The clash of the synthons: crystal structures of benzimidazole–alcohol–carboxylic acids†

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The crystal structures of a series of compounds containing protonated benzimidazole functions are reported. Hydrogen bonds are always seen in the plane of the benzimidazole but, in opposition to our previous work, stacking interactions between the benzimidazole cations are not invariably observed. In zwitterionic benzimidazole carboxylic acid compounds, a *gauche* conformation is often adopted which allows a Coulombic attraction between carboxylate and benzimidazolonium functions.

Introduction

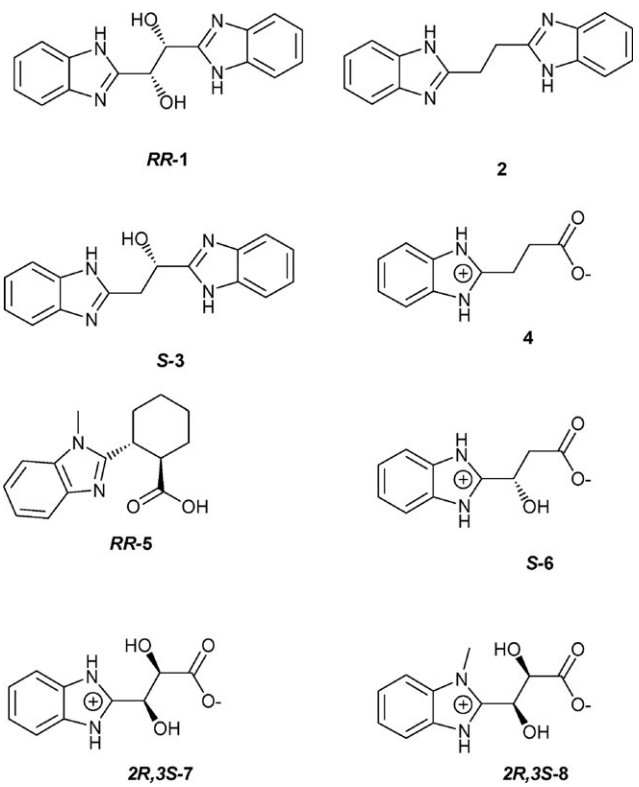
While the prediction of crystal structure in general remains a problem, much work has been carried out to understand the nature of interactions between molecules in organic crystals. The supramolecular synthon approach of Desiraju[1] identifies frequently observed intermolecular interactions which may be regarded as synthons which build up the three-dimensional structure of the crystal. For a molecule which carries several functions capable of participation in a synthon, the question arises as to whether all synthons can be formed, and if not, which will predominate. As a rule of thumb, we might expect that hydrogen-bonding synthons will dominate, but this will of course depend upon the strength of the hydrogen bonds involved.[2]

We have recently synthesised a series of benzimidazole carboxylic acids with or without alcohol functions appended to the ethylene bridge between the carboxylate and the benzimidazole. Our interest in these molecules was principally motivated by their use as ligands related to the bisbenzimidazole **1** which has been shown to act as a versatile ligand, acting as a tridentate facial ligand to a single metal,[3] but also capable of forming polynuclear species in which the alcohol function is deprotonated and acts as a bridging ligand.[4,5] However, we note that these molecules contain three functions capable of participating in synthons: the carboxylic acid, the alcohols, and the benzimidazoles which we have shown to participate readily in stacking interactions when protonated.[6,7] It therefore seemed of interest to study the crystal structures of the free ligands which can show stacking interactions between protonated benzimidazoles and hydrogen bonding between benzimidazolonium cations, carboxylates and alcohol functions. The molecules studied are shown in Scheme 1.

Results

Synthesis

The complexes were prepared by the Phillips reaction[8] involving refluxing the appropriate aryl diamine with carboxylic acid. Compound **1** has been reported previously by us,[3] and compound **3** by Taffs *et al.*[9] The procedure for the synthesis of



Scheme 1 Compounds studied in this work.

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† Electronic supplementary information (ESI) available: Drawings of all structures showing numbering and thermal ellipsoids. Details of hydrogen bonding. CCDC reference numbers 683798–683805. For ESI and crystallographic data in CIF or other electronic format see DOI:10.1039/b717018a

Table 1 Details of X-ray crystal structure determinations

	[*RR*-**1**H_2]Cl_2·2H_2O	[*RR*,*SS*-**1**H_2]Cl_2·EtOH·H_2O	[*S*-**3**H_2]Cl_2·2H_2O	**4**	*RR*,*SS*-**5**	*S*-**6**	2*R*,3*S*-**7**·2H_2O	2*R*,3*S*-**8**
Formula	$(C_{16}H_{16}N_4O_2)Cl_2(H_2O)_2$	$(C_{16}H_{16}N_4O_2)Cl_2(C_2H_6O)(H_2O)$	$(C_{16}H_{16}N_4O)Cl_2(H_2O)_2$	$C_{10}H_{10}N_2O_2$	$C_{15}H_{18}N_2O_2$	$C_{10}H_{10}N_2O_3$	$C_{10}H_{10}N_2O_4(H_2O)_2$	$C_{11}H_{12}N_2O_4$
M_r	403.3	431.4	387.3	190.2	258.4	206.2	258.3	236.3
Diffractometer	Stoe IPDS	Stoe IPDS	Stoe IPDS	Stoe IPDS	Stoe IPDS	Stoe IPDS	Stoe IPDS	Stoe IPDS
System	Monoclinic	Triclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Orthorhombic	Orthorhombic
Space group	*C*2	$P\bar{1}$	$P2_1$	$P2_1/c$	$P2_1$	$P2_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	13.1840(16)	8.0790(5)	8.5668(9)	16.1313(16)	11.4467(10)	4.6354(5)	6.8790(3)	10.5317(8)
b/Å	7.5135(7)	8.2010(6)	12.2524(11)	5.0524(4)	9.5194(6)	10.4827(15)	10.3028(7)	10.5831(9)
c/Å	9.5583(12)	16.3774(13)	9.3375(10)	11.8012(13)	13.1539(10)	10.2152(12)	15.9544(8)	9.4968(10)
α/°	90	84.534(9)	90	90	90	90	90	90
β/°	104.607(15)	84.929(9)	103.982(12)	109.906(11)	108.810(9)	101.112(13)	90	90
γ/°	90	71.783(8)	90	90	90	90	90	90
V/Å^3	916.2(2)	1024.1(1)	951.1(2)	904.4(2)	1356.8(2)	487.07(11)	1130.74(11)	1058.5(2)
T/K	180	150	220	200	200	220	200	200
Z	2	2	2	4	4	2	4	4
μ(Mo-Kα)/mm^{-1}	0.385	0.350	0.363	0.100	0.085	0.106	0.127	0.115
D_c/g cm^{-3}	1.462	1.399	1.352	1.397	1.265	1.406	1.517	1.482
Refl. measured	8657	12 392	11 939	8753	16 126	7468	17 918	14 185
R_{int}	0.065	0.033	0.061	0.058	0.059	0.047	0.053	0.061
Observed	1753	3326	2169	1054	2897	1575	2140	1414
No. variables	133	280	241	133	348	138	219	172
R(*F*)	0.039	0.036	0.043	0.032	0.032	0.031	0.032	0.031
wR(*F*)	0.038	0.036	0.042	0.032	0.031	0.031	0.032	0.030
S (all)	1.35(3)	1.45(2)	1.49(2)	1.21(1)	1.50(2)	1.66(4)	1.62(4)	1.38(3)
Flack param.	−0.02(10)		0.03(19)		0.5[a]	0[a]	0[a]	0[a]
Solution	SIR97	SIR97	SIR97	SIR97	SIR97	SIR97	SIR97	SIR97
Packing coeff.	0.700	0.690	0.661	0.705	0.677	0.681	0.732	0.723

[a] Fixed.

the mono-benzimidazole carboxylic acids followed that used by Matthews.[10] Compounds containing benzimidazole and carboxylic acids crystallised as neutral compounds. In the absence of a carboxylic acid function the compound was isolated as a hydrochloride salt (Table 1).

Crystal structure analysis

(*RR*)-1,2-Bis(1*H*-benzimidazol-2-onium)-1,2-ethanediol dichloride dihydrate, [*RR*-1H$_2$]Cl$_2$·2H$_2$O. This structure allows us to study the effect of perturbing the basic bis-benzimidazole compound **2** by the addition of two alcohol functions. The structures of salts of $[\mathbf{2}H_2]^{2+}$ have been discussed previously[6] and shows head-to tail stacking of benzimidazolonium cations to give sheets which are linked by hydrogen bonding to the counter ions. In [**1**H$_2$]Cl$_2$·2H$_2$O the benzimidazoles stack (Fig. 1) but only as pairs in distinction to the columns observed for $[\mathbf{2}H_2]^{2+}$. We assume that this arises from the steric effect of the alcohol functions. This motif forms a chain along the *z* axis.

The alcohol O–H bonds of the cations are directed approximately perpendicular to the planes of the benzimidazoles and hydrogen bond to chloride ions which form part of a {Cl$_2$(OH$_2$)$_2$} lozenge, each chloride ion being bridged by two water molecules acting as hydrogen bond donors. The {Cl$_2$(OH$_2$)$_2$} lozenges link cations which are separated by four stacking distances along the *x* axis, and link the chains into sheets (Fig. 2).

Finally, the water molecules of the lozenges act as hydrogen bond acceptors from the NH protons of benzimidazoles in the neighbouring sheets, thus linking the sheets into a three dimensional structure (Fig. 3). All hydrogen bond donors are thus satisfied. The structure of [**1**H$_2$](NO$_3$)$_2$ described as a racemate was reported recently[11] and is isostructural to the enantiopure compound [*RR*-**1**H$_2$]Cl$_2$·2H$_2$O, also crystallising in space group *C*2 even though the starting material was racemic, suggesting that spontaneous resolution has occurred. In this compound the nitrate anion also satisfies all H-bond donors.

(*RR*,*SS*)-1,2-Bis(1*H*-benzimidazol-2-onium)-1,2-ethanediol dichloride hydrate, [(*RR*,*SS*)-1H$_2$]Cl$_2$·H$_2$O·C$_2$H$_5$OH. The crystal structure of the racemate shows many similarities with the previous one. The cation again shows a *trans*-conformation, but no longer lies on a twofold axis, and the two benzimidazole planes are inclined at 46.57(6)° to each other. The cations again form stacked chains with interplane distances of 3.46 and 3.30 Å (Fig. 4), the two components of a stacked pair being related by a centre of inversion.

One of the chloride ions links the chains by hydrogen bonding to NH groups of one benzimidazole (Fig. 5) and the other links the alcohol functions. The water and ethanol of crystallisation act as H-bond acceptors for the second benzimidazole, and as H-bond donors to the chloride ions.

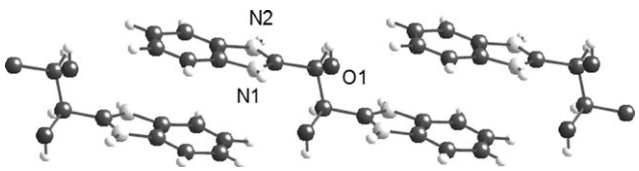

Fig. 1 Stacking between benzimidazole cations in [*RR*-**1**H$_2$]Cl$_2$·2H$_2$O. The crystallographic *z* axis runs horizontally.

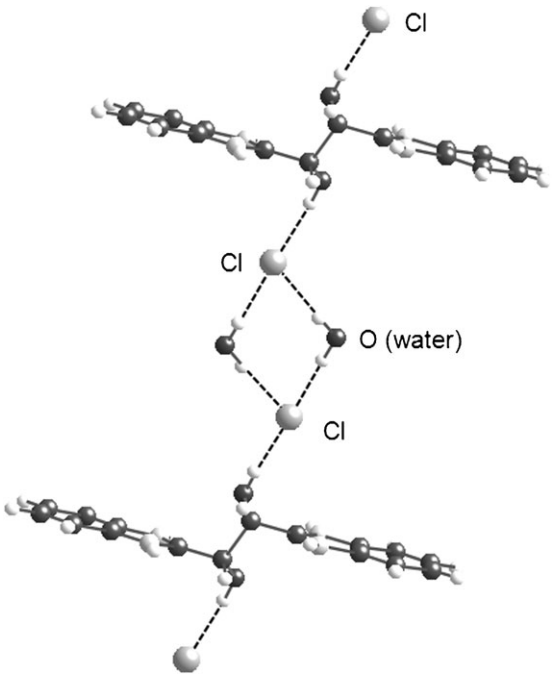

Fig. 2 Hydrogen bonding between alcohol functions and chloride ions in [*RR*-**1**H$_2$]Cl$_2$·2H$_2$O.

(1*S*)-1,2-Bis(1*H*-benzimidazol-2-onium)ethanol dichloride dihydrate, [*S*-3H$_2$]Cl$_2$·2H$_2$O. The structure of the hydrochloride salt of *S*-**3** is actually rather more complicated than that of *RR*-**1** since the twofold symmetry axis of *RR*-**1**H^{2+} is missing. The cation has essentially the same *trans* conformation as *RR*-**1**H^{2+} with the two benzimidazole planes in the molecule nearly parallel (interplane angle 1.3°). The cations form a zigzag motif along the *y* axis and are related by a twofold screw axis (Fig. 6). The zigzag motifs are aligned in the *xy*

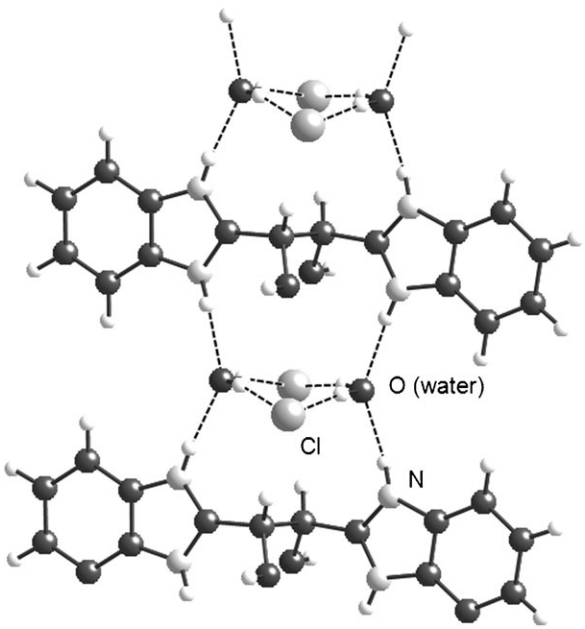

Fig. 3 Hydrogen bonding between benzimidazolonium cations and lattice water in [*RR*-**1**H$_2$]Cl$_2$·2H$_2$O.

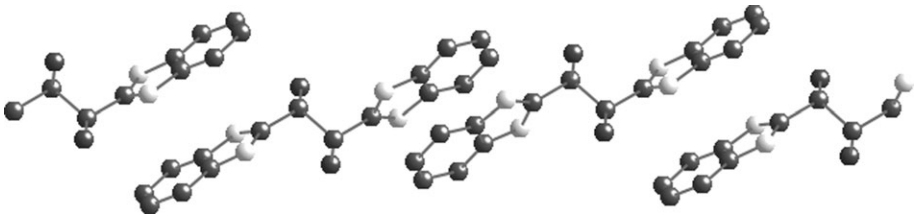

Fig. 4 Chains of [(*RR*,*SS*)-**1**H_2] cations. The stacking pairs are related by a centre of inversion.

plane to form a corrugated sheet, but there are no strong stacking interactions as observed for **2**H^{2+}. The benzimidazole units interleave, but the overlap is poor, and the molecular planes are inclined at about 20°. One of the phenyl hydrogens lies 3.3 Å above the centre of the phenyls below it in the chain which may suggest a C–H···π interaction. The chloride ions and the two water molecules lie in the furrows of the sheets. Each benzimidazole cation hydrogen bonds to one water molecule and one chloride. The alcohol function acts as a H-bond donor to one of the chlorides.

Crystal structure of 3-(1*H*-benzimidazol-2-yl)propanoic acid (4)

The molecule is found in zwitterionic form and adopts an unexpected *gauche* conformation which bends the carboxylate back towards the benzimidazolonium cation in a way reminiscent of a scorpion's tail. The distance between the benzimidazole C2 atom and the nearest carboxylate oxygen is only 2.886(2) Å (Fig. 7) and is presumably due to a coulombic attraction.

Each molecule forms hydrogen bonds to four other molecules with the N–H bonds acting as donors and the carboxylates as acceptors, forming sheets in the *yz* plane (Fig. 8). The sheets have the phenyl groups protruding on one side and the $–CH_2CH_2–$ groups protruding on the other. They are stacked along the *x*-axis in alternate orientation so that the aromatic side of one sheet is in contact with aromatic sheet of the next. No aromatic stacking interactions are observed and this may be a result of the interaction with the carboxylate. This structure is essentially identical to the room temperature structure published previously[12] which has erroneously an extra hydrogen on the carboxylic acid.

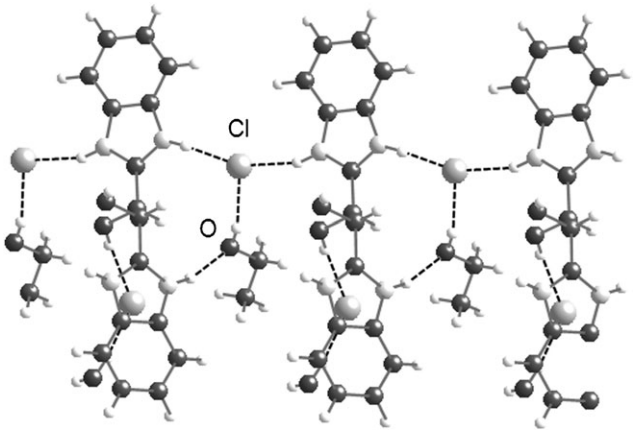

Fig. 5 Hydrogen bonding between chains in [(*RR*,*SS*)-**1**H_2]Cl_2.

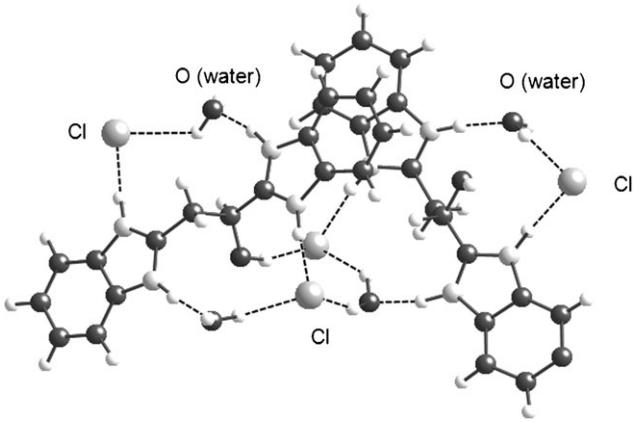

Fig. 6 Structure of [*S*-**3**H_2]Cl_2·$2H_2O$ looking down *x* axis with the twofold screw axis lying horizontally. Hydrogen atoms have been omitted for clarity.

Crystal structure of *trans*-2-(1-methylbenzimidazol-2-yl)-cyclohexanoic acid (*RR*,*SS*-5)

This compound is unusual in not adopting a zwitterionic structure. The different C–O distances confirm the localisation of the proton on the carboxylic acid rather than the benzimidazole. The benzimidazole moiety adopts a *syn*-conformation with respect to the cyclohexane ring which was identified as more favourable in our previous work.[7] The molecules are linked by hydrogen bonds between the carboxylic acid of one molecule and the benzimidazole of the following, forming a C(7) motif[13] propagated along the *y* axis (Fig. 9). There is no stacking, but one of the phenyl hydrogen atoms lies about 3 Å above the centre of the phenyl of the previous molecule of the chain, and this may be a weak C–H hydrogen bond. The chirality of the molecules alternates along the chain:

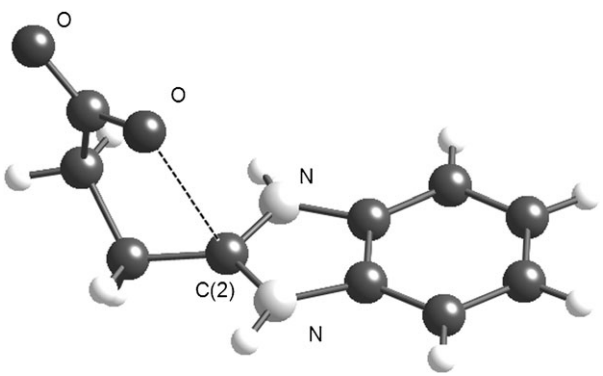

Fig. 7 The *gauche* conformation of **4** showing the carboxylate–benzimidazole interaction.

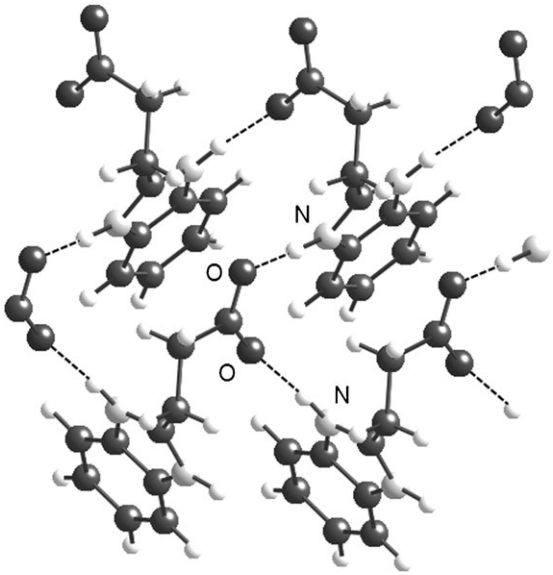

Fig. 8 Hydrogen bonded sheets in **4**.

–*RR*–*SS*–*RR*–, and, although the compound is racemic, it crystallises in a non-centrosymmetric space group ($P2_1$), the two enantiomers not being related by a symmetry element. The observation of $Z' > 1$ is not unusual when hydrogen bonding is important.[14] The non-zwitterionic nature of the compound might be a means of avoiding unfavourable steric interaction between a protonated benzimidazole and the axial hydrogens of the cyclohexane ring.

Crystal structure of (3*S*)-3(1*H*-benzimidazol-2-yl)-3-hydroxypropanoic acid (*S*-6)

The zwitterionic compound adopts a *gauche* conformation similar to than seen for **4** and again shows a short distance (2.778(5) Å) between a carboxylate oxygen and the benzimidazole C2. The molecules are arranged in columns along *x*

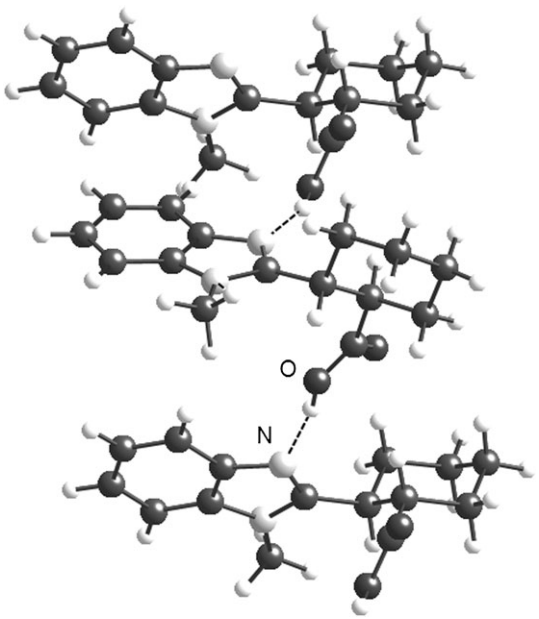

Fig. 9 The C(7) chain motif in **5**.

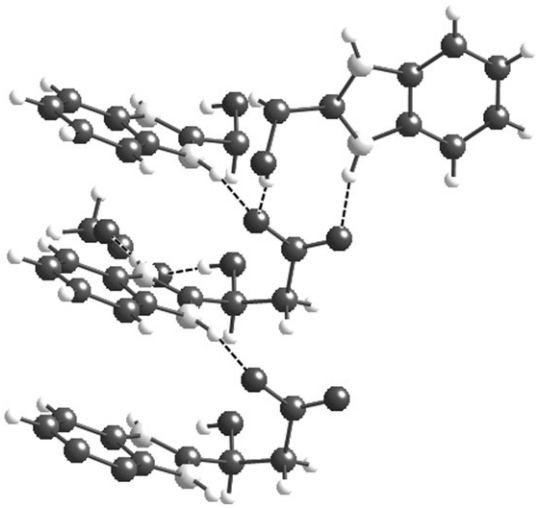

Fig. 10 The molecules of *S*-**6** are arranged in columns along *x* (vertical) and hydrogen bond to neighbouring columns related by a displacement along *y*.

with the benzimidazole planes at approximately 45° to the *x* axis. The NH groups hydrogen bond, one to a carboxylate in the next column along *y* and the other to a carboxylate of a neighbouring molecule in the same column. The carboxylate accepts two hydrogen bonds from a NH group and alcohol function in the next column, forming a $R_2^2(9)$ motif. One of the carboxylate atoms also accepts a hydrogen bond from a NH group below it in the column. The linking of molecules along *x* and *y* gives sheets with the phenyl groups projecting alternately above and below the sheets (Fig. 10).

Crystal structure of (2*R*,3*S*)-3-(1*H*-benzimidazol-2-yl)-2,3-dihydroxypropanoic acid dihydrate (*R*,*S*-7·2H$_2$O)

The compound adopts a zwitterionic structure with the benzimidazolonium and the carboxylate approximately *trans*. There is a stacking interaction between the benzimidazole cations along the *x* axis. There is a very complicated three-dimensional network of hydrogen bonds. The benzimidazolonium cations form one hydrogen bond to a neighboring carboxylate and one to a water molecule. The proximal alcohol does not hydrogen bond, and the distal one acts as a donor to a water

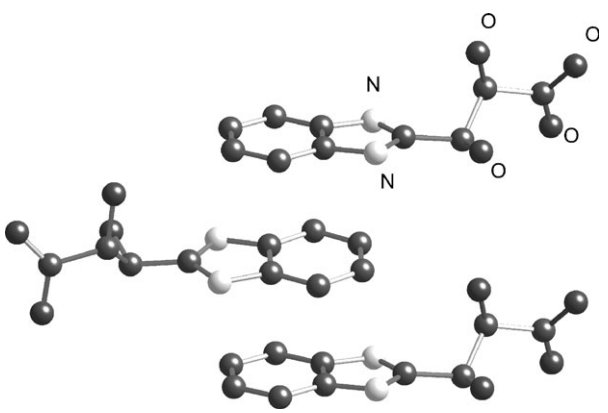

Fig. 11 Stacking between molecules of **7**. Hydrogens have been omitted for clarity.

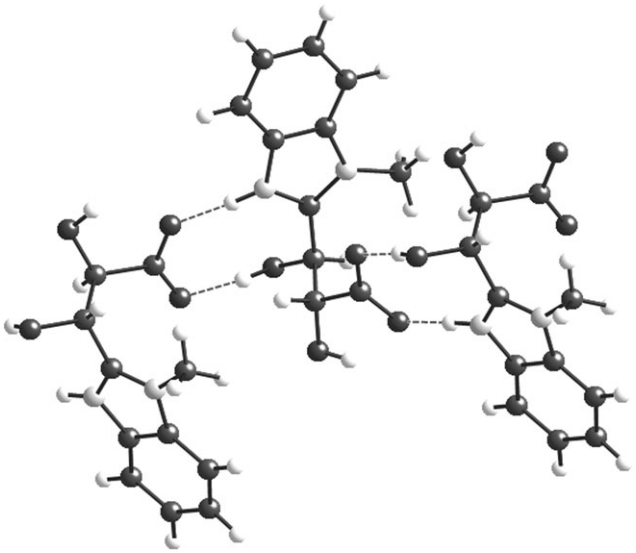

Fig. 12 Tapes of **8** showing the $R_2^2(9)$ hydrogen bonding motif.

molecule. One carboxylate oxygen bonds to a benzimidazolonium and two water molecules, and the other to two water molecules. The two water molecules acts as hydrogen bond donors to two carboxylates and acceptors from an alcohol and a NH bond, respectively (Fig. 11).

Crystal structure of (2*R*,3*S*)-3-(1-methylbenzimidazol-2-yl)-2,3-dihydroxypropanoic acid (*R*,*S*-8)

The compound is found in zwitterionic form with the carboxylate deprotonated, and the benzimidazole protonated. The *gauche* conformation in the solid state has the distal alcohol function *trans* to the benzimidazole and the carboxylate anion is again close to the benzimidazolonium cation (C···O distance 2.873(5) Å). This results in the NH^+ function and the proximal alcohol lying on one side and the carboxylate lying on the other. The molecules are linked into tapes by hydrogen bonds between the carboxylate on one molecule and the NH^+ and proximal alcohol functions on the next (Fig. 12) forming a $R_2^2(9)$ motif similar to **6**. The N–H···O bond, which is charge assisted, is significantly shorter than the O–H···O bond. The resulting tapes pack together to form the structure. No stacking interactions are observed and the distal alcohol function does not appear to be involved in hydrogen bonding.

Discussion

Four intermolecular interactions have been observed in the eight crystal structures reported here: (i) the stacking of benzimidazolonium cations; (ii) the protonated NH functions of the benzimidazolonium cations acting as H-bond donors to anions or solvent molecules; (iii) hydrogen bonding involving the alcohol functions when present; (iv) an interaction between anions and the benzimidazolonium cation shown by a short anion–benzimidazolonium C2 distance.

The protonated benzimidazoles act as hydrogen-bond donors in all cases. This is not surprising since unprotonated benzimidazole is already a good H donor[15] and protonated benzimidazole which has a pK_a around 5[16] will be stronger. In most cases studied here the resulting hydrogen bonds are charge assisted,[2] although in three cases donation to solvent molecules is observed, and in **5** the benzimidazole is not protonated and acts as an acceptor from the protonated carboxylic acid. The predictable behaviour of the N^+–H group as an H-bond donor has been established previously for pyridinium groups by Orpen and co-workers,[17–19] and Hosseini and co-workers have used the amidinium ion as a source of hydrogen bond donors to build up networks.[20–22] This type of hydrogen bond donation was observed in our previous work,[6,7] and the benzimidazolonium cation may be classed as a highly reliable H-bond donor. It is possible to control the dimensionality of the H-bonding by methylation at one of the nitrogens. We may note that the directionality of the hydrogen bonds is such that these interactions will lie in the plane of the cation, and thus leave free the region above or below the cation. It is in this region that stacking interactions will be found, and thus the hydrogen bonding by the benzimidazole cations and stacking do not interfere with each other.

In the compounds where carboxylate is present, it always acts as an H-bond acceptor from the NH functions. This agrees with its strong hydrogen bond acceptance power.[23] In the chloride salts the hydrogen bond acceptor power of chloride[23] would lead one to anticipate that it would bind preferentially to the N^+–H units, but in general there are not enough chloride ions per cation for a simple 1 : 1 association, and in $[RR\text{-}\mathbf{1}H_2]Cl_2{\cdot}2H_2O$ the N^+–H units all bind to lattice water, itself H-bonded to chloride.

In our previous work stacking interactions were always observed with the sole exception of 1,3,5-tris(1-methylbenzimidalol-2-onium)cyclohexane tribromide.[7] In the compounds studies here, stacking was only observed clearly in three of the compounds (*RR* and *RR*,*SS* **1** and 2*R*,3*S*-**7**), and there was some overlap between benzimidazoles in **3**. In **4**, **5**, **6** and **8** we observe a short distance between the benzimidazole C2 atom and a carboxylate oxygen, less than 2.9 Å for the zwitterionic species and less than 3.0 Å for the non-zwitterionic **5**. We attribute this interaction to coulombic attraction. The presence of the anionic atom above the benzimidazole plane precludes stacking, and the two interactions are thus mutually exclusive. With the carboxylates, this interaction is favoured by its intramolecular nature, but will have an energetic price associated with the *gauche* conformation. It is not clear why 2*R*,3*S*-**7**, which could equally show this interaction, prefers to adopt a structure with stacking, but this suggests that the energies of the two types of interaction are comparable, and we may note that this compound shows the highest packing coefficient. Re-examination of the structure of 1,3,5-tris(1-methylbenzimidalol-2-onium)cyclohexane tribromide mentioned above has shown an anion···C2 interaction between the bromide and each benzimidazolonium moiety, and this would be the explanation of the absence of stacking. This example shows incidentally that the coulombic attraction may be intermolecular as well as intramolecular.

The alcohol functions when present generally show hydrogen bonding, typically as donors, but there are two alcohol groups (in 2*R*,3*S*-**7** and 2*R*,3*S*-**8**, respectively) which do not take part in hydrogen bonding. The presence of alcohol functions will of course introduce additional hydrogen

bonding, and these additional hydrogen bonds may prevent the efficient stacking of the cations since they will not in general lie in the plane of the benzimidazoles.

The compounds discussed here comprise three salts, four zwitterions, and one neutral molecule. It may be asked whether it is reasonable to discuss the structures of these three classes of compound together. We believe that this is the case, and that it is justified by the similarity of the interactions noted in the eight compounds. In an ionic compound there will of course be an electrostatic attraction between ions of opposite charge, but this attraction is non-directed, and will lead essentially to a close-packed structure. However, close-packed structures are also common for molecular crystals, and indeed the packing coefficients of the ionic structures show no significant differences from those of the molecular structures. The coulombic attraction is not observed in the ionic structures where it might be expected to be dominant, but in three of the four zwitterionic structures.

The strongest interactions observed in these compounds would appear to be the hydrogen bonds involving the NH groups followed by those involving alcohol functions. The stacking interactions and the coulombic attraction would seem to be comparable and weaker than the other two. In spite of their relative weakness, stacking interactions can play an important role in the structure when they are exerted in a direction orthogonal to the strong hydrogen bonding as in the case of salts of the cation $[\mathbf{2}H_2]^{2+}$.[6] This has also been observed in other systems such as the anthracene-resorcinol constructs of Aoyama and co-workers where the stacking interactions are equally orthogonal to the hydrogen bonding.[24]

Experimental

General

Solvents and starting materials were purchased from Fluka AG (Buchs, Switzerland) and were used without further purification unless otherwise stated. UV-Vis spectra: Cary IE or Perkin-Elmer Lambda-5 UV/VIS/NIR spectrometers; quartz cells of 1 or 0.1 cm path lengths; $\lambda_{max}(\varepsilon)$ in nm. IR spectra: Perkin-Elmer Spectrum-One instrument; ν in cm^{-1}. 1D and 2D NMR spectra: Bruker Avance-400 machine at 400 (^1H) and 101 MHz (^{13}C) at 22 °C; chemical shifts δ in ppm with respect to $SiMe_4$, J in Hz. MS: Electrospray mass spectra (ES-MS) were recorded on the Finigan MAT SSQ 7000 instrument of the Mass Spectroscopy Laboratory University of Geneva; in m/z (rel. %). Elemental analyses were performed by Dr H. Eder, University of Geneva.

Synthesis of compounds

Bisbenzimidazoles: (2*R*,3*R*)-1,2-bis(1*H*-benzimidazol-2-onium)-1,2-ethanediol dichloride dihydrate ([*RR*-1H$_2$]Cl$_2$·2H$_2$O). 1,2-Phenylenediamine (10.00 g, 92.5 mmol) and 2*S*,3*S*-(−)-tartaric acid (6.94 g, 46.3 mmol) were dissolved in 200 mL 4 M hydrochloric acid. The solution was heated to reflux for 24 h. On cooling, green crystals of the chloride salt of the protonated ligand formed. The crystals were filtered off and dissolved in 200 mL water and treated with activated carbon under reflux for 2 h. After filtration, the solution was allowed to cool to room temperature to give a white precipitate. The precipitate was then filtered off, washed with acetone and dried under vacuum (3.41 g, 25%). A solution of the product (1 g) in ethanol (40 mL) and water (2.5 mL) was prepared. Slow diffusion of dimethoxyethane vapours into this solution led to the formation of colourless crystals suitable for X-ray structure, within three days.

^1H NMR (400 MHz, solvent DMSO, 293 K, ppm): 7.80 (m, 4H, Ar); 7.55 (m, 4H, Ar); 5.95 (s, 2H, CH). ^{13}C (101 MHz, solvent DMSO, 293 K, ppm): 153.01 (Ar C); 132.00 (Ar C); 126.10 (Ar C); 114.68 (Ar C); 68.97 (CH). IR (cm^{-1}): ν_{max} 3169–2727 (br s), 1619 (m), 1561 (m), 1518 (m), 1486 (m), 1454 (m), 1381 (m), 1300 (s), 1219 (s), 1077 (s), 844 (s), 794 (s), 750 (s), 615 (s), 435 (s). UV-Vis absorption (T = 22 °C/10^{-4} M/EtOH/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 279(19 400); 272(17 200). Mass spectrum: m/z 295.3 (M − H$^+$, 100). Melting point >250 °C.

(*rac*)-1,2-Bis(1*H*-benzimidazol-2-onium)-1,2-ethanediol dichloride monoethanol monohydrate ([*RR*,*SS*-1H$_2$]Cl$_2$·H$_2$O·C$_2$H$_5$OH). 1,2-Phenylenediamine (10.00 g, 92.5 mmol) and DL-tartaric acid (6.94 g, 46.3 mmol) were dissolved in 200 mL 4 M hydrochloric acid. The solution was heated to reflux for 24 h. On cooling, green crystals of the chloride salt of the protonated ligand formed. The crystals were filtered off and dissolved in 200 mL water and treated with activated carbon under reflux for 2 h. After filtration, the solution was allowed to cool to room temperature to give a white precipitate. The precipitate was then filtered off, washed with acetone and dried under vacuum (4.5 g, 33%). A solution of the product (1 g) in ethanol (40 mL) and water (2.5 mL) was prepared. Slow evaporation of this solution led to the formation of colourless crystals suitable for X-ray structure, within five days. ^1H NMR (400 MHz, solvent DMSO, 293 K, ppm): 7.80 (m, 4H, Ar *RR*); 7.55 (m, 4H, Ar *RR*); 5.95 (s, 2H, CH *RR*). ^{13}C (101 MHz, solvent DMSO, 293 K, ppm): 152.96 (Ar C); 131.85 (Ar C); 126.13 (Ar C); 114.66 (Ar C); 68.91 (CH). IR (cm^{-1}): ν_{max} 3162–2724 (br s), 1623 (m), 1572 (m), 1515 (m), 1485 (m), 1460 (m), 1370 (s), 1294 (s), 1248 (m), 1234 (m), 1205 (m), 1219 (s), 1100 (s), 1073 (s), 1019 (m), 816 (s), 788 (s), 741 (s), 620 (s), 535 (s), 498 (s), 434 (s). UV-Vis absorption (T = 22 °C/10^{-4} M/EtOH/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 279 (14 900); 272 (13 200). Mass spectrum: m/z 295.3 (M − H$^+$, 100). Melting point >250 °C.

(*S*)-1,2-Bis(1*H*-benzimidazol-2-onium)ethanol dichloride dihydrate ([*S*-3H$_2$]Cl$_2$·2H$_2$O). 1,2-phenylenediamine (10.81 g, 100 mmol) and *S*(−)-malic acid (6.70 g, 50 mmol) were dissolved in 75 mL 6 M hydrochloric acid. The solution was heated to reflux for 17 h. The chloride salt of the protonated ligand formed as a green powder on cooling. The solid was filtered off and dissolved in methanol–ethanol (1 : 1) and treated with activated carbon under reflux for 4 h. After filtration, the solution was allowed to cool to room temperature to give a white precipitate. The precipitate was then filtered, washed with diethyl ether and dried under vacuum (11.36 g, 65%). A saturated solution of the product in methanol (5 mL) with water (200 μL) was prepared. Slow diffusion of

dimethoxyethane vapours into this solution led to the formation of colourless crystals suitable for X-ray structure.

Elemental analysis. Found: C, 53.84; H, 4.75; N, 15.65%; $C_{16}H_{16}N_4OCl_2 \cdot 1/3H_2O$ requires C, 53.79; H, 4.70; N, 15.68%; ^{1}H NMR (400 MHz, solvent DMSO, 298 K, ppm): 7.81 (m, 4H, Ar); 7.55 (m, 4H, Ar); 5.91 (dd, J = 4.2 and 8.6 Hz, 1H, CH); 4.11 (dd, J = 4.2 and 15 Hz, 1H, CH_2); 3.84 (dd, J = 8.6 and 15 Hz, 1H, CH_2). ^{13}C (101 MHz, solvent DMSO, 298 K, ppm): 154.37; 149.73; 132.15; 131.50; 126.15; 126.02; 114.77; 114.39; 63.92; 33.60. IR (cm^{-1}): ν_{max} 3277 (br s), 2800–2550 (br s), 1626 (s), 1575 (s), 1520 (m), 1487 (m), 1457 (s), 1408 (m), 1304 (m), 1221 (s), 1185 (m), 1097 (s), 1019 (s), 945 (s), 897 (s), 810 (m), 750 (s), 623 (s). Mass spectrum: m/z 279 ($M - H^+$,100).

Benzimidazole carboxylic acids: (2*R*,3*S*)-3-(1*H*-benzimidazol-2-yl)-2,3-dihydroxypropanoic acid (2*R*,3*S*-7). (*R*,*S*)-3-(1*H*-Benzimidazol-2-yl)-2,3-dihydroxypropanoic acid was prepared by a modified literature method.[10] 1,2-Phenylenediamine (2.5 g, 23.3 mmol) and (2*R*,3*R*)-tartaric acid (3.5 g, 23.3 mmol) were dissolved in 50 ml of 4 M hydrochloric acid. The solution was heated to reflux for 16 h. On cooling, green pale crystals were formed. The crystals were filtered and dried (precipitate A) The remaining filtrate was cooled to −20 °C overnight and the resulting precipitate (B) was filtered and removed. Precipitate A was dissolved using the mother-liquor of the second crystallization. The solution was stirred at 5 °C and basified with 0.880 ammonia solution slowly until the pH of the solution was strongly alkaline, pH = 9, when a fawn-colored precipitate formed, which was filtered off and dried. This step removed the unwanted fully condensed bis(benzimidazole) by-product (confirmed with NMR analysis). The temperature of the filtrate was maintained at 5 °C and concentrated HCl was added slowly until pH 5. The solution was stirred rapidly at this stage and after 30 min a white precipitate formed (if no precipitate formed at this stage the volume was reduced until the first sign of precipitation). The solution was left at −20 °C overnight and filtered, then washed with cold water and finally diethyl ether to yield the pure yellow pale solid (1.3 g, yield = 25%). The ligand is soluble in H_2O, ethanol and methanol, insoluble in CH_3CN, acetone and hexane.

Recrystallisation: 100 mg of ligand is dissolved in a mixture of acetone–ethanol (50 : 50). The solution is filtered to remove eventual dust and led to slow evaporation within twenty days of white crystals formed. The crystals obtained were suitable for X-ray structure analysis. The crystals for analysis were dried under vacuum.

^{1}H NMR (400 MHz, solvent D_2O, 293 K, ppm): 7.68 (m, 2H, Ar); 7.42 (m, 2H, Ar); 5.47 (d, J = 2.4 Hz, 1H, CH); 4.47 (d, J = 2.4 Hz, 1H, CH). ^{13}C (101 MHz, solvent D_2O, 293 K, ppm): 176.5 (COOH); 154.7 (C=N); 134.5 (C–N); 124.5 (Ar C); 114.5 (Ar C); 74.4 (CH), 69.1 (CH). IR (cm^{-1}): ν_{max} 3154 (m), 3047 (m), 1697 (m), 1587 (w), 1484 (s), 1439 (m), 1401 (w), 1333 (m), 1309 (m), 1266 (m), 1118 (m), 1111 (m), 1064 (m), 1022 (s), 898 (w), 999 (s), 951 (m), 887 (s), 844 (s), 819 (m), 790 (s), 738 (w), 653 (m), 619 (m), 522 (m). UV-Vis absorption. (T = 22 °C/10^{-4} M/H_2O/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 276 (12 527); 270 (13 300); 244 (8700). Mass spectrum: m/z 223.4 (MH^+, 100%), 245.3 (MNa^+, 28%). Elemental analysis. Found: C, 52.35; H, 5.70; N, 10.98%; $C_{10}H_{10}N_2O_4 \cdot 0.5C_2H_6O \cdot 0.5H_2O$ requires C, 51.97; H, 5.55; N, 11.02% (this formula was confirmed by NMR study).

The other benzimidazole carboxylic acids were synthesised in a similar way except for compound **4** which was prepared following the method of Taffs.[9] The appropriate 1,2-aminobenzene was used (1,2-phenylenediamine for compounds **4**, **6** and **7** and *N*-methyl-1,2-phenylenediamine for compounds **5** and **8**) and the starting dicarboxylic acid was (*S*)-2-hydroxysuccinic acid (compounds **3** and **6**), succinic acid (compound **4**), (*R*,*S*)-cyclohexane-1,2-dicarboxylic acid (compound **5**) and (*R*,*R*)-tartaric acid (compound **8**).

3-(1*H*-Benzimidazol-2-yl)propanoic acid (4). (2.4 g, yield = 54%), ^{1}H NMR (400 MHz, solvent D_2O, 293 K, ppm): 12.2 (s, 1H, N–H); 7.45 (m, 2H, Ar); 7.10 (m, 2H, Ar); 3.04 (t, J = 8 Hz, 2H, CH_2); 2.78 (t, J = 8 Hz, 2H, CH_2). ^{13}C (101 MHz, solvent D_2O, 293 K, ppm): 174 (COOH); 154 (C=N); 121 (Ar C); 31.5 (CH_2), 24 (CH_2). IR (cm^{-1}): ν_{max} 2916 (m), 2445 (br), 1920 (br), 1622 (m), 1583 (s), 1504 (m), 1401 (s), 1305 (m), 1210 (m), 1181 (m), 1003 (w), 987 (w), 853 (m), 751 (s), 697 (m), 661 (m), 607 (s), 564 (s), 456 (m). UV-Vis absorption. (T = 22 °C/10^{-4} M/H_2O/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 281 (7500); 275 (7000); 245 (6000). Mass spectrum: m/z 191.4 (MH^+, 100), 213.5 (MNa^+, 10). Elemental analysis. Found: C, 63.03; H, 5.12; N, 14.67%; $C_{10}H_{10}N_2O_2$ requires C, 63.15; H, 5.3; N, 14.73%.

***trans*-2-(1-Methylbenzimidazol-2-yl)cyclohexanoic acid (5).** (2.05 g, Yield = 34%), ^{1}H NMR (400 MHz, solvent DMSO, 293 K, ppm): 11.97 (s, 1H, COOH); 7.5 (m, 2H, Ar); 7.15 (m, 2H, Ar); 3.78 (s, 3H, CH_3); 3.16 (td, J = 6 Hz, 1H, C^1H-bzim); 2.93 (td, J = 6 Hz, 1H, C^2H–COOH); 2.11 (d, 1H, C^3H); 1.94 (d, 1H, C^6H); 1.80 (m, 2H, C^4H + C^5H); 1.42 (m, 4H, C^3H + C^6H + C^4H + C^5H). ^{13}C (101 MHz, solvent DMSO, 293 K, ppm): 176.5 (COOH); 158.65 (C^7=N); 142.6 (Ar C^8); 135.9 (Ar C^{13}); 121.8 (Ar C^{11}); 121.5 (Ar C^{10}); 118.8 (C^9), 110.2 (Ar C^{12}); 47.2 (C^2); 36.9 (C^1); 31.7 (C^6), 30.1 (C^3); 29.8 ($C^{14}H_3$); 25.6 (C^5); 25.5 (C^4). IR (cm^{-1}): ν_{max} 3057 (w), 2932 (s) (O–H str.), 2853 (m), 2449–2326 (br m), 1890 (m), 1694 (s) (C=O str.), 1570 (w), 1476 (s), 1449 (s), 1417 (s), 1235 (s) (C–O str.), 1005 (s), 948 (s), 890 (m), 846 (m), 742 (s), 667 (s), 605 (m), 580 (m), 538 (m), 513 (m), 479 (m), 454 (m), 391 (m). Mass spectrum: m/z 259.3 (MH^+, 100), 241.1 ($MH^+ - H_2O$, 86). UV-Vis absorption (T = 22 °C/10^{-4} M/EtOH/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 254 (6500), 276 (7300), 283 (7600). Elemental analysis. Found: C, 69.72; H, 7.06; N, 10,85%. $C_{15}H_8N_2O_2$ requires C, 69.74; H, 7.02; N, 10.84.

(*S*)-3-(1*H*-Benzimidazol-2-yl)-3-hydroxypropanoic acid (6). (2.1 g, yield = 44%), ^{1}H NMR (400 MHz, solvent D_2O, 293 K, ppm): 7.7 (m, 2H, Ar); 7.52 (m, 2H, Ar); 5.52 (d, J = 2.4 Hz, 1H, CH); 2.95 (d, J = 2.4 Hz, 2H, CH_2). ^{13}C (101 MHz, solvent D_2O, 293 K, ppm): 175 (COOH); 156 (C=N); 133 (C–N); 130 (C–N); 126 (Ar C); 132 (Ar C); 126 (Ar C); 114 (Ar C); 64 (CH), 43 (CH_2). IR (cm^{-1}): ν_{max} 3395 (s), 3024 (s), 1637 (m), 1597 (m), 1527 (m), 1491 (m), 1464 (w), 1402 (m), 1312 (w), 1142 (s), 1070 (w), 1002 (w), 926 (m), 894 (m), 793 (s), 673 (w), 593 (s), 559 (m), 541 (w). UV-Vis absorption (T = 22 °C/10^{-4} M/H_2O/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 278 (10 625); 271 (8800); 245

(7200). Mass spectrum: m/z 207.4 (MH^+, 100), 229.5 (MNa^+, 24). Elemental analysis. Found: C, 57.89; H, 5.02; N, 13.45%. $C_{10}H_{10}N_2O_3$ requires C, 58.25; H, 4.89; N, 13.58%.

(2*R*,3*S*)-3-(1-Methylbenzimidazol-2-yl)-2,3-dihydroxypropanoic acid (8). (3.3 g, yield = 67%), ^{1}H NMR (400 MHz, solvent D_2O, 293 K, ppm): 7.73 (m, 2H, Ar); 7.56 (m, 2H, Ar); 5.64 (d, J = 2.4 Hz, 1H, CH); 4.40 (d, J = 2.4 Hz, 1H, CH); 4.02 (s, 3H, CH_3). ^{13}C (101 MHz, solvent D_2O, 293 K, ppm): 175.7 (COOH); 152.5 (C=N); 133.1 (C–N); 130.8 (C–N); 126.1 (Ar C); 125.8 (Ar C); 114.3 (Ar C); 112.1 (Ar C); 73.3 (CH), 67.4 (CH); 31.3 (CH_3). IR (cm^{-1}): ν_{max} 3403 (s), 3046 (s), 1639 (m), 1597 (m), 1531 (m), 1486 (m), 1467 (w), 1402 (w), 1342 (w), 1249 (m), 1145 (m), 1081 (w), 1007 (w), 927 (m), 898 (m), 873 (w), 793 (s), 751 (w), 677 (w), 593 (s), 559 (m), 541 (w). UV-Vis absorption (T = 22 °C/10^{-4} M/H_2O/l = 1 cm) λ_{max}/nm (ε_{max}/dm^3 mol^{-1} cm^{-1}): 278 (12 453); 269 (12 800); 245 (9200). Mass spectrum: m/z 237.4 (MH^+, 100%), 259.5 (MNa^+, 50%). Elemental analysis. Found: C, 55.66; H, 5.16; N, 11.89%. $C_{11}H_{12}N_2O_4$ requires C, 55.93; H, 5.12; N, 11.86%.

X-Ray crystallography

The structures were measured at low temperature using a Stoe IPDS image plate detector and Mo-Kα radiation. Structures were solved using direct methods (SIR97[25]) and refined using the XTAL3.2 set of programs.[26] Additional calculations used ORTEP.[27] No particular difficulties were encountered with these structures. For cases where no atom heavier than oxygen was present, the absolute structure parameter was fixed, and the configuration was assumed to be that of the chiral starting material. Hydrogens bound to nitrogen or oxygen were observed and refined; others were calculated.

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For crystallographic data in CIF or other electronic format see DOI: 10.1039/b717018a

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