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Quadrupolar [1$_4$](*meta–ortho*)$_2$Azolophanes. Intramolecular C–H···N and to Water C–H···O Hydrogen Bonding Revealed by X-Ray Diffraction[1]

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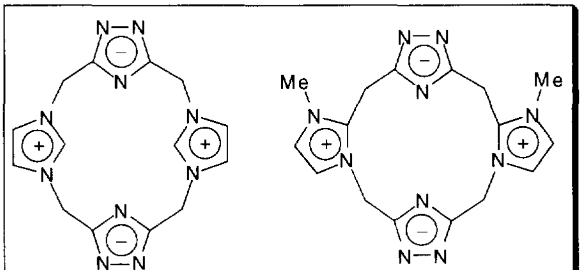
Abstract: The first X-ray crystallographic diffraction of an example of the title heterophanes built up from heterocyclic betaine subunits is reported and its quadrupolar character is confirmed. The crystal packing of **2·4H$_2$O** is mainly governed by hydrogen-bonding networks, *strong* intermolecular interactions with water together with *weak* interactions, either intramolecular or with water. Copyright © 1996 Elsevier Science Ltd

Diffraction studies of supramolecular systems —natural and synthetic— have revealed details of structure and bonding, and the different types of Donor-H···Acceptor interaction play a significant role in the organization of the solid-state, e.g. in self–assembly and in molecular recognition[2,3] as well as in crystal engineering.[4] Heterophanes have very different structures but none is related to the quadrupolar [1$_4$]azolophanes **1** and **2**, whose structures are, indeed, without precedent in the literature.[1a] Single–crystal diffraction analysis is a valuable tool for structural elucidation of imidazolium(pyridinium) azolate inner salts with different spacers,[5,6] and also for the recently reported [1$_4$]*meta*azolophane **1**.[7]

Here we describe results of X–ray analyses of the quadrupolar [1$_4$]azolophane **2·4H$_2$O**, which shed light on details of the structure, bonding and importance of the crystal packing controlled by hydrogen–bonding networks.



1 **2**

In contrast with the corresponding dipolar building blocks,[8] the tendency for hydration has been overcome, which permitted ^{1}H NMR spectra to be recorded in D_2O, and a clear shielding effect for the CH and CH_2 protons of the quadrupolar systems **1** and **2** was detected (Figure1).[1,9]

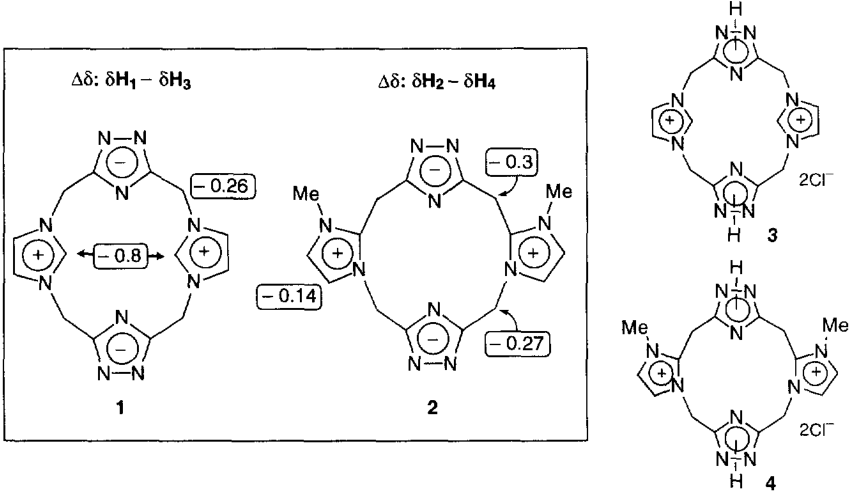
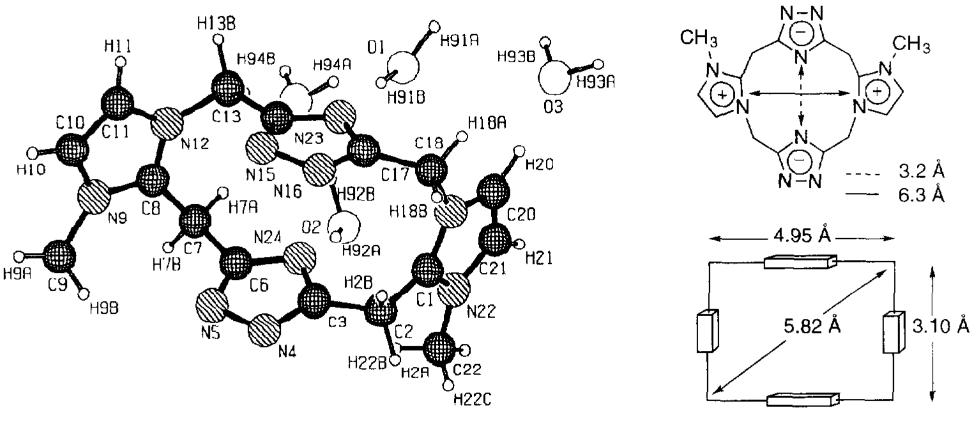


Figure 1. ^{1}H NMR chemical shift –ppm, D_2O– difference between *bis*-betaines **1** and **2** and the corresponding precursors **3** and **4**

The *bis*-betaine molecular structure of **2·4H$_2$O** is shown in Figure 2, along with an atom labeling scheme[10a] and macrocyclic dimensions. The asymmetric unit contains one macrocycle complexed with four H_2O molecules by H–bond interactions,[10b] and the molecular dimensions according to the weighted least-squares reference plane defined by C2-C7-C13-C18 methylene carbon atoms are: *ca.* 3.10 × 4.95 Å.



(a) (b)

Figure 2. (a) Crystallographically determined structure of the quadrupolar [14](*meta-ortho*)$_2$azolophane **2·4H$_2$O**; perspective molecular diagram including hydrogen atoms and the four water molecules showing the atom numbering scheme used in the X-ray diffraction analysis.[10a] (b) Molecular macrocyclic dimensions of **2·4H$_2$O**

The molecular shape may be described by the spatial arrangement within the four heteroaromatic planes and also by their inclination with respect to the reference plane, as well as the significant non-bonding distances related to the macrocyclic dimensions listed in Table 1. The spatial orientation within the four heteroaromatic rings –which constitute the walls of the macrocyclic system– adopted a geometry s which can be described by the dihedral angles formed by the weighted least-squares planes **A** and **C** is 23.8° and 14.7° for **B** and **D** –a flattened disposition–. Conversely, those angles formed by the imidazolium (**A** or **C**) and the *s*-triazolate (**B** or **D**) rings range between 88° to 92° –markedly upright– in a nearly perpendicular conformation. Noteworthy are the differing relative spatial orientation in both cation residues **A**, **C** and also in the *s*-triazolate nuclei **B** and **D** to the reference plane (**E**). Inspection of the orientation of the C10, C21, N23, and N24 atoms with respect to the reference plane (**E**) shows that the C10 and C21 imidazolium carbon atoms are oriented on opposite sides of the reference plane, 2.77 Å and 3.26 Å respectively, and the N23 and N24 *s*-triazolate nitrogen atoms are located on the upper side of the rim 0.38 Å and 0.41 Å respectively. Bond distances and angles are close to those described previously for the [1$_4$]*meta*azolophane **1**[7] and also within crown ether structures for the π-excessive rings.[11]

Table 1. Significative non-bonding distances (Å) and dihedral angles (°) for *bis*-betaine **2·H$_2$O**[a]

	macrocyclic dimensions (Å)		dihedral angles (°)
C1···C8[b]	6.162	A-B[c]	88.0
C2···C7[b]	4.950	A-C[c]	23.8
C2···C13[b]	5.689	A-D[c]	88.0
C2···C18[b]	3.118	A-E[c]	96.9
N4···N16[b]	3.727	B-C[c]	97.4
N5···N15[b]	3.717	B-D[c]	14.7
C7···C13[b]	3.080	B-E[c]	59.5
C7···C18[b]	5.950	C-D[c]	91.8
N12···N19[b]	6.299	C-E[c]	120.5
C13···H18[b]	4.952	D-E[c]	74.0
N23···N24[b]	3.201		
C10···E[d,e]	2.771		
C21···E[d,e]	-3.265		
N23···E[d,f]	-0.382		
N24···E[d,f]	-0.409		

[a]Atom numbering scheme:[10a] (a) IUPAC; (b) used for X-ray data. [b]Macrocyclic molecular dimensions (see Figure 3). [c]Dihedral angles formed by least-squares planes: Plane A: C1-N19-C20-C21-N22; Plane B: C3-N4-N5-C6-N24; Plane C: C8-N9-C10-C11-N12; Plane D: C14-N15-N16-C17-N23; Plane E: C2-C7-C13-C18. [d]Distance (Å) between the indicated atom and the reference plane (E). [e]Orientation of C-10 and C-21 atoms: On opposite sides of the reference plane E. [f]Orientation of N-23 and N-24 atoms: On the same side of the reference plane E.

X-ray diffraction provides evidence for the H-bonding network,[10b,12] which has a crucial role in the crystal structure of **2·4H$_2$O**, and the conformation adopted of the quadrupolar system within the hydrated monocrystal is shown in Figure 3.

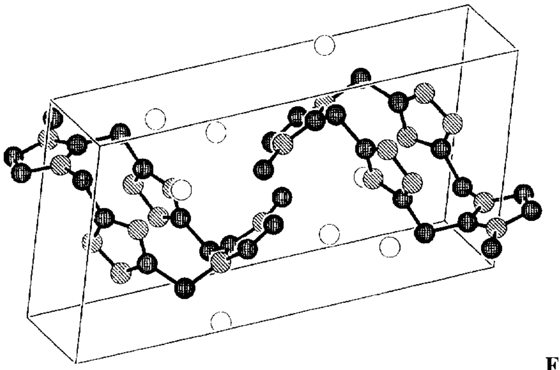


Figure 3. Unit cell packing diagram for **2·4H$_2$O**

Consequently, our crystallographic study revealed an embroidered pattern made by hydrogen bonds.[10b] The strongest hydrogen-bonding interactions were intermolecular *via* O-H···O and O-H···N –the acceptor centre is water and the π-excessive residues respectively– with an average distance of 1.78 Å (H···A), 2.80 Å (O···A), and the O–H···A angle was found to be *ca.* 170° (see Table 2).

Table 2. Significative H-bonding interactions for *bis*-betaine **2·4H$_2$O**, distances (Å) and angles (°)

O1-H91A···N4	2.477 Å; 150.8°	O1···N4	3.477 Å
O1-H91A···N5	1.736 Å; 176.1°	O1···N5	2.832 Å
O1-H91B···N23	1.811 Å; 174.6°	O1···N23	2.810 Å
O2-H92A···N24	1.873 Å; 164.9°	O2···N24	2.864 Å
O3-H93B···N4	1.751 Å; 175.3°	O3···N4	2.825 Å
O4-H94B···N16	1.783 Å; 175.1°	O4···N16	2.742 Å
O2-H92B···O^f	1.805 Å; 168.0°	O2···O4	2.793 Å
O3-H93A···O2	1.800 Å; 170.2°	O3···O2	2.867 Å
O4-H94A···O1	1.820 Å; 162.8°	O4···O1	2.741 Å
C2-H2B···N16	2.933 Å; 112.5°	C2···N16	3.450 Å
C9-H9A···N16	2.721 Å; 161.7°	C9···N16	3.645 Å
C9-H9A···N15	2.543 Å; 133.8°	C9···N15	3.281 Å
C9-H9B···N5	2.758 Å; 130.1°	C9···N5	3.456 Å
C10-H10···N4	2.713 Å; 131.8°	C10···N4	3.431 Å
C11-H11···N23	2.708 Å; 152.7°	C11···N23	3.633 Å
C13-H13B···N15	2.704 Å; 150.3°	C13···N15	3.631 Å
C22-H22A···N5	2.646 Å; 135.8°	C18···O3	3.253 Å
C18-H18A···O3	2.307 Å; 163.2°	C20···O3	3.281 Å
C20-H20···O3	2.478 Å; 135.5°	C21···O1	3.426 Å
C21-H21···O1	2.599 Å; 143.1°	C21···O2	3.338 Å
C21-H21···O2	2.748 Å; 119.8°	C22···O1	3.492 Å
C22-H22A···O1	2.598 Å; 154.9°		

The evidence of weak intramolecular C-H···N and to water C-H···O hydrogen-bonding in **$2a{\cdot}4H_2O$** is noteworthy (Figure 4). The average H-bond geometry is: 2.5 Å (H···Acceptor), 3.4 Å (Donor···Acceptor) and $\theta \geq 112.5°$ (Table 2). On examination the weak intramolecular contacts,[10b] the closest centroid···H–C distances of *ca.* 2.7 Å are between the highly π-excessive ring **B** or **D** and the *N*-methyl group of a cationic residue or a methylene interannular linker respectively (Table 3).

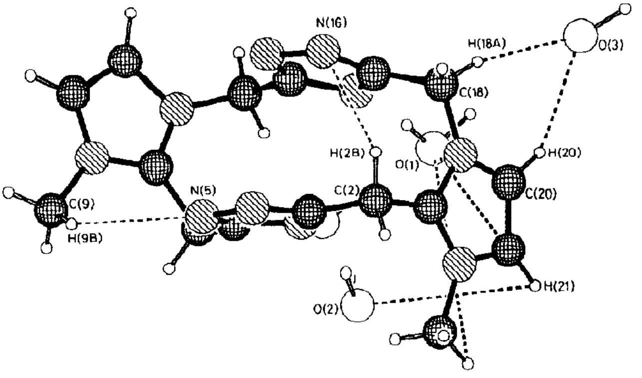


Figure 4. Weak C–H···N and C–H···O hydrogen bonding interactions in compound **$2{\cdot}4H_2O$**: C–H···N ≤ 2.933 Å; C···N ≤ 3.631 Å; $\theta \geq 112.5°$; C-H···O ≤ 2.748 Å; C···O ≤ 3.492 Å; $\theta \geq 119.8°$.

Table 3. Selected centroid···H–C and centroid···H–O interactions, distances (Å) and angles (°)[a,b]

Donor–H	Donor···Acceptor	H···Acceptor	Donor–H···Acceptor
O1-H91A	O1···Fb (1)	H91A···Fb (1)	O1-H91A···Fb (1)
1.098 (0.007)	3.771 (0.016)	2.706 (0.017)	163.30 (0.70)
C22-H22A	C22···Fb (1)	H22A···Fb (1)	C22-H22A···Fb (1)
0.960 (0.005)	3.267 (0.012)	2.759 (0.012)	113.81 (0.42)
C13-13B	C13···Fd (2)	H13B···Fd (2)	C13-H13B···Fd (2)
1.026 (0.033)	3.622 (0.015)	2.628 (0.035)	163.09 (2.63)

[a] Fa, Fb, Fc, and Fd labels– Centroid and Heterocycle in parenthesis–: Fa (Imidazolium **A**), Fb (Triazolate **B**), Fc (Imidazolium **C**) and Fd (Triazolate **D**).

[b] Equivalent positions: (1) -x+1,-y,-z+1; (2) -x+1,-y+1,-z.

The single–crystal X-ray structure of *bis*-betaine **2** validated its quadrupolar nature and provided the best demonstration of its structure. Moreover, the diffraction analysis gave further insight into the intramolecular C–H···N and to water C–H···O hydrogen bonding network.

Experimental Section

Single–Crystal X-ray Determination of *bis*-Betaine $2{\cdot}4H_2O$. Crystallographic data were collected on an Enraf-Nonius CAD4 single crystal diffractometer with MoKα radiation and a graphite crystal monochromator. Unit cell dimensions were determined from the least-squares fit of 25 reflections within the θ ranges shown in Table 4.

Table 4. Crystal, Data Collection and Refinement Parameters for *bis*-Betaine **2·4H$_2$O**[a]

formula	$C_{16}H_{18}N_{10}{\cdot}4H_2O$
crystal color	colorless
crystal size/mm	0.33 x 0.33 x 0.26
symmetry	triclinic, $P\bar{1}$
unit-cell determination	least-squares fit from 25 reflections ($10° < \theta < 15°$)
unit cell dimension	
a/Å	8.354(11)
b/Å	9.26(4)
c/Å	14.35(4)
α/deg	81.0(3)
β/deg	73.2(2)
γ/deg	68.1(3)
packing: V/Å, Z	985(5), 2
d_o/g cm^{-3}, M, F(000)	1.425, 422.47, 448
μ/cm^{-1}, T/K	0.107, 200
λ/Å	0.71073
technique	diffractometer: Enraf-Nonius CAD-4 single crystal graphite crystal monochromator: MoKα, ω-2θ scans
scan time	1 min per reflection
number of reflections	
measured	4685
independent	3433
observed	2516[2σ(I)criterion]
R_{int}	0.0432
standard reflections	3 reflections every 60 min
range h, k, l	-9, -10, 0 to 9, 10, 17
drift correction	1.00-1.18
absorption corr; XABS2	0.8674-1.000
solution and refinements	direct methods; full matrix least-squares on F_o^2
parameters: no. of var	324
final shift/error	0.001
weighting scheme	$[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w=1/[\sigma^2(F_o^2) + (0.0779*P)^2 + 0.52*P]$ where $P=(\mathrm{Max}(F_o^2,0) + 2*F_c^2)/3$ with $\sigma^2(F_o^2)$ from counting statistics.
max. thermal value/Å^2	U[O(3)]= 0.0718
final ΔF peaks/e Å^{-3}	0.314, 0.328
final R and R_w [$I>2\sigma(I)$]	0.0468, 0.1193
R and R_w (all data)	0.0793, 0.1383

[a] Solvent of recrystallization: 96 % ethanol.[10b]

The reflections were measured using the ω-2θ scan technique with a variable scan rate and a maximum scan time of 60 s per reflection. The intensity was checked through out data collection by monitoring 3 standard reflections every 60 min. Final drift corrections are shown in Table 4. A profile analysis was performed on all reflections.[13a,b] Lorentz and polarization correction were applied and the data were reduced to F_o^2 values. The structure was solved by direct methods using the program SHELXS90.[13c] Isotropic full-matrix least-squares refinement on F^2 using SHELXL93[13d] converged to R=0.15. An empirical absorption correction was applied using XABS2.[13e] Maximum and minimum correction factors are shown in Table 4. Hydrogen atoms were located at the last stages of the refinement by Fourier Synthesis, ignoring reflections above $2\theta = 25°$.CH_3 groups and solvent water molecules were considered as ideal and their hydrogen atoms were geometrically placed. Hydrogen atoms of methyl groups were refined riding on their parent atoms. Further refinements included anisotropic thermal parameters for all non-hydrogen atoms. All hydrogen atoms were isotropically refined with a common thermal parameter, excluding those of the solvent which were refined with different thermal parameters for each molecule. The minimized function was $[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w=1/[\sigma^2(F_o^2)+(0.0779*P)^2+0.52*P]$ where $P=(\mathrm{Max}(F_o^2,0)+2*F_c^2)/3$ with $\sigma^2(F_o^2)$ from counting statistics. The maximum shift to e.s.d. ratio and the final ΔF peaks are shown in Table 4. Atomic scattering factors were taken from ref 13f. The plots were made using the EUCLID package.[13g] Geometrical calculations were made with PARST.[13h] All crystallographic calculations were carried out at the University of OVIEDO on the Scientific Computer Center and X-ray Group VAX-Computers.

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10. a)The atom numbering scheme for X-ray data is not the same as the IUPAC numbering system used for NMR data.[1] b) The crystals of $\mathbf{2{\cdot}4H_2O}$ were grown from 96% ethanol. Unfortunately, it is not yet possible to obtain suitable single–crystals in anhydrous conditions. In fact, the crystal packing of the macrocycle it is dominated by H–bonding involving water molecules. It would be relevant however to grow single–crystals in *anhydrous conditions* to see if a packing geometry dominated by π–π stacking interactions between positively and negatively charge rings would result instead.
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