioate (**47e**, 555 mg, 2 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (3 mL) was added. The reaction mixture was stirred at 50 °C for 4 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 4:1 → 1:1) afforded **52e** as white solid (280 mg, 0.66 mmol, 66%).

mp: 83-86 °C

¹H-NMR (600 MHz, CDCl₃) δ/ppm : 7.81-7.78 (m, 2H), 7.74-7.70 (m, 4H), 7.69-7.63 (m, 3H), 7.49-7.39 (m, 3H), 6.88-6.84 (m, 4H), 3.84 (s, 3H), 3.83 (s, 3H).

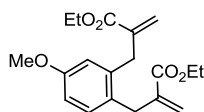
¹³C-NMR (150 MHz, CDCl₃) δ/ppm : 195.4, 195.0, 163.5, 163.5, 143.0, 141.1, 139.3, 138.6, 132.2, 132.2, 130.3, 130.3, 130.0, 129.0, 128.3, 128.2, 127.7, 127.2, 113.6, 113.5, 55.4, 55.4.

MS (EI, 70 eV) m/z (%): 423 (27), 422 (100), 315 (37), 299 (11), 135 (46).

HRMS (EI) for C₂₈H₂₂O₄ calculated: 422.1518 [M⁺], found: 422.1510.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2935 (W), 2838 (W), 1656 (M), 1650 (M), 1620 (W), 1595 (S), 1574 (M), 1556 (W), 1508 (M), 1461 (M), 1450 (M), 1420 (M), 1314 (M), 1309 (M), 1291 (M), 1251 (VS), 1173 (S), 1154 (S), 1110 (M), 1077 (W), 1024 (M), 947 (M), 930 (M), 902 (W), 843 (M), 817 (M), 790 (M), 781 (M), 756 (S), 699 (M).

3.10.15 Diethyl 2,2'-((4-methoxy-1,2-phenylene)bis(methylene))diacrylate (**52f**)



The aluminium reagent **50d** was prepared according to **TP18A** from 2-bromo-4-methoxyphenyl trifluoromethanesulfonate (**49d**, 670 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis

indicated a yield of 53% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -78 °C. $\text{CuCN}\cdot 2\text{LiCl}$ (1 M in THF, 0.4 mL, 0.4 mmol) was added at -78 °C before ethyl 2-(bromomethyl)acrylate (**43**, 752 mg, 4 mmol) was added subsequently. The reaction mixture was allowed to slowly warm to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 6:1) afforded **52f** as colorless oil (200 mg, 0.60 mmol, 51%).

$^1\text{H-NMR}$ (300 MHz, C_6D_6) δ /ppm: 7.01 (d, $J = 8.6$ Hz, 1H), 6.80 (d, $J = 2.8$ Hz, 1H), 6.66 (dd, $J = 8.3$ Hz, 2.8 Hz), 6.29-6.24 (m, 2H), 5.19-5.14 (m, 2H), 3.97 (q, $J = 7.2$ Hz, 2H), 3.94 (q, $J = 7.2$ Hz, 2H), 3.33 (s, 3H), 0.93 (t, $J = 7.2$ Hz, 3H), 0.91 (t, $J = 7.2$ Hz, 3H).

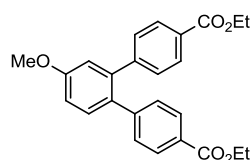
$^{13}\text{C-NMR}$ (75 MHz, C_6D_6) δ /ppm: 166.7, 166.6, 159.1, 140.9, 140.4, 138.9, 131.6, 129.4, 125.7, 125.3, 116.2, 112.4, 60.6, 60.6, 54.7, 35.6, 34.7, 14.1, 14.1.

MS (EI, 70 eV) m/z (%): 332 (20) [M^+], 287 (16), 286 (13), 259 (20), 258 (100), 241 (17), 240 (27), 229 (14), 213 (24), 186 (12), 185 (50), 184 (23), 183 (10), 173 (21), 159 (16), 158 (17).

HRMS (EI) for $\text{C}_{19}\text{H}_{24}\text{O}_5$ calculated: 332.1624 [M^+], found: 332.1620.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ / cm^{-1} : 3415 (W), 2981 (W), 2837 (W), 1712 (VS), 1631 (M), 1609 (M), 1580 (W), 1502 (M), 1465 (M), 1446 (M), 1432 (M), 1391 (W), 1368 (M), 1253 (VS), 1214 (S), 1194 (S), 1158 (S), 1132 (VS), 1113 (S), 1096 (S), 1025 (S), 949 (M), 861 (M), 817 (M), 752 (W).

3.10.16 Diethyl 4'-methoxy-[1,1':2',1''-terphenyl]-4,4''-dicarboxylate (**52g**)



The aluminium reagent **50d** was prepared according to **TP18A** from 2-bromo-4-methoxyphenyl trifluoromethanesulfonate (**49d**, 670 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl_3 (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 55% bimetallic (1.10 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of ethyl 4-iodobenzoate (**51c**, 604 mg, 2.2 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (4mL) was added. The reaction mixture was stirred at 50 °C for 4 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether/DCM = 10:1:1) afforded **52g** as yellow oil (388 mg, 0.96 mmol, 87%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.03-7.96 (m, 4H), 7.17, (d, $J = 8.6$ Hz, 1H), 7.11-7.05 (m, 4H), 6.92 (d, $J = 2.7$ Hz, 1H), 6.82 (dd, $J = 8.5$ Hz, $J = 2.6$ Hz, 1H), 4.08 (q, $J = 7.2$ Hz, 2H), 4.07 (q, $J = 7.2$ Hz, 2H), 3.38 (s, 3H), 0.97 (t, $J = 7.1$ Hz, 3H), 0.96 (t, $J = 7.1$ Hz, 3H).

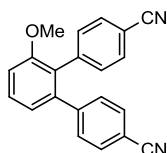
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.0, 165.9, 159.9, 146.1, 145.9, 141.2, 132.5, 132.2, 130.2, 130.1, 129.7, 129.7, 129.6, 129.1, 116.3, 114.0, 60.8, 60.7, 55.0, 14.2, 14.2.

MS (EI, 70 eV) m/z (%): 405 (16), 404 (100), 359 (23), 215 (16).

HRMS (EI) for C₂₅H₂₄O₅ calculated: 404.1624 [M⁺], found: 404.1617.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2978 (W), 2836 (VW), 1709 (S), 1602 (M), 1575 (W), 1566 (W), 1557 (W), 1519 (W), 1509 (VW), 1479 (M), 1464 (M), 1444 (W), 1419 (W), 1396 (W), 1366 (M), 1322 (W), 1308 (M), 1266 (VS), 1221 (S), 1212 (S), 1176 (S), 1098 (VS), 1051 (M), 1015 (S), 1002 (M), 880 (W), 854 (M), 822 (M), 816 (M), 774 (S), 745 (W), 729 (W), 719 (M), 709 (S), 642 (VW), 634 (VW), 616 (W).

3.10.17 3'-Methoxy-[1,1':2',1''-terphenyl]-4,4''-dicyanide (52h)



The aluminium reagent **50e** was prepared according to **TP18B** from 2-bromo-6-methoxyphenyl trifluoromethanesulfonate (**49e**, 670 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 56% bimetallic (1.12 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 4-iodobenzonitrile (**51d**, 916 mg, 4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in DMPU (2 mL) and THF (2 mL) was added. The reaction mixture was stirred at 50 °C for 4 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 3:1) afforded **52h** as white solid (224 mg, 0.72 mmol, 64%).

mp: 195-198 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.43-7.34 (m, 5H), 7.49-7.01 (m, 4H), 6.97 (dd, $J = 8.6$ Hz, $J = 1.0$ Hz, 1H), 6.92 (dd, $J = 7.7$ Hz, $J = 1.1$ Hz, 1H), 3.69 (s, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 156.6, 145.4, 141.3, 140.5, 131.9, 131.6, 131.4, 130.3, 129.6, 127.4, 122.3, 118.7, 118.5, 110.9, 110.6, 110.5, 55.8.

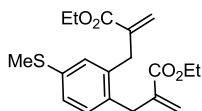
MS (EI, 70 eV) m/z (%): 311 (20), 310 (100), 295 (11), 265 (14).

HRMS (EI) for C₂₁H₁₄ON₂ calculated: 310.1106 [M⁺], found: 310.1101.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3012 (W), 2964 (W), 2917 (W), 2849 (W), 2837 (W), 2361 (W), 2226 (M), 1604 (M), 1579 (M), 1550 (W), 1509 (W), 1490 (W), 1466 (S), 1454 (M), 1435 (M), 1399 (M), 1300

(M), 1271 (M), 1252 (S), 1212 (W), 1196 (W), 1181 (M), 1147 (W), 1121 (M), 1099 (M), 1025 (M), 1014 (M), 1004 (M), 962 (W), 863 (W), 847 (M), 828 (S), 799 (VS), 755 (M), 737 (W), 697 (W).

3.10.18 Diethyl 2,2'-((4-(methylthio)-1,2-phenylene)bis(methylene))diacrylate (**52i**)



The aluminium reagent **50f** was prepared according to **TP18A** from 2-bromo-4-(methylthio)phenyl trifluoromethanesulfonate (**49f**, 702 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 55% bimetallic (1.10 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -30 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**43**, 463 mg, 2.4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **52i** as yellow oil (278 mg, 0.80 mmol, 72%).

¹H-NMR (400 MHz, C₆D₆) δ/ppm: 7.12 (d, *J* = 2.1 Hz, 1H), 6.99 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.26-6.21 (m, 2H), 5.14-5.10 (m, 2H), 3.96 (q, *J* = 7.0 Hz, 2H), 3.94 (q, *J* = 7.0 Hz, 2H), 3.63 (s, 4H), 2.02 (s, 3H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H).

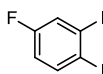
¹³C-NMR (100 MHz, C₆D₆) δ/ppm: 166.5, 166.5, 140.4, 140.1, 138.3, 137.4, 134.4, 131.0, 128.8, 125.8, 125.6, 125.4, 60.6, 60.6, 35.3, 34.9, 15.5, 14.1, 14.1.

MS (EI, 70 eV) *m/z* (%): 349 (12), 348 (49), 303 (13), 276 (11), 275 (15), 274 (100), 199 (16), 188 (16), 174 (12), 161 (13), 154 (15), 153 (23), 128 (17), 115 (13), 82 (15).

HRMS (EI) for C₁₉H₂₄O₄S calculated: 348.1395 [M⁺], found: 348.1388.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2980 (W), 2921 (W), 1710 (VS), 1630 (M), 1596 (W), 1560 (VW), 1488 (W), 1477 (W), 1464 (W), 1442 (W), 1427 (W), 1367 (M), 1299 (M), 1274 (M), 1249 (S), 1202 (M), 1174 (M), 1131 (VS), 1095 (M), 1024 (M), 948 (M), 898 (W), 861 (W), 816 (M), 763 (VW), 728 (VW), 644 (W).

3.10.19 4-Fluoro-1,2-diiodobenzene (**52j**)



The aluminium reagent **50g** was prepared according to **TP18B** from 2-bromo-4-fluorophenyl trifluoromethanesulfonate (**49g**, 646 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 48% bimetallic (0.96 mmol). The solution containing the aluminium reagent was separated from the

remaining aluminium powder and transferred to a new flask containing dried LiCl (254 mg, 6 mmol). The reaction mixture was stirred at 20 °C for 20 min before I₂ (2.3 g, 9 mmol) was added. The reaction mixture was stirred 30 min before being quenched with sat. aqueous Na₂S₂O₃ solution (10 mL). Flash column chromatographical purification on silica gel (isohexane) afforded **52j** as colorless oil (281 mg, 0.81 mmol, 84%, 41% overall).

¹H-NMR (400 MHz, DMSO-*d*⁶) δ /ppm: 7.91-7.77 (m, 2H), (7.02 (td, *J* = 8.8 Hz, *J* = 2.9 Hz, 1H).

¹³C-NMR (100 MHz, DMSO-*d*⁶) δ /ppm: 161.7 (d, *J* = 249 Hz), 140.6 (d, *J* = 8 Hz), 126.7 (d, *J* = 24 Hz), 117.7 (d, *J* = 21 Hz), 109.7, 109.6.

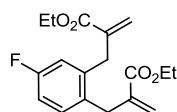
¹⁹F-NMR (376 MHz, DMSO-*d*⁶) δ /ppm: -113.58.

MS (EI, 70 eV) *m/z* (%): 347 (100), 220 (28), 127 (11), 126 (14), 94 (41), 93 (10), 84 (15), 63 (38).

HRMS (EI) for C₆H₃FI₂: calculated: 347.8308 [M⁺], found: 347.8300.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3077 (W), 3003 (W), 2922 (W), 2850 (W), 2817 (W), 2454 (W), 2409 (W), 2080 (W), 2052 (W), 1876 (W), 1781 (W), 1723 (W), 1570 (S), 1514 (W), 1446 (VS), 1411 (M), 1388 (M), 1363 (M), 1252 (S), 1203 (VS), 1152 (W), 1124 (W), 1074 (M), 1006 (S), 941 (W), 859 (S), 847 (S), 804 (S), 725 (W), 708 (W), 675 (W), 657 (W).

3.10.20 Diethyl 2,2'-((4-fluoro-1,2-phenylene)bis(methylene))diacrylate (**52k**)



The aluminium reagent **50g** was prepared according to **TP18B** from 2-bromo-4-fluorophenyl trifluoromethanesulfonate (**49g**, 646 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 66% bimetallic (1.32 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing dried LiCl (254 mg, 6 mmol) and anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -30 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**43**, 541 mg, 2.8 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **52k** as colorless oil (276 mg, 0.86 mmol, 65%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 6.86-6.80 (m, 2H), 6.69 (td, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 6.24-6.18 (m, 2H), 5.07-5.03 (m, 2H), 3.94 (q, *J* = 7.0 Hz, 2H), 3.92 (q, *J* = 7.0 Hz, 2H), 3.57 (s, 2H), 3.52 (s, 2H), 0.92 (t, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.4, 166.3, 162.2 (d, $J = 244$ Hz), 140.2 (d, $J = 1$ Hz), 139.9 (d, $J = 7$ Hz), 139.6 (d, $J = 0.4$ Hz), 133.1 (d, $J = 3$ Hz), 131.9 (d, $J = 8$ Hz), 126.0, 125.6, 116.9 (d, $J = 22$ Hz), 113.7 (d, $J = 21$ Hz), 60.7, 60.6, 35.2 (d, $J = 2$ Hz), 34.6, 14.1, 14.0.

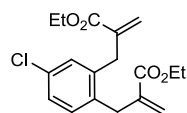
¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -116.38.

MS (EI, 70 eV) m/z (%): 320 (7), 247 (18), 246 (100), 228 (14), 227 (33), 216 (15), 174 (13), 173 (67), 172 (40), 171 (25), 161 (14), 147 (22), 146 (31).

HRMS (EI) for C₁₈H₂₁FO₄ calculated: 320.1424 [M⁺], found: 320.1416.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2982 (W), 1711 (VS), 1631 (W), 1611 (W), 1590 (W), 1497 (M), 1478 (W), 1465 (W), 1445 (W), 1430 (W), 1405 (W), 1368 (W), 1298 (M), 1276 (M), 1248 (S), 1209 (M), 1173 (M), 1130 (VS), 1095 (M), 1025 (M), 974 (M), 949 (M), 919 (W), 865 (M), 831 (W), 816 (M), 756 (W), 715 (VW), 670 (VW), 648 (VW)

3.10.21 Diethyl 2,2'-((4-chloro-1,2-phenylene)bis(methylene))diacrylate (**52l**)



The aluminium reagent **50h** was prepared according to **TP18B** from 2-bromo-4-chlorophenyl trifluoromethanesulfonate (**49h**, 679 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 38% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing dried LiCl (254 mg, 6 mmol) and anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -30 °C. CuCN·2 LiCl (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before ethyl 2-(bromomethyl)acrylate (**43**, 772 mg, 4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 10:1) afforded **52l** as colorless oil (214 mg, 0.6 mmol, 85%).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.12 (d, $J = 2.2$ Hz, 1H), 7.00 (dd, $J = 8.0$ Hz, $J = 2.2$ Hz, 1H), 6.78 (d, $J = 8.3$ Hz, 1H), 6.22-6.16 (m, 2H), 5.04-5.00 (m, 2H), 3.94 (q, $J = 7.2$ Hz, 2H), 3.92 (q, $J = 7.2$ Hz, 2H), 3.54 (s, 2H), 3.50 (s, 2H), 0.91 (t, $J = 7.2$ Hz, 3H), 0.90 (t, $J = 7.1$ Hz, 3H).

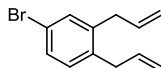
¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 166.3, 166.2, 139.9, 139.7, 139.6, 136.1, 132.8, 131.8, 130.3, 127.1, 126.1, 125.8, 60.7 (2C), 35.0, 34.7, 14.1 (2C).

MS (EI, 70 eV) m/z (%): 291 (20), 290 (16), 264 (34), 262 (100), 246 (12), 245 (13), 244 (29), 233 (13), 218 (15), 217 (21), 216 (35), 209 (21), 191 (21), 190 (22), 189 (64), 188 (39), 187 (11), 181 (12), 177 (19), 163 (13), 162 (23), 155 (14), 154 (26), 153 (40), 152 (18), 149 (11), 128 (22), 127 (15), 115 (17).

HRMS (EI) for C₁₈H₂₁ClO₄ calculated: 336.1128 [M⁺], found: 336.1122.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2982 (W), 1712 (VS), 1632 (M), 1597 (W), 1571 (W), 1486 (M), 1465 (W), 1446 (W), 1428 (W), 1403 (M), 1368 (M), 1326 (W), 1299 (M), 1275 (M), 1251 (S), 1218 (M), 1201 (M), 1173 (M), 1132 (VS), 1111 (S), 1095 (M), 1025 (S), 949 (M), 895 (M), 864 (M), 832 (M), 816 (M), 726 (W).

3.10.22 1,2-Diallyl-4-bromobenzene (52m)



The aluminium reagent **50i** was prepared according to **TP18B** from 2-bromo-4-bromophenyl trifluoromethanesulfonate (**49i**, 768 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl_3 (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 38% bimetallic (0.76 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous $\text{Zn}(\text{OAc})_2$ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before being cooled to -30 °C. $\text{CuCN} \cdot 2 \text{LiCl}$ (1 M in THF, 0.2 mL, 0.2 mmol) was added at -30 °C before allyl bromide (**51e**, 484 mg, 4 mmol) was added subsequently. The reaction mixture was stirred at -30 °C for 1 h and slowly warmed to 20 °C before being quenched with HCl (2 M, 2 mL). Flash column chromatographical purification on silica gel (isohexane) afforded **52m** as colorless liquid (110 mg, 0.46 mmol, 61%).

$^1\text{H-NMR}$ (300 MHz, C_6D_6) δ/ppm : 7.27 (d, $J = 1.8 \text{ Hz}$, 1H), 7.18 (dd, $J = 8.2 \text{ Hz}$, $J = 2.2 \text{ Hz}$, 2H), 6.69 (d, $J = 8.0 \text{ Hz}$, 2H), 5.75-5.58 (m, 2H), 4.96-4.88 (m, 2H), 4.85-4.77 (m, 2H), 3.03-2.97 (m, 2H).

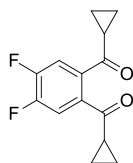
$^{13}\text{C-NMR}$ (75 MHz, C_6D_6) δ/ppm : 140.6, 137.0, 136.6, 136.3, 132.7, 131.6, 129.8, 120.6, 116.3, 116.0, 36.8, 36.6.

MS (EI, 70 eV) m/z (%): 238 (28), 236 (30), 157 (32), 142 (60), 141 (20), 130 (13), 129 (61), 128 (100), 127 (15), 116 (43), 115 (53).

HRMS (EI) for $\text{C}_{12}\text{H}_{13}\text{Br}$ calculated: 236.0201 [M^+], found: 236.0198.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3080 (W), 3005 (W), 2979 (W), 2912 (W), 2851 (W), 1835 (VW), 1638 (M), 1590 (W), 1567 (W), 1481 (M), 1431 (M), 1411 (W), 1396 (W), 1295 (W), 1252 (W), 1169 (W), 1094 (W), 992 (M), 912 (VS), 882 (M), 858 (M), 821 (M), 793 (M), 677 (W).

3.10.23 (4,5-Difluoro-1,2-phenylene)bis(cyclopropylmethanone) (52n)



The aluminium reagent **50j** was prepared according to **TP18B** from 2-bromo-4,5-difluorophenyl trifluoromethanesulfonate (**49j**, 682 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl_3 (33 mg,

0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 45% bimetallic (0.90 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of *S*-phenyl cyclopropanecarbothioate (**51f**, 713 mg, 4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in DMPU (4 mL) was added. The reaction mixture was stirred at 50 °C for 4 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 3:1) afforded **51g** as colorless oil (100 mg, 0.40 mmol, 44%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 6.93 (t, *J* = 8.8 Hz, 2H), 1.69-1.62 (m, 2H), 1.24-1.13 (m, 4H), 0.62-0.50 (m, 4H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 200.4, 151.0 (dd, *J* = 256 Hz, *J* = 15 Hz), 138.0 (t, *J* = 4 Hz), 117.7-117.1 (m), 20.5, 12.5.

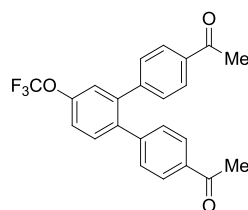
¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -133.66.

MS (EI, 70 eV) *m/z* (%): 250 (18), 223 (12), 222 (91), 221 (100), 209 (61), 194 (58), 193 (40), 191 (41), 181 (23), 180 (50), 166 (15), 165 (37), 164 (24), 163 (17), 153 (11), 151 (44), 141 (16), 133 (24), 127 (18), 113 (18), 112 (24), 69 (44), 55 (13), 41 (58).

HRMS (EI) for C₁₄H₁₂F₂O₄ calculated: 250.0805 [M⁺], found: 250.0800.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3054 (W), 3012 (W), 2922 (VW), 2852 (VW), 1676 (S), 1600 (S), 1505 (M), 1444 (W), 1418 (W), 1384 (S), 1298 (VS), 1215 (W), 1198 (M), 1178 (W), 1133 (S), 1094 (M), 1064 (W), 1039 (M), 1007 (S), 948 (S), 899 (M), 871 (S), 852 (M), 810 (M), 790 (M), 763 (M), 747 (M), 729 (M).

3.10.24 1,1'-(4'-(Trifluoromethoxy)-[1,1':2',1''-terphenyl]-4,4''-diyl)diethanone (**52o**)



The aluminium reagent **50k** was prepared according to **TP18B** from 2-bromo-4-(trifluoromethoxy)phenyl trifluoromethanesulfonate (**49k**, 682 mg, 2 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 53% bimetallic (1.08 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 4'-bromoacetophenone (**51g**, 796 mg, 4 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in DMPU (4 mL) was added. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 4 mL).

Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 3:1 → 1:1) afforded **52o** as colorless oil (166 mg, 0.42 mmol, 45%).

¹H-NMR (600 MHz, CDCl₃) δ /ppm: 7.84-7.80 (m, 4H), 7.46 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 7.30 (s, br, 1H), 7.20 (m, 4H), 2.58 (s, 3H), 2.57 (s, 3H).

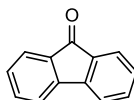
¹³C-NMR (150 MHz, CDCl₃) δ /ppm: 197.61, 197.58, 148.9 (q, J = 2 Hz), 144.6, 144.5, 141.2, 138.1, 135.9, 135.7, 132.0, 129.94, 129.88, 128.31, 128.26, 122.7, 120.5 (q, J = 258 Hz), 120.4, 26.59, 26.58.

¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -133.66.

MS (EI, 70 eV) m/z (%): 399 (14), 398 (57), 384 (24), 383 (100), 43 (14).

HRMS (EI) for C₂₃H₁₇F₃O₃ calculated: 398.1130 [M⁺], found: 398.1133.

3.10.25 9*H*-Fluoren-9-one (**54a**)



The aluminium reagent **46a** was prepared according to **TP17** from 1,2-dibromobenzene (**45a**, 472 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 4 mL THF at 50 °C for 4 h. Iodolysis indicated a yield of 55% bimetallic (1.10 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 2-iodobenzoyl chloride (**53**, 850 mg, 3 mmol) and Pd(PPh₃)₄ (88 mg, 0.076 mmol) in NMP (3 mL) was added. The reaction mixture was stirred at 20 °C for 1 h before being quenched with HCl (2 M, 5 mL). Flash column chromatographical purification on silica gel (isohexane/DCM = 4:1) afforded **54a** as yellow solid (119 mg, 0.66 mmol, 60%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.61-7.57 (m, 2H), 7.43-7.39 (m, 4H), 7.25-7.19 (m, 2H).

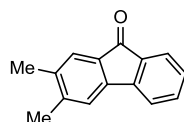
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 193.8, 144.3, 134.6, 134.1, 129.0, 124.2, 120.3.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3059 (W), 1712 (S), 1671 (M), 1610 (M), 1598 (M), 1470 (W), 1450 (M), 1295 (M), 1250 (M), 1190 (M), 1149 (M), 1097 (M), 1015 (W), 928 (W), 915 (S), 877 (W), 810 (W), 730 (VS), 666 (M).

MS (EI, 70 eV) m/z (%): 181 (14), 180 (100), 152 (26), 151 (16), 58 (14), 43 (34).

HRMS (EI) for C₁₃H₈O calculated: 180.0575 [M⁺], found: 180.0569.

3.10.26 2,3-Dimethyl-9*H*-fluoren-9-one (**54b**)



The aluminium reagent **46b** was prepared according to **TP17** from 3,4-dibromotoluene (**45b**, 500 mg, 2 mmol), LiCl (254 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 51% bimetallic (1.02 mmol). The solution containing the aluminium reagent was separated from the remaining aluminium powder and transferred to a new flask containing anhydrous Zn(OAc)₂ (734 mg, 4 mmol). The resulting suspension was stirred for 20 minutes at 20 °C before a solution of 2-iodobenzoyl chloride (**53**, 850 mg, 3 mmol) and Pd(PPh₃)₄ (88 mg, 0.076 mmol) in NMP (3 mL) was added. The reaction mixture was stirred at 20 °C for 1 h before being quenched with HCl (2 M, 5 mL). Flash column chromatographical purification on silica gel (isohexane/DCM = 4:1) afforded **54b** as yellow solid (54 mg, 0.66 mmol, 73%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.56 (d, J = 6.9 Hz, 1H), 7.33 (s, 1H), 7.03-6.92 (m, 2H), 6.84 (s, 1H), 6.80-6.74 (m, 1H), 1.82 (s, 3H), 1.76 (s, 3H).

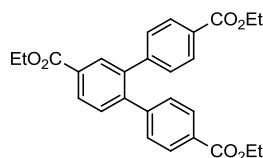
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 192.7, 144.5, 143.2, 142.4, 137.2, 134.8, 133.7, 132.6, 128.3, 125.4, 123.8, 121.5, 119.5, 20.0, 19.2.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3009 (W), 2919 (W), 2857 (W), 1737 (M), 1704 (S), 1667 (M), 1599 (S), 1446 (M), 1405 (M), 1384 (M), 1367 (M), 1298 (M), 1274 (M), 1234 (S), 1190 (M), 1176 (M), 1161 (M), 1120 (W), 1102 (M), 1074 (W), 1041 (M), 1020 (M), 982 (M), 961 (W), 897 (W), 878 (M), 869 (M), 847 (W), 804 (W), 765 (S), 736 (VS), 700 (M), 680 (M).

MS (EI, 70 eV) m/z (%): 208 (100).

HRMS (EI) for C₁₅H₁₂O calculated: 208.0888 [M⁺], found: 208.0882.

3.10.27 Triethyl [1,1':2',1''-terphenyl]-4,4',4''-tricarboxylate (**57**)



The zinc reagent **55f** was prepared according to **TP18A** from ethyl 3-bromo-4-(((trifluoromethyl)sulfonyl)oxy)benzoate (**49l**, 754 mg, 2 mmol), LiCl (254 mg, 6 mmol), Zn-powder (523 mg, 8 mmol) and InCl₃ (33 mg, 0.15 mmol). The reaction was carried out in 2 mL THF at 50 °C for 12 h. Iodolysis indicated a yield of 40% bimetallic (0.8 mmol). The solution containing the zinc reagent was separated from the remaining zinc powder and transferred to a new flask. A solution of ethyl 4-iodobenzoate (**56**, 359 mg, 1.3 mmol) and PEPPSI-*i*Pr (19 mg, 0.028 mmol) in NMP (4 mL) was added. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 4 mL). Flash column chromatographical purification on silica gel (isohexane/diethyl ether = 3:1) afforded **57** as yellow oil (185 mg, 0.51 mmol, 64%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 8.25 (d, $J = 1$ Hz, 1H), 8.14 (d, $J = 8.0$ Hz, $J = 1.8$ Hz, 1H), 7.10 (d, 7.6 Hz, 1H), 4.15 (q, $J = 7.2$ Hz, 2H), 4.01 (q, $J = 7.2$ Hz, 4H), 1.02 (t, $J = 7.1$ Hz, 3H), 0.90 (t, $J = 7.1$ Hz, 6H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 165.5 (2C), 165.4, 144.6, 144.6, 143.7, 139.9, 131.7, 130.7, 130.5, 129.7, 129.6, 129.5, 129.4, 129.4, 129.0, 60.8, 60.5, 60.4, 13.9, 13.8, 13.8.

3.11 ESI Mass Spectrometry of 1,2-dialuminium reagents

3.11.1 General Considerations

Sample solutions were transferred into a gas-tight syringe and administered into the ESI source of an HCT quadrupole ion trap mass spectrometer (Bruker Daltonik) at a flow rate of 0.30 ml h⁻¹. The ESI source was operated with nitrogen both as spraying gas (0.7 bar backing pressure) and drying gas (5 L min⁻¹, 60 °C) at a voltage of 3 kV. Ion transfer and trapping parameters similar to those reported previously¹⁹² were applied (except for a trap drive of 40). For collision-induced dissociation (CID) experiments, the mass-selected ions were accelerated by excitation voltages (of peak-to-peak amplitudes V_{exc}) and allowed to collide with the He background gas present in the ion trap (2 mTorr estimated pressure, 40 ms collision time).

3.11.2 Additional Figures

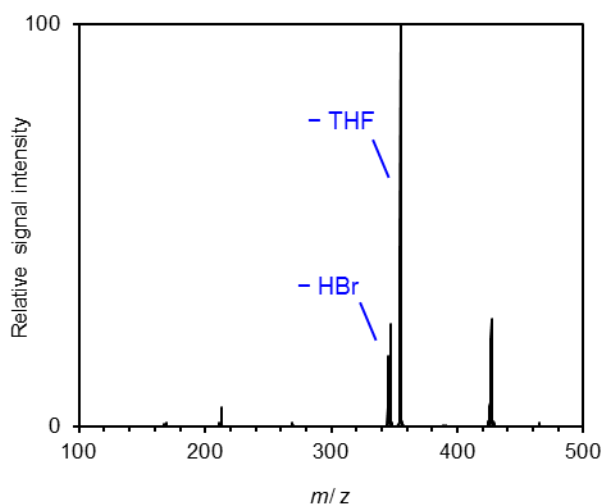


Figure 26: Mass spectrum of mass-selected $m/z = 427$ and its fragment ions produced upon collision-induced dissociation ($V_{\text{exc}} = 0.20$ V, HCT ion trap).

¹⁹² K. Koszinowski, *J. Am. Chem. Soc.* **2010**, *132*, 6032-6040.

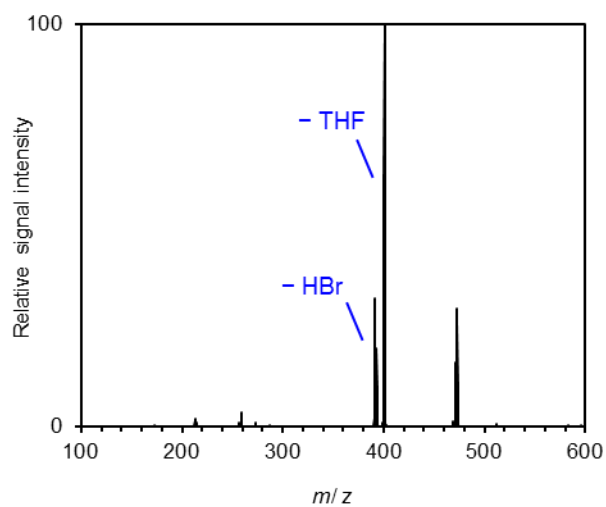


Figure 27: Mass spectrum of mass-selected $m/z = 473$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

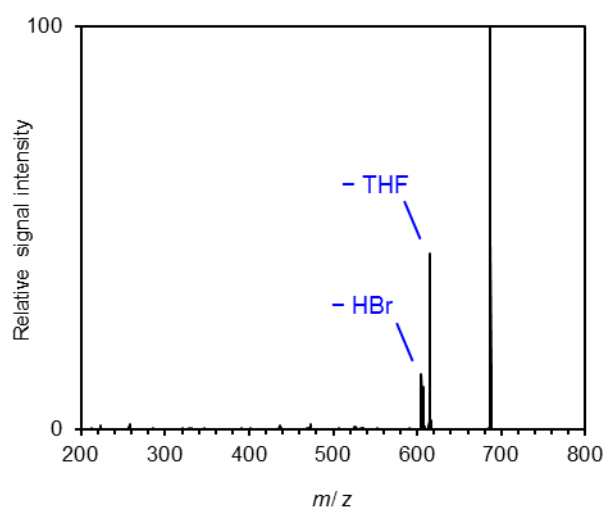


Figure 28: Mass spectrum of mass-selected $m/z = 687$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

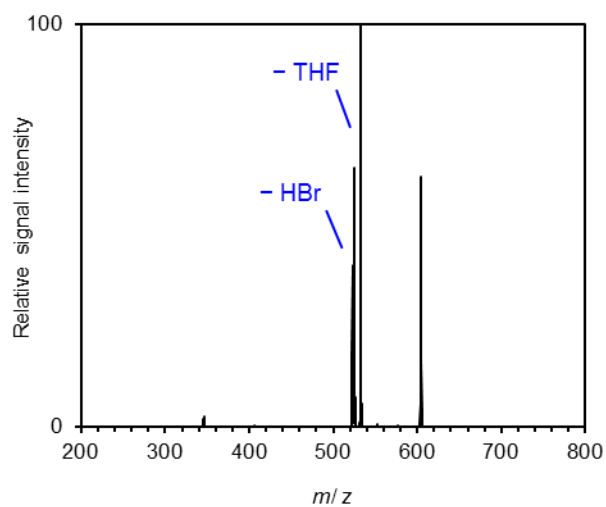


Figure 29: Mass spectrum of mass-selected $m/z = 605$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

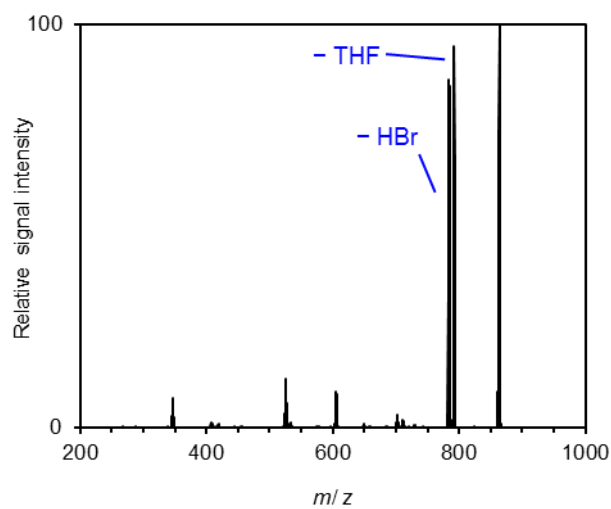


Figure 30: Mass spectrum of mass-selected $m/z = 865$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

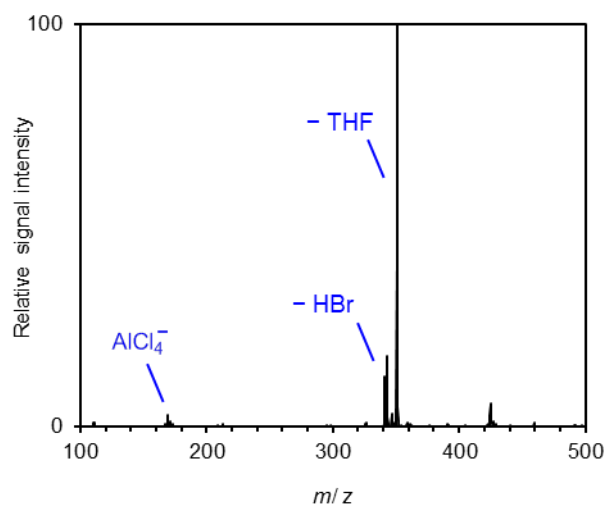


Figure 31: Mass spectrum of mass-selected $m/z = 423$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

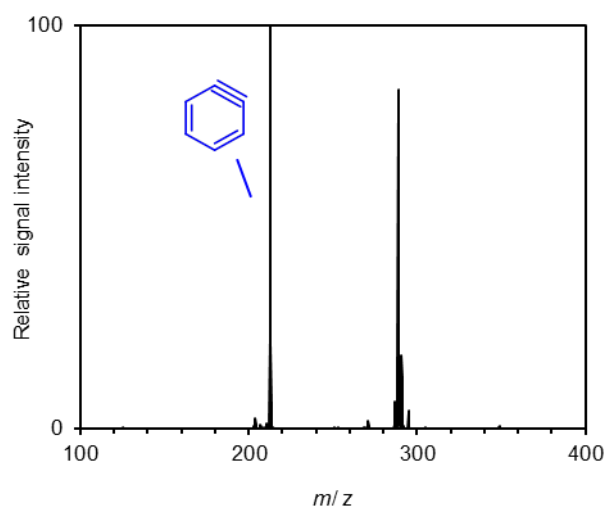


Figure 32: Mass spectrum of mass-selected $m/z = 289$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

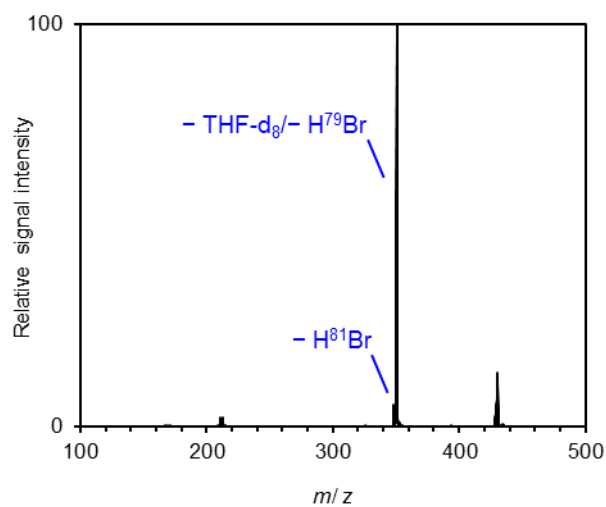


Figure 33: Mass spectrum of mass-selected $m/z = 431$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

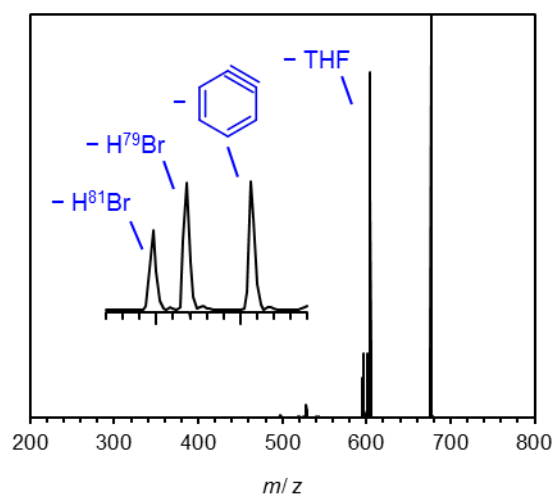


Figure 34: Mass spectrum of mass-selected $m/z = 677$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT ion trap).

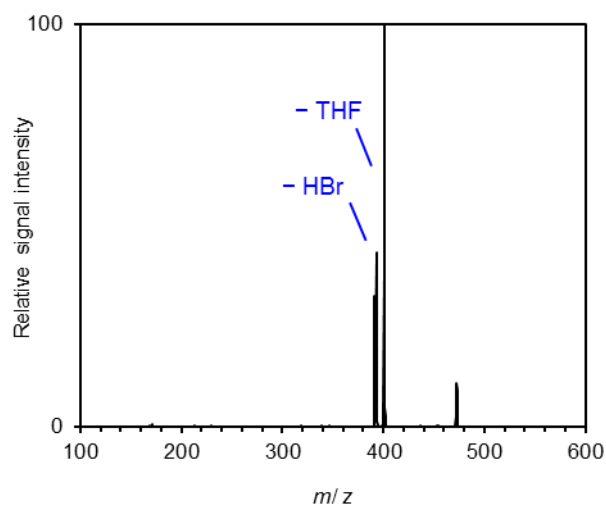
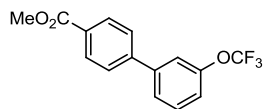


Figure 35: Mass spectrum of mass-selected $m/z = 473$ and its fragment ions produced upon collision-induced dissociation ($V_{exc} = 0.20$ V, HCT¹ ion trap).

3.12 Direct Cross-Coupling of Aluminium Reagents

3.12.1 Methyl 3'-(trifluoromethoxy)-[1,1'-biphenyl]-4-carboxylate (**71**)



The aluminium reagent **2j** was prepared according to **TP2** from 1-iodo-3-trifluoromethoxy benzene (**1j**, 1152 mg, 4 mmol), LiCl (254 mg, 6 mmol), Al-powder (324 mg, 12 mmol) and InCl₃ (27 mg, 0.12 mmol). The reaction was carried out in 4 mL THF at 50 °C for 1 h. One half of the solution containing the aluminium reagent was used for the subsequent reaction. The cross-coupling was carried out according to **TP19** using a solution of methyl 4-iodobenzoate (**70**, 367 mg, 1.4 mmol) and PdCl₂(ttmp)₂ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 6 h before being quenched with HCl (2 M, 3 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 30:1) afforded **71** as white solid (300 mg, 72%).

mp: 67-68 °C.

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.08-8.05 (m, 2H), 7.17-7.15 (m, 1H), 7.11-7.08 (m, 2H), 6.97-6.94 (m, 1H), 6.89-6.85 (m, 1H), 6.84-6.80 (m, 1H), 3.48 (s, 3H).

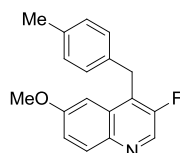
¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.0, 149.6 (q, *J* = 2 Hz), 143.4, 142.0, 130.1, 130.0, 129.9, 126.9, 125.5, 120.8 (q, *J* = 257 Hz), 119.9 (q, *J* = 1 Hz), 119.8 (q, *J* = 1 Hz), 51.3.

MS (EI, 70 eV) *m/z* (%): 297 (14), 296 (78), 266 (16), 265 (100), 237 (10), 152 (10), 139 (10).

HRMS (EI) for C₁₅H₁₁F₃O₃: calculated: 296.0660 [M⁺], found: 296.0665.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2958 (W), 1720 (S), 1608 (W), 1586 (W), 1567 (VW), 1486 (W), 1476 (W), 1444 (W), 1432 (W), 1398 (W), 1283 (S), 1235 (S), 1217 (S), 1194 (VS), 1176 (S), 1153 (VS), 1124 (M), 1109 (S), 1043 (M), 1016 (M), 999 (W), 975 (W), 954 (M), 941 (M), 912 (W), 889 (W), 856 (M), 826 (M), 802 (M), 770 (S), 744 (M), 706 (S), 682 (W).

3.12.2 3-Fluoro-6-methoxy-4-(4-methylbenzyl)quinoline (**73a**)



The aluminium reagent **19h** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 4-methylbenzyl chloride (**18h**, 281 mg, 2 mmol). The reaction was carried out at 25 °C for 3 h. The cross-coupling was carried out according to **TP19** using a solution of 3-fluoro-4-iodo-6-methoxyquinoline (**72a**, 424 mg, 1.4 mmol) and PdCl₂(ttmp)₂ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with sat. aqueous NaHCO₃.

solution (5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 5:1) afforded **73a** as colourless solid (365 mg, 93%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 8.67 (d, *J* = 1.3 Hz, 1H), 8.04 (d, *J* = 9.2 Hz, 1H), 7.34-7.24 (m, 1H), 7.18 (d, *J* = 2.6 Hz, 1H), 7.14-7.04 (m, 4H), 4.37 (d, *J* = 1.6 Hz, 2H), 3.84 (s, 3H), 2.28 (s, 3H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 158.7, 155.0 (d, *J* = 252 Hz), 141.1 (d, *J* = 2 Hz), 137.8 (d, *J* = 30 Hz), 136.2, 134.8 (d, *J* = 1 Hz), 131.1, 129.4, 129.4 (d, *J* = 4 Hz), 128.2 (d, *J* = 1 Hz), 120.7 (d, *J* = 3 Hz), 102.4 (d, *J* = 5 Hz), 77.2, 55.5, 29.8 (d, *J* = 4 Hz), 21.0.

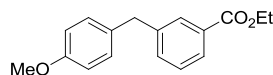
¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -132.27.

MS (EI, 70 eV): *m/z* (%) = 282 (22), 281 (100), 280 (25), 266 (23), 251 (12), 250 (22), 249 (11), 248 (11), 235 (16), 234 (26), 125 (14), 85 (11), 71 (17), 57 (22), 43 (18).

HRMS (EI) for C₁₈H₁₆F₄NO calculated: 281.1216 [M⁺], found 281.1220.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2997 (W), 2954 (W), 2938 (W), 2872 (W), 1621 (M), 1607 (M), 1574 (W), 1508 (S), 1471 (M), 1457 (M), 1445 (M), 1426 (M), 1416 (W), 1357 (M), 1325 (M), 1310 (M), 1298 (W), 1263 (M), 1225 (VS), 1207 (S), 1181 (M), 1128 (M), 1109 (W), 1077 (M), 1032 (S), 1022 (M), 1013 (M), 909 (M), 894 (W), 871 (W), 848 (W), 823 (VS), 810 (M), 782 (S), 770 (S), 752 (M), 742 (W), 706 (W).

3.12.3 Ethyl 3-(4-methoxybenzyl)benzoate (**73b**)



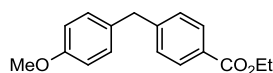
The aluminium reagent **19i** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 4-methoxybenzyl chloride (**18i**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h. The cross-coupling reaction was carried out according to **TP19** using a solution of ethyl 3-iodobenzoate (**72b**, 386 mg, 1.4 mmol) and PdCl₂(ttmp)₂ (50 mg, 0.04 mmol) in 8 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **73b** as colourless oil (135 mg, 36%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 8.00-7.83 (m, 2H), 7.43-7.34 (m, 2H), 7.14 (dd, *J* = 8.3 Hz, 0.5 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.00 (s, 2H), 3.81 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 166.7, 158.2, 141.9, 133.4, 132.7, 130.7, 129.9, 129.9, 128.5, 127.4, 114.0, 61.0, 55.3, 40.9, 14.4.

MS (EI, 70 eV): *m/z* (%) = 270 (100) [M⁺], 241 (18), 225 (17), 197 (32), 164 (11), 121 (16).

HRMS (EI) for C₁₇H₁₈O₃: calculated: 270.1256 [M⁺], found 270.1252.

3.12.4 Ethyl 4-(4-methoxybenzyl)benzoate (73c)

The aluminium reagent **19i** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 4-methoxybenzyl chloride (**18i**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 5 h. The cross-coupling reaction was carried out according to **TP19** using a solution of ethyl 4-bromobenzoate (**72c**, 386 mg, 1.4 mmol) and $\text{PdCl}_2(\text{tppp})_2$ (50 mg, 0.04 mmol) in 8 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (pentane/diethyl ether = 10:1) afforded **73c** as white solid (261 mg, 69%).

mp: 46-47 °C.

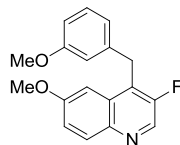
$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ /ppm: 8.17-8.12 (m, 2H), 7.03-6.98 (m, 2H), 6.91-6.86 (m, 2H), 6.78-6.73 (m, 2H), 4.14 (q, $J = 7.2$ Hz, 2H), 3.64 (s, 2H), 3.31 (s, 3H), 1.02 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ /ppm: 166.2, 158.8, 147.1, 132.5, 130.2, 130.1, 129.1, 114.3, 60.7, 54.7, 41.1, 14.3, 2.7.

MS (EI, 70 eV) m/z (%): 271 (19), 270 (100) [M^+], 225 (26), 197 (39), 178 (35), 165 (12), 150 (19), 149 (27), 133 (78), 124 (25), 121 (18), 109 (20), 105 (16), 77 (12), 73 (27), 61 (24), 45 (33), 43 (17).

HRMS (EI) for $\text{C}_{17}\text{H}_{18}\text{O}_3$; calculated: 270.1256 [M^+], found: 270.1252.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3000 (W), 2978 (W), 2972 (W), 2910 (W), 2836 (W), 2362 (VW), 1710 (VS), 1670 (W), 1609 (M), 1585 (W), 1575 (W), 1511 (S), 1471 (M), 1452 (W), 1444 (W), 1430 (W), 1414 (W), 1397 (W), 1378 (W), 1364 (M), 1304 (W), 1278 (S), 1242 (VS), 1174 (S), 1126 (S), 1105 (S), 1032 (S), 1019 (S), 922 (W), 876 (W), 857 (W), 850 (W), 843 (W), 831 (M), 819 (M), 790 (M), 764 (M), 743 (S), 713 (W), 693 (W).

3.12.5 3-fluoro-6-methoxy-4-(3-methoxybenzyl)quinoline (73d)

The aluminium reagent **19j** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 3-methoxybenzyl chloride (**18j**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 12 h. The cross-coupling was carried out according to **TP19** using a solution of 3-fluoro-4-iodo-6-methoxyquinoline (**72a**, 424 mg, 1.4 mmol) and $\text{PdCl}_2(\text{tppp})_2$ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with sat. aqueous NaHCO_3 solution (5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 5:2) afforded **73d** as offwhite solid (323 mg, 78%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.64 (d, J = 1.0 Hz, 1H), 8.13 (dd, J = 9.1 Hz, 0.4 Hz, 1H), 7.11-7.06 (m, 1H), 7.04 (d, J = 2.6 Hz, 1H), 6.99-6.92 (m, 1H), 6.83 (t, J = 2.0 Hz, 1H), 6.72-6.67 (m, 1H), 6.58 (ddd, J = 8.3 Hz, 2.6 Hz, 0.9 Hz, 1H), 4.11 (d, J = 0.9 Hz, 2H), 3.24 (s, 3H), 3.20 (s, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 160.2, 158.6, 155.2 (d, J = 253 Hz), 142.2 (d, J = 2 Hz), 139.8 (d, J = 1 Hz), 138.1 (d, J = 29 Hz), 132.1, 129.6, 129.3 (d, J = 3 Hz), 127.2 (d, J = 13 Hz), 120.4 (d, J = 1 Hz), 120.1 (d, J = 3 Hz), 114.3, 111.7, 102.3 (d, J = 5.3 Hz), 54.4, 54.2, 29.8 (d, J = 3.7 Hz).

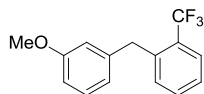
¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -133.0.

MS (EI, 70 eV) m/z (%): 298 (17), 297 (100), 282 (11), 266 (15), 85 (15), 71 (23), 57 (25), 43 (13).

HRMS (EI) for C₁₈H₁₆FNO₂ calculated: 297.1165 [M⁺], found 297.1155.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 3010 (W), 2973 (W), 2962 (W), 2925 (W), 2840 (W), 2814 (W), 1620 (M), 1608 (M), 1583 (M), 1556 (W), 1507 (M), 1485 (M), 1455 (S), 1444 (M), 1416 (M), 1363 (M), 1323 (M), 1285 (S), 1264 (M), 1226 (S), 1215 (VS), 1189 (M), 1176 (W), 1144 (S), 1132 (S), 1096 (W), 1081 (W), 1044 (S), 1027 (S), 1020 (S), 962 (W), 924 (W), 906 (M), 884 (W), 878 (W), 860 (W), 826 (S), 780 (S), 769 (S), 748 (W), 738 (M), 692 (M), 672 (W).

3.12.6 1-(3-Methoxybenzyl)-2-(trifluoromethyl)benzene (73e)



The aluminium reagent **19j** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 3-methoxybenzyl chloride (**18j**, 313 mg, 2 mmol). The reaction was carried out at 25 °C for 12 h. The cross-coupling was carried out according to **TP19** using a solution of 2-iodobenzotrifluoride (**72d**, 381 mg, 1.4 mmol) and PdCl₂(ttmpp)₂ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 24 h before being quenched with sat. aqueous NaHCO₃ solution (5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohehexane/diethyl ether = 60:1) afforded **73e** as colorless oil (261 mg, 70%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 7.44 (d, J = 7.4 Hz, 1H), 7.08-7.00 (m, 1H), 6.98-6.87 (m, 2H), 6.83-6.74 (m, 1H), 6.74-6.68 (m, 1H), 6.70-6.59 (m, 2H), 4.06 (s, 2H), 3.27 (s, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 160.1, 141.1 (q, J = 1 Hz), 139.5 (q, J = 2 Hz), 151.5, 131.5 (q, J = 1 Hz), 129.4, 127.6 (q, J = 24 Hz), 126.0, 125.6 (q, J = 6 Hz), 124.0 (q, J = 274 Hz), 121.4, 114.9, 111.7, 54.2, 37.7 (q, J = 2 Hz).

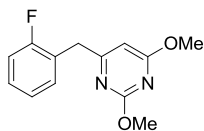
¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -59.4.

MS (EI, 70 eV) m/z (%): 267 (16) 266 (100) 197 (10) 183 (12) 121 (20) 59 (12).

HRMS (EI) for C₁₅H₁₃F₃O calculated: 266.0918 [M⁺], found 266.0911.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2942 (W), 2837 (W), 1600 (M), 1584 (M), 1489 (M), 1455 (M), 1438 (M), 1310 (VS), 1258 (M), 1148 (S), 1107 (VS), 1059 (S), 1051 (S), 1036 (VS), 996 (W), 958 (W), 935 (W), 876 (W), 786 (M), 764 (S), 719 (M), 693 (M), 655 (M).

3.12.7 4-(2-Fluorobenzyl)-2,6-dimethoxypyrimidine (73f)



The aluminium reagent **19f** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 2-fluorobenzyl chloride (**18f**, 289 mg, 2 mmol). The reaction was carried out at 25 °C for 6 h. The cross-coupling was carried out according to **TP19** using a solution of 4-iodo-2,6-dimethoxypyrimidine (**72e**, 372 mg, 1.4 mmol) and $\text{PdCl}_2(\text{ttmp})_2$ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with sat. aqueous NaHCO_3 solution (5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 4:1) afforded **73f** as colourless oil (237 mg, 68%).

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ/ppm : 7.02-6.95 (m, 1H), 6.81-6.67 (m, 3H), 6.06 (s, 1H), 3.77 (s, 2H), 3.64 (d, $J = 1.4$ Hz, 3H), 3.50 (d, $J = 1.3$ Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, C_6D_6) δ/ppm : 172.1, 169.8, 164.0 (d, $J = 246$ Hz), 159.9, 131.5 (d, $J = 4$ Hz), 128.3 (d, $J = 8$ Hz), 125.0 (d, $J = 16$ Hz), 123.9 (d, $J = 4$ Hz), 115.1 (d, $J = 22$ Hz), 99.9 (d, $J = 5$ Hz), 53.9, 52.9, 36.4 (d, $J = 3$ Hz).

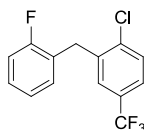
$^{19}\text{F-NMR}$ (282 MHz, C_6D_6) δ/ppm : -117.5.

MS (EI, 70 eV) m/z (%): 248 (48) 247 (59) 230 (14) 229 (100) 109 (13).

HRMS (EI) for $\text{C}_{13}\text{H}_{13}\text{FN}_2\text{O}_2$: calculated: 248.0961 [M^+], found 248.0937.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 2955 (W), 1583 (S), 1565 (S), 1492 (M), 1479 (M), 1455 (S), 1382 (M), 1349 (VS), 1282 (W), 1230 (M), 1206 (M), 1146 (M), 1099 (S), 1057 (M), 1039 (M), 984 (W), 931 (M), 868 (W), 848 (W), 830 (M), 780 (W), 754 (S), 734 (M), 712 (W), 701 (W), 685 (W).

3.12.8 1-Chloro-2-(2-fluorobenzyl)-4-(trifluoromethyl)benzene (73g)



The aluminium reagent **19f** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 2-fluorobenzyl chloride (**18f**, 289 mg, 2 mmol). The reaction was carried out at 25 °C for 6 h. The cross-coupling was carried out according to **TP19** using a solution of 2-bromo-1-chloro-4-(trifluoromethyl)benzene (**72f**, 363 mg, 1.4 mmol) and $\text{PdCl}_2(\text{ttmp})_2$ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 24 h before being quenched with HCl (2 M,

5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 8:1) afforded **73g** as colorless oil (170 mg, 42%).

¹H-NMR (300 MHz, CDCl₃) δ /ppm: 7.26-7.18 (m, 1H), 6.90-6.79 (m, 2H), 6.78-6.68 (m, 2H), 6.65 (q, J = 3.9 Hz, 3.3 Hz, 2H), 3.77 (d, J = 3.4 Hz, 2H).

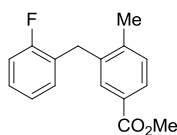
¹³C-NMR (75 MHz, CDCl₃) δ /ppm: 160.9 (d, J = 245 Hz), 138.3 (d, J = 1 Hz), 137.9 (q, J = 2 Hz), 130.5 (d, J = 4 Hz), 130.0, 129.9, 129.0 (q, J = 32 Hz), 128.4 (d, J = 8 Hz), 125.4, 125.2 (d, J = 15 Hz), 124.5 (q, J = 4 Hz), 124.0 (q, J = 272 Hz), 123.9 (d, J = 4 Hz), 122.7, 115.2 (d, J = 22 Hz), 32.1 (d, J = 4 Hz).

MS (EI, 70 eV) m/z (%): 290 (19), 288 (63), 254 (18), 253 (100), 233 (22), 184 (23), 183 (41), 109 (17), 97 (13), 85 (23), 83 (15), 71 (29), 69 (17), 59 (12), 57 (44), 55 (19), 43 (25), 41 (13).

HRMS (EI) for C₁₄H₉ClF₄: calculated: 288.0329 [M⁺], found 288.0327.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 1610 (W), 1587 (W), 1492 (M), 1457 (W), 1435 (W), 1412 (W), 1333 (S), 1322 (S), 1278 (M), 1257 (W), 1233 (M), 1167 (S), 1122 (VS), 1102 (M), 1094 (M), 1080 (VS), 1046 (M), 1035 (M), 943 (W), 932 (W), 921 (W), 906 (W), 897 (W), 863 (W), 847 (W), 826 (S), 778 (W), 753 (S), 724 (M), 692 (W), 658 (VW).

3.12.9 Methyl 3-(2-fluorobenzyl)-4-methylbenzoate (**73h**)



The aluminium reagent **19f** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl₃ (13 mg, 0.06 mmol) and 2-fluorobenzyl chloride (**18f**, 289 mg, 2 mmol). The reaction was carried out at 25 °C for 6 h. The cross-coupling was carried out according to **TP19** using a solution of 3-bromo-4-methylbenzoate (**72g**, 321 mg, 1.4 mmol) and PdCl₂(ttmp)₂ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with HCl (2 M, 5 mL). The aqueous layer was extracted with diethyl ether, DCM and ethyl acetate and the combined organic extracts were dried (Na₂SO₄) and concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 8:1) afforded **73h** as colorless oil (160 mg, 44%).

¹H-NMR (400 MHz, C₆D₆) δ /ppm: 8.01 (m, 2H), 6.88 (d, J = 8.3 Hz, 1H), 6.85-6.76 (m, 2H), 6.74-6.65 (m, 2H), 3.77 (s, 2H), 3.49 (s, 3H), 1.91 (s, 3H).

¹³C-NMR (100 MHz, C₆D₆) δ /ppm: 166.4, 160.9 (d, J = 245 Hz), 141.9, 137.7 (d, J = 1 Hz), 133.4, 131.0 (d, J = 4 Hz), 130.4, 130.2 (d, J = 4 Hz), 128.6, 126.8, 126.6, 123.9 (d, J = 3.7 Hz), 114.9 (d, J = 22 Hz), 51.0, 31.7 (d, J = 3 Hz), 19.0 (d, J = 1 Hz).

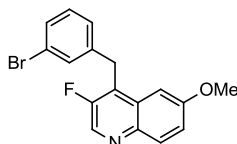
¹⁹F-NMR (282 MHz, C₆D₆) δ /ppm: -117.5.

MS (EI, 70 eV) m/z (%): 258 (11), 227 (11), 70 (13), 61 (21), 45 (14), 43 (100).

HRMS (EI) for C₁₆H₁₅FO₂ calculated: 258.1056 [M⁺], found 258.1050.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3031 (W), 2952 (W), 1717 (S), 1611 (W), 1585 (W), 1489 (M), 1454 (M), 1435 (M), 1410 (W), 1380 (W), 1295 (S), 1265 (S), 1229 (S), 1193 (M), 1171 (M), 1152 (W), 1121 (S), 1100 (M), 1091 (M), 1033 (W), 1002 (M), 942 (W), 926 (W), 912 (W), 898 (W), 836 (M), 786 (W), 753 (VS), 712 (W), 702 (W), 681 (W).

3.12.10 4-(3-Bromobenzyl)-3-fluoro-6-methoxyquinoline (73i)



The aluminium reagent **19u** was prepared according to **TP8** using aluminium powder (162 mg, 6 mmol), InCl_3 (13 mg, 0.06 mmol) and 3-bromobenzyl chloride (**18u**, 411 mg, 2 mmol). The reaction was carried out at 25 °C for 12 h. The cross-coupling was carried out according to **TP19** using a solution of 3-fluoro-4-iodo-6-methoxyquinoline (**72a**, 424 mg, 1.4 mmol) and $\text{PdCl}_2(\text{ttmp})_2$ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 50 °C for 12 h before being quenched with sat. aqueous NaHCO_3 solution (5 mL). The aqueous layer was extracted with diethyl ether and the combined organic extracts were concentrated *in vacuo*. Flash column chromatographical purification of the crude residue on silica gel (isohexane/diethyl ether = 5:1) afforded **73i** as offwhite solid (293 mg, 60%).

mp: 67-68 °C.

$^1\text{H-NMR}$ (300 MHz, C_6D_6) δ/ppm : 8.59 (d, $J = 0.8$ Hz, 1H), 8.09 (d, $J = 9.1$ Hz, 1H), 7.36-7.34 (m, 1H), 7.10-7.03 (m, 2H), 6.86 (d, $J = 2.5$ Hz, 1H), 6.72 (d, $J = 7.7$ Hz, 1H), 6.58 (t, $J = 7.9$ Hz, 1H), 3.90 (s, 2H), 3.25 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, C_6D_6) δ/ppm : 159.1, 155.4 (d, $J = 253$ Hz), 142.4 (d, $J = 3$ Hz), 140.9 (d, $J = 1$ Hz), 138.4 (d, $J = 28$ Hz), 132.5 (d, $J = 1$ Hz), 131.7 (d, $J = 1$ Hz), 130.5 (d, $J = 46$ Hz), 129.3 (d, $J = 3$ Hz), 126.8 (d, $J = 1$ Hz), 126.7, 126.6, 123.1, 120.5 (d, $J = 3$ Hz), 102.4 (d, $J = 5$ Hz), 54.9, 29.6 (d, $J = 4$ Hz).

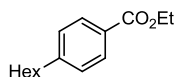
$^{19}\text{F-NMR}$ (376 MHz, C_6D_6) δ/ppm : -132.5.

MS (EI, 70 eV) m/z (%): 348 (14), 347 (100), 346 (20), 345 (98), 235 (19), 234 (29), 223 (12), 222 (17), 125 (14).

HRMS (EI) for $\text{C}_{17}\text{H}_{13}\text{BrFNO}$: calculated: 345.0165 [M^+], found: 345.0157.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}/\text{cm}^{-1}$: 3052 (W), 3015 (W), 2936 (W), 2838 (W), 1620 (S), 1594 (M), 1568 (M), 1509 (S), 1472 (M), 1457 (M), 1438 (M), 1426 (S), 1379 (W), 1360 (M), 1314 (M), 1306 (M), 1264 (S), 1237 (VS), 1221 (VS), 1188 (M), 1169 (S), 1141 (M), 1095 (W), 1086 (W), 1071 (M), 1034 (S), 1008 (S), 999 (M), 916 (W), 898 (M), 876 (M), 856 (M), 838 (M), 826 (S), 793 (M), 764 (S), 738 (M), 708 (M), 686 (M), 678 (M), 662 (W).

3.12.11 Ethyl 4-hexylbenzoate (75)



The aluminium reagent **34c** was prepared according to **TP14** from 1-bromohexane (**33c**, 330 mg, 2 mmol), LiBr (521 mg, 6 mmol), Al-powder (162 mg, 6 mmol) and PbCl₂ (17 mg, 0.06 mmol). The reaction was carried out in 2 mL THF at 50 °C for 48 h. The cross-coupling reaction was carried out according to **TP19** using a solution of ethyl 4-iodobenzoate (**74**, 386 mg, 1.4 mmol), and PdCl₂(ttmp)₂ (50 mg, 0.04 mmol) in 4 mL DMF. The reaction mixture was stirred at 20 °C for 15 min and quenched with HCl (5 mL). Flash column chromatographical purification on silica gel (pentane/diethyl ether = 60:1) afforded **75** as colorless liquid (186 mg, 57%).

¹H-NMR (300 MHz, C₆D₆) δ /ppm: 7.97-7.91 (m, 2H), 7.24-7.21 (m, 2H), 4.35 (q, $J = 7.2$ Hz, 2H), 2.68-2.61 (m, 2H), 1.67-1.55 (m, 2H), 1.38 (t, $J = 7.2$ Hz, 3H), 1.34-1.24 (m, 6H), 0.91-0.84 (m, 3H).

¹³C-NMR (75 MHz, C₆D₆) δ /ppm: 166.7, 148.4, 137.7, 131.0, 129.6, 128.4, 127.9, 60.7, 36.0, 31.7, 31.1, 28.9, 22.6, 14.4, 14.

MS (EI, 70 eV) m/z (%): 234 (22), 207 (13), 189 (55), 164 (13), 163 (25), 136 (21), 134 (15), 127 (12), 113 (13), 111 (13), 106 (13), 99 (21), 97 (22), 91 (11), 90 (53), 85 (51), 83 (22), 71 (76), 70 (17), 68 (25), 57 (100), 56 (25), 55 (41), 43 (80), 42 (46).

HRMS (EI) for C₁₅H₂₂O₂: calculated: 234.1620 [M⁺], found: 234.1617.

FT-IR (Diamond-ATR, neat) $\tilde{\nu}$ /cm⁻¹: 2956 (W), 2929 (M), 2857 (W), 1715 (S), 1611 (W), 1464 (W), 1415 (W), 1392 (W), 1367 (W), 1309 (W), 1270 (VS), 1177 (M), 1104 (S), 1022 (M), 851 (W), 761 (M), 726 (W), 703 (M).