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CHROMIUM-CATALYZED ARYL-ALKYL CROSS-COUPLING REACTIONS

- AND -

REGIOSELECTIVE REMOTE LITHIATION OF (HETERO)ARENES AND PREPARATION OF POLYFUNCTIONALIZED (HETERO)ARENES

von

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aus

Dinkelsbühl

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ERKLÄRUNG

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EIDESSTATTLICHE VERSICHERUNG

Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

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Parts of this Ph.D. Thesis have been published

1) "Chromium-Catalyzed Cross-Coupling Reactions of Alkylmagnesium Reagents with Halo-Quinolines and Activated Aryl Chlorides"
A. B. Bellan, O. M. Kuzmina, V. A. Vetsova, P. Knochel, *Synthesis* **2017**, *49*, 188.

2) "Highly Regioselective Remote Lithiation of Functionalized 1,3-bis-Silylated Arenes"
A. B. Bellan, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 1838.

3) "Steric Hindrance Triggered Remote Lithiations of Bulky Silyl Substituted Arenes"
A. B. Bellan, P. Knochel, *Synthesis* **2019**, *accepted article*.

“The greatest challenge to any thinker is

stating the problem in a way that will allow a solution.”

Bertrand Russel

Abbreviations

Ac	acetyl
acac	acetylacetonate
aq.	aqueous
ATR	attenuated total reflection
Bu	butyl
Bz	benzoyl
calc.	calculated
dba	*trans*,*trans*-dibenzylideneacetone
DMF	*N*,*N*-dimethylformamide
e.g.	*exempli gratia*, for example
EI	electron ionization (MS)
equiv.	equivalent(s)
Et	ethyl
EX	electrophile
FG	functional group
GC	gas chromatography
Hal	halogen
Het	undefined heteroaryl substituent
HRMS	high resolution mass spectrometry
i	*iso*
i.e.	*id est*, that is
IR	infrared spectroscopy
J	coupling constant (NMR)
M	mol L^{-1}
Me	methyl
Met	metal
mol%	equiv.•10^{-2}
m.p.	melting point
MS	mass spectrometry
NFSI	*N*-Fluorobenzenesulfonimide
NMP	*N*-Metyl-2-pyrrolidone
NMR	nuclear magnetic resonance
PG	protecting group
Ph	phenyl
Piv	pivaloyl
PMDTA	*N*,*N*,*N'*,*N''*,*N''*-pentamethyldiethylenetriamine

ppm	parts per million
Pr	propyl
R	undefined organic substituent
sat.	saturated
t	*tert*
TBAF	tetra-*N*-butylammonium fluoride
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	*N*,*N*,*N'*,*N'*-tetramethylethylenediamine
TMP	2,2,6,6-tetramethylpiperidine
TP	typical procedure
vol	volume

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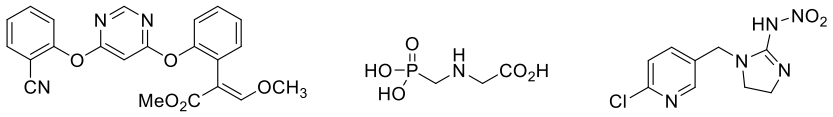
A. INTRODUCTION

1 General Introduction

In the 20th century the world population has increased from 1.6 billion to 6.1 billion people.[1] Since then humanity continued to grow to approximately 7.7 billion up to the beginning of 2019 and is projected to grow up to 12.3 billion by the end of this century.[2] This growth was facilitated by great scientific achievements throughout the last century. The Haber-Bosch process, patented in 1908, allowed the use of the unreactive atmospheric nitrogen to bind it into valuable ammonia, which can be used as fertilizer in crop production or as vantage point for explosives used in both, industrial and military areas.[3] It is estimated that currently 40% of the human population is dependent on food grown, using nitrogen based fertilizers generated from this process. Agricultural research nowadays is focused on providing high yielding and robust crops, as well as crop protection chemicals such as fungicides like azoxystrobin,[4] herbicides like glyphosate[5] or insecticides like imidacloprid[6] (Scheme 1).



Scheme 1: Currently used crop protecting agents in agriculture.

However, even though these compounds are among the most widely used representatives of their classes, they are not without criticism. While azoxystrobin is not known to be harmful towards mammals, birds and insects, the compound itself and its degradation products pose a considerable risk for aquatic life.[7] The herbicide glyphosate, which got a lot of media coverage in recent years, received a new evaluation by the "International Agency for Research on Cancer" regarding its cancerogenity in 2015 and was therein classified as "probably cancerogenic to humans".[8] Finally, the neonicotinoide family of pesiticides, of which imidacloprid is a prominent member, is considered to be one of the

[1] United Nations, Department of Economic and Social Affairs, Population Division, *World Population Prosepects: The 2017 Revision, Key Findings and Advance Table*, ESA/P/WP/248.
[2] a) P. Gerland, A. E. Raftery, H. Ševčíková, N. Li, D. Gu, T. Spoorenberg, L. Alkema, B. K. Fosdick, J. Chunn, N. Lalic, G. Bay, T. Buettner, G. K. Heilig, J. Wilmoth, *Science*, **2014**, *346*, 234. b) *United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision, custom data acquired via website.*
[3] J. W. Erisman, M. A. Sutton, J. Galloway, Z. Klimont, W. Winiwarter, *Nature Geoscience* **2008**, *1*, 636.
[4] a) M. E. Matheron, M. Porchas, *Plant Disease* **2000**, *84*, 454; b) J. R. Bertelsen, E. de Neergard, V. Smedegaard-Petersen, *Plant Pathology* **2001**, *50*, 190.
[5] S. B. Powles, *Proc. Natl. Acad. Sci. U. S. A.* **2010**, *107*, 955.
[6] D. Bai, S. C. R. Lummis, W. Leicht, H. Breer, D. B. Sattelle, *Pestic. Sci.* **1991**, *33*, 197.
[7] a) European Food Safety Authority, *EFSA Journal* **2010**, *8*, 1542; b) J. L. Kunz, C. G. Ingersoll, K. L. Smalling, A. A. Elskus, K. M. Kuivila, *Environ. Toxicol. Chem.* **2017**, *36*, 2308.
[8] IARC Working Group, *IARC Monog. Prog.* **2015**, *112*, 321.

reasons for the bee colony collapse disorder.[9] All these issues warrant the development of improved agents to diminish the potential side-effects as well as improve their performance.

In 1928 Fleming's discovery of penicillin, the first antibiotic, allowed the treatment of bacterially based infections such as streptococcal meningitis.[10] Precise numbers how many lives were saved by antibiotics or specifically the penicillin class of antibiotics are not known, however considering that approximately one third of all deaths at the beginning of the 20th century were related to infectious diseases and that this number decreased to about 4% by the end of the last century, their impact on the growth and well being of our society can not be overestimated.[11] However, antibiotic resistance has become a serious threat to the progress made. The time span between the release of an antibiotic and the discovery of a resistant strain of a bacterial class has steadily decreased to the point that in the same year levofloxacin was released on the US market, a levofloxacin-resistant pneumococcus was found.[12] Therefore, to maintain our ability to fight against bacterial infections, efficient and fast development of novel antibiotic classes and derivatives thereof is necessary.

Synthetic organic chemistry presents itself as a reliable tool in the development and modification of molecules, which ultimately might help in the pressing issues of our time. Regioselective activation and modifications of carbon based molecules are the quintessential backbone of organic chemistry. Modern synthetic approaches for the preparation of complex molecules rely heavily on organometallic chemistry, which offers a wide array of efficient, regioselective and unique transformations, making it an invaluable discipline.[13]

[9] a) A. Decouryte, J. Devillers in *Insect Nicotinic Acetylcholine Receptors. Advances in Experimental Medicine and Biology Vol. 683*, (Eds.: S. H. Thany), Springer, New York **2010**, p. 85; b) European Food Safety Authority, *EFSA Journal* **2013**, *11*, 3066.

[10] R. Gaynes, *Emerg Infect Dis.* **2017**, *23*, 849.

[11] N. Kardos, A. L. Demain, *Appl. Microbiol. Biotechnol.* **2011**, *92*, 677.

[12] C. L. Ventola, *Pharmacy and Therapeutics* **2015**, *40*, 277.

[13] For a general review, see: a) P. Knochel, H. Leuser, L.-Z. Gong, S. Perrone, F. Kneisel in *Handbook of Functionalized Organometallics*, (Eds.: P. Knochel), Wiley-VCH, Weinheim **2005**. b) P. Knochel, P. Millot, A. L. Rodriguez, C. E. Tucker in *Organic reactions*, (Eds.: L. E. Overman), Wiley & Sons Inc., New York, **2001**, p. 1.

2 Organometallic Chemistry

Organometallic compounds contain a carbon-metal bond (C-Met), which gives the carbon the characteristics of a carbon-nucleophile equivalent. The first compound considered to be an organometallic reagent was prepared in 1757 by the French pharmacist and chemist Louis-Claude Cadet de Gassicourt, called "Cadet's fuming liquid".[14] By mixing and heating As_2O_3 and KOAc, a red liquid was distilled, consisting of cacodyl $(Me_2As)_2$ and cacodyl oxide $(Me_2As)_2O$. Following this discovery several other organometallic reagents were discovered, among these were organozinc reagents like diethylzinc by Franklin (1849)[15] or organomagnesium reagents by Grignard (1900).[16] The common trait among these organometallic reagents is the polarization of the carbon-metal bond. However, the degree of this polarization has significant influence on the reactivity, stability and functional group tolerance of these reagents. Compounds with a high ionic character, such as organolithiums, are highly reactive, but often need cryogenic reaction temperatures[13a] and need to be stored in hydrocarbon solvents to avoid degradation by ethereal solvents.[17] Also, due to their high reactivity, functional group tolerance is comparatively low, which can lead to side reactions. On the other hand, organometallic reagents with a lower ionic character, which contain a more covalent bond, have higher functional group tolerance but may need additional activation for certain reactions.[18] In general, the polarization of a carbon metal bond can be deduced by the electronegativity difference of the carbon atom and the metal attached to it (Scheme 2).[19]

Met	Li	Sm	La	Mg	Al	Zn	B
ΔEN(C-Met)	1.53	1.43	1.42	1.27	1.03	0.84	0.49

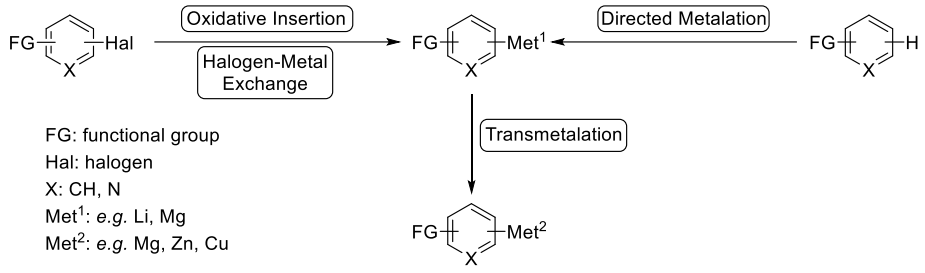
Bond polarization decreases

Functional group tolerance increases
Stability increases
Reactivity decreases

Scheme 2: Electronegativity differences (ΔEN) between carbon and commonly used metals, calculated according to Allred-Rochow electronegativities (the most commonly assigned electronegativities were used, considering the dependency upon the state of hybridization).

The most common preparation methods of organometallic reagents are the direct oxidative insertion of a metal, the halogen-metal exchange and the directed metalation. Additionally, organometallic reagents can be transmetalated to more electronegative metals *via* the corresponding metal halides (Scheme 3).

[14] D. Seyferth, *Organometallics* **2001**, *20*, 14888.
[15] E. Frankland, *Liebigs Ann. Chem.* **1849**, *71*, 171.
[16] V. Grignard, *Compt. Rend. Acad. Sci. Paris* **1900**, *130*, 1322.
[17] H. Gilman, B. J. Gaj, *J. Org. Chem.* **1957**, *22*, 1165.
[18] J. Shannon, D. bernier, D. Rawson, S. Woodward, *Chem. Commun.* **2007**, 3945.
[19] Electronegativities according to the Allred-Rochow scale were used: A. L. Allred, E. G. Rochow, *J. Inorg. Nucl. Chem.* **1958**, *5*, 264.

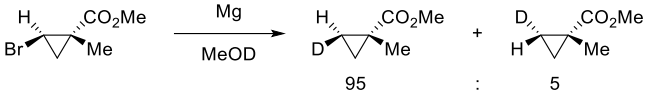


Scheme 3: Most frequently used preparation methods of organometallic reagents.

2.1 Oxidative Insertion

The oxidative insertion of a metal into a carbon-halogen bond is the most used preparation method for organometallic reagents. Many important reagents for both academic research and industrial use, like *n*butyllithium, phenylmagnesium bromide or diethylzinc, are prepared by direct oxidative addition of the metal into the corresponding carbon-halogen bond. The following elaboration focuses mainly on the preparation of organomagnesium (Grignard) reagents, since the mechanism of the magnesium insertion is well studied and understood.

The widely accepted mechanism for the oxidative addition of magnesium is a radical pathway *via* a sequence of single electron transfers (SET).[20] Due to the radical nature of the reaction, partial to full racemization is a substantial problem. Experimental findings suggest, that both outer- as well as inner-sphere radicals can be formed during the SET, which explains the sometimes encountered partial retention of chirality (Scheme 4).[21]

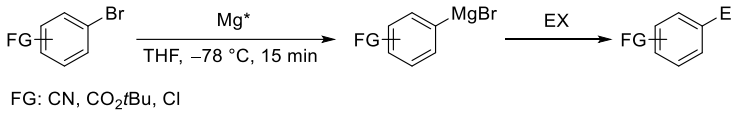


Scheme 4: Example for an unsual retention of chirality during a magnesium insertion.

Furthermore, the metal surface needs to be activated prior to use, to remove the passivation layer formed upon the metals exposure to air. Commonly used reagents for this activation include iodine, 1,2-dibromoethane or diisobutylaluminium hydride.[22] The original protocol for the preparation of organomagnesium reagents had severe drawbacks. High temperatures (30–60 °C), long reaction times (up to 23 h) and intensive activation steps limited the functional group tolerance as well as the applicability of this procedure.[23] Rieke and co-workers developed a preparation method for

[20] a) H. R. Rogers, C. L. Hill, Y. Fujiwara, R. J. Rogers, H. L. Mitchell, G. M. Whitesides, *J. Am. Chem. Soc.* **1980**, *102*, 217; b) H. M. Walborsky, J. Rachon, *J. Am. Chem. Soc.* **1989**, *111*, 1897; c) Z.-N. Chen, G. Fu, X. Xu, *Org. Biomol. Chem.* **2012**, *10*, 9491.
[21] a) W. Kirmse, J. Rode, K. Rode, *Chem. Ber.* **1986**, *119*, 3672; b) H. M. Walborsky, *Acc. Chem. Res.* **1990**, *23*, 286.
[22] a) H. Gilman, R. H. Kirby, *Rec. Trav. Chim.* **1935**, *54*, 577; b) D. E. Pearson, D. Cowan, J. D. Beckler, *J. Org. Chem.* **1959**, *24*, 504; c) U. Tilstam, H. Weinmann, *Org. Proc. Res. Dev.* **2002**, *6*, 906.
[23] H. E. Ramsden, A. E. Balint, W. R. Whitford, J. J. Walburn, R. Cserr, *J. Org. Chem.* **1957**, *22*, 1202.

unpassivated metals with a high surface, by reducing a solution of a metal halide salt using alkali metals such as lithium and a catalytic amount of an electron carrier like naphthalene or biphenyls.[24] The generated highly active magnesium (Rieke magnesium) performs the oxidative addition reaction at cryogenic temperatures within minutes, while tolerating sensitive functional groups like esters, nitriles or intermediary formed ketones (Scheme 5).

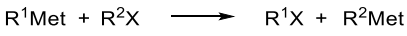


Scheme 5: Preparation of functionalized organomagnesium reagents using Rieke Magnesium.

Further improvements were presented by Knochel and co-workers with their LiCl mediated magnesium insertion.[25] The simple addition of LiCl facilitates the oxidative addition of commercial magnesium enabling the reaction to be performed even at −20 °C often within 30 min. Also, due to the fast reaction times and low temperatures needed, a high functional group tolerance was obtained. It was possible to prepare o*rtho*-magnesiated benzonitrile at ambient temperature within 30 min, whereas 5 h were necessary in the absence of LiCl and considerable amounts of decomposition were observed. This method of promoting metal insertion reactions was extended to several other metals such as zinc, aluminium or indium.[26]

2.2 Halogen-Metal Exchange

Another method to prepare organometallic reagents from organic halides is the halogen-metal exchange. Therein, an already metalated reagent replaces the halide with its own metal, taking on the previous halide (Scheme 6).[27]

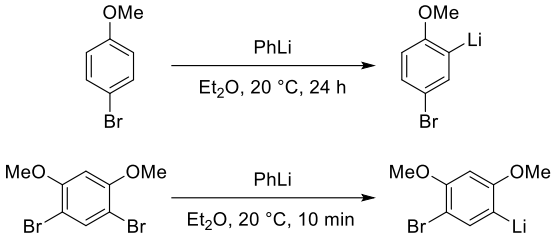


Scheme 6: Schematic representation of a halogen-metal exchange.

In 1931, Prévost reported the first bromine-magnesium exchange after cinnamyl bromide was treated with ethylmagnesium bromide to furnish cinnamylmagnesium bromide.[28] The group of Wittig was the

[24] a) R. D. Rieke, *Science* **1989**, *246*, 1260; b) J.-S. Lee, R. Velarde-Ortiz, A. Guijarro, J. R. Wurst, R. D. Rieke, *J. Org. Chem.* **2000**, *65*, 5428.
[25] F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed*. **2008**, *47*, 6802.
[26] a) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040; b) Y.-H. Chen, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 7648; c) T. D. Blümke, Y.-H. Chen, Z. Peng, P. Knochel, *Nat. Chem.* **2010**, *2*, 313.
[27] For a general overview, see: a) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Ed.* **2003**, *42*, 4302; b) D. Tilly, F. Chevallier, F. Mongin, P. C. Gros, *Chem. Rev.* **2014**, *114*, 1207; c) D. S. Ziegler, B. Wei, P. Knochel, *Chem. Eur. J.* **2019**, *25*, 2695.
[28] C. Prévost, *Bull. Soc. Chim. Fr.* **1931**, *49*, 1372.

first to identify and report the halogen-lithium exchange in 1938.[29] After an *ortho*-lithiation of 4-bromoanisole by phenyllithium was observed, they investigated this metalation with different aryl methyl ethers. However, when 1,3-dimethoxy-4,6-dibromobenzene was treated with phenyllithium no metalation occurred but instead a bromine was exchanged by lithium (Scheme 7).

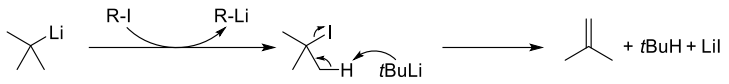


Scheme 7: Experiments conducted by Wittig and co-workers leading to the first identified halogen-lithium exchange.

Shortly after, Gilman and co-workers reported their independent discovery of a halogen-lithium exchange.[30] Contrary to the earlier approach *n*butyllithium was used instead of phenyllithium. It is important to note that several other groups were close to observe the halogen-lithium exchange more than 10 years earlier, however due to the "established" radical theory they identified products like 1-butyl-4-methylbenzene as products of a radical recombination or of a novel approach toward a Wurtz type reaction.[31]

The halogen-metal exchange is an equilibrium reaction, whose driving force is the formation of the most stable organometallic species.[13a,32] The stability of the organometallic species is dependent on the hybridization of the carbon atom ($sp > sp^2_{vinyl} > sp^2_{aryl} > sp^3_{prim} > sp^3_{sek} > sp^3_{tert}$) and the influence of stabilizing electron withdrawing groups. A problem of the halogen-metal exchange is the *in situ* formed organo halide. It can lead to decomposition of the newly formed organometallic reagent *via* an elimination side reaction or form unwanted sideproducts in the following reactions like transition metal catalyzed cross-coupling reactions.[33] The elimination side reaction is particularly evident for tertiary aliphatic lithium exchange reagents such as *t*butyllithium. Therefore, the exchange reagent is often used with an excess of 1.0 equiv. to promote the elimination by the exchange reagent and keep the desired metalated species intact (Scheme 8).

[29] G. Wittig, U. Pockels, H. Dröge, *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 1903.
[30] H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106.
[31] a) C. S. Marvel, F. D. Hager, D. D. Coffman, *J. Am. Chem. Soc.* **1927**, *49*, 2323; b) K. Ziegler, F. Crössmann, H. Kleiner, O. Schäfer, *Justus Liebigs Ann. Chem.* **1929**, *473*, 1.
[32] a) H. J. S. Winkler, H. Winkler, *J. Am. Chem. Soc.* **1966**, *88*, 964; b) H. J. S. Winkler, H. Winkler, *J. Am. Chem. Soc.* **1966**, *88*, 969.
[33] a) H. Neumann, D. Seebach, *Tetrahedron Lett.* **1976**, *17*, 4839; b) C. B. Rauhut, C. A. Vu, F. F. Fleming, P. Knochel, *Org. Lett.* **2008**, *10*, 1187.



Scheme 8: Iodine-lithium exchange with an additional equivalent of *t*BuLi to intercept the intermediary formed *t*BuI.

Especially for the halogen-lithium exchange, low temperatures are a necessity to facilitate a certain degree of functional group tolerance as shown earlier by the groups of Köbrich and Parham.[34] It is therefore favorable, that the rates of the halogen-exchange reaction often exceed possible side reactions, even at −78 °C.[35]

To circumvent the need of these extreme cryogenic temperatures and to increase the functional group tolerance the attention was moved to less electropositive metals, to generate more general and stable organometallic species. The groups of Knochel and Cahiez reported the use of convenient *i*PrMgBr and iPr$_2$Mg to generate magnesiated arenes by iodine-magnesium exchange at −40 °C within less than 60 min.[36] The reaction tolerated functional groups like ethyl esters, nitriles or amides and selectively exchanged iodide in the presence of a bromide. Organomagnesium reagents bearing the highly sensitive nitro-group were prepared from *ortho*-iodonitroarenes at −40 °C within minutes in good yields using phenyl or mesityl magnesium reagents.[37] As they are less reactive than their corresponding lithium exchange reagents, magnesium based exchange reagents struggle with the replacement of bromides if they are not additionally activated by electron-withdrawing groups, even if stronger exchange reagents like iPr$_2$Mg are used.[38] Oshima and co-workers were able to perform fast bromine-magnesium exchange reactions of electron-rich bromoarenes at 0 °C by using highly reactive lithium trialkylmagnesium-ate complexes.[39] Also, functional groups like nitriles or amides were tolerated if the reaction was performed at −78 °C. Further improvements were made by Knochel and co-workers with their introduction of the "Turbo-Grignard".[40] This reagent, consisting of LiCl complexed *i*PrMgCl, performed a fast bromine-magnesium exchange reaction, while tolerating sensitive groups like esters or nitriles even at −15 °C. Compared to previous exchange reagents like iPr$_2$Mg or *i*PrMgCl, higher yields were obtained and lower reagent amounts were needed using *i*PrMgCl•LiCl (Scheme 9).

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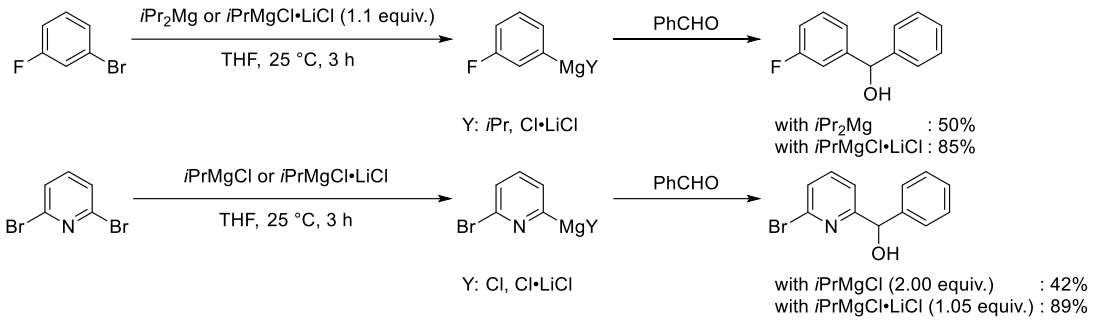
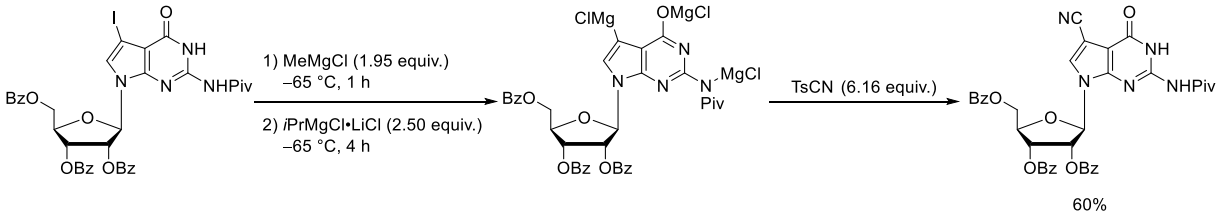
[34] a) G. Köbrich, P. Bruck, *Chem. Ber.* **1970**, *103*, 1412; b) W. E. Parham, C. K. Bradsher, *Acc. Chem. Res.* **1982**, *15*, 300.
[35] W. F. Bailey, J. J. Patricia, T. T. Nurmi, W. Wang, *Tetrahedron Lett.* **1986**, *27*, 1861; b) I. S. Aidhen, J. R. Ahuja, *Tetrahedron Lett.* **1992**, *33*, 5431.
[36] a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1701; b) G. Varchi, A. Ricci, G. Cahiez, P. Knochel, *Tetrahedron* **2000**, *56*, 2727.
[37] a) I. Sapountzis, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 1610; b) I. Sapountzis, H. Dube, R. Lewis, P. Knochel, *J. Org. Chem.* **2005**, *70*, 2445.
[38] M. Abarbri, F. Dehmel, P. Knochel, *Terahedron Lett.* **1999**, *40*, 7449.
[39] a) K. Kitagawa, A. Inoue, H. Shinokubo, K. Oshima, *Angew. Chem. Int. Ed.* **2000**, *39*, 2481; b) A. Inoue, K. Kitagawa, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2001**, *66*, 4333.
[40] a) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333; *Angew. Chem.* **2004**, *116*, 3396; b) L. Shit, Y. Chu, P. Knochel, H. Mayr, *Angew. Chem. Int. Ed.* **2008**, *47*, 202; c) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2012**, *14*, 2602.



Scheme 9: Bromine-magnesium exchange with various magnesium reagents, highlighting the improvements by the "Turbo-Grignard".

*i*PrMgCl•LiCl also tolerateed the highly sensitive triazene group, whereas uncomplexed *i*PrMgCl lead to the formation of sideproducts.[41] Furthermore, the reagent tolerated functionalized substrates like nucleosides and performed the halogen-metal exchange even if there were already negative charges present in the molecule (Scheme 10).[42]

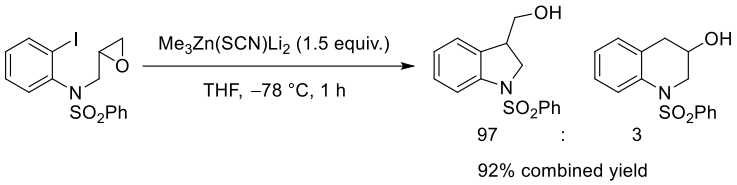


Scheme 10: Preparation of a functionalized nucleoside *via* *i*PrMgCl•LiCl mediated magnesiation.

Recently, Knochel and co-workers reported a novel class of halogen-magnesium exchange reagents, which can prepare organomagnesium reagents in important industrial non-polar solvents like toluene and hydrocarbons.[43] The toluene soluble reagents were prepared by mixing the magnesium alkoxide $Mg(OR)_2$ (R = 2-ethylhexyl) with 1.0 or 2.0 equiv. of *s*BuLi forming *s*BuMgOR•LiOR and *s*Bu_2Mg•2LiOR, respectively. These reagents performed the bromine-magnesium exchange of electron-rich bromides within minutes. For example, the exchange of 4-bromoanisole using *i*PrMgCl•LiCl was finished after 27 h in THF and does not occur in toluene at all. Whereas, the novel *s*BuMgOR•LiOR afforded the organomagnesium reagent in 85% yield after only 15 min and can go as high as 99% after addition of TMEDA. Aditionally, the also reported *s*Bu_2Mg•2LiOR (0.6 equiv.) used with the additive PMDTA (0.6 equiv.) is the first reported reagent mixture to perform the chlorine-magnesium exchange on electron rich substrates.

[41] C.-Y. Liu, P. Knochel, *Org. Lett.* **2005**, *7*, 2543.
[42] T. Brückl, I. Thoma, A. J. Wagner, P. Knochel, T. Carell, *Eur. J. Org. Chem.* **2010**, 6517.
[43] D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701.

Finally, exchange reagents for more electropositive metals such as manganese,[44] zinc[45] and copper[46] have been developed. Especially, the halogen-zinc exchange was studied thoroughly as zinc reagents can be used for a wide array of reactions like transition metal catalyzed cross-coupling reactions[47] or for the synthesis of functionalized ketones *via* acylation reactions.[48] As organozinc reagents are even less polarized than their corresponding organomagnesium species, an additional activation was necessary for the halogen-zinc exchange. Therefore, tri- or tetra-alkyl zincates were used as exchange reagents. However, an excess of the metalated reagent (up to 4.50 equiv. of metalated alkyl reagent) and cryogenic reaction temperatures were often needed (Scheme 11).[49]



Scheme 11: Zincate mediated iodine-zinc exchange, followed by an intramolecular epoxide opening.

Knochel and co-workers were able to circumvent the previously reported excess of organometallic reagent by adding a catalytic amount of Li(acac) (10%) to iPr$_2$Zn (0.6 equiv.) in a solvent mixture of Et$_2$O/NMP (1:10) at 25 °C.[45c,d] In their proposed mechanism an initial iodine-zinc exchange takes place. The newly formed mixed zinc reagent, which was also observed as main product in the absence of Li(acac), was complexed by the acac ligand to form an intermediary zincate species, which was then capable of performing a second exchange reaction. This bisarylacetylaceton zincate collapsed, releasing the diarylzinc species and regenerating the Li(acac) (Scheme 12). They were able to perform this exchange reaction on various aryl iodides bearing both electron-withdrawing and electron-donating groups and even sensitive functional groups like free aldehydes were tolerated on the aryl iodides.

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[44] a) R. Inoue, H. Shinokubo, K. Oshima, *Tetrahedron Lett.* **1996**, *37*, 5377; b) H. Kakiya, R. Inoue, H. Shinokubo, K. Oshima, *Tetrahedron Lett.* **1997**, *38*, 3275; c) R. Inoue, H. Shinokubo, K. Oshima, *J. Org. Chem.* **1998**, *63*, 910; d) H. Kakiya, H. Shinokubo, K. Oshima, *Tetrahedron* **2001**, *57*, 10063.

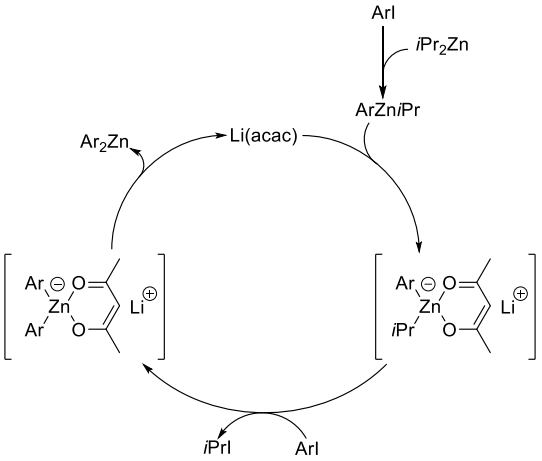
[45] a) Y. Kondo, M. Fujinami, M. Uchiyama, T. Sakamoto, *J. Chem. Soc., Perkin Trans. 1* **1997**, 799; b) Y. Kondo, T. Komine, M. Fujinami, M. Uchiyama, T. Sakamoto, *J. Comb. Chem.* **1999**, *1*, 123; c) F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 1017; d) L.-Z. Gong, P. Knochel, *Synlett* **2005**, 267.

[46] a) Y. Kondo, T. Metsudaira, J. Sato, N. Murata, T. Sakamoto, *Angew. Chem. Int. Ed.* **1996**, *35*, 736; b) C. Piazza, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 3263; c) F. F. Fleming, Z. Zhang, W. Liu, P. Knochel, *J. Org. Chem.* **2005**, *70*, 2200.

[47] a) S. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705; b) A. Krasovskiy, B. H. Lipshutz, *Org. Lett.* **2011**, *13*, 3818.

[48] a) E.-i. Negishi, V. Bagheri, S. Chatterjee, F.-T. Luo, J. A. Miller, A. T. Stoll, *Terahedron Lett.* **1983**, *24*, 5181; b) Y. Zhang, T. Rovis, *J. Am. Chem. Soc.* **2004**, *126*, 15964; c) A. Krasovski, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040; d) A. D. Benischke, M. Leroux, I. Knoll, P. Knochel, *Org. Lett.* **2016**, *18*, 3626.

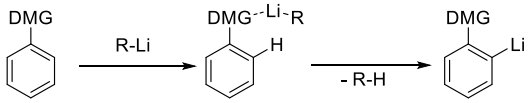
[49] a) M. Uchiyama, M. Koike, M. Kameda, Y. Kondo, T. Sakamoto, *J. Am. Chem. Soc.* **1996**, *118*, 8733; b) M. Uchiyama, M. Kameda, O. Mishima, N. Yokoyama, M. Koike, Y. Kondo, T. Sakamoto, *J. Am. Chem. Soc.* **1998**, *20*, 4934; c) M. Uchiyama, T. Furuyama, M. Kobayashi, Y. Matsumoto, K. Tanaka, *J. Am. Chem. Soc.* **2006**, *128*, 8404.



Scheme 12: Proposed mechanism of the Li(acac) catalyzed iodine-zinc exchange using *i*Pr_2Zn.

2.3 Directed Metalation

Organometallic reagents can also be prepared *via* deprotometalation of C-H bonds using alkyl metal or metal amide bases. Among the earliest reported examples of a lithiation mediated by an alkyllithium reagent was the preparation of 9-fluorenyllithium from the reaction of ethyllithium with fluorene by Schlenk in 1928.[50] A decade later, Wittig[51] and Gilman[52] independently reported their experiments leading selectively to *ortho*-lithiated anisole. This seminal work led to the concept of directed *ortho* metalation (DoM), which describes the phenomenon of aromatic C-H metalations adjacent to a directing metalation group (DMG).[53] DMGs are functional groups that enable the kinetic metalation of their *ortho*-position either by a coordination induced proximity effect,[54] in which they act as lewis-basic moieties coordinating to the lewis-acidic metal of the organometallic base, or by an electronic effect, wherein the C-H bond is acidified using the electron withdrawing effect of the DMG (Scheme 13). Commonly considered to be strong DMGs are *e.g.* amides, carbamates, sulfonamides or the oxazolyl group, whereas halides, ethers or amines are in general weak DMGs.[53b]

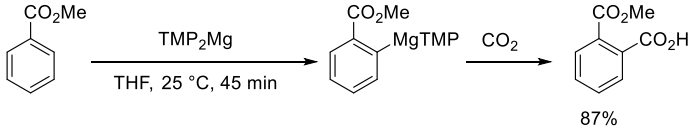


Scheme 13: Schematic representation of a coordination induced *ortho*-lithiation.

[50] W. Schlenk, E. Bergmann, *Justus Liebigs Ann. Chem.* **1928**, *463*, 98.
[51] G. Wittig, U. Pockels, H. Dröge, *Chem. Ber.* **1938**, *71*, 1903.
[52] H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109.
[53] For a generel overview, see: a) H. W. Gschwend, H. R. Rodriguez, *Org. React.* **1979**, *26*, 1; b) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; c) J. Epsztajn, A. Józwiak, A. K. Szczesniak, *Curr. Org. Chem.* **2006**, *10*, 1817.
[54] a) M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206; b) V. H. Gessner in *Ideas in Chemistry and Molecular Sciences: Advances in Synthetic Chemistry*, (Eds.: B. Pignataro), Wiley-VCH, Weinheim **2010**.

Traditionally, highly reactive organolithium bases like PhLi or the butyllithiums have been used for these directed metalations. Additionally, the metalation rate and substrate scope of these reagents can further be increased through the application of additives like the tertiary amine TMEDA[55] or the alkali metal alcoholate KO*t*Bu (often called LiCKOR base or Schlosser's base).[56] However, the tendency to attack electrophilic functional groups and to undergo halogen-lithium exchange reactions made the development of more tolerant bases necessary.[57] Sterically hindered amides (MetNRR') are viable alternatives as their sterical bulk limits nucleophilic attacks, and they cannot perform halogen-exchange reactions. The most commonly used lithium amides are TMPLi, $LiN(SiMe_3)_2$ and $LiN(iPr)_2$.[58] However, the formed organolithium species still has limited functional group tolerance and their high reactivity can lead to multiple metalations, especially when used for the metalation of azines.

Analog to the halogen-metal exchange reagents, the implementation of less electropositive metals like magnesium or zinc led to an increased tolerance towards sensitive functional groups and higher metalation temperatures could be used. Pioneering work by Hauser[59] showed that Et_2NMgBr and iPr_2NMgBr are suitable bases for the enolization of esters while fully avoiding the acylation of the amide. Decades later, Eaton and co-workers reported the two magnesium amide bases TMPMgBr and TMP_2Mg which were capable of performing DoM's on very sensitive substrates like methyl benzoate (Scheme 14).[60]



Scheme 14: Directed *ortho*-magnesiation of methyl benzoate using TMP_2Mg.

Further interest into the subject was generated, when Mulzer and co-workers showed that TMPMgCl efficiently and regioselectively metalates pyridine carboxamides, carbamates and derivatives thereof, whereas lithium bases like *t*BuLi and TMPLi afforded mixtures of regioisomers, while needing

[55] a) D. B. Collum, *Acc. Chem. Res.* **1992**, *25*, 448; b) M. A. Nichols, P. G. Williard, *J. Am. Chem. Soc.* **1993**, *115*, 1568; c) H. J. Reich, D. P. Green, M. A. Medina, W. S. Goldenberg, B. Ö. Gudmundsson, R. R. Dykstra, N. H. Phillips, *J. Am. Chem. Soc.* **1998**, *120*, 7201. d) V. H. Gessner, C. Däschlein, C. Strohmann, *Chem. Eur. J.* **2009**, *15*, 3320; e) H. J. Reich, *Chem. Rev.* **2013**, *113*, 7130.

[56] a) M. Schlosser, S. Strunk, *Tetrahedron Lett.* **1984**, *25*, 741; b) M. Schlosser, *Pure & Appl. Chem.* **1988**, *60*, 1627; c) M. Schlosser, *Angew. Chem. Int. Ed.* **2005**, *44*, 376.

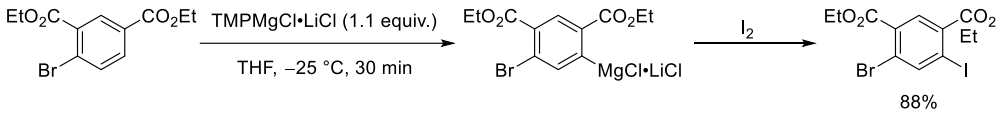
[57] a) H. W. Gschwend, A. Hamdan, *J. Org. Chem.* **1975**, *40*, 2008; b) P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356.

[58] a) R. A. Olofson, C. M. Dougherty, *J. Am. Chem. Soc.* **1973**, *95*, 581; b) R. A. Olofson, C. M. Dougherty, *J. Am. Chem. Soc.* **1973**, *95*, 582;

[59] a) C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295; b) F. C. Frostick, C. R. Hauser, *J. Am. Chem. Soc.* **1949**, *71*, 1350.

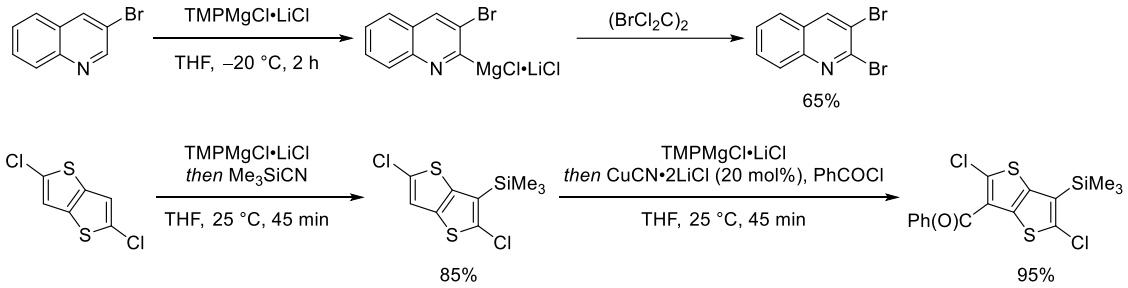
[60] a) P. E. Eaton, C.-H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016; b) P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc.* **1993**, *115*, 11370; c) K. W. Henderson, W. J. Kerr, *Chem. Eur. J.* **2001**, *7*, 3430.

cryogenic temperatures to avoid decomposition and side reactions.[61] This highlighted the applicability of magnesium amides in organic synthesis. However, an issue were the long reaction times needed and the low solubility in THF. Furthermore, procedures used a considerable excess of the respective base, which was indefensible from an atom economic point of view. Knochel and co-workers were able to solve these issues with their introduction of Turbo-Hauser bases.[62] Similar to the improvements seen for halogen-metal exchange reagents, the addition of LiCl to TMPMgCl considerably enhanced the kinetic basicity and solubility of the magnesium amide. The reagent can easily be prepared by magnesiation of TMP-H with *i*PrMgCl•LiCl and batches of this reagent are storeable for long periods of time. Substrates like brominated isophtalic esters were regioselectively magnesiated using only 1.1 equivalents of the novel TMPMgCl•LiCl base within 30 minutes (Scheme 15).



Scheme 15: Regioselective magnesiation of an isophtalic ester using TMPMgCl•LiCl.

Additionally, both electronpoor[63] and electronrich[64] heteroarenes were metalated using TMPMgCl•LiCl (Scheme 16).

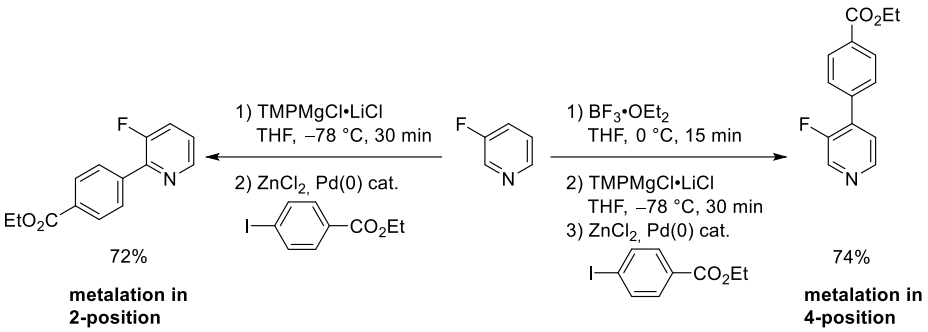


Scheme 16: Synthesis of functionalized electronpoor and electronrich heteroarenes using TMPMgCl•LiCl.

Also, *N*-heterocycles can be activated by addition of a Lewis-acid like BF_3•OEt_2. This activation allows for a change of regioselectivity or can enable the metalation at all. A prominent example is the metalation of 3-fluoropyridine, wherein a metalation in the absence of BF_3•OEt_2 regioselectively leads

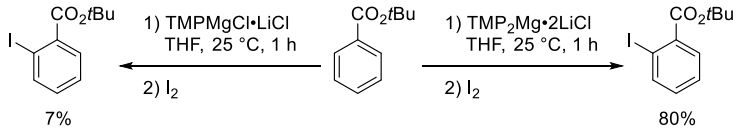
[61] a) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414; b) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *Justus Liebigs Ann. Chem.* **1995**, 1441; c) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *Synthesis* **1995**, 1225.
[62] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; *Angew. Chem.* **2006**, *118*, 3024; b) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794; c) M. Balkenhohl, P. Knochel, *Synopen* **2018**, *2*, 78.
[63] a) Boudet, J. R. Lachs, P. Knochel, *Org. Lett.* **2007**, *9*, 5525; b) C. J. Rohbogner, G. C. Clososki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1503; c) L. D. Tran, O. Daugulis, *Org. Lett.* **2010**, *12*, 4277; d) C. J. Rohbogner, S. Wirth, P. Knochel, *Org. Lett.* **2010**, *12*, 1984.
[64] a) T. Kunz, P. Knochel, *Chem. Eur. J.* **2011**, *17*, 866; b) F. M. Piller, P. Knochel, *Synthesis* **2011**, 1751.

in 2-position, while in the presence of BF_3•OEt_2 the 4-position is magnesiated selectively (Scheme 17).[65]



Scheme 17: Change in regioselectivity for the metalation of 3-fluoropyridine by addition of BF_3•OEt_2.

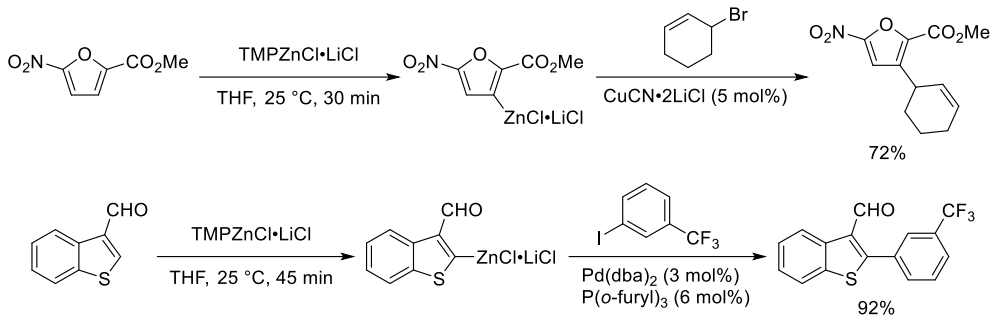
However, some substrates were not sufficiently metalated by TMPMgCl•LiCl or made higher reaction temperatures necessary, which often hinders functional group tolerance. The more reactive TMP_2Mg•2LiCl enabled the metalation of these substrates.[66] Thus, *t*butylbenzoate could efficiently be metalated using TMP_2Mg•2LiCl, wheras TMPMgCl•LiCl only afforded traces of the magnesiated benzoate (Scheme 18).



Scheme 18: Comparison between TMPMgCl•LiCl and TMP_2Mg•2LiCl for the metalation of *t*butyl benzoate.

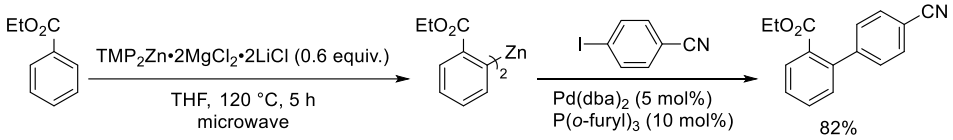
The tolerance of functional groups was further improved with the introduction of the kinetically active zinc amide TMPZnCl•LiCl.[67] The base and its formed organozinc reagents tolerate highly sensitive functional groups like aldehydes or nitro groups (Scheme 19).

[65] a) M. Jaric, B. A. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 5451; *Angew. Chem.* **2010**, *122*, 5582; b) M. Jaric, B. A. Haag, S. M. Manolikakes, P. Knochel, *Org. Lett.* **2011**, *13*, 2306; c) S. M. Manolikakes, M. Jaric, K. Karaghiosoff, P. Knochel, *Chem. Commun.* **2013**, *49*, 2124.
[66] G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681; *Angew. Chem.* **2007**, *119*, 7825.
[67] a) M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837; b) T. Bresser, G. Monzon, M. Mosrin, P. Knochel, *Org. Process Res. Dev.* **2010**, *14*, 1299; c) F. Gosselin, S. J. Savage, N. Blaquiere, S. T. Staben, *Org. Lett.* **2012**, *14*, 862; d) S. L. McDonald, C. E. Hendrick, Q. Wang, *Angew. Chem. Int. Ed.* **2014**, *53*, 4667.



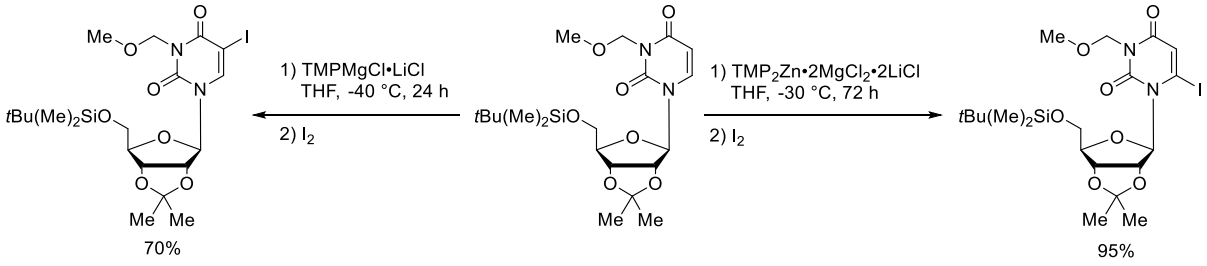
Scheme 19: Zincation of electronrich heteroarenes bearing highly sensitive functional groups, using TMPZnCl•LiCl.

Another valuable addition to the toolset of organometallic chemists was $TMP_2Zn•2MgCl_2•2LiCl$.[68] It presents itself as a more powerful metalation reagent while largely maintaining the functional group tolerance of TMPZnCl•LiCl. The zincation of the previously shown thianaphtene-3-carboxaldehyde is completed within 15 min. Sensitive heterocycles like the easily decomposing oxadiazole can be metalated at 25 °C. Additionally, this base was shown to be stable at elevated temperatures and be used in a microwave reactor (Scheme 20).[69]



Scheme 20: Microwave enabled zincation of ethyl benzoate.

Finally, during their studies on the functionalization of nucleosides, Knochel and co-worker were able to show that $TMP_2Zn•2MgCl_2•2LiCl$ can behave as a complementary base to TMPMgCl•LiCl, allowing for a change of regioselecivity of the metalation (Scheme 21).[70]

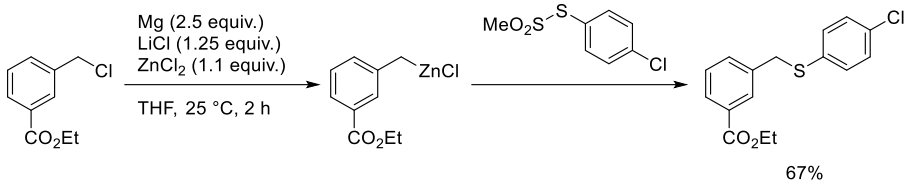


Scheme 21: Different regioselective metalations of a protected uridine, dependent on the choice of metalated amide.

[68] S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685.
[69] S. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705.
[70] L. Klier, E. Aranzamendi, D. Ziegler, J. Nickel, K. Karaghiosoff, T. Carell, P. Knochel, *Org. Lett.* **2016**, *18*, 1068.

2.4 Transmetalation

Transmetalations offers another approach towards various organometallic reagents by treating a metalated reagent with the salt of a different metal. In general, the driving force of this metal metathesis is the formation of the most covalent bond *i.e.* it is possible to transmetalate an organolithium reagent using $ZnCl_2$, whereas the generation of an organolithium reagent by treatment of an organozinc reagent with LiCl is not possible. The general use of transmetalations is the preparation of more stable, functional group tolerant organometallic reagents and to enable specific reactions like a Negishi cross-coupling reaction or a copper-catalyzed allylation. A transmetalation is possible as either a followup reaction, *e.g.* after a successful metalation or halogen-metal exchange, or as an *in situ* process, where the metal salt is already present when the metalated reagent is prepared to immediately transmetalate it (Scheme 22).[71]



Scheme 22: Preparation of a functionalized benzylzinc reagent *via* a magnesium insertion-*in situ* transmetalation sequence.

[71] a) A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824; b) F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 7192; c) A. Frischmuth, M. Fernández, N. M. Barl, F. Achrainer, H. Zipse, G. Berionni, H. Mayr, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 7928; d) M. R. Becker, P. Knochel, *Angew. Chem. Int. Ed.* **2015**, *54*, 12501; e) M. Ketels, M. A. Ganieck, N. Weidmann, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 12770.

3 Transition Metal Catalyzed Cross-Coupling Reactions

A frequent application of organometallic reagents are transition metal catalyzed cross-coupling reactions.[72] Even though metal mediated homocoupling reactions like the Wurtz,[73] Pinacol[74] or Glaser[75] coupling reactions have been known since the mid 19th century. The first report of a selective cross-coupling reaction was in 1955 by Cadiot and Chodkiewicz.[76] They described the copper(I)-catalyzed cross-coupling reaction of a terminal alkyne with a haloalkyne, which selectively led to mixed 1,3-diynes. In the 1970s the groups of Kumada and Corriu,[77] Heck,[78] Sonogashira,[79] Negishi,[80] Stille[81] and Suzuki[82] reported the first palladium- and nickel-catalyzed cross-coupling reactions of organometallic reagents with organohalides, which enabled the C-C bond formation between two sp^2-hybridized carbon centers. New elaborate catalytic systems[83] have been developed which allowed this reaction to find widespread use in both academic and industrial synthesis of complex organic molecules.[84] However, prices for palladium have been steadily rising and almost tripled within the last 3 years, leading to a current all time high.[85] And although nickel shows a similar chemical behavior and is comparatively inexpensive, severe toxicity issues limit its use on industrial scale.[86] The search for catalytically active replacement metals is therefore of utmost importance. In recent years' first row transition metals like

[72] C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062.
[73] A. Wurtz, *Justus Liebigs Ann. Chem.* **1855**, *96*, 364.
[74] R. Fittig, *Justus Liebigs Ann. Chem.* **1859**, *110*, 17.
[75] a) C. Glaser, *Chem. Ber.* **1869**, *2*, 422; b) C. Glaser, *Justus Liebigs Ann. Chem.* **1870**, *154*, 137.
[76] a) W. Chodkiewicz, P. Cadiot, *C. R. Hebd. Seances Acad. Sci.* **1955**, *241*, 1055; b) W. Chodkiewicz, *Ann. Chim. Paris* **1957**, *2*, 819.
[77] a) R. J. P. Corriu, J. P. Masse, *J. Chem. Soc., Chem. Commun.* **1972**, 144a; b) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374.
[78] a) R. F. Heck, J. P. Nolley, *J. Org. Chem.* **1972**, *37*, 2320; b) H. A. Dieck, R. F. Heck, *J. Am. Chem. Soc.* **1974**, *96*, 1133.
[79] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467.
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[81] D. Milstein, J. K. Stille, *J. Am. Chem. Soc.* **1978**, *100*, 3636.
[82] N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, *20*, 3437.
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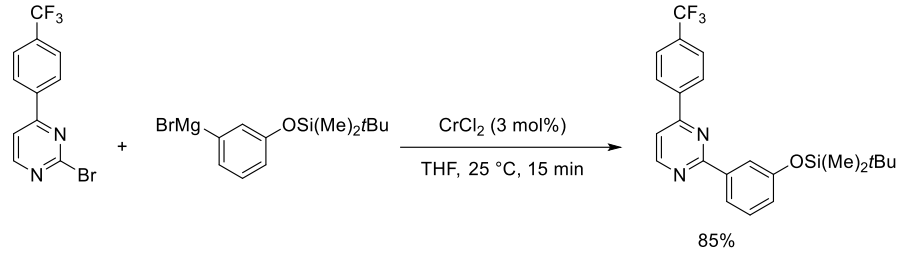
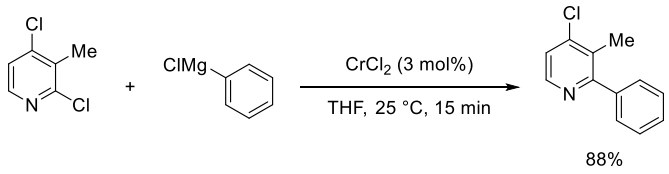
[84] *Palladium-Catalyzed Coupling Reactions: Practical Aspects and Future Developments*, (Eds.: Á. Molnár), Wiley-VCH, Weinheim **2013**.
[85] world market prices: 1214 €/31.1 g; https://www.finanzen.net/rohstoffe/palladiumpreis; retrieved in January 2019.
[86] a) world market prices: 10.36 €/1 kg; https://www.finanzen.net/rohstoffe/nickelpreis; retrieved in January 2019; b) *Handbook on the Toxicology of Metals* (Eds.: L. Friberg, G. F. Nordberg, V. B. Vouk), Elsevier, Amsterdam, **1986**; c) K. S. Kasprzak, B. A. Diwan, J. M. Rice, M. Misra, C. W. Riggs, R. Olinski, M. Dizdaroglu, *Chem. Res. Toxicol.* **1992**, *5*, 809.

iron[87] and cobalt[88] have been studied extensively. Iron and cobalt cost only a fraction of palladium and are less toxic than nickel. Additionally, the reactivity and substrate scope of these metals has been shown to be comparable to classic palladium or nickel based cross-coupling reactions. However, the cross-coupling reactions of iron and cobalt are often contaminated with homocoupling side products of the used organometallic reagent. These are difficult to separate and decrease the efficiency of the reaction. However, the transition metal chromium has shown promising properties aswell. In 2013 a seminal study by Knochel and co-workers showed that arylmagnesium reagents react efficiently with (hetero)arene halides (Scheme 23).[89] These cross-coupling reactions proceeded quickly and were often finished within 15 min at 25 °C, while no homocoupling formation was observed during the reaction.



Scheme 23: Chromium-catalyzed cross-coupling of a 2-bromopyrimidine derivative and an aryl Grignard reagent.

Additional research by the Knochel group has shown, that chromium catalyzes selectively the arylation of a halide adjacent to a heteroatom, even if other halides are present (Scheme 24).[90]



Scheme 24: Regioselective arylation of a dichlorinated pyridine in the presence of $CrCl_2$.

Furthermore, both amination and oxidative coupling reactions catalyzed by chromium have been reported.[91] Finally, the group of Zheng has shown that chromium halides can perform cross-coupling reactions between arylmagnesium reagents and aryl methyl ethers or aryl pyridyl ethers as electrophiles.[92]

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[87] for a general overview, see: a) A. Fürstner, A. Leitner, M. Méndez, H. Krause, *J. Am. Chem. Soc.* **2002**, *124*, 13856; b) I. Bauer, H.-J. Knölker, *Chem. Rev.* **2015**, *115*, 3170; c) D. Haas, J. M. Hamann, R. Greiner, P. Knochel, *ACS Catal.* **2016**, *6*, 1540; d) T. L. Mako, J. A. Byers, *Inorg. Chem. Front.* **2016**, *3*, 766; e) A. Piontek, E. Bisz, M. Szostak, *Angew. Chem. Int. Ed.* **2018**, *57*, 11116.

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[89] A. K. Steib, O. M. Kuzmina, S. Fernandez, D. Flubacher, P. Knochel, *J. Am. Chem. Soc.* **2013**, *135*, 15346.

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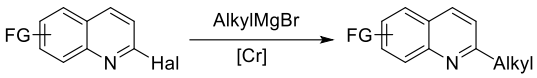
[92] a) X. Cong, H. Tang, X. Zeng, *J. Am. Chem. Soc.* **2015**, *137*, 14367; b) F. Fan, J. Tang, M. Luo, X. Zeng, *J. Org. Chem.* **2018**, *83*, 13549.

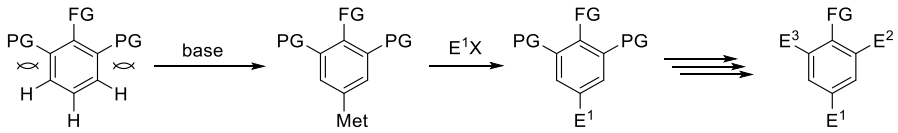
4 Objectives

Based on previous results on transition metal catalyzed cross-coupling reactions, the scope of chromium based coupling reactions should be expanded. Especially as they show a low tendency to undergo side reactions such as homocouplings, which are often present in related reactions of metals like iron or cobalt. Notably alkylations of *N*-arenes and electron-deficient substrates would be a valuable addition to the scope of chromium-catalyzed C-C bond formations, considering the high reactivity of alkylmagnesium reagents towards electrophilic reagents and their tendency to undergo halogen-magnesium exchange reactions (Scheme 25).



Scheme 25: Schematic representation of the chromium-catalyzed alkylation of a halogenated quinoline.

Furthermore, an expansion of regioselective metalations would be of major interest. The general tendency of metalations toward the *ortho*-position of a directing group, due to coordination induced proximity effects and inductive electronic effects, is a common motiv in organometallic chemistry. Remote metalations would be a valuable tool to simplify the generation of various substitution patterns. As inductive electronic effects are proximity based, an alternative steric directing effect seems feasible. The necessary shielding groups should be chosen large enough to avoid the metalation of their immediate *ortho*-positions and their removal needs to be possible to add additional synthetic value. The utility of these remote functionalized substrates needs to be shown regarding both their scalability and their followup functionalizations (Scheme 26).[93]



Scheme 26: General depiction of a sterically induced remote metalation and its application for the generation of 1,2,3,5-tetrafunctionalized arenes.

[93] This project was based on preliminary experiments by Dr. Johannes Nickel, see: J. Nickel, Dissertation, LMU München, **2016**.

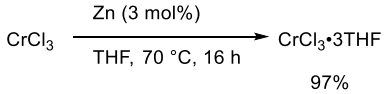
B. RESULTS AND DISCUSSION

1 Chromium-Catalyzed Cross-Coupling Reactions of Alkylmagnesium Reagents with Halo-Quinolines and Activated Aryl Chlorides

1.1 Introduction

Although palladium-[94] and nickel-catalyzed[95] cross-coupling reactions using organomagnesium reagents are well known, alternative cross-couplings using transition-metal catalysts such as iron,[87,96] cobalt[97] or copper[98] salts are cost efficient options and have therefore been studied with great attention. Recently, it was reported that chromium(II) chloride catalyzes the cross-coupling of various aryl- and heteroarylmagnesium reagents with electron-deficient aryl and heteroaryl halides.[89,90,92,99] Chromium(II) chloride also catalyzes the direct oxidative arylation of pyridines, aryl oxazolines and imines with aryl Grignard reagents.[91a] In addition, *N*-heterocyclic chlorides were aminated *via* chromium catalysis.[91b]

Herein, a simple procedure is reported, which allows the cross-coupling of alkylmagnesium reagents with electron-deficient unsaturated substrates using $CrCl_3$•3THF, a THF soluble chromium catalyst.[100] This complex was prepared by Soxhlet extraction of $CrCl_3$ with THF and a catalytic amount of zinc powder (Scheme 27).



Scheme 27: Preparation of the THF-soluble $CrCl_3$•3THF complex.

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[98] a) S. Thapa, A. Kafle, S. K. Gurung, A. Montoya, P. Riedel, R. Giri, *Angew. Chem. Int. Ed.* **2015**, *54*, 8236; b) Y.-A. Chen, S. S. Badsara, W.-T. Tsai, C.-F. Lee, *Synthesis* **2015**, *47*, 181.

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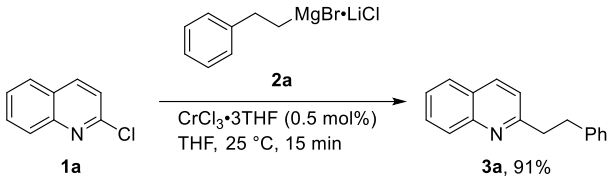
1.2 Alkylation of quinolines and isoquinolines

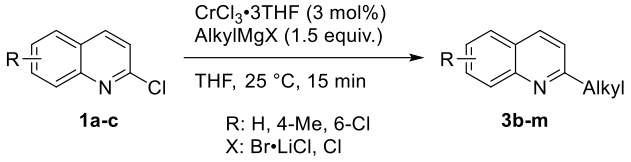
In a preliminary experiment, 2-chloroquinoline (**1a**) was treated with phenylethylmagnesium bromide (**2a**) (1.5 equiv.), prepared from the corresponding alkyl bromide and Mg/LiCl, in the presence of $CrCl_3$•3THF (3 mol%) at 25 °C.[25] Full conversion was observed after 15 min and the desired cross-coupling product **3a** was obtained in 91% isolated yield. In contrast to other transition metals such as iron or cobalt, no homo-coupling byproducts were observed. Furthermore, the catalyst loading could be reduced from 3 mol% to 0.5 mol% with no decrease in yield (Scheme 28).

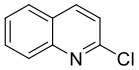
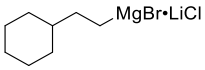
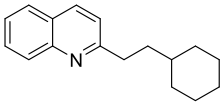
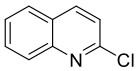
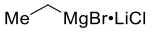
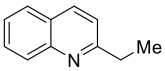
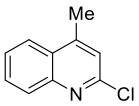
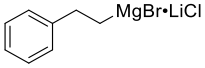
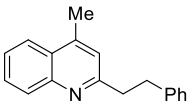
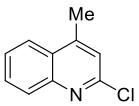
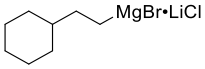
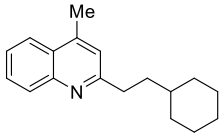
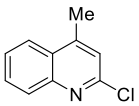
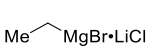
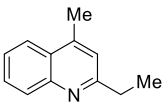
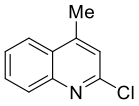
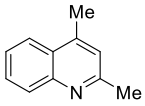
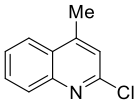
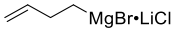
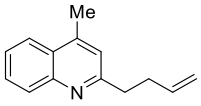
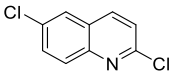
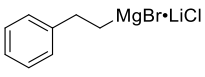
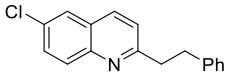
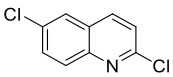
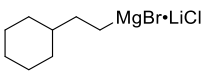
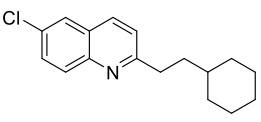


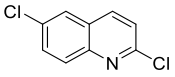
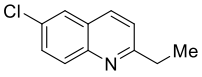
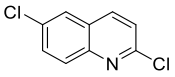
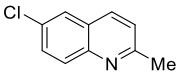
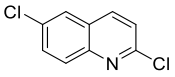
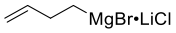
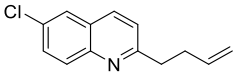
Scheme 28: Chromium(III)-catalyzed cross-coupling of 2-chloroquinoline (**1a**) and Grignard reagent **2a.**

This coupling reaction could be extended to primary alkylmagnesium derivatives such as **2b-c** and the 2-alkylated quinolines **3b-c** were obtained in 65–79% yield under the same reaction conditions (Table 1, entries 1–2). All organomagnesium reagents except **2d**, were complexed by LiCl, however control experiments using Grignard reagent **2a** without LiCl did not lead to differences in yield or reaction times. The related 2-chloro-4-methylquinoline (**1b**) reacted similarly with the Grignard reagents **2a–e** leading, within 15 min at 25 °C, to the 2-alkylated quinolines **3d–h** in 56–82% yield (entries 3–7). Electron-deficient 2,6-dichloroquinoline (**1c**) underwent a regioselective cross-coupling reaction with alkylmagnesium reagents **2a–e**, furnishing the expected 2-alkylated 6-chloroquinolines **3i–m** in 58–84% yield (entries 8–12).

Table 1: Chromium-catalyzed cross-coupling reactions of alkylmagnesium reagents **2a–e** with quinolines **1a–c**.

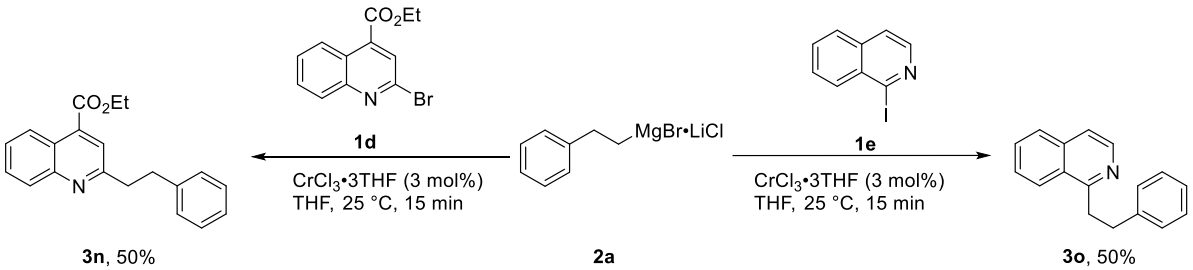


Entry	Electrophile	Magnesium reagent	Product/Yield[a]
			
1	**1a**	**2b**	**3b**, 79%
			
2	**1a**	**2c**	**3c**, 65%
			
3	**1b**	**2a**	**3d**, 82%
			
4	**1b**	**2b**	**3e**, 79%
			
5	**1b**	**2c**	**3f**, 79%
		MeMgCl	
6	**1b**	**2d**	**3g**, 56%
			
7	**1b**	**2e**	**3h**, 69%
			
8	**1c**	**2a**	**3i**, 58%
			
9	**1c**	**2b**	**3j**, 77%

10	 **1c**	 **2c**	 **3k**, 63%
11	 **1c**	**2d**	 **3l**, 83%
12	 **1c**	 **2e**	 **3m**, 84%

[a] Yield of isolated, analytically pure product.

The reaction scope could be extended and functionalized 2-bromoquinoline **1d** as well as 1-iodoisoquinoline (**1e**) reacted well with the alkylmagnesium reagent **2a**, tolerating an ethyl ester and avoiding possible halogen-metal exchanges, affording the expected products **3n-o** in 50% yield each (Scheme 29).

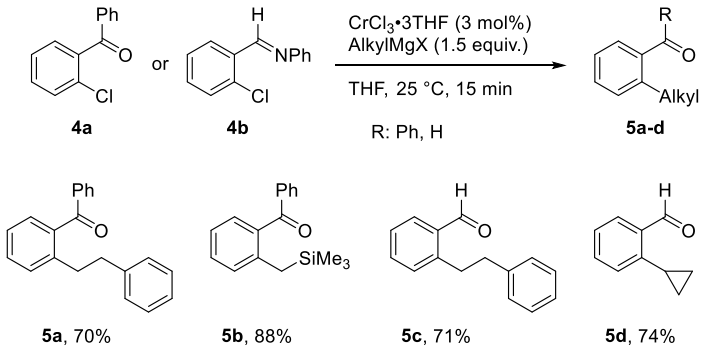


Scheme 29: Cross-coupling reaction of quinoline **1d** and isoquinoline **1e** with Grignard reagent **2a**.

1.3 Alkylation of electron-deficient aryl chlorides

Interestingly, alkylmagnesium halides also reacted smoothly with aryl chlorides bearing an electron-withdrawing function, such as the benzoyl group or an imine, in *ortho*-position. Thus, the Grignard reagent **2a** reacted with 2-chlorobenzophenone (**4a**) in the presence of $CrCl_3$•3THF (3 mol%) within 15 min at 25 °C, furnishing the alkylated benzophenone **5a** in 70% yield (Scheme 30). Using the less reactive Grignard reagent Me_3SiCH_2MgCl•LiCl (**2f**) provided benzophenone **5b** in 88% yield, while completely avoiding the formation of a potential Peterson-olefination byproduct.[101] Also, imine **4b** was readily alkylated with **2a** producing, after acidic hydrolysis, the *ortho*-alkylated benzaldehyde **5c** in 71% yield. Even though secondary alkylmagnesium halides normally undergo cross-coupling reactions in moderate yield,[102] cyclopropylmagnesium bromide complexed with lithium chloride (**2g**) underwent a rapid cross-coupling with **4b** leading to the aldehyde **5d** in 74% yield.

[101] J. S. Clark, F. Romiti, *Angew. Chem. Int. Ed.* **2013**, *52*, 10072.
[102] D. H. Burns, J. D. Miller, H.-K. Chan, M. O. Delaney, *J. Am. Chem. Soc.* **1997**, *119*, 2125.

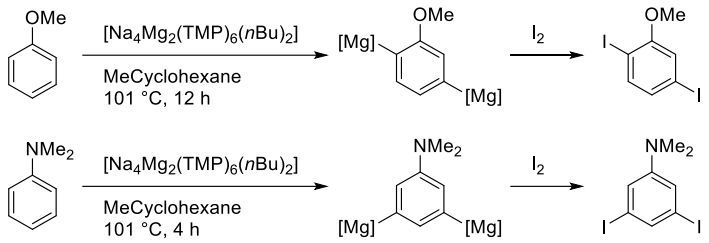


Scheme 30: Chromium-catalyzed cross-coupling reactions of electron-deficient aryl chlorides **4a** and **4b**.

2 Regioselective Remote-Lithiation of 1,3-bis-Silylated (Hetero)Arenes

2.1 Introduction

The metalation of arenes and heteroarenes is an important functionalization method of these unsaturated cyclic systems.[103] Usually a functional group is used to direct metalations into the *ortho* position.[104] However, metalation in *meta* or *para* positions are rare. Recently, the groups of Mulvey, O'Hara and others described selective *meta*-functionalizations using mixed alkali-metal-mediated metalations allowing the double functionalization of various aromatics in *ortho-meta*' or even in *meta-meta*' positions (Scheme 31).[105]



Scheme 31: Mulvey and O'Hara's double metalation and reaction with iodine.

Additionally, the groups of Gaunt and Wu investigated a copper-catalyzed oxidative C-H-coupling leading to a *meta*-arylation of aniline derivatives.[106] Using removable nitrile containing tethers, the groups of Yu[107] and Tan[108] were able to perform *meta* C-H activations using palladium-catalyzed Heck reactions (Scheme 32).

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[103] a) J. Clayden, *Organolithiums: Selectivity for Synthesis* (Eds.: J. E. Baldwin, R. M. Williams), Pergamon, Oxford, **2002**; b) F. Mongin, A. Harrison-Marchand, *Chem. Rev.* **2013**, *113*, 7563; c) D. Tilly, F. Chevallier, F. Mongin, P. C. Gros, *Chem. Rev.* **2014**, *114*, 1207.

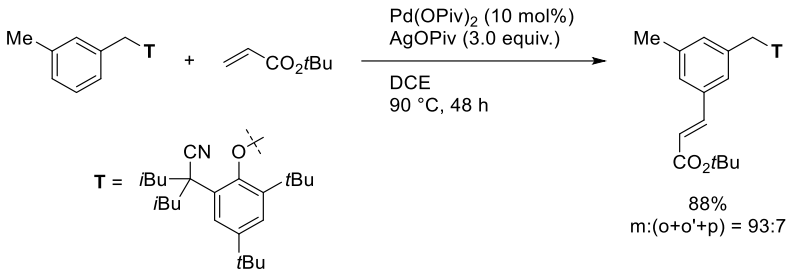
[104] a) P. Beak, V. Snieckus, *Acc. Chem. Res.* **1982**, *15*, 306; b) D. R. Ray, Z. Song, S. G. Smith, P. Beak, *J. Am. Chem. Soc.* **1988**, *110*, 8145; c) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; d) K. M. Bertini, P. Beak, *J. Am. Chem. Soc.* **2001**, *123*, 315; e) S. Usui, Y. Hashimoto, J. V. Morey, A. E. H. Wheatley, M. Uchiyama, *J. Am. Chem. Soc.* **2007**, *129*, 15102; f) D. I. Coppi, A. Salomone, F. M. Perna, V. Capriati, *Angew. Chem. Int. Ed.* **2012**, *51*, 7532.

[105] a) D. R. Armstrong, W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, *Angew. Chem. Int. Ed.* **2006**, *45*, 3775; *Angew. Chem.* **2006**, *118*, 3859; b) R. E. Mulvey, *Acc. Chem. Res.* **2009**, *42*, 743; c) A. J. Martinez-Martinez, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, *Science* **2014**, 346, 834; see also: d) C. J. Rohbogner, G. C. Closoki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1503; *Angew. Chem.* **2008**, *120*, 1526; e) J. P. Flemming, M. B. Berry, J. M. Brown, *Org. Biomol. Chem.* **2008**, *6*, 1215.

[106] a) R. J. Phipps, M. J. Gaunt, *Science* **2009**, *323*, 1593; b) B. Chen, C.-L. Hou, Y.-X. Li, Y.-D. Wu, *J. Am. Chem. Soc.* **2011**, *133*, 7668.

[107] a) D. Leow, G. Li, T.-S. Mei, J.-Q. Yu, *Nature* **2012**, *486*, 518; b) L. Wan, N. Dastbaravardeh, G. Li, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 18056; c) G. Yang, P. Lindovska, D. Zhu, J. Kim, P. Wang, R.-Y. Tang, M. Movassaghi, J.-Q. Yu, *J. Am. Chem. Soc.* **2014**, *136*, 10807; d) R.-Y. Tang, G. Li, J.-Q. Yu, *Nature* **2014**, *507*, 215; e) L. Fang, T. G. Saint-Denis, B. L. H. Taylor, S. Ahlquist, K. Hong, S. Liu, L. Han, K. N. Houk, J.-Q. Yu, *J. Am. Chem. Soc.* **2017**, *139*, 10702; f) G. Yang, D. Zhu, P. Wang, R.-Y. Tang, J.-Q. Yu, *Chem. Eur. J.* **2018**, *24*, 3434.

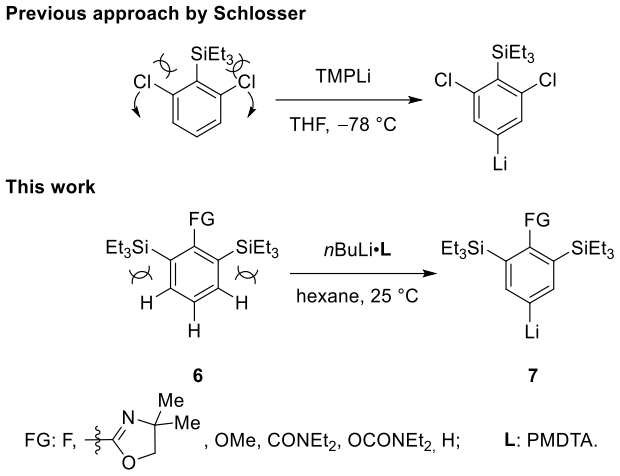
[108] S. Lee, H. Lee, K. L. Tan, *J. Am. Chem. Soc.* **2013**, *135*, 18778.



Scheme 32: *Meta* C-H activation, using the Thorpe-Ingold effect for an end-on nitrile-palladium coordination, reported by Yu and co-workers.

Yu and co-workers performed an oxidative Pd-catalyzed Catellani-reaction, changing the regioselectivity of the C-H activation from *ortho* to the *meta* position.[109] The Ackermann group reported a *meta*-selective ruthenium-catalyzed C-H alkylation using secondary alkyl halides.[110] Maiti and co-workers observed a *para*-selective oxidative acylation of arenes employing enol ethers as acylating reagents.[111] Pioneering work by the Schlosser group showed that a bulky silyl-substituent between two chlorides on a benzene ring results in a buttress effect, which kinetically favors the meta-metalation relative to the halides.[112] Therefore a remote metalation using the direct sterical bulk of two silyl groups was envisioned. Herein, a convenient, more general, 5-lithiation of arenes of type **6**, leading to remote-substituted aryllithiums of type **7** is reported (Scheme 33).

[109] a) X.-C. Wang, W. Gong, L.Z. Fang, R.-Y. Zhu, S. Li, K. M. Engle, J.-Q. Yu, *Nature* **2015**, *519*, 334; b) P. Wang, G.-C. Li, P. Jain, M. E. Farmer, J. He, P.-X. Shen, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 14092; c) P. Wang, M.E. Farmer, X. Huo, P. Jain, P.-X. Shen, M. Ishoey, J. E. Bradner, S. R. Wisniewski, M. D. Eastgate, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 9269; d) Q. Ding, S. Ye, G. Cheng, P. Wang, M. E. Farmer, J.-Q. Yu, *J. Am. Chem. Soc.* **2017**, *139*, 417; e) H. Shi, A. N. Herron, Y. Shao, Q. Shao, J.-Q. Yu, *Nature* **2018**, *58*, 581.
[110] N. Hofmann, L. Ackermann, *J. Am. Chem. Soc.* **2013**, *135*, 5877.
[111] A. Maji, A. Dahiya, G. Lu, T. Bhattacharya, M. Brochetta, G. Zanoni, P. Liu, D. Maiti, *Nat. Commun.* **2018**, *9*, 3582.
[112] a) C. Heiss, E. Marzi, M. Schlosser, *Eur. J. Org. Chem.* **2003**, 4625; b) J. Gorecka, C. Heiss, R. Scopelliti, M. Schlosser, *Org. Lett.* **2004**, *6*, 4591; c) M. Schlosser, C. Heiss, E. Marzi, R. Scopelliti, *Eur. J. Org. Chem.* **2006**, 4398; d) C. Heiss, E. Marzi, F. Mongin, M. Schlosser, *Eur. J. Org. Chem.* **2007**, 669; e) T. Klis, S. Lulinski, J. Serwatowski, *Curr. Org. Chem.* **2008**, *12*, 1479.



Scheme 33: A buttress induced remote lithiation, reported by Schlosser and co-workers, and an extension to sterically hindered bis-silylated arenes of type **6**.

2.2 Optimization of the metalation conditions and investigation of the shielding trialkylsilyl group

First, the conditions for the lithiation of the model substrate 2,6-bis(triethylsilyl)fluorobenzene (**6a**) were investigated. The formation of the lithiated arene **7a** was determined by quenching reaction aliquots with MeSSMe leading to the thioether **8a**. No lithiation was observed with standard lithium bases (Table 2, entries 1-4). The addition of TMEDA, a common reactivity enhancing agent of alkyllithium reagents, had no effect (entries 5-6).[113] However, addition of PMDTA[114] to either *n*BuLi or *s*BuLi afforded the expected metalation product **7a** in 43% and 29% yield respectively, indicating that *n*BuLi is the superior alkyllithium base for these systems (entries 7-8). To improve the incomplete metalation, the amount of base was increased from 1.5 equiv. to 3.0 equiv. raising the yield to 58% (entry 9). Surprisingly, Schlosser's base (*n*BuLi•KO*t*Bu)[115] drastically decreased the product yield to 9% (entry 10). Finally, changing from ethereal solvents to non-coordinating hexane improved the lithiation considerably and the reaction of **6a** with *n*BuLi•PMDTA led, after quench with MeSSMe, to an increased yield of 65% isolated product of **8a** (entry 11). Realizing, that non-coordinating *n*hexane was the best solvent for the lithiation, TMEDA was tested again, still not leading to product formation (entry 12). Longer homologes of PMDTA like 1,1,4,7,10,10-hexamethyltriethylenetetramine

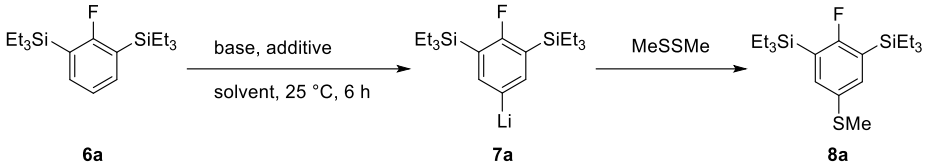
[113] a) C. Heiss, E. Marzi, M. Schlosser, *Eur. J. Org. Chem.* **2003**, 4625; b) J. Gorecka, C. Heiss, R. Scopelliti, M. Schlosser, *Org. Lett.* **2004**, *6*, 4591; c) M. Schlosser, C. Heiss, E. Marzi, R. Scopelliti, *Eur. J. Org. Chem.* **2006**, 4398; d) C. Heiss, E. Marzi, F. Mongin, M. Schlosser, *Eur. J. Org. Chem.* **2007**, 669; e) T. Klis, S. Lulinski, J. Serwatowski, *Curr. Org. Chem.* **2008**, *12*, 1479.

[114] a) G. Katsoulos, S. Takagishi, M. Schlosser, *Synlett* **1991**, 731; b) C. Strohmann, V. H. Gessner, *Angew. Chem. Int. Ed.* **2007**, *46*, 4566; *Angew. Chem.* **2007**, *119*, 4650; c) M. Porcs-Makkay, A. Komáromi, G. Lukács, G. Simig *Tetrahedron* **2008**, *64*, 1029; d) V. H. Gessner, C. Däschlein, C. Strohmann, *Chem. Eur. J.* **2009**, *15*, 3320; e) A.-C. Pöppler, H. Keil, D. Stalke, M. John, *Angew. Chem. Int. Ed.* **2012**, *51*, 7843; *Angew. Chem.* **2012**, *124*, 7963.

[115] a) M. Schlosser, *J. Organomet. Chem.* **1967**, *8*, 9; b) P. Benrath, M. Kaiser, T. Limbach, M. Mondeshki, J. Klett, *Angew. Chem. Int. Ed.* **2016**, *55*, 10886; *Angew. Chem.* **2016**, *128*, 11045; c) e-EROS Encyclopedia of Reagents for Organic Synthesis: *n*-Butyllithium–Potassium *t*-Butoxide, DOI: 10.1002/9780470842898.rb398m.pub2.

(HMTETA) or tris[2-(dimethylamino)ethyl]-amine (Me_6TREN) were tested in an attempt to increase the lithium-chelation (entries 13-14). Surprisingly, these additives did not lead to product formation. Additionally, the bidentate additives *trans-N,N,N',N'*-tetramethylcyclohexane-1,2-diamine (Me_4DACH) and $Me_2N(CH_2)_2OLi$[116] afforded no product either (entries 15-16).

Table 2: Optimization of the lithiation of bis-silylated fluorobenzene **6a**.



6a **7a** **8a**

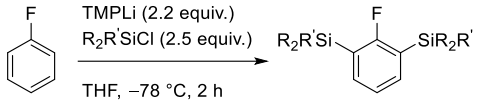
Entry	Li reagent	Additive	Equiv.	Solvent	Yield [%][a]
1	*n*BuLi	-	1.5	Et_2O	0
2	*s*BuLi	-	1.5	Et_2O	0
3	*t*BuLi	-	1.5	Et_2O	0
4	TMPLi	-	1.5	THF	0
5	*n*BuLi	TMEDA	1.5	Et_2O	0
6	*s*BuLi	TMEDA	1.5	Et_2O	0
7	*n*BuLi	PMDTA	1.5	Et_2O	43
8	*s*BuLi	PMDTA	1.5	Et_2O	29
9	*n*BuLi	PMDTA	3.0	Et_2O	58
10	*n*BuLi	PMDTA/KO*t*Bu	3.0	Et_2O	9
11	***n*BuLi**	**PMDTA**	**3.0**	***n*hexane**	**71 (65)[b]**
12	*n*BuLi	TMEDA	3.0	*n*hexane	0
13	*n*BuLi	HMTETA	3.0	*n*hexane	0
14	*n*BuLi	Me_6TREN	3.0	*n*hexane	0
15	*n*BuLi	Me_4DACH	3.0	*n*hexane	0
16	*n*BuLi	$Me_2N(CH_2)_2OLi$	3.0	*n*hexane	0

[a] Yield of the thioether determined by GC analysis of reaction aliquots quenched with MeSSMe, using undecane as internal standard. [b] Yield of analytically pure isolated product.

With these metalation conditions in hand, the nature of the trialkylsilyl-group necessary for a regioselective remote lithiation was investigated. Therefore, several 2,6-bis-silyl fluorobenzenes were prepared (Table 3). Trimethylsilyl chloride and triethylsilyl chloride afforded the desired products in 88% and 95% yield, respectively (entries 1-2). However, the more sterically hindered triisopropyl chloride and *t*butyldimethylsilyl chloride led only to the mono-silylated products (entries 3-4).

[116] P. Gros, Y. Fort, G. Queguiner, P. Caubère, *Tetrahedron Lett*. **1995**, *36*, 4791.

Table 3: Preparation of various sterically hindered bis-silylated fluorobenzenes.



Entry	R	R´	Yield [%]
1	Me	Me	88[a]
2	Et	Et	95[a]
3	*i*Pr	*i*Pr	0[b]
4	Me	*t*Bu	0[b]

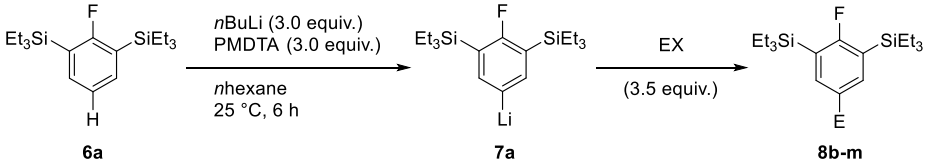
[a] Yield of analytically pure isolated product. [b] Only mono-silylated product was observed.

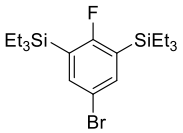
Finally, submitting bis(trimethylsilyl)fluorobenzene to the previously established metalation protocol and treatment with MeSSMe afforded a complex mixture of unidentifiable products. Therefore, the triethylsilyl group was the optimal sterically hindered trialkylsilyl group for this remote lithiation.

2.3 Preparation of 5-functionalized arenes

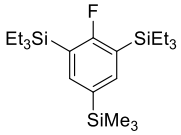
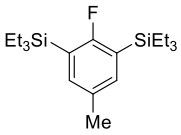
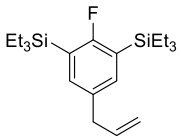
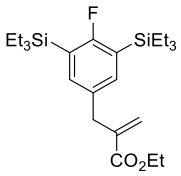
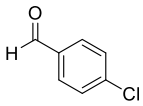
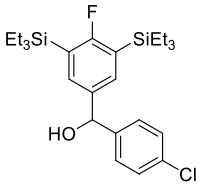
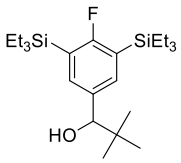
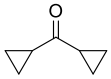
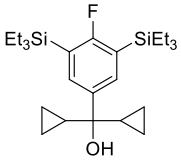
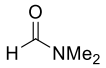
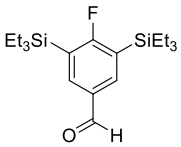
The aryllithium **7a** generated under these optimized conditions was treated with various electrophiles leading regiospecifically to 5-substituted fluorobenzenes **8a–m** in 51–89% yield (Table 4). Thus, a bromination was best performed by transmetallating **7a** with $ZnCl_2$ followed by quenching with bromine in THF to afford bromobenzene **8b** in 89% yield. Treatment of **7a** with Me_3SiCl furnished the silyl derivative **8c** in 83% yield. A methylation was achieved with methyl iodide affording the arene **8d** in 74% yield. Allylations with allylic bromides of the zinc derivative of **7a** in the presence of 10% CuCN•2LiCl[117] furnished the allylated products **8e–f** in 68–82% yield. Trapping with aldehydes or ketones produced the desired alcohols **8g–l** in 61–80% yield. Acylations were successful with DMF, a Weinreb amide,[118] CO_2 or ethyl cyanoformate leading to the carbonyl derivatives **8j–m** in 51–74% yield.

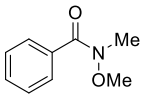
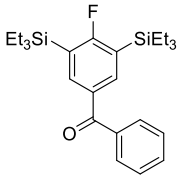
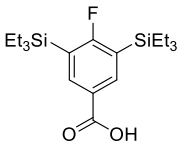
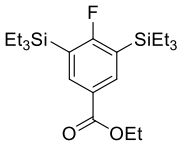
Table 4: 5-lithiation of fluorobenzene **6a**, leading to functionalized arenes of type **8**.



Entry	Electrophile	Product	Yield (%)[a]
1	Br_2	 **8b**	89[b]

[117] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390.
[118] S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, *22*, 3815.

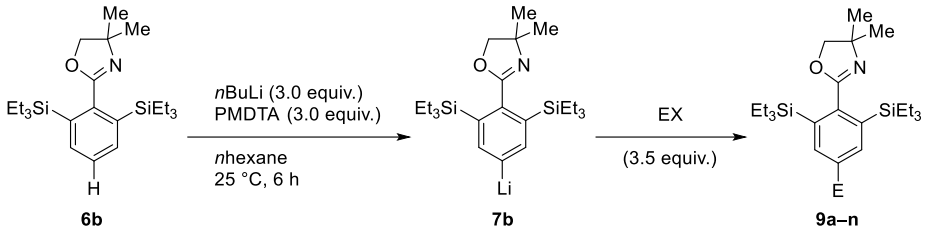
	Me_3SiCl		
2		**8c**	83
	MeI		
3		**8d**	74
			
4		**8e**	82[b,c]
			
5		**8f**	68[b,c]
			
6		**8g**	61
			
7		**8h**	80
			
8		**8l**	76
			
9		**8j**	74

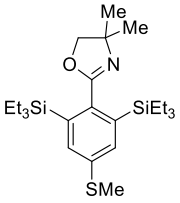
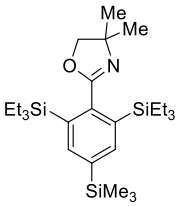
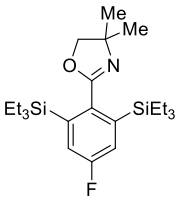
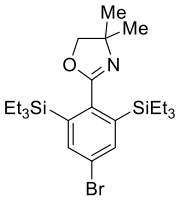
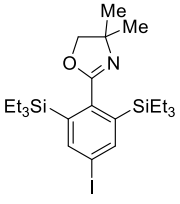
10		 **8k**	71
11	CO_2	 **8l**	63
12		 **8m**	51[d]

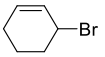
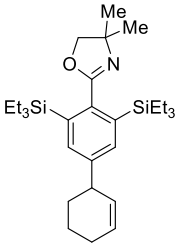
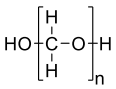
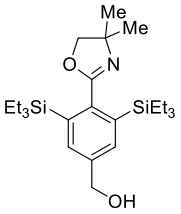
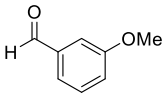
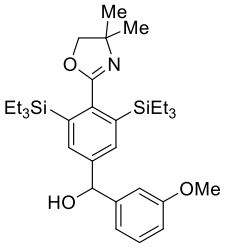
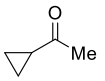
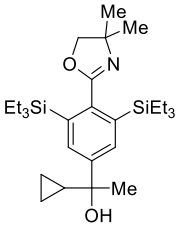
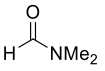
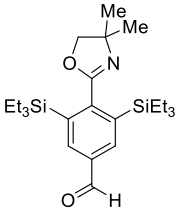
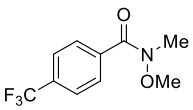
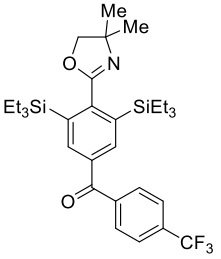
[a] Yield of analytically pure isolated product. [b] $ZnCl_2$ (3.0 equiv.) was added. [c] CuCN•2LiCl (10 mol%) was added. [d] $MgCl_2$ (3.0 equiv.) was added.

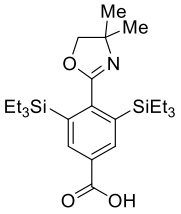
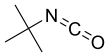
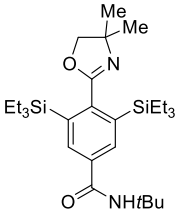
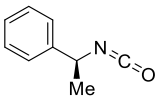
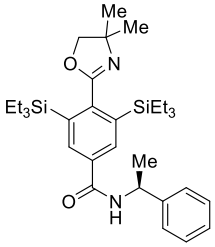
It was assumed, that the fluoro-substituent of the bis-silyl arene **6a** was essential for a fast metalation. However, after preparing analogs of **6a** such as oxazolylbenzene **6b**, it was apparent that other factors than the substituents electronegativity were important for such remote lithiations. Thus, oxazolyl derivative **6b** was smoothly metalated with *n*BuLi•PMDTA (3.0 equiv., 25 °C, 6 h) to provide the lithiated arene **7b** (Table 5). Quenching **7b** with MeSSMe led to the corresponding thioether **9a** in 89% isolated yield (entry 1). Trisilylbenzene **9b** was obtained after treating lithium reagent **7b** with trimethylsilyl chloride in 89% yield (entry 2). Halogenation was achieved by either reacting **7b** with NFSI affording the fluorinated arene **9c** in 62% yield (entry 3) or by transmetallating the lithium species with $ZnCl_2$ and adding the zinc reagent to a THF solution of the elemental halogen to yield bromide **9d** (this reaction was performed on a 30 mmol scale with no decrease in yield) and iodide **9e** in 88-96% yield respectively (entries 4–5). A copper-catalyzed allylation of the zinc intermediate with 3-bromocyclohexene furnished **9f** in 86% yield (entry 6). Primary, secondary and tertiary benzylic alcohols **9g–i** were accessible after reaction with paraformaldehyde, aldehydes and ketones in 79–86% yield (entries 7–9). The formylation using DMF yielded benzaldehyde **9j** in 67% yield (entry 10). Finally, various acylation reactions successfully led to the respective ketone, acid or amides **9k–n** in 68–70% yield (entries 11–14).

Table 5: 5-Lithiation of oxazolyl arene **6b** and reaction with various electrophiles leading to functionalized arenes of type **9**.



Entry	Electrophile	Product	Yield (%)[a]
1	MeSSMe	 **9a**	89
2	Me_3SiCl	 **9b**	89
3	NFSI	 **9c**	62
4	Br_2	 **9d**	96[b,c]
5	I_2	 **9e**	88[b]

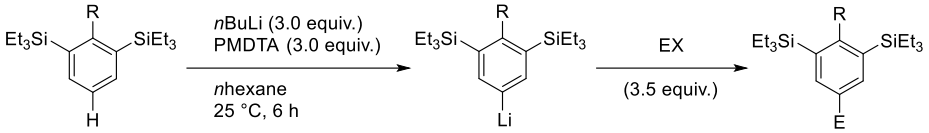
6		 **9f**	86[b,d]
7		 **9g**	79
8		 **9h**	84
9		 **9i**	86
10		 **9j**	67
11		 **9k**	70

12	CO_2	 **9l**	68
13		 **9m**	70
14		 **9n**	68

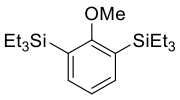
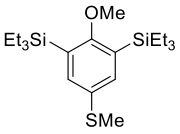
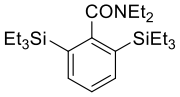
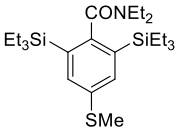
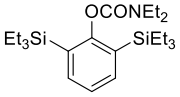
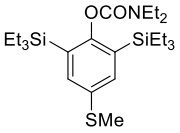
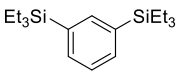
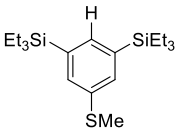
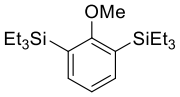
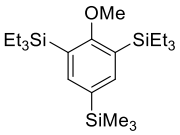
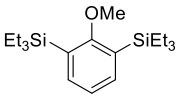
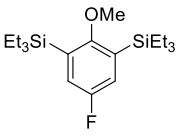
[a] Yield of analytically pure isolated product. [b] $ZnCl_2$ (3.0 equiv.) was added. [c] Performed on a 30 mmol scale. [d] CuCN•2LiCl (10 mol%) was added.

To investigate the influence of coordinating groups, the bis-silyl arenes **6c–e** were prepared. Their lithiated intermediates **7c–e** were treated with MeSSMe affording the corresponding thioethers **10a–12a** in 38–48% yield, indicating that the oxazolyl group has unique properties for this metalation (Table 6, entries 1–3). The unsubstituted bis-silyl benzene **6f** was metalated and the reaction of the lithiated species **7f** with MeSSMe furnished thioether **13a** in 42% yield, comparable to the previously mentioned arenes (entry 4). Metalation of and reaction of the lithiated arenes **7c-f** with various electrophiles led to the functionalized arenes **10**-**13** in 34-58% yield (entries 5-17).

Table 6: 5-Lithiation of various functionalized bis-silyl arenes and their reaction with electrophiles.



R = OMe, $CONEt_2$, $OCONEt_2$, H

Entry	Substrate	Electrophile	Product	Yield (%)[a]
		MeSSMe		
1	**6c**		**10a**	44
		MeSSMe		
2	**6d**		**11a**	38
		MeSSMe		
3	**6e**		**12a**	48[b]
		MeSSMe		
4	**6f**		**13a**	42
		Me_3SiCl		
5	**6c**		**10b**	39
		NFSI		
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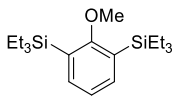
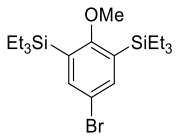
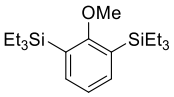
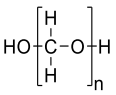
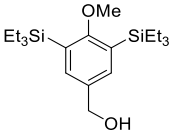
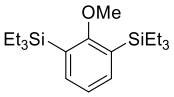
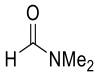
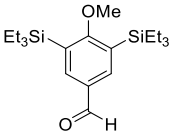
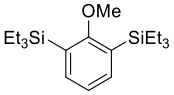
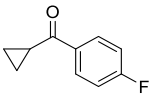
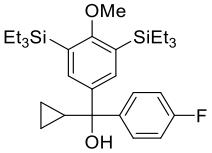
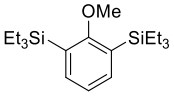
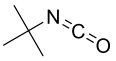
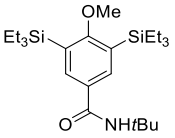
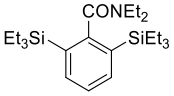
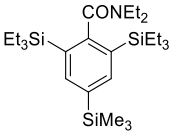
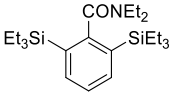
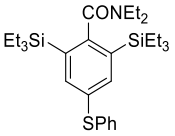
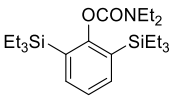
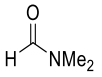
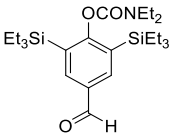
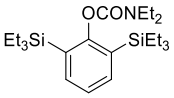
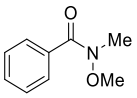
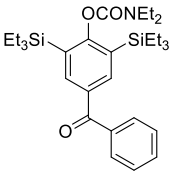
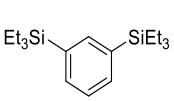
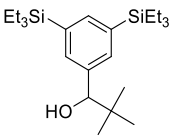
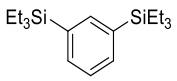
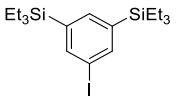
		Br_2		
7	**6c**		**10d**	51[c]

				
8	**6c**		**10e**	39
				
9	**6c**		**10f**	38
				
10	**6c**		**10g**	44
				
11	**6c**		**10h**	38
		Me_3SiCl		
12	**6d**		**11b**	46
		PhSSPh		
13	**6d**		**11c**	44
				
14	**6e**		**12b**	34[b]
				
15	**6e**		**12c**	44[b]
				

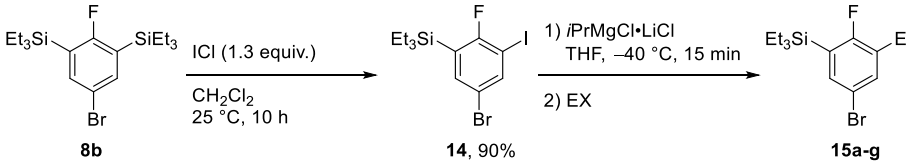
16	**6f** 	I_2	**13b** 	58
17	**6f**		**13c**	43[c]

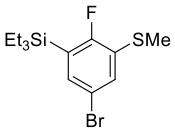
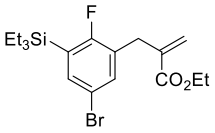
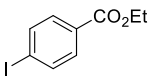
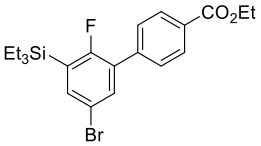
[a] Yield of analytically pure isolated product. [b] The metalation temperature was −10 °C. [c] $ZnCl_2$ (3.0 equiv.) was added.

2.4 Preparation of 1,2,3,5-tetrasubstituted arenes

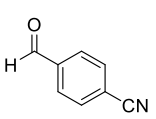
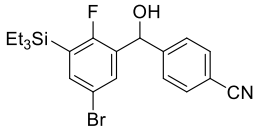
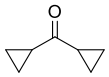
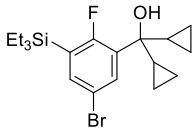
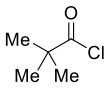
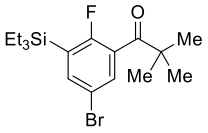
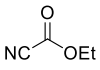
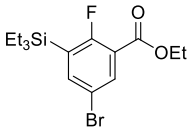
To demonstrate the utility of the prepared remote functionalized bis-silyl arenes, partially and fully desilylated derivatives were prepared. Therefore, halobenzene **8b** underwent a selective *ipso*-iodinative desilylation with ICl, providing aryl iodide **14** in 90% yield.[119] A selective iodine-magnesium exchange on **14** (*i*PrMgCl•LiCl, −40 °C, 15 min) furnished an aryl magnesium intermediate, which was quenched with a range of electrophiles affording the mono-silanes **15a–g** in 71–94% yield (Table 7, entries 1-7).[40a]

Table 7: Trifunctional mono-silanes of type **15** prepared by selective iododesilylation, followed by iodine-magnesium exchange and electrophile quenchings.



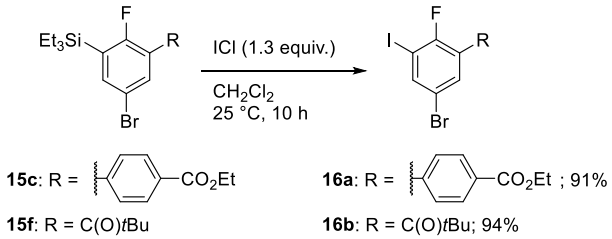
Entry	Electrophile	Product	Yield (%)[a]
1	MeSSMe	**15a** 	73
2		**15b** 	71[b]
3		**15c** 	93[c]

[119] G. Félix, J. Dunoguès, F. Pisciotti, R. Calas, *Angew. Chem. Int. Ed.* **1977**, *16*, 488; *Angew. Chem.* **1977**, *89*, 502.

4		 **15d**	76
5		 **15e**	74
6		 **15f**	94[d]
7		 **15g**	77

[a] Yield of analytically pure isolated product. [b] CuCN•2LiCl (10 mol%) was added. [c] $ZnCl_2$ (1.1 equiv.), $Pd(dba)_2$ (2 mol%) and $P(2\text{-furyl})_3$ (4 mol%) were added. [d] CuCN•2LiCl (1.1 equiv.) was added.

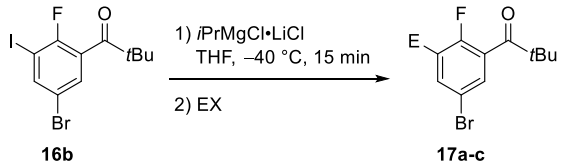
Subsequent treatment of arenes **15c** and **15f** with ICl afforded the silyl-free iodo-arenes **16a-b** in 91–94% yield (Scheme 34).



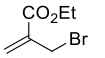
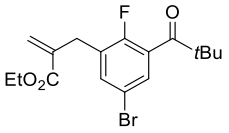
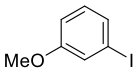
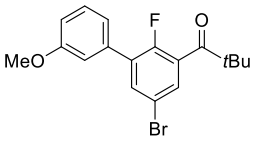
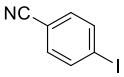
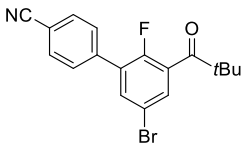
Scheme 34: Iododesilylation of mono-silyl arenes **15** affording iodoarenes of type **16**.

An iodine-magnesium exchange on iodoketone **16b** and quenching with an electrophile led to the tetrasubtituted fluorobenzenes **17a–c** in 73–82% yield (Table 8, entries 1-3).

Table 8: Tetrasubstituted arenes of type **17** prepared by iodine-magnesium exchange, followed by transmetallation and reaction with an electrophile.

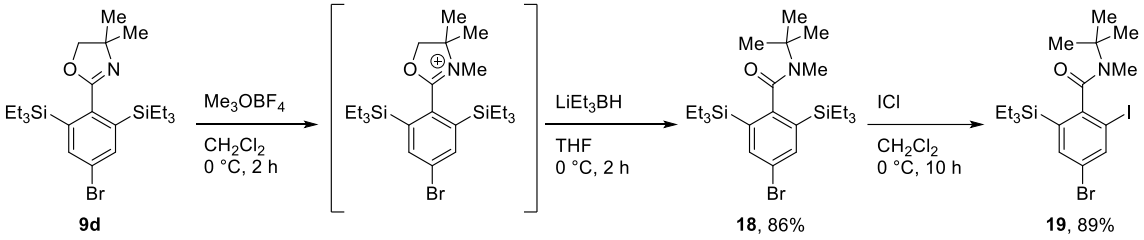


Entry	Electrophile	Product	Yield (%)[a]

			
1		**17a**	73[b]
			
2		**17b**	82[c]
			
3		**17c**	75[c]

[a] Yield of analytically pure isolated product. [b] CuCN•2LiCl (10 mol%) was added. [c] $ZnCl_2$ (1.1 equiv.), $Pd(dba)_2$ (2 mol%) and $P(2\text{-furyl})_3$ (4 mol%) were added.

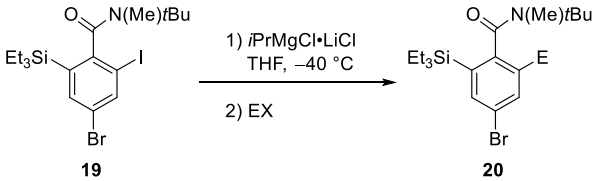
Additionally, the oxazolyl arenes of type **9** were converted into partially- and fully-desilylated amides and lactones *via* short reaction sequences. Thus, in a one-pot procedure, oxazolyl arene **9d** was methylated using Me_3OBF_4 (1.05 equiv., 0 °C, 2 h) followed by a reductive ring opening with $LiEt_3BH$ (1.2 equiv., −78 °C, 4 h), affording the benzamide **18** in 86% yield (Scheme 35).[120] Treatment of **18** with ICl provided iodoarene **19** in 89% yield.



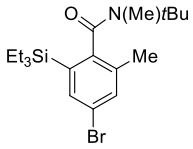
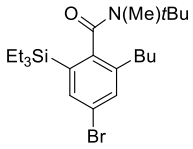
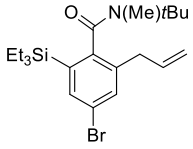
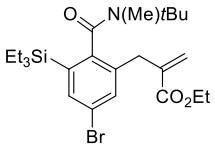
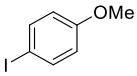
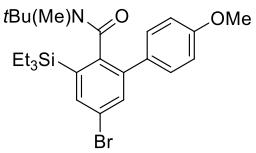
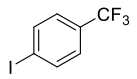
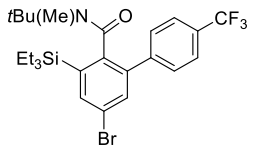
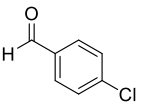
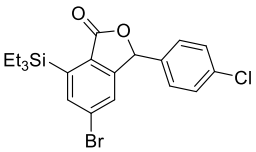
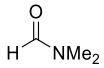
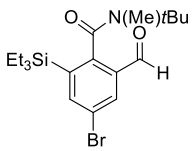
Scheme 35: Alkylation and reductive ring-opening of oxazoline **9d**, followed by iododesilylation leading to iodobenzamide **19**.

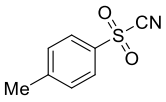
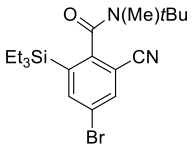
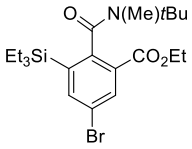
Selective iodine-magnesium exchange of benzamide **19** and treatment of the intermediate magnesium species with various electrophiles afforded the mono-silyl arenes **20a–j** in 65–99% yield (Table 9, entries 1-10).

Table 9: Iodine-magnesium exchange of benzamide **19** followed by reaction with electrophiles furnishing amides and lactones of type **20**.



[120] a) E. M. Fry, *J. Org. Chem.* **1950**, *15*, 802; b) A. I. Meyers, M. Shimano, *Tetrahedron Lett.* **1993**, *34*, 4893.

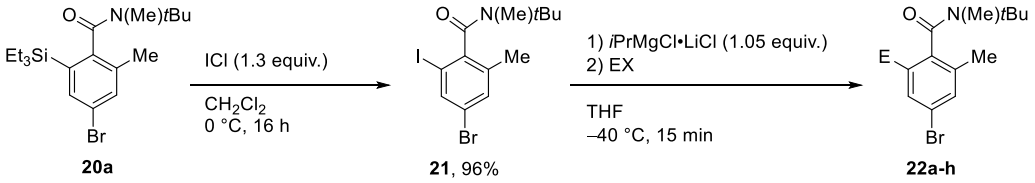
Entry	Electrophile	Product	Yield (%)[a]
1	–	 **20a**	91[b]
2	–	 **20b**	69[c]
3		 **20c**	93[d]
4		 **20d**	95[d]
5		 **20e**	65[e]
6		 **20f**	77[e]
7		 **20g**	68[f]
8		 **20h**	74

9		 **20i**	72
10		 **20j**	99

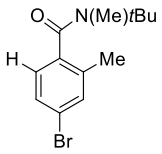
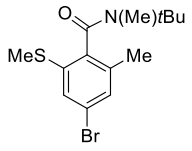
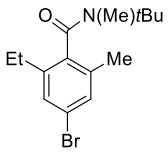
[a] Yield of analytically pure isolated product. [b] MeLi•LiBr (1.05 equiv.) at −78°C was used instead of *i*PrMgCl•LiCl. [c] *n*BuLi (1.05 equiv.) at −78°C was used instead of *i*PrMgCl•LiCl. [d] CuCN•2LiCl (10 mol%) was added. [e] $ZnCl_2$ (1.1 equiv.), $Pd(dba)_2$ (2 mol%) and P(2-furyl)$_3$ (4 mol%) were added. [f] The crude benzylic alcohol was heated in refluxing 1,4-dioxane.

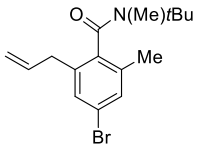
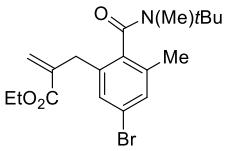
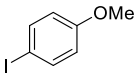
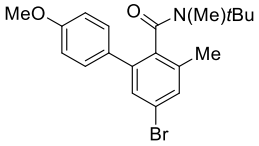
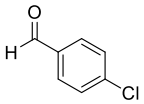
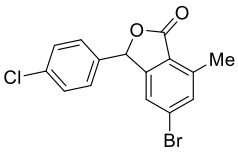
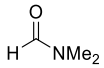
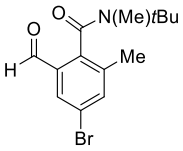
The mono-silyl benzamide **20a** was further iodo-desilylated with ICl, leading to iodoarene **21** in 96% yield. Subsequent iodine-magnesium exchange followed by reaction with different electrophiles furnished the desired silyl-free tetrasubstituted arenes **22a–h** in 61–86% yield (Table 10, entries 1-8).

Table 10: Iododesilylation of amide **20a** followed by a iodine-magnesium exchange and reaction with elecrophiles affording tetrasubstituted arenes of type **22**.



20a **21**, 96% **22a-h**

Entry	Electrophile	Product	Yield (%)[a]
1	NH_4Cl	 **22a**	86
2	MeSSMe	 **22b**	83
3	EtI	 **22c**	61[b]

4		 **22d**	66[c]
5		 **22e**	68[c]
6		 **22f**	71[d]
7		 **22g**	61[e]
8		 **22h**	86

[a] Yield of analytically pure isolated product. [b] *t*BuLi (2.05 equiv.) at −78°C was used instead of *i*PrMgCl•LiCl. [c] CuCN•2LiCl (10 mol%) was added. [d] $ZnCl_2$ (1.1 equiv.), $Pd(dba)_2$ (2 mol%) and $P(2\text{-furyl})_3$ (4 mol%) were added. [e] The crude benzylic alcohol was refluxed in 1,4-dioxane.

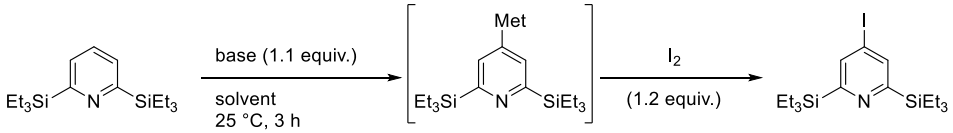
2.5 Preparation of 4-functionalized pyridines

Based on the promising results for the remote lithiation of functionalized benzenes, an extension towards the 4-lithiation of pyridines was explored. Therefore, the readily available 2,6-bis(triethylsilyl)pyridine (**23**) was prepared and its metalation was investigated. As a result of the inherent lower pK_a values of pyridines, a lower amount of base could be used (1.1 equiv. instead of 3.0 equiv.).[121] The formation of the metalated pyridine was checked by quenching reaction aliquots with I_2 in THF (Table 11). Treatment of **23** with the alkyllithium reagents *n*BuLi and *t*BuLi in *n*hexane as well as the isopropylmagnesiumchloride lithium chloride complex led to no lithiation (entries 1-3).[40a] Furthermore, no metalation was observed employing the lithium amide bases LiHMDS and TMPLi or

[121] a) K. Shen, Y. Fu, J.-N. Li, L. Liu, Q.X. Guo, *Tetrahedron* **2007**, *63*, 1568; b) M. Hedidi, G. Bentabed-Ababsa, A. Derdour, Y. S. Halauko, O. A. Ivashkevich, V. E. Matulis, F. Chevallier, T. Roisnel, V. Dorcet, F. Mongin, *Tetrahedron* **2016**, *72*, 2196.

the Knochel-Hauser base TMPMgCl•LiCl (entries 4-6).[62a] Addition of the deaggregating TMEDA to *n*BuLi was inefficient as well (entry 7). However, PMDTA turned out to be the superior additive for the 4-lithiation forming the intermediary lithiated pyridine **24**, which reacted with I_2 affording the iodinated pyridine **25a** in 95% GC yield (entry 8).

Table 11: Optimization of the 4-metalation of 2,6-bis(triethylsilyl)pyridine (**23**).



Met = Li, MgCl•LiCl

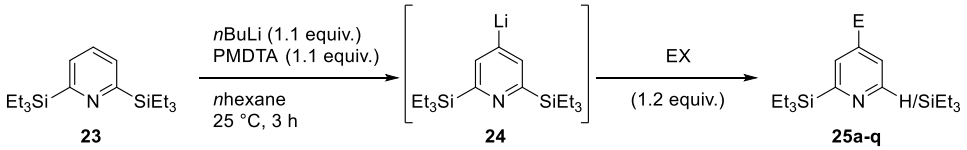
Entry	Base	Solvent	Yield (%)[a]
1	*n*BuLi	*n*hexane	0
2	*t*BuLi	*n*hexane	0
3	*i*PrMgCl•LiCl	THF	0
4	LiHMDS	THF	0
5	TMPLi	THF	0
6	TMPMgCl•LiCl	THF	0
7	*n*BuLi•TMEDA	*n*hexane	0
8	*n*BuLi•PMDTA	*n*hexane	95

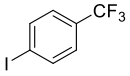
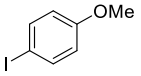
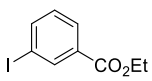
[a] Yield of the iodide determined by GC analysis of reaction aliquots quenched with I_2, using undecane as internal standard.

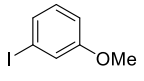
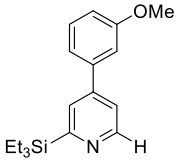
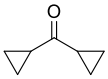
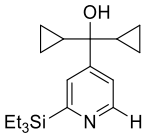
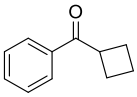
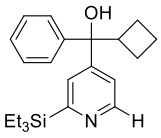
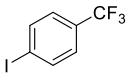
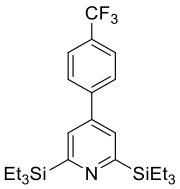
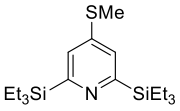
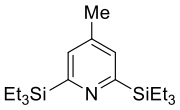
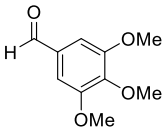
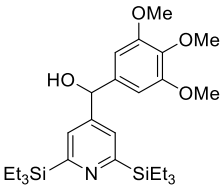
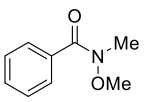
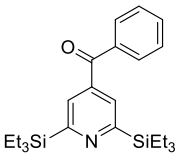
Using these optimized conditions, 4-functionalized pyridines of type **25a–q** were prepared in 60–96% yield (Table 12). Thus, **24** was treated with I_2 affording the mono-silyl iodide **25a** in 89% yield (entry 1). A copper-catalyzed allylation with allylic bromides led, after transmetalation of **24** with $ZnCl_2$, to the allylated pyridine **25b** in 62% yield (entry 2). Furthermore, the zinc derivative of **24** was successfully used for Pd-catalyzed Negishi cross-coupling reactions furnishing the heterobiphenyls **25c–f** in 60–96% yield (entries 3–6). Addition of **24** to ketones provided the tertiary alcohols **25g–h** in 63–71% yield (entries 7–8). Surprisingly, all functionalized pyridines **25a–h** were selectively mono-desilylated during purification *via* silica flash column chromatography using silica gel as stationary phase. To keep both triethylsilyl-groups intact, the reaction leading to **25c** was repeated and NEt_3 (2 vol%) was added to the eluent for flash column chromatography. The corresponding bis-silylated biaryl **25i** was isolated in 75% yield (entry 9). This, in comparison to **25c**, lower yield can be explained by a still occurring partial protodesilylation of pyridine **25i**. Using this modified purification protocol, the bis-silylated thioether **25j**, picoline **25k** and benzylic alcohol **25l** were prepared by reaction with corresponding electrophiles and by purification using NEt_3 (2 vol%) as an additive to the eluent in 62–90% yield (entries 10–11). Acylations of **24** with Weinreb-amides, cyanoformates, chloro formamides and isocyanates afforded the carbonyl derivatives **25m–q** in 66–88% yield (entries 12–17).

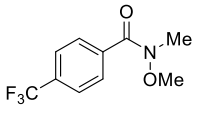
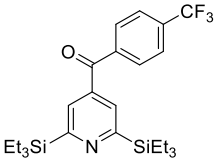
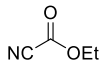
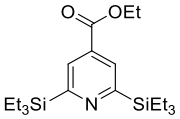
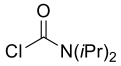
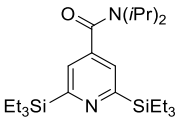
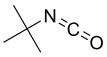
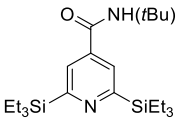
Surprisingly, no NEt_3 additive was necessary to maintain both silyl function during purification. The most likely reason for this observation is a protonated cationic intermediate formed on the acidic stationary phase. Electron rich substituents stabilize the cationic intermediate, promoting its formation and allowing the following protodesilylation. However, electron withdrawing groups destabilize potential cations and the corresponding electron-poor pyridines are therefore more inert to silica induced protodesilylation.

Table 12: 4-Lithiation of pyridine **23**, leading to functionalized pyridines of type **25**.



Entry	Electrophile	Product	Yield (%)[a]
1	I_2	**25a**	89
2		**25b**	62[b]
3		**25c**	96[c]
4		**25d**	83[c]
5		**25e**	73[c]

			
6		**25f**	60[c]
			
7		**25g**	71
			
8		**25h**	63
			
9		**25i**	75[c,d]
	MeSSMe		
10		**25j**	66[d]
	MeI		
11		**25k**	90[d]
			
12		**25l**	62[d]
			
13		**25m**	78

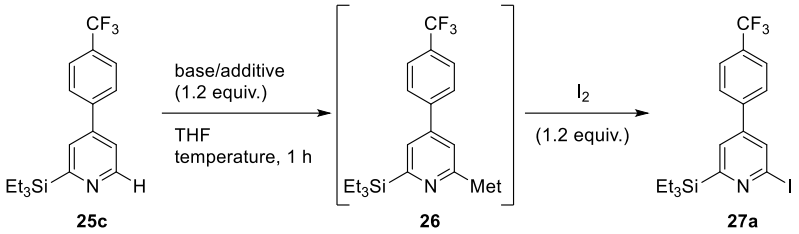
			
14		**25n**	76
			
15		**25o**	88[e]
			
16		**25p**	67
			
17		**25q**	66

[a] Yield of analytically pure isolated product. [b] $ZnCl_2$ (1.1 equiv.) and CuCN•2LiCl (10 mol%) were added. [c] $ZnCl_2$ (1.1 equiv.) and $Pd(PPh_3)_4$ (2 mol%) were added. [d] NEt_3 was used during column chromatographical purification. [e] $MgCl_2$ (1.0 equiv.) was added.

2.6 Preparation of polyfunctionalized pyridines

To emphasize the synthetic value of this remote functionalization, follow-up metalations of the pyridines of type **25** were investigated. The formation of metalated intermediate **26** was determined by quenching reaction aliquots with I_2 leading to iodo pyridine **27a** (Table 13). Thus, mono-silyl pyridine **25c** was treated with the lithium amide bases LiHMDS and TMPLi. Whereas LiHMDS did not form the desired iodide, TMPLi formed the iodinated pyridine **27a** in 17% yield, while leaving large amounts of **25c** unreacted (entries 1–2). Applying the magnesium amides TMPMgCl•LiCl and TMP_2Mg•2LiCl without additives led to no conversion of the starting material, independent of the temperature used (entries 3–6).[62,66] Adding BF_3•OEt_2 for an additional Lewis Acid activation was ineffective for TMPMgCl•LiCl at cryogenic temperatures (entries 7–8).[65] However, at 0 °C full conversion of **25c** was observed and iodide **27a** was obtained in 86% yield (74% isolated yield) (entry 9). TMP_2Mg•2LiCl reacted after addition of BF_3•OEt_2 even at −40 °C affording the iodinated pyridine **27a** in 61% yield (entry 10). Finally, the TMP_2Mg•2LiCl/BF_3•OEt_2 mixture at 0 °C raised the yield of **27a** to 78% (entry 11).

Table 13: Base screening for the *ortho*-metalation of pyridine **25c**.



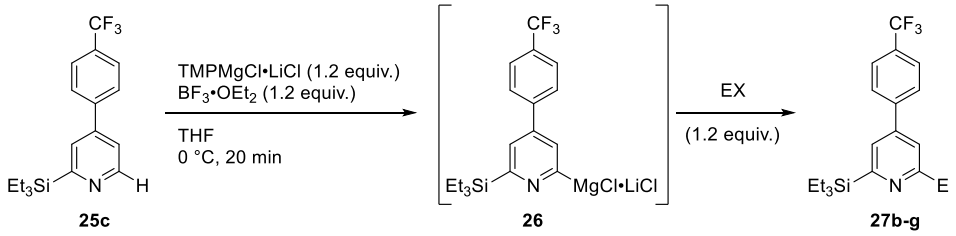
Met: Li, MgX

Entry	Base	Additive	Temperature	Yield (%)[a]
1	LiHMDS		−40 °C	0
2	TMPLi		−40 °C	17
3	TMPMgCl•LiCl		−78 °C	0
4	TMPMgCl•LiCl		−40 °C	0
5	TMPMgCl•LiCl		0 °C	0
6	TMP_2Mg•2LiCl		−40 °C	0
7	TMPMgCl•LiCl	BF_3•OEt_2	−78 °C	0
8	TMPMgCl•LiCl	BF_3•OEt_2	−40 °C	0
9	TMPMgCl•LiCl	BF_3•OEt_2	0 °C	86[b] (74)[c]
10	TMP_2Mg•2LiCl	BF_3•OEt_2	−40 °C	61
11	TMP_2Mg•2LiCl	BF_3•OEt_2	0 °C	78

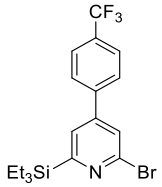
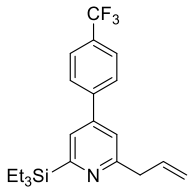
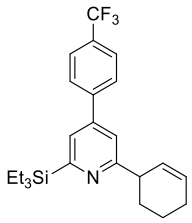
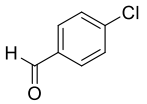
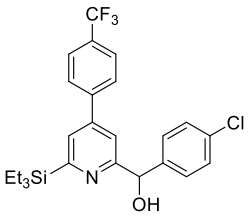
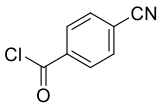
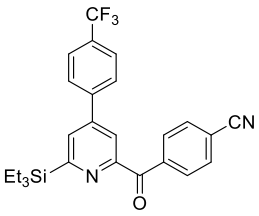
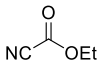
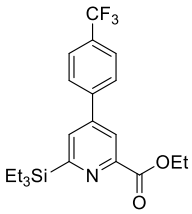
[a] Yield of the iodide **27a** determined by GC analysis of reaction aliquots quenched with I_2, using undecane as internal standard. [b] The metalation was finished within 20 min. [c] Yield of analytically pure isolated product.

TMPMgCl•LiCl and BF_3•OEt_2 at 0 °C were deemed the most efficient mixture for this *ortho*-metalation and were used for the functionalization of **25c** (Table 14). Therefore, the pyridylmagnesium species **26** was treated with bromine leading to 2-bromopyridine **27b** in 83% yield (entry 1). Copper-catalyzed allylations with allylic bromides furnished the allylated products **27c–d** in 52–73% yield (entries 2–3). Reaction of **26** with 4-chlorobenzaldehyde afforded benzylic alcohol **27e** in 61% yield (entry 4). A copper-mediated acylation provided phenone **27f** in 78% yield (entry 5). Finally, the reaction of **26** with ethyl cyanoformate led to ethyl picolinate **27g** in 65% yield (entry 6).

Table 14: BF_3•OEt_2 mediated *ortho*-magnesiation of pyridine **25c** leading to functionalized pyridines of type **27**.

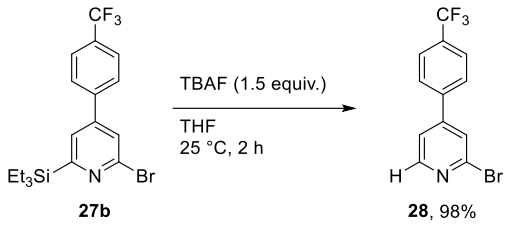


Entry	Electrophile	Product	Yield (%)[a]

1	Br_2	 **27b**	83
2		 **27c**	73[b]
3		 **27d**	52[b]
4		 **27e**	61
5		 **27f**	78[c]
6		 **27g**	65

[a] Yield of analytically pure isolated product. [b] CuCN•2LiCl (10 mol%) was added. [c] CuCN•2LiCl (1.2 equiv.) was added.

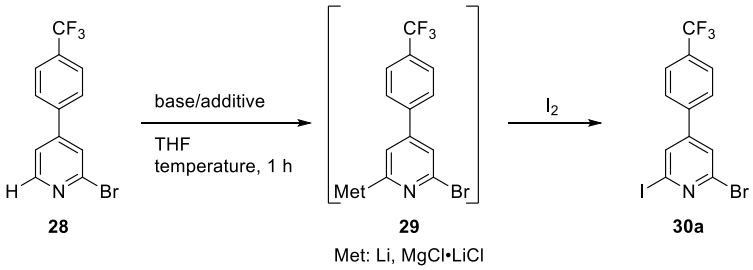
The second triethylsilyl group was readily removed by treating **27b** with TBAF affording the disubstituted pyridine **28** in 98% yield (Scheme 36).



Scheme 36: Protodesilylation of pyridine **27b** using TBAF.

The disubstituted pyridine **28** was treated with different metal-amides to obtain metalated pyridines of type **29** (Table 15). Reaction of **28** with lithium-amide TMPLi led to the decomposition of the halopyridine (entry 1). TMPMgCl•LiCl afforded the desired dihalo-pyridine **30a** in 44% yield (entry 2). Surprisingly, contrary to the metalation of mono-silyl pyridine **25c**, addition of BF_3•OEt_2 led to a decrease in product formation (entry 3). Due to the fact that longer reaction times led to decomposition of **29**, the base amount was steadily increased. This raised the formation of **30a** to 66% (for 2.0 equiv.) and 93% (96% isolated yield, for 4.0 equiv.) (entries 4–5). Also, the zinc-amide TMPZnCl•LiCl was tested, however no product was formed (entry 6).

Table 15: Screening of the metalation conditions of pyridine **28**.



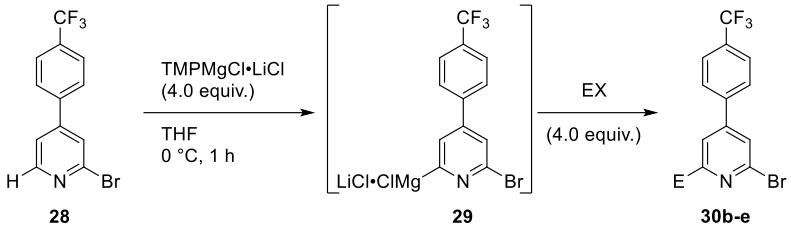
Entry	Base	Equivalents	Additive	Temperature	Yield(%)[a]
1	TMPLi	1.2	–	−40 °C	0
2	TMPMgCl•LiCl	1.2	–	0 °C	44
3	TMPMgCl•LiCl	1.2	BF_3•OEt_2	0 °C	30
4	TMPMgCl•LiCl	2.0	–	0 °C	66
5	TMPMgCl•LiCl	4.0	–	0 °C	93(97)[b]
6	TMPZnCl•LiCl	1.2	–	0 °C	0

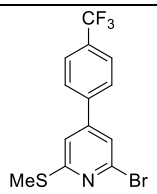
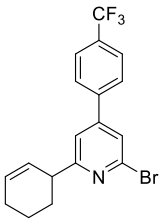
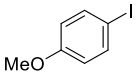
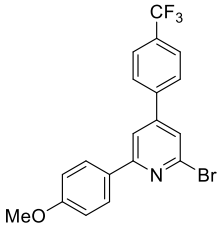
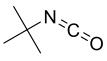
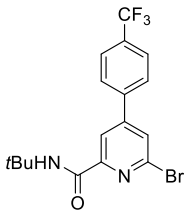
[a] Yield of the iodide **30a** determined by GC analysis of reaction aliquots quenched with I_2, using undecane as internal standard. [b] Yield of analytically pure isolated product.

Using these optimized conditions, several trisubstituted pyridines of type **30** were prepared (Table 16). Magnesium pyridine **29** was treated with MeSSMe leading to the methyl thioether **30b** in 86% yield (entry 1). A copper-catalyzed allyation using 3-bromocyclohexene provided **30c** in 97% yield (entry 2). A Pd-catalyzed cross-coupling reaction of the zinc derivative of **29** and iodoanisole afforded **30d** in

83% yield (entry 3). Finally, an acylation using *t*butyl isocyanate furnished amide **30d** in 79% yield (entry 4).

Table 16: Preparation of trisubstituted pyridines of type **30** from bromopyridine **28**.



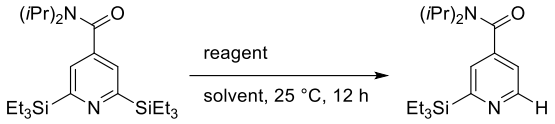
Entry	Electrophile	Product	Yield (%)[a]
1	MeSSMe	 **30b**	86
2		 **30c**	97[b]
3		 **30d**	83[c]
4		 **30e**	79

[a] Yield of analytically pure isolated product. [b] CuCN•2LiCl (10 mol%) was added. [c] $ZnCl_2$ (1.1 equiv.), $Pd(dba)_2$ (2 mol%) and P(2-furyl)$_3$ (4 mol%) were added.

2.7 Protodesilylation and functionalization of electron-deficient pyridines

To gain access to substitution patterns different from the 2,4,6-pyridines of type **30**, the directing group bearing **25p** was to be functionalized. As mentioned in chapter 2.5 electron withdrawing substituents in 4-position inhibited the protodesilylation during flash column chromatography. Therefore, the deprotection of the electron-deficient pyridine **25p** to mono-silyl pyridine **31** was explored (Table 17). Stirring **25p** in a suspension of silica gel in hexane did not lead to deprotected pyridine (entry 1). Furthermore, the strong desilylation reagent TBAF left both triethylsilyl groups intact (entry 2). Also, acid mediated protodesilylation was ineffective for a solution of HCl (2 M in MeOH) (entry 3). However, acetic acid selectively cleaved one silyl-group affording pyridine **31** in 83% yield (entry 4).

Table 17: Investigation regarding the protodesilylation of pyridine **25p** toward **31**.



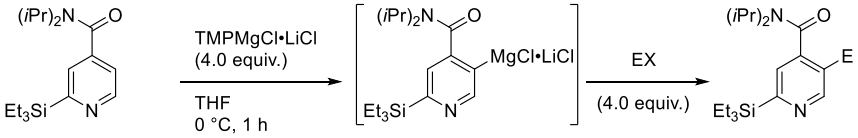
25p **31**

Entry	Reagent	Solvent	Yield(%)[a]
1	silica gel	hexane	-
2	TBAF	THF	-
3	HCl	MeOH	-
4	acetic acid	–	83

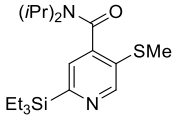
[a] Yield of analytically pure isolated product.

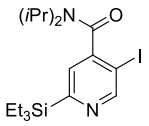
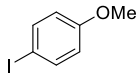
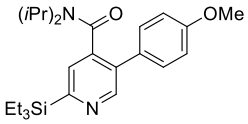
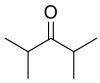
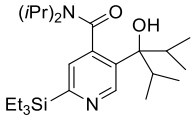
Similarly to pyridine **28** an excess of the magnesium amide TMPMgCl•LiCl (4.0 equiv.) was necessary to ensure full conversion to the metalated pyridine **32**. Thus, metalation of **31** led to the 5-magnesiated pyridine **32**, which reacted with MeSSMe to furnish thioether **33a** in 71% yield (Table 18, entry 1). Reaction of **32** with iodine afforded the 3-iodopyridine **33b** in 47% yield (entry 2). A palladium-catalyzed cross-coupling of the zinc species, obtained after transmetalation using a $ZnCl_2$ solution, with 4-iodoanisole successfully provided biaryl **33c** in 43% yield (entry 3). Finally, the reaction of **32** with a sterically hindered ketone led to benzylic alcohol **33d** in 66% yield (entry 4).

Table 18: *Ortho*-metalation of amide **31** leading to trisubstituted pyridines of type **33**.



31 **32** **33**

Entry	Electrophile	Product	Yield (%)[a]
	MeSSMe		

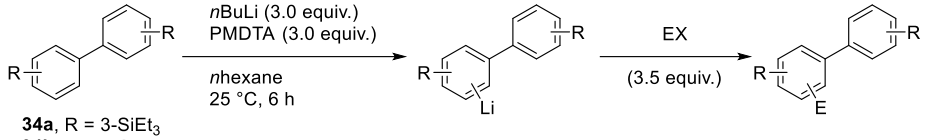
1	I_2	**33a** 	71
2		**33b** 	47
3		**33c** 	43[b]
4		**33d**	66

[a] Yield of analytically pure isolated product. [b] $ZnCl_2$ (1.1 equiv.), $Pd(dba)_2$ (2 mol%) and P(2-furyl)$_3$ (4 mol%) were added.

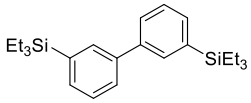
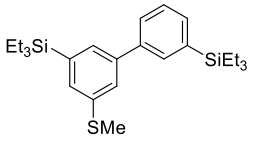
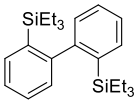
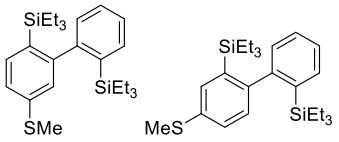
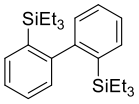
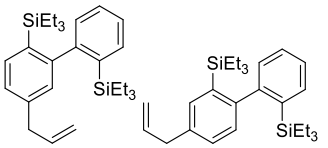
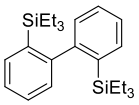
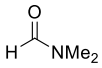
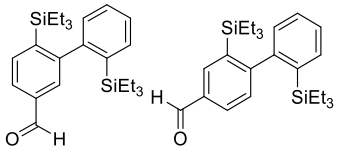
2.8 Remote lithiation of bis(triethylsilyl)-biphenyls

Finally, this remote lithiation was extended to biphenyl derivatives. Whereas the lithiation of 3,3'-bis(triethylsilyl)-1,1'-biphenyl (**34a**) and its reaction with MeSSMe afforded thioether **35** as a single regioisomer in 38% yield (Table 19, entry 1), 2,2'-bis(triethylsilyl)-1,1'-biphenyl (**34b**) led to a 6:1 mixture of 4-thioether (**36a**) and 5-thioether (**37a'**) in 62% yield (entry 2). The same product ratio was observed for the copper-catalyzed allylation and the formylation, which afforded the mixtures **36b**/**36b'** and **36c**/**36c'** in 69% and 66% respectively (entries 3–4).

Table 19: Remote lithiation of sterically hindered biphenyls of type **34**.



34a, R = 3-$SiEt_3$
34b, R = 2-$SiEt_3$

Entry	Biphenyl	Electrophile	Products	Yield(%)[a]
		MeSSMe		
1	**34a**		**35**	38
		MeSSMe		
2	**34b**		**36a** **36a'**	53/9
				
3	**34b**		**36b** **36b'**	59/10[b]
				
4	**34b**		**36c** **36c'**	57/9

[a] Yield of analytically pure isolated product. The regioisomer ratio was determined by NMR analysis. [b] $ZnCl_2$ (3.0 equiv.) and CuCN•2LiCl (10 mol%) were added.

3 Summary

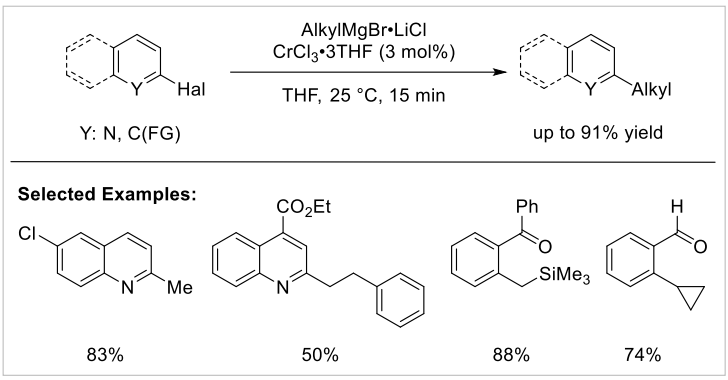
In summary, this thesis was focused on two major topics.

First, the alkylation of halo quinolines and activated aryl chlorides by alkylgrignard reagents *via* chromium catalysis was investigated. The THF soluble $CrCl_3$•3THF complex was able to alkylate *ortho*-halogenated quinolines and electron-deficient 2-chloro arenes at room temperature within minutes. This reaction tolerated sensitive functional groups like ethyl esters and ketones at 25 °C. The alkylation occurred regioselectively with halides adjacent to a benzoazine nitrogen atom, while other halides were present within the molecule. Furthermore, no considerable amount of halogen-magnesium exchange was observed if halides like bromine or iodine were used. Finally, this reaction proceeded without the formation of homocoupling side products, which are common for the cross-coupling reactions of the related first row transition metals like iron and cobalt.

Second, a novel protocol for the preparation of remote functionalized arenes and heteroarenes was developed. The convenient base *n*BuLi•PMDTA allowed for the regiospecific remote lithiation of bis-triethylsilyl substituted unsaturated ring systems. These lithiated intermediates were then quenched with various electrophiles, affording 5-substituted benzenes and 4-substituted pyridines. Subsequent short reaction sequences allowed for the preparation of 1,2,3,5-tetrasubstituted benzenes and trisubstituted pyridines. Finally, this protocol was applied to the remote metalation of bis-triethylsilyl substituted biphenylic systems.

3.1 Chromium-Catalyzed Cross-Coupling Reactions of Alkylmagnesium Reagents with Halo-Quinolines and Activated Aryl Chlorides

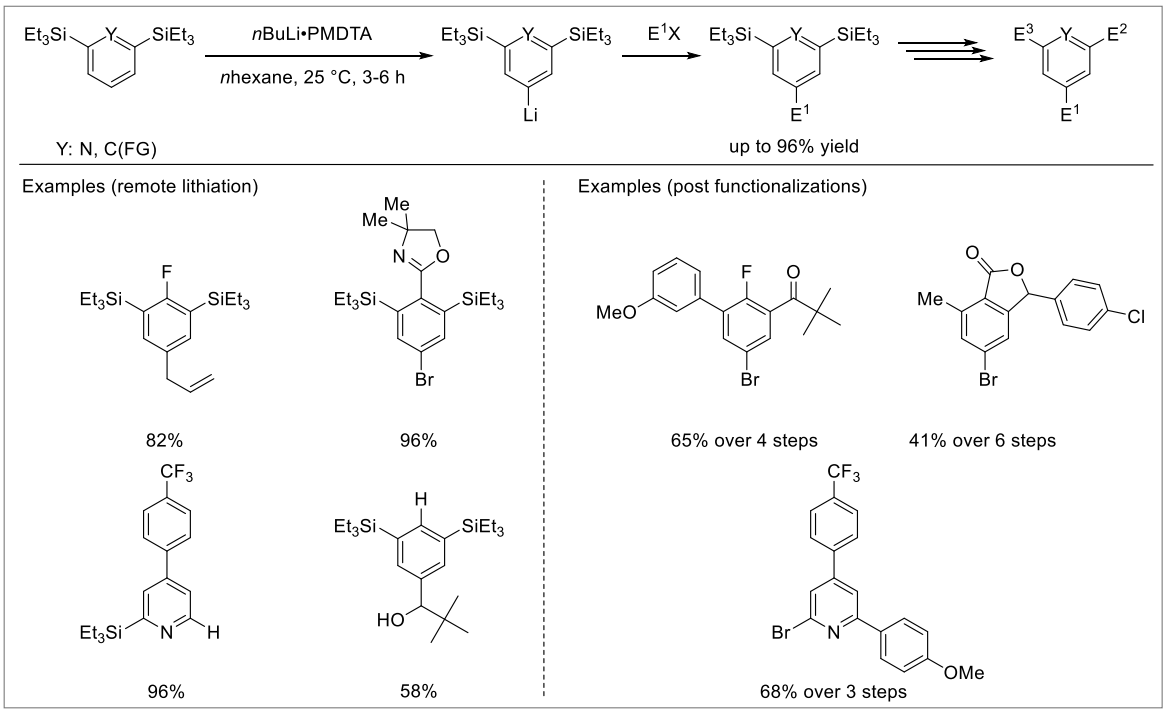
A range of alkylated quinolines, isoquinolines, benzophenones and benzaldehydes were prepared *via* chromium-catalyzed aryl-alkyl cross-coupling reaction. Various primary and secondary alkylmagnesium reagents reacted readily with halogenated electron-deficient aromatic ring systems using $CrCl_3$•3THF within 15 min at 25 °C. This reaction protocol was able to tolerated sensitive carbonyl bearing groups like esters and ketones and no halogen-magnesium exchange was observed for the higher halides bromine or iodine. The catalyst loading for the cross-coupling reaction was reduced down to 0.5 mol%, while no decrease in product yield was observed, highlighting the catalytic activity of chromium. Furthermore, no homocoupling side products, which are common for other first row transition metal catalyzed coupling reactions, were observed (Scheme 37).



Scheme 37: Chromium-catalyzed alkylation reactions, leading to 2-alkylated (hetero)arenes.

3.2 Regioselective Remote-Lithiation of 1,3-bis-Silylated (Hetero)Arenes

The regioselective remote lithiation of bis-triethylsilylated benzenes, pyridines and biphenyls using the activated base mixture *n*BuLi•PMDTA was described. Electrophilic trapping reactions led to a broad range of remote functionalized arenes and pyridines, demonstrating that remote functionalization can be achieved without the use of elaborate catalyst systems. The high practicality of this method was highlighted by reactions on scales up to 30 mmol without a decrease in yield. The subsequent full or partial functionalization of the obtained remote functionalized bis-silyl arenes either by a sequence of iodo-desilylation, iodine-magnesium exchanges and reactions with electrophiles, or by proto-desilylation, directed metalation and reaction with electrophiles, demonstrates the full synthetic value of the used triethylsily groups and the method overall (Scheme 38).



Scheme 38: Summary of regioselective remote-lithiation of 1,3-bis-silylated (hetero)arenes.

C. EXPERIMENTAL PART

1 General Considerations

If not otherwise stated, all reactions have been carried out using standard Schlenk-techniques in flame-dried glassware under argon. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H-NMR (25 °C) and capillary GC.

1.1 Solvents

Solvents were dried according to standard methods by distillation from drying agents as stated below and were stored under argon. Otherwise they were obtained from commercial sources and used without further purification.

THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen and stored over molecular sieves.
Et_2O was freshly distilled from sodium benzophenone ketyl under argon and stored over molecular sieves.
***n*Hexane** was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen and stored over molecular sieves.
Dichloromethane was continuously refluxed and freshly distilled from CaH_2 under nitrogen.

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**[40a] was prepared by careful addition of *i*PrCl (78.54 g, 91.3 mL, 1.00 mol, 1.0 equiv.) to a suspension of Mg (26.74 g, 1.1 mol, 1.1 equiv.) and LiCl (46.63 g, 1.1 mol, 1.1 equiv.) in dry THF (900 mL). The reaction mixture was stirred for 12 h and afterwards the floating particles were allowed to settle. The solution was cannulated into a flame-dried and argon flushed Schlenk-flask and its concentration was determined by titration against I_2 in THF.[122]
***n*BuLi, *s*BuLi, *t*BuLi** solutions in hexane were purchased from Albemarle and their concentration was determined by titration against *N*-benzylbenzamide in THF at −20 °C.[123]
TMPH was purchased from Albemarle, freshly distilled from CaH_2 and stored over argon.

[122] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890.
[123] A. F. Burchat, J. M. Chong, N. Nielsen, *J. Organomet. Chem.* **1997**, *542*, 281.

PMDTA was purchased from TCI, distilled from sodium benzophenone ketyl under argon and stored in a Schlenk flask.

BF_3•OEt_2 was distilled prior to use and stored under argon.

CuCN•2LiCl[117] solution (1.00 M in THF) was prepared by drying CuCN (44.78 g, 500 mmol, 1.0 equiv.) and LiCl (42.39 g, 1.00 mol, 2.0 equiv.) in a Schlenk-flask under vacuum for 5 h at 150 °C. After cooling to 25 °C, dry THF (480 mL) was added and the suspension was stirred until all salts were dissolved. Then dry THF was added until a previously set 500 mL mark was matched.

$MgCl_2$ solution (0.50 M in THF) was prepared by suspending Mg turnings (6.68 g, 275 mmol) in dry THF (500 mL) in a flame-dried and argon flushed Schlenk-flask. Then 1,2-dichloroethane (24.74 g, 19.70 mL, 250 mmol) was added carefully over 1 h (strong gas evolution), while the temperature was kept below 25 °C. The reaction mixture was stirred overnight at 25 °C until gas evolution was complete.

$ZnCl_2$ solution (1.00 M in THF) was prepared by drying $ZnCl_2$ (68.15 g, 500 mmol, 1.0 equiv.) in a Schlenk-flask under vacuum for 5 h at 150 °C. After cooling to 25 °C, dry THF (480 mL) was added and stirred until all salts were dissolved. Then, dry THF was added until a previously set 500 mL mark was matched.

TMPLi solution in THF was prepared by addition of *n*BuLi (38.2 mL, 2.62 M in hexane, 100 mmol, 1.0 equiv.) to a solution of TMPH (14.13 g, 16.87 mL, 100 mmol, 1.0 equiv.) in THF (100 mL) at −40 °C. The mixture was allowed to warm up to 0 °C and its concentration was determined by titration against *N*-benzylbenzamide in THF at –20 °C.

TMPMgCl•LiCl[62a] was prepared by addition of TMPH (14.83 g, 17.72 mL, 105 mmol, 1.05 equiv.) to *i*PrMgCl•LiCl (95.24 mL, 1.05 M, 100 mmol, 1.00 equiv.) at 25 °C. The mixture was stirred for 48 h until all gas evolution ceased. The concentration was determined by titration against benzoic acid in THF using 4-(phenylazo)diphenylamine as indicator.

1.3 Chromatography

Flash column chromatography was performed using SiO_2 60 (0.040–0.063 mm, 230–400 mesh ASTM) from Merck.

Thin layer chromatography (TLC) was performed using aluminum plates covered with SiO_2 (Merck 60, F–254). Spots were visualized by UV light irradiation and/or by staining of the TLC plate with one of the solutions below, followed by heating with a heat gun.

- $KMnO_4$ (0.3 g), K_2CO_3 (20 g) and KOH (0.3 g) in water (300 mL).
- $Ce(SO_4)_2$ (5.0 g), $(NH_4)_6Mo_7O_{24}$•$4H_2O$ (25 g) and concentrated H_2SO_4 (50 mL) in water (450 mL).
- Neat iodine absorbed on silica gel.

1.4 Analytical data

NMR spectra were recorded on *Bruker* ARX 200, AC 300, WH 400 or AMX 600 instruments. Chemical shifts are reported as δ-values in parts-per-million (ppm) relative to the residual solvent peak: $CDCl_3$ (δ_H: 7.26; δ_C: 77.16). For the observation of the observed signal multiplicities, the following abbreviations and combinations thereof were used: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet) and br (broad). If not otherwise noted, the coupling constants given are either H-H or H-F coupling constants for proton signals and C-F coupling constants for carbon signals.

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

Infrared spectra were recorded from 4000–650 cm^{-1} on a Perkin Elmer Spectrum BX-59343 instrument. For detection a Smiths Detection DuraSampl IR II Diamond ATR sensor was used. The main absorption peaks are reported in cm^{-1}.

Gas chromatography (GC) was performed with instruments of the type Hewlett-Packard 6890 or 5890 Series II, using a column of the tyoe HP 5 (Hewlett-Packard, 5% phenylmethylpolysiloxane; length: 10 m, diameter: 0.25 mm, film thickness 0.25 μm). The detection was accomplished using a flame ionization detector.

Mass spectra (MS) and high resolution mass spectra (HRMS) were recorded on a Finnigan MAT 95Q or Finnigan MAT 90 instrument for electron impact ionization (EI). For the combination of gas chromatography with mass spectroscopic detection, a GC–MS of the type Hewlett-Packard 6890/MSD 5793 networking was used (column: HP 5–MS, Hewlett–Packard; 5% phenylmethylpolysiloxane; length: 15 m, diameter: 0.25 mm, film thickness: 0.25 μm).

2 Chromium-Catalyzed Cross-Coupling Reactions of Alkyl

2.1 Preparation of the $CrCl_3$•3THF solution

Preparation of $CrCl_3$•3THF (0.1 M)[100]

A dry and argon flushed Soxhlet extraction apparatus was charged with anhydrous $CrCl_3$ (5.0 g, 31.6 mmol, 1.0 equiv.) and zinc dust (62 mg, 0.95 mmol, 0.03 equiv.). The reaction mixture was extracted for 24 h with refluxing THF (250 mL). The mixture was allowed to cool to room temperature and the THF was removed *in vacuo*. The violet solid (11.5 g, 97%) was stored in a Schlenk flask under argon.

10 mL of THF were added and the Cr(III) complex was partially dissolved. This solution was transferred into a tared Schlenk-flask under argon and the THF was removed *in vacuo*. The weight of the resulting solid was determined and enough THF was added to obtain a 0.1 M solution.

2.2 Typical Procedures (TP)

Preparation of Alkylmagnesium reagents[25]

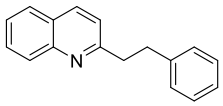
A dry and argon flushed Schlenk-flask, equipped with a stirring bar and a septum, was charged with Mg turnings (292 mg, 12 mmol, 1.2 equiv.) and LiCl (509 mg, 12 mmol, 1.2 equiv.). The solids were dried *in vacuo* at 400 °C for 3 min. After cooling to 25 °C the flask was flushed with argon and THF (8 mL) was added. The suspension was cooled to 0 °C and the corresponding alkyl bromide (10 mmol, 1.0 equiv.) was added dropwise. After the addition was finished, the mixture was allowed to slowly warm to 25 °C. The concentration of the Grignard reagent was determined by iodometric titration.[122]

Typical procedure for the Chromium-Catalyzed Cross-Couplings of Alkylmagnesium Reagents (TP1):

A dry and argon-flushed 10 mL Schlenk-tube, equipped with a stirring bar and a septum, was charged with a solution of $CrCl_3$·3THF (0.1 M in THF, 0.15 mL, 0.015 mmol, 0.03 equiv.), the corresponding (hetero)aryl halide (0.5 mmol, 1.0 equiv.) and THF (2.5 mL). The alkylmagnesium bromide solution (0.75 mmol, 1.5 equiv.) was added dropwise over 2 min by syringe at room temperature. After 15 min, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (1 mL) and diluted with water (4 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3x20 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed *in vacuo* and the crude product was purified by flash column chromatography furnishing the respective title compound.

2.3 Chromium-Catalyzed Cross-Coupling Reaction of Alkylmagnesium bromides and (Hetero)aryl halides

2-Phenylethylquinoline (3a)



A cross-coupling reaction was performed according to **TP1** between 2-chlorquinoline (**1a**, 81 mg) and Grignard reagent **2a** (0.85 mL, 0.88 M) with a catalyst loading of $CrCl_3 \cdot 3THF$ (2.5 µmol, 25 µL, 0.5 mol%). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3a** (106 mg, 91%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.14 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.39 – 7.21 (m, 6H), 3.34 (dd, *J* = 9.8, 6.3 Hz, 2H), 3.21 (dd, *J* = 9.7, 6.3 Hz, 2H).

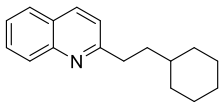
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.87, 148.03, 141.57, 136.30, 129.49, 128.91, 128.59, 128.47, 127.61, 126.86, 126.08, 125.87, 121.64, 41.08, 36.03.

MS (EI, 70 eV): *m/z* (%) = 233 (95), 232 (100), 217 (17), 156 (55), 129 (23), 128 (14), 115 (11), 91 (15).

HRMS (EI): *m/z* calc. for $[C_{17}H_{15}N]$: 233.1204 $[M]^{\bullet+}$; found: 233.1204.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3026 (w), 2923 (w), 2856 (vw), 1618 (w), 1599 (s), 1502 (s), 1452 (m), 1425 (m), 1310 (w), 819 (vs), 748 (vs), 694 (vs).

2-(2-Cyclohexylethyl)quinoline (3b)



A cross-coupling reaction was performed according to **TP1** between 2-chlorquinoline (**1a**, 81 mg) and Grignard reagent **2b** (0.87 mL, 0.86 M). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3b** (95 mg, 79%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.03 (dd, *J* = 10.9, 8.7 Hz, 2H), 7.74 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.66 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.45 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 1H), 3.01 – 2.92 (m, 2H), 1.85 – 1.76 (m, 2H), 1.75 – 1.60 (m, 5H), 1.39 – 1.29 (m, 1H), 1.29 – 1.08 (m, 3H), 1.04 – 0.90 (m, 2H).

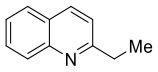
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.50, 147.95, 136.22, 129.34, 128.85, 127.52, 126.73, 125.65, 121.40, 37.83, 37.79, 36.94, 33.35, 26.72, 26.42.

MS (EI, 70 eV): *m/z* (%) = 156 (38), 144 (10), 143 (100).

HRMS (EI): *m/z* calc. for $[C_{17}H_{14}N]$: 238.1590 $[M-H]^{\bullet+}$; found: 238.1592.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2919 (vs), 2848 (s), 1600 (s), 1561 (w), 1502 (s), 1447 (m), 1425 (m), 824 (vs), 749 (s).

2-Ethylquinoline (3c)



A cross-coupling reaction was performed according to **TP1** between 2-chlorquinoline (**1a**, 81 mg) and Grignard reagent **2c** (0.65 mL, 1.15 M). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3c** (51 mg, 65%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.04 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.47 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 3.00 (q, *J* = 7.6 Hz, 2H), 1.39 (t, *J* = 7.6 Hz, 3H).

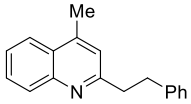
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.12, 147.94, 136.45, 129.44, 128.89, 127.58, 126.81, 125.75, 120.95, 32.45, 14.18.

MS (EI, 70 eV): *m/z* (%) = 157 (55), 156 (100), 129 (22), 128 (15).

HRMS (EI): *m/z* calc. for $[C_{11}H_{10}N]$: 156.0808 $[M-H]^{\bullet+}$; found: 156.0806.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2969 (w), 2933 (vw), 1618 (w), 1602 (m), 1504 (s), 1426 (w), 839 (vs), 753 (m).

4-Methyl-2-phenylethylquinoline (3d)



A cross-coupling reaction was performed according to **TP1** between 2-chloro-4-methylquinoline (**1b**, 89 mg) and Grignard reagent **2a** (0.82 mL, 0.91 M). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3d** (101 mg, 82%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.07 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.34 – 7.15 (m, 5H), 7.11 (s, 1H), 3.24 (dd, *J* = 10.3, 5.8 Hz, 2H), 3.14 (dd, *J* = 10.0, 5.5 Hz, 2H), 2.67 (s, 3H).

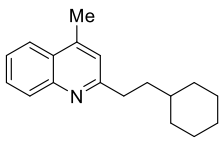
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.65, 147.94, 144.42, 141.81, 129.54, 129.24, 128.65, 128.53, 127.01, 126.11, 125.69, 123.79, 122.40, 41.14, 36.14, 18.85.

MS (EI, 70 eV): *m/z* (%) = 247 (100), 87 (246), 232 (28), 231 (13), 170 (67), 143 (32), 116 (12), 115 (19), 91 (12).

HRMS (EI): *m/z* calc. for $[C_{18}H_{17}N]$: 247.1361 $[M]^{\bullet+}$; found: 247.1356.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3061 (w), 3027 (w), 2923 (w), 1602 (vs), 1562 (w), 1496 (w), 1450 (m), 754 (vs), 699 (s).

2-(2-Cyclohexylethyl)-4-methylquinoline (3e)



A cross-coupling reaction was performed according to **TP1** between 2-chloro-4-methylquinoline (**1b**, 89 mg) and Grignard reagent **2b** (0.87 mL, 0.86 M). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3e** (100 mg, 79%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.08 – 8.00 (m, 1H), 7.90 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.64 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.46 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.11 (d, *J* = 1.1 Hz, 1H), 2.98 – 2.85 (m, 2H), 2.63 (d, *J* = 1.0 Hz, 3H), 1.85 – 1.77 (m, 2H), 1.76 – 1.58 (m, 5H), 1.41 – 1.08 (m, 4H), 1.03 – 0.83 (m, 2H).

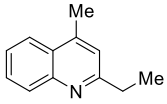
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.17, 147.75, 144.19, 129.34, 129.02, 126.79, 125.40, 123.61, 122.08, 37.89, 37.82, 36.83, 33.35, 26.73, 26.42, 18.74.

MS (EI, 70 eV): *m/z* (%) = 253 (2), 170 (37), 158 (11), 157 (100).

HRMS (EI): *m/z* calc. for $[C_{18}H_{23}N]$: 253.1830 $[M]^{\bullet+}$; found: 253.1825.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2919 (m), 2848 (m), 2360 (vw), 1602 (m), 1561 (w), 1446 (m), 754 (vs).

2-Ethyl-4-methylquinoline (3f)



A cross-coupling reaction was performed according to **TP1** between 2-chloro-4-methylquinoline (**1b**, 89 mg) and Grignard reagent **2c** (0.65 mL, 1.15 M). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3g** (68 mg, 79%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.04 (dd, *J* = 8.5, 0.7 Hz, 1H), 7.91 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.65 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.47 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.12 (d, *J* = 1.0 Hz, 1H), 2.94 (q, *J* = 7.6 Hz, 2H), 2.64 (s, 3H), 1.37 (t, *J* = 7.6 Hz, 3H).

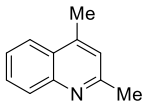
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.74, 147.72, 144.37, 129.35, 129.07, 126.82, 125.45, 123.63, 121.58, 32.29, 18.75, 14.16.

MS (EI, 70 eV): *m/z* (%) = 171 (48), 170 (76), 70 (12), 61 (18), 45 (15), 43 (100).

HRMS (EI): *m/z* calc. for $[C_{12}H_{12}N]$: 170.0970 $[M-H]^{\bullet+}$; found: 170.0964.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2969 (w), 2933 (w), 2873 (vw), 1604 (m), 1562 (w), 1507 (vw), 1448 (w), 862 (w), 754 (vs).

2,4-Dimethylquinoline (3g)



A cross-coupling reaction was performed according to **TP1** between 2-chloro-4-methylquinoline (**1b**, 89 mg) and commercial MeMgCl **2d** (0.32 mL, 2.34 M). After purification by flash column

chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3f** (44 mg, 56%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.01 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.95 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.50 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.14 (d, *J* = 1.2 Hz, 1H), 2.70 (s, 3H), 2.67 (s, 3H).

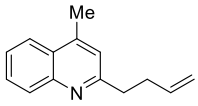
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 158.82, 147.80, 144.34, 129.26, 126.69, 125.56, 123.74, 122.87, 25.40, 18.77.

MS (EI, 70 eV): *m/z* (%) = 157 (100), 156 (19), 115 (13), 44 (12).

HRMS (EI): *m/z* calc. for [$C_{11}H_{11}N$]: 157.0891 [M]$^{\bullet+}$; found: 157.0883.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (vw), 2922 (vw), 1604 (vs), 1564 (w), 1447 (w), 859 (w), 758 (vs).

2-(But-3-en-1-yl)-4-methylquinoline (3h)



A cross-coupling reaction was performed according to **TP1** between 2-chloro-4-methylquinoline (**1b**, 89 mg) and Grignard reagent **2e** (0.88 mL, 0.85 M). After purification by flash column chromatography (9:1, *i*hexane:ethyl acetate) the title compound **3h** (63 mg, 69%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.08 – 8.00 (m, 1H), 7.94 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.49 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.13 (d, *J* = 1.1 Hz, 1H), 5.93 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.04 – 4.95 (m, 1H), 3.06 – 2.97 (m, 2H), 2.66 (d, *J* = 1.0 Hz, 3H), 2.63 – 2.53 (m, 2H).

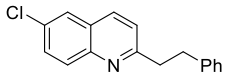
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.78, 147.82, 144.36, 137.90, 129.43, 129.16, 126.92, 125.60, 123.70, 122.21, 115.24, 38.55, 33.97, 18.82.

MS (EI, 70 eV): *m/z* (%) = 197 (58), 184 (100), 170 (62), 157 (72), 144 (92), 130 (15), 115 (32).

HRMS (EI): *m/z* calc. for [$C_{14}H_{15}N$]: 197.1204 [M]$^{\bullet+}$; found: 197.1207.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3063 (vw), 2975 (vw), 2921 (vw), 1602 (m), 1561 (w), 1508 (w), 1446 (w), 1411 (w), 910 (m), 860 (m), 754 (vs).

6-Chloro-2-phenethylquinoline (3i)



A cross-coupling reaction was performed according to **TP1** between 2,6-dichloroquinoline (**1c**, 99 mg) and Grignard reagent **2a** (0.87 mL, 0.86 M). After purification by flash column chromatography (19:1, *i*hexane:ethyl acetate) the title compound **3i** (78 mg, 58%) was obtained as a colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.99 (d, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.72 (d, *J* = 2.4 Hz, 1H), 7.61 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.33 – 7.16 (m, 6H), 3.30 – 3.24 (m, 2H), 3.20 – 3.11 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.18, 146.40, 141.39, 135.29, 131.47, 130.57, 130.31, 128.57, 128.50, 127.42, 126.26, 126.14, 122.51, 40.95, 35.80.

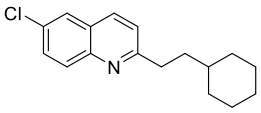
MS (EI, 70 eV): *m/z* (%) = 266 (100), 192 (17), 190 (48), 163 (18), 91 (26).

HRMS (EI): *m/z* calc. for [$C_{17}H_{13}{}^{35}ClN$]: 266.0731 [M−H]$^{\bullet+}$; found: 266.0726.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2949 (vw), 2924 (w), 2856 (w), 1594 (s), 1558 (w), 1488 (s), 1452 (w), 1308 (w), 1073 (s), 830 (m), 820 (s), 699 (vs).

m.p. (°C): 94.6 – 95.8 °C

6-Chloro-2-(2-cyclohexylethyl)quinoline (3j)



A cross-coupling reaction was performed according to **TP1** between 2,6-dichloroquinoline (**1c**, 99 mg) and Grignard reagent **2b** (0.87 mL, 0.86 M). After purification by flash column chromatography (19:1, *i*hexane:ethyl acetate) the title compound **3j** (105 mg, 77%) was obtained as a colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.96 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 2.4 Hz, 1H), 7.60 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 3.02 – 2.91 (m, 2H), 1.86 – 1.76 (m, 2H), 1.75 – 1.61 (m, 4H), 1.41 – 1.12 (m, 4H), 1.03 – 0.90 (m, 2H), 0.90 – 0.80 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.96, 146.40, 135.37, 131.33, 130.57, 130.27, 127.39, 126.28, 122.39, 37.89, 37.70, 36.94, 33.40, 26.77, 26.47.

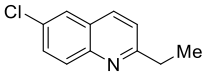
MS (EI, 70 eV): *m/z* (%) = 273 (3), 192 (12), 190 (38), 176 (100).

HRMS (EI): *m/z* calc. for [$C_{17}H_{20}{}^{35}ClN$]: 273.1284 [M]$^{\bullet+}$; found: 273.1292.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2919 (s), 2849 (m), 1599 (m), 1557 (vw), 1489 (s), 1447 (w), 1072 (m), 875 (m), 829 (vs), 810 (w).

m.p. (°C): 69.2 – 70.3 °C

6-Chloro-2-ethylquinoline (3k)



A cross-coupling reaction was performed according to **TP1** between 2,6-dichloroquinoline (**1c**, 99 mg) and Grignard reagent **2c** (0.65 mL, 1.15 M). After purification by flash column chromatography (29:1, *i*hexane:ethyl acetate) the title compound **3k** (60 mg, 63%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.02 – 7.94 (m, 2H), 7.76 (d, *J* = 2.4 Hz, 1H), 7.61 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 2.99 (q, *J* = 7.7 Hz, 2H), 1.39 (t, *J* = 7.6 Hz, 3H).

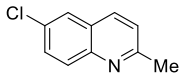
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.49, 146.36, 135.54, 131.40, 130.58, 130.34, 127.44, 126.30, 121.91, 32.41, 14.02.

MS (EI, 70 eV): *m/z* (%) = 190 (100), 164 (16), 143 (22), 128 (13).

HRMS (EI): *m/z* calc. for [$C_{11}H_9{}^{35}ClN$]: 190.0418 [M−H]$^{\bullet+}$; found: 190.0412.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2970 (w), 2934 (vw), 2874 (vw), 1598 (m), 1490 (s), 1302 (w), 1188 (w), 1074 (w), 897 (m), 876 (m), 829 (vs).

6-Chloro-2-methylquinoline (3l)



A cross-coupling reaction was performed according to **TP1** between 2,6-dichloroquinoline (**1c**, 99 mg) and Grignard reagent **2d** (0.32 mL, 2.34 M). After purification by flash column chromatography (19:1, *i*hexane:ethyl acetate) the title compound **3l** (74 mg, 83%) was obtained as a colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.95 (d, *J* = 2.3 Hz, 1H), 7.93 (d, *J* = 3.2 Hz, 1H), 7.74 (d, *J* = 2.4 Hz, 1H), 7.60 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 2.73 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 159.49, 146.36, 135.33, 131.39, 130.39, 127.18, 126.29, 123.00, 25.49.

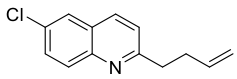
MS (EI, 70 eV): *m/z* (%) = 177 (100), 162 (11), 142 (26), 140 (11), 115 (21), 43 (29).

HRMS (EI): *m/z* calc. for [$C_{10}H_8{}^{35}ClN$]: 177.0345 [M]$^{\bullet+}$; found: 177.0343.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (w), 2916 (w), 1597 (s), 1557 (w), 1489 (s), 1369 (m), 1066 (m), 885 (m), 833 (vs), 805 (s).

m.p. (°C): 95.2 – 96.0 °C.

2-(But-3-en-1-yl)-6-chloroquinoline (3m)



A cross-coupling reaction was performed according to **TP1** between 2,6-dichloroquinoline (**1c**, 99 mg) and Grignard reagent **2e** (0.88 mL, 0.85 M). After purification by flash column chromatography (39:1, *i*hexane:ethyl acetate) the title compound **3m** (90 mg, 84%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.97 – 7.90 (m, 2H), 7.71 (d, *J* = 2.3 Hz, 1H), 7.58 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 5.90 (ddt, *J* = 16.9, 10.2, 6.5 Hz, 1H), 5.06 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.98 (dd, *J* = 10.3, 1.6 Hz, 1H), 3.12 – 2.97 (m, 2H), 2.70 – 2.47 (m, 2H).

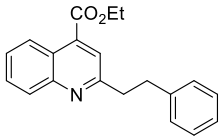
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.40, 146.35, 137.57, 135.31, 131.42, 130.54, 130.28, 127.39, 126.23, 122.37, 115.46, 38.49, 33.69.

MS (EI, 70 eV): *m/z* (%) = 216 (100), 204 (15), 190 (38), 177 (31), 163 (18), 140 (27).

HRMS (EI): *m/z* calc. for [$C_{13}H_{11}{}^{35}ClN$]: 216.0575 [M−H]$^{\bullet+}$; found: 216.0568.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3076 (vw), 2920 (vw), 1640 (w), 1598 (s), 1556 (w), 1488 (s), 1072 (m), 909 (s), 875 (s), 829 (vs), 811 (s).

Ethyl 2-phenethylquinoline-4-carboxylate (3n)



A cross-coupling reaction was performed according to **TP1** between ethyl 2-bromoquinoline-4-carboxylate (**1d**, 140 mg) and Grignard reagent **2a** (0.87 mL, 0.86 M). After purification by flash column chromatography (19:1, *i*hexane:ethyl acetate) the title compound **3n** (76 mg, 50%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.69 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.12 (dt, *J* = 8.4, 1.0 Hz, 1H), 7.76 – 7.69 (m, 2H), 7.58 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.32 – 7.22 (m, 4H), 7.22 – 7.14 (m, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 3.38 – 3.27 (m, 2H), 3.23 – 3.09 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H).

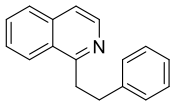
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.49, 161.33, 149.00, 141.34, 135.53, 129.75, 129.54, 128.61, 128.54, 127.37, 126.19, 125.52, 123.74, 122.80, 61.89, 40.90, 35.74, 14.41.

MS (EI, 70 eV): *m/z* (%) = 305 (100), 274 (46), 231 (28), 199 (16), 91 (21), 71 (43), 57 (63), 43 (93).

HRMS (EI): *m/z* calc. for $[C_{20}H_{19}O_2N]$: 305.1416 $[M]^{\bullet+}$; found: 305.1408.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3063 (vw), 3027 (vw), 2981 (vw), 1721 (vs), 1594 (m), 1507 (w), 1371 (w), 1268 (m), 1242 (vs), 1200 (s), 1147 (m), 1026 (m), 797 (w), 776 (m), 750 (w), 699 (m).

1-Phenethylisoquinoline (3o)



A cross-coupling reaction was performed according to **TP1** between 1-iodoisoquinoline (**1e**, 128 mg) and Grignard reagent **2a** (0.87 mL, 0.86 M). After purification by flash column chromatography (19:1, *i*hexane:ethyl acetate) the title compound **3o** (58 mg, 50%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.41 (d, *J* = 5.7 Hz, 1H), 8.11 – 8.05 (m, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.51 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.47 (dd, *J* = 5.8, 0.9 Hz, 1H), 7.28 – 7.23 (m, 4H), 7.20 – 7.12 (m, 1H), 3.58 – 3.51 (m, 2H), 3.18 – 3.10 (m, 2H).

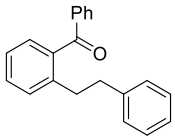
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.12, 142.03, 142.00, 136.33, 129.94, 128.59, 128.55, 127.53, 127.21, 127.01, 126.16, 125.16, 119.54, 37.39, 35.59.

MS (EI, 70 eV): *m/z* (%) = 232 (100), 217 (17), 156 (41), 129 (35), 115 (19), 91 (17), 43 (12).

HRMS (EI): *m/z* calc. for $[C_{17}H_{14}N]$: 232.1121 $[M-H]^{\bullet+}$; found: 232.1117.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3052 (vw), 3026 (vw), 2929 (vw), 1622 (w), 1586 (w), 1562 (m), 1496 (m), 1453 (w), 1388 (w), 1358 (w), 823 (s), 744 (vs), 699 (vs).

(2-Phenethylphenyl)(phenyl)methanone (5a)



A cross-coupling reaction was performed according to **TP1** between 2-chlorobenzophenone (**4a**, 434 mg, 2.0 mmol) and Grignard reagent **2a** (3.49 mL, 0.86 M) with $CrCl_3 \cdot 3THF$ (0.6 mL, 0.06 mmol). After purification by flash column chromatography (29:1, *i*hexane:ethyl acetate) the title compound **5a** (400 mg, 1.4 mmol, 70%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.78 – 7.68 (m, 2H), 7.56 – 7.47 (m, 1H), 7.42 – 7.31 (m, 3H), 7.24 (dd, *J* = 7.6, 1.5 Hz, 2H), 7.20 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.18 – 7.10 (m, 2H), 7.10 – 6.99 (m, 3H), 2.99 – 2.88 (m, 2H), 2.85 – 2.75 (m, 2H).

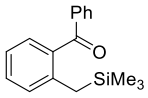
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 198.60, 141.56, 140.84, 138.53, 137.90, 133.22, 130.45, 130.33, 130.25, 128.80, 128.49, 128.47, 128.33, 125.95, 125.48, 38.18, 35.60.

MS (EI, 70 eV): *m/z* (%) = 286 (2), 195 (100), 177 (13), 165 (20), 91 (22).

HRMS (EI): *m/z* calc. for $[C_{21}H_{18}O]$: 286.1358 $[M]^{\bullet+}$; found: 286.1353.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3061 (vw), 3025 (vw), 2925 (w), 2860 (vw), 1662 (vs), 1597 (w), 1494 (w), 1448 (m), 1314 (w), 1267 (m), 927 (w), 757 (m), 698 (vs).

Phenyl(2-((trimethylsilyl)methyl)phenyl)methanone (5b)



A cross-coupling reaction was performed according to **TP1** between 2-chlorobenzophenone (**4a**, 108 mg) and Grignard reagent **2f** (1.03 mL, 0.73 M). After purification by flash column chromatography (39:1, *i*hexane:ethyl acetate) the title compound **5b** (118 mg, 88%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.80 (d, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.18 – 7.09 (m, 2H), 2.35 (s, 2H), -0.05 (s, 9H).

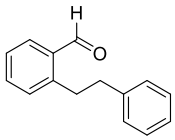
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 198.57, 141.19, 138.38, 136.45, 132.86, 130.39, 130.33, 130.26, 130.11, 128.40, 123.35, 24.34, -1.25.

MS (EI, 70 eV): *m/z* (%) = 267 (100), 253 (24), 178 (14), 165 (23), 149 (18), 111 (12), 73 (47), 69 (18), 57 (12), 43 (24).

HRMS (EI): *m/z* calc. for $[C_{17}H_{19}O^{28}Si]$: 267.1200 $[M-H]^{\bullet+}$; found: 267.1184.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3061 (vw), 2953 (vw), 2897 (vw), 1659 (s), 1597 (w), 1447 (w), 1262 (s), 1246 (s), 1152 (m), 927 (m), 837 (vs), 760 (m), 699 (vs).

2-Phenylethylbenzaldehyde (5c)



A cross-coupling reaction was performed according to **TP1** between 1-(2-chlorophenyl)-*N*-phenylmethanimine (**4b**, 108 mg) and Grignard reagent **2a** (0.87 mL, 0.86 M). The reaction mixture was stirred with 2 M HCl (2 mL) for 1 h before workup. After purification by flash column chromatography (39:1, *i*hexane:ethyl acetate) the title compound **5c** (75 mg, 71%) was obtained as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.18 (s, 1H), 7.82 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.48 (td, *J* = 7.5, 1.5 Hz, 1H), 7.38 (td, *J* = 7.5, 1.3 Hz, 1H), 7.32 – 7.25 (m, 2H), 7.24 – 7.16 (m, 4H), 3.37 – 3.29 (m, 2H), 2.94 – 2.87 (m, 2H).

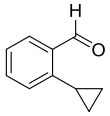
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 192.43, 144.39, 141.27, 133.88, 133.85, 132.53, 131.33, 128.67, 128.50, 126.80, 126.22, 38.36, 35.03.

MS (EI, 70 eV): *m/z* (%) = 210 (16), 192 (10), 132 (12), 91 (100), 65 (29), 61 (11), 43 (48).

HRMS (EI): *m/z* calc. for [$C_{15}H_{14}O$]: 210.1045 [M]$^{\bullet+}$; found: 210.1028.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3062 (vw), 3026 (vw), 2924 (vw), 2859 (vw), 1691 (vs), 1599 (m), 1573 (w), 1495 (w), 1452 (w), 1191 (w), 755 (s), 724 (w), 698 (s).

2-Cyclopropylbenzaldehyde (5d)



A cross-coupling reaction was performed according to **TP1** between 1-(2-chlorophenyl)-*N*-phenylmethanimine (**4b**, 108 mg) and Grignard reagent **2g** (0.86 mL, 0.87 M). The reaction mixture was stirred with 2 M HCl (2 mL) for 1 h before workup. After purification by flash column chromatography (39:1, *i*hexane:ethyl acetate) the title compound **5d** (54 mg, 74%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.60 (s, 1H), 7.82 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.48 (td, *J* = 7.6, 1.6 Hz, 1H), 7.36 – 7.27 (m, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 2.63 (tt, *J* = 8.5, 5.3 Hz, 1H), 1.14 – 1.04 (m, 2H), 0.82 – 0.76 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 192.87, 146.22, 134.99, 134.11, 130.16, 126.72, 126.22, 11.92, 8.61.

MS (EI, 70 eV): *m/z* (%) = 145 (22), 131 (69), 128 (21), 115 (100), 103 (44), 90 (49), 77 (32), 63 (29), 51 (23).

HRMS (EI): *m/z* calc. for [$C_{10}H_9O$]: 145.0648 [M−H]$^{\bullet+}$; found: 145.0651.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3005 (vw), 2854 (vw), 2758 (vw), 1689 (vs), 1599 (m), 1489 (w), 1288 (vw), 1224 (w), 1191 (w), 1030 (vw), 823 (w), 757 (m).

3 Regioselective Remote-Lithiation of 1,3-bis-Silylated (Hetero)Arenes

3.1 Typical Procedures

Typical procedure for the preparation of o,o'-bissilylated arenes via an in situ lithiation and silylation sequence (TP2):

A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding arene (1.0 equiv.) and silyl chloride (2.4 equiv.) in dry THF (0.5–1.0 M solution). The resulting solution was cooled to −78 °C and TMPLi (2.2 equiv.) was added dropwise. The mixture was allowed to warm to 25 °C and was subsequently quenched with sat. aq. NH_4Cl. The aqueous phase was extracted with ethyl acetate (3 x 30 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Typical procedure for the preparation of o,o'-bissilylated arenes via in situ silylation of dibromo arenes (TP3):

A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding dibromoarene (1.0 equiv.) and silyl chloride (2.5 equiv.) in dry THF (0.5–1.0 M solution). The resulting solution was cooled to −78 °C and *n*BuLi (2.2 equiv.) was added dropwise. The mixture was slowly warmed to 25 °C and subsequently quenched with sat. aq. NH_4Cl. The aqueous phase was extracted with ethyl acetate (3 x 30 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Typical procedure for the preparation of para-lithiated arenes using *n*BuLi•PMDTA followed by the reaction with an electrophile (TP4):

A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding bissilylated arene (1.0 equiv.) in dry *n*hexane (0.5 M solution) and PMDTA (3.0 equiv.) was added. The solution was stirred at 25 °C and *n*BuLi (3.0 equiv.) was added in one portion. After 6 h, the reaction mixture was cooled to –20 °C and THF (1 mL) or a metal salt solution (3.0 equiv.) were added, immediately followed by the corresponding electrophile (3.5 equiv.). The reaction mixture was allowed to warm to 25 °C, quenched with a sat. aq. NH_4Cl solution (or sat. aq. $Na_2S_2O_3$ for halogenolysis) and extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Typical procedure for the iododesilylation using ICl (TP5):

A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding silylated arene (1.0 equiv.) in dry CH_2Cl_2 (0.5 M solution) and ICl (1.3 equiv.) was

added in one portion at 25 °C. After 10 h, a sat. aq. $Na_2S_2O_3$ (20 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Typical procedure for the iodine/magnesium-exchange with *i*PrMgCl•LiCl followed by the reaction with an electrophile (TP6):

A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding iodoarene (1.0 equiv.) in dry THF (0.5 M solution) and was cooled to –40 °C. *i*PrMgCl•LiCl (1.05 equiv.) was added dropwise and the mixture was stirred for 15 min. Then the electrophile (1.1 equiv.) was added in one portion and the mixture was allowed to warm to 25 °C. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Typical procedure for the magnesiation of pyridines using BF_3•OEt_2 and TMPMgCl•LiCl followed by the reaction with an electrophile (TP7):

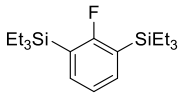
A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the monosilylated pyridine **25c** (1.0 equiv.) in dry THF (0.5 M solution) and was cooled to 0 °C. TMPMgCl•LiCl (1.2 equiv.) was added in one portion, immediately followed by BF_3•OEt_2 (1.2 equiv.) and the mixture was stirred for 20 min. Then the electrophile (1.2 equiv.) was added in one portion and the mixture was allowed to warm to 25 °C. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Typical procedure for the magnesiation of pyridines with TMPMgCl•LiCl followed by the reaction with an electrophile (TP8):

A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding pyridine in dry THF (0.5 mL) and was cooled to 0 °C. TMPMgCl•LiCl (0.50 mL, 1.05 M in THF, 0.52 mmol, 4.0 equiv.) was added dropwise and the mixture was stirred for 60 min. Then the electrophile (0.52 mmol, 4.0 equiv.) was added in one portion and the mixture was allowed to warm to 25 °C. A sat. aq. NH_4Cl solution (5 mL, or sat. aq. $Na_2S_2O_3$ for halogenolysis) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

3.2 Preparation of bis-silylated (hetero)arenes

(2-fluoro-1,3-phenylene)bis(triethylsilane) (6a)



According to **TP2**, fluorobenzene (9.61 g, 100 mmol) and triethylchlorosilane (42 mL, 250 mmol) were dissolved in THF (150 mL). TMPLi (129 mL, 220 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (31.0 g, 95 mmol, 95%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.47 (dd, *J* = 7.2, 5.7 Hz, 2H), 7.17 (td, *J* = 7.2, 1.7 Hz, 1H), 1.08 – 0.97 (m, 18H), 0.97 – 0.85 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 172.39 (d, *J* = 236.0 Hz), 137.52 (d, *J* = 12.4 Hz), 123.65 (d, *J* = 3.0 Hz), 122.28 (d, *J* = 37.2 Hz), 7.56 (d, *J* = 0.9 Hz), 3.74 (d, *J* = 2.0 Hz).

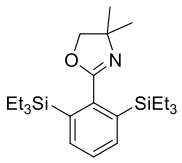
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −84.69.

MS (EI, 70 eV): *m/z* (%) = 324 (1), 268 (11), 267 (38), 240 (10), 239 (41), 211 (30), 161 (19), 105 (11), 77 (10), 70 (19), 61 (21), 45 (17), 43 (100).

HRMS (EI): *m/z* calc. for $[C_{18}H_{33}F^{28}Si_2]$: 324.2105 $[M]^{\bullet+}$; found: 324.2102.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2910 (w), 2874 (m), 1581 (w), 1457 (w), 1417 (w), 1384 (s), 1376 (s), 1239 (w), 1214 (w), 1190 (w), 1150 (vw), 1126 (w), 1003 (s), 972 (w), 818 (m), 773 (vs), 748 (vs), 717 (vs), 686 (s).

2-(2,6-bis(triethylsilyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (6b)



According to **TP2**, 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (8.76 g, 50 mmol) and triethylchlorosilane (21 mL, 125 mmol) were dissolved in THF (100 mL). TMPLi (65 mL, 110 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a slight yellow solid (16.4 g, 40.6 mmol, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.54 (d, *J* = 7.4, 2H), 7.32 (dd, *J* = 7.8, 7.2, 1H), 4.12 (s, 2H), 1.45 (s, 6H), 0.97 – 0.79 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.31, 141.88, 136.42, 136.33, 127.31, 78.83, 68.50, 29.26, 7.75, 4.32.

MS (EI, 70 eV): *m/z* (%) = 403 (1), 303 (14), 302 (77), 292 (23), 290 (12), 274 (51), 264 (51), 250 (12), 246 (87), 236 (15), 232 (40), 219 (32), 218 (36), 204 (18), 191 (32), 190 (18), 188 (11), 179 (15), 163

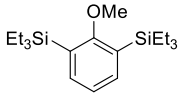
(35), 162 (19), 161 (29), 160 (14), 159 (13), 153 (24), 151 (15), 149 (13), 147 (11), 145 (11), 135 (30), 133 (23), 132 (29), 131 (25), 117 (12), 105 (19).

HRMS (EI): *m*/*z* calc. for [$C_{23}H_{41}NO^{28}Si_2$]: 403.2727 [M]$^{\bullet+}$; found: 403.2724.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3044 (vw), 2951 (m), 2935 (w), 2905 (w), 2869 (m), 1662 (m), 1557 (vw), 1463 (w), 1455 (w), 1414 (w), 1394 (w), 1364 (w), 1340 (w), 1279 (m), 1247 (w), 1234 (m), 1206 (w), 1162 (w), 1091 (m), 1036 (m), 1009 (s), 975 (m), 957 (s), 922 (m), 795 (w), 780 (s), 761 (s), 716 (vs), 690 (vs), 669 (m).

m.p. (°C): 69.3–70.8.

(2-methoxy-1,3-phenylene)bis(triethylsilane) (6c)



According to **TP3**, 1,3-dibromo-2-methoxybenzene (5.04 g, 19 mmol) and triethylchlorosilane (8.0 mL, 47.5 mmol) were dissolved in THF (40 mL). *n*BuLi (16.4 mL, 2.55 M in hexane, 41.8 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (5.1 g, 15 mmol, 80%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.43 (d, *J* = 7.2 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 3.67 (s, 3H), 1.03 – 0.76 (m, 30H).

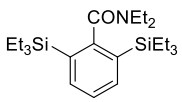
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 172.33, 138.24, 128.64, 123.18, 63.65, 7.74, 4.27.

MS (EI, 70 eV): *m/z* (%) = 307 (5), 297 (25), 280 (14), 279 (100), 269 (12), 251 (89), 223 (71), 221 (17), 195 (47), 193 (23), 191 (12), 179 (14), 167 (27), 165 (24), 163 (17), 161 (30), 151 (22), 137 (19), 135 (13), 133 (46), 131 (18), 117 (65), 115 (12), 111 (11), 107 (14), 105 (15), 97 (12), 91 (13), 89 (84), 87 (27), 61 (26), 59 (13).

HRMS (EI): *m*/*z* calc. for [$C_{17}H_{31}O^{28}Si_2$]: 307.1913 [M–Et]$^{\bullet+}$; found: 307.1910.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (w), 2874 (m), 1562 (w), 1457 (w), 1416 (w), 1370 (s), 1236 (w), 1209 (m), 1170 (vw), 1148 (vw), 1120 (w), 1076 (vw), 1014 (s), 1003 (s), 973 (w), 960 (w), 809 (w), 769 (vs), 717 (vs), 682 (m).

***N*,*N*-diethyl-2,6-bis(triethylsilyl)benzamide (6d)**



According to **TP2**, *N*,*N*-diethylbenzamide (3.36 g, 30 mmol) and triethylchlorosilane (12.6 mL, 75 mmol) were dissolved in THF (60 mL). TMPLi (39 mL, 66 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (10.3 g, 25.5 mmol, 85%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.53 (d, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 3.54 (q, *J* = 7.2 Hz, 2H), 2.99 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.00 – 0.62 (m, 33H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 172.39, 149.62, 136.05, 133.46, 125.94, 43.29, 38.71, 13.33, 12.89, 7.68, 3.92.

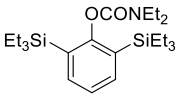
MS (EI, 70 eV): *m/z* (%) = 404 (1), 377 (31), 376 (100), 318 (19), 260 (21), 232 (16), 87 (19), 59 (16).

HRMS (EI): *m/z* calc. for $[C_{23}H_{42}NO^{28}Si_2]$: 404.2805 $[M–H]^{\bullet+}$; found: 404.2804.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (s), 2908 (m), 2872 (s), 1627 (vs), 1456 (m), 1434 (m), 1380 (m), 1363 (m), 1280 (s), 1235 (m), 1219 (m), 1155 (w), 1124 (w), 1094 (m), 1062 (w), 1001 (vs), 962 (m), 872 (w), 795 (vs), 782 (vs), 720 (vs), 682 (s).

m.p. (°C): 77.8–79.3.

2,6-bis(triethylsilyl)phenyl diethylcarbamate (6e)



According to **TP2**, phenyl diethylcarbamate (1.93 g, 10 mmol) and triethylchlorosilane (4.2 mL, 25 mmol) were dissolved in THF (20 mL). TMPLi (18.6 mL, 22 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 29:1) afforded the title compound as a colorless oil (3.3 g, 7.8 mmol, 78%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.47 (d, *J* = 7.2 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 3.59 (q, *J* = 7.2 Hz, 2H), 3.37 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.96 – 0.90 (m, 18H), 0.78 (dtd, *J* = 8.5, 7.2, 3.8 Hz, 12H).

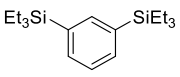
^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 161.68, 154.85, 137.60, 129.75, 124.73, 40.78, 40.69, 13.94, 13.01, 7.59, 3.66.

MS (EI, 70 eV): *m/z* (%) = 392 (80), 278 (32), 221 (14), 202 (14), 179 (12), 151 (30), 133 (16), 100 (100), 72 (63).

HRMS (EI): *m/z* calc. for $[C_{21}H_{38}NO_2{}^{28}Si_2]$: 392.2441 $[M−Et]^{\bullet+}$; found: 392.2442.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2936 (w), 2909 (w), 2874 (m), 1714 (vs), 1573 (w), 1458 (w), 1422 (m), 1371 (s), 1350 (w), 1315 (vw), 1270 (vs), 1236 (w), 1211 (vw), 1178 (m), 1148 (vs), 1118 (s), 1070 (w), 1003 (s), 962 (m), 935 (w), 772 (s), 756 (m), 720 (vs), 684 (m).

1,3-bis(triethylsilyl)benzene (6f)



According to **TP3**, 1,3-dibromobenzene (11.8 g, 50 mmol) and triethylchlorosilane (21 mL, 125 mmol) were dissolved in THF (100 mL). *n*BuLi (43.1mL, 2.55 M in hexane, 110 mmol) was slowly added to

the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (14.9 g, 48.6 mmol, 97%).

^{1}H-NMR: (400 MHz, Chloroform-*d*) δ 7.62 (dd, *J* = 2.2, 1.2 Hz, 1H), 7.48 (dd, *J* = 7.3, 1.3 Hz, 2H), 7.32 (ddd, *J* = 7.7, 6.8, 0.7 Hz, 1H), 1.01 – 0.94 (m, 18H), 0.83 – 0.74 (m, 12H).

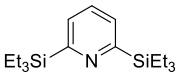
^{13}C-NMR: (101 MHz, $CDCl_3$) δ / ppm = 140.32, 136.27, 134.68, 127.05, 7.57, 3.56.

MS (EI, 70 eV): *m/z* (%) = 306 (1), 278 (11), 277 (71), 249 (76), 221 (100), 217 (14), 189 (23), 165 (18), 163 (12), 161 (20), 137 (31), 135 (17), 135 (11), 133 (31), 131 (12), 115 (36), 107 (19), 105 (16), 96 (10), 87 (16).

HRMS (EI): *m/z* calc. for $[C_{18}H_{34}{}^{28}Si_2]$: 306.2199 $[M]^{\bullet+}$; found: 306.2197.

IR: 2952 (m), 2909 (w), 2874 (m), 1457 (w), 1415 (w), 1361 (w), 1236 (w), 1106 (m), 1002 (m), 972 (w), 778 (vs), 729 (s), 714 (vs), 685 (s).

2,6-bis(triethylsilyl)pyridine (23)



In a modified version of **TP3**, 2,6-dibromopyridine (47.38 g, 200 mmol) and triethylchlorosilane (80 mL, 480 mmol, 2.4 equiv.) were dissolved in THF (400 mL). *n*BuLi (173 mL, 2.55 M in hexane, 440 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by vacuum distillation (160 °C, 1.5 mbar) afforded the title compound as a colorless oil (41.5 g, 135 mmol, 67%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.41 (dd, *J* = 8.3, 6.8 Hz, 1H), 7.34 – 7.30 (m, 2H), 1.01 – 0.95 (m, 18H), 0.87 – 0.80 (m, 12H).

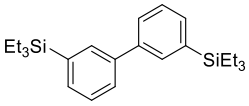
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.29, 131.02, 128.15, 7.59, 3.29.

MS (EI, 70 eV): *m/z* (%) = 306 (6), 280 (14), 279 (100), 278 (42), 251 (92), 250 (22), 223 (84), 222 (68), 220 (20), 195 (30), 194 (12), 192 (34), 165 (10), 164 (32), 162 (19), 136 (29), 134 (16), 132 (13), 106 (17), 97 (11), 59 (11).

HRMS (EI): *m/z* calc. for $[C_{17}H_{32}N^{28}Si_2]$: 306.2073 $[M-H]^{\bullet+}$; found: 306.2068.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (w), 2873 (m), 1559 (vw), 1548 (vw), 1457 (w), 1414 (w), 1237 (w), 1129 (vw), 1003 (m), 982 (w), 971 (w), 791 (s), 751 (m), 715 (vs), 686 (s).

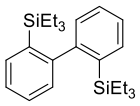
3,3'-bis(triethylsilyl)-1,1'-biphenyl (34a)



According to **TP3**, 3,3'-dibromo-1,1'-biphenyl (6.24 g, 20 mmol) and triethylchlorosilane (8.4 mL, 50 mmol) were dissolved in THF (40 mL). *n*BuLi (17.3 mL, 2.55 M in hexane, 44 mmol) was slowly added to the mixture at −78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (7.56 g, 19.8 mmol, 99%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.72 (dd, *J* = 2.0, 1.0 Hz, 2H), 7.59 (dq, *J* = 7.7, 1.4 Hz, 2H), 7.51 (dq, *J* = 7.2, 1.2 Hz, 2H), 7.46 (t, *J* = 7.4 Hz, 2H), 1.08 – 0.99 (m, 18H), 0.92 – 0.82 (m, 12H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 140.99, 138.14, 133.33, 133.17, 128.15, 127.88, 7.61, 3.57.
MS (EI, 70 eV): *m/z* (%) = 382 (28), 353 (64), 325 (75), 297 (27), 269 (32), 241 (39), 217 (27), 213 (62), 209 (13), 205 (19), 201 (18), 199 (51), 189 (47), 183 (33), 181 (100), 180 (14), 161 (19), 133 (22), 105 (22), 87 (15), 77 (31).
HRMS (EI): *m/z* calc. for $[C_{24}H_{38}{}^{28}Si_2]$: 382.2512 $[M]^{\bullet+}$; found: 382.2506.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2908 (w), 2873 (w), 1460 (w), 1415 (w), 1377 (vw), 1359 (vw), 1236 (w), 1120 (w), 1004 (m), 972 (vw), 832 (vw), 779 (w), 716 (vs), 705 (vs), 678 (m).

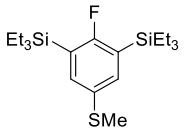
2,2'-bis(triethylsilyl)-1,1'-biphenyl (34b)



According to **TP3**, 1,2-dibromobenzene (7.08 g, 30 mmol) and triethylchlorosilane (12.6 mL, 75 mmol) were dissolved in THF (60 mL). *n*BuLi (25.9 mL, 2.55 M in hexane, 66 mmol) was slowly added to the mixture at –78 °C. Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless solid (2.1 g, 5.5 mmol, 37%).
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.58 – 7.53 (m, 2H), 7.35 – 7.28 (m, 4H), 7.15 – 7.10 (m, 2H), 0.85 – 0.76 (m, 18H), 0.59 – 0.31 (m, 12H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 151.09, 135.99, 135.40, 130.33, 127.61, 126.13, 7.73, 4.32.
MS (EI, 70 eV): *m/z* (%) = 382 (1), 227 (15), 209 (60), 199 (17), 181 (53), 115 (62), 87 (100), 59 (30).
HRMS (EI): *m/z* calc. for $[C_{24}H_{38}{}^{28}Si_2]$: 382.2512 $[M]^{\bullet+}$; found: 382.2511.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2910 (w), 2872 (w), 1456 (w), 1416 (w), 1233 (w), 1121 (w), 1007 (w), 995 (m), 970 (w), 710 (vs), 675 (m).
m.p. (°C): 89.9–91.4.

3.3 Preparation of 5-functionalized (hetero)arenes via remote lithiation

(2-fluoro-5-(methylthio)-1,3-phenylene)bis(triethylsilane) (8a)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by MeSSMe (0.31 mL, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (241 mg, 0.65 mmol, 65%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.32 (d, *J* = 5.0 Hz, 2H), 2.48 (s, 3H), 0.98 (t, *J* = 7.6 Hz, 18H), 0.85 (q, *J* = 8.2, 7.4 Hz, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.79 (d, *J* = 235.2 Hz), 136.87 (d, *J* = 12.5 Hz), 132.30 (d, *J* = 2.9 Hz), 123.42 (d, *J* = 38.2 Hz), 17.59, 7.50, 3.59 (d, *J* = 2.1 Hz).

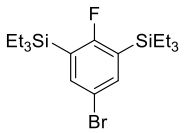
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −89.83.

MS (EI, 70 eV): *m/z* (%) = 370 (32), 285 (22), 257 (15), 229 (20), 207 (28), 201 (26), 199 (11), 197 (41), 179 (100), 171 (10), 151 (15), 125 (13), 123 (19), 105 (21), 95 (10), 91 (10), 87 (19), 77 (61), 75 (30), 59 (12).

HRMS (EI): *m/z* calc. for [$C_{19}H_{35}{}^{19}FS^{28}Si_2$]: 370.1982 [M]$^{\bullet+}$; found: 370.1976.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (s), 2909 (m), 2874 (m), 1566 (w), 1457 (w), 1436 (vw), 1419 (w), 1386 (vs), 1271 (vw), 1238 (w), 1219 (w), 1195 (m), 1144 (s), 1090 (vw), 1003 (vs), 967 (m), 872 (vw), 858 (w), 785 (vs), 743 (vs), 718 (vs), 688 (m), 670 (vs).

(5-bromo-2-fluoro-1,3-phenylene)bis(triethylsilane) (8b)



According to **TP4**, fluorobenzene **6a** (9.73 g, 30.0 mmol) and PMDTA (18.8 mL, 90.0 mmol) were dissolved in *n*hexane (60 mL). *n*BuLi (35.3 mL, 2.55 M in hexane, 90.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (90 mL, 1.0 M in THF, 90.0 mmol, 3.0 equiv.) was added, followed by a solution of Br_2 (5.41 mL, 105 mmol) in THF (30 mL). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (10.7 g, 26.5 mmol, 89%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.43 (d, *J* = 4.7 Hz, 2H), 1.00 – 0.91 (m, 18H), 0.88 – 0.76 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.92 (d, *J* = 236.1 Hz), 139.60 (d, *J* = 12.9 Hz), 125.95 (d, *J* = 39.7 Hz), 117.77 (d, *J* = 2.9 Hz), 7.45, 3.50 (d, *J* = 1.7 Hz).

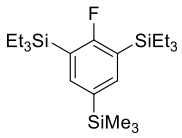
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −88.69 (t, *J* = 5.0 Hz).

MS (EI, 70 eV): *m/z* (%) = 402 (2), 319 (71), 317 (73), 291 (51), 289 (50), 289 (50), 263 (39), 261 (37), 241 (45), 239 (44), 235 (46), 233 (47), 231 (35), 229 (34), 213 (100), 211 (100), 189 (35), 179 (52), 151 (40), 149 (46), 133 (84), 131 (46), 123 (54), 105 (65), 103 (55), 87 (56), 77 (98), 75 (67).

HRMS (EI): *m/z* calc. for [$C_{18}H_{32}{}^{79}Br^{19}F^{28}Si_2$]: 402.1210 [M]$^{\bullet+}$; found: 402.1203.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (s), 2936 (m), 2909 (m), 2874 (m), 1571 (w), 1457 (w), 1418 (w), 1377 (vs), 1269 (w), 1238 (w), 1211 (m), 1193 (m), 1120 (vs), 1003 (vs), 972 (w), 883 (m), 861 (vw), 779 (vs), 744 (vs), 721 (vs), 687 (m).

(2-fluoro-5-(trimethylsilyl)-1,3-phenylene)bis(triethylsilane) (8c)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by Me_3SiCl (0.45 mL, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (330 mg, 0.83 mmol, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.57 (d, *J* = 6.3 Hz, 2H), 1.04 – 0.95 (m, 18H), 0.92 – 0.83 (m, 12H), 0.29 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 173.40 (d, *J* = 238.0 Hz), 142.81 (d, *J* = 11.5 Hz), 134.37 (d, *J* = 3.6 Hz), 121.36 (d, *J* = 35.5 Hz), 7.60 (d, *J* = 0.8 Hz), 3.84 (d, *J* = 1.6 Hz), -0.76.

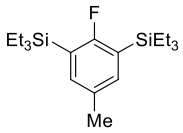
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −84.30 (t, *J* = 5.6 Hz).

MS (EI, 70 eV): *m/z* (%) = 381 (7), 339 (40), 311 (54), 283 (55), 255 (24), 247 (37), 237 (20), 227 (37), 219 (73), 209 (38), 207 (16), 191 (26), 179 (17), 163 (44), 161 (16), 136 (17), 135 (31), 133 (31), 131 (15), 127 (16), 119 (15), 77 (22), 75 (24), 73 (100), 59 (16).

HRMS (EI): *m/z* calc. for [$C_{20}H_{38}F^{28}Si_3$]: 381.2265 [M−Me]$^{\bullet+}$; found: 381.2259.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2910 (w), 2875 (m), 1562 (w), 1457 (w), 1418 (w), 1392 (m), 1260 (w), 1248 (m), 1224 (w), 1200 (vw), 1095 (m), 1003 (m), 974 (w), 873 (vs), 833 (vs), 788 (s), 758 (m), 749 (m), 718 (vs), 687 (s), 677 (m), 670 (m).

(2-fluoro-5-methyl-1,3-phenylene)bis(triethylsilane) (8d)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by iodomethane (0.22 mL, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (251 mg, 0.74 mmol, 74%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.21 (d, *J* = 5.3 Hz, 2H), 2.35 (d, *J* = 1.0 Hz, 3H), 1.06 – 0.95 (m, 18H), 0.92 – 0.81 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.70 (d, *J* = 233.5 Hz), 137.91 (d, *J* = 12.2 Hz), 132.32 (d, *J* = 3.0 Hz), 121.89 (d, *J* = 37.1 Hz), 20.95, 7.59, 3.73 (d, *J* = 1.7 Hz).

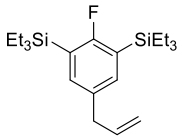
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −90.76.

MS (EI, 70 eV): *m/z* (%) = 338 (1), 281 (14), 253 (33), 225 (40), 197 (26), 193 (14), 179 (11), 175 (66), 169 (37), 167 (14), 165 (27), 161 (10), 151 (17), 147 (100), 145 (23), 137 (12), 123 (11), 121 (10), 119 (20), 105 (13), 95 (11), 77 (32), 75 (14).

HRMS (EI): *m*/*z* calc. for $[C_{19}H_{35}{}^{19}F^{28}Si_2]$: 338.2261 $[M]^{\bullet+}$; found: 338.2254.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2937 (w), 2910 (w), 2874 (m), 1578 (m), 1457 (w), 1418 (w), 1393 (vs), 1277 (vw), 1238 (w), 1218 (m), 1192 (m), 1111 (w), 1099 (w), 1003 (s), 972 (w), 914 (m), 873 (w), 789 (vs), 745 (vs), 715 (vs), 689 (vs).

(5-allyl-2-fluoro-1,3-phenylene)bis(triethylsilane) (8e)



According to **TP4**, fluorobenzene **6a** (162 mg, 0.5 mmol) and PMDTA (0.32 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol, 3.0 equiv.) and CuCN•2LiCl (0.05 mL, 1.0 M in THF, 0.05 mmol, 0.1 equiv.) were added, followed by allyl bromide (0.15 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (149 mg, 0.41 mmol, 82%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.17 (d, *J* = 5.3 Hz, 2H), 6.05 – 5.88 (m, 1H), 5.08 (d, *J* = 1.6 Hz, 1H), 5.05 (dq, *J* = 6.1, 1.7 Hz, 1H), 3.39 – 3.32 (m, 2H), 1.01 – 0.91 (m, 18H), 0.88 – 0.76 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.88 (d, *J* = 234.4 Hz), 137.77, 137.37 (d, *J* = 12.3 Hz), 134.33 (d, *J* = 2.9 Hz), 121.95 (d, *J* = 37.3 Hz), 115.60, 39.56 (d, *J* = 1.4 Hz), 7.43, 3.56 (d, *J* = 1.7 Hz).

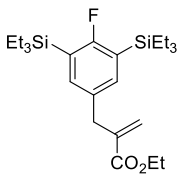
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −89.77 (t, *J* = 5.1 Hz).

MS (EI, 70 eV): *m/z* (%) = 364 (3), 307 (19), 279 (32), 251 (32), 223 (19), 219 (33), 207 (19), 203 (17), 201 (66), 195 (33), 193 (22), 191 (31), 189 (14), 183 (15), 181 (35), 173 (100), 165 (35), 163 (72), 151 (25), 145 (49), 143 (42), 117 (38), 115 (27), 105 (25), 103 (32), 91 (18), 87 (19), 77 (52), 75 (70), 59 (14).

HRMS (EI): *m/z* calc. for [$C_{21}H_{37}F^{28}Si_2$]: 364.2418 [M]$^{\bullet+}$; found: 364.2415.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2909 (w), 2874 (m), 1658 (s), 1598 (w), 1566 (m), 1457 (w), 1447 (w), 1418 (w), 1395 (w), 1378 (m), 1317 (w), 1276 (vs), 1222 (m), 1198 (w), 1168 (m), 1099 (s), 1001 (s), 970 (vs), 921 (w), 842 (w), 779 (vs), 755 (vs), 708 (vs), 689 (vs).

ethyl 2-(4-fluoro-3,5-bis(triethylsilyl)benzyl)acrylate (8f)



According to **TP4**, fluorobenzene **6a** (162 mg, 0.5 mmol) and PMDTA (0.32 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol, 3.0 equiv.) and CuCN•2LiCl (0.05 mL, 1.0 M in THF, 0.05 mmol, 0.1 equiv.) were added, followed by ethyl 2-(bromomethyl)acrylate[124] (0.24 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (149 mg, 0.34 mmol, 68%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.18 (d, *J* = 5.3 Hz, 2H), 6.22 (d, *J* = 1.5 Hz, 1H), 5.37 (q, *J* = 1.5 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.61 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.98 – 0.92 (m, 18H), 0.85 – 0.79 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.14 (d, *J* = 234.9 Hz), 167.13, 141.04 (d, *J* = 0.9 Hz), 138.04 (d, *J* = 12.4 Hz), 133.29 (d, *J* = 2.9 Hz), 125.74, 122.12 (d, *J* = 37.5 Hz), 60.84, 37.50 (d, *J* = 1.4 Hz), 14.28, 7.51 (d, *J* = 0.7 Hz), 3.65 (d, *J* = 1.6 Hz).

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −89.42 (t, *J* = 4.7 Hz).

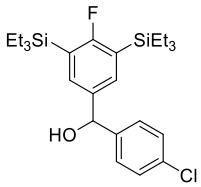
MS (EI, 70 eV): *m/z* (%) = 436 (1), 333 (10), 299 (10), 281 (10), 277 (10), 249 (14), 229 (14), 227 (21), 226 (13), 225 (100), 217 (12), 209 (38), 207 (49), 201 (10), 199 (16), 191 (12), 155 (20), 149 (10), 145 (11), 143 (13), 129 (21), 128 (14), 117 (10), 115 (12), 103 (16), 93 (28), 87 (10), 84 (12), 78 (14), 77 (14), 75 (40), 59 (10).

[124] J. Villieras, M. Rambaud, *Synthesis* **1982**, 924.

HRMS (EI): *m/z* calc. for [$C_{24}H_{41}FO_2{}^{28}Si_2$]: 436.2629 [M]$^{\bullet+}$; found: 436.2617.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2937 (m), 2909 (m), 2874 (m), 1717 (s), 1629 (w), 1577 (w), 1457 (m), 1392 (vs), 1324 (w), 1299 (w), 1279 (w), 1220 (m), 1192 (s), 1133 (s), 1104 (vs), 1003 (s), 947 (m), 921 (w), 788 (vs), 748 (vs), 718 (vs), 686 (vs).

(4-chlorophenyl)(4-fluoro-3,5-bis(triethylsilyl)phenyl)methanol (8g)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by 4-chlorobenzaldehyde (492 mg, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (282 mg, 0.61 mmol, 61%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.33 (d, *J* = 5.2 Hz, 2H), 7.32 – 7.30 (m, 4H), 5.80 (s, 1H), 2.24 (s, 1H), 0.98 – 0.89 (m, 18H), 0.84 – 0.76 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.89 (d, *J* = 236.9 Hz), 142.47, 138.13 (d, *J* = 2.9 Hz), 135.89 (d, *J* = 12.9 Hz), 133.33, 128.69, 127.88, 122.73 (d, *J* = 37.9 Hz), 75.58 (d, *J* = 1.3 Hz), 7.52, 3.63 (d, *J* = 1.7 Hz).

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −86.67 (t, *J* = 5.6 Hz).

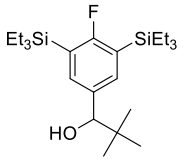
MS (EI, 70 eV): *m/z* (%) = 464 (9), 410 (12), 409 (42), 408 (35), 407 (100), 382 (10), 381 (30), 380 (22), 353 (18), 352 (13), 351 (52), 333 (13), 315 (35), 314 (19), 313 (72), 277 (11), 193 (12), 165 (14), 139 (15), 138 (11), 87 (16), 77 (28), 59 (21), 43 (17).

HRMS (EI): *m/z* calc. for [$C_{25}H_{38}Cl^{19}FO^{28}Si_2$]: 464.2134 [M]$^{\bullet+}$; found: 464.2125.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3261 (w), 2953 (s), 2935 (m), 2908 (m), 2874 (s), 1576 (m), 1490 (m), 1456 (w), 1415 (m), 1388 (s), 1241 (m), 1219 (w), 1193 (m), 1102 (vs), 1013 (vs), 1004 (vs), 963 (m), 926 (m), 905 (w), 853 (w), 839 (m), 829 (m), 783 (s), 748 (vs), 727 (vs), 713 (vs), 690 (vs).

m.p. (°C): 50.2–52.4.

1-(4-fluoro-3,5-bis(triethylsilyl)phenyl)-2,2-dimethylpropan-1-ol (8h)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by trimethylacetaldehyde (301 mg, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (330 mg, 0.80 mmol, 80%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.31 (d, *J* = 5.4 Hz, 2H), 4.39 (d, *J* = 2.0 Hz, 1H), 1.83 (d, *J* = 2.4 Hz, 1H), 0.98 – 0.92 (m, 18H), 0.90 (s, 9H), 0.87 – 0.79 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.79 (d, *J* = 235.8 Hz), 136.63 (d, *J* = 12.5 Hz), 136.54, 121.10 (d, *J* = 37.5 Hz), 82.27 (d, *J* = 1.2 Hz), 35.84 (d, *J* = 0.9 Hz), 26.01, 7.53 (d, *J* = 0.8 Hz), 3.70 (d, *J* = 1.7 Hz).

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −87.99 (t, *J* = 5.7 Hz).

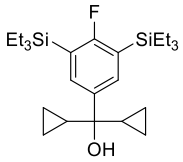
MS (EI, 70 eV): *m/z* (%) = 392 (8), 354 (24), 353 (100), 229 (14), 225 (27), 221 (11), 219 (15), 209 (13), 207 (28), 201 (24), 193 (17), 163 (17), 149 (17), 145 (35), 143 (12), 141 (12), 129 (19), 128 (17), 115 (13), 105 (13), 103 (11), 91 (17), 87 (39), 77 (24), 75 (43), 59 (27).

HRMS (EI): *m/z* calc. for [$C_{23}H_{41}F^{28}Si_2$]: 392.2731 [M−H_2O]$^{\bullet+}$; found: 392.2727.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3393 (br vw), 2952 (m), 2873 (m), 1684 (w), 1577 (w), 1456 (w), 1417 (w), 1393 (m), 1291 (w), 1221 (m), 1194 (m), 1102 (s), 1058 (m), 1004 (s), 943 (m), 904 (m), 875 (w), 783 (s), 719 (vs), 686 (vs), 668 (vs), 655 (s).

m.p. (°C): 46.8–48.9.

Dicyclopropyl(4-fluoro-3,5-bis(triethylsilyl)phenyl)methanol (8i)



According to **TP4**, fluorobenzene **6a** (162 mg, 0.5 mmol) and PMDTA (0.32 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by dicyclopropylketone (286 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (165 mg, 0.38 mmol, 76%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.64 (d, *J* = 5.4 Hz, 2H), 1.47 (d, *J* = 2.7 Hz, 1H), 1.18 (tt, *J* = 8.4, 5.5 Hz, 2H), 1.02 – 0.94 (m, 18H), 0.90 – 0.81 (m, 12H), 0.61 – 0.49 (m, 4H), 0.44 – 0.35 (m, 4H).

^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 171.44 (d, *J* = 235.6 Hz), 141.13 (d, *J* = 2.9 Hz), 135.23 (d, *J* = 12.4 Hz), 121.03 (d, *J* = 37.3 Hz), 73.94 (d, *J* = 1.0 Hz), 20.80, 7.58, 3.77 (d, *J* = 1.6 Hz), 1.96, 0.48.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −88.99 (t, *J* = 5.5 Hz).

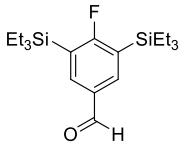
MS (EI, 70 eV): *m/z* (%) = 434 (1), 406 (22), 302 (22), 245 (29), 243 (34), 225 (30), 217 (58), 215 (36), 197 (59), 195 (32), 189 (20), 187 (22), 169 (40), 167 (100), 166 (33), 165 (95), 155 (23), 153 (63), 152 (42), 141 (46), 128 (23), 115 (25), 105 (35), 103 (28), 87 (97), 77 (97), 75 (83), 59 (57).

HRMS (EI): *m/z* calc. for $[C_{25}H_{43}FO^{28}Si_2]$: 434.2836 $[M]^{\bullet+}$; found: 434.2831.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3307 (br w), 3006 (vw), 2952 (s), 2909 (m), 2874 (s), 1577 (w), 1457 (m), 1398 (s), 1340 (w), 1222 (w), 1153 (w), 1123 (w), 1094 (s), 1017 (s), 999 (vs), 977 (s), 897 (s), 851 (vw), 818 (vw), 788 (vs), 752 (vs), 720 (vs), 685 (s).

m.p. (°C): 48.5–50.2.

4-fluoro-3,5-bis(triethylsilyl)benzaldehyde (8j)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by dimethylformamide (0.27 mL, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (260 mg, 0.74 mmol, 74%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.98 (s, 1H), 7.93 (d, *J* = 5.4 Hz, 2H), 1.01 – 0.92 (m, 18H), 0.89 (ddt, *J* = 9.1, 6.9, 1.1 Hz, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 191.66, 175.87 (d, *J* = 246.3 Hz), 140.09 (d, *J* = 14.8 Hz), 132.36 (d, *J* = 2.4 Hz), 124.05 (d, *J* = 39.2 Hz), 7.43, 3.46 (d, *J* = 1.7 Hz).

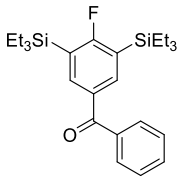
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −75.00 (t, *J* = 5.7 Hz).

MS (EI, 70 eV): *m/z* (%) = 351 (1), 285 (100), 283 (14), 267 (55), 265 (17), 257 (99), 239 (50), 229 (45), 227 (11), 225 (10), 211 (26), 209 (19), 203 (13), 201 (84), 199 (11), 183 (50), 179 (23), 161 (22), 149 (12), 139 (11), 137 (11), 131 (11), 117 (20), 115 (19), 105 (12), 91 (47), 89 (12), 87 (13), 77 (48), 75 (62), 63 (13), 59 (12).

HRMS (EI): *m/z* calc. for $[C_{19}H_{32}FO^{28}Si_2]$: 351.1976 $[M-H]^{\bullet+}$; found: 351.1964.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2937 (w), 2910 (w), 2875 (m), 1692 (s), 1568 (m), 1457 (w), 1418 (w), 1390 (m), 1364 (s), 1291 (w), 1217 (m), 1195 (w), 1095 (s), 1003 (s), 976 (w), 929 (s), 907 (m), 795 (s), 772 (m), 755 (vs), 719 (vs), 689 (s).

(4-fluoro-3,5-bis(triethylsilyl)phenyl)(phenyl)methanone (8k)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by *N*-methoxy-*N*-methylbenzamide (578 mg, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (306 mg, 0.71 mmol, 71%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.91 (dd, *J* = 5.4, 1.2 Hz, 2H), 7.81 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.61 – 7.54 (m, 1H), 7.48 (td, *J* = 7.5, 1.2 Hz, 2H), 1.02 – 0.93 (m, 18H), 0.93 – 0.82 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 196.04, 174.70 (d, *J* = 243.6 Hz), 140.18 (d, *J* = 13.9 Hz), 137.88, 133.14 (d, *J* = 2.5 Hz), 132.40, 130.07, 128.26, 122.79 (d, *J* = 38.6 Hz), 7.40, 3.49.

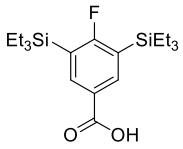
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −78.64 (t, *J* = 5.8 Hz).

MS (EI, 70 eV): *m/z* (%) = 428 (1), 400 (23), 399 (81), 390 (14), 389 (49), 372 (19), 371 (71), 362 (16), 361 (69), 344 (21), 343 (100), 341 (33), 333 (54), 316 (14), 315 (88), 305 (20), 287 (33), 285 (18), 277 (18), 259 (38), 257 (15), 237 (22), 229 (24), 213 (16), 207 (20), 178 (21), 165 (73), 105 (76), 77 (52), 75 (28).

HRMS (EI): *m/z* calc. for $[C_{25}H_{37}{}^{19}FO^{28}Si_2]$: 428.2367 $[M]^{\bullet+}$; found: 428.2354.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2937 (w), 2909 (w), 2874 (m), 1658 (s), 1566 (m), 1464 (w), 1457 (w), 1447 (w), 1395 (w), 1378 (m), 1317 (w), 1276 (vs), 1221 (m), 1198 (w), 1168 (m), 1099 (s), 1001 (s), 970 (vs), 921 (w), 843 (w), 779 (vs), 755 (vs), 733 (s), 707 (vs), 697 (vs), 688 (vs).

4-fluoro-3,5-bis(triethylsilyl)benzoic acid (8l)



According to **TP4**, fluorobenzene **6a** (324 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 m, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added. A second glass vessel, which was connected by teflon tubing, was charged with dry ice, bubbling CO_2 into the reaction mixture. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 8:2) afforded the title compound as a colorless solid (231 mg, 0.63 mmol, 63%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.20 (d, *J* = 5.4 Hz, 2H), 1.07 – 0.82 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 175.76 (d, *J* = 245.0 Hz), 172.51, 140.49 (d, *J* = 14.4 Hz), 124.95 (d, *J* = 2.5 Hz), 123.34 (d, *J* = 39.2 Hz), 7.47, 3.56.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −76.94.

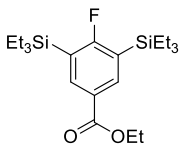
MS (EI, 70 eV): *m/z* (%) = 339 (4), 312 (26), 311 (88), 284 (20), 283 (100), 256 (17), 255 (60), 227 (10), 217 (44), 199 (31), 127 (17), 77 (10), 43 (26).

HRMS (EI): *m/z* calc. for [$C_{17}H_{28}{}^{19}FO_2{}^{28}Si_2$]: 339.1612 [M−Et]$^{\bullet+}$; found: 339.1603.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (s), 2936 (m), 2896 (m), 2872 (m), 2650 (w), 2552 (w), 1684 (vs), 1576 (s), 1456 (w), 1436 (w), 1418 (w), 1383 (s), 1291 (vs), 1235 (m), 1221 (s), 1199 (m), 1162 (s), 1102 (s), 1079 (w), 1004 (vs), 960 (s), 947 (s), 903 (s), 778 (vs), 751 (vs), 733 (s), 712 (vs), 691 (s), 671 (m).

m.p. (°C): 116.8–118.6.

Ethyl 4-fluoro-3,5-bis(triethylsilyl)benzoate (8m)



According to **TP4**, fluorobenzene **6a** (162 mg, 0.5 mmol) and PMDTA (0.32 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and $MgCl_2$ (3.0 mL, 0.5 M in THF, 1.5 mmol, 3.0 equiv.) was added, followed by ethyl cyanoformate (0.17 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (102 mg, 0.26 mmol, 51%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.09 (d, *J* = 5.4 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 0.99 – 0.93 (m, 18H), 0.90 – 0.82 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 175.05 (d, *J* = 243.4 Hz), 166.61, 139.59 (d, *J* = 14.0 Hz), 126.08 (d, *J* = 2.9 Hz), 122.87 (d, *J* = 38.6 Hz), 61.01, 14.51, 7.46, 3.53.

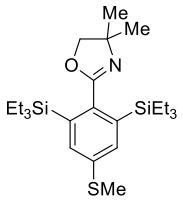
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -78.78 (t, *J* = 5.6 Hz).

MS (EI, 70 eV): *m/z* (%) = 367 (1), 357 (17), 339 (13), 329 (27), 311 (20), 301 (27), 283 (22), 273 (13), 218 (12), 217 (100), 189 (17), 181 (12), 161 (11), 133 (14), 131 (11), 77 (15), 75 (17).

HRMS (EI): *m/z* calc. for [$C_{19}H_{32}FO_2{}^{28}Si_2$]: 367.1925 [M–Et]$^{\bullet+}$; found: 367.1919.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2938 (w), 2910 (w), 2875 (m), 1720 (vs), 1576 (m), 1457 (w), 1418 (w), 1386 (m), 1365 (m), 1269 (vs), 1239 (m), 1217 (m), 1173 (w), 1128 (vs), 1003 (s), 975 (w), 922 (w), 866 (w), 786 (s), 771 (s), 750 (s), 720 (s), 687 (m), 656 (m).

4,4-dimethyl-2-(4-(methylthio)-2,6-bis(triethylsilyl)phenyl)-4,5-dihydrooxazole (9a)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by MeSSMe (0.16 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (201 mg, 0.45 mmol, 89%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.39 (s, 2H), 4.10 (s, 2H), 2.49 (s, 3H), 1.43 (s, 6H), 1.03 – 0.71 (m, 30H).

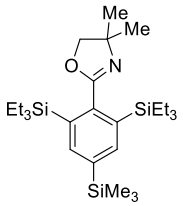
^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 164.03, 138.28, 137.82, 137.29, 133.82, 78.78, 68.46, 29.19, 15.54, 7.77, 4.34.

MS (EI, 70 eV): *m/z* (%) = 421 (10), 420 (29), 366 (46), 348 (54), 338 (59), 320 (44), 310 (75), 292 (72), 282 (22), 281 (16), 265 (27), 264 (23), 255 (13), 237 (26), 225 (55), 209 (26), 207 (47), 199 (21), 196 (14), 181 (16), 125 (24), 45 (18), 44 (66), 42 (100), 41 (16).

HRMS (EI): *m/z* calc. for $[C_{22}H_{38}NOS^{28}Si_2]$: 420.2213 $[M-Et]^{\bullet+}$; found: 420.2213.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2935 (m), 2906 (w), 2872 (m), 1652 (m), 1549 (w), 1463 (w), 1419 (w), 1397 (w), 1363 (w), 1343 (w), 1285 (w), 1238 (m), 1209 (w), 1182 (w), 1132 (m), 1119 (m), 1037 (s), 1001 (s), 961 (s), 921 (w), 868 (w), 778 (s), 721 (vs), 688 (s).

2-(2,6-bis(triethylsilyl)-4-(trimethylsilyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (9b)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by trimethylsilyl chloride (0.22 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a yellow oil (211 mg, 0.44 mmol, 89%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.70 (s, 2H), 4.11 (s, 2H), 1.44 (s, 6H), 1.04 – 0.73 (m, 30H), 0.26 (s, 9H).

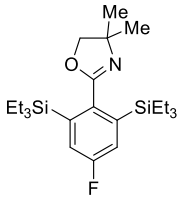
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.41, 141.26, 138.45, 136.33, 134.86, 78.87, 68.46, 29.22, 7.81, 4.48, -1.10.

MS (EI, 70 eV): *m/z* (%) = 461 (22), 446 (77), 392 (31), 375 (29), 374 (100), 364 (31), 347 (14), 346 (53), 337 (11), 336 (469), 319 (17), 318 (91), 308 (16), 304 (11), 291 (25), 290 (40), 263 (21), 262 (15), 252 (10), 235 (23), 234 (15), 233 (11), 225 (17), 207 (35), 161 (10), 159 (10), 73 (35), 41 (10).

HRMS (EI): *m/z* calc. for $[C_{25}H_{46}NO^{28}Si_3]$: 460.2887 $[M-Me]^{\bullet+}$; found: 460.2881.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2908 (w), 2891 (w), 2873 (m), 1654 (m), 1464 (w), 1418 (vw), 1400 (vw), 1363 (w), 1342 (vw), 1287 (w), 1248 (m), 1184 (vw), 1036 (s), 1002 (m), 961 (m), 875 (s), 850 (s), 835 (vs), 782 (s), 720 (vs), 689 (s).

2-(4-fluoro-2,6-bis(triethylsilyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (9c)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by *N*-fluorobenzenesulfonimide (552 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (131 mg, 0.31 mmol, 62%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.21 (d, *J* = 9.2, 2H), 4.11 (s, 2H), 1.44 (s, 6H), 1.02 – 0.75 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.50 (d, *J* = 37.5 Hz), 160.80, 140.64 (d, *J* = 3.7 Hz), 137.59 (d, *J* = 3.2 Hz), 122.67 (d, *J* = 19.2 Hz), 78.88, 68.51, 29.19, 7.66, 4.20.

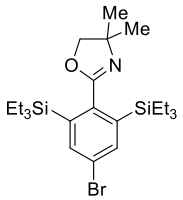
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −114.3 (t, *J* = 9.2).

MS (EI, 70 eV): *m/z* (%) = 420 (1), 320 (12), 310 (14), 308 (15), 292 (10), 282 (24), 268 (21), 264 (15), 250 (36), 225 (10), 222 (15), 181 (11), 150 (11).

HRMS (EI): *m/z* calc. for $[C_{23}H_{39}FNO^{28}Si_2]$: 420.2554 $[M-H]^{\bullet+}$; found: 420.2551.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2937 (w), 2908 (w), 2873 (m), 1654 (m), 1570 (m), 1458 (w), 1418 (w), 1399 (w), 1342 (w), 1281 (m), 1218 (s), 1182 (m), 1106 (vw), 1040 (m), 1001 (s), 961 (m), 930 (m), 882 (w), 860 (vw), 777 (s), 721 (vs), 691 (s).

2-(4-bromo-2,6-bis(triethylsilyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (9d)



According to **TP4**, oxazolylbenzene **6b** (12.1 mg, 30.0 mmol) and PMDTA (18.8 mL, 90.0 mmol) were dissolved in *n*hexane (60 mL). *n*BuLi (35.3 mL, 2.55 M in hexane, 90.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (90 mL, 1.0 M in THF, 90 mmol, 3.0 equiv.) was added, followed by a solution of Br_2 (5.41 mL, 105 mmol) in THF (30 mL). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (13.9 g, 28.7 mmol, 96%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.62 (s, 2H), 4.11 (s, 2H), 1.43 (s, 6H), 1.07 – 0.74 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.54, 140.38, 140.10, 138.75, 124.14, 78.92, 68.60, 29.15, 7.66, 4.19.

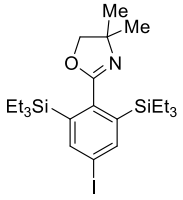
MS (EI, 70 eV): *m/z* (%) = 454 (10), 452 (8), 380 (28), 370 (41), 354 (14), 352 (15), 344 (53), 342 (51), 326 (21), 324 (18), 316 (13), 314 (13), 299 (15), 281 (13), 258 (12), 256 (11), 230 (10), 227 (17), 226 (11), 225 (88), 212 (10), 209 (27), 207 (41), 93 (11), 81 (10), 79 (10), 75 (14), 45 (10), 44 (21), 42 (100).

HRMS (EI): *m/z* calc. for $[C_{21}H_{35}{}^{79}BrNOS^{28}Si_2]$: 452.1441 $[M-Et]^{\bullet+}$; found: 452.1439.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2906 (w), 2873 (m), 1656 (m), 1537 (vw), 1461 (w), 1418 (vw), 1393 (w), 1341 (vw), 1276 (w), 1238 (w), 1179 (vw), 1109 (m), 1037 (s), 1003 (s), 959 (m), 921 (w), 881 (w), 777 (s), 755 (w), 723 (vs), 691 (m).

m.p. (°C): 48.5–50.4.

2-(4-iodo-2,6-bis(triethylsilyl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (9e)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol, 3.0 equiv) was added, followed by a solution of I_2 (444 mg, 1.75 mmol) in THF (1 mL). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (232 mg, 0.44 mmol, 88%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.82 (s, 2H), 4.10 (s, 2H), 1.43 (s, 6H), 0.99 – 0.72 (m, 30H).

^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 163.59, 144.75, 140.87, 140.25, 136.32, 78.92, 68.63, 29.17, 7.68, 4.18.

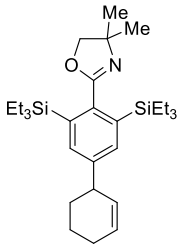
MS (EI, 70 eV): *m/z* (%) = 500 (91), 447 (30), 428 (100), 418 (40), 401 (13), 400 (63), 391 (10), 390 (54), 373 (15), 372 (90), 362 (11), 345 (27), 344 (24), 317 (22), 316 (11), 314 (10), 289 (23), 288 (10), 287 (12), 279 (14), 261 (16), 155 (12), 127 (20), 44 (16), 42 (15), 41 (12).

HRMS (EI): *m/z* calc. for $[C_{21}H_{35}INO^{28}Si_2]$: 500.1302 $[M-Et]^{\bullet+}$; found: 500.1302.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2905 (w), 2872 (m), 1652 (m), 1533 (vw), 1460 (w), 1418 (vw), 1392 (w), 1365 (vw), 1340 (vw), 1277 (w), 1237 (w), 1177 (vw), 1102 (w), 1037 (m), 1002 (s), 958 (m), 922 (w), 879 (vw), 776 (s), 755 (m), 721 (vs), 688 (s), 674 (s).

m.p. (°C): 72.2–74.0.

2-(3,5-bis(triethylsilyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-yl)-4,4-dimethyl-4,5-dihydrooxazole (9f)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol, 3.0 equiv.) and CuCN•2LiCl (0.05 mL, 1.0 M in THF, 0.05 mmol, 0.1 equiv.) were added, followed by 3-bromocyclohex-1-ene (0.20 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (207 mg, 0.43 mmol, 86%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.37 (s, 2H), 5.96 – 5.88 (m, 1H), 5.75 – 5.67 (m, 1H), 4.11 (s, 2H), 3.39 (ddt, *J* = 8.1, 5.5, 2.8 Hz, 1H), 2.13 – 2.04 (m, 2H), 2.05 – 1.94 (m, 1H), 1.82 – 1.47 (m, 2H), 1.43 (s, 7H), 0.99 – 0.79 (m, 30H).

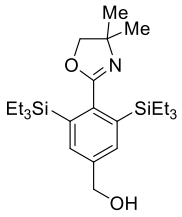
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.64, 144.65, 139.33, 136.21, 135.87, 129.95, 128.62, 78.83, 68.36, 41.80, 32.64, 29.22, 25.16, 20.98, 7.80, 4.40.

MS (EI, 70 eV): *m/z* (%) = 482 (1), 455 (36), 454 (100), 382 (10), 344 (10), 326 (12), 312 (15), 284 (12), 243 (11), 225 (30), 215 (14), 209 (16), 207 (46), 183 (10), 181 (11), 81 (13), 79 (12), 75 (14), 59 (14).

HRMS (EI): *m/z* calc. for $[C_{29}H_{48}NO^{28}Si_2]$: 482.3274 $[M-H]^{\bullet+}$; found: 482.3275.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2950 (m), 2933 (m), 2908 (m), 2872 (m), 1652 (m), 1460 (w), 1418 (w), 1343 (w), 1287 (w), 1238 (w), 1206 (w), 1183 (w), 1127 (vw), 1040 (m), 1001 (s), 960 (m), 782 (s), 720 (vs), 690 (s), 669 (m).

(4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)phenyl)methanol (9g)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by paraformaldehyde (53 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (172 mg, 0.40 mmol, 79%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.52 (s, 2H), 4.70 (s, 2H), 4.11 (s, 2H), 1.66 (s, 1H), 1.44 (s, 6H), 1.03 – 0.77 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.16, 141.32, 139.07, 136.95, 134.98, 78.83, 68.52, 65.75, 29.23, 7.78, 4.31.

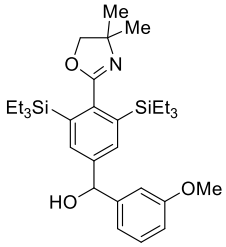
MS (EI, 70 eV): *m/z* (%) = 433 (1), 419 (100), 406 (11), 405 (30).

HRMS (EI): *m/z* calc. for $[C_{24}H_{43}NO_2{}^{28}Si_2]$: 433.2832 $[M]^{\bullet+}$; found: 433.2831.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3281 (br w), 2954 (m), 2937 (m), 2898 (m), 2876 (s), 1653 (m), 1454 (m), 1419 (w), 1398 (w), 1367 (w), 1343 (w), 1283 (s), 1237 (m), 1203 (m), 1180 (w), 1125 (w), 1045 (vs), 1002 (vs), 957 (vs), 933 (m), 913 (m), 880 (m), 861 (w), 783 (s), 759 (s), 718 (vs), 693 (s), 681 (m).

m.p. (°C): 181.7–183.6.

(4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)phenyl)(3-methoxyphenyl)methanol (9h)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting

solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by 3-methoxybenzaldehyde (238 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (227 mg, 0.42 mmol, 84%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.54 (s, 2H), 7.22 (t, *J* = 8.0, 1H), 6.90 (dt, *J* = 7.5, 1.6, 2H), 6.82 – 6.76 (m, 1H), 5.79 (s, 1H), 4.11 (s, 2H), 3.75 (s, 3H), 2.56 (s, 1H), 1.43 (s, 6H), 0.89 (td, *J* = 8.1, 7.4, 3.2, 18H), 0.86 – 0.80 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.29, 159.81, 145.51, 141.87, 140.98, 136.72, 134.58, 129.53, 119.04, 113.56, 111.71, 78.84, 76.24, 68.39, 55.25, 29.14, 7.70, 4.28.

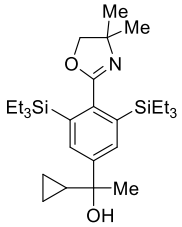
MS (EI, 70 eV): *m/z* (%) = 539 (1), 512 (12), 511 (34), 510 (100).

HRMS (EI): *m/z* calc. for $[C_{31}H_{49}NO_3{}^{28}Si_2]$: 539.3251 $[M]^{\bullet+}$; found: 539.3236.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3212 (br w), 2953 (m), 2900 (m), 2872 (m), 2829 (w), 1648 (m), 1601 (m), 1464 (m), 1344 (w), 1285 (m), 1256 (s), 1204 (m), 1180 (w), 1156 (m), 1047 (vs), 1003 (s), 955 (s), 935 (m), 892 (w), 850 (w), 785 (s), 761 (s), 725 (s), 694 (s).

m.p. (°C): 140.5–142.4.

1-cyclopropyl-1-(4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)phenyl) ethan-1-ol (9i)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by cyclopropyl methyl ketone (0.17 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (210 mg, 0.43 mmol, 86%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.72 (s, 2H), 4.11 (s, 2H), 1.70 (s, 1H), 1.49 (s, 4H), 1.44 (s, 5H), 1.22 (tt, *J* = 8.2, 5.7 Hz, 1H), 0.98 – 0.90 (m, 18H), 0.90 – 0.82 (m, 12H), 0.54 – 0.31 (m, 4H).

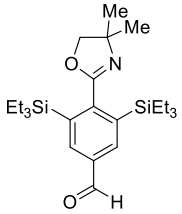
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.41, 145.58, 140.20, 135.98, 133.23, 78.82, 73.40, 68.37, 29.16, 28.42, 22.86, 7.76, 4.37, 1.90, 1.19.

MS (EI, 70 eV): *m/z* (%) = 458 (55), 299 (16), 281 (14), 227 (19), 226 (14), 225 (100), 209 (32), 207 (49), 191 (10), 42 (80).

HRMS (EI): *m/z* calc. for $[C_{26}H_{44}NO_2{}^{28}Si_2]$: 458.2911 $[M-Et]^{\bullet+}$; found: 458.2908.

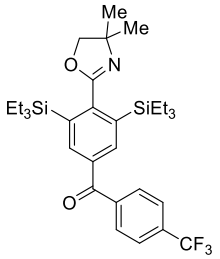
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3275 (vw), 2952 (w), 2906 (w), 2873 (w), 1652 (w), 1460 (w), 1419 (vw), 1403 (vw), 1383 (vw), 1365 (w), 1343 (w), 1285 (w), 1236 (w), 1208 (vw), 1182 (vw), 1112 (m), 1094 (w), 1037 (m), 1018 (m), 1001 (m), 960 (m), 915 (m), 901 (w), 782 (m), 721 (vs), 687 (s).
m.p. (°C): 98.6–100.1.

4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)benzaldehyde (9j)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by dimethylformamide (0.14 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless oil (145 mg, 0.34 mmol, 67%).
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.04 (s, 1H), 8.02 (s, 2H), 4.15 (s, 2H), 1.45 (s, 6H), 1.02 – 0.75 (m, 30H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 192.95, 163.37, 147.62, 138.12, 137.64, 134.07, 79.06, 68.75, 29.08, 7.58, 4.11.
MS (EI, 70 eV): *m/z* (%) = 402 (34), 348 (35), 331 (16), 330 (75), 320 (46), 303 (10), 302 (69), 292 (77), 275 (14), 274 (100), 272 (11), 264 (22), 247 (30), 246 (42), 236 (11), 219 (30), 218 (20), 209 (14), 191 (29), 190 (15), 189 (14), 181 (16), 163 (22), 145 (19), 143 (12).
HRMS (EI): *m/z* calc. for $[C_{22}H_{36}NO_2{}^{28}Si_2]$: 402.2285 $[M-Et]^{\bullet+}$; found: 402.2282.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2935 (m), 2907 (w), 2873 (m), 1722 (w), 1702 (s), 1654 (m), 1576 (w), 1464 (w), 1418 (w), 1395 (w), 1365 (w), 1342 (w), 1279 (m), 1239 (m), 1207 (m), 1180 (w), 1140 (vw), 1116 (vw), 1038 (s), 1002 (vs), 960 (s), 913 (s), 892 (w), 858 (w), 782 (s), 717 (vs), 685 (s).

(4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)phenyl)(4-(trifluoromethyl)-phenyl)methanone (9k)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide (408 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (201 mg, 0.35 mmol, 70%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.96 (s, 2H), 7.90 (d, *J* = 8.1 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 4.17 (s, 2H), 1.47 (s, 6H), 1.01 – 0.80 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 195.89, 163.42, 146.33, 140.73 (q, *J* = 1.1 Hz), 137.73, 137.61, 134.84, 133.98 (q, *J* = 32.7 Hz), 130.34, 125.43 (q, *J* = 3.7 Hz), 123.82 (q, *J* = 272.7 Hz), 79.10, 68.80, 29.15, 7.65, 4.20.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −63.04.

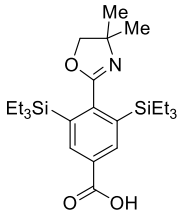
MS (EI, 70 eV): *m/z* (%) = 546 (100), 492 (28), 475 (23), 474 (70), 447 (21), 446 (70), 445 (23), 419 (10), 418 (38), 390 (20), 362 (10), 307 (12), 224 (13), 210 (15), 207 (10), 195 (11), 176 (17), 173 (17), 165 (23), 145 (17), 126 (10), 43 (12), 42 (16), 41 (17).

HRMS (EI): *m/z* calc. for $[C_{29}H_{39}F_3NO_2{}^{28}Si_2]$: 546.2471 $[M-Et]^{\bullet+}$; found: 546.2480.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2948 (w), 2935 (w), 2905 (w), 2872 (w), 1656 (s), 1572 (vw), 1462 (vw), 1407 (w), 1324 (s), 1277 (s), 1246 (w), 1165 (s), 1132 (vs), 1106 (m), 1064 (s), 1042 (s), 1015 (m), 977 (s), 960 (m), 923 (w), 860 (m), 783 (s), 719 (vs), 681 (s).

m.p. (°C): 64.8–66.7.

4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)benzoic acid (9l)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added. A second glass vessel, which was connected by teflon tubing, was charged with dry ice, bubbling CO_2 into the mixture. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (152 mg, 0.34 mmol, 68%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.25 (s, 2H), 4.18 (s, 2H), 1.51 (s, 6H), 1.06 – 0.60 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.40, 164.37, 146.16, 137.86, 137.16, 128.29, 79.30, 68.61, 29.04, 7.54, 4.08.

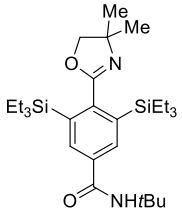
MS (EI, 70 eV): *m/z* (%) = 447 (1), 420 (10), 419 (28), 418 (100).

HRMS (EI): *m/z* calc. for [$C_{24}H_{41}NO_3{}^{28}Si_2$]: 447.2625 [M]$^{\bullet+}$; found: 447.2612.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (m), 2935 (m), 2907 (m), 2873 (s), 1692 (s), 1648 (s), 1579 (w), 1458 (m), 1418 (w), 1395 (w), 1345 (w), 1277 (m), 1239 (s), 1208 (m), 1155 (w), 1139 (m), 1125 (m), 1054 (m), 1040 (m), 1002 (vs), 959 (s), 921 (m), 889 (w), 853 (m), 774 (vs), 756 (m), 719 (vs), 688 (vs).

m.p. (°C): 172.8–174.9.

***N*-(*tert*-butyl)-4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3,5-bis(triethylsilyl)benzamide (9m)**



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by *tert*-butyl isocyanate (0.20 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (175 mg, 0.35 mmol, 70%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.84 (s, 2H), 5.88 (s, 1H), 4.11 (s, 2H), 1.47 (s, 9H), 1.43 (s, 6H), 0.98 – 0.77 (m, 30H).

^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 167.40, 163.54, 144.56, 137.27, 134.47, 134.04, 78.86, 68.64, 51.70, 29.12, 28.97, 7.68, 4.23.

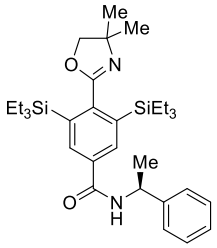
MS (EI, 70 eV): *m/z* (%) = 473 (100), 225 (22), 207 (12), 42 (16).

HRMS (EI): *m/z* calc. for [$C_{26}H_{45}N_2O_2{}^{28}Si_2$]: 473.3020 [M−Et]$^{\bullet+}$; found: 473.3017.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3383 (br vw), 2955 (m), 2935 (w), 2872 (w), 1643 (s), 1576 (vw), 1514 (s), 1454 (w), 1392 (w), 1364 (w), 1341 (vw), 1301 (w), 1284 (w), 1238 (m), 1202 (w), 1182 (w), 1156 (vw), 1036 (m), 1000 (s), 960 (m), 909 (m), 775 (m), 725 (vs), 683 (m).

m.p. (°C): 106.5–108.4.

(*S*)-4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-*N*-(1-phenylethyl)-3,5-bis(triethylsilyl)benzamide (9n)



According to **TP4**, oxazolylbenzene **6b** (202 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by (*S*)-(1-isocyanatoethyl)benzene (258 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (186 mg, 0.34 mmol, 68%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.90 (s, 2H), 7.43 – 7.34 (m, 4H), 7.31 – 7.26 (m, 1H), 6.25 (d, *J* = 7.7 Hz, 1H), 5.34 (p, *J* = 7.1 Hz, 1H), 4.13 (s, 2H), 1.63 (d, *J* = 6.9 Hz, 3H), 1.45 (s, 6H), 0.97 – 0.83 (m, 30H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.28, 163.53, 144.96, 143.39, 137.55, 134.67, 133.00, 128.93, 127.60, 126.26, 78.95, 68.71, 49.47, 29.17, 22.10, 7.73, 4.31.

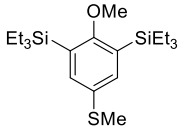
MS (EI, 70 eV): *m/z* (%) = 521 (25), 281 (14), 225 (44), 209 (19), 208 (10), 207 (72), 191 (16), 105 (40), 104 (100), 103 (56), 102 (13), 91 (11), 79 (10), 78 (66), 77 (43).

HRMS (EI): *m/z* calc. for $[C_{30}H_{45}N_2O_2{}^{28}Si_2]$: 521.3020 $[M-Et]^{\bullet+}$; found: 521.3016.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3308 (vw), 2953 (w), 2933 (w), 2872 (w), 2359 (vw), 1655 (w), 1625 (s), 1577 (w), 1524 (s), 1456 (w), 1418 (vw), 1401 (vw), 1375 (vw), 1363 (w), 1332 (w), 1283 (m), 1242 (w), 1207 (w), 1162 (w), 1124 (w), 1036 (m), 1001 (m), 959 (m), 912 (w), 864 (vw), 782 (m), 727 (vs), 699 (vs), 666 (s).

m.p. (°C): 168.0–169.8.

(2-methoxy-5-(methylthio)-1,3-phenylene)bis(triethylsilane) (10a)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by S_2Me_2 (0.31 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (84 mg, 0.22 mmol, 44%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.33 (s, 2H), 3.65 (s, 3H), 2.47 (s, 3H), 0.99 – 0.92 (m, 18H), 0.89 – 0.79 (m, 12H).

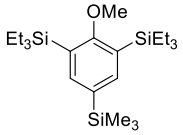
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.54, 137.51, 131.70, 129.80, 63.67, 17.40, 7.71, 4.19.

MS (EI, 70 eV): *m/z* (%) = 382 (1), 197 (16), 179 (31), 151 (15), 137 (10), 135 (24), 117 (56), 107 (42), 91 (20), 89 (100), 87 (38), 77 (22), 75 (13), 61 (51), 59 (27).

HRMS (EI): *m/z* calc. for $[C_{20}H_{38}OS^{28}Si_2]$: 382.2182 $[M]^{\bullet+}$; found: 382.2177.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (w), 2873 (m), 1541 (vw), 1456 (w), 1375 (s), 1210 (s), 1137 (m), 1101 (w), 1003 (vs), 968 (w), 781 (s), 719 (vs), 663 (m).

(2-methoxy-5-(trimethylsilyl)-1,3-phenylene)bis(triethylsilane) (10b)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by trimethylsilylchloride (0.22 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (79 mg, 0.19 mmol, 39%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.59 (s, 2H), 3.69 (s, 3H), 1.02 – 0.93 (m, 18H), 0.91 – 0.81 (m, 12H), 0.26 (s, 9H).

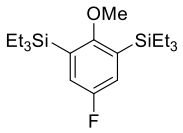
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 173.11, 143.56, 133.46, 127.52, 63.52, 7.79, 4.42, -0.78.

MS (EI, 70 eV): *m/z* (%) = 393 (6), 369 (37), 352 (25), 351 (100), 341 (18), 323 (66), 295 (50), 267 (30), 265 (22), 249 (25), 247 (70), 239 (21), 235 (19), 221 (22), 219 (19), 207 (20), 193 (33), 191 (21), 179 (25), 163 (22), 161 (23), 117 (30), 89 (66), 87 (32), 73 (57), 61 (27), 59 (25).

HRMS (EI): *m/z* calc. for $[C_{26}H_{41}O^{28}Si_3]$: 393.2465 $[M\text{-}Me]^{\bullet+}$; found: 393.2457.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (w), 2874 (w), 1537 (w), 1457 (w), 1417 (vw), 1382 (m), 1247 (m), 1215 (w), 1107 (m), 1003 (m), 974 (vw), 869 (vs), 834 (vs), 782 (s), 718 (vs), 686 (s).

(5-fluoro-2-methoxy-1,3-phenylene)bis(triethylsilane) (10c)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by *N*-fluorobenzenesulfonimide (582 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (71 mg, 0.20 mmol, 40%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.05 (d, *J* = 8.4 Hz, 2H), 3.65 (s, 3H), 0.95 (td, *J* = 7.1, 1.1 Hz, 18H), 0.90 – 0.78 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 158.98 (d, *J* = 245.0 Hz), 138.24, 131.43 (d, *J* = 3.7 Hz), 123.72 (d, *J* = 20.7 Hz), 63.87, 7.63, 4.07.

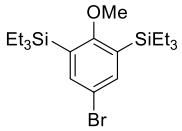
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -121.97 (t, *J* = 8.4 Hz).

MS (EI, 70 eV): *m/z* (%) = 325 (3), 297 (27), 269 (23), 241 (24), 213 (16), 211 (42), 197 (10), 189 (23), 185 (10), 183 (12), 169 (23), 163 (11), 155 (19), 153 (16), 151 (24), 149 (11), 133 (42), 131 (12), 125 (28), 123 (13), 117 (53), 115 (22), 109 (15), 107 (16), 93 (10), 91 (34), 89 (100), 87 (46), 77 (32), 75 (11), 61 (30), 59 (20).

HRMS (EI): *m/z* calc. for [$C_{17}H_{30}FO^{28}Si_2$]: 325.1819 [M–Et]$^{\bullet+}$; found: 325.1820.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2909 (w), 2874 (m), 1572 (vw), 1457 (w), 1418 (vw), 1372 (vs), 1236 (w), 1200 (m), 1163 (w), 1003 (s), 960 (w), 881 (w), 776 (s), 717 (vs).

(5-bromo-2-methoxy-1,3-phenylene)bis(triethylsilane) (10d)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol) was added, followed by a solution of Br_2 (0.09 mL, 1.75 mmol) in THF (1 mL). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (106 mg, 0.26 mmol, 51%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.45 (s, 2H), 3.65 (s, 3H), 0.99 – 0.89 (m, 18H), 0.89 – 0.78 (m, 12H).

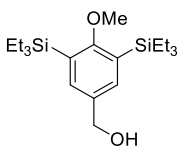
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.03, 140.33, 132.39, 117.83, 63.73, 7.64, 4.07.

MS (EI, 70 eV): *m/z* (%) = 414 (2), 360 (15), 359 (60), 358 (15), 357 (55), 331 (28), 329 (30), 303 (10), 301 (15), 273 (11), 244 (10), 165 (12), 151 (11), 150 (12), 118 (13), 117 (100), 115 (22), 89 (32), 87 (24), 61 (15), 59 (19), 57 (15), 55 (11), 43 (69).

HRMS (EI): *m/z* calc. for [$C_{19}H_{35}{}^{79}BrO^{28}Si_2$]: 414.1410 [M]$^{\bullet+}$; found: 414.1407.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2909 (w), 2874 (m), 1456 (w), 1417 (vw), 1368 (s), 1238 (w), 1207 (m), 1114 (s), 1003 (s), 973 (w), 882 (w), 772 (s), 721 (vs), 683 (m).

(4-methoxy-3,5-bis(triethylsilyl)phenyl)methanol (10e)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by paraformaldehyde (53 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (72 mg, 0.20 mmol, 39%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.40 (s, 2H), 4.64 (s, 2H), 3.67 (s, 3H), 1.63 (s, 1H), 0.99 – 0.92 (m, 18H), 0.90 – 0.80 (m, 12H).

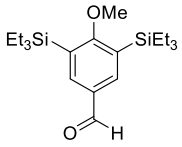
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 172.06, 137.38, 135.00, 129.01, 65.72, 63.64, 7.74, 4.22.

MS (EI, 70 eV): *m/z* (%) = 366 (1), 310 (21), 309 (69), 281 (23), 253 (12), 205 (15), 203 (45), 117 (13), 89 (14), 87 (12), 85 (15), 71 (22), 61 (14), 59 (12), 57 (33), 45 (15), 43 (100).

HRMS (EI): *m*/*z* calc. for $[C_{20}H_{38}O_2{}^{28}Si_2]$: 366.2410 $[M]^{\bullet+}$; found: 366.2398.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3299 (br vw), 2951 (m), 2909 (w), 2873 (m), 1557 (w), 1456 (w), 1417 (w), 1376 (s), 1210 (s), 1108 (m), 1003 (vs), 917 (vw), 889 (vw), 780 (s), 717 (vs), 685 (s).

4-methoxy-3,5-bis(triethylsilyl)benzaldehyde (10f)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by dimethylformamide (0.14 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (69 mg, 0.19 mmol, 38%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.96 (s, 1H), 7.94 (s, 2H), 3.74 (s, 3H), 0.98 – 0.83 (m, 30H).

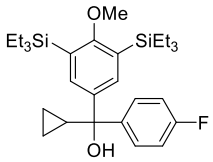
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 192.17, 177.39, 140.63, 131.53, 130.08, 63.55, 7.73, 7.65, 4.00.

MS (EI, 70 eV): 335 (26), 325 (46), 307 (100), 297 (39), 279 (75), 277 (12), 269 (25), 267 (13), 251 (55), 249 (20), 241 (22), 223 (44), 221 (15), 213 (12), 207 (13), 195 (28), 193 (24), 191 (17), 183 (20), 179 (36), 165 (52), 163 (15), 161 (24), 149 (16), 145 (14), 135 (14), 117 (41), 107 (16), 91 (23), 89 (79), 87 (24), 61 (34), 59 (18).

HRMS (EI): *m*/*z* calc. for $[C_{18}H_{31}O_2{}^{28}Si_2]$: 335.1863 $[M–Et]^{\bullet+}$; found: 335.1855.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2909 (w), 2874 (m), 1698 (s), 1571 (w), 1554 (w), 1456 (w), 1417 (w), 1380 (w), 1358 (m), 1212 (s), 1101 (s), 1003 (vs), 926 (m), 782 (m), 721 (vs), 684 (m).

Cyclopropyl(4-fluorophenyl)(4-methoxy-3,5-bis(triethylsilyl)phenyl)methanol (10g)



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by cyclopropyl 4-fluorophenyl ketone (0.25 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a slight yellow oil (110 mg, 0.22 mmol, 44%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.46 (s, 2H), 7.41 – 7.35 (m, 2H), 7.02 – 6.92 (m, 2H), 3.67 (s, 3H), 1.87 (d, *J* = 0.8 Hz, 1H), 1.56 (tt, *J* = 8.2, 5.5 Hz, 1H), 0.94 – 0.87 (m, 18H), 0.84 – 0.75 (m, 12H), 0.69 – 0.61 (m, 1H), 0.58 – 0.39 (m, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.46, 161.84 (d, *J* = 245.0 Hz), 143.50 (d, *J* = 3.1 Hz), 140.58, 137.11, 128.57 (d, *J* = 8.3 Hz), 127.89, 114.51 (d, *J* = 21.0 Hz), 63.57, 21.98, 7.70, 4.28, 2.38, 1.40.

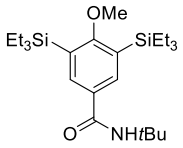
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -116.49 – -116.64 (m).

MS (EI, 70 eV): *m/z* (%) = 482 (1), 443 (15), 254 (13), 252 (14), 249 (12), 225 (17), 209 (12), 207 (39), 203 (14), 202 (19), 196 (13), 189 (10), 183 (12), 165 (11), 123 (100), 117 (30), 115 (12), 109 (25), 107 (20), 105 (11), 103 (24), 89 (78), 87 (76), 77 (12), 75 (37), 61 (39), 59 (54).

HRMS (EI): *m*/*z* calc. for $[C_{29}H_{43}FO^{28}Si_2]$: 482.2836 $[M–H_2O]^{\bullet+}$; found: 482.2829.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (w), 2874 (m), 1603 (vw), 1553 (vw), 1506 (m), 1457 (w), 1418 (w), 1379 (m), 1314 (vw), 1221 (s), 1158 (w), 1107 (s), 1002 (vs), 898 (w), 839 (m), 777 (s), 719 (vs), 684 (m).

***N*-(*tert*-butyl)-4-methoxy-3,5-bis(triethylsilyl)benzamide (10h)**



According to **TP4**, anisole derivative **6c** (168 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by *tert*-butyl isocyanate (0.20 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (83 mg, 0.19 mmol, 38%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.74 (s, 2H), 5.82 (s, 1H), 3.68 (s, 3H), 1.47 (s, 9H), 0.98 – 0.90 (m, 18H), 0.90 – 0.80 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 174.68, 167.57, 136.90, 130.72, 129.16, 63.58, 51.61, 29.06, 7.69, 4.12.

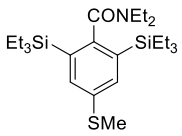
MS (EI, 70 eV): *m/z* (%) = 434 (1), 406 (19), 380 (13), 379 (32), 378 (100), 351 (16), 350 (53), 322 (12), 318 (10), 294 (10), 217 (14), 89 (12), 87 (11), 57 (24), 43 (17).

HRMS (EI): *m/z* calc. for $[C_{24}H_{44}NO_2{}^{28}Si_2]$: 434.2911 $[M–H]^{\bullet+}$; found: 434.2899.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3318 (vw), 2953 (m), 2909 (w), 2874 (w), 1634 (m), 1573 (w), 1532 (m), 1448 (w), 1365 (m), 1313 (m), 1211 (s), 1165 (vw), 1104 (m), 1003 (s), 908 (m), 785 (w), 729 (vs).

m.p. (°C): 56.4 – 58.2.

***N*,*N*-diethyl-4-(methylthio)-2,6-bis(triethylsilyl)benzamide (11a)**



According to **TP4**, benzamide **6d** (203 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by dimethyl disulfide (0.16 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (86 mg, 0.19 mmol, 44%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.37 (s, 2H), 3.51 (q, *J* = 7.2 Hz, 2H), 2.98 (q, *J* = 7.2 Hz, 2H), 2.49 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H), 0.93 – 0.80 (m, 30H).

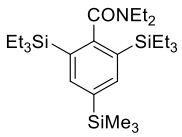
^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 172.08, 146.39, 135.81, 134.38, 133.74, 43.31, 38.74, 15.82, 13.36, 12.85, 7.67, 3.82.

MS (EI, 70 eV): *m/z* (%) = 451 (1), 424 (13), 423 (29), 422 (100).

HRMS (EI): *m/z* calc. for $[C_{29}H_{46}NOS^{28}Si_2]$: 451.2760 $[M]^{\bullet+}$; found: 451.2767.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (w), 2873 (m), 1631 (s), 1548 (w), 1457 (w), 1423 (m), 1378 (w), 1281 (m), 1237 (w), 1129 (m), 1065 (w), 1002 (s), 968 (w), 870 (w), 794 (vs), 721 (vs), 686 (s).

***N*,*N*-diethyl-2,6-bis(triethylsilyl)-4-(trimethylsilyl)benzamide (11b)**



According to **TP4**, benzamide **6d** (203 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by trimethylsilylchloride (0.22 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless solid (110 mg, 0.23 mmol, 46%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.66 (s, 2H), 3.54 (q, *J* = 7.2 Hz, 2H), 3.00 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.96 – 0.64 (m, 30H), 0.27 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 172.46, 149.82, 141.05, 136.61, 131.84, 43.31, 38.63, 13.36, 12.90, 7.73, 4.05, -1.04.

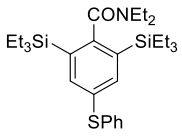
MS (EI, 70 eV): *m/z* (%) = 476 (1), 450 (15), 449 (37), 448 (100), 43 (17).

HRMS (EI): *m/z* calc. for $[C_{26}H_{50}NO^{28}Si_3]$: 476.3200 $[M–H]^{\bullet+}$; found: 476.3202.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (s), 2909 (w), 2872 (m), 1622 (s), 1473 (w), 1456 (w), 1426 (m), 1379 (w), 1286 (m), 1248 (m), 1069 (w), 1002 (m), 881 (w), 851 (vs), 800 (m), 766 (w), 726 (vs), 689 (m).

m.p. (°C): 67.6 – 69.2.

***N*,*N*-diethyl-4-(phenylthio)-2,6-bis(triethylsilyl)benzamide (11c)**



According to **TP4**, benzamide **6d** (203 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by diphenyl disulfide (382 mg, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as an orange oil (112 mg, 0.22 mmol, 44%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.42 (d, *J* = 0.8 Hz, 2H), 7.35 – 7.28 (m, 4H), 7.27 – 7.23 (m, 1H), 3.52 (q, *J* = 7.2 Hz, 2H), 3.00 (q, *J* = 7.2 Hz, 2H), 1.25 (td, *J* = 7.3, 0.7 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.88 – 0.60 (m, 30H).

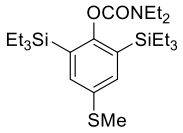
^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 171.98, 148.03, 137.72, 135.38, 135.08, 133.77, 131.38, 129.32, 127.30, 43.29, 38.75, 13.32, 12.81, 7.58, 3.75.

MS (EI, 70 eV): *m/z* (%) = 512 (1), 486 (10), 485 (38), 484 (100), 368 (13), 340 (16), 225 (16), 213 (15), 207 (34), 109 (13), 87 (23), 75 (12), 59 (24).

HRMS (EI): *m/z* calc. for $[C_{29}H_{46}NOS^{28}Si_2]$: 512.2839 $[M–H]^{\bullet+}$; found: 512.2836.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2908 (w), 2873 (m), 1632 (s), 1545 (w), 1473 (w), 1457 (m), 1423 (m), 1378 (w), 1280 (m), 1222 (w), 1124 (m), 1067 (w), 1001 (s), 872 (w), 793 (vs), 722 (vs), 688 (vs).

4-(methylthio)-2,6-bis(triethylsilyl)phenyl diethylcarbamate (12a)



In a modified version of **TP4**, carbamate **6e** (177 mg, 0.42 mmol) and PMDTA (0.26 mL, 1.26 mmol) were dissolved in *n*hexane (1 mL) and cooled to –10 °C. *n*BuLi (0.50 mL, 2.55 M in hexane, 1.26 mmol) was added and the resulting solution was stirred for 6 h at –10 °C. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by MeSSMe (0.13 mL, 1.47 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (94 mg, 0.20 mmol, 48%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.35 (s, 2H), 3.56 (q, *J* = 7.2 Hz, 2H), 3.36 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.95 – 0.91 (m, 18H), 0.81 – 0.75 (m, 12H).

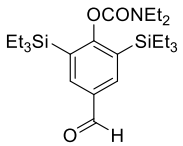
^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 159.69, 154.78, 136.50, 133.80, 130.78, 40.78, 40.73, 17.04, 13.90, 12.96, 7.55, 3.60.

MS (EI, 70 eV): *m/z* (%) = 438 (5), 324 (16), 281 (23), 225 (59), 209 (30), 208 (13), 207 (100), 191 (21), 103 (53), 100 (50), 75 (77), 72 (35), 58 (10), 56 (12), 44 (28), 42 (56).

HRMS (EI): *m*/*z* calc. for $[C_{22}H_{40}NO_2S^{28}Si_2]$: 438.2318 $[M-Et]^{\bullet+}$; found: 438.2318.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2936 (w), 2873 (m), 1714 (vs), 1552 (vw), 1457 (w), 1424 (w), 1375 (s), 1271 (s), 1223 (w), 1183 (m), 1136 (vs), 1003 (s), 963 (m), 782 (s), 726 (vs), 688 (s).

4-formyl-2,6-bis(triethylsilyl)phenyl diethylcarbamate (12b)



According to **TP4**, carbamate **6e** (177 mg, 0.42 mmol) and PMDTA (0.26 mL, 1.26 mmol) were dissolved in *n*hexane (1 mL) and cooled to –10 °C. *n*BuLi (0.50 mL, 2.55 M in hexane, 1.26 mmol) was added and the resulting solution was stirred for 6 h at –10 °C. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by dimethylformamide (0.11 mL, 1.47 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a slight yellow oil (65 mg, 0.14 mmol, 34%).

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 10.00 (s, 1H), 7.97 (s, 2H), 3.58 (q, *J* = 7.2 Hz, 2H), 3.37 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.96 – 0.90 (m, 18H), 0.88 – 0.76 (m, 12H).

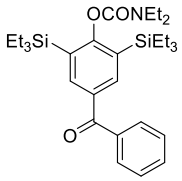
^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 192.09, 166.35, 154.02, 139.49, 132.61, 131.55, 40.82, 40.69, 13.73, 12.78, 7.34, 3.35.

MS (EI, 70 eV): *m/z* (%) = 448 (1), 422 (18), 421 (55), 420 (40), 179 (11), 168 (12), 100 (100), 72 (23).

HRMS (EI): *m*/*z* calc. for $[C_{24}H_{42}NO_3{}^{28}Si_2]$: 448.2703 $[M–H]^{\bullet+}$; found: 448.2693.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (w), 2909 (w), 2874 (w), 1716 (s), 1696 (s), 1564 (w), 1457 (w), 1424 (m), 1380 (m), 1363 (m), 1272 (s), 1221 (m), 1178 (m), 1145 (vs), 1100 (s), 1003 (s), 961 (m), 936 (m), 807 (w), 784 (m), 726 (vs), 671 (m).

4-benzoyl-2,6-bis(triethylsilyl)phenyl diethylcarbamate (12c)



According to **TP4**, carbamate **6e** (211 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL) and cooled to –10 °C.. *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h at –10 °C. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by *N*-methoxy-*N*-methylbenzamide (0.27 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a slight yellow oil (116 mg, 0.22 mmol, 44%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.92 (s, 2H), 7.85 – 7.80 (m, 2H), 7.61 – 7.55 (m, 1H), 7.50 – 7.44 (m, 2H), 3.60 (q, *J* = 7.2 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.98 – 0.88 (m, 18H), 0.85 – 0.75 (m, 12H).

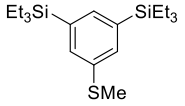
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 196.63, 164.95, 154.36, 139.81, 137.95, 133.71, 132.40, 130.47, 130.21, 128.27, 40.93, 40.82, 13.87, 12.94, 7.50, 3.54.

MS (EI, 70 eV): *m/z* (%) = 496 (19), 255 (17), 207 (35), 105 (12), 100 (100), 72 (55).

HRMS (EI): *m*/*z* calc. for $[C_{28}H_{42}NO_3{}^{28}Si_2]$: 496.2703 $[M–Et]^{\bullet+}$; found: 496.2703.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (w), 2909 (w), 2874 (w), 1715 (s), 1657 (m), 1568 (vw), 1457 (w), 1426 (w), 1375 (m), 1315 (w), 1267 (vs), 1219 (w), 1183 (m), 1146 (vs), 1099 (s), 1002 (s), 967 (s), 852 (vw), 778 (s), 728 (s), 712 (vs), 691 (s).

(5-(methylthio)-1,3-phenylene)bis(triethylsilane) (13a)



According to **TP4**, arene **6f** (153 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by MeSSMe (0.16 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (74 mg, 0.21 mmol, 42%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.37 (s, 1H), 7.36 (s, 2H), 2.49 (s, 3H), 0.97 (t, *J* = 7.7 Hz, 18H), 0.84 – 0.73 (m, 12H).

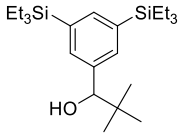
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 137.22, 137.16, 136.78, 132.95, 16.24, 7.55, 3.48.

MS (EI, 70 eV): *m/z* (%) = 352 (4), 263 (28), 261 (17), 253 (100), 252 (17), 251 (60), 250 (10), 236 (15), 235 (13), 219 (17), 187 (13), 45 (10), 44 (20), 42 (57).

HRMS (EI): *m/z* calc. for $[C_{19}H_{36}S^{28}Si_2]$: 352.2076 $[M]^{\bullet+}$; found: 352.2069.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (s), 2936 (m), 2909 (m), 2874 (s), 1547 (w), 1458 (w), 1415 (w), 1363 (w), 1237 (w), 1143 (m), 1006 (m), 968 (w), 796 (s), 731 (vs), 718 (vs), 691 (m).

1-(3,5-bis(triethylsilyl)phenyl)-2,2-dimethylpropan-1-ol (13b)



According to **TP4**, arene **6f** (307 mg, 1.0 mmol) and PMDTA (0.63 mL, 3.0 mmol) were dissolved in *n*hexane (2 mL). *n*BuLi (1.18 mL, 2.55 M in hexane, 3.0 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (2 mL) was added, followed by trimethylacetaldehyde (0.38 mL, 3.5 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (228 mg, 0.58 mmol, 58%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.55 (t, *J* = 1.2 Hz, 1H), 7.44 (d, *J* = 1.2 Hz, 2H), 4.42 (s, 1H), 2.00 (s, 1H), 1.03 – 0.98 (m, 18H), 0.94 (s, 9H), 0.87 – 0.78 (m, 12H).

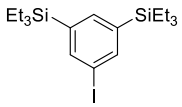
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 140.08, 139.40, 135.27, 133.98, 82.90, 35.80, 26.08, 7.55, 3.58.

MS (EI, 70 eV): *m/z* (%) = 374 (8), 345 (30), 335 (34), 317 (40), 289 (51), 260 (16), 258 (13), 231 (47), 205 (17), 203 (82), 201 (19), 189 (13), 175 (100), 173 (39), 163 (13), 159 (14), 151 (31), 147 (13), 145 (41), 144 (18), 143 (16), 141 (19), 133 (30), 131 (24), 129 (34), 128 (32), 123 (38), 115 (22), 105 (15), 103 (23), 87 (68), 75 (17), 59 (45).

HRMS (EI): *m/z* calc. for $[C_{23}H_{42}{}^{28}Si_2]$: 374.2825 $[M–H_2O]^{\bullet+}$; found: 374.2822.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3455 (vw), 2952 (m), 2908 (w), 2874 (m), 1737 (vw), 1458 (w), 1416 (w), 1363 (w), 1235 (w), 1143 (w), 1055 (w), 1005 (s), 973 (w), 863 (vw), 801 (s), 719 (vs), 678 (s).

(5-iodo-1,3-phenylene)bis(triethylsilane) (13c)



According to **TP4**, arene **6f** (153 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol) was added, followed by a solution of I_2 (444 mg, 1.75 mmol) in THF (1 mL). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (93 mg, 22 mmol, 43%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.77 (d, *J* = 1.0 Hz, 2H), 7.53 (t, *J* = 1.1 Hz, 1H), 1.01 – 0.93 (m, 18H), 0.83 – 0.74 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 143.00, 140.27, 138.84, 96.88, 7.46, 3.40.

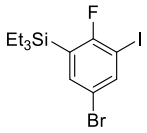
MS (EI, 70 eV): *m/z* (%) = 432 (11), 405 (10), 404 (29), 403 (100), 376 (16), 375 (53), 348 (12), 347 (48), 173 (12), 159 (18), 145 (14), 87 (15), 59 (13), 43 (42).

HRMS (EI): *m/z* calc. for $[C_{18}H_{33}I^{28}Si_2]$: 432.1165 $[M]^{\bullet+}$; found: 432.1165.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2908 (w), 2873 (m), 1529 (w), 1457 (w), 1414 (w), 1367 (w), 1235 (w), 1135 (s), 1099 (m), 1003 (s), 972 (w), 860 (w), 787 (vs), 716 (vs), 687 (vs).

3.4 Preparation of 1,2,3,5-tetrasubstituted arenes

(5-bromo-2-fluoro-3-iodophenyl)triethylsilane (14)



According to **TP5**, bis(triethylsilyl)benzene **8c** (2.49 g, 6.17 mmol) was dissolved in CH_2Cl_2 (12 mL) and ICl (1.3 g, 8.0 mmol) was added in one portion. Purification by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (2.3 g, 5.54 mmol, 90%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.86 (dd, *J* = 5.7, 2.4 Hz, 1H), 7.38 (dd, *J* = 4.0, 2.3 Hz, 1H), 1.01 – 0.77 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.71 (d, *J* = 240.1 Hz), 142.27 (d, *J* = 2.1 Hz), 138.47 (d, *J* = 11.4 Hz), 127.32 (d, *J* = 36.9 Hz), 117.67 (d, *J* = 3.3 Hz), 82.65 (d, *J* = 33.2 Hz), 7.36, 3.33 (d, *J* = 1.7 Hz).

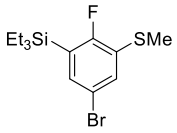
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −83.73 (t, *J* = 4.5 Hz).

MS (EI, 70 eV): *m/z* (%) = 416 (20), 414 (21), 359 (69), 357 (70), 331 (97), 329 (97), 260 (46), 258 (44), 249 (20), 247 (20), 232 (46), 231 (74), 230 (45), 229 (76), 222 (23), 220 (24), 203 (60), 167 (39), 151 (39), 149 (24), 141 (26), 127 (24), 123 (20), 104 (16), 93 (100), 87 (18), 77 (16), 75 (19), 65 (20).

HRMS (EI): *m/z* calc. for $[C_{12}H_{17}{}^{79}BrFI^{28}Si]$: 413.9312 $[M]^{\bullet+}$; found: 413.9306.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2909 (w), 2875 (w), 1538 (w), 1457 (w), 1404 (vs), 1373 (w), 1218 (m), 1109 (w), 1074 (s), 1004 (s), 974 (w), 868 (m), 836 (w), 725 (vs), 690 (s).

(5-bromo-2-fluoro-3-(methylthio)phenyl)triethylsilane (15a)



According to **TP6**, iodoarene **14** (208 mg, 0.5 mmol) was dissolved in THF (1 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.48 mL, 1.10 M in THF, 0.53 mmol) was added dropwise. After 15 min, dimethyl disulfide (0.05 mL, 0.55 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (123 mg, 0.37 mmol, 73%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.30 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.20 (dd, *J* = 4.0, 2.4 Hz, 1H), 2.45 (s, 3H), 1.00 – 0.91 (m, 9H), 0.90 – 0.76 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.98 (d, *J* = 238.4 Hz), 134.72 (d, *J* = 12.0 Hz), 130.84 (d, *J* = 3.2 Hz), 127.99 (d, *J* = 23.9 Hz), 126.18 (d, *J* = 34.7 Hz), 117.56 (d, *J* = 3.0 Hz), 15.15 (d, *J* = 2.3 Hz), 7.41, 3.40 (d, *J* = 1.5 Hz).

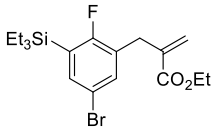
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −101.30 (t, *J* = 5.3 Hz).

MS (EI, 70 eV): *m/z* (%) = 336 (51), 334 (54), 296 (33), 294 (32), 278 (60), 276 (58), 268 (16), 266 (16), 250 (80), 248 (82), 235 (18), 233 (20), 226 (74), 198 (100), 197 (30), 183 (15), 173 (16), 169 (28), 155 (24), 151 (16), 134 (20), 123 (68), 121 (32), 77 (33), 75 (16).

HRMS (EI): *m/z* calc. for [$C_{13}H_{20}{}^{79}BrFS^{28}Si$]: 334.0222 $[M]^{\bullet+}$; found: 334.0214.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2934 (w), 2909 (w), 2873 (m), 1540 (w), 1456 (w), 1401 (vs), 1375 (s), 1237 (w), 1203 (s), 1112 (vs), 1003 (s), 972 (w), 852 (m), 834 (m), 789 (m), 725 (vs), 661 (s).

Ethyl 2-(5-bromo-2-fluoro-3-(triethylsilyl)benzyl)acrylate (15b)



According to **TP6**, iodoarene **14** (208 mg, 0.5 mmol) was dissolved in THF (1 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.48 mL, 1.10 M in THF, 0.53 mmol) was added dropwise. After 15 min, CuCN•2LiCl (0.05 mL, 1.0 M in THF, 0.05 mmol, 0.1 equiv.) was added, followed by ethyl 2-(bromomethyl)acrylate (89 mg, 0.55 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (142 mg, 0.35 mmol, 71%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.37 – 7.27 (m, 2H), 6.27 (d, *J* = 1.1 Hz, 1H), 5.45 (t, *J* = 1.2 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.60 (d, *J* = 1.5 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.02 – 0.90 (m, 9H), 0.88 – 0.77 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.62, 164.58 (d, *J* = 241.4 Hz), 138.36, 136.74 (d, *J* = 12.6 Hz), 135.01 (d, *J* = 5.0 Hz), 127.64 (d, *J* = 22.0 Hz), 126.70, 126.55 (d, *J* = 35.2 Hz), 116.98 (d, *J* = 3.0 Hz), 61.05, 31.23 (d, *J* = 3.0 Hz), 14.26, 7.42, 3.44 (d, *J* = 1.6 Hz).

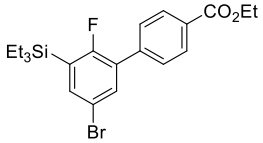
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −107.15 (t, *J* = 5.4 Hz).

MS (EI, 70 eV): *m/z* (%) = 400 (3), 345 (17), 343 (17), 315 (50), 313 (50), 297 (11), 259 (14), 257 (14), 225 (16), 223 (16), 221 (11), 206 (25), 205 (21), 195 (11), 193 (12), 141 (13), 128 (23), 116 (11), 115 (100), 114 (14), 105 (16), 93 (18), 77 (43), 75 (24), 65 (13).

HRMS (EI): *m/z* calc. for [$C_{18}H_{26}BrFO_2{}^{28}Si$]: 400.0869 $[M]^{\bullet+}$; found: 400.0860.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2936 (w), 2909 (w), 2875 (w), 1717 (vs), 1635 (w), 1414 (m), 1300 (m), 1277 (m), 1251 (m), 1193 (s), 1161 (vs), 1133 (vs), 1004 (s), 947 (m), 870 (m), 830 (m), 817 (w), 725 (vs), 662 (s).

Ethyl 5'-bromo-2'-fluoro-3'-(triethylsilyl)-[1,1'-biphenyl]-4-carboxylate (15c)



According to **TP6**, iodoarene **14** (830 mg, 2.0 mmol) was dissolved in THF (4 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (1.91 mL, 1.10 M in THF, 2.1 mmol) was added dropwise. After 15 min, $ZnCl_2$ (2.0 mL, 1.0 M in THF, 2.0 mmol, 1.0 equiv.) was added, followed by $Pd(dba)_2$ (23 mg, 0.04 mmol, 0.02 equiv.), P(*o*-furyl)$_3$ (19 mg, 0.08 mmol, 0.04 equiv.) and ethyl 4-iodobenzoate (550 mg, 2.0 mmol, 1.0 equiv.). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (810 mg, 1.85 mmol, 93%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.13 – 8.09 (m, 2H), 7.62 – 7.54 (m, 3H), 7.44 (dd, *J* = 3.9, 2.5 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.04 – 0.80 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.43, 162.93 (d, *J* = 243.2 Hz), 139.52 (d, *J* = 1.7 Hz), 138.18 (d, *J* = 12.8 Hz), 134.41 (d, *J* = 3.8 Hz), 130.13, 129.83, 129.70 (d, *J* = 19.8 Hz), 129.18 (d, *J* = 3.2 Hz), 127.83 (d, *J* = 36.2 Hz), 117.53 (d, *J* = 3.0 Hz), 61.24, 14.49, 7.47, 3.48 (d, *J* = 1.7 Hz).

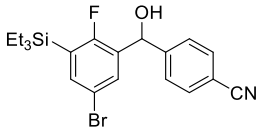
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −106.83 (t, *J* = 5.3 Hz).

MS (EI, 70 eV): *m/z* (%) = 438 (17), 436 (17), 391 (14), 382 (15), 381 (68), 379 (71), 354 (17), 353 (100), 352 (17), 351 (97), 325 (53), 323 (53), 279 (20), 277 (19), 261 (72), 259 (74), 227 (14), 217 (29), 207 (18), 199 (60), 197 (18), 179 (42), 178 (71), 177 (14), 176 (19), 170 (18), 165 (37), 154 (24), 153 (25), 152 (75), 151 (43), 150 (71), 77 (24), 65 (29).

HRMS (EI): *m/z* calc. for $[C_{21}H_{26}{}^{79}BrFO_2{}^{28}S_1]$: 436.0869 $[M]^{\bullet+}$; found: 436.0858.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (w), 2936 (w), 2909 (w), 2874 (w), 1718 (vs), 1611 (w), 1457 (w), 1430 (w), 1397 (m), 1269 (vs), 1194 (s), 1101 (vs), 1058 (s), 1019 (s), 856 (s), 837 (w), 776 (s), 701 (vs), 679 (m), 653 (m).

4-((5-bromo-2-fluoro-3-(triethylsilyl)phenyl)(hydroxy)methyl)benzonitrile (15d)



According to **TP6**, iodoarene **14** (208 mg, 0.5 mmol) was dissolved in THF (1 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.48 mL, 1.10 M in THF, 0.53 mmol) was added dropwise. After 15 min, 4-cyanobenzaldehyde (72 mg, 0.55 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (160 mg, 0.38 mmol, 76%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.65 – 7.61 (m, 2H), 7.60 – 7.57 (m, 1H), 7.54 – 7.49 (m, 2H), 7.37 (dd, *J* = 4.2, 2.5 Hz, 1H), 6.12 (s, 1H), 2.36 (s, 1H), 0.96 – 0.88 (m, 9H), 0.85 – 0.76 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.92 (d, *J* = 240.8 Hz), 147.61, 138.24 (d, *J* = 13.0 Hz), 132.57, 131.74, 131.54 (d, *J* = 4.4 Hz), 127.36 (d, *J* = 35.2 Hz), 127.01 (d, *J* = 1.4 Hz), 118.79, 117.90 (d, *J* = 2.9 Hz), 111.70, 69.08 (d, *J* = 3.0 Hz), 7.37, 3.41 (d, *J* = 1.6 Hz).

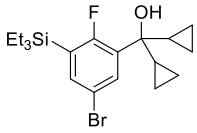
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −107.91 (t, *J* = 5.4 Hz).

MS (EI, 70 eV): *m/z* (%) = 419 (1), 281 (21), 270 (16), 268 (18), 227 (11), 226 (11), 225 (88), 209 (41), 208 (13), 207 (100), 191 (24), 190 (20), 130 (30), 128 (17), 119 (10), 95 (12), 93 (11), 82 (13), 81 (62), 80 (14), 79 (62), 77 (16), 75 (19), 42 (18).

HRMS (EI): *m/z* calc. for [$C_{20}H_{23}{}^{79}BrFNO^{28}Si$]: 419.0716 [M]$^{\bullet+}$; found: 419.0708.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3435 (br w), 2953 (m), 2908 (w), 2874 (m), 2230 (m), 1609 (w), 1503 (vw), 1456 (w), 1412 (s), 1386 (m), 1237 (w), 1209 (w), 1154 (vs), 1048 (m), 1018 (s), 1004 (s), 881 (m), 833 (s), 818 (s), 768 (m), 723 (vs), 682 (s).

(5-bromo-2-fluoro-3-(triethylsilyl)phenyl)dicyclopropylmethanol (15e)



According to **TP6**, iodoarene **14** (208 mg, 0.5 mmol) was dissolved in THF (1 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.48 mL, 1.10 M in THF, 0.53 mmol) was added dropwise. After 15 min, dicyclopropyl ketone (0.06 mL, 0.55 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (148 mg, 0.37 mmol, 74%).

^{1}H-NMR (400 MHz, CDCl$_3$): δ / ppm = 7.72 (dd, *J* = 7.1, 2.6 Hz, 1H), 7.32 (dd, *J* = 3.8, 2.6 Hz, 1H), 1.43 – 1.34 (m, 2H), 1.26 (s, 1H), 1.01 – 0.92 (m, 9H), 0.89 – 0.78 (m, 6H), 0.67 – 0.58 (m, 2H), 0.55 – 0.46 (m, 2H), 0.39 – 0.31 (m, 4H).

^{13}C-NMR (101 MHz, CDCl$_3$): δ / ppm = 163.62 (d, *J* = 240.4 Hz), 136.92 (d, *J* = 13.3 Hz), 135.79 (d, *J* = 18.4 Hz), 132.10 (d, *J* = 5.6 Hz), 127.11 (d, *J* = 38.0 Hz), 117.20 (d, *J* = 2.6 Hz), 73.28 (d, *J* = 4.5 Hz), 19.90 (d, *J* = 3.9 Hz), 7.48 (d, *J* = 0.8 Hz), 3.63 (d, *J* = 1.9 Hz), 2.23 (d, *J* = 2.2 Hz), 0.53 (d, *J* = 1.4 Hz).

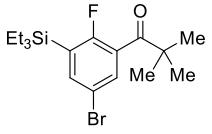
^{19}F-NMR: (377 MHz, CDCl$_3$): δ / ppm = −106.83 (t, *J* = 5.3 Hz).

MS (EI, 70 eV): *m/z* (%) = 382 (6), 380 (6), 359 (16), 357 (17), 172 (11), 167 (28), 166 (21), 165 (69), 153 (26), 152 (53), 146 (11), 141 (13), 139 (13), 128 (18), 115 (20), 105 (24), 87 (36), 77 (100), 75 (47), 65 (11).

HRMS (EI): *m/z* calc. for [$C_{19}H_{26}{}^{79}BrF^{28}Si$]: 380.0971 [M−$H_2O$]$^{\bullet+}$; found: 380.0959.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3087 (vw), 3009 (vw), 2954 (m), 2874 (m), 1457 (w), 1406 (vs), 1378 (m), 1308 (w), 1270 (w), 1237 (w), 1206 (w), 1157 (m), 1133 (w), 1121 (w), 1000 (vs), 915 (m), 879 (m), 865 (w), 835 (m), 826 (m), 742 (vs), 692 (m), 670 (vw), 658 (m).

1-(5-bromo-2-fluoro-3-(triethylsilyl)phenyl)-2,2-dimethylpropan-1-one (15f)



According to **TP6**, iodoarene **14** (3.0 g, 7.2 mmol) was dissolved in THF (14 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (6.9 mL, 1.10 M in THF, 7.6 mmol) was added dropwise. After 15 min, CuCN•2LiCl (7.9 mL, 1.0 M in THF, 7.9 mmol, 1.1 equiv.) and trimethylacetyl chloride (1.06 mL, 8.6 mmol, 1.2 equiv.) were added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (2.5 g, 6.8 mmol, 94%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.45 (dd, *J* = 4.2, 2.5 Hz, 1H), 7.25 (dd, *J* = 5.9, 2.5 Hz, 1H), 1.22 (d, *J* = 1.0 Hz, 8H), 0.98 – 0.91 (m, 10H), 0.87 – 0.79 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 208.96 (d, *J* = 1.4 Hz), 160.87 (d, *J* = 240.2 Hz), 138.96 (d, *J* = 12.4 Hz), 131.05 (d, *J* = 5.3 Hz), 130.17 (d, *J* = 27.7 Hz), 127.67 (d, *J* = 35.3 Hz), 116.87 (d, *J* = 3.0 Hz), 44.99, 26.43 (d, *J* = 1.9 Hz), 7.16 (d, *J* = 0.7 Hz), 3.19 (d, *J* = 1.7 Hz).

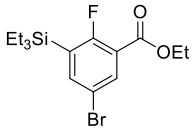
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −102.26 (t, *J* = 5.2 Hz).

MS (EI, 70 eV): *m/z* (%) = 372 (1), 318 (14), 317 (98), 316 (14), 315 (100), 142 (16), 77 (17).

HRMS (EI): *m/z* calc. for $[C_{17}H_{26}{}^{79}Br^{19}FO^{28}Si]$: 372.0920 $[M]^{\bullet+}$; found: 372.0910.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (m), 2936 (w), 2909 (w), 2875 (m), 1699 (s), 1588 (w), 1478 (w), 1458 (w), 1405 (vs), 1366 (w), 1279 (w), 1224 (w), 1173 (vs), 1039 (m), 990 (vs), 931 (w), 877 (m), 824 (m), 769 (w), 729 (vs), 696 (m).

Ethyl 5-bromo-2-fluoro-3-(triethylsilyl)benzoate (15g)



According to **TP6**, iodoarene **14** (208 mg, 0.5 mmol) was dissolved in THF (1 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.48 mL, 1.10 M in THF, 0.53 mmol) was added dropwise. After 15 min, ethyl cyanoformate (0.06 mL, 0.55 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a yellow oil (139 mg, 0.38 mmol, 77%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.01 (dd, *J* = 6.5, 2.6 Hz, 1H), 7.58 (dd, *J* = 3.8, 2.6 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.00 – 0.80 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.08 (d, *J* = 254.4 Hz), 163.62 (d, *J* = 4.5 Hz), 142.78 (d, *J* = 13.4 Hz), 135.59 (d, *J* = 1.6 Hz), 129.06 (d, *J* = 35.6 Hz), 120.36 (d, *J* = 15.7 Hz), 116.90 (d, *J* = 3.4 Hz), 61.78, 14.39, 7.38 (d, *J* = 0.7 Hz), 3.35 (d, *J* = 1.7 Hz).

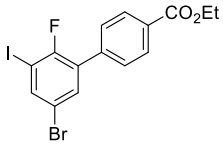
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −99.35 (t, *J* = 5.1 Hz).

MS (EI, 70 eV): *m/z* (%) = 362 (8), 360 (7), 321 (41), 317 (26), 315 (28), 305 (64), 303 (100), 277 (80), 275 (80), 273 (49), 267 (44), 265 (44), 249 (28), 247 (44), 245 (38), 231 (46), 229 (49), 224 (30), 223 (37), 221 (30), 219 (32), 217 (30), 205 (35), 203 (39), 201 (37), 196 (31), 141 (25), 139 (39), 93 (55), 77 (35), 75 (26), 65 (39).

HRMS (EI): *m/z* calc. for $[C_{15}H_{22}{}^{79}BrFO_2{}^{28}Si]$: 360.0556 $[M]^{\bullet+}$; found: 360.0548.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (m), 2937 (w), 2910 (w), 2875 (w), 1734 (s), 1716 (s), 1591 (m), 1457 (w), 1415 (vs), 1364 (w), 1282 (vs), 1239 (vs), 1210 (vs), 1123 (vs), 1102 (vs), 1004 (s), 891 (m), 833 (m), 786 (vs), 728 (vs), 693 (m), 657 (m).

Ethyl 5'-bromo-2'-fluoro-3'-iodo-[1,1'-biphenyl]-4-carboxylate (16a)



According to **TP5**, triethylsilylbenzene **15c** (570 mg, 1.30 mmol) was dissolved in CH_2Cl_2 (3 mL) and ICl (341 mg, 2.1 mmol) was added in one portion. Purification by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless solid (530 mg, 1.18 mmol, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.15 – 8.08 (m, 2H), 7.88 (dd, *J* = 5.1, 2.4 Hz, 1H), 7.57 – 7.51 (m, 3H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.23, 157.91 (d, *J* = 248.0 Hz), 140.93, 138.29 (d, *J* = 1.9 Hz), 133.66 (d, *J* = 2.9 Hz), 130.72, 130.35 (d, *J* = 17.3 Hz), 129.96, 129.02 (d, *J* = 3.1 Hz), 117.76 (d, *J* = 4.0 Hz), 83.60 (d, *J* = 28.7 Hz), 61.35, 14.48.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −98.72 (ddt, *J* = 6.6, 5.0, 1.7 Hz).

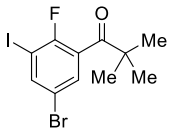
MS (EI, 70 eV): *m/z* (%) = 450 (23), 448 (23), 422 (29), 420 (32), 405 (49), 403 (47), 296 (27), 250 (17), 248 (18), 202 (13), 201 (14), 170 (13), 169 (29), 168 (36), 149 (13), 148 (19), 127 (100).

HRMS (EI): *m/z* calc. for [$C_{15}H_{11}{}^{79}BrFIO_2$]: 447.8971 [M]$^{\bullet+}$; found: 447.8962.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3062 (vw), 2999 (vw), 2979 (vw), 2910 (vw), 2362 (vw), 2338 (vw), 1707 (vs), 1609 (w), 1543 (vw), 1477 (vw), 1443 (s), 1383 (w), 1366 (w), 1280 (vs), 1227 (m), 1186 (m), 1126 (s), 1105 (s), 1040 (m), 1016 (m), 910 (vw), 856 (s), 772 (vs), 701 (vs), 676 (m).

m.p. (°C): 121.6–124.4.

1-(5-bromo-2-fluoro-3-iodophenyl)-2,2-dimethylpropan-1-one (16b)



According to **TP5**, triethylsilylbenzene **15f** (2.55 g, 6.83 mmol) was dissolved in CH_2Cl_2 (14 mL) and ICl (1.44 g, 8.9 mmol) was added in one portion. Purification by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless solid (2.47 g, 6.42 mmol, 94%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.90 (dd, *J* = 5.3, 2.3 Hz, 1H), 7.24 (dd, *J* = 5.2, 2.3 Hz, 1H), 1.24 (d, *J* = 1.0 Hz, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 207.18 (d, *J* = 1.5 Hz), 156.18 (d, *J* = 245.0 Hz), 142.05 (d, *J* = 1.3 Hz), 130.52 (d, *J* = 24.8 Hz), 130.45 (d, *J* = 4.1 Hz), 117.40 (d, *J* = 3.8 Hz), 83.12 (d, *J* = 28.6 Hz), 45.30, 26.59 (d, *J* = 1.7 Hz).

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −95.58 (t, *J* = 5.3 Hz).

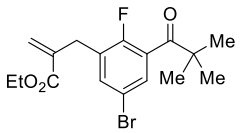
MS (EI, 70 eV): *m/z* (%) = 384 (18), 225 (42), 209 (14), 207 (18), 127 (100).

HRMS (EI): *m/z* calc. for [$C_{11}H_{11}{}^{79}Br^{19}FIO$]: 383.9022 [M]$^{\bullet+}$; found: 383.9012.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3063 (vw), 2977 (m), 2936 (w), 2873 (w), 1695 (vs), 1549 (w), 1429 (vs), 1383 (m), 1277 (m), 1238 (m), 1222 (m), 1152 (vs), 1093 (w), 982 (s), 895 (w), 871 (vs), 837 (m), 776 (w), 751 (s), 703 (m).

m.p. (°C): 71.0–73.9.

Ethyl 2-(5-bromo-2-fluoro-3-pivaloylbenzyl)acrylate (17a)



According to **TP6**, iodoarene **16b** (39 mg, 0.1 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.10 mL, 1.10 M in THF, 0.11 mmol) was added dropwise. After 15 min, CuCN•2LiCl (0.01 mL, 1.0 M in THF, 0.01 mmol, 0.1 equiv.) and ethyl 2-(bromomethyl)acrylate (21 mg, 0.11 mmol) were added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (27 mg, 0.07 mmol, 73%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.38 (dd, *J* = 6.3, 2.5 Hz, 1H), 7.15 (dd, *J* = 5.3, 2.5 Hz, 1H), 6.30 (d, *J* = 1.0 Hz, 1H), 5.52 (t, *J* = 1.2 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.63 (s, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.23 (d, *J* = 0.9 Hz, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 208.65, 166.34, 155.41 (d, *J* = 246.8 Hz), 137.74, 134.68 (d, *J* = 4.5 Hz), 130.85 (d, *J* = 23.1 Hz), 129.05 (d, *J* = 18.0 Hz), 128.62 (d, *J* = 5.0 Hz), 127.32, 116.43 (d, *J* = 3.5 Hz), 61.20, 45.19, 31.08 (d, *J* = 3.0 Hz), 26.62 (d, *J* = 1.9 Hz), 14.27.

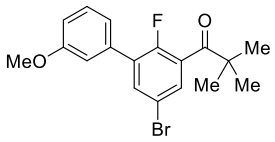
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −119.67 (t, *J* = 6.0 Hz).

MS (EI, 70 eV): *m/z* (%) = 370 (3), 315 (55), 313 (50), 133 (16), 61 (15), 57 (54), 45 (14), 43 (100), 41 (19).

HRMS (EI): *m/z* calc. for [$C_{17}H_{20}{}^{79}BrFO_3$]: 370.0580 [M]$^{\bullet+}$; found: 370.0580.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2974 (w), 2936 (vw), 2907 (vw), 2872 (vw), 1699 (vs), 1633 (w), 1479 (w), 1453 (m), 1395 (w), 1367 (w), 1285 (m), 1254 (m), 1205 (s), 1186 (vs), 1139 (vs), 1096 (vw), 1057 (m), 1024 (m), 950 (w), 868 (m), 839 (vw), 817 (w), 665 (w).

1-(5-bromo-2-fluoro-3'-methoxy-[1,1'-biphenyl]-3-yl)-2,2-dimethylpropan-1-one (17b)



According to **TP6**, iodoarene **16b** (39 mg, 0.1 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.10 mL, 1.10 M in THF, 0.11 mmol) was added dropwise. After 15 min, $ZnCl_2$ (0.10 mL, 1.0 M in THF, 0.10 mmol, 1.0 equiv.) was added, followed by $Pd(dba)_2$ (1 mg, 0.002 mmol, 0.02 equiv.), P(*o*-furyl)$_3$ (1 mg, 0.004 mmol, 0.04 equiv.) and 3-iodoanisole (26 mg, 0.11 mmol, 1.1 equiv.). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a colorless oil (30 mg, 0.08 mmol, 82%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.59 (dd, *J* = 6.6, 2.5 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.24 (dd, *J* = 5.1, 2.5 Hz, 1H), 7.07 (dtd, *J* = 7.6, 1.7, 0.9 Hz, 1H), 7.03 (dt, *J* = 3.1, 1.6 Hz, 1H), 6.95 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 3.85 (s, 3H), 1.27 (d, *J* = 1.0 Hz, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 208.71, 159.82, 153.99 (d, *J* = 248.0 Hz), 135.15 (d, *J* = 1.3 Hz), 134.11 (d, *J* = 3.5 Hz), 131.72 (d, *J* = 5.6 Hz), 131.52 (d, *J* = 13.4 Hz), 129.83, 129.10 (d, *J* = 5.0 Hz), 121.49 (d, *J* = 2.9 Hz), 116.77 (d, *J* = 3.6 Hz), 114.80 (d, *J* = 3.1 Hz), 114.28, 55.52, 45.27, 26.64 (d, *J* = 1.8 Hz).

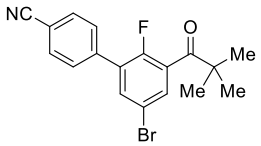
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −119.97 (t, *J* = 6.0 Hz).

MS (EI, 70 eV): *m/z* (%) = 364 (1), 200 (18), 170 (12), 158 (12), 157 (100), 57 (15).

HRMS (EI): *m/z* calc. for [$C_{18}H_{18}{}^{79}BrFO_2$]: 364.0474 $[M]^{\bullet+}$; found: 364.0468.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2968 (w), 2934 (w), 2871 (vw), 2835 (vw), 1698 (vs), 1601 (m), 1581 (m), 1564 (w), 1461 (m), 1426 (s), 1393 (w), 1365 (w), 1307 (m), 1278 (m), 1227 (s), 1206 (vs), 1180 (m), 1113 (m), 1048 (s), 992 (s), 869 (m), 838 (w), 782 (m), 761 (w), 726 (w), 700 (vs), 680 (m).

5'-bromo-2'-fluoro-3'-pivaloyl-[1,1'-biphenyl]-4-carbonitrile (17c)



According to **TP6**, iodoarene **16b** (39 mg, 0.1 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.10 mL, 1.10 M in THF, 0.11 mmol) was added dropwise. After 15 min, $ZnCl_2$ (0.10 mL, 1.0 M in THF, 0.10 mmol, 1.0 equiv.) was added, followed by $Pd(dba)_2$ (1 mg, 0.002 mmol, 0.02 equiv.), P(*o*-furyl)$_3$ (1 mg, 0.004 mmol, 0.04 equiv.) and 4-iodobenzonitrile (25 mg, 0.11 mmol, 1.1 equiv.). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 99:1) afforded the title compound as a yellow oil (27 mg, 0.08 mmol, 75%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.78 – 7.73 (m, 2H), 7.62 (dq, *J* = 8.3, 1.7 Hz, 2H), 7.58 (dd, *J* = 6.6, 2.5 Hz, 1H), 7.32 (dd, *J* = 5.1, 2.5 Hz, 1H), 1.27 (d, *J* = 0.9 Hz, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 208.02, 153.92 (d, *J* = 249.1 Hz), 138.39 (d, *J* = 1.4 Hz), 133.80 (d, *J* = 2.9 Hz), 132.58, 131.89 (d, *J* = 23.6 Hz), 130.44 (d, *J* = 5.2 Hz), 129.85 (d, *J* = 3.2 Hz), 128.82 (d, *J* = 57.6 Hz), 118.51, 117.22 (d, *J* = 3.7 Hz), 112.62, 45.31, 26.59 (d, *J* = 1.7 Hz).

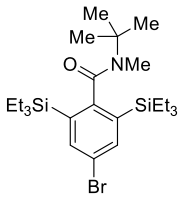
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −120.14 (t, *J* = 5.4 Hz).

MS (EI, 70 eV): *m/z* (%) = 361 (1), 304 (21), 302 (21), 196 (13), 195 (100), 168 (41), 57 (60).

HRMS (EI): *m/z* calc. for [$C_{18}H_{15}{}^{81}BrFNO$]: 361.0301 [M]$^{\bullet+}$; found: 361.0299.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2970 (w), 2933 (vw), 2871 (vw), 2229 (w), 1696 (vs), 1608 (w), 1509 (vw), 1478 (w), 1446 (s), 1410 (w), 1392 (m), 1365 (w), 1302 (m), 1279 (m), 1228 (m), 1210 (vs), 1182 (w), 1116 (s), 1035 (vw), 1020 (w), 984 (s), 876 (w), 842 (vs), 834 (vs), 793 (vw), 768 (vw), 760 (w), 736 (w), 719 (w), 668 (s).

4-bromo-*N*-(*tert*-butyl)-*N*-methyl-2,6-bis(triethylsilyl)benzamide (18)



Trimethyloxonium tetrafluoroborate (777 mg, 5.25 mmol, 1.05 equiv) was added to a solution of oxazolylbenzene **9d** (2.41 g, 5.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) at 0 °C. The mixture was allowed to warm to 25 °C. After 2 h, the dichloromethane was removed *in vacuo* and a solution of lithium triethylborohydride (6.0 mL, 1.0 M in THF, 6.0 mmol, 1.2 equiv.) was added at 0 °C. The resulting solution was stirred for another 4 h. The reaction mixture was quenched with a sat. aq. NH_4Cl (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (2.15 g, 4.31 mmol, 86%)

^{1}H-NMR (599 MHz, $CDCl_3$): δ / ppm = 7.60 (s, 2H), 2.53 (s, 3H), 1.54 (s, 9H), 0.94 – 0.85 (m, 30H).

^{13}C-NMR (151 MHz, $CDCl_3$): δ / ppm = 172.58, 151.07, 139.21, 136.29, 121.89, 57.60, 35.49, 28.58, 7.54, 3.83.

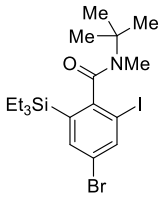
MS (EI, 70 eV): *m/z* (%) = 470 (17), 468 (15), 412 (16), 385 (22), 384 (100), 383 (27), 382 (97), 326 (18), 324 (18).

HRMS (EI): *m/z* calc. for [$C_{22}H_{39}{}^{79}BrNO^{28}Si_2$]: 468.1754 [M−Et]$^{\bullet+}$; found: 468.1749.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2933 (m), 2909 (w), 2874 (m), 1636 (s), 1536 (w), 1457 (m), 1362 (m), 1341 (m), 1236 (m), 1225 (m), 1112 (m), 1037 (s), 1002 (s), 970 (m), 883 (w), 788 (s), 719 (vs), 689 (vs).

m.p. (°C): 58.1–61.7.

4-bromo-*N*-(*tert*-butyl)-2-iodo-*N*-methyl-6-(triethylsilyl)benzamide (19)



According to **TP5**, bis(triethylsilyl)benzene **18** (3.42 g, 6.85 mmol) was dissolved in CH_2Cl_2 (15 mL) and ICl (1.45 g, 8.9 mmol) was added in one portion. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (3.1 g, 6.07 mmol, 89%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.96 (d, *J* = 1.9, 1H), 7.57 (d, *J* = 1.9, 1H), 2.73 (s, 3H), 1.56 (s, 9H), 1.00 – 0.71 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.04, 148.27, 141.96, 139.14, 138.35, 121.84, 95.41, 57.97, 34.12, 28.13, 7.46, 3.47.

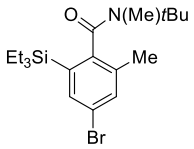
MS (EI, 70 eV): *m/z* (%) = 482 (10), 480 (10), 426 (100), 425 (18), 424 (100), 296 (10), 127 (22), 42 (11).

HRMS (EI): *m/z* calc. for $[C_{16}H_{24}{}^{79}BrINO^{28}Si]$: 479.9855 $[M-Et]^{\bullet+}$; found: 479.9852.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (w), 2928 (w), 2912 (w), 2893 (w), 2870 (w), 1636 (vs), 1548 (w), 1517 (w), 1472 (w), 1455 (w), 1415 (vw), 1362 (m), 1237 (w), 1202 (w), 1178 (vw), 1157 (vw), 1105 (s), 1085 (m), 1031 (s), 997 (s), 867 (w), 798 (w), 763 (w), 734 (vs), 704 (s), 689 (s), 660 (vw).

m.p. (°C): 76.7–77.7.

4-bromo-*N*-(*tert*-butyl)-*N*,2-dimethyl-6-(triethylsilyl)benzamide (20a)



In a modified version of **TP6**, iodoarene **19** (510 mg, 1.0 mmol) was dissolved in THF (2.0 mL). The mixture was cooled to −78 °C and MeLi•LiBr (0.74 mL, 1.42 M in Et_2O, 1.05 mmol) was added dropwise. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (362 mg, 0.91 mmol, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.44 – 7.42 (m, 1H), 7.31 – 7.30 (m, 1H), 2.69 (s, 3H), 2.22 (s, 3H), 1.54 (s, 9H), 1.06 – 0.67 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.81, 144.19, 136.49, 136.06, 135.49, 133.70, 121.75, 57.34, 33.62, 28.10, 19.01, 7.51, 3.60.

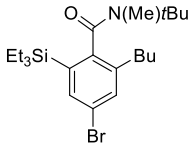
MS (EI, 70 eV): *m/z* (%) = 370 (10), 368 (10), 315 (14), 314 (100), 313 (17), 312 (100).

HRMS (EI): *m/z* calc. for $[C_{17}H_{27}{}^{79}BrNO^{28}Si]$: 368.1045 $[M-Et]^{\bullet+}$; found: 368.1043.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2908 (w), 2874 (w), 1624 (vs), 1556 (w), 1455 (m), 1363 (vs), 1212 (w), 1187 (m), 1155 (w), 1110 (s), 1044 (vs), 1007 (s), 972 (w), 910 (vw), 883 (m), 798 (m), 730 (vs), 692 (s).

m.p. (°C): 74.6–76.1.

4-bromo-*N*-(*tert*-butyl)-2-butyl-*N*-methyl-6-(triethylsilyl)benzamide (20b)



In a modified version of **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –78 °C and *n*BuLi (0.08 mL, 2.55 M, 0.21 mmol) was added dropwise. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a yellow oil (61 mg, 0.14 mmol, 69%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.43 (d, *J*=2.0, 1H), 7.34 (d, *J*=2.0, 1H), 2.66 (s, 3H), 2.58 – 2.38 (m, 2H), 1.71 – 1.55 (m, 2H), 1.54 (s, 9H), 1.36 (h, *J*=7.4, 2H), 0.96 – 0.88 (m, 15H), 0.88 – 0.81 (m, 3H).

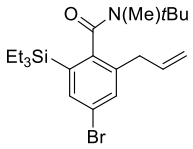
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.69, 143.77, 140.45, 136.45, 136.03, 132.57, 121.91, 57.29, 34.23, 32.85, 32.48, 28.14, 23.11, 14.09, 7.55, 3.66.

MS (EI, 70 eV): *m/z* (%) = 412 (22), 410 (20), 402 (17), 357 (23), 356 (100), 355 (36), 354 (100), 353 (10), 326 (16), 324 (14), 57 (37), 43 (51), 41 (18).

HRMS (EI): *m/z* calc. for [$C_{20}H_{33}{}^{79}BrNO^{28}Si$]: 410.1515 [M−Et]$^{\bullet+}$; found: 410.1507.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2932 (w), 2873 (w), 1636 (vs), 1557 (w), 1458 (m), 1362 (vs), 1212 (w), 1185 (w), 1113 (m), 1040 (vs), 1003 (m), 871 (w), 800 (w), 723 (vs), 692 (s).

2-allyl-4-bromo-*N*-(*tert*-butyl)-*N*-methyl-6-(triethylsilyl)benzamide (20c)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, CuCN•2LiCl (0.02 mL, 0.02 mmol, 0.1 equiv.) and allyl bromide (0.02 mL, 0.22 mmol) were added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (79 mg, 0.19 mmol, 93%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.46 (d, *J*=2.1, 1H), 7.35 (d, *J*=2.0, 1H), 5.97 – 5.84 (m, 1H), 5.13 (dt, *J*=2.3, 1.1, 1H), 5.10 (dq, *J*=9.0, 1.6, 1H), 3.43 – 3.12 (m, 2H), 2.67 (s, 3H), 1.54 (s, 9H), 0.99 – 0.68 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.56, 143.70, 137.72, 136.66, 136.55, 135.89, 132.82, 122.08, 117.31, 57.42, 36.45, 34.33, 28.13, 7.52, 3.64.

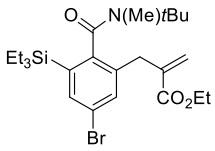
MS (EI, 70 eV): *m/z* (%) = 396 (8), 394 (8), 341 (16), 340 (100), 339 (18), 338 (99), 336 (11), 309 (19), 307 (20), 228 (19), 199 (12), 115 (10).

HRMS (EI): *m/z* calc. for $[C_{19}H_{29}{}^{79}BrNO^{28}Si]$: 394.1202 $[M-Et]^{\bullet+}$; found: 394.1199.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2932 (w), 2872 (w), 1623 (s), 1555 (w), 1478 (w), 1457 (w), 1364 (s), 1212 (m), 1183 (m), 1149 (w), 1107 (m), 1043 (s), 1004 (s), 919 (m), 872 (m), 798 (m), 726 (vs), 691 (s).

m.p. (°C): 60.4 – 62.0.

Ethyl 2-(5-bromo-2-(tert-butyl(methyl)carbamoyl)-3-(triethylsilyl)benzyl)acrylate (20d)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, CuCN•2LiCl (0.02 mL, 0.02 mmol, 0.1 equiv.) and ethyl 2-(bromomethyl)acrylate (0.03 mL, 0.22 mmol) were added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (94 mg, 0.19 mmol, 95%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.48 (d, *J*=2.0, 1H), 7.24 (d, *J*=2.0, 1H), 6.33 (d, *J*=1.1, 1H), 5.40 (d, *J*=1.4, 1H), 4.19 (q, *J*=7.1, 2H), 3.64 – 3.42 (m, 2H), 2.69 (s, 3H), 1.50 (s, 9H), 1.26 (t, *J*=7.1, 3H), 0.97 – 0.70 (m, 15H).

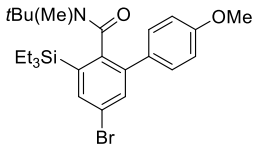
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.27, 166.87, 144.19, 138.17, 136.93, 136.84, 136.47, 132.75, 128.05, 122.03, 61.00, 57.38, 34.34, 34.15, 28.04, 14.31, 7.51, 3.62.

MS (EI, 70 eV): *m/z* (%) = 468 (16), 466 (18), 413 (22), 412 (99), 411 (30), 410 (100), 384 (12), 382 (10), 381 (12), 379 (13), 366 (28), 365 (12), 364 (27), 338 (32), 336 (34), 309 (24), 307 (25), 280 (10), 278 (10), 256 (13), 234 (10), 228 (16), 199 (11).

HRMS (EI): *m/z* calc. for $[C_{22}H_{33}{}^{79}BrNO_3{}^{28}Si]$: 466.1413 $[M-Et]^{\bullet+}$; found: 466.1406.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (m), 2910 (w), 2874 (w), 1716 (s), 1636 (vs), 1557 (w), 1459 (m), 1363 (vs), 1299 (w), 1279 (w), 1251 (m), 1210 (s), 1149 (s), 1107 (vs), 1041 (vs), 950 (w), 870 (w), 800 (m), 730 (vs), 692 (s).

5-bromo-*N*-(*tert*-butyl)-4'-methoxy-*N*-methyl-3-(triethylsilyl)-[1,1'-biphenyl]-2-carboxamide (20e)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, $ZnCl_2$ (0.2 mL, 0.2 mmol) was added, followed $Pd(dba)_2$ (2 mg, 0.004 mmol, 0.02 equiv.), P(*o*-furyl)$_3$ (2 mg, 0.008 mmol, 0.04 equiv) and 4-iodoanisole (51 mg, 0.22 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (64 mg, 0.13 mmol, 65%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.59 (d, *J* = 2.1 Hz, 1H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.34 – 7.30 (m, 2H), 6.91 – 6.85 (m, 2H), 3.82 (s, 3H), 2.35 (s, 3H), 1.18 (s, 9H), 1.01 – 0.77 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.14, 159.47, 143.17, 140.54, 137.81, 137.26, 133.55, 132.06, 130.62, 121.90, 113.60, 57.12, 55.54, 33.93, 27.88, 7.61, 3.74.

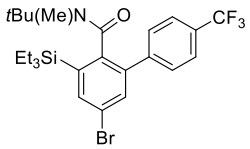
MS (EI, 70 eV): *m/z* (%) = 462 (25), 460 (29), 407 (25), 406 (82), 405 (28), 404 (100), 403 (10), 57 (16), 55 (10), 43 (26), 41 (10).

HRMS (EI): *m/z* calc. for $[C_{23}H_{31}{}^{79}BrNO_2{}^{28}Si]$: 460.1307 $[M-Et]^{\bullet+}$; found: 460.1316.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (w), 2930 (w), 2906 (w), 2873 (w), 1629 (s), 1608 (m), 1510 (s), 1457 (m), 1363 (vs), 1291 (w), 1248 (vs), 1211 (m), 1177 (m), 1108 (m), 1041 (vs), 1029 (s), 1002 (s), 878 (w), 835 (vs), 799 (m), 771 (m), 729 (vs), 690 (s).

m.p. (°C): 100.1 – 101.7.

5-bromo-*N*-(*tert*-butyl)-*N*-methyl-3-(triethylsilyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxamide (20f)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, $ZnCl_2$ (0.2 mL, 0.2 mmol) was added, followed $Pd(dba)_2$ (2 mg, 0.004 mmol, 0.02 equiv.), P(*o*-furyl)$_3$ (2 mg, 0.008 mmol, 0.04 equiv) and 4-iodobenzotrifluoride (60 mg, 0.22 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (81 mg, 0.15 mmol, 77%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.66 (d, *J* = 2.0 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 2.0 Hz, 1H), 2.36 (s, 3H), 1.12 (s, 9H), 1.01 – 0.77 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.62, 143.10 (q, *J* = 1.2 Hz), 142.96, 139.27, 138.30, 133.11, 130.13 (q, *J* = 32.6 Hz), 129.85, 125.09 (q, *J* = 3.7 Hz), 124.24 (q, *J* = 272.1 Hz), 122.09, 57.23, 33.98, 27.63, 7.57, 3.69.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.6.

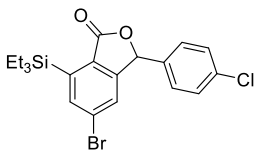
MS (EI, 70 eV): *m/z* (%) = 500 (4), 498 (4), 442 (26), 440 (26), 299 (17), 281 (16), 227 (20), 226 (13), 225 (100), 209 (29), 207 (47), 191 (10), 42 (72).

HRMS (EI): *m/z* calc. for $[C_{23}H_{28}{}^{81}BrF_3NO^{28}Si]$: 500.1055 $[M-Et]^{\bullet+}$; found: 500.1054.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2957 (w), 2880 (vw), 1626 (s), 1557 (w), 1472 (w), 1398 (w), 1366 (m), 1323 (vs), 1254 (w), 1191 (w), 1166 (s), 1127 (vs), 1107 (vs), 1073 (vs), 1038 (vs), 1015 (vs), 974 (w), 882 (w), 848 (vs), 801 (m), 720 (s), 685 (w), 659 (w).

m.p. (°C): 82.4 – 84.2.

5-bromo-3-(4-chlorophenyl)-7-(triethylsilyl)isobenzofuran-1(3H)-one (20g)



Iodoarene **19** (255 mg, 0.5 mmol) was dissolved in THF (1 mL). The mixture was cooled to -40 °C and *i*PrMgCl•LiCl (0.48 mL, 1.10 M in THF, 0.53 mmol) was added dropwise. After 15 min, 4-chlorobenzaldehyde (77 mg, 0.55 mmol) was added and the mixture was allowed to warm up to 25 °C. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude benzylic alcohol was dissolved in 1,4-dioxane (2 mL) and HCl (0.5 mL, 2.0 M in H_2O) was added. The solution was heated to 85 °C for 24 h. After cooling to 25 °C a sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (148 mg, 0.34 mmol, 68%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.7 (dd, *J*=1.7, 0.6, 1H), 7.4 (dd, *J*=1.7, 0.9, 1H), 7.4 – 7.3 (m, 2H), 7.2 – 7.2 (m, 2H), 6.3 (s, 1H), 1.1 – 0.9 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.22, 151.44, 142.51, 139.95, 135.58, 134.81, 129.47, 129.43, 128.78, 128.38, 126.36, 80.84, 7.68, 2.97.

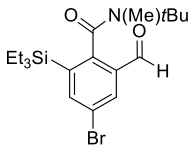
MS (EI, 70 eV): *m/z* (%) = 409 (100), 408 (22), 407 (74), 163 (14), 44 (12), 43 (26).

HRMS (EI): *m/z* calc. for $[C_{18}H_{17}{}^{79}Br^{35}ClO_2{}^{28}Si]$: 406.9870 $[M-Et]^{\bullet+}$; found: 406.9851.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (m), 2935 (w), 2911 (w), 2875 (w), 1767 (vs), 1636 (w), 1566 (m), 1489 (w), 1464 (w), 1406 (w), 1308 (w), 1282 (m), 1231 (w), 1201 (m), 1167 (m), 1086 (vs), 1058 (s), 1005 (vs), 972 (w), 848 (m), 816 (m), 721 (vs), 693 (s).

m.p. (°C): 88.0 – 90.1.

4-bromo-*N*-(*tert*-butyl)-2-formyl-*N*-methyl-6-(triethylsilyl)benzamide (20h)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, dimethylformamide (0.02 mL, 0.22 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (61 mg, 0.15 mmol, 74%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.05 (s, 1H), 8.01 (d, *J*=2.1, 1H), 7.83 (d, *J*=2.1, 1H), 2.65 (s, 3H), 1.57 (s, 9H), 1.09 – 0.72 (m, 15H).

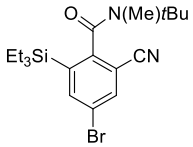
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 189.91, 169.58, 146.57, 144.15, 138.85, 133.75, 131.57, 122.95, 58.21, 34.89, 28.03, 7.45, 3.62.

MS (EI, 70 eV): *m/z* (%) = 396 (1), 327 (22), 326 (100), 324 (31), 270 (12), 268 (12), 56 (22).

HRMS (EI): *m/z* calc. for $[C_{18}H_{27}{}^{79}BrNO_2{}^{28}Si]$: 396.0994 $[M-Me]^{\bullet+}$; found: 396.0988.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2909 (w), 2873 (m), 1696 (vs), 1638 (vs), 1555 (m), 1458 (m), 1380 (s), 1353 (s), 1251 (m), 1219 (s), 1181 (s), 1099 (m), 1042 (vs), 1003 (s), 890 (m), 799 (m), 725 (vs), 692 (s).

4-bromo-*N*-(*tert*-butyl)-2-cyano-*N*-methyl-6-(triethylsilyl)benzamide (20i)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, *p*-tosylcyanide (40 mg, 0.22 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (59 mg, 0.14 mmol, 72%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.82 (d, *J* = 2.0 Hz, 1H), 7.75 (d, *J* = 2.0 Hz, 1H), 2.81 (s, 3H), 1.57 (s, 9H), 1.00 – 0.76 (m, 15H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 168.48, 147.01, 142.97, 140.20, 135.21, 121.90, 116.20, 111.35, 57.89, 34.13, 27.52, 7.29, 3.27.

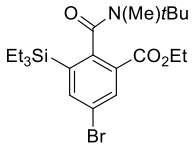
MS (EI, 70 eV): *m/z* (%) = 381 (3), 379 (4), 324 (19), 323 (100), 267 (10), 265 (10), 225 (24), 207 (12), 72 (10), 56 (12).

HRMS (EI): *m*/*z* calc. for [$C_{17}H_{24}{}^{79}BrNO^{28}Si$]: 379.0841 [M−Et]$^{\bullet+}$; found: 379.0839.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (w), 2872 (w), 1635 (vs), 1552 (w), 1472 (w), 1366 (vs), 1188 (m), 1156 (w), 1103 (m), 1047 (m), 1006 (s), 877 (m), 862 (m), 801 (m), 728 (vs), 694 (m).

m.p. (°C): 64.8 – 68.4.

Ethyl 5-bromo-2-(*tert*-butyl(methyl)carbamoyl)-3-(triethylsilyl)benzoate (20j)



According to **TP6**, iodoarene **19** (102 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, ethyl chloroformate (0.02 mL, 0.22 mmol) was added in one portion. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (90 mg, 0.20 mmol, 99%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.97 (d, *J*=2.1, 1H), 7.73 (d, *J*=2.1, 1H), 4.30 (qd, *J*=7.1, 1.9, 2H), 2.62 (s, 3H), 1.52 (s, 9H), 1.34 (t, *J*=7.1, 3H), 0.96 – 0.78 (m, 15H).

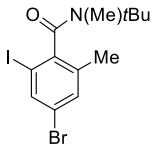
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.72, 165.37, 145.38, 142.29, 137.65, 133.20, 129.97, 121.43, 61.54, 57.40, 34.54, 27.95, 14.36, 7.47, 3.59.

MS (EI, 70 eV): *m*/*z* (%) = 428 (6), 426 (5), 372 (26), 371 (11), 370 (26), 327 (13), 326 (100), 325 (26), 324 (100), 323 (11), 313 (14), 311 (14), 298 (23), 296 (23), 270 (12), 268 (13).

HRMS (EI): *m*/*z* calc. for [$C_{19}H_{29}{}^{81}BrNO_3{}^{28}Si$]: 428.1080 [M–Et]$^{\bullet+}$; found: 428.1072.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (w), 2909 (w), 2874 (w), 1729 (s), 1642 (vs), 1555 (w), 1459 (m), 1360 (s), 1267 (vs), 1233 (s), 1175 (m), 1118 (vs), 1103 (vs), 1041 (vs), 1002 (s), 888 (w), 862 (vw), 794 (m), 721 (vs), 690 (s), 665 (w).

4-bromo-*N*-(*tert*-butyl)-2-iodo-*N*,6-dimethylbenzamide (21)



According to **TP5**, triethylsilylbenzene **20a** (550 mg, 1.38 mmol) was dissolved in CH_2Cl_2 (3 mL) and ICl (292 mg, 1.8 mmol) was added in one portion. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (544 mg, 1.33 mmol, 96%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.82 – 7.72 (m, 1H), 7.33 – 7.26 (m, 1H), 2.74 (s, 3H), 2.26 (s, 3H), 1.55 (s, 9H).

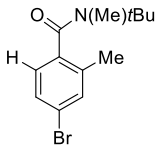
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 169.91, 143.26, 138.52, 137.05, 133.01, 121.79, 92.90, 57.57, 32.92, 28.07, 19.60.

MS (EI, 70 eV): *m/z* (%) = 411 (5), 409 (4), 325 (98), 323 (100), 170 (11), 168 (11), 127 (13), 89 (13).

HRMS (EI): *m/z* calc. for [$C_{13}H_{17}{}^{79}BrINO$]: 408.9538 [M]$^{\bullet+}$; found: 408.9536.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2974 (w), 2959 (w), 2921 (w), 2869 (vw), 1633 (vs), 1571 (m), 1543 (w), 1473 (m), 1455 (m), 1373 (vs), 1364 (vs), 1257 (w), 1212 (m), 1183 (w), 1149 (w), 1103 (s), 1044 (vs), 876 (w), 855 (m), 780 (w), 753 (w), 709 (m).

4-bromo-*N*-(*tert*-butyl)-*N*,2-dimethylbenzamide (22a)



According to **TP6**, iodoarene **21** (82 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, a sat. aq. solution of NH_4Cl (1 mL) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (49 mg, 0.17 mmol, 86%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.35 – 7.29 (m, 2H), 7.01 (d, *J*=8.0, 1H), 2.73 (s, 3H), 2.27 (s, 3H), 1.52 (s, 9H).

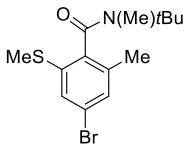
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.45, 138.44, 136.06, 133.31, 129.24, 127.30, 122.13, 57.06, 33.84, 28.15, 18.72.

MS (EI, 70 eV): *m/z* (%) = 284 (2), 282 (2), 199 (98), 197 (100), 171 (14), 169 (14), 90 (11), 89 (15).

HRMS (EI): *m/z* calc. for [$C_{13}H_{17}{}^{79}BrNO$]: 282.0494 [M−H]$^{\bullet+}$; found: 282.0491.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2959 (w), 2922 (vw), 1632 (vs), 1588 (m), 1562 (vw), 1472 (m), 1454 (m), 1364 (vs), 1255 (w), 1199 (m), 1156 (w), 1086 (m), 1046 (vs), 875 (m), 822 (m), 767 (w).

4-bromo-*N*-(*tert*-butyl)-*N*,2-dimethyl-6-(methylthio)benzamide (22b)



According to **TP6**, iodoarene **21** (62 mg, 0.15 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.14 mL, 1.10 M in THF, 0.16 mmol) was added dropwise. After 15 min, dimethyl disulfide (0.02 mL, 0.17 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (41 mg, 0.12 mmol, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.17 (d, *J* = 1.7, 1H), 7.13 (d, *J* = 1.8, 1H), 2.74 (s, 3H), 2.44 (s, 3H), 2.21 (s, 3H), 1.55 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 169.04, 137.77, 136.64, 136.00, 130.06, 126.44, 121.96, 57.39, 32.74, 28.19, 18.71, 16.23.

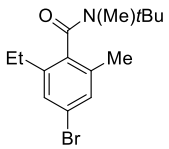
MS (EI, 70 eV): *m/z* (%) = 331 (1), 329 (1), 258 (41), 245 (100), 244 (17), 243 (99), 242 (18), 230 (14), 228 (14), 136 (28), 135 (27), 121 (20), 88 (11), 72 (23).

HRMS (EI): *m/z* calc. for $[C_{14}H_{20}{}^{79}BrNOS]$: 329.0449 $[M]^{\bullet+}$; found: 329.0440.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2959 (w), 2922 (w), 1627 (vs), 1561 (m), 1453 (m), 1373 (vs), 1255 (w), 1211 (m), 1183 (w), 1157 (w), 1109 (m), 1047 (vs), 895 (w), 842 (s), 798 (m), 768 (w), 730 (w).

m.p. (°C): 109.1–110.6.

4-bromo-*N*-(*tert*-butyl)-2-ethyl-*N*,6-dimethylbenzamide (22c)



In a modified version of **TP6**, iodoarene **21** (82 mg, 0.20 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –78 °C and *t*BuLi (0.21 mL, 1.95 M in heptane, 0.41 mmol, 2.05 equiv.) was added dropwise. After 15 min, iodoethane (0.2 mL, 0.22 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (38 mg, 0.12 mmol, 61%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.20 – 7.18 (m, 1H), 7.18 – 7.15 (m, 1H), 2.71 (s, 3H), 2.58 – 2.47 (m, 2H), 2.20 (t, *J*=0.7, 3H), 1.54 (s, 9H), 1.20 (t, *J*=7.6, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.67, 141.46, 137.86, 135.31, 130.51, 128.96, 121.65, 57.13, 33.06, 28.19, 25.78, 18.70, 14.78.

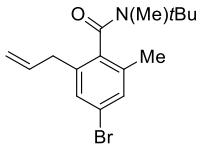
MS (EI, 70 eV): *m/z* (%) = 313 (3), 311 (4), 228 (11), 227 (100), 226 (77), 225 (100), 224 (77), 146 (27), 118 (15), 117 (37), 115 (34), 91 (11), 81 (15), 79 (13).

HRMS (EI): *m/z* calc. for $[C_{15}H_{22}{}^{79}BrNO]$: 311.0885 $[M]^{\bullet+}$; found: 311.0882.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2957 (w), 2922 (w), 1632 (vs), 1575 (m), 1453 (m), 1361 (vs), 1258 (vw), 1210 (m), 1157 (w), 1113 (w), 1043 (vs), 855 (s), 821 (m), 759 (w), 741 (vw).

m.p. (°C): 82.6 – 84.5.

2-allyl-4-bromo-*N*-(*tert*-butyl)-*N*,6-dimethylbenzamide (22d)



According to **TP6**, iodoarene **21** (62 mg, 0.15 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.14 mL, 1.10 M in THF, 0.16 mmol) was added dropwise. After 15 min, CuCN•2LiCl (0.02 mL, 0.02 mmol, 0.1 equiv.) was added, followed by allyl bromide (0.02 mL, 0.17 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (32 mg, 0.10 mmol, 66%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.20 – 7.18 (m, 2H), 5.96 – 5.81 (m, 1H), 5.13 – 5.09 (m, 1H), 5.08 (t, *J*=1.4, 1H), 3.31 – 3.26 (m, 2H), 2.70 (s, 3H), 2.21 (s, 3H), 1.54 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.3, 137.8, 137.6, 135.9, 135.4, 130.8, 129.7, 121.5, 116.9, 57.1, 36.8, 33.1, 28.1, 18.6.

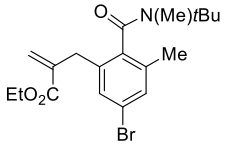
MS (EI, 70 eV): *m/z* (%) = 325 (1), 323 (1), 252 (19), 239 (32), 238 (81), 237 (33), 236 (88), 211 (22), 209 (23), 158 (10), 157 (64), 130 (90), 129 (100), 128 (52), 115 (64), 84 (18).

HRMS (EI): *m/z* calc. for [$C_{16}H_{22}{}^{79}BrNO$]: 323.0885 [M]$^{\bullet+}$; found: 323.0880.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (vw), 2958 (w), 2920 (w), 2854 (vw), 1632 (vs), 1576 (m), 1473 (w), 1457 (w), 1362 (vs), 1259 (w), 1208 (m), 1156 (w), 1111 (w), 1094 (w), 1044 (vs), 1002 (w), 922 (m), 857 (m), 830 (w), 780 (vw), 759 (vw), 683 (w).

m.p. (°C): 74.3 – 76.4.

Ethyl 2-(5-bromo-2-(*tert*-butyl(methyl)carbamoyl)-3-methylbenzyl)acrylate (22e)



According to **TP6**, iodoarene **21** (82 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, CuCN•2LiCl (0.02 mL, 1.0 M in THF, 0.02 mmol, 0.1 equiv.) was added, followed by ethyl 2-(bromomethyl)acrylate (89 mg, 0.22 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (54 mg, 0.14 mmol, 68%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.21 – 7.18 (m, 1H), 7.15 – 7.11 (m, 1H), 6.31 (q, *J* = 1.1, 1H), 5.48 (q, *J* = 1.4, 1H), 4.18 (q, *J* = 7.1, 2H), 3.66 – 3.42 (m, 2H), 2.71 (s, 3H), 2.24 – 2.18 (m, 3H), 1.51 (s, 9H), 1.26 (t, *J* = 7.1, 3H).

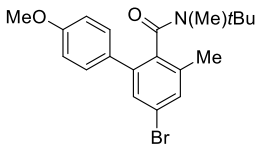
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.23, 166.77, 138.38, 138.30, 136.56, 135.63, 131.25, 129.91, 127.82, 121.58, 60.98, 57.21, 34.54, 33.14, 28.12, 18.74, 14.32.

MS (EI, 70 eV): *m/z* (%) = 397 (3), 395 (3), 280 (56), 279 (23), 268 (40), 266 (43), 240 (12), 239 (41), 238 (31), 237 (42), 236 (35), 235 (43), 209 (13), 207 (18), 186 (17), 158 (100), 157 (33), 156 (14), 155 (14), 145 (14), 143 (17), 130 (51), 129 (65), 128 (75), 127 (13), 115 (33), 84 (17), 81 (24), 79 (23), 72 (17), 56 (22).

HRMS (EI): *m/z* calc. for [$C_{19}H_{26}{}^{79}BrNO_3$]: 395.1096 [M]$^{\bullet+}$; found: 395.1094.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2926 (w), 1714 (vs), 1633 (vs), 1577 (s), 1475 (m), 1456 (m), 1366 (vs), 1300 (m), 1256 (s), 1209 (s), 1136 (s), 1107 (s), 1046 (vs), 1025 (s), 950 (w), 860 (m), 836 (w), 817 (w).

5-bromo-*N*-(*tert*-butyl)-4'-methoxy-*N*,3-dimethyl-[1,1'-biphenyl]-2-carboxamide (22f)



According to **TP6**, iodoarene **21** (82 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, $ZnCl_2$ (0.2 mL, 1.0 M in THF, 0.2 mmol, 1.0 equiv.) was added, followed $Pd(dba)_2$ (2 mg, 0.004 mmol, 0.02 equiv.), P(*o*-furyl)$_3$ (2 mg, 0.008 mmol, 0.04 equiv) and 4-iodoanisole (51 mg, 0.22 mmol) were added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (55 mg, 0.14 mmol, 71%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.39 – 7.34 (m, 2H), 7.32 – 7.31 (m, 1H), 7.30 – 7.29 (m, 1H), 6.91 – 6.87 (m, 2H), 3.83 (s, 3H), 2.44 (s, 3H), 2.29 (s, 3H), 1.30 (s, 9H).

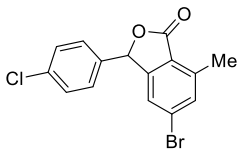
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.22, 159.48, 139.77, 137.34, 136.36, 131.72, 131.60, 130.37, 130.05, 121.56, 113.71, 57.03, 55.48, 32.96, 27.97, 19.09.

MS (EI, 70 eV): *m/z* (%) = 391 (18), 389 (17), 334 (18), 332 (18), 306 (14), 304 (18), 303 (77), 224 (34), 181 (14), 153 (16), 152 (18), 61 (14), 57 (18), 45 (15), 43 (100).

HRMS (EI): *m/z* calc. for [$C_{20}H_{24}{}^{79}BrNO_2$]: 389.0990 [M]$^{\bullet+}$; found: 389.0990.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2957 (w), 2923 (w), 1738 (vw), 1631 (vs), 1567 (w), 1512 (s), 1456 (m), 1364 (vs), 1286 (m), 1246 (vs), 1213 (m), 1178 (s), 1104 (m), 1044 (vs), 833 (vs).

5-bromo-3-(4-chlorophenyl)-7-methylisobenzofuran-1(3H)-one (22g)



Iodoarene **21** (62 mg, 0.15 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.14 mL, 1.10 M in THF, 0.16 mmol) was added dropwise. After 15 min, 4-chlorobenzaldehyde (23 mg, 0.17 mmol) was added and the mixture was allowed to warm to 25 °C. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude benzylic alcohol was dissolved in 1,4-dioxane (1 mL) and HCl (0.2 mL, 2.0 M in H_2O) was added. The solution was heated to 85 °C for 24 h. After cooling to 25 °C a sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x

10 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (31 mg, 0.09 mmol, 61%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.48 – 7.45 (m, 1H), 7.39 – 7.35 (m, 2H), 7.25 – 7.18 (m, 3H), 6.26 (s, 1H), 2.71 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 169.60, 151.54, 141.71, 135.63, 134.76, 134.54, 129.49, 129.35, 128.41, 123.63, 122.13, 80.56, 17.35.

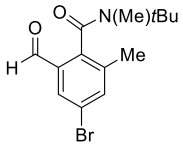
MS (EI, 70 eV): *m/z* (%) = 338 (14), 336 (11), 303 (36), 301 (37), 199 (96), 198 (38), 197 (100), 196 (39), 178 (18), 176 (22), 170 (10), 168 (10), 165 (20), 163 (10), 139 (21), 118 (10), 89 (30), 77 (10).

HRMS (EI): *m/z* calc. for [$C_{15}H_{10}{}^{79}BrClO_2$]: 335.9553 [M]$^{\bullet+}$; found: 335.9549.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (vw), 2919 (vw), 2851 (vw), 1760 (vs), 1589 (m), 1490 (m), 1455 (w), 1404 (w), 1377 (vw), 1333 (w), 1282 (m), 1235 (m), 1204 (m), 1089 (m), 1055 (m), 1007 (vs), 848 (m), 810 (m), 767 (m), 670 (m).

m.p. (°C): 120.6–122.1.

4-bromo-*N*-(*tert*-butyl)-2-formyl-*N*,6-dimethylbenzamide (22h)



According to **TP6**, iodoarene **21** (82 mg, 0.2 mmol) was dissolved in THF (0.5 mL). The mixture was cooled to –40 °C and *i*PrMgCl•LiCl (0.19 mL, 1.10 M in THF, 0.21 mmol) was added dropwise. After 15 min, dimethylformamide (0.02 mL, 0.22 mmol) was added. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (54 mg, 0.17 mmol, 86%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.95 (s, 1H), 7.88 – 7.82 (m, 1H), 7.61 – 7.55 (m, 1H), 2.71 (s, 3H), 2.31 (d, *J* = 0.7 Hz, 3H), 1.58 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 189.74, 168.53, 140.15, 138.76, 136.93, 133.50, 130.25, 122.27, 57.82, 33.32, 28.08, 18.15.

MS (EI, 70 eV): *m/z* (%) = 256 (20), 255 (16), 254 (23), 253 (17), 227 (76), 225 (83), 199 (33), 198 (26), 197 (33), 196 (32), 1194 (11), 171 (13), 170 (16), 169 (11), 168 (17), 118 (46), 90 (38), 89 (100), 81 (20), 79 (20), 77 (12), 63 (25), 56 (36), 42 (12).

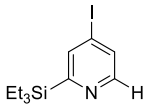
HRMS (EI): *m/z* calc. for [$C_{13}H_{15}{}^{79}BrNO_2$]: 296.0286 [M−Me]$^{\bullet+}$; found: 296.0284.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2977 (w), 2956 (w), 2922 (w), 1695 (s), 1635 (vs), 1577 (m), 1473 (m), 1457 (m), 1400 (m), 1364 (vs), 1245 (m), 1221 (s), 1173 (w), 1156 (m), 1105 (m), 1045 (vs), 950 (m), 867 (vs), 841 (m), 770 (w), 740 (m), 683 (m).

m.p. (°C): 111.3–113.2.

3.5 Preparation of 4-functionalized pyridines

4-iodo-2-(triethylsilyl)pyridine (25a)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by elemental iodine (152 mg, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (142 mg, 0.44 mmol, 89%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.40 (dd, *J* = 5.2, 0.7 Hz, 1H), 7.80 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.57 (dd, *J* = 5.2, 1.9 Hz, 1H), 1.01 – 0.93 (m, 9H), 0.89 – 0.78 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 168.47, 150.63, 138.80, 131.98, 105.43, 7.44, 2.98.

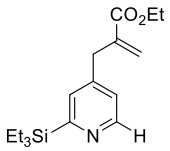
MS (EI, 70 eV): *m/z* (%) = 318 (21), 308 (12), 291 (100), 290 (44), 280 (20), 263 (44), 262 (59), 252 (23), 235 (20), 234 (89), 232 (38), 205 (12), 155 (23), 127 (37).

HRMS (EI): *m/z* calc. for [$C_{11}H_{17}IN^{28}Si$]: 318.0175 [M−H]$^{\bullet+}$; found: 318.0167.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3189 (w), 3073 (w), 3017 (w), 2996 (w), 2949 (m), 2892 (w), 2869 (m), 1637 (m), 1594 (s), 1579 (vs), 1558 (s), 1490 (m), 1457 (m), 1418 (s), 1399 (s), 1348 (m), 1297 (m), 1254 (m), 1222 (s), 1205 (m), 1139 (s), 1077 (m), 1049 (w), 1008 (s), 999 (s), 986 (m), 917 (w), 844 (m), 805 (vs), 734 (vs), 691 (vs).

m.p. (°C): 86.9–88.5.

Ethyl 2-((2-(triethylsilyl)pyridin-4-yl)methyl)acrylate (25b)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (0.55 mL, 1.0 M in THF, 0.55 mmol, 1.1 equiv.) and CuCN•2LiCl (0.05 mL, 1.0 M in THF, 0.05 mmol, 0.1 equiv.) were added, followed by ethyl 2-(bromomethyl)acrylate (116 mg, 0.6 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (95 mg, 0.31 mmol, 62%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.67 – 8.63 (m, 1H), 7.29 – 7.27 (m, 1H), 7.04 – 6.97 (m, 1H), 6.26 (q, *J* = 0.9 Hz, 1H), 5.48 (t, *J* = 1.3 Hz, 1H), 4.18 – 4.10 (m, 2H), 3.60 – 3.54 (m, 2H), 1.21 (tt, *J* = 7.1, 0.9 Hz, 3H), 0.93 (tq, *J* = 7.3, 1.1 Hz, 9H), 0.86 – 0.77 (m, 6H).

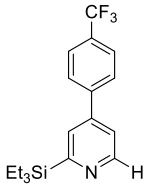
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.52, 166.19, 150.27, 145.41, 138.93, 130.56, 126.93, 123.14, 61.00, 37.70, 14.17, 7.44, 3.00.

MS (EI, 70 eV): *m/z* (%) = 304 (5), 278 (10), 277 (46), 276 (100), 248 (20), 220 (22).

HRMS (EI): *m/z* calc. for $[C_{17}H_{26}NO_2{}^{28}Si]$: 304.1733 $[M-H]^{\bullet+}$; found: 304.1735.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2910 (w), 2874 (m), 2361 (vw), 2340 (vw), 1717 (vs), 1715 (vs), 1635 (w), 1586 (m), 1457 (w), 1414 (w), 1298 (m), 1184 (s), 1141 (s), 1094 (w), 1018 (s), 948 (m), 858 (w), 818 (w), 719 (vs), 689 (s).

2-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridine (25c)



In a modified version of **TP4**, pyridine **23** (3.08 g, 10.0 mmol) and PMDTA (2.30 mL, 11 mmol, 1.1 equiv.) were dissolved in *n*hexane (10 mL). *n*BuLi (4.31 mL, 2.55 m in hexane, 11 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (11 mL, 1.0 m in THF, 11 mmol, 1.1 equiv.) was added, followed by $Pd(PPh_3)_4$ (231 mg, 0.2 mmol, 0.02 equiv.) and 4-iodobenzotrifluoride (3.3 g, 12.0 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless oil (3.25 g, 9.6 mmol, 96%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.88 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.78 – 7.69 (m, 4H), 7.65 (dd, *J* = 2.0, 0.9 Hz, 1H), 7.39 (dd, *J* = 5.1, 2.0 Hz, 1H), 1.05 – 0.99 (m, 9H), 0.96 – 0.87 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.59, 150.91, 144.67, 142.68, 130.94 (q, *J* = 33.0 Hz), 127.84, 127.67, 126.16 (q, *J* = 3.7 Hz), 124.18 (q, *J* = 272.0 Hz), 120.73, 7.57, 3.12.

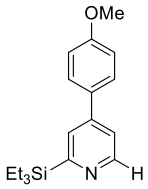
^{19}F-NMR: (101 MHz, $CDCl_3$): δ / ppm = −62.64.

MS (EI, 70 eV): *m/z* (%) = 336 (35), 326 (15), 310 (17), 309 (100), 308 (60), 298 (15), 284 (15), 282 (10), 281 (75), 280 (54), 270 (19), 253 (57), 252 (94), 250 (84), 223 (32), 204 (55), 154 (10), 151 (20).

HRMS (EI): *m/z* calc. for $[C_{18}H_{21}F_3N^{28}Si]$: 336.1395 $[M-H]^{\bullet+}$; found: 336.1389.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (w), 2911 (w), 2875 (w), 2361 (vw), 2342 (vw), 1618 (vw), 1585 (m), 1539 (w), 1457 (vw), 1413 (vw), 1322 (vs), 1238 (vw), 1166 (s), 1125 (vs), 1110 (s), 1071 (vs), 1044 (w), 1016 (s), 988 (w), 857 (w), 826 (vs), 714 (vs), 689 (m).

4-(4-methoxyphenyl)-2-(triethylsilyl)pyridine (25d)



In a modified version of **TP4**, pyridine **23** (3.08 g, 10.0 mmol) and PMDTA (2.4 mL, 11.0 mmol, 1.1 equiv.) were dissolved in *n*hexane (10 mL). *n*BuLi (4.3 mL, 2.55 M in hexane, 11.0 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (11 mL, 1.0 M in THF, 11.0 mmol, 1.1 equiv.) was added, followed by $Pd(PPh_3)_4$ (231 mg, 0.2 mmol, 0.02 equiv.) and 4-iodoanisole (2.81 g, 12.0 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless oil (2.49 g, 8.3 mmol, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.79 (dd, *J* = 5.2, 0.9 Hz, 1H), 7.64 (dd, *J* = 2.0, 0.9 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.35 (dd, *J* = 5.2, 2.0 Hz, 1H), 7.03 – 6.97 (m, 2H), 3.85 (s, 3H), 1.07 – 0.97 (m, 9H), 0.97 – 0.84 (m, 6H).

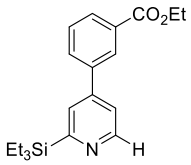
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.61, 160.45, 150.63, 145.45, 131.15, 128.29, 127.41, 120.14, 114.60, 55.46, 7.56, 3.11.

MS (EI, 70 eV): *m/z* (%) = 298 (14), 294 (18), 293 (12), 272 (17), 271 (63), 270 (35), 243 (28), 242 (14), 215 (15), 214 (30), 212 (13), 186 (17), 185 (100), 183 (13), 170 (29), 142 (32), 115 (17), 107 (16), 70 (11), 61 (14), 45 (12).

HRMS (EI): *m/z* calc. for $[C_{18}H_{24}NO^{28}Si]$: 298.1627 $[M-H]^{\bullet+}$; found: 298.1630.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3041 (vw), 3021 (vw), 2966 (w), 2938 (w), 2842 (vw), 1606 (m), 1592 (m), 1577 (m), 1540 (w), 1521 (m), 1486 (m), 1457 (m), 1405 (m), 1288 (m), 1257 (m), 1224 (m), 1185 (m), 1116 (w), 1036 (s), 1016 (s), 990 (m), 847 (m), 827 (m), 805 (vs), 719 (m).

ethyl 3-(2-(triethylsilyl)pyridin-4-yl)benzoate (25e)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (0.55 mL, 1.0 M in THF, 0.55 mmol, 1.1 equiv.) was added, followed by $Pd(PPh_3)_4$ (12 mg, 0.01 mmol, 0.02 equiv.) and ethyl 3-iodobenzoate (166 mg, 1.2 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as an orange oil (125 mg, 0.37 mmol, 73%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.86 (dd, *J* = 5.1, 0.9 Hz, 1H), 8.30 (t, *J* = 1.8 Hz, 1H), 8.10 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.80 (ddd, *J* = 7.7, 2.0, 1.2 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 5.2, 2.0 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.04 – 0.98 (m, 9H), 0.95 – 0.87 (m, 6H).

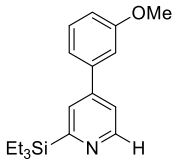
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.21, 166.33, 150.74, 145.13, 139.30, 131.51, 131.47, 129.85, 129.25, 128.33, 127.78, 120.70, 61.37, 14.44, 7.54, 3.11.

MS (EI, 70 eV): *m/z* (%) = 340 (31), 330 (13), 314 (18), 313 (100), 312 (49), 302 (11), 296 (11), 288 (12), 286 (12), 285 (76), 284 (38), 274 (11), 257 (60), 256 (61), 254 (26), 228 (11), 226 (50), 183 (11), 182 (41), 180 (13), 154 (30), 115 (21), 106 (10).

HRMS (EI): *m/z* calc. for $[C_{20}H_{26}NO_2{}^{28}Si]$: 340.1733 $[M-H]^{\bullet+}$; found: 340.1725.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (w), 2908 (w), 2873 (w), 2360 (vw), 2340 (vw), 2326 (vw), 1718 (s), 1581 (m), 1540 (w), 1457 (w), 1436 (w), 1367 (w), 1307 (m), 1281 (w), 1243 (vs), 1172 (w), 1108 (s), 1084 (m), 1059 (w), 1016 (m), 844 (w), 814 (w), 757 (vs), 717 (vs), 692 (s), 672 (s).

4-(3-methoxyphenyl)-2-(triethylsilyl)pyridine (25f)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and $ZnCl_2$ (0.55 mL, 1.0 M in THF, 0.55 mmol 1.1 equiv.) was added, followed by $Pd(PPh_3)_4$ (12 mg, 0.01 mmol, 0.02 equiv.) and 3-iodoanisole (140 mg, 1.2 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a yellow oil (90 mg, 0.30 mmol, 60%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.83 (dd, *J* = 5.2, 0.9 Hz, 1H), 7.66 (dd, *J* = 2.0, 0.9 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.21 (ddd, *J* = 7.6, 1.7, 0.9 Hz, 1H), 7.15 (dd, *J* = 2.6, 1.7 Hz, 1H), 6.98 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 3.88 (s, 3H), 1.07 – 0.98 (m, 9H), 0.96 – 0.86 (m, 6H).

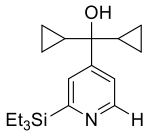
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.82, 160.25, 150.60, 146.03, 140.48, 130.27, 128.01, 120.79, 119.68, 114.02, 113.21, 55.51, 7.57, 3.13.

MS (EI, 70 eV): *m/z* (%) = 298 (31), 288 (13), 281 (20), 271 (62), 270 (33), 246 (15), 243 (49), 242 (28), 232 (14), 225 (61), 215 (46), 214 (65), 212 (52), 209 (27), 208 (14), 207 (100), 191 (19), 185 (53), 170 (15), 169 (34), 155 (15), 154 (23), 116 (17), 115 (19), 104 (14), 78 (15).

HRMS (EI): *m/z* calc. for $[C_{18}H_{24}NO^{28}Si]$: 298.1627 $[M-H]^{\bullet+}$; found: 298.1619.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (w), 2908 (w), 2872 (w), 2835 (w), 1592 (s), 1584 (vs), 1548 (s), 1507 (w), 1477 (s), 1433 (m), 1407 (s), 1297 (s), 1216 (vs), 1172 (s), 1090 (w), 1054 (s), 1031 (s), 998 (m), 872 (m), 856 (m), 822 (vs), 777 (vs), 714 (vs), 691 (vs).

Dicyclopropyl(2-(triethylsilyl)pyridin-4-yl)methanol (25g)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by dicyclopropyl ketone (0.07 mL, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (108 mg, 0.36 mmol, 71%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.72 (dd, *J* = 5.2, 0.9 Hz, 1H), 7.64 (dd, *J* = 2.0, 0.9 Hz, 1H), 7.35 (dd, *J* = 5.2, 2.0 Hz, 1H), 1.90 (s, 1H), 1.19 – 1.10 (m, 2H), 1.02 – 0.95 (m, 9H), 0.92 – 0.82 (m, 6H), 0.64 – 0.51 (m, 4H), 0.45 – 0.30 (m, 4H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.60, 153.47, 149.94, 127.03, 119.87, 73.30, 20.34, 7.56, 3.15, 2.25, 0.15.

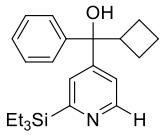
MS (EI, 70 eV): *m/z* (%) = 302 (20), 284 (15), 276 (15), 100 (275), 274 (52), 264 (11), 256 (13), 250 (10), 248 (12), 247 (85), 246 (34), 223 (14), 219 (56), 218 (56), 216 (16), 205 (22), 200 (13), 198 (10), 176 (13), 172 (15), 156 (11), 130 (16).

HRMS (EI): *m/z* calc. for $[C_{18}H_{28}NO^{28}Si]$: 302.1940 $[M-H]^{\bullet+}$; found: 302.1935.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3122 (br w), 3088 (w), 3008 (w), 2948 (m), 2929 (w), 2870 (m), 2361 (vw), 2340 (vw), 1588 (m), 1543 (w), 1456 (w), 1418 (w), 1374 (w), 1319 (w), 1237 (m), 1187 (m), 1141 (w), 1098 (w), 1033 (m), 1010 (s), 998 (vs), 959 (w), 919 (m), 883 (m), 820 (s), 751 (m), 722 (vs), 707 (vs), 689 (vs).

m.p. (°C): 75.4–77.4.

Cyclobutyl(phenyl)(2-(triethylsilyl)pyridin-4-yl)methanol (25h)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by cyclobutyl phenyl ketone (212 mg, 0.60 mmol,

1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (111 mg, 0.31 mmol, 63%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.60 (dd, *J* = 5.2, 0.9 Hz, 1H), 7.50 (dd, *J* = 2.0, 0.9 Hz, 1H), 7.37 – 7.27 (m, 4H), 7.26 – 7.19 (m, 1H), 7.08 (dd, *J* = 5.2, 2.0 Hz, 1H), 3.36 (tdd, *J* = 9.3, 8.2, 7.1 Hz, 1H), 2.43 (s, 1H), 2.14 – 1.64 (m, 6H), 0.99 – 0.89 (m, 9H), 0.88 – 0.78 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.82, 152.03, 150.05, 145.11, 128.45, 127.46, 127.23, 126.48, 120.41, 77.99, 43.74, 23.10, 22.51, 17.18, 7.50, 3.08.

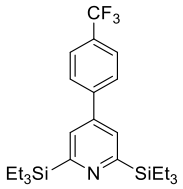
MS (EI, 70 eV): *m/z* (%) = 352 (4), 325 (35), 324 (18), 297 (21), 296 (11), 281 (22), 269 (19), 268 (20), 225 (65), 213 (15), 212 (13), 209 (30), 208 (14), 207 (100), 191 (21), 168 (15), 167 (22), 115 (20), 105 (31), 91 (11), 84 (12), 78 (13), 77 (18), 42 (19).

HRMS (EI): *m/z* calc. for $[C_{22}H_{30}NO^{28}Si]$: 352.2097 $[M–H]^{\bullet+}$; found: 352.2096.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3115 (br, w), 3057 (w), 2980 (w), 2951 (m), 2921 (w), 2869 (m), 2360 (vw), 2342 (vw), 1585 (m), 1446 (m), 1242 (w), 1195 (w), 1148 (m), 1098 (w), 1073 (w), 998 (vs), 969 (m), 906 (w), 821 (m), 771 (m), 735 (vs), 692 (vs).

m.p. (°C): 139.2 – 141.6.

2,6-bis(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridine (25i)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to –20 °C and $ZnCl_2$ (0.55 mL, 1.0 M in THF, 1.1 equiv.) was added, followed by $Pd(PPh_3)_4$ (12 mg, 0.01 mmol, 0.02 equiv.) and 4-iodobenzotrifluoride (163 mg, 0.6 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1, 2 vol% NEt_3) afforded the title compound as colorless oil (170 mg, 0.38 mmol, 75%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.78 – 7.68 (m, 4H), 7.51 (s, 2H), 1.08 – 0.97 (m, 18H), 0.95 – 0.84 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.19, 143.80, 141.93, 130.53 (q, *J* = 32.7 Hz), 127.76, 126.08, 126.01 (q, *J* = 3.7 Hz), 124.30 (q, *J* = 272.0 Hz), 7.63, 3.33.

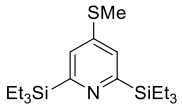
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = δ -62.54.

MS (EI, 70 eV): *m/z* (%) = 451 (1), 423 (14), 395 (10), 299 (11), 281 (11), 250 (14), 227 (22), 226 (14), 225 (100), 209 (36), 207 (53), 191 (13), 127 (22), 84 (14), 78 (15), 42 (12).

HRMS (EI): *m/z* calc. for $[C_{24}H_{36}F_3N^{28}Si_2]$: 451.2338 $[M]^{\bullet+}$; found: 451.2323.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2936 (w), 2910 (w), 2874 (m), 2360 (vw), 2336 (vw), 2324 (vw), 1576 (w), 1521 (w), 1457 (w), 1413 (w), 1322 (vs), 1238 (w), 1166 (s), 1128 (vs), 1109 (s), 1076 (s), 1059 (m), 1017 (s), 972 (w), 840 (vs), 815 (m), 757 (w), 715 (vs), 690 (s).

4-(methylthio)-2,6-bis(triethylsilyl)pyridine (25j)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by dimethyldisulfide (0.06 mL, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1, 2 vol% NEt_3) afforded the title compound as a colorless oil (117 mg, 0.33 mmol, 66%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.15 (s, 2H), 2.46 (s, 3H), 1.03 – 0.94 (m, 18H), 0.89 – 0.77 (m, 12H).

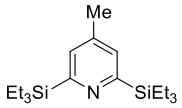
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.47, 144.90, 124.47, 13.68, 7.57, 3.28.

MS (EI, 70 eV): *m/z* (%) = 353 (3), 326 (21), 325 (100), 324 (36), 298 (13), 297 (81), 296 (12), 269 (63), 268 (44), 266 (15), 241 (23), 238 (20), 210 (19), 182 (31), 180 (13), 178 (10), 154 (11), 152 (17), 120 (17), 115 (32), 106 (15), 87 (12), 59 (15).

HRMS (EI): *m/z* calc. for $[C_{18}H_{35}NS^{28}Si_2]$: 353.2029 $[M]^{\bullet+}$; found: 353.2030.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (m), 2873 (m), 2361 (vw), 2342 (vw), 1542 (s), 1507 (w), 1457 (w), 1437 (w), 1414 (w), 1366 (w), 1237 (w), 1176 (w), 1162 (w), 1003 (s), 979 (m), 854 (w), 814 (s), 793 (w), 750 (s), 714 (vs), 688 (vs).

4-methyl-2,6-bis(triethylsilyl)pyridine (25k)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by methyl iodide (0.04 mL, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1 + 2 vol% NEt_3) afforded the title compound as a colorless oil (144 mg, 0.45 mmol, 90%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.15 (d, *J* = 0.6 Hz, 2H), 2.28 (t, *J* = 0.6 Hz, 3H), 1.03 – 0.94 (m, 18H), 0.87 – 0.76 (m, 12H).

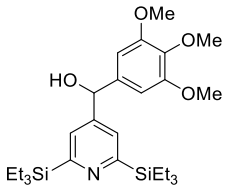
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.66, 141.18, 129.31, 21.41, 7.62, 3.32.

MS (EI, 70 eV): *m/z* (%) = 321 (2), 294 (14), 293 (100), 292 (40), 265 (76), 264 (13), 237 (61), 236 (42), 234 (14), 209 (17), 206 (19), 179 (23), 178 (16), 176 (12), 151 (15), 150 (17), 148 (13), 146 (11), 122 (24), 120 (26).

HRMS (EI): *m/z* calc. for [$C_{18}H_{35}N^{28}Si_2$]: 321.2308 [M]$^{\bullet+}$; found: 321.2306.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (m), 2873 (m), 1579 (w), 1457 (w), 1414 (w), 1375 (w), 1236 (w), 1003 (s), 982 (w), 972 (w), 856 (w), 816 (s), 756 (s), 715 (vs), 691 (vs).

(2,6-bis(triethylsilyl)pyridin-4-yl)(3,4,5-trimethoxyphenyl)methanol (25l)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by 3,4,5-trimethoxybenzaldehyde (118 mg, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 8:2, 2 vol% NEt_3) afforded the title compound as a yellow solid (157 mg, 0.31 mmol, 62%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.35 (d, *J* = 0.7 Hz, 2H), 6.55 (s, 2H), 5.66 (d, *J* = 3.4 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 6H), 2.59 (dd, *J* = 3.5, 0.9 Hz, 1H), 1.02 – 0.91 (m, 18H), 0.89 – 0.78 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.40, 153.37, 146.18, 138.90, 137.53, 125.59, 103.79, 75.86, 60.92, 56.08, 7.55, 3.25.

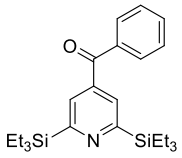
MS (EI, 70 eV): *m/z* (%) = 503 (32), 502 (12), 501 (24), 477 (14), 476 (35), 475 (100), 474 (33), 473 (22), 447 (19), 359 (11), 273 (13), 87 (12), 59 (12).

HRMS (EI): *m/z* calc. for [$C_{27}H_{45}NO_4{}^{28}Si_2$]: 503.2887 [M]$^{\bullet+}$; found: 503.2886.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3503 (br w), 2952 (m), 2907 (w), 2873 (m), 1592 (m), 1506 (m), 1457 (s), 1415 (m), 1334 (w), 1231 (s), 1180 (w), 1124 (vs), 1059 (m), 998 (s), 833 (w), 817 (s), 762 (m), 740 (s), 715 (vs), 678 (s).

m.p. (°C): 60.3 – 63.4.

(2,6-bis(triethylsilyl)pyridin-4-yl)(phenyl)methanone (25m)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by *N*-methoxy-*N*-methylbenzamide (0.09 mL, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (161 mg, 0.39 mmol, 78%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.89 – 7.80 (m, 2H), 7.63 (tt, *J* = 7.0, 1.3 Hz, 1H), 7.56 (s, 2H), 7.51 (tt, *J* = 7.6, 1.6 Hz, 2H), 1.03 – 0.96 (m, 18H), 0.90 – 0.82 (m, 12H).

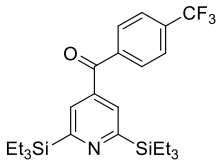
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 197.46, 167.47, 139.31, 136.59, 133.38, 130.40, 128.62, 126.44, 7.55, 3.23.

MS (EI, 70 eV): *m/z* (%) = 411 (74), 383 (65), 382 (54), 381 (100), 355 (46), 354 (23), 353 (32), 327 (36), 326 (50), 325 (22), 324 (32), 296 (39), 268 (32), 240 (43), 212 (25), 210 (34), 167 (24), 149 (23), 144 (56), 135 (34), 105 (23), 87 (32), 77 (22), 59 (37).

HRMS (EI): *m/z* calc. for $[C_{24}H_{37}NO^{28}Si_2]$: 411.2414 $[M]^{\bullet+}$; found: 411.2408.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2909 (m), 2873 (m), 2360 (vw), 2340 (vw), 1668 (s), 1597 (w), 1522 (w), 1457 (w), 1448 (m), 1415 (w), 1375 (w), 1317 (w), 1282 (s), 1236 (m), 1172 (m), 1120 (w), 1001 (s), 971 (s), 819 (m), 790 (s), 777 (w), 755 (m), 733 (s), 710 (vs), 690 (vs), 654 (s).

(2,6-bis(triethylsilyl)pyridin-4-yl)(4-(trifluoromethyl)phenyl)methanone (25n)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide (160 mg, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (183 mg, 0.38 mmol, 76%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.96 – 7.91 (m, 2H), 7.81 – 7.75 (m, 2H), 7.55 (s, 2H), 1.03 – 0.96 (m, 18H), 0.91 – 0.83 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 196.37, 168.00, 139.53, 138.39, 134.64 (q, *J* = 32.5 Hz), 130.55, 126.17, 125.69 (q, *J* = 3.8 Hz), 123.72 (q, *J* = 272.8 Hz), 7.54, 3.21.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -63.08.

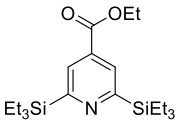
MS (EI, 70 eV): *m/z* (%) = 479 (52), 451 (37), 450 (37), 449 (55), 423 (23), 422 (13), 421 (16), 395 (20), 394 (24), 393 (13), 364 (15), 336 (16), 308 (25), 206 (16), 197 (14), 192 (25), 183 (20), 178 (44),

173 (31), 169 (34), 167 (15), 164 (100), 163 (22), 155 (53), 154 (14), 145 (40), 139 (44), 130 (22), 126 (17), 87 (52), 59 (50).

HRMS (EI): *m/z* calc. for $[C_{25}H_{36}F_3NO^{28}Si_2]$: 479.2288 $[M]^{\bullet+}$; found: 479.2279.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2935 (w), 2912 (w), 2874 (m), 2360 (vw), 2336 (vw), 2326 (vw), 1675 (m), 1457 (w), 1409 (m), 1375 (w), 1323 (vs), 1313 (s), 1279 (s), 1238 (w), 1169 (s), 1132 (vs), 1108 (m), 1066 (vs), 1018 (s), 976 (s), 856 (m), 816 (s), 771 (m), 716 (vs), 668 (s).

Ethyl 2,6-bis(triethylsilyl)isonicotinate (25o)



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and $MgCl_2$ (1 mL, 0.5 M in THF, 0.5 mmol, 1.0 equiv.) was added, followed by ethyl cyanoformate (0.06 mL, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (168 mg, 0.44 mmol, 88%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.85 (s, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.02 – 0.95 (m, 18H), 0.91 – 0.83 (m, 12H).

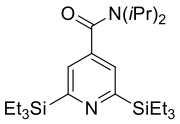
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.75, 167.12, 132.65, 126.34, 61.55, 14.40, 7.50, 3.22.

MS (EI, 70 eV): *m/z* (%) = 379 (1), 351 (32), 350 (100), 323 (27), 322 (32), 320 (12), 295 (20), 294 (30), 292 (12), 266 (14), 264 (22), 236 (25), 208 (25), 180 (15), 87 (16), 59 (13).

HRMS (EI): *m/z* calc. for $[C_{20}H_{37}NO_2{}^{28}Si_2]$: 379.2363 $[M]^{\bullet+}$; found: 379.2360.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (m), 2936 (w), 2910 (w), 2874 (m), 1729 (vs), 1534 (w), 1457 (w), 1415 (w), 1375 (w), 1280 (vs), 1238 (w), 1173 (s), 1151 (vs), 1109 (w), 1005 (s), 973 (w), 861 (vw), 814 (m), 768 (w), 715 (vs), 691 (vs).

***N*,*N*-diisopropyl-2,6-bis(triethylsilyl)isonicotinamide (25p)**



In a modified version of **TP4**, pyridine **23** (3.08 g, 10.0 mmol) and PMDTA (2.4 mL, 11.0 mmol, 1.1 equiv.) were dissolved in *n*hexane (10 mL). *n*BuLi (4.3 mL, 2.55 M in hexane, 11.0 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and THF (10 mL) was added, followed by *N*,*N*-diisopropylcarbamoyl chloride (1.96 g,

12 mmol, 1.2 equiv). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (2.91 g, 6.7 mmol, 67%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.21 (s, 2H), 3.72 (s, 1H), 3.52 (s, 1H), 1.64 – 1.47 (m, 6H), 1.19 – 1.07 (m, 6H), 1.02 – 0.92 (m, 18H), 0.89 – 0.78 (m, 12H).

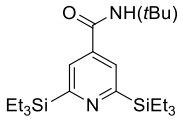
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.30, 166.99, 140.82, 123.98, 51.04, 46.13, 20.81, 7.52, 3.20.

MS (EI, 70 eV): *m/z* (%) = 434 (13), 423 (14), 407 (15), 406 (53), 405 (44), 392 (18), 391 (65), 378 (31), 363 (30), 361 (16), 350 (34), 349 (30), 347 (13), 321 (13), 305 (100), 291 (18), 289 (13), 277 (94), 249 (23), 247 (81), 246 (23), 225 (18), 219 (17), 207 (41), 192 (17), 87 (62), 84 (16), 75 (22), 59 (54).

HRMS (EI): *m/z* calc. for $[C_{24}H_{46}N_2O^{28}Si_2]$: 434.3149 $[M]^{\bullet+}$; found: 434.3141.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (m), 2935 (m), 2909 (w), 2873 (m), 2360 (vw), 2343 (vw), 1635 (s), 1517 (vw), 1438 (m), 1370 (m), 1330 (s), 1237 (w), 1206 (m), 1154 (w), 1135 (w), 1003 (s), 974 (w), 889 (w), 824 (s), 714 (vs), 704 (vs), 691 (vs).

***N*-(*tert*-butyl)-2,6-bis(triethylsilyl)isonicotinamide (25q)**



In a modified version of **TP4**, pyridine **23** (154 mg, 0.50 mmol) and PMDTA (0.12 mL, 0.55 mmol, 1.1 equiv.) were dissolved in *n*hexane (1 mL). *n*BuLi (0.22 mL, 2.55 M in hexane, 0.55 mmol, 1.1 equiv.) was added and the resulting solution was stirred for 3 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by *tert*-butyl isocyanate (0.07 mL, 0.60 mmol, 1.2 equiv.). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (134 mg, 0.33 mmol, 66%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.52 (s, 2H), 5.98 (s, 1H), 1.47 (s, 9H), 0.99 – 0.93 (m, 18H), 0.88 – 0.80 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.55, 167.02, 137.86, 124.34, 52.01, 28.87, 7.50, 3.18.

MS (EI, 70 eV): *m/z* (%) = 406 (4), 395 (11), 378 (10), 350 (12), 349 (65), 321 (30), 319 (23), 299 (11), 293 (10), 291 (10), 281 (11), 265 (14), 263 (21), 235 (28), 227 (21), 226 (12), 225 (100), 209 (38), 207 (44), 191 (11), 179 (23), 149 (10), 105 (20), 87 (34), 84 (11), 78 (13), 75 (28), 59 (34).

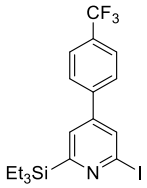
HRMS (EI): *m/z* calc. for $[C_{22}H_{42}N_2O^{28}Si_2]$: 406.2836 $[M]^{\bullet+}$; found: 406.2834.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3351 (br w), 2953 (m), 2936 (m), 2909 (m), 2874 (m), 2361 (vw), 2337 (vw), 1638 (s), 1523 (vs), 1456 (m), 1414 (w), 1395 (m), 1361 (m), 1308 (s), 1218 (s), 1193 (m), 1167 (w), 1116 (w), 1013 (s), 972 (m), 909 (w), 896 (w), 816 (s), 736 (vs), 713 (vs), 693 (vs).

m.p. (°C): 146.5–148.9.

3.6 Preparation of polyfunctionalized pyridines

2-iodo-6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridine (27a)



According to **TP7**, pyridine **25c** (169 mg, 0.5 mmol) was dissolved in THF (1 mL). TMPMgCl•LiCl (0.49 mL, 1.22 M in THF, 0.6 mmol) was added, followed by BF_3•OEt_2 (0.07 mL, 0.6 mmol). After 20 min elemental iodine (152 mg, 0.6 mmol, 1.2 equiv.) was added. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (171 mg, 0.37 mmol, 74%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.81 (d, *J* = 1.6 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.56 (dd, *J* = 1.7, 0.8 Hz, 1H), 1.05 – 0.98 (m, 9H), 0.93 – 0.84 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.11, 146.46, 141.10, 131.55, 131.36 (q, *J* = 32.5 Hz), 127.70, 127.19, 126.24 (q, *J* = 3.7 Hz), 124.06 (q, *J* = 272.5 Hz), 121.08, 7.48, 3.06.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.69.

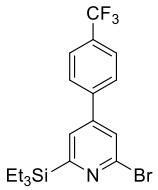
MS (EI, 70 eV): *m/z* (%) = 462 (9), 435 (36), 434 (18), 407 (18), 406 (14), 378 (21), 376 (11), 250 (10), 204 (15), 202 (18), 155 (30), 128 (10), 127 (100).

HRMS (EI): *m/z* calc. for $[C_{18}H_{20}F_3IN^{28}Si]$: 462.0362 $[M–H]^{\bullet+}$; found: 462.0355.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2950 (w), 2908 (w), 2873 (m), 2358 (vw), 2341 (vw), 1619 (vw), 1571 (m), 1505 (s), 1457 (w), 1408 (w), 1353 (w), 1322 (vs), 1282 (m), 1240 (w), 1163 (vs), 1121 (vs), 1097 (vs), 1073 (vs), 1054 (s), 1016 (vs), 977 (m), 897 (w), 877 (w), 835 (vs), 776 (s), 737 (s), 708 (vs).

m.p. (°C): 40.3 – 42.1.

2-bromo-6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridine (27b)



A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the monosilylated pyridine **25d** (1.01 g, 3.0 mmol, 1.0 equiv.) in dry THF (6 mL) and was cooled to 0 °C. TMPMgCl•LiCl (3 mL, 1.2 M in THF, 3.6 mmol, 1.2 equiv.) was added in one portion, immediately followed by BF_3•OEt_2 (0.44 mL, 3.6 mmol, 1.2 equiv.) and the mixture was stirred for 20 min. Then, elemental bromine (0.20 mL, 3.9 mmol, 1.3 equiv.) in THF (6 mL) was added dropwise and the mixture was allowed to warm to 25 °C. A sat. aq. $Na_2S_2O_3$ solution (5 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed

with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a slight yellow solid (1.04 g, 2.5 mmol, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.77 – 7.73 (m, 2H), 7.71 – 7.66 (m, 2H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 1.05 – 0.98 (m, 9H), 0.94 – 0.85 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.19, 147.54, 144.21, 141.23, 131.45 (q, *J* = 32.6 Hz), 127.75, 127.01, 126.28 (q, *J* = 3.8 Hz), 124.99, 124.05 (q, *J* = 272.2 Hz), 7.50, 3.04.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.72.

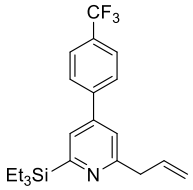
MS (EI, 70 eV): *m/z* (%) = 416 (23), 414 (23), 404 (17), 389 (68), 388 (42), 387 (69), 386 (47), 361 (34), 360 (42), 359 (35), 358 (44), 350 (24), 348 (24), 333 (19), 332 (53), 331 (20), 330 (53), 328 (35), 250 (23), 222 (24), 204 (70), 202 (100), 151 (19), 109 (22), 107 (25).

HRMS (EI): *m/z* calc. for [$C_{18}H_{20}{}^{79}Br^{19}F_3N^{28}Si$]: 414.0500 [M−H]$^{\bullet+}$; found: 414.0493.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2958 (w), 2904 (w), 2874 (w), 1620 (w), 1571 (m), 1508 (s), 1463 (w), 1410 (w), 1354 (w), 1323 (vs), 1283 (m), 1163 (s), 1112 (vs), 1073 (vs), 1017 (vs), 979 (m), 959 (m), 877 (m), 837 (vs), 789 (s), 738 (m), 708 (vs).

m.p. (°C): 53.9–55.7.

2-allyl-6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridine (27c)



According to **TP7**, pyridine **25c** (169 mg, 0.5 mmol) was dissolved in THF (1 mL). TMPMgCl•LiCl (0.49 mL, 1.22 M in THF, 0.6 mmol) was added, followed by BF_3•OEt_2 (0.07 mL, 0.6 mmol). After 20 min CuCN•2LiCl (0.05 mL, 1.0 M in THF, 0.1 equiv.) was added, followed by allyl bromide (0.05 mL, 0.6 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (138 mg, 0.37 mmol, 73%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.74 (t, *J* = 1.1 Hz, 4H), 7.50 (t, *J* = 2.0 Hz, 1H), 7.27 (t, *J* = 1.8 Hz, 1H), 6.18 (ddtd, *J* = 15.5, 10.1, 6.8, 1.7 Hz, 1H), 5.26 – 5.11 (m, 2H), 3.73 – 3.69 (m, 2H), 1.05 (ddt, *J* = 8.3, 7.0, 1.5 Hz, 9H), 0.92 (qt, *J* = 6.9, 1.8 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.13, 160.90, 145.01, 143.19, 136.48, 130.71 (q, *J* = 32.5 Hz), 127.70, 126.03 (q, *J* = 3.8 Hz), 125.40, 124.26 (q, *J* = 272.2 Hz), 119.64, 116.58, 43.44, 7.63, 3.25.

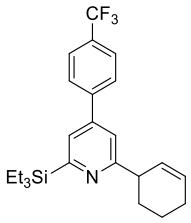
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.69.

MS (EI, 70 eV): *m/z* (%) = 376 (4), 227 (23), 226 (13), 225 (100), 218 (13), 216 (12), 214 (12), 209 (34), 207 (46), 191 (11), 151 (12), 91 (11), 84 (20), 78 (20), 42 (19).

HRMS (EI): *m/z* calc. for [$C_{21}H_{25}F_3N^{28}Si$]: 376.1708$^{\bullet+}$; found: 376.1701.

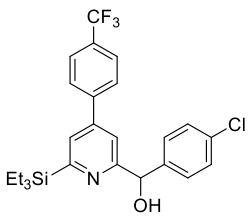
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2958 (w), 2912 (w), 2879 (w), 2365 (vw), 2333 (vw), 2229 (w), 1653 (m), 1585 (m), 1533 (w), 1405 (w), 1320 (vs), 1260 (m), 1162 (s), 1123 (vs), 1113 (vs), 1076 (m), 1062 (s), 1010 (s), 971 (m), 905 (w), 844 (s), 778 (m), 730 (s), 717 (s), 700 (s), 680 (m).
m.p. (°C): 79.5 – 81.7.

2-(cyclohex-2-en-1-yl)-6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridine (27d)



According to **TP7**, pyridine **25c** (1.01 g, 3.0 mmol) was dissolved in THF (6 mL). TMPMgCl•LiCl (2.95 mL, 1.22 M in THF, 3.6 mmol) was added, followed by BF_3•OEt_2 (0.44 mL, 3.6 mmol). After 20 min CuCN•2LiCl (0.3 mL, 1.0 M in THF, 0.3 mmol, 0.1 equiv.) was added, followed by 3-bromocyclohex-1-ene (0.42 mL, 3.6 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as an orange oil (652 mg, 1.56 mmol, 52%).
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.72 (d, *J* = 0.8 Hz, 4H), 7.45 (d, *J* = 1.8 Hz, 1H), 7.26 (d, *J* = 1.9 Hz, 1H), 5.98 – 5.84 (m, 2H), 3.79 – 3.63 (m, 1H), 2.19 – 2.05 (m, 3H), 1.87 – 1.60 (m, 3H), 1.11 – 0.83 (m, 15H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.80, 165.99, 144.88, 143.50 (q, *J* = 1.3 Hz), 130.62 (q, *J* = 32.6 Hz), 129.32, 128.90, 127.75, 127.72, 126.00 (q, *J* = 3.9 Hz), 124.29 (q, *J* = 272.0 Hz), 118.44, 44.25, 30.50, 25.30, 21.26, 7.66, 3.32.
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.62.
MS (EI, 70 eV): *m/z* (%) = 417 (22), 406 (15), 390 (24), 389 (100), 388 (39), 361 (51), 360 (28), 351 (16), 333 (50), 332 (69), 330 (46), 328 (22), 326 (27), 304 (31), 302 (33), 300 (40), 276 (83), 274 (35), 264 (22), 250 (35), 225 (56), 209 (25), 207 (56), 151 (20).
HRMS (EI): *m/z* calc. for $[C_{24}H_{30}F_3N^{28}Si]$: 417.2100 $[M]^{\bullet+}$; found: 417.2094.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (w), 2911 (w), 2874 (w), 1585 (w), 1539 (vw), 1457 (vw), 1322 (vs), 1166 (s), 1125 (vs), 1110 (s), 1072 (s), 1016 (s), 827 (s), 716 (vs), 689 (m).

(4-chlorophenyl)(6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)pyridin-2-yl)methanol (27e)



According to **TP7**, pyridine **25c** (169 mg, 0.5 mmol) was dissolved in THF (1 mL). TMPMgCl•LiCl (0.49 mL, 1.22 M in THF, 0.6 mmol) was added, followed by BF_3•OEt_2 (0.07 mL, 0.6 mmol). After 20 min 4-chlorobenzaldehyde (146 mg, 0.6 mmol) was added. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 8:2) afforded the title compound as a colorless solid (146 mg, 0.31 mmol, 61%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.71 (d, *J* = 8.2 Hz, 2H), 7.64 – 7.60 (m, 2H), 7.57 (dt, *J* = 1.6, 0.8 Hz, 1H), 7.39 – 7.29 (m, 4H), 7.15 – 7.12 (m, 1H), 6.15 (s, 1H), 5.78 (s, 1H), 1.05 (td, *J* = 7.9, 1.3 Hz, 9H), 1.00 – 0.90 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.44, 160.43, 146.18, 142.25, 142.14, 133.83, 131.16 (q, *J* = 32.8 Hz), 128.96, 128.62, 127.79, 127.30, 126.14 (q, *J* = 3.8 Hz), 124.08 (q, *J* = 272.3 Hz), 118.60, 74.27, 7.60, 3.19.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.69.

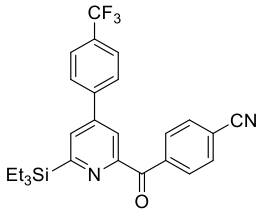
MS (EI, 70 eV): *m/z* (%) = 477 (56), 452 (13), 451 (42), 450 (41), 449 (100), 448 (38), 447 (10), 421 (13), 403 (10), 376 (11), 375 (22), 311 (14), 178 (13), 103 (17), 75 (44), 47 (12), 43 (12).

HRMS (EI): *m/z* calc. for [$C_{25}H_{27}ClF_3NO^{28}Si$]: 477.1503 [M]$^{\bullet+}$; found: 477.1495.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3219 (br, vw), 2952 (w), 2936 (w), 2909 (w), 2872 (w), 2361 (vw), 2344 (vw), 1618 (vw), 1591 (m), 1539 (w), 1489 (w), 1411 (w), 1323 (vs), 1241 (w), 1165 (s), 1110 (vs), 1063 (vs), 1014 (vs), 965 (w), 915 (w), 893 (w), 840 (s), 832 (s), 806 (m), 766 (w), 741 (m), 726 (vs), 701 (s), 672 (m).

m.p. (°C): 78.1 – 80.9.

4-(6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)picolinoyl)benzonitrile (27f)



According to **TP7**, pyridine **25c** (169 mg, 0.5 mmol) was dissolved in THF (1 mL). TMPMgCl•LiCl (0.49 mL, 1.22 M in THF, 0.6 mmol) was added, followed by BF_3•OEt_2 (0.07 mL, 0.6 mmol). After 20 min CuCN•2LiCl (0.60 mL, 1.0 M in THF, 1.2 equiv.) was added, followed by 4-cyanobenzoyl chloride (99 mg, 0.6 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (183 mg, 0.39 mmol, 78%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.35 – 8.30 (m, 2H), 8.29 (d, *J* = 1.8 Hz, 1H), 7.87 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.78 (dd, *J* = 8.4, 2.2 Hz, 4H), 1.04 – 0.97 (m, 9H), 0.94 – 0.87 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 192.33, 167.35, 154.78, 146.16, 141.65, 140.14, 131.77, 131.54, 131.35 (q, *J* = 32.9 Hz), 130.10, 127.73, 126.26 (q, *J* = 3.8 Hz), 124.02 (q, *J* = 272.2 Hz), 121.68, 118.35, 115.76, 7.43, 3.06.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.68.

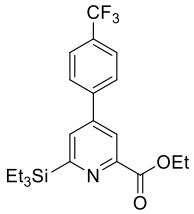
MS (EI, 70 eV): *m/z* (%) = 466 (5), 438 (20), 437 (12), 381 (20), 380 (43), 337 (19), 281 (20), 265 (14), 225 (74), 209 (31), 208 (14), 207 (100), 184 (13), 151 (11), 130 (24), 75 (17).

HRMS (EI): *m/z* calc. for $[C_{26}H_{25}F_3N_2O^{28}Si]$: 466.1688 $[M]^{\bullet+}$; found: 466.1678.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2959 (w), 2940 (w), 2912 (w), 2881 (w), 2360 (vw), 2342 (vw), 2229 (w), 1653 (s), 1617 (w), 1584 (w), 1558 (w), 1533 (w), 1405 (w), 1321 (vs), 1260 (s), 1161 (s), 1124 (vs), 1113 (vs), 1076 (m), 1063 (s), 1010 (s), 971 (m), 905 (w), 844 (vs), 817 (m), 778 (s), 731 (s), 717 (s), 697 (vs).

m.p. (°C): 122.5 – 124.9.

Ethyl 6-(triethylsilyl)-4-(4-(trifluoromethyl)phenyl)picolinate (27g)



According to **TP7**, pyridine **25c** (169 mg, 0.5 mmol) was dissolved in THF (1 mL). TMPMgCl•LiCl (0.49 mL, 1.22 M in THF, 0.6 mmol) was added, followed by BF_3•OEt_2 (0.07 mL, 0.6 mmol). After 20 min ethyl cyanoformate (0.06 mL, 0.6 mmol) was added. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless oil (134 mg, 0.33 mmol, 65%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.20 (d, *J* = 1.8 Hz, 1H), 7.81 – 7.73 (m, 5H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.10 – 1.00 (m, 9H), 1.00 – 0.86 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 168.61, 165.93, 149.75, 145.45, 141.96, 131.20 (q, *J* = 32.5 Hz), 129.91, 127.74, 126.20 (q, *J* = 3.8 Hz), 124.09 (q, *J* = 272.2 Hz), 121.95, 61.77, 14.34, 7.49, 3.17.

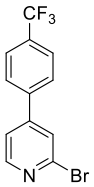
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = -62.69.

MS (EI, 70 eV): *m/z* (%) = 380 (100), 370 (45), 353 (10), 352 (51), 324 (17), 294 (46), 268 (10), 262 (11), 252 (21), 250 (13), 240 (58), 225 (38), 223 (18), 222 (38), 209 (16), 207 (25), 203 (13), 202 (98), 177 (10), 175 (15), 151 (31), 103 (33), 93 (29), 87 (16), 75 (75), 63 (11), 59 (20).

HRMS (EI): *m/z* calc. for $[C_{19}H_{21}F_3NO_2{}^{28}Si]$: 380.1294 $[M-Et]^{\bullet+}$; found: 380.1288.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (w), 2911 (vw), 2875 (w), 2360 (vw), 2337 (vw), 1743 (w), 1717 (m), 1589 (w), 1321 (vs), 1250 (s), 1211 (w), 1166 (s), 1125 (vs), 1111 (vs), 1075 (m), 1060 (vs), 1015 (s), 841 (s), 788 (m), 717 (s), 696 (s).

2-bromo-4-(4-(trifluoromethyl)phenyl)pyridine (28)



A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with mono-silyl pyridine **27b** (363 mg, 0.87 mmol, 1.0 equiv.) in dry THF (1.6 mL). A solution of tetrabutylammonium fluoride (1.3 mL, 1.0 M in THF, 1.3 mmol, 1.5 equiv.) was added and the mixture was stirred for 2 h. Afterwards a sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 8:2) afforded the title compound as a colorless solid (258 mg, 0.85 mmol, 98%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.46 (dd, *J* = 5.2, 0.7 Hz, 1H), 7.80 – 7.68 (m, 5H), 7.47 (dd, *J* = 5.2, 1.6 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 150.83, 149.92, 143.27, 140.42, 131.81 (q, *J* = 32.7 Hz), 127.68, 126.39 (q, *J* = 3.8 Hz), 126.22, 123.96 (q, *J* = 272.4 Hz), 121.08.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.78.

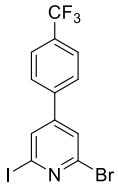
MS (EI, 70 eV): *m/z* (%) = 303 (42), 301 (42), 240 (30), 222 (63), 203 (13), 202 (100), 153 (14).

HRMS (EI): *m*/*z* calc. for $[C_{12}H_7{}^{79}BrF_3N]$: 300.9714 $[M]^{\bullet+}$; found: 300.9707.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3054 (vw), 3025 (vw), 2938 (vw), 1586 (s), 1526 (m), 1458 (w), 1374 (m), 1322 (vs), 1173 (s), 1113 (vs), 1070 (vs), 1040 (vs), 1017 (s), 988 (m), 972 (m), 831 (vs), 800 (s), 755 (s), 744 (s), 701 (s).

m.p. (°C): 123.5–124.5.

2-bromo-6-iodo-4-(4-(trifluoromethyl)phenyl)pyridine (30a)



According to **TP8**, the metalated pyridine was treated with elemental iodine (127 mg, 0.53 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (54 mg, 0.13 mmol, 97%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.90 (d, *J* = 1.4 Hz, 1H), 7.76 (dt, *J* = 8.1, 0.7 Hz, 2H), 7.68 (dt, *J* = 8.1, 0.8 Hz, 2H), 7.66 (d, *J* = 1.4 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 150.80, 141.55, 138.88 (q, *J* = 1.2 Hz), 132.17 (q, *J* = 33.0 Hz), 132.12, 127.66, 126.42 (q, *J* = 3.7 Hz), 125.54, 123.77 (q, *J* = 272.4 Hz), 116.48.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.88.

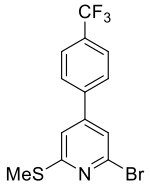
MS (EI, 70 eV): *m/z* (%) = 429 (27), 427 (28), 320 (17), 318 (17), 302 (30), 300 (30), 282 (10), 280 (10), 222 (12), 221 (100), 220 (15), 202 (11), 201 (13), 200 (10), 171 (20), 127 (40).

HRMS (EI): *m/z* calc. for $[C_{12}H_6{}^{79}Br^{19}F_3IN]$: 426.8680 $[M]^{\bullet+}$; found: 426.8668.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2928 (vw), 2913 (vw), 2859 (vw), 1570 (vs), 1508 (vs), 1352 (m), 1321 (vs), 1282 (s), 1163 (vs), 1107 (vs), 1072 (vs), 1052 (vs), 1014 (vs), 978 (m), 880 (m), 836 (vs), 814 (s), 757 (vs), 737 (vs), 713 (m).

m.p. (°C): 133.1–135.2.

2-bromo-6-(methylthio)-4-(4-(trifluoromethyl)phenyl)pyridine (30b)



According to **TP8**, the metalated pyridine was treated with dimethyl disulfide (0.05 mL, 0.53 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a yellow oil (39 mg, 0.11 mmol, 86%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.75 – 7.71 (m, 2H), 7.69 – 7.64 (m, 2H), 7.36 (d, *J* = 1.4 Hz, 1H), 7.31 (d, *J* = 1.3 Hz, 1H), 2.61 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.19, 149.40, 142.45, 140.49 (d, *J* = 1.4 Hz), 131.72 (q, *J* = 32.8 Hz), 127.64, 126.29 (q, *J* = 3.8 Hz), 123.98 (q, *J* = 272.3 Hz), 121.34, 118.47, 13.75.

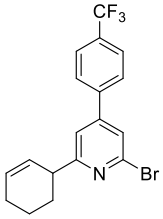
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.81.

MS (EI, 70 eV): *m/z* (%) = 349 (100), 347 (97), 346 (95), 303 (17), 301 (17), 253 (13), 225 (41), 222 (27), 221 (31), 209 (17), 207 (30), 203 (12), 202 (94), 175 (15), 171 (17), 153 (30), 140 (15), 81 (28), 79 (28).

HRMS (EI): *m/z* calc. for $[C_{13}H_9{}^{79}Br^{19}F_3NS]$: 346.9591 $[M]^{\bullet+}$; found: 346.9585.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2926 (w), 2853 (vw), 2360 (vw), 2335 (vw), 1576 (m), 1516 (s), 1355 (m), 1321 (vs), 1288 (m), 1166 (s), 1124 (vs), 1110 (vs), 1073 (vs), 1057 (vs), 1016 (s), 957 (w), 832 (vs), 789 (s), 757 (s), 743 (m), 718 (w).

2-bromo-6-(cyclohex-2-en-1-yl)-4-(4-(trifluoromethyl)phenyl)pyridine (30c)



According to **TP8**, after 60 min CuCN•2LiCL (0.02 mL, 1.0 M in THF, 0.02 mmol, 0.15 equiv.) was added to the metalated pyridine followed by 3-bromocyclohexene (0.06 mL, 0.53 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless oil (48 mg, 0.13 mmol, 97%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.74 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 1.4 Hz, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 6.01 – 5.95 (m, 1H), 5.84 – 5.78 (m, 1H), 3.71 – 3.61 (m, 1H), 2.21 – 2.06 (m, 3H), 1.81 – 1.60 (m, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.96, 150.15, 142.39, 140.98, 131.52 (q, *J* = 33.0 Hz), 130.14, 127.73, 127.71, 126.23 (q, *J* = 3.6 Hz), 123.99 (q, *J* = 272.1 Hz), 123.57, 118.94, 43.81, 30.60, 25.07, 20.86.

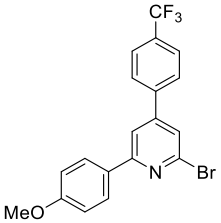
^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.67.

MS (EI, 70 eV): *m/z* (%) = 383 (19), 381 (18), 380 (12), 368 (12), 366 (12), 354 (51), 352 (53), 342 (11), 340 (11), 339 (10), 317 (26), 315 (26), 303 (19), 302 (100), 300 (13), 274 (17), 272 (11), 261 (11), 204 (11), 202 (18).

HRMS (EI): *m/z* calc. for [$C_{18}H_{15}{}^{79}Br^{19}F_3N_3$]: 381.0340 [M]$^{\bullet+}$; found: 381.0330.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3024 (vw), 2932 (w), 2860 (vw), 2835 (vw), 2361 (vw), 2337 (vw), 1589 (m), 1529 (s), 1385 (w), 1321 (vs), 1166 (s), 1123 (vs), 1110 (vs), 1062 (s), 1016 (s), 914 (w), 835 (vs), 797 (m), 758 (s), 723 (m), 708 (m).

2-bromo-6-(4-methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)pyridine (30d)



According to **TP8**, $ZnCl_2$ (0.53 mL, 1.0 M in THF, 0.53 mmol, 4.0 equiv.) was added, followed by $Pd(dba)_2$ (1.5 mg, 2.6 µmol, 0.02 equiv.), $P(o\text{-furyl})_3$ (1.2 mg, 5.2 µmol, 0.04 equiv.) and 4-iodoanisole (37 mg, 0.16 mmol, 1.2 equiv.). The reaction mixture was allowed to warm to 25 °C and was stirred for another 2 h. Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 19:1) afforded the title compound as a colorless solid (44 mg, 0.11 mmol, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.03 – 7.95 (m, 2H), 7.80 – 7.70 (m, 5H), 7.53 (d, *J* = 1.3 Hz, 1H), 7.01 – 6.96 (m, 2H), 3.87 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.31, 158.89, 150.42, 142.91, 141.03, 131.57 (q, *J* = 32.9, 32.0, 32.0 Hz), 130.11, 128.61, 127.69, 126.28 (q, *J* = 3.8 Hz), 124.01 (q, *J* = 272.2 Hz), 123.55, 116.75, 114.35, 55.52.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.67.

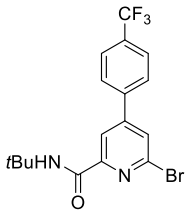
MS (EI, 70 eV): *m/z* (%) = 409 (97), 408 (20), 407 (100), 366 (13), 364 (13), 328 (20), 313 (10), 301 (13), 285 (44), 284 (12), 281 (10), 227 (10), 225 (27), 216 (13), 215 (10), 214 (20), 209 (11), 207 (45), 189 (20), 81 (11), 79 (11).

HRMS (EI): *m/z* calc. for [$C_{19}H_{13}{}^{79}Br^{19}F_3NO$]: 407.0133 [M]$^{\bullet+}$; found: 407.0126.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1607 (w), 1586 (m), 1526 (m), 1516 (m), 1456 (vw), 1419 (vw), 1405 (vw), 1382 (w), 1323 (vs), 1256 (m), 1171 (s), 1113 (vs), 1072 (s), 1044 (m), 1015 (m), 830 (vs), 807 (m), 765 (m), 659 (vw).

m.p. (°C): 102.4–104.7.

6-bromo-*N*-(*tert*-butyl)-4-(4-(trifluoromethyl)phenyl)picolinamide (30e)



According to **TP8**, the metalated pyridine was treated with *tert*-butyl isocyanate (43 mg, 0.52 mmol). Purification by flash column chromatography (silica gel, *i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless solid (41 mg, 0.10 mmol, 79%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.38 (d, *J* = 1.6 Hz, 1H), 7.79 (d, *J* = 1.6 Hz, 1H), 7.76 (s, 4H), 1.50 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.68, 152.54, 150.88, 141.11, 139.72, 131.94 (q, *J* = 33.1 Hz), 127.85, 127.58, 126.32 (q, *J* = 3.8 Hz), 123.78 (q, *J* = 273.0 Hz), 119.10, 51.39, 28.67.

^{19}F-NMR: (377 MHz, $CDCl_3$): δ / ppm = −62.82.

MS (EI, 70 eV): *m/z* (%) = 385 (1), 299 (12), 281 (15), 227 (18), 226 (13), 225 (100), 218 (11), 216 (11), 209 (46), 207 (76), 191 (21), 151 (10), 86 (14), 84 (41), 78 (14), 73 (11), 42 (72).

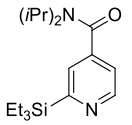
HRMS (EI): *m/z* calc. for [$C_{16}H_{13}{}^{79}BrF_3N_2O$]: 385.0163 [M−Me]$^{\bullet+}$; found: 385.0166.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3388 (w), 3079 (vw), 3061 (vw), 2976 (w), 2937 (vw), 2361 (vw), 2344 (vw), 1670 (vs), 1593 (m), 1517 (vs), 1457 (m), 1321 (vs), 1266 (m), 1225 (w), 1166 (s), 1114 (vs), 1073 (s), 1057 (vs), 1017 (s), 884 (w), 837 (s), 783 (s), 758 (s), 722 (s).

m.p. (°C): 133.1–134.8.

3.7 Preparation of partially functionalized electron-deficient pyridines

N,*N*-diisopropyl-2-(triethylsilyl)isonicotinamide (31)



Bis-silyl pyridine **25p** (1.5 g, 3.45 mmol, 1.0 equiv.) was dissolved in glacial acetic acid (15 mL) and stirred at 25 °C for 2 h. A sat. aq. solution of Na_2CO_3 solution was added until the gas evolution ceased and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash column chromatography (*i*hexane/ethyl acetate = 9:1) afforded the title compound as a colorless oil (920 mg, 2.87 mmol, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.81 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.34 (dd, *J* = 1.8, 1.0 Hz, 1H), 7.09 (dd, *J* = 5.0, 1.7 Hz, 1H), 3.69 (s, 1H), 3.51 (s, 1H), 1.53 (d, *J* = 6.8 Hz, 6H), 1.25 – 1.04 (m, 6H), 0.99 – 0.93 (m, 9H), 0.90 – 0.81 (m, 6H).

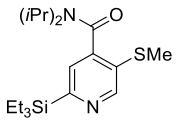
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 169.14, 167.40, 150.47, 143.81, 125.91, 119.02, 51.10, 46.20, 20.74, 7.45, 2.96.

MS (EI, 70 eV): *m/z* (%) = 319 (4), 309 (27), 292 (37), 291 (79), 281 (23), 277 (50), 264 (30), 263 (54), 249 (40), 236 (81), 235 (100), 233 (22), 221 (21), 219 (31), 207 (32), 193 (25), 192 (29), 191 (89), 179 (16), 177 (20), 163 (74), 149 (34), 135 (23), 133 (50), 106 (23), 87 (19).

HRMS (EI): *m/z* calc. for [$C_{18}H_{31}N_2O^{28}Si$]: 319.2206 $[M–H]^{\bullet+}$; found: 319.2197.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2936 (w), 2910 (w), 2874 (m), 2357 (vw), 2340 (vw), 1632 (vs), 1539 (w), 1456 (m), 1438 (s), 1370 (s), 1339 (vs), 1202 (m), 1135 (m), 1100 (w), 1037 (m), 1003 (m), 843 (w), 778 (w), 720 (vs), 697 (vs).

N,*N*-diisopropyl-5-(methylthio)-2-(triethylsilyl)isonicotinamide (33a)



A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with pyridine **31** (48 mg, 0.15 mmol, 1.0 equiv.) in dry THF (0.5 mL) and was cooled to 0 °C. TMPMgCl•LiCl (0.43 mL, 1.05 M in THF, 0.45 mmol, 3.0 equiv.) was added dropwise and the mixture was stirred for 60 min. Then dimethyldisulfide (0.04 mL, 0.45 mmol, 3.0 equiv.) was added in one portion and the mixture was allowed to warm to 25 °C. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (*i*hexane/ethyl acetate = 9:1) afforded the title compound as an orange oil (39 mg, 0.11 mmol, 71%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.72 (d, *J* = 0.8 Hz, 1H), 7.14 (d, *J* = 0.8 Hz, 1H), 3.50 (dp, *J* = 17.7, 6.7 Hz, 2H), 2.52 (s, 3H), 1.57 (d, *J* = 6.8 Hz, 6H), 1.13 (dd, *J* = 67.8, 6.5 Hz, 6H), 1.00 – 0.91 (m, 9H), 0.89 – 0.78 (m, 6H).

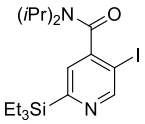
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.33, 163.33, 149.01, 143.73, 130.01, 125.20, 51.29, 46.23, 20.84, 16.33, 7.47, 3.01.

MS (EI, 70 eV): *m/z* (%) = 366 (10), 355 (16), 338 (47), 337 (54), 323 (54), 319 (22), 310 (51), 295 (17), 282 (76), 265 (38), 261 (25), 238 (48), 237 (100), 232 (73), 223 (20), 210 (25), 209 (33), 207 (24), 181 (16), 179 (26), 154 (21), 152 (70), 124 (30), 106 (17), 87 (39), 84 (33), 59 (30).

HRMS (EI): *m/z* calc. for $[C_{19}H_{34}N_2OS^{28}Si]$: 366.2161 $[M]^{\bullet+}$; found: 366.2158.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2933 (w), 2873 (m), 2362 (vw), 2342 (vw), 1634 (vs), 1437 (s), 1369 (m), 1345 (vs), 1286 (m), 1212 (w), 1162 (w), 1136 (w), 1109 (w), 1048 (s), 1006 (m), 972 (w), 888 (w), 856 (w), 789 (m), 720 (vs), 700 (vs).

5-iodo-*N*,*N*-diisopropyl-2-(triethylsilyl)isonicotinamide (33b)



A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the pyridine **31** (64 mg, 0.20 mmol, 1.0 equiv.) in dry THF (0.5 mL) and was cooled to 0 °C. TMPMgCl•LiCl (0.57 mL, 1.05 M in THF, 0.60 mmol, 3.0 equiv.) was added dropwise and the mixture was stirred for 60 min. Then elemental iodine (152 mg, 0.6 mmol, 3.0 equiv.) was added in one portion and the mixture was allowed to warm to 25 °C. A sat. aq. $Na_2S_2O_3$ solution (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (*i*hexane/ethyl acetate = 9:1) afforded the title compound as a yellow solid (42 mg, 0.09 mmol, 47%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.06 (d, *J* = 0.8 Hz, 1H), 7.20 (d, *J* = 0.8 Hz, 1H), 3.50 (dhept, *J* = 26.6, 6.7 Hz, 2H), 1.58 (dd, *J* = 6.8, 4.3 Hz, 6H), 1.27 (d, *J* = 6.7 Hz, 3H), 1.06 (d, *J* = 6.6 Hz, 3H), 0.99 – 0.92 (m, 9H), 0.87 – 0.79 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 168.11, 166.17, 157.90, 148.65, 126.29, 91.79, 51.48, 46.40, 20.92, 20.84, 20.81, 20.17, 7.42, 2.92.

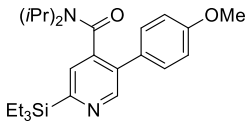
MS (EI, 70 eV): *m/z* (%) = 446 (1), 127 (100).

HRMS (EI): *m/z* calc. for $[C_{18}H_{31}IN_2O^{28}Si]$: 446.1250 $[M]^{\bullet+}$; found: 446.1244.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2947 (w), 2930 (w), 2872 (w), 1637 (vs), 1448 (m), 1437 (m), 1368 (s), 1343 (s), 1282 (m), 1209 (w), 1155 (w), 1135 (w), 1108 (w), 1003 (s), 972 (w), 889 (m), 856 (w), 782 (s), 742 (s), 722 (s), 688 (s).

m.p. (°C): 95.9 – 97.8.

_N_,_N_-diisopropyl-5-(4-methoxyphenyl)-2-(triethylsilyl)isonicotinamide (33c)



A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the pyridine **31** (64 mg, 0.20 mmol, 1.0 equiv.) in dry THF (0.5 mL) and was cooled to 0 °C. TMPMgCl•LiCl (0.57 mL, 1.05 M in THF, 0.60 mmol, 3.0 equiv.) was added dropwise and the mixture was stirred for 60 min. Then $ZnCl_2$ (0.6 mL, 1.0 m in THF, 0.6 mmol, 3.0 equiv.) was added, followed by $Pd(dba)_2$ (2 mg, 0.04 mmol, 0.02 equiv.), P(2-furyl)$_3$ (2 mg, 0.08 mmol, 0.04 equiv) and 4-iodoanisole (51 mg, 0.22 mmol, 1.1 equiv.). The mixture was warmed to 25 °C and stirred for 2 h. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (*i*hexane/ethyl acetate = 9:1) afforded the title compound as a yellow oil (37 mg, 0.09 mmol, 43%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.81 (d, *J* = 0.8 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.31 (d, *J* = 0.8 Hz, 1H), 6.98 – 6.91 (m, 2H), 3.83 (s, 3H), 3.29 (dp, *J* = 15.6, 6.8 Hz, 2H), 1.53 (d, *J* = 6.8 Hz, 3H), 1.32 (d, *J* = 6.8 Hz, 3H), 1.03 – 0.96 (m, 9H), 0.93 – 0.84 (m, 9H), 0.41 (d, *J* = 6.6 Hz, 3H).

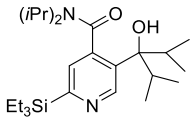
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 168.76, 165.08, 159.94, 150.32, 142.04, 130.93, 130.64, 129.19, 126.57, 114.19, 55.46, 50.83, 45.95, 20.93, 20.70, 19.74, 19.66, 7.51, 3.06.

MS (EI, 70 eV): *m/z* (%) = 426 (40), 399 (23), 398 (89), 397 (57), 383 (100), 371 (22), 370 (85), 369 (25), 355 (40), 342 (67), 341 (52), 339 (35), 298 (59), 297 (24), 269 (24), 239 (48), 225 (23), (212), 211 (24), 207 (51), 196 (62), 130 (23), 87 (34), 59 (28).

HRMS (EI): *m/z* calc. for [$C_{25}H_{38}N_2O_2{}^{28}Si$]: 426.2703 [M]$^{\bullet+}$; found: 426.2696.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (m), 2933 (m), 2909 (w), 2873 (m), 2361 (vw), 2340 (vw), 1627 (vs), 1610 (s), 1510 (s), 1441 (vs), 1369 (m), 1349 (s), 1319 (m), 1292 (m), 1247 (vs), 1180 (s), 1036 (s), 995 (s), 890 (w), 834 (s), 808 (m), 793 (w), 719 (vs), 701 (vs).

5-(3-hydroxy-2,4-dimethylpentan-3-yl)-_N_,_N_-diisopropyl-2-(triethylsilyl)isonicotinamide (33d)



A dry and argon flushed flask, equipped with a magnetic stirring bar and a septum, was charged with the pyridine **31** (64 mg, 0.20 mmol, 1.0 equiv.) in dry THF (0.5 mL) and was cooled to 0 °C. TMPMgCl•LiCl (0.57 mL, 1.05 M in THF, 0.60 mmol, 3.0 equiv.) was added dropwise and the mixture was stirred for 60 min. Then diisopropyl ketone (0.11 mL, 0.6 mmol, 3.0 equiv.) was added in one portion and the mixture was allowed to warm to 25 °C. A sat. aq. NH_4Cl solution (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were

washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (*i*hexane/ethyl acetate = 8:2) afforded the title compound as a yellow oil (57 mg, 0.13 mmol, 66%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.73 (d, *J* = 0.8 Hz, 1H), 7.11 (d, *J* = 0.8 Hz, 1H), 3.58 (hept, *J* = 6.7 Hz, 1H), 3.48 (hept, *J* = 6.8 Hz, 1H), 3.01 (d, *J* = 1.1 Hz, 1H), 2.33 (hept, *J* = 6.8 Hz, 1H), 2.21 (hept, *J* = 6.8 Hz, 1H), 1.54 (d, *J* = 1.8 Hz, 3H), 1.53 (d, *J* = 1.8 Hz, 3H), 1.15 (d, *J* = 6.6 Hz, 3H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.99 – 0.79 (m, 29H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 172.54, 163.14, 149.60, 142.50, 136.13, 126.99, 82.33, 51.01, 46.00, 36.54, 35.40, 20.52, 20.49, 20.37, 20.11, 18.16, 18.08, 17.17, 16.95, 7.49, 3.00.

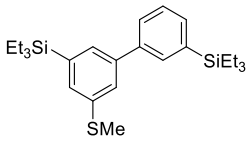
MS (EI, 70 eV): *m/z* (%) = 416 (2), 299 (10), 290 (16), 281 (23), 225 (76), 209 (32), 208 (13), 207 (100), 191 (18), 176 (23), 130 (17), 86 (19), 84 (25), 75 (13).

HRMS (EI): *m*/*z* calc. for $[C_{25}H_{44}N_2O^{28}Si]$: 416.3223 $[M-H_2O]^{\bullet+}$; found: 416.3222.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (s), 2934 (m), 2873 (m), 2360 (vw), 2342 (vw), 1616 (vs), 1440 (vs), 1379 (s), 1368 (s), 1342 (vs), 1294 (m), 1279 (m), 1210 (m), 1162 (m), 1066 (m), 1036 (m), 1000 (vs), 896 (m), 846 (w), 796 (m), 723 (vs), 701 (vs), 676 (s).

3.8 Preparation of remote functionalized bis(triethylsiyl)-biphenyls

(5-(methylthio)-[1,1'-biphenyl]-3,3'-diyl)bis(triethylsilane) (35)



According to **TP4**, biphenyl **34a** (191 mg, 0.5 mmol) and PMDTA (0.31 mL, 1.5 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.59 mL, 2.55 M in hexane, 1.5 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to −20 °C and THF (1 mL) was added, followed by S_2Me_2 (0.16 mL, 1.75 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (81 mg, 0.19 mmol, 38%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.67 (dt, *J* = 1.9, 0.8 Hz, 1H), 7.55 (dt, *J* = 7.6, 1.7 Hz, 1H), 7.50 (dt, *J* = 7.3, 1.3 Hz, 1H), 7.45 (td, *J* = 2.9, 1.4 Hz, 3H), 7.38 (dd, *J* = 1.8, 1.0 Hz, 1H), 2.55 (s, 3H), 1.06 – 0.97 (m, 18H), 0.90 – 0.79 (m, 12H).

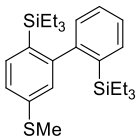
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 141.68, 140.45, 138.87, 138.15, 138.03, 133.32, 133.16, 131.22, 130.25, 128.05, 127.78, 126.07, 16.11, 7.47, 7.47, 3.43, 3.40.

MS (EI, 70 eV): *m/z* (%) = 428 (5), 299 (10), 281 (15), 227 (17), 226 (12), 225 (100), 209 (44), 208 (10), 207 (80), 191 (20), 151 (10), 42 (20).

HRMS (EI): *m/z* calc. for $[C_{25}H_{40}S^{28}Si_2]$: 428.2389 $[M]^{\bullet+}$; found: 428.2385.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (m), 2908 (w), 2873 (w), 1556 (w), 1457 (w), 1415 (w), 1363 (w), 1236 (w), 1140 (w), 1119 (w), 1005 (m), 968 (w), 853 (w), 805 (w), 716 (vs).

(5-(methylthio)-[1,1'-biphenyl]-2,2'-diyl)bis(triethylsilane) (36a)



According to **TP4**, biphenyl **34b** (172 mg, 0.45 mmol) and PMDTA (0.28 mL, 1.35 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.53 mL, 2.55 M in hexane, 1.35 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by dimethyldisulfide (0.14 mL, 1.58 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (102 mg, 0.24 mmol, 53%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.58 – 7.54 (m, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.36 – 7.27 (m, 2H), 7.20 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.14 – 7.10 (m, 1H), 6.99 (d, *J* = 2.0 Hz, 1H), 2.47 (s, 3H), 0.87 – 0.75 (m, 18H), 0.61 – 0.28 (m, 12H).

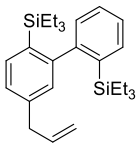
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 151.51, 150.59, 138.10, 135.95, 135.80, 135.49, 132.00, 130.18, 127.71, 127.68, 126.31, 123.70, 15.07, 7.75, 7.69, 4.39, 4.29.

MS (EI, 70 eV): *m/z* (%) = 428 (1), 413 (19), 285 (11), 273 (18), 255 (40), 245 (11), 227 (25), 165 (13), 115 (33), 105 (13), 87 (100), 59 (36).

HRMS (EI): *m/z* calc. for [$C_{25}H_{40}S^{28}Si_2$]: 428.2389 [M]$^{\bullet+}$; found: 428.2382.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (w), 2908 (w), 2872 (w), 1573 (w), 1455 (w), 1420 (w), 1239 (w), 1086 (w), 1055 (w), 1003 (m), 966 (w), 821 (w), 769 (m), 715 (vs), 685 (m).

(5-allyl-[1,1'-biphenyl]-2,2'-diyl)bis(triethylsilane) (36b)



According to **TP4**, biphenyl **34b** (172 mg, 0.45 mmol) and PMDTA (0.28 mL, 1.35 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.53 mL, 2.55 M in hexane, 1.35 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and $ZnCl_2$ (1.5 mL, 1.0 M in THF, 1.5 mmol) and CuCN•2LiCl (0.05 mL, 0.05 mmol, 0.1 equiv.) were added, followed by allylbromide (0.14 mL, 1.58 mmol). Purification of the crude product by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a colorless oil (112 mg, 0.27 mmol, 59%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.60 – 7.55 (m, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.20 – 7.12 (m, 2H), 6.99 (d, *J* = 1.9 Hz, 1H), 6.14 – 5.90 (m, 1H), 5.17 – 5.04 (m, 2H), 3.43 – 3.38 (m, 2H), 0.82 (td, *J* = 7.9, 1.2 Hz, 18H), 0.64 – 0.26 (m, 12H).

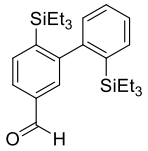
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 151.24, 151.16, 139.40, 137.20, 135.95, 135.66, 135.44, 133.21, 130.75, 130.29, 127.58, 126.41, 126.08, 116.11, 40.26, 7.74, 7.73, 4.36, 4.32.

MS (EI, 70 eV): *m/z* (%) = 422 (1), 306 (10), 267 (45), 250 (16), 249 (100), 239 (14), 221 (38), 217 (12), 115 (40), 105 (14), 87 (98), 59 (36).

HRMS (EI): *m/z* calc. for [$C_{27}H_{42}{}^{28}Si_2$]: 422.2825 [M]$^{\bullet+}$; found: 422.2819.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951 (w), 2908 (w), 2873 (w), 1458 (w), 1415 (w), 1235 (vw), 1094 (w), 1003 (m), 973 (vw), 913 (w), 770 (w), 711 (vs), 677 (m).

2',6-bis(triethylsilyl)-[1,1'-biphenyl]-3-carbaldehyde (36c)



According to **TP4**, biphenyl **34b** (172 mg, 0.45 mmol) and PMDTA (0.28 mL, 1.35 mmol) were dissolved in *n*hexane (1 mL). *n*BuLi (0.53 mL, 2.55 M in hexane, 1.35 mmol) was added and the resulting solution was stirred for 6 h. Afterwards, the mixture was cooled to –20 °C and THF (1 mL) was added, followed by dimethylformamide (0.12 mL, 1.58 mmol). Purification of the crude product

by flash column chromatography (silica gel, *i*hexane) afforded the title compound as a yellow oil (106 mg, 0.26 mmol, 57%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.02 (s, 1H), 7.82 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.34 (pd, *J* = 7.4, 1.6 Hz, 2H), 7.12 – 7.07 (m, 1H), 0.80 (td, *J* = 7.9, 3.7 Hz, 18H), 0.59 – 0.27 (m, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 192.70, 151.93, 149.60, 145.16, 136.11, 136.08, 135.70, 135.30, 131.16, 130.16, 127.87, 126.73, 126.67, 7.69, 7.64, 4.46, 4.17.

MS (EI, 70 eV): *m/z* (%) = 410 (1), 381 (13), 209 (20), 115 (21), 105 (14), 87 (100), 59 (43).

HRMS (EI): *m*/*z* calc. for $[C_{25}H_{38}O^{28}Si]$: 410.2461 $[M]^{\bullet+}$; found: 410.2461.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (w), 2909 (w), 2873 (w), 1701 (s), 1457 (w), 1416 (vw), 1376 (w), 1237 (w), 1174 (w), 1121 (vw), 1091 (vw), 1003 (m), 962 (vw), 706 (vs).