Inorg. Chem. **2004**, *43*, 2018–2020

Inorganic Chemistry

Article

An Improved Method for the Synthesis of [*closo*-$B_{12}(OH)_{12}]^{-2}$

Michael J. Bayer and M. Frederick Hawthorne*

Department of Chemistry and Biochemistry, University of California, Los Angeles,
607 Charles E. Young Drive East, Los Angeles, California 90095-1569

Received October 3, 2003

The dicesium salt of the icosahedral borane anion dodecahydroxy-*closo*-dodecaborate(2–), *closo*-$Cs_2B_{12}(OH)_{12}$, Cs_2**4**, was prepared using an improved synthetic pathway. Heating cesium dodecahydro-*closo*-dodecaborate, *closo*-$Cs_2B_{12}H_{12}$, Cs_2**1**, with 30% hydrogen peroxide added in successive increments at 105–110 °C provided Cs_2**4** in 95% yield. Reaction progress was monitored using ^{1}H-decoupled ^{11}B NMR while ^{17}O NMR provides the most reliable way to detect the presence of peroxides in the reaction solution. The reaction may be safely increased in scale to afford Cs_2**4** in multigram quantities.

Introduction

Since *closo*-borane dianions and *closo*-carboranes are regarded as three-dimensional aromatic species[1] and their reactivity and bonding properties have received attention due to analogy with arenes, the substitution chemistry of the parent species of polyhedral boranes and carboranes, *closo*-$[B_{12}H_{12}]^{2-}$ (**1**),[2] continues to be intensively investigated.[3] Twelve-fold substitution of **1**, *closo*-$[1\text{-}CB_{11}H_{12}]^-$ (**2**), and the three isomeric dicarbaboranes (*closo*-1,2-, 1,7-, and 1,12-$C_2B_{10}H_{12}$) has been accomplished providing hydrophobic derivatives such as *closo*-$[B_{12}Cl_{12}]^{2-}$,[4] *closo*-$[CB_{11}(CH_3)_{12}]^-$,[5] and *closo*-1,12-$C_2B_{10}(CH_3)_{12}$,[6] respectively. Recently, we have reported the B-perhydroxylation of **1**, **2**, and *closo*-1,12-$(HOCH_2)_2$-1,12-$C_2B_{10}H_{10}$ (**3**) by treatment with hot aqueous 30% hydrogen peroxide leading to *closo*-$Cs_2B_{12}(OH)_{12}$ (Cs_2**4**), *closo*-Cs[1-H−$CB_{11}(OH)_{11}$] (Cs**5**), and *closo*-1,12-$(H)_2$-1,12-$C_2B_{10}(OH)_{10}$ (**6**), respectively.[7,8] Per-substituted borane clusters of all types generally have potential applications as hydrophobic space-filling pharmacophores,[9] weakly coordinating anions,[10] components of radioimaging reagents,[11] or drug delivery systems, and as targets for boron neutron capture therapy.[12] These so-called camouflaged polyhedral borane derivatives[13] serve as cores for the synthesis of dendrimer-like derivatives known as closomers.[14] Very recently it has been demonstrated that the spherical sheath of hydroxyl groups in **4** can be fully derivatized affording closomeric dodecaesters[14,15] and dodecaethers,[16,17] respectively. Furthermore, dodecaborates bearing twelve organic linkers with terminal functionality were synthesized[18] for biomedical applications. In order to implement the full potential of compound Cs_2**4** an improved synthetic method has been sought for this salt, since the yields were not consistent using previously published syntheses.[7,8] In addition, it was imperative to safely increase the scale of Cs_2**4**

---

* Author to whom correspondence should be addressed. E-mail: mfh@chem.ucla.edu.

(1) Schleyer, P. v. R.; Najafian, K. *Inorg. Chem.* **1998**, *37*, 3454−3470 and references therein.

(2) Pitochelli, A. R.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1960**, *82*, 3228−3229.

(3) Muetterties, E. L.; Knoth, W. H. *Polyhedral Boranes*; M. Dekker: New York, 1968.

(4) Knoth, W. H.; Miller, H. C.; Sauer, J. C.; Balthis, J. H.; Chia, Y. T.; Muetterties, E. L. *Inorg. Chem.* **1964**, *3*, 159−167.

(5) King, B. T.; Janousek, Z.; Grüner, B.; Trammell, M.; Noll, B. C.; Michl, J. *J. Am. Chem. Soc.* **1996**, *118*, 3313−3314.

(6) Jiang, W.; Knobler, C. B.; Mortimer, M. D.; Hawthorne, M. F. *Angew. Chem.* **1995**, *107*, 1470−1473; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1332−1334.

(7) Peymann, T.; Herzog, A.; Knobler, C. B.; Hawthorne, M. F. *Angew. Chem.* **1999**, *111*, 1129−1132; *Angew. Chem., Int. Ed.* **1999**, *38*, 1062−1064.

(8) Peymann, T.; Knobler, C. B.; Khan, S. I.; Hawthorne, M. F. *J. Am. Chem. Soc.* **2001**, *123*, 2182−2185.

(9) Friedmann, S. H.; DeCamp, D. L.; Sijbesma, R. P.; Srdanov, G.; Wudl, F.; Kenyon, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 6506−6509.

(10) Reed, C. A. *Acc. Chem. Res.* **1998**, *31*, 133−139.

(11) Hawthorne, M. F.; Maderna, A. *Chem. Rev.* **1999**, *99*, 3421−3434.

(12) Soloway, A. H.; Tjarks, W.; Barnum, B. A.; Rong, F. G.; Barth, R. F.; Codogni, I. M.; Wilson, J. G. *Chem. Rev.* **1998**, *98*, 1515−1562.

(13) Rockwell, J. J.; Herzog, A.; Peymann, T.; Knobler, C. B.; Hawthorne, M. F. *Curr. Sci.* **2000**, *78*, 405−409.

(14) Maderna, A.; Knobler, C. B.; Hawthorne, M. F. *Angew. Chem.* **2001**, *113*, 1709−1712; *Angew. Chem., Int. Ed.* **2001**, *40*, 1662−1664.

(15) Thomas, J.; Hawthorne, M. F. *Chem. Commun.* **2001**, *18*, 1884−1885.

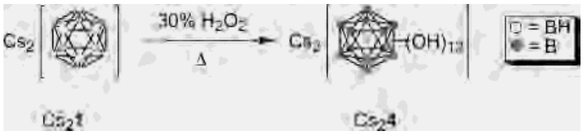
(16) Peymann, T.; Knobler, C. B.; Khan, S. I.; Hawthorne, M. F. *Angew. Chem.* **2001**, *113*, 1713−1715; *Angew. Chem., Int. Ed.* **2001**, *40*, 1664−1667.

(17) Huertas, R.; Peymann, T.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.*, to be submitted.

(18) Li, T.; Bayer, M. J.; Maderna, A.; Khan, S. I.; Hawthorne, M. F. *J. Am. Chem. Soc.*, to be submitted.

10.1021/ic030289w CCC: $27.50

Scheme 1



synthesis to multigram quantities in order to extend the chemistry of this very versatile species.

Results and Discussion

The hydroxylation of Cs_2**1** (Scheme 1) carried out according to the described[7,8] protocol led to inconsistent yields of Cs_2**4**. Reinvestigation of this reaction confirmed the supposition that the per-B-hydroxylated species is thermodynamically less stable than boric acid. Consequently, once kinetic conditions exist for the formation of boric acid in the reaction mixture (easily detected by ^{11}B NMR spectroscopy) the formation of additional boric acid is favored over product leading to a reduced yield of Cs_2**4**. The use of excess 30% hydrogen peroxide (40 mL per g of Cs_2**1**)[7,8] or a reaction temperature above 120 °C increases the loss of Cs_2**4** through boric acid formation.

Another problem which sometimes occurred while using an excess of H_2O_2 was the failure of Cs_2**4** to precipitate even after a reaction time of 12 days, and in these cases the separation of Cs_2**4** from excess H_2O_2 presented difficulties. The removal of hydrogen peroxide under vacuum is unsafe and not recommended, especially when the solution contains polyhedral hydroborates and the destruction of excess hydrogen peroxide with HBr[19] or catalytic amounts of MnO_2[20] increases the concentration of unwanted ions and is not attractive.

To overcome these problems, a search was carried out for an improved synthesis of Cs_2**4** which would provide higher yields allowing a scale-up of the procedure with a minimum of risk. The method of choice which evolved utilized proportionally less hydrogen peroxide and lower reaction temperatures than those previously[7,8] employed. Thus, a minimal amount of 30% hydrogen peroxide is initially employed to completely dissolve Cs_2**1** at 105 °C (about 15−20 mL of 30% H_2O_2 for 2.5 g of Cs_2**1**). The reaction temperature is always maintained below 110 °C, and precipitation of the Cs^+ salts of hydroxylated products begins after 3−5 days. After 5 days the ^{11}B NMR spectrum of the supernatant reaction solution indicates the progress of the reaction. If the reaction is not complete, an additional 2 mL of 30% H_2O_2 (small-scale procedure) is added and the reaction is continued for two additional days. This procedure is repeated until the ^{11}B NMR spectrum of the supernatant reaction solution exhibits only one singlet at −17.1 ppm. Figure 1 shows the time-dependent product distribution in the aqueous phase as determined using ^1H-decoupled ^{11}B NMR spectra. The solubilities of boric acid, hydroxylated intermediates, and Cs_2**4** are sufficiently high to allow the assumption that equilibrium of the supernatant solution and the precipitated solids exists near the conclusion of the reaction and well before.

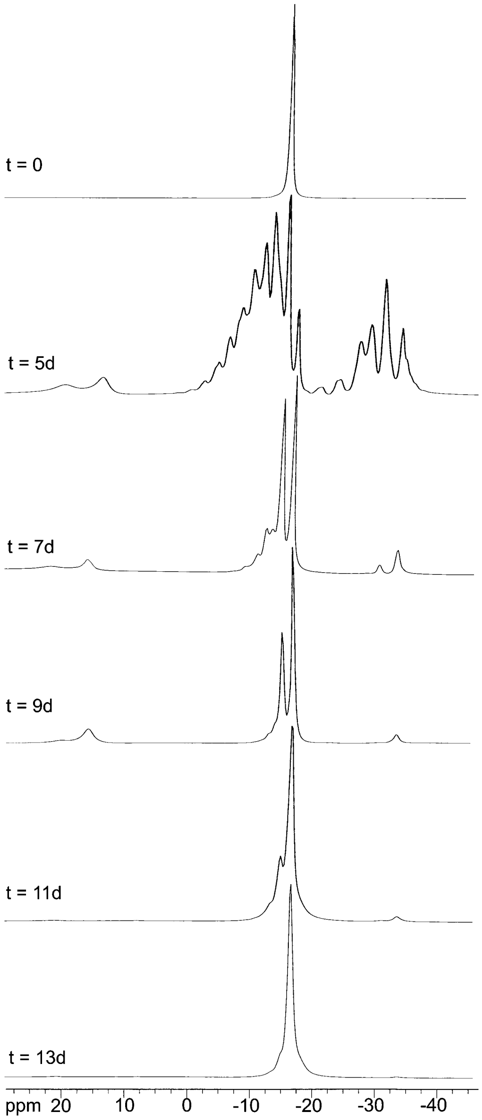


Figure 1. Proton-decoupled ^{11}B NMR spectra of the hydroxylation process of Cs_2**1** showing the course of the reaction as a function of time.[21]

Starting with one signal in the ^1H-decoupled ^{11}B NMR spectrum of Cs_2**1**, the formation of various partially hydroxylated dodecaborates is observed as a collection of resonances representing ^{11}B environments present in solution. Finally, only one symmetrical singlet (Cs_2**4**) is observed, signaling the completion of the reaction. It is noteworthy that no boric acid has been formed (^{11}B resonance at 20 ppm) in the reaction even after 12 days. In general, small-scale reactions (0.5 to 2.5 g of Cs_2**1**) are completed within 5−9 days.

The precipitate obtained after the completion of the reaction was collected by filtration. Since Cs_2**4** is partially

---

(19) Herzog, A.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.* **2001**, *123*, 12791−12797.

(20) Zhou, H.; Shen, Y. F.; Wang, J. Y.; Chen, X.; O'Young, C.-L.; Suib, S. L. *J. Catal.* **1998**, *176*, 321−328.

(21) The proton-decoupled ^{11}B NMR spectra shown in Figure 1 were obtained during the scaled-up reaction described in the Experimental Section, and they are generally representative of all hydroxylation reactions, regardless of size. The only variable is the reaction time, which depends upon the amount of starting material Cs_2**1** and H_2O_2 employed at the beginning of the reaction, and subsequently.

soluble in water, the filtrate was examined for the presence of H_2O_2, which must be destroyed before evaporation to dryness to achieve increased recovery. It was found that the most reliable and sensitive way to detect the presence of H_2O_2 in the filtrate is through the use of ^{17}O NMR spectroscopy, since hydrogen peroxide exhibits a signal at 174 ppm.[22] If excess hydrogen peroxide remains in the filtrate, the filtrate is stirred for another 2 days at 105 °C to destroy H_2O_2 by thermal soaking. When the presence of H_2O_2 is no longer detected by NMR, the filtrate is concentrated to 3−5 mL and an additional NMR search for peroxides is carried out. Once peroxide-free, the residue obtained by evaporation of this filtrate is dried and the residue is combined with the originally precipitated reaction product, washed with cold water, and dried under vacuum to give Cs_2**4** in 95% yield. This result led to an increase in the scale of the reaction to 15 g of Cs_2**1**.

In conclusion, an improved synthetic method leading to Cs_2**4** is described. Less hydrogen peroxide, a lower reaction temperature, and reaction control via ^{11}B NMR provides higher yields of Cs_2**4** than previously[7,8] described. Furthermore, a convenient method for the detection of H_2O_2 (^{17}O NMR) and its thermal decomposition without the introduction of additional reagents is provided. The great advantages of this method are high yields and the feasibility of safe, multigram scale-up.

Experimental Section

CAUTION! *On the scale and under the conditions described here, no explosions have occurred during the synthesis of Cs*$_2$***4****. Nevertheless, this does not rule out the possibility of such an event when dealing with polyhedral boranes, hydroborates, or carboranes and hydrogen peroxide. Departure from the reported procedure is not recommended, and extreme precautions should always be taken to ensure the identity and purity of all reagents. The use of adequate shielding to contain possible explosions is mandatory.*

General Procedures. Pure *closo*-$K_2B_{12}H_{12}$, K_2**1**,[2,23] was obtained from Callery Chemical Co. (BASF). The dicesium salt, Cs_2**1**, was precipitated upon adding an aqueous solution of CsCl to aqueous K_2**1**.[24] The resulting salt was recrystallized from hot water. The ^1H-decoupled ^{11}B NMR spectra were obtained with a Bruker AM-500 spectrometer at 160 MHz and externally referenced to $BF_3 \cdot Et_2O$; peaks upfield of the reference are designated as negative. Electrospray ionization mass spectra (ESI-MS) were recorded by injection of an aqueous solution into an ion spray source with the mass spectrometer operating in the negative-ion mode. Infrared data were obtained using KBr pellets.

Dicesium Dodecahydroxy-*closo*-dodecaborate ($Cs_2$4). To Cs_2**1** (15.0 g, 36.8 mmol) was added 30% hydrogen peroxide (30 mL), and the mixture was heated to 105 °C. Additional H_2O_2 was added slowly with vigorous stirring in 10 mL portions until all of the Cs_2**1** was dissolved (6 × 10 mL of H_2O_2 was added over a period of 1 h) and the solution stirred for 5 days at 105−110 °C. The ^{11}B NMR of the supernatant reaction mixture then indicated that the hydroxylation reaction was not complete. The reaction mixture was treated with H_2O_2 (20 mL) and stirred for an additional 2 days at 105 °C and the ^{11}B NMR examined. This procedure was repeated until the ^{11}B NMR of the supernatant reactant mixture contained only one signal. (Three such additions were made, i.e., 3 × 20 mL of H_2O_2 and 3 × 2 days reaction time; in total: 170 mL of 30% H_2O_2, 13 days reaction time.) Precipitation of hydroxylated material begins between the fifth and the eighth day. Following each new addition of H_2O_2, the white precipitate present initially became yellow during heating to 105−110 °C and colorless after 2−3 h at this temperature. After completion of the reaction, the Cs_2**4** was separated by filtration and washed with cold water and the filtrate stored at 4 °C overnight to obtain additional product, which was separated by filtration and washed with cold water to give additional Cs_2**4**. In order to isolate additional product, the filtrate was checked for H_2O_2 (detected by ^{17}O NMR spectroscopy at 174 ppm[22]) and heated at 105−110 °C for an additional 2 days to destroy H_2O_2, if detected. In the event that no peroxides were detected the filtrate was directly concentrated to 5 mL and checked again for peroxides. Once peroxide-free, the solvent was removed and the residue washed with cold water and dried under vacuum, leading to an additional 5% yield of Cs_2**4**. Total yield: 20.9 g, 94.6%. The analytical data were in agreement with those reported previously:[7,8]

^{11}B NMR (H_2O) $\delta = -17.1$; IR (KBr pellet) $1/\lambda$ (cm^{-1}) = 3370 (s, v br), 1190 (s), 1127 (s), 714 (m); ESI-MS $m/z = 335.1$ [H**1**]$^-$.

Acknowledgment. We gratefully acknowledge the support of this research by the National Science Foundation for its research grant (CHE-0111718) and equipment grants (CHE-9610080, CHE-9808175, CHE-9974928, and CHE-00782990).

IC030289W

---

[22] Rodger, C.; Sheppard, N.; McFarlane, C.; McFarlane, W. In *NMR and the Periodic Table*; Harris, R. K., Mann, B. E., Eds.; Academic Press: London, 1978; pp 383−419.

[23] Miller, H. C.; Miller, N. E.; Muetterties, E. L. *Inorg. Chem.* **1964**, *3*, 1456−1463.

[24] Aftandilian, V. D.; Miller, H. C.; Parshall, G. W.; Muetterties, E. L. *Inorg. Chem.* **1962**, *1*, 734−737.