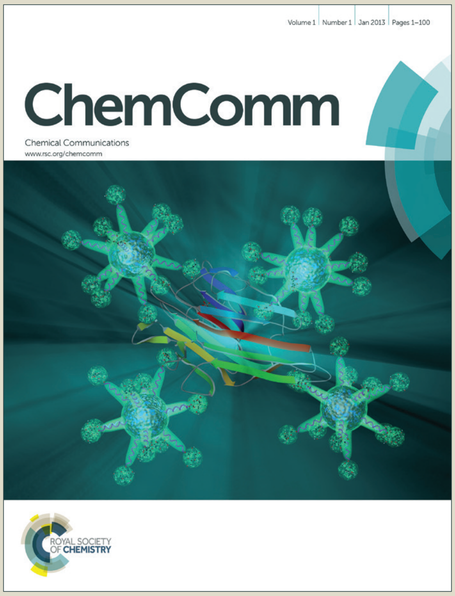
ChemComm

This article can be cited before page numbers have been issued, to do this please use: G. Kehr, G. Erker, C. G. Daniliuc, D. W. Stephan and C. Eller, *Chem. Commun.*, 2015, DOI: 10.1039/C5CC01806D.



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

View Article Online
DOI: 10.1039/C5CC01806D

Journal Name

RSCPublishing

COMMUNICATION

Thiophene Synthesis by 1,1-Carboboration

Cite this: DOI: 10.1039/x0xx00000x

Christina Eller,[a,b] Gerald Kehr,[a] Constantin G. Daniliuc,[a‡] Douglas W. Stephan,*[b] Gerhard Erker*[a]

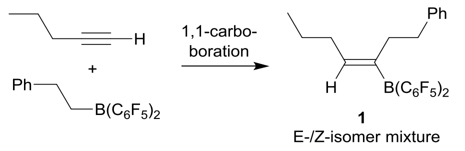
Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Reaction of bis(*tert*-butylethynyl)sulfide with the boron Lewis acid reagents X-B(C_6F_5)$_2$ (X = CH_3, Cl, C_6F_5) in pentane at r.t. gave the respective borylated thiophenes in a sequence of 1,1-carboboration reactions. In contrast, bis(phenylethynyl)-sulfide reacted with B(C_6F_5)$_3$ only in a 2:1 molar ratio to give a benzothiophene derivative.

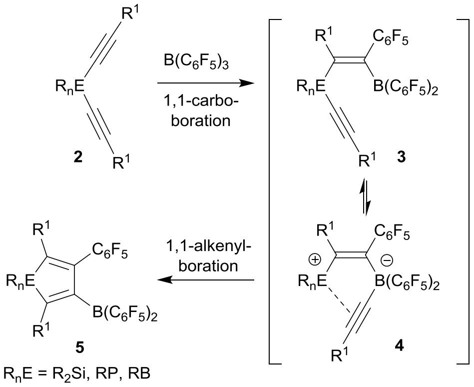
The 1,1-carboboration reaction has become an increasingly attractive alternative to the 1,2-hydroboration reaction for making substituted alkenylboranes.[1] Using strongly electrophilic R-B(C_6F_5)$_2$ boranes has resulted in a major improvement of the 1,1-carboboration reaction since now alkynes with conventional organic substituents could undergo this reaction under mild conditions to give **1** (Scheme 1).[2-4]



Scheme 1

With geminal diacetylenes (**2**), sequential alkyne 1,1-carboboration reactions (**3**) followed by intramolecular 1,1-alkenylboration of **4** have resulted in the formation of heterocyclic elementacyclopentadienes (**5**). Siloles,[5,6] phospholes[7] and even boroles[8,9] have been prepared by facile one-pot procedures in this way (Scheme 2).[10,11] In this manuscript, we describe an extension of this 1,1-carboboration protocol to the preparation of a series of thiophenes.[11] Suitably substituted linked thiophenes play an important role in organic materials chemistry.[12]

Treatment of bis(phenylethynyl)sulfide **6a**[13] with 0.5 molar equiv. of B(C_6F_5)$_3$ in pentane gave a red solution. After 2 d at 25 °C the mixture was worked up to give the substituted benzothiophene product **8a** in 58% yield. Compound **8a** was characterized by X-ray diffraction (Figure 1). The X-ray crystal structure analysis shows the planar benzothiophene framework with a phenyl substituent at the α-position of the thiophene ring and a C_6F_5 substituent at the β-carbon atom. The annulated phenylene ring has phenyl groups on C4, C6 and C7 and bears a SH substituent on C5.



Scheme 2

Analogous treatment of *bis*(*p*-tolylethynyl)sulfide **6b** with B(C_6F_5)$_3$ (0.5 molar equiv.) afforded the analogous benzothiophenethiol product **8b** in 40% yield after chromatographic workup. Again, the ^{19}F NMR signals were typical of a single C_6F_5 substituent and the ^{1}H NMR spectrum showed the expected SH signal. Also all expected ^{13}C NMR resonances were observed and the formation of **8b** was confirmed by X-ray diffraction (see the Supporting Information).

Compounds **8a,b** are obtained by a hydrolytic cleavage of the S-B(C_6F_5)$_2$ linkage during the workup procedure. The proposed precursors **7a,b** were confirmed by a series of 2D NMR experiments in which the formation of the compounds **7** was observed *in situ*. Three of the four Ph substituents and the single C_6F_5 group at the thiophene ring exhibit hindered rotation at room temperature on the NMR time

DOI: 10.1039/C5CC01806D

scale. The S-$B(C_6F_5)_2$ moiety gives rise to inequivalent C_6F_5 groups and consequently shows two sets of three ^{19}F NMR resonances (see Supporting Information). The *in situ* experiments also confirmed the 2 : 1 **6a** : $B(C_6F_5)_3$ stoichiometry of the reaction, as the corresponding reaction in a 1 : 1 molar ratio invariably gave a mixture of **7a** and a 0.5 molar equivalents of unused borane (identified by ^{19}F NMR spectroscopy). Similar monitoring of the *in situ* reaction between **6b** and $B(C_6F_5)_3$ showed NMR signals of the intermediate S[B] product **7b** (see the Supporting Information).

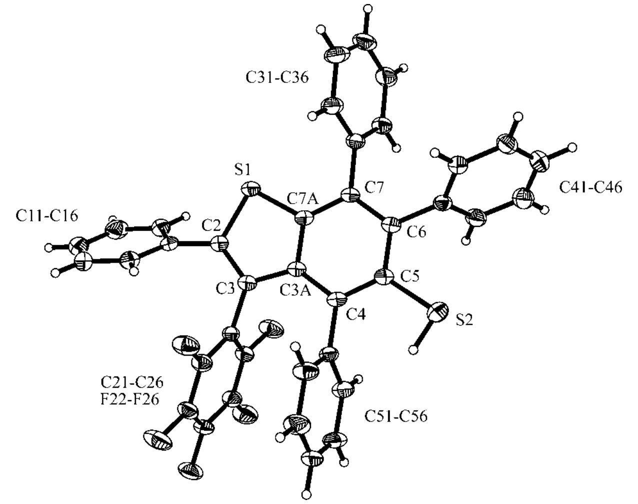
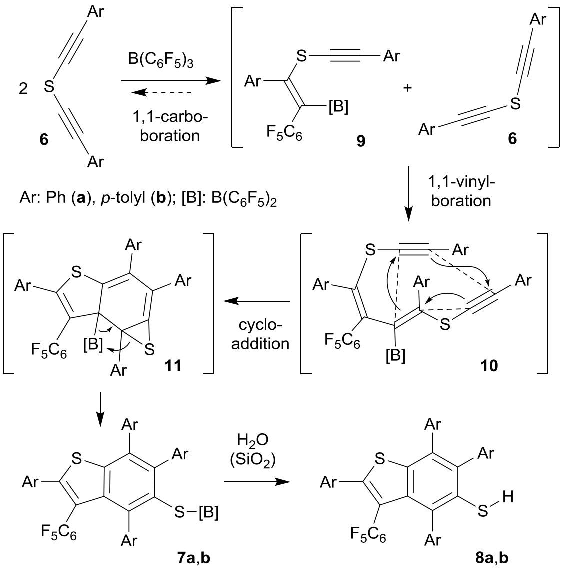
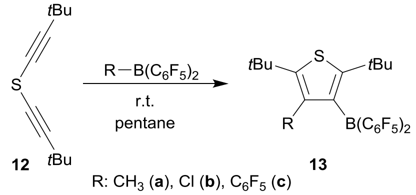


Figure 1. A view of the molecular structure of compound **8a** (thermal ellipsoids are shown with 30% probability).



Scheme 3

Scheme 3 provides a possible mechanistic pathway for the selective formation of the 2 : 1 carboboration product of compound **6** with $B(C_6F_5)_3$. Initial 1,1-carboboration at one arylalkynyl unit effects transfer of the C_6F_5 group generating the alkenylborane intermediate **9**. Subsequent intermolecular 1,1-vinylboration reaction with a second equivalent of **6** generates **10** which thermally undergoes an intramolecular ring-closing [2+2+2]cycloaddition reaction forming **11**. Finally Lewis acid induced opening of the thiirane ring gave the observed product **7** which was converted to the thiol derivative **8** on hydrolysis during the work-up.



Scheme 4

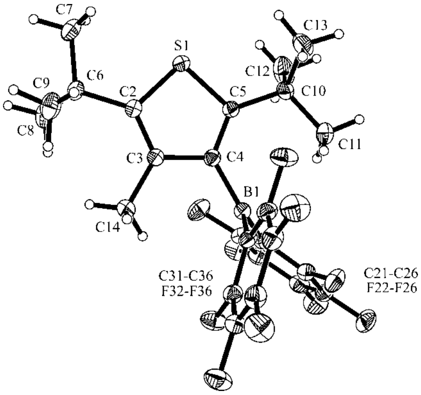


Figure 2. Molecular structure of the borylthiophene derivative **13a** (thermal ellipsoids are shown with 30% probability).

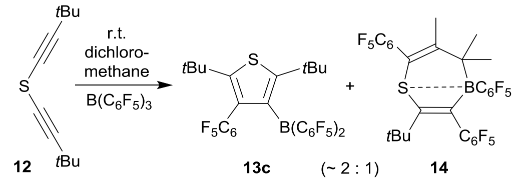
In contrast the reaction of bis(*tert*-butylethynyl)sulfide (**12**)[13] with a small series of $RB(C_6F_5)_2$ reagents in pentane gave the respective borylated thiophene derivatives (Scheme 4). For example, the reaction of bis(*tert*-butylethynyl)sulfide (**12**) with $MeB(C_6F_5)_2$[14] in pentane solution for 10 days resulted in a yellow solution that on cooling to −35 °C yielded the product **13a** in 50% yield. $^{1}H/^{13}C$ NMR data showed signals attributed to inequivalent *tert*-butyl substituents and a methyl substituent. The $B(C_6F_5)_2$ substituent showed a ^{11}B NMR resonance (δ 63.9) and ^{19}F NMR features ($\Delta\delta^{19}F_{m,p}$ = 15.3) typical of a planar tricoordinated boron center. The product **13a** was also characterized by X-ray diffraction (Figure 2) confirming the nature of this borylthiophene product with a pair of *tert*-butyl substituents bonded to the α-carbon atoms and methyl and $B(C_6F_5)_2$ substituents on the *β*-carbon atoms of the thiophene ring. This confirms selective migration of the methyl group from boron to carbon during the 1,1-carboboration.[2]

In a similar fashion reactions of bis(*tert*-butylethynyl)sulfide (**12**) with the $ClB(C_6F_5)_2$ or $B(C_6F_5)_3$ afforded **13b** or **13c** in 45% and 50% yield, respectively. NMR data and X-ray crystal structures (see the Supporting Information) confirmed chloride and C_6F_5 migrations yielding the β-substituted thiophenes.

Interestingly repetition of the reaction between the bis(*tert*-butylethynyl)sulfide (**12**) and $B(C_6F_5)_3$ in the polar solvent dichloromethane, monitored by NMR spectroscopy, showed a slightly different outcome. After ca. 30 min. two new compounds were formed and identified as the products **13c**, and the new compound **14** in a **13c** : **14** ≈ 2 : 1 molar ratio (Scheme 5). Slow evaporation of the dichloromethane solvent at −35 °C eventually gave single crystals of

View Article Online
DOI: 10.1039/C5CC01806D

product **14** (Figure 3). In solution compound **14** shows a ^{11}B NMR resonances (δ 7.7) consistent with a tetracoordinated borate fragment, while the ^{19}F NMR signals are consistent with three C_6F_5 substituents. The ^{1}H/^{13}C NMR resonances correspond to a single methyl substituent and a pair of geminal methyl group in addition to a *tert*-butyl substituent. These data together with the results of an X-ray diffraction analysis confirmed that compound **14** contains a seven-membered ring featuring a bis(alkenyl)sulfide fragment subunit interacting with the transannular B-C_6F_5 group (B1-S1 2.073(2) Å). The unsaturated C_3-bridge is a tetrasubstituted allyl unit with a CMe_2 unit adjacent to boron and the remaining C(Me)=C(C_6F_5) group connecting it to sulfur.



Scheme 5

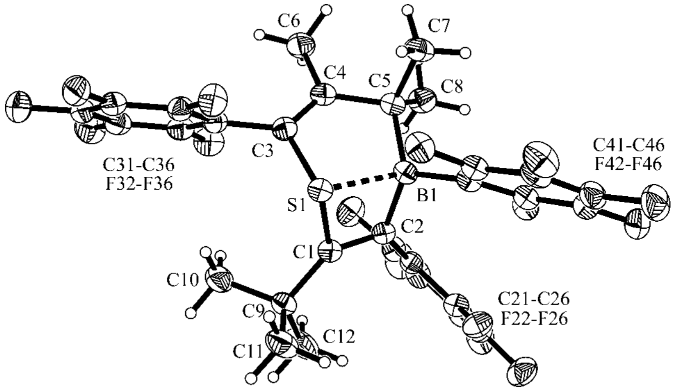
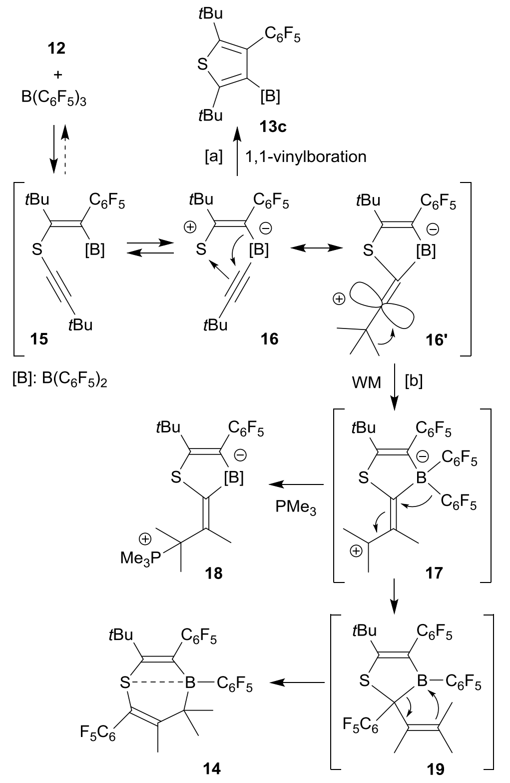


Figure 3. A projection of the molecular structure of compound **14**. Thermal ellipsoids are shown with 30% probability.

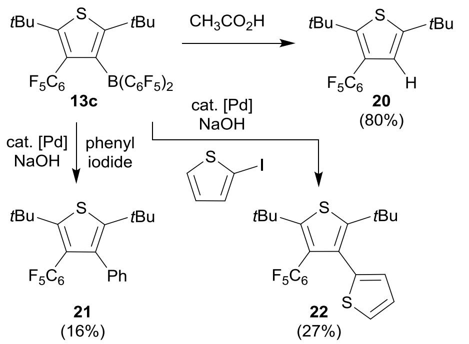
The products **13c** and **14** are formed in competing pathways (Scheme 6). We assume a reaction pathway of the 1,1-carboboration reaction that is similar to that proposed by Wrackmeyer et al.[15,16] This should then proceed by means of a reactive intermediate **16**[15] formed subsequently to the initial 1,1-carboboration step at the first alkynyl unit (**15**). The intramolecular 1,1-vinylboration starting from the intermediate **16** would directly give the thiophene derivative **13c** (pathway [a] in Scheme 6). It is well conceivable that reaction branching might be occur at the stage of the intermediate **16** ↔ **16'**,[16] involving the Wagner-Meerwein rearrangement step from the tert-butyl group at the activated bridging alkynyl group (**16'**) to enter into a typical carbenium ion pathway via **17** (which was successfully trapped by PMe_3 to give **18** (see the Supporting Information)) and **19** to give the observed competing product **14** (pathway [b] in Scheme 6).

The boryl substituent at these thiophenes can be removed by protonolysis: treatment of *in situ* generated **13c** with excess acetic acid in pentane solution (r.t., 2 h) gave the trisubstituted thiophene derivative **20** in 80% yield (Scheme 7).



Scheme 6. WM: Wagner-Meerwein rearrangement

Alternatively, **13c** was subjected to a Suzuki-Miyaura cross-coupling reaction with phenyl iodide. This afforded replacement of the boryl substituent by a phenyl group to give **21** (Scheme 7). Cross coupling with α-iodothiophene gave the bis(thiophene) derivative **22** (Scheme 7). Both compounds were isolated and characterized by spectroscopy and X-ray diffraction (see the Supporting Information and Figure 4). In the case of **22** the attachment of the 2-thienyl substituent at the β-carbon atom (C4) of the central tetra-substituted thiophene ring was confirmed by the X-ray crystal structure analysis: it exhibits a marked deviation from planarity (θ C5A-C4A-C6A-S2A 93.2(3)°).



Scheme 7

With this study we have the extended sequential 1,1-carboboration/ 1,1-vinylboration reaction scheme to the synthesis of thiophene derivatives. A limited series of intermolecular variants to yield functionalized benzothiophenes and intramolecular variants yielding substituted boryl-thiophenes was described and these borylsubstituted heteroarenes were shown to be amenable to cross-coupling reactions.

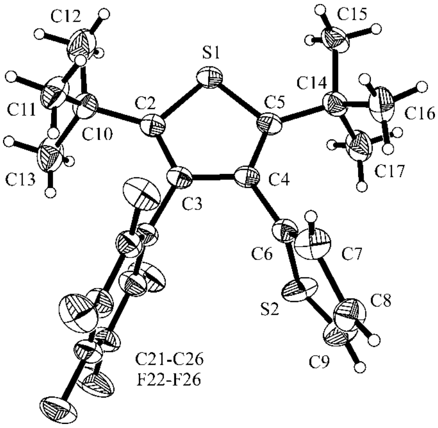


Figure 4. A projection of the bis(thienyl) product **22** [thermal ellipsoids are shown with 30% probability; only one molecule of two found in the asymmetric unit is shown (molecule A)].

Our present study shows that the 1,1-carboboration reaction yielding the thiophene **13c** is competing with a carbocation route. We cannot decide whether these two pathways are representing different reaction branches from the beginning or if the branching occurs at the stage of a common intermediate such as e.g. the zwitterion **16** ↔ **16'** which offers an attractive route to the assumed carbenium ion intermediate **17**. In dichloromethane both the products of the 1,1-carboboration and the competing carbenium ion route are experimentally observable and discernable. This observation will probably be useful for designing selective additional applications of the unique 1,1-carboboration reaction and its subsequent reaction sequences in order to further extend the scope of application of this attractive carbon-carbon bond forming reaction. We think that this new synthetic scheme might become a welcome methodical addition to the existing variants of thiophene syntheses.

Financial support from the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

Notes and references

[a] Organisch-Chemisches Institut der Universität Münster, Corrensstraße 40, 48149 Münster, Germany; E-Mail: erker@uni-muenster.de; Fax: +49-251-8336503.
[b] Department of Chemistry University of Toronto, 80 St. George Street, Toronto, ON, M5S 3H6, Canada.

‡ X-ray crystal structure analysis

† Electronic Supplementary Information (ESI) available: Detailed description of the experiments, characterization of all compounds and crystal structure data as CIF files (CCDC numbers are 1044969 to 1044977): See DOI: 10.1039/c000000x/

1 B. Wrackmeyer, *Coord. Chem. Rev*. 1995, **145,** 125; b) B. Wrackmeyer, *Heteroat. Chem.* 2006, **17**, 188.

2 a) C. Chen, F. Eweiner, B. Wibbeling, R. Fröhlich, S. Senda, Y. Ohki, K. Tatsumi, S. Grimme, G. Kehr and G. Erker, *Chem. Asian J.* 2010, **5**, 2199; b) C. Chen, G. Kehr, R. Fröhlich and G. Erker, *J. Am. Chem. Soc.* 2010, **132**, 13594; c) C. Chen, R. Fröhlich, G. Kehr and G. Erker, *Org. Lett*. 2011, **13**, 62.

3 Review: G. Kehr and G. Erker, *Chem. Commun*., 2012, **48**, 1839.

4 a) C. Jiang, O. Blacque and H. Berke, Organometallics 2010, 29, 125; b) C. Fan, W. Piers, M. Parvez and R. McDonald, Organometallics 2010, 29, 5132.

5 a) R. Köster, G. Seidel, J. Süß and B. Wrackmeyer, *Chem. Ber*. 1993, **126**, 1107; b) R. Köster, G. Seidel, I. Klopp, C. Krüger, G. Kehr, J. Süß and B. Wrackmeyer, *Chem. Ber*. 1993, **126**, 1385; c) B. Wrackmeyer, G. Kehr and J. Süß, J. *Chem. Ber*. 1993, **126**, 2221; d) B. Wrackmeyer, O. L. Tok, E. V. Klimkina, W. Milius, *Eur. J. Inorg. Chem*. 2010, 2276.

6 a) G. Dierker, J. Ugolotti, G. Kehr, R. Fröhlich and G. Erker, *Adv. Synth. Catal.* 2009, **351**, 1080; b) J. Ugolotti, G. Kehr, R. Fröhlich and G. Erker, *Chem. Commun.*, 2010, **46**, 3016.

7 a) J. Möbus, Q. Bonnin, K. Ueda, R. Fröhlich, K. Itami, G. Kehr and G. Erker, *Angew. Chem. Int. Ed.,* 2012, **51**, 1954; b) J. Möbus, A. Galstyan, A. Feldmann, C. G. Daniliuc, R. Fröhlich, C. A. Strassert, G. Kehr and G. Erker, *Chem. Eur. J.*, 2014, **20**, 11883.

8 a) F. Ge, G. Kehr, C. G. Daniliuc and G. Erker, *J. Am. Chem. Soc.* 2014, **136**, 68; b) F. Ge, G. Kehr, C. G. Daniliuc and G. Erker, *Organometallics*, 2015, **34**, 229.

9 For 1,1-carboboration reactions to group 4 metallacyclopentadienes see e.g.: a) A. Sebald and B. Wrackmeyer, *J. Chem. Soc., Chem. Commun.* 1983, 1293; b) A. Sebald and B. Wrackmeyer, *J. Organomet. Chem*. 1986, **304**, 271; c) B. Wrackmeyer, A. Pedall and J. Weidinger, *J. Organomet. Chem.* 2002, **649**, 225.

10 For a zirconocene route to thiophenes see e.g. S. A. Johnson, F.-Q. Liu, M. C. Suh, S. Zürcher, M. Haufe, S. S. H. Mao and T. Don Tilley, *J. Am. Chem. Soc*. 2003, **125**, 4199.

11 C. Eller, C. G. Daniliuc, R. Fröhlich, G. Kehr and G. Erker, *Organometallics* 2013, **32**, 384.

12 E.g. a) A. Wakamiya, K. Mori, T. Araki and S. Yamaguchi, *J. Am. Chem. Soc.* 2009, **131**, 10850; b) G. C. Welch and G. C. Bazan, *J. Am. Chem. Soc.* 2011, **133**, 4632; c) A. Iida and S. Yamaguchi, *J. Am. Chem. Soc.* 2011, **133**, 6952; d) S. Saito, K. Matsuo and S. Yamaguchi, *J. Am. Chem. Soc.* 2012, **134**, 9130; e) Z. B. Henson, K. Müllen and G. C. Bazan, *Nat. Chem.* 2012, **4**, 699; f) J. A. Love, I. Nagao, Y. Huang, M. Kuik, V. Gupta, C. J. Takacs, J. E. Coughlin, L. Qi, T. S. van der Poll, E. J. Kramer, A. J. Heeger, T.-Q. Nguyen and G. C. Bazan, G. C. *J. Am. Chem. Soc*. 2014, **136**, 3597.

13 Q. Su, Z.-J. Zhao, F. Xu. P.-C. Lou, K. Zhang, D.-X. Xie, L. Shi, Q.-Y. Cai, Z.-H. Peng and D.-L. An, *Eur. J. Org. Chem*. 2013, 1551.

14 $B(C_6F_5)_3$: a) A. G. Massey and A. J. Park, *J. Organomet. Chem.* 1964, **2**, 245; b) C. Wang, G. Erker, G. Kehr, K. Wedeking and R. Fröhlich, *Organometallics* 2005, **24**, 4760; $MeB(C_6F_5)_2$: see ref. 2c; $ClB(C_6F_5)_2$: J. D. Parks, W. E. Piers and G. P. A. Yap, *Organometallics* 1998, **17**, 5492.

15 a) B. Wrackmeyer, K. Horchler and R. Boese, *Angew. Chem. Int. Ed.* 1989, **28**, 1500; b) B. Wrackmeyer, G. Kehr and R. Boese. *Angew. Chem. Int. Ed.* 1991, **30**, 1370; c) B. Wrackmeyer, S. Kundler and R. Boese, *Chem. Ber.* 1993, **126**, 1361; d) B. Wrackmeyer, S. Kundler, W. Milius and R. Boese, *Chem. Ber*. 1994, **127**, 333.

16 a) B. Wrackmeyer, G. Kehr, A. Sebald and J. Kümmerlen, *Chem. Ber*. 1992, **125**, 1597; b) B. Wrackmeyer, G. Kehr and S. Willbold, *J. Organomet. Chem.* 1999, **590**, 93; c) B. Wrackmeyer, P. Thoma, S. Marx, T. Bauer and R. Kempe, *Eur. J. Inorg. Chem.* 2014, 2103.

View Article Online
DOI: 10.1039/C5CC01806D

TOC