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B-Mercaptocarboranes: A New Synthetic Route

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A novel route for synthesis of B-mercaptocarboranes is described. The reaction proceeds through Pd-catalyzed iodine exchange with the sulfur nucleophile TIPS–SH in mono- and diiodinated *ortho-*, *meta-*, and *para-*carboranes. Self-assembled monolayers of selected B-mercaptocarboranes on a gold surface were analyzed by X-ray photoelectron spectroscopy and their water contact angles were assessed.

Introduction

In the last decade, the branch of surface science dedicated to the formation, characterization, and search for applications of thiol-based self-assembled monolayers (SAMs) has grown into a vast independent area of investigation.^[1] Many different kinds of organic, inorganic, and organometallic thiols have been used for the preparation of SAMs, including B- and C-mercaptocarboranes,^[2] which are unique with regard to their chemical stability, hydrophobicity, and rigidity.^[3]

The application of thiolated borane clusters in the preparation of SAMs was first reported nearly 15 years ago,^[4] but further development of this fascinating intersection of inorganic chemistry and surface science has been hindered by the lack of a general method for the synthesis of various B-mercaptocarboranes. These compounds are of potentially great interest to the surface science community as a result of their uneven electron-density distribution within the carborane cage and the consequent effects on electron density at the mercapto group. Such variation allows for fine-tuning the properties of carborane-based SAMs.

To date, all methods for the synthesis of B-mercaptocarboranes described in the literature have relied on electrophilic substitution reactions of carboranes.^[5] However, this type of reactions proceeds only under very harsh conditions, and the regiochemistry of the reaction is limited to substitution in the 9- and 12-positions in *ortho*-carborane, 9- and 10-positions in *meta*-carborane, and 2-position in *para*-carborane.

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A vast number of mono- and polyiodinated *closo*-carboranes have been reported,^[6] some of which have already been successfully used in various Pd-catalyzed cross-coupling reactions, such as the Suzuki–Miyaura, Mizoroki–Heck, and Buchwald–Hartwig reactions to name a few.^[7] Herein, we describe a Pd-catalyzed approach to the synthesis of B-mercaptocarboranes starting from *closo*-iodocarboranes that uses commercially available triisopropylsilanethiol.

Results and Discussion

Initially, to optimize the reaction conditions for a Pdcatalyzed thiolation of an iodocarborane, we used 3-iodo-1,2-dicarba-*closo*-dodecaborane (**1a**) with Pd(PPh₃)₄ as the catalyst (Scheme 1). TIPS-protected sodium thiolate, TIPS– SNa, was chosen initially as the sulfur nucleophile, and it was prepared separately through the reaction of TIPS–SH with NaH. When the cross-coupling reaction was carried out in anhydrous dioxane at 90 °C, the desired 3-(TIPS– S)-1,2-dicarba-*closo*-dodecaborane (**2a**) was obtained along with the 3-(TIPS–S)-7,8-dicarba-*nido*-undecaborate anion in a 3:2 molar ratio. To avoid deboronation, we decreased the reaction temperature and generated the thiolate anion in situ. By running the reaction for 3–4 d at 40 °C using the Pd catalyst (10 mol-%), TIPS–SH (1 equiv.), and anhydrous



Scheme 1. Synthesis of 3-mercapto-1,2-dicarba-*closo*-dodecaborane **3a**.



 K_3PO_4 (3 equiv.), we were able to produce desired *closo*-product **2a** in 95% yield.

Using optimized reagent ratios and reaction temperatures in each case, we also successfully prepared 8-(TIPS-S)-1,2-dicarba-closo-dodecaborane (2b), 9-(TIPS-S)-1,2-dicarba-closo-dodecaborane (2c), 9,12-(TIPS-S)₂-1,2-dicarbacloso-dodecaborane (2d), 9-(TIPS-S)-1,7-dicarba-closo-dodecaborane (2e), 2-(TIPS-S)-1,12-dicarba-*closo*-dodecaborane (2f), and 2,9-(TIPS-S)₂-1,12-dicarba-*closo*-dodecaborane (2g). Compounds 2a-g were easily deprotected by using an equivalent molar amount of either dilute aqueous HCl or a solution of tetrabutylammonium fluoride (ТВАF, 1 м in THF) to give corresponding compounds 3a-g. It is interesting to note that for compounds 2a, 2f, and 2g, in which the (TIPS-S) group is connected to the most electron-deficient boron atom, complete deprotection required the shortest incubation time. Compound 2a even underwent partial deprotection during chromatographic purification on silica gel. In contrast, compounds **2b-d** required heating to 40 °C during deprotection with dilute HCl, and deprotection of compound 2e required treatment with TBAF. Reaction conditions and yields of (TIPS-S)-carboranes 2a-g and mercaptocarboranes 3a-g are presented in Table 1.

Table 1. Reaction conditions and yields of compounds 2a-h and 3a-h.

Entry	Starting iodocarborane 1	Cb-(S–TIPS) 2 (<i>T</i> /time/yield ^[a]) ^[b]	Cb-SH 3 (<i>T</i> /time/yield) ^[b]
1	$3-I-o-C_2B_{10}H_{11}$ (1a)	2a (40/90/95)	3a (20/24/91)
2	$8-I-o-C_2B_{10}H_{11}$ (1b)	2b (100/24/64)	3b (40/120/84)
3	9-I- o -C ₂ B ₁₀ H ₁₁ (1c)	2c (100/24/88)	3c (40/24/91)
4	$9,12-I_2-o-C_2B_{10}H_{10}$ (1d)	2d (100/24/56)	3d (40/72/89)
5	9-I- m -C ₂ B ₁₀ H ₁₁ (1e)	2e (100/24/99)	3e (20/24/63) ^[c]
6	$2-I-p-C_2B_{10}H_{11}$ (1f)	2f (100/24/79)	3f (20/24/95)
7	$2,9-I_2-p-C_2B_{10}H_{10}$ (1g)	2g (100/24/70)	3g (20/72/83)
8	$3,9-I_2-o-C_2B_{10}H_{10}$ (1h)	2h (20/24/– ^[d])	3h (40/0.25/61) ^[e]

[a] Isolated yield. [b] °C/h/%. [c] TBAF/THF. [d] The protecting group appeared to have been removed during the acid workup. [e] Acid workup.

As the electron density distribution in carboranes affects their reactivity, we decided to try the thiol coupling reaction using a nonsymmetrically substituted diiodo-*ortho*-carborane, 3,9-diioodo-1,2-dicarba-*closo*-dodecaborane (1h). This compound contains iodine substituents in the electron-deficient B(3)-position and the electron-rich B(9)-position of the *ortho*-carborane cage.

Considering that compound **1a** reacted with the sulfur nucleophile at a much lower temperature compared with **1c**, we expected the two iodinated vertices of **1h** to exhibit a difference in reactivity. When **1h** was reacted with TIPS–SH (1 equiv.) in dioxane in the presence of anhydrous K_3PO_4 (3 equiv.) and Pd(PPh₃)₄ (10 mol-%) at room temperature, the deprotected monothiolated derivative 3-mercapto-9-iodo-1,2-dicarba-*closo*-dodecaborane (**3h**) was produced (Table 1, entry 8). The iodine at the B(9)-position thus remained available for further functionalization. The loss of the protective TIPS group was most likely due to its re-

moval during the acid workup. Notably, this is the first example of a Pd-catalyzed cross-coupling reaction in carborane chemistry that proceeds at room temperature.

To further investigate the versatility of the Pd-catalyzed reaction, we used mercaptocarborane **3c** as a sulfur nucleophile in the reaction with iodocarborane **1c** (Scheme 2). This reaction proceeded without destruction of the carborane cages and gave desired bis(carboranyl) sulfide **4** in 44% isolated yield.



Scheme 2. Synthesis of bis(carboranyl) sulfide 4.

We obtained X-ray diffraction-quality single crystals of compound **3g** and performed X-ray structure analysis. The compound was found to contain a *para*-carborane unit in which the boron atoms at the B(2)- and B(9)-positions, situated *para* with respect to each other, are bonded to thiol groups (Figure 1). The asymmetric unit contains two crystallographically unique halves of the molecule, and the other half in each case was generated by inversion through the center of each carborane cage. Because of symmetry, the B(2)–S(2) and B(9)–S(9) distances are indistinguishable and averaged 1.850(2) Å for the two crystallographically unique halves. This value agrees well with the 1.840–1.877 Å range reported for B–S distances in several structurally characterized *ortho*-carborane thiols.^[2c]



Figure 1. ORTEP representation of $2,9-(HS)_2-1,12$ -dicarba-*closo*-dodecaborane (**3g**) drawn at the 40% probability level.

As an initial demonstration of the applicability of these compounds in surface-modification experiments, SAMs of **3a** and **3c** were prepared on a gold surface. X-ray photoelectron spectroscopy (XPS) was used to probe the nature of the sulfur–gold bonds at the gold/monolayer interface of each SAM sample. The static water contact angles were also



determined to gain insight into the hydrophobic/hydrophilic nature of the monolayers and to permit qualitative determination of the hydrophobic B–H bond orientation.^[2c]

Because **3a** has a substituent on the electron-deficient B(3) atom and **3c** has a substituent on the electron-rich B(9) atom, the two molecules could be expected to differ somewhat in their binding energies and static water contact angles. The XPS spectra of monolayers of both **3a** and **3c** showed characteristic S $2p^{3/2}$ peaks at binding energies of 161.8 and 161.9 eV, respectively, attributable to a Au–S thiolate bond. These binding energies are in good agreement with values reported by others for similar compounds.^[2c]

The measured static water contact angle in the case of the SAM of **3a** was 80°, whereas the angle for the SAM of **3c** was 62° .^[8] These differing contact angle values can be qualitatively explained by the orientation of the acidic carborane C–H bonds relative to the gold surface. When the carborane C–H bonds are distal to the gold surface (for **3c**), the surface is more hydrophilic. When the C–H bonds are proximal to the gold surface (for **3a**), the B–H bonds are exposed to the solvent, and this results in a more hydrophobic surface.

Conclusions

In summary, we have developed a new synthetic route for the Pd-catalyzed preparation of previously inaccessible mono- and di-B-mercapto(*ortho-*, *meta-*, and *para-*)carboranes from iodocarboranes. The thiol-substituted carboranes prepared by this method readily form SAMs on gold surfaces.

Experimental Section

General Methods: All non-aqueous reactions were carried out under an atmosphere of dry argon in oven-dried glassware. All reagents were used as purchased. Triisopropylsilanethiol (TIPS–SH), anhydrous K_3PO_4 , anhydrous AlCl₃, Pd(PPh₃)₄, and anhydrous 1,4-dioxane (99.8%) were obtained from Sigma–Aldrich. TBAF (1 M in THF) was obtained from TCI America. Flash column chromatography was performed by using 63–200 µm silica gel (Merck). Thin-layer chromatography (TLC) was performed by using 60 F₂₅₄ silica gel plates (Merck). Visualization of the TLC plates was accomplished with UV light and PdCl₂/HCl/methanol stain.

General Protocol for the Preparation of TIPS–S-carboranes 2a– c,e,f: A reaction vial equipped with a magnetic stir bar and fitted with a Teflon[®]/rubber membrane screw cap was charged with iodocarborane (0.100 mmol), TIPS–SH (0.200 mmol), anhydrous K_3PO_4 (0.300 mmol), and Pd(PPh₃)₄ (0.0100 mmol). The vial was then evacuated and backfilled with argon. Dioxane (1 mL per 0.1 mmol of iodocarborane) was added by syringe, and the reaction mixture was stirred in a preheated oil bath. Upon completion of the reaction, as confirmed by NMR spectroscopy and TLC, compounds **2a–c,e,f** were isolated by flash chromatography (hexane/ DCM, 1:1). For the preparation of compounds **2d** and **2g** containing two substituents, the amounts of reagents used were as follows: iodocarborane (0.100 mmol), TIPS–SH (0.400 mmol), anhydrous K_3PO_4 (0.600 mmol), and Pd(PPh₃)₄ (0.0200 mmol).

General Protocol for the Deprotection of 2a-d,f,g: An aqueous 1 M HCl solution (0.1 mL) was added to a solution of the corresponding protected mercaptocarborane (0.100 mmol) in a mixture of CHCl₃ (3 mL) and MeOH (1 mL). The reaction mixture was stirred at 20 or 40 °C (Table 1) under TLC control. Upon completion of the reaction, the solution was concentrated in vacuo, and the residue was treated by flash chromatography (hexane/DCM, 1:1). Details for the deprotection of 2e in the presence of TBAF/THF are given in the Supporting Information.

Supporting Information (see footnote on the first page of this article): Experimental procedures; NMR, MS, and XPS spectra; contact angles, X-ray diffraction data.

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[8] For comparison, the measured water contact angle for bare gold was 72°.

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