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ORIGINAL PAPER

Crystal Engineering: A Unique Cyclic Assembly of a 40 Membered Module Composed from Two Alternating Units Each of Benzenehexacarboxylic Acid (Mellitic Acid, MA) and 2,5-Bis-(4-pyridyl)-1,3,4-oxadiazole (4-BPO): Assembly of Modules to Macromolecules by Intermolecular Hydrogen Bonding

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Abstract Individually prepared, equivalent amounts of 2,5-bis-(4-pyridyl)-1,3,4-oxadiazole (4-BPO) and benzenehexacarboxylic acid (mellitic acid, MA) when mixed, deposited long rods, whose X-ray structure showed a unique assembly of 40 membered planar modules composed from two alternating units each of MA and 4-BPO, rather than the anticipated helical profile. Several novel features of complexes of MA with organic molecules are seen here. In almost all cases the intermolecular hydrogen bonding between MA anions is so stable that the MA anions and the complementary cations lie in separate planes. This barrier is overcome in the present case. The basic module associates to form quartets by very simple hydrogen bonding of the carboxylic groups of MA. The quartet assembly is characterized by the rotation of the left hand pair compared to the right hand pair. The mode of the macromolecular assembly is clear, that is, they are layered in alternating planes. Space group: $P2_1/c$ with $a = 9.181(1)$ Å, $b = 9.624(1)$ Å, $c = 29.390(2)$ Å, and $\beta = 94.626(4)°$. The modules are embedded in an extensively hydrogen bonded MA network. The assembly profile of MA and 4-BPO is unique and should be a harbinger for the design of novel functional assemblies. The 40-membered module mimics the self-assemblies of peptides and can be important in the design of "Haptens" from simple molecules.

Keywords Macrocyclic module (40) · Non-covalent self-assembly · Modules to supramolecules

Introduction

Benzenehexacarboxylic acid (mellitic acid, MA) where the six carboxylic groups are arranged around a benzene core, suggests itself as a unit for examining diverse types of molecular topology by the choice of the organic bases in salt formation. In spite of the fact that several complexes of MA with organic counterparts have been studied by X-ray crystallography, factors that control the topology still remain elusive. Extensive investigations by us have shown that the options available are limited, arising out of preference by MA anions for the formation of hydrogen bonding networks, either as sheets or ribbons, resulting in the placement of the anions and cations in separate domains. Thus, it has become a challenge to design complexes of MA with organic bases where they intermingle, overcoming the advantages of isolation. This is accomplished in the present work.

A general profile of complexes of MA with organic bases would be helpful for predicting the nature of new complexes. In the case of MA^{-2} anions, they form extended sheets, in an approximate hexagonal arrangement, that may or may not incorporate water molecules. The cations generally are organized orthogonal to the anion sheets. MA^{-4} anions assemble as uninterrupted ribbons, mediated by pairs of direct MA–MA hydrogen bonds that form 14 membered ring structures. The continuing interest in MA–organic salts arises from the promise they have shown in the formation of structures with varied properties, the unknown potential they hold, and the hope that designs of MA salts with a measure of predictability become possible by choice of the organic bases.

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The versatility of MA, in forming crystalline salts with organic bases, is illustrated with a few examples:

The crystal arising from MA and 2,2′-bipyridyl (BP) has the unusual composition MA$_8$BP$_{16}$(H$_2$O)$_{28}$ Sheets of MA^{-2} are interspersed by infinite stacks of orthogonally disposed mono protonated BP. The deprivation of water molecules, at $\sim$140 °C, that play a major role in the structure (Fig. 1a), clearly shows channels (Fig. 1b) that can be filled by water or ammonia, thus demonstrating the potential of such salts in the design of macroporous materials [1].

In the dense and hard ionic crystal MA^{-5} 2.5 EDA^{2+} (where EDA is ethylene diamine) the MA^{-5} ions form a continuous ribbon by strong OH···O=C hydrogen bonds, rather than sheets, as in Fig. 1. Each MA^{-5} in the ribbon is surrounded by EDA^{2+} ions and water molecules as shown in Fig. 2. The enormous flexibility of M^{-n} ions in crafting tightly packed salts with counter ions is exhibited where a complicated energy balancing system is naturally in place [2].

An unusual anion–cation interlocking system resulted from MA–phenanthroline complexation (MA–PL) (Fig. 3a). The structural representation highlights perfect stacking of PL$^+$ at 3.5 Å intervals. The complex is marginally semiconducting.

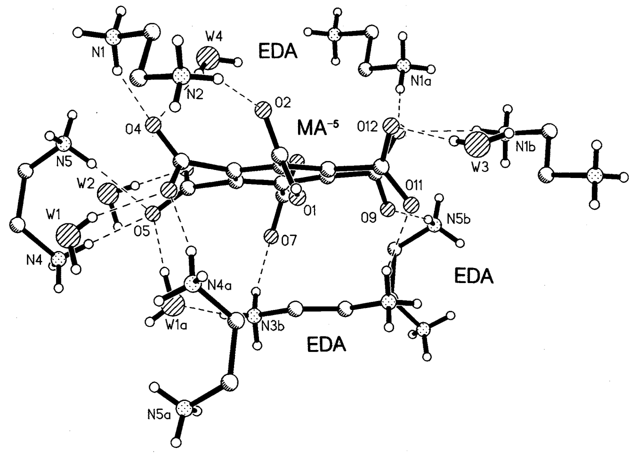


Fig. 2 Tightly packed ionic crystal MA^{-5}. 2.5 EDA^{2+}. Hydrogen bonds are represented by dashed lines [2]. The view is looking down the ribbon in the center with only one MA^{-5} ion shown

Another unique feature of the MA–PL complex are the continuous sheets that form the hydrogen bonded MA^{-2} counter ion. Interestingly these sheets have a profile shown in Fig. 3b where a central MA^{-2} ion connects to four surrounding MA^{-2}

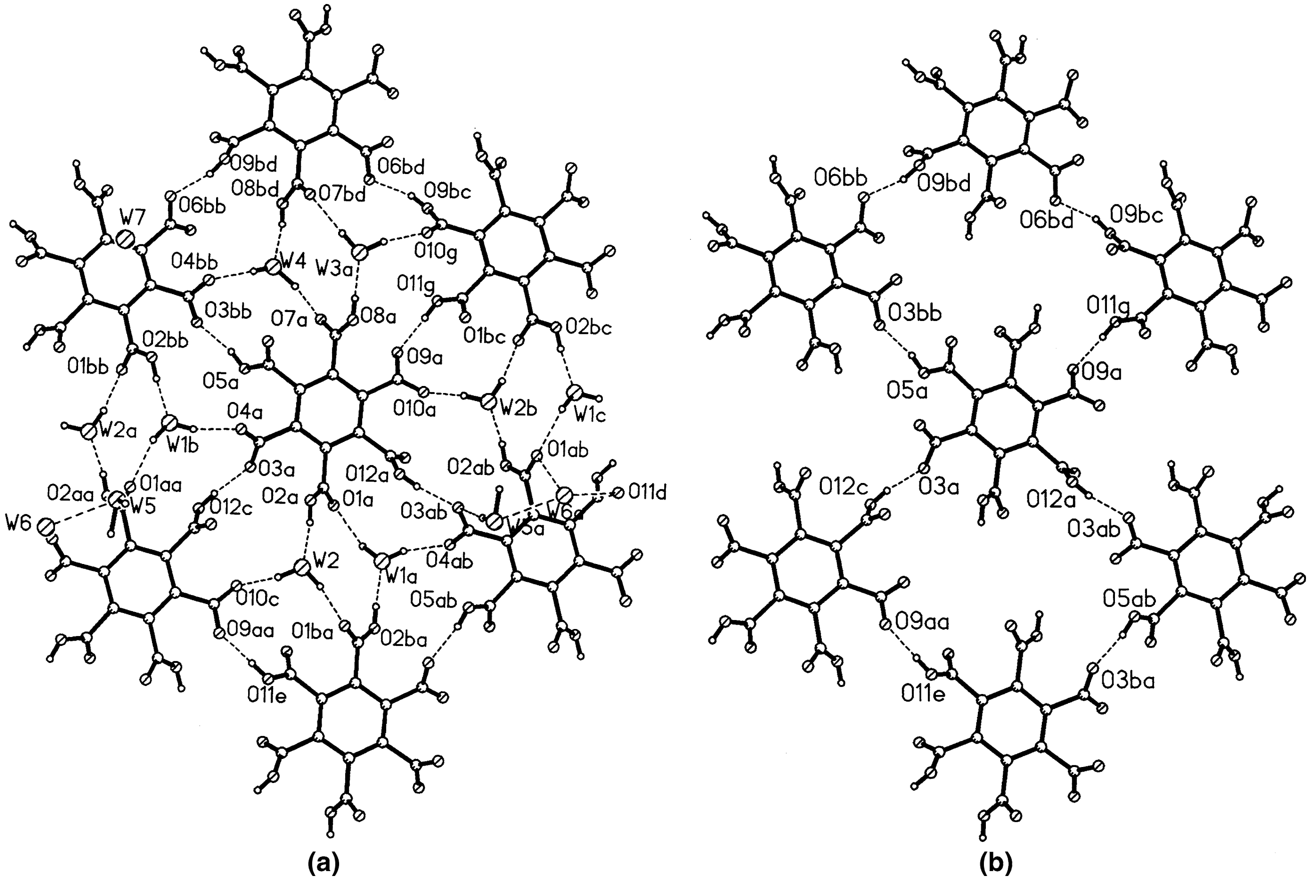
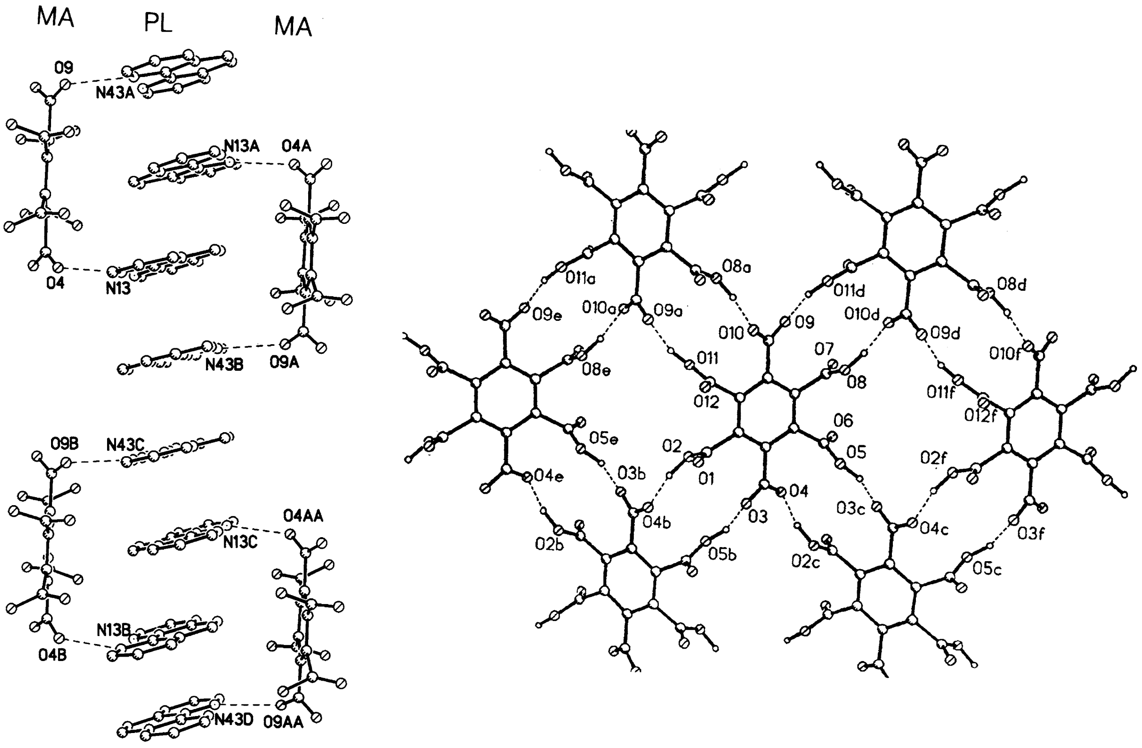


Fig. 1 (**a**) The mellitic acid ion (MA^{-2}) layer with water molecules in the MA–BP crystal. (**b**) Open channels arising from the loss of water at 140 °C in the MA–BP crystal [1]

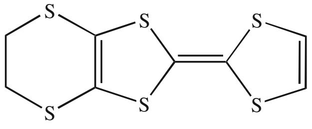


(a) (b)

Fig. 3 (**a**) An infinite interlocked assembly of MA–PL complex [1]. (**b**) Sheet structure of MA^{-2} in the MA–PL complex at right angles to (**a**). There are no water molecules in the crystal. Each MA^{-2} ion participates with 8 hydrogen bonds to form the sheet

ions by four pairs of hydrogen bonds without any intervening H_2O molecules.

The general profile of salts of MA with organic bases, as composed of ribbons or layers of MA anions with the positive counter ion held separately, and in favorable cases as stacks that could elicit π–π interaction, could be used in several designs. In an imaginative approach, endeavors were made to encapsulate stacks of tetrathiafulvalene (TTF) radical cation with MA counter ions. Initial efforts produced crystals of MA^{-2}(TTF$^{+\cdot}$)$_2$ which, having the profile in which stacks of TTF$^{+\cdot}$ were encapsulated in a MA anion helix, pairing interactions failed to produce the desired magnetic material. Interestingly the salt profile changed when TTF was replaced by EDTTTF [3].



EDTTTF

In this complex, two-dimensional sheets of MA^{-2} sandwich stacks of cation layers of the EDTTTF that results in an effective π–π interaction to produce a conducting crystal. A side view is presented in Fig. 4.

The above brief account gives an idea of the potential of MA–organic salt complexes. The work reported in the present paper highlights yet another novel and unique property of these systems. This work resulted from a search for compounds that may provide helical structures with MA and led to the identification of 2,5-bis-(4-pyridyl)-1,3,4-oxadiazole (4-BPO). The genesis for this expectation arose from the report that oxadiazoles flanked by pyridines at the the 4-location (4-BPO) complexes with mesitoic acid to form turn structures that further assemble to triple helices [4]. These turn structures simply arise as shown in Fig. 5 by tandem arrangement of mesitoic acid and 4-BPO. The triple helix formation involves modules as shown below harboring acids that form salts with the base of the neighboring strings.

Experimental

Materials and Methods

Melting points were recorded on a Fischer–John's apparatus and are uncorrected. Infrared spectra were recorded

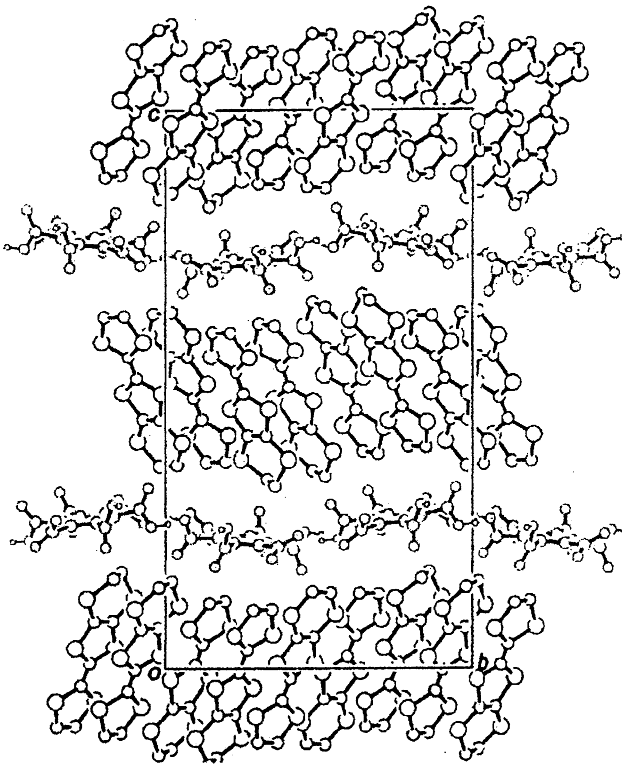


Fig. 4 Side view of the MA anionic sheets and the EDTTTF cation layers in the MA EDTTTF salt [3]

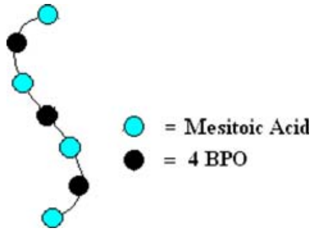
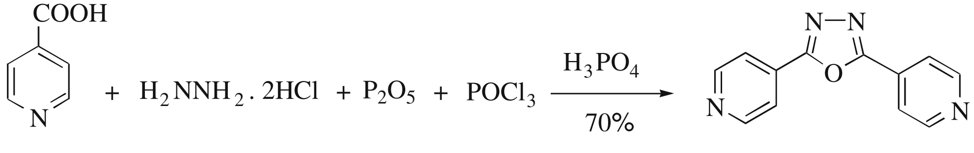


Fig. 5 Tandem arrangement of mesitoic acid and 4-BPO

on a Thermo Nicolet Nexus 760 spectrophotometer as KBr pellets and prominent peaks expressed in cm^{-1}.

2,5-Bis-(4-pyridyl)-1,3,4-oxadiazole (4-BPO) was prepared by reacting isonicotinic acid with hydrazine dihydrochloride in the presence of P_2O_5, $POCl_3$, and H_3PO_4 [5]:



m.p. 189 °C

Table 1 Crystallographic data and structure refinement for the MA^{-2}–4-BPO^{2+} complex

Identification	CCDC# 682881
Empirical formula	$(C_{12}H_4O_{12})^{-2} \cdot (C_{12}H_{10}N_4O)^{+2} \cdot 2.5H_2O$
Molecular weight	606.39
Chemical, m.p., °C	>300
Temperature, K	293°
Wavelength, Å	1.5418
Space group	$P2_1/c$
a, Å	9.181(1)
b, Å	9.624(1)
c, Å	29.390(2)
β, °	94.63
Volume, $Å^3$	2588.4(4)
Z	4
Density (calc.) (mg/mm^3)	1.556
Absorption coefficient, *μ* (mm^{-1})	1.17
F(000)	1,240
Color	Pale yellow
Shape	Rods
Crystal size, mm	0.28 × 0.20 × 0.18
Limiting indices	$0 \leq h \leq 10$
	$-1 \leq k \leq 11$
	$-30 \leq l \leq 33$
Reflections collected	3808
Reflections observed $>4\sigma(F)$	2682
Goodness to fit	1.01
Final *R* indices [I > 2(I)]	0.063
Extinc. Coeff.	0.0021
Larg. Diff. peak and hole, $e/Å^3$	0.40/−0.36
Param./Restr./Data	413/0/2682

Mellitic Acid (MA)–2,5-Bis-(4-pyridyl)-1,3,4-Oxadiazole (4-BPO) Complex, MA–BPO

A solution of MA (0.034 g, 0.1 mmoL) in MeOH (1 mL) was admixed with a solution of 4-BPO (0.022 g, 0.1 mmoL) in MeOH (2 mL). The resulting solution immediately deposited small cubic crystals. This solid was crystallized from hot water to give small rod like crystals within one day; M.p: > 300 °C.

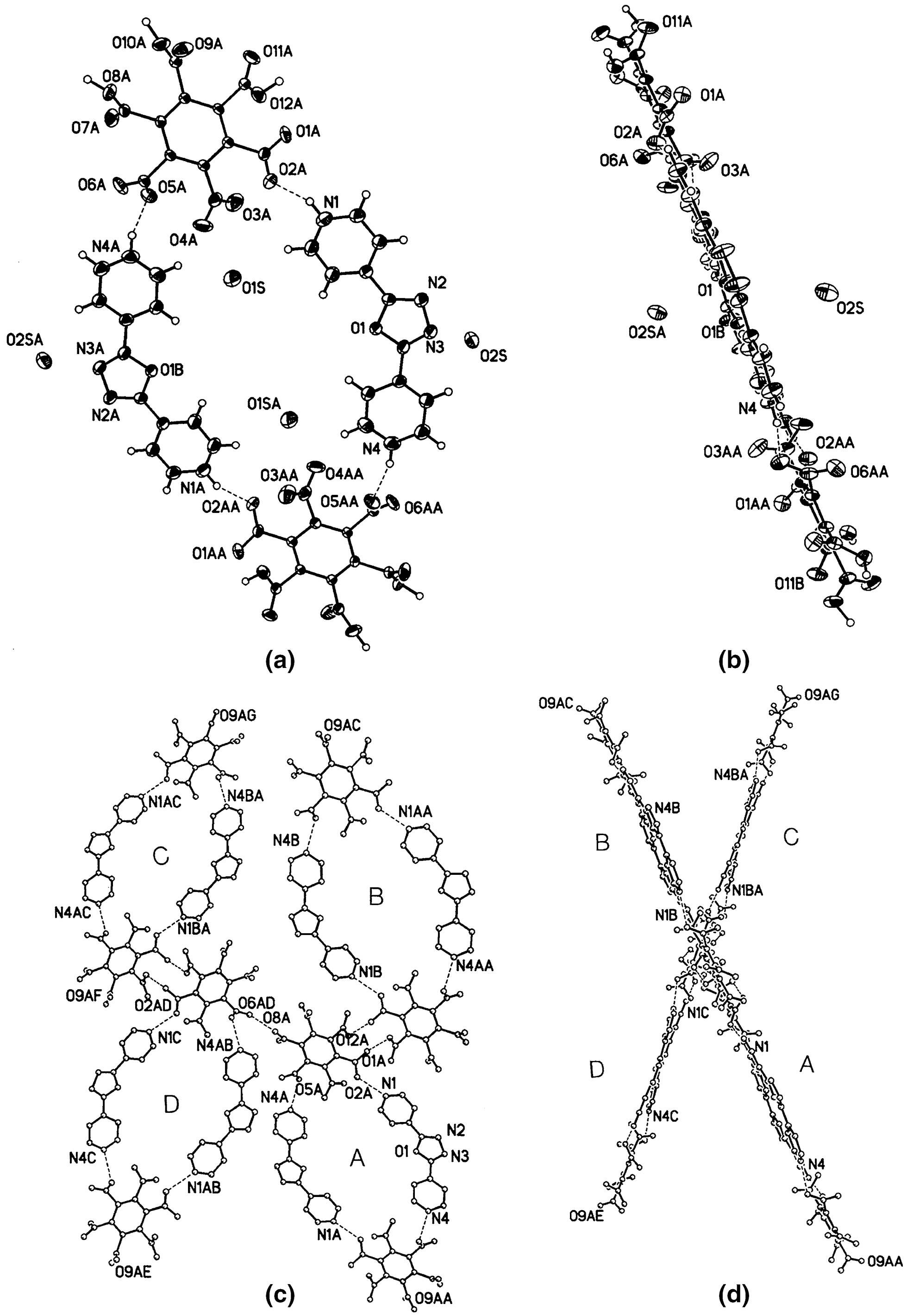


Fig. 6 (**a**) The primary module of MA^{-2}–BPO^{2+} complex, a novel and unusual 40-membered macrocycle generated from pairs of MA and 4-BPO. The thermal ellipsoids are shown at the 50% probability. (**b**) An edge-on view of the macrocycle shows that all rings are nearly coplanar and that many of the CO and OH bonds in the MA molecules are directed out of the plane. (**c**) A quartet assembly of four basic units by simple hydrogen bonding. (**d**) An edge-on view of the quartet shown in (**c**)

The aqueous filtrate on standing for three days deposited an additional batch of long rod like crystals. The IR spectrum of the crystals clearly indicated that the desired salt was formed. One of these crystals was used for X-ray diffraction analysis.

M.p: > 300 °C; Yield: 0.018 g; IR (KBr): 3422 (s, br), 1710 (m), 1636 (s), 1443 (m), 1248 (m), 624 (m) cm^{-1}. The two crops of crystals were identical, except for size.

X-ray Structure Analysis

Single crystal X-ray data were collected at room temperature on a P4 Bruker automated four-circle diffractometer in the $\theta/2\theta$ mode, with a constant speed of 10 deg/min, 1.5° scan width, and $2\theta_{\max} \approx 115°$ (resolution 0.9 Å), using Cu-Kα radiation ($\lambda = 1.54178$ Å), and a graphite monochromator. Parameters and details are listed in Table 1.

Table 2 Hydrogen bonds

Donor	Acceptor	D–A (Å)	H–A (Å)	D–H–A (°)
N1	O2A	2.595	1.75	155
N4	O5A[a]	2.642	1.78	160
O4A	O1S	2.667		
O8A	O6A[b]	2.531	1.47	176
O10A	O2S[c]	2.633	1.57	160
O12A	O1A[d]	2.550	1.53	174
O1S	O3A[e]	2.904		
O1S	O11A[f]	2.912		
O2S	O7A[e]	2.840		
O3S′	O1A[f]	2.75		

Symmetry equivalents: [a] −x, 2 − y, −z; [b] −x, −½ + y, −½ − z; [c] x, ½ − y, −½ + z; [d] 1 − x, −y, −z; [e] −x, 1 − y, −z; [f] x, 1 + y, z

The solution of the crystal structure showed the formation of a 40-membered macrocycle arising from four $NH^{+}\cdots{}^{-}O–C$ hydrogen bonds that link pairs of alternating units of MA^{-2} and BPO^{2+}, Fig. 6a, into discrete modules. Water molecules O1S within the macrocycle and O2S outside the macrocycle participate in well-determined hydrogen bonds, Table 2. Full matrix least-squares yield U_{eq} thermal values of 0.026–0.050 for the atoms in the organic entity and values of 0.06 and 0.05 for O1S and O2S. However, there is “empty volume” between the modules for which difference maps indicate a probable third water molecule O3S that is distributed among several sites. One partially occupied site containing O3S′, that is consistent with a hydrogen bond to atom O1A in the module, appears to be stable. Other sites, such as O3S″ have not been stable in the least-squares refinement.

The programs used are those in the SHELXTL package [6]. Tables of coordinates, bond lengths and angles, anisotropic thermal parameters, and hydrogen coordinates are deposited with the Cambridge Crystallographic Data Centre, CCDC# 682881. Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ: (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Results and Discussion

As already mentioned, the energetics of the usual organic salts derived from MA lead to separate cation and anion assemblies. One of our long standing objectives has been to discover a system that may overcome this natural tendency so that an integrated cation–anion module is formed. Consequently the results obtained from the X-ray crystal structure of MA–4-BPO are gratifying in that the primary module (Fig. 6a) has the acid (MA^{-2}) and base (BPO^{2+}) ions neatly integrated. The module shows a unique profile of a 40-membered ring held by four strong $NH^{+}\cdots O^{-}–C$ hydrogen bonds where the N···O distances are only 2.59 and 2.64 Å, Table 2. An edge-on view of the basic module shows coplanarity of the 40-membered macrocycle (Fig. 6b), except for the rotated carboxyl groups in MA.

An analysis of this crystal structure has enabled a better understanding of the novel and unique properties of the primary module. The basic module assembles to a quartet (Fig. 6c) by the pair of OH···O=C bonds connecting carbonyl groups of MA around a center of symmetry. The distances involving atoms O1A and O12A are 2.55 Å. This pair of hydrogen bonds connects modules A and B and a similar pair of hydrogen bonds connects modules C and D. To complete the quartet of modules, the A, B pair is joined to the C, D pair of modules by only one hydrogen bond, between O8A and O6AB in Fig. 6c, with an O···O distance of 2.53 Å. The

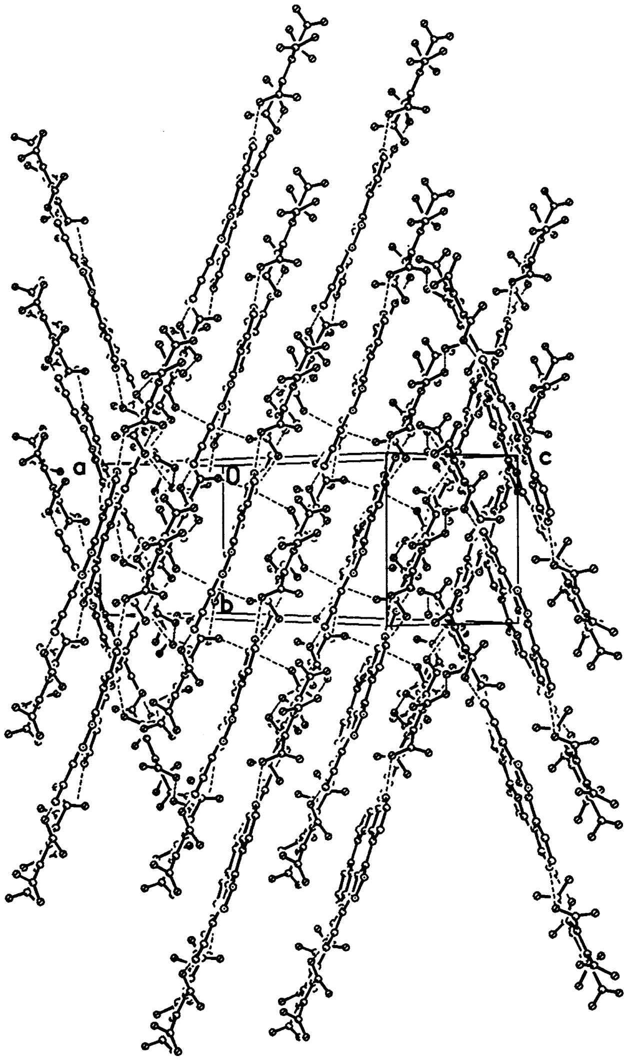


Fig. 7 An extended packing diagram of the modules that shows the layer-like arrangements. The unit cell is inscribed with light lines

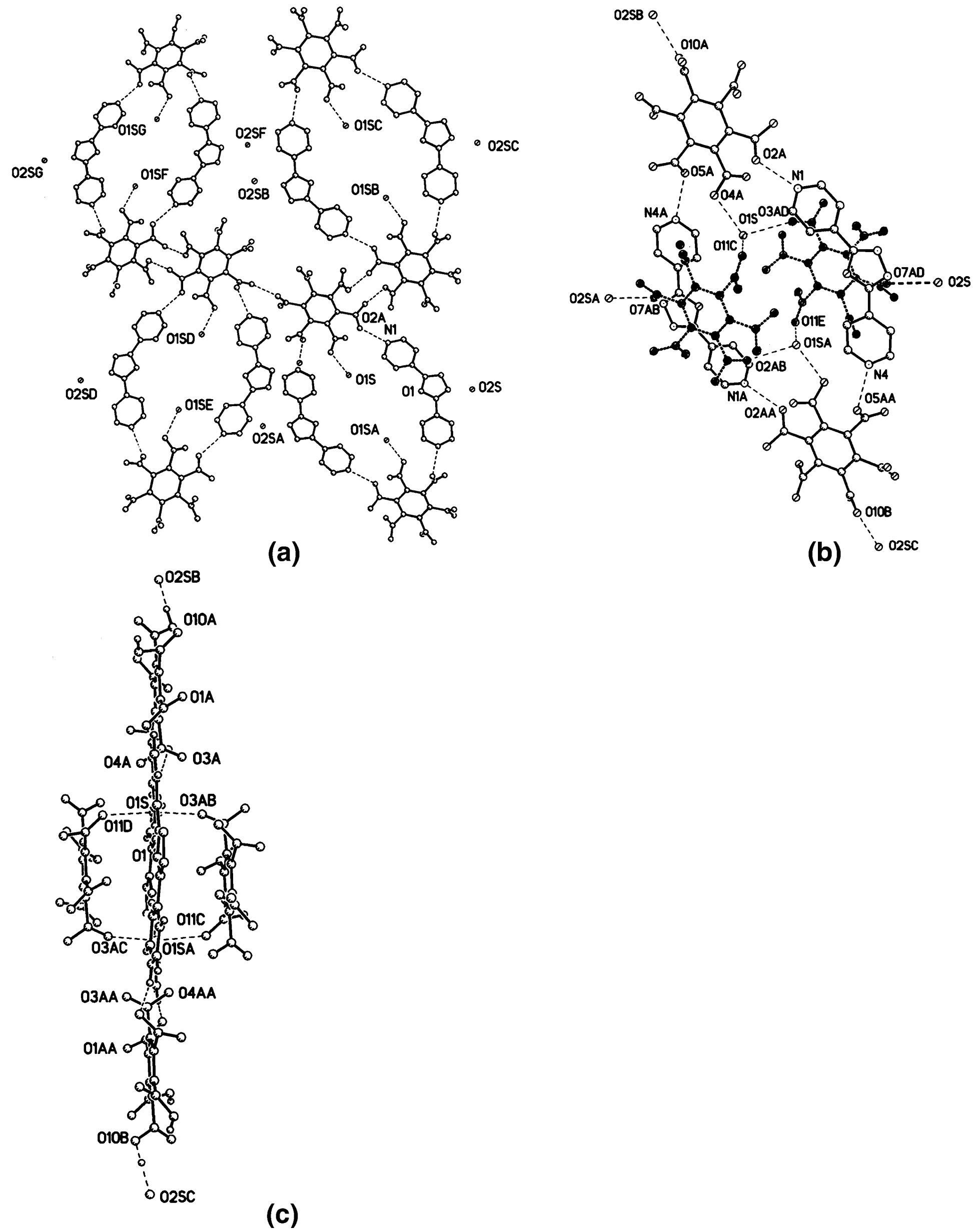


Fig. 8 (**a**) Water molecules both inside and outside the macrocycles. (**b**) One complete module shown layered between MA moieties (darkened atoms) on either side of BPO moieties. Two water molecules within the cavity participate in three hydrogen bonds each. (**c**) Edge-on view of (**b**). The two BPO moieties are superimposed in the center of the diagram

listing of hydrogen bonds in Table 2 shows that the NH···O=C bonds in the macrocycle and the OH···O=C bonds between modules in the quartet are very strong, 2.53 to 2.64 Å, while the hydrogen bonds involving the H_2O molecules (O1S, O2S, and O3S′) are considerably weaker with O···O values of 2.67–2.91 Å. Furthermore, the many O9A carbonyl oxygens on the periphery of the quartet do not participate in any hydrogen bonding, thus contributing to the separation of quartets from each other. There is no center of symmetry within a quartet. A simple explanation for the radical change in the structural profile could be that an initially formed intermediate where MA is linked to two units of 4-BPO at the 1, 3 locations is ideally oriented to form the 40-membered cycle with another unit of MA. Basic to this may also be the fact that the initially formed macromolecule prefers to form multiplexes by hydrogen bonding rather than having separate identities (vide infra).

Of interest is the characterization of the quartet assembly shown in Fig. 6c when viewed edge-on, as in Fig. 6d. The mean plane of the A, B pair of modules is rotated by ~40° from the C, D pair of modules. The mode of the macromolecular assembly is layering, as shown in Fig. 7.

The basic modular scaffolds described above are assembled to tertiary structures by making use of the free carboxylic groups of MA and water molecules present inside and outside the macrocycle as shown in Fig. 8a. The unique pair of carboxylic groups that project into the module are hydrogen bonded to the water molecules O1S and O1SA inside the ring as shown in Fig. 8b. The process makes use of all sites available for hydrogen bond formation except for carbonyl O9. The intricate nature of this operation is illustrated in Fig. 8b and c. In Fig. 8b extra-modular MA (shown with darkened atoms above and below the cavity of the module) also hydrogen bond with the water O1S and O1SA inside the module. The same group of atoms is shown in Fig. 8c at right angles to Fig. 8b. Figure 8c also illustrates the layering of separate modules, in which MA^{-2} ions alternate with BPO^{2+} ions, at distances >3.7 Å, a value that does not indicate any particular attraction. The acceptance of two and only two water molecules within the basic module opens avenues to take advantage of the pair of carboxylic groups of the module that project into the macro-ring that are spaced by 11.78 Å for molecular recognition. Such studies are planned with 1,ω-diamines, $H_2N(CH_2)_nNH_2$ having $n = 7$ or 8.

The assembly profile of MA and 4-BPO is unique and should be a harbinger for the design of novel functional assemblies. The 40-membered module mimics the self-assemblies of peptides and can be important in the design of “Haptens” from simple molecules.

An analysis of the present results do indeed show that the expected alternate hydrogen bonding between the acid and 4-BPO took place and underwent simple dimer formation that forms the basic 40-membered unit (Fig. 6a), that further assembled to macrocyles. The differences in the structural profile of compounds having the common base 4-BPO but differing acids, mesitoic acid and MA, is noteworthy. It appears that the extra carboxylic groups in the latter could provide kinetic advantages for the formation of the basic module (Fig. 6a).

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