A Simple Route to C-Monosubstituted Carborane Derivatives

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A procedure is reported for the conversion of *tert*-butyldimethylsilyl chloride and *closo*-1,2-$C_2B_{10}H_{12}$ (1) to the corresponding silylcarborane derivative 2 in 99% yield. Compound 2 served as a valuable synthon to other monosubstituted carboranyl derivatives. Lithiation and reaction at the carborane 2-vertex with a variety of mono- and difunctional electrophiles under mild conditions formed the corresponding silylated products. Subsequent deprotection with tetrabutylammonium fluoride produced the corresponding monosubstituted carborane derivatives in high yield.

Introduction

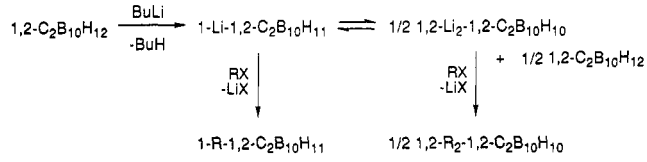
The selective synthesis of monosubstituted icosahedral 1,2-$C_2B_{10}H_{12}$ carborane derivatives is currently of great synthetic importance. Especially noteworthy are their use in the cytotoxic boron–neutron capture reaction, ^{10}B (n, α) ^7Li, as the basis of a binary method for cancer therapy (BNCT),[2a] and the recent discovery of radiometallacarborane reagents suitable for radiomedical application as immunoconjugates.[2b-d] Unfortunately, many of the complex organic structures desired are not always possible to attain via known synthetic routes to mono-C-Substituted 1,2-$C_2B_{10}H_{12}$ species.[3,4]

The most generally useful preparation of *o*-carborane derivatives utilizes the reaction of a terminal alkyne and a solution of $B_{10}H_{12}$(ligand)$_2$ species such as $B_{10}H_{12}[(C_2H_5)_2S]_2$.[4,5] The limited number of easily available alkyne derivatives makes this route only marginally useful. The second method of preparation requires the monolithiation of 1,2-$C_2B_{10}H_{12}$ at carbon followed by the use of the resulting monolithiocarborane as a nucleophile. Preparation of 1-Li-1,2-$C_2B_{10}H_{11}$ is complicated by an equilibrium that exists between the monolithiocarborane, the dilithiocarborane, and the unsubstituted carborane which usually leads to product mixtures.[6]

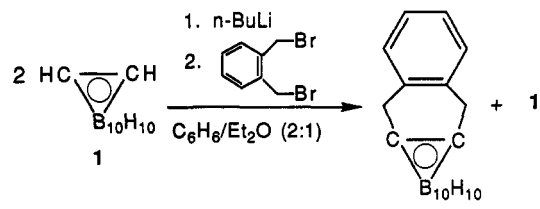
Earlier work with carborane derivatives in the areas of BNCT and radioimmunoconjugates often employed methyl and/or phenyl C-substituted blocking groups.[1,7] Unfortunately, the resultant compounds frequently possessed steric and electronic properties which were deleterious to those actually required for these applications.

In earlier studies we have shown the *tert*-butyldimethylsilyl (TBDMS) moiety to be an effective protecting group for a single carbon vertex of 1,2-$C_2B_{10}H_{12}$.[8] In the present paper we discuss these syntheses and extend our study to include other carborane derivatives.

Scheme I



Scheme II



Results and Discussion

The synthesis of bridged carboranes (e.g., 4) was central to our development of radiometallacarborane reagents. We had originally hoped to prepare these species via metalation followed by electrophilic attack at the metalated carborane carbon atom. Reaction of 1.0 molar equiv of 1 with 1.0 equiv of n-BuLi in a 2:1 C_6H_6/Et_2O solution established the equilibrium (Scheme I). Subsequent addition of a solution of 0.5 equiv of α,α'-dibromo-*o*-xylene afforded only the exocyclic ring derivative (Scheme II).[9] A second route we developed to 4 utilized (hydroxymethyl)carborane as the starting material.[10] Even though 4 was obtained, the low overall yield (4%) and lengthy synthesis (8 steps from decaborane) highlighted the need for a versatile carborane protecting group.

Our interest in silyl protecting groups stemmed from the ease with which C-substituted silyl carboranes could be synthesized and from the already developed methodology of silyl protecting groups in other areas of organic chemistry.[11] Protecting groups initially investigated included trimethylsilyl and thiophenyl moieties. The corresponding monosubstituted *o*-carborane derivatives were prepared, albeit as mixtures of mono- and disubstituted products as well as starting material which were difficult to separate. Both moieties were found to be displaced in the subsequent lithiation step which led only to the exocyclic product.[7] An attempt to synthesize the mono-*tert*-butyldiphenylsilyl *o*-carborane derivative proved to be futile, presumably due to steric constraints. We then turned our

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(2) (a) Hawthorne, M. F. *Pure Appl. Chem.* **1991**, *63*(3), 327 and references therein. (b) Hawthorne, M. F.; Varadarajan, A.; Knobler, C. B.; Chakrabarti, S.; Paxton, R. J.; Beatty, B. G.; Curtis, F. L. *J. Am. Chem. Soc.* **1990**, *112*, 5365. (c) Varadarajan, A.; Johnson, S. E.; Chakrabarti, S.; Gomez, F. A.; Knobler, C. B.; Hawthorne, M. F. In press. (d) Paxton, R. J.; Beatty, B. G.; Hawthorne, M. F.; Varadarajan, A.; Williams, L. E.; Curtis, F. L.; Knobler, C. B.; Beatty, J. D.; Shively, J. E. *Proc. Natl. Acad. Sci. U.S.A.* **1991**, *88*, 3387.

(3) Fein, M. M.; Bobinski, J.; Dvorak, J.; Smith, H. F.; Schwartz, N. N.; Cohen, M. S. *Inorg. Chem.* **1963**, *2*, 1111.

(4) Grafstein, D.; Bobinski, J.; Dvorak, J.; Smith, H. F.; Schwartz, N. N.; Cohen, M. S.; Fein, M. M. *Inorg. Chem.* **1963**, *2*, 1120.

(5) Heying, T. L.; Ager, J. W.; Clark, S. L.; Mangold, D. J.; Goldstein, H. L.; Hillman, M.; Polak, R. J.; Szymanski, J. W. *Inorg. Chem.* **1963**, *2*, 1089.

(6) Zakharkin, L. I.; Grebenikov, A. V.; Kazantsev, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1967**, 2077.

(7) Hawthorne, M. F. Unpublished results.

(8) Gomez, F. A.; Johnson, S. E.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1991**, *113*, 5913.

(9) Zakharkin, L. I.; Kazantsev, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, 568.

(10) Zakharkin, L. I.; Brattsev, V. A.; Stanko, V. I. *Zh. Obshch. Khim.* **1966**, *36*, 886.

(11) Greene, T. W. *Protective Groups in Organic Synthesis*; John Wiley and Sons: New York, 1981.

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Scheme III

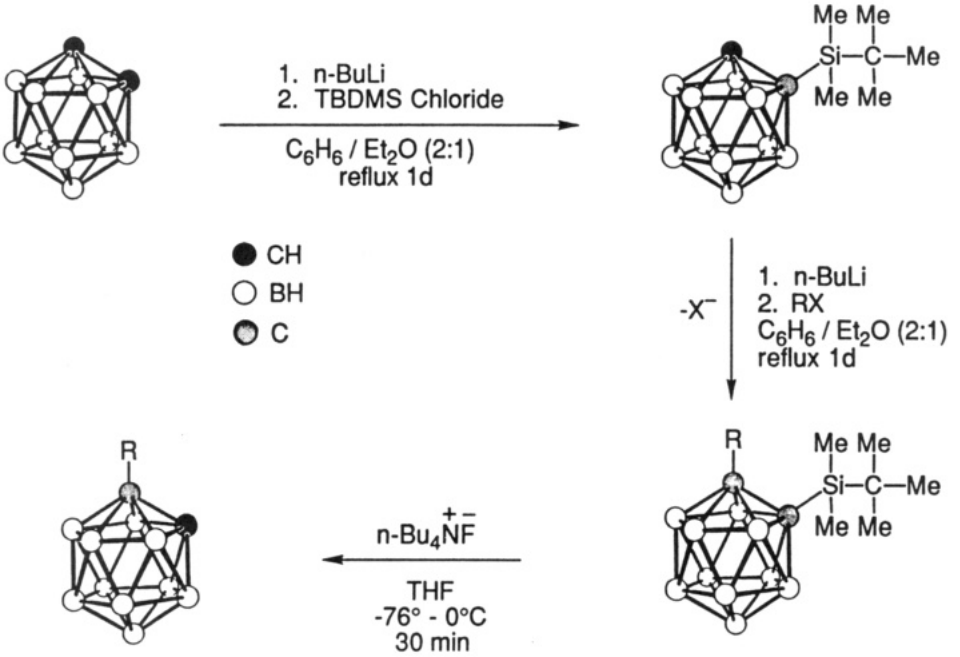
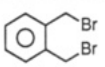
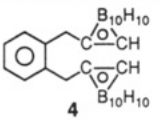
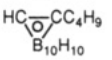
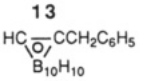
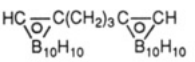
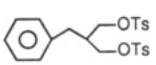
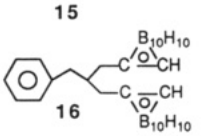
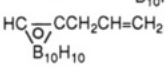
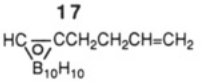
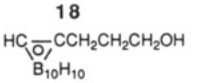


Table I. Protected and Deprotected *closo*-1,2-$C_2B_{10}H_{12}$ Derivatives

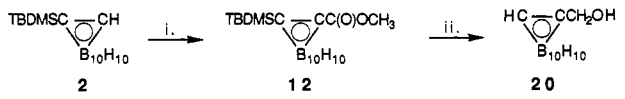
substrate (RX)	protected product (RTBDMS)	protected product yield, %	deprotected product (RH)	deprotected product yield, %
	**3**	74	 **4**	94
$n\text{-}C_4H_9Br$	**5**	80	 **13**	90
$C_6H_5CH_2Br$	**6**	61	 **14**	70
$Br(CH_2)_3Br$	**7**	61	 **15**	88
	**8**	56	 **16**	87
$BrCH_2CH{=}CH_2$	**9**	79	 **17**	71
$BrCH_2CH_2CH{=}CH_2$	**10**	81	 **18**	63
	**11**	84	 **19**	95

attention to the *tert*-butyldimethylsilyl (TBDMS) group. Corey had earlier demonstrated the TBDMS moiety to be an outstanding protecting group for alcohols.[12]

Reaction of **1** with 1.1 equiv of n-BuLi at 0 °C in a 2:1 C_6H_6/Et_2O solution established the equilibrium shown in Scheme I. The lithiated component of this equilibrium then reacted with 1 equiv of *tert*-butyldimethylsilyl chloride at 35 °C to produce **2** in 99% yield. Under high vacuum, unreacted starting material sublimed at 70 °C while the pure product distilled at 120 °C. Compound **2** was characterized by a combination of ^1H, ^{11}B, and ^{13}C NMR, IR, and mass spectroscopy. The ^1H NMR spectrum of **2** exhibits two sharp upfield resonances associated with the Si-substituted alkyl groups, a broad downfield carborane C–H resonance, and broad B–H resonances consistent for carborane cages. The ^{11}B NMR spectrum exhibits six resonances in a 1:1:2:2:2:2 ratio and the IR contains a characteristic band at 2585 cm^{-1} consistent with the B–H stretching mode. Addition of 0.5 molar equiv of α,α'-dibromo-*o*-xylene to the lithio derivative of **2**, formed by the

(12) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

Scheme IV[a]



2 12 20

[a] (i) (a) n-BuLi, (b) $ClC(O)OCH_3$; (ii) $LiAlH_4$.

addition of n-BuLi at 0 °C in 2:1 C_6H_6/Et_2O, afforded **3** in 74% yield (Scheme III). Deprotection of **3** with n-$Bu_4N^+F^-$ in THF (−76 °C to 0 °C) for 20 min yielded **4** (71% overall), which was characterized both spectroscopically and by an X-ray diffraction study.[13]

From Table I it can be seen that the lithio derivative of **2** reacts in good yield with a variety of mono- and difunctional electrophiles under mild conditions to form the corresponding silylated products. As expected, these silylated species do not exhibit a carborane C–H resonance in their ^1H NMR spectra and they show a downfield shift for the carborane carbon resonances in the ^{13}C NMR spectrum consistent with disubstituted *o*-carborane derivatives. Subsequent desilylation produces the desired C-substituted and C-bridged carborane derivatives, in high yields. Spectra obtained with previously reported carboranes[14] were in agreement with published data and the new compounds were characterized via NMR, IR, and mass spectroscopy.

The synthesis of alkylene-linked carboranes such as **15** is virtually impossible using earlier methods. This difficulty may be attributed to the lithiocarborane equilibrium (Schemes I and II) whereby undesired exocyclic side products predominate. The silylcarborane reagent **2** made it possible to synthesize such species. To 2.2 equiv of **2** was added 2.3 equiv of n-BuLi at 0 °C in 2:1 C_6H_6/Et_2O. A solution of 1,3-dibromopropane (1.0 equiv) was then reacted with lithio **2** to produce **7** in 61% yield. Subsequent deprotection of **7** with n-$Bu_4N^+F^-$ in THF (−76 °C to 0 °C) for 20 min afforded **15** in 88% yield.

C-Alkenyl-*o*-carboranes containing terminal vinyl groups have been generally prepared by the reaction of $B_{10}H_{12}$-(ligand)$_2$ species with the corresponding alkenylacetylenes.[3,14] This appears to be the preferred method although alkenylcarboranes have also been obtained by the action of alkenyl halides on *C*-metallacarboranes[15] or carboranyl Grignards.[4] We here report the synthesis of alkenylcarboranes **17** and **18** using a simplified procedure. Addition of the appropriate bromoalkene to a solution of lithio **2** afforded **9** and **10**. Subsequent deprotection of these derivatives with n-$Bu_4N^+F^-$ in THF gave **17** and **18** in 56% and 51% overall yields, respectively.

Alcohol derivatives of *o*-carborane cannot be prepared directly from acetylenic alcohols and $B_{10}H_{12}$(ligand)$_2$ compounds since the borane cage is degraded by hydroxyl groups. The normal route to carboranyl alcohols involves the esterification of the corresponding acetylenic alcohol. The resulting ester is then allowed to react with a bisligand decaborane compound and the resulting carboranyl ester is then converted to the alcohol by transesterification,[16] lithium aluminum hydride reduction,[15] or by hydrolysis.[4,9,14,16] We were able to synthesize (hydroxymethyl)carborane[10] (**20**) in two steps from **2** in 66% overall yield (Scheme IV). Methyl chloroformate reacts with lithio-**2** to form the methyl ester **12**, which when reacted with $LiAlH_4$ in THF affords **20**. To our knowledge there is no precedent for $LiAlH_4$ cleavage of TBDMS moieties.[12] An attempt to deprotect **12** with n-$Bu_4N^+F^-$ to give the methyl ester of *o*-carborane carboxylic acid yielded only *o*-carborane.

Lithiation of 1,7-$C_2B_{10}H_{12}$ (**21**) followed by reaction with *tert*-butyldimethylsilyl chloride is not selective and yields both mono- and disilylated products. Under high vacuum, unreacted starting material easily sublimed at 60 °C while the product distilled at 90 °C to afford **22** as a clear liquid in only 40% yield. The adjacent carbon atoms in 1,2-$C_2B_{10}H_{12}$ provide a steric requirement unfavorable for disilylation. On the other hand, the carbon atoms lie further from each other in 1,7-$C_2B_{10}H_{12}$, thereby yielding a mixture of silylation products. Reaction of methyl iodide with the monolithio derivative of **22** gave **23** in 90% yield. Subsequent deprotection with TBAF afforded 1-CH_3-1,7-$C_2B_{10}H_{11}$[17] (**24**) in 57% yield.

As shown above the TBDMS group presents the proper balance of steric requirements which allow the selective monosilylation of **1** and retention of the C–Si bond in **2** during subsequent reactions. Even though additional metalation by alkali metal reagents is possible, the TBDMS moiety in **2** provides efficient steric protection from attack by an additional *tert*-butyldimethylsilyl chloride molecule.

Conclusions

The utility of the monosilyl-protected carborane **2** is illustrated in the development of functionalized precursors of bridged metallacarborane systems employed for the complexation of radiometal ions (Venus Flytrap Clusters) and their subsequent conjugation to monoclonal antibodies.[2b-d] The monoprotected carborane is also employed as a precursor in the synthesis of compounds required for boron neutron capture studies. The generality of the new synthon described here coupled with the high yields obtained offers a valuable tool for organic transformations on carborane cages. The TBDMS protecting group makes monosubstituted carborane derivatives quite accessible and supplants classical routes to these derivatives. Consequently, the ability to easily form both previously reported and new carborane compounds will open the door to new chemical, biological, and medicinal applications of the carboranes.

Experimental Section

General Considerations. Syntheses are described using a simplified nomenclature system.[18] Standard glovebox, Schlenk, and vacuum-line techniques were employed for all manipulation of air- and moisture-sensitive compounds. Reaction solvents were reagent grade and were distilled from appropriate drying agents under nitrogen before use. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl; benzene was distilled from potassium benzophenone ketyl. Deuteriated solvents were obtained from Cambridge Isotope Laboratories. *tert*-Butyldimethylsilyl chloride and *n*-butyllithium (2.5 M solution in hexanes) (Aldrich) were used as received.

Physical Measurements. Proton (^1H NMR) and carbon (^{13}C NMR) spectra were obtained on a Bruker AF 200 spectrophotometer at 200.133 and 50.324 MHz, respectively. Boron (^{11}B

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(14) Grimes, R. N. *Carboranes*; Academic Press, Inc.: New York, 1970.
(15) Heying, T. L.; Ager, J. W.; Clark, S. L.; Alexander, R. P.; Papetti, S.; Reid, J. A.; Trotz, S. I. *Inorg. Chem.* **1963**, *2*, 1097.
(16) Fein, M. M.; Grafstein, D.; Paustian, J. E.; Bobinski, J.; Lichstein, B. M.; Mayes, N.; Schwartz, N. N.; Cohen, M. S. *Inorg. Chem.* **1963**, *2*, 1115.
(17) Grafstein, D.; Dvorak, J. *Inorg. Chem.* **1963**, *2*, 1128.
(18) Throughout this paper, the terms silyl-*o*-carboranyl and silyl-*m*-carboranyl refer to substituent groups derived from 1-substituted-2-(*tert*-butyldimethylsilyl)-1,2-dicarba-*closo*-dodecaborane and 1-substituted-7-(*tert*-butyldimethylsilyl)-1,7-dicarba-*closo*-dodecaborane, respectively. The terms *o*-carboranyl and *m*-carboranyl refer to substituted 1,2-dicarba-*closo*-dodecaborane and 1,7-dicarba-*closo*-dodecaborane derivatives, respectively.

NMR) spectra were obtained at 160.46 MHz on a Bruker AM 500 spectrometer. Chemical shifts for ^1H and ^{13}C NMR spectra were referenced to $SiMe_4$ (0.00 ppm) and measured with respect to residual protons in deuterated solvents. Chemical shift values for ^{11}B spectra were referenced relative to external $BF_3{\cdot}OEt_2$ (0.00 ppm). Coupling constants (J) are given in hertz. Resonances observed upfield of the references were assigned negative chemical shift values in all cases. Infrared spectra were obtained as Nujol mulls and were recorded on a Beckman FT-1100 instrument. Electron impact mass spectra were obtained on an AEI Ltd. Model MS-902 sector filled double-focusing spectrometer, and xenon FAB mass spectra were obtained on an AEI Ltd. Model MS-9 spectrometer.

Silyl-*o*-carborane 2. To a solution of 1,2-dicarba-*closo*-dodecaborane (1) (85.0 g, 589 mmol) in a dry benzene/diethyl ether (2:1) mixture (500 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (247 mL, 619 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and *tert*-butyldimethylsilyl chloride (97.7 g, 647.9 mmol) in a benzene/diethyl ether (2:1) mixture (150 mL) was added dropwise but rapidly. The solution was refluxed overnight and then quenched with 250 mL of water and transferred to a separatory funnel and diluted with 500 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 300 mL). The combined extracts were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. Sublimation at 80 °C (1×10^{-3} mmHg) removed unreacted 1,2-dicarba-*closo*-dodecaborane(12). The product **2** distilled at 120 °C in 99% yield (150 g, 581 mmol): mp 54–56 °C. IR (Nujol, cm^{-1}): 2920, 2585, 1415, 1365, 1265, 1175, 1130, 1073, 1030, 1000, 930, 863, 837, 820, 800, 774, 721. ^1H NMR ($(CD_3)_2CO$): 4.26 (s, 1 H), 1.05 (s, 9 H), 0.30 (s, 9 H). ^{13}C NMR ($(CD_3)_2CO$): 67.2, 62.1, 27.1, 19.7, −4.6. ^{11}B NMR (acetone): 0.24 (d, 1 B), −1.87 (d, 1 B), −7.05 (d, 2 B), −10.48 (d, 2 B), −11.79 (d, 2 B), −12.66 (d, 2 B). High resolution MS (FAB): m/z calcd for $C_8H_{26}{}^{11}B_{10}Si$ 258.2758, found 258.4924. Anal. Calcd for $C_8H_{26}B_{10}Si$: C, 37.17; H, 10.14; B, 41.82; Si, 10.87. Found: C, 37.15; H, 10.14; B, 41.82; Si, 10.65.

α,α′-*o*-Bis(silyl-*o*-carboranyl)-*o*-xylene 3. To a solution of **2** (77.6 g, 300 mmol) in a dry benzene/diethyl ether (2:1) mixture (400 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (132 mL, 313 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and a solution of α,α′-dibromo-*o*-xylene (43.6 g, 165 mmol) in a benzene/diethyl ether (2:1) mixture (100 mL) was added dropwise with stirring. After refluxing overnight the solution was quenched with 200 mL of water, transferred to a separatory funnel, and diluted with 200 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 200 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude white solids were washed with petroleum ether and the nonsoluble solids **3** collected in 74% yield (68.7 g, 111 mmol): mp 220–222 °C. IR (Nujol, cm^{-1}): 2922, 2564, 1255, 1205, 1077, 830, 819, 767. ^1H NMR ($(CD_3)_2CO$): 7.36 (s, 4 H), 3.72 (s, 4 H), 1.21 (s, 18 H), 0.57 (s, 12 H). ^{13}C NMR ($(CD_3)_2CO$): 135.0, 133.4, 128.9, 82.0, 74.9, 41.0, 27.9, 21.1, −2.3. ^{11}B NMR (acetone): 0.96 (d, 2 B), −3.60 (d, 2 B), −7.91 (d, 4 B), −8.85 (d, 4 B), −9.46 (d, 4 B), −10.56 (d, 4 B). MS (EI): m/z calcd for $C_{24}H_{58}{}^{11}B_{20}Si_2$ 619.12, found 619.60. Anal. Calcd for $C_{24}H_{58}B_{20}Si_2$: C, 46.56; H, 9.44; B, 34.93; Si, 9.07. Found: C, 46.38; H, 9.28; B, 34.93; Si, 9.00.

α,α′-Di-*o*-carboranyl-*o*-xylene (4). A solution of **3** (63.6 g, 103 mmol) in dry THF (500 mL) was cooled to −76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (216 mL, 216 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature and then 300 mL of water was added. The solution was diluted with 400 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 300 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. Chromatography on silica (33% diethyl ether/hexane) afforded **4** as a white solid in 97% yield (39.0 g, 99.8 mmol): mp 185–186 °C. IR (Nujol, cm^{-1}): 3040, 2920, 2570, 1113, 1096, 1063, 1017, 935, 765, 725. ^1H NMR ($(CD_3)_2CO$): 7.28 (m, 4 H), 4.51 (s, 2 H), 3.74 (s, 4 H). ^{13}C NMR ($(CD_3)_2CO$): 134.9, 133.0, 129.2, 75.8, 62.4, 40.7. ^{11}B NMR (acetone): −2.09 (d, 2 B), −5.10 (d, 2 B), −9.03 (d, 4 B), −11.10 (d, 10 B), −12.24 (d, 2 B). MS (EI): m/z calcd for $C_{12}H_{30}{}^{11}B_{20}$ 390.59, found 390.36. Anal. Calcd for $C_{12}H_{30}B_{20}$: C, 36.90; H, 7.74; B, 55.36. Found: C, 36.87; H, 7.65; B, 55.08.

1-(Silyl-*o*-carboranyl)butane 5. To a solution of **2** (1.52 g, 5.88 mmol) in a dry benzene/diethyl ether (2:1) mixture (40 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (2.59 mL, 6.47 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and 1-bromobutane (0.70 mL, 6.52 mmol) was added dropwise with stirring. After refluxing for 4 h, the solution was quenched with 10 mL of water, transferred to a separatory funnel, and diluted with 50 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give white solid **5** in 80% yield (1.5 g, 4.8 mmol): mp 34–36 °C. IR (Nujol, cm^{-1}): 2925, 2581, 1260, 1075, 820. ^1H NMR ($(CD_3)_2CO$): 2.29 (t, 2 H, J = 8.4), 1.54 (m, 2 H), 1.33 (m, 2 H), 1.10 (s, 9 H), 0.91 (t, 3 H, J = 7.2), 0.38 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 82.8, 77.3, 38.2, 32.9, 27.9, 22.8, 20.8, 14.0, −2.3. ^{11}B NMR (acetone): −0.17 (d, 1 B), −4.37 (d, 1 B), −7.71 (d, 2 B), −10.52 (d, 6 B). MS (EI): m/z calcd for $C_{12}H_{34}{}^{11}B_{10}Si - CH_3$ 299.57, found 299.

α-(Silyl-*o*-carboranyl)toluene 6. To a solution of **2** (2.4 g, 9.3 mmol) in a dry benzene/diethyl ether (2:1) mixture (50 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (4.1 mL, 10.2 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and benzyl bromide (1.2 mL, 10.2 mmol) was added dropwise with stirring. After refluxing for 3 h, the solution was quenched with 20 mL of water, transferred to a separatory funnel, and diluted with 50 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The white solids were recrystallized from petroleum ether to give **6** in 61% yield (2.0 g, 5.7 mmol): mp 94–97 °C. IR (Nujol, cm^{-1}): 2929, 2574, 1257, 1029, 1013, 1003, 990, 931, 841, 815, 797. ^1H NMR ($(CD_3)_2CO$): 7.30 (m, 5 H), 3.61 (s, 2 H), 1.19 (s, 9 H), 0.51 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 136.8, 130.7, 129.2, 128.9, 128.6, 82.7, 76.3, 43.9, 28.0, 21.0, −2.1. ^{11}B NMR (acetone): 0.68 (d, 1 B), −3.45 (d, 1 B), −7.16 (d, 2 B), −9.49 (d, 6 B). MS (EI): m/z calcd for $C_{15}H_{32}{}^{11}B_{10}Si$ 348.62, found 348.

1,3-Bis(silyl-*o*-carboranyl)propane 7. To a solution of **2** (8.0 g, 30.9 mmol) in a dry benzene/diethyl ether (2:1) mixture (100 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (13.6 mL, 34.0 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and 1,3-dibromopropane (1.7 mL, 17.0 mmol) was added dropwise with stirring. After refluxing for 5 h, the solution was quenched with 30 mL of water, transferred to a separatory funnel, and diluted with 100 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 200 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The white solids were washed with petroleum ether and the nonsoluble solids **7** collected in 61% yield (5.2 g, 9.4 mmol); mp 195–196 °C. IR (Nujol, cm^{-1}): 2928, 2583, 1259, 1087, 840, 820. ^1H NMR ($CDCl_3$): 2.13 (m, 4 H), 1.78 (m, 2 H), 1.05 (s, 18 H), 0.31 (s, 12 H). ^{13}C NMR ($CDCl_3$): 80.2, 76.1, 36.8, 30.5, 27.5, 20.4, −2.4. ^{11}B NMR (chloroform): −0.09 (d, 2 B), −4.21 (d, 2 B), −7.83 (d, 4 B), −10.77 (d, 12 B). MS (EI): m/z calcd for $C_{19}H_{56}{}^{11}B_{20}Si_2$ 557.05, found 557. Anal. Calcd for $C_{19}H_{56}B_{20}Si_2$: C, 40.97; H, 10.13; B, 38.82; Si, 10.08. Found: C, 40.78; H, 9.86; B, 39.00; Si, 9.89.

2-Benzyl-1,3-bis(silyl-*o*-carboranyl)propane 8. To a solution of **2** (49.0 g, 190 mmol) in a dry benzene/diethyl ether (2:1) mixture (400 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (100 mL, 199 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and a solution of 2-benzyl-1,3-bis(*p*-toluenesulfonyloxy)propane[20] (45.0 g, 94.8 mmol) in a benzene/diethyl ether (2:1) mixture (200 mL)

was added dropwise with stirring. After refluxing overnight, the solution was quenched with 200 mL of water, transferred to a separatory funnel, and diluted with 200 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 200 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude white solids were washed with petroleum ether and the nonsoluble solids 8 collected in 56% yield (34.4 g, 53.2 mmol): mp 172–174 °C. IR (Nujol, cm^{-1}): 3070, 2950, 2559, 1417, 1395, 1260, 1089, 1072, 1005, 838, 818, 795, 737, 702. ^1H NMR ($CDCl_3$): 7.26 (m, 5 H), 2.71 (d, 2 H, J = 5.7), 2.24 (ddd, 4 H, J' = 48.3, J'' = 17.2, J''' = 4.0), 2.32 (m, 1 H), 1.05 (s, 18 H), 0.25 (s, 6 H), 0.20 (s, 6 H). ^{13}C NMR ($CDCl_3$): 137.9, 129.0, 127.4, 80.4, 76.0, 41.3, 41.0, 40.5, 27.7, 20.5, –2.2, –2.4. ^{11}B NMR (chloroform): 0.58 (d, 2 B), –3.51 (d, 2 B), –7.76 (d, 4 B), –10.38 (d, 12 B). MS (EI): m/z calcd for $C_{26}H_{62}{}^{11}B_{20}Si_2$, 647.18, found 647. Anal. Calcd for $C_{26}H_{52}B_{20}Si_2$: C, 48.25; H, 9.65; B, 33.41. Found: C, 48.25; H, 9.44; B, 33.18.

3-(Silyl-*o*-carboranyl)-1-propene 9. To a solution of 2 (4.0 g, 15.5 mmol) in a dry benzene/diethyl ether (2:1) mixture (50 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (6.8 mL, 17.0 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and allyl bromide (1.5 mL, 17.0 mmol) was added dropwise with stirring. After refluxing overnight, the solution was quenched with 30 mL of water, transferred to a separatory funnel, and diluted with 100 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give 9 in 79% yield (3.7 g, 12.2 mmol): mp 43–45 °C. IR (Nujol, cm^{-1}): 3083, 2924, 2600, 1949, 1862, 1643, 1466, 1417, 1394, 1363, 1293, 1263, 1167, 1126, 1070, 1031, 987, 931, 825, 792, 725. ^1H NMR ($(CD_3)_2CO$): 5.78 (m, 1 H), 5.10 (m, 2 H), 3.05 (d, 2 H, J = 7.0), 1.12 (s, 9 H), 0.41 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 133.8, 119.6, 81.2, 76.3, 42.1, 27.9, 20.9, –2.2. ^{11}B NMR (acetone): 0.72 (d, 2 B), –3.50 (d, 2 B), –6.97 (d, 4 B), –9.75 (d, 2 B). MS (EI): m/z calcd for $C_{11}H_{30}{}^{11}B_{10}Si - C_4H_9$ 241.44, found 241.

4-(Silyl-*o*-carboranyl)-1-butene 10. To a solution of 2 (1.6 g, 6.2 mmol) in a dry benzene/diethyl ether (2:1) mixture (35 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (2.7 mL, 6.8 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and 4-bromo-1-butene (0.7 mL, 6.8 mmol) was added dropwise with stirring. After refluxing overnight, the solution was quenched with 20 mL of water transferred to a separatory funnel and diluted with 100 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give 10 in 81% yield based on recovered 2 (1.3 g, 4.0 mmol): mp 50–52 °C. IR (Nujol, cm^{-1}): 2906, 2582, 1643, 1255, 1075, 1029, 993, 926, 730, 838, 818, 795. ^1H NMR ($(CD_3)_2CO$): 5.77 (m, 1 H), 5.05 (m, 2 H), 2.35 (m, 4 H), 1.10 (s, 9 H), 0.39 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 136.2, 116.6, 82.0, 77.4, 37.5, 34.6, 27.9, 20.9, –2.2. ^{11}B NMR (acetone): 1.65 (d, 1 B), –2.45 (d, 1 B), –5.75 (d, 2 B), –8.66 (d, 6 B). MS (EI): m/z calcd for $C_{12}H_{32}{}^{11}B_{10}Si - C_4H_9$ 255.47, found 254.

3-(Silyl-*o*-carboranyl)-1-propanol 11. To a solution of 2 (2.7 g, 10.6 mmol) in a dry benzene/diethyl ether (2:1) mixture (40 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (4.7 mL, 11.7 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and trimethylene oxide (0.8 mL, 12.7 mmol) was added dropwise with stirring. After refluxing overnight, the solution was quenched with 20 mL of water transferred to a separatory funnel and diluted with 100 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give 11 in 84% yield (2.8 g, 8.9 mmol): mp 81–83 °C. IR (Nujol, cm^{-1}): 3356, 2916, 2506, 1309, 1257, 1167, 1049, 954, 928, 903, 820, 730. ^1H NMR ($(CD_3)_2CO$): 3.89 (s, 1 H), 3.55 (t, 2 H, J = 5.7), 2.43 (m, 2 H), 1.73 (m, 2 H), 1.09 (s, 9 H), 0.38 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 82.9, 77.5, 61.0, 35.5, 34.0, 28.0, 20.8, –2.3. ^{11}B NMR (acetone): 1.64 (d, 1 B), –2.55 (d, 1 B), –5.83 (d, 2 B), –8.57 (d, 6 B). MS (EI): m/z calcd for $C_{11}H_{32}{}^{11}B_{10}Si - C_4H_9$ 259.46, found 258.

Silyl-*o*-carboranecarboxylic Acid Methyl Ester 12. To a solution of 2 (0.93 g, 3.61 mmol) in a dry benzene/diethyl ether (2:1) mixture (35 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (1.59 mL, 3.97 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and methyl chloroformate (0.31 mL, 3.97 mmol) was added dropwise with stirring. After refluxing overnight, the solution was quenched with 20 mL of water transferred to a separatory funnel and diluted with 50 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give a white solid (12) in 93% yield (1.1 g, 3.5 mmol): mp 67–70 °C. IR (Nujol, cm^{-1}): 2901, 2578, 1755, 1266, 1071, 1028, 963, 840, 792. ^1H NMR ($(CD_3)_2CO$): 3.87 (s, 3 H), 1.06 (s, 9 H), 0.29 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 161.2, 76.8, 75.5, 55.9, 27.4, 20.8, –3.8. ^{11}B NMR (acetone): 0.80 (d, 1 B), –0.98 (d, 1 B), –7.15 (d, 2 B), –9.56 (d, 4 B), –10.76 (d, 2 B). MS (EI): m/z calcd for $C_{10}H_{28}{}^{11}B_{10}O_2Si - C_4H_9$ 259.21, found 259.41.

1-*o*-Carboranylbutane (13). A solution of 5 (1.48 g, 4.70 mmol) in dry THF (30 mL) was cooled to –76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (5.65 mL, 5.65 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature upon which 20 mL water was added. The solution was diluted with 50 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give 13 as a clear oil in 90% yield (0.84 g, 4.19 mmol): mp oil. Spectroscopic data were in agreement with literature.[19,21] IR (Nujol, cm^{-1}): 2951, 2572, 1128, 1115, 1066, 1020, 723. ^1H NMR ($(CD_3)_2CO$): 4.53 (s, 1 H), 2.32 (t, 2 H), 1.48 (m, 2 H), 1.28 (m, 2 H), 0.88 (t, 3 H). ^{13}C NMR ($(CD_3)_2CO$): 76.9, 63.0, 37.9, 31.9, 22.6, 13.8. ^{11}B NMR (acetone): –2.90 (d, 1 B), –6.14 (d, 1 B), –9.63 (d, 2 B), –11.45 (d, 2 B), –11.91 (d, 2 B), –13.11 (d, 2 B).

α-*o*-Carboranyltoluene (14). A solution of 6 (1.0 g, 2.5 mmol) in dry THF (25 mL) was cooled to –76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (5.1 mL, 5.1 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 10 mL of water was added. The solution was diluted with 50 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give 14 as a white solid in 70% yield (0.4 g, 1.8 mmol): mp 55–57 °C. Spectroscopic data were in agreement with literature.[22] IR (Nujol, cm^{-1}): 2918, 2571, 1322, 1105, 1078, 1060, 1019, 759, 726 (s), 701. ^1H NMR ($(CD_3)_2CO$): 7.31 (m, 5 H), 4.34 (s, 1 H), 3.64 (s, 2 H). ^{13}C NMR ($(CD_3)_2CO$): 135.9, 130.7, 129.4, 128.8, 76.4, 62.1, 43.8. ^{11}B NMR (acetone): –2.58 (d, 1 B), –5.74 (d, 1 B), –9.33 (d, 2 B), –11.09 (d, 2 B), –12.00 (d, 2 B), –12.82 (d, 2 B). High-resolution MS (FAB): m/z calcd for $C_9H_{18}{}^{11}B_{10}$ 234.3538, found 234.2391.

1,3-Di-*o*-carboranylpropane (15). A solution of 7 (2.5 g, 4.5 mmol) in dry THF (100 mL) was cooled to –76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (9.2 mL, 9.2 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 20 mL of water was added. The solution was diluted with 100 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The

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white solids were washed with petroleum ether and the nonsoluble solids **15** collected in 88% yield (1.3 g, 4.0 mmol): mp >285 °C. IR (Nujol, cm^{-1}): 2916, 2579, 1126, 1016, 1000, 723. ^1H NMR ($(CD_3)_2CO$): 4.62 (s, 2 H), 2.37 (m, 4 H, J = 8.4), 1.75 (m, 2 H). ^{13}C NMR ($(CD_3)_2CO$): 76.0, 62.9, 36.8, 29.5. ^{11}B NMR (acetone): -2.42 (d, 2 B), -5.56 (d, 2 B), -9.21 (d, 4 B), -11.05 (d, 4 B), -11.44 (d, 4 B), -12.59 (d, 4 B). MS (EI): m/z calcd for $C_7H_{28}{}^{11}B_{20}$ 328.52, found 329. Anal. Calcd for $C_7H_{28}B_{20}$: C, 25.59; H, 8.59; B, 65.82. Found: C, 25.81; H, 8.39; B, 65.51.

2-Benzyl-1,3-di-*o*-carboranylpropane (16). A solution of **8** (33.8 g, 52.2 mmol) dry THF (300 mL) was cooled to -76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (110 mL, 110 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 300 mL of water was added. The solution was diluted with 400 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 300 mL). The combined extracts were dried over anhydrous $MgSO_4$, concentrated in vacuo, and washed with petroleum ether to afford **16** as a white solid in 87% yield (19.1 g, 45.6 mmol): mp 208–211 °C. IR (Nujol, cm^{-1}): 3060, 2950, 2605, 1310, 1081, 722. ^1H NMR ($(CD_3)_2CO$): 7.30 (m, 5 H), 4.55 (s, 2 H), 2.73 (d, 2 H, J = 6.9), 2.43 (dd, 4 H, J = 9.7), 2.24 (m, 1 H). ^{13}C NMR ($(CD_3)_2CO$): 139.0, 129.7, 129.3, 127.4, 75.6, 64.4, 41.7, 40.5, 40.2. ^{11}B NMR (acetone): -2.24 (d, 2 B), -5.10 (d, 2 B), -9.07 (d, 4 B), -11.24 (d, 8 B), -12.48 (d, 4 B). MS (EI): m/z calcd for $C_{14}H_{34}{}^{11}B_{20}$, 418.65, found 418.50.

3-*o*-Carboranyl-1-propene (17). A solution of **9** (3.2 g, 10.7 mmol) in dry THF (35 mL) was cooled to -76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (11.8 mL, 11.8 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 20 mL of water was added. The solution was diluted with 100 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give **17** as a white solid in 71% yield (1.4 g, 7.5 mmol): mp oil. Spectroscopic data were in agreement with literature.[15] IR (neat, cm^{-1}): 2960, 2584, 1862, 1640, 1460, 1435, 1304, 1209, 1113, 1067, 928, 725. ^1H NMR ($(CD_3)_2CO$): 5.78 (m, 1 H), 5.20 (s, 1 H), 4.50 (s, 1 H), 3.07 (d, 2 H, J = 7.3). ^{13}C NMR ($(CD_3)_2CO$): 132.8, 120.5, 75.3, 62.2, 41.9. ^{11}B NMR (acetone): -3.68 (d, 1 B), -10.27 (d, 7 B), -12.95 (d, 2 B), -14.31 (d, 2 B).

4-*o*-Carboranyl-1-butene (18). A solution of **10** (1.4 g, 4.3 mmol) in dry THF (35 mL) was cooled to -76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (4.3 mL, 4.3 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 20 mL of water was added. The solution was diluted with 100 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give **18** as a white solid in 63% yield (0.5 g, 2.7 mmol): mp oil. Spectroscopic data were in agreement with literature.[4] IR (neat, cm^{-1}): 3068, 2931, 2589, 1643, 1450, 1121, 1070, 1018, 923, 725. ^1H NMR ($(CD_3)_2CO$): 5.75 (m, 1 H), 5.04 (m, 2 H), 4.61 (s, 1 H), 2.42 (m, 2 H), 2.25 (m, 2 H). ^{13}C NMR ($(CD_3)_2CO$): 136.4, 116.5, 76.3, 63.1, 37.3, 33.7. ^{11}B NMR (acetone): -2.40 (d, 1 B), -5.50 (d, 1 B), -9.08 (d, 2 B), -10.96 (d, 4 B), -12.51 (d, 2 B).

3-*o*-Carboranyl-1-propanol (19). A solution of **11** (2.5 g, 7.9 mmol) in dry THF (70 mL) was cooled to -76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (7.9 mL, 7.9 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 20 mL of water was added. The solution was diluted with 100 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give **19** as a white solid in 95% yield (1.5 g, 7.5 mmol): mp oil. Spectroscopic data were in agreement with literature.[9] IR (Nujol, cm^{-1}): 3322, 2929, 2597, 1640, 1450, 1368, 1250, 1121, 1039, 944, 836, 723. ^1H NMR ($(CD_3)_2CO$): 4.44 (s, 1 H), 4.07 (s, 1 H), 3.49 (t, 2 H, J = 5.9), 2.38 (m, 2 H), 1.67 (m, 2 H). ^{11}B NMR (acetone): -2.45 (d, 1 B), -5.74 (d, 1 B), -9.21 (d, 2 B), -11.07 (d, 4 B), -12.63 (d, 2 B).

***o*-Carboranylmethanol (20).** To a solution of **12** (113 mg, 0.36 mmol) in dry THF (30 mL) at 0 °C was added a 1.0 M solution of lithium aluminum hydride (0.50 mL, 0.50 mmol) dropwise with stirring. The solution remained at 40 °C for 2 h, was quenched with 3 mL of water, and was transferred to a separatory funnel and diluted with 20 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 20 mL). The combined extracts were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give **20** as a white solid in 71% yield (44 mg, 0.25 mmol): mp 229–230 °C. Spectroscopic data were in agreement with literature.[9] IR (Nujol, cm^{-1}): 3391, 2924, 2615, 1119, 1039, 723. ^1H NMR ($(CD_3)_2CO$): 5.45 (t, 1 H), 4.58 (s, 1 H), 4.09 (s, 2 H). ^{13}C NMR ($(CD_3)_2CO$): 77.9, 65.1, 60.0. ^{11}B NMR (acetone): -3.14 (d, 1 B), -5.46 (d, 1 B), -9.42 (d, 2 B), -11.60 (d, 2 B), -12.87 (d, 2 B), -13.11 (d, 2 B).

Attempted Synthesis of *o*-Carboranecarboxylic Acid Methyl Ester. A solution of **12** (0.9 g, 2.8 mmol) in dry tetrahydrofuran (30 mL) was cooled to -76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (3.1 mL, 3.1 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and then 5 mL of water was added. The solution was diluted with diethyl ether (50 mL) and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was determined by proton and carbon NMR to be 1,2-$C_2B_{10}H_{12}$.

Silyl-*m*-carborane 22. To a solution of 1,7-dicarbadodecaborane (**21**) (25.0 g, 173.5 mmol) in a dry benzene/diethyl ether (2:1) mixture (300 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (76.3 mL, 190.8 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and *tert*-butyldimethylsilyl chloride (27.5 g, 182.1 mmol) in a benzene/diethyl ether (2:1) mixture (100 mL) was added dropwise but rapidly. The solution was refluxed overnight, quenched with 100 mL of water, transferred to a separatory funnel, and diluted with 200 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (3 × 200 mL). The combined extracts were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. Sublimation at 60 °C (1 × 10^{-3} mmHg) removed unreacted 1,7-dicarbadodecaborane(12). The product **22** distilled at 90 °C in 40% yield (17.8 g, 68.7 mmol): mp liquid. IR (Nujol, cm^{-1}): 2938, 2596, 1467, 1411, 1394, 1365, 1256, 1135, 1087, 1050, 1007, 986, 931, 872, 837, 826, 803, 787, 730. ^1H NMR ($(CD_3)_2CO$): 3.62 (s, 1 H), 1.01 (s, 9 H), 0.18 (s, 9 H). ^{13}C NMR ($(CD_3)_2CO$): 65.6, 59.2, 27.1, 19.6, -3.9. ^{11}B NMR (acetone): -3.85 (d, 2 B), -8.97 (d, 2 B), -10.96 (d, 4 B), -14.51 (d, 2 B). High-resolution MS (EI): m/z calcd for $C_8H_{26}{}^{11}B_{10}Si - C_4H_9$, 201.3761, found 202.1984.

(Silyl-*m*-carboranyl)methane 23. To a solution of **22** (1.6 g, 6.2 mmol) in a dry benzene/diethyl ether (2:1) mixture (50 mL) at 0 °C was added a 2.5 M solution of n-BuLi in hexane (2.7 mL, 6.9 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to ambient temperature. The solution was cooled to 0 °C and methyl iodide (0.4 mL, 6.6 mmol) was added dropwise with stirring. After refluxing overnight, the solution was quenched with 20 mL of water, transferred to a separatory funnel, and diluted with 50 mL of diethyl ether. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 50 mL). The combined filtrates were then dried over anhydrous $MgSO_4$ and concentrated in vacuo to give white solid **23** in 90% yield (1.5 g, 5.6 mmol): mp 41–43 °C. IR (Nujol, cm^{-1}): 2918, 2597, 1391, 1254, 1191, 1069, 1005, 931, 823, 731, 674. ^1H NMR ($(CD_3)_2CO$): 1.75 (s, 3 H), 1.02 (d, 9 H), 0.18 (s, 6 H). ^{13}C NMR ($(CD_3)_2CO$): 74.2, 66.0, 27.2, 25.0, 19.7, -3.8. ^{11}B NMR (acetone): -0.32 (d, 1 B), -8.14 (d, 3 B), -8.71 (d, 2 B), -10.51 (d, 2 B), -11.97 (d, 2 B).

***m*-Carboranylmethane (24).** A solution of **23** (1.5 g, 5.5 mmol) in dry THF (50 mL) was cooled to -76 °C and a 1.0 M solution of tetrabutylammonium fluoride in THF (5.8 mL, 5.8 mmol) was added dropwise with stirring. The mixture was allowed to stir for 30 min while being warmed to room temperature, and

then 7 mL of water was added. The solution was diluted with 30 mL of diethyl ether and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with additional Et_2O (2 × 100 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was sublimed at 70 °C (1 × 10^{-3} mmHg) to give **24** as a white solid in 57% yield (0.5 g, 3.1 mmol): mp 195–198 °C. Spectroscopic data were in agreement with literature.[19] IR (Nujol, cm^{-1}): 2918, 2600, 1336, 1252, 1139, 1055, 1002, 933, 838, 784, 726. ^1H NMR ($(CD_3)_2CO$): 3.45 (s, 1 H), 1.74 (s, 3 H). ^{13}C NMR ($(CD_3)_2CO$): 71.6, 56.9, 26.2. ^{11}B NMR (acetone): −2.68 (d, 1 B), −9.20 (d, 1 B), −9.94 (d, 4 B), −12.45 (d, 2 B), −15.81 (d, 2 B).

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Registry No. 1, 16872-09-6; 2, 135457-04-4; 3, 138490-21-8; 4, 135481-15-1; 5, 135457-07-7; 6, 138490-22-9; 7, 138490-23-0; 8, 138490-24-1; 9, 138490-25-2; 10, 138490-26-3; 11, 138490-27-4; 12, 138490-28-5; 13, 23835-38-3; 14, 17526-10-2; 15, 93784-70-4; 16, 138490-29-6; 17, 30619-60-4; 18, 17522-80-4; 19, 23835-93-0; 20, 19610-34-5; 21, 51999-28-1; 22, 138490-30-9; 23, 138490-31-0; 24, 17378-55-1; *tert*-butyldimethylsilyl chloride, 18162-48-6; α,α′-dibromo-*o*-xylene, 91-13-4; 1-bromobutane, 109-65-9; benzyl bromide, 100-39-0; 1,3-dibromopropane, 109-64-8; 2-benzyl-1,3-bis(*p*-toluenesulfonyloxy)propane, 86103-46-0; allyl bromide, 106-95-6; 4-bromo-1-butene, 5162-44-7; trimethylene oxide, 503-30-0; methyl chloroformate, 79-22-1.

Regiospecific Synthesis of the Aminoimidazoquinoxaline (IQx) Mutagens from Cooked Foods

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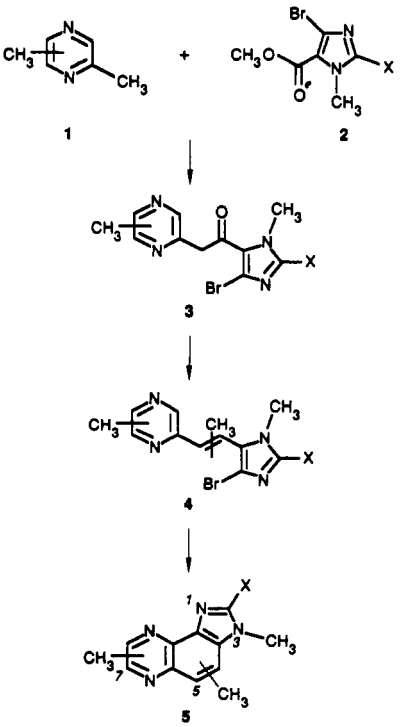
A versatile regiospecific synthesis has been developed to prepare the six dimethyl- and trimethyl-substituted 2-aminoimidazoquinoxaline (IQx) regioisomers **35**, **36**, **37**, **38**, **39**, and **40** for complete and unambiguous characterization. The key reaction step in the synthetic sequence for these angular tricycles is a photodehydrohalogenative cyclization of suitably substituted pyrazinylimidazolylethylene intermediates derived from common pyrazine and fully functionalized imidazole precursors. The reaction sequence developed allows for versatility in the substitution pattern as well as total regioisomeric control for the synthesis of all possible methyl and polymethyl analogues of IQx. Comparison of the physical properties among the isomeric di- and trimethyl-IQx's has established the value of unambiguous regiospecific synthesis for structural assignments in this food mutagen series.

Among the mutagens and potential carcinogens formed when protein-containing foods are cooked at high temperatures,[1] the dimethyl- and trimethyl-2-aminoimidazo-[4,5-*f*]quinoxalines (the IQx's) are among the most potent.[2] The isolation from cooked food, assignment of structure, and synthesis have been reported for a number of these dimethyl- and trimethyl-2-amino-IQx's.[3,4,5] Most of the synthetic methods encounter regioisomer problems at one or more stages or are restricted to a single substitution pattern.[6,7] Furthermore, since the various cooked food

Scheme I. Synthetic Plan



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