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FROM CAGES TO WEDGES AND CLEFTS: DESIGN OF SOME NOVEL HOSTS BASED ON cis, syn, cis-TRIQUINANE FRAMEWORK

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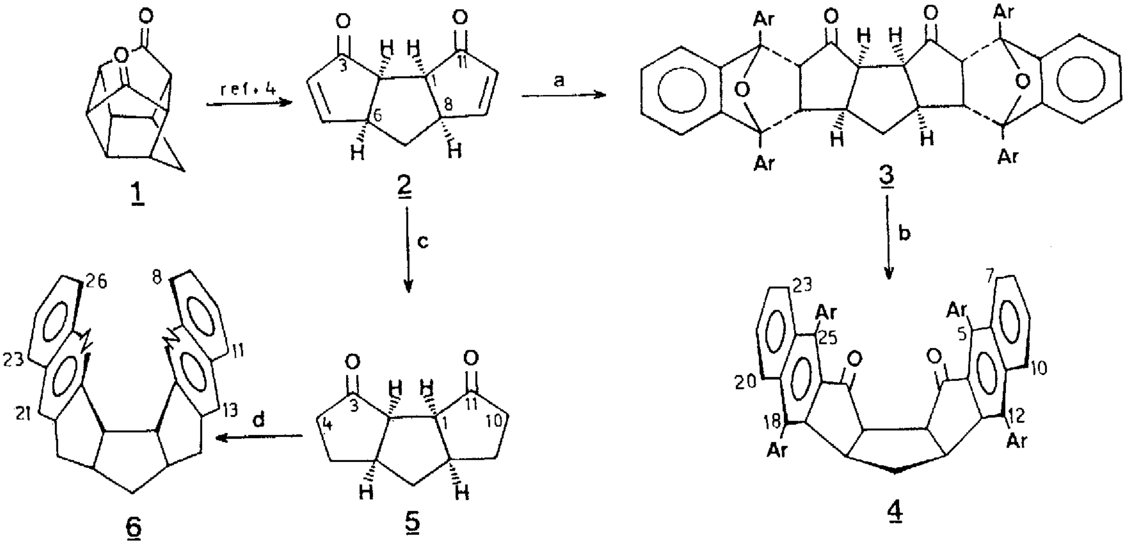
Summary: Annulation of aromatic rings on the folded cis,syn,cis-triquinane backbone has led to the design of potential host systems 4 and 6 whose crystal structures have been determined.

Molecular recognition employing wholly synthetic compounds, designed and assembled to function as molecular receptors or hosts for diverse chemical species, is an area of ascending importance.[1] In recent years, synthetic chemists have endeavoured to craft many receptor molecules which possess rigid structures and incorporate a range of topological features and binding sites.[1] As a part of our interest[2] in the area, we report here the creation of two novel shapes to serve as potential hosts by restructuring the abundantly available Cookson's caged-dione 1 (PCUD)[3] via uncaging and aromatic annulations.

Reaction of cis,syn,cis-triquinane bis-enone 2, accessible from PCUD in one step,[4] with excess of diphenylisobenzofuran in refluxing toluene furnished a 1:2 cycloadduct 3 (60%)[5] whose gross structure was revealed through its spectral characteristics. Acid mediated aromatisation of 3 smoothly led to 4 (64%) having bis-naphthoannulation at the C_4-C_5 and C_9-C_{10} positions of the triquinane framework. While the formulation of 4 was commensurate with its 300 MHz ^{1}H NMR and ^{13}C NMR spectral data,[5] its full stereostructure was elucidated via single crystal X-ray structural analysis, Fig.1.[6] The key nonbonded intramolecular separations are shown in Table 1 and the dihedral angle between the naphthalene rings (i.e., the angle between the extended planes of the aromatic rings) is 46.5°. This data provides a definitive indication of the existence of a molecular cleft in 4 with a pronounced lipophilic posterior and strategically placed carbonyl recognition sites.

To achieve annulations at C_3-C_4 and C_{10}-C_{11} positions of the triquinane moiety, the bis-enone



Reagents & Yields: (a) diphenylisobenzofuran (2.2 equiv.), toluene, Δ ,16h, 60%. (b) 98% H_2SO_4-gl.AcOH (1:10), 60°C, 6h, 64%. (c) 10% Pd/C-H_2, EtOAc, quant. (d) 2-aminobenzaldehyde (3 equiv.), EtOH - 15% KOH-MeOH, Δ, 6h, 27%.

Fig.1: Molecular Structure of 4

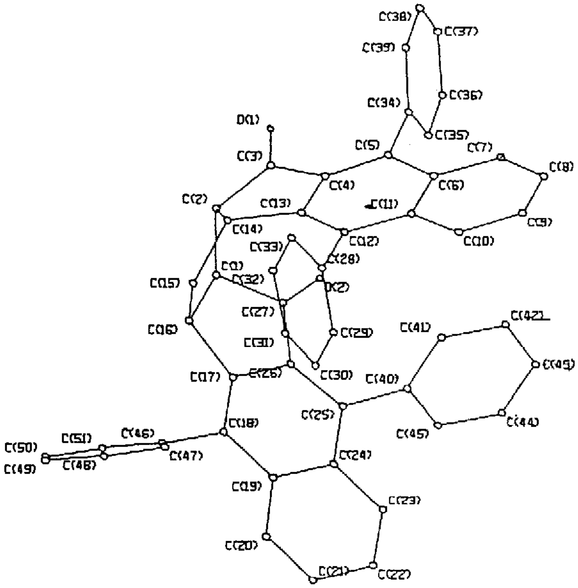


Table 1

Selected Interatomic Distances in 4

From	To	Distance (Å)
C(10)	C(20)	7.705
C(7)	C(23)	7.843
C(12)	C(18)	5.064
C(5)	C(25)	5.392

Fig.2: Molecular Structure of 6

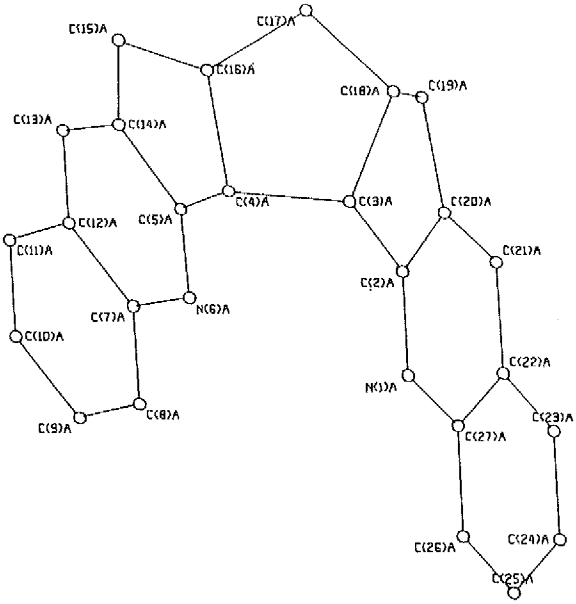


Table 2

Selected Interatomic Distances in 6

From	To	Distance (Å)
C(8)	C(26)	4.950
C(11)	C(23)	7.389
N(1)	N(6)	3.186
C(13)	C(21)	5.761

2 was reduced to the tetrahydro dione 5 and subjected to double Freidlaender condensation employing excess of 2-aminobenzaldehyde as the reacting partner.[10] The bis-quinolinotriquinane 6 (27%) was obtained, as planned, and its 500 MHz ^{1}H NMR and ^{13}C NMR values were in agreement with its formulation. However, unequivocal support for stereostructure 6 was achieved through single crystal X-ray diffraction studies, Fig.2.[11] Significant interatomic distances in 6 are shown in Table 2 and the dihedral angle between the planes of two quinoline rings is 65.2°. Thus, there is a clear evidence that the two quinoline moieties are twisted with respect to one another and form a 'wedge-like' shape with the two nitrogen atoms occupying proximal positions.[12]

In short, we have demonstrated that the folded triquinane framework can be readily elaborated into different shapes by choosing the sites of annulation. Further efforts in the area, particularly towards the enclosed polyaza cavity systems and recognition studies with 4 and 6 are currently underway.[13]

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5. All new compounds were fully characterised. Selected spectral data are as follows : (4): ^{1}H NMR (DMSO-d$_6$, 300 MHz) δ 1.3 (m, 1H), 1.7 (m, 1H), 3.45 (m, 2H), 3.85 (m, 2H), 6.62 (d, 2H), 6.71 (d, 2H), 7.18 (q, 4H), 7.3 - 7.6 (m, 20H). ^{13}C NMR (CDCl$_3$, 25 MHz) δ 45.8, 57.6, 125.8, 125.9, 126.8, 127.4, 127.6, 128.1, 128.4, 128.7, 129.0, 129.3, 129.8, 130.1, 130.3, 130.7, 130.9, 132.7, 135.6, 136.0, 137.7, 139.5, 146.8, 203.4. (6): ^{1}H NMR (CDCl$_3$, 500 MHz) δ 1.45 (ddd, 1H), 2.39 (dd, 2H), 2.64 (ddd, 1H), 3.13 (dd, 2H), 3.30 (m, 2H), 4.27 (dd, 2H), 7.36 (m, 2H), 7.45 (m, 2H), 7.53 (d, 2H), 7.60 (d, 4H). ^{13}C NMR (CDCl$_3$, 25 MHz) δ 37.2, 39.7, 44.8, 56.1, 125.3, 127.1, 127.4, 127.8, 129.3, 130.1, 135.8, 147.4, 167.1.

6. Crystal data for 4: $C_{51}H_{34}O_2$, M = 678.8, Triclinic, P$\bar{1}$, a = 11.172(3), b = 12.968(4), c = 15.372(3) Å, α = 61.52(2), β = 64.68(2), γ = 74.82(3), U = 1764.9 A^3, D$_c$ = 1.28 gCm^{-3}, μ = 0.5 Cm^{-1}, F(000) = 712, Z = 2. CuKα intensity data were collected on an Enraf Nonius CAD-4 diffractometer, for a crystal of size 0.3 x 0.12 x 0.12 mm, up to (sin Θ)/λ = 0.497 Å^{-1}, using ω-2Θ scans. Of the 3814 reflections measured, 3792 were considered observed. Lorentz and polarization corrections were applied. The structure was solved by direct methods by 'saytan' option[7] of MULTAN[8]. The E map computed with the best set of phases revealed 47 of the 53 non-H atoms. A weighted Fourier based on these 47 atoms gave the complete structure. 33 of the 34 H-atoms were located from difference Fourier maps computed at various stages of refinement. The H-atom bonded to C(49) was fixed geometrically. Full-matrix least-squares refinement on F's using SHELX400[9] with the H-atoms refined isotropically and all others refined anisotropically, converged at R = 0.063 for 2655 reflections [I > 1.5σ (I)] and 611 parameters. Individual weights, $w = [\sigma^2 F + 0.0017 \times F^2]^{-1}$, wR = 0.056. Maximum Δ/σ = 0.529; Maximum and minimum electron densities in the final difference Fourier map are 0.24 and -0.28 eA^{-3}.

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11. Crystal data for 6 : $C_{25}H_{20}N_2$, M = 348.4, Triclinic, P$\bar{1}$, a = 12.183(3), b = 12.611(3), c = 15.507(3) Å, α = 67.32(2), β = 73.49(2), γ = 58.15(2), U = 1856.7 A^3, D$_c$ = 1.25 gCm^{-3}, μ = 0.5 Cm^{-1}, F(000) = 736, Z = 4. CuKα intensity data were collected on an Enraf Nonius CAD-4 diffractometer, for a crystal of size 0.18 x 0.1 x 0.06 mm, Θlimit 55°, ω-2Θ scans. 3824 reflections were considered observed. Lorentz and polarization corrections were applied. The structure was solved by direct methods using 'saytan' option[7] of MULTAN[8]. The E map computed with the best set of phases revealed both the molecules in the asymmetric unit completely. However, data for only one of them is given in Fig.2 and Table 2. The H-atoms were fixed geometrically. Full-matrix least-squares refinement on F's using SHELX400[9], with the non-H-atoms refined anisotropically, and the H-atoms fixed, converged at R = 0.085 for 2671 reflections [F > 3σ(F)] and 488 parameters. Individual weights, $w = [\sigma^2(F) + 0.0018 \times F^2]^{-1}$, wR = 0.089. Maximum Δ/σ = 0.160; Maximum and minimum electron densities within + 0.3 e/A^3.

12. Atomic coordinates, bond lengths & angles and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre.
13. GM thanks UGC for support of this research through Special Assistance and COSIST Programmes in Organic Synthesis.

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