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6.1 Introduction

Boron is a peculiar and intriguing element, and, mainly because of its particular electronic configuration, can give rise to an eclectic and complex chemistry. In view of the context of the book in which this chapter is included, we will limit our discussion to some basic elements of boron chemistry, both from inorganic and organic chemistry viewpoints. During the past, and also in the present, its unique properties have stimulated not only the development of preparative and theoretical chemistry, but also industrial and technological applications [1].

Looking at the periodic table (Fig. 6.1), boron is located at the top of group 13, being the only non-metal in this group. Moreover, its chemical behavior has many similarities with the following element, carbon, and its diagonal neighbor, silicon. Then, like them, it has a strong tendency to form covalent bonds, but it differs clearly from them as it has four bonding orbitals, but only three external electrons, so it can be defined as electron deficient. This feature has a dramatic effect on its chemistry and is the main reason for the choice of boron in medicinal chemistry, together with its large cross-section for neutron capture, as it is possible to easily incorporate boron atoms in organic compounds.

Historically, boron has long been used for the production of borosilicate glasses. Boron was first isolated, although in impure form, by Davy, Gay-Lussac, and Thénard in 1808. Only in 1892 was a quite pure form obtained by Moissan, who prepared elemental boron by the reduction of B_2O_3 with Mg, while high-purity boron was obtained only in the past century. Among the methods available for elemental boron production, the most effective for obtaining high-purity material is the reduction of boron compounds (e.g., halides) with H_2 at high temperature on a heated tantalum filament; the crystallinity improves by increasing the temperatures, and the crystal structure is also temperature dependent. The name, introduced by Davy, derives from its main source (*borax*) and from its behavior, similar to that of carbon.

Boron is relatively scarce in the earth's crust (about 10 ppm), being found as borate minerals or borosilicates, with the main deposits being found in California and Turkey. Other isolated deposits have also been found in Argentina, Chile, Russia, China, and Peru.

Only silicates have more complex structures than boron compounds, and various allotropic forms of boron itself are known.

6.2 Elemental Boron

6.2.1 Structure

The many-sided properties of boron are reflected in the unique complexity of its allotropic modifications. The origin of such complexity is the tactics used by boron to try to solve the problem of having more atomic orbitals than electrons. Metal compounds, which have a similar situation, usually solve the problem by metallic

1 H																	2 He
3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba	57 La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
87 Fr	88 Ra	89 Ac	104 Db	105 Jl	106 Rf	107 Bh	108 Hn	109 Mt									

Metal
Metalloid
Non metal

58 Ce	59 Pr	60 Nd	61 Pm	63 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	102 Lr

Fig. 6.1 Schematic representation of the periodic table

bonds, but boron's small size and high ionization energy lead to a much more pronounced tendency to form covalent bonds. The final result is that the most represented structural unit in various boron allotropes is the B-12 icosahedron, which also occurs in metal borides, boron hydrides, and boron-carbon hydrides.

As the B-12 icosahedral packing is not very efficient, leaving empty spaces even in the closely packed α -rhombohedral form, other allotropic modifications can accommodate extra atoms (boron or others) such as in α -tetragonal boron in which 2C or 2N atoms, each 50 B atoms, seem to be required to form this phase.

The crystal structures of more polymorphs have been elucidated, such as β -rhombohedral, while others, e.g., the β -tetragonal phase, are even more complex and elusive [2].

It is important to emphasize that the structural representation of boron and boron compounds (such as in Fig. 6.2) simply represents the geometry of the cluster of boron atoms, but does not describe the compounds in terms of localized bonds containing couples of electrons between pairs of atoms. Later, we will briefly describe the electronic behavior of the boron atoms involved in bond formation.

6.2.2 Physical Properties

Natural boron has two stable isotopes, namely ^{10}B and ^{11}B , with a natural abundance of about 20 and 80 %, respectively. Small variations in their concentration are observed. For instance, borates from California are more abundant in ^{11}B , whereas those from Turkey are more abundant in ^{10}B , thus preventing a precise determination of the atomic weight (Table 6.1). Both isotopes show a nuclear spin, allowing

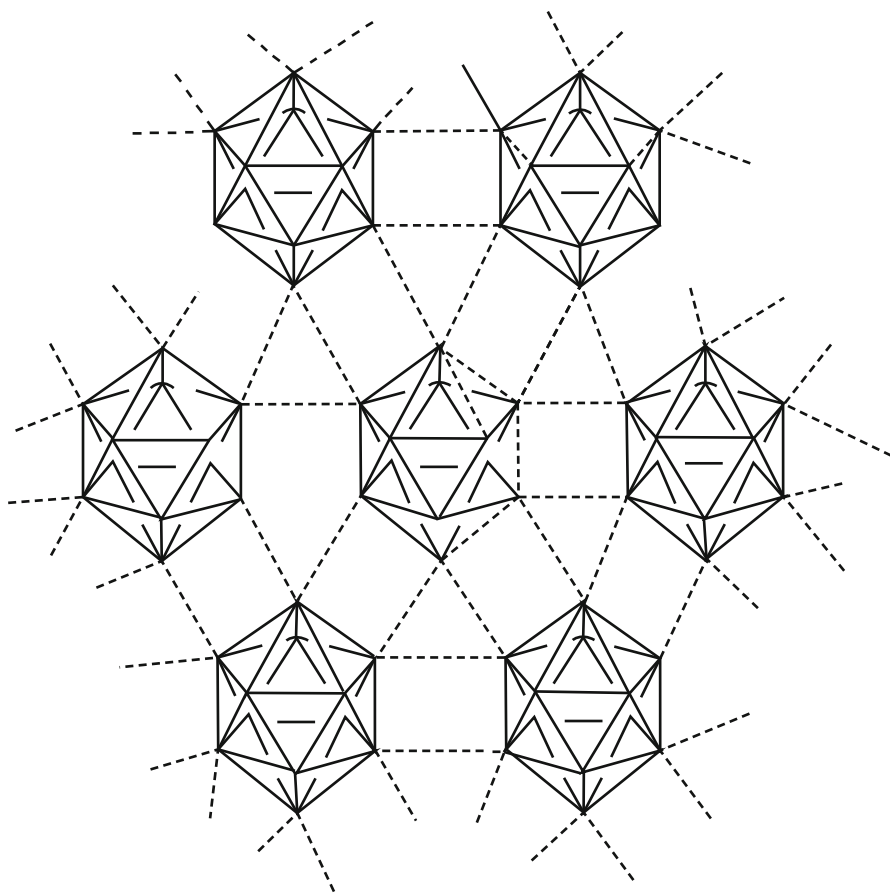


Fig. 6.2 Representation of the structure of the basal plane of α -rhombohedral boron in a quite densely packed arrangement of boron icosahedra

Table 6.1 Physical information

Atomic number	5
Relative atomic mass ($^{12}\text{C} = 12.000$)	10.811(7)
Melting point (β -rhombohedral)/K	2,352
Boiling point/K	4,000
Density/kg m ³	2,340 (293 K)
Ground state electron configuration	[He]2s ² 2p ¹

the use of NMR spectroscopy for the structural characterization of boron-containing compounds, with the ^{11}B isotope being generally preferred [3].

A relevant nuclear property of the ^{10}B isotope is the high cross section for neutron capture, which has opened the possibility of the therapeutic use of boron compounds for boron neutron capture therapy (BNCT) (Table 6.2).

Table 6.2 Boron isotopes

Nuclide	¹⁰ B	¹¹ B
Relative mass	10.01294	11.00931
Natural abundance (%)	19.055–20.316	80.945–79.684
Half-life	Stable	Stable
Nuclear spin parity	3	3/2
Cross section for neutron capture (barns) 1 barn 10 ⁻²⁸ m ²	3,835	0.005

The ionization energies are 800.6, 2,427.1, and 3,659.7 kJ/mol, much larger than those of the other elements of the same group. The electronegativity is 2.0, close to that of H (2.1), but lower than that of C (2.5), which means that the polarity of the B–H bond is reversed with respect to that of the C–H bond, a factor that plays a role in the hydroboration reaction. The physical properties are difficult to determine precisely because of the polymorphisms and difficulty obtaining high purity. Elemental boron has low density, extreme hardness (close to that of diamonds), and very low conductivity, and appears as a dark powder.

6.2.3 Chemical Properties

The chemistry of boron is probably the most complex and varied of all the elements in the periodic table. The last 50 years have seen tremendous developments in boron chemistry, with many different structures being elucidated and the nature of bonding better understood.

The main features that influence the chemical behavior of boron are its small size, high ionization energy, and electronegativity that is close to that of C and H (and Si), leading to an unusual ability to form covalent bonds.

Similar to C and Si, it shows a marked propensity to form covalent molecular compounds, but it differs sharply from them in having one less valence electron with respect to the number of valence orbitals, being therefore electron deficient. Therefore, although the presence of three external electrons accounts for its propensity to form trivalent compounds, much of its chemistry derives from the tendency to act as an electron-pair acceptor and to give multicenter bonds. Finally, it has a high affinity for oxygen, which is the basis of the vast chemistry of oxygen derivatives.

Different classes of boron compounds can thus be recognized; we have tentatively divided boron compounds in the following classes:

1. Boron–oxygen compounds
2. Other boron-heteroatom compounds (we will focus on halides and B–N derivatives)
3. Metal borides
4. Boron hydrides (including boron clusters, carboranes, and metal derivatives thereof)
5. Organoboron compounds (molecular species containing localized B–C bonds)

6.3 Classes of Boron Compounds

6.3.1 Boron-Oxygen Compounds

Boron always occurs in nature as oxygen compounds, and it has never been found as an element or bound to other elements [4]. As for elemental boron, borides and boranes, boron–oxygen compounds show an enormous structural complexity and variety. Moreover, a large number of organic boron compound containing B–O bonds are known (namely BPA) and have found many application in synthesis.

The main oxide derivative of boron is boric oxide, B_2O_3 , which can be prepared by cautious dehydration of boric acid. Its structure consists of a network of trigonal BO_3 units in which boron atoms are linked through oxygen atoms.

It is largely employed for the preparation of borosilicate glasses.

Hydrolysis of most inorganic boron compounds gives boric acid, $B(OH)_3$, which is mainly obtained by acid treatment of aqueous solutions of borax ($Na_2B_4O_7 \cdot H_2O$). It forms white crystals in which the molecules are connected by a network of hydrogen bonds. Partial dehydration of $B(OH)_3$ above 100° yields metaboric acid HBO_2 , whose structure is shown in Fig. 6.3.

Boric acid is a very weak acid having a pK_a of 9.25. Its acid behavior is not due to a proton donation, but to its reaction with water as a Lewis acid accepting an OH and releasing a proton, as shown in Fig 6.4:

Boric acid is highly reactive towards alcohols and easily forms esters. Moreover boric acid, as well as other boron–oxygen compounds (e.g., boronic acids), is able to form acetal-like derivatives with diols [5]. This elevated affinity for diols strongly influences the pK_a of boric acid; for example, the complexation with mannitol leads to a pK_a of 5.15 according to Fig. 6.5.

Also in borate salts a complex structural variability is observed, and they have been intensively studied for their industrial relevance, as they are found in many minerals. Some common features are recognized. Boron can link three or four oxygen atoms, forming trigonal or tetrahedric structures, polynuclear anions are formed by sharing a single vertex oxygen, and they can be hydrated, can contain boric acid units and form polymeric structures [6] (Fig. 6.6).

Examples of frequent units containing tri- or tetracoordinated boron are shown in the previous figure.

6.3.2 Other Boron–Heteroatom Compounds

6.3.2.1 Boron Halides

Boron halides can be found either as monomeric boron trihalides, which have been extensively studied, or polynuclear derivatives, including halogenated polyhedral compounds. We will limit our discussion to trihalides, which are the most important for industrial application. Indeed, this class of boron derivatives is involved in the preparation of elemental boron and used as catalysts for a variety of organic

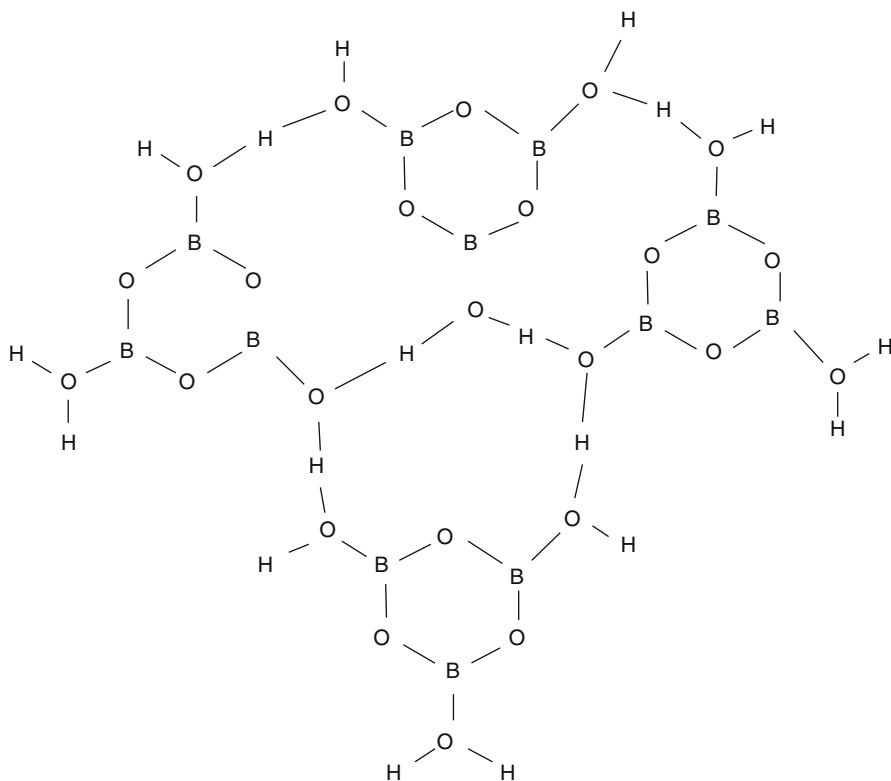


Fig. 6.3 Metaboric acid

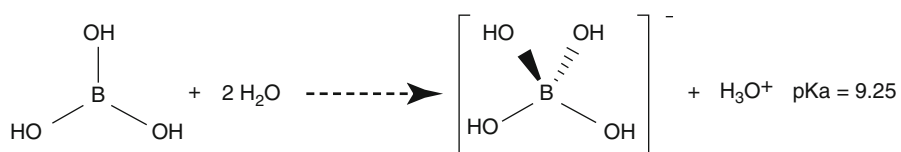


Fig. 6.4 Acidity properties of boric acid

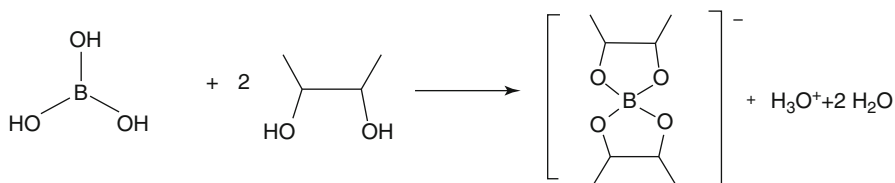


Fig. 6.5 Increased boric acid acidity by complexation

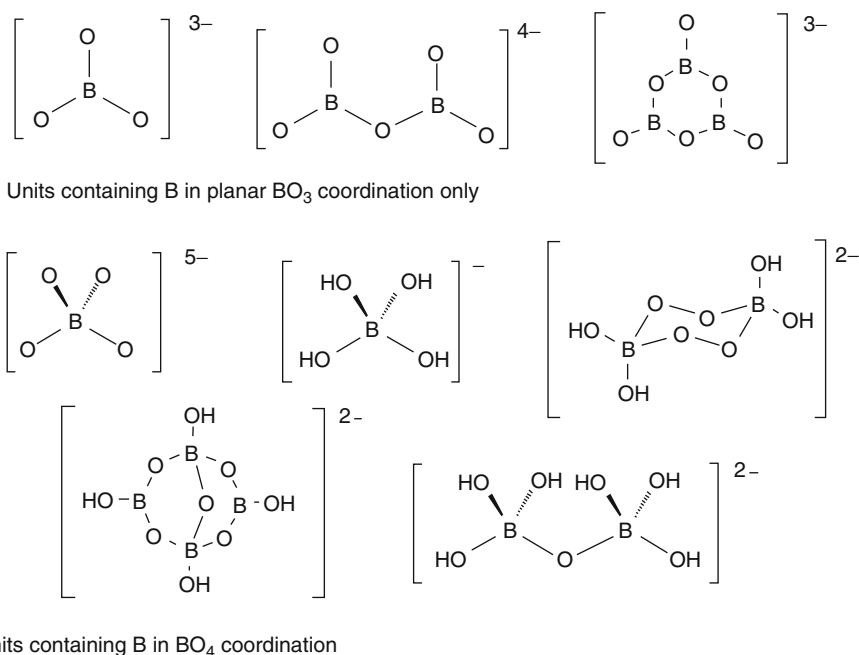


Fig. 6.6 Common units in boron oxo-compounds

reactions, such as the Friedel-Crafts reaction [7], olefin polymerization [8], cracking of hydrocarbons [9], and nitration and sulfonation of aromatic compounds.

Boron trihalides are very volatile and highly reactive compounds. Structurally they are planar trigonal molecules like organoboranes; they are very strong Lewis acids because of the combined effects of the empty p orbital and of the electronegativity of the bound halogens. The B–X bond energies are very high, and the bond distances are shorter than those expected for a single bond. This can be attributed to an overlap between the empty orbital on boron with halogen lone-pair containing orbitals [10].

When mixed, different boron trihalides give rise to a rapid halogen exchange, forming mixtures of mixed halides: $\text{BX}_3 + \text{BY}_3 \rightarrow \text{BX}_3 + \text{BY}_3 + \text{BX}_2\text{Y} + \text{BXY}_2$.

Boron trifluoride can be obtained by fluorination of borates with CaF_2 or HF in the presence of concentrated sulfuric acid. Boron trichloride and tribromide are obtained by treating boron oxide with elemental bromine or chlorine, respectively, in the presence of carbon, while boron triiodide is prepared by reacting elemental iodine with sodium or lithium borohydride.

Like the other Lewis acids, boron trihalides form stable complexes with Lewis bases such as ethers or amines (Fig. 6.7). The stability of the adducts follows the order $\text{BF}_3 < \text{BCl}_3 < \text{BBr}_3 < \text{BI}_3$, most likely because of the previously mentioned

Fig. 6.7 BCl_3 -trimethylamine complex

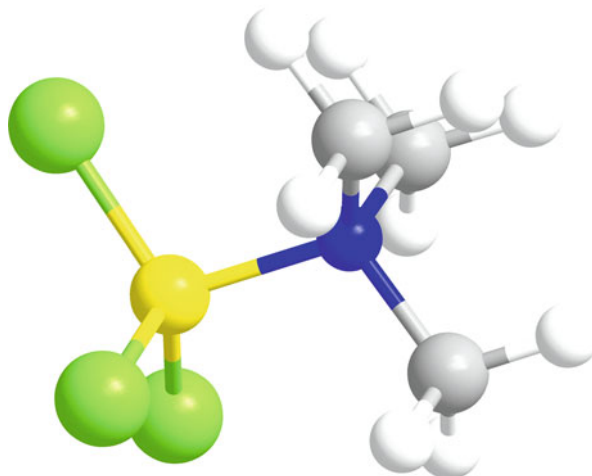


Table 6.3 Properties of B, C and N

Element	B	C	N
Valence electrons	3	4	5
Electronegativity	2.0	2.5	3.0
Radius (Å)	0.88	0.77	0.70

orbital interaction, geometry reorganization from trigonal to tetrahedral, and the electronegativity effect, with a complex interplay between these factors [11].

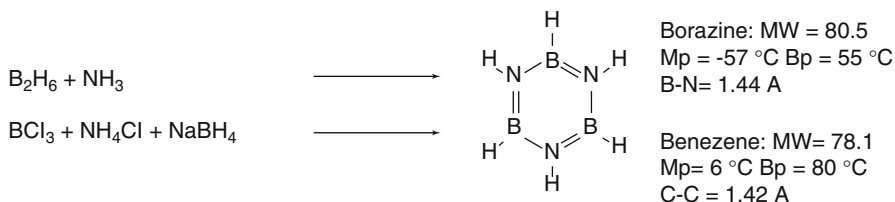
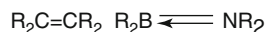
6.3.2.2 Boron–Nitrogen Compounds

Boron–nitrogen compounds have raised considerable interest for three main reasons: the electronegativities of the three elements, including carbon, are quite similar, with that of carbon being intermediate between nitrogen and boron; they have similar sizes, and, very importantly, the B–N unit is isoelectronic with a C–C bond (Table 6.3). The features of the B–N bond in amine–borane complexes have been discussed to a large extent. Usually such bonds are represented as follows: $\text{R}_3\text{N} \rightarrow \text{BX}_3$ or $\text{R}_3\text{N}^+ = \text{BX}_3^-$, which suggests that the origin of the bond is a donation of a pair of electrons from nitrogen to boron. However, it does not mean that nitrogen becomes positively charged and boron negatively, as the electron density distribution depends on the atoms' characteristics, mainly electronegativity.

Calculation indicates that there is a decrease of positive charge on boron and a decrease of electron density on nitrogen, but without reversal of charge.

A similar situation is found in compounds of the type shown in Fig. 6.8, from which the isoelectronic analogy with alkenes is evident.

From the electronic point of view, however, the previous consideration can be applied also to this type of compounds. The possibility of replacing a single or double carbon–carbon bond with a B–N or B=N unit has opened the possibility

Fig. 6.8 Analogy between C=C and B=N bonds**Fig. 6.9** Borazine synthesis and properties

obtaining a large number of new classes of compounds, but the discussion is beyond the scope of this chapter.

However, a particular example deserves to be mentioned, namely borazine, shown in the following figure (Fig. 6.9):

Borazine is prepared by the reaction of diborane with ammonia or, more efficiently, by the reaction of BCl_3 and NH_4Cl , followed by reduction with $NaBH_4$.

Borazine can be considered as an analog of benzene and, actually looking at their physical properties, they appear quite similar. Moreover, borazine has a structural similarity to benzene, being a planar, regular hexagonal ring, and discussions on its aromaticity are still ongoing [12]. However, the analogies do not go further as borazine's chemical behavior shows few aromatic properties. In fact, borazine can easily yield addition reactions, usually initiated by nucleophiles reacting with boron atoms.

Apart from discrete molecules, boron–nitrogen compounds can also be found in boron nitrides, which are isoelectronic with graphite and have a similar hexagonal layer structure; other structures are known, but obtaining them requires harsh conditions. Differently from graphite, however, boron nitride has the layers superposed, having B on one layer located on N on the adjacent layer; moreover, boron nitrides have good electric conductivity and high chemical resistance. For these reasons, boron nitrides are mainly applied in ceramic materials and composites [13].

6.3.3 Metal Borides

6.3.3.1 Properties and Preparation

Boron is able to form metal-rich binary compounds showing, a surprising variability in stoichiometry and structural motifs, as well as some non-stoichiometric derivatives or ternary and more complex combinations. The boron-metal ratio can vary from rich metal compounds, e.g., M_3B , to very rich boron derivatives, such as MB_{66} ; X-ray diffraction has been a powerful technique for their structural elucidation. Beyond academic attention, these compounds also stimulate a significant industrial interest because of their relevant physical and chemical properties.

Metal borides are, in fact, exceptionally hard, non-volatile, chemically inert, and refractory (ceramic) materials with melting points often exceeding 3,000 °C.

They are usually obtained as powders, but can be made up into the desired shape by standard metallurgical and ceramic techniques, and can be applied in heavy-duty apparatuses, such as turbine blades, rocket nozzles, and combustion chambers, as well as having nuclear applications because of the very high neutron capture cross section even with high-energy neutrons. Metal borides can be obtained with a variety of methods either for laboratory or industrial preparation. The main method for small-scale preparation is the direct combination of the elements at high temperature; all the other methods are based on the reduction of boron and/or metal oxides or halides exploiting boron or metal itself, or external reductants (e.g., C, other metals, and H_2), or by electrolysis of molten salts.

6.3.3.2 Structure of Borides

As already found for other classes of boron compounds, also in this case a structural variability is observed. Metal-rich borides can contain isolated boron atoms, or, alternatively, boron can form pairs, linear or branched chains, as well as planar networks. Increasing the percentage of boron results in a predominant occurrence of B–B bonds in which boron is present as icosahedral units, and the metal atoms are located in specific cavities or vacant sites. A compound that is strictly structurally related to rhombohedral elemental boron is boron carbide, for which the formula B_4C was originally proposed, but is not better written as $B_{13}C_2$, although the stoichiometry can slightly differ from that. It is interesting to remember that boron carbide was first prepared in 1899, and it is produced in large amounts, but still waits for a conclusive structural characterization [14].

Figure 6.10 shows a pictorial representation of boron carbide in which icosahedron units are clearly visible, joined by C–B–C units, besides B–B bonds.

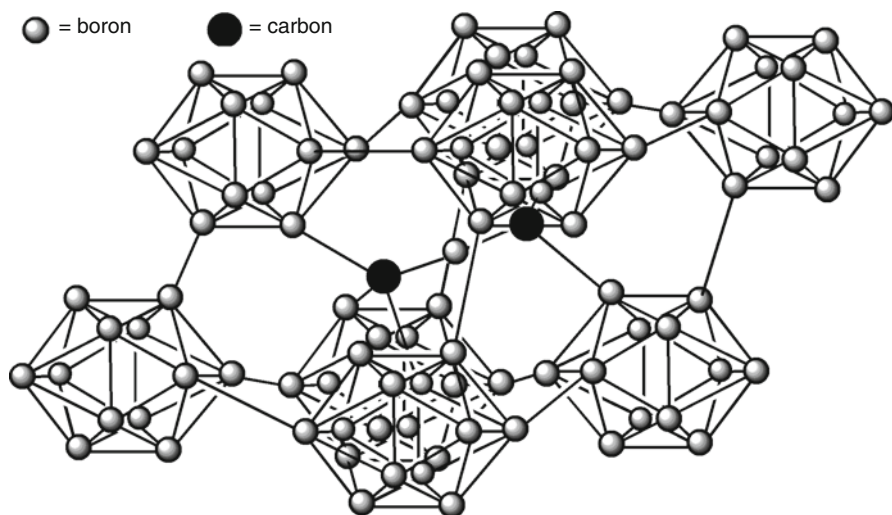


Fig. 6.10 Structure of boron carbide

Other metal borides with large electropositive metals such as lanthanides have simpler structures. For example, MB_{12} has a structure similar to that of NaCl in which the 12 boron atoms form a cubic octahedral cluster that behaves like the Cl^- ion in NaCl crystals, and MB_6 compounds form CsCl-type structures in which Cl^- is replaced by an octahedral B_6 . From the structural complexity and properties of borides, it is apparent that boron bonding (and more generally, in inorganic compounds) is inadequately described as ionic, covalent, or metallic. A more appropriate description requires the use of a molecular orbital approach. We will briefly discuss such problems in the borane section.

6.4 Boranes

6.4.1 General Features

Borane chemistry was initially explored at the beginning of the twentieth century thanks to investigations of Stock. Later, the inorganic chemistry of boranes and related carbaboranes attracted tremendous research interest for different reasons: the new principles involved in borane structures, the intriguing properties of bonds in boranes, which constituted a serious problem for Lewis electronic theory and forced the development of molecular orbital theory, and, finally, an extensive reactivity peculiar to this class of compounds. This part of the story ended with the 1976 Nobel Prize to Lipscomb for his “studies on boranes, which have illuminated problems of chemical bonding.” Besides these investigations of the theoretical and inorganic aspects, Brown, a young chemist who joined the Schlesinger group as a Ph.D. student, started up the study of the reactivity of boranes with organic compounds. This was the beginning of a rapid development of new reagents and new reactions in organic chemistry, which culminated with a second Nobel Prize awarded to Brown in 1979 (shared with Wittig) for “their development of the use of boron- and phosphorus-containing compounds, respectively, into important reagents in organic synthesis.”

Boron is the only element other than carbon that can make a complex and extended series of hydrides. Comparing the structures of boron hydrides with those of carbon hydrides (or, better hydrocarbons) shows that while carbon hydrides have a tendency to form chains and rings, boranes prefer to give rise to three-dimensional clusters (Fig. 6.11).

6.4.2 Chemical Bonding in Boranes

The understanding of the structure of boranes started with the determination of the structure of decaborane [15] by Harker, who showed the existence of an icosahedral structure together with four hydrogen atoms bridging couples of boron atoms. Later on, the structure of diborane was demonstrated, showing the presence of bridging H

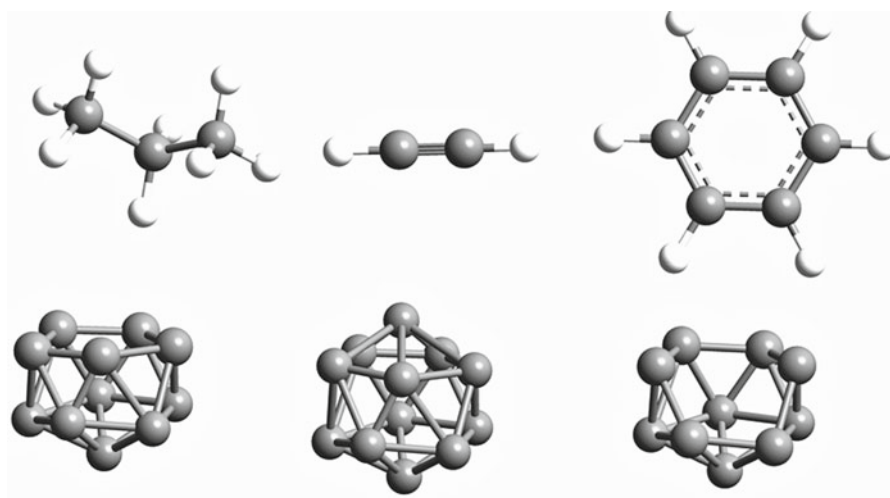


Fig. 6.11 Comparison between carbon and boron hydride structures

atoms. To explain such structures, the concept of a tricentric bond, namely three centers and two electrons, was initially introduced in 1949 by Longuet-Higgins [16]. The concept was then applied to higher boranes and developed by the Lipscomb group [17]. In bonding theory, atomic orbitals can be linearly combined to give molecular orbitals; in localized bonds, a pair of atomic orbitals is combined to give two molecular orbitals, one bonding and one antibonding. The pair of electrons occupies the lower energy bonding orbital. In a more general situation, linear combination of n atomic orbitals gives rise to n molecular orbitals, which can be bonding, antibonding, and non-bonding. As a consequence, not only two center, but also three or multicenter orbitals can be obtained by calculation.

When applied to the B–H–B bond in diborane, the molecular orbital theory gives rise to the orbitals shown in Fig. 6.12 in which only the bonding orbital is occupied, essentially meaning that the two electrons are used to keep three atoms together.

In a similar way, for more complex boron clusters, also three-center bonds can be described for boron atoms; in Fig. 6.12b, a pictorial representation of the three-center boron orbital overlap is shown.

More complex structures with clusters of boron atoms can also be obtained, for which this concept of multicenter bonds explains the stability of such polyhedral boranes.

Structure and bonding descriptions were attained through a topological theory by Lipscomb [17], and the relation between electron counting and cluster geometry resulted in Wade's rules in 1971 [18]. These aspects will not be described in detail as they are beyond the scope of this chapter.

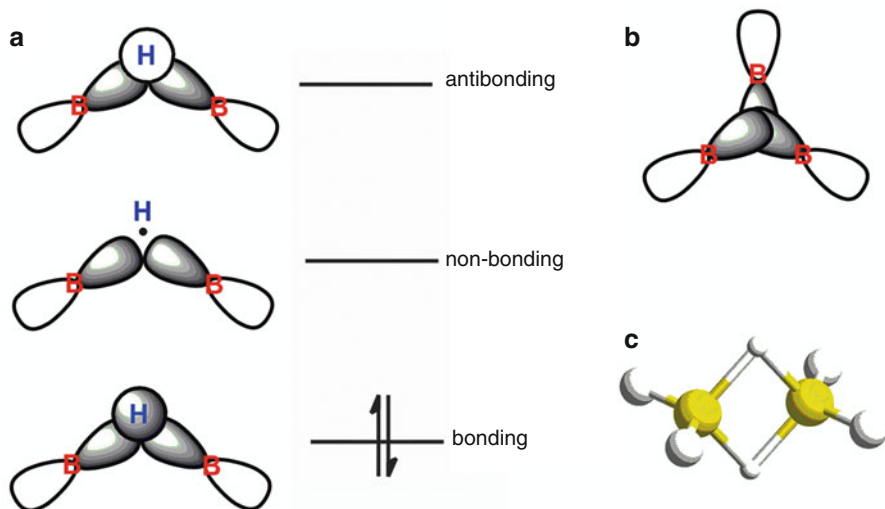


Fig. 6.12 Three-center bond in boranes: (a) B–H–B orbitals; (b) B₃ orbitals overlap; (c) diborane

6.4.3 Structure of Boranes

Three main structures of boranes can be envisaged together with two other minor classes:

- *Closo*-boranes with a polyhedral closed structure of the general formula B_nH_n²⁻
- *Nido*-boranes having a non-closed structure and the formula B_nH_{n+4} or B_nH_{n+3}⁻
- *Arachno*-boranes with an even more open structure and the formula B_nH_{n+6}

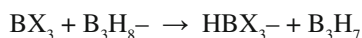
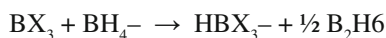
Besides these, two supplementary groups have been classified: *hypno*-boranes, for which adducts are known, and *conjuncto*-boranes, which are derived by linking together the above-mentioned structures (at least five different structures have been identified).

Boranes are usually named by indicating the number of B atoms with a Latin prefix with the number of H atoms in parentheses, e.g., B₅H₉ pentaborane(9); anion names end in “ate” and contain both the number of B and H atoms and the charge, e.g., B₃H₈⁻ is octahydrotriborate(1-). Additional information on the structure (*closo*-, *nido*-, etc.) can be included (in italics).

Figure 6.13 shows few examples of the possible borane structures.

6.4.4 Preparation and Reactivity of Boranes

Low terms can be obtained thanks to the availability of anionic monoborane, e.g., BH₄⁻ or B₃H₈⁻, which allows easy access to diborane or B₃H₇, respectively.



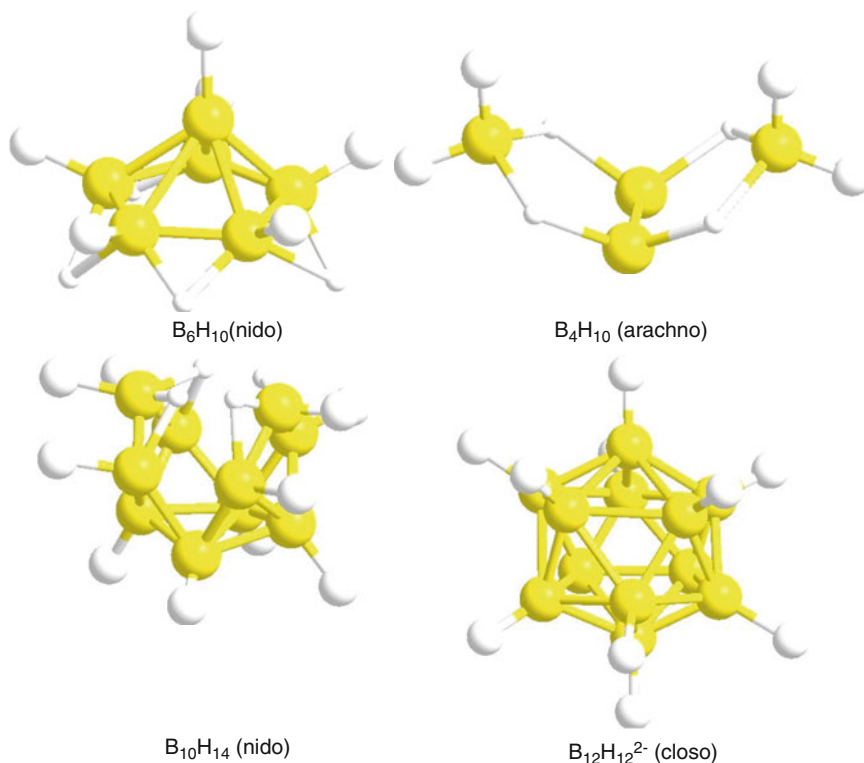
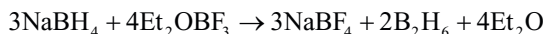


Fig. 6.13 Some borane structures

Diborane can be obtained on a small scale by the reaction of NaBH_4 and Et_2OBF_3 in diglyme and used directly without isolation:



Higher terms are typically obtained by thermolysis of smaller boranes. The elucidation of the thermal behavior of boranes took a long time from its first observation by Stock because of the complexity of the system and the instability of intermediates, requiring reliable tools for product analysis and detailed mechanistic studies. Precise optimization of the reaction conditions can allow obtaining an acceptable yield of intermediate boranes.

Boranes are extremely reactive compounds, and many of them are pyrophoric and ignite spontaneously in air. This tendency and, more generally, the reactivity are very high in *arachno*-boranes and decrease in *nido*-derivatives; in general, reactivity decreases with increasing molecular weight. *Closo*-boranes are surprisingly stable, suggesting the concept of three-dimension aromaticity [19].

The chemistry of the lower terms of boranes, namely BH_4^- and B_2H_6 , will be discussed, together with few information on boron clusters in the context of BNCT compounds.

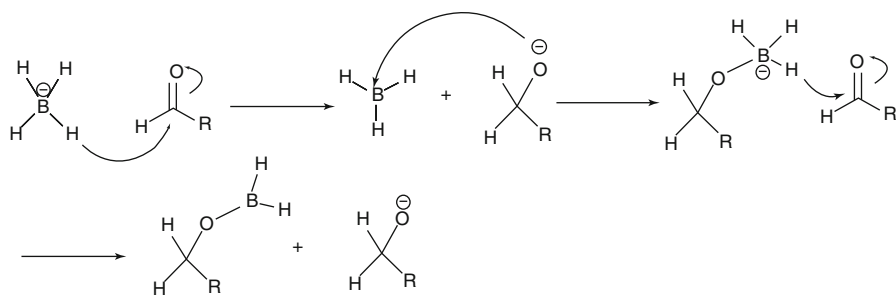


Fig. 6.14 Mechanism of NaBH_4 reduction of carbonyl compounds

Boron hydrides have been widely used in both the laboratory and industrial applications. One of the most commonly used hydrides is sodium borohydride, which is cheap, easy to handle, and can be used in protic solvents. Sodium borohydride allows for the reduction of electrophilic compounds including aldehydes, ketones, imines and related derivatives, and, to some extent, esters [20].

In carbonyl reduction, the hydrogen atom, together with the pair of electrons from the B–H bond, will be transferred to the carbon atom of the C=O group (Fig. 6.14).

Though no hydride ion, H^- , is actually involved in the reaction, the transfer of a hydrogen atom with an attached pair of electrons can be regarded as a ‘hydride transfer’. The oxyanion produced in the first step can help stabilize the electron-deficient BH_3 molecule by adding to its empty *p* orbital. Now a tetravalent boron anion is formed again and could transfer a second hydrogen atom (with its pair of electrons) to another molecule of carbonyl compound.

The alkoxyborane intermediate then reduces a second molecule of the carbonyl compound, and the reaction can continue until all hydrides are consumed, so that BH_4^- is able to reduce four molecules of carbonyl derivative. From the above mechanism, the interplay between tri- and tetracoordination on the boron atom can be easily noticed.

An alternative to BH_4^- , B_2H_6 is also able to reduce carbonyl compounds. As such, it is a gaseous substance, but it can be tamed by complexation with Et_2O or Me_2S . Although at first glance borane appears similar to borohydride, it is not an ion, which is the basis of the difference in its reactivity. Whereas borohydride prefers to react with the most electrophilic carbonyl groups, the reactivity of borane is dominated by its tendency to accept an electron pair into its empty *p* orbital, thus showing its soft Lewis acid properties. In the context of carbonyl group reductions, this means that it reduces electron-rich carbonyl groups fastest. As a consequence, apart from aldehydes and ketones, it is able to reduce amides to the corresponding amines efficiently, whereas the reduction of esters is very slow. On the other hand, borane is able to reduce carboxylic acids very efficiently as it initially forms a borate anhydride with the carboxylic group, making the carbonyl group much more electrophilic. In fact, in carboxylic derivatives, the carbonyl group is usually less electrophilic than in other carbonyl compounds, e.g., ketones, because of conjugation between the carbonyl group and the lone pair of the sp^3 hybridized oxygen atom, but, in these boron esters,

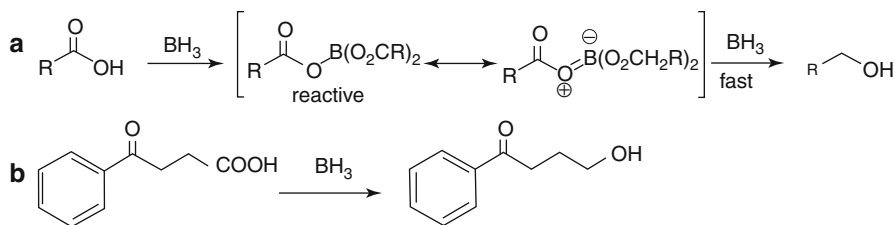


Fig. 6.15 Reduction of carboxylic acids with borane: **(a)** schematic mechanism; **(b)** example of selectivity

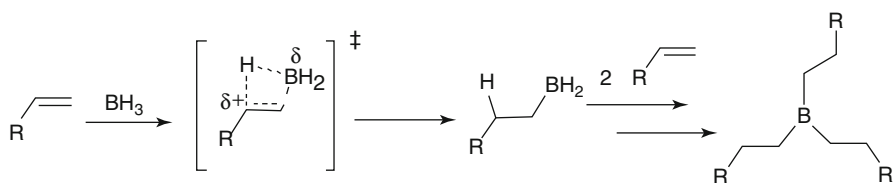


Fig. 6.16 Addition of borane to alkenes

the oxygen next to the boron has to share its lone pair between the carbonyl group and the boron's empty p orbital, so they are considerably more reactive than normal esters (Fig. 6.15a). In this way, it is even possible to reduce a carboxylic acid in the presence of a ketone (Fig. 6.15b).

The most relevant reaction of borane, however, is the hydroboration of alkenes and alkynes, which was discovered and developed by Brown, who was awarded the 1979 Nobel Prize, as previously mentioned [21]. Hydroboration is an electrophilic addition reaction of borane to multiple bonds. It is a regioselective reaction as the boron shows a tendency to attack preferentially the less substituted carbon atom of the multiple bond in a so-called anti-Markovnikov approach. This behavior has an electronic justification, as the more electrophilic boron preferentially attacks the carbon atom, which leads to the formation of a better stabilized positive charge on the more substituted carbon atom in the transition state. Besides electronic reasons, steric factors also play a major role in the regioselectivity. Looking at the transition state, it is also apparent that the reaction is stereospecific, with the boron and the hydrogen atoms approaching the same face of the double bond (Fig. 6.16). The reaction can go further by adding two other alkene molecules.

Alkyl boranes are easily converted in other derivatives. Their oxidation with hydrogen peroxide in basic conditions leads to the corresponding alcohol; the hydroxyl group replaces boron with retention of the configuration. The mechanism, shown in Fig. 6.17, once more illustrates the ability of boron to go back and forth between planar neutral structures and anionic tetrahedral structures.

Superior boron clusters have also been explored [22], but the discussion will be limited here to some information on *nido*-decaborane $B_{10}H_{14}$ and to just an example of *closo*-dodecaborane $B_{12}H_{12}^{2-}$ in the context of BNCT.

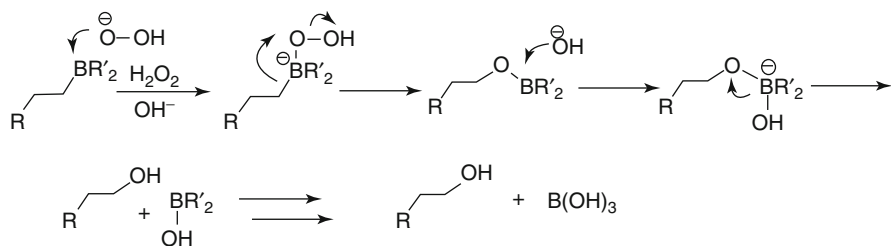
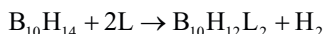


Fig. 6.17 Oxidation of organoboranes

Nido-B₁₀H₁₄ is probably the most studied among polyhedral boranes and has been produced in the past in large amounts for potential application in high-power fuels. It can be obtained on a small scale by pyrolysis of diborane at 100–200°C in the presence of weak Lewis bases. Decaborane is insoluble in water, but freely soluble in many organic solvents; however, its reactivity strongly limits the range of solvents that can be used. Decaborane behaves as a relatively strong protic acid and can be titrated in hydroalcoholic solutions showing a pK_a of 2.70. Deprotonation can also be observed using other strong bases such as MeO[−], NH₂[−], etc.

Treatment of decaborane with donor ligands gives rise to replacement of two hydrogen atoms:



The ligand can be either inorganic or organic, neutral or anionic. Ligands can activate decaborane for several types of reactions, including degradation reactions in the presence of protic compounds, e.g., alcohols:



Another example of reactions of activated decaborane will be considered later.

Decaborane can undergo reactions in which boron or other atoms are incorporated to give an expanded cluster. In this way, metallaboranes can be generated easily.

Closo-boranes, obtained by pyrolysis, are very stable. They are relatively reactive towards electrophiles, but much less so with nucleophiles. An important substituted derivative of this class is BSH, (sodium mercaptoundecahydrododecaborate, Na₂B₁₂H₁₁SH), which is currently being used for clinical trials in BNCT. It can be obtained from B₁₂H₁₂^{2−} by a reaction with *N*-methylthiopyrrolidone [23], as shown in Fig. 6.18:

6.5 Carboranes

Carboranes [24] (or, better, carbaboranes) can be structurally seen as boron clusters in which one or more of the BH groups in boranes are substituted by a CH. The different number of external electrons introduced in the cluster by a formal B to C

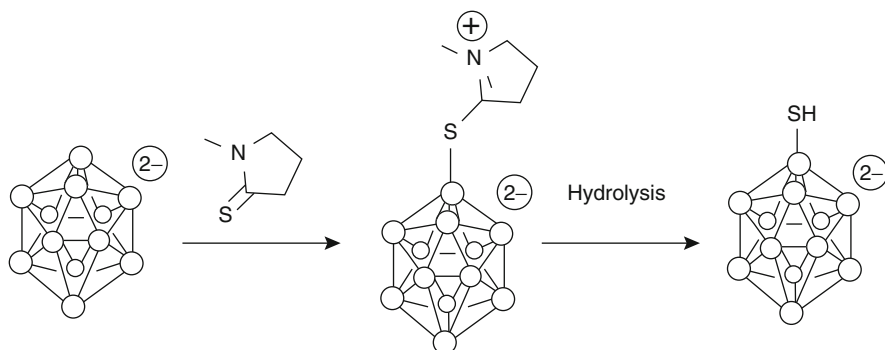


Fig. 6.18 A preparation of BSH

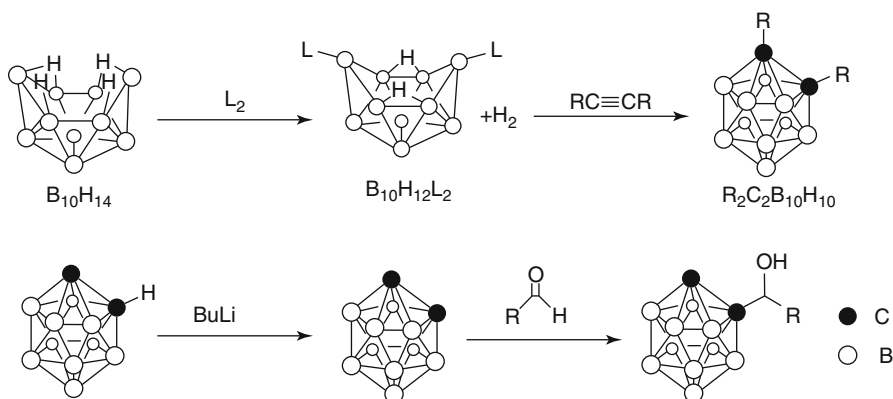


Fig. 6.19 Preparation of substituted carboranes

substitution is compensated by the elimination of an H atom involved in a three-center bond. The most represented carboranes have the stable *closo* structure and can be obtained by pyrolytic reaction between a borane and an alkyne. As for boranes, many substitution derivatives, including metallocarboranes, have been extensively studied and even today are still of great interest. Only the icosahedral carborane $C_2B_{10}H_{12}$ will be briefly considered in this context. The three isomeric $C_2B_{10}H_{12}$ (*ortho*-, *meta*- and *para*- according to the relative position of the carbon atoms) are by far the most studied because of their easy preparation and great stability.

Two main strategies for the preparation of substituted carboranes are usually exploited (Fig. 6.19):

- The addition of ligand-activated decaborane to alkynes
- The addition of deprotonated carboranes to electrophiles as carbon atoms in decaborane are quite acidic (pK_a around 23).

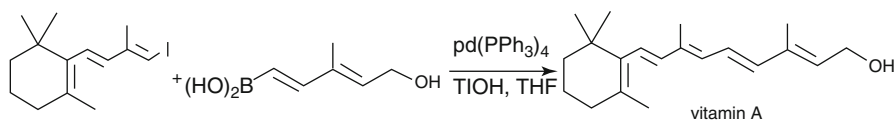


Fig. 6.20 Suzuki vitamin A synthesis

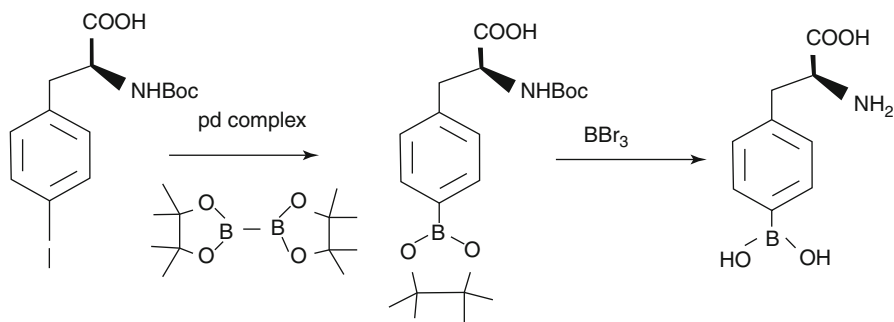


Fig. 6.21 Palladium-catalyzed synthesis of BPA

Although carboranes are usually stable, they are sensitive to bases such as HO^- , MeO^- , R_2NH , giving rise to the *nido*-derivative by extraction of a boron atom [25]. A large number of structures containing carboranes have been synthesized with the above and other strategies [26].

6.6 Organoboron Compounds

Besides reactivity concerns, boron chemistry has been extensively studied in a number of other aspects. The ability of boron to form stable bonds with carbon allows its easy incorporation in organic molecules. Many carbon-carbon bond-forming reactions exploiting organoborane are known [27]. Of particular interest are aryl and vinylboronic acids, which can be applied for carbon-carbon bond-forming reactions, such as Suzuki coupling [28].

Boronic acids can be obtained in a variety of ways, with the reaction of vinyl or aryl lithium or Grignard reagents with triethylborate followed by hydrolysis being the most common methods. Such a reaction has also been applied for the synthesis of 4-borono-L-phenylalanine, BPA, a compound approved for clinical use in BNCT together with BSH [29].

A large number of compounds have been synthesized exploiting Suzuki cross-coupling. The synthesis of vitamin A reported in Fig. 6.20 is just one example [30].

Boronic acids can also be obtained from palladium-catalyzed cross coupling, and this approach has been used for the synthesis of BPA. One example is reported in Fig. 6.21 starting from partially protected 4-iodophenylalanine and bis-pinacolato diboronate in the presence of a Pd catalyst [31].

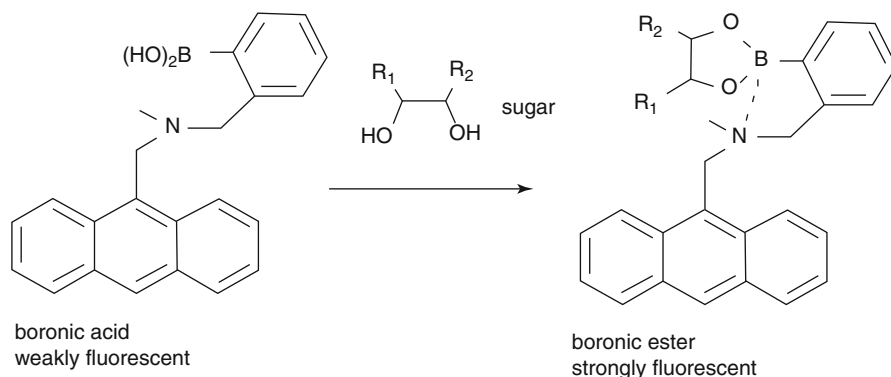


Fig. 6.22 Boronic acids as sugar sensors

Finally, boronic acid also has other applications apart from synthesis. As previously mentioned, it can provide stable boron acetals with diols and has been used as a protecting group to give better solubility in water, as in the case of the complex between BPA and fructose, or as an analytical tool for selective sugar recognition based on fluorescence variations (Fig. 6.22) [32].

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