

## Preparation and Structural Properties of Hydroxy- and Alkoxy-[2.2.1]metacyclophanes<sup>1</sup>

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The asymmetric **4a** and symmetric conformers **4b** of a trimethoxy[2.2.1]metacyclophane were isolated and the structures were established by <sup>1</sup>H NMR spectroscopy and X-ray crystallography. The trihydroxy[2.2.1]-**5** and dihydroxy(methoxy)[2.2.1]metacyclophane **6** were obtained by demethylation of isomers **4a** and **4b**, respectively. Treatment of compound **5** with ethyl bromoacetate afforded only the tris(ethoxycarbonylmethoxy)[2.2.1]metacyclophane **7**. On the other hand the bis(ethoxycarbonylmethoxy)(methoxy)[2.2.1]-**8** and ethoxycarbonylmethoxy(hydroxy)(methoxy)[2.2.1]metacyclophane **9** were obtained from compound **6**. It was found that compounds **4a** and **7** assume a '2,1-alternate' conformation, whereas, on the other hand, compounds **4b**, **6**, **8** and **9** have a '2,2-alternate' conformation. In the case of compound **5** both '2,1-alternate' and '2,2-alternate' conformers were detected by <sup>1</sup>H NMR spectroscopy. The chiralities of compounds **4a** and **9** were confirmed by their <sup>1</sup>H NMR spectrum in the presence of Pirkle's reagent.

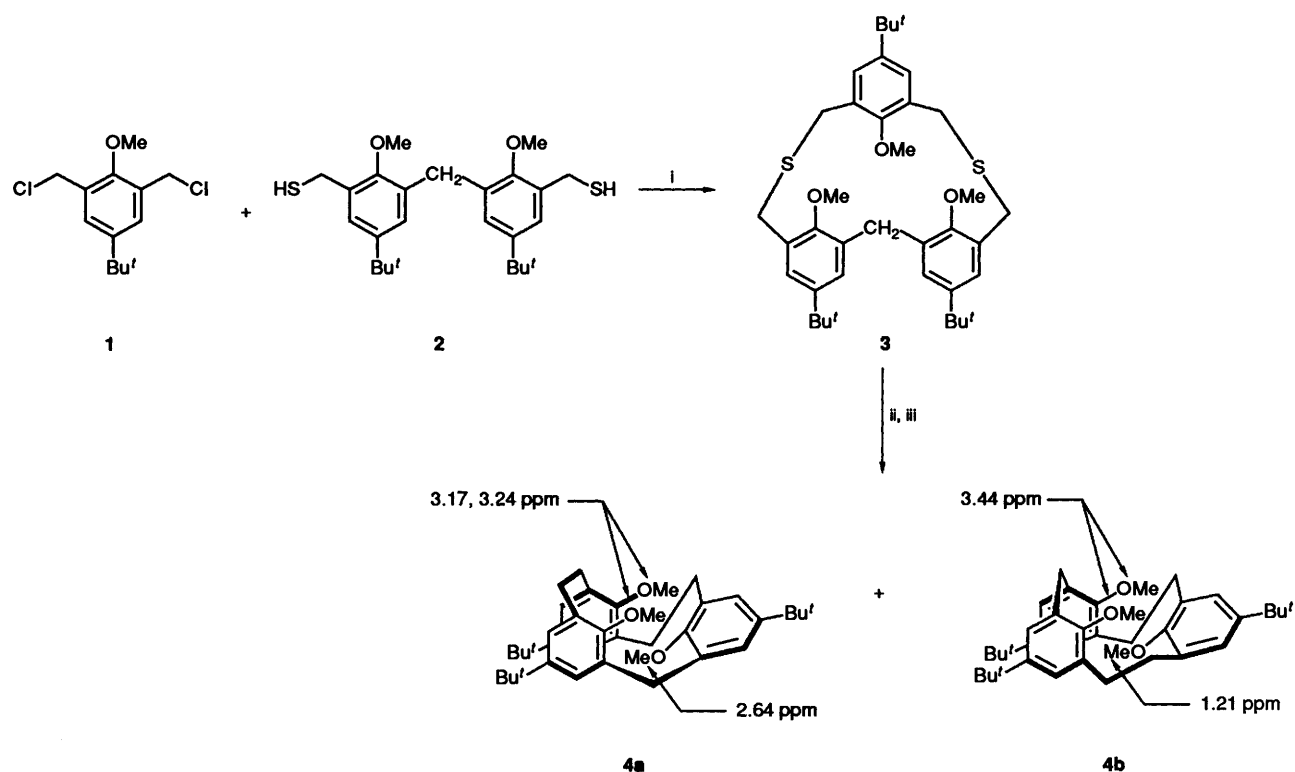
Recently, conformational characteristics of macrocyclic cyclophanes,<sup>2</sup> especially, those of calix[*n*]arenes<sup>3</sup> ([1,*n*]MCPs),<sup>†</sup> have been intensively investigated. Reports on calixarenes which have more than four aromatic rings are abundant; however, it is surprising that knowledge of MCPs having three aromatic rings, including calix[3]arenes,<sup>4</sup> is very limited. It is reported that trimethyl[2.2.2]MCP<sup>5</sup> adopts a 'folded inwards' conformation and that [2.1.1]MCP<sup>6a</sup> prefers a 'stepped' conformation rather than a 'folded inwards' one. Temperature-dependent <sup>1</sup>H NMR spectra for [2.2.0]MCP<sup>6b</sup> suggested that rapid conformational changes occur; however, its general conformation is uncertain. From these points of view we have been quite interested in conformational behaviour of these kinds of MCPs. We now describe the preparation of methoxy-, hydroxy- and ethoxycarbonylmethoxy-[2.2.1]MCPs and their conformational properties as well.

### Results and Discussion

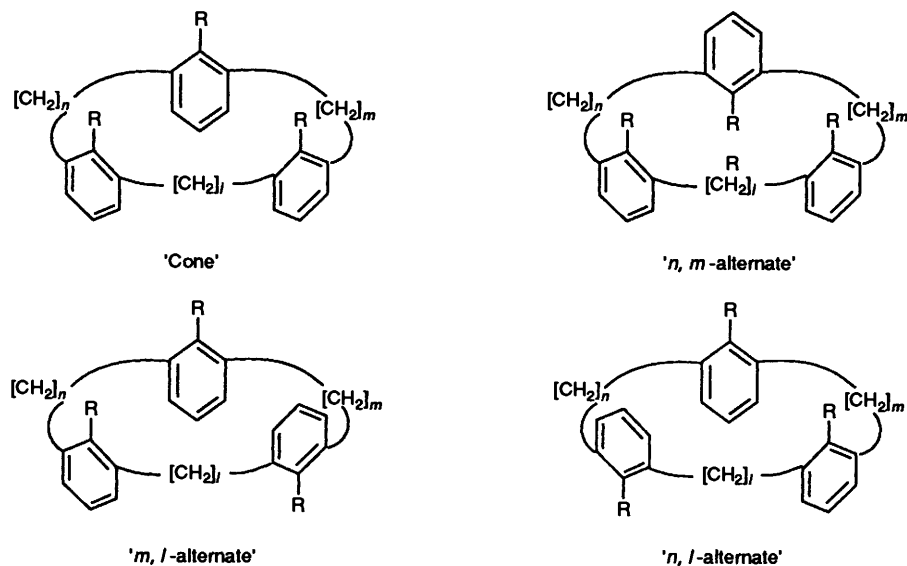
**Preparation and Conformational Properties.**—The preparation of compound **4** is shown in Scheme 1. High-diluted coupling reaction of substrates **1** and **2** gave the dithia[3.3.1]MCP **3** in 61% yield. Oxidation of **3** by *m*-chloroperbenzoic acid (MCPBA), followed by pyrolysis at 450 °C (0.6 mmHg) afforded the trimethoxy[2.2.1]MCP as a 2:1 mixture of **4a** and **4b** in 60% yield. Two conformers were isolated, in 21 and 17% yield, respectively, by column chromatography. In the <sup>1</sup>H NMR spectrum of one of the conformers, three methoxy groups were observed each as a singlet, and each of equal intensity, as well as *tert*-butyl signals. On the other hand, the spectrum of the other conformer showed the methoxy and *tert*-butyl protons each as a pair of singlets in a 1:2 intensity ratio. Therefore we deduced that the former isomer assumes the asymmetric conformation **4a** (*C*<sub>1</sub> symmetry) and that the latter isomer has a symmetric conformation **4b** (*C*<sub>s</sub> symmetry) as shown in Scheme 1. For convenience in describing conformers of [*n.m.l*]MCPs such as those presented here they are classified as four discrete conformers, which can be designated as 'cone,' '*n,m*-alternate,' '*m,l*-alternate' and '*n,l*-alternate' shown in Fig. 1. Thus,

conformers **4a** and **4b** can be assigned as '2,1-alternate' and '2,2-alternate,' respectively. In both conformers one of the three methoxy groups exhibits an upfield shift ( $\delta$  2.64 in **4a** and 1.21 in **4b**). Such upfield shifts might arise from a strong shielding effect of the aromatic rings. The X-ray crystallographic analysis of conformers **4a** and **4b** (Figs. 2 and 3) clearly indicates that one methoxy group is directed into the cavity between the other aromatic rings. However, the methoxy protons of conformer **4b** experience a greater shift than do the corresponding protons of isomer **4a**, which can be explained by the methoxy group of conformer **4b** being located more deeply in the cavity than is that of conformer **4a**. Interconversion between conformers **4a** and **4b** did not occur under severe conditions such as heating in dimethyl sulfoxide (DMSO) at 180 °C or in the solid state at 400 °C. In demethylation of compounds **4a** and **4b** with BBr<sub>3</sub>, the trihydroxy[2.2.1]MCP **5** was obtained from conformer **4a** (52%); on the other hand, the dihydroxy(methoxy)[2.2.1]MCP **6** instead of compound **5** was obtained, in 59% yield, in which only two of the three methoxy groups of conformer **4b** had reacted (Scheme 2). We suggest that one methoxy group of conformer **4b**, located deep in the cavity, is inert to the attack of BBr<sub>3</sub>. The <sup>1</sup>H NMR spectrum of compound **5** revealed that it exists as a mixture of two conformers at 27 °C as indicated by Table 1. It was found that the ratio **5a**:**5b** was 1:2; however, at higher temperature (60–100 °C in toluene) broadening of *tert*-butyl and aromatic protons was observed, which is supposedly due to the conformational interconversion between the conformers **5a** and **5b**. In the <sup>1</sup>H NMR spectrum of the dihydroxy(methoxy)[2.2.1]MCP **6** the hydroxy and methoxy protons were observed at  $\delta$  5.41 and 1.42, each as a singlet, respectively. Thus compound **6** was determined to assume a symmetric conformation such as **4b**. Ionophoric calix[4]arenes carrying an ethoxycarbonylmethoxy group are capable of binding some alkali and alkaline earth metals or of extracting them from an aqueous metal picrate solution into an organic medium, as is evidenced by a bathochromic shift of the UV-visible absorption of a picrate anion.<sup>7</sup> Hence, the reaction of compounds **5** and **6** with ethyl bromoacetate in the presence of NaH was carried out in order to obtain [2.2.1]MCP ionophores. The trihydroxy[2.2.1]MCPs **5** afforded the desired tris(ethoxycarbonylmethoxy)[2.2.1]MCP **7**. Compound **7** is believed to assume the '2,1-alternate' conformation since its <sup>1</sup>H

<sup>†</sup> MCP = metacyclophane.



**Scheme 1** Reagents and conditions: i, CsOH, NaBH<sub>4</sub>; ii, MCPBA; iii, 450 °C, 0.6 mmHg



**Fig. 1** Conformations of  $[n.m.l]$ metacyclophanes

**Table 1** <sup>1</sup>H NMR spectra data of the trimethoxy[2.2.1]MCP 5

Conformer	$\delta_{\text{H}}^a$	
	OH	Bu <sup>t</sup>
2,1-Alternate <b>5a</b>	2.82(1 H)	1.16(9 H)
	3.80(1 H)	1.25(9 H)
	4.65(1 H)	1.37(9 H)
2,2-Alternate <b>5b</b>	2.82(1 H)	1.25(18 H)
	5.45(2 H)	1.37(9 H)

<sup>a</sup> In CDCl<sub>3</sub> at 27 °C.

NMR spectrum revealed the presence of three pairs of *tert*-butyl and ethoxy groups. Considering steric repulsion between an ethoxycarbonylmethoxy group and the benzene rings, the '2,2-

alternate' conformation seems to be unfavourable for triester **7**. Dihydroxy derivative **6** afforded the bis(ethoxycarbonylmethoxy)(methoxy)[2.2.1]MCP **8** and the ethoxycarbonylmethoxy(hydroxy)(methoxy)[2.2.1]MCP **9** (Scheme 3). In the <sup>1</sup>H NMR spectrum of compound **8** an upfield shift of the methoxy signal ( $\delta$  1.23) was observed. The *tert*-butyl protons appeared as two singlets whose intensity ratio was 1:2. These facts suggest that compound **8** assumes the '2,2-alternate' conformation. Similar to compound **8**, the methoxy group of compound **9** appeared at a high magnetic field ( $\delta$  1.29); on the other hand, the three *tert*-butyl groups showed three singlets of equal intensity. Thus, compound **9** can be defined as an asymmetric '2,2-alternate' conformer. The UV spectrum of an alkali metal picrate solution was not influenced by addition of calixarene **7**, **8** or **9**, indicating a lack of complexation between these MCPs and alkali metals. This result implies such a

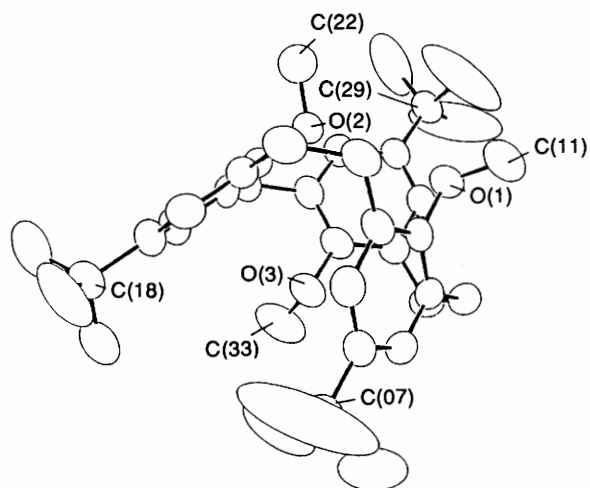


Fig. 2 Perspective view of conformer 4a: *tert*-butyl and methoxy carbon and oxygen atoms are numbered

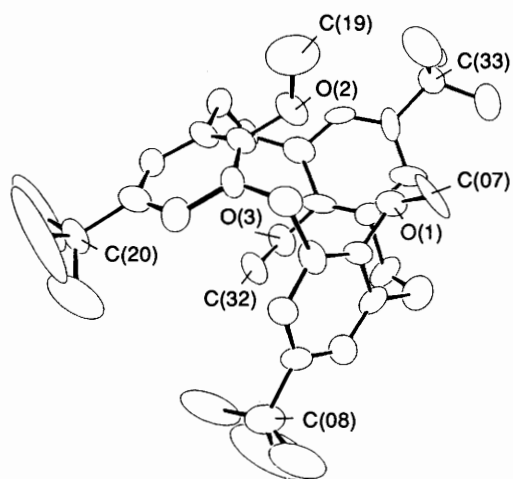
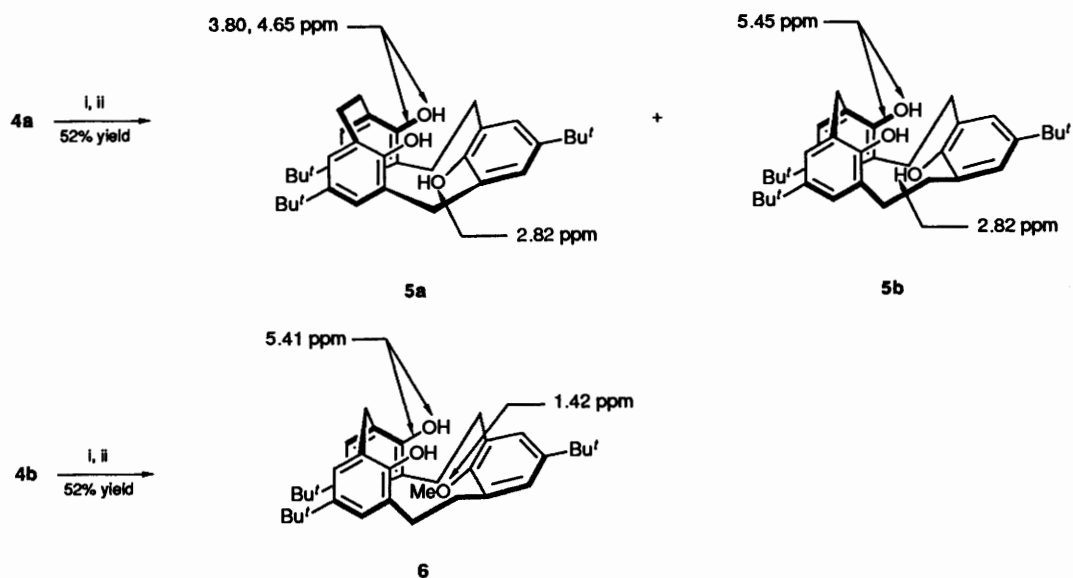
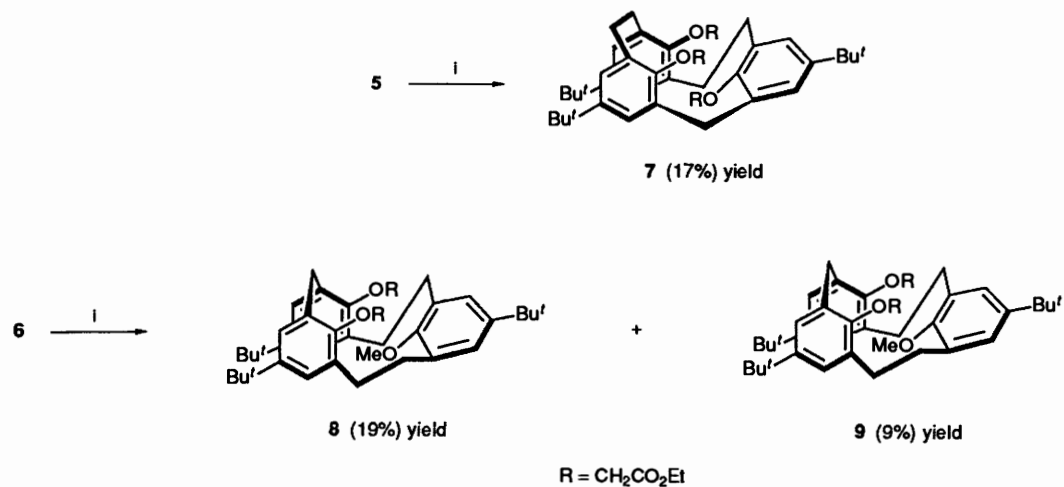


Fig. 3 Perspective view of conformer 4b: *tert*-butyl, methoxy carbon and oxygen atoms are numbered



Scheme 2 Reagents: i,  $\text{BBr}_3$ ; ii, water



Scheme 3 Reagents: i, NaH,  $\text{BrCH}_2\text{CO}_2\text{Et}$

conformation as an 'alternate' one is not suitable for effective complexation with metals and that a 'cone' conformation is essential for such complexation.

*Chiralities.*—Recently, chiral calixarenes have been reported by many groups.<sup>8</sup> Böhmer and co-workers<sup>9</sup> demonstrated the chirality of dissymmetric calix[4]arenes with  $C_2$  and  $C_4$

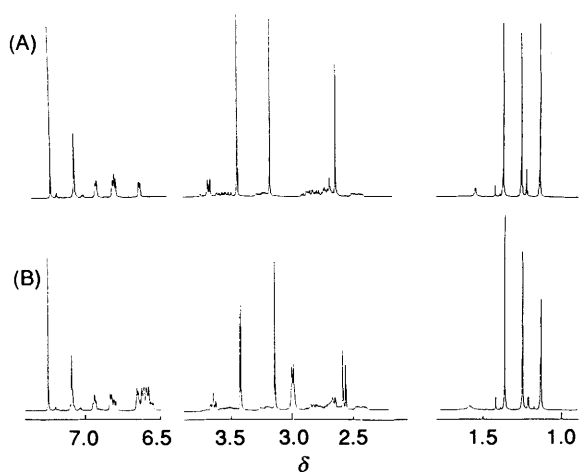


Fig. 4 Partial  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ; 270 MHz); (A) **4a**, (B) **4a** + Pirkle's reagent

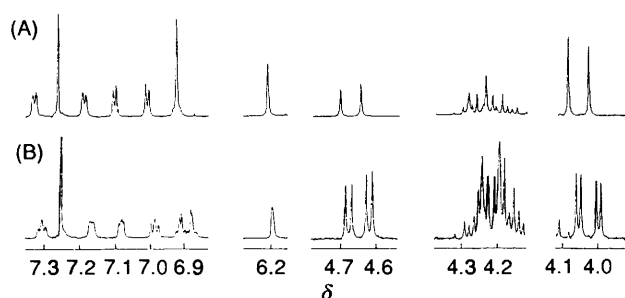


Fig. 5 Partial  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ; 270 MHz); (A) **9**, (B) **9** + Pirkle's reagent



symmetry by interaction with Pirkle's reagent **10** [(S)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol]. Of the [2.2.1]MCPs prepared here, compounds **4a**, **7** and **9** were expected to have a plane of chirality, because MCPs **4a** and **7** which have the same three substituents are fixed as  $C_1$  symmetrical conformers and, on the other hand, the MCP **9** with three different substituents does not show a conformational change.  $^1\text{H}$  NMR spectra of compounds **4a** and **9** in the absence and the presence of reagent **10** are shown in Figs. 4 and 5. In the spectrum of compound **9** two singlet peaks of the *tert*-butyl groups and all peaks of the aromatic and bridged protons were doubled on addition of reagent **10**. It was reported<sup>9</sup> that hydroxy groups which do not participate in intramolecular hydrogen bonding are necessary for an effective interaction between chiral calix[4]arenes and reagent **10**. Although compound **4a** does not have a hydroxy group, a similar effect was observed on addition of reagent **10**; that is, one singlet peak of the *tert*-butyl group, two singlet peaks of the methoxy groups, and all peaks of the aromatic and bridged protons were also doubled. These facts suggest that methoxy and hydroxy groups of calixarenes **4a** and **9** play an important role in co-ordination with reagent **10**. On the other hand, the spectrum of compound **7** was not influenced upon addition of reagent **10**, since this reagent should co-ordinate at the ester sites of compound **7** which are located far from the cyclophane skeleton.

## Experimental

**General.**—All m.p.s were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded on a Nippon Bunko IR-700 spectrometer as KBr pellets.  $^1\text{H}$  NMR spectra (internal  $\text{Me}_4\text{Si}$ ) were measured in  $\text{CDCl}_3$  at  $25^\circ\text{C}$  on a Nippon Denshi JEOL GSX-270 NMR spectrometer unless stated otherwise. *J*-Values are given in Hz. Mass spectra were recorded on a Nippon Denshi JMS-O1SA-2 mass spectrometer at 75 eV using a direct-inlet system. Column chromatography was carried out on silica gel (Wako gel, C-300).

**6,15,22-Tri-*tert*-butyl-9,18,25-trimethoxy-2,11-dithia[3.3.1]-MCP 3.**—To a stirred, refluxing mixture of  $\text{CsOH}$  (18.2 g, 108 mmol) and  $\text{NaBH}_4$  (2.04 g, 54 mmol) in  $\text{EtOH}$  (4  $\text{dm}^3$ ) was added a solution of substrates **1** (6.87 g, 27 mmol) and **2** (11.8 g, 27 mmol) in a mixture of benzene (100  $\text{cm}^3$ ) and ethanol (400  $\text{cm}^3$ ) dropwise from a Hershberg funnel. After the addition was complete (90 h) the reaction mixture was concentrated, and then extracted with dichloromethane. The extract was washed with water, dried and evaporated under reduced pressure to leave a residue, which was chromatographed with an 8:2 mixture of hexane–ethyl acetate as eluent to afford compound **3** (9.17 g, 61%) as prisms, m.p.  $88\text{--}89^\circ\text{C}$  (from  $\text{EtOH}$ ) (Found: C, 73.6; H, 8.7%;  $M^+$ , 620.  $\text{C}_{38}\text{H}_{52}\text{O}_3\text{S}_2$  requires C, 73.50; H, (8.44%; *M*, 620);  $\delta_{\text{H}}$  1.24 (27 H, s), 3.38 (3 H, br s), 3.60 (6 H, s), 1.80–4.40 (10 H, m), 7.04 (2 H, s) and 7.22 (4 H, br s).

**5,13,20-Tri-*tert*-butyl-8,16,23-trimethoxy[2.2.1]MCP 4.**—After a solution of compound **3** (5.58 g, 8.93 mmol) and MCPBA (10.0 g, 47.4 mmol) in dichloromethane (500  $\text{cm}^3$ ) had been stirred at room temperature for 2 h, it was washed with water, dried ( $\text{MgSO}_4$ ), and evaporated under reduced pressure to give the sulfone derivative (5.08 g, 83%). Without further purification, the sulfone derivative was pyrolysed at  $450^\circ\text{C}$  under reduced pressure (0.4–0.6 mmHg) according to the reported method.<sup>10</sup> The pyrolysate was dissolved in dichloromethane and chromatographed with benzene as eluent. From the first eluate ( $R_f$ : 0.57), conformer **4b** was isolated (0.69 g, 17%) as needles, m.p.  $256\text{--}258^\circ\text{C}$  (from  $\text{EtOH}$ ) (Found: C, 81.7; H, 9.7%;  $M^+$ , 556.  $\text{C}_{33}\text{H}_{52}\text{O}_3$  requires C, 81.97; H, 9.41%; *M*, 565);  $\delta_{\text{H}}$  1.21 (21 H, s), 1.40 (9 H, s), 2.28–3.00 (10 H, m), 3.44 (6 H, s), 6.90 (2 H, d, *J* 3.0), 7.00 (2 H, d, *J* 3.0) and 7.16 (2 H, s). From the second eluate ( $R_f$ : 0.49) was isolated conformer **4a** (0.87 g, 21%) as prisms, m.p.  $169\text{--}171^\circ\text{C}$  (from  $\text{EtOH}$ ) (Found: C, 81.8; H, 9.7%;  $M^+$ , 556);  $\delta_{\text{H}}$  1.12 (9 H, s), 1.24 (9 H, s), 1.36 (9 H, s), 2.20–3.00 (10 H, m), 2.69 (3 H, s), 3.17 (3 H, s), 3.24 (3 H, s), 6.67 (1 H, d, *J* 3.0), 6.79 (1 H, d, *J* 3.0), 6.90 (1 H, d, *J* 3.0) and 7.09 (2 H, s).

**5,13,20-Tri-*tert*-butyl-8,16,23-trihydroxy[2.2.1]MCP 5.**—To a stirred solution of conformer **4a** (0.1 g, 0.18 mmol) in dry dichloromethane at  $0^\circ\text{C}$  was added dropwise a solution of  $\text{BBr}_3$  (1.50 g, 5.98 mmol) in dry dichloromethane. After the reaction mixture had been stirred for 24 h at room temperature, it was poured into ice-water. The mixture was stirred for a further 3 h at room temperature and extracted with dichloromethane (100  $\text{cm}^3$ ). The extract was washed with water, dried ( $\text{MgSO}_4$ ), and evaporated under reduced pressure to leave a residue which, on recrystallization, gave compound **5** (49.5 mg, 52%) as plates, m.p.  $150\text{--}153^\circ\text{C}$  (from  $\text{EtOH}$ ) (Found: C, 81.4; H, 8.9%;  $M^+$ , 514.  $\text{C}_{35}\text{H}_{46}\text{O}_3$  requires C, 81.67; H, 9.01%; *M*, 514);  $\nu_{\text{max}}/\text{cm}^{-1}$  3870 (OH);  $\delta_{\text{H}}$  1.16, 1.25 and 1.37 (total 27 H, each s), 2.48–4.20 (10 H, m), 2.82, 3.80, 4.65 and 5.45 (total 3 H, each s), 6.65–7.10 (4 H, m) and 7.25 (2 H, s).

**5,13,20-Tri-*tert*-butyl-16,23-dihydroxy-8-methoxy[2.2.1]-MCP 6.**—The reaction of conformer **4b** with  $\text{BBr}_3$  under similar conditions to that of **4a** gave title compound **6** (59%) as needles,

**Table 2** Fractional atomic co-ordinates for compound **4b**

	x	y	z
O(1)	0.3118(3)	0.4147(8)	0.613
O(2)	0.3121(3)	0.4109(8)	0.7938(5)
O(3)	0.1649(2)	0.7533(7)	0.7052(7)
C(1)	0.2195(5)	0.455(1)	0.5455(5)
C(2)	0.1634(5)	0.399(1)	0.5296(6)
C(3)	0.1388(4)	0.261(1)	0.5636(6)
C(4)	0.1764(4)	0.1884(9)	0.6149(6)
C(5)	0.2297(4)	0.2391(9)	0.6349(6)
C(6)	0.2531(4)	0.367(1)	0.6002(5)
C(7)	0.3537(4)	0.314(1)	0.5789(9)
C(8)	0.0801(5)	0.189(2)	0.5393(7)
C(9)	0.0862(7)	0.104(2)	0.4746(9)
C(10)	0.0383(8)	0.333(3)	0.504(2)
C(11)	0.0397(6)	0.243(4)	0.600(1)
C(12)	0.2593(3)	0.1677(9)	0.7024(9)
C(13)	0.2545(4)	0.365(1)	0.8121(6)
C(14)	0.2290(4)	0.236(1)	0.7726(6)
C(15)	0.1717(5)	0.173(2)	0.7936(7)
C(16)	0.1419(5)	0.267(1)	0.8547(7)
C(17)	0.1667(4)	0.402(1)	0.8851(6)
C(18)	0.2237(4)	0.446(1)	0.8624(6)
C(19)	0.3594(7)	0.324(2)	0.8306(9)
C(20)	0.0783(4)	0.207(1)	0.8728(7)
C(21)	0.0470(8)	0.114(3)	0.811(1)
C(22)	0.0561(7)	0.290(3)	0.937(1)
C(23)	0.0814(7)	0.030(2)	0.886(2)
C(24)	0.2461(4)	0.608(1)	0.8927(6)
C(25)	0.2277(4)	0.754(1)	0.8474(6)
C(26)	0.2272(3)	0.7521(8)	0.7008(8)
C(27)	0.2558(5)	0.760(1)	0.7755(7)
C(28)	0.3177(4)	0.779(1)	0.7672(5)
C(29)	0.3499(3)	0.7883(9)	0.705(1)
C(30)	0.3205(5)	0.777(1)	0.6338(7)
C(31)	0.2572(4)	0.759(1)	0.6393(5)
C(32)	0.1364(4)	0.594(1)	0.699(1)
C(33)	0.4185(4)	0.805(1)	0.705(1)
C(34)	0.4436(6)	0.814(3)	0.6248(9)
C(35)	0.4436(6)	0.651(2)	0.736(1)
C(36)	0.4345(6)	0.947(2)	0.747(1)
C(37)	0.2230(6)	0.751(1)	0.5640(6)
C(38)	0.2448(5)	0.608(1)	0.5098(6)

m.p. 223–227 °C (from EtOH) (Found: C, 81.6; H, 9.1%;  $M^+$ , 528.  $C_{36}H_{48}O_3$  requires C, 81.77; H, 9.15%;  $M$ , 528);  $\nu_{\max}/\text{cm}^{-1}$  3850 (OH);  $\delta_{\text{H}}$  1.21 (18 H, s), 1.41 (12 H, s), 2.61–4.72 (10 H, m), 5.43 (2 H, s), 6.93 (2 H, d,  $J$  2.6), 6.99 (2 H, d,  $J$  2.6) and 7.41 (2 H, s).

5,13,20-Tri-tert-butyl-8,16,23-tris(ethoxycarbonylmethoxy)-[2.2.1]MCP **7**.—Under dry  $N_2$  was stirred a suspension of compound **5** (0.1 g, 0.19 mmol) and NaH (0.18 g, 4.66 mmol) in a 1:1 mixture of dry dimethylformamide (DMF) and tetrahydrofuran (THF) (10  $\text{cm}^3$ ) for 1 h. Then ethyl bromoacetate (0.2 g, 1.19 mmol) was added to the suspension and the mixture was stirred under reflux for 12 h. After most of the solvent and the excess of bromoacetate had been removed under reduced pressure to leave a residue, ice-water (10  $\text{cm}^3$ ) was poured onto the residue and the mixture was extracted with dichloromethane. The extract was washed with water, dried ( $MgSO_4$ ), and evaporated under reduced pressure. The resultant residue was chromatographed with a mixture of hexane–ethyl acetate (9:1) to yield compound **7** (23.1 mg, 17%) as prisms, m.p. 95–97 °C (from aq. MeOH) (Found: C, 73.2; H, 8.1%;  $M^+$ , 772.  $C_{47}H_{64}O_9$  requires C, 73.07; H, 8.35%;  $M$ , 772);  $\delta_{\text{H}}$  1.12 (9 H, s), 1.21 (3 H, t,  $J$  7.2), 1.24 (9 H, s), 1.25 (3 H, t,  $J$  7.4), 1.27 (3 H, t,  $J$  7.2), 1.31 (9 H, s), 1.33 (9 H, s), 2.51–4.49 (22 H, m), 6.69 (1 H, d,  $J$  2.2), 6.88 (1 H, d,  $J$  2.2), 6.92 (1 H, d,  $J$  2.2), 7.00 (1 H, d,  $J$  2.3) and 7.14–7.18 (2 H, m).

**Table 3** Intramolecular distances (Å) and angles (°) for compound **4b**

(a) Bonds			
O(1)–C(6)	1.402(11)	C(18)–C(24)	1.560(15)
O(1)–C(7)	1.413(13)	C(1)–C(6)	1.450(13)
C(26)–O(3)	1.406(9)	C(1)–C(38)	1.553(13)
C(26)–C(31)	1.30(2)	C(5)–C(6)	1.356(13)
C(26)–C(27)	1.50(2)	C(5)–C(4)	1.362(13)
C(28)–C(27)	1.412(14)	C(5)–C(12)	1.51(2)
C(28)–C(29)	1.34(2)	C(29)–C(33)	1.554(11)
O(2)–C(13)	1.393(11)	C(25)–C(24)	1.533(14)
O(2)–C(19)	1.46(2)	C(4)–C(3)	1.374(14)
C(14)–C(13)	1.420(14)	C(33)–C(34)	1.55(2)
C(14)–C(15)	1.447(15)	C(33)–C(36)	1.46(2)
C(14)–C(12)	1.55(2)	C(33)–C(35)	1.53(2)
C(30)–C(31)	1.440(14)	C(16)–C(20)	1.556(15)
C(30)–C(29)	1.45(2)	C(20)–C(22)	1.44(3)
C(17)–C(18)	1.398(14)	C(20)–C(23)	1.51(2)
C(17)–C(16)	1.38(2)	C(20)–C(21)	1.53(3)
O(3)–C(32)	1.490(11)	C(37)–C(38)	1.627(15)
C(2)–C(1)	1.373(15)	C(3)–C(8)	1.521(15)
C(2)–C(3)	1.423(14)	C(8)–C(11)	1.49(3)
C(13)–C(18)	1.328(14)	C(8)–C(9)	1.38(2)
C(31)–C(37)	1.561(14)	C(8)–C(10)	1.66(3)
C(15)–(16)	1.51(2)		
C(27)–C(25)	1.44(2)		
(b) Angles			
C(6)–O(1)–C(7)	112.7(7)	C(1)–C(38)–C(37)	104.6(8)
O(3)–C(26)–C(27)	112(1)	O(1)–C(6)–C(5)	121.1(8)
O(3)–C(26)–C(31)	125(1)	C(1)–C(6)–C(5)	120.9(9)
C(31)–C(26)–C(27)	122.8(8)	C(27)–C(25)–C(24)	112.8(8)
C(27)–C(26)–C(29)	129(1)	C(5)–C(4)–C(3)	125.0(8)
C(13)–O(2)–C(19)	115.8(9)	C(29)–C(33)–C(34)	112(1)
C(13)–O(2)–C(15)	121(1)	C(29)–C(33)–C(36)	109(1)
C(13)–C(14)–C(12)	121.0(8)	C(29)–C(33)–C(35)	106.9(9)
C(15)–C(14)–C(12)	118.0(9)	C(34)–C(33)–C(36)	111(1)
C(31)–C(30)–C(29)	113.6(9)	C(34)–C(33)–C(35)	104(1)
C(18)–C(17)–C(16)	118(1)	C(36)–C(33)–C(35)	114(1)
C(26)–O(3)–C(32)	114.8(6)	C(17)–C(16)–C(15)	123(1)
C(1)–C(2)–C(3)	123.1(9)	C(17)–C(16)–C(20)	124(1)
O(2)–C(13)–C(14)	118.1(8)	C(15)–C(16)–C(20)	113(1)
O(2)–C(13)–C(18)	120.5(9)	C(16)–C(20)–C(22)	109(1)
C(14)–C(13)–C(18)	121.3(9)	C(16)–C(20)–C(23)	108(1)
C(26)–C(31)–C(30)	125.4(9)	C(16)–C(20)–C(21)	116(1)
C(26)–C(31)–C(37)	118.9(9)	C(22)–C(20)–C(23)	112(2)
C(30)–C(31)–C(37)	115.7(9)	C(22)–C(20)–C(21)	132(1)
C(14)–C(15)–C(16)	113(1)	C(23)–C(20)–C(21)	69(1)
C(26)–C(27)–C(28)	109.6(9)	C(31)–C(37)–C(38)	114.0(9)
C(26)–C(27)–C(25)	128.1(9)	C(18)–C(24)–C(25)	115.5(8)
C(28)–C(27)–C(25)	122(1)	C(14)–C(12)–C(5)	108.3(7)
C(17)–C(18)–C(13)	123(1)	C(2)–C(3)–C(4)	115.2(9)
C(17)–C(18)–C(24)	115.0(9)	C(2)–C(3)–C(8)	123(1)
C(13)–C(18)–C(24)	121.3(9)	C(4)–C(3)–C(8)	121.8(9)
C(2)–C(1)–C(6)	116.9(8)	C(3)–C(8)–C(11)	102(1)
C(2)–C(1)–C(38)	122.6(9)	C(3)–C(8)–C(9)	111(1)
C(6)–C(1)–C(38)	120.5(9)	C(3)–C(8)–C(10)	108(1)
C(6)–C(5)–C(4)	118.9(9)	C(11)–C(8)–C(9)	147(2)
C(6)–C(5)–C(12)	121.1(8)	C(11)–C(8)–C(10)	74(2)
C(4)–C(5)–C(12)	119.4(8)	C(9)–C(8)–C(10)	96(2)
C(28)–C(29)–C(30)	119.5(8)		
C(28)–C(29)–C(33)	123(1)		
C(30)–C(29)–C(33)	117(1)		
O(1)–C(6)–C(1)	118.0(8)		

5,13,20-Tri-tert-butyl-16,23-bis(ethoxycarbonylmethoxy)-8-methoxy[2.2.1]MCP **8** and 5,13,20-Tri-tert-butyl-16-(ethoxycarbonylmethoxy)-23-hydroxy[2.2.1]MCP **9**.—Compound **6** was treated as compound **5** in the preparation of compound **7**. Column chromatography with a 1:1 mixture of dichloromethane–hexane as eluent gave compound **8** (19%) as needles, m.p. 133–134 °C (from aq. MeOH) (Found: C, 75.8; H, 8.5%;  $M^+$ , 700.  $C_{44}H_{60}O_7$  requires C, 75.40; H, 8.63%;  $M$ , 700);  $\nu_{\max}/\text{cm}^{-1}$  1760 (C=O);  $\delta_{\text{H}}$  1.22 (18 H, s), 1.23 (3 H, s), 1.27 (3 H, t,  $J$  7.1), 1.33 (9 H, s), 2.46–2.61 (2 H, m), 2.74–2.85 (4 H, m), 3.29 (1 H, d,  $J$  12.5), 3.56–3.72 (2 H, m), 4.17 (4 H, q,  $J$  7.1), 4.35

(2 H, d,  $J$  15.5), 4.46 (2 H, d,  $J$  15.5), 4.63 (1 H, d,  $J$  12.5), 6.97 (2 H, d,  $J$  2.5), 7.06 (2 H, d,  $J$  2.5) and 7.25 (2 H, s).

Further elution gave compound **9** (9%) as needles, m.p. 178–180 °C (from aq. MeOH) (Found: C, 77.8; H, 8.7%;  $M^+$ , 614.  $C_{40}H_{54}O_5$  requires C, 78.14; H, 8.85%;  $M$ , 614);  $\nu_{\max}/\text{cm}^{-1}$  3490 (OH) and 1758 (C=O);  $\delta_{\text{H}}$  1.21 (9 H, s), 1.23 (9 H, s), 1.28 (3 H, t,  $J$  7.2), 1.29 (3 H, s), 1.34 (9 H, s), 2.50–2.96 (6 H, m), 3.10–5.32 (3 H, m), 4.06 (1 H, d,  $J$  15), 4.12–4.32 (3 H, m), 4.68 (1 H, d,  $J$  15), 6.17 (1 H, s), 6.92 (2 H, s), 7.00 (1 H, d,  $J$  2.6), 7.10 (1 H, d,  $J$  2.6), 7.18 (1 H, d,  $J$  2.6) and 7.32 (1 H, d,  $J$  2.6).

**Crystal-structure Determinations.**—Crystal data for **4a** were reported in ref. 1a. Atomic co-ordinates, bond lengths and angles, and thermal parameters of conformer **4a** are deposited at the Cambridge Crystallographic Data Centre.\*

**Crystal data for conformer 4b:**  $C_{38}H_{52}O_3$ , Orthorhombic,  $a = 22.5437(55)$ ,  $b = 8.4226(22)$ ,  $c = 18.0367(37)$  Å,  $\beta = 90.000^\circ$ ,  $V = 3424.7$  Å<sup>3</sup>, space group  $P_{na21}$  (No. 33),  $Z = 4$ ,  $D_x = 1.080$  g cm<sup>-3</sup>, needles. Data were collected on an Enraf-Nonius CAD-4 diffractometer,  $\theta$ - $2\theta$  scan type, graphic-monochromated Mo-K $\alpha$  radiation,  $\lambda = 0.71073$  Å. Of 8228 independent reflections collected in the range  $1 \leq \theta \leq 35^\circ$  1839 with  $I_0 > 3\sigma(I_0)$  were taken as observed. The crystal did not show any significant decay during the data collection. Positional parameters were determined by direct methods using MULTAN-82, and were refined by full-matrix least-squares calculations with all non-hydrogen atoms treated anisotropically using the scheme  $w = 4F_0^2/\sigma^2(F_0^2)^2$  to give the final residuals:  $R = 0.095$ ,  $R_w = 0.134$ . Fractional atomic co-ordinates are given in Table 2, and intramolecular bond-lengths and angles are given in Table 3. Thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.\*

\* See Instructions to Authors, January issue (section 5.6.3).

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