Synthesis of *pseudo*-Ribofuranoses by Stereocontrolled Reactions on 4-Hydroxycyclopent-2-enylmethanol Derivatives

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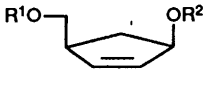
The diol **3** is a major product formed from a Prins reaction on cyclopentadiene and was readily converted into the derivatives **4–7**. The latter compounds were obtained in states of high optical purity by using both enzyme-catalysed hydrolysis and esterification reactions. Osmium tetraoxide transformed the ene diol derivatives **4–7** into the corresponding alcohols **8–11**. In this way the alcohol (+)-**6** was used to prepare (−)-*pseudo*-β-ribofuranose (−)-**2**, and the alcohol (−)-**4** was used to synthesize (+)-*pseudo*-α-ribofuranose (+)-**1**.

There is current interest in the preparation of *pseudo*-α-ribofuranose (+)-**1**[1] and *pseudo*-β-ribofuranose (+)-**2**,[2] especially in connection with studies aimed at unravelling the mechanism of the biosynthesis of aristeromycin. We report a novel synthesis of the cyclopentane derivatives (+)-**1** and (−)-**2** in states of high optical purity, using an enzyme-catalysed esterification reaction to obtain a suitable chiral synthon.

Results and Discussion

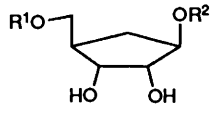
The diol (±)-**3** is readily obtained from the mixture resulting from the treatment of cyclopentadiene with formaldehyde in formic acid.[3] The primary hydroxy group can be protected preferentially such that the triphenylmethyl (trityl) derivatives **4** and **5**[4] and the *tert*-butyldimethylsilyl derivatives **6** and **7** are freely available as the racemates. Furthermore the cyclopentenols **4** and **6** can be obtained in optically active form by using enzyme-catalysed reactions. Thus the acetates **5** and **7** were hydrolysed using selected enzymes as catalysts (Table 1) and aq. acetone as the solvent. While the acetate **5** was stable to hydrolysis in the presence of porcine pancreatic lipase (PPL), pig liver esterase (PLE) catalysed slow hydrolysis of compound **5** to give the alcohol (−)-**4** of modest optical purity. In contrast *Pseudomonas fluorescens* lipase (PFL)-catalysed hydrolysis of the ester **5** gave the alcohol (+)-**4** in excellent optical purity. Similarly the ester (±)-**7** was hydrolysed enantiospecifically by the same enzyme to give the alcohol (+)-**6** and recovered ester (−)-**7** in optically pure states. {The enantiomeric excesses were determined by ^{1}H NMR spectroscopy employing tris-[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) as chiral shift reagent}.

The alcohol **4** can also be resolved by a PFL-catalysed acetylation process utilising vinyl acetate as the solvent and acyl donor, adjusting the reaction time so as to obtain the acetate or the alcohol in a state of high optical purity (Table 2).[4] The absolute configurations of the materials isolated from the enzyme-catalysed reactions were ascertained by further derivatization (*vide infra*). Note that, as expected, hydrolysis of the ester **5** and esterification of the alcohol **4**, as catalysed by PFL, take place on the substrates possessing the same absolute configuration.

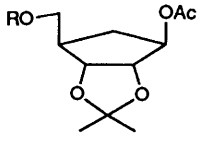


3 $R^1 = R^2 = H$
4 $R^1 = CPh_3$, $R^2 = H$
5 $R^1 = CPh_3$, $R^2 = Ac$
6 $R^1 = SiBu^tMe_2$, $R^2 = H$
7 $R^1 = SiBu^tMe_2$, $R^2 = Ac$

Further transformations of the compounds **3–7** towards *pseudo*-β-ribofuranose **2** are readily accomplished using osmium tetraoxide (cat.), and *N*-methylmorpholine *N*-oxide (NMO) in aq. acetone. In accordance with Kishi's guidelines[5] hydroxylation takes place from the face of the double bond distant from the adjacent hydroxy or acetate group to give the corresponding products **2**, **8–11** (Table 3). (These experiments were conducted on racemic materials and the products were fully characterised as the corresponding diesters **12** and **13**.) Furthermore the alcohol (+)-**6** was converted into the bis-*tert*-butyldimethylsilyl derivative and oxidized with osmium tetraoxide in the prescribed manner to give the diol (+)-**14**. Deprotection, acetylation, chromatography and de-esterification gave tetraol (−)-**2** (Scheme 1) with an optical rotation {$[\alpha]_D$ -10.5×10^{-1} deg cm^2 g^{-1} (*c* 1.0, MeOH)} opposite to that reported earlier for authentic (1*R*,2*S*,3*R*,4*R*)-1,2,3-trihydroxy-4-hydroxymethylcyclopentane (*pseudo*-β-ribofuranose) **2**.[6]



8 $R^1 = CPh_3$, $R^2 = H$
9 $R^1 = CPh_3$, $R^2 = Ac$
10 $R^1 = SiBu^tMe_2$, $R^2 = H$
11 $R^1 = SiBu^tMe_2$, $R^2 = Ac$



12 R = Ac
13 $R = SiBu^tMe_2$

The tritylated diol (−)-**4** was acetylated to give compound **5**, which was bis-hydroxylated using osmium tetraoxide to afford the diol **9**; this was converted in two steps into the acetonide **15**, which was in turn oxidized to the ketone **16**, reduction of which with sodium borohydride and deprotection gave (+)-*pseudo*-α-ribofuranose **1** in an optically pure state {$[\alpha_D]$ 46.7 (*c* 0.4, MeOH)} (Scheme 2). The efficiency of the synthesis of tetraol **1** from diol **3** meant that it was ideally suited for the preparation of labelled tetraols **17** and **18**, compounds that may be helpful in delineating the biosynthesis of aristeromycin. Thus the deuteriated compound (±)-**17** was prepared from compound **19** in an overall yield of 70%.

Table 1 Hydrolysis of the acetates **5** and **7**, using enzymes as catalysts

Substrate	Enzyme	Conversion (%)	Acetone (% v/v)	Time (*t*/h)	Product (ee)
5	Pig liver esterase (PLE)	4	11	96	(−)-(4) (65)
5	Porcine pancreatic lipase (PPL)	<1	6.25	96	
5	*Pseudomonas fluorescens* lipase (PFL)	25	15	16.5	(+)-(4) (>95)
7	*Pseudomonas fluorescens* lipase (PFL)	50	17	20	(+)-(6) (>95)

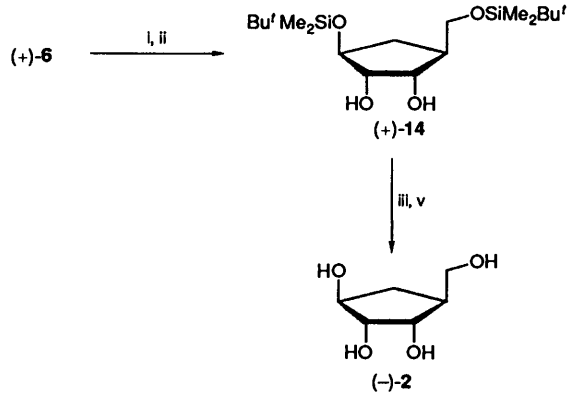
Table 2 Acetylation of the alcohol **4** using *Pseudomonas fluorescens* lipase in vinyl acetate

Time (*t*/h)	Isolated yield (+)-**5** (ee)	Isolated yield (−)-**4** (ee)
46	22 (>95)	50 (82)
75	50 (85)	46 (96)

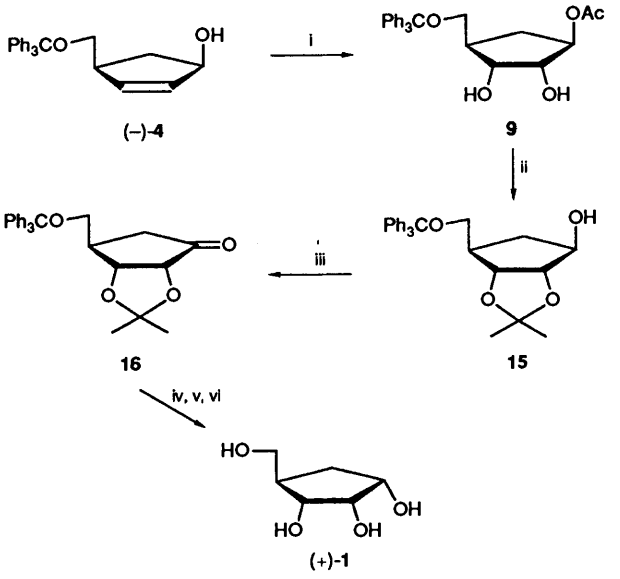
Table 3 Oxidation of cyclopentene derivatives **3**–**7** by using osmium tetraoxide[a]

Substrate	Product	Yield (%)
3	**1**	87
4	**8**	81
5	**9**	89
6	**10**	84
7	**11**	96

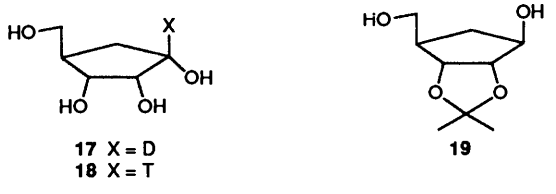
[a] 0.01 mol equiv. OsO_4, 1.1 mol equiv. *N*-methylmorpholine *N*-oxide, acetone–water (10:1).



Scheme 1 *Reagents*: i, Bu^{t}Me$_2$SiCl, imidazole, 4-(dimethylamino)-pyridine (DMAP), CH_2Cl_2; ii, OsO_4 (cat.), NMO, aq. acetone; iii, Bu_4NF (TBAF) tetrahydrofuran (THF); iv, Ac_2O, pyridine, DMAP, CH_2Cl_2; v, NaOMe, MeOH



Scheme 2 *Reagents and conditions*: i, Ac_2O, pyridine, DMAP, CH_2Cl_2; then OsO_4, NMO; ii, 2,2-dimethoxypropane, toluene-*p*-sulfonic acid (PTSA); then NaOMe, MeOH; iii, pyridinium chlorochromate (PCC), 4 Å sieves, CH_2Cl_2; iv, $NaBH_4$, 90% aq. EtOH; v, 80% aq. AcOH; then Amberlyst (H^+) resin, aq. THF



Experimental

Ethyl acetate and light petroleum (boiling range 60–80 °C unless otherwise stated) were distilled prior to use. Dichloromethane was distilled from calcium hydride and stored over 4 Å molecular sieves.

Thin-layer chromatography (TLC) was performed using precoated glass plates (Merck silica gel 60F 254). The plates were visualised using UV light (254 nm) and/or phosphomolybic acid in ethanol, or *p*-anisaldehyde in glacial acetic acid, or basic potassium permanganate. Flash chromatography (chromatography) was performed using Merck silica 60 (40–63 μm).

IR spectra were recorded using a Perkin-Elmer 881 spectrophotometer. ^1H and ^{13}C NMR spectra were measured using a Bruker AM 250 spectrometer operating at 250 MHz and 62.9 MHz, respectively. *J*-Values are given in Hz. Mass spectral data were obtained at the SERC Centre, Swansea. Optical rotations were measured on an AA-1000 polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}.

M.p.s were measured on an Electrothermal capillary melting point apparatus and are not corrected.

(3β,5β)-(±) and (3R,5S)-(−) 3-Acetoxy-5-(triphenylmethoxymethyl)cyclopentene **5**.—Acetic anhydride (1.6 cm^3, 1.73 g, 0.02 mol), pyridine (2.5 cm^3, 2.45 g, 0.031 mol) and DMAP (333.5 mg, 2.7 mmol, 0.4 mol equiv.) were added to a solution of (±)-4β-(triphenylmethoxymethyl)cyclopent-2-en-1β-ol **4**[3] (2.48 g, 7.8 mmol) in dry dichloromethane (18 cm^3). After 1.5 h the solvent was removed by evaporation and the residue was chromatographed over silica gel [(8:1) light petroleum–EtOAc] to give (±)-3β-acetoxy-5β-(triphenylmethoxymethyl)-cyclopentene **5** (2.76 g, 99%), R_f 0.4 [light petroleum–EtOAc, (4:1)] as an oil.

(−)-(3*R*,5*S*)-3-Acetoxy-5-(triphenylmethoxymethyl)cyclopentene was synthesized from (1*R*,4*S*)-(triphenylmethoxymethyl)cyclopent-2-enol in an identical procedure; $[\alpha]_D^{22}$ −20.2 (*c* 1.2, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3062, 3030, 2916, 2868, 1732, 1597, 1490, 1366, 1240, 1154 and 1067; δ_H(250 MHz; $CDCl_3$) 1.60 (1 H, ddd, *J* 14.5, 4.5 and 4.5, 4-H), 2.00 (3 H, s, AcO), 2.51 (1 H, ddd, *J* 14.5, 8 and 8, 4-H), 2.90–3.04 (1 H, m, 5-H), 3.05–3.20 (2 H, m, 6-H_2), 5.64–5.73 (1 H, m, 3-H), 5.89 (1 H, ddd, *J* 5.5, 2 and 2, 1-H), 6.13 (1 H, ddd, *J* 5.5, 1 and 2, 2-H) and 7.21–7.58 (15 H, m, Ph); δ_C($CDCl_3$) 21.28 (CH_3, $MeCO_2$), 33.72 (CH_2, C-4), 45.10 (CH, C-5), 67.04 (CH_2, C-6), 79.65 (CH, C-3), 86.37 (C, Ph_3C), 126.94 (CH, Ph), 127.75 (CH, Ph), 128.79 (CH, Ph), 130.41 (CH, C-1), 138.49 (CH, C-2), 144.27 (C, Ph) and 170.88 (C, $MeCO_2$).

Enzymic Resolution of (±)-4β-(*Triphenylmethoxymethyl*)*cyclopent-2-en*-1β-*ol* **4**.—PFL (325 mg, 4550 units) was added to a solution of (±)-4β-(triphenylmethoxymethyl)cyclopent-2-en-1β-ol **4** (529 mg, 1.49 mmol) in vinyl acetate (30 cm^3). After 75 h at room temperature, the enzyme was removed by filtration and the residue was washed with ethyl acetate. The combined filtrate and washings were concentrated under reduced pressure and the residue (656 mg) was purified by chromatography over silica gel [(4:1) light petroleum–EtOAc]. The first compound to be eluted was (3*S*,5*R*)-(+)-3-acetoxy-5-(triphenylmethoxymethyl)cyclopentene **5** (296 mg, 50%), R_f 0.42, as an oil; $[\alpha]_D^{21}$ +16.2 (*c* 1.5, $CHCl_3$) (85% ee). This was followed by (1*R*,4*S*)-(−)-4-(triphenylmethoxymethyl)cyclopent-2-enol **4** (244 mg, 46%), R_f 0.16 as a solid, m.p. 113–114 °C; $[\alpha]_D^{24}$ −72 (*c* 1.2, $CHCl_3$) (95.5% ee).

Enzyme-catalysed Hydrolysis of (±)-3β-*Acetoxy*-5β-(*triphenylmethoxymethyl*)*cyclopentene* (±)-**5** *using PLE, PPL and PFL.—Using PLE.* A potassium phosphate buffer solution (8 cm^3; pH 7) was added to a solution of (±)-**5** (150.5 mg, 0.38 mmol) in acetone (0.9 cm^3). PLE (100 mm^3, 253 units) was added and the mixture was stirred for four days. The reaction mixture was extracted with diethyl ether (2 × 10 cm^3) and the combined extracts were dried (anhydrous magnesium sulfate), filtered, and concentrated under reduced pressure. The residue (126.2 mg) was chromatographed over silica gel [(4:1) light petroleum–EtOAc] to give first (3*S*,5*R*)-(+)-3-acetoxy-5-(triphenylmethoxymethyl)cyclopentene **5** (110.4 mg, 73%), R_f 0.42, as an oil, followed by (1*R*,4*S*)-4-(triphenylmethoxymethyl)-cyclopent-2-enol **4** (4.9 mg, 4%), R_f 0.19, as a solid, m.p. 112–113 °C; $[\alpha]_D^{25}$ −45.6 (*c* 0.2, $CHCl_3$) (65% ee).

Using PPL. A potassium phosphate buffer solution (8 cm^3; pH 7) was added to a solution of (±)-**5** (160.9 mg, 0.40 mmol) in acetone (0.5 cm^3). PPL (80 mg, 1064 units) was added and the mixture was stirred for four days with negligible hydrolysis by TLC analysis (<1%).

Using PFL. A potassium phosphate buffer solution (6 cm^3; pH 7) was added to a solution of (±)-**5** in acetone (0.9 cm^3). PFL (40 mg, 560 units) was added and the mixture was stirred for 16.5 h. The mixture was extracted with diethyl ether (3 × 15 cm^3) and the combined extracts were dried (anhydrous magnesium sulfate). The solvent was removed by evaporation and the residue was chromatographed [(4:1) light petroleum–EtOAc] over silica gel to give recovered starting material **5** (69.7 mg, 66%) followed by (1*S*,4*R*)-(+)-4-(triphenylmethoxymethyl)cyclopent-2-enol **4** (23.5 mg, 25%) (>95% ee) as a solid, m.p. 112–113 °C; $[\alpha]_D^{26}$ +63.2 (*c* 0.5, $CHCl_3$). ^{1}H and ^{13}C NMR spectra were identical with those of the racemic compound.

(±)-4β-(tert-*Butyldimethylsiloxymethyl*)*cyclopent-2-en*-1β-*ol* **6**.—*tert*-Butyldimethylsilyl chloride (2.36 g, 0.016 mol, 1 mol. equiv.), imidazole (2.38 g, 0.035 mol, 2.2 mol equiv.) and DMAP (69.2 mg, 0.57 mmol, 0.04 mol. equiv.) were added to a cooled (0 °C) solution of the mixed *cis*-1,4- and 1,2-diols obtained from the Prins reaction on cyclopentadiene[3] (1.78 g, 0.02 mol) in dry dichloromethane (98 cm^3) under argon. After being stirred for 3 h at 0 °C, the solids were removed by filtration and washed with dichloromethane. The combined filtrate and washings were concentrated under reduced pressure. The residue (5.93 g) was purified by chromatography on silica gel [(9:1) light petroleum–EtOAc] to give (±)-4β-(tert-*butyldimethylsiloxymethyl*)*cyclopent-2-en*-1β-*ol* **6** (1.03 g, 29%), R_f 0.19, as a liquid; ν_{max}(neat)/cm^{-1} 3394, 2957, 2933, 2893, 2859, 1614, 1385, 1254 and 1084; δ_H(250 MHz; $CDCl_3$) 0.05 (6 H, s, 2 × Me), 0.87 (9 H, s, Bu^t), 1.49 (1 H, ddd, *J* 14, 2 and 2, 5-H), 2.26 (1 H, ddd, *J* 14, 7 and 8.5, 5-H), 2.70–2.80 (2 H, m, 4-H and OH), 3.56 (1 H, dd, *J* 4 and 10, 6-H), 3.61 (1 H, dd, *J* 3.5 and 10, 6-H), 4.50–4.64 (1 H, m, 1-H), 4.73 (1 H, dd, *J* 2.5 and 5.5, 3-H) and 5.90 (1 H, ddd, *J* 5.5, 2 and 2, 2-H); δ_C($CDCl_3$) −5.51 (CH_3, 2 × Me), 18.48 (C, Bu^t), 25.96 (CH_3, Bu^t), 37.03 (CH_2, C-5), 46.47 (CH, C-4), 64.80 (CH_2, C-6), 75.67 (CH, C-1), 134.85 (CH, C-3) and 135.24 (CH, C-2) (Found: for $[M + NH_4 - H_2O]^+$, 228.1784. $C_{12}H_{24}O_2Si$ requires $[M + NH_4 - H_2O]^+$, 228.1784).

(±)-3β-*Acetoxy*-5β-(tert-*butyldimethylsiloxymethyl*)*cyclopentene* **7**.—A solution of the (±)-alcohol **6** (1.03 g, 4.5 mmol) in dry dichloromethane (12 cm^3) was treated with acetic anhydride (0.85 cm^3, 0.99 mg, 9.10 mmol) and pyridine (0.55 cm^3, 0.54 mg, 6.8 mmol) in the presence of DMAP (55.0 mg, 0.45 mmol) for 2 h. The solvent was removed by evaporation and the residue (2.14 g) was chromatographed over silica gel [(10:1) light petroleum–EtOAc] to give (±)-3β-acetoxy-5β-(*tert*-butyldimethylsiloxymethyl)cyclopentene **7** (1.14 g, 94%), R_f 0.34, as an oil; ν_{max}(neat)/cm^{-1} 2934, 2860, 1736, 1365, 1242 and 1082; δ_H(250 MHz; $CDCl_3$) 0.03 (6 H, s, 2 × Me), 0.87 (9 H, s, Bu^t), 1.50 (1 H, ddd, *J* 14.5, 4.5 and 4.5, 4-H), 2.00 (3 H, s, AcO), 2.40 (1 H, ddd, *J* 14.5, 8 and 8, 4-H), 2.68–2.86 (1 H, m, 5-H), 3.53 (2 H, d, *J* 7, 6-H_2), 5.55–5.68 (1 H, m, 3-H), 5.82 (1 H, ddd, *J* 5.5, 3.5 and 2, 1-H) and 6.02 (1 H, ddd, *J* 5.5, 2 and 1, 2-H); δ_C($CDCl_3$) −5.39 (CH_3, 2 × Me), 18.27 (C, Bu^t), 21.17 (CH_3, AcO), 25.86 (CH_3, Bu^t), 33.01 (CH_2, C-4), 47.36 (CH, C-5), 66.89 (CH_2, C-6), 79.56 (CH, C-3), 130.36 (CH, C-1), 138.35 (CH, C-2) and 170.72 (C, $MeCO_2$) *m*/*z* (EI) 271 [(M^+ + H), 3%], 211 [(M − Ac), 97%].

Enzymic Resolution of (±)-3β-*Acetoxy*-5β-(tert-*butyldimethylsiloxymethyl*)*cyclopentene* **7**.—A potassium phosphate buffer solution (12.5 cm^3; pH 7) was added dropwise to a vigorously stirred solution of (±)-3β-acetoxy-5β-(*tert*-butyldimethylsiloxymethyl)cyclopentene **7** (203.5 mg, 0.75 mmol) in acetone (2.5 cm^3). PFL (97.8 mg, 1369 units) was added and the mixture was stirred for 15 h. An extra aliquot (98 mg, 1369 units) of lipase was added and the mixture was stirred for 5 h, whereupon 50% hydrolysis was observed by TLC and pH change (*i.e.* the volume of 0.01 mol dm^{-3} aq. sodium hydroxide required to neutralize the acetic acid formed during the reaction). The reaction mixture was extracted with diethyl ether (4 × 40 cm^3) and the combined extracts were dried (anhydrous magnesium sulfate). The solids were removed by filtration and the filtrate was concentrated under reduced pressure. The residue (180 mg) was chromatographed over silica gel [(9:1) light petroleum–EtOAc]. The first compound to be eluted was (3*R*,5*S*)-(−)-3-acetoxy-5-(*tert*-butyldimethylsiloxymethyl)-cyclopentene **7** (88.0 mg, 43%), R_f 0.38, as an oil; $[\alpha]_D^{25}$ −4.2 (*c* 1.8, $CHCl_3$) (>95% ee); IR, ^{1}H and ^{13}C NMR spectra were identical with those of the racemic compound. This was followed by (1*S*,4*R*)-(+)-4-(*tert*-butyldimethylsiloxymethyl)-cyclopent-2-enol **6** (71.8 mg, 42%), R_f 0.14, as a volatile liquid; $[\alpha]_D^{25}$ +49.6 (*c* 1.4, $CHCl_3$) (>95% ee); IR, ^{1}H and ^{13}C NMR spectra were identical with those of the racemic compound.

Standard Procedure for Bis-hydroxylation of Alkenes **3–7** *using Osmium Tetraoxide.*—A 0.01 mol dm^{-3} solution of osmium tetraoxide in butan-1-ol (0.01 mol equiv.) was added dropwise to a cooled (0 °C) solution of the cyclopentene derivative in an acetone–water mixture (10:1; 0.5 mol dm^{-3}). NMO (1.1 mol equiv.) was added and the reaction mixture was allowed to warm up to room temperature. After the mixture had been stirred for 15 h, sodium metabisulfite (solid, 2–3 mol equiv.) was added and the mixture was stirred for an additional 10 min. The reaction mixture was diluted with acetone and then filtered through a Celite/silica plug. The residue was washed with acetone and the combined filtrate and washings were concentrated under reduced pressure. The residue was purified by chromatography on silica gel.

Standard Procedure for Preparation of the Isopropylidene Derivatives of cis*-diols* **8–11**.—A solution of the diol in 2,2-dimethoxypropane (0.1–0.2 mol dm^{-3}) was stirred in the presence of a catalytic amount of PTSA (~0.1 mol equiv.) under nitrogen. Once the reaction was complete (TLC) the acid was neutralized with solid sodium hydrogen carbonate. The solids were removed by filtration and the residue was washed with dichloromethane. The combined filtrate and washings were concentrated under reduced pressure and the residue was purified by chromatography over silica gel.

(±)-4β-(*Triphenylmethoxymethyl*)*cyclopentane*-1β,2α,3α-*triol* **8**.—(±)-4β-(Triphenylmethoxymethyl)cyclopent-2-en-1β-ol **4** (256 mg, 0.72 mmol) was bis-hydroxylated and worked up as described in the standard procedure. The residue (593 mg) was chromatographed over silica gel [(1:1), CH_2Cl_2–EtOAc] to give (±)-4β-(*triphenylmethoxymethyl*)*cyclopentane*-1β,2α,3α-*triol* **8** (228 mg, 81%), R_f 0.11, as a solid, m.p. 107–111 °C; ν_{max}(KBr)/cm^{-1} 3361, 3060, 2932, 2865, 1487, 1219, 1121, 1089 and 1060; δ_H(250 MHz; CD_3OD) 1.33 (1 H, ddd, *J* 11.5, 6.5 and 6.5, 5-H), 2.08–2.32 (2 H, m, 4- and 5-H), 3.06–3.25 (2 H, m, 6-H_2), 3.70 (1 H, dd, *J* 5 and 5, 2-H), 3.90 (1 H, dd, *J* 5 and 5, 3-H), 3.95–4.09 (1 H, m, 1-H) and 7.15–7.53 (15 H, m, Ph); δ_C(CD_3OD) 34.12 (CH_2, C-5), 44.24 (CH, C-4), 66.58 (CH_2, C-6), 74.72 (CH, C-2), 76.74 (CH, C-1), 79.70 (CH, C-3), 87.74 (C, Ph_3C), 128.04 (CH, Ph), 128.76 (CH, Ph), 129.93 (CH, Ph) and 145.64 (C, Ph). The compound was further characterised as the triacetate, m.p. 138–139.5 °C (Found: M^+, 516.2148. $C_{31}H_{32}O_7$ requires *M*, 516.2148).

(±)-4β-(tert-*Butyldimethylsiloxymethyl*)*cyclopentane*-1β,2α,3α-*triol* **10**, (±)-1β-*acetoxy*-4β-*acetoxymethyl*-2α,3α-(*isopropylidenedioxy*)*cyclopentane* **12** *and* (±)-4β-*hydroxymethyl*-2α,3α-(*isopropylidenedioxy*)*cyclopentan*-1β-*ol* **19**.—The (±)-alkene **6** (58.3 mg, 0.26 mmol) was bis-hydroxylated and worked up as described in the standard procedure. The residue (103 mg) was chromatographed over silica gel [(10:1), $CHCl_3$–MeOH] to give (±)-4β-(*tert*-butyldimethylsiloxymethyl)cyclopentane-1β,2α,3α-triol **10** (56.5 mg, 84%), R_f 0.2 [EtOAc–CH_2Cl_2 (2:1)] as an oil; ν_{max}(neat)/cm^{-1} 3373, 2933, 2892, 2860, 1388, 1359, 1254 and 1101; δ_H(250 MHz; CD_3OD) 0.08 (6 H, s, 2 × Me), 0.92 (9 H, s, Bu^t), 1.31 (1 H, ddd, *J* 12.5, 7.5 and 7, 5-H), 1.95–2.20 (2 H, m, 4- and 5-H), 3.63–3.71 (3 H, m, 1-H and 6-H_2), 3.86 (1 H, dd, *J* 5.5 and 5.5, 3-H) and 3.93–4.03 (1 H, m, 2-H); δ_C(CD_3OD) −5.15 (CH_3, 2 × Me), 19.22 (C, Bu^t), 26.50 (CH_3, Bu^t), 33.36 (CH_2, C-5), 46.16 (CH, C-4), 65.92 (CH_2, C-6), 74.19 (CH, C-1), 76.82 (CH, C-3) and 79.72 (CH, C-2).

The (±)-triol **10** (50.1 mg, 0.19 mmol) was dissolved in 2,2-dimethoxypropane (0.1 cm^3) and PTSA (10 mg) was added. The reaction mixture was stirred at room temperature until TLC analysis showed complete reaction (*ca.* 3 h). After work-up in the standard fashion and chromatography over silica gel [(9:1), $CHCl_3$–MeOH] (±)-4β-hydroxymethyl-2α,3α-(isopropylidenedioxy)cyclopentane-1β-ol **19** (29.0 mg, 81%), R_f 0.1 [EtOAc–CH_2Cl_2 (2:1)] was obtained as an oil. (Note that the *tert*-butyldimethylsilyl protecting group was lost under the reaction conditions.)

This diol **19** (29.0 mg, 0.15 mmol) was dissolved in dry dichloromethane (0.5 cm^3) and treated with a mixture of acetic anhydride (0.06 cm^3, 65.3 mg, 0.64 mmol) and pyridine (0.06 cm^3, 58.5 mg, 0.74 mmol) in the presence of DMAP (5 mg) for 1 h. The solvent was removed by evaporation and the residue was chromatographed over silica gel [(4:1) light petroleum–EtOAc] to give (±)-1β-*acetoxy*-4β-*acetoxymethyl*-2α,3α-(*isopropylidenedioxy*)*cyclopentane* **12** (40.1 mg, 96%), R_f 0.15, as an oil; ν_{max}(neat)/cm^{-1} 2989, 2940, 1739, 1371, 1234, 1162 and 1034; δ_H(250 MHz; $CDCl_3$) 1.26 and 1.42 (each 3 H, each s, Me_2C), 1.54–1.64 (1 H, m, 5-H), 2.00 (3 H, s, AcO), 2.05 (3 H, s, AcO), 2.26–2.55 (2 H, m, 4- and 5-H), 4.02 (2 H, d, *J* 7.5, 6-H_2), 4.50 (2 H, s, 2- and 3-H) and 5.04 (1 H, dd, *J* 2.5 and 5.5, 1-H); δ_C($CDCl_3$) 20.81 and 21.05 (CH_3, 2 × $MeCO_2$), 24.18 and 26.55 (CH_3, Me_2C), 31.80 (CH_2, C-5), 44.39 (CH, C-4), 65.03 (CH_2, C-6), 79.17 (CH, C-1), 82.33 (CH, C-2), 84.79 (CH, C-3), 111.07 (C, Me_2C) and 169.78 and 170.82 (C, 2 × $MeCO_2$) (Found: $[M + H]^+$, 273.1338, $C_{13}H_{20}O_6$ requires $[M + H]^+$, 273.1338).

(±)-3β-*Acetoxy*-5β-(tert-*butyldimethylsiloxymethyl*)*cyclopentane*-1α,2α-*diol* **11** *and* 1β-*Acetoxy*-4β-(tert-*butyldimethylsiloxymethyl*)-2α,3α-(*isopropylidenedioxy*)*cyclopentane* **13**.—The (±)-alkene **7** (119 mg, 0.44 mmol) was bis-hydroxylated and worked up as described in the standard procedure. The residue (205 mg) was chromatographed on silica gel [(9:1), CH_2Cl_2–acetone] to give (±)-3β-*acetoxy*-5β-(tert-*butyldimethylsiloxymethyl*)*cyclopentane*-1α,2α-*diol* **11** (128 mg, 96%), R_f 0.17, as an oil; ν_{max}(neat)/cm^{-1} 3423, 2957, 2935, 2895, 2861, 1736, 1373, 1253, 1105 and 1031; δ_H(250 MHz; $CDCl_3$) 0.03 (6 H, s, 2 × Me), 0.83 (9 H, s, Bu^t), 1.34 (1 H, ddd, *J* 13.5, 6 and 8, 4-H), 1.99 (3 H, s, AcO), 2.05–2.17 (1 H, m, 5-H), 2.26 (1 H, ddd, *J* 13.5, 8.5 and 8.5, 4-H), 3.24 (1 H, br s, OH), 3.54 (1 H, dd, *J* 5.5 and 10, 6-H), 3.62–3.74 (2 H, m, 6-H and OH), 3.89 (2 H, s, 1- and 2-H) and 4.84–4.95 (1 H, m, 3-H); δ_C($CDCl_3$) −5.57 and −5.53 (CH_3, 2 × Me), 18.17 (C, Bu^t), 20.98 (CH_3, AcO), 25.83 (CH_3, Bu^t), 29.42 (CH_2, C-4), 44.51 (CH, C-5), 64.31 (CH_2, C-6), 74.08 (CH, C-1), 76.62 (CH, C-2), 79.41 (CH, C-3) and 171.48 (C, $MeCO_2$).

The isopropylidene derivative **13** of the diol **11** (124 mg, 0.41 mmol) was prepared and worked up as described in the standard procedure. The residue (141 mg) was chromatographed on silica gel [(3:1) light petroleum–EtOAc] to give (±)-1β-*acetoxy*-4β-(tert-*butyldimethylsiloxymethyl*)-2α,3α-(*isopropylidenedioxy*)*cyclopentane* **13** (125 mg, 89%), R_f 0.49, as an oil; ν_{max}(neat)/cm^{-1} 2935, 2893, 2861, 1746, 1374, 1238, 1211, 1162, 1093 and 1044; δ_H(250 MHz; $CDCl_3$) 0.03 (6 H, s, 2 × Me), 0.87 (9 H, s, Bu^t), 1.24 and 1.41 (each 3 H, each s, Me_2C), 1.53–1.68 (1 H, m, 5-H), 1.99 (3 H, s, AcO), 2.18–2.31 (2 H, m, 4- and 5-H), 3.50 (1 H, dd, *J* 6.5 and 10.5, 6-H), 3.57 (1 H, dd, *J* 7 and 10, 6-H), 3.42 (1 H, br d, *J* 6, 2-H), 3.48 (1 H, br d, *J* 5.5, 3-H) and 4.96–5.06 (1 H, m, 1-H); δ_C($CDCl_3$) −5.46 and −5.43 (CH_3, 2 × Me), 18.23 (C, Bu^t), 21.00 (CH_3, $MeCO_2$), 24.35 (CH_3, Me_AC), 25.84 (CH_3, Bu^t), 26.75 (CH_3, Me_BC), 31.58 (CH_2, C-5), 47.21 (CH, C-4), 63.67 (CH_2, C-6), 79.68 (CH, C-1), 81.74 (CH, C-3), 84.87 (CH, C-2), 110.98 (C, Me_2C) and 169.80 (C, $MeCO_2$) (Found: $[M + H]^+$, 345.2097. $C_{17}H_{32}O_5Si$ requires $[M + H]^+$, 345.2097).

(1α,2α,3β,5β)-(±) *and* (1R,2R,3R,5S)-(−)-3-*Acetoxy*-5-(*triphenylmethoxymethyl*)*cyclopentane*-1,2-*diol* **9**.—(±)-3β-Acetoxy-5β-(triphenylmethoxymethyl)cyclopentene **5** (1.66 g, 4.2 mmol) was bis-hydroxylated and worked up as described in the standard procedure. The residue was purified by chromato-

graphy over silica gel [(9:1), CH_2Cl_2–acetone] to give (±)-3β-acetoxy-5β-(triphenylmethoxymethyl)cyclopentane-1α,2α-diol **9** (1.60 g, 89%), R_f 0.28, as a foam, m.p. 37–41 °C.

(1*R*,2*R*,3*R*,5*S*)-(−)-3-Acetoxy-5-(triphenylmethoxymethyl)-cyclopentane-1,2-diol was synthesized from (3*R*,5*S*)-(−)-3-acetoxy-5-(triphenylmethoxymethyl)cyclopentene in an identical manner; m.p. 37–41 °C; $[\alpha]_D^{25}$ −13.8 (*c* 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3423, 3061, 2928, 1729, 1489, 1372, 1245, 1070 and 1032; δ_H(250 MHz; $CDCl_3$) 1.35–1.46 (1 H, m, 4-H), 2.05 (3 H, s, AcO), 2.26–2.47 (2 H, m, 4- and 5-H), 2.86 (1 H, br s, OH), 3.14 (1 H, dd, *J* 6.5 and 9, 6-H), 3.23–3.37 (2 H, m, 6-H and OH), 3.93–4.04 (2 H, m, 1- and 2-H), 4.90–5.02 (1 H, m, 3-H), 7.21–7.37 (9 H, m, ArH) and 7.40–7.55 (6 H, m, ArH); δ_C($CDCl_3$) 21.04 (CH_3, *Me*CO_2), 30.25 (CH_2, C-4), 42.92 (CH, C-5), 65.28 (CH_2, C-6), 74.81 (CH, C-2), 76.87 (CH, C-1), 79.91 (CH, C-3), 86.88 (C, Ph_3C), 127.11 (CH, Ph), 127.88 (CH, Ph), 128.69 (CH, Ph), 143.92 (C, Ph) and 171.72 (C, Me*C*O_2).

(1β,2α,3α,4β)-(±) *and* (1R,2S,3R,4R)-(−)-2,3-*Isopropylidenedioxy*-4-(*triphenylmethoxymethyl*)*cyclopentan*-1-*ol* **15**.—The isopropylidene derivative of the (±)-diol **9** (2.58 g, 5.97 mmol) was synthesized as described in the standard procedure. The residue (2.40 g) was purified by chromatography over silica gel [(3:1) light petroleum–EtOAc] to give (±)-1β-acetoxy-2α,-3α-isopropylidenedioxy-4β-(triphenylmethoxymethyl)cyclopentane (2.31 g, 82%), R_f 0.41, as a foam. {(1R,2S,3R,4R)-(−)-1-*Acetoxy*-2,3-*isopropylidenedioxy*-4-(*triphenylmethoxymethyl*)-*cyclopentane* was synthesized from (1*R*,2*R*,3*R*,5*S*)-(−)-3-acetoxy-5-(triphenylmethoxymethyl)cyclopentane-1,2-diol in an identical procedure; $[\alpha]_D^{24}$ −28.6 (*c* 0.99 in $CHCl_3$)}; ν_{max}(neat)/cm^{-1} 3063, 2987, 2938, 1738, 1490, 1374, 1240, 1159 and 1043; δ_H(250 MHz; $CDCl_3$) 1.29 and 1.47 (each 3 H, each s, Me_2C), 1.60–1.74 (1 H, m, 5-H), 1.79 (3 H, s, AcO), 2.37 (1 H, ddd, *J* 14, 6 and 7.5, 5-H), 2.50–2.66 (1 H, m, 4-H), 3.09 (2 H, d, *J* 7.5, 6-H_2), 4.35 (1 H, d, *J* 6, 2-H), 4.51 (1 H, d, *J* 6, 3-H), 4.59–5.04 (1 H, m, 1-H) and 7.18–7.58 (15 H, m, Ph); δ_C($CDCl_3$) 20.98 (CH_3, *Me*CO_2), 24.32 and 26.70 (CH_3, Me_2C), 32.05 (CH_2, C-5), 45.44 (CH, C-4), 64.53 (CH_2, C-6), 79.56 (CH, C-1), 82.56 (CH, C-2), 84.79 (CH, C-3), 86.58 (C, Ph_3C), 110.84 (C, Me_2C), 126.98 (CH, Ph), 127.78 (CH, Ph), 128.72 (CH, Ph), 144.17 (C, Ph) and 169.83 (C, MeCO_2). (Found: M^+, 472.2250. $C_{30}H_{32}O_5$ requires M^+, 472.2250).

Sodium methoxide (42.0 mg, 0.78 mmol) was added to a solution of the above (±)-acetate (2.31 g, 4.89 mmol) in methanol (29 cm^3). After the mixture had been stirred for 3.5 h, the solvent was removed by evaporation and the residue (2.40 g) was chromatographed over silica gel [(3:1) light petroleum–EtOAc] to give (±)-2α,3α-isopropylidenedioxy-4β-(triphenylmethoxymethyl)cyclopentane-1β-ol **15** (2.02 g, 96%), R_f 0.19, as a hygroscopic foam.

(1R,2S,3R,4R)-(−)-2,3-*Isopropylidenedioxy*-4-(*triphenylmethoxymethyl*)*cyclopentanol* was synthesized from (1*R*,2*S*,-3*R*,4*R*)-(−)-1-acetoxy-2,3-isopropylidenedioxy-4-(triphenylmethoxymethyl)cyclopentane by an identical procedure; $[\alpha]_D^{27}$ −13.5 (*c* 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3450, 3063, 3031, 2988, 2935, 1489, 1375, 1261, 1210, 1157 and 1037; δ_H(250 MHz; $CDCl_3$) 1.30 and 1.42 (each 3 H, each s, Me_2C), 1.48–1.66 (1 H, m, 5-H), 2.26–2.45 (2 H, m, 4- and 5-H), 2.75 (1 H, br d, *J* 6.5, OH), 3.21 (1 H, dd, *J* 5 and 9.5, 6-H), 3.37 (1 H, dd, *J* 5 and 9.5, 6-H), 4.08–4.18 (1 H, m, 1-H), 4.42 (1 H, d, *J* 6, 2-H), 4.55 (1 H, d, *J* 6, 3-H), 7.18–7.37 (9 H, m, ArH) and 7.40–7.53 (6 H, m, ArH); δ_C($CDCl_3$) 24.36 and 26.80 (CH_3, Me_2C), 35.48 (CH_2, C-5), 45.72 (CH, C-4), 65.35 (CH_2, C-6), 77.18 (CH, C-1), 83.31 (CH, C-2), 87.54 (C, Ph_3C), 87.75 (CH, C-3), 110.34 (C, Me_2C), 127.19 (CH, Ph), 127.90 (CH, Ph), 128.79 (CH, Ph) and 143.56 (C, Ph) (Found: M^+, 430.2144. $C_{28}H_{30}O_4$ requires M^+, 430.2144).

(1S,2S,3R,4R)-(+)-4-(*Hydroxymethyl*)*cyclopentane*-1,2,3-*triol*-(pseudo-α-*Ribofuranose*) (+)-**1**.—A solution of the (±) alcohol **15** (293 mg, 0.68 mmol) in dry dichloromethane (3 cm^3) was added to a mixture of PCC (366 mg, 1.70 mmol) and powdered 4 Å molecular sieves (510 mg) under argon. After the mixture had been stirred for 1 h at room temp., diethyl ether (3 cm^3) was added and the solids were removed by filtration through a Celite/silica plug. The solids were washed with diethyl ether and the combined filtrate and washings were concentrated under reduced pressure. The crude ketone (±)-**16** (267 mg, 91%) was used without further purification; however, it can be purified by chromatography over silica gel [(3:1) light petroleum–EtOAc] to give (±)-2α,3α-*isopropylidenedioxy*-4β-(*triphenylmethoxymethyl*)*cyclopentanone* **16** (R_f 0.36) as a solid, m.p. 175–178 °C; ν_{max}(KBr)/cm^{-1} 2986, 2959, 2925, 1752, 1491, 1377, 1264, 1218, 1152 and 1064; δ_H(250 MHz; $CDCl_3$) 1.32 and 1.43 (each 3 H, each s, Me_2C), 2.24 (1 H, dd, *J* 1 and 18.5, 5-H), 2.50–2.60 (1 H, m, 4-H), 2.80 (1 H, dd, *J* 9.5 and 18.5, 5-H), 3.23–3.35 (2 H, m, 6-H_2), 4.39 (1 H, *J* 5.5, 2-H), 4.45 (1 H, d, *J* 5.5, 3-H) and 7.18–7.42 (15 H, m, Ph); δ_C($CDCl_3$) 24.71 and 26.81 (CH_3, Me_2C), 37.61 (CH_2, C-5 and CH, C-4), 64.88 (CH_2, C-6), 79.07 (C-2), 81.48 (CH, C-3), 87.77 (C, Ph_3C), 111.40 (C, Me_2C), 127.24 (CH, Ph), 127.96 (CH, Ph), 128.64 (CH, Ph), 143.43 (C, Ph) and 213.52 (C, C-1) (Found: C, 78.1; H, 6.5. $C_{28}H_{28}O_4$ requires C, 78.5; H, 6.6. Found: $[M + NH_4]^+$, 446.2331. $C_{28}H_{28}O_4$ requires $[M + NH_4]^+$, 446.2331).

The crude ketone (±)-**16** (267 mg) was dissolved in 90% aq. ethanol (6 cm^3) and cooled to 0 °C. Sodium borohydride (368 mg, 1.80 mmol) was added and the mixture was stirred for 2 h at 0 °C. Saturated aq. ammonium chloride was added dropwise until the effervescence had ceased and the solvent was then removed by evaporation. The residue was redissolved in chloroform (10 cm^3) and washed with water (5 cm^3). The organic phase was concentrated under reduced pressure (336 mg) and was purified by chromatography over silica gel [(4:1) light petroleum–EtOAc] to give (±)-2α,3α-isopropylidenedioxy-4β-(triphenylmethoxymethyl)cyclopentan-1α-ol (235 mg, 80%), R_f 0.16, as a foam, m.p. 40–46 °C.

(1S,2S,3R,4R)-(−)-2,3-*Isopropylidenedioxy*-4-(*triphenylmethoxymethyl*)*cyclopentanol* was synthesized from the corresponding (1*R*,2*S*,3*R*,4*R*)-(−)-2,3-isopropylidenedioxy-4-(triphenylmethoxymethyl)cyclopentanol (−)-**15** in an identical procedure; $[\alpha]_D^{25}$ −9.7 (*c* 1.1, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3460, 3060, 3028, 2989, 2938, 1488, 1377, 1258, 1208, 1157, 1075 and 1035; δ_H(250 MHz; $CDCl_3$) 1.34 and 1.53 (each 3 H, each s, Me_2C), 1.81–2.01 (2 H, m, 5-H_2), 2.32–2.45 (1 H, m, 4-H), 2.50 (1 H, d, *J* 8.5, OH), 3.05 (1 H, dd, *J* 6 and 9.5, 6-H), 3.11 (1 H, dd, *J* 6.5 and 9.5, 6-H), 4.10–4.26 (1 H, m, 1-H), 4.42–4.51 (2 H, m, 2- and 3-H), 7.21–7.37 (9 H, m, ArH) and 7.42–7.54 (6 H, m, ArH); δ_C($CDCl_3$) 24.40 and 26.23 (CH_3, Me_2C), 25.38 (CH_2, C-5), 42.26 (CH, C-4), 64.52 (CH_2, C-6), 71.75 (CH, C-1), 79.58 (CH, C-2), 82.91 (CH, C-3), 86.94 (C, Ph_3C), 111.28 (C, Me_2C), 127.09 (CH, Ph), 127.87 (CH, Ph), 128.72 (CH, Ph) and 143.97 (C, Ph) (Found: $[M - CPh_3]^+$, 187.0970. $C_{28}H_{30}O_4$ requires $[M - CPh_3]^+$, 187.0970).

A solution of the (−)-alcohol (262 mg, 0.61 mmol) in 80% aq. acetic acid (10 cm^3) was heated at 80 °C for 30 min. The solvent was removed by evaporation and the residue of crude (1*S*,2*S*,3*R*,4*R*)-4-hydroxymethyl-2,3-(isopropylidenedioxy)-cyclopentanol was redissolved in a THF–water mixture (1:1; 9 cm^3). Amberlyst 15 (H^+) ion-exchange resin (110.3 mg) was added and the mixture was heated for 15 h at 60 °C. The resin was removed by filtration and was then washed with methanol. The combined filtrate and washings were concentrated under reduced pressure. The residue was chromatographed on silica gel [(3:1) $CHCl_3$–MeOH] to give (1S,2S,3R,4R)-(+)-4-(*hydroxymethyl*)*cyclopentane*-1,2,3-*triol* (+)-**1** (69.6 mg, 77%),

R_f 0.14, as an oil; $[\alpha]_D^{27}$ +46.4 (*c* 0.80, MeOH); ν_{max}(neat)/cm^{-1} 3344, 2931, 1331, 1107 and 1020; δ_H(250 MHz; CD_3OD) 1.60 (1 H, ddd, *J* 14, 6.5 and 7.5, 5-H), 1.92 (1 H, ddd, *J* 14, 4 and 10, 5-H), 2.24–2.38 (1 H, m, 4-H), 3.54 (2 H, d, *J* 5.5, CH_2), 3.83–3.94 (2 H, m, 2- and 3-H) and 4.06–4.15 (1 H, m, 1-H); δ_C(CD_3OD) 33.79 (CH_2, C-5), 47.7 (CH, C-4), 64.71 (CH_2, C-6), 73.74 (CH, C-1), 75.26 (CH, C-2) and 75.39 (CH, C-3). (Found: $[M + NH_4]^+$, 166.1079. $C_6H_{12}O_4$ requires $[M + NH_4]^+$, 166.1079).

(1α,2α,3β,5β)-(±)- *and* (1S,2S,3S,5R)-3-(tert-*Butyldimethylsiloxy*)-5-(tert-*butyldimethylsiloxymethyl*)*cyclopentane*-1,2-*diol* **14** *and* (1S,2R,3S,4S)-(−)-4-(*hydroxymethyl*)*cyclopentane*-1,2,3-*triol* (−)-**2**.—*tert*-Butyldimethylsilyl chloride (7.39 g, 0.049 mol), imidazole (6.66 g, 0.1 mol) and DMAP (80 mg) were added to a cooled (0 °C) solution of the diol **3**[3] (1.86 g) in dry dichloromethane (100 cm^3). After being stirred for 1 h at 0 °C, the solids were removed by filtration and the residue was washed with dichloromethane. The combined filtrate and washings were concentrated under reduced pressure and the residue was chromatographed over silica gel [(2:1) light petroleum (40–60 °C)–CH_2Cl_2] to give (±)-3β-(*tert*-butyldimethylsiloxy)-5β-(*tert*-butyldimethylsiloxymethyl)cyclopentene (5.48 g, 98%), R_f 0.39, as an oil.

[(3*S*,5*R*)-(+)-3-(*tert*-Butyldimethylsiloxy)-5-(*tert*-butyldimethylsiloxymethyl)cyclopentene was synthesized from (1*S*,4*R*)-(+)-4-(hydroxymethyl)cyclopent-2-enol (+)-**3** in an identical procedure; $[\alpha]_D^{26}$ +14.2 (*c* 2.0, $CHCl_3$)]; ν_{max}(neat)/cm^{-1} 2958, 2933, 2891, 2860, 1603, 1364, 1251, 1051 and 1082; δ_H(250 MHz; $CDCl_3$) 0.05 and 0.10 (12 H, 2 × s, 4 × Me), 0.92 (18 H, s, 2 × Bu^t), 1.34 (1 H, ddd, *J* 13.5, 5.5 and 5.5, 4-H), 2.29 (1 H, ddd, *J* 13.5, 7.5 and 7.5, 4-H), 2.65–2.78 (1 H, m, 5-H), 3.50 (2 H, d, *J* 7, 6-H_2), 4.60–4.89 (1 H, m, 3-H), 4.75 (1 H, ddd, *J* 5.5, 2 and 2, 1-H) and 5.86 (1 H, d, *J* 5.5, 2-H); δ_C($CDCl_3$) −5.31 and −4.58 (CH_3, 4 × Me), 18.16 and 18.34 (C, 2 × Bu^t), 25.94 (CH_3, 2 × Bu^t), 37.30 (CH_2, C-4), 47.36 (CH, C-5), 67.67 (CH_2, C-6), 77.29 (CH, C-3), 134.46 (CH, C-1) and 135.07 (CH, C-2).

The (±)-alkene (550 mg, 1.60 mmol) was bis-hydroxylated and worked up as described in the standard procedure. The residue (761 mg) was purified by chromatography on silica gel (2% MeOH–CH_2Cl_2) to give (±)-3β-(*tert*-butyldimethylsiloxy)-5β-(*tert*-butyldimethylsiloxymethyl)cyclopentane-1,2-diol **14** (567 mg, 94%), R_f 0.16, as a solid, m.p. 51–52 °C. {(1*S*,2*S*,3*S*,5*R*)-(+)-3-(*tert*-Butyldimethylsiloxy)-5-(*tert*-butyldimethylsiloxymethyl)cyclopentane-1,2-diol (+)-**14** was synthesized from (3*S*,5*R*)-(+)-3-(*tert*-butyldimethylsiloxy)-5-(*tert*-butyldimethylsiloxymethyl)cyclopentene in an identical procedure; m.p. 41–43 °C; $[\alpha]_D^{27}$ +18.9 (*c* 1.2, $CHCl_3$) and $[\alpha]_D^{24}$ +16.9 (*c* 1.0, $CHCl_3$)}; ν_{max}($CHCl_3$)/cm^{-1} 3554, 2955, 2933, 2893, 2859, 1386, 1250 and 1061; δ_H(250 MHz; $CDCl_3$) 0.03 and 0.05 (12 H, 2 × s, 4 × Me), 0.84 and 0.90 (18 H, 2 s, 2 × Bu^t), 1.09–1.23 (1 H, m, 4-H), 1.99–2.23 (2 H, m, 4- and 5-H), 2.73 (1 H, s, OH), 2.86 (1 H, s, OH), 3.57 (1 H, dd, *J* 8 and 9.5, 6-H), 3.70–3.83 (2 H, m, 3- and 6-H) and 3.96–4.09 (2 H, m, 1- and 2-H); δ_C($CDCl_3$) −5.54, −5.48 and −4.83 (CH_3, 4 × Me), 17.94 and 18.20 (C, 2 × Bu^t), 25.77 and 25.89 (CH_3, 2 × Bu^t), 33.48 (CH_2, C-4), 44.47 (CH, C-5), 66.41 (CH_2, C-6), 76.03 (CH, C-2), 76.61 (CH, C-3) and 79.02 (CH, C-1).

TBAF (1 mol dm^{-3} solution in THF; 1.2 cm^3, 1.20 mmol) was added to a solution of (1*S*,2*S*,3*S*,5*R*)-(+)-3-(*tert*-butyldimethylsiloxy)-5-(*tert*-butyldimethylsiloxymethyl)cyclopentane-1,2-diol **14** (101 mg, 0.27 mmol) in dry THF (7 cm^3). After being stirred for 2 h under argon, the solvent was removed by evaporation and the residue was redissolved in dry dichloromethane (1 cm^3). Acetic anhydride (0.5 cm^3, 541 mg, 5.30 mmol), pyridine (0.5 cm^3, 490 mg, 6.2 mmol) and DMAP (~5 mg) were added and the mixture was stirred for 1 h. The solvent was removed by evaporation and the residue (817 mg) was chromatographed on silica gel (2% MeOH–CH_2Cl_2) to give (1S,2R,3S,4S)-(+)-1,2,3-*triacetoxy*-4-(*acetoxymethyl*)cyclopentane (84.4 mg, 99%), R_f 0.18 as an oil; $[\alpha]_D^{23}$ +5.3 (*c* 0.79, $CHCl_3$) {lit.,[2] $[\alpha]_D^{21}$ −5.3 (*c* 0.79, $CHCl_3$) for the opposite enantiomer}, ν_{max}(neat)/cm^{-1} 2956, 1737, 1369, 1222 and 1043; δ_H(250 MHz; $CDCl_3$) 1.26–1.42 (1 H, m, 5-H), 1.98, 2.00 and 2.01 (12 H, 3 × s, 4 × AcO), 2.37–2.53 (2 H, m, 4- and 5-H), 4.06 (2 H, d, *J* 5.5, 6-H_2), 5.04–5.13 (2 H, m, 1- and 2-H) and 5.17 (1 H, dd, *J* 5 and 5, 3-H); δ_C($CDCl_3$) 20.48, 20.53, 20.63 and 20.80 (CH_3, 4 × $MeCO_2$), 30.02 (CH_2, C-5), 39.63 (CH, C-4), 64.48 (CH_2, C-6), 72.79 (CH, C-2), 75.01 (CH, C-3), 75.29 (CH, C-1) and 169.60, 169.88, 170.06 and 170.75 (C, $MeCO_2$) (Found: $[M + NH_4]^+$, 334.1502. $C_{14}H_{20}O_8$ requires $[M + NH_4]^+$, 334.1502).

The tetra-acetate (67.0 mg, 0.21 mmol) was dissolved in methanol (6.2 cm^3), and the solution was cooled to 0 °C and treated with sodium methoxide (33.3 mg, 0.62 mmol). The mixture was stirred for 3.5 h at 0 °C and then neutralized with Amberlite IR-120 (H^+) ion-exchange resin. The resin was removed by filtration and then washed with methanol. The combined filtrate and washing were concentrated under reduced pressure. The residue (85.3 mg) was chromatographed on silica gel [(3:1) $CHCl_3$–MeOH] to give (1S,2R,3S,4S)-(−)-(*hydroxymethyl*)*cyclopentane*-1,2,3-*triol* (−)-**2** (28.2 mg, 90%), R_f 0.18, as a solid;* m.p. 124–127 °C; $[\alpha]_D^{26}$ −10.55 (*c* 1.0, MeOH) {lit.,[6] $[\alpha]_D^{23}$ +8.8 (*c* 2.9, MeOH) for the opposite enantiomer}; ν_{max}(KBr)/cm^{-1} 3369, 2933, 1341, 1118 and 1039; δ_H(250 MHz, CD_3OD) 1.24 (1 H, ddd, *J* 13.5, 6.5 and 8, 5-H), 1.96–2.13 (1 H, m, 4-H), 2.20 (1 H, ddd, *J* 13.5, 7 and 9, 5-H), 3.54 (1 H, dd, *J* 6.5 and 10.5, 6-H), 3.63 (1 H, dd, *J* 5.5 and 10.5, 6-H), 3.69 (1 H, dd, *J* 5 and 5, 3-H), 3.86 (1 H, dd, *J* 5.5, 2-H) and 3.99 (1 H, ddd, *J* 5, 7 and 7, 1-H); δ_C(CD_3OD) 35.74 (CH_2, C-5), 46.13 (CH, C-4), 65.37 (CH_2, C-6), 74.66 (CH, C-2), 76.80 (CH, C-1) and 79.70 (CH, C-3) (Found: $[M + NH_4]^+$, 166.1079. $C_6H_{12}O_4$ requires $[M + NH_4]^+$, 166.1079).

(1α,2α,3α,4β)-(±)-4-(*Hydroxymethyl*)(1-^{2}H)*cyclopentane*-1,2,3-*triol* **17**.—*tert*-Butyldiphenylsilyl chloride (0.26 cm^3, 275 mg, 1.0 mmol), imidazole (146 mg, 2.15 mmol) and DMAP (~10 mg) were added to a cooled (0 °C) solution of the (±)-diol **19** (183 mg, 0.97 mmol) in dry dichloromethane (14 cm^3) under argon. After 30 min, solids were removed by filtration and washed with dichloromethane. The combined filtrate and washings were concentrated under reduced pressure and the residue was purified by chromatography over silica gel [(3:1) light petroleum–EtOAc] to give (±)-4β-(*tert*-butyldiphenylsiloxymethyl)-2α,3α-(isopropylidenedioxy)cyclopentan-1β-ol (250 mg).

This silyl ether (2.78 g) was oxidized with PCC (4.73 g, 21.9 mmol) in the presence of 4 Å molecular sieves (3.71 g) as described above. After the mixture had been stirred for 15 min under argon, diethyl ether (260 cm^3) was added and the reaction mixture was filtered through a Celite/silica plug. The filtrate was concentrated under reduced pressure to give crude 4β-(*tert*-butyldiphenylsiloxymethyl)-2α,3α-(isopropylidenedioxy)cyclopentanone (2.33 g) as an oil.

The crude ketone (2.33 g) was dissolved in 90% aq. ethanol (96 cm^3) and the solution was cooled to 0 °C. Sodium borodeuteride (770 mg, 0.018 mol) was added slowly and the mixture was stirred for 1 h at 0 °C. Saturated aq. ammonium chloride was added dropwise until the effervescence had ceased and the solvent was then removed by evaporation. The residue was redissolved in chloroform (50 cm^3) and the solution was

* Depending on the moisture content the tetraol was more commonly obtained as an oil.

washed with water (50 cm^3). The organic phase was concentrated under reduced pressure and the residue (3.23 g) was chromatographed over silica gel [(3:1) light petroleum–EtOAc] to give (±)-4β-(tert-*butyldiphenylsiloxymethyl*)-1,2α,3α-(*isopropylidenedioxy*)(1-^{2}H)*cyclopentan*-1α-*ol* (2.47 g, 89%), R_f 0.3; ν_{max}(neat)/cm^{-1} 3539, 3074, 2936, 2862, 1378, 1251, 1211, 1160, 1109 and 1042; δ_H(250 MHz; $CDCl_3$) 1.11 (9 H, s, Bu^t), 1.40 and 1.55 (each 3 H, each s, Me_2C), 1.89–1.99 (2 H, m, 5-H_2), 2.24–2.38 (1 H, m, 4-H), 2.58 (1 H, s, OH), 3.56 (1 H, dd, *J* 5.5 and 10.5, 6-H), 3.65 (1 H, dd, *J* 5.5 and 10.5, 6-H), 4.47 (1 H, d, *J* 6, 2-H), 5.54 (1 H, dd, *J* 1.5 and 6, 3-H), 7.34–7.53 (6 H, m, ArH) and 7.63–7.76 (4 H, m, ArH); δ_C($CDCl_3$) 19.20 (C, Bu^t), 24.31 and 26.19 (CH_3, Me_2C), 26.93 (CH_3, Bu^t), 35.23 (CH_2, C-5), 44.04 (CH, C-4), 65.20 (CH_2, C-6), 71.42 (CD, t, *J* 23, C-1), 79.60 (CH, C-2), 82.77 (CH, C-3), 111.21 (C, Me_2C), 127.76 (CH, Ph), 129.79 (CH, Ph), 133.28 (C, Ph), 135.58 (CH, Ph) and 135.63 (CH, Ph) (Found: $[M + H]^+$, 428.2367. $C_{25}H_{33}DO_4Si$ requires $[M + H]^+$, 428.2367).

TBAF (1 mol dm^{-3} solution in THF; 9 cm^3, 9.0 mmol) was added to a solution of the (±)-alcohol (2.58 g, 6.04 mmol) in dry THF (60 cm^3). After being stirred for 1 h at room temperature, the solvent was removed by evaporation and the residue was chromatographed over silica gel [(9:1) CH_2Cl_2–EtOH] to give (±)-4β-(hydroxymethyl)-2α,3α-(isopropylidenedioxy)(1-^{2}H)cyclopentan-1α-ol (1.14 g) as an oil; ν_{max}(neat)/cm^{-1} 3419, 2987, 2939, 2876, 1377, 1210, 1161, 1133 and 1076; δ_H(250 MHz; $CDCl_3$) 1.34 and 1.53 (each 3 H, each s, each Me_2C), 1.68–1.81 (1 H, m, 5-H), 1.88 (1 H, dd, *J* 7.5 and 13.5, 5-H), 2.10 (1 H, br s, 6-OH), 2.19–2.32 (1 H, m, 4-H), 2.53 (1 H, s, 1-OH), 3.47 (1 H, dd, *J* 7 and 10.5, 6-H), 3.60 (1 H, dd, *J* 5.5 and 10.5, 6-H), 4.46 (1 H, d, *J* 6, 2-H) and 4.52 (1 H, dd, *J* 2 and 6, 3-H); δ_C($CDCl_3$) 24.25 and 26.07 (CH_3, Me_2C), 34.39 (CH_2, C-5), 44.22 (CH, C-4), 63.38 (CH_2, C-6), 71.05 (CD, t, *J* 22.7, C-1), 79.54 (CH, C-2), 82.49 (CH, C-3) and 111.38 (C, Me_2C) (Found: $[M + H]^+$, 190.1190. $C_9H_{15}DO_4$ requires $[M + H]^+$, 190.1190).

The (±)-diol (1.12 g, 5.90 mmol) was dissolved in a mixture of THF and water (1:1; 100 cm^3), Amberlyst 15 (H^+) ion-exchange resin (916 mg) was added, and the mixture was heated at 65 °C for 15 h. The resin was removed by filtration and the filtrate was concentrated under reduced pressure. The residue (2.0 g) was chromatographed over silica gel [(3:1) $CHCl_3$–MeOH] to give (±)-4β-(*hydroxymethyl*)(1-^{2}H)*cyclopentane*-1α,2α-*triol* **17** (850 mg, 96%), R_f 0.15, as an oil; ν_{max}(neat)/cm^{-1} 3341, 2927, 1329, 1189, 1088 and 1019; δ_H(250 MHz; CD_3OD) 1.65 (1 H, dd, *J* 7.5 and 14, 5-H), 1.88 (1 H, dd, *J* 10 and 14, 5-H), 2.17–2.31 (1 H, m, 4-H), 3.47–3.62 (2 H, m, 6-H_2) and 3.73–3.86 (2 H, m, 2- and 3-H); δ_C(CD_3OD) 33.72 (CH_2, C-5), 47.10 (CH, C-4), 67.80 (CH_2, C-6), 72.63 (CD, t, *J* 22.4, C-1), 75.10 (CH, C-2) and 75.45 (CH, C-3) (Found: $[M + NH_4]^+$, 167.1142. $C_6H_{11}DO_4$ requires $[M + NH_4]^+$, 167.1142).

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