Intramolecular O–H · · · π hydrogen bond found in [2.2]metacyclophane systems: spectral properties and X-ray crystallographic analysis of 8-hydroxymethyl[2.2]metacyclophanes

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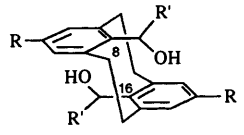
In 5-*tert*-butyl-8-hydroxymethyl[2.2]metacyclophanes 3b–h and *meso*-8,8′-(1,2-dihydroxyethane-1,2-diyl)bis(5-*tert*-butyl[2.2]metacyclophane) *meso*-4, the hydroxy group forms an intramolecular O–H · · · π hydrogen bond with the opposing benzene ring as is indicated by IR spectroscopy. This is confirmed in the cases of the 13-*tert*-butyl derivative 3h and *meso*-4 by X-ray crystallographic analyses.

Introduction

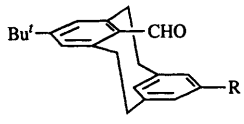
O–H · · · π Hydrogen bonds between hydroxy groups and the π-electrons of aromatic rings, and acetylenic and olefinic bonds have been studied spectroscopically in the last 3–4 decades[1] since they often play an important role in determining the conformation of various organic molecules,[1–3] in host–guest chemistry[4] and in biological systems.[5] However, it is sometimes difficult to identify O–H · · · π hydrogen bonds, since their interactions are weak; the binding energy of O–H · · · π hydrogen bonds is estimated to be < 4.0 kcal mol^{-1}.[6] Recently, several X-ray crystallographic analyses have been carried out in order to verify short non-bonded distances between hydroxy groups and an aromatic ring or an acetylenic bond.[2–4]

In the [2.2]metacyclophane ([2.2]MCP) structure,[7] an internal hydroxy group at positions 8 or 16 is expected to interact with π-electrons of the opposing benzene ring. The preparation of 8,16-di(hydroxymethyl)[2.2]MCP **1** has been reported[8] previously, however, without any mention of such an interaction.

In this paper, studies of O–H · · · π hydrogen bonding in 8-hydroxymethyl[2.2]MCP **3** and bis(hydroxy[2.2]MCP) **4** are discussed on the basis of the IR spectra and X-ray crystallographic analyses.

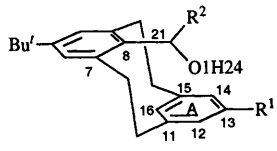


1



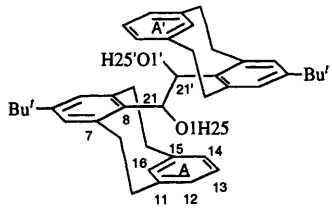
2

2a R = H
b R = Br
c R = OMe
d R = Bu^t



3

3a R^1 = H, R^2 = H
b R^1 = H, R^2 = Me
c R^1 = H, R^2 = Et
d R^1 = H, R^2 = CH_2Ph
e R^1 = H, R^2 = $CH_2C_6H_4Br$-*p*
f R^1 = Br, R^2 = CH_2Ph
g R^1 = OMe, R^2 = CH_2Ph
h R^1 = Bu^t,



meso-**4**

(±)-**4**

Results and discussion

Synthesis

8-Hydroxymethyl[2.2]MCP **3a** was prepared by reduction of 8-formyl[2.2]MCP **2a**[7a] and **3b–h** by Grignard reactions of **2**[7a] in good yields. A *meso*- and (±)- mixture (49:51) of bis-(hydroxy[2.2]MCP) **4** was prepared in 74% yield by a coupling reaction of **2a** using $TiCl_3(DME)_{1.5}$ and Zn–Cu[9] in DME. Each isomer was separated by column chromatography and identified by means of chiral HPLC.

IR spectra

The absorption bands due to the hydroxy stretching vibration (ν_{OH}) of compounds **3** and **4** are listed in Table 1. Due to a strong intermolecular O–H · · · O hydrogen bond, the band of **3a** appears at 3418 cm^{-1} as a broad peak in the solid state (KBr), while it appears at 3614 cm^{-1} as a sharp peak in solution (5×10^{-4} M, CCl_4).

In contrast, alkyl and benzyl derivatives **3b–h** show the bands at very similar positions in the solid state (3545–3574 cm^{-1}) and

Table 1 Absorption peaks for the hydroxy stretching vibration (ν_{OH}/cm^{-1}) of [2.2]MCPs **3** and **4** at 25 °C

	ν_{OH}/cm^{-1}	
	KBr	CCl_4 (5×10^{-4} M)
3a	3418 (208)[a]	3614 (16)[a]
3b	3549 (23)[a]	3564 (20)[a]
3c	3558	3566
3d	3558	3558
3e	3558	3558
3f	3574	3576
3g	3551	3550
3h	3545	3546
meso-**4**	3554	3552
(±)-**4**	3534	3546

[a] Values in parentheses are half band widths ($\nu_{\frac{1}{2}}$/cm^{-1}).

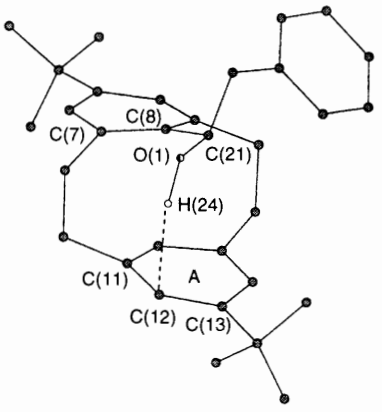


Fig. 1 Stereo-view drawing of **3h** showing the intramolecular O–H · · · π hydrogen bond. Selected bond distance (Å) and bond angle (°): O(1)–H(24) 1.08(5), C(21)–O(1)–H(24) 105(2)

in solution (3546–3576 cm^{-1}). These bands are relatively sharp as compared with that of **3a** in the solid state. These facts suggest for **3b–h** a similar conformational preference for the C(8)–C(21) bond in both solid and solution states, the absence of an intermolecular O–H · · · O hydrogen bond and the presence of a weak intramolecular O–H · · · π hydrogen bond[1,2] between the hydroxy group and π-electrons of the opposing benzene ring (A-ring). A substituent (R^1) on the A-ring could be expected to have an influence on the strength of the O–H · · · π hydrogen bond.

While in **3g** (R^1 = OMe) and **3h** (R^1 = Bu^t) with an electron-donating substituent ν_{OH} shows a low-wavenumber shift as compared to **3d** (R^1 = H), the degree of the shift is larger for the inductive *tert*-butyl group ($\Delta\nu$ = 12–13 cm^{-1}) than the resonant methoxy group ($\Delta\nu$ = 7–8 cm^{-1}). A high-wavenumber shift ($\Delta\nu$ = 16–18 cm^{-1}) was observed in **3f** with the weakly electron-withdrawing bromo substituent. It must be noted, however, that steric as well as electronic characteristics of the substituent may contribute to the degree of shift $\Delta\nu$.

From IR spectra, an intramolecular O–H · · · π hydrogen bond is also suggested to be present in *meso*-**4** and (±)-**4**. An X-ray crystallographic analysis of the *meso*-isomer is described below.

X-Ray crystallographic analysis

X-Ray crystallographic analyses of **3h** and *meso*-**4** were performed at −90 °C. No phase transformation in the temperature range −90 °C to +25 °C could be detected by differential scanning calorimetry. The stereo-view drawings of **3h** and *meso*-**4** are shown in Fig. 1 and Fig. 2, and intramolecular short contacts are listed in Table 2.

The hydroxy group of **3h** is located inside of the [2.2]MCP-subunit with the C(7)–C(8)–C(21)–O(1) torsional angle of 13.55

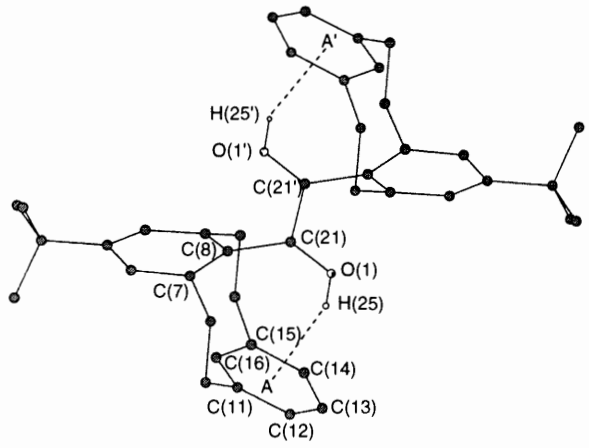


Fig. 2 Stereo-view drawing of *meso*-**4** showing the intramolecular O–H · · · π hydrogen bond. Selected bond distance (Å) and bond angle (°): O(1)–H(25) 0.75(3), C(21)–O(1)–H(25) 122(3)

(0.76)°. The hydrogen atom H(24) of the hydroxy group lies above the π-electrons on the peripheral region of the A-ring and is only 2.17(4) Å away from carbon atom C(12); the distances from H(24) to carbon atoms C(11) and C(13), are 2.46(4) and 2.70(3) A, respectively. The angle between O(1)–H(24) · · · C(12) is 165(3)°, showing the edge type O–H · · · π hydrogen bond in **3h**.

In *meso*-**4**, the two hydroxy groups are arranged antiperiplanar to each other with O(1)–C(21)–C(21′)–O(1′) torsional angle of *ca.* 180°. The hydroxy group is directed towards the benzene ring (A-ring) of the [2.2]MCP-subunit with a C(7)–C(8)–C(21)–O(1) torsional angle of 66.74 (0.38)°. The hydrogen atom H(25) is positioned just over the centroid of the A-ring at a short distance of only *ca.* 2.2 Å and the O(1)–H(25) · · · centroid angle is *ca.* 160°. Thus, an O–H · · · π hydrogen bond of a centroid type is found in *meso*-**4**. The hydrogen atom H(25) mainly interacts with carbons C(12) and C(13). The distances between H(25) and C(12) and (13) are in the range of 2.54(3) Å and 2.58(3) Å, respectively, with the angles O(1)–H(25) · · · C(12) and O(1)–H(25) · · · C(13) being 143(3)° and 172(4)°.

Experimental

All melting points are uncorrected. IR spectra were measured as KBr pellets and in carbon tetrachloride. ^{1}H NMR spectra were determined in deuteriochloroform at 270 MHz with a JEOL EX-270 instrument. Mass spectra were measured on a JEOL JMS-01-SG-2 machine at 75eV using a direct inlet system. Elemental analysis was performed on a YANAKO MT-5 instrument. HPLC analysis was performed on Nippon Bunkou 880-PU [Nippon Bunkou 875-UV detector, Daicel CHIRAL OD column (4.6 mm × 250 cm) and hexane–isopropyl alcohol (90:10)]. Differential scanning calorimetry was performed on SEIKO DSC 220C instrument. Column chromatography was carried on silica gel (Wako C-300). Ether refers to diethyl ether.

5-*tert*-Butyl-8-hydroxymethyl[2.2]metacyclophane 3a

Sodium borohydride (76 mg, 2.0 mmol) in methanol (2 ml) was added dropwise at room temperature to a suspension of **2a** (292 mg, 1.0 mmol) in methanol (10 ml) and the mixture was stirred at room temperature for 20 min. It was then poured into ice–water and extracted with ether. The extract was washed with water, dried ($MgSO_4$) and evaporated *in vacuo* to leave a residue which was chromatographed with hexane–ether as eluent to give **2** (86%, 252 mg, 0.857 mmol) as colourless prisms, mp 95–96 °C (from hexane) (Found: C, 85.39; H, 9.01. $C_{21}H_{26}O$ requires C, 85.67; H, 8.90%); ν_{max}(KBr)/cm^{-1} 3418, 2954, 1597, 1480, 1361, 1180, 1001, 863, 784 and 716;

Table 2 Intramolecular non-bonded atomic distances (Å) and angles (°) for **3h** and *meso*-**4**

	3h	*meso*-**4**
OH···C(11)	2.46(4)	2.72(3)
OH···C(12)	2.17(4)	2.54(3)
OH···C(13)	2.70(3)	2.58(3)
OH···C(14)	3.26(4)	2.70(3)
OH···C(15)	3.47(4)	2.88(3)
OH···C(16)	3.18(4)	2.95(3)
O···C(11)	3.332(7)	3.208(3)
O···C(12)	3.223(6)	3.175(3)
O···C(13)	3.574(5)	3.324(3)
O···C(14)	3.891(5)	3.406(3)
O···C(15)	3.997(5)	3.450(3)
O···C(16)	3.817(6)	3.432(3)
O–H···C(11)	138(3)	125(3)
O–H···C(12)	165(3)	143(3)
O–H···C(13)	139(4)	172(4)
O–H···C(14)		158(4)
O–H···C(15)		135(4)
O–H···C(16)		125(3)

Values in parentheses are estimated standard deviations.

$\nu_{max}(CCl_4)/cm^{-1}$ 3614; δ_H(270 MHz, $CDCl_3$) 0.69 (1 H, br s, D_2O-exchange, OH), 1.36 (9 H, s, Bu^t), 2.19 (2 H, dt, *J* 5.0 and 11.9, C_2H_4), 2.75 (2 H, dt, *J* 4.3 and 11.9, C_2H_4), 2.79 (2 H, s, CH_2OH), 2.93–3.08 (4 H, m, C_2H_4), 3.73 (1 H, br s, ArH), 7.08 (3 H, s, ArH) and 7.12 (2 H, s, ArH); *m/z* 294 (M^+, 100%).

General procedure for reactions with Grignard reagents

Preparation of 5-*tert*-butyl-8-(1-hydroxyethyl)[2.2]metacyclophane 3b. To a suspension of methylmagnesium iodide [prepared from magnesium ribbon (122 mg, 5.0 mmol) and iodomethane (710 mg, 0.31 ml, 5.0 mmol)] in dry ether (5 ml) was added dropwise **2a** (146 mg, 0.5 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was heated under reflux for 0.5 h. After being cooled to room temperature, the reaction mixture was poured into ice-cooled 10% aq. hydrochloric acid and extracted with ether. The extract was washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to leave a residue which was chromatographed with hexane–ether as eluent to give **3b** (91%, 140 mg, 0.454 mmol) as colourless prisms, mp 80–82 °C (from hexane) (Found: C, 85.38; H, 9.32. $C_{22}H_{28}O$ requires C, 85.66; H, 9.15%); ν_{max}(KBr)/cm^{-1} 3549, 2946, 1593, 1443, 1360, 1331, 1263, 1183, 1115, 1049, 892, 866, 795, 755 and 725; $\nu_{max}(CCl_4)/cm^{-1}$ 3564; δ_H(270 MHz, $CDCl_3$) −0.54 (1 H, s, D_2O-exchange, OH), 0.94 [3 H, d, *J* 6.6, CH(OH)CH_3], 1.37 (9 H, s, Bu^t), 2.21–2.36 (2 H, m, C_2H_4), 2.72 (1 H, dt, *J* 4.0 and 12.2, C_2H_4), 2.94–3.12 (4 H, m, C_2H_4), 3.36 (1 H, dt, *J* 4.0 and 12.2, C_2H_4), 3.62 (1 H, br s, ArH), 4.16 (1 H, q, *J* 6.6, C*H*OH), 7.04 and 7.07 (each 1 H, each d, *J* 7.3, ArH), 7.10 and 7.13 (each 1 H, each d, *J* 2.0, ArH) and 7.21 (1 H, t, *J* 7.3, ArH); *m/z* 263 [(M − CH(OH)Me)$^+$, 30], 207 (92) and 57 (100%).

5-*tert*-Butyl-8-(1-hydroxypropyl)[2.2]metacyclophane 3c. To a suspension of ethylmagnesium bromide [prepared from magnesium ribbon (122 mg, 5.0 mmol) and bromoethane (545 mg, 0.37 ml, 5.0 mmol)] in dry ether (5 ml) was added dropwise **2a** (117 mg, 0.40 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was stirred at room temperature for 10 min. It was worked up as described in the general procedure to give **3c** (110 mg, 0.342 mmol, 86%), as colourless prisms, mp 79–81 °C (from hexane) (Found: C, 85.49; H, 9.34. $C_{23}H_{30}O$ requires C, 85.66; H, 9.38%); ν_{max}(KBr)/cm^{-1} 3558, 3048, 2960, 2926, 2868, 1594, 1478, 1454, 1361, 1179, 1110, 1074, 1037, 1019, 969, 864 and 786; $\nu_{max}(CCl_4)/cm^{-1}$ 3566; δ_H(270 MHz, $CDCl_3$) −0.57 (1 H, s, D_2O-exchange, OH), 0.51 (3 H, t, *J* 7.6, CH_2CH_3), 1.12 [2 H, dq, *J* 7.0 and 7.6, CH(OH)CH_2], 1.37 (9 H, s, Bu^t), 2.20–2.39 (2 H, m, C_2H_4), 2.73 (1 H, dt, *J* 4.3 and 11.9, C_2H_4), 2.92–3.15 (4 H, m, C_2H_4), 3.32 (1 H, dt, *J* 4.3 and 11.9, C_2H_4), 3.63 (1 H, br s, ArH), 3.88 (1 H, t, *J* 7.0, C*H*OH), 7.04 and 7.07 (each 1 H, each d, *J* 7.6, ArH), 7.11 and 7.12 (each 1 H, each d, *J* 2.0, ArH) and 7.23 (1 H, t, *J* 7.6, ArH); *m/z* 322 (M^+, 3), 304 [(M − H_2O)$^+$, 5] and 263 [(M − CH(OH)Et)$^+$, 100%].

5-*tert*-Butyl-8-(1-hydroxy-2-phenylethyl)[2.2]metacyclophane 3d. To a suspension of benzylmagnesium chloride [prepared from magnesium ribbon (243 mg, 10.0 mmol) and benzyl chloride (1.27 g, 1.15 ml, 10.0 mmol)] in dry ether (10 ml) was added dropwise **2a** (292 mg, 1.0 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was stirred at room temperature for 5 min. It was then worked up as described in the general procedure to give **3d** (344 mg, 0.895 mmol, 90%) as colourless prisms, mp 23–25 °C (Found: C, 87.54; H, 8.30. $C_{28}H_{32}O$ requires C, 87.45; H, 8.39%); ν_{max}(KBr)/cm^{-1} 3558, 3026, 2950, 1594, 1495, 1478, 1452, 1361, 1182, 1040, 864, 788, 723 and 697; $\nu_{max}(CCl_4)/cm^{-1}$ 3558; δ_H(270 MHz, $CDCl_3$) −0.45 (1 H, s, D_2O-exchange, OH), 1.37 (9 H, s, Bu^t), 2.15–2.35 (2 H, m, C_2H_4), 2.36 [1 H, dd, *J* 5.6 and 13.5, CH(OH)CH_2], 2.57 [1 H, dd, *J* 8.3 and 13.5, CH(OH)CH_2], 2.67 (1 H, dt, *J* 4.9 and 11.9, C_2H_4), 2.85–3.08 (4 H, m, C_2H_4), 3.49 (1 H, dt, *J* 3.6 and 11.9, C_2H_4), 3.68 (1 H, br s, ArH), 4.16 (1 H, dd, *J* 5.6 and 8.3, C*H*OH) and 6.76–7.20 (10 H, m, ArH); *m/z* 366 [(M − H_2O)$^+$, 62], 263 [(M − CH(OH)CH_2Ph)$^+$, 68] and 261 (100%).

5-*tert*-Butyl-8-[1-hydroxy-2-(4-bromophenyl)ethyl][2.2]metacyclophane 3e. To a suspension of *p*-bromobenzylmagnesium bromide [prepared from magnesium ribbon (122 mg, 5.0 mmol) and *p*-bromobenzyl bromide (1.25 g, 5.0 mmol)] in dry ether (5 ml) was added dropwise **2a** (117 mg, 0.4 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was stirred at room temperature for 10 min. It was then worked up as described in the general procedure to give **3e** (159 mg, 0.343 mmol, 86%) as colourless prisms, mp 35–37 °C (Found: C, 72.78; H, 6.86. $C_{28}H_{31}OBr$ requires C, 72.57; H, 6.74%); ν_{max}(KBr)/cm^{-1} 3558, 2962, 2864, 1593, 1486, 1440, 1403, 1361, 1182, 1102, 1071, 1044, 1011, 803, 790, 746 and 728; $\nu_{max}(CCl_4)/cm^{-1}$ 3558; δ_H(270 MHz, $CDCl_3$) −0.46 (1 H, s, D_2O-exchange, OH), 1.37 (9 H, s, Bu^t), 2.01–2.30 (2 H, m, C_2H_4), 2.32 [1 H, dd, *J* 5.9 and 13.2, CH(OH)CH_2], 2.52 [1 H, dd, *J* 7.6 and 13.2, CH(OH)CH_2], 2.64 (1 H, dt, *J* 4.3 and 12.2, C_2H_4), 2.90–3.08 (4 H, m, C_2H_4), 3.43 (1 H, dt, *J* 4.3 and 12.2, C_2H_4), 3.67 (1 H, br s, ArH), 4.13 (1 H, dd, *J* 5.9 and 7.6, C*H*OH), 6.64 and 7.19 (each 2 H, each d, *J* 8.6, ArH) and 6.98–7.21 (5 H, m, ArH); *m/z* 464 (M^+, 5), 462 (M^+, 5) and 209 (100%).

13-Bromo-5-*tert*-butyl-8-(1-hydroxy-2-phenylethyl)[2.2]metacyclophane 3f. To a suspension of benzylmagnesium chloride [prepared from magnesium ribbon (73 mg, 3.0 mmol) and benzyl chloride (380 mg, 0.35 ml, 3.0 mmol)] in dry ether (3 ml) was added dropwise **2b** (111 mg, 0.30 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was stirred at room temperature for 5 min. It was worked up as described in the general procedure to give **3f** (120 mg, 0.259 mmol, 86%) as colourless prisms, mp 33–35 °C (Found: C, 72.40; H, 6.83. $C_{28}H_{31}OBr$ requires C, 72.57; H, 6.74%); ν_{max}(KBr)/cm^{-1} 3574, 3082, 3050, 3026, 2950, 2864, 1593, 1561, 1495, 1453, 1361, 1289, 1216, 1181, 1037, 880, 852, 791 and 698; $\nu_{max}(CCl_4)/cm^{-1}$ 3576; δ_H(270 MHz, $CDCl_3$) −0.22 (1 H, s, D_2O-exchange, OH), 1.36 (9 H, s, Bu^t), 2.18 and 2.99 (each 1 H, each dt, *J* 5.3 and 12.2, C_2H_4), 2.40 [1 H, dd, *J* 5.9 and 13.5, CH(OH)CH_2], 2.61 [1 H, dd, *J* 7.6 and 13.5, CH(OH)CH_2], 2.68 (1 H, dt, *J* 4.3 and 12.2, C_2H_4), 2.85–3.08 (4 H, m, C_2H_4), 3.53 (1 H, dt, *J* 4.3 and 12.2, C_2H_4), 3.54 (1 H, br s, ArH), 4.20 (1 H, dd, *J* 5.9 and 7.6, C*H*OH), 6.76–6.82 (2 H, m, ArH), 7.01 and 7.14 (each 1 H, each d, *J* 1.8, ArH), 7.06–7.12 (3 H, m, ArH) and 7.16 and 7.22 (each 1 H, each t, *J* 2.0, ArH); *m/z* 446 [(M − H_2O)$^+$ 100] and 444 [(M − H_2O)$^+$, 47%].

5-*tert*-Butyl-13-methoxy-8-(1-hydroxy-2-phenylethyl)[2.2]-metacyclophane 3g. To a suspension of benzylmagnesium chloride [prepared from magnesium ribbon (73 mg, 3.0 mmol) and benzyl chloride (380 mg, 0.35 ml, 0.30 mmol)] in dry ether (3 ml) was added dropwise **2c** (97 mg, 0.3 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was stirred at room temperature for 5 min. It was then worked up as described in the general procedure to give **3g** (116 mg, 0.280 mmol, 93%) as colourless prisms, mp 24–26 °C (Found: C, 83.73; H, 8.32. $C_{29}H_{34}O_2$ requires C, 84.02; H, 8.27%); ν_{max}(KBr)/cm^{-1} 3551, 3026, 2950, 2864, 1587, 1455, 1431, 1336, 1289, 1147, 1057, 1000, 927, 887, 862 and 848; ν_{max}(CCl_4)/cm^{-1} 3550; δ_H(270 MHz, $CDCl_3$) −0.14 (1 H, s, D_2O-exchange, OH), 1.36 (9 H, s, Bu^t), 2.23 and 2.33 (each 1 H, each dt, *J* 5.3 and 11.9, C_2H_4), 2.41 [1 H, dd, *J* 5.9 and 13.2, CH(OH)C*H*$_2$], 2.61 [1 H, dd, *J* 7.6 and 13.2, CH(OH)C*H*$_2$], 2.66 (1 H, dt, *J* 5.3 and 11.9, C_2H_4), 2.70–3.05 (4 H, m, C_2H_4), 3.33 (1 H, br s, ArH), 3.54 (1 H, dt, *J* 4.3 and 11.9, C_2H_4), 3.75 (3 H, s, OMe), 4.24 (1 H, dd, *J* 5.9 and 7.6, C*H*OH), 6.57 and 6.62 (each 1 H, each dd, *J* 1.3 and 2.3, ArH), 6.76–6.82 (2 H, m, ArH), 6.99 and 7.13 (each 1 H, each d, *J* 1.8, ArH) and 7.04–7.11 (3 H, m, ArH); *m*/*z* 414 (M^+, 2), 293 [(M − CH(OH)CH_2Ph)$^+$, 74] and 237 (100%).

5,13-Di-*tert*-butyl-8-(1-hydroxy-2-phenylethyl)[2.2]metacyclophane 3h. To a suspension of benzylmagnesium chloride [prepared from magnesium ribbon (146 mg, 6.0 mmol) and benzyl chloride (760 mg, 0.69 ml, 6.0 mmol)] in dry ether (6 ml) was added dropwise **2d** (209 mg, 0.60 mmol) in dry ether (1 ml) within 1 min at room temperature under argon and the reaction mixture was stirred at room temperature for 5 min. It was then worked up as described in the general procedure to give **3h** (242 mg, 0.549 mmol, 92%) as colourless plates, mp 119–120 °C (from hexane) (Found: C, 87.05; H, 9.31. $C_{32}H_{40}O$ requires C, 87.22; H, 9.15%); ν_{max}(KBr)/cm^{-1} 3545, 3032, 2950, 1591, 1496, 1453, 1361, 1275, 1215, 1182, 1102, 1061, 1039, 889, 863, 725 and 694; ν_{max}(CCl_4)/cm^{-1} 3546; δ_H(270 MHz, $CDCl_3$) −0.33 (1 H, s, D_2O-exchange, OH), 1.30 and 1.35 (each 9 H, each s, Bu^t), 2.15–3.08 [9 H, m, C_2H_4 and CH(OH)CH_2], 3.51 (1 H, dt, *J* 4.0 and 11.6, C_2H_4), 3.55 (1 H, br s, ArH), 4.10 (1 H, dd, *J* 5.6 and 6.9, C*H*OH), 6.64–6.72 (2 H, m, ArH), 6.94 and 7.12 (each 1 H, each d, *J* 2.0, ArH) and 6.98–7.11 (5 H, m, ArH); *m*/*z* 319 [(M − CH(OH)CH_2Ph)$^+$, 5] and 57 (100%).

Preparation of *meso*- and (±)-8,8′-(1,2-dihydroxyethane-1,2-diyl)bis(5-*tert*-butyl[2.2]metacyclophane) 4. To a suspension of $TiCl_3(DME)_{1.5}$ (1.88 g, 6.5 mmol) in dry 1,2-dimethoxyethane (30 ml) was added zinc–copper couple (1.78 g, 15.0 mmol) under argon and the mixture was heated under reflux for 2 h. After the mixture had been cooled to room temperature, a solution of **2a** (475 mg, 1.62 mmol) in dry 1,2-dimethoxyethane (3 ml) was added dropwise to it at room temperature within 1 min. The mixture was then stirred at room temperature for 30 min after which it was diluted with ether (30 ml), filtered through a pad of Florisil, washed with ether and dichloromethane, and evaporated *in vacuo*. The residue was chromatographed with hexane–ether as eluent to give *meso*-**4** (174 mg, 0.296 mmol, 37%) as colourless needles and (±)-**4** (180 mg, 0.308 mmol, 38%) as colourless needles.

meso-**4**. Mp 255–257 °C (from ethanol) (Found: C, 85.95; H, 8.64. $C_{42}H_{50}O_2$ requires C, 85.96; H, 8.59%); ν_{max}(KBr)/cm^{-1} 3554, 2960, 2862, 1594, 1478, 1439, 1361, 1217, 1179, 1101, 1036, 790 and 730; ν_{max}(CCl_4)/cm^{-1} 3552; δ_H(270 MHz, $CDCl_3$) −0.28 (2 H, s, D_2O-exchange, OH), 1.34 (18 H, s, Bu^t), 1.98–2.09 (4 H, m, C_2H_4), 2.33 (2 H, dt, *J* 4.6 and 11.9, C_2H_4), 2.41–2.53 (4 H, m, C_2H_4), 2.72–2.84 (4 H, m, C_2H_4), 3.04 (2 H, dt, *J* 4.6 and 11.9, C_2H_4), 3.54 (2 H, br s, ArH), 3.71 (2 H, s, C*H*OH), 6.75 (4 H, s, ArH), 6.91 (2 H, d, *J* 7.3, ArH), 6.95 (2 H, d, *J* 7.6, ArH) and 7.08 (2 H, dd, *J* 7.3 and 7.6, ArH); *m*/*z* 293 [(M/2)$^+$, 10] and 57 (100%).

(±)-**4**. Mp 204–205 °C (from hexane) (Found: C, 86.26; H, 8.55. $C_{42}H_{50}O_2$ requires C, 85.96; H, 8.59%); ν_{max}(KBr)/cm^{-1} 3534, 2950, 2866, 1595, 1478, 1437, 1361, 1179, 1048, 865, 790 and 724; ν_{max}(CCl_4)/cm^{-1} 3546; δ_H(270 MHz, $CDCl_3$) −0.50 (2 H, s, D_2O-exchange, OH), 1.28 (18 H, s, Bu^t), 1.98 (2 H, dt, *J* 5.3 and 11.9, C_2H_4), 2.12 (2 H, dt, *J* 5.3 and 11.9, C_2H_4), 2.33 (2 H, dt, *J* 4.3 and 11.9, C_2H_4), 2.51 (2 H, ddd, *J* 2.3, 5.3 and 11.9, C_2H_4), 2.69–2.84 (4 H, m, C_2H_4), 2.89 (2 H, ddd, *J* 2.3, 4.3 and 11.9, C_2H_4), 3.25 (2 H, dt, *J* 4.3 and 11.9, C_2H_4), 3.41 (2 H, br s, ArH), 3.74 (2 H, s, C*H*OH), 6.50 and 6.88 (each 2 H, each d, *J* 2.0, ArH), 6.90 and 6.93 (each 2 H, each d, *J* 7.4, ArH) and 7.10 (2 H, t, *J* 7.4, ArH); *m*/*z* 293 [(M/2)$^+$, 10] and 57 (100%).

X-Ray crystal structure determination of 3h

Crystal data. Colourless plate (from hexane, approximate dimensions of 0.10 × 0.20 × 0.20 mm). $C_{32}H_{40}O$, *M* = 440.67, triclinic, space group *P*$\bar{1}$ (No. 2), *a* = 11.771(7) Å, *b* = 12.351(3) Å, *c* = 10.298(2) Å, α = 101.79(2)°, β = 111.37(4)°, γ = 68.71(4)°, *V* = 1294.6 Å^3, *Z* = 2, D_c = 1.13 g cm^{-3}; monochromated Cu-Kα radiation, λ = 1.541 84 Å.

Data collection, structure solution and refinement. Data were collected on an Enraf-Nonius CAD-4 diffractometer using ω–2θ scans at a temperature of −90 ± 1 °C. A total of 4667 reflections were collected, of which 4397 were unique. The structure was solved by direct methods (SIR 88)[10] and refined by full-matrix least squares calculation to give *R* = 0.059, R_w = 0.063 for 1768 independent observed reflections [$|F_o^2| > 3\sigma(F_o^2)$, 2° < θ < 65°]. The remaining atoms were located in succeeding difference Fourier syntheses. All non-hydrogen atoms were anisotropically treated. Hydrogen atoms were located, and their positions and isotropic thermal parameters were refined. All calculations were performed on a MicroVAX 3100 computer using MolEN.[11]

X-Ray crystal structure determination of *meso*-4

Crystal data. Colourless needle (from ethanol, approximate dimensions of 0.13 × 0.26 × 0.06 mm). $C_{42}H_{50}O_2$, *M* = 586.87, triclinic, space group *P*$\bar{1}$ (No. 2), *a* = 10.386(1) Å, *b* = 11.026(4) Å, *c* = 8.061(2) Å, α = 105.89 (3)°, β = 103.00(2)°, γ = 71.73(2)°, *V* = 833.3 Å^3, *Z* = 1, D_c = 1.17 g cm^{-3}; monochromated Cu-Kα radiation, λ = 1.541 84 Å.

Data collection, structure solution and refinement. Data were collected on an Enraf-Nonius CAD-4 diffractometer using ω–2θ scans at a temperature of −90 ± 1 °C. A total of 3051 reflections were collected, of which 2827 were unique. The structure was solved by direct methods (SIR 88)[10] and refined by full-matrix least squares calculation to give *R* = 0.053, R_w = 0.063 for 1807 independent observed reflections [$|F_o^2| > 3\sigma(F_o^2)$, 2° < θ < 65°]. The remaining atoms were located in succeeding difference Fourier syntheses. All non-hydrogen atoms were anisotropically treated. Hydrogen atoms were located, and their positions and isotropic thermal parameters were refined. All calculations were performed on a MicroVAX 3100 computer using MolEN.[11]

Atomic coordinates, thermal parameters and bond lengths and angles for **3h** and *meso*-**4** have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/17.

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