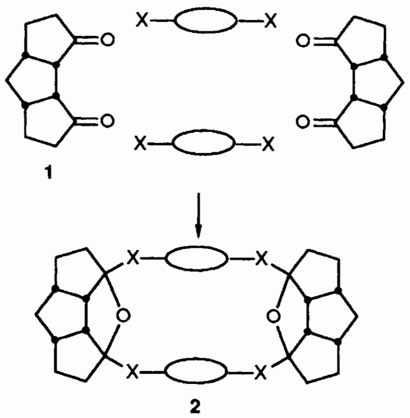
Triquinane-derived Macrocyclic Cyclophane Hosts

Goverdhan Mehta,*[a] Chebiyyam Prabhakar,[a] Munirathinam Nethaji[b] and Kailasam Venkatesan[c]

[a] *School of Chemistry, University of Hyderabad, Hyderabad 500 134, India*
[b] *Department of Inorganic & Physical Chemistry, Indian Institute of Science, Bangalore 560 012, India*
[c] *Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India*

A one step stereoselective assembly of novel macrocyclic cyclophane hosts **4a** and **b** from readily available *cis,syn,cis*-triquinane dione and 4,4′-dianilinoalkanes is described.

Cyclophanes and in particular [*n*.1.*n*.1]cyclophanes have received considerable attention in recent years as macrocyclic hosts for a variety of guest molecules.[1] The cyclophane cavities have proved to be versatile probes for evaluating aromatic–aromatic and donor–acceptor interactions as well as solvent effects in host–guest complexation.[2] Readily available *cis,syn,cis*-triquinane dione **1**,[3] with rigid, folded topology and transannularly interacting carbonyl groups,[3,4] appealed to us as an interesting substrate for the construction of macrocyclic polyquinanophanes *e.g.* **2**, employing suitable aromatic spacers, Scheme 1. Herein, we report that **1** indeed engages 4,4′-dianilinoalkane units, which function as aromatic spacers and cavity walls, to assemble novel cyclophanes through a multi-molecular, multi-event sequence in which as many as eight σ bonds are formed in a one-pot reaction.



Scheme 1

Stirring a 1 : 3 mixture of **1** and 4,4′-methylenedianiline **3a** in glacial acetic acid (6–8 h, 30 °C) followed by chromatography (silica gel) led to the isolation of macrocyclic cyclophane **4a** in *ca.* 15% yield as the major characterisable product. The structure of **4a** was deduced by fast atom bombardment MS (M^+ 680), 500 MHz ^1H NMR (Table 1) and 100 MHz ^{13}C NMR.† In particular, the symmetry element (20 line ^{13}C NMR with single resonance at δ 40.0 due to the two equivalent methylenes of the methylenedianiline spacers) and the presence of 1,4- and 1,2,4-substituted aromatic moieties, with the mutual shielding of the protons of the proximal, face-to-face aromatic rings (*cf.* H_a, H_b in **4a** and **b** and **6b**, Table 1), comprising the cyclophane-wall, strongly supported the as-

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† *Selected spectral data* for **4a**: ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.6, 34.2, 35.9, 38.3, 40.0, 42.0 (2C), 42.5, 58.2, 66.2, 73.0, 74.0, 114.0, 114.5, 127.5, 128.6, 130.6, 131.6, 142.5, 143.2

4b: ^{13}C NMR (50 MHz, $CDCl_3$): δ 29.5, 34.1, 35.5, 35.8, 38.3, 41.9, 42.8, 57.9, 66.4, 72.8, 74.3, 113.9, 114.8, 125.5, 126.6, 128.1, 128.8, 129.0, 132.5, 142.1, 143.3.

6a: ^{13}C NMR (25.0 MHz, $CDCl_3$): δ 29.4, 34.2, 35.9, 38.2, 41.9, 42.1, 42.5, 58.3, 66.7, 73.0, 74.1, 114.5, 114.9, 116.9, 118.5, 127.0, 127.5, 127.7, 128.9, 145.0, 146.2.

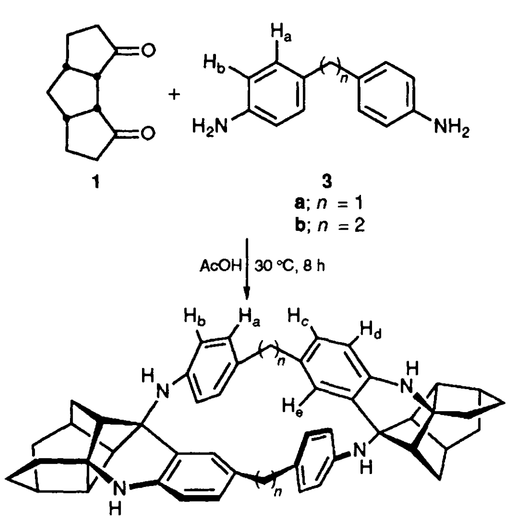
6b: ^{13}C NMR (25.0 MHz, $CDCl_3$): δ 20.2, 20.8, 29.5, 34.2, 35.8, 38.1, 41.9, 42.1, 42.7, 58.2, 66.5, 73.1, 74.1, 114.6, 115.1, 125.9, 127.5, 127.7, 127.8, 128.2, 129.4, 142.4, 144.0.

6c: ^{13}C NMR (25.0 MHz, $CDCl_3$): δ 29.5, 33.7, 35.7, 38.1, 41.8, 42.0, 43.0, 55.5, 57.7, 65.9, 73.2, 74.4, 113.1, 113.3, 114.4, 115.5, 117.3, 130.3, 136.7, 140.1, 151.5, 153.9

Table 1 Chemical shifts (δ) of aromatic protons[a]

Entry	H_a	H_b	H_c	H_d	H_e
3a	6.90	6.54	—	—	—
4a	6.51	6.03	6.80	6.49	6.96
4b	6.68	6.10	6.89	6.52	7.02
6b	6.80	6.26	6.80	6.44	7.16

[a] H_a, H_b, H_c and H_d: doublets (*J ca.* 9 Hz); H_e: singlet.

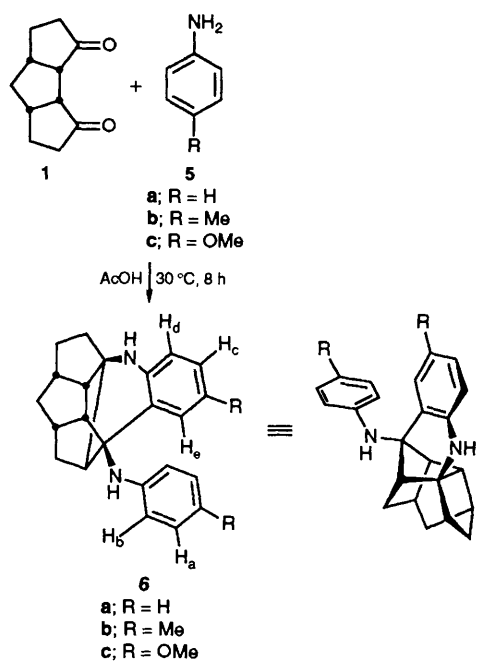


Scheme 2

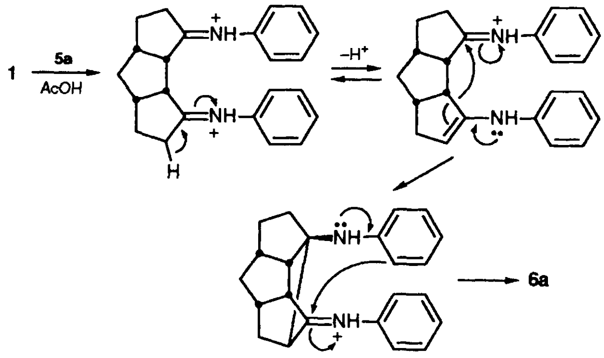
signed structure.‡ The occurrence of a novel transannular cyclisation in the triquinane moiety enroute to **4a** was unravelled by the comparison of the ^{13}C NMR values of the alicyclic carbons of **4a** with those of the product **6a** obtained from **1** and aniline; the X-ray crystal structure has been determined (*vide infra*).§

As with **4a**, expanded cyclophane **4b** was obtained from **1** and 4,4′-ethylenedianiline **3b** in *ca.* 15% yield, Scheme 2.† Energy minimized[5] modelled structures of **4a** and **b** provide an indication of the size of the cavity (channel-like) with face-to-face aromatic rings *ca.* 9.4 and 4.8 Å apart in **4a** and 10.5 and 4.8 Å in **4b**.

As a model for the complex events observed in the reaction between **1** and **3a** and **b**, the reaction of the triquinane dione **1** with aniline **5a**, *p*-toluidine **5b** and *p*-anisidine **5c** was studied. In each case, a major 1 : 2 addition product was obtained **6a**, **b** and **c**, respectively (30–40% yield), Scheme 3. The structure of the aniline addition product **6a** was solved by single crystal X-ray structure determination which clearly revealed the transannular C–C bond formation within the triquinane moiety. A perspective is shown in Fig. 1.§ The structures of **6b** and **c** follow from the close resemblance of their ^1H and ^{13}C NMR spectral data with **6a**.† A plausible mechanism for the formation of **6a** from **1** is shown in Scheme 4 and an extension



Scheme 3



Scheme 4

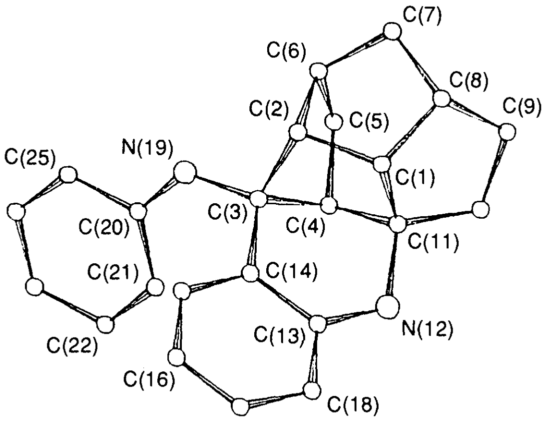


Fig. 1 A perspective view of **6a**

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‡ While for **4a** and **b** two identical polyquinane derived carbocyclic fragments have been depicted, a diastereoisomeric structure with the two carbocyclic moieties having an enantiomeric relationship cannot be ruled out. However, the shape and size of the cyclophane core remains essentially the same in the two diastereoisomeric forms.

§ *Crystal data* for **6a**: $C_{23}H_{24}N_2$, monoclinic, space group $P2_1/a$, a = 12.049(1), b = 10.804(6), c = 12.960(1) Å, β = 92.07(1)°, V = 1686.0(1) Å^3, Z = 4, D_c = 1.294 g cm^{-3}, Mo-Kα (λ = 0.7107 Å), μ = 0.705 cm^{-1} $F(000)$ = 704. Intensity data were collected on an Enraf-Nonius CAD-4 diffractometer in the w/2θ scan mode. A total of 3362 reflections were measured of which 2953 were 'unique' and 2577 were 'observed' with $|F_o| \geq 5.0\sigma|F_o|$. The intensity was corrected for Lorentz and polarisation but not for absorption. The structure was solved by SHELXS-86 and the full-matrix least-squares refinement on $|F_o|$ with non-H atoms anisotropic and H-atoms isotropic converged to an R-factor of 0.057, R_w = 0.043. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

of this mechanism could be invoked to explain the formation of **4a** and **b** from **1** and **3a** and **b**, respectively.¶

In summary, we have observed a new transannular cyclisation in the triquinane system **1**, which promotes the assembly of the novel macrocyclic hosts **4a** and **b** in the presence of spacers **3a** and **b**, respectively, in a one-pot reaction. The host–guest chemistry of **4a** and **b** is currently being pursued.

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¶ Alternative mechanisms, differing in minor details, for the formation of **6a** from **1** are also possible.

References

1 K. Odashima, A. Itai, Y. Iitaka and K. Koga, *J. Am. Chem. Soc.*, 1980, **102**, 2504; K. Odashima, A. Itai, Y. Iitaka, Y. Arata and K. Koga, *Tetrahedron Lett.*, 1980, 4347. Reviews: F. Diederich, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 362; C. Seel and F. Vogtle, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 528; D. Philip and J. F. Stoddart, *Synlett*, 1991, 445; H.-J. Schneider, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1417.

2 S. B. Ferguson, E. M. Sanford, E. M. Seward and F. Diederich, *J. Am. Chem. Soc.*, 1991, **113**, 5410 and references cited therein.

3 G. Mehta, A. Srikrishna, A. V. Reddy and M. S. Nair, *Tetrahedron*, 1981, **37**, 4543.

4 G. Mehta, K. S. Rao, N. Krishnamurthy, V. Srinivas and D. Balasubramanian, *Tetrahedron*, 1989, **45**, 2743; G. Mehta, C. Prabhakar, N. Krishnamurthy and M. S. Nair, *Synth. Commun.*, 1990, **20**, 3467.

5 N. L. Allinger, *J. Am. Chem. Soc.*, 1977, **99**, 8122; N. L. Allinger and Y. H. Yuh, *QCPE*, 1980, **11**, 395.