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Communications to the Editor

Synthesis and Structure of the Polyhedral $[\mu\text{-}B_{20}H_{17}OH]^{2-}$ Borane Anion Containing Both Oxygen- and Hydrogen-Bridge Bonds

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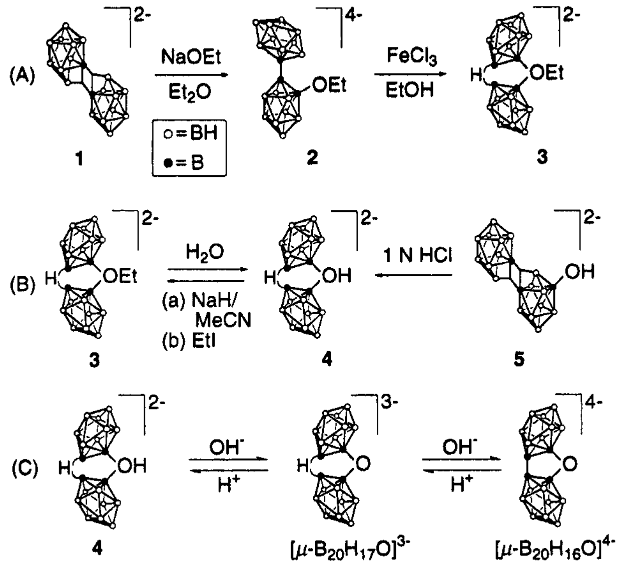
The syntheses of derivatives of the polyhedral borane anion $[n\text{-}B_{20}H_{18}]^{2-}$ (**1**) have been the subject of considerable research because of their potential application in the boron neutron capture therapy (BNCT) of cancer.[1] The synthesis of the hydroxyl-substituted anion $[ae\text{-}B_{20}H_{17}OH]^{4-}$ and its isomer $[a^2\text{-}B_{20}H_{17}OH]^{4-}$ have been reported,[2] and their oxidation by aqueous ferric ion has been shown to produce $[n\text{-}B_{20}H_{17}OH]^{2-}$ (**5**).[2] Reinvestigation of this chemistry has led to the discovery of a new isomer of $[B_{20}H_{17}OH]^{2-}$: an unprecedented oxygen-, hydrogen-bridged polyhedral borane anion, $[1,1'\text{-}(\mu\text{-H})\text{-}2,2'\text{-}(\mu\text{-OH})\text{-}1\text{-}(1'\text{-}B_{10}H_8)B_{10}H_8)]^{2-}$, designated as $[\mu\text{-}B_{20}H_{17}OH]^{2-}$ (**4**). Oxygen-substituted derivatives of **4** are readily accessible by simple alkylation reactions, giving this boron-rich anion the potential to conjugate to a variety of organic substrates. We report here the synthesis, structure, and reactions of the oxygen and hydrogen doubly bridged polyhedral borane anion $[\mu\text{-}B_{20}H_{17}OH]^{2-}$.

The addition of $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$[3] to a stirred suspension of NaOEt (prepared *in situ* from NaH and EtOH) in dry diethyl ether afforded $Na_4[1\text{-}(2'\text{-}B_{10}H_9)\text{-}2\text{-}(OC_2H_5)B_{10}H_8]$ (designated $Na_4[ae\text{-}B_{20}H_{17}OC_2H_5]$, $Na_4[$**2**$]$)[4] in high yield (Scheme 1A). The room temperature ferric ion oxidation of **2** in anhydrous ethanol produced $[1,1'\text{-}(\mu\text{-H})\text{-}2,2'\text{-}(\mu\text{-}OC_2H_5)\text{-}1\text{-}(1'\text{-}B_{10}H_8)B_{10}H_8)]^{2-}$ (**3**, $[\mu\text{-}B_{20}H_{17}OC_2H_5]^{2-}$), isolated in 64% yield as its tetramethylammonium salt.[5] The structural identity of $[Me_4N]_2[$**3**$]$ has been confirmed by X-ray crystallographic analysis.[6]

The hydrolysis of **3** to $[\mu\text{-}B_{20}H_{17}OH]^{2-}$ (**4**)[7] was accomplished in 75% isolated yield by heating a solution of $[Me_4N]_2[\mu\text{-}B_{20}H_{17}OC_2H_5]$ in H_2O at the boiling point for 24 h (Scheme 1B). In order to ascertain the fate of the ethyl group of **3**, this reaction was also performed with D_2O as the solvent. Examination of the product mixture by ^1H NMR indicated the presence of EtOD although some ethylene could also have been formed.

Scheme 1



The $[\mu\text{-}B_{20}H_{17}OH]^{2-}$ anion was also obtained from the rearrangement of its known isomer $[n\text{-}B_{20}H_{17}OH]^{2-}$ (**5**).[2] Heating a solution of $[Me_4N]_2[$**5**$]$ in 1 N HCl for 14 d resulted in a solution whose ^{11}B NMR indicated almost complete conversion of **5** to **4**. After recrystallization, the isolation of $[Me_4N]_2[$**4**$]$ was accomplished in 43% yield. When pure **4** was subjected to the same conditions, **5** was not observed, demonstrating that the rearrangement is irreversible.

The anion **4** has been characterized by ^{11}B NMR spectroscopy, electrospray ionization mass spectroscopy (ESI-MS), and X-ray crystallography. An ORTEP drawing[8] of the structure of the **4** anion is shown in Figure 1. This polyhedral borane anion consists of two $[B_{10}H_{10}]^{2-}$ fragments bridged by both oxygen and hydrogen atoms. As a consequence of the bridging atoms between the two borane cages, a six-membered B−H−B−B−O−B ring is formed. The bond distances within the two B_{10} cages are normal and similar to those found in other $[B_{10}H_{10}]^{2-}$ structures. The hydrogen atom of the −OH group lies essentially in the plane of the six-membered ring, and there is a hydrogen bond within the crystal between this hydrogen atom and a solvent water molecule. The three-coordinate oxygen atom of **4** exhibits essentially planar geometry. The sum of the three angles about oxygen is 353.7°. This geometry has been observed previously in species with tricoordinate oxygen bound to boranes and carboranes.[9]

A hydrogen atom bridges the two apical boron atoms of the two borane cages. A similar bridging hydrogen was recently

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(1) (a) Shelly, K.; Feakes, D. A.; Hawthorne, M. F.; Schmidt, P. G.; Krisch, T. A.; Bauer, W. F. *Proc. Natl. Acad. Sci. U.S.A.* **1992**, *89*, 9039−9043. (b) Feakes, D. A.; Shelly, K.; Knobler, C. B.; Hawthorne, M. F. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 3029−3033.

(2) Hawthorne, M. F.; Pilling, R. L.; Garrett, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 4740.

(3) (a) Lipscomb, W. N. *Proc. Natl. Acad. Sci. U.S.A.* **1961**, *47*, 1791. (b) Pilling, R. L.; Hawthorne, M. F.; Pier, E. A. *J. Am. Chem. Soc.* **1964**, *86*, 3568.

(4) Spectroscopic data for **2**. $^{11}B\{^1H\}$ NMR (ppm, H_2O): 9.8 (1B, apical B−B); 3.6 (1B, apical B−H); −1.5 (1B, apical B−H); −3.3 (1B, B−O); −9.3 (1B, apical); −23.4, −26.1, −28.9, and −34.5 (total 15B, equatorial B−H). ^1H NMR (ppm, CD_3CN): 3.52 (q, J_{HH} = 7 Hz, B−O−CH_2); 0.90 (t, J_{HH} = 7 Hz, −CH_3). ^{13}C NMR (ppm, D_2O): 78.26 (B−O−CH_2), 13.15 (−CH_3).

(5) Spectroscopic data for **3**. $^{11}B\{^1H\}$ NMR (ppm, H_2O): 13.9 (2B, B−B); 6.6 (2B, apical B−H); −8.9 (2B, B−O−B); −19.8, −20.5, −26.6, and −29.3 (total 14B, equatorial B−H). Electrospray MS (*m/z*): 138.6 $\{B_{20}H_{17}OC_2H_5\}^{2-}$; 279.0 $\{(H)(B_{20}H_{17}OC_2H_5)\}^{1-}$; 296.0 $\{(H)(H_2O)(B_{20}H_{17}OC_2H_5)\}^{1-}$; 352.4 $\{(Me_4N)(B_{20}H_{17}OC_2H_5)\}^{1-}$. The compound was ion-exchanged to the sodium salt in H_2O/CH_3CN (1:1) solution using Bio-Rad AG50W-X8, 50−100 mesh cation exchange resin. ^1H NMR (ppm, CD_3CN): 3.15 (q, J_{HH} = Hz, B−O−CH_2); 0.74 (t, J_{HH} = 7 Hz, −CH_3). ^{13}C NMR (ppm, D_2O): 76.01 (B−O−CH_2), 13.98 (−CH_3).

(6) Li, F.; Kane, R. R.; Shelly, K.; Knobler, C. B.; Hawthorne, M. F. Manuscript in preparation.

(7) Spectroscopic data for **4**. $^{11}B\{^1H\}$ NMR (ppm, H_2O): 11.1 (2B, B−B); 2.6 (2B, apical B−H); −4.4 (2B, B−O−B); −20.8, −21.9, and −29.6 (total 14B, equatorial B−H). Electrospray MS (*m/z*): 125.2 $\{B_{20}H_{17}OH\}^{2-}$; 324.4 $\{(Me_4N)(B_{20}H_{17}OH)\}^{1-}$.

(8) $[Me_4N]_2[$**4**$]$ crystallized in the orthorhombic space group $Pbc2_1$ (standard setting $Pca2_1$, No. 29) with a = 12.327(4) Å, b = 13.476(4) Å, c = 16.360(5) Å, V = 2718 Å^3, and Z = 4. Data were collected on a Syntex P1 diffractometer modified by Professor C.E. Strouse of this department, using Cu Kα radiation, to a maximum 2θ = 115°, giving 1944 unique reflections, and the structure was solved by direct methods. The final discrepancy indices were R = 0.069, R_w = 0.086, and GOF = 2.50 for 1313 independent reflections with $I > 3\sigma(I)$.

(9) Peymann, T.; Lork, E.; Gabel, D. *Inorg. Chem.* **1996**, *35*, 1355−1360 and references therein.

S0002-7863(96)01385-6 CCC: $12.00

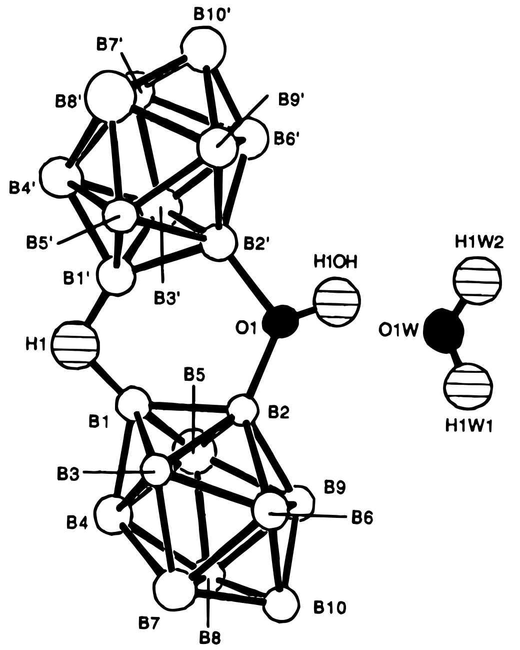

Figure 1. ORTEP representation of the **4** anion showing the atom numbering scheme. For purposes of clarity, the terminal B−H hydrogens have been omitted. Some selected interatomic distances (Å) and angles (deg) are as follows (estimated standard deviations in parentheses): O1−B2 = 1.474(7), O1−B2′ = 1.491(7), B1−B2 = 1.673(9), B1′−B2′ = 1.662(9), B1−B1′ = 1.907(9), B1−H1 = 1.25(6), B1′−H1 = 1.17(6), O1−H(1OH) = 0.908, H(1OH)−O(1W) = 1.809; B2−O1−B2′ = 114.4(7), O1−B2−B1 = 113.2(8), B2−B1−B1′ = 99.0(7), B1−B1′−B2′ = 101.2(7), B1′−B2′−O1 = 111.6(8), B1−H1−B1′ = 104(8), B2′−O1−H(1OH) = 109.1(11), B2−O1−H(1OH) = 130.2(11).

structurally identified in $[a^2\text{-}B_{20}H_{19}]^{3-}$.[10] The apical intercage B(1)−B(1′) separation in **4** is 1.907(9) Å. This is much longer than the intercage B−B bond in $[a^2\text{-}B_{20}H_{18}]^{4-}$ (1.699(4) Å),[11] but it is comparable to the analogous boron−boron distance in the hydrogen-bridged structure of $[a^2\text{-}B_{20}H_{19}]^{3-}$ (1.936(6) Å).[10] In contrast to the structures determined for $[a^2\text{-}B_{20}H_{19}]^{3-}$ and $[a^2\text{-}B_{20}H_{18}]^{4-}$, the B(10)−B(1)−B(1′)−B(10′) array of **4** is nonlinear because of geometrical constraints imposed by the bridging oxygen atom. To our knowledge, **4** is the first polyhedral borane to be simultaneously bridged by both an oxygen and a hydrogen atom which has been crystallographically characterized.

Both the hydroxyl and the bridging hydrogens of **4** are acidic (Scheme 1C). Dissolution of the anion **4** in water produces an acidic solution (pH ≈ 2) due to the ionization of the hydroxyl proton and the formation of $[\mu\text{-}B_{20}H_{17}O]^{3-}$.[12] The aqueous titration of this acidic solution produces no observable changes in the ^{11}B NMR spectrum of the anion. The K_a of the hydroxyl proton is estimated to be 10^{-3}.[13]

The deprotonation of the hydrogen bridge of $[\mu\text{-}B_{20}H_{17}O]^{3-}$ occurs only in strongly basic solution (Scheme 1C). The removal of this proton results in the formation of $[\mu\text{-}B_{20}H_{16}O]^{4-}$, which can easily be distinguished from $[\mu\text{-}B_{20}H_{17}O]^{3-}$ in the ^{11}B NMR spectrum.[14] The estimated pK_a of this hydrogen bridge is approximately 13,[13] and therefore it is much less acidic than the hydrogen bridge in $[a^2\text{-}B_{20}H_{19}]^{3-}$ (pK_a = 7.3).[15] This remarkable difference in acidity is likely the result of the structures and relative stabilities of the conjugate bases of these two acids. The conjugate base $[a^2\text{-}B_{20}H_{18}]^{4-}$, formed by the deprotonation of $[a^2\text{-}B_{20}H_{19}]^{3-}$, has a stable, strain-free structure,[11] in which the *exo*-polyhedral boron orbitals that form the B−B bond are directed toward one another along the B−B vector. In the corresponding $[\mu\text{-}B_{20}H_{16}O]^{4-}$ ion, overlap of the *exo*-polyhedral orbitals of the apical boron atoms provides a bent B−B bond of diminished stability due to the geometric constraints imposed by the bridging oxygen atom. Thus, the deprotonation of $[\mu\text{-}B_{20}H_{17}O]^{3-}$ results in a five-membered ring whose internal strain is no longer relieved by the presence of the hydrogen bridging the two apical boron atoms.

A demonstration of the facile alkylation of **4** is provided by heating the $[\mu\text{-}B_{20}H_{17}O]^{3-}$ ion with ethyl iodide in MeCN to produce **3** in 88% yield (Scheme 1B). The efficacious alkylation reaction of this oxygen-bridged polyhedral borane anion provides a route to oxygen-substituted species. The derivatization of **4** with organic substrates will lead to a variety of derivatives having potential utility in BNCT. We are continuing the exploration of this novel chemistry.

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Supporting Information Available: Experimental procedures, details of the crystallographic data collection, and tables giving positional and thermal parameters, bond lengths, bond angles, and torsion angles for $[Me_4N]_2[\mathbf{4}]$ (17 pages). See any current masthead page for ordering and Internet access instructions.

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[10] Watson-Clark, R.; Knobler, C. B.; Hawthorne, M. F. *Inorg. Chem.* **1996**, *35*, 2963−2966.

[11] Ng, L.; Ng, B. K.; Knobler, C. B.; Hawthorne, M. F. *Inorg. Chem.* **1992**, *31*, 3669.

[12] Aqueous solutions of **3** are essentially neutral and exhibit one weakly acidic proton, identifying the hydroxyl hydrogen of **4** as the strong acid.

[13] The pK_a of the hydroxyl hydrogen was estimated from the pH of the half-neutralization volume of an aqueous titration. The pK_a of the bridging hydrogen was estimated from integration of ^{11}B spectra at several pH values near the pK_a.

[14] Spectroscopic data for $[\mu\text{-}B_{20}H_{16}O]^{4-}$. $^{11}B\{^1H\}$ NMR (ppm, H_2O, pH ≈ 13.5): 13.8 (2B, B−B); 7.3 (2B, B−O); −8.4 (2B, apical B−H); −22.6 (8B, equatorial B−H); −29.5 (4B, equatorial B−H); −34.8 (2B, equatorial B−H).

[15] Chamberland, B. L.; Muetterties, E. L. *Inorg. Chem.* **1964**, *3*, 1450−1456.