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Synthesis of a new lattice inclusion host belonging to the tetrahalo aryl family

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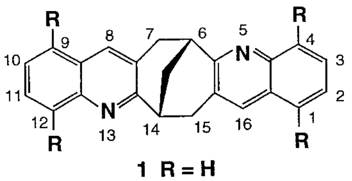
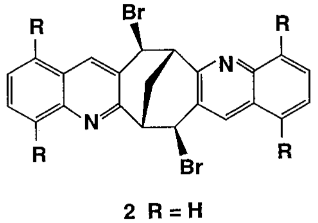
Abstract—The tetrabromo diquinoline derivative **3** has been synthesised and its dichloromethane compound investigated by X-ray crystallography. This racemic host acts in an unusual manner by assembling into achiral molecular staircases and including the guests in parallel channels between these. Compound **3** belongs to a newly identified family of lattice inclusion hosts whose structural characteristics are described here for the first time. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

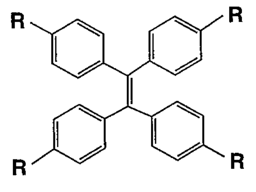
The synthesis of new inclusion hosts is an active area of contemporary chemistry, driven by their application in analytical separation and material sciences,[1,2] and also our quest to understand the roles played by intermolecular forces in supramolecular assembly.[3–5] A useful distinction can be made between hosts where a pre-formed receptor interacts with the guest species, and those inclusion compounds which result from the combination of host–guest interactions present throughout their crystal lattice. While the behaviour of the former compounds (such as crown ethers, cryptands, and calixarenes) lends itself to efficient modelling, the properties of the latter group (such as thiourea, tetraaryl porphyrins, and the bile acids) are less predictable and the design of new lattice inclusion hosts remains problematic. Recent years have, however, seen notable advances in the preparation of new lattice inclusion hosts. This progress has arisen through chance discovery, successful modification of known structures, and from growing awareness of the types of molecular structure likely to exhibit inclusion properties.[6,7]



1 R = H
3 R = Br



2 R = H
4 R = Br



5

	R =
a	H
b	F
c	Cl
d	Br
e	I

Recently, we have moved from studying inclusion systems which assemble through relatively strong hydroxy group hydrogen bonding[8] to those[9,10] which involve the interplay of a combination of weaker supramolecular synthons[11] (such as aryl–aryl,[12–14] C–H···N[15] and halogen–halogen[16,17] interactions). For example, while the diquinoline **1** packs efficiently in the solid state without inclusion properties, its dibromo analogue **2** is an excellent lattice inclusion host with a preference for trapping small polyhalo guests.[18] A major packing mode for both compounds is the edge–edge aryl C–H···N dimer which provides an efficient means of accommodating both enantiomers of the racemic material in their crystals.[19] This favourable interaction is no longer possible in the halogenated molecules **3** and **4**. We report here that the tetrabromide **3** is an effective new host molecule and we define the new tetrahalo aryl lattice inclusion family to which it belongs.

Keywords: inclusion; host compounds; supramolecular chemistry; X-ray crystal structures; intermolecular forces; halogenation.

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Table 1. Numerical details of the solution and refinement of the structure $(\mathbf{3})_2\cdot(CH_2Cl_2)$

Formula	$(C_{23}H_{14}Br_4N_2)_2\cdot(CH_2Cl_2)$
Formula mass	1361
Space group	$C2/c$
a (Å)	27.417(6)
b (Å)	12.202(2)
c (Å)	13.819(3)
β (Å)	100.824(9)
V (Å^3)	4541(2)
T (°C)	21(1)
Z	4
$D_{calc.}$ (g cm^{-3})	1.99
Radiation, λ (Å)	CuKα, 1.5418
μ (cm^{-1})	99.8
Scan mode	$\theta/2\theta$
$2\theta_{max.}$ (°)	120
Number of intensity measurements	3356
Criterion for observed reflection	$I/\sigma(I)>3$
Number of independent observed reflections	1946
Number of reflections (m) in final refinement	1946
Number of variables (n) in final refinement	150
$R=\sum^m\lvert\Delta F\rvert\sum^m\lvert F_0\rvert$	0.069
$R_w=[\sum^m w\lvert\Delta F\rvert^2/\sum^m w\lvert F_0\rvert^2]^{1/2}$	0.099
$s=[\sum^m w\lvert\Delta F\rvert^2/(m-n)]^{1/2}$	1.93
Crystal decay	1–0.96
Maximum, minimum transmission coefficients	0.60, 0.30

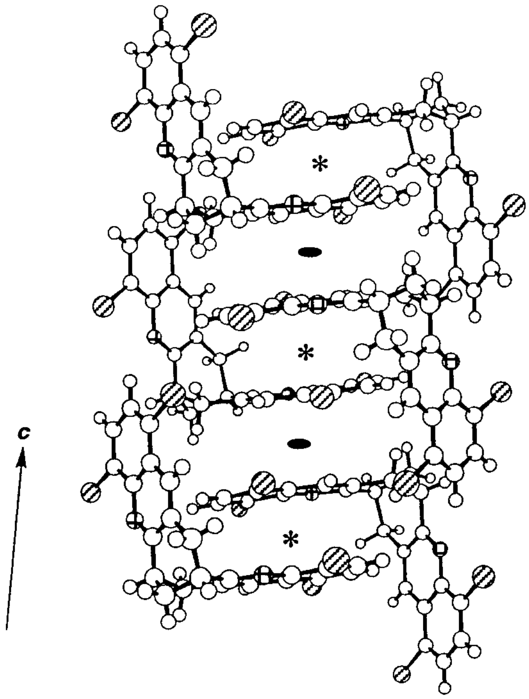

Figure 1. Staircase assembly present in the structure $(\mathbf{3})_2\cdot(CH_2Cl_2)$. The steps formed by one aromatic wing of the host molecules **3** are edge-on in the centre of the diagram, with the surrounds formed by the second wings pointing up (left) and down (right) along *c*. Symbolism used: bromine (diagonal stripes), nitrogen (cross hatching), centre of symmetry (star), and twofold axis (ellipse).

2. Results and discussion

Quinoline is known to undergo bromination at its 5- and 8-positions using a mixture of bromine, sulfuric acid, and silver sulfate.[20] Application of this reaction protocol to the diquinoline derivative **1** gave the analogous 1,4,9,12-tetrabromide **3** in 49% yield, and subsequent benzylic bromination using *N*-bromosuccinimide in CCl_4 produced the hexabromide **4** in 89% yield. No evidence of any inclusion properties was found for **4** where slow concentration of test solutions tended to yield gums rather than crystalline material. In contrast, compound **3** trapped many test solvents and here the X-ray crystal structure of its novel inclusion compound $(\mathbf{3})_2\cdot(CH_2Cl_2)$ is described. Numerical details pertaining to the data collection, data processing, and refinement of this structure are given in Table 1.

The two planar aromatic wings of **3** give it an approximately V-shaped geometry, but additional twisting around the central alicyclic ring generates C_2 symmetry. Presence of the four bromine atoms rules out the possibility of dimeric edge–edge aryl C–H···N interactions but increases the likelihood of aryl–aryl and interhalogen packing motifs being involved. In fact, molecules of **3** assemble into molecular staircases oriented along *c* as shown in Fig. 1. The steps of each staircase are built up using one wing of the molecules, with the surrounds of the staircase comprising the second wings. These surrounds are directed upwards on one side, and downwards on the other side of the staircase.

Adjacent steps assemble through offset aryl–aryl face–face stacking, but there are two types of inter-step region which are alternately related by inversion and twofold axes along the staircase. The centrosymmetric step-pairs have one bromine atom from each molecule located directly over an aryl ring of the other and this pair is additionally stabilised by aryl edge–face interactions between the outer edges of the steps and the aromatic surrounds. In contrast, the twofold step-pairs only involve offset aryl–aryl face–face interactions and have their bromine atoms oriented away from the aryl stacking. It is well known that planar molecules may sometimes stack giving staircase structures as, for example, the phthalocyanine derivatives recently described by Nolte[21] where chiral staircases were produced. This is not the case here since the staircases formed by **3** incorporate centres of symmetry along *c* (see Fig. 1) and hence all the staircases are achiral and identical.

The net outcome in the crystal is assembly in the *ab* plane of translation-related staircases with approximately hexagonal cross-section. Four of the hexagon edges are formed by the aromatic surrounds along *c*, but the remaining two opposed edges are slightly concave with exposed nitrogen and bromine atoms. Dichloromethane guest molecules, which are disordered over two sites, occupy interstitial channels between two concave edges belonging to adjacent staircases (Fig. 2). The aromatic surrounds of each staircase associate with those of its neighbours through centrosymmetric offset aryl–aryl face–face interactions. The structure is further stabilised by both host–host Br···Br and host–guest Br···Cl attractions. In addition, there are C–H···halogen interactions where the C–H can be either host or guest.

Lattice inclusion host **3** functions quite differently to previously reported examples and is quite versatile since it

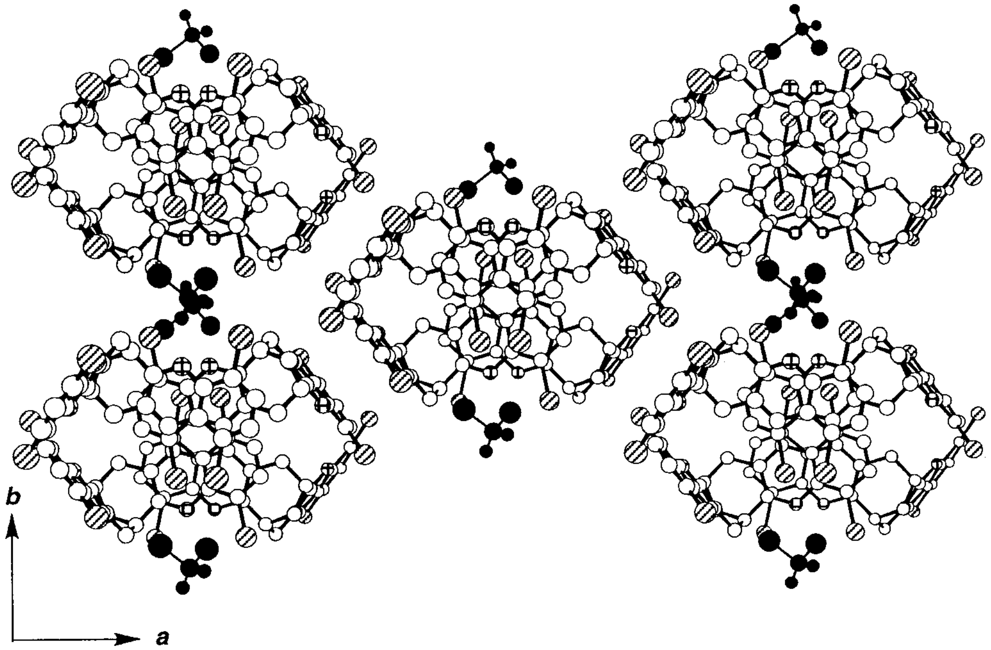

Figure 2. Packing of the host staircases and dichloromethane guests in $(\mathbf{3})_2\cdot(CH_2Cl_2)$. Host hydrogen atoms are omitted for clarity and the guests are coloured black. The staircases, with their steps in the centre, have a hexagonal cross-section when projected in the *ab* plane. Four faces are formed by the aromatic surrounds and the remaining two opposed faces are slightly concave. Disordered guest molecules (both positions illustrated) occupy channels between the concave edges of two adjacent staircases.

also includes guests as diverse as toluene, tetrahydrofuran, and 1,1,2,2-tetrachloroethane. The structures of these compounds are currently under investigation, but more importantly at this stage we wish to highlight the synthetic potential for new lattice inclusion hosts based on the structural characteristics of **3** and the tetrahalo hosts **5b–d** described recently by Tanaka et al.[22–24]

We identify these compounds as being the first examples of a new tetrahalo aryl family of lattice inclusion hosts, and we predict that many further examples will exist. Since **3** has a twisted V-geometry and **5** is propeller-shaped, further compounds of this group are likely to be structurally and geometrically diverse. Hence there is no reason why the supramolecular behaviour and crystal packing of new examples should necessarily resemble those of either **3** or **5b–d**.

Weber has recognised that molecules containing inclined planar groups are especially prone to having inclusion properties.[25,26] Hence, compounds with edge–edge or edge–face aligned aromatic groups sometimes result in three-dimensional shapes which pack inefficiently by themselves. In such cases guest inclusion can increase the crystal packing density. Combination of these principles with the presence of halogen substitution at the molecular extremities characterises this new class of hosts. A further defining characteristic of this new group of hosts is that the parent hydrogen-substituted derivative may exhibit no inclusion properties in its own right (as demonstrated by both parents **1** and **5a**). Introduction of halo-substituents provides additional intermolecular host–host and host–guest packing possibilities over the hydrocarbon compound, such as halogen–halogen, halogen–hydrogen, and halogen–π synthons. On the other hand, halogen substitution additional to the extremity positions (as in compound **4**) is detrimental to molecular inclusion.

3. Experimental

NMR data were recorded using a Bruker ACF300 instrument (300 MHz for ^1H, 75.4 MHz for ^{13}C) as solutions in $CDCl_3$ at 25°C. Proton coupling constants are given in hertz (Hz) and carbon substitution was determined using the DEPT procedure. MS data (EI) were recorded on a VG Quattro triple quadrupole instrument.

3.1. General

3.1.1. 1,4,9,12-Tetrabromo-6,7,14,15-tetrahydro-6,14-methanocycloocta[1,2-*b*:5,6-*b*′]diquinoline 3. Diquinoline **1**[18,19] (189.9 mg, 0.59 mmol) and Ag_2SO_4 (498.8 mg, 2.45 mmol) were dissolved in H_2SO_4 (98%, 2 cm^3) with warming, then the solution was allowed to cool and bromine (0.5 cm^3) added dropwise. The mixture was stoppered, stirred at room temperature for 3 h, then poured into aq. NaOH (2 M; 40 cm^3) and solid Na_2SO_3 added until all excess bromine had been reduced. The suspension was extracted with dichloromethane (3×50 cm^3), the combined organic extracts dried ($MgSO_4$), then solvent was evaporated from the filtrate under reduced pressure to give a fine yellow-brown solid. Recrystallisation from dichloromethane–methanol gave **3** as a buff solid (172 mg, 46%), mp 269–272°C (Found: C, 40.81; H, 2.65; N, 3.70. $C_{23}H_{14}N_2Br_4$ requires C, 40.98; H, 2.69; N, 4.15%); ν_{max} (paraffin mull) (cm^{-1}) 1610w, 1590w, 1445w, 1425w, 1260w, 1220w, 1200w, 1130w, 1010m, 950m, 935w, 820m, 800m; δ_H 2.58 (t, 2H, J=3.0 Hz, H17), 3.43 and 3.49 (d, 2H, J_{AB}=16.9 Hz, H7/15), 3.59 and 3.65 (dd, 2H,

J_{AB}=16.9 Hz, J_{BX}=2.7 Hz, H7/15), 3.97 (dt, 2H, $J_{6,7}$/$J_{14,15}$=2.7 Hz, H6/14), 7.52 (d, 2H, *J*=8.0 Hz), 7.79 (d, 2H, *J*=8.0 Hz), 8.07 (s, 2H, H8/16); δ_C 28.5 (CH_2, C17), 36.1 (CH, C6/14), 38.3 (CH_2, C7/15), 120.6 (C), 124.1 (C), 127.7 (C), 129.7 (CH), 130.8 (C), 132.2 (CH), 136.1 (CH), 144.6 (C), 163.2 (C); *m/z*: 642 (M^+, four ^{81}Br, 0.1%), 640 (M^+, ^{79}Br/three ^{81}Br, 0.3), 638 (M^+, two ^{79}Br/two ^{81}Br, 0.35), 636 (M^+, three $^{79}Br/^{81}Br$, 0.2), 634 (M^+, four ^{79}Br, 0.1), 86 (76), 84 (100), 69 (29), 55 (41), 51 (51), 49 (99).

3.1.2. 1,4,7α,9,12,15α-Hexabromo-6,7,14,15-tetrahydro-6α,14α-methanocycloocta[1,2-*b*:5,6-*b*′]diquinoline 4. A mixture of tetrabromide **3** (86 mg, 0.14 mmol) and *N*-bromosuccinimide (62.4 mg, 0.35 mmol) was refluxed in CCl_4 for 2.5 h. The cooled solution was filtered and solvent evaporated from the filtrate under reduced pressure to give a yellow foam. This was eluted through a column of silica (5 g) using dichloromethane–petrol (1:1) to give **4** as a light yellow foam (95.7 mg, 89%), mp 294–296°C (Found: C, 34.37; H, 2.00; N, 3.18. $C_{23}H_{12}N_2Br_6$ requires C, 34.71; H, 1.52; N, 3.52%); δ_H 3.23 (t, 2H, $J_{17,6}$/$J_{17,14}$=3.1 Hz, H17), 4.22 (dt, 2H, $J_{6,17}$/$J_{14,17}$=2.8 Hz, $J_{6,7}$/$J_{14,15}$=2.6 Hz, H6/14), 5.81 (d, 2H $J_{7,6}$/$J_{15,14}$=2.6 Hz, H7/15), 7.59 (d, 2H, *J*=8.0 Hz), 7.87 (d, 2H, *J*=8.2 Hz), 8.35 (s, 2H, H8/16); δ_C 20.2 (CH_2, C17), 44.1 (CH, C6/C14), 51.1 (CH, C7/15), 121.0 (C), 124.5 (C), 128.1 (C), 130.7 (CH), 131.4 (C), 133.8 (CH), 139.2 (CH), 145.6 (C), 157.0 (C); *m/z* 796 (M^+, three ^{79}Br/three ^{81}Br, 1%), 717 [$(M-^{79}Br)^+$, 3], 635 (6), 554 (3), 475 (5), 394 (4), 151 (46), 149 (100), 121 (55), 119 (47).

3.1.3. Solution and refinement of the crystal structure. Reflection data were measured with an Enraf-Nonius CAD-4 diffractometer in $\theta/2\theta$ scan mode graphite monochromated copper radiation (λ=1.5418 Å). Data were corrected for absorption.[27] Reflections with $I > 3\sigma(I)$ were considered observed. The structure was determined by direct phasing (SIR92[28]) and Fourier methods. The CH_2Cl_2 guest was modelled as a rigid group with twofold symmetry. The guest was disordered over two sites (occupancies 0.512 and 0.488), both of which were located near the twofold axis. The four bromine atoms were refined anisotropically, with the thermal motion of the remainder of the host molecule being defined as a 15 parameter TLX group (where T is the translation tensor, L is the libration tensor and X is the origin of libration). The guest thermal motion was described by a single TL group.[29] Reflection weights used were $1/\sigma^2(F_0)$, with $\sigma(F_0)$ being derived from $\sigma(I_0) = [\sigma^2(I_0) + (0.04I_0)^2]^{1/2}$. The weighted residual is defined as $R_w = (\sum w\Delta^2/\sum wF_0^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray crystallography.[30]

4. Supporting information available

Crystallographic data (cif) have been deposited with the Cambridge Crystallographic Data Centre (deposition number CCDC 152353). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-0-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgements

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