Camouflaged Polyhedral Species

The three isomers of the icosahedral $C_2B_{10}H_{12}$ (1,2- or *ortho*-; 1,7- or *meta*-; and 1,12- or *para*-) carboranes and the isoelectronic polyhedral borane dianion $B_{12}H_{12}^{2-}$ are uniquely suited to play the role of building-blocks in the construction of molecular scaffolding and stereochemically rigid platforms. These versatile components often provide sites for further functionalization of the macrostructure or to add other interesting chemical properties. This versatility has lead to the formation of several different types of structural motifs, including carborods, mercuracarborands, carboracycles, and camouflaged carboranes and polyhedral borane anions. This section of the web site will focus on the latter of these structural types, the camouflaged carboranes and polyhedral borane anions. The term camouflaged carborane or polyhedral borane describes a molecule in which all, or very nearly all, the B–H vertices have been substituted by a typical organic substituent. The resulting polyhedral borane derivative, which has a borane core stabilized by multicenter electron delocalization, is shrouded by a periphery of organic substituents. Hence, camouflaged carboranes demonstrate chemical properties indicative of their hybrid nature between that of the thermally and chemically stable carboranes and boranes and the substitutionally versatile aliphatic hydrocarbons.

Electrophilic substitution of hydrogen by halogenation or alkylation at B–H vertices of the carboranes is a well-known reaction. However, it was our initial report of the high-yield synthesis of per-B-methyl *para*-carborane by the methylation of *para*-carborane with methyl triflate and a catalytic amount of triflic acid that initiated the development of a new class of unprecedented molecules, the camouflaged carboranes. This remarkable chemoselectivity leaves the C–H vertices free for further functionalization using other means. The complete methylation of all the vertices of *para*-carborane can be accomplished if 1,12-dimethyl-1,12-dicarba-*closo*-dodecaborane is methylated using methyl triflate and triflic acid, producing dodecamethyl-1,12-dicarba-*closo*-dodecaborane(12) in excellent yield, 91%. Figure 1a presents a view of a space-filling model of this novel icosahedral hydrocarbon-like molecule. Radical photochlorination of decamethyl-*para*-carborane using chlorine in carbon tetrachloride under UV irradiation forms decakis(dichloromethyl)-1,12-dicarba-*closo*-dodecaborane(12) in high yield, 88%. This more extensively camouflaged carborane is depicted in Figure 1b as a ball and stick structure showing the rigorous stereochemical orientation of the $–CHCl_2$ substituents. The extensive steric crowding observed in the space-filling diagram of deca(dichloromethyl)-*para*-carborane accounts for the selective chlorination of only two of the three hydrogen atoms present on each methyl group. These and other camouflaged carboranes are currently under investigation as modules for the formation of the molecular assemblies (carborods, carboracycles, mercuracarborands, and pharmacophore groups) described in other sections of this web page.

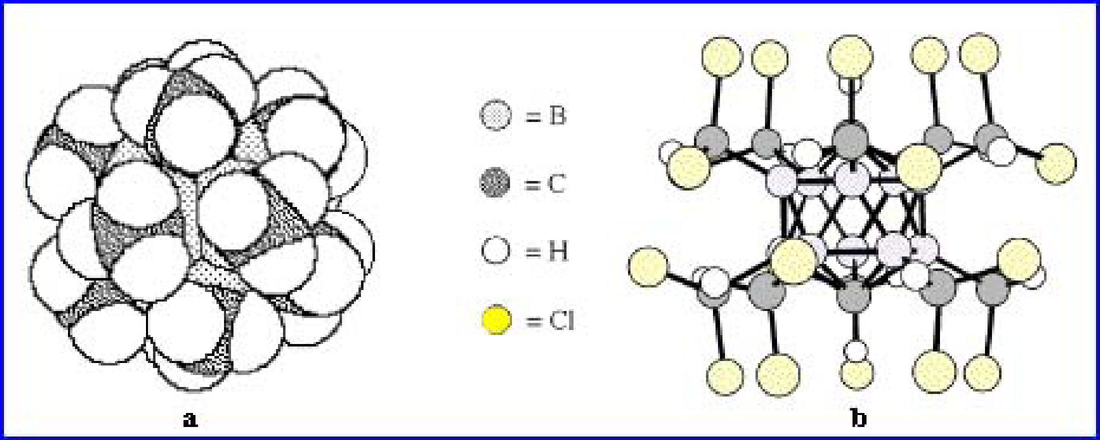

Figure 1. a, Space-filling representation of *para*-$C_2B_{10}(CH_3)_{12}$ and **b**, ball and stick representation of *para*-$C_2B_{10}H_2(CHCl_2)_{10}$

Another application which is of particular interest is the possible adoption of these camouflaged icosahedral carboranes as the bases of an inventory of large, hydrophobic and biodegradation-resistant pharmacophore groups and their potential functionalization for use in drug discovery. A comparison of the calculated van der Waals diameters of dodecamethyl-*para*-carborane (990 pm), deca(dichloromethyl)-*para*-carborane (1440 pm) and a well-known hydrophobe, C_{60} (1070 pm) shows the similar volumes of these three molecules. In order to permit either of these camouflaged carboranes to be used as pharmacophore groups, reactions which provide further functionalization of the carboranes needed to be developed. The photochlorination results demonstrate that reactions characteristic of aliphatic hydrocarbons can be utilized to functionalize the organic shroud surrounding the delocalized polyhedral cage bonding of the carborane scaffolding. This hydrocarbon-like reactivity was further exploited through adaptation of the Barton photochemical oximation reaction.

By focusing on functionalization at one of the ten available methyl groups of per-*B*-methyl-*para*-carborane, isomerically pure monofunctional products can be prepared. The Barton reaction is an example of an intramolecular regiospecific radical reaction capable of activating methyl C–H bonds. The rigid geometry of an appropriately carbon-substituted deca-methyl-*para*-carborane is ideally suited for the Barton reaction which through the photochemical decomposition of a nitrite ester function produces NO and an alkoxy radical in close proximity to a C–H bond. The nitrite- substituted carborane was prepared from the reaction of deca-*B*-methyl-1-hydroxymethyl-1,12-dicarba-*closo*-dodecaborane(12) and nitrosyl chloride in pyridine in excellent yield, 95%. The ensuing photolysis of this product in benzene produces the boron-substituted hydroximino alcohol in 42% to 25% yields. Figure 2 shows a few of the organic conversions which are feasible using this versatile hydroxyimino alcohol-substituted camouflaged carborane.

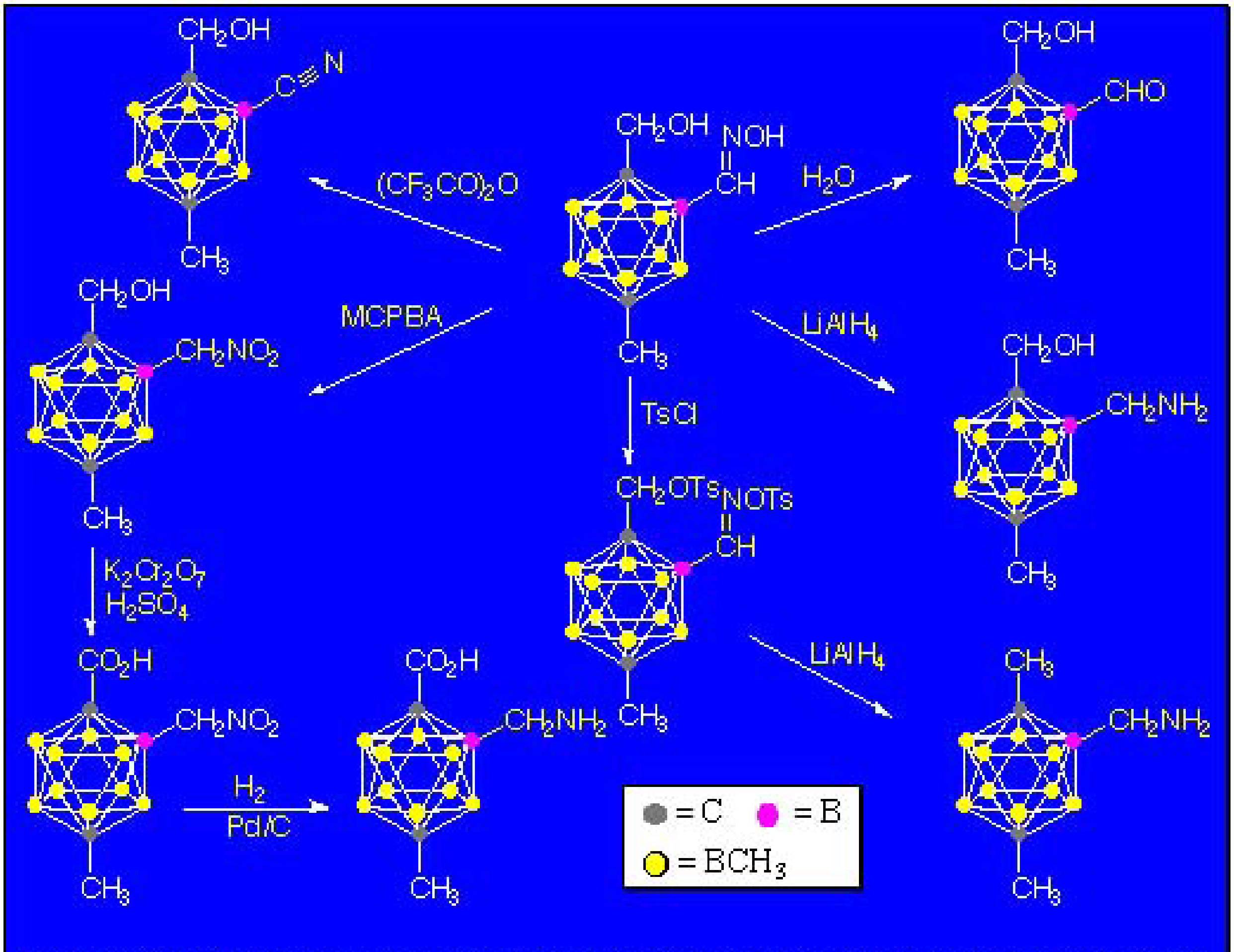

Figure 2. Possible interconversions of the Barton photochemical oximation product; new pharmaphores.

Having successfully developed a synthetic approach to decamethyl- and dodecamethyl-*para*-carboranes, it became feasible to attempt the similar methylation of 1,2- and 1,7-$C_2B_{10}H_{12}$ and at the same time perhaps increase the yields of decamethyl- and dodecamethyl-*para*-carborane. A new procedure employing $AlCl_3$ in neat CH_3I solvent easily methylated *para*-carborane in high yield by substitution of all available B–H vertices. This procedure allowed for the preparation of 4,5,7,8,9,10,11,12-octamethyl-1,2-dicarba-*closo*-dodecaborane(12) and 4,5,6,8,9,10,11,12-octamethyl-1,7-dicarba-*closo*-dodecaborane(12) derivatives of 1,2- and 1,7-$C_2B_{10}H_{12}$ after 50 h using either 1 or 10 equivalents of $AlCl_3$. In both cases the two equivalent B–H vertices nearest the 1,2- or 1,7- pairs of C–H vertices were not susceptible to electrophilic substitution.

The class of camouflaged carboranes was further extended to include a *nido*-carborane anion with the preparation of 1,2,4,5,6,9,10,11-octamethyl-7,8-dicarba-undecaborate(–1) through the base-mediated deboration of *closo*-1,2-$C_2B_{10}(CH_3)_8H_4$. Not surprisingly, the octa-*B*-methylated, *closo*-carborane was quite resistant to degradation. However, complete conversion to the corresponding *nido*-carborane anion was accomplished by treatment of the *closo*-carborane with an excess of potassium ethoxide in dimethoxyethane solution in a high-pressure vessel at 200°C for 14 hours.

When prontonated, this camouflaged *nido*-carborane demonstrates enhanced stability over that of the similar, non-camouflaged, *nido*-7,8-$C_2B_9H_{13}$. While simple heating of *nido*-7,8-$C_2B_9H_{13}$ results in dehydrogenation to form *closo*-1,8-$C_2B_9H_{11}$, the camouflaged *nido*-carborane must be passed over a bed of silica in order to induce dehydrogenation. Interestingly, *nido*-7,8-$C_2B_9H_{13}$ is inert in the presence of silica. The resulting crystalline product is a mixture of two isomers of *closo*-1,8-$C_2B_9(CH_3)_8H_3$, resulting from the differing positions of the unique B–H vertex. From this isomeric mixture, a single pure compound was prepared by methylation of the single B–H vertex present in each isomer to produce 2,3,4,5,6,7,9,10,11-nonamethyl-1,8-dicarbaundecaborane (11), *closo*-1,8-$C_2B_9(CH_3)_9H_2$, by reaction with $MeI/AlCl_3$ at the reflux temperature for 8 hours, in 95% yield.

The series of neutral, monoanionic ($CB_{11}(CH_3)_{12}^-$ prepared by Michl and coworkers), and dianionic camouflaged carboranes was completed with our recent report of the total methylation of $B_{12}H_{12}^{2-}$. Permethylation occurred when $Cs_2B_{12}H_{12}$ was first treated with a mixture of methyl iodide and trimethylaluminum (6 days, 45°C) giving $Cs_2B_{12}(CH_3)_{11}I$ followed by the reaction of this intermediate with neat trimethylaluminum. Figure 3a presents an ORTEP representation of this extraordinary dianion. As in the cases of the permethylated carborane and monocarbon carborane anion analogs, the icosahedral surface of $B_{12}(CH_3)_{12}^{2-}$ presents a virtual forest of hydrophobic methyl groups even though some salts of this species display solubility in water. This amphiphilic ion may serve as a weakly coordinating dianion in a variety of applications. In addition, functionalized modifications of this species could serve as pharmacophores. Of particular interest was the fact that cyclic voltammetry in acetonitrile produced a reversible one-electron oxidation at 0.41 V. Chemical oxidation with Ce^{4+} ion in the same solvent led to the isolation of the bright blue, air-stable anion radical $B_{12}(CH_3)_{12}^{-}$ in good yield (66%). Figure 3b is an ORTEP representation of this anion radical. Not surprisingly, structural features of the diamagnetic dianion and the paramagnetic anion radical are essentially identical.

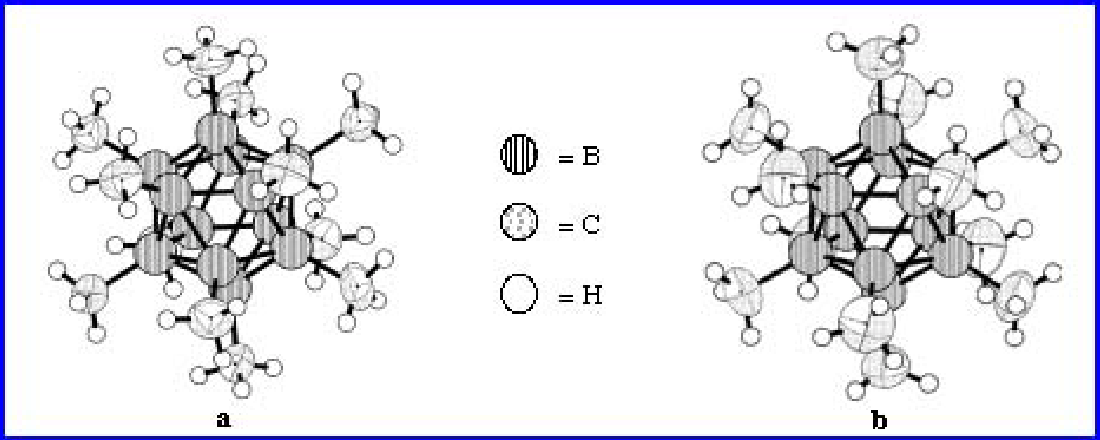

Figure 3. ORTEP representation of **a**, $[B_{12}(CH_3)_{12}]^{2-}$ and **b** the $[B_{12}(CH_3)_{12}]^{-}$ radical.

The methyl camouflaged species described above demonstrate the amplification of aromatic polyhedral borane chemistry by the prudent application of organic chemistry and the emergence of a novel family of organoboranes, the camouflaged carboranes and polyhedral boranes.

The development of successful routes for the electrophilic polymethylation of icosahedral carboranes and the $B_{12}H_{12}^{2-}$ ion provides species equipped with hydrophobic hydrocarbon surfaces, thereby spawning the field of hydrophobically-camouflaged carboranes and polyhedral boranes. As a consequence, the possible existence of similar structures presenting hydrophobically-camouflaged surfaces offered a synthetic challenge. While the oxidation of boranes is highly exothermic and reminiscent of high-performance aircraft fuels, rocket propellants, and explosives, moderation of this reaction using relatively weak oxidants with stabilized icosahedral borane derivatives offered a challenging pathway to polyhydroxylated products. Our approach proved to be successful using 30% hydrogen peroxide as the solvent and oxidant at the reflux temperatures with $B_{12}H_{12}^{2-}$, $CB_{11}H_{12}^{-}$ and 1,12-$(CH_2OH)_2$-1,12-$C_2B_{10}H_{10}$ as substrates. Figure 4 presents the structure of $B_{12}(OH)_{12}^{2-}$. In each case all B–H vertices were converted to their B–OH counterparts in variable yield, Cs_2*closo*-$B_{12}(OH)_{12}$ 65%, Cs *closo*-1-H-1-$CB_{11}(OH)_{10}$ 31%, and *closo*-1,12-H_2-1,12-$C_2B_{10}(OH)_{10}$ 80%, respectively.

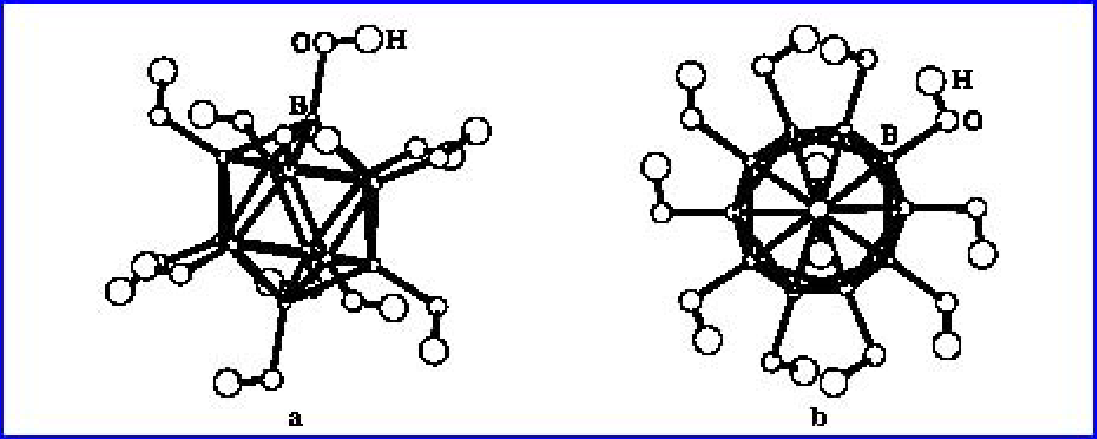

Figure 4. ORTEP representation of the $[B_{12}(OH)_{12}]^{2-}$ ion **a**, side view and **b** top view.

The properties of the $B_{12}(OH)_{12}^{2-}$ ion are of particular interest since this structure offers a unique geometric platform for formation of extended structures such as dendrimers (closomers). An unexpected property is the facile aggregation of the disodium salt which has very limited water solubility. Sodium ions coordinate with the –OH surface and provide intercage bonding. The dicesium salt is freely soluble in water since cesium is too large to effectively coordinate with the $B_{12}(OH)_{12}^{2-}$ ion. While $B_{12}(OH)_{12}^{2-}$ may be viewed as an intermediate in the hydrolysis of $B_{12}H_{12}^{2-}$ to boric acid, it still retains aromatic character and twenty-six cage-bonding electrons available for chemical reduction reactions. The chemistry of these novel polyhydroxylated carborane and borane derivatives is being actively pursued including dendrimer (closomer) synthesis.

The chemistry described above exemplifies the great similarity between aromatic polyhedral borane chemistry and the aromatic branch of organic chemistry. Modular syntheses with carboranes and polyhedral borane derivatives as well as the discovery of a variety of camouflaged derivatives clearly reveals the tentacles of organic chemistry reaching into the polyhedral borane field. Thus, the conflux of boron and carbon chemistries is broadened and strengthened. Combination of this new chemistry with previously elucidated metal chemistry provides a totally manmade field of chemistry of infinite scope.

Selected References

Wei Jiang, Carolyn B. Knobler, Mark D. Mortimer, and M. Frederick Hawthorne, "A Camouflaged Icosahedral Carborane: Dodecamethyl-1,12-dicarba-*closo*-dodecarborane(12) and Related Compounds," *Angew. Chem.*, *34*, 1332, (**1995**).

Axel Herzog, Carolyn B. Knobler and M. Frederick Hawthorne, “Adaptation of the Barton Reaction to Carborane Chemistry: The Synthesis and Reactivity of 2-Hydroxyimino-1-hydroxymethylnona-*B*-methyl-1,12-dicarba-*closo*-dodecaborane(12),” *Angew. Chem.*, *37*, 1552, (**1998**).

Axel Herzog, Andreas Maderna, George N. Harakas, Carolyn B. Knobler and M. Frederick Hawthorne, “A Camouflaged *Nido*-Carborane Anion: Facile Synthesis of Octa-*B*-methyl-1,2-dicarba-*closo*-dodecaborane(12) and Its Deboration Reaction,” *Chem. Eur. J.*, *5*, 1212, **(1999)**.

Toralf Peymann, Carolyn B. Knobler, and M. Frederick Hawthorne, “An Unpaired Electron Incarcerated Within an Icosahedral Borane Cage: Synthesis and Crystal Structure of the Blue, Air-Stable $\{[closo\text{-}B_{12}(CH_3)_{12}]^{\bullet}\}^{-}$ Radical,” *Chem. Comm.*, 2039 (**1999**).

Toralf Peymann, Axel Herzog, Carolyn B. Knobler, and M. Frederick Hawthorne, “Aromatic Polyhedral Hydroxyborates: Bridging Boron Oxides and Boron Hydrides,” *Angew. Chem. Int. Ed.*, *38*(8), 1061, (**1999)**.