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Microbial Oxidation in Synthesis: Preparation of (+)- and (-)-Pinitol from Benzene

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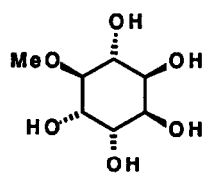
Abstract: Microbial oxidation with *Pseudomonas putida* of benzene affords *cis*-1,2-dihydroxycyclohexa-3,5-diene (2) which may be converted in five steps and 49% overall yield to (±)-pinitol. Resolution of an intermediate alcohol (6) with menthoxyacetyl chloride provides optically pure materials which may be independently transformed to (+)- or (-)-pinitol. Demethylation conditions for pinitol together with further reactions of (2) and related compounds were investigated.

The cyclitol natural product (+)-pinitol (1) has been shown to be a feeding stimulant for the larvae of the yellow butterfly *Eurema hecabe mandarina* [1] and also inhibits larval growth of *Heliothis zea* on soybeans.[2] More interestingly, however, (1) has recently been shown to have significant hypoglycemic and antidiabetic activity in normal and alloxan-induced diabetic albino mice and is free from acute toxicity.[3]



(1)

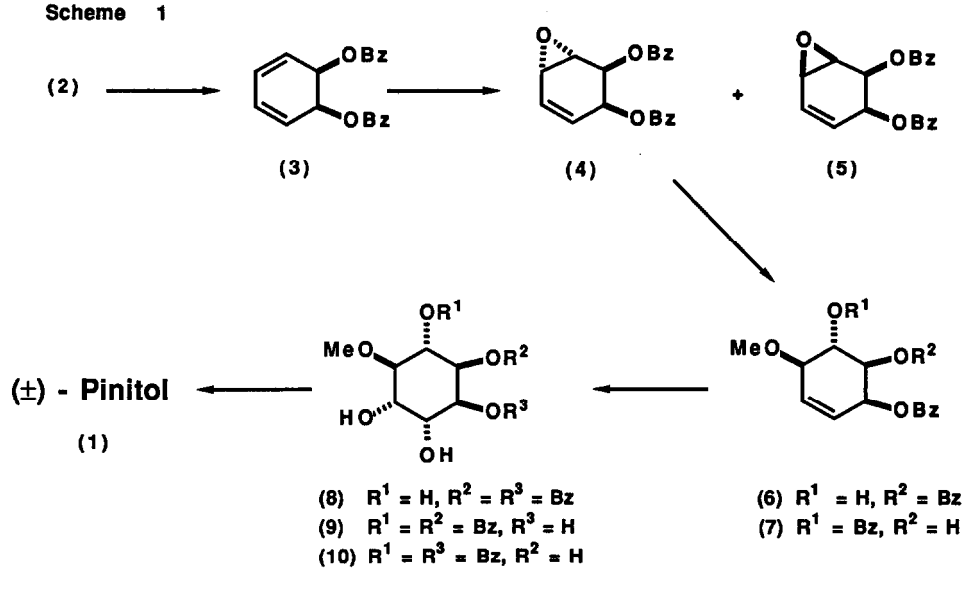
As a route to (1)[4] we have chosen to exploit the strategically important process which permits the ready transformation of benzene to *cis*-1,2-dihydroxycyclohexa-3,5-diene (2) using a microbial oxidation with *Pseudomonas putida*.[5] The product diene diol (2) is well suited to further chemical elaboration[6] and is particularly appropriate for the preparation of cyclitol compounds.[7] The significance of the microbial oxidation step derives from the fact that it achieves the direct conversion of an aromatic substrate to an oxidised intermediate not presently available by a single conventional chemical reaction.

(2)

In order to define the synthetic steps from (2) to pinitol (1) we initially studied reactions in the racemic series. Benzoylation of (2) under standard conditions gave the dibenzoate (3) (84%). Selective epoxidation of (3) with m-CPBA in buffered (pH8) dichloromethane gave (4) and (5) in 73 and 17% yields, respectively. These were readily separated by column chromatography and their structures confirmed by X-ray crystallography.[8] Compound (4) reacted with methanol in the presence of camphorsulphonic acid to give the ring-opened product (6) in an expected highly regioselective and stereoselective fashion and in quantitative yield. Work-up of this reaction necessitated the use of dilute aqueous solutions of sodium bicarbonate since with more concentrated solutions some rearrangement (up to 13%) of the benzoyl group was noticed, affording compound (7).[9] Treatment of (6) (or the mixture of (6) and (7)) with osmium tetroxide under catalytic conditions with N-methylmorpholine-N-oxide (NMO) as co-oxidant produced triols (8) and (9) in a 5:1 ratio (65%). Hydrolysis of this mixture with aqueous methanol/triethylamine produced an essentially quantitative yield of (±)-pinitol (1). The product was identical by spectroscopic methods to an authentic sample of natural (+)-pinitol.[10]

Interestingly, when (6) was oxidised with stoichiometric OsO_4 only a very low yield (4%) of hydroxylated material was obtained, presumably due to problems associated with cleavage of the intermediate osmate ester. However, use of t-butylhydroperoxide as co-oxidant in the catalytic reaction proved to be superior to NMO and an 80% yield of triols (8), (9) and (10) could be achieved. As before these triols were hydrolysed (separately or as a mixture) to racemic pinitol (Scheme 1).

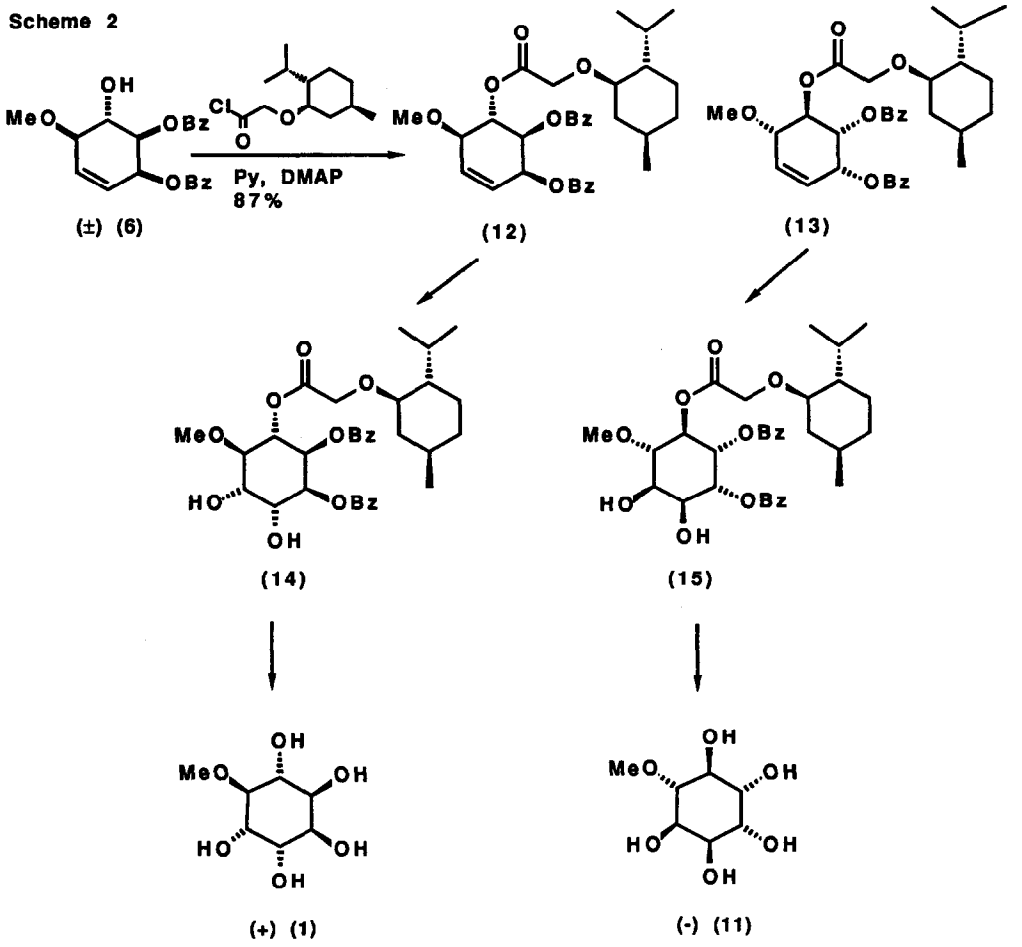
Scheme 1



Use of the most efficient sequence of reactions, therefore, makes pinitol available in 49% overall yield from benzene in just six steps.

Following the success of this racemic route we were keen to prepare optically pure materials and especially to synthesize the unnatural (-)-pinitol isomer (11) for biological evaluation and comparison with the (+)-antipode. For this reason we chose to adopt a resolution approach which involved the preparation of menthoxyacetic ester diastereoisomers (12) and (13) from the racemic alcohol (6).[11] These were readily separable by HPLC and could be independently oxidised to the corresponding diols (14) and (15), which were then hydrolysed to the natural (+)-pinitol (1) or (-)-pinitol (11) using the previously established procedures (Scheme 2). The synthetic material was identical in all respects with a sample of the natural product (1).[10] This work constitutes the first total synthesis of (1) and its antipode (11).

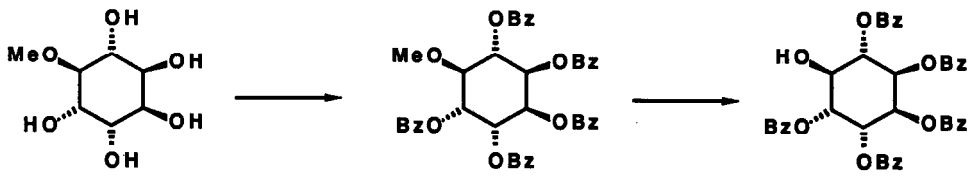
Scheme 2



In addition, we have investigated other methods for the resolution of the intermediates in these and related reaction sequences. The details of these studies will be reported later during our work with other cyclitol systems.

In connection with other work we have also developed a potentially useful demethylation reaction of pinitol. For example, the pentabenzoate (16) was prepared from (1) in 97% yield by standard methods. This, upon treatment with excess tetrabutylammonium iodide and boron trifluoride etherate[12] afforded the hydroxy derivative (17) in 57% yield (100% based upon recovered starting material) (Scheme 3). A variety of other reagents (TMS-I, Me_2BBr, TMS-Br, HCl/TFA) failed to effect this transformation.

Scheme 3

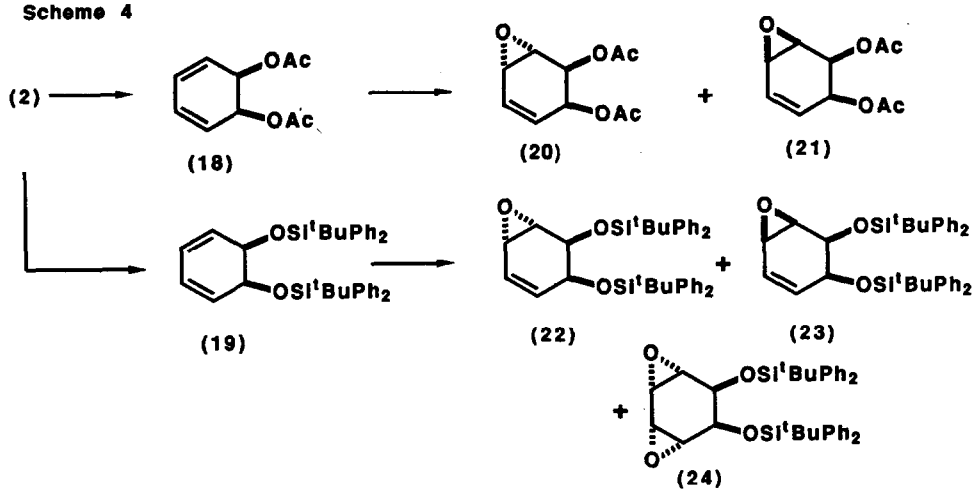


(1) (16) (17)

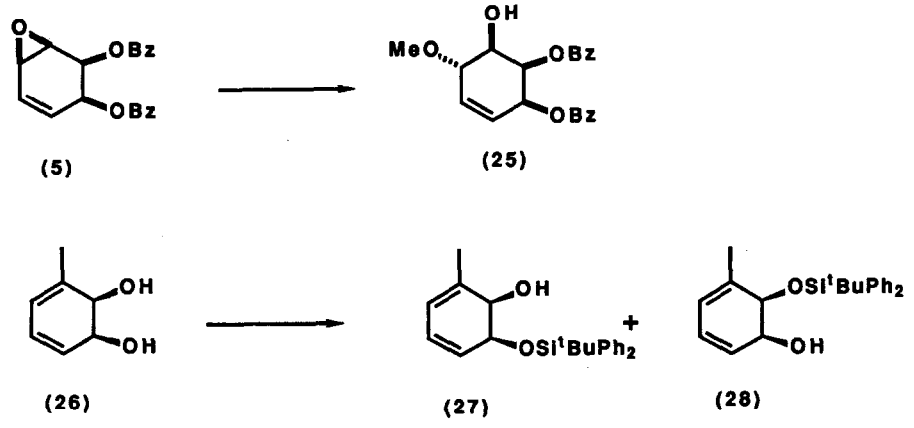
Owing to current interest in the use of the diene diol (2) as a novel starting material for organic synthesis, we report here several additional reactions which may well find applications in the future. For example, the *cis*-glycol functionality of (2) can also be protected as the diacetate (18) or bis-t-butyldiphenylsilyl ether (19). Both (18) and (19) may be epoxidised using m-CPBA (Scheme 4). For the diacetate (18), two epoxides (20) and (21) are obtained in a ratio in accord with the epoxidation of (3). However, oxidation of (19) is markedly more selective, owing to the steric bulk of the silyl group, producing the α-epoxide (22) in an excellent 77% yield, together with only small amounts (5%) of the β-epoxide (23) and a bis epoxide (24).

Reaction of (5) with methanol affords a single ring opened product (25). Also, treatment of the cyclohexadiene diol (26), obtained by microbial oxidation of toluene,[13] was found to undergo selective silylation with t-butylchlorodiphenylsilane (1 eq) to give the hydroxyl differentiated compound (27) as the major product, together with small amounts of (28) (Scheme 5).[14]

Scheme 4



Scheme 5



In summary, this paper describes further uses of the strategically important microbial oxidation reaction of aromatic compounds to cyclohexadiene diol.[15]

Acknowledgements

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Experimental.

IR spectra were recorded on a Perkin Elmer 983G Infrared Spectrometer. ^{1}NMR spectra were recorded in $CDCl_3$ using a Bruker AM-500, Bruker WH-400, Jeol GSX-270, Bruker WM 250 and Jeol FX-90Q. Mass spectra were recorded on a VG-7070B instrument and microanalyses were performed in the Imperial College Chemistry microanalytical laboratory. Optical rotations were measured on an Optical Activity AA-1000 polarimeter. Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Chromatography refers to column chromatography on Merck Kieselgel 60 (230-400 mesh); petrol refers to petroleum ether b.p. 40-60°C and ether to diethyl ether. Compound numbering for NMR purposes follows systematic nomenclature.

***cis* -3,5-Cyclohexadiene-1,2-diol dibenzoate (3).** Benzoyl chloride (11.4 ml, 98.2 mmol) was added dropwise to a stirred solution of *cis* -3,5-cyclohexadiene-1,2-diol (2) (5.00g, 44.6mmol) and DMAP (0.100g, 0.819mmol) in pyridine (200ml) at 0°C under argon. After 2 1/2h, the mixture was brought to RT and stirred overnight. Dilute aqueous copper (II) sulphate solution was added and, after a further 15min, the mixture was extracted with ether (x2). The combined extracts were washed successively with copper sulphate solution, water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (15% ether - petrol) of the residue afforded the *dibenzoate* (3) (12.0g, 84%) as a white solid, m.p. 90.5 - 91.5°C; ν_{max} ($CHCl_3$) 3059, 1717, 1601, 1584, 1490 and 1450 cm^{-1}; δ (250 MHz) 8.17 - 7.91 (4H, m, Ph), 7.56 - 7.46 (2H, m, Ph), 7.42 - 7.30 (4H, m, Ph), 6.25 - 6.15 (2H, m, 4-H and 5-H), 6.12 - 6.01 (2H, m, 3-H, and 6-H), 5.88 (2H, t, J 1.3 Hz, 1-H and 2-H); m/z 320 (M^+), 198 (M^+ -$PhCO_2H$), 122 ($PhCO_2H^+$), 105 ($PhCO^+$) and 77 (Ph^+). (Found: C, 75.18, H, 4.98. $C_{20}H_{16}O_4$ requires C, 74.99; H, 5.03%).

(1α, 2α, 5β, 6β)-5,6-Epoxy-3-cyclohexene-1,2-diol dibenzoate (4) and (1α,2α,5α, 6α)-5,6-Epoxy-3-cyclohexene-1,2-diol dibenzoate (5). The diene (3) (12.0g, 37.5 mmol) was dissolved in DCM (250 ml) and pH 8 phosphate buffer solution (250 ml) added. mCPBA (8.49g, 90%, 44.3 mmol) was added portionwise to the vigorously stirred biphasic mixture. After stirring at RT for 22h, the mixture was extracted with DCM and the extracts washed with 10% aqueous sodium sulphite solution (x1), dilute aqueous sodium bicarbonate solution (x1) and water (x1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (20-25% ether-petrol, gradient elution) of the residue afforded the *vinyl epoxides* (4) (9.2g, 73%) and (5) (2.1g, 17%), both as white solids. Less polar: (4) m.p. 95.5°C; ν_{max} (film) 3061, 3029, 1723, 1600, 1583, 1490, 1449, 1272, 1113, and 707 cm^{-1}, δ (400 MHz), 8.06-7.89 (4H, m, Ph), 7.62-7.30 (6H, m, Ph), 6.28 (1H, ddd, J 10.5, 3.5 and 3.0 Hz, 4-H), 6.23 (1H, ddd, J 3.5, 3.0 and 1.5 Hz, 1-H), 5.96 (1H, dq, J 10.0 and 1.5 Hz, 3-H), 5.79 (1H, ddd, J 4.5, 2.5 and 2.0 Hz, 2-H), 3.76 (1H, t, J 3.5 Hz, 6-H), 3.55 (1H, td, J 3.5 and 1.5 Hz, 5-H); m/z 336 (M^+), 214 (M^+-$PhCO_2H$), 198 (M^+-$PhCO_2H$-O), 105 ($PhCO^+$) and 77 (Ph^+). (Found: M^+, 336.0995. $C_{20}H_{16}O_5$ requires M, 336.0998). (Found: C, 71.10; H, 4.72. $C_{20}H_{16}O_5$ requires C, 71.42; H, 4.80%). More polar: (5), m.p. 129°C, ν_{max} ($CHCl_3$) 3027, 1717, 1601, 1584, 1490, 1450, 1315 and 1118 cm^{-1}; δ (400 MHz) 8.35-8.05 (2H, m, Ph), 8.05-7.85 (2H, m, Ph), 7.65-7.30 (6H, m, Ph), 6.42 (1H, dd, J 10.0 and 4.0 Hz, 4-H), 6.21 (1H, ddd, J 10.0, 6.5 and 2.0 Hz, 3-H), 5.93 (1H, ddd, J, 6.5, 5.0 and 2.0 Hz, 2-H), 5.60 (1H, dd, J, 5.0 and 1.0 Hz,

1-H), 3.82 (1H, m, 6-H), 3.57 (1H, td, J 4.0 and 2.0 Hz, 5-H); m/z 336 (M^+), 214 (M^+-$PhCO_2H$) and 105 ($PhCO^+$). (Found: C, 71.28, H, 4.71. $C_{20}H_{16}O_5$ requires. C, 71.42, H, 4.80%).

(1α, 2β, 3β, 6β)-6-Methoxy-4-cyclohexene-1,2,3-triol 2,3-dibenzoate(6). Camphorsulphonic acid monohydrate (106 mg, 0.423 mmol) was added to a stirred mixture of the epoxide (4) (1.01g, 3.00 mmol) in chloroform (5 ml) and methanol (10 ml) at RT. After 22 1/2 h, the reaction was poured into chloroform and washed with dilute aqueous sodium bicarbonate solution (x1). The aqueous layer was re-extracted with chloroform (x 3) and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (40% ether-petrol) of the residue afforded the *alcohol* (6) (1.1g, 100%) as a white solid, m.p. 108°C; ν_{max} (film) 3487, 3064, 2934, 1718, 1601, 1584, 1491, 1451, 1281 and 1097 cm^{-1}; δ (400 MHz) 8.05 -7.90 (4H, m, Ph), 7.60-7.30 (6H, m, Ph), 6.13 (1H, dd, J 10.0 and 2.0 Hz, 5-H), 6.02 (1H, ddd, J 10.0, 5.0 and 2.0 Hz, 4-H), 5.94 (1H, dd, J 5.0 and 4.5 Hz, 3-H), 5.35 (1H, dd, J 11.0 and 4.5 Hz, 2-H), 4.40 (1H, dd, J 11.0 and 7.5 Hz, 1-H), 3.99 (1H, dtd, J 7.5, 2.0 and 0.75 Hz, 6-H), 3.59 (3H, s, MeO-), 2.55 (1H, br s, -OH); m/z 368 (M^+), 336 (M^+-MeOH) and 105 ($PhCO^+$). (Found: M^+, 368,1257. $C_{21}H_{20}O_6$ requires M, 368.1260). (Found: C, 68.49; H, 5.61. $C_{21}H_{20}O_6$ requires C, 68.47; H, 5.47%).

DL-1,2-Di-*O*-benzoyl-4-*O*-methyl-*chiro*-inositol (8) and DL-2,3-Di-*O*-benzoyl-4-*O*-methyl-*chiro*-inositol (9). Osmium tetroxide (*ca.* 1mg, 4 μmol) was added to a stirred solution of the olefin (6) (153 mg, 0.415 mmol) and N-methylmorpholine-N-oxide (0.101 ml of a 58% w/w aqueous solution, 0.498 mmol) in 10:3:1 t-butanol/THF/water (9 ml), at RT. After 3 1/2 days, a slurry of dilute aqueous sodium sulphite solution and talc was added, and, after a further 15 min, the mixture filtered through a pad of talc. The filtrate was extracted with ether and the extracts washed with brine (x1). After re-extracting the combined aqueous layers with ether (until TLC indicated that any residual organic material had been removed), the combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (40% ether -petrol) of the residue afforded the *starting olefin* (16 mg, 10%). Continued elution (75% ethyl acetate - petrol) yielded the *triols* (8) and (9) (97 mg, 58%) as a white foam and a 5:1 mixture of regioisomers, ν_{max} (film) 3436, 3066, 2934, 1724, 1602, 1585, 1491, 1451, 1280, 1113, and 710cm^{-1}; Major (8): δ (250 MHz, $CDCl_3$ + D_2O shake) 8.03- 7.88 (4H, m Ph), 7.67 - 7.30 (6H, m, Ph), 5.78 (1H, t, J 3.8 Hz, 1-H), 5.63 (1H, dd, J 9.5 and 3.0 Hz, 2-H), 4.26 (1H, t, J 3.8 Hz, 6-H), 4.20 (1H, t, J 9.0 Hz, 3-H), 3.99 (1H, dd, J 9.5 and 3.5 Hz, 5-H), 3.74 (3H, s, MeO-) 3.62 (1H, t, J 9.0 Hz, 4-H). Minor: (9) δ (250 MHz, $CDCl_3$ + D_2O shake) 8.03 - 7.88 (4H, m, Ph), 7.67 - 7.30 (6H, m, Ph), 5.89 (1H, t, J 9.5 Hz, 3-H), 5.63 (1H, dd, J 9.5 and 3.0 Hz, 2-H), 4.41 (1H, t, J 3.3 Hz, 1-H or 6-H), ~4.27 (1H, 6-H or 1-H), 4.12 (1H, dd, J 9.0 and 3.5 Hz, 5-H), 3.56 (1H, t, J 9.0 Hz, 4-H), 3.51 (3H, s, MeO^-); m/z 402 (M^+), 384 (M^+ - H_2O), 352 (M^+ - H_2O - MeOH), 280 (M^+- $PhCO_2H$), 262 (M^+-H_2O-$PhCO_2H$), 191 (M^+-H-2PhCO), 158 (M^+-2 $PhCO_2H$), 140 (M^+-H_2O-2$PhCO_2H$) and 105 ($PhCO^+$). (Found: M^+, 402.1309. $C_{21}H_{22}O_8$ requires 402.1315).

DL-1,2-Di-*O*-benzoyl-4-*O*-methyl-*chiro*-inositol (8) and DL-2,3-Di-*O*-benzoyl-4-*O*-methyl-*chiro*-inositol (9) and DL-1,3-Di-*O*-benzoyl-4-*O*-methyl-*chiro*-inositol (10). Tetraethylammonium acetate tetrahydrate (37 mg, 0.14 mmol) and t-butylhydroperoxide (0.126 ml of a 70% aqueous solution, 0.908 mmol) were

added successively to a solution of the olefin (6) (209mg, 0.567 mmol) in acetone (1.5 ml) at RT. After the salt had dissolved, the mixture was cooled to 0°C whereupon osmium tetroxide (*ca* 0.3 mg, 1μmol) was added. The solution was stirred at 0°C for 1 1/2h and then at RT for 3 days. The mixture was diluted with ether, cooled to 0°C and 10% aqueous sodium sulphite solution added. After stirring at RT for 2h, solid sodium chloride was added until the aqueous phase was saturated and the biphasic mixture then stirred for a further 10 min. The ethereal layer was separated and washed with brine (x2). The combined aqueous layers were re-extracted with ether (x2) and the combined organic extracts then dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (50% ether-petrol) of the residue afforded the *triol* (10) (50mg, 22%) as a colourless oil, ν_{max} (film) 3450, 1720, 1275, 1120, 1100 and 708 cm^{-1}; δ(250 MHz) 8.16-8.00 (4H, m Ph), 7.65-7.54 (2H, m, Ph), 7.54-7.40 (4H, m, Ph), 5.62-5.50 (2H, m, 1-H and 3-H), 4.35 (1H, br d, J 9.0 Hz, 2-H or 5-H), 4.27 (1H, t, J 3.5 Hz, 6-H), 3.94 (1H, dd, J 9.0 and 3.5 Hz, 5-H or 2-H), 3.74 (1H, t, J 9.0 Hz, 4-H), 3.55 (3H, s, MeO-), 3.10 (1H, br s, -OH), 2.89 (1H, br s, -OH), 2.55 (1H, br s, -OH). Continued elution (75% ether-petrol) afforded the *triols* (8) and (9) (133 mg, 58%) as a white foam and a 1:1.2 mixture of regioisomers, identical spectral properties to previously prepared material.

Preparation of (±)-Pinitol (1). The mixture of dibenzoates (8) and (9) (20 mg, 0.050 mmol) was stirred in 1:5:1 triethylamine/methanol/water (1 ml) at RT. After 3h, the mixture was poured into water and washed with ether (x2). The ethereal washings were re-extracted with water (x2) and the combined aqueous extracts evaporated *in vacuo*. Column chromatography (1:2 chloroform -IPA; material preadsorbed onto silica from aqueous solution) of the residue afforded (±)-pinitol (10 mg, 100%) as a white solid with spectral properties identical to an authentic sample of pinitol: δ (250 MHz, D_2O, HOD = 4.63), 3.75 (2H, m, 1-H and 6-H), 3.54 (2H, m, 2-H and 5-H), 3.41 (1H, t, J 9.4 Hz, 4-H), 3.34 (3H, s, MeO^-), 3.08 (1H, t, J 9.4 Hz, 3-H); m/z 194 (M^+), 158 ($M^+ - 2H_2O$), 144 ($M^+ - H_2O$-MeOH) and 73 ($MH^+ - 5H_2O$-MeOH). (Found: M^+, 194.0792. $C_7H_{14}O_6$ requires M, 194.0790).

[1S-(1α, 2β, 5β,6β)]-[5,6-Di(benzoyloxy)-2-methoxy-3-cyclohexen-1-yl] (l)-menthoxyacetate (12) and [1R-(1α, 2β, 5β, 6β)]-[5,6-Di(benzoyloxy)-2-methoxy-3-cyclohexen-1-yl] (l)-menthoxyacetate (13). Oxalyl chloride (0.030 ml, 0.34 mmol) was added dropwise to a stirred solution of l-menthoxyacetic acid (67 mg, 0.31 mmol) and DMF (3 drops) in DCM (0.5 ml) at RT under argon. After 3 1/2h, the volatiles were removed *in vacuo*, the residue taken up in DCM (1ml) and added to a solution of the alkenol (6) (64 mg. 0.17 mmol) and DMAP (few crystals) in pyridine (1 ml) at RT under argon. After stirring at RT for 2 days, dilute aqueous copper (II) sulphate solution was added and, after a further 5 min, the mixture was extracted with ether. The extracts were washed successively with copper sulphate solution, water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (20% ether-petrol) of the residue afforded the *menthoxyacetate esters* (12) and (13) (80 mg, 82%) as a colourless oil and a 1:1 mixture of diastereomers. Continued elution (50% ether-petrol) yielded the *starting alcohol* (6) (7 mg, 11%) as a white solid, spectral properties identical to previously prepared material.

HPLC (1.5" diameter Dynamax 83-141-C column (normal phase); 3% IPA-petrol, 32 ml min^{-1}) effected separation of the diastereomers.[16] Less polar: (12), retention time 15 min; $[\alpha]_D^{21}$ +141.4°(c 1.09, $CHCl_3$), ν_{max} (film)

1602, 1585, 1491, 1276, 1106 and 711cm^{-1} δ (250 MHz) 8.10-7.98 (2H, m, Ph), 7.93-7.84 (2H, m, Ph), 7.63-7.28 (6H, m, Ph), 6.13-6.08 (2H, m, 3-H and 4-H), 5.99 (1H, dd, J 11.3 and 7.8 Hz, 1-H), 5.91 (1H, m, 5-H), 5.39 (1H, dd, J 11.3 and 4.0 Hz, 6-H), 4.19 (1H, d, J 7.8 Hz, 2-H), 4.08 (1H, d, J 16.3 Hz, C(O)C$\underline{H}_2$O), 3.96 (1H, d, J 16.3 Hz, C(O)C$\underline{H}_2$O), 3.47 (3H, s, MeO-), 3.00 (1H, td, J 10.8 and 4.0 Hz, C(O)C$\underline{H}_2$O), 2.17 (1H, septet d, J 6.9 and 2.8 Hz, Me$_2$C$\underline{H}$-), 1.78 (1H, m), 1.60-1.50 (2H, m), 1.28-1.03 (2H, m), 0.90-0.64 (12H, m, including 0.84 (d, J 6.9 Hz, Me), 0.77 (d, J 6.8 Hz, Me), 0.69 (d, J, 6.8 Hz, Me)); m/z 564 (M$^+$), 533 (MH$^+$-MeOH), 442 (M$^+$- PhCO$_2$H), 410 (M$^+$-PhCO$_2$H-MeOH), 395 (M$^+$-C$_{11}$H$_{21}$O), 351 (M$^+$-C$_{12}$H$_{21}$O$_3$), 288 (M$^+$-2PhCO$_2$H-MeOH), 149 (M$^+$-2PhCO$_2$H-MeOH-C$_{10}$H$_{19}$) and 105 (PhCO$^+$). (Found:M$^+$, 564.2709. C$_{33}$H$_{40}$O$_8$ requires M, 564.2723 (Found: C, 69.95; H, 7.18. C$_{33}$ H$_{40}$O$_8$ requires C,70.19; H,7.14%). More polar: (13) retention time 17 min; $[\alpha]_D^{21}$ -186.7 (c 0.94, CHCl$_3$), ν_{max} (film) 1768, 1725, 1602, 1585, 1276, 1106 and 711cm^{-1}; δ (250 MHz) 8.10-7.98 (2H, m, Ph), 7.93-7.84 (2H, m, Ph), 7.63-7.28 (6H, m, Ph), 6.13-6.07 (2H, m, 3H and 4-H), 5.98 (1H, dd, J 10.9 and 7.8Hz, 1-H), 5.91 (1H, m, 5-H), 5.38 (1H, dd, J 11..3 and 4.1 Hz, 6-H), 4.19 (1H, d, J 8.1 Hz, 2-H), 4.14 (1H, d, J 16.6 Hz, C(O)C$\underline{H}_2$O-), 3.91 (1H, d, J 16.9 Hz, C(O)C$\underline{H}_2$O-), 3.46 (3H, s, MeO-), 2.93 (1H, td, J 10.6 and 4.1 Hz, C(O)CH$_2$OC$\underline{H}$-), 2.14 (1H, septet d, J. 6.9 and 2.6 Hz, Me$_2$C$\underline{H}$-), 1.85 (1H, m), 1.59-1.49 (2H, m), 1.38-0.60 (14H, m, including 0.81 (d, J 6.8 Hz, $\underline{Me}_2$CH-), 0.81 (d, J 6.0Hz, Me), 0.63 (d, J 6.8 Hz, $\underline{Me}_2$CH-)); m/z 564 (M$^+$), 533 (MH$^+$-MeOH), 442 (M$^+$-PhCO2H), 410 (M$^+$-PhCO$_2$H-MeOH), 395 (M$^+$-C$_{11}$H$_{21}$O), 351 (M$^+$-C$_{12}$H$_{21}$O$_3$), 288 (M$^+$-2PhCO$_2$H-MeOH), 149 (M$^+$-2PhCO$_2$H-MeOH-C$_{10}$H$_{19}$) and 105 (PhCO$^+$). (Found: M$^+$, 564.2696. C$_{33}$H$_{40}$O$_8$ requires M, 564.2723). (Found: C, 70.26; H, 7.34. C$_{33}$H$_{40}$O$_8$ requires C,70.19; H, 7.14%).

(1L-1,2-DI-*O*-benzoyl-4-*O*-methyl-*chiro*-inosityloxy)-(l)-menthoxyacetate (14). Osmium tetroxide (*ca.* 0.5mg, 2 μmol) was added to a stirred solutin of the olefin (12) (108 mg, 0.191 mmol) and N-methylmorpholine-N-oxide (0.046 ml of a 58% w/w aqueous solution, 0.23 mmol) in 10:3:1 t-butanol/THF/water (4 ml) at RT. After 5 days, a slurry of dilute aqueous sodium sulphite solution and talc was added and, after a further 1h, the mixture filtered through a pad of talc. The filtrate was extracted with ether and the extracts washed with brine (x1) . After re-extracting the combined aqueous layers with ether the combined organic extracts were dried (MgSO$_4$) and evaporated *in vacuo*. Column chromatography (65% ether-petrol) of the residue afforded the *diol* (14) (111 mg, 97%) as a colourless oil, $[\alpha]_D^{20}$ +99.2° (c 4.5, CHCl$_3$); ν_{max} (film) 3452, 1764, 1725, 1601, 1584, 1490, 1450, 1275, 1026 and 712 cm^{-1}; δ (500 MHz) 7.97 (2H, d, J 8.0 Hz, Ph), 7.86 (2H, d, J 8.0 Hz, Ph), 7.58 (1H, t, J 7.0 Hz, Ph), 7.49-7.41 (3H, m, Ph), 7.30 (2H, t J 7.0 Hz, Ph), 5.77 (1H, t, J 3.5 Hz, 1-H), 5.74 (1H, t, J 10.0 Hz, 3-H), 5.66 (1H, dd, J 10.5 and 3.0 Hz, 2-H), 4.29 (1H, q, J 3.3 Hz, 6-H), 4.05 (1H, d, J 16.5 Hz, C(O)C$\underline{H}_2$O-), 4.02 (1H, m, 5-H), 3.99 (1H, d, J 16.5 Hz, C(O)C$\underline{H}_2$O-), 3.73 (1H, t, J 9.5 Hz, 4-H), 3.59 (3H, s, MeO-), 3.19 (1H, br s, -OH), 2.99 (1H, td, J 10.5 and 4.0 Hz, C(O)CH$_2$OC$\underline{H}$-), 2.81 (1H, br s, -OH), 2.14 (1H, septet d, J 7.0 and 2.5 Hz, Me$_2$C$\underline{H}$-), 1.80 (1H, br d, J 11.5 Hz), 1.57-1.50 (2H, m), 1.21-0.66 (14H, m, including 0.81 (d, J 7.0 Hz, Me$_2$CH-), 0.74 (d, J 6.5 Hz, Me), 0.68 (d, J 7.0 Hz, Me$_2$C$\underline{H}$-)); m/z 598 (M$^+$), 444 (M$^+$-PhCO$_2$H-MeOH), 426 (M$^+$-PhCO$_2$H-MeOH-H$_2$O), 385 (M$^+$-C$_{12}$H$_{21}$O$_3$) 322 (M$^+$- 2 PhCO$_2$H-MeOH), 262 (M$^+$-C$_{12}$H$_{21}$O$_3$-H$_2$O-PhCO), 140 (M$^+$-C$_{12}$H$_{21}$O$_3$-PhCO$_2$H-H$_2$O-PhCO), 122 (PhCO$_2$H$^+$) and 105 (PhCO$^+$). (Found: M$^+$, 598.2769. C$_{33}$H$_{42}$O$_{10}$ requires M, 598.2778). (Found: C,66.00; H,7.15. C$_{33}$H$_{42}$O$_{10}$ requires C, 66.20; H, 7.07%).

(1D-1,2-Di-*O*-benzoyl-4-*O*-methyl-*chiro*-inosityloxy)-(l)-menthoxyacetate (15). Osmium tetroxide (*ca.* 1mg, 4 μmol) was added to a stirred solutin of the olefin (13) (105 mg, 0.186 mmol) and N-methylmorpholine-N-oxide (0.045 ml of a 58% w/w aqueous solution, 0.22 mmol) in 10:3:1 t-butanol/THF/water (46ml) at RT. After 5 days, a slurry of dilute aqueous sodium sulphite solution and talc was added and, after a further 1h, the mixture filtered through a pad of talc. The filtrate was extracted with ether and the extracts washed with brine (x1) . After re-extracting the combined aqueous layers with ether, the combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (65% ether-petrol) of the residue afforded the *diol* (15) (100 mg, 90%) as a white foam, $[\alpha]_D^{20}$ -169.9° (c 1.9, $CHCl_3$); ν_{max} (film) 3436, 1765, 1726, 1601, 1276, 1114, and 711 cm^{-1} δ (500 MHz) 7.97 (2H, d, J 8.0 Hz, Ph), 7.86 (2H, d, J 8.0 Hz, Ph), 7.58 (1H, t, J 7.0 Hz, Ph), 7.49-7.41 (3H, m, Ph), 7.30 (2H, t J 7.0 Hz, Ph), 5.77 (1H, t, J 3.5 Hz, 1-H), 5.74 (1H, t, J 10.0 Hz, 3-H), 5.66 (1H, dd, J 10.5 and 3.0 Hz, 2-H), 4.29 (1H, br s, 6-H), 4.09 (1H, d, J 16.5 Hz, C(O)C$\underline{H}_2$O-), 4.02 (1H, br d, J 10.0 Hz, 5-H), 3.93 (1H, d, J 16.5 Hz, C(O)C$\underline{H}_2$O-), 3.73 (1H, t, J 9.5 Hz, 4-H), 3.58 (3H, s, MeO-), 3.02 (1H, br s, -OH), 2.91 (1H, td, J 10.5 and 4.0 Hz), C(O)CH_2OC$\underline{H}$-), 2.78 (1H, br s, -OH), 2.12 (1H, septet d, J 7.0 and 2.5 Hz, $Me_2C\underline{H}$-), 1.84 (1H, br d, J 12.5 Hz), 1.54-1.47 (2H, m), 1.26-0.56 (14H, m, including 0.78 (d, J 7.0 Hz), 0.59 (d, J 7.0 Hz)); m/z 598 (M^+), 444 (M^+-$PhCO_2H$-MeOH), 385 (M^+-$C_{12}H_{21}O_3$), 262 (M^+-$C_{12}H_{21}O_3$-H_2O-PhCO) and 105 ($PhCO^+$). (Found: M^+, 598.2769. $C_{33}H_{42}O_{10}$ requires M, 598.2778). (Found; C, 66.08; H, 7.34. $C_{33}H_{42}O_{10}$ requires C, 66.20; H, 7.07%).

Preparation of (+)-Pinitol (1). The triester (14) (28mg, 0.047 mmol) was stirred in 1:5:1 triethylamine/methanol/water (1ml) at RT. After 68h, the volatiles were removed *in vacuo*, the residue taken up in water and washed with ether (x2). The etereal washings were re-extracted with water (x2) and the combined aqueous extract freeze-dried. Column chromatography (1:2 chloroform - IPA; material preadsorbed onto silica from an aqueous solution) of the residue afforded (+)-*pinitol* (9.1 mg, 100%) as a white solid, $[\alpha]_D^{20}$ +61.5° (c 0.27, H_2O), (authentic sample, +61.2° (c 0.26, H_2O)); δ (500 MHz, D_2O, $\underline{H}OD$ = 4.74), 3.96-3.94 (2H, m, 1-H and 6-H), 3.76 (1H, dd, J 10.0 and 2.8 Hz, 2-H or 5-H), 3.71 (1H, dd, J 10.0 and 2.8 Hz, 5-H or 2-H), 3.60 (1H, t, J 9.7 Hz, 4-H), 3.54 (3H, s, MeO^-), 3.29 (1H, t, J 9.7 Hz, 3-H); other spectral properties identical to previously prepared racemic material.

Preparation of (-)-Pinitol (11). The triester (15) (23mg, 0.038 mmol) was stirred in 1:5:1 triethylamine/methanol/water (1ml) at RT. After 23 1/2h, the volatiles were removed *in vacuo*, the residue taken up in water and washed with ether (x2). The ethereal washings were re-extracted with water (x2) and the combined aqueous extracts freeze-dried. Column chromatography (1:2 chloroform- IPA; material preadsorbed onto silica from an aqueous solution) of the residue afforded (-)-*pinitol* (7 mg, 100%) as a white solid, $[\alpha]_D^{20}$ -61.4° (c 0.21, H_2O), spectral properties identical with previously prepared (+)-enantiomer.

1D-1,2,3,5,6-Penta-*O*-benzoyl-4-*O*-methyl-*chiro*-inositol (16). Benzoyl chloride (0.200 ml, 1.72 mmol) was added to a stirred solution of (+)-pinitol (40 mg, 0.21mmol) and DMAP (catalytic amount) in pyridine (1.5 ml) at RT

under argon. After 23h, dilute aqueous copper (II) sulphate solution was added and the mixture extracted with ether. The organic extracts were washed with copper sulphate solution (x2), water (x2) and brine (x1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (25% ether-petrol) of the residue afforded the *pentabenzoate* (16) (143 mg, 97%) as a white glass, $[a]_D^{20}$ +62.7° (c 0.3, $CHCl_3$); vmax (film) 1732, 1601, 1449, 1265, 1109 and 708cm^{-1}; δ (270 MHz) 8.25-7.86 (12H, m, Ph), 7.75-7.25 (18H, m, Ph), 6.25-5.90 (5H,m, 1-H,2-H, 3-H, 5-H, 6-H), 4.23 (1H, t, J 6.5 Hz, 4-H), 3.55 (3H, s, MeO-); m/z 714 (M^+), 683(M^+-MeOH), 609 (M^+-PhCO), 593 (M^+-$PhCO_2$), 487 (MH^+-$PhCO_2$-PhCO), 473 (MH^+-2$PhCO_2$), 441 (MH^+-MeOH-2$PhCO_2$), 348 (M^+-3$PhCO_2H$) and 105 ($PhCO^+$). (Found: M^+-$PhCO_2$, 593.1827. $C_{35}H_{29}O_9$ requires M, 593.1812).

1D-1,2,3,5,6-Penta-*O*-benzoyl-*chiro*-inositol(17). Boron trifluoride etherate (0.065 ml, 0.53 mmol) was added dropwise to a stirred solution of the methyl ether (16) (38 mg, 0.053 mmol) and n-tetra butylammonium iodide (196 mg, 0.53 mmol) in deuterochloroform (1 ml) at RT under argon. The reaction was stirred at RT for 14 1/2h, at reflux for 24h and then allowed to cool to RT. The mixture was poured into DCM, washed with dilute aqueous sodium bicarbonate solution (x1) , dilute aqueous sodium thiosulphate solution (x1) and water (x1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (25-40% ether-petrol, gradient elution) of the residue afforded the *starting ether* (16) (19 mg, 50%) and the *alcohol* (17) (21 mg, 57%), both as white glasses. Less polar: (16), spectral data identical to previously prepared material. More polar: (17), $[a]_D^{20}$ +46.2° (c 0.9, $CHCl_3$); vmax (film) 3482, 1727, 1266, 1109 and 708 cm^{-1}; δ (90 MHz) 8.25-7.15 (25H, m, Ph), 6.10-5.75 (5H, m, 1-H, 2-H, 3-H, 5-H, 6-H), 4.60 (1H, t, J 7.5 Hz, 4-H); m/z 699 (M^+-H), 683 (M^+-OH), 579 (M^+-$PhCO_2$), 474 (M^+-$PhCO_2$-PhCO), 456 (M^+-2$PhCO_2H$), 438 (M^+-2$PhCO_2H$-H_2O), 352 (M^+-$PhCO_2H$-$PhCO_2$-PhCO), 334 (M^+-3$PhCO_2H$), 230 (M^+-2$PhCO_2H$-2$PhCO_2$-PHCO), 122 (PhCO2H^+), 105 ($PhCO^+$) and 77 (Ph^+). (Found: M^+-2$PhCO_2H$-H_2O, 438.1106. $C_{27}H_{18}O_6$ requires 438.1103).

***cis*-3,5-cyclohexadiene-1,2-diol diacetate (18).** Acetic anhydride (5 ml, 53 mmol) and pyridine (15 ml) were stirred together at RT under argon for 1/2h. The mixture was cooled to 0°C and the diol (2) (2.09g, 18.6 mmol) added. After stirring at 0°C for 1h, the reaction was brought to RT and stirred for 3 1/2 days. The volatiles were removed *in vacuo* and column chromatography (dichloromethane) of the residue afforded the *diacetate* (18) (2.95g, 81%) as low-melting, white flakey needles, m.p. < 29°C; ν_{max} (film) 3053, 1733, 1369, 1244 and 1063 cm^{-1}; δ (250 MHz) 6.15-6.06 (2H, m, 4-H and 5-H), 5.92-5.82 (2H, m, 3-H and 6-H), 5.51 (2H, t, J 1.1 Hz, 1-H and 2-H), 2.05 (6H, s, Me_2); m/z 196 (M^+), 154 (M^+-C_2H_2O), 137 (M^+-$MeCO_2$), 112 (M^+-2C_2H_2O), 94 (M^+-H_2O-2C_2H_2O) and 43 ($MeCO^+$). (Found: M^+, 196.0734. $C_{10}H_{12}O_4$ requires M, 196.0736). (Found: C, 61.49; H, 6.33. $C_{10}H_{12}O_4$ requires C, 61.21; H, 6.17%).

Preparation of (1α, 2α, 5β, 6β)-5,6-Epoxy-3-cyclohexene-1,2-diol diacetate (20) and (1α, 2α, 5α, 6α)-5,6-Epoxy-3-cyclohexene-1,2-diol diacetate (21). The diene (18) (250 mg, 1.27 mmol) was dissolved in 1,2-dichloroethane (10 ml) and pH 8 phosphate buffer solution (10 ml) added. mCPBA (270 mg, 90%, 1.41 mmol) was added portion-wise to the vigorously stirred biphasic mixture. After stirring at RT for 2 days, the

mixture was extracted with chloroform and the extracts washed with 10% aqueous sodium sulphite solution (x1), dilute aqueous sodium bicarbonate solution (x1) and water (x1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (30-40% ether-petrol, gradient elution) of the residue afforded the *vinyl epoxides* (20) (201 mg, 75%) and (21) (31 mg, 12%), both as white solids. Less polar: (20), m.p. 74.5°C; ν_{max} (film), 3020, 1741, 1370, 1240 and 1040 cm^{-1}; δ (250 MHz) 6.14 (1H, ddd, J 10.0, 4.0 and 3.0 Hz, 4-H), 5.82 (1H, ddd, J 5.5, 3.0 and 1.5 Hz, 1-H), 5.71 (1H, dq, J 10.0 and 1.5 Hz, 3-H) 5.39 (1H, ddd, J. 5.0, 3.0 and 2.0 Hz, 2-H), 3.50 (1H, t, J 3.5 Hz, 6-H), 3.41 (1H, td, J 3.8 and 1.5 Hz, 5-H), 2.07 (3H, s, Me), 2.03 (3H, s, Me); m/z 212 (M^+), 183 (M^+-HCO), 170 (M^+-C_2H_2O), 141 (M^+-HCO-C_2H_2O), 128 (M^+-$2C_2H_2O$), 110 (M^+-$2C_2H_2O$-H_2O), 99 (M^+-HCO-$2C_2H_2O$), 94 (M^+-$2C_2H_2O$-H_2O-O), 81 (M^+-HCO-$2C_2H_2O$-H_2O) and 43 (CH_3CO^+). (Found: M^+, 212.0679. $C_{10}H_{12}O_5$ requires M, 212.0685). (Found: C, 56.70; H, 6.03. $C_{10}H_{12}O_5$ requires C, 56.60; H, 5.70%). More polar: (21), m.p. 97.5-98.5°C; ν_{max} (film) 1735, 1370, 1240, 1031 and 840 cm^{-1}; δ (250 MHz) 6.29 (1H, dd, J 9.5 and 4.0 Hz, 4-H), 5.97 (1H, ddd, J. 9.5, 6.5 and 2.0 Hz, 3-H), 5.54 (1H, ddd, J 6.5, 5.5 and 2.0 Hz, 2-H), 5.22 (1H, dd, J 5.5 and 1.0 Hz, 1-H) 3.58 (1H, ddd, J 4.5, 2.0 and 1.5 Hz, 6-H), 3.42 (1H, td, J. 4.0 and 2.0 Hz, 5-H), 2.11 (3H, s, Me), 2.08 (3H, s, Me); m/z 213 (MH^+), 212 (M^+), 183 (M^+-HCO), 170 (M^+-C_2H_2O), 141 (M^+-HCO-C_2H_2O), 128 (M^+-$2C_2H_2O$), 110 (M^+-$2C_2H_2O$-H_2O) and 43 (CH_3CO^+). (Found: M^+, 212.0679. $C_{10}H_{12}O_5$ requires M, 212.0685).

***cis*-5,6-Bis(t-butyldiphenylsilyloxy)-1,3-cyclohexadiene(19).** t-Butylchorodiphenylsilane (2.55 ml, 9.81 mmol) was added dropwise to a stirred solution of the diol (2) (0.500g, 4.46 mmol) and imidazole (1.34g, 19.7 mmol) in DMF (7 ml) at RT under argon. After 90 min, the mixture was poured into ether and washed with water (x2) and brine (x1). The combined aqueous layers were re-extracted with ether (x1) and the combined organic extracts dried (Na_2SO_4) and evaporated *in vacuo*. Column chromatography (petrol) of the residue afforded the *bis-silyl ether* (19) (2.4g, 92%) as a white solid, m.p. 115-116°C; ν_{max} (DCM) 3030, 2981, 1423 and 1111 cm^{-1}; δ (90 MHz) 7.80-7.60 (8H, m, Ph), 7.45-7.15 (12H, m, Ph), 5.65 (4H, br s, 1-H, 2-H, 3-H, and 4-H), 4.20 (2H, br s, 5-H and 6-H), 1.05 (18H, s, $^tBu_2$); m/z 588 (M^+), 332 (M^+-TBDPSOH), 275 (M^+-TBDPSOH-^tBu), 199 (Ph_2SiOH^+) and 77 (Ph^+). (Found: M^+, 588.2875. $C_{38}H_{44}O_2Si$ requires M, 588.2880).

(3α, 4α, 5β, 6β)-3,4-Bis(t-butyldiphenylsilyloxy)-5,6-epoxy-1-cyclohexene (22), (3α, 4α, 5α, 6α)-3,4-Bis(t-butyldiphenylsilyloxy)-5,6-epoxy-1-cyclohexene (23) and (1α, 2α,3β, 4β,5β, 6β)-1,2-Bis(t-butyldiphenylsilyloxy)-3,4,5,6-diepoxy-cyclohexane (24). The diene (19) (290mg, 0.492 mmol) was dissolved in 1,2-dichoroethane (6 ml) and pH 8 phosphate buffer solution (6 ml) added. mCPBA (260mg, 80%, 1.21 mmol) was added portion wise to the vigorously stirred biphasic mixture. After 1h, the mixture was extracted with 10% aqueous sodium sulphite solution (x1), dilute aqueous sodium bicarbonate solution (x1) and water (x1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (3-5% ether-petrol, gradient elution) afforded the *vinyl epoxides* (22) (229 mg, 77%) and (23) (16 mg, 5%) and the *bisepoxide* (24) (14 mg, 5%), all as white foams. Least polar: (22), ν_{max} (DCM) 3048, 2930, 1469, 1397 and 1110 cm^{-1}; δ (400 MHz) 7.80-7.25 (20H, m, Ph), 5.82 (1H, dt, J 10.0 and 2.5 Hz, 1-H), 5.77 (1H, dq, J 10.0 and 1.5 Hz, 2-H), 4.47 (1H, m, 4-H), 4.32 (1H, m, 3-H),

3.10-3.04 (2H, m, 5-H and 6-H), 1.10 (18H, s, $^tBu_2$); m/z 604 (M^+), 588 (M^+-O), 547 (M^+-^{t}Bu), 275 (M^+- TBDPSOH-^{t}Bu-O) and 199 (Ph_2SiOH^+). (Found: M^+, 604.2822. $C_{38}H_{44}O_3Si_2$ requires 604.2829). More Polar: (23), ν_{max} (DCM) 3059, 2930, 2857, 1602 and 1423 cm^{-1}; δ (250 MHz) 7.90-7.58 (8H, m, Ph), 7.55-7.25 (12H, m, Ph), 5.75 (1H, dd, J 10.0 and 4.0 Hz, 1-H), 5.38 (1H, ddd, J 10.0, 6.3 and 2.0 Hz, 2-H), 4.35 (1H, ddd, J 5.9, 4.7 and 2.2 Hz, 3-H), 3.92 (1H, dd, J 4.4 and 1.0 Hz, 4-H), 3.10 (1H, m, 5-H), 3.05 (1H, m, 6-H), 1.10 (18H, s, $^tBu_2$); m/z 604 (M^+), 588 (M^+-O), 547 (M^+-^{t}Bu), 291 (M^+-TBDPSOH-^{t}Bu), and 199 (Ph_2SiOH^+). (Found: M^+, 604.2822. $C_{38}H_{44}O_3Si_2$ requires M, 604.2829). Most polar: (24), ν_{max} (DCM) 3061, 2930, 2858, 1602, 1266 and 1112 cm^{-1}; δ (400 MHz) 7.82-7.75 (6H, m, Ph), 7.63-7.58 (3H, m, Ph), 7.47-7.27 (11H, m, Ph), 4.40 (1H, m, 2-H), 4.10 (1H, dd, J 4.0 and 1.5 Hz, 1-H), 3.25 (1H, ddd, J. 4.5, 2.0 and 1.0 Hz, 5-H), 3.15 (1H, dd, J 4.0 and 2.0 Hz, 4-H), 2.88 (1H, ddd, J 4.0, 3.5 and 1.0 Hz, 3-H), 2.82 (1H, dt, J 4.5 and 1.5 Hz, 6-H), 1.13 (9H, s, ^{t}Bu), 1.10 (9H, s ^{t}Bu); m/z 563 (M^+-^{t}Bu) and 199 (Ph_2SiOH^+).

Preparation of (1α, 2α, 3α, 6β)-6-Methoxy-4-cyclohexene-1,2,3-triol 2,3-dibenzoate (25). Camphorsulphonic acid monohydrate (31 mg, 0.12 mmol) was added to a stirred mixture of the epoxide (5) (104 mg, 0.309 mmol) in chloroform (1 ml) and methanol (1 ml). After 8h, the reaction was poured into chloroform and washed with saturated aqueous sodium bicarbonate solution. The aqueous layer was re-extracted with chloroform (x2) and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (20%, then 50% ether-petrol) afforded the *alcohol* (25) (106 mg, 93%) as a colourless oil, ν_{max} (film) 3469, 3065, 1718, 1601, 1584, 1491, 1451 1281, 1098 and 711 cm^{-1}; d (250 MHz) 8.03-7.99 (2H, m, Ph), 7.88-7.84 (2H, m, Ph), 7.61-7.28 (6H, m, Ph), 6.11 (1H, dt, J 10.4 and 2.1 Hz, 4-H or 5-H), 5.96 (1H, m, 2-H or 3-H), 5.91 (1H, m, 3-H or 2-H), 5.83 (1H, dm, J 10.4 Hz, 5-H or 4-H), 4.21-4.13 (2H, m, 1-H and 6-H), 3.56 (3H, s, MeO^-); m/z 246 (M^+-$PhCO_2H$), 204 ($MeOCH{=}CH{-}CH{=}CHO_2CPh^+$) and 105 ($PhCO^+$). (Found: M^+-$PhCO_2H$, 246.0905. $C_{14}H_{14}O_4$ requires M, 246.0892).

(1R-*cis*)-6-t-butyldiphenylsilyloxy-2-methyl-2,4-cyclohexadien-1-ol (27) and (1S-*cis*)-6-t-Butyldiphenylsilyloxy-5-methyl-2,4-cyclohexadien-1-ol (28). t-Butylchlorodiphenylsilane (1.08 ml, 4.16 mmol) was added to a stirred solution of the diol (26) (525mg, 4.16mmol) and imidazole (623 mg, 9.15 mmol) in DMF (5 ml) at RT under argon. After stirring overnight at RT, the mixture was poured into ether and washed with water (x3). The aqueous layers were re-extracted with ether (x1) and the combined organic extracts washed with brine (x1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (5% ether-petrol) of the residue afforded the *alcohols* (27) (652mg, 43%) and (28) (212 mg, 14%), both as colourless oils. Less polar: (28), $[\alpha]_D^{20}$ +24.3° (c 1.2, $CHCl_3$), ν_{max} (film) 3554, 3046, 2930, 1588, 1426, 1111 and 702 cm^{-1}; δ (90 MHz) 7.80-7.55 (4H, m, Ph), 7.50-7.15 (6H, m, Ph), 5.85-5.35 (3H, m, 3-H, 4-H and 5-H), 4.45 (1H, m, 6-H), 3.80 (1H, t, J 5.5 Hz, 1-H), 2.65 (1H, d, J 5.5 Hz, OH), 1.85 (3H, s, Me), 1.10 (9H, s, ^{t}Bu); m/z 364 (M^+), 346 (M^+ -H_2O), 307 (M^+ -^{t}Bu), 289 (M^+ - H_2O-^{t}Bu), 229 (M^+ -^{t}Bu-Ph), 199 (Ph_2SiOH^+) and 77 (Ph^+). (Found: M^+, 364.1851. $C_{23}H_{28}O_2Si$ requires M, 364.1859). More polar: (29), $[\alpha]_D^{20}$ +4.4° (c 0.5, $CHCl_3$), ν_{max} (film), 3562, 3045,1588, 1425, 1110 and 703cm^{-1}; δ (90 MHz) 7.75-7.55 (4H, m, Ph), 7.50-7.15 (6H, m, Ph), 6.00-5.55 (3H, m, 2-H, 3-H and 4-H), 4.30 (1H, br d, J 6.0 Hz, 6-H), 3.95 (1H, q, J 5.5 Hz, 1-H), 2.30

(1H, d, J 6.0 Hz, -OH), 1.70 (3H, s, Me), 1.10 (9H, s, ^{t}Bu); m/z 364 (M^{+}), 289 (M^{+}-H_2O-^{t}Bu) 229 (M^{+}-^{t}Bu-Ph), 211 (M^{+}-H_2O-^{t}Bu-Ph) and 199 (Ph_2SiOH^{+}). (Found: M^{+}, 364.1851. $C_{23}H_{28}O_2Si$ requires M, 364.1859).

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16. Typically, 200-250 mg of the mixture of (12) and (13) could be separated on a single HPLC run using this system; average recovery 85-90%.