Enclathration of morpholinium cations by Dianin's compound: salt formation by partial host-to-guest proton transfer

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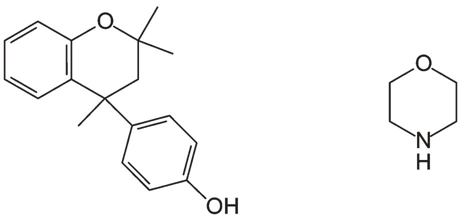
In spite of partial deprotonation upon inclusion of morpholine, Dianin's compound maintains its well-known clathrate structure in the solid state.

The inclusion behaviour of Dianin's compound (4-*p*-hydroxyphenyl-2,2,4-trimethylchroman) (**1**, Scheme 1) is arguably one of the most recognised archetypes of solid state supramolecular chemistry. Since its discovery nearly a century ago,[1] many crystal structures involving Dianin's compound as a host have been reported. The most remarkable feature of these structures is that they comprise a homomorphic series with regard to the skeletal framework formed by the host compound.[2] The chiral molecules crystallise as a racemate with six molecules situated about a site of $\bar{3}$ symmetry to form a cyclic, hexameric arrangement of O–H···O hydrogen bonds between phenolic groups of alternating *R* and *S* stereoisomers. Three like-isomers project above the plane of the hydrogen bonded ring of oxygen atoms while their enantiomers are directed below the plane. The hydrogen bonded hexamers are stacked in columns perpendicular to the hydrogen bonded ring such that the *R* and *S* components of adjacent units interdigitate to form a relatively large hourglass-shaped interstitial cavity of approximately 240 Å^3. The hydrogen bonded hexagonal ring is clearly recognised as a major structure-directing feature of this system. Indeed, this packing mode persists despite synthetic modifications such as thiolation of the phenolic group,[3] removal of one of the 2-methyl groups[4] and replacement of the oxygen heteroatom by S[5] or Se.[6]

One of the stated goals of crystal engineering is to assemble structures with predictable and tuneable packing arrangements. To this end, a reasonable strategy is to employ host molecules that generally pack in a consistent fashion despite incorporation of a wide variety of guest species, or even in the absence of guest molecules. Zeolites and some metal–organic frameworks are well-known to exhibit such structural consistency, but only a small number of analogous organic molecular crystalline systems have been identified to date.[7]


1
2

Scheme 1 Dianin's compound (**1**) and morpholine (**2**).

While organic host–guest systems generally harness many weak intermolecular interactions to encapsulate guests,[8] the utilisation of ionic interactions for such purposes is less common. In the majority of known cases either the host is cationic, or the precise taxonomy of host and guest is open to interpretation.[9] The transfer of a proton from the host molecule to the guest is the most obvious route to an anionic host framework. However, despite such a seemingly small structural modification, removal of a proton can reasonably be expected to cause a major perturbation of the host framework relative to that observed for the neutral host.[10] This is easily rationalised since deprotonation can significantly alter the electrostatic topology of a molecule, as well as its properties as either a hydrogen bond donor or acceptor, and these factors are well-known to dictate crystal packing.

As part of our ongoing studies of the inclusion chemistry of Dianin's compound and its derivatives,[11] we have investigated the enclathration of relatively large guest molecules such as morpholine (**2**, Scheme 1). Slow evaporation of a concentrated solution of Dianin's compound in morpholine yielded crystals suitable for X-ray structural analysis.† The asymmetric unit consists of six molecules of Dianin's compound (four neutral and two deprotonated), as well as two morpholinium cations. Structures with such large values of Z' are relatively unusual and generally warrant investigating the possibility of a misassigned space group. Two similar sets of molecules, each comprised of three molecules of Dianin's compound (two neutral and one deprotonated) and one protonated morpholinium cation, can be distinguished. Each set of four molecules forms the basis of a crystallographically unique one-dimensional column aligned parallel to [100] (one situated along x,0,0 and the other along x,½,½). A detailed analysis of the structure reveals that the latter column can be exactly mapped onto the former by an inversion operation through ¼,¾,¼, followed by a threefold rotation about [100]. However, the unit cell cannot be reindexed as trigonal and the apparent symmetry can reasonably be considered to be non-crystallographic.

Overall, the structure is remarkably similar to those of all the previously reported clathrates of Dianin's compound, although no disorder is apparent in $\mathbf{1}_3\cdot\mathbf{2}$. Until now, Dianin's compound has only been crystallised in trigonal space groups which have generally necessitated modelling the guest molecules as being disordered. We also note that solid state structures containing deprotonated Dianin's compound have not been reported to date. The present structure retains the characteristic hourglass cavity shape and two morpholinium cations are encapsulated in each cavity (Fig. 1). The most significant difference between the present

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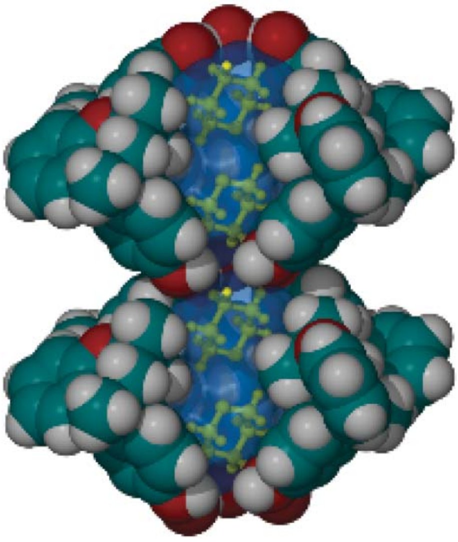

Fig. 1 Molecular cages (semi-transparent blue surfaces) formed by Dianin's compound encapsulate the protonated morpholine molecules (yellow, ball-and-stick). The Dianin's molecules nearest the viewer have been removed in order to reveal the contents of the cavities.

structure and that of the neutral host is the considerable perturbation of the hydrogen bonded motif that forms the nodes of the one-dimensional host columns (Fig. 2).

The cyclic hydrogen bonded motif, considered critical for the stabilisation of the neutral host structure, is interrupted as a result of deprotonation of two of the phenolic hydroxyl groups. Instead of six intermolecular host···host hydrogen bonds, only four are now formed (Fig. 2b). The loss of two energetically important hydrogen bonds is compensated for by the formation of a total of four hydrogen bonds from the protonated amines of two morpholinium guests to the phenolic oxygen atoms of deprotonated and neutral Dianin's compound molecules (Fig. 3). This occurs on both sides of the nodes of the one-dimensional column of host molecules such that a hexameric hydrogen bonded chair [···O–H···O(···H–O)···H–N–H···O–H···O(···H–O)···H–N–H···] is formed. The two morpholinium guest ions that participate in this cyclic hydrogen bonded pattern are situated in adjacent interstitial cavities.

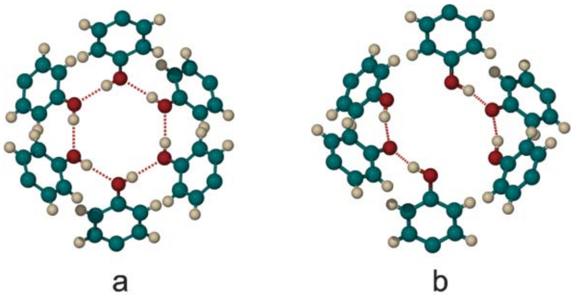

Fig. 2 (a) Ball-and-stick representation of the hexagonally hydrogen bonded phenolic OH groups characteristic to neutral Dianin's compound host systems and (b) a distorted "hexagon" showing how two Dianin's compound molecules hydrogen bond to the nearest deprotonated molecule in the anionic host system.

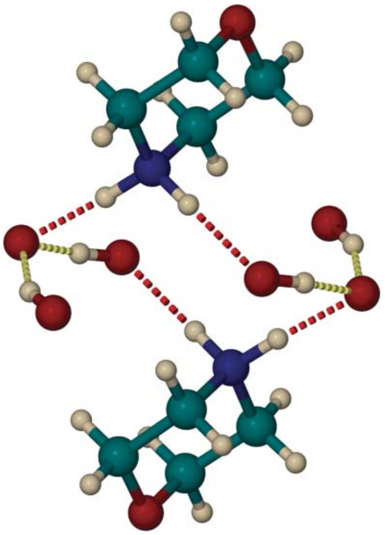

Fig. 3 Hydrogen bonded network formed between the six phenolic groups and the morpholinium guests. Hydrogen bonds between OH and O^- are shown as yellow dotted bonds. The red dotted bonds indicate hydrogen bonds associated with the protonated amine group of morpholine.

It is of interest to survey a selection of Dianin's compound clathrate structures by considering the free volumes of the interstitial cavities as well as the static volumes of the guest molecules (and their disordered models where applicable) in order to rationalise host : guest (H : G) ratios. A H : G ratio of 6 : 1 implies one guest molecule per cavity whereas a ratio of 3 : 1 implies two guest molecules per cavity. For example, the formic and acetic acid clathrates[12] have H : G = 3 : 1 while the carbon tetrachloride,[13] chloroform,[14] propionate[12] and *p*-xylene[15] clathrates have H : G = 6 : 1. The two smallest organic acids form hydrogen bonded dimers within the lattice voids. However, the cavity space is presumably not large enough to accommodate the other types of guest molecules in pairs (we note that complementarity of shape is also important). Since morpholinium is larger than $CHCl_3$ and comparable in size to CCl_4 (Fig. 4), it is at first surprising that the morpholinium clathrate structure has H : G = 3 : 1. However, as noted above, the morpholinium cations are hydrogen bonded to the phenolic host oxygen atoms and there is thus some van der Waals overlap between host and guest. It is interesting to note that disruption of the hexagonal hydrogen bonded motif normally observed in Dianin's compound structures results in no significant change in the shape or volume of the interstitial cavity (Fig. 5). We also note that there is some van der

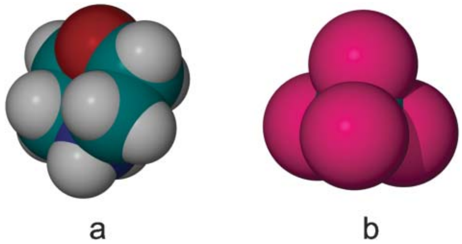

Fig. 4 Size–shape comparison of (a) morpholinium and (b) carbon tetrachloride shown in van der Waals representation.

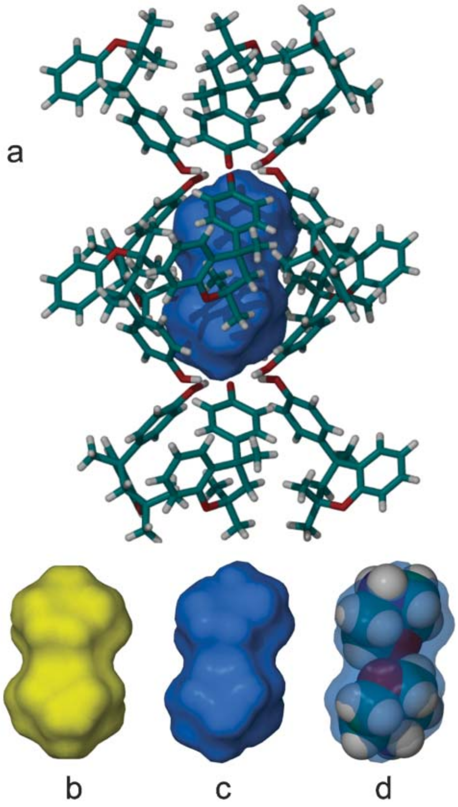

Fig. 5 Surfaces representing the molecular cavities in Dianin's compound structures: (a) columnar packing of the host, (b) the cavity formed by the CCl_4 clathrate, (c) corresponding view of the cavity containing morpholinium and (d) the cavity occupied by two morpholinium molecules shown in van der Waals representation. We calculate the cavity volume to be 237 Å^3 for $\mathbf{1}_3$·**2** and 238 Å^3 for $\mathbf{1}_6$·CCl_4.[16]

Waals overlap between the two morpholinium ions in each cavity (Fig. 5d). A relatively short C–H···O hydrogen bond (C···O = 3.11 Å and ∠C–H···O = *ca.* 128°) is formed between the two guest molecules. This close contact allows the two morpholine molecules to form a compact dimer which fills the cavity with a high packing efficiency of approximately 73.5%. Such close packing between host and guest is likely to contribute significantly towards minimisation of the overall lattice energy.

In the twenty four previously reported structures involving Dianin's compound, no guest molecules have been shown to disrupt the hydrogen bonding pattern of the host framework. We have now probed the proclivity for Dianin's compound to crystallise in its peculiar fashion with the conclusion that molecular topology is also a key factor. Although this is not particularly surprising, our observations do raise fundamental questions about the poorly understood process of crystallisation. In this particular case, is the solution of **1** in **2** an equilibrium mixture of neutral as well as ionised host and guest molecules that simply self-assemble in the correct proportions to yield the observed structure? Alternatively, does crystallisation of neutral species occur first, followed by a proton transfer event to facilitate optimisation of the lattice energy?

Notes and references

† Crystal data for $\mathbf{1}_3$·**2**: $C_{58}H_{69}NO_7$, M = 892.14, colorless prism, 0.25 × 0.10 × 0.10 mm^3, triclinic, space group $P\bar{1}$ (No. 2), a = 11.0956(8), b = 16.0377(11), c = 26.6878(19) Å, α = 89.935(2), β = 89.9310(10), γ = 77.3870(10)°, V = 4634.4(6) Å^3, Z = 4, D_c = 1.279 g cm^{-3}, F_{000} = 1920, MoKα radiation, λ = 0.71073 Å, T = 100(2) K, $2\theta_{max}$ = 56.7°, 29582 reflections collected, 20505 unique (R_{int} = 0.0382). Final GooF = 1.071, $R1$ = 0.0849, $wR2$ = 0.1624, R indices based on 14269 reflections with $I > 2\sigma(I)$ (refinement on F^2), 1240 parameters, 0 restraints. Lp and absorption corrections applied, μ = 0.083 mm^{-1}. The structure was solved and refined using the SHELX-97 suite of programs[17] and the X-Seed[18] interface. The figures were prepared using X-Seed, POV-Ray[19] and Connolly's Molecular Surface Package.[16] CCDC 273461. See http://dx.doi.org/10.1039/b507726e for crystallographic data in CIF or other electronic format.

1 A. P. Dianin, *J. Russ. Phys. Chem. Soc.*, 1914, **31**, 1310.
2 P. Finocchiaro and S. Failla, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vögtle, Elsevier Science, Oxford, 1996, vol. 6.
3 A. D. U. Hardy, D. D. MacNicol, J. J. McKendrick and D. R. Wilson, *J. Chem. Soc., Chem. Commun.*, 1977, **166**, 292.
4 J. H. Gall, A. D. U. Hardy, J. J. McKendrick and D. D. MacNicol, *J. Chem. Soc., Perkin Trans. 2*, 1979, 376.
5 D. D. MacNicol, H. H. Mills and F. B. Wilson, *J. Chem. Soc. D*, 1969, 1332.
6 D. D. MacNicol, P. R. Mallinson, R. A. B. Keates and F. B. Wilson, *J. Inclusion Phenom.*, 1987, **5**, 373.
7 (*a*) J. L. Atwood, L. J. Barbour and A. Jerga, *Science*, 2002, **296**, 2367; (*b*) J. L. Atwood, L. J. Barbour, A. Jerga and B. L. Schottel, *Science*, 2002, **298**, 1000; (*c*) G. D. Andreetti, R. Ungaro and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1979, 1005; (*d*) M. Migata and K. Sada, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vögtle, Elsevier Science, Oxford, 1996, vol. 6; (*e*) J. Szejtli and T. Osa, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vögtle, Elsevier Science, Oxford, 1996, vol. 3.
8 G. R. Desiraju, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vögtle, Elsevier Science, Oxford, 1996, vol. 6.
9 (*a*) P. O. Brown, G. D. Enright and J. A. Ripmeester, *J. Supramol. Chem.*, 2002, **2**, 497; (*b*) T. N. Parac, D. L. Caulder and K. N. Raymond, *J. Am. Chem. Soc.*, 1998, **120**, 8003; (*c*) Q. Li, H.-Y. Hu, C.-K. Lam and T. C. W. Mak, *J. Supramol. Chem.*, 2002, **2**, 473; (*d*) J. Alvarez, Y. Wang, W. Ong and A. E. Kaifer, *J. Supramol. Chem.*, 2001, **1**, 269.
10 (*a*) J. L. Atwood, L. J. Barbour and A. Jerga, *J. Am. Chem. Soc.*, 2002, **124**, 2122; (*b*) H. Mansikkamäki, M. Nissinen and K. Rissanen, *Chem. Commun.*, 2002, **17**, 1902; (*c*) J. Alvarez, Y. Wang, W. Ong and A. E. Kaifer, *J. Supramol. Chem.*, 2001, **1**, 269; (*d*) T. Kaneda, S. Umeda, Y. Ishizaki, H.-S. Kuo, S. Misumi, Y. Kai, N. Kanehisa and N. Kasai, *J. Am. Chem. Soc.*, 1989, **111**, 1881.
11 (*a*) C. Esterhuysen, M. W. Bredenkamp and G. O. Lloyd, *Acta Crystallogr., Sect. C*, 2005, **C61**, o32; (*b*) G. O. Lloyd and M. W. Bredenkamp, *Acta Crystallogr., Sect. E*, 2005, **E61**, o1512.
12 R. W. H. Small, *Acta Crystallogr., Sect. B*, 2003, **59**, 141.
13 W. Abriel, A. DuBois, M. Zakrzewski and M. A. White, *Can. J. Chem.*, 1990, **68**, 1352.
14 J. C. Flippen, J. Karle and I. L. Karle, *J. Am. Chem. Soc.*, 1970, **92**, 3749.
15 G. D. Enright, C. I. Ratcliffe and J. A. Ripmeester, *Mol. Phys.*, 1999, **97**, 1193.
16 *MSROLL program*. A probe radius of 1.2 Å was used to calculate all cavity and molecular volumes. See M. L. Connolly, *Science*, 1983, **221**, 709.
17 G. M. Sheldrick, *SHELX-97: Structure solution and refinement programs*, University of Göttingen, 1997.
18 (*a*) L. J. Barbour, *J. Supramol. Chem.*, 2001, **1**, 189; (*b*) J. L. Atwood and L. J. Barbour, *Cryst. Growth Des.*, 2003, **3**, 3.
19 http://www.povray.org.