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Boronic acids in the design and synthesis of supramolecular assemblies☆

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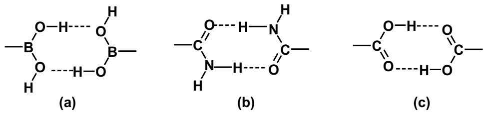
Abstract—Supramolecular assemblies of phenylboronic and 4-methoxyphenylboronic acids with 4,4′-bipyridine and an assembly of phenylboronic acid with 1,2-bis(4-pyridyl)ethene, which were obtained due to the formation of O–H···N hydrogen bonds between hetero N-atoms and –B(OH)$_2$ are reported. Further, a centrosymmetric cyclic C–H···O hydrogen bonding dimer is identified in the crystal structure of 4-methoxyphenylboronic acid.

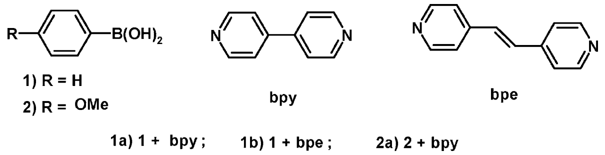
In recent times, boronic acids (which possess –B(OH)$_2$ as a functional moiety) have been widely used as reagents for the targeted synthesis of compounds having applications in the areas of pharmaceuticals, agrochemicals etc.[1] For instance, Suzuki cross-coupling reactions of pyridylboronic acids to yield novel heteroarylpyridines is one of the recent examples reported in the literature.[2] Boronic acids are also being utilized as inhibitors of proteases, sensors for carbohydrates, etc.[3] Since these interactions proceed through molecular recognition, the involvement of the –B(OH)$_2$ unit could be envisaged as involving formation of noncovalent bonds (such as hydrogen bonds). A recent report[4] of molecular tectons in the form of three-dimensional channel networks, employing tetraboronic acids, obtained due to the hydrogen bonding patterns formed by –B(OH)$_2$, is another superb example to encourage further consideration of the ability of boronic acids in molecular recognition phenomena.

To date, except for the structure determination of a few boronic acids and a molecular complex between phenylboronic acid and a phenylnitronyl nitroxide radical (synthesized for the purpose of magnetic studies), the systematic exploration of a hydrogen bonding network of these acids, in the construction of supramolecular assemblies having binary or ternary components has not been studied.[5] Analysis of the few crystal structures of boronic acids[6] reveals that the hydrogen bonding patterns formed by –B(OH)$_2$ have a close relationship with that of –CONH$_2$ and –COOH groups, as shown in Scheme 1.



Scheme 1.

Hence, we were attracted to boronic acids to investigate their utilization for generating different types of supramolecular assemblies, following crystal engineering principles.[7–10] For this purpose, we have considered the synthesis of molecular complexes of phenylboronic acid and its various derivatives with aza-donor molecules like 4,4′-bipyridine (***bpy***), *trans*-1,2-bis(4-pyridyl)ethene (***bpe***), etc. hoping that the constituents would interact with each other through O–H···N hydrogen bonds, a well-recognized hydrogen bonding pattern in molecular recognition and supramolecular synthesis.[11]



Keywords: Boronic acids; O–H···N hydrogen bonds; Supramolecular synthesis; C–H···pi interactions; Molecular recognition.

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Thus, co-crystallization of phenylboronic acid, **1** with ***bpy*** and ***bpe***, from CH_3OH, gave molecular complexes **1a**[12] and **1b**[13] in a 1:2 and 1:1 molar ratio, respectively. In **1b**, however, we also found a water molecule in the asymmetric unit. Co-crystallization of **2** with ***bpy*** yielded a molecular complex **2a**[14] in a 2:1 ratio, but we were not able to obtain good quality single crystals between **2** and ***bpe***. All the crystal structures were determined using the SHELXTL package.[15] The molecular arrangement in these complexes (**1a**, **1b** and **2a**) is shown in Figures 1–3, respectively.

In the complex **1a**, molecules of **1** and ***bpy*** interact with each other, as anticipated, forming O–H···N hydrogen bonds between hetero nitrogen atoms and $–B(OH)_2$ groups (Fig. 1 (top)). However, it is interesting to note that the hydroxyl groups are arranged in a *syn* manner, unlike in the known crystal structures of boronic acids. In such a recognition pattern, molecules of **1** are held together by two ***bpy*** molecules through O–H···N and C–H···N hydrogen bonds, with H···N distances of 1.86 and 2.93 Å,[16] respectively, constituting molecular tapes. Further, these tapes form a three-dimensional arrangement such that **1** is sandwiched between ***bpy*** molecules (Fig. 1 (bottom)). In this three-dimensional arrangement, adjacent ***bpy*** molecules along the stacking direction are held together by edge type π–π interactions (3.65 Å). However, the molecular tapes perpendicular to the stacking direction are held together by C–H···π interactions (2.89 Å) formed between C–H groups of ***bpy*** and the Ph moiety of **1** (see inset in Fig. 1).

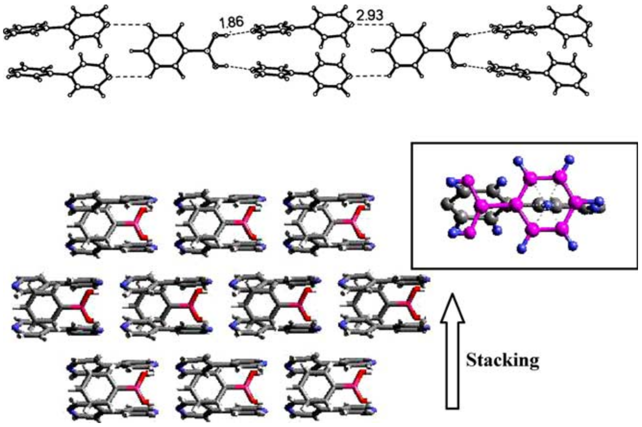

Figure 1. Molecular recognition between **1** and ***bpy*** through O–H···N and C–H···N hydrogen bonds (top); Three-dimensional arrangement of **1** and ***bpy*** in the molecular complex, **1a** (bottom); C–H···π interaction between **1** and ***bpy*** (inset).

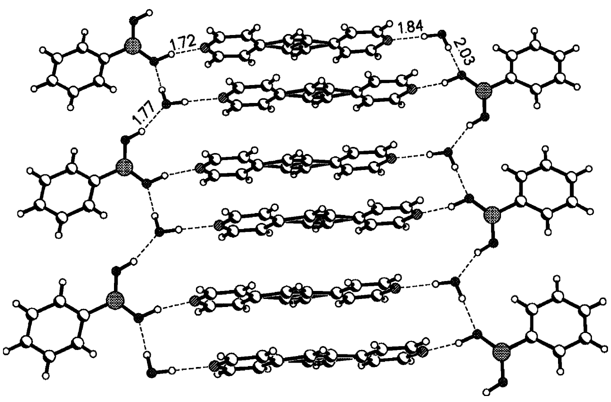

Figure 2. A ladder structure formed between **1** and ***bpe*** with the latter forming rungs separated by a distance of 3.70 Å.

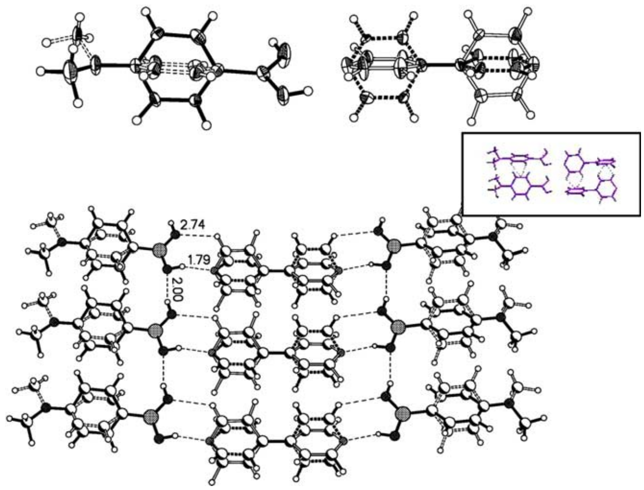

Figure 3. ORTEP diagram of the molecular contents, in the disordered form, in the molecular complex, **2a** (top); Arrangement of *bpy* molecules, as spacers, in between the molecules of **2**, by forming O–H···N and C–H···O pairwise hydrogen bonds (bottom); C–H···π interactions between the adjacent units shown for one set of disordered molecules for clarity (inset).

In the complex, **1b**, the basic recognition pattern between **1** and ***bpe***[17] is similar to the one noted between **1** and ***bpy*** in **1a**, with an H···N distance of 1.72 Å. Nevertheless, further packing of the supramolecules constitutes a quite fascinating network, yielding a ladder structure. This network has molecules of **1** and water together forming rods by interacting through O–H···O hydrogen bonds (H···O, 1.77, 2.03 Å) while ***bpe*** molecules are inserted between these rods as rungs, forming O–H···N hydrogen bonds with both **1** (H···N, 1.72 Å) and water (1.84 Å) as shown in Figure 2. In such an arrangement, the rungs (***bpe*** molecules) are separated by a distance of 3.70 Å. In general, only a few ladder structures are known in organic supramolecular assemblies, compared to organic–inorganic hybrids.[18] Thus, the complex **1b** serves as a further illustrative example of organic ladders.

In the complex **2a**, the structural features are much more intriguing in both molecular and supramolecular aspects. Firstly, the –Ph moieties of **2** and ***bpy***, as well as the –OMe group on **2** are disordered as shown in Figure 3 (top). Further, it is evident that the two hydroxyl groups adopt *syn* and *anti* conformations compared with the *syn* only conformation found in **1a** and **1b**. However, the basic interaction between **2** and ***bpy*** remains the same as noted in **1a** and **1b**, by forming O–H···N hydrogen bonds (H···N, 1.79 Å), but, as part of a cyclic pattern, in association with an additional C–

H···O hydrogen bond (H···O, 2.74 Å), resembling the interaction between –COOH and ***bpy***.

Thus, in complex **2a**, ***bpy*** molecules insert between the molecules of **2** as spacers and the adjacent units are held together by O–H···O hydrogen bonds (H···O, 2.00 Å) formed through the *anti* –OH groups, as shown in Figure 3. Further, in this arrangement the adjacent molecules of **2**, as well as ***bpy***, are held by strong C–H···π interactions (2.40–3.12 Å), (see inset in Fig. 3 (bottom)). However, the nature of these interactions is quite different to that noted in **1a**. The C–H···π interactions in **2a** are the result of the interaction of the –CH group with an edge of the –Ph moiety rather than at the centroid and further, the interactions are formed between homomeric molecules (**2**···**2**, ***bpy***···***bpy***).

It is known that, in the parent crystal structure of ***bpy***,[19] the molecular structure is perfectly ordered—hence, the observed disorder in the molecular constituents in **2a** could be attributed to the molecular recognition between **2** and ***bpy***, if the molecular structure of **2** is also ordered in its parent crystal structure. However, crystallographic studies on **2** were not available from the literature,[5] hence, we carried out its structure determination[20] by crystallization from CH_3OH. The crystals of **2**, do indeed possess fully ordered molecules as shown in Figure 4 (top), thus, accounting for the disorder and homomeric C–H···π interactions in **2a** to the molecular recognition process.

However, the packing of molecules in the crystal lattice of **2** revealed quite interesting features, demonstrating the intriguing hydrogen bonding patterns of boronic acid structures. A two-dimensional arrangement of the molecules in the form of a layer is shown in Figure 4 (bottom). Interestingly, the –B(OH)$_2$ group interacts with the neighboring molecules through O–H···O hydrogen bonds (H···O, 1.82 and 2.05 Å) with the involvement of both *syn* and *anti* hydrogen atoms of –B(OH)$_2$, yielding a cyclic pattern. Further, the molecules related by the center of inversion are held together by C–H···O hydrogen bonds (H···O, 2.59 Å), formed between –OCH$_3$ groups in the form of cyclic dimers.

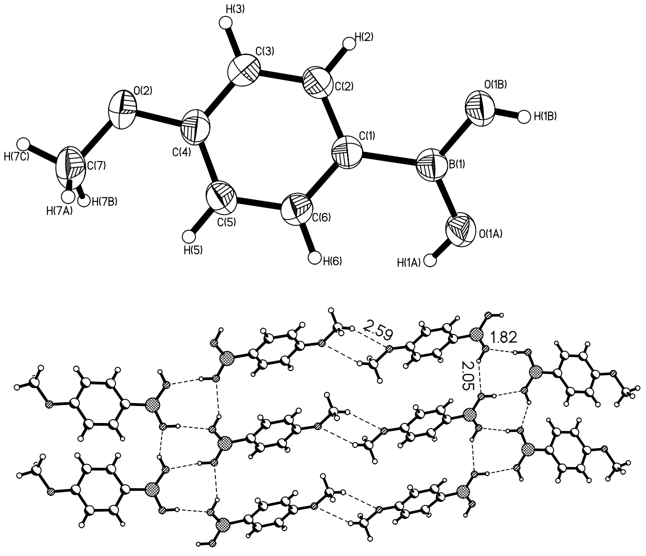

Figure 4. ORTEP drawing of the molecular structure of 4-methoxyphenylboronic acid, **2** (top). Arrangement of molecules in the crystal structure of **2** (bottom). Notice the dimeric hydrogen bonding pattern formed by the –OCH$_3$ groups.

A comparison of packing of the molecules in the structures of **2** and **2a** (Figs. 3 and 4) reveals that complex **2a**, is indeed a result of replacement of molecules of **2** held together by C–H···O dimers by ***bpy*** molecules. Thus, the complex **2a** further demonstrates the analogy between the packing of molecules in the parent crystal structures and in the supramolecular assemblies to perform supramolecular synthesis through a knowledge of the parent crystal structures.

In conclusion, we have demonstrated the utilization of boronic acids for the creation of supramolecular assemblies of varied networks in the form of sandwich, ladder and molecular blocks. Among the structural highlights, we note that the *syn* conformation of –B(OH)$_2$ (in **1a** and **1b**) and the strong C–H···π interactions (**1a** and **2a**) are important features, which are to be explored further to evaluate their influence as structure directing parameters. Further, we believe that these findings will also have immense impact on the further development of exotic architectures involving the –B(OH)$_2$ moiety, either by itself or in conjunction with other functional moieties like –COOH, –CONH$_2$ etc. Further experiments are in progress in these directions.

Acknowledgements

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12. Crystal data for **1a**: ($C_{26}H_{23}O_2N_4B$), $M = 434.29$, orthorhombic, *Fdd2*; $a = 26.519(23)$, $b = 9.245(8)$, $c = 17.612(15)$ Å, $V = 4318(6)$ Å^3, $Z = 8$, $D_{calcd} = 1.336\ g\,cm^{-3}$, $F(000) = 1824$, λ (Mo-Kα) = 0.71073 Å, $T = 140(2)$ K, reflections collected/unique 4496/1428 ($R_{ini} = 0.018$). Final GooF = 1.030, $R_1 = 0.052$, $wR_2 = 0.129$, 197 parameters, μ (Mo-Kα) = 0.086 mm^{-1}, R indices based on 1300 reflections with $I > 2\sigma(I)$ (refinement on F^2), absorption corrections applied. CCDC 220094.
13. Crystal data for **1b**: ($C_{18}H_{19}O_3N_2B$), $M = 322.16$, monoclinic, $P2_1/c$; $a = 6.860(2)$, $b = 19.092(5)$, $c = 12.829(3)$ Å, $\beta = 96.47(1)°$, $V = 1669.7(7)$ Å^3, $Z = 4$, $D_{calcd} = 1.282\ g\,cm^{-3}$, $F(000) = 680$, λ (Mo-Kα) = 0.71073 Å, $T = 140(2)$ K, reflections collected/unique 7183/2407 ($R_{ini} = 0.028$). Final GooF = 0.891, $R_1 = 0.040$, $wR_2 = 0.111$, μ (Mo-Kα) = 0.087 mm^{-1}, R indices based on 1965 reflections with $I > 2\sigma(I)$ (refinement on F^2), absorption corrections applied. CCDC 220095.
14. Crystal data for **2a**: ($C_{24}H_{26}O_6N_2B_2$), $M = 460.09$, monoclinic, $C2/c$; $a = 23.736(6)$, $b = 5.216(1)$, $c = 18.544(5)$ Å, $\beta = 96.11(1)°$, $V = 2282.7(10)$ Å^3, $Z = 4$, $D_{calcd} = 1.339\ g\,cm^{-3}$, $F(000) = 968$, λ (Mo-Kα) = 0.71073 Å, $T = 140(2)$ K, reflections collected/unique 4594/1645 ($R_{ini} = 0.108$). Final GooF = 0.891, $R_1 = 0.046$, $wR_2 = 0.082$, μ (Mo-Kα) = 0.095 mm^{-1}, R indices based on 901 reflections with $I > 2\sigma(I)$ (refinement on F^2), absorption corrections applied. CCDC 220096.
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20. Crystal data for **2**: ($C_7H_9O_3B$), $M = 151.95$, monoclinic, $P2_1/n$; $a = 11.259(3)$, $b = 5.064(1)$, $c = 13.878(3)$ Å, $\beta = 111.04(1)°$, $V = 738.5(3)$ Å^3, $Z = 4$, $D_{calcd} = 1.367\ g\,cm^{-3}$, $F(000) = 320$, λ (Mo-Kα) = 0.71073 Å, $T = 140(2)$ K, reflections collected/unique 3009/1065 ($R_{ini} = 0.025$). Final GooF = 0.998, $R_1 = 0.046$, $wR_2 = 0.082$, μ (Mo-Kα) = 0.103 mm^{-1}, R indices based on 876 reflections with $I > 2\sigma(I)$ (refinement on F^2), absorption corrections applied. CCDC 222652.