242 *Inorg. Chem.* **1993**, *32*, 242–243

A Convenient Synthesis of Carboranyl Aldehydes from (Hydroxymethyl)carboranes

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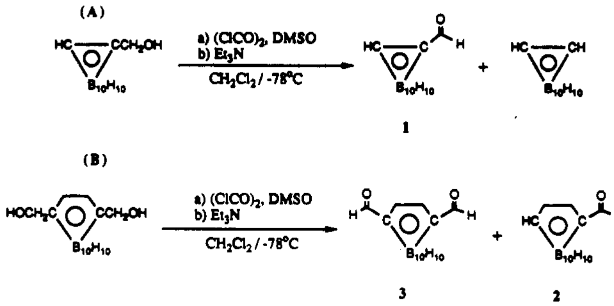
The *C*-formyl derivatives of carboranes are important to the further development of organocarborane chemistry. However, the chemistry of carboranyl aldehydes and their application in the synthesis of other carborane derivatives has been studied in only a few limited cases[1-3] due to the lack of a convenient synthesis of these rare precursors. Only a few methods have been reported for the synthesis of carboranyl aldehydes, and these include the ozonization of vinyl-*o*-carboranes,[2,4] the hydrogenation of *o*-carboranyl acid chlorides over a palladium catalyst in boiling xylene[5] or in the presence of trimethylsilane,[6] and the reaction of 1-phenyl-2-cyano-*o*-carborane with diisobutylaluminum hydride and water.[7] Another method utilizes acid hydrolysis of *C*-formylcarborane acetals to afford *C*-formylcarboranes in 40–63% yield.[5,8]

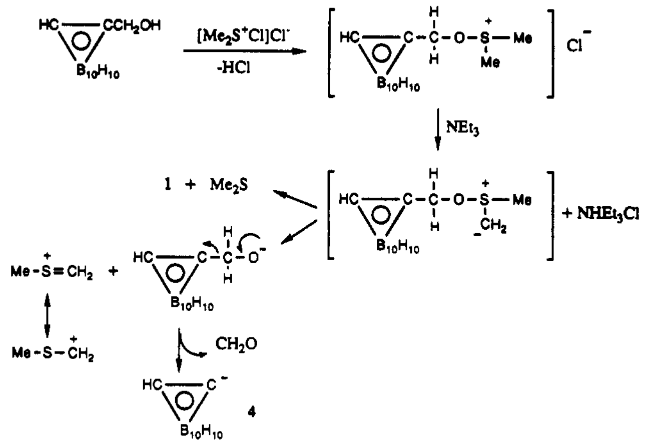
It was reported that the oxidation of (hydroxymethyl)-*o*-carborane with CrO_3 or permanganate did not yield the desired aldehyde[9] nor did mild oxidation with DMSO.[10] Since the Swern oxidation has proved to be very useful in the transformation of primary alcohols to aldehydes,[11] we decided to explore this reaction for the conversion of (hydroxymethyl)carboranes to the corresponding aldehydes.[12] Our results are reported herein.

Reaction of (hydroxymethyl)-*o*-carborane with DMSO, oxalyl chloride, and Et_3N in methylene chloride at −78 °C affords *o*-carboranyl aldehyde (**1**) in 43% yield. The side product is *o*-carborane (12%) (Scheme IA). Similarly, the oxidation of bis(hydroxymethyl)-*m*-carborane gave bis(*C*-formyl)-*m*-carborane (**3**) in 41% yield along with the formation of a small amount of *m*-carboranyl aldehyde (**2**) (7%) (Scheme IB). The oxidation of bis(hydroxymethyl)-*o*-carborane under Swern oxidation conditions gave oils which could not be characterized. To our knowledge, bis(*C*-formyl)-*o*-carborane has not been successfully synthesized. The attempt to prepare it from the acid hydrolysis of bis(diethoxymethyl)-*o*-carborane gave only the cyclic *o*-carboranyl ether.[6]

Scheme I



Scheme II



The oxidations of a variety of alcohols with dimethyl sulfoxide "activated" by numerous electrophiles were studied in the past, and oxalyl chloride was found to be the most generally effective.[11] The yields of carbonyl derivatives were typically over 95%. The relatively low yield of carboranyl aldehydes obtained from the Swern oxidation of (hydroxymethyl)carboranes may be due to the facile formation of the carboranyl anion **4**, which is well documented in the literature[1] and arises due to the strong electron-withdrawing character of the carborane cage. The proposed reaction pathways (Scheme II) are analogous to those suggested by Swern et al.[14]

The ^{13}C NMR spectra of carboranyl aldehydes are reported here for the first time. The chemical shifts of the carbonyl carbon are 184.1 ppm for *C*-formyl-*o*-carborane, 187.4 ppm for *C*-formyl-*m*-carborane, and 184.2 ppm for bis(*C*-formyl)-*m*-carborane, respectively. In comparison, chemical shifts for the more common aliphatic aldehydes range from 203 to 199 ppm.[15] The upfield shift of the resonance of the carbonyl carbon is undoubtedly due to the enhanced electron-withdrawing properties of the carborane cage.[15]

The two-step synthesis of carboranyl aldehydes in moderate yield from *o*- or *m*-carborane precursors is quite convenient. This method is comparable to the acid hydrolysis of carboranyl acetals.[8] Even though the hydrogenation of the acid halides of carboranes in the presence of triethylsilane produces carboranyl aldehydes in higher yields, it requires three steps to prepare the precursor carboranyl acid chlorides. The reaction also takes 22–60 h to complete.[6] The Swern oxidation of (hydroxymethyl)carboranes provides a new entry to the chemistry of carboranyl aldehydes, which, in turn, will open the door to other new carborane derivatives of importance to material science and biomedicine.

Experimental Section

General Methods. Standard Schlenk line techniques were employed for all manipulations of air- and moisture-sensitive compounds. All solvents were dried and distilled before use. DMSO and CH_2Cl_2 were freshly distilled over CaH_2, and Et_3N was distilled over KOH. Oxalyl chloride was purchased from Aldrich and used without further purification. (Hydroxymethyl)-*o*-carborane and bis(hydroxymethyl)-*m*-carborane were prepared according to the literature methods.[16,17] Melting points are

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(12) A high-yield (85%) synthesis of *C*-formyl-*o*-carborane according to Corey's method[13] from the reaction of the (hydroxymethyl)-*o*-carborane with *N*-chlorosuccinimide and dimethyl sulfide was achieved by Ji Li and Maitland Jones, Jr., private communication.

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uncorrected. IR spectra of KBr pellets were recorded with a Beckman FT-1100 instrument. ^1H, ^{13}C, and ^{11}B NMR spectra were recorded with Bruker AF 200, AM 360, and AM 500 spectrometers. Chemical shifts for ^1H and ^{13}C NMR spectra were referenced to the residual protons and carbons in deuterated solvents. Chemical shift values for ^{11}B spectra were referenced relative to external $BF_3{\cdot}OEt_2$ (δ 0.0 ppm with negative δ value upfield). Electron impact mass spectra were obtained on an AEI Ltd. Model MS-902 sector-filled double-focusing spectrometer.

***C*-Formyl-*o*-carborane (1).** A solution of CH_2Cl_2 (20 mL) and oxalyl chloride (1.6 mL, 12.0 mmol) was placed in a 250-mL Schlenk flask. The solution was cooled in a dry ice/acetone bath, and DMSO (1.96 mL, 27.6 mmol) in 5 mL of CH_2Cl_2 was added dropwise to the magnetically stirred oxalyl chloride solution at −78 °C. The evolution of gas was observed, (hydroxymethyl)-*o*-carborane (1.25 g, 7.14 mmol) in 10 mL of CH_2Cl_2 was added, and stirring was continued for 15 min. Et_3N (7.0 mL, 50.2 mmol) was added, and the reaction mixture was allowed to warmed to room temperature. Water (50 mL) was then added, and the aqueous phase was extracted three times with CH_2Cl_2 (3 × 10 mL). The combined organic phase was washed with H_2O and dried over $MgSO_4$. The filtered solution was concentrated to a yellowish oil from which 700 mg of waxy solid was obtained by extraction with pentane. Sublimation of the solid, followed by chromatography on silica gel by eluting with ether/hexane (15:75), gave 120 mg of *o*-carborane and 534 mg of **1** (43%): mp 207–209 °C [lit.[5] mp 208–209 °C]; IR (KBr) 2610 (B–H), 1750 (C=O) cm^{-1}; ^1H NMR (200 MHz, acetone-d_6) δ 9.49 (s, 1H), 4.97 (s, 1H, carborane H), 0.7–4.0 (m, 10H); ^{13}C NMR (90.56 MHz, $CDCl_3$) δ 184.1 (*C*HO), 74.3 (carborane C), 54.1 (carborane C); ^{11}B NMR (160.46 MHz, acetone) δ −2.2, −8.7, −12.6 (2:2:6).

Bis(*C*-formyl)-*m*-carborane (3) and *C*-Formyl-*m*-carborane (2). A solution of CH_2Cl_2 (20 mL) and 2.0 M oxalyl chloride in CH_2Cl_2 (10.78 mL, 21.56 mmol) was placed in a 250-mL Schlenk flask. The solution was cooled in a dry ice/acetone bath, and DMSO (3 mL, 43.12 mmol) was added dropwise to the magnetically stirred oxalyl chloride solution at −78 °C. The evolution of gas was observed, bis(hydroxymethyl)-*m*-carborane (2 g, 9.8 mmol) in 15 mL of CH_2Cl_2 was added, and stirring was continued for 10 min. Et_3N (11 mL, 80 mmol) was added, and the reaction mixture was allowed to warm to room temperature. The reaction was quenched with 20 mL H_2O. The water layer was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic phase was washed with H_2O (3 × 15 mL) and dried over $MgSO_4$. The organic solvent was evaporated, and the oil obtained was extracted with pentane to give a yellowish solid. The solid was chromatographed on a silica gel column eluted with a mixture of 25% ether in hexane to give 110 mg of **2** (6%) and then 810 mg of **3** (41%). **3**: mp 162–163 °C [lit.[6] mp 164 °C]; IR (KBr) 2642 (B–H), 1755 (C=O) cm^{-1}; ^1H NMR (200 MHz, acetone-d_6) δ 9.39 (s, 2H, C*H*O), 1.0–4.5 (m, 10H); ^{13}C NMR (90.56 MHz, $CDCl_3$) δ 184.2 (*C*HO), 78.3 (carborane C); ^{11}B NMR (160 MHz, Et_2O) δ −5.6, −9.6, −11.4, −15.3 (2:2:4:2). **2**: mp 212–214 °C [lit.[5] mp 213–214 °C]; IR (KBr, cm^{-1}) ^1H NMR (200 MHz, acetone-d_6) δ 9.24 (s, 1H, C*H*O), 3.92 (s, 1H, carborane H), 1.0–4.2 (m, 10H, B*H*); ^{11}B NMR (160.46 MHz, Et_2O) δ −5.9, −9.8, −11.9, −15.8 (2:2:3:3); ^{13}C NMR (90.56 MHz, acetone-d_6) δ 187.1 (*C*HO), 79.5 (carborane C), 57.5 (carborane C); MS *m/z* 171 (M^+ − 1, 35%).

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