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Crystal structures of 2-(*N*,*N*-dimethylaminoalkyl)ferroceneboronic acids and their diol derivatives. The quest for a B–N intramolecular bond in the solid state

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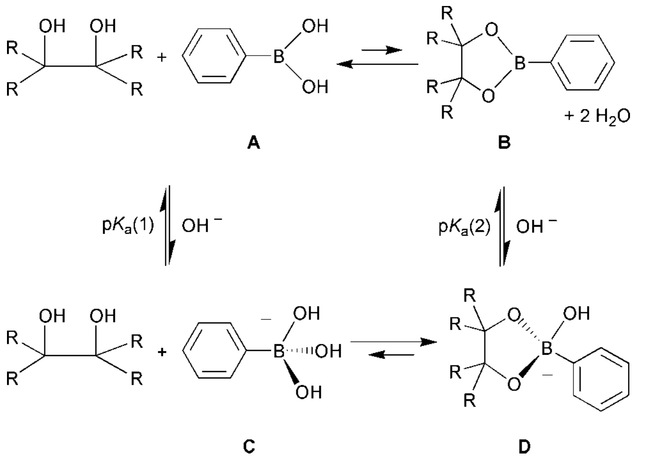
Received (in Cambridge, UK) 12th March 2001, Accepted 20th March 2001
First published as an Advance Article on the web 18th April 2001

The crystal structures of (*S*,*S*)-2-(*N*,*N*-dimethyl-1-aminoethyl)ferroceneboronic acid (**2**), (*S*,*S*)-1-(*N*,*N*-dimethyl-1-aminoethyl)-2-(4,4,5,5-tetraphenyl-1,3,2-dioxaborolan-2-yl)ferrocene (**3**), *rac*-2-(*N*,*N*-dimethylaminomethyl)-ferroceneboronic acid (**rac-4**), (*S*)-[(1*S*,2*S*,3*R*,5*S*)-pinane-1,2-diyl] 2-(*N*,*N*-dimethylaminomethyl)ferroceneboronate (**5**) are presented. In connection with our studies of boronic acid-based carbohydrate sensors, we aimed at verifying the existence of an intramolecular B–N bond in these compounds; however, such a bond was not found. This fact, and other structural elements and similarities of the four compounds, are discussed.

Introduction

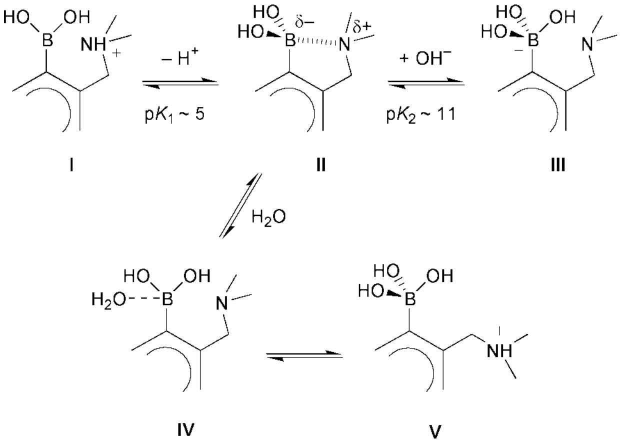
Aromatic boronic acids have recently gained considerable attention for their potential applications as carbohydrate sensors.[1–6] In aqueous solution boronic acids form cyclic esters (from hereon also named complexes) with diols according to the equilibria in Scheme 1. As indicated, the formation of a neutral boronate ester (**B**) is generally highly disfavored in aqueous solution and only hydroxyboronates (**D**) will exist in fair amounts. Since the pK_a of the boronate ester is approximately 1–2 units less than that of the boronic acid,[7,8] it follows that complex formation only results if the pK_a value of the boronic acid is comparable with or less than the pH of the solution. This requirement limits the use of simple boronic acids (pK_a ~9) for sensor purposes at neutral pH.



Scheme 1 Equilibria between boronic acids and diols in aqueous solution.

Twenty years ago Wulff *et al.* discovered that the exchange rate between free diols and diol esters of boronic acids were greatly enhanced by neighboring amino functionalities in the boronic acids.[9,10] On the basis of their NMR studies they discovered a strong but kinetically labile B–N interaction in *o*-(*N*,*N*-dimethylaminomethyl)benzeneboronic acid derivatives. They also showed that this interaction expands the pH-range within which a tetrahedral boron atom exists. Accordingly, this allows a strong binding of diols even at neutral pH. Scheme 2 shows the relevant equilibria in such a system; only the forms **II**, **III** and **V** can give strong interactions with diols. We anticipate that only the zwitterionic form **V** exists in substantial amounts when other factors prevent the formation of a B–N bond.

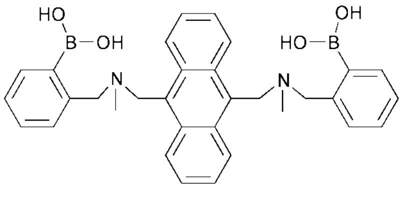
Since the early studies by Wulff the B–N interactions in a number of boronate esters and boroxins have been confirmed in the crystalline state. A general picture of a strong B–N bond of approximately 1.5 to 1.8 Å emerges from the literature.[11]



Scheme 2 Equilibria of 2-(*N*,*N*-dimethylaminomethyl)-substituted boronic acids in aqueous solution.

Recently the B–N concept was used by Shinkai's group in the design of a fluorescent glucose sensor (**1**)[12] as well as an electrochemical sensor (**2**),[13] where the interaction between the boronic acid and the carbohydrate at neutral pH was believed to be facilitated by favorable intramolecular B–N interactions. An

DOI: 10.1039/b102377m



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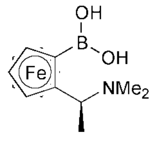

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obvious difference between the two systems is the bi- *versus* mono-dentate binding mode, but the general concept of B–N interactions seemed to be the same. However, there are some geometrical differences, in that the first system comprises a six-membered phenyl ring whereas the latter is attached on the five-membered cyclopentadienyl ring. This might suggest a longer B–N distance in the ferrocene system.

From binding studies of **1** and **2** with D-glucose, a large difference in their complexation constants at neutral pH was observed. Compared to the very strong binding observed for the anthracene bisboronic acid **1**, the glucose binding by the non-oxidized ferroceneboronic acid was almost unmeasurable. In our opinion this difference cannot be explained only by the mono- *versus* the bi-dentate binding mode. A recent study by Moore and Wayner[14] on unsubstituted ferroceneboronic acid gave very similar complexation constants to those of compound **2**, so we wondered whether structural parameters, which could prevent a strong B–N interaction, might be a more feasible explanation for the negligible binding of glucose in the ferrocene case. In the preceding paper we have reported on **2** and its sorbitol complex in aqueous solution and provided evidence that no intramolecular B–N bonding is present under these conditions.[15] Furthermore, with titration studies we showed that, at neutral pH, ferroceneboronic acid **2** was present as as the mono-cationic species **I** (Scheme 2).

In the present crystallographic study we disclose the molecular structures of **2** and its benzopinacol ester **3**, as well as two closely related structures, in a quest for an intramolecular B–N bond in the solid state in this type of compound.

Results and discussion

Synthesis

The optically pure (*S*,*S*)-2-(*N*,*N*-dimethyl-1-aminoethyl)-ferroceneboronic acid (**2**) was first prepared by Silva and coworkers.[16] However, these authors erroneously designated the compound they prepared as (*S*,*R*) which is not in accordance with the generally accepted nomenclature deduced by Ugi.[17] We have repeated their synthesis, starting from the optically pure (−)-(*S*)-(*N*,*N*-dimethyl-1-aminoethyl)ferrocene to verify the stereochemistry and the sign of the reported rotation of the compound. Due to the moderate yield obtained by the published method (47%) we slightly modified the procedure. By lithiation with *sec*-butyllithium instead of *n*-butyllithium we were able to obtain (+)-(*S*,*S*)-**2** in 72% yield after crystallization from EtOAc–pentane. The product had a slightly higher optical rotation than previously reported.

For reasons we shall return to below, we made several attempts to crystallize a diol-protected derivative of **2**. We investigated several diols from our stock but all the boronates were *very* soluble, even in pentane. However, with benzopinacol we were able to obtain the boronate **3**, which crystallized from toluene.

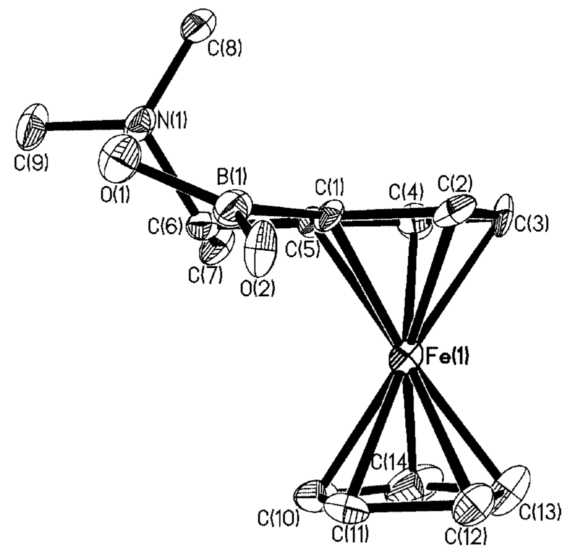
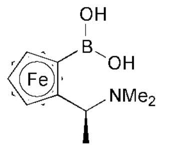
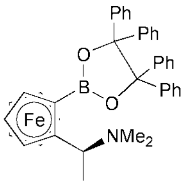


Fig. 1 View of (*S*,*S*)-2-(*N*,*N*-dimethyl-1-aminoethyl)ferroceneboronic acid (**2**). The thermal ellipsoids are drawn at a 50% probability level. The hydrogen atoms have been omitted for clarity.

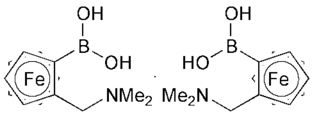
The racemic 2-(*N*,*N*-dimethylaminomethyl)ferroceneboronic acid (**rac-4**) was prepared by the method of Marr *et al.*[18] and crystallized from toluene–heptane or EtOAc. Two morphologically different racemates (**rac-4a**) and (**rac-4b**) were obtained (cubes and needles, respectively). The two diastereomeric (+)-pinanediol esters of **rac-4** were synthesized by reacting **rac-4** with equimolar amounts of (+)-pinanediol in toluene (Dean–Stark). The resulting red oil was left in the freezer for several months, after which time one of the two diastereomers (**5**) crystallized.



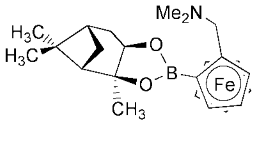
(+)-(S,S)-**2**



(+)-(S,S)-**3**



rac-4



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Crystal structures

Crystal structures of compounds **2**, **3**, **rac-4a**, **rac-4b** and **5** (Figs. 1–4) were obtained. These compounds can be divided into two groups, one of which comprises the free boronic acids **2** and **rac-4**, and the other one the diol-boronates **3** and **5**. Crystal data for the compounds are listed in Table 1 and selected bond lengths, angles and torsion angles are listed in Table 2. The labeling of the atoms in the molecules is shown in Figs. 1–4. The Fe–C bond lengths in the five structures are in

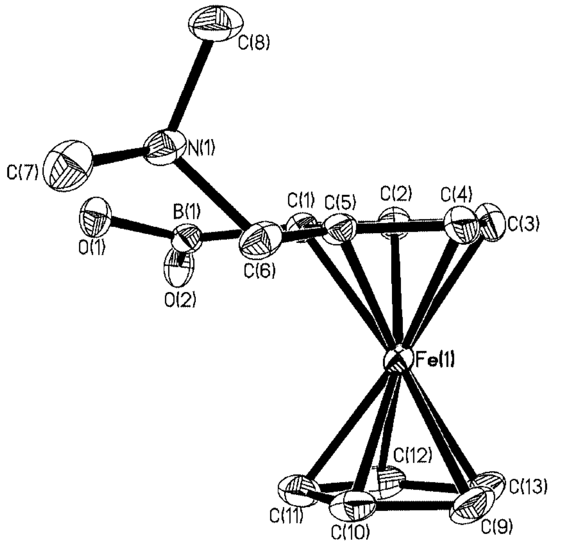

Fig. 2 View of *rac*-2-(*N*,*N*-dimethylaminomethyl)ferroceneboronic acid (**rac-4**). The thermal ellipsoids are drawn at a 50% probability level. The hydrogen atoms have been omitted for clarity.

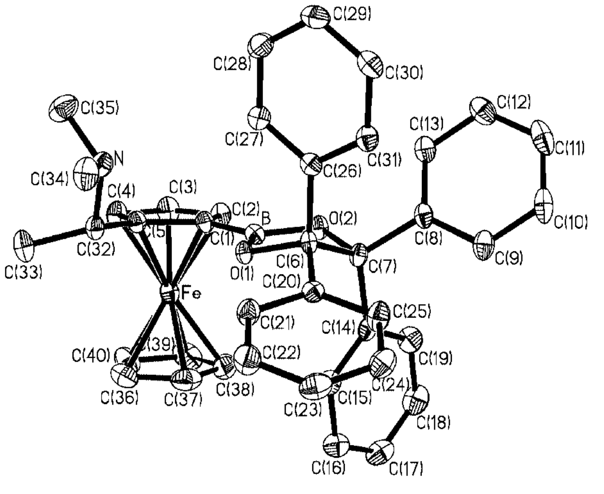

Fig. 3 View of (*S*,*S*)-1-(*N*,*N*-dimethyl-1-aminoethyl)-2-(4,4,5,5-tetraphenyl-1,3,2-dioxaborolan-2-yl)ferrocene (**3**). The thermal ellipsoids are drawn at a 50% probability level. The hydrogen atoms have been omitted for clarity.

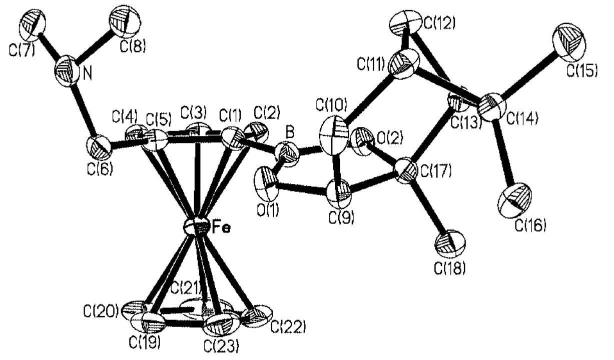

Fig. 4 View of (*S*)-[(1*S*,2*S*,3*R*,5*S*)-pinane-1,2-diyl] 2-(*N*,*N*-dimethylaminomethyl)ferroceneboronate (**5**). The thermal ellipsoids are drawn at a 50% probability level. The hydrogen atoms have been omitted for clarity.

the range 2.022–2.065 Å and the coordination around the Fe(II) ions is in agreement with the results found in similar compounds, *e.g.*, in ferrocene itself.[19] The cyclopentadienyl rings of the ferrocene moieties are almost eclipsed in all the structures. The rings are planar and the angles between them are 1.6(4) and 0.6(4)° for the two molecules in **2**, 1.5(2)° in **3**, 3.1(1) and 2.9(1)° in **rac-4a** 3.3(6) and 2.2(6)° in **rac-4b**, and 2.8(3)° in **5**. The molecules in **rac-4b** are similar to those of **rac-4a** and, because the structure of **rac-4b** is less accurate than the structure of **rac-4a**, the bond lengths, angles and torsion angles of the molecules in **rac-4b** are omitted here. The distances from the planes of the cyclopentadienyl rings to the Fe(II) ions in the five structures are in the range 1.635–1.650 Å. This is in agreement with the distances found in some substituted [1]ferrocenophanes[20] and in two azaferrocenes.[21]

In **2** and **rac-4** the bond lengths, angles and torsion angles of both the boronic acid moieties and the aminoalkyl groups are quite similar. In **2** the ethyl carbon atoms, C(6) and C(20), are located in the plane of the substituted cyclopentadienyl rings, whereas the methyl carbon atoms, C(7) and C(21) are 0.18(1) and 0.04(1) Å below the plane, respectively. The methyl carbon atoms thus lie close to the cyclopentadienyl plane and the NMe_2 groups are outside the ring planes, as also found in [1-(*N*,*N*-dimethylammonium)ethyl]ferrocene tartrate dihydrate.[22] In **rac-4a** we observe an analogous placing of the methyl carbon atoms C(6) and C(9), being 0.076(2) and 0.056(2) Å below the plane. In **2** both *N*-methyl groups are in a *gauche* orientation with respect to C(7).

In **2** and **rac-4** there are, in each of the molecules, intramolecular hydrogen bonds between the nitrogen atom and one of the oxygen atoms in the $B(OH)_2$ group. In **2** the hydrogen bonds are the O(1)–H(1O) · · · N(1) bond [2.690(5) Å] and the O(3)–H(3O) · · · N(2) bond [2.686(5) Å (D · · · A)]. In **rac-4a** the O(1)–H(1O) · · · N(1) bond is 2.653(1) and the O(3)–H(3O) · · · N(2) bond is 2.672(1) Å. In **rac-4b** the two hydrogen bonds are 2.627(8) and 2.667(8) Å. As a consequence of the hydrogen bonding in **2** and **rac-4**, the plane of the $B(OH)_2$ groups is twisted approximately 20 degrees relative to the cyclopentadienyl ring. To our knowledge no comparable structure of the unsubstituted ferroceneboronic acid has yet been published.

The crystal packing in **2** and **rac-4** are influenced by hydrogen bonds. In **2** the hydrogen bonds are the O(2)–H(2O) · · · O(3) ($x + 1, y, z$) [2.782(5) Å] and the O(4)–H(4O) · · · O(1) ($x - 1, y, z$) [2.771(5) Å (D · · · A)]. In **rac-4a** the hydrogen bonds are the O(2)–H(2O) · · · O(3) ($1/2 - x, -1/2 + y, 1/2 - z$) [2.732(1) Å] and the O(4)–H(4O) · · · O(1) ($1½ - x, 1/2 + y, 1/2 - z$) [2.704(1) Å (D · · · A)]. In **rac-4b** the two hydrogen bonds are the O(2)–H(2O) · · · O(3) ($-x, 2 - y, z - 1/2$) bond [2.766(7) Å] and the O(4)–H(4O) · · · O(1) ($-x, 2 - y, z + 1/2$) bond [2.709(7) Å (D · · · A)].

The B–N distances are 3.288(8) and 3.287(8) Å for the two molecules in **2**, 3.305(2) Å for the two molecules in **rac-4a** and 3.28(1) and 3.29(1) Å in **rac-4b**, whereas the optimal distance for a B–N bond, as mentioned above, is 1.5–1.8 Å. Consequently, there are no intramolecular B–N bonds in these compounds as opposed to the structure of, *e.g.*, 2-{2-[1-(dimethylamino)-1-methylethyl]phenyl}-4,4-diphenyl-1,3,2-dioxaborolane,[23] where an intramolecular B–N bond of 1.747(2) Å is found. However, when comparing the ferrocene structures **2** and **4** determined in this paper with the above mentioned compound there are several factors which may explain why the B–N bond does not form in molecules **2** and **4**. Firstly, the intramolecular hydrogen bonding present in the free boronic acids **2** and **rac-4** may be more favorable than the B–N interaction, as the latter will lead to severe distortion of bond lengths and angles and induce steric repulsions between the unsubstituted cyclopentadienyl ring and both a N-Me group and a B-OH group. Secondly, there is an obvious geometrical difference to take into account, in that the ferrocenes comprise 1,2-substituted five-membered rings, whereas the benzene derivative is, of course, a 1,2-substituted six-membered ring, the former having a considerably longer optimal B–N distance

Table 1 Crystallographic data for compounds **2**, **3**, **4a**, **4b**, **5**

	2	**3**	**4a**	**4b**	**5**
Formula	$C_{14}H_{20}BFeNO_2$	$C_{40}H_{38}BFeNO_2$	$C_{13}H_{18}BFeNO_2$	$C_{13}H_{18}BFeNO_2$	$C_{23}H_{32}BFeNO_2$
FW	300.97	631.37	286.94	286.94	421.16
T/K	120(2)	120(2)	120(2)	120(2)	120(2)
Crystal system	Orthorhombic	Monoclinic	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$	$P2_1/n$	$Pca2_1$	$P2_1$
a/Å	7.2501(15)	9.866(2)	12.452(3)	21.431(4)	7.3162(15)
b/Å	16.807(3)	13.168(3)	12.858(3)	6.1956(12)	11.887(2)
c/Å	23.309(5)	11.968(2)	17.078(3)	20.414(4)	12.622(3)
β/°		92.55(3)	104.77(3)		104.73(3)
V/Å^3	2840.2(10)	1553.3(5)	2643.9(9)	2710.6(9)	1061.6(4)
Z	8	2	8	8	2
D_x/g cm^{-3}	1.408	1.350	1.442	1.406	1.317
$\mu_{(\mathrm{Mo}K\alpha)}$/mm^{-1}	1.058	0.523	1.132	1.104	0.728
Crystal colour	Yellow	Orange	Yellow–brown	Pale yellow	Yellow
Crystal size/mm	0.50 × 0.06 × 0.05	0.35 × 0.30 × 0.25	0.35 × 0.30 × 0.20	0.40 × 0.08 × 0.02	0.33 × 0.20 × 0.15
θ-range/°	1.49–29.74	1.70–29.45	1.82–29.68	1.90–29.71	1.67–29.52
Measured reflections	20153	10719	17656	17557	7453
Unique reflections	7330	7330	6747	6844	4780
Reflections with $[I > 2\sigma(I)]$	3819	6224	5865	3866	4359
R(int)	0.1404	0.0194	0.0158	0.1247	0.0231
Transm. factors	1.0000–0.8786	1.0000–0.8346	1.0000–0.9018	1.0000–0.8382	1.0000–0.8140
Refined param	349	406	325	325	253
$R1$[a] (obs. data)	0.0664	0.0310	0.0231	0.0788	0.0447
$wR2$[b] (all data)	0.1143	0.0728	0.0653	0.1533	0.1111
Goodness-of-fit	0.930	1.036	1.051	1.052	1.037
Max, min $\Delta\rho$/e Å^{-3}	−0.655 and 0.449 (near Fe(1))	−0.238 and 0.217 (near Fe and O(2))	−0.308 and 0.388 (near Fe(1) and B(2))	−0.548 and 1.310 (near Fe(2))	−0.336 and 0.481 (near Fe)

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma w|F^2_o - F^2_c|^2/\Sigma wF_o^4]^{1/2}$.

(~2.6 Å compared to ~2.2 Å without alteration of bond length and angles).

Now we turn to the crystal structures of the two boronates **3** and **5**. These molecules were synthesized, not only in order to avoid interference from the hydrogen bonding as discussed above, but also because it is well known that boronates have a more electrophilic boron atom than the corresponding free acids and so make stronger interactions with donor atoms. Nevertheless, as we shall discuss below, no B–N interactions were found.

In **3** the bond lengths and angles of the amino substituted ethyl group are like those of **2** and **4**, whereas the torsion angles differ slightly. In **3** the lone pair of the nitrogen atom is roughly directed towards the O(1) atom, the N(1)···O(1) and the N(1)···O(2) distances being 3.315(2) and 4.772(2) Å, respectively. The change in conformation of the substituent in **3** could be due to the lack of hydrogen bonds. The ethyl carbon atom C(32) is 0.032(4) Å above, and the methyl carbon atom C(33) is 0.381(5) Å below the plane of the ring. The methyl carbon atom here lies clearly between the planes of two cyclopentadienyl rings. The conformation of the aminoalkyl side chain places one *N*-methyl group nearly *gauche* to the C(33) methyl group. In the BO_2C_2 ring in **3** the B–O bond lengths are like those of the $B(OH)_2$ groups in **2** and **rac-4** and are in agreement with the values found in 2,3-dimethylbutane-2,3-diyl (3-benzoyl-2-phenylisoxazolidin-4-yl)boronic ester.[24] The B–O bond lengths are, however, shorter than those found in 2-{2-[1-(dimethylamino)-1-methylethyl]phenyl}-4,4-diphenyl-1,3,2-dioxaborolane [1.436(2) and 1.435(2) Å].[23] In the latter structure the tetrahedral character[11] of the boron atom is 53%. In the BO_2C_2 ring of **3** the O–C bonds are shorter and the C–C bond longer than the equivalent bonds (C–O 1.505, 1.533 and C–C 1.509 Å) in 2,3-dimethylbutane-2,3-diyl (3-benzoyl-2-phenylisoxazolidin-4-yl)boronic ester.[24] In the five-membered BO_2C_2 ring the angles and the twist conformation are in agreement with the values found in 2,3-dimethylbutane-2,3-diyl (3-benzoyl-2-phenylisoxazolidin-4-yl)boronic ester.[24]

In the aminoalkyl group of **5** the bond lengths and angles, except for the bond angle N–C(6)–C(5) of 116.8(3)°, are quite similar to those found in the other four structures reported here. The carbon atom C(6) is 0.041(5) Å below the plane of the cyclopentadienyl ring and the N–C(6)–C(5) group is almost perpendicular to the plane of the ring. The lone pair on the nitrogen atom is directed away from the ring and the shortest N···O distance is the N···O(1) distance of 3.947(4) Å. The bond lengths and angles of the pinane-1,2-diyl substituent are in agreement with those found in (1*S*,2*S*,3*R*,5*S*)-pinanediol pyrrolidine-(2*R**)-boronate hydrochloride.[25] In the BO_2C_2 moiety the B–O and the O–C bonds are quite similar to those found in **3**, whereas the C–C bond of 1.559(4) Å is shorter than the values of 1.594(2) Å found in **3**. The O–C–O angles in **5** are 105.2(2) and 103.7(2)°, whereas in **3** they are 100.8(1) and 100.0(1)°. The bond lengths and angles in **5** are in agreement with those found in (1*S*,2*S*,3*R*,5*S*)-pinanediol pyrrolidine-(2*R**)-boronate hydrochloride.[25] The five-membered ring containing B, O(1) and O(2) has an envelope conformation. The two six-membered rings C(9)–C(10)–C(11)–C(12)–C(13)–C(17) and C(9)–C(10)–C(11)–C(14)–C(13)–C(17) are both in an E-form. The conformation of the rings are in agreement with those found in (1*S*,2*S*,3*R*,5*S*)-pinanediol pyrrolidine-(2*R**)-boronate hydrochloride.[25]

As expected, there are no classic hydrogen bonds in the structures of **3** and **5** and the C–H···A bonds are weak. The B–N distance is 3.524(3) Å in **3** and 4.094(4) Å in **5**. Consequently, there are no intramolecular B–N bonds in the solid state in any of the five compounds studied here.

Simple considerations based on model building and simple calculations (MM2) seem to indicate that one of the major factors preventing the formation of the B–N bond may be steric interactions with the unsubstituted cyclopentadienyl ring upon forming the five-membered azaborolane ring. We plan to do more exact calculations on the system in the near future.

Conclusion

From the results presented in this study we were not able to find an intramolecular B–N bond in the solid state in any of the five

Table 2 Selected bond lengths (Å), bond angles and torsion angles (°) for **2**, **3**, **4a** and **5**

	2	**4a**
C(1)–B(1)	1.548(8)	1.562(2)
B(1)–O(1)	1.370(6)	1.370(2)
B(1)–O(2)	1.371(7)	1.361(2)
C(5)–C(6)	1.508(7)	1.505(2)
C(6)–N(1)	1.499(6)	1.477(2)
C(6)–C(7)	1.515(7)	
N(1)–C(8/7)	1.473(6)	1.468(2)
N(1)–C(9/8)	1.477(6)	1.467(2)
C(15/14)–B(2)	1.562(8)	1.562(2)
C(19/18)–C(20/19)	1.523(7)	1.508(2)
B(2)–O(3)	1.363(7)	1.374(2)
B(2)–O(4)	1.335(7)	1.355(2)
C(20/19)–N(2)	1.482(6)	1.477(2)
C(20)–C(21)	1.525(7)	
N(2)–C(22/20)	1.464(6)	1.461(2)
N(2)–C(23/21)	1.468(6)	1.465(2)
O(1)–B(1)–O(2)	119.3(5)	120.79(11)
O(1)–B(1)–C(1)	121.4(5)	120.51(11)
O(2)–B(1)–C(1)	119.3(5)	118.70(11)
C(5)–C(1)–B(1)	129.0(5)	127.57(11)
C(1)–C(5)–C(6)	125.2(5)	126.09(11)
N(1)–C(6)–C(5)	107.8(4)	111.95(10)
O(3)–B(2)–O(4)	121.2(5)	120.89(11)
O(3)–B(2)–C(15/14)	120.5(5)	120.94(11)
O(4)–B(2)–C(15/14)	118.2(5)	118.17(11)
C(19/18)–C(15/14)–B(2)	130.0(5)	128.00(11)
C(15/14)–C(19/18)–C(20/19)	124.6(4)	125.98(11)
N(2)–C(20/19)–C(19/18)	109.3(4)	112.20(10)
C(7)–C(6)–C(5)–C(1)	172.0(5)	
N(1)–C(6)–C(5)–C(1)	59.9(6)	−54.4(2)
O(1)–B(1)–C(1)–C(5)	−26.3(9)	21.2(2)
O(2)–B(1)–C(1)–C(5)	156.2(5)	−159.5(1)
C(21)–C(20)–C(19)–C(15)	−178.1(5)	
N(2)–C(20/19)–C(19/18)–C(15/14)	53.7(7)	51.9(2)
O(3)–B(2)–C(15/14)–C(19/18)	−24.5(9)	−21.6(2)
O(4)–B(2)–C(15/14)–C(19/18)	158.4(5)	159.1(1)
	3	**5**
C(1)–B	1.531(3)	1.540(5)
B–O(1)	1.376(2)	1.370(4)
B–O(2)	1.378(2)	1.370(4)
O(1)–C(6/9)	1.450(2)	1.444(4)
O(2)–C(7/17)	1.455(2)	1.458(4)
C(6/9)–C(7/17)	1.594(2)	1.559(4)
C(5)–C(32/6)	1.509(3)	1.498(4)
C(32)–C(33)	1.536(3)	
C(32/6)–N	1.478(2)	1.462(4)
N–C(34/7)	1.452(3)	1.443(5)
N–C(35/8)	1.450(3)	1.448(5)
C(5)–C(1)–B	129.7(2)	128.4(3)
O(1)–B–O(2)	112.3(2)	113.4(3)
O(1)–B–C(1)	127.0(2)	124.8(3)
O(2)–B–C(1)	120.7(2)	121.8(3)
C(1)–C(5)–C(32/6)	124.5(2)	127.7(3)
N–C(32/6)–C(5)	108.9(2)	116.8(3)
C(33)–C(32)–C(5)–C(1)	−163.6(2)	
C(33)–C(32)–N–C(34)	77.9(2)	
N–C(32/6)–C(5)–C(1)	68.4(3)	93.7(4)
O(1)–B–C(1)–C(5)	3.3(4)	8.2(5)
O(2)–B–C(1)–C(5)	−175.4(2)	−172.4(3)

structures studied. For the compounds **2** and **rac-4** the formation of an intramolecular hydrogen bond, which determines the orientation of the ferrocene substituents seems to prevail over a conceivable B–N bond. For the boronates **3** and **5** we have no clear cut explanation why the normally very energetically favorable B–N bond does not form. Even with the quite bulky diol used in order to facilitate crystallization of the compounds, we do not believe that steric interactions originating from the diol moieties are the principal explanation. We rather anticipate that the electronic structure of the ferrocene core may cause the required distortions of the C_{Fe}–C_{Fe}–X binding angles to be highly unfavorable compared to the energy gain by formation of a B–N bond. In the structure of 2,2-dimethylpropane-1,3-diyl [*o*-(dimethylaminomethyl)phenyl]boronate we have recently seen severe distortions of the benzene–substituent angles to allow for a 1.76 Å B–N bond there.[26] For comparison, a number of ferrocenes with 1,2-appended five-membered rings containing a three-carbon bridging fragment are known. As expected, large distortions of the binding angles around the ferrocene moiety and of the C–C bond lengths are observed. In, *e.g.*, *rac*-4-ferrocenyl-4a,5,6,8a-tetrahydro-4a,5,8-trimethyl-4*H*-indeno[2,3-*a*]ferrocene[27] the two C–C bonds in the carbon bridge are 1.571(5) and 1.611(5) Å and in *endo*-1,7-diphenyl-3,4-(3-*tert*-butylferroceno)-8,9-benzo-10-oxatricyclo[5.2.1.$0^{2,4}$]-deca-3,8-diene[28] † C–C distances of 1.557(4) and 1.584(4) Å are found. The bond angles around the two carbon atoms shared with the ferrocene ring in these two compounds are 110, 110 and 140°, whereas in the structures presented in this work with no five-membered ring formed the angles are 110, 125 and 125°.

As mentioned in the introduction, our parallel study of **2** and its sorbitol complex in solution gave no evidence of a B–N bond;[15] with this, and the results of the present investigation, the use of ferroceneboronic acid **2** as a scaffold for future designs of carbohydrate sensors for neutral pH measurements must surely be seriously questioned.

The quest for an intramolecular B–N bond in this type of electrochemically active sensor, however, persists in our laboratory. Currently we are preparing some new analogs of **2** in which, we believe, we will have a better chance of obtaining the B–N interaction needed for carbohydrate sensing capability at neutral pH.

Experimental

General

^{1}H NMR spectra were recorded at 25 °C at 400 MHz. Chemical shifts are reported in ppm. The spectra in $CDCl_3$ are referenced internally the residual solvent peak at 7.26 ppm. Evaporations were performed *in vacuo* on a rotary evaporator at 40–50 °C. Melting points are uncorrected.

Materials

All chemicals used were of reagent grade and all solvents were of HPLC-grade.

X-Ray crystallography ‡

The crystals of the compounds are cooled to 120 K using a Cryostream nitrogen gas cooler system. The data were collected on a Siemens SMART platform diffractometer with a CCD area sensitive detector. The structures were solved by direct methods and refined by full-matrix least-squares against F^2 of all data. In all the structures the non-hydrogen atoms were refined anisotropically. The hydrogen atoms could in all structures be located from electron-density difference maps, but were at calculated positions using a riding model with C–H = 0.95–1.00 Å, O–H = 0.84 Å and fixed thermal parameters [$U(H) = 1.2U$ for attached atom]. In **2** the hydrogen atoms attached to O(3) and O(4) were refined with fixed distance of 0.84 Å and fixed thermal parameters. The Flack *x*-parameter is −0.00(3) for **2**, −0.025(10) for **3** and 0.02(2) for **5**, indicating

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† The IUPAC name for this compound is (η-cyclopentadienyl)(3-6η-17-oxapentacyclo[8.6.1.$0^{2,7}$.$0^{3,7}$.$0^{11,16}$]heptadeca-3,5,11,13,15-pentaenyl)iron.

‡ CCDC reference number 160671–160675. See http://www.rsc.org/suppdata/p2/b1/b102377m/ for crystallographic files in .cif or other electronic format.

that this is the correct absolute structure.[29,30] For **4b** the absolute structure could not be determined reliably. Programs used for data collection, data reduction and absorption were SMART, SAINT and SADABS.[31,32] The program SHELXTL 95[33] was used to solve the structures and for molecular graphics. PLATON[34] was used for molecular geometry calculations.

Syntheses

(*S*,*S*)-2-(*N*,*N*-Dimethyl-1-aminoethyl)ferroceneboronic acid (2). (*S*)-(*N*,*N*-Dimethyl-1-aminoethyl)ferrocene (1.00 g, 3.89 mmol) was dissolved in dry ether (20 mL) under a nitrogen atmosphere. The solution was cooled to 0 °C and *sec*-BuLi (1.2 M, 3.5 mL) was added dropwise. The orange solution was left at 0 °C for 1 h and allowed to reach room temperature over 30 min. Then the mixture was cooled to −100 °C and freshly distilled $(MeO)_3B$ (0.90 mL, 8.1 mmol) was added, quickly, in one portion.[35] The mixture was allowed to stand overnight, slowly reaching room temperature and then hydrolyzed at 0 °C with water (20 mL). The phases were separated and the aqueous phase was extracted twice with ether (25 mL). The combined organic phase was washed twice with brine, dried over Na_2SO_4 and evaporated to a orange solid material. Recrystallization from EtOAc–pentane yielded 0.50 g of orange needles. Mp[36] 139–142 °C (lit.[16] 142–145 °C), $[\alpha]_D^{25} = +104.2°$ ($c = 0.5$, EtOH) [lit.[16] $[\alpha]_D^{22} = +98°$ ($c = 1$, EtOH)]. Evaporation of the mother liquor and recrystallization gave another 0.34 g. Mp 136–142 °C, $[\alpha]_D^{25} = +104.0°$ ($c = 0.5$, EtOH). The total yield was 72%. ^{1}H and ^{13}C NMR data for both samples were in accordance with those previously published.[16]

(*S*,*S*)-1-(*N*,*N*-Dimethyl-1-aminoethyl)-2-(4,4,5,5-tetraphenyl-1,3,2-dioxaborolan-2-yl)ferrocene (3). (*S*,*S*)-2-(*N*,*N*-Dimethyl-1-aminoethyl)ferroceneboronic acid (**2**) (50 mg, 0.17 mmol) and recrystallized benzopinacol (61 mg, 0.17 mmol) were refluxed in benzene (50 mL) for 2 h in a Dean–Stark apparatus. Approximately 25 mL of solvent was collected and discarded and the remaining solvent was removed *in vacuo* to yield a brownish residue. Crystallizing twice from toluene with filtration gave shining red–orange crystals. Mp 220–222 °C. ^{1}H NMR ($CHCl_3$) δ 7.35 (m, 8H), 7.10 (m, 12H), 4.67 (dd, 1H), 4.47 (t, 1H), 4.45 (dd, 1H), 4.08 (q, 1H, $J = 7$ Hz), 4.07 (s, 5H), 2.02 (s, 6H), 1.49 (d, 3H, $J = 7$ Hz). MALDI-TOF MS: 632 (MH^+) +587 ($MH^+ - NHMe_2$).

***rac*-2-(*N*,*N*-Dimethylaminomethyl)ferroceneboronic acid (rac-4).** This compound was prepared by the method of Marr *et al.*[18] Crystallization from toluene–heptane gave a mixture of crystals **rac-4a** (blocks) and **rac-4b** (needles).

(*S*)-[(1*S*,2*S*,3*R*,5*S*)-Pinane-1,2-diyl 2-(*N*,*N*-dimethylaminomethyl)ferroceneboronate (5). This compound was prepared by the same method as **3**. Upon evaporation a viscous orange oil was obtained. This was left in the freezer for 3–4 months with occasional trituration. After initial crystal formation, approximately half of the oil crystallized. The oil was decanted and the residual oily crystals were isolated by fast washing with pentane at −10 °C. (The crystals were *very* soluble in pentane and all other "stock" solvents.) Mp 65–75 °C. ^{1}H NMR ($CHCl_3$) δ 4.41, 4.39, 4.34, 4.09, 3.69 (d, 1H, $J = 13$ Hz), 3.39 (d, 1H, $J = 13$ Hz), 2.43 (m, 1H), 2.27 (m, 1H), 2.20 (s, 6H), 2.15 (t, 1H), 2.00–1.90 (m, 3H), 1.48 (s, 3H), 1.32 (s, 3H), 1.31 (d, 1H, $J = 10$ Hz), 0.90 (s, 3H). MS FAB+ = 422.1 (MH^+).

Acknowledgement

Author J. C. N. thanks The Danish Technical Research Council for financial support (grant no. 9900690).

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