# (-)-Quinic Acid in Organic Synthesis. Part 4.<sup>1</sup> Syntheses of Cyclophellitol and its (1*R*,6*S*)-, (2*S*)-, (1*R*,2*S*,6*S*)-Diastereoisomers

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Cyclophellitol 1 and its (1R,6S)-, (2S)-, (1R,2S,6S)-diastereoisomers 2, 3 and 4 are constructed from quinic acid involving the following key steps: regioselective cyclic sulfate ring opening, regiospecific oxidative elimination and an epoxidation. Diastereoisomers 1, 2, 3 and 4 are characterized as their corresponding tetraacetates 5, 6, 7 and 8.

Cyclophellitol {(1S,2R,3S,4R,5R,6R)-5-hydroxymethyl-7-oxabicyclo[4.1.0]heptane-2,3,4-triol} 1 was isolated from the culture filtrates of a mushroom, *Phellinus sp.*, by the Umezawa group in 1989.<sup>2</sup> The absolute configuration of cyclophellitol 1 was established by X-ray crystallographic analysis which disclosed a fully oxygenated cyclohexane corresponding to a carba analogue of D-glucopyranose.<sup>2</sup> Cyclophellitol 1 was found to inhibit 50% of the almond  $\beta$ -D-glucosidase activity at a concentration of 0.8 µg cm<sup>-3</sup>.<sup>2</sup> The value is lower than the IC<sub>50</sub> values † of 1-deoxynojirimycin (30 µg cm<sup>-3</sup>) and castanospermine (12 µg cm<sup>-3</sup>). Also, it showed no antimicrobial activity and no cytotoxicity on NIH 3T3 cells, Molt-4 cells and P388 cells at 100 µg cm<sup>-3</sup>.<sup>2</sup>.<sup>3</sup>

Structurally, cyclophellitol 1 is a unique pseudopyranose with a  $\beta$ -epoxide moiety. The epoxide, the three hydroxy groups and the hydroxymethyl group in compound 1 have the configuration of  $\beta$ -D-glucose. Since cyclophellitol, a  $\beta$ -Dglucosidase inhibitor, has a  $\beta$ -epoxide, the  $\alpha$ -epoxide 2 might act as an  $\alpha$ -D-glucosidase inhibitor. Along this vein of reasoning, the unnatural diastereoisomeric epoxides 3 and 4, which are structurally related to  $\beta$ -D-mannose and  $\alpha$ -D-mannose respectively (Fig. 1) might be inhibitors of the corresponding glycosidases. The syntheses of cyclophellitol 1 and its (1*R*,6*S*)-, (2*S*)-, (1*R*,2*S*,6*S*)-diastereoisomers 2, 3 and 4 may help to clarify their mode of action in glycosidase inhibition.

The isolation and first total synthesis of cyclophellitol 1 was achieved by the Japanese group.<sup>4,5</sup> The synthesis started from an unnatural sugar, L-glucose, and proceeded through an intramolecular nitrile oxide cycloaddition (INOC) to construct the cyclohexane ring as the key step. The other fabrication of cyclophellitol 1 included an enantiospecific synthesis<sup>6</sup> from L-quebrachitol and a racemic synthesis<sup>7</sup> from a Diels-Alder adduct. Recently, the (1R,6S)- and (1R,2S,6S)-diastereoisomers 2 and 4 have been synthesized from D-galactose via the INOC strategy and have been shown to be a specific  $\alpha$ -Dglucosidase inhibitor and a-D-mannosidase inhibitor, respectively.<sup>5,8</sup> As part of our programme on the use of quinic acid 9 as a homochiral precursor in organic synthesis, we have already described enantiospecific syntheses of an antitumour agent COTC {2-crotonyloxymethyl-(4R,5R,6R)-4,5,6-trihydroxycyclohex-2-enone},  ${}^9$  pseudo- $\beta$ -D-fructopyranose,  ${}^{10}$  pseudo- $\beta$ -D-mannopyranose,  ${}^{10}$  pseudo- $\alpha$ -D-mannopyranose,  ${}^1$  and pseudo- $\alpha$ -D-mannopyranose,  ${}^1$  $\alpha$ -D-glucopyranose.<sup>1</sup> Recent work from other research groups employing (-)-quinic acid 9 as the starting material include the synthesis of  $1\alpha$ ,25-dihydroxy-19-norvitamin D<sub>3</sub>,<sup>11</sup> antibiotic (+)-negamycin,<sup>12</sup> and the A-ring precursor for daunomycin.<sup>13</sup> This paper describes in detail the versatility of this approach by facile syntheses of diastereoisomers 1, 2, 3 and 4.14

Our synthetic plan is shown in Fig. 2. The sites to be modified in (-)-quinic acid 9 are C-5 (deoxygenation of the tertiary alcohol and reduction of carboxyl group), C-1, C-6 (intro-



Fig. 1 Structural relationship between sugars and cyclohexane oxide inhibitors of glycosidases



Retention of configuration for 3 and 4 Inversion of configuration for 1 and 2

 $<sup>\</sup>dagger$  The IC<sub>50</sub> value reflects the amount of compound required for 50% inhibition of the enzyme under the standard assay conditions.

Fig. 2 Synthetic plan

duction of an epoxide stereoselectively), C-2 (inversion of hydroxy group for compounds 1 and 2), C-3 (inversion of configuration) and C-4 (introduction of a hydroxy group stereoselectively). All the four target compounds share three common stereogenic centres at C-3, C-4 and C-5, so our synthetic plan was to establish the hydroxy groups at C-3, C-4 and the hydroxymethyl group at C-5 first. Then we would need to address the stereocentre at C-2. Lastly, we would have to fabricate an epoxide moiety between C-1 and C-6 with the correct stereochemistry.

The route to cyclophellitol 1 and its (1R,6S)-diastereoisomer 2 is illustrated in Scheme 1. The conversion of quinic acid 9 into



Scheme 1 Reagents and conditions: i, cyclohexanone,  $H_2SO_4$  or  $H_3PO_4$  (cat.) (83%); ii, 5 steps, see ref. 1; iii, NaH, THF, 0 °C then benzyl (Bn) bromide, Bu<sub>4</sub>NI (cat.), reflux, overnight (82%); iv, CF<sub>3</sub>CO<sub>2</sub>H, CH<sub>2</sub>Cl<sub>2</sub>, room temp., 24 h (90%); v, triethylamine, thionyl chloride, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C; vi, NaIO<sub>4</sub>, RuCl<sub>3</sub> (cat.), CCl<sub>4</sub>, CH<sub>3</sub>CN, H<sub>2</sub>O, 0 °C  $\rightarrow$ room temp., 1 h (89%); vii, Bu<sub>4</sub>NI, THF, reflux, then H<sub>2</sub>SO<sub>4</sub>, H<sub>2</sub>O (83%); viii, (CH<sub>3</sub>CO)<sub>2</sub>O (Ac<sub>2</sub>O), pyridine, DMAP (cat.), CH<sub>2</sub>Cl<sub>2</sub>, room temp., 24 h (95%); vi, DBU, xylene, reflux (83%); x, NaOMe (cat.), MeOH, room temp. (95%)

the alcohol 11 followed a modified reaction sequence developed by us.<sup>1</sup> The lactone 10 was synthesized previously using Gero's procedure<sup>15</sup> by boiling a mixture of compound 9, cyclohexanone, Dowex 50 WX8 resin (H<sup>+</sup>), DMF and benzene with the azeotropic removal of water. In this work, we followed a simplified protocol developed by Stoodley<sup>16</sup> for its preparation by boiling compound 9 and cyclohexanone in the presence of a catalytic amount of H<sub>2</sub>SO<sub>4</sub> or H<sub>3</sub>PO<sub>4</sub>, with the azeotropic removal of water. We found this procedure more convenient and thus the lactone 10 was readily obtained in 83% yield from compound 9, which was converted into the alcohol 11 in six steps<sup>1</sup> with an overall yield of 41.6%. Blocking of the hydroxy group in compound 11 with benzyl bromide gave the

benzyl ether 12 in 82% yield. Hydrolysis of the cyclohexylidene ring in 12 using trifluoroacetic acid (TFA) in CH<sub>2</sub>Cl<sub>2</sub> gave the diol 13 in 90% yield. According to the Sharpless protocol,<sup>17</sup> the diol 13 was treated with thionyl chloride in the presence of triethylamine at 0 °C to give the cyclic sulfite 14, which was oxidised with catalytic RuO<sub>4</sub> in CCl<sub>4</sub>-CH<sub>3</sub>CN-H<sub>2</sub>O at 0 °C, to give the cyclic sulfate 15. The cyclic sulfate 15 could be prepared in 89% yield without isolation of the cyclic sulfite 14. The artifice of this reaction lies in the removal of the triethylamine since it was reported that the amine would inactivate the ruthenium catalyst.<sup>17</sup> The <sup>1</sup>H NMR spectrum of compound 15 showed two protons deshielded to  $\delta$  4.91 and 5.10, attributable to those attached to the cyclic sulfate moiety. The IR spectrum showed the characteristic S=O vibration at 1210 cm<sup>-1</sup> and in the mass spectrum, the  $M^+ - C_7 H_7$  fragment was observed at m/z419.

The cyclic sulfate moiety has been described as an epoxide analogue and is readily opened in an  $S_N 2$  manner by a number of nucleophiles such as the azide, benzoate, acetate, hydride, fluoride, etc.<sup>18</sup> The high reactivity of cyclic sulfates has been attributed to the ring strain, even though the origin of the ring strain is not very clear. In addition to the ring strain, the good leaving ability of the ROSO<sub>3</sub><sup>-</sup> moiety makes the five-membered cyclic sulfate very reactive towards various reagents.<sup>18</sup>

Ring opening of the cyclic sulfate 15 with  $Bu_4NI$  in refluxing THF provided the iodo alcohol 16 in 83% yield, after acidic work-up. The regioselectivity of the initial attack was identified by acetylation of the hydroxy group in compound 16 with  $Ac_2O$ -pyridine-4-dimethylaminopyridine (DMAP)-CH<sub>2</sub>Cl<sub>2</sub> to give the iodo acetate 17. The <sup>1</sup>H NMR spectrum of compound 17 showed an apparent triplet at  $\delta$  5.49 with coupling constants of J 3.5 Hz, confirming that the hydroxy group in compound 16 was attached to C-2 and at the axial position. Treatment of the iodo acetate 17 with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)<sup>19</sup> in refluxing xylene\* afforded the alkene 18 in 83% yield. Methanolysis of the acetate 18 furnished the allylic alcohol 19.

It was envisaged that the  $ROSO_3^-$  moiety after the nucleophilic attack can only be hydrolysed in the presence of acid,<sup>17,18,20</sup> so treatment of the intermediate **20** (obtained from nucleophilic attack of compound **15** with Bu<sub>4</sub>NI) directly with DBU and then with aq. acid gave the desired allylic alcohol **19** in 61% yield (Scheme 2). The cyclic sulfate **15** could also be elaborated to compound **19** by the Sharpless–Reich protocol.<sup>21</sup> Thus, treatment of the sulfate **15** with the phenyl selenide anion



Scheme 2 Reagents and conditions: i,  $Bu_4NI$ , THF, reflux; ii, DBU, xylene, reflux,  $H_2SO_4$ ,  $H_2O$ , THF (61%); iii, PhSeNa, EtOH, THF, 0 °C $\rightarrow$ room temp.,  $H_2SO_4$ ,  $H_2O$  (80%); iv, MCPBA,  $CH_2Cl_2$ , -40 °C $\rightarrow$ room temp., then  $Pr_2^iNEt$ , toluene, 80 °C (72%)

<sup>\*</sup> The reaction was unsuccessful when THF or toluene was used.

(generated from the hydride reduction of diphenyl diselenide) in tetrahydrofuran (THF) followed by acid hydrolysis formed the *trans*-diaxial seleno-alcohol **21** as the sole product in 80% yield. The selenoxide produced from the oxidation of compound **21** with *meta*-chloroperbenzoic acid (MCPBA) at -70 °C was treated with diisopropylethylamine (Hünig's base) to give compound **19** in 58% overall yield (Scheme 2). The phenomenon that the *syn*-elimination occurs away from the hydroxy group appears to be general.<sup>21</sup> The regioselectivity of the initial attack by the selenide anion was confirmed by the allylic alcohol **19** obtained.

Thus, we have shown three ways of transforming the cyclic sulfate 15 into the allylic alcohol 19. Among the three methods, the second method, *i.e.*, the *in situ* elimination of the iodide 20, was the most satisfactory in terms of both the yield and the number of steps involved. Remarkably, the ring opening of the cyclic sulfate 15 by the iodide or by the selenide was highly regioselective. This fact can be rationalized according to the effect of neighbouring polar substituents on the development of the S<sub>N</sub>2 transition state.<sup>22</sup> As shown in Fig. 3, the transition state 15a arising from nucleophilic attack at C-1 would exert a dipole which is aligned with the existing dipole at C-2, and thus the energy of the transition state XC-2 would evoke two such dipole-dipole interactions, which would be influenced by two dipoles at C-1 and C-3, resulting in an even less favourable transition state 15b.

The hydroxy group in the allylic alcohol 19 is of opposite stereochemistry to the C-2 hydroxy group in cyclophellitol 1, so our next objective was to invert the hydroxy group in compound 19 by the Mitsunobu reaction.<sup>23</sup> Treatment of the allylic alcohol 19 with benzoic acid, triphenylphosphine (PPh<sub>3</sub>) and diisopropyl azodicarboxylate (DIAD) in toluene at 0 °C gave the  $\beta$ -benzoate 22 in 93% yield. Epoxidation of the double bond in compound 22 with MCPBA in CH<sub>2</sub>Cl<sub>2</sub> gave a mixture of inseparable diastereoisomeric oxiranes 23a and 23b in 66% combined yield (<sup>1</sup>H NMR, 30:70). Debenzoylation of the inseparable oxiranes 23a and 23b with K<sub>2</sub>CO<sub>3</sub> in anhydrous MeOH gave two epoxy alcohols 24 and 25 in 95% isolated yield with a ratio of 27:73, respectively. The assignment of the stereochemistry of 24 and 25 was made by comparison with the major oxirane obtained from the epoxidation of the allylic alcohol 26. Thus, methanolysis of the  $\beta$ -benzoate 22 with NaOMe in anhydrous MeOH afforded compound 26 in 94% yield which underwent the hydroxy-directed <sup>24</sup> MCPBA epoxidation to give compounds 24 and 25 in 70% yield, with a ratio of 6:94, respectively. The major oxirane should have the epoxide ring syn<sup>24</sup> to the alcohol and therefore was assigned as the  $\beta$ epoxide 25. In order to reverse the stereoselectivity of the epoxidation, the hydroxy group in 26 was blocked with the bulky tert-butyldimethyl silyl (TBDMS) group. Treatment of compound 26 with TBDMSCl-imidazole-DMAP in DMF gave the silyl ether 27 in 91% yield. MCPBA Epoxidation of 27 furnished two diastereoisomeric oxiranes 28 and 29 in 72% isolated yield with a respective ratio of 61:39 favouring the  $\alpha$ oxirane. The assignment of the stereochemistry of the oxiranes was made simply by desilylation of the compounds 28 and 29

Fig. 3 Transition states for nucleophilic ring opening of compound 15

OBr

OBn

15b

BnOCH<sub>2</sub>

OBn

Nu OBn`\

158

BnOCH<sub>2</sub>

2019



separately with Bu<sub>4</sub>NF, affording compounds 24 and 25 respectively in 94% yields. Finally, hydrogenolysis of the antiepoxy alcohol 24 with a catalytic amount of 5% palladium on charcoal in EtOH gave cyclophellitol 1 in 93% yield. The melting point and optical rotation of synthetic 1 were in accord with those reported by the Umezawa group;<sup>2</sup> m.p. 146-148 °C;  $[\alpha]_{D}^{23} + 100 (c \ 0.3, H_2O) \{\text{lit.}, ^2 \text{ m.p. } 149 - 151 \text{ }^\circ\text{C}; [\alpha]_{D}^{27} + 103 (c \ 0.3, H_2O) \}$ 0.5, H<sub>2</sub>O). Acetylation of cyclophellitol 1 with Ac<sub>2</sub>O-pyridine-DMAP gave its tetraacetate 5 in 91% yield. The <sup>1</sup>H and <sup>13</sup>C NMR data were identical to those reported by the Vogel group<sup>7</sup> for racemic 5, m.p. 105–106 °C;  $[\alpha]_D^{23}$  +100 (c 0.2, CHCl<sub>3</sub>) (lit.,<sup>7</sup> oil). Similarly, hydrogenolysis of the syn-epoxy alcohol 25 with a catalytic amount of 5% palladium on charcoal in EtOH gave the (1R, 6S)-diastereoisomer 2 in quantitative yield. The melting point and optical rotation of synthetic 2 were in good agreement with those reported by the Umezawa group;<sup>4.5</sup> m.p. 155–157 °C;  $[\alpha]_D^{23}$  +83.3 (c 0.3, H<sub>2</sub>O) {lit.,<sup>4.5</sup> m.p. 150–152 °C;  $[\alpha]_D^{25}$  +80 (c 0.4, H<sub>2</sub>O)}. Acetylation of the isomer 2 with Ac<sub>2</sub>O-pyridine-DMAP gave its tetraacetate 6 in 83% yield, oil;  $[\alpha]_{D}^{21}$  + 90.4 (c 0.7, CHCl<sub>3</sub>).

Alternatively, the allyl acetate 18 was used for the synthesis of the (2S)- and (1R,2S,6S)-diastereoisomers 3 and 4. MCPBA Epoxidation of the alkene 18 in boiling  $CH_2Cl_2$  gave two oxiranes 30 and 31 in 77% isolated yield, with a respective ratio of 45:55. Methanolysis of the epoxy acetates 30 and 31 separately gave the corresponding epoxy alcohols 32 and 33 in 94% and 91% yield, respectively. The assignment of the stereochemistry of the oxiranes 32 and 33 was established by the hydroxy-directed MCPBA epoxidation<sup>24</sup> of the allylic alcohol 19, which gave solely the *syn*-epoxy alcohol 32 in 95% yield.

Using the said strategy, blocking of the hydroxy group in 19 with TBDMSCl gave the silyl ether 34 in 96% yield. MCPBA Epoxidation of compound 34 gave two diastereoisomeric oxiranes 35 and 36 in 67% isolated yield, with a respective ratio of 24:76. Their stereochemistries were assigned based upon desilylation and comparison with compounds 32 and 33. Thus the oxiranes 32 and 33 could be obtained from the allylic alcohol 19 in three steps with 14% and 46% overall yield, respectively.

Finally, hydrogenolysis of the syn-epoxy alcohol 32 with a catalytic amount of 5% palladium on charcoal in EtOH gave the (2S)-diastereoisomer 3 in 91% yield, for the first time, m.p. 148–150 °C;  $[\alpha]_{D}^{24}$  + 7.0 (c 0.4, H<sub>2</sub>O). Acetylation of compound 3 with Ac<sub>2</sub>O-pyridine-DMAP gave its tetraacetate 7 in 91% yield, m.p. 111.5–113 °C;  $[\alpha]_{D}^{23}$  – 55.3 (c 0.4, CHCl<sub>3</sub>). Similarly, hydrogenolysis of the *anti*-epoxy alcohol 33 with a catalytic amount of 5% palladium on charcoal in EtOH gave the (1*R*,2*S*,6*S*)-diastereoisomer 4 in 89% yield. The melting point and optical rotation of synthetic 4 are compared with those obtained from the Umezawa group;<sup>8</sup> 4, m.p. 129–131 °C;  $[\alpha]_{D}^{23}$  – 39.5 (c 0.9, H<sub>2</sub>O) {lit.,<sup>8</sup> oil;  $[\alpha]_{D}^{25}$  – 76 (c 0.1, H<sub>2</sub>O)}. Acetylation of compound 4 with Ac<sub>2</sub>O-pyridine-DMAP gave the new tetraacetate 8 in 93% yield, m.p. 74–75 °C;  $[\alpha]_{D}^{22}$  0.0 (c 0.4, CHCl<sub>3</sub>).

It is noteworthy that the presence of the oxirane moiety in compounds 1 to 8 could be established by <sup>13</sup>C NMR spectroscopy; the two carbons bearing the oxirane moiety (C-1,6) in compounds 1 to 4 resonated in the range from  $\delta$  54.4 to 58.2, whereas those in compounds 5 to 8 resonated in the range from  $\delta$  50.8 to 54.7.

In conclusion, cyclophellitol 1 and its (1R,6S)-diastereoisomer 2 could be synthesized from (-)-quinic acid 9 in 17 steps with 4.5% overall yield and in 15 steps with 8.6% overall yield, respectively. On the other hand, the (2S)- and (1S,2S,6R)diastereoisomers 3 and 4 could be synthesized from (-)-quinic acid 9 in 13 steps with 12.6% overall yield and in 15 steps with 6.0% overall yield, respectively. Remarkably, the diastereoisomers 2 and 3 could also be obtained stereoselectively by hydroxy-directed MCPBA expoxidation of the allylic alcohols 26 and 19, respectively.

#### **Experimental**

M.p.s were measured on a Reichert Microscope apparatus and are uncorrected. A Bruker WM 250 spectrometer was used to obtain <sup>1</sup>H (250 MHz) and <sup>13</sup>C (62.9 MHz) NMR spectra. All spectra were measured on solutions of the compound in deuteriochloroform with Me<sub>4</sub>Si (TMS) as internal standard, unless otherwise stated. Chemical shifts are reported as parts per million (ppm) using the  $\delta$  scale. Coupling constants (J) are reported in Hz. IR spectra were recorded on a Nicolet 205 FTIR spectrometer. EI- and CI(isobutane)-mass spectra were recorded on a VG 7070F mass spectrometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter using chloroform as solvent, unless otherwise stated;  $[\alpha]_D$  values are recorded in 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup>. Elemental analyses were carried out at either the Shanghai Institute of Organic Chemistry, Academic Sinica, China or at MEDAC Ltd., Department of Chemistry, Brunel Unisversity, Uxbridge, Middlesex UB8 3PM, United Kingdom. All reactions were monitored by thin layer chromatography (TLC) performed on a Merck precoated silica gel 60F254 plates, and compounds were visualised with a spray (5% w/v dodecamolybdophosphoric acid in ethanol) and subsequent heating. Flash chromatography was carried out on columns of Merck Keisel gel 60 (230-400 mesh). All solvents were reagent grade. Pyridine was distilled from barium oxide and stored in the presence of potassium hydroxide pellets. THF was freshly distilled from Na-benzophenone ketyl under nitrogen. CH<sub>2</sub>Cl<sub>2</sub> Was distilled from P<sub>2</sub>O<sub>5</sub> and stored over 4 Å molecular sieves. DMF was distilled over CaH<sub>2</sub> under reduced pressure and stored over 3 Å molecular sieves under nitrogen.

Cyclophellitol 1.—To a suspension of palladium on charcoal (60 mg; 5% w/w) in absolute EtOH (1.5 cm<sup>3</sup>) under H<sub>2</sub> at atmospheric pressure was added a solution of the benzylated compound 24 (189.3 mg, 0.424 mmol) in absolute EtOH (8

cm<sup>3</sup>). The suspension was stirred for 2 h at room temp. and filtered through a pad of Celite. The residue was washed with methanol (30 cm<sup>3</sup>) and concentration of the filtrate, followed by flash chromatography [chloroform–methanol (3:1 v/v)] gave cyclophellitol 1 (69.4 mg, 93%) as colourless needles, m.p. 146–148 °C (MeOH), [lit.,<sup>2</sup> 149–151 °C (H<sub>2</sub>O)];  $R_{\rm f}$  0.32 [chloroform–methanol (3:1)] (Found: C, 47.7; H, 6.9. C<sub>7</sub>H<sub>12</sub>O<sub>5</sub> requires C, 47.7; H, 6.9%);  $[\alpha]_{\rm D}^{23}$  + 100 (c 0.3, H<sub>2</sub>O) {lit.,<sup>2</sup>  $[\alpha]_{\rm D}^{27}$  + 103 (c 0.5, H<sub>2</sub>O)};  $\nu_{\rm max}({\rm KBr})/{\rm cm^{-1}}$  3400 and 3490 (OH);  $\delta_{\rm H}({\rm D}_{2}{\rm O}, {\rm DOH}$  at 4.80) 2.10 (1 H, m, 5-H), 3.18–3.26 (2 H, m, 1-H and 4-H), 3.35 (1 H, dd, J 8.4 and 10.0, 3-H), 3.54 (1 H, br d, J 3.6, 6-H), 3.75–3.83 (2 H, m, 2-H and 8-H) and 3.98 (1 H, dd, J 3.8 and 11.3, 8'-H);  $\delta_{\rm C}({\rm D}_{2}{\rm O}, {\rm dixane} \delta$  67.4) 44.3, 56.8, 56.9, 61.4, 67.8, 71.7 and 77.1; *m/z* (CI) 177 (MH<sup>+</sup>).

# (1R,2R,3S,4R,5R,6S)-5-Hydroxymethyl-7-oxabicyclo-

[4.1.0]*heptane*-2,3,4-*triol* **2**.—Similar catalytic hydrogenolysis of the benzylated compound **25** (235.5 mg, 0.528 mmol) as above gave, after flash chromatography [chloroform–methanol (2:1 v/v)], the (1*R*,6*S*)-diastereoisomer **2** (92.6 mg, 100%) as colourless needles, m.p. 155–157 °C (MeOH), [lit.,<sup>4,5</sup> 150–152 °C (MeOH)]; *R*<sub>f</sub> 0.32 [chloroform–methanol (2:1 v/v)] (Found: C, 47.5; H, 6.9. C<sub>7</sub>H<sub>12</sub>O<sub>5</sub> requires C, 47.7; H, 6.9%);  $[\alpha]_D^{23}$  +83.3 (*c* 0.3, H<sub>2</sub>O), {lit.,<sup>4.5</sup>  $[\alpha]_D^{25}$  +80 (*c* 0.4, H<sub>2</sub>O)}; *v*<sub>max</sub>(KBr)/cm<sup>-1</sup> 3244 and 3322 (OH);  $\delta_H(D_2O)$  2.04 (1 H, m, 5-H), 3.30–3.47 (4 H, m), 3.78 (1 H, dd, *J* 5.9 and 11.3, 8-H) and 3.89–3.95 (2 H, m);  $\delta_C(D_2O)$  45.0, 55.8, 58.2, 61.3, 70.4, 72.1 and 74.0; *m/z* (CI) 177 (MH<sup>+</sup>).

(1S,2S,3S,4R,5R,6R)-5-*Hydroxymethyl*-7-*oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* 3.—Similar catalytic hydrogenolysis of compound **32** (255.9 mg, 0.574 mmol) as above afforded, after flash chromatography [chloroform–methanol (5:2 v/v)], the (2S)*diastereoisomer* **3** (92.1 mg, 91%) as colourless needles, m.p. 148–150 °C (MeOH);  $R_f$  0.28 [chloroform–methanol (5:2 v/v)] (Found: C, 47.6; H, 6.9. C<sub>7</sub>H<sub>12</sub>O<sub>5</sub> requires C, 47.7; H, 6.9%); [ $\alpha$ ]<sub>D</sub><sup>24</sup> + 7.0 (*c* 0.4, H<sub>2</sub>O);  $\nu_{max}$ (KBr)/cm<sup>-1</sup> 3440 and 3470 (OH);  $\delta_H$ (D<sub>2</sub>O) 2.11 (1 H, m, 5-H), 3.42–3.58 (4 H, m), 3.84 (1 H, dd, *J* 8.0 and 11.0, 8-H), 4.00 (1 H, dd, *J* 4.2 and 11.0, 8'-H) and 4.38 (1 H, t, *J* 4.5);  $\delta_C$ (D<sub>2</sub>O) 44.8, 54.4, 56.9, 61.8, 66.4, 66.7 and 73.2; *m/z* (CI) 177 (MH<sup>+</sup>).

(1R,2S,3S,4R,5R,6S)-5-*Hydroxymethyl*-7-*oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* 4.—Similar catalytic hydrogenolysis of compound 33 (723.5 mg, 1.62 mmol) provided, after chromatography [chloroform–methanol (3:1 v/v)], the (1*R*,2*S*,6*S*)diastereoisomer 4 (254.6 mg, 89%) as colourless plates, m.p. 129–131 °C (MeOH), [lit.,<sup>8</sup> oil]; *R*<sub>f</sub> 0.30 [chloroform– methanol (3:1)] (Found: C, 47.6; H, 6.9. C<sub>7</sub>H<sub>12</sub>O<sub>5</sub> requires C, 47.7; H, 6.9%);  $[\alpha]_{D}^{23}$  – 39.5 (*c* 0.9, H<sub>2</sub>O), {lit.,<sup>12</sup>  $[\alpha]_{D}^{25}$  – 76 (*c* 0.1, H<sub>2</sub>O)};  $\nu_{max}(KBr)/cm^{-1}$  3364 and 3426 (OH);  $\delta_{H}(D_{2}O)$ 2.05 (1 H, m, 5-H), 3.32 (1 H, d, *J* 3.7), 3.43 (1 H, t, *J* 2.9), 3.50– 3.60 (2 H, m), 3.78 (1 H, dd, *J* 6.8 and 11.3, 8-H), 3.92 (1 H, dd, *J* 3.7 and 11.3, 8'-H) and 4.43 (1 H, br s);  $\delta_{C}(D_{2}O)$  45.3, 55.6, 56.6, 61.6, 66.7, 68.0 and 71.2; *m/z* (CI) 177 (MH<sup>+</sup>).

(1R,2S,3S,4R,5R,6R)-2,3,4-*Tri*-O-*acetyl*-5-*acetoxymethyl*-7oxabicyclo[4.1.0]*heptane*-2,3,4-*triol* 5.—A solution of cyclophellitol 1 (17.4 mg, 0.099 mmol), acetic anhydride (0.3 cm<sup>3</sup>) and a crystal of 4-dimethylaminopyridine (DMAP) in pyridine (1.5 cm<sup>3</sup>) was stirred at room temp. for 12 h. The solution was diluted with CH<sub>2</sub>Cl<sub>2</sub> (4 cm<sup>3</sup>) and an aq. saturated solution of NH<sub>4</sub>Cl (1.5 cm<sup>3</sup>) was added. The aq. phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 4 cm<sup>3</sup>) and the combined organic extracts were washed with brine (2 × 4 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (1:2 v/v)] gave the *tetraacetate* 5 (31.0 mg, 91%) as colourless needles, m.p. 105–106 °C;  $R_f$  0.44 [hexane-diethyl ether (1:3 v/v)] (Found: C, 52.0; H, 5.8.  $C_{15}H_{20}O_9$  requires C, 52.3; H, 5.85%);  $[\alpha]_{D^3}^{D^3} + 100$  (c 0.2);  $v_{max}(film)/cm^{-1}$  1752 (C=O);  $\delta_H$  1.99 (3 H, s, Ac), 2.04 (3 H, s, Ac), 2.09 (3 H, s, Ac), 2.10 (3 H, s, Ac), 2.50 (1 H, m, 5-H), 3.15 (1 H, d, J 3.5, 1-H), 3.46 (1 H, br d, J 3.5, 6-H), 4.16 (1 H, dd, J 7.3 and 11.3, 8-H), 4.31 (1 H, dd, J 4.2 and 11.3, 8'-H), 5.02 (1 H, t, J 10, 4-H) and 5.0–5.19 (2 H, m, 2-H, 3-H);  $\delta_C$  20.5 (×2), 20.7 (×2), 39.8, 53.2, 54.7, 62.1, 66.5, 71.1, 72.4, 169.6, 169.7, 169.9 and 170.5; m/z (EI) 345 (MH<sup>+</sup>, 6%), 182 (13) and 43 (100).

(1S,2S,3S,4R,5R,6S)-2,3,4-*Tri*-O-*acetyl*-5-*acetoxymethyl*-7oxabicyclo[4.1.0]*heptane*-2,3,4-*triol* 6.—Similar acetylation of the epoxide 2 (10.0 mg, 0.057 mmol) and work-up as above gave the *tetraacetate* 6 (16.2 mg, 83%) as a colourless oil;  $R_f$  0.43 [hexane-diethyl ether (1:3 v/v)] (Found: C, 52.1; H, 6.0. C<sub>15</sub>H<sub>20</sub>O<sub>9</sub> requires C, 52.3; H, 5.85%);  $[\alpha]_{2}^{21}$  +90.4 (c 0.7);  $\nu_{max}(film)/cm^{-1}$  1748 (C=O);  $\delta_{\rm H}$  2.00 (3 H, s, Ac), 2.03 (3 H, s, Ac), 2.11 (3 H, s, Ac), 2.12 (3 H, s, Ac), 2.52 (1 H, m, 5-H), 3.22 (1 H, d, J 3.9, 6-H), 3.49 (1 H, dd, J 1.6 and 3.9, 1-H), 4.11 (1 H, dd, J 5.2 and 11.7, 8-H), 4.22 (1 H, dd, J 3.4 and 11.7, 8'-H), 5.07 (1 H, dd, J 9.9 and 12.0, 4-H), 5.27 (1 H, dd, J 9.1 and 9.9, 3-H) and 5.34 (1 H, dd, J 1.8 and 9.1, 2-H);  $\delta_{\rm C}$  20.5 (× 2), 20.6, 20.7, 40.4, 53.5, 54.2, 62.2, 68.7, 70.1, 71.4, 169.5, 169.8, 170.4 and 170.5; m/z (EI) 345 (MH<sup>+</sup>, 6%), 182 (40) and 43 (100).

(1R,2R,3S,4R,5R,6R)-2,3,4-*Tri-O-acetyl-5-acetoxymethyl-7-oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* 7.—Similar acetylation of the epoxide 3 (18.2 mg, 0.103 mmol) as above furnished, after flash chromatography [hexane-diethyl ether (2:5 v/v)], the *tetraacetate* 7 (32.3 mg, 91%) as colourless needles, m.p. 111.5-113 °C;  $R_{\rm f}$  0.37 [hexane-diethyl ether (1:3)] (Found: C, 52.4; H, 5.85. C<sub>15</sub>H<sub>20</sub>O<sub>9</sub> requires C, 52.3; H, 5.85%);  $[\alpha]_{D}^{23}$  - 55.3 (*c*0.4);  $\nu_{\rm max}$ (film)/cm<sup>-1</sup> 1744 (C=O);  $\delta_{\rm H}$  2.02 (3 H, s, Ac), 2.06 (3 H, s, Ac), 2.10 (3 H, s, Ac), 2.15 (3 H, s, Ac), 2.47 (1 H, m, 5-H), 3.44 (1 H, dd, J 2.5 and 3.8, 6-H), 3.48 (1 H, dd, J 3.8 and 4.1, 1-H), 4.25 (1 H, dd, J 7.6 and 11.2, 8-H), 4.29 (1 H, dd, J 5.5 and 11.2, 8'-H), 4.98 (1 H, dd, J 5.3 and 9.3, 3-H), 5.14 (1 H, dd, J 7.9 and 9.3, 4-H) and 5.51 (1 H, t, J 4.8, 2-H);  $\delta_{\rm C}$  20.4, 20.5, 20.6, 20.7, 40.0, 50.8, 53.7, 62.5, 66.0, 66.3, 69.2, 169.4, 169.7, 170.2 and 170.5; *m/z* (EI) 345 (MH<sup>+</sup>, 68%) and 182 (100).

(1S,2R,3S,4R,5R,6S)-2,3,4-*Tri-O-acetyl-5-acetoxymethyl-7-oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* **8**.—Similar acetylation of the epoxide **4** (15.8 mg, 0.090 mmol), as above furnished, after flash chromatography [hexane–diethyl ether (1:2 v/v)], the *tetraacetate* **8** (28.8 mg, 93%) as a white solid, m.p. 74–75 °C;  $R_f$  0.46 [hexane–diethyl ether (1:3 v/v)] (Found: C, 52.35; H, 5.8. C<sub>15</sub>H<sub>20</sub>O<sub>9</sub> requires C, 52.3; H, 5.85%);  $[\alpha]_{\text{D}}^{22}$  0.0 (c 0.4);  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1747 (C=O);  $\delta_{\text{H}}$  1.92 (3 H, s, Ac), 1.98 (3 H, s, Ac), 2.05 (3 H, s, Ac), 2.11 (3 H, s, Ac), 2.46 (1 H, m, 5-H), 3.13 (1 H, d, J 3.2, 6-H), 3.26 (1 H, t, J 3.2, 1-H), 4.09 (1 H, dd, J 6.8 and 11.5, 8-H), 4.22 (1 H, dd, J 4.1 and 11.5, 8'-H), 5.08 (1 H, dd, J 3.0 and 10.7, 3-H); 5.18 (1 H, dd, J 8.5 and 10.7, 4-H) and 5.71 (1 H, t, J 3.0, 2-H);  $\delta_{\text{C}}$  20.4 (×2), 20.6 (×2), 40.5, 52.9 (×2), 62.6, 65.9, 67.2, 69.1, 169.4, 169.7, 169.9 and 170.4; *m*/z (EI) 345 (MH<sup>+</sup>, 20%) and 182 (100).

3,4-O-Cyclohexylidene-1,3,4-trihydroxycyclohexane-1,5-carbolactone 10.<sup>16</sup>—A mixture of (–)-quinic acid (1,3,4,5-tetrahydroxycyclohexanecarboxylic acid) 9 (100 g, 0.52 mol) and cyclohexanone (152 cm<sup>3</sup>, 1.56 mol) containing conc. phosphoric acid (10 drops) was heated under reflux for 30 min. The solution was then distilled for *ca.* 2.5 h until all the water (*ca.* 19 cm<sup>3</sup>) was removed. The yellow solution was left to cool and ethyl acetate (160 cm<sup>3</sup>), potassium hydrogen carbonate (16 g) and anhydrous sodium sulfate (16 g) were added. The mixture was stirred until neutral, as shown by pH paper, filtered and the filtrate concentrated to leave a yellow solid. Recrystallisation of the 2021

solid from chloroform-hexane (1:1 v/v) gave the title compound 10 (110 g, 83%) as colourless needles, m.p. 140–142 °C (lit.,<sup>15</sup> 139–141 °C);  $R_f 0.30$  [hexane-diethyl ether (1:2)];  $[\alpha]_{D}^{21}$  – 30.4 (c 1.0) {lit.,<sup>15</sup>  $[\alpha]_{D}^{20}$  – 33 (c 1.1)};  $v_{max}$ (film)/cm<sup>-1</sup> 3425 (OH) and 1797 (lactone C=O);  $\delta_H 1.40$ –1.75 (10 H, m), 2.18 (1 H, dd, J 14 and 3), 2.34 (2 H, m), 2.66 (1 H, d, J 12), 3.04 (1 H, bs, OH), 4.31 (1 H, ddd, J 6, 2.3 and 1.2), 4.48 (1 H, td, J 7 and 2.85) and 4.74 (1 H, dd, J 6 and 2.5); m/z (EI) 254 (M<sup>+</sup>, 24%) and 211 (M<sup>+</sup> - C<sub>3</sub>H<sub>7</sub>, 100).

(1R,2R,3S,4R,5R)-3,4-Di-O-benzyl-5-benzyloxymethyl-1,2-O-cyclohexylidenecyclohexane-1,2,3,4-tetraol 12.—Sodium hydride (80%, 30 mg, 1.04 mmol) was washed with dry hexane  $(2 \times 1 \text{ cm}^3)$  and suspended in dry THF (5 cm<sup>3</sup>) under nitrogen at 0 °C. A solution of the alcohol 11 (304.5 mg, 0.695 mmol) in THF (2 cm<sup>3</sup>) was added dropwise and the mixture was stirred for 1 h. Benzyl bromide (0.165 cm<sup>3</sup>, 1.39 mmol) was then added dropwise, followed by the addition of a catalytic amount of tetrabutylammonium iodide. The mixture was stirred at 60 °C for 12 h and then methanol (1 cm<sup>3</sup>) was slowly added, followed by the addition of water (3 cm<sup>3</sup>). The organic solvent was removed under reduced pressure, chloroform (10 cm<sup>3</sup>) was then added to the residue and the aq. layer was then extracted with chloroform  $(4 \times 4 \text{ cm}^3)$ . The combined extracts were washed with brine  $(3 \times 3 \text{ cm}^3)$ , dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (3:1 v/v)] provided the *title compound* 12 (300 mg, 82%) as a white solid, m.p. 82.5-83 °C (diethyl etherhexane); R<sub>f</sub> 0.31 [hexane-diethyl ether (1:1)] (Found: C, 76.9; H, 7.4.  $C_{34}H_{40}O_5$  requires C, 77.2; H, 7.6%);  $[\alpha]_D^{20} + 28.8(c 1.0)$ ;  $v_{max}(film)/cm^{-1}$  3000–3100 (aromatic C-H);  $\delta_{H}$  1.4–2.0 (13 H, m), 3.52 (2 H, br d, J 4.3), 3.65 (1 H, dd, J 8.7 and 3.9, 3-H), 3.76 (1 H, t, J 8.7, 4-H), 4.06-4.14 (1 H, m, 1-H), 4.31 (1 H, t, J 4.4, 2-H), 4.47 (2 H, s, OCH<sub>2</sub>Ph), 4.77 (2 H, s, OCH<sub>2</sub>Ph), 4.50 and 4.89 (2 H, ABq, J 10.9, OCH<sub>2</sub>Ph) and 7.27-7.42 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 528 (M<sup>+</sup>, 4%), 437 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 7) and 91 (100).

(1R,2R,3S,4R,5R)-3,4-Di-O-benzyl-5-benzyloxymethylcyclohexane-1,2,3,4-tetraol 13.-To a solution of the compound 12 (157 mg, 0.297 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 cm<sup>3</sup>) was added trifluoroacetic acid (TFA) (2 drops) and H<sub>2</sub>O (1 drop). The mixture was stirred at room temp. for 24 h and poured into an aq. solution of NaHCO3 (5% w/v, 1 cm<sup>3</sup>). The aq. phase was extracted with  $CH_2Cl_2$  (3 × 2 cm<sup>3</sup>). The combined extracts were washed with brine  $(2 \times 1 \text{ cm}^3)$ , dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate followed by flash chromatography [hexane-ethyl acetate (4:5 v/v)] provided the title compound 13 (120 mg, 90%) as plates, m.p. 110.5-112 °C (hexane-diethyl ether);  $R_f$  0.40 [hexane-ethyl acetate (2:3)] (Found: C, 75.2; H, 7.2. C<sub>28</sub>H<sub>32</sub>O<sub>5</sub> requires C, 75.0; H, 7.2%);  $[\alpha]_{D}^{20} + 26.3 (c 1.2); v_{max}(film)/cm^{-1} 3450 (OH); \delta_{H} 1.63 (1 H, m),$ 1.83-1.90 (2 H, m), 3.45 (1 H, dd, J 9.2 and 2.8), 3.50-3.65 (3 H, m), 3.70 (1 H, dd, J10.5 and 9.3), 4.16 (1 H, t, J2.75, 2-H), 4.47 (2 H, s, OCH<sub>2</sub>Ph), 4.70 (2 H, s, OCH<sub>2</sub>Ph), 4.50 and 4.86 (2 H, ABq, J 10.8, OCH<sub>2</sub>Ph) and 7.21-7.61 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI)  $357 (M^+ - C_7 H_7, 5\%)$  and 91 (100).

(1R,2R,3S,4R,5R)-3,4-Di-O-benzyl-5-benzyloxymethyl-1,2-O,O-sulfinyl-cyclohexane-1,2,3,4-tetraol 14.—To a solution of the diol 13 (223.7 mg, 0.50 mmol), triethylamine (0.28 cm<sup>3</sup>, 2 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 cm<sup>3</sup>) at 0 °C was added thionyl chloride (0.054 cm<sup>3</sup>, 0.75 mmol) over 5 min. The reaction mixture was diluted with cold diethyl ether (25 cm<sup>3</sup>) and washed with cold water (2 × 15 cm<sup>3</sup>) and brine (15 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (1:1 v/v)] provided the *title compound* 14 (230 mg, 93%) as colourless needles, m.p. 99.5–102 °C;  $R_f$  0.40 [hexane–diethyl ether (1:1)] (Found; C, 67.5; H, 6.1.  $C_{28}H_{30}O_6S$  requires C, 68.0, H, 6.1%)  $[\alpha]_D^{20}$  + 62.3 (c 0.5);  $v_{max}(film)/cm^{-1}$  1211 (S=O) and 810–850 (S-O-C);  $\delta_H$ 1.69–1.82 (2 H, m), 2.16–2.23 (1 H, m), 3.48–3.55 (2 H, m), 3.72 (1 H, t, J 7.8), 4.85 (1 H, dd, J 7.3 and 3.7), 4.44 (2 H, s), 4.48 (1 H, d, J 11), 4.68 (1 H, d, J 11.8), 4.76 (1 H, d, J 10.4), 4.77 (1 H, d, J 10.8), 4.87–4.93 (1 H, m), 5.14 (1 H, t, J 4.6) and 7.21–7.36 (15 H, m); m/z (EI) 403 (M<sup>+</sup> –  $C_7H_7$ , 4%) and 91 (100).

(1R,2R,3S,4R,5R)-3,4-Di-O-benzyl-5-benzyloxymethyl-1,2-O,O-sulfonyl-cyclohexane-1,2,3,4-tetraol 15.—To a solution of the diol 13 (88 mg, 0.198 mmol), triethylamine (0.110 cm<sup>3</sup>, 0.792 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 cm<sup>3</sup>) at 0 °C was added thionyl chloride  $(0.05 \text{ cm}^3, 0.69 \text{ mmol})$  over 5 min. The reaction mixture was diluted with cold diethyl ether (12 cm<sup>3</sup>) and washed with cold water  $(2 \times 12 \text{ cm}^3)$  and brine  $(10 \text{ cm}^3)$ . The organic solution was dried (MgSO<sub>4</sub>) and filtered. The filtrate was concentrated and the residual triethylamine was removed under high vacuum (ca. 1 h). The solid residue was dissolved in  $CCl_4$  (5 cm<sup>3</sup>) and MeCN (5  $cm^3$ ), and the solution cooled in an ice-bath. Cold water (8 cm<sup>3</sup>) was added followed by a catalytic amount of RuCl<sub>3</sub>·H<sub>2</sub>O and NaIO<sub>4</sub> (85 mg, 0.396 mmol). After 1 h, diethyl ether (15 cm<sup>3</sup>) was added and the two layers were separated. The aq. layer was extracted with diethyl ether  $(2 \times 5 \text{ cm}^3)$  and the combined organic extracts were washed with brine  $(2 \times 5)$  $cm^3$ ), dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (2:3 v/v] provided the *title compound* 15 (89.9 mg, 89%) as a white solid, m.p. 106.5-108 °C; R<sub>f</sub> 0.35 [hexane-diethyl ether (2:3)] (Found: C, 65.65; H, 5.75. C<sub>28</sub>H<sub>30</sub>O<sub>7</sub>S requires C, 65.9, H, 5.9%);  $[\alpha]_{D}^{20} + 27.8 (c \ 0.9); v_{max}(film)/cm^{-1} 1210 (S=O) and 810-$ 850 (S-O-C);  $\delta_{\rm H}$  1.61–1.68 (1 H, m), 2.13–2.35 (2 H, m), 3.49 (2 H, d, J 5.0), 3.69–3.77 (2 H, m), 4.45 (2 H, s), 4.45 (1 H, d, J 10.9), 4.70 (1 H, d, J 11.8), 4.73 (1 H, d, J 12.6), 4.78 (1 H, d, J 12.0), 4.86–4.95 (1 H, m), 5.09–5.11 (1 H, m) and 7.17–7.37 (15 H, m); m/z (EI) 419 (M<sup>+</sup> – C<sub>7</sub>H<sub>7</sub>, 9%) and 91 (100).

## (1R,2R,3R,4S,6R)-1,2-Di-O-benzyl-6-benzyloxymethyl-4iodocyclohexane-1,2,3-triol 16.—A solution of the cyclic sulfate 15 (127 mg, 0.249 mmol), Bu<sub>4</sub>NI (110 mg, 0.299 mmol) in THF (12 cm<sup>3</sup>) was heated under reflux for 6 h under nitrogen. Conc. $H_2SO_4$ (15 mm<sup>3</sup>) and $H_2O$ (4 mm<sup>3</sup>) were added and the solution stirred for 30 min at 60 °C. An excess of NaHCO<sub>3</sub> (100 mg) was added and the mixture stirred for 25 min. The mixture was filtered through a pad of silica gel topped with Celite and washed with CH<sub>2</sub>Cl<sub>2</sub>. Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (3:1 v/v)] afforded the title compound 16 as a colourless oil (116 mg, 83%); R<sub>f</sub> 0.60 [hexane-diethyl ether (1:1)] (Found: C, 60.5; H, 5.5. $C_{28}H_{31}IO_4$ requires C, 60.2; H, 5.6%; $[\alpha]_D^{22} + 46.4$ (c 1.4); $v_{max}$ (film)/cm<sup>-1</sup> 3440 (OH); $\delta_{H}$ 1.8–2.3 (3 H, m), 2.73 (1 H, d, J 2.05, OH), 3.47 (1 H, dd, J 9.1 and 2.9, 7-H), 3.67 (1 H, dd, J 9.1 and 4.9, 7'-H), 3.78 (1 H, t, J 8.7, 1-H), 4.14 (1 H, dd, J 8.7 and 2.9, 2-H), 4.20 (1 H, br s, 3-H), 4.39-4.53 (4 H, m, 4-H and OCH<sub>2</sub>Ph), 4.60 and 4.69 (2 H, ABq, J 11.4, OCH<sub>2</sub>Ph), 4.79 (1 H, d, J 10.9, OCH<sub>2</sub>Ph) and 7.21-7.41 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 558 (M<sup>+</sup>, 2%), 467 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 32) and 91 (100).

(1R,2R,3R,4S,6R)-3-O-Acetyl-1,2-di-O-benzyl-6-benzyloxymethyl-4-iodocyclohexane-1,2,3-triol 17.—To a mixture of the iodo alcohol 16 (669.4 mg, 1.20 mmol), pyridine (0.213 cm<sup>3</sup>, 2.64 mmol) and a catalytic amount of DMAP in dry CH<sub>2</sub>Cl<sub>2</sub> was added acetic anhydride (0.125 cm<sup>3</sup>, 1.32 mmol) at room temp. The solution was stirred at this temp. for 24 h, then poured into a solution of saturated NH<sub>4</sub>Cl (8 cm<sup>3</sup>) and the aq. phase extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 8 cm<sup>3</sup>). The combined organic extracts were washed with brine (2 × 8 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (3:1 v/v)] afforded the *title compound* 17 (680.5 mg, 95%) as a colourless oil;  $R_{\rm f}$  0.55 [hexane-diethyl ether (2:1 v/v)] (Found: 60.1; H, 5.4. C<sub>30</sub>-H<sub>33</sub>IO<sub>5</sub> requires C, 60.0; H, 5.5%);  $[\alpha]_D^{28}$  + 59.5 (c 1.2);  $v_{\rm max}({\rm film})/{\rm cm}^{-1}$  1744 (C=O);  $\delta_{\rm H}$  2.04–2.19 (3 H, m), 2.13 (3 H, br s, Ac), 3.50 (1 H, dd, J 9.1 and 2.9, 7-H), 3.70 (1 H, dd, J 9.1 and 4.9, 7'-H), 3.75 (1 H, t, J 9.0, 1-H), 4.29 (1 H, dd, J 9.0 and 3.5, 2-H), 4.43–4.50 (3 H, m, OCH<sub>2</sub>Ph), 4.55 and 4.65 (2 H, ABq, J 11.2, OCH<sub>2</sub>Ph), 4.83 (1 H, d, J 10.9, OCH<sub>2</sub>Ph), 5.19 (1 H, t, J 3.5, 3-H) and 7.22–7.35 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 509 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 13%), 493 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>O, 23), 403 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub> - C<sub>7</sub>H<sub>6</sub>O, 46) and 91 (100).

(1R,2R,3R,4R)-1-O-Acetyl-2,3-di-O-benzyl-4-benzyloxymethylcyclohex-5-ene-1,2,3-triol 18.-A solution of the iodo acetate 17 (1.15 g, 1.92 mmol), 1,8-diazabicyclo[5.4.0]undec-7ene (DBU) (0.57 cm<sup>3</sup>, 3.83 mmol) in xylene (25 cm<sup>3</sup>) was heated to reflux under nitrogen for 12 h. The mixture was cooled and filtered through a pad of silica gel topped with Celite and washed with diethyl ether (30 cm<sup>3</sup>). Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (5:2 v/v)] gave the title compound 18 (0.75 g, 83%) as a colourless oil;  $R_f 0.48$  [hexane-diethyl ether (2:1 v/v)] (Found: C, 76.5; H, 6.7.  $C_{30}H_{32}O_5$  requires C, 76.25; H, 6.8%);  $[\alpha]_D^{22}$  – 19.7 (c 1.2);  $v_{max}(film)/cm^{-1}$  1735 (C=O);  $\delta_{H}$  2.11 (3 H, br s, Ac), 2.50 (1 H, m, 4-H), 3.50 (1 H, dd, J 9.0 and 6.0, 7-H), 3.61 (1 H, dd, J9.0 and 4.0, 7'-H), 3.73 (1 H, dd, J9.7 and 3.7, 2-H), 3.82 (1 H, t, J 9.7, 3-H), 4.40–4.63 (4 H, m, OCH<sub>2</sub>Ph), 4.72 (1 H, J 11.5, OCH<sub>2</sub>Ph), 4.92 (1 H, d, J 11.0, OCH<sub>2</sub>Ph), 5.67 (1 H, dd, J 4.8 and 3.2, 1-H), 5.76 (1 H, ddd, J 9.6, 4.8 and 2.6, 6-H), 5.93 (1 H, dd, J 9.6 and 2.3, 5-H) and 7.21-7.33 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 381 ( $M^+ - C_7 H_7, 9\%$ ), 275 ( $M^+ - C_7 H_7 - C_7 H_6 O, 32$ ) and 91 (100).

(1R,2R,3R,4R)-2,3-Di-O-benzyl-4-benzyloxymethylcyclohex-5-ene-1,2,3-triol 19.—Method A. A solution of the allyl acetate 18 (185.6 mg, 0.393 mmol) and a catalytic amount of sodium methoxide in anhydrous methanol (10 cm<sup>3</sup>) was stirred at room temp. for 15 h. The mixture was filtered through a pad of silica gel topped with Celite and washed with ethyl acetate (20 cm<sup>3</sup>). Concentration of the filtrate, followed by flash chromatography [hexane-diethylether (1:1 v/v)] gave the title compound 19 (160.3 mg, 95%) as a colourless oil;  $R_f 0.35$  [hexane-diethyl ether (1:1 v/v)]; (Found: C, 78.0; H, 7.05. C<sub>28</sub>H<sub>30</sub>O<sub>4</sub> requires C, 78.1; H, 7.0%);  $[\alpha]_{D}^{28}$  + 54.3 (c 1.3);  $\nu_{max}(\text{film})/\text{cm}^{-1}$  3450 (OH);  $\delta_{H}$  2.45– 2.53 (1 H, m, 4-H), 2.61 (1 H, br s, OH), 3.44 (1 H, dd, J 9.0 and 6.4, 7-H), 3.58 (1 H, dd, J 9.0 and 4.3, 7'-H), 3.65 (1 H, dd, J 9.2 and 4.1, 2-H), 3.81 (1 H, t, J 9.2, 3-H), 4.31 (1 H, br s, 1-H), 4.22 and 4.48 (2 H, ABq, J 12.5, OCH<sub>2</sub>Ph), 4.68 and 4.77 (2 H, ABq, J 11.7, OCH<sub>2</sub>Ph), 4.51 and 4.88 (2 H, ABq, J 11.1, OCH<sub>2</sub>Ph), 5.82 (2 H, br s, 5-H and 6-H) and 7.24–7.36 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 339 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 9%) and 91 (100).

Method B. A solution of the cyclic sulfate 15 (220 mg, 0.431 mmol),  $Bu_4NI$  (191.2 mg, 0.518 mmol) in THF (30 cm<sup>3</sup>) was heated at reflux for 6 h under nitrogen. The solvent was then evaporated and xylene (30 cm<sup>3</sup>) and DBU (0.142 cm<sup>3</sup>, 0.950 mmol) were added to the residue. The solution was heated under reflux for a further 24 h and then cooled, THF (30 cm<sup>3</sup>) and conc.  $H_2SO_4$  (0.2 cm<sup>3</sup>) were both added and the solution stirred for 1 h. An excess of NaHCO<sub>3</sub> was added and the solution stirred until neutralised, as shown by pH paper. The mixture was then filtered through a pad of silica gel topped with Celite. Concentration of the filtrate, followed by flash chromatography [hexane-ethyl acetate (3:1 v/v)] gave the title compound 19 (113.6 mg, 61%) as a colourless oil.

Method C. To a solution of the compound 21 (181.4 mg, 0.309 mmol) in  $CH_2Cl_2$  (5 cm<sup>3</sup>) at -70 °C was added MCPBA (125.5

mg, 0.618 mmol). The solution was stirred for 10 min and then allowed to rise to room temp. Diisopropylethylamine (0.161 cm<sup>3</sup>, 0.927 mmol) and toluene (5 cm<sup>3</sup>) were added to the colourless solution, which was heated at 80 °C for 1 h. The resultant yellow solution was poured into an aq. saturated solution of NH<sub>4</sub>Cl (2 cm<sup>3</sup>) and the aq. phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 3 cm<sup>3</sup>). The combined organic extracts were then washed with brine (2 × 2 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate, followed by flash chromatography [hexane-diethyl ether (2:1 v/v)] gave the title compound **19** (96 mg, 72%) as a colourless oil.

(1R,2R,3R,4S,6R)-1,2-Di-O-benzyl-6-benzyloxymethyl-4phenylselenocyclohexane-1,2,3-triol 21.-Diphenyl diselenide (9.5 mg, 0.030 mmol) was dissolved in absolute ethanol  $(4 \text{ cm}^3)$ and sodium borohydride (2.3 mg, 0.061 mmol) was then added under nitrogen at 0 °C. The cyclic sulfate 15 (25.9 mg, 0.051 mmol) in THF (2 cm<sup>3</sup>) was added and the solution stirred for 2 h at 0 °C. Conc.  $H_2SO_4$  (0.06 cm<sup>3</sup>) and water (0.04 cm<sup>3</sup>) were then added and the solution stirred for 2 h at room temp. Anhydrous Na<sub>2</sub>CO<sub>3</sub> was added with stirring until neutral, as shown by pH paper. The mixture was filtered through a pad of silica gel topped with Celite. Concentration of the filtrate, followed by flash chromatography [hexane-diethyl ether (2:1 v/v] gave the *title compound* 21 (23.8 mg, 80%) as a colourless oil;  $R_f 0.50$  [hexane-diethyl ether (1:1 v/v)] (Found: C, 69.2; H, 6.05.  $C_{34}H_{36}O_4$ Se requires C, 69.5; H, 6.2%);  $[\alpha]_D^{22} + 12.4 (c$ 1.7);  $v_{\text{max}}(\text{film})/\text{cm}^{-1}$  3450 (OH);  $\delta_{\text{H}}$  1.93 (1 H, dt, J 14.1 and 3.3), 2.08-2.12 (1 H, m), 2.29-2.37 (1 H, m), 2.68 (1 H, d, J 1.6, OH), 3.50 (1 H, dd, J 9.1 and 3.2, 7-H), 3.62-3.67 (2 H, m, 4-H, 7'-H), 3.74 (1 H, t, J 9.0, 1-H), 4.02 (1 H, dd, J 9.0 and 3.0, 2-H), 4.11 (1 H, br s, 3-H), 4.41 and 4.47 (2 H, ABq, J 12.2, OCH<sub>2</sub>Ph), 4.51 and 4.80 (2 H, ABq, J 10.9, OCH<sub>2</sub>Ph), 4.61 and 4.69 (2 H, ABq, J 11.5, OCH<sub>2</sub>Ph) and 7.21-7.50 (20 H, m, OCH<sub>2</sub>Ph and SePh); m/z (EI) 558 (M<sup>+</sup>, 10%), 497 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 3), 391 (M<sup>+</sup> - $C_7H_7 - C_7H_7O$ , 15) and 91 (100).

(1S,2R,3R,4R)-1-O-Benzoyl-2,3,-di-O-benzyl-4-benzyloxymethylcyclohex-5-ene-1,2,3-triol 22.--A solution of the allylic alcohol 19 (589.7 mg, 1.37 mmol), PPh<sub>3</sub> (539.6 mg, 2.06 mmol) and benzoic acid (251.2 mg, 2.06 mmol) in toluene (20 cm<sup>3</sup>) was stirred under nitrogen at 0 °C for 15 min. Diisopropyl azodicarboxylate (DIAD) (0.459 cm<sup>3</sup>, 2.26 mmol) was added dropwise over 10 min and the yellow solution was stirred for 30 min at room temp. Concentration of the solution gave a yellow oil which was flash chromatographed [hexane-diethyl ether (8:1) followed by hexane-diethyl ether (5:1 v/v) to give the title compound 22 (680.0 mg, 93%) as colourless needles, m.p. 54.5-55.5 °C;  $R_f$  0.30 [hexane-diethyl ether (5:1)] (Found: C, 78.4; H, 6.4. C<sub>35</sub>H<sub>34</sub>O<sub>5</sub> requires C, 78.6; H, 6.4%); [a]<sub>D</sub><sup>28</sup> +215.6 (c 1.2);  $\nu_{max}$ (film)/cm<sup>-1</sup> 1718 (C=O);  $\delta_{\rm H}$  2.63 (1 H, m, 4-H), 3.50-3.65 (2 H, m, H-7 and H-7'), 3.81 (1 H, t, J 9.8, 3-H), 3.99 (1 H, dd, J 9.8 and 8.0, 2-H), 4.42 and 4.48 (2 H, ABq, J 12.2, OCH<sub>2</sub>Ph), 4.76 and 4.86 (2 H, ABq, J 11.3, OCH<sub>2</sub>Ph), 4.50 and 4.92 (2 H, ABq, J 11.0, OCH<sub>2</sub>Ph), 5.66 (1 H, ddd, J 10.0, 2.5 and 2.35, 5-H), 5.77, (1 H, br d, J 10, 6-H), 5.83 (1 H, m, 1-H) and 7.14-8.01 (20 H, m, OCH<sub>2</sub>Ph and OCOPh); m/z (EI) 443 ( $M^+ - C_7 H_7$ , 19%), 337 ( $M^+ - C_7 H_7 - C_7 H_6 O$ , 32) and 91 (100).

(1S,2R,3R,4S,5R,6R)- and (1R,2S,3R,4S,5R,6R)-3-O-Benzoyl-4,5-di-O-benzyl-6-benzyloxymethyl-1,2-epoxycyclohexane-3,4,5-triol **23a** and **23b**.—To a solution of the alkene **22** (231 mg, 0.433 mmol) in CH<sub>2</sub>Cl<sub>2</sub>  $(10 \text{ cm}^3)$  was added MCPBA (112.0 mg, 0.649 mmol) at room temp. and stirred for 48 h, and then diluted with CH<sub>2</sub>Cl<sub>2</sub>  $(10 \text{ cm}^3)$ . The solution was washed with an aq. solution of NaOH  $(0.75 \text{ mol dm}^{-3}, 8 \text{ cm}^3)$ . The aq. phase was then extracted with CH<sub>2</sub>Cl<sub>2</sub>  $(3 \times 8 \text{ cm}^3)$  and the 2023

combined organic extracts were washed with brine  $(2 \times 8 \text{ cm}^3)$ , dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate, followed by flash chromatography [hexane-diethyl ether (7:2 v/v)] gave an inseparable mixture of the diastereoisomeric oxiranes 23a and 23b (156.2 mg, 66%) as a semi-solid.

(1S,2R,3S,4R,5R,6R)- and (1R,2R,3S,4R,5R,6S)-3,4-Di-Obenzyl-5-benzyloxymethyl-7-oxabicyclo[4.1.0]heptane-2,3,4triol 24 and 25.—Method A. To the inseparable diastereoisomeric mixture of the oxiranes 23a and 23b (150.2 mg, 0.273 mmol) in anhydrous methanol (15 cm<sup>3</sup>) was added a catalytic amount of anhydrous potassium carbonate. The mixture was stirred at room temp. for 15 h. Concentration of the solution, followed by flash chromatography [hexane-diethyl ether (1:1 v/v] gave compound 24 (31.1 mg, 25.5%) and then compound 25 (84.8 mg, 69.5%), both as white solids. Compound 24; m.p. 76.5-78.5 °C; R<sub>f</sub> 0.50 [hexane-diethyl ether (1:2)] (Found: C, 75.3; H, 6.8.  $C_{28}H_{30}O_5$  requires C, 75.3; H, 6.8%);  $[\alpha]_D^{23} + 111.1$  $(c \ 0.4); v_{\text{max}}(\text{film})/\text{cm}^{-1} 3380 \text{ (OH)}; \delta_{\text{H}} 2.26 \text{ (1 H, d, } J 3.8, \text{ OH)},$ 2.32 (1 H, m, 5-H), 3.12 (1 H, d, J 3.6), 3.27 (1 H, dd, J 9.6 and 9.1, 7-H), 3.37 (1 H, dd, J 9.6 and 7.6, 7'-H), 3.44 (1 H, m, 2-H), 3.59 (1 H, t, J 8.8, 4-H), 3.73 (1 H, dd, J 8.8 and 3.9, 3-H), 3.91 (1 H, dd, J7.5 and 3.6), 4.50 and 4.56 (2 H, ABq, J12.2, OCH<sub>2</sub>Ph), 4.43 and 4.81 (2 H, ABq, J 10.9, OCH<sub>2</sub>Ph), 4.67 and 4.92 (2 H, ABq, J11.7, OCH<sub>2</sub>Ph) and 7.18-7.36 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI)  $355 (M^+ - C_7 H_7, 71\%)$  and 91 (100). Compound 25; m.p. 112.5–113.0 °C;  $R_f 0.42$  [hexane-diethyl ether (1:2 v/v)] (Found: C, 75.6; H, 6.9.  $C_{28}H_{30}O_5$  requires C, 75.3; H, 6.8%);  $[\alpha]_D^{28} + 86.4 (c \ 0.6); v_{max}(film)/cm^{-1} 3350 (OH); \delta_H 2.26 (1 H, d, d)$ J 4.8, OH), 2.22–2.27 (1 H, m, 5-H), 3.19 (1 H, d, J 4.0, 1-H), 3.38 (1 H, dd, J 4.0 and 1.8, 6-H), 3.46-3.66 (4 H, m, 3-H, 4-H, 7-H and 7'-H), 3.97-4.03 (1 H, m, 2-H), 4.36 and 4.45 (2 H, ABq, J 12.1, OCH<sub>2</sub>Ph), 4.42 and 4.84 (2 H, ABq, J 11.2, OCH<sub>2</sub>Ph), 4.70 and 4.93 (2 H, ABq, J 11.4, OCH<sub>2</sub>Ph) and 7.18–7.35 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 355 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 16%) and 91 (100).

Method B for compound 24. To a solution of the epoxide 28 (279.1 mg, 0.498 mmol) in dry THF (6 cm<sup>3</sup>) was added  $Bu_4NF$  (1.0 mol dm<sup>-3</sup> solution in THF, 0.548 cm<sup>3</sup>, 0.548 mmol). The mixture was stirred at room temp. for 10 min, filtered through a pad of silica gel topped with Celite and washed with diethyl ether (30 cm<sup>3</sup>). Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (1:1 v/v)] afforded the title compound 24 (209.9 mg, 94%) as a white solid.

Method B for compound 25. To a solution of the epoxide 29 (211.1 mg, 0.377 mmol) in dry THF (8 cm<sup>3</sup>) was added  $Bu_4NF$  (1.0 mol dm<sup>-3</sup> solution in THF, 0.42 cm<sup>3</sup>, 0.420 mmol). The mixture was stirred at room temp. for 45 min, filtered through a pad of silica gel topped with Celite, and washed with ethyl acetate (25 cm<sup>3</sup>). Concentration of the filtrate followed by flash chromatography [hexane-diethyl ether (1:1 v/v)] afforded the title compound 25 (158.5 mg, 94%) as a white solid.

Method C. Similar MCPBA epoxidation of the allylic alcohol **26** (80.9 mg, 0.198 mmol) as for the preparation of oxiranes **23a** and **23b** gave, after flash chromatography [hexane-diethyl ether (1:1 v/v)], compound **24** (3.7 mg, 4%) and then compound **25** (55.8 mg, 66%), both as white solids.

(1S,2R,3R,4R)-2,3-*Di*-O-*benzyl*-4-*benzyloxymethylcyclohex*-5-*ene*-1,2,3-*triol* **26**.—A solution of the benzoate **22** (198 mg, 0.371 mmol) and a catalytic amount of sodium methoxide in anhydrous methanol (8 cm<sup>3</sup>) was stirred at room temp. for 12 h. Concentration of the solution, followed by addition of diethyl ether (15 cm<sup>3</sup>) gave a pad of inorganic solid which was removed by filtration through a pad of Celite. Concentration of the filtrate, followed by flash chromatography [hexane–diethyl ether (3:2 v/v)] gave the *title compound* **26** (149.3 mg, 94%) as colourless needles, m.p. 55.0–56.5 °C;  $R_f$  0.22 [hexane–diethyl ether (2:1 v/v)] (Found: C, 78.4; H, 7.0.  $C_{28}H_{30}O_4$  requires C, 78.1; H, 7.0%); [ $\alpha$ ]<sub>D</sub><sup>3</sup> + 137.3 (c 0.8);  $\nu_{max}$ (film)/cm<sup>-1</sup> 3450 (OH);  $\delta_{\rm H}$  2.16 (1 H, d, J 4.83, OH), 2.54–2.62 (1 H, m, 4-H), 3.47–3.57 (2 H, m, 7-H and 7'-H), 3.62 (1 H, dd, J 9.1 and 7.0, 2-H), 3.73 (1 H, t, J 9.1, 3-H), 4.26–4.32 (1 H, m, 1-H), 4.41 and 4.47 (2 H, ABq, J 12.3, OCH<sub>2</sub>Ph), 4.50 and 4.86 (2 H, ABq, J 11.1, OCH<sub>2</sub>Ph), 4.73 and 4.95 (2 H, ABq, J 11.6, OCH<sub>2</sub>Ph), 5.69 (2 H, br s, 5-H and 6-H) and 7.21–7.26 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 339 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 11%) and 91 (100).

(1S,2S,3R,4S)-2,3-Di-O-benzyl-5-benzyloxymethyl-1-O-tertbutyldimethylsilylcyclohex-5-ene-1,2,3-triol 27.--A solution of the allylic alcohol 26 (541.6 mg, 1.26 mmol), imidazole (428.7 mg, 6.30 mmol), TBDMSCl (664 mg, 3.78 mmol) and a catalytic amount of DMAP in dry DMF (12 cm<sup>3</sup>) was stirred at room temp. for 9 h. Water (10 cm<sup>3</sup>) and diethyl ether (20 cm<sup>3</sup>) were added and the aq. phase was extracted with diethyl ether  $(3 \times 10 \,\mathrm{cm^3})$ . The combined organic extracts were washed with brine  $(2 \times 8 \text{ cm}^3)$ , dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate, followed by flash chromatography [hexanediethyl ether (12:1 v/v)] provided the *title compound* 27 (624.9 mg, 91.2%) as a colourless oil;  $R_f 0.37$  [hexane-diethyl ether (12:1 v/v)] (Found: C, 75.3; H, 8.3.  $C_{34}H_{44}O_4Si$  requires C, 75.0; 8.1%);  $[\alpha]_D^{23} + 120.0$  (c 0.3);  $v_{max}(film)/cm^{-1}$  3000–3100 (aromatic C-H);  $\delta_{\rm H}$  0.09 (3 H, s, SiMe), 0.11 (3 H, s, SiMe), 0.91 (9 H, s, Bu'), 2.55 (1 H, m, 4-H), 3.50 (2 H, br d, J 4.1, 7-H and 7'-H), 3.61–3.65 (2 H, m, 2-H and 3-H), 4.36-4.48 (4 H, m, 1-H and OCH<sub>2</sub>Ph), 4.86 (1 H, d, J 11.2, OCH<sub>2</sub>Ph), 4.89 (2 H, br s, OCH<sub>2</sub>Ph), 5.53 (1 H, dt, J 2.0 and 10.5) and 5.59 (1 H, dt, J 1.5 and 10.5; 5-H and 6-H) and 7.12-7.34 (15 H, m, OCH<sub>2</sub>Ph); m/z (CI) 544 (M<sup>+</sup>, 4%), 453 (M<sup>+</sup> -  $C_7H_7$ , 5), 438 (M<sup>+</sup> -  $C_7H_6O$ , 3) and 91 (100).

(1R,2S,3S,4R,5R,6R)- and (1S,2S,3S,4R,5R,6S)-3,4-Di-Obenzyl-5-benzyloxymethyl-2-O-tert-butyldimethylsilyl-7-oxabicyclo[4.1.0]heptane-2,3,4-triol 28 and 29.-To a solution of the alkene 27 (624.9 mg, 1.15 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (15 cm<sup>3</sup>) was added MCPBA (595 mg, 3.45 mmol) at room temp. The mixture was heated under reflux for 40 h and then poured into an aq. solution of Na<sub>2</sub>CO<sub>3</sub> (10% w/v, 5 cm<sup>3</sup>). The aq. phase was extracted with  $CHCl_3$  (3 × 10 cm<sup>3</sup>) and the combined organic extracts were washed with brine  $(2 \times 5 \text{ cm}^3)$ , dried (MgSO<sub>4</sub>) and filtered. Concentration of the filtrate, followed by flash chromatography [hexane-diethyl ether (10:1 v/v)] provided firstly the less polar title compounds 28 (281.7 mg, 44%), followed by compound 29 (179.0 mg, 28%), both as colourless oils. Compound 28;  $R_f 0.44$  [hexane-diethyl ether (6:1 v/v)] (Found: C, 72.9; H, 7.9. C<sub>34</sub>H<sub>44</sub>O<sub>5</sub>Si requires C, 72.8; H, 7.9%);  $[\alpha]_{D}^{22}$  + 62.6 (c 1.2);  $v_{max}$ (film)/cm<sup>-1</sup> 3000–3100 (aromatic C-H);  $\delta_{\rm H}$  0.10 (3 H, s, SiMe), 0.17 (3 H, s, SiMe), 0.93 (9 H, s, Bu'), 2.30 (1 H, m, 5-H), 3.04 (1 H, d, J 3.60, 6-H), 3.22 (1 H, t, J 10.0, 4-H), 3.39 (1 H, dd, J 10.0 and 7.8, 3-H), 3.44 (1 H, br d, J 3.2, 1-H), 3.56 (1 H, t, J 8.8, 7-H), 3.73 (1 H, dd, J 8.8 and 3.5, 7'-H), 4.00 (1 H, d, J 7.8, 2-H), 4.35 (1 H, d, J 10.0, OCH<sub>2</sub>Ph), 4.51 (2 H, br s, OCH<sub>2</sub>Ph), 4.74-4.81 (3 H, m, OCH<sub>2</sub>Ph) and 7.08-7.32 (15 H, m, OCH<sub>2</sub>Ph); m/z (EI) 469 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 3%) and 91 (100)

Compound **29**;  $R_f$  0.31 [hexane-diethyl ether (6:1 v/v)] (Found: C, 72.8; H, 8.0.  $C_{34}H_{44}O_5$ Si requires C, 72.8; H, 7.9%);  $[\alpha]_D^{23} + 67.3 (c 1.5); v_{max}(film)/cm^{-1} 3000-3100 (aromatic C-H); <math>\delta_H 0.09 (3 \text{ H}, \text{s}, \text{SiMe}), 0.17 (3 \text{ H}, \text{s}, \text{SiMe}), 0.94 (9 \text{ H}, \text{s}, \text{Bu}', 2.22 (1 \text{ H}, \text{m}, 5-\text{H}), 3.16 (1 \text{ H}, \text{d}, J4.0, 6-\text{H}), 3.24 (1 \text{ H}, \text{dd}, J4.0 \text{ and } 1.9, 1-\text{H}), 3.41-3.60 (4 \text{ H}, \text{m}, 3-\text{H}, 4-\text{H}, 7-\text{H} \text{ and } 7'-\text{H}), 4.09 (1 \text{ H}, \text{dd}, J8.0 \text{ and } 1.9, 2-\text{H}), 4.36 (1 \text{ H}, \text{d}, J11.1, \text{OC}H_2\text{Ph}), 4.45 \text{ and } 4.37 (2 \text{ H}, \text{ABq}, J12.2, \text{OC}H_2\text{Ph}), 4.77-4.87 (3 \text{ H}, \text{m}, \text{OC}H_2\text{Ph}) \text{ and } 7.08-7.36 (15 \text{ H}, \text{m}, \text{OC}H_2\text{Ph}); m/z (\text{EI}) 469 (M^+ - C_7\text{H}_7, 6\%), 363 (M^+ - C_7\text{H}_7 - C_7\text{H}_6\text{O}, 6) \text{ and } 91 (100).$ 

(1R,2S,3S,4S,5R,6R)- and (1S,2R,3S,4S,5R,6R)-3-O-Acetyl-4,5-di-O-benzyl-6-benzyloxymethyl-1,2-epoxycyclohexane-3,4, 5-triol 30 and 31.-Similar MCPBA epoxidation of the allyl acetate 18 (1.507 g, 3.19 mmol) as for the preparation of oxiranes 23a and 23b gave, after gradient elution flash chromatography [hexane-diethyl ether (3:1 v/v) followed by hexane-diethyl ether (2:1 v/v)], initially the less polar title compound 31 (663.3 mg, 43%) as a colourless oil, followed by compound 30 (535.4 mg, 34%) as a white solid. Compound 30; m.p. 59–61 °C;  $R_f 0.36$  [hexane-ethyl acetate (3:1 v/v)] (Found: C, 73.8; H, 6.5.  $C_{30}H_{32}O_6$  requires C, 73.75; H, 6.6%);  $[\alpha]_D^{24}$ +4.8 (c 2.7);  $\nu_{max}(film)/cm^{-1}$  1738 (C=O);  $\delta_H$  2.16 (3 H, s, Ac), 2.33 (1 H, m, 6-H), 3.41 (1 H, t, J 4.0), 3.47-3.54 (2 H, m), 3.58 (1 H, dd, J 8.6 and 4.8), 3.67 (1 H, t, J 8.7), 3.76 (1 H, dd, J 8.9 and 5.0), 4.41 and 4.75 (2 H, ABq, J 11.1, OCH<sub>2</sub>Ph), 4.50 and 4.56 (2 H, ABq, J 12.3, OCH<sub>2</sub>Ph), 4.53 and 4.60 (2 H, ABq, J 11.7, OCH<sub>2</sub>Ph), 5.50 (1 H, t, J 4.6, 3-H) and 7.19-7.35 (15 H, m, OCH<sub>2</sub>*Ph*); m/z (EI) 397 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 7%), 291 (M<sup>+</sup> - $C_7H_7 - C_7H_6O$ , 29) and 91 (100).

Compound **31**;  $R_f$  0.52 [hexane–ethyl acetate (3:1 v/v)] (Found: C, 74.1; H, 6.8.  $C_{30}H_{32}O_6$  requires C, 73.75; H, 6.6%);  $[\alpha]_D^{24}$  + 14.3 (*c* 2.0);  $v_{max}(film)/cm^{-1}$  1747 (C=O);  $\delta_H$  2.16 (3 H, s, Ac), 3.29 (1 H, m, 6-H), [3.21 (1 H, d, *J* 3.4) and 3.27 (1 H, t, *J* 3.1), H-1 and H-2], 3.56 (1 H, dd, *J* 9.3 and 5.4, 7-H), 3.63 (1 H, dd, *J* 9.3 and 3.6, 7'-H), 3.67–3.78 (2 H, m, 4-H and 5-H), 4.38 and 4.51 (2 H, ABq, *J* 12.1, OCH<sub>2</sub>Ph), 4.41 and 4.83 (2 H, ABq, *J* 11.2, OCH<sub>2</sub>Ph), 4.53 and 4.68 (2 H, ABq, *J* 11.2, OCH<sub>2</sub>Ph), 5.84 (1 H, br s, 3-H), 6.98–7.37 (15 H, m, OCH<sub>2</sub>Ph); *m/z* (EI) 397 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 7%), 291 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub> - C<sub>7</sub>H<sub>6</sub>O, 72) and 91 (100).

(1S,2S,3S,4R,5R,6R)-3,4-*Di*-O-*benzyl*-5-*benzyloxymethyl*-7oxabicyclo[4.1.0]*heptane*-2,3,4-*triol* **32**.—*Method* A. A solution of the epoxy acetate **30** (111.4 mg, 0.228 mmol), and a catalytic amount of anhydrous potassium carbonate in dry methanol (5 cm<sup>3</sup>) was stirred at room temp. for 12 h. Concentration of the solvent, followed by flash chromatography [hexane–diethyl ether (2:3 v/v)] gave the *title compound* **32** (95.8 mg, 94%) as a white solid, m.p. 78–80 °C;  $R_f$  0.36 [hexane–diethyl ether (1:2 v/v)] (Found: C, 74.9; H, 7.0. C<sub>28</sub>H<sub>30</sub>O<sub>5</sub> requires C, 75.3; H, 6.8%); [ $\alpha$ ]<sub>D</sub><sup>23</sup> +42.1 (*c* 0.8);  $\nu_{max}$ (film)/cm<sup>-1</sup> 3450 (OH);  $\delta_{H}$  2.29– 2.34 (1 H, m), 2.65 (1 H, br d, J 6.0), 3.38 (1 H, t, J 4.0), 3.47–3.58 (3 H, m), 3.62–3.74 (2 H, m), 3.66 (1 H, t, J 8.9), 3.71 (1 H, dd, J 8.9 and 5.6), 4.27 (1 H, m), 4.48 and 4.55 (2 H, ABq, J 12.1), 4.59 and 4.62 (2 H, ABq, J 11.9), 4.43 and 4.71 (2 H, ABq, J 11.3) and 7.20–7.35 (15 H, m); *m/z* (EI) 355 (M<sup>+</sup> – C<sub>7</sub>H<sub>7</sub>, 19%), 249 (M<sup>+</sup> – C<sub>7</sub>H<sub>7</sub> – C<sub>7</sub>H<sub>6</sub>O, 9) and 91 (100).

Method B. To a solution of the epoxide 35 (15.2 mg, 0.027 mmol) in dry THF (2 cm<sup>3</sup>) was added  $Bu_4NF$  (1.0 mol dm<sup>-3</sup> solution in THF, 0.033 cm<sup>3</sup>, 0.03 mmol). The mixture was stirred at room temp. for 2 h. Concentration of the solvent, followed by flash chromatography [hexane-diethyl ether (1:2 v/v)] afforded the *title compound* 32 (11.1 mg, 92%) as a white solid.

Method C. Similar MCPBA epoxidation of the allyl alcohol 19 (283.8 mg, 0.660 mmol) as in the preparation of the oxiranes 23a and 23b gave, after flash chromatography [hexane-diethyl ether (2:3 v/v)], the *title compound* 32 (279.9 mg, 95%) as a white solid.

(1R,2S,3S,4R,5R,6S)-3,4-Di-O-benzyl-5-benzyloxymethyl-7oxabicyclo[4.1.0]heptane-2,3,4-triol**33**.—Method A. A solutionof the epoxy acetate**31**(91.4 mg, 0.187 mmol), and a catalyticamount of anhydrous potassium carbonate in dry methanol (5cm<sup>3</sup>) was stirred at room temp. for 4 h. Concentration of thesolvent followed by flash chromatography [hexane-diethylether (3:2 v/v)] gave the*title compound***33**(76.1 mg, 91%) as a white solid, m.p. 50-52 °C; R<sub>f</sub> 0.36 [hexane-diethyl ether (1:1)] (Found: C, 75.25; H, 6.6. C<sub>28</sub>H<sub>30</sub>O<sub>5</sub> requires C, 75.3; H, 6.8%);  $[\alpha]_{D}^{25}$  + 30.2 (c 1.2);  $v_{max}(\text{film})/\text{cm}^{-1}$  3450 (OH);  $\delta_{H}$  2.25 (1 H, ddd, J 8.8, 5.4 and 3.6), 2.80 (1 H, d, J 2.8), 3.19 (1 H, d, J 3.5), 3.33 (1 H, t, J 3.1), 3.51 (1 H, dd, J 9.2 and 5.6), 3.56 (1 H, d, J 3.5), 3.62 (1 H, dd, J 10.1 and 3.2), 3.71 (1 H, dd, J 9.9 and 8.6), 4.40-4.45 (1 H, m), 4.40 and 4.48 (2 H, ABq, J 12.2), 4.42 and 4.81 (2 H, ABq, J 11.1), 4.62 and 4.71 (2 H, ABq, J 11.5) and 7.18-7.35 (15 H, m); m/z (EI) 355 (M<sup>+</sup> – C<sub>7</sub>H<sub>7</sub>, 13%) and 91 (100).

Method B. To a solution of the epoxide 36 (12.1 mg, 0.0216 mmol) in dry THF (2 cm<sup>3</sup>) was added tetrabutylammonium fluoride ( $1.0 \text{ mol } \text{dm}^{-3}$  solution in THF;  $0.026 \text{ cm}^3$ , 0.024 mmol). The mixture was stirred at room temp. for 3 h, then concentration of the solvent, followed by flash chromatography [hexane-diethyl ether (1:1 v/v)] afforded the title compound 33 (9.1 mg, 94%) as a white solid.

(1R,2S,3R,4S)-2,3-Di-O-benzyl-4-benzyloxymethyl-1-(O-tertbutyldimethylsilyl)cyclohex-5-ene-1,2,3-triol 34.—Similar silylation of the allylic alcohol 19 (247.4 mg, 0.575 mmol) as for the preparation of compound 27 afforded, after flash chromatography [hexane-diethyl ether (12:1 v/v)], the *title* compound 34 (302.2 mg, 96%) as a colourless oil;  $R_f$  0.42 [hexane-diethyl ether (10:1 v/v)] (Found: C, 74.9; H, 8.2.  $C_{34}H_{44}O_4Si$  requires C, 75.0; H, 8.1%);  $[\alpha]_D^{22} - 1.3$  (c 1.5);  $v_{\rm max}$ (film)/cm<sup>-1</sup> 3000–3100 (aromatic C-H);  $\delta_{\rm H}$  0.06 (3 H, s, SiMe), 0.09 (3 H, s, SiMe), 0.91 (9 H, s, Bu<sup>t</sup>), 2.46 (1 H, m), 3.42 (1 H, dd, J 8.93 and 6.6), 3.56-3.63 (2 H, m), 3.88 (1 H, dd, J 8.45 and 7.0), 4.41-4.44 (3 H, m), 4.52 and 4.80 (2 H, ABq, J 11.5), 4.63 and 4.73 (2 H, ABq, J 12.1), 5.71 (2 H, br d, J 2.0) and 7.21–7.36 (15 H, m); m/z (EI) 453 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 2%), 438  $(M^+ - C_7 H_6 O, 3)$  and 91 (100).

(1R,2R,3S,4R,5R,6R)- and (1S,2R,3S,4R,5R,6S)-3,4-Di-Obenzyl-5-benzyloxymethyl-2-O-tert-butyldimethylsilyl-7-oxa-

bicyclo[4.1.0]heptane-2,3,4-triol 35 and 36.—Similar MCPBA epoxidation of the alkene 34 (58.6 mg, 0.107 mmol) as in the preparation of the oxiranes 23a and 23b gave, after flash chromatography [hexane-diethyl ether (8:1 v/v) followed by hexane-diethyl ether (5:1 v/v)], initially the title compound 36 (30.8 mg, 51.2%), followed by compound **35** (9.6 mg, 15.9\%), both as colourless oils. Compound 35;  $R_f 0.24$  [hexane-diethyl ether (5:1 v/v)] (Found: C, 72.3; H, 8.0. C<sub>34</sub>H<sub>44</sub>O<sub>5</sub>Si requires C, 72.8; H, 7.9%;  $[\alpha]_D^{26}$  -1.9 (c 1.1);  $v_{max}(film)/cm^{-1}$  3000-3100 (aromatic C-H);  $\delta_{\rm H}$  0.12 (3 H, s, SiMe), 0.14 (3 H, s, SiMe), 1.00 (9 H, s, Bu<sup>t</sup>), 2.33 (1 H, m), 3.24 (1 H, t, J 3.8), 3.40–3.55 (3 H, m), 3.64-3.76 (2 H, m), 4.40 and 4.59 (2 H, ABq, J 11.6), 4.40 (1 H, t, J 4.2), 4.47 and 4.59 (2 H, ABq, J 11.9), 4.53 and 4.69 (2 H, ABq, J 12.2) and 7.15–7.35 (15 H, m); m/z (EI) 469 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 11%) and 91 (100).

Compound 36;  $R_f 0.36$  [hexane-diethyl ether (7:1 v/v)] (Found: C, 72.5; H, 7.9. C<sub>34</sub>H<sub>44</sub>O<sub>5</sub>Si requires C, 72.8; H, 7.9%);  $[\alpha]_D^{25}$  +11 (c 1.1);  $\nu_{max}(\text{film})/\text{cm}^{-1}$  3000–3100 (aromatic C-H);  $\delta_{\rm H}$  0.07 (3 H, s, SiMe), 0.10 (3 H, s, SiMe), 0.93 (9 H, s, Bu<sup>t</sup>), 2.26 (1 H, m), 3.15 (1 H, dd, J 3.5 and 3.0), 3.20 (1 H, d, J 3.5), 3.47 (1 H, dd, J9.3 and 6.4), 3.52-3.61 (2 H, m), 3.77 (1 H, dd, J9.9 and 8.8), 4.35 and 4.45 (2 H, ABq, J 12), 4.43 and 4.80 (2 H, ABq, J 11.3), 4.50 (1 H, t, J2.6), 4.67 (2 H, br s) and 7.17-7.36 (15 H, m); m/z (EI) 469 (M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>, 11%) and 91 (100).

### **Acknowledgements**

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