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A new method for the synthesis of boronate macrocycles

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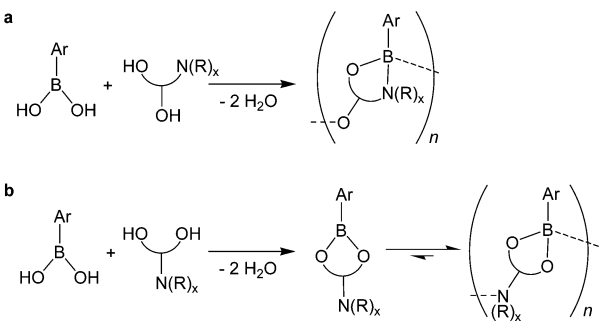
The condensation of aryl boronic acids with 2,3-dihydroxypyridine gives boronates, which self-assemble to form tetrameric macrocycles as evidenced by X-ray crystallographic analyses.

The utilization of boron compounds as building blocks for the construction of macrocyclic two- and three-dimensional assemblies is an emerging topic in supramolecular chemistry.[1] Similar to many transition metal complexes, boron compounds may form directional bonds, which are thermodynamically stable but kinetically labile. This feature allows error correction processes to occur during assembly reactions, a characteristic that is of central importance for the synthesis of complex structures. As starting materials, aryl boronic acids appear to be of special interest since many derivatives are commercially available. Furthermore, aryl boronic acids are known to easily undergo condensation reactions with various diols to form boronic esters,[2] a reaction that appears to be a good entry point for the formation of more complex structures.

First results in this area have been reported by Höpfl and Farfán.[3] They have successfully employed the reaction outlined in Scheme 1(a) for the construction of di-, tri- and tetranuclear boron macrocycles with ring sizes between 10 and 20 atoms. A different strategy, which—to the best of our knowledge—has not been investigated so far, is depicted in Scheme 1(b). Again, an aryl boronic acid is reacted with a tridentate amino dialcohol. But now, the ligand has two *adjacent* hydroxy groups. Consequently, it is expected that an O–B–O′ chelate is formed initially which can then assembly to give the macrocycle. The main difference between the two reactions is that for the latter pathway, macrocyclization occurs *via* formation of dative B–N bonds[4] and not *via* strong covalent B–O bonds.

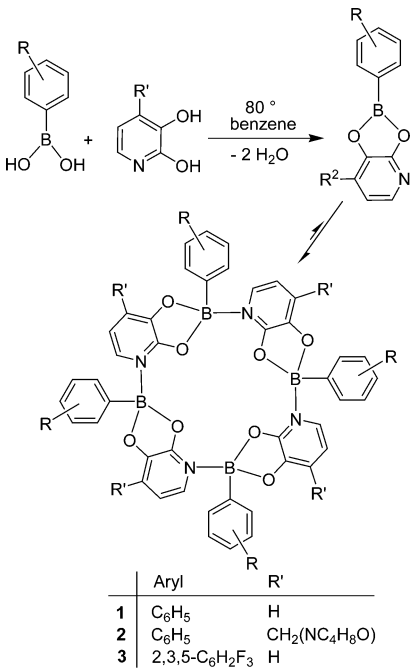
In order to test the feasibility of the latter approach, we have first examined the reaction between phenyl boronic acid and 2,3-dihydroxypyridine. This ligand was chosen because it has been successfully employed in transition metal based self-assembly reactions using metal fragments with a (pseudo)tetrahedral coordination geometry.[5] Furthermore, several derivatives are easily accessible which would allow to fine-tune the electronic properties and the solubility of the resulting assemblies.[6] In order to efficiently remove the by-product water, the reaction was performed in benzene under reflux using a Dean–Stark trap to separate the azeotropic benzene–water mixture. Upon cooling of the benzene solution, the product (**1**) precipitated as a white powder (isolated yield: 51%).[7]†



Scheme 1 Different strategies to synthesize macrocyclic boronates: (a) macrocyclization *via* covalent B–O bonds; (b) macrocyclization *via* dative B–N bonds.

Compound **1** is well soluble in organic solvents such as chloroform. This is in contrast to macrocycles prepared by the method depicted in Scheme 1(a), which were often found to display a very limited solubility.[3] The ^{1}H and ^{13}C NMR spectra of **1** indicated that a highly symmetrical complex had formed because only one set of signals was found for the phenyl group as well as for the pyridine ligand. Since NMR spectroscopy is not suited to determine the association number *n*, we have investigated the molecular structure of **1** in the solid state by single crystal X-ray analysis.‡ It was found that a tetrameric assembly had formed (Fig. 1). As expected, the boronic acid has undergone a condensation reaction with the two adjacent hydroxy groups to give a five-membered cyclic ester and the pyridine N-atom forms a dative bond to the next boron centre. Overall, the macrocycle displays a perfect S_4 symmetry. The planes of the heterocyclic ligands are nearly orthogonal to each other forming a molecular square. It is interesting to note that organometallic halfsandwich complexes of Ru^{II}, Rh^{III}, and Ir^{III}, which likewise display a (pseudo)tetrahedral coordination geometry, form exclusively trimeric macrocycles with the same bridging heterocycle.[5] Apparently, the smaller boron atom is able to switch the assembly process entirely from $n = 3$ to $n = 4$.

In order to test the flexibility of the synthetic approach, we have investigated whether substitutions of the bridging ligand and on the aryl group are tolerated. This is indeed possible as evidenced by the successful preparation of complexes **2** and **3** (Scheme 2).† For the synthesis of complex **2**, a ligand with a morpholinomethyl group in



Scheme 2 Synthesis of the tetrameric boronates **1–3**.

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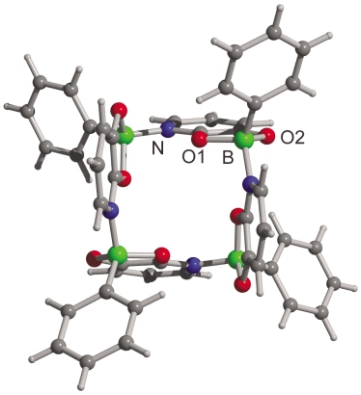

Fig. 1 Molecular structure of **1** in the crystal.

position 4 was employed[8] and for complex **3**, the commercially available 2,3,6-trifluorophenyl boronic acid was used. The self-assembly reactions are not affected by these substitutions. This was confirmed by NMR spectroscopy and single crystal X-ray analyses.‡ For complex **2**, the presence of stereogenic boron centres is manifested by the presence of two diastereotopic methylene protons, which give rise to two doublets in the ^{1}H NMR spectrum. The structures of **2** and **3** in the crystal are very similar to that of **1** although a crystallographic S_4 symmetry is no longer present. A comparison of important bond length and angles is given in Table 1.

The B–N and the B–O bonds of the complexes **2** and **3** are slightly shorter than those found for **1**. This leads to an overall contraction of the macrocycles as reflected by the reduced B···B distances of **2** and **3**. The O–B–N angles found for all complexes are close to the 109.5° expected for a perfect tetrahedral geometry. The B–N bond lengths are of special interest because they represent a key element of the macrocyclic framework. Dative B–N bonds can range from 1.57 to 2.91 Å.[4] The average B–N bond length of the complexes **1–3** is 1.59 Å. This is shorter than what is typically found for tetrahedral boronates with N-donor ligands, which show a value around 1.69 Å. The simple adduct between 4-methylpyridine and 2-phenyl-1,3,2-benzodioxaborole, for example, displays a B–N bond length of 1.654 Å in the crystal.[9]

The data described above suggest that the B–N bonds in **1–3** are thermodynamically rather stable. In order to investigate the kinetic stability of the assemblies, we have performed scrambling experiments. Equimolar amounts of complex **1** and **2** were dissolved in $CDCl_3$. Even after 24 h, the ^{1}H NMR spectrum of the mixture was unchanged, indicating that no mixed species had formed. Apparently, the macrocycles are kinetically rather inert.

In summary, we have described a new method for the synthesis of macrocyclic boronate complexes. It seems likely that this synthetic concept can be expanded by employing other tridentate ligands such as 3,4-dihydroxy-2-methylpyridine, 2-hydroxynicotinic acid, or 2,3-dihydroxyquinoline, all of which have successfully been employed in transition metal-based self-assembly reactions.[10,11] Furthermore, it should be possible to replace aryl with alkyl boronic acids which would significantly enhance the structural diversity that is accessible. Preliminary results indicate that this is indeed possible.[12]

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Table 1 Selected distances (Å) and angles (°) for the compounds **1–3**

	B–N	B–O1	B–O2	B···B′[a]	O2–B–N	O1–B–N
1	1.601(2)	1.529(2)	1.496(2)	5.624(2)	110.1(1)	105.1(1)
2[b]	1.587(6)	1.524(5)	1.481(5)	5.318(7)	108.8(3)	106.0(3)
3[b]	1.58(1)	1.506(9)	1.487(9)	5.31(1)	109.0(6)	108.0(6)

[a] The distance between the boron atoms opposite to each other is given. [b] Averaged values are given.

Notes and references

† A suspension of phenyl boronic acid (219 mg, 1.8 mmol) and 2,3-dihydroxypyridine (200 mg, 1.8 mmol) in freshly distilled benzene (60 mL) was heated under reflux using a Dean–Stark trap. After 15 h, the suspension was filtered hot. Upon cooling, a white precipitate formed which was isolated and dried under vacuum. (yield: 180 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.61 (t, ^3J = 7 Hz, 4 H, pyridine), 6.67 (d, ^3J = 6 Hz, 4 H, pyridine), 6.99 (d, ^3J = 7 Hz, 4 H, pyridine), 7.05–7.35 (m, 20 H, phenyl); ^{13}C NMR (400 MHz, $CDCl_3$): δ 114.17, 115.78, 127.69, 128.09, 128.12, 132.04, 151.26, 163.83; ^{11}B NMR (400 MHz, $CDCl_3$): δ 11.5; elemental analysis (%) calc. for $C_{44}H_{32}B_4N_4O_8$: C 67.07, H 4.09, N 7.11; obtained: C 67.32, H 4.18, N 6.86. The synthesis of **2** (yield: 84%) and **3** (yield: 84%) was performed analogously using 2,3-dihydroxy-4-morpholinomethyl-pyridine and 2,3,6-$C_6H_2F_3B(OH)_2$. All reactions were carried out under an inert atmosphere (N_2). Crystals were obtained by slow diffusion of pentane into solutions of the respective complexes in CH_2Cl_2 (**1**) or benzene (**2**, **3**).

‡ *Crystal data* for **1**: $C_{44}H_{32}B_4N_4O_8$, M = 787.98, tetragonal, a = 16.7128(8), c = 13.9916(11) Å, V = 3908.1(4) Å^3, T = 140(2) K, space group $I4_1/a$ (no. 88), Z = 4, μ(Mo-K$_\alpha$) = 0.091 mm^{-1}, 11 750 reflections collected, 1729 independent reflections, R_{int} = 0.0384, R_1 [$I > 2\sigma(I)$] = 0.0347, wR_2 (all data) = 0.0943. For **2**: $C_{78.5}H_{86}B_4N_8O_{12}$, M = 1376.79, orthorhombic, a = 26.3143(18), b = 28.029(2), c = 20.2248(11) Å, V = 14917.2(17) Å^3, T = 140(2) K, space group *Iba*2 (no. 45), Z = 8, μ(Mo-K$_\alpha$) = 0.082 mm^{-1}, 44 532 reflections collected, 12 697 independent reflections, R_{int} = 0.0756, R_1 [$I > 2\sigma(I)$] = 0.0625, wR_2 (all data) = 0.1498. For **3**: $C_{56}H_{32}B_4F_{12}N_4O_8$, M = 1160.10, triclinic, a = 13.538(4), b = 13.595(10), c = 13.813(12) Å, α = 80.64(7), β = 85.41(4), γ = 80.58(4)°, V = 2471(3) Å^3, T = 140(2) K, space group $P\bar{1}$ (no. 2), Z = 2, μ(Mo-K$_\alpha$) = 0.133 mm^{-1}, 16 104 reflections collected, 8192 independent reflections, R_{int} = 0.1172, R_1 [$I > 2\sigma(I)$] = 0.0774, wR_2 (all data) = 0.2432. CCDC 233235–233237. See http://www.rsc.org/suppdata/cc/b4/b402510e/ for crystallographic data in CIF or other electronic format.

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