New Triquinane-based Host Molecules: Binding with Diamines

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Synthesis of several shape-specific hosts through heteroaromatic annulation on *cis,syn,cis*-triquinanedione **1** and X-ray crystal structure determination of one of them, **4a**, is reported. Preliminary results of complexation between cleft **5a** and diamines are reported.

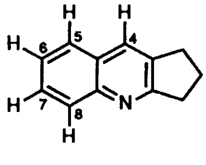
Efforts directed towards the design of molecular receptors or hosts with varying size, shape and recognition sites for diverse chemical species (guests) have attained a pre-eminent position in contemporary research.[1] As a result of these endeavours, an impressive number of macrocyclic (closed) and non-macrocyclic (cleft,[1b] cavity,[2a,b] tweezer,[2c] clip[2d] *etc.*) receptors have been crafted, which engage a variety of guest molecules predominantly through hydrogen bonding and/or π-stacking interactions. The underlying rationale behind the creation of non-macrocyclic receptors is the installation of aromatic surfaces on rigid, topologically biased backbone structures. In this context, we were attracted by the prospect of utilising the readily available *cis,syn,cis*-triquinane system with rigid, folded topology for creating different shapes by grafting aromatic rings and binding sites.[3] Herein we describe the preparation of several hosts based on the triquinane system and report on the binding characteristics of one of them.

The *cis,syn,cis*-triquinane dione **1**, readily accessible from Cookson's caged dione **2**[4] *via* efficient reductive uncaging protocols,[5] was subjected to Friedlander condensation[2a] with 2-aminobenzaldehyde **3a** in the presence of alcoholic KOH (Scheme 1) to furnish **4a** (16%), **5a** (15%), **6a** (22%) and **7** (7%). Thus, three different shapes, a wedge **4a**, a cleft **5a** and a hybrid of the two **6a**, could be generated in a single step. The 500 MHz ^{1}H NMR and ^{13}C NMR spectroscopic data readily enabled a distinction to be made between the symmetrical bisquinolinotriquinanes **4a**, **5a** and the unsymmetrical analogue **6a**. Further, a comparison of the highfield ^{1}H NMR shifts of the aromatic protons in **4a** and **5a** with the model compound cyclopenta[*b*]quinoline **8**[6] revealed the wedge-like structure of **4a** in which the resonances of 4- and 5-H, being proximal on the quinoline moieties, are strongly shielded (*ca.* 0.3 ppm); while the distal 7- and 8-H protons are hardly affected (Table 1).

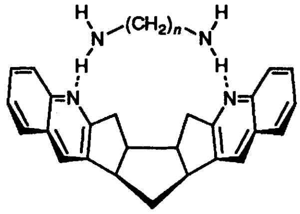
Table 1 ^{1}H NMR shifts of quinoline protons in a model compound **8** and the hosts **4a** and **5a** at 500 MHz[a]

	δ_H				
Compound	4-H	5-H	6-H	7-H	8-H
8	7.76	7.65	7.40	7.58	8.00
4a	7.44	7.43	7.38	7.59	7.94
5a	7.76	7.62	7.38	7.55	7.92

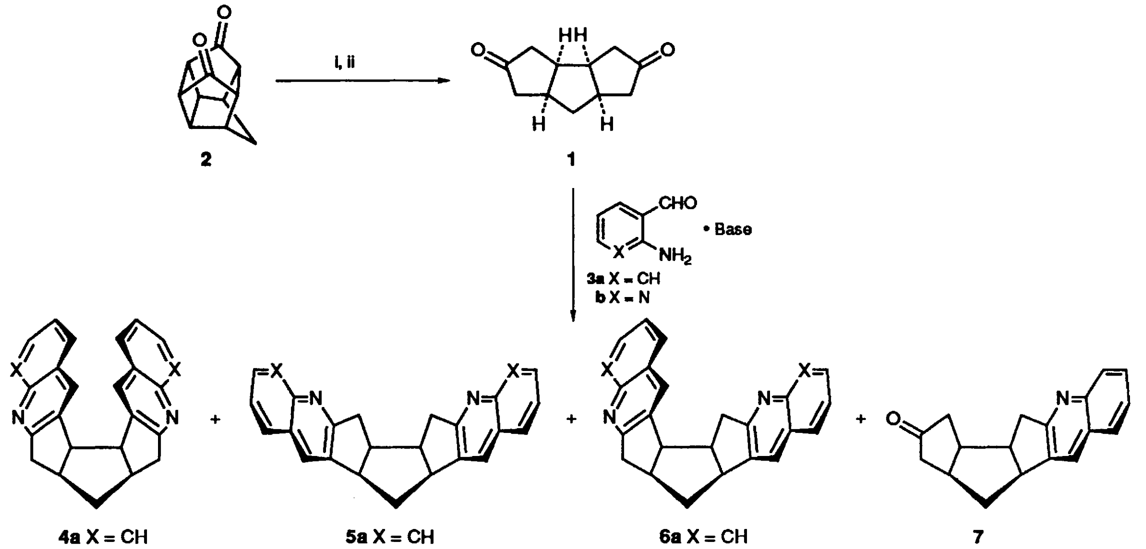
[a] For convenience, quinoline numbering has been followed to assign aromatic protons throughout this paper.



8



9 *n* = 2, 3



Scheme 1 *Reagents:* i, Zn–AcOH; ii, Na–K alloy, TMSCl (ref. 5)

Table 2 Selected interatomic distances

Atoms		Distance (Å)
N(1)	N(9)	6.379(2)
C(11)	C(26)	8.395(3)
C(14)	C(23)	6.191(3)
C(16)	C(21)	3.666(2)

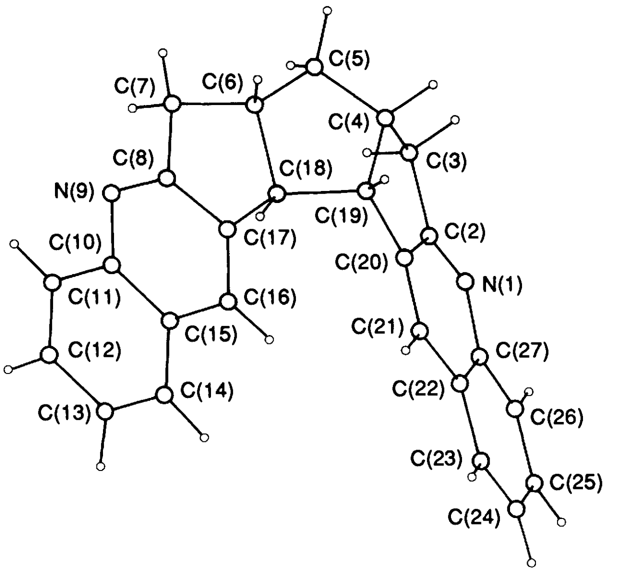


Fig. 1 Crystal structure of **4a**

In the cleft-like structure **5a**, the quinoline protons exhibit only a small shielding. However, the assignments of structures **4a** and **5a** to the wedge and cleft, respectively, were fully secured through the X-ray crystal structure determination of **4a** whose molecular structure is depicted in Fig. 1. Selected interatomic distances that vouch for its wedge-like shape are indicated in Table 2.

In an analogous manner, the dione **1** on Friedlander condensation[2a] with 2-aminopyridine-3-carbaldehyde **3b** in ethanol in the presence of piperidine furnished the bis-naphthyridinotriquinanes **4b**, **5b** and **6b** in 82% yield. The formulae **4b**–**6b** were arrived at by comparison of their ^1H and ^{13}C NMR spectroscopic data with that of the corresponding quinolino compounds **4a**–**6a**. However, in this case a clean separation between **4b** and **6b** was not achieved.

The separation of *ca.* 5 Å between the two aromatic surfaces in the vicinity of the nitrogen binding sites in the hosts **4**–**6** makes them less suitable as aromatic binding hosts. However, the N ··· N distance of *ca.* 5.3 Å in the cleft **5a** presented the possibility of binding with aliphatic diamines through trans-annular hydrogen-bond promoted bridging. Consequently, **5a** was titrated with ethane-1,2-diamine and propane-1,3-diamine in $CDCl_3$. The 300 MHz ^1H NMR spectroscopic results are presented in Table 3. The deshielding of the guest NH protons and the consistent shielding of all the quinoline aromatic protons provided definitive indication of binding as indicated in **9**; the aromatic proton shielding being more pronounced in the case of propane-1,3-diamine as compared with ethane-1,2-diamine. Further support for the bridging shown in **9** came from the NMR spectroscopic data of the titration of **5a** with propylamine, which showed comparable deshielding of the NH proton but the aromatic protons remain practically unchanged. Thus, in **9** the aromatic surfaces reorganise to accommodate the diamine guests as is evident from the altered mutual shieldings. Preliminary estimates of $-\Delta G^0$ values for the binding of the diamines is in the range of 1–2 kcal* and accord well with a bridge structure similar to **9**. Further complexation studies with the new host systems are currently being pursued.

Experimental

Friedlander Condensation of Dione **1** *with 2-Aminobenzaldehyde* **3a**.—A mixture of dione **1** (200 mg, 1.12 mmol), **3a** (424 mg, 3.48 mmol) and 15% KOH–methanol (0.2 cm^3) in absolute ethanol (25 cm^3) was refluxed for 4 h. Dilution with water, extraction with ethyl acetate followed by work-up and chromatography (SiO_2 gel) furnished **4a** (62 mg, 16%), **5a** (60 mg, 15%), **6a** (86 mg, 22%) and **7** (20 mg, 7%). All the compounds were characterised on the basis of elemental analyses and spectroscopic data. Selected data is as follows: **4a**: m.p. 214–215 °C, δ_H($CDCl_3$; 500 MHz) 1.46 (1 H, m), 2.64 (3 H, m), 3.26 (m, 4 H), 4.19 (2 H, q), 7.38 (2 H, m), 7.42 (2 H, d, *J* 1.13),† 7.44 (2 H, s), 7.59 (2 H, m) and 7.94 (2 H, d, *J* 8.39); δ_C(25.0 MHz) 39.3, 41.4, 44.1, 52.8, 125.6, 126.8, 127.7, 128.4, 128.7, 131.9, 135.3, 147.8 and 167.8 (Found: C, 86.4; H, 5.8; N, 8.1. $C_{25}H_{20}N_2$ requires C, 86.21; H, 5.75; N, 8.04%).

5a: m.p. > 250 °C, δ_H($CDCl_3$; 500 MHz) 1.85 (1 H, m), 2.96 (3 H, m), 3.28 (2 H, dd, J_1 17.59, J_2 8.6), 3.38 (2 H, m), 4.00 (2 H, dd, J_1 15.79, J_2 7.8), 7.38 (2 H, m), 7.55 (2 H, m), 7.62 (2 H, d, *J* 8.13), 7.76 (2 H, s) and 7.92 (2 H, d, *J* 8.43); δ_C(25.0 MHz) 35.8, 39.7, 45.8, 50.0, 125.5, 127.4, 128.3, 128.4, 130.1, 139.5, 139.7, 147.5 and 166.5 (Found: C, 86.25; H, 5.75; N, 8.05. $C_{25}H_{20}N_2$ requires C, 86.21; H, 5.75; N, 8.04%).

6a: m.p. 231–233 °C; δ_H($CDCl_3$; 500 MHz) 1.62 (1 H, m), 2.51 (1 H, m), 2.90 (1 H, m), 3.00 (1 H, dd, J_1 17.7, J_2 7.8), 3.29 (3 H, m), 3.64 (1 H, m), 3.91 (1 H, dd, J_1 16.49, J_2 8.3), 4.18 (1 H, t), 7.40 (1 H, t), 7.47 (1 H, t), 7.54 (1 H, t), 7.60 (1 H, t), 7.68 (1 H, d, *J* 8.1), 7.76 (1 H, d, *J* 8.1), 7.83 (1 H, s), 7.86 (1 H, d, *J* 8.4), 7.94 (1 H, d, *J* 8.4) and 7.97 (1 H, s); δ_C(25.0 MHz) 36.6, 39.4, 39.5, 44.2, 46.0, 50.4, 50.7, 125.7, 125.8, 127.3, 127.5, 127.8, 128.1, 128.2, 128.7, 129.0, 130.5, 133.4, 136.0, 138.2, 147.4, 166.1 and 167.0 (Found: C, 86.3; H, 5.7; N, 8.1. $C_{25}H_{20}N_2$ requires C, 86.21; H, 5.75; N, 8.04%).

Crystal data for **4a**. $C_{25}H_{20}N_2$, $M = 348.4$, monoclinic, $P2_1/C$, $a = 6.180(1)$ Å, $b = 14.894(3)$ Å, $c = 19.107(3)$ Å, $\beta = 93.01(2)$, $V = 1756.3$ Å^3, $D_c = 1.31$ g cm^{-3}, $\mu = 5.6$ cm^{-1}, $F(000) = 736$, $Z = 4$. Intensity data were collected on an Enraf-Nonius CAD-4 diffractometer, for a crystal of size 0.82 × 0.2 × 0.14 mm. 3233 Reflections were measured out of which 2824 reflections were found to be unique and 2585 reflections were considered observed $[F \geq 3\sigma(F)]$. Lorentz and polarisation corrections were applied. The structure was solved by direct methods using MULTAN (Germain, Main & Woolfson, 1971). Full matrix least squares refinement on F's using SHELX 400 (Sheldrick, 1976), with the non-H atoms refined anisotropically and the H-atoms fixed, converged at $R = 0.042$ for 324 varied parameters. Individual weights, $W = [\sigma^2(F) + WF^2]^{-1}$ was 0.001 and $R_w = 0.048$. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.‡

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* 1 cal = 4.184 J.

† *J* values are given in Hz throughout.

‡ For full details of the CCDC deposition scheme see, 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1992, Issue 1.

Table 3 $\Delta\delta_{max}$ Values obtained from 300 MHz ^{1}H NMR spectra for complexation of **5a** with various amines in $CDCl_3$

Guest	$\Delta\delta_{max}$ ppm[a]					
	4-H	5-H	6-H	7-H	8-H	NH[b]
Propylamine	−0.006	−0.005	−0.007	−0.005	−0.008	0.21
Ethane-1,2-diamine	−0.02	−0.02	−0.02	−0.02	−0.03	0.13
Propane-1,3-diamine	−0.07	−0.07	−0.06	−0.07	−0.08	0.28

[a] $\Delta\delta_{max}$ for guest at 1:2.5 equiv. (host to guest) and $\Delta\delta_{max}$ for host at 1:5 equiv. [b] Separate studies with guests indicated that the NH shifts reported here do not arise from self-association.

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