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High Yield C-Derivatization of Weakly Coordinating Carborane Anions

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Abstract

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. Attachment of a carborane anion to a polymer has allowed exploitation of immobilization chemistry in cation-selective sensor technology. C-arylation takes advantage of the unique scaffold of a carborane anion in rigid rod supramolecular chemistry.

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 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 metallations. 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

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

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that chromatographic purification is unnecessary. High yield C-cyanation of undecahalogenated carboranes has very recently been reported. ¹⁵ These findings makes sense within 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 CHB₁₁H₁₁. This is borne out by DFT theory at the B3LYP/6-311+G(d,p) level using dimethylsulfoxide in the IEFPCM solvation model. A 16 kcal.mole⁻¹ decrease in acidity of the C-H bond between CHB₁₁H₅Br₆ and CHB₁₁H₁₁ is calculated. Similarly, the electron withdrawing effect of B-halogen substituents will more favorably polarize the Li-C bond in 1-Li-CB₁₁H₅Br₆ towards 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 $_{5}$ Br $_{6}$], conveniently prepared from the Me $_{3}$ NH $^{+}$ salt and 2 equiv. of butyl lithium. ¹⁶ 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.

Experimental

All experimental manipulations were carried out using standard drybox or Schlenk tube inert atmospheric techniques. Spectrochemical grade tetrahydrofuran (THF), acetonitrile and diethylether (Fischer) were distilled from sodium/benzophenone. Cs(CHB₁₁H₅Br₆) was prepared as previously described. ¹ Other commercially available chemicals were reagent grade and were degassed and dried over 4A molecular sieves for 1 week prior to use. All solvent evaporations were performed at reduced pressure on a rotary evaporator. ¹¹B, ¹H, ¹⁹F and ³¹P NMR spectra were obtained on a Bruker Avance 300 MHz spectrometer. ¹¹B chemical shifts were referenced to BF₃-OEt₂ as an external reference in a capillary within the sample tube. ¹H chemical shifts were measured relative to internal residual protons from the lock solvent and referenced to (CH₃)₄Si (0.0 ppm). ¹⁹F chemical shifts were referenced to CFCl₃ (0.0 ppm). ³¹P chemical shifts were referenced to 85% aqueous H₃PO₄ (0.0 ppm) in a capillary. Electrospray ionization mass spectrometry data were obtained on an Agilent 6200 LC TOF in anionic mode. IR data were recorded on a Perkin Elmer Spectrum 100 Series as KBr pellets.

DFT calculations were carried out on $CB_{11}H_{12}^-$ and $CHB_{11}H_5Br_6^-$ at B3LYP/6-311+G(d,p) level with the Gaussian 03 system of programs. The intrinsic gas phase acidities of the carborane anions were calculated according to the following thermodynamic heterolytic equilibrium, analogous to work¹⁷,18 on neutral species:

$$HA^- \rightarrow A^{2-} + H^+$$

The absence of imaginary frequencies was taken as the criterion of a true minimum. The gas phase values of ΔG_{acid} were then recalculated using the IEFPCM solvation model with DMSO as a solvent. The resultant ΔG_{acid} values were: $CB_{11}H_{12}^- = 325.75$ and $CHB_{11}H_5Br_6^- = 309.58$ kcal.mol⁻¹.

$[Me_3NH][closo-1-H-CB_{11}H_5Br_6]$

[Cs][CHB $_{11}$ H $_{5}$ Br $_{6}$] (8.27 g, 11 mmole) 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 $_{3}$ NH]Cl (3.15 g, 33 mmole) 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-CB₁₁H₅Br₆]

In a typical reaction, [Me₃NH][closo-1-H-CB₁₁H₅Br₆] (0.1–3 g) was dissolved in sufficient THF (\sim 10 mL/g) to give a clear solution. Butyl lithium in hexanes (1.6 M, 2.1 molar equivalents) 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 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.

[Me₄N][closo-1-Me₃Si-CB₁₁H₅Br₆]

To a THF solution of Li[1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.1251g, 0.185 mmol), Me₃SiCl (~.5 mL) was added dropwise over 5 min. After stirring for 24 hrs, the flask was removed from the inert atmosphere and the solvent evaporated. The resulting white solid was dissolved in water (45 mL) transferred to a beaker. A pellet of sodium hydroxide was added to neutralize any remaining Me₃SiCl 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 Me₄NCl (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, Me₄N], 0.096 ppm [s, 9H, Me₃Si]. ¹¹B 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 Me₃Si-CB₁₁H₅Br₆⁻ 688.7000, found 688.6996.

[Me₄N][closo-1-iPr₃Si-CB₁₁H₅Br₆]

This was prepared from [Me₃NH][CHB₁₁H₅Br₆] (0.1467g, 0.217 mmol) and iPr₃SiCl in a similar manner to [Me₄N][closo-1-Me₃Si-CB₁₁H₅Br₆] above except that the crude product was extracted into diethylether (45 mL) for the initial filtration before dissolving in water (30 mL). Yield: 0.173g, 94%). ¹H NMR (d_6 -acetone): δ 3.46 [s, 12H, Me₄N], 1.17 [m, 21H, i-Pr₃Si]. ¹¹B 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 (iPr)₃Si-CB₁₁H₅Br₆ -772.7939, found 772.7930.

$[Me_4N][closo-1-C_3H_5-CB_{11}H_5Br_6]$

To THF solution of Li[1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.1525g, 0.225 mmol) was added allyl iodide (~1mL) dropwise over the course of 5 mins. Light was excluded by wrapping the flask in Al foil and the reaction stirred for 24 hours before exposing to air and evaporating the solvent to dryness. The white solid was dissolved in water (45mL) 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 Me₄NCl (200 mg, 1.8 mmol) 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, Me₄N], 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 - $CB_{11}H_5Br_6$ 656.6917, found 656.6913.

$[Me_4N][closo-1-CH_2(C_6H_5)-CB_{11}H_5Br_6]$

This was prepared from Li[1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.1401g, 0.207 mmol) and benzyl bromide (~0.25 mL) in a similar manner to [Me₄N] [*closo*-1-C₃H₅-CB₁₁H₅Br₆] above (0.243g, 90%). 1 H NMR (d_6 -acetone): δ 3.46 [s, 12H, Me₄N], 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)], $^{-1}$ 6.84 [d, 5B, B(2–6), J_{BH} 501.8 Hz]. M/z: calcd. for C₇H₇-CB₁₁H₅Br₆ $^{-}$ 706.7074, found 706.7061.

Li[closo-1-(t-butyl)₂P-CB₁₁H₅Br₆]

This was prepared from Li[1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.2350g, 0.347 mmol) and di-t-butylchlorophosphine (.065 mL). The reaction was allowed to stir for 1 hour at room temperature followed by 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].

$[Me_4N][closo-1-C_6F_5-CB_{11}H_5Br_6]$

This was prepared from Li[1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.2708 g, 0.400 mmol) and C_6F_6 (~1 mL) in a similar manner to [Me₄N][*closo*-1-Me₃Si-CB₁₁H₅Br₆] 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%). ₁₁B 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]. ¹⁹F 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 -CB₁₁H₅Br₆ 782.6446, found 782.6459.

$[Me_4N][closo-1-C_6F_{11}-CB_{11}H_5Br_6]$

This was prepared from Li[1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.3051 g, 0.451 mmol and perfluoro-1-hexene (0.150 g, 0.5 mmol) in a similar manner to [Me₄N] [*closo*-1-Me₃Si-CB₁₁H₅Br₆] 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 solvent gave an oil that solidified to a brown solid (0.3682 g, 91.1%). ¹¹B 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]. ¹⁹F 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.

$[Me_4N][closo-1-C_3F_5-CB_{11}H_5Br_6]$

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 (\sim 1mL) was pre-condensed at -78 °C then transferred to a heavy walled reaction vessel at dry ice temperature containing THF (5 mL) and Li[closo-1-Li-CB₁₁H₅Br₆] generated from [Me₃NH][CHB₁₁H₅Br₆] (0.4510 g, 0.666 mmol). The resulting yellow solution was allowed to stir for 3 hours before gradually removing the excess hexafluoropropene under 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), filtered through a fine frit and the filtrate

evaporated to dryness. The crude product was dissolved in water (35 mL) and Me₄NCl (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%). ¹¹B 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]. ¹⁹F NMR: -67.56 [dd, CF₂(sp^3), J_{FF} 23.5, 10.7 Hz], -122.60 [dm, CF, J_{FF} 146.1, 23.7 Hz], -160.60 [d, CF₂(sp^2), J_{FF} 145.3 Hz]. M/z: calcd. for C₃F₅CB₁₁H₅Br₆⁻ 746.6446, found 746.6458.

Cs[closo-1-Merrifield Peptide Resin-CB₁₁H₅Br₆]

To THF solution [Li][1-Li-CB $_{11}H_5Br_6$] generated from [Me $_3$ NH][CHB $_{11}H_5Br_6$] (0.2330 g, 0.344 mmol) was added Merrifield's Peptide Resin (0.185g, 1.95 mmol Cl/g, 1.05 equiv.) was added. 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 3 aliquots of THF (50 mL). All filtrates were collected and the solvent evaporated. To the residue, deionized water (20 mL) was added. ^{11}B NMR of this solution showed no detectable signals. To the filtrate, 2 drops of HNO $_3$ were added, followed AgNO $_3$ (1 mL, 0.5 M). The resulting white precipitate of AgCl was filtered onto a fine frit and dried (0.048g, 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 hours at 90° C before obtaining an IR spectrum.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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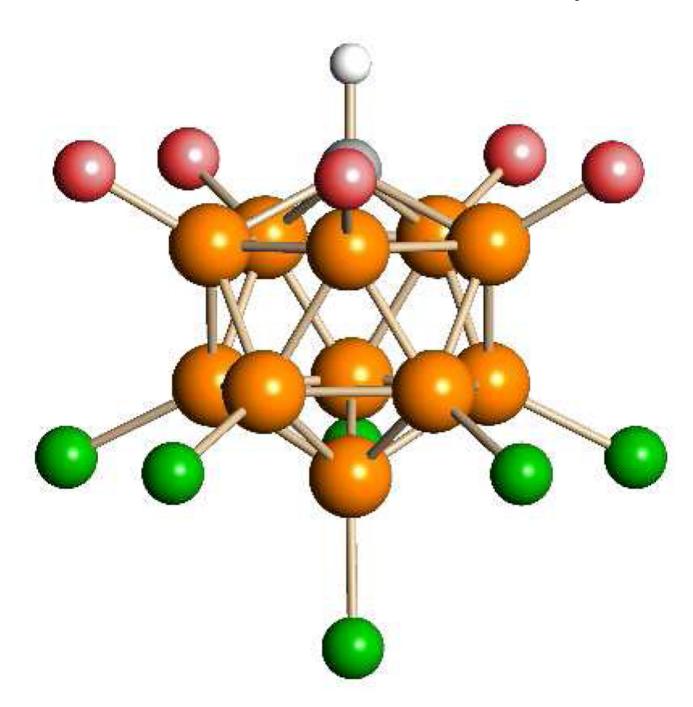


Figure 1. Carborane anions $CHB_{11}H_5X_6^-$ and $CHB_{11}X_{11}^-$ (gray = C, white = H, red = H or halogen, green = halogen).

C-functionalization of the 1-Li–CB₁₁H₅Br₆⁻ anion (o denotes boron vertex).