Clathrate formation between halogenated species

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Analysis of X-ray crystallographic data reveals how the *exo,exo*-dibromodiquinoline derivative **4** encloses small halogenated guests as clathrate structures.

Clathrate compounds can result where molecules of a pure compound are unable to achieve efficient crystal packing by themselves.[1] This provides a strong driving force for inclusion of suitable guests but makes the design of new lattice inclusion systems a considerable synthetic challenge.[2]

Reaction of racemic bicyclo[3.3.0]octane-2,6-dione **1** and *o*-aminobenzaldehyde **2** gives the Friedländer condensation[3] product **3**† (Scheme 1). Molecules of this diquinoline derivative pack together efficiently in the solid phase and so exhibit no inclusion properties. Benzylic bromination of **3** affords the racemic dibromide **4**† which, in marked contrast, is an efficient host molecule. This change in behaviour was anticipated since its C_2 symmetry provides a favourable scissor topology[4] and since the *exo*-bromine sensor groups[4] destabilise potential aryl offset face–face attractions[5] and provide additional modes for intermolecular packing.[6]
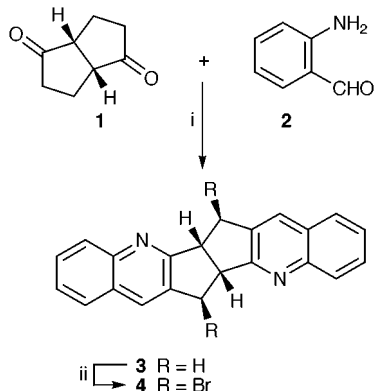
Scheme 1 *Reagents and conditions*: i, NaOH, H_2O, MeOH, 75%; ii, NBS, CCl_4, 78%.

Crystallisation of **4** from $MeCCl_3$ gave crystals of **4**·$(MeCCl_3)_{0.5}$ whose structure‡ in space group $C2/c$ was determined by single crystal X-ray determination. Pairs of host molecules, related by a two-fold axis, enclose each disordered guest within a molecular pen of nearly square cross-section where the aromatic faces of **4** act as the surrounding fences (Fig. 1). If these host pairs were covalently linked at the corners of this structure the result would be a cyclophane[7] but, in fact,
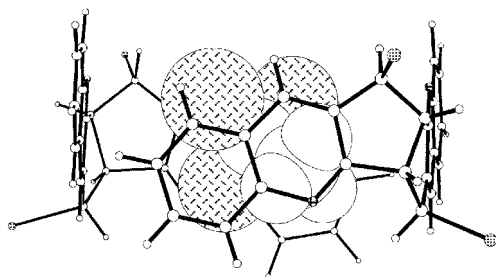
Fig. 1 Side view of the square molecular pen of **4**·$(MeCCl_3)_{0.5}$ showing the two host molecules (framework representation) acting as fences enclosing a $MeCCl_3$ guest (space-filling representation). The guest chlorine atoms are indicated by cross-hatching.

Table 1 Potential and actual supramolecular synthons operating in the clathrate structure **4**·$(MeCCl_3)_{0.5}$

Supramolecular synthon	Partners	Atoms involved	Distances/Å
Aryl offset face–face[a]	Host–host[b]	Ar···Ar	3.55
Aryl edge–face[a]	Host–host	Ar-*H*···*Ar*	Not present
Aryl C–H···N dimer[c] (centrosymmetric)	Host–host[d]	C–H···N	3.38
		C–H···N	2.47
Interhalogen[e]	Host–host[b]	Br···Br	3.69
Interhalogen[e]	Host–guest	Br···Cl	Not present
Aryl-halogen[f]	Host–guest[b]	Ar···Cl[g]	3.48, 3.77, 3.81, 3.98[h]
Aryl-alkyl[c]	Host–guest[b]	*Ar*···H_3C[g]	3.65, 3.66
Interhalogen[e]	Guest–guest	Cl···Cl	Not present

[a] Ref. 10. [b] Within layers. [c] Ref. 5. [d] Between layers. [e] Ref. 11. [f] Ref. 12. [g] Aromatic ring centroids used. [h] Values under 4.00 Å only.

there is not even significant intermolecular attraction. Although pens thus only result from the net outcome of all lattice attractions (see Table 1) in the clathrate it is convenient to retain this term as a descriptor. There is a planar array of pens (Fig. 2) all constructed using the same enantiomer of **4**, and the slightly offset adjacent layers of pens are built from the second enantiomer.

Comparatively strong intermolecular forces (such as hydroxy group hydrogen bonding) are not used in the design of host **4**. Instead, a number of relatively weak interactions such as aryl offset face–face, aryl edge–face, aryl C–H···N dimer, aryl–halogen and interhalogen attractions are available for potential combinations of **4** and $MeCCl_3$. Since it is the best overall combination of these synthons[6] (along with size, shape and conformational factors) which determines the structure, some of
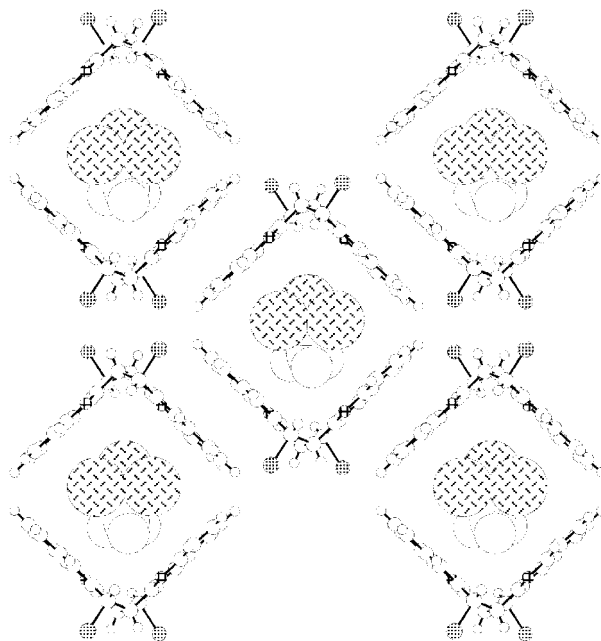
Fig. 2 Top view of part of a layer of the square molecular pens in **4**·$(MeCCl_3)_{0.5}$ showing how these are arranged in regular rows. The host bromine atoms are stippled and guest chlorine atoms cross-hatched. $MeCCl_3$ guests are shown in just one of their disorder positions.
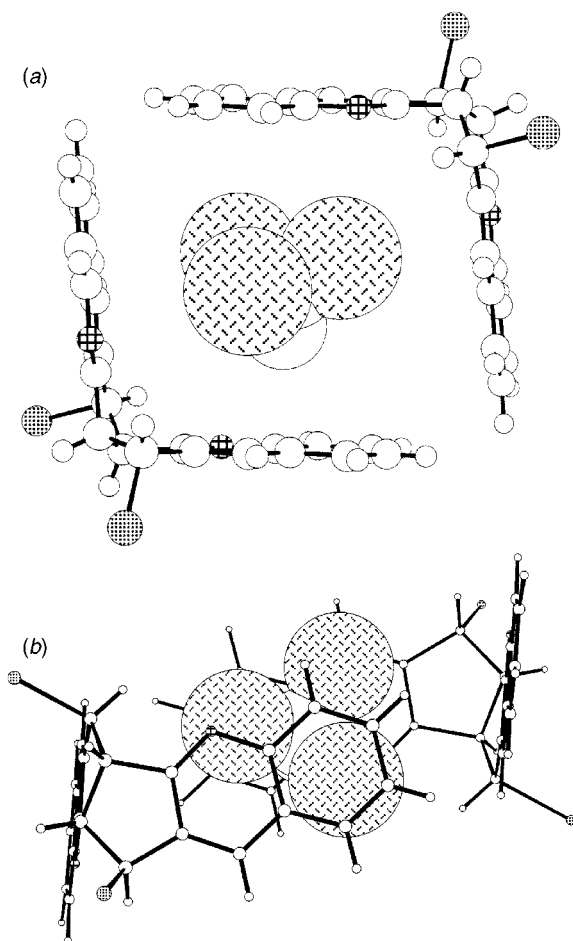
Fig. 3 (*a*) One of the two types of parallelogram-shaped molecular pens present in the clathrate structure **4**·(CHCl₃)₀.₅. (*b*) Side view of the inclusion compound showing its overall parallelepiped geometry.

these turn out not to be used in **4**·(MeCCl₃)₀.₅ while others (including the aryl C–H···N dimer[5]) do play a major role (Table 1).

The central bicyclic ring of the host molecule potentially allows considerable conformational mobility since, for example, the much flatter bis(*N*-oxide) derivative of **3**† has an angle of 133.4° between the normals to the two aromatic planes. It is significant that the two aromatic faces of **4** are almost orthogonal in the MeCCl₃ compound (97.7°). This allows maximisation of aryl–halogen and aryl–alkyl interactions between the π-deficient quinoline host and the nearly spherical electron-rich guest. Hence host **4** exhibits molecular tweezer characteristics[8,9] whereby two host molecules wrap around each MeCCl₃ guest.

The detailed energetic interplay changes with differing guests. Crystals of **4**·(CHCl₃)₀.₅ were obtained from CHCl₃ solution. This structure‡ is more complex, but pairs of host molecules still enclose disordered guests in the same manner despite the changes in guest and space group (*P*2₁/*c*). Each molecular pen is now centrosymmetric and there are two crystallographically distinct pens (A and B) present in the lattice (angles 97.6 and 100.8° respectively). Both have a more

parallelogram-like cross-section than previously (Fig. 3) and they stack alternately (-A-B-A-B-A-). Where these stacks abut, however, there is no layer formation. The pens are not parallel to each other along the stacks, but rather tilt somewhat back and forth.

The same types of intermolecular attractions operate in this second clathrate, but with different geometries. Unexpectedly, although the versatile aryl C–H···N dimer still operates between opposite enantiomers of **4**, this time it is non-centrosymmetric with two distinct *C*–H···*N* distances (3.45 and 3.49 Å). This is the first reported example of such behaviour for this motif.[5]

These preliminary results reveal the dibromide **4** to be an unusual new lattice inclusion host. The interplay of host–guest attractions results in molecular enclosure tailored to the requirements of the particular guest. The further inclusion behaviour of this host compound is under active investigation.

Notes and references

† The structures of all new compounds are based on IR, MS, ¹H and ¹³C NMR spectroscopy and single crystal X-ray structural determinations.
‡ *Crystal data* for **4**·MeCCl₃: C₂₂H₁₄Br₂N₂·(C₂H₃Cl₃)₀.₅, M = 532.9, monoclinic, a = 17.006(9), b = 18.764(4), c = 13.421(7) Å, β = 92.05(3)°, U = 4280(3) Å³, T = 294(1) K, space group *C*2/*c* (no. 15), monochromated Mo-Kα radiation, λ = 0.7107 Å, Z = 8, D_c = 1.65 Mg m⁻³, μ(Mo-Kα) = 39.5 cm⁻¹, 3761 reflections measured, 1519 unique (R_{int} = 0.056) which were used in all calculations. The final R was 0.059, and $wR(F)$ 0.069 (observed data). For **4**·CHCl₃: C₂₂H₁₄Br₂N₂·(CHCl₃)₀.₅, M = 525.9, monoclinic, a = 14.832(7), b = 16.754(5), c = 18.084(9) Å, β = 110.80(2)°, U = 4201(3) Å³, T = 294(1) K, space group *P*2₁/*c* (no. 14), monochromated Cu-Kα radiation, λ = 1.5418 Å, Z = 8, D_c = 1.66 Mg m⁻³, μ(CuKα) = 68.2 cm⁻¹, 7879 reflections measured, 4503 unique (R_{int} = 0.027) which were used in all calculations. The final R was 0.051, and $wR(F)$ 0.071 (observed data). Both structures were determined by direct phasing (SIR92) and Fourier methods. CCDC 182/1452. See http://www.rsc.org.suppdata/cc/1999/2389/ for crystallographic data in .cif format.

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