

Recent advances in the field of camouflaged carboranes and polyhedral boranes

Juston J. Rockwell, Axel Herzog, Toralf Peymann, Carolyn B. Knobler and M. Frederick Hawthorne*

Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California 90095-1569, USA

The initial permethylation of 1,12- $C_2B_{10}H_{12}$ resulted in the development of a new class of molecules, the camouflaged carboranes and polyhedral boranes. Following this original report, this class has expanded to include the polymethylation of other carboranes and polyhedral boranes, namely 1,2- $C_2B_{10}H_{12}$, 1,7- $C_2B_{10}H_{12}$, and $B_{12}H_{12}^{2-}$ and others. A new addition to this class includes the per-B-hydroxylated carboranes and polyhedral boranes. The characteristics of these molecules demonstrate their hybrid nature between carboranes/boranes and aliphatic hydrocarbons. Recent advances in the field of camouflaged carboranes and polyhedral boranes are presented.

OF all of the elements of the periodic table, only neighbouring carbon and boron share the properties of self-bonding (catenation) and the support of electron-delocalized structures based upon these catenated frameworks. Carbon catenation, of course, leads to the immense field of organic chemistry. Boron catenation provides the *nido*-, *arachno*-, and *hypho*-boranes, which may be considered as the borane equivalents of aliphatic hydrocarbons, and the discrete families of *closo*-borane derivatives which bear a formal resemblance to the aromatic hydrocarbons, heterocycles, and metallocenes. Aside from these analogies, boron and carbon chemistries are also important to each other through their extravagant ability to mix in ways not available to other element-pairs. Thus, the conflux of boron and carbon chemistries effectively provides a new element-pair for exploitation in a variety of novel ways.

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 isostructural 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 are

often used for functionalization of the macrostructure or to add other interesting chemical properties. This versatility has led to the formation of several different types of structural motifs¹⁻⁴. This paper will focus on just one 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 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 versatile aliphatic hydrocarbons.

Electrophilic halogenation or alkylation of hydrogen at B-H vertices of the carboranes is a well-known reaction⁵⁻⁷. The methylation of *para*-carborane with methyl triflate and a catalytic amount of triflic acid at reflux temperature for 20 h cleanly affords the per-B-methylated carborane in 89% yield⁸. Under these conditions, only a small portion, less than 5%, of undecamethylcarborane is observed in the GC/MS of the crude reaction mixture. This demonstrates the remarkable chemoselectivity of methylation towards the B-H vertices. The camouflaged per-B-methylated carborane leaves the C-H vertices so inaccessible that even though they can be lithiated by phenyl lithium, they cannot be methylated by methyl iodide. The complete methylation of all the vertices of *para*-carborane can be accomplished if 1,12-dimethyl-1,12-dicarba-*closo*-dodecaborane⁹ is methylated using methyl triflate and triflic acid, producing dodecamethyl-1,12-dicarba-*closo*-dodecaborane(12) in excellent yield, 91% (ref. 8). Figure 1a presents a view of a space-filling model of this novel icosahedral hydrocarbon-like molecule. Radical photochlorination of one of these apparent hydrocarbons, decamethyl-*para*-carborane, by chlorine in carbon tetrachloride under UV irradiation at ambient temperature for eight hours forms decakis(dichloromethyl)-1,12-

*For correspondence. (e-mail: mfh@chem.ucla.edu)

This paper is dedicated to Prof. S. S. Krishnamurthy on the occasion of his 60th birthday.

dicarba-*closo*-dodecaborane(12) in high yield, 88%. This further camouflaged carborane is depicted in Figure 1 *b* as a ball and stick structure showing the rigorous stereochemical orientation of the $-\text{CHCl}_2$ 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 methyl hydrogen atoms. Systematic chlorination using stoichiometric amounts of *N*-chlorosuccinimide showed that initial chlorination of the methyl group activates the second C–H bond toward chlorination. Likely due to the extensive steric crowding around decamethyl-*para*-carborane camouflaged carborane as well as unfavorable bond strengths, the bromination of decamethyl-*para*-carborane was unsuccessful.

An application which is of particular interest is the possible adoption of these camouflaged icosahedral carboranes as pharmacophore groups possessing hydrophobic properties and potential functionalization for further reactions¹⁰. 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 similar volumes of these three molecules. In order to permit either of these camouflaged carboranes to be used as pharmacophore groups, further functionalization of the carboranes is 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 reaction¹¹.

By focusing on functionalization at one of the ten available methyl groups of per-*B*-methyl-*para*-carborane, isomerically pure products can be prepared. While the radical chlorination resulted in only one isomer due to steric constraints, radical-mediated reactions are generally nonselective. However, the Barton reaction is an example of an intramolecular regioselective

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. It has been shown that the Barton reaction occurs through a cyclic six-membered transition state containing the alkoxy radical and the activated C–H bond¹². The oxime product is then formed following a 1,5-hydrogen shift, collapse of the NO-alkyl radical pair, and isomerization of the nitroso derivative.

The appropriate functionality on the carbon atom of the carborane, a nitrite, was prepared from the reaction of deca-*B*-methyl-1-hydroxymethyl-1,12-dicarba-*closo*-dodecaborane(12)¹¹ and nitrosyl chloride in pyridine in excellent yield, 95%. The ensuing photolysis of this product in benzene produces the boron-substituted hydroximinolalcohol in 42% to 25% yields with varying amounts of starting material and the N–N linked nitroso dimer intermediate isolated from the reaction mixture. Figure 2 shows a few of the organic conversions which are feasible using this versatile hydroxyiminoalcohol-substituted camouflaged carborane.

Having successfully developed a synthetic approach to decamethyl- and dodecamethyl-*para*-carboranes by triflate mediated electrophilic methylation of all available B–H vertices, it became feasible to attempt the similar methylation of 1,2- and 1,7- $\text{C}_2\text{B}_{10}\text{H}_{12}$ 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- $\text{C}_2\text{B}_{10}\text{H}_{12}$ after 50 h using either 1 or 10 equivalents of AlCl_3 (ref. 13). In both cases the two equivalent B–H vertices nearest the 1,2- or 1,7-pairs of C–H vertices escaped reaction. This is not an unexpected result due to the reduced ground-state electron density at these positions. In fact, the 'exhaustive' iodination of 1,2-, 1,7- and 1,12- $\text{C}_2\text{B}_{10}\text{H}_{12}$ resulted in the exact same selectivity and extent of substitution as the methylation reactions described above¹⁴.

This same synthetic scheme was employed to methylate 1-[1'-1',2'-dicarba-*closo*-dodecaborane(12)]-1,2-dicarba-*closo*-dodecaborane(12)^{15,16}, *bis-ortho*-carborane, resulting in quantitative formation of 8,9,10,12,8',9',10',12'-octamethyl-*bis-ortho*-carborane after 5 days. Again, methylation occurred at the eight B–H vertices of the dimer with the highest electron densities.

The class of camouflaged carboranes was extended to include a *nido*-carborane with the preparation of 1,2,4,5,6,9,10,11-octamethyl-7,8-dicarba-undecabo-

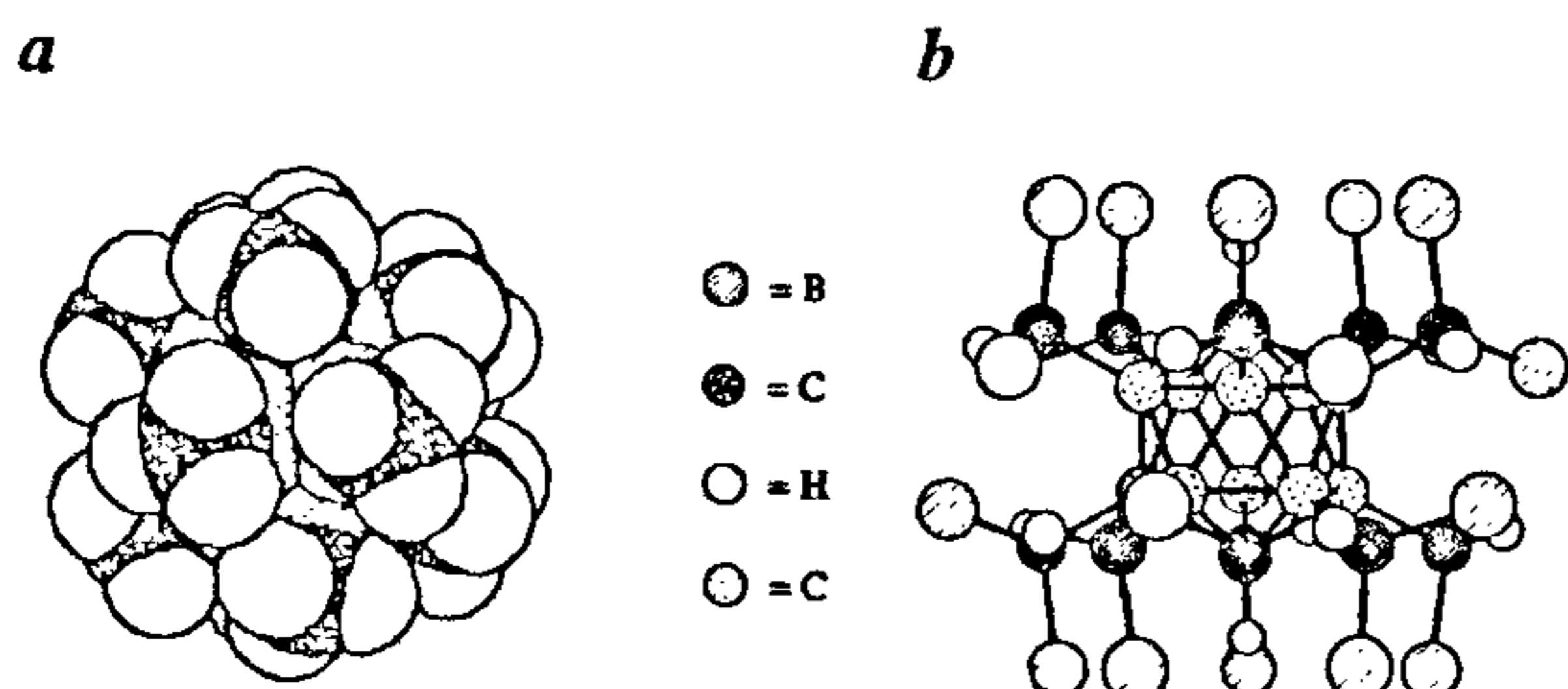


Figure 1. *a*, Space-filling representation of dodecamethyl-*para*-carborane; *b*, Ball and stick representation of deca(dichloromethyl)-*para*-carborane.

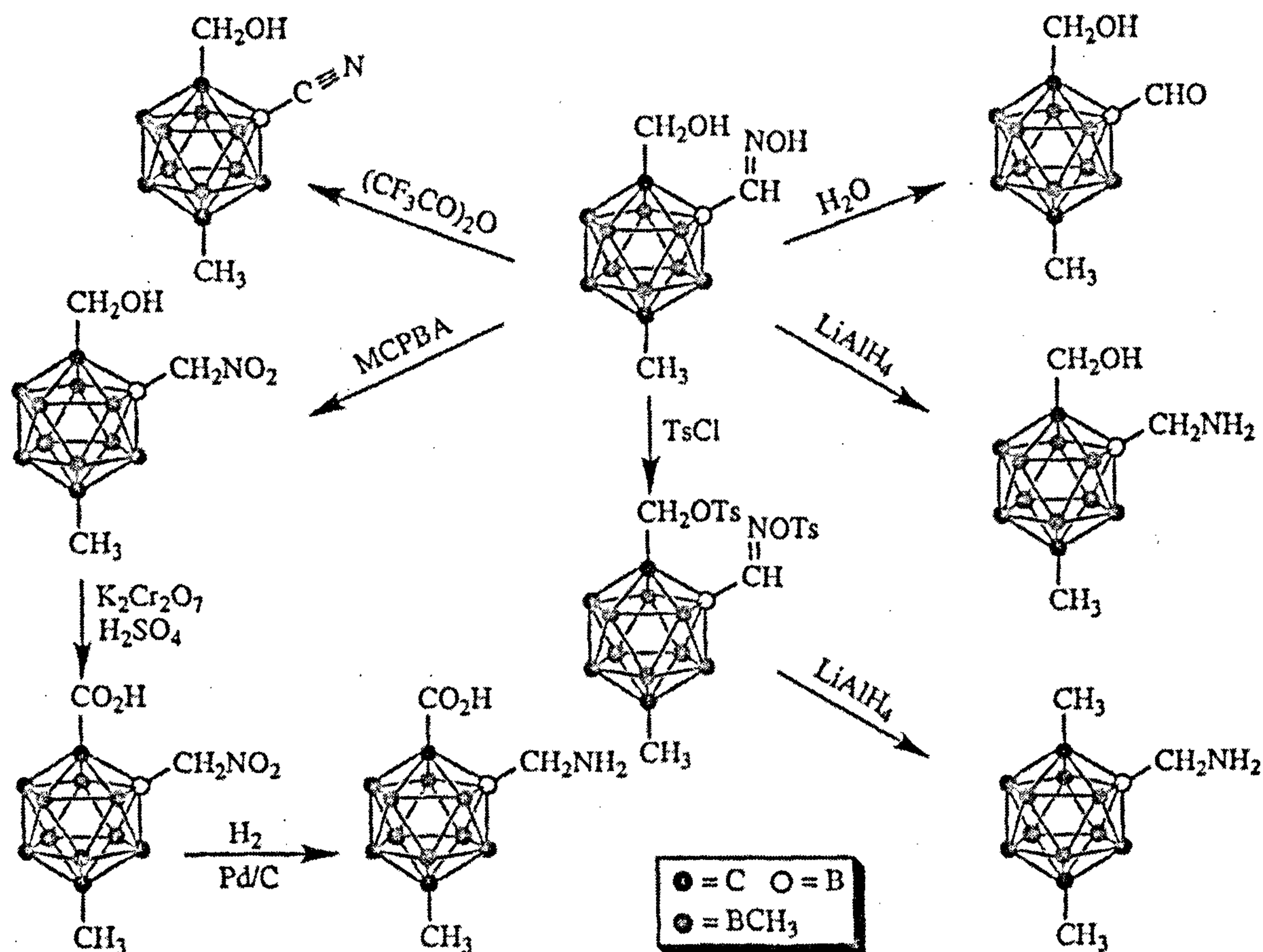


Figure 2. Possible interconversions of the Barton photochemical oximation product.

rate(-1) through the base-mediated deboration^{17,18} of *closo*-1,2- $C_2B_{10}Me_8H_4$. Not surprisingly, the *octa*-*B*-methylated, *closo*-carborane was quite resistant to degradation. However, complete conversion to the corresponding *nido*-carborane 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 h. The crude potassium salt was converted to the *bis*(triphenylphosphoranylidene) ammonium (PPN⁺) salt by treatment of the crude reaction mixture with PPNCl in absolute ethanol followed by crystallization from a saturated solution. The acid form of this camouflaged *nido*-carborane was prepared by treatment of the crude reaction mixture with aqueous HCl and sublimation from the resulting oily solid.

Again the camouflage carborane demonstrates enhanced stability toward hydrolysis in organic solvents over that of the similar, non-camouflaged, *nido*-7,8- $C_2B_9H_{13}$ (ref. 19). 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- $C_2B_9Me_8H_3$, result-

ing in 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 to produce 2,3,4,5,6,7,9,10,11-nonamethyl-1,8-dicarbundecaborane(11), *closo*- $C_2B_9Me_9H_2$, by reaction with MeI/ $AlCl_3$ at reflux temperature for 8 h, in 95% yield.

With the permethylation results summarized above and the report of the permethylation of the $[CB_{11}H_{12}]^-$ by Michl and coworkers²⁰ using an alkylation method based upon methyl triflate which followed, the series of neutral, monoanionic, and dianionic camouflaged carboranes was complete with the recent report of the methylation of $[B_{12}H_{12}]^{2-}$ (ref. 21). 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 new ion. The hypothesis that methylation occurred by successive iodination followed by methylation was confirmed when $[closo-B_{12}H_{11}]^{2-}$ was selectively converted to $[closo-B_{12}H_{11}CH_3]^{2-}$ when treated with trimethylaluminum and heated at reflux temperature. Note that conversion of B-I bonds to B-alkyl bonds in this manner offers an alternative route to the palladium-catalysed alkylation of

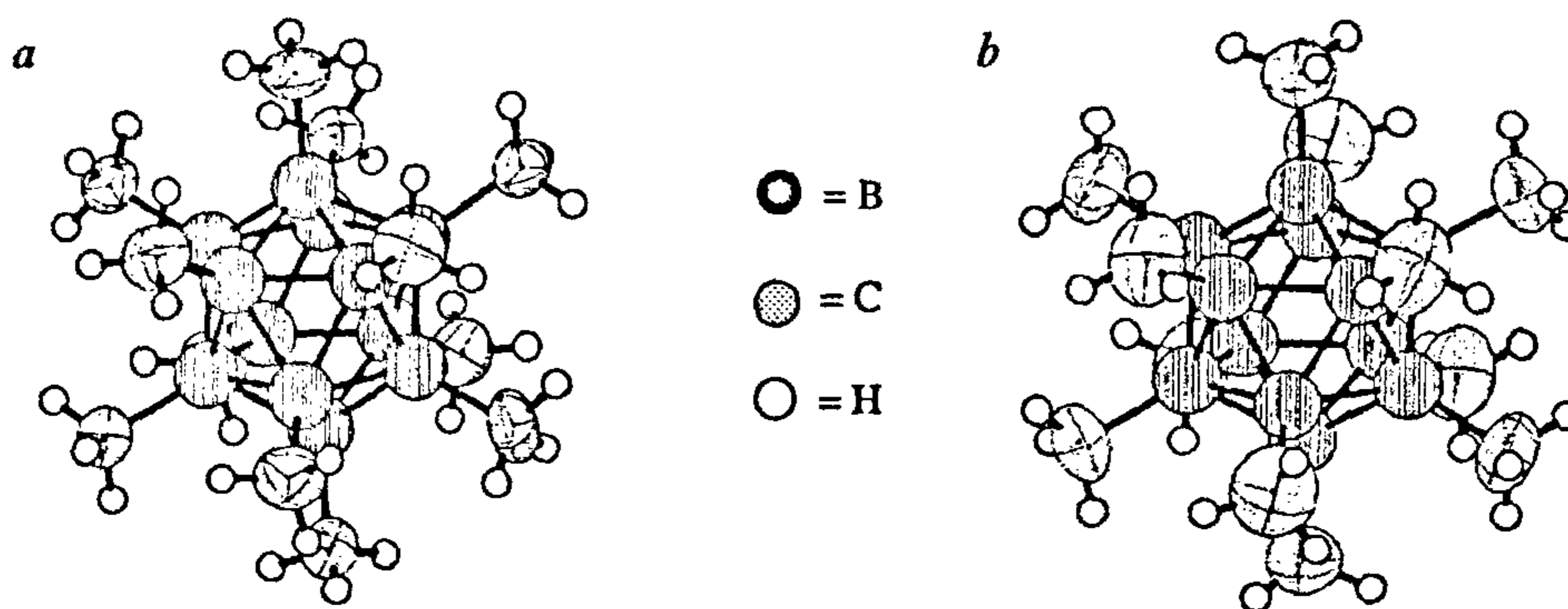


Figure 3. ORTEP representations of (a), $[\text{B}_{12}(\text{CH}_3)_{12}]^{2-}$ and (b), the $[\text{B}_{12}(\text{CH}_3)_{12}]^-$ radical.

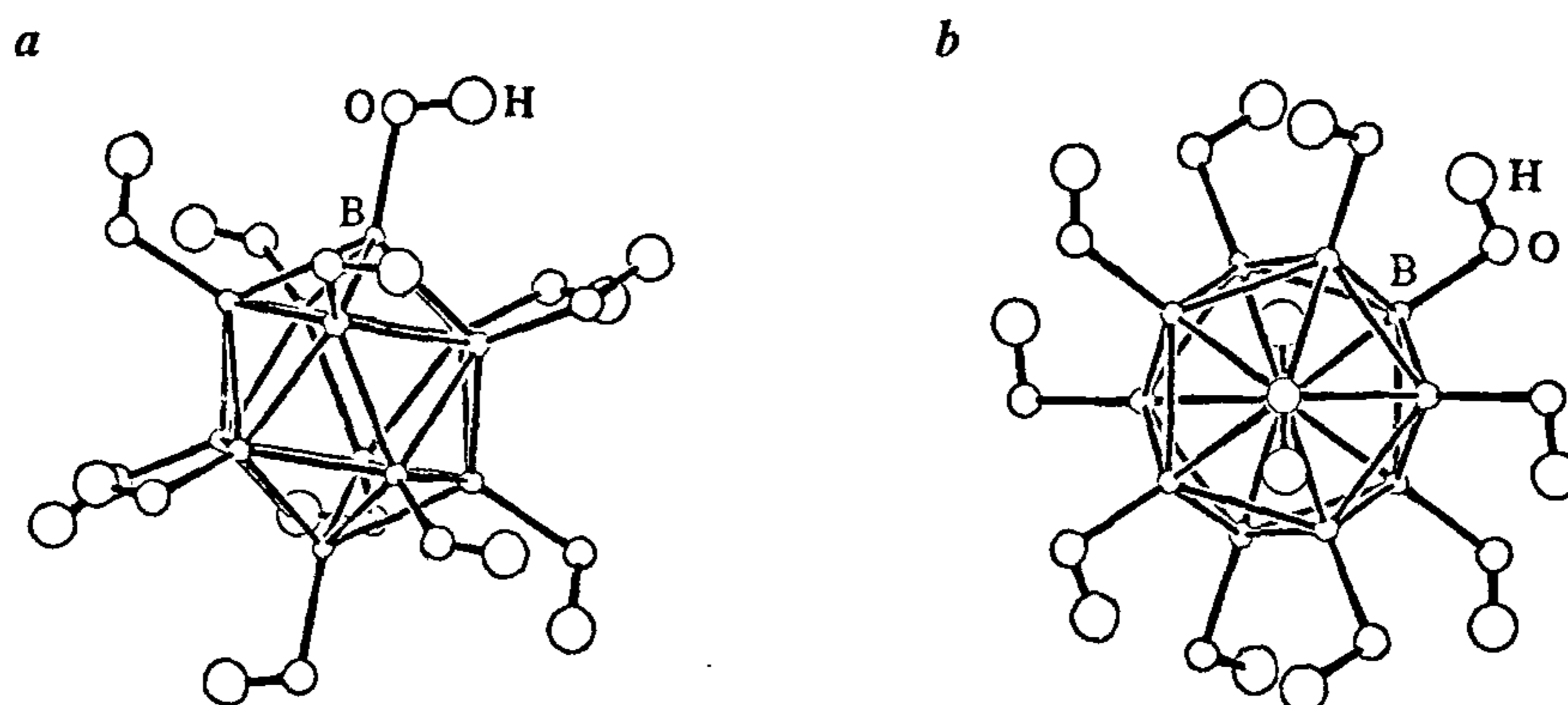


Figure 4. ORTEP representation of the $[\text{B}_{12}(\text{OH})_{12}]^{2-}$ ion *a*, side view and *b*, top view.

$[\text{closo-B}_{12}\text{H}_{12}]^{2-}$ with Grignard reagents²². As in the cases of the permethylated carborane and monocarbon anion analogs, the icosahedral surface of $[\text{B}_{12}(\text{CH}_3)_{12}]^{2-}$ presents a virtual forest of hydrophobic methyl groups even though 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 $[\text{B}_{12}(\text{CH}_3)_{12}]^-$ in good yield (66%)²³. Figure 3 *b* is an ORTEP representation of this anion radical. Bonding features of the diamagnetic dianion and the paramagnetic anion radical are essentially identical. The analogous neutral $[\text{CB}_{11}(\text{CH}_3)_{12}]$ radical reported by King *et al.*²⁴ is also bright blue and structurally very similar to the isoelectronic anion 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 an electrophilic polymethylation of icosahedral carboranes and the $[\text{B}_{12}\text{H}_{12}]^{2-}$ ion provides species equipped with hydrophobic hydrocarbon surfaces, spawning the field of hydrophobically-camouflaged carboranes and polyhedral boranes. As a consequence, the possible existence of similar structures presenting hydrophilically-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 approach to polyhydroxylated products. This approach proved to be successful²⁵ using 30% hydrogen peroxide as the solvent and oxidant at reflux temperatures with $[\text{B}_{12}\text{H}_{12}]^{2-}$, $[\text{CB}_{11}\text{H}_{12}]^-$ and 1,12- $(\text{CH}_2\text{OH})_2$ -1,12- $\text{C}_2\text{B}_{10}\text{H}_{10}$ as substrates. Figure 4 presents the structure of $[\text{B}_{12}(\text{OH})_{12}]^{2-}$. In each case all B-H vertices were converted to their B-OH counterparts in variable yield, $\text{Cs}_2[\text{closo-B}_{12}(\text{OH})_{12}]$ 65%, $\text{Cs}[\text{closo-1-H-1-CB}_{11}(\text{OH})_{10}]$ 31%, and closo-1,12-H_2 -1,12- $\text{C}_2\text{B}_{10}(\text{OH})_{10}$ 80%, respectively. The higher yield of the hydroxy-substituted carborane demonstrates the greater kinetic stability of the carborane toward degradation to the thermodynamic product, boric acid. The

lower kinetic stability of [*closo*-1-H-1-CB₁₁(OH)₁₀]⁻ is likely due to its overall molecular electronic polarization compared to the two centrosymmetric molecules.

The -CH₂OH substituents present on the *para*-carborane derivative provide some solubility of the carborane derivative in 30% H₂O₂ and are removed *in situ* by conversion to -COOH groups and subsequent decarboxylation. The properties of the [B₁₂(OH)₁₂]²⁻ ion are of particular interest since this structure offers a unique geometric platform for formation of extended structures such as dendrimers. An unexpected property is the facile aggregation of the disodium salt which has very limited water solubility. Sodium ions appear to 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 [B₁₂(OH)₁₂]²⁻ ion. While [B₁₂(OH)₁₂]²⁻ may be viewed as an intermediate in the hydrolysis of [B₁₂H₁₂]²⁻ to boric acid, it still retains aromatic character and twenty-six cage-bonding electrons available for chemical reactions. The chemistry of these novel polyhydroxylated carborane and borane derivatives is being actively pursued.

Conclusions

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 the discovery of a variety of camouflaged derivatives clearly reveal the tentacles of organic chemistry reaching into the polyhedral borane field. Thus, the conflux of boron and carbon chemistries is broadened.

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