# (−)-Quinic Acid in Organic Synthesis. Part 4.[1] Syntheses of Cyclophellitol and its (1*R*,6*S*)-, (2*S*)-, (1*R*,2*S*,6*S*)-Diastereoisomers

**Tony K. M. Shing* and Vincent W.-F. Tai**
*Department of Chemistry, The Chinese University of Hong Kong, Shatin, Hong Kong*

Cyclophellitol **1** and its (1*R*,6*S*)-, (2*S*)-, (1*R*,2*S*,6*S*)-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 {(1*S*,2*R*,3*S*,4*R*,5*R*,6*R*)-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.[2] 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.[2] Cyclophellitol **1** was found to inhibit 50% of the almond β-D-glucosidase activity at a concentration of 0.8 μg $cm^{-3}$.[2] The value is lower than the $IC_{50}$ values† of 1-deoxynojirimycin (30 μg $cm^{-3}$) and castanospermine (12 μg $cm^{-3}$). Also, it showed no antimicrobial activity and no cytotoxicity on NIH 3T3 cells, Molt-4 cells and P388 cells at 100 μg $cm^{-3}$.[2,3]

Structurally, cyclophellitol **1** is a unique pseudopyranose with a β-epoxide moiety. The epoxide, the three hydroxy groups and the hydroxymethyl group in compound **1** have the configuration of β-D-glucose. Since cyclophellitol, a β-D-glucosidase inhibitor, has a β-epoxide, the α-epoxide **2** might act as an α-D-glucosidase inhibitor. Along this vein of reasoning, the unnatural diastereoisomeric epoxides **3** and **4**, which are structurally related to β-D-mannose and α-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.[4,5] 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[6] from L-quebrachitol and a racemic synthesis[7] from a Diels–Alder adduct. Recently, the (1*R*,6*S*)- and (1*R*,2*S*,6*S*)-diastereoisomers **2** and **4** have been synthesized from D-galactose *via* the INOC strategy and have been shown to be a specific α-D-glucosidase inhibitor and α-D-mannosidase inhibitor, respectively.[5,8] 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-(4*R*,5*R*,6*R*)-4,5,6-trihydroxycyclohex-2-enone},[9] pseudo-β-D-fructopyranose,[10] pseudo-β-D-mannopyranose,[10] pseudo-α-D-mannopyranose,[1] and pseudo-α-D-glucopyranose.[1] Recent work from other research groups employing (−)-quinic acid **9** as the starting material include the synthesis of 1α,25-dihydroxy-19-norvitamin $D_3$,[11] antibiotic (+)-negamycin,[12] and the A-ring precursor for daunomycin.[13] This paper describes in detail the versatility of this approach by facile syntheses of diastereoisomers **1**, **2**, **3** and **4**.[14]

† The $IC_{50}$ value reflects the amount of compound required for 50% inhibition of the enzyme under the standard assay conditions.

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-

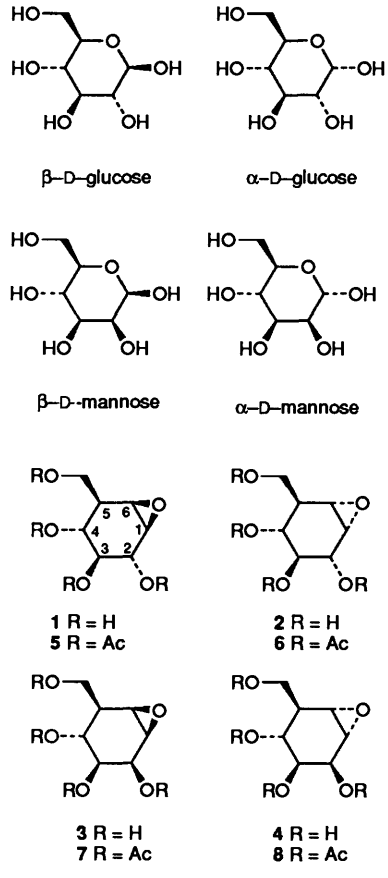



**Fig. 1** Structural relationship between sugars and cyclohexane oxide inhibitors of glycosidases

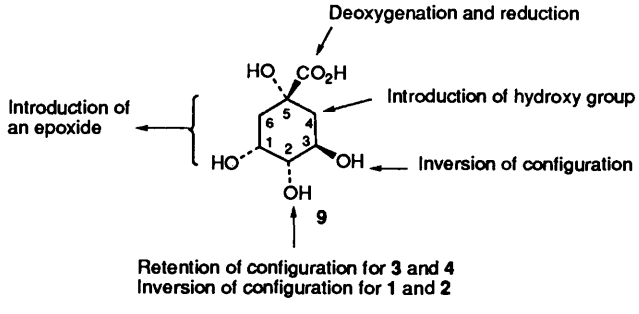
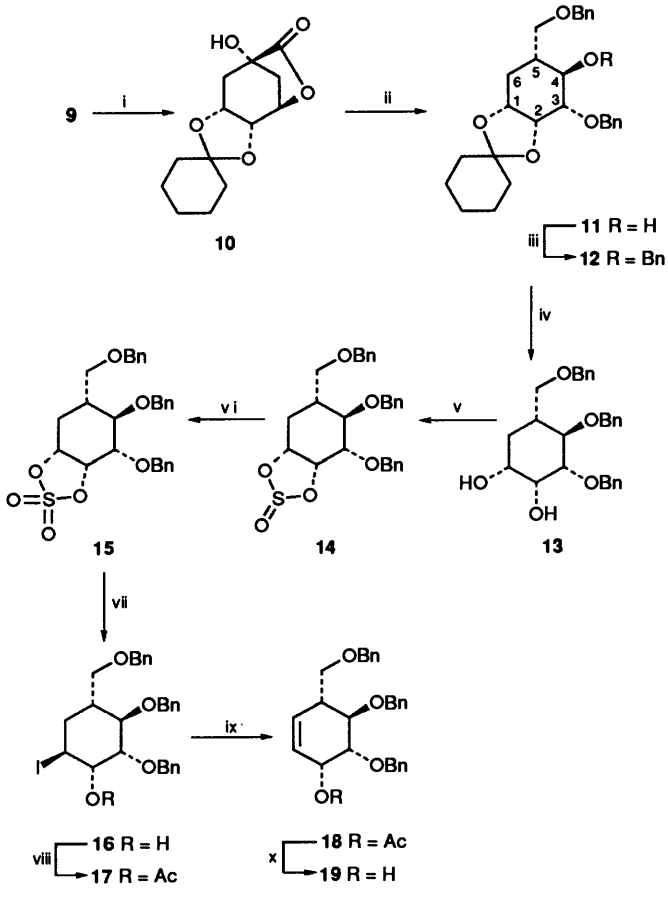



**Fig. 2** Synthetic plan

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 (1*R*,6*S*)-diastereoisomer **2** is illustrated in Scheme 1. The conversion of quinic acid **9** into



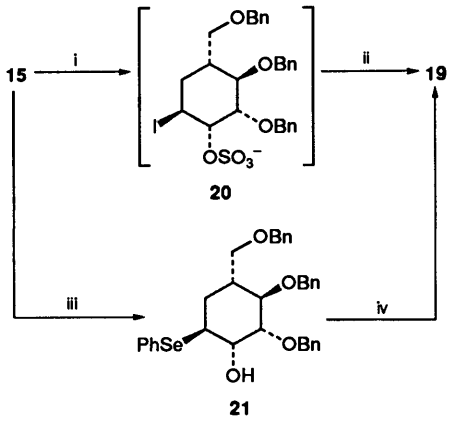

**Scheme 1** *Reagents and conditions:* i, cyclohexanone, $H_2SO_4$ or $H_3PO_4$ (cat.) (83%); ii, 5 steps, see ref. 1; iii, NaH, THF, 0 °C then benzyl (Bn) bromide, $Bu_4NI$ (cat.), reflux, overnight (82%); iv, $CF_3CO_2H$, $CH_2Cl_2$, room temp., 24 h (90%); v, triethylamine, thionyl chloride, $CH_2Cl_2$, 0 °C; vi, $NaIO_4$, $RuCl_3$ (cat.), $CCl_4$, $CH_3CN$, $H_2O$, 0 °C→room temp., 1 h (89%); vii, $Bu_4NI$, THF, reflux, then $H_2SO_4$, $H_2O$ (83%); viii, $(CH_3CO)_2O$ ($Ac_2O$), pyridine, DMAP (cat.), $CH_2Cl_2$, room temp., 24 h (95%); ix, DBU, xylene, reflux (83%); x, NaOMe (cat.), MeOH, room temp. (95%)

the alcohol **11** followed a modified reaction sequence developed by us.[1] The lactone **10** was synthesized previously using Gero's procedure[15] by boiling a mixture of compound **9**, cyclohexanone, Dowex 50 WX8 resin ($H^+$), DMF and benzene with the azeotropic removal of water. In this work, we followed a simplified protocol developed by Stoodley[16] for its preparation by boiling compound **9** and cyclohexanone in the presence of a catalytic amount of $H_2SO_4$ or $H_3PO_4$, 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[1] 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 $CH_2Cl_2$ gave the diol **13** in 90% yield. According to the Sharpless protocol,[17] 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 $RuO_4$ in $CCl_4$–$CH_3CN$–$H_2O$ 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.[17] The $^1H$ 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 $cm^{-1}$ and in the mass spectrum, the $M^+ - C_7H_7$ fragment was observed at *m/z* 419.

The cyclic sulfate moiety has been described as an epoxide analogue and is readily opened in an $S_N2$ manner by a number of nucleophiles such as the azide, benzoate, acetate, hydride, fluoride, etc.[18] 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 $ROSO_3^-$ moiety makes the five-membered cyclic sulfate very reactive towards various reagents.[18]

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)–$CH_2Cl_2$ to give the iodo acetate **17**. The $^1H$ 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)[19] 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,[17,18,20] so treatment of the intermediate **20** (obtained from nucleophilic attack of compound **15** with $Bu_4NI$) 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.[21] Thus, treatment of the sulfate **15** with the phenyl selenide anion



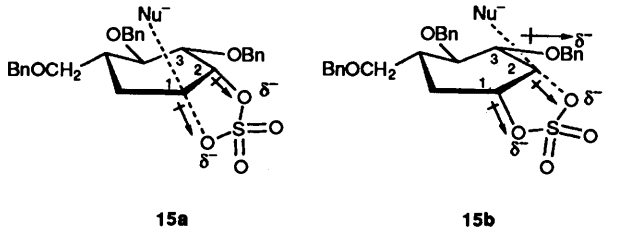

**Scheme 2** *Reagents and conditions:* i, $Bu_4NI$, THF, reflux; ii, DBU, xylene, reflux, $H_2SO_4$, $H_2O$, THF (61%); iii, PhSeNa, EtOH, THF, 0 °C→room temp., $H_2SO_4$, $H_2O$ (80%); iv, MCPBA, $CH_2Cl_2$, −40 °C→room temp., then $Pr^i_2NEt$, toluene, 80 °C (72%)

* 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.[21] The regioselectivity of the initial attack by the selenide anion was confirmed by the allylic alcohol **19** obtained.

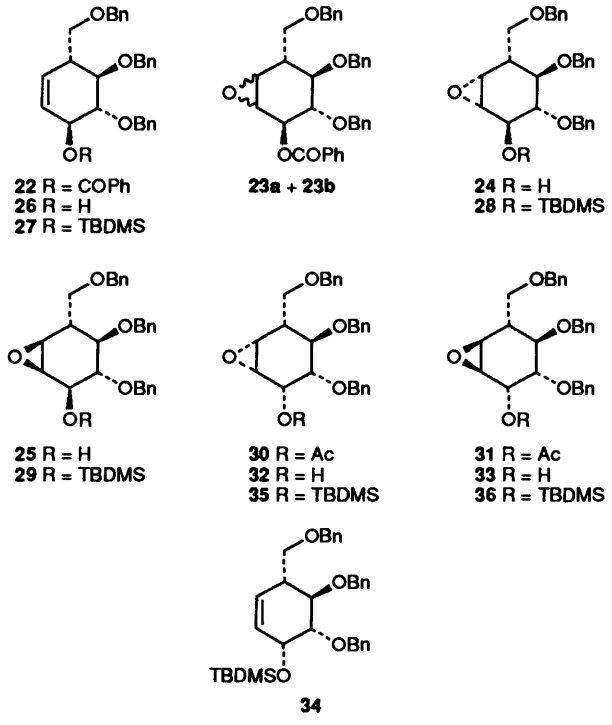
Thus, we have shown three ways of transforming the cyclic sulfate **15** into the allylic alcohol **19**. Among the three methods, the second method, *i.e.*, the *in situ* elimination of the iodide **20**, was the most satisfactory in terms of both the yield and the number of steps involved. Remarkably, 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 $S_N2$ transition state.[22] 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 would be correspondingly increased.[22] Nucleophilic attack at C-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.[23] Treatment of the allylic alcohol **19** with benzoic acid, triphenylphosphine ($PPh_3$) and diisopropyl azodicarboxylate (DIAD) in toluene at 0 °C gave the β-benzoate **22** in 93% yield. Epoxidation of the double bond in compound **22** with MCPBA in $CH_2Cl_2$ gave a mixture of inseparable diastereoisomeric oxiranes **23a** and **23b** in 66% combined yield ($^1H$ NMR, 30:70). Debenzoylation of the inseparable oxiranes **23a** and **23b** with $K_2CO_3$ 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 β-benzoate **22** with NaOMe in anhydrous MeOH afforded compound **26** in 94% yield which underwent the hydroxy-directed[24] 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*[24] to the alcohol and therefore was assigned as the β-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 α-oxirane. The assignment of the stereochemistry of the oxiranes was made simply by desilylation of the compounds **28** and **29**




**15a** **15b**

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




**22** R = COPh
**26** R = H
**27** R = TBDMS

**23a** + **23b**

**24** R = H
**28** R = TBDMS

**25** R = H
**29** R = TBDMS

**30** R = Ac
**32** R = H
**35** R = TBDMS

**31** R = Ac
**33** R = H
**36** R = TBDMS

**34**

separately with $Bu_4NF$, affording compounds **24** and **25** respectively in 94% yields. Finally, hydrogenolysis of the *anti*-epoxy 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;[2] m.p. 146–148 °C; $[\alpha]_D^{23}$ +100 (*c* 0.3, $H_2O$) {lit.,[2] m.p. 149–151 °C; $[\alpha]_D^{27}$ +103 (*c* 0.5, $H_2O$)}. Acetylation of cyclophellitol **1** with $Ac_2O$–pyridine–DMAP gave its tetraacetate **5** in 91% yield. The $^1H$ and $^{13}C$ NMR data were identical to those reported by the Vogel group[7] for racemic **5**, m.p. 105–106 °C; $[\alpha]_D^{23}$ +100 (*c* 0.2, $CHCl_3$) (lit.,[7] oil). Similarly, hydrogenolysis of the *syn*-epoxy alcohol **25** with a catalytic amount of 5% palladium on charcoal in EtOH gave the (1*R*,6*S*)-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;[4,5] m.p. 155–157 °C; $[\alpha]_D^{23}$ +83.3 (*c* 0.3, $H_2O$) {lit.,[4,5] m.p. 150–152 °C; $[\alpha]_D^{25}$ +80 (*c* 0.4, $H_2O$)}. Acetylation of the isomer **2** with $Ac_2O$–pyridine–DMAP gave its tetraacetate **6** in 83% yield, oil; $[\alpha]_D^{21}$ +90.4 (*c* 0.7, $CHCl_3$).

Alternatively, the allyl acetate **18** was used for the synthesis of the (2*S*)- and (1*R*,2*S*,6*S*)-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[24] 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 (2*S*)-diastereoisomer **3** in 91% yield, for the first time, m.p. 148–150 °C; $[\alpha]_D^{24}$ +7.0 (*c* 0.4, $H_2O$). Acetylation of compound **3** with $Ac_2O$–pyridine–DMAP gave its tetraacetate **7** in 91% yield, m.p. 111.5–113 °C; $[\alpha]_D^{23}$ −55.3 (*c* 0.4, $CHCl_3$). 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;[8] **4**, m.p. 129–131 °C; $[\alpha]_D^{23}$ −39.5 (*c* 0.9, $H_2O$) {lit.,[8] oil; $[\alpha]_D^{25}$ −76 (*c* 0.1, $H_2O$)}. Acetylation of compound **4** with $Ac_2O$–pyridine–DMAP gave the new tetraacetate **8** in 93% yield, m.p. 74–75 °C; $[\alpha]_D^{22}$ 0.0 (*c* 0.4, $CHCl_3$).

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

In conclusion, cyclophellitol **1** and its (1*R*,6*S*)-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 (2*S*)- and (1*S*,2*S*,6*R*)-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 $^1H$ (250 MHz) and $^{13}C$ (62.9 MHz) NMR spectra. All spectra were measured on solutions of the compound in deuteriochloroform with $Me_4Si$ (TMS) as internal standard, unless otherwise stated. Chemical shifts are reported as parts per million (ppm) using the δ 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 $10^{-1}$ deg $cm^2$ $g^{-1}$. 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 $60F_{254}$ 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. $CH_2Cl_2$ Was distilled from $P_2O_5$ and stored over 4 Å molecular sieves. DMF was distilled over $CaH_2$ 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 $cm^3$) under $H_2$ at atmospheric pressure was added a solution of the benzylated compound **24** (189.3 mg, 0.424 mmol) in absolute EtOH (8 $cm^3$). The suspension was stirred for 2 h at room temp. and filtered through a pad of Celite. The residue was washed with methanol (30 $cm^3$) 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.,[2] 149–151 °C ($H_2O$)]; $R_f$ 0.32 [chloroform–methanol (3:1)] (Found: C, 47.7; H, 6.9. $C_7H_{12}O_5$ requires C, 47.7; H, 6.9%); $[\alpha]_D^{23}$ +100 (*c* 0.3, $H_2O$) {lit.,[2] $[\alpha]_D^{27}$ +103 (*c* 0.5, $H_2O$)}; $\nu_{max}$(KBr)/$cm^{-1}$ 3400 and 3490 (OH); $\delta_H$($D_2O$, 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); $\delta_C$($D_2O$, dioxane δ 67.4) 44.3, 56.8, 56.9, 61.4, 67.8, 71.7 and 77.1; *m*/*z* (CI) 177 ($MH^+$).

(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.,[4,5] 150–152 °C (MeOH)]; $R_f$ 0.32 [chloroform–methanol (2:1 v/v)] (Found: C, 47.5; H, 6.9. $C_7H_{12}O_5$ requires C, 47.7; H, 6.9%); $[\alpha]_D^{23}$ +83.3 (*c* 0.3, $H_2O$), {lit.,[4,5] $[\alpha]_D^{25}$ +80 (*c* 0.4, $H_2O$)}; $\nu_{max}$(KBr)/$cm^{-1}$ 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 ($MH^+$).

(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. $C_7H_{12}O_5$ requires C, 47.7; H, 6.9%); $[\alpha]_D^{24}$ +7.0 (*c* 0.4, $H_2O$); $\nu_{max}$(KBr)/$cm^{-1}$ 3440 and 3470 (OH); $\delta_H$($D_2O$) 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); $\delta_C$($D_2O$) 44.8, 54.4, 56.9, 61.8, 66.4, 66.7 and 73.2; *m*/*z* (CI) 177 ($MH^+$).

(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.,[8] oil]; $R_f$ 0.30 [chloroform–methanol (3:1)] (Found: C, 47.6; H, 6.9. $C_7H_{12}O_5$ requires C, 47.7; H, 6.9%); $[\alpha]_D^{23}$ −39.5 (*c* 0.9, $H_2O$), {lit.,[12] $[\alpha]_D^{25}$ −76 (*c* 0.1, $H_2O$)}; $\nu_{max}$(KBr)/$cm^{-1}$ 3364 and 3426 (OH); $\delta_H$($D_2O$) 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); $\delta_C$($D_2O$) 45.3, 55.6, 56.6, 61.6, 66.7, 68.0 and 71.2; *m*/*z* (CI) 177 ($MH^+$).

(1R,2S,3S,4R,5R,6R)-2,3,4-*Tri*-O-*acetyl*-5-*acetoxymethyl*-7-*oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* **5**.—A solution of cyclophellitol **1** (17.4 mg, 0.099 mmol), acetic anhydride (0.3 $cm^3$) and a crystal of 4-dimethylaminopyridine (DMAP) in pyridine (1.5 $cm^3$) was stirred at room temp. for 12 h. The solution was diluted with $CH_2Cl_2$ (4 $cm^3$) and an aq. saturated solution of $NH_4Cl$ (1.5 $cm^3$) was added. The aq. phase was extracted with $CH_2Cl_2$ (4 × 4 $cm^3$) and the combined organic extracts were washed with brine (2 × 4 $cm^3$), dried ($MgSO_4$) 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%); $[\alpha]_D^{23}$ +100 (*c* 0.2); $\nu_{max}$(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 ($MH^+$, 6%), 182 (13) and 43 (100).

(1S,2S,3S,4R,5R,6S)-2,3,4-*Tri*-O-*acetyl*-5-*acetoxymethyl*-7-*oxabicyclo*[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. $C_{15}H_{20}O_9$ requires C, 52.3; H, 5.85%); $[\alpha]_D^{21}$ +90.4 (*c* 0.7); $\nu_{max}$(film)/cm$^{-1}$ 1748 (C=O); $\delta_H$ 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); $\delta_C$ 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 ($MH^+$, 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; $R_f$ 0.37 [hexane–diethyl ether (1:3)] (Found: C, 52.4; H, 5.85. $C_{15}H_{20}O_9$ requires C, 52.3; H, 5.85%); $[\alpha]_D^{23}$ −55.3 (*c* 0.4); $\nu_{max}$(film)/cm$^{-1}$ 1744 (C=O); $\delta_H$ 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); $\delta_C$ 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 ($MH^+$, 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. $C_{15}H_{20}O_9$ requires C, 52.3; H, 5.85%); $[\alpha]_D^{22}$ 0.0 (*c* 0.4); $\nu_{max}$(film)/cm$^{-1}$ 1747 (C=O); $\delta_H$ 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); $\delta_C$ 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 ($MH^+$, 20%) and 182 (100).

3,4-O-*Cyclohexylidene*-1,3,4-*trihydroxycyclohexane*-1,5-*carbolactone* **10**.[16]—A mixture of (−)-quinic acid (1,3,4,5-tetrahydroxycyclohexanecarboxylic acid) **9** (100 g, 0.52 mol) and cyclohexanone (152 cm$^3$, 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$^3$) was removed. The yellow solution was left to cool and ethyl acetate (160 cm$^3$), 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 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.,[15] 139–141 °C); $R_f$ 0.30 [hexane–diethyl ether (1:2)]; $[\alpha]_D^{21}$ −30.4 (*c* 1.0) {lit.,[15] $[\alpha]_D^{20}$ −33 (*c* 1.1)}; $\nu_{max}$(film)/cm$^{-1}$ 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 ($M^+$, 24%) and 211 ($M^+ - C_3H_7$, 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 × 1 cm$^3$) and suspended in dry THF (5 cm$^3$) under nitrogen at 0 °C. A solution of the alcohol **11** (304.5 mg, 0.695 mmol) in THF (2 cm$^3$) was added dropwise and the mixture was stirred for 1 h. Benzyl bromide (0.165 cm$^3$, 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$^3$) was slowly added, followed by the addition of water (3 cm$^3$). The organic solvent was removed under reduced pressure, chloroform (10 cm$^3$) was then added to the residue and the aq. layer was then extracted with chloroform (4 × 4 cm$^3$). The combined extracts were washed with brine (3 × 3 cm$^3$), dried ($MgSO_4$) 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 ether–hexane); $R_f$ 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); $\nu_{max}$(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, $OCH_2Ph$), 4.77 (2 H, s, $OCH_2Ph$), 4.50 and 4.89 (2 H, ABq, *J* 10.9, $OCH_2Ph$) and 7.27–7.42 (15 H, m, $OCH_2Ph$); *m/z* (EI) 528 ($M^+$, 4%), 437 ($M^+ - C_7H_7$, 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 $CH_2Cl_2$ (5 cm$^3$) was added trifluoroacetic acid (TFA) (2 drops) and $H_2O$ (1 drop). The mixture was stirred at room temp. for 24 h and poured into an aq. solution of $NaHCO_3$ (5% w/v, 1 cm$^3$). The aq. phase was extracted with $CH_2Cl_2$ (3 × 2 cm$^3$). The combined extracts were washed with brine (2 × 1 cm$^3$), dried ($MgSO_4$) 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. $C_{28}H_{32}O_5$ requires C, 75.0; H, 7.2%); $[\alpha]_D^{20}$ +26.3 (*c* 1.2); $\nu_{max}$(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, *J* 10.5 and 9.3), 4.16 (1 H, t, *J* 2.75, 2-H), 4.47 (2 H, s, $OCH_2Ph$), 4.70 (2 H, s, $OCH_2Ph$), 4.50 and 4.86 (2 H, ABq, *J* 10.8, $OCH_2Ph$) and 7.21–7.61 (15 H, m, $OCH_2Ph$); *m/z* (EI) 357 ($M^+ - C_7H_7$, 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$^3$, 2 mmol) in $CH_2Cl_2$ (10 cm$^3$) at 0 °C was added thionyl chloride (0.054 cm$^3$, 0.75 mmol) over 5 min. The reaction mixture was diluted with cold diethyl ether (25 cm$^3$) and washed with cold water (2 × 15 cm$^3$) and brine (15 cm$^3$), dried ($MgSO_4$) 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); $\nu_{max}$(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 ($M^+ - C_7H_7$, 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$^3$, 0.792 mmol) in $CH_2Cl_2$ (5 cm$^3$) at 0 °C was added thionyl chloride (0.05 cm$^3$, 0.69 mmol) over 5 min. The reaction mixture was diluted with cold diethyl ether (12 cm$^3$) and washed with cold water (2 × 12 cm$^3$) and brine (10 cm$^3$). The organic solution was dried ($MgSO_4$) 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$^3$) and MeCN (5 cm$^3$), and the solution cooled in an ice-bath. Cold water (8 cm$^3$) was added followed by a catalytic amount of $RuCl_3 \cdot H_2O$ and $NaIO_4$ (85 mg, 0.396 mmol). After 1 h, diethyl ether (15 cm$^3$) was added and the two layers were separated. The aq. layer was extracted with diethyl ether (2 × 5 cm$^3$) and the combined organic extracts were washed with brine (2 × 5 cm$^3$), dried ($MgSO_4$) 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; $R_f$ 0.35 [hexane–diethyl ether (2:3)] (Found: C, 65.65; H, 5.75. $C_{28}H_{30}O_7S$ requires C, 65.9, H, 5.9%); $[\alpha]_D^{20}$ +27.8 (*c* 0.9); $\nu_{max}$(film)/cm$^{-1}$ 1210 (S=O) and 810–850 (S-O-C); $\delta_H$ 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 ($M^+ - C_7H_7$, 9%) and 91 (100).

(1R,2R,3R,4S,6R)-1,2-*Di*-O-*benzyl*-6-*benzyloxymethyl*-4-*iodocyclohexane*-1,2,3-*triol* **16**.—A solution of the cyclic sulfate **15** (127 mg, 0.249 mmol), $Bu_4NI$ (110 mg, 0.299 mmol) in THF (12 cm$^3$) was heated under reflux for 6 h under nitrogen. Conc. $H_2SO_4$ (15 mm$^3$) and $H_2O$ (4 mm$^3$) were added and the solution stirred for 30 min at 60 °C. An excess of $NaHCO_3$ (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 $CH_2Cl_2$. 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%); $R_f$ 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); $\nu_{max}$(film)/cm$^{-1}$ 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 OC*H*$_2$Ph), 4.60 and 4.69 (2 H, ABq, *J* 11.4, OC*H*$_2$Ph), 4.79 (1 H, d, *J* 10.9, OC*H*$_2$Ph) and 7.21–7.41 (15 H, m, OCH$_2$*Ph*); *m/z* (EI) 558 ($M^+$, 2%), 467 ($M^+ - C_7H_7$, 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$^3$, 2.64 mmol) and a catalytic amount of DMAP in dry $CH_2Cl_2$ was added acetic anhydride (0.125 cm$^3$, 1.32 mmol) at room temp. The solution was stirred at this temp. for 24 h, then poured into a solution of saturated $NH_4Cl$ (8 cm$^3$) and the aq. phase extracted with $CH_2Cl_2$ (2 × 8 cm$^3$). The combined organic extracts were washed with brine (2 × 8 cm$^3$), dried ($MgSO_4$) 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; $R_f$ 0.55 [hexane–diethyl ether (2:1 v/v)] (Found: 60.1; H, 5.4. $C_{30}H_{33}IO_5$ requires C, 60.0; H, 5.5%); $[\alpha]_D^{28}$ +59.5 (*c* 1.2); $\nu_{max}$(film)/cm$^{-1}$ 1744 (C=O); $\delta_H$ 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, OC*H*$_2$Ph), 4.55 and 4.65 (2 H, ABq, *J* 11.2, OC*H*$_2$Ph), 4.83 (1 H, d, *J* 10.9, OC*H*$_2$Ph), 5.19 (1 H, t, *J* 3.5, 3-H) and 7.22–7.35 (15 H, m, OCH$_2$*Ph*); *m/z* (EI) 509 ($M^+ - C_7H_7$, 13%), 493 ($M^+ - C_7H_7O$, 23), 403 ($M^+ - C_7H_7 - C_7H_6O$, 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-7-ene (DBU) (0.57 cm$^3$, 3.83 mmol) in xylene (25 cm$^3$) 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$^3$). 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); $\nu_{max}$(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, *J* 9.0 and 4.0, 7′-H), 3.73 (1 H, dd, *J* 9.7 and 3.7, 2-H), 3.82 (1 H, t, *J* 9.7, 3-H), 4.40–4.63 (4 H, m, OC*H*$_2$Ph), 4.72 (1 H, *J* 11.5, OC*H*$_2$Ph), 4.92 (1 H, d, *J* 11.0, OC*H*$_2$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$_2$*Ph*); *m/z* (EI) 381 ($M^+ - C_7H_7$, 9%), 275 ($M^+ - C_7H_7 - C_7H_6O$, 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$^3$) 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$^3$). Concentration of the filtrate, followed by flash chromatography [hexane–diethyl ether (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. $C_{28}H_{30}O_4$ requires C, 78.1; H, 7.0%); $[\alpha]_D^{28}$ +54.3 (*c* 1.3); $\nu_{max}$(film)/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, OC*H*$_2$Ph), 4.68 and 4.77 (2 H, ABq, *J* 11.7, OC*H*$_2$Ph), 4.51 and 4.88 (2 H, ABq, *J* 11.1, OC*H*$_2$Ph), 5.82 (2 H, br s, 5-H and 6-H) and 7.24–7.36 (15 H, m, OCH$_2$*Ph*); *m/z* (EI) 339 ($M^+ - C_7H_7$, 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$^3$) was heated at reflux for 6 h under nitrogen. The solvent was then evaporated and xylene (30 cm$^3$) and DBU (0.142 cm$^3$, 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$^3$) and conc. $H_2SO_4$ (0.2 cm$^3$) were both added and the solution stirred for 1 h. An excess of $NaHCO_3$ 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$^3$) 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 $cm^3$, 0.927 mmol) and toluene (5 $cm^3$) 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 $NH_4Cl$ (2 $cm^3$) and the aq. phase was extracted with $CH_2Cl_2$ (3 × 3 $cm^3$). The combined organic extracts were then washed with brine (2 × 2 $cm^3$), dried ($MgSO_4$) 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*-4-*phenylselenocyclohexane*-1,2,3-*triol* **21**.—Diphenyl diselenide (9.5 mg, 0.030 mmol) was dissolved in absolute ethanol (4 $cm^3$) 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 $cm^3$) was added and the solution stirred for 2 h at 0 °C. Conc. $H_2SO_4$ (0.06 $cm^3$) and water (0.04 $cm^3$) were then added and the solution stirred for 2 h at room temp. Anhydrous $Na_2CO_3$ 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. $C_{34}H_{36}O_4Se$ requires C, 69.5; H, 6.2%); $[\alpha]_D^{22}$ +12.4 (*c* 1.7); $\nu_{max}$(film)/$cm^{-1}$ 3450 (OH); $\delta_H$ 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, OC*H*$_2$Ph), 4.51 and 4.80 (2 H, ABq, *J* 10.9, OC*H*$_2$Ph), 4.61 and 4.69 (2 H, ABq, *J* 11.5, OC*H*$_2$Ph) and 7.21–7.50 (20 H, m, OCH$_2$*Ph* and Se*Ph*); *m/z* (EI) 558 ($M^+$, 10%), 497 ($M^+ - C_7H_7$, 3), 391 ($M^+ - C_7H_7 - C_7H_7O$, 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), $PPh_3$ (539.6 mg, 2.06 mmol) and benzoic acid (251.2 mg, 2.06 mmol) in toluene (20 $cm^3$) was stirred under nitrogen at 0 °C for 15 min. Diisopropyl azodicarboxylate (DIAD) (0.459 $cm^3$, 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. $C_{35}H_{34}O_5$ requires C, 78.6; H, 6.4%); $[\alpha]_D^{28}$ +215.6 (*c* 1.2); $\nu_{max}$(film)/$cm^{-1}$ 1718 (C=O); $\delta_H$ 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, OC*H*$_2$Ph), 4.76 and 4.86 (2 H, ABq, *J* 11.3, OC*H*$_2$Ph), 4.50 and 4.92 (2 H, ABq, *J* 11.0, OC*H*$_2$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$_2$*Ph* and OCO*Ph*); *m/z* (EI) 443 ($M^+ - C_7H_7$, 19%), 337 ($M^+ - C_7H_7 - C_7H_6O$, 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 $CH_2Cl_2$ (10 $cm^3$) was added MCPBA (112.0 mg, 0.649 mmol) at room temp. and stirred for 48 h, and then diluted with $CH_2Cl_2$ (10 $cm^3$). The solution was washed with an aq. solution of NaOH (0.75 mol $dm^{-3}$, 8 $cm^3$). The aq. phase was then extracted with $CH_2Cl_2$ (3 × 8 $cm^3$) and the combined organic extracts were washed with brine (2 × 8 $cm^3$), dried ($MgSO_4$) 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*-O-*benzyl*-5-*benzyloxymethyl*-7-*oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* **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 $cm^3$) 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; $R_f$ 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); $\nu_{max}$(film)/$cm^{-1}$ 3380 (OH); $\delta_H$ 2.26 (1 H, d, *J* 3.8, 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, *J* 7.5 and 3.6), 4.50 and 4.56 (2 H, ABq, *J* 12.2, OC*H*$_2$Ph), 4.43 and 4.81 (2 H, ABq, *J* 10.9, OC*H*$_2$Ph), 4.67 and 4.92 (2 H, ABq, *J* 11.7, OC*H*$_2$Ph) and 7.18–7.36 (15 H, m, OCH$_2$*Ph*); *m/z* (EI) 355 ($M^+ - C_7H_7$, 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); $\nu_{max}$(film)/$cm^{-1}$ 3350 (OH); $\delta_H$ 2.26 (1 H, 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, OC*H*$_2$Ph), 4.42 and 4.84 (2 H, ABq, *J* 11.2, OC*H*$_2$Ph), 4.70 and 4.93 (2 H, ABq, *J* 11.4, OC*H*$_2$Ph) and 7.18–7.35 (15 H, m, OCH$_2$*Ph*); *m/z* (EI) 355 ($M^+ - C_7H_7$, 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 $cm^3$) was added $Bu_4NF$ (1.0 mol $dm^{-3}$ solution in THF, 0.548 $cm^3$, 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 $cm^3$). 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 $cm^3$) was added $Bu_4NF$ (1.0 mol $dm^{-3}$ solution in THF, 0.42 $cm^3$, 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 $cm^3$). 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 $cm^3$) was stirred at room temp. for 12 h. Concentration of the solution, followed by addition of diethyl ether (15 $cm^3$) 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%); $[\alpha]_D^{23}$ +137.3 (*c* 0.8); $\nu_{max}$(film)/cm$^{-1}$ 3450 (OH); $\delta_H$ 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, OC*H*$_2$Ph), 4.50 and 4.86 (2 H, ABq, *J* 11.1, OC*H*$_2$Ph), 4.73 and 4.95 (2 H, ABq, *J* 11.6, OC*H*$_2$Ph), 5.69 (2 H, br s, 5-H and 6-H) and 7.21–7.26 (15 H, m, OCH$_2$*Ph*); *m*/*z* (EI) 339 (M$^+$ − $C_7H_7$, 11%) and 91 (100).

(1S,2S,3R,4S)-2,3-*Di*-O-*benzyl*-5-*benzyloxymethyl*-1-O-*tert*-*butyldimethylsilylcyclohex*-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$^3$) was stirred at room temp. for 9 h. Water (10 cm$^3$) and diethyl ether (20 cm$^3$) were added and the aq. phase was extracted with diethyl ether (3 × 10 cm$^3$). The combined organic extracts were washed with brine (2 × 8 cm$^3$), dried ($MgSO_4$) and filtered. Concentration of the filtrate, followed by flash chromatography [hexane–diethyl 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); $\nu_{max}$(film)/cm$^{-1}$ 3000–3100 (aromatic C-H); $\delta_H$ 0.09 (3 H, s, SiMe), 0.11 (3 H, s, SiMe), 0.91 (9 H, s, Bu$^t$), 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 OC*H*$_2$Ph), 4.86 (1 H, d, *J* 11.2, OC*H*$_2$Ph), 4.89 (2 H, br s, OC*H*$_2$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$_2$*Ph*); *m*/*z* (CI) 544 (M$^+$, 4%), 453 (M$^+$ − $C_7H_7$, 5), 438 (M$^+$ − $C_7H_6O$, 3) and 91 (100).

(1R,2S,3S,4R,5R,6R)- *and* (1S,2S,3S,4R,5R,6S)-3,4-*Di*-O-*benzyl*-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 $CH_2Cl_2$ (15 cm$^3$) 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 $Na_2CO_3$ (10% w/v, 5 cm$^3$). The aq. phase was extracted with $CHCl_3$ (3 × 10 cm$^3$) and the combined organic extracts were washed with brine (2 × 5 cm$^3$), dried ($MgSO_4$) 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. $C_{34}H_{44}O_5Si$ requires C, 72.8; H, 7.9%); $[\alpha]_D^{22}$ +62.6 (*c* 1.2); $\nu_{max}$(film)/cm$^{-1}$ 3000–3100 (aromatic C-H); $\delta_H$ 0.10 (3 H, s, SiMe), 0.17 (3 H, s, SiMe), 0.93 (9 H, s, Bu$^t$), 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, OC*H*$_2$Ph), 4.51 (2 H, br s, OC*H*$_2$Ph), 4.74–4.81 (3 H, m, OC*H*$_2$Ph) and 7.08–7.32 (15 H, m, OCH$_2$*Ph*); *m*/*z* (EI) 469 (M$^+$ − $C_7H_7$, 3%) and 91 (100).

Compound **29**; $R_f$ 0.31 [hexane–diethyl ether (6:1 v/v)] (Found: C, 72.8; H, 8.0. $C_{34}H_{44}O_5Si$ requires C, 72.8; H, 7.9%); $[\alpha]_D^{23}$ +67.3 (*c* 1.5); $\nu_{max}$(film)/cm$^{-1}$ 3000–3100 (aromatic C-H); $\delta_H$ 0.09 (3 H, s, SiMe), 0.17 (3 H, s, SiMe), 0.94 (9 H, s, Bu$^t$, 2.22 (1 H, m, 5-H), 3.16 (1 H, d, *J* 4.0, 6-H), 3.24 (1 H, dd, *J* 4.0 and 1.9, 1-H), 3.41–3.60 (4 H, m, 3-H, 4-H, 7-H and 7'-H), 4.09 (1 H, dd, *J* 8.0 and 1.9, 2-H), 4.36 (1 H, d, *J* 11.1, OC*H*$_2$Ph), 4.45 and 4.37 (2 H, ABq, *J* 12.2, OC*H*$_2$Ph), 4.77–4.87 (3 H, m, OC*H*$_2$Ph) and 7.08–7.36 (15 H, m, OCH$_2$*Ph*); *m*/*z* (EI) 469 (M$^+$ − $C_7H_7$, 6%), 363 (M$^+$ − $C_7H_7$ − $C_7H_6O$, 6) 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, OC*H*$_2$Ph), 4.50 and 4.56 (2 H, ABq, *J* 12.3, OC*H*$_2$Ph), 4.53 and 4.60 (2 H, ABq, *J* 11.7, OC*H*$_2$Ph), 5.50 (1 H, t, *J* 4.6, 3-H) and 7.19–7.35 (15 H, m, OCH$_2$*Ph*); *m*/*z* (EI) 397 (M$^+$ − $C_7H_7$, 7%), 291 (M$^+$ − $C_7H_7$ − $C_7H_6O$, 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); $\nu_{max}$(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, OC*H*$_2$Ph), 4.41 and 4.83 (2 H, ABq, *J* 11.2, OC*H*$_2$Ph), 4.53 and 4.68 (2 H, ABq, *J* 11.2, OC*H*$_2$Ph), 5.84 (1 H, br s, 3-H), 6.98–7.37 (15 H, m, OCH$_2$*Ph*); *m*/*z* (EI) 397 (M$^+$ − $C_7H_7$, 7%), 291 (M$^+$ − $C_7H_7$ − $C_7H_6O$, 72) and 91 (100).

(1S,2S,3S,4R,5R,6R)-3,4-*Di*-O-*benzyl*-5-*benzyloxymethyl*-7-*oxabicyclo*[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$^3$) 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. $C_{28}H_{30}O_5$ requires C, 75.3; H, 6.8%); $[\alpha]_D^{23}$ +42.1 (*c* 0.8); $\nu_{max}$(film)/cm$^{-1}$ 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$^+$ − $C_7H_7$, 19%), 249 (M$^+$ − $C_7H_7$ − $C_7H_6O$, 9) and 91 (100).

*Method B*. To a solution of the epoxide **35** (15.2 mg, 0.027 mmol) in dry THF (2 cm$^3$) was added $Bu_4NF$ (1.0 mol dm$^{-3}$ solution in THF, 0.033 cm$^3$, 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*-7-*oxabicyclo*[4.1.0]*heptane*-2,3,4-*triol* **33**.—*Method A*. A solution of the epoxy acetate **31** (91.4 mg, 0.187 mmol), and a catalytic amount of anhydrous potassium carbonate in dry methanol (5 cm$^3$) was stirred at room temp. for 4 h. Concentration of the solvent followed by flash chromatography [hexane–diethyl ether (3:2 v/v)] gave the *title compound* **33** (76.1 mg, 91%) as a

white solid, m.p. 50–52 °C; $R_f$ 0.36 [hexane–diethyl ether (1:1)] (Found: C, 75.25; H, 6.6. $C_{28}H_{30}O_5$ requires C, 75.3; H, 6.8%); $[\alpha]_D^{25}$ +30.2 (*c* 1.2); $\nu_{max}$(film)/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 ($M^+ - C_7H_7$, 13%) and 91 (100).

*Method B.* To a solution of the epoxide **36** (12.1 mg, 0.0216 mmol) in dry THF (2 cm$^3$) was added tetrabutylammonium fluoride (1.0 mol dm$^{-3}$ solution in THF; 0.026 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-tert-*butyldimethylsilyl*)*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); $\nu_{max}$(film)/cm$^{-1}$ 3000–3100 (aromatic C-H); $\delta_H$ 0.06 (3 H, s, SiMe), 0.09 (3 H, s, SiMe), 0.91 (9 H, s, Bu$^t$), 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 ($M^+ - C_7H_7$, 2%), 438 ($M^+ - C_7H_6O$, 3) and 91 (100).

(1R,2R,3S,4R,5R,6R)- *and* (1S,2R,3S,4R,5R,6S)-3,4-*Di*-O-*benzyl*-5-*benzyloxymethyl*-2-O-tert-*butyldimethylsilyl*-7-*oxabicyclo*[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. $C_{34}H_{44}O_5Si$ requires C, 72.8; H, 7.9%); $[\alpha]_D^{26}$ −1.9 (*c* 1.1); $\nu_{max}$(film)/cm$^{-1}$ 3000–3100 (aromatic C-H); $\delta_H$ 0.12 (3 H, s, SiMe), 0.14 (3 H, s, SiMe), 1.00 (9 H, s, Bu$^t$), 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 ($M^+ - C_7H_7$, 11%) and 91 (100).

Compound **36**; $R_f$ 0.36 [hexane–diethyl ether (7:1 v/v)] (Found: C, 72.5; H, 7.9. $C_{34}H_{44}O_5Si$ requires C, 72.8; H, 7.9%); $[\alpha]_D^{25}$ +11 (*c* 1.1); $\nu_{max}$(film)/cm$^{-1}$ 3000–3100 (aromatic C-H); $\delta_H$ 0.07 (3 H, s, SiMe), 0.10 (3 H, s, SiMe), 0.93 (9 H, s, Bu$^t$), 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, *J* 9.3 and 6.4), 3.52–3.61 (2 H, m), 3.77 (1 H, dd, *J* 9.9 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, *J* 2.6), 4.67 (2 H, br s) and 7.17–7.36 (15 H, m); *m/z* (EI) 469 ($M^+ - C_7H_7$, 11%) and 91 (100).

## Acknowledgements

We thank the Croucher Foundation for financial support.

## References

1 For Part 3, see T. K. M. Shing, Y.-X. Cui and Y. Tang, *J. Chem. Soc., Chem. Commun.*, 1991, 756; *Tetrahedron*, 1992, **48**, 2349.
2 S. Atsumi, K. Umezawa, H. Iinuma, H. Naganawa, H. Nakamura, Y. Iitaka and T. Takeucki, *J. Antibiotics.*, 1990, **43**, 49.
3 S. Atsumi, H. Iinuma, C. Nosaka and K. Umezawa, *J. Antibiotics.*, 1990, **43**, 1579.
4 K. Tatsuta, Y. Niwata, K. Umezawa, K. Toshima and M. Nakata, *Tetrahedron Lett.*, 1990, **31**, 1171.
5 K. Tatsuta, Y. Niwata, K. Umezawa, K. Toshima and M. Nakata, *Carbohydr. Res.*, 1991, **222**, 189.
6 T. Akiyama, M. Ohnari, H. Shima, S. Ozaki, *Synlett.*, 1991, 831.
7 V. Moritz and P. Vogel, *Tetrahedron Lett.*, 1992, **33**, 5343.
8 K. Tatsuta, Y. Niwata, K. Umezawa, K. Toshima and M. Nakata, *J. Antibiotics.*, 1991, **44**, 456, 912.
9 T. K. M. Shing and Y. Tang, *J. Chem. Soc., Chem. Commun.*, 1990, 312; *Tetrahedron*, 1990, **46**, 6575.
10 T. K. M. Shing and Y. Tang, *J. Chem. Soc., Chem. Commun.*, 1990, 748; *Tetrahedron*, 1991, **47**, 4571.
11 K. L. Perlman, R. E. Swenson, H. E. Paaren, H. K. Schnoes and H. F. DeLuca, *Tetrahedron Lett.*, 1992, **33**, 7663.
12 C. D. Maycock, M. T. Barros, A. G. Santos and L. S. Godinho, *Tetrahedron Lett.*, 1992, **33**, 4633.
13 B. M. Johnson and K. P. C. Vollhardt, *Synlett.*, 1990, 209.
14 T. K. M. Shing and V. W.-F. Tai, *J. Chem. Soc., Chem. Commun.*, 1993, 995.
15 D. Mercier, J. Leboul, J. Cléophax and S. D. Gero, *Carbohydr. Res.*, 1971, **20**, 299.
16 J. D. Elliott, A. B. Kelson, N. Purcell and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2441.
17 B. M. Kim and K. B. Sharpless, *Tetrahedron Lett.*, 1989, **30**, 655; Y. Gao and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 7538.
18 For a review on the chemistry of cyclic sulfate, see B. B. Lohray, *Synthesis*, 1992, 1035.
19 H. Oediger, F. Möller and K. Eiter, *Synthesis*, 1972, 591.
20 G. F. Cooper, K. E. McCarthy and M. G. Martin, *Tetrahedron Lett.*, 1992, **33**, 5895.
21 K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, 1973, **95**, 2697; S. Knapp, A. B. J. Naughton and T. M. Murali Dhar, *Tetrahedron Lett.*, 1992, **33**, 1025.
22 J. G. Buchanan, in *MTP International Review of Science, Organic chemistry series one*, ed. A. O. Aspinall, Vol. 7, University Park Press, U.S.A., 1973, p. 33.
23 O. Mitsunobu, *Synthesis*, 1981, 1.
24 H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1957, 1958.

*Paper* 4/00423J
*Received* 24*th January* 1994
*Accepted* 14*th March* 1994