The first members of the octasubstituted naphthalene spider-host series with type I (*abababab*) conformation: gateway to new nano-host gas storage materials†

Louis J. Farrugia,* James H. Gall, David D. MacNicol* and Ross MacSween

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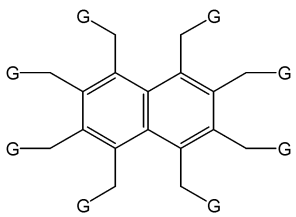
Octakis(*m*-tolyloxymethyl)naphthalene, the first Type I spider host produced, crystallises from tetraglyme forming a novel channel structure with the host molecule attaining exact D_2 symmetry. The (flexible) channel structure is retained for guest CS_2, the host now only having exact C_2 symmetry. The octa-sulfone octakis(*m*-tolylsulfonylmethyl)naphthalene is also of Type I in its triclinic DMSO clathrate. DNMR establishes a substantial difference in molecular flexibilities in solution.

There continues to be intense interest in the design of new crystalline inclusion compounds, in particular those formed by *families* of organic host molecules.[1,2] The spider host series,[3] devised in Glasgow, features conformational versatility and exhibits an extraordinarily wide range of inclusion behaviour; from the uniquely specific inclusion of well-ordered acetone in octakis(4-(2-phenylpropan-2-yl) phenylthio)naphthalene[4] to the very general inclusion of many guests by octakis-(3,4-dimethylphenylthio)naphthalene.[5]



1 G = Br
2 G = OPh
3 G = OPh-3Me
4 G = SPh
5 G = SPh-3Me
6 G = SO_2Ph
7 G = SO_2Ph-3Me

Fourteen host-molecule conformations have been classified,[6] corresponding to *trans* arrangements for *peri*-related groups. Although several of these have been encountered, ranging in symmetry from D_2 to C_1, the attractive Type I (*abababab*) host conformation of D_2 symmetry has remained elusive until now. Seeking to access this previously unknown Type I conformation, we prepared suitably designed two-atom link spider hosts, the first atom corresponding to a methylene group directly attached to the central naphthalene core of the molecule.‡ Such molecules proved readily accessible by persubstitution of octakis(bromomethyl)naphthalene[7] **1** (itself obtained by bromination of octamethylnaphthalene)[8] by judiciously chosen nucleophiles.

Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland, UK. E-mail: davemcn@chem.gla.ac.uk; Fax: +44 (0)141 330 4888; Tel: +44 (0)141 330 4378

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Among the first candidate molecules prepared in good yield§ were the octakis(aryloxymethyl)naphthalenes **2** and **3**. The structures of **2–7** were established from ^{1}H and ^{13}C NMR, MS and microanalytical data: for **3** and **7** also by single crystal X-ray diffraction. Compound **2**, recrystallised from a wide variety of aromatic and non-aromatic solvents, revealed a complete absence of inclusion behaviour. However, *meta*-substitution of the side-chain aromatic rings as in **3** transformed the situation completely. Compound **3** is a very versatile host, forming many crystalline inclusion compounds with non-stoichiometric host–guest ratios, *e.g.* benzene (1 : 1.32), toluene (1 : 1.50), 1,4-dioxane (1 : 1.69), anisole (1 : 0.96), THF (1 : 1.1), tetraglyme (1 : 0.71) and squalene (1 : 0.32), all ratios determined by ^{1}H NMR. The tetraglyme adduct was found to be tetragonal, space group $P4/ncc$. The host molecule **3**, illustrated in Fig. 1, is located on a point of 222 symmetry and so is constrained to be exactly D_2 symmetric. It possesses the desired Type I (*abababab*) conformation and features a modest non-planarity of the central naphthalenecore; the twist angle around the naphthalene central bond is 14.38(16)°. A view of the packing of **3** is shown in Fig. 2(a), looking down the *c*-axis. There are two four-fold symmetric channels running through the unit cell. The long axis of the naphthalene is oriented exactly along the crystallographic *c*-axis, unlike the situation for octakis(*m*-tolylthio)naphthalene (which has a D_2 symmetric Type II (*aabbaabb*) conformation) where the long molecular axis lies exactly normal to the *c*-axis.[6] The tetraglyme guest in **3** was non-commensurately disordered and not located.

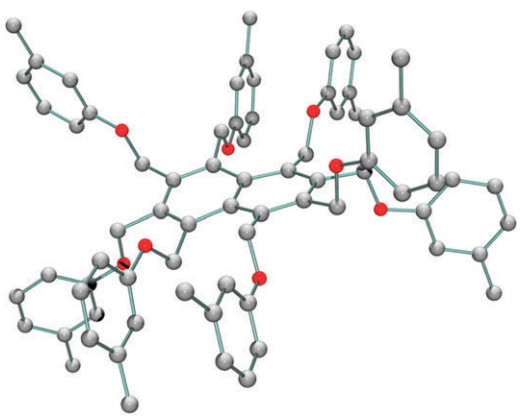

Fig. 1 Molecular structure of **3**, showing the Type I (*abababab*) conformation. H atoms omitted for clarity.

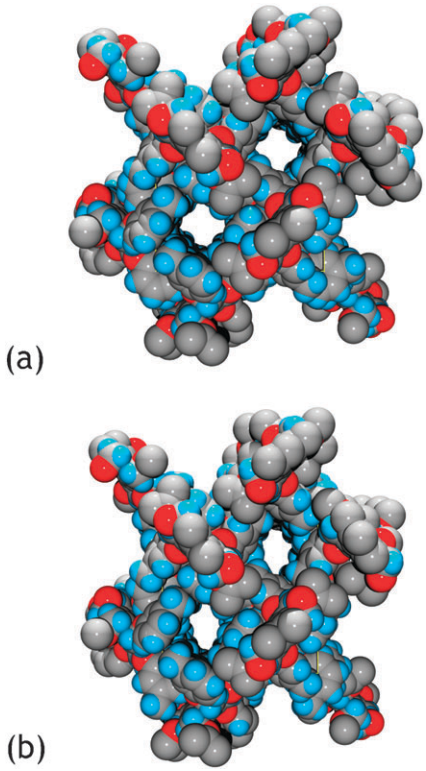

Fig. 2 Space-filling views of the unit cell packing for compound **3** looking down the *c* axis in (a) the tetraglyme inclusion compound and (b) the CS_2 inclusion compound. Guest molecules are not shown to emphasise the differing channel shapes.

From carbon disulfide solution, unexpectedly, an orthorhombic adduct was formed with host–guest ratio of 1 : 3.28 and space group *Pccn*. The host packing is shown in Fig. 2(b) again looking down the *c*-axis but now that of the orthorhombic cell. Two channels per cell still exist but these now possess only two-fold rotational symmetry, rather than the four-fold symmetry of the tetragonal adduct. Three crystallographically independent CS_2 guest molecules, one on a C_2 axis, were located, appearing almost like chock blocks in the molecularly comprised chimney. The presence of these channels, especially in view of the retention of the volatile guest CS_2 component (bp 46 °C), is interesting and brings to mind the elegant study by Sozzani and coworkers of CH_4 absorption by tris(*o*-phenylenedioxy)cyclotriphosphazene.[9] This suggests that gas absorption by **3** may well merit study, though it is not yet known whether the channel structure is stable in the absence of guest molecules. However it is worth noting that the isomorphous octakis-(*m*-tolylthio)naphthalene mentioned above retains enclathrated CH_4 for months[3] and that the same 'open' host packing is present in the stable empty-cage form. Interestingly, in this case small windows of approximately 2 Å diameter exist at the top and bottom of each cage, thus presenting an opportunity for the possible pressure and temperature-dependent reversible storage of molecular hydrogen. Atwood and coworkers have stressed the importance[10] of thermal motion of the host in allowing small guest species to pass through thermally enlarged apertures in the low density polymorph of *p*-*tert*-butylcalix[4]-arene. In order to expand the Type I family members, we analogously prepared octathioethers **4** and **5** from **1**. Oxidation

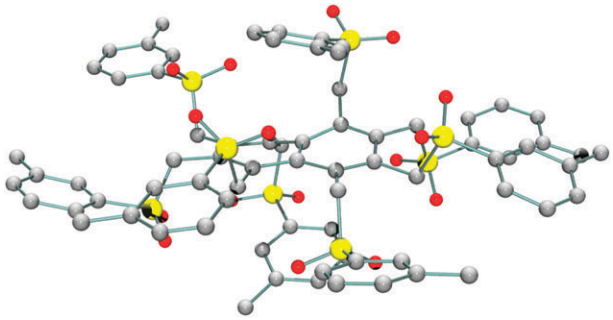

Fig. 3 A view looking approximately along the central naphthalene C–C bond of host **7** in its DMSO clathrate, H atoms and DMSO omitted for clarity. The chiral host molecule has non-crystallographic C_2 symmetry.

of these compounds with hydrogen peroxide in glacial acetic acid gave sulfones **6** and **7**, respectively. Again highlighting[3] the power of *meta*-substitution to promote inclusion behaviour, compound **6** was devoid of host properties whilst **7** formed a crystalline inclusion compound from DMSO, with a host/guest ratio of 1 : 2. This true clathrate is triclinic. Two centrosymmetrically related host molecules occupy general positions in the unit cell, but nonetheless possess the Type I conformation shown in Fig. 3. An unusual feature of this conformation is that two *peri*-related *m*-tolyl rings point inwards and lie roughly parallel to the central naphthalene core of the molecule. Two crystallographically independent DMSO guests, one disordered, are accommodated in a moderately large closed void.

The situation in solution is of conformational interest. The observation of two sharp AB quartets [centred at δ_H 4.28 and 4.66, with ν_{AB} and J_{AB} 29.2, 16.0 and 247.1, 15.6 Hz, respectively] for the diastereotopic protons of the two non-equivalent methylene groups in the 400 MHz ^{1}H NMR spectrum of **7** in CCl_2DCCl_2D at 373 K is consistent with the presence and slow enantiomerisation, on the NMR time-scale, of the chiral Type I conformation in solution. From the absence of detectable lifetime broadening, one may place a *lower limit* on the free energy of activation for enantiomerisation of **7** at *ca.* 19.5 kcal mol^{-1}. This raises the intriguing possibility of optically resolving **7** or analogues with even bulkier side-chains, for use as potential chiral ligands. It may be noted that transition metal complexes of **5**, for example (even when a single metal atom is coordinated), will be expected to have much higher barriers since *all* side chains must undergo a 180° rotation to produce the enantiomeric form. Interestingly, the topomerisation barrier shows a marked dependence upon the *effective* bulkiness of the side-chain groups, and coalescences[11] of AB quartets observed for **3** and **5** allow measurement of $\Delta G^{\#}$ values ($\kappa = \frac{1}{2}$), namely 10.5 ± 0.3 kcal mol^{-1} (at 231 K) for **3** (in $CDCl_3$) and 14.3 ± 0.2 kcal mol^{-1} (at 313 K) for **5** (in CCl_4). Thus formal replacement of oxygen by the larger sulfur atom leads to an approximately 4 kcal mol^{-1} increase in $\Delta G^{\#}$. For our starting material **1**, featuring a bulky bromine side-chain atom, we find a value for $\Delta G^{\#}$ of 15.8 ± 0.2 kcal mol^{-1} (at 342 K) in CCl_4, in accordance with an independent literature finding for **1** in CCl_2DCCl_2D solution.¶

Finally, it may be noted that compounds described above are the first examples of two-atom link spider hosts; their synthesis represents a significant expansion of this conformationally fascinating host series. We thank the University of Glasgow (Loudon Bequest) for financial support (to RM).

Notes and references

‡ Interestingly the ordering of the two-atom link components appears to be crucial. For example, when the sulfur atom is directly bonded to the naphthalene, as in octakis(3,4-dichlorobenzylthio)naphthalene, no evidence for Type I behaviour has been found (C. S. Frampton, D. D. MacNicol, R. MacSween, unpublished results). This molecule has, however, significant host properties and X-ray analysis of its triclinic *p*-chlorotoluene adduct (host/guest ratio 2 : 3) has revealed a not uncommon Type III (*abbabaab*) (C_{2h}) host conformation. Promotion of the Type I conformation may, in part at least, reflect a more favourable juxtapositioning of hydrogen atoms between adjacent methylene groups directly attached to the naphthalene core when the side-chains adopt an *anti*-arrangement.

§ Experimental procedure for the preparation of **2**: **1** (0.25 g, 0.29 mmol, 1 eq.) in DMF (5 mL) was added to sodium phenolate in ethanol, prepared from phenol (0.229 g, 2.44 mmol) and sodium (0.056 g, 2.44 mmol, 8.5 eq.). The reaction mixture was stirred at 50 °C, with diethyl ether (5 mL) and water (5 mL) added after 30 minutes. The organic layer was dried and the solvent removed to give the crude solid. After recrystallisation from diethyl ether/iso-propanol, product **2** was obtained as a solid (0.157 g, 56%), mp 170–174 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (m, 8H), 6.97 (m, 8H), 6.88 (m, 12H), 6.71 (m, 12H), 5.41 (s, 8H), 5.39 (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 157.9, 138.1, 137.0, 133.9, 129.8, 129.5, 121.6, 121.3, 115.2, 114.7, 65.3, 64.1; MS (FAB+) *m*/*z* 976.9 [M+] $C_{66}H_{66}O_8$, calc. as 976.4. Compound **3** was prepared analogously in 68% yield, mp 154–155 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (m, 4H), 6.89 (t, J = 7.8 Hz, 4H), 6.69 (d, J = 7.5 Hz, 4H), 6.56 (m, 8H), 6.54 (m, 8H), 6.47 (s, 4H), 5.38 (s, 8H), 5.35 (s, 8H), 2.18 (s, 12H), 2.07 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 157.9, 139.8, 139.4, 138.1, 137.0, 133.9, 129.5, 129.1, 122.4, 122.0, 116.0, 115.2, 112.3, 112.1, 65.3, 64.1, 21.76, 21.70; MS (FAB+) *m*/*z* 1089.0 [M+], $C_{74}H_{72}O_8$, calc. as 1088.5. Experimental procedure for the preparation of **4**: **1** (0.25 g, 0.29 mmol, 1 eq.) was added to the lithium salt of thiophenol (0.253 g, 2.30 mmol, 8 eq.) and 2.5 M *n*-butyl lithium (1.1 mL, 2.30 mmol, 8 eq.) at 0 °C, in dry THF (5 mL). The reaction mixture was stirred at room temperature, and after 2 hours water (2 mL) and chloroform (5 mL) were added. The organic layer was dried and the solvent removed, to give the product **4** (0.40 g, 32%), mp 177–178 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (m, 40H), 5.10 (broad s, 8H), 4.52 (broad s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 136.2, 135.5, 131.8, 130.7, 129.2, 129.0, 128.8, 126.8, 126.2, 37.1, 33.7; MS (FAB+) *m*/*z* [M+] 1104.7, $C_{66}H_{56}S_8$, calc. as 1104.2. Compound **5** was prepared analogously to **4**, in 40% yield, mp 128–130 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (m, 32H), 5.22 (broad s, 8H), 4.52 (broad s, 8H), 4.56 (broad s, 8H), 2.19 (s, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 138.5, 137.0, 136.4, 136.2, 135.7, 131.9, 131.1, 129.3, 128.8, 128.6, 127.7, 127.6, 127.0, 125.7, 36.7, 33.8, 21.3, 21.2; MS (FAB+) *m*/*z* 1216.6 [M+], $C_{74}H_{72}S_8$, calc. as 1216.3. Experimental procedure for the preparation of **6**: compound **4** (0.144 g, 0.130 mmol, 1 eq.) was added to a solution of hydrogen peroxide (30% in water) (2.03 mL) and acetic acid (20.0 mL) and the reaction mixture was refluxed with water (2 mL) added after 2 hours. Filtration afforded the solid product **6** (0.144 g, 81%), mp > 294 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.3 Hz, 8H), 7.71 (m, 4H), 7.51 (m, 28H), 7.44 (m, 8H), 5.56 (d, J = 15.6 Hz, 4H), 4.87 (m, 8H), 4.50 (d, J = 16.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 138.3, 135.1, 134.9, 131.9, 130.5, 130.2, 128.2, 128.0, 60.2, 56.3; MS (FAB+) [m + 2H] 1362.6, $C_{66}H_{56}O_{16}S_8$ [plus two hydrogens], calc. as 1362.1. Compound **7** was prepared analogously from **5**, in 72% yield, mp 268–270 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (m, 32H), 5.46 (d, J = 15.6 Hz, 4H), 4.80 (d, J = 15.6 Hz, 4H), 4.67 (d, J = 16.0 Hz, 4H), 4.47 (d, J = 16.0 Hz, 4H), 2.37 (s, 12H), 2.26 (s, 12H); MS (FAB+) *m*/*z* 1473.7 [m + H], $C_{74}H_{73}O_{16}S_8$, calc. 1473.3. Crystal data for **3** (tetraglyme adduct): $C_{74}H_{72}O_8$, M = 1089.32, colourless prism, 0.5 × 0.46 × 0.32 mm, tetragonal, space group $P4/ncc$, a = 16.5680(2), c = 26.0484(4) Å, V = 7150.25(16) Å^3, Z = 4, D_c = 1.012 g cm^{-3}, F_{000} = 2320, Nonius KappaCCD, Mo-K$_\alpha$ radiation, λ = 0.71073 Å, T = 150(2) K, θ_{max} = 26.02, 86 187 reflections collected, 3522 unique (R_{int} = 0.0483). Final *GooF* = 1.124, R_1(obs) = 0.0789, wR_2(all) 0.2709, with $I > 2\sigma(I)$, refinement on F^2, 188 parameters, 0 restraints. The tetraglyme solvent molecules were not located crystallographically and their contribution to the structure factors were estimated using the SQUEEZE algorithm in PLATON (A. L. Spek, *J. Appl. Crystallogr.*, 2003, **26**, 7). Crystal data for **3**: $C_{76}H_{72}O_8{\cdot}3.27(CS_2)$, M = 1339.01, colourless prism, 0.7 × 0.7 × 0.5 mm, orthorhombic, space group *Pccn*, a = 15.7611(9), b = 17.0636(9), c = 26.4663(15) Å, V = 7117.9(7) Å^3, Z = 4, D_c = 1.250 g cm^{-3}, F_{000} = 2817.8, Nonius KappaCCD, Mo-K$_\alpha$ radiation, λ = 0.71073 Å, T = 150(2) K, θ_{max} = 26.08, 45 331 reflections collected, 6960 unique (R_{int} = 0.056). Final *GooF* = 1.145, R_1(obs) = 0.0777, wR_2(all) 0.2134, with $I > 2\sigma(I)$, refinement on F^2, 440 parameters, 0 restraints. Crystal data for **7**: $C_{74}H_{72}O_{16}S_8{\cdot}2(C_2H_6OS)$, M = 1630.05, colourless prism, 0.42 × 0.25 × 0.15 mm, triclinic, space group $P\bar{1}$, a = 15.3025, b = 15.9172(6), c = 17.7176(5) Å, α = 92.3101(18), β = 97.8882(19), γ = 115.8882(16)°, V = 3836.4(2) Å^3, Z = 2, D_c = 1.411 g cm^{-3}, F_{000} = 1712, Nonius KappaCCD, Mo-K$_\alpha$ radiation, λ = 0.71073 Å, T = 150(2) K, θ_{max} = 26.11, 54 852 reflections collected, 14 970 unique (R_{int} = 0.0611). Final *GooF* = 1.049, R_1(obs) = 0.074, wR_2(all) 0.2089, with $I > 2\sigma(I)$, refinement on F^2, 966 parameters, 0 restraints.

¶ See S. Simaan, V. Marks, H. E. Gottlieb, A. Stanger and S. E. Biali, *J. Org. Chem.*, 2003, **68**, 637. The authors and C. S. Frampton have also shown by single-crystal X-ray analysis of **1** at 100 K the completely regular alternation of Br atoms above and below the mean plane of **1.** Refinement in space group *Fdd2* gives a final R_1 value of 3.7%.

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