Radical Cyclisation Reactions Leading to Polyhydroxylated Cyclopentane Derivatives: Synthesis of (1*R*,2*R*,3*S*,4*R*)- and (1*S*,2*S*,3*R*,4*S*)-4-Hydroxyethylcyclopentane-1,2,3-triol

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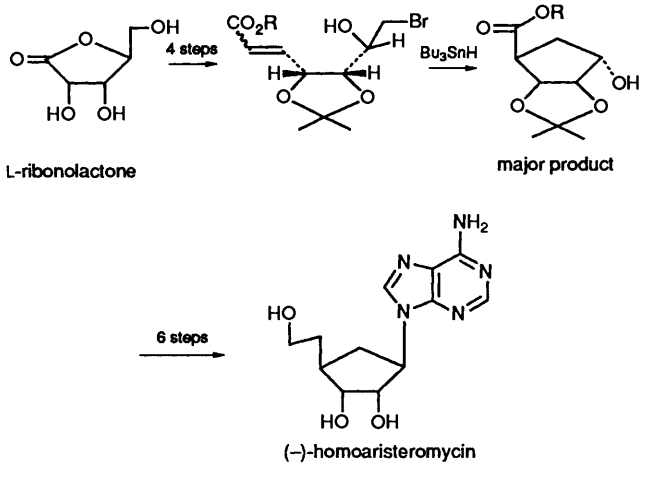
The tetraol (−)-**1** has been prepared from a derivative of (D)-allose **3**. The stereoselective carbocyclization reaction (**8** ⟹ **11**) formed the key step in this sequence. The enantiomeric cyclopentane derivative (+)-**1** was also prepared from compound **3**. In this synthesis the cyclization of compound **18** to provide the carbocycle **19** features as the critical carbon–carbon bond forming reaction.

The synthesis of perhydroxylated cyclopentane derivatives has been of interest for some time in connection with, *inter alia*, the preparation of carbocyclic nucleosides[1] and the biosynthesis of aristeromycin.[2] We have contributed to this area of research, almost always utilising cyclopentadiene as the starting material, and embroidering this diene so as to obtain the required pattern of substituents using a series of stereocontrolled reactions.[3] However, in a synthesis of (−)-homoaristeromycin we took (L)-ribonolactone as the starting point and employed a radical cyclisation reaction as the key step (Scheme 1).[4]



Scheme 1

The cyclisation step was styled on work described by Wilcox and Thomasco[5] who also used an acetonide ring to hold the radical centre close to an enester moiety which acted as the radicalophile. In this paper we show that the two enantiomers of the tetraol **1** can be conveniently prepared from D-allose by radical cyclisation reactions involving acyclic compounds. The retrosynthetic strategy is outlined in Fig. 1.

Thus the readily available protected (D)-allose **2**[6] was benzylated and partially hydrolysed by concentrated hydrochloric acid[7] to give the diol **3** (75% yield) (Scheme 2). The primary hydroxy group was converted into a halogen atom using triphenylphosphine and carbon tetrabromide in pyridine[8] to afford the bromide **4** (71%). The reaction was complete within 9 min and the dibrominated species was not observed. Silylation of the remaining hydroxy group was achieved in a standard fashion and the resultant compound **5** was hydrolysed with 80% aqueous acetic acid to furnish the diol **6** (96%). Smooth oxidative cleavage occurred on treatment of **6** with sodium periodate in aqueous methanol to give an almost quantitative yield of the aldehyde **7**. This aldehyde was not

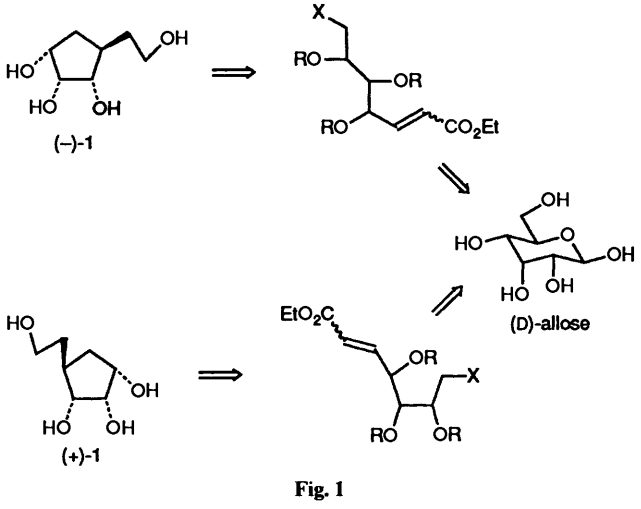


Fig. 1

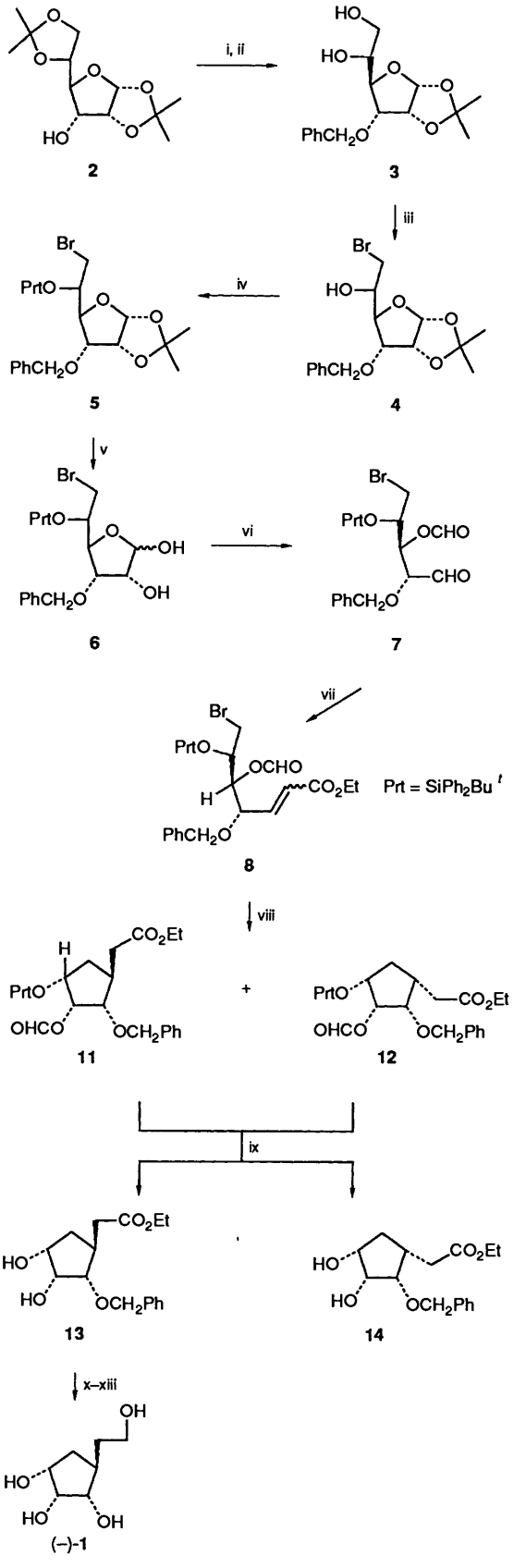
Table 1 Ratio of products obtained on cyclization of compounds (*E*)-**8** and (*Z*)-**8**

Compound	Yield (%)	Ratio **11**:**12**
(*E*)-**8**	77	8:1
(*Z*)-**8**	43	19.5:1

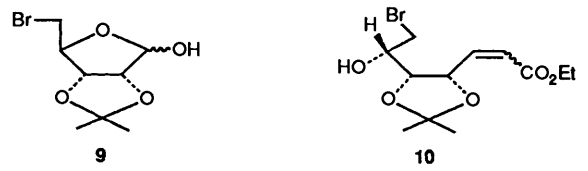
rigorously purified but was treated with (ethoxycarbonylmethylene) triphenylphosphorane to give the (*Z*)- and (*E*)-alkenes **8** in the ratio 1:9 (85% yield from **6**). The two isomers were easily distinguished by NMR spectroscopy. The (*Z*)-alkene showed a smaller coupling of the vinylic protons (*J* 11.8 Hz) than the (*E*)-alkene (*J* 16 Hz).

The predominance of the *E*-alkene is not unexpected when considering the results of the vast majority of Wittig reactions involving a stabilized ylide. However Wilcox has shown that the lactol **9** undergoes an analogous Wittig reaction to give the (*Z*)-alkene (*Z*)-**10** and (*E*)-alkene (*E*)-**10** in the ratio 10:1.[9] *Inter alia* the restriction in mobility caused by the presence of the isopropylidene group is obviously a decisive factor in controlling the stereochemical outcome of the latter Wittig reaction.

Cyclisation of the two α,β-unsaturated esters **8** gave the required compound **11** and a small quantity of the epimer **12**. From a preparative point of view it was not necessary to treat the unsaturated esters separately since both gave excess of the required isomer (Table 1). The configuration of the major compound formed was elucidated by NMR spectroscopy; the NOE observed between CH_2CO_2Et and 1-H (4.9%) was



Scheme 2 *Reagents and conditions:* i, $PhCH_2Br$, NaH, THF; ii, HCl (conc.), MeOH; iii, CBr_4, PPh_3, pyridine; iv, Me_3CSiPh_2Cl, imidazole, dimethylaminopyridine, CH_2Cl_2; v, 80% $MeCO_2H$, H_2O; vi, $NaIO_4$, H_2O, MeOH; vii, $EtO_2CCHPPh_3$, $PhCO_2H$, C_6H_6; viii, Bu_3SnH, AIBN, benzene; ix, TBAF, THF; x, $(MeO)_2CMe_2$, $HO_3SC_6H_4Me$, 2.5 h; xi, Bu^i_2AlH, ether; xii, H_2, Pd–C; xiii, Amberlyst 15 (H^+) resin, THF–H_2O (1:1)



particularly informative. The formation of compound **11** as the major product was anticipated on the basis of earlier work.[3,5,10]

The mixtures of esters **11** and **12** were treated with tetrabutylammonium fluoride to give the diols **13** (82%) and **14** (8%) which were separated by chromatography over silica. The major product was converted into the target tetrol (−)-**1**{$[\alpha]_D^{25}$ −46.3 (*c* 0.23 MeOH)} in four steps (64% overall yield).

The synthesis of the enantiomeric tetraol (+)-**1** is shorter, composed of seven steps from the protected (D)-allose **3** but has two steps of modest (albeit non-optimised) yield (Scheme 3). Thus periodate cleavage of the diol **3** furnished the aldehyde **15**. The appropriate Wittig reaction gave the ester **16** [ratio of (*Z*)- and (*E*)-isomers, 1:19] (80% from **3**). [The predominance of the (*E*)-enesters was in accord with results obtained by Tronchet and Gentile.[11]] Ethane-1,2-diol in the presence of anhydrous zinc(II) chloride reacted with the ester **16** to give the dithiolane **17** (68%) as the sole isolated product.[12] Silylation of the latter compound was accomplished in quantitative yield to give the desired compound **17**. There were no signs of the formation of the disilylated compound. Carbocyclisation of the heptenyl derivative **18** using tributyltin hydride and AIBN (azoisobutyronitrile) in refluxing benzene gave the required cyclopentanol **19** directly.[13] The configuration of the product **19** was determined by NMR spectroscopy [*e.g.* the NOE between CH_2CO_2Et and 3-H 3%)] and further chemical transformations (*v.i.*). The yield for the cyclisation step was low (26%). Part of the problem could be ascribed to the slow desulfurisation under the reaction conditions. A second stage desulfurisation using Raney nickel was attempted but tin impurities in the reaction mixture seemed to interfere with the catalyst. No other diastereoisomer appeared to be formed in the cyclisation step but, in view of the low yield that was obtained, it would be folly to suggest that the cyclisation was a specific process. Reduction of the ester **19** with diisobutylaluminium hydride furnished the triol **20**: loss of the silyl-protecting group was observed in this, the second low yield (31%) reaction. Debenzylation of **20** gave the target compound (+)-**1**{$[\alpha]_D^{25}$ +49.1 (*c* 0.74, MeOH)] in practically quantitative yield. Despite the two bad steps (which we did not try to improve) the sequence **3** ⇒ (+)-**1** has an overall yield of 4.4% and is extremely easy to perform on a large scale.

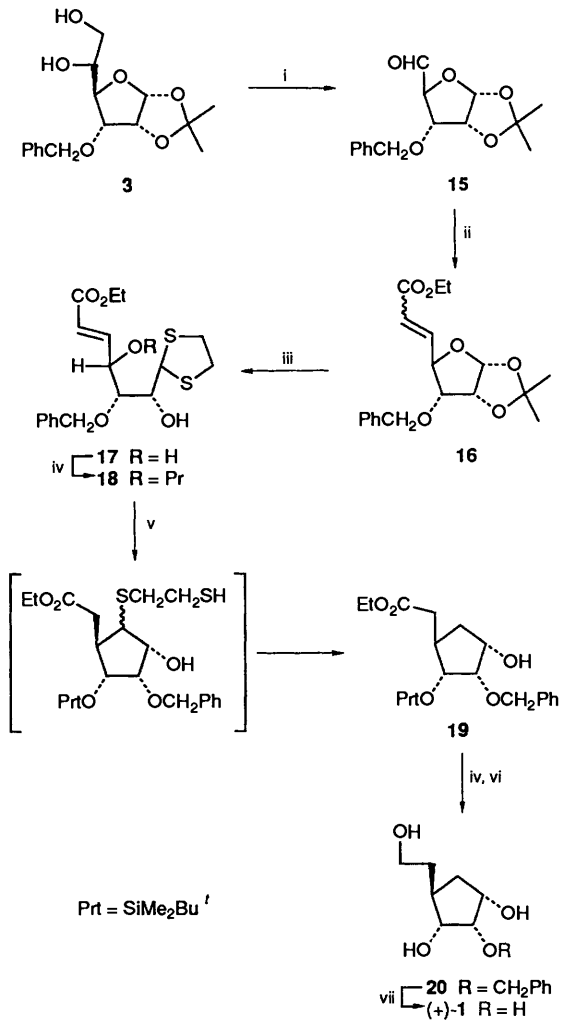
Thus the enantiomers of 4-hydroxyethylcyclopentane-1,2,3-triol **1** are available from a common precursor.

Experimental

Ethyl acetate (AcOEt) and light petroleum (b.p. 60–80 °C) were distilled prior to use. When anhydrous conditions were required the solvents were dried as follows. Tetrahydrofuran (THF) and diethyl ether (referred to as ether) were dried and distilled from sodium metal and benzophenone prior to use. Benzene, dichloromethane (CH_2Cl_2), and pyridine were distilled from calcium hydride and stored over 4 Å molecular sieves.

TLC was performed on pre-coated glass plates (Merck silica gel 60F 254). The plates were visualised using UV light (254 nm) and/or phosphomolybdic acid in ethanol or *p*-anisaldehyde in glacial acetic acid or basic potassium permanganate as appropriate.

Flash chromatography performed over silica (Merck silica



Scheme 3 *Reagents and conditions:* i, $NaIO_4$, H_2O, MeOH; ii, $EtO_2CCHPPh_3$, benzoic acid, THF; iii, $ZnCl_2$, $HSCH_2CH_2SH$, CH_2Cl_2; iv, Me_2SiBu^tCl, imidazole, *N,N*-dimethylaminopyridine, CH_2Cl_2; v, Bu_3SnH, AIBN, C_6H_6; vi, Bu^i_2AlH, CH_2Cl_2; vii, H_2, Pd/C

60, 40–63 μm) was used to purify all products, unless stated otherwise and is referred to simply as chromatography.

IR spectra were obtained using a Perkin-Elmer 881 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained using a Bruker AM 250 machine operating at 250 and 62.9 MHz respectively. *J*-Values are given in Hz.

Both low and high resolution mass spectra were obtained from the SERC mass spectroscopy service at Swansea. Spectra were obtained by electron impact (EI) at 70 eV, chemical ionisation (CI) using ammonia or fast atomic bombardment (FAB) where appropriate.

Optical rotations were obtained using an AA-1000 polarimeter. $[\alpha]_D$ Values are given in units of 10^{-1} deg cm^2 g^{-1}.

M.p.s, determined on an Electrothermal capillary melting point apparatus, are reported as °C and are not corrected.

(+)-3-*Benzyloxy*-1,2-*isopropylidenedioxy*-α-D-*allofuranose* **3**.[7]—A solution of 1,2;5,6-di-*O*-isopropylidene-α-D-allose **2** (10.5 g, 38.6 mmol) in dry THF (93 cm^3) was added dropwise with stirring under nitrogen to a suspension of sodium hydride [60% dispersion in oil, washed with P_2O_5 dried light petroleum (40–60 °C), 3.50 g, 87.5 mmol] in THF (15 cm^3) at 0 °C. Once the addition had been completed, the mixture was allowed to warm to room temp. and stirred for 45 min after which deprotonation was judged to be complete. The solution was recooled to 0 °C, tetrabutylammonium iodide (0.14 g, 0.38 mmol) and benzyl bromide (5.0 cm^3, 7.19 g, 42.0 mmol) were added. The mixture was refluxed until the reaction was judged complete by TLC (approximately 1 h). The cooled mixture was filtered through a thick Celite plug to remove excess of sodium hydride and the fine sodium bromide suspension. The residue was washed with dry THF (approximately 15 cm^3) and the combined filtrate and washings were concentrated under reduced pressure to a thick yellow syrup (18.8 g) of crude 3-benzyloxy-1,2;5,6-di(isopropylidenedioxy)-α-D-allofuranose. This was used directly in the next step without any further purification.

A solution of the above benzyl derivative in a mixture of methanol (94 cm^3), water (9 cm^3) and concentrated hydrochloric acid (0.5 cm^3) was stirred for 23 h at room temp. The mixture was neutralised with concentrated ammonia solution and concentrated under reduced pressure to a syrup. This was redissolved in ethyl acetate (80 cm^3) and washed with water (2 × 80 cm^3). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure to give the crude product (11.7 g). This was purified by chromatography on silica gel (EtOAc–light petroleum, 2:1) to give (+)-3-benzyloxy-1,2-isopropylidenedioxy-α-D-allofuranose **3** (8.99 g, 75%, R_f 0.2) as a thick syrup; $[\alpha]_D^{28}$ +108.2 (*c* 1.45 in $CHCl_3$), [lit.,[14] $[\alpha]_D^{25}$ +103 (*c* 0.6 in MeOH)]; ν_{max}(neat)/cm^{-1} 3495br s (OH_{str}), 2988s (CH_{str}), 2937s (CH_{str}), 1378, 1217, 1167, 1128 and 1024s ($C–O_{str}$ and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.32, 1.56 (each 3 H, each s, Me_2C), 3.10 (1 H, br s, OH), 3.35 (1 H, br s, OH), 3.63 (2 H, br s, 6-CH_2), 3.92 (2 H, dd, *J* 4.5 and 9, 3-H and 5-H), 4.07 (1 H, dd, *J* 3 and 9, 4-H), 4.50–4.56 (2 H, m, $PhCH_A$ and 2-H), 4.72 (1 H, d, *J* 11.5, $PhCH_B$), 5.72 (1 H, d, *J* 4, 1-H) and 7.29–7.37 (5 H, m, Ph); *m/z* (EI) 311 (M^+ + H).

(+)-3-*Benzyloxy*-6-*bromo*-1,2-*isopropylidenedioxy*-6-*deoxy*-α-D-*allofuranose* **4**.—Triphenylphosphine (10.8 g, 41.3 mmol, 2 equiv.) was added to a solution of the diol (6.37 g, 20.5 mmol) in pyridine (300 cm^3) at 0 °C under a nitrogen atmosphere. This was followed by the dropwise addition of a carbon tetrabromide solution (7.26 g, 21.9 mmol, 1.1 equiv.) in pyridine (26 cm^3) with stirring. This was washed through with additional pyridine (10 cm^3) and the mixture was heated at 60 °C for 9 min. Methanol (62 cm^3) was added, at room temp., to quench the reaction and the mixture was concentrated under reduced pressure to a syrup of the crude product **4** (25.1 g). The crude mixture was chromatographed on silica gel (EtOAc–CH_2Cl_2, 4:96) to give (+)-3-*benzyloxy*-6-*bromo*-1,2-*isopropylidenedioxy*-6-*deoxy*-α-D-*allofuranose* **4** (5.44 g, 71%, R_f 0.4, light petroleum–EtOAc, 1:1) as a thick colourless oil; $[\alpha]_D^{27}$ +91.1 (*c* 1.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3484br s (OH_{str}), 2987s (CH_{str}), 2935s (CH_{str}), 1373, 1217, 1166, 1108 and 1026s (CO_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.36, 1.60 (each 3 H, each s, Me_2C), 2.64 (1 H, d, *J* 2, OH), 3.43 (1 H, dd, *J* 7.6 and 10.7, 6-H), 3.54 (1 H, dd, *J* 3.5 and 10.7, 6-H), 3.91 (1 H, dd, *J* 4.4 and 8.5, 3-H), 3.90–4.07 (1 H, m, 5-H), 4.13 (1 H, dd, *J* 4.7 and 8.5, 4-H), 4.54–4.62 (2 H, m, $PhCH_A$ and 2-H), 4.78 (1 H, d, *J* 11.6, $PhCH_B$), 5.73 (1 H, d, *J* 3.7, 1-H) and 7.32–7.40 (5 H, m, Ph); δ_C($CDCl_3$) 26.67, 26.87 (CH_3, Me_2C), 34.74 (CH_2, C-6), 71.73 (CH, C-5), 72.13 (CH_2, $PhCH_2$), 77.60 (CH, C-2), 78.06 (CH, C-3), 78.66 (CH, C-4), 104.25 (CH, C-1), 113.37 (C, Me_2C), 128.07 (CH, Ph), 128.16 (CH, Ph), 128.55 (CH, Ph) and 137.17 (C, Ph) (Found: $[M + NH_4]^+$ 390.0916. $C_{16}H_{21}{}^{79}BrO_5$ requires $[M + NH_4]^+$ 390.0916).

(+)-3-*Benzyloxy*-6-*bromo*-5-tert-*butyldiphenylsiloxy*-1,2-*isopropylidenedioxy*-6-*deoxy*-α-D-*allofuranose* **5**.—Imidazole (3.40 g, 0.05 mol, 6 equiv.) and DMAP (87.8 mg, 0.70 mmol, 0.8 equiv.) were added to a solution of the 1,2-*O*-isopropylidene derivative **4** (3.03 g, 8.20 mmol) in dry dichloromethane (94

cm^3) under argon, followed by the dropwise addition of *tert*-butyldiphenylsilyl chloride (6.5 cm^3, 8.25 g, 0.03 mol, 3.6 equiv.) with stirring. After 17 h at room temp., saturated ammonium chloride solution (approximately 180 cm^3) was added and both phases were separated. The aqueous phase was extracted with ethyl acetate (3 × 250 cm^3) and the combined organic phases were dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure. The residue (11.8 g) was chromatographed on silica [CH_2Cl_2–light petroleum (40–60 °C), 8:2] to give (+)-3-*benzyloxy*-6-*bromo*-5-tert-*butyldiphenylsiloxy*-1,2-*isopropylidenedioxy*-6-*deoxy*-α-D-*allofuranose* **5** (4.24 g, 85%, R_f 0.45) as a thick oil: $[\alpha]_D^{24}$ +55.5 (*c* 1.6 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2934s (CH_{str}), 2861s (CH_{str}), 1111 and 1027s (C–O_{str} and Si–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.05 (9 H, s, 3 × CH_3), 1.37, 1.55 (each 3 H, each s, Me_2C), 3.17 (1 H, dd, *J* 5.5 and 10, 6-H), 3.45 (1 H, dd, *J* 8 and 10, 6-H), 4.17 (1 H, dd, *J* 4.5 and 8.5, 3-H), 4.27–4.35 (1 H, m, 5-H), 4.42 (1 H, dd, *J* 1.5 and 8.5, 4-H), 4.52–4.63 (2 H, m, $PhCH_A$ and 2-H), 4.84 (1 H, d, *J* 12, $PhCH_B$), 5.48 (1 H, d, *J* 3.5, 1-H), 7.32–7.53 (11 H, m, Ph) and 7.61–7.79 (4 H, m, Ph); δ_C($CDCl_3$) 19.49 (C, Bu^t), 26.78, 26.96 (CH_3, Me_2C), 27.11 (CH_3, Bu^t), 31.58 (CH_2, C-6), 71.86 (CH_2, PhCH_2), 72.65 (CH, C-5), 76.11 (CH, C-4), 77.58 (CH, C-2), 79.28 (CH, C-3), 104.04 (CH, C-1), 113.01 (C, Me_2C), 127.58 (CH, Ph), 127.63 (CH, Ph), 128.05 (CH, Ph), 128.10 (CH, Ph), 128.56 (CH, Ph), 129.80 (CH, Ph), 133.08 (C, Ph), 133.71 (C, Ph), 135.98 (CH, Ph), 136.08 (CH, Ph) and 137.49 (C, Ph) (Found: $[M + NH_4]^+$ 628.2094. $C_{32}H_{39}{}^{79}BrO_5Si$ requires $[M + NH_4]^+$ 628.2094).

3-*Benzyloxy*-6-*bromo*-5-tert-*butyldiphenylsiloxy*-6-*deoxy*-D-*allofuranose* **6**.—A solution of the 1,2-*O*-isopropylidene derivative **5** (2.16 g, 3.8 mmol) in 80% aqueous acetic acid (97 cm^3) was heated at 65 °C for 15.5 h. The solvent was removed under reduced pressure to yield the crude anomeric mixture of the diol **6** (2.56 g). This was chromatographed on silica gel (2% EtOAc–CH_2Cl_2) to give 3-benzyloxy-6-bromo-5-*tert*-butyldiphenylsiloxy-6-deoxy-D-allofuranose **6** (1.93 g, 96%, R_f 0.38) as a syrup; ν_{max}(neat)/cm^{-1} 3540br s (OH_{str}), 3072s (CH_{str}), 3009s (CH_{str}), 2936s (CH_{str}), 2897s (CH_{str}), 2863s (CH_{str}), 1111 and 1002s (C–O_{str}, OH_{def} and SiO_{str}); δ_H(250 MHz; $CDCl_3$) 1.08 (9 H, s, Bu^t), 2.84 (1 H, d, *J* 10, OH), 3.03 (1 H, dd, *J* 8 and 10, 6-H), 3.16 (1 H, dd, *J* 3 and 10, 6-H), 3.47 (1 H, d, *J* 10, OH), 3.92–4.08 (2 H, m, 5-H and 3-H), 4.18 (1 H, dd, *J* 3 and 6.5, 4-H), 4.53 (1 H, dd, *J* 3 and 3, 2-H) 4.63 (1 H, d, *J* 11.5, $PhCH_A$), 4.71 (1 H, d, *J* 11.5, $PhCH_B$), 5.13 (1 H, dd, *J* 3.5 and 3.5, 1-H), 7.34–7.58 (11 H, m, Ph) and 7.61–7.79 (4 H, m, Ph).

(4R,5R,6S)-*Ethyl* 4-*Benzyloxy*-7-*bromo*-6-tert-*butyldiphenylsilyloxy*-5-*formyloxyhept*-2-*enoate* **8**.—An aqueous solution of sodium metaperiodate (890 mg, 4.20 mmol) in water (6.2 cm^3) was added dropwise to a stirred solution of the diol **6** (1.93 g, 3.40 mmol) in methanol (16 cm^3). After 2.5 h at room temp., the solvent was removed by evaporation and the solid residue was extracted with chloroform (6 × 30 cm^3). The combined extracts were dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure to a gum of (2R,3S,4S)-2-*benzyloxy*-5-*bromo*-4-(tert-*butyldiphenylsilyloxy*)-3-*formyloxypentanal* **7** (2.11 g) which was used directly in the next stage without further purification.

The aldehyde **7** was redissolved in dry benzene (5 cm^3) and added dropwise to a cooled (0 °C) suspension of (ethoxycarbonylmethylene)triphenylphosphorane (3.55 g, 0.01 mol) and benzoic acid (40.2 mg, 0.33 mmol) in dry benzene (8 cm^3). Extra dry benzene (2 cm^3) was used to wash the aldehyde through and the mixture was allowed to warm to room temp. After stirring for 15 h under argon, water (8 cm^3) was added followed by ether (25 cm^3). The two phases were separated and the aqueous phase was extracted with ether (25 cm^3). The combined organic extracts were washed with brine (30 cm^3), dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure. The residue (5.99 g) was chromatographed on silica gel (light petroleum–EtOAc, 8:1); with care both isomers could be separated in a E:Z ratio of 9:1 in a total yield of 84%. The first to be eluted was (−)-(2Z)-(4R,5R,6S)-*ethyl* 4-*benzyloxy*-7-*bromo*-6-tert-(*butyldiphenylsiloxy*)-5-*formyloxyhept*-2-*enoate* (*Z*)-**8** (191 mg, 9%, R_f 0.25, light petroleum–EtOAc, 8:1) as an oil; $[\alpha]_D^{26}$ −14.8 (*c* 0.45 in $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2932s (CH_{str}), 2860s (CH_{str}), 1720s (C=O_{str}), 1650w (C=C_{str}), 1166 and 1106s (C–O_{str} and Si–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.08 (9 H, s, Bu^t), 1.29 (3 H, t, *J* 7, CH_3CH_2), 3.25 (1 H, dd, *J* 5.5 and 10.5, 7-H), 3.63 (1 H, dd, *J* 6.5 and 10.5, 7-H), 4.13–4.30 (3 H, m, CH_2CH_3 and 6-H), 4.45 (1 H, d, *J* 12, $PhCH_A$), 4.53 (1 H, d, *J* 12, $PhCH_B$), 5.30–5.36 (1 H, m, 4-H), 5.52 (1 H, dd, *J* 7 and 8.5, 5-H), 5.92–5.61 (2 H, m, 2-H and 3-H), 7.16–7.53 (11 H, m, Ph), 7.61–7.82 (4 H, m, Ph) and 7.97 (1 H, s, OCHO). This was followed by (+)-(2E)-(4R,5R,6S)-*ethyl* 4-*benzyloxy*-7-*bromo*-6-tert-*butyldiphenylsilyloxy*)-5-*formyloxyhept*-2-*enoate* (*E*)-**8** (1.57 g, 72%, R_f 0.19, light petroleum–EtOAc, 8:1) as an oil; $[\alpha]_D^{23}$ +19.8 (*c* 2.6 in $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2933s (CH_{str}), 2345s (CH_{str}), 1721s (C=O_{str}), 1653w (C=C_{str}), 1366, 1274, 1160 and 1108s (C–O_{str} and Si–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.13 (9 H, s, Bu^t), 1.32 (3 H, t, *J* 7, CH_3CH_2), 3.35 (1 H, dd, *J* 2.5 and 6, 7-H), 3.54 (1 H, dd, *J* 3 and 6, 7-H), 4.10–4.18 (1 H, m, 6-H), 4.23 (2 H, q, *J* 7, CH_2CH_3), 4.41–4.53 (2 H, m, $PhCH_A$ and 4-H), 4.63 (1 H, d, *J* 12, $PhCH_B$), 5.40 (1 H, dd, *J* 5 and 5, 5-H), 5.94 (1 H, dd, J_{2-4} 1 and J_{2-3} 16, 2-H), 6.73 (1 H, dd, J_{3-4} 7 and J_{3-2} 16, 3-H), 7.29–7.55 (11 H, m, Ph), 7.66–7.84 (4 H, m, Ph) and 7.96 (1 H, s, OCHO); δ_C($CDCl_3$) 14.26 (CH_3, CH_3CH_2), 19.39 (C, Bu^t), 27.04 (CH_3, Bu^t), 33.62 (CH_2, C-7), 60.58 (CH_2, CH_2CH_3), 71.19 (CH_2, PhCH_2), 72.07 (CH, C-6), 74.86 (CH, C-5), 76.03 (CH, C-4), 125.44 (CH, C-2), 127.78 (CH, Ph), 127.80 (CH, Ph), 127.92 (CH, Ph), 127.97 (CH, Ph), 128.56 (CH, Ph), 130.18 (CH, Ph), 130.31 (CH, Ph), 132.26 (C, Ph), 132.96 (C, Ph), 136.03 (CH, Ph), 136.09 (CH, Ph), 137.23 (C, Ph), 142.53 (CH, C-3), 159.50 (C, CO_2Et) and 165.42 (C, OCHO) (Found: $[M + NH_4]^+$ 656.2043. $C_{33}H_{39}{}^{79}BrO_6Si$ requires $[M + NH_4]^+$ 656.2043).

(1R,2R,3S,4R)- *and* (1R,2R,3S,4S)-3-*Benzyloxy*-1-tert-*butyldiphenylsilyloxy*-4-*ethoxycarbonylmethyl*-2-*formyloxycyclopentane* **11**, **12**.—Tributyltin hydride (0.41 cm^3, 444 mg, 1.6 mmol) and AIBN (azoisobutyronitrile, 400 mg, 2.4 mmol) were added to a solution of the alkene (*E*)-**8** (490 mg, 0.77 mmol) in dry benzene (18 cm^3) under argon. After 9 h at reflux, the solvent was removed by evaporation and the residue was dissolved in acetonitrile (35 cm^3). This was washed with hexane (3 × 35 cm^3) and the combined hexane washes were back-extracted with acetonitrile (2 × 35 cm^3). The combined acetonitrile extracts were concentrated under reduced pressure and the residue (1.0 g) was chromatographed on silica gel (light petroleum–EtOAc, 8:1) to give an inseparable mixture of (1R,2R,3S,4R)- *and* (1R,2R,3S,4S)-3-*benzyloxy*-1-tert-*butyldiphenylsilyloxy*-4-*ethoxycarbonylmethyl*-2-*formyloxypentane* **11** and **12** (332 mg, 77%, R_f 0.16) in a ratio of 8:1 * respectively, as an oil; ν_{max}(neat)/cm^{-1} 2934s (CH_{str}), 2861s (CH_{str}), 1718s (C=O_{str}), 1171 and 1107s (C–O_{str} and Si–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.05 (9 H, s, Bu^t), 1.18 (3 H, t, *J* 7, CH_3CH_2), 1.52 (1 H, ddd, *J* 13.5, 6.5 and 8.5, 2-H), 2.06–2.25 (2 H, m, 5-H and 2-H), 2.45 (1 H, dd, *J* 5 and 15, 5′-H), 2.60–2.79 (1 H, br m, 4-H), 3.46 (1 H, dd, *J* 3.2 and 9.5, 3-H), 4.04 (2 H, q, *J* 7, CH_2CH_3), 4.20 (1 H, ddd, *J* 8, 8 and 3.7, 1-H), 4.30 (1 H, d, *J* 11.5, $PhCH_A$), 4.59 (1 H, d, *J* 11.5, $PhCH_B$), 5.37 (1 H, dd, *J* 3.7 and 3.2, 2′-H), 7.21–

* Diastereoisomeric ratio was determined by NMR spectroscopy; NMR data correspond to the major isomer only.

7.58 (11 H, m, Ph), 7.63–7.87 (4 H, m, Ph) and 8.27 (1 H, s, OCHO); δ_C($CDCl_3$) 14.16 (CH_3, CH_3CH_2), 19.07 (C, Bu^t), 26.81 (CH_3, Bu^t), 35.81 (CH_2, C-5), 37.62 (CH, C-4), 37.69 (CH_2, C-2), 60.23 (CH_2, CH_2CH_3), 70.60 (CH, C-2), 72.41 (CH_2, PhCH_2), 72.95 (CH, C-1), 81.10 (CH, C-3), 127.69 (CH, Ph), 127.64 (CH, Ph), 127.81 (CH, Ph), 127.99 (CH, Ph), 128.38 (CH, Ph), 129.82 (CH, Ph), 129.88 (CH, Ph), 133.37 (C, Ph), 133.70 (C, Ph), 135.72 (CH, Ph), 135.76 (CH, Ph), 137.72 (C, Ph), 160.54 (C, OCHO) and 172.14 (C, CO_2Et) (Found: $[M + NH_4]^+$ 578.2938. $C_{33}H_{40}O_6Si$ requires $[M + NH_4]^+$ 578.2938).

(−)-(1R,2R,3S,4R)- *and* (1R,2R,3S,4S)-3-*Benzyloxy*-4-*ethoxycarbonylmethylcyclopentane*-1,2-*diol* **13** *and* **14**.—Tetrabutyl ammonium fluoride (1 mol dm^{-3} solution in THF, 0.35 cm^3, 0.35 mmol) was added dropwise to a solution of the diastereoisomeric mixture of silyl-derivatives **11** and **12** (72.0 mg, 0.13 mmol) in dry THF (2 cm^3) under argon. After stirring for 15 h, the solvent was removed by evaporation and the residue was chromatographed on silica gel (CH_2Cl_2–acetone, 9:1) to yield the pure products in a total yield of 90%. Careful chromatography achieved total separation of the diastereoisomers. The first to be eluted was (−)-(1R,2R,3S,4S)-3-*benzyloxy*-4-*ethoxycarbonylmethylcyclopentane*-1,2-*diol* **14** (3.4 mg, 8%, R_f 0.21) as an oil; $[\alpha]_D^{26}$ −41.2 (*c* 0.33 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3447br s (OH_{str}), 2943s (CH_{str}), 1731s (C=O_{str}), 1259, 1186, 1114 and 1029s (C–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.24 (3 H, t, *J* 7, CH_3CH_2), 1.47–1.53 (1 H, m, 5_A-H), 2.23–2.51 (4 H, m, OH, 4-H, 5_B-H and 2_A-H), 2.63 (1 H, dd, *J* 7.5 and 16, 2_B-H), 2.96 (1 H, d, *J* 7, OH), 3.88–4.02 (3 H, m, 1-H, 2-H and 3-H), 4.11 (2 H, q, *J* 7, CH_2CH_3), 4.58 (1 H, d, *J* 11.5, $PhCH_A$), 4.73 (1 H, d, *J* 11.5, $PhCH_B$) and 7.28–7.42 (5 H, m, Ph) (Found: $[M + NH_4]^+$ 295.1545. $C_{16}H_{22}O_5$ requires $[M + NH_4]^+$ 295.1545). This was followed by (−)-(1R,2R,3S,4R)-3-*benzyloxy*-4-*ethoxycarbonylmethylcyclopentane*-1,2-*diol* **13** (31.0 mg, 82%, R_f 0.17, CH_2Cl_2–acetone, 9:1); $[\alpha]_D^{25}$ −33.3 (*c* 0.3 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3447br s (OH_{str}), 2934s (CH_{str}), 1731s (C=O_{str}), 1259, 1186, 1114 and 1029s (C–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.24 (3 H, t, *J* 7, CH_3CH_2), 1.53 (1 H, ddd, *J* 14.5, 6.5 and 8.5, 5-H), 2.05 (1 H, ddd, *J* 14.5, 3.5 and 9, 5-H), 2.24 (1 H, dd, *J* 8 and 15, CHHCO$_2$Et), 2.42 (1 H, dd, *J* 6.5 and 15, CHHCO$_2$Et), 2.55–2.74 (2 H, m, 4-H and OH), 2.87 (1 H, br s, OH), 3.61 (1 H, dd, *J* 5.5 and 5.5, 3-H), 3.95–4.16 (4 H, m, CH_2CH_3, 1-H and 2-H), 5.61 (2 H, s, PhCH_2) and 7.24–7.45 (5 H, m, Ph); δ_C($CDCl_3$) 14.20 (CH_3, CH_3CH_2), 36.18 (CH_2, C-5), 37.80 (CH, C-4), 38.13 (CH_2, C-2), 60.43 (CH_2, CH_2CH_3), 71.65 (CH, C-2), 71.81 (CH, C-1), 72.55 (CH_2, PhCH_2), 83.51 (CH, C-3), 127.91 (CH, Ph), 128.06 (CH, Ph), 128.56 (CH, Ph), 137.59 (C, Ph) and 172.15 (C, CO_2Et) (Found: $[M + H]^+$ 295.1545. $C_{16}H_{22}O_5$ requires $[M + H]^+$ 295.1545).

(−)-(1R,2R,3S,4R)-4-(2′-*Hydroxyethyl*)*cyclopentane*-1,2,3-*triol* (−)-**1**.—A solution of the diol **13** (31.0 mg, 0.11 mmol) in 2,2-dimethoxypropane (0.5 cm^3, 361 mg, 4.10 mmol) was stirred in the presence of a catalytic amount of toluene-*p*-sulfonic acid (approximately 5 mg) under nitrogen. After 2.5 h, the mixture was diluted with acetone (1 cm^3) and the acid was neutralised with sodium hydrogen carbonate (solid). The solids were removed by filtration and the filtrate was concentrated under reduced pressure. The residue (36.5 mg) was chromatographed on silica gel (light petroleum–EtOAc, 3:1) to give (−)-(1R,2R,3S,4R)-3-*benzyloxy*-4-*ethoxycarbonylmethyl*-1,2-*isopropylidenedioxycyclopentane* (31.6 mg, 90%), R_f 0.36); $[\alpha]_D^{24}$ −101.8 (*c* 1.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2986s (CH_{str}), 2937s (CH_{str}), 1732s (C=O_{str}), 1375, 1207, 1163, 1123, 1089 and 1039s (C–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.13–1.26 (4 H, m, CH_3CH_2 and 5-H), 1.32, 1.53 (each 3 H, each s, Me_2C), 1.99 (1 H, dd, *J* 6 and 14, 5-H), 2.11 (1 H, dd, *J* 8.5 and 14.5, CHHCO$_2$Et), 2.50–2.69 (2 H, m, CHHCO$_2$Et and 4-H), 3.22 (1 H, ddd, *J* 10, 1.5 and 4.5, 3-H), 4.09 (2 H, q, *J* 7, CH_2CH_3), 4.47–4.56 (3 H, m, $PhCH_A$, 1-H and 2-H), 4.81 (1 H, d, *J* 12, $PhCH_B$) and 7.21–7.42 (5 H, m, Ph); δ_C($CDCl_3$) 14.19 (CH_3, CH_3CH_2), 24.14, 26.07 (CH_3, Me_2C), 33.93 (CH_2, C-5), 36.21 (CH, C-4), 36.37 (CH_2, CH_2CO_2Et), 60.20 (CH_2, CH_2CH_3), 71.60 (CH, C-2), 76.59 (CH, C-1), 77.75 (CH_2, PhCH_2), 83.03 (CH, C-3), 110.27 (C, Me_2C), 127.70 (CH, Ph), 127.94 (CH, Ph), 128.32 (CH, Ph), 138.27 (C, Ph) and 172.43 (C, CO_2Et) (Found: $[M + H]^+$ 335.1827. $C_{19}H_{26}O_5$ requires $[M + H]^+$ 335.1858).

DIBAL-H (1 mol dm^{-3} solution in THF, 0.70 cm^3, 0.70 mmol) was added dropwise to a solution of the above ester (56.1 mg, 0.20 mmol) in ether (2 cm^3), at −78 °C under argon with stirring. After 3.5 h at −78 °C, the mixture was warmed to 0 °C and methanol (0.12 cm^3) was added slowly followed by 4 mol dm^{-3} sodium hydroxide (5 cm^3). The reaction mixture was stirred for an extra 0.5 h then allowed to warm to room temp. and extracted with dichloromethane (5 × 5 cm^3). The combined extracts were dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure. The residue (63.5 mg) was chromatographed on silica gel (light petroleum–EtOAc, 1:1) to give (−)-(1R,2S,3S,4R)-3-*benzyloxy*-4-(2′-*hydroxyethyl*)-1,2-(*isopropylidenedioxy*)*cyclopentane* (42.3 mg, 86%, R_f 0.22) as a colourless oil; $[\alpha]_D^{26}$ −122.2 (*c* 1.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3441br s (OH_{str}), 3034m (CH_{str}), 2933s (CH_{str}), 1376, 1207, 1165 and 1085s (C–O_{str} and OH_{def}); δ_H(250 MHz, $CDCl_3$) 1.12–1.26 (1 H, m, 5-H), 1.34, 1.53 (each 3 H, each s, Me_2C), 1.63 (2 H, dd, *J* 6.5 and 12.5, 1′-CH_2), 1.91 (1 H, dd, *J* 6.5 and 14, 5-H), 2.17–2.37 (1 H, m, 4-H), 2.80 (1 H, t, *J* 6, OH), 3.24 (1 H, dd, *J* 4.5 and 10.5, 3-H), 3.56–3.76 (2 H, m, 2′-CH_2), 4.48–4.61 (3 H, m, 1-H, 2-H and $PhCH_A$), 4.84 (1 H, d, *J* 11.5, $PhCH_B$) and 7.26–7.46 (5 H, m, Ph); δ_C($CDCl_3$) 24.16, 26.03, (CH_2, Me_2C), 35.15 (CH_2, C-5), 35.67 (CH_2, C-1′), 37.98 (CH, C-4), 61.98 (CH_2, C-2′), 71.57 (CH_2, PhCH_2), 77.03 (CH, C-2), 77.91 (CH, C-1), 84.27 (CH, C-3), 110.25 (C, Me_2C), 127.96 (CH, Ph), 128.30 (CH, Ph), 128.46 (CH, Ph) and 137.52 (C, Ph) (Found: $[M + H]^+$ 293.1753. $C_{17}H_{24}O_4$ requires $[M + H]^+$ 293.1753).

A solution of the above benzyl ether (41.1 mg, 0.14 mmol) in ethanol (1 cm^3) was added dropwise to a suspension of 10% palladium on carbon catalyst (approximately 10 mg) in ethanol (1 cm^3). The mixture was stirred under a positive atmosphere of hydrogen for 15.5 h. The catalyst was removed by filtration through Celite and the residue was washed with ethanol. The combined filtrate and washings were concentrated under reduced pressure to give the crude diol (27.9 mg) as an oil. This was purified by chromatography on silica gel (CH_2Cl_2–MeOH, 15:1) to give (−)-(1R,2S,3S,4R)-3-*hydroxy*-4-(2′-*hydroxyethyl*)-1,2-(*isopropylidenedioxy*)*cyclopentane* (25.2 mg, 89%, R_f 0.13, CH_2Cl_2–acetone, 9:1) as a white solid; m.p. 111–112 °C; $[\alpha]_D^{26}$ −46.2 (*c* 0.45 in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3439br s (OH_{str}), 2923s (CH_{str}), 1379, 1207, 1159, 1095 and 1043s (C–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.10–1.26 (1 H, m, 5-H), 1.32, 1.47 (each 3 H, each s, Me_2C), 1.54–1.77 (2 H, m, 1′-CH_2), 1.84–2.00 (2 H, m, 5-H and 4-H), 2.97–3.13 (1 H, br m, OH), 3.24–3.37 (1 H, br s, OH), 3.37–3.50 (1 H, br m, 2′-H), 3.61–3.82 (2 H, m, 2′-H and 3-H), 4.45 (1 H, dd, *J* 5.5 and 5.5, 1-H) and 4.55 (1 H, dd, *J* 5 and 5, 2-H); δ_C($CDCl_3$) 24.04, 25.82 (CH_3, Me_2C), 34.91 (CH_2, C-5), 35.61 (CH_2, C-1′), 41.10 (CH, C-4), 62.13 (CH_2, C-2′), 77.94 (CH, C-2), 77.98 (CH, C-1), 78.98 (CH, C-3) and 110.34 (C, Me_2C) (Found: 203.1283. $C_{10}H_{18}O_4$ requires $[M + H]^+$ 203.1283).

A solution of the above isopropylidene derivative (24.9 mg, 0.12 mmol) in THF (1 cm^3) and water (1 cm^3) was heated at 65 °C with Amberlyst 15 (H^+) ion exchange resin (39.2 mg). After 4 h the resin was removed by filtration and the solids were washed with methanol. The combined filtrate and washings

were concentrated under reduced pressure to give the crude tetraol (−)-**1** (23.8 mg) as an oil. The residue was purified by chromatography on silica gel ($CHCl_3$–MeOH, 3:1) to give (−)-(1R,2R,3S,4R)-4-(2-*hydroxyethyl*)*cyclopentane*-1,2,3-*triol* (−)-**1** (18.4 mg, 92%, R_f 0.23) as an oil;* $[\alpha]_D^{26}$ −46.3 (*c* 0.23 in MeOH); ν_{max}(KBr)/cm^{-1} 3371br s (OH_{str}), 2933s (CH_{str}), 1116 and 1050s (C–O_{str} and OH_{def}); δ_H(250 MHz; CD_3OD) 1.42–1.59 (2 H, m, 5-H and 1′-H), 1.76 (1 H, ddd, *J* 20.5, 7 and 7, 1′-H), 1.92 (1 H, ddd, *J* 13.5, 4.5 and 9.5, 5-H), 2.07–2.25 (1 H, m, 4-H), 3.54–3.67 (3 H, m, 2′-CH_2 and 3-H), 3.85 (1 H, dd, *J* 4.5 and 4.5, 2-H) and 4.06 (1 H, ddd, *J* 7, 4.5 and 4.5, 1-H); δ_C(CD_3OD) 37.36 (CH_2, C-5), 38.46 (CH_2, C-1′), 41.51 (CH, C-4), 62.02 (CH_2, C-2′), 72.31 (CH, C-2), 74.97 (CH, C-1) and 78.79 (CH, C-3) (Found: $[M + NH_4]^+$ 180.1236. Calc. for $C_7H_{14}O_4$ $[M + NH_4]^+$ 180.1236).

Ethyl 3-[(2′R,3′R,4′R,5′R)-3′-*Benzyloxy*-4′,5′-*isopropylidenedioxytetrahydrofuran*-2-*yl*]*prop*-2-*enoate* **16**.—A solution of sodium metaperiodate (1.50 g, 7.0 mmol) in water (8 cm^3) was added dropwise, with stirring, to a solution of the diol **3** (1.17 g, 3.77 mmol) in methanol 15 cm^3). After 30 min at room temp., the solvent was removed by evaporation and the solid residue was extracted with chloroform (4 × 10 cm^3). The combined extracts were dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure to yield the crude (1*R*,-2*R*,3*R*)-3-benzyloxy-1,2-(isopropylidenedioxy)-α-D-*ribo*-pentodialdofuranose **15** (1.19 g) which was used directly in the next stage without further purification.

Benzoic acid (46.0 mg, 0.38 mmol) was added to a cooled (−20 °C) solution of (ethoxycarbonylmethylene)triphenylphosphorane (2.62 g, 7.52 mmol) in dry THF (38 cm^3), under argon, followed by a solution of the freshly prepared aldehyde (1.19 g) in dry THF (8 cm^3). The aldehyde was washed through with extra dry THF (3 cm^3) and the straw coloured solution was allowed to warm to room temp. After stirring for 4.5 h, the excess ylide reagent was quenched with water (6 cm^3) and the reaction mixture was extracted with ether (4 × 15 cm^3). The combined extracts were washed with saturated brine (50 cm^3), dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure. The residue (3.82 g) was purified by chromatography on silica gel (4:1, light petroleum–EtOAc) to give the alkene in a total yield of 80%. Careful chromatography enabled both compounds to be separated giving a *Z*:*E* ratio of 1:19. The first to be eluted was (+)-(2E)-*ethyl* 3-[(2′R,3′R,4′R,-5′R)-3′-*benzyloxy*-4′,5′-*isopropylidenedioxytetrahydrofuran*-2′-*yl*]*prop*-2-*enoate* (*E*)-**16** (1.0 g, 76%, R_f 0.2, light petroleum–EtOAc, 4:1) as an oil; $[\alpha]_D^{25}$ +50.6 (*c* 1.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2987s (CH_{str}), 2940m (CH_{str}), 2873m (CH_{str}), 1718s (C=O_{str}), 1660m (C=C_{str}), 1304, 1264, 1215, 1169, 1089 and 1025s (C–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.29 (3 H, t, *J* 7, CH_3CH_2), 1.37, 1.61 (each 3 H, each s, Me_2C), 3.52 (1 H, dd, *J* 4 and 9, 3′-H), 4.20 (2 H, q, *J* 7, CH_2CH_3), 4.54–4.66 (3 H, m, $PhCH_A$, 4′-H and 2′-H), 4.73 (1 H, d, *J* 12, $PhCH_B$), 5.76 (1 H, d, *J* 3.5, 5′-H), 6.12 (1 H, dd, $J_{2-2'}$ 1.5 and J_{2-3} 15.5, 2-H), 6.91 (1 H, dd, $J_{3-2'}$ 5 and J_{3-2} 15.5, 3-H) and 7.24–7.47 (5 H, m, Ph); δ_C($CDCl_3$) 14.21 (CH_3, CH_3CH_2), 26.49, 26.76 (CH_3, Me_2C), 60.42 (CH_2, CH_2CH_3), 72.48 (CH_2, $PhCH_2$), 77.05 (CH, C-4′ or C-2′), 77.52 (CH, C-2′ or C-4′), 82.07 (CH, C-3′), 104.08 (CH, C-5′), 113.22 (C, Me_2C), 122.51 (CH, C-2), 128.00 (CH, Ph), 128.10 (CH, Ph), 128.48 (CH, Ph), 137.19 (C, Ph), 143.47 (CH, C-3) and 165.96 (C, CO_2Et) (Found: $[M + H]^+$ 366.1917. $C_{19}H_{24}O_6$ requires $[M + NH_4]^+$ 366.1917). This was followed by (−)-(2Z)-*ethyl* 3-[(2′R,3′R,4′R,5′R)-3′-*benzyloxy*-4′,5′-*isopropylidenedioxytetrahydrofuran*-2′-*yl*]*prop*-2-*enoate* (*Z*)-**16** (53.5 mg, 4%, R_f 0.14, light petroleum–EtOAc, 4:1) as an oil; $[\alpha]_D^{26}$ −18.7 (*c* 0.58 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2984s (CH_{str}), 2934s (CH_{str}), 2871m (CH_{str}), 1710s (C=O_{str}), 1650m (C=C_{str}), 1375, 1295, 1163, 1087 and 1014s (C–O_{str}); δ_H(250 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 7, CH_3CH_2), 1.36, 1.65 (each 3 H, each s, Me_2C), 3.52 (1 H, dd, *J* 4 and 9, 3′-H), 4.17 (2 H, q, *J* 7, CH_2CH_3), 4.53–4.64 (2 H, m, $PhCH_A$ and 4′-H), 4.71 (1 H, d, *J* 12.5, $PhCH_B$), 5.67–5.78 (2 H, m, 5′-H and 2′-H), 5.89–5.99 (2 H, m, 2-H and 3-H) and 7.20–7.46 (5 H, m, Ph); δ_C($CDCl_3$) 14.11 (CH_3, CH_3CH_2), 26.80, 26.85 (CH_3, Me_2C), 60.35 (CH_2, CH_2CH_3), 72.10 (CH_2, $PhCH_2$), 73.47 (CH, C-2′), 77.91 (CH, C-4′), 82.47 (CH, C-3′), 104.14 (CH, C-5′), 113.27 (C, Me_2C), 124.36 (CH, C-2), 127.75 (CH, Ph), 128.04 (CH, Ph), 128.31 (CH, Ph), 137.69 (C, Ph), 142.88 (CH, C-3) and 165.24 (C, CO_2Et).

(−)-(2E)-(4R,5R,6R)-5-*Benzyloxy*-4,6-*dihydroxy*-7-(1′,3′-*dithiolan*-2′-*yl*)*hept*-2-*enoate* **17**.—Anhydrous zinc chloride (1.76 g, 0.01 mol) was added to a cooled (−10 °C) solution of the 4,5-*O*-isopropylidene derivative **16** (1.21 g, 3.48 mmol) in dry dichloromethane (14 cm^3) followed by the dropwise addition of ethane-1,2-dithiol (1.6 cm^3, 1.80 g, 0.19 mol) under argon. After stirring for 16 h, the solvent was removed by evaporation and the residue was dissolved in ethyl acetate (80 cm^3). Saturated aqueous sodium hydrogen carbonate (11 cm^3) was added followed by ethyl acetate (320 cm^3) and the resulting precipitate was removed by filtration. The solids were washed with ethyl acetate (80 cm^3) and the combined filtrate and washings were washed with brine (3 × 80 cm^3). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure. The residue (2.78 g) was chromatographed on silica gel (3:2, light petroleum–EtOAc) to give (−)-(2E)-(4R,5R,6R)-5-*benzyloxy*-4,6-*dihydroxy*-7-(1′,3′-*dithiolan*-2′-*yl*)-*hept*-2-*enoate* **17** (909 mg, 68%) as a white solid; m.p. 57–58 °C; $[\alpha]_D^{30}$ −5.12 (*c* 0.45 in $CHCl_3$) and $[\alpha]_D^{28}$ −6.6 (*c* 1.1 in $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3482br s (OH_{str}), 2985s (CH_{str}), 2931s (CH_{str}), 1703s, (C=O_{str}), 1654s (C=C_{str}), 1304, 1272, 1202, 1172, 1087 and 1034s (C–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.29 (3 H, t, *J* 7, CH_3CH_2), 2.88 (1 H, d, *J* 5, 6-OH), 2.93 (1 H, d, *J* 4, 4-OH), 3.13–3.36 (4 H, m, $-SCH_2CH_2S-$), 3.55 (1 H, dd, *J* 5 and 7.5, 5-H), 3.82 (1 H, ddd, *J* 7.5, 3.5 and 5, 6-H), 4.20 (2 H, q, *J* 7, CH_2CH_3), 4.58–4.73 (3 H, m, $PhCH_2$ and 4′-H), 4.99 (1 H, d, *J* 3.5, 2′-H), 6.15 (1 H, dd, *J* 1.5 and 15.5, 2-H), 7.10 (1 H, dd, *J* 5 and 15.5, 3-H) and 7.24–7.47 (5 H, m, Ph); δ_C($CDCl_3$) 14.24 (CH_3, CH_3CH_2), 38.95, 39.00 (CH_2, $-SCH_2CH_2S-$), 56.23 (CH, C-2′), 60.41 (CH_2, CH_2CH_3), 72.21 (CH, C-4), 74.27 (CH_2, $PhCH_2$), 74.99 (CH, C-6), 83.65 (CH, C-5), 121.77 (CH, C-2), 128.12 (CH, Ph), 128.24 (CH, Ph), 128.58 (CH, Ph), 137.36 (C, Ph), 146.20 (CH, C-3) and 166.36 (C, CO_2Et) (Found: $[M + NH_4]^+$ 402.1409. $C_{18}H_{24}O_5S_2$ requires 402.1409).

(−)-(2E)-(4R,5S,6R)-5-*Benzyloxy*-4-tert-*butyldimethylsilyloxy*-7-(1′,3′-*dithiolan*-2′-*yl*)-6-*hydroxyhept*-2-*enoate* **18**.—*tert*-Butyldimethylsilyl chloride (712 mg, 4.73 mmol, 2.2 equiv.), imidazole (665 mg, 9.76 mmol, 4.6 equiv.) and DMAP (108 mg, 0.89 mmol, 0.4 equiv.) were added to a solution of the dithiolane **17** (807 mg, 2.10 mmol) in dry dichloromethane (27 cm^3) under argon. After stirring for 24 h at room temp. the solid was removed by filtration and the filtrate was concentrated under reduced pressure. The residue (2.03 g) was chromatographed on silica gel (4:1, light petroleum–EtOAc) to give (−)-(2E)-(4R,-5S,6R)-5-*benzyloxy*-4-tert-*butyldimethylsilyloxy*-7-(1′,3′-*dithiolan*-2′-*yl*)-6-*hydroxyhept*-2-*enoate* **18** (1.05 g, 100%, R_f 0.17) as an oil; $[\alpha]_D^{22}$ −31.2 (*c* 1.25 in $CHCl_3$) and $[\alpha]_D^{23}$ −28.9 (*c* 1.35 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3483br s (OH_{str}), 3068w (CH_{str}), 3035w (CH_{str}), 2958s (CH_{str}), 2934s (CH_{str}), 2895s (CH_{str}), 2861s (CH_{str}), 1721s (C=O_{str}), 1658s (C=C_{str}), 1369,

* Depending on moisture content the tetraol can also be obtained as a solid.

1255, 1172 and 1115s (C–O_{str}, Si–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 0.08, 0.11 (6 H, 2 × 2, 2 × Me), 0.97 (9 H, s, Bu^t), 1.29, (3 H, t, *J* 7, CH_3CH_2), 2.65 (1 H, d, *J* 5.5, OH), 3.09–3.36 (4 H, m, $-SCH_2CH_2S-$), 3.59 (1 H, dd, *J* 2.5, 8.5, 5-H), 3.69 (1 H, ddd, *J* 8.5, 2.5 and 5.5, 6-H), 4.18 (2 H, q, *J* 7, CH_2CH_3), 4.57 (1 H, d, *J* 11, $PhCH_A$), 4.79 (1 H, ddd, *J* 5.5, 1.5 and 2.5, 4-H), 4.91 (1 H, d, *J* 11, $PhCH_B$), 5.00 (1 H, d, *J* 2.5, 2′-H), 6.08 (1 H, dd, *J* 1.5, 15.5, 5′-H), 7.05 (1 H, dd, *J* 5.5, 15.5, 3-H) and 7.21–7.40 (5 H, m, Ph); δ_C($CDCl_3$) −4.78, −4.55 (CH_3, 2 × Me), 14.26 (CH_3, CH_3CH_2), 18.15 (C, Bu^t), 25.91 (CH_3, Bu^t), 38.97, 39.06 (CH_2,–SCH_2CH_2S–), 56.31 (CH, C-2′), 60.38 (CH_2, CH_2CH_3), 73.63 (CH, C-4), 73.80 (CH, C-6), 74.60 (CH_2, $PhCH_2$), 85.41 (CH, C-5), 122.24 (CH, C-2), 127.76 (CH, Ph), 128.19 (CH, Ph), 128.38 (CH, Ph), 138.08 (C, Ph), 146.78 (CH, C-3) and 166.23 (C, CO_2Et) (Found: $[M + H]^+$ 499.2008. $C_{24}H_{38}O_5S_2Si$ requires $[M + H]^+$ 499.2008).

(+)-(1S,2S,3R,4R)-*Ethyl 2-Benzyloxy*-3-tert-*butyldimethylsiloxy*-4-*ethoxycarbonylmethylcyclopentan*-1-*ol* **19**.—Tributyltin hydride (0.6 cm^3, 659 mg, 2.3 mmol) and AIBN (171 mg, 1 mmol) were added to a solution of the dithiolane **18** (163 mg, 0.4 mmol) in dry benzene (8 cm^3) under argon. After 34 h at reflux temperature, the solvent was removed by evaporation and the residue was dissolved in acetonitrile (5 cm^3). This was washed with hexane (3 × 5 cm^3) and the combined hexane washes were back-extracted with acetonitrile (3 × 5 cm^3). The combined acetonitrile extracts were concentrated under reduced pressure and the residue was dissolved in dichloromethane (4 cm^3). This was washed successively with 2 mol dm^{-3} sodium hydroxide (2 cm^3), aqueous potassium fluoride solution (0.35 mol dm^{-3}, 2.5 cm^3) and water (2.5 cm^3). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel (6:1, light petroleum–EtOAc) to give (+)-(1S,2S,3R,4R)-*ethyl 2-benzyloxy*-3-tert-*butyldimethylsilyloxy*-4-*ethoxycarbonylmethylcyclopentan*-1-*ol* **19** (22.1 mg, 17%, R_f 0.21, 4:1, light petroleum–EtOAC) as an oil; $[\alpha]_D^{24}$ +26.5 (*c* 1.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3536br s (OH_{str}), 2934s (CH_{str}), 2860s (CH_{str}), 1735s (C=O_{str}), 1254, 1145, 1091 and 1031s (C–O_{str}, Si–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 0.1 (6 H, s, 2 × Me), 0.9 (9 H, s, Bu^t), 1.25 (3 H, t, *J* 7, CH_3CH_2), 1.51–1.66 (1 H, m, 5′-H), 2.03–2.34 (2 H, m, 5-H and CH_2CO_2Et), 2.42 (1 H, dd, *J* 6 and 15, CH_2CO_2Et), 2.52–2.70 (1 H, m, 4-H), 3.11 (1 H, d, *J* 10, OH), 3.64 (1 H, dd, *J* 4 and 4, 2-H), 3.92 (1 H, dd, *J* 4 and 4, 3-H), 4.06–4.26 (3 H, m, CH_2CH_3 and 1-H), 4.66 (1 H, d, *J* 11.5, $PhCH_A$), 4.79 (1 H, d, *J* 11.5, $PhCH_B$) and 7.24–7.42 (5 H, m, Ph); δ_C($CDCl_3$) −4.96, −4.59 (CH_3, 2 × Me), 14.22 (CH_3, CH_3CH_2), 18.03 (C, Bu^t), 25.79 (CH_3, Bu^t), 37.26 (CH_2, C-5), 38.35 (CH_2, CCO_2Et), 39.94 (CH, C-4), 60.40 (CH_2, CH_2CH_3), 70.49 (CH, C-3), 72.49 (CH_2, $PhCH_2$), 78.22 (CH, C-1), 80.57 (CH, C-2), 127.65 (CH, Ph), 127.76 (CH, Ph), 128.34 (CH, Ph), 138.33 (C, Ph) and 172.19 (C, CO_2Et) (Found: $[M + H]^+$ 409.2410. $C_{22}H_{36}O_5Si$ requires $[M + H]^+$ 409.2410).

(+)-(1S,2S,3R,4S)-1,2,3,4-(2′-*Hydroxyethyl*)*cyclopentane*-1,2,3-*triol* (+)-**1**.—*tert*-Butyldimethylsilyl chloride (24.3 mg, 0.16 mmol) imidazole (24.2 mg, 0.36 mmol) and DMAP (approximately 5 mg) were added to a solution of the alcohol **19** (24.4 mg, 0.06 mmol) in dry dichloromethane (0.5 cm^3) under argon. After stirring for 3 h at room temp., the solvent was removed by evaporation and the residue was chromatographed on silica gel (9:1, light petroleum–EtOAc) to give (+)-(1S,2S,3R,4S)-2-*benzyloxy*-1,3-*bis*(tert-*butyldimethylsilyloxy*)-4-*ethoxycarbonylmethylcyclopentane* (28.8 mg, 92%, R_f 0.35) as a white waxy solid; m.p. 45–38 °C; $[\alpha]_D^{24}$ +47.45 (*c* 1.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2932s (CH_{str}), 2857s (CH_{str}), 1729s (C=O_{str}), 1251 and 1076s (C–O_{str} and Si–O_{str}); δ_H(250 MHz; $CDCl_3$) 0.04, 0.05, 0.06, 0.08 (12 H, 4 × 2, 4 × Me), 0.91, 0.92 (18 H, 2 × 2, 2 × Bu^t), 1.26 (3 H, t, *J* 7, CH_3CH_2), 1.67 (1 H, ddd, *J* 13.5, 8.5 and 6.5, 5-H), 2.00–2.23 (2 H, m, 5-H and CH_2CO_2Et), 2.58 (1 H, dd, *J* 4 and 15, CH_2CO_2Et), 2.62–2.76 (1 H, m, 4-H), 3.62 (1 H, dd, *J* 3.5 and 3.5, 2-H), 3.78 (1 H, dd, *J* 3.5 and 9.5, 3-H), 4.05–4.25 (3 H, m, CH_2CH_3 and 1-H), 4.76 (1 H, d, *J* 12, $PhCH_A$), 4.95 (1 H, d, *J* 12, $PhCH_B$), 7.21–7.37 (3 H, m, Ph) and 7.40–7.47 (2 H, m, Ph); δ_C($CDCl_3$) −4.96, −4.82, −4.60, −4.33 (CH_3, 4 × Me), 14.25 (CH_3, CH_3CH_2), 18.13 (C, Bu^t), 25.88 (CH_3, Bu^t), 35.71 (CH_2, C-5), 37.46 (CH_2), 39.31 (CH, C-4), 60.16 (CH_2, CH_2CH_3), 72.11 (CH, C-3), 73.16 (CH_2, $PhCH_2$), 76.66 (CH, C-1), 82.42 (CH, C-2), 127.02 (CH, Ph), 127.52 (CH, Ph), 128.03 (CH, Ph), 139.67 (C, Ph) and 172.78 (C, COEt) (Found: $[M + H]^+$ 528.3280. $C_{28}H_{50}O_5Si_2$ requires $[M + H]^+$ 528.3280).

A solution of the above ester (165 mg, 0.32 mmol) in dry dichloromethane (9 cm^3), under argon, was cooled to −10 °C and DIBAL-H (1 mol dm^{-3} solution in toluene, 3.5 cm^3, 3.5 mmol) was added dropwise with stirring. Extra DIBAL-H (1.5 cm^3, 1.5 mmol) was added after 5 h and the reaction mixture was allowed to warm to room temp. The reaction mixture was stirred for an additional 17 h before it was recooled to −78 °C and methanol (1.7 cm^3) was added dropwise. The mixture was warmed to room temp. slowly and the resultant gel was extracted with ethyl acetate (5 × 15 cm^3). The combined extracts were concentrated under reduced pressure and the residue (89.3 mg) was purified by chromatography on silica gel (EtOAc to EtOAc–MeOH, 8:1) to give (+)-(1S,2S,3R,4S)-*benzyloxy*-4-(2′-*hydroxyethyl*)*cyclopentane*-1,3-*diol* (24.3 mg, 31%, R_f 0.14, EtOAc) as an oil; $[\alpha]_D^{25}$ +16.5 (*c* 0.51 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3342br s (OH_{str}), 2925s (CH_{str}), 1350, 1120 and 1054s (C–O_{str} and OH_{def}); δ_H(250 MHz; $CDCl_3$) 1.32 (1 H, ddd, *J* 14, 5.5 and 10, 5_A-H), 1.61 (2 H, dd, *J* 6.5 and 13, 1′-CH_2), 2.00 (1 H, ddd, *J* 14, 2.5 and 8.5, 5_B-H), 2.13–2.30 (1 H, m, 4-H), 2.68 (2 H, br s, 2 × OH), 3.03 (1 H, br s, OH), 3.60–3.82 (4 H, m, 2′-CH_2, 2-H and 3-H), 4.12–4.24 (1 H, m, 1-H), 4.73 (2 H, s, $PhCH_2$) and 7.29–7.45 (5 H, m, Ph); δ_C($CDCl_3$) 36.76 (CH_2, C-5), 37.18 (CH_2, C-1′), 42.15 (CH, C-4), 61.82 (CH_2, C-2′), 70.97 (CH, C-3), 73.35 (CH_2, $PhCH_2$), 76.69 (CH, C-1), 80.25 (CH, C-2), 128.05 (CH, Ph), 128.22 (CH, Ph), 128.67 (CH, Ph) and 137.54 (C, Ph) (Found: $[M + H]^+$ 253.1440. $C_{14}H_{20}O_4$ requires $[M + H]^+$ 253.1440).

A solution of the above triol (23.8 mg, 0.09 mmol) in ethanol (0.5 cm^3) was added dropwise to a suspension of 10% palladium on carbon catalyst (approximately 10 mg) in ethanol (0.2 cm^3). An extra aliquot of ethanol (0.5 cm^3) was used to wash the triol through and the reaction mixture was stirred under a positive atmosphere of hydrogen for 48 h. The catalyst was removed by filtration through Celite and the residue was washed with ethanol. The combined filtrate and washings were concentrated under reduced pressure to give the crude tetraol (+)-**1** (30.4 mg). This was purified by chromatography on silica gel (3:1, $CHCl_3$–MeOH) to give (+)-(1*S*,2*S*,3*R*,4*S*)-4-(2′-hydroxyethyl)cyclopentane-1,2,3-triol (+)-**1** (14.9 mg, 97%, R_f 0.24) as an oil; $[\alpha]_D^{24}$ +49.1 (*c* 0.74 in MeOH) and $[\alpha]_D^{25}$ +48.3 (*c* 0.74 in MeOH); ν_{max}(neat)/cm^{-1} 3351br s (OH_{str}), 2928s (CH_{str}) and 1051br s (C–O_{str} and OH_{def}); δ_H(250 MHz; CD_3OD) 1.40–1.60 (2 H, m, 5-H and 1′-H), 1.74 (1 H, ddd, *J* 20.5, 7 and 7, 1′-H), 1.85–2.00 (1 H, m, 5-H), 2.07–2.26 (1 H, m, 4-H), 3.50–3.70 (3 H, m, 2′-CH_2 and 3-H), 3.86 (1 H, dd, *J* 4.5 and 4.5, 2-H) and 4.06 (1 H, ddd, *J* 7, 4.5 and 4.5, 1-H); δ_C($CDCl_3$) 37.34 (CH_2, C-5), 38.46 (CH_2, C-1′), 41.55 (CH, C-4), 61.99 (CH_2, C-2′), 72.43 (CH, C-2), 74.96 (CH, C-1) and 78.78 (CH, C-3) (Found: $[M + H]^+$ 163.0970. Calc. for $C_7H_{14}O_4$ $[M + H]^+$ 163.0970).

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