Dissertation zur Erlangung des Doktorgrades
der Fakultät für Chemie und Pharmazie
der Ludwig-Maximilians-Universität München

Regioselective Magnesiations of Aromatics and Heterocycles Using *s*Bu_2Mg and Bis-Magnesium Amides in Hydrocarbon Solvents

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aus

Landshut, Deutschland

2022

ERKLÄRUNG

Diese Dissertation wurde im Sinne von § 7 der Promotionsordnung vom 28. November 2011 von Herrn Prof. Dr. Paul Knochel betreut.

EIDESTATTLICHE VERSICHERUNG

Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

München, den 10.12.2022

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(Andreas Hess)

Dissertation eingereicht am:	15.12.2022
1. Gutachter:	Prof. Dr. Paul Knochel
2. Gutachter:	Prof. Dr. Oliver Trapp
Mündliche Prüfung am:	02.02.2023

This work was carried out from June 2020 to February 2023 under the guidance of Prof. Dr. Paul Knochel at the Department of Chemistry of the Ludwig-Maximilians-Universität, Munich.

Firstly, I would like to express my appreciation to Prof. Dr. Paul Knochel for giving me the great opportunity to do my master as well as my Ph.D. thesis in his group. I am grateful for his supporting guidance during my scientific journey and the fruitful discussions not only about chemistry.

I also would like to thank Prof. Dr. Oliver Trapp for agreeing to be the second reviewer of this thesis, as well as Prof. Dr. Konstantin Karaghiosoff, Prof. Dr. Franz Bracher, Prof. Dr. Thomas Carell and Prof. Dr. Thomas Klapötke for their interest shown in this manuscript by accepting to be referees.

I am very grateful to Clemence Hamze, Johannes Harenberg and Alisa Sunagatullina for proofreading my thesis and for their careful corrections.

Additionally, I am very thankful for the friendly and unconditional support of Prof. Dr. Konstantin Karghiosoff and his time for measuring NMR-spectra and crystal structures.

I thank all past and present co-workers I have met in the Knochel group for their kindness and help. Special thanks go to the members of Lab F2.017 Alexander Kremsmair and Alisa Sunagatullina for being the best lab mates one could imagine inside and outside the lab.

I want to thank Ferdinand Lutter and Simon Graßl for giving me fruitful advices in the beginning of my Ph.D. Especially, I want to thank Dr. Nurtalya Alandini for her valuable and fruitful help in the projects. Also, I thank my former students Florian Trauner, Sabrina Dörrich, Jan Prohaska, Can Gülen, Areta Mourati and Yusuf Gürsoy for their excellent contributions in the course of their internships.

Finally, I would like to thank my parents and all my friends for their endless and unconditional support and motivation for finishing this thesis. Each of you supported me anytime and under any circumstances. You contributed to this thesis way more you might expect.

For my parents

List of Publications

First Author

1) A. Hess, J. P. Prohaska, S. B. Doerrich, F. Trauner, F. H. Lutter, S. Lemaire, S. Wagschal, K. Karaghiosoff, P. Knochel, *Chem. Sci.* **2021***, 12*, 8424-8429.

2) A. Hess, H. C. Guelen, N. Alandini, A. Mourati, Y. C. Guersoy, P. Knochel, *Chem. Eur. J.* **2022**, *28*, e202103700.

3) A. Hess, N. Alandini, Y. C. Guersoy, P. Knochel, *Angew. Chem. Int. Ed.* **2022**, *61*, e202206176.

4) A. Hess, N. Alandini, H. C. Guelen, J. P. Prohaska, P. Knochel, *Chem. Commun.* **2022**, *58*, 8774-8777.

Reviews

5) A. Kremsmair, J. H. Harenberg, K. Schwaerzer, A. Hess, P. Knochel, *Chem. Sci.* **2021**, *12*, 6011-6019.

6) A. Hess, A. Kremsmair, P. Knochel, Lithium Dichloro(2,2,6,6-tetramethylpiperidinato)-Magnesiate. In *Encyclopedia of Reagents for Organic Synthesis* **2022**.

7) A. Kremsmair, A. Hess, B. Heinz, P. Knochel, *Chem. Eur. J.* **2022**, *28*, e202103269.

Table of Contents

Abbreviations

Ar	undefined aryl substitutent
aq. sat.	*aqueous*, saturated
calc.	calculated
conc.	concentrated
***c*Hex**	*cyclo*-hexyl
d	doublet (NMR)
DG	directing group
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
d.r.	diastereomeric ratio
EI	electron ionization (MS)
equiv	equivalents
ESI	electrospray ionization (MS)
FG	functional group
GC	gas chromatography
HRMS	high resolution mass spectroscopy
***i*Pr**	*iso*-propyl
IR	infrared
LDA	lithium diisopropylamide
M	mol/L
Met	Metal
m.p.	melting point
MS	mass spectrometry
NMR	nuclear magnetic resonance
ppm	parts per million
q	quartet (NMR)
R	undefined organic substituent
r.t.	room temperature
***s*Bu**	*sec*-butyl
s	singulet (NMR)
t	triplet (NMR)
***t*Bu**	*tert*-butyl
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethan-1,2-diamin
TBS	*tert*-butyldimethylsilyl
THF	tetrahydrofuran
TMP	2,2,6,6-tetramethylpiperidyl
TMS	trimethylsilyl
TP	typical procedure
UV	ultraviolet

A. INTRODUCTION

1. General Introduction

In the context of a rapidly developing world, problems such as epidemics, still incurable diseases and increasingly diminishing resources are considered as major challenges today. Increasing population, rising age of the population as well as a claim for high living standards all over the world create a demand for safe supply in food, pharmaceuticals and new materials. Major contributions to the development and progress in all of these fields are provided by organic chemists.[1] As an example, about 75% of the top 200 drugs by worldwide sales in 2016 contain small organic molecules as the active pharmaceutical ingredient.[2] A range of these best-selling drugs can be produced over several steps including reactions using organometallic reagents.[3] Organometallic reagents can be defined as bases, nucleophiles and catalysts and their reactivity strongly depends on the polarity of the non-metal-metal bond. For instance, reagents bearing a high ionic character such as lithium or sodium organometallics display an outstanding reactivity towards a broad range of electrophiles but are accompanied with lower stability, the requirement of low reaction temperatures and low functional group tolerance.[4] However, organomagnesium reagents are defined with a comparable more covalent non-metal-metal bond and eventually offer higher stability and functional group tolerance. Due to their even more pronounced covalent character of the non-metal-metal bond, organozinc or -boron reagents show an exceptional high functional group compatibility, which is in turn accompanied with low reactivity towards electrophiles.[5]

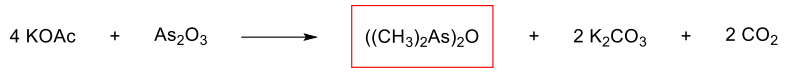
In the course of increasingly complex synthetic challenges and the highly useful properties just mentioned, there is still great potential for the development of new organometallic reagents. This work deals with the preparation of new organomagnesium reagents in industrially relevant, non-etheral solvents and their use for the deprotometalation of complex, functionalized systems under convenient reaction conditions.

[1] M. MacCoss, T. A. Baillie, *Science* **2004**, *303*, 1810-1813.
[2] G. Sedelmeier, J. Sedelmeier, *Chimia* **2017**, *71*, 730-730.
[3] M. Baumann, I. R. Baxendale, *Beilstein J. Org. Chem.* **2013**, *9*, 2265-2319.
[4] J. Clayden, *Organolithiums: Selectivity for Synthesis.* Elsevier, **2002**.
[5] P. Knochel, *Handbook of Functionalized Organometallics*, Wiley-VCH, **2005**.

2. Preparation of Organomagnesium Reagents

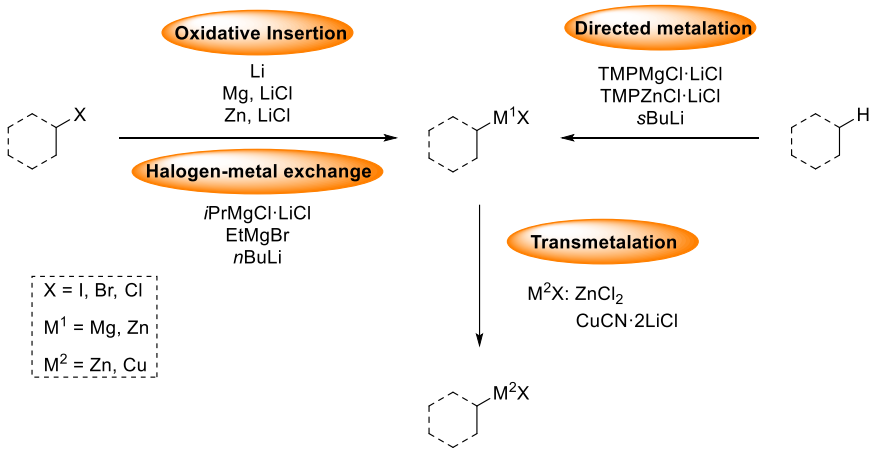
2.1 Overview

The first preparation of an organometallic reagent was described in 1760 by *de Gassicourt*. Reaction of potassium acetate with arsenic trioxide furnished a mixture of dicacodyl and cacodyl oxide further known as *Cadet´s fuming liquid* (Scheme 1).[6]



Scheme 1: Preparation of *Cadet´s fuming liquid*.

Pioneering contributions of *Frankland*[7] and *Grignard*[8] established the field of organometallic chemistry and opened up numerous possibilities to access polyfunctional magnesium and zinc organometallic reagents. The three most commonly used strategies comprise oxidative insertion, halogen-metal exchange and directed metalation. Another approach is provided by transmetalation (Scheme 2).

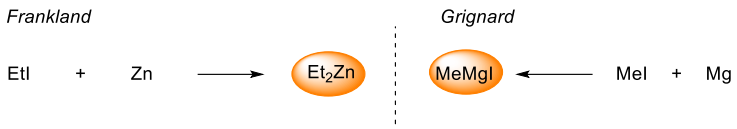


Scheme 2: Various approaches to organometallic reagents.

[6] D. Seyferth, *Organometallics* **2001**, *8*, 1488-1498.
[7] E. von Frankland, *Justus Liebigs Ann. Chem.* **1849**, *71*, 171-213.
[8] V. Grignard, *Compt. Rend.* **1900**, *130*, 1322.

2.2 Oxidative Insertion

In 1849 *Frankland* reported the preparation of diethyl- and ethylzinc iodide by reacting ethyliodide with granulated zinc, which can be considered as the first described oxidative insertion of a metal into a carbon-halogen bond.[9] However, the most common direct insertion of a metal into a carbon-halogen bond was discovered by *Grignard* in 1900 by reacting methyliodide with magnesium turnings in diethylether providing the first described organomagnesium reagent (Scheme 3).[10]

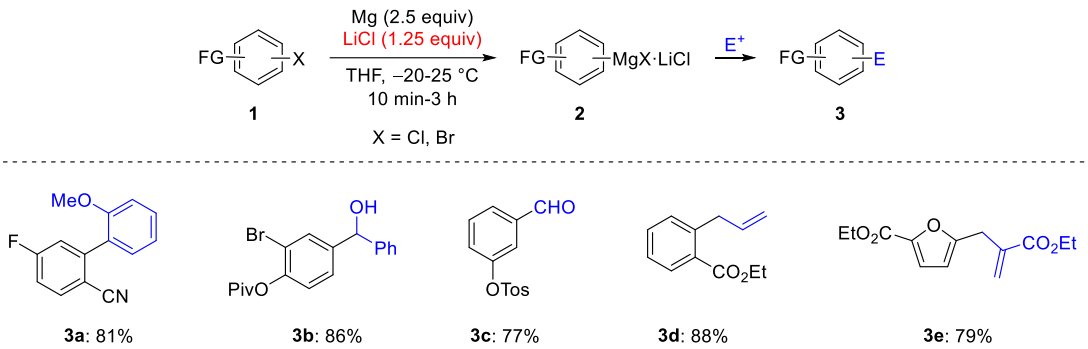


Scheme 3: Pioneering work by *Frankland* and *Grignard*.

These findings created the basis of organometallic chemistry and provided a powerful tool to form new carbon-carbon bonds in organic synthesis. The exact mechanism for the magnesium insertion is still not clear but radical pathways are generally accepted.[11] Due to a naturally occurring passivation layer on the metal surface, the magnesium metal needs to be activated. A range of reagents such as 1,2-dibromoethane,[12] iodine,[13] $FeCl_2$[14] or DIBAL-H[15] proved to be highly efficient. Such a direct oxidative insertion has several advantages since it is atom economical[16] and magnesium turnings are one of the cheapest reagents for the formation of organometallic species. Usually, this transformation only takes place at temperatures from 30-60 °C,[17] which can be considered as a serious limitation if functional groups are present in the targeted system. However, in 2008 *Knochel* and co-workers reported a convenient preparation of polyfunctional aryl magnesium reagents by a direct magnesium insertion in the presence of LiCl under mild conditions.[18] LiCl serves several purposes such as solubilizing the resulting organomagnesium compound, promoting the initial electron transfer by the electrophilic activation of the aromatic ring through complexation[19] and facilitating the charge separation.[20]

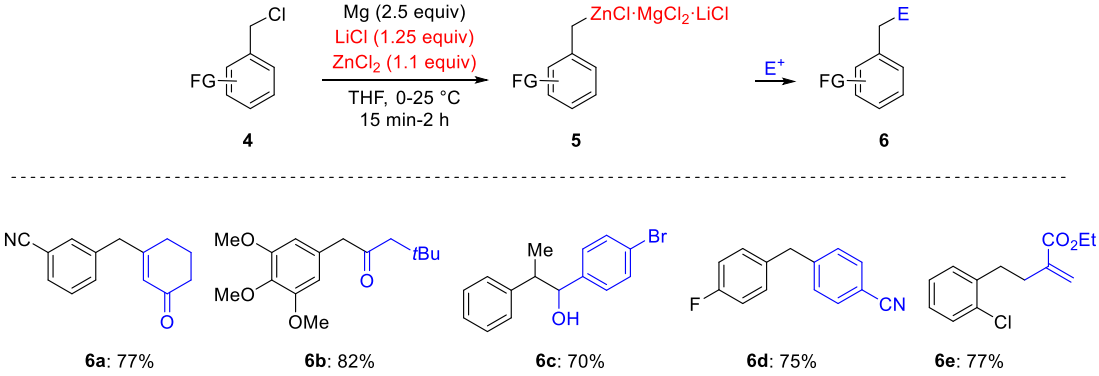
An unprecedented range of functional groups was present in the substrates of type **1** and the resulting functionalized organomagnesium reagents **2** were reacted with various electrophiles affording the desired products of type **3** (Scheme 4).

[9] E. von Frankland, *Justus Liebigs Ann. Chem.* **1849**, *71*, 171-213.
[10] V. Grignard, *Compt. Rend.* **1900**, *130*, 1322.
[11] H. Walborsky, *Acc. Chem. Res.* **1990**, *23*, 286-293.
[12] G. Wilkinson, F. G. A. Stone, E. W. Abel, *The Synthesis, Reactions and Structures of Organometallic Compounds*, Pergamon Press, **1982**.
[13] H. Gold, M. Larhed, P. Nilsson, *Synlett* **2005**, *10*, 1596-1600.
[14] B. Bogdanović, M. Schwickardi, *Angew. Chem. Int. Ed.* **2000**, *39*, 4610-4612.
[15] U. Tilstam, H. Weinmann, *Org. Process Res. Dev.* **2002**, *6*, 906-910.
[16] B. M. Trost, *Science* **1991**, *254*, 1471-1477.
[17] H. E. Ramsden, A. E. Balint, W. R. Whitford, J. J. Walburn, R. Cserr, *J. Org. Chem.* **1957**, *22*, 1202-1206.
[18] F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802-6806.
[19] N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358-12359.
[20] C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, Wiley-VCH, **2003**.



Scheme 4: LiCl-promoted insertion into aryl halides **1** bearing functional groups.

The methodology was extended to the preparation of benzylic zinc chlorides **5** by the direct insertion of magnesium into benzylic chlorides **4** in the presence of LiCl and $ZnCl_2$.[21] Compared to the direct zinc insertion,[22] the reported magnesium insertion in the presence of zinc chloride is remarkably faster and proceeds at lower temperatures. Subsequent reaction with various electrophiles such as aldehydes, acid chlorides, enones and Pd-catalyzed cross-coupling reactions provided a range of polyfunctional building blocks of type **6** (Scheme 5).

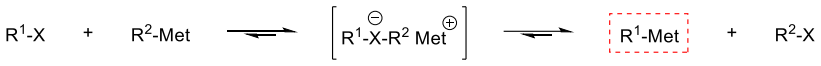


Scheme 5: Direct insertion of magnesium into benzylic chlorides **4** in the presence of LiCl and $ZnCl_2$.

[21] A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824-5826.
[22] a) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107-1110; b) M. A. Schade, A. Metzger, S. Hug, P. Knochel, *Chem. Commun.* **2008**, 3046-3048. c) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040-6044.

2.3 Halogen-Metal Exchange

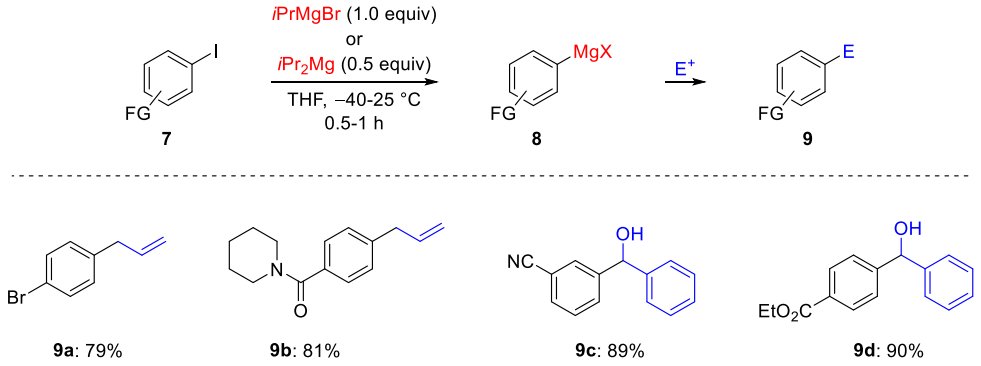
Starting from organic halides, an alternative approach to access organometallic reagents is the exchange reaction with another organometallic reagent. In general, the driving force for this reaction type is the formation of a more stable organometallic species compared to the exchange reagent itself ($sp > sp^2_{vinyl} > sp^2_{aryl} > sp^3_{prim} > sp^3_{sec}$).[23] From a mechanistic insight, the reaction of an organic halide R^1-X with an organometallic R^2-Met produces a halogenate complex $R^1R^2X^-Met^+$, which after subsequent decomposition provides the most stable organometallic species (Scheme 6).[24]



Scheme 6: General equation for the halogen-metal exchange.

The first halogen-metal exchange was reported by *Wittig*[25] and *Gilman*[26] in means of a bromine-lithium exchange and proved its synthetic utility over the years for preparing a wide range of organolithium reagents.[27] However, the high reactivity and instability of organolithium compounds requires very low reaction temperatures down to -100 °C to allow a moderate functional group tolerance.[28]

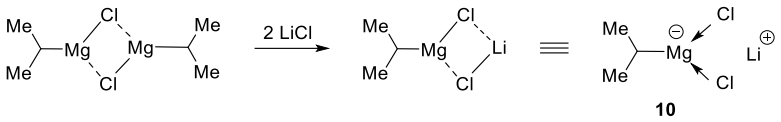
Concerning the halogen-magnesium exchange, *Prévost* pioneered by reacting cinnamyl bromide with ethylmagnesium bromide in 1931.[29] After further pioneering work of *Villieras*,[30] *Knochel* and co-workers reported an iodine-magnesium exchange on organic halides **7** bearing sensitive functional groups such as esters or nitro groups using *i*Pr_2Mg or *i*PrMgBr (Scheme 7).[31]



Scheme 7: Iodine.magnesium exchange using *i*PrMgBr or *i*Pr_2Mg.

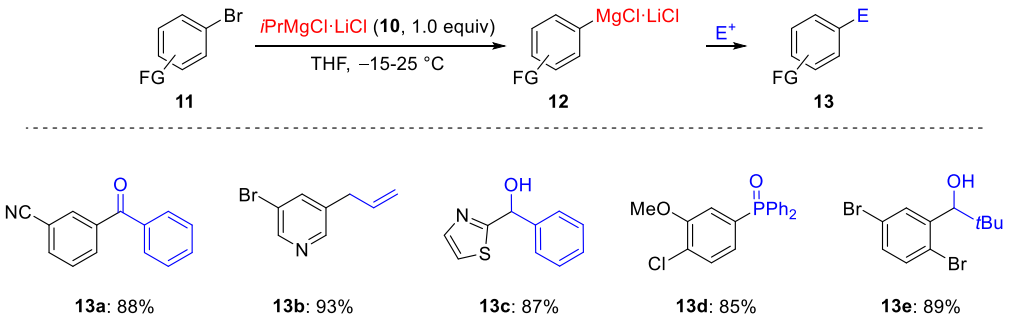
[23] D. Hauk, S. Lang, A. Murso, *Org. Process Res. Dev.* **2006**, *10*, 733-738.
[24] H. J. Reich, A. W. Sanders, A. T. Friedler, M. J. Bevan, *J. Am. Chem. Soc.* **2002**, *124*. 13386-13387.
[25] G. Wittig, U. Pockels, H. Dröge, *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 1903-1912.
[26] H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106-109.
[27] R. Chinchilla, C. Nájera, M. Yus, *Tetrahedron* **2005**, *61*, 3139-3176.
[28] W. E. Parham, L. D. Jones, *J. Org. Chem.* **1976**, *41*, 2704-2706.
[29] C. Prévost, *Bull. Soc. Chim. Fr.* **1931**, *49*, 1372.
[30] J. Villiears, *Bull. Soc. Chim. Fr.* **1967**, *5*, 1520.
[31] a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1701-1703; b) W. Dohle, D. M. Lindsay, P. Knochel, *Org. Lett.* **2001**, *3*, 2871-2873.

A major improvement was the addition of one equivalent LiCl furnishing the reagent *i*PrMgCl·LiCl **10**, also called *Turbo-Grignard*.[32] The addition of LiCl cleaves the aggregates of *i*PrMgCl, enhancing the solubility and reactivity. A schematic illustration of *i*PrMgCl·LiCl (**10**) is depicted in Scheme 8.



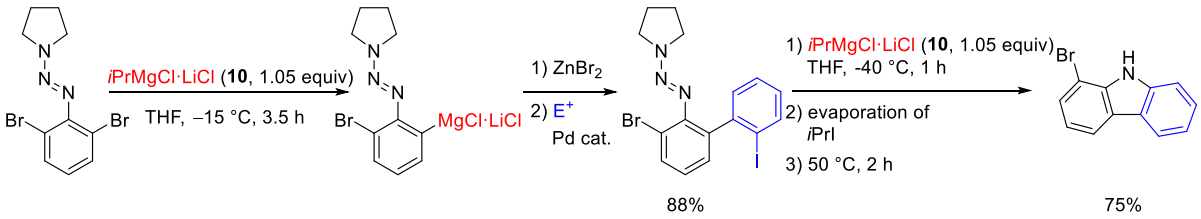
Scheme 8: Effect of LiCl on *i*PrMgCl.

Initially, *i*PrMgCl·LiCl **10** was shown to be highly effective for the preparation of a broad range of functionalized aryl- and heteroarylmagnesium reagents **12** starting from cheap and readily available aryl bromides **11**. The reactions proceeded within a convenient temperature range and various valuable building blocks of type **13** were obtained (Scheme 9).



Scheme 9: LiCl-mediated Br/Mg exchange using *i*PrMgCl·LiCl **10**.

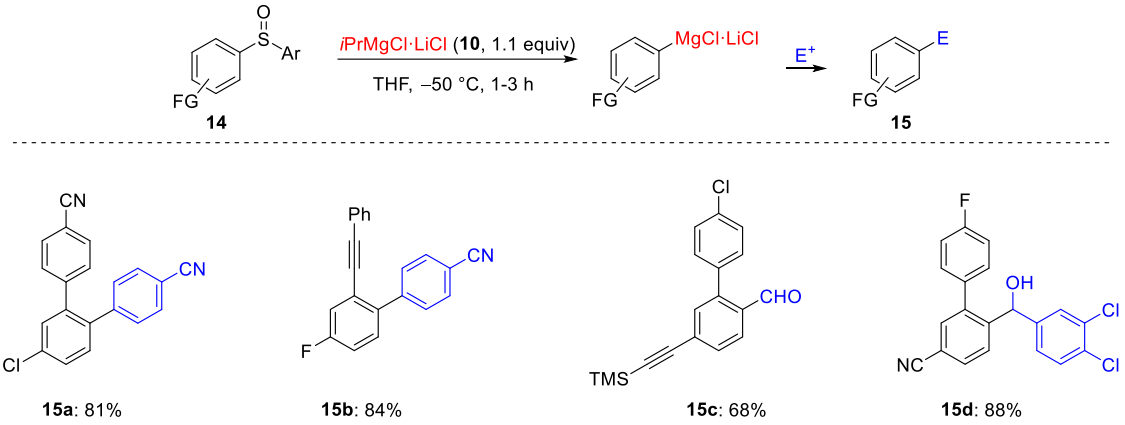
The methodology was extended to the preparation of polyfunctional arylmagnesium reagents bearing a triazene moiety. The triazene functionality is a convenient way to protect a diazonium salt and to carry this reactive functionality through several steps. It has also proved its utility as a linker in solid-phase combinatorial synthesis.[33] Thus, the generated magnesiated derivatives reacted with various electrophiles affording polyfunctional triazenes, which can be readily converted to the corresponding aryl iodides or carbazole derivatives (Scheme 10).[34]



Scheme 10: Preparation of carbazole derivatives by consecutive halogen/Mg exchange reactions.

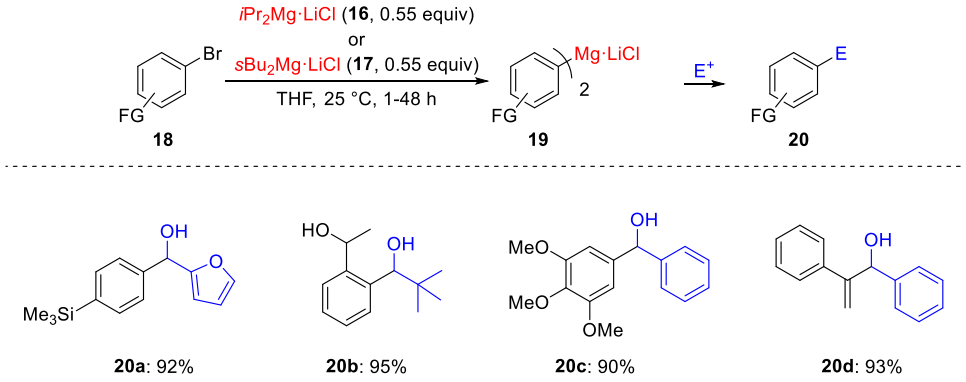
[32] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333-3336.
[33] a) D. B. Kimball, M. M. Haley, *Angew. Chem. Int. Ed.* **2002**, *41*, 3338-3351; b) J. S. Moore, *Acc. Chem. Res.* **1997**, *30*, 402-407.
[34] C.-Y. Liu, P. Knochel, *Org. Lett.* **2005**, *7*, 2543-2546.

*i*PrMgCl·LiCl **10** was also the reagent of choice for the diverse functionalization of arenes bearing a sulfoxide moiety **14** by a so far barely described sulfoxide-magnesium exchange reaction.[35] Thus, by using the chameleon chemical behaviour of the sulfoxide moiety, a range of highly functionalized arenes of type **15** were efficiently generated (Scheme 11).[36]



Scheme 11: Functionalization of arenes **14** by sulfoxide-magnesium exchange.

In 2006, *Knochel* and co-workers reported the preparation and the exceptional reactivities of the reagents *i*Pr_2Mg·LiCl **16** and *s*Bu_2Mg·LiCl **17**.[37] These reagents displayed outstanding reactivity in a Br/Mg-exchange on very challenging, electron-rich aryl systems **18** as well as alkenyl bromides. The produced dialkyl magnesiates **19** are of general synthetic value and a range of highly functionalized electron-rich products of type **20** could be prepared (Scheme 12).

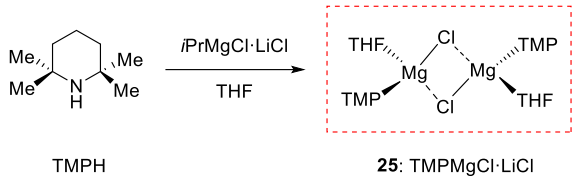


Scheme 12: Br-magnesium exchange on electron-rich, challenging arenes **18** and olefins.

[35] a) S. Ogawa, N. Furukawa, *J. Org. Chem.* **1991**, *56*, 5723-5726; b) M. Annunziata, M. Capozzi, C. Cardellichio, F. Naso, G. Spina, P. Tortorella, *J. Org. Chem.* **2001**, *66*, 5933-5936; c) T. Yamamoto, S. Ogawa, M. Sugawara, Y. Kawai, R. Sato, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 460-467.
[36] C. B. Rauhut, L. Melzig, P. Knochel, *Org. Lett.* **2008**, *10*, 3891-3894.
[37] A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 159-162.

2.4 Directed Metalation

While both, oxidative insertion or halogen-metal exchange require the presence of a halogen-carbon bond, organometallic reagents can also be prepared by directed metalation of a hydrogen-carbon bond. Initially discovered by *Gilman*[38] and *Wittig*,[39] the directed metalation strategy was developed by *Snieckus*,[40] *Hauser*,[41] *Eaton*[42] and *Mulzer*.[43] Alkyllithiums such as *n*BuLi, *s*BuLi or *t*BuLi and strong lithium amides such as lithium diisoproylamide (LDA, **21**) or TMPLi (TMP = 2,2,6,6-tetramethylpiperidine) **22** are commonly used for such metalations.[44] Despite the frequent use of lithium reagents for metalations in chemical literature, the high reactivity of organolithium reagents hampers their use for highly functionalized substrates and requires low reaction temperatures. Thus, alternative organometallic reagents displaying higher functional group tolerance are desired. In 1947, *Hauser* and *Walker* developed organomagnesium amides of the type R_2NMgX (X = Br, Cl) and $(R_2N)_2Mg$, known as *Hauser* bases.[45] Based on these encouraging results, *Eaton* reported the preparation of TMP_2Mg **23** and its use for the magnesiation of arenes,[46] which was further investigated by *Mulzer* using TMPMgCl **24**. These early amide bases however tended to form aggregates resulting in solubility issues and low kinetic basicity, thus requiring a large excess of the used organometallic base.[47] A huge improvement was achieved by *Knochel* and co-workers by developing a highly reactive LiCl-solubilized magnesium amide base TMPMgCl·LiCl **25**, which can be smoothly prepared by treating *i*PrMgCl·LiCl **10** with TMPH in THF. The resulting base showed a range of valuable properties comprising excellent solubility, high kinetic basicity and stability (Scheme 13).[48]

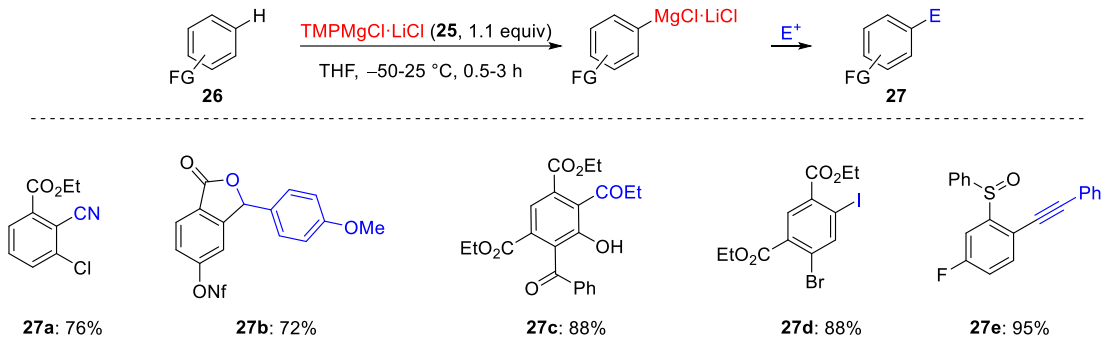


TMPH **25**: TMPMgCl·LiCl

Scheme 13: Preparation of TMPMgCl·LiCl **25**.

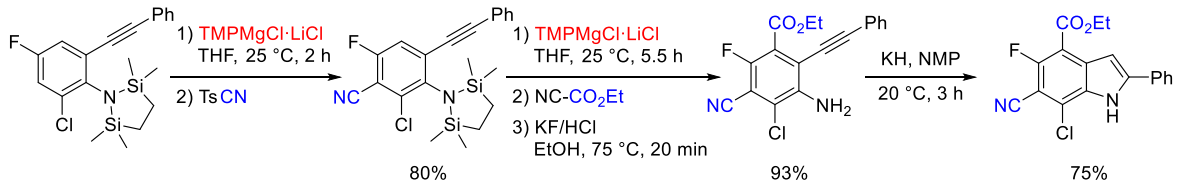
[38] H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109-112.
[39] G. Wittig, G. Fuhrmann, *Ber. Dtsch. Chem. Ges.* **1940**, *73*, 1197-1218.
[40] V. Snieckus, *Chem. Rev.* **1990**, *90*, 879-933.
[41] a) C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295-297; b) F. C. Frostick, C. R. Hauser, *J. Am. Chem. Soc.* **1949**, *71*, 1350-1352.
[42] P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016-8018.
[43] a) W. Schlecker, A. Huth, E. ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414-8416; b) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *Liebigs Ann.* **1995**, 1441-1446; c) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *Synthesis* **1995**, 1225-1227.
[44] a) M. Schlosser, *Angew. Chem. Int. Ed.* **2005**, *44*, 376-393; b) P. Beak, V. Snieckus, *Acc. Chem. Res.* **1982**, *15*, 306-312; c) M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206-2225.
[45] C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295-297.
[46] a) P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016-8018; b) P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc.* **1993**, 115, 11370-11375.
[47] W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414-8416.
[48] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961; b) P. García-Álvarez, D. V. Graham, E. Hevia, A. R. Kennedy, J. Klett, R. E. Mulvey, C. T. O'Hara, S. Weatherstone, *Angew. Chem. Int. Ed.* **2008**, *47*, 8079-8081.

TMPMgCl·LiCl **25** allowed the efficient magnesiation of a range of highly functionalized aromatic compounds **26** bearing sensitive functional groups such as esters, ketones, carbamates, anilines, sulfones and nitriles providing arenes of type **27** (Scheme 14).[49]



Scheme 14: Regioselective magnesiation of arenes **26** bearing sensitive functional groups using TMPMgCl·LiCl.

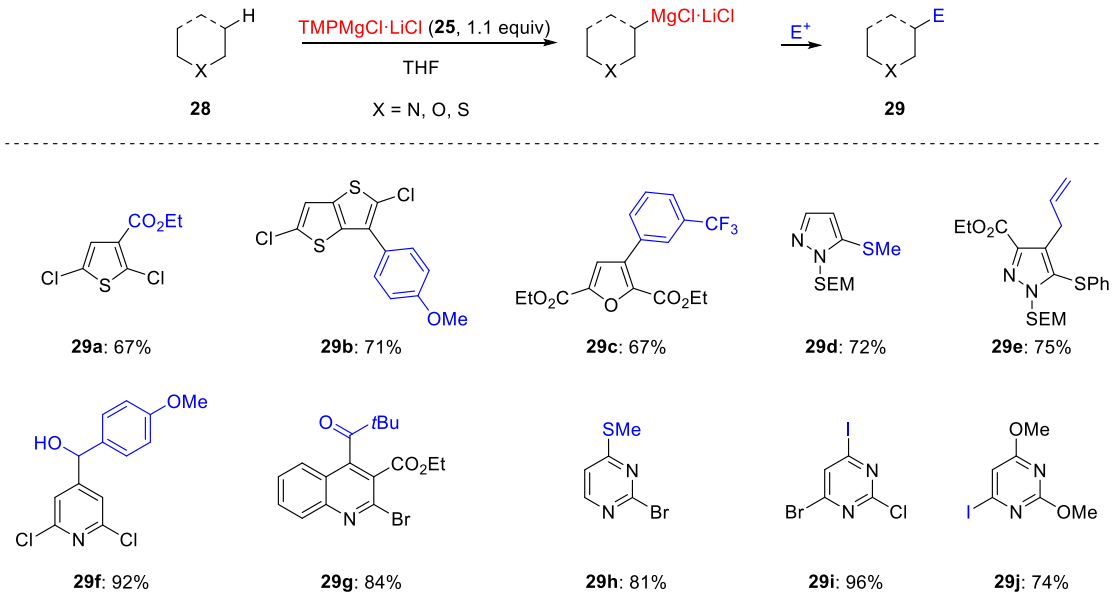
Furthermore, successive magnesiations using TMPMgCl·LiCl **25** on readily available protected aniline derivatives allowed the preparation of hexasubtituted anilines which can be smoothly transformed to highly functionalized indole derivatives (Scheme 15).[50]



Scheme 15: Successive magnesiations of aniline derivative with TMPMgCl·LiCl leading to a polyfunctional indole.

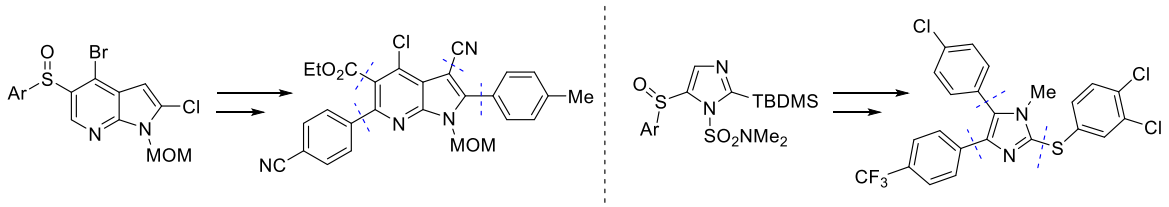
TMPMgCl·LiCl (**25**) also proved to be very useful for the selective magnesiation of a wide range of heterocycles **28** such as thiophenes,[51] furans[52] and *N*-heterocycles (pyridines, quinolines, pyrimidines, pyrazoles).[53] Both electron-rich and electron-poor heteroaromatic compounds were readily metalated, while the presence of electron-withdrawing substituents considerably facilitates the magnesiation. The developed methodologies provided an immense library of pharmaceutical relevant, highly functionalized scaffolds **29** (Scheme 16).

[49] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961; b) J. Clayden, C. C. Stimson, M. Keenan, *Chem. Commun.* **2006**, 1393-1394; c) J. Högermeier, H.-U. Reissig, *Adv. Synth. Catal.* **2009**, *351*, 2747-2763; d) A. H. Stoll, P. Knochel, *Org. Lett.* **2008**, *10*, 113-116; e) C. B. Rauhut, L. Melzig, P. Knochel, *Synthesis* **2009**, 1041-1048; d) T. Bresser, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *123*, 1954-1958.
[50] a) A. H. Stoll, P. Knochel, *Org. Lett.* **2008**, *10*, 113-116; b) C. Koradin, W. Dohle, A. L. Rodriguez, B. Schmid, P. Knochel, *Tetrahedron Lett.* **2003**, *59*, 1571-1587; c) A. Arcadi, S. Cacchi, G. Fabrizi, F. Marinelli, L. M. Parisi, *J. Org. Chem.* **2005**, *70*, 6213-6217.
[51] F. M. Piller, P. Knochel, *Org. Lett.* **2009**, *11*445-448.
[52] a) F. Piller, P. Knochel, *Synthesis* **2011**, 1751-1758; b) L. Melzig, C. B. Rauhut, P. Knochel, *Chem. Commun.* **2009**, 3536-3538.
[53] a) C. Despotopoulou, L. Klier, P. Knochel, *Org. Lett.* **2009**, *11*, 3326-3329; b) A. Krasovskiy, V. Krasovkskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *118*, 3024-3027; c) S. H. Wunderlich, C. J. Rohbogner, A. Unsinn, P. Knochel, *Org. Process Res. Dev.* **2010**, *14*, 339-345; d) N. Boudet, J. R. Lachs, P. Knochel, *Org. Lett.* **2007**, *9*, 5525-5528; e) C. J. Rohbogner, S. Wirth, P. Knochel, *Org. Lett.* **2010**, *12*, 1984-1987; f) M. Mosrin, P. Knochel, *Org. Lett.* **2008**, *10*, 2497-2500; g) M. Mosrin, N. Boudet, P. Knochel, *Org. Biomol. Chem.* **2008**, *6*, 3237-3239.



Scheme 16: Regioselective magnesiation of heterocycles **28** using TMPMgCl·LiCl (**25**).

Remarkably, TMPMgCl·LiCl **25** can be also used in several key steps for the full functionalization of pharmaceutically relevant scaffolds such as *N*-heterocycles. Thus, sequences consisting of directed metalations and halogen/sulfoxide-magnesium exchange reactions provided fully functionalized 7-azaindoles and imidazoles (Scheme 17).[54]

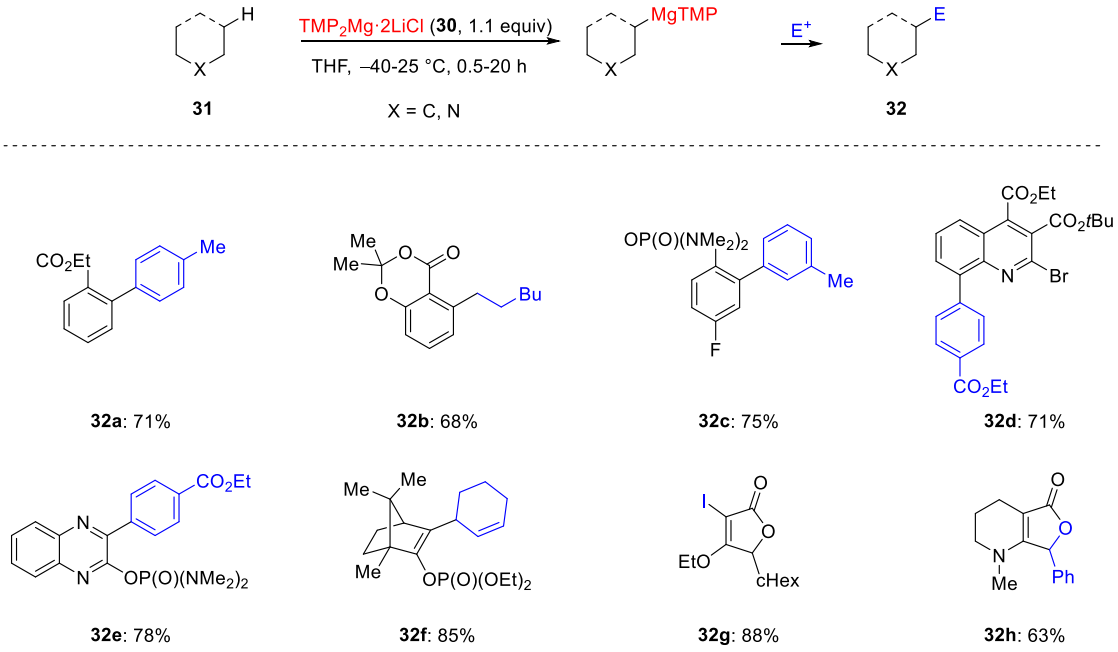


Scheme 17: Full functionalization of heterocyclic *N*-scaffolds by directed metalation and halogen- or sulfoxide-magnesium exchange reactions.

Aromatics bearing electron-donating substituents or weakly electron-accepting substituents are difficult to magnesiate with TMPMgCl·LiCl **25** at low temperatures. Considerably long reaction times are required which result in the observation of competitive side reactions. Thus, the development of a stronger base was desired which was realized by the organomagnesium amide $TMP_2Mg·2LiCl$ **30**, which can be smoothly prepared by treatment of TMPMgCl·LiCl **25** with TMPLi **22** within 0.5 h.[55] The high basicity of $TMP_2Mg·2LiCl$ **30** allowed the magnesiation of otherwise difficult accessible

[54] a) N. M. Barl, E. Sansiaume-Dagousset, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2013**, *52*, 10093-10096; b) C. Sämann, E. Coya, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 1430-1434.
[55] G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *119*, 7825-7828.

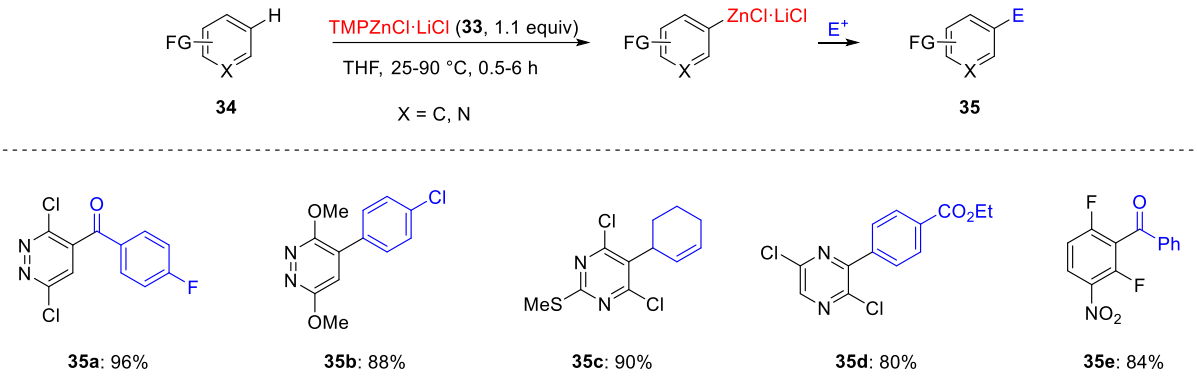
substrates comprising aromatics,[56] heterocycles[57] and even non-aromatic systems **31** and gave access to highly functionalized substrates of type **32** (Scheme 18).[58]



Scheme 18: Magnesiation of challenging substrates **31** using $TMP_2Mg·2LiCl$ **30**.

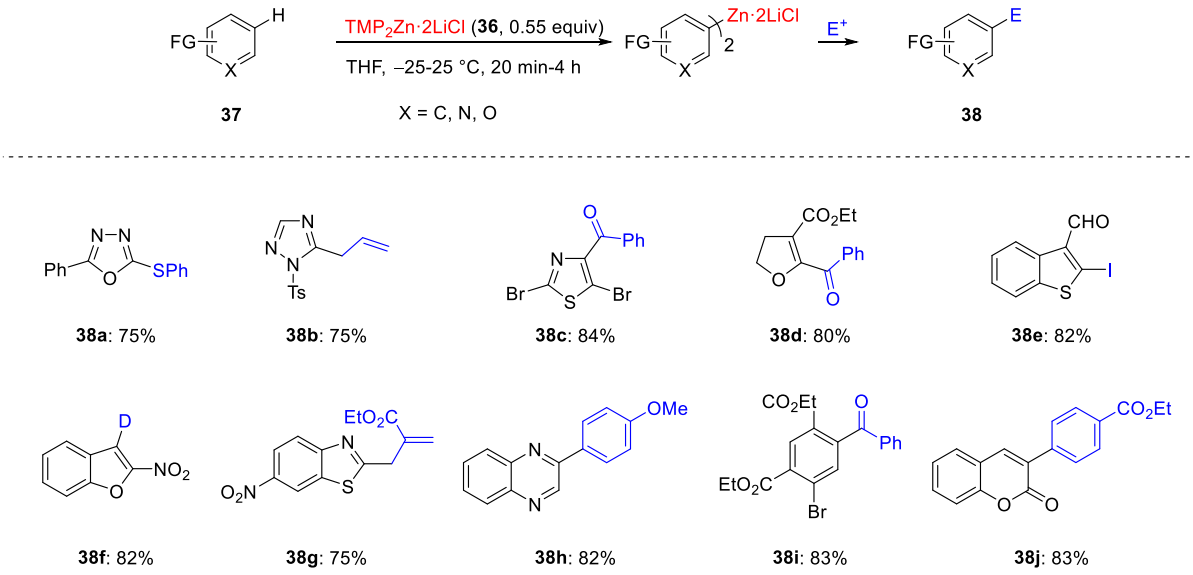
The above-mentioned TMP-magnesium bases TMPMgCl·LiCl (**25**) and $TMP_2Mg·2LiCl$ (**30**) displayed a high tolerance towards important functional groups such as nitriles, esters and aryl ketones but there are still a number of relevant functional groups, such as nitro, aldehyde, methyl ketone or electron-poor *N*-heterocycles, which are not compatible with these magnesium bases. The use of zinc as the cation was especially appropriate, since it is a low-cost, non-toxic metal and the resulting aryl or heteroaryl zinc reagents are compatible with sensitive functional groups.[59] Treatment of TMPLi (**22**) with $ZnCl_2$ in THF produced the LiCl-solubilized base TMPZnCl·LiCl **33**, which is stable at room temperature.[60] Zincations with this reagent were usually performed at convenient non-cryogenic temperatures and were compatible with a wide range of sensitive, functionalized scaffolds such as those of type **34** (Scheme 19).[61]

[56] C. J. Rohbogner, G. C. Clososki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *120*, 1526-1530.
[57] a) N. Boudet, S. R. Dubbaka, P. Knochel, *Org. Lett.* **2008**, *10*, 1715-1718; b) C. Despotopoulou, C. Gignoux, D- McConnell, P. Knochel, *Synthesis* **2009**, 3661-3671.
[58] a) F. M. Piller, T. Bresser, M. K. R. Fischer, P. Knochel, *J. Org. Chem.* **2010**, *75*, 4365-4375; b) T. Bresser, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *123*, 1954-1958.
[59] P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker, *Org. React.* **2001**, *58*, 417-731.
[60] M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837-1840.
[61] a) T. Bresser, G. Monzon, M. Mosrin, P. Knochel, *Org. Process Res. Dev.* **2010**, *14*, 1299-1303; b) F. Crestey, P. Knochel, *Synthesis* **2010**, 1097-1106; c) M. Mosrin, T. Bresser, P. Knochel, *Org. Lett.* **2009**, *11*, 3406-3409.



Scheme 19: Regioselective zincation of sensitive heterocycles and arenes **34** bearing sensitive functional groups using TMPZnCl·LiCl **33**.

Nevertheless, TMPZnCl·LiCl (**33**) usually failed in the efficient zincation of relatively unreactive unsaturated substrates. Thus, there was a need for a more powerful zinc base, which was realized in the form of $TMP_2Zn·2MgCl_2·2LiCl$ **36** (abbreviated as $TMP_2Zn·2LiCl$). Combination of TMPMgCl·LiCl (**25**) with 0.5 equivalents $ZnCl_2$ resulted in the quantitative formation of the above mentioned reagent,[62] whereas LiCl ensured a good solubility of the base and $MgCl_2$ considerably enhanced its kinetic basicity. The developed base allowed the efficient zincation of sensitive heterocycles such as 1,3,4-oxadiazoles and 1,2,4-triazoles, quinoxalines and moderate reactive substrates such as coumarin or ethyl benzoate of general type **37** (Scheme 20).[63] A range of valuable building blocks of type **38** were obtained.

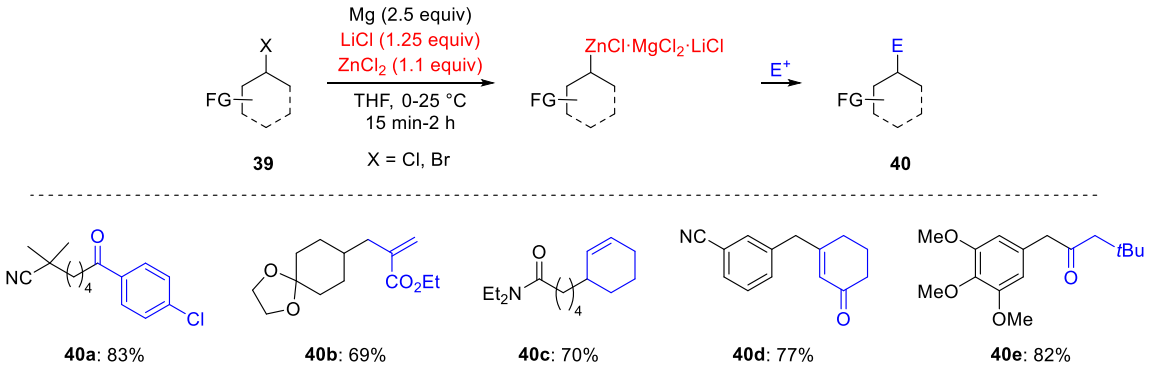


Scheme 20: Regioselective zincation of sensitive heterocycles and unreactive arenes **37** bearing sensitive functional groups using $TMP_2Zn·2LiCl$ **36**.

[62] S. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685-7688.
[63] a) T. Bresser , P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 1914-1917; b) Z. Dong, G. C. Clososki, S. Wunderlich, A. Unsinn, J. Li, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 457-468.

2.5 Transmetalation

Transmetalation reactions can be considered as key transformations in synthetic organic chemistry allowing adjustment of the reactivity of the particular organometallic reagent. Hereby, undesired side reactions can be avoided. The most common procedure is the treatment of an organometallic species R^1-Met^1 with a metal salt of type Met^2-X_n producing the new desired organometallic of type R^1-Met^2. As previously mentioned, the driving force is the formation of a stronger carbon-metal bond, e.g. with a more covalent character. Organozinc reagents display high stability, a highly covalent C-Met bond and a wide range of synthetic applications. Thus, a transformation starting from various reactive organometallics such as organolithiums and organomagnesiums is feasible.[64] Usually, the transformation is realized by treatment of the more reactive organometallics with a suitable zinc salt. *Knochel* and co-workers developed a new method for the preparation of highly functionalized organozinc reagents by oxidative magnesium insertion into aryl-halide bonds in the presence of $ZnCl_2$. Since the oxidative insertion of magnesium proceeds remarkably faster than the insertion of zinc, this method allowed the use of rather unreactive halides **39**. A range of functional groups such as esters or nitriles could be tolerated, since the transmetalation proceeds faster than a possible attack of the formed organomagnesium reagent and allowed access to a range of polyfunctional arenes of type **40**.[65]



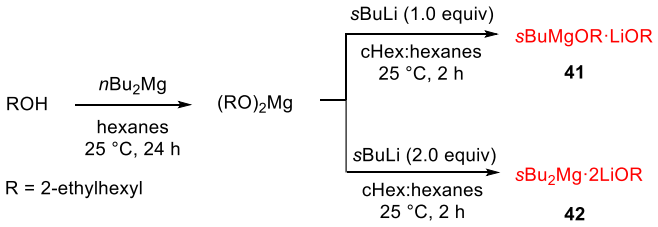
Scheme 21: In situ transmetalation of organomagnesium reagents formed by oxidative insertion.

Furthermore, both organozinc and organomagnesium reagents could be efficiently transmetalated to the corresponding copper reagents by using CuCN·2LiCl. The formed organocopper displayed excellent reactivity towards selective acylation, allylation and 1,4-addition reactions.[66]

[64] P. Knochel, *Handbook of Functionalized Organometallics, Vol. 1 and 2,* Wiley-VCH, Weinheim, **2005**.
[65] a) A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824-5826; b) T. D. Blümke, F. M. Piller, P. Knochel, *Chem. Commun.* **2010**, *46*, 4082-4084.
[66] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2392-2394.

2.6 Organometallic Reagents in Hydrocarbons

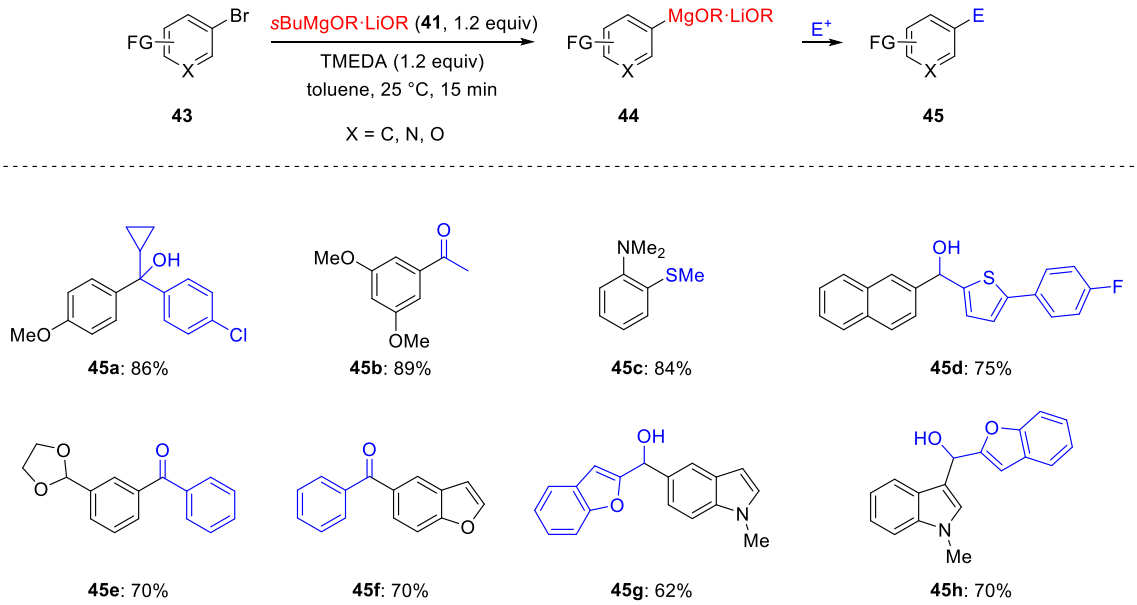
Organometallic-based reactions are commonly carried out in etheral solvents such as diethyl ether and THF providing high solubility and enhanced reactivity. These solvents display some drawbacks such as safety hazards as well as carcinogenetic properties.[67] Furthermore, only a few methods have been reported for the preparation of organometallics in non-polar solvents such as hydrocarbons.[68] Organometallic reagents may display original and unusual reactivities in these weakly-coordinating solvents. Additionally, hydrocarbons are industrially friendly solvents, since they improve aqueous extraction during work-up.[69] Thus, *Knochel* and co-workers developed the novel magnesium alkoxide reagents *s*BuMgOR·LiOR **41** and *s*Bu_2Mg·2LiOR (R = 2-ethylhexyl) **42** in industrially friendly toluene. Both reagents can be obtained by treating the alkoxide $(RO)_2Mg$ with one or two equivalents *s*BuLi in particular. The alkoxide itself is readily available by reacting commercial *n*Bu_2Mg with 2-ethylhexanol (Scheme 22).[70]



Scheme 22: Preparation of new organomagnesium reagents **41** and **42** in hydrocarbons.

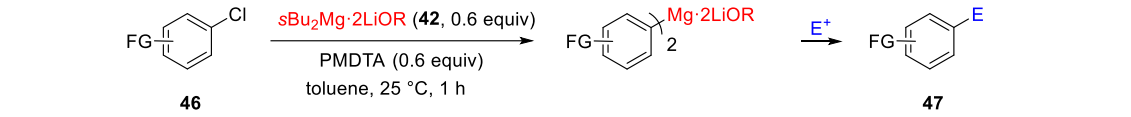
These two reagents proved to be outstanding powerful reagents for the Br/Mg exchange with aryl and heteroaryl bromides **43** producing highly soluble aryl and heteroaryl magnesium alkoxides **44** in toluene. The addition of *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TMEDA) or *N*,*N*,*N'*,*N''*,*N'''*-pentamethyldiethylenetriamine (PMDTA) further improved the reactivity.[71] The formed Grignard reagents **44** showed excellent reactivity with a broad range of electrophiles such as aldehydes, ketones, allyl bromides, acyl chlorides, epoxides and aziridines and provided various polyfunctional arenes and heteroarenes of type **45** (Scheme 23).

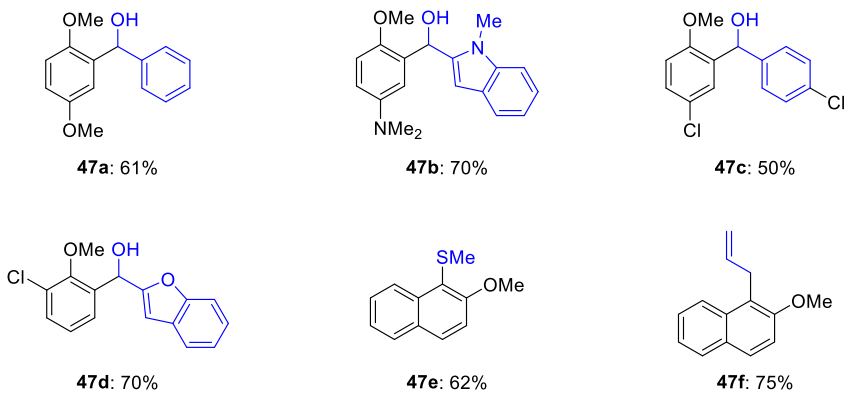
[67] A. Jordan, C. G. J. Hall, L. R. Thorp, H. F. Sneddon, *Chem. Rev.* **2022**, *122*, 6749-6794.
[68] a) C. G. Screttas, M. Micha-Screttas, *J. Organomet. Chem.* **1985**, *290*, 1-13; b) T. Iida, T. Wada, K. Tomimoto, T. Mase, *Tetrahedron Lett.* **2001**, *42*, 4841-4844; c) E. S. Baillie, T. D. Blümke, A. R. Kennedy, W. Clegg, J. klett, L. Russo, M. de Tullio, E. Hevia, *Chem. Commun.* **2014**, *50*, 12859-12862.
[69] L. Delhaye, A. Ceccato, P. Jacobs, C. Köttgen, A. Merschaert, *Org. Process Res. Dev.* **2007**, *11*, 160-164.
[70] D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701-6704.
[71] F. M. Perna, A. Salomone, M. Dammacco, S. Florio, V. Capriati, *Chem. Eur. J.* **2011**, *17*, 8216-8225.



Scheme 23: Br/Mg exchange with (hetero)aryl bromides **43** using sBuMgOR·LiOR **41**.

Remarkably, the reagent *s*Bu_2Mg·2LiOR **42** proved its outstanding reactivity by facilitating the first described Cl/Mg exchange with various electron-rich aryl chlorides **46** (Scheme 24).

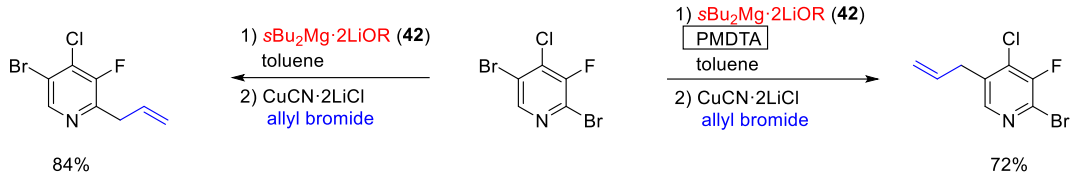




Scheme 24: First Cl/Mg exchange with aryl chlorides using sBu$_2$Mg·2LiOR (**42**).

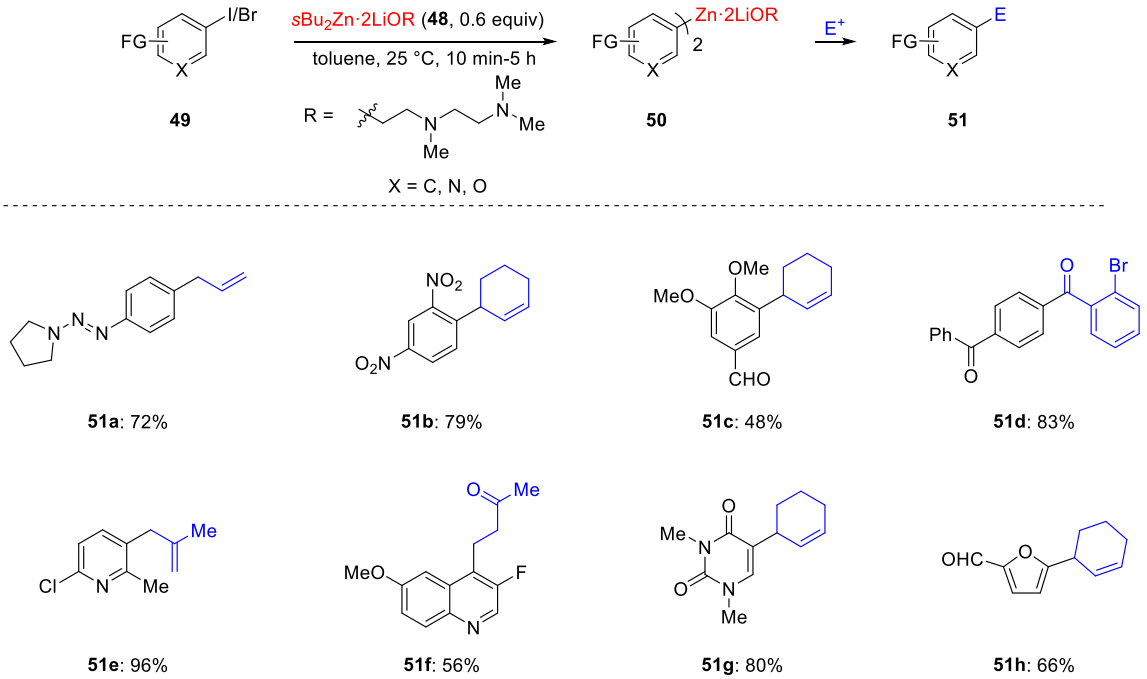
The use of *s*Bu_2Mg·2LiOR **42** was extended to the regioselective Br/Mg exchange with various dibromo-arenes and –heteroarenes. The regioselectivity of the exchange was finely tuned by the coordination preference of lithium, which can be switched by the addition of Lewis donors such as PMDTA (Scheme 25).[72]

[72] A. Desaintjean, T. Haupt, L. J. Bole, N. R. Judge, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 1513-1518.



Scheme 25: Selective Br/Mg exchange of polyhalogenated (hetero)arenes using *s*Bu$_2$Mg·2LiOR (**42**).

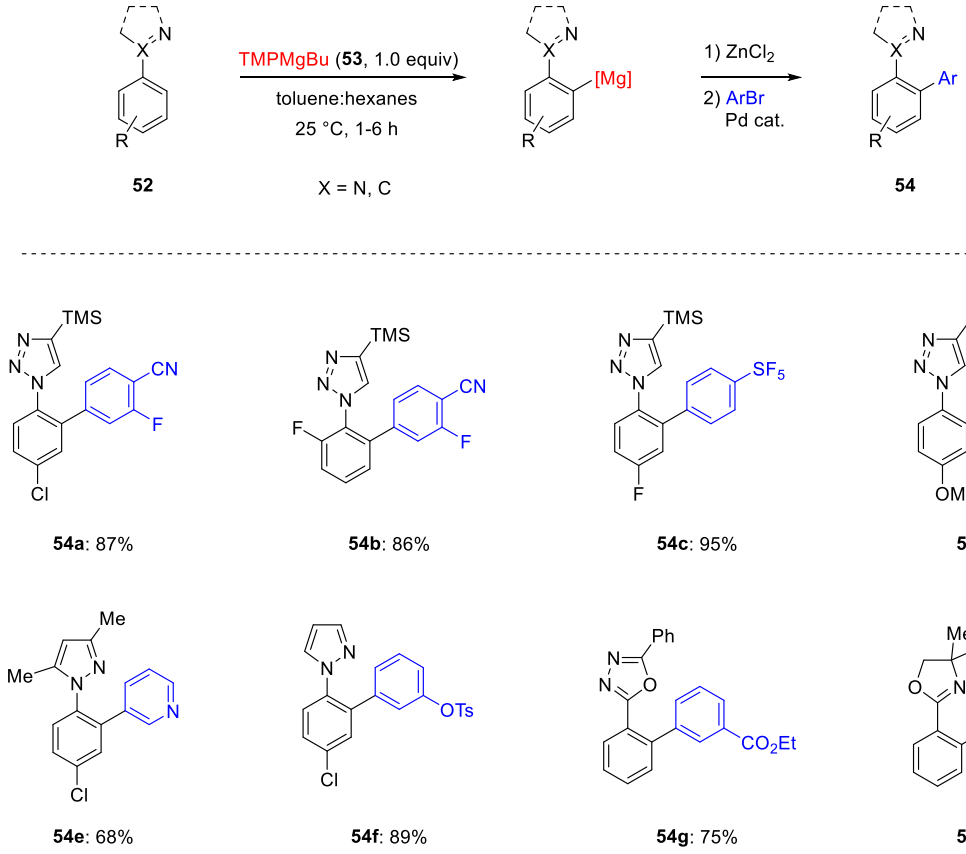
Encouraged by these outstanding results, *Knochel* and co-workers developed the complementary bimetallic zinc reagent *s*Bu$_2$Zn·2LiOR (R = CH_2CH_2N-$(CH_3)CH_2CH_2N(CH_3)_2$)) **48** allowing the highly efficient I/Zn or Br/Zn exchange with arenes bearing highly sensitive functional groups such as triazines, ketones, aldehydes or nitro groups. The reagent was readily obtained by reacting Et_2Zn in toluene with two equivalents of the alcohol (25 °C, 4 h) affording the corresponding ethylzinc alkoxides co-complexed with the corresponding alcohol.[73] Further reaction with *s*BuLi (two equivalents) produced the desired bimetallic reagent **48**, which can be stored at 25 °C for months without significant loss of reactivity. The performed exchange reactions processed at room temperature and the in situ generated zinc organometallics of type **50** showed excellent reactivity towards a range of electrophiles (Scheme 26) and provided a range of sensitive substrates **51**. Structural and spectroscopic studies suggested the formation of a highly reactive lithium *bis*(alkyl)bis-(alkoxy)zincate.[74]



Scheme 26: I/Zn and Br/Zn exchange on (hetero)aryl halides **49** using *s*Bu$_2$Zn·2LiOR (**48**).

[73] M. S. Hill, G. Kociok-Köhn, K. C. Molloy, D. C. Stanton, *Main Group Met. Chem.* **2015**, *38*, 61.
[74] M. Balkenhohl, D. S. Ziegler, A. Desaintjean, L. J. Bole, A. R. Kennedy, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 12898-12902.

N-aryl azole scaffolds of type **52** are ubiquitous moieties present in a range of experimental and marketed drugs.[75] As part of an ongoing development program, the selective and efficient metalation of aryl-1*H*-1,2,3-triazoles on the aryl ring became emergent. Established metalation agents such as TMPLi (**22**), LDA (**21**), TMPMgCl·LiCl (**25**) or $TMP_2Mg·2LiCl$ (**30**) showed unsatisfying results comprising undesired metalation at the heterocycle itself and led to decomposition. Well-established strategies involve transition-metal catalyzed C-H arylations, requiring harsh conditions and often leading to *bis*-arylated products.[76] Knochel and co-workers developed an approach avoiding the use of a coordinating solvent such as THF, which competes with the nitrogen atom of the azole ring in complexation of the base,[77] by using TMPMgBu **53** in hexanes.[78] The highly ortho-selective magnesiations were usually conducted at room temperature and subsequent Negishi cross-coupling furnished hardly-accessible pharmaceutical relevant substrates of type **54** (Scheme 27).



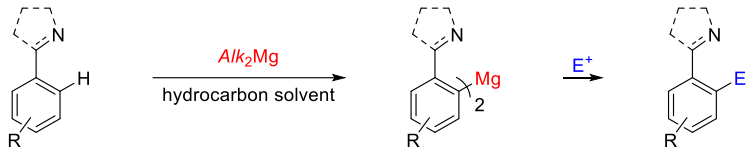
Scheme 27: Regioselective ortho-magnesiation of aryl azoles **52** using TMPMgBu (**53**) in hexanes.

[75] a) T. D. Penning, J. J. Talley, W. E. Perkins, K. Seibert, Y. Y. Zhang, *J. Med. Chem.* **1997**, *40*, 1347-1365; b) D. J. Pinto, M. J. Orwat, S. Koch, K. A. Rossi, R. M. Knabb, *J. Med. Chem.* **2007**, *50*, 5339-5356.
[76] D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174-238.
[77] M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206-2225.
[78] F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, *Nature Commun.* **2020**, *11*, 4443.

3. Objectives

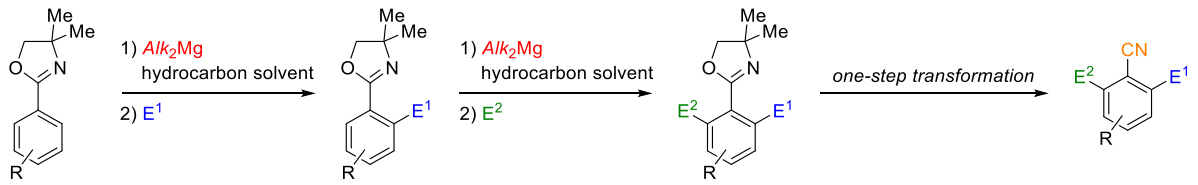
C-C bond forming reactions are essential tools in modern synthetic organic chemistry. As described above, organometallic reagents are commonly used for this kind of tranformations and find broad applications in providing highly functionalized and pharmaceutically relevant structures. In particular, the directed metalation on a C-H bond can for instance be realized by the use of a range of mostly amide based organomagnesium reagents such as TMPMgCl·LiCl or TMP_2Mg·2LiCl. The corresponding Grignard reagents are commonly prepared in etheral solvents providing high solubility and activity and their preparation as well as properties in hydrocarbon solvents are barely described.

Preliminary results provide a highly regioselective and mild *ortho*-functionalization of aryl azoles at the aryl moiety by using the mixed magnesium amide base TMPMgBu in hexanes as the solvent. This motifs can be nowadays considered as core structures in modern pharmaceutical development and the desired transformation was so far only realized by transition-metal catalyzed C-H arylation under harsh conditions. Additionally, the predomimant formation of undesired *ortho,ortho´*-functionalized arenes limits the applicability of this C-H activation strategy. However, an excess of aryl halides as electrophile in Negishi cross-coupling sequences was mandatory to compensate the formation of undesired side-products. Thus, a simple hydrocarbons soluble and readily available *bis*-alkylmagnesium reagent overcoming this problem and still ensuring the desired regioselectivity should be developed (Scheme 28). Furthermore, the general reactivity towards a range of functionalized and sensitive arenes should be explored.



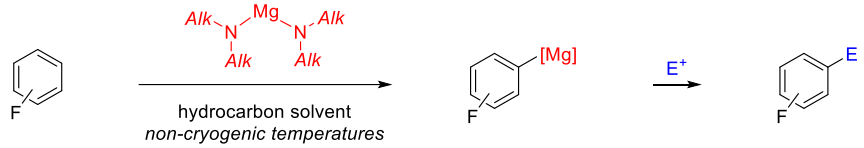
Scheme 28: Regioselective magnesiation of aryl azoles using a *bis*-alkylmagnesium reagent.

Aromatic nitriles are key intermediates in organic synthesis providing access to a range of *N*-heterocycles or further transformations. Usually, they can be prepared from various precursors such as aromatic aldehydes, hydrocarbons, carboxylic acid derivatives, halides or benzylic derivatives. The oxazoline moiety is a readily available functional group developed in pioneering work by *Meyers* showing applications as protecting group of carboxylic acids, as versatile ligands and as very strong metal-directing group. This heterocycle is often difficult to cleave and usually requires very harsh conditions. Furthermore, a direct conversion to the corresponding nitrile is barely described. The aim of the second project is the development of a successive *ortho,ortho´*-functionalization of aryl oxazolines and the subsequent transformation to their corresponding nitriles. This methodology would in general valorize the chemistry of aryl oxazolines and provide otherwise difficult accessible aryl nitriles (Scheme 29).



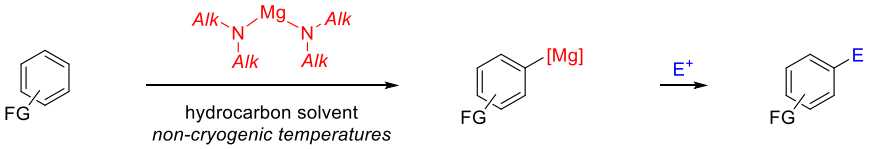
Scheme 29: Successive *ortho,ortho´*-magnesiations of aryl oxazolines followed by a one-step transformation to their corresponding nitriles.

The special nature of fluorine affects the properties of biologically active molecules by for instance enhanced binding interactions, metabolic stability, changes in physical properties and selective reactivities. The metalation of fluorinated aromatics may be complicated by the formation of undesired and highly reactive aryne side products and thus usually requires cryogenic reaction temperatures to supress these side reactions. Due to the increasing demand of highly functionalized fluorinated aromatics, the third project aims at the development of a hydrocarbon soluble magnesiation agent for these above mentioned targets. It is anticipated that magnesiated fluoroaromatics should be significantly more stable in hydrocarbons and could be generated under convenient non-cryogenic conditions. Apart from this, due to the high cost of TMPH, a more economically benign amine should be tested for its suitability as component in the organometallic base (Scheme 30).



Scheme 30: Non-cryogenic magnesiations of fluorinated arenes in hydrocarbons.

The regioselective and efficient metalation of arenes bearing sensitive functional groups and sensitive heteroarenes is usually realized by using highly active magnesium- and zinc amides in etheral solvents such as THF under cryogenic conditions. Cryogenic conditions are mandatory in order to supress undesired side reactions with functional groups or decomposition reactions. The use of complementary reagents in hydrocarbon solvents and investigation of their reactivity is barely described. Thus, a hydrocarbon soluble magnesium amide allowing the magnesiation of sensitive arenes and heteroarenes under non-cryogenic conditions should be developed in the last project (Scheme 31).



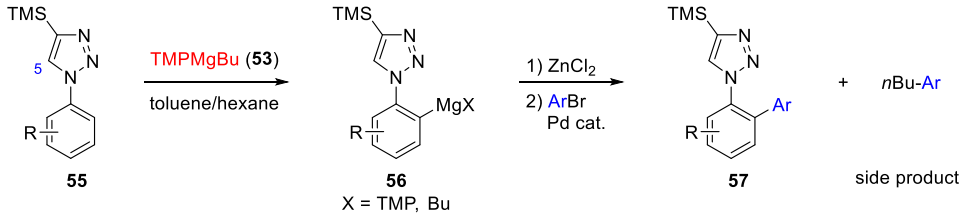
Scheme 31: Non-cryogenic magnesiations of arenes bearing sensitive functional groups.

B. RESULTS AND DISCUSSION

1. Directed Regioselective *Ortho*,*Ortho*´-Magnesiations of Aromatics and Heterocycles Using *s*Bu_2Mg in Toluene

1.1 Introduction

The directed magnesiation of arenes and heteroarenes is an important synthetic tool for the preparation of polyfunctional aryl- and heteroaryl-magnesium organometallics.[79] Mixed magnesium and lithium amides $R_2NMgX{\cdot}LiCl$ are usually the most efficient reagents for such metalations.[80] Recently, the regioselective metalation of various pharmaceutically relevant aryl azoles such as **55** was examined.[81] It was found that standard metal amides such as LDA (**21**) or TMPLi **22** (TMP = 2,2,6,6-tetramethylpiperidyl) gave the metalated products **56** with poor regioselectivity, due to a competitive deprotonation at the 5 position of the triazole ring of **55**. The best result was achieved in toluene[82] using the alkylmagnesium amide TMPMgBu[83] **53** prepared from commercial Bu_2Mg in hexanes, which provided after cross-coupling with aryl bromides various products of type **57**. Although this base was highly regioselective in toluene, an excess of ArBr was required to compensate the formation of the Ar-*n*Bu side-product, originating from a faster cross-coupling of the *n*Bu moiety compared to the metalated azole **56** (Scheme 32).



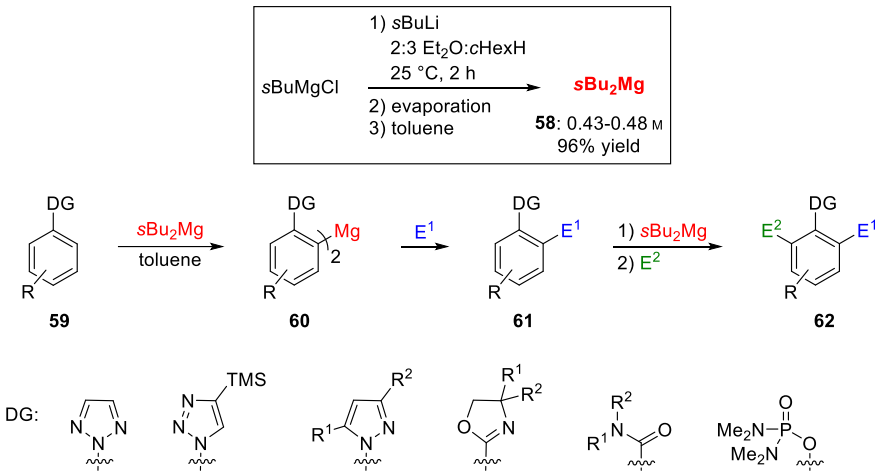
Scheme 32: Regioselective magnesiation and subsequent Negishi cross-coupling of aryl azoles (**55**) using TMPMgBu (**53**) in toluene/hexane.

While commercially available Bu_2Mg contained a 60:40 mixture of *n*Bu_2Mg and *s*Bu_2Mg, only small amounts of the branched coupling side-product Ar-*s*Bu were found, suggesting that the secondary alkyl moiety was reacting much slower than the primary one.

[79]a) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3802-3824; b) K. W. Henderson, W. J. Kerr, *Chem. Eur. J.* **2001**, *7*, 3430-3437; c) C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295-297; d) J. Wei, W.-X. Zhang, Z. Xi, *Org. Chem. Front.* **2014**, *1*, 983-987.
[80]a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961; b) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681-7684; c) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794-9824; d) P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016-8018; e) P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc.* **1993**, *115*, 11370-11375.
[81]F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, *Nat. Comm.* **2020**, *11*, 4443.
[82]D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701-6704.
[83]a) E. Hevia, A. R. Kennedy, R. E. Mulvey, S. Weatherstone, *Angew. Chem. Int. Ed.* **2004**, *43*, 1709-1712; b) B. Conway, E. Hevia, A. R. Kennedy, R. E. Mulvey, S. Weatherstone, *Dalton Trans.* **2005**, 1532-1544.

Below, the preparation of *s*Bu$_2$Mg[84] **58** is reported, which avoided these side reactions and significantly increased the metalation scope. Thus, it was shown that *s*Bu$_2$Mg **58** was an improved magnesiation reagent, which allowed a highly *ortho*-regioselective magnesiation of arenes **59** bearing various directing groups (DG), leading after trapping of the resulting diarylmagnesium species **60** with various electrophiles E^1 to products of type **61**. These polyfunctional arenes were in several cases magnesiated again using *s*Bu$_2$Mg producing, after addition of a second different electrophile E^2, valuable 1,2,3-polyfunctional arenes of type **62**.

The reaction of *s*BuMgCl in diethyl ether with *s*BuLi (1.0 equiv) in cyclohexane at 25 °C (2 h) gave, after solvent evaporation under vacuum, redissolution in toluene and filtration, a 0.43–0.48 M solution of *s*Bu$_2$Mg **58** in 96% yield.[85]



E^1, E^2: aldehydes, ketones, allylic halides, acyl chlorides, Weinreb amides, aryl halides (Negishi cross-coupling).

Scheme 33: Regioselective magnesiation and *ortho,ortho'*-functionalization of arenes and heteroarenes using *s*Bu$_2$Mg **58** in toluene.

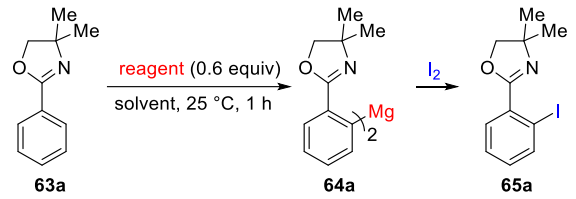
[84] a) L. J. Bole, N. R. Judge, E. Hevia, *Angew. Chem. Int. Ed.* **2021**, *133*, 7704-7709; b) C. W. Kamienski, J. F. Eastham, *J. Organometal. Chem.* **1967**, *8*, 542-546.

[85] This reagent still contained 0.5 equiv of Et$_2$O, having the formula *s*Bu$_2$Mg·0.5Et$_2$O (determined by ^{1}H-NMR analysis) that is abbreviated *s*Bu$_2$Mg for the sake of clarity. The toluene solution of *s*Bu$_2$Mg **58** can be stored at -30 °C for at least 1 week. See Experimental Section.

1.2 Optimization Studies

In preliminary experiments, a smooth magnesiation of oxazoline **63a** with a toluene solution of 0.6 equiv of sBu$_2$Mg leading to the diarylmagnesium **64a** (Table 1) was observed. A full conversion to the diarylmagnesium species was achieved within 1 hour at 25 °C and the iodolyzed product **65a** was isolated in 80% yield (entry 1). sBu$_2$Mg gave also good results in cyclohexane or THF, albeit in lower yields (entries 2-3). cHex$_2$Mg in toluene delivered the desired product **65a** in only 46% yield and other bases such as Ph$_2$Mg, (TMSCH$_2$)$_2$Mg and tBu$_2$Mg or sBuMgCl[86] did not give any conversion (entries 4-8).

Table 1: Magnesiation of oxazoline **63a** using various magnesium reagents in various solvents at 25 °C. [a] Calibrated GC-yield using undecane as internal standard. [b] 1.2 equiv of sBuMgCl were used. [c] Isolated yield.

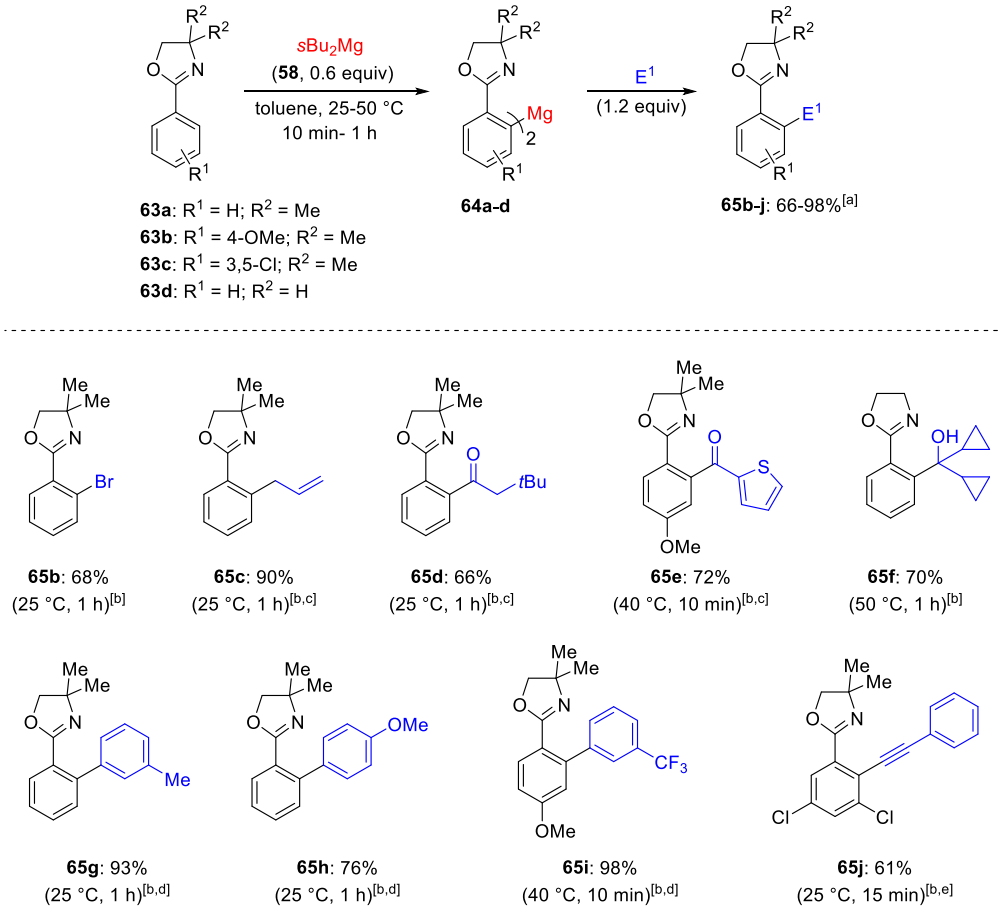


Entry	Reagent	Solvent	Yield[a]
1	sBu$_2$Mg	toluene	91% (80)[c]
2	sBu$_2$Mg	THF	73%
3	sBu$_2$Mg	cyclohexane	64%
4	cHex$_2$Mg	toluene	46%
5	tBu$_2$Mg	toluene	0%
6	(TMSCH$_2$)$_2$Mg	toluene	0%
7	Ph$_2$Mg	toluene	0%
8	sBuMgCl[b]	ether/toluene	0%

1.3 Regioselective Magnesiations of Aryl Oxazolines

Therefore, a range of oxazolines (**63a-d**) were magnesiated selectively on the aryl ring and the resulting diarylmagnesiums (**64a-d**) underwent Negishi cross-couplings[87], copper-catalyzed allylation or acylation,[88] *in situ* Sonogashira cross-coupling[89] or trapping reactions with tetrachlorodibromoethane or dicyclopropylketone, leading to the mono-*ortho* substituted oxazolines **65b**–**j** in 68-98% yield (Scheme 34).

[86] A. Marxer, M. Siegrist, *Helv. Chim. Acta* **1974**, *57*, 1988-2000.
[87] A. O. King, N. Okukado, E.-I. Negishi, *J. Chem. Soc., Chem. Comm.* **1977**, *19*, 683-684.
[88] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390-2392.
[89] a) K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *50*, 4467-4470; b) M. Mosrin, T. Bresser, P. Knochel, *Org. Lett.* **2009**, *11*, 3406-3409.

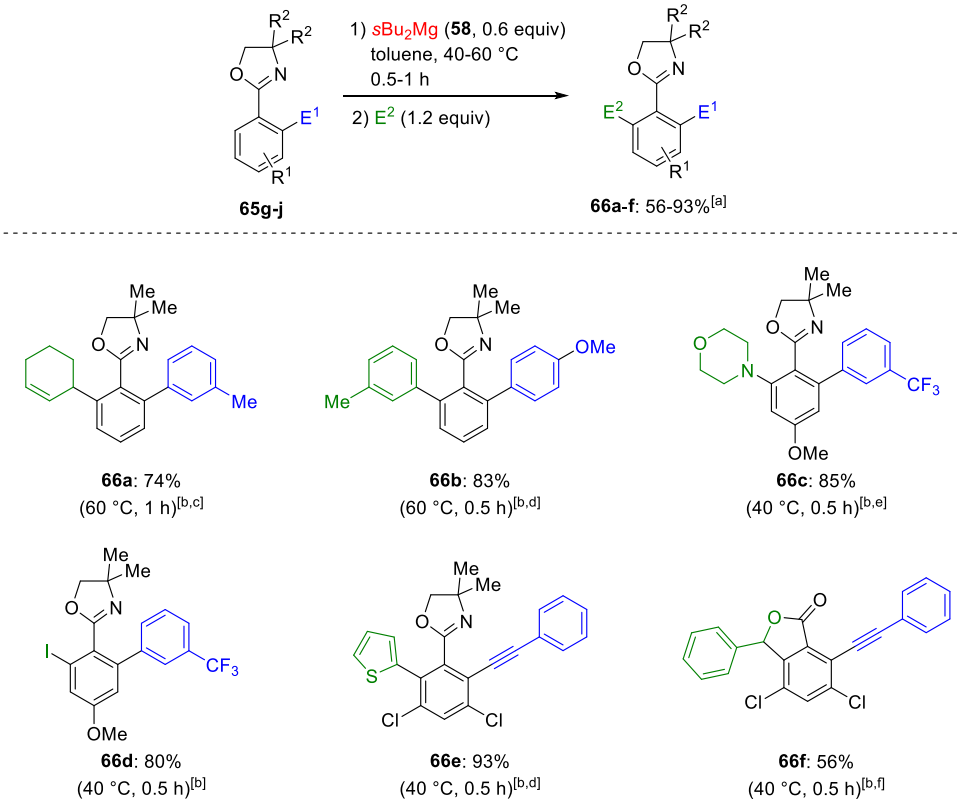


Scheme 34: Regioselective magnesiation of oxazolines **63a-d** with *s*Bu_2Mg **58** leading, *via* diarylmagnesium species **64a-d**, to functionalized oxazolines **65b-j**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] The reaction was catalyzed by CuCN·2LiCl (20 mol%). [d] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [$PdCl_2$(dppf)] (5 mol%, dppf = diphenylphosphinoferrocene) and an aryl halide (0.83 equiv). [e] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv), subsequent iodine quench (1.1 equiv) and Sonogashira cross-coupling with CuI (4 mol%), $Pd(dba)_2$ (3 mol%, dba = dibenzylideneacetone), tri-(2-furyl)-phosphine (6 mol%) and phenylacetylene (1.3 equiv).

Most of the C-H activation methods currently available for the arylation of aryl azoles were performed by using transition metal catalysts and suffered from the unwanted formation of symmetrical *bis*-arylated products and the selective preparation of unsymmetrical *ortho-ortho'*-bis functionalized[90] aryl azoles remained challenging.[91] It was found that various oxazolines **65g-j** were again regioselectively magnesiated at 40-60 °C with *s*Bu_2Mg in toluene (Scheme 35).[92] The intermediate diarylmagnesium species were further functionalized by a copper-catalyzed allylation, Negishi cross-coupling, cobalt-

[90] a) A. J. Martinez-Martinez, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, *Science* **2014**, *346*, 834-837; b) A. J. Martinez-Martinez, S. Justice, B. J. Fleming, A. R. Kennedy, I. D. H. Oswald, C. T. O'Hara, *Sci. Adv.* **2017**, *3*, e1700832.
[91] a) M. Simonetti, D. M. Cannas, X. Just-Baringo, I. J. Vitorica-Yrezabal, I. Larrosa, *Nat. Chem.* **2018**, *10*, 724-731; b) L. Ackermann, A. Althammer, R. Born, *Tetrahedron* **2008**, *64*, 6115-6124; c) S. Oi, H. Sato, S. Sugawara, Y. Inoue, *Org. Lett.* **2008**, *10*, 1823-1826; d) C. J. Teskey, S. M. A. Sohel, D. L. Bunting, S. G. Modha, M. F. Greaney, *Angew. Chem. Int. Ed.* **2017**, *56*, 5263-5266; e) O. Daugulis, V. G. Zaitsev, *Angew. Chem. Int. Ed.* **2005**, *44*, 4046-4048.
[92] A. I. Meyers, W. B. Avila, *J. Org. Chem.* **1981**, *46*, 3881-3886.

catalyzed electrophilic amination[93] and iodolysis furnishing the desired products **66a-e** in 74-93% yield. Interestingly, magnesiation of **65j** followed by trapping with benzaldehyde and subsequent treatment with 6 M HCl provided lactone **66f** in 56% yield.[94]



Scheme 35: Regioselective magnesiation of mono-functionalized oxazolines **65g-j**, leading to *ortho*,*ortho'*-functionalized oxazolines **66a-f**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] The reaction was catalyzed by CuCN·2LiCl (20 mol%). [d] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [$PdCl_2$(dppf)] (5 mol%) and an aryl iodide (0.83 equiv). [e] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a cobalt-catalyzed electrophilic amination with $CoCl_2$ (5 mol%) and morpholino benzoate (1.2 equiv). [f] Obtained after addition of benzaldehyde (1.2 equiv) followed by treatment with 6 M HCl.

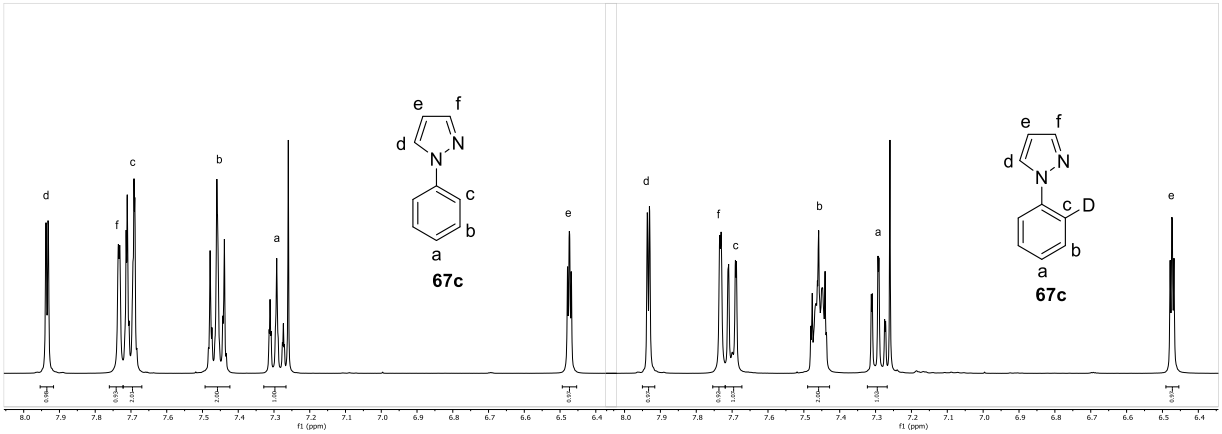
To demonstrate the versatility of the oxazoline directing group, the strongly sterical hindered *ortho*,*ortho'*-functionalized oxazoline **66b** was successfully converted to the corresponding nitrile **66g** using thionyl chloride and DMF[95] in 92% yield (Scheme 36).[96]

[93] a) A. M. Berman, J. S. Johnson, *J. Am. Chem. Soc.* **2004**, *126*, 5680-5681; b) A. M. Berman, J. S. Johnson, *J. Org. Chem.* **2005**, *70*, 364-366; c) M. Campbell, J. S. Johnson, *Org. Lett.* **2007**, *9*, 1521-1524; d) Y.-H. Chen, S. Graßl, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 1108-1111; e) S. Graßl, Y.-H. Chen, C. Hamze, C. P. Tüllmann, P. Knochel, *Org. Lett.* **2019**, *21*, 494-497.
[94] C. A. Boulet, G. A. Poulton, *Heterocycles* **1989**, *28*, 405.
[95] a) O. Fischer, A. Muller, A. Vilsmeier, *J. Prakt. Chem.* **1925**, *109*, 69-87; b) G. Jones, S. P. Stanforth, *Org. React.* **2000**, *56*, 355.
[96] H. Petersen, US2003/13895, 2003, A1.

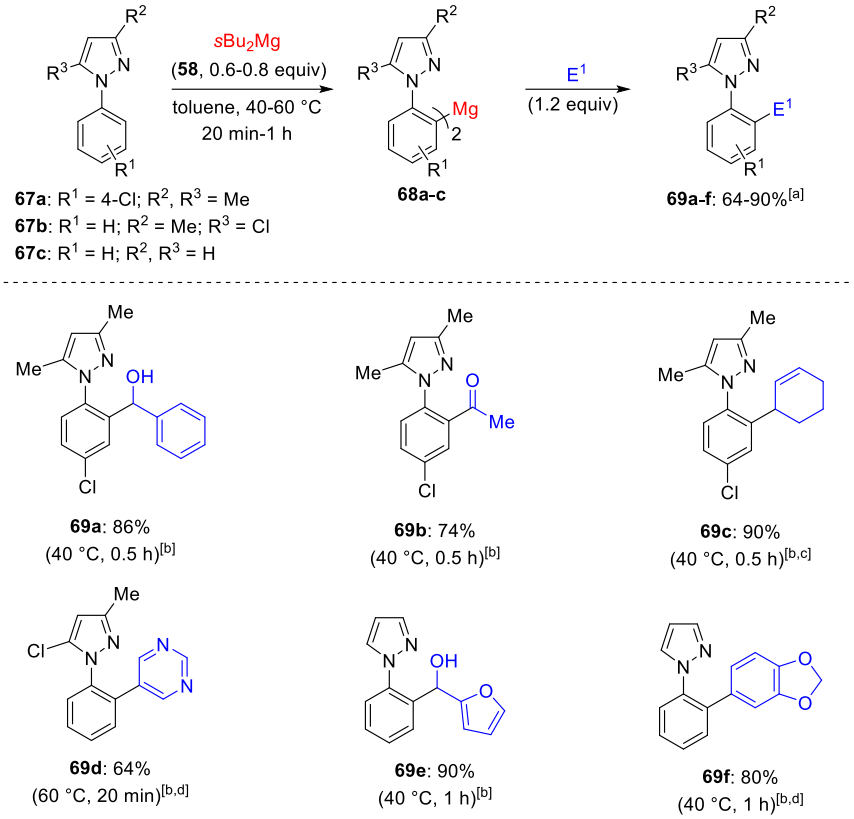
Scheme 36: Transformation of *ortho*,*ortho'*-functionalized oxazoline **66b** to the corresponding nitrile **66g**. [a] Isolated yield.

1.4 Regioselective Magnesiations of Aryl Pyrazoles

In the next step, the magnesiation of various *N*-arylpyrazoles (**67a**–**c**) was examined. *s*Bu_2Mg **58** proved also to be an excellent base for the regioselective magnesiation of *N*-aryl pyrazole **67a**, affording the corresponding *bis*-arylmagnesium species **68a** after 0.5 h at 40 °C. After addition of benzaldehyde or Weinreb amide MeCON(OMe)Me, alcohol **69a** and ketone **69b** were obtained in 74-86% yield (Scheme 38). Copper-catalyzed allylation with 3-bromocyclohex-1-ene produced the pyrazole **69c** (90% yield). Interestingly, *N*-arylpyrazoles **67b** and **67c** although bearing relatively acidic protons at the heterocyclic ring were selectively magnesiated at the *ortho*-position of the phenyl ring. In particular, unsubstituted pyrazole **67c** was metalated in 94% yield and >98:1:1 selectivity, as determined by deuterolysis of a reaction aliquot (Scheme 37). These results further confirmed the key role of the coordination at the *N*(2) atom of the pyrazole to direct the metalation selectively on the aryl ring in a non-polar solvent like toluene. Thus, the functionalized pyrazoles **69d-f** were obtained after Negishi cross-coupling with 5-bromopyrimidine, 5-bromobenzo[*d*][1,3]dioxole or addition of furfural in 64-90% yield.

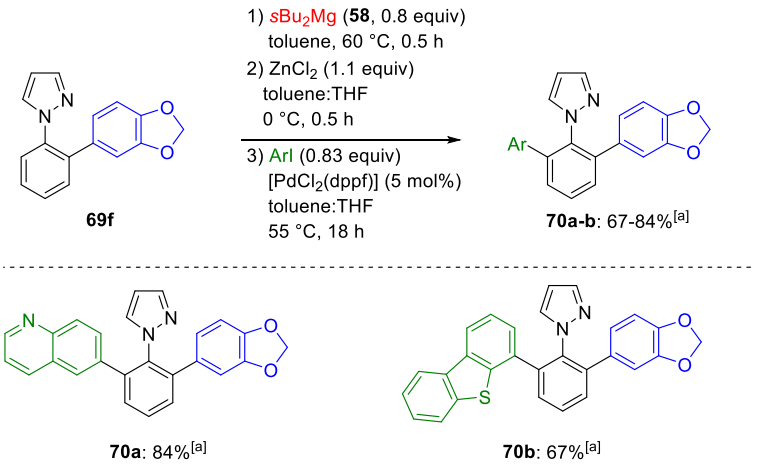


Scheme 37: Deuterolysis experiment on unsubstituted pyrazole **67c**.



Scheme 38: Regioselective magnesiation of *N*-arylpyrazoles **67a-c** with *s*Bu2Mg **58** leading, *via* diarylmagnesium species **68a-c**, to functionalized *N*-arylpyrazoles **69a-f**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] The reaction was catalyzed by CuCN·2LiCl (20 mol%). [d] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross coupling with [$PdCl_2$(dppf)] (5 mol%) and an aryl bromide (0.83 equiv).

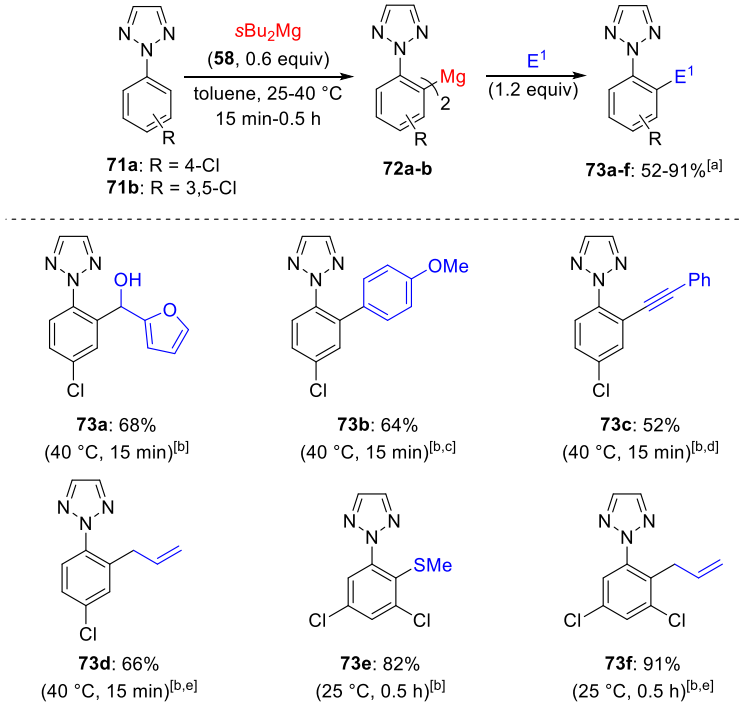
We also achieved an unsymmetrical *ortho*,*ortho'*-functionalization and mono-substituted pyrazole **69f** was selectively magnesiated at 60 °C (0.5 h) and trapped by Negishi cross-coupling with 6-iodoquinoline and 4-iododibenzo[*b*,*d*]thiophene providing the products **70a-b** in 67-84% yield (Scheme 39).



Scheme 39: Regioselective magnesiation of mono-functionalized *N*-aryl pyrazole **69f** with *s*Bu2Mg **58** leading to *ortho*,*ortho'*-functionalized *N*-aryl pyrazoles **70a-b**. [a] All yields refer to isolated compounds.

1.5 Regioselective Magnesiations of Aryl Triazoles

The functionalization of less common heterocycles is of key importance for pharmaceutical applications.[97] Thus, the metalation of symmetrical 2-aryl-2*H*-1,2,3-triazoles **71a-b** was then investigated (Scheme 40).[98] After metalation of **71a** with 0.6 equiv of *s*Bu$_2$Mg **58** for 15 min at 40 °C, the resulting *bis*-arylmagnesium species **72a** was then trapped with furfural, affording the functionalized 1,2,3-triazole **73a** in a 68% yield. Further trapping reactions such as Negishi cross-coupling, copper-catalyzed allylation and oxidative alkynylation with (phenylethynyl)lithium[99] led to 2-aryl-1,2,3-triazoles **73b-d** in 52-66% yield. Similarly, 1,2,3-triazole **71b** was readily magnesiated at 25 °C (0.5 h) as shown by the quantitative formation of a single regioisomer by NMR-analysis of a deuterolyzed reaction aliquot. Further quenching reactions of **72b** like thiomethylation and allylation furnished triazoles **73e-f** in 82-91% yield.



Scheme 40: Regioselective magnesiation of 2-aryl-2*H*-1,2,3-triazoles **71a-b** with *s*Bu$_2$Mg **58** leading, *via* diarylmagnesium species **72a-b**, to functionalized 2-aryl-2*H*-1,2,3-triazoles **73a-f**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] Obtained after transmetalation with ZnCl$_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [PdCl$_2$(dppf)] (5 mol%) and an aryl halide (0.83 equiv). [d] Obtained after transmetalation with CuCN·2LiCl (1.2 equiv) and subsequent addition of (phenylethynyl)lithium (2.0 equiv), followed by addition of chloranil (1.3 equiv). [e] The reaction was catalyzed by CuCN·2LiCl (20 mol%).

[97] a) V. M. Ahrens, K. Bellmann-Sickert, A. G. Beck-Sickinger, *Future Med. Chem.* **2012**, *4*, 1567-1586; b) C. R. Dass, P. F. M. Choong, *Peptides* **2006**, *27*, 3020-3028.
[98] a) J. L. Riebsommer, *J. Org. Chem.* **1948**, *13*, 815-821; b) G. F. Myachina, T. G. Ermakova, N. P. Kuznetsova, R. G. Sultangareev, L. I. Larina, L. V. Klyba, G. T. Suchanov, B. A. Trofimov, *Chem. Heterocycl. Cmpd.* **2010**, *46*, 79; c) S. Shi, W. Liu, P. He, C. Kuang, *Org. Biomol. Chem.* **2014**, *12*, 3576-3580.
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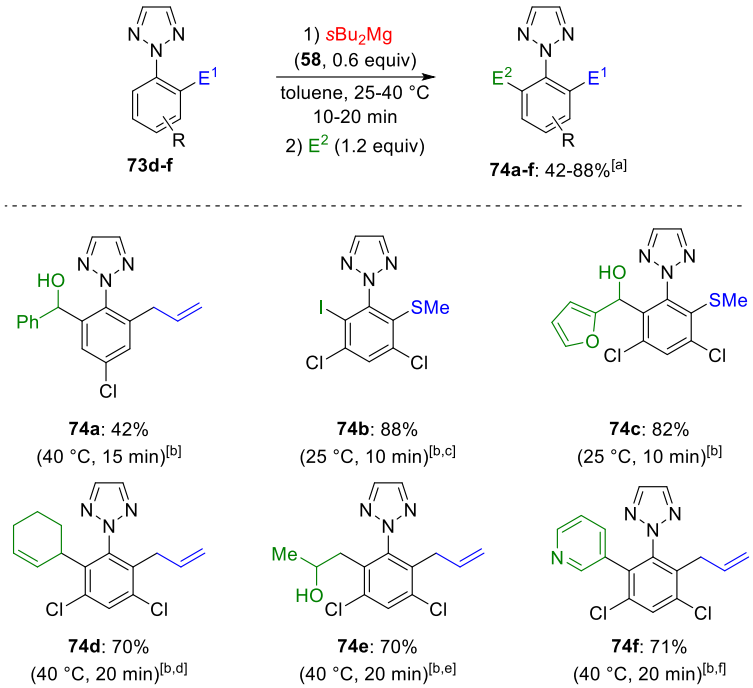
A second functionalization was performed on *N*-aryl triazoles **73d-f** using again *s*Bu_2Mg in toluene, followed by quench with a different electrophile (E^2) (Scheme 41). A complete magnesiation of **73d** with *s*Bu_2Mg was achieved within 15 min at 40 °C and a subsequent reaction with benzaldehyde produced the mixed *bis*-functionalized 1,2,3-triazole **74a** in 42% yield. Similarly, **73e** and **73f** were magnesiated under the standard conditions and the resulting *bis*-arylmagnesium species were trapped with a different electrophile (E^2) leading to a range of unsymmetrical functionalized 1,2,3-triazoles **74b-f** in 70–88% yield.

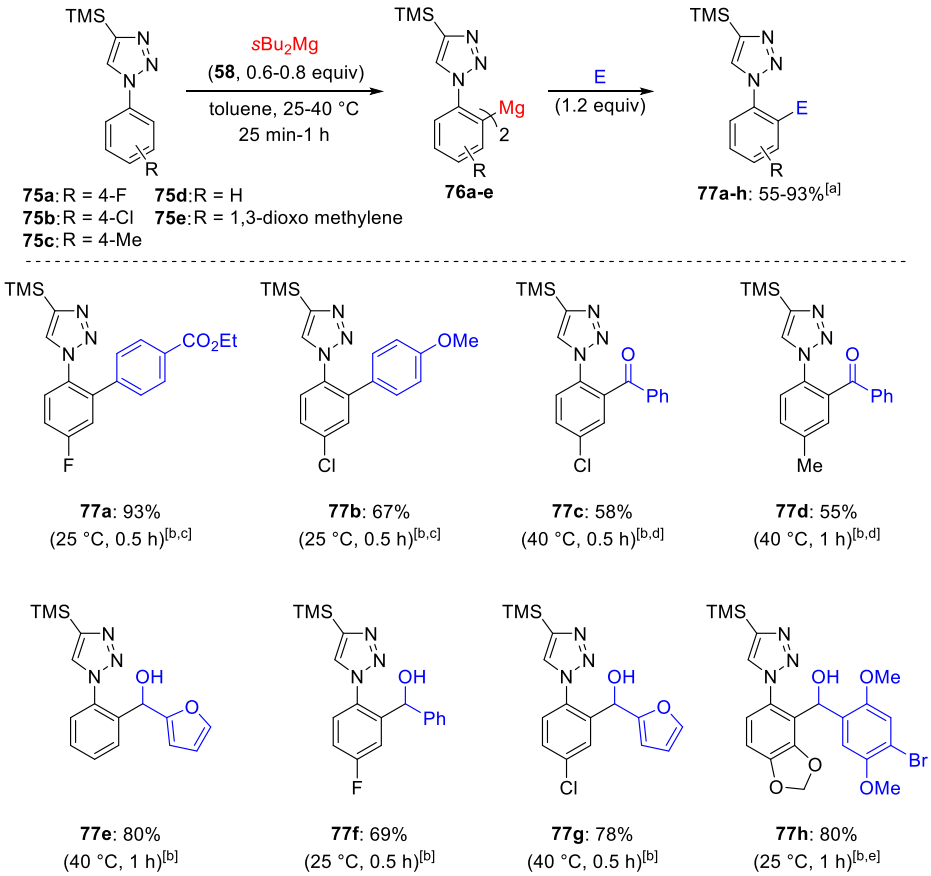


Scheme 41: Regioselective magnesiation of mono-functionalized 2-aryl-2*H*-1,2,3-triazoles **73d-f** with *s*Bu_2Mg **58** leading to *ortho*,*ortho'*-functionalized 2-aryl-2*H*-1,2,3-triazoles **74a-f**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] The regioselectivity was determined by crystal structure analysis, see Experimental Section. [d] The reaction was catalyzed by CuCN·2LiCl (20 mol%). [e] The reaction was catalyzed by CuI (10 mol%). [f] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [$PdCl_2$(dppf)] (5 mol%) and an aryl bromide (0.83 equiv).

Finally, the metalation of 1-aryl-1*H*-1,2,3-triazoles such as **75a-e** was investigated and it was found that *s*Bu_2Mg **58** led to a highly regioselective magnesiation at the *ortho*-position of the aryl ring in toluene (25–40 °C, 0.5–1 h), affording the *bis*-aryl-magnesium species **76a** in 75% yield and 97:3 regioselectivity (Scheme 42). This new metalation procedure occurred twice as fast as the previously reported TMPMgBu base **53**.[100] 1,2,3-Triazoles **77a** and **77b** were isolated in 93% and 67% yields respectively after Negishi cross-couplings with only 0.83 equiv of aryl bromide. Copper-catalyzed

[100] F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, *Nat. Comm.* **2020**, *11*, 4443.

acylation with benzoyl chloride led to products **77c** and **77d** in 55-58% yield and quenching with various aldehydes afforded compounds **77e-h** in 69-80% yield.



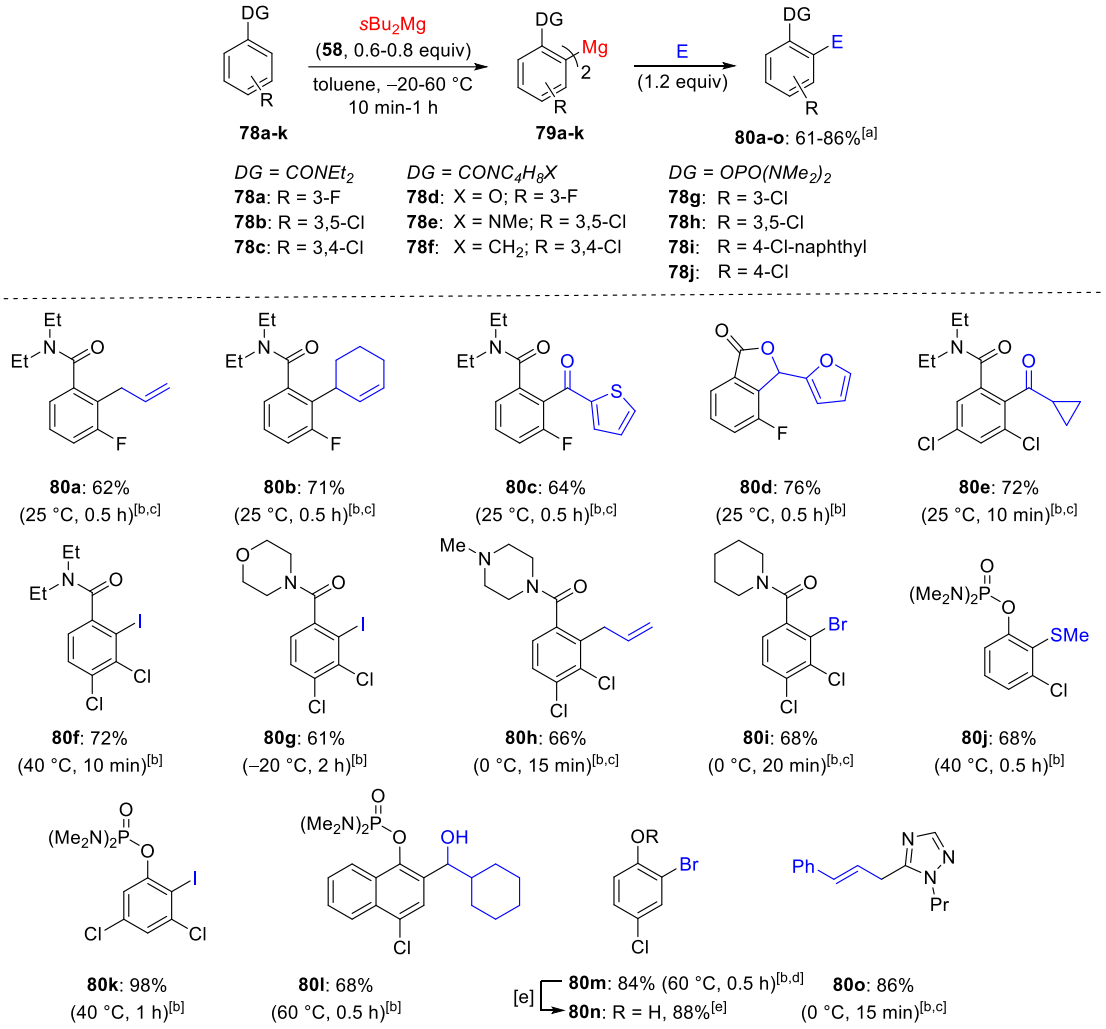
Scheme 42: Regioselective magnesiation of 1-aryl-2*H*-1,2,3-triazoles **75a-e** with sBu_2Mg **58** leading, *via* diarylmagnesium species **76a-e**, to functionalized 1-aryl-2*H*-1,2,3-triazoles **77a-h**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [$PdCl_2$(dppf)] (5 mol%) and an aryl halide (0.83 equiv).[d] The reaction was catalyzed by CuCN·2LiCl (20 mol%). [e] The regioselectivity was determined by crystal structure analysis, see experimental section.

1.6 Regioselective Magnesiations of Arenes

Remarkably, *s*Bu_2Mg **58** was also an excellent base for the magnesiation of various arenes bearing directing groups such as a tertiary amide or phosphorodiamidate (**78a-j**; Scheme 43).[101] The addition of *s*Bu_2Mg to the aromatic amide **78a** in toluene led to a clean magnesiation within 0.5 h at room temperature. The resulting diarylmagnesium species **79a** was then further allylated with allyl and

[101] a) P. Beak, G. R. Brubaker, R. J. Farney, *J. Am. Chem. Soc.* **1976**, *98*, 3621-3627; b) P. Beak, R. A. Brown, *J. Org. Chem.* **1977**, *42*, 1823-1824; c) P. Bowles, J. Clayden, M. Helliwell, C. McCarthy, M. Tomkinson, N. Westlund, *J. Chem. Soc., Perkin Trans. 1* **1997**, 2607-2616; d) J.-C. Cuevas, P. Patil, V. Snieckus, *Tetrahedron Lett.* **1989**, *30*, 5841-5844; e) W. H. Puterbaugh, C. R. Hauser, *J. Org. Chem.* **1964**, *29*, 853-856; f) M. Watanabe, V. Snieckus, *J. Am. Chem. Soc.* **1980**, *102*, 1457-1460; g) F. Hintze, D. Hoppe, *J. Org. Chem.* **1990**, *55*, 1375-1379; h) H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109-112; i) G. Wittig, G. Fuhrman, *Chem. Ber.* **1940**, *73*, 1197-1218; j) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879-933.

cyclohexenyl bromides, leading to **80a** and **80b** in 62% and 71% yield respectively. Copper-catalyzed acylation of **79a** with thiophene-2-carbonyl chloride or trapping with furfural furnished the ketone **80c** (64% yield) and the lactone **80d** (76% yield).[102]



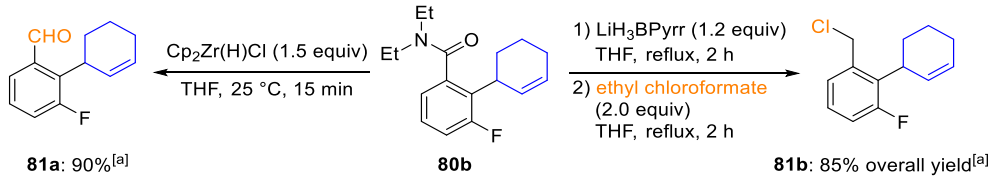
Scheme 43: Regioselective magnesiation of various arenes bearing an amide or a phosphorodiamidate directing group as well as 1-propyl-1,2,4-triazole **78a-k** with sBu$_2$Mg **58** leading, via diarylmagnesium species **79a-k**, to functionalized arenes **80a-o**. [a] All yields refer to isolated compounds. [b] The reaction was catalyzed by CuCN·2LiCl (20 mol%). [d] R = P(O)(NMe$_2$)$_2$. [e] Obtained after treating **80m** with 2 M HCl in dioxane (105 °C, 1 h).

Similarly, the amides **78b-f** afforded with the same magnesiation/trapping sequence the polyfunctional amides (**80e-i**) in 61-72% yield. Various phosphorodiamidates (**78g-j**) were also metalated with *s*Bu$_2$Mg at 40-60 °C (0.5-1 h) providing the diarylmagnesiums **79g-j**, which were trapped with a range of electrophiles (MeSSO$_2$Me, I$_2$, *c*HexCHO and (BrCCl$_2$)$_2$) furnishing the phenol derivatives **80j-m** in 68-98% yield. Removal of the phosphorodiamidate group[103] in **80m** was achieved with a 2 M HCl treatment in dioxane (105 °C, 1 h) leading to phenol **80n** in 88% yield. Interestingly, 1-propyl-1,2,4-

[102] W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *24*, 5673-5676.
[103] a) M. Watanabe, M. Date, K. Kawanishi, M. Tsukazaki, S. Furukawa, *Chem. Pharm. Bull.* **1989**, *37*, 2564-2566; b) C. J. Rohbogner, S. Wirth, P. Knochel, *Org. Lett.* **2010**, *9*, 1984-1987.

triazole (**78k**) was magnesiated with *s*Bu_2Mg **58** and allylated with cinnamyl bromide providing the *N*-heterocycle **80o** in 86% yield.[104]

We performed some further transformations leading to polyfunctionalized 1,2,3-trisubstituted arenes to show the utility of these magnesiations. The newly prepared amide **80b** was thus selectively reduced with $Cp_2Zr(H)Cl$[105] (25 °C, 15 min) to the aldehyde **81a** in 90% yield. A two-step transformation consisting of a reduction with the complex borohydride LiH_3BPyrr (Pyrr = pyrrolidino)[106] followed by a treatment with ethyl chloroformate[107] provided the benzylic chloride **81b** in 85% overall yield (Scheme 44).



81a: 90%[a] **80b** **81b**: 85% overall yield[a]

Scheme 44: Synthetic transformations of magnesiated product **80b**. [a] All yields refer to isolated compounds.

1.7 Summary

In summary, a new preparation of *s*Bu_2Mg in toluene was developed and its utility for the directed magnesiation of various aromatic and heterocyclic systems including pharmaceutically relevant *N*-arylated pyrazoles as well as *N*-arylated 1,2,3-triazoles was shown. This method provided a unique access to varius diarylmagnesium reagents in toluene under mild reaction conditions. Furthermore, a range of arenes bearing various directing groups such as an oxazoline, phosphorodiamidate or an amide were magnesiated with *s*Bu_2Mg. Remarkably, a second unsymmetrical *ortho*,*ortho'*-functionalization was achieved in the case of aryl oxazolines, *N*-aryl pyrazoles as well as *N*-aryl triazoles, leading to valuable synthetic intermediates of potential pharmaceutical relevance.

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2. Preparation of Polyfunctionalized Aromatic Nitriles from Aryl Oxazolines

2.1 Introduction

The preparation of highly substituted aromatic compounds is of great importance for pharmaceutical, agrochemical and material science applications.[108] Especially, the selective preparation of *ortho*,*ortho'*-trisubstituted aromatics are of importance. Various C-H activation methods allowed such *ortho*,*ortho'*-functionalizations,[109] however unsymmetrical *ortho*,*ortho'*-derivatives were difficult to prepare.[110] Above, it was shown that the magnesiation of various *N*-aryl azoles[111] including aryl oxazolines may be achieved by selective metalation using the powerful base *s*Bu_2Mg **58** in toluene.[112] Although, such *ortho*,*ortho'*-arylated heterocycles were useful on themselves but the generation of heterocycle-free 1,2,3-trisubstituted arenes would greatly enhance their synthetic potential.[113] Thus, the preparation of newly *ortho*,*ortho'*-functionalized aryl oxazolines would be much more relevant, if the oxazoline moiety could be converted to a carboxylate derivative.[114] Such a conversion would valorize in general the chemistry of aryl oxazolines developed in pioneering work by Meyers, since this heterocycle is often difficult to cleave.[115] Aromatic nitriles are key intermediates for the preparation of various *N*-heterocycles and represent valuable target molecules for various applications.[116]

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[110] a) A. J. Martínez-Martínez, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, *Science* **2014**, *346*, 834-837; b) A. J. Martínez-Martínez, S. Justice, B. J. Fleming, A. R. Kennedy, I. D. Oswald, C. T. O'Hara, *Sci. Adv.* **2017**, *3*; c) M. Simonetti, D. M. Cannas, X. Just-Baringo, I. J. Vitorica-Yrezabal, I. Larrosa, *Nat. Chem.* **2018**, *10*, 724-731; d) L. Ackermann, A. Althammer, R. Born, *Tetrahedron* **2008**, *64*, 6115-6124; e) S. Oi, H. Sato, S. Sugawara, Y. Inoue, *Org. Lett.* **2008**, *10*, 1823-1826; f) C. J. Teskey, S. M. Sohel, D. L. Bunting, S. G. Modha, M. F. Greaney, *Angew. Chem. Int. Ed.* **2017**, *56*, 5263-5266; g) O. Daugulis, V. G. Zaitsev, *Angew. Chem. Int. Ed.* **2005**, *44*, 4046-4048.

[111] F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, *Nat. Commun.* **2020**, *11*, 4443.

[112] A. Hess, J. P. Prohaska, S. B. Doerrich, F. Trauner, F. H. Lutter, S. Lemaire, S. Wagschal, K. Karaghiosoff, P. Knochel, *Chem. Sci.* **2021**, *12*, 8424-8429.

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[115] a) T. G. Gant, A. Meyers, *Tetrahedron* **1994**, *50*, 2297-2360; b) A. Meyers, E. Mihelich, *Angew. Chem. Int. Ed.* **1976**, *15*, 270-281.

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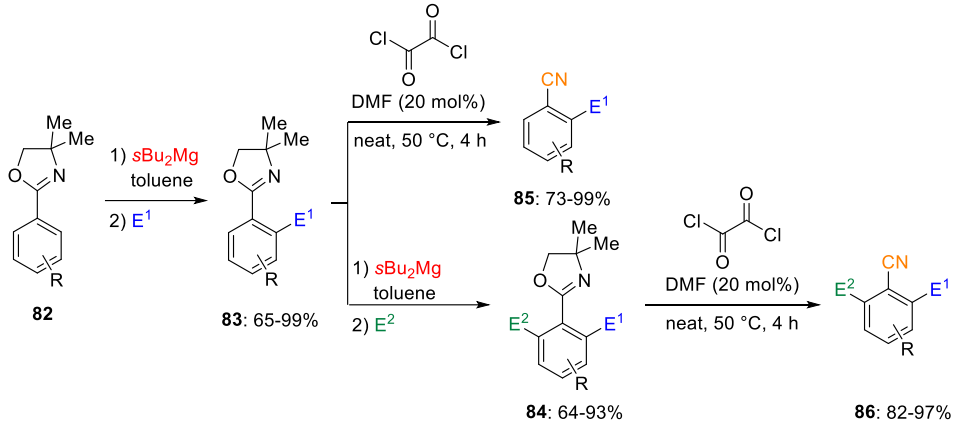
They are usually prepared from various precursors such as aromatic aldehydes,[117] hydrocarbons,[118] carboxylic acid derivatives,[119] halides[120] or benzylic derivatives.[121] In preliminary experiments, it was noticed that aryl oxazolines may be converted under harsh conditions (refluxing of a 2:1 mixture of thionyl chloride and DMF at 75 °C for 2 h) to the corresponding aromatic nitriles.[122]

Below, the successive magnesiations of aryl oxazolines of type **82** providing *ortho*-substituted aryl oxazolines of type **83** and *ortho*,*ortho'*-substituted aryl oxazolines of type **84** and their conversion to the corresponding nitriles **85** and **86** is reported (Scheme 45).



Scheme 45: Regioselective magnesiations of aryl oxazolines **82** using *s*Bu2Mg **58** in toluene furnishing *ortho*- and *ortho*,*ortho'*-substituted oxazolines **83** and **84** and subsequent conversion to the corresponding nitriles **85** and **86**.

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2.2 Preparation of *Ortho*-Functionalized Aryl Oxazolines

First, a range of mono-*ortho*-substituted aryl oxazolines of type **83** were produced starting from aryl oxazolines of type **82**[123] by magnesiation with sBu$_2$Mg[124] in toluene (0.48 M) prepared by the reaction of *s*BuMgCl with *s*BuLi (Scheme 46). In a typical experiment, the phenyl oxazoline **82a** was treated with sBu$_2$Mg (**58**, 0.6 equiv) for 1 h at 25 °C leading to the diarylmagnesium intermediate **87a** in toluene, which after transmetalation with $ZnCl_2$ (1M in THF, 1.1 equiv) and Negishi cross-coupling[125] with 1-iodo-3-trifluorobenzene (0.83 equiv, 55 °C, 2 h) and $PdCl_2$(dppf) (5 mol%, dppf = diphenylphosphinoferrocene) furnished the *ortho*-substituted oxazoline **83a** in 73% yield of analytically pure isolated product. Similarly, starting from **82a** and **82b**, the related 2-arylated oxazolines **83b-f** were obtained in 76-99% yield. Also, the 3,5-dichlorophenyl oxazoline **82c** and the 3-fluorophenyl oxazoline **82d** were magnesiated with sBu$_2$Mg at 25 °C for 15 min furnishing the diarylmagnesium intermediates **87c** and **87d**. Trapping with various electrophiles such as iodine, tosyl cyanide, ethyl cyanoformate or (hetero)aryl iodides (Negishi cross-coupling using $Pd(dba)_2$ (3 mol%, dba = dibenzylideneacetone and tfp (6 mol%, tfp = tri(*o*-furyl)phosphine) gave the expected products **83g-m** in 70-98% yield. Electron-rich substituted aryl oxazolines such as **82e** and **82f** as well as the 2-naphthyl oxazoline **82g**[126] were metalated with sBu$_2$Mg **58** as well as with TMPMgCl·LiCl[127] **25** and were trapped with typical electrophiles providing the *ortho*-substituted oxazolines **83n-r** in 65-98% yield. Finally, the 1,4-bisoxazolyl benzene **82h** [128] or thienyl oxazoline **82i** were converted to the *ortho*-substituted oxazolines **83s-v** in 92-98% yield.

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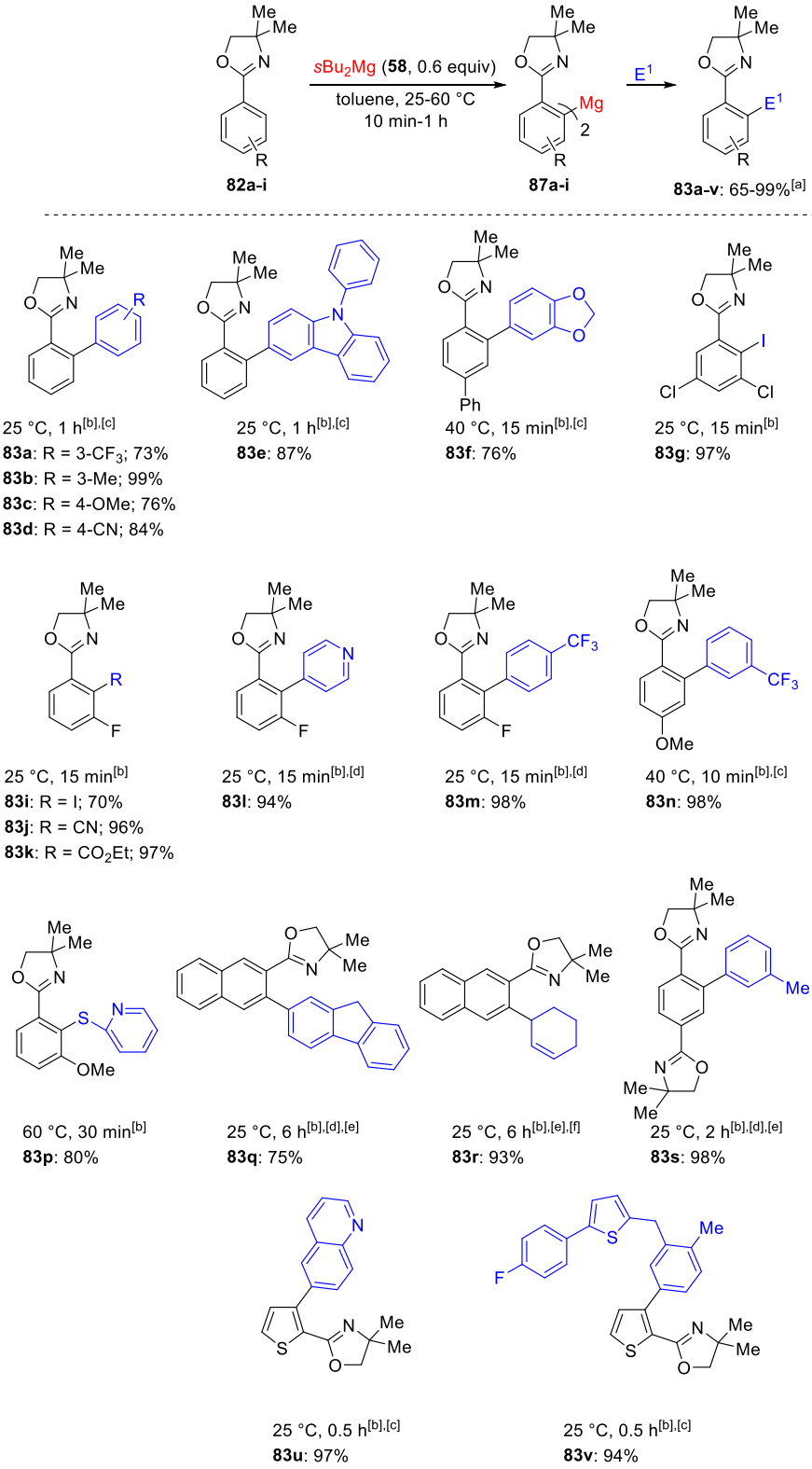
[127] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961; b) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794-9824; c) W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *8*, 5673-5676; d) A. Unsinn, C. J. Rohbogner, P. Knochel, *Adv. Synth. Catal.* **2013**, *355*, 1553-1560.
[128] V. Nasufović, P. Then, F. Dröge, M. Duong, C. Kaether, B. Dietzek, R. Heintzmann, H.-D. Arndt, *Org. Biomol. Chem.* **2021**, *19*, 574-578.

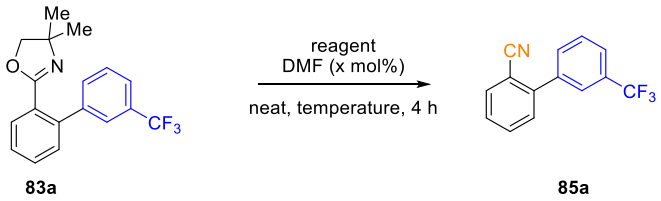


Scheme 46: Regioselective magnesiation of oxazolines **82a-i** with sBu_2Mg leading, *via* diarylmagnesium intermediates **87a-i**, to functionalized oxazolines **83a-v**. [a] All yields refer to analytically pure isolated compounds. [b] Magnesiation conditions. [c] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [$PdCl_2$(dppf)] (5 mol%) and an aryl bromide or iodide (0.83 equiv). [d] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with $Pd(dba)_2$ (3 mol%), tfp (6 mol%) and an aryl bromide or iodide (0.83 equiv). [e] TMPMgCl·LiCl (2.0-3.0 equiv) was used for the magnesiation.[20] [f] The reaction was catalyzed by CuCN·2LiCl (20 mol%).

2.3 Optimization studies

With these oxazolines in hand, various optimization experiments for their conversion to the corresponding nitriles were conducted. Thus, the oxazoline **83a** was submitted to various conditions, leading to nitrile **85a**. Thionyl chloride (used as solvent) was ineffective in the absence of DMF (entry 1 of Table 2) or in the presence of DMF (20 mol%) at 25 °C (entry 2). Heating to 50 °C, which presumably generates an intermediate immonium reagent ($Me_2N{=}C(H)Cl_2$); *Vilsmeier* reagent)[23] led to the nitrile **85a** in 64% calibrated GC-yield (entry 3). Switching thionyl chloride to oxalyl chloride as solvent (0.2 M solutions) already provided **85a** at 25 °C (entries 4 and 5). Increasing the reaction temperature to 50 °C afforded the desired nitrile **85a** in quantitative GC-yield (98% isolated yield; entry 6). Using toluene as solvent and oxalyl chloride in small excess (2.0 equiv) was not satisfactory (entry 7).

Table 2: Optimization of the dehydration reaction of oxazoline **83a** to nitrile **85a**. [a] Calibrated GC-yield using undecane as internal standard. [b] Isolated yield. [c] 2.0 equiv of $(COCl)_2$ in toluene were used.

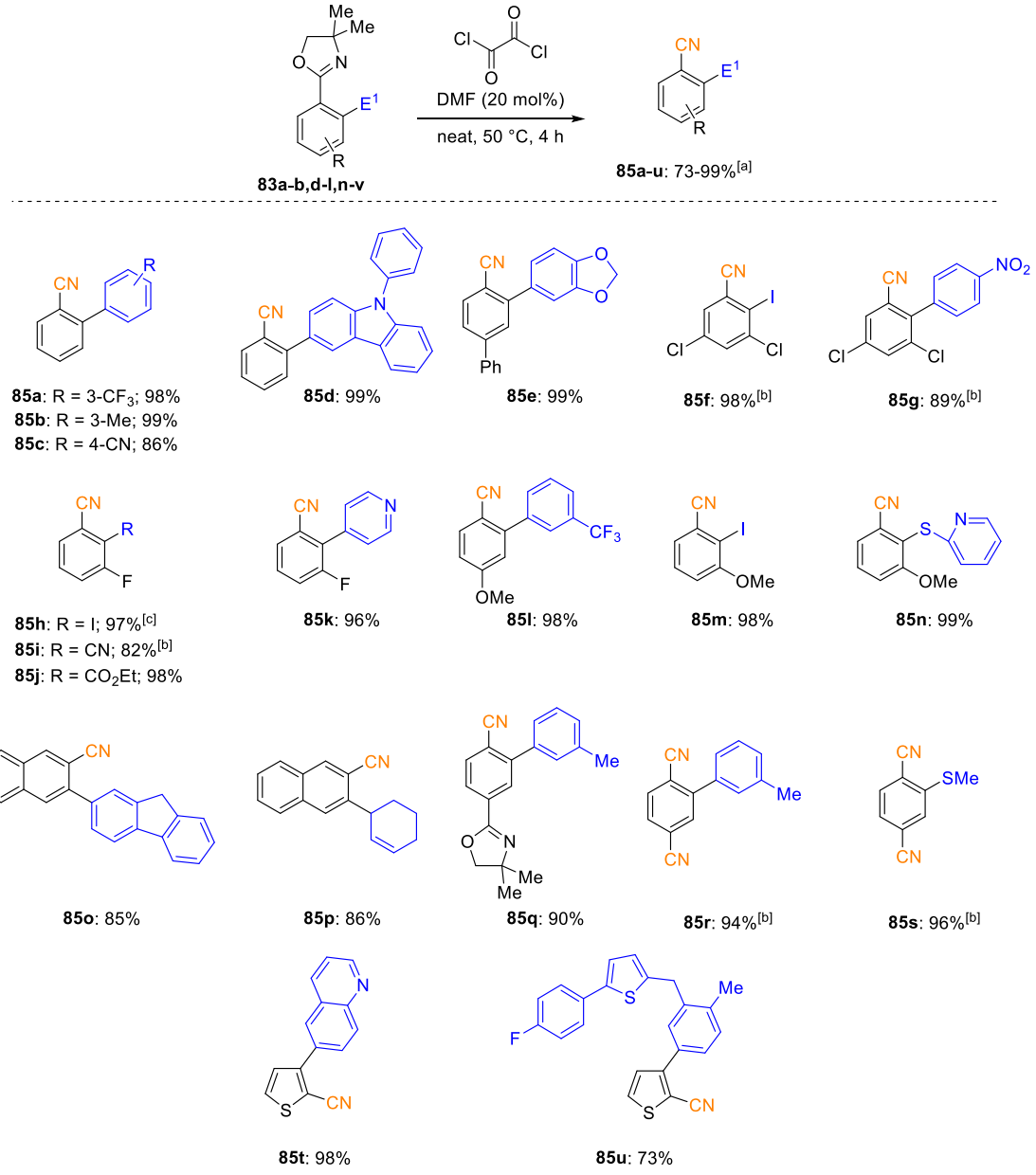


83a **85a**

Entry	Reagent	DMF (mol%)	Temperature (°C)	Yield (%)[a]
1	$SOCl_2$	0	25	0
2	$SOCl_2$	20	25	0
3	$SOCl_2$	20	50	64
4	$(COCl)_2$	0	25	traces
5	$(COCl)_2$	20	25	47
6	$(COCl)_2$	20	50	100 (98)[b]
7	$(COCl)_2$	20	50	47

2.4 Preparation of *Ortho*-Functionalized Aromatic Nitriles

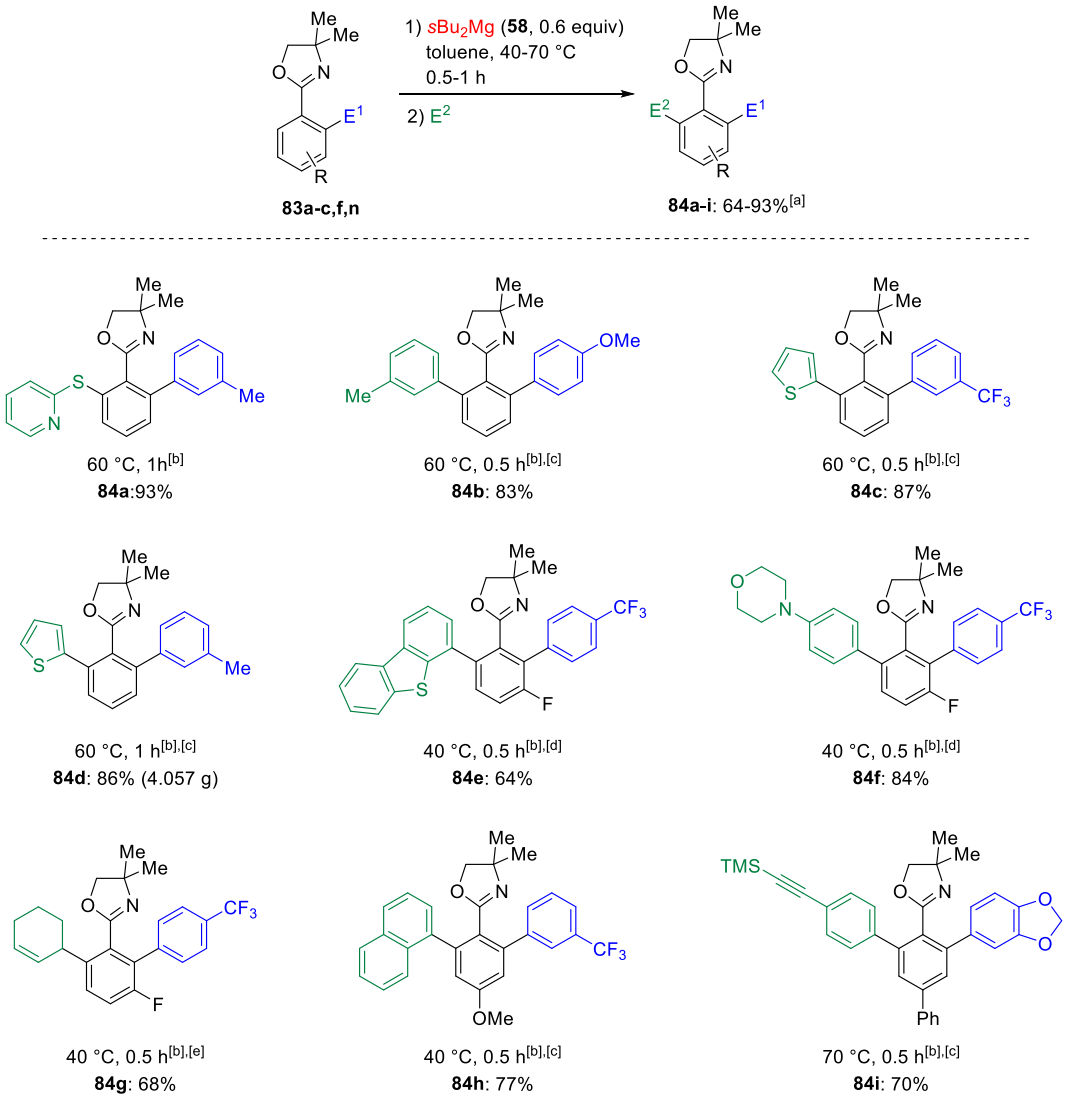
With these optimized conditions in hand, the particular *ortho*-substituted aryl oxazolines **83a-b,d-l,n-v** were converted to the corresponding nitriles **85a-u** in 73-99% yield (Scheme 47). Various functional groups like a CN, NO_2, CO_2Et, cyclohexenyl or thiopyridyl were compatible with the mild reaction conditions of this cyanation procedure.



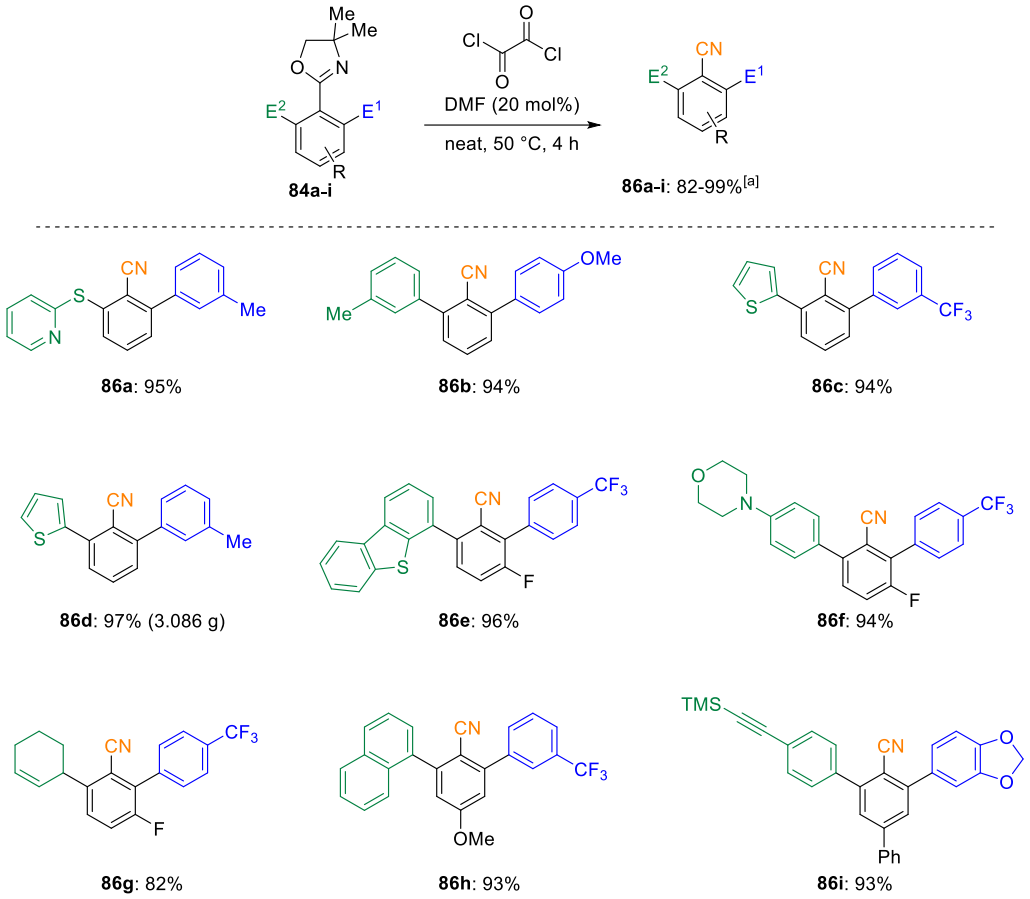
Scheme 47: Transformation of ortho-functionalized oxazolines **83a-b,d-l,n-v** to the corresponding nitriles **85a-u**. [a] All yields refer to isolated compounds. [b] $SOCl_2$: DMF 2:1 (70 °C, 4 h) was used. [c] 5 h reaction time.

2.5 Preparation of *Ortho*,*Ortho'*-Functionalized Aryl Oxazolines and the Corresponding Nitriles

After these encouraging results, various *ortho*,*ortho'*-disubstituted oxazolines **84a-i** were prepared using *s*Bu_2Mg (0.6 equiv) in toluene between 40-70 °C within 0.5-1 h reaction time and in 64-93% isolated yield (Scheme 48). Fortunately, the aryl oxazolines **84a-i** were readily converted in the corresponding nitriles **86a-i** in 82-99% yield (Scheme 49). Remarkably, the scale-up of this cyanation was performed in the case of **84d** providing the nitrile **86d** in multigram-scale (3.1 g were prepared) in 97% isolated yield.



Scheme 48: Regioselective magnesiation of *ortho*-functionalized oxazolines **83a-c**,**f**,**n** with sBu_2Mg **58** leading to *ortho*,*ortho'*-functionalized oxazolines **86a-i**. [a] All yields refer to isolated compounds. [b] Magnesiation conditions. [c] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with [$PdCl_2$(dppf)] (5 mol%) and an aryl halide (0.83 equiv). [d] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling with $Pd(dba)_2$ (3 mol%), tfp (6 mol%) and an aryl halide (0.83 equiv). [e] The reaction was catalyzed by CuCN·2LiCl (20 mol%).



Scheme 49: Transformation of *ortho*,*ortho'*-functionalized oxazolines **84a-i** to the corresponding nitriles **86a-i**. [a] All yields refer to isolated compounds.

2.6 Nucleophilic Aromatic Substitution on *Ortho*-(methoxy)aryl Oxazolines and Preparation of their Corresponding Nitriles

Furthermore, *ortho*-methoxy substituted aryl oxazolines **88a** and **88b** were treated with various nucleophiles, as previously described by *Meyers*,[129] resulting in substituted products of type **89**. Thus, the reaction of the reaction of **88a** with *c*HexMgCl or *exo*-norbornylmagnesium bromide[130] (25 °C, 1 h) produced the alkylated derivatives **89a-b** in 81-96% yield (Scheme 50). Treatment of **88b** with piperidyllithium or vinylmagnesium bromide provided the aminated and vinylated products **89c** and **89d** respectively (62-90% yield). Applying the cyanation procedure afforded the aryl nitriles **90a-c** in 90-97% yield. Treatment of the alkylated oxazoline **89a** with *s*Bu_2Mg (60 °C, 1 h) and subsequent Negishi cross-coupling furnished the *ortho*,*ortho'*-functionalized aryl oxazoline **91** in 80% yield, which was converted to the corresponding aromatic nitrile **92** in 99% yield. Reacting the readily available 2-

[129] a) A. Meyers, R. Gabel, E. D. Mihelich, *J. Org. Chem.* **1978**, *43*, 1372-1379; b) A. Meyers, R. Gabel, *J. Org. Chem.* **1977**, *42*, 2653-2654; c) A. Meyers, M. Reuman, R. A. Gabel, *J. Org. Chem.* **1981**, *46*, 783-788.
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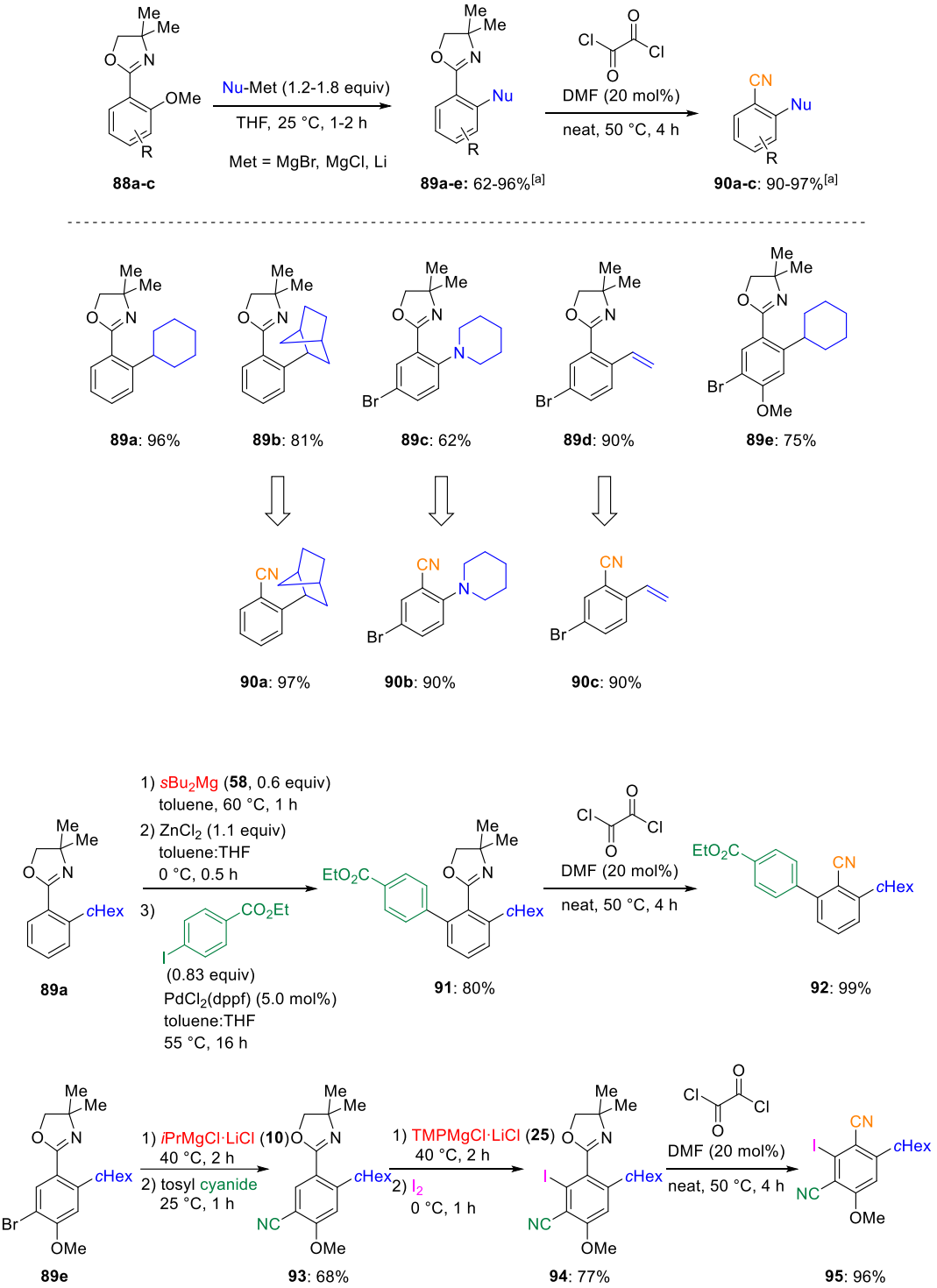
methoxy oxazoline **88c** with *c*HexMgCl (25 °C, 1 h) furnished the ortho-substituted oxazoline (**89e**) in 75% yield.

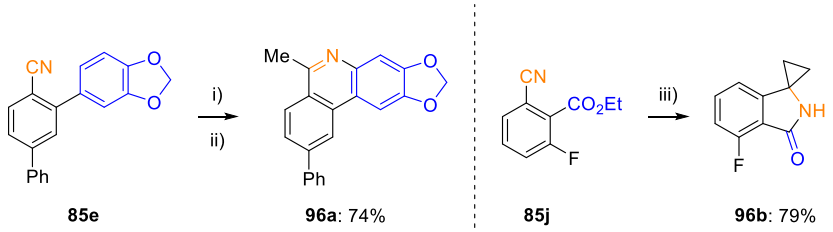


Scheme 50: Nucleophilic aromatic substitution on *ortho*-(methoxy)aryl oxazolines **88a-c** furnishing functionalized aryl oxazolines **89a-e** and subsequent transformation to the corresponding nitriles **90a-c**. Multiple functionalizations on aryl oxazolines **89a** and **89e** and subsequent transformation to the corresponding nitriles **92** and **95**. [a] All yields refer to isolated compounds.

Br/Mg-exchange with *i*PrMgCl·LiCl[131] **10** produced an intermediate functionalized aryl magnesium derivative, which after treatment with tosyl cyanide (25 °C, 1 h) gave the nitrile **93** in 68% yield. Subsequent magnesiation with TMPMgCl·LiCl **25** followed by an iodolysis of the intermediate Grignard species led to the polyfunctional aryl iodide **94** in 77% yield, which was converted by the usual procedure into the penta-substituted dinitrile **95** in 96% yield demonstrating the versatility of this approach for preparing highly substituted aryl nitriles.

2.7 Postfunctionalizations and Tentative Mechanism

Some of these nitriles were converted to cyclized derivatives by diverse methods. Thus, the nitrile **85e** was converted to the phenanthridine **96a** by an imino radical cyclization in 74% yield.[132] Treatment of **85j** using the Kulinkovich procedure (Ti(O*i*Pr)$_4$ and EtMgBr)[133] in ether (25 °C, 1 h) furnished a spirocyclic lactam **96b** in 79% yield.[134]

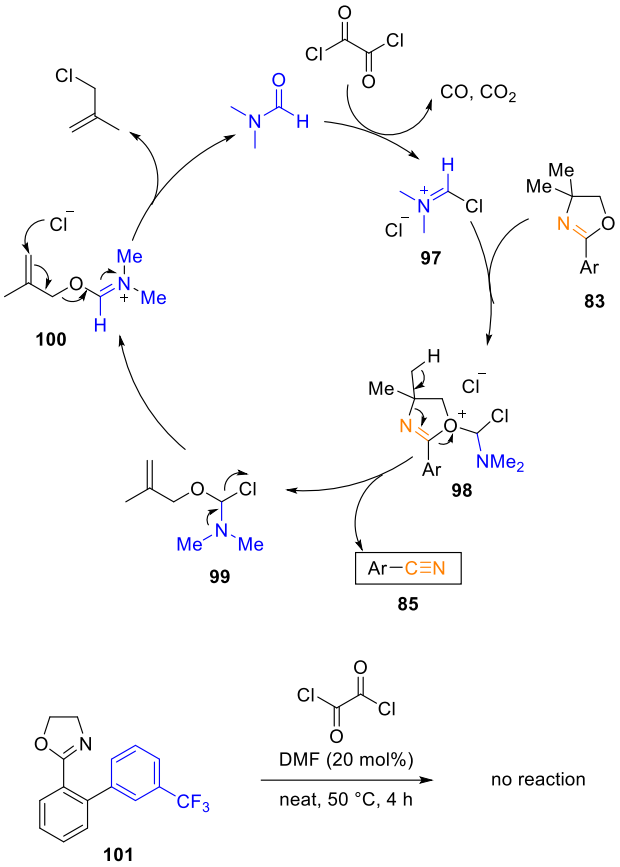


85e **96a**: 74% **85j** **96b**: 79%

Scheme 51: Transformation of aryl nitriles **85e** and **85j** to cyclic derivatives **96a** and **96b**. All yields refer to isolated compounds. Reaction conditions: i) MeLi (2.0 equiv), THF, 0 °C, 15 min. ii) H_2O, I_2 (4.0 equiv), K_2CO_3 (3.0 equiv), THF, 60 °C, 2 h. iii) Ti(O*i*Pr)$_4$ (1.1 equiv), EtMgBr (2.0 equiv), Et_2O, 25 °C, 1 h.

A tentative reaction mechanism was proposed in Scheme 52. Thus, DMF was first converted with oxalyl chloride to the *Vilsmeier* reagent **97**. Its reaction with the aryl oxazoline **83** provided the oxonium ion **98** which by a fragmentation led to the aryl nitrile **85** and to the amino-derivative **99** which gave the iminium chloride **100** regenerating DMF and methallyl chloride in a further fragmentation step. Interestingly, the use of an aryl oxazoline such as **101** missing the two methyl groups necessary in the fragmentation process leading to a nitrile, gave no reaction under the established standard conditions.

[131] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333-3336.
[132] A. Kishi, K. Moriyama, H. Togo, *J. Org. Chem.* **2018**, *83*, 11080-11088.
[133] K. Cha, O. G. Kulinkovich, *Org. React.* **2004**,1-160.
[134] P. Bertus, J. Szymoniak, *J. Org. Chem.* **2003**, *68*, 7133-7136.



Scheme 52: Tentative reaction mechanism of the conversion of aryl oxazoline **83** to the aromatic nitrile **85**.

2.8 Summary

In summary, a novel method for preparing highly functionalized tri-, tetra- and penta-substituted aromatic nitriles was developed. Successive magnesiations with *s*Bu_2Mg in toluene followed by trapping with a broad range of electrophiles associated with an efficient conversion of the oxazolyl directing group to a nitrile using oxalyl chloride and catalytic amounts of DMF (50 °C, 4 h) valorized the chemistry of aryl oxazolines.

3. Regioselective Magnesiations of Fluorinated Arenes and Heteroarenes Using Magnesium-*bis*-Diisopropylamide (MBDA) in Hydrocarbons

3.1 Introduction

Fluorinated aromatics are important scaffolds present in numerous pharmaceuticals and agrochemicals.[135] The special nature of fluorine imparts a range of useful properties, including enhanced binding interactions, metabolic stability, changes in physical properties[136] and selective reactivities.[137] The regioselective metalation of such aromatics using lithium bases may be complicated by the formation of aryne side-products requiring cryogenic temperatures for such lithiations.[138] Due to the increasing importance of polyfunctionalized fluorinated aromatics, it was intentioned to develop a convenient magnesiation of fluorinated unsaturated substrates since it is anticipated that magnesiated fluoroaromatics should be significantly more stable and easy to handle.[139] A range of magnesium amides in THF suitable for metalations have been reported.[140] Among them, the mixed lithium magnesium amides TMPMgCl·LiCl **25**,[141] TMP_2Mg·2LiCl **30**[142] and $[t\text{Bu}(i\text{Pr})\text{N}]_2\text{Mg}$·2LiCl[143] **102** have recently found many applications. The TMP group in combination with LiCl proved to be important for providing a monomeric, highly soluble base with remarkable reactivity.[144] However, due to the high cost of TMPH compared to DA (diisopropylamine),[145] the preparation of a new DA-based magnesium amide in hexanes would be economically valuable. Previous reports of *Kondo* and *Sakamoto* have already described the magnesiation of indoles in THF with $(i\text{Pr}_2\text{N})_2\text{Mg}$ **103** and related

[135] a) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320-330; b) E. P. Gillis, K. J. Eastman, M. D. Hill, D. J. Donnelly, N. A. Meanwell, *J. Med. Chem.* **2015**, *58*, 8315-8359.
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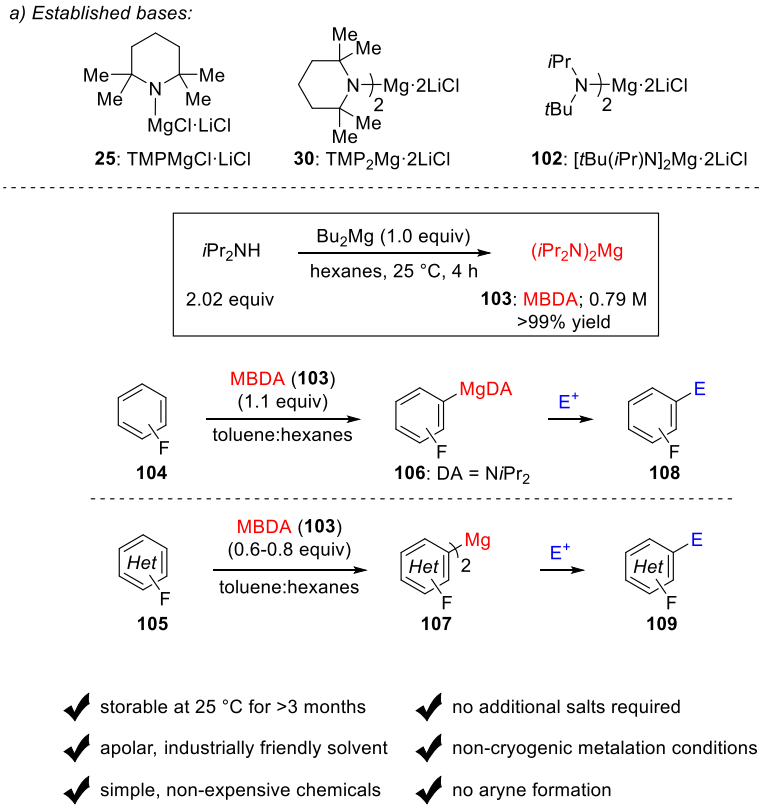
[137] a) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470-477; b) J. Iskra, A. Decker, *Halogenated Heterocycles: Synthesis, Application and Environment, Vol. 27*, Springer Science & Business Media, **2012**; c) O. Planas, F. Wang, M. Leutzsch, J. Cornella, *Science* **2020**, *367*, 313-317; d) Q. Wang, Q. Tao, H. Dong, C. Ni, X. Xie, J. Hu, *Angew. Chem. Int. Ed.* **2021**, *133*, 27524-27529; e) A. Liu, C. Ni, Q. Xie, J. Hu, *Angew. Chem. Int. Ed.* **2022**, *61*, e202115467.
[138] a) P. L. Coe, A. J. Waring, T. D. Yarwood, *J. Chem. Soc. Perkin Trans. I* **1995**, 2729-2737; b) Marzi, J. Gorecka, M. Schlosser, *Synthesis* **2004**, 1609-1618; c) E. Marzi, C. Bobbio, F. Cottet, M. Schlosser, *Eur. J. Org. Chem.* **2005**, 2116-2123; d) C. Heiss, E. Marzi, F. Mongin, M. Schlosser, *Eur. J. Org. Chem.* **2007**, 669-675; e) M. Schlosser, *Synlett* **2007**, 3096-3102; f) J.-A. García-López, M. F. Greaney, *Chem. Soc. Rev.* **2016**, *45*, 6766-6798.
[139] a) A. Unsinn, C. J. Rohbogner, P. Knochel, *Adv. Synth. Catal.* **2013**, *355*, 1553-1560; b) T. Dos Santos, H. P. Orenha, V. E. Murie, R. Vessecchi, G. C. Clososki, *Org. Lett.* **2021**, *23*, 7396-7400; c) A Y.-J. Wu, G. J. Porter, D. B. Frennesson, M. G. Saulnier, *J. Org. Chem.* **2022,** *87*, 2559-2568.
[140] a) P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016-8018; b) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *Liebigs Ann.* **1995**, 1441-1446; c) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3802-3824; d) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794-9824.
[141] A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961.
[142] G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681-7684.
[143] C. J. Rohbogner, S. H. Wunderlich, G. C. Clososki, P. Knochel, *Eur. J. Org. Chem.* **2009**, 1781-1795.
[144] P. García-Álvarez, D. V. Graham, E. Hevia, A. R. Kennedy, J. Klett, R. E. Mulvey, C. T. O'Hara, S. Weatherstone, *Angew. Chem. Int. Ed.* **2008**, *47*, 8079-8081.
[145] The price of TMPH is more than 100 times superior to the price of DA.

bases.[146] Also, *Lessène* and *Bordeau* reported the regio- and stereo-selective generation of silyl enol ethers with magnesium-*bis*-diisopropylamide (MBDA) **103**.[147] The use of an apolar, industrially friendly[148] solvent compared to THF should suppress any aryne formation and allow magnesiations at non-cryogenic temperatures. Thus, treating *i*Pr$_2$NH (DA) with commercially available Bu$_2$Mg[149] in hexanes (25 °C, 4 h) produced a light-yellow ca. 0.8 M solution of magnesium-*bis*-diisopropylamide **103** (MBDA) in quantitative yield. This solution was storable at ambient temperature for more than three months without decomposition or loss of activity. In the following, a base is reported that allowed the magnesiation of various fluorinated aromatics and heterocycles of type **104** and **105** in a convenient temperature range (−20 °C to 70 °C) leading to the corresponding organomagnesium species **106** or **107** (depending on the stoichiometry of base **103** used).[150] After quenching with typical electrophiles such as aldehydes, ketones, allylic bromides, disulfides or aryl halides, a range of polyfunctionalized fluorinated aromatics and heterocycles of type **108** and **109** were obtained in 52-96% yield (Scheme 53).



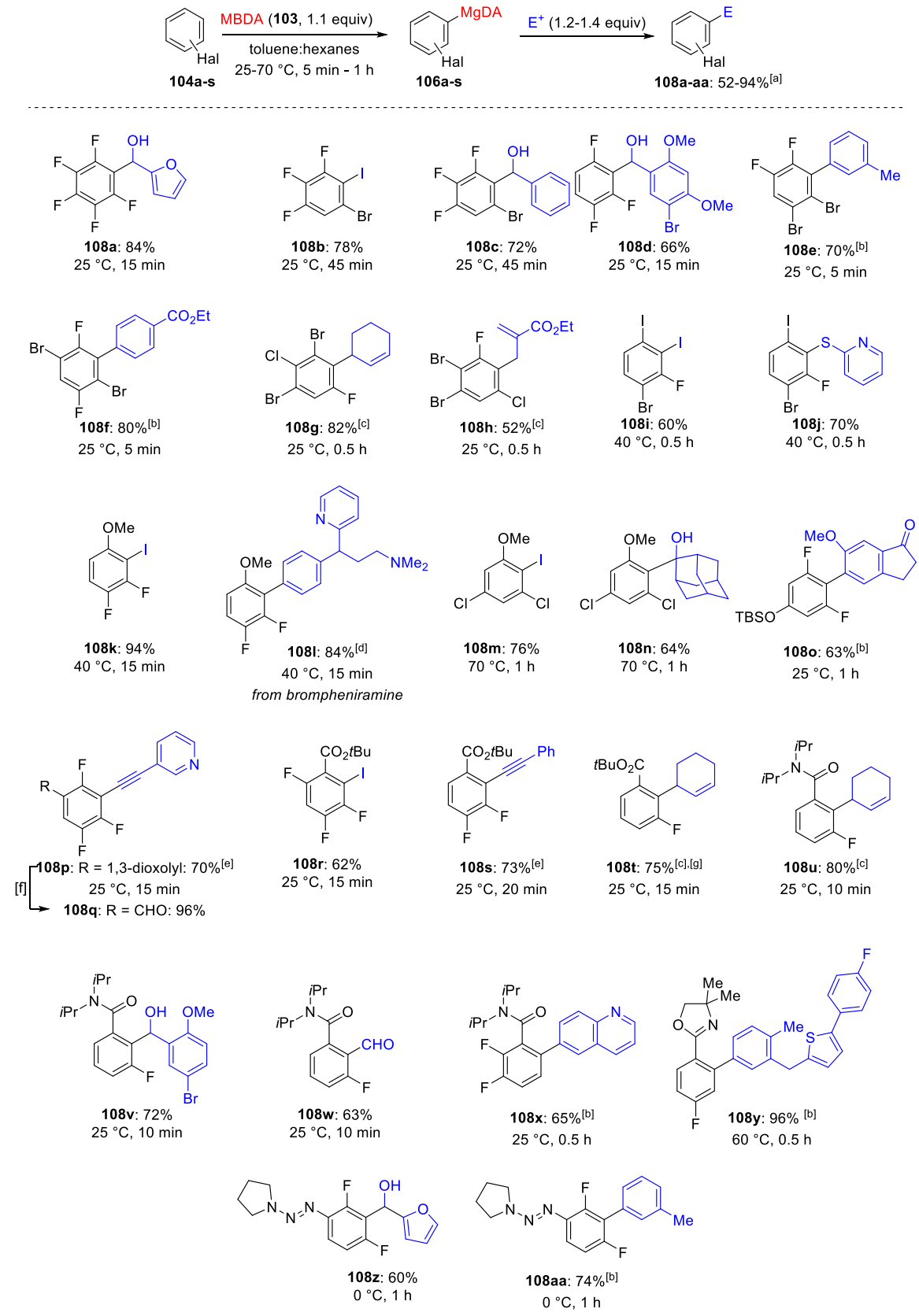
Scheme 53: Valuable magnesium amide bases and the preparation of MBDA **103** and its reaction with fluoroarenes **104** or heteroarenes **105**.

[146] Y. Kondo, A. Yoshida, T. Sakamoto, *J. Chem. Soc. Perkin Trans. I* **1996**, 2331-2332.
[147] G. Lessène, R. Tripoli, P. Cazeau, C. Biran, M. Bordeau, *Tetrahedron Lett.* **1999**, *40*, 4037-4040.
[148] A. Jordan, C. G. J. Hall, L. R. Thorp, H. F. Sneddon, *Chem. Rev.* **2022**, *122*, 6749-6794.
[149] Commercial Bu$_2$Mg is a mixture of *n*Bu$_2$Mg and *s*Bu$_2$Mg (ca. 60:40 ratio) and is available from Sigma-Aldrich and Albermarle.
[150] The use of 0.5 equiv of MBDA **103** did not lead to full conversion in most cases.

3.2 Regioselective Magnesiation of Fluorinated Arenes

Thus, various halogenated fluoroaromatics such as pentafluorobenzene (**104a**), 5-bromo-1,2,3-trifluorobenzene (**104b**), 1,2,4-trifluorobenzene (**104c**), 1,2-dibromo-4,5-difluorobenzene (**104d**), 1,4-dibromo-2,5-difluorobenzene (**104e**), 1,3-dibromo-2-chloro-5-fluorobenzene (**104f**), and 1,2-dibromo-5-chloro-3-fluorobenzene (**104g**) were all readily magnesiated with MBDA (**103**, 1.1 equiv) in toluene:hexanes at 25 °C within 5-45 min as indicated by iodolysis of reaction aliquots. The resulting arylmagnesium amides (**106a-g**) were quenched with several electrophiles (1.2-1.4 equiv) such as iodine, aldehydes, aryl iodides (Negishi cross-coupling)[151] and allylic bromides leading to the desired products **108a-h** in 52-84% yield. The organomagnesium amides **106a-g** proved to be thermally stable and for example the reagent **106e** was stable in hexanes at 40 °C for four days without significant decomposition. In no cases aryne-derived side products were observed. Various electron-rich substitutents such as an iodide, methoxy, TBS-O or 1,3-dioxolane in aromatic substrates **104h-l** were similarly metalated with MBDA **103**. However, due to the increased electronic density of these ring systems, higher magnesiation temperatures and longer reaction times were required (25-70 °C, 15 min-1 h; see Scheme 54). After quenching with various electrophiles the desired functionalized aromatics **108m-p** were obtained in 60-94% yield. Electron-withdrawing substituents such as *t*-butyl esters were compatible with a metalation using MBDA **103**. Thus, the *tert*-butyl benzoates **104m**, **104n** and **104o** were readily magnesiated at 25 °C within 15-20 min. Interestingly, in the case of *tert*-butyl 3-fluorobenzoate (**104o**) a metalation with MBDA **103** in toluene:hexanes was complicated by a competitive reaction with the ester function. This side reaction was widely suppressed by the addition of 3 equivalents THF accelerating this magnesiation.[152] Quenching with typical electrophiles gave the fluorobenzoates **108r-t** in 62-75% yield. Although fluorobenzonitriles were not magnesiated with MBDA due to extensive reaction of the cyano group, the corresponding *N*,*N*-diisopropylamido derivatives **104p** and **104q** were magnesiated at 25 °C and reacted well in various trapping reactions affording the polyfunctional amides **108u-x** in 63-80% yield. Also, the fluorinated aryl oxazoline **104r** was successfully magnesiated at 60 °C (0.5 h) providing, after a Negishi cross-coupling, the polyfunctional biphenyl **108y** in 96% yield. Finally, the triazene **104s** was smoothly magnesiated with MBDA at 0 °C (1 h) and trapping with furfural or cross-coupling gave the poly-substituted triazenes **108z-aa** in 60-74% yield.[153]

[151] A. O. King, N. Okukado, E.-i. Negishi, *J. Chem. Soc., Chem. Commun.* **1977**, 683-684.
[152] D. Djukanovic, B. Heinz, F. Mandrelli, S. Mostarda, P. Filipponi, B. Martin, P. Knochel, *Chem. Eur. J.* **2021**, *27*, 13977-13981.
[153] A crystal structure of **108aa** confirmed the proposed structure. See Experimental Section.



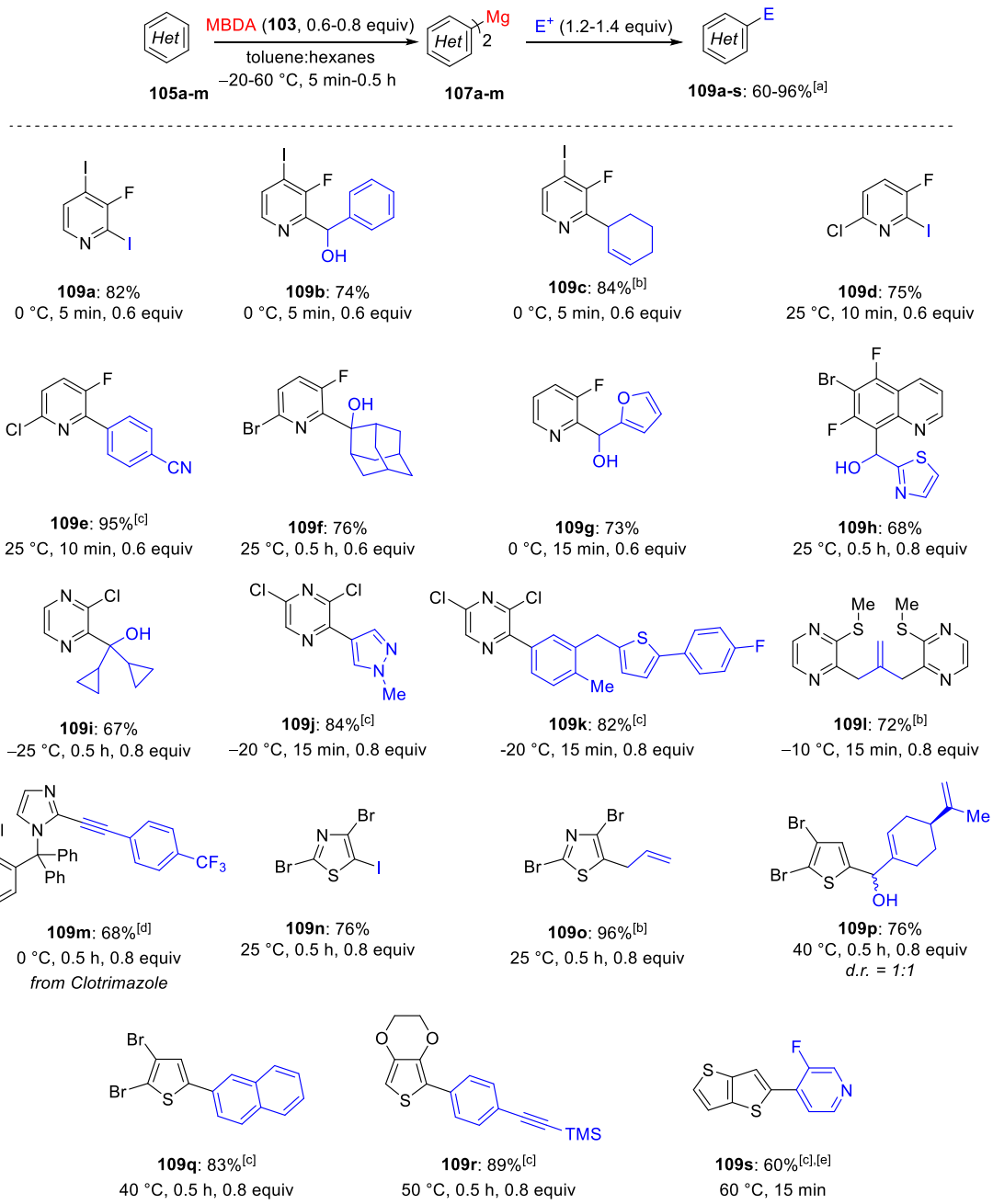
Scheme 54: Regioselective magnesiation of fluorinated arenes **104a-s** with MBDA **103** leading to arylmagnesium species **106a-s** and after electrophile trapping to functionalized arenes **108a-aa**. a) All yields refer to isolated compounds. b) Obtained after transmetalation with $ZnCl_2$ (1.4 equiv) and a palladium-catalyzed cross-coupling with an aryl iodide (0.83 equiv) using

$Pd(dba)_2$ (3 mol%, dba = dibenzylideneacetone), tfp (6 mol%, tfp = tri-(2-furyl)-phosphine).[154] c) The reaction was catalyzed by CuCN·2LiCl (20 mol%). d) Obtained after transmetalation with $ZnCl_2$ (1.4 equiv) and a palladium-catalyzed cross-coupling with an aryl bromide (0.83 equiv) using [$PdCl_2$(dppf)] (5 mol%). e) Obtained after transmetalation with $ZnCl_2$ (1.4 equiv), subsequent iodine quench (1.1 equiv) and Sonogashira cross-coupling with an alkyne (1.3 equiv) using CuI (4 mol%), $Pd(dba)_2$ (3 mol%), tfp(6 mol%).[19] f) Reaction conditions: conc. HCl, THF:H_2O, 25 °C, 0.5 h. g) 3 equiv. of THF were added.

3.3 Regioselective Magnesiation of Heteroarenes

MBDA was an excellent base for the metalation of heterocycles **105**. The formation of a *bis*-heteroaryl magnesium intermediate of type **107** was performed in most cases using 0.6-0.8 equivalents of MBDA **103**. Various trapping reactions with iodine, allylic bromides, aryl iodides (Negishi cross-coupling), ketones, aldehydes and alkynes (Sonogashira cross-coupling) provided a range of fluorinated or halogenated heterocycles **109a-r** in 60-96% yield (Scheme 55). Thus, fluoropyridines **105a-d**, polyfluorinated quinoline **105e**, 2-chloropyrazine **105f**, 2,6-dichloropyrazine **105g** as well as thiomethylpyrazine **105h** were magnesiated between −25 and 25 °C within a few minutes. Quenching with typical electrophiles afforded the expected products in 67-96% yield. Five-membered heterocycles such as the antifungal drug clotrimazole **105i**, 2,4-dibromothiazole **105j**, 2,3-dibromothiophene **105k** or 3,4-ethylenedioxythiophene **105l** were magnesiated between 25 °C and 50 °C giving the expected diheteroarylmagnesium derivatives of type **107** which after electrophile quench provided the heterocycles **109m-r** in 68-96% yield. Finally, in the case of thieno[3,2-*b*]thiophene **105m** the magnesiation required 1.1 equivalents of MBDA (**103**). Pd-catalyzed cross-coupling with 4-iodo-3-fluoropyridine **105a** afforded the product **109s** in 60% yield.

[154] V. Farina, *Adv. Synth. Catal.* **2004**, *346*, 1553-1582.

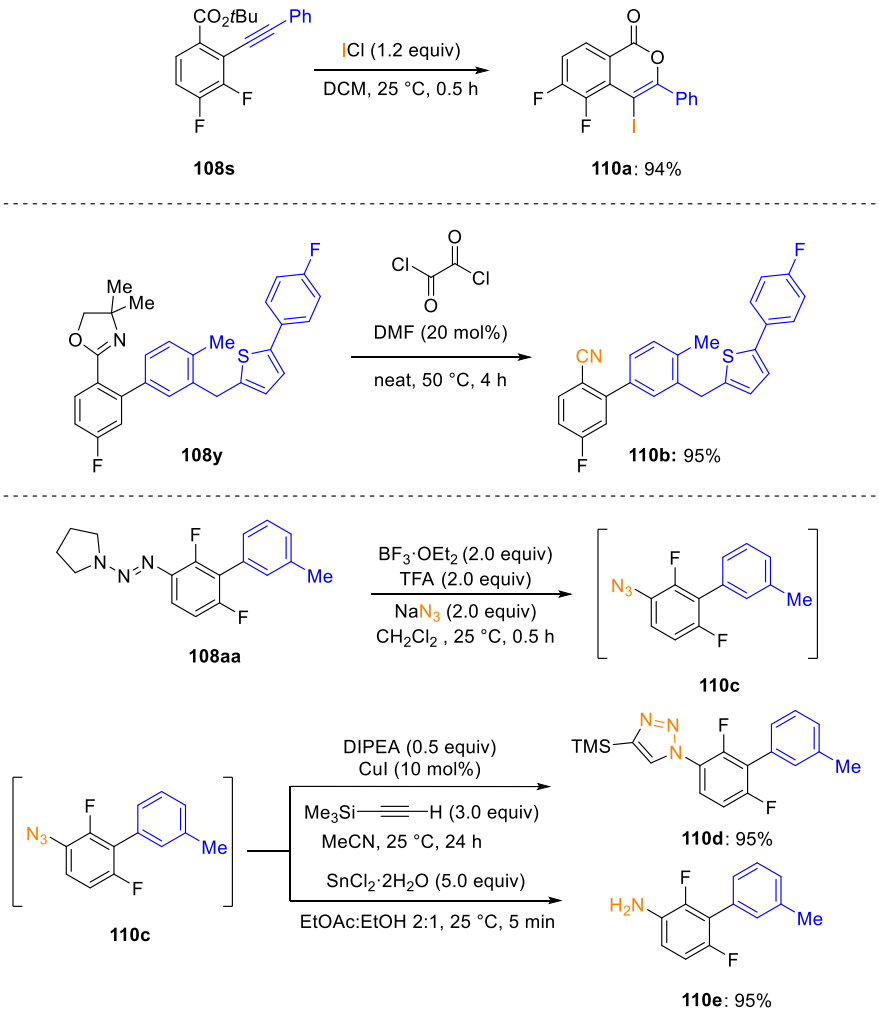


Scheme 55: Regioselective magnesiation of heteroarenes **105a-m** with MBDA **103** leading to diheteroarylmagnesium species **107a-m** and after electrophile trapping to functionalized arenes **109a-s**. a) All yields refer to isolated compounds. b) The reaction was catalyzed by CuCN·2LiCl (20 mol%). c) Obtained after transmetalation with $ZnCl_2$ (1.4 equiv) and a palladium-catalyzed cross-coupling with an aryl iodide (0.83 equiv) using $Pd(dba)_2$ (3 mol%), tfp (6 mol%). d) Obtained after transmetalation with $ZnCl_2$ (1.4 equiv), subsequent iodine quench (1.1 equiv) and Sonogashira cross-coupling with an alkyne (1.3 equiv) using CuI (4 mol%), $Pd(dba)_2$ (3 mol%), tfp (6 mol%). e) 1.1 equiv of MBDA **103** were used.

3.4 Postfunctionalizations and NMR-Studies

Some products of type **108** (Scheme 54) were readily post-functionalized funrishing more complex fluorinated molecules (Scheme 56). Thus, the benzoate **108s** underwent a ring closure with ICl leading

to the fluorinated isocoumarine **110a** in 94% yield.[155] Also, the aryl oxazoline **108y** was converted to the corresponding fluoronitrile **110b** under Vilsmeier-Haack conditions in 95% yield.[156] Finally, the triazene[157] **108aa** gave the key aryl azide **110c** by treatment with $BF_3 \cdot OEt_2$, trifluoroacetic acid (TFA) and sodium azide which by click-reaction with trimethylsilylacetylene afforded the triazole **110d** in 95% yield.[158] Reduction of **110c** with $SnCl_2$ furnished the difluoroaniline **110e** in 95% yield.[159]

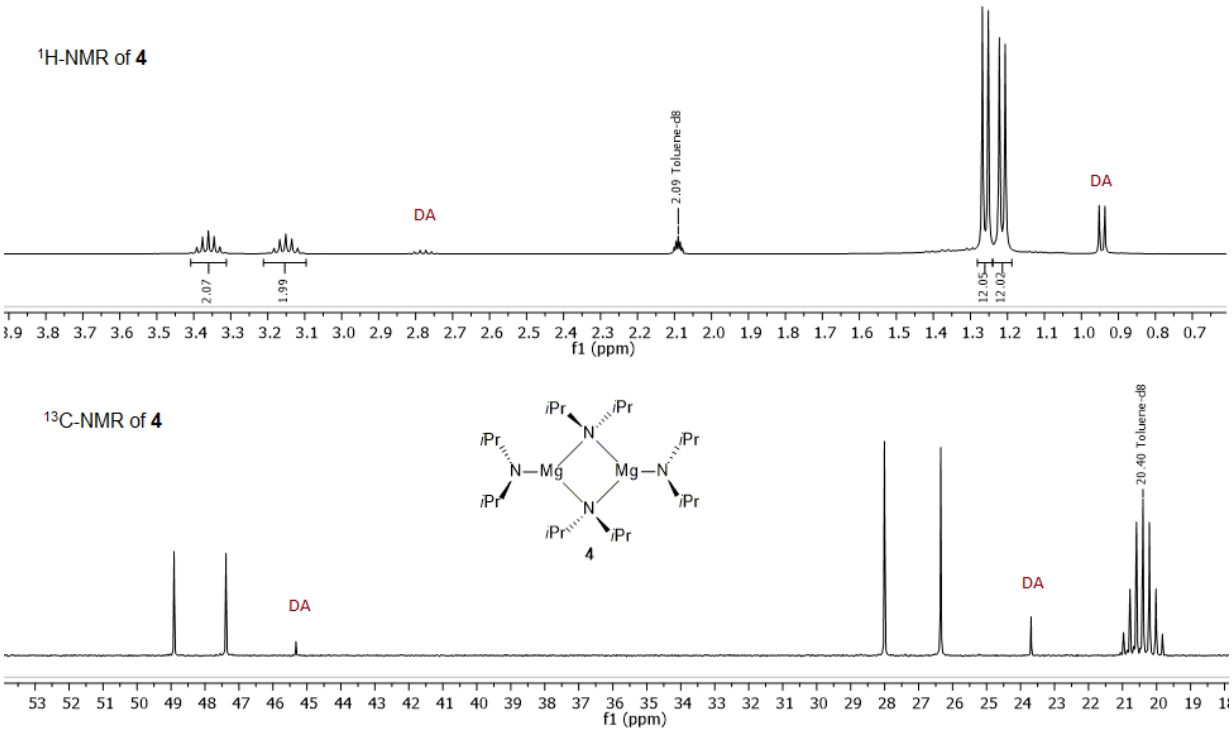


Scheme 56: Postfunctionalizations of fluoroarenes **108s, 108y** and **108aa** providing highly functionalized fluoroarenes.

Furthermore, ^{1}H- and ^{13}C-NMR studies revealed a dimeric structure of MBDA (**103**) in toluene-d_8 as shown by a typical pattern showing two sets of signals (Scheme 57).[160] Also, ^{1}H- and ^{19}F-NMR spectra

[155] T. Yao, R. C. Larock, *J. Org. Chem.* **2003**, *68*, 5936-5942.
[156] a) A. Vilsmeier, A. Haack, *Ber. Chem. Dtsch. Ges.* **1927**, *60*, 119-122.; b) A. Hess, H. C. Guelen, N. Alandini, A. Mourati, Y. C. Guersoy, P. Knochel, *Chem. Eur. J.* **2022**, *28*, e202103700.
[157] M. L. Gross, D. H. Blank, W. M. Welch, *J. Org. Chem.* **1993**, *58*, 2104-2109.
[158] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004-2021.
[159] K. R. Gee, J. Keana, *Synth. Commun.* **1993**, *23*, 357-360.
[160] a) M. Westerhausen, *Inorg. Chem.* **1991**, *30*, 96-101; b) M. M. Olmstead, W. J. Grigsby, D. R. Chacon, T. Hascall, P. P. Power, *Inorganica Chim. Acta* **1996**, *251*, 273-284; c) A. Harrison-Marchand, F. Mongin, *Chem. Rev.* **2013**, *113*, 7470-7562.

of ArMgDA confirmed the expected stoichiometry for arenes by addition of 1.1 equivalents of MBDA (**103**).[161]



Scheme 57: ^{1}H and ^{13}C NMR spectra of MBDA (**103**) in toluene-d_8.

3.5 Summary

In summary, a new hydrocarbon soluble base MBDA was developed that allowed a non-cryogenic magnesiation of various fluoroarenes and heterocyclic fluoro-derivatives. The resulting organomagnesium intermediates of type ArMgDA or Het_2Mg showed high stability and no aryne-formation was observed in any case. Reaction with various electrophiles provided a range of valuable fluorinated and pharmaceutically relevant building blocks.

[161] See Experimental Section.

4. Regioselective Magnesiations of Functionalized Arenes and Heteroarenes using TMP_2Mg in Hydrocarbons[162]

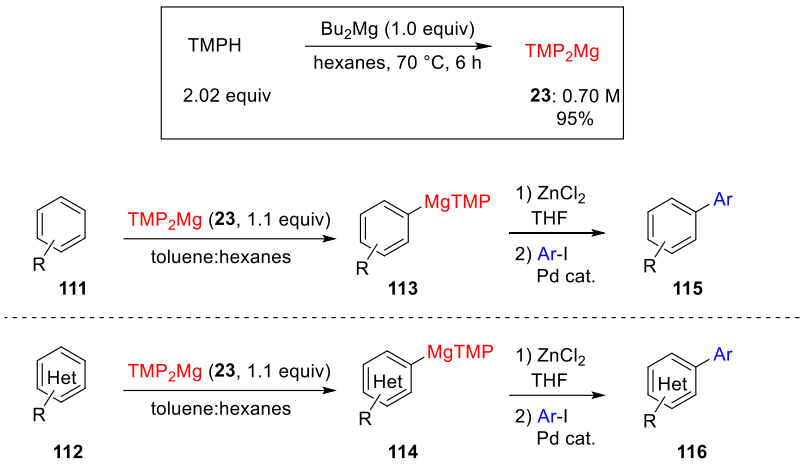
4.1 Introduction

The regioselective metalation of aromatics and heterocycles is an important method for the preparation of highly functionalized derivatives present in numerous pharmaceuticals and agrochemicals.[163] Although the directed lithiation of such arenes and heteroarenes has been extensively studied, the high reactivity of the resulting aryllithiums has precluded the presence of sensitive functional groups and therefore limits the scope of this metalation strategy.[164] A much broader scope was achieved by directed magnesiations,[165] using mixed sterically hindered and well soluble bases such as TMPMgCl·LiCl[166] (**25**) or $TMP_2Mg·2LiCl$[167] (**30**) in THF. The high polarity of THF gave a high reactivity to bases **25** and **30** as well as to the resulting (hetero)arylmagnesium reagents. However, for many applications including industrial processes, the use of less polar solvents was desirable.[168] Above, $(i Pr_2N)_2Mg$ (magnesium-*bis*-diisopropylamide; MBDA) **103** in hexanes was reported as an excellent base for the magnesiation of fluorosubstituted arenes and heterocycles.[169] However, the base **103** was not compatible with important functional groups such as ethyl esters and carbamates.

In the following, the preparation of a new base TMP_2Mg[170] **23** in hexanes and its use for the magnesiation of arenes **111** and heteroarenes **112** providing arylmagnesium amides of type **113** and **114** is reported. The further reaction with various aryl iodides in the presence of a Pd-catalyst gave access to a variety of biaryl derivatives of type **115** and **116** (Scheme 58).[171]

[162] Adapted with permission from (A. Hess, N. Alandini, H. C. Guelen, J. P. Prohaska, P. Knochel, *Chem. Commun.* **2022**, *58*, 8774-8777). Copyright (2022) Royal Society of Chemistry.
[163] a) R. Chinchilla, C. Nájera, M. Yus, *Tetrahedron* **2005**, *61*, 3139-3176; b) S. D. Roughley, A. M. Jordan, *J. Med. Chem.* **2011**, *54*, 3451-3479; c) J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, *4*, 2337-2347; d) J. A. Bull, J. J. Mousseau, G. Pelletier, A. B. Charette, *Chem. Rev.* **2012**, *112*, 2642-2713; e) Z. Nairoukh, M. Cormier, I. Marek, *Nature Rev. Chem.* **2017**, *1*, 0035.
[164] a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879-933; b) J. Clayden, *Organolithiums: selectivity for synthesis* **2002**, *23*, Elsevier; c) M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206-2225; d) M. Schlosser, F. Mongin, *Chem. Soc. Rev.* **2007**, *36*, 1161-1172.
[165] a) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3802-3824; b) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794-9824.
[166] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961; b) W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *8*, 5673-5676; c) M. Mosrin, P. Knochel, *Org. Lett.* **2008**, *10*, 2497-2500.
[167] a) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681-7684; b) C. J. Rohbogner, G. C. Clososki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1503-1507.
[168] a) L. Delhaye, A. Ceccato, P. Jacobs, C. Köttgen, A. Merschaert, *Org. Process Res. Dev.* **2007**, *11*, 160-164; b) A. Jordan, C. G. J. Hall, L. R. Thorp, H. F. Sneddon, *Chem. Rev.* **2022**, *122*, 6749-6794; c) L. J. Bole, N. R. Judge, E. Hevia, *Angew. Chem. Int. Ed.* **2021**, *60*, 7626-7631.
[169] A. Hess, N. Alandini, Y. C. Guersoy, P. Knochel, *Angew. Chem. Int. Ed.* **2022**, e202206176.
[170] P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016-8018.
[171] A. O. King, N. Okukado, E.-i. Negishi, *J. Chem. Soc., Chem. Commun.* **1977**, 683.

The amide base TMP_2Mg **23** was easily obtained by the reaction of TMPH with commercially available Bu_2Mg[172] in hexanes at 70 °C for 6 h, giving a 0.65-0.70 M solution in 95% yield.

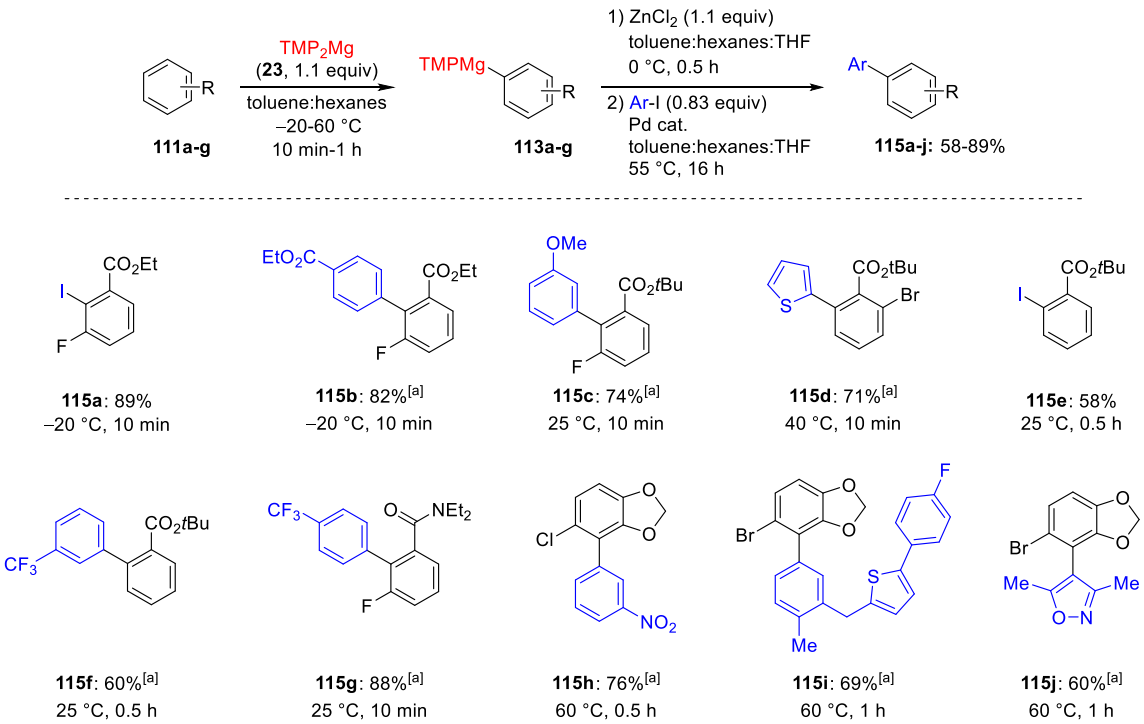


Scheme 58: Preparation of TMP_2Mg **23** in hexanes and regioselective magnesiation of arenes or heteroarenes **111** and **112** furnishing (hetero)arylmagnesium amides **113** and **114** followed by Negishi cross-coupling providing the desired products **115** and **116**.

4.2 Regioselective Magnesiations of Arene Derivatives

Initially, ethyl 3-fluorobenzoate **111a** was treated with TMP_2Mg (**23**, 1.1 equiv) in toluene:hexanes at −20 °C and a full conversion of **111a** within 10 min to the corresponding arylmagnesium amide **113a** was observed. Subsequent iodolysis furnished the aryl iodide **115a** in 89% yield, whereas transmetalation at 0 °C with $ZnCl_2$ (1 M solution in THF) followed by a Negishi cross-coupling with ethyl 4-iodobenzoate at 55 °C and in the presence of $Pd(dba)_2$ (3 mol%, dba = dibenzylideneacetone) and tfp (6 mol%, tfp = tri-(2-furyl)-phosphine)[173] furnished after 16 h the desired product **115b** in 82% yield. Unfortunately, the use of 0.5 equiv TMP_2Mg **23** did not allow to produce the expected diarylmagnesium species in satisfying yield. Therefore 1.1 equiv of **23** were used to produce magnesium amides of type **113**. With *tert*-butyl benzoates **111b-d**, it was possible to perform magnesiations with **23** at 25-40 °C within 30 min (Scheme 59). After performing trapping reactions such as cross-coupling or iodolysis, the desired products **115c-f** were obtained in 58-74% yield. *N*,*N*-Diethyl-3-fluorobenzamide **111e** underwent efficient magnesiation with TMP_2Mg **23** at 25 °C within 10 min. Transmetalation with $ZnCl_2$ and subsequent Pd-catalyzed cross-coupling with 4-iodotrifluoromethylbenzene (55 °C, 16 h) furnished the biphenyl **115g** in 88% yield. Furthermore, more electron-rich aromatic chlorides and bromides could also be metalated with **23** at 60 °C (0.5-1 h) giving the cross-coupling products **115h-j** in 60-76% yield.

[172] Commercial Bu_2Mg is a mixture of $n Bu_2Mg$ and $s Bu_2Mg$ (ca. 60:40 ratio) and is available from Sigma-Aldrich and Albermarle.
[173] V. Farina, *Adv. Synth. Catal.* **2004**, *346*, 1553-1582.

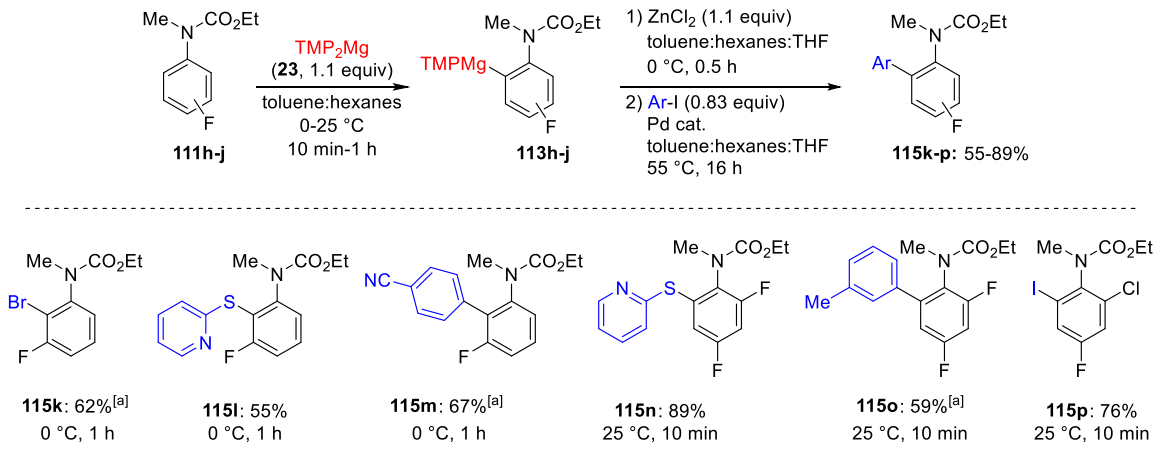


Scheme 59: Regioselective magnesiation of arene derivatives **111a-g** leading to arylmagnesium amides **113a-g** and after Pd-catalyzed cross-coupling to functionalized products **115a-j**. All yields refer to isolated compounds. [a] Obtained after transmetalation with $ZnCl_2$ (2.4 equiv) and a palladium-catalyzed cross-coupling with an aryl iodide (0.83 equiv) using $Pd(dba)_2$ (3 mol%, dba = dibenzylideneacetone) and tfp (6 mol%, tfp = tri-(2-furyl)-phosphine).

4.3 Regioselective Magnesiations of Aniline Derivatives

The metalation of aniline derivatives is an important synthetic reaction for the preparation of functionalized amino-substituted arenes.[174] Thus, various fluoro-substituted *N*-methyl ethyl carbamates (**111h-j**) were magnesiated with TMP_2Mg **23** at temperatures between 0 °C and 25 °C leading to the magnesium amides **113h-j** (Scheme 60). Trapping with various electrophiles such as $(BrCl_2C)_2$, $(PyrS)_2$, I_2 and Ar-I in the presence of a Pd-catalyst gave the desired substituted aniline derivatives **115k-p** in 55-89% yield.

[174] a) A. H. Stoll, P. Knochel, *Org. Lett.* **2008**, *10*, 113-116; b) A. Antoft-Finch, T. Blackburn, V. Snieckus, *J. Am. Chem. Soc.* **2009**, *131*, 17750-17752; c) G. Monzón, I. Tirotta, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 10624-10627.

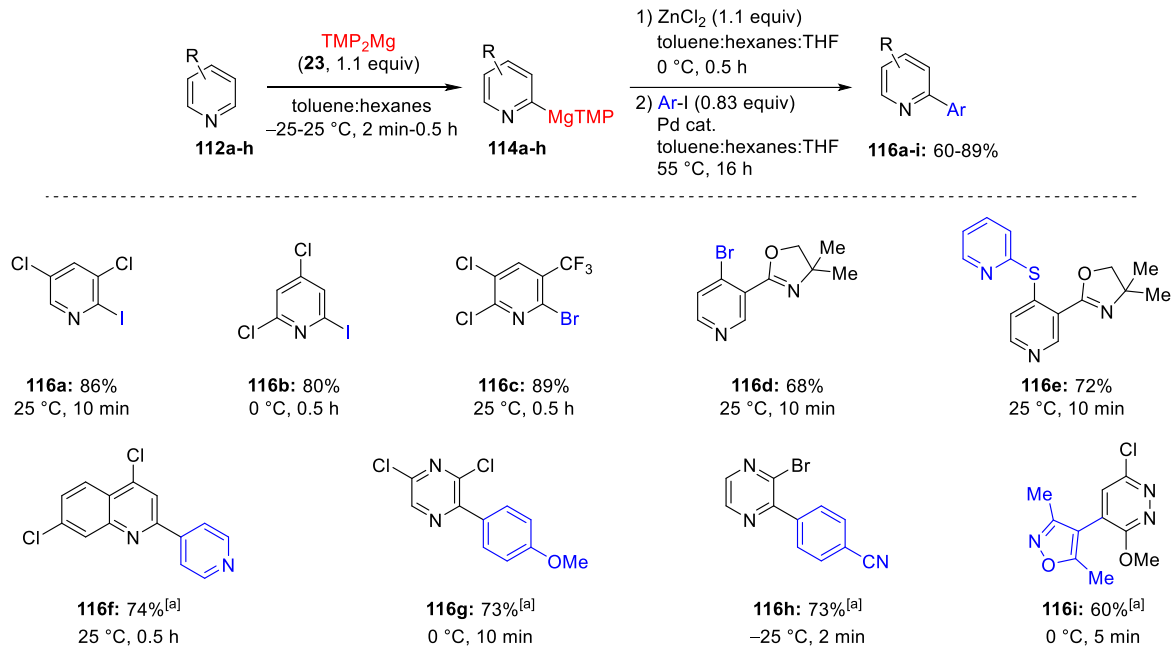


Scheme 60: Regioselective magnesiation of aniline derivatives **111h-j** leading to arylmagnesium amides **113h-j** and after quench to functionalized products **115k-p**. All yields refer to isolated compounds. [a] Obtained after transmetalation with $ZnCl_2$ (2.4 equiv) and a Pd-catalyzed cross-coupling with an aryl iodide (0.83 equiv) using $Pd(dba)_2$ (3 mol%) and tfp (6 mol%).

4.4 Regioselective Magnesiations of Six-Membered *N*-Heterocycles

TMP_2Mg **23** proved to be an excellent reagent for the mild and regioselective magnesiation of six-membered *N*-heterocycles such as pyridines, quinolines, pyrazines or pyridazines.[175] Thus, the chlorinated pyridines **112a-c** were readily magnesiated at 0 °C to 25 °C within 0.5 h affording the corresponding heteroarylmagnesium amides **114a-c** (Scheme 61). Halogenation using iodine and $(BrCl_2C)_2$ gave the polyfunctional pyridines **116a-c** in 80-89% yield. Interestingly, in the case of 4,4-dimethyl-2-(pyridin-3-yl)-4,5-dihydrooxazole **112d** the strong directing power of the dimethyloxazoline group[176] caused the exclusive magnesiation at the 4-position. Treatment of **112d** with **23** at 25 °C and subsequent electrophilic trapping with $(BrCl_2C)_2$ or $(PyrS)_2$ provided the derivatives **116d** and **116e** in 68-72% yield. Quinoline **112e** was magnesiated with **23** at 25 °C for 0.5 h giving the heteroarylmagnesium amide **114e** in quantitative yield. Negishi cross-coupling of **114e** with 4-iodopyridine provided the building block **116f** in 74% yield. Sensitive heterocycles such as pyrazines (**112f-g**) and pyridazine **112h** were also magnesiated with **23** at convenient temperatures from −25 °C to 0 °C within a few minutes. Subsequent transmetalation with $ZnCl_2$, followed by a Negishi cross-coupling generated the valuable *N*-heterocycles **116g-i** in 60-73% yield.

[175] a) M. Miah, V. Snieckus, *J. Org. Chem.* **1985**, *50*, 5436-5438; b) M. Mosrin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 1468-1477; c) M. Mosrin, T. Bresser, P. Knochel, *Org. Lett.* **2009**, *11*, 3406-3409; d) M. Jaric, B. A. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 5451-5455; e) H. K. Khartabil, P. C. Gros, Y. Fort, M. F. Ruiz-López, *J. Am. Chem. Soc.* **2010**, *132*, 2410-2416; f) M. Jaric, B. A. Haag, S. M. Manolikakes, P. Knochel, *Org. Lett.* **2011**, *13*, 2306-2309.
[176] T. G. Gant, A. Meyers, *Tetrahedron* **1994**, *50*, 2297-2360.

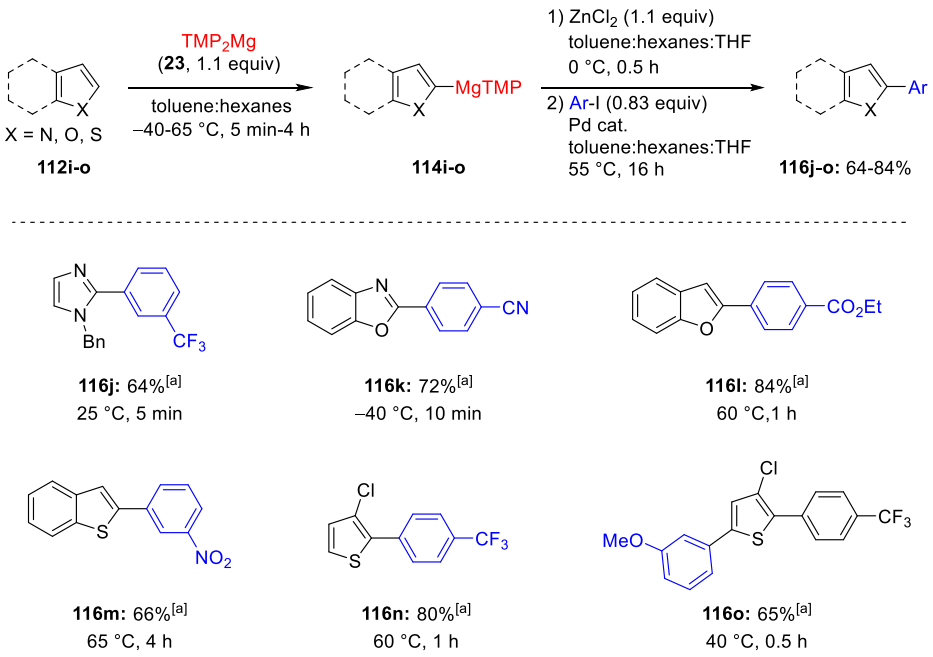


Scheme 61: Regioselective magnesiation of *N*-heterocycles **112a-h** leading to heteroarylmagnesium amides **114a-h** and after quench to functionalized products **116a-i**. All yields refer to isolated compounds. [a] Obtained after transmetalation with $ZnCl_2$ (2.4 equiv) and a Pd-catalyzed cross-coupling with an aryl iodide (0.83 equiv) using $Pd(dba)_2$ (3 mol%), tfp (6 mol%).

4.5 Regioselective Magnesiations of Five-Membered Heterocycles

In a next step, the magnesiation of five-membered heterocycles such as imidazoles, benzoxazoles, benzofuran and thiophene derivatives followed by Negishi cross-coupling reactions was examined (Scheme 62).[177] Thus, the treatment of imidazole **112i** with TMP_2Mg **23** (25 °C, 5 min) and reaction with the corresponding aryl iodide furnished the diaryl **116j** in 64% yield. Benzoxazole **112j** required a reaction temperature of -40 °C for an efficient magnesiation due to its high sensitivity. Nevertheless, the cross-coupling proceeded efficiently giving the desired product in 72% yield (**116k**). Notably, both benzofuran (**112k**) and benzothiophene (**112l**) were only efficiently magnesiated at elevated temperatures of 60-65 °C in 1-4 h to afford the heteroarylmagnesium amides **114k** and **114l**. Cross-coupling with 4-iodobenzoate and 1-iodo-3-nitrobenzene provided the heterocyclic products **116l** and **116m** in 66-84% yield. Furthermore, 3-chlorothiophene was also treated with TMP_2Mg (**23**) and the resulting magnesium reagent reacted with the corresponding aryl iodide after transmetalation with $ZnCl_2$ to give **116n** in 80% yield. A further magnesiation of **116n** was achieved at 40 °C (0.5 h) and the reaction with 3-iodo anisole gave a 2,3,5-functionalized thiophene **116o** in 65% yield.

[177] a) L. Melzig, C. B. Rauhut, P. Knochel, *Chem. Commun.* **2009**, 3536-3538; b) G. W. Gribble, *Metalation of Azoles and Related Five-Membered Ring Heterocycles* **2012**, *29*, Springer. c) C. Saemann, E. Coya, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 1430-1434.

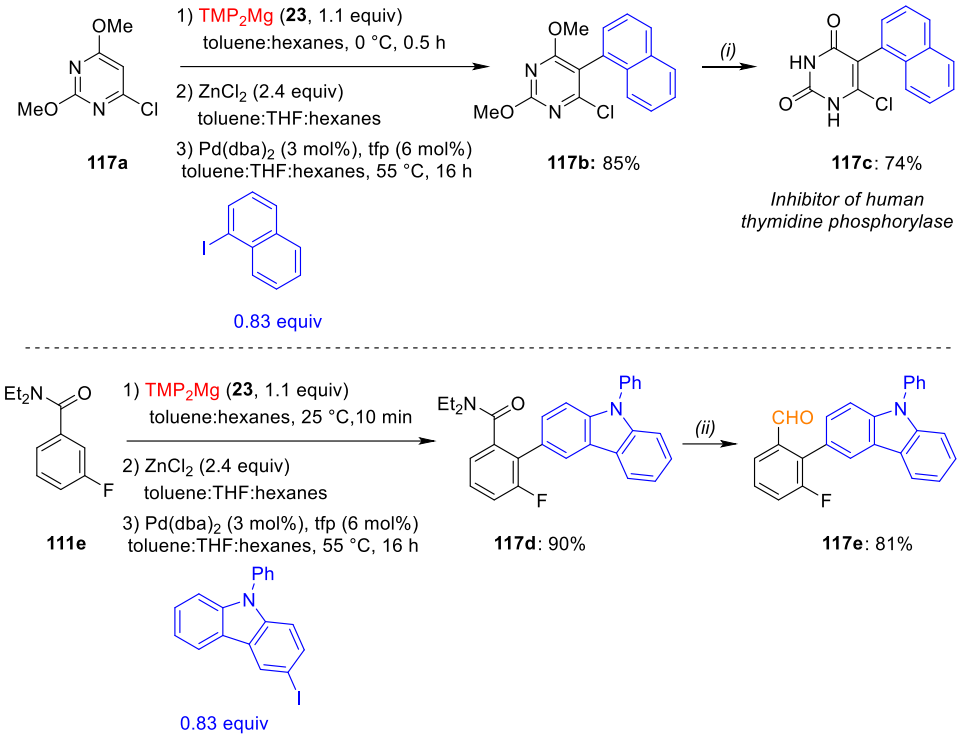


Scheme 62: Regioselective magnesiation of five-membered heterocycles **112i-o** leading to heteroarylmagnesium amides **114i-o** and after Pd-catalyzed cross-coupling to functionalized products **116j-o**. All yields refer to isolated compounds. [a] Obtained after transmetalation with $ZnCl_2$ (2.4 equiv) and a Pd-catalyzed cross-coupling with an aryl iodide (0.83 equiv) using $Pd(dba)_2$ (3 mol%), tfp (6 mol%).

4.6 Synthetic Applications

The commercially available uracil derivative **117a** was magnesiated with TMP_2Mg **23** at 0 °C for 0.5 h and functionalized by cross-coupling with 1-iodonaphthalene. The coupling product **117b** was obtained in 85% yield and was readily transformed by hydrolysis with aqueous hydrochloric acid into an inhibitor of the human thymidine phosphorylase (**117c**) in 74% yield.[178] Finally, *N*,*N*-diethyl-3-fluorobenzamide **111e** was magnesiated under standard conditions and submitted to a Negishi cross-coupling with 3-iodo-9-phenylcarbazole leading to the desired product **117d** in 90% yield. This amide was selectively reduced to the corresponding aldehyde **117e** by using the Schwartz reagent (Scheme 63).[179]

[178] R. Nencka, I. Votruba, H. Hřebabecký, P. Jansa, E. Tloušťová, K. Horská, M. Masojídková, A. Holý, *J. Med. Chem.* **2007**, *50*, 6016-6023.
[179] a) J. M. White, A. R. Tunoori, G. I. Georg, *J. Am. Chem. Soc.* **2000**, *122*, 11995-11996; b) Y. Zhao, V. Snieckus, *Org. Lett.* **2014**, *16*, 390-393.



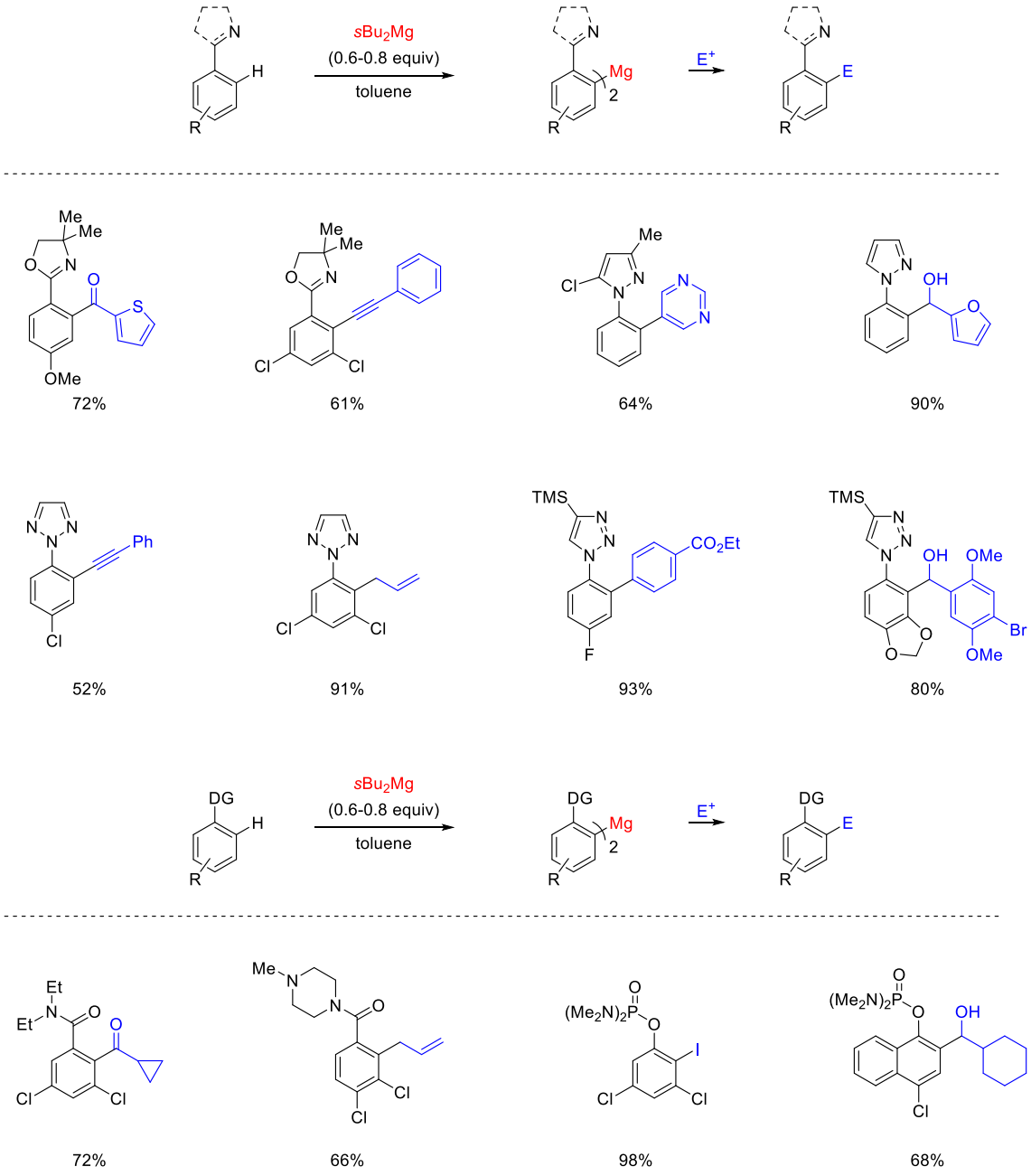
Scheme 63: Magnesiations of uracil derivative **117a** and benzamide **111e** with TMP_2Mg **23** and further transformations. Reaction conditions: (i) conc. HCl, THF:dioxane, reflux, 2 h; (ii) $Cp_2Zr(H)Cl$ (1.5 equiv), THF, 25 °C, 0.5 h.

4.7 Conclusion

In summary, a regioselective magnesiation of arenes and heteroarenes using TMP_2Mg in hydrocarbons under mild reaction conditions was developed. This method was compatible with various aromatic substrates bearing ethyl esters or carbamates. Subsequent Negishi cross-couplings with a broad range of aryl iodides or quenching with various electrophiles gave access to a range of valuable functionalized arenes and heteroarenes in good to excellent yields.

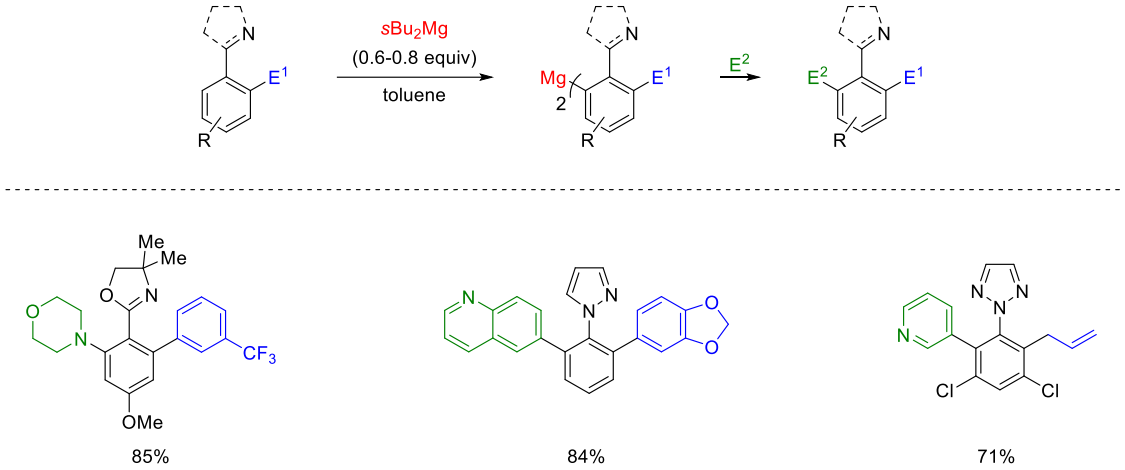
5. Summary

In this thesis, three new hydrocarbon-soluble organomagnesium reagents were developed, which could be all obtained in excellent yields. The reagent *s*Bu_2Mg as a solution in toluene allowed the regioselective and mild *ortho*-magnesiation of sensitive and pharmaceutically relevant aryl azoles as well as arenes bearing various directing groups such as an oxazoline, phosphorodiamidate or an amide (Scheme 64).



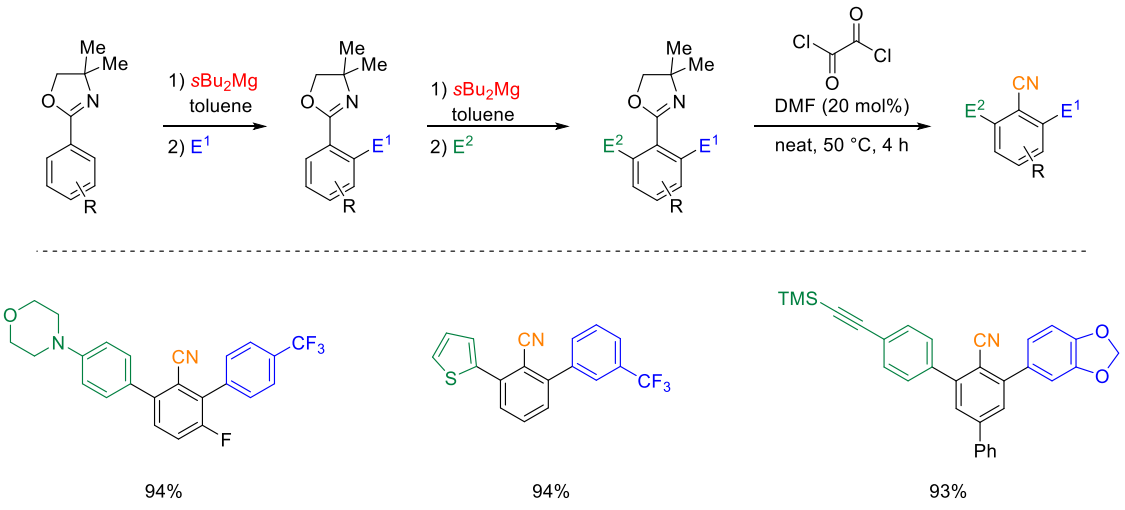
Scheme 64: Regioselective magnesiation of aryl azoles and arenes using *s*Bu_2Mg in toluene.

In the case of aryl oxazolines, *N*-aryl pyrazoles as well as *N*-aryl triazoles a second unsymmetrical *ortho,ortho´*- functionalization was achieved (Scheme 65).



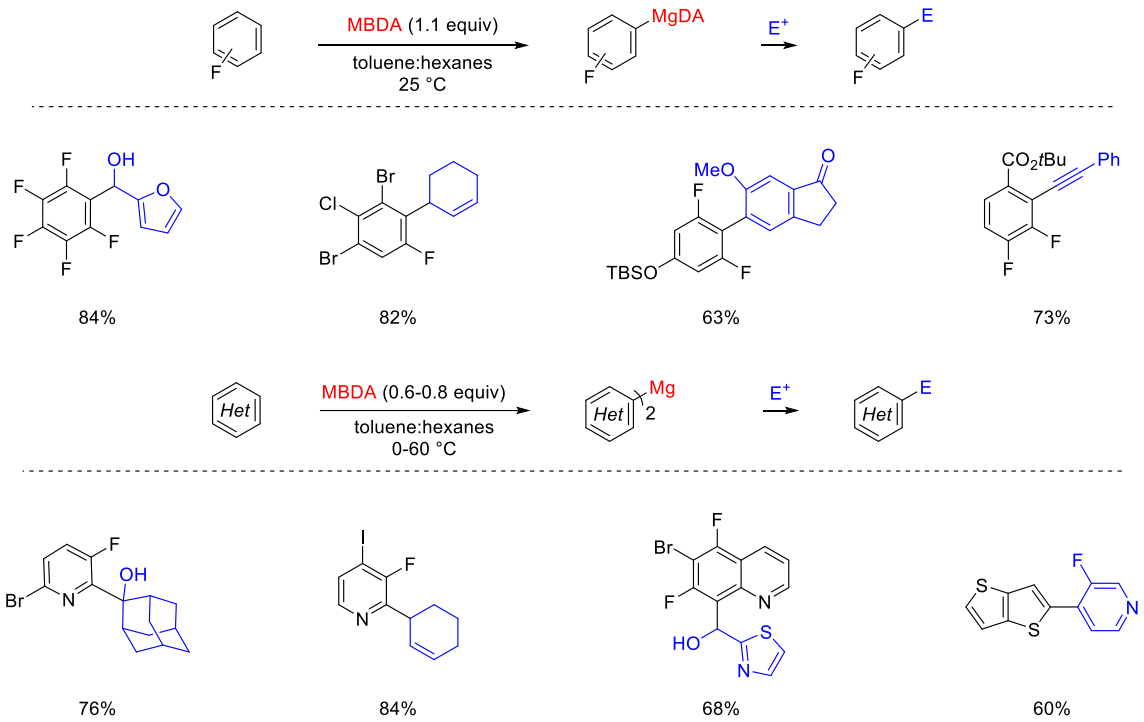
Scheme 65: *Ortho,ortho´*-functionalization of various aryl azoles.

The second part of this thesis comprised the development of a new method for the preparation of highly functionalized aromatic nitriles. Successive magnesiations of aryl oxazolines with *s*Bu$_2$Mg in toluene provided a range of *ortho,ortho´*-functionalized aryl oxazolines which could be converted to the corresponding nitriles in an efficient one-step sequence by treatment with oxalyl chloride and catalytic amounts of DMF (Scheme 66).



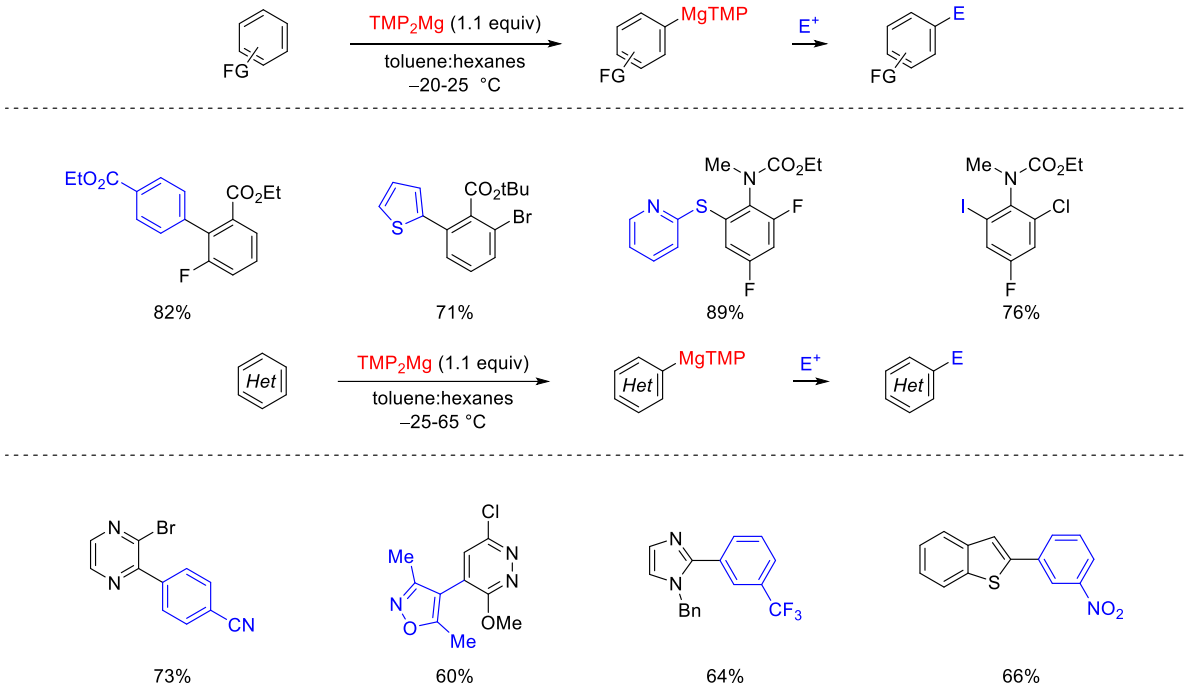
Scheme 66: Transformation of *ortho,ortho´*-functionalized oxazolines to the corresponding nitriles.

Based on the pharmaceutical relevance and increasing demand for highly functionalized fluorinated arenes, a new strategy for their efficient magnesiation using the new hexane-soluble reagent magnesium-*bis*-diisopropylamide (MBDA) was developed. The reagent itself shows long stability and allowed the magnesiation of various fluoroaromatics and heteroarenes without the formation of undesired aryne side-products under non-cryogenic conditions (Scheme 67). Furthermore, NMR studies revealed a dimeric structure of the reagent in solution and gave valuable insights into the nature of organometallic species in hydrocarbons.



Scheme 67: Regioselective magnesiations of fluoroaromatics and heteroarenes using MBDA in hydrocarbons.

The reagent MBDA was not compatible with important functional groups such as ethyl esters or carbamates. Thus, the last part of this thesis described the development of the hexane-soluble reagent TMP_2Mg, which showed excellent properties for the regioselective magnesiation of various arenes bearing functional groups and sensitive heteroarenes under very mild conditions (Scheme 68).



Scheme 68: Regioselective magnesiations of arenes bearing functional groups and sensititve heteroarenes using TMP_2Mg in hydrocarbons.

C. EXPERIMENTAL SECTION

1. General Considerations

All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF, toluene and hexanes were continuously refluxed and freshly distilles from sodium benzophenone ketyl under nitrogen and stored over molecular sieves. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H-NMR and capillary GC.

1.1 Solvents

Solvents were dried according to standard procedures by distillation over drying agents and stored under argon.

CH_2Cl_2 was predried over $CaCl_2$ and distilled from CaH_2.

Et_2O was treated with phtalic anhydride and sodium, heated to reflux for 6 h and distilled.

Toluene was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen and then stored over molecular sieves.

Solvents for column chromatography were distilled prior to use.

1.2 Reagents

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

***i*PrMgCl·LiCl** solution in THF was obtained from Albemarle.

***n*BuLi** solution in hexanes was obtained from Albemarle.

***s*BuLi** solution in cyclohexane was obtained from Albemarle.

***s*BuMgCl** solution in Et_2O was obtained from Sigma-Aldrich.

Bu_2Mg solution in hexanes was obtained from Albemarle.

Preparation of a $ZnCl_2$ solution in THF

A $ZnCl_2$ solution (1 M) was prepared by drying $ZnCl_2$ (200 mmol, 27.3 g) in a Schlenk-flask under vacuum at 140 °C for 5 h. After cooling, dry THF (200 mL) was added and stirring continued until the salt was dissolved.

Preparation of a CuCN·2LiCl solution in THF

A CuCN·2LiCl 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-flask under vacuum at 140 °C for 12 h. After cooling, dry THF (80 mL) was added and stirring was continued until the salts were dissolved.

Preparation of *s*Bu_2Mg (58) in toluene

A dry and argon-flushed Schlenk-flask equipped with a stirring bar and a septum, was charged with *s*BuMgCl (10.2 mL, 20 mmol, 1.95 M in Et_2O, 1.00 equiv). Then *s*BuLi (12.8 mL, 20 mmol, 1.56 M in cyclohexane, 1.00 equiv) was added at room temperature under vigorous stirring. The resulting suspension was stirred for 2 h at room temperature. The solvents were removed under vacuum followed by addition of dry toluene (40 mL). The resulting suspension was vigorously stirred and allowed to settle overnight. The colourless solution was carefully transferred by cannula using a syringe filter and titrated (benzoic acid and 4-(phenylazo)diphenylamine as indicator, 0.43-0.48 M, 96% yield) prior use.

Preparation of TMPMgCl·LiCl (25) in THF

A dry and argon flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with freshly titrated *i*PrMgCl·LiCl (100 mL, 1.2 M in THF, 120 mmol). TMPH (19.8 g, 126 mmol, 1.05 equiv) was added dropwise at room temperature until gas evolution ceased (ca. 24 h). The solution was titrated with benzoic acid and 4-(phenylazo)diphenylamine as indicator prior use.

Preparation of Magnesium-bis-diisopropylamide MBDA (103) in hexanes

A dry and argon-flushed Schlenk-flask equipped with a stirring bar and a septum, was charged with Bu_2Mg (67.1 mL, 50 mmol, 0.75 M in hexanes, 1.00 equiv). Then diisopropylamine (14.3 mL, 101 mmol, 2.02 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 4 h. The slightly yellow solution was titrated (benzoic acid and 4-(phenylazo)diphenylamine as indicator, 0.79 M, >99% yield) prior use.

Preparation of TMP_2Mg (23) in hexanes

A dry and argon-flushed Schlenk-flask equipped with a stirring bar and a septum, was charged with 2,2,6,6-Tetramethylpiperidine (3.44 mL, 20.2 mmol, 2.02 equiv). Then *n*Bu_2Mg (13.5 mL, 10 mmol, 0.74 M in hexane, 1.00 equiv) was added dropwise at 0 °C. The resulting cloudy mixture was refluxed for 6 h. The resulting yellow solution was titrated (benzoic acid and 4-(phenylazo)diphenylamine as indicator, 0.65-0.70 M, 95% yield) prior use.

1.3 Content Determination of Organometallic Reagents

Titration of Organomagnesium Reagents Using Benzoic Acid

Accurately weighted aliquots of benzoic acid and 4-(phenylazo)diphenylamine were dissolved in dry THF. The resulting yellow solution was cooled to 0 °C and the organomagnesium reagent was added till the colour completely changed to deep purple. Thus, the concentration of the active species (in mmol/mL) is determined and thereof the yield of the magnesium reagent.[180]

Organolithium reagents were titrated against isopropanol using 1,10-phenantrolin as indicator in THF.[181]

1.4 Chromatography

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

Thin layer chromatography was performed using SiO_2 pre-coated aluminium plates (Merck 60, F-254). The chromatograms were examined under UV light at 254 nm and/or by staining of the TLC plate with one of the solutions given below followed by heating with a heat gun:

Seebach's stain: Phosphomolybdic acid (2.5 g), $Ce(SO_4)_2$ (1.0 g), conc. H_2SO4 (6 mL), H_2O (94 mL).

$KMnO_4$ stain: $KMnO_4$ (3.0 g), K_2CO_3 (20 g), 5% NaOH solution (5 mL), water (300 mL).

1.5 Analytical Data

^{1}H-NMR and **^{13}C-NMR** spectra were recorded on VARIAN Mercury 200, BRUKER ARX 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments. Chemical shifts are reported as values in ppm relative to tetramethylsilane. CDCl3 peaks were set to 7.26 ppm in ^{1}H NMR and 77.16 ppm in ^{13}C NMR experiments. The following abbreviations were used to characterize signal multiplicities: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), hept (heptett) as well as m (multiplet).

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 ionization energy of 70 eV. For coupled gas chromatography/mass spectrometry, a HEWLETT-PACKARD HP

[180] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890-891.
[181] H.-S. Lin, A. Paquette, *Synth. Commun.* **1994**, *24*, 2503-2506.

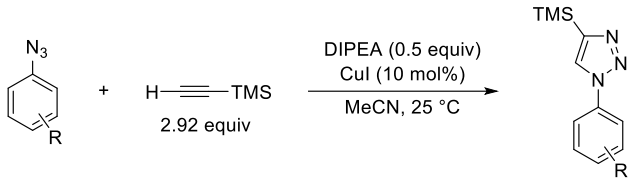
6890/MSD 5973 GC/MS system was used. Molecular fragments are reported starting at a relative intensity of 10-20%.

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. The main absorption peaks are reported in cm^{-1}.

Melting points (m.p.) were determined on a BÜCHI B-540 melting point apparatus and are uncorrected.

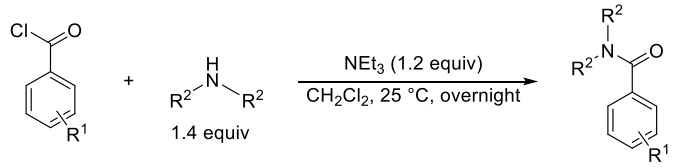
2. Typical Procedures

2.1 TP1: Typical Procedure for the Preparation of 1-aryl-4-trimethylsilyl-1*H*-1,2,3-triazoles



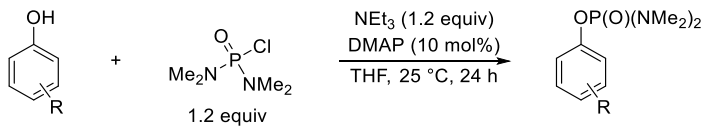
A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding aromatic azide (30.0 mmol, 1.0 equiv) and dissolved in dry acetonitrile (20 mL). Copper(I)-iodide (3.0 mmol, 10 mol%), trimethylsilylacetylene (87.7 mmol, 2.92 equiv) and DIPEA (15.0 mmol, 0.5 equiv) were added and the reaction mixture was stirred for a indicated time at room temperature. The reaction mixture was quenched with water, filtered through a short pad of celite and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

2.2 TP2: Typical Procedure for the Preparation of Aryl Amides



A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding aromatic acid chloride (20.0 mmol, 1.0 equiv) and dissolved in dry dichloromethane (20 mL). NEt_3 (24.0 mmol, 1.2 equiv) was added and the corresponding amine (28.0 mmol, 1.4 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched with sat. aq. $NaHCO_3$ solution and extracted with dichloromethane (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude products were purified by flash column chromatography.

2.3 TP3: Typical Procedure for the Preparation of Aryl Phosphordiamidate Derivatives



The described preparation was performed according to a modified literature procedure.[182] A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding phenol (20.0 mmol, 1.0 equiv) and DMAP (2.0 mmol, 10 mol%) and subsequently dissolved in dry THF (20 mL). NEt_3 (24.0 mmol, 1.2 equiv) and *N*,*N*,*N'*,*N'*-tetramethylphosphordiamidic chloride (24.0 mmol, 1.2 equiv) were added and the reaction mixture was stirred for 24 h at room temperature. The mixture was quenched with brine (20 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude products were purified by flash column chromatography.

2.4 TP4: Typical Procedure for the Regioselective Metalation and Functionalization of Aryl Azoles and Arenes using *s*Bu_2Mg in Toluene

A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding substrate (1.0 equiv) in dry toluene (0.5 M solution). The resulting solution was stirred at indicated temperature and *s*Bu_2Mg (**58**, 0.60-0.80 equiv) was added dropwise. The completion of the metalation was checked by GC-analysis of reaction aliquots quenched with iodine, using undecane as internal standard. Subsequent reactions with electrophiles (1.2 equiv) were carried out under the indicated conditions. After complete conversion, the mixture was quenched with sat. aq. NH_4Cl solution and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography using an indicated eluent afforded the corresponding title compounds.

2.5 TP5: Typical Procedure for the Regioselective Metalation and Functionalization of 2-(Hetero)aryl Oxazolines using TMPMgCl·LiCl

A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding 2-aryl oxazoline (1.0 equiv) in dry THF (0.5 M solution). The resulting solution was stirred at indicated temperature and TMPMgCl·LiCl (**25**, 1.20-2.00 equiv) was added dropwise. The completion of the metalation was checked by GC-analysis of reaction aliquots quenched with iodine, using undecane as internal standard. Subsequent reactions with electrophiles (1.2 equiv) were carried out under the indicated conditions. After complete conversion, the mixture was quenched with sat. aq. NH_4Cl solution and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography using an indicated eluent afforded the corresponding title compounds.

[182] M. Balkenhohl, B. Heinz, T. Abegg, P. Knochel, *Org. Lett.* **2018**, *24*, 8057-8060.

2.6 TP6: Typical Procedure for the Preparation of Functionalized Aromatic Nitriles from Aryl Oxazolines using Oxalyl Chloride and Catalytic Amounts of DMF

A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding 2-aryl oxazoline (0.2 mmol). Oxalyl chloride (1 mL) was added and the resulting solution was cooled to 0 °C. DMF (3 µL) was added dropwise and the reaction mixture was stirred at 50 °C for the indicated time. The completion of the deprotection was checked by GC-analysis of reaction aliquots quenched with a sat. aqueous $NaHCO_3$ solution. After complete conversion, the mixture was cooled to 0 °C, quenched with a sat. aqueous $NaHCO_3$ solution and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography using an indicated eluent afforded the corresponding title compounds.

2.7 TP7: Typical Procedure for the Regioselective Metalation and Functionalization of Fluorinated Arenes and Heteroarenes using MBDA in Hexanes

A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding starting material (1.0 equiv) in dry toluene (0.5 M solution). The resulting solution was stirred at indicated temperature and MBDA (**103**, 0.60-1.10 equiv) was added dropwise. The completion of the metalation was checked by GC-analysis of reaction aliquots quenched with iodine, using undecane as internal standard. Subsequent reactions with electrophiles (1.2-1.4 equiv) were carried out under the indicated conditions. After complete conversion, the mixture was quenched with sat. aq. NH_4Cl solution and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography using an indicated eluent afforded the corresponding title compounds.

2.8 TP8: Typical Procedure for the Preparation of Aryl Carbamate Derivatives

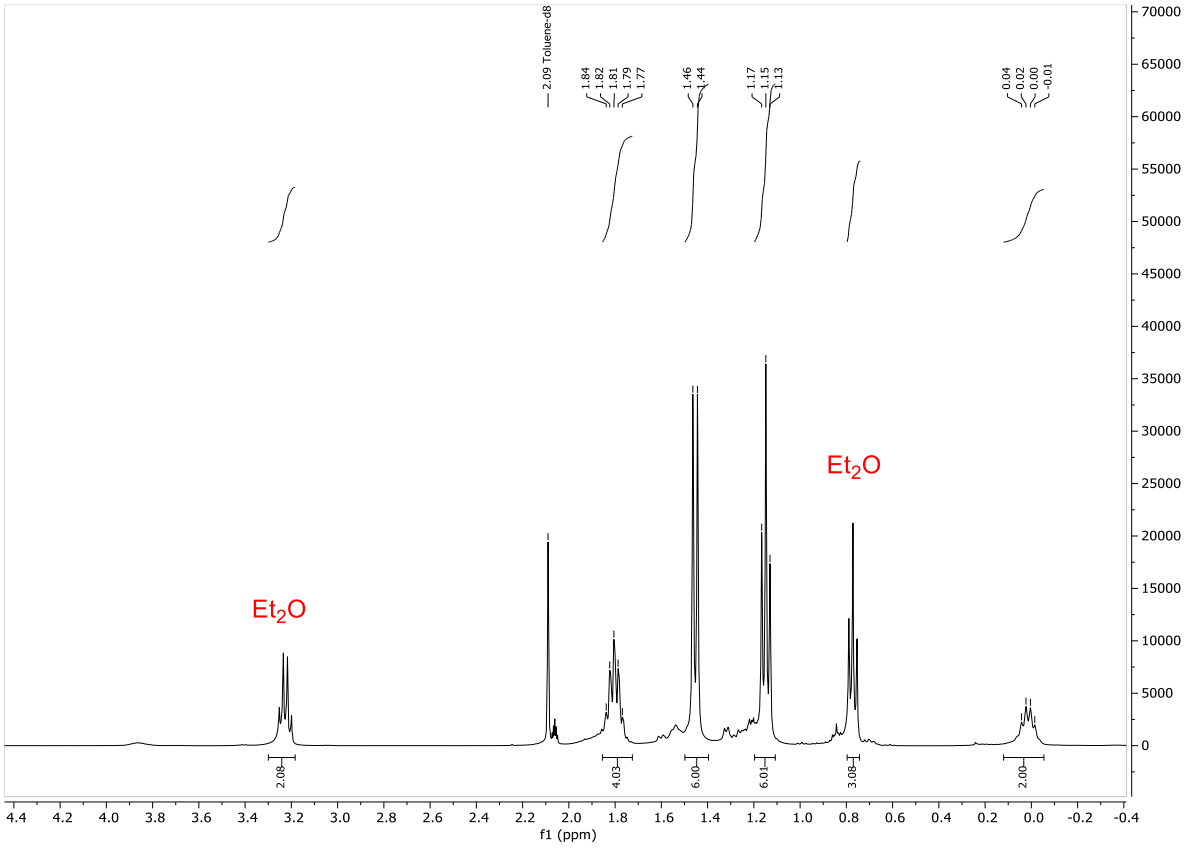
A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding aniline (20.0 mmol, 1.0 equiv) and subsequently dissolved in dry DCM (25 mL). NEt_3 (24.0 mmol, 1.2 equiv) and ethyl chloroformate (24.0 mmol, 1.2 equiv) were added at 0 °C and the reaction mixture was allowed to warm up to room temperature and stirred for 16 h. The mixture was quenched with brine (20 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude products were purified by flash column chromatography.

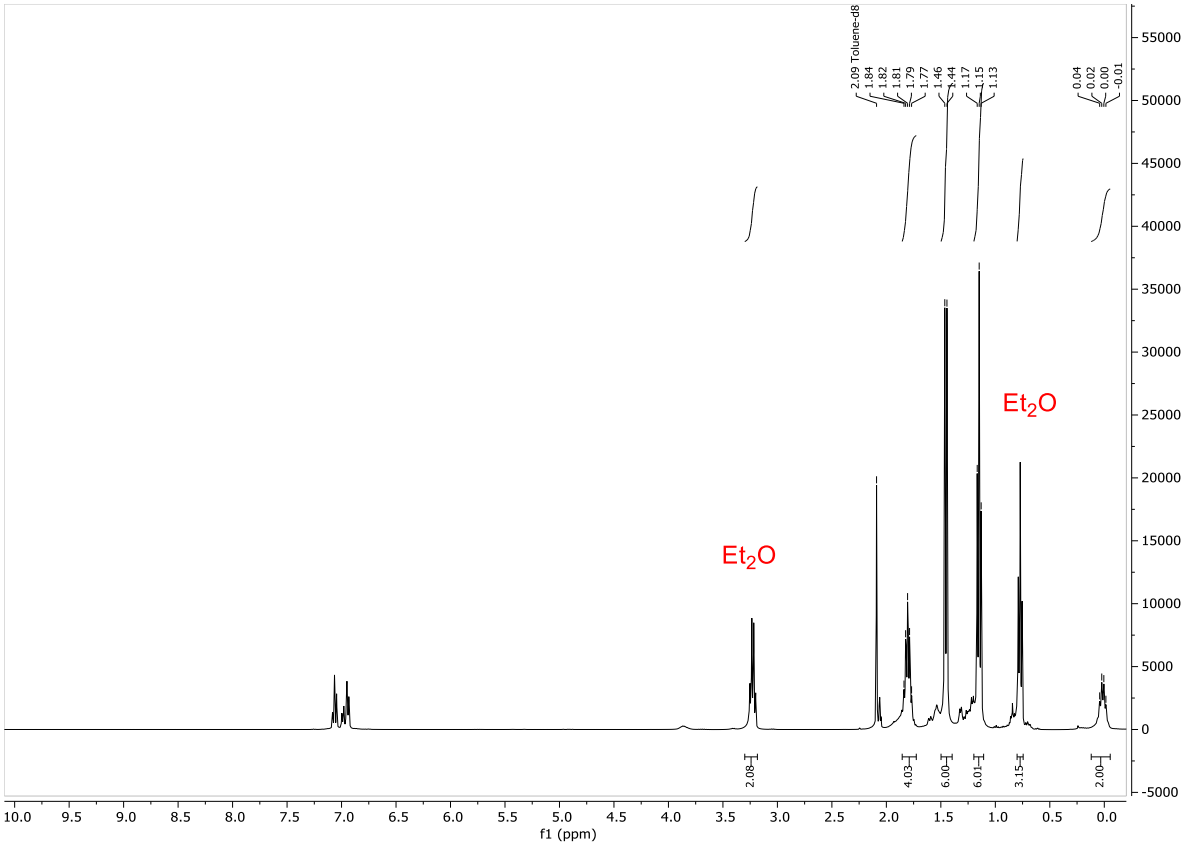
2.9 TP9: Typical Procedure for the Regioselective Metalation and Functionalization of Arenes and Heteroarenes using TMP_2Mg in Hexanes

A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding substrate (1.0 equiv) in dry toluene (0.5 M solution). The resulting solution was stirred at indicated temperature and TMP_2Mg (**23**, 1.1 equiv) was added dropwise. The completion of the metalation was checked by GC-analysis of reaction aliquots quenched with iodine, using undecane as internal standard. Subsequent reactions with electrophiles were carried out under the indicated conditions. After complete conversion, the mixture was quenched with sat. aq. NH_4Cl solution and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography using an indicated eluent afforded the corresponding title compounds.

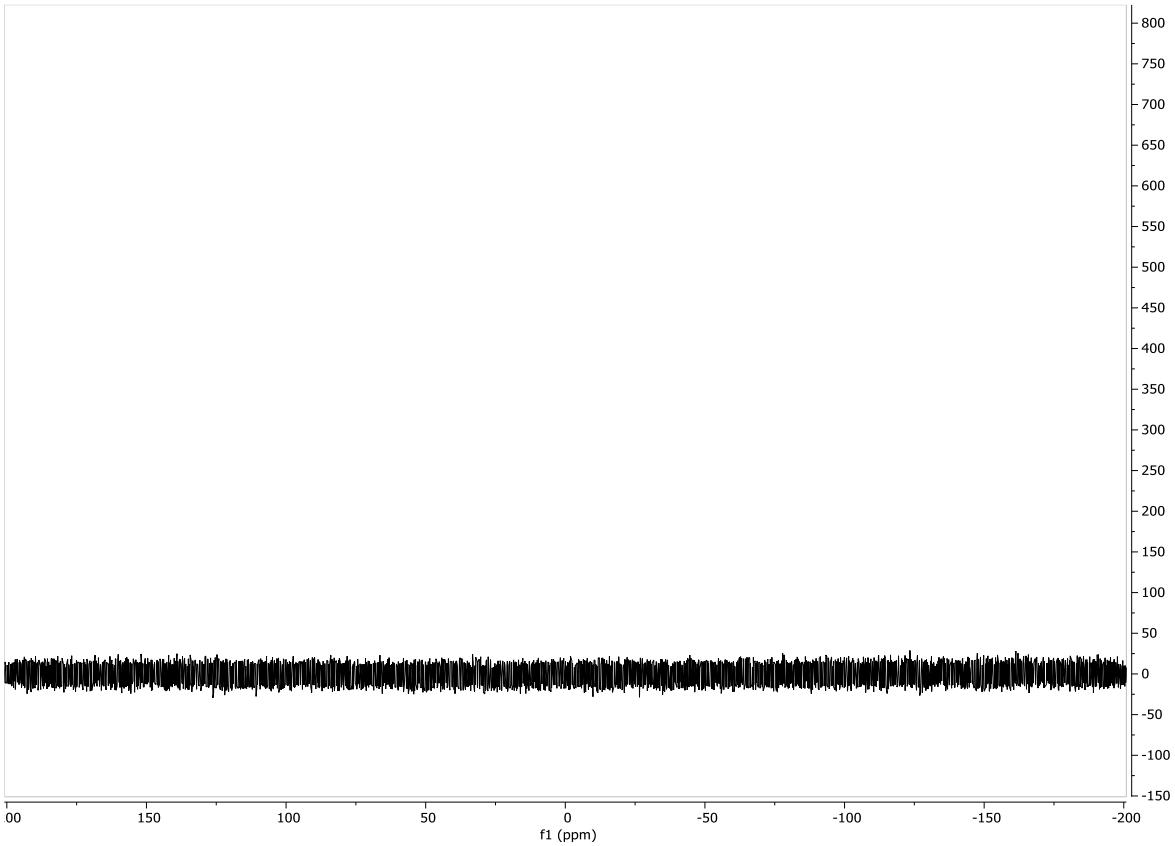
3. Directed Regioselective *Ortho*,*Ortho´*-Magnesiations of Aromatics and Heterocycles Using *s*Bu_2Mg in Toluene

3.1 NMR Studies on *s*Bu_2Mg





^{7}Li-NMR of *s*BuMg in toluene-d$_{8}$

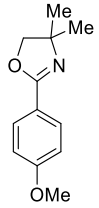


The amount of complexed ether was determined as 0.5 equiv with respect to 1.0 equiv *s*Bu_2Mg **58**. The presence of Lithium was excluded by ^{7}Li-NMR.

^{1}H NMR (400 MHz, Toluene-d_8) δ (ppm) = 1.80 (pd, *J* = 7.2, 2.0 Hz, 4H), 1.45 (d, *J* = 7.9 Hz, 6H), 1.15 (t, *J* = 7.2 Hz, 6H), 0.02 (hept, *J* = 8.5 Hz, 2H).

3.2 Preparation of Starting Materials

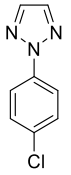
2-(4-Methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (63b)



2-(4-Methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**63b**) was prepared according to a literature procedure.[183]

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.92–7.87 (m, 2H), 6.93–6.88 (m, 2H), 4.09 (s, 2H), 3.84 (s, 3H), 1.38 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 162.0, 130.0, 120.2, 113.66, 79.1, 67.3, 55.3, 28.4.

2-(4-Chlorophenyl)-2*H*-1,2,3-triazole (73a)



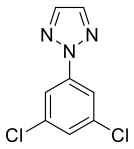
2-(4-Chlorophenyl)-2*H*-1,2,3-triazole (**73a**) was prepared according to modified literature procedures.[184] 4-chlorophenylhydrazine hydrochloride (8.95 g, 50.0 mmol, 1.0 equiv) was suspended in water (100 mL). Sodium acetate trihydrate (20.41 g, 150.0 mmol, 3.0 equiv) was added followed by dropwise addition of an aqueous solution of glyoxal (40% in water, 3.63 mL, 25.0 mmol, 0.5 equiv).

[183] D. A. Gutierrez, W.-C. C. Lee, Y. Shen, J. J. Li, *Tetrahedron Lett.* **2016**, *57*, 5372-5376.
[184] a) J. L. Riebsommer, *J. Org. Chem.* **1948**, *13*, 815-821. (b) G. F. Myachina, T. G. Ermakova, N. P. Kuznetsova, R. G. Sultangareev, L. I. Larina, L. V. Klyba, G. T. Suchanov, B. A. Trofimov, *Chem. Heterocycl. Cmpd.* **2010**, *46*, 79-81.

The reaction mixture was vigorously stirred for 2 h. The yellow precipitate was filtrated, dried and used without further purification. A dry and argon flushed three-necked flask, equipped with a magnetic stirring bar, reflux condenser and a septum, was charged with the dry osazone and diluted in toluene (25 mL). Copper(II) triflate (0.27 g, 3 mol%) was added and the reaction mixture was heated to reflux for 48 h. The reaction mixture was cooled to room temperature, filtered through a short pad of celite and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, ihexane/EtOAc = 99:1) affording 2-(4-Chlorophenyl)-2*H*-1,2,3-triazole as an orange solid (**73a**, 2.991 g, 16.7 mmol, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.08–8.00 (m, 2H), 7.82 (s, 2H), 7.49–7.42 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 138.8, 136.2, 133.6, 129.8, 120.5.

2-(3,5-Dichlorophenyl)-2*H*-1,2,3-triazole (73b)

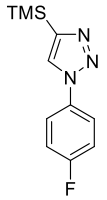


2-(3,5-Dichlorophenyl)-2*H*-1,2,3-triazole (**73b**) was prepared according to modified literature procedures.[184] 3,5-dichlorophenylhydrazine hydrochloride (14.16 g, 80.0 mmol, 1.0 equiv) was suspended in water (160 mL). Sodium acetate trihydrate (32.66 g, 240.0 mmol, 3.0 equiv) was added followed by dropwise addition of an aqueous solution of glyoxal (40% in water, 5.81 mL, 40.0 mmol, 0.5 equiv). The reaction mixture was vigorously stirred for 2 h. The yellow precipitate was filtrated, dried and used without further purification. A dry and argon flushed three-necked flask, equipped with a magnetic stirring bar, reflux condenser and a septum, was charged with the dry osazone and diluted in toluene (40 mL). Copper(II) triflate (0.95 g, 3 mol%) was added and the reaction mixture was heated to reflux for 48 h. The reaction mixture was cooled to room temperature, filtered through a short pad of celite and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, ihexane/EtOAc = 99:1) affording 2-(3,5-dichlorophenyl)-2*H*-1,2,3-triazole as a brown solid (**73b**, 4.691 g, 22.0 mmol, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.04 (d, *J* = 1.9 Hz, 2H), 7.84 (s, 2H), 7.34 (t, *J* = 1.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 140.9, 136.4, 135.8, 127.4, 117.5.

1-(4-Fluorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (75a)



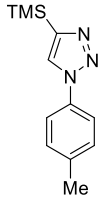
1-(4-Fluorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75a**) was prepared according to **TP 1** using 1-azido-4-fluorobenzene. The reaction was complete after 48 h. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) affording the desired compound as a pale brown solid (**75a**, 5.72 g, 24.3 mmol, 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.89 (s, 1H), 7.74–7.68 (m, 2H), 7.24–7.18 (m, 2H), 0.38 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.2, 160.8, 147.3, 133.2, 133.1, 127.1, 122.5, 122.5, 116.5, 116.2, -1.4.

Analytical data was equivalent to literature.[185]

1-(*p*-Tolyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (75c)



1-(*p*-Tolyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75c**) was prepared according to **TP 1** using 1-azido-4-methylbenzene. The reaction was complete after 24 h. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) affording the desired compound as a pale brown solid (**75c**, 4.33 g, 18.7 mmol, 62% yield).

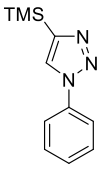
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.89 (s, 1H), 7.64–7.58 (m, 2H), 7.33–7.28 (m, 2H), 2.42 (s, 3H), 0.37 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.2, 139.6, 135.9, 131.2, 128.2, 121.8, 22.2, 0.0.

Analytical data was equivalent to literature.[185]

1-Phenyl-4-(trimethylsilyl)-1*H*-1,2,3-triazole (75d)

[185] F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. lemaire, S. Wagschal, P. Knochel, *Nature Commun.* **2020**, *11*, 4443.



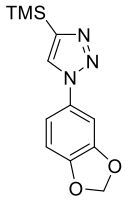
1-Phenyl-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75d**) was prepared according to **TP 1** using azidobenzene. The reaction was complete after 48 h. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) affording the desired compound as a pale brown solid (**75d**, 4.35 g, 20.0 mmol, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.94 (s, 1H), 7.78–7.70 (m, 2H), 7.56–7.47 (m, 2H), 7.47–7.38 (m, 1H), 0.38 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.3, 137.1, 129.8, 128.7, 127.3, 120.9, -0.9.

Analytical data was equivalent to literature.[185]

1-(Benzo[*d*][1,3]dioxol-5-yl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (75e)



1-(Benzo[*d*][1,3]dioxol-5-yl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75e**) was prepared according to **TP 1** using 5-azidobenzo[*d*][1,3]dioxole. The reaction was complete after 48 h. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) affording the desired compound as a pale brown solid (**75e**, 4.28 g, 16.4 mmol, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.83 (s, 1H), 7.24 (d, *J* = 2.2 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.07 (s, 2H), 0.37 (s, 9H).

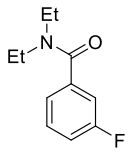
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 149.8, 149.3, 147.8, 132.3, 128.8, 115.7, 109.6, 104.1, 103.3, 0.0.

MS (EI, 70 eV): m/z (%) = 236 (39), 233 (17), 218 (100), 190 (23), 168 (11).

HRMS (EI) for $C_{12}H_{15}N_3O_2Si$: calc. $[M-CH_3N_2]^{2\bullet}$: 218.0637, found: 218.0629.

IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3128 (vw), 2952 (w), 2897 (w), 1507 (m), 1484 (w), 1470 (m), 1463 (m), 1376 (w), 1246 (s), 1233 (m), 1205 (m), 1193 (m), 1170 (w), 1126 (m), 1108 (w), 1042 (s), 989 (m), 938 (m), 884 (m), 840 (vs), 818 (s), 806 (s), 799 (s), 756 (s), 726 (w), 690 (m).

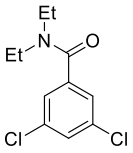
***N,N*-Diethyl-3-fluorobenzamide (78a)**



N,N-Diethyl-3-fluorobenzamide (**78a**) was prepared according to **TP 2** using 3-fluorobenzoyl chloride and diethylamine. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) affording the desired compound as a colorless liquid (**78a**, 3.87 g, 19.8 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.36 (dtd, *J* = 7.5, 5.6, 2.3 Hz, 1H), 7.14 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.08 (ddt, *J* = 8.7, 7.0, 2.0 Hz, 2H), 3.63–3.15 (m, 4H), 1.35–1.02 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 169.8–161.3 (d, *J* = 847.21 Hz), 139.3 (d, *J* = 6.7 Hz), 130.3 (d, *J* = 8.1 Hz), 121.9 (d, *J* = 3.2 Hz), 116.2 (d, *J* = 21.0 Hz), 113.6 (d, *J* = 22.7 Hz).
Analytical data was equivalent to literature.[186]

3,5-Dichloro-*N,N*-diethylbenzamide (78b)

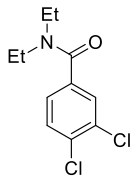


3,5-Dichloro-*N,N*-diethylbenzamide (**78b**) was prepared according to **TP 2** using 3,5-dichlorobenzoyl chloride and diethylamine. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) affording the desired compound as a colorless solid (**78b**, 4.92 g, 20.0 mmol, 100% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.37 (t, *J* = 1.9 Hz, 1H), 7.23 (d, *J* = 1.9 Hz, 2H), 3.36 (dq, *J* = 115.6, 7.3 Hz, 4H), 1.16 (dt, *J* = 44.0, 7.4 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.2, 139.9, 135.3, 129.3, 124.8, 43.3, 39.5, 14.2, 12.8.
Analytical data was equivalent to literature.[187]

3,4-Dichloro-*N,N*-diethylbenzamide (78c)

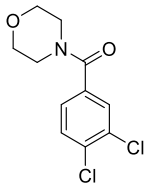
[186] R. J. Mills, N. J. Taylor, V. Snieckus, *J. Org. Chem.* **1989**, *54*, 4372-4374.
[187] M. Demas, G. J. Javadi, L. M. Bradley, D. A. Hunt, *J. Org. Chem.* **2000**, *21*, 7201-7202.



3,4-Dichloro-*N,N*-diethylbenzamide (**78c**) was prepared according to **TP 2** using 3,4-dichlorobenzoyl chloride and diethylamine. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) affording the desired compound as a colorless oil (**78c**, 5.09 g, 20.0 mmol, 100% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (dd, *J* = 5.1, 3.1 Hz, 2H), 7.20 (dd, *J* = 8.2, 1.9 Hz, 1H), 3.77–3.06 (m, 4H), 1.42–1.03 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.8, 137.0, 133.5, 132.9, 130.6, 128.6, 125.7, 43.4, 39.5, 14.2, 12.8.
Analytical data was equivalent to literature.[188]

(3,4-Dichlorophenyl)(morpholino)methanone (78d)

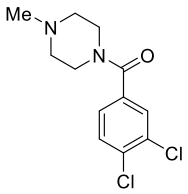


(3,4-Dichlorophenyl)(morpholino)methanone (**78d**) was prepared according to **TP 2** using 3,4-dichlorobenzoyl chloride and morpholine. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1 to 1:1) affording the desired compound as a yellow solid (**78d**, 5.04 g, 19.3 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.48–7.41 (m, 2H), 7.19–7.15 (m, 1H), 3.53 (d, *J* = 120.1 Hz, 8H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.0, 135.0, 134.4, 133.1, 130.7, 129.4, 126.4, 66.8.
Analytical data was equivalent to literature.[189]

(3,4-Dichlorophenyl)(4-methylpiperazin-1-yl)methanone (78e)

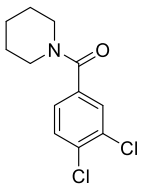
[188] K. Shichijo, M. Fujitsuka, Y. Hisaeda, H. Shimakoshi, *J. Organomet. Chem.* **2020**, *907*, 121058.
[189] A. Althammer, L. Ackermann, *Angew. Chem. Int. Ed.* **2007**, *46*, 1627-1629.



(3,4-Dichlorophenyl)(4-methylpiperazin-1-yl)methanone (**78e**) was prepared according to **TP 2** using 3,4-dichlorobenzoyl chloride and *N*-methylpiperazine. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) affording the desired compound as an orange solid (**78e**, 5.217 g, 19.1 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53–7.47 (m, 2H), 7.24 (dd, *J* = 8.2, 2.0 Hz, 1H), 3.60 (d, *J* = 139.7 Hz, 4H), 2.32 (s, 7H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 167.8, 135.6, 134.1, 133.0, 130.6, 129.3, 126.4, 46.0.
MS (EI, 70 eV): m/z (%) = 229 (28), 227 (46), 180 (14), 174 (52), 172 (82), 146 (12), 144 (19), 110 (23), 108 (69), 99 (20), 84 (10), 83 (16), 82 (18), 75 (17), 74 (22), 70 (67), 58 (34), 56 (22), 42 (32).
HRMS (EI) for $C_{12}H_{14}Cl_2N_2O$: calc. [M]: 272.0483, found: 272.0480.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 2946 (m), 2930 (m), 2859 (m), 1626 (vs), 1587 (m), 1553 (m), 1475 (m), 1461 (m), 1434 (vs), 1402 (m), 1377 (m), 1368 (m), 1352 (w), 1346 (w), 1287 (s), 1277 (s), 1258 (m), 1251 (s), 1235 (m), 1178 (w), 1148 (w), 1140 (w), 1132 (m), 1125 (m), 1105 (m), 1030 (m), 1003 (m), 954 (w), 895 (m), 881 (m), 851 (s), 835 (m), 807 (w), 793 (w), 781 (w), 753 (m), 710 (w), 670 (m), 660 (m).

(3,4-Dichlorophenyl)(piperidin-1-yl)methanone (78f)



(3,4-Dichlorophenyl)(piperidin-1-yl)methanone (**78f**) was prepared according to **TP 2** using 3,4-dichlorobenzoyl chloride and piperidine. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) affording the desired compound as a white solid (**78f**, 4.827 g, 18.7 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.50–7.43 (m, 2H), 7.21 (dd, *J* = 8.2, 1.9 Hz, 1H), 3.78–3.22 (m, 4H), 1.73–1.44 (m, 6H).

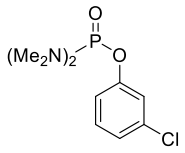
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.8, 136.3, 133.7, 132.9, 130.5, 129.1, 126.2, 48.8, 43.3, 26.5, 25.5, 24.5.

MS (EI, 70 eV): m/z (%) = 258 (63), 257 (12), 256 (100), 174 (15), 172 (24), 108 (15).

HRMS (EI) for $C_{12}H_{13}Cl_2NO$: calc. [M]: 257.0374, found: 257.0375.

IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 2950 (w), 2929 (m), 2868 (w), 2845 (w), 2794 (m), 2769 (w), 1630 (vs), 1585 (m), 1549 (w), 1476 (w), 1455 (m), 1438 (vs), 1373 (m), 1362 (m), 1295 (s), 1289 (s), 1275 (s), 1265 (m), 1253 (m), 1239 (m), 1204 (w), 1170 (m), 1141 (s), 1128 (s), 1089 (w), 1073 (w), 1052 (m), 1029 (vs), 1000 (s), 913 (m), 903 (m), 848 (vs), 840 (m), 790 (s), 777 (m), 750 (vs), 712 (w), 681 (m), 665 (m).

3-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (78g)



3-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78g**) was prepared according to **TP 3** using 3-chlorophenol. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) affording the desired compound as a colorless liquid (**78g**, 3.37 g, 12.8 mmol, 64% yield).

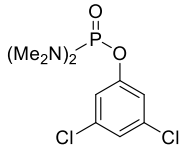
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.25–7.18 (m, 2H), 7.14–7.08 (m, 2H), 2.72 (d, *J* = 10.1 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 151.9, 134.7, 130.3, 124.4, 120.7, 118.4, 36.7.

^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 16.1.

Analytical data was equivalent to literature.[190]

3,5-Dichlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (78h)

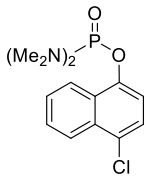


[190] C. J. Rohbogner, G. Clososki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1503-1507.

3,5-Dichlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78h**) was prepared according to **TP 3** using 3,5-dichlorophenol. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) affording the desired compound as a colorless liquid (**78h**, 5.08 g, 17.1 mmol, 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.11 (d, *J* = 1.0 Hz, 3H), 2.70 (d, *J* = 10.2 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.4, 135.3, 124.6, 119.2, 36.6.
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 16.3.
MS (EI, 70 eV): m/z (%) = 189 (29), 188 (47), 135 (100), 92 (11).
HRMS (EI) for $C_{10}H_{15}Cl_2N_2O_2P$: calc. [M- C_2H_6N]: 251.9748, found: 251.9740.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 2928 (w), 2896 (w), 2811 (vw), 1582 (m), 1572 (s), 1455 (w), 1428 (m), 1305 (m), 1294 (m), 1246 (m), 1228 (m), 1218 (m), 1177 (m), 1096 (m), 1068 (w), 988 (s), 952 (vs), 847 (m), 830 (w), 809 (s), 787 (s), 756 (s), 674 (m), 665 (m).

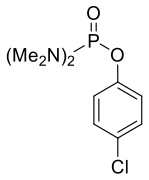
4-Chloronaphtyl *N,N,N′,N′*-tetramethylphosphorodiamidate (78i)



4-Chloronaphtyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78i**) was prepared according to **TP 3** using 4-chloronaphtol. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) affording the desired compound as a colorless solid (**78i**, 5.82 g, 18.6 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.31–8.17 (m, 2H), 7.63 (dddd, *J* = 19.5, 8.2, 6.9, 1.4 Hz, 2H), 7.51 (s, 2H), 2.80 (d, *J* = 10.1 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) =146.4, 146.3, 131.6, 127.4, 126.7, 125.8, 124.7, 121.9, 114.3, 36.8.
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 16.29.
MS (EI, 70 eV): m/z (%) = 312 (13), 149 (10), 135 (100).
HRMS (EI) for $C_{14}H_{18}ClN_2O_2P$: calc. [M]: 312.0794, found: 312.0787.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 2923 (w), 2889 (w), 2847 (w), 2799 (w), 1593 (w), 1503 (w), 1477 (w), 1454 (m), 1417 (w), 1371 (m), 1313 (m), 1254 (m), 1222 (s), 1179 (m), 1147 (m), 1115 (w), 1047 (m), 1025 (w), 1000 (s), 984 (s), 950 (m), 856 (s), 836 (s), 759 (vs), 707 (m), 674 (m), 656 (m).
Melting point: M.p. = 111 °C

4-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (78j)

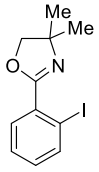


4-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78j**) was prepared according to **TP 3** using 4-chlorophenol. The crude product was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:4) affording the desired compound as a yellow liquid (**78j**, 4.95 g, 18.8 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.30–7.26 (m, 2H), 7.17–7.12 (m, 2H), 2.72 (d, *J* = 10.1 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.0, 129.5, 129.3, 121.5, 36.6.
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 16.24.
Analytical data was equivalent to literature.[190]

3.3 Preparation of Compounds

2-(2-Iodophenyl)-4,4-dimethyl-4,5-dihydrooxazole (65a)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**63a**, 85 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, the reaction mixture was cooled to 0 °C and iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**65a**, 143 mg, 0.40 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.90 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.57 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.10 (td, *J* = 7.7, 1.7 Hz, 1H), 4.14 (s, 2H), 1.42 (s, 6H).

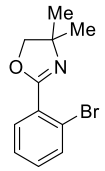
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.8, 140.1, 134.2, 131.5, 130.5, 127.8, 94.7, 79.4, 68.2, 28.2.

MS (EI, 70 eV): m/z (%) = 300 (19), 286 (10), 285 (100), 257 (35), 229 (26), 228 (13), 144 (27), 131 (15), 130 (15), 103 (18).

HRMS (EI): for $C_{11}H_{12}INO$: calc. [M+]: 300.9964; found: 300.9957.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2964 (m), 2925 (w), 2888 (w), 1652 (m), 1584 (w), 1560 (w), 1461 (m), 1428 (m), 1382 (w), 1363 (m), 1349 (m), 1304 (s), 1248 (w), 1213 (m), 1187 (m), 1123 (w), 1081 (s), 1031 (s), 1023 (w), 1014 (s), 976 (w), 961 (s), 920 (m), 866 (w), 818 (w), 760 (s), 738 (w), 726 (vs), 707 (w), 694 (m).

2-(2-Bromophenyl)-4,4-dimethyl-4,5-dihydrooxazole (65b)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**63a**, 85 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, the reaction mixture was cooled to 0 °C and 1,2-dibromotetrachloroethane (244 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**65b**, 87 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.62 (ddd, *J* = 9.2, 7.7, 1.6 Hz, 2H), 7.32 (td, *J* = 7.5, 1.4 Hz, 1H), 7.26 (td, *J* = 7.7, 1.9 Hz, 1H), 4.13 (s, 2H), 1.41 (s, 6H).

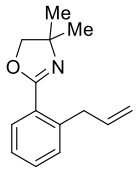
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.2, 133.9, 131.9, 131.6, 130.7, 127.4, 122.2, 79.8, 68.4, 28.6.

MS (EI, 70 eV): m/z (%) = 240 (10), 239 (99), 238 (10), 237 (100), 224 (26), 222 (26), 211 (50), 209 (51), 184 (15), 183 (69), 182 (15), 181 (72), 180 (15), 130 (12), 103 (15).

HRMS (EI): for $C_{11}H_{12}BrNO$: calc. [M-H^+]: 252.0024; found: 252.0016.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3187 (w), 3068 (w), 2967 (m), 2929 (w), 2892 (w), 1655 (s), 1590 (w), 1565 (w), 1474 (m), 1462 (m), 1433 (m), 1383 (w), 1352 (m), 1310 (s), 1250 (m), 1214 (m), 1187 (m), 1128 (w), 1087 (s), 1024 (vs), 986 (m), 962 (s), 921 (m), 869 (w), 819 (w), 762 (vs), 730 (vs), 703 (m), 685 (m).

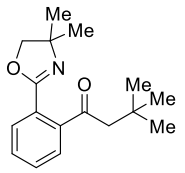
2-(2-Allylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (65c)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**63a**, 85 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, allyl bromide (52 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**65c**, 98 mg, 0.45 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.78 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.41 (td, *J* = 7.4, 1.5 Hz, 1H), 7.31–7.27 (m, 2H), 6.02 (ddt, *J* = 17.6, 9.6, 6.6 Hz, 1H), 5.07 (dtd, *J* = 14.9, 3.6, 1.9 Hz, 2H), 4.11 (s, 2H), 3.81 (dt, *J* = 6.6, 1.6 Hz, 2H), 1.42 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.6, 140.1, 137.5, 130.6, 130.2, 130.0, 126.0, 115.5, 78.7, 67.8, 38.3, 28.4.
MS (EI, 70 eV): m/z (%) = 214 (69), 201 (14), 200 (100), 176 (11), 160 (19), 158 (10), 146 (12), 143 (20), 142 (14), 130 (10), 129 (12), 128 (13), 117 (16), 116 (13), 115 (53).
HRMS (EI): for $C_{14}H_{17}NO$: calc. [M+]: 215.1310; found: 215.1304.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3075 (w), 2964 (m), 2928 (w), 2890 (w), 2382 (vw), 2303 (vw), 2205 (vw), 2131 (vw), 2051 (vw), 1934 (vw), 1638 (s), 1601 (w), 1575 (w), 1491 (w), 1462 (w), 1445 (w), 1409 (w), 1382 (w), 1363 (w), 1349 (m), 1305 (m), 1279 (w), 1248 (w), 1214 (w), 1189 (m), 1164 (w), 1121 (w), 1066 (w), 1050 (m), 1035 (vs), 992 (m), 967 (m), 914 (m), 869 (w), 820 (w), 773 (m), 747 (s), 730 (m), 696 (s), 672 (w).

1-(2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phenyl)-3,3-dimethylbutan-1-one (65d)

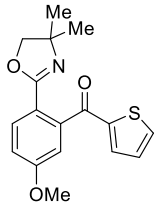


According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**63a**, 85 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, 3,3-

dimethylbutanoyl chloride (81 mg, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 12 h at 25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**65d**, 90 mg, 0.33 mmol, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.83–7.78 (m, 1H), 7.52–7.41 (m, 2H), 7.38 (dd, *J* = 7.4, 1.6 Hz, 1H), 4.07 (s, 2H), 2.74 (s, 2H), 1.38 (s, 6H), 1.03 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 204.7, 143.1, 130.7, 129.7, 129.6, 126.9, 125.9, 79.5, 68.1, 54.7, 31.4, 29.7, 28.1, 23.8.
MS (EI, 70 eV): m/z (%) = 216 (25), 203 (12), 202 (100), 186 (60), 160 (70), 148 (51), 146 (21), 130 (86).
HRMS (EI): for $C_{17}H_{23}NO_2$: calc. [M-CH_3]: 258.1494; found: 258.1487.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3066 (vw), 2957 (m), 2869 (m), 2361 (vw), 1709 (s), 1691 (m), 1653 (s), 1595 (w), 1574 (w), 1478 (m), 1463 (m), 1447 (w), 1398 (w), 1384 (m), 1363 (s), 1351 (s), 1312 (s), 1266 (m), 1249 (m), 1231 (s), 1215 (m), 1184 (s), 1122 (w), 1106 (w), 1073 (m), 1059 (m), 1044 (s), 1035 (s), 1008 (s), 989 (m), 964 (s), 912 (m), 869 (w), 818 (w), 770 (s), 745 (m), 697 (vs).

(2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-5-methoxyphenyl)(thiophen-2-yl)methanone (65e)

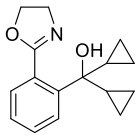


According to **TP 4**, to a mixture of 2-(4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**63b**, 103 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 20 min, thiophene-2-carbonyl chloride (64 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 12 h at 25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a yellow oil (**65e**, 142 mg, 0.45 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.91 (d, *J* = 8.6 Hz, 1H), 7.66 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.26 (d, *J* = 2.2 Hz, 1H), 7.07–6.99 (m, 3H), 3.87 (s, 3H), 3.71 (s, 2H), 1.13 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 188.6, 161.8, 144.7, 141.4, 134.0, 131.3, 127.9, 115.9, 113.1, 79.7, 55.6, 27.7.

MS (EI, 70 eV): m/z (%) = 315 (15), 287 (16), 286 (100), 271 (12), 270 (72), 259 (15), 231 (35), 216 (25), 201 (12), 160 (16).
HRMS (EI): for $C_{17}H_{17}NO_3S$: calc. [M+]: 315.0929; found: 315.0921.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3074 (vw), 2964 (w), 2927 (w), 2894 (w), 2839 (vw), 1716 (vw), 1647 (vs), 1600 (s), 1568 (m), 1509 (w), 1500 (m), 1460 (m), 1411 (s), 1383 (w), 1351 (s), 1319 (m), 1311 (m), 1294 (vs), 1231 (vs), 1184 (m), 1146 (w), 1109 (m), 1081 (w), 1060 (m), 1044 (m), 1025 (vs), 988 (w), 962 (m), 931 (m), 919 (m), 859 (m), 832 (m), 799 (s), 759 (s), 739 (s), 722 (s), 685 (m), 654 (w).

Dicyclopropyl(2-(4,5-dihydrooxazol-2-yl)phenyl)methanol (65f)

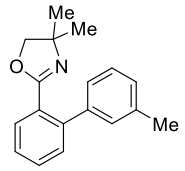


According to **TP 4**, to a mixture of 2-phenyl-4,5-dihydrooxazole (**63d**, 64 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu$_2$Mg (**58**, 0.30 mmol, 0.6 equiv) at 50 °C. After 1 h, dicyclopropyl ketone (74 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 2 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:2) afforded the title compound as a white solid (**65f**, 90 mg, 0.35 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.48 (d, *J* = 7.6 Hz, 1H), 7.08 (td, *J* = 7.5, 1.2 Hz, 1H), 7.01 (td, *J* = 7.5, 1.1 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 3.88 (s, 1H), 3.52 (t, *J* = 5.3 Hz, 2H), 3.23 (t, *J* = 5.3 Hz, 2H), 0.91 (tt, *J* = 8.3, 5.4 Hz, 2H), 0.19–0.05 (m, 4H), 0.00–-0.13 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.3, 148.7, 130.8, 129.9, 128.2, 123.1, 120.8, 88.8, 62.0, 49.2, 18.0, 1.0, 0.0.

MS (EI, 70 eV): m/z (%) = 227 (11), 226 (100), 216 (34), 198 (21), 185 (61), 184 (46), 172 (13), 128 (12).
HRMS (EI): for $C_{16}H_{19}NO_2$: calc. [M+]: 257.1416; found: 257.1412.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3178 (w), 3085 (w), 3004 (w), 2951 (w), 2921 (w), 2903 (w), 2856 (w), 1679 (vs), 1610 (w), 1479 (w), 1467 (m), 1427 (w), 1367 (w), 1357 (m), 1330 (w), 1303 (m), 1272 (m), 1132 (m), 1121 (m), 1111 (m), 1093 (m), 1075 (s), 1057 (m), 1043 (m), 1019 (s), 990 (w), 952 (s), 918 (m), 897 (m), 872 (m), 862 (m), 838 (w), 821 (w), 815 (w), 786 (m), 777 (s), 756 (s), 721 (m), 675 (s), 660 (w).
Melting point: M.p. = 86 °C.

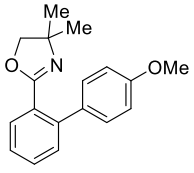
4,4-dimethyl-2-(3'-methyl-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (65g)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**63a**, 0.85 mL, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (183 mg, 5 mol%) and 3-iodotoluene (0.53 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**65g**, 1.03 g, 3.88 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.71 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.48 (td, *J* = 7.5, 1.4 Hz, 1H), 7.37 (ddd, *J* = 14.6, 7.5, 1.4 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.25–7.19 (m, 2H), 7.18–7.12 (m, 1H), 3.83 (s, 2H), 2.38 (s, 3H), 1.31 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 141.7, 141.0, 137.5, 130.4, 130.1, 129.1, 128.0, 127.0, 125.5, 79.6, 67.5, 28.0, 21.5.
MS (EI, 70 eV): m/z (%) = 265 (19), 264 (100), 210 (13), 209 (18), 192 (14), 179 (28), 178 (14), 165 (22), 152 (10).
HRMS (EI): for $C_{18}H_{19}NO$: calc. [M^+]: 265.1467; found: 265.1461.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2964 (m), 2944 (w), 2942 (w), 2939 (w), 2925 (m), 2922 (m), 2915 (w), 2912 (w), 2889 (w), 2886 (w), 1676 (w), 1656 (s), 1652 (s), 1606 (w), 1604 (w), 1600 (w), 1479 (w), 1473 (m), 1471 (m), 1462 (m), 1456 (m), 1446 (m), 1363 (m), 1349 (m), 1311 (m), 1212 (w), 1190 (w), 1188 (w), 1113 (w), 1076 (m), 1067 (w), 1065 (w), 1043 (s), 1041 (m), 1034 (s), 988 (w), 964 (m), 920 (w), 918 (w), 790 (m), 769 (m), 755 (vs), 699 (s).

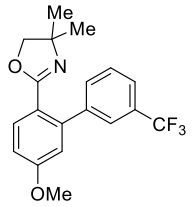
2-(4'-Methoxy-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (65h)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**63a**, 85 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (15 mg, 5 mol%) and 4-bromoanisole (53 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**65h**, 89 mg, 0.32 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.70 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39–7.31 (m, 4H), 6.95–6.90 (m, 2H), 3.85 (s, 3H), 3.83 (s, 2H), 1.31 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.1, 158.9, 141.2, 133.6, 130.4, 130.2, 130.0, 129.4, 127.8, 126.7, 113.4, 79.5, 67.4, 55.3, 40.8, 28.0, 23.8.
MS (EI, 70 eV): m/z (%) = 281 (19), 280 (100), 225 (29), 195 (11).
HRMS (EI): for $C_{18}H_{19}NO_2$: calc. [M-H$^+$]: 280.1338; found: 280.1332.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3138 (vw), 3064 (vw), 2964 (m), 2892 (w), 2837 (w), 1652 (m), 1611 (m), 1580 (w), 1565 (vw), 1517 (s), 1483 (m), 1462 (m), 1446 (m), 1413 (vw), 1383 (w), 1363 (w), 1351 (m), 1295 (m), 1243 (vs), 1212 (m), 1177 (s), 1107 (w), 1075 (m), 1036 (vs), 1017 (m), 1001 (m), 988 (w), 963 (m), 920 (w), 869 (w), 832 (s), 804 (m), 761 (vs), 727 (m), 704 (m), 662 (w).

2-(5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (65i)

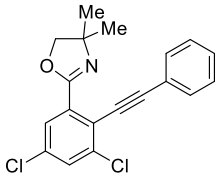


According to **TP 4**, to a mixture of 2-(4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**63b**, 1.026 g, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 40 °C. After 20 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (183 mg, 5 mol%) and 1-iodo-3-(trifluoromethyl)benzene (0.60 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude

product by flash column chromatography (silica gel, *i*hexane/Et_2O = 1:1) afforded the title compound as a brown solid (**65i**, 1.62 g, 4.05 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.76 (d, J = 8.6 Hz, 1H), 7.66–7.55 (m, 3H), 7.51 (t, J = 7.6 Hz, 1H), 6.93 (dd, J = 8.6, 2.6 Hz, 1H), 6.86 (d, J = 2.6 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 2H), 1.26 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.7, 160.9, 141.8, 141.7, 132.0, 131.4, 131.3, 130.5, 130.1, 129.8, 129.5, 128.4, 125.3, 125.3, 125.2, 125.2, 125.1, 123.8, 123.8, 123.8, 123.7, 122.7, 120.1, 115.5, 112.8, 79.0, 67.2, 55.3, 27.8.
MS (EI, 70 eV): m/z (%) = 349 (20), 348 (100), 263 (38), 258 (18), 215 (14).
HRMS (EI): for $C_{19}H_{18}F_3NO_2$: calc. [M-H$^+$]: 348.1211; found: 348.1199.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2988 (vw), 2974 (w), 2945 (w), 2942 (w), 2937 (vw), 2933 (vw), 2931 (vw), 2927 (vw), 2905 (vw), 2901 (vw), 2886 (w), 2843 (vw), 1635 (s), 1608 (s), 1579 (w), 1568 (w), 1513 (w), 1464 (m), 1448 (w), 1432 (w), 1423 (w), 1365 (w), 1350 (m), 1334 (s), 1314 (s), 1295 (s), 1276 (m), 1244 (m), 1212 (s), 1195 (m), 1178 (s), 1165 (vs), 1139 (s), 1110 (s), 1095 (s), 1080 (s), 1068 (s), 1034 (m), 1025 (vs), 1002 (w), 986 (m), 964 (m), 959 (m), 932 (m), 927 (m), 914 (m), 907 (m), 895 (s), 809 (s), 788 (m), 774 (vw), 771 (vw), 768 (vw), 758 (w), 743 (vw), 716 (m), 706 (m), 701 (vs), 687 (w), 664 (m).
Melting point: M.p. = 70 °C.

2-(3,5-dichloro-2-(phenylethynyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (65j)

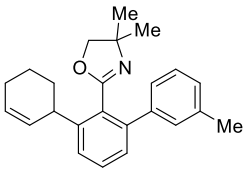


According to **TP 4**, to a mixture of 2-(3,5-dichlorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**63c**, 0.732 g, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 1.80 mmol, 0.6 equiv) at 25 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (3.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. Iodine (0.838 g, 3.30 mmol, 1.1 equiv) dissolved in THF (2 mL) was added and the reaction mixture was allowed to stir 1 h at 25 °C. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (52 mg, 3 mol%), CuI (23 mg, 4 mol%), tfp (42 mg, 6 mol%) and NEt_3 (10 mL). The freshly prepared arylzinc reagent followed by phenylacetylene (0.43 mL, 3.90 mmol, 1.3 equiv) were added and the reaction mixture was stirred overnight at 25 °C. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/Et_2O = 9:1) afforded the title compound as a yellow oil (**65j**, 633 mg, 1.84 mmol, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.73 (d, *J* = 2.1 Hz, 1H), 7.58–7.53 (m, 3H), 7.37 (tt, *J* = 4.0, 2.7 Hz, 3H), 4.17 (s, 2H), 1.42 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.3, 143.4, 138.1, 133.8, 131.7, 131.0, 129.0, 128.4, 128.2, 100.4, 84.1, 79.6, 68.3, 28.4.
MS (EI, 70 eV): m/z (%) = 344 (22), 342 (36), 331 (11), 330 (61), 329 (18), 328 (100), 326 (17), 289 (16), 253 (11), 238 (14), 237 (18), 207 (32), 201 (14), 190 (19), 163 (13), 158 (26), 156 (39), 43 (54), 42 (25).
HRMS (EI): for $C_{19}H_{15}Cl_2NO$: calc. [M-H$^+$]: 342.0452; found: 342.0445.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3079 (vw), 3057 (vw), 2965 (w), 2928 (w), 2892 (w), 2866 (vw), 2219 (w), 1651 (m), 1623 (m), 1596 (w), 1576 (m), 1541 (w), 1492 (m), 1475 (vw), 1461 (w), 1450 (m), 1442 (m), 1412 (m), 1382 (w), 1363 (w), 1347 (m), 1338 (w), 1296 (m), 1251 (w), 1214 (w), 1188 (m), 1157 (w), 1148 (w), 1116 (m), 1077 (w), 1063 (m), 1025 (vw), 988 (m), 969 (s), 915 (w), 893 (w), 891 (w), 861 (s), 819 (vw), 792 (m), 753 (vs), 729 (w), 688 (s), 672 (w), 667 (w).

4,4-dimethyl-2-(3''-methyl-1,2,3,4-tetrahydro-[1,1':3',1''-terphenyl]-2'-yl)-4,5-dihydrooxazole (66a)

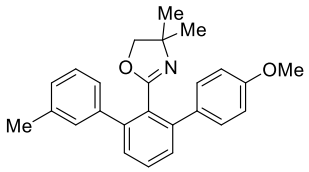


According to **TP 4**, to a mixture of 4,4-dimethyl-2-(3'-methyl-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**65g**, 133 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 60 °C. After 1 h, 3-bromocyclohexene (70 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a colorless liquid (**66a**, 129 mg, 0.37 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 (t, *J* = 7.7 Hz, 1H), 7.34–7.21 (m, 5H), 7.19–7.12 (m, 1H), 6.00–5.91 (m, 1H), 5.76 (dq, *J* = 10.3, 2.2 Hz, 1H), 3.88–3.80 (m, 2H), 3.77 (tq, *J* = 5.5, 2.7 Hz, 1H), 2.39 (s, 3H), 2.18–2.06 (m, 3H), 1.77 (tdd, *J* = 10.2, 6.8, 4.9 Hz, 1H), 1.66–1.54 (m, 2H), 1.20 (d, *J* = 16.2 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.7, 145.5, 142.1, 141.1, 137.2, 130.2, 129.7, 129.4, 128.6, 127.9, 127.8, 127.8, 127.4, 126.6, 125.9, 78.9, 67.8, 65.9, 38.7, 32.2, 27.9, 27.8, 25.0, 21.4, 21.2.
MS (EI, 70 eV): m/z (%) = 345 (22), 290 (40), 289 (20), 288 (100), 274 (17), 273 (14), 272 (15), 271 (17), 270 (13), 255 (14), 244 (10), 222 (23), 215 (22), 202 (22), 189 (12), 179 (13), 178 (13), 165 (21).
HRMS (EI): for $C_{24}H_{27}NO$: calc. [M-H$^+$]: 345.2093; found: 345.2085.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3027 (w), 3019 (w), 2965 (m), 2962 (m), 2960 (m), 2952 (w), 2949 (w), 2926 (m), 2923 (m), 2900 (w), 2898 (w), 2897 (w), 2895 (w), 2889 (w), 2886 (w), 2883 (w), 2878 (w), 2875 (w), 2872 (w), 2870 (w), 2868 (w), 2865 (w), 2862 (w), 2859 (w), 2856 (w), 2844 (w), 2834 (w), 1661 (s), 1606 (w), 1584 (w), 1577 (w), 1459 (m), 1447 (m), 1433 (w), 1363 (w), 1345 (w), 1313 (w), 1285 (m), 1274 (w), 1265 (w), 1253 (w), 1246 (w), 1208 (w), 1196 (w), 1188 (w), 1178 (w), 1175 (w), 1172 (w), 1095 (w), 1035 (vs), 1000 (w), 987 (w), 962 (m), 945 (w), 943 (w), 940 (w), 936 (w), 930 (w), 917 (m), 905 (w), 891 (w), 882 (w), 871 (w), 806 (w), 781 (s), 759 (s), 741 (m), 733 (w), 722 (m), 703 (vs).

2-(4''-methoxy-3-methyl-[1,1':3',1''-terphenyl]-2'-yl)-4,4-dimethyl-4,5-dihydrooxazole (66b)



According to **TP 4**, to a mixture of 2-(4'-Methoxy-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**65h**, 1.0 g, 3.55 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (3.91 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (132 mg, 5 mol%) and 3-iodotoluene (0.38 mL, 2.95 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a brown solid (**66b**, 0.914 g, 2.46 mmol, 83% yield).

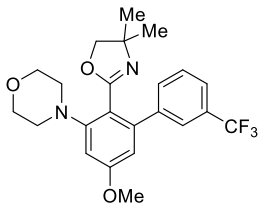
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 1.4 Hz, 1H), 7.26 (d, *J* = 3.4 Hz, 3H), 7.18 – 7.11 (m, 1H), 6.94 – 6.88 (m, 2H), 3.84 (s, 3H), 3.62 (s, 2H), 2.36 (s, 3H), 0.96 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.0, 142.4, 141.8, 140.7, 137.3, 133.3, 130.1, 129.7, 129.3, 128.6, 128.3, 127.9, 127.8, 126.0, 113.3, 79.0, 67.6, 55.3, 27.4, 21.4.
MS (EI, 70 eV): m/z (%) = 371 (26), 370 (100), 298 (11).

HRMS (EI): for $C_{25}H_{25}NO_2$: calc. [M^+]: 371.1885; found: 371.1833.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2972 (w), 2950 (w), 2928 (w), 2925 (w), 2919 (w), 2916 (w), 2914 (w), 2899 (w), 2878 (w), 2877 (w), 2864 (w), 2833 (w), 1658 (m), 1635 (w), 1610 (m), 1605 (m), 1587 (w), 1582 (w), 1574 (w), 1515 (s), 1461 (m), 1454 (s), 1441 (s), 1419 (w), 1403 (w), 1402 (w), 1382 (w), 1379 (w), 1364 (m), 1345 (w), 1303 (w), 1293 (m), 1289 (m), 1283 (m), 1242 (vs), 1212 (m), 1202 (w), 1186 (m), 1171 (s), 1150 (w), 1120 (w), 1106 (m), 1092 (m), 1077 (w), 1043 (m), 1036 (vs), 1010 (w), 987 (m), 978 (w), 964 (m), 931 (w), 920 (w), 907 (m), 888 (w), 865 (w), 833 (s), 821 (m), 809 (s), 803 (s), 792 (w), 786 (vs), 762 (s), 729 (w), 716 (w), 713 (m), 702 (s).

Melting point: M.p. = 84 °C.

4-(2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)morpholine (66c)



According to **TP 4**, to a mixture of 2-(5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**65i**, 64 mg, 0.20 mmol, 1.0 equiv) in toluene (0.4 mL) was added *s*Bu_2Mg (**58**, 0.12 mmol, 0.6 equiv) at 40 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.24 mL, 1.00 M in THF, 1.20 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $CoCl_2$ (1.3 mg, 5 mol%) and morpholino benzoate (50 mg, 0.24 mmol, 1.2 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was stirred at 25 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a white solid (**66c**, 73 mg, 0.17 mmol, 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.67 (d, *J* = 1.9 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 6.57 (d, *J* = 2.4 Hz, 1H), 3.82 (m, 9H), 3.13 – 3.01 (m, 4H), 1.07 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.1, 160.9, 153.8, 143.3, 141.6, 132.2, 130.6, 130.3, 130.0, 129.6, 128.4, 125.6, 125.6, 125.5, 125.5, 125.5, 124.2, 124.1, 124.1, 124.0, 122.8, 117.7, 109.5, 106.1, 78.8, 67.5, 67.4, 55.4, 53.1, 27.9.

MS (EI, 70 eV): m/z (%) = 404 (46), 403 (29), 389 (58), 377 (16), 376 (17), 375 (77), 361 (23), 360 (26), 359 (39), 348 (75), 347 (26), 346 (54), 331 (26), 321 (38), 320 (33), 319 (100), 306 (19), 305 (22),

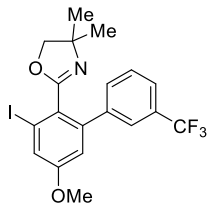
303 (45), 301 (36), 285 (17), 283 (19), 263 (50), 258 (28), 235 (19), 220 (25), 215 (20), 207 (33), 201 (19), 188 (18), 165 (18), 164 (20), 43 (58), 42 (22).

HRMS (EI): for $C_{23}H_{25}F_3N_2O_3$: calc. [M^+]: 434.1817; found: 434.1823.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2963 (m), 1663 (m), 1591 (m), 1575 (m), 1466 (m), 1454 (m), 1437 (m), 1418 (m), 1362 (s), 1347 (m), 1331 (m), 1323 (s), 1315 (m), 1305 (m), 1292 (m), 1260 (m), 1236 (m), 1210 (m), 1198 (m), 1187 (w), 1175 (m), 1165 (s), 1148 (s), 1127 (vs), 1110 (vs), 1093 (s), 1075 (s), 1045 (m), 1027 (s), 982 (m), 964 (m), 927 (m), 922 (m), 916 (m), 910 (m), 870 (m), 863 (s), 856 (s), 816 (m), 806 (s), 768 (m), 757 (m), 706 (s).

Melting point: M.p. = 117 °C.

2-(3-iodo-5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (66d)



According to **TP 4**, to a mixture of 2-(5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**65i**, 64 mg, 0.20 mmol, 1.0 equiv) in toluene (0.4 mL) was added *s*Bu_2Mg (**58**, 0.12 mmol, 0.6 equiv) at 40 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and iodine (61 mg, 0.24 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a yellow oil (**66d**, 74 mg, 0.16 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69 (dt, *J* = 1.9, 1.0 Hz, 1H), 7.64–7.56 (m, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.41 (d, *J* = 2.5 Hz, 1H), 6.85 (d, *J* = 2.5 Hz, 1H), 3.90 (s, 2H), 3.83 (s, 3H), 1.14 (s, 6H).

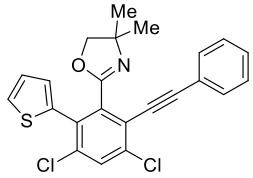
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.2, 160.3, 142.9, 140.8, 132.1, 130.9, 130.6, 130.3, 130.0, 128.8, 126.7, 125.6, 125.6, 125.5, 125.5, 124.8, 124.7, 124.7, 124.6, 124.0, 122.8, 115.6, 97.6, 79.4, 68.1, 55.8, 27.7.

MS (EI, 70 eV): m/z (%) = 475 (18), 474 (93), 389 (14), 388 (100), 383 (24), 376 (22), 332 (21), 305 (11), 257 (11), 242 (16), 226 (12), 220 (10), 219 (12), 214 (11), 213 (15), 207 (27), 206 (15), 165 (14), 164 (24).

HRMS (EI): for $C_{19}H_{17}F_3INO_2$: calc. [M-H^+]: 474.0178; found: 474.0170.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3012 (vw), 2976 (w), 2972 (w), 2969 (w), 2945 (w), 2942 (w), 2935 (w), 2931 (w), 2912 (vw), 2904 (vw), 2902 (vw), 2880 (vw), 2865 (vw), 2858 (vw), 2841 (vw), 1736 (s), 1667 (m), 1590 (m), 1546 (m), 1492 (w), 1464 (m), 1436 (w), 1428 (w), 1395 (w), 1373 (m), 1359 (w), 1348 (w), 1331 (vs), 1305 (m), 1270 (m), 1238 (vs), 1214 (s), 1165 (s), 1158 (s), 1125 (vs), 1095 (m), 1082 (m), 1073 (s), 1044 (s), 1035 (s), 1024 (vs), 1002 (w), 985 (w), 960 (m), 937 (w), 918 (w), 904 (w), 874 (w), 861 (w), 856 (w), 845 (w), 827 (vw), 803 (s), 787 (w), 744 (w), 733 (w), 703 (s), 666 (s).

2-(3,5-dichloro-2-(phenylethynyl)-6-(thiophen-2-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (66e)

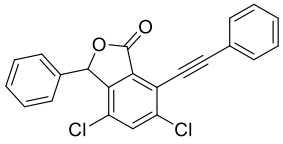


According to **TP 4**, to a mixture of 2-(3,5-dichloro-2-(phenylethynyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (**65j**, 68 mg, 0.2 mmol, 1.0 equiv) in toluene (0.4 mL) was added *s*Bu_2Mg (**58**, 0.12 mmol, 0.6 equiv) at 40 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.22 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (8 mg, 5 mol%) and 2-iodothiophene (16 µL, 0.17 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**66e**, 66 mg, 0.15 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.64 (s, 1H), 7.55–7.48 (m, 2H), 7.46–7.42 (m, 1H), 7.35 (qd, *J* = 4.4, 1.4 Hz, 3H), 7.07 (d, *J* = 3.2 Hz, 2H), 3.88 (s, 2H), 1.13 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.1, 136.6, 135.9, 135.1, 135.0, 132.3, 131.5, 130.8, 129.2, 128.9, 128.2, 126.9, 126.2, 122.2, 121.9, 98.6, 82.9, 79.5, 68.0, 29.5, 27.6.
MS (EI, 70 eV): m/z (%) = 281 (33), 266 (11), 265 (11), 225 (39), 209 (18), 208 (13), 207 (100), 191 (21), 43 (42), 42 (12).
HRMS (EI): for $C_{23}H_{17}Cl_2NOS$: calc. [M+]: 425.0408; found: 425.0396.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2960 (m), 2958 (m), 2945 (m), 2921 (s), 2892 (m), 2887 (m), 2871 (w), 2866 (w), 2853 (m), 1740 (w), 1674 (m), 1492 (m), 1462 (m), 1447 (m), 1442 (m), 1424 (m), 1396 (w), 1363 (w), 1339 (w), 1307 (w), 1262 (m), 1237 (m), 1206 (s), 1177 (m), 1162 (m), 1093 (s), 1083

(m), 1069 (m), 1052 (m), 1033 (w), 1022 (w), 988 (m), 968 (s), 927 (w), 888 (m), 872 (w), 866 (m), 863 (w), 847 (m), 829 (w), 820 (w), 807 (m), 762 (s), 757 (s), 698 (s), 686 (vs), 667 (m).
Melting point: M.p. = 126 °C.

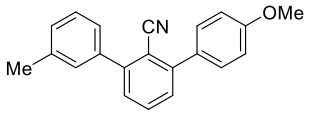
4,6-dichloro-3-phenyl-7-(phenylethynyl)isobenzofuran-1(3*H*)-one (66f)



According to **TP 4**, to a mixture of 2-(3,5-dichloro-2-(phenylethynyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (**65j**, 68 mg, 0.2 mmol, 1.0 equiv) in toluene (0.4 mL) was added *s*Bu_2Mg (**58**, 0.12 mmol, 0.6 equiv) at 40 °C. After 0.5 h, benzaldehyde (26 µL, 0.24 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. & M HCl (4 mL) was added and the reaction mixture was stirred at 25 °C overnight. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a white solid (**66f**, 42 mg, 0.11 mmol, 56% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.77–7.70 (m, 2H), 7.68 (s, 1H), 7.46–7.35 (m, 6H), 7.26–7.21 (m, 2H), 6.30 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.5, 145.6, 138.5, 134.8, 133.7, 132.4, 129.9, 129.7, 129.0, 128.7, 128.6, 128.5, 128.2, 122.1, 120.7, 104.3, 81.2, 80.9.
MS (EI, 70 eV): m/z (%) = 381 (14), 380 (61), 379 (22), 378 (100), 302 (13), 300 (20), 299 (21), 286 (12), 274 (51), 273 (12), 272 (79), 264 (12), 263 (67), 261 (36), 250 (30), 245 (12), 243 (19), 212 (23), 210 (69), 175 (19), 174 (46), 131 (24), 130 (15), 125 (18), 105 (92), 77 (25).
HRMS (EI): for $C_{22}H_{12}Cl_2O_2$: calc. [M+]: 378.0214; found: 378.0208.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3066 (w), 2961 (w), 2959 (w), 2945 (w), 2924 (w), 2922 (w), 2898 (w), 2896 (w), 2872 (w), 2869 (w), 2866 (w), 2864 (w), 2853 (w), 2210 (w), 1764 (m), 1754 (vs), 1733 (w), 1723 (w), 1720 (w), 1717 (w), 1700 (w), 1683 (w), 1674 (w), 1671 (w), 1669 (w), 1663 (w), 1652 (w), 1647 (w), 1492 (m), 1453 (s), 1441 (m), 1388 (w), 1322 (m), 1300 (w), 1270 (m), 1263 (m), 1210 (w), 1194 (s), 1178 (m), 1174 (m), 1167 (w), 1162 (w), 1158 (w), 1109 (w), 1106 (w), 1091 (vs), 1073 (m), 1069 (m), 1050 (w), 1038 (w), 1036 (w), 1026 (m), 1011 (w), 993 (w), 980 (s), 969 (w), 922 (w), 910 (m), 881 (m), 829 (w), 804 (m), 796 (m), 785 (m), 764 (m), 757 (vs), 723 (m), 710 (w), 709 (w), 701 (vs), 696 (m), 685 (s), 674 (m), 669 (w), 667 (w).
Melting point: M.p. = 148 °C.

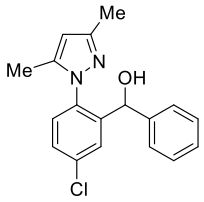
4''-methoxy-3-methyl-[1,1':3',1''-terphenyl]-2'-carbonitrile (66g)



2-(4''-methoxy-3-methyl-[1,1':3',1''-terphenyl]-2'-yl)-4,4-dimethyl-4,5-dihydrooxazole (**66b**, 75 mg, 0.20 mmol, 1.0 equiv) was dissolved in $SOCl_2$ (2 mL) and DMF (1 mL) was added dropwise at 25 °C. The reaction mixture was refluxed for 2 h and subsequently cooled to 0 °C. Water was carefully added and the reaction mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a yellow solid (**66g**, 55 mg, 0.18 mmol, 92% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.63 (t, *J* = 7.8 Hz, 1H), 7.57–7.52 (m, 2H), 7.43 (ddd, *J* = 7.6, 6.4, 1.2 Hz, 2H), 7.40–7.38 (m, 3H), 7.28–7.26 (m, 1H), 7.05–7.00 (m, 2H), 3.87 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.0, 147.1, 146.6, 138.7, 138.3, 132.2, 131.0, 130.3, 129.8, 129.4, 128.6, 128.5, 128.4, 126.1, 118.3, 114.1, 110.2, 55.4, 21.5.
MS (EI, 70 eV): m/z (%) = 299 (100), 298 (55), 284 (31), 283 (11), 255 (27), 254 (20), 241 (29), 240 (26).
HRMS (EI): for $C_{21}H_{17}NO$: calc. [M+]: 299.1310; found: 299.1305.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3013 (vw), 2957 (w), 2953 (w), 2945 (w), 2921 (w), 2920 (w), 2896 (w), 2877 (w), 2874 (w), 2871 (w), 2853 (w), 2844 (w), 2220 (w), 1733 (vw), 1662 (w), 1660 (w), 1652 (w), 1609 (m), 1581 (w), 1577 (w), 1575 (w), 1559 (w), 1558 (vw), 1515 (s), 1496 (w), 1490 (w), 1475 (vw), 1455 (s), 1442 (m), 1436 (m), 1419 (w), 1404 (w), 1394 (w), 1375 (w), 1364 (w), 1323 (vw), 1307 (w), 1298 (m), 1283 (m), 1247 (s), 1211 (w), 1202 (w), 1178 (s), 1151 (w), 1121 (w), 1110 (m), 1093 (w), 1077 (w), 1067 (w), 1043 (m), 1024 (s), 999 (w), 988 (w), 985 (w), 980 (w), 964 (w), 950 (w), 932 (vw), 917 (w), 907 (w), 888 (w), 872 (w), 833 (m), 828 (s), 809 (m), 804 (m), 785 (vs), 770 (s), 751 (m), 735 (w), 726 (w), 717 (w), 712 (w), 703 (s).
Melting point: M.p. = 83 °C.

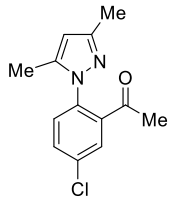
(5-Chloro-2-(3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl)(phenyl)methanol (69a)



According to **TP 4**, to a mixture of 1-(4-chlorophenyl)-3,5-dimethyl-1*H*-pyrazole (**67a**, 103 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 30 min, benzaldehyde (62 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 7:1) afforded the title compound as a white solid (**69a**, 135 mg, 0.43 mmol, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.23–7.13 (m, 3H), 7.09–7.05 (m, 3H), 5.77 (s, 1H), 5.61 (s, 1H), 2.27 (s, 3H), 1.78 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 149.1, 144.0, 141.6, 141.2, 130.5, 128.9, 128.2, 127.8, 127.0, 125.4, 106.4, 72.8, 13.3, 11.2.
MS (EI, 70 eV): m/z (%) = 314 (43), 313 (26), 312 (100), 311 (34), 310 (26), 297 (15), 295 (18), 294 (19), 283 (13), 282 (16), 280 (27), 266 (37), 255 (18), 234 (29), 232 (48), 229 (12), 228 (13), 216 (12), 207 (34), 151 (17), 104 (22), 82 (16), 77 (20), 76 (28), 62 (27), 57 (12).
HRMS (EI): for $C_{18}H_{17}ClN_2O$: calc. [M+]: 312.1029; found: 312.1033.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3166 (m), 3059 (w), 3030 (w), 2923 (m), 2853 (m), 2733 (w), 2663 (w), 2563 (w), 2479 (w), 2360 (w), 2243 (w), 1932 (w), 1735 (w), 1700 (w), 1670 (w), 1595 (w), 1573 (w), 1555 (m), 1492 (m), 1472 (m), 1455 (m), 1417 (m), 1397 (m), 1379 (m), 1371 (m), 1338 (w), 1317 (m), 1292 (w), 1269 (w), 1242 (m), 1195 (w), 1179 (m), 1161 (w), 1139 (w), 1121 (w), 1091 (m), 1077 (m), 1049 (m), 1035 (s), 1026 (m), 982 (w), 962 (w), 918 (w), 906 (m), 889 (m), 850 (w), 832 (s), 773 (s), 751 (s), 699 (vs), 671 (w), 658 (w).
Melting point: M.p. = 179 °C.

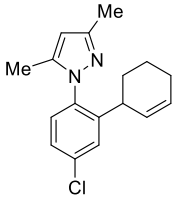
1-(5-Chloro-2-(3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl)ethan-1-one (69b)



According to **TP 4**, to a mixture of 1-(4-chlorophenyl)-3,5-dimethyl-1*H*-pyrazole (**67a**, 103 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 30 min, *N*-methoxy-*N*-methyl acetamide (65 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as an orange solid (**69b**, 92 mg, 0.37 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.67 (d, *J* = 2.4 Hz, 1H), 7.53 (dd, *J* = 8.4, 2.5 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 6.04 (s, 1H), 2.27 (s, 3H), 2.14 (d, *J* = 0.7 Hz, 3H), 1.90 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 198.9, 150.0, 140.8, 138.9, 134.8, 131.7, 129.1, 129.0, 107.2, 28.2, 13.4, 11.5.
MS (EI, 70 eV): m/z (%) = 235 (31), 234 (12), 233 (100).
HRMS (EI): for $C_{13}H_{13}ClN_2O$: calc. [M+]: 248.0716; found: 248.0713.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3070 (vw), 2922 (w), 2854 (w), 2360 (vw), 1700 (vw), 1684 (vs), 1637 (vw), 1593 (w), 1570 (w), 1558 (m), 1542 (vw), 1508 (w), 1492 (s), 1467 (m), 1441 (w), 1410 (m), 1396 (m), 1376 (w), 1362 (w), 1351 (m), 1288 (w), 1274 (m), 1256 (m), 1229 (s), 1178 (vw), 1131 (w), 1114 (vw), 1098 (m), 1082 (w), 1042 (vw), 1029 (m), 1012 (w), 976 (w), 890 (m), 835 (s), 811 (vs), 764 (w), 731 (w), 689 (w), 663 (vw).
Melting point: M.p. = 82 °C.

1-(5-Chloro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-yl)-3,5-dimethyl-1*H*-pyrazole (69c)

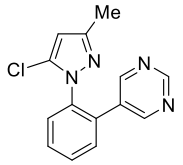


According to **TP 4**, to a mixture of 1-(4-chlorophenyl)-3,5-dimethyl-1*H*-pyrazole (**67a**, 103 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After

30 min, 3-bromocyclohexene (70 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 18:1) afforded the title compound as a yellow solid (**69c**, 129 mg, 0.45 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.34 (d, *J* = 2.4 Hz, 1H), 7.24 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 5.95 (s, 1H), 5.90 (ddt, *J* = 10.0, 5.1, 2.8 Hz, 1H), 5.59–5.53 (m, 1H), 3.15 (s, 1H), 2.27 (s, 3H), 2.12–1.95 (m, 5H), 1.83 (d, *J* = 12.0 Hz, 1H), 1.68 (ddt, *J* = 16.4, 5.9, 3.7 Hz, 1H), 1.54–1.35 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.7, 146.7, 140.5, 136.4, 134.9, 129.4, 129.3, 129.0, 128.9, 126.7, 105.3, 36.1, 31.4, 24.7, 21.1, 13.6, 11.5.
MS (EI, 70 eV): m/z (%) = 288 (23), 286 (77), 285 (30), 273 (30), 272 (18), 271 (100), 257 (22), 254 (17), 245 (17), 243 (57), 231 (34), 228 (23), 217 (27), 205 (22), 191 (15), 190 (26), 180 (15), 168 (17), 167 (29), 164 (16), 162 (52), 154 (18), 153 (15), 152 (23), 115 (17), 96 (15).
HRMS (EI): for $C_{17}H_{19}ClN_2$: calc. [M+]: 286.1237; found: 286.1233.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3021 (vw), 2933 (m), 2859 (w), 2839 (w), 2360 (vw), 1731 (w), 1595 (vw), 1569 (vw), 1553 (m), 1496 (s), 1470 (m), 1445 (w), 1433 (w), 1415 (m), 1389 (w), 1378 (w), 1365 (m), 1343 (w), 1310 (w), 1298 (vw), 1279 (vw), 1267 (vw), 1241 (w), 1220 (vw), 1184 (w), 1154 (vw), 1136 (w), 1118 (w), 1091 (m), 1077 (w), 1042 (w), 1028 (m), 1014 (w), 991 (w), 984 (w), 931 (vw), 910 (w), 898 (w), 883 (m), 859 (w), 832 (vs), 810 (w), 795 (m), 775 (w), 753 (w), 726 (m), 718 (m), 683 (vw), 669 (w), 662 (w).
Melting point: M.p. = 94 °C.

5-(2-(5-Chloro-3-methyl-1*H*-pyrazol-1-yl)phenyl)pyrimidine (69d)

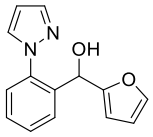


According to **TP 4**, to a mixture of 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole (**67b**, 96 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 60 °C. After 20 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (15 mg, 5 mol%) and 5-bromopyrimidine (67 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a yellow oil (**69d**, 72 mg, 0.27 mmol, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.15 (s, 1H), 8.51 (s, 2H), 7.73–7.51 (m, 4H), 6.07 (s, 1H), 2.28 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.9, 155.9, 150.5, 136.1, 132.8, 132.3, 130.4, 130.2, 130.1, 129.2, 128.5, 105.9, 14.0.
MS (EI, 70 eV): m/z (%) = 236 (15), 235 (100), 208 (14), 207 (10), 194 (15), 167 (18), 140 (16).
HRMS (EI): for $C_{14}H_{11}ClN_4$: calc. [M-H$^+$]: 269.0594; found: 269.0586.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3118 (vw), 3039 (w), 2929 (w), 2855 (vw), 1725 (vw), 1578 (w), 1549 (m), 1524 (s), 1497 (m), 1462 (m), 1421 (m), 1408 (vs), 1373 (m), 1362 (m), 1278 (w), 1187 (m), 1163 (w), 1117 (w), 1087 (w), 1011 (m), 1002 (m), 992 (m), 972 (w), 912 (w), 781 (m), 765 (vs), 750 (m), 726 (vs), 672 (w).

(2-(1*H*-Pyrazol-1-yl)phenyl)(furan-2-yl)methanol (69e)



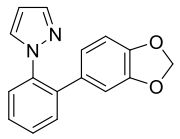
According to **TP 4**, to a mixture of 1-phenyl-1*H*-pyrazole (**67c**, 65 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu$_2$Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 1 h, furfural (50 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a brown solid (**69e**, 108 mg, 0.45 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.71 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.65 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.46–7.36 (m, 3H), 7.34–7.30 (m, 1H), 7.28–7.26 (m, 2H), 6.43 (t, *J* = 2.2 Hz, 1H), 6.27 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.18 (dt, *J* = 3.3, 1.0 Hz, 1H), 5.72 (d, *J* = 1.1 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.5, 141.6, 140.5, 139.2, 136.9, 130.6, 130.2, 129.1, 128.6, 125.1, 110.2, 107.2, 106.5, 68.3.
MS (EI, 70 eV): m/z (%) = 223 (30), 212 (29), 211 (100), 209 (29), 197 (51), 195 (26), 193 (39), 184 (80), 183 (59), 181 (19), 172 (18), 171 (47), 169 (30), 168 (16), 167 (30), 166 (25), 156 (29), 144 (17), 130 (25), 117 (21), 115 (37), 89 (17).
HRMS (EI): for $C_{14}H_{12}N_2O_2$: calc. [M+]: 240.0899; found: 240.0892.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3244 (w), 3240 (w), 3091 (w), 2923 (vw), 1601 (w), 1583 (vw), 1515 (w), 1490 (m), 1458 (w), 1424 (w), 1398 (m), 1331 (w), 1316 (m), 1283 (w), 1270 (w), 1211 (m),

1197 (m), 1182 (m), 1166 (vw), 1142 (m), 1129 (w), 1103 (vw), 1068 (w), 1056 (m), 1046 (s), 1026 (m), 1012 (s), 985 (w), 950 (m), 922 (m), 914 (w), 881 (w), 865 (w), 830 (w), 802 (m), 769 (s), 757 (vs), 732 (vs), 717 (s), 698 (m), 677 (w), 663 (m).

Melting point: M.p. = 91 °C.

1-(2-(benzo[*d*][1,3]dioxol-5-yl)phenyl)-1H-pyrazole (69f)



According to **TP 4**, to a mixture of 1-phenyl-1*H*-pyrazole (**67c**, 0.65 mL, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (182 mg, 5 mol%) and 5-bromobenzo[d][1,3]dioxole (0.50 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a brown solid (**69f**, 879 mg, 3.33 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.65 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.61–7.55 (m, 1H), 7.49–7.41 (m, 3H), 7.15 (dd, *J* = 2.4, 0.7 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.60 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.54 (d, *J* = 1.7 Hz, 1H), 6.24 (dd, *J* = 2.4, 1.8 Hz, 1H), 5.95 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.7, 147.0, 140.3, 138.5, 136.4, 132.4, 131.3, 131.0, 128.3, 128.2, 126.6, 122.2, 108.9, 108.4, 106.5, 101.1.

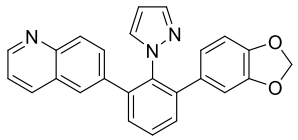
MS (EI, 70 eV): m/z (%) = 264 (20), 263 (100), 205 (15).

HRMS (EI): for $C_{16}H_{12}N_2O_2$: calc. [M+]: 264.0899; found: 264.0891.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2892 (w), 1733 (vw), 1607 (w), 1576 (vw), 1517 (m), 1505 (m), 1477 (vs), 1460 (s), 1435 (m), 1416 (m), 1393 (s), 1337 (m), 1329 (m), 1239 (s), 1218 (vs), 1192 (m), 1148 (w), 1126 (w), 1107 (m), 1097 (m), 1036 (s), 1021 (s), 1012 (m), 935 (s), 915 (m), 891 (m), 877 (m), 863 (w), 861 (w), 836 (vw), 809 (m), 749 (vs), 744 (vs), 726 (m), 715 (m), 701 (w), 699 (w), 694 (vw), 675 (w), 667 (w), 659 (w).

Melting point: M.p. = 97 °C.

6-(3-(benzo[d][1,3]dioxol-5-yl)-2-(1H-pyrazol-1-yl)phenyl)quinolone (70a)



According to **TP 4**, to a mixture of 1-(2-(benzo[*d*][1,3]dioxol-5-yl)phenyl)-1*H*-pyrazole (**69f**, 53 mg, 0.20 mmol, 1.0 equiv) in toluene (0.4 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.24 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (8 mg, 5 mol%) and 6-iodoquinoline (43 mg, 0.17 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a brown oil (**70a**, 55 mg, 0.14 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.06 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.68–7.48 (m, 4H), 7.41–7.34 (m, 3H), 7.12 (d, *J* = 2.4 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.63 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.57 (d, *J* = 1.8 Hz, 1H), 6.07 (t, *J* = 2.1 Hz, 1H), 5.93 (s, 2H).

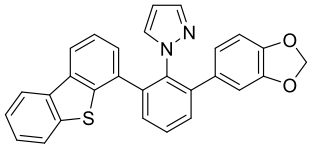
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.6, 147.6, 147.4, 147.1, 140.3, 139.9, 139.7, 137.3, 136.7, 136.5, 132.5, 132.5, 130.7, 130.2, 130.0, 129.4, 129.1, 128.1, 127.4, 122.1, 121.5, 108.8, 108.3, 106.6, 101.2.

MS (EI, 70 eV): m/z (%) = 281 (17), 252 (14), 225 (41), 209 (20), 207 (64), 191 (17).

HRMS (EI): for $C_{25}H_{17}N_3O_2$: calc. [M+]: 391.1321; found: 391.1315.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (w), 2924 (m), 2855 (w), 1741 (m), 1517 (w), 1502 (m), 1492 (m), 1464 (s), 1435 (m), 1410 (w), 1390 (w), 1354 (w), 1341 (w), 1241 (m), 1227 (m), 1157 (m), 1154 (m), 1109 (m), 1091 (m), 1083 (m), 1037 (vs), 1022 (s), 976 (s), 937 (vs), 914 (vs), 870 (s), 841 (s), 829 (m), 799 (s), 763 (s), 754 (s), 736 (m), 731 (m), 698 (w), 673 (w), 668 (w).

1-(2-(benzo[d][1,3]dioxol-5-yl)-6-(dibenzo[b,d]thiophen-4-yl)phenyl)-1H-pyrazole (70b)



According to **TP 4**, to a mixture of 1-(2-(benzo[*d*][1,3]dioxol-5-yl)phenyl)-1H-pyrazole (**69f**, 53 mg, 0.20 mmol, 1.0 equiv) in toluene (0.4 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.24 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dppf)Cl_2$ (8 mg, 5 mol%) and 4-iododibenzo[*b*,*d*]thiophene (53 mg, 0.17 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:1) afforded the title compound as a white solid (**70b**, 51 mg, 0.12 mmol, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.17–8.12 (m, 1H), 8.03 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.84–7.78 (m, 1H), 7.67 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.64–7.56 (m, 2H), 7.49–7.42 (m, 2H), 7.32–7.26 (m, 2H), 7.07–7.01 (m, 2H), 6.71 (d, *J* = 8.1 Hz, 1H), 6.66 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.60 (d, *J* = 1.7 Hz, 1H), 5.92 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.2, 146.8, 140.0, 139.5, 139.3, 139.3, 138.7, 136.8, 135.7, 135.4, 133.1, 132.2, 131.9, 130.8, 129.1, 128.9, 126.7, 126.6, 124.3, 124.1, 122.5, 121.9, 121.6, 120.3, 108.6, 107.9, 105.7, 100.8.

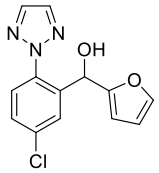
MS (EI, 70 eV): m/z (%) = 447 (26), 446 (74), 445 (100).

HRMS (EI): for $C_{28}H_{18}N_2O_2S$: calc. [M-H$^+$]: 445.1011; found: 445.1010.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2962 (vw), 2959 (w), 2957 (w), 2954 (w), 2950 (vw), 2945 (vw), 2922 (w), 2918 (w), 2914 (w), 2901 (w), 2896 (w), 2892 (w), 2889 (w), 2887 (w), 2884 (w), 2882 (w), 2876 (w), 2874 (w), 2866 (w), 2864 (w), 2862 (w), 2853 (w), 1517 (w), 1502 (m), 1492 (m), 1480 (w), 1462 (m), 1440 (m), 1436 (m), 1419 (w), 1411 (w), 1392 (m), 1385 (w), 1339 (w), 1315 (w), 1304 (w), 1259 (w), 1257 (w), 1242 (m), 1227 (s), 1195 (w), 1178 (w), 1157 (vw), 1155 (vw), 1107 (w), 1084 (w), 1038 (s), 1022 (m), 937 (m), 911 (m), 894 (w), 890 (w), 882 (w), 877 (w), 874 (w), 872 (w), 870 (w), 868 (w), 865 (w), 863 (w), 804 (m), 793 (m), 749 (vs), 737 (m), 732 (m), 727 (m), 722 (s), 705 (m), 692 (w).

Melting point: M.p. = 152 °C.

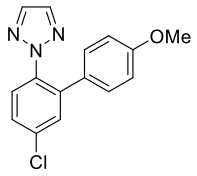
(5-Chloro-2-(2*H*-1,2,3-triazol-2-yl)phenyl)(furan-2-yl)methanol (73a)



According to **TP 4**, to a mixture of 2-(4-chlorophenyl)-2*H*-1,2,3-triazole (**71a**, 90 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 15 min, furfural (50 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a brown oil (**73a**, 92 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (s, 2H), 7.75–7.69 (m, 1H), 7.48–7.42 (m, 2H), 7.32 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.28 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.17 (dt, *J* = 3.3, 1.0 Hz, 1H), 5.98 (d, *J* = 0.9 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 153.3, 142.3, 137.0, 136.4, 135.7, 134.9, 129.8, 129.2, 126.2, 110.2, 107.3, 67.2.
MS (EI, 70 eV): m/z (%) = 277 (23), 275 (64), 260 (26), 259 (20), 258 (71), 257 (22), 248 (32), 247 (37), 246 (84), 231 (26), 230 (20), 228 (19), 221 (38), 220 (41), 219 (100), 208 (22), 207 (39), 206 (62), 204 (22), 202 (18), 192 (29), 191 (34), 164 (22), 163 (17), 140 (16), 124 (25), 123 (18), 115 (18), 95 (42), 81 (31), 75 (18), 70 (83), 63 (17), 43 (78), 42 (43), 41 (16).
HRMS (EI): for $C_{13}H_{10}ClN_3O_2$: calc. [M+]: 275.0462; found: 275.0457.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3380 (w), 3143 (w), 3120 (w), 2923 (vw), 2852 (vw), 2363 (vw), 1794 (w), 1714 (w), 1700 (w), 1652 (w), 1594 (w), 1488 (s), 1410 (s), 1370 (w), 1290 (w), 1260 (w), 1225 (w), 1181 (m), 1148 (m), 1122 (w), 1100 (m), 1072 (m), 1049 (w), 1010 (s), 962 (s), 948 (vs), 902 (w), 883 (m), 819 (vs), 783 (m), 735 (s), 675 (w), 656 (vw).

2-(5-Chloro-4'-methoxy-[1,1'-biphenyl]-2-yl)-2*H*-1,2,3-triazole (73b)

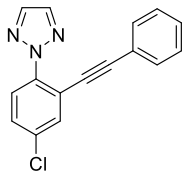


According to **TP 4**, to a mixture of 2-(4-chlorophenyl)-2*H*-1,2,3-triazole (**71a**, 539 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 1.80 mmol, 0.6 equiv) at 40 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (3.3 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (110 mg, 5 mol%) and 4-bromoanisole (0.31 mL, 2.50 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**73b**, 455 mg, 1.60 mmol, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69 (s, 2H), 7.54 – 7.49 (m, 2H), 7.42 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.96–6.92 (m, 2H), 6.81–6.76 (m, 2H), 3.79 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.3, 139.1, 136.8, 135.3, 135.1, 131.0, 129.5, 129.2, 127.9, 127.6, 113.8, 55.2.
MS (EI, 70 eV): m/z (%) = 287 (11), 286 (31), 285 (36), 284 (100), 269 (10), 188 (22), 153 (18), 126 (10).
HRMS (EI): for $C_{15}H_{12}ClN_3O$: calc. [M+]: 285.0669; found: 285.0671.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3125 (vw), 3060 (vw), 3038 (vw), 3001 (vw), 2956 (w), 2932 (w), 2835 (w), 1609 (m), 1580 (w), 1516 (m), 1488 (s), 1462 (m), 1441 (w), 1410 (m), 1401 (m), 1368 (w), 1289 (m), 1250 (s), 1242 (s), 1178 (s), 1149 (m), 1128 (w), 1110 (m), 1099 (m), 1075 (m), 1056 (w), 1036 (m), 1024 (m), 1007 (w), 961 (s), 950 (s), 884 (w), 819 (vs), 776 (m), 745 (w), 728 (vw), 670 (w).

2-(4-Chloro-2-(phenylethynyl)phenyl)-2*H*-1,2,3-triazole (73c)



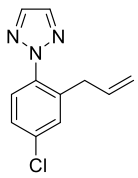
According to **TP 4**, to a mixture of 2-(4-chlorophenyl)-2*H*-1,2,3-triazole (**71a**, 539 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 1.80 mmol, 0.6 equiv) at 40 °C. After 15 min, the further procedure was adopted and modified from literature.[191] The reaction mixture was cooled to -50 °C and CuCN·2LiCl (3.6 mL, 1.0 M in THF, 1.2 equiv) was added dropwise and the mixture was stirred for 25 min. (phenylethynyl)lithium (6.00 mmol; prepared by adding *n*BuLi (6.00 mmol) to a 0.5 M solution of phenylacetylen (6.00 mol) in THF at 0 °C and stirring for 30 min) was added dropwise to the resulting cuprate and the mixture was stirred for 1 h at -50 °C. The reaction mixture was cooled to -78 °C, and a solution of chloranil (959 mg, 3.90 mmol, 1.3 equiv) in dry THF (20 mL) was added slowly over a period of 45 min. The reaction mixture was then warmed to -50 °C and stirred for 3 h. Et_2O (30 mL) was poured into the crude reaction mixture and the reaction mixture was then filtered through celite and the residue washed with Et_2O (ca. 100 mL). The organic phase was washed with NH_4OH (2 M, 2 x 30 mL) and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash column

[191] S. R. Dubbaka, M. Kienle, H. Mayr, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 9093-9096.

chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a brown oil (**73c**, 432 mg, 1.54 mmol, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) =7.90 (s, 2H), 7.71–7.66 (m, 2H), 7.45–7.40 (m, 3H), 7.33 (dd, *J* = 5.3, 2.0 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 139.2, 135.7, 134.1, 133.3, 131.6, 129.0, 128.9, 128.3, 125.9, 122.5, 119.7, 95.2, 84.6.
MS (EI, 70 eV): m/z (%) = 278 (20), 254 (32), 253 (16), 252 (100), 223 (12), 217 (31), 190 (41), 163 (19).
HRMS (EI): for $C_{16}H_{10}ClN_3$: calc. [M+]: 279.0563; found: 279.0559.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3284 (vw), 3061 (vw), 2966 (w), 2927 (vw), 2873 (vw), 2223 (w), 1683 (m), 1599 (w), 1571 (m), 1497 (s), 1484 (s), 1442 (m), 1406 (s), 1262 (w), 1149 (m), 1103 (s), 1068 (m), 1024 (w), 961 (s), 945 (s), 893 (m), 820 (vs), 753 (vs), 728 (s), 688 (vs), 669 (w).

2-(2-Allyl-4-chlorophenyl)-2*H*-1,2,3-triazole (73d)

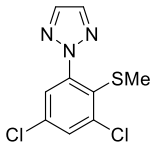


According to **TP 4**, to a mixture of 2-(4-chlorophenyl)-2*H*-1,2,3-triazole (**71a**, 539 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 1.80 mmol, 0.6 equiv) at 40 °C. After 15 min, allyl bromide (0.31 mL, 3.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.6 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a white solid (**73d**, 433 mg, 1.98 mmol, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (s, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.38–7.30 (m, 2H), 5.81 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.06–4.93 (m, 2H), 3.48 (dt, *J* = 6.7, 1.6 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 138.2, 137.1, 135.8, 135.6, 135.2, 131.1, 127.6, 127.4, 117.4, 36.4.
MS (EI, 70 eV): m/z (%) = 206 (32), 205 (10), 204 (100), 164 (14), 155 (12), 128 (12), 115 (10).
HRMS (EI): for $C_{11}H_{10}ClN_3$: calc. [M+]: 219.0563; found: 219.0558.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3134 (w), 3121 (w), 3076 (vw), 2926 (w), 2856 (vw), 1882 (vw), 1854 (vw), 1635 (w), 1600 (w), 1490 (m), 1437 (w), 1414 (m), 1407 (m), 1375 (w), 1304 (w), 1255

(w), 1188 (w), 1157 (m), 1132 (m), 1103 (m), 1095 (m), 1070 (m), 1045 (w), 1005 (m), 956 (s), 945 (m), 920 (s), 883 (m), 871 (m), 815 (vs), 751 (m), 705 (w), 677 (m), 660 (w).
Melting point: M.p. = 63 °C.

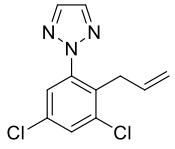
2-(3,5-Dichloro-2-(methylthio)phenyl)-2*H*-1,2,3-triazole (73e)



According to **TP 4**, to a mixture of 2-(3,5-dichlorophenyl)-2*H*-1,2,3-triazole (**71b**, 1.070 g, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 25 °C. After 30 min, *S*-methyl methanethiosulfonate (0.57 mL, 6.00 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 2 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a brown solid (**73e**, 1.062 g, 4.08 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.90 (s, 2H), 7.61 (d, *J* = 2.3 Hz, 1H), 7.48 (d, *J* = 2.3 Hz, 1H), 2.24 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 144.7, 141.3, 135.9, 134.6, 131.8, 130.9, 126.3, 19.0.
MS (EI, 70 eV): m/z (%) = 260 (49), 258 (73), 245 (38), 243 (56), 227 (61), 225 (100), 205 (44), 203 (71), 202 (11), 191 (12), 190 (12), 189 (20), 188 (23), 168 (27), 167 (13), 160 (19), 158 (26), 141 (10), 123 (15), 119 (24), 92 (10), 78 (16), 69 (29).
HRMS (EI): for $C_9H_7Cl_2N_3S$: calc. [M+]: 258.9738; found: 258.9735.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3141 (vw), 3122 (vw), 3075 (w), 3059 (w), 2995 (vw), 2919 (w), 1768 (vw), 1738 (vw), 1574 (s), 1545 (m), 1439 (m), 1406 (s), 1346 (m), 1313 (w), 1249 (w), 1184 (w), 1146 (m), 1119 (m), 1067 (w), 1047 (w), 979 (m), 958 (vs), 899 (m), 885 (w), 870 (s), 828 (s), 821 (vs), 791 (s), 723 (m), 701 (w), 672 (w), 654 (w).
Melting point: M.p. = 53 °C.

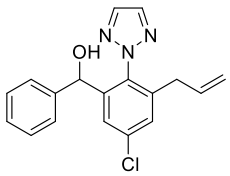
2-(2-Allyl-3,5-dichlorophenyl)-2*H*-1,2,3-triazole (73f)



According to **TP 4**, to a mixture of 2-(3,5-dichlorophenyl)-2*H*-1,2,3-triazole (**71b**, 1.070 g, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 25 °C. After 30 min, allyl bromide (0.52 mL, 6.00 mmol, 1.2 equiv) and CuCN·2LiCl (1.0 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a red solid (**73f**, 1.150 g, 4.53 mmol, 91% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.86 (s, 2H), 7.55–7.49 (m, 2H), 5.79 (ddt, *J* = 16.3, 10.1, 6.2 Hz, 1H), 4.97 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.87 (dq, *J* = 17.1, 1.7 Hz, 1H), 3.59 (dt, *J* = 6.1, 1.6 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 135.7, 133.7, 132.6, 132.0, 130.2, 125.2, 116.5, 32.8.
MS (EI, 70 eV): m/z (%) = 239 (62), 237 (100), 207 (20), 149 (15), 57 (11), 44 (67), 43 (42).
HRMS (EI): for $C_{11}H_9Cl_2N_3$: calc. [M+]: 253.0174; found: 253.0181.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3136 (w), 3084 (w), 2360 (w), 1733 (w), 1635 (m), 1589 (s), 1565 (m), 1466 (m), 1455 (m), 1447 (m), 1436 (m), 1428 (m), 1411 (s), 1283 (w), 1256 (w), 1184 (w), 1146 (m), 1129 (m), 1119 (m), 1076 (m), 1061 (m), 998 (m), 960 (s), 936 (m), 920 (s), 907 (s), 857 (vs), 825 (m), 818 (s), 807 (m), 782 (s), 705 (m), 672 (w).
Melting point: M.p. = 58 °C.

(3-Allyl-5-chloro-2-(2*H*-1,2,3-triazol-2-yl)phenyl)(phenyl)methanol (74a)



According to **TP 4**, to a mixture of 2-(2-allyl-4-chlorophenyl)-2*H*-1,2,3-triazole (**73d**, 110 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 15 min, benzaldehyde (62 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**74a**, 67 mg, 0.21 mmol, 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (s, 2H), 7.40 (d, *J* = 2.4 Hz, 1H), 7.37–7.26 (m, 4H), 7.22–7.16 (m, 2H), 5.73 (ddt, *J* = 16.9, 10.0, 6.8 Hz, 1H), 5.43 (d, *J* = 4.2 Hz, 1H), 5.04 (dq, *J* = 10.1, 1.5 Hz, 1H), 4.95 (dq, *J* = 17.0, 1.6 Hz, 1H), 3.56–3.47 (m, 1H), 3.11 (dd, *J* = 6.8, 1.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 143.3, 140.9, 140.0, 136.1, 135.2, 134.6, 129.6, 128.2, 127.6, 127.1, 126.0, 117.3, 71.2, 35.6.

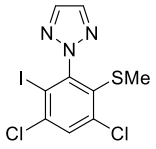
MS (EI, 70 eV): m/z (%) = 325 (13), 324 (25), 309 (22), 308 (37), 307 (72), 306 (21), 299 (24), 297 (78), 272 (17), 270 (16), 268 (100), 254 (16), 219 (36), 204 (15), 203 (49), 202 (34), 192 (15), 190 (66), 189 (19), 152 (17), 128 (16), 115 (21), 105 (75), 77 (48).

HRMS (EI): for $C_{18}H_{16}ClN_3O$: calc. [M+]: 325.0982; found: 325.0979.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3320 (m), 3132 (w), 3109 (m), 2955 (w), 2919 (m), 2849 (w), 1639 (w), 1589 (w), 1578 (w), 1456 (m), 1435 (m), 1418 (m), 1363 (w), 1315 (m), 1307 (w), 1227 (m), 1186 (w), 1153 (m), 1117 (w), 1061 (s), 1007 (m), 967 (s), 956 (s), 938 (m), 893 (m), 865 (m), 842 (m), 825 (m), 777 (m), 758 (m), 697 (vs), 684 (m), 668 (m).

Melting point: M.p. = 84 °C.

2-(3,5-Dichloro-2-iodo-6-(methylthio)phenyl)-2*H*-1,2,3-triazole (74b)



According to **TP 4**, to a mixture of 2-(3,5-dichloro-2-(methylthio)phenyl)-2*H*-1,2,3-triazole (**73e**, 130 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 25 °C. After 10 min, the reaction mixture was cooled to 0 °C and iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a brown solid (**74b**, 169 mg, 0.44 mmol, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.93 (s, 2H), 7.79 (s, 1H), 2.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.8, 140.8, 140.2, 135.5, 135.3, 131.2, 100.8, 18.9.

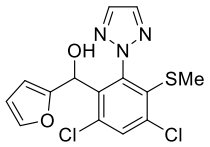
MS (EI, 70 eV): m/z (%) = 384 (100), 371 (13), 369 (21), 354 (26), 352 (35), 332 (21), 331 (11), 330 (33), 317 (33), 316 (12), 315 (38), 227 (11), 225 (16), 202 (21), 190 (17), 189 (13), 188 (24), 157 (12), 155 (16), 153 (41), 70 (43), 69 (33), 44 (12).

HRMS (EI): for $C_9H_6Cl_2IN_3S$: calc. [M+]: 384.8704; found: 384.8698.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3139 (vw), 3126 (w), 2920 (w), 2361 (vw), 1543 (w), 1517 (w), 1432 (m), 1411 (m), 1391 (s), 1277 (m), 1234 (w), 1160 (m), 1155 (s), 1131 (m), 1073 (m), 1062 (m), 1057 (m), 968 (m), 961 (vs), 872 (s), 823 (vs), 792 (m), 699 (w), 682 (w).

Melting point: M.p. = 97 °C.

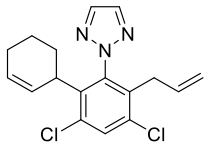
(4,6-Dichloro-3-(methylthio)-2-(2*H*-1,2,3-triazol-2-yl)phenyl)(furan-2-yl)methanol (74c)



According to **TP 4**, to a mixture of 2-(3,5-dichloro-2-(methylthio)phenyl)-2*H*-1,2,3-triazole (**73e**, 130 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 25 °C. After 10 min, furfural (50 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**74c**, 136 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.79 (s, 1H), 7.77–7.67 (m, 2H), 7.16 (dt, *J* = 1.8, 0.9 Hz, 1H), 6.11 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.06 (d, *J* = 9.9 Hz, 1H), 5.86–5.80 (m, 1H), 4.38 (d, *J* = 11.0 Hz, 1H), 2.21 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.7, 144.3, 141.7, 140.8, 136.6, 135.7, 135.5, 135.3, 132.8, 110.2, 105.3, 66.8, 19.0.
MS (EI, 70 eV): m/z (%) = 354 (100), 341 (15), 339 (27), 338 (15), 336 (16), 327 (15), 325 (22), 288 (23), 287 (30), 286 (33), 285 (41), 279 (17), 277 (24), 273 (13), 271 (24), 230 (12), 97 (12), 95 (61), 70 (94), 69 (22), 41 (23), 40 (16).
HRMS (EI): for $C_{14}H_{11}Cl_2N_3O_2S$: calc. [M+]: 354.9949; found: 354.9944.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3410 (w), 3122 (w), 3066 (vw), 2980 (vw), 2925 (w), 1733 (m), 1562 (m), 1536 (m), 1505 (w), 1431 (s), 1410 (s), 1373 (m), 1241 (m), 1188 (w), 1143 (s), 1108 (s), 1045 (s), 1003 (s), 960 (vs), 905 (s), 883 (m), 823 (vs), 807 (m), 793 (m), 733 (vs), 702 (w).

2-(3-Allyl-4,6-dichloro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-yl)-2*H*-1,2,3-triazole (74d)

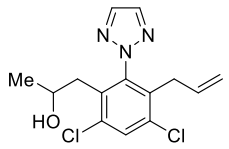


According to **TP 4**, to a mixture of 2-(2-allyl-3,5-dichlorophenyl)-2*H*-1,2,3-triazole (**73f**, 127 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 20 min, 3-bromocyclohexene (70 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product

by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a colorless oil (**74d**, 117 mg, 0.35 mmol, 70 % yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.89–7.71 (m, 2H), 7.60 (s, 1H), 5.67 (ddt, *J* = 16.6, 10.1, 6.4 Hz, 1H), 5.38–5.16 (m, 2H), 4.95 (dq, *J* = 10.1, 1.5 Hz, 1H), 4.81 (dq, *J* = 17.1, 1.7 Hz, 1H), 3.01–2.77 (m, 2H), 2.12–1.71 (m, 6H), 1.43 (d, *J* = 13.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 141.1, 140.6, 134.8, 133.5, 133.2, 133.0, 127.2, 116.8, 76.7, 38.7, 33.4, 27.8, 23.8, 22.7.
MS (EI, 70 eV): m/z (%) =334 (46), 332 (74), 320 (57), 318 (91), 305 (42), 304 (38), 298 (63), 280 (69), 279 (56), 278 (100), 277 (75), 276 (66), 265 (35), 264 (39), 243 (40), 242 (45), 241 (47), 240 (37), 238 (37), 236 (63), 234 (41), 229 (49), 214 (57), 207 (40), 206 (49), 204 (40), 201 (57), 180 (53), 178 (35), 165 (96), 153 (42), 152 (87), 139 (52).
HRMS (EI): for $C_{17}H_{17}Cl_2N_3$: calc. [M^+]: 333.0800; found: 333.0793.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3027 (vw), 2927 (vw), 2866 (vw), 2252 (vw), 1639 (vw), 1578 (vw), 1554 (vw), 1455 (vw), 1433 (vw), 1413 (vw), 1380 (vw), 1219 (vw), 1178 (vw), 1148 (vw), 1110 (vw), 1011 (vw), 994 (vw), 962 (w), 821 (w), 804 (vw), 652 (vw).

2-(3-Allyl-4,6-dichloro-2-(2*H*-1,2,3-triazol-2-yl)phenyl)propan-2-ol (74e)



According to **TP 4**, to a mixture of 2-(2-allyl-3,5-dichlorophenyl)-2*H*-1,2,3-triazole (**73f**, 51 mg, 0.20 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.12 mmol, 0.6 equiv) at 40 °C. After 20 min, the reaction mixture was cooled to 0 °C and CuI (8 mg, 5 mol%) was added and the reaction mixture was stirred for 1 h at 0 °C. Propylene oxide (42 µL, 0.24 mmol, 1.2 equiv) was added dropwise and the reaction mixture was stirred for further 4 h at 0 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a yellow oil (**74e**, 42 mg, 0.14 mmol, 70% yield).

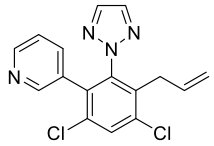
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.92 (s, 2H), 7.64 (s, 1H), 5.67 (ddt, *J* = 16.7, 10.1, 6.3 Hz, 1H), 4.94 (dq, *J* = 10.1, 1.5 Hz, 1H), 4.81 (dq, *J* = 17.0, 1.6 Hz, 1H), 4.07 (dtq, *J* = 12.5, 6.2, 3.3, 2.4 Hz, 1H), 3.14 (ddt, *J* = 15.0, 6.6, 1.5 Hz, 1H), 3.05–2.97 (m, 2H), 2.77 (dd, *J* = 14.1, 4.0 Hz, 1H), 1.95 (dd, *J* = 14.1, 9.5 Hz, 1H), 1.13 (d, *J* = 6.2 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 140.9, 135.4, 135.0, 133.6, 133.4, 133.2, 132.2, 116.8, 66.2, 38.6, 33.5, 24.5.

MS (EI, 70 eV): m/z (%) = 269 (25), 268 (13), 267 (39), 266 (11), 256 (11), 254 (62), 253 (14), 252 (100), 239 (10), 197 (12), 45 (17), 43 (14).

HRMS (EI): for $C_{14}H_{15}Cl_2N_3O$: calc. [M-H$^+$]: 310.0514; found: 310.0509.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3426 (w), 3080 (vw), 2969 (w), 2930 (w), 2360 (w), 1638 (w), 1581 (m), 1569 (w), 1558 (m), 1456 (m), 1436 (vs), 1411 (s), 1387 (w), 1374 (m), 1286 (w), 1206 (w), 1148 (m), 1110 (s), 1083 (m), 1050 (m), 987 (m), 960 (vs), 932 (s), 916 (s), 893 (m), 874 (m), 820 (s), 802 (m), 777 (m), 756 (w), 740 (w).

3-(3-Allyl-4,6-dichloro-2-(2*H*-1,2,3-triazol-2-yl)phenyl)pyridine (74f)



According to **TP 4**, to a mixture of 2-(2-allyl-3,5-dichlorophenyl)-2*H*-1,2,3-triazole (**73f**, 127 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu$_2$Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 20 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl$_2$ (15 mg, 5 mol%) and 3-bromopyridine (40 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a yellow oil (**74f**, 98 mg, 0.30 mmol, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.45 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.31 (dd, *J* = 2.3, 0.9 Hz, 1H), 7.76 (s, 1H), 7.57 (s, 2H), 7.44 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.15 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H), 5.73 (ddt, *J* = 16.6, 10.0, 6.4 Hz, 1H), 4.98 (dq, *J* = 10.0, 1.5 Hz, 1H), 4.85 (dq, *J* = 17.1, 1.6 Hz, 1H), 3.18 (dt, *J* = 6.4, 1.6 Hz, 2H).

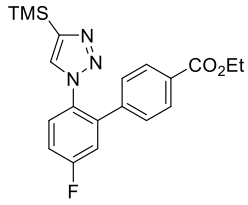
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 149.9, 149.5, 141.1, 137.2, 136.3, 136.0, 135.9, 135.6, 133.4, 133.1, 132.4, 130.7, 122.9, 117.6, 33.9.

MS (EI, 70 eV): m/z (%) = 332 (14), 330 (22), 319 (11), 318 (12), 317 (63), 316 (23), 315 (100), 302 (11), 275 (11), 263 (18), 261 (23), 239 (12), 205 (11), 191 (11).

HRMS (EI): for $C_{16}H_{12}Cl_2N_4$: calc. [M$^+$]: 330.0439; found: 330.0434.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2962 (vw), 2253 (vw), 2151 (vw), 2020 (vw), 1639 (vw), 1581 (vw), 1441 (vw), 1411 (vw), 1379 (vw), 1193 (vw), 1150 (vw), 1100 (vw), 1027 (vw), 962 (vw), 823 (vw), 664 (vw).

Ethyl 5'-fluoro-2'-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)-[1,1'-biphenyl]-4-carboxylate (77a)



According to **TP 4**, to a mixture of 1-(4-fluorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75a**, 118 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (15 mg, 5 mol%) and ethyl 4-bromobenzoate (69 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 12:1) afforded the title compound as a yellow oil (**77a**, 148 mg, 0.39 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.97–7.91 (m, 2H), 7.61 (dd, *J* = 9.6, 5.1 Hz, 1H), 7.26–7.22 (m, 2H), 7.12 (s, 1H), 7.12–7.08 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 0.21 (s, 9H).

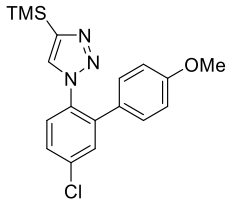
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.2, 165.3, 162.8, 147.8, 141.9, 139.9, 139.8, 132.5, 131.6, 131.1, 130.1, 130.0, 129.6, 118.9, 118.7, 117.4, 117.2, 62.5, 15.5, 0.0.

MS (EI, 70 eV): m/z (%) = 356 (10), 355 (28), 354 (31), 340 (17), 326 (13), 312 (12), 297 (13), 296 (54), 283 (14), 282 (48), 269 (13), 268 (50), 267 (100), 266 (13), 252 (18), 238 (19), 222 (16), 209 (12), 169 (14), 75 (15), 73 (20).

HRMS (EI): for $C_{20}H_{22}FN_3O_2Si$: calc. [M]: 383.1465, found: 383.1448.

IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3121 (vw), 3073 (vw), 2980 (vw), 2956 (w), 2900 (vw), 1713 (s), 1608 (w), 1588 (w), 1567 (w), 1517 (m), 1501 (m), 1478 (w), 1408 (w), 1391 (w), 1367 (w), 1271 (s), 1248 (s), 1200 (w), 1184 (m), 1147 (m), 1101 (s), 1034 (m), 1018 (m), 984 (m), 892 (w), 838 (vs), 775 (s), 758 (m), 737 (w), 705 (s), 670 (w).

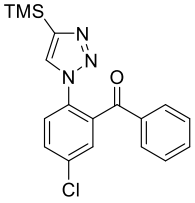
1-(5-Chloro-4'-methoxy-[1,1'-biphenyl]-2-yl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (77b)



According to **TP 4**, to a mixture of 1-(4-chlorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75b**, 126 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (15 mg, 5 mol%) and 4-bromoanisole (53 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**77b**, 101 mg, 0.28 mmol, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 2.3 Hz, 1H), 7.45 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.09 (s, 1H), 6.96–6.90 (m, 2H), 6.82–6.76 (m, 2H), 3.78 (s, 3H), 0.22 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.9, 147.6, 139.5, 136.6, 134.8, 132.3, 131.9, 130.8, 129.6, 129.3, 129.0, 115.3, 56.5, 0.0.
MS (EI, 70 eV): m/z (%) = 329 (30), 328 (25), 327 (84), 315 (24), 314 (20), 313 (74), 312 (12), 284 (21), 283 (17), 282 (56), 280 (21), 279 (100), 271 (17), 264 (10), 139 (18), 73 (24).
HRMS (EI): for C18H20ClN3OSi: calc. [M+]: 357.1064; found: 357.1059
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2957 (w), 2900 (vw), 2838 (vw), 1609 (m), 1579 (vw), 1516 (m), 1496 (s), 1464 (m), 1443 (w), 1427 (w), 1378 (vw), 1292 (w), 1248 (s), 1201 (m), 1179 (m), 1149 (m), 1125 (w), 1112 (w), 1095 (w), 1042 (m), 1034 (m), 1008 (w), 996 (w), 982 (m), 884 (w), 832 (vs), 821 (vs), 775 (m), 758 (s), 725 (w), 708 (w), 698 (w), 680 (w), 659 (w).

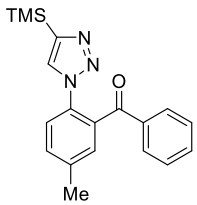
(5-Chloro-2-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)phenyl)(phenyl)methanone (77c)



According to **TP 4**, to a mixture of 1-(4-chlorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75b**, 126 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, benzoyl chloride (70 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 12 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**77c**, 103 mg, 0.29 mmol, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69–7.57 (m, 6H), 7.47 (ddt, *J* = 8.7, 7.1, 1.4 Hz, 1H), 7.34–7.28 (m, 2H), 0.19 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.6, 137.2, 137.0, 136.8, 135.1, 132.9, 131.5, 131.2, 130.6, 129.8, 127.4, 0.0.
MS (EI, 70 eV): m/z (%) = 313 (30), 312 (18), 311 (100), 105 (52), 77 (29), 73 (10).
HRMS (EI): for $C_{18}H_{18}ClN_3OSi$: calc. [M]: 355.0908, found: 355.0914.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3117 (w), 2954 (w), 2854 (vw), 1733 (vw), 1658 (m), 1595 (w), 1583 (vw), 1573 (vw), 1497 (m), 1478 (w), 1449 (w), 1408 (w), 1394 (w), 1314 (w), 1278 (m), 1268 (m), 1247 (m), 1202 (m), 1176 (w), 1158 (w), 1136 (vw), 1113 (w), 1090 (w), 1069 (w), 1041 (m), 1025 (w), 1000 (w), 984 (m), 956 (w), 939 (vw), 904 (vw), 891 (vw), 833 (vs), 805 (m), 786 (m), 760 (m), 740 (m), 708 (s), 695 (m), 661 (w).

(5-Methyl-2-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)phenyl)(phenyl)methanone (77d)



According to **TP 4**, to a mixture of 1-(*p*-tolyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75c**, 116 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 60 min, benzoyl chloride (70 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 12 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**77d**, 93 mg, 0.28 mmol, 55% yield).

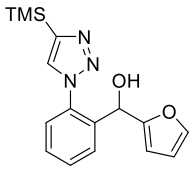
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.61–7.40 (m, 7H), 7.31–7.27 (m, 2H), 2.50 (s, 3H), 0.19 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 196.8, 148.2, 141.1, 137.7, 135.7, 134.6, 134.1, 133.6, 131.6, 130.5, 129.6, 126.0, 22.5, 0.0.

MS (EI, 70 eV): m/z (%) = 307 (22), 292 (26), 291 (100).

HRMS (EI): for $C_{19}H_{21}N_3OSi$: calc. [M]: 335.1454, found: 335.1477.

IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3080 (w), 2957 (w), 2923 (vw), 2852 (vw), 1730 (w), 1660 (s), 1605 (w), 1597 (w), 1581 (w), 1509 (m), 1450 (w), 1406 (w), 1318 (w), 1312 (w), 1287 (m), 1247 (m), 1211 (w), 1198 (m), 1179 (m), 1161 (w), 1108 (w), 1039 (m), 1002 (w), 982 (w), 976 (m), 971 (m), 958 (w), 932 (w), 908 (vw), 836 (vs), 824 (vs), 797 (m), 757 (m), 738 (s), 702 (vs), 686 (m), 662 (w).

Furan-2-yl(2-(4-(trimethylsilyl)-1H-1,2,3-triazol-1-yl)phenyl)methanol (77e)



According to **TP 4**, to a mixture of 1-phenyl-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75d**, 109 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu$_2$Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 1 h, furfural (50 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a slight yellow solid (**77e**, 126 mg, 0.40 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.67 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.58 (s, 1H), 7.55 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.49 (td, *J* = 7.6, 1.6 Hz, 1H), 7.33 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.24 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.24 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.09 (dt, *J* = 3.3, 1.0 Hz, 1H), 5.74 (s, 1H), 0.37 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 155.3, 148.1, 143.1, 138.4, 136.6, 131.8, 131.3, 131.0, 130.3, 111.6, 108.3, 68.4, 0.0.

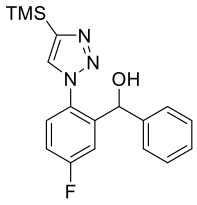
MS (EI, 70 eV): m/z (%) = 313 (17), 284 (14), 270 (15), 269 (13), 268 (56), 252 (18), 224 (12), 212 (18), 204 (21), 202 (22), 196 (88), 195 (16), 194 (17), 187 (15), 180 (17), 168 (10), 167 (31), 166 (33), 115 (22), 75 (74), 73 (100).

HRMS (EI): for $C_{16}H_{19}N_3O_2Si$: calc. [M]: 313.1247, found: 313.1234.

IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3272 (w), 3141 (vw), 2954 (w), 1500 (m), 1459 (w), 1390 (vw), 1347 (vw), 1251 (m), 1208 (m), 1183 (w), 1156 (w), 1148 (m), 1105 (w), 1072 (w), 1051 (m), 1029 (m), 1013 (m), 987 (w), 929 (w), 842 (vs), 807 (m), 760 (s), 747 (s), 731 (m), 709 (w), 680 (vw), 667 (w).

Melting point: M.p. = 107 °C.

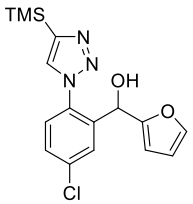
(5-Fluoro-2-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)phenyl)(phenyl)methanol (77f)



According to **TP 4**, to a mixture of 1-(4-fluorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75a**, 118 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, benzaldehyde (62 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a white solid (**77f**, 118 mg, 0.35 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.43 (dd, *J* = 9.2, 2.9 Hz, 1H), 7.29 (s, 1H), 7.25–7.17 (m, 4H), 7.12 (ddd, *J* = 8.7, 7.5, 2.8 Hz, 1H), 7.07–7.02 (m, 2H), 5.79 (s, 1H), 0.31 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 165.7, 163.2, 147.6, 144.2, 144.1, 142.4, 132.3, 129.6, 129.1, 129.0, 128.9, 127.4, 117.8, 117.6, 116.7, 116.5, 72.8, 0.0.
MS (EI, 70 eV): m/z (%) = 313 (21), 312 (56), 298 (31), 296 (15), 256 (18), 239 (28), 236 (28), 225 (15), 224 (100), 223 (18), 222 (71) 220 (69), 207 (14), 204 (14), 198 (47), 183 (23), 170 (12), 75 (11), 73 (27).
HRMS (EI): for $C_{18}H_{20}FN_3OSi$: calc. [M]: 341.1360, found: 341.1366.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3223 (w), 3030 (vw), 2953 (w), 1618 (vw), 1594 (w), 1501 (m), 1488 (w), 1455 (w), 1421 (w), 1348 (vw), 1263 (m), 1250 (m), 1202 (m), 1152 (m), 1142 (m), 1099 (w), 1055 (m), 1044 (m), 1039 (m), 1017 (w), 989 (m), 957 (m), 917 (vw), 891 (w), 835 (vs), 822 (s), 765 (w), 749 (m), 744 (s), 702 (s), 663 (w), 656 (w).
Melting point: M.p. = 118 °C.

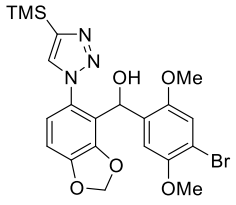
(5-Chloro-2-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)phenyl)(furan-2-yl)methanol (77g)



According to **TP 4**, to a mixture of 1-(4-chlorophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75b**, 126 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, furfural (50 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a colorless solid (**77g**, 134 mg, 0.39 mmol, 78% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.71 (d, *J* = 2.3 Hz, 1H), 7.51 (s, 1H), 7.44 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.28–7.25 (m, 2H), 6.25 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.08 (dt, *J* = 3.4, 0.9 Hz, 1H), 5.74 (s, 1H), 0.34 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.6, 148.2, 143.4, 140.1, 137.3, 134.8, 131.9, 130.8, 130.3, 128.0, 111.6, 108.8, 67.5, 0.0.
MS (EI, 70 eV): m/z (%) = 317 (16), 303 (11), 301 (25), 285 (11), 245 (10), 238 (10), 235 (15), 231 (21), 229 (68), 228 (20), 200 (13), 199 (13), 167 (15), 166 (18), 115 (10), 81 (21), 75 (75), 73 (100), 45 (12).
HRMS (EI): for $C_{16}H_{18}ClN_3O_2Si$: calc. [M+]: 347.0857; found: 347.0851.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3213 (w), 3142 (w), 2959 (w), 2360 (w), 1498 (m), 1484 (w), 1457 (w), 1406 (w), 1318 (w), 1298 (vw), 1286 (vw), 1251 (m), 1211 (m), 1183 (w), 1159 (w), 1152 (m), 1119 (w), 1092 (w), 1077 (vw), 1056 (m), 1043 (m), 1010 (m), 989 (w), 927 (w), 889 (w), 871 (w), 838 (vs), 817 (s), 806 (m), 786 (m), 757 (m), 742 (s), 713 (m), 681 (w), 657 (w).
Melting point: M.p. = 136 °C.

(4-Bromo-2,5-dimethoxyphenyl)(5-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)benzo[*d*][1,3]dioxol-4-yl)methanol (77h)

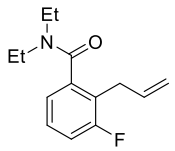


According to **TP 4**, to a mixture of 1-(benzo[*d*][1,3]dioxol-5-yl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (**75e**, 126 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg·(**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, 4-bromo-2,5-dimethoxybenzaldehyde (147 mg, 0.60 mmol, 1.2 equiv) dissolved in toluene (1 mL) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel,

*i*hexane/EtOAc = 4:1 to 1:1) afforded the title compound as a colorless solid (**77h**, 201 mg, 0.40 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.23 (s, 1H), 6.80 (t, *J* = 4.1 Hz, 2H), 6.76 (s, 1H), 6.67 (d, *J* = 8.2 Hz, 1H), 6.14 (d, *J* = 13.9 Hz, 2H), 5.97 (s, 1H), 3.80 (s, 3H), 3.49 (s, 3H), 0.31 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.6, 148.4, 132.4, 131.1, 130.0, 123.4, 120.9, 116.9, 111.2, 110.4, 108.6, 103.7, 65.8, 61.7, 57.5, 23.9, 22.3, 15.5, 0.0.
MS (EI, 70 eV): m/z (%) = 463 (14), 462 (11), 448 (10), 390 (12), 388 (18), 358 (13), 355 (12), 332 (23), 263 (19), 262 (97), 246 (47), 217 (25), 297 (24), 111 (11), 99 (11), 97 (23), 85 (46), 84 (11), 83 (23), 75 (50), 74 (11), 73 (93), 71 (61), 70 (14), 67 (10), 57 (83), 56 (17), 55 (32), 44 (100), 43 (57), 43 (33), 41 (24).
HRMS (EI): for $C_{21}H_{24}BrN_3O_5Si$: $[M-O]^{\bullet+}$: 489.0714, found: 489.0719.
IR (Diamond-ATR, neat): $\tilde{\nu}$/cm^{-1} = 3142 (w), 2359 (w), 1492 (s), 1453 (m), 1409 (w), 1378 (m), 1323 (m), 1275 (w), 1250 (m), 1241 (m), 1210 (s), 1180 (m), 1138 (w), 1071 (s), 1048 (s), 1034 (s), 1004 (m), 934 (w), 889 (w), 843 (vs), 817 (s), 761 (s), 736 (m), 709 (m), 668 (m).
Melting point: M.p. = 201 °C.

2-Allyl-*N*,*N*-diethyl-3-fluorobenzamide (80a)



According to **TP 1**, to a mixture of *N*,*N*-diethyl-3-fluorobenzamide (**78a**, 98 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, allyl bromide (52 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a colorless oil (**80a**, 73 mg, 0.31 mmol, 62% yield).

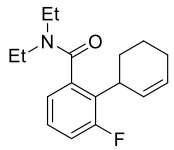
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.25–7.18 (m, 1H), 7.04 (ddd, *J* = 9.6, 8.2, 1.2 Hz, 1H), 6.97 (dd, *J* = 7.5, 1.2 Hz, 1H), 5.97–5.85 (m, 1H), 5.08–4.98 (m, 2H), 3.79 (s, 1H), 3.46–3.23 (m, 3H), 3.08 (p, *J* = 6.6 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 169.1, 169.1, 162.5, 160.1, 139.1, 139.0, 135.0, 135.0, 128.0, 127.9, 124.0, 123.8, 121.3, 121.3, 116.0, 115.7, 115.5, 43.0, 38.7, 30.7, 13.8, 12.7.

MS (EI, 70 eV): m/z (%) = 282 (10), 281 (61), 266 (32), 265 (13), 253 (13), 250 (10), 248 (13), 225 (23), 221 (20), 209 (12), 208 (12), 207 (92), 197 (17), 192 (13), 191 (19), 163 (31), 162 (100), 149 (12), 147 (24), 135 (18), 134 (58), 133 (76), 115 (48), 109 (16), 73 (33).

HRMS (EI): for $C_{14}H_{18}FNO$: calc. [M-H$^+$]: 234.1294; found: 234.1289.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3080 (vw), 2976 (w), 2936 (w), 2876 (vw), 1629 (vs), 1613 (m), 1578 (m), 1482 (m), 1456 (s), 1427 (s), 1381 (m), 1365 (m), 1348 (w),1315 (m), 1287 (s), 1244 (m), 1231 (m), 1220 (m), 1207 (w), 1186 (w), 1159 (w), 1130 (w), 1095 (m), 1070 (w), 1016 (w), 994 (w), 960 (w), 939 (w), 915 (m), 884 (w), 844 (m), 793 (s), 752 (m), 676 (w).

***N*,*N*-Diethyl-6-fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxamide (80b)**



According to **TP 4**, to a mixture of *N*,*N*-diethyl-3-fluorobenzamide (**78a**, 976 mg, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu$_2$Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, 3-bromocyclohexene (0.81 mL, 7.00 mmol, 1.4 equiv) and CuCN·2LiCl (1.0 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1 to 4:1) afforded the title compound as a pink oil (**80b**, 974 mg, 3.54 mmol, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.19 (tt, *J* = 7.9, 4.8 Hz, 1H), 6.99 (ddt, *J* = 11.2, 8.2, 1.5 Hz, 1H), 6.92 (ddd, *J* = 7.7, 3.8, 1.2 Hz, 1H), 5.85–5.70 (m, 1H), 5.61 (dt, *J* = 9.7, 1.9 Hz, 1H), 3.87–3.03 (m, 5H), 2.20–1.72 (m, 5H), 1.66–1.52 (m, 1H), 1.23 (q, *J* = 7.3 Hz, 3H), 1.05 (dt, *J* = 11.5, 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 169.3, 163.2, 163.1, 160.7, 160.6, 139.0, 139.0, 139.0, 129.7, 129.5, 129.4, 129.0, 128.8, 128.0, 127.9, 127.8, 127.7, 127.3, 127.2, 121.3, 121.1, 116.5, 116.3, 116.1, 43.0, 42.8, 38.7, 38.4, 37.9, 36.7, 29.1, 28.8, 24.6, 24.5, 22.8, 13.9, 12.7, 12.5.

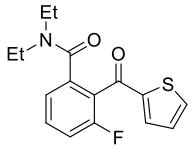
MS (EI, 70 eV): m/z (%) = 275 (29), 260 (23), 246 (17), 220 (30), 203 (17), 202 (100), 201 (86), 187 (17), 185 (35), 184 (62), 183 (54), 175 (18). 174 (14), 173 (17), 170 (11), 165 (32), 159 (25), 153 (11), 152 (13), 147 (25), 146 (42), 133 (37), 109 (12), 72 (13).

HRMS (EI): for $C_{17}H_{22}FNO$: calc. [M+]: 275.1685; found: 275.1681.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3020 (w), 2971 (w), 2933 (m), 2874 (w), 2836 (w), 2363 (vw), 1629 (vs), 1609 (m), 1574 (w), 1479 (m), 1454 (s), 1425 (s), 1380 (m), 1364 (w), 1347 (w), 1315 (m), 1288 (s), 1265 (w), 1238 (m), 1222 (m), 1190 (w), 1160 (w), 1135 (w), 1119 (m), 1099 (w), 1067 (w),

1047 (w), 1014 (w), 987 (w), 952 (w), 928 (w), 900 (w), 878 (vw), 850 (w), 833 (m), 799 (s), 746 (s), 720 (m), 703 (w), 654 (vw).

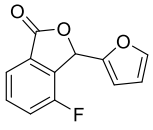
_N_,_N_-Diethyl-3-fluoro-2-(thiophene-2-carbonyl)benzamide (80c)



According to **TP 4**, to a mixture of *N*,*N*-diethyl-3-fluorobenzamide (**78a**, 98 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, thiophene-2-carbonyl chloride (64 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 12 h at 25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a yellow oil (**80c**, 97 mg, 0.32 mmol, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.72 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.57–7.45 (m, 2H), 7.23–7.16 (m, 2H), 7.10 (dd, *J* = 4.9, 3.8 Hz, 1H), 3.40 (q, *J* = 7.1 Hz, 2H), 3.25 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 184.3, 167.9, 160.3, 157.8, 143.9, 138.7, 136.2, 135.5, 131.7, 128.4, 125.5, 125.4, 122.2, 116.6, 116.4, 43.4, 38.9, 13.7, 12.1.
MS (EI, 70 eV): m/z (%) = 234 (22), 233 (100), 213 (15), 205 (17), 189 (11), 186 (11), 185 (12), 157 (20), 133 (13), 110 (23), 72 (18).
HRMS (EI): for $C_{16}H_{16}FNO_2S$: calc. [M-H$^+$]: 304.0808; found: 304.0804.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3078 (vw), 2975 (w), 2935 (w), 2876 (vw), 1626 (vs), 1606 (s), 1572 (m), 1516 (m), 1483 (m), 1449 (s), 1429 (s), 1409 (vs), 1382 (m), 1355 (m), 1314 (m), 1283 (vs), 1243 (s), 1212 (m), 1165 (w), 1142 (w), 1123 (m), 1100 (w), 1081 (w), 1069 (w), 1048 (m), 1017 (w), 956 (w), 934 (w), 914 (w), 883 (m), 844 (s), 826 (w), 802 (s), 767 (m), 742 (s), 724 (s), 689 (w), 680 (w).

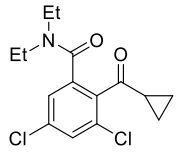
4-Fluoro-3-(furan-2-yl)isobenzofuran-1(3*H*)-one (80d)



According to **TP 4**, to a mixture of *N*,*N*-diethyl-3-fluorobenzamide (**78a**, 98 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 30 min, furfural (50 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was warmed to 60 °C and stirred for further 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a red solid (**80d**, 83 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.79 (d, *J* = 7.5 Hz, 1H), 7.66–7.58 (m, 1H), 7.46–7.36 (m, 2H), 6.54 (s, 1H), 6.46 (dd, *J* = 3.3, 0.7 Hz, 1H), 6.40 (dd, *J* = 3.3, 1.8 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.5, 158.3, 155.8, 147.0, 144.3, 132.3, 132.3, 132.1, 129.6, 121.7, 121.7, 121.3, 121.1, 111.1, 110.7, 73.1.
MS (EI, 70 eV): m/z (%) = 218 (47), 217 (11), 191 (10), 190 (85), 174 (57), 173 (23), 162 (32), 147 (10), 146 (100), 134 (11), 133 (33), 126 (10), 125 (11), 123 (24), 122 (19), 120 (21), 95 (11), 94 (17), 75 (10).
HRMS (EI): for $C_{12}H_7FO_3$: calc. [M+]: 218.0379; found: 218.0372.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 515 (vw), 3121 (vw), 3079 (vw), 2925 (vw), 2853 (vw), 1900 (vw), 1770 (s), 1764 (s), 1732 (w), 1725 (w), 1603 (m), 1501 (w), 1483 (s), 1386 (vw), 1342 (w), 1312 (w), 1288 (m), 1254 (m), 1245 (s), 1181 (w), 1156 (m), 1152 (m), 1083 (s), 1070 (m), 1050 (m), 1016 (m), 985 (m), 936 (m), 925 (s), 887 (m), 868 (m), 823 (s), 796 (w), 751 (s), 741 (vs), 668 (w).
Melting point: M.p. = 87 °C.

3,5-Dichloro-2-(cyclopropanecarbonyl)-*N*,*N*-diethylbenzamide (80e)



According to **TP 4**, to a mixture of 3,5-dichloro-*N*,*N*-diethylbenzamide (**78b**, 738 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 2.40 mmol, 0.8 equiv) at 25 °C. After 10 min cyclopropanecarbonyl chloride (0.33 mL, 3.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.6 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 12 h at 25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**80e**, 675 mg, 2.15 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.43 (d, *J* = 1.9 Hz, 1H), 7.18 (d, *J* = 1.9 Hz, 1H), 3.45 (q, *J* = 7.1 Hz, 2H), 3.18 (q, *J* = 7.2 Hz, 2H), 2.39 (tt, *J* = 7.8, 4.5 Hz, 1H), 1.32–1.26 (m, 2H), 1.18–1.08 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 203.6, 167.2, 138.7, 137.4, 135.6, 131.7, 129.8, 124.6, 43.4, 39.1, 23.2, 14.0, 13.7, 12.3.

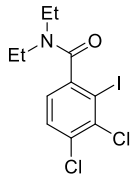
MS (EI, 70 eV): m/z (%) = 222 (38), 215 (30), 214 (21), 213 (49), 212 (33), 199 (20), 197 (30), 186 (28), 184 (44), 180 (10), 178 (32), 174 (20), 172 (32), 160 (13), 151 (13), 150 (24), 149 (38), 143 (12), 115 (25), 108 (13), 72 (100).

HRMS (EI): for $C_{15}H_{17}Cl_2NO_2$: calc. [M-H$^+$]: 312.0558; found: 312.0552.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3048 (w), 2972 (w), 2933 (w), 2362 (vw), 1680 (m), 1620 (vs), 1580 (m), 1551 (m), 1478 (m), 1455 (m), 1428 (m), 1371 (s), 1361 (m), 1346 (m), 1316 (m), 1285 (m), 1265 (w), 1228 (m), 1202 (m), 1183 (m), 1121 (w), 1103 (m), 1087 (m), 1063 (w), 1035 (m), 1015 (w), 984 (s), 949 (w), 928 (w), 861 (s), 829 (m), 795 (m), 762 (m), 729 (w).

Melting point: M.p. = 91 °C.

3,4-Dichloro-*N*,*N*-diethyl-2-iodobenzamide (80f)



According to **TP 4**, to a mixture of 3,4-dichloro-*N*,*N*-diethylbenzamide (**78c**, 123 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 10 min, the reaction mixture was cooled to 0 °C and iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a brown solid (**80f**, 134 mg, 0.36 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.49 (d, *J* = 8.1 Hz, 1H), 7.02 (d, *J* = 8.1 Hz, 1H), 3.84 (dtd, *J* = 14.3, 7.2, 0.9 Hz, 1H), 3.28 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.22–3.02 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.9, 144.2, 137.9, 132.1, 130.5, 125.1, 98.7, 42.8, 39.0, 13.9, 12.2.

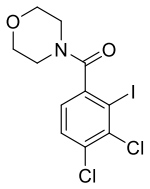
MS (EI, 70 eV): m/z (%) = 371 (16), 370 (14), 369 (21), 300 (43), 298 (75), 270 (11), 246 (24), 244 (27), 207 (15), 174 (12), 172 (19), 145 (11), 143 (19), 85 (11), 83 (16), 71 (17), 70 (11), 69 (20), 57 (35), 56 (23), 55 (14), 43 (100), 42 (27), 41 (12), 40 (15).

HRMS (EI): for $C_{11}H_{12}Cl_2INO$: calc. [M-H$^+$]: 369.9262; found: 369.9260.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2996 (w), 2972 (w), 2932 (w), 2873 (w), 2365 (vw), 1888 (vw), 1609 (vs), 1568 (m), 1537 (w), 1520 (w), 1463 (m), 1444 (m), 1419 (s), 1384 (m), 1366 (m), 1343 (m), 1337 (m), 1319 (m), 1292 (s), 1247 (w), 1221 (m), 1201 (m), 1163 (m), 1147 (m), 1112 (m), 1108 (m), 1089 (m), 1068 (m), 1048 (m), 1012 (w), 950 (w), 895 (m), 820 (s), 800 (s), 777 (m), 760 (m), 713 (m), 659 (m).

Melting point: M.p. = 103 °C.

(3,4-Dichloro-2-iodophenyl)(morpholino)methanone (80g)



According to **TP 4**, to a mixture of (3,4-dichlorophenyl)(morpholino)methanone (**78d**, 130 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at -20 °C. After 2 h, iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h at 0 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1 to 1:1) afforded the title compound as a yellow solid (**80g**, 118 mg, 0.31 mmol, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.52 (d, *J* = 8.2 Hz, 1H), 7.02 (d, *J* = 8.1 Hz, 1H), 3.89-3.73 (m, 5H), 3.60 (ddd, *J* = 11.6, 6.3, 3.2 Hz, 1H), 3.28 (ddd, *J* = 13.4, 6.4, 3.3 Hz, 1H), 3.18 (ddd, *J* = 13.4, 6.6, 3.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.2, 143.1, 138.2, 132.7, 130.7, 125.2, 98.5, 66.6, 47.1, 42.0.

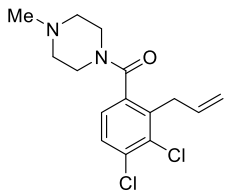
MS (EI, 70 eV): m/z (%) = 386 (22), 385 (25), 384 (35), 383 (32), 302 (11), 300 (63), 298 (100), 272 (15), 270 (20), 260 (12), 258 (19), 174 (15), 172 (24), 146 (10), 145 (20), 144 (16), 143 (30), 108 (25), 86 (38), 74 (18), 56 (37), 55 (19), 41 (12).

HRMS (EI): for $C_{11}H_{10}Cl_2INO_2$: calc. [M-H^+]: 384.9133; found: 384.9127.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3066 (vw), 2957 (m), 2869 (m), 2361 (vw), 1709 (s), 1691 (m), 1653 (s), 1595 (w), 1574 (w), 1478 (m), 1463 (m), 1447 (w), 1398 (w), 1384 (m), 1363 (s), 1351 (s), 1312 (s), 1266 (m), 1249 (m), 1231 (s), 1215 (m), 1184 (s), 1122 (w), 1106 (w), 1073 (m), 1059 (m), 1044 (s), 1035 (s), 1008 (s), 989 (m), 964 (s), 912 (m), 869 (w), 818 (w), 770 (s), 745 (m), 697 (vs).

Melting point: M.p. = 134 °C.

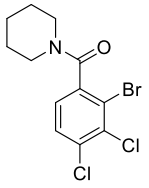
(2-Allyl-3,4-dichlorophenyl)(4-methylpiperazin-1-yl)methanone (80h)



According to **TP 4**, to a mixture of (3,4-dichlorophenyl)(4-methylpiperazin-1-yl)methanone (**78e**, 137 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg·(**58**, 0.40 mmol, 0.8 equiv) at 0 °C. After 15 min, allyl bromide (52 µL, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a brown oil (**80h**, 104 mg, 0.33 mmol, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$): 7.38 (d, *J* = 8.1 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 1H), 5.88 (dddd, *J* = 17.3, 10.1, 7.4, 5.2 Hz, 1H), 5.13–4.98 (m, 2H), 3.87 (dd, *J* = 11.5, 6.0 Hz, 1H), 3.77–3.52 (m, 3H), 3.19 (dtdt, *J* = 13.2, 10.5, 7.1, 3.6 Hz, 2H), 2.46 (dtq, *J* = 18.7, 7.1, 3.5 Hz, 2H), 2.36–2.20 (m, 5H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.3, 137.5, 136.7, 134.5, 134.4, 134.3, 128.9, 125.3, 117.3, 55.4, 55.0, 47.6, 46.5, 42.0, 36.2.
MS (EI, 70 eV): m/z (%) = 281 (16), 225 (38), 209 (22), 208 (13), 207 (100), 192 (16), 191 (25), 151 (11), 150 (13), 149 (38), 133 (15), 115 (40), 99 (11), 97 (39), 85 (14), 73 (27), 70 (45), 56 (10), 42 (13).
HRMS (EI): for $C_{15}H_{18}Cl_2N_2O$: calc. [M+]: 312.0796; found: 312.0790.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3077 (vw), 2936 (w), 2847 (w), 2791 (w), 2357 (w), 2331 (vw), 1717 (w), 1632 (vs), 1579 (m), 1460 (m), 1447 (m), 1427 (s), 1383 (m), 1291 (s), 1273 (s), 1266 (s), 1243 (m), 1171 (m), 1143 (m), 1122 (m), 1092 (w), 1071 (m), 1025 (m), 1000 (s), 915 (m), 894 (w), 824 (m), 777 (m), 668 (w).

(2-Bromo-3,4-dichlorophenyl)(piperidin-1-yl)methanone (80i)

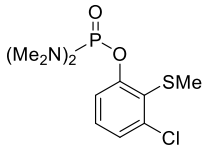


According to **TP 4**, to a mixture of (3,4-dichlorophenyl)(piperidin-1-yl)methanone (**78f**, 129 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 0 °C. After

20 min, 1,2-dibromotetrachloroethane (244 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h at 0 C°. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**80i**, 115 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (d, *J* = 8.2 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 3.80–3.66 (m, 2H), 3.17 (qdd, *J* = 13.2, 7.1, 3.8 Hz, 2H), 1.66 (tt, *J* = 13.9, 5.4 Hz, 5H), 1.51–1.41 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.1, 139.2, 134.3, 133.9, 129.6, 125.4, 121.1, 47.8, 42.6, 26.2, 25.4, 24.4.
MS (EI, 70 eV): m/z (%) = 338 (14), 337 (40), 336 (32), 335 (85), 334 (21), 333 (50), 258 (41), 257 (10), 256 (65), 254 (44), 252 (100), 250 (59), 226 (13), 224 (29), 222 (17), 172 (15), 145 (11), 143 (18), 108 (15), 84 (16), 83 (11), 55 (23), 42 (22), 41 (22).
HRMS (EI): for $C_{12}H_{12}BrCl_2NO$: calc. [M-H$^+$]: 334.9479; found: 333.9389.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2942 (m), 2921 (w), 2861 (m), 2353 (vw), 1630 (vs), 1572 (m), 1467 (m), 1458 (m), 1447 (m), 1441 (m), 1424 (vs), 1351 (m), 1284 (m), 1278 (m), 1272 (s), 1258 (m), 1250 (m), 1240 (m), 1188 (m), 1166 (m), 1146 (w), 1117 (m), 1059 (w), 1028 (m), 1004 (s), 955 (w), 932 (vw), 896 (m), 852 (m), 823 (vs), 790 (m), 762 (m), 730 (m), 721 (m), 667 (m).
Melting point: M.p. = 111 °C.

3-Chloro-2(methylsulfanyl)phenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (80j)



According to **TP 4**, to a mixture of 3-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78g**, 131 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 40 °C. After 30 min, *S*-methyl methanethiosulfonate (57 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**80j**, 106 mg, 0.34 mmol, 68% yield).

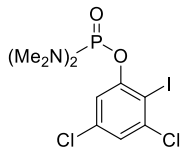
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.35 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.24–7.17 (m, 2H), 2.77 (d, *J* = 10.1 Hz, 12H), 2.41 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 153.8, 140.1, 130.3, 129.7, 125.5, 118.7, 36.7, 18.3.
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 15.9.

MS (EI, 70 eV): m/z (%) = 265 (29), 264 (83), 263 (27), 261 (87), 200 (11), 173 (21), 154 (13), 135 (100), 92 (12).

HRMS (EI): for $C_{11}H_{18}ClN_2O_2PS$: calc. [M+]: 308.0515; found: 308.0506.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3471 (vw), 3065 (vw), 2994 (vw), 2923 (w), 2893 (w), 2851 (w), 2809 (w), 1589 (w), 1573 (w), 1564 (m), 1474 (w), 1438 (s), 1304 (m), 1220 (s), 1179 (m), 1107 (vw), 1068 (w), 987 (s), 929 (vs), 777 (s), 754 (s), 736 (m), 719 (m), 700 (vw), 682 (w), 667 (m).

2-Iodo-3,5-Dichlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (80k)



According to **TP 4**, to a mixture of 3,5-Dichlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78h**, 148 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 1 h, iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h at 0 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a yellow oil (**80k**, 209 mg, 0.49 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.44 (dd, *J* = 2.2, 1.1 Hz, 1H), 7.24 (d, *J* = 2.2 Hz, 1H), 2.75 (d, *J* = 10.3 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 153.3, 140.1, 135.5, 124.5, 117.8, 92.0, 36.9.

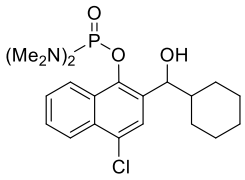
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 16.5.

MS (EI, 70 eV): m/z (%) = 297 (31), 295 (47), 135 (100), 44 (29).

HRMS (EI): for $C_{10}H_{14}Cl_2IN_2O_2P$: calc. [M-I]: 295.0170; found: 295.0173.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2942 (m), 2921 (w), 2861 (m), 2353 (vw), 1630 (vs), 1572 (m), 1467 (m), 1458 (m), 1447 (m), 1441 (m), 1424 (vs), 1351 (m), 1284 (m), 1278 (m), 1272 (s), 1258 (m), 1250 (m), 1240 (m), 1188 (m), 1166 (m), 1146 (w), 1117 (m), 1059 (w), 1028 (m), 1004 (s), 955 (w), 932 (vw), 896 (m), 852 (m), 823 (vs), 790 (m), 762 (m), 730 (m), 721 (m), 667 (m).

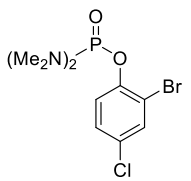
4-Chloro-2-(cyclohexyl(hydroxy)methyl)phenyl *N,N,N′,N′* tetramethylphosphorodiamidate (80l)



According to **TP 4**, to a mixture of 4-Chloronaphtyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78i**, 156 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 60 °C. After 30 min, cyclohexan carboxaldehyde (73 µL, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a white solid (**80l**, 144 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.26–8.20 (m, 1H), 8.05–7.98 (m, 1H), 7.70 (s, 1H), 7.64–7.55 (m, 2H), 4.73 (d, *J* = 10.0 Hz, 1H), 2.89 (d, *J* = 10.0 Hz, 6H), 2.60 (d, *J* = 9.8 Hz, 6H), 2.49–2.40 (m, 1H), 1.97–1.78 (m, 2H), 1.71–1.52 (m, 2H), 1.38–1.04 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 142.9, 133.0, 130.8, 128.7, 128.4, 127.1, 126.5, 125.6, 124.7, 122.1, 71.6, 41.4, 36.9, 30.7, 26.5, 25.8.
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 15.9.
MS (EI, 70 eV): m/z (%) = 270 (11), 254 (17), 219 (18), 191 (12), 135 (100).
HRMS (EI): for $C_{21}H_{30}ClN_2O_3P$: calc. [M-H_2O]: 406.1582; found: 406.1572.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3325 (w), 2951 (w), 2921 (s), 2851 (m), 2815 (w), 1743 (vw), 1597 (w), 1455 (w), 1449 (w), 1360 (m), 1307 (m), 1254 (w), 1213 (m), 1195 (s), 1160 (m), 1124 (m), 1083 (s), 1068 (m), 1027 (m), 995 (vs), 971 (m), 954 (m), 910 (w), 850 (s), 789 (m), 784 (w), 776 (s), 757 (s), 706 (s), 674 (w), 669 (w).
Melting point: M.p. = 155 °C.

2-Bromo-4-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (80m)

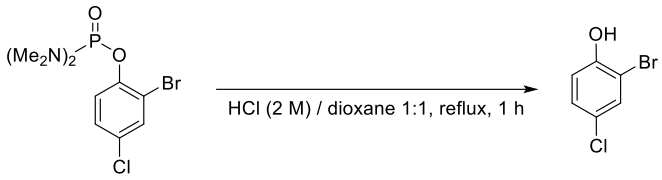


According to **TP 4**, to a mixture of 4-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**78j**, 657 mg, 2.50 mmol, 1.0 equiv) in toluene (5 mL) was added *s*Bu_2Mg (**58**, 2.00 mmol, 0.8 equiv) at

60 °C. After 30 min, 1,2-dibromotetrachloroethane (1.14 g, 3.50 mmol, 1.4 equiv) dissolved in THF (5 mL) was added dropwise and the reaction mixture was stirred for 1 h at 0 C°. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:4) afforded the title compound as a yellow oil (**80m**, 699 mg, 2.10 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53 (dd, *J* = 2.5, 1.0 Hz, 1H), 7.44 (dd, *J* = 8.8, 1.1 Hz, 1H), 7.21 (dd, *J* = 8.8, 2.6 Hz, 1H), 2.73 (d, *J* = 10.2 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.5, 132.8, 129.4, 128.5, 121.5, 114.7, 114.6, 36.7.
^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) = 16.1.
MS (EI, 70 eV): m/z (%) = 263 (20), 261 (63), 135 (100).
HRMS (EI): for $C_{10}H_{15}BrClN_2O_2P$: calc. [M+]: 339.9743; found: 339.9740.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3461 (vw), 3089 (vw), 2997 (vw), 2926 (w), 2895 (w), 2852 (w), 2810 (w), 2363 (vw), 1733 (vw), 1647 (vw), 1579 (vw), 1470 (vs), 1379 (w), 1304 (m), 1262 (m), 1223 (s), 1180 (m), 1149 (w), 1096 (w), 1068 (w), 1046 (m), 985 (vs), 904 (vs), 866 (m), 823 (m), 790 (vs), 758 (vs), 684 (s), 659 (w).

2-Bromo-4-chlorophenol (80n)

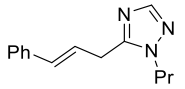


The procedure was adopted from literature.[192] 2-Bromo-4-Chlorophenyl *N,N,N′,N′*-tetramethylphosphorodiamidate (**80m**, 171 mg, 0.50 mmol, 1.0 equiv) was dissolved in a mixture of HCl (2 M) and dioxane (1:1, 5 mL). The reaction mixture was warmed to reflux for 1 h. The reaction mixture was extracted with Et_2O (3 x 10 mL). Purification by short path flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**80n**, 91 mg, 0.44 mmol, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 (d, *J* = 2.5 Hz, 1H), 7.13 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 1H), 5.40 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.9, 131.1, 129.0, 125.6, 116.6, 110.1.
Analytical data was equivalent to literature.[193]

[192] C. J. Rohbogner, S. Wirth, P. Knochel, *Org. Lett.* **2010**, *9*, 1984-1987.
[193] P. Suresh, S. Annalakshmi, K. Pitchumani, *Tetrahedron* **2007**, *63*, 4959-4967.

5-Cinnamyl-1-propyl-1*H*-1,2,4-triazole (80o)

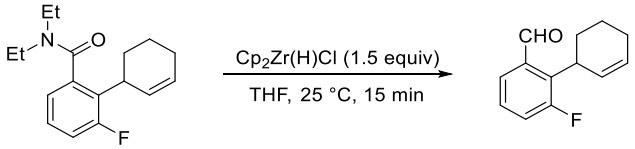


According to **TP 1**, to a mixture of 1-propyl-1*H*-1,2,4-triazole (**78k**, 56 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 0 °C. After 15 min, cinnamyl bromide, (118 mg, 0.60 mmol, 1.2 equiv) and CuCN·2LiCl (0.1 mL, 1.0 M in THF, 20 mol%) were added at -25 °C and the mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a colorless oil (**80o**, 98 mg, 0.43 mmol, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.91 (s, 1H), 7.42 – 7.28 (m, 6H), 6.53 (dt, *J* = 15.9, 1.7 Hz, 1H), 6.35 (dt, *J* = 15.9, 6.5 Hz, 1H), 4.11 (t, *J* = 7.2 Hz, 2H), 3.78 (dd, *J* = 6.5, 1.5 Hz, 2H), 1.93 (h, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 153.0, 150.3, 136.4, 133.0, 128.6, 127.7, 126.3, 123.1, 49.9, 29.7, 23.2, 11.1.
MS (EI, 70 eV): m/z (%) = 227 (41), 226 (30), 212 (57), 199 (14), 198 (39), 184 (54), 170 (17), 157 (13), 145 (20), 144 (11), 136 (15), 130 (13), 129 (12), 128 (15), 125 (34), 117 (17), 116 (10), 115 (72), 110 (46), 97 (56), 96 (21), 91 (16), 84 (100), 83 (22).
HRMS (EI): for $C_{14}H_{17}N_3$: calc. [M+]: 227.1422; found: 227.1415.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3057 (w), 3026 (w), 2964 (m), 2930 (m), 2876 (w), 2853 (w), 1733 (w), 1598 (w), 1510 (m), 1482 (s), 1460 (m), 1448 (s), 1399 (m), 1384 (m), 1347 (w), 1274 (s), 1225 (w), 1184 (m), 1136 (m), 1040 (m), 1030 (m), 966 (vs), 927 (w), 899 (w), 876 (m), 806 (w), 770 (m), 732 (vs), 692 (vs), 676 (m).

3.4 Synthetic Transformations

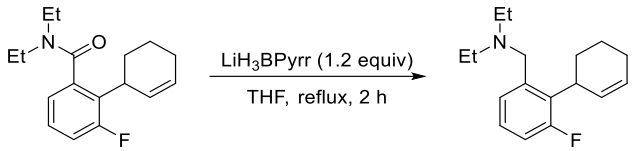
6-Fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (81a)



The title compound was prepared according to a literature procedure.[194] A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with $Cp_2Zr(H)Cl$ (77 mg, 0.30 mmol, 1.5 equiv). A solution of *N*,*N*-diethyl-6-fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxamide (**80b**, 55 mg, 0.20 mmol, 1.0 equiv) in dry THF (1 mL) was added and the reaction mixture was stirred for 15 min at 25 °C. Purification by short path flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a colorless oil (**81a**, 37 mg, 0.18 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 10.57 (s, 1H), 7.72 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.39–7.25 (m, 2H), 5.92–5.77 (m, 2H), 4.35 (h, *J* = 5.2, 3.9 Hz, 1H), 2.25–1.75 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 191.4, 162.4, 160.0, 136.5, 135.3, 130.3, 127.8, 127.7, 127.5, 125.4, 121.0, 120.8, 33.4, 31.8, 24.6, 22.9.
MS (EI, 70 eV): m/z (%) = 204 (14), 203 (13), 187 (11), 186 (81), 185 (69), 183 (13), 176 (24), 175 (100), 171 (33), 170 (14), 165 (51), 163 (37), 162 (40), 160 (17), 159 (19), 149 (35), 148 (12), 147 (44), 146 (42), 135 (20), 134 (13), 133 (64), 121 (14), 115 (16), 109 (16).
HRMS (EI): for $C_{13}H_{13}FO$: calc. [M+]: 204.0950; found: 204.0945.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3069 (vw), 3021 (vw), 2928 (w), 2859 (w), 2836 (w), 2764 (vw), 2732 (vw), 2363 (vw), 1687 (s), 1652 (vw), 1604 (m), 1574 (w), 1457 (m), 1447 (m), 1434 (w), 1396 (w), 1271 (w), 1239 (vs), 1221 (m), 1205 (m), 1192 (w), 1186 (w), 1135 (w), 1078 (vw), 1031 (vw), 987 (w), 950 (w), 929 (w), 899 (w), 876 (w), 847 (w), 791 (s), 776 (m), 760 (m), 744 (m), 735 (s), 720 (m), 679 (m).

_N_-Ethyl-_N_-((6-fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)ethanamine



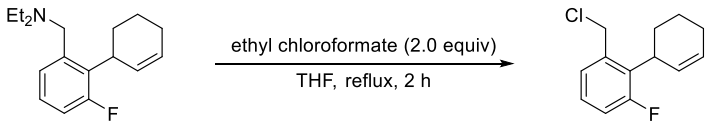
The title compound was prepared according to a literature procedure.[195] A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with *N*,*N*-diethyl-6-fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxamide (**80b**, 138 mg, 0.50 mmol, 1.0 equiv). Lithium pyrrolidinoborohydride (0.60 mL, 0.60 mmol, 1 M in THF, 1.2 equiv) was added dropwise and the reaction mixture was heated to reflux for 2 h. The reaction was quenched by slow addition of 3M HCl (2 mL). The aqueous layer was separated, layered with Et_2O and NaOH was added until the

[194] J. M. White, A. R. Tunoori, G. I. Georg, *J. Am. Chem. Soc.* **2000**, *122*, 11995-11996.
[195] G. B. Fisher, J. C. Fuller, J. Harrison, C. T. Goralski, B. Singaram, *Tetrahedron Lett.* **1993**, *34*, 1091-1094.

reaction mixture was strongly basic to litmus. The organic layer was separated, the aqueous layer extracted with Et_2O (3 x 10 mL) and the combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1 to 4:1) afforded the title compound as a colorless oil (114 mg, 0.44 mmol, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.13–7.04 (m, 2H), 6.94–6.86 (m, 1H), 5.79–5.71 (m, 1H), 5.64 (ddt, *J* = 10.1, 3.0, 1.6 Hz, 1H), 3.97 (dtd, *J* = 9.8, 4.8, 2.4 Hz, 1H), 3.59 (d, *J* = 13.4 Hz, 1H), 3.49 (d, *J* = 13.4 Hz, 1H), 2.47 (p, *J* = 7.1 Hz, 4H), 2.23–1.61 (m, 6H), 1.01 (t, *J* = 7.1 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 140.3, 132.5, 132.4, 130.7, 126.6, 126.5, 125.9, 125.6, 114.9, 114.6, 56.2, 46.5, 35.1, 28.7, 24.7, 23.2, 11.8.
MS (EI, 70 eV): m/z (%) = 189 (14), 188 (29), 187 (16), 173 (30), 161 (11), 160 (98), 159 (100), 153 (10), 147 (49), 146 (48), 135 (11), 133 (36), 123 (18), 109 (11).
HRMS (EI): for $C_{17}H_{24}FN$: calc. [M+]: 261.1893; found: 261.1891.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3019 (w), 2967 (s), 2930 (s), 2856 (m), 2834 (m), 2796 (m), 2722 (w), 1652 (vw), 1612 (w), 1577 (m), 1464 (vs), 1383 (m), 1371 (m), 1291 (m), 1239 (vs), 1220 (m), 1198 (m), 1164 (m), 1133 (m), 1118 (w), 1058 (m), 1003 (m), 928 (w), 899 (w), 876 (m), 847 (w), 804 (s), 790 (s), 764 (vs), 746 (vs), 734 (vs), 718 (s), 655 (w).

2'-(Chloromethyl)-6'-fluoro-1,2,3,4-tetrahydro-1,1'-biphenyl (81b)



A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with *N*-ethyl-*N*-((6-fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)ethanamine (69 mg, 0.26 mmol, 1.0 equiv) in dry THF (1 mL). Ethyl chloroformate (50 µL, 0.52 mmol, 2.0 equiv) was added dropwise and the reaction mixture was heated to reflux for 2 h. Purification by short path flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a colorless oil (**81b**, 56 mg, 0.25 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.22–7.12 (m, 2H), 7.00 (ddd, *J* = 10.9, 7.7, 1.8 Hz, 1H), 5.84 (ddt, *J* = 10.4, 5.3, 2.9 Hz, 1H), 5.69 (dp, *J* = 10.1, 1.6 Hz, 1H), 4.69 (s, 2H), 3.86 (ddh, J = 9.8, 4.8, 2.5 Hz, 1H), 2.27–2.07 (m, 2H), 2.05–1.68 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.1, 160.7, 137.8, 132.3, 132.1, 129.7, 127.7, 127.7, 127.1, 127.1, 126.5, 126.5, 116.7, 116.5, 43.9, 35.3, 29.3, 24.6, 23.0.

MS (EI, 70 eV): m/z (%) = 224 (22), 189 (27), 188 (16), 160 (24), 159 (16), 147 (46), 146 (21), 137 (13), 133 (21), 125 (18), 123 (18), 113 (14), 112 (21), 111 (34), 110 (13), 109 (28), 97 (48), 96 (22), 95 (44), 91 (15), 85 (39), 84 (23), 83 (53), 82 (19), 81 (47), 79 (18), 71 (61), 70 (30), 69 (58), 67 (30), 57 (100), 56 (28), 55 (73), 43 (85), 42 (72), 40 (53).

HRMS (EI): for $C_{13}H_{14}ClF$: calc. [M+]: 224.0768; found: 224.0773.

3.5 X-Ray Crystallography

Single crystals of compound **74b**, suitable for X-ray diffraction, were obtained by slow evaporation of CH_2Cl_2 solution. The crystals were introduced into perfluorinated oil and a suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation (λ = 0.71071 Å).

Data collection and data reduction were performed with the CrysAlisPro software.[196] Absorption correction using the multiscan method was applied. The structures were solved with SHELXS-97,[197] refined with SHELXL-97[198] and finally checked using PLATON.[199] Details for data collection and structure refinement are summarized in Table 5.

CCDC-2061337 contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

[196] Program package 'CrysAlisPro 1.171.40.82a (Rigaku OD, 2020)'.
[197] Sheldrick, G. M. (1997) SHELXS-97: *Program for Crystal Structure Solution*, University of Göttingen, Germany.
[198] Sheldrick, G. M. (1997) SHELXL-97: *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany.
[199] Spek, A. L. (1999) PLATON: *A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands.

Table 3: Details for X-ray data collection and structure refinement for compound **74b**

	74b
Empirical formula	$C_9H_6Cl_2IN_3S$
Formula mass	386.03
T[K]	123(2)
Crystal size [mm]	0.40 × 0.25 × 0.05
Crystal description	colorless platelet
Crystal system	orthorhombic
Space group	*Iba*2
a [Å]	29.5021(13)
b [Å]	9.0794(3)
c [Å]	9.4820(4)
α [°]	90.0
β [°]	90.0
γ [°]	90.0
V [Å^3]	2539.86(18)
Z	8
$\rho_{calcd.}$ [g cm^{-3}]	2.019
μ [mm^{-1}]	3.082
F(000)	1472
Θ range [°]	2.34 – 25.24
Index ranges	$-36 \leq h \leq 36$
	$-11 \leq k \leq 11$
	$-11 \leq l \leq 11$
Reflns. collected	15592
Reflns. obsd.	2254
Reflns. unique	2462 (R_{int} = 0.0560)
R_1, wR_2 (2σ data)	0.0317, 0.0722
R_1, wR_2 (all data)	0.0369, 0.0757
GOOF on F^2	1.059
Peak/hole [e Å^{-3}]	1.370 / -0.491

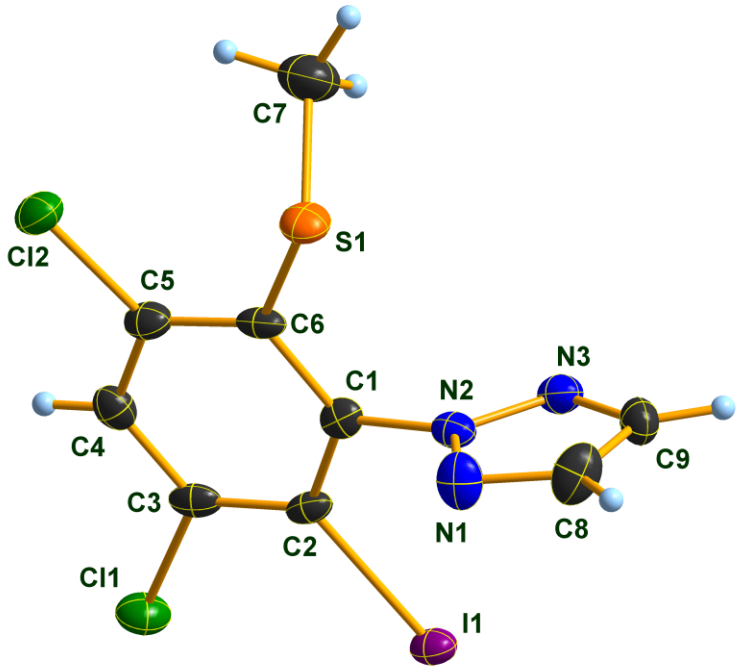


Figure 1: Molecular structure of compound **74b** in the crystal. DIAMOND[200] representation; thermal ellipsoids are drawn at 50 % probability level.

Table 4: Selected bond lengths (Å) of compound **74b**.

I1 – C2	2.095(7)	N3 – C9	1.323(10)
S1 – C6	1.779(9)	C3 – C4	1.381(11)
S1 – C7	1.798(10)	C4 – C5	1.390(11)
Cl1 – C3	1.745(8)	C6 – C5	1.386(12)
N1 – C8	1.311(12)	C8 – C9	1.374(17)
N1 – N2	1.332(9)	N2 – N3	1.330(9)
C1 – C2	1.408(11)	Cl2 – C5	1.733(8)
C1 – C6	1.411(11)	C2 – C3	1.379(11)
C1 – N2	1.412(10)		

Table 5: Selected bond angles (°) of compound **74b**.

C6 – S1 – C7	101.5(4)	C5 – C6 – C1	117.2(7)
C8 – N1 – N2	102.6(8)	C5 – C6 – S1	124.4(6)
C2 – C1 – C6	121.7(7)	C1 – C6 – S1	118.1(6)
C2 – C1 – N2	118.9(7)	C6 – C5 – C4	122.0(8)
C6 – C1 – N2	119.3(7)	C6 – C5 – Cl2	120.8(6)
N3 – N2 – N1	115.3(6)	C4 – C5 – Cl2	117.2(6)
N3 – N2 – C1	123.3(6)	N1 – C8 – C9	110.5(9)

[200] DIAMOND, Crystal Impact GbR., Version 3.2i.

N1 – N2 – C1	121.4(6)	N3 – C9 – C8	108.3(8)
C3 – C2 – C1	118.2(7)	C2 – C3 – C4	121.7(7)
C3 – C2 – I1	122.2(6)	C2 – C3 – Cl1	121.2(6)
C1 – C2 – I1	119.7(6)	C4 – C3 – Cl1	117.1(6)
C9 – N3 – N2	103.3(7)	C3 – C4 – C5	119.3(8)

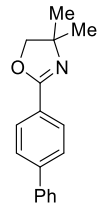
Table 6: Selected torsion angles (°) of compound **74b**.

C8 – N1 – N2 – C1	-179.8(7)	C2 – C1 – C6 – C5	0.1(11)
C2 – C1 – N2 – N3	82.3(9)	N2 – C1 – C6 – C5	-175.0(6)
C6 – C1 – N2 – N3	-102.5(8)	C2 – C1 – C6 – S1	174.4(5)
C2 – C1 – N2 – N1	-96.3(9)	N2 – C1 – C6 – S1	-0.8(9)
C6 – C1 – N2 – N1	78.9(9)	C7 – S1 – C6 – C5	-66.7(7)
C6 – C1 – C2 – C3	-0.4(10)	C7 – S1 – C6 – C1	119.5(7)
N2 – C1 – C2 – C3	174.7(6)	C1 – C6 – C5 – C4	-0.5(11)
C6 – C1 – C2 – I1	180.0(5)	S1 – C6 – C5 – C4	-174.3(6)
N2 – C1 – C2 – I1	-4.9(9)	C1 – C6 – C5 – Cl2	175.9(6)
N1 – N2 – N3 – C9	-1.4(9)	S1 – C6 – C5 – Cl2	2.1(10)
C1 – N2 – N3 – C9	179.9(7)	C3 – C4 – C5 – C6	1.2(11)
C1 – C2 – C3 – C4	1.1(11)	C3 – C4 – C5 – Cl2	-175.4(6)
I1 – C2 – C3 – C4	-179.3(5)	N2 – N1 – C8 – C9	-1.(1)
C1 – C2 – C3 – Cl1	-175.1(5)	N2 – N3 – C9 – C8	0.7(9)
I1 – C2 – C3 – Cl1	4.5(9)	N1 – C8 – C9 – N3	0.2(11)
C2 – C3 – C4 – C5	-1.5(11)		

4. Preparation of Polyfunctionalized Aromatic Nitriles from Aryl Oxazolines

4.1 Preparation of Starting Materials

2-([1,1'-Biphenyl]-4-yl)-4,4-dimethyl-4,5-dihydrooxazole (82b)



The compound was prepared according to a modified literature procedure.[201] 3-methoxybenzoyl chloride (10.83 g, 50 mmol, 1.0 equiv) and Et_3N (14 mL, 100 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (100 mL) and 2-amino-2-methyl-1-propanol (5.75 mL, 60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude amide intermediate was dissolved in dry CH_2Cl_2 (80 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (4.65 mL, 60 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (2 g, 50 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) afforded the title compound as a white solid (**82b**, 6.41 g, 25.5 mmol, 51% yield).

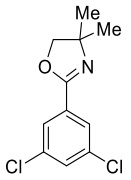
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.05–7.98 (m, 2H), 7.67–7.60 (m, 4H), 7.49–7.42 (m, 2H), 7.41–7.34 (m, 1H), 4.13 (s, 2H), 1.40 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1, 144.0, 140.4, 129.0, 128.8, 128.0, 127.3, 127.1, 127.0, 79.3, 67.8, 28.6.

Analytical data was consistent with literature.[202]

[201] D. A. Gutierrez, W.-C. C. Lee, Y. Shen, J. J. Li, *Tetrahedron Lett.* **2016**, *57*, 5372-5376.
[202] D. Göbel, N. Clamor, E. Lork, B. J. Nachtsheim, *Org. Lett.* **2019**, *21*, 5373-5377.

2-(3,5-Dichlorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (82c)



The compound was prepared according to a modified literature procedure.[203] 3,5-dichlorobenzoyl chloride (10.47 g, 50 mmol, 1.0 equiv) and Et_3N (14 mL, 100 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (100 mL) and 2-amino-2-methyl-1-propanol (5.75 mL, 60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude amide intermediate was dissolved in dry CH_2Cl_2 (80 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (4.65 mL, 60 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (2 g, 50 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) afforded the title compound as a colorless oil (**82c**, 5.96 g, 24.4 mmol, 49% yield).

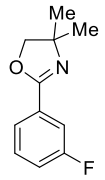
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.82 (d, *J* = 2.0 Hz, 2H), 7.43 (t, *J* = 2.0 Hz, 1H), 4.11 (s, 2H), 1.36 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.4, 135.5, 131.4, 131.3, 127.1, 79.9, 68.4, 28.8.

Analytical data was consistent with literature.[204]

[203] D. A. Gutierrez, W.-C. C. Lee, Y. Shen, J. J. Li, *Tetrahedron Lett.* **2016**, *57*, 5372-5376.
[204] R. A. Y. Jones, A. R. Katritzky, P. G. Lehman, B. B. Saphiro, *J. Chem. Soc. B* **1971**, 1308-1315.

2-(3-Fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (82d)

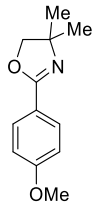


The compound was prepared according to a modified literature procedure. 3-fluorobenzoyl chloride (6.08 mL, 50 mmol, 1.0 equiv) and Et_3N (14 mL, 100 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (100 mL) and 2-amino-2-methyl-1-propanol (5.75 mL, 60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude amide intermediate was dissolved in dry CH_2Cl_2 (80 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (4.65 mL, 60 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (2 g, 50 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) afforded the title compound as a colorless oil (**82d**, 6.46 g, 33.4 mmol, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.75–7.67 (m, 1H), 7.62 (ddt, *J* = 10.2, 5.7, 2.7 Hz, 1H), 7.35 (dtt, *J* = 8.3, 5.7, 3.1 Hz, 1H), 7.13 (tdt, *J* = 8.5, 5.3, 2.7 Hz, 1H), 4.14 (s, 2H), 1.36 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.8, 161.4, 161.2, 161.1, 130.3, 130.3, 130.0, 130.0, 124.0, 124.0, 118.3, 118.1, 115.5, 115.2, 79.4, 67.9, 28.5.
Analytical data was consistent with literature.[205]

[205] D. T. Witiak, S. Goswami, G. E. Milo, *J. Org. Chem.* **1988**, *53*, 345-352.

2-(4-Methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (82e)

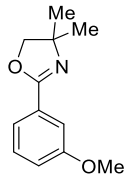


The compound was prepared according to a modified literature procedure. 4-methoxybenzoyl chloride (4.27 g, 25 mmol, 1.0 equiv) and Et_3N (7 mL, 50 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (60 mL) and 2-amino-2-methyl-1-propanol (2.88 mL, 30 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added, and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed in vacuo. The crude amide intermediate was dissolved in dry CH_2Cl_2 (50 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (2.32 mL, 30 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed in vacuo. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (1 g, 25 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 94:6) afforded the title compound as a colorless oil (**82e**, 2.87 g, 14 mmol, 56% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.92–7.87 (m, 2H), 6.93–6.88 (m, 2H), 4.09 (s, 2H), 3.84 (s, 3H), 1.38 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.0, 130.0, 120.2, 113.66, 79.1, 67.3, 55.3, 28.4.
Analytical data was consistent with literature.[206]

[206] J. C. Clinet, E. Dunach, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1983**, *105*, 6710-6712.

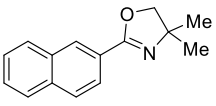
2-(3-Methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (82f)



The compound was prepared according to a modified literature procedure.[203] 3-methoxybenzoyl chloride (6.82 mL, 50 mmol, 1.0 equiv) and Et_3N (14 mL, 100 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (100 mL) and 2-amino-2-methyl-1-propanol (5.75 mL, 60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude amide intermediate was dissolved in dry CH_2Cl_2 (80 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (4.65 mL, 60 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (2 g, 50 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 94:6) afforded the title compound as a colorless oil (**82f**, 4.82 g, 23.5 mmol, 47% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.52 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.46 (dd, *J* = 2.7, 1.5 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.01 (ddd, *J* = 8.3, 2.7, 1.0 Hz, 1H), 4.10 (s, 2H), 3.84 (s, 3H), 1.38 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1, 159.6, 129.5, 120.8, 118.1, 112.6, 79.2, 67.7, 55.6, 28.5.
Analytical data was consistent with literature.[207]

4,4-Dimethyl-2-(naphthalen-2-yl)-4,5-dihydrooxazole (82g)

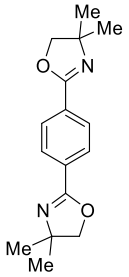


[207] A. I. Meyers, W. B. Avila, *J. Org. Chem.* **1981**, *46*, 3881-3886.

The compound was prepared according to a modified literature procedure.[4] 2-naphthoyl chloride (9.532 g, 50 mmol, 1.0 equiv) and Et_3N (14 mL, 100 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (100 mL) and 2-amino-2-methyl-1-propanol (5.75 mL, 60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude amide intermediate was dissolved in dry CH_2Cl_2 (80 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (4.65 mL, 60 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (2 g, 50 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a white solid (**82g**, 7.998 g, 35.5 mmol, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.47–8.42 (m, 1H), 8.02 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.94–7.82 (m, 3H), 7.58–7.48 (m, 2H), 4.17 (s, 2H), 1.43 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.3, 134.8, 132.8, 129.0, 128.8, 128.2, 127.9, 127.6, 126.6, 125.5, 125.0, 79.3, 67.8, 28.6.
Analytical data was consistent with literature.[208]

1,4-Bis(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzene (82h)



The compound was prepared according to a modified literature procedure.[209] Terephthaldehyde (3.04 g, 22.6 mmol, 1.0 equiv) and 2-amino-2-methylpropan-1-ol (4.17 g, 46.8 mmol, 2.05 equiv) were

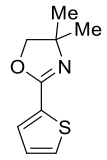
[208] D. Göbel, N. Clamor, E. Lork, B. J. Nachtsheim, *Org. Lett.* **2019**, *21*, 5373-5377.
[209] B. T. Hahn, K. Schwekendiek, F. Glorius, B. Gschwend, A. Pfaltz, *Org. Synth.* **2008**, *85*, 267-277.

dissolved in dry CH_2Cl_2 (80 mL), to which molecular sieves 4 A (2 g) were added. The mixture was stirred for 23 h at room temperature. The flask was cooled to 0 °C and NBS (9.08 g, 45.4 mmol, 2.0 equiv) was added in portions. The mixture was stirred for 10 min at 0 °C, the cooling bath was removed, and stirring was continued for 3 h at 25 °C. The mixture was filtered and the solid residue was washed with EtOAc (150 mL) and sat. $NaHCO_3$ (100 mL) solution. The phases were separated and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**82h**, 4.9 g, 18.0 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.96 (s, 4H), 4.12 (s, 4H), 1.39 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.7, 130.6, 128.3, 79.4, 67.9, 28.6.
Analytical data was consistent with literature.[210]

4,4-Dimethyl-2-(thiophen-2-yl)-4,5-dihydrooxazole (82i)



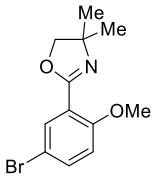
The compound was prepared according to a modified literature procedure.[203] 2-thiophenecarbonyl chloride (5.35 mL, 50 mmol, 1.0 equiv) and Et_3N (14 mL, 100 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (100 mL) and 2-amino-2-methyl-1-propanol (5.75 mL, 60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dilute HCl (30 mL) was added and the organic phase was washed with brine (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude amide intermediate was dissolved in dry CH_2Cl_2 (80 mL) and Et_3N (8.3 mL, 60 mmol, 1.2 equiv) was added at 0 °C. The reaction was stirred for 0.5 h at 0 °C followed by dropwise addition of mesyl chloride (4.65 mL, 60 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was washed with dilute HCl (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude mesylate intermediate was diluted in ethanol (30 mL) and NaOH (2 g, 50 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 0.5 h and subsequently diluted with ethyl acetate. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, filtered and the solvent was

[210] A. R. Katritzky, C. Cai, K. Suzuki, S. K. Singh, *J. Org. Chem.* **2004**, *69*, 811-814.

removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a colorless oil (**82i**, 2.87 g, 15.8 mmol, 32% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.44 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.07 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.10 (s, 2H), 1.38 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.9, 130.8, 130.3, 129.7, 127.7, 79.6, 68.1, 28.5.
Analytical data was consistent with literature.[211]

2-(5-Bromo-2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (88b)



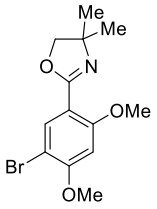
The compound was prepared according to a modified literature procedure.[209] 5-bromo-2-methoxybenzaldehyde (10.00 g, 47.0 mmol, 1.0 equiv) and 2-amino-2-methylpropan-1-ol (5.0 mL, 51.7 mmol, 1.10 equiv) were dissolved in dry CH_2Cl_2 (100 mL), to which molecular sieves 4 A (5 g) were added. The mixture was stirred for 23 h at room temperature. The flask was cooled to 0 °C and K_2CO_3 (17.54 g, 127 mmol, 2.7 equiv) followed by NBS (15.06 g, 84.6 mmol, 1.8 equiv) was added in portions. The mixture was stirred for 10 min at 0 °C, the cooling bath was removed, and stirring was continued for 12 h at 25 °C. The mixture was filtered and the solid residue was washed with EtOAc (150 mL) and sat. $NaHCO_3$ (100 mL) solution. The phases were separated and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a yellow oil (**xxb**, 11.17 g, 39.9 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.86 (d, *J* = 2.6 Hz, 1H), 7.48 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.83 (d, *J* = 8.9 Hz, 1H), 4.09 (s, 2H), 3.87 (s, 3H), 1.39 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.2, 157.6, 134.9, 134.0, 119.4, 113.6, 112.5, 79.2, 67.7, 56.5, 28.4.
MS (EI, 70 eV): m/z (%) = 241 (27), 212 (96), 210 (100), 209 (25), 186 (20), 161 (20), 118 (64)
HRMS (EI): for $C_{12}H_{14}BrNO_2$: calc. [M^+]: 283.0208; found: 283.0202.

[211] H. C. Aspinall, O. Beckingham, M. D. Farrar, N. Greeves, C. D. Thomas, *Tetrahedron Lett.* **2011**, *52*, 5120-5123.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2964 (m), 1641 (m), 1593 (m), 1486 (s), 1461 (s), 1439 (m), 1407 (m), 1348 (m), 1302 (m), 1268 (vs), 1252 (s), 1207 (s), 1180 (s), 1142 (m), 1067 (m), 1039 (s), 1022 (s), 989 (m), 965 (s), 878 (m), 807 (s), 679 (m).

2-(5-Bromo-2,4-dimethoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (88c)



The compound was prepared according to a modified literature procedure.[209] 5-bromo-2,4-dimethoxybenzaldehyde (4.00 g, 16.0 mmol, 1.0 equiv) and 2-amino-2-methylpropan-1-ol (1.69 mL, 17.6 mmol, 1.10 equiv) were dissolved in dry CH_2Cl_2 (50 mL), to which molecular sieves 4 A (2 g) were added. The mixture was stirred for 23 h at room temperature. The flask was cooled to 0 °C and K_2CO_3 (5.97 g, 43.2 mmol, 2.7 equiv) followed by NBS (5.13 g, 28.8 mmol, 1.8 equiv) was added in portions. The mixture was stirred for 10 min at 0 °C, the cooling bath was removed, and stirring was continued for 12 h at 25 °C. The mixture was filtered and the solid residue was washed with EtOAc (150 mL) and sat. $NaHCO_3$ (100 mL) solution. The phases were separated and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:2) afforded the title compound as a white solid (**xxc**, 2.95 g, 9.4 mmol, 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.96 (s, 1H), 6.47 (s, 1H), 4.06 (s, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 1.37 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.0, 159.4, 158.8, 135.5, 111.4, 102.0, 96.8, 78.9, 67.5, 56.7, 56.4, 28.5.

MS (EI, 70 eV): m/z (%) = 300 (28), 298 (30), 272 (39), 270 (41), 242 (63), 240 (66), 230 (49), 214 (72), 212 (77), 191 (100), 148 (90).

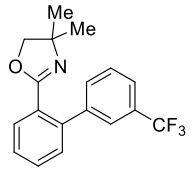
HRMS (EI): for $C_{13}H_{16}BrNO_3$: calc. [M^+]: 313.0314; found: 313.0304.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2959 (w), 2925 (w), 1645 (m), 1624 (s), 1602 (s), 1563 (w), 1502 (m), 1458 (s), 1433 (m), 1407 (s), 1375 (m), 1347 (s), 1323 (m), 1285 (s), 1269 (s), 1249 (m), 1212 (vs), 1208 (vs), 1175 (s), 1060 (m), 1032 (s), 1024 (vs), 992 (m), 977 (m), 952 (m), 921 (m), 908 (m), 873 (w), 818 (w), 807 (vs), 740 (w), 688 (s).

Melting point: M.p. = 62 °C.

4.2 Preparation of Functionalized 2-Aryl Oxazolines

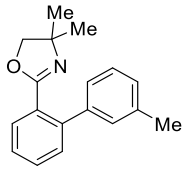
4,4-Dimethyl-2-(3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (83a)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**82a**, 0.85 mL, 5.0 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.0 mmol, 0.6 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (110 mg, 5 mol%) and 1-iodo-3-(trifluoromethyl)benzene (0.60 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a brown oil (**83a**, 1.172 g, 3.67 mmol, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.78 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.65 (tt, *J* = 1.7, 0.9 Hz, 1H), 7.60 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.55–7.48 (m, 2H), 7.45–7.36 (m, 2H), 3.80 (s, 2H), 1.28 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.2, 142.0, 140.2, 131.8, 131.8, 130.8, 130.8, 130.5, 130.2, 130.2, 129.9, 128.7, 128.4, 128.1, 127.9, 125.7, 125.6, 125.5, 125.5, 125.5, 124.1, 124.0, 124.0, 124.0, 122.9, 120.2, 79.6, 67.8, 28.1.
MS (EI, 70 eV): m/z (%) = 319 (19), 318 (100), 264 (10), 233 (59), 228 (31), 220 (12), 208 (19), 201 (14).
HRMS (EI): for $C_{18}H_{16}F_3NO$: calc. [M-H$^+$]: 318.1106; found: 318.1100.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3070 (vw), 2969 (w), 2929 (w), 2892 (vw), 1681 (vw), 1677 (w), 1654 (m), 1651 (m), 1634 (w), 1600 (w), 1593 (w), 1480 (w), 1475 (w), 1462 (w), 1449 (w), 1447 (w), 1438 (w), 1427 (m), 1365 (w), 1350 (w), 1332 (vs), 1311 (m), 1281 (m), 1257 (w), 1244 (m), 1212 (w), 1177 (m), 1162 (s), 1120 (vs), 1095 (m), 1072 (s), 1037 (s), 1024 (m), 1001 (w), 987 (w), 964 (m), 919 (m), 870 (w), 824 (w), 804 (m), 769 (m), 757 (s), 737 (w), 700 (s), 675 (m), 659 (w), 654 (m).

4,4-Dimethyl-2-(3'-methyl-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (83b)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**82a**, 0.85 mL, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (183 mg, 5 mol%) and 3-iodotoluene (0.53 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**83b**, 1.03 g, 3.88 mmol, 93% yield).

The compound was obtained in a 20 mmol scale in 99% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.71 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.48 (td, *J* = 7.5, 1.4 Hz, 1H), 7.37 (ddd, *J* = 14.6, 7.5, 1.4 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.25–7.19 (m, 2H), 7.18–7.12 (m, 1H), 3.83 (s, 2H), 2.38 (s, 3H), 1.31 (s, 6H).

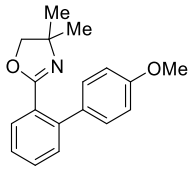
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 141.7, 141.0, 137.5, 130.4, 130.1, 129.1, 128.0, 127.0, 125.5, 79.6, 67.5, 28.0, 21.5.

MS (EI, 70 eV): m/z (%) = 265 (19), 264 (100), 210 (13), 209 (18), 192 (14), 179 (28), 178 (14), 165 (22), 152 (10).

HRMS (EI): for $C_{18}H_{19}NO$: calc. [M^+]: 265.1467; found: 265.1461.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2964 (m), 2944 (w), 2942 (w), 2939 (w), 2925 (m), 2922 (m), 2915 (w), 2912 (w), 2889 (w), 2886 (w), 1676 (w), 1656 (s), 1652 (s), 1606 (w), 1604 (w), 1600 (w), 1479 (w), 1473 (m), 1471 (m), 1462 (m), 1456 (m), 1446 (m), 1363 (m), 1349 (m), 1311 (m), 1212 (w), 1190 (w), 1188 (w), 1113 (w), 1076 (m), 1067 (w), 1065 (w), 1043 (s), 1041 (m), 1034 (s), 988 (w), 964 (m), 920 (w), 918 (w), 790 (m), 769 (m), 755 (vs), 699 (s).

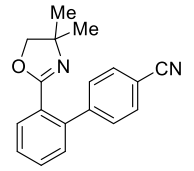
2-(4'-Methoxy-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83c)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**82a**, 85 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (15 mg, 5 mol%) and 4-bromoanisole (53 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**83c**, 89 mg, 0.32 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.70 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39–7.31 (m, 4H), 6.95–6.90 (m, 2H), 3.85 (s, 3H), 3.83 (s, 2H), 1.31 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.1, 158.9, 141.2, 133.6, 130.4, 130.2, 130.0, 129.4, 127.8, 126.7, 113.4, 79.5, 67.4, 55.3, 40.8, 28.0, 23.8.
MS (EI, 70 eV): m/z (%) = 281 (19), 280 (100), 225 (29), 195 (11).
HRMS (EI): for $C_{18}H_{19}NO_2$: calc. [M-H$^+$]: 280.1338; found: 280.1332.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3138 (vw), 3064 (vw), 2964 (m), 2892 (w), 2837 (w), 1652 (m), 1611 (m), 1580 (w), 1565 (vw), 1517 (s), 1483 (m), 1462 (m), 1446 (m), 1413 (vw), 1383 (w), 1363 (w), 1351 (m), 1295 (m), 1243 (vs), 1212 (m), 1177 (s), 1107 (w), 1075 (m), 1036 (vs), 1017 (m), 1001 (m), 988 (w), 963 (m), 920 (w), 869 (w), 832 (s), 804 (m), 761 (vs), 727 (m), 704 (m), 662 (w).

2'-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-[1,1'-biphenyl]-4-carbonitrile (83d)

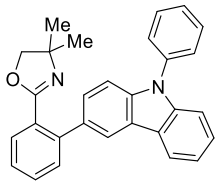


According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**82a,** 85 µL, 0.50 mmol, 1.0 equiv),) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 1 h, the

resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (15 mg, 5 mol%) and 4-iodobenzonitrile (95 mg, 0.415 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 3:1) afforded the title compound as a brown solid (**83d**, 97 mg, 0.35 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.82–7.77 (m, 1H), 7.70–7.65 (m, 2H), 7.53 (m, 1H), 7.50–7.47 (m, 2H), 7.44 (td, J = 7.6, 1.4 Hz, 1H), 7.36–7.31 (m, 1H), 3.81 (s, 2H), 1.27 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.9, 146.2, 140.0, 131.9, 130.9, 130.5, 130.1, 129.4, 128.4, 128.0, 119.1, 111.1, 79.6, 67.9, 28.2.
MS (EI, 70 eV): m/z (%) = 276 (19), 275 (100), 221 (13), 205 (19), 204 (55), 203 (20), 190 (47), 177 (22).
HRMS (EI): for $C_{18}H_{16}N_2O$: calc. [M^+]: 275.1184; found: 275.1178.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3065 (vw), 2964 (m), 2926 (w), 2888 (w), 2868 (w), 2226 (m), 1655 (s), 1651 (s), 1634 (m), 1608 (m), 1485 (m), 1475 (w), 1462 (m), 1447 (m), 1400 (w), 1364 (m), 1350 (m), 1309 (m), 1282 (w), 1247 (w), 1212 (w), 1180 (m), 1075 (m), 1060 (m), 1036 (vs), 1006 (m), 987 (w), 962 (m), 920 (w), 840 (s), 769 (s), 760 (vs), 731 (m), 699 (m).
Melting point: M.p. = 154 °C.

4,4-Dimethyl-2-(2-(9-phenyl-9*H*-carbazol-3-yl)phenyl)-4,5-dihydrooxazole (83e)

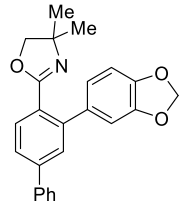


According to **TP 4**, to a mixture of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**82a**, 0.53 mL, 3.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 1.80 mmol, 0.6 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (3.6 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (66 mg, 3 mol%) and 3-iodo-9-phenyl-9*H*-carbazole (0.919 g, 2.49 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**83e**, 0.906 g, 2.17 mmol, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.21 (d, *J* = 1.7 Hz, 1H), 8.11 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.62 (h, *J* = 6.2 Hz, 4H), 7.55–7.35 (m, 8H), 7.33–7.27 (m, 1H), 3.76 (s, 2H), 1.31 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.5, 142.3, 141.4, 140.3, 137.8, 133.2, 130.7, 130.6, 130.5, 130.1, 128.3, 127.6, 127.2, 126.7, 126.7, 126.2, 123.6, 123.4, 120.4, 120.2, 110.0, 109.5, 79.7, 67.6, 28.3.
MS (EI, 70 eV): m/z (%) = 417 (29), 416 (100), 417 (22), 339 (18), 249 (24).
HRMS (EI): for $C_{18}H_{19}NO$: calc. [M^+]: 416.1889; found: 416.1885.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3120 (vw), 3034 (vw), 2960 (m), 2896 (w), 2833 (w), 1650 (m), 1628 (m), 1580 (w), 1565 (vw), 1517 (s), 1483 (m), 1465 (m), 1444 (m), 1412 (vw), 1383 (w), 1364 (w), 1351 (m), 1295 (m), 1243 (vs), 1212 (m), 1174 (s), 1110 (w), 1076 (m), 1032 (vs), 1017 (m), 1001 (m), 988 (w), 963 (m), 920 (w), 869 (w), 832 (s), 804 (m), 761 (vs), 727 (m), 704 (m), 662 (w).

2-(3-(Benzo[d][1,3]dioxol-5-yl)-[1,1'-biphenyl]-4-yl)-4,4-dimethyl-4,5-dihydrooxazole (83f)



According to **TP 4**, to a mixture of 2-([1,1'-biphenyl]-4-yl)-4,4-dimethyl-4,5-dihydrooxazole (**82b**, 1.257 g, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 40 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (183 mg, 5 mol%) and 5-bromobenzo[d][1,3]dioxole (0.50 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 5:1) afforded the title compound as a brown solid (**83f**, 1.170 g, 3.15 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.81–7.75 (m, 1H), 7.69–7.61 (m, 2H), 7.61–7.56 (m, 2H), 7.50–7.43 (m, 2H), 7.42–7.35 (m, 1H), 6.96–6.90 (m, 2H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.00 (s, 2H), 3.88 (s, 2H), 1.33 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.8, 147.6, 147.1, 143.4, 141.8, 140.3, 135.3, 130.9, 129.0, 128.0, 127.4, 126.9, 125.7, 122.1, 109.2, 108.2, 101.3, 79.7, 67.7, 28.2.

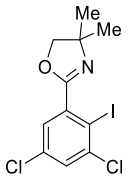
MS (EI, 70 eV): m/z (%) = 371 (26), 370 (100), 315 (31), 299 (34), 298 (18), 285 (13), 240 (11).

HRMS (EI): for $C_{24}H_{21}NO_3$: calc. [M-H$^+$]: 370.1443; found: 370.1439.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2966 (w), 2948 (w), 2940 (w), 2923 (w), 2912 (w), 2888 (w), 2878 (w), 1657 (m), 1600 (w), 1500 (m), 1478 (m), 1460 (m), 1450 (w), 1434 (m), 1401 (m), 1382 (w), 1364 (w), 1356 (m), 1336 (w), 1305 (m), 1256 (m), 1242 (s), 1213 (s), 1184 (m), 1156 (w), 1132 (w), 1108 (m), 1069 (s), 1038 (s), 1012 (m), 983 (w), 966 (m), 957 (m), 934 (m), 924 (m), 905 (m), 895 (m), 870 (m), 835 (s), 828 (s), 818 (m), 812 (m), 792 (m), 758 (vs), 738 (m), 732 (m), 723 (m), 712 (m), 694 (s), 672 (w), 653 (m).

Melting point: M.p. = 117 °C.

2-(3,5-Dichloro-2-iodophenyl)-4,4-dimethyl-4,5-dihydrooxazole (83g)



According to **TP 4**, to a mixture of 2-(3,5-dichlorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82c**, 0.977 g, 4.00 mmol, 1.0 equiv) in toluene (8 mL) was added *s*Bu_2Mg (**58**, 2.40 mmol, 0.6 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and iodine (2.03 g, 8.0 mmol, 2.0 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a yellow solid (**83g**, 1.427 g, 3.86 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.52 (d, *J* = 2.4 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 4.16 (s, 2H), 1.42 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1, 141.1, 138.7, 135.0, 130.4, 128.6, 97.6, 80.0, 68.6, 28.3.

MS (EI, 70 eV): m/z (%) = 368 (31), 355 (60), 353 (100), 338 (23), 327 (22), 325 (37), 299 (30), 298 (44), 297 (51), 197 (42), 172 (59), 170 (95), 133 (47).

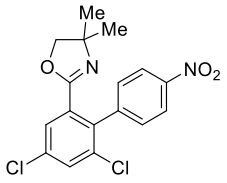
HRMS (EI): for $C_{11}H_{10}Cl_2INO$: calc. [M+]: 368.9184; found: 368.9178.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2970 (w), 2957 (w), 2929 (w), 2927 (w), 2925 (w), 2922 (vw), 2917 (vw), 2895 (w), 1660 (s), 1635 (vw), 1626 (vw), 1568 (w), 1564 (w), 1544 (w), 1460 (w), 1456 (w), 1412 (w), 1406 (w), 1385 (w), 1381 (m), 1366 (m), 1348 (m), 1296 (s), 1245 (w), 1216 (w), 1190

(m), 1178 (m), 1173 (m), 1158 (w), 1135 (w), 1104 (s), 1087 (m), 1020 (w), 960 (m), 950 (s), 936 (m), 889 (m), 874 (w), 860 (vs), 843 (w), 840 (w), 833 (vw), 820 (s), 793 (w), 791 (w), 786 (vw), 750 (m), 740 (vw), 738 (vw), 734 (vw), 726 (m), 705 (vw).

Melting point: M.p. = 108 °C.

2-(4,6-Dichloro-4'-nitro-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83h)



According to **TP 4**, to a mixture of 2-(3,5-dichlorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82c**, 122 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 4-iodonitrobenzene (107 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 96:4) afforded the title compound as a yellow solid (**83h**, 134 mg, 0.37 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.30–8.24 (m, 2H), 7.74 (d, *J* = 2.1 Hz, 1H), 7.61 (d, *J* = 2.2 Hz, 1H), 7.47–7.40 (m, 2H), 3.71 (s, 2H), 1.15 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.6, 147.6, 144.0, 136.6, 135.0, 134.6, 131.6, 130.7, 128.8, 123.2, 79.8, 68.1, 28.0.

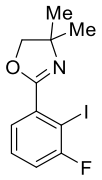
MS (EI, 70 eV): m/z (%) = 363 (41), 293 (10), 291 (16), 279 (15), 277 (24), 246 (14), 235 (14), 233 (22), 213 (32), 212 (14), 211 (100), 175 (13).

HRMS (EI): for $C_{17}H_{14}Cl_2N_2O_3$: calc. [M-H$^+$]: 363.0303; found: 363.0297.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2980 (w), 2942 (w), 2931 (w), 2925 (w), 2920 (w), 2921 (vw), 2917 (vw), 2873 (w), 1664 (s), 1632 (vw), 1629 (vw), 1567 (w), 1552 (w), 1543 (w), 1462 (w), 1454 (w), 1418 (w), 1402 (w), 1395 (w), 1371 (m), 1366 (m), 1344 (m), 1292 (s), 1239 (w), 1208 (w), 1190 (m), 1175 (m), 1173 (w), 1155 (w), 1133 (w), 1101 (s), 1082 (m), 1019 (w), 965 (m), 952 (s), 931 (m), 884 (m), 873 (w), 861 (vs), 842 (w), 840 (w), 836 (vw), 820 (s), 788 (vw), 752 (m),

Melting point: M.p. = 101 °C.

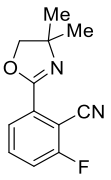
2-(3-Fluoro-2-iodophenyl)-4,4-dimethyl-4,5-dihydrooxazole (83i)



According to **TP 4**, to a mixture of 2-(3-fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82d**, 0.386 g, 2.00 mmol, 1.0 equiv) in toluene (4 mL) was added *s*Bu_2Mg (**58**, 1.20 mmol, 0.6 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and iodine (1.03 g, 4.0 mmol, 2.0 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a yellow solid (**83i**, 0.450 g, 1.41 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.39–7.29 (m, 2H), 7.11 (tdd, *J* = 7.9, 2.0, 0.7 Hz, 1H), 4.16 (d, *J* = 0.7 Hz, 2H), 1.43 (d, *J* = 0.6 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1 (d, *J* = 2.6 Hz), 162.0 (d, *J* = 244.6 Hz), 136.6 (d, *J* = 1.8 Hz), 129.9 (d, *J* = 8.2 Hz), 126.3 (d, *J* = 3.2 Hz), 117.1 (d, *J* = 25.0 Hz), 83.5 (d, *J* = 27.0 Hz), 79.7, 68.5, 28.4.
MS (EI, 70 eV): m/z (%) = 318 (33), 304 (10), 303 (100), 288 (16), 275 (26), 247 (33), 246 (52), 162 (12), 121 (10).
HRMS (EI): for $C_{11}H_{11}FINO$: calc. [M+]: 318.9869; found: 318.9862.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2984 (vw), 2973 (w), 2941 (vw), 2932 (vw), 2888 (vw), 2875 (vw), 2869 (vw), 2858 (vw), 1686 (vw), 1666 (m), 1637 (vw), 1593 (w), 1562 (w), 1472 (w), 1461 (m), 1438 (vw), 1436 (vw), 1424 (m), 1381 (vw), 1363 (w), 1350 (m), 1331 (vw), 1315 (m), 1276 (w), 1241 (s), 1220 (vw), 1187 (w), 1169 (w), 1115 (m), 1078 (m), 1028 (vw), 1018 (vw), 1007 (vw), 969 (s), 954 (w), 941 (m), 907 (m), 898 (m), 834 (m), 818 (w), 791 (vs), 762 (vw), 754 (vw), 724 (m), 707 (w), 693 (w).
Melting point: M.p. = 99 °C.

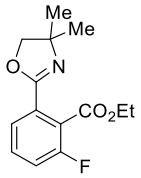
2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-6-fluorobenzonitrile (83j)



According to **TP 4**, to a mixture of 2-(3-fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82d**, 96 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.3 mmol, 0.6 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and tosyl cyanide (108 mg, 0.60 mmol, 1.2 equiv) dissolved in toluene (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a yellow solid (**83j**, 104 mg, 0.48 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.85 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.61 (ddd, *J* = 8.4, 7.9, 5.5 Hz, 1H), 7.32 (td, *J* = 8.5, 1.1 Hz, 1H), 4.20 (s, 2H), 1.41 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.3 (d, *J* = 259.3 Hz), 159.3 (d, *J* = 252.7 Hz), 159.0 (d, *J* = 3.0 Hz), 134.2 (d, *J* = 9.0 Hz), 132.5, 126.0 (d, *J* = 3.4 Hz), 118.5 (d, *J* = 20.4 Hz), 112.3, 101.2 (d, *J* = 17.0 Hz), 80.0, 68.6, 28.4.
MS (EI, 70 eV): m/z (%) = 217 (11), 204 (12), 203 (100), 188 (22), 147 (93).
HRMS (EI): for $C_{12}H_{11}FN_2O$: calc. [M+]: 218.0855; found: 218.0851.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3012 (vw), 2982 (w), 2951 (vw), 2911 (vw), 2881 (vw), 2872 (vw), 2783 (vw), 1680 (vw), 1655 (m), 1634 (vw), 1594 (w), 1536 (w), 1470 (w), 1447 (m), 1439 (vw), 1420 (m), 1371 (vw), 1360 (w), 1355 (m), 1333 (vw), 1314 (m), 1276 (w), 1238 (s), 1224 (vw), 1180 (w), 1160 (w), 1112 (m), 1083 (m), 1035 (vw), 1033 (vw), 1000 (vw), 968 (s), 954 (w), 941 (m), 909 (m), 868 (m), 833 (m), 814 (w), 785 (vs), 766 (vw), 755 (vw), 730 (m), 710 (w), 684 (w).
Melting point: M.p. = 85 °C.

Ethyl 2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-6-fluorobenzoate (83k)



According to **TP 4**, to a mixture of 2-(3-fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82d**, 270 mg, 1.40 mmol, 1.0 equiv) in toluene (2.8 mL) was added *s*Bu_2Mg (**58**, 0.84 mmol, 0.6 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and ethylcyano formate (0.20 mL, 1.68 mmol, 1.2 equiv) was added dropwise and the reaction mixture was stirred for 2 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a yellow oil (**83k**, 361 mg, 1.36 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.41 (ddd, *J* = 8.3, 7.8, 5.5 Hz, 1H), 7.21 (ddd, *J* = 9.3, 8.4, 1.1 Hz, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 4.07 (s, 2H), 1.41–1.33 (m, 9H).

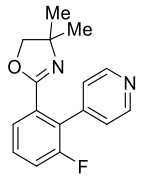
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 165.1, 160.0 (d, *J* = 3.1 Hz), 130.9 (d, *J* = 8.5 Hz), 127.9 (d, *J* = 4.0 Hz), 125.1 (d, *J* = 3.3 Hz), 122.9 (d, *J* = 19.5 Hz), 118.5 (d, *J* = 21.6 Hz), 79.7, 68.3, 62.1, 28.3, 14.2.

MS (EI, 70 eV): m/z (%) = 250 (24), 206 (33), 205 (12), 204 (100), 178 (10), 166 (28), 148 (49).

HRMS (EI): for $C_{14}H_{16}FNO_3$: calc. [M-H$^+$]:264.1036; found: 264.1029.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2897 (w), 1736 (s), 1653 (m), 1608 (m), 1579 (m), 1471 (w), 1458 (s), 1385 (w), 1365 (m), 1353 (m), 1313 (s), 1266 (vs), 1247 (s), 1191 (m), 1174 (m), 1124 (m), 1105 (s), 1095 (m), 1060 (s), 1017 (m), 976 (s), 936 (m), 906 (m), 874 (w), 856 (w), 834 (w), 804 (s), 736 (s), 707 (m).

2-(3-Fluoro-2-(pyridin-4-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (83l)



According to **TP 4**, to a mixture of 2-(3-fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82d**, 96 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 4-iodopyridine (85 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 8 h. Purification of the crude product by flash column chromatography (silica gel, EtOAc) afforded the title compound as a brown oil (**83l**, 106 mg, 0.39 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.68–8.62 (m, 2H), 7.60 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 7.43 (ddd, *J* = 8.3, 7.7, 5.3 Hz, 1H), 7.32–7.27 (m, 2H), 7.27–7.24 (m, 1H), 3.78 (s, 2H), 1.23 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.7 (d, *J* = 3.3 Hz), 159.4 (d, *J* = 247.9 Hz), 149.5, 142.5, 130.4 (d, *J* = 3.2 Hz), 130.1 (d, *J* = 8.7 Hz), 126.8 (d, *J* = 17.2 Hz), 126.0 (d, *J* = 3.5 Hz), 124.7 (d, *J* = 1.6 Hz), 118.2 (d, *J* = 22.8 Hz), 79.6, 68.0, 28.1.

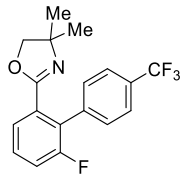
MS (EI, 70 eV): m/z (%) = 270 (16), 269 (100), 215 (15), 199 (19), 184 (40).

HRMS (EI): for $C_{16}H_{15}FN_2O$: calc. [M-H$^+$]: 269.1090; found: 269.1085.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3401 (w), 3073 (w), 3031 (w), 2968 (m), 2930 (w), 2894 (w), 1656 (s), 1611 (s), 1598 (s), 1574 (m), 1546 (m), 1505 (vw), 1455 (s), 1410 (m), 1385 (w), 1364 (m),

1353 (s), 1312 (s), 1283 (w), 1244 (s), 1218 (m), 1189 (m), 1167 (m), 1112 (s), 1078 (m), 1022 (vw), 975 (vs), 907 (m), 824 (s), 798 (vs), 751 (s), 738 (s), 711 (w), 666 (vw).
Melting point: M.p. = 85 °C.

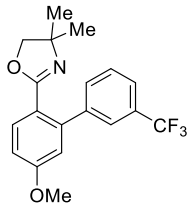
2-(6-Fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83m)



According to **TP 4**, to a mixture of 2-(3-fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82d**, 580 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 1.80 mmol, 0.6 equiv) at 25 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (3.30 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (52 mg, 3 mol%), tfp (42 mg, 6 mol%) and 1-iodo-4-(trifluoromethyl)benzene (0.37 ml, 2.49 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 8:1) afforded the title compound as a brown solid (**83m**, 846 mg, 2.44 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69–7.64 (m, 2H), 7.60–7.56 (m, 1H), 7.50–7.46 (m, 2H), 7.41 (td, *J* = 8.0, 5.3 Hz, 1H), 7.29–7.23 (m, 1H), 3.75 (s, 2H), 1.22 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.0 (d, *J* = 3.4 Hz), 159.5 (d, *J* = 246.9 Hz), 138.0, 130.7, 130.1 (d, *J* = 1.6 Hz), 130.0 (q, *J* = 33.0 Hz), 129.6 (d, *J* = 8.8 Hz), 128.1 (d, *J* = 17.3 Hz), 125.9 (d, *J* = 3.5 Hz), 124.9 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.0 Hz), 79.7, 67.9, 28.1.
MS (EI, 70 eV): m/z (%) = 337 (19), 336 (100), 282 (12), 251 (50), 246 (32), 238 (11), 226 (10).
HRMS (EI): for $C_{18}H_{15}F_4NO$: calc. [M-H$^+$]: 336.1012; found: 336.1007.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2978 (w), 2937 (vw), 2920 (vw), 2890 (w), 2878 (vw), 1646 (m), 1619 (w), 1580 (w), 1568 (w), 1465 (w), 1406 (w), 1366 (w), 1352 (m), 1323 (s), 1314 (s), 1279 (w), 1241 (m), 1223 (w), 1188 (m), 1173 (m), 1158 (m), 1124 (s), 1102 (vs), 1076 (m), 1066 (s), 1037 (w), 1021 (m), 1008 (m), 987 (m), 974 (s), 957 (m), 922 (vw), 904 (m), 848 (s), 834 (m), 819 (w), 794 (m), 784 (m), 753 (m), 740 (m), 728 (s), 713 (w), 666 (m).
Melting point: M.p. = 56 °C.

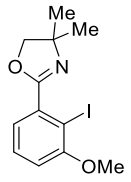
2-(5-Methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83n)



According to **TP 4**, to a mixture of 2-(4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82e**, 1.026 g, 5.00 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**, 3.00 mmol, 0.6 equiv) at 40 °C. After 20 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.5 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (183 mg, 5 mol%) and 1-iodo-3-(trifluoromethyl)benzene (0.60 mL, 4.15 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/Et_2O = 1:1) afforded the title compound as a brown solid (**83n**, 1.62 g, 4.05 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.76 (d, *J* = 8.6 Hz, 1H), 7.66–7.55 (m, 3H), 7.51 (t, *J* = 7.6 Hz, 1H), 6.93 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.86 (d, *J* = 2.6 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 2H), 1.26 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.1, 161.3, 142.1, 142.0, 132.3, 131.7 (d, *J* = 1.6 Hz), 130.3 (q, *J* = 32.1 Hz), 128.7, 125.5 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.2 Hz), 124.1 (q, *J* = 3.8 Hz), 120.4, 115.9, 113.1, 79.4, 67.5, 55.6, 28.1.
MS (EI, 70 eV): m/z (%) = 349 (20), 348 (100), 263 (38), 258 (18), 215 (14).
HRMS (EI): for $C_{19}H_{18}F_3NO_2$: calc. [M-H$^+$]: 348.1211; found: 348.1199.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2988 (vw), 2974 (w), 2945 (w), 2942 (w), 2937 (vw), 2933 (vw), 2931 (vw), 2927 (vw), 2905 (vw), 2901 (vw), 2886 (w), 2843 (vw), 1635 (s), 1608 (s), 1579 (w), 1568 (w), 1513 (w), 1464 (m), 1448 (w), 1432 (w), 1423 (w), 1365 (w), 1350 (m), 1334 (s), 1314 (s), 1295 (s), 1276 (m), 1244 (m), 1212 (s), 1195 (m), 1178 (s), 1165 (vs), 1139 (s), 1110 (s), 1095 (s), 1080 (s), 1068 (s), 1034 (m), 1025 (vs), 1002 (w), 986 (m), 964 (m), 959 (m), 932 (m), 927 (m), 914 (m), 907 (m), 895 (s), 809 (s), 788 (m), 774 (vw), 771 (vw), 768 (vw), 758 (w), 743 (vw), 716 (m), 706 (m), 701 (vs), 687 (w), 664 (m).
Melting point: M.p. = 70 °C.

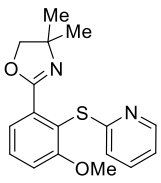
2-(2-Iodo-3-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (83o)



According to **TP 4**, to a mixture of 2-(3-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82f**, 205 mg, 1.00 mmol, 1.0 equiv) in toluene (2 mL) was added *s*Bu_2Mg (**58**, 0.8 mmol, 0.8 equiv) at 60 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and iodine (2.54 g, 10.0 mmol, 2.0 equiv) dissolved in THF (10 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a yellow solid (**83o**, 1.07 g, 3.23 mmol, 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.31 (dd, *J* = 8.2, 7.6 Hz, 1H), 7.11 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.86 (dd, *J* = 8.3, 1.4 Hz, 1H), 4.15 (s, 2H), 3.89 (s, 3H), 1.42 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.3, 158.5, 136.8, 129.4, 122.9, 112.3, 88.0, 79.6, 68.3, 56.8, 28.4.
MS (EI, 70 eV): m/z (%) = 331 (49), 316 (11), 315 (100), 300 (16), 287 (11), 259 (25), 258 (36), 174 (20), 161 (41), 146 (34), 133 (18), 132 (11), 117 (17).
HRMS (EI): for $C_{12}H_{14}INO_2$: calc. [M+]: 331.0069; found: 331.0064.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3016 (vw), 2969 (w), 2960 (m), 2936 (w), 2933 (w), 2924 (w), 2911 (w), 2893 (w), 2890 (w), 2864 (w), 2862 (w), 2836 (w), 2834 (w), 1665 (m), 1652 (w), 1634 (w), 1587 (w), 1582 (w), 1575 (w), 1563 (m), 1475 (w), 1465 (s), 1438 (w), 1418 (m), 1383 (w), 1359 (m), 1317 (s), 1283 (w), 1260 (vs), 1234 (w), 1183 (m), 1172 (m), 1124 (m), 1091 (m), 1039 (vs), 1018 (m), 1011 (m), 990 (w), 981 (w), 957 (s), 924 (m), 894 (w), 885 (w), 880 (w), 823 (w), 814 (w), 781 (vs), 722 (m), 711 (w), 692 (m).
Melting point: M.p. = 109 °C.

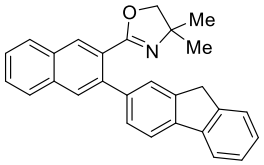
2-(3-Methoxy-2-(pyridin-2-ylthio)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (83p)



According to **TP 4**, to a mixture of 2-(3-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**82f**, 205 mg, 1.00 mmol, 1.0 equiv) in toluene (2 mL) was added *s*Bu_2Mg (**58**, 0.8 mmol, 0.8 equiv) at 60 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and 2,2′-dipyridyl disulfide (270 mg, 1.20 mmol, 1.2 equiv) dissolved in toluene (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:4) afforded the title compound as a yellow solid (**83p**, 225 mg, 0.80 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.35 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.41–7.34 (m, 1H), 7.29 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.3 Hz, 1H), 6.93 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1H), 6.73 (dt, *J* = 8.1, 1.0 Hz, 1H), 3.99 (s, 2H), 3.77 (s, 3H), 1.25 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.4, 161.1, 160.2, 149.1, 136.5, 136.4, 131.0, 122.6, 120.6, 119.5, 118.6, 113.5, 79.6, 67.9, 56.4, 28.2.
MS (EI, 70 eV): m/z (%) = 284 (16), 283 (100), 211 (16).
HRMS (EI): for $C_{17}H_{18}N_2O_2S$: calc. [M-H$^+$]: 313.1013; found: 313.1006.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3051 (w), 3005 (w), 2969 (m), 2959 (w), 2922 (m), 2916 (m), 2909 (w), 2852 (w), 1742 (w), 1666 (m), 1573 (s), 1561 (s), 1469 (s), 1461 (m), 1447 (s), 1429 (m), 1418 (vs), 1363 (m), 1355 (m), 1315 (s), 1278 (m), 1269 (s), 1252 (w), 1189 (m), 1128 (s), 1038 (vs), 985 (m), 960 (s), 957 (s), 927 (m), 782 (s), 764 (s), 736 (s), 729 (s), 723 (s), 721 (s), 716 (m), 714 (m).
Melting point: M.p. = 75 °C.

2-(3-(9*H*-Fluoren-2-yl)naphthalen-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83q)



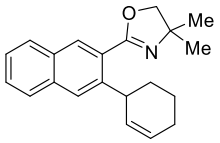
The metalation itself was prepared according to a literature procedure.[212] According to **TP 5**, to a mixture of 4,4-dimethyl-2-(naphthalen-2-yl)-4,5-dihydrooxazole (**82g**, 113 mg, 0.50 mmol, 1.0 equiv) in THF (1 mL) was added TMPMgCl·LiCl (**25**, 1.5 mmol, 3.0 equiv) at 25 °C. After 6 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 3-iodofluorene (121 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was

[212] D. Göbel, N. Clamor, E. Lork, B. J. Nachtsheim, *Org. Lett.* **2019**, *21*, 5373-5377.

placed in an oil bath at 55 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**83q**, 121 mg, 0.31 mmol, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.30 (s, 1H), 7.95–7.80 (m, 6H), 7.75–7.68 (m, 1H), 7.61–7.28 (m, 7H), 3.97 (s, 2H), 3.82 (s, 2H), 1.36 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 171.3, 164.3, 143.6, 143.3, 141.7, 140.9, 140.0, 138.7, 134.3, 131.8, 130.7, 129.3, 128.4, 128.0, 127.7, 127.5, 127.0, 126.9, 126.7, 126.6, 125.3, 125.2, 120.1, 119.6, 79.8, 67.7, 60.6, 37.1, 28.3, 21.2, 14.3.
MS (EI, 70 eV): m/z (%) = 389 (42), 388 (100), 333 (10), 317 (16), 316 (11), 303 (20), 302 (13), 289 (12), 42 (16).
HRMS (EI): for $C_{28}H_{23}NO$: calc. [M-H$^+$]: 388.1701; found: 388.1696.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2961 (m), 1665 (s), 1657 (s), 1649 (s), 1642 (s), 1631 (s), 1620 (s), 1612 (s), 1605 (s), 1597 (s), 1580 (m), 1572 (m), 1484 (m), 1467 (s), 1461 (s), 1451 (s), 1444 (s), 1402 (m), 1364 (m), 1358 (m), 1346 (m), 1328 (m), 1294 (s), 1192 (s), 1178 (m), 1065 (s), 995 (s), 769 (s).
Melting point: M.p. = 134 °C.

2-(3-(Cyclohex-2-en-1-yl)naphthalen-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83r)



The metalation itself was prepared according to a literature procedure. According to **TP 5**, to a mixture of 4,4-dimethyl-2-(naphthalen-2-yl)-4,5-dihydrooxazole (**82g**, 113 mg, 0.50 mmol, 1.0 equiv) in THF (1 mL) was added TMPMgCl·LiCl (**25**, 1.5 mmol, 3.0 equiv) at 25 °C. After 6 h, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.2 mL, 20 mol%, 1M in THF) and 3-bromocyclohexen (70 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 5:1) afforded the title compound as a yellow oil (**83r**, 143 mg, 0.47 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.22 (s, 1H), 7.86–7.76 (m, 2H), 7.73 (s, 1H), 7.46 (dddd, *J* = 22.6, 8.2, 6.8, 1.3 Hz, 2H), 6.00 (dtd, *J* = 9.8, 3.6, 2.2 Hz, 1H), 5.89–5.76 (m, 1H), 4.47 (dp, *J* = 5.9, 2.9 Hz, 1H), 4.13 (d, *J* = 1.9 Hz, 2H), 2.11 (dt, *J* = 9.6, 6.9 Hz, 3H), 2.01–1.81 (m, 1H), 1.70–1.60 (m, 2H), 1.43 (s, 6H).

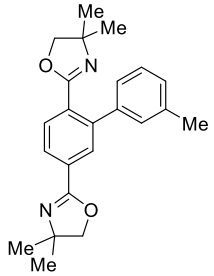
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.9, 142.8, 139.5, 134.3, 131.3, 130.6, 130.5, 128.7, 128.2, 127.5, 127.4, 127.3, 126.4, 125.9, 123.9, 78.9, 68.2, 54.1, 37.6, 33.7, 32.0, 28.5, 25.3, 25.1, 24.8, 20.7, 18.2.

MS (EI, 70 eV): m/z (%) = 306 (26), 305 (100), 304 (55), 250 (30), 221 (26), 215 (15), 42 (29).

HRMS (EI): for $C_{21}H_{23}NO$: calc. [M^+]: 305.1780; found: 305.1774.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2926 (s), 2888 (m), 1642 (vs), 1463 (m), 1457 (m), 1362 (m), 1349 (m), 1292 (m), 1285 (m), 1193 (s), 1118 (m), 1113 (m), 1027 (s), 1017 (s), 980 (m), 903 (m), 880 (m).

2,2'-(3'-Methyl-[1,1'-biphenyl]-2,5-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole) (83s)



According to **TP 5**, to a mixture of 1,4-bis(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzene (**82h**, 545 mg, 2.00 mmol, 1.0 equiv) in THF (5 mL) was added TMPMgCl·LiCl (**25**, 4.0 mmol, 2.0 equiv) at 25 °C. After 2 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (2.80 mL, 1.00 M in THF, 1.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (32 mg, 3 mol%), tfp (28 mg, 6 mol%) and 3-iodotoluene (0.21 ml, 1.66 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1, 5% Et_3N) afforded the title compound as a yellow oil (**83s**, 589 mg, 1.63 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.96 (d, *J* = 1.8 Hz, 1H), 7.91 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.26–7.22 (m, 2H), 7.20 (dt, *J* = 7.4, 1.6 Hz, 1H), 7.13 (dp, *J* = 7.4, 1.0 Hz, 1H), 4.11 (s, 2H), 3.80 (s, 2H), 2.37 (d, *J* = 0.8 Hz, 3H), 1.38 (s, 6H), 1.29 (s, 6H).

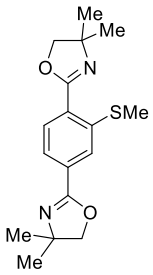
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.5, 161.6, 142.1, 140.4, 137.7, 130.6, 130.3, 130.0, 130.0, 129.2, 128.3, 128.0, 126.7, 125.6, 79.8, 79.3, 68.0, 67.8, 28.5, 28.1, 21.5.

MS (EI, 70 eV): m/z (%) = 363 (21), 362 (100), 347 (19), 226 (26), 210 (18), 173 (43).

HRMS (EI, 70 eV): for $C_{23}H_{26}N_2O_2$: calc. [M^+]: 362.1994; found: 362.1989.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2973 (m), 2949 (w), 2941 (w), 2939 (w), 2928 (m), 2924 (m), 2918 (w), 2911 (w), 2892 (w), 2884 (w), 1678 (w), 1657 (s), 1652 (s), 1606 (w), 1604 (w), 1600 (w), 1479 (w), 1473 (m), 1471 (m), 1462 (m), 1456 (m), 1446 (m), 1363 (m), 1349 (m), 1311 (m), 1223 (w), 1192 (w), 1185 (w), 1111 (w), 1076 (m), 1067 (w), 1065 (w), 1043 (s), 1041 (m), 1034 (s), 984 (w).

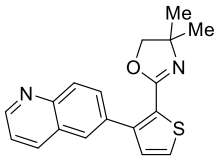
2,2'-(2-(Methylthio)-1,4-phenylene)bis(4,4-dimethyl-4,5-dihydrooxazole) (83t)



According to **TP 5**, to a mixture of 1,4-bis(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzene (**82h**, 136 mg, 0.50 mmol, 1.0 equiv) in THF (1 mL) was added TMPMgCl·LiCl (**25**, 1.0 mmol, 2.0 equiv) at 25 °C. After 2 h, *S*-Methyl methanethiosulfonate (80 µL, 0.80 mmol, 1.60 equiv) was added and the reaction mixture was stirred for 2 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1,) afforded the title compound as a brown solid (**83t**, 147 mg, 0.46 mmol, 92% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.96 (s, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.69 (dd, *J* = 8.1, 1.6 Hz, 1H), 4.11 (s, 2H), 4.07 (s, 2H), 2.50 (s, 3H), 1.42 (s, 6H), 1.38 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.5, 160.8, 141.3, 130.3, 130.2, 128.3, 127.9, 123.9, 123.5, 79.3, 68.0, 28.5.
MS (EI, 70 eV): m/z (%) = 318 (22), 304 (16), 303 (100), 285 (16), 249 (14), 231 (26), 229 (10), 175 (14).
HRMS (EI): for $C_{17}H_{22}N_2O_2S$: calc. [M^+]: 318.1402; found: 318.1393.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2868 (m), 1643 (s), 1488 (w), 1475 (w), 1451 (m), 1363 (w), 1347 (m), 1305 (m), 1267 (w), 1247 (w), 1204 (m), 1191 (m), 1108 (w), 1058 (w), 1033 (vs), 990 (w), 966 (m), 920 (m), 867 (w), 766 (m), 758 (m), 749 (m), 728 (m), 695 (m).
Melting point: M.p. = 80 °C.

4,4-Dimethyl-2-(3-(quinolin-6-yl)thiophen-2-yl)-4,5-dihydrooxazole (83u)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-(thiophen-2-yl)-4,5-dihydrooxazole (**82i**, 91 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dppf)Cl_2$ (18 mg, 5 mol%) and 6-iodoquinoline (106 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a brown solid (**83u**, 124 mg, 0.40 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.93 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.20–8.13 (m, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.90 (d, *J* = 2.1 Hz, 1H), 7.80 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.47 (d, *J* = 5.1 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.17 (d, *J* = 5.1 Hz, 1H), 3.92 (s, 2H), 1.33 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.2, 150.7, 147.8, 143.8, 136.4, 134.5, 131.5, 131.0, 128.8, 128.4, 128.0, 127.7, 125.8, 121.5, 79.6, 67.7, 28.2.

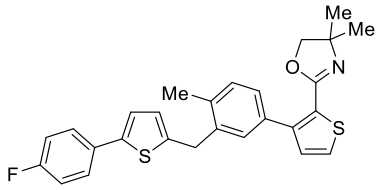
MS (EI, 70 eV): m/z (%) =307 (100), 222 (33), 236 (27), 308 (18), 235 (12), 237 (10).

HRMS (EI): for $C_{18}H_{16}N_2OS$: calc. [M^+]: 308.0983; found: 308.0973.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3068 (w), 2960 (w), 2924 (m), 2892 (w), 2854 (w), 1627 (vs), 1592 (m), 1568 (w), 1496 (m), 1471 (w), 1458 (m), 1435 (m), 1427 (m), 1388 (m), 1378 (m), 1372 (m), 1363 (m), 1358 (w), 1344 (w), 1318 (w), 1302 (w), 1268 (w), 1246 (w), 1210 (m), 1189 (w), 1173 (m), 1125 (w), 1110 (w), 1078 (w), 1029 (vs), 985 (w), 964 (m), 949 (m), 922 (m), 912 (w), 887 (m), 864 (w), 846 (vs), 820 (w), 798 (m), 780 (vs), 770 (m), 764 (m), 714 (w), 674 (s).

Melting point: M.p. = 125 °C.

2-(3-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)thiophen-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (83v)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-(thiophen-2-yl)-4,5-dihydrooxazole (**82i**, 91 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 25 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (18 mg, 5 mol%) and 2-(4-fluorophenyl)-5-(5-iodo-2-methylbenzyl)thiophene (170 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a brown oil (**83v**, 182 mg, 0.39 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53–7.45 (m, 2H), 7.38 (d, *J* = 5.1 Hz, 1H), 7.32 (d, *J* = 1.9 Hz, 1H), 7.28 (d, *J* = 1.9 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.09–6.99 (m, 4H), 6.70 (dt, *J* = 3.7, 1.1 Hz, 1H), 4.13 (d, *J* = 3.0 Hz, 2H), 3.88 (s, 2H), 2.36 (s, 3H), 1.28 (s, 6H).

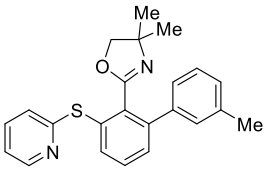
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.6, 144.4, 143.4, 141.7, 137.7, 135.9, 134.0, 131.1, 130.6, 130.2, 127.8 (d, *J* = 53.6 Hz), 127.2 (d, *J* = 7.9 Hz), 126.3, 124.7, 122.8, 115.9 (d, *J* = 21.7 Hz), 79.6, 67.3, 34.2, 28.2, 19.5.

MS (EI, 70 eV): m/z (%) = 461 (31), 460 (100), 389 (24), 228 (10), 211 (66), 210 (18), 191 (77), 184 (16), 139 (10).

HRMS (EI): for $C_{27}H_{24}FNOS_2$: calc. [M-H$^+$]: 460.1205; found: 460.1205.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3068 (vw), 2966 (m), 2925 (w), 2892 (w), 1633 (s), 1602 (w), 1573 (vw), 1548 (w), 1508 (vs), 1462 (m), 1432 (m), 1378 (w), 1364 (m), 1346 (m), 1300 (m), 1285 (w), 1229 (s), 1208 (m), 1197 (m), 1159 (m), 1114 (w), 1097 (m), 1078 (w), 1026 (vs), 990 (w), 955 (m), 942 (m), 915 (w), 856 (m), 832 (s), 799 (vs), 773 (w), 745 (s), 724 (w), 712 (w), 681 (w), 662 (w).

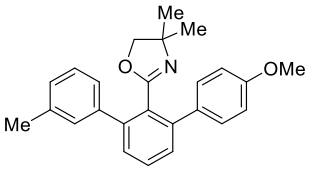
4,4-Dimethyl-2-(3'-methyl-3-(pyridin-2-ylthio)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (84a)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-(3'-methyl-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**83b**, 796 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added *s*Bu_2Mg (**58**, 1.8 mmol, 0.6 equiv) at 60 °C. After 1 h, the reaction mixture was cooled to 0 °C and 2,2′-dipyridyl disulfide (793 mg, 3.60 mmol, 1.2 equiv) dissolved in toluene (6 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a green oil (**84a**, 1.049 g, 2.80 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.39 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.61 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.52–7.40 (m, 3H), 7.31–7.23 (m, 3H), 7.14 (ttd, *J* = 5.4, 4.4, 3.8, 2.3 Hz, 1H), 6.96 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 6.87 (dt, *J* = 8.1, 1.0 Hz, 1H), 3.86 (s, 2H), 2.35 (s, 3H), 1.01 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.5, 160.7, 149.3, 143.8, 139.8, 137.6, 137.0, 135.0, 134.2, 131.4, 130.8, 130.5, 129.6, 128.4, 128.1, 126.0, 122.0, 120.0, 79.3, 68.0, 27.6, 21.5.
MS (EI, 70 eV): m/z (%) = 374 (11), 373 (13), 301 (33), 297 (18), 296 (100), 276 (14), 242 (28), 211 (10).
HRMS (EI): for $C_{23}H_{22}N_2OS$: calc. [M-H$^+$]: 373.1375; found: 373.1369.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 =3046 (w), 2950 (w), 2920 (w), 2855 (w), 2853 (w), 2848 (w), 2225 (w), 2223 (w), 2221 (w), 2167 (w), 1736 (w), 1733 (w), 1606 (w), 1572 (s), 1556 (s), 1447 (s), 1414 (vs), 1379 (w), 1281 (w), 1261 (w), 1206 (w), 1179 (w), 1171 (w), 1169 (w), 1167 (w), 1148 (m), 1114 (s), 1098 (m), 1086 (m), 1071 (w), 1063 (w), 1043 (m), 999 (w), 985 (m), 889 (w), 881 (w), 806 (m), 781 (s), 758 (vs), 742 (s), 727 (w), 720 (s), 702 (vs).

2-(4''-Methoxy-3-methyl-[1,1':3',1''-terphenyl]-2'-yl)-4,4-dimethyl-4,5-dihydrooxazole (84b)

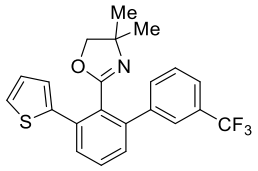


According to **TP 4**, to a mixture of 2-(4'-Methoxy-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83c**, 1.0 g, 3.55 mmol, 1.0 equiv) in toluene (10 mL) was added *s*Bu_2Mg (**58**,

3.00 mmol, 0.6 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (3.91 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dppf)Cl_2$ (132 mg, 5 mol%) and 3-iodotoluene (0.38 mL, 2.95 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a brown solid (**84b**, 0.914 g, 2.46 mmol, 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 1.4 Hz, 1H), 7.26 (d, *J* = 3.4 Hz, 3H), 7.18 – 7.11 (m, 1H), 6.94 – 6.88 (m, 2H), 3.84 (s, 3H), 3.62 (s, 2H), 2.36 (s, 3H), 0.96 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.0, 142.4, 141.8, 140.7, 137.3, 133.3, 130.1, 129.7, 129.3, 128.6, 128.3, 127.9, 127.8, 126.0, 113.3, 79.0, 67.6, 55.3, 27.4, 21.4.
MS (EI, 70 eV): m/z (%) = 371 (26), 370 (100), 298 (11).
HRMS (EI): for $C_{25}H_{25}NO_2$: calc. [M^+]: 371.1885; found: 371.1833.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2972 (w), 2950 (w), 2928 (w), 2925 (w), 2919 (w), 2916 (w), 2914 (w), 2899 (w), 2878 (w), 2877 (w), 2864 (w), 2833 (w), 1658 (m), 1635 (w), 1610 (m), 1605 (m), 1587 (w), 1582 (w), 1574 (w), 1515 (s), 1461 (m), 1454 (s), 1441 (s), 1419 (w), 1403 (w), 1402 (w), 1382 (w), 1379 (w), 1364 (m), 1345 (w), 1303 (w), 1293 (m), 1289 (m), 1283 (m), 1242 (vs), 1212 (m), 1202 (w), 1186 (m), 1171 (s), 1150 (w), 1120 (w), 1106 (m), 1092 (m), 1077 (w), 1043 (m), 1036 (vs), 1010 (w), 987 (m), 978 (w), 964 (m), 931 (w), 920 (w), 907 (m), 888 (w), 865 (w), 833 (s), 821 (m), 809 (s), 803 (s), 792 (w), 786 (vs), 762 (s), 729 (w), 716 (w), 713 (m), 702 (s).
Melting point: M.p. = 84 °C.

4,4-Dimethyl-2-(3-(thiophen-2-yl)-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (84c)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-(3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**83a**, 160 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dppf)Cl_2$ (13 mg,

3 mol%) and 2-iodothiophene (42 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a brown oil (**84c**, 144 mg, 0.36 mmol, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.77 (d, *J* = 1.9 Hz, 1H), 7.69–7.59 (m, 2H), 7.56–7.46 (m, 3H), 7.38–7.31 (m, 2H), 7.22 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.05 (dd, *J* = 5.1, 3.5 Hz, 1H), 3.75 (s, 2H), 0.96 (s, 6H).

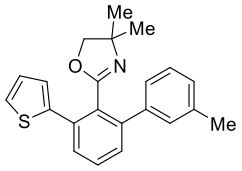
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.7, 141.3, 141.3, 141.2, 135.0, 132.5 (d, *J* = 1.5 Hz), 130.3 (q, *J* = 32.1 Hz), 130.0, 129.7, 129.1, 128.6, 128.3, 127.1, 127.1, 126.1, 125.8 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 272.5 Hz), 79.1, 67.9, 27.5.

MS (EI, 70 eV): m/z (%) = 401 (23), 400 (100), 380 (12), 330 (10), 329 (57), 328 (27), 315 (16), 308 (24), 290 (13), 260 (42), 259 (12).

HRMS (EI): for $C_{22}H_{18}F_3NOS$: calc. [M-H$^+$]: 400.0983; found: 400.0977.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2994 (w), 2962 (w), 2950 (w), 2941 (w), 2918 (w), 2902 (w), 2884 (w), 2816 (w), 1657 (m), 1622 (w), 1500 (m), 1473 (m), 1464 (m), 1450 (w), 1419 (m), 1403 (m), 1386 (w), 1360 (w), 1348 (m), 1336 (w), 1300 (m), 1250 (m), 1232 (s), 1196 (s), 1187 (m), 1149 (w), 1130 (w), 1102 (m), 1057 (s), 1048 (s), 1022 (m), 980 (w), 973 (m), 952 (m), 930 (m), 918 (m), 909 (m), 885 (m), 868 (m), 831 (s), 823 (s), 816 (m), 811 (m), 775 (m), 757 (vs), 745 (m), 738 (vs), 732 (m), 721 (m), 707 (m), 690 (s), 681 (w), 662 (m).

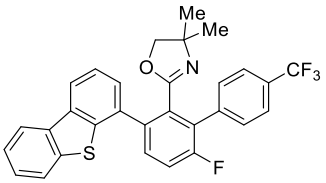
4,4-Dimethyl-2-(3'-methyl-3-(thiophen-2-yl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (84d)



According to **TP 4**, to a mixture of 4,4-dimethyl-2-(3'-methyl-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**83b**, 4.343 g, 16.37 mmol, 1.0 equiv) in toluene (34 mL) was added *s*Bu_2Mg (**58**, 9.82 mmol, 0.6 equiv) at 60 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (18.01 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (600 mg, 5 mol%) and 2-iodothiophene (1.60 mL, 13.59 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 8:1) afforded the title compound as a yellow oil (**84d**, 4.057 g, 11.68 mmol, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (s, 1H), 7.46 (d, *J* = 3.2 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.29 – 7.26 (m, 2H), 7.25 (d, *J* = 1.2 Hz, 1H), 7.20 (dd, *J* = 3.5, 1.2 Hz, 1H), 7.17 – 7.12 (m, 1H), 7.04 (dd, *J* = 5.1, 3.5 Hz, 1H), 3.73 (s, 2H), 2.37 (d, *J* = 0.8 Hz, 3H), 1.00 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.0, 142.9, 141.6, 140.4, 137.3, 134.6, 129.8, 129.3, 129.2, 129.2, 128.1, 128.1, 127.8, 126.9, 126.9, 126.0, 125.8, 79.1, 67.7, 27.5, 21.4.
MS (EI, 70 eV): m/z (%) = 347 (23), 346 (100), 275 (14), 274 (40), 261 (11), 260 (12).
HRMS (EI): for $C_{22}H_{21}NOS$: calc. [M-H$^+$]: 346.1266; found: 346.1259.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2977 (m), 2938 (w), 2931 (w), 2925 (m), 2922 (m), 2910 (w), 2894 (w), 2889 (w), 2878 (w), 1681 (w), 1677 (s), 1653 (s), 1639 (s), 1610 (w), 1606 (w), 1580 (w), 1475 (w), 1470 (m), 1464 (m), 1460 (m), 1451 (m), 1440 (m), 1356 (m), 1348 (m), 1339 (m), 1288 (m), 1201 (w), 1193 (w), 1167 (w), 1105 (w), 1066 (m), 1054 (w), 1043 (w), 1041 (s), 1039 (m), 1021 (s), 1014 (s), 985 (w), 960 (m), 924 (w), 905 (w), 782 (m), 764 (m), 759 (vs), 685 (s).

2-(3-(Dibenzo[*b*,*d*]thiophen-4-yl)-6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (84e)



According to **TP 4**, to a mixture of 2-(6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83m**, 169 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%)and 4-iododibenzo[*b*,*d*]thiophene (129 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a yellow solid (**84e**, 140 mg, 0.27 mmol, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.20–8.13 (m, 2H), 7.84–7.79 (m, 1H), 7.70–7.59 (m, 6H), 7.52–7.43 (m, 4H), 7.37 (dd, *J* = 9.1, 8.5 Hz, 1H), 3.35 (s, 2H), 0.71 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.5, 159.1 (d, *J* = 249.5 Hz), 140.1, 139.8, 137.3, 136.6, 135.8 (d, *J* = 5.9 Hz), 134.1, 131.4, 130.9 (d, *J* = 8.5 Hz), 130.6, 130.2, 129.7 (q, *J* = 152.6 Hz), 127.9,

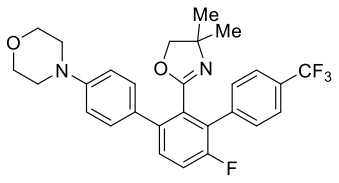
127.2 (q, *J* = 320.3 Hz), 127.0, 124.9 (q, *J* = 3.8 Hz), 124.6, 124.3, 123.0, 121.9, 121.1, 117.3 (d, *J* = 22.7 Hz), 79.2, 67.8, 27.3.

MS (EI, 70 eV): m/z (%) = 520 (15), 519 (54), 518 (100), 433 (19).

HRMS (EI): for $C_{30}H_{21}F_4NOS$: calc. [M-H$^+$]: 518.1202; found: 518.1186.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3025 (w), 2939 (w), 2925 (w), 2908 (w), 2892 (w), 2851 (w), 2811 (w), 1743 (m), 1618 (w), 1523 (m), 1488 (m), 1473 (m), 1462 (w), 1434 (m), 1388 (m), 1370 (w), 1351 (w), 1344 (m), 1329 (w), 1284 (m), 1267 (m), 1212 (s), 1174 (s), 1166 (m), 1146 (w), 1135 (w), 1059 (m), 1046 (s), 1037 (s), 1003 (m), 985 (w), 966 (m), 952 (m), 942 (m), 918 (m), 900 (m), 887 (m), 857 (m), 823 (s), 820 (s), 814 (m), 811 (m), 766 (m), 756 (m), 748 (m).

4-(2'-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-4'-fluoro-4''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4-yl)morpholine (84f)



According to **TP 4**, to a mixture of 2-(6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83m**, 169 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%)and 4-(4-iodophenyl)morpholine (120 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a white solid (**84f**, 175 mg, 0.35 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.70–7.63 (m, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.41–7.34 (m, 3H), 6.94–6.89 (m, 2H), 3.92–3.84 (m, 4H), 3.57 (s, 2H), 3.22–3.16 (m, 4H), 0.88 (s, 6H).

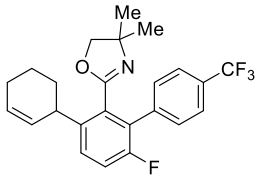
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.1 (d, *J* = 3.1 Hz), 158.3 (d, *J* = 246.6 Hz), 150.9, 138.2 (d, *J* = 3.8 Hz), 137.7, 131.2, 131.1 (d, *J* = 2.0 Hz), 130.6, 130.2, 129.8, 129.1 (q, *J* = 181.0 Hz), 128.9 (q, *J* = 301.5 Hz), 124.8 (q, *J* = 3.8 Hz), 117.0 (d, *J* = 22.5 Hz), 116.0, 115.2, 79.2, 67.8, 67.0, 49.3, 31.1, 27.5.

MS (EI, 70 eV): m/z (%) = 499 (19), 497 (100), 426 (77), 383 (10), 369 (18), 368 (83), 367 (21), 340 (37), 339 (27), 320 (16), 271 (17), 257 (11), 207 (11).

HRMS (EI): for $C_{28}H_{26}F_4N_2O_2$: calc. [M-H$^+$]: 497.1852; found: 497.1847.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2359 (s), 2341 (s), 2327 (s), 1683 (m), 1670 (m), 1653 (s), 1616 (m), 1558 (m), 1521 (m), 1506 (m), 1466 (s), 1457 (m), 1321 (vs), 1318 (vs), 1235 (s), 1165 (s), 1130 (s), 1120 (vs), 1111 (vs), 1083 (s), 1065 (s), 991 (m), 925 (s), 839 (m), 826 (vs), 807 (s).

2-(4'-Fluoro-4''-(trifluoromethyl)-1,2,3,4-tetrahydro-[1,1':3',1''-terphenyl]-2'-yl)-4,4-dimethyl-4,5-dihydrooxazole (84g)



According to **TP 4**, to a mixture of 2-(6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83m**, 169 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu$_2$Mg (**58**, 0.30 mmol, 0.6 equiv) at 40 °C. After 0.5 h, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.2 mL, 20 mol%, 1M in THF) and 3-bromocyclohexen (70 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 96:4) afforded the title compound as a white solid (**84g**, 142 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69–7.62 (m, 2H), 7.52 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.31 (dd, *J* = 8.7, 5.3 Hz, 1H), 7.17 (t, *J* = 8.9 Hz, 1H), 5.94 (dtd, *J* = 9.9, 3.7, 2.4 Hz, 1H), 5.68 (dq, *J* = 9.8, 2.3, 1.8 Hz, 1H), 3.81–3.72 (m, 2H), 3.63 (ddp, *J* = 8.3, 5.4, 2.7 Hz, 1H), 2.18–2.00 (m, 3H), 1.77–1.66 (m, 1H), 1.63–1.49 (m, 2H), 1.08 (d, *J* = 14.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.2 (d, *J* = 3.1 Hz), 157.7 (d, *J* = 245.3 Hz), 141.6 (d, *J* = 3.8 Hz), 138.0 (d, *J* = 1.6 Hz), 130.5 (d, *J* = 1.3 Hz), 130.3 (d, *J* = 3.0 Hz), 130.1 (q, *J* = 32.3 Hz), 129.7, 129.4, 129.3, 127.9 (d, *J* = 17.3 Hz), 124.8 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 273.3 Hz), 117.0 (d, *J* = 22.3 Hz), 79.1, 68.0, 38.5, 32.2, 27.9, 27.8, 25.0, 21.1.

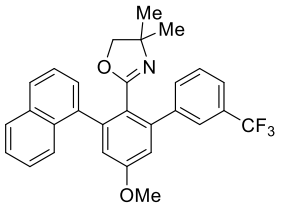
MS (EI, 70 eV): m/z (%) = 418 (16), 417 (65), 362 (48), 360 (50), 345 (30), 344 (100), 340 (15), 327 (21), 316 (32), 294 (18).

HRMS (EI): for $C_{24}H_{23}F_4NO$: calc. [M$^+$]: 417.1716; found: 417.1711.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3065 (vw), 3063 (vw), 2225 (w), 1487 (w), 1446 (w), 1427 (m), 1333 (s), 1323 (m), 1300 (m), 1261 (m), 1254 (m), 1182 (m), 1167 (m), 1162 (m), 1103 (vs), 1094 (s),

1077 (s), 1051 (m), 1023 (m), 1000 (w), 993 (w), 986 (w), 981 (vw), 979 (vw), 974 (vw), 969 (vw), 959 (w), 952 (vw), 948 (vw), 932 (w), 922 (m), 910 (vw), 882 (w), 834 (m), 811 (m), 806 (m), 761 (vs), 745 (m), 713 (m), 708 (m), 704 (vs), 658 (s).

2-(5-Methoxy-3-(naphthalen-1-yl)-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (84h)



According to **TP 4**, to a mixture of 2-(5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83n**, 175 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with Pd(dppf)Cl_2 (13 mg, 3 mol%) and 1-iodonaphtalene (61 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a colorless oil (**84h**, 152 mg, 0.32 mmol, 77% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.89–7.82 (m, 2H), 7.78 (dt, *J* = 2.4, 1.1 Hz, 1H), 7.76–7.66 (m, 2H), 7.60 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.56–7.37 (m, 5H), 7.00 (d, *J* = 0.6 Hz, 2H), 3.89 (s, 3H), 3.21 (d, *J* = 1.3 Hz, 2H), 0.52 (d, J = 40.2 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.0, 160.0, 143.0, 141.6, 138.1, 132.9 (q, *J* = 107.8 Hz), 132.0, 128.8, 128.0 (q, *J* = 2.2 Hz), 127.3, 126.6, 126.2, 125.8, 125.6, 125.0, 122.0, 115.6, 114.8, 78.7, 67.3, 55.7, 27.0.

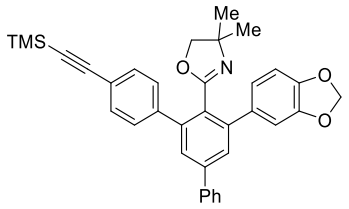
MS (EI, 70 eV): m/z (%) = 401 (23), 400 (100), 380 (12), 330 (10), 329 (57), 328 (27), 315 (16), 308 (24), 290 (13), 260 (42), 259 (12).

HRMS (EI): for $C_{25}H_{25}NO_2$: calc. [M^+]: 371.1885; found: 371.1833.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3049 (w), 2941 (w), 2933 (w), 2911 (w), 2895 (w), 2884 (w), 2800 (w), 1763 (m), 1609 (w), 1533 (m), 1489 (m), 1470 (m), 1466 (w), 1443 (m), 1421 (m), 1372 (w), 1359 (w), 1348 (m), 1325 (w), 1313 (m), 1252 (m), 1210 (s), 1178 (s), 1165 (m), 1149 (w), 1130 (w), 1066

(m), 1051 (s), 1040 (s), 1009 (m), 970 (m), 949 (m), 933 (m), 922 (m), 902 (m), 880 (m), 862 (m), 827 (s), 822 (s), 819 (m), 811 (m), 775 (m), 764 (m).

2-(5'-(Benzo[d][1,3]dioxol-5-yl)-4''-((trimethylsilyl)ethynyl)-[1,1':3',1''-terphenyl]-4'-yl)-4,4-dimethyl-4,5-dihydrooxazole (84i)



According to **TP 4**, to a mixture of 2-(3-(benzo[d][1,3]dioxol-5-yl)-[1,1'-biphenyl]-4-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83f**, 186 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.30 mmol, 0.6 equiv) at 70 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%)and ((4-iodophenyl)ethynyl)trimethylsilane (125 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 92:8) afforded the title compound as a yellow solid (**84i**, 158 mg, 0.29 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.70–7.62 (m, 2H), 7.58 (d, *J* = 1.9 Hz, 1H), 7.54 (d, *J* = 1.8 Hz, 1H), 7.52–7.42 (m, 6H), 7.41–7.36 (m, 1H), 7.04–6.96 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.99 (s, 2H), 3.68 (s, 2H), 1.03 (s, 6H), 0.27 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.3, 147.4, 147.1, 142.6, 142.4, 142.2, 141.1, 140.1, 134.6, 131.7, 129.0, 128.9, 128.1, 127.8, 127.4, 127.3, 126.7, 122.6, 122.3, 109.7, 108.1, 105.1, 101.2, 94.8, 79.2, 67.9, 27.7, 0.1.

MS (EI, 70 eV): m/z (%) = 544 (20), 543 (20), 542 (100), 263 (11).

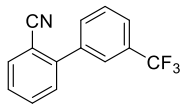
HRMS (EI): for $C_{35}H_{33}NO_3Si$: calc. [M-H$^+$]: 542.2151; found: 542.2150.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2964 (w), 2927 (w), 2901 (w), 2890 (w), 2882 (w), 2159 (w), 2144 (w), 1664 (m), 1596 (w), 1566 (w), 1503 (m), 1493 (m), 1472 (w), 1459 (m), 1434 (w), 1401 (w), 1364 (w), 1352 (w), 1332 (w), 1295 (w), 1245 (s), 1224 (m), 1190 (w), 1171 (w), 1123 (w), 1106 (m), 1084 (w), 1045 (m), 1039 (m), 1032 (m), 1014 (w), 980 (w), 956 (m), 945 (m), 930 (w), 917 (w), 910 (w), 890 (m), 862 (s), 839 (vs), 820 (s), 805 (m), 788 (m), 768 (s), 760 (m), 744 (m), 724 (m), 696 (s), 671 (w), 658 (m).

Melting point: M.p. = 177 °C.

4.3 Preparation of Functionalized Nitriles

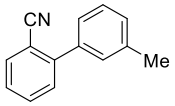
3'-(Trifluoromethyl)-[1,1'-biphenyl]-2-carbonitrile (85a)



According to **TP 6**, to a mixture of 4,4-dimethyl-2-(3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**83a**, 64 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**85a**, 49 mg, 0.198 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84–7.76 (m, 3H), 7.76–7.61 (m, 3H), 7.56–7.48 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 144.3, 139.3, 134.3, 133.5, 132.6 (d, *J* = 1.5 Hz), 131.7 (q, *J* = 32.6 Hz), 130.5, 129.7, 128.8, 126.1 (q, *J* = 3.7 Hz), 126.0 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 273.8 Hz), 118.7, 111.9.
MS (EI, 70 eV): m/z (%) = 248 (15), 247 (100), 227 (28), 226 (26), 208 (25), 197 (10), 182 (17), 177 (13).
HRMS (EI): for $C_{14}H_8F_3N$: calc. [M+]: 247.0609; found: 247.0603.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3065 (vw), 3063 (vw), 2225 (w), 1487 (w), 1446 (w), 1427 (m), 1333 (s), 1323 (m), 1300 (m), 1261 (m), 1254 (m), 1182 (m), 1167 (m), 1162 (m), 1103 (vs), 1094 (s), 1077 (s), 1051 (m), 1023 (m), 1000 (w), 993 (w), 986 (w), 981 (vw), 979 (vw), 974 (vw), 969 (vw), 959 (w), 952 (vw), 948 (vw), 932 (w), 922 (m), 910 (vw), 882 (w), 834 (m), 811 (m), 806 (m), 761 (vs), 745 (m), 713 (m), 708 (m), 704 (vs), 658 (s).
Melting point: M.p. = 62 °C.

3'-Methyl-[1,1'-biphenyl]-2-carbonitrile (85b)

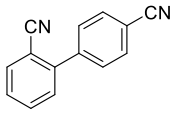


According to **TP 6**, to a mixture of 4,4-dimethyl-2-(3'-methyl-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**83b**, 53 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless liquid (**85b**, 38 mg, 0.197 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.76 (dd, J = 7.8, 1.4 Hz, 1H), 7.64 (td, J = 7.7, 1.4 Hz, 1H), 7.51 (dd, J = 7.9, 1.3 Hz, 1H), 7.46–7.34 (m, 4H), 7.27 (d, J = 4.5 Hz, 1H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 145.8, 138.6, 138.2, 133.9, 132.9, 130.2, 129.6, 129.6, 128.8, 127.6, 126.0, 118.9, 111.4, 21.6.
MS (EI, 70 eV): m/z (%) = 193 (48), 192 (100), 191 (10), 190 (12), 165 (62).
HRMS (EI): for $C_{14}H_{11}N$: calc. [M+]: 193.0891; found: 193.0885.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3060 (vw), 3030 (vw), 2948 (vw), 2921 (vw), 2222 (m), 1607 (w), 1596 (w), 1587 (w), 1566 (w), 1479 (w), 1471 (m), 1441 (m), 1379 (vw), 1286 (w), 1270 (w), 1196 (vw), 1186 (vw), 1164 (w), 1110 (w), 1095 (vw), 1052 (vw), 1038 (vw), 1000 (vw), 956 (vw), 910 (vw), 887 (w), 862 (vw), 792 (m), 758 (vs), 741 (s), 701 (s), 676 (vw), 673 (vw).

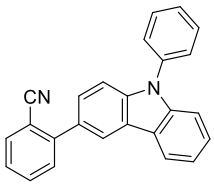
[1,1'-Biphenyl]-2,4'-dicarbonitrile (85c)



According to **TP 6**, to a mixture of 2'-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-[1,1'-biphenyl]-4-carbonitrile (**83d**, 55 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**85c**, 35 mg, 0.172 mmol, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.81 (dd, *J* = 8.5, 6.7 Hz, 3H), 7.75–7.65 (m, 3H), 7.57–7.49 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 143.4, 142.5, 134.0, 133.2, 132.6, 129.9, 129.6, 128.8, 118.4, 118.0, 112.7, 111.3.
MS (EI, 70 eV): m/z (%) = 205 (15, 204 (100), 203 (22), 177 (30), 150 (16), 76 (12), 75 (18), 74 (18).
HRMS (EI): for $C_{14}H_8N_2$: calc. [M+]: 204.0687; found: 204.0682.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3091 (w), 3066 (w), 3038 (w), 2958 (w), 2924 (m), 2921 (m), 2844 (w), 2227 (s), 2225 (m), 2169 (m), 2166 (m), 1607 (w), 1594 (w), 1481 (m), 1445 (m), 1404 (m), 1281 (w), 1265 (w), 1188 (w), 1165 (w), 1055 (w), 998 (w), 967 (w), 849 (vs), 764 (vs), 759 (vs), 749 (m), 743 (m), 723 (m).
Melting point: M.p. = 156 °C.

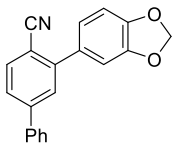
2-(9-Phenyl-9*H*-carbazol-3-yl)benzonitrile (85d)



According to **TP 6**, to a mixture of 4,4-dimethyl-2-(2-(9-phenyl-9*H*-carbazol-3-yl)phenyl)-4,5-dihydrooxazole (**83e**, 83 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**85d**, 68 mg, 0.197 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.33 (d, *J* = 1.8 Hz, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 7.84–7.78 (m, 1H), 7.71–7.58 (m, 7H), 7.54–7.41 (m, 5H), 7.32 (ddd, *J* = 8.0, 5.3, 2.8 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 146.5, 141.6, 141.1, 137.5, 133.9, 132.9, 130.6, 130.2, 130.1, 127.9, 127.3, 127.1, 126.9, 126.5, 123.8, 123.3, 120.9, 120.7, 120.4, 119.4, 111.6, 110.1.
MS (EI, 70 eV): m/z (%) = 345 (24), 344 (100), 342 (12), 171 (15).
HRMS (EI): for $C_{25}H_{16}N_2$: calc. [M+]: 344.1313; found: 344.1306.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3047 (w), 2952 (w), 2931 (w), 2853 (w), 2848 (w), 2225 (w), 2221 (w), 2167 (w), 1736 (w), 1733 (w)1595 (m), 1498 (s), 1486 (w), 1474 (m), 1473 (m), 1471 (m), 1467 (m), 1458 (s), 1456 (s), 1453 (s), 1441 (s), 1427 (w), 1425 (w), 1360 (m), 1331 (m), 1322 (w), 1300 (m), 1248 (m), 1234 (s), 1179 (m), 1167 (m), 1166 (m), 1158 (w), 1153 (w), 1151 (w), 1135 (w), 892 (w), 814 (m), 812 (m), 759 (vs), 747 (vs), 729 (s), 723 (m), 697 (vs), 682 (m).
Melting point: M.p. = 78 °C.

3-(Benzo[*d*][1,3]dioxol-5-yl)-[1,1'-biphenyl]-4-carbonitrile (85e)

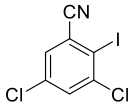


According to **TP 6**, to a mixture of 2-(3-(benzo[*d*][1,3]dioxol-5-yl)-[1,1'-biphenyl]-4-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83f**, 74 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude

product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a white solid (**85e**, 59 mg, 0.197 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.80 (d, *J* = 8.0 Hz, 1H), 7.70–7.67 (m, 1H), 7.66–7.60 (m, 3H), 7.53–7.40 (m, 3H), 7.12–7.06 (m, 2H), 6.94 (dd, *J* = 7.7, 0.8 Hz, 1H), 6.05 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.4, 148.2, 145.8, 145.8, 139.3, 134.3, 132.2, 129.3, 128.9, 128.8, 127.4, 126.1, 123.0, 119.0, 109.8, 109.4, 108.8, 101.6.
MS (EI, 70 eV): m/z (%) = 300 (21), 299 (100), 298 (46), 271 (11), 242 (10), 240 (20), 213 (12), 149 (21).
HRMS (EI): for $C_{20}H_{13}NO_2$: calc. [M+]: 299.0946; found: 299.0941.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3032 (w), 2962 (w), 2946 (w), 2917 (w), 2907 (w), 2882 (w), 2852 (w), 2217 (m), 2196 (w), 2167 (w), 1597 (m), 1584 (w), 1503 (m), 1495 (m), 1476 (s), 1454 (w), 1438 (m), 1394 (m), 1338 (w), 1259 (m), 1245 (s), 1219 (m), 1198 (w), 1179 (m), 1157 (w), 1120 (w), 1104 (m), 1078 (w), 1036 (s), 1012 (m), 960 (w), 933 (s), 916 (w), 907 (m), 892 (m), 874 (w), 847 (m), 834 (m), 814 (s), 804 (m), 758 (vs), 740 (s), 720 (w), 706 (w), 687 (vs), 658 (w).
Melting point: M.p. = 115 °C.

3,5-Dichloro-2-iodobenzonitrile (85f)



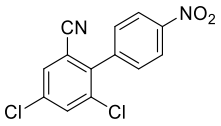
According to **TP 6**, to a mixture of 2-(3,5-dichloro-2-iodophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**83g**, 74 mg, 0.20 mmol, 1.0 equiv) in thionyl chloride (1 mL) was added DMF (0.5 mL) dropwise at 0 °C. The reaction mixture was heated at reflux for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**85f**, 58 mg, 0.196 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.65 (d, *J* = 2.3 Hz, 1H), 7.49 (d, *J* = 2.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 142.0, 135.7, 133.1, 132.2, 124.2, 118.2, 101.2.
MS (EI, 70 eV): m/z (%) = 298 (62), 296 (100), 199 (22), 197 (35), 135 (11), 133 (38), 126 (11), 99 (15).
HRMS (EI): for $C_7H_2Cl_2IN$: calc. [M+]: 296.8609; found: 296.8603.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3062 (w), 2943 (w), 2933 (w), 2929 (w), 2924 (w), 2923 (w), 2919 (w), 2230 (w), 2220 (w), 1742 (w), 1557 (w), 1539 (m), 1525 (w), 1450 (w), 1447 (w), 1436 (w), 1433 (w), 1421 (w), 1399 (m), 1384 (w), 1373 (m), 1291 (w), 1259 (w), 1253 (w), 1219 (m), 1203 (w),

1175 (m), 1132 (m), 1127 (w), 1122 (w), 1112 (s), 1086 (m), 1075 (w), 1061 (w), 1056 (w), 1053 (w), 1029 (w), 1021 (m), 961 (w), 959 (w), 894 (m), 880 (m), 873 (vs), 821 (s), 793 (m), 787 (m), 785 (m), 781 (m), 778 (m), 766 (m), 750 (m), 748 (m), 739 (m), 736 (m), 732 (m), 730 (m), 728 (m), 725 (m), 721 (m), 716 (m), 714 (m), 697 (w), 691 (s), 685 (w).

Melting point: M.p. = 151 °C.

4,6-Dichloro-4'-nitro-[1,1'-biphenyl]-2-carbonitrile (85g)



According to **TP 6**, to a mixture of 2-(4,6-dichloro-4'-nitro-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83h**, 73 mg, 0.20 mmol, 1.0 equiv) in thionyl chloride (1 mL) was added DMF (0.5 mL) dropwise at 0 °C. The reaction mixture was heated at reflux for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 92:8) afforded the title compound as a yellow solid (**85g**, 52 mg, 0.177 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.43–8.35 (m, 2H), 7.78 (d, *J* = 2.1 Hz, 1H), 7.71 (d, *J* = 2.1 Hz, 1H), 7.62–7.53 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.5, 140.8, 140.3, 135.9, 135.3, 134.5, 131.6, 130.9, 124.1, 115.7, 115.6.

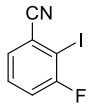
MS (EI, 70 eV): m/z (%) = 291 (15), 235 (15), 233 (24), 213 (31), 212 (13), 211 (100), 175 (10).

HRMS (EI, 70 eV): for $C_{13}H_6Cl_2N_2O_2$: calc. [M^+]: 291.9806; found: 291.9800.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3050 (w), 2940 (w), 2937 (w), 2925 (w), 2913 (w), 2236 (w), 2209 (w), 1611 (w), 1552 (w), 1534 (m), 1529 (w), 1460 (w), 1444 (w), 1435 (w), 1426 (w), 1396 (m), 1382 (w), 1341 (m), 1277 (w), 1256 (w), 1215 (m), 1200 (w), 1164 (m), 1130 (m), 1126 (w), 1120 (w), 1097 (s), 1086 (m), 1071 (w), 1064 (w), 1055 (w), 1052 (w), 1024 (w), 1022 (m), 973 (w), 955 (w), 888 (m), 879 (m), 848 (vs), 818 (s), 791 (m), 786 (m), 784 (m), 772 (m), 759 (m), 752 (m), 745 (m), 740 (m), 733 (m), 732 (m), 729 (m), 724 (m), 711 (m), 703 (m), 695 (m),

Melting point: M.p. = 151 °C.

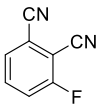
3-Fluoro-2-iodobenzonitrile (85h)



According to **TP 6**, to a mixture of 2-(3-fluoro-2-iodophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**83i**, 64 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**85h**, 48 mg, 0.194 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.45 (td, *J* = 3.4, 2.3 Hz, 2H), 7.32–7.24 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.8, 161.3, 130.7 (d, *J* = 8.3 Hz), 130.4 (d, *J* = 3.7 Hz), 122.6 (d, *J* = 2.9 Hz), 119.9 (d, *J* = 24.3 Hz), 118.5 (d, *J* = 3.4 Hz), 87.1 (d, *J* = 29.0 Hz).
MS (EI, 70 eV): m/z (%) = 246 (100), 148 (20), 100 (16).
HRMS (EI): for C_7H_3FIN: calc. [M+]: 246.9294; found: 246.9289.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3055 (w), 2948 (w), 2937 (w), 2920 (w), 2228 (w), 2223 (w), 1740 (w), 1560 (w), 1535 (m), 1529 (w), 1454 (w), 1432 (w), 1418 (w), 1385 (m), 1375 (m), 1288 (w), 1257 (w), 1255 (w), 1221 (m), 1200 (w), 1179 (m), 1131 (m), 1125 (w), 1119 (w), 1107 (s), 1082 (m), 1073 (w), 1065 (w), 1057 (w), 1033 (w), 1025 (m), 964 (w), 896 (m), 884 (m), 844 (vs), 814 (s), 790 (m), 786 (m), 779 (m), 772 (m), 765 (m), 746 (m), 735 (m), 730 (m), 722 (m), 715 (m), 694 (w), 688 (w).
Melting point: M.p. = 94 °C.

3-Fluorophthalonitrile (85i)



According to **TP 6**, to a mixture of 2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-6-fluorobenzonitrile (**83j**, 44 mg, 0.20 mmol, 1.0 equiv) in thionyl chloride (1 mL) was added DMF (0.5 mL) dropwise at 0 °C. The reaction mixture was heated at reflux for 6 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a white solid (**85i**, 24 mg, 0.164 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.78 (ddd, *J* = 8.6, 7.8, 5.2 Hz, 1H), 7.65 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.53 (td, *J* = 8.5, 1.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.7, 162.1, 135.6 (d, *J* = 9.0 Hz), 129.7 (d, *J* = 3.7 Hz), 121.4 (d, *J* = 19.8 Hz), 117.4 (d, *J* = 2.0 Hz), 114.4 (d, *J* = 3.7 Hz), 110.7, 105.2 (d, *J* = 18.3 Hz).

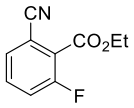
MS (EI, 70 eV): m/z (%) = 146 (100), 119 (16).

HRMS (EI): for $C_8H_3FN_2$: calc. [M+]: 146.0280; found: 146.0274.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3038 (w), 2940 (w), 2933 (w), 2929 (w), 2242 (w), 2237 (w), 1745 (w), 1620 (w), 1551 (m), 1520 (w), 1448 (w), 1421 (w), 1418 (w), 1388 (m), 1379 (m), 1269 (w), 1259 (w), 1259 (w), 1212 (m), 1202 (w), 1177 (m), 1128 (m), 1121 (w), 1115 (w), 1102 (s), 1079 (m), 1069 (w), 1061 (w), 1047 (w), 1036 (w), 1023 (m), 935 (w), 909 (w), 890 (m), 871 (m), 805 (vs), 791 (m), 786 (m), 779 (m), 772 (m), 765 (m), 746 (m), 735 (m), 730 (m), 722 (m), 715 (m), 694 (w), 688 (w).

Melting point: M.p. = 64 °C.

Ethyl 2-cyano-6-fluorobenzoate (85j)



According to **TP 6**, to a mixture of ethyl 2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-6-fluorobenzoate (**83k**, 133 mg, 0.5 mmol, 1.0 equiv) in thionyl chloride (1 mL) was added DMF (0.5 mL) dropwise at 0 °C. The reaction mixture was heated at reflux for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**85j**, 43 mg, 0.17 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.64–7.54 (m, 2H), 7.4 –7.36 (m, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1 (d, *J* = 4.4 Hz), 159.5, 133.3 (d, *J* = 9.5 Hz), 130.1 (d, *J* = 3.8 Hz), 123.4 (d, *J* = 16.0 Hz), 121.7 (d, *J* = 22.5 Hz), 116.3, 114.1, 63.0, 14.1.

MS (EI, 70 eV): m/z (%) = 178 (10), 165 (22), 148 (100), 123 (15), 121 (20).

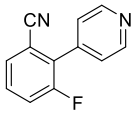
HRMS (EI): for $C_{10}H_8FNO$: calc. [M+]: 193.0539; found: 193.0533.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3021 (w), 2940 (w), 2932 (w), 2929 (w), 2338 (w), 2295 (w), 1801 (w), 1552 (w), 1530 (m), 1512 (w), 1449 (w), 1426 (w), 1409 (w), 1392 (m), 1388 (m), 1375 (m), 1263 (w), 1256 (w), 1252 (w), 1209 (m), 1204 (w), 1148 (m), 1138 (m), 1121 (w), 1117 (w), 1102 (s), 1088 (m), 1082 (w), 1071 (w), 1064 (w), 1044 (w), 1039 (m), 931 (w), 892 (m), 888 (m), 876 (vs), 810

(s), 792 (m), 783 (m), 774 (m), 765 (m), 753 (m), 746 (m), 733 (m), 722 (m), 708 (m), 690 (w), 684 (w).

Melting point: M.p. = 102 °C.

3-Fluoro-2-(pyridin-4-yl)benzonitrile (85k)



According to **TP 6**, to a mixture of 2-(3-fluoro-2-(pyridin-4-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (**83l**, 54 mg, 0.20 mmol, 1.0 equiv) oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a white solid (**85k**, 38 mg, 0.192 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.82–8.76 (m, 2H), 7.67–7.61 (m, 1H), 7.53 (td, *J* = 8.1, 5.1 Hz, 1H), 7.49–7.41 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.7, 158.2, 150.3, 139.4, 131.0 (d, *J* = 8.9 Hz), 130.4 (d, *J* = 17.8 Hz), 129.9 (d, *J* = 4.0 Hz), 124.5 (d, *J* = 1.8 Hz), 121.2 (d, *J* = 22.7 Hz), 116.8 (d, *J* = 4.1 Hz), 113.9 (d, *J* = 4.3 Hz).

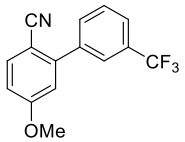
MS (EI, 70 eV): m/z (%) = 199 (12), 198 (100), 197 (67), 171 (19), 145 (13), 144 (11).

HRMS (EI): for $C_{12}H_7FN_2$: calc. [M+]: 198.0593; found: 198.0587.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3065 (w), 2997 (w), 2941 (w), 2920 (w), 2902 (w), 2890 (w), 2849 (w), 2236 (m), 1607 (m), 1597 (m), 1574 (m), 1549 (w), 1456 (s), 1413 (m), 1285 (m), 1247 (s), 1223 (w), 1092 (w), 1078 (w), 994 (w), 970 (w), 957 (s), 825 (s), 803 (vs), 774 (m), 750 (m), 728 (s), 672 (w), 665 (w).

Melting point: M.p. = 126 °C.

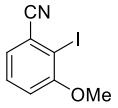
5-Methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-carbonitrile (85l)



According to **TP 6**, to a mixture of 2-(5-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83n**, 70 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**85l**, 54 mg, 0.195 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.81–7.69 (m, 4H), 7.67–7.59 (m, 1H), 7.00 (dd, *J* = 6.7, 2.5 Hz, 2H), 3.91 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.0, 146.0, 139.0, 135.7, 132.2, 131.4 (q, *J* = 32.6 Hz), 129.4, 125.7 (q, *J* = 4.0 Hz), 124.0 (q, *J* = 272.6 Hz), 118.7, 115.8, 114.1, 103.3, 55.9.
MS (EI, 70 eV): m/z (%) = 278 (16), 277 (100), 234 (18).
HRMS (EI): for $C_{15}H_{10}F_3NO$: calc. [M+]: 277.0714; found: 277.0709.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3020 (vw), 2950 (vw), 2918 (vw), 2844 (vw), 2216 (m), 1600 (m), 1591 (m), 1575 (w), 1569 (w), 1500 (w), 1498 (w), 1490 (m), 1481 (w), 1469 (w), 1430 (w), 1407 (w), 1338 (m), 1317 (m), 1312 (m), 1268 (m), 1249 (m), 1227 (m), 1184 (w), 1178 (m), 1148 (m), 1114 (vs), 1095 (m), 1075 (s), 1038 (w), 1026 (m), 999 (w), 988 (w), 923 (w), 898 (w), 871 (s), 839 (s), 809 (m), 790 (w), 724 (w), 710 (m), 697 (s), 666 (m).
Melting point: M.p. = 117 °C.

2-Iodo-3-methoxybenzonitrile (85m)

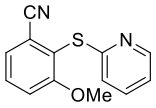


According to **TP 6**, to a mixture of 2-(2-iodo-3-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**83o**, 66 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**85m**, 56 mg, 0.198 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.41 (dd, *J* = 8.4, 7.7 Hz, 1H), 7.23 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.99 (dd, *J* = 8.4, 1.3 Hz, 1H), 3.93 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.3, 130.1, 126.6, 122.3, 119.6, 114.5, 91.3, 56.9.
MS (EI, 70 eV): m/z (%) = 258 (100), 243 (16), 215 (11), 117 (22).
HRMS (EI): for C_8H_6INO: calc. [M+]: 258.9494; found: 258.9488.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3079 (vw), 3066 (vw), 2967 (w), 2938 (w), 2934 (w), 2920 (w), 2853 (w), 2228 (m), 1963 (w), 1578 (w), 1561 (m), 1462 (s), 1438 (m), 1419 (s), 1407 (m), 1290 (m), 1268 (vs), 1255 (s), 1229 (m), 1188 (m), 1172 (w), 1151 (w), 1063 (s), 1024 (m), 1015 (m), 1011 (m), 982 (w), 916 (w), 894 (m), 797 (s), 790 (vs), 756 (w), 732 (w), 704 (m).
Melting point: M.p. = 126 °C.

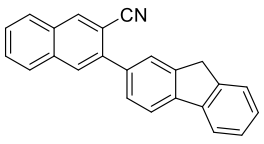
3-Methoxy-2-(pyridin-2-ylthio)benzonitrile (85n)



According to **TP 6**, to a mixture of 2-(3-methoxy-2-(pyridin-2-ylthio)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (**83p**, 63 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a white solid (**85n**, 48 mg, 0.198 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.41–8.30 (m, 1H), 7.50 (td, *J* = 7.6, 5.0 Hz, 2H), 7.44–7.36 (m, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.01 (dd, *J* = 7.7, 5.5 Hz, 2H), 3.82 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.7, 158.1, 149.9, 136.7, 131.6, 126.0, 122.5, 121.6, 121.0, 120.5, 117.3, 115.9, 56.6.
MS (EI, 70 eV): m/z (%) = 212 (12), 211 (100).
HRMS (EI): for $C_{13}H_{10}N_2OS$: calc. [M-H$^+$]: 241.0436; found: 241.0423.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3078 (w), 3007 (w), 2922 (m), 2853 (w), 2838 (w), 2232 (m), 1571 (s), 1557 (s), 1466 (s), 1454 (s), 1427 (s), 1410 (s), 1288 (m), 1273 (vs), 1184 (m), 1144 (m), 1122 (m), 1109 (s), 1062 (s), 1051 (s), 1042 (m), 985 (m), 896 (m), 876 (w), 794 (vs), 757 (vs), 733 (m), 728 (s), 724 (s), 720 (m), 717 (s), 715 (m), 711 (m).
Melting point: M.p. = 114 °C.

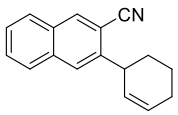
3-(9*H*-Fluoren-2-yl)-2-naphthonitrile (85o)



According to **TP 6**, to a mixture of 2-(3-(9*H*-fluoren-2-yl)naphthalen-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83q**, 78 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**85o**, 54 mg, 0.170 mmol, 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.38 (s, 1H), 8.00 (s, 1H), 7.98–7.82 (m, 6H), 7.71–7.57 (m, 3H), 7.46–7.32 (m, 2H), 4.02 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 143.8, 143.8, 142.2, 141.2, 140.2, 136.9, 136.1, 135.0, 131.3, 129.6, 129.3, 128.3, 128.2, 128.1, 127.6, 127.3, 127.1, 125.9, 125.3, 120.4, 120.2, 119.2, 109.8, 37.2.
MS (EI, 70 eV): m/z (%) = 318 (28), 317 (100), 316 (20), 314 (17), 158 (13).
HRMS (EI): for $C_{24}H_{15}N$: calc. [M+]: 317.1204; found: 317.1200.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1626 (w), 1592 (w), 1449 (w), 1401 (w), 898 (m), 838 (m), 771 (m), 756 (m).
Melting point: M.p. = 236 °C.

3-(Cyclohex-2-en-1-yl)-2-naphthonitrile (85p)

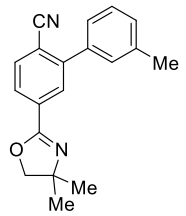


According to **TP 6**, to a mixture of 2-(3-(cyclohex-2-en-1-yl)naphthalen-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83r**, 31 mg, 0.10 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a colorless oil (**85p**, 20 mg, 0.086 mmol, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.23 (s, 1H), 7.84 (td, *J* = 7.4, 6.7, 1.2 Hz, 2H), 7.75 (s, 1H), 7.60 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H), 7.53 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 6.08 (dtd, *J* = 9.9, 3.7, 2.2 Hz, 1H), 5.78 (dq, *J* = 10.0, 2.4 Hz, 1H), 3.96 (ddt, *J* = 8.6, 5.8, 2.8 Hz, 1H), 2.29–2.12 (m, 3H), 1.76–1.58 (m, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 143.8, 135.3, 135.0, 131.0, 130.3, 129.1, 128.2, 128.1, 128.0, 127.4, 127.0, 118.5, 110.6, 39.7, 31.5, 25.1, 20.5.
MS (EI, 70 eV): m/z (%) = 234 (14), 233 (79), 232 (100), 230 (28), 229 (37), 228 (12), 225 (27), 218 (34), 205 (31), 190 (53), 165 (28), 126 (12).
HRMS (EI): for $C_{17}H_{15}N$: calc. [M+]: 233.1204; found: 233.1203.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2921 (vs), 2850 (s), 2219 (w), 1461 (m), 1454 (w), 1446 (w), 1377 (w), 1260 (w), 901 (w).

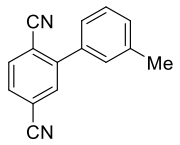
5-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-3'-methyl-[1,1'-biphenyl]-2-carbonitrile (85q)



According to **TP 6**, to a mixture of 2,2'-(3'-methyl-[1,1'-biphenyl]-2,5-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole) (**83s**, 72 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**85q**, 51 mg, 0.180 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (d, *J* = 1.7 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.42–7.35 (m, 3H), 7.31–7.28 (m, 1H), 3.92 (s, 2H), 2.44 (s, 3H), 1.54 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 165.8, 146.4, 139.3, 138.8, 137.4, 134.2, 130.1, 129.5, 128.9, 128.6, 126.0, 125.7, 118.1, 113.9, 55.0, 51.3, 25.4, 21.6.
MS (EI, 70 eV): m/z (%) = 291 (100), 263 (30), 251 (10), 235 (54), 234 (37), 220 (39), 220 (10), 191 (31), 177 (16), 165 (15), 165 (11), 164 (34).
HRMS (EI): for $C_{19}H_{20}N_2O$: calc. [M+]: 291.1497; found: 291.1491.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3299 (w), 3034 (w), 2983 (w), 2973 (w), 2964 (w), 2944 (w), 2938 (w), 2924 (w), 2920 (w), 2910 (w), 2898 (w), 2226 (w), 1637 (s), 1600 (m), 1586 (w), 1564 (m), 1552 (m), 1539 (s), 1504 (w), 1488 (w), 1469 (m), 1462 (m), 1456 (m), 1440 (m), 1424 (m), 1400 (w), 1385 (m), 1365 (m), 1333 (m), 1300 (m), 1257 (m), 1098 (w), 1076 (w), 1048 (w), 1025 (w), 1016 (w), 982 (w), 970 (w), 944 (w), 929 (m), 914 (w), 898 (m), 884 (w), 848 (m), 841 (m), 819 (w), 786 (s), 770 (m), 746 (m), 735 (s), 728 (s), 719 (m), 706 (vs), 694 (m), 675 (s), 669 (s), 652 (m).
Melting point: M.p. = 171 °C.

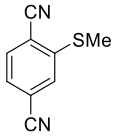
3'-Methyl-[1,1'-biphenyl]-2,5-dicarbonitrile (85r)



According to **TP 6**, to a mixture of 2,2'-(3'-methyl-[1,1'-biphenyl]-2,5-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole) (**83s**, 72 mg, 0.20 mmol, 1.0 equiv) in thionyl chloride (1 mL) was added DMF (0.5 mL) dropwise at 0 °C. The reaction mixture was heated at reflux for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**85r**, 41 mg, 0.188 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.87 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.81 (dd, *J* = 1.6, 0.6 Hz, 1H), 7.71 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.45–7.39 (m, 1H), 7.33 (tdd, *J* = 7.5, 1.9, 0.9 Hz, 3H), 2.47 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 146.9, 139.1, 136.1, 134.5, 133.6, 130.7, 130.6, 129.4, 129.2, 125.9, 117.3, 117.2, 116.8, 115.6, 21.6.
MS (EI, 70 eV): m/z (%) =
HRMS (EI): for $C_8H_3FN_2$: calc. [M+]:; found:.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3100 (w), 3081 (w), 3051 (w), 2946 (w), 2940 (w), 2919 (w), 2902 (w), 2892 (w), 2885 (w), 2854 (w), 2830 (w), 2232 (s), 2206 (w), 2192 (w), 2140 (w), 1932 (w), 1859 (w), 1799 (w), 1738 (w), 1716 (w), 1669 (w), 1610 (w), 1606 (w), 1587 (w), 1550 (w), 1485 (m), 1470 (w), 1463 (w), 1446 (m), 1425 (m), 1408 (w), 1398 (m), 1374 (w), 1320 (w), 1312 (w), 1283 (m), 1265 (s), 1196 (m), 1176 (w), 1163 (w), 1135 (w), 1128 (w), 1096 (w), 1049 (m), 1000 (w), 966 (w), 946 (w), 933 (m), 912 (m), 904 (s), 893 (m), 837 (s), 809 (m), 780 (vs), 755 (w), 744 (m), 731 (w), 712 (s), 700 (vs), 684 (w), 662 (m).
Melting point: M.p. = 180 °C.

2-(Methylthio)terephthalonitrile (85s)

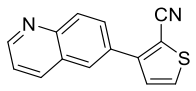


According to **TP 6**, to a mixture of 2,2'-(2-(methylthio)-1,4-phenylene)bis(4,4-dimethyl-4,5-dihydrooxazole) (**83t**, 64 mg, 0.20 mmol, 1.0 equiv) in thionyl chloride (1 mL) was added DMF (0.5 mL) dropwise at 0 °C. The reaction mixture was heated at reflux for 5 h. Purification of the crude

product by flash column chromatography (silica gel, *i*hexane/EtOAc = 8:1) afforded the title compound as a white solid (**85s**, 33 mg, 0.192 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.53–7.45 (m, 2H), 2.61 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 146.4, 134.0, 128.3, 127.9, 117.2, 117.1, 115.4, 114.9, 15.5.
MS (EI, 70 eV): m/z (%) = 174 (100), 173 (70), 160 (18), 159 (21), 147 (11), 146 (35), 142 (27), 141 (69), 132 (12), 129 (14), 128 (31), 114 (15), 101 (11).
HRMS (EI): for $C_9H_6N_2S$: calc. [M+]: 174.0252; found: 174.0246.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2359 (s), 2341 (s), 2327 (s), 1683 (m), 1670 (m), 1653 (s), 1616 (m), 1558 (m), 1521 (m), 1506 (m), 1466 (s), 1457 (m), 1321 (vs), 1318 (vs), 1235 (s), 1165 (s), 1130 (s), 1120 (vs), 1111 (vs), 1083 (s), 1065 (s), 991 (m), 925 (s), 839 (m), 826 (vs), 807 (s).
Melting point: M.p. = 96 °C.

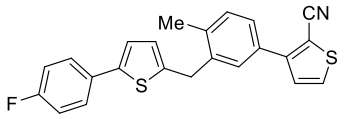
3-(Quinolin-6-yl)thiophene-2-carbonitrile (85t)



According to **TP 6**, to a mixture of 4,4-dimethyl-2-(3-(quinolin-6-yl)thiophen-2-yl)-4,5-dihydrooxazole (**83u**, 62 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a white solid (**85t**, 46 mg, 0.195 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.97 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.30–8.16 (m, 3H), 8.00 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.68 (d, *J* = 5.2 Hz, 1H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.41 (d, *J* = 5.1 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 151.5, 150.6, 148.2, 136.7, 132.5, 131.3, 130.6, 129.1, 128.6, 128.4, 127.3, 122.1, 114.9, 105.3.
MS (EI, 70 eV): m/z (%) = 237 (14), 236 (100), 209 (17), 164 (11).
HRMS (EI): for $C_{14}H_8N_2S$: calc. [M+]: 236.0408; found: 236.0402.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3108 (w), 3057 (w), 3034 (w), 2209 (m), 2188 (vw), 2180 (vw), 2169 (w), 1592 (w), 1570 (w), 1502 (m), 1432 (w), 1404 (m), 1388 (w), 1374 (w), 1346 (w), 1319 (w), 1276 (w), 1242 (vw), 1232 (w), 1186 (w), 1162 (m), 1125 (w), 1105 (vw), 1073 (w), 1050 (vw), 1030 (vw), 958 (w), 920 (m), 897 (m), 856 (m), 838 (vs), 796 (s), 778 (m), 771 (m), 748 (vs), 720 (vw), 706 (w), 678 (m).
Melting point: M.p. = 155 °C.

3-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)thiophene-2-carbonitrile (85u)



According to **TP 6**, to a mixture of 2-(3-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)thiophen-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**83v**, 92 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 10:1) afforded the title compound as a white solid (**85u**, 57 mg, 0.195 mmol, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.61–7.44 (m, 6H), 7.33–7.26 (m, 2H), 7.08–6.98 (m, 3H), 6.76–6.70 (m, 1H), 4.19 (s, 2H), 2.38 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.4, 161.0, 151.5, 142.7, 141.8, 139.2, 138.0, 132.0, 131.4, 131.3, 130.9 (d, J = 3.3 Hz), 128.9, 128.4, 127.3 (d, J = 8.0 Hz), 126.4 (d, J = 4.3 Hz), 122.9 (d, J = 1.3 Hz), 115.8 (d, J = 21.7 Hz), 115.1, 104.1, 34.2, 19.5.

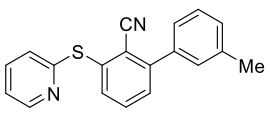
MS (EI, 70 eV): m/z (%) = 391 (10), 390 (29), 389 (29), 388 (13), 374 (18), 212 (17), 211 (100), 210 (21), 196 (16), 191 (76), 189 (11), 184 (11), 178 (26), 171 (11), 152 (10), 139 (32), 133 (40), 127 (10), 45 (39).

HRMS (EI): for $C_{23}H_{16}FNS_2$: calc. [M+]: 389.0708; found: 389.0708.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3105 (w), 3037 (vw), 2988 (vw), 2962 (vw), 2918 (w), 2891 (w), 2884 (vw), 2858 (w), 2851 (w), 2210 (m), 2186 (w), 2176 (w), 2168 (w), 2159 (w), 2142 (vw), 2129 (vw), 1881 (vw), 1634 (vw), 1600 (w), 1573 (vw), 1548 (w), 1529 (vw), 1507 (vs), 1468 (m), 1439 (m), 1421 (m), 1376 (w), 1362 (w), 1300 (w), 1276 (vw), 1256 (vw), 1229 (vs), 1180 (w), 1158 (s), 1128 (w), 1096 (m), 1080 (w), 1045 (w), 1032 (w), 1012 (w), 999 (vw), 955 (w), 891 (w), 856 (m), 831 (vs), 798 (vs), 774 (w), 742 (vs), 709 (w), 685 (w), 665 (w).

Melting point: M.p. = 154 °C.

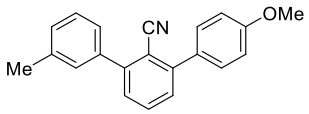
3'-Methyl-3-(pyridin-2-ylthio)-[1,1'-biphenyl]-2-carbonitrile (86a)



According to **TP 6**, to a mixture of 4,4-dimethyl-2-(3'-methyl-3-(pyridin-2-ylthio)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**84a**, 75 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**86a**, 59 mg, 0.194 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.36 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.62 – 7.45 (m, 3H), 7.39 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.27 (d, *J* = 5.6 Hz, 3H), 7.20 – 7.11 (m, 2H), 7.00 (dd, *J* = 7.5, 4.9 Hz, 1H), 2.33 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.6, 150.2, 147.9, 138.5, 138.0, 137.2, 137.0, 133.9, 132.7, 130.2, 129.7, 129.6, 128.7, 126.1, 123.4, 121.3, 116.7, 116.5, 21.6.
MS (EI, 70 eV): m/z (%) = 302 (19), 301 (100), 287 (10), 276 (13).
HRMS (EI): for $C_{19}H_{14}N_2S$: calc. [M-H$^+$]: 301.0799; found: 301.0794.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3019 (vw), 2979 (w), 2972 (w), 2967 (w), 2939 (w), 2909 (w), 2896 (w), 2889 (w), 2866 (w), 2849 (w), 2836 (w), 2481 (w), 2358 (w) 1755 (vw), 1670 (w), 1650 (w), 1594 (m), 1584 (w), 1572 (w), 1566 (w), 1552 (w), 1529 (vw), 1511 (s), 1499 (w), 1482 (w), 1463 (vw), 1452 (s), 1439 (m), 1427 (m), 1411 (w), 1400 (w), 1390 (w), 1377 (w), 1356 (w), 1322 (vw), 1317 (w), 1301 (m), 1274 (m), 1239 (s), 1209 (w), 1203 (w), 1185 (s), 1162 (w), 1111 (w), 1090 (w), 1084 (w), 1069 (w), 1047 (m), 1028 (s), 988 (w), 981 (w), 973 (w), 954(w), 944(w), 914 (w), 906 (w), 881 (w), 872 (w), 862 (m), 855 (m), 820 (s), 807 (m), 778 (vs), 764 (s), 751 (m), 735 (w), 710 (s).
Melting point: M.p. = 85 °C.

4''-Methoxy-3-methyl-[1,1':3',1''-terphenyl]-2'-carbonitrile (86b)



According to **TP 6**, to a mixture of 2-(4''-methoxy-3-methyl-[1,1':3',1''-terphenyl]-2'-yl)-4,4-dimethyl-4,5-dihydrooxazole (**84b**, 74 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**86b**, 56 mg, 0.188 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.63 (t, *J* = 7.8 Hz, 1H), 7.57–7.52 (m, 2H), 7.43 (ddd, *J* = 7.6, 6.4, 1.2 Hz, 2H), 7.40–7.38 (m, 3H), 7.28–7.26 (m, 1H), 7.05–7.00 (m, 2H), 3.87 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.0, 147.1, 146.6, 138.7, 138.3, 132.2, 131.0, 130.3, 129.8, 129.4, 128.6, 128.5, 128.4, 126.1, 118.3, 114.1, 110.2, 55.4, 21.5.

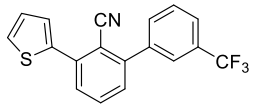
MS (EI, 70 eV): m/z (%) = 299 (100), 298 (55), 284 (31), 283 (11), 255 (27), 254 (20), 241 (29), 240 (26).

HRMS (EI): for $C_{21}H_{17}NO$: calc. [M+]: 299.1310; found: 299.1305.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2957 (w), 2953 (w), 2945 (w), 2921 (w), 2920 (w), 2896 (w), 2877 (w), 2874 (w), 2871 (w), 2853 (w), 2844 (w), 2220 (w), 1733 (vw), 1662 (w), 1660 (w), 1652 (w), 1609 (m), 1581 (w), 1577 (w), 1575 (w), 1559 (w), 1558 (vw), 1515 (s), 1496 (w), 1490 (w), 1475 (vw), 1455 (s), 1442 (m), 1436 (m), 1419 (w), 1404 (w), 1394 (w), 1375 (w), 1364 (w), 1323 (vw), 1307 (w), 1298 (m), 1283 (m), 1247 (s), 1211 (w), 1202 (w), 1178 (s), 1151 (w), 1121 (w), 1110 (m), 1093 (w), 1077 (w), 1067 (w), 1043 (m), 1024 (s), 999 (w), 988 (w), 985 (w), 980 (w), 964 (w), 950 (w), 932 (vw), 917 (w), 907 (w), 888 (w), 872 (w), 833 (m), 828 (s), 809 (m), 804 (m), 785 (vs), 770 (s), 751 (m), 735 (w), 726 (w), 717 (w), 712 (w), 703 (s).

Melting point: M.p. = 83 °C.

3-(Thiophen-2-yl)-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-carbonitrile (86c)



According to **TP 6**, to a mixture of 4,4-dimethyl-2-(3-(thiophen-2-yl)-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**84c**, 80 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**86c**, 62 mg, 0.188 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.80 (t, *J* = 3.8 Hz, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.69 – 7.61 (m, 4H), 7.47 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.43 (dd, *J* = 6.3, 2.6 Hz, 1H), 7.18 (dd, *J* = 5.1, 3.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 146.0, 139.4, 139.3, 132.8, 132.5, 131.3 (q, *J* = 26.9 Hz), 129.6, 129.3, 129.1, 128.4, 128.4, 127.8, 126.0 (q, *J* = 3.8 Hz), 125.7 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 270.8 Hz), 117.8, 109.7.

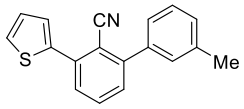
MS (EI, 70 eV): m/z (%) = 330 (19), 329 (100), 328 (31), 308 (25), 261 (13), 260 (74), 259 (12).

HRMS (EI): for $C_{18}H_{10}F_3NS$: calc. [M+]: 329.0486; found: 329.0482.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3115 (vw), 3065 (vw), 2959 (vw), 2924 (vw), 2854 (vw), 2221 (w), 1812 (vw), 1732 (vw), 1615 (vw), 1574 (w), 1521 (vw), 1490 (vw), 1466 (w), 1432 (m), 1334 (s),

1280 (m), 1255 (m), 1226 (w), 1188 (w), 1158 (m), 1136 (m), 1101 (s), 1071 (s), 1057 (m), 995 (m), 918 (w), 907 (m), 859 (m), 845 (w), 807 (w), 799 (s), 711 (s), 706 (m), 675 (m).
Melting point: M.p. = 112 °C.

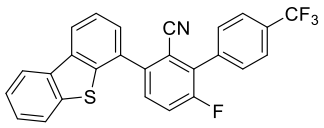
3'-Methyl-3-(thiophen-2-yl)-[1,1'-biphenyl]-2-carbonitrile (86d)



According to **TP 6**, to a mixture of 4,4-dimethyl-2-(3'-methyl-3-(thiophen-2-yl)-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (**84d**, 4.031 g, 11.60 mmol, 1.0 equiv) in oxalyl chloride (30 mL) was added DMF (0.18 mL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) afforded the title compound as a yellow solid (**86d**, 3.086 g, 11.21 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.65–7.56 (m, 3H), 7.45 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.43–7.35 (m, 4H), 7.30–7.26 (m, 1H), 7.17 (dd, *J* = 5.1, 3.7 Hz, 1H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.9, 139.8, 139.0, 138.6, 138.4, 132.5, 129.8, 129.7, 129.2, 128.8, 128.6, 128.3, 128.2, 127.4, 126.2, 118.2, 109.7, 21.6.
MS (EI, 70 eV): m/z (%) = 276 (11), 275 (60), 274 (100), 456 (100), 228 (10), 227 (19).
HRMS (EI): for $C_{18}H_{13}NS$: calc. [M-H$^+$]: 274.0691; found: 274.0687.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3035 (vw), 2957 (w), 2922 (vw), 2897 (w), 2874 (vw), 2359 (vw), 2219 (w), 2166 (w), 2156 (w), 1593 (m), 1559 (w), 1502 (m), 1490 (m), 1454 (m), 1436 (w), 1407 (w), 1394 (w), 1350 (w), 1332 (w), 1244 (s), 1226 (s), 1182 (w), 1124 (w), 1102 (w), 1078 (vw), 1038 (m), 1022 (w), 937 (w), 913 (m), 891 (w), 860 (s), 838 (vs), 811 (s), 784 (m), 760 (s), 729 (s), 696 (s), 673 (m), 668 (m).
Melting point: M.p. = 98 °C.

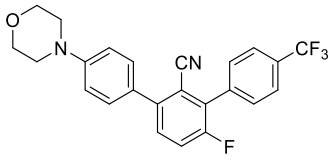
3-(Dibenzo[*b,d*]thiophen-4-yl)-6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carbonitrile (86e)



According to **TP 6**, to a mixture of 2-(3-(dibenzo[*b,d*]thiophen-4-yl)-6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**84e**, 104 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 92:8) afforded the title compound as a yellow solid (**86e**, 86 mg, 0.192 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.26 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.24–8.19 (m, 1H), 7.87–7.76 (m, 4H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.59–7.47 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 139.5, 139.3, 136.6, 135.7, 135.3, 133.0, 132.8, 132.3, 131.7, 131.6, 131.5, 131.4, 130.6 (d, *J* = 1.7 Hz), 127.9, 127.4, 125.8 (q, *J* = 3.9 Hz), 125.1 (d, *J* = 24.7 Hz), 124.0 (q, *J* = 275.0 Hz), 122.9, 122.3 (d, *J* = 22.2 Hz), 120.9 (d, *J* = 23.1 Hz), 116.0, 114.1.
MS (EI, 70 eV): m/z (%) = 448 (28), 447 (100), 446 (36), 445 (13), 426 (10), 379 (23), 378 (87), 377 (50), 376 (16), 375 (16), 225 (21), 214 (17), 213 (62), 207 (30), 189 (43), 188 (37), 187 (21), 139 (20), 73 (13).
HRMS (EI): for $C_{26}H_{13}F_4NS$: calc. [M+]: 447.0705; found: 447.0700.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3074 (vw), 2924 (vw), 2854 (vw), 2360 (vw), 2226 (vw), 1620 (w), 1576 (vw), 1490 (vw), 1470 (w), 1456 (vw), 1443 (w), 1418 (w), 1404 (vw), 1378 (w), 1327 (s), 1310 (m), 1288 (w), 1268 (m), 1254 (m), 1194 (w), 1173 (s), 1108 (vs), 1071 (s), 1060 (m), 1050 (w), 1022 (m), 969 (m), 934 (w), 910 (vw), 863 (w), 837 (s), 799 (m), 790 (w), 772 (vw), 763 (w), 748 (vs), 726 (m), 719 (w), 706 (w), 684 (m), 668 (w), 663 (w), 652 (w).
Melting point: M.p. = 236 °C.

4'-Fluoro-4-morpholino-4''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-2'-carbonitrile (86f)



According to **TP 6**, to a mixture of 4-(2'-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-4'-fluoro-4''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4-yl)morpholine (**84f**, 50 mg, 0.10 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a white solid (**86f**, 40 mg, 0.094 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.82–7.76 (m, 2H), 7.65 (dq, *J* = 7.7, 1.0 Hz, 2H), 7.54–7.41 (m, 4H), 7.05–6.98 (m, 2H), 3.92–3.86 (m, 4H), 3.30–3.22 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.4, 156.9, 151.6, 143.3 (d, *J* = 3.9 Hz), 135.7, 132.4 (d, *J* = 18.0 Hz), 131.5, 131.3 (d, *J* = 8.4 Hz), 131.2, 130.6 (d, *J* = 1.6 Hz), 130.0, 128.3, 125.7 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 270.4 Hz), 120.7 (d, *J* = 22.8 Hz), 117.0 (d, *J* = 3.9 Hz), 115.3, 112.4 (d, *J* = 4.0 Hz), 66.9, 48.7.

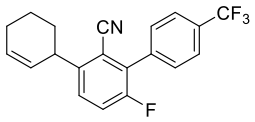
MS (EI, 70 eV): m/z (%) = 426 (26), 368 (35), 340 (16), 299 (13), 281 (32), 265 (10), 226 (10), 225 (77), 208 (13), 207 (100), 191 (21).

HRMS (EI): for $C_{24}H_{18}F_4N_2O$: calc. [M^+]: 426.1355; found: 426.1352.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2850 (m), 1702 (s), 1691 (s), 1679 (vs), 1660 (vs), 1650 (s), 1641 (m), 1630 (s), 1613 (m), 1483 (s), 1357 (m), 1314 (m), 1245 (m), 1239 (m), 1137 (m), 986 (s), 796 (s), 773 (m), 766 (m).

Melting point: M.p. = 167 °C.

4'-Fluoro-4''-(trifluoromethyl)-1,2,3,4-tetrahydro-[1,1':3',1''-terphenyl]-2'-carbonitrile (86g)



According to **TP 6**, to a mixture of 2-(4'-fluoro-4''-(trifluoromethyl)-1,2,3,4-tetrahydro-[1,1':3',1''-terphenyl]-2'-yl)-4,4-dimethyl-4,5-dihydrooxazole (**84g**, 42 mg, 0.10 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 96:4) afforded the title compound as a white solid (**86g**, 28 mg, 0.082 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.82–7.73 (m, 2H), 7.65–7.59 (m, 2H), 7.45–7.32 (m, 2H), 6.04 (dtd, *J* = 9.9, 3.7, 2.2 Hz, 1H), 5.71–5.61 (m, 1H), 3.93 (ddp, *J* = 8.3, 5.5, 2.8 Hz, 1H), 2.25–2.09 (m, 3H), 1.71 (qtd, *J* = 13.4, 6.8, 3.8 Hz, 2H), 1.53 (ddd, *J* = 9.4, 8.1, 3.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.7 (d, *J* = 247.8 Hz), 147.6 (d, *J* = 3.8 Hz), 135.8 (d, *J* = 1.5 Hz), 131.8 – 131.6 (m), 131.3 (d, *J* = 32.7 Hz), 130.7, 130.5 (d, *J* = 1.7 Hz), 129.7 (d, *J* = 8.4 Hz), 127.8, 125.7 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 272.9 Hz), 120.6 (d, *J* = 22.6 Hz), 116.0 (d, *J* = 4.0 Hz), 113.4 (d, *J* = 4.0 Hz), 39.9, 31.7, 24.9, 20.8.

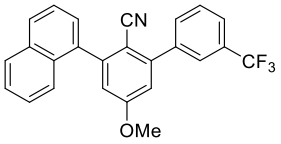
MS (EI, 70 eV): m/z (%) = 345 (20), 344 (100), 316 (28), 248 (5).

HRMS (EI): for $C_{20}H_{15}F_4N$: calc. [M-H^+]: 344.1062; found: 344.1056.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2921 (w), 2863 (w), 2840 (w), 2228 (w), 1620 (w), 1473 (m), 1434 (w), 1405 (w), 1328 (s), 1310 (m), 1282 (w), 1265 (m), 1253 (m), 1193 (w), 1169 (s), 1119 (vs), 1109 (vs), 1066 (s), 1019 (s), 986 (w), 969 (m), 904 (w), 889 (w), 854 (w), 837 (s), 752 (w), 727 (m), 691 (w).

Melting point: M.p. = 129 °C.

5-Methoxy-3-(naphthalen-1-yl)-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-carbonitrile (86h)



According to **TP xx**, to a mixture of 2-(5-methoxy-3-(naphthalen-1-yl)-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**84h**, 95 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**86h**, 75 mg, 0.186 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.96 (tt, *J* = 8.0, 1.1 Hz, 2H), 7.90–7.84 (m, 2H), 7.73 (dt, *J* = 8.2, 1.1 Hz, 1H), 7.67–7.47 (m, 6H), 7.07 (q, *J* = 2.5 Hz, 2H), 3.93 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.0, 148.0, 146.7, 139.3, 136.1, 133.7, 132.4, 131.4, 131.2 (q, *J* = 32.3 Hz), 129.3, 129.2, 128.6, 127.4, 126.8, 126.2, 125.8 (q, *J* = 3.8 Hz), 125.6 (q, *J* = 3.8 Hz), 125.2 (d, *J* = 1.7 Hz), 123.9 (q, *J* = 272.5 Hz), 117.4, 116.2, 115.2, 104.6, 55.9.

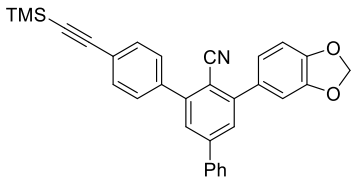
MS (EI, 70 eV): m/z (%) = 404 (25), 403 (100), 402 (22), 382 (22), 359 (12), 352 (14), 334 (17), 332 (14), 291 (10).

HRMS (EI): for $C_{25}H_{16}F_3NO$: calc. [M+]: 403.1184; found: 403.1180.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3056 (w), 3005 (w), 2933 (w), 2853 (w), 2224 (w), 2223 (w), 2218 (m), 2213 (w), 1732 (w), 1586 (s), 1567 (m), 1508 (w), 1492 (w), 1463 (m), 1415 (m), 1394 (m), 1347 (s), 1321 (s), 1312 (s), 1217 (s), 1200 (m), 1166 (s), 1152 (s), 1143 (m), 1120 (vs), 1098 (s), 1073 (s), 1057 (m), 1055 (m), 1037 (m), 1024 (m), 999 (w), 993 (m), 905 (m), 873 (m), 861 (m), 802 (s), 790 (m), 789 (m), 777 (vs), 766 (m), 763 (w), 723 (w), 718 (m), 703 (s), 671 (m).

Melting point: M.p. = 130 °C.

5'-(Benzo[*d*][1,3]dioxol-5-yl)-4''-((trimethylsilyl)ethynyl)-[1,1':3',1''-terphenyl]-4'-carbonitrile (86i)



According to **TP 6**, to a mixture of 2-(5'-(benzo[*d*][1,3]dioxol-5-yl)-4''-((trimethylsilyl)ethynyl)-[1,1':3',1''-terphenyl]-4'-yl)-4,4-dimethyl-4,5-dihydrooxazole (**84i**, 54 mg, 0.10 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a colorless oil (**86i**, 44 mg, 0.093 mmol, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.69–7.56 (m, 8H), 7.53–7.42 (m, 3H), 7.13–7.08 (m, 2H), 6.97–6.92 (m, 1H), 6.04 (s, 2H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.4, 148.0, 147.3, 146.7, 145.3, 139.0, 138.7, 132.5, 132.3, 129.3, 129.1, 129.0, 127.8, 127.5, 127.2, 123.8, 123.2, 118.1, 109.6, 108.9, 108.7, 104.6, 101.6, 95.9, 0.1.

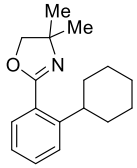
MS (EI, 70 eV): m/z (%) = 472 (20), 471 (59), 457 (31), 456 (100), 228 (10), 227 (19).

HRMS (EI): for $C_{31}H_{25}NO_2Si$: calc. [M+]: 471.1655; found: 471.1648.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 3035 (vw), 2957 (w), 2922 (vw), 2897 (w), 2874 (vw), 2359 (vw), 2219 (w), 2166 (w), 2156 (w), 1593 (m), 1559 (w), 1502 (m), 1490 (m), 1454 (m), 1436 (w), 1407 (w), 1394 (w), 1350 (w), 1332 (w), 1244 (s), 1226 (s), 1182 (w), 1124 (w), 1102 (w), 1078 (vw), 1038 (m), 1022 (w), 937 (w), 913 (m), 891 (w), 860 (s), 838 (vs), 811 (s), 784 (m), 760 (s), 729 (s), 696 (s), 673 (m), 668 (m).

Melting point: M.p. = 82 °C.

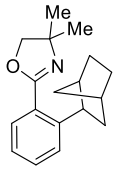
2-(2-Cyclohexylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (89a)



2-(2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**88a**, 1.03 g, 5.00 mmol, 1.0 equiv) was dissolved in THF (10 mL) and *c*HexMgCl (5 mL, 2 M in Et_2O, 10 mmol, 2.0 equiv) was added dropwise at room temperature. The reaction mixture was stirred for 1 h at room temperature and was quenched with brine. The aqueous layer was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**89a**, 1.23 g, 4.8 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.59–7.53 (m, 1H), 7.40–7.29 (m, 2H), 7.18 (td, *J* = 7.4, 1.5 Hz, 1H), 4.08 (s, 2H), 3.24 (ddt, *J* = 11.6, 6.1, 3.1 Hz, 1H), 1.95–1.70 (m, 6H), 1.46–1.34 (m, 10H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.3, 147.6, 130.5, 129.7, 127.8, 126.2, 125.5, 79.0, 68.0, 40.5, 34.3, 28.5, 27.2, 26.4.
Analytical data was equivalent to literature.[213]

2-(2-((2*S*)-Bicyclo[2.2.1]heptan-2-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (89b)



2-(2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**88a**, 0.205 g, 1.00 mmol, 1.0 equiv) was dissolved in THF (2 mL) and ((2*S*)-bicyclo[2.2.1]heptan-2-yl)magnesium bromide (2.38 mL, 0.84 M in Et_2O, 2 mmol, 2.0 equiv) was added dropwise at room temperature. The reaction mixture was stirred for 1 h at room temperature and was quenched with brine. The aqueous layer was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) afforded the title compound as a colorless oil (**89b**, 0.218 g, 0.81 mmol, 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.58 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.38–7.32 (m, 2H), 7.17 (ddd, *J* = 7.6, 6.1, 2.6 Hz, 1H), 4.08 (s, 2H), 3.44–3.37 (m, 1H), 2.38–2.31 (m, 2H), 1.74 (ddd, *J* = 11.7, 9.0, 2.3 Hz, 1H), 1.68–1.50 (m, 5H), 1.39 (s, 6H), 1.26 (tdd, *J* = 7.8, 3.6, 1.6 Hz, 1H), 1.17 (dtd, *J* = 9.7, 2.9, 1.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.6, 146.9, 130.3, 130.1, 128.5, 125.9, 125.2, 79.1, 67.9, 43.8, 43.1, 39.0, 37.1, 36.3, 30.6, 29.2, 28.6, 28.5.

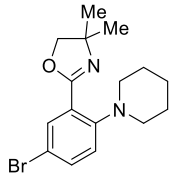
[213] G. Cahiez, F. Lepifre, P. Ramiandrasoa, *Synthesis* **1999**, *12*, 2138-2144.

MS (EI, 70 eV): m/z (%) = 269 (16), 241 (16), 240 (100), 228 (18), 214 (23), 213 (55), 200 (11), 169 (16), 168 (73), 158 (52), 141 (19), 115 (23).

HRMS (EI): for $C_{18}H_{23}NO$: calc. [M-H$^+$]: 269.1780; found: 269.1777.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2868 (m), 1643 (s), 1488 (w), 1475 (w), 1451 (m), 1363 (w), 1347 (m), 1305 (m), 1267 (w), 1247 (w), 1204 (m), 1191 (m), 1108 (w), 1058 (w), 1033 (vs), 990 (w), 966 (m), 920 (m), 867 (w), 766 (m), 758 (m), 749 (m), 728 (m), 695 (m).

2-(5-Bromo-2-(piperidin-1-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (89c)



Piperidine (60 µL, 0.60 mmol, 1.2 equiv) was dissolved in THF (1 mL) and *n*BuLi (0.37 mL, 1.62 M in cyclohexane, 0.60 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and added to a solution of 2-(5-bromo-2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**88b**, 0.142 g, 0.5 mmol, 1.0 equiv) in THF (1 mL) at room temperature. The reaction mixture was stirred for 0.5 h and quenched with brine. The aqueous layer was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**89c**, 103 mg, 0.31 mmol, 62% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.73 (d, *J* = 2.5 Hz, 1H), 7.40 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 1H), 4.08 (s, 2H), 3.00–2.93 (m, 4H), 1.69 (p, *J* = 5.6 Hz, 4H), 1.56 (m, 2H), 1.38 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.7, 151.8, 134.3, 134.2, 123.1, 119.9, 113.0, 79.4, 67.4, 53.2, 28.5, 26.1, 24.3.

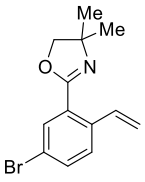
MS (EI, 70 eV): m/z (%) = 337 (21), 335 (23), 281 (65), 279 (69), 266 (20), 252 (39), 250 (41), 225 (100), 223 (96), 183 (33), 155 (30), 130 (29).

HRMS (EI): for $C_{16}H_{21}BrN_2O$: calc. [M-H$^+$]: 335.0759; found: 335.0756.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1631 (m), 1478 (s), 1470 (s), 1461 (s), 1452 (s), 1444 (s), 1382 (s), 1232 (m), 1197 (m), 1172 (m), 1108 (s), 1036 (m), 1023 (s), 985 (s), 926 (vs), 877 (s), 847 (m), 833 (vs).

Melting point: M.p. = 75 °C.

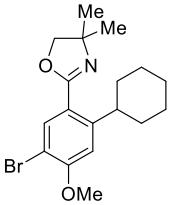
2-(5-Bromo-2-vinylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (89d)



2-(5-bromo-2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**88b**, 0.142 g, 0.5 mmol, 1.0 equiv) was dissolved in THF (1 mL) and vinylmagnesium bromide (0.8 mL, 1 M in THF, 0.80 mmol, 1.6 equiv) was added dropwise at room temperature. The reaction mixture was stirred for 1 h at room temperature and was quenched with brine. The aqueous layer was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 3:1) afforded the title compound as a colorless oil (**89d**, 125 mg, 0.45 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.91 (d, *J* = 2.1 Hz, 1H), 7.54–7.37 (m, 3H), 5.70 (dd, *J* = 17.5, 1.2 Hz, 1H), 5.34 (dd, *J* = 10.9, 1.2 Hz, 1H), 4.08 (s, 2H), 1.39 (d, *J* = 0.9 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.0, 136.9, 134.6, 133.7, 132.8, 128.2, 127.9, 121.2, 116.5, 79.1, 68.4, 28.5.
MS (EI, 70 eV): m/z (%) = 281 (24), 280 (100), 279 (24), 278 (98), 223 (25), 145 (21), 102 (19), 55 (31), 42 (87).
HRMS (EI): for $C_{13}H_{14}BrNO$: calc. [M-H$^+$]: 278.0181; found: 278.0175.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1641 (s), 1583 (m), 1481 (s), 1462 (m), 1363 (m), 1347 (m), 1300 (s), 1260 (m), 1211 (m), 1197 (m), 1096 (m), 1041 (vs), 1031 (s), 988 (s), 966 (s), 915 (s), 896 (m), 880 (m), 826 (vs), 796 (s).

2-(5-Bromo-2-cyclohexyl-4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (89f)

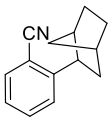


2-(5-bromo-2,4-dimethoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**88c**, 1.26 g, 4.00 mmol, 1.0 equiv) was dissolved in THF (10 mL) and *c*HexMgCl (3.2 mL, 2 M in Et_2O, 10 mmol, 1.6 equiv) was added dropwise at room temperature. The reaction mixture was stirred for 1 h at room temperature and

was quenched with brine. The aqueous layer was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a white solid (**89f**, 1.09 g, 2.98 mmol, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.83 (s, 1H), 6.81 (s, 1H), 4.04 (s, 2H), 3.92 (s, 3H), 3.42 (ddd, *J* = 11.4, 8.3, 3.0 Hz, 1H), 1.92–1.80 (m, 5H), 1.80–1.72 (m, 1H), 1.37 (m, 10H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.7, 157.4, 149.5, 134.7, 121.3, 109.6, 108.1, 78.8, 68.0, 56.3, 40.3, 34.3, 28.5, 27.0, 26.3.
MS (EI, 70 eV): m/z (%) = 366 (22), 312 (33), 311 (52), 309 (58), 283 (31), 267 (97), 265 (100), 254 (41), 196 (47), 115 (42).
HRMS (EI): for $C_{18}H_{24}BrNO_2$: calc. [M-H$^+$]: 364.0912; found: 364.0911.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1640 (vs), 1632 (m), 1589 (s), 1492 (s), 1459 (s), 1446 (s), 1377 (m), 1344 (m), 1318 (m), 1305 (s), 1262 (s), 1252 (s), 1188 (s), 1183 (s), 1057 (s), 1044 (vs), 991 (s), 969 (s), 903 (s), 844 (s), 694 (s).
Melting point: M.p. = 90 °C.

2-((2*S*)-Bicyclo[2.2.1]heptan-2-yl)benzonitrile (90a)

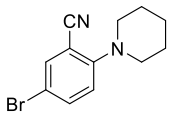


According to **TP 6**, to a mixture of 2-(2-((2*S*)-bicyclo[2.2.1]heptan-2-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (**89b**, 54 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a colorless oil (**90a**, 38 mg, 0.193 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.60 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.50 (td, *J* = 7.8, 1.5 Hz, 1H), 7.37 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.23 (td, *J* = 7.6, 1.2 Hz, 1H), 3.13 (dd, *J* = 9.2, 5.5 Hz, 1H), 2.44–2.36 (m, 2H), 1.98 (ddd, *J* = 11.8, 9.1, 2.4 Hz, 1H), 1.71–1.43 (m, 5H), 1.39–1.23 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 151.5, 133.2, 132.7, 125.9, 118.7, 112.6, 45.6, 42.5, 38.8, 37.0, 36.5, 30.5, 28.7.
MS (EI, 70 eV): m/z (%) = 196 (15), 182 (18), 180 (10), 169 (13), 168 (18), 130 (100), 129 (21), 115 (12).
HRMS (EI): for $C_{14}H_{15}N$: calc. [M-H$^+$]: 196.1126; found: 196.1120.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2869 (m), 2221 (m), 1598 (w), 1481 (w), 1475 (w), 1448 (m), 1312 (w), 1298 (w), 1212 (w), 1034 (w), 756 (vs), 741 (m).

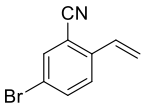
5-Bromo-2-(piperidin-1-yl)benzonitrile (90b)



According to **TP 6**, to a mixture of 2-(5-bromo-2-(piperidin-1-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (**89c**, 644 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 199:1) afforded the title compound as a white solid (**90b**, 48 mg, 0.180 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.62 (d, *J* = 2.4 Hz, 1H), 7.52 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.85 (d, *J* = 8.9 Hz, 1H), 3.19–3.11 (m, 4H), 1.76 (p, *J* = 5.8 Hz, 4H), 1.66–1.57 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 155.9, 136.7, 136.4, 120.4, 117.4, 112.6, 107.3, 53.1, 26.1, 24.0.
MS (EI, 70 eV): m/z (%) = 266 (48), 265 (98), 264 (48), 263 (100), 236 (68), 234 (71), 209 (32), 207 (34), 182 (57), 180 (60).
HRMS (EI): for $C_{12}H_{13}BrN_2$: calc. [M-H$^+$]: 263.0184; found: 263.0179.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2221 (m), 1586 (m), 1485 (vs), 1463 (m), 1450 (s), 1442 (m), 1391 (m), 1379 (s), 1357 (m), 1342 (m), 1280 (m), 1271 (m), 1261 (w), 1231 (vs), 1214 (m), 1177 (m), 1155 (m), 1128 (s), 1105 (m), 1025 (m), 923 (m), 881 (m), 858 (m), 846 (m).
Melting point: M.p. = 102 °C.

5-Bromo-2-vinylbenzonitrile (90c)

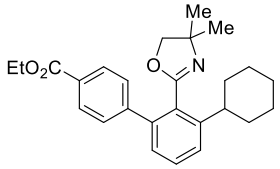


According to **TP 6**, to a mixture of 2-(5-bromo-2-vinylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**89d**, 56 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a white solid (**xxc**, 38 mg, 0.18 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.75 (d, *J* = 2.1 Hz, 1H), 7.67 (ddd, *J* = 8.5, 2.1, 0.6 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.01 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.95 (d, *J* = 17.4 Hz, 1H), 5.58 (d, *J* = 11.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 139.7, 136.2, 135.3, 132.1, 127.0, 121.5, 119.8, 116.5, 112.9.
MS (EI, 70 eV): m/z (%) = 208 (55), 206 (54), 128 (65), 127 (13), 101 (18), 83 (25), 61 (15), 42 (100).
HRMS (EI): for C_9H_6BrN: calc. [M^+]: 206.9684; found: 206.9676.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2224 (m), 1931 (w), 1863 (w), 1753 (w), 1630 (w), 1585 (m), 1573 (w), 1546 (w), 1470 (m), 1461 (m), 1452 (m), 1433 (w), 1427 (w), 1417 (m), 1402 (w), 1385 (m), 1366 (w), 1315 (w), 1287 (w), 1277 (w), 1266 (m), 1257 (w), 1249 (w), 1210 (w), 1172 (m), 1108 (s), 1080 (m), 1028 (m), 985 (s), 967 (w), 926 (vs), 877 (s), 847 (s), 833 (vs), 756 (w).
Melting point: M.p. = 66 °C.

Ethyl 3'-cyclohexyl-2'-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-[1,1'-biphenyl]-4-carboxylate (91)



According to **TP 4**, to a mixture of 2-(2-cyclohexylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**89a**, 129 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added *s*Bu_2Mg (**58**, 0.40 mmol, 0.8 equiv) at 60 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.55 mL, 1.00 M in THF, 1.10 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dppf)Cl_2$ (18 mg, 5 mol%) and 4-iodo ethylbenzoate (70 µL, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 18 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 7:1) afforded the title compound as a brown oil (**91**, 133 mg, 0.33 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.08–8.02 (m, 2H), 7.53–7.48 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.34 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.17 (dd, *J* = 7.5, 1.3 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 2H), 2.80 (tt, *J* = 11.8, 3.2 Hz, 1H), 1.98–1.70 (m, 6H), 1.34 (dt, *J* = 61.6, 7.1 Hz, 7H), 1.18 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.8, 161.6, 147.3, 146.1, 141.0, 129.8, 129.2, 129.1, 127.7, 127.0, 125.5, 79.1, 68.0, 61.1, 41.5, 34.4, 28.1, 27.2, 26.3, 14.5.

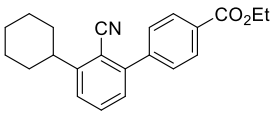
MS (EI, 70 eV): m/z (%) = 333 (33), 332 (100), 305 (15), 304 (79), 288 (42), 232 (19), 217 (13), 216 (15), 204 (33), 203 (27), 190 (11).

HRMS (EI): for $C_{22}H_{23}NO_2$: calc. [M+]: 333.1729; found: 333.1716.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2925 (m), 2910 (w), 2888 (w), 2850 (w), 2231 (w), 2222 (w), 2210 (w), 2185 (w), 2180 (w), 2166 (m), 1707 (s), 1674 (w), 1608 (w), 1588 (w), 1576 (w), 1461 (w), 1445 (m), 1404 (w), 1395 (w), 1370 (w), 1302 (w), 1275 (s), 1258 (m), 1182 (m), 1172 (m), 1112 (m), 1102 (s), 1020 (m), 1001 (w), 982 (w), 864 (w), 850 (w), 808 (m), 770 (vs), 754 (m), 718 (w), 708 (s), 692 (w).

Melting point: M.p. = 113 °C.

Ethyl 2'-cyano-3'-cyclohexyl-[1,1'-biphenyl]-4-carboxylate (92)



According to **TP 6**, to a mixture of ethyl 3'-cyclohexyl-2'-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-[1,1'-biphenyl]-4-carboxylate (**91**, 81 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 4 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 7:1) afforded the title compound as a white solid (**92**, 66 mg, 0.198 mmol, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.21–8.13 (m, 2H), 7.65–7.56 (m, 3H), 7.41 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.31 (dd, *J* = 7.7, 1.1 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.11 (ddt, *J* = 11.6, 8.3, 3.4 Hz, 1H), 2.05–1.76 (m, 6H), 1.55–1.45 (m, 3H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.35–1.21 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.4, 152.9, 145.2, 143.4, 132.7, 130.6, 129.9, 129.1, 127.5, 125.8, 117.3, 111.0, 61.3, 43.1, 34.0, 26.7, 26.1, 14.5.

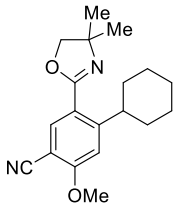
MS (EI, 70 eV): m/z (%) = 333 (33), 332 (100), 305 (15), 304 (79), 288 (42), 232 (19), 217 (13), 216 (15), 204 (33), 203 (27), 190 (11).

HRMS (EI): for $C_{22}H_{23}NO_2$: calc. [M+]: 333.1729; found: 333.1716.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2925 (m), 2910 (w), 2888 (w), 2850 (w), 2231 (w), 2222 (w), 2210 (w), 2185 (w), 2180 (w), 2166 (m), 1707 (s), 1674 (w), 1608 (w), 1588 (w), 1576 (w), 1461 (w), 1445 (m), 1404 (w), 1395 (w), 1370 (w), 1302 (w), 1275 (s), 1258 (m), 1182 (m), 1172 (m), 1112 (m), 1102 (s), 1020 (m), 1001 (w), 982 (w), 864 (w), 850 (w), 808 (m), 770 (vs), 754 (m), 718 (w), 708 (s), 692 (w).

Melting point: M.p. = 113 °C.

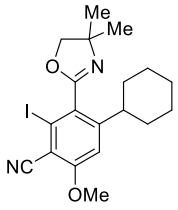
4-Cyclohexyl-5-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-methoxybenzonitrile (93)



To a mixture of 2-(5-bromo-2-cyclohexyl-4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**89e**, 0.702 g, 1.92 mmol, 1.0 equiv) in THF (3.8 mL) was added *i*PrMgCl·LiCl (**10**, 4.61 mmol, 2.4 equiv) at 40 °C. After 2 h, the reaction mixture was cooled to 0 °C and tosyl cyanide (0.835 g, 4.61 mmol, 2.4 equiv) was added and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) afforded the title compound as a yellow solid (**93**, 0.422 g, 1.15 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.87 (s, 1H), 6.88 (s, 1H), 4.05 (s, 2H), 3.95 (s, 3H), 3.53 (tt, *J* = 11.2, 2.9 Hz, 1H), 1.85 (ddd, *J* = 13.0, 9.9, 2.7 Hz, 5H), 1.81–1.73 (m, 1H), 1.46–1.21 (m, 10H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.4, 160.9, 156.0, 135.6, 120.8, 116.1, 109.1, 99.0, 78.8, 68.2, 56.1, 40.8, 33.9, 28.4, 26.8, 26.2.
MS (EI, 70 eV): m/z (%) =
HRMS (EI): for $C_{16}H_{21}BrN_2O$: calc. [M-H$^+$]:; found:.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1640 (vs), 1632 (m), 1589 (s), 1492 (s), 1459 (s), 1446 (s), 1377 (m), 1344 (m), 1318 (m), 1305 (s), 1262 (s), 1252 (s), 1188 (s), 1183 (s), 1057 (s), 1044 (vs), 991 (s), 969 (s), 903 (s), 844 (s), 694 (s).
Melting point: M.p. = 153 °C.

4-Cyclohexyl-3-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-iodo-6-methoxybenzonitrile (94)

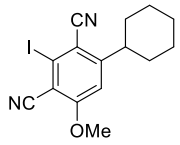


According to **TP 5**, to a mixture of 4-cyclohexyl-5-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-methoxybenzonitrile (**93**, 94 mg, 0.30 mmol, 1.0 equiv) in THF (0.6 mL) was added TMPMgCl·LiCl (**25**, 0.9 mmol, 3.0 equiv) at 40 °C. After 2 h, the reaction mixture was cooled to 0 °C and iodine

(230 mg, 0.90 mmol, 3.0 equiv) dissolved in THF (1 mL) was added and the mixture was stirred for 1 h at 0 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a white solid (**94**, 98 mg, 0.23 mmol, 77% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 6.84 (s, 1H), 4.16 (s, 2H), 3.94 (s, 3H), 2.71 (ddt, *J* = 11.4, 8.8, 3.3 Hz, 1H), 1.88 (ddd, *J* = 21.3, 10.8, 3.4 Hz, 4H), 1.79–1.72 (m, 1H), 1.45 (s, 6H), 1.40–1.22 (m, 5H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.2, 162.0, 154.6, 128.7, 117.4, 108.9, 108.5, 103.0, 79.7, 68.5, 56.5, 43.3, 33.9, 28.2, 26.8, 26.0.
MS (EI, 70 eV): m/z (%) = 438 (53), 437 (32), 383 (100), 382 (83), 354 (74), 350 (36), 338 (86), 325 (67), 227 (36), 140 (25).
HRMS (EI): for $C_{19}H_{23}IN_2O_2$: calc. [M^+]: 438.0804; found: 438.0799.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2918 (m), 2229 (m), 1659 (vs), 1585 (s), 1537 (s), 1466 (s), 1445 (m), 1390 (s), 1347 (s), 1307 (s), 1268 (m), 1258 (m), 1190 (m), 1134 (s), 1123 (s), 1058 (s), 1007 (s), 986 (s), 977 (vs), 955 (m), 921 (m).
Melting point: M.p. = 221 °C.

4-Cyclohexyl-2-iodo-6-methoxyisophthalonitrile (95)



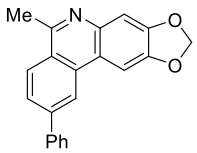
According to **TP 6**, to a mixture of 4-cyclohexyl-3-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-iodo-6-methoxybenzonitrile (**94**, 88 mg, 0.20 mmol, 1.0 equiv) in oxalyl chloride (1 mL) was added DMF (3 µL, 20 mol%) at 0 °C. The reaction mixture was heated at 50 °C for 5 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**95**, 70 mg, 0.192 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 6.89 (s, 1H), 4.00 (s, 3H), 3.05 (tt, *J* = 11.6, 3.1 Hz, 1H), 1.97–1.86 (m, 4H), 1.81 (dddt, *J* = 15.2, 5.1, 3.4, 1.7 Hz, 1H), 1.52–1.22 (m, 5H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.6, 160.1, 118.0, 116.3, 114.2, 110.4, 108.9, 106.7, 56.9, 44.6, 33.5, 26.4, 25.8.
MS (EI, 70 eV): m/z (%) = 366 (95), 336 (45), 324 (100), 311 (78), 310 (63), 309 (51), 280 (35), 126 (89.
HRMS (EI): for $C_{15}H_{15}IN_2O$: calc. [M^+]: 366.0229; found: 366.0221.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1660 (vs), 1585 (vs), 1543 (m), 1537 (s), 1466 (s), 1462 (s), 1452 (s), 1444 (s), 1390 (s), 1365 (m), 1348 (s), 1307 (vs), 1269 (m), 1259 (s), 1191 (s), 1125 (s), 1069 (m), 1059 (s), 1008 (s), 980 (vs), 954 (m).
Melting point: M.p. = 228 °C.

4.4 Synthetic Transformations

5-Methyl-2-phenyl-[1,3]dioxolo[4,5-*b*]phenanthridine (96a)



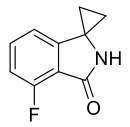
The compound was prepared according to a modified literature procedure.[214] To a solution of 3-(benzo[*d*][1,3]dioxol-5-yl)-[1,1'-biphenyl]-4-carbonitrile (**85e**, 30 mg, 0.10 mmol) in dry THF (0.4 mL) was added MeLi (0.12 mL, 0.20 mmol, 1.6 M in Et_2O, 2.0 equiv) dropwise at 0 °C. The reaction mixture was stirred for 15 min at room temperature. H_2O (0.4 mL) was added to the mixture, followed by addition of iodine (39 mg, 0.15 mmol, 1.50 equiv) and K_2CO_3 (42 mg, 0.3 mmol, 3.0 equiv) at 0 °C. The obtained reaction mixture was stirred for 2 h at 60 °C. Saturated Na_2SO_3 aqueous solution (5 mL) was added and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 4:1) afforded the title compound as a brown solid (**96a**, 23 mg, 0.074 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.55 (d, *J* = 1.7 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 7.90 (s, 1H), 7.85 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.80–7.74 (m, 2H), 7.58–7.51 (m, 2H), 7.50–7.43 (m, 2H), 6.13 (s, 2H), 3.01 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.6, 149.4, 147.7, 142.9, 141.4, 140.7, 133.0, 129.2, 128.2, 127.8, 127.2, 126.0, 124.2, 120.4, 119.7, 107.4, 101.9, 99.5, 23.2.
MS (EI, 70 eV): m/z (%) = 314 (21), 313 (100), 42 (25).
HRMS (EI): for $C_{21}H_{15}NO_2$: calc. [M+]: 313.1103; found: 313.1100.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 1619 (s), 1612 (s), 1599 (s), 1580 (s), 1573 (s), 1500 (s), 1494 (s), 1479 (s), 1468 (s), 1461 (s), 1453 (s), 1440 (s), 1433 (s), 1427 (s), 1414 (m), 1402 (m), 1390 (m), 1380 (s), 1371 (s), 1365 (m), 1359 (m), 1335 (m), 1270 (s), 1231 (vs), 1201 (s), 1182 (m), 1170 (s), 1074 (s), 1037 (s), 947 (s), 940 (s), 865 (m), 829 (s), 791 (s), 769 (s), 761 (vs), 756 (vs).

[214] A. Kishi, K. Moriyama, H. Togo, *J. Org. Chem.* **2018**, *83*, 11080-11088.

Melting point: M.p. = 179 °C.

4'-Fluorospiro[cyclopropane-1,1'-isoindolin]-3'-one (96b)



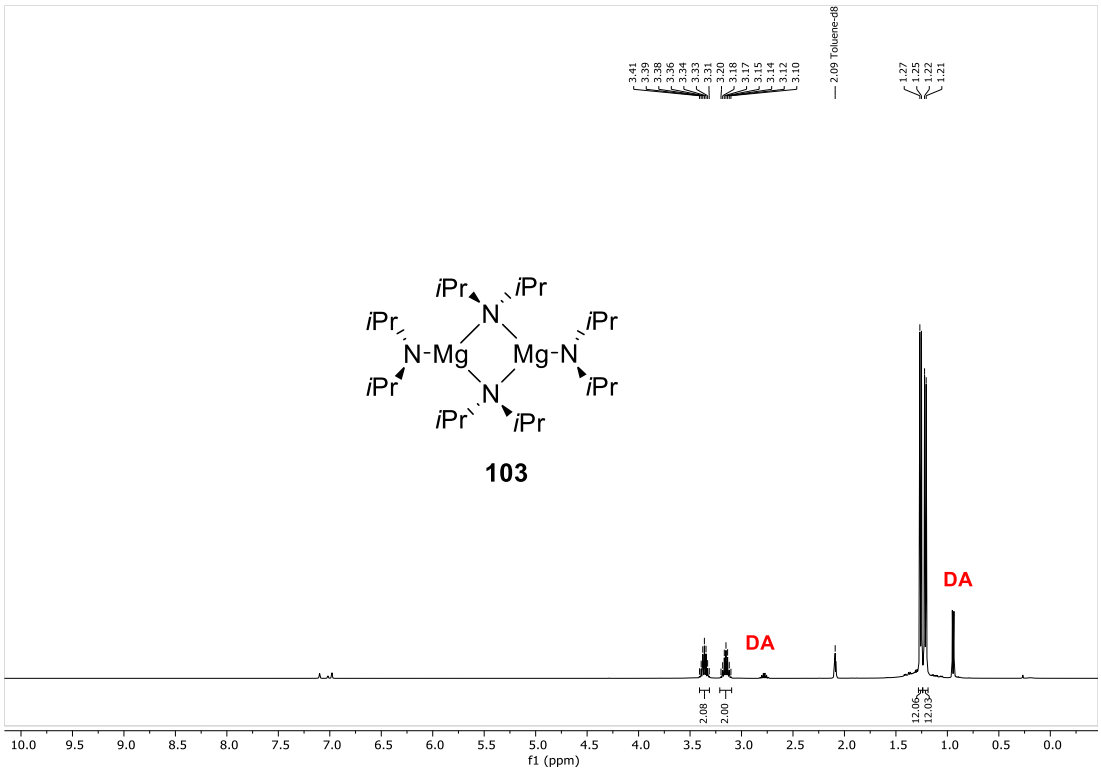
The compound was prepared according to a modified literature procedure.[215] Ethyl 2-cyano-6-fluorobenzoate (**85j**, 19 mg, 0.10 mmol, 1.0 equiv) was dissolved in Et_2O and $Ti(O\textit{i}Pr)_4$ (40 µL, 0.11 mmol, 1.1 equiv) was added at room temperature. EtMgBr (70 µL, 0.20 mmol, 3M in Et_2O, 2.0 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. 1 N HCl (1 mL) and CH_2Cl_2 (5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, CH_2Cl_2/Acetone = 7:1) afforded the title compound as a yellow solid (**96b**, 14 mg, 0.079 mmol, 79% yield).

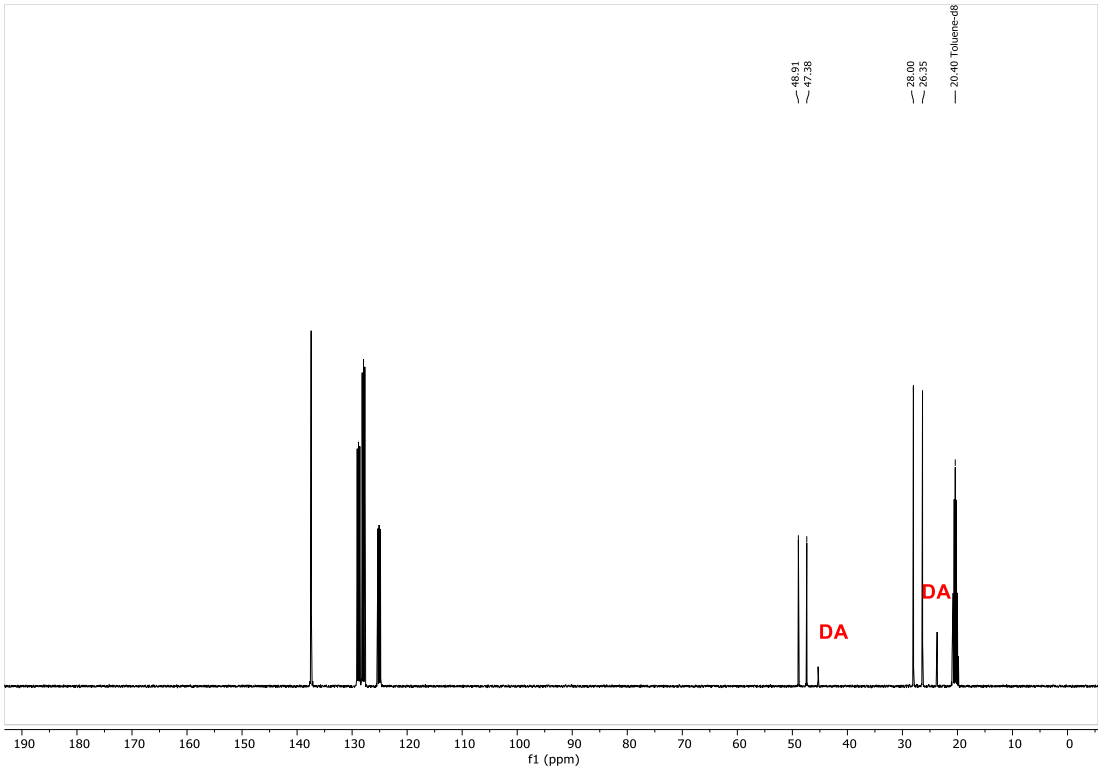
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.12 (s, 1H), 7.49 (td, *J* = 7.9, 4.7 Hz, 1H), 7.10–7.02 (m, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 1.72–1.64 (m, 2H), 1.47–1.41 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.3, 159.2 (d, *J* = 259.8 Hz), 152.1 (d, *J* = 3.5 Hz), 134.0 (d, *J* = 7.9 Hz), 119.3 (d, *J* = 13.5 Hz), 114.3 (d, *J* = 19.7 Hz), 114.0 (d, *J* = 4.1 Hz), 41.9 (d, *J* = 1.5 Hz), 29.8, 14.5.
MS (EI, 70 eV): m/z (%) = 178 (10), 177 (100), 176 (77), 150 (21), 148 (32), 121 (22), 94 (16).
HRMS (EI): for $C_{10}H_8FNO$: calc. [M+]: 177.0590; found: 177.0583.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm-1 = 2850 (m), 1702 (s), 1691 (s), 1679 (vs), 1660 (vs), 1650 (s), 1641 (m), 1630 (s), 1613 (m), 1483 (s), 1357 (m), 1314 (m), 1245 (m), 1239 (m), 1137 (m), 986 (s), 796 (s), 773 (m), 766 (m).
Melting point: M.p. = 140 °C.

[215] P. Bertus, J. Szymoniak, *J. Org. Chem*. **2003**, *68*, 7133-7136.

5. Regioselective Magnesiations of Fluorinated Arenes and Heteroarenes Using Magnesium-bis-Diisopropylamide (MBDA) in Hydrocarbons

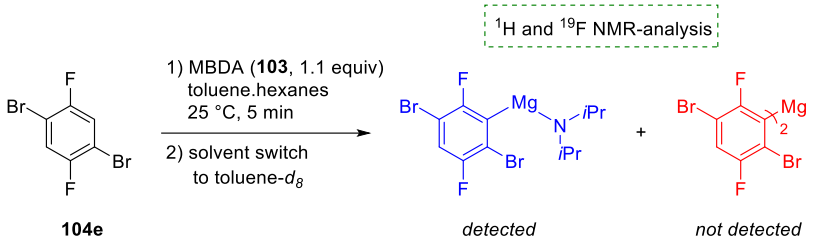
5.1 NMR-Studies



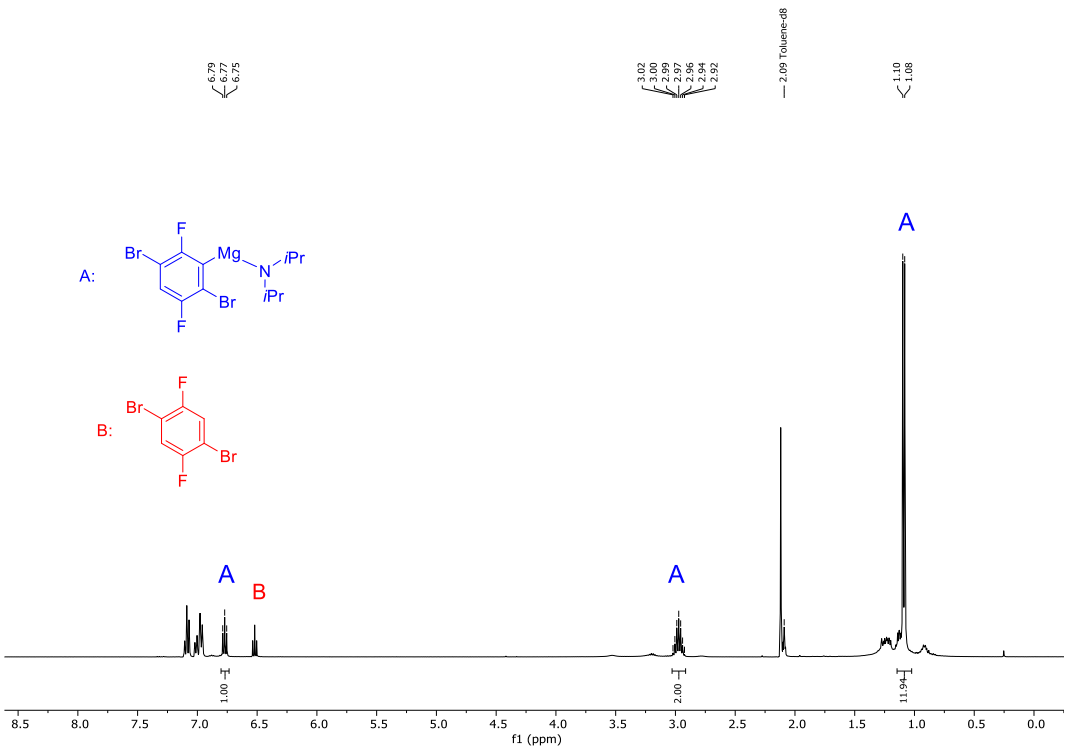


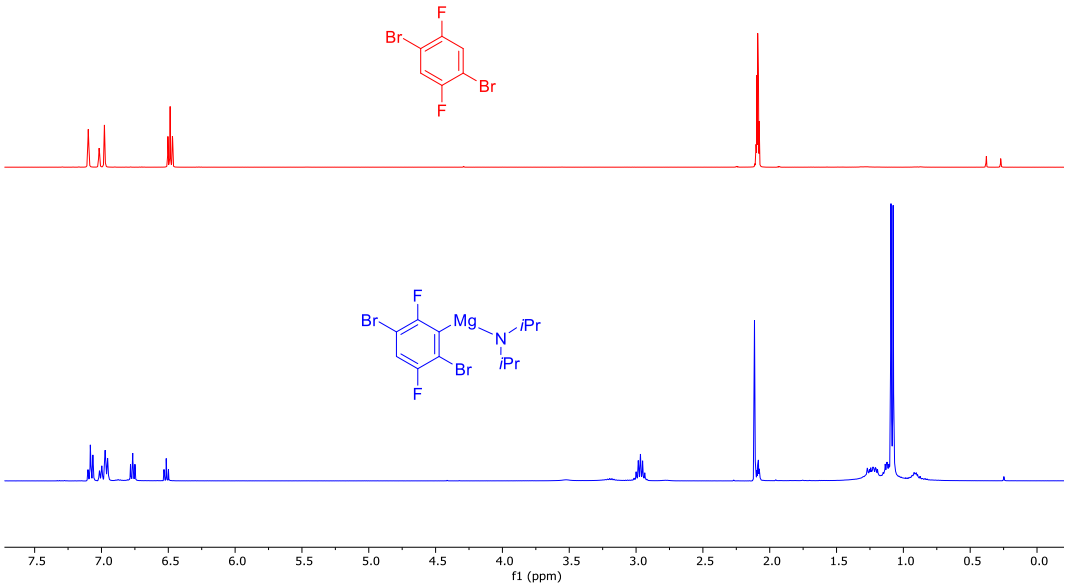
^{1}H NMR (400 MHz, tol-d_8): δ (ppm) = 3.36 (hept, *J* = 6.3 Hz, 2H), 3.15 (hept, *J* = 6.4 Hz, 2H), 1.26 (d, *J* = 6.3 Hz, 12H), 1.21 (d, *J* = 6.4 Hz, 12H).

^{13}C NMR (101 MHz, tol-d_8): δ (ppm) = 48.9, 47.4, 28.0, 26.3.

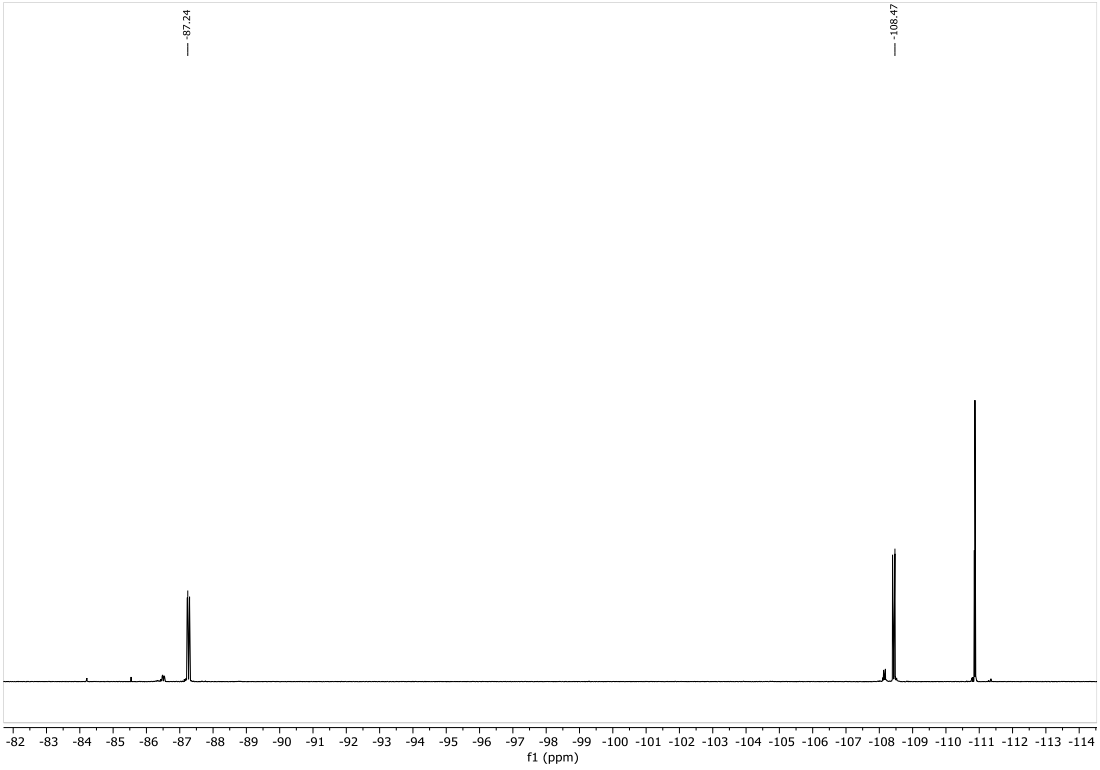


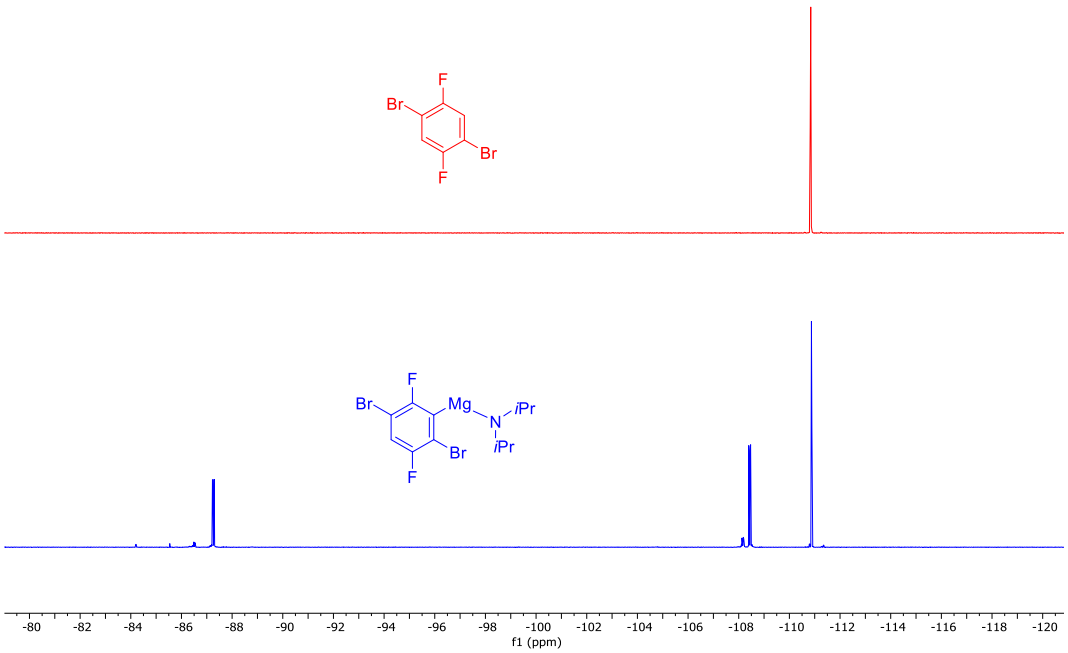
^{1}H-NMR Spectra:





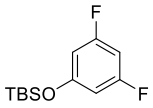
^{19}F-NMR Spectra:




F
Br
Br
F
F
Br
Mg
N
iPr
iPr
Br
F
-80 -82 -84 -86 -88 -90 -92 -94 -96 -98 -100 -102 -104 -106 -108 -110 -112 -114 -116 -118 -120
f1 (ppm)

5.2 Preparation of Starting Materials

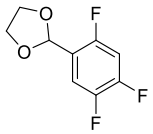
***Tert-butyl*(3,5-difluorophenoxy)dimethylsilane (104k)**



3,5-difluorophenol (4.00 g, 30.70 mmol, 1.0 equiv) and imidazole (4.18 g, 61.40 mmol, 2.2 equiv) were dissolved in DMF (40 mL). The reaction mixture was cooled to 0 °C and TBS-Cl (5.09 g, 33.80 mmol, 1.1 equiv) was added in portions. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched by addition of water and extracted with DCM (3 x 30 mL). The combined organic layers were washed with water (2 x 20 mL) and brine (20 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 199:1) afforded the title compound as a colorless oil (**104k**, 6.00 g, 24.56 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 6.43 (tt, *J* = 9.1, 2.3 Hz, 1H), 6.39–6.32 (m, 2H), 0.97 (s, 9H), 0.22 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.6 (dd, *J* = 246.4, 16.1 Hz), 157.8 (t, *J* = 14.1 Hz), 104.1–103.7 (m), 97.3 (t, *J* = 25.9 Hz), 25.7, 18.3, -4.4.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -110.2.
MS (EI, 70 eV): m/z (%) = 205 (21), 187 (100), 80 (11).
HRMS (EI): for $C_{12}H_{18}F_2OSi$: calc. [M+]: 244.1095; found: 244.1088.

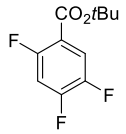
2-(2,4,5-Trifluorophenyl)-1,3-dioxolane (104l)



2,4,5-trifluorobenzaldehyde (3.16 mL, 28.00 mmol, 1.0 equiv), ethylene glycol (1.87 mL, 33.60 mmol, 1.2 equiv) and $TsOH \cdot H_2O$ (107 mg, 2 mol%) were dissolved in toluene (40 mL) and the reaction mixture was refluxed overnight. After cooling to room temperature, water (20 mL) was added and the reaction mixture was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 96:4) afforded the title compound as a white solid (**104l**, 3.474 g, 17.0 mmol, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.37 (ddd, *J* = 10.4, 8.9, 6.4 Hz, 1H), 6.94 (td, *J* = 9.7, 6.3 Hz, 1H), 6.01 (d, *J* = 1.3 Hz, 1H), 4.18–4.09 (m, 2H), 4.09–4.00 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.2 (ddd, *J* = 248.6, 9.7, 2.7 Hz), 150.7 (ddd, *J* = 252.7, 14.6, 12.4 Hz), 146.9 (ddd, *J* = 245.2, 12.6, 3.7 Hz), 122.0 (dt, *J* = 14.7, 4.5 Hz), 115.9 (ddd, *J* = 20.4, 5.4, 1.7 Hz), 105.9 (dd, *J* = 27.2, 21.1 Hz), 97.8 (d, *J* = 3.1 Hz), 65.6.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -121.1, -132.3, -142.3.
MS (EI, 70 eV): m/z (%) = 203 (80), 185 (100), 159 (97), 144 (46), 125 (19).
HRMS (EI): for $C_9H_7F_3O_2$: calc. [M+]: 204.0398; found: 204.0391.

***Tert-butyl* 2,4,5-trifluorobenzoate (104m)**

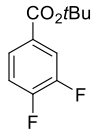


2,4,5-trifluorobenzoyl chloride (2.94 mL, 23.10 mmol, 1.0 equiv) was dissolved in dry DCM (40 mL). The reaction mixture was cooled to 0 °C and KO*t*Bu (2.851 g, 25.41 mmol, 1.1 equiv) was added in portions. The mixture was stirred for 1 h and then allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched by addition of water (20 mL) and was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 94:6) afforded the title compound as a colorless oil (**104m**, 4.364 g, 18.79 mmol, 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.71 (ddd, *J* = 10.5, 8.9, 6.6 Hz, 1H), 6.96 (td, *J* = 9.8, 6.2 Hz, 1H), 1.58 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.7 (d, *J* = 4.5 Hz), 157.8 (ddd, *J* = 259.4, 9.9, 2.7 Hz), 152.8 (ddd, *J* = 257.9, 14.4, 12.0 Hz), 146.4 (ddd, *J* = 246.3, 12.7, 3.9 Hz), 120.0 (dt, *J* = 20.3, 2.3 Hz), 117.0 (dt, *J* = 11.6, 4.5 Hz), 107.0 (dd, *J* = 28.7, 20.8 Hz), 82.9, 28.2.
The analytical data were consistent with literature values.[216]

[216] M. Al-Masum, A. Hira, S. Chrisman, N. T. Nguyen, *Tetrahedron Lett.* **2019**, *60*, art. no. 150936.

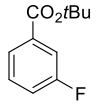
***Tert-butyl* 3,4-difluorobenzoate (104n)**



3,4-difluorobenzoyl chloride (2.30 mL, 20.00 mmol, 1.0 equiv) was dissolved in dry DCM (40 mL). The reaction mixture was cooled to 0 °C and KO*t*Bu (2.360 g, 22.00 mmol, 1.1 equiv) was added in portions. The mixture was stirred for 1 h and then allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched by addition of water (20 mL) and was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a colorless oil (**104n**, 3.724 g, 17.40 mmol, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.83–7.73 (m, 2H), 7.23–7.15 (m, 1H), 1.59 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.9, 153.4 (dd, *J* = 255.0, 12.7 Hz), 150.1 (dd, *J* = 249.3, 13.0 Hz), 129.2 (dd, *J* = 5.4, 3.6 Hz), 126.4 (dd, *J* = 7.3, 3.7 Hz), 118.9 (dd, *J* = 18.4, 1.6 Hz), 117.2 (d, *J* = 17.8 Hz), 82.0, 28.3.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -131.4, -137.1.
MS (EI, 70 eV): m/z (%) = 159 (12), 141 (100), 63 (16).
HRMS (EI): for $C_{11}H_{12}F_2O_2$: calc. [M+]: 214.0805; found: 214.0815.

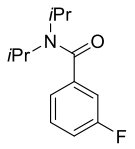
***Tert-butyl* 3-fluorobenzoate (104o)**



3-fluorobenzoyl chloride (4.20 mL, 35.00 mmol, 1.0 equiv) was dissolved in dry DCM (50 mL). The reaction mixture was cooled to 0 °C and KO*t*Bu (4.000 g, 38.50 mmol, 1.1 equiv) was added in portions. The mixture was stirred for 1 h and then allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched by addition of water (20 mL) and was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 94:6) afforded the title compound as a colorless oil (**104o**, 5.235 g, 26.68 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.78 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.66 (ddd, *J* = 9.5, 2.7, 1.5 Hz, 1H), 7.38 (td, *J* = 8.0, 5.6 Hz, 1H), 7.21 (tdd, *J* = 8.3, 2.7, 1.1 Hz, 1H), 1.59 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.7 (d, *J* = 2.9 Hz), 162.6 (d, *J* = 246.5 Hz), 134.4 (d, *J* = 7.3 Hz), 129.9 (d, *J* = 7.7 Hz), 125.2 (d, *J* = 3.0 Hz), 119.6 (d, *J* = 21.3 Hz), 116.4 (d, *J* = 22.9 Hz), 81.7, 28.3.
The analytical data were consistent with literature values.[217]

3-Fluoro-*N*,*N*-diisopropylbenzamide (104p)

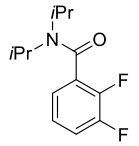


3-fluorobenzoyl chloride (2.40 mL, 20.00 mmol, 1.0 equiv) and Et_3N (3.90 mL, 28.00 mmol, 1.4 equiv) were dissolved in dry DCM (40 mL). The reaction mixture was cooled to 0 °C and diisopropylamine (3.96 mL, 28.00 mmol, 1.4 equiv) was added dropwise. The mixture was stirred for 1 h and then allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched by addition of water (20 mL) and was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**104p**, 4.437 g, 19.90 mmol, quant. yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.35 (td, *J* = 7.9, 5.6 Hz, 1H), 7.12–6.97 (m, 3H), 3.65 (d, *J* = 92.0 Hz, 2H), 1.83–0.90 (m, 12H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 169.6 (d, *J* = 2.3 Hz), 162.7 (d, *J* = 247.8 Hz), 141.0 (d, *J* = 6.6 Hz), 130.4 (d, *J* = 8.1 Hz), 121.4 (d, *J* = 3.2 Hz), 115.8 (d, *J* = 21.1 Hz), 113.1 (d, *J* = 22.5 Hz), 20.8.
The analytical data were consistent with literature values.[218]

[217] S. W. Wright, D. L. Hagemann, A. S. Wright, L. D. McClure, *Tetrahedron Lett.* **1997**, *38*, 7345-7348.
[218] L. Wang, L. Ackermann, *Chem. Comm.* **2014**, *50*, 1083-1085.

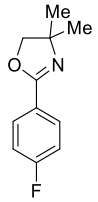
2,3-Difluoro-*N*,*N*-diisopropylbenzamide (104q)



2,3-difluorobenzoyl chloride (2.48 mL, 20.00 mmol, 1.0 equiv) and Et_3N (3.90 mL, 28.00 mmol, 1.4 equiv) were dissolved in dry DCM (40 mL). The reaction mixture was cooled to 0 °C and diisopropylamine (3.96 mL, 28.00 mmol, 1.4 equiv) was added dropwise. The mixture was stirred for 1 h and then allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched by addition of water (20 mL) and was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**104q**, 4.236 g, 17.56 mmol, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.19–7.07 (m, 2H), 7.01 (ddt, *J* = 8.6, 5.3, 1.7 Hz, 1H), 3.71 (pd, *J* = 6.7, 1.3 Hz, 1H), 3.54 (hept, *J* = 6.8 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 6H), 1.29–1.02 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.4, 150.5 (dd, *J* = 238.4, 13.0 Hz), 129.1 (dd, *J* = 235.7, 14.8 Hz), 129.1 (d, *J* = 16.1 Hz), 125.1 (dd, *J* = 6.6, 4.4 Hz), 122.6 (t, *J* = 3.5 Hz), 117.5 (d, *J* = 17.1 Hz), 51.4, 46.4, 20.7 (t, *J* = 29.1 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -136.9, -141.5.
MS (EI, 70 eV): m/z (%) = 241 (11), 226 (11), 198 (19), 184 (16), 141 (100).
HRMS (EI): for $C_{13}H_{17}F_2NO$: calc. [M+]: 241.1278; found: 241.1274.

2-(4-Fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (104r)

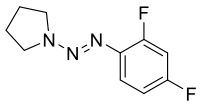


4-fluorobenzaldehyde (2.60 mL, 25.00 mmol, 1.0 equiv) and 2-amino-2-methylpropan-1-ol (2.80 mL, 30.00 mmol, 1.2 equiv) were dissolved in dry CH_2Cl_2 (40 mL), to which molecular sieves 4 A (2 g) were added. The mixture was stirred for 23 h at room temperature. The flask was cooled to 0 °C and NBS (9.08 g, 45.4 mmol, 1.8 equiv) was added in portions. The mixture was stirred for 10 min at 0 °C, the cooling bath was removed, and stirring was continued for 3 h at 25 °C. The mixture was filtered and

the solid residue was washed with EtOAc (150 mL) and sat. NaHCO3 (100 mL) solution. The phases were separated and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over MgSO4, filtered and the solvent was removed in vacuo. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a colorless oil (**104r**, 3.965 g, 20.52 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.75–7.67 (m, 1H), 7.62 (ddt, *J* = 10.2, 5.7, 2.7 Hz, 1H), 7.35 (dtt, *J* = 8.3, 5.7, 3.1 Hz, 1H), 7.13 (tdt, *J* = 8.5, 5.3, 2.7 Hz, 1H), 4.14 (s, 2H), 1.36 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.6 (d, *J* = 246.0 Hz), 161.1 (d, *J* = 3.2 Hz), 130.3 (d, *J* = 8.3 Hz), 130.0 (d, *J* = 8.0 Hz), 124.0 (d, *J* = 3.1 Hz), 118.2 (d, *J* = 21.2 Hz), 115.3 (d, *J* = 23.5 Hz), 79.4, 67.9, 28.5.
The analytical data were consistent with literature values.[219]

(*E*)-1-((2,4-Difluorophenyl)diazenyl)pyrrolidine (104s)



The compound was prepared according to a literature procedure.[220] A solution of 2,4-difluoroaniline (2.582 g, 20.00 mmol, 1.0 equiv) in 4 mL of conc. HCl was cooled in an ice bath while a solution of $NaNO_2$ (1.38 g, 20.00 mmol, 1.0 equiv) in 10 mL of cold water was added dropwise. The resulting solution of the diazonium salt was stirred at 0 °C for 0.5 h and then added at once to a solution of pyrrolidine (1.81 mL, 22.00 mmol, 1.1 equiv) in 1 M KOH (20 mL). The reaction mixture was stirred for 0.5 h at 0 °C and was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as an orange solid (**104s**, 3.259 g, 15.43 mmol, 77% yield).

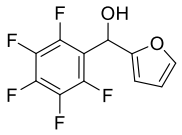
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 (td, *J* = 9.0, 6.2 Hz, 1H), 6.89–6.75 (m, 2H), 3.80 (d, *J* = 75.3 Hz, 4H), 2.12–1.95 (m, 5H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.1 (dd, *J* = 245.5, 11.3 Hz), 156.0 (dd, *J* = 251.5, 11.9 Hz), 136.3 (dd, *J* = 8.0, 3.8 Hz), 119.8 (dd, *J* = 9.4, 3.2 Hz), 111.1 (dd, *J* = 21.9, 3.8 Hz), 104.4 (dd, *J* = 25.9, 24.1 Hz), 51.3, 46.6, 23.9.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -115.7, -124.2.

[219] D. T. Witiak, S. Goswami, G. E. Milo, *J. Org. Chem.* **1988**, *53*, 345-352.
[220] C.-Y. Liu, P. Knochel, *Org. Lett.* **2005**, *13,* 2543-2546.

MS (EI, 70 eV): m/z (%) = 141 (100), 113 (10), 63 (6).
HRMS (EI): for $C_{10}H_{11}F_2N_3$: calc. [M+]: 211.0921; found: 211.0913.

5.3 Preparation of Compounds

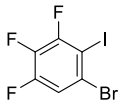
Furan-2-yl(perfluorophenyl)methanol (108a)



According to **TP 7**, to a mixture of pentafluorobenzene (**104a**, 56 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and furfural (58 µL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**108a**, 110 mg, 0.42 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 (dd, *J* = 1.9, 0.8 Hz, 1H), 6.37 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.31 (d, *J* = 3.4 Hz, 1H), 6.16 (d, *J* = 8.3 Hz, 1H), 2.83 (d, *J* = 8.4 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.3, 146.7–143.5 (m), 143.2, 142.7–139.7 (m), 139.3–136.2 (m), 114.6 (t, *J* = 16.4 Hz), 110.8, 107.8 (d, *J* = 1.2 Hz), 63.1–60.8 (m).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -143.0, -154.0, -161.4.
MS (EI, 70 eV): m/z (%) = 264 (28), 247 (33), 236 (82), 194 (100), 187 (29), 169 (60), 97 (23).
HRMS (EI): for $C_{11}H_5F_5O_2$: calc. [M+]: 264.0210; found: 264.0217.

1-Bromo-3,4,5-trifluoro-2-iodobenzene (108b)

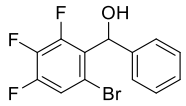


According to **TP 7**, to a mixture of 5-bromo-1,2,3-trifluorobenzene (**104b**, 60 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 45 min, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude

product by flash column chromatography (silica gel, pentane) afforded the title compound as a colorless liquid (**108b**, 132 mg, 0.39 mmol, 78% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.42 (ddd, *J* = 9.2, 6.7, 2.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.9 (ddd, *J* = 70.2, 10.9, 4.2 Hz), 150.4 (ddd, *J* = 75.7, 11.0, 4.3 Hz), 138.6 (ddd, *J* = 257.1, 18.1, 15.6 Hz), 123.3 (ddd, *J* = 9.2, 5.1, 1.4 Hz), 116.6 (dd, *J* = 20.8, 3.6 Hz), 85.8 (ddd, *J* = 24.6, 4.5, 1.9 Hz).
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -101.9, -132.1, -156.6.
MS (EI, 70 eV): m/z (%) = 130 (100), 126 (10), 99 (12), 80 (33).
HRMS (EI): for C_6HBrF_3I: calc. [M+]: 335.8258; found: 335.8248.

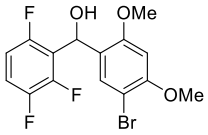
(6-Bromo-2,3,4-trifluorophenyl)(phenyl)methanol (108c)



According to **TP 7**, to a mixture of 5-bromo-1,2,3-trifluorobenzene (**104b**, 60 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 45 min, the reaction mixture was cooled to 0 °C and benzaldehyde (78 µL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a pale yellow oil (**108c**, 114 mg, 0.36 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40–7.27 (m, 7H), 6.34 (d, *J* = 8.0 Hz, 1H), 2.94–2.81 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 151.9 (ddd, *J* = 34.4, 10.7, 4.6 Hz), 149.4 (ddd, *J* = 33.6, 10.8, 4.5 Hz), 141.6–141.1 (m), 140.9, 139.2–138.5 (m), 128.7, 128.5–128.3 (m), 128.0, 125.6 (d, *J* = 1.4 Hz), 117.2 (dd, *J* = 19.9, 4.0 Hz), 116.3–115.8 (m), 73.3 (d, *J* = 1.8 Hz).
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -133.0, -158.4.
MS (EI, 70 eV): m/z (%) = 317 (44), 315 (46), 238 (31), 219 (40), 79 (67), 42 (100).
HRMS (EI): for $C_{13}H_8BrF_3O$: calc. [M+]: 315.9711; found: 315.9697.

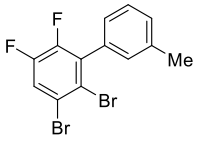
(5-Bromo-2,4-dimethoxyphenyl)(2,3,6-trifluorophenyl)methanol (108d)



According to **TP 7**, to a mixture of 1,2,4-trifluorobenzene (**104c**, 52 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and 5-bromo-2,4-dimethoxybenzaldehyde (172 mg, 0.70 mmol, 1.4 equiv) dissolved in toluene (1 mL) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a white solid (**108d**, 125 mg, 0.33 mmol, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.60 (q, *J* = 1.1 Hz, 1H), 7.09–7.00 (m, 1H), 6.78 (tdd, *J* = 9.4, 3.8, 2.2 Hz, 1H), 6.43 (s, 1H), 6.29 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.08 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.7 (dd, *J* = 5.9, 2.8 Hz), 157.1, 156.8, 155.3 (dd, *J* = 5.9, 2.8 Hz), 150.3 (dd, *J* = 14.5, 8.6 Hz), 148.9 (dd, *J* = 13.6, 3.6 Hz), 147.8 (dd, *J* = 14.6, 8.6 Hz), 146.4 (dd, *J* = 13.5, 3.6 Hz), 131.4 (t, *J* = 2.3 Hz), 123.3 (d, *J* = 1.1 Hz), 120.8 (dd, *J* = 18.0, 12.8 Hz), 116.5 (ddd, *J* = 19.4, 10.4, 1.7 Hz), 111.4 (ddd, *J* = 25.1, 6.4, 4.1 Hz), 102.3, 96.8, 64.0 (td, *J* = 3.0, 1.9 Hz), 56.8, 56.2.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -118.8, -137.1, -142.3.
MS (EI, 70 eV): m/z (%) = 377 (43), 375 (46), 247 (29), 245 (31), 158 (32), 137 (28), 70 (13), 42 (100).
HRMS (EI): for $C_{15}H_{12}BrF_3O_3$: calc. [M+]: 375.9922; found: 375.9920.

2,3-dibromo-5,6-difluoro-3'-methyl-1,1'-biphenyl (108e)

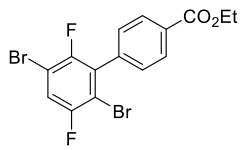


According to **TP 7**, to a mixture of 1,2-dibromo-4,5-difluorobenzene (**104d**, 136 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 5 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 3-iodotoluene

(54 µl, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, pentane) afforded the title compound as a colorless oil (**108e**, 104 mg, 0.29 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.55 (dd, *J* = 9.3, 7.5 Hz, 1H), 7.42–7.35 (m, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.11–7.06 (m, 2H), 2.43 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.7 (dd, *J* = 218.1, 13.8 Hz), 147.2 (dd, *J* = 214.3, 13.8 Hz),138.3, 134.8 (d, *J* = 15.9 Hz), 134.3 (d, *J* = 2.2 Hz), 130.2 (d, *J* = 1.3 Hz), 129.8, 128.5, 126.6 (d, *J* = 1.3 Hz), 121.7 (d, *J* = 4.0 Hz), 120.9 (d, *J* = 20.6 Hz), 119.5 (dd, *J* = 7.8, 4.7 Hz), 21.6.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -133.4, -135.5.
MS (EI, 70 eV): m/z (%) = 363 (32), 361 (76), 359 (39), 201 (73), 43 (41), 42 (100).
HRMS (EI): for $C_{13}H_8Br_2F_2$: calc. [M+]: 359.8961; found: 359.8951.

Ethyl 2',5'-dibromo-3',6'-difluoro-[1,1'-biphenyl]-4-carboxylate (108f)

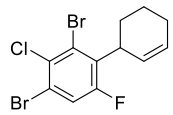


According to **TP 7**, to a mixture of 1,4-dibromo-2,5-difluorobenzene (**104e**, 136 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 5 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 4-iodo ethylbenzoate (72 µl, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a yellow solid (**108f**, 137 mg, 0.33 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.20–8.14 (m, 2H), 7.46–7.36 (m, 3H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.2, 156.7 (d, *J* = 3.7 Hz), 154.2 (dd, *J* = 17.3, 3.5 Hz), 151.7 (d, *J* = 3.3 Hz), 137.5 (d, *J* = 1.9 Hz), 132.1 (d, *J* = 21.2 Hz), 131.1, 130.0 (d, *J* = 1.4 Hz), 129.8, 119.9 (d, *J* = 27.7 Hz), 110.5 (dd, *J* = 22.7, 2.2 Hz), 108.7 (dd, *J* = 25.0, 9.6 Hz), 61.4, 14.5.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -106.9, -108.2.
MS (EI, 70 eV): m/z (%) = 419 (39), 391 (54), 376 (51), 374 (100), 372 (54), 268 (48), 187 (50).

HRMS (EI): for $C_{15}H_{10}Br_2F_2O_2$: calc. [M+]: 417.9016; found: 417.9009.

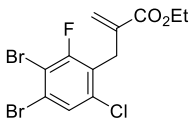
2',4'-dibromo-3'-chloro-6'-fluoro-1,2,3,4-tetrahydro-1,1'-biphenyl (108g)



According to **TP 7**, to a mixture of 1,3-dibromo-2-chloro-5-fluorobenzene (**104f**, 144 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 0.5 h, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.1 mL, 20 mol%, 1M in THF) and 3-bromocyclohexen (70 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel,pentane) afforded the title compound as a white solid (**108g**, 152 mg, 0.41 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.33 (d, *J* = 9.9 Hz, 1H), 5.83–5.76 (m, 1H), 5.59 (dt, *J* = 10.1, 2.5 Hz, 1H), 4.05 (tdd, *J* = 9.2, 7.7, 4.8, 2.4 Hz, 1H), 2.20–2.02 (m, 2H), 1.99–1.86 (m, 2H), 1.79–1.63 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.7, 158.2, 134.7 (d, *J* = 14.8 Hz), 131.3, 128.1 (d, *J* = 2.0 Hz), 127.1, 126.2, 120.9–120.4 (m), 27.7, 24.6, 22.8.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -109.9.
MS (EI, 70 eV): m/z (%) = 369 (38), 367 (54), 313 (46), 182 (36), 180 (100), 67 (31), 43 (36).
HRMS (EI): for $C_{12}H_{10}Br_2ClF$: calc. [M+]: 365.8822; found: 365.8824.

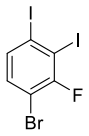
Ethyl 2-(3,4-dibromo-6-chloro-2-fluorobenzyl)acrylate (108h)



According to **TP 7**, to a mixture of 1,2-dibromo-5-chloro-3-fluorobenzene (**104g**, 144 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 0.5 h, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.1 mL, 20 mol%, 1M in THF) and ethyl 2-(bromomethyl)acrylate (97 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel,pentane) afforded the title compound as a colorless oil (**108h**, 104 mg, 0.26 mmol, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53 (d, *J* = 1.9 Hz, 1H), 6.24 (d, *J* = 1.6 Hz, 1H), 5.17 (d, *J* = 2.0 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.78 (q, *J* = 1.9 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.3, 158.5 (d, *J* = 251.9 Hz), 136.1, 135.4 (d, *J* = 6.4 Hz), 129.3 (d, *J* = 3.9 Hz), 125.6, 125.1 (d, *J* = 20.3 Hz), 124.1 (d, *J* = 1.5 Hz), 111.9 (d, *J* = 24.6 Hz), 61.2, 29.1 (d, *J* = 2.6 Hz), 14.3.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -96.9.
MS (EI, 70 eV): m/z (%) = 364 (23), 219 (15), 167 (100).
HRMS (EI): for $C_{12}H_{10}Br_2ClFO_2$: calc. [M+]: 397.8720; found: 397.8726.

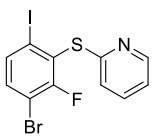
1-bromo-2-fluoro-3,4-diiodobenzene (108i)



According to **TP 7**, to a mixture of 1-bromo-2-fluoro-4-iodobenzene (**104h**, 150 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 40 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, pentane) afforded the title compound as a white solid (**108i**, 129 mg, 0.30 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.55 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.32–7.26 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.3 (d, *J* = 247.7 Hz), 135.5 (d, *J* = 4.2 Hz), 134.7, 108.4, 107.6, 97.7 (d, *J* = 27.9 Hz).
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -70.4.
MS (EI, 70 eV): m/z (%) = 427 (91), 425 (100), 126 (52).
HRMS (EI): for $C_6H_2BrFI_2$: calc. [M+]: 425.7413; found: 425.7397.

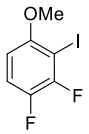
2-((3-bromo-2-fluoro-6-iodophenyl)thio)pyridine (108j)



According to **TP 7**, to a mixture of 1-bromo-2-fluoro-4-iodobenzene (**104h**, 150 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 40 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and 2,2′-dipyridyl disulfide (132 mg, 0.60 mmol, 1.2 equiv) dissolved in toluene (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 94:6) afforded the title compound as a white solid (**108j**, 145 mg, 0.35 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.38 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.68 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.53 (ddd, *J* = 8.0, 7.4, 1.9 Hz, 1H), 7.35 (dd, *J* = 8.5, 6.6 Hz, 1H), 7.05 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 6.99 (dt, *J* = 8.0, 1.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.4 (d, *J* = 251.8 Hz), 157.5, 150.1, 137.0, 136.2 (d, *J* = 4.5 Hz), 136.0 (d, *J* = 1.4 Hz), 126.1 (d, *J* = 20.6 Hz), 121.2, 120.7, 110.4 (d, *J* = 24.4 Hz), 108.3 (d, *J* = 2.3 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -86.9.
MS (EI, 70 eV): m/z (%) = 283 (33), 281 (33), 203 (22), 61 (15) 50 (14), 43 (100).
HRMS (EI): for $C_{11}H_6BrFINS$: calc. [M+]: 408.8433; found: 408.8432.

1,2-difluoro-3-iodo-4-methoxybenzene (108k)

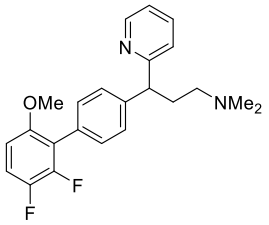


According to **TP 7**, to a mixture of 1,2-difluoro-4-methoxybenzene (**104i**, 58 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 40 °C. After 15 min, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 94:6) afforded the title compound as a yellow solid (**108k**, 128 mg, 0.47 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.13 (q, *J* = 9.2 Hz, 1H), 6.54 (ddd, *J* = 9.2, 3.7, 2.1 Hz, 1H), 3.86 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 155.4 (dd, *J* = 4.0, 2.3 Hz), 150.9 (dd, *J* = 244.7, 14.9 Hz), 144.9 (dd, *J* = 244.5, 15.2 Hz), 116.8 (dd, *J* = 18.6, 1.9 Hz), 105.4 (dd, *J* = 6.0, 3.3 Hz), 75.6 (d, *J* = 23.6 Hz), 57.1.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -113.2, -144.5.
MS (EI, 70 eV): m/z (%) = 269 (100), 254 (44), 226 (24), 42 (75).

HRMS (EI): for $C_7H_5F_2IO$: calc. [M+]: 269.9353; found: 269.9346.

3-(2',3'-difluoro-6'-methoxy-[1,1'-biphenyl]-4-yl)-N,N-dimethyl-3-(pyridin-2-yl)propan-1-amine (108l)



According to **TP 7**, to a mixture of 1,2-difluoro-4-methoxybenzene (**104i**, 58 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 40 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $PdCl_2$(dppf) (18 mg, 5 mol%) and brompheniramine (132 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, DCM/MeOH = 96:4) afforded the title compound as a brown oil (**108l**, 135 mg, 0.35 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.59–8.53 (m, 1H), 7.57 (tdd, *J* = 7.7, 1.8, 1.0 Hz, 1H), 7.41–7.29 (m, 4H), 7.20 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.17–7.00 (m, 2H), 6.61 (ddd, *J* = 9.3, 3.8, 1.9 Hz, 1H), 4.21 (t, *J* = 7.6 Hz, 1H), 3.69 (d, *J* = 1.1 Hz, 3H), 2.81 (dtd, *J* = 25.4, 9.6, 8.3, 5.1 Hz, 3H), 2.64 (s, 6H), 2.59–2.45 (m, 1H).

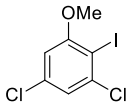
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.4, 153.1 (dd, *J* = 4.9, 2.2 Hz), 149.4, 149.3, 149.3, 146.9 (d, *J* = 14.0 Hz), 144.5 (d, *J* = 14.2 Hz), 141.9, 137.0, 131.0 (d, *J* = 1.8 Hz), 129.3 (d, *J* = 2.2 Hz), 127.6, 123.8, 122.0, 120.1 (d, *J* = 14.0 Hz), 115.1 (d, *J* = 1.9 Hz), 105.9 (dd, *J* = 6.5, 3.6 Hz), 56.8, 56.3, 50.4, 43.3, 29.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -139.0, -147.3.

MS (EI, 70 eV): m/z (%) = 336 (22), 335 (100), 320 (57), 207 (11), 159 (15).

HRMS (EI): for $C_{23}H_{24}F_2N_2O$: calc. [M+]: 382.1857; found: 382.1851.

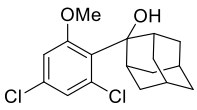
1,5-dichloro-2-iodo-3-methoxybenzene (108m)



According to **TP 7**, to a mixture of 3,5-dichloroanisole (**104j**, 88 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 70 °C. After 1 h, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a white solid (**108m**, 116 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.12 (d, *J* = 2.1 Hz, 1H), 6.67 (d, *J* = 2.1 Hz, 1H), 3.88 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.3, 140.4, 135.6, 121.7, 109.5, 89.2, 57.1.
MS (EI, 70 eV): m/z (%) = 303 (18), 301 (28), 88 (18), 60 (10), 46 (100).
HRMS (EI): for $C_7H_5Cl_2IO$: calc. [M+]: 301.8762; found: 301.8768.

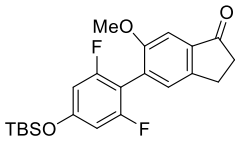
(1r,5R,7S)-2-(2,4-dichloro-6-methoxyphenyl)adamantan-2-ol (108n)



According to **TP 7**, to a mixture of 3,5-dichloroanisole (**104j**, 88 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 70 °C. After 1 h, the reaction mixture was cooled to 0 °C and adamantan-2-one (105 mg, 0.70 mmol, 1.4 equiv) dissolved in toluene (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as a white solid (**108n**, 103 mg, 0.32 mmol, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.01 (d, *J* = 2.2 Hz, 1H), 6.80 (d, *J* = 2.2 Hz, 1H), 3.81 (s, 3H), 3.31 (s, 2H), 2.96 (q, *J* = 3.1 Hz, 1H), 2.58–2.52 (m, 1H), 2.42 (dt, *J* = 12.6, 3.1 Hz, 2H), 2.13–1.91 (m, 5H), 1.80–1.69 (m, 2H), 1.64–1.53 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.7, 135.1, 133.3, 130.5, 125.5, 112.1, 80.7, 56.3, 47.4, 39.7, 37.9, 37.2, 36.7, 36.6, 36.5, 35.5, 34.0, 33.6, 27.9, 27.0, 26.8.
MS (EI, 70 eV): m/z (%) = 202 (12), 70 (12), 61 (15), 46 (13), 45 (100).
HRMS (EI): for $C_{17}H_{20}Cl_2O_2$: calc. [M+]: 326.0840; found: 326.0832.

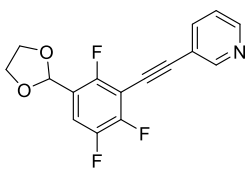
5-(4-((tert-butyldimethylsilyl)oxy)-2,6-difluorophenyl)-6-methoxy-2,3-dihydro-1H-inden-1-one (108o)



According to **TP 7**, to a mixture of tert-butyl(3,5-difluorophenoxy)dimethylsilane (**104k**, 122 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 5-iodo-6-methoxy-2,3-dihydro-1H-inden-1-one (120 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow solid (**108o**, 104 mg, 0.26 mmol, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.37 (s, 1H), 7.30 (s, 1H), 6.50–6.44 (m, 2H), 3.83 (s, 3H), 3.15–3.09 (m, 2H), 2.77–2.71 (m, 2H), 1.00 (s, 9H), 0.26 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 207.0, 160.6 (dd, *J* = 239.6, 11.0 Hz), 157.5, 157.1 147.3, 138.4, 130.2, 126.4, 107.8, 104.4, 103.8 (d, *J* = 27.9 Hz), 56.2, 37.1, 34.3, 29.9, 25.7, 25.2, 22.5, 18.3, 14.2, -4.3.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -112.1.
MS (EI, 70 eV): m/z (%) = 404 (37), 348 (48), 347 (100), 42 (27).
HRMS (EI): for $C_{22}H_{26}F_2O_3Si$: calc. [M-C_4H_9]: 347.0931; found: 347.0939.

3-((3-(1,3-dioxolan-2-yl)-2,5,6-trifluorophenyl)ethynyl)pyridine (108p)

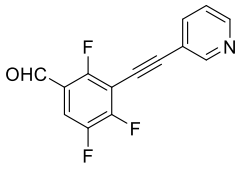


According to **TP 7**, to a mixture of 2-(2,4,5-trifluorophenyl)-1,3-dioxolane (**104l**, 102 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 0.5 h. Iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added

dropwise and the reaction mixture was stirred for 1 h. . A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%), CuI (4 mg, 4 mol%)and Et_3N (3 mL). The freshly prepared arylzinc reagent followed by 3-ethynyl pyridine (73 mg, 0.7 mmol, 1.4 equiv) were added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a yellow solid (**108p**, 108 mg, 0.35 mmol, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.80 (dd, *J* = 2.1, 0.9 Hz, 1H), 8.60 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.85 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.41–7.28 (m, 2H), 6.03 (d, *J* = 1.1 Hz, 1H), 4.17–4.01 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.5 (dt, *J* = 254.4, 2.9 Hz), 152.5, 152.2 (dd, *J* = 15.1, 5.3 Hz), 149.7, 146.8 (ddd, *J* = 246.3, 12.1, 3.7 Hz), 138.9, 123.2, 122.0 (dt, *J* = 14.4, 4.9 Hz), 119.4, 115.8 (ddd, *J* = 20.6, 5.3, 1.6 Hz), 103.8 (dt, *J* = 14.3, 1.4 Hz), 97.7 (d, *J* = 3.0 Hz), 97.0 (t, *J* = 3.5 Hz), 78.4 (d, *J* = 3.7 Hz), 65.6.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -115.1, -118.6, -128.8.
MS (EI, 70 eV): m/z (%) = 302 (27), 301 (93), 284 (100), 129 (39), 55 (45), 42 (90).
HRMS (EI): for $C_{16}H_{10}F_3NO_2$: calc. [M+]: 305.0664; found: 305.0658.

2,4,5-trifluoro-3-(pyridin-3-ylethynyl)benzaldehyde (108q)



3-((3-(1,3-dioxolan-2-yl)-2,5,6-trifluorophenyl)ethynyl)pyridine (**108p**, 31 mg, 0.10 mmol, 1.0 equiv) was dissolved in THF (1 mL). The reaction mixture was cooled to 0 C° and conc. HCl (3 drops) was added. The reaction mixture was allowed to warm to room temperature and stirred for 0.5 h. The reaction was quenched by addition of sat. $NaHCO_3$ solution (5 mL) and extracted with EtOAc (3 x 10 mL). Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 2:1) afforded the title compound as a white solid (**108q**, 25 mg, 0.096 mmol, 96% yield).

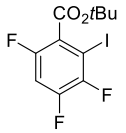
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 10.29 (d, *J* = 2.9 Hz, 1H), 8.83 (d, *J* = 2.1 Hz, 1H), 8.64 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.89 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.69 (td, *J* = 9.0, 6.2 Hz, 1H), 7.40–7.32 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 184.3 (dt, *J* = 6.7, 1.5 Hz), 160.8 (d, *J* = 262.9 Hz), 156.4–153.3 (m), 152.6, 152.5, 150.1, 149.2–148.7 (m), 146.6–146.2 (m), 139.0, 123.3, 121.3–120.3 (m), 118.9, 115.5 (dt, *J* = 19.8, 2.9 Hz), 105.6–104.8 (m), 98.5 (t, *J* = 3.5 Hz), 97.8, 65.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -118.7, -120.6, -138.6.

MS (EI, 70 eV): m/z (%) = 262 (13), 261 (100).

HRMS (EI): for $C_{14}H_6F_3NO$: calc. [M+]: 261.0401; found: 261.0408.

Tert-butyl 3,4,6-trifluoro-2-iodobenzoate (108r)



According to **TP 7**, to a mixture of tert-butyl 2,4,5-trifluorobenzoate (**104m**, 116 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a brown solid (**108r**, 112 mg, 0.31 mmol, 62% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.02 (ddd, *J* = 9.5, 8.4, 6.1 Hz, 1H), 1.61 (s, 9H).

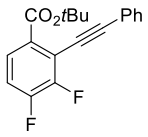
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.6, 154.6 (ddd, *J* = 252.6, 10.5, 3.6 Hz), 149.7 (ddd, *J* = 228.1, 12.2, 4.0 Hz), 147.5 (ddd, *J* = 225.1, 13.8, 4.7 Hz), 126.1 (dd, *J* = 21.6, 4.4 Hz), 106.5 (dd, *J* = 27.6, 21.5 Hz), 84.7, 82.2 (dd, *J* = 26.1, 5.2 Hz), 28.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -117.8, -129.3, -141.0.

MS (EI, 70 eV): m/z (%) = 306 (100), 305 (66), 260 (44), 233 (54), 73 (59), 42 (87).

HRMS (EI): for $C_{11}H_{10}F_3IO_2$: calc. [M+]: 357.9678; found: 357.9676.

Tert-butyl 3,4-difluoro-2-(phenylethynyl)benzoate (108s)

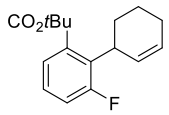


According to **TP 7**, to a mixture of tert-butyl 3,4-difluorobenzoate (**104n**, 107 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 20 min, the resulting diarylmagnesium was transmetalated with a ZnCl2 solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. Iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added

dropwise and the reaction mixture was stirred for 1 h. . A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%), CuI (4 mg, 4 mol%)and Et_3N (3 mL). The freshly prepared arylzinc reagent followed by phenylacetylene (77 µL, 0.7 mmol, 1.4 equiv) were added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**108s**, 117 mg, 0.37 mmol, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.68 (ddd, *J* = 8.8, 5.1, 1.9 Hz, 1H), 7.62–7.56 (m, 2H), 7.38 (tt, *J* = 3.8, 2.3 Hz, 3H), 7.16 (td, *J* = 9.0, 7.4 Hz, 1H), 1.60 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.2 (d, *J* = 2.6 Hz), 152.5 (dd, *J* = 242.1, 19.8 Hz), 151.5 (dd, *J* = 239.8, 9.8 Hz) 131.9, 130.9 (d, *J* = 3.5 Hz), 129.2, 128.6, 126.7–126.4 (m), 122.9, 116.4 (d, *J* = 17.6 Hz), 115.1–114.6 (m), 101.1 (d, *J* = 5.2 Hz), 82.5, 80.2 (d, *J* = 3.8 Hz), 28.3.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -132.0, -132.3.
MS (EI, 70 eV): m/z (%) = 259 (13), 258 (100), 240 (16), 200 (14).
HRMS (EI): for $C_{19}H_{16}F_2O_2$: calc. [M+]: 314.1118; found: 314.1121.

Tert-butyl 6-fluoro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxylate (108t)



According to **TP 7**, to a mixture of 3 tert-butyl 3-fluorobenzoate (**104o**, 392 mg, 2.00 mmol, 1.0 equiv) in toluene (4 mL) and THF (0.49 mL, 3.0 equiv) was added MBDA (**103**, 2.20 mmol, 1.1 equiv) at 25 °C. After 15 min, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.4 mL, 20 mol%, 1M in THF) and 3-bromocyclohexen (0.32 mL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a colorless oil (**108t**, 414 mg, 1.50 mmol, 75% yield).

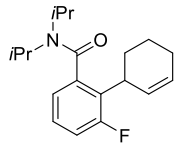
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.33 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.19 (td, *J* = 7.9, 5.1 Hz, 1H), 7.07 (ddd, *J* = 11.2, 8.1, 1.4 Hz, 1H), 5.81–5.73 (m, 1H), 5.64 (ddt, *J* = 10.1, 3.3, 1.7 Hz, 1H), 3.96 (ddq, *J* = 9.9, 5.1, 2.5 Hz, 1H), 2.23–2.00 (m, 3H), 1.96–1.81 (m, 2H), 1.76–1.64 (m, 1H), 1.58 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.7 (d, *J* = 3.7 Hz), 162.2 (d, *J* = 249.0 Hz), 136.0 (d, *J* = 5.1 Hz), 132.4 (d, *J* = 13.1 Hz), 129.8 (d, *J* = 1.3 Hz), 127.4 (d, *J* = 9.0 Hz), 126.6 (d, *J* = 2.7 Hz), 124.7 (d, *J* = 3.3 Hz), 118.4 (d, *J* = 23.0 Hz), 82.3, 36.9, 29.1 (d, *J* = 2.0 Hz), 28.3, 24.8, 23.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -112.9.

MS (EI, 70 eV): m/z (%) = 202 (100), 201 (62), 184 (57), 173 (19), 146 (27).

HRMS (EI): for $C_{17}H_{21}FO_2$: calc. [M+]: 276.1526; found: 276.1534.

6-fluoro-*N*,*N*-diisopropyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxamide (108u)



According to **TP 7**, to a mixture of 3-fluoro-*N*,*N*-diisopropylbenzamide (**104p**, 112 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.1 mL, 20 mol%, 1M in THF) and 3-bromocyclohexen (70 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 92:8) afforded the title compound as a white solid (**108u**, 120 mg, 0.40 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.17 (tt, *J* = 7.9, 5.2 Hz, 1H), 6.96 (dddd, *J* = 11.1, 8.3, 2.6, 1.3 Hz, 1H), 6.86 (ddd, *J* = 7.6, 4.2, 1.3 Hz, 1H), 5.77 (dddd, *J* = 14.7, 10.0, 4.5, 2.6 Hz, 1H), 5.62 (dddd, *J* = 11.9, 10.1, 3.9, 1.8 Hz, 1H), 3.77–3.34 (m, 3H), 2.22–1.99 (m, 3H), 1.94–1.74 (m, 2H), 1.67-1.51 (m, 7H), 1.18–1.05 (m, 6H).

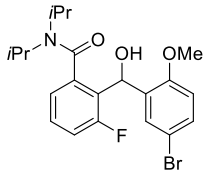
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 169.2 (dd, *J* = 10.0, 3.0 Hz), 162.2 (d, *J* = 250.1 Hz), 140.6 (dd, *J* = 13.9, 4.9 Hz), 129.8 (d, *J* = 13.6 Hz), 129.5–129.2 (m), 127.9 (dd, *J* = 33.7, 9.0 Hz), 127.3 (dd, *J* = 4.5, 2.1 Hz), 121.0 (d, *J* = 3.5 Hz), 120.4 (d, *J* = 3.5 Hz), 116.0 (dd, *J* = 22.6, 17.4 Hz), 50.9 (d, *J* = 9.8 Hz), 45.9 (d, *J* = 4.5 Hz), 38.1, 37.0, 29.1 (dd, *J* = 24.2, 2.3 Hz), 24.8 (d, *J* = 8.8 Hz), 23.1 (d, *J* = 5.4 Hz), 20.9 – 20.3 (m).

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -112.2.

MS (EI, 70 eV): m/z (%) = 202 (100), 201 (75), 185 (55), 165 (35), 146 (34), 133 (36).

HRMS (EI): for $C_{19}H_{26}FNO$: calc. [M+]: 303.1998; found: 303.1994.

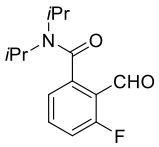
2-((5-bromo-2-methoxyphenyl)(hydroxy)methyl)-3-fluoro-*N*,*N*-diisopropylbenzamide (108v)



According to **TP 7**, to a mixture of 3-fluoro-*N*,*N*-diisopropylbenzamide (**104p**, 112 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the reaction mixture was cooled to 0 °C and 5-bromo-2-methoxybenzaldehyde (151 mg, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 6:1) afforded the title compound as a white solid (**108v**, 157 mg, 0.36 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.79 (dd, *J* = 2.6, 1.1 Hz, 1H), 7.30 (ddd, *J* = 8.6, 2.6, 0.7 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.13 (ddd, *J* = 9.7, 8.2, 1.3 Hz, 1H), 6.89 – 6.85 (m, 1H), 6.60 (d, *J* = 8.6 Hz, 1H), 6.22 (dq, *J* = 11.4, 1.2 Hz, 1H), 6.08 (d, *J* = 11.2 Hz, 1H), 3.57 (s, 3H), 3.30 (dp, *J* = 25.2, 6.7 Hz, 2H), 1.46 (d, *J* = 6.9 Hz, 3H), 1.40 (d, *J* = 6.7 Hz, 3H), 1.06 (d, *J* = 6.6 Hz, 3H), 0.29 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 171.6 (d, *J* = 3.1 Hz), 161.0 (d, *J* = 249.0 Hz), 155.4, 137.8 (d, *J* = 2.2 Hz), 134.0 (d, *J* = 1.8 Hz), 131.0, 130.9, 130.5, 130.4, 128.3 (d, *J* = 9.3 Hz), 122.5 (d, *J* = 3.7 Hz), 116.5 (d, *J* = 24.9 Hz), 113.5, 112.0, 64.0 (d, *J* = 8.7 Hz), 60.5, 55.7, 51.5, 46.5, 21.3, 20.2, 20.2, 20.0.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -114.1.
MS (EI, 70 eV): m/z (%) = 404 (36), 241 (59), 220 (40), 183 (100), 170 (81).
HRMS (EI): for $C_{21}H_{25}BrFNO_3$: calc. [M+]: 437.1002; found: 437.0993.

3-fluoro-2-formyl-*N*,*N*-diisopropylbenzamide (108w)

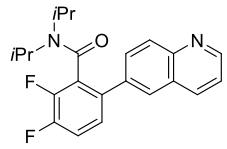


According to **TP 7**, to a mixture of 3-fluoro-*N*,*N*-diisopropylbenzamide (**104p**, 670 mg, 3.00 mmol, 1.0 equiv) in toluene (6 mL) was added MBDA (**103**, 3.30 mmol, 1.1 equiv) at 25 °C. After 10 min, the

reaction mixture was cooled to 0 °C and DMF (0.69 mL, 9.00 mmol, 3.0 equiv) was added dropwise and the reaction mixture was stirred for 1 h at room temperature. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 2:1) afforded the title compound as a white solid (**108w**, 477 mg, 1.90 mmol, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 10.37 (s, 1H), 7.58 (ddd, *J* = 8.4, 7.6, 5.3 Hz, 1H), 7.16 (ddd, *J* = 10.5, 8.4, 1.0 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 3.52 (dp, *J* = 9.6, 6.8 Hz, 2H), 1.60 (d, *J* = 6.9 Hz, 7H), 1.10 (d, *J* = 6.7 Hz, 7H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 186.8, 167.9, 164.8 (d, *J* = 260.2 Hz), 141.0, 136.1, 122.3 (d, *J* = 3.8 Hz), 120.9 (d, *J* = 8.6 Hz), 116.4 (d, *J* = 20.6 Hz), 51.4 (d, *J* = 7.4 Hz), 46.1 (d, *J* = 7.5 Hz), 20.5.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -119.0.
MS (EI, 70 eV): m/z (%) = 208 (13), 166 (23), 151 (100), 123 (31), 100 (10), 75 (10).
HRMS (EI): for $C_{14}H_{18}FNO_2$: calc. [M+]: 251.1322; found: 251.1324.

2,3-difluoro-*N*,*N*-diisopropyl-6-(quinolin-6-yl)benzamide (108x)



According to **TP 7**, to a mixture of 2,3-difluoro-N,N-diisopropylbenzamide (**104q**, 121 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 25 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 6-iodoquinoline (106 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) afforded the title compound as a yellow solid (**108x**, 99 mg, 0.27 mmol, 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.96 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.22–8.13 (m, 2H), 8.10 (d, *J* = 2.1 Hz, 1H), 7.85 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.46 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.32–7.23 (m, 2H), 3.52 (hept, *J* = 6.6 Hz, 1H), 3.23 (hept, *J* = 6.8 Hz, 1H), 1.54 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.33 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.5 (d, *J* = 2.5 Hz), 151.1, 150.7 (dd, *J* = 249.4, 13.7 Hz), 147.7, 146.9 (dd, *J* = 249.4, 14.0 Hz), 136.6, 136.2 (d, *J* = 1.9 Hz), 134.5–134.4 (m), 130.8, 129.8,

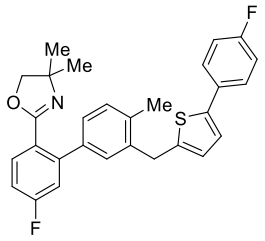
128.5, 128.3, 128.0, 125.8 (dd, *J* = 6.3, 3.7 Hz), 121.9, 117.1 (d, *J* = 17.2 Hz), 51.3, 46.2, 20.9, 20.5, 20.0, 19.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -137.5, -141.0.

MS (EI, 70 eV): m/z (%) = 333 (12), 269 (15), 268 (100), 240 (14).

HRMS (EI): for $C_{22}H_{22}F_2N_2O$: calc. [M+]: 368.1700; found: 368.1695.

2-(5-fluoro-3'-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4'-methyl-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (108y)



According to **TP 7**, to a mixture of 2-(4-fluorophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**104r**, 163 mg, 0.84 mmol, 1.0 equiv) in toluene (1.70 mL) was added MBDA (**103**, 0.92 mmol, 1.1 equiv) at 60 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (1.0 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (15 mg, 3 mol%), tfp (12 mg, 6 mol%) and 2-(4-fluorophenyl)-5-(5-iodo-2-methylbenzyl)thiophene (280 mg, 0.69 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1 to 1:1) afforded the title compound as a yellow oil (**108y**, 313 mg, 0.66 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.74 (dd, *J* = 8.6, 5.8 Hz, 1H), 7.50–7.45 (m, 2H), 7.27 (t, *J* = 1.2 Hz, 1H), 7.23 (d, *J* = 1.3 Hz, 2H), 7.09 (dd, *J* = 9.5, 2.6 Hz, 1H), 7.07–7.00 (m, 4H), 6.67 (dd, *J* = 3.6, 1.2 Hz, 1H), 4.15 (d, *J* = 1.3 Hz, 2H), 3.77 (s, 2H), 2.38 (s, 3H), 1.26 (s, 6H).

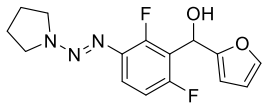
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.8 (d, *J* = 239.9 Hz),163.3, 162.1 (d, *J* = 236.2 Hz), 144.0 (d, *J* = 8.4 Hz), 143.3 (d, *J* = 1.0 Hz), 141.7, 138.2 (d, *J* = 1.7 Hz), 138.0, 136.1, 132.7 (d, *J* = 9.0 Hz), 130.9 (d, *J* = 3.4 Hz), 130.5, 129.5, 127.2 (d, *J* = 8.0 Hz), 126.8, 126.0, 124.0 (d, *J* = 3.0 Hz), 122.7 (d, *J* = 1.2 Hz), 117.3 (d, *J* = 22.0 Hz), 115.8 (d, *J* = 21.7 Hz), 114.0 (d, *J* = 21.5 Hz), 79.6, 67.4, 34.3, 28.1, 19.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -109.9, -115.0.

MS (EI, 70 eV): m/z (%) = 240 (19), 239 (16), 222 (13), 196 (29), 191 (100), 178 (16), 139 (22).

HRMS (EI): for $C_{29}H_{25}F_2NOS$: calc. [M-H$^+$]: 472.1547; found: 472.1539.

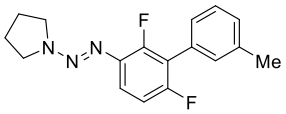
(*E*)-(2,6-difluoro-3-(pyrrolidin-1-yldiazenyl)phenyl)(furan-2-yl)methanol (108z)



According to **TP 7**, to a mixture of (*E*)-1-((2,4-difluorophenyl)diazenyl)pyrrolidine (**104s**, 211 mg, 1.00 mmol, 1.0 equiv) in toluene (2 mL) was added MBDA (**103**, 1.10 mmol, 1.1 equiv) at 0 °C. After 1 h, furfural (0.12 mL, 1.40 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 8:1 to 4:1) afforded the title compound as a brown oil (**108z**, 173 mg, 0.60 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.44–7.37 (m, 2H), 6.86 (td, *J* = 9.4, 1.7 Hz, 1H), 6.32 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.23 (d, *J* = 3.3 Hz, 1H), 6.19 (s, 1H), 4.06–3.52 (m, 4H), 2.13–1.97 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.9 (dd, *J* = 239.0, 5.9 Hz), 154.1, 154.1 (dd, *J* = 243.3, 7.9 Hz), 142.7, 119.1 (dd, *J* = 10.0, 3.6 Hz), 117.4–116.9 (m), 111.5 (dd, *J* = 23.2, 3.9 Hz), 110.5, 107.3, 63.0–62.0 (m).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -120.3, -129.1.
MS (EI, 70 eV): m/z (%) = 239 (27), 140 (100), 94 (26), 84 (25), 70 (27), 40 (34).
HRMS (EI): for $C_{15}H_{15}F_2N_3O_2$: calc. [M+]: 307.1132; found: 307.1141.

(*E*)-1-((2,6-difluoro-3'-methyl-[1,1'-biphenyl]-3-yl)diazenyl)pyrrolidine (108aa)

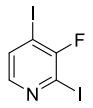


According to **TP 7**, to a mixture of (*E*)-1-((2,4-difluorophenyl)diazenyl)pyrrolidine (**104s**, 845 mg, 4.00 mmol, 1.0 equiv) in toluene (8.0 mL) was added MBDA (**103**, 4.40 mmol, 1.1 equiv) at 0 °C. After 1 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (5.6 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (64 mg, 3 mol%), tfp (56 mg, 6 mol%) and 3-iodotoluene (0.43 mL, 3.32 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column

chromatography (silica gel, *i*hexane/EtOAc = 98:2) afforded the title compound as an orange solid (**108aa**, 741 mg, 2.46 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.43–7.28 (m, 4H), 7.21 (ddt, *J* = 7.5, 2.2, 1.0 Hz, 1H), 6.91 (td, *J* = 9.0, 1.8 Hz, 1H), 3.82 (d, *J* = 70.6 Hz, 4H), 2.41 (s, 3H), 2.11–1.98 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.4 (dd, *J* = 245.5, 6.2 Hz), 153.3 (dd, *J* = 251.5, 7.0 Hz), 137.9, 136.6 (dd, *J* = 9.1, 3.8 Hz), 131.2 (t, *J* = 1.8 Hz), 129.7, 129.0, 128.2, 127.5 (t, *J* = 1.9 Hz), 119.0 (dd, *J* = 19.6, 18.0 Hz), 118.1 (dd, *J* = 9.6, 3.3 Hz), 111.1 (dd, *J* = 23.7, 4.0 Hz), 23.9, 21.6.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -119.6, -128.4.
MS (EI, 70 eV): m/z (%) = 231 (26), 203 (100), 201 (14), 188 (48), 183 (21).
HRMS (EI): for $C_{17}H_{17}F_2N_3$: calc. [M+]: 301.1391; found: 301.1377.

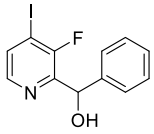
3-fluoro-2,4-diiodopyridine (109a)



According to **TP 7**, to a mixture of 3-fluoro-4-iodopyridine (**105a**, 112 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.30 mmol, 0.6 equiv) at 0 °C. After 5 min, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a brown solid (**109a**, 142 mg, 0.41 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (d, *J* = 4.9 Hz, 1H), 7.65 (t, *J* = 4.7 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.7 (d, *J* = 255.4 Hz), 147.0 (d, *J* = 6.2 Hz), 134.1, 105.4 (d, *J* = 31.8 Hz), 91.1 (d, *J* = 26.2 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -81.9.
MS (EI, 70 eV): m/z (%) = 70 (11), 61 (13), 45 (14), 44 (14), 43 (100).
HRMS (EI): for $C_5H_2FI_2N$: calc. [M+]: 348.8261; found: 348.8255.

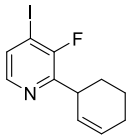
(3-fluoro-4-iodopyridin-2-yl)(phenyl)methanol (109b)



According to **TP 7**, to a mixture of 3-fluoro-4-iodopyridine (**105a**, 112 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.30 mmol, 0.6 equiv) at 0 °C. After 5 min, the reaction mixture was cooled to 0 °C and benzaldehyde (78 µL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a white solid (**109b**, 120 mg, 0.37 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.04 (d, *J* = 5.0 Hz, 1H), 7.66 (t, *J* = 4.8 Hz, 1H), 7.42–7.26 (m, 6H), 5.97 (d, *J* = 2.2 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.3 (d, *J* = 256.3 Hz), 149.2 (d, *J* = 19.0 Hz), 144.4 (d, *J* = 6.2 Hz), 141.7, 133.9, 128.7, 128.2, 127.8, 127.1, 126.9 (d, *J* = 1.7 Hz), 93.7 (d, *J* = 23.3 Hz), 70.5 (d, *J* = 3.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -106.9.
MS (EI, 70 eV): m/z (%) = 328 (16), 61 (11), 45 (10), 44 (100).
HRMS (EI): for $C_{12}H_9FINO$: calc. [M+]: 328.9713; found: 328.9692.

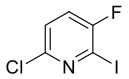
2-(cyclohex-2-en-1-yl)-3-fluoro-4-iodopyridine (109c)



According to **TP 7**, to a mixture of 3-fluoro-4-iodopyridine (**105a**, 112 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.30 mmol, 0.6 equiv) at 0 °C. After 5 min, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.1 mL, 20 mol%, 1M in THF) and 3-bromocyclohexen (70 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 97:3) afforded the title compound as a colorless oil (**109c**, 127 mg, 0.42 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.00 (d, *J* = 5.0 Hz, 1H), 7.54 (t, *J* = 4.7 Hz, 1H), 5.97 (ddt, *J* = 10.1, 5.0, 2.7 Hz, 1H), 5.75–5.66 (m, 1H), 3.91 (qp, *J* = 5.1, 2.5 Hz, 1H), 2.24–1.98 (m, 3H), 1.90–1.82 (m, 1H), 1.77–1.64 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.3 (d, *J* = 255.9 Hz), 153.5 (d, *J* = 16.5 Hz), 145.6 (d, *J* = 6.6 Hz), 132.3, 129.3, 127.3 (d, *J* = 1.3 Hz), 92.7 (d, *J* = 24.2 Hz), 37.9 (d, *J* = 2.2 Hz), 28.9, 24.8, 21.7.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -107.7.
MS (EI, 70 eV): m/z (%) = 207 (6), 70 (11), 63 (18), 61 (13), 44 (12), 41 (100).
HRMS (EI): for $C_{11}H_{11}FIN$: calc. [M+]: 302.9920; found: 302.9908.

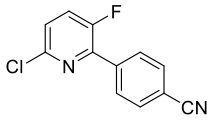
6-chloro-3-fluoro-2-iodopyridine (109d)



According to **TP 7**, to a mixture of 2-chloro-5-fluoropyridine (**105b**, 49 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 10 min, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a colorless oil (**109d**, 96 mg, 0.38 mmol, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.25–7.19 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.9 (d, *J* = 257.2 Hz), 145.6 (d, *J* = 3.0 Hz), 125.0, 124.8 (d, *J* = 3.2 Hz), 124.7, 104.6 (d, *J* = 31.2 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -105.1.
MS (EI, 70 eV): m/z (%) = 256 (27), 131 (32), 129 (100), 109 (35), 94 (12).
HRMS (EI): for C_5H_2ClFIN: calc. [M+]: 256.8904; found: 256.8897.

4-(6-chloro-3-fluoropyridin-2-yl)benzonitrile (109e)



According to **TP 7**, to a mixture of 2-chloro-5-fluoropyridine (**105b**, 49 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 10 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 4-iodobenzonitrile (120 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) afforded the title compound as a white solid (**109e**, 96 mg, 0.41 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.18–8.10 (m, 2H), 7.81–7.74 (m, 2H), 7.53 (dd, *J* = 10.0, 8.6 Hz, 1H), 7.35 (dd, *J* = 8.6, 3.1 Hz, 1H).

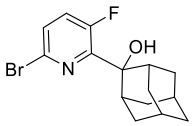
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.0 (d, *J* = 261.3 Hz), 146.0 (d, *J* = 2.7 Hz), 143.6 (d, *J* = 12.4 Hz), 138.1 (d, *J* = 5.8 Hz), 132.4, 129.5 (d, *J* = 7.1 Hz), 128.0 (d, *J* = 23.1 Hz), 125.6 (d, *J* = 5.1 Hz), 118.6, 113.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -125.3.

MS (EI, 70 eV): m/z (%) = 234 (24), 232 (81), 205 (13), 198 (12), 197 (100), 177 (21), 170 (28), 150 (26).

HRMS (EI): for $C_{12}H_6ClFN_2$: calc. [M+]: 232.0204; found: 232.0196.

(1r,5R,7S)-2-(6-bromo-3-fluoropyridin-2-yl)adamantan-2-ol (109f)



According to **TP 7**, to a mixture of 2-bromo-5-fluoropyridine (**105c**, 88 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and adamantan-2-one (105 mg, 0.70 mmol, 1.4 equiv) dissolved in toluene (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 94:6) afforded the title compound as a white solid (**109f**, 122 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 (dd, *J* = 8.4, 3.1 Hz, 1H), 7.32–7.27 (m, 1H), 2.76 (s, 2H), 2.38 (dd, *J* = 12.8, 3.1 Hz, 3H), 2.22 (s, 1H), 1.94–1.68 (m, 10H).

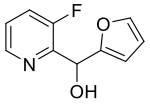
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.0 (d, *J* = 261.1 Hz), 153.0 (d, *J* = 11.5 Hz), 134.1 (d, *J* = 2.5 Hz), 128.2 (d, *J* = 4.9 Hz), 127.8 (d, *J* = 24.0 Hz), 78.2 (d, *J* = 4.6 Hz), 37.7, 35.1, 35.0, 34.9, 32.8, 27.0, 26.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -121.8.

MS (EI, 70 eV): m/z (%) = 61 (12), 44 (10), 42 (100).

HRMS (EI): for $C_{15}H_{17}BrFNO$: calc. [M+]: 325.0478; found: 325.0464.

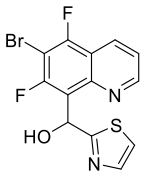
(3-fluoropyridin-2-yl)(furan-2-yl)methanol (109g)



According to **TP 7**, to a mixture of 3-fluoropyridine (**105d**, 43 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.30 mmol, 0.6 equiv) at 0 °C. After 15 min, the reaction mixture was cooled to 0 °C and furfural (58 µL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a white solid (**109g**, 71 mg, 0.37 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.45 (d, *J* = 4.7 Hz, 1H), 7.47–7.29 (m, 3H), 6.37–6.28 (m, 1H), 6.20 (d, *J* = 3.3 Hz, 1H), 6.09–6.01 (m, 1H), 5.58–4.84 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.5 (d, *J* = 258.3 Hz), 154.1, 146.4 (d, *J* = 16.1 Hz), 144.1 (d, *J* = 5.2 Hz), 142.8, 124.7 (d, *J* = 3.7 Hz), 123.8 (d, *J* = 18.2 Hz), 110.4, 107.6, 64.0 (d, *J* = 1.8 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -125.7.
MS (EI, 70 eV): m/z (%) = 193 (46), 164 (100), 136 (55), 97 (56), 81 (36) 68 (41).
HRMS (EI): for $C_{10}H_8FNO_2$: calc. [M+]: 193.0539; found: 193.0532.

(6-bromo-5,7-difluoroquinolin-8-yl)(thiazol-2-yl)methanol (109h)

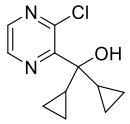


According to **TP 7**, to a mixture of 6-bromo-5,7-difluoroquinoline (**105e**, 122 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and thiazole-2-carbaldehyde (70 µL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 3:1) afforded the title compound as a yellow solid (**109h**, 121 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.83 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.43 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.70 (d, *J* = 11.1 Hz, 1H), 7.61 (d, *J* = 3.3 Hz, 1H), 7.48 (dd, *J* = 8.5, 4.4 Hz, 1H), 6.70 (d, *J* = 11.1 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 175.3 (d, *J* = 2.4 Hz), 155.7 (ddd, *J* =255.6,183.2, 57.4, 6.8 Hz), 150.7, 145.6 (dd, *J* = 8.6, 4.2 Hz), 142.8, 130.5 (dd, *J* = 4.0, 2.1 Hz), 121.4 (t, *J* = 2.6 Hz), 119.6, 119.0 (dd, *J* = 16.6, 5.4 Hz), 117.2 (dd, *J* = 17.2, 1.8 Hz), 97.7 (d, *J* = 23.5 Hz), 97.4 (d, *J* = 23.5 Hz), 69.2 (d, *J* = 4.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -105.6, -111.7.
MS (EI, 70 eV): m/z (%) = 271 (15), 244 (10), 242 (12), 163 (11), 86 (26), 70 (11), 61 (14), 45 (14), 43 (100).
HRMS (EI): for $C_{13}H_7BrF_2N_2OS$: calc. [M+]: 355.9431; found: 355.9421.

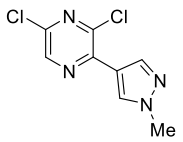
(3-chloropyrazin-2-yl)dicyclopropylmethanol (109i)



According to **TP 7**, to a mixture of 2-chloropyrazine (**105f**, 45 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at -25 °C. After 0.5 h, the reaction mixture dicyclopropylketone (79 µL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**109i**, 75 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.37 (s, 2H), 4.84 (s, 1H), 1.89 (tt, *J* = 8.3, 5.2 Hz, 2H), 0.79 (dtd, *J* = 9.5, 5.6, 4.1 Hz, 2H), 0.48 (tdd, *J* = 8.7, 6.0, 4.0 Hz, 2H), 0.20 – 0.05 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.5, 147.3, 142.5, 139.1, 71.6, 17.2, 1.5, -0.7.
MS (EI, 70 eV): m/z (%) = 185 (26), 183 (82), 181 (23), 155 (21), 142 (29), 140 (90), 128 (64), 112 (69), 111 (100), 69 (74).
HRMS (EI): for $C_{11}H_{13}ClN_2O$: calc. [M+]: 224.0716; found: 224.0711.

3,5-dichloro-2-(1-methyl-1H-pyrazol-4-yl)pyrazine (109j)

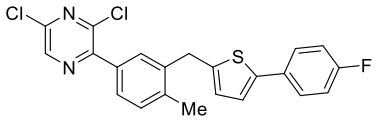


According to **TP 7**, to a mixture of 2,6-dichloropyrazine (**105g**, 75 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at -20 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 4-iodo-1-methyl-1H-pyrazole

(86 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 3:1) afforded the title compound as a yellow solid (**109j**, 79 mg, 0.35 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.45 (s, 1H), 8.24 (s, 1H), 8.19 (s, 1H), 3.99 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 144.8, 143.0, 142.7, 141.9, 140.5, 131.8, 118.0, 39.5.
MS (EI, 70 eV): m/z (%) = 229 (63), 227 (100), 195 (29), 193 (91), 168 (14), 166 (43).
HRMS (EI): for $C_8H_6Cl_2N_4$: calc. [M+]: 227.9970; found: 227.9963.

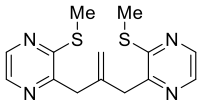
3,5-dichloro-2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrazine (109k)



According to **TP 7**, to a mixture of 2,6-dichloropyrazine (**105g**, 75 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at -20 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 2-(4-fluorophenyl)-5-(5-iodo-2-methylbenzyl)thiophene (169 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) afforded the title compound as a yellow oil (**109k**, 146 mg, 0.34 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.57 (s, 1H), 7.67 (d, *J* = 2.0 Hz, 1H), 7.64 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.51–7.45 (m, 2H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.07–6.99 (m, 3H), 6.74–6.69 (m, 1H), 4.20 (s, 2H), 2.41 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1 (d, *J* = 246.8 Hz), 151.1, 145.4, 145.0, 142.6, 141.9, 141.8, 138.6 (d, *J* = 36.6 Hz), 133.0, 130.8 (d, *J* = 3.4 Hz), 130.5 (d, *J* = 13.6 Hz), 128.0, 127.2 (d, *J* = 8.0 Hz), 126.3, 122.8 (d, *J* = 1.2 Hz), 115.9, 115.6, 34.1, 19.5.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -114.9.
MS (EI, 70 eV): m/z (%) = 430 (62), 429 (29), 428 (90), 413 (20), 252 (64), 250 (100), 191 (53), 178 (20).
HRMS (EI): for $C_{22}H_{15}Cl_2FN_2S$: calc. [M+]: 428.0317; found: 428.0312.

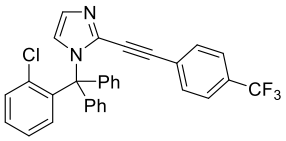
3,3'-(2-methylenepropane-1,3-diyl)bis(2-(methylthio)pyrazine) (109l)



According to **TP 7**, to a mixture of 2-(methylthio)pyrazine (**105h**, 63 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at -10 °C. After 15 min, the reaction mixture was cooled to -25 °C and CuCN·2LiCl (0.1 mL, 20 mol%, 1M in THF) and 3-bromo-2-(bromomethyl)prop-1-ene (35 µL, 0.3 mmol, 0.6 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 2:1) afforded the title compound as a brown solid (**109l**, 56 mg, 0.18 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.25 (d, *J* = 2.7 Hz, 2H), 8.16 (d, *J* = 2.7 Hz, 2H), 4.93 (t, *J* = 1.2 Hz, 2H), 3.64 (d, *J* = 1.3 Hz, 4H), 2.51 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.7, 152.4, 141.6, 140.9, 138.3, 116.1, 41.3, 13.0.
MS (EI, 70 eV): m/z (%) = 289 (23), 257 (42), 179 (13), 165 (100), 150 (20), 131 (12).
HRMS (EI): for $C_{14}H_{16}N_4S_2$: calc. [M+]: 304.0816; found: 304.0811.

1-((2-chlorophenyl)diphenylmethyl)-2-((4-(trifluoromethyl)phenyl)ethynyl)-1*H*-imidazole (109m)

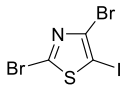


According to **TP 7**, to a mixture of clotrimazole (**105i**, 173 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 0 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 0.5 h. Iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%), CuI (4 mg, 4 mol%)and Et_3N (3 mL). The freshly prepared arylzinc reagent followed by 1-ethynyl-4-(trifluoromethyl)benzene (0.11 mL, 0.7 mmol, 1.4 equiv) were added and the reaction mixture was placed in an oil bath at 55 °C for 2 h. Purification of the crude product by flash column chromatography (silica gel,

DCM/MeOH = 98:2) afforded the title compound as a brown oil (**109m**, 175 mg, 0.34 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.46–7.40 (m, 3H), 7.31 (qd, *J* = 4.2, 3.6, 2.0 Hz, 8H), 7.24–7.17 (m, 5H), 7.11–7.06 (m, 2H), 7.04–6.98 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 140.3, 139.6, 135.9, 133.0, 132.6, 131.9, 131.6, 130.8, 129.9, 128.2, 128.1, 127.9, 126.6, 126.0, 125.3, 125.2, 125.1 (q, *J* = 3.8 Hz), 125.1, 125.0, 123.9 (q, *J* = 271.6 Hz), 122.6, 92.5, 83.4, 76.4.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -62.9.
MS (EI, 70 eV): m/z (%) = 278 (36), 276 (100), 238 (31), 235 (36), 165 (62).
HRMS (EI): for $C_{31}H_{20}ClF_3N_2$: calc. [M+]: 512.1267; found: 512.1262.

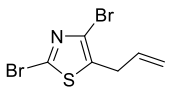
2,4-dibromo-5-iodothiazole (109n)



According to **TP 7**, to a mixture of 2,4-dibromothiazole (**105j**, 121 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and iodine (152 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 199:1) afforded the title compound as a brown solid (**109n**, 141 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = no proton signals existing.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 140.3, 134.0, 74.7.
MS (EI, 70 eV): m/z (%) = 368 (12), 243 (48), 241 (100), 134 (77), 81 (22).
HRMS (EI): for C_3Br_2INS: calc. [M+]: 366.7163; found: 366.7158.

5-allyl-2,4-dibromothiazole (109o)

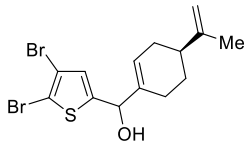


According to **TP 7**, to a mixture of 2,4-dibromothiazole (**105j**, 121 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 25 °C. After 0.5 h, the reaction

mixture was cooled to -25 °C and CuCN·2LiCl (0.1 mL, 20 mol%, 1M in THF) and allyl bromide (69 µL, 0.6 mmol, 1.2 equiv) were added and the mixture was stirred for 0.5 h at -25 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 199:1) afforded the title compound as a yellow oil (**109o**, 135 mg, 0.48 mmol, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 5.94–5.82 (m, 1H), 5.23–5.19 (m, 1H), 5.17 (d, *J* = 1.4 Hz, 1H), 3.53–3.45 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 136.6, 134.0, 133.4, 122.6, 118.4, 32.0.
MS (EI, 70 eV): m/z (%) = 282 (16), 203 (18), 201 (19), 124 (15), 123 (100).
HRMS (EI): for $C_6H_5Br_2NS$: calc. [M+]: 280.8509; found: 280.8504.

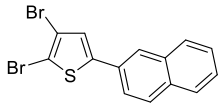
(4,5-dibromothiophen-2-yl)((S)-4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methanol (109p)



According to **TP 7**, to a mixture of 2,3-dibromothiophene (**105k**, 57 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 40 °C. After 0.5 h, the reaction mixture was cooled to 0 °C and (*S*)-(-)-perillaldehyde (0.11 mL, 0.70 mmol, 1.4 equiv) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C and then allowed to warm to room temperature and stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a yellow oil (**109p**, 150 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 6.75 (dd, *J* = 6.0, 1.1 Hz, 1H), 5.91 (td, *J* = 4.8, 4.2, 1.6 Hz, 1H), 5.23 (t, *J* = 3.8 Hz, 1H), 4.77–4.70 (m, 2H), 2.27–1.92 (m, 5H), 1.84 (ddq, *J* = 12.7, 5.0, 2.0 Hz, 1H), 1.74 (s, 3H), 1.45 (tdd, *J* = 12.7, 10.3, 4.7 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 149.5, 149.4, 148.6, 148.3, 138.3, 137.9, 126.8, 126.8, 125.2, 125.0, 113.2, 110.4, 110.4, 109.1, 74.6, 74.3, 41.1, 41.0, 30.6, 30.5, 27.4, 24.2, 24.0, 20.9.
MS (EI, 70 eV): m/z (%) = 268 (55), 254 (31), 171 (65), 115 (41), 91 (100).
HRMS (EI): for $C_{14}H_{16}Br_2OS$: calc. [M-2H$^+$]: 387.9132; found: 387.9126.

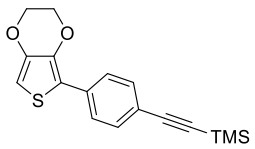
2,3-dibromo-5-(naphthalen-2-yl)thiophene (109q)



According to **TP 7**, to a mixture of 2,3-dibromothiophene (**105k**, 57 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 40 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 2-iodonaphthalene (105 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, pentane) afforded the title compound as a white solid (**109q**, 127 mg, 0.35 mmol, 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.23–8.13 (m, 1H), 7.96–7.86 (m, 2H), 7.60–7.46 (m, 4H), 7.07 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 143.4, 133.9, 131.5, 130.6, 129.9, 129.6, 128.6, 128.3, 127.1, 126.5, 125.3, 125.2, 114.0, 111.0.
MS (EI, 70 eV): m/z (%) = 209 (13), 208 (100), 164 (65), 163 (88), 104 (11).
HRMS (EI): for $C_{14}H_8Br_2S$: calc. [M+]: 365.8713; found: 365.8705.

((4-(2,3-dihydrothieno[3,4-b][1,4]dioxin-5-yl)phenyl)ethynyl)trimethylsilane (109r)

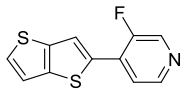


According to **TP 7**, to a mixture of 2,3-dihydrothieno[3,4-b][1,4]dioxine (**105l**, 53 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.40 mmol, 0.8 equiv) at 50 °C. After 0.5 h, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and ((4-iodophenyl)ethynyl)trimethylsilane (130 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of

the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a yellow solid (**109r**, 111 mg, 0.37 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.71–7.63 (m, 2H), 7.48–7.41 (m, 2H), 6.33 (s, 1H), 4.34–4.31 (m, 2H), 4.27–4.22 (m, 2H), 0.26 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 142.4, 138.9, 133.5, 132.3, 125.7, 125.5, 120.9, 117.0, 105.4, 98.5, 94.7, 64.9, 64.5.
MS (EI, 70 eV): m/z (%) = 317 (17), 314 (81), 299 (100), 217 (12).
HRMS (EI): for $C_{17}H_{18}O_2SSi$: calc. [M+]: 314.0797; found: 314.0790.

3-fluoro-4-(thieno[3,2-b]thiophen-2-yl)pyridine (109s)

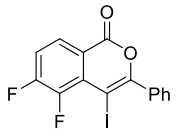


According to **TP 7**, to a mixture of thieno[3,2-b]thiophene (**105m**, 70 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added MBDA (**103**, 0.55 mmol, 1.1 equiv) at 70 °C. After 15 min, the resulting diarylmagnesium was transmetalated with a $ZnCl_2$ solution (0.70 mL, 1.00 M in THF, 1.4 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (8 mg, 3 mol%), tfp (7 mg, 6 mol%) and 3-fluoro-4-iodopyridine (93 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 12 h. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) afforded the title compound as a brown solid (**109s**, 58 mg, 0.25 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.53 (d, *J* = 3.2 Hz, 1H), 8.41 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.89 (t, *J* = 0.8 Hz, 1H), 7.57–7.48 (m, 2H), 7.30 (d, *J* = 5.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 155.5 (d, *J* = 259.3 Hz), 146.2 (d, *J* = 5.0 Hz), 140.8 (d, *J* = 3.7 Hz), 140.3 (d, *J* = 1.7 Hz), 139.3 (d, *J* = 25.4 Hz), 135.9 (d, *J* = 4.0 Hz), 129.7, 129.6, 121.8 (d, *J* = 9.6 Hz), 121.3, 119.6.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -128.9.
MS (EI, 70 eV): m/z (%) = 236 (10), 235 (16), 234 (100), 63 (15), 61 (10), 41 (63).
HRMS (EI): for $C_{11}H_6FNS_2$: calc. [M+]: 234.9926; found: 234.9914.

5.4 Synthetic Transformations

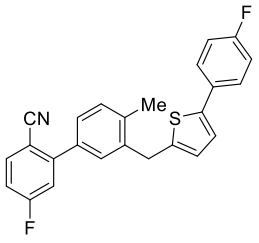
5,6-difluoro-4-iodo-3-phenyl-1*H*-isochromen-1-one (110a)



Tert-butyl 3,4-difluoro-2-(phenylethynyl)benzoate (**108s**, 31 mg, 0.10 mmol, 1.0 equiv) was dissolved in dry DCM (1 mL). The reaction mixture was cooled to 0 C° and iodine monochloride (7 µL, 0.12 mmol, 1.2 equiv)) was added. The reaction mixture was allowed to warm to room temperature and stirred for 0.5 h. The reaction was quenched by addition of sat. $Na_2S_2O_3$ solution (5 mL) and extracted with EtOAc (3 x 10 mL). Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 96:4) afforded the title compound as a white solid (**110a**, 36 mg, 0.094 mmol, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.20 (ddd, *J* = 8.9, 5.2, 1.9 Hz, 1H), 7.84–7.60 (m, 2H), 7.52–7.47 (m, 3H), 7.42 (td, *J* = 8.9, 6.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.9, 157.2, 155.4 (dd, *J* = 258.5, 13.8 Hz), 145.4 (dd, *J* = 261.2, 14.8 Hz), 135.5, 130.8, 130.7, 130.1, 129.7, 128.7, 128.4, 126.9 (dd, *J* = 8.8, 5.1 Hz), 118.4 (d, *J* = 19.1 Hz), 118.2–117.8 (m), 58.9 (t, *J* = 4.1 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -120.6, -138.6.
MS (EI, 70 eV): m/z (%) = 384 (14), 383 (100), 355 (30), 229 (22), 201 (39), 105 (49), 77 (31).
HRMS (EI): for $C_{15}H_7F_2IO_2$: calc. [M+]: 383.9459; found: 383.9455.

5-fluoro-3'-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4'-methyl-[1,1'-biphenyl]-2-carbonitrile (110b)

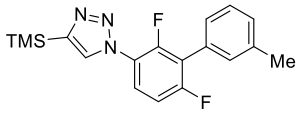


A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with 2-(5-fluoro-3'-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4'-methyl-[1,1'-biphenyl]-2-yl)-4,4-dimethyl-4,5-dihydrooxazole (**108y**, 47 mg, 0.10 mmol). Oxalyl chloride (0.50 mL) was added and the

resulting solution was cooled to 0 °C. DMF (1 drop) was added and the reaction mixture was stirred at 50 °C for 4 h. The mixture was cooled to 0 °C and quenched with a sat. aqueous $NaHCO_3$ solution and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a white solid (**110b**, 38 mg, 0.095 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.62 (dd, *J* = 8.6, 5.5 Hz, 1H), 7.38–7.34 (m, 2H), 7.29–7.24 (m, 2H), 7.19 (d, *J* = 7.7 Hz, 1H), 7.08 (dd, *J* = 9.2, 2.6 Hz, 1H), 6.99 (ddd, *J* = 8.7, 7.8, 2.6 Hz, 1H), 6.93 (d, *J* = 3.6 Hz, 1H), 6.92–6.86 (m, 2H), 6.60 (dt, *J* = 3.7, 1.1 Hz, 1H), 4.07 (s, 2H), 2.27 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 164.9 (d, *J* = 256.6 Hz), 162.2 (d, *J* = 246.7 Hz), 148.5 (d, *J* = 9.2 Hz), 142.6 (d, *J* = 1.0 Hz), 141.8, 139.0, 138.0, 136.2 (d, *J* = 9.7 Hz), 135.2 (d, *J* = 1.7 Hz), 131.2, 130.9 (d, *J* = 3.3 Hz), 129.7, 127.3 (d, *J* = 8.0 Hz), 127.2, 126.5, 122.9 (d, *J* = 1.2 Hz), 118.3, 117.4 (d, *J* = 22.7 Hz), 115.9 (d, *J* = 21.8 Hz), 115.1 (d, *J* = 22.7 Hz), 107.5 (d, *J* = 3.2 Hz), 34.2, 19.5.
^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -103.1, -115.1.
MS (EI, 70 eV): m/z (%) = 401 (58), 223 (100), 191 (54), 178 (21), 133 (28).
HRMS (EI): for $C_{25}H_{17}F_2NS$: calc. [M+]: 401.1050; found: 401.1047.

1-(2,6-difluoro-3'-methyl-[1,1'-biphenyl]-3-yl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole (110d)



(*E*)-1-((2,6-difluoro-3'-methyl-[1,1'-biphenyl]-3-yl)diazenyl)pyrrolidine (**108aa**, 150 mg, 0.50 mmol, 1.0 equiv) and NaN_3 (65 mg, 1.0 mmol, 2.0 equiv) were suspended in DCM (1 mL). $BF_3{\cdot}OEt_2$ (0.12 mL, 1.0 mmol, 2.0 equiv) and CF_3COOH (80 µL, 1.0 mmol, 2.0 equiv) were added and the reaction mixture was stirred for 0.5 h at 25 °C. The reaction mixture was quenched by addition of water and was extracted with DCM (3 x 10 mL), dried over $MgSO_4$ and the solvent was removed in vacuo. The crude product was purified through a short silica plug and the obtained azide **110c** was directly used for the next step.
The crude azide **110c** was dissolved in MeCN (1 mL) and DIPEA (43 µL, 0.25 mmol, 0.5 equiv), ethynyltrimethylsilane (0.21 mL, 1.5 mmol, 3.0 equiv) followed by CuI (19 mg, 10 mol%) were added. The reaction mixture was stirred at 25 °C for 24 h, quenched by addition of water and extracted with DCM (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 9:1) afforded the title compound as a pale yellow solid (**110d**, 163 mg, 0.48 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.98 (d, *J* = 3.1 Hz, 1H), 7.82 (td, *J* = 8.7, 5.5 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.28–7.21 (m, 3H), 7.11 (td, *J* = 8.8, 1.7 Hz, 1H), 2.38 (d, *J* = 1.3 Hz, 3H), 0.35 (s, 9H).

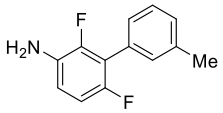
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.5 (dd, *J* = 251.5, 6.2 Hz), 151.3 (dd, *J* = 252.0, 7.4 Hz), 147.1, 138.3, 130.8 (t, *J* = 1.7 Hz), 130.2 (d, *J* = 7.2 Hz), 129.7, 128.5, 127.8, 127.3 (t, *J* = 1.8 Hz), 124.6 (dd, *J* = 10.2, 1.5 Hz), 122.4 (dd, *J* = 12.2, 3.9 Hz), 120.1 (dd, *J* = 20.5, 18.1 Hz), 112.5 (dd, *J* = 24.5, 3.9 Hz), 21.5, -1.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -111.9, -123.0.

MS (EI, 70 eV): m/z (%) = 315 (56), 300 (99), 184 (100), 77 (76).

HRMS (EI): for $C_{18}H19F_2N_3Si$: calc. [M+]: 343.1310; found: 343.1300.

2,6-difluoro-3'-methyl-[1,1'-biphenyl]-3-amine (110e)



(*E*)-1-((2,6-difluoro-3'-methyl-[1,1'-biphenyl]-3-yl)diazenyl)pyrrolidine (**108aa**, 60 mg, 0.20 mmol, 1.0 equiv) and NaN_3 (26 mg, 0.4 mmol, 2.0 equiv) were suspended in DCM (1 mL). $BF_3{\cdot}OEt_2$ (50 µL, 0.4 mmol, 2.0 equiv) and CF_3COOH (30 µL, 0.4 mmol, 2.0 equiv) were added and the reaction mixture was stirred for 0.5 h at 25 °C. The reaction mixture was quenched by addition of water and was extracted with DCM (3 x 10 mL), dried over $MgSO_4$ and the solvent was removed in vacuo. The crude product was purified through a short silica plug and the obtained azide **110c** was directly used for the next step. The crude azide **110c** was dissolved in EtOAc (2 mL) and EtOH (1 mL) followed by addition of $SnCl_2{\cdot}2H_2O$ (225 mg, 1.0 mmol, 5.0 equiv) and the reaction mixture was stirred at room temperature for 5 min. The reaction was quenched by addition of water (2 mL) and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography (silica gel, ihexane/EtOAc = 4:1) afforded the title compound as a colorless oil (**110e**, 42 mg, 0.19 mmol, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.36 (t, *J* = 7.5 Hz, 1H), 7.31–7.25 (m, 2H), 7.22 (ddt, *J* = 7.7, 1.9, 0.9 Hz, 1H), 6.81 (td, *J* = 9.0, 1.7 Hz, 1H), 6.71 (td, *J* = 9.2, 5.4 Hz, 1H), 3.63 (s, 2H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.7 (dd, *J* = 238.8, 5.9 Hz), 148.4 (dd, *J* = 241.1, 6.8 Hz), 137.9, 131.2 (d, *J* = 3.1 Hz), 131.1–131.0 (m), 129.6, 129.0, 128.2, 127.4 (t, *J* = 1.9 Hz), 118.7 (dd, *J* = 20.1, 17.0 Hz), 115.3 (dd, *J* = 9.2, 4.8 Hz), 111.1 (dd, *J* = 23.8, 4.0 Hz), 21.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = -128.3, -135.3.

MS (EI, 70 eV): m/z (%) = 220 (14), 219 (100), 198 (37), 170 (10).

HRMS (EI): for $C_{13}H_{11}F_2N$: calc. [M+]: 219.0860; found: 219.0854.

5.5 X-Ray Crystallography

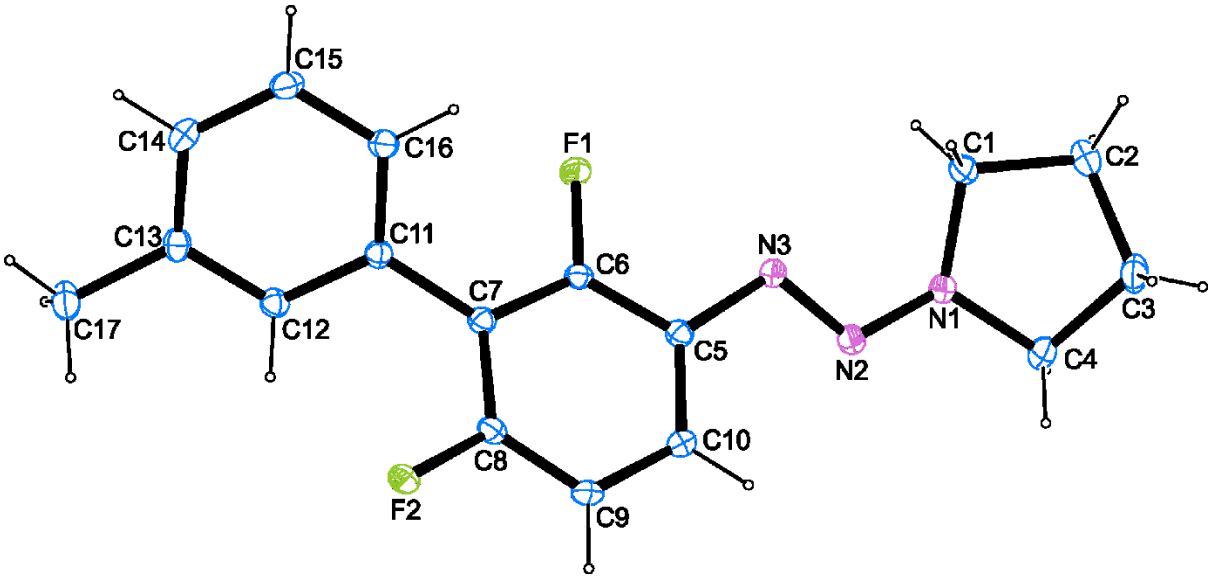


Figure 2: X-ray crystal structure of **108aa** (CCDC 2156072).

Experimental details

The X-ray intensity data of *CCDC 2156072* were measured on a Bruker D8 Venture TXS system equipped with a multilayer mirror monochromator and a Mo Kα rotating anode X-ray tube (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The structure was solved and refined using the Bruker SHELXTL Software Package. All hydrogen atoms have been calculated in ideal geometry riding on their parent atoms. The figures have been drawn at the 25% ellipsoid probability level.

Table 7: Crystallographic data of **108aa** (CCDC 2156072).

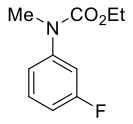
	108aa
net formula	$C_{17}H_{17}F_2N_3$
M_r/g mol^{-1}	301.33
crystal size/mm	0.160 × 0.120 × 0.080
T/K	173.(2)
radiation	MoKα
diffractometer	'Bruker D8 Venture TXS'
crystal system	monoclinic
space group	'P 1 21/c 1'

a/Å	6.8655(2)
b/Å	7.5245(2)
c/Å	28.4353(9)
α/°	90
β/°	91.5810(10)
γ/°	90
V/Å^3	1468.39(7)
Z	4
calc. density/g cm^{-3}	1.363
μ/mm^{-1}	0.100
absorption correction	Multi-Scan
transmission factor range	0.96–0.99
refls. measured	25010
R_{int}	0.0330
mean σ(I)/I	0.0232
θ range	2.866–27.483
observed refls.	3033
x, y (weighting scheme)	0.0806, 0.5799
hydrogen refinement	constr
Flack parameter	?
refls in refinement	3358
parameters	201
restraints	0
$R(F_{obs})$	0.0610
$R_w(F^2)$	0.1570
S	1.203
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.546
min electron density/e Å^{-3}	−0.451

6. Regioselective Magnesiations of Functionalized Arenes and Heteroarenes using TMP_2Mg in Hydrocarbons

6.1 Preparation of Starting Materials

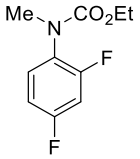
Ethyl (3-fluorophenyl)(methyl)carbamate (111h)



Ethyl (3-fluorophenyl)(methyl)carbamate (**111h**) was prepared according to **TP 8** using 3-fluoro -N-methylaniline. The crude product was purified by flash column chromatography (silica gel, pentane/EtOAc = 6:1) affording the desired compound as a colorless oil (**111h**, 3.15 g, 16 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.33 – 7.21 (m, 1H), 7.07 – 6.97 (m, 2H), 6.94 – 6.86 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.30 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.6 (d, *J* = 245.8 Hz), 155.4, 144.9 (d, *J* = 9.9 Hz), 129.7 (d, *J* = 9.3 Hz), 120.8, 112.9 (d, *J* = 24.0 Hz), 112.6 (d, *J* = 21.1 Hz), 62.0, 37.4, 14.6.
MS (EI, 70 eV): m/z (%) = 197 (36), 169 (18), 138 (52), 125 (40), 124 (100), 122 (11), 97 (23), 96 (11), 95 (10), 77 (10), 75 (10).
HRMS (EI): for $C_{10}H_{12}FNO_2$: calc. [M+]: 197.0852; found: 197.0843.

Ethyl (2-fluoro-4-fluorophenyl)(methyl)carbamate (111i)

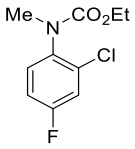


Ethyl (2-fluoro-4-fluorophenyl)(methyl)carbamate (**111i**) was prepared according to **TP 8** using 2-fluoro-4-fluoro-N-methylaniline. The crude product was purified by flash column chromatography (silica gel, pentane/EtOAc = 6:1) affording the desired compound as a colorless oil (**111i**, 3.25 g, 15.2 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.20 (s, 1H), 6.94 – 6.77 (m, 2H), 4.31 – 4.01 (m, 2H), 3.22 (s, 3H), 1.42 – 1.07 (m, 3H).Rotamers.

^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.6 (d, *J* = 11.4 Hz), 160.1 (d, *J* = 11.2 Hz), 155.6, 129.7, 111.4 (dd, *J* = 22.3, 3.8 Hz), 104.8 (t, *J* = 25.4 Hz), 62.0, 37.5, 14.5.
MS (EI, 70 eV): m/z (%) = 215 (13), 156 (58), 143 (52), 142 (100), 140 (13), 123 (11), 95 (13).
HRMS (EI): for $C_{10}H_{11}F_2NO_2$: calc. [M+]: 215.0758; found: 215.0748.

Ethyl (2-chloro-4-fluorophenyl)(methyl)carbamate (111j)

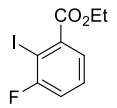


Ethyl (2-chloro-4-fluorophenyl)(methyl)carbamate (**111j**) was prepared according to **TP 8** using 2-chloro-4-fluoro-N-methylaniline. The crude product was purified by flash column chromatography (silica gel, pentane/EtOAc = 6:1) affording the desired compound as a colorless oil (**111j**, 3.85 g, 16.6 mmol, 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.31 – 7.14 (m, 2H), 6.99 (ddd, *J* = 8.8, 7.8, 2.9 Hz, 1H), 4.26 – 4.00 (m, 2H), 3.18 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). Rotamers.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.2 (d, *J* = 250.2 Hz), 155.6, 136.8 (d, *J* = 4.0 Hz), 133.8 (d, *J* = 10.8 Hz), 130.3 (d, *J* = 9.3 Hz), 117.4 (d, *J* = 25.7 Hz), 114.8 (d, *J* = 22.0 Hz), 61.9, 37.0, 14.6.
MS (EI, 70 eV): m/z (%) = 196 (27), 172 (10), 158 (58), 123 (14), 122 (15), 95 (13).
HRMS (EI): for $C_{10}H_{12}ClFNO_2$: calc. [M+]: 232.0535; found: 232.0531.

6.2 Preparation of Compounds

Ethyl 3-fluoro-2-iodobenzoate (115a)

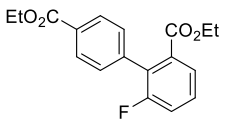


According to **TP 9**, to a solution of ethyl 3-fluorobenzoate (**111a**, 74 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at -20 °C and the reaction mixture was stirred for 1 h. The resulting arylmagnesium was then cooled to 0 °C and iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h.

Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 98:2) afforded the title compound as a colorless oil (**115a**, 261 mg, 0.45 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53 (ddd, *J* = 7.7, 1.5, 0.7 Hz, 1H), 7.35 (td, *J* = 8.0, 5.3 Hz, 1H), 7.17 (td, *J* = 8.0, 1.5 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.0 (d, *J* = 2.7 Hz), 162.2 (d, *J* = 245.0 Hz), 138.1 (d, *J* = 1.6 Hz), 129.7 (d, *J* = 8.2 Hz), 126.3 (d, *J* = 3.3 Hz), 118.0 (d, *J* = 25.4 Hz), 82.7 (d, *J* = 27.2 Hz), 62.0, 14.2.
MS (EI, 70 eV): m/z (%) = 265 (49), 248 (96), 220 (29), 126 (98), 94 (100), 93 (13), 92 (11), 75 (21), 74 (33), 68 (32), 50 (10).
HRMS (EI): for $C_9H_8FIO_2$: calc. [M+]: 293.9553; found: 293.9547.

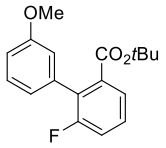
Diethyl 6-fluoro-(1,1'-biphenyl)-2,4'-dicarboxylate (115b)



According to **TP 9**, to a solution of ethyl 3-fluorobenzoate (**111a**, 74 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at -20 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and ethyl 4-iodobenzoate (70 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 9:1) afforded the title compound as a yellow oil (**115b**, 107 mg, 0.34 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.10 (d, *J* = 8.4 Hz, 2H), 7.71 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.43 (td, *J* = 8.0, 5.2 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.30 (ddd, *J* = 9.4, 8.3, 1.3 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.05 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.9 (d, *J* = 3.5 Hz), 166.5, 159.5 (d, *J* = 246.9 Hz), 139.1, 133.3 (d, *J* = 2.5 Hz), 130.2, 129.7, 129.4, 129.3, 129.2, 128.9, 127.2, 125.7 (d, *J* = 3.6 Hz), 119.0 (d, *J* = 23.2 Hz), 61.3, 61.1, 14.4, 13.7.
MS (EI, 70 eV): m/z (%) = 271 (28), 243 (17), 199 (19), 170 (17), 75 (17), 73 (100).
HRMS (EI): for $C_{18}H_{17}FO_4$: calc. [M+]: 316.1111; found: 316.1103.

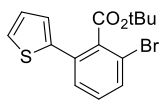
***Tert*-Butyl 6-fluoro-3'-methoxy-[1,1'-biphenyl]-2-carboxylate (115c)**



According to **TP 9**, to a solution of *tert*-butyl 3-fluorobenzoate (**111b**, 98 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 3-iodoanisole (56 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 95:5) afforded the title compound as a yellow oil (**115c**, 94 mg, 0.31 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.57 (d, *J* = 5.8 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.35 – 7.30 (m, 1H), 7.27 – 7.20 (m, 1H), 6.94 (ddd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 6.91 – 6.88 (m, 1H), 6.85 (s, 1H), 3.81 (s, 3H), 1.22 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.0 (d, *J* = 3.4 Hz), 159.7 (d, *J* = 246 Hz), 159.4, 135.9, 135.8 (d, *J* = 2.5 Hz), 129.3, 129.1, 128.9 (d, *J* = 8.6 Hz), 125.2 (d, *J* = 3.5 Hz), 122.2, 118.3 (d, *J* = 23.5 Hz), 115.0, 113.7, 81.9, 55.4, 27.6.
MS (EI, 70 eV): m/z (%) = 247 (14), 246 (100), 245 (15), 229 (37), 202 (15), 186 (19), 172 (13), 171 (11), 170 (20), 159 (10), 157 (25).
HRMS (EI): for $C_{18}H_{19}FO_3$: calc. [M+]: 302.1318; found: 302.1312.

***Tert*-Butyl 2-bromo-6-(thiophen-2-yl)benzoate (115d)**

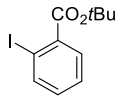


According to **TP 9**, to a solution of *tert*-butyl 2-bromobenzoate (**111c**, 129 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 40 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 2-Iodothiophene (42 µL,

0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 100:1) afforded the title compound as a white solid (**115d**, 101 mg, 0.30 mmol, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.54 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.39 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.36 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.24 (t, *J* = 7.9 Hz, 1H), 7.17 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.05 (dd, *J* = 5.1, 3.6 Hz, 1H),1.43 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 166.5, 140.1, 136.8, 133.8, 132.0, 129.9, 129.3, 127.6, 127.4, 126.5, 119.7, 83.3, 27.9.
MS (EI, 70 eV): m/z (%) = 284 (14), 283 (100), 282 (11), 281 (97), 266 (27), 264 (27), 250 (22), 248 (23), 158 (33), 115 (10), 114 (11), 57 (27), 40 (15).
HRMS (EI): for $C_{15}H_{15}BrO_2S$: calc. [M+]: 337.9976; found: 337.9970.

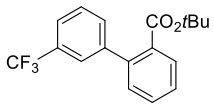
***Tert*-Butyl 2-iodobenzoate (115e)**



According to **TP 9**, to a solution of *tert*-butylbenzoate (**111d**, 89 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. The reaction mixture was heated to 50 °C and stirred for 30 min. The resulting arylmagnesium was then cooled to 0 °C and iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 98:2) afforded the title compound as a pale yellow oil (**115e**, 88 mg, 0.29 mmol, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.94 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.68 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.37 (td, *J* = 7.5, 1.2 Hz, 1H), 7.10 (td, *J* = 7.6, 1.7 Hz, 1H), 1.62 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 166.3, 141.0, 137.5, 132.1, 130.6, 127.9, 93.6, 82.81, 28.3.
MS (EI, 70 eV): m/z (%) = 247 (100), 230 (56).
HRMS (EI): for $C_{11}H_{13}IO_2$: calc. [M+]: 303.9960; found: 303.9955.

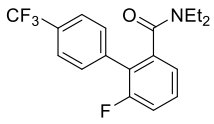
***Tert*-Butyl 3'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate (115f)**



According to **TP 9**, to a solution of *tert*-butylbenzoate (**111d**, 89 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 50 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dppf)Cl_2$ (15 mg, 2 mol%) and 1-iodo-3-(trifluoromethyl)benzene (60 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 10:1) afforded the title compound as a yellow oil(**115f**, 80 mg, 0.25 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.87 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.63 (d, *J* = 6.2 Hz, 1H), 7.58 (s, 1H), 7.56 – 7.49 (m, 3H), 7.45 (td, *J* = 7.6, 1.4 Hz, 1H), 7.31 (dd, *J* = 7.6, 1.4 Hz, 1H), 1.25 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.5, 142.9, 140.8, 132.8, 131.9, 131.0, 130.5, 130.3 (q, *J* = 30.5 Hz), 130.1, 128.5, 127.8, 125.5 (q, *J* = 3.9 Hz), 124.2 (q, *J* = 272 Hz), 123.7 (q, *J* = 3.8 Hz), 81.6, 27.6.
MS (EI, 70 eV): m/z (%) = 267 (10), 266 (77), 282 (11), 265 (53), 250 (15), 249 (100), 229 (60), 201 (63), 152 (17).
HRMS (EI): for $C_{18}H_{17}F_3O_2$: calc. [M+]: 322.1181; found: 322.1175.

***N*,*N*-Diethyl-6-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxamide (115g)**

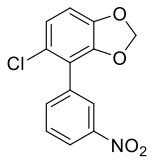


According to **TP 9**, to a solution of *N*,*N*-diethyl-3-fluorobenzamide (**111e**, 98 mg, 0.5 mmol, 1.0 equiv.) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%), TFP (7 mg, 6 mol%) and 1-iodo-4-(trifluoromethyl)benzene (61 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction

mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 1:1) afforded the title compound as a white solid (**115g**, 122 mg, 0.36 mmol, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.64 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.37 (m, 1H), 7.21 – 7.14 (m, 2H), 3.78 – 2.58 (m, 4H), 0.83 (t, *J* = 7.1 Hz, 3H), 0.74 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 168.1, 158.9 (d, *J* = 249.0 Hz), 138.8 (d, *J* = 1.9 Hz), 136.3 (d, *J* = 1.5 Hz), 130.2, 130.1, 129.9 (q, *J* = 8.6 Hz), 124.8 (q, *J* = 3.8 Hz), 124.5 (d, *J* = 16.5 Hz), 123.8 (q, *J* = 270 Hz), 122.1 (d, *J* = 3.7 Hz), 116.0 (d, *J* = 22.9 Hz), 115.9 (d, J = 21.7 Hz), 113.4 (d, J = 22.7 Hz), 42.1, 38.0, 13.3, 11.4.
MS (EI, 70 eV): m/z (%) = 339 (13), 338 (67), 318 (11), 268 (15), 267 (100), 219 (45), 194 (18), 170 (35).
HRMS (EI): for $C_{18}H_{17}F_4NO$: calc. [M+]: 339.1246; found: 339.1193.

5-Chloro-4-(3-nitrophenyl)benzo-1,3-dioxole (115h)

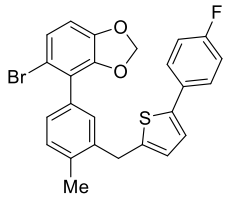


According to **TP 9**, to a solution of 5-chlorobenzo-1,3-dioxole (**111f**, 58 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 60 °C. After one hour, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 1-Iodo-3-nitrobenzene (103 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 99:1) afforded the title compound as a white solid (**115h**, 88 mg, 0.32 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.37 (t, *J* = 2.0 Hz, 1H), 8.26 (ddd, *J* = 8.1, 2.3, 1.0 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.02 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 148.1, 146.6, 146.5, 136.4, 134.6, 129.1, 125.3, 124.8, 123.1, 122.8, 120.1, 108.9, 102.1.

MS (EI, 70 eV): m/z (%) = 279 (31), 278 (14), 277 (100), 276 (24), 260 (12), 230 (17), 175 (22), 173 (71), 168 (21), 139 (25), 138 (29), 137 (22).
HRMS (EI): for $C_{13}H_8ClNO_4$: calc. [M+]: 277.0142; found: 277.0137.

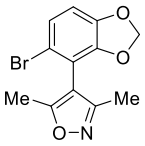
5-Bromo-4-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)benzo-1,3-dioxole (115i)



According to **TP 9**, to a solution of 5-bromo-1,3-benzodioxole (**111g**, 60 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 60 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%), TFP (7 mg, 6 mol%) and 2-(4-fluorophenyl)-5-(5-iodo-2-methylbenzyl)thiophene (169 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, hexane/EtOAc = 20:1) afforded the title compound as a white solid (**115i**, 138 mg, 0.29 mmol, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53 – 7.46 (m, 2H), 7.36 – 7.25 (m, 3H), 7.17 (d, *J* = 8.3 Hz, 1H), 7.09 – 7.00 (m, 3H), 6.73 (d, *J* = 3.6 Hz, 1H), 6.70 (d, *J* = 8.3 Hz, 1H), 5.96 (s, 2H), 4.19 (s, 2H), 2.39 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.1 (d, *J* = 246.5 Hz), 147.0, 146.5, 143.1, 141.6, 138.1, 136.7, 132.6, 131.2, 131.0 (d, *J* = 3.3 Hz), 130.4, 128.4, 127.2 (d, *J* = 7.9 Hz), 126.3, 125.7, 124.5, 122.8 (d, *J* = 1.3 Hz), 115.8 (d, *J* = 21.7 Hz), 114.6, 108.6, 101.7, 34.2, 19.5.
MS (EI, 70 eV): m/z (%) = 483 (13), 482 (50), 481 (12), 480 (49), 304 (14), 303 (90), 302 (15), 301 (91), 223 (15), 207 (20), 195 (57), 192 (11), 191 (100), 189 (10), 178 (11), 167 (13), 165 (25), 152 (20), 139 (16), 133 (17).
HRMS (EI): for $C_{25}H_{18}BrFO_2S$: calc. [M+]: 480.0195; found: 480.0189.

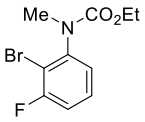
4-(5-Bromobenzo-1,3-dioxol-4-yl)-3,5-dimethylisoxazole (115j)



According to **TP 9**, to a solution of 5-bromo-1,3-benzodioxole (**111g**, 60 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 60 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%), TFP (7 mg, 6 mol%)and 4-iodo-3,5-dimethylisoxazole (93 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 9:1) afforded the title compound as a white solid (**115j**, 74 mg, 0.25 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.15 (d, *J* = 8.3 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 5.99 (q, *J* = 1.3 Hz, 2H), 2.30 (s, 3H), 2.18 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.3, 159.5, 147.6, 147.0, 125.6, 116.2, 113.3, 110.6, 109.7, 101.9, 12.12, 10.8.
MS (EI, 70 eV): m/z (%) = 297 (12), 296 (94), 295 (12), 294 (100), 253 (20), 251 (21), 216 (22), 213 (80), 212 (14), 211 (82), 210 (14), 201 (37), 200 (15), 188 (13), 175 (11), 154 (14), 152 (14), 147 (29), 146 (10), 119 (16), 18 (10), 91 (24), 89 (22).
HRMS (EI): for $C_{12}H_{10}BrNO_3$: calc. [M+]: 294.9844; found: 294.9839.

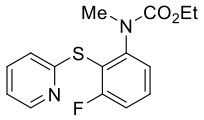
Ethyl (3-fluoro-2-bromophenyl)(methyl)carbamate (115k)



According to **TP 9**, to a solution of ethyl (3-fluorophenyl)(methyl)carbamate (**111h**, 98 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 0 °C. After 1 h, 1,2-dibromotetrachloroethane (195 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise to the resulting arylmagnesium at 0 °C and the reaction mixture was warmed up to room temperature and stirred for an additional 2 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 8:1) afforded the title compound as a pale yellow solid (**115k**, 86 mg, 0.31 mmol, 62% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.35 – 7.28 (m, 1H), 7.13 – 6.96 (m, 2H), 4.30 – 3.39 (m, 2H), 3.18 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). rotamers.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 159.9 (d, *J* = 248.4 Hz), 155.4, 144.0, 128.8 (d, *J* = 9.1 Hz), 124.8 (d, *J* = 3.2 Hz), 115.5 (d, *J* = 22.6 Hz), 111.1 (d, *J* = 20.3 Hz), 62.1, 37.1, 14.7.
MS (EI, 70 eV): m/z (%) = 203 (18), 201 (18), 196 (23), 168 (100), 136 (10), 123 (14), 122 (16).
HRMS (EI): for $C_{10}H_{12}BrFNO_2$: calc. [M+]: 276.0030; found: 276.0029.

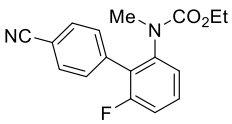
Ethyl (3-fluoro-2-(pyridin-2-ylthio)phenyl)(methyl)carbamate (115l)



According to **TP 9**, to a solution of ethyl (3-fluorophenyl)(methyl)carbamate (**111h**, 98 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 0 °C. After 1 h, 2,2'-dipyridyldisulfide (165 mg, 0.75 mmol, 1.5 equiv) dissolved in toluene (1 mL) was added dropwise to the resulting arylmagnesium at 0 °C and the reaction mixture was warmed up to room temperature and stirred for an additional 2 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 4:1) afforded the title compound as a pale yellow solid (**115l**, 85 mg, 0.27 mmol, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.35 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.51 – 7.41 (m, 2H), 7.19 – 7.13 (m, 2H), 7.03 – 6.93 (m, 2H), 4.00 (q, *J* = 7.0 Hz, 2H), 3.17 (s, 3H), 1.07 (t, *J* = 7.1 Hz, 3H). rotamers.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 163.5 (d, *J* = 250.1 Hz), 158.4, 155.5, 149.6, 136.5, 131.4 (d, *J* = 9.8 Hz), 124.3, 120.9, 120.2, 118.45 (d, *J* = 18.3 Hz), 115.3 (d, *J* = 23.5 Hz), 61.9, 37.9, 14.6.
MS (EI, 70 eV): m/z (%) = 306 (15), 273 (29), 260 (10), 233 (16), 232 (11), 215 (10), 213 (11), 205 (11), 204 (100), 201 (50), 199 (12), 186 (10), 168 (14), 154 (49), 80 (29).
HRMS (EI): for $C_{15}H_{15}FN_2O_2S$: calc. [M+]: 306.0838; found: 306.0831.

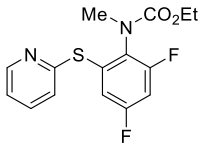
Ethyl (4'-cyano-6-fluoro-(1,1'-biphenyl)-2-yl)(methyl)carbamate (115m)



According to **TP 9**, to a solution of ethyl (3-fluorophenyl)(methyl)carbamate (**111h**, 197 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 0 °C. After 1 h, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%), TFP (7 mg, 6 mol%) and 4-iodobenzonitrile (95 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 4:1) afforded the title compound as a colorless oil (**115m**, 83 mg, 0.28 mmol, 67% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) = 7.71 (d, *J* = 8.0 Hz, 2H), 7.49 – 7.34 (m, 3H), 7.21 – 7.05 (m, 2H), 4.15 – 3.86 (m, 2H), 2.96 (s, 3H), 1.07 (t, *J* = 7.1 Hz, 3H). rotamers.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.8 (d, *J* = 248.4 Hz), 155.2, 142.5, 137.5, 132.2, 132.1, 130.6, 130.5, 130.1, 126.4 (d, *J* = 15.4 Hz), 124.1, 118.7, 115.1 (d, *J* = 22.7 Hz), 112.0, 62.0, 38.0, 14.7.
MS (EI, 70 eV): m/z (%) = 298 (36), 253 (10), 239 (10), 226 (15), 225 (100), 224 (17), 223 (40), 210 (72), 198 (13), 195 (11), 182 (11).
HRMS (EI): for $C_{17}H_{15}FN_2O_2$: calc. [M+]: 298.1118; found: 298.1111.

Ethyl (2,4-difluoro-6-(pyridin-2-ylthio)phenyl)(methyl)carbamate (115n)

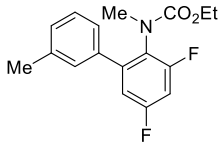


According to **TP 9**, to a solution of ethyl (2-fluoro-4-fluorophenyl)(methyl)carbamate (**111i**, 108 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, 2,2'-dipyridyldisulfide (165 mg, 0.75 mmol, 1.5 equiv) dissolved in toluene (1 mL) was added dropwise to the resulting arylmagnesium at 0 °C and the reaction mixture was warmed up to room temperature and stirred for an additional 2 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 4:1) afforded the title compound as a yellow oil (**115n**, 144 mg, 0.44 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.36 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.55 – 7.48 (m, 1H), 7.44 – 7.29 (m, 1H), 7.07 – 6.96 (m, 2H), 4.11 (s, 2H), 3.24 (s, 3H), 1.13 (s, 3H). Rotamers.

^{13}C NMR (151 MHz, $CDCl_3$): δ (ppm) = 161.7 (dd, *J* = 250.7, 3.4 Hz), 158.9, 158.7 (dd, *J* = 253.0, 4.8 Hz), 157.3, 155.4, 149.6 (d, *J* = 26.1 Hz), 137.5, 136.8, 121.1, 120.8, 120.4, 119.68, 111.6 (dd, *J* = 24.2, 4.1 Hz), 108.1 (t, *J* = 22.2 Hz), 62.1, 37.4, 14.5.
MS (EI, 70 eV): m/z (%) = 223 (11), 222 (100), 78 (30), 73 (10).
HRMS (EI): for $C_{15}H_{14}F_2N_2O_2S$: calc. [M+]: 324.0744; found: 324.0738.

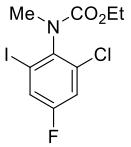
Ethyl (3,5-difluoro-3'-methyl-[1,1'-biphenyl]-2-yl)(methyl)carbamate (115o)



According to **TP 9**, to a solution of ethyl (2-fluoro-4-fluorophenyl)(methyl)carbamate (**111i**, 108 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%), TFP (7 mg, 6 mol%) and 3-iodotoluene (53 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 4:1) afforded the title compound as a colorless oil (**115o**, 75 mg, 0.31 mmol, 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.36 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.20 (m, 4H), 6.97 (td, *J* = 8.9, 1.8 Hz, 1H), 4.17 – 4.07 (m, 2H), 3.25 (s, 3H), 2.41 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). Rotamers.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 171.3, 158.5 (dd, *J* = 248.6, 6.4 Hz), 156.7, 155.8, 138.1, 131.0, 129.4, 128.7, 128.3, 127.9, 127.4, 119.6 (t, *J* = 19.2 Hz), 111.5 (dd, *J* = 24.1, 4.0 Hz), 62.1, 37.6 (d, *J* = 1.8 Hz), 21.5, 14.7.
MS (EI, 70 eV): m/z (%) = 305 (18), 246 (12), 233 (16), 232 (18), 61 (16), 44 (13), 42 (100).
HRMS (EI): for $C_{17}H_{17}F_2NO_2$: calc. [M+]: 305.1227; found: 305.1222.

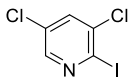
Ethyl (2-chloro-4-fluoro-6-iodophenyl)(methyl)carbamate (115p)



According to **TP 9**, to a solution of ethyl (2-chloro-4-fluorophenyl)(methyl)carbamate (**111j**, 116 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise at 0 °C to the resulting arylmagnesium and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 9:1) afforded the title compound as a pale yellow oil (**115p**, 130 mg, 0.38 mmol, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.34 – 7.20 (m, 1H), 7.00 (dd, *J* = 8.8, 7.0 Hz, 1H), 4.34 – 3.94 (m, 2H), 3.17 (d, *J* = 1.8 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). Rotamers.
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.6 (d, *J* = 248.0 Hz), 155.4, 139.2 (d, *J* = 3.7 Hz), 137.2, 130.1 (d, *J* = 8.8 Hz), 114.2 (d, *J* = 25.6 Hz), 88.3 (d, *J* = 28.7 Hz), 62.2, 36.9, 14.7.
MS (EI, 70 eV): m/z (%) = 321 (15), 60 (13), 45 (13), 43 (100), 232 (11), 215 (10), 213 (11), 205 (11), 204 (100), 201 (50), 199 (12), 186 (10), 168 (14), 154 (49), 80 (29).
HRMS (EI): for $C_{10}H_{10}ClFINO_2$: calc. [M+]: 356.9429; found: 356.9438.

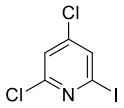
3,5-Dichloro-2-iodopyridine (116a)



According to **TP 9**, to a solution of 3,5-dichloropyridine (**112a**, 74 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the reaction mixture was cooled to 0 °C and iodine (153 mg, 0.60 mmol, 1.2 equiv) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 95:5) afforded the title compound as a pale yellow solid (**116a**, 116 mg, 0.425 mmol, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.26 (d, *J* = 2.3 Hz, 1H), 7.67 (d, *J* = 2.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.1, 138.8, 135.9, 132.1, 118.4.
MS (EI, 70 eV): m/z (%) = 276 (10), 274 (63), 272 (100), 165 (15), 163 (23), 147 (43), 145 (65), 126 (17), 111 (13), 109 (39).
HRMS (EI): for $C_5H_2Cl_2IN$: calc. [M+]: 272.8609; found: 272.8604.

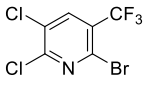
2,4-Dichloro-6-iodopyridine (116b)



According to **TP 9**, to a solution of 2,4-dichloropyridine (**112b**, 54 µL, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, the reaction mixture was cooled to 0 °C and iodine (254 mg, 1.0 mmol, 2 equiv.) dissolved in THF (1 mL) was added dropwise and the reaction mixture was stirred for 1 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 99:1) afforded the title compound as a pale yellow solid (**116b**, 109 mg, 0.4 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.70 (d, *J* = 1.5 Hz, 1H), 7.34 (d, *J* = 1.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 151.1, 145.9, 133.6, 123.9, 115.3.
MS (EI, 70 eV): m/z (%) = 274 (13), 272 (21), 163 (13), 149 (10), 147 (64), 145 (100), 127 (15), 126 (15), 111 (19), 109 (56), 75 (10).
HRMS (EI): for $C_5H_2Cl_2IN$: calc. [M+]: 272.8609; found: 272.8603.

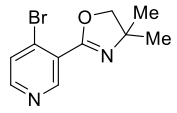
2-Bromo-5,6-dichloro-3-(trifluoromethyl)pyridine (116c)



According to **TP 9**, to a solution of 2,3-dichloro-5-(trifluoromethyl)pyridine (**112c**, 107 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, 1,2-dibromotetrachloroethane (227 mg, 0.70 mmol, 1.4 equiv) dissolved in THF (1 mL) was added dropwise to the resulting arylmagnesium at 0 °C and the reaction mixture was warmed up to room temperature and stirred for an additional 2 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc 98:2) afforded the title compound as a yellow solid (**116c**, 131 mg, 0.33 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.02 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 151.4, 138.4 (q, *J* = 5.1 Hz), 135.6, 130.3, 127.9 (q, *J* = 34.1 Hz), 121.4 (q, *J* = 273.5 Hz).
MS (EI, 70 eV): m/z (%) = 296 (31), 294 (71), 292 (45), 215 (63), 213 (100), 144 (10), 84 (17), 68 (12).
HRMS (EI): for $C_6HBrCl_2F_3N$: calc. [M+]: 292.8622; found: 292.8614.

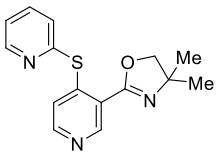
2-(4-Bromopyridin-3-yl)-4,4-dimethyl-4,5-dihydrooxazole (116d)



According to **TP 9**, to a solution of 4,4-dimethyl-2-(pyridin-3-yl)-4,5-dihydrooxazole (**112d**, 88 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 10 min, 1,2-dibromotetrachloroethane (227 mg, 0.70 mmol, 1.4 equiv) dissolved in THF (1 mL) was added dropwise to the resulting arylmagnesium at 0 °C and the reaction mixture was warmed up to room temperature and stirred for an additional 2 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc 1:1) afforded the title compound as a yellow solid (**116d**, 85 mg, 0.33 mmol, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.84 (d, *J* = 0.5 Hz, 1H), 8.42 (d, *J* = 5.4 Hz, 1H), 7.58 (dd, *J* = 5.4, 0.5 Hz, 1H), 4.16 (s, 2H), 1.43 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.4, 151.4, 151.3, 132.5, 128.5, 126.7, 79.5, 68.5, 28.3.
MS (EI, 70 eV): m/z (%) = 240 (88), 238 (91), 225 (22), 223 (22), 212 (44), 210 (44), 185 (45), 183 (16), 182 (100), 103 (23), 76 (17).
HRMS (EI): for $C_{10}H_{11}ON_2Br$: calc. [M+]: 254.0055; found: 254.0051.

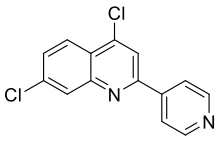
4,4-Dimethyl-2-(4-(pyridin-2-ylthio)pyridin-3-yl)-4,5-dihydrooxazole (116e)



According to **TP 9**, to a solution of 4,4-dimethyl-2-(pyridin-3-yl)-4,5-dihydrooxazole (**112d**, 35 mg, 0.20 mmol, 1.0 equiv) in toluene (0.4 mL) was added TMP_2Mg (**23**, 0.22 mmol, 1.1 equiv) at 25 °C. After 10 min, 2,2'-dipyridyldisulfide (66 mg, 0.30 mmol, 1.5 equiv) dissolved in toluene (0.5 mL) was added dropwise to the resulting arylmagnesium at 0 °C and the reaction mixture was warmed up to room temperature and stirred for an additional 2 h. Purification of the crude product by flash column chromatography (silica gel, EtOAc 100%) afforded the title compound as a yellow solid (**116e**, 41 mg, 0.14 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.90 (s, 1H), 8.67 (ddd, *J* = 4.8, 2.0, 0.9 Hz, 1H), 8.31 (d, *J* = 5.5 Hz, 1H), 7.75 (td, *J* = 7.7, 1.9 Hz, 1H), 7.65 – 7.58 (m, 1H), 7.32 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 6.86 (dd, *J* = 5.6, 0.6 Hz, 1H), 4.09 (s, 2H), 1.41 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 159.1, 154.4, 151.3, 150.3, 150.2, 149.3, 137.8, 129.6, 123.5, 121.8, 121.7, 78.8, 77.4, 68.8, 28.5.
MS (EI, 70 eV): m/z (%) = 208 (10), 207 (100), 153 (11), 78 (10).
HRMS (EI): for $C_{15}H_{15}N_3OS$: calc. [M+]: 285.0936; found: 285.0930.

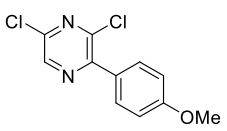
4,7-Dichloro-2-(pyridin-4-yl)quinoline (116f)



According to **TP 9**, to a solution of 4,7-dichloroquinoline (**112e**, 99 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 25 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (4.8 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%), TFP (7 mg, 6 mol%) and 4-iodopyridine (85 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 8:1) afforded the title compound as a white solid (**116f**, 84 mg, 0.30 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.79 – 8.76 (m, 2H), 8.73 (d, *J* = 4.7 Hz, 1H), 8.28 (d, *J* = 9.1 Hz, 1H), 7.76 (d, *J* = 9.1 Hz, 1H), 7.52 (d, *J* = 4.6 Hz, 1H), 7.35 – 7.29 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.9, 149.7, 147.9, 144.9, 142.9, 136.9, 135.3, 129.3, 125.7, 125.6, 125.5, 121.6.
MS (EI, 70 eV): m/z (%) = 276 (10), 274 (64), 272 (100), 239 (22), 106 (12).
HRMS (EI): for $C_{14}H_7Cl_2N_2$: calc. [M+]: 272.9986; found: 272.9978.

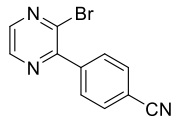
3,5-Dichloro-2-(4-methoxyphenyl)pyrazine (116g)



According to **TP 9**, to a solution of 2,6-dichloropyrazine (**112f**, 75 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 0 °C. After 10 min, the resulting arylmagnesium was transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 4-iodoanisole (97 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 15:1) afforded the title compound as a white solid (**116g**, 89 mg, 0.30 mmol, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.56 (s, 1H), 7.80 (d, *J* = 8.9 Hz, 2H), 7.02 (d, *J* = 8.9 Hz, 2H), 3.88 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 161.1, 151.0, 145.2, 144.6, 141.9, 131.2, 113.9, 55.6.
MS (EI, 70 eV): m/z (%) = 257 (110), 286 (10), 256 (64), 255 (12), 254 (100), 219 (31), 210 (11), 44 (14), 43 (12).
HRMS (EI): for $C_{11}H_8O_1N_2Cl_2$: calc. [M+]: 254.0014; found: 254.0015.

4-(Benzoxazol-2-yl)benzonitrile (116h)

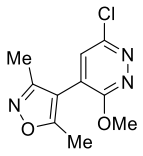


According to **TP 9**, to a solution of 2-bromopyrazine (**112g**, 18 µL, 0.2 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.22 mmol, 1.1 equiv) at -25 °C. After 2 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (0.48 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (4 mg, 3 mol%) and TFP (3 mg, 6 mol%) and 4-iodobenzonitrile (39 mg, 0.17 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 4:1) afforded the title compound as a white solid (**116h**, 32 mg, 0.12 mmol, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.64 (d, *J* = 2.4 Hz, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 7.90 (d, *J* = 8.6 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 153.6, 143.5, 142.6, 141.5, 139.7, 132.0, 130.3, 118.4, 113.4.
MS (EI, 70 eV): m/z (%) = 260 (25), 258 (25), 181 (12), 180 (100), 153 (35), 129 (17).

HRMS (EI): for $C_{11}H_6BrN_3$: calc. [M+]: 258.9745; found: 258.9739.

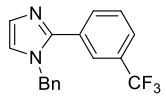
4-(6-Chloro-3-methoxypyridazin-4-yl)-3,5-dimethylisoxazole (116i)



According to **TP 9**, to a solution of 3-chloro-6-methoxypyridazine (**112h**, 72 mg, 0.50 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 0 °C. After 5 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 4-iodo-3,5-dimethylisoxazole (93 mg, 0.42 mmol, 0.83 equiv).The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 2:1) afforded the title compound as a white solid(**116i**, 60 mg, 0.25 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.23 (s, 1H), 4.13 (s, 3H), 2.37 (s, 3H), 2.21 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 168.4, 162.0, 158.7, 151.0, 130.2, 123.4, 108.6, 55.6, 12.2, 10.9.
MS (EI, 70 eV): m/z (%) = 226 (31), 224 (100), 198 (23), 196 (16), 182 (28), 182 (17), 169 (12), 158 (16), 157 (16), 156 (50), 155 (53), 130 (11), 128 (33).
HRMS (EI): for $C_{10}H_{10}O_2N_3Cl$: calc. [M+]: 239.0462; found: 239.0455.

1-Benzyl-2-(3-(trifluoromethyl)phenyl)-1*H*-imidazole (116j)

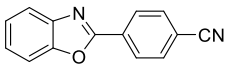


According to **TP 9**, to a solution of 1-benzylimidazole (**112i**, 79 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 0 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 1-iodo-3-

(trifluoromethyl)benzene (60 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 1:1) afforded the title compound as a colorless oil (**116j**, 80 mg, 0.26 mmol, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = δ 7.84 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.39 – 7.28 (m, 3H), 7.21 (d, *J* = 1.3 Hz, 1H), 7.12 – 7.05 (m, 2H), 7.03 (d, *J* = 1.3 Hz, 1H), 5.21 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 146.6, 136.5, 131.7, 131.7, 131.3, 131.1 (q, *J* = 32.6 Hz), 129.3, 129.1, 128.2, 126.5, 125.7 (q, *J* = 3.8 Hz), 125.4 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.5 Hz) 122.2, 50.6.
MS (EI, 70 eV): m/z (%) = 302 (23), 91 (100).
HRMS (EI): for $C_{17}H_{13}N_2F_3$: calc. [M+]: 302.1031; found: 302.1024.

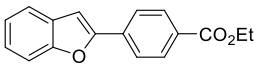
4-(Benzoxazol-2-yl)benzonitrile (116k)



According to **TP 9**, to a solution of benzoxazole (**112j**, 60 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at -40 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 4-iodobenzonitrile (95 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 1:1) afforded the title compound as a white solid (**116k**, 66 mg, 0.30 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.31 (d, *J* = 8.5 Hz, 2H), 7.77 (d, *J* = 8.6 Hz, 3H), 7.63 – 7.53 (m, 1H), 7.47 – 7.33 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 160.9, 150.9, 141.9, 132.7, 131.1, 127.9, 126.2, 125.1, 120.6, 118.2, 114.7, 110.9.
MS (EI, 70 eV): m/z (%) = 221 (15), 220 (100), 192 (20).
HRMS (EI): for $C_{14}H_8N_2O$: calc. [M+]: 220.0637; found: 220.0631.

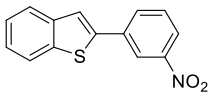
Ethyl 4-(benzofuran-2-yl)benzoate (116l)



According to **TP 9**, to a solution of benzofuran (**112k**, 55 µL, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at -20 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and ethyl 4-iodobenzoate (70 µL, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/diethyl ether = 9:1) afforded the title compound as a yellow oil (**116l**, 93 mg, 0.35 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.12 (d, *J* = 8.5 Hz, 2H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.61 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H), 7.55 (dq, *J* = 8.2, 0.9 Hz, 1H), 7.33 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.15 (d, *J* = 0.9 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$): δ (ppm) = 166.3, 155.3, 154.8, 134.5, 130.2, 130.1, 129.0, 125.2, 124.7, 123.3, 121.4, 111.5, 103.5, 61.2, 14.5.
MS (EI, 70 eV): m/z (%) = 266 (100), 239 (14), 238 (89), 222 (14), 221 (93), 193 (28), 166 (13), 165 (99), 164 (31), 163 (33), 139 (13).
HRMS (EI): for $C_{17}H_{14}O_3$: calc. [M+]: 266.0943; found: 266.0937.

2-(3-Nitrophenyl)benzo[b]thiophene (116m)

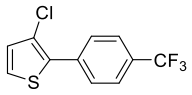


According to **TP 9**, to a solution of benzothiophene (**112l**, 67 mg, 0.5 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 0.55 mmol, 1.1 equiv) at 65 °C. After one hour, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (1.2 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (9 mg, 3 mol%) and TFP (7 mg, 6 mol%) and 1-iodo-3-nitrobenzene (100 mg, 0.415 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column

chromatography (silica gel, pentane/EtOAc = 9:1) afforded the title compound as a yellow solid (**116m**, 69 mg, 0.27 mmol, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.56 (t, *J* = 2.0 Hz, 1H), 8.18 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 8.02 – 7.98 (m, 1H), 7.88 – 7.80 (m, 2H), 7.68 (s, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.44 – 7.34 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.8, 141.2, 140.4, 139.8, 136.2, 132.2, 130.1, 125.4, 125.1, 124.2, 122.8, 122.5, 121.5, 121.1.
MS (EI, 70 eV): m/z (%) = 256 (12), 255 (79), 209 (17), 208 (84), 197 (13), 166 (13), 165 (100), 164 (21), 163 (35), 139 (13).
HRMS (EI): for $C_{14}H_9NO_2S$: calc. [M+]: 255.0354; found: 255.0349.

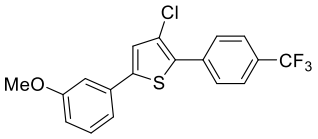
3-Chloro-2-(4-(trifluoromethyl)phenyl)thiophene (116n)



According to **TP 9**, to a solution of 3-chlorothiophene (**112m**, 371 µL, 4 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 4.4 mmol, 1.1 equiv) at 60 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (9.6 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (69 mg, 3 mol%) and TFP (56 mg, 6 mol%) and 1-iodo-4-(trifluoromethyl)benzene (0.5 mL, 3.32 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 1:1) afforded the title compound as a white solid (**116n**, 698 mg, 2.65 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.79 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 5.4 Hz, 1H), 7.04 (d, *J* = 5.4 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 135.8, 135.7, 134.5, 130.0 (d, *J* = 32.7 Hz), 129.6, 128.9, 125.6 (q, *J* = 3.8 Hz), 124.9, 122.5, 123.7 (q, *J* = 204.1 Hz), 120.5.
MS (EI, 70 eV): m/z (%) = 263 (35), 261 (100), 207 (20), 183 (28), 182 (12).
HRMS (EI): for $C_{11}H_6ClF_3S$: calc. [M+]: 261.9831; found: 261.9827.

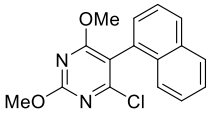
3-Chloro-5-(3-methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)thiophene (116o)



According to **TP 9**, to a solution of 3-Chloro-2-(4-(trifluoromethyl)phenyl)thiophene (**116n**, 52 mg, 0.2 mmol, 1.0 equiv) in toluene (0.4 mL) was added TMP_2Mg (**23**, 0.22 mmol, 1.1 equiv) at 40 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (0.48 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (4 mg, 3 mol%) and TFP (3 mg, 6 mol%) and 1-iodo-3-methoxybenzene (18 µL, 0.14 mmol, 0.7 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, hexane 100%) afforded the title compound as a yellow oil (**116o**, 33 mg, 0.09 mmol, 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (d, *J* = 7.5 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.38 – 7.29 (m, 1H), 7.23 (s, 1H), 7.18 (ddd, *J* = 7.7, 1.7, 0.9 Hz, 1H), 7.11 (dd, *J* = 2.5, 1.7 Hz, 1H), 6.90 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 3.87 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 146.6, 136.5, 131.8, 131.4, 131.1 (q, *J* = 32.6 Hz), 129.3, 129.2, 128.2, 126.5, 125.8 (q, *J* = 3.8 Hz), 125.5 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.5 Hz), 122.3, 50.6.
MS (EI, 70 eV): m/z (%) = 370 (35), 369 (19), 368 (100), 325 (22), 304 (17).
HRMS (EI): for $C_{18}H_{12}OClF_3S$: calc. [M+]: 368.0249; found: 368.0244.

4-Chloro-2,6-dimethoxy-5-(naphthalen-1-yl)pyrimidine (117b)

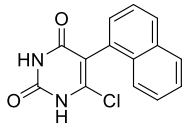


According to **TP 9**, to a solution of 4-chloro-2,6-dimethoxypyrimidine (**117a**, 349.6 mg, 2 mmol, 1.0 equiv) in toluene (1 mL) was added TMP_2Mg (**23**, 2.2 mmol, 1.1 equiv) at 0 °C. After 30 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (4.8 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (35 mg, 3 mol%) and TFP (28 mg, 6 mol%) and 1-iodonaphthalene (243 µL, 1.66 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column

chromatography (silica gel, pentane/diethyl ether = 6:1) afforded the title compound as a white solid (**117b**, 418 mg, 1.39 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.96 – 7.90 (m, 2H), 7.58 – 7.42 (m, 4H), 7.36 (dd, *J* = 7.0, 1.2 Hz, 1H), 4.10 (s, 3H), 3.87 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 170.4, 163.8, 160.9, 133.6, 131.7, 129.8, 129.0, 128.6, 128.38, 126.5, 126.1, 125.4, 124.8, 112.5, 55.5, 55.0.
MS (EI, 70 eV): m/z (%) = 302 (31), 301 (16), 300 (100), 299 (31), 285 (15), 271 (16), 270 (16), 265 (37), 250 (41), 235 (28), 233 (16), 220 (24), 207 (32), 206 (29), 205 (15), 193 (31), 192 (15), 191 (19), 180 (28), 179 (24), 178 (23), 165 (44), 164 (68), 152 (21), 139 (19), 137 (15).
HRMS (EI): for $C_{16}H_{13}O_2N_2Cl$: calc. [M+]: 300.0666; found: 300.0658.

6-Chloro-5-(naphthalen-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (117c)



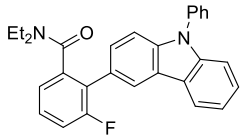
The title compound was prepared according to a literature procedure.[221] A dry and argon flushed 25 mL round-bottom-flask, equipped with a magnetic stirring bar and a septum, was charged with 4-Chloro-2,6-dimethoxy-5-(naphthalen-1-yl) pyrimidine (**117b**, 0.25 mmol), concentrated hydrochloric acid (0.5 mL), THF (0.4 mL), and dioxane (0.4 mL). The resulting mixture was heated to reflux. After 2 h, the reaction mixture was allowed to cool down and half of the volume was removed by evaporation. Water (2 mL) was then added and the mixture was boiled for 1-2 min. After refrigerating for 2 h, the crystals were filtered and washed with water and diethyl ether. The title compound was obtained as a white powder (**117c**, 50 mg, 0.18 mmol, 74% yield).

^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ (ppm) = 12.25 (s, 1H), 11.54 (s, 1H), 7.99 – 7.92 (m, 2H), 7.74 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.60 – 7.45 (m, 3H), 7.39 (dd, *J* = 7.1, 1.3 Hz, 1H).
^{13}C NMR (101 MHz, $(CD_3)_2SO$): δ (ppm) = 162.95, 150.5, 143.9, 133.7, 132.4, 130.4, 129.4, 128.9, 128.7, 126.8, 126.4, 125.9, 125.6, 110.7.
MS (EI, 70 eV): m/z (%) = 302 (31), 301 (16), 300 (100), 299 (31), 285 (15), 271 (16), 270 (16), 265 (37), 250 (41), 235 (28), 233 (16), 220 (24), 207 (32), 206 (29), 205 (15), 193 (31), 192 (15), 191 (19), 180 (28), 179 (24), 178 (23), 165 (44), 164 (68), 152 (21), 139 (19), 137 (15).

[221] R. Nencka, I. Votruba, H. Hřebabecký, P. Jansa, E. Tloušťová, K. Masojídková, A. Holý, *J. Med. Chem.* **2007**, *50*, 24, 6016-6023.

HRMS (EI): for $C_{14}H_9ClN_2O_2$: calc. [M+]: 272.0353; found: 272.0340.

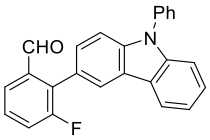
N,*N*-Diethyl-3-fluoro-2-(9-phenyl-9*H*-carbazol-3-yl)benzamide (117d)



According to **TP 9**, to a solution of *N*,*N*-diethyl-3-fluorobenzamide (**111e**, 390 mg, 2 mmol, 1.0 equiv.) in toluene (4 mL) was added TMP_2Mg (**23**, 2.2 mmol, 1.1 equiv) at 25 °C. After 10 min, the resulting arylmagnesium with transmetalated with a $ZnCl_2$ solution (4.8 mL, 1.00 M in THF, 2.40 equiv) at 0 °C for 30 min. A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum was charged with $Pd(dba)_2$ (35 mg, 3 mol%), TFP (28 mg, 6 mol%) and 3-iodo-9-phenyl-9H-carbazole (612 mg, 1.66 mmol, 0.83 equiv). The freshly prepared arylzinc reagent was added and the reaction mixture was placed in an oil bath at 55 °C for 16 h. Purification of the crude product by flash column chromatography (silica gel, pentane/EtOAc = 1:1) afforded the title compound as a white solid (**117d**, 651 mg, 1.49 mmol, 90% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) = 8.22 (s, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.54 (m, 4H), 7.53 – 7.46 (m, 2H), 7.44 – 7.40 (m, 3H), 7.38 (td, *J* = 8.1, 5.1 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.24 – 7.18 (m, 2H), 3.69 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.11 (dq, *J* = 14.3, 7.2 Hz, 1H), 2.88 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.69 (dq, *J* = 14.1, 7.0 Hz, 1H), 0.81 (t, *J* = 7.1 Hz, 3H), 0.70 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$): δ (ppm) = 169.22 (d, *J* = 3.0 Hz), 159.58 (d, *J* = 247.0 Hz), 141.2, 140.5, 139.5, 137.4, 129.9, 128.9 (d, *J* = 8.6 Hz), 127.9 (d, *J* = 1.7 Hz), 127.6, 127.0, 126.9 (d, *J* = 16.5 Hz), 126.1, 124.3, 123.3, 123.2, 122.5 (d, *J* = 3.7 Hz), 121.8 (d, *J* = 1.5 Hz), 120.5, 120.1, 116.1 (d, *J* = 23.3 Hz), 109.8, 109.4, 42.4, 38.3, 13.6, 11.9.
MS (EI, 70 eV): m/z (%) = 437 (27), 436 (100), 435 (14), 365 (33), 364 (57), 363 (11), 336 (10), 335 (15), 257 (12), 181 (23), 72 (10).
HRMS (EI): for $C_{29}H_{25}FN_2O$: calc. [M+]: 436.1951; found: 436.1945.

3-Fluoro-2-(9-phenyl-9*H*-carbazol-3-yl)benzaldehyde (117e)



The title compound was prepared according to a literature procedure.[222] A dry and argon flushed Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with $Cp_2Zr(H)Cl$ (77 mg, 0.30 mmol, 1.5 equiv). A solution of N,N-diethyl-3-fluoro-2-(9-phenyl-9H-carbazol-3-yl)benzamide (**117d**, 87 mg, 0.2 mmol, 1.0 equiv) in dry THF (1 mL) was added and the reaction mixture was stirred for 30 min at 25 °C. Purification by short path flash column chromatography (silica gel, ihexane/EtOAc = 4:1) afforded the title compound as a yellow oil (**117e**, 59 mg, 0.16 mmol, 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.92 (d, *J* = 0.8 Hz, 1H), 8.18 – 8.07 (m, 2H), 7.89 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.69 – 7.57 (m, 4H), 7.55 – 7.39 (m, 7H), 7.33 (ddd, *J* = 8.0, 5.3, 2.9 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = δ 191.68 (d, *J* = 3.9 Hz), 160.10 (d, *J* = 247.2 Hz), 141.4, 140.8, 137.3, 136.2 (d, *J* = 2.4 Hz), 133.8 (d, *J* = 16.5 Hz), 130.0, 128.7 (d, *J* = 7.8 Hz), 128.6, 127.8, 127.2, 126.6, 123.4, 123.2 (d, *J* = 3.6 Hz), 123.0, 122.9, 121.6, 120.8 (d, *J* = 23.2 Hz), 120.5, 120.4, 110.1, 109.7.
MS (EI, 70 eV): m/z (%) = 366 (26), 365 (100), 364 (15), 338 (14), 337 (55), 336 (52), 335 (19), 311 (26), 259 (10), 258 (17), 241 (10), 157 (10).
HRMS (EI): for $C_{25}H_{16}FNO$: calc. [M+]: 365.1216; found: 365.1213.

[222] J. M. White, A. R. Tunoori, G. I. Georg, *J. Am. Chem. Soc.* **2000**, *122*, 11995-11996.