Title
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Journal
Inorganic Chemistry, 49(11)

ISSN
0020-1669

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Publication Date
2010-06-07

DOI
10.1021/ic100053u

Peer reviewed

4726 *Inorg. Chem.* **2010**, *49*, 4726–4728
DOI: 10.1021/ic100053u

Inorganic Chemistry
Communication

High Yield C-Derivatization of Weakly Coordinating Carborane Anions

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Received January 9, 2010

Unlike the "parent" carborane anion $CHB_{11}H_{11}^-$, halogenated carborane anions such as $CHB_{11}H_5Br_6^-$ can be readily C-functionalized in high yield and purity, enhancing their utility as weakly coordinating anions.

B-halogenated icosahedral carborane anions such as $CHB_{11}H_5X_6^-$ and $CHB_{11}X_{11}^-$ (X = halogen; Figure 1) are particularly useful members of a class of exceptionally inert, weakly coordinating anions[1−5] whose versatility might be further tailored by suitable C-derivatization chemistry. Long-chain hydrocarbon "tails" formed by C-alkylation should lower the lattice energies of salts, increase their solubilities in low dielectric solvents, and allow better exploitation of reactive cations in catalysis. Applications in surfactant chemistry can also be envisioned. Similarly, C-fluorocarbon tails should improve the solubility of carborane ion pairs in fluorocarbon solvents, where catalytic applications have been reported.[6] Attachment of a carborane anion to a polymer has allowed exploitation of immobilization chemistry in cation-selective sensor technology.[7] C-arylation takes advantage of the unique scaffold of a carborane anion in rigid rod supramolecular chemistry.[8,9]

Despite these promising applications, the C-derivatization chemistry of carborane anions has progressed rather slowly. Most work has been performed on the "parent" carborane anion, $CHB_{11}H_{11}^-$, but is frequently hampered by modest yields and difficult separations from starting material. Being ionic rather than neutral, the chromatographic separation of different carborane anions is not trivial on a synthetic scale. The activation of $CHB_{11}H_{11}^-$ via C-lithiation with butyl lithium appears to be essentially quantitative,[10] but the partial regeneration of starting material during subsequent reactions with electrophiles is common, despite careful control of the conditions. Alkylation of 1-Li-$CB_{11}H_{11}^-$ with alkyl halides gives mixed results. While the yields for methylations are frequently quite high,[2,11−14] they drop to 63% for ethylation of $CHB_{11}H_{11}^-$ and are even lower for most other alkylations, silylations, phosphinations, and metalations.[2,10] The yields of C-monohalogenated products, 1-X-$CB_{11}H_{11}^-$, have been raised to 81−96% by careful attention to conditions, but chromatography purification is still recommended for most derivatives.[11]

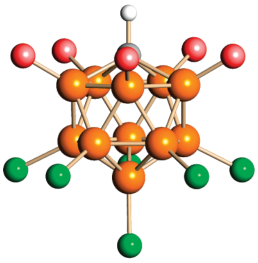

Figure 1. Carborane anions $CHB_{11}H_5X_6^-$ and $CHB_{11}X_{11}^-$ (gray = C, white = H, red = H or halogen, green = halogen).

We now report that, when these C-functionalization reactions are performed on an already halogenated carborane anion such as $CHB_{11}H_5Br_6^-$, rather than on the unfunctionalized parent $CHB_{11}H_{11}^-$, isolated yields are generally excellent and compound purity is sufficiently high that chromatographic purification is unnecessary. High yield C-cyanation of undecahalogenated carboranes has very recently been reported.[15] These findings makes sense within

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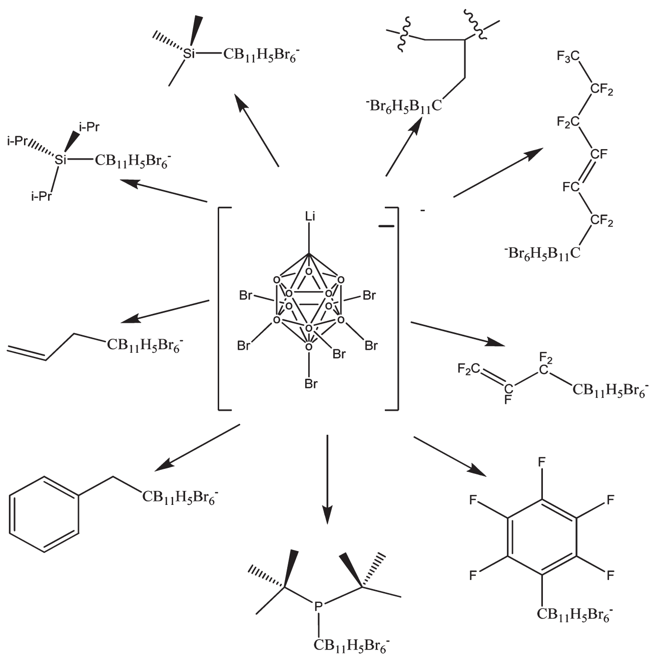
Scheme 1. C-Functionalization of the 1-Li $-CB_{11}H_5Br_6^-$ Anion (o denotes boron vertex)



the context of known carborane reactivity patterns.[2] C-lithiation is a deprotonation reaction and the C−H bond in B-halogenated carborane anions is more acidic than in the parent $CHB_{11}H_{11}^-$. This is borne out by DFT theory[16,17] at the B3LYP/6-311+G(d,p) level using dimethylsulfoxide in the IEFPCM solvation model. A 16 kcal mol^{-1} increase in the acidity of the C−H bond from $CHB_{11}H_{11}^-$ to $CHB_{11}H_5Br_6^-$ is calculated. Similarly, the electron withdrawing effect of B-halogen substituents will more favorably polarize the Li−C bond in 1-Li-$CB_{11}H_5Br_6^-$ toward clean replacement of Li^+ by an electrophile.

Scheme 1 summarizes the representative C-functionalization chemistry reported in the present work.

For convenience and solubility reasons, the preferred starting material is the dilithio derivative Li[1-Li-$CB_{11}H_5Br_6$], conveniently prepared from the Me_3NH^+ salt and 2 equiv of butyl lithium.[18] Trialkylsilyl, allyl, benzyl (including Merrifield resin), perfluoroaryl, and perfluoroallenyl electrophiles, supplied as halides, illustrate the scope of the reactivity. When performed in a careful manner, isolated yields were >90%. Products were isolated by straightforward solvent extractions, avoiding tedious HPLC protocols. Excellent product purity was indicated both by clean NMR and IR spectroscopies as well as the absence of starting material in anionic mode electrospray mass spectrometry.

There is every reason to believe that the same efficient C-functionalization chemistry can be applied to other halogenated carborane anions.

[Me_3NH][*closo*-1-H-$CB_{11}H_5Br_6$]. [Cs][$CHB_{11}H_5Br_6$] (8.27 g, 11 mmol) was suspended in deionized water (325 mL) and the suspension heated to boiling to effect dissolution. The hot solution was filtered through a medium porosity frit and the filtrate reheated to boiling. [Me_3NH]Cl (3.15 g, 33 mmol) was added, resulting in a thick white precipitate. The solution was allowed to stir at a gentle boil for 5 min before being removed from heat. After cooling to room temperature, the suspension was further cooled in an ice bath. After 30 min, the suspension was filtered onto a 30 mL fine porosity frit and washed with aliquots of deionized water (300 mL). After air drying overnight, the product was transferred to a glass vial, dried overnight in a convection oven at 95 °C (7.24 g (97%), and stored in a drybox.

Li[*closo*-1-Li-$CB_{11}H_5Br_6$]. In a typical reaction, [Me_3NH]-[closo-1-H-$CB_{11}H_5Br_6$] (0.1−3 g) was dissolved in sufficient THF (~10 mL/g) to give a clear solution. Butyl lithium in hexanes (1.6 M, 2.1 mol equiv) was then added dropwise over the course of minutes, maintaining a clear solution. If a white precipitate formed, additional THF was added to effect dissolution. The solvent volume was then reduced under a vacuum by ca. 50% to remove butane and trimethylamine. THF was added to redissolve any white precipitate, and the clear solution was immediately used for subsequent reactions.

[Me_4N][*closo*-1-Me_3Si-$CB_{11}H_5Br_6$]. To a THF solution of Li[1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.1251 g, 0.185 mmol) was added Me_3SiCl (~.5 mL) dropwise over 5 min. After stirring for 24 h, the flask was removed from the inert atmosphere and the solvent evaporated. The resulting white solid was dissolved in water (45 mL) and transferred to a beaker. A pellet of sodium hydroxide was added to neutralize any remaining Me_3SiCl and acidic byproducts. The solution was heated to boiling and filtered while hot using a fine frit. The resulting clear solution was reduced in volume to 20 mL by boiling, and Me_4NCl (200 mg, 1.8 mmol) was added. A white precipitate formed, which was isolated by filtration onto a fine frit, washed with water, and vacuum-dried (0.135 g, 88%). ^1H NMR (d_6-acetone): δ 3.46 [s, 12H, Me_4N], 0.096 ppm [s, 9H, Me_3Si]. ^{11}B NMR: +0.49 [s, 1B, B(12)], −7.52 [s, 5B, B(7−11)], −17.49 ppm [d, 5B, B(2−6), J_{BH} 503.2 Hz]. *m*/*z* calcd for Me_3Si-$CB_{11}H_5Br_6^-$: 688.7000. Found: 688.6996.

[Me_4N][*closo*-1-*i*Pr_3Si-$CB_{11}H_5Br_6$] was prepared from [Me_3NH][$CHB_{11}H_5Br_6$] (0.1467 g, 0.217 mmol) and *i*Pr_3SiCl in a similar manner to [Me_4N][*closo*-1-Me_3Si-$CB_{11}H_5Br_6$] above, except that the crude product was extracted into diethylether (45 mL) for the initial filtration before dissolving in water (30 mL). Yield: 0.173 g, 94%. ^1H NMR (d_6-acetone): δ 3.46 [s, 12H, Me_4N], 1.17 [m, 21H, *i*-Pr3Si]. ^{11}B NMR: 1.21 [s, 1B, B(12)], −7.70 [s. 5B, B(7−11)], −16.82 [d, 5B, B(2−6), J_{BH} 498.3 Hz]. *m*/*z* calcd for (*i*Pr)$_3$Si-$CB_{11}H_5Br_6^-$: 772.7939. Found: 772.7930.

[Me_4N][*closo*-1-C_3H_5-$CB_{11}H_5Br_6$]. To a THF solution of Li[1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.1525 g, 0.225 mmol) was added allyl iodide (~1 mL) dropwise over the course of 5 min. Light was excluded by wrapping the flask in Al foil, and the reaction stirred for 24 h before being exposed to air and evaporating the solvent to dryness. The white solid was dissolved in water (45 mL), yielding a clear solution which was transferred to a beaker, boiled, and filtered hot through a fine frit. The resulting solution was reduced in volume to 20 mL before adding Me_4NCl (200 mg, 1.8 mmol),

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which yielded a white precipitate, which was isolated on a fine frit, washed with water, and vacuum-dried (0.152 g, 92%). ^{1}H NMR (d_6-acetone): δ 3.46 [s, 12H, Me_4N], 2.57 [d, 2H, methylene, J_H 7.2 Hz], 4.99 [m, 2H, vinyl], 5.63 [m, 1H, vinyl]. ^{11}B NMR: −2.29 [s, 1B, B(12)], −8.85 [s. 5B, B(7−11)], −16.97 [d, 5B, B(2−6), J_{BH} 522 Hz]. *m*/*z* calcd for $C_3H_5\text{-}CB_{11}H_5Br_6^-$: 656.6917. Found: 656.6913.

[Me$_4$N][*closo*-1-CH$_2$(C$_6$H$_5$)-CB$_{11}$H$_5$Br$_6$] was prepared from Li[1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.1401 g, 0.207 mmol) and benzyl bromide (~0.25 mL) in a similar manner to [Me_4N][*closo*-1-$C_3H_5{-}CB_{11}H_5Br_6$] above (0.243 g, 90%). ^{1}H NMR (d_6-acetone): δ 3.46 [s, 12H, Me_4N], 3.15 [s, 2H, methylene], 7.12 [m, 2H, phenyl], 7.27 [m, 3H, phenyl]. ^{11}B NMR: −2.29 [s, 1B, B(12)], −8.79 [s, 5B, B(7−11)], −16.84 [d, 5B, B(2−6), J_{BH} 501.8 Hz]. *m*/*z* calcd for $C_7H_7\text{-}CB_{11}H_5Br_6^-$: 706.7074. Found: 706.7061.

Li[*closo*-1-(*t*-butyl)$_2$P-CB$_{11}$H$_5$Br$_6$] was prepared from Li[1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.2350 g, 0.347 mmol) and di-*t*-butylchlorophosphine (0.065 mL). The reaction was allowed to stir for 1 h at room temperature, followed by the removal of ca. 85% of the solvent. Only NMR data were collected due to the extreme sensitivity of the product to oxygen. ^{1}H NMR (d_3-acetonitrile): δ 1.18 [d, 18 H, *t*-butyl, J_{PH} 32.2 Hz]. ^{31P} NMR: −151.40 [s, 1P]. ^{11}B NMR: −1.13 [s, 1B, B(12)], −8.69 [s. 5B, B(7−11)], −15.20 [d, 5B, B(2−6), J_{BH} 551.9 Hz].

[Me$_4$N][*closo*-1-C$_6$F$_5$−CB$_{11}$H$_5$Br$_6$] was prepared from Li[1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.2708 g, 0.400 mmol) and C_6F_6 (~1 mL) in a similar manner to [Me_4N][*closo*-1-$Me_3Si\text{-}CB_{11}H_5Br_6$] above, except that the crude yellow product was extracted into diethylether (45 mL) for the initial filtration before dissolving in water (45 mL). (If a large excess of C_6F_6 is not used, multiple substitution occurs.) Yield of off-white solid: 0.323 g, 94%. ^{11}B NMR: +.049 [s, 1B, B(12)], −8.55 [s. 5B, B(7−11)], −15.85 [d, 5B, B(2−6), J_{BH} 495.9 Hz]. ^{19}F NMR: −133.53 [broad, *o*-F], −154.70 [tt, *p*-F, J_{FF} 22.9, 5.1 Hz], −162.9531 [m, *m*-F]. *m*/*z* calcd for $C_6F_5\text{-}CB_{11}H_5Br_6^-$: 782.6446. Found: 782.6459.

[Me$_4$N][*closo*-1-C$_6$F$_{11}$-CB$_{11}$H$_5$Br$_6$] was prepared from Li[1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.3051 g, 0.451 mmol and perfluoro-1-hexene (0.150 g, 0.5 mmol) in a similar manner to [Me_4N][*closo*-1-$Me_3Si\text{-}CB_{11}H_5Br_6$] above except that the crude brown product was extracted into diethylether (45 mL) for the initial filtration before evaporation and dissolution in water (45 mL). An additional extraction of the final product into dichloromethane (10 mL) followed filtration through a fine frit, and evaporation of the solvent gave an oil that solidified to a brown solid (0.3682 g, 91.1%). ^{11}B NMR: +0.049 [s, 1B, B(12)], −8.55 [s, 5B, B(7−11)], −15.85 [d, 5B, B(2−6), J_{BH} 487.5 Hz]. ^{19}F NMR: −157.73 [d, alkene, J_{FF} 144.5 Hz], −146.70 [d, alkene, J_{FF} 137.37 Hz], −127.70 [m, *CF$_2$*], −118.75 [m, *CF$_2$*], −84.67 [dd, *CF$_2$*, J_{FF} 31.7, 9.93 Hz], −80.73[t, *CF$_3$*, J_{FF} 8.6 Hz]. *m*/*z* calcd for $C_6F_{11}CB_{11}H_5Br_6^-$: 896.6351. Found: 893.6390.

[Me$_4$N][*closo*-1-C$_3$F$_5$−CB$_{11}$H$_5$Br$_6$]. ***Caution!*** *Extreme care should be exercised when confining hexafluoropropene (B.Pt. −28 °C) to glass Schlenkware. All reactions must be maintained at dry ice temperatures to avoid explosion.* In heavy walled Schlenkware, hexafluoropropene (~1 mL) was precondensed at −78 °C and then transferred to a heavy walled reaction vessel at dry ice temperature containing THF (5 mL) and Li[*closo*-1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.4510 g, 0.666 mmol). The resulting yellow solution was allowed to stir for 3 h before gradually removing the excess hexafluoropropene under a vacuum. The reaction was then allowed to warm to room temperature and the solvent removed under reduced pressure to give a colorless residue. This was extracted into diethylether (50 mL) and filtered through a fine frit and the filtrate evaporated to dryness. The crude product was dissolved in water (35 mL), and Me_4NCl (200 mg, 1.8 mmol) was added. The resulting white precipitate was isolated by filtration onto a fine frit, washed with water and vacuum-dried (0.4608 g, 92.7%). ^{11}B NMR: +1.82 [s, 1B, B(12)], −8.60 [s. 5B, B(7−11)], −17.52 [d, 5B, B(2−6), J_{BH} 504.2 Hz]. ^{19}F NMR: −67.56 [dd, CF$_2$(sp^3), J_{FF} 23.5, 10.7 Hz], −122.60 [dm, *CF*, J_{FF} 146.1, 23.7 Hz], −160.60 [d, CF$_2$-(sp^2), J_{FF} 145.3 Hz]. *m*/*z* calcd for $C_3F_5CB_{11}H_5Br_6^-$: 746.6446. Found: 746.6458.

Cs[*closo*-1-Merrifield Peptide Resin-CB$_{11}$H$_5$Br$_6$]. To a THF solution [Li][1-Li-$CB_{11}H_5Br_6$] generated from [Me_3NH][$CHB_{11}H_5Br_6$] (0.2330 g, 0.344 mmol) was added Merrifield's Peptide Resin (0.185 g, 1.95 mmol Cl/g, 1.05 equiv). The reaction was allowed to stir for 1 week, yielding a yellow powder which was filtered onto a medium frit and was washed thoroughly with three aliquots of THF (50 mL). All filtrates were collected and the solvent evaporated. To the residue was added deionized water (20 mL). The ^{11}B NMR of this solution showed no detectable signals. To the filtrate were added two drops of HNO_3, followed by $AgNO_3$ (1 mL, 0.5 M). The resulting white precipitate of AgCl was filtered onto a fine frit and dried (0.048 g, 0.99 equiv). The resin was suspended in water and CsCl (1 g, 6 mmol) added. The suspension was stirred for 1 day before collecting the resin by filtration onto a medium frit and washing with water. The faintly pale product was oven-dried for 2 h at 90 °C before obtaining an IR spectrum.

Acknowledgment. We thank the National Science Foundation (CHE-0841428 and 0742001) for support. M.J.N. was a MARCU* trainee supported by award T34GM062756 from the National Institute of General Medical Sciences.

Supporting Information Available: General experimental conditions, NMR and mass spectra for all new compounds (18 pages). This material is available free of charge via the Internet at http://pubs.acs.org.