Dissertation zur Erlangung des Doktorgrades

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REGIOSELECTIVE FUNCTIONALIZATION OF AROMATICS AND HETEROCYCLES BEARING A *BIS*-SILYL-METHYL GROUP,

ONE-POT PROCEDURE FOR THE PREPARATION OF TERTIARY AMINES *VIA* IMINIUM IONS

AND PREPARATION OF NEW BENZODITHIOPHENE BUILDING BLOCKS FOR COVALENT ORGANIC FRAMEWORKS

von

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Erklärung

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Eidesstattliche Versicherung

Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

München, ...

.....

Veronika Werner

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Veronika Werner, Thomas Klatt, Masaya Fujii, Jenifer Markiewicz, Yitzhak Apeloig, Paul Knochel: "Preparation and Regioselective Metalation of *Bis*(trimethylsilyl)methyl-Substituted Aryl Derivatives", *Chem. Eur. J.* **2014**, *20(27)*, 8338-8342.

Dana D. Medina, Julian Rotter, Yinghong Hu, Mirjam Dogru, Veronika Werner, Florian Auras, John Markiewicz, Paul Knochel, Thomas Bein: "Room Temperature Synthesis of Covalent Organic Framework Films through Vapor Assisted Conversion", *J. Am. Chem. Soc.* **2015**, *accepted for publication*.

Veronika Werner, Mario Ellwart, Andreas J. Wagner, Paul Knochel: "Preparation of Tertiary Amines by the Reaction of Iminium Ions Derived from Unsymmetrical Aminals with Zinc and Magnesium Organometallics", *manuscript submitted*.

Thomas Klatt, Veronika Werner, Marina G. Maximova, D. Didier, Yitzhak Apeloig, Paul Knochel: "Preparation and Regioselective Magnesiation or Lithiation of *Bis*(trimethylsilyl)methyl-Substituted Heteroaryls for the Generation of Highly Functionalized Heterocycles", *manuscript submitted*.

Review Articles:

Nadja M. Barl, Veronika Werner, Christoph Sämann, Paul Knochel: "The Halogen/Magnesium-Exchange Using *i*PrMgCl·LiCl and Related Exchange Reagents", *Heterocycles* **2014**, *88(2)*, 827-844.

MEINER FAMILIE

“Wissenschaft:

Es ist nicht ihr Ziel, der unendlichen Weisheit eine Tür zu öffnen,

sondern eine Grenze zu setzen dem unendlichen Irrtum”

BERTOLD BRECHT

(1898 - 1956)

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A: INTRODUCTION

1. OVERVIEW

"Every aspect of the world today – even politics and international relations – is affected by chemistry."[1] This statement of Linus Pauling in 1984 counts more than ever nowadays, as a growing population, climate change and shrinking fossil fuel reserves are challenging today's society worldwide. As a consequence, scientists' efforts should be directed towards solving existing or predicted social and global problems regarding energy, materials, the environment, natural disasters, water, food and health.[2] Chemistry in general and especially organic chemistry is providing and constantly developing practical solutions to these threats by creating new substances, ranging from small molecules to highly complex materials and establishing efficient synthetic methodologies that can be applied in large production processes.[3] In this context, today's organic chemists attempt both to understand structures and characteristics of substances in detail and to create new compounds with desirable properties and functions.[2] The organometallic chemistry helps to fulfill this task by providing a useful and ever growing toolbox of methods and reagents. Its origin lies in the 19th century with the synthesis of diethylzinc by *Frankland*, the first discovery of a carbon-metal bond.[4] Another milestone was set by *Grignard* at the beginning of the 20th century, who prepared the first isolable organomagnesium compound.[5] Since then, a wide range of various main-group or transition metal based organometallics, has been investigated and successfully used as both catalysts and reagents in organic synthesis.[6] The reactivity of these reagents can be fine-tuned by the choice of the metal. Strong polarized carbon-metal bonds, like carbon-lithium, carbon-sodium and carbon-magnesium bonds, are closely connected to a high reactivity towards electrophiles accompanied by low chemical selectivity.[7] Handling of these mostly unstable organometallics is only possible at low temperatures and in solvents with moderate polarity.[6] To achieve better selectivities and higher functional group tolerances, less reactive organometallic reagents, like organozinc- and organoboron-compounds, have found various applications.[8] Their decreased reactivity, derived from a rather covalent carbon-metal bond, is accompanied with an increased stability and allows their handling at higher temperatures. The field of organometallic chemistry is a constantly developing and expanding research sector. Discoveries of new synthetic methods, utilizing organometallic reagents will help to face future preparational problems.

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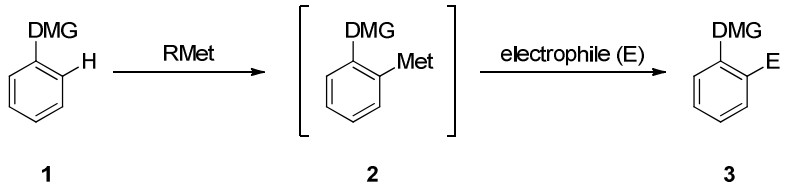
[1] a) L. Pauling, *Chem. Eng. News* **1984**, April 16, 54. b) A. J. Bard, G. M. Whitesides, R. N. Zare, F. W. McLafferty, *Acc. Chem. Res.* **1995**, *28*, 91.
[2] R. Noyori, *Nat. Chem.* **2009**, *1*, 5.
[3] a) B. M. Trost, *Science* **1991**, *254*, 147. b) B. M. Trost, *Angew. Chem. Int. Ed.* **1995**, *34*, 259.
[4] a) E. Frankland, *Liebigs Ann. Chem.* **1848**, *71*, 171. b) E. Frankland, *J. Chem. Soc.* **1848**, *2*, 263.
[5] a) V. Grignard, *Ann. Chim.* **1901**, *24*, 433. b) V. Grignard, *Compt. Rend. Acad. Sci. Paris* **1900**, *130*, 1322.
[6] P. Knochel, *Handbook of Functionalized Organometallics, Vol. 1 and 2*, Wiley-VCH, Weinheim, Germany, **2005**.
[7] G. Wu, M. Huang, *Chem. Rev.* **2006**, *106*, 2596.
[8] a) P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117. b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457.

2. REGIOSELECTIVE METALATION OF BTSM-FUNCTIONALIZED AROMATICS

2.1. Directed *ortho*-Metalation

With the independent discovery of *Gilman* and *Bepp*[9] in 1939 and *Wittig* and *Fuhrman*[10] in 1940, the *ortho* lithiation of anisole is considered as pioneering work for the "directed *ortho* metalation" (D*o*M) strategy to prepare 1,2-disubstituted (hetero-)aromatics. This preliminary work resulted in fundamental reactivity studies of the D*o*M process by *Gilman*[11] and later by *Hauser* and his students,[12] who also systematically expanded the scope of directed metalation groups (DMGs). This concept has proven to be of great importance, as many modern synthetic targets, in particular those of interest for pharmaceuticals and agrochemistry, constitute of a (hetero-)aromatic moiety. Their preparation and regiospecific functionalization are of high interest.[13,14] In the last decades, *Snieckus* and coworkers contributed enormously to this research field by extended studies of different DMGs, especially amides and carbamates.[15] The term D*o*M is defined as the deprotonation of a site *ortho* to a heteroatom-containing DMG (**1**) by a strong base, normally an alkyllithium reagent. This reaction leads to an *ortho* metalated species (**2**), which yields the 1,2-disubstituted products **3**, after treatment with various electrophiles (Scheme 1).



Scheme 1: Preparation of 1,2-disubstituted aromatics *via* directed *ortho* metalation.

The combination of D*o*M with a transition metal-catalyzed cross-coupling reaction has proven to be a useful strategy in synthesis and has found widespread application for the preparation of biologically interesting aromatic and heteroaromatic compounds. For instance, Merck published an efficient large scale synthesis of 3-bromo-6-chloro-phenanthrene-9,10-dione (**4**) using a combined D*o*M-Suzuki cross-coupling sequence in 2008 (Scheme 2).[16]

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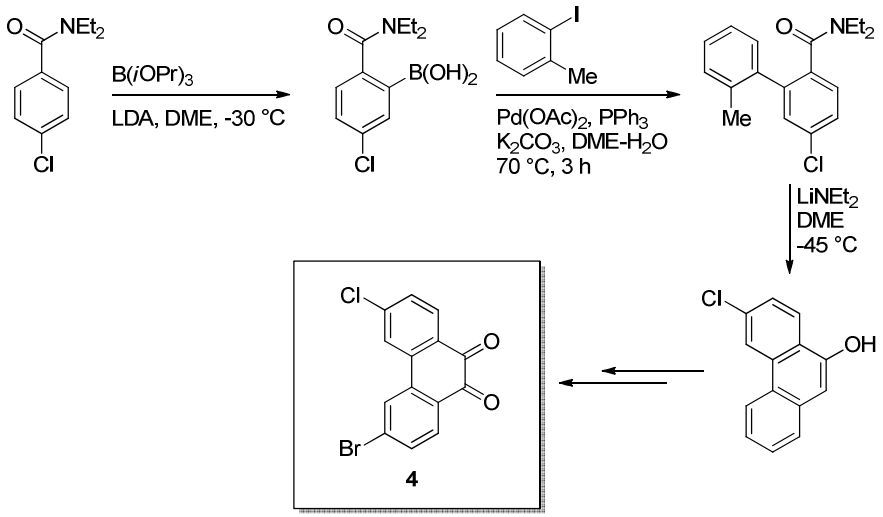
[9] H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109.
[10] G. Wittig, G. Fuhrmann, *Chem. Ber.* **1940**, *73*, 1197.
[11] H. Gilman, J. W. Morton, *Organic Reactions, Vol. 8*, Wiley, New York, **1954**.
[12] a) W. H. Puterbaugh, C. R. Hauser, *J. Org. Chem.* **1964**, *29*, 853. b) D. W. Slocum, D. I. Sugarman, *Adv. Chem. Ser.* **1974**, *130*, 227.
[13] D. Lednicer, L. A. Mitscher, *The Organic Chemistry of Drug Design, Vol. 1-3*, Wiley-Interscience, New York, **1977**.
[14] W. Sneader, *Drug Discovery: The Evolution of Modern Medicines*, Wiley, Chichester, **1985**.
[15] For selected reviews see: a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879. b) E. J.-G. Anctil, V. Snieckus, *J. Organomet. Chem.* **2002**, *653*, 150. c) J. Board, J. L. Cosman, T. Rantanen, S. P. Singh, V. Snieckus, *Platin. Met. Rev.* **2013**, *57*, 234.
[16] J. Limanto, B. T. Dorner, F. W. Hartner, L. Tan, *Org. Process Res. Dev.* **2008**, *12*, 1269.

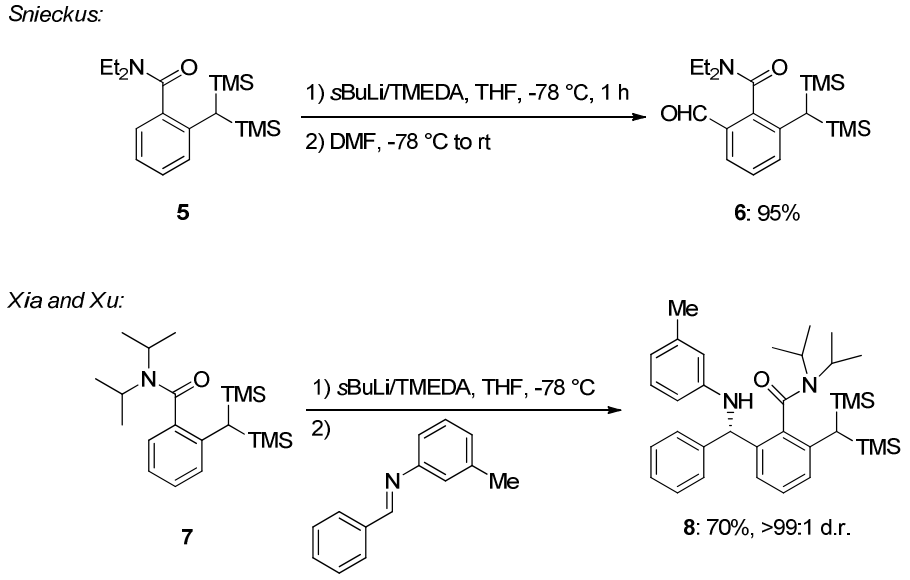


Scheme 2: Merck's large scale preparation of 3-bromo-6-chloro-phenanthrene-9,10-dione (**4**).

2.2. The BTSM-Group

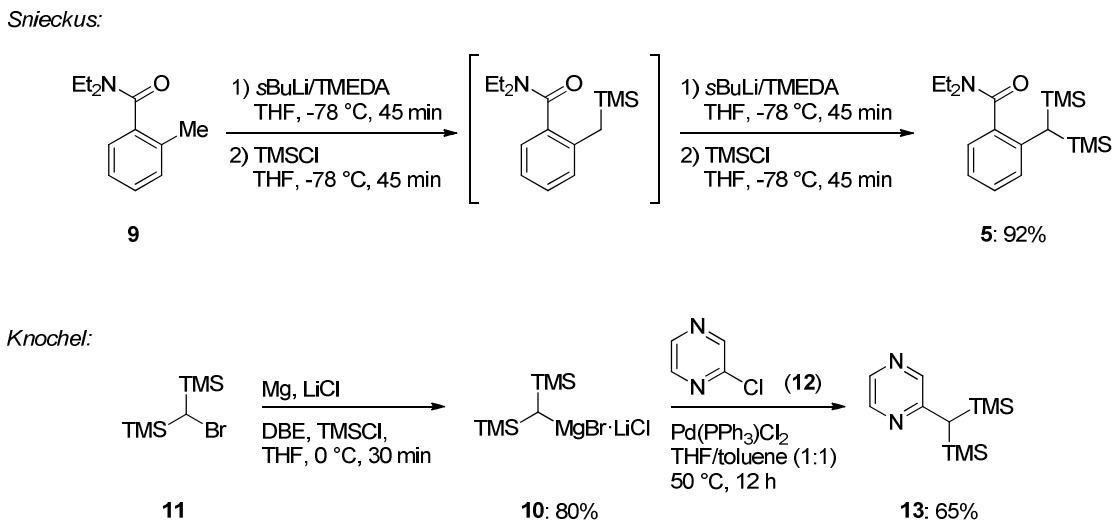
In 1983, *Snieckus* reported a systematic study of directed metalation combined with silicon protection of an *ortho* methyl-group.[17] Inspired by the observation of *Beak* and coworkers that metalation of 2-isopropyl-*N,N*-diethylbenzamide occurs at the *ortho* rather than the benzylic site,[18] *Snieckus* and coworkers showed that two TMS-groups sufficiently mask the *ortho* methyl-group in *o*-toluamide (**5**). The lithiation at the more acidic benzylic position is here prevented, furnishing only the 1,2,3-trisubstituted arene **6**, after quenching with DMF (Scheme 3). Also, the group of *Xia* and *Xu* successfully used this *bis*(trimethylsilyl)methyl-group (BTSM) in metalation studies of *o*-methylbenzamides (**7**) to yield exclusively the amine **8** (Scheme 3).[19]

[17] a) R. J. Mills, V. Snieckus, *J. Org. Chem.* **1983**, *48*, 1565. b) R. J. Mills, N. J. Taylor, V. Snieckus, *J. Org. Chem.* **1989**, *54*, 4372.
[18] P. Beak, A. Tse, J. Hawkins, C.-W. Chen, S. Mills, *Tetrahedron* **1983**, *39*, 1983.
[19] X. F. Bai, W. H. Deng, Z. Xu, F. W. Li, Y. Deng, C. G. Xia, L. W. Xu, *Chem. Asian J.* **2014**, *9*, 1108.



Scheme 3: Regioselective lithiation of various benzamides reported by Snieckus, Xia and Xu.

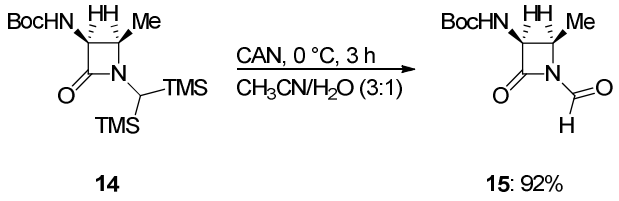
For the introduction of both TMS groups to the toluamide-system, a double lithiation with *s*BuLi of **9** followed by subsequent trapping with TMSCl was usually performed (Scheme 4).[17] As this method involves harsh conditions, accompanied by a low functional group tolerance, *Knochel* and coworkers reported an alternative way by using the Grignard reagent $(Me_3Si)_2CHMgBr{\cdot}LiCl$ (**10**) to introduce the whole BTSM-group *via* a *Kumada-Corriu* cross-coupling reaction.[20,21] This Grignard reagent **10** was obtained after LiCl-mediated magnesium insertion into (bromomethylene)*bis*(trimethylsilane) (**11**) and furnished after reaction with 2-chloropyrazine (**12**) the BTSM-substituted pyrazine derivative **13** (Scheme 4).



Scheme 4: Snieckus' and Knochel's method for the preparation of BTSM-substituted compounds.

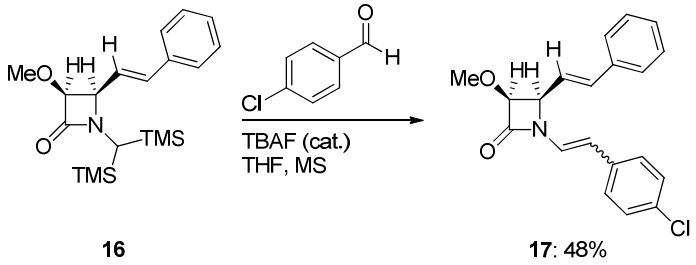
[20] a) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374. b) R. J. P. Corriu, J. P. Masse, *J. Chem. Soc., Chem. Commun.* **1972**, 144a.
[21] K. Groll, S. M. Manolikakes, X. Mollat du Jourdin, M. Jaric, A. Bredihhin, K. Karaghiosoff, T. Carell, P. Knochel, *Angew. Chem.* **2013**, *125*, 6909; *Angew. Chem. Int. Ed.* **2013**, *52*, 6776.

The easy and smooth removal of TMS-groups using TBAF·$3H_2O$[22] (tetra-*n*-butylammonium fluoride), hypothesizes this BTSM-group as versatile synthetic tool for the preparation of polyfunctionalized toluene derivatives. Despite its benzylic methyl-protection abilities, the BTSM-group is also known to undergo other useful transformations,[23] for example in the Wittig rearrangement and Prins cyclization,[24] which make this group generally applicable in organic synthesis.[25] *Palomo* and coworkers reported that oxidation of a nitrogen-attached BTSM-group with CAN ($[Ce(NH_4)_2(NO_3)_6]$) converts the *bis*silyl-group of **14** into a formyl group, leading to the β-lactam **15** (Scheme 5).[23a]



Scheme 5: Oxidation of the β-lactam **14** using CAN.

When the BTSM-lactam **16** is treated with catalytic amounts of TBAF in the presence of an aldehyde, a *Peterson Olefination*[26] reaction proceeds and the corresponding olefin **17** is obtained (Scheme 6).[23b]

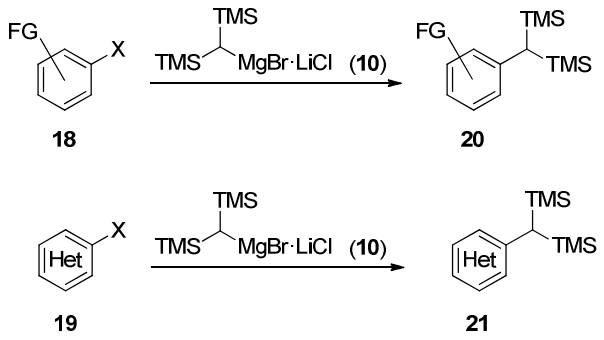


Scheme 6: Peterson Olefination of the β-lactam **16**.

2.3. Objectives

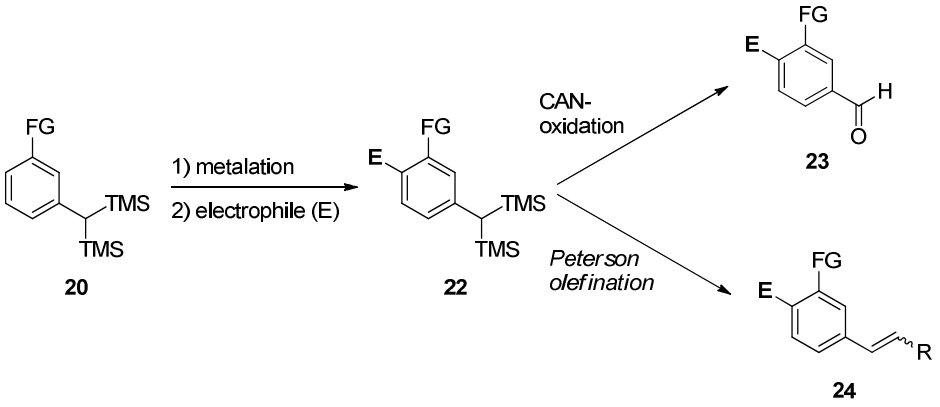
The work consisted of finding a general protocol for the cross-coupling reaction of the Grignard reagent **10** with various functionalized aromatic (**18**) and heterocyclic halides (**19**), furnishing the BTSM-substituted products **20** and **21** (Scheme 7).

[22] a) M. Reiffen, R. W. Hoffmann, *Tetrahedron Lett.* **1978**, 1107. b) A. Couture, H. Cornet, E. Deniau, P. Grandclaudon, S. Lebrun, *J. Chem. Soc., Perkin Trans 1* **1997**, 469.
[23] a) C. Palomo, J. M. Aizpurua, M. Legido, A. Mielgo, R. Galarza, *Chem. Eur. J.* **1997**, *3*, 1432. b) J. Lasarte, C. Palomo, J. P. Picard, J. Dunogues, J. M. Aizpurua, *J. Chem. Soc. Chem. Commun.* **1989**, 72. c) C. Palomo, J. M. Aizpurua, J. M. García, I. Ganboa, F. P. Cossio, B. Lecea, C. López, *J. Org. Chem.* **1990**, *55*, 2498. d) A. R. Bassindale, R. J. Ellis, J. C. Y. Lau, P. G. Taylor, *J. Chem. Soc., Perkin Trans 2* **1986**, 593.
[24] a) X. Sun, J. Lei, C. Sun, Z. Song, L. Yan, *Org. Lett.* **2012**, *14*, 1094. b) J. Lu, Z. Song, Y. Zhang, Z. Gan, H. Li, *Angew. Chem. Int. Ed.* **2012**, *51*, 5367.
[25] For a detailed review of the BTSM-group see: J.-P. Picard, *Can. J. Chem.* **2000**, *78*, 1363.
[26] D. J. Peterson, *J. Org. Chem.* **1968**, *33*, 780.



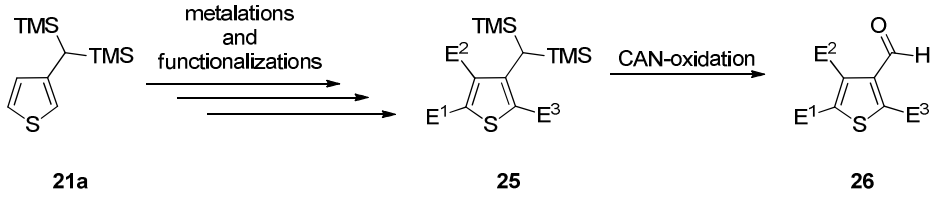
Scheme 7: Kumada-Corriu cross-coupling of different (hetero-)aromatic halides with **10**.

Then, regioselective metalations of *meta*-substituted BTSM derivatives (**19**) were tried out, utilizing the high sterical demand of the *bis*-silyl-methyl substituent. Finally, CAN-oxidations and *Peterson olefination* reactions are predicted to transform the obtained functionalized arenes (**22**) into the corresponding aldehydes (**23**) and olefins (**24**) (Scheme 8).



Scheme 8: Regioselective metalation of **19** with subsequent CAN-oxidation and Peterson olefination.

Within this context, a BTSM-thiophene derivative (**21a**) was aimed to be fully functionalized by stepwise, regioselective metalation reactions. Transformation of **25** into the corresponding aldehydes (**26**) would provide tetrasubstituted thiophene-carbaldehydes, which cannot be prepared easily *via* other methods (Scheme 9).

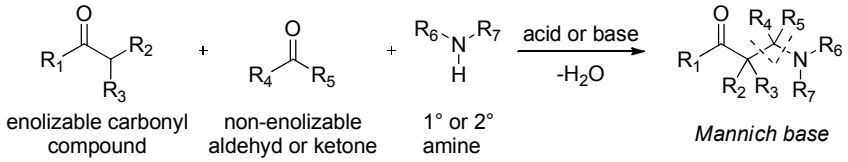


Scheme 9: Full-functionalization of the thiophene **21a** and subsequent CAN-oxidation.

3. GENERATION OF TERTIARY AMINES *VIA* IMINIUM IONS

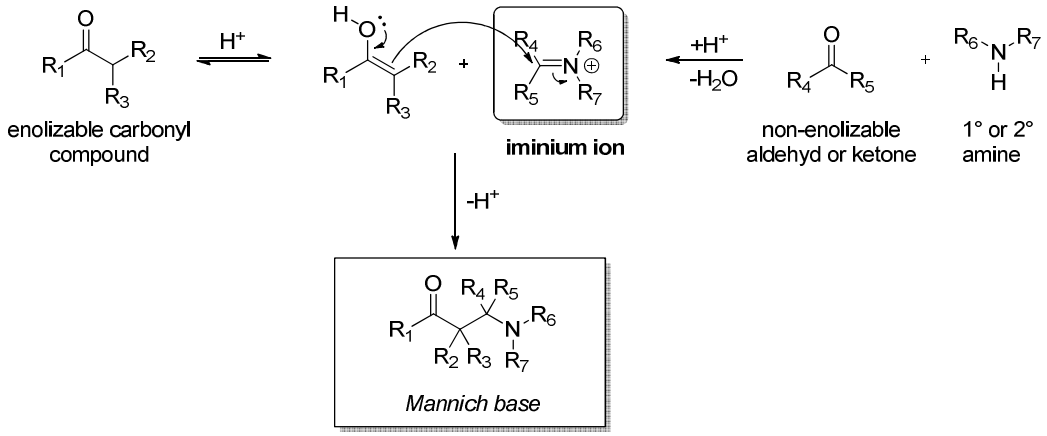
3.1. The Mannich Reaction

Aminoalkylation covers only one of many ways to introduce amino-functions into molecules. Although the aminoalkylation of CH-acidic compounds was described earlier,[27] *Carl Mannich* was first to extend this chemistry into a broad based synthetic methodology and thereby generating one of the most important C-C bond forming reactions, namely the *Mannich reaction*.[28] This reaction describes the condensation of an enolizable aldehyde (or ketone) with a primary or secondary amine (or ammonia) and a non enolizable aldehyde (or ketone), furnishing a β-aminocarbonyl compound, also known as *Mannich base* (Scheme 10).



Scheme 10: General features of the Mannich reaction.

The first step in this aminoalkylation includes the condensation of the non-enolizable carbonyl with the amine providing an iminium ion. This ion reacts further with the enolized carbonyl in an *aldol-type reaction*[29] to the *Mannich base* (Scheme 11).



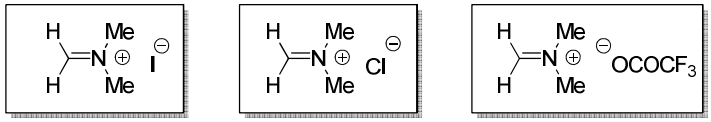
Scheme 11: Mechanism of the Mannich reaction.

[27] C. M. van Marle, B. Tollens, *Ber.* **1903**, *36*, 1351.
[28] a) C. Mannich, *J. Chem. Soc. Abstracts* **1917**, *112*, 634. b) C. Mannich, *Arch. Pharm.* **1917**, *255*, 261. For selected reviews see: c) M. Arend, B. Westermann, N. Risch, *Angew. Chem. Int. Ed.* **1998**, *37*, 1044. d) A. Córdova, *Acc. Chem. Res.* **2004**, *37*, 102. e) J. M. Verkade, L. J. van Hemert, P. J. Quaedflieg, F. P. Rutjes, *Chem. Soc. Rev.* **2008**, *37*, 29. f) G. Roman, *Eur. J. Med. Chem.* **2015**, *89*, 743.
[29] a) R. Kane, *J. Prakt. Chem.* **1838**, *15*, 129. b) R. Kane, *Ann. Phys. Chem. Ser. 2* **1838**, *44*, 475. c) T. Mukaiyama, *Org. React.* **1982**, *28*, 203.

When formaldehyde is employed as non-enolizable carbonyl component, the substrate is converted into the corresponding *Mannich base* through an aminomethylation process. The hereby formed iminium ion exhibits powerful electrophilic properties that come along with a high hygroscopic character and sensitivity towards hydrolysis.

3.2. Iminium salts

Iminium salts are wildly used electrophiles for aminoalkylation reactions and their preparation can be achieved by different methods. Besides the condensation of amines with aldehydes, like in the *Mannich reaction*, the alkylation of imines[30] or the cleavage of aminals[31,32] and *N*,*O*-acetals[33] imply alternative pathways. The most commonly used iminium salts for aminomethylation reactions are namely the *Eschenmoser salt* (**27**),[34] *Tietze's* chloride salt (**28**)[32] and the iminium trifluoroacetate (**29**) first introduced by *Potier*[35] (Figure 1).

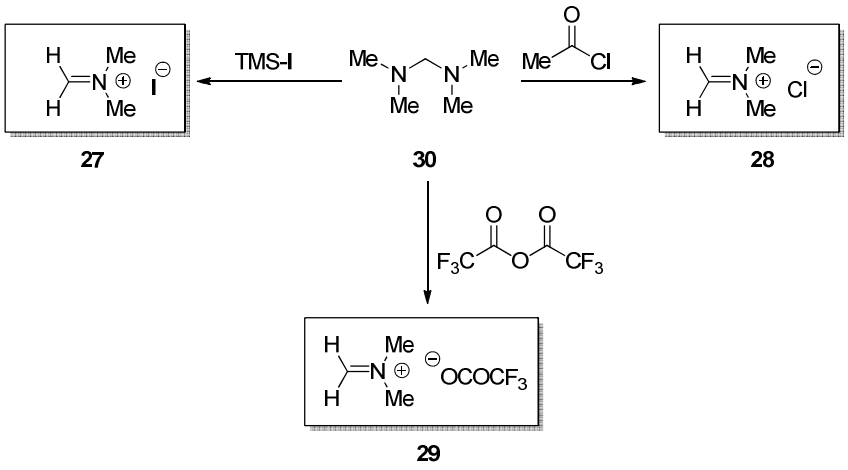


27 Eschenmoser's salt | **28** Tietze | **29** Potier

Figure 1: Eschenmoser's, Tietze's and Potier's iminium salts.

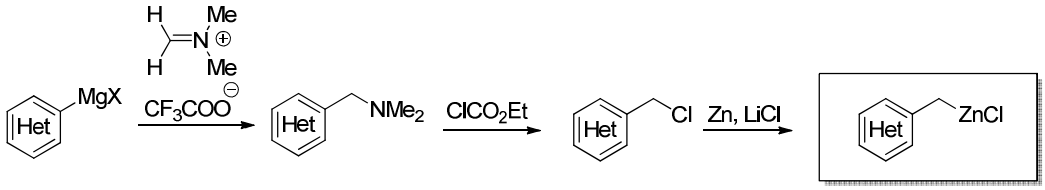
Whereas both salts **27** and **28** are typical solids, the trifluoroacetate **29** is a distillable liquid.[36] The anhydrous preparation of theses salts can be achieved by the cleavage of the commercially available aminal *N,N,N′,N′*-tetramethylmethanediamine (**30**) with either TMSI (for **27**), acetyl chloride (for **28**) or trifluoroacetic anhydride (TFAA; for **29**) (Scheme 12).

[30] H. Böhme, M. Haake, *Adv. Org. Chem.* **1976**, *9*, 107.
[31] H. Böhme, K. Hartke, *Chem. Ber.* **1960**, *93*, 1305.
[32] G. Kinast, L. F. Tietze, *Angew. Chem.* **1976**, *88*, 261. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 239.
[33] a) C. Rochin, O. Babot, J. Dunoguès, F. Duboudin, **1986**, 228. b) H. K. Hombrecher, G. Horter, *Liebigs Ann. Chem.* **1991**, 219.
[34] a) T. A. Bryson, G. H. Bonitz, C. J. Reichel, R. E. Dardis, *J. Org. Chem.* **1980**, *45*, 524. b) J. Schreiber, H. Maag, N. Hashimoto, A. E. Eschenmoser, *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 330.
[35] A. Ahond, A. Cavé, C. Kan-Fan, H.-P. Husson, J. de Rostolan, P. Potier, *J. Am. Chem. Soc.* **1986**, *90*, 5622.
[36] N. Holy, R. Fowler, E. Burnett, R. Lorenz, *Tetrahedron* **1979**, *35*, 613.



Scheme 12: Preparation of the iminium salts **27**-**29**.

All three iminium salts (**27**-**29**) are widely used for dimethylaminomethylation of aromatics and heterocycles by the reaction with various organometallics.[37,38] This was recently employed by *Knochel* and coworkers in the preparation of benzyl chloride precursors for the preparation of heteroarylmethylzinc reagents (Scheme 13).[39]



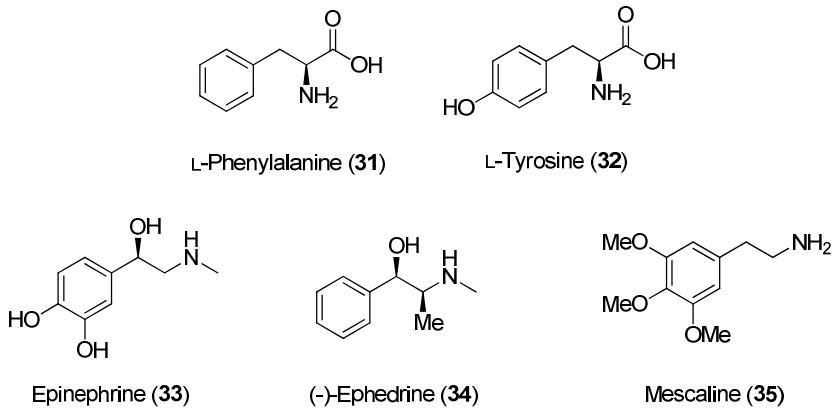
Scheme 13: Preparation of heteroarylmethylzinc reagents.

Although this method has been proven to be an efficient way to introduce a dimethylaminomethyl-group to aromatic systems, a few drawbacks are limiting the versatility of this reaction, regarding the preparation of more functionalized aminomethyl derivatives. The commercial availability of the corresponding aminals as well as their handling, leads to a restricted application of this reaction because of the aminals quite sensitive character[40] and only a few examples to be found in the literature.[38,41]

[37] a) G. D. Hartman, W. Halczenko, *Tetrahedron Lett.* **1987**, *28*, 3241. b) I. K. Sebhat, Y.-L. Tan, D. A. Widdowson, R. Wilhelm, A. J. P. White, D. J. Williams, *Tetrahedron* **2000**, *56*, 6121. c) D. W. Slocum, T. L. Reece, R. D. Sandlin, T. K. Reinscheld, P. E. Whitley, *Tetrahedron Lett.* **2009**, *50*, 1593.
[38] a) M. S. Cooper, H. Heaney, *Tetrahedron Lett.* **1986**, *27*, 5011. b) M. S. Cooper, R. A. Fairhurst, R. Heaney, P. G., R. F. Wilkins, *Tetrahedron* **1989**, *45*, 1155.
[39] N. M. Barl, E. Sansiaume-Dagousset, G. Monzon, A. J. Wagner, P. Knochel, *Org. Lett.* **2014**, *16*, 2422.
[40] V. Jurčík, R. Wilhelm, *Tetrahedron* **2004**, *60*, 3205.
[41] a) N. Gommermann, C. Koradin, P. Knochel, *Synthesis* **2002**, 2143. b) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker, *Org. React.* **2001**, *58*, 417. c) N. Millot, C. Piazza, S. Avolio, P. Knochel, *Synthesis* **2000**, 941. d) B. E. Love, *J. Org. Chem.* **2007**, *72*, 630.

3.3. Phenethylamines

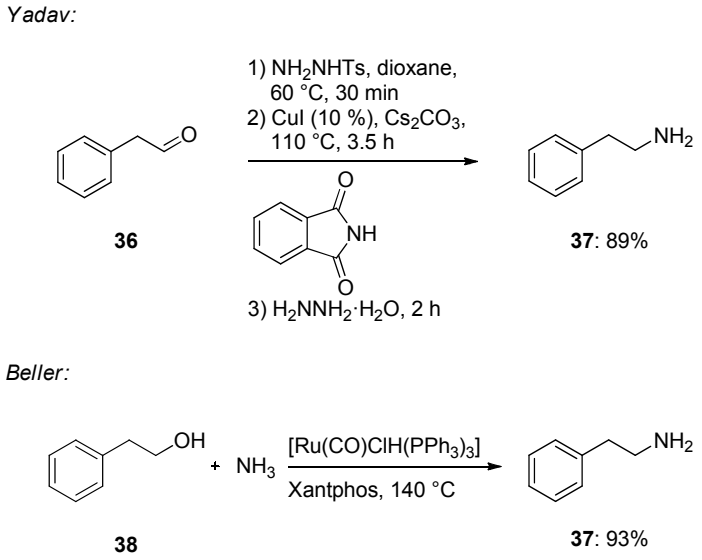
Phenethylamines represent an important class of amines and are well known for their psychoactive and stimulating effects. Surprisingly, little modification of the basic structure is required to elicit significant alterations in neurochemical and behavioral actions.[42] Prominent representatives of this subclass are the amino acids phenylalanine (**31**) and tyrosine (**32**),[43] the hormone and neurotransmitter epinephrine (**33**),[44] as well as the monoalkaloids ephedrine (**34**)[45] and mescaline (**35**)[46] (Scheme 14).



Scheme 14: L-phenylalanine, L-tyrosine, epinephrine, (-)-ephedrine and mescaline.

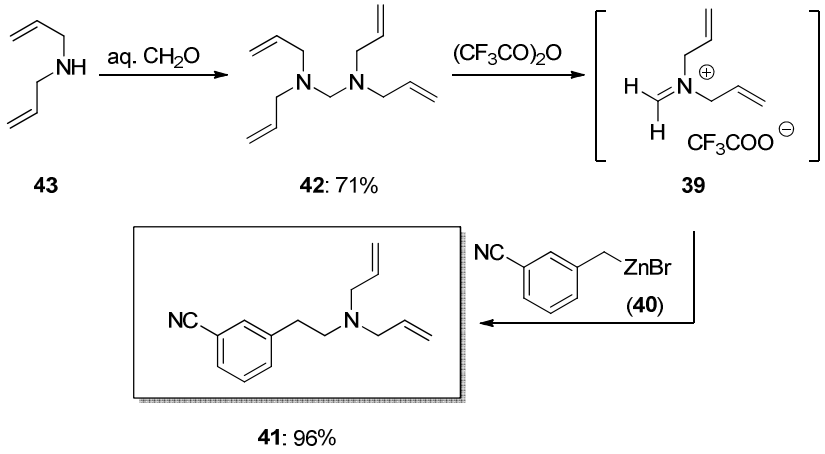
The preparation of phenethylamines can be achieved by different methods. *Yadav* and coworkers described the conversion of 2-phenylacetaldehyde (**36**) into 2-phenylethanamine (**37**) *via* a one-pot Gabriel synthesis,[47] *Beller* and coworkers transformed 2-phenylethanol (**38**) into the corresponding amine (**37**) by a ruthenium catalyzed amination procedure using ammonia (Scheme 15).[48]

[42] a) S. L. Hill, S. H. Thomas, *Clin. Toxicol.* **2011**, *49*, 705. b) T. A. Smith, *Pythochemistry* **1977**, *16*, 9.
[43] a) L. Wang, P. G. Schultz, *Angew. Chem. Int. Ed.* **2004**, *44*, 34. b) S. E. Gibson , N. Guillo, M. J. Tozer, *Tetrahedron* **1999**, *55*, 585.
[44] a) G. Rona, *J. Mol. Cell Cardiol.* **1985**, *17*, 291. b) I. J. Elenkov, R. L. Wilder, G. P. Chrousos, E. S. Vizi, *Pharmacol. Rev.* **2000**, *52*, 595. c) S. Guimaraes, D. Moura, *Pharmacol. Rev.* **2001**, *53*, 319.
[45] E. A. Abourashed, A. T. El-Alfy, I. A. Khan, L. Walker, *Phytother. Res.* **2003**, *17*, 703.
[46] a) G. K. Aghajanian, G. J. Marek, *Neuropsychopharmocology* **1999**, *21*, 2S. b) G. K. Aghajanian, G. J. Marek, *Brain Res. Rev.* **2000**, *3*, 302. c) O. M. Friedman, K. N. Parameswaran, S. Burstein, *J. Med. Chem.* **1963**, *6*, 227.
[47] A. K. Yadav, L. D. S. Yadav, *RSC Adv.* **2014**, *4*, 34764.
[48] S. Imm, S. Bahn, M. Zhang, L. Neubert, H. Neumann, F. Klasovsky, J. Pfeffer, T. Haas, M. Beller, *Angew. Chem. Int. Ed.* **2011**, *50*, 7599.



Scheme 15: Yadav's and Beller's methods for the preparation of 2-phenylethanol.

Also, the reduction of nitrostyrenes,[49] azides,[50] nitriles[51] or phenylacetamides[52] as well as the substitution of the corresponding halides with secondary amines is reported in the literature.[53] A different approach was established by *Knochel* and coworkers, who constructed the phenethyl-moiety by the reaction of an iminium ion (**39**) with a benzylic zinc reagent **40**, furnishing the amine **41**.[41a] The iminium trifluoroacetate **39** was prepared *via Tietze's* method from the corresponding aminal **42**, which was obtained after treatment of the respective secondary amine **43** with an aqueous formaldehyde solution (Scheme 16).



Scheme 16: Knochel's method for the preparation of a functionalized phenethylamine.

[49] M. Kohno, S. Sasao, S.-I. Murahashi, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1252.
[50] T. Hattori, A. Tsubone, Y. Sawama, Y. Monguchi, H. Sajiki, *Tetrahedron* **2014**, *70*, 4790.
[51] a) C. Gunanathan, M. Hölscher, W. Leitner, *Eur. J. Inorg. Chem.* **2011**, 3381. b)J. H. Short, D. A. Dunnigan, C. W. Ounst, *Tetrahedron* **1973**, *29*, 1931.
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[53] a) R. D. Schoenwald, C. F. Barfknecht, *Antiglaucoma Drug Compositions Containing Phenalkylamines*, US5322859, **1994**. b) V. Desobry, P. Murer, A. Schuwey, *Thermal and Photoinitiated Radical Polymerisation in the Presence of an Addition Fragmentation Agent*, WO2000011041, **2000**.

3.4. Objectives

The aim of this work was the development of a one-pot procedure for the preparation of tertiary amines *via* the reaction of organometallics with iminium ions. We envisioned that the iminium salt **29** could be used to prepare new unsymmetrical aminals of type **44** by the reaction of **29** with metallic amides of type **45.** These amides **45** were prepared by deprotonation of the corresponding amine R^1R^2NH (**46**) with CH_3Met (Met = Li, MgX). The treatment of the obtained aminals **44** with TFAA, will regioselectively provide the iminium salt **47**. It is expected that the acylation of aminals **44** with TFAA occurs selectively on the least sterically hindered nitrogen of the *N*,*N*-acetal. The resulting functionalized iminium salt **47** may react with various organometallics (R^3-Met), leading to polyfunctional tertiary amines of type **49-51** (Figure 2).

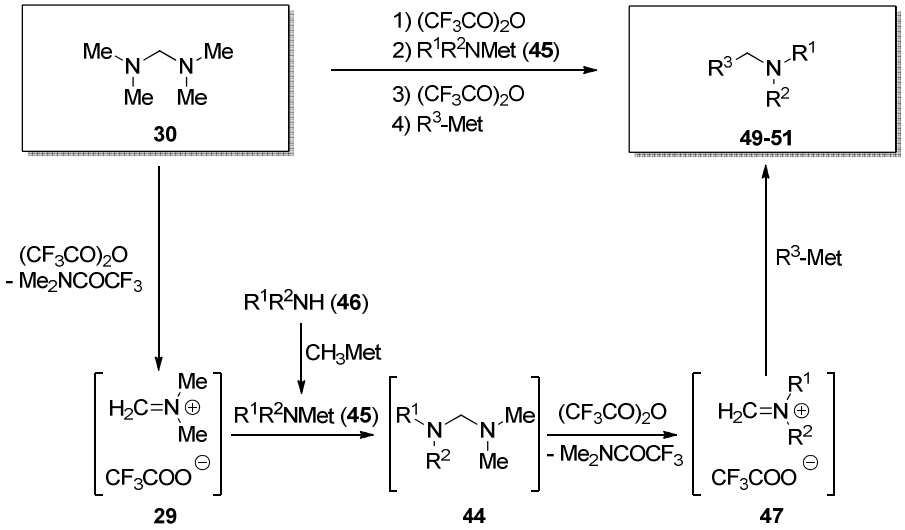
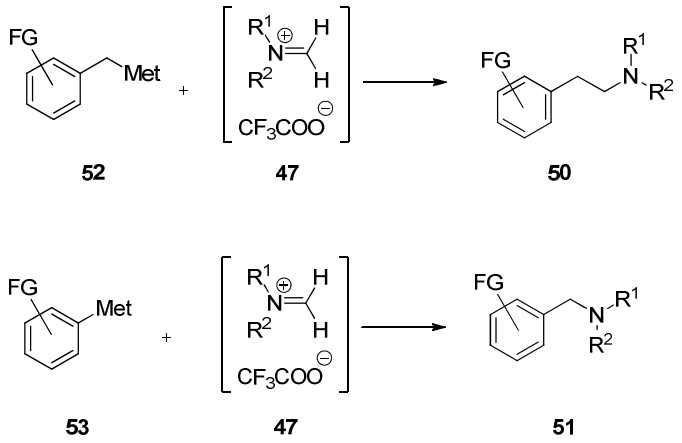


Figure 2: Envisioned one-pot procedure for the preparation of tertiary amines of types **49-51**.

Within this reaction sequence, various phenethylamines (**50**) and benzylamines (**51**) are to be prepared by using ether benzylic (**52**) or aryl-organometallics (**53**).



Scheme 17: Preparation of various phenethyl- (**50**) and benzylamines (**51**).

4. NEW BUILDING BLOCKS FOR COVALENT ORGANIC FRAMEWORKS

4.1. Porous Materials

Ordered porous materials are of high interest for science and technology because of their ability to interact with atoms, ions and molecules, not only at their surfaces but throughout their structures.[54] Several applications using porous materials are known, including ion exchange, gas storage, catalysis, molecular separation and sensor developments.[55] These applications are thereby critically dependent on the size, shape and volume of the pores. In the last few years, the generation of new materials with a predictable, distinct and accurate porosity has become an interesting field for organic chemists to create organic frameworks incorporating these properties in an inexpensive and tunable manner.

4.2. Covalent Organic Frameworks

Covalent organic frameworks (COFs) are organic, crystalline and highly porous networks, composed of a defined amount of different organic building blocks that offer great rigidness, high regularity, low densities and fixed porosity. The linkages between the single moieties in COFs are exclusively covalent, which highlighted them with excellent thermal stability. The slightly reversible nature of these linkages enables the generation of highly ordered structures through a self-assembling mechanism. The most common connection strategies of the single building blocks include boroxines,[56] imines,[57] borosilicates[58] and boronate esters.[59] The most prominent linkage in these frameworks constitutes a reversible boronate ester condensation, resulting from the reaction of boronic acids with poly diol compounds, a process of great ease, high efficiency and without the need for catalysts or other reagents. The first COF, reported by *Yaghi* and coworkers,[56a] was composed of 2,3,6,7,10,11-hexahydroxytriphenylene **54** (HHTP) and 1,4-phenylenediboronic acid (**55**), resulting in a two-dimensional hexagonal layered structure, which is held together in the third dimension by π-stacking (Figure 3).

[54] M. E. Davis, *Nature* **2002**, *417*, 813.
[55] For selected reviews see: a) C. J. Rhodes, *Annu. Rep. Prog. Chem., Sect. C: Phys. Chem.* **2007**, *103*, 287. b) K. Moller, T. Bein, *Chem. Soc. Rev.* **2013**, *42*, 3689. c) N. Stock, S. Biswas, *Chem. Rev.* **2012**, *112*, 933. d) X. Feng, X. Ding, D. Jiang, *Chem. Soc. Rev.* **2012**, *41*, 6010. e) S. Y. Ding, W. Wang, *Chem. Soc. Rev.* **2013**, *42*, 548. f) H. C. Zhou, J. R. Long, O. M. Yaghi, *Chem. Rev.* **2012**, *112*, 673.
[56] a) A. P. Côté, A. I. Benin, N. W. Ockwig, M. O'Keeffe, A. J. Matzger, O. M. Yaghi, *Science* **2005**, *310*, 1166. b) S. Ean, J. Guo, J. Kim, H. Ihee, D. Jiang, *Angew. Chem. Int. Ed.* **2009**, *48*, 5439.
[57] a) F. J. Uribe-Romo, J. R. Hunt, H. Furukawa, C. Klock, M. O'Keeffe, O. M. Yaghi, *J. Am. Chem. Soc.* **2009**, *131*, 4570. b) F. J. Uribe-Romo, C. J. Doonan, H. Furukawa, K. Oisaki, O. M. Yaghi, *J. Am. Chem. Soc.* **2011**, *133*, 11478. c) N. C. Duncan, B. P. Hay, E. W. Hagaman, R. Custelcean, *Tetrahedron* **2012**, *68*, 53.
[58] J. R. Hunt, C. J. Doonan, J. D. LeVangie, A. P. Côté, O. M. Yaghi, *J. Am. Chem. Soc.* **2008**, *130*, 11872.
[59] a) R. W. Tilford, W. R. Gemmill, H.-C. zur Loye, J. J. Lavigne, *Chem. Mat.* **2006**, *18*, 5296. b) M. Dogru, A. Sonnauer, A. Gavryushin, P. Knochel, T. Bein, *Chem. Commun.* **2011**, *47*, 1707. c) M. Dogru, A. Sonnauer, S. Zimdars, M. Döblinger, P. Knochel, T. Bein, *Cryst. Eng. Comm.* **2013**, *15*, 1500.

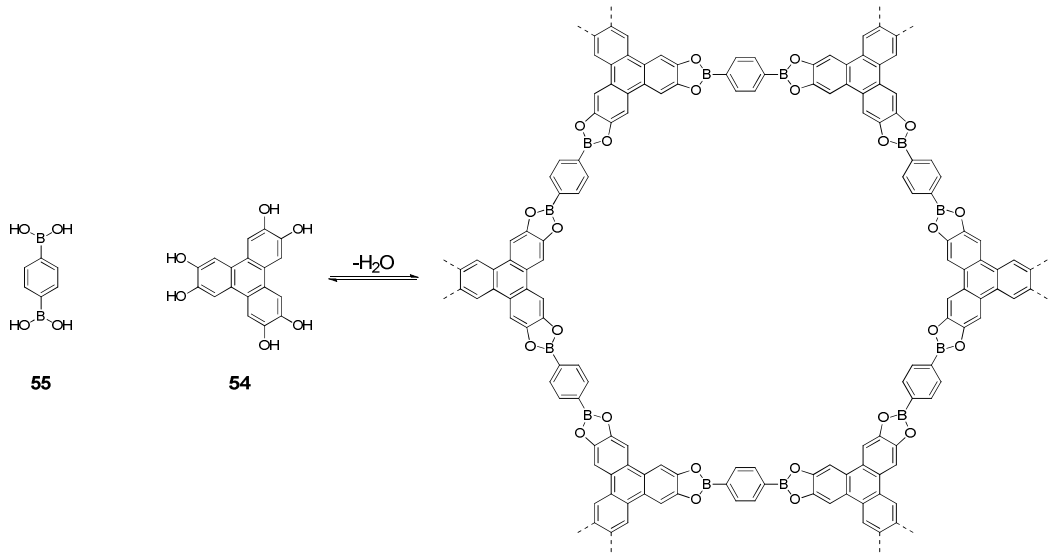


Figure 3: Structure of the first reported COF by Yaghi.

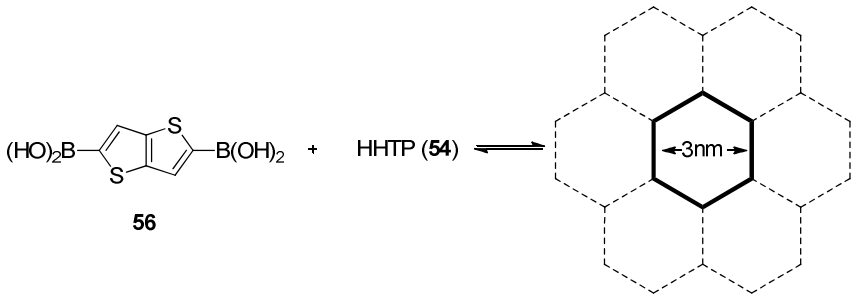
After this pioneering work of *Yaghi* in 2005, the design and preparation of new COFs with precisely controlled pore sizes and pore environment, derived from the corresponding fine tuned organic building blocks became a prominent research field in the last decade.[60] Until now, there are only a few known applications for COFs. The most established applications of these networks are for gas storage, for example incorporating hydrogen.[61] Additionally, the group of *Jiang* synthesized a framework which shows high luminescent properties, absorbs a wide range of photons of different wavelengths and allows energy transfer and migration.[62] In 2013, the groups of *Bein* and *Knochel* published a photoconductive thienothiophene-based COF, which showed charge transfer properties after building an ordered donor-acceptor network with incorporated fullerene derivatives.[63] The hereby used diboronate-linker (**56**) contains a thienothiophene-motif as core element and after condensation with HHTP (**54**), the corresponding hexagonal network was built with high surface area and 3 nm open pore system illustrated in Figure 4.

[60] For selected articles see: a) P. Kuhn, M. Antonietti, A. Thomas, *Angew. Chem. Int. Ed.* **2008**, *47*, 3450. b) E. D. Spitler, W. R. Dichtel, *Nat. Chem.* **2010**, *2*, 672. c) D. N. Bunck, W. R. Dichtel, *Angew. Chem. Int. Ed.* **2012**, *51*, 1885. d) J. F. Dienstmaier, A. M. Gigler, A. J. Goetz, P. Knochel, T. Bein, A. lyapin, S. Reichlmaier, W. M. Heckl, M. Lackinger, *ACS Nano* **2011**, *5*, 9737. e) A. Nagai, Z. Guo, X. Feng, S. Jin, X. Chen, X. Ding, D. Jiang, *Nat. Commun.* **2011**, *2*, 536. f) S. Jin, X. Ding, X. Feng, M. Supur, K. Furukawa, S. Takahashi, ;. Addicoat, M. E. El-Khouly, T. Nakamura, S. Irle, S. Fukuzumi.A. Nagai, D. Jiang, *Angew. Chem. Int. Ed.* **2013**, *52*, 2017. For a review see: g) M. Dogru, T. Bein, *Chem. Commun.* **2014**, *50*, 5531.

[61] a) Rudkevich, D. M. *Eur. J. Org. Chem.* **2007**, 3255. b) H. Furukawa, O. M. Yaghi, *J. Am. Chem. Soc.* **2009**, *131*, 8875.

[62] Wan, S.; Guo, J.; Kim, J.; Ihee, H.; Jiang, D. *Angew. Chem. Int. Ed.* **2008**, *47*, 8826.

[63] M. Dogru, M. Handloser, F. Auras, T. Kunz, D. Medina, A. Hartschuh, P. Knochel, T. Bein, *Angew. Chem. Int. Ed.* **2013**, *125*, 2992.



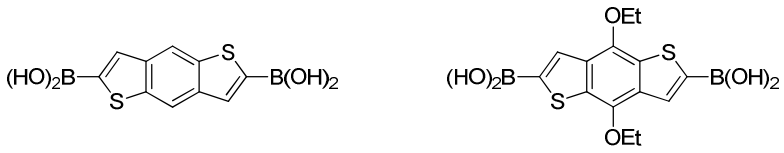
56

Figure 4: The thienothiophene diboronate building block (**56**).

As the field of organic heterojunctions are of great interest for organic photovoltaic devices,[56a] the use of COFs as electron-hole conducting material is promising in the field of organic materials. The integration of larger and more functionalized building blocks into COFs, leading to greater pore sizes and hopefully to new characteristics of the network, is a subject that looks promising for the development of new organic materials.

4.3. Objectives

The aim of this work was to prepare new benzo[1,2-*b*:4,5-*b'*]dithiophene-based diboronate linker (benzodithiophene = BDT) for the integration in covalent organic frameworks (Figure 5).

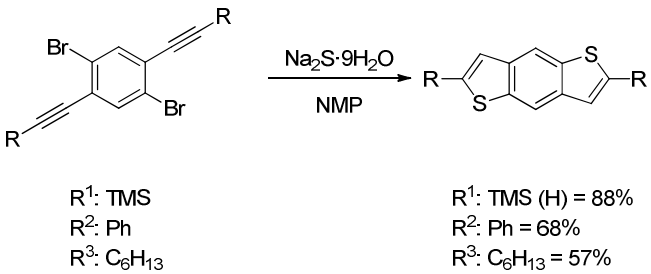


57 **58**

Figure 5: New benzodithiophene-based diboronate linker.

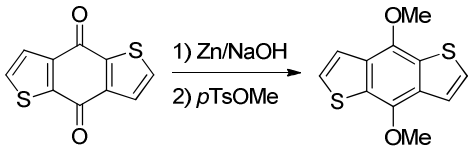
Only few examples are known in the literature for the preparation of the BDT scaffold. [64] Regarding the use of cheap starting materials and the possibility of large gram-synthesis, the reported method of *Takimiya* and coworkers tried out to obtain desired linkers (Scheme 18).[65]

[64] a) P. Beimling, G. Koßmehl, *Chem. Ber.* **1986**, *119*, 3198. b) J. G. Laquindanum, H. E Katz, A. J. Lovinger, A. Dodabalapur, Adv. Mater. **1997**, *9*, 36. c) K. Takimiya, Y. Konda, H. Ebata, N. Niihara, T. Otube, *J. Org. Chem.* **2005**, *70*, 10596.
[65] T. Kashiki, S. Shinamura, M. Kohara, E. Miyazaki, K. Takimiya, M. Ikeda, and H. Kuwabara, *Org. Lett.* **2009**, *11*, 2473.



Scheme 18: Preparation of the BDT-scaffold by Takimiya.

A synthesis based on the research by *Beimlinger* and *Koßmehl via* reduction of a quinone seems to be the best choice for the diethoxy-precursor (Scheme 19).[64a]



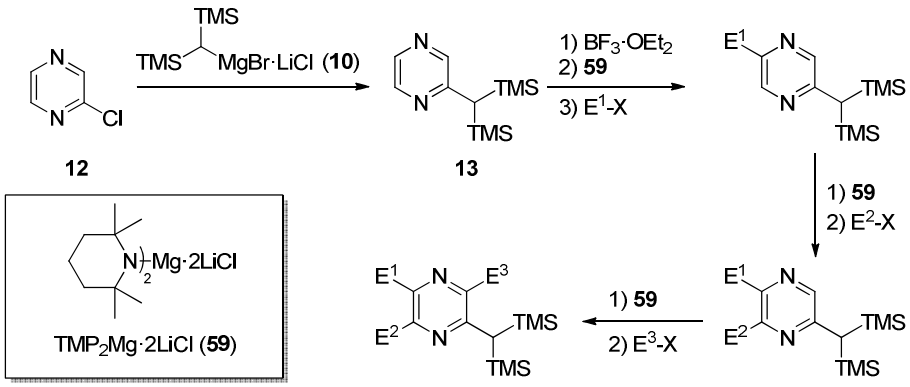
Scheme 19: Synthesis the BDT-scaffold by Beimlinger and Koßmehl.

B: RESULTS AND DISCUSSION

1. REGIOSELECTIVE FUNCTIONALIZATION OF AROMATICS AND HETEROCYCLES BEARING A BULKY *BIS*-SILYL-METHYL GROUP

1.1. Introduction

The regioselective metalation of aromatics is an important synthetic task, since functionalized arenes are essential building blocks of pharmaceuticals and agrochemicals.[66] Whereas numerous strategies have been elaborated for performing regioselective lithiations[67], the use of the BTSM-group was pioneered by Snieckus.[17] Recently, *Knochel* and coworkers have shown that the pyrazine scaffold can be fully functionalized starting from a BTSM-substituted pyrazine (**13**) using the magnesium base $TMP_2Mg\cdot 2LiCl$ (**59**)[68] (Scheme 20).[21]



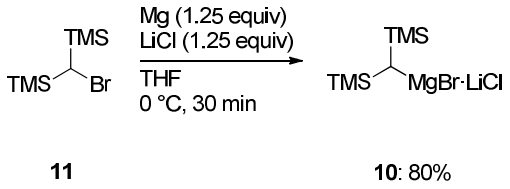
Scheme 20: Regioselective full-functionalization of the pyrazine scaffold using the BTSM-group.

To explore the scope and limitations of this *bis*-silyl-methyl group and its use in regioselective functionalization reactions of other aromatics and heterocycles would be of high interest.

1.2. Preparation of BTSM-Substituted Aromatics

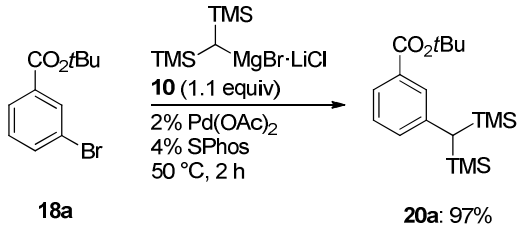
The Grignard reagent $(Me_3Si)_2CHMgBr\cdot LiCl$ (**10**) was prepared by the reaction of $(Me_3Si)_2CHBr$ (**11**; 1.0 equiv) with magnesium turnings (1.25 equiv) in the presence of LiCl (1.25 equiv) within 30 min at 0 °C, as described by Groll et. *al*. (Scheme 21).[21] Titration of the organomagnesium reagent **10** with iodine in THF indicated a concentration of 0.6 M (80% yield).

[66] L. Ackermann, *Modern Arylation Methods*, Wiley-VCH, Weinheim, Germany, **2009**.
[67] M. Schlosser, *Angew. Chem. Int. Ed.* **2005**, *44*, 376.
[68] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958. b) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681. c) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem.* **2011**, *123*, 9968; *Angew. Chem. Int. Ed.* **2011**, *50*, 9794.



Scheme 21: Preparation of **10** *via* magnesium insertion in the presence of LiCl.

In preliminary experiments, *tert*-butyl 3-bromobenzoate (**18a**) underwent a smooth *Kumada-Corriu* cross-coupling with the Grignard reagent $(Me_3Si)_2CHMgBr{\cdot}LiCl$ (**10**; 1.1 equiv, 50 °C, 2 h) using 2% $Pd(OAc)_2$ and 4% SPhos[69] and the BTSM-substituted benzoic ester (**20a**) was obtained in 97% yield (Scheme 22).



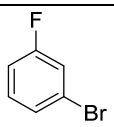
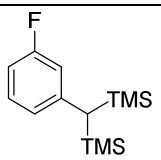
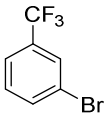
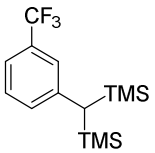
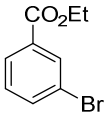
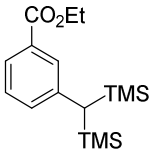
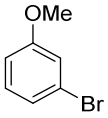
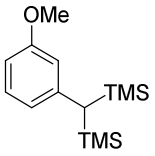
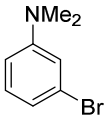
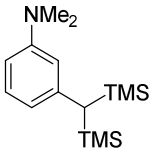
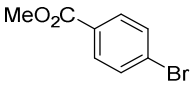
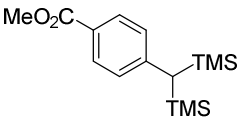
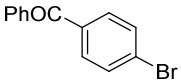
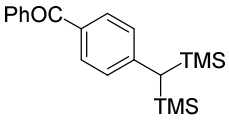
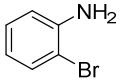
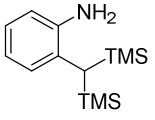
Scheme 22**:** Kumada-Corriu cross coupling of **18a** with **10**.

This cross-coupling procedure could be extended to a range of aromatic bromides bearing either electron-donating or electron-withdrawing substituents. Thus, the *meta*-substituted aryl bromides **18b-18f** underwent the cross-coupling reaction with the Grignard reagent **10** and the corresponding BTSM-functionalized aromatic derivatives (**20b-20f**) were isolated in 88-95% yield (Table 1, entries 1-5). Also, the *para*-substituted methyl 4-bromobenzoate (**18g**) was transformed into the corresponding cross-coupling product **20g** in 89% yield (entry 6).[70] Even a keto-function could be tolerated in this cross-coupling and the bromobenzophenone **18h** was converted to **20h** in 72% yield (entry 7).[70] Also, the unprotected aniline derivative **18i** furnished the corresponding cross-coupling product **20i** by using 3 equivalents of the Grignard reagent **10** and toluene as cosolvent (THF/toluene = 1:2, 80 °C 24 h). The resulting aniline **20i** was isolated in 60% yield (entry 8).

[69] a) S. D. Walker, T. E. Barder, J. R. Martinelli, S. L. Buchwald, *Angew. Chem.* **2004**, *116*, 1907; *Angew. Chem. Int. Ed.* **2004**, *43*, 1871. b) T. E. Barder, S. D. Walker, J. R. Martinelli, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 4685. c) R. A. Altmann, S. L. Buchwald, *Nat. Protoc.* **2007**, *2*, 3115. d) R. Martin, S. L. Buchwald, *Acc. Chem. Res.* **2008**, *41*, 1461.

[70] These experiments were performed by T. Klatt and are given here for the sake of completeness.

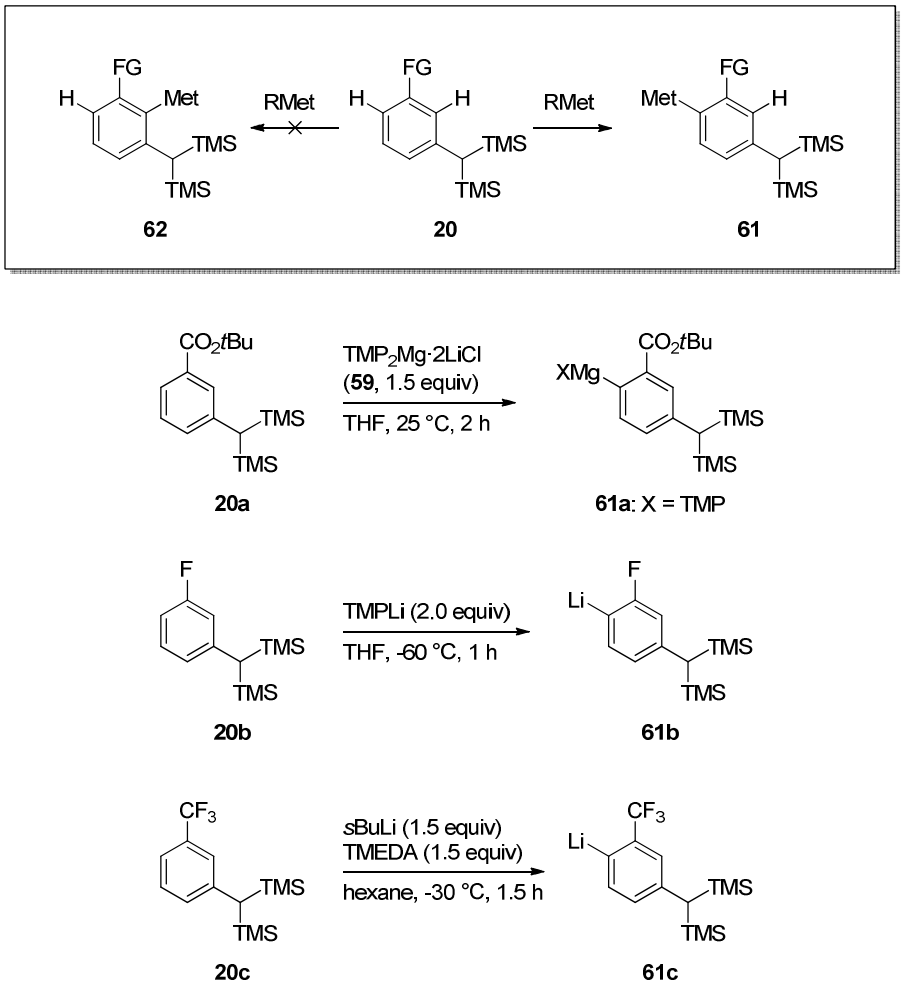
Table 1: Products of type **20** obtained by *Kumada-Corriu* cross-coupling reaction of various aryl bromides (**18**) with **10**.

Entry	Electrophile	Product[a]
		
1	**18b**	**20b**: 92%
		
2	**18c**	**20c**: 91%
		
3	**18d**	**20d**: 91%
		
4	**18e**	**20e**: 95%
		
5	**18f**	**20f**: 88%
		
6	**18g**	**20g**: 89%[70]
		
7	**18h**	**20h**: 72%[70]
		
8	**18i**	**20i**: 60%[b]

[a] Isolated yields of analytically pure product. [b] The cross-coupling was performed by using 3.0 equivalents of **10** in a 2:1 mixture of THF/toluene at 80 °C for 24 h.

1.3. Regioselective Functionalization of BTSM-Substituted Derivatives

The prepared BTSM-substituted aromatics of type **20** were submitted to metalation reactions using various Li- or Mg-bases. In all cases, a regioselective metalation at the least hindered position of the aromatic substrate **20** was observed, leading to the lithiated or magnesiated species **61** and not to the more sterically hindered organometallic **62** (Scheme 23).



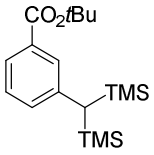
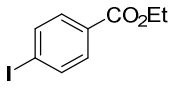
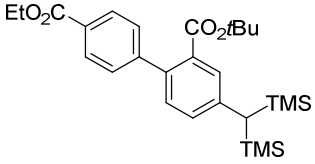
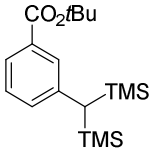
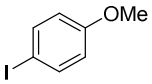
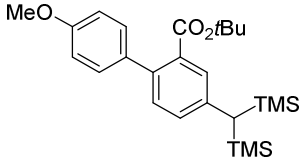
Scheme 23: Regioselective metalation of aromatics of type **20** using various Li- or Mg-bases.

For the metalation of the benzoate **20a** bearing a sensitive ester function, the use of TMPMgCl·LiCl[68] (**63**) did not lead to complete conversion. Therefore, the stronger base $TMP_2Mg·2LiCl$ (**59**) was applied for a selective metalation. Thus, treatment of **20a** with $TMP_2Mg·2LiCl$ (**59**, 1.5 equiv) in THF (25 °C, 2 h) led to the Grignard reagent **61a**. After transmetalation with $ZnCl_2$ (1.5 equiv), a Pd-catalyzed *Negishi* cross-coupling[71] reaction with ethyl 4-iodobenzoate or 4-iodoanisole (Table 2,

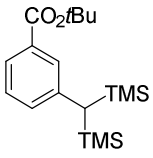
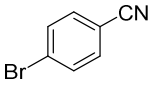
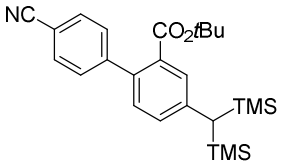
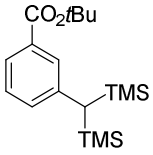
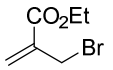
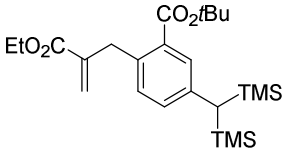
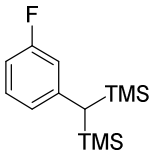
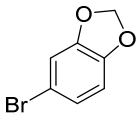
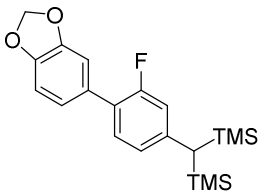
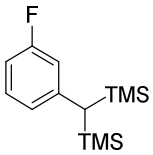
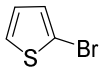
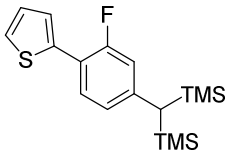
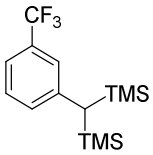
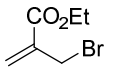
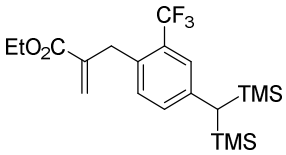
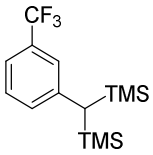
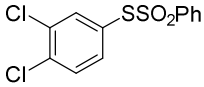
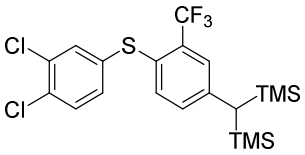
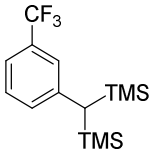
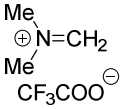
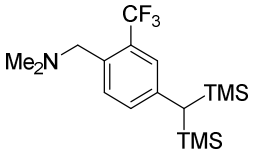
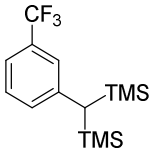
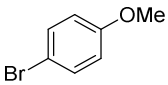
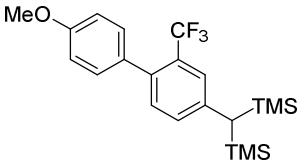
[71] a) A. King, N. Okukado, E. Negishi, *J. Org. Chem.* **1977**, *42*, 1821. b) E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340. c) Ø. Rist, M. Begtrup, *J. Chem. Soc., Perkin Tran. 1* **2001**, 1566. d) X. Zeng, M. Quian, Q. Hu, E. Negishi, *Angew. Chem. Int. Ed.* **2004**, *43*, 2259. e) A. de Meijere, P. von Zezschwitz, S. Braese, *Acc. Chem. Res.* **2005**, *38*, 413. f) J.-X. Wang, J. McCubbin, M. Jin, R. Laufer, Y. Mao, A. Crew, M. Mulvihill, V. Snieckus, *Org. Lett.* **2008**, *10*, 2923. g) G. Manolikakes, M. Schade, C. Munoz Hernandez, H. Mayr, P. Knochel, *Org. Lett.* **2008**, *10*, 2765. h) Z. Dong, G. Manolikakes, J. Li, P. Knochel, *Synthesis* **2009**, 681.

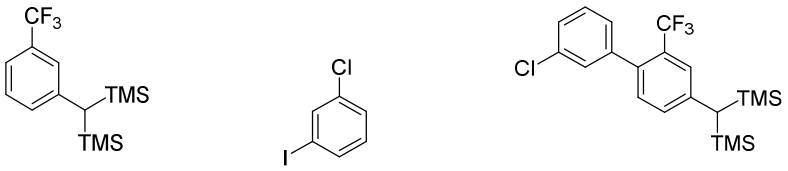
entries 1-2) in THF (50 °C, 12 h) using 2% $Pd(dba)_2$ (dba = dibenzylideneacetone) and 4% tfp (tfp = tri(2-furyl)phosphine)[72] led to the corresponding biphenyls **22a**-**b** in 88-93% yield. The cross-coupling reaction with 4-bromobenzonitrile using 2% $Pd(OAc)_2$ and 4% SPhos as the catalytic system (50 °C, 12 h) furnished the nitrile **22c** in 88% yield (entry 3). In the presence of CuCN·2LiCl (1.5 equiv), a reaction with ethyl (2-bromomethyl)acrylate[73] gave the allylated product **22d** in 92% yield (entry 4).[74] The less sensitive substrate **20b** was conveniently lithiated with TMPLi (2.0 equiv) in THF (-60 °C, 1 h) leading to the aryllithium reagent **61b** (Scheme 2). Transmetalation with $ZnCl_2$ (2.1 equiv) and subsequent cross-coupling reaction with 5-bromobenzo[*d*][1,3]dioxole led to the expected product **22e** in 95% yield (entry 5). Moreover, the cross-coupling with 2-iodothiophene furnished the biaryl **22f** in 96% yield (entry 6). For the metalation of **20c**, *s*BuLi (1.5 equiv) and TMEDA (1.5 equiv) in hexane[75] (-30 °C, 1.5 h) led to the *ortho*-lithiated species **61c,** which underwent, after transmetalation with $ZnCl_2$ (1.5 equiv), a copper-catalyzed allylation with ethyl 2-(bromomethyl)acrylate to the allylated product **22g** in 57% yield (entry 7). The aryllithium species **61c** reacted directly with *O*-phenyl 3,4-dichlorobenzenesulfonothioate to afford the thioether **22h** in 60% yield (entry 8). Transmetalation to the magnesium-species (using 1.5 equiv $MgCl_2$·LiCl) and subsequent reaction with *N*,*N*-dimethyl(methylene)iminium trifluoroacetate (**29**) furnished the corresponding benzylamine **22i** in 62% yield (entry 9). Transmetalation of **61c** with $ZnCl_2$ and subsequent Pd-catalyzed cross-coupling reactions with 1-bromo-4-methoxybenzene and 1-chloro-3-iodobenzene gave the biphenyls **22j** and **22k** in 64% and 77% yield, respectively (entries 10 and 11).

Table 2: Products of type **22** obtained by metalation of **20** followed by reaction with different electrophiles.

Entry	Substrate	Electrophile	Product[a]
1	 **20a**		 **22a**: 88%[b], [c]
2	 **20a**		 **22b**: 93%[b], [c]

[72] V. Farina, B. Krishnan, *J. Am. Chem. Soc.* **1991**, *113*, 9585.
[73] a) M. Rambaud, J. Villiéras, *Synthesis* **1984**, 406. b) J. Villiéras, M. Rambaud, *Synthesis* **1982**, 924.
[74] This reaction was performed by T. Klatt und is given here for the sake of completeness.
[75] S. O. de Silva, M. Watanabe, V. Snieckus, *J. Org. Chem.* **1979**, *44*, 4802.

3		**20a**		 **22c**: 88%[b], [d]
4		**20a**		 **22d**: 92% [b], [e]
5		**20b**		 **22e**: 95%[f], [d]
6		**20b**		 **22f**: 96%[f], [c]
7		**20c**		 **22g**: 57%[g], [e]
8		**20c**		 **22h**: 60%[g]
9		**20c**	 **29**	 **22i**: 62%[g], [h]
10		**20c**		 **22j**: 77%[g], [d]



11 **20c** **22k**: 64%[g], [c]

[a] Isolated yields of analytically pure product. [b] Metalation conditions: $TMP_2Mg \cdot 2LiCl$ (1.5 equiv), 25 °C, 2 h. [c] Cross-coupling conditions: $ZnCl_2$, 2% $Pd(dba)_2$, 4% tfp, 50 °C, 12 h. [d] Cross-coupling conditions: $ZnCl_2$, 2% $Pd(OAc)_2$, 4% SPhos, 50 °C, 12 h. [e] $CuCN \cdot 2LiCl$ (1.5 equiv) was added. [f] Metalation conditions: TMPLi (2equiv), -60 °C, 1 h. [g] Metalation conditions: *s*BuLi (1.5 equiv), TMEDA (1.5 equiv), hexane, -30 °C, 1.5 h. [h] $MgCl_2$ (1.5 equiv) was added.

The presence or absence of the BTSM-group allows to switch the metalation regioselectivity. Thus, an aryl bromide of type **18** (FG is an electron-withdrawing substituent) is preferentially metalated in position 2 leading to products of type **64/65** after quenching with an electrophile (Figure 6). On the other hand, the metalation of substrate **20** proceeds at the least sterically hindered position 6, leading to products of type **22/23** after quenching with an electrophile. In this sequence, the final group R present in **64/65** or **22/23** is either a BTSM-group (**64** and **22**) or a formyl group (CHO) (**65** and **23**).

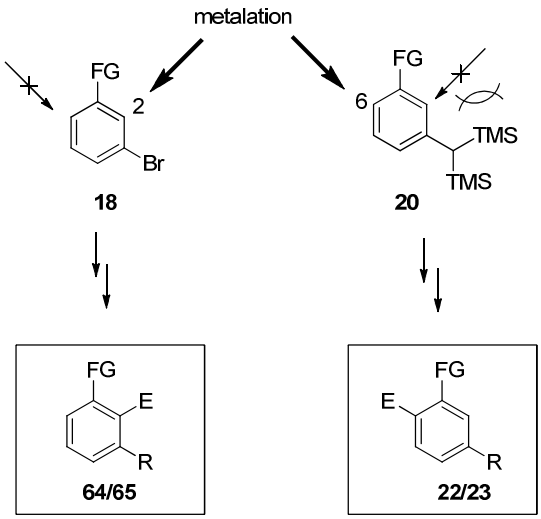
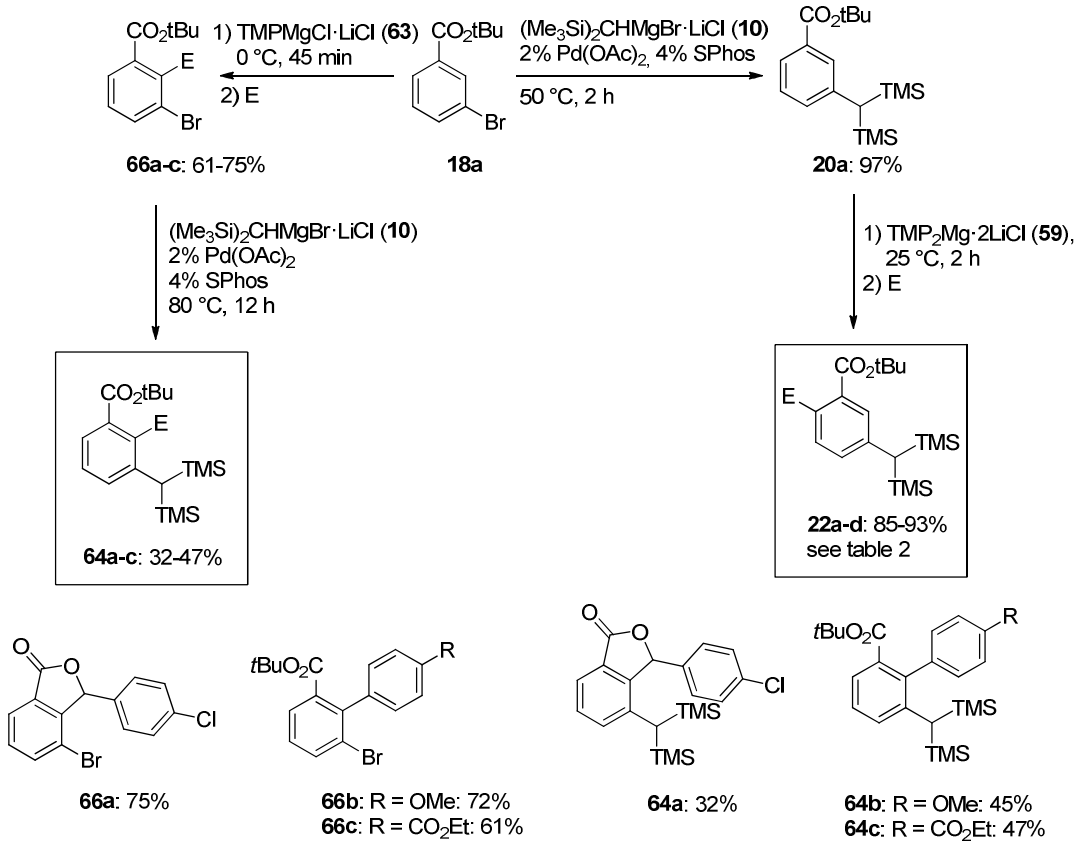


Figure 6: Regioselective metalation of substrates of type **18** and **20**.

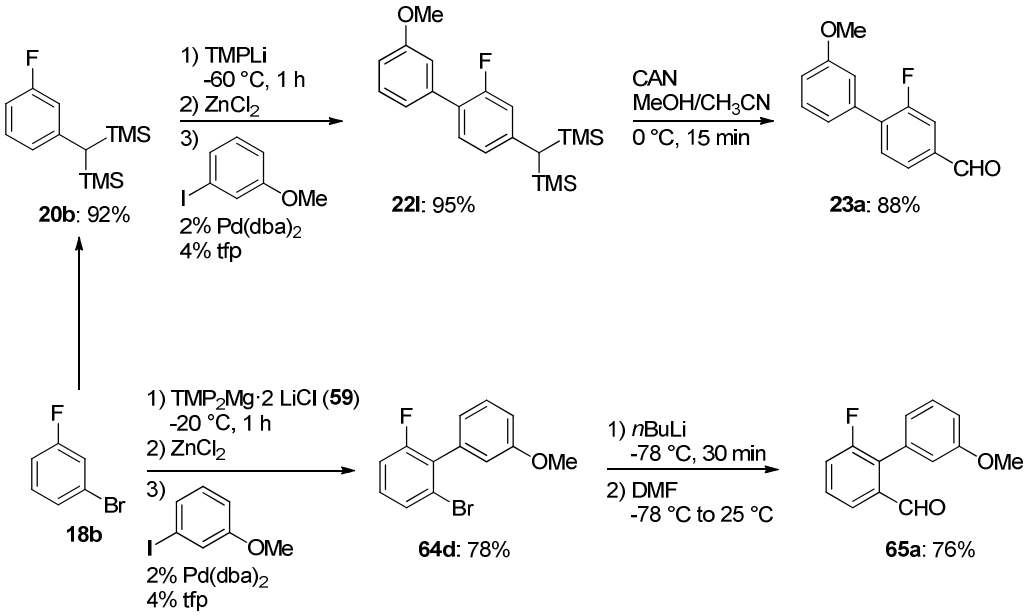
Thus, the ester **18a** was smoothly metalated by TMPMgCl·LiCl (**63**; 1.5 equiv) in THF (0 °C, 45 min; Scheme 4). Direct addition to 4-chlorobenzaldehyde furnished the lactone **66a** in 75% yield. Alternatively, transmetalation of the magnesiated species with $ZnCl_2$ (1.6 equiv) and subsequent Pd-catalyzed cross-coupling reactions with 4-iodo-anisole or ethyl 4-iodobenzoate gave the biphenyls **66b** and **66c** in 61-72% yield. A *Kumada* cross-coupling of the *ortho*-substituted substrates **66a-c** with the Grignard reagent **10** required harsher conditions (80 °C, 12 h) and the BTSM-products **64a-c** were isolated in 32-47% yield. The resulting products **64a-c** have a complementary regioisomeric substitution pattern compared to the BTSM-substituted arenes **22a-d** already described in Table 2 (entries 1-4) (Scheme 24).



Scheme 24: Orthogonal functionalization of **18a** and **20b** by regioselective magnesiation.

A similar regioselectivity switch was performed with the 3-substituted aryl fluorides **18b** and **20b** (Scheme 25).[76] Thus, treatment of **18b** with $TMP_2Mg·2LiCl$ (**59**; 1.1 equiv, -20 °C, 1 h) led to a 2-magnesiated intermediate, which after transmetalation with $ZnCl_2$ (1.2 equiv) reacted in a Pd-catalyzed cross-coupling with 3-iodo-anisole furnishing the biphenyl **64d** in 78% yield. A Br/Li-exchange was then performed on the arene **64d** with *n*BuLi (1.1 equiv) in THF (-78 °C, 30 min) affording a lithiated species, which was trapped with DMF (2 equiv) to give the benzaldehyde **65a** in 76% yield. Complementary, the metalation of **20b** with TMPLi (2 equiv, -60 °C, 1 h) followed by a transmetalation with $ZnCl_2$ (2.1 equiv) and subsequent *Negishi* cross-coupling with 1-iodo-3-methoxybenzene afforded the biphenyl **22l** in 95% yield. Oxidation of **22l** with CAN (5 equiv, 0 °C) in a 3:1 mixture of methanol/acetonitrile (0 °C, 10 min) furnished the benzaldehyde derivative **23a** in 88% yield.

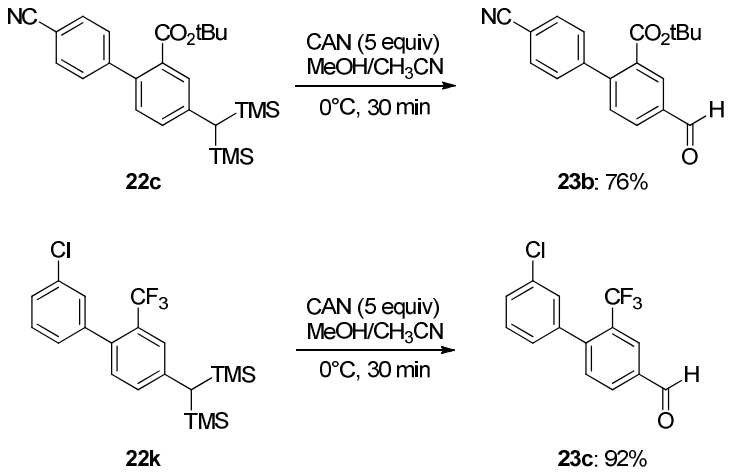
[76]These reactions were performed by T. Klatt and are given here for the sake of completeness.



Scheme 25: Generation of orthogonal functionalized benzaldehydes **23a** and **65a**

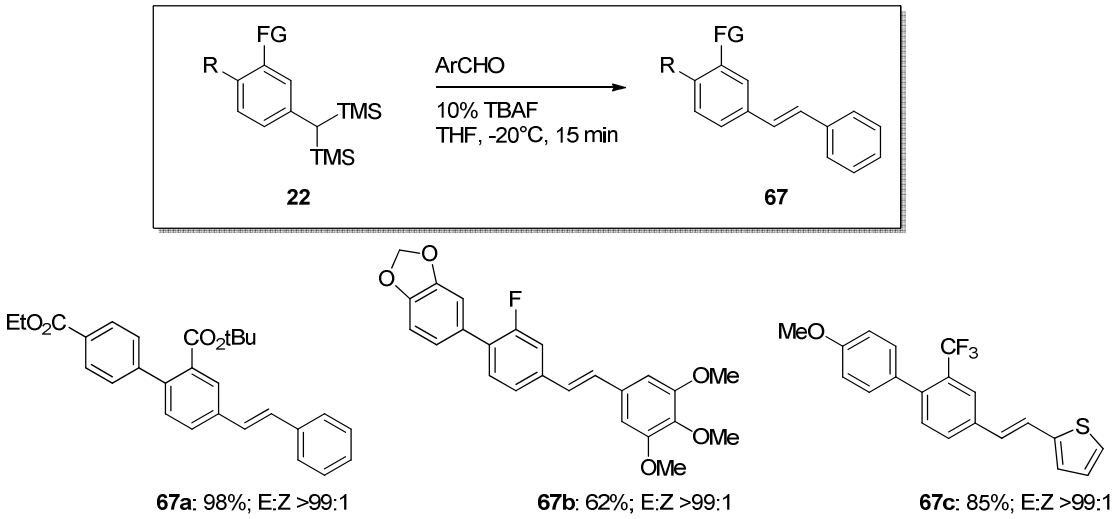
1.4. Transformation of the BTSM-Group

In order to show the utility of the BTSM-group, several polyfunctional BTSM-substituted arenes have been converted into the corresponding aldehydes using the oxidation method of *Palomo*.[23a] Thus, the biphenyls **22c** and **22k** provided after treatment with CAN (5 equiv) the corresponding aldehydes **23b-c** in 76-92% yield (Scheme 26).



Scheme 26: Oxidation of **22c** and **22k** into the corresponding aldehydes **23b** and **23c**.

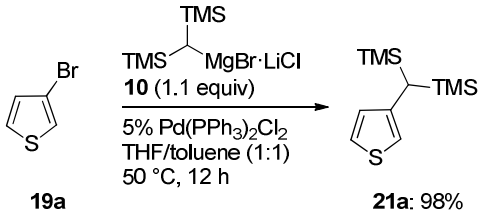
Another convenient transformation of the BTSM-group represents the *Peterson Olefination*. Hereby, the *bis*-silyl-methyl group reacts with an aldehyde-function in an elimination reaction to alkenes, catalyzed by a fluoride source. A *Peterson olefination* reaction was performed on the biphenyl **22a** using benzaldehyde (1.2 equiv) in the presence of 10% TBAF in THF (-20 °C, 15 min) leading to the stilbene derivative **67a** (>99% *E*) in 98% yield. The biphenyls **22e** and **22j** reacted in a similar fashion with 3,4,5-trimethoxybenzaldehyde and thiophene-2-carbaldehyde catalyzed by TBAF to the corresponding alkenes **67b** and **67c** (>99% *E*) in 62 and 85% yield, respectively (Scheme 27).



Scheme 27: Peterson olefination of substrates of type **22** to stilbene derivatives of type **67**.

1.5. Preparation of BTSM-Substituted Heteroaromatics

Groll et. *al* already established the cross-coupling of $(Me_3Si)_2CHMgBr{\cdot}LiCl$ (**10**) with some pyridine- and pyrazine-bromides and chlorides.[77] In order to expand the scope and show the versatility of this reaction, various heteroaromatic bromides have been used within a *Kumada-Corriu* cross-coupling reaction. Therefore, 3-bromothiophene (**19a**) reacted with the Grignard reagent **10** (1.1 equiv, THF/toluene (1:1), 50 °C, 12 h) and (thiophen-3-ylmethylene)*bis*(trimethylsilane) (**21a**) was obtained in 98% yield (Scheme 28).[78]



Scheme 28: Kumada-Corriu cross-coupling of **19a** with **10** to obtain **21a**.

For heterocyclic compounds bearing sensitive functional groups and iodides, a *Negishi* cross-coupling was established using the less reactive zinc reagent $(Me_3Si)_2CHZnCl{\cdot}MgBrCl{\cdot}LiCl$ (**10b**) achieved by a transmetalation of **10** with $ZnCl_2$ (1.05 equiv, 1 M in THF, 25 °C, 30 min).[78] By using either the Grignard reagent **10** or the zinc reagent **10b** a broad range of heteroaromatic bromides and iodides could be converted into the corresponding BTSM-functionalized derivatives (Figure 7).[78]

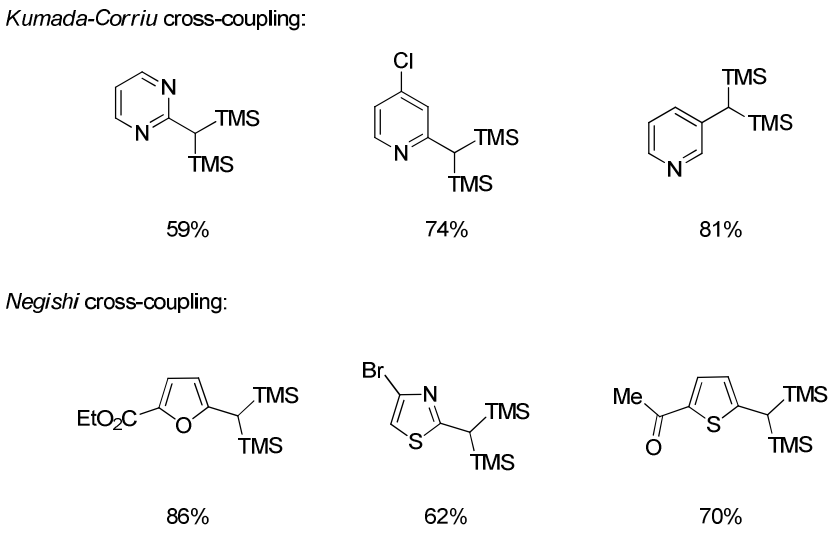
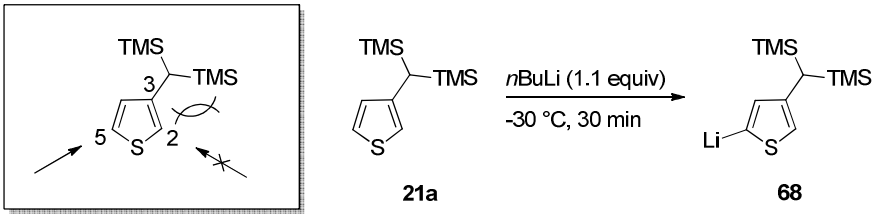


Figure 7: Various BTSM-substituted heteroaromatics obtained by either a Kumada-Corriu or a Negishi cross-coupling.[78]

[77] K. Groll, Dissertation, LMU-München, **2013**.
[78] These reactions were performed by T. Klatt and are given here for the sake of completeness.

1.6. Regioselective Functionalization of the Thiophene Scaffold

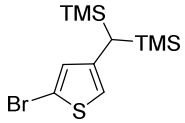
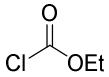
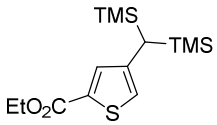
The introduction of the BTSM-group to the thiophene scaffold on position 3 allows now the regioselective metalation of the heterocycle in position 5 and not in position 2, due to sterical hindrance. It was shown that (thiophen-3-ylmethylene)*bis*(trimethylsilane) (**21a**) was selectively metalated in position 5 by the reaction with *n*BuLi in (-30 °C, 30 min), affording the lithiated species **68** (Scheme 29).

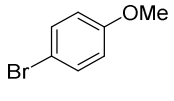
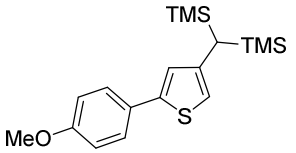
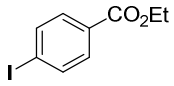
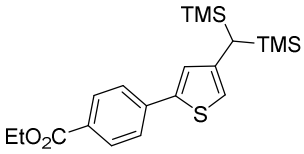
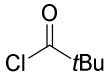
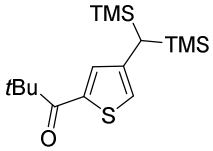


Scheme 29: Regioselective lithiation of **21a**.

The lithiated species **68** reacted with a range of different electrophiles. Thus treatment with 1,2-dibromo-1,1,2,2-tetrachloroethane (1.2 equiv, -30 °C) led to the brominated compound **69** in 98% yield (Table 3, entry 1). The reaction with ethyl chloroformate (1.2 equiv, -30 °C) afforded the ethyl ester **70** in 76% yield (entry 2). After transmetalation with $ZnCl_2$ (1.1 equiv), a Pd-catalyzed *Negishi* cross-coupling reaction with 4-bromo-anisole (0.9 equiv) in THF (50 °C, 12 h) using 2% $Pd(OAc)_2$ and 4% SPhos afforded **71** in 91% yield (entry 3). The cross-coupling reaction with ethyl 4-iodobenzoate (0.9 equiv, 50 °C, 12 h) using 2% $Pd(dba)_2$ and 4% tfp, furnished the ester **72** in 91% (entry 4). In the presence of CuCN·2LiCl (1.2 equiv), a reaction with pivaloyl chloride gave the ketone **73** in 61% yield (entry 5).

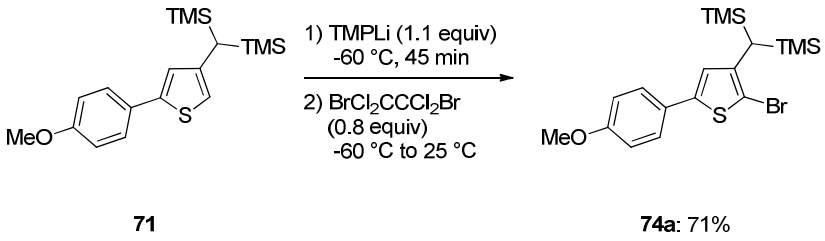
Table 3: Products **69-73** obtained by metalation of **19a** and reaction with different electrophiles.

Entry	Electrophile	Product Yield[a]
1	$BrCl_2CCCl_2Br$	 **69**: 98%
2		 **70**: 76%

3		 **71**: 91%[b]
4		 **72**: 91%[c]
5		 **73**: 61%[d]

[a] Isolated yields of analytically pure product. [b]Cross-coupling conditions: $ZnCl_2$, 2% $Pd(OAc)_2$, 4% SPhos, 50 °C, 12 h. [c] Cross-coupling conditions: $ZnCl_2$, 2% $Pd(dba)_2$, 4% tfp, 50 °C, 12 h. [d] CuCN·2LiCl was added.

A second metalation reaction on a few disubstituted thiophenes was then investigated and it could be demonstrated that the metalation again took place in a regioselective manner. For the anisyl-functionalized thiophene (**71)** the position next to the sulfur was found to be the most reactive one despite the position next to the aryl substituent. Therefore, the reaction of ((5-(4-methoxyphenyl)thiophen-3-yl)methylene)*bis*(trimethylsilane) (**71**) with TMPLi (1.1 equiv, -60 °C, 45 min) in THF, followed by the addition of dibromo-1,1,2,2-tetrachloroethane (0.8 equiv) furnished the trisubstituted thiophene derivative **74a** in 71% yield (Scheme 30).



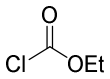
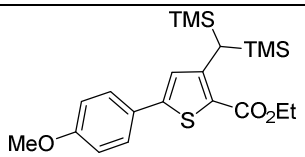
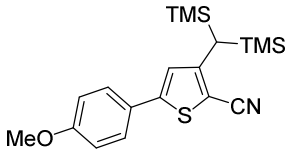
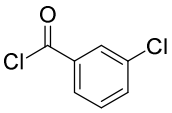
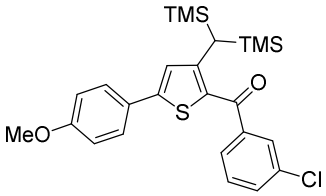
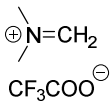
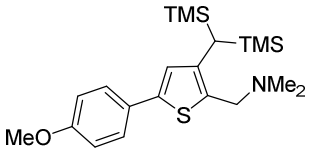
71 **74a**: 71%

Scheme 30: Lithiation of **71** followed by the reaction with dibromo-1,1,2,2-tetrachloroethane.

After successful lithiation with TMPLi, the reaction with ethyl chloroformate (1.2 equiv) or *p*-toluenesulfonyl cyanide (1.2 equiv) led to the ethyl ester **74b** or the nitrile **74c** in 62% and 59% yield (Table 4, entry 1-2). Transmetalation with $ZnCl_2$ (1.2 equiv, -60 °C, 30 min), followed by the reaction with CuCN·2LiCl (1.2 equiv, -60 °C, 30 min) and subsequent acylation reaction with 3-chlorobenzoyl chloride (0.9 equiv) furnished the ketone **74d** in 85% yield (entry 2). An analogous transmetalation

with $MgCl_2 \cdot LiCl$ (1.2 equiv) and subsequent reaction with *N*,*N*-dimethyl(methylene)iminium trifluoroacetate (**29**) gave the corresponding amine **74e** in 72% yield.

Table 4: Products of type **74** obtained by lithiation of **71** followed by reaction with different electrophiles.

Entry	Electrophile	Product Yield[a]
1		 **74b**: 62%
2	TosCN	 **74c**: 59%
3		 **74d**: 85%[b]
4	 **29**	 **74e**: 72%[c]

[a] Isolated yields of analytically pure product. [b] CuCN·2LiCl was added. [c] $MgCl_2 \cdot LiCl$ was added.

Interestingly, it was found that the metalation of the ester **70** and the ketone **73** occurs selectively next to the carbonyl-function and not next to the sulfur as it happens for the anisyl-derivative **71**. The directing effect of the carbonyl-group results in a switch of reactive sides in this case. Therefore, the metalation of the disubstituted thiophene derivatives **70** and **73** led after quenching with an electrophile exclusively to one product (of type **75** in the case of **70** and of type **76** in the case of **73**) (Figure 8).

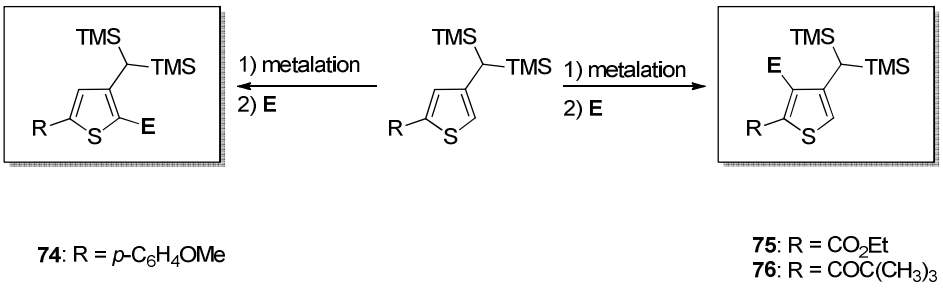
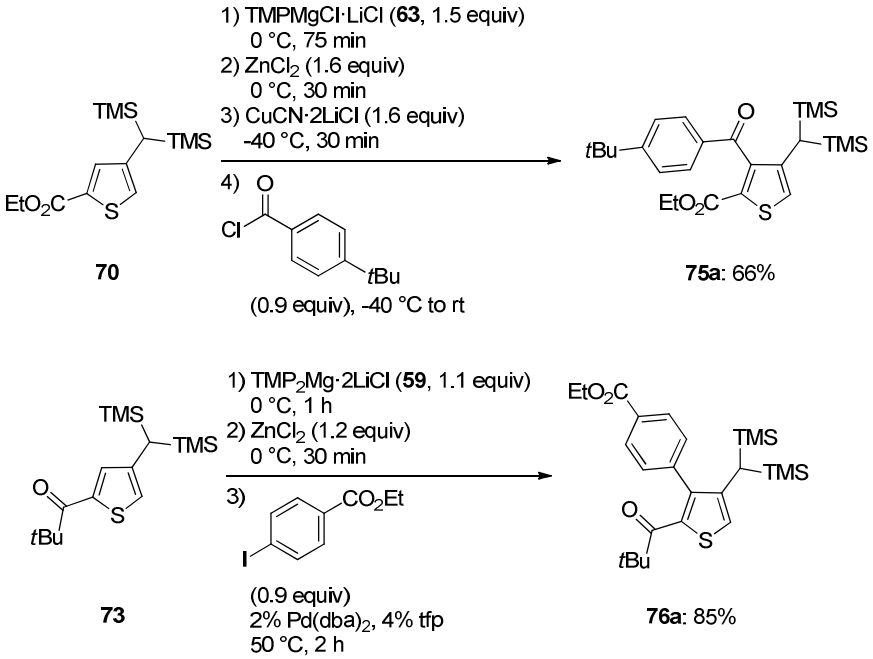


Figure 8: Switch of reactive sides during the metalation sequence of some disubstituted thiophene-derivatives.

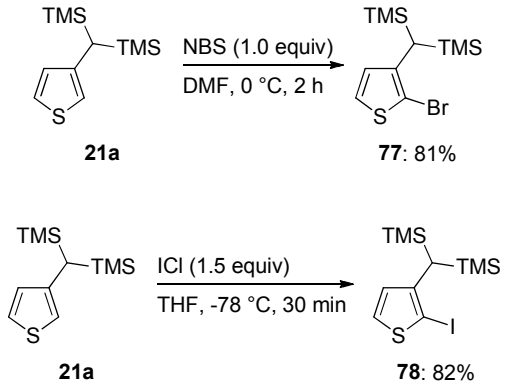
For the metalation of the ethyl ester **70**, TMPMgCl·LiCl (**63**; 1.5 equiv, 0 °C, 75 min) was found to give the best results. After transmetalation to zinc ($ZnCl_2$, 1.6 equiv), the reaction with 4-(*tert*-butyl)benzoyl chloride (0.9 equiv) in the presence of CuCN·2LiCl (1.6 equiv) results in the trisubstituted thiophene derivative **75a** in 66% yield (Scheme 31). In the case of the ketone **73**, the stronger base TMP_2Mg·2LiCl (**59**; 1.1 equiv, 0 °C, 1 h) was applied for a selective metalation. After transmetalation with $ZnCl_2$ (1.2 equiv), subsequent cross-coupling reaction with ethyl 4-iodobenzoate (0.9 equiv, 50 °C, 12 h), using $Pd(dba)_2$ (2%) and tfp (4%) as the catalytic system, furnished the biaryl **76a** in 85% yield (Scheme 31).



Scheme 31: Regioselective metalation of the carbonyls **70** and **73** and subsequent transformations to **75a** and **76a**, respectively.

So far, the BTSM-substituent has proven as useful tool in regioselective metalation strategies by allowing the stepwise and directed functionalization of the thiophene scaffold. Another useful observation was made regarding direct halogenation-reactions. It can be observed, that the

bromination of **21a** using NBS (1.0 equiv, DMF, 0 °C, 2 h) results in the 2-brominated species **77** (81%) exclusively (Scheme 32). The same directing effect can be observed for the iodination of **21a** with ICl (1.5 equiv, THF, -78 °C, 30 min). The ((2-iodothiophen-3-yl)methylene)*bis*(trimethylsilane) (**78**) was isolated in 82% yield (Scheme 32).



Scheme 32: Direct bromination and iodination of **21a** results in the 2-halogenated species **77** and **78**, respectively.

The regioselectivity in this halogenation reaction is not surprising, as it is known for 3-substituted thiophene derivatives, bearing an alkyl-group or any halide, that the bromination or iodination takes place in position 2, next to the substituent.[79] The opposite directing effect is described in the literature, when the substituent in position 3 is a carbonyl function, for example an aldehyde-group. Here position 5 is favored over position 2 (Figure 9).[80]

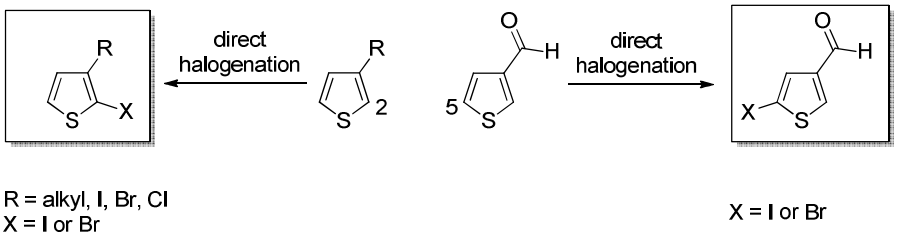


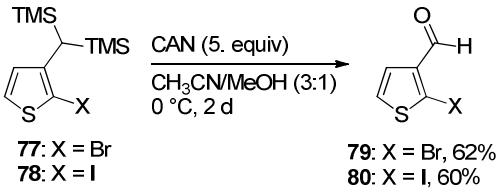
Figure 9: Regioselective halogenations reaction dependent of the nature of the substituent.

This behavior can be explained by the rules of electrophilic aromatic substitution. For five-membered heterocycles like thiophenes, furanes and pyrroles, the heteroatom in the ring strongly activates the aromatic ring system compared to benzene and directs the aromatic substitution to both *ortho* sites. In addition to this, alkyl groups and halides are also favoring electrophilic substitution in *ortho* position

[79] a) R. Wu, J. S. Schumm, D. L. Pearson, J. M. Tour, *J. Org. Chem.* **1996**, *61*, 6906. b) S. S. Gunathilake, H. D. Magurudeniya, P. Huang, H. Nguyen, E. A. Rainbolt, M. C. Stefan, M. C. Biewer, *Polym. Chem.* **2013**, *4*, 5216. c) S. K. Sontag, J. A. Bilbrey, N. E. Huddleston, G. R. Sheppard, W. D. Allen, J. Locklin, *J. Org. Chem.* **2014**, *79*, 1836. d) J. Marshall, B. C. Schroeder, H. Bronstein, I. Meager, S. Rossbauer, N. Yaacobi-Gross, E. Buchaca-Domingo, T. D. Anthopoulos, N. Stingelin, P. Beavis, M. Heeney, *Macromolecules* **2014**, *47*, 89.

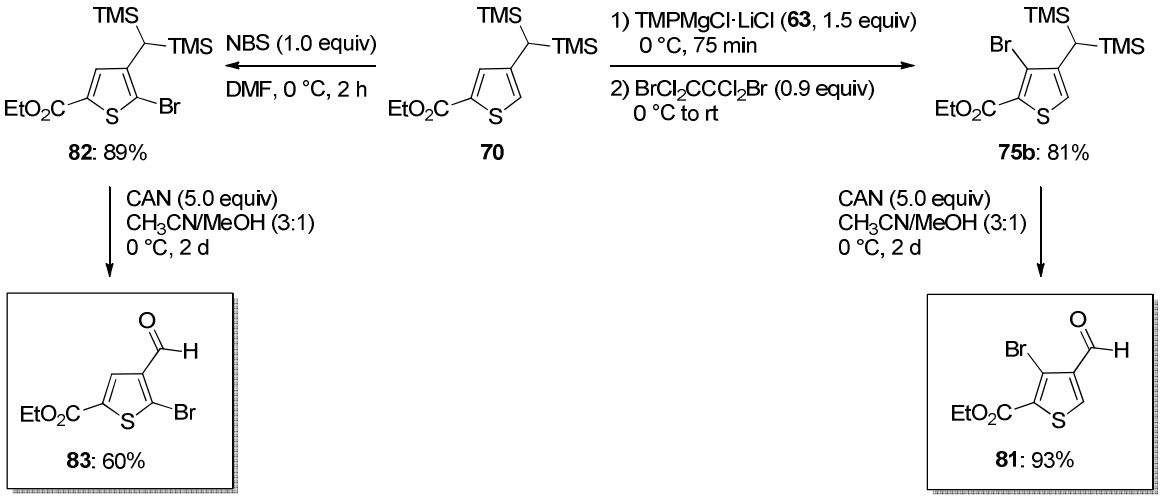
[80] a) J. Eras, C. Galvez, F. Garcia, *J. Heterocyclic Chem.* **1984**, *21*, 215. b) K.-H. Lee, K. Morino, A. Sudo, T. Endo, *J. Polym. Sci. Pol. Chem.* **2011**, *49*, 1190.

due to the +I effect (in the case of the alkyl-substituent) and the +M effect (for halides). Carbonyl-substituents are deactivating the ring and are thereby *meta*-directing by disfavoring the *ortho/para* sites for electrophilic attack. The BTSM-group, as a masked methyl group, favors the halogenation of **21a** in *ortho* position due to the +I effect, furnishing the products **77** and **78** (Scheme 32). After converting the *bis*-silyl-methyl-substituents into formyl-groups (CAN, 5 equiv, MeOH/CH_3CN, 0 °C, 2 days) the corresponding aldehydes **79** and **80** with the *ortho*-substitution pattern were obtained (Scheme 33).



Scheme 33: CAN-oxidation of **77** and **78** for the preparation of aldehydes **79** and **80**.

The combined concepts of regioselective metalation and electrophilic substitution allow the preparation of orthogonal functionalized thiophene-3 carbaldehydes. To exemplify this, ethyl 4-(*bis*(trimethylsilyl)methyl)thiophene-2-carboxylate (**70**) was metalated using TMPMgCl·LiCl (**63**; 1.5 equiv, 0 °C, 75 min) and quenched with dibromo-1,1,2,2-tetrachloroethane (0.9 equiv, 0 °C) affording **75a** in 81% yield. Oxidation with CAN (5.0 equiv, 0 °C, 2 d) results in the 2,3,4-substituted aldehyde **81** in 93% yield.[81] On the other hand, when **70** is treated with NBS (1.0 equiv, DMF, 0 °C, 2 h), the brominated species **82** is obtained in 89% yield, which gives the 2,3,5-substituted aldehyde **83** (60%) after CAN-mediated oxidation (5.0 equiv, 0 °C, 2 d) (Scheme 34).



Scheme 34: Preparation of orthogonal functionalized aldehydes **81** and **83**.

[81]This reaction was performed by T. Klatt and is given here for the sake of completeness.

To summarize and highlight the usefulness of the BTSM-substituent, appropriate conditions for the functionalization of the last position have to be found to complete the regioselective and step-wise full-functionalization of the thiophene-scaffold (Figure 10).

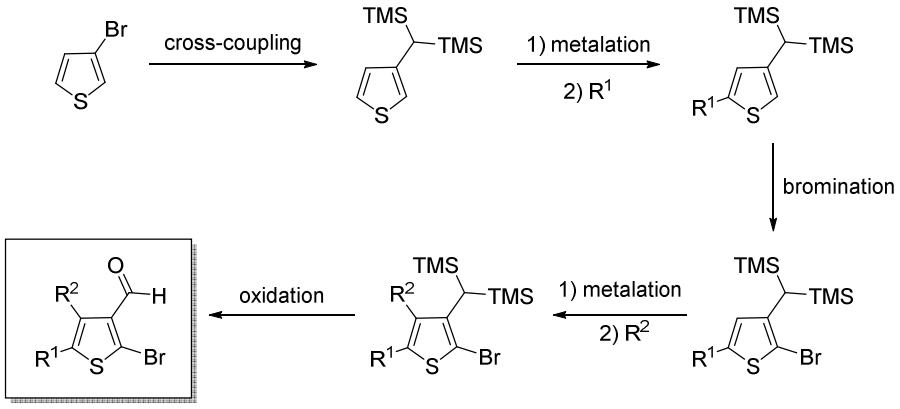
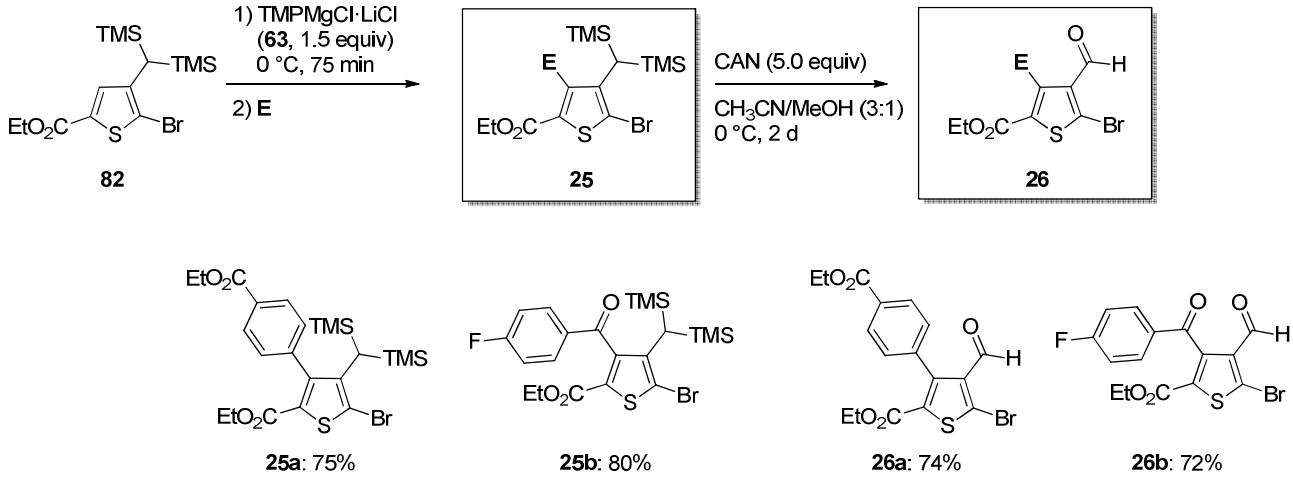


Figure 10: Synthesis-strategy for the preparation of a full-functionalized thiophene-scaffold.

For the finalization of the full-functionalization, the metalation of **82** was achieved with TMPMgCl·LiCl (**63**; 1.5 equiv, 0 °C, 75 min). After addition of $ZnCl_2$ (1.6 equiv, 0 °C, 30 min), a Pd-catalyzed cross-coupling reaction with ethyl 4-iodobenzoate (0.9 equiv, 50 °C, 12 h) was performed, using 2% $Pd(dba)_2$ and 4% tfp to provide the tetrasubstituted thiophene derivative **25a** in 75% yield. In the presence of CuCN·2LiCl (1.6 equiv, -40 °C, 30 min), the reaction with 4-fluorobenzoyl chloride (0.9 equiv) gave the ketone **25b** in 80% yield. CAN-mediated oxidation (5.0 equiv) of both tetra-substituted scaffolds were accomplished within 2 days at 0 °C to end up with the full-functionalized thiophene derivatives **26a** and **26b**[82] in 72-74% yield (Scheme 35).



Scheme 35: Preparation of the tetrasubstituted thiophene derivatives of type **25** and **26**.

[82] The CAN-oxidation was performed by T. Klatt and is given here for the sake of completeness.

2. ONE-POT PROCEDURE FOR THE PREPARATION OF TERTIARY AMINES *VIA* IMINIUM IONS

2.1. Introduction

Polyfunctional amines are ubiquitous in organic chemistry and numerous preparation methods have been reported.[83,84] Especially, the addition of organometallic reagents to iminium ions constitutes a useful synthesis of tertiary amines.[37,38,39] *Potier* reported the first preparation of *N,N*-dimethyl(methylene)iminium trifluoroacetate (**29**) from trimethylamine oxide.[35] This synthesis was considerably improved by *Tietze*, who reported a preparation by the reaction of *N,N,N′,N′*-tetramethyl-methanediamine (TMDAM, **30**) with trifluoroacetic anhydride (TFAA).[32] The aim of this work was the development of a one-pot procedure for the preparation of tertiary amines *via* the reaction of organometallics with iminium ions. It was envisioned, that the iminium salt **29**, derived from the acylation reaction of **30** with TFAA, could be used to prepare new unsymmetrical aminals of type **44** by the reaction with metallic amides of type **45.** The corresponding amides **45** were prepared by deprotonation of the secondary amines of type **46** with CH_3Met (Met = Li, MgX). The treatment of the obtained aminals **44** with TFAA will lead to the acylation of the sterically less hindered nitrogen (in this case the Me_2N-group) and provide the iminium salt **47** regioselectively. The resulting new iminium trifluoroacetate **47** may react with various organometallic reagents (R^3-Met), leading to polyfunctional tertiary amines of type **49-51** (Figure 11).

[83] For recent publications see: a) K. Okano, H. Tokuyama, T. Fukuyama, *Chem. Commun.* **2014**, *50*, 13650. b) A. E. Enyong, B. Moasser, *J. Org. Chem.* **2014**, *79*, 7553. c) W. Chen. Y. Kang, R. G. Wilde, D. Seidel *Angew. Chem. Int. Ed.* **2014**, *53*, 5178.

[84] a) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069. b) B. H. Yang, S. L. Buchwald, *J. Organomet. Chem.* **1999**, *574*, 125. c) B. List, *Tetrahedron* **2002**, *58*, 5573. d) R. I. Storer, D. E. Carrera, Y. Ni, D. W. C. MacMillan *J. Am. Chem. Soc.* **2006**, *128*, 84. d) M. Kienle, S. R. Dubbaka, K. Brade, P. Knochel, *Eur. J. Org. Chem.* **2007**, 4166. e) J. L. Klinkenberg, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2011**, *50*, 86. f) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780.

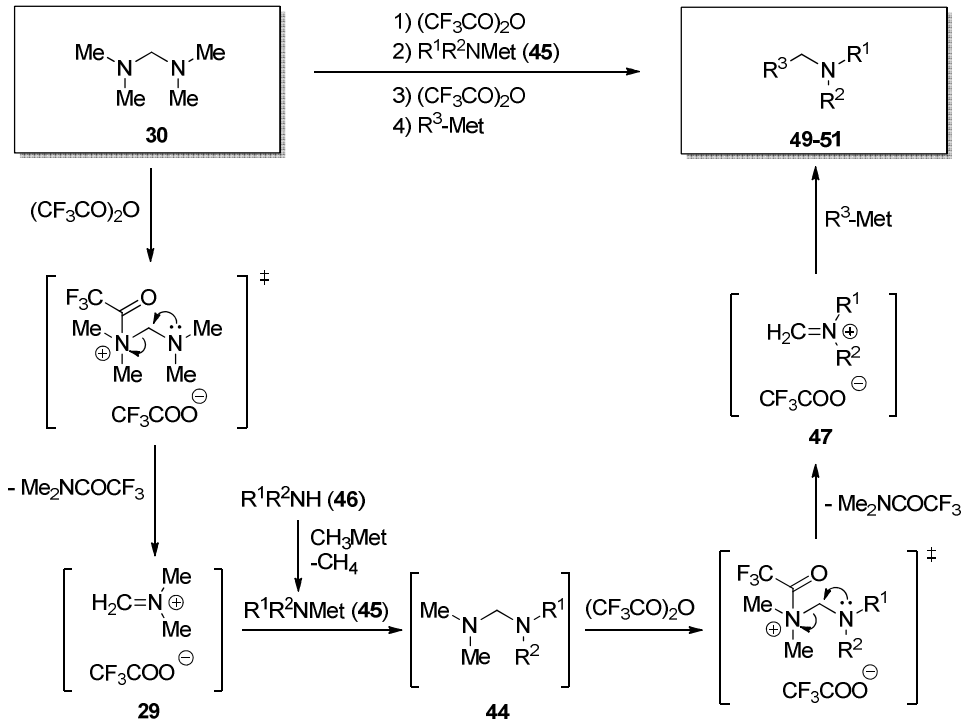
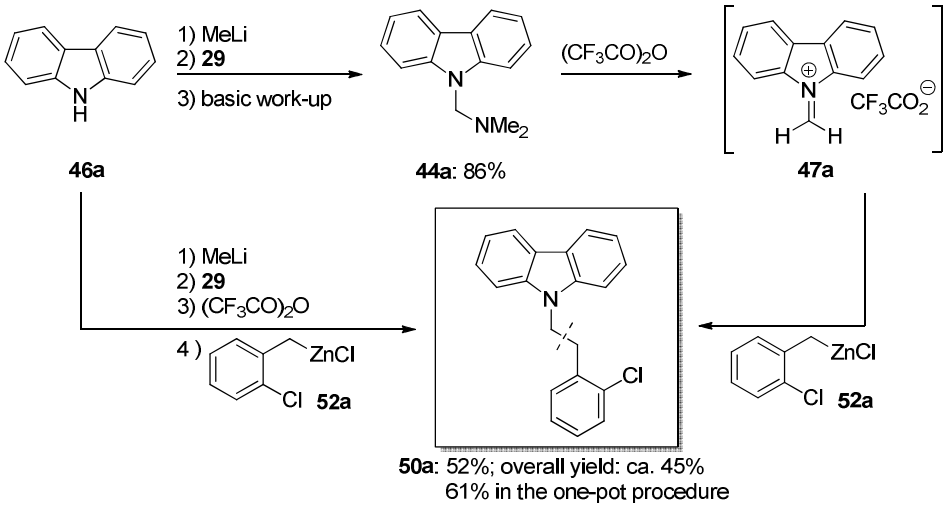


Figure 11: Envisioned mechanism of the one-pot procedure for the preparation of tertiary amines **49**.

2.2. One-Pot Procedure for the Preparation of Tertiary Amines

Although a convenient one-pot procedure has been developed (Table 5), the isolation of the unsymmetrical aminal of type **44** has been performed in the special case of 9*H*-carbazole (**46a**) (Scheme 36). Thus, the treatment of a THF solution of **46a** with MeLi (1.1 equiv, 1.6 M in Et_2O, -78 °C, 30 min) provided the corresponding lithium amide, which was added to the iminium trifluoroacetate (**29**), generated by the addition of TFAA (1.0 equiv) to TMDAM (**30**; 1.0 equiv, CH_2Cl_2, 0 °C, 15 min). This resulted in the clean formation of the mixed aminal **44a**,[85] which was isolated after a basic work-up in 86% yield. The reaction of the aminal (**44a**) with TFAA (1.0 equiv, CH_2Cl_2, -78 °C, 15 min) led selectively to a new iminium trifluoroacetate (**47a**) which was treated with the benzylic zinc reagent **52a**[86] furnishing the expected tertiary amine **50a** in 52% yield (45% overall yield in this two-step procedure). To avoid the isolation of the sensitive mixed aminal **44a**, a convenient one-pot procedure was developed, allowing the isolation of the tertiary amine **50a** in 61% yield (Scheme 36).



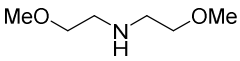
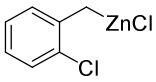
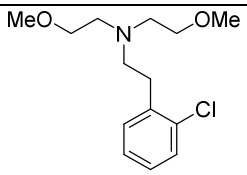
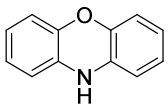
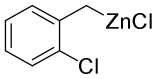
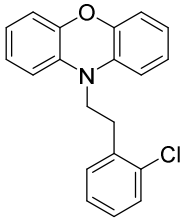
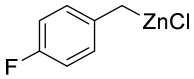
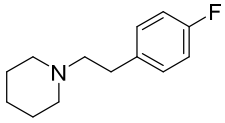
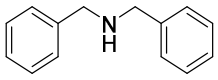
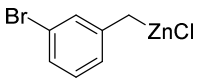
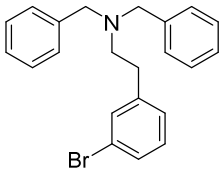
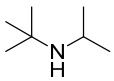
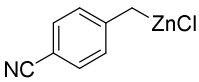
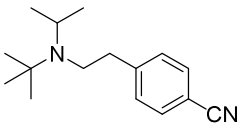
Scheme 36: Preparation of mixed aminal **44a** and subsequent conversion to the tertiary amine **50a**.

[85] B. E. Love, *J. Org, Chem.* **2007**, *72*, 630.
[86] a) A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, *44*, 5824; b) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett*. **2008**, *10*, 1107; c) A. Metzger, M. A. Schade, G. Manolikakes, P. Knochel, *Chem. Asian J.* **2008**, *3*, 1678.

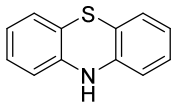
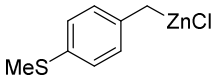
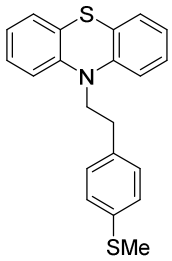
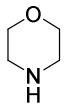
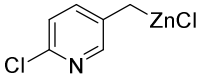
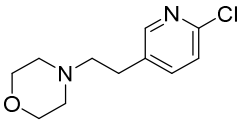
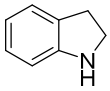
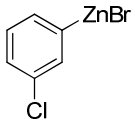
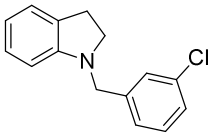
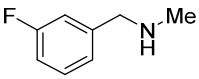
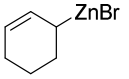
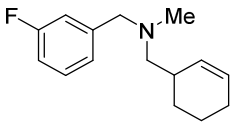
2.3. One-Pot Preparation of Tertiary Amines by Using Various Zinc Reagents

This one-pot procedure has proven to be general and a range of functionalized amines of type **46** as well as a variety of benzylic zinc reagents **52a-e** can be utilized, leading to various phenethylamines (**50b-g**) in 62-92% overall yield (Table 5, entries 1-6).

Table 5: Phenethylamines (**50**), benzylamines (**51**) and homoallylic amines (**49**) obtained by the one-pot procedure of amines of type 46 with various zinc reagents.

Entry	Amine	Zinc Reagent[a]	Product Yield[b]
1	 **46b**	 **52a**	 **50b**: 92%[87]
2	 **46c**	 **52a**	 **50c**: 77%
3	 **46d**	 **52b**	 **50d**: 82%[87]
4	 **46e**	 **25c**	 **50e**: 72%
5	 **46f**	 **25d**	 **50f**: 72%[88]

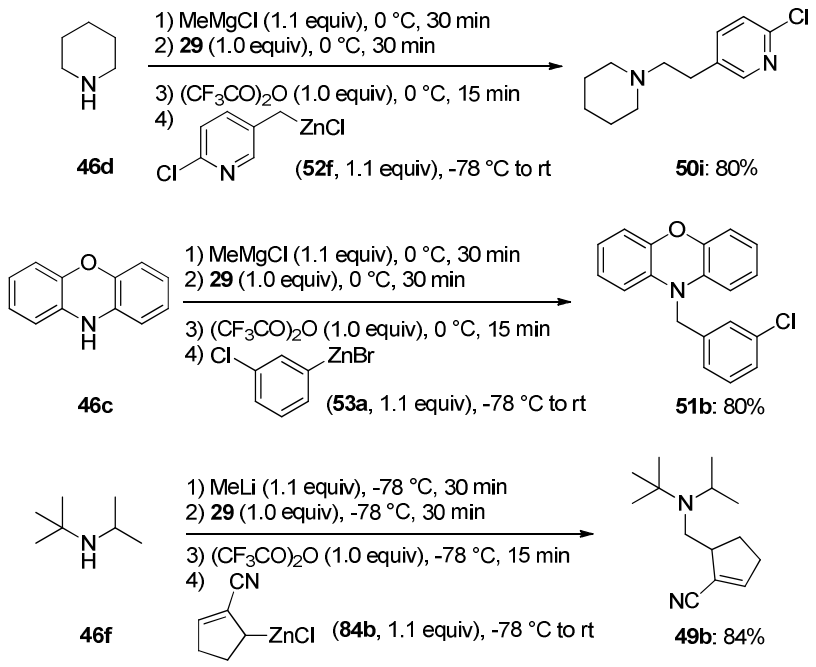
[87] These experiments were performed by Dr. Andreas J. Wagner and are mentioned here for the sake of completeness.
[88] This experiment was performed by Mario Ellwart and are mentioned here for the sake of completeness.

			
6	**46g**	**52e**	**50g**: 62%
			
7	**46h**	**52f**	**50h**: 79%[89]
			
8	**46i**	**53a**	**51a**: 66%[90]
			
9	**46j**	**84a**	**49a**: 76%[90]

[a] The concentration of the zinc reagent was determined by iodometric titration. [b] Isolated yield of analytically pure product.

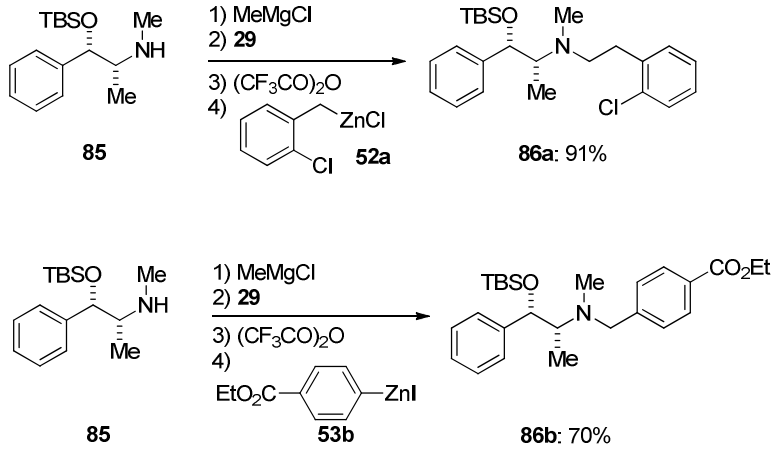
Interestingly, heterocyclic benzylic zinc reagents,[39] such as ((6-chloropyridin-3-yl)methyl)zinc chloride (**52f**) provided an entry to heterocyclic phenethylamines like **50h** (entry 6) and **50i** (Scheme 37).[89] Other classes of zinc reagents[91] were successfully used in this homologative synthesis of tertiary amines. Thus, the aminomethylation of the arylzinc bromide (**53a**) with indoline (**46i**) or phenoxazine (**46c**) provided the benzylamines **51a** (entry 8) and **51b**[90] (Scheme 37) in 66-80% yield. Also, functionalized allylic zinc reagents,[92] such as cyclohex-2-en-1-ylzinc bromide (**84a**) or the cyano-functionalized (2-cyanocyclopent-2-en-1-yl)zinc chloride (**84b**) were added to iminium ions of type **47**, generated from the two amines 1-(3-fluorophenyl)-*N*-methylmethanamine (**46j**) and the sterically hindered aliphatic amine **46f**, furnishing the expected homoallylic amines **49a** (entry 9) and **49b** (Scheme 37) in 76-84% yield.[90]

[89] These experiments were performed by Dr. Andreas J. Wagner and are mentioned here for the sake of completeness.
[90] These experiments were performed by Mario Ellwart and are mentioned here for the sake of completeness.
[91] a) P. Knochel, P. Jones, *Organozinc Reagents*, Oxford University Press, New York, **1999**. b) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker, *Org. React.* **2001**, *58*, 417. c) B. Haag, M. Mosrin, I. Hiriyakkanavar, V. Malakhov, P. Knochel, *Angew. Chem.* **2011**, *123*, 9968. *Angew. Chem. Int. Ed.* **2011**, *50*, 9794.
[92] a) H. Ren, G. Dunet, P. Mayer, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 5376; b) C. Sämann, P. Knochel, *Synthesis* **2013**, 1870.



Scheme 37: One-pot procedure for the generation of tertiary amines of type **49**-**50** by using benzylic, aryl and allylic zinc reagents.

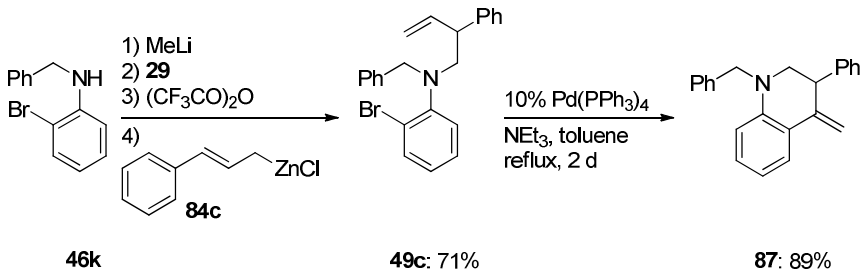
Ephedrine has found several pharmaceutical applications and is especially valuable for the treatment of obesity.[45] Our homologative amination procedure allows to convert the (+)-ephedrine derivative **85** to the benzylic and phenethylic amines **86a-86b** in 70-91% yield (Scheme 38).



Scheme 38: Homologation of the (+)-ephedrine derivative **85** into the corresponding tertiary amines of type **86**.

The high functional group tolerance of this procedure enabled the synthesis of functionalized precursors suitable for cyclization reactions. This was demonstrated in the homologation of the amine **46k**, which led to an intermediate iminium ion that reacted *regioselectively* with cinnamylzinc chloride

(**84c**) to the polyfunctional aniline **49c** in 71% yield.[93]A subsequent Heck cyclization[94] led selectively to the *exo*-methylene quinolidine (**87**) in 89% yield (Scheme 39).[93]



Scheme 39: Heck reaction of the aniline derivative **49c** obtained by the one-pot reaction of aniline **46k** and cinnamylzinc chloride (**84c**).

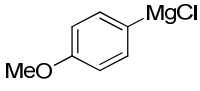
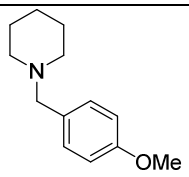
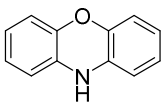
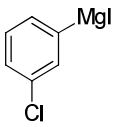
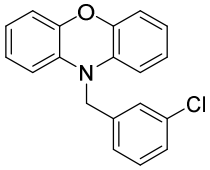
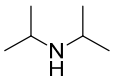
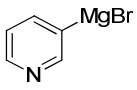
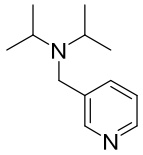
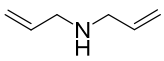
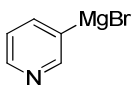
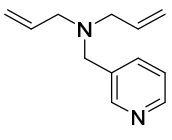
[93]These reactions were performed by Mario Ellwart and are mentioned here forthe sake of completeness.

[94] a) L. F. Tietze, T. Nöbel, M. Spescha, *J. Am. Chem. Soc.***1998**, *120*, 8971. For selected reviews see: b) A. de Meijere, F. E. Meyer, *Angew. Chem. Int. Ed.* **1995**, *33*, 2379. c) G. C. Fu, *Acc. Chem. Res.* **2008**, *41*, 1555. d) A. T. Lindhardt, T. Skrydstrup, *Chem. Eur. J.* **2008**, *14*, 8756. e) X-F. Wu, P.Anbarasan, H. Neumann, M. Beller, *Angew. Chem.* **2010**, *122*, 9231; *Angew. Chem. Int. Ed.***2010**, *49*, 9047. f) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644.

2.4. One-Pot Preparation of Tertiary Amines by Using Grignard Reagents

Finally, aryl and heteroaryl Grignard reagents[95] were used in this one-pot homologative amination, furnishing highly functionalized benzylamines of type **51**. Thus, piperidine (**46d**) and phenoxazine (**46c**) were converted into the corresponding benzylamines **51c**[96] and **51b** in 76-77% yield, using the Grignard reagents **53c** and **53d** (Table 6, entries 1-2). Also pyridin-3-ylmagnesium bromide (**53e**)[96] reacted with diisopropylamine (**46l**) and diallylamine (**46m**) in this one-pot procedure, furnishing the corresponding amines **51d-e** in 70-71% yield (entries 3-4). The pyrimidine derivative (2,4-dimethoxypyrimidin-5-yl)magnesium bromide (**5f**) provided the heterocyclic amine **51f** in 61% yield (entry 5).[97]

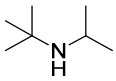
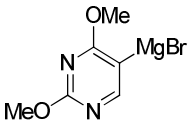
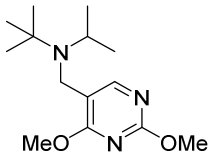
Table 6: Products of type **51** obtained by the one-pot procedure of amines of type **46** with various Grignard reagents.

Entry	Amine	Grignard Reagent[a]	Product Yield[b]
1	 **46c**	 **53c**	 **51c**: 76%[96]
2	 **46d**	 **53d**	 **51b**: 77%
3	 **46l**	 **53e**	 **51d**: 71%[96]
4	 **46m**	 **53e**	 **51e**: 70%[96]

[95] a) P. Knochel, W. Dohle, N. Gommermann, F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Ed.* **2003**, *42*, 4302. b) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333. c) G. Manolikakes, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 205.

[96] These reactions were performed by Dr. Andreas J. Wagner and are mentioned here for the sake of completeness.

[97] This reaction was performed by Mario Ellwart and is mentioned here for the sake of completeness.

			
5	**46f**	**53f**	**51f**: 61%[97]

[a] The concentration of the Grignard reagent was determined by iodometric titration. [b] Isolated yields of analytically pure product.

3. PREPARATION OF NEW BENZODITHIOPHENE BUILDING BLOCKS FOR COVALENT ORGANIC FRAMEWORKS

3.1. Introduction

The incorporation of novel functionalized building blocks into covalent organic frameworks and the further exploration of these networks is a promising subject for the development of new organic materials. Anthracenes and especially heteroanthracenes like benzodithiophene derivatives find various applications in organic materials as organic thin film transistors (OTFT)[98] and organic light-emitting diodes (OLED).[99] For this reason, two benzodithiophene-based diboronate linkers were prepared for the generation of new classes of COFs (Figure 12).

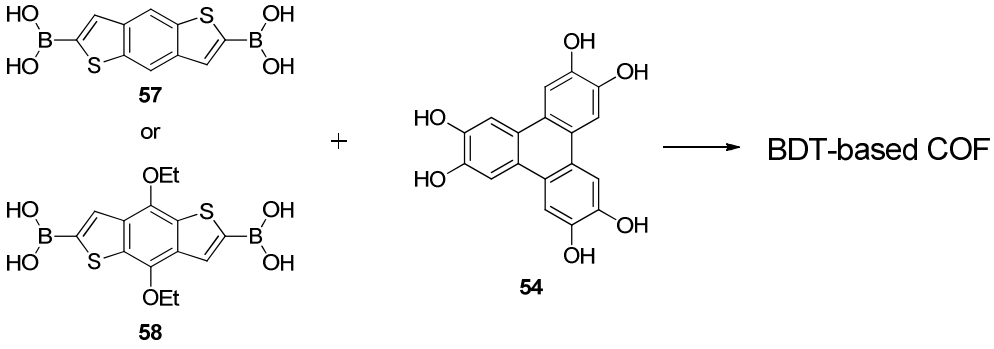
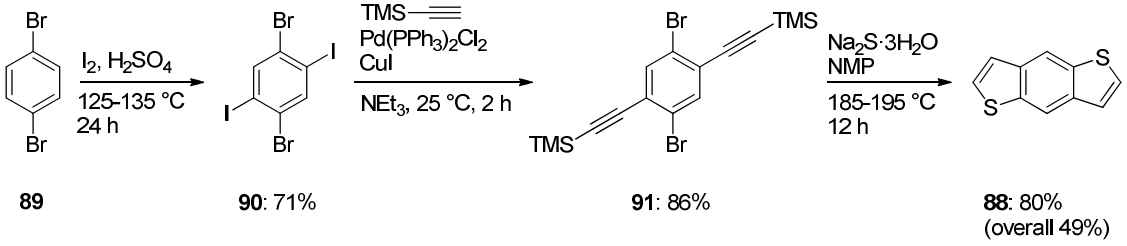


Figure 12: BDT-based diboronate linkers **57** and **58** for the generation of new COFs.

3.2. Preparation of the BDT Scaffolds

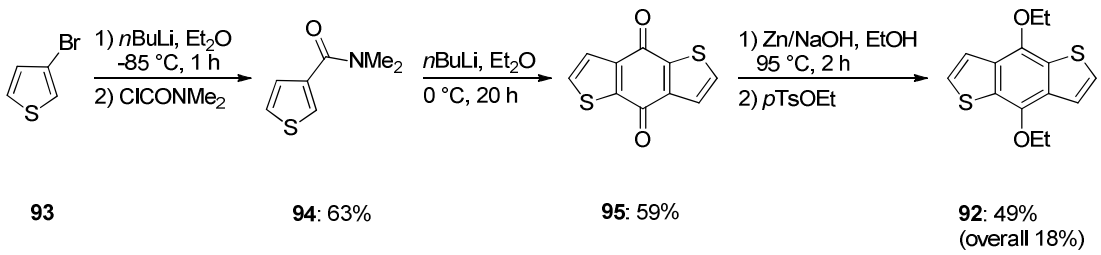
Benzo[1,2-*b*:4,5-*b'*]dithiophene (**88**) was prepared according to a modified literature procedure starting from commercially available 1,4-dibromobenzene **89** (Scheme 40).[65] Treatment of **89** with iodine in sulfuric acid provides the 1,4-dibromo-2,5-diiodobenzene **90**, which was submitted to a double *Sonogashira* cross-coupling reaction, affording the di-acetylene **91**. Subsequent reaction with sodium sulfide in NMP results in a double ring-closing reaction furnishing the benzo[1,2-*b*:4,5-*b'*]dithiophene **88** in 49% overall yield.

[98] a) Horowitz, G. *Adv. Mater.* **1998**, *10*, 165. b) Katz, H. E.; Bao, Z. N.; Gilat, S. L. *Acc. Chem. Res.* **2001**, *34*, 359. c) Sirringhaus, H.; Tessler, N.; Friend, R. H.; *Science* **1998**, *280*, 1741.
[99] Anthony, J. E. *Chem. Rev.* **2006**, *106*, 5028.



Scheme 40: Preparation of **88** *via* double Sonogashira reaction.

The preparation of 4,8-diethoxybenzo[1,2-*b*:4,5-*b'*]dithiophene **92** was performed according to a modified literature procedure, starting from the commercially available 3-bromothiophene **93** (Scheme 41).[64a,100] After a Br/Li-exchange, reaction with dimethylcarbamoyl chloride provided the amide **94**. Metalation with *n*BuLi and dimerization furnished the quinone derivative **95**. Zinc-mediated reduction followed by the addition of ethyl *p*-toluenesulfonate gave 4,8-diethoxybenzo[1,2-*b*:4,5-*b'*]dithiophene **92** in 18% overall yield.

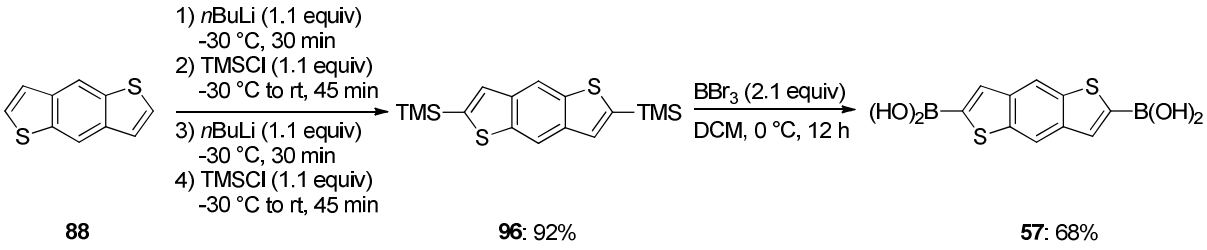


Scheme 41: Preparation of 4,8-diethoxybenzo[1,2-b:4,5-b']dithiophene **92**.

[100] a) P. Lucas, N. El Mehdi, H. A. Ho, D. Bélanger, L. Breau, *Synthesis* **2000**, 1253. b) D. W. Slocum, P. L. Gierer, *J. Org. Chem.* **1976**, *41*, 3668. c) Y. Wang, S. R. Parkin, M. D. Watson, *Org. Lett.* **2008**, *10*, 4421.

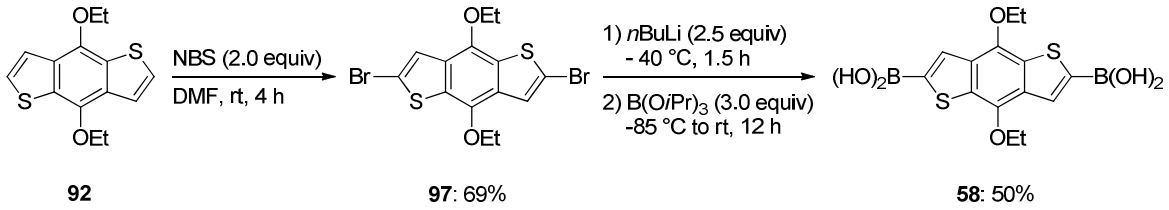
3.3. Preparation of the BDT-Linker

The benzo[1,2-*b*:4,5-*b'*]dithiophene-2,6-diyldiboronic acid **57** was prepared as illustrated in Scheme 42. The first part of the synthesis involves a stepwise double metalation and silyl-protection sequence, using *n*BuLi (1.1 equiv, -30 °C, 30 min) and chloro trimethylsilane (1.1 equiv, -30 °C to rt, 45 min) to obtain 2,6-*bis*(trimethylsilyl)benzo[1,2-*b*:4,5-*b'*]dithiophene (**96**) in 92% yield. The cleavage of the TMS-groups with BBr_3 (2.1 equiv, DCM, 0 °C, 12 h) followed by a basic work up afforded the linear diboronic acid linker **57** in 68% yield.



Scheme 42: Preparation of the linear linker **57**.

A different approach was followed for the preparation of the diboronic acid linker (**58**) bearing two ethoxy-groups, as BBr_3 is known to cleave ether-groups. Thus, 4,8-diethoxybenzo[1,2-*b*:4,5-*b'*]dithiophene **92** was treated with NBS (2.0 equiv, 0 °C, 4 h) in DMF to provide the dibromide **97** in 69% yield. Double Br/Li exchange using *n*BuLi (2.5 equiv, -40 °C, 1.5 h) followed by the addition of tri*iso*propyl borate furnished the diboronic acid linker **58** in 50% yield (Scheme 43).



Scheme 43: Preparation of the BDT-linker **58** *via* bromination and double Br/Li-exchange reaction.

3.4. Integration of the Diboronic Acid Linkers in Covalent Organic Frameworks

The formation of the COF was achieved by condensation of the free boronic acid linker **57** with HHTP (**54**) as trimeric linker, resulting in a highly ordered covalent organic network (**BDT-COF 1**) (Figure 13).[101] For the linear diethoxy-derivative **58** the COF was made using a 1:1 mixture of **57** and **58** and HHTP (**54**) (BDT-COF 2). One of the honeycomb-shaped pores of **BDT-COF 2** is illustrated in Figure 14.[101]

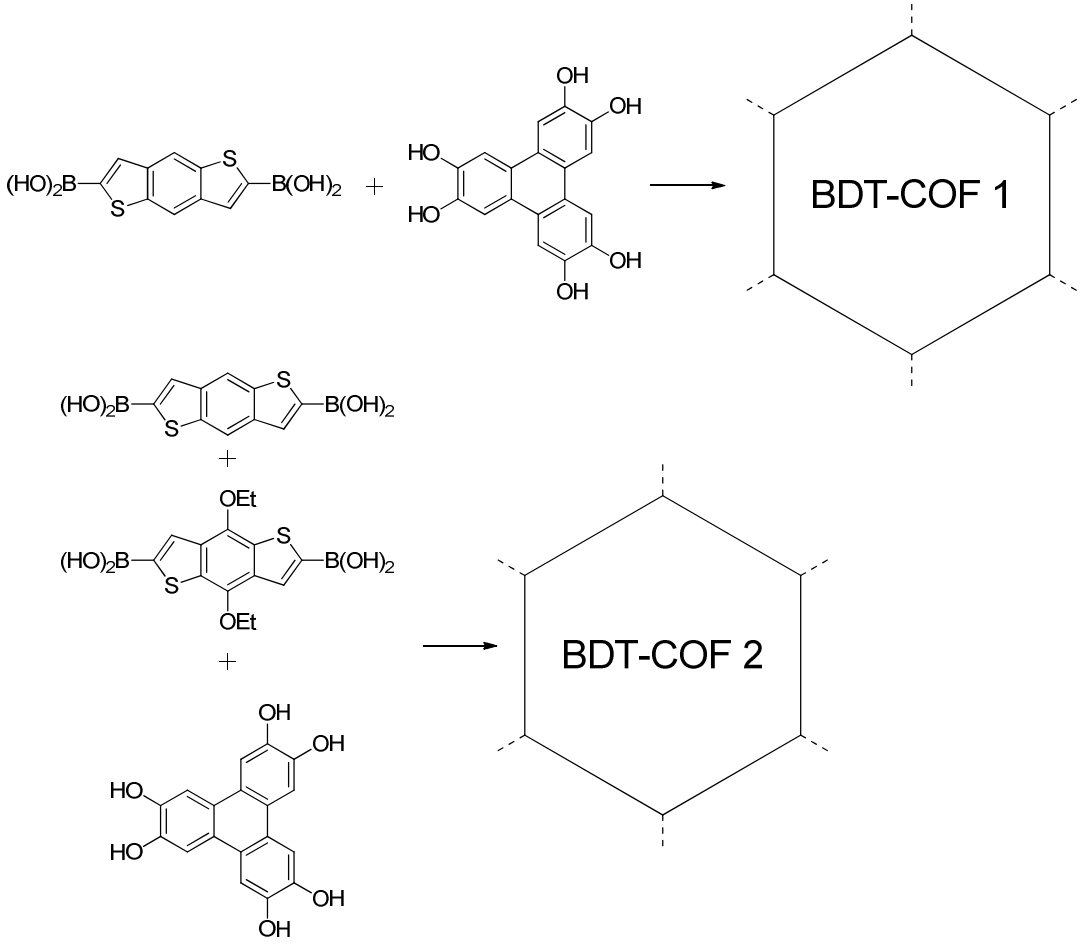


Figure 13: Condensation of the BDT-linker (**57** and **58**) and HHTP for the formation of the **BDT-COF 1** and **BDT-COF 2**.

[101] These experiments were performed by Dr. M. Dogru and Dr. Dana D. Medina and are mentioned here for the sake of completeness

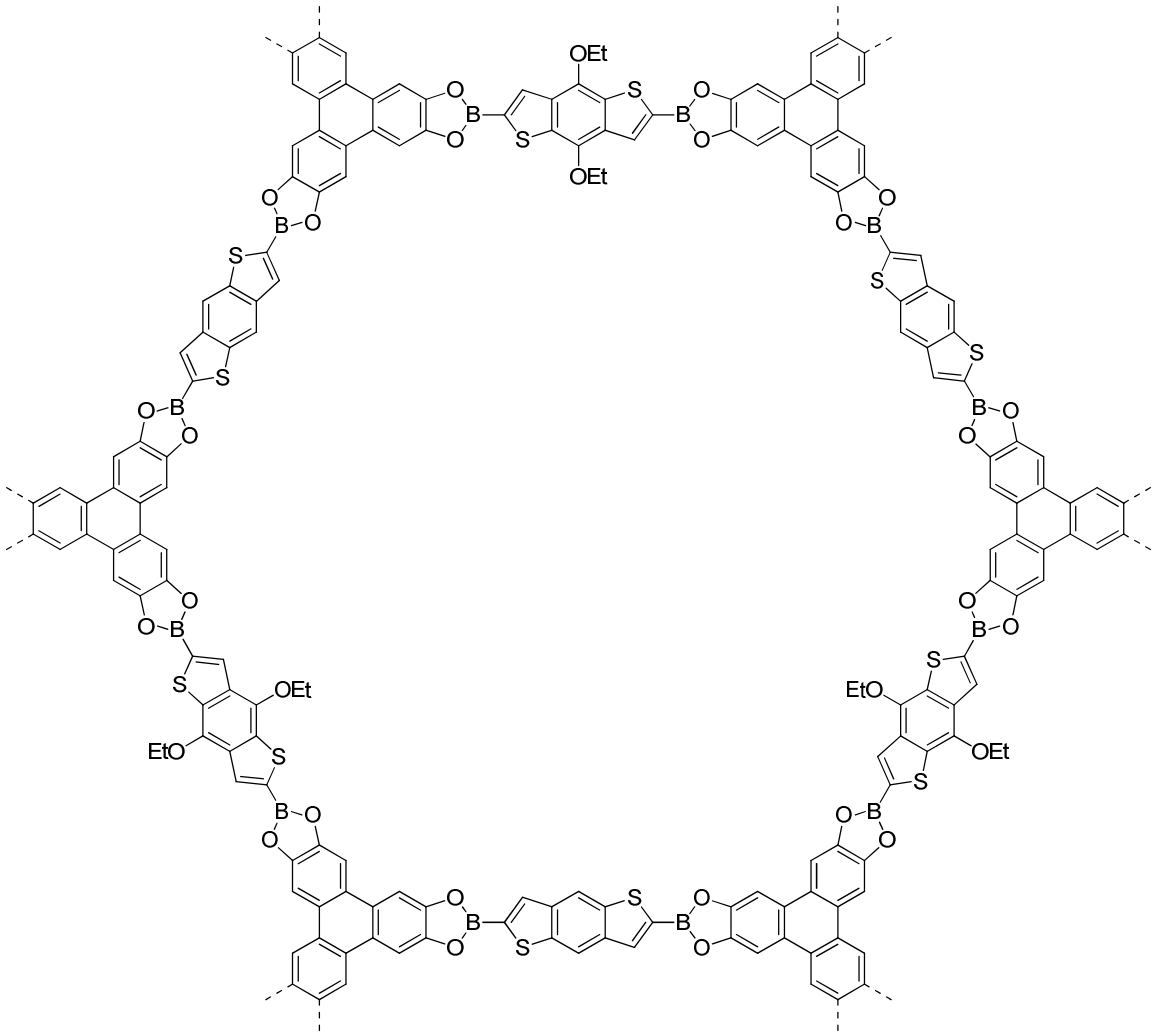


Figure 14: Honeycomb-structure of a pore from the **BDT-COF 2**.

4. SUMMARY

This work was focused on the development of a general cross-coupling procedure for the preparation of functionalized *bis*(trimethylsilyl)methyl-substituted (BTSM) aromatics and heterocycles. The regioselective functionalization of these substrates as well as the transformation of the BTSM-group into an aldehyde function or an olefin has been investigated. Furthermore, a convenient one-pot procedure for the generation of tertiary amines *via* the reaction of iminium ions with various organometallic reagents has been established. In the last part of this thesis, the preparation of two new benzodithiophene-based diboronate derivatives as building blocks for covalent organic frameworks has been realized.

4.1. Regioselective Functionalization of Aromatics and Heterocycles Bearing a Bulky *bis*-Silyl-Methyl Group

In summary, we have developed a simple procedure for the preparation of BTSM-functionalized arenes using a *Kumada-Corriu* cross-coupling. A range of functional groups, such as esters, ketones or amino groups were tolerated in this cross-coupling reaction (Figure 15).

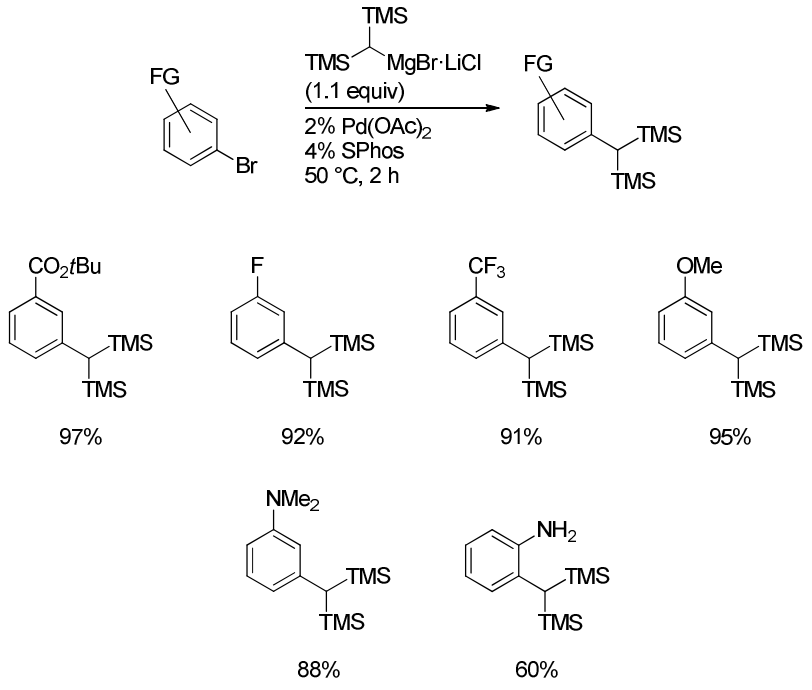


Figure 15: Examples of aromatic BTSM-derivatives obtained *via Kumada-Corriu* cross-coupling.

The bulky BTSM-group allows the regioselective metalation of different arenes and provides a route to various 1,2,4-trisubstituted aromatic compounds (Figure 16).

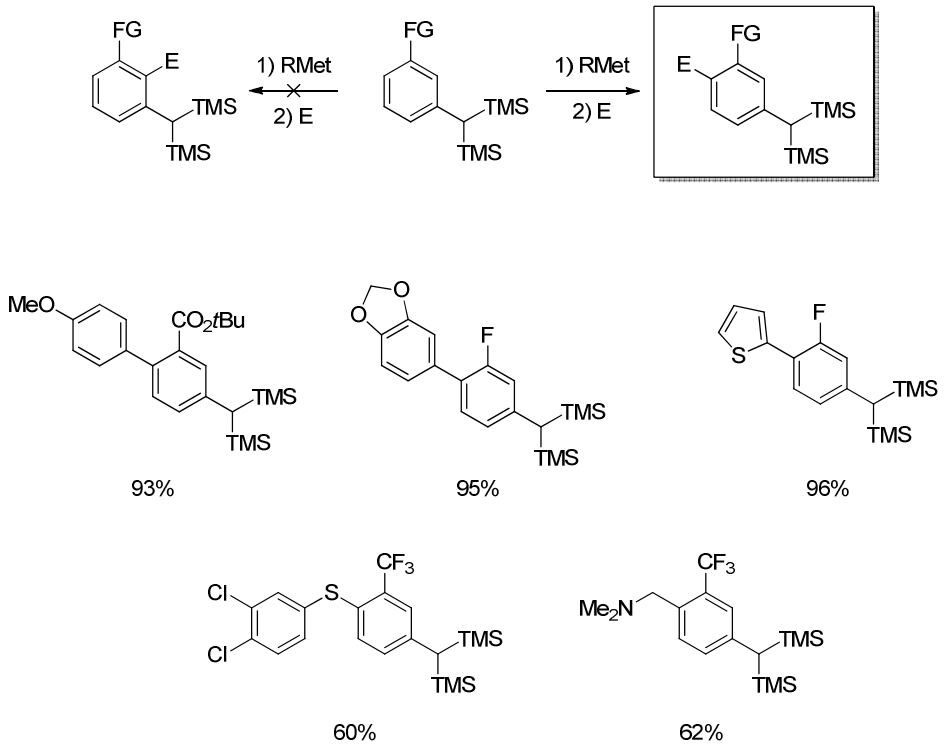


Figure 16: Examples obtained *via* the regioselective metalation of various BTSM-substituted aromatics.

Peterson Olefination reactions and CAN-mediated oxidations of the BTSM-functionalized arenes provided various aldehydes and *E*-stilbenes (Figure 17).

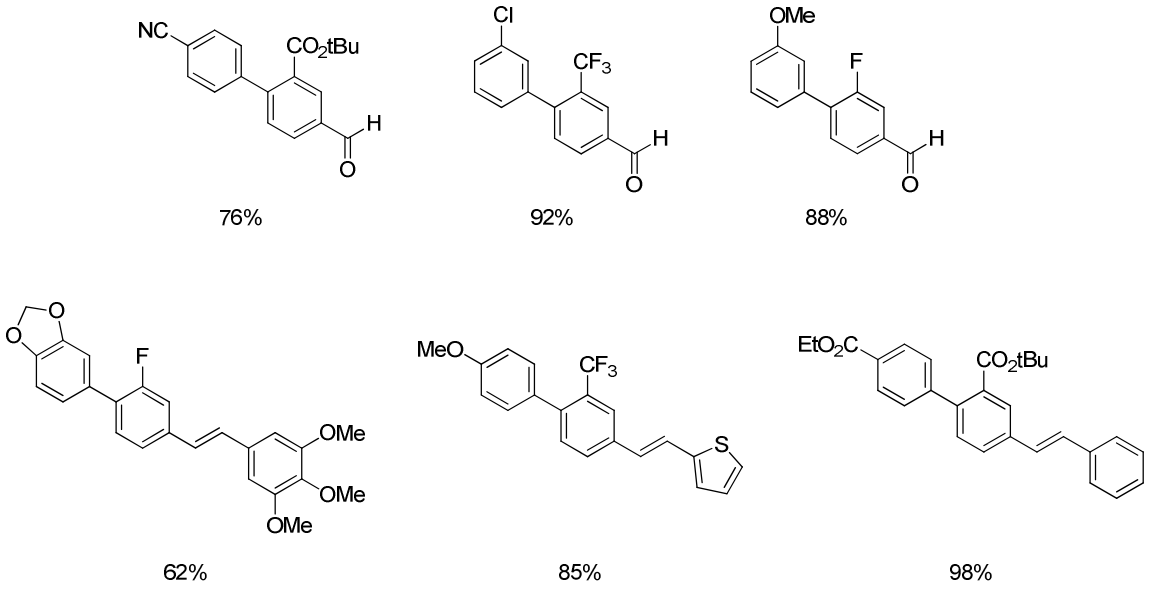


Figure 17: Examples of aldehydes and olefins obtained *via Peterson Olefination* reactions or CAN-oxidations.

The utility of the BTSM-substituent was demonstrated in the preparation sequence for orthogonal substituted thiophene-3-carbaldehydes (Figure 18).

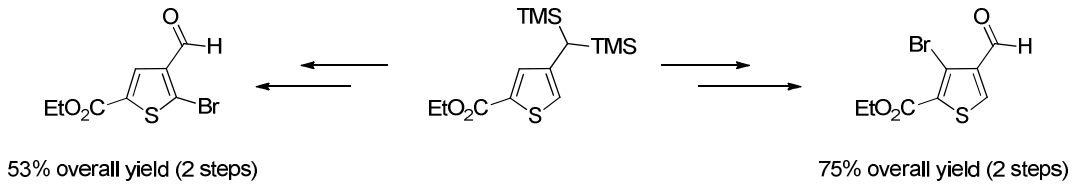


Figure 18: Preparation of orthogonal substituted thiophene-3-carbaldehydes.

The BTSM-substituent was further used for the step-wise full-functionalization of the thiophene scaffold in a regioselective manner (Figure 19).

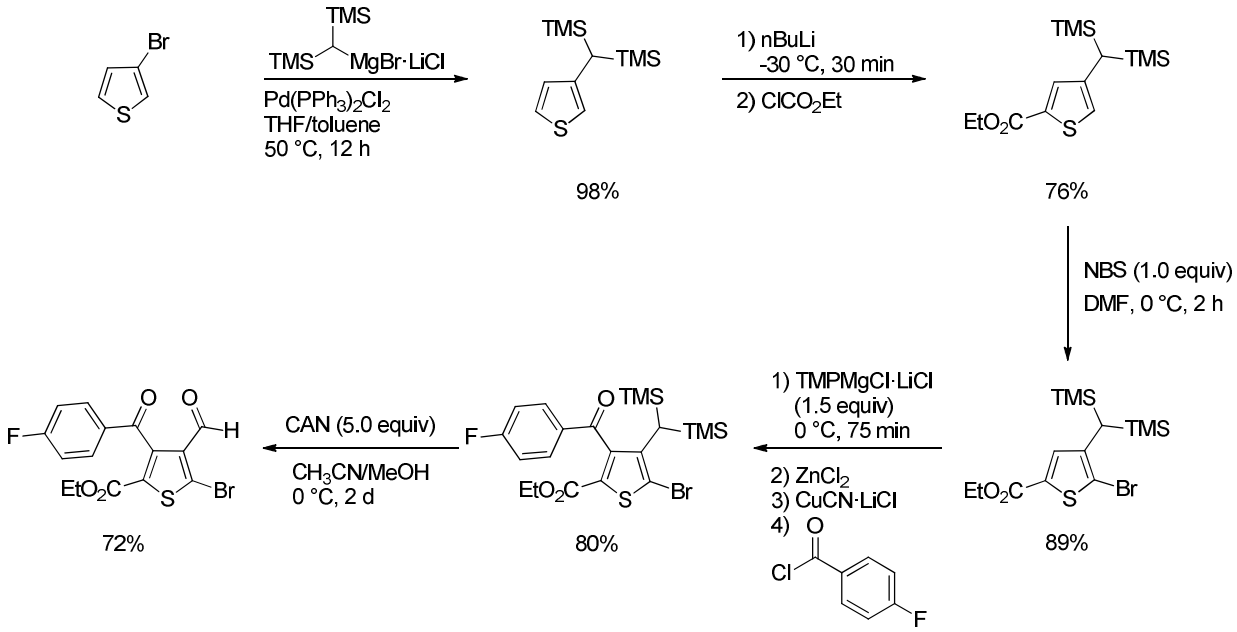
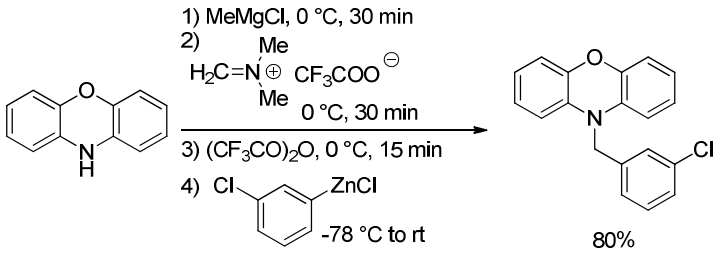
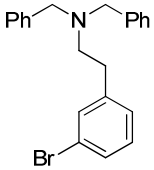


Figure 19: Full-functionalization of the thiophene-scaffold.

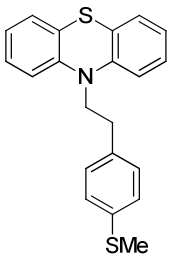
4.2. One-Pot Procedure for the Preparation of Tertiary Amines *via* Iminium Ions

In summary, a general synthesis of novel mixed aminals using Tietze's iminium salt was established. Their treatment with TFAA provided an entry to new polyfunctional iminium salts, which were trapped by numerous zinc and magnesium organometallics leading to a range of valuable amines using a convenient one-pot procedure. This reaction sequence allows to prepare complex amines, including benzylamines, biorelevant phenethylamines and ephedrine derivatives.





72%



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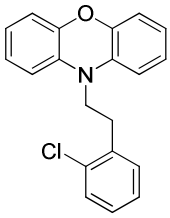
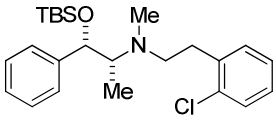


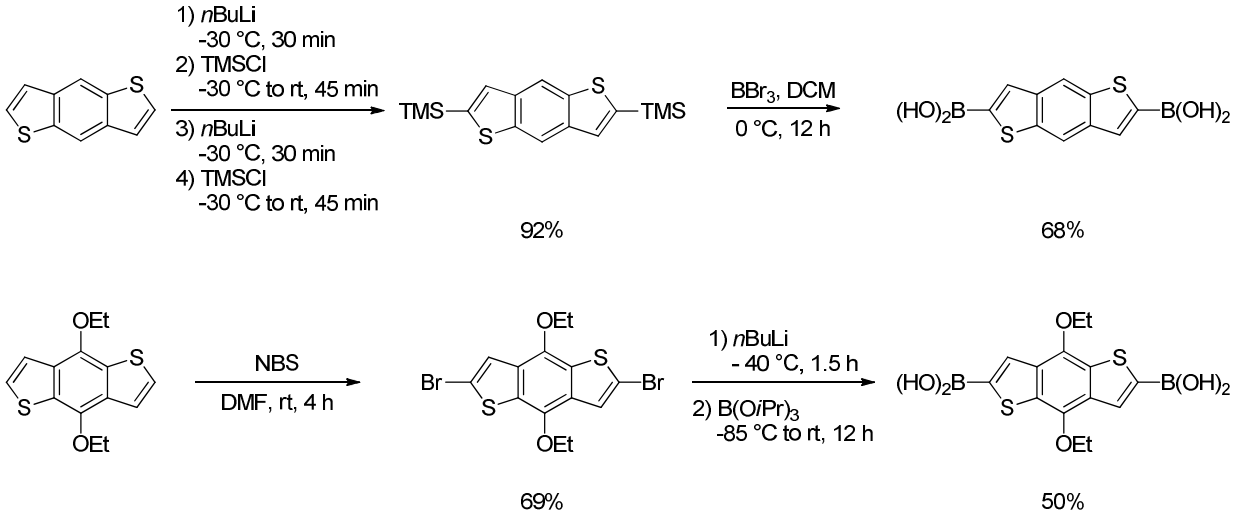
77%



91%

4.3. Preparation of New Benzodithiophene Building Blocks for Covalent Organic Frameworks

In the last part of this thesis, two new linear benzodithiophene-diboronate derivatives as building blocks for covalent organic frameworks have been prepared (Scheme 44).



Scheme 44: Preparation of two benzodithiophene-diboronate derivatives.

C: EXPERIMENTAL SECTION

1. GENERAL CONSIDERATIONS

All reactions were carried out with magnetic stirring and, if the reagents were air or moisture sensitive, in flame-dried glassware under argon. Syringes which were used to transfer reagents and solvents were purged with argon prior to use.

1.1. Solvents

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

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

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

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

Et_2O was predried over calcium hydride and dried with the solvent purification system SPS 400-2 from INNOVATIVE TECHNOLOGIES INC.

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

Pyridine was dried over KOH and distilled.

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

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

Triethylamine was dried over KOH and distilled.

Solvents for column chromatography were distilled on a rotary evaporator prior to use.

1.2. Reagents

All reagents were obtained from commercial sources and used without further purification unless otherwise stated. Liquid aldehydes, amines and acid chlorides were distilled prior to use. Following compounds were prepared according to literature procedures: $(TMS)_2CHBr$ (**11**)[102], **52a**[86], **52c**[86], **52e**[86], **53a**[91], **53b**[91], **53d**[95].

***i*PrMgCl·LiCl** solution in THF was purchased from Rockwood Lithium GmbH.

MeMgCl solution in THF was purchased from Rockwood Lithium GmbH.

[102] N. Wiberg, G. Wagner, G. Müller, J. Rieden, *J. Organomet. Chem.* **1984**, *271*, 381.

MeLi solution in Et_2O was purchased from Rockwood Lithium GmbH.

***n*BuLi** solution in hexane was purchased from Rockwood Lithium GmbH.

***s*BuLi** solution in hexane was purchased from Rockwood Lithium GmbH.

***t*BuLi** solution in hexane was purchased from Rockwood Lithium GmbH.

TMPMgCl·LiCl was prepared according to a literature procedure.[103]

TMP_2Mg·2LiCl was prepared according to a literature procedure.[104]

TMPLi was prepared by the slow addition of *n*BuLi (2.17 mL, 2.30 M in hexane, 5.00 mmol) to a solution of TMPH (0.85 mL, 5.00 mmol) in THF (5 mL) at -40 °C and stirring the reaction mixture for 30 min at -40 °C.

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

$MgCl_2$·LiCl solution (0.5 M in THF) was prepared by placing LiCl (424 mg, 10 mmol) in a *Schlenk*-flask and heating at 400 °C (heatgun) for 15 min under high vacuum. Then, Mg turnings (243 mg, 10 mmol) were added, followed by absolute THF (5 mL). Afterwards 1,2-dichloroethane (0.79 mL, 10 mmol) was added in one portion. The reaction was started by gentle warming of the reaction mixture. Once the reaction was started, the mixture was cooled by further addition of THF (15 mL) and stirred until all salts were dissolved.

$ZnCl_2$ solution (1.00 M in THF) was prepared by drying $ZnCl_2$ (136 g, 100 mmol) in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, dry THF (100 mL) was added and stirring was continued until the salt was dissolved.

1.3. Content Determination of Organometallic Reagents

Organozinc and **organomagnesium** reagents were titrated against I_2 in THF.

Organolithium reagents were titrated against anhydrous 2-propanole using 1,10-phenanthroline as indicator in THF.

TMPMgCl·LiCl and **TMP_2Mg·2LiCl** were titrated against benzoic acid using 4-(phenylazo)diphenylamine as indicator in THF.

TMPLi were titrated using phenyl benzamide as titrating agent and indicator in THF.

[103]A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem*. **2006**, *118*, 3024; *Angew. Chem. Int. Ed*. **2006**, *45*, 2958.
[104]G. Clososki, C. Rohbogner, P. Knochel, *Angew. Chem*. **2007**, *119*, 7825; *Angew. Chem. Int. Ed*. **2007**, *46*, 7681.

1.4. Chromatography

Flash column chromatography was performed using silica gel 60 (0.040-0.063 mm) and aluminum oxide 90 (0.063-0.200) from Merck.

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

- $KMnO_4$ (3.0 g), 5 drops of conc. H_2SO_4 in water (300 mL).

- Phosphomolybdic acid (5.0 g), $Ce(SO_4)_2$ (2.0 g) and conc. H_2SO_4 (12 mL) in water (230 mL).

- Ninhydrin (1.5 G), EtOH (100 mL) and conc. AcOH (3.0 mL).

1.5. Analytical Data

NMR spectra were recorded on VARIAN Mercury 200, BRUKER AXR 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to tetramethylsilane. For the characterization of the observed signal multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet) as well as br (broadened).

Mass spectroscopy: High resolution (HRMS) and low resolution (MS) spectra were recorded on a FINNIGAN MAT 95Q instrument. Electron impact ionization (EI) was conducted with an electron energy of 70 eV. For the coupled gas chromatography / mass spectrometry, a HEWLETT-PACKARD HP 6890 / MSD 5973 GC/MS system was used.

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

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

2. REGIOSELECTIVE FUNCTIONALIZATION OF AROMATICS AND HETEROCYCLES BEARING A BULKY *BIS*-SILYL-METHYL GROUP

2.1. Typical Procedures (TP)

Typical Procedure 1 for the cross-coupling of 18 with aryl bromides (TP 1):

In a dry argon flushed *Schlenk*-flask, the aryl bromide (**18**, 1.0 equiv), $Pd(OAc)_2$ (0.02 equiv) and SPhos (0.04 equiv) were suspended in dry THF (0.3 M). Then, $(TMS)_2CHMgBr \cdot LiCl$ (**10**, 1.1 equiv, 0.6 M in THF) was added and the reaction mixture was stirred at the indicated temperature and time. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with sat. aq NH_4Cl solution and using undecane as internal standard.

Typical Procedure 2 for the magnesiation of 20a with $TMP_2Mg \cdot 2LiCl$ (TP 2):

In a dry argon flushed *Schlenk*-flask, $TMP_2Mg \cdot 2LiCl$ (**59**, 1.5 equiv, 0.6 M in THF) was placed and the ester **20a** (1.0 equiv) was added at 25 °C. The reaction mixture was stirred at this temperature for 2 h. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

Typical Procedure 3 for the lithiation of 20b with TMPLi (TP 3):

In a dry argon flushed *Schlenk*-flask, the arene **20b** (1.0 equiv) was dissolved in THF (0.5 M) and cooled to -60 °C. Then, TMPLi (2.0 equiv, 0.63 M in THF) was added dropwise and the reaction mixture was stirred at this temperature for 1 h. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

Typical Procedure 4 for the lithiation of 20c with *s*BuLi and TMEDA (TP 4):

In a dry argon flushed *Schlenk*-flask, the arene **20c** (1.0 equiv) was dissolved in dry *n*-hexane (0.5 M) and cooled to -30 °C. Then, TMEDA (*N,N,N',N'*-tetramethylethane-1,2-diamine; 1.5 equiv) and *s*BuLi (1.5 equiv, 1.45 M in THF) were added dropwise and the reaction mixture was stirred at this temperature for 1 h. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

Typical Procedure 5 for the oxidation of the BTSM-substituted arenes with CAN (TP 5):

In a dry argon flushed *Schlenk*-flask, the BTSM-substituted compound (1.0 equiv) was dissolved in a 3:1 mixture of CH_3CN:MeOH (0.015 M) and cooled to 0 °C. Then, ceric ammonium nitrate (CAN; 5.0

equiv) was added and the reaction mixture was stirred at this temperature for 30 min. The completion of the reaction was checked by GC analysis of reaction aliquots.

Typical Procedure 6 for the Peterson olefination of the BTSM-substituted arenes (TP 6):

In a dry argon flushed *Schlenk*-flask, the BTSM-substituted compound (1.0 equiv) and the aldehyde (1.2 equiv) were dissolved in THF (0.0625 M) and cooled to -20 °C. Then, TBAF (tetra-*n*-butylammonium fluoride; 0.1 equiv, 1.0 M in THF) was added dropwise and the reaction mixture was stirred at this temperature for 15 min.

Typical Procedure 7 for the lithiation of 21a with *n*BuLi (TP 7):

In a dry argon flushed *Schlenk*-flask, the arene **21a** (1.0 equiv) was dissolved in THF (0.2 M) and cooled to -30 °C. Then, *n*BuLi (1.1 equiv, 2.35 M in hexane) was added dropwise and the reaction mixture was stirred at this temperature for 30 min. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

Typical Procedure 8 for the lithiation of 71 with TMPLi (TP 8):

In a dry argon flushed *Schlenk*-flask, the arene **71** (1.0 equiv) was dissolved in THF (1.0 M) and cooled to -60 °C. Then, freshly prepared TMPLi (1.1 equiv, 0.63 M in THF) was added dropwise and the reaction mixture was stirred at this temperature for 45 min. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

Typical Procedure 9 for the magnesiation of 70 with TMPMgCl·LiCl (TP 9):

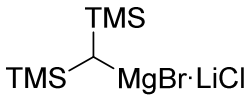
In a dry argon flushed *Schlenk*-flask, TMPMgCl·LiCl (**63**; 1.5 equiv, 1.2 M in THF) was placed and the carbonyl compound **70** (1.0 equiv) was added at 0 °C. The reaction mixture was stirred at this temperature for 75 min. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

Typical Procedure 10 for the magnesiation of 73 with $TMP_2Mg·2LiCl$ (TP 10):

In a dry argon flushed *Schlenk*-flask, the arene **73** (1.0 equiv) was dissolved in THF (1.0 M) and cooled to 0 °C. Then, $TMP_2Mg·2LiCl$ (**59**; 1.5 equiv, 0.6 M in THF) was added at 0 °C and the reaction mixture was stirred at this temperature for 1 h. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with iodine and using undecane as internal standard.

2.2. Preparation of Starting Material

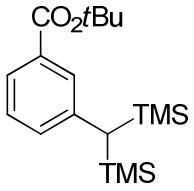
Preparation of the Grignard Reagent $(Me_3Si)_2CHMgBr \cdot LiCl$ (10)



LiCl (1.59 g, 37.5 mmol, 1.25 equiv) was placed in a dry argon flushed *Schlenk*-flask and dried for 10 min at 450 °C (heat gun) under high vacuum (10^{-2} mbar). Mg turnings (0.91 g, 37.5 mmol, 1.25 equiv) were added and the flask was evacuated again and refilled with argon. Then, THF (30 mL) was added and after addition of chlorotrimethylsilane (33 mg, 0.04 mL, 0.30 mmol) and 1,2-dibromoethane (56 mg, 0.03 mL, 0.30 mmol), the suspension was heated until ebullition occurred. The flask was cooled to 0 °C and *bis*(trimethylsilyl)methylbromide (**11**;18 g, 30 mmol, 1.0 equiv) was added dropwise. After stirring for 30 min at 0 °C, the solids were allowed to settle and the supernatant solution was carefully cannulated to a new dry and argon flushed *Schlenk*-flask. Titration of the organomagnesium reagent **10** against iodine in THF gave a concentration of 0.60 M (80%).

2.3. Preparation of BTSM-Functionalized Aromatics

Synthesis of *tert*-butyl 3-(*bis*(trimethylsilyl)methyl)benzoate (20a)



According to **TP 1**, the cross-coupling of *tert*-butyl 3-bromobenzoate (**18a**; 257 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 2 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 50:1) to give **20a** as colorless oil (326 mg, 97%).

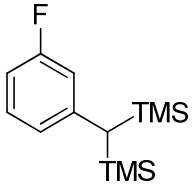
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm =7.66 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.59 (t, *J* = 1.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.04-7.13 (m, 1H), 1.59 (s, 9H), 1.56 (s, 1H), 0.03 (s, 18H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.1, 143.4, 132.7, 131.7, 129.5, 127.8, 124.4, 80.6, 29.5, 28.2, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}= 2950, 2897, 2847, 1710, 1700, 1597, 1575, 1476, 1456, 1430, 1392, 1373, 1365, 1290, 1253, 1246, 1162, 1151, 1106, 1081, 1036, 999, 932, 920, 914, 866, 838, 829, 815, 775, 764, 746, 695, 692, 687, 664.

MS (70 eV, EI): *m/z* (%) = 336 (1, M^+), 280 (23), 265 (18), 264 (20), 190 (24), 162 (14), 73 (31), 70 (11), 61 (17), 57 (14), 45 (14), 43 (100).

HRMS (EI) for **$C_{18}H_{32}O_2Si_2$** (336.1941): found: 336.1952 (M^+).

Synthesis of ((3-fluorophenyl)methylene)*bis*(trimethylsilane) (20b)



According to **TP 1**, the cross-coupling of 1-bromo-3-fluorobenzene (**18b**; 175 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF

(3.5 mL) with $(TMS)_2CHMgBr \cdot LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 2 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 99:1) to give **20b** as a yellow oil (234 mg, 92%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.13 (d, J = 6.4 Hz, 1H), 6.70 (t, J = 7.1 Hz, 2H), 6.63 (m, 1H), 1.51 (s, 1H), 0.03 (s, 18H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 163.0 (d, J = 244 Hz), 146.3 (d, J = 8 Hz), 129.4 (d, J = 9 Hz), 124.5, 115.2 (d, J = 22 Hz), 110.2 (d, J = 21 Hz), 30.1, 0.3.

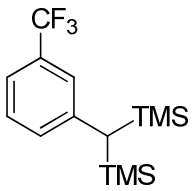
^{19}F-NMR (282 MHz, $CDCl_3$): δ/ppm = -114.4.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}=2953, 2896, 2834, 1610, 1582, 1483, 1439, 1284, 1265, 1248, 1177, 1159, 1131, 1070, 1036, 1002, 946, 940, 888, 866, 825, 768, 737, 685.

MS (70 eV, EI): *m/z* (%) = 254 (5, M^+), 239 (16), 166 (42), 163 (10), 162 (54), 161 (18), 147 (38), 145 (17), 135 (10), 134 (15), 73 (100), 59 (10), 45 (17).

HRMS (EI) for **$C_{13}H_{23}FSi_2$** (254.1322): found: 254.1313 (M^+).

Synthesis of ((3-(trifluoromethyl)phenyl)methylene)*bis*(trimethylsilane) (20c)



According to **TP 1**, the cross-coupling of 1-bromo-3-(trifluoromethyl)benzene (**18c**; 225 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr \cdot LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 2 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **20c** as a colorless oil (277 mg, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm =7.29 (d, J = 4.7 Hz, 2H), 7.17 (s, 1H), 7.07 - 7.14 (m, 1H), 1.59 (s, 1H), 0.03 (s, 18H).

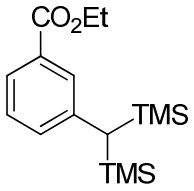
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm =144.5, 131.8, 130.3 (q, J = 31.9 Hz), 128.3, 124.9 (q, J = 2.8 Hz), 124.4 (q, J = 272.2 Hz), 120.1 (q, J = 3.8 Hz), 30.0, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2898, 2836, 1607, 1591, 1487, 1456, 1442, 1325, 1315, 1251, 1200, 1158, 1123, 1090, 1073, 1035, 1000, 976, 907, 891, 864, 836, 826, 768, 743, 721, 704, 688, 671, 661.

MS (70 eV, EI): *m/z* (%) = 304 (1, M^+), 216 (18), 130 (17), 115 (19), 91 (16), 83 (15), 77 818), 73 (100), 45 (15).

HRMS (EI) for $\mathbf{C_{14}H_{23}F_3Si_2}$ (304.1290): found: 304.1277 (M^+).

Synthesis of ethyl 3-(*bis*(trimethylsilyl)methyl)benzoate (20d)



According to **TP 1**, the cross-coupling of ethyl 3-bromobenzoate (**18d**; 229 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 1.83 mL, 1.1 mmol, 0.6 M in THF, 1.1 equiv) was completed within 2 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 50:1) to give **20d** as a colorless oil (281 mg, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.72 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.63 (t, *J* = 1.7 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.07 - 7.16 (m, 1H), 4.35 (q, *J* = 7.0 Hz, 2H), 1.58 (s, 1H), 1.39 (t, *J* = 7.1 Hz, 3H), 0.03 (s, 18H).

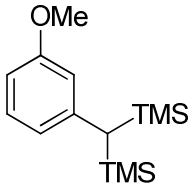
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 192.7, 167.0, 167.0, 143.7, 130.2, 128.0, 124.5, 60.7, 29.6, 14.3, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2898, 2833, 1718, 1600, 1580, 1481, 1434, 1419, 1392, 1367, 1307, 1273, 1249, 1198, 1169, 1157, 1104, 1079, 1029, 999, 924, 865, 836, 829, 827, 771, 755, 745, 695, 688, 656.

MS (70 eV, EI): *m/z* (%) = 308 (42, M^+), 293 (22), 279 (11), 264 (11), 263 (17), 220 (13), 191 (14), 190 (62), 162 (43), 147 (29), 145 (10), 73 (100), 59 (11), 45 (14).

HRMS (EI) for $\mathbf{C_{16}H_{28}O_2Si_2}$ (308.1628): found: 308.1622 (M^+).

Synthesis of ((3-methoxyphenyl)methylene)*bis*(trimethylsilane) (20e)



According to **TP 1**, the cross-coupling of 1-bromo-3-methoxybenzene (**18e**; 187 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr \cdot LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 2 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **20e** as colorless oil (253 mg, 95%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.10 (td, *J* = 7.8 Hz, J = 2.6, 1H), 6.55 (m, 3H), 3.77 (s, 3H), 1.47 (s, 1H), 0.03 (s, 18H).

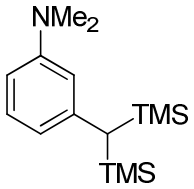
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 159.3, 144.8, 128.8, 121.5, 114.6, 108.3, 55.0, 29.8, 0.2.

IR (Diamond-ATR, neat): $\tilde{V}$ / cm^{-1} = 2951, 2898, 2833, 1603, 1597, 1591, 1577, 1484, 1465, 1435, 1295, 1256, 1247, 1190, 1173, 1165, 1140, 1037, 937, 930, 918, 915, 883, 863, 833, 826, 771, 769, 734, 698, 685, 667, 653.

MS (70 eV, EI): *m/z* (%) = 266 (46, M^+), 251 (27), 179 (17), 178 (100), 73 (86), 59 (11), 45 (11).

HRMS (EI) for **$C_{14}H_{26}OSi_2$** (266.1522): found: 266.1522 (M^+).

Synthesis of 3-(*bis*(trimethylsilyl)methyl)-*N*,*N*-dimethylaniline (20f)



According to **TP 1**, the cross-coupling of 3-bromo-*N*,*N*-dimethylaniline (**18f**; 200 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr \cdot LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 2 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 100:1) to give **20f** as a yellow oil (246 mg, 88%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.07 (t, *J* = 7.9 Hz, 1H), 6.55 – 6.40 (m, 3H), 2.93 (s, 6H), 1.46 (s, 1H), 0.04 (s, 18H).

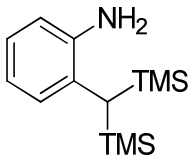
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 149.9, 144.0, 128.5, 119.1, 114.2, 108.7, 41.2, 29.8, 0.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2950, 2896, 2830, 2799, 1684, 1595, 1575, 1560, 1495, 1456, 1435, 1346, 1262, 1246, 1205, 1181, 1162, 1135, 1092, 1061, 1036, 995, 975, 886, 876, 864, 832, 826, 771, 761, 743, 737, 723, 717, 698, 685, 667, 653.

MS (70 eV, EI): *m/z* (%) = 279 (100, M^+), 278 (22), 265 (18), 264 (40), 208 (14), 207 (74), 206 (19), 205 (21), 192 (13), 191 (55), 190 (14), 178 (16), 176 (13), 73 (89), 59 (12), 45 (13).

HRMS (EI) for **$C_{15}H_{29}NSi_2$** (279.1839): found: 279.1813 (M^+).

Synthesis of 2-(*bis*(trimethylsilyl)methyl)aniline (20i)



According to **TP 1**, the cross-coupling 2-bromoaniline (**18i**; 172 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry toluene (2.1 mL) with $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 4.17 mL, 2.5 mmol, 3.0 equiv, 0.6 M in THF) was completed within 24 h at 80 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (Al_2O_3, *iso*hexane:EtOAc = 100:1) to give **20i** as a red oil (151 mg, 60%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 6.91 – 6.86 (m, 2H), 6.74 – 6.66 (m, 2H), 3.42 (s, *br*, 2H), 1.37 (s, 1H), 0.05 (s, 18H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 143.1, 129.0, 128.1, 124.1, 118.9, 116.1, 20.9, 0.4.

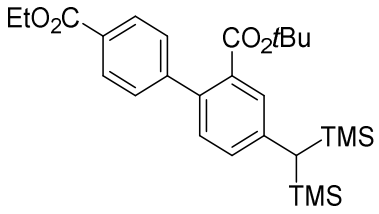
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3460, 3368, 3061, 3019, 2951, 2896, 2854, 1618, 1578, 1489, 1451, 1436, 1419, 1400, 1303, 1263, 1247, 1201, 1163, 1019, 932, 862, 832, 791, 771, 745, 703, 685, 667, 653.

MS (70 eV, EI): *m/z* (%) = 251 (21, M^+), 247 (11), 236 (48), 220 (11), 178 (17), 148 (32), 74 (12), 73 (100), 71 (16), 69 (15), 57 (22), 55 (15), 44 (12), 41 (43).

HRMS (EI) for **$C_{13}H_{25}NSi_2$** (251.1526): found: 251.1517 (M^+).

2.4. Regioselective Functionalization of the BTSM-substituted Aromatics

Synthesis of 2-*tert*-butyl 4'-ethyl 4-(*bis*(trimethylsilyl)methyl)biphenyl-2,4'-dicarboxylate (22a)



tert-Butyl 3-(*bis*(trimethylsilyl)methyl)benzoate (**20a**; 337 mg, 1.0 mmo, 1.0 equivl) was metalated according to **TP 2** using $TMP_2Mg \cdot 2LiCl$ (**59**; 2.5 mL, 1.5 mmol, 1.5 equiv, 0.6 M in THF). The reaction mixture was cooled to -20 °C and $ZnCl_2$ (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. Then, $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and ethyl 4-iodobenzoate (221 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 20:1) to give **22a** as white crystals (341 mg, 88%).

M.p.: 98.4 – 100.2 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.05 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 1.7 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.11 - 7.15 (m, 1H), 7.03 - 7.09 (m, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 1.61 (s, 1H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.28 (s, 9H), 0.07 (s, 18H).

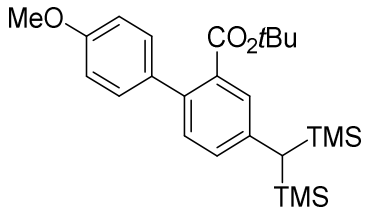
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 167.8, 166.6, 146.9, 143.3, 136.3, 131.9, 131.1, 130.2, 130.2, 129.1, 128.7, 128.6, 81.2, 60.9, 29.4, 27.6, 14.3, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2969, 2951, 2931, 2899, 2831, 1721, 1719, 1609, 1478, 1457, 1451, 1402, 1367, 1364, 1299, 1288, 1269, 1249, 1244, 1200, 1174, 1160, 1134, 1123, 1110, 1102, 1095, 1027, 1006, 934, 906, 865, 855, 838, 796, 790, 780, 765, 756, 738, 733, 719, 704, 688, 677, 660.

MS (70 eV, EI): *m/z* (%) = 484 (4, M^+), 429 (23), 428 (56), 413 (21), 340 (15), 338 (17), 310 (12), 267 (12), 266 (35), 265 (100), 237 (12), 191 (10), 147 (11), 75 (10), 73 (50), 57 (14).

HRMS (EI) for **$C_{27}H_{40}O_4Si_2$** (484.2465): found: 484.2461 (M^+).

Synthesis of *tert*-butyl 4-(*bis*(trimethylsilyl)methyl)-4'-methoxy-[1,1'-biphenyl]-2-carboxylate (22b)



tert-Butyl 3-(*bis*(trimethylsilyl)methyl)benzoate (**20a**; 337 mg, 1.0 mmol, 1.0 equiv) was metalated according to **TP 2** using $TMP_2Mg \cdot 2LiCl$ (**59**; 2.5 mL, 1.5 mmol, 1.5 equiv, 0.6 M in THF). The reaction mixture was cooled to -20 °C and $ZnCl_2$ (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. Then, $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and 4-iodoanisole (187 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 20:1) to give **22b** as white crystals (329 mg, 93%).

M.p.: 99.3 – 100.9 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.34 (d, *J* = 1.9 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 1H), 7.02 (dd, *J* = 7.9, 2.1 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 3H), 1.57 (s, 1H), 1.32 (s, 9H), 0.06 (s, 18H).

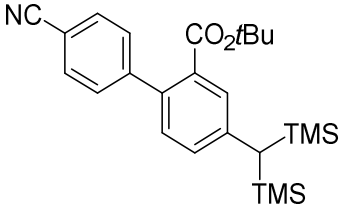
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 168.5, 158.6, 141.9, 136.8, 134.4, 132.2, 130.9, 130.3, 129.9, 129.7, 113.3, 80.8, 55.3, 29.1, 27.7, 0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952, 2836, 1701, 1601, 1479, 1458, 1408, 1367, 1294, 1274, 1243, 1187, 1173, 1156, 1135, 1107, 1038, 936, 920, 865, 836, 826, 803, 792, 775, 747, 734, 686.

MS (70 eV, EI): *m/z* (%) = 442 (13, M^+), 371 (15), 298 (12), 297 (19), 296 (100), 253 (10), 222 (15), 147 (12), 73 (46).

HRMS (EI) for **$C_{25}H_{38}O_3Si_2$** (442.2359): found: 442.2360 (M^+).

Synthesis of *tert*-butyl 4-(bis(trimethylsilyl)methyl)-4'-cyano-[1,1'-biphenyl]-2-carboxylate (22c)



tert-Butyl 3-(*bis*(trimethylsilyl)methyl)benzoate (**20a**; 337 mg, 1.0 mmol, 1.0 equiv) was metalated according to **TP 2** using $TMP_2Mg{\cdot}2LiCl$ (**59**; 2.5 mL, 1.5 mmol, 1.5 equiv, 0.6 M in THF). The reaction mixture was cooled to -20 °C and $ZnCl_2$ (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. Then, $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), SPhos (16.4 mg, 0.04 mmol) and 4-bromobenzonitrile (146 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 20:1) to give **22c** as a white solid (308 mg, 88%).

M.p.: 101.8 – 102.4 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.66 (d, *J* = 8.0 Hz, 2H), 7.45 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.09 - 7.08 (m, 2H), 1.62 (s, 1H), 1.29 (s, 9H), 0.07 (s, 18H).

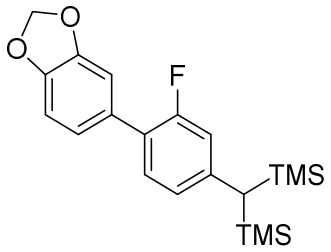
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 167.3, 147.1, 144.0, 135.5, 131.7, 131.6, 131.3, 130.4, 130.1, 129.5, 119.1, 110.3, 81.4, 29.6, 27.7, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2899, 2229, 1712, 1608, 1481, 1412, 1394, 1364, 1294, 1282, 1250, 1244, 1206, 1171, 1160, 1137, 1108, 1103, 1027, 937, 915, 861, 838, 792, 783, 772, 747, 736, 688, 668.

MS (70 eV, EI): *m/z* (%) = 437 (1, M^+), 382 (28), 381 (93), 366 (27), 365 (16), 293 (20), 292 (11), 291 (42), 263 (11), 248 (11), 217 (11), 75 (13), 73 (100), 57 (32).

HRMS (EI) for **$C_{25}H_{35}NO_2Si_2$** (437.2206): found: 437.2197 (M^+).

Synthesis of ((4-(benzo[*d*][1,3]dioxol-5-yl)-3-fluorophenyl)methylene)*bis*(trimethylsilane) (22e)



((3-Fluorophenyl)methylene)*bis*(trimethylsilane) (**20b**; 254 mg, 1.0 mmol, 1.0 equiv) was metalated according to **TP 3** using TMPLi (3.17 mL, 2.0 mmol, 2.0 equiv, 0.63 M in THF). Then, $ZnCl_2$ (2.1 mL, 2.1 mmol, 2.1 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), SPhos (16.4 mg, 0.04 mmol) and 5-bromobenzo[*d*][1,3]dioxole (161 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x

30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **22e** as a white solid (285 mg, 95%).

M.p.: 65.7 – 66.1 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm =7.20 (t, *J* = 8.3 Hz, 1H), 6.97 - 7.08 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.65 - 6.78 (m, 2H), 5.99 (s, 2H), 1.53 (s, 1H), 0.06 (s, 18H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 160.7 (d, *J* = 247 Hz), 147.6, 146.7, 145.0, 144.9, 130.0 (d, *J* = 1 Hz), 129.7 (d, *J* = 4 Hz), 124.8, 123.4 (d, *J* = 14 Hz), 122.3 (d, *J* = 3 Hz), 109.4 (d, *J* = 4 Hz), 108.2, 101.0, 29.7, 0.1.

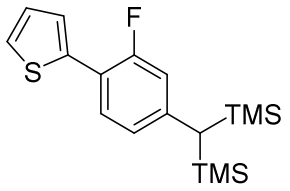
^{19}F-NMR (282 MHz, $CDCl_3$): δ / ppm = -119.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951, 2923, 2898, 2865, 2850, 2778, 1619, 1556, 1501, 1478, 1413, 1335, 1307, 1244, 1226, 1118, 1100, 1037, 956, 880, 863, 857, 836, 829, 814, 780, 769, 734, 685.

MS (70 eV, EI): *m/z* (%) = 375 (23), 374 (77, M^+), 359 (21), 287 (14), 286 (63), 283 (11), 282 (44), 273 (14), 268 (13), 267 (56), 165 (14), 73 (100).

HRMS (EI) for **$C_{20}H_{27}FO_2Si_2$** (374.1534): found: 374.1517 (M^+).

Synthesis of ((3-fluoro-4-(thiophen-2-yl)phenyl)methylene)*bis*(trimethylsilane) (22f)



((3-Fluorophenyl)methylene)*bis*(trimethylsilane) (**20b**; 254 mg, 1.0 mmol. 1.0 equiv) was metalated according to **TP 3** using TMPLi (3.17 mL, 2.0 mmol, 2.0 equiv, 0.63 M in THF). Then, $ZnCl_2$ (2.1 mL, 2.1 mmol, 2.1 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and 2-iodothiophene (168 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **22f** as colorless oil (258 mg, 96%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.50 – 7.46 (m, 1H), 7.42 (d, *J* = 4.98 Hz, 1H), 7.30 (d, *J* = 5.25 Hz, 1H), 7.11 – 7.08 (m, 1H), 6.75 (s, 1H), 6.71 (d, *J* = 3.59 Hz, 1H), 1.54 (s, 1H), 0.06 (s, 18H).

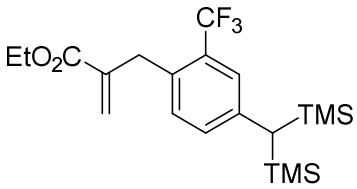
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 158.8 (d, *J* = 249 Hz), 145.3 (d, *J* = 8 Hz), 137.7 (d, *J* = 4 Hz), 128.1 (2C), 127.5, 125.1 (d, *J* = 6 Hz), 124.6 (d, *J* = 4 Hz), 117.3, 117.1, 29.9, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951, 2895, 2834, 1617, 1555, 1489, 1433, 1422, 1354, 1292, 1281, 1248, 1234, 1209, 1169, 1150, 1136, 1124, 1116, 1080, 1033, 969, 940, 877, 864, 824, 779, 771, 748, 736, 720, 687, 676.

MS (70 eV, EI): *m/z* (%) = 337 (19), 336 (66, M^+), 321 (24), 249 (17), 248 (76), 245 (20), 244 (75), 243 (18), 230 (18), 229 (93), 216 (22), 201 (14), 73 (100).

HRMS (EI) for **$C_{17}H_{25}FSSi_2$** (336.1200): found: 316.1194 (M^+).

Synthesis of ethyl 2-(4-(*bis*(trimethylsilyl)methyl)-2-(trifluoromethyl)benzyl)acrylate (22g)



((3-(Trifluoromethyl)phenyl)methylene)*bis*(trimethylsilane) (**20c**; 304 mg, 1.0 mmol, 1.0 equiv) was metalated according to **TP 4** using *s*BuLi (1.03 mL, 1.5 mmol, 1.5 equiv, 1.45 M in hexane) and TMEDA (0.22 mL, 174 mg, 1.5 mmol, 1.5 equiv). Then, $ZnCl_2$ (1.5 mL, 1.5 mmol, 1.0 M in THF) was added. The mixture was kept at this temperature for 15 min before a 1.0 M solution of CuCN·2LiCl (1.5 mL, 1.5 mmol) and ethyl 2-(bromomethyl)acrylate (290 mg, 1.5 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (5 mL), extracted with EtOAc (3 x 15 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **22g** as a colorless oil (356 mg, 57%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.21 (d, *J* = 1.7 Hz, 1H), 6.99 - 7.11 (m, 2H), 6.27 (d, *J* = 1.1 Hz, 1H), 5.16 (d, *J* = 1.4 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.76 (s, 2H), 1.55 (s, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 0.02 (s, 18H).

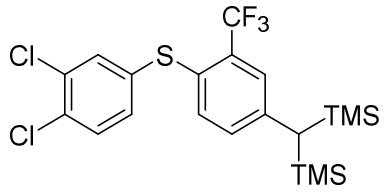
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.8, 142.2, 139.9, 131.7, 131.2, 130.0, 128.5 (q, *J* = 29 Hz), 126.4, 125.8, 124.5 (q, *J* = 274 Hz), 60.7, 33.9, 29.4, 14.0, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2900, 2833, 1718, 1635, 1612, 1499, 1421, 1314, 1301, 1262, 1250, 1214, 1189, 1151, 1117, 1053, 1032, 902, 856, 835, 828, 768, 688, 672.

MS (70 eV, EI): *m/z* (%) = 416 (23, M^+), 328 (14), 173 (16), 155 (25), 77 (39), 73 (100), 61 (12), 45 (11), 43 (74).

HRMS (EI) for $\mathbf{C_{20}H_{31}F_3O_2Si_2}$ (416.1815): found: 416.1806 (M^+).

Synthesis of ((4-((3,4-dichlorophenyl)thio)-3-(trifluoromethyl)phenyl)methylene)*bis*-(trimethylsilane) (22h)



((3-(Trifluoromethyl)phenyl)methylene)bis(trimethylsilane) (**20c**; 304 mg, 1.0 mmol) was metalated according to **TP 4** using *s*BuLi (1.03 mL, 1.5 mmol, 1.5 equiv, 1.45 M in hexane) and TMEDA (0.22 mL, 174 mg, 1.5 mmol, 1.5 equiv). Then, $MgCl_2$ (3.0 mL, 1.5 mmol, 0.5 M in THF) was added. The mixture was kept at this temperature for 15 min, was then allowed to warm up to 25 °C. The solvent was evaporated under vacuum (10^{-2} mbar) and THF (2 mL) was then added slowly under vigorous stirring. The mixture was cooled to -20 °C and *S*-(3,4-dichlorophenyl) benzenesulfonothioate (479 mg, 1.5 mmol, 1.5 equiv) dissolved in THF (5 mL) was added dropwise. The reaction mixture was allowed to warm up to 25 °C, quenched with sat. aq NH_4Cl solution (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **22h** as white crystals (287 mg, 60%).

M.p.: 56.4 – 59.5 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.29 – 7.25 (m, 2H), 7.21 (s, 1H), 7.13 (d, J = 2.2 Hz, 1H), 7.03 (dd, J = 8.2, 1.8 Hz, 1H), 6.94 (dd, J = 8.3, 2.2 Hz, 1H), 1.59 (s, 1H), 0.00 (s, 18H).

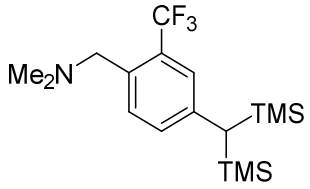
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 145.8, 137.5, 136.4, 133.1, 132.5, 131.9 (q, J = 30 Hz), 130.7, 130.6, 130.6, 128.4, 127.1, 125.7, 123.6 (q, J = 274 Hz), 30.4, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2952, 2896, 2837, 1589, 1568, 1546, 1474, 1460, 1415, 1371, 1364, 1311, 1249, 1204, 1174, 1159, 1155, 1128, 1107, 1091, 1031, 1026, 963, 952, 908, 901, 853, 826, 816, 804, 777, 768, 747, 742, 727, 709, 699, 689, 674, 668.

MS (70 eV, EI): *m/z* (%) = 482 (10), 480 (13, M^+), 394 (11), 392 (15), 389 (12), 387 (15), 355 (15), 353 (37), 275 (10), 77 (16), 73 (100), 45 (12).

HRMS (EI) for $\mathbf{C_{20}H_{25}Cl_2F_3SSi_2}$ (480.0545): found: 480.0542 (M^+).

Synthesis of 1-(4-(*bis*(trimethylsilyl)methyl)-2-(trifluoromethyl)phenyl)-*N,N*-dimethyl-methanamine (22i)



((3-(Trifluoromethyl)phenyl)methylene)*bis*(trimethylsilane) (**20c**; 304 mg, 1.0 mmol) was metalated according to **TP 4** using *s*BuLi (1.03 mL, 1.5 mmol, 1.5 equiv, 1.45 M in hexane) and TMEDA (0.22 mL, 174 mg, 1.5 mmol, 1.5 equiv). Then, $MgCl_2$ (3.0 mL, 1.5 mmol, 0.5 M in THF) was added. The mixture was kept at this temperature for 15 min, was then allowed to warm up to 25 °C. The solvent was evaporated under vacuum (10^{-2} mbar) and THF (2 mL) was then added slowly under vigorous stirring. Another dry and argon flushed Schlenk-flask was charged with *N,N,N',N'*-tetramethylmethanediamine (0.21 mL, 1.5 mmol 1.5 equiv) and anhydrous CH_2Cl_2 to obtain a 1 M solution. After cooling to 0 °C, neat trifluoroacetic anhydride (0.21 mL, 1.5 mmol, 1.5 equiv) was added dropwise and the solution was allowed to warm up to 25 °C and stirring was continued for 5 min. The so prepared solution of methylene(dimethyl)iminium trifluoroacetate (**29**) was then cannulated dropwise to the Grignard reagent at 0 °C. The reaction mixture was allowed to warm up to 25 °C, quenched with sat. aq $NaHCO_3$ solution (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 9:1) to give **22i** as colorless oil (224 mg, 62 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.51 (d, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 1.9 Hz, 1H), 7.08 (d, *J* = 8.3, 1H), 3.53 (s, 2H), 2.27 (s, 6H), 1.55 (s, 1H), 0.02 (s, 18H).

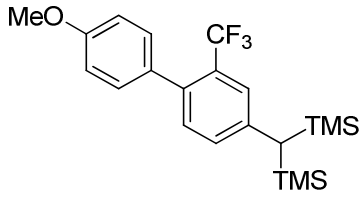
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 142.4, 131.8, 130.6, 128.7, 128.1 (q, *J* = 29 Hz), 125.4, 124.6 (q, *J* = 274 Hz), 59.2, 45.5, 29.4, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2950, 2899, 2860, 2819, 2772, 1495, 1458, 1442, 1432, 1420, 1369, 1313, 1264, 1249, 1214, 1191, 1177, 1156, 1147, 1117, 1097, 1056, 1031, 898, 863, 835, 826, 786, 771, 766, 741, 735, 688, 677, 671.

MS (70 eV, EI): *m/z* (%) = 362 (21), 361 (68, M^+), 346 (21), 273 (10), 229 (48), 225 (15), 129 (22), 128 (18), 117 (20), 115 (19), 102 (14), 77 (35), 73 (92), 58 (100), 45 (12), 43 (12).

HRMS (EI) for $\mathbf{C_{17}H_{30}F_3NSi_2}$ (361.1869): found: 361.1855 (M^+).

Synthesis of ((4'-methoxy-2-(trifluoromethyl)biphenyl-4-yl)methylene)*bis*(trimethyl-silane) (22j)



((3-(Trifluoromethyl)phenyl)methylene)*bis*(trimethylsilane) (**20c**; 304 mg, 1.0 mmol) was metalated according to **TP 4** using sBuLi (1.03 mL, 1.5 mmol, 1.5 equiv, 1.45 M in hexane) and TMEDA (0.22 mL, 174 mg, 1.5 mmol, 1.5 equiv). Then, $ZnCl_2$ (1.5 mL, 1.5 mmol, 1.0 M in THF) was added. The mixture was kept at this temperature for 15 min, was then allowed to warm up to 25 °C. The solvent was evaporated under vacuum (10^{-2} mbar) and THF (2 mL) was then added slowly under vigorous stirring. $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), SPhos (16.4 mg, 0.04 mmol) and 4-bromoanisole (150 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **22j** as yellow oil (253 mg, 77%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm =7.21 - 7.31 (m, 3H), 7.04 - 7.17 (m, 2H), 6.88 - 6.97 (m, 2H), 3.85 (s, 3H), 1.62 (s, 1H), 0.07 (s, 18H).

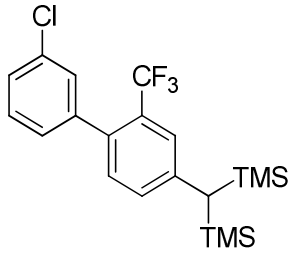
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 158.9, 142.7, 135.9, 132.5, 132.0, 131.2, 130.2, 127.9 (q, J = 29 Hz), 125.9, 124.4 (q, J = 274 Hz), 113.1, 55.2, 29.5, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2899, 2836, 1606, 1576, 1509, 1488, 1443, 1418, 1311, 1245, 1241, 1197, 1166, 1150, 1122, 1107, 1069, 1035, 897, 862, 826, 808, 799, 768, 762, 690, 686, 672.

MS (70 eV, EI): *m/z* (%) = 410 (39, M^+), 396 (18), 395 (56), 380 (10), 379 (40), 323 (11), 322 (48), 303 (17), 289 (12), 288 (10), 287 (17), 245 (13), 227 (15), 226 (26), 213 (15), 209 (10), 191 (32), 179 (41), 77 (21), 73 (100), 61 (10), 59 (10), 45 (10), 43 (60).

HRMS (EI) for **$C_{21}H_{29}F_3OSi_2$** (410.1709): found: 410.1700 (M^+).

Synthesis of ((3'-chloro-2-(trifluoromethyl)biphenyl-4-yl)methylene)bis(trimethylsilane) (22k)



((3-(Trifluoromethyl)phenyl)methylene)*bis*(trimethylsilane) (**20c**; 304 mg, 1.0 mmol) was metalated according to **TP 4** using *s*BuLi (1.03 mL, 1.5 mmol, 1.5 equiv, 1.45 M in hexane) and TMEDA (0.22 mL, 174 mg, 1.5 mmol, 1.5 equiv). Then, $ZnCl_2$ (1.5 mL, 1.5 mmol, 1.0 M in THF) was added. The mixture was kept at this temperature for 15 min, was then allowed to warm up to 25 °C. The solvent was evaporated under vacuum (10^{-2} mbar) and THF (2 mL) was then added slowly under vigorous stirring. $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and 1-chloro-3-iodobenzene (191 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. The reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **22k** as colorless oil (258 mg, 64%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm =7.27 - 7.38 (m, 4H), 7.20 - 7.25 (m, 1H), 7.12 (s, 2H), 1.64 (s, 1H), 0.07 (s, 18H).

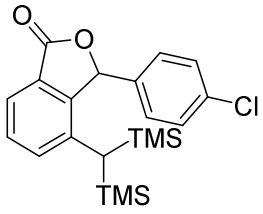
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 143.8, 141.8, 134.6, 134.5, 133.5, 131.5, 131.3, 129.3, 128.9, 127.8 (q, J = 30 Hz), 127.4, 126.0, 124.1 (q, J = 274 Hz), 29.8, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2899, 2839, 1608, 1596, 1561, 1537, 1502, 1470, 1420, 1313, 1250, 1170, 1121, 1068, 1034, 1023, 902, 857, 826, 786, 766, 701, 681, 669.

MS (70 eV, EI): *m/z* (%) = 414 (3, M^+), 326 (20), 322 (12), 191 (26), 77 (10), 73 (61), 61 (15), 45 (13), 42 (100).

HRMS (EI) for **$C_{20}H_{26}ClF_3Si_2$** (414.1214): found: 414.1204 (M^+).

Synthesis of 4-(*bis*(trimethylsilyl)methyl)-3-(4-chlorophenyl)*iso*benzofuran-1(3H)-one (64a)



According to **TP 1**, the cross-coupling of **66a** (323 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry toluene (2.1 mL) with $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 4.17 mL, 2.5 mmol, 2.5 equiv, 0.6 M in THF) was completed within 12 h at 80 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **64a** as a yellow oil (129 mg, 32%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.68 (d, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 8.3 Hz, 2H), 6.15 (s, 1H), 1.37 (s, 1H), 0.01 (s, 9H), -0.30 (s, 9H).

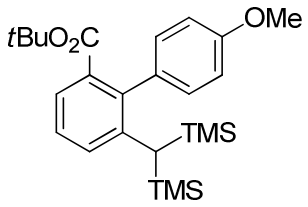
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 170.8, 146.2, 140.0, 135.5, 134.6, 134.0, 129.7, 129.7, 129.2, 125.9, 120.7, 82.5, 24.4, 0.3, -0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2899, 2856, 1764, 1607, 1587, 1493, 1475, 1412, 1335, 1286, 1263, 1250, 1196, 1159, 1106, 1090, 1069, 1052, 1024, 1016, 993, 924, 857, 837, 826, 773, 759, 751, 730, 683, 681, 675, 655.

MS (70 eV, EI): *m/z* (%) = 402 (11, M^+), 387 (13), 241 (12), 240 (24), 239 (28), 235 (14), 214 (10), 212 (34), 205 (54), 73 (100), 57 (12), 45 (10).

HRMS (EI) for **$C_{21}H_{27}ClO_2Si_2$** (402.1238): found: 402.1237 (M^+).

Synthesis of *tert*-butyl 6-(*bis*(trimethylsilyl)methyl)-4'-methoxy-[1,1'-biphenyl]-2-carboxylate (64a)



According to **TP 1**, the cross-coupling of **66b** (363 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 12 h at 80 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 97:3) to give **64a** as colorless oil (199 mg, 45%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm =7.35 (dd, J = 7.5, 1.7 Hz, 1 H), 7.25 - 7.20 (m, 1 H), 7.15 - 7.11 (m, 1 H), 7.07 - 6.99 (m, 2 H), 6.94 - 6.88 (m, 2 H), 3.88 - 3.82 (m, 3 H), 1.26 - 1.12 (m, 9 H) 1.73 (s, 1 H), 0.14 - 0.11 (m, 18 H).

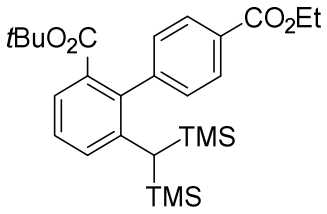
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 169.3, 158.6, 143.1, 138.8, 135.7, 133.0, 131.4, 130.4, 126.6, 123.8, 113.2, 81.0, 55.4, 27.8, 24.2, 0.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2897, 2836, 1707, 1611, 1514, 1438, 1391, 1367, 1299, 1242, 1175, 1126, 1105, 1087, 1038, 1019, 1000, 943, 857, 838, 827, 803, 790, 761, 746, 686, 662.

MS (70 eV, EI): *m/z* (%) = 442 (9, M^+), 386 (18), 371 (11), 297 (20), 296 (58), 295 (12), 268 (19), 253 (19), 224 (11), 223 (31), 222 (13), 73 (100), 57 (18).

HRMS (EI) for **$C_{25}H_{38}O_3Si_2$** (442.2359): found: 442.2356 (M^+).

Synthesis of 2-(*tert*-butyl) 4'-ethyl 6-(*bis*(trimethylsilyl)methyl)-[1,1'-biphenyl]-2,4'-dicarboxylate (64c)



According to **TP 1**, the cross-coupling of **66c** (405 mg, 1.0 mmol, 1.0 equiv) catalyzed by $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and SPhos (16.4 mg, 0.04 mmol) in dry THF (3.5 mL) with $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was completed within 12 h at 80 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 97:3) to give **64c** as colorless oil (227 mg, 47%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.06 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.6 Hz, 1H), 7.31 – 7.16 (m, 4H), 4.40 (q, J = 7.1 Hz, 2H), 2.03 (s, 1H), 1.42 (t, J = 7.2 Hz, 3H), 1.16 (s, 9H), -0.05 (s, 18H).

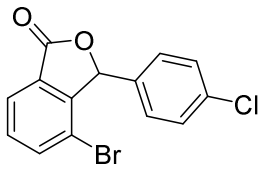
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 168.3, 166.6, 145.8, 142.4, 138.2, 134.4, 130.7, 130.2, 128.9, 128.8, 127.1, 124.3, 81.1, 61.0, 27.6, 24.4, 14.3, 0.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2899, 2873, 1716, 1608, 1585, 1477, 1454, 1392, 1367, 1301, 1269, 1257, 1248, 1230, 1174, 1127, 1109, 1099, 1089, 1035, 1025, 1004, 939, 837, 829, 826, 790, 777, 765, 757, 735, 723, 709, 687, 677, 668, 666, 659.

MS (70 eV, EI): *m/z* (%) = 484 (1, M^+), 430 (10), 429 (27), 428 (74), 427 (14), 413 (11), 399 (15), 311 (13), 310 (22), 309 (45), 267 (11), 266 (26), 265 (57), 237 (20), 193 (24), 192 (16), 165 (11), 73 (100), 57 (24).

HRMS (EI) for $\mathbf{C_{27}H_{40}O_4Si_2}$ (484.2465): found: 484.2463 (M^+).

Synthesis of 4-bromo-3-(4-chlorophenyl)*iso*benzofuran-1(3H)-one (66a)



In a dry argon flushed *Schlenk*-flask, *tert*-butyl 3-bromobenzoate (**18a**; 257 mg, 1.0 mmol, 1.0 equiv) was dissolved in THF (1.0 mL) and cooled to 0 °C. Then, TMPMgCl·LiCl (**63**; 1.25 mL, 1.5 mmol, 1.5 equiv, 1.2 M in THF) was added dropwise and the reaction mixture was stirred at this temperature for 45 min. The mixture was then cooled to -20 °C and 4-chlorobenzaldehyde (280 mg, 2.0 mmol, 2.0 equiv) dissolved in THF (3 mL) was added dropwise. The reaction mixture was allowed to warm up to 25 °C, quenched with sat. aq NH_4Cl solution (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 9:1) to give **66a** as a white solid (241 mg, 75%).

M.p.: 114.5 – 116.6 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.96 (d, *J* = 7.5 Hz, 1H), 7.81 (d, *J* = 7.7 Hz 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.29 (s, 1H).

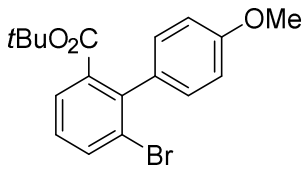
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 168.8, 147.8, 138.0, 135.7, 132.6, 131.5, 129.9, 129.1, 128.5, 124.7, 117.8, 82.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1771, 1490, 1456, 1415, 1331, 1290, 1246, 1194, 1123, 1091, 1062, 1042, 1015, 978, 972, 848, 836, 823, 810, 758, 747, 721.

MS (70 eV, EI): *m/z* (%) = 326 (23), 324 (91), 322 (72, M^+), 289 (99), 287 (100), 245 (41), 243 (41), 213 (20), 211 (20), 201 (24), 199 (74), 185 (39), 184 (25), 183 (38), 164 (38), 163 (67), 139 (86), 111 (23), 75 (70).

HRMS (EI) for $\mathbf{C_{14}H_8BrClO_2}$ (321.9396): found: 321.9389 (M^+).

Synthesis of *tert*-Butyl 6-bromo-4'-methoxy-[1,1'-biphenyl]-2-carboxylate (66b)



In a dry argon flushed *Schlenk*-flask, *tert*-butyl 3-bromobenzoate (**18a**; 257 mg, 1.0 mmol, 1.0 equiv) was dissolved in THF (1.0 mL) and cooled to 0 °C. Then, TMPMgCl·LiCl (**63**; 1.25 mL, 1.5 mmol, 1.5 equiv, 1.2 M in THF) was added dropwise and the reaction mixture was stirred at this temperature for 45 min. Then, $ZnCl_2$ (1.5 mL, 1.5 mmol, 1.5 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and 4-iodoanisole (187 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (5 mL), extracted with EtOAc (3 x 15 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **66b** as a colorless solid (209 mg, 72%).

M.p.: 85.3 – 87.0 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.74 (d, J = 7.74 Hz, 1H), 7.64 (d, J = 7.46 Hz, 1H), 7.23 – 7.20 (m, 1H), 7.15 (d, J = 8.57 Hz, 2H), 6.95 (d, J = 8.57 Hz, 2H), 3.85 (s, 3H), 1.20 (s, 9H).

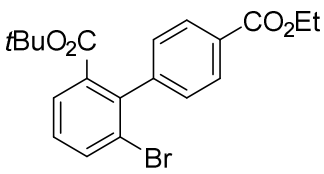
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 167.2, 159.1, 140.9, 136.5, 134.7, 132.6, 130.5, 128.4, 127.8, 125.3, 113.2, 81.7, 55.3, 27.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3011, 2997, 2977, 2956, 2935, 2911, 2837, 1699, 1612, 1587, 1551, 1514, 1465, 1431, 1370, 1366, 1295, 1242, 1184, 1181, 1169, 1141, 1112, 1079, 1033, 1020, 999, 845, 832, 816, 810, 804, 775, 752, 746, 727, 714, 708.

MS (70 eV, EI): *m/z* (%) = 364 (17), 362 (19, M^+), 309 (15), 308 (99), 307 (18), 306 (100), 291 (14), 289 (12), 210 (12), 167 (10), 139 (37), 57 (17), 41 (13).

HRMS (EI) for **$C_{18}H_{19}BrO_3$** (362.0518): found: 362.0506 (M^+).

Synthesis of 2-(*tert*-butyl) 4'-ethyl 6-bromo-[1,1'-biphenyl]-2,4'-dicarboxylate (66c)



In a dry argon flushed *Schlenk*-flask, *tert*-butyl 3-bromobenzoate (**18a**; 257 mg, 1.0 mmol, 1.0 equiv) was dissolved in THF (1.0 mL) and cooled to 0 °C. Then, TMPMgCl·LiCl (**63**; 1.25 mL, 1.5 mmol, 1.5 equiv, 1.2 M in THF) was added dropwise and the reaction mixture was stirred at this temperature for 45 min. Then, $ZnCl_2$ (1.5 mL, 1.5 mmol, 1.5 equiv, 1.0 M in THF) was added and the resulting solution was stirred for 15 min. $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and ethyl 4-iodobenzoate (221 mg, 0.8 mmol, 0.8 equiv) were added and the resulting solution was stirred for 12 h at 50 °C. Then, the reaction mixture was quenched with sat. aq NH_4Cl solution (5 mL), extracted with EtOAc (3 x 15 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **66c** as a colorless oil (198 mg, 61%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.09 (d, J = 8.22 Hz, 2H), 7.79 – 7.73 (m, 2H), 7.32 – 7.29 (m, 3H), 4.40 (q, J = 7.17 Hz, 2H), 1.40 (t, J = 7.06 Hz, 3H), 1.16 (s, 9H).

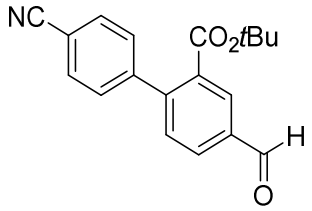
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.4, 166.4, 145.0, 140.6, 135.4, 135.2, 129.6, 129.4, 129.1, 129.0, 128.4, 124.3, 82.1, 61.0, 27.5, 14.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978, 2934, 2906, 2872, 1708, 1610, 1556, 1476, 1456, 1434, 1402, 1392, 1367, 1268, 1195, 1171, 1141, 1109, 1097, 1081, 1025, 1004, 881, 848, 812, 777, 766, 753, 731, 705, 680, 677, 666, 657, 653.

MS (70 eV, EI): *m/z* (%) = 404 (2, M^+), 351 (22), 350 (99), 349 (24), 348 (96), 322 (57), 321 (12), 320 (58), 306 (19), 305 (99), 304 (29), 303 (100), 261 (15), 259 (16), 232 (11), 230 (11), 196 (22), 180 (15), 168 (24), 152 (36), 151 (45), 150 (33), 139 (15), 57 (51), 43 (10), 41 (26).

HRMS (EI) for **$C_{20}H_{21}BrO_4$** (404.0623): found: 404.0615 (M^+).

Synthesis of *tert*-butyl 4'-cyano-4-formylbiphenyl-2-carboxylate (23b)



According to **TP 5**, the oxidation of **22c** (438 mg, 1.0 mmol, 1.0 equiv) with CAN (2.74 g, 5.0 mmol, 5.0 equiv) was completed within 30 min at 0 °C. CF_3COOH (5 mL) was added and the reaction mixture was stirred for further 15 min. Then, the reaction mixture was quenched with H_2O (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 9:1) to give **23b** as yellow crystals (234 mg, 76%).

M.p.: 97.3 – 99.2 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.11 (s, 1H), 8.34 (d, *J* = 1.7 Hz, 1H), 8.04 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.73 (d, *J* = 7.7 Hz, 2H), 7.39 - 7.51 (m, 3H), 1.31 (s, 9H).

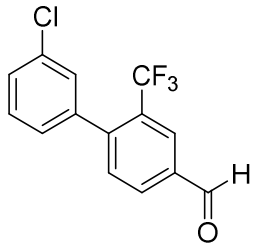
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 190.8, 165.9, 145.8, 145.4, 140.5, 135.9, 133.5, 131.9, 131.2, 131.0, 129.1, 118.5, 111.8, 82.7, 27.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3007, 2976, 2225, 1700, 1603, 1472, 1455, 1419, 1366, 1313, 1306, 1249, 1198, 1159, 1140, 1112, 1006, 933, 854, 844, 832, 827, 796, 763, 703, 653.

MS (70 eV, EI): *m/z* (%) = 307 (1, M^+), 252 (57), 251 (100), 250 (33), 234 (39), 177 (11), 57 (35), 56 (11).

HRMS (EI) for **$C_{19}H_{17}NO_3$** (307.1208): found: 307.1297 (M^+).

Synthesis of 3'-chloro-2-(trifluoromethyl)biphenyl-4-carbaldehyde (23c)



According to **TP 5**, the oxidation of **22k** (415 mg, 1.0 mmol, 1.0 equiv) with CAN (2.74 g, 5.0 mmol, 5.0 equiv) was completed within 30 min at 0 °C. CF_3COOH (5 mL) was added and the reaction mixture was stirred for further 15 min. Then, the reaction mixture was quenched with H_2O (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **23c** as yellow oil (262 mg, 92%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.12 (s, 1H), 8.27 (d, *J* = 1.7 Hz, 1H), 8.09 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.36 - 7.46 (m, 2H), 7.34 (d, *J* = 1.9 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 190.3, 145.6, 140.1, 135.6, 134.0, 132.9, 131.9, 129.7 (q, *J* = 31 Hz), 129.3, 128.6, 128.6, 127.7 (q, *J* = 5 Hz), 126.8 (q, *J* = 2 Hz), 123.3 (q, *J* = 274 Hz).

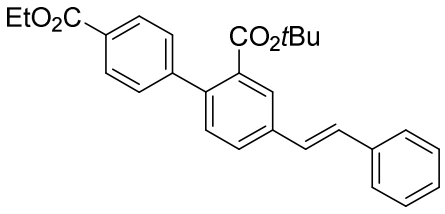
^{19}F-NMR (282 MHz, $CDCl_3$): δ/ppm = -57.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3068, 2838, 2735, 1703, 1612, 1596, 1562, 1469, 1429, 1410, 1374, 1315, 1281, 1246, 1173, 1122, 1100, 1081, 1065, 1024, 1006, 999, 917, 905, 891, 841, 784, 769, 759, 752, 701, 691, 669, 660.

MS (70 eV, EI): *m/z* (%) = 286 (27), 285 (37), 284 (100, M^+), 283 (76), 235 (14), 220 (18), 219 (12), 201 (11).

HRMS (EI) for **$C_{14}H_8ClF_3O$** (284.0216): found: 284.0200 (M^+).

Synthesis of (*E*)-2-*tert*-butyl 4'-ethyl 4-styrylbiphenyl-2,4'-dicarboxylate (67a)



According to **TP 6**, the biphenyl **22a** (229 mg, 1.0 mmol, 1.0 equiv) reacted with benzaldehyde (127 mg, 0.12 mL, 1.2 mmol, 1.2 equiv) catalyzed by TBAF (0.1 mL, 0.1 mmol, 0.1 equiv, 1.0 M in THF) at -20 °C within 15 min. Then, the reaction mixture was quenched with sat. aq. NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 19:1) to give **67a** as white crystals (326 mg, 76%, E:Z > 99:1).

M.p.: 111.3 – 113.2 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.11 (d, *J* = 8.3 Hz, 2H), 7.97 (d, *J* = 1.7 Hz, 1H), 7.64 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.51 - 7.59 (m, 2H), 7.34 - 7.45 (m, 4H), 7.27 - 7.34 (m, 2H), 7.18 (d, *J* = 8.6 Hz, 2H), 4.41 (q, *J* = 7.0 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H), 1.28 (s, 9H).

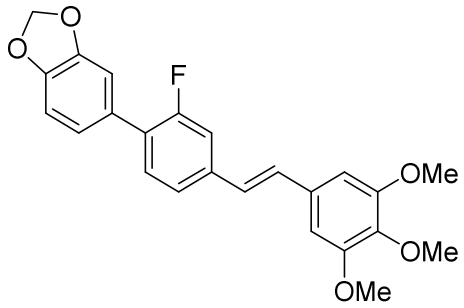
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 167.5, 166.5, 146.3, 140.0, 137.0, 136.9, 133.1, 130.8, 130.2, 129.3, 129.1, 128.7, 128.6, 128.6, 128.0, 127.9, 127.1, 126.7, 81.7, 61.0, 27.6, 4.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2983, 2927, 2922, 2910, 2851, 1717, 1711, 1699, 1674, 1671, 1606, 1595, 1479, 1452, 1446, 1412, 1393, 1369, 1306, 1293, 1279, 1270, 1253, 1214, 1196, 1174, 1162, 1152, 1144, 1128, 1117, 1106, 1102, 1087, 1045, 1026, 1020, 1004, 990, 982, 969, 961, 946, 937, 928, 916, 907, 878, 870, 861, 853, 847, 829, 825, 794, 776, 757, 751, 743, 735, 724, 708, 706, 694, 688, 680, 672, 667, 664, 661, 653.

MS (70 eV, EI): *m/z* (%) = 428 (38, M^+), 373 (26), 372 (100), 327 (16), 253 (8), 252 (9).

HRMS (EI) for **$C_{28}H_{28}O_4$** (428.1988): found: 428.1976 (M^+).

Synthesis of (*E*)-5-(2-fluoro-4-(3,4,5-trimethoxystyryl)phenyl)benzo[*d*][1,3]dioxole (67b)



According to **TP 6**, the biphenyl **22e** (375 mg, 1.0 mmol, 1.0 equiv) reacted with 3,4,5-trimethoxybenzaldehyde (235 mg, 1.2 mmol, 1.2 equiv) catalyzed by TBAF (0.1 mL, 0.1 mmol, 0.1 equiv, 1.0 M in THF) at -20 °C within 15 min. Then, the reaction mixture was quenched with sat. aq. NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 8:2) to give **67b** as white crystals (253 mg, 62%, E:Z > 99:1).

M.p.: 98.5 – 101.3 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.41 – 7.29 (m, 3H), 7.09 – 7.00 (m, 4H), 6.91 – 6.88 (m, 1H), 6.75 (s, 2H), 6.01 (s, 2H), 3.93 (s, 6H), 3.88 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 159.8 (d, J = 247 Hz), 153.4, 147.7, 147.2, 138.2, 138.2 (d, J = 8 Hz), 132.6, 130.6 (d, J = 4 Hz), 129.8, 129.4, 129.3, 127.6 (d, J = 14 Hz), 122.6 (d, J = 3 Hz), 122.5 (d, J = 3 Hz), 113.4 (d, J = 24 Hz), 109.4 (d, J = 4 Hz), 108.4, 103.7, 101.2, 61.0, 56.1.

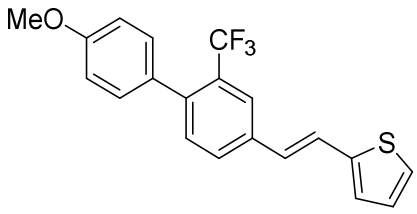
^{19}F-NMR (282 MHz, $CDCl_3$): δ/ppm = -118.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2997, 2936, 2881, 2834, 1583, 1505, 1501, 1481, 1463, 1456, 1436, 1432, 1417, 1339, 1328, 1225, 1185, 1151, 1123, 1102, 1035, 1005, 1003, 979, 976, 952, 932, 929, 887, 882, 878, 870, 867, 861, 852, 841, 838, 835, 804, 775, 730, 728, 658, 656.

MS (70 eV, EI): *m/z* (%) = 409 (28), 408 (100, M^+), 394 (17), 393 (55), 333 (6), 249 (6), 221 (5), 220 (8), 196 (7), 181 (6), 140 (6), 139 (9), 110 (5), 43 (10).

HRMS (EI) for **$C_{24}H_{21}FO_5$** (408.1373): found: 408.1370 (M^+).

Synthesis of (*E*)-2-(2-(4'-Methoxy-2-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)vinyl)thiophene (67c)



According to **TP 6**, the biphenyl **22j** (411 mg, 1.0 mmol, 1.0 equiv) reacted with thiophene-2-carbaldehyde (135 mg, 0.11 mL, 1.2 mmol, 1.2 equiv) catalyzed by TBAF (0.1 mL, 0.1 mmol, 0.1 equiv, 1.0 M in THF) at -20 °C within 15 min. Then, the reaction mixture was quenched with sat. aq. NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 8:2) to give **67c** as white crystals (306 mg, 85%, E:Z > 99:1).

M.p.: 127.4 – 129.1 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.80 (s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.35 – 7.24 (m, 5H), 7.13 (d, J = 3.3 Hz, 1H), 7.05 – 6.99 (m, 2H), 6.94 (d, J = 8.6 Hz, 2H), 3.86 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 159.2, 142.2, 139.9 (q, J = 2 Hz), 136.1, 132.8, 131.9, 130.8, 130.1 (q, J = 1 Hz), 128.9 (q, J = 29 Hz), 128.5, 127.7, 126.9, 126.4, 125.0, 124.1 (q, J = 274 Hz), 123.3, 113.2, 55.2.

^{19}F-NMR (282 MHz, $CDCl_3$): δ/ppm = -57.3.

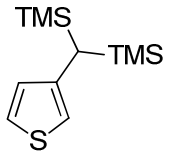
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3010, 2964, 2963, 2944, 2910, 2842, 1610, 1514, 1489, 1487, 1471, 1464, 1458, 1456, 1445, 1431, 1409, 1317, 1299, 1292, 1290, 1282, 1268, 1249, 1248, 1225, 1177, 1168, 1138, 1123, 1108, 1078, 1065, 1044, 1034, 1018, 999, 968, 955, 939, 929, 921, 910, 907, 901, 887, 873, 870, 866, 864, 853, 835, 820, 801, 791, 787, 782, 775, 774, 767, 763, 759, 756, 754, 746, 738, 733, 725, 716, 704, 688, 685, 682, 680, 675, 669, 666, 655, 651.

MS (70 eV, EI): *m/z* (%) = 362 (6), 361 (19), 360 (100, M^+), 345 (9), 276 (4), 233 (3), 180 (6).

HRMS (EI) for **$C_{20}H_{15}F_3OS$** (360.0796): found: 360.0800 (M^+).

2.5. Preparation of the BTSM-Substituted Heterocycles

Synthesis of (thiophen-3-ylmethylene)*bis*(trimethylsilane) (21a)



In a dry argon flushed *Schlenk*-flask 3-bromothiophene (**19a**, 163 mg, 1.0 mmol, 1.0 equiv) and $Pd(PPh_3)_2Cl_2$ (35 mg, 0.05 mmol, 5 mol%) were suspended in 2.5 mL dry THF and 2.5 mL dry toluene. Then, $(TMS)_2CHMgBr{\cdot}LiCl$ (**10**; 1.83 mL, 1.1 mmol, 1.1 equiv, 0.6 M in THF) was added and the reaction mixture was stirred at 50 °C for 12 h. After completion of the reaction, the mixture was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **21a** as colorless oil (237 mg, 98%).

^{1}H-NMR (400 MHz, CDCl3): δ / ppm = 7.17 (dd, J = 5.0 and 3.0 Hz, 1H), 6.72 (dd, J = 4.7 and 1.4 Hz, 1H), 6.57 (dd, J = 2.8 and 1.4 Hz, 1H), 1.68 (s, 1H), 0.07-0.04 (m, 18H).

^{13}C-NMR (75 MHz, CDCl3): δ / ppm = 141.7, 129.6, 124.3, 117.0, 23.9, 0.2.

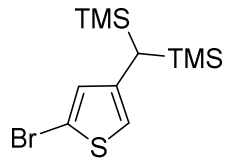
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2898, 2835, 1520, 1423, 1373, 1248, 1166, 1032, 940, 924, 827, 766, 751, 685, 639.

MS (EI, 70 eV): *m/z* (%) = 242 (34), 227 (15), 207 (20), 154 (100), 73 (61), 55 (15).

HRMS (EI) for $\mathbf{C_{11}H_{22}SSi_2}$ (242.0981): 242.0981 (M^+).

2.6. Regioselective Functionalization of the BTSM-substituted Thiophene Scaffold

Synthesis of ((5-bromothiophen-3-yl)methylene)bis(trimethylsilane) (69)



According to **TP 7**, the lithiation of **21a** (242 mg, 1.0 mmol, 1.0 equiv) with *n*BuLi (0.47 mL, 1.1 mmol, 1.1 equiv, 2.35 M in hexane) was completed after 30 min at -30 °C. Then, 1,2-dibromo-1,1,2,2-tetrachloroethane (391 mg, 1.2 mmol, 1.2 equiv) in THF (1.2 mL) was slowly added at -30 °C and the reaction mixture was allowed to warm up to room temperature. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **69** as yellow oil (315 mg, 98%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 6.65 (d, *J* = 1.7 Hz, 1H), 6.46 (d, *J* = 1.7 Hz, 1H), 1.58 (s, 1H), 0.02 (s, 18H).

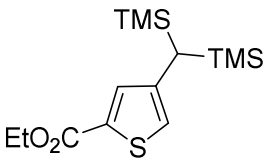
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 142.7, 131.8, 118.4, 110.7, 24.5, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2898, 2836, 1522, 1401, 1353, 1248, 1209, 1152, 1031, 983, 931, 923, 857, 825, 763, 727, 686.

MS (EI, 70 eV): *m/z* (%) = 322 (19), 320 (19, M^+), 307 (21), 305 (18), 243 (11), 242 (23), 241 (100), 234 (42), 232 (37), 213 (19), 168 (11), 167 (49), 153 (19), 73 (25).

HRMS (EI) for $\mathbf{C_{11}H_{21}{}^{79}BrSSi_2}$ (320.0086): 320.0087 (M^+).

Synthesis of ethyl 4-(*bis*(trimethylsilyl)methyl)thiophene-2-carboxylate (70)



According to **TP 7**, the lithiation of **21a** (242 mg, 1.0 mmol, 1.0 equiv) with *n*BuLi (0.47 mL, 1.1 mmol, 1.1 equiv, 2.35 M in hexane) was completed after 30 min at -30 °C. Then, ethyl chloroformate (130 mg, 1.2 mmol, 1.2 equiv) in THF (1.2 mL) was slowly added at -30 °C and the reaction mixture was allowed to warm up to room temperature. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration,

the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 100:1) to give **70** as yellow oil (239 mg, 76%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.41 (d, *J* = 1.5 Hz, 1H), 8.81 (d, *J* = 1.5 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.64 (s, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.03 (s, 18H).

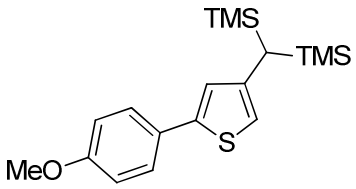
^{13}C-NMR (100 MHz, $CDCl_3$): δ/ ppm = 162.4, 143.0, 135.0, 132.8, 124.5, 61.0, 24.1, 14.3, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2899, 2838, 1708, 1536, 1416, 1370, 1278, 1247, 1217, 1158, 1126, 1069, 1030, 953, 873, 836, 826, 761, 687.

MS (EI, 70 eV): *m/z* (%) = 314 (33, M^+), 269 (11), 257 (17), 226 (22), 196 (33), 168 (21), 153 (10), 147 (11), 137 (28), 75 (11), 73 (100), 45 (18), 43 (11).

HRMS (EI) for $C_{14}H_{26}O_2SSi_2$ (314.1192): 314.1183 (M^+).

Synthesis of ((5-(4-methoxyphenyl)thiophen-3-yl)methylene)*bis*(trimethylsilane) (71)



According to **TP 7**, the lithiation of **21a** (242 mg, 1.0 mmol, 1.0 equiv) with *n*BuLi (0.47 mL, 1.1 mmol, 1.1 equiv, 2.35 M in hexane) was completed after 30 min at -30 °C. $ZnCl_2$ (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF) was slowly added at -30 °C and the resulting solution was stirred for 30 min and allowed to warm up to room temperature. Then, $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), SPhos (16.4 mg, 0.04 mmol) and 4-bromoanisole (168 mg, 0.9 mmol, 0.9 equiv) were added and the reaction mixture was stirred for 12 h at 50 °C. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 100:1) to give **71** as yellow oil (285 mg, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.49 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 2H), 6.82 (s, 1H), 6.46 (s, 1H), 3.82 (s, 3H), 1.62 (s, 1H), 0.05 (s, 18H).

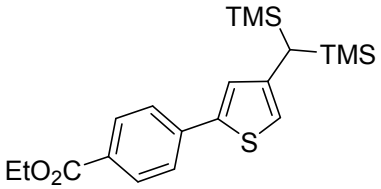
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 158.9, 142.5, 129.2, 127.7, 126.8, 124.6, 115.8, 114.2, 55.3, 24.1, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3001, 2952, 2899, 2835, 1610, 1505, 1464, 1442, 1416, 1360, 1291, 1246, 1177, 1154, 1108, 1034, 982, 926, 859, 823, 792, 765, 722, 687, 658.

MS (EI, 70 eV): *m/z* (%) = 348 (37, M^+), 276 (10), 261 (10), 260 (38), 73 (100), 45 (14), 43 (11).

HRMS (EI) for $C_{18}H_{28}OSSi_2$ (348.1399): 348.1392 (M^+).

Synthesis of ethyl 4-(4-(*bis*(trimethylsilyl)methyl)thiophen-2-yl)benzoate (72)



According to **TP 7**, the lithiation of **21a** (242 mg, 1.0 mmol, 1.0 equiv) with *n*BuLi (0.47 mL, 1.1 mmol, 1.1 equiv, 2.35 M in hexane) was completed after 30 min at -30 °C. $ZnCl_2$ (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF) was slowly added at -30 °C and the resulting solution was stirred for 30 min and allowed to warm up to room temperature. Then, $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and ethyl 4-iodobenzoate (248 mg, 0.9 mmol, 0.9 equiv) were added and the reaction mixture was stirred for 12 h at 50 °C. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 100:1) to give **72** as a yellow oil (320 mg, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.02 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 1.2 Hz, 1H), 6.62 (d, J = 1.2 Hz, 1H), 4.39 (q, J = 7.2 Hz, 2H), 1.66 (s, 1H), 1.41 (t, J = 7.2 Hz, 3H), 0.06 (s, 18H).

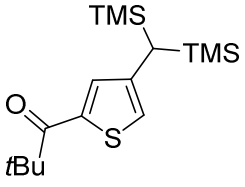
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.3, 143.3, 141.7, 138.9, 130.1, 128.8, 126.8, 125.1, 118.4, 60.9, 24.2, 14.3, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2899, 2836, 1713, 1605, 1503, 1427, 1408, 1366, 1272, 1247, 1181, 1104, 1022, 984, 927, 862, 851, 835, 768, 730, 693, 686.

MS (EI, 70 eV): *m/z* (%) = 390 (69, M^+), 375 (16), 303 (12), 302 (46), 272 (25), 244 (38), 229 (17), 213 (24), 73 (100), 45 (13).

HRMS (EI) for $C_{20}H_{30}O_2SSi_2$ (390.1505): 390.1498 (M^+).

Synthesis of 1-(4-(*bis*(trimethylsilyl)methyl)thiophen-2-yl)-2,2-dimethylpropan-1-one (73)



According to **TP 7**, the lithiation of **21a** (242 mg, 1.0 mmol, 1.0 equiv) with *n*BuLi (0.47 mL, 1.1 mmol, 1.1 equiv, 2.35 M in hexane) was completed after 30 min at -30 °C. After the addition of $ZnCl_2$ (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF), the reaction mixture was stirred for 30 min at this temperature before CuCN·2LiCl (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF) was added. After another 30 min, pivaloyl chloride (108 mg, 0.9 mmol, 0.9 equiv) was added and the resulting solution was allowed to warm up to room temperature and stirred overnight. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 100:1) to give **73** as a colorless oil (179 mg, 61%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.39 (d, *J* = 0.8 Hz, 1H), 6.84 (d, *J* = 0.8 Hz, 1H), 1.63 (s, 1H), 1.37 (s, 9H), 0.03 (s, 18H).

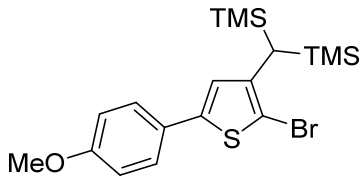
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 198.8, 142.7, 141.2, 133.8, 125.0, 43.7, 28.2, 24.0, -0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2902, 2873, 1648, 1476, 1401, 1366, 1249, 1180, 1129, 1030, 967, 868, 836, 826, 794, 768, 736, 688, 663.

MS (EI, 70 eV): *m/z* (%) = 326 (28, M^+), 285 (11), 284 (18), 283 (63), 269 (16), 238 (13), 195 (12), 73 (100), 57 (26), 45 (12), 41 (15).

HRMS (EI) for **$C_{16}H_{30}OSSi_2$** (326.1556): 326.1549 (M^+).

Synthesis of ((2-bromo-5-(4-methoxyphenyl)thiophen-3-yl)methylene)*bis*(trimethylsilane) (74a)



According to **TP 8**, the lithiation of **71** (349 mg, 1.0 mmol, 1.0 equiv) with TMPLi (1.75 mL, 1.1 mmol, 1.1 equiv, 0.63 M in THF) was completed within 45 min at -60 °C. Then, 1,2-dibromo-1,1,2,2-tetrachloroethane (261 mg, 0.8 mmol, 0.8 equiv) in THF (1.0 mL) was slowly added at -60 °C and the reaction mixture was allowed to warm up to room temperature. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **74a** as a light brown solid (243 mg, 71%).

M.p.: 83.0 – 84.8 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.35 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.68 (s, 1H), 3.75 (s, 3H), 1.80 (s, 1H), 0.00 (s, 18H).

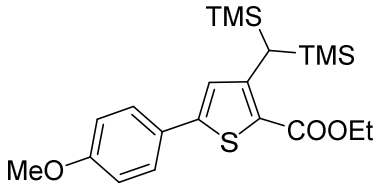
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 159.3, 142.6, 142.4, 126.9, 126.6, 122.0, 114.3, 104.7, 55.4, 23.0, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2956, 2897, 2837, 1606, 1544, 1508, 1454, 1342, 1292, 1258, 1249, 1178, 1167, 1038, 1030, 974, 928, 860, 832, 816, 792, 768, 713, 689, 662.

MS (EI, 70 eV): m/z (%) = 428 (22), 426 (20, M^+), 349 (13), 348 (25), 347 (80), 274 (23), 273 (43), 260 (14), 259 (60), 216 (14), 201 (11), 73 (100).

HRMS (EI) for **$C_{18}H_{27}{}^{79}BrOSSi_2$** (426.0505): 426.0502 (M^+).

Synthesis of ethyl 3-(*bis*(trimethylsilyl)methyl)-5-(4-methoxyphenyl)thiophene-2-carboxylate (74b)



According to **TP 8**, the lithiation of **71** (349 mg, 1.0 mmol, 1.0 equiv) with TMPLi (1.75 mL, 1.1 mmol, 1.1 equiv, 0.63 M in THF) was completed within 45 min at -60 °C. Then, ethyl chloroformate (130 mg, 1.2 mmol, 1.2 equiv) in THF (1.2 mL) was slowly added at -60 °C and the reaction mixture was allowed to warm up to room temperature. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 100:1) to give **74b** as a white solid (261 mg, 62%).

M.p.: 93.5 – 95.4 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.54 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.88 (s, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.44 (s, 1H), 1.36 (t, *J* = 7.2 Hz, 3H), 0.06 (s, 18H).

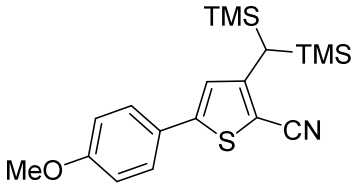
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 163.5, 160.0, 153.4, 147.6, 127.3, 126.4, 124.9, 121.1, 114.4, 60.2, 55.4, 23.5, 14.4, 0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2892, 2839, 1680, 1605, 1538, 1504, 1435, 1416, 1364, 1268, 1248, 1210, 1180, 1167, 1114, 1074, 1044, 1026, 1017, 869, 838, 828, 794, 768, 763, 722, 688, 666, 655.

MS (EI, 70 eV): *m/z* (%) = 420 (33, M^+), 391 (12), 377 (30), 376 (29), 375 (17), 333 (26), 287 (26), 286 (13), 260 (24), 259 (14), 219 (13), 147 (76), 75 (21), 73 (85), 69 (12), 57 (12), 55 (12), 45 (12), 44 (100), 43 (37), 41 (17).

HRMS (EI) for $\mathbf{C_{21}H_{32}O_3SSi_2}$ (420.1611): 420.1606 (M^+).

Synthesis of 3-(*bis*(trimethylsilyl)methyl)-5-(4-methoxyphenyl)thiophene-2-carbonitrile (74c)



According to **TP 8**, the lithiation of **71** (349 mg, 1.0 mmol, 1.0 equiv) with TMPLi (1.75 mL, 1.1 mmol, 1.1 equiv, 0.63 M in THF) was completed within 45 min at -60 °C. Then, *p*-toluenesulfonyl cyanide (217 mg, 1.2 mmol, 1.2 equiv) was added slowly to the reaction mixture as a solution in THF (1.2 mL) and the resulting solution was allowed to warm up to room temperature. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 100:1) to give **74c** as white crystals (220 mg, 59%).

M.p.: 138.5 – 139.8 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.49 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 6.83 (s, 1H), 3.84 (s, 3H), 2.09 (s, 1H), 0.10 (s, 18H).

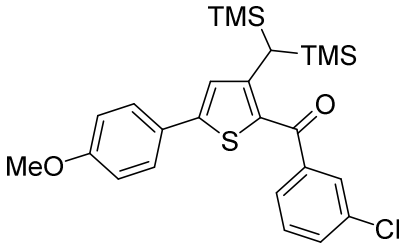
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 160.5, 156.6, 149.9, 127.5, 125.5, 122.2, 115.6, 114.5, 99.9, 55.4, 26.1, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2932, 2898, 2836, 2202, 1606, 1503, 1433, 1416, 1300, 1256, 1245, 1194, 1180, 1115, 1037, 990, 866, 835, 826, 794, 772, 692, 654.

MS (EI, 70 eV): *m/z* (%) = 374 (31), 373 (90, M^+), 359 (15), 358 (45), 285 (34), 274 (13), 260 (11), 259 (52), 73 (100), 45 (18).

HRMS (EI) for $\mathbf{C_{19}H_{27}NOSSi_2}$ (373.1352): 373.1346 (M^+).

Synthesis of (3-(*bis*(trimethylsilyl)methyl)-5-(4-methoxyphenyl)thiophen-2-yl)(3-chlorophenyl)methanone (74d)



According to **TP 8**, the lithiation of **71** (349 mg, 1.0 mmol, 1.0 equiv) with TMPLi (1.75 mL, 1.1 mmol, 1.1 equiv, 0.63 M in THF) was completed within 45 min at -60 °C. After the addition of $ZnCl_2$ (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF), the reaction mixture was stirred for 30 min at this temperature before CuCN·2LiCl (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF) was added. After another 30 min, 3-chlorobenzoyl chloride (158 mg, 0.9 mmol, 0.9 equiv) was added and the resulting solution was allowed to warm up to room temperature and stirred overnight. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 1000:1) to give **74d** as yellow crystals (373 mg, 85%).

M.p.: 155.3 – 157.0 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.65 (s, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 6.91 (s, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.75 (s, 3H), 3.36 (s, 1H), 0.00 (s, 18H).

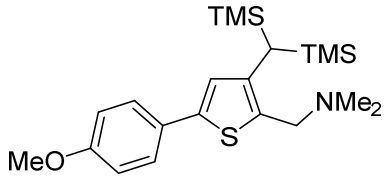
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 188.0, 160.4, 155.0, 149.8, 142.9, 134.2, 131.3, 129.4, 129.3, 128.7, 127.5, 126.7, 125.9, 125.6, 114.5, 55.4, 24.1, 0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}= 2955, 2900, 2884, 2838, 1626, 1500, 1418, 1292, 1250, 1178, 1031, 867, 839, 826, 807, 793, 782, 770, 740, 687, 654.

MS (EI, 70 eV): *m/z* (%) = 486 (6, M^+), 471 (10), 413 (12), 412 (16), 379 (14), 378 (38), 363 (17), 73 (100).

HRMS (EI) for **$C_{25}H_{31}ClO_2SSi_2$** (486.1272): 486.1272 (M^+).

Synthesis of 1-(3-(*bis*(trimethylsilyl)methyl)-5-(4-methoxyphenyl)thiophen-2-yl)-N,N-dimethylmethanamine (74e)



According to **TP 8**, the lithiation of **71** (349 mg, 1 mmol, 1.0 equiv) with TMPLi (1.75 mL, 1.1 mmol, 1.1 equiv) was completed within 45 min at -60 °C. Then, $MgCl_2 \cdot LiCl$ (2.4 mL, 1.2 mmol, 1.2 equiv, 0.5 M in THF) was added and the reaction mixture was stirred for 30 min and allowed to warm up to room temperature. Another dry and argon flushed *Schlenk*-flask was charged with *N,N,N',N'*-tetramethylmethanediamine (**30**; 0.21 mL, 1.5 mmol 1.5 equiv) and anhydrous CH_2Cl_2 to obtain a 1.0 M solution. After cooling to 0 °C, neat trifluoroacetic anhydride (0.21 mL, 1.5 mmol, 1.5 equiv) was added dropwise and the solution was allowed to warm up to room temperature and stirring was continued for 5 min. The previously prepared Grignard reagent was then dropwise cannulated to the so obtained solution of methylene(dimethyl)iminium trifluoroacetate (**29**) at 0 °C. The reaction mixture was allowed to warm up to room temperature, quenched with sat. aq $NaHCO_3$ solution (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$.After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (Al_2O_3, *iso*hexane:EtOAc = 9:1) to give **74e** as yellow oil (288 mg, 72%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.42 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.73 (s, 1H), 3.77 (s, 3H), 3.43 (s, 2H), 2.28 (s, 6H), 1.64 (s, 1H), 0.00 (s, 18H).

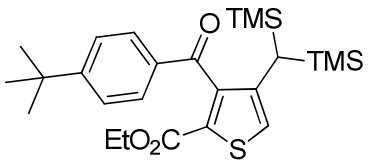
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 158.8, 140.6, 138.9, 127.8, 126.5, 123.3, 114.2, 108.7, 57.1, 55.3, 45.6, 21.5, 0.4, 0.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}=2950, 2899, 2854, 2835, 2771, 1610, 1510, 1463, 1455, 1440, 1351, 1291, 1246, 1176, 1126, 1109, 1030, 1016, 888, 860, 832, 823, 793, 767, 725, 687.

MS (EI, 70 eV): *m/z* (%) = 405 (23, M^+), 363 (16), 362 (36), 361 (80), 360 (53), 347 (12), 346 (12), 345 (13), 289 (12), 288 (25), 287 (78), 286 (13), 274 (21), 273 (44), 73 (100), 58 (33), 44 (12).

HRMS (EI) for **$C_{21}H_{35}NOSSi_2$** (405.1978): 405.1971 (M^+).

Synthesis of ethyl 4-(*bis*(trimethylsilyl)methyl)-3-(4-(tert-butyl)benzoyl)thiophene-2-carboxylate (75a)



According to **TP 9**, the magnesiation of **70** (315 mg, 1.0 mmol, 1.0 equiv) with TMPMgCl·LiCl (**63**, 1.25 mL, 1.5 mmol, 1.5 equiv, 1.2 M in THF) was completed within 75 min at 0 °C. After the addition of $ZnCl_2$ (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF), the reaction mixture was stirred for 30 min at this temperature before CuCN·2LiCl (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF) was added. After another 30 min, 4-(*tert*-butyl)benzoyl chloride (177 mg, 0.9 mmol, 0.9 equiv) was added and the resulting solution was allowed to warm up to room temperature and stirred overnight. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:Et_2O = 100:1) to give **75a** as a yellow oil (313 mg, 66%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.70 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 6.92 (s, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 1.49 (s, 1H), 1.30 (s, 9H), 0.91 (t, *J* = 7.2 Hz, 3H), -0.04 (s, 18H).

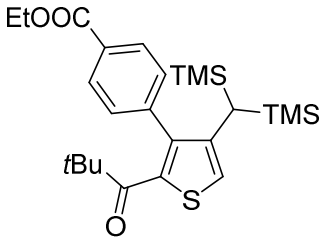
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 194.0, 161.5, 157.1, 145.5, 143.5, 135.2, 130.9, 129.3, 125.3, 123.6, 61.3, 35.1, 31.0, 20.6, 13.5, 0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}=2956, 2904, 2871, 1709, 1666, 1604, 1518, 1463, 1419, 1368, 1277, 1249, 1175, 1111, 1101, 1051, 1021, 936, 878, 835, 768, 728, 685, 675, 655.

MS (EI, 70 eV): *m/z* (%) = 474 (1, M^+), 459 (21), 417 (21), 401 (11), 389 (14), 374 (10), 373 (33), 301 (10), 300 (19), 299 (55), 227 (14), 73 (100), 57 (19), 45 (13).

HRMS (EI) for **$C_{25}H_{38}O_3SSi_2$** (475.2152, M^++ H^+): 475.2149.

Synthesis of ethyl 4-(4-(*bis*(trimethylsilyl)methyl)-2-pivaloylthiophen-3-yl)benzoate (76a)



According to **TP 10**, the magnesiation of **73** (327 mg, 1.0 mmol, 1.0 equiv) with $TMP_2Mg·2LiCl$ (**59**, 1.8 mL, 1.1 mmol, 1.1 equiv, 0.60 M in THF) was completed within 75 min at 0 °C. After the addition of $ZnCl_2$ (1.2 mL, 1.2 mmol, 1.2 equiv, 1.0 M in THF), the reaction mixture was stirred for 30 min at this temperature. Then, $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and ethyl 4-iodobenzoate (248 mg, 0.9 mmol, 0.9 equiv) were added and the reaction mixture was stirred for 12 h at 50 °C. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **76a** as a yellow solid (363 mg, 85%).

M.p.: 108.9 – 110.6 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.08 (d, J = 8.3 Hz, 2H), 7.49 (s, 1H), 7.42 (d, J = 8.3 Hz, 2H), 4.39 (q, J = 7.0 Hz, 2H), 1.92 (s, 1H), 1.42-1.38 (m, 12H), 0.00 (s, 18H).

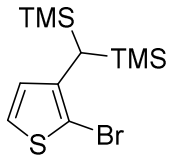
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 198.7, 166.2, 141.0, 140.0, 139.6, 138.9, 133.5, 129.8, 129.8, 129.5, 61.1, 43.8, 28.2, 20.9, 14.3, 0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}=2970, 2952, 2901, 2864, 1714, 1647, 1606, 1476, 1428, 1404, 1364, 1270, 1262, 1249, 1170, 1143, 1100, 1032, 1019, 976, 889, 870, 856, 836, 796, 772, 754, 705, 689, 665.

MS (EI, 70 eV): *m/z* (%) = 474 (10, M^+), 445 (11), 417 (17), 402 (29), 401 (74), 73 (100), 57 (20).

HRMS (EI) for **$C_{25}H_{38}O_3SSi_2$** (474.2080): 474.2065 (M^+).

Synthesis of ((2-bromothiophen-3-yl)methylene)*bis*(trimethylsilane) (77)



In a dry argon flushed *Schlenk*-flask, **21a** (242 mg, 1.0 mmol, 1.0 equiv) was dissolved in dry DMF (2 mL) and cooled to 0 °C. Then, *N*-bromosuccinimide (178 mg, 1.0 mmol, 1.0 equiv) was added in one portion and the reaction mixture was allowed to warm up to room temperature and stirred for 2 h. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **77** as colorless oil (315 mg, 81%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.18 (d, J = 5.5 Hz, 1H), 6.67 (d, J = 5.5 Hz, 1H), 1.90 (s, 1H), 0.03 (s, 18H).

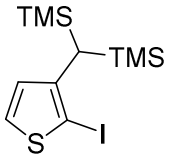
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 141.5, 127.3, 124.4, 106.3, 22.6, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}=2953, 2898, 2846, 1523, 1395, 1356, 1248, 1170, 1036, 992, 945, 880, 865, 837, 825, 767, 703, 685.

MS (EI, 70 eV): *m/z* (%) = 322 (5), 320 (5, M^+), 242 (11), 241 (51), 167 (36), 154 (12), 153 (76), 152 (9), 151 (11), 110 (10), 73 (100), 45 (17).

HRMS (EI) for **$C_{11}H_{21}BrSSi_2$** (320.0086): 320.0071 (M^+).

Synthesis of ((2-iodothiophen-3-yl)methylene)*bis*(trimethylsilane) (78)



In a dry argon flushed *Schlenk*-flask, **21a** (242 mg, 1.0 mmol, 1.0 equiv) was dissolved in dry THF (5 mL) and cooled to -78 °C. Then, iodine monochloride (243 mg, 1.5 mmol, 1.5 equiv) in THF (1.5 mL) was added in one portion and the reaction mixture was stirred for 30 min. The reaction was quenched with sat. aq $Na_2S_2O_3$ solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **78** as colorless oil (302 mg, 82%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.39 (d, *J* = 5.4 Hz, 1H), 6.63 (d, *J* = 5.4 Hz, 1H), 1.84 (s, 1H), 0.04 (s, 18H).

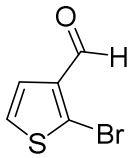
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 147.0, 129.8, 126.4, 73.3, 25.6, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}= 2952, 2897, 2838, 1513, 1385, 1353, 1248, 1164, 1034, 938, 880, 864, 837, 825, 767, 728, 707, 685.

MS (EI, 70 eV): *m/z* (%) = 369 (2), 241 (32), 167 (35), 153 (48), 73 (100), 45 (16).

HRMS (EI) for **$C_{11}H_{21}ISSi_2$** (369.0029, M^++ H^+): 369.0027.

Synthesis of 2-bromothiophene-3-carbaldehyde (79)



According to **TP 11**, to **77** (321 mg, 1.0 mmol, 1.0 equiv) in 17 mL MeOH and 50 mL CH_3CN was added CAN (2.74 g, 5.0 mmol, 5.0 equiv) in one portion and the resulting mixture was stirred for 2 days. CF_3COOH (5 mL) was added and the reaction mixture was stirred for further 15 min. Then, the reaction mixture was quenched with H_2O (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 20:1) to give **79** as yellow oil (118 mg, 62%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.93 (s, 1H), 7.36 (d, J = 5.8 Hz, 1H), 7.28 (d, J = 5.8 Hz, 1H).

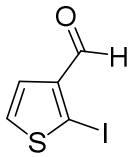
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 184.6, 138.5, 126.9, 126.2, 125.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1}=3109, 3087, 2852, 2828, 2778, 2720, 1683, 1661, 1514, 1426, 1377, 1226, 1087, 1004, 992, 891, 818, 714, 658.

MS (EI, 70 eV): *m/z* (%) = 192 (72), 191 (100), 190 (73), 189 (95, M^+), 163 (10), 161 (10), 83 (14), 82 (44), 81 (19), 57 (14), 45 (14).

HRMS (EI) for **$C_5H_3{}^{79}BrOS$** (189.9088): 189.9070 (M^+).

Synthesis of 2-iodothiophene-3-carbaldehyde (80)



According to **TP 11**, to **78** (368 mg, 1.0 mmol, 1.0 equiv) in 17 mL MeOH and 50 mL CH_3CN was added CAN (2.74 g, 5.0 mmol, 5.0 equiv) in one portion and the resulting mixture was stirred for 2 days. CF_3COOH (5 mL) was added and the reaction mixture was stirred for further 15 min. Then, the reaction mixture was quenched with H_2O (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 50:1) to give **80** as a yellow solid (143 mg, 60%).

M.p.: 64.9 – 66.7 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.72 (s, 1H), 7.49 (d, J = 5.5 Hz, 1H), 7.31 (d, J = 5.5 Hz, 1H).

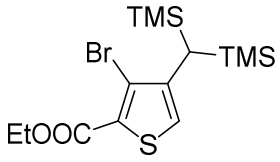
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 186.9, 141.6, 132.0, 126.9, 88.9.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3115, 3077, 2846, 2821, 2765, 1662, 1649, 1620, 1507, 1372, 1356, 1225, 1171, 979, 818, 725.

MS (EI, 70 eV): *m/z* (%) = 238 (100, M^+), 237 (76), 110 (26), 84 (12), 82 (32), 81 (15), 57 (14), 45 (11).

HRMS (EI) for **C_5H_3IOS** (237.8949): 237.8958 (M^+).

Synthesis of ethyl 4-(*bis*(trimethylsilyl)methyl)-3-bromothiophene-2-carboxylate (75b)



According to **TP 9**, the magnesiation of **70** (315 mg, 1.0 mmol, 1.0 equiv) with TMPMgCl·LiCl (**63**, 1.25 mL, 1.5 mmol, 1.5 equiv, 1.2 M in THF) was completed within 75 min at 0 °C. Then, 1,2-dibromo-1,1,2,2-tetrachloroethane (293 mg, 0.9 mmol, 0.9 equiv) in THF (1.0 mL) was slowly added at 0 °C and the reaction mixture was allowed to warm up to room temperature. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **75b** as a reddish solid (287 mg, 81%).

M.p.: 59.3 – 61.1 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 6.90 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.13 (s, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 0.00 (s, 18H).

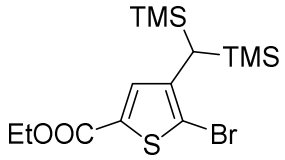
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm =161.0, 144.6, 126.7, 121.8, 121.0, 61.2, 21.6, 14.3, -0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3097, 2951, 2898, 2855, 1712, 1511, 1422, 1342, 1251, 1244, 1222, 1174, 1079, 1028, 975, 883, 835, 825, 795, 782, 768, 752, 689, 664.

MS (EI, 70 eV): *m/z* (%) = 394 (22), 392 (23, M^+), 379 (15), 377 (15), 365 (14), 363 (16), 276 (38), 274 (33), 217 (10), 195 (10), 167 (10), 147 (11), 92 (16), 73 (100), 45 (12).

HRMS (EI) for **$C_{14}H_{25}{}^{79}BrO_2SSi_2$** (392.0297): 392.0285 (M^+).

Synthesis of ethyl 4-(*bis*(trimethylsilyl)methyl)-5-bromothiophene-2-carboxylate (82)



In a dry argon flushed *Schlenk*-flask, **70** (315 mg, 1.0 mmol, 1.0 equiv) was dissolved in dry DMF (2 mL) and cooled to 0 °C. Then, *N*-bromosuccinimide (178 mg, 1.0 mmol, 1.0 equiv) was added in one portion and the reaction mixture was allowed to warm up to room temperature and stirred for 2 h. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **82** as red oil (287 mg, 81%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.30 (s, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.84 (s, 1H), 1.32 (t, *J* = 7.2 Hz, 3H), 0.00 (s, 18H).

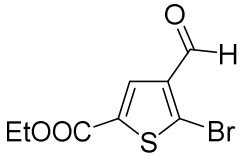
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 161.5, 143.2, 132.5, 132.2, 114.7, 61.2, 23.0, 14.3, -0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2900, 2852, 1712, 1541, 1408, 1348, 1278, 1248, 1204, 1161, 1070, 1035, 961, 864, 836, 826, 768, 748, 689.

MS (EI, 70 eV): m/z (%) = 394 (23), 392 (20, M^+), 325 (30), 313 815), 383 (53), 276 (17), 274 (18), 225 (10), 195 (48), 167 (15), 139 (11), 111 (14), 97 (19), 95 (12), 85 (18), 83 (17), 81 (13), 73 (100), 71 (19), 69 (21), 57 (30), 55 (20), 45 (16), 43 (20).

HRMS (EI) for $\mathbf{C_{14}H_{25}{}^{79}BrO_2SSi_2}$ (392.0297): 392.0287(M^+).

Synthesis of ethyl 5-bromo-4-formylthiophene-2-carboxylate (83)



According to **TP 11**, to **75b** (393 mg, 1.0 mmol, 1.0 equiv) in 17 mL MeOH and 50 mL CH_3CN was added CAN (2.74 g, 5.0 mmol, 5.0 equiv) in one portion and the resulting mixture was stirred for 2 days. CF_3COOH (5 mL) was added and the reaction mixture was stirred for further 15 min. Then, the reaction mixture was quenched with H_2O (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 100:1) to give **81** as yellow oil (158 mg, 60%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.85 (s, 1H), 7.89 (s, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

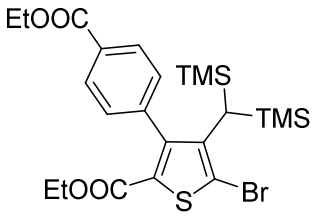
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 184.1, 160.5, 138.9, 135.2, 131.3, 130.1, 62.0, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3094, 2987, 2926, 2858, 1700, 1672, 1532, 1440, 1379, 1364, 1282, 1168, 1067, 872, 856, 749, 689.

MS (EI, 70 eV): *m/z* (%) = 264 (51, M^+), 262 (49), 236 (49), 235 (41), 236 (46), 233 (36), 220 (14), 219 (98), 218 (14), 217 (100), 191 (11), 189 (10), 82 (55), 81 (35), 45 (11), 43 (12).

HRMS (EI) for **$C_8H_7{}^{79}BrO_3S$** (261.9299): 261.9303 (M^+).

Synthesis of ethyl 4-(*bis*(trimethylsilyl)methyl)-5-bromo-3-(4-(ethoxycarbonyl)phenyl)thiophene-2-carboxylate (25a)



According to **TP 9**, the magnesiation of **82** (393 mg, 1.0 mmol, 1.0 equiv) with TMPMgCl·LiCl (**63**, 1.25 mL, 1.5 mmol, 1.5 equiv) was completed within 75 min at 0 °C. After the addition of $ZnCl_2$ (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF), the reaction mixture was stirred for 30 min at this temperature. Then, $Pd(dba)_2$ (11.5 mg, 0.02 mmol), tfp (9.29 mg, 0.04 mmol) and ethyl 4-iodobenzoate (248 mg, 0.9 mmol, 0.9 equiv) were added and the reaction mixture was stirred for 12 h at 50 °C. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 50:1) to give **25a** as yellow crystals (366 mg, 75%).

M.p.: 99.8 – 101.1 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.07 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 1.51 (s, 1H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.00 (s, 18H).

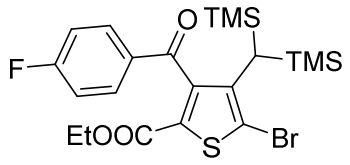
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.3, 160.9, 147.9, 144.7, 141.4, 129.9, 129.9, 129.1, 112.4, 105.2, 61.0, 61.0, 21.7, 14.3, 13.9, 1.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2983, 2955, 2898, 2852, 1715, 1611, 1427, 1366, 1341, 1271, 1248, 1214, 1152, 1100, 1086, 1023, 981, 837, 770, 763, 713, 695, 686.

MS (EI, 70 eV): *m/z* (%) = 540 (1, M^+), 481 (10), 479 (8), 469 (11), 467 (9), 462 (12), 461 (32), 423 (13), 395 (13), 393 (10), 351 (19), 349 (19), 433 (15), 343 (53), 271 (12), 73 (100), 45 (12).

HRMS (EI) for **$C_{23}H_{33}BrO_4SSi_2$** (540.0821): 540.0837 (M^+).

Synthesis of ethyl 4-(*bis*(trimethylsilyl)methyl)-5-bromo-3-(4-fluorobenzoyl)thiophene-2-carboxylate (25b)



According to **TP 9**, the magnesiation of **82** (393 mg, 1.0 mmol, 1.0 equiv) with TMPMgCl·LiCl (**63**, 1.25 mL, 1.5 mmol, 1.5 equiv) was completed within 75 min at 0 °C. After the addition of $ZnCl_2$ (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF), the reaction mixture was stirred for 30 min at this temperature and cooled down to -40 °C, before CuCN·2LiCl (1.6 mL, 1.6 mmol, 1.6 equiv, 1.0 M in THF) was added. After another 30 min, 4-fluorobenzoyl chloride (143 mg, 0.9 mmol, 0.9 equiv) was added and the resulting solution was allowed to warm up to room temperature and stirred overnight. The reaction was quenched with sat. aq NH_4Cl solution (30 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 100:1) to give **25b** as yellow crystals (371 mg, 80%).

M.p.: 83.6 – 85.2 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.85-7.79 (m 2H), 7.14-7.08 (m, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 1.41 (s, 1H), 1.05 (t, *J* = 7.2 Hz, 3H), 0.00 (s, 18H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 192.1, 162.7 (d, *J* = 244.0 Hz), 160.3, 146.2, 143.8, 133.4 (d, *J* = 3.1 Hz), 132.0 (d, *J* = 9.5 Hz), 130.0, 115.8 (d, *J* = 22.1 Hz), 113.5, 61.7, 22.2, 13.7, 1.5.

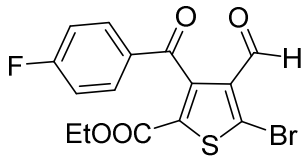
^{19}F-NMR (282 MHz, $CDCl_3$): δ/ppm = -103.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954, 2900, 2856, 1695, 1663, 1594, 1524, 1505, 1476, 1416, 1410, 1370, 1335, 1291, 1261, 1244, 1228, 1190, 1150, 1118, 1104, 1095, 1059, 1020, 1006, 981, 863, 835, 792, 774, 766, 750, 700, 688, 682, 669.

MS (EI, 70 eV): *m/z* (%) = 514, (1, M^+), 501 (18), 499 (17), 488 (12), 487 (38), 496 (11), 485 (35), 443 (14), 441 (12), 436 (15), 435 (48), 325 (16), 323 (14), 318 (11), 317 (50), 123 (23), 95 (13), 73 (100), 45 (13).

HRMS (EI) for **$C_{21}H_{28}{}^{79}BrFO_3SSi_2$** (514.0465): 514.0451 (M^+).

Synthesis of ethyl 5-bromo-3-(4-fluorobenzoyl)-4-formylthiophene-2-carboxylate (26b)



According to **TP 11**, to **25b** (515 mg, 1.0 mmol, 1.0 equiv) in 17 mL MeOH and 50 mL CH_3CN was added CAN (2.74 g, 5.0 mmol, 5.0 equiv) in one portion and the resulting mixture was stirred for 2 days. CF_3COOH (5 mL) was added and the reaction mixture was stirred for further 15 min. Then, the reaction mixture was quenched with H_2O (10 mL), extracted with EtOAc (3 x 30 mL) and dried over $MgSO_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 10:1) to give **26b** as a yellow oil (277 mg, 72%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.84 (s, 1H), 7.85-7.79 (m, 2H), 7.14-7.08 (m, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 189.4, 183.3, 166 (d, *J* = 255.8 Hz), 159.5, 144.7, 137.6, 132.9 (d, *J* = 3.1 Hz), 132.0, 131.4 (d, *J* = 9.5 Hz), 130.9, 115.9 (d, *J* = 22.1 Hz), 62.5, 13.7.

^{19}F-NMR (282 MHz, $CDCl_3$): δ/ppm = -103.9

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2927, 2858, 2362, 2339, 1717, 1694, 1683, 1597, 1529, 1504, 1438, 1367, 1274, 1247, 1234, 1219, 1152, 1133, 1100, 1057, 1018, 1010, 974, 944, 884, 838, 817, 797, 770, 746, 726.

MS (EI, 70 eV): *m/z* (%) = 386 (12), 384 (15, M^+), 341 (10), 340 (36), 339 (20), 338 (30), 337 (15), 313 (12), 311 (19), 310 (24), 231 (59), 204 (20), 176 (14), 123 (89), 95 (100), 75 (29), 43 (14).

HRMS (EI) for **$C_{15}H_{10}BrFO_4S$** (383.9467): 383.9465 (M^+).

3. ONE-POT PROCEDURE FOR THE PREPARATION OF TERTIARY AMINES *VIA* IMINIUM IONS

3.1. Typical Procedures (TP)

Typical Procedure 1 for the One-Pot Procedure of Tertiary Amines Using MeMgCl (TP 1)

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with *N*,*N*,*N'*,*N'*-tetramethylmethanediamine (**30**, 1.0 equiv) and anhydrous CH_2Cl_2 to obtain a 1.0 M solution. After cooling to 0 °C, trifluoroacetic anhydride (1.0 equiv) was added dropwise and the solution was allowed to stirr for 15 min at 0 °C.

A second dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding amine (1.0 equiv) and THF to obtain a 0.2 M solution. After cooling to 0 °C, MeMgCl (1.1 equiv) was added dropwise and the solution was stirred for 30 min. Next, the magnesium amide was added over 15 min to the previously prepared methylene(dimethyl)iminium trifluoroacetate (**29**) at 0 °C and stirring was continued for another 30 min. After, trifluoroacetic anhydride (1.0 equiv) was added, resulting in the formation of a white precipitate and the mixture was stirred for 15 min. Finally, the desired organomagnesium / organozinc reagent (1.1 equiv) was added at -78°C and the reaction was allowed to warm up to room temperature at which the precipitate dissolved completely. The crude mixture was quenched with sat. aq $NaHCO_3$ and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with sat. aq NaCl and the solvent was removed *in vacuo*.

Typical Procedure 2 for the One-Pot Procedure of Tertiary Amines Using MeLi (TP 2)

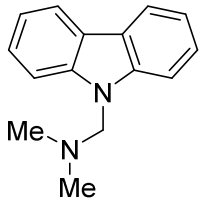
A dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with *N*,*N*,*N'*,*N'*-tetramethylmethanediamine (**30**; 1.0 equiv) and anhydrous CH_2Cl_2 to obtain a 1.0 M solution. After cooling to 0 °C, trifluoroacetic anhydride (1.0 equiv) was added dropwise and the solution was allowed to stirr for 15 min at 0 °C.

A second dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding amine (1.0 equiv) and THF to obtain a 0.2 M solution. After cooling to 0 °C, MeLi (1.1 equiv) was added dropwise and the solution was stirred for 30 min. Next, the magnesium amide was added over 15 min to the previously prepared methylene(dimethyl)iminium trifluoroacetate (**29**) at 0 °C and stirring was continued for another 30 min. After, trifluoroacetic anhydride (1.0 equiv) was added, resulting in the formation of a white precipitate and the mixture was stirred for 15 min. Finally, the desired organomagnesium / organozinc reagent (1.1 equiv) was added at -78 °C and the reaction was allowed to warm up to room temperature at which the precipitate

dissolved completely. The crude mixture was quenched with sat. aq $NaHCO_3$ and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with sat. aq NaCl and the solvent was removed *in vacuo*.

3.2. One-Pot Preparation of Tertiary Amines

1-(9*H*-carbazol-9-yl)-*N*,*N*-dimethylmethanamine (44a)



A dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with *N*,*N*,*N'*,*N'*-tetramethylmethanediamine (**30**, 0.10 g, 1.0 mmol, 1.0 equiv) and anhydrous DCM (1.0 mL). After cooling to 0 °C, trifluoroacetic anhydride (0.21 g, 1.0 mmol, 1.0 equiv) was added dropwise and the solution was allowed to stirr for 15 min at 0 °C.

A second dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with 9*H*-carbazole (0.17 g, 1.0 mmol, 1.0 equiv) and 5 mL THF. After cooling to -78 °C, MeMgCl (0.35 mL, 1.1 mmol, 1.1 equiv, 3.12 M in THF) was added dropwise and the solution was stirred for 30 min. Next, the lithium amide was added over 15 min to the previously prepared methylene(dimethyl)iminium trifluoroacetate (**29**) at -78 °C and stirring was continued for another 30 min. The reaction was quenched with sat. aq $NaHCO_3$ and extracted with DCM (3 x 20 mL). The combined organic layers were washed with sat. aq NaCl and the solvent was removed *in vacuo*. The pure product **44a** was obtained as white solid (193 mg, 86%).

M.p.: 74.0 – 74.9 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.10 (d, J = 7.7 Hz, 2H), 7.55-7.41 (m, 4H), 7.26-7.23 (m, 2H), 4.86 (s, 2H), 2.37 (s, 6H).

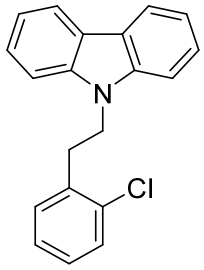
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 141.1, 125.8, 123.1, 120.2, 119.3, 109.5, 66.2, 43.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3418, 3044, 2975, 2944, 2864, 2827, 2777, 1595, 1485, 1465, 1451, 1438, 1382, 1344, 1336, 1326, 1233, 1195, 1154, 1064, 1014, 856, 749, 733, 722.

MS (EI, 70 eV): *m/z* (%) = 224 (5, M^+), 180 (10), 167 (22), 58 (100).

HRMS (EI) for $\mathbf{C_{15}H_{16}N_2}$ (180.0808, M^+ - NMe_2): found: 180.0804.

9-(2-chlorophenethyl)-9*H*-carbazole (50a)



Prepared according to **TP 2** from 9*H*-carbazole (**46a**, 0.17 g, 1.0 mmol, 1.0 equiv) 2-chlorobenzylzinc chloride (**52a**; 0.69 mL, 1.1 mmol, 1.1 equiv, 1.60 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 99:1) afforded **50a** as white crystals (186 mg, 61%).

M.p.: 78.7 – 80.7 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.13 (d, *J* = 7.6 Hz, 2H), 7.50-7.43 (m, 5H), 7.28-7.25 (m, 2H), 7.19 (td, *J* = 7.5 Hz, *J* = 2.0 Hz, 1H), 7.12-7.06 (m, 2H), 4.61-4.57 (m, 2H), 2.32-3.28 (m, 2H).

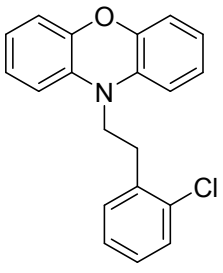
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 140.2, 136.1, 134.0, 131.2, 129.6, 128.3, 127.1, 125.7, 122.9, 120.3, 118.9, 108.5, 42.6, 33.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3050, 3022, 2948, 2929, 2881, 2858, 1959, 1917, 1884, 1850,1808, 1761, 1627, 1597, 1484, 1462, 1452, 1347, 1332, 1324, 1238, 1210, 1182, 1150, 1053, 995, 924, 878, 841, 745, 719, 682,

MS (EI, 70 eV): *m/z* (%) = 305 (12, M^+), 181 (13), 180 (100), 152 (12).

HRMS (EI) for **$C_{20}H_{16}ClN$** (305.0971): found: 305.0967 (M^+).

Synthesis of 10-(2-chlorophenethyl)-10*H*-phenoxazine (50c)



Prepared according to **TP 1** from 10*H*-phenoxazine (**46c**; 183 mg, 1.0 mmol 1.0 equiv) and 2-chlorobenzylzinc chloride (**52a**; 0.69 mL, 1.1 mmol, 1.1 equiv, 1.60 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 49:1) afforded **50c** as a yellow solid (247 mg, 77%).

M.p.: 105.3 – 106.5 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.40 (dd, *J* = 7.46 Hz, *J* = 1.38 Hz, 1H), 7.35 (dd, *J* = 7.46 Hz, *J* = 1.94 Hz, 1H), 7.28-7.18 (m, 2H), 6.85-6.80 (m, 2H), 6.68-6.63 (m, 6H), 3.76-3.71 (m, 2H), 3.11-3.06 (m, 2H).

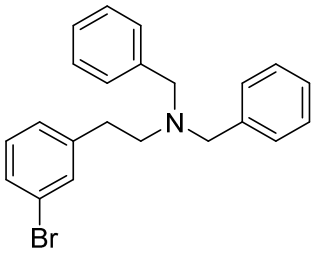
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 144.9, 136.3, 134.0, 132.9, 131.0, 129.7, 128.2, 127.3, 123.7, 121.0, 115.5, 111.3, 43.7, 29.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3066, 3052, 2360, 2341, 1627, 1592, 1569, 1560, 1487, 1472, 1462, 1380, 1308, 1270, 1216, 1201, 1128, 1054, 910, 841, 742, 730, 682.

MS (EI, 70 eV): *m/z* (%) = 321 (16, M^+), 197 (18), 196 (100), 182 (11), 77 (7).

HRMS (EI) for **$C_{20}H_{16}{}^{35}ClNO$** (321.0920): found: 321.0910 (M^+).

Synthesis of *N,N*-dibenzyl-2-(3-bromophenyl)ethan-1-amine (50e)



Prepared according to **TP 1** from dibenzylamine (**46e**; 197 mg, 1.0 mmol, 1.0 equiv) and 2-chlorobenzylzinc chloride (**25c**; 0.69 mL, 1.1 mmol, 1.1 equiv, 1.60 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 19:1) afforded **50e** as yellow oil (273 mg, 72%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.33-7.24 (m, 12H), 7.10 (t, *J* = 7.7 Hz, 1H), 7.00-6.98 (m, 1H), 3.63 (s, 4H), 2.77-2.70 (m, 4H).

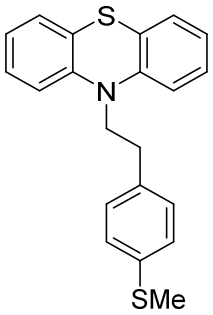
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 143.0, 139.5, 131.9, 129.7, 128.9, 128.6, 128.2, 127.5, 126.8, 122.2, 58.3, 54.6, 33.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3084, 3061, 3026, 2947, 2930, 2795, 2716, 1596, 1567, 1494, 1474, 1452, 1425, 1366, 1247, 1202, 1119, 1071, 1027, 997, 976, 803, 776, 731, 693, 669.

MS (EI, 70 eV): *m/z* (%) = 380 (2, M^+), 211 (14), 210 (79), 181 (6), 118 (5), 92 (9), 91 (100).

HRMS (EI) for **$C_{22}H_{22}BrN$** (378.0852, $M^+ - H^+$): found: 378.0852.

Synthesis of 10-(4-(methylthio)phenethyl)-10*H*-phenothiazine (50g)



Prepared according to **TP 1** from 10*H*-phenothiazine (**46g**; 199 mg, 1.0 mmol 1.0 equiv) and (4-(methylthio)benzyl)zinc chloride (**52e**; 4.40 mL, 1.1 mmol, 1.1 equiv, 0.25 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 49:1) afforded **50g** as a colorless oil (217 mg, 62%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.26-7.16 (m, 8H), 6.98-6.91 (m, 4H), 4.11-4.03 (m, 2H), 3.11-3.03 (m, 2H), 2.49 (s, 3H).

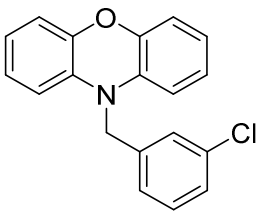
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 145.0, 136.3, 136.1, 129.2, 127.6, 127.3, 127.2, 125.4,122.7, 115.6, 48.9, 33.0, 16.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3059, 3016, 2978, 2917, 2855, 1733, 1592, 1570, 1493, 1486, 1455, 1442, 1368, 1333, 1284, 1248, 1234, 1205, 1179, 1126, 1104, 1094, 1039, 808, 743, 727, 696, 659.

MS (EI, 70 eV): *m/z* (%) = 349 (7, M^+), 212 (49), 199 (99), 198 (51), 180 (71), 167 (39), 138 (36), 137 (69), 91 (17), 43 (100).

HRMS (EI) for **$C_{21}H_{19}NS_2$** (349.0959): found: 349.0944 (M^+).

Synthesis of 10-(3-chlorobenzyl)-10*H*-phenoxazine (51b)



Prepared according to **TP 1** from 10*H*-phenoxazine (**46c**; 183 mg, 1 mmol, 1.0 equiv) and 3-chlorophenylzinc chloride (**53a**; 2.75 mL, 1.1 mmol, 1.1 equiv, 0.40 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 99:1) afforded **51b** as a white solid (246 mg, 80%).

Prepared also according to **TP 1** from 10*H*-phenoxazine (**46c**, 183 mg, 1 mmol, 1.0 equiv) and 3-chlorophenylmagnesium bromide (**53d**, 1.4 mL, 0.80 M in THF, 1.1 mmol, 1.1 equiv). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 99:1) afforded **51b** as a white solid (246 mg, 77%).

M.p.: 114.8 – 115.9 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.21-7.09 (m, 4H), 6.62-6.57 (m, 6H), 6.20 (d, *J* = 6.83 Hz, 2H), 4.65 (s, 2H).

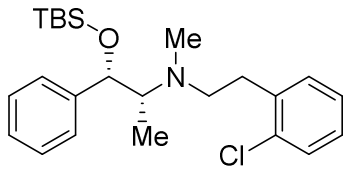
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 145.1, 138.8, 134.9, 133.5, 130.2, 127.5, 126.1, 124.1, 123.7, 121.5, 115.4, 112.1, 49.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3070, 3056, 3025, 2943, 2924, 2888, 2854, 1628, 1591, 1578, 1488, 1475, 1463, 1428, 1378, 1325, 1313, 1294, 1272, 1253, 1200, 1186, 1130, 1082, 1051, 1004, 910, 867, 850, 825, 768, 727, 708, 678.

MS (EI, 70 eV): *m/z* (%) = 307 (11, M^+), 183 (14), 182 (100), 127 (5).

HRMS (EI) for **$C_{19}H_{14}{}^{35}ClNO$** (307.0764): found: 307.0757 (M^+).

Synthesis of (1*S*, 2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-*N*-(2-chlorophenethyl)-*N*-methyl-1-phenylpropan-2-amine (86a)



Prepared according to **TP 1** from (1*S*,2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylpropan-2-amine (**85**; 279 mg, 1.0 mmol, 1.0 equiv) and 2-chlorobenzylzinc chloride (**52a**; 0.69 mL, 1.1 mmol, 1.1 equiv, 1.60 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 49:1) afforded **86a** as colorless oil (380 mg, 91%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.34-7.23 (m, 6H), 7.15-7.08 (m, 3H), 4.63 (d, *J* = 5.9 Hz, 1H), 2.81 (qi, *J* = 6.6 Hz, 1H), 2.71-2.61 (m, 4H), 2.32 (s, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.02 (s, 3H), -0.30 (s, 3H).

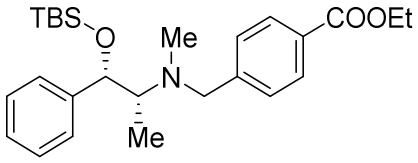
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 145.3, 138.7, 134.2, 131.2, 129.6, 127.9, 127.6, 127.1, 127.0, 127.0, 65.8, 54.6, 38.4, 33.0, 26.2, 18.4, 9.7, -4.0, -4.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2956, 2929, 2886, 2856, 2796, 1472, 1360, 1251, 1082, 1053, 1028, 1006, 863, 834, 816, 774, 747, 698, 680, 675.

MS (EI, 70 eV): *m/z* (%) = 417 (1, M^+), 402 (1), 198 (35), 197 (12), 196 (100), 139 (19), 103 (12), 73 (17).

HRMS (EI) for $\mathbf{C_{24}H_{36}{}^{35}ClNOSi}$ (402.2025, M^+-CH_3): found: 402.2024.

Synthesis of ethyl 4-((((1*S*, 2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-1-phenylpropan-2-yl)(methyl)amino)methyl)benzoate (86b)



Prepared according to **TP 1** from (1*S*,2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylpropan-2-amine (**85**; 279 mg, 1.0 mmol, 1.0 equiv) and (4-(ethoxycarbonyl)phenyl)zinc iodide (**53b**; 1.7 mL, 1.1 mmol, 1.1 equiv, 0.65 M in THF). Purification of the crude product by flash chromatography (Al_2O_3, *iso*hexane/EtOAc = 99:1) afforded **86b** as colorless oil (309 mg, 70%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.80 (d, *J* = 8.4 Hz, 2H), 7.28-7.20 (m, 5H), 6.96 (d, *J* = 8.4 Hz, 2H), 4.56 (d, *J* = 7.2 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 3.60-3.46 (m, 2H), 2.79 (qi, *J* = 6.6 Hz, 1H), 2.12 (s, 3H), 1.35 (t, *J* = 7.0, 3H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.83 (s, 9H), 0.0 (s, 3H), -0.29 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.7, 145.8, 144.8, 129.2, 128.7, 128.1, 127.6, 126.9, 126.9, 64.9, 60.7, 58.7, 37.3, 25.8, 18.1, 14.4, 9.1, -4.4, -5.0.

IR (Diamond-ATR, neat): $\tilde{V}$ / cm^{-1} = 2957, 2930, 2857, 2794, 1717, 1611, 1472, 1452, 1413, 1365, 1272, 1258, 1172, 1105, 1098, 1084, 1060, 1020, 863, 834, 775, 756, 699.

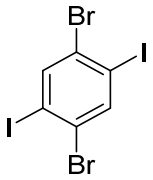
MS (EI, 70 eV): *m/z* (%) = 441 (1, M^+), 221 (15), 220 (100), 163 (28), 73 (7).

HRMS (EI) for $\mathbf{C_{26}H_{39}NO_3Si}$ (440.2626, M^+-H^+): found: 440.2616.

4. PREPARATION OF NEW BENZODITHIOPHENE BUILDING BLOCKS FOR COVALENT ORGANIC FRAMEWORKS

4.1. Preparation of Starting Materials

Synthesis of 1,4-Dibromo-2,5-diiodobenzene (90)



The reaction was performed as described in the literature.[105] A solution of *p*-dibromobenzene (**89**; 23.60 g, 100 mmol, 1.0 equiv) in concentrated sulfuric acid (300 mL) was heated to 125-135 °C. Iodine (96.40 g, 380 mmol, 3.8 equiv) was added portion wise, the reaction was stirred at 125-135 °C for one day and then cooled to room temperature. The reaction mixture was poured into ice water, the precipitate dissolved in DCM and extracted with sat. aq $Na_2S_2O_3$ (3 x 250 mL). The organic extracts were washed with sat. aq NaCl solution (200 mL) and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* and recrystallization from benzene afforded **90** as a white solid (34.6 g, 71%)

M.p.: 179.8 – 181.5 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.05 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 142.7, 129.6, 101.7.

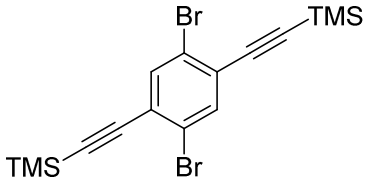
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3066, 2415, 2130, 1935, 1736, 1431, 1408, 1280, 1187, 1122, 1106, 1012, 999, 875.

MS (70 eV, EI): *m/z* (%) = 489 (47), 487 (100), 485 (55, M^+), 360 (23), 358 (12), 127 (17), 126 (18), 74 (35), 73 (11), 44 (17).

HRMS (EI) for **$C_6H_2Br_2I_2$** (485.6613): found: 485.6611 (M^+).

[105] S. H. Chanteau, J. M. Tour, *J. Org. Chem.* **2003**, *68*, 8750.

Synthesis of 1,4-Dibromo-2,5-*bis*(trimethylsilylethynyl)benzene (91)



To a solution of **90** (24.4 g, 50 mmol, 1.0 equiv) in triethylamine (300 mL) was added trimethylsilylacetylene (19.6 g, 200 mmol, 4.0 equiv), $PdCl_2(PPh_3)_2$ (350 mg, 0.5 mmol, 1 mol%) and CuI (190 mg, 1.0 mmol, 2 mol%) and the mixture was stirred for 2 h. After evaporation of the solvent *in vacuo*, the precipitate was dissolved in DCM (200 mL) and extracted with sat. aq NH_4Cl solution (3 x 200 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. Purification by flash chromatography (silica, *iso*hexane) and recrystallization from heptane afforded **91** as white crystals (18.4 g, 86%).

M.p.: 122.8 – 124.5 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.68 (s, 2 H), 0.28 (s, 18H).

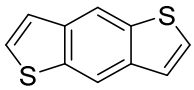
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 136.8, 126.8, 124.1, 103.4, 101.7, 0.10.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2896, 2165, 1738, 1462, 1341, 1246, 1196, 1062, 836, 760, 700.

MS (70 eV, EI) *m/z* (%) = 429 (17), 428 (12), 427 (41), 425 (18, M^+), 415 (13), 414 (50), 413 (25), 412 (100), 411 (22), 410 (45), 199 (16), 82 (22), 81 (23), 80 (12), 79 (27), 78 (15), 73 (17).

HRMS for **$C_{16}H_{20}Br_2Si_2$** (425.9470): found: 425.9464 (M^+).

Synthesis of Benzo[1,2-*b*:4,5-*b*']dithiophene (88)



The reaction was performed as described in the literature.[65] To a suspension of sodium sulfide trihydrate (containing ~ 60 % Na_2S, 5.20 g, 39.6 mmol, 4.0 equiv) in NMP (100 mL), 1,4-dibromo-2,5-*bis*(trimethylsilylethynyl)benzene (**91**; 4.28 g, 10.0 mmol, 1.0 equiv.) was added. Then, the mixture was heated at 185-195 °C for 12 h. After cooling to room temperature, the mixture was poured into the fourfold volume of sat. aq NH_4Cl (400 mL). The resulting precipitate was filtrated over celite, and dissolved in DCM (1.0 L). After washing with sat. aq NaCl solution (3 x 750 mL), and drying over $MgSO_4$, the solvent was evaporated *in vacuo* and the resulting crude product was purified

by column chromatography (silica, *iso*hexane). Benzo[1,2-*b*:4,5-*b*']dithiophene (**88**) was afforded as colorless crystals (1.52 g, 80%).

M.p.: 198.7 – 200.7 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.37 (d, *J* = 5.5 Hz, 2H), 7.48 (d, *J* = 5.5 Hz, 2H), 8.33 (s, 2H).

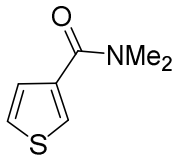
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 137.8, 137.5, 127.4, 123.3, 117.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3070, 1732, 1512, 1445, 1377, 1324, 1292, 1177, 1079, 1053, 890, 864, 834, 784, 734, 676.

MS (70 eV, EI): *m/z* (%) = 191 (10), 190 (100, M^+), 145 (16), 102 (11), 95 (30), 82 (13), 69 (15).

HRMS (EI) for **$C_{10}H_6S_2$** (189.9911): found: 189.9912 (M^+).

Synthesis of *N,N*-dimethyl-3-thiophenecarboxamide (94)



The reaction was performed as described in the literature.[106] In a dry argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, 3-bromothiophene (16.3 g, 9.37 ml, 100 mmol, 1.0 equiv) was dissolved in dry Et_2O (560 ml) and cooled down to -85 °C. Then, *n*BuLi (46.8 mL, 110 mmol, 1.1 equiv, 2.35 M in hexane) was added dropwise and the solution was stirred for 1 h at the given temperature. Next, dimethylcarbamoyl chloride (21.5 g, 200 mmol, 2.0 equiv) was added and the reaction mixture was allowed to warm up to room temperature and stirred overnight. The solution was quenched with sat. aq NH_4Cl solution (300 mL),extracted with Et_2O (3 x 200 mL) and dried over Na_2SO_4. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane:EtOAc = 8:2) to give **94** as a yellow oil (9.78 g, 63%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.52 (dd, *J* = 2.9 Hz, J = 1.0 Hz, 1H), 7.31 (dd, *J* = 5.0 Hz, J = 2.9 Hz, 1H), 7.21 (dd, *J* = 5.0 Hz , *J* = 1.0 Hz, 1H), 3.08 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 167.1, 137.0, 127.5, 126.6, 125.8.

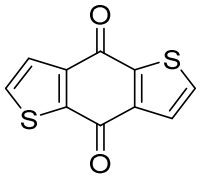
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3528, 3081, 2931, 1615, 1526, 1493, 1447, 1409, 1362, 1262, 1228, 1179, 1141, 1083, 1060, 1023, 952, 915, 885, 854, 816, 796, 739, 704, 676.

MS (EI, 70 eV): *m/z* (%) = 155 (43, M^+), 122 (13), 111 (100), 83 (15).

[106] P. Lucas, N. El Mehdi, H. A. Ho, D. Bélanger, L. Breau, *Synthesis* **2000**, *9*, 1253.

HRMS (EI) for **C_9H_4ONS** (155.0405): found: 155.0399 (M^+).

Synthesis of benzo[1,2-*b*:4,5-*b*']*bis*thiophene-4,8-dione (95)



The reaction was performed as described in the literature.[107] In a dry argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, **94** (7.65 g, 49.3 mmol, 1.0 equiv) was dissolved in Et_2O (165 mL) and *n*BuLi (23.1 mL, 54.2 mmol, 1.1 equiv, 2.35 M in hexane) was slowly added at 0 °C. The resulting mixture was stirred for 20 h and allowed to warm up to room temperature. The reaction was diluted with ice-cold water (300 mL) and the precipitate was filtered off, washed with water (250 mL) and dried *in vacuo*. The crude product **95** was obtained as a green solid (3.20 g, 59%) and was used without further purification.

M.p.: 262.6 – 264.0 °C

^{1}H-NMR (400 MHz, acetone-*d6*): δ / ppm= 8.07 (d, J = 5.0 Hz, 2H), 7.65 (d, J = 5.0 Hz, 2H).

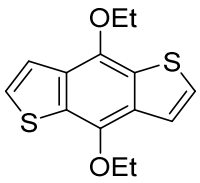
^{13}C-NMR (75 MHz, acetone-*d6*): δ / ppm= 174.2, 144.8, 142.8, 134.7, 126.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3284, 3094, 3077, 1831, 1704, 1643, 1621, 1541, 1505, 1493, 1416, 1382, 1281, 1199, 1097, 1008, 919, 848, 834, 764, 754, 725, 694.

MS (EI, 70 eV): *m/z* (%) = 222 (10), 220 (100, M^+), 192 (55).

HRMS (EI) for **$C_{10}H_4O_2S_2$** (219.9653): found: 219.9647 (M^+).

Synthesis of 4,8-diethoxybenzo[1,2-*b*:4,5-*b*']*dit*hiophene (92)



The reaction was performed based on the literature.[64a] A mixture of **95** (1.10 g, 4.99 mmol, 1.0 equiv), zinc dust (0.981 g, 15.0 mmol, 3.0 equiv), NaOH (10 mL) and EtOH (10 mL) was stirred at 95 °C for 2 h. Ethyl *p*-toluenesulfonate (3.00 g, 15.0 mmol, 3.0 equiv) was added and the resulting solution was stirred at 95 °C for further 3 h. The reaction mixture was allowed to cool down to room temperature

[107] D. W. Slocum, P. L. Gierer, *J. Org. Chem.* **1976**, *41*, 3668.

and was diluted with DCM (70 mL). The aqueous layer was extracted with DCM (4 × 100 mL) and the combined organic fractions were dried over Na_2SO_4. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane/DCM = 3:1) to give **92** as a colorless solid (0.675 g, 49%).

M.p.: 96.9 – 102.6 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.46 (d, J = 5.5 Hz, 2H), 7.35 (d, J = 5.5 Hz, 2H), 4.35 (q, J = 7.0 Hz, 4H), 1.47 (t, J = 7.0 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 144.3, 131.8, 130.4, 126.0, 120.3, 69.4, 16.1.

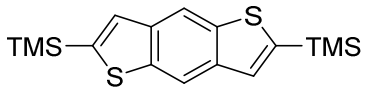
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3100, 2980, 2873, 1892, 1515, 1477, 1436, 1372, 1347, 1199, 1106, 1085, 1029, 977, 873, 810, 752, 736, 695, 661.

MS (EI, 70 eV): *m/z* (%) = 278 (27, M^+), 223 (11), 222 (13), 221 (100), 111 (37), 44 (31), 43 (80).

HRMS (EI) for **$C_{14}H_{14}O_2S_2$** (278.0435): found: 278.0428 (M^+).

4.2. Preparation of the BDT-Linker

Synthesis of 2,6-*Bis*(trimethylsilyl)benzo[1,2-*b*:4,5-*b*']*dit*hiophene (96)



In a flame-dried *Schlenk*-flask, equipped with a magnetic stirring-bar, an argon inlet and a septum, benzo[1,2-*b*:4,5-*b'*]*dit*hiophene (**88**, 1.90 g, 10.0 mmol, 1.0 equiv) was dissolved in THF (50.0 mL). The solution was cooled down to -30 °C and *n*BuLi (4.68 mL, 11.0 mmol, 1.1 equiv, 2.35 M in hexane) was added dropwise. After stirring for 30 min, chloro trimethylsilane (1.40 mL, 11.0 mmol, 1.1 equiv) was added and the solution was allowed to warm up to room temperature. After 45 min, the solution was again cooled to -30 °C, *n*BuLi and TMSCl were added as described before and the mixture was allowed to warm up to room temperature. The reaction was quenched with sat. aq $NaHCO_3$ (30 mL), extracted with diethyl ether (3 x 30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, *i*hexane) afforded **96** as a white solid (3.08 g, 92 %).

M.p.: 189.2 – 190.9 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.29 (s, 2H), 7.49 (s, 2H), 0.42 (s, 18H).

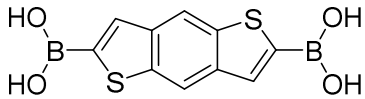
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 144.0, 141.1, 139.5, 130.2, 116.4, 0.04.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 1739, 1506, 1439, 1367, 1246, 1170, 1059, 963, 866, 833, 752, 697.

MS (70 eV, EI): *m/z* (%) = 336 (12), 335 (22), 334 (100, M^+), 321 (13), 320 (19), 319 (71), 152 (24), 73 (30).

HRMS (EI) for **$C_{16}H_{22}S_2Si_2$** (334.0701): found: 334.0685 (M^+).

Synthesis of benzo[1,2-*b*:4,5-*b*']*bis*thiophene-2,6-diyldiboronic acid (57)



2,6-Di(trimethylsilyl)benzo[1,2-*b*:4,5-*b*']dithiophene (**96**, 1.67 g, 5 mmol, 1.0 equiv) was dissolved in dry DCM (20 mL) and cooled to 0 °C. BBr_3 (1.0 mL, 10.5 mmol, 2.1 equiv) was added and the reaction mixture was stirred for 12 h. The reaction was quenched by adding 1 M NaOH/ice mixture (40 mL) and the phases were separated. The aqueous phase was washed with DCM (2x 20 mL), then

adjusted to pH 7 with 2 M HCl and extracted with ethyl acetate (3x 20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo* to afford **57** as a white solid (0.95 g, 68%).

M.p.: 313.1 – 315.2 °C

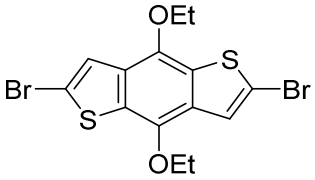
^{1}H-NMR (400 MHz, acetone-*d6*): δ / ppm = 8.44 (s, 2H), 8.00 (s, 2H).

^{13}C-NMR (100 MHz, acetone-*d6*): δ / ppm = 140.4, 139.6, 131.9, 117.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3351, 1541, 1435, 1398, 1366, 1341, 1312, 1177, 1163, 1106, 1033, 866, 645.

HRMS (ESI) for **$C_{10}H_8B_2O_4S_2$** (276.9966, M^+-H^+): found: 276.9973.

Synthesis of 2,6-dibromo-4,8-diethoxybenzo[1,2-*b*:4,5-*b*']*dit*hiophene (97)



In a dry argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, **92** (1.39 g, 5.0 mmol, 1.0 equiv) was dissolved in DMF (25 mL) and cooled down to 0 °C. *N*-bromosuccinimide (1.78 g, 10.0 mmol, 2.0 equiv) was added in one portion and the resulting solution was warmed to room temperature and stirred for 4 h. The reaction mixture was diluted with water (100 mL) and extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with water (6 × 100 mL) and dried over Na_2SO_4. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (silica, *iso*hexane) to give **97** as a colorless solid (1.50 g, 69%).

M.p.: 158.7 – 161.9 °C

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.41 (s, 2H), 4.26 (q, *J* = 7.0 Hz, 4H), 1.44 (t, *J* = 7.0 Hz, 6H).

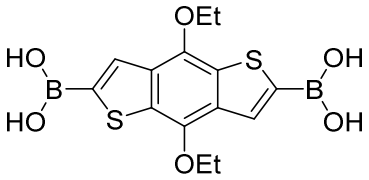
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 142.3, 131.4, 131.1, 123.2, 115.0, 69.7, 16.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2980, 2927, 2886, 1905, 1520, 1479, 1442, 1370, 1350, 1265, 1170, 1104, 1042, 999, 935, 894, 873, 809, 689, 668.

MS (EI, 70 eV): *m/z* (%) = 434 (23, M^+), 409 (25), 407 (44), 405 (22), 381 (54), 380 (18), 379 (100), 378 (14), 377 (47), 300 (30), 298 (28), 191 (16), 189 (11), 109 (11), 61 (12), 45 (11), 43 (70).

HRMS for **$C_{14}H_{12}O_2Br_2S_2$** (433.8640): found: 433.8649.

Synthesis of 4,8-diethoxybenzo[1,2-*b*:4,5-*b'*]*bis*thiophene-2,6-diyldiboronic acid (58)



In a dry argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, **97** (434 mg, 1.00 mmol, 1.0 equiv) was dissolved in THF (8 mL) and cooled down to -40°C. *n*BuLi (1.06 mL, 2.5 mmol, 2.5 equiv, 2.35 M in hexane) was added and the resulting solution was stirred for 1.5 h and cooled down to -85 °C. Then, tri*iso*propyl borate (0.69 mL, 3.0 mmol, 3.0 equiv) was added and the reaction mixture was allowed to warm up to room temperature and stirred overnight. The solution was diluted with half-conc. aq NH_4Cl solution (25 mL). The alkaline solution was acidified to pH 6 (with 2.0 M HCl) and was extracted with ethyl acetate (3 × 150 mL) and the combined organic layers were dried over Na_2SO_4. After filtration, the solvents were evaporated *in vacuo.* The crude product was suspended in *iso*hexane (70 mL) and the mixture was stirred at room temperature for 5 h. The precipitate was filtered off and dried *in vacuo.* **58** was obtained as green solid (184 mg, 50%) and was used without further purification.

M.p.: 271.9 - 274.3 °C

^{1}H-NMR (400 MHz, acetone-*d6*): δ / ppm= 8.14 (s, 2H), 4.39 (q, J = 7.2 Hz, 4H), 1.47 (t, J = 7.2 Hz, 6H).

^{13}C-NMR (75 MHz, acetone-*d6*): δ / ppm= 145.5, 135.1, 134.5, 130.3, 70.4, 16.8.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3209, 2978, 1532, 1445, 1373, 1344, 1320, 1161, 1084, 1046, 989, 959, 850, 788, 700.

HRMS (ESI) for $\mathbf{C_{14}H_{15}O_6B_2S_2}$ (365.0496): found: 365.0501 (M^+).

D: APPENDIX

LIST OF ABBREVIATIONS

aq	aqueous
BDT	benzo[1,2-*b*;4,5-*b'*]dithiophene
br.	broad
BTSM	*bis*(trimethylsilyl)methyl
Bu	butyl
cat.	catalytic
CAN	ceric(IV) ammonium nitrate
COF	covalent organic framework
conc.	concentrated
d	doublet
dba	dibenzylideneacetone
DBE	1,2-dibromoethane
DCM	dichloromethane
DME	dimethylether
DMF	dimethylformamide
DMG	directed metalation group
D*o*M	directed *ortho* metalation
E	electrophile
equiv.	equivalent
Et	ethyl
FG	functional group
GC	gas chromatography
h	hour
Hal	halogen

HHTP	2,3,6,7,10,11-hexahydroxytriphenylene
HRMS	high resolution mass spectroscopy
IR	infra-red
i	iso
J	coupling constant (NMR)
LDA	lithium diisopropylamide
LG	leaving group
M	molarity
m	meta
m	multiplet
Me	methyl
Met	metal
min	minute
MOF	metal organic framework
mol.	mole
mp.	melting point
MS	mass spectroscopy
Ms	molecular sieves
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
o	ortho
OLED	organic light-emitting diode
OTFT	organic thin film transistors
p	para
PG	protecting group
Ph	phenyl

Pr	propyl
prim	primary
q	quartet
rt	room temperature
s	singlet
sat	saturated
*s*Bu	*sec*-butyl
sec	secondary
s.m.	starting material
t	triplet
*t*Bu	*tert*-butyl
TBAF	tetra-*n*-butylammonium fluoride
TBS	*tert*-butyldimethylsilyl
TEA	triethylamine
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMDAM	*N,N,N',N'*-tetramethylmethanediamine
TMEDA	*N,N,N',N'*-tetramethylethylenediamine
TMS	trimethylsilyl
TMP	2,2,6,6-tetramethylpiperidyl
TP	typical procedure

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PUBLICATIONS

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