Review Article www.ijcps.com

International Journal of Chemical and Pharmaceutical Sciences
2013, Sep., Vol. 4 (3)

ISSN: 0976-9390
IJCPS

Overview of structure, properties and derivatives of boronic acid

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ABSTRACT

A boronic acid is an alkyl or aryl substituted boric acid containing a carbon–boron bond belonging to the larger class of organoboranes. Boronic acids act as Lewis acids. Their unique feature is that they are capable of forming reversible covalent complexes with sugars, amino acids, hydroxamic acids, etc. (molecules with vicinal, (1,2) or occasionally (1,3) substituted Lewis base donors (alcohol, amine, carboxylate)). The pKa of a boronic acid is ~9, but they can form tetrahedral boronate complexes with pKa ~7. They are occasionally used in the area of molecular recognition to bind to saccharides for fluorescent detection or selective transport of saccharides across membranes. Boronic acids are used extensively in organic chemistry as chemical building blocks and intermediates predominantly in the Suzuki coupling. A key concept in its chemistry is transmetallation of its organic residue to a transition metal. The compound bortezomib with a boronic acid group is a drug used in chemotherapy. The boron atom in this molecule is a key substructure because through it certain proteasomes are blocked that would otherwise degrade proteins.

Keywords: Boronic acid, Organoboranes.

1. INTRODUCTION

Structurally, boronic acids are trivalent boron-containing organic compounds that possess one alkyl substituent (i.e., a C–B bond) and two hydroxyl groups to f ill the re- maining valences on the boron atom (Figure 1.1). With only six valence electrons and a consequent def iciency of two electrons, the sp2-hybridized boron atom possesses a vacant p orbital. This low-energy orbital is orthogonal to the three substituents, which are oriented in a trigonal planar geometry. Unlike carboxylic acids, their carbon ana- logues, boronic acids are not found in nature. These abiotic compounds are derived synthetically from primary sources of boron such as boric acid, which is made by the acidif ication of borax with carbon dioxide. Borate esters, the main precursors for boronic acid derivatives, are made by simple dehydration of boric acid with alcohols. The first preparation and isolation of a boronic acid was reported by Frankland in18601. By treating diethylzinc with triethylborate, the highly air-sensitive triethylb- orane was obtained, and its slow oxidation in ambient air eventually provided ethyl- boronic acid. Boronic acids are the products of the second oxidation of boranes. Their stability to atmospheric oxidation is considerably superior to that of borinic acids, which result from the first oxidation of boranes. The product of a third oxidation of boranes, boric acid, is a very stable and a relatively benign compound to humans [1].

Their unique properties as mild organic Lewis acids and their mitigated reactivity prof ile, coupled with their stability and ease of handling, make boronic acids a particularly attractive class of synthetic intermediates. Moreover, because of their low toxicity and their ultimate degradation into the environmentally friendly boric acid, boronic acids can be regarded as "green" compounds. They are solids that tend to exist as mixtures of oligomeric anhydrides, in particular the cyclic six-membered boroxines (Figure 1.1). For this reason and other considerations outlined below, the corresponding boronic esters are often preferred as synthetic intermediates. Although other classes of organoboron compounds have found tremendous utility in organic synthesis.

1.1. General types and nomenclature of boronic acid derivatives

The reactivity and properties of boronic acids is highly dependent upon the nature of their single

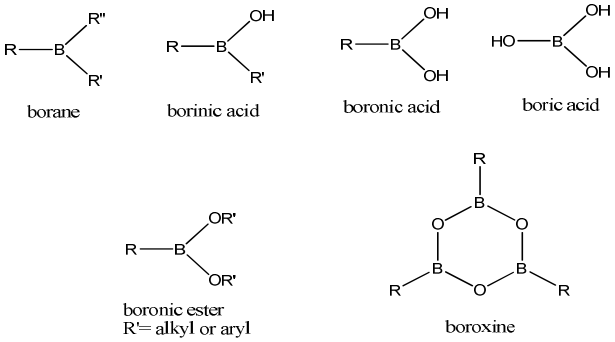

Fig. 1.1 Oxygenated organoboron compounds

variable substituent; more specifically, by the type of carbon group (R) directly bonded to boron. In the same customary way as for other functional groups, boronic acids are classif ied conveniently in subtypes such as alkyl-, alkenyl-, alkynyl-, and aryl- boronic acids

When treated as an independent substituent, the pref ix borono is employed to name the boronyl group (e.g., 3-boronoacrolein). For cyclic derivatives such as boron- ic esters, the IUPAC RB-1-1 rules for small heterocycles (i.e., the Hantzsch–Widman system) are employed along with the pref ix "boro". Thus, saturated five- and six- membered cyclic boronic esters are, respectively, named as dioxaborolanes and dioxaborinanes. For example, the formal name of the pinacol ester of phenylboronic acid is 2-phenyl-4, 4, 5, 5-tetramethyl-1,3,2-dioxaborolane. The corresponding nitrogen analogues are called diazaborolidines and diazaborinanes , and the mixed nitro- gen–oxygen heterocycles are denoted by the prefix oxaza. Unsaturated heterocycles are named as boroles.

1.2. Boronicacids-structure and bonding

The X-ray crystal structure of phenylboronic acid (1, Figure 1.2) was reported in 1977 by Rettig and Trotter [2]. The crystals are orthorhombic, and each asymmetric unit consists of two distinct molecules, bound through a pair of O–H---O hydrogen bonds.The CBO2 plane is quite coplanar with the benzene ring, with a respective twist around the C–B bond of 6.6°and 21.4° for the two independent molecules of PhB(OH)2. Each dimeric ensemble is also linked with hydrogen bonds to four other similar units to give an infinite array of layers. X-ray crys- tallographic analysis of other arylboronic acids like *p*-methoxyphenyl boronic acid (2) [3] and 4 -carboxy-2-nitrophenyl boronic acid (3, Figure1.2) [4] are consistent with this pattern. Recently, the structures of two heterocyclic boronic acids, 2-bromo- and2-chloro-5-pyridylboronic acids (4 and 5), were reported[5]. Whereas the boronic acid group has a trigonal geometry and is fairly coplanar with the benzene ring in structures 1and 2, and 4 and 5, it is almost perpendicular to the ring in 3. This is likely due to a combination of two factors: minimization of steric strain with the ortho-nitro group, and also because of a possible interaction between one oxygen of the nitro group and the trigonal boron atom. Inspired by the structural behavior of phenylboronic acid and its propensity to form hydrogen-bonded dimers, Wuest and co-workers recently reported the design of new diamond-like porous solids from the crystallization of tetrahedral-shaped tetraboronic acid 6 (Figure 1.2)[6]. Recently, phenyl- and *p*-methoxyphenyl boronic acids were found to co-crystallize with 4,4′-bipyridine into similar supramolecular assemblies involving hydrogen bonds between B(OH)2 groups and the bipyridine nitrogens[7]. With a range of approximately 1.55–1.59 Å, the C–B bond of boronic acids and esters is slightly longer than typical C–C single bonds . The average C–B bond en- ergy is also slightly less than that of C–C bonds (323 vs. 358 kJ mol–1)[8]. Consistent with strong B–O bonds, the B–O distances of tricoordinate boronic acids such as phenylboronic acid are fairly short, and lie in the range 1.35–1.38 Å. These values are slightly larger than those observed in boronic esters. For example, the B–O bond distances found in the X-ray crystallographic structures of trityloxymethyl pinacolate boronic esters (e.g., 7 in Figure1.2) are in the range 1.31–1.35 Å, and the dioxaborolane unit of these derivatives is nearly planar[9]. The X-ray crystallographic structure of cyclic hemiester 8 (Figure 1.2) has been described. Like phenylboronic acid, this compound also crystallizes as a hydrogen-bonded dimer; however, without the extended network because of the absence of a second hydroxyl group. The cyclic nature of this derivative induces a slight deviation from planarity for the tricoordinate boronate unit, as well as a distortion of the bond angles. The endocyclic B–O bond in is slightly longer than the B–OH bond. This is attributed to the geometrical constraints of the ring, which prevents effective lone pair conjugation between the end cyclic oxygen and the vacant orbital of boron.

To complete boron's octet, boronic acids and their esters may also coordinate basic molecules and exist as stable tetracoordinated adducts. For example, the X-ray crystallographic structure of the diethanolamine adduct of phenylboronic acid (9, Figure1.2), which was also reported by Rettig and Trotter[10], conf irmed the transannular B–N bridge long suspected from other spectroscopic evidence such as NMR . This dative B–N bond is 1.67 Å long.

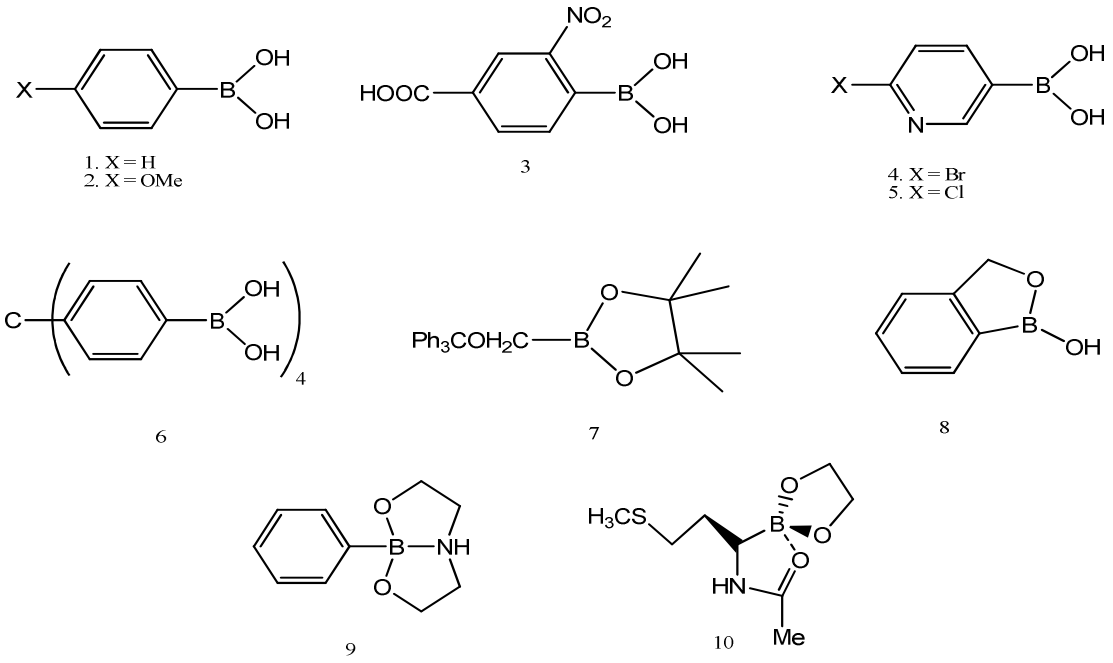

Fig. 1.2 Boronic acid derivatives analysed by X-ray crystallography

This interaction induces a strong Nδ+–Bδ– dipole that points away from the plane of the aryl ring – an effect that was elegantly exploited in the design of a diboronate paraquat receptor. When tetracoordinated, such as in structures 9 or 10 (Figure 1.2), the B–O bond of boronic esters increases to about 1.43–1.47 Å, which is as much as 0.10 Å longer than the corresponding bonds in tricoordinate analogues. These markedly longer B–O bonds are comparable to normal C–O ether linkages (~1.43 Å). These comparisons emphasize the considerable strength of B–O bonds in trigonal boronic acid derivatives[11]. This bond strength originates from conjugation between the lone pairs on the oxygens and boron's vacant orbital, which confers partial double bond character to the B–O linkage. It was estimated that formation of tetrahedral adducts (e.g., with NH3) may result in a loss of as much as 50 kJ mol–1 of B–O bond energy compared to the tricoordinate boronate. Not surprisingly, trigonal B–O bonds are much stronger than the average C–O bonds of ethers (519 vs. 384 kJ mol–1).

Fig. 1.3 Model compounds for boronate hypercoordination

In rare instances where geometrical factors allow it, boronic acid derivatives may become hypervalent. For example, catechol ester 11 (Figure 1.3) was found by X-ray crystallographic analysis to be pentacoordinated in a highly symmetrical fashion as a result of the rigidly held ether groups, which are perfectly positioned to each donate lone pair electrons to both lobes of the vacant p orbital of boron. The boronyl group of this two-electron three-atom center is planar, in a sp2 hybridization state, and the resulting structure has a slightly distorted

trigonal bipyramidal geometry. The corresponding diamine 12, however, behaved quite differently and demonstrat- ed coordination with only one of the two NMe2 groups due to electronegativity differences (B = 2.05, C = 2.55) and notwithstanding the electronic deficiency of boron, which is mitigated by the two electron-donating oxy- gen atoms (vide supra), the inductive effect of a boronate group should be that of a weak electron-donor. The 13C NMR alpha effect of a boronate group is very small[12]. Conversely, the def icient valency of boron and its relatively similar size to carbon has long raised the intriguing question of possible pi-conjugation between carbon and boron in aryl- and alkenylboronic acids and esters. NMR data and other evidence like UV and photoelectron spectroscopy, and LCAO-MO calculations, suggest that B–C conjugation occurs to a modest extent in alkenylboranes, and is probably minimal for the considerably less acidic boronate derivatives.

1.3. Physical properties and handling

Most boronic acids exist as white crystalline solids that can be handled in air without special precautions. At ambient temperature, boronic acids are chemically stable and most display shelf-stability for long periods. They do not tend to diproportionate into their corresponding borinic acid and boric acid even at high tem- peratures. To minimize atmospheric oxidation and autoxidation, however, they should be stored under an inert atmosphere. When dehydrated, either with a water- trapping agent or through co-evaporation or high vacuum, boronic acids form cyclic and linear oligomeric anhydrides such as the trimeric boroxines (Figure 1.1). Fortunately, this is often inconsequential when boronic acids are employed as synthetic in-termediates. Many of their most useful reactions, including the Suzuki cross-coupling, proceed regardless of the hydrated state (i.e., free boronic acid or boronic anhydride). Anhydride formation, however, may complicate analysis and characterization efforts. Furthermore, upon exposure to air, dry sam- ples of boronic acids may be prone to decompose rapidly, and boronic anhydrides were proposed as initiators of the autoxidation process. For this reason, it is of- ten better to store boronic acids in a slightly moist state. Incidentally, commercial samples tend to contain a small percentage of water that helps in their long-term preservation.

Due to their facile dehydration, boronic acids tend to provide somewhat unreliable melting points. This inconvenience, and the other above-mentioned problems associated with anhydride formation, largely explains the popu- larity of boronic esters as surrogates of boronic acids. The Lewis acidity of boronic acids and the hydrogen bond donating capability of their hydroxyl groups combine to lend a polar character to most of these compounds. Although the polarity of the boronic acid head can be mitigated by a relatively hy-drophobic tail as the boron substituent, most small boronic acids are amphiphilic. Phenylboronic acid, for instance, has a benzene–water partition ratio of. The partial solubility of many boronic acids in both neutral water and polar organic sol- vents often complicates isolation and purification efforts.

1.4. Safety considerations

Most boronic acids pres- ent no particular toxicity compared to other organic compounds. Small water-sol- uble boronic acids demonstrate low toxicity levels, and are excreted largely un-changed by the kidney[13] . Larger fat-soluble boronic acids are moderately toxic. Boronic acids present no particular environmental threat, and the ultimate fate of all boronic acids in air and aqueous media is their slow oxidation into boric acid. The latter is a relatively innocuous compound, and may be toxic only under high daily doses [13]. A single acute ingestion of boric acid does not even pose a threatening poisoning effect in humans unless it is accompanied by other health malfunctions such as dehydration.

1.5. Acidic character

By virtue of their def icient valence, boronic acids possess a vacant p orbital. This char-acteristic confers them unique properties as mild organic Lewis acids that can coordinate basic molecules. By doing so, the resulting tetrahedral adducts acquire a carbon-like conf iguration. Thus, despite the presence of two hydroxyl groups, the acidic character of most boronic acids is not that of a Brønsted acid (i.e., oxyacid) but usually that of a Lewis acid When coordinated with an anionic ligand, although the resulting negative charge is formally drawn on the boron atom, it is in fact spread out on the three heteroatoms.

1.6. Chemical stability

1.6.1. Ligand exchange and disproportionation

Several favorable factors contribute to the stability of boronic acids and their esters. Substitution of the carbon-containing group of boronic acids with other substituents is a slow process, and B–C/B–O bond metatheses to give the corresponding disproportionation products (trialkylborane, borinic acid or boric acid) is thermodynamically unfavored. Similarly, thermodynamic considerations make the exchange of the hydroxyl substituents of boronic acids with other ligands quite unfavorable. Sub-stitution with alcohols or diols to form boronic

esters usually requires dehydration techniques to drive the reaction forward. In general, from the B–X bond energies of all possible boronic acid derivatives (RBX2), free boronic acids remain unchanged when dissolved in solutions containing other potential anionic ligands . The only type of B–X bond stronger than a B–O bond is the B–F bond.

1.6.2. Atmospheric oxidation

A signif icant thermodynamic drive for C–B bond oxidation comes as a direct conse- quence of the huge difference between B–O and B–C bond energies. Heats of reaction for the oxidative cleavage of methylboronic acid with water and hydrogen peroxide are –112 and –345 kJ mol–1, respectively. Yet, fortunately for syn- thetic chemists, oxidative cleavage of the B–C bond of boronic acid derivatives with water or oxygen is a kinetically slow process and most boronic acids can be manipu- lated in air and are stable in water over a wide pH range. This is particularly true for aryl- and alkenylboronic acids, and, in general, samples of all types of boronic acids tend to be signif icantly more stable when moist [14,15]. Presumabl, coordination of water or hydroxide ions to boron protects boronic acids from the action of oxygen . Exceptionally, the highly electron-poor arylboronic acid 4 -carboxy-2-nitrophenylboronic acid was reported to undergo slow oxida- tion to the corresponding phenol when left in aqueous basic solutions (pH 9). Conversely, basic aqueous solutions of alkylboronate ions were claimed to be highly tolerant of air oxidation. Free alkylboronic acids, however, are quite prone to slow atmospheric oxidation and variable amounts of the corresponding alcohols may form readily when dried samples are left under ambient air with no precautions. Likewise, solutions of arylboronic acids in tetrahydrofuran devoid of stabilizer may turn rapidly into the corresponding phenols. The propensity of alkylboronic acids to undergo autoxidation depends on the degree of substitution, with primary alkyl substituents being less reactive than secondary and tertiary alkyl substituents. More potent ox- idants such as peroxides readily oxidize all types of boronic acids and their corresponding esters. Hence, this ease of oxidation must be kept in mind when handling boronic acids.

1.6.3. Protolytic deboration

Most types of boronic acids are highly resistant to protolysis of the C–B bond in neu- tral aqueous solutions, even at high temperatures. For example, p-tolylboronic acid was recovered unchanged after[16] hours in boiling water, but it was completely deboronated to toluene after 6 hours under pressure at 130 –150 °C 78. On the other hand, arylboronic acids can be quite readily deboronated in highly acidic or basic aqueous solutions. In particular, ortho-substituted and especially electron-poor arylboronic acids are notorious for their propensity to protodeboronate under basic aqueous conditions a process that can be exacerbated by exposure to light. Consequently, competitive deboronation may plague some reactions of boronic acids like the Suzuki cross-coupling reaction, which is often carried out under basic aqueous conditions.

Under strongly acidic aqueous conditions, however, the more electron-rich arylboronic acids deboronate faster. For example, p-carboxyphenylboronic acid is more tolerant than phenylboronic acid to the highly acidic conditions of ring nitration under fuming nitric acid and concentrated sulfuric acid. Kuivila and co-workers [17,18] have studies the effect of acid, temperature, and ring substitution of arylboronic acids on the kinetics of electrophilic protolytic deboronation with strong aqueous acid. A relatively complex behavior was found, and at least two possible pH-dependant mechanisms were proposed. In contrast to their behavior with aqueous acids, most arylboronic acids and esters appear to be very resistant to non-aqueous acids, as evidenced by their recovery from reaction processes using strong organic acids. For example, a phenolic methoxymethyl ether was deprotected with a 2:1 CH2Cl2–CF3CO2H mixture that left intact a pinacol boronic ester functionality[19]. Exceptionally, one report emphasized that arylboronic acids can be protodeboronated thermally by prolonged heating in ref luxing ethereal solvents In contrast to arylboronic acids, early reports document the great stability of alkyl- boronic acids under aqueous acidic solutions. For example,various simple alkyl- boronic acids were unaffected by prolonged heating in 40% aqueous HBr or HI. Like arylboronic acids, however, deboronation is observed in hot basic aqueous solutions. Alkenylboronic esters undergo protonolysis in ref luxing AcOH, and alkynylboronic acids were reported to be quite unstable in basic aqueous solutions, all types of boronic acids can being protodeboronated by means of metal-promote.

1.6.4. Boroxines

Boroxines are the cyclotrimeric anhydrides of boronic acids. They are isoelectronic to benzene and, by virtue of the vacant orbital on boron, may possess partial aromatic character. Several theoretical and experimental studies have addressed the nature and structure of these derivatives 20-26 in

particular, X-ray crystallographic analysis of triphenylboroxine conf irmed that it is virtually flat. Boroxines are easily produced by the simple dehydration of boronic acids, either thermally through azeotrop- ic removal of water or by exhaustive drying over sulfuric acid or phosphorus pentoxide.

These compounds can be employed invariably as substrates in many of the same synthetic transformations known to affect boronic acids, but they are rarely sought as synthetic products. In one rare example of application, the formation of boroxine cross-linkages has been employed to immobilize blue-light emitting oligof luorene diboronic acids [27]. Samples of boroxines may also contain oligomeric acyclic analogues, and they are sensitive to autoxidation when dried exhaustively. A recent study examined the thermodynamic param- eters of boroxine formation in water. Using 1H NMR spectroscopy, the reaction was found to be reversible at room temperature, and the equilibrium constants, relatively small ones, were subject to substituent effects. For example, boroxines with a para electron-withdrawing group have smaller equilibrium con- stants. This observation was interpreted as an outcome of a back reaction (i.e., borox- ine hydrolysis) facilitated by the increased electrophilicity of boron. Steric effects also come into play, as indicated by a smaller K for ortho-tolylboronic acid than for the para isomer. Variable temperature studies provided useful thermodynamic informa- tion, which was consistent with a signif icant entropic drive for boroxine formation due to the release of three molecules of water.

1.6.5. Boronic esters

By analogy with carboxylic acids, replacement of the hydroxyl groups of boronic acids by alkoxy or aryloxy groups provides esters. By losing the hydrogen bond donor capability of the hydroxyl groups, boronic esters are less polar and easier to handle. They also serve as protecting groups to mitigate the particular reactivity of boron–car- bon bonds. Most boronic esters with a low molecular weight are liquid at room tem- perature and can be conveniently purif ied by distillation. Exceptionally, the trity-loxymethyl esters described above (7, Figure 1.2) are crystalline solids.

1.6.6. Boronic acid diol sugar equilibrium

The reversible formation of boronic esters by the interaction of boronic acids and polyols in water was f irst examined in the seminal study of Lorand and Edwards. This work followed an equally important study on the elucidation of the structure of the borate ion. By measuring the complexation equilibrium between phenyl-boronic acid and several model diols and monosaccharides using the method of pH depression, ester formation was shown to be more favorable in solutions of high pH where the boronate ion exists in high concentrations (Equation 1, Figure 1.4). This study also conf irmed the Lewis acid behavior of boronic acids and the tetracoordinate structure of their conjugate base, i.e., the hydroxyboronate anion. Another conclusion is that free boronic acids have lower Lewis acid strengths than their neutral complexes with 1, 2-diols. For example, the p*K*a of PhB(OH)2 decreases from 8.8 to 6.8 and 4.5 upon formation of cyclic esters with glucose and fructose, re- spectively [27]. To explain the favorable thermodynamic effect seen at high pH (Equation 1) in comparison to neutral pH (Equation 2), it was hypothesized that the formation of hydroxyboronate complexes of 1,2-diols is accompanied by a signif icant release of angle strain, resulting from the rehybridization of boron from sp2 to sp3 (i.e., 120° vs. 109° bond angles).

Pizer and co-workers reported a series of investigations on the equilibria and mechanism of complexation between boric acid or boronic acids with polyols and other ligands in water. Early work by this group and others showed that the stability constants of complexes increase when the aryl substituent on the boronic acid is electron poor, who is consistent with the proposal of Lorand and Edwards that views formation of hydroxyboronate complexes as the drive for release of angle strain. Using methylboronic acid and simple 1,2- and 1,3-diols, equilibrium con-stants were measured both by pH titration and 11B NMR spectroscopy . Constants of 2.5, 5.5 and 38 were found for 1,3-propanediol, 1,2-ethanediol and 1,2,3- propanetriol respectively, with the latter binding preferentially with a 1,2-diol unit. Kinetic studies performed by the temperature-jump relaxation method revealed for- ward and reverse rate constants, and established that the lower Stability constants of six-membered boronic esters compared to the five-membered ones is the result of a faster reverse reaction for the former[28]. Quite importantly, this work confirmed that the tetracoordinate hydroxyboronate anion is much more reactive than the trigonal neutral boronic acid in forming esters with diols (at least 104 times faster), with forward rate constants in the range 103–104 M–1 s–1.

It was suggested that the high re- activity of the boronate anion could be interpreted in terms of an associative transi- tion state involvingproton transfer and hydroxide displacement within a pentacoor- dinated boron.

In the past decade, interest in the interaction between boronic acids and cis-diols has developed tremendously due to applications in the development of receptors and sensors for saccharides. As with simple polyols discussed above, the binding of carbohydrates to boronic acids is subject to the same geometrical requirement for a coplanar diol unit. In fact, in water, boronic acid receptors bind to glucose in the furanose form, which presents a very favorable, coplanar 1, 2-diol. This observation concurs with the absence of complexation between boronic acids and non-reducing sugars (glycosides) and the low aff inity of1→4 linked oligosaccharides such as lactose. Fluorescent catechol derivatives such as the dye alizarin red S (ARS) also form covalent adducts with boronic acids in water, and this equilibrium has recently been used as a competitive color- and fluorescence-based assay for both qualitative and quantitative determination of saccharide binding. Using the ingenious ARS assay, Springsteen and Wang presented an interesting cautionary tale from discrepancies found in the measurements of boronic acid–diol binding constants based on the above-mentioned method of pH depression. The latter method may not always reliably provide the true overall equi- librium constants. Indeed, these measurements are complicated by the multiple states of ionization of the boronic acid and the resulting ester (neutral trigonal or tetrahedral hydroxyboronate), the pronounced effect of the solvent, pH and buffer components, and the concentration of these species on the equilibrium.

1.6.7. Synthesis of boronic acid and their esters

The increasing importance of boronic acids as synthetic intermediates has justif ied the development of new, mild and eff icient methods to provide access to a large pool. Of particular interest is the synthesis of arylboronic acids substituted with a wide range of other functional groups.As a consequence of their growing popularity and improvements in methods available for their preparation, many functionalized boronic acids have become available from several commercial sources. Although several methods, like the oxidation or hydrolysis of trialkylboranes, have signif icant historical and fundamental relevance, this section is devoted mainly to modern methods of practical value to synthetic chemists.

1.6.8. Aryl boronic esters

Arylboronic acids remain the most popular class of boronic acids. Their popularity in medicinal chemistry is due in large part to their role as cross-coupling partners for the synthesis of biaryl units, which are present in the structure of several pharmaceutical.

1.6.9. Electrophilic trapping of arylmetal intermediates with borates

One of the f irst and, probably, still the cheapest and most common way of synthesiz- ing arylboronic acids involves the reaction of a hard organometallic intermediate (i.e., lithium or magnesium) with a borate ester at low temperature. The corresponding zinc and cadmium species are much less effective [29,30].

1.7. Other methods

Harrity and co-workers described the application of 2-substituted 1-alkynylboronic esters in the Dötz cycloaddition of Fisher chromium carbene complexes, affording in a highly regioselective fashion a novel class of hydroxy-naphthyl boron pinacolates. These reaction products also provided, upon treatment with ceric ammonium nitrate, the corresponding quinone boronic esters.

1.8. Alkyl boronic acid

Alkenylboronic acids constitute another class of highly useful synthetic intermedi- ates. They are particularly popular as partners in the Suzuki–Miyaura cross-coupling reaction for the synthesis of dienes and other unsaturated units present in many natural products. Several methods are available for the synthesis of a wide range of alkenylboronic acids with different substitution patterns.

Acknowledgment

Authors are grateful to Department of Science and Technology (DST) New-Delhi (India) for providing financial assistance to (Banasthali Centre for Education and Research in Basic Sciences) under their CURIE (Consolidation of University Research for innovation and Excellence in Women University) programme.

2. REFRENCES

1. Groziak M. **Am. J. Therap.**, 2001; 8; 321–328.
2. Rettig SJ and Trotter J. **Can. J. Chem.,** 1977; 55; 3071–3075.
3. Cambridge Crystallographic Database Compound (CCDC) number 222652.
4. Soundararajan S, Duesler EN, Hageman JH, **Acta Crystallogr. C,** 1993**;** 49; 690 – 693.
5. Parry PR, Wang C, Batsanov AS, Bryce MR and Tarbit B. **J. Org. Chem.,** 2002; 67; 7541–7543. (CCDC numbers: bromide,184781 and 184782; chloride, 184783)

6. Fournier JH, Maris T, Wuest JD, Guo W, Galoppini E. **J. Am. Chem. Soc.,** 2003;125; 1002–1006.
7. Pedireddi VR, Seethalekshmi N. **Tetrahedron Lett.,** 2004; 45; 1903 -1906.
8. Sana M, Leroy G and Wilante C. **Organometallics**, 1991**;** 10; 264 –270.
9. Ho OC, Soundararajan R, Lu J, Matteson DS, Wang Z, Chen X, Wei M, Willett RD, **Organometallics**, 1995; 14:2855–2860.
10. Zhdankin VV, Persichini PJ, Zhang L, Fix S and Kiprof P. **Tetrahedron Lett.,** 1999**;** 40: 6705–670.
11. Rettig SJ and Trotter J. **Can. J. Chem.,** 1975**;** 53; 1393–1401.
12. Yamashita M, Kamura K, Yamamoto Y and Akiba KY. **Chem. Eur. J.** 2002; 8: 2976 –2979.
13. Yamamoto Y and Moritani I. **J. Org. Chem.,** 1975; 40; 3434 –3437.
14. Soloway AH, Whitman B and Messer JR. **J. Pharm. Exp. Ther.,** 1960; 129; 310 –314.
15. Soloway AH and Whitman B and Messer JR. **J. Med. Pharm. Chem.,** 1962**;** 7; 640.
16. Johnson JR, Van Campen MG, Jr O Grummit. **J. Am. Chem. Soc.,** 1938; 60; 111–115.
17. Johnson JR and Van Campen MG. **J. Am. Chem. Soc., 1938;** 60; 121–124.
18. Soloway AH. **J. Am. Chem. Soc.,** 1959**;** 81; 3017–3019.
19. Kuivila HG and Nahabedian KV. **J. Am.Chem. Soc.,** 1961; 83; 2164–2166.
20. Nahabedian KV and Kuivila HG. **J. Am. Chem. Soc.,** 1961; 83; 2167–2174.
21. Porter RF and Gupta SK. **J. Phys. Chem.,** 1964; 68; 280 –289.
22. Wason SK and Porter RF. **J. Phys. Chem.,** 1964; 68; 1443–1447.
23. Grimm FA, Barton L and Porter RF. **Inorg. Chem.,** 1968**;** 71309–1316.
24. Chang CH, Porter RF and Bauer SH. **In- org. Chem.,** 1969; 8; 1689–1693.
25. Brock CP, Minton RP and Niedenzu K. **Acta Crystallogr. Sect. C,** 1987; 43;1775–1779.
26. Torssell JA and Lazzeretti P. **J. Phys. Chem.,** 1990; 94; 1723–1724.
27. Tokunaga Y, Ueno H, Shimomura Y and Seo T, **Heterocycles,** 2002**;** 57; 787–790.
28. Bielecki M, Eggert H, Norrild JC. **J. Chem. Soc., Perkin Trans.,** 1999; 2: 449– 455.
29. Gilman H and Moore LO. **J. Am. Chem. Soc.,** 1958; 80; 3609–3611.
30. Das S, Alexeev VL, Sharma AC, Geib SJ and Asher SA. **Tetrahedron Lett., 2003.**