# New Cyclophane Hosts: Polyether-Bridged Hexaoxacyclophanes

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The polyether-bridged hexaoxacyclophane (**3**) has been shown by *X*-ray crystallography to include a $CH_2Cl_2$ molecule within its molecular cavity.

The conformational properties of the free hexaoxacyclophane (**1**) displayed[1] in the solid state encouraged us to progress to the incorporation of polyether ribbons between the two *m*-xylylene rings in (**1**) in order to increase the rigidity of the cyclophane unit and introduce a potential alkali-metal cation binding site. In this communication, we (i) report on the synthesis of the polyether-bridged hexaoxacyclophanes (**2**) and (**3**), and (ii) illustrate by *X*-ray crystallography how (**3**) includes a $CH_2Cl_2$ molecule within its molecular cavity in the solid state.

As a result of separate reactions [$Cs_2CO_3$/MeCN/reflux/24—28 h] of bis(4-hydroxyphenyl) ether[2] with 1,8-bis[2,6-bis(bromomethyl)phenoxy]-3,6-dioxaoctane[3] and 1,11-bis(2,6-bis(bromomethyl)phenoxy)-3,6,9-trioxaundecane[3] respectively (**2**) [3%, m.p. 239—242 °C, *M*, 754 (f.a.b.m.s.); δ($CD_2Cl_2$) 3.28—3.30 (8 H, s and m), 3.78—383 (4 H, m), 5.05 (8 H, s), 6.78—7.01 (16 H, $A_2B_2$), 7.22 (2 H, t, *J* 7.5 Hz), 7.50 (4 H, d, *J* 7.5 Hz) was isolated after preparative t.l.c. [$SiO_2$/$CHCl_3$–EtOAc (20:1, v/v)] and (**3**) [7%, m.p. 257—260 °C, *M*, 798 (f.a.b.m.s.), δ($CD_2Cl_2$) 3.50—3.57 (8 H, m), 3.63—3.66 (4 H, m), 3.82—3.87 (4 H, m), 5.14 (8 H, s), 6.74—7.03 (16 H, $A_2B_2$), 7.21 (2 H, t, *J* 7.5 Hz), and 7.52 (4 H, d, *J* 7.5 Hz) was isolated after column chromatography [$SiO_2$/$CH_2Cl_2$–$Et_2O$ (20:1, v/v)]. Single crystals of (**3**) suitable for *X*-ray crystallography were grown from $CH_2Cl_2$–hexane.

# New Cyclophane Hosts: A Hexaoxacyclophane

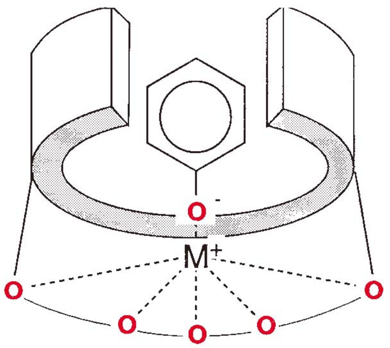
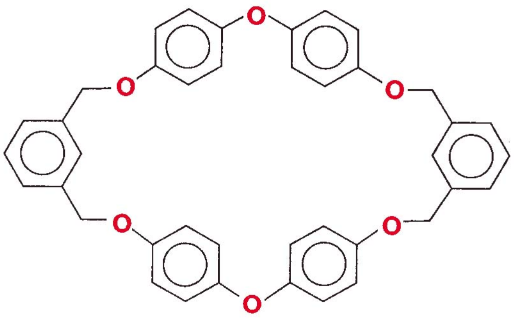


**Figure 1.** Diagrammatic representation of a potential bireceptor molecule for alkali metal phenoxides



(1)

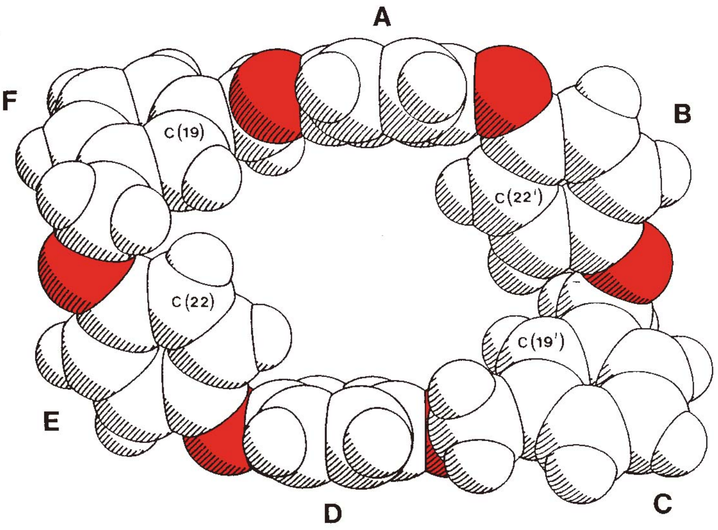


**Figure 2.** Space-filling representation of the solid state structure of (**1**): the oxygen atoms are shown in red

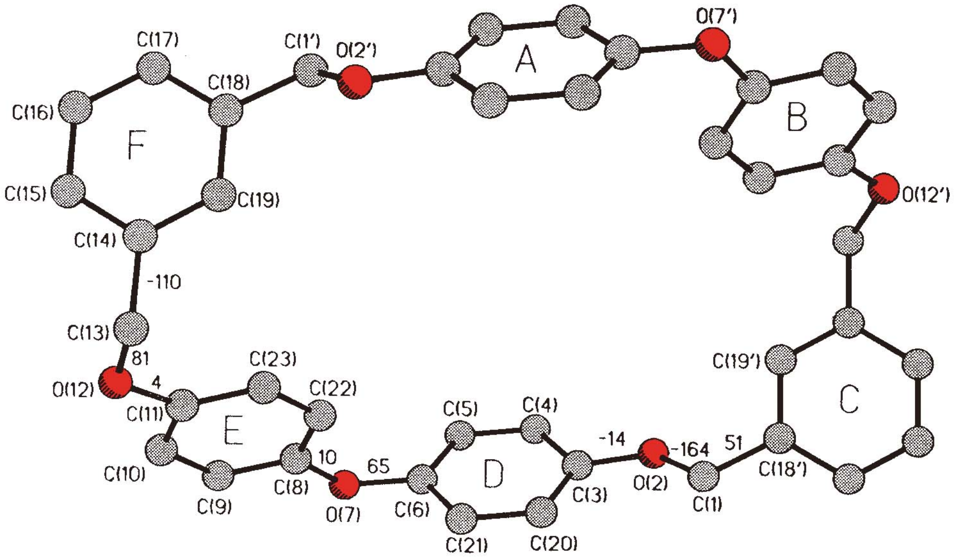


**Figure 3.** The solid-state structure of (**1**) giving the atomic numbering scheme and selected torsional angles: the carbon and oxygen atoms are shown in grey and red, respectively. Note that there is a non-linearity of 9° between the O(7)–C(8) and C(11)–O(12) bonds emanating from ring E (and from ring B)

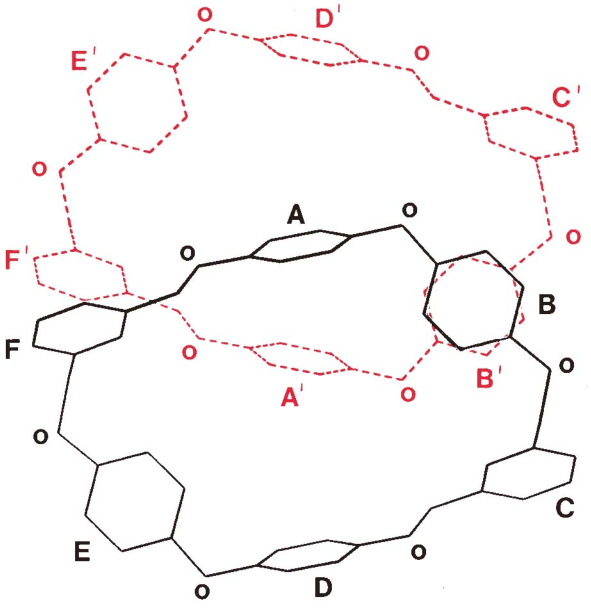


**Figure 4.** The packing of adjacent molecules (red and black) of (**1**) in the crystal. Aromatic ring centroid-centroid distances (Å), angles (°) between their mean planes: AA′, 4.77, 20; BB′, 3.83, 6; FF′, 4.70, 19

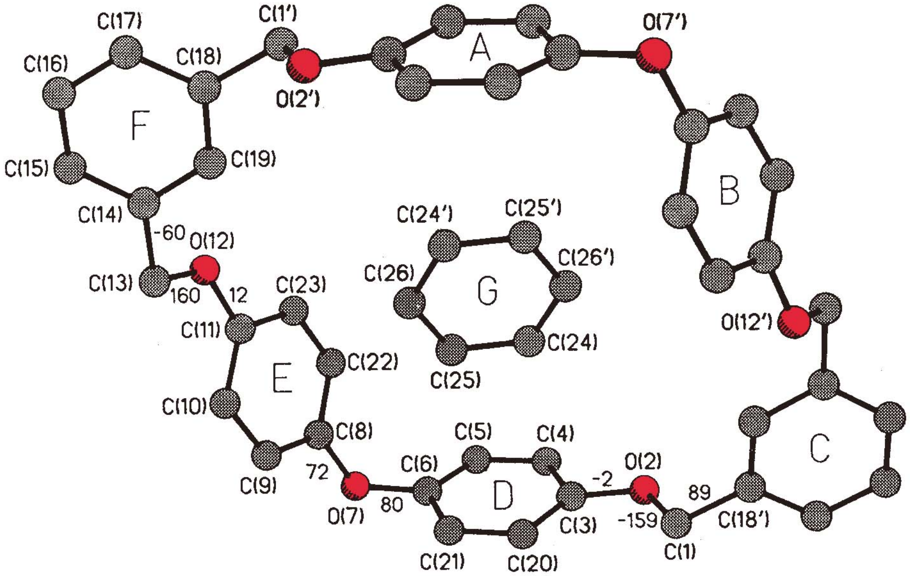


**Figure 5.** The solid-state structure of (**1**)•$C_6H_6$ giving the aromatic numbering scheme and selected torsional angles: the carbon and oxygen atoms are shown in grey and red, respectively

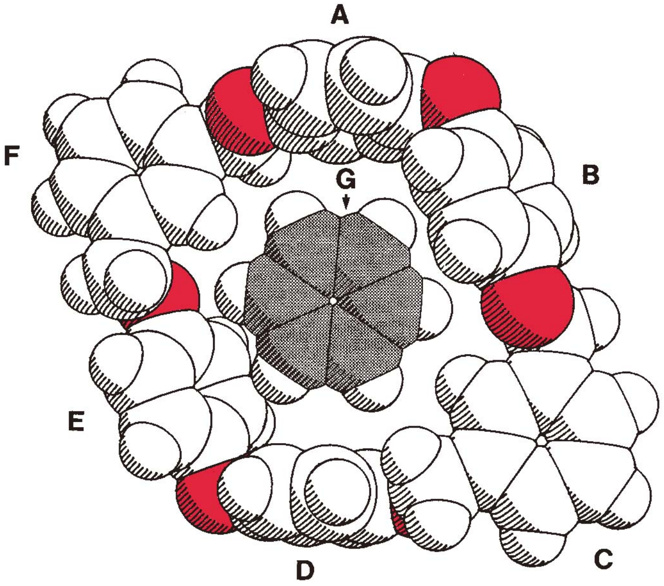


**Figure 6.** Space-filling representation of the solid-state structure of (**1**)•$C_6H_6$ corresponding to the view of the framework representation illustrated in Figure 5: the oxygen atoms are shown in red and the encapsulated benzene molecule is highlighted in grey

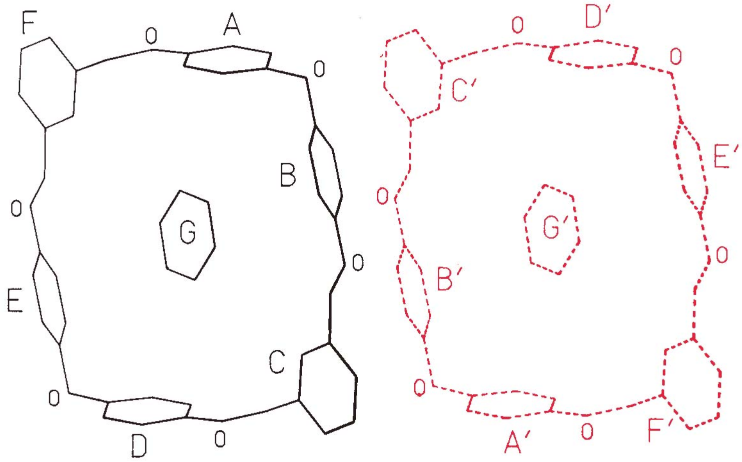


**Figure 7.** The packing of adjacent supermolecules (red and black) of (**1**)•$C_6H_6$ in the crystal

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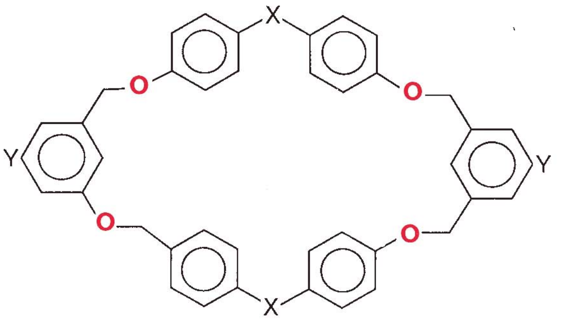
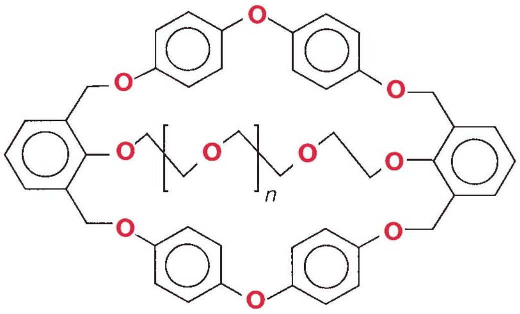
Formulae



(1) X = O; Y = H (4) X = $CMe_2$; Y = $NO_2$



(2) *n* = 1 (3) *n* = 2

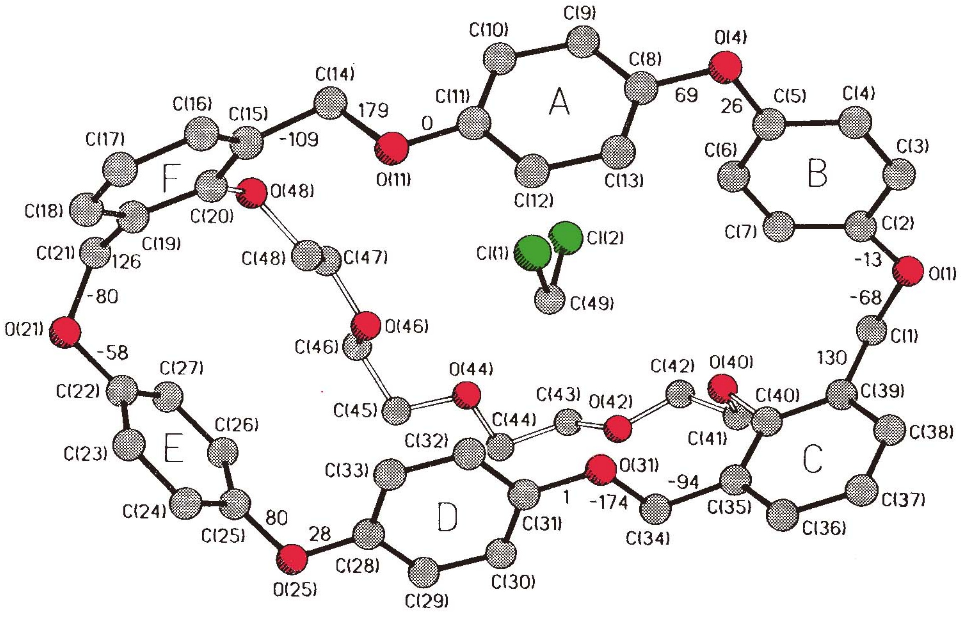


**Figure 1.** The solid-state structure of (**3**)·$CH_2Cl_2$ giving the atomic numbering scheme and selected torsional angles: the carbon, oxygen, and chlorine atoms are shown in grey, red and green, respectively. The angles between the O(1)–C(2) and C(5)–O(4) and O(25)–C(25) and C(22)–O(21) bonds are 8 and 2°, respectively

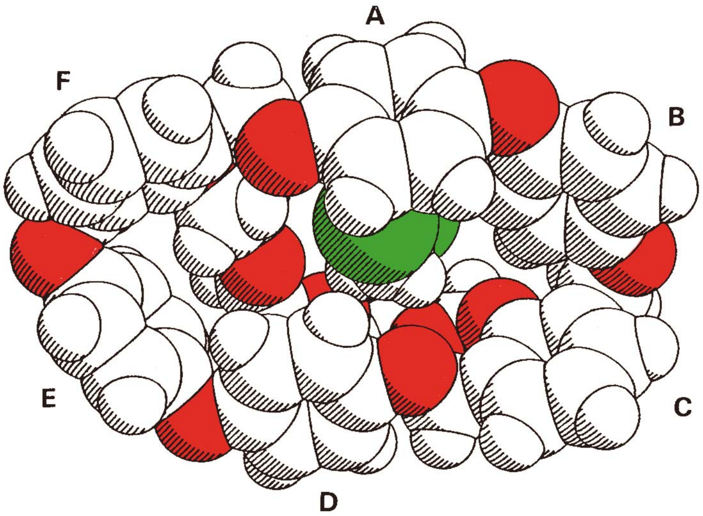


**Figure 2.** Space-filling representation of the solid state structure of (**3**)•$CH_2Cl_2$ corresponding to the view of the framework representation illustrate in Figure 1: the oxygen and chlorine atoms are shown in red and green, respectively

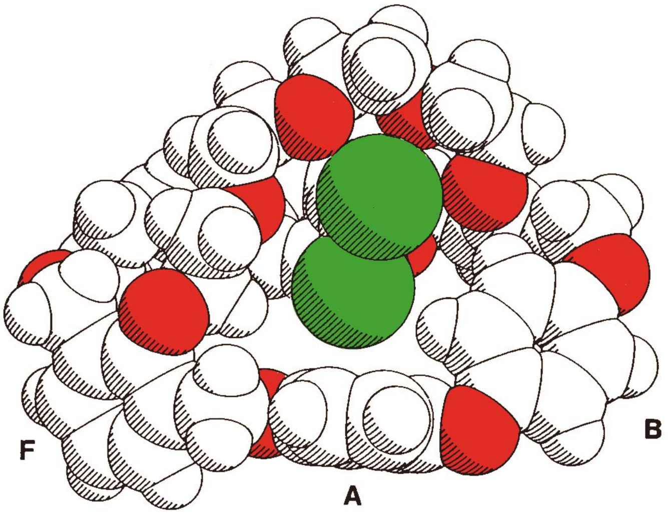


**Figure 3.** Space-filling representation of the solid state structure of (**3**)•$CH_2Cl_2$ looking into the molecular cave of (**1**): the oxygen and chlorine atom are shown in red and green, respectively

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The *X*-ray crystal structure* of (**3**) reveals (Figures 1 and 2) that the conformation of its hexaoxacyclophane unit changes from that adopted[1] in (**1**). The aromatic rings A and D are no longer parallel but they are folded in towards each other and so partially fill the macrocyclic ring aperture that was present[1] in (**1**). However, the bridging polyether ribbon, together with the aromatic rings F, A, and B form (Figure 3) the boundary to a sizable molecular cave in which a $CH_2Cl_2$ molecule[4] resides.† The closest contacts to this encapsulated substrate are between one of the $CH_2$ protons [on C(49)] of $CH_2Cl_2$ and the two oxygen atoms, O(44) and O(40), of the bridging polyether ribbon in (**3**), namely 2.51 and 2.55 Å, respectively.‡ In common with (**1**), aromatic rings A and B, and D and E, of the two diphenyl ether units are approximately orthogonal to each other. Again, in both cases, these geometries are produced by two non-zero torsional components about the O(4)–C(5), O(4)–C(8), and O(25)–C(25), O(25)–C(28) bonds, respectively (Figure 1). Approximate coplanarity[5] of the methyleneoxy units with the aromatic rings A, B and D is retained; however, the C(21)–O(21) bond is rotated by 58° out-of-the-plane of aromatic ring E. The conformation of the polyether ribbon linking C(40) with C(20) has the torsional angle sequence $g^-g^+g^-a$ for the four contiguous O–C–C–O units.

The solubility properties of (**2**) and (**3**) are very different: whilst (**2**) is virtually insoluble in most organic solvents, (**3**) is readily soluble in, for example, $CHCl_3$ and $CH_2Cl_2$. As in the case of (**1**),[1] when 1 molar equivalent of potassium *p*-nitrophenolate was added to a $CD_2Cl_2$ solution (*ca.* 6 mM) of (**3**), insignificantly small displacements (*ca.* 0.03 p.p.m.) in the chemical shifts of the protons on the anion relative to those for the same protons in the free potassium *p*-nitrophenolate in $CD_2Cl_2$ were observed.§ Dynamic $^1H$ n.m.r. spectroscopy ($CD_2Cl_2$) indicates that (**3**) undergoes a conformational inversion process as a result of passage of the polyether ribbon through the middle of the cyclophane (*cf.* ref. 6). The singlet for the benzylic methylene protons in (**3**) at room temperature separates out into an AB system below −83 °C. The barrier to conformational inversion was increased by only 2.7 kJ mol$^{-1}$ from 36.7 to 39.4 kJ mol$^{-1}$ on addition of 1 molar equivalent of potassium *p*-nitrophenolate to (**3**). And so we conclude that any complexation is very small and that it is going to be necessary to add a second polyether ribbon (*i.e.* form a macrocyclic polyether) across the floor of the cyclophane.

## Acknowledgements

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## References

1 G. R. Brown, S. S. Chana, A. M. Z. Slawin, J. F. Stoddart, and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, preceding communication.
2 G. Koga, M. Yasaka, and Y. Nakano, *Org. Prep. Proced.*, 1969, **1(3)**, 205.
3 D. R. Alston, A. M. Z. Slawin, J. F. Stoddart, D. J. Williams, and R. Zarzycki, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 692.
4 For other examples of $CH_2Cl_2$ (and $CHCl_3$) molecules included within the cavities of synthetic neutral host molecules, see F. Vögtle, H. Puff, E. Friedrichs, and W. M. Müller, *J. Chem. Soc., Chem. Commun.*, 1983, 1398; F. Vögtle and W. M. Müller, *J. Incl. Phenom.*, 1984, **1**, 369; I. Tabushi, K. Yamamura, H. Nonoguchi, K. Hirotsu, and T. Higuchi, *J. Am. Chem. Soc.*, 1984, **106**, 2621; J. Canceill, M. Cesario, A. Collet, J. Guilhem, and C. Pascard, *J. Chem. Soc., Chem. Commun.*, 1985, 361; J. Canceill, M. Cesario, A. Collet, J. Guilhem, and C. Pascard, *ibid.*, p. 361; J. Canceill, M. Cesario, A. Collet, J. Guilhem, C. Riche, and C. Pascard, *ibid.*, 1986, 339; J. Canceill, L. Lacombe, and A. Collet, *J. Am. Chem. Soc.*, 1986, **104**, 4230; A. W. Coleman, S. G. Bott, and J. L. Atwood, *J. Incl. Phenom.*, 1986, **4**, 247; I. Goldberg and K. M. Doxsee, *ibid.*, p. 303; J. Jazwinski, J.-M. Lehn, R. Méric, J.-P. Vigneron, M. Cesario, J. Guilhem, and C. Pascard, *Tetrahedron Lett.*, 1987, **28**, 3489.
5 *cf.* A. Makriyannis and S. Fesik, *J. Am. Chem. Soc.*, 1982, **104**, 6462; L. I. Kruse and J. K. Cha, *J. Chem. Soc., Chem. Commun.*, 1982, 1329; J. D. Mersh, J. K. M. Sanders, and S. A. Maitlin, *ibid.*, 1983, 306.
6 D. R. Alston, A. M. Z. Slawin, J. F. Stoddart, and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 821; H. M. Colquhoun, J. F. Stoddart, and D. J. Williams, *ibid.*, 1986, **25**, 487.

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* *Crystal data for compound* (**3**). $C_{48}H_{46}O_{11}\cdot CH_2Cl_2$, $M = 883.8$, triclinic, $a = 9.524(3)$, $b = 14.953(5)$, $c = 17.278(7)$ Å, $\alpha = 112.40(3)$, $\beta = 89.83(3)$, $\gamma = 98.53(3)°$, $U = 2\,246$ Å$^3$, space group $P\bar{1}$, $Z = 2$, $D_c = 1.31$ g cm$^{-3}$, $\mu$(Cu-$K_\alpha$) = 18 cm$^{-1}$. The structure was solved by direct methods and refined anisotropically to give $R = 0.066$, $R_w = 0.066$ for 3 985 independent observed reflections [$|F_0| \geq 3\sigma(|F_0|)$, $\theta \leq 55°$]. Data were measured on a Nicolet R3m diffractometer with Cu-$K_\alpha$ radiation (graphite monochromator) using ω-scans. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See 'Instructions for Authors (1989),' *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

† When a tetrahydrofuran (THF) solution of (**3**) was allowed to evaporate, single crystals containing THF and suitable for *X*-ray crystallography were isolated. The results of this investigation will be reported at a later date.

‡ Note, however, that there are no significant intermolecular short contacts between symmetry related (**3**)·$CH_2Cl_2$ molecular complexes.

§ Interestingly, when attempts were made to record the negative-ion f.a.b.m.s. of (**3**):potassium *p*-nitrophenolate in *m*-nitrobenzyl alcohol (*m*NBA) as the matrix, a peak was observed at *m/z* 951 for $[M + m\text{NBA}]^-$. This observation suggests that (**3**) is complexing with *m*NBA under the conditions of the f.a.b. experiment, *i.e.* *m*NBA is present in large excess.