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1,1-Carboboration Route to Substituted Naphthalenes

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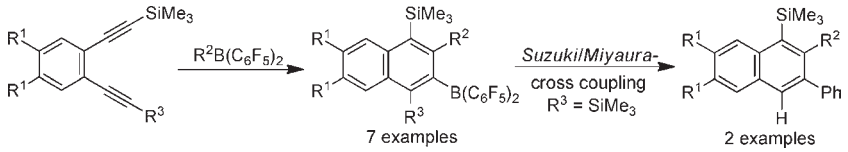
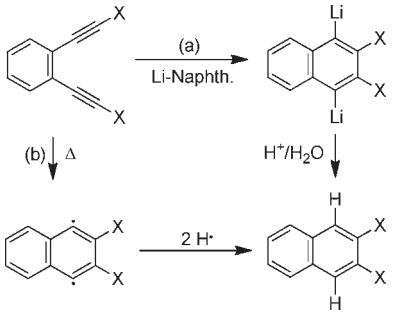
ABSTRACT



1,2-Bis(alkynyl)benzene derivatives react with strongly electrophilic boranes to yield in boryl-functionalized bulky naphthalene derivatives by means of a sequence of 1,1-carboboration reactions. These substrates can be functionalized by transition metal catalyzed cross-coupling reactions.

1,2-Bis(alkynyl)benzenes feature the correct number of π-functionalized carbon atoms necessary for ring closure reactions to yield the naphthalene framework, but they are lacking a pair of σ-substitutents at the central sp-carbon atoms of the acetylenic moieties. In other words, the substrates **1** possess the wrong formal carbon oxidation states for a direct conversion to the respective naphthalene nucleus. Therefore, reductive cyclizations and related multistep processes needed to be developed for the bis(alkynyl)benzene to naphthalene interconversion. Typical examples include the reductive coupling induced by stoichiometric Li-naphthalenide (see Scheme 1, pathway a).[1] Metal or thermally induced variants of the Bergman cyclization, i.e., a diradical pathway, eventually including H-abstraction, provide interesting alternatives (Scheme 1, pathway b).[2]

Scheme 1



We have recently shown that the strongly electrophilic borane $B(C_6F_5)_3$[3] undergoes rapid 1,1-carboboration reactions with a variety of 1-alkynes to yield the respective alkenylboranes.[4] At elevated temperatures, even internal alkynes underwent this reaction, which constitutes a novel C−C bond activation process.[5,6]

We have used such modern versions of the "Wrackmeyer 1,1-carboboration reaction"[7−9] to form siloles[10] or

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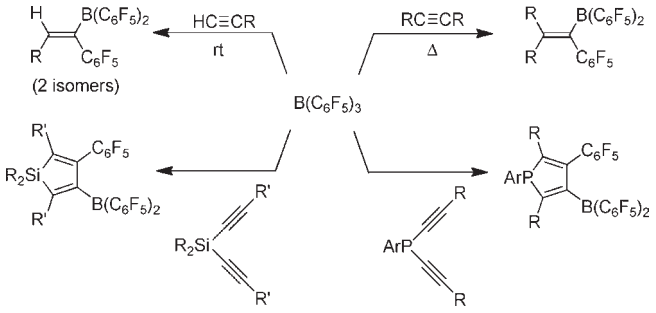
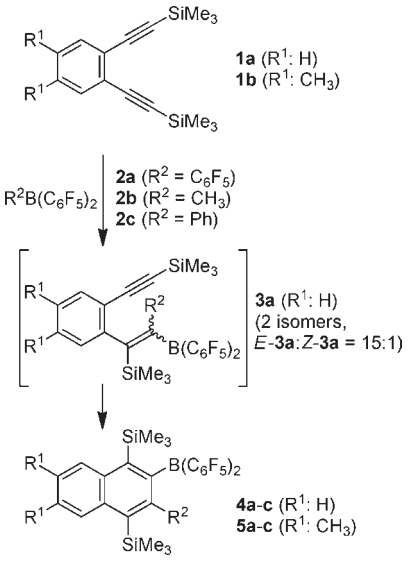
Scheme 2



Scheme 3



phospholes[11] from their respective acetylenic precursors (see Scheme 2). We have now been able to extend these series of sequential 1,1-carboboration reactions to 1,2-bis(alkynyl)benzene/$B(C_6F_5)_3$ systems to form the respective naphthalene derivatives in a novel, straightforward way. In this account, we present some selected examples describing this new development.

The starting material of our study, 1,2-bis(trimethylsilylethynyl)benzene (**1a**), was prepared by Sonogashira coupling of *o*-diiodobenzene with trimethylsilylacetylene according to a literature procedure.[12] The *o*-xylene derived bisacetylene substrate (**1b**) was synthesized analogously.[13] The compounds **1** were then reacted with the boranes **2**. The reaction of $B(C_6F_5)_3$ with **1a** is a typical example. The components were mixed in toluene at room temperature and kept at reflux temperature overnight to ensure complete conversion. Workup of the reaction mixture then gave the product **4a** as a yellow solid in 85% yield. Compound **4a** was characterized by X-ray diffraction (single crystals were obtained by slow evaporation of the solvent of a solution of **4a** in *n*-pentane at −40 °C). The X-ray crystal structure analysis confirmed the ring closure reaction of the phenylene linked bis-acetylenic starting material by a sequence of 1,1-carboboration reactions to give the respective tetrasubstituted naphthalene framework.

It contains the newly formed arene C2−C3 linkage (1.439(4)Å) with the adjacent $C(sp^2)$−$C(sp^2)$ bonds (C1−C2 1.397 Å, C3−C4 1.383(4) Å). The pair of Me_3Si-groups is now found at the naphthalene carbon atoms C1 (C1−Si11 1.905(3) Å) and C4 (C4−Si41 1.915(3) Å). The boryl substituent [$-B(C_6F_5)_2$] is found bonded to C2 (B1−C2 1.568(4) Å), and the remaining $-C_6F_5$ substituent that was shifted from boron to carbon during the 1,1-carboboration reaction is found at C3 (C3−C51 1.501(4) Å). The plane of the C_6F_5 substituent is rotated by 98.3° relative to the naphthalene framework. Similary, the coordination plane of the adjacent trigonal-planar boron substituent (sum of the C−B−C angles at boron: 359.8°) is rotated from the naphthalene plane by 62.1° (see Figure 1).

In solution, compound **4a** features the NMR signals of the pair of Me_3Si-substituents [^1H δ 0.17, −0.05 (each 9H)] and a ^{11}B NMR resonance (δ 65) typical of a tricoordinated boron center with this substituent combination. The ^{19}F NMR features of the $-B(C_6F_5)_2$ moiety show the typical large separation of the *m*- and *p*-F signals (BC_6F_5[a]: $\Delta\delta^{19}F_{m,p}$ = 21.6, $\Delta\delta^{19}F_{m',p}$ = 22.2; BC_6F_5[b]: $\Delta\delta^{19}F_{m,p}$ = 14.2, $\Delta\delta^{19}F_{m',p}$ = 17.3; measurement at 253 K)[14] and the signals of the single C-bound $-C_6F_5$ group.

Analogous treatment of the substrate **1a** with $CH_3B(C_6F_5)_2$ (**2b**)[15] proceeded with high chemoselectivity to give the product **4b** in 87% yield, which was formed by predominant migration of the methyl substituent in the respective 1,1-carboboration step. The product (see Scheme 3) shows the typical NMR signals of the $-B(C_6F_5)_2$ group

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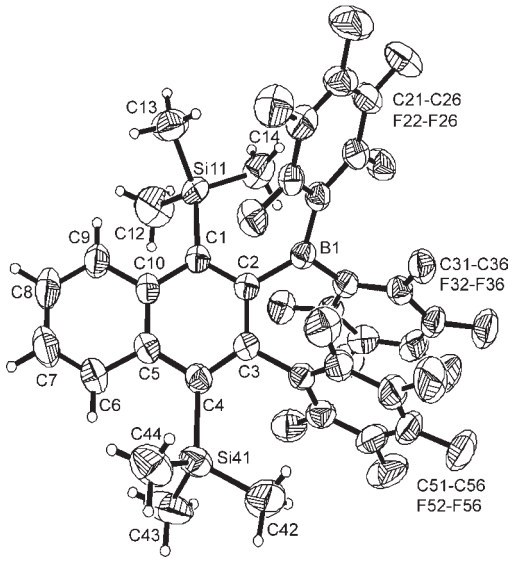

Figure 1. A view of the molecular structure of the borylnaphthalene product **4a**.

[δ 65 (^{11}B), δ −126.7, −144.3, −161.2 (^{19}F)] and the NMR resonances of the $-CH_3$ substituent at the adjacent naphthalene position at δ 2.35 (^{1}H, 3H) and δ 27.3 (^{13}C), respectively. Treatment of **1a** with $PhB(C_6F_5)_2$ (**2c**)[16] proceeded analogously to yield the tetrasubstituted naphthalene derivative **4c** (85% isolated, see Scheme 3; for details see the Supporting Information).

We have also reacted the *o*-xylene derived bis-acetylene substrate **1b** with the **2a**–**c** reagents. In each case, we did isolate the corresponding hexasubstituted naphthalenes in high yields [**5a**: 90%, **5b**: 91%, **5c**: 58%; see Scheme 3]. The products were characterized by C,H-elemental analysis and by spectroscopy; compound **5a** was also characterized by X-ray diffraction. The structural analysis confirmed the substitution pattern resulting from the series of consecutive 1,1-carboboration reactions that formed these compounds. The structural parameters of compound **5a** are similar to those of **4a** (for details see the Supporting Information; see also Figure 2).

We assume that the 1,2-bis(alkynyl)benzene + borane transformation to give the naphthalene derivatives proceeds by means of a sequence of 1,1-carboboration reactions. This was supported by the observation of a respective intermediate stage when we carried out the reaction under milder conditions with direct monitoring by NMR. Thus, the treatment of **1a** with $B(C_6F_5)_3$ (**2a**) in toluene-d_8 at room temperature rapidly resulted in the formation of a ca. 15:1 mixture of a pair of 1:1 reaction products, which we tentatively have assigned the structure of the two geometrical isomers (*E*/*Z*-**3a**) of the 1,1-carboboration product of one of the pendant —C≡C—$SiMe_3$ groups (see Scheme 3).

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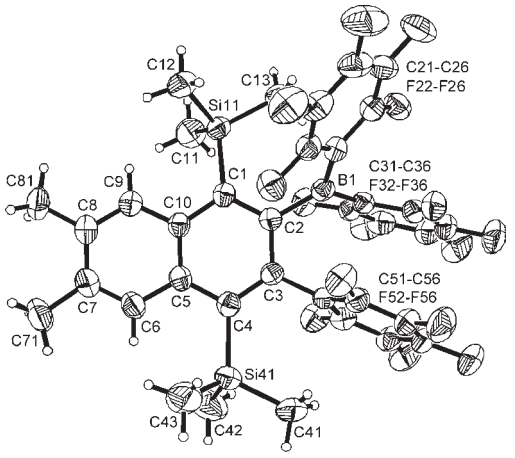
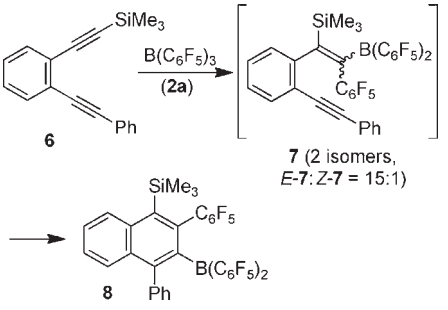


Figure 2. Molecular structure of compound **5a**.

The major **3a** isomer was tentatively assigned as *E*-isomer, which shows the ^{1}H NMR signals of a pair of Me_3Si-groups at δ 0.32 and −0.02 (each 9H) and ^{13}C NMR signals of the remaining alkynyl unit at δ 104.0 (C≡) and 99.0 (≡C[Si]). The newly formed olefinic C(sp^2) carbon atom adjacent to the aromatic ring (=C[Si]) is found at δ 170.0 (corresponding =C[B] not located). Intermediate **3a** exhibits a ^{11}B NMR resonance at δ 63 and, most importantly, the ^{19}F NMR signals of the relocated single $-C_6F_5$ group [δ −133.6 (*o*), −153.6 (*p*), −162.5 (*m*)] separated from the double intensity trio of the respective $-B(C_6F_5)_2$ ^{19}F NMR resonances (δ −125.6 (*o*), −144.1 (*p*), −160.4 (*m*)]. Warming of the sample for ca. 1 d at 50 °C eventually resulted in a close to complete conversion to the naphthalene derivative **4a**.

Scheme 4



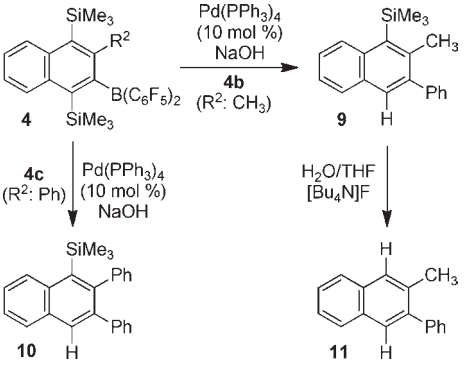
The reaction of the unsymmetrical bis(alkynyl)benzene starting material **6** with $B(C_6F_5)_3$ under analogous reaction conditions took a similar course. At room temperature, we observed the rapid formation of a 15:1 mixture of two isomers, to which we also tentatively assign the structures of the *E*/*Z*-isomers of the initial 1,1-carboboration product. From the spectroscopic data, we assume that this first 1,1-carboboration step was taking place regioselectively at the —C≡C—$SiMe_3$ section of the starting material **6**

(see Scheme 4). The major isomer of **7** features a ^{11}B NMR signal at δ 67, a Me_3Si- ^1H NMR resonance at δ 0.00, and the ^{13}C NMR resonance of the adjacent alkenyl carbon atom (=C[Si]) at δ 169.7. We monitored the typical sets of ^{19}F NMR features of the $=C(C_6F_5)B(C_6F_5)_2$ moiety (for details see the Supporting Information). The remaining —C≡C—Ph substituent shows its acetylenic ^{13}C NMR features at δ 94.3 and 88.4. Warming to 50 °C for ca. 1 day led to conversion of the 1,1-carboboration intermediate **7** to the respective naphthalene derivative **8** with a similar qualitative rate, as it was observed for the **3a** to **4a** conversion.

The series of strongly electrophilic bulky naphthylboranes that have become readily available by our advanced 1,1-carboboration route are likely to become interesting Lewis acids in their own right, e.g., for applications in frustrated Lewis pair chemistry.[17,18] Since they are also reactive tricoordinate arylborane derivatives, we have employed these new products as reagents in Suzuki–Miyaura cross-coupling reactions.[19] For this purpose, we have treated the example **4b** (R^1 = H, R^2 = CH_3) with phenyl iodide and aqueous NaOH base with a catalytic quantity of $Pd(PPh_3)_4$ (10 mol %) in THF (70 °C, 12 h). The cross-coupling reaction proceeded chemoselectively with by far predominant transfer of the newly formed naphthyl substituent at boron to give the phenyl-substituted naphthalene derivative **9** that was isolated in good yield (93%) (see Scheme 5). The product was identified by C,H-elemental analysis and by spectroscopy. The latter revealed that the product **9** contained only a single remaining $-SiMe_3$ substituent. Apparently, the $-SiMe_3$ substituent at the α-position to the boryl group of the starting material **4b** was selectively replaced by hydrogen under these specific reaction conditions, potentially by means of OH^- addition to the borane[20] in the course of the overall Pd-catalyzed cross-coupling sequence, which eventually resulted in the C–C coupling between the two aromatic residues. The ^1H NMR signal of the newly introduced —H substituent at the "right" naphthalene arene ring of **9** was located at δ 7.62 (s, 1H) (for details see the Supporting Information).

We have also removed the remaining $-SiMe_3$ substituent of the cross-coupling product **9** by treatment with tetra-*n*-butylammonium fluoride in THF. After aqueous work-up, we isolated the naphthalene derivative **11** in 98% yield [^1H NMR: δ 7.71, 7.75 (naphthalene 1-H, 4-H), δ 2.42 (CH_3)].

Scheme 5



Cross-coupling of the phenyl substituted borylnaphthalene system **4c** with PhI (10 mol % $Pd(PPh_3)_4$, NaOH, 70 °C, 12 h) gave the corresponding mono-desilylated naphthalene derivative **10** (see Scheme 5 and the Supporting Information).

Our study shows that the modern variants of the 1,1-carboboration reaction and its sequences of multiple consecutive 1,1-carboborations have become powerful tools for C–C bond formation. We have converted examples of readily available bis(alkynyl)arenes in very simple one-pot procedures to highly substituted, very bulky borylated naphthalene derivatives. These may serve as useful novel arylboron *Lewis* acids, e.g., for interesting new applications in FLP chemistry. These newly formed naphthylboranes serve as suitable components in cross-coupling reactions. This demonstrates an increasing synthetic potential of 1,1-carboboration chemistry.[21]

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Supporting Information Available. Experimental procedures and spectroscopic data for starting materials (**1a**, **1b**, **6**) and all new compounds (**4a–c**, **5a–c**, **8–11**). Description of in situ preparation and NMR analysis of the intermediates **3a** and **7**. Time-dependent NMR measurements for the intermediates **3a** and **7** and CIF files of **4a**, **5a**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.