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MICROBIAL OXIDATION IN SYNTHESIS: PREPARATION OF *MYO*-INOSITOL PHOSPHATES AND RELATED CYCLITOL DERIVATIVES FROM BENZENE.†

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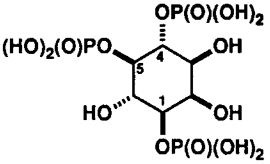
Abstract: *Pseudomonas putida* oxidation of benzene affords *cis*-3,5-cyclohexadiene-1,2-diol (2) which is used as a novel precursor for the synthesis of D- and L-*myo*-inositol 1,4,5-trisphosphates, (-)-(1) and (+)-(1). The versatility of this approach to functionalised cyclitols is illustrated in the synthesis of *myo*-inositol 1-phosphate (19), 6-deoxy, 6-deoxy-6-fluoro, and 6-deoxy-6-methyl *myo*-inositols (31), (37) and (43), and their 1,4,5-trisphosphate derivatives (33), (39) and (45).

Following the discovery and full characterisation of brain phospholipids by Ballou in 1961,[1] and the observation in 1975 by Michell [2] that the receptor controlled hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP_2) releases D-*myo*-inositol 1,4,5-trisphosphate (IP_3), a fundamental cell-signal transduction mechanism has been elucidated.[3] This has led to a sudden increase in interest in the inositol lipids, in particular IP_3 (1) which acts as a second messenger by binding to specific receptors on the endoplasmic reticulum stimulating the release of calcium from intracellular stores. The secondary messengers generated in the phosphatidylinositol (PI) cycle are known to regulate a large array of cellular processes including secretion, metabolism, contraction and proliferation.



(±)(1)

Although knowledge of this phosphoinositide cell signalling system has expanded enormously in recent years, still many facets remain unclear, hence there is an increased demand for improved supplies of natural

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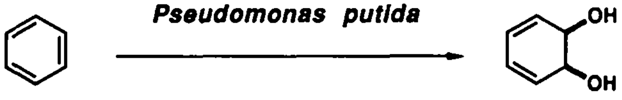
† Dedicated to Professor David Ollis F.R.S on the occasion of his 65th birthday.

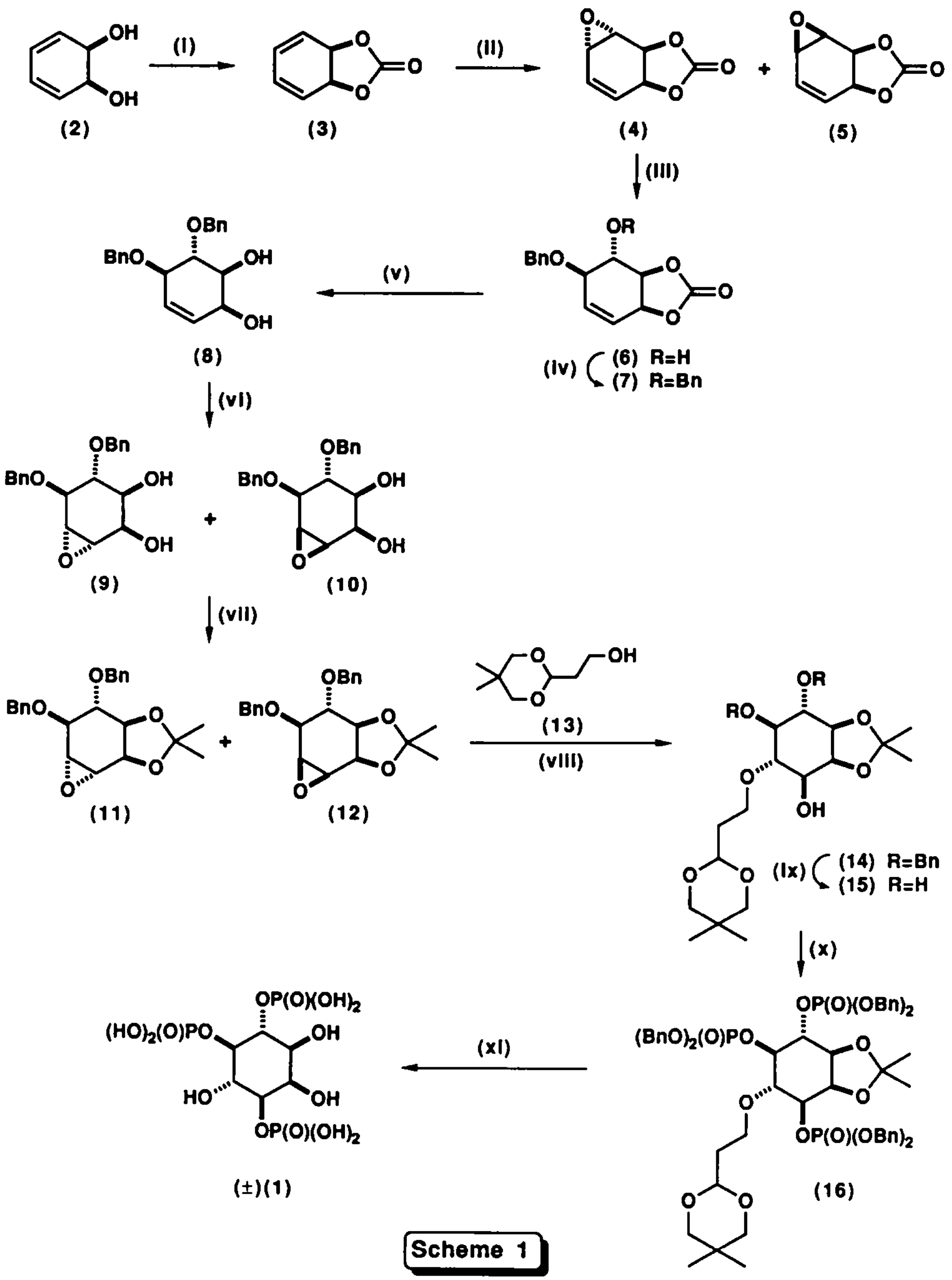
products and of novel analogues[4] to probe these mechanisms in more detail. The role of the synthetic chemist is therefore crucial to these studies.

The efficient synthesis of IP_3 (1) and other inositol phosphates on the PI pathway provides a challenging problem, since there is a need to devise appropriate protection/deprotection steps to facilitate the construction of the specific substitution patterns in the correct homochiral form. While there are now several reported syntheses of D-(-)-IP_3,[5] we chose to adopt a conceptually different approach[6] which introduces the required six stereogenic centres in a sequential fashion starting from benzene. We have previously shown[7] the strategic importance of microbial oxidation using *Pseudomonas putida*[8] as a method for converting benzene to *cis*-3,5-cyclohexadiene-1,2-diol (2) which is useful as a cyclitol precursor.[9] The significance of this biotransformation stems from the fact that benzene is converted directly into an oxidised intermediate not presently available by a single, conventional chemical reaction.



(2)

As the diol (2) is now commercially available it serves as a novel building block for organic synthesis. In order to test the feasibility of using (2) for the synthesis of IP_3, and its analogues, we concentrated our initial efforts on the racemic series, although a homochiral route was developed and is discussed later. The cyclic carbonate (3) was prepared from (2) simply by treatment with sodium methoxide and dimethyl carbonate at room temperature. This was epoxidised stereoselectively using *m*-chloroperbenzoic acid (mCPBA) to give the α- and β-epoxides (4) and (5) in a 4.6:1 ratio. Regioselective ring opening of (4) with benzyl alcohol catalysed by camphorsulphonic acid gave (6) which, on benzylation with benzyl bromide and silver (I) oxide, afforded the dibenzyl ether (7) in excellent yield. In this way, four of the necessary oxygen functionalities were introduced with the 4,5 groups similarly protected for later phosphorylation. It should, however, be noticed that by suitable changes in protecting groups the 4,5 hydroxyl groups could be differentiated at this stage should alternative substitution patterns be needed. Various methods were then investigated for introducing the remaining hydroxyl groups in (7). Hydrolysis of (7) with aqueous triethylamine in methanol gave the diol (8) in which the hydroxyl groups are ideally placed for directed epoxidation of the cyclohexene double bond. This epoxidation proceeded slowly with mCPBA to give the epoxides (9) and (10) in a 1:9 ratio, and although these could be separated it was found to be more convenient to convert these diols to the acetonides (11) and (12) prior to separation (scheme 1).



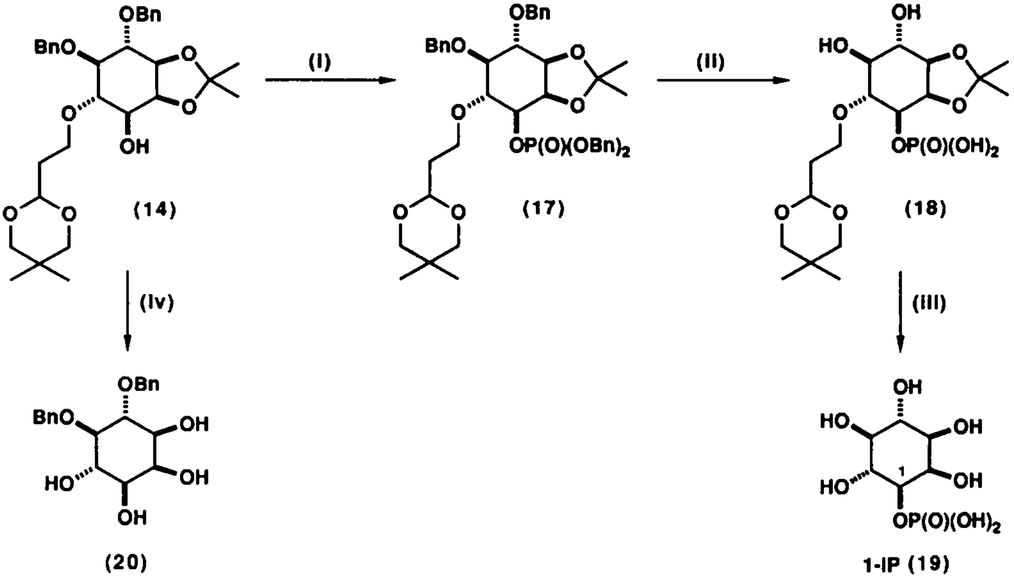
Scheme 1

(i) $(MeO)_2CO$, MeO^-Na^+, MeOH; (ii) mCPBA, DCM, 47% over 2 steps; (iii) BnOH, CSA, DCM, 85%; (iv) BnBr, Ag_2O, DMF, 81%; (v) Et_3N/MeOH/ H_2O, 100%; (vi) mCPBA, pH 8, DCM, 97%; (vii) 2,2-Dimethoxypropane, CSA, DCM, 74%; (viii) (13), NaH, HMPA/THF, 95°C, 44h, 43%; (ix) H_2, 10% Pd-C, EtOH, 23.5h, 100%; (x) ^nBuLi, $^iPr_2NH$, THF, tetrabenzylpyrophosphate, -30°C-RT, 62%; (xi) a. H_2, 10% Pd-C, EtOH, 4 days; b. 80% aq. TFA, 4h, 86% overall.

Molecular mechanics (MM2) calculations[10] suggested that the preferred conformation of the major epoxide (12) was a well-defined boat. Excellent agreement between the calculated values of the ^1H nmr coupling constants for (12) and the observed values indicated that this was also the conformation adopted in solution. Later, X-ray crystal structure determination of a related epoxide (52) suggested a slightly distorted boat in the solid state conformation. From these studies and steric considerations we were confident that regioselective ring opening of (12) by an oxygen nucleophile would occur at the C-6 carbon centre to establish the required relative stereochemistry. However, for IP_3 synthesis, a protected form of this oxygen nucleophile was required which would be compatible with the later proposed synthetic steps. This proved to be more difficult than expected. Consequently we have developed the use of the sodium salt of 5,5-dimethyl-1,3-dioxane-2-ethanol (13) as a new hydroxide equivalent.[7] This sterically unencumbered alkoxide was designed such that, at a later stage, acidic hydrolysis would release a β-alkoxy aldehyde, which would spontaneously undergo β-elimination to afford the free hydroxyl group. The parent alcohol (13) was obtained from acrolein by reaction with benzyl alcohol and 2,2-dimethylpropane-1,3-diol under Piasecki's conditions[11] to enable a one-pot Michael addition and carbonyl protection sequence, followed by hydrogenolysis of the benzyl group. Pleasingly, reaction of the epoxide (12) with the sodium salt of (13) in hexamethylphosphoramide/THF at 95°C selectively gave the ring-opened product (14) albeit in rather modest yield (43%). The *myo*-inositol stereochemistry of the alcohol (14) was confirmed by a combination of nmr studies and molecular mechanics (MM2) calculations. A COSY-90 experiment enabled the connectivities of the signals in the 500 MHz spectrum of (14) to be established and the observed coupling constants to be assigned. The experimental *J* values were found to be in excellent agreement with those calculated from the minimum energy conformation of (14).

Catalytic hydrogenolysis of (14) gave the triol (15) which, upon reaction with three equivalents of n-butyllithium and tetrabenzylpyrophosphate,[12] produced the fully protected 1,4,5-trisphosphate (16) in good overall yield. Deprotection of (16) was readily achieved by hydrogenolysis and subsequent treatment with moist trifluoroacetic acid to give IP_3 (1) in 86% yield (scheme 1). Purification was achieved by anion exchange HPLC[13] (Spherisorb S5SAX) using 0.2M ammonium formate buffer at pH4 as a mobile phase, followed by freeze-drying to remove the buffer, and subsequent lyophilisation. The synthetic (±)-(1) was identical by nmr and HPLC to an authentic sample.

The intermediates prepared in scheme 1 were also suitable for cyclitol synthesis. For example, reaction of (14) with tetrabenzylpyrophosphate gave the 1-phosphate derivative (17) which, upon debenzylation by catalytic hydrogenolysis, afforded (18). This was then deprotected under acidic conditions (4:1 TFA/H_2O) to give inositol 1-phosphate (1-IP) (19), which is also one of the metabolic products of the PI cycle (scheme 2).

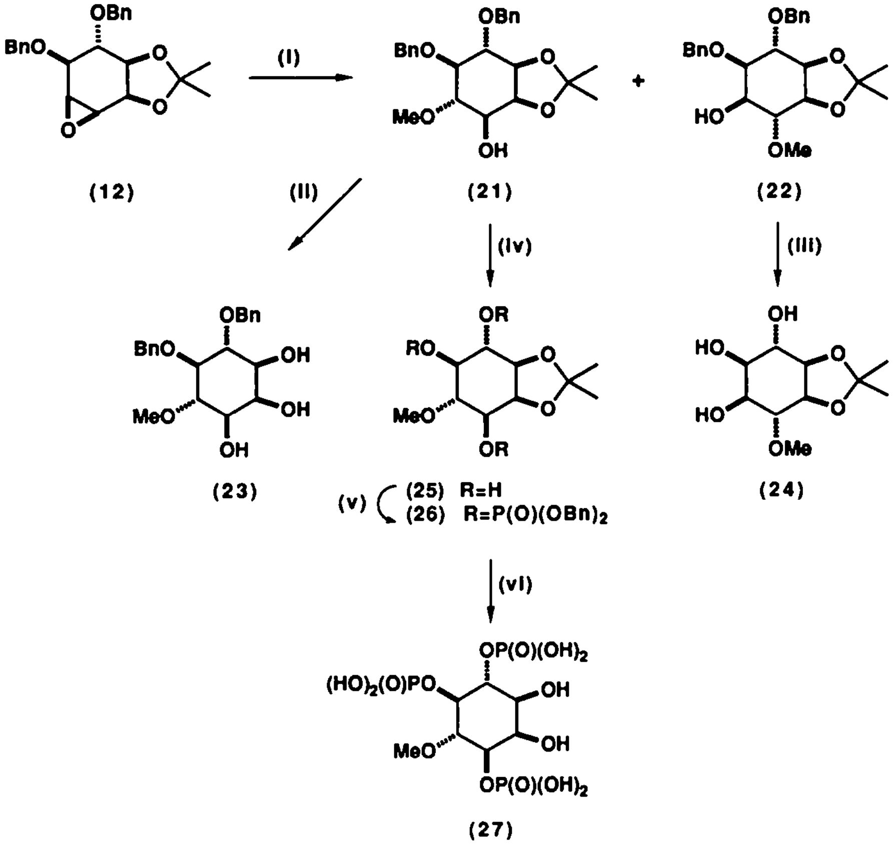


Scheme 2

(i) ^nBuLi, $^iPr_2NH$, THF, tetrabenzylpyrophosphate, -30°C-RT, 57%; (ii) H_2, 10% Pd-C, EtOH, 100%; (iii) 80% aq. TFA, 4h, 21%; (iv) 80% aq. TFA, 15h.

As a possible route to other inositol phosphates, alcohol (14) was deprotected to the tetraol (20) using trifluoroacetic acid (scheme 2). In principle this route could afford either the 1,2,3,6-tetraphosphate by phosphorylation and deprotection, or, by appropriate reactions, the 4,5-bisphosphate.

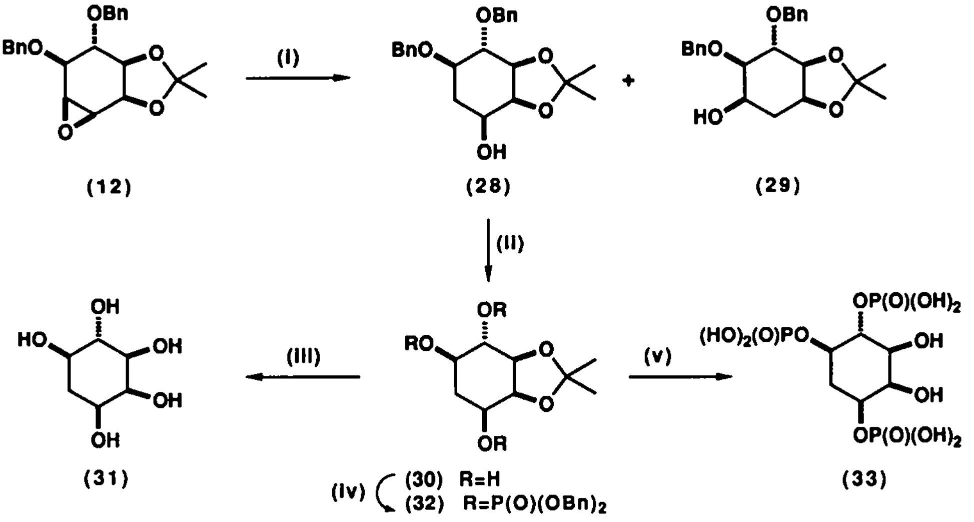
In an effort to extend this chemistry to the preparation of a range of novel 6-substituted analogues,[4d,6b] we have studied the ring opening of the epoxide (12) with a variety of nucleophiles. Reaction of (12) with methanolic sodium methoxide afforded a 3.6:1 ratio of ring-opened products (21) and (22). These compounds are also the precursors of various cyclitols. Deprotection of (21) with 80% trifluoroacetic acid gave (23), while, upon catalytic hydrogenolysis, (22) gave the triol (24). Compound (21) may also be converted to a 1,4,5-trisphosphate analogue *via* a sequence of reactions involving removal of the benzyl groups to furnish (25), phosphorylation with tetrabenzylpyrophosphate to give the trisphosphate (26), and finally deprotection to afford (27) using trimethylsilyl bromide (scheme 3).



Scheme 3

(i) MeO^-Na^+, MeOH, reflux, 72h, 95%; (ii) 80% aq. TFA, 19h, 61%; (iii) H_2, 10% Pd-C, EtOH, 45h, 100%; (iv) H_2, 10% Pd-C, EtOH, 23h, 100%; (v) ^nBuLi, $^iPr_2NH$, THF, DMSO, tetrabenzylpyrophosphate, -30°C-RT, 61% ; (vi) a.TMSBr, DCM, 55 min; b. H_2O, 80 min, 62% overall.

Ring opening of the epoxide (12) with lithium aluminium hydride gave (28) and (29) in 76% and 12% yields respectively.[14] Following debenzylation of (28) to give the triol (30), two pathways were followed. Firstly, removal of the acetonide protecting group afforded the 6-deoxy cyclitol (31). Alternatively, treatment with tetrabenzylpyrophosphate gave (32). Compound (32) was then transformed to the trisphosphate (33) by reaction with trimethylsilyl bromide in dichloromethane at room temperature in 79% yield (scheme 4). Compound (33) constitutes the 6-deoxy derivative of IP_3.

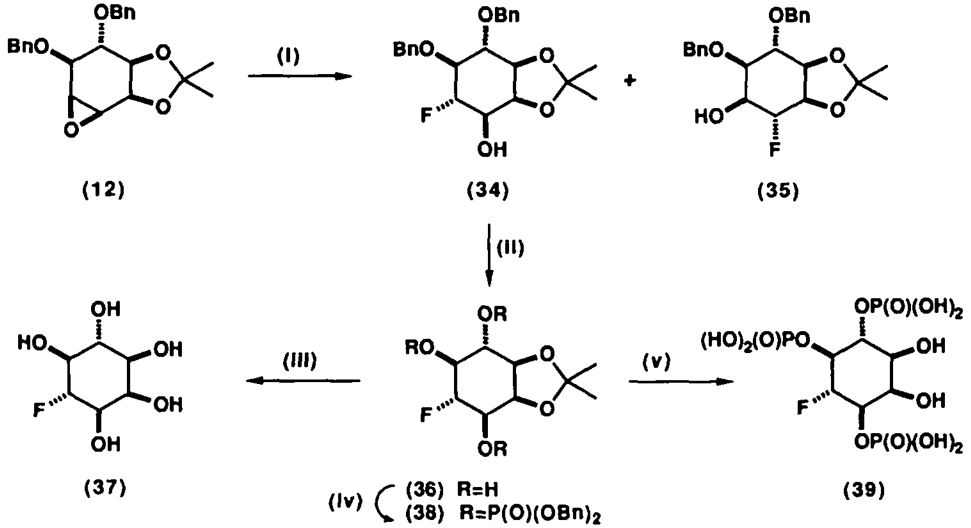


Scheme 4

(i) $LiAlH_4$, Et_2O, reflux, 2h, 88%; (ii) H_2, 10% Pd-C, EtOH, 39h, 100%; (iii) 80% aq. TFA, 4h, 97%; (iv) $^{n}BuLi$, $^{i}Pr_2NH$, THF, tetrabenzylpyrophosphate, -30°C-RT, 56% ; (v) a. TMSBr, DCM, 65 min; b. H_2O, 80 min, 79% overall.

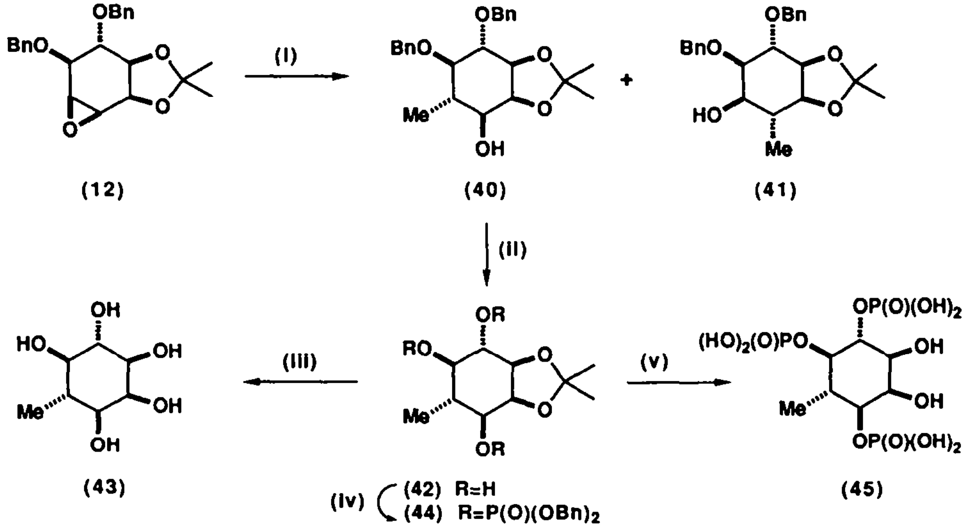
By a similar sequence of reactions, the 6-fluoro analogue was prepared from the key epoxide (12). Thus, treatment of (12) with tris(dimethylamino)sulphur (trimethylsilyl)difluoride (TASF)[15] in THF at reflux gave the fluorohydrins (34) and (35) as a readily separable 4:1 mixture. Debenzylation of (34) as before gave the triol (36). This, upon reaction with 80% trifluoroacetic acid, gave the 6-fluoro *myo*-inositol derivative (37). Reaction of (36) with tetrabenzylpyrophosphate in the normal way afforded (38). This was again fully deprotected to yield the parent 6-fluoro IP_3 analogue (39) in good yield (scheme 5).

Finally in this study of 6-substituted analogue synthesis, the epoxide (12) was reacted with lithium dimethyl(cyano)copper (I)[16] to give the alcohols (40) and (41), with excellent selectivity (21:1) and high overall yield (76%). By analogy to the previous sequences, (40) was hydrogenolysed to the triol (42) and further deprotected (4:1 TFA/H_2O) to afford the 6-methyl cyclitol (43). Alternatively, phosphorylation of triol (42) gave (44), which on deprotection with trimethylsilyl bromide afforded the trisphosphate (45) (scheme 6). To this point we have shown the versatility of this novel approach to cyclitols and *myo*-inositol phosphates. A large number of structures and substitution patterns are therefore available, many of which would be difficult to obtain by standard modifications of *myo*-inositol itself.



Scheme 5

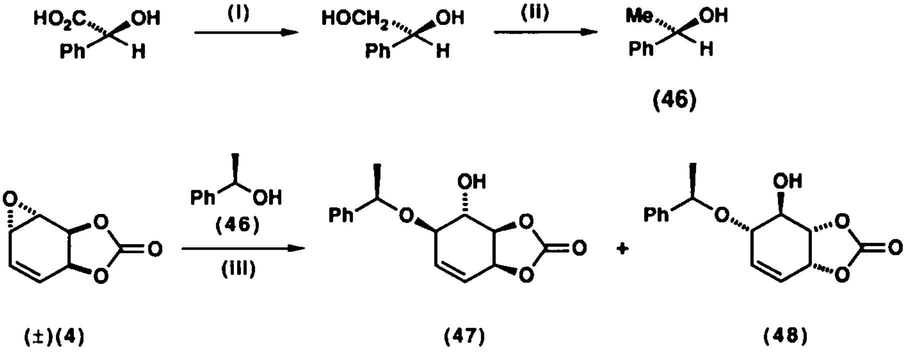
(i) TASF, THF, reflux, 4 days, 74%; (ii) H_2, 10% Pd-C, EtOH, 17h, 100%; (iii) 80% aq. TFA, 4h, 100%; (iv) ^nBuLi, $^iPr_2NH$, THF, tetrabenzylpyrophosphate, -30°C-RT, 77% ; (v) a. TMSBr, DCM, 65 min; b. H_2O, 80 min, 93% overall.



Scheme 6

(i) $Me_2Cu(CN)Li_2$, THF, -30°C, 22h, 74%; (ii) H_2, 10% Pd-C, EtOH, 16h, 97%; (iii) 80% aq. TFA, RT, 5h, 81%; (iv) ^nBuLi, $^iPr_2NH$, THF, tetrabenzylpyrophosphate, -30°C-RT, 41% ; (v) a. TMSBr, DCM, RT, 65 min; b. H_2O, 80 min, 82% overall.

The remaining problem to be addressed is that of obtaining compounds in optically pure form. Indeed an approach which would also produce the enantiomeric series could be useful for biological evaluation purposes. For this reason we have chosen a resolution procedure, but one which does not add any further steps to the reaction sequence. The key to this process was the regioselective ring opening of the epoxide (4) with a homochiral benzyl alcohol, (R)-(+)-*sec*-phenethyl alcohol (46). While (46) is commercially available, it is relatively expensive. Consequently, we have modified a preparative route[17] from (S)-(+)-mandelic acid which readily provides the alcohol (46) in multigramme quantities. Reduction of the mandelic acid with borane dimethylsulphide (BMS) to give the diol, followed by selective primary tosylation and reduction with lithium aluminium hydride gave (46) (scheme 7).

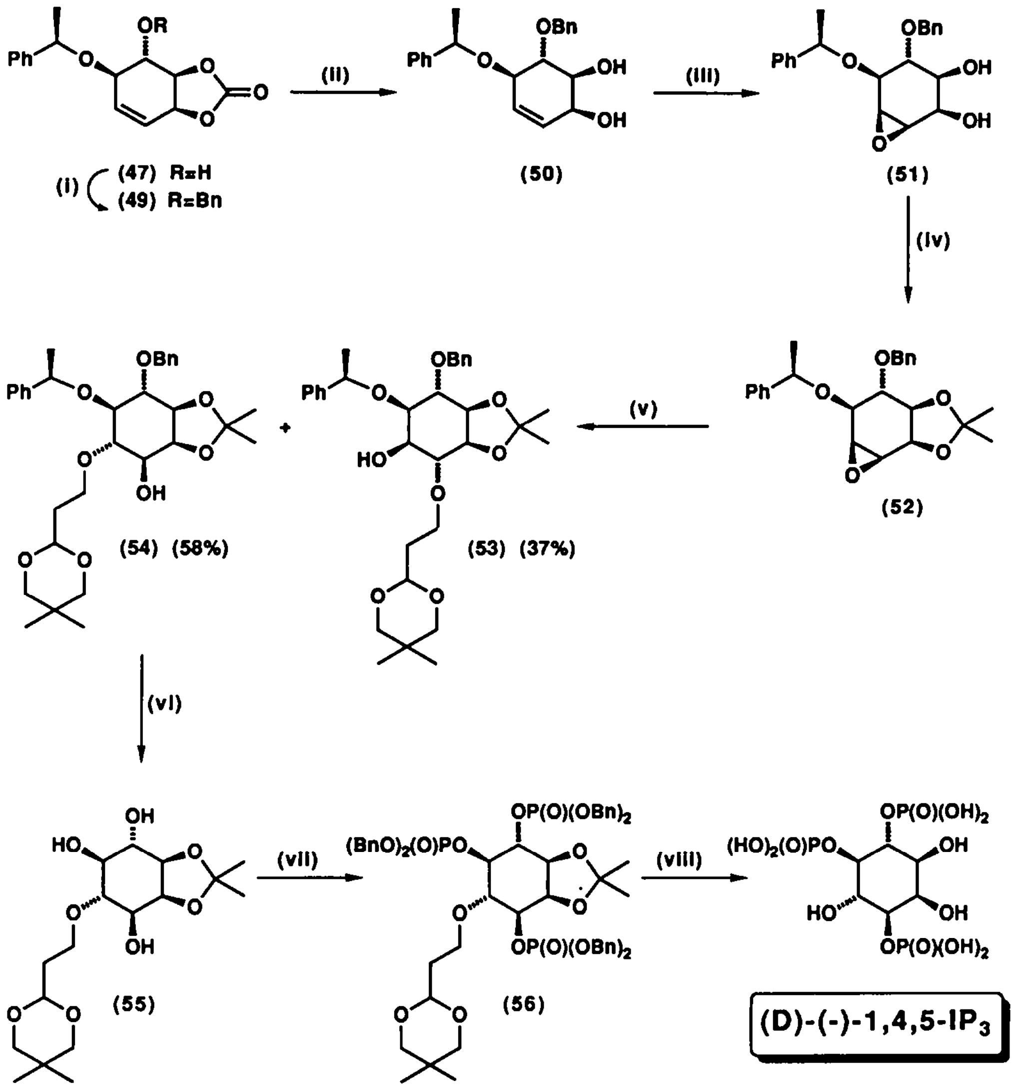


Scheme 7

(i) $Me_2S.BH_3$, THF, 2h, 64% overall; (ii) a. TsCl, py, 0°C - RT; b. $LiAlH_4$, Et_2O/THF, 22h, 48% overall; (iii) cat. $HBF_4.OEt_2$, DCM, 67%.

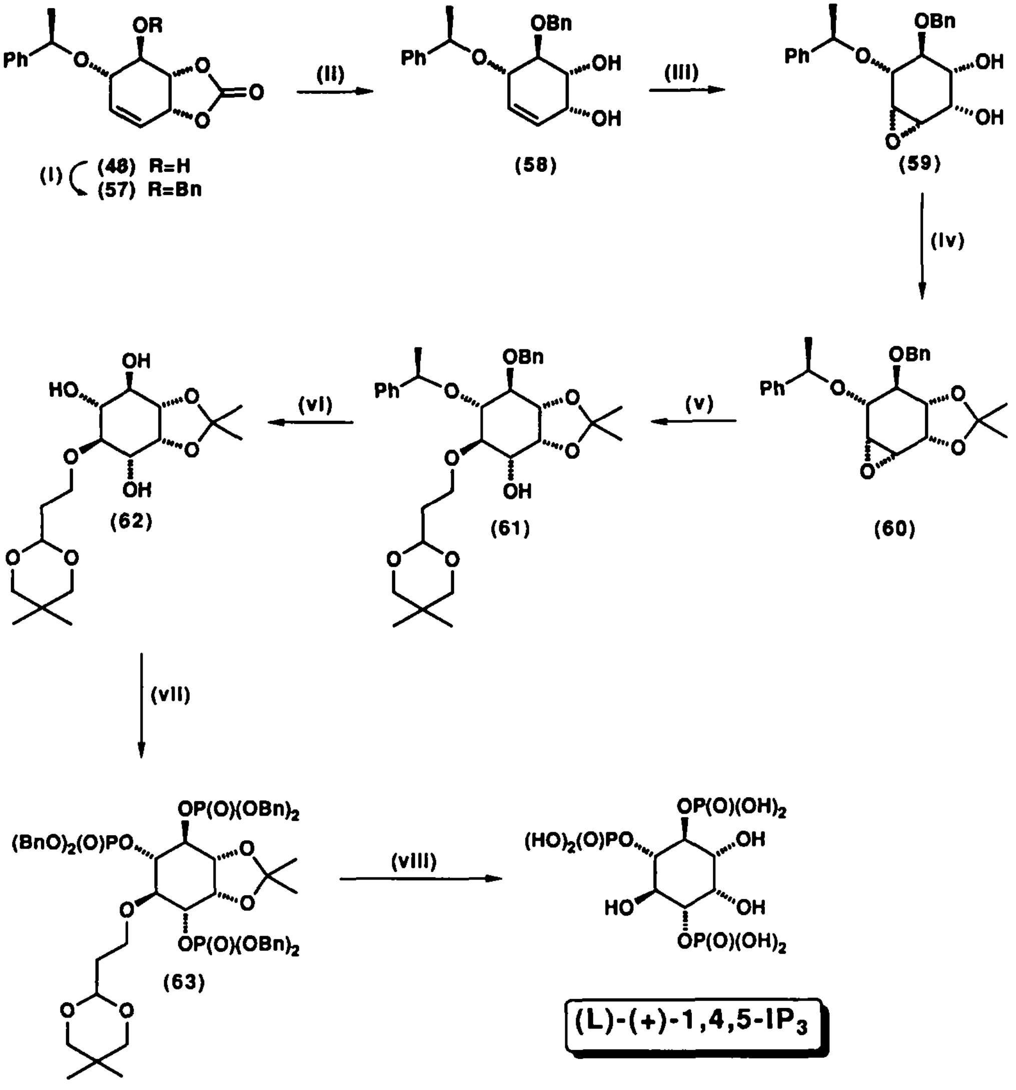
Reaction of (46) with the epoxide (4) using a catalytic amount of $HBF_4.OEt_2$ in dichloromethane gave the diastereoisomeric alcohols (47) and (48) in the expected 1:1 ratio in 67% yield (scheme 7). After separation, (47) and (48) could be processed separately to D-(-)-*myo*-inositol 1,4,5-trisphosphate (-)-(1) or L-(+)-*myo*-inositol 1,4,5-trisphosphate (+)-(1). In order to determine the absolute configuration of the diastereoisomers (47) and (48) we resorted to X-ray crystallography of a later derivative. Much of the synthetic route to the (-)- and (+)-IP_3 compounds follows the previously established methods for the racemic compounds.

For D-(-)-IP_3, the diastereoisomer (47) was benzylated to furnish (49), and then hydrolysed using the mild $Et_3N/MeOH/H_2O$ conditions to give the diol (50) in essentially quantitative yield. This underwent hydroxyl-directed epoxidation with mCPBA to give the β-epoxide (51) in 87% yield, together with a small amount (5%) of



Scheme 8

(i) BnBr, Ag_2O, DMF, 3 days, 100%; (ii) Et_3N/MeOH/H_2O, 3 days, 99%; (iii) mCPBA, DCM, 87%;
(iv) 2,2-Dimethoxypropane, CSA, DCM, 89%; (v) (13), NaH, TMEDA, 110°C, 3 days, 95% combined yield;
(vi) H_2, 10% Pd-C, EtOH, 16 h, 100%; (vii) $^{n}BuLi$, $^{i}Pr_2NH$, THF, tetrabenzylpyrophosphate, -30°C-RT, 67%;
(viii) a. H_2, 10% Pd-C, EtOH, 48 h; b. 80% aq. TFA, 4h, 88% overall.



Scheme 9

(i) BnBr, Ag_2O, DMF, 4 days, 81%; (ii) $Et_3N/MeOH/H_2O$, 3 days, 97%; (iii) mCPBA, DCM, 72%; (iv) 2,2-Dimethoxypropane, CSA, DCM, 91%; (v) (13), TMEDA, 110°C, 3 days, 92% combined yield; (vi) H_2, 10% Pd-C, EtOH, 100%; (vii) $^{n}BuLi$, $^{i}Pr_2NH$, THF, tetrabenzylpyrophosphate, 65%; (viii) a. H_2, 10% Pd-C, EtOH; b. 80% aq. TFA, RT, 4h, 80% overall.

the corresponding α isomer which was readily removed by silica gel chromatography. The *cis*-diol (51) was protected as the acetonide (52) in the normal fashion. X-ray crystallographic studies[18] on (52) confirmed the absolute stereochemistry of the system and in addition provided important structural proof of the relative placement of oxygen substituents together with solid state conformational information. Regioselective ring opening of (52) with the hydroxide equivalent (13) discussed previously, in tetramethylethylenediamine (TMEDA), gave (54) and (53) in 58% and 37% yields, respectively. After separation, (54) was deprotected using catalytic hydrogenolysis to remove simultaneously the benzyl and chiral phenethyl substituents to provide the triol (55). The remaining steps in the synthesis followed the previous method to give (56) and ultimately D-(-)-*myo*-inositol 1,4,5-trisphosphate (-)-(1) in optically pure form, identical with an authentic sample in all respects (scheme 8).

Finally, in scheme 9 the preparation of the enantiomeric L-(+)-*myo*-inositol 1,4,5-trisphosphate (+)-(1) is presented, following essentially the same route as described for the D-(-) series.

Overall we have described a novel strategy, involving sequential introduction of oxygen substituents, from benzene to a wide range of *myo*-inositol phosphates and cyclitol derivatives. This chemistry is different to previous approaches to these important molecules which rely on the protection/deprotection of *myo*-inositol. It also allows entry to the optically pure materials without the need for further synthetic steps. Furthermore, this route gives access to derivatives and selectively protected species not readily obtainable by other methods. All of this chemistry hinges on the use of the strategically important biotransformation, microbial oxidation of benzene by *Pseudomonas putida* to *cis*-1,2-dihydroxycyclohexa-3,5-diene.

Acknowledgements

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Experimental

^{1}H nmr spectra were recorded in $CDCl_3$ unless otherwise stated using a Jeol FX 90Q, Bruker WM 250, Jeol GSX 270, Bruker WH 400 or Bruker AM 500 nmr spectrometer. ^{31}P nmr spectra were recorded at 101 MHz on a Bruker WM 250 or at 202 Mhz on a Bruker AM 500 spectrometer and referenced relative to H_3PO_4 as external standard. ^{19}F nmr spectra were recorded at 84 MHz on a Jeol FX 90Q spectrometer and referenced relative to $CFCl_3$. Infra-red spectra were recorded on a Perkin-Elmer 983G spectrometer. Mass spectra were recorded using VG 7070B, VG 12-253 and VG ZAB-E instruments; microanalyses were performed in the Imperial College Chemistry Department microanalytical laboratory. Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Optical rotations were measured using an Optical Activity AA-1000 polarimeter. Molecular modelling was performed using the MACROMODEL package,[10] on an Evans and Sutherland PS-390 graphics terminal. Diethyl ether (ether) and tetrahydofuran (THF) solvents were distilled from sodium-benzophenone ketyl; dichloromethane (DCM) from phosphorus pentoxide; toluene from sodium; acetonitrile and dimethyl sulphoxide (DMSO) from calcium hydride. Other solvents and reagents were purified by standard procedures as necessary. Petrol refers to light petroleum ether, b.p. 40-60°C, and was redistilled prior to use. Analytical thin layer chromatography was performed on pre-coated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualised by ultra-violet light, acidic ammonium molybdate (IV), basic potassium permanganate or iodine as appropriate. Preparative chromatography was performed under pressure on Merck Kieselgel 60 (230-400 mesh) unless otherwise stated. Numbering for ^{1}H nmr assignments follows the systematic (IUPAC) nomenclature. Coupling constants are measured in Hertz.

(3aα,6α,7α,7aα)-6,7-Epoxy-3a,6,7,7a-tetrahydrobenzo[d]-1,3-dioxol-2-one (4) and (3aα,6β,7β,7aα)-6,7-Epoxy-3a,6,7,7a-tetrahydrobenzo[d]-1,3-dioxol-2-one (5).- Freshly prepared sodium methoxide (0.1 ml of a 1M solution in methanol, 10 mmol) was added dropwise to a solution of diol (2) (112 mg, 1 mmol) in dimethyl carbonate (1.7 ml) and methanol (0.2 ml) at RT under argon, and stirred for 20 min. A small aliquot was removed, solvent evaporated *in vacuo* (bath temperature 22 °C) and the resulting solid was washed with a small volume of chilled (-20°C) ether and chilled (-20°C) petrol (b.p. 30-40°C) to afford the *cyclic carbonate* (3) as a beige-coloured solid, m.p. ~ 90°C (dec.); ν_{max} (film) 1763, 1365, 1332, 1175, 1038 and 750 cm^{-1}; δ (250 MHz) 6.16-6.03 (2H, m, 5-H and 6-H), 5.86-5.73 (2H, m, 4-H and 7-H), 5.40-5.26 (2H, t, J 1.6 Hz, 3a-H and 7a-H); m/z 138 (M$^+$), 94 (M$^+$-CO_2) and 66 (M$^+$-CO_2-CO); Found: M$^+$, 138.0320. $C_7H_6O_3$ requires M, 138.0317; Found: C, 60.93; H, 4.34. $C_7H_6O_3$ requires C, 60.87; H, 4.38. The remaining solution was diluted with DCM (2 ml), and mCPBA (0.30 g, 2.0 mmol) was added portionwise. After stirring at RT for 40h, the mixture was extracted with DCM and washed successively with aqueous sodium sulphite solution (x 1), aqueous sodium bicarbonate solution (x 1) and water (x 3), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (45-70% ether-petrol, gradient elution) of the residue afforded the *epoxides* (4) (73 mg, 47%) and (5) (16 mg, 10%) as white solids. Less polar (4), m.p. 87-89°C; ν_{max} (film) 3075, 3024, 1789, 1356, 1178 and 1059 cm^{-1}; δ (400 MHz) 6.38 (1H, ddd, J 10.3, 4.0 and 1.5 Hz, 5-H), 5.86 (1H, ddd, J 10.5, 2.8 and 1.3 Hz, 4-H), 5.29 (1H, dd, J 8.8 and 1.8 Hz, 7a-H), 4.97 (1H, ddd, J 8.8, 2.8 and 1.5 Hz, 3a-H), 3.67 (1H, dd, J 3.5 and 1.8 Hz, 7-H), 3.46 (1H, tt, J 3.9 and 1.0 Hz, 6-H); m/z 154 (M$^+$), 110 (M$^+$-CO_2), 94 (M$^+$-CO_2-O), 81 (M$^+$-CO_2-HCO) and 68 (M$^+$-CO_2-CO-C_2H_2); Found: M$^+$, 154.0262. $C_7H_6O_4$ requires M, 154.0266; Found: C, 54.50; H 3.91. $C_7H_6O_4$ requires C, 54.55; H 3.92%.

More polar, m.p. 107.5-108.5°C; ν_{max} (film) 1792, 1341, 1174 and 1048 cm^{-1}; δ (400 MHz) 6.55 (1H, dd, J 10.0 and 4.0 Hz, 5-H), 6.06 (1H, ddt, J 10.0, 5.5 and 1.3 Hz, 4-H), 5.22 (1H, br t, J 6.8 Hz, 3a-H), 5.08 (1H, ddd, J 8.0, 3.5 and 1.0 Hz, 7a-H), 3.77 (1H, m, 7-H), 3.57 (1H, tt, J 4.0 and 1.8 Hz, 6-H); m/z 154

(M^+), 110 (M^+-CO_2), 94 (M^+-CO_2-O), 81 (M^+-CO_2-HCO) and 68 (M^+-CO_2-CO-C_2H_2); Found: M^+, 154.0262. $C_7H_6O_4$ requires M, 154.0266; Found: C, 54.33; H 3.93. $C_7H_6O_4$ requires C, 54.55; H 3.92%.

(3aα,6β,7α,7aα)-6-(Benzyloxy)-3a,6,7,7a-tetrahydro-7-hydroxybenzo[d]-1,3-dioxol-2-one (**6**).- Camphorsulphonic acid monohydrate (1.36 g, 5.43 mmol) was added to a stirred solution of benzyl alcohol (14 ml, 135 mmol) and the epoxide (4) (4.21 g, 27.3 mmol) in DCM (150 ml) at RT under argon. After 23 1/2 h, the solution was poured into DCM and washed with dilute aqueous sodium bicarbonate solution (x 1). The aqueous layer was re-extracted (x 3) and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (25% ether-petrol to remove excess benzyl alcohol, then 75% ether-petrol) of the residue afforded the *alcohol* (6) (6.09 g, 85%) as a white solid, m.p. 53-54°C; ν_{max} (film) 3450, 1798, 1356, 1171 and 1053 cm $^{-1}$; δ (250 MHz) 7.40-7.25 (5H, m, Ph), 6.10 (1H, d, J 10.0 Hz, 5-H), 5.86 (1H, ddd, J 10.0, 3.4 and 2.0 Hz, 4-H), 5.06 (1H, br d, J 8.3 Hz, 3a-H), 4.77 (1[illegible], d, J 12 Hz, $PhC\underline{H}_2O$-), 4.69 (1H, d, J 12 Hz, $PhC\underline{H}_2O$-), 4.64 (1H, t, J 8.6 Hz, 7a-H), 3.89 (1H, dq, J 8.[illegible]nd 1.8 Hz, 6-H), 3.80 (1H, td, J 8.5 and 2.4 Hz, 7-H), 3.15 (1H, br s, -OH); m/z 262 (M^+), 176 (M^+-CO_2-[illegible]H_3O), 107 ($PhCH_2O^+$) and 91 ($PhCH_2^+$); Found: M^+, 262.0843. $C_{14}H_{14}O_5$ requires M, 262.0841; Found: C, 63.88; H, 5.36. $C_{14}H_{14}O_5$ requires C, 64.11; H, 5.38%.

(3aα,6β,7α,7aα)-6,7-Bis(benzyloxy)-3a,6,7,7a-tetrahydrobenzo[d]-1,3-dioxol-2-one (**7**).- Freshly prepared silver (I) oxide (3.08 g, 13.3 mmol) was added to a stirred solution of the alcohol (6) (2.18 g, 8.31 mmol) and benzyl bromide (3.5 ml, 29 mmol) in DMF (80 ml) at RT under argon, and the mixture stirred vigorously in the dark for 39.5h. The mixture was diluted with ether, filtered through a pad of silica which was then washed copiously with ether and DCM, and the filtrate evaporated *in vacuo*. The residue was dissolved in ether, washed with water (x 3) and brine (x 1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (40-50% ether-petrol, gradient elution) of the residue afforded the *benzyl ether* (7) (2.36 g, 81%) as a white solid, m.p. 68.5-69.5°C; ν_{max} (film) 1801, 1175, 1113 and 1050cm^{-1}; δ (500 MHz) 7.45-7.26 (10H, m, Ph), 6.12 (1H, dt, J 10.0 and 1.5 Hz, 5-H), 5.88 (1H, ddd, J 10.0, 4.0 and 2.0 Hz, 4-H), 5.10 (1H, ddt, J 8.0, 4.0 and 2.0 Hz, 3a-H), 4.89 (1H, d, J 11.0 Hz, $PhC\underline{H}_2O$-), 4.84 (1H, d, J 11.0 Hz, $PhC\underline{H}_2O$-), 4.77 (1H, d, J 12.0 Hz, $PhC\underline{H}_2O$-), 4.75 (1H, t, J 8.0 Hz, 7a-H), 4.72 (1H, d, J 12.0 Hz, $PhC\underline{H}_2O$-), 4.03 (1H, dq, J 8.0 and 2.0 Hz, 6-H), 3.74 (1H, t, J 8.4 Hz, 7-H); m/z 352 (M^+), 261 (M^+-$PhCH_2$), 107 ($PhCH_2O^+$) and 91 ($PhCH_2^+$); Found: M^+-$PhCH_2$, 261.0762. $C_{14}H_{13}O_5$ requires M-$PhCH_2$, 261.0763; Found: C, 71.86; H, 5.77. $C_{21}H_{20}O_5$ requires C, 71.58; H, 5.72%.

(1α,2α,5α,6β)-5,6-Bis(benzyloxy)-3-cyclohexene-1,2-diol (**8**).- The carbonate (7) (3.12 g, 8.85 mmol) was stirred in 1:5:1 triethylamine/methanol/water (105 ml) at RT. After 90h, the volatiles were removed *in vacuo* and the residue extracted with DCM. The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo* to afford the *diol* (8) (2.89 g, 100%) as a white gummy solid, ν_{max} (film) 3406, 3061, 3030, 1114, 1070, 737 and 698 cm^{-1}; δ (250 MHz) 7.45-7.26 (10H, m, Ph), 5.89 (2H, d, J 2.0 Hz, 3-H and 4-H), 4.93 (1H, d, J 11.6 Hz, $PhC\underline{H}_2O$-), 4.73 (1H, d, J 11.6 Hz, $PhC\underline{H}_2O$-), 4.70 (1H, d, J 11.6 Hz, $PhC\underline{H}_2O$-), 4.65 (1H, d, J 11.6 Hz, $PhC\underline{H}_2O$-), 4.31 (1H, br s, 2-H), 4.08 (1H, d, J 6.5 Hz, 5-H), 3.91 (1H, dd, J 9.0 and 6.5 Hz, 6-H), 3.72 (1H, dd, J 9.0 and 4.0 Hz, 1-H), 3.16 (1H, br s, -OH), 2.92 (1H, br s, -OH); m/z 326 (M^+), 308 (M^+-H_2O), 235 (M^+-$PhCH_2$), 176 ($PhCH_2OCH$=CH-CH_2-CHO^+), 112 (M^+-2($PhCH_2O$)), 107 ($PhCH_2O^+$) and 91 ($PhCH_2^+$); Found: M^+, 326.1515. $C_{20}H_{22}O_4$ requires M, 326.1518.

***(1α,2α,3β,4α,5α,6α)-3,4-Bis(benzyloxy)-5,6-epoxycyclohexane-1,2-diol* (10)**.- The olefin (8) (1.37 g, 5.30 mmol) was dissolved in DCM (70 ml) and pH 8 phosphate buffer solution (70 ml) added. mCPBA (3.43 g, 80%, 15.9 mmol) was added portionwise to the vigorously stirred biphasic mixture. After stirring at RT for 112h, the mixture was extracted with DCM. The organic extract was washed successively with dilute aqueous sodium sulphite solution (x 1), dilute aqueous sodium bicarbonate solution (x 1) and water (x 1), dried ($MgSO_4$) and evaporated *in vacuo* to afford the *epoxy diols* (9) and (10) (1.75 g, 97%) as a white solid and a 1:9 mixture of epoxide stereoisomers. Column chromatography (ether-ethyl acetate) of a small portion of the mixture permitted spectroscopic characterisation of the major *epoxide* (10), ν_{max} (film) 3390, 3010 and 1074 cm^{-1}; δ (500 MHz) 7.48-7.16 (10H, m, Ph), 4.76 (1H, d, J 12.0 Hz, PhC$\underline{H_2}$O-), 4.69 (1H, d, J 12.0 Hz, PhC$\underline{H_2}$O-), 4.64 (1H, d, J 12.0 Hz, PhC$\underline{H_2}$O-), 4.57 (1H, d, J 12.0 Hz, PhC$\underline{H_2}$O-), 4.18 (1H, br s, 1-H or 2-H), 3.92 (1H, t, J 3.4 Hz, 3-H or 4-H), 3.82-3.74 (2H, m, 4-H or 3-H and 2-H or 1-H), 3.56-3.54 (2H, m, 5-H and 6-H), 2.90 (1H, br s, -OH), 2.78 (1H, br s, -OH); m/z 342 (M$^+$), 251 (M$^+$-$PhCH_2$), 107 ($PhCH_2O^+$) and 91 ($PhCH_2^+$); Found: M$^+$, 342.1467. $C_{20}H_{22}O_5$ requires M, 342.1467.

***(3aα,4α,5β,6α,7α,7aα)-4,5-Bis(benzyloxy)-6,7-epoxyhexahydro-2,2-dimethylbenzo[d]-1,3-dioxole* (11) *and (3aα,4α,5β,6β,7β,7aα)-4,5-Bis(benzyloxy)-6,7-epoxyhexahydro-2,2-dimethylbenzo[d]-1,3-dioxole* (12)**.- The mixture of epoxy diols (9) and (10) (1.749 g, 5.11 mmol) was dissolved in DCM (22 ml) at RT under argon and 2,2-dimethoxypropane (50 ml) added. Camphorsulphonic acid monohydrate (64 mg, 0.26 mmol) was added and the reaction stirred at RT for 105 min. The mixture was poured into DCM and washed with dilute aqueous sodium bicarbonate solution (x 1) and water (x 1). The aqueous layers were re-extracted with DCM (x 1) and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (20-40% ether-petrol, gradient elution) of the residue afforded the *epoxy acetonides* (11) (0.163 g, 8% over 3 steps) and (12) (1.425 g, 72% over 3 steps), as a colourless oil and white solid respectively. Less polar (11), ν_{max} (film) 2989, 1382, 1371, 1248, 1220, 1074, 1040, 736 and 698 cm^{-1}; δ (400 MHz) 7.41-7.26 (10H, m, Ph), 4.88 (1H, d, J 11.5 Hz, PhC$\underline{H_2}$O-), 4.81 (1H, d, J 11.5 Hz, PhC$\underline{H_2}$O-), 4.78 (1H, d, J 11.5 Hz, PhC$\underline{H_2}$O-), 4.74 (1H, d, J 11.5 Hz, PhC$\underline{H_2}$O-), 4.58 (1H, d, J 6.0 Hz, 7a-H), 4.01 (1H, dd, J 7.0 and 6.0 Hz, 3a-H), 3.60 (1H, d, J 8.0 Hz, 5-H), 3.56 (1H, t, J 8.5 Hz, 4-H), 3.43 (1H, d, J 3.5 Hz, 6-H), 3.33 (1H, d, J 3.5 Hz, 7-H), 1.47 (3H, s, Me), 1.40 (3H, s, Me); m/z 382 (M$^+$), 367 (M$^+$-Me), 291 (M$^+$-$PhCH_2$) and 91 ($PhCH_2^+$); Found: M$^+$, 382.1769. $C_{23}H_{26}O_5$ requires M, 382.1780; Found: C, 72.13; H 6.96. $C_{23}H_{26}O_5$ requires C, 72.23; H, 6.85%.

More polar (12), m.p. 85-86°C; ν_{max} (film) 2930, 1380, 1210, 1068, 911, 737 and 699 cm^{-1}; δ (400 MHz) 7.41-7.26 (10H, m, Ph), 4.88 (1H, d, J 11.4 Hz, PhC$\underline{H_2}$O-), 4.85 (1H, d, J 11.9 Hz, PhC$\underline{H_2}$O-), 4.76 (1H, d, J 11.3 Hz, PhC$\underline{H_2}$O-), 4.74 (1H, d, J 11.9 Hz, PhC$\underline{H_2}$O-), 4.53 (1H, dd, J 8.1 and 2.0 Hz, 7a-H), 4.15 (1H, t, J 7.7 Hz, 3a-H), 3.91 (1H, dd, J 9.3 and 7.4 Hz, 4-H), 3.79 (1H, d, J 9.3 Hz, 5-H), 3.43-3.41 (2H, m, 6-H and 7-H), 1.54 (3H, s, Me), 1.38 (3H, s, Me); m/z 367 (M$^+$-Me), 291 (M$^+$-$PhCH_2$), 185 (M$^+$-Me-2($PhCH_2$)) and 91 ($PhCH_2^+$); Found: M$^+$-Me, 367.1546. $C_{22}H_{23}O_5$ requires M-Me, 367.1545); Found: C, 72.27; H, 6.87. $C_{23}H_{26}O_5$ requires C, 72.23; H, 6.85%.

***5,5-Dimethyl-1,3-dioxane-2-ethanol* (13)**.- Tosic acid monohydrate (0.29 g, 1.5 mmol) was added to a solution of 2,2-dimethylpropane-1,3-diol (15.6 g, 150 mmol), benzyl alcohol (34.2 ml, 330 mmol) and acrolein (6.68 ml, 100 mmol) in chloroform (100 ml) at RT under argon. The mixture was refluxed with removal of the water produced by Soxhlet extraction through 4Å molecular sieves. After 52h, the reaction was allowed to cool to RT, diluted with DCM and washed with dilute aqueous sodium bicarbonate solution. The aqueous phase was re-extracted and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (0-10% ether-perol, gradient elution) afforded 2-(2-benzyloxyethyl)-5,5-dimethyl-1,3-dioxane (21.5 g, 86%) as a colourless liquid, ν_{max} (film) 2954, 2853 and 1100 cm^{-1}; δ (270 MHz) 7.40-7.26 (5H, m, Ph), 4.60 (1H, t, J 5.0 Hz, 2-H), 4.50 (2H, s, $PhC\underline{H}_2O$-), 3.60 (2H, t, J 7.0 Hz, 2'-H_2), 3.60 (2H, d, J 11.0 Hz, 4-H and 6-H), 3.45 (2H, d, J 11.0 Hz, 4-H and 6-H), 1.95 (2H, td, J 7.0 and 5.0 Hz, 1'-H_2), 1.15 (3H, s, Me), 0.70 (3H, s, Me); m/z 249 (M^+-H), 159 (M^+-$PhCH_2$), 115 (M^+-$PhCH_2OCH_2CH_2$), 107 ($PhCH_2O^+$) and 91 ($PhCH_2^+$); Found; M^+-H, 249.1497. $C_{15}H_{21}O_3$ requires M-H, 249.1491; Found: C, 72.00; H, 8.98. $C_{15}H_{22}O_3$ requires C, 71.97; H, 8.86%. 10% Palladium on activated charcoal (Lancaster) (1.25 g, 10% w/w) was added to a solution of 2-(2-benzyloxyethyl)-5,5-dimethyl-1,3-dioxane (12.53 g, 50.5 mmol) in ethanol (240 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 2h the flask was reflushed with argon, the mixture filtered through a pad of celite and the solvents evaporated *in vacuo*. Column chromatography (30-50% ether-petrol, gradient elution) of the residue afforded the *alcohol* (13) (7.03 g, 88%) as a volatile, colourless liquid, ν_{max} (film) 3426, 2954, 2851, 1471, 1394, 1138, 1099, 1061, 1040, 1015 and 919 cm^{-1}; δ (270 MHz) 4.65 (1H, t, J 5.0 Hz, 2-H), 3.80 (2H, q, J 6.0 Hz, 2'-H_2), 3.65 (2H, d, J 11.5 Hz, 4-H and 6-H), 3.45 (2H, d, J 11.0 Hz, 4-H and 6-H), 2.55 (1H, t, J 6.0 Hz, -OH), 1.90 (2H, q, J 5.0 Hz, 1'-H_2), 1.10 (3H, s, Me), 0.75 (3H, s, Me); m/z 159 (M^+-H) and 115 (M^+-CH_2CH_2OH); Found: C, 59.81; H, 10.34. $C_8H_{16}O_3$ requires C, 59.97; H, 10.07 %.

***DL-4,5-Di-O-benzyl-6-O-[2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol* (14)**.- The dioxane alcohol (13) (1 ml) was added dropwise to sodium hydride (39 mg of 60% dispersion, 0.98 mmol) at RT under argon. When the effervescence had ceased (*ca.* 35 min), HMPA (0.5 ml) was added, the mixture stirred for a further 15 min and then a solution of the epoxide (12) (24.5 mg, 0.064 mmol) in THF (0.5 ml) added dropwise. The mixture was stirred at RT for 3h, at 95°C for 44h and then allowed to cool to RT. Water was added and, after 5 min, the mixture extracted with ether. The extract was washed with water (x 5) (until no HMPA remained) and brine (x 1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (25-80% ether-petrol, gradient elution) of the residue afforded the *alcohol* (14) (15 mg, 43%) as a colourless oil, ν_{max} (film) 3452, 1092 and 1041 cm^{-1}; δ (500 MHz) 7.37-7.26 (10H, m, Ph), 4.87 (1H, d, J 11.3 Hz, $PhC\underline{H}_2O$-), 4.81 (1H, d, J 10.8 Hz, $PhC\underline{H}_2O$-), 4.73 (1H, d, J 10.8 Hz, $PhC\underline{H}_2O$-), 4.72 (1H, d, J 11.3 Hz, $PhC\underline{H}_2O$-), 4.63 (1H, t, J 4.9 Hz, 2"-H), 4.45 (1H, dd, J 5.3 and 3.9 Hz, 2-H), 4.19 (1H, dd, J 6.8 and 5.5 Hz, 3-H), 4.10 (1H, m, 1'-H), 4.08 (1H, br s, -OH), 3.82-3.76 (2H, m, 1-H and 1'-H), 3.73 (1H, dd, J 9.3 and 6.8 Hz, 4-H), 3.64-3.59 (3H, m, 6-H, 4"-H and 6"-H), 3.43 (1H, d, J 11.4 Hz, 4"-H or 6"-H), 3.42 (1H, d, J 11.4 Hz, 6"-H or 4"-H), 3.38 (1H, t, J 9.1 Hz, 5-H), 2.01-1.87 (2H, m, 2'-H_2), 1.50 (3H, s, Me_2C-O), 1.40 (3H, s, Me_2C-O), 1.20 (3H, s, Me_2C-C), 0.70 (3H, s, Me_2C-C); m/z 542 (M^+), 541 (M^+-H), 527 (M^+-Me), 451 (M^+-$PhCH_2$), 345 (M^+-Me-2($PhCH_2$)), 161 ($C_8H_{17}O_3^+$), 143 ($C_8H_{15}O_2^+$), 115 ($C_6H_{11}O_2^+$) and 91 ($PhCH_2^+$); Found: M^+, 542.2869. $C_{31}H_{42}O_8$ requires M, 542.2880.

***DL-6-O-[2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol* (15)**.- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the dibenzyl ether (14) (26 mg, 0.048 mmol) in ethanol (2 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 23.5 h, the flask was reflushed with argon the mixture filtered through a pad of celite, which was washed copiously with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (15) (17 mg, 100%) as a thick oil, ν_{max} (film) 3426, 2922, 1375, 1242, 1219, 1104 and 867 cm^{-1}; δ (500 MHz) 4.62 (1H, t, J 4.9 Hz, 2"-H), 4.38 (1H, dd, J 5.1

and 4.3 Hz, 2-H), 3.97 (1H, dd, J 7.4 and 5.2 Hz, 3-H), 3.95-3.93 (2H, m, 1'-H_2), 3.75 (1H, dd, J 9.1 and 4.2 Hz, 1-H), 3.68 (1H, dd, J 10.1 and 7.5 Hz, 4-H), 3.60 (2H, dt, J 11.1 and 2.6 Hz, 4"-H and 6"-H), 3.41 (2H, d, J 12.5 Hz, 4"-H and 6"-H), 3.40 (1H, t, J 9.1 Hz, 6-H), 3.25 (1H, dd, J 10.0 and 9.2 Hz, 5-H), 1.94 (2H, ddd, J 10.2, 5.7 and 4.5 Hz, 2'-H_2), 1.51 (3H, s, Me_2C-O), 1.35 (3H, s, Me_2C-O), 1.15 (3H, s, Me_2C-C), 0.68 (3H, s, Me_2C-C); m/z 361 (M^+-H), 347 (M^+-Me), 142 ($C_8H_{14}O_2^+$) and 115 ($C_6H_{11}O_2^+$); Found: M^+-H, 361.1871. $C_{17}H_{29}O_8$ requires M-H, 361.1862.

DL-6-O-[2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol 1,4,5-tris(dibenzylphosphate) **(16)**.- n-Butyllithium (0.141 ml of a 1.55 M solution in hexanes, 0.219 mmol) was added dropwise to a solution of the triol (15) (22 mg, 0.061 mmol) in THF (2 ml) at -28°C under argon. Diisopropylamine (0.036 ml, 0.26 mmol) was immediately added and the mixture stirred at -28 - -22°C for 15 min. Tetrabenzylpyrophosphate (123 mg, 0.228 mmol) was added in one portion and the reaction allowed to warm gradually to +2°C over 85 min and then stirred at O°C for 180 min. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (30-90% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (16) (34 mg, 62% over 2 steps) as a thick oil, ν_{max} (film) 3033, 1278 and 1015 cm^{-1}; ^1H nmr δ (500 MHz) 7.45-7.15 (30H, m, Ph), 5.11-4.96 (12H, m, $PhC\underline{H_2}O$-), 4.89 (1H, q, J 7.9 Hz, 4-H), 4.72 (1H, td, J 8.1 and 3.2 Hz, 1-H), 4.56-4.50 (2H, m, 2-H and 5-H), 4.41 (1H, t, J 5.2 Hz, 2"-H), 4.24 (1H, t, J 6.8 Hz, 3-H), 3.98 (1H, dd, J 7.2 and 4.9 Hz, 6-H), 3.77 (1H, dt, J 9.2 and 6.6 Hz, 1'-H), 3.68 (1H, dt, J 9.2 and 6.9 Hz, 1'-H), 3.46 (2H, d, J 11.2 Hz, 4"-H and 6"-H), 3.30 (2H, d, J 10.9 Hz, 4"-H and 6"-H), 1.83 (2H, m, 2'-H_2), 1.47 (3H, s, Me_2C-O), 1.24 (3H, s, Me_2C-O), 1.10 (3H, s, Me_2C-C), 0.63 (3H, s, Me_2C-C); ^1H-coupled ^{31}P nmr δ (101 MHz) -1.07 (q, J 8.0 Hz), -1.38 (q, J 7.5 Hz), -1.44 (q, J 7.0 Hz); m/z (FAB+ve) 1144 (MH^+) and 91 ($PhCH_2^+$); Found: MH^+, 1143.3826. $C_{59}H_{70}O_{17}P_3$ requires MH, 1143.3778.

DL-myo-Inositol 1,4,5-trisphosphate **(1)**.- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the protected trisphosphate (16) (21 mg, 0.018 mmol) in ethanol (4 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 4 days, the flask was reflushed with argon, and the mixture filtered through a pad of celite, which was washed exhaustively with ethanol, water and finally ethanol again. The volatiles were removed *in vacuo* and the residue freeze-dried to afford the fully debenzylated material. This was stirred in 80% aqueous trifluoroacetic acid (*ca.* 2 ml) at RT for 4h. After removing the volatiles *in vacuo*, the residue was again freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 4.6 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 1 ml min^{-1}) afforded 1,4,5-IP_3 (1) (8 mg, 86%), retention time 5 min ; δ (500 MHz, D_2O, pH 9.2) 4.17 (1H, br s, 2-H), 3.99 (1H, q, J 8.6 Hz, 4-H), 3.80-3.68 (3H, m, 1-H, 5-H and 6-H), 3.55 (1H, dd, J 9.8 and 3.0 Hz, 3-H); m/z (FAB+ve) 421 (MH^+), 323 (MH^+-H_3PO_4), 126 ($C_6H_6O_3^+$) and 109 ($C_6H_5O_2^+$).

DL-4,5-Di-O-benzyl-6-O-[2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol 1-(dibenzylphosphate) **(17)**.- n-Butyllithium (0.061 ml of a 1.6 M solution in hexanes, 0.097 mmol) was added dropwise to a solution of the alcohol (14) (44 mg, 0.081 mmol) in THF (4 ml) at -35°C under argon. Diisopropylamine (0.017 ml, 0.12mmol) was immediately added and the mixture stirred at -30 - -25°C for 20 min. Tetrabenzylpyrophosphate (52 mg, 0.097 mmol) was added in one portion and the reaction allowed to warm gradually to +2°C over 4h. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (50% ether-petrol) of the residue afforded the *monophosphate* (17) (37 mg, 57% over 2 steps) as a colourless oil, ν_{max} (film) 3030, 2952, 1452, 1380, 1275, 1216, 1088, 1018, 736 and 697 cm^{-1}; ^1H nmr δ (500 MHz) 7.36-7.26 (20H, m, Ph), 5.10-5.08 (4H, m, $(PhC\underline{H}_2O)_2P$-), 4.81 (1H, d, J 11.5 Hz, $PhC\underline{H}_2O$-), 4.76 (1H, d, J 10.9 Hz, $PhC\underline{H}_2O$-), 4.73 (1H, d, J 10.9 Hz, $PhC\underline{H}_2O$-), 4.69 (1H, d, J 11.5 Hz, $PhC\underline{H}_2O$-), 4.60 (1H, td, J 8.2 and 3.8 Hz, 1-H), 4.52 (1H, dd, J 6.5 and 3.8 Hz, 2-H), 4.51 (1H, t, J 5.2 Hz, 2"-H), 4.19 (1H, t, J 6.4 Hz, 3-H), 3.88-3.80 (3H, m, 1'-H_2 and 6-H), 3.76 (1H, dd, J 9.0 and 6.8 Hz, 4-H), 3.49 (1H, dd, J 4.2 and 2.7 Hz, 4"-H or 6"-H), 3.47 (1H, dd, J 4.2 Hz and 2.7 Hz, 4"-H or 6"-H), 3.41 (1H, dd, J 8.9 and 7.5 Hz, 5-H), 3.31 (1H, d, J 11.2 Hz, 4"-H or 6"-H), 3.26 (1H, d, J 11.2 Hz, 4"-H or 6"-H), 1.90 (2H, m, 2'-H_2), 1.47 (3H, s, Me_2C-O), 1.28 (3H, s, Me_2C-O), 1.13 (3H, s, Me_2C-C), 0.63 (3H, s, Me_2C-C); ^1H-coupled ^{31}P nmr δ (202 MHz) -2.01 (sext, J 7.4 Hz); m/z (FAB+ve) 804 (MH^+), 661 (MH^+-$C_8H_{15}O_2$) and 571; Found: MH^+, 803.3560. $C_{45}H_{56}O_{11}P$ requires MH, 803.3560.

***DL-myo-Inositol 1-phosphate* (19).**- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the protected monophosphate (17) (34 mg, 0.042 mmol) in ethanol (15ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 36h, the flask was reflushed with argon, and the mixture filtered through a pad of celite, which was washed exhaustively with ethanol and DCM. The volatiles were removed *in vacuo* to afford fully debenzylated material (18). This was stirred in 80% aqueous trifluoroacetic acid (*ca.* 2 ml) at RT for 4h. After removing the volatiles *in vacuo*, the residue was again freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 4.6 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 1 ml min^{-1}) afforded 1-IP (19) (2.3 mg, 21%), retention time 4.5 min ; δ (500 MHz, D_2O) 4.10 (1H, br s, 2-H), 3.79 (1H, m, 1-H), 3.61 (1H, m, 6-H), 3.50 (1H, t, J 9.5 Hz, 4-H), 3.41 (1H, d, J 10.1 Hz, 3-H), 3.19 (1H, t, J 9.2 Hz, 5-H); m/z (FAB+ve) 261 (MH^+); Found: MH^+, 261.0375. $C_6H_{14}O_9P$ requires MH, 261.0375.

***DL-5,6-Di-O-benzyl-myo-inositol* (20).**- The dioxanyl ether (14) (2 mg, 0.004 mmol) was stirred in 80% aqueous trifluoroacetic acid (0.5 ml) at RT. After 15 1/2 h, the volatiles were removed *in vacuo* and the residue freeze-dried and subsequently washed with a small volume of deuterochloroform to afford the tetraol (20), δ (500 MHz, D_2O) 7.45-7.25 (10H, m, Ph), 4.74-4.63 (partly obscured by HOD, $PhC\underline{H}_2O$-), 3.92 (1H, t, J 2.8 Hz, 2-H), 3.63 (1H, t, J 9.7 Hz, 4-H or 5-H or 6-H), 3.61 (1H, t, J 9.7 Hz, 4-H or 5-H or 6-H), 3.54 (1H, dd, J 10.1 and 2.8 Hz, 1-H or 3-H), 3.41 (1H, dd, J 10.1 and 2.9 Hz, 3-H or 1-H), 3.28 (1H, t, J 9.4 Hz, 4-H or 5-H or 6-H); m/z 360 (M^+), 269 (M^+-$PhCH_2$), 251 (M^+-$PhCH_2$-H_2O) and 91 ($PhCH_2^+$); Found: M^+-$PhCH_2$, 269.1021. $C_{13}H_{17}O_6$ requires M-$PhCH_2$, 269.1025.

***DL-4,5-Di-O-benzyl-2,3-O-isopropylidene-6-O-methyl-myo-inositol* (21) *and DL-2,3-Di-O-benzyl-4,5-O-isopropylidene-6-O-methyl-muco-inositol* (22).**- Freshly prepared sodium methoxide (4 ml of a 1.0M solution in methanol, 4 mmol) was added dropwise to a stirred solution of the epoxide (12) (310 mg, 0.81 mmol) in methanol at RT under argon. The mixture was heated at reflux for 72h, then cooled to RT and water carefully added. After 5 min, the mixture was extracted with ether and the extracts washed with water (x 1). The aqueous layer was re-extracted with ether and the combined ethereal extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (50-70% ether-petrol, gradient elution) of the residue afforded the *alcohols* (22) (69 mg, 21%) and (21) (249 mg, 74%), both as colourless oils. Less polar (22), ν_{max} (film) 3471, 2933, 1452, 1370, 1219, 1100, 737 and 698 cm^{-1}; δ (500 MHz) 7.40-7.26 (10H, m, Ph), 4.78 (1H, d, J

11.6 Hz, PhC$\underline{H}_2$O-), 4.75 (1H, d, J 11.7 Hz, PhC$\underline{H}_2$O-), 4.70 (1H, d, J 11.6 Hz, PhC$\underline{H}_2$O-), 4.64 (1H, d, J 11.7 Hz, PhC$\underline{H}_2$O-), 4.28 (1H, t, J 5.5 Hz, 5-H), 4.20 (1H, t, J 5.6 Hz, 4-H), 3.98 (1H, dd, J 6.9 and 5.1 Hz, 3-H or 6-H), 3.94 (1H, m, 1-H), 3.75 (1H, dd, J 6.9 and 3.3 Hz, 2-H), 3.68 (1H, dd, J 6.9 and 5.3 Hz, 3-H or 6-H), 3.50 (3H, s, MeO-), 2.63 (1H, d, J 5.6 Hz, -OH), 1.50 (3H, s, Me_2C-), 1.36 (3H, s, Me_2C-); m/z 414 (M^+), 399 (M^+-Me), 323 (M^+-$PhCH_2$), 259 (M^+-$PhCH_2O$-MeO-OH) and 91 ($PhCH_2^+$); Found: M^+-Me 399.1803. $C_{11}H_{21}O_6$ requires M-Me, 399.1808; Found: C, 69.45; H 7.38. $C_{12}H_{24}O_6$ requires C, 69.54; H 7.30%.

More polar (21), ν_{max} (film) 3458, 2930, 1377, 1217, 1156, 1073, 866, 737 and 698 cm^{-1}; δ (500 MHz) 7.42-7.26 (10H, m, Ph), 4.85 (1H, d, J 11.3 Hz, PhC$\underline{H}_2$O-), 4.80 (1H, d, J 11.3 Hz, PhC$\underline{H}_2$O-), 4.73 (1H, d, J 11.3 Hz, PhC$\underline{H}_2$O-), 4.72 (1H, d, J 11.3 Hz, PhC$\underline{H}_2$O-), 4.43 (1H, dd, J 6.0 and 3.8 Hz, 2-H), 4.23 (1H, t, J 6.4 Hz, 3-H), 3.85 (1H, dd, J 8.3 and 3.8 Hz, 1-H), 3.84 (1H, dd, J 9.0 and 6.8 Hz, 4-H), 3.59 (3H, s, MeO-), 3.56 (1H, t, J 7.9 Hz, 6-H), 3.41 (1H, dd, J 9.0 and 7.5 Hz, 5-H), 2.57 (1H, br s, -OH), 1.51 (3H, s, Me-C), 1.40 (3H, s, Me-C); m/z 414 (M^+), 399 (M^+-Me), 323 (M^+-$PhCH_2$), 277 (MH^+-$PhCH_2O$-MeO) and 91 ($PhCH2^+$); Found: M^+, 414.2050. $C_{12}H_{24}O_6$ requires M, 414.2042; Found: C, 69.27; H, 7.38. $C_{12}H_{24}O_6$ requires C, 69.54; H, 7.30%.

DL-4,5-Di-O-benzyl-6-O-methyl-myo-inositol (23).- The acetonide (21) (42 mg, 0.10 mmol) was stirred in 80% aqueous trifluoroacetic acid (1 ml) at RT. After 19h, the volatiles were removed *in vacuo* and the residue extracted with ether and washed with dilute aqueous sodium bicarbonate solution (x 4). The aqueous layers were re-extracted with ether (x 1) (no residual triol present by TLC), and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (ethyl acetate) of the residue afforded the *triol* (23) (23 mg, 61%) as a white solid, m.p. 165°C; ν_{max} (film) 3339, 1123, 1051, 1034, 717 and 694 cm^{-1}; δ (500 MHz) 7.40-7.28 (10H, m, Ph), 4.95 (1H, d, J 11.3 Hz, PhC$\underline{H}_2$O-), 4.86 (2H, s, PhC$\underline{H}_2$O-), 4.73 (1H, d, J 11.3 Hz, PhC$\underline{H}_2$O-), 4.17 (1H, t, J 2.7 Hz, 2-H), 3.76 (1H, t, J 9.5 Hz, 4-H or 5-H or 6-H), 3.67 (3H, s, MeO-), 3.55-3.47 (3H, m, 1-H, 3-H and 4-H or 5-H or 6-H), 3.41 (1H, t, J 9.2 Hz, 4-H or 5-H or 6-H), 2.57 (2H, br s, -OH), 2.41 (1H, br d, J 3.7 Hz, -OH); m/z 374 (M^+), 338 (M^+-2(H_2O)), 290 (M^+-2(H_2O)-OH-MeO) and 283 (M^+-$PhCH_2O$); Found: M^+, 374.1720. $C_{21}H_{26}O_6$ requires M, 374.1729; Found: C, 67.02; H, 7.16. $C_{21}H_{26}O_6$ requires C, 67.36; H, 7.00%.

DL-4,5-O-Isopropylidine-6-O-methyl-muco-inositol (24).- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the dibenzyl ether (22) (32mg, 0.077 mmol) in ethanol (1 ml) at RT under argon. The mixture was stirred vigorously under a hydrogen atmosphere for 45.5h, the flask was then flushed with argon and the mixture filtered through a pad of celite. The celite was washed exhaustively with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (24) (18 mg, 100%) as a colourless oil, ν_{max} (film) 3407, 1372, 1220, 1092 and 1013 cm^{-1}; δ (500 MHz) 4.21 (1H, t, J 5.3 Hz, 5-H), 4.11 (1H, t, J 6.5 Hz, 4-H), 3.98 (1H, dd, J 5.2 and 4.2 Hz, 1-H), 3.93 (1H, dd, J 8.5 and 7.3 Hz, 3-H), 3.73 (1H, dd, J 8.7 and 3.7 Hz, 2-H), 3.66 (1H, t, J 5.2 Hz, 6-H), 3.51 (3H, s, MeO-), 1.52 (3H, s, Me_2C-), 1.35 (3H, s, Me_2C-); m/z 219 (M^+-Me) and 187 (M^+-Me-MeOH); Found: M^+-Me, 219.0875. $C_9H_{15}O_6$ requires M-Me, 219.0869.

DL-2,3-O-Isopropylidene-6-O-methyl-myo-inositol (25).- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the dibenzyl ether (21) (50 mg, 0.12 mmol) in ethanol (2 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 23h the flask was reflushed with argon, and the mixture filtered through a pad of celite which was washed copiously with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (25) (28 mg, 100%) as an amorphous white solid, ν_{max} (film) 3423, 1381, 1266, 1243, 1220, 1054, 1003, 866 and 736 cm^{-1}; δ (500 MHz) 4.39 (1H, dd, J 5.7 and 4.2 Hz, 2-H), 4.03 (1H, dd, J 7.4 and 5.9 Hz, 3-H), 3.86 (1H, dd, J 7.7 and 4.1 Hz, 1-H), 3.78 (1H, dd, J 9.7 and 7.5 Hz, 4-H), 3.64 (3H, s, MeO-), 3.40 (1H, t, J 7.9 Hz, 6-H), 3.35 (1H, t, J 9.0 Hz, 5-H), 1.54 (3H, s, Me_2C-), 1.38 (3H, s, Me_2C-); m/z 235 (MH^+) and 219 (M^+-Me); Found: M^+-Me, 219.0875. $C_9H_{15}O_6$ requires M-Me, 219.0869.

DL-2,3-O-Isopropylidene-6-O-methyl-myo-inositol 1,4,5-tris(dibenzylphosphate) **(26).**- DMSO (0.02 ml) was added to a solution of the triol (25) (33 mg, 0.14 mmol) in THF (5.5 ml) at RT under argon and the solution cooled to -20°C. n-Butyllithium (0.327 ml of a 1.55 M solution in hexanes, 0.507 mmol) was added dropwise followed by diisopropylamine (0.083 ml, 0.59 mmol). After 15 min at -20 - -15°C, tetrabenzylpyrophosphate (284 mg, 0.527 mmol) was added in one portion with the temperature at -15°C. The mixture was allowed to warm gradually to +2°C over 40 min and then stirred at O°C for 130 min. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (30-80% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (26) (75 mg, 61% over 2 steps) as a thick oil, ν_{max} (film) 3033, 1277, 1018, 739 and 697 cm^{-1}; ^{1}H nmr δ (500 MHz) 7.45-7.15 (30H, m, Ph), 5.11-4.98 (12H, m, $PhC\underline{H}_2O$-), 4.80 (1H, td, J 8.8 and 6.8 Hz, 5-H or 4-H), 4.67 (1H, td, J 8.2 and 3.8 Hz, 1-H), 4.52 (1H, dd, J 6.2 and 3.8 Hz, 2-H), 4.47 (1H, td, J 8.8 and 6.6 Hz, 4-H or 5-H), 4.20 (1H, t, J 6.4 Hz, 3-H), 3.81 (1H, dd, J 8.2 and 6.8 Hz, 6-H), 3.38 (3H, s, MeO-), 1.51 (3H, s, Me_2C-), 1.24 (3H, s, Me_2C-); ^{1}H-decoupled ^{31}P nmr δ (101 MHz), -1.04 (s), -1.18 (s), -1.40 (s); m/z (FAB+ve) 1037 (MNa^+), 1015 (MH^+) and 91 ($PhCH_2^+$); Found: C, 61.42; H, 5.89. $C_{52}H_{57}O_{15}P_3$ requires C, 61.54; H, 5.66%.

DL-6-O-Methyl-myo-inositol 1,4,5-trisphosphate **(27).**- Bromotrimethylsilane (0.025 ml, 0.19 mmol) was added dropwise to a stirred solution of the trisphosphate (26) (20 mg, 0.020 mmol) in DCM (1 ml) at RT under argon. After 55 min, the volatiles were removed *in vacuo*, the residue stirred with water (1 ml) for 80 min and then freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 4.6 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 1 ml min^{-1}) afforded the *trisphosphate* (27) (5.3 mg, 62%), retention time 6 min ; ^{1}H nmr δ (500 MHz, D_2O, pH 9.4) 4.15 (1H, br s, 2-H), 4.04 (1H, q, J 8.5 Hz, 4-H or 5-H), 3.87 (1H, q, J 9.2 Hz, 5-H or 4-H), 3.83 (1H, t, J 8.7 Hz, 6-H), 3.51 (1H, br d, J 8.8 Hz, 3-H), 3.45-3.35 (4H, m, including s at δ 3.42 (1-H and MeO-)); ^{31}P nmr δ (101 MHz, D_2O, pH 9.4), 6.78 (1P, s), 5.31 (1P, s), 3.64 (1P, s); m/z (FAB+ve) 435 (MH^+), 126 ($C_6H_6O_3^+$) and 109 ($C_6H_5O_2^+$); Found: MH^+, 434.9868. $C_7H_{18}O_{15}P_3$ requires MH, 434.9859.

(3aα,4β,6β,7α,7aα)-6,7-Bis(benzyloxy)hexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-4-ol **(28)** ***and (3aα,5β,6β,7α,7aα)-6,7-Bis(benzyloxy)hexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-5-ol*** **(29).**- A solution of the epoxide (12) (315 mg, 0.824 mmol) in ether (13 ml) was added to a stirred suspension of lithium aluminium hydride (88mg, 2.3 mmol) in ether (5 ml) under argon. The mixture was heated at reflux for 2h and then allowed to cool to RT. Water was added dropwise to give a white precipitate which was stirred for 40 min. The mixture was diluted with ethyl acetate, solid sodium bicarbonate added to form a crunchy solid and the mixture filtered. The solids were washed with ethyl acetate and the filtrate evaporated *in vacuo*. Column chromatography (40-75% ether-petrol, gradient elution) of the residue afforded the *alcohols* (29) (38 mg, 12%) and (28) (241 mg, 76%), both as colourless oils. Less polar (29), ν_{max} (film) 3492, 1368, 1241, 1218, 1091 and 1047cm^{-1}; δ (500MHz) 7.42-7.26 (10H, m, Ph), 4.92 (1H, d, J 11.3 Hz, $PhC\underline{H}_2O$-), 4.82 (1H, d, J 11.3 Hz, $PhC\underline{H}_2O$), 4.76 (1H, d, J 11.9 Hz, $PhC\underline{H}_2O$-), 4.71 (1H, d, J 11.9 Hz, $PhC\underline{H}_2O$-), 4.32 (1H, td, J 4.7 and 2.8 Hz, 3a-H), 4.14-4.11 (2H, m, 5-H and 7a-H), 4.00 (1H, dd, J 9.6 and 6.9 Hz, 7-H), 3.33 (1H, dd, J 9.6 and 2.7 Hz, 6-H), 2.75 (1H, d, J 6.6 Hz, -OH), 2.43 (1H, dt, J 15.8 and 3.4 Hz, 4 eq-H), 1.78 (1H, ddd, J 15.9, 4.4 and 3.6 Hz, 4 ax-H), 1.50 (3H, s, Me), 1.36 (3H, s, Me): m/z 384 (M^+), 369 (M^+-Me), 293 (M^+-$PhCH_2$), 202 (M^+-2($PhCH_2$)), 107 ($PhCH_2O^+$) and 91 ($PhCH_2^+$); Found: M^+, 384.1945. $C_{23}H_{28}O_5$ requires M, 384.1937; Found: C, 72.14; H, 7.48. $C_{23}H_{28}O_5$ requires C, 71.85; H, 7.34%.

More polar (28), ν_{max} (film) 3432, 1380, 1241, 1218 and 1065 cm^{-1}; δ (500 MHz) 7.40-7.26 (10H, m, Ph), 4.86 (1H, d, J 11.5 Hz, $PhC\underline{H}_2O$-), 4.78 (1H, d, J 11.5 Hz, $PhC\underline{H}_2O$-), 4.67 (2H, s, $PhC\underline{H}_2O$-), 4.29 (1H, dd, J 5.3 and 4.2 Hz, 3a-H), 4.16 (1H, t, J 6.2 Hz, 7a-H), 3.89 (1H, ddt, J 10.9, 8.2 and 4.2 Hz, 4-H), 3.70 (1H, dd, J 8.8 and 6.6 Hz, 7-H), 3.42 (1H, ddd, J 10.4, 8.9 and 4.8 Hz, 6-H), 2.16 (1H, d, J 8.6 Hz, -OH), 2.15 (1H, dt, J 12.7 and 4.2 Hz, 5 eq-H), 1.87 (1H, dt, J 12.7 and 10.7 Hz, 5 ax-H), 1.50 (3H, s, Me), 1.39 (3H, s, Me); m/z 384 (M^+), 369 (M^+-Me), 293 (M^+-$PhCH_2$) and 187 (MH^+-$PhCH_2O$); Found: C, 71.65; H, 7.56. $C_{23}H_{28}O_5$ requires C, 71.85; H, 7.34%.

***(3aα,4α,5β,7β,7aα)-Hexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-4,5,7-triol* (30)**.- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the dibenzyl ether (28) (71 mg, 0.18 mmol) in ethanol (6 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 39h the flask was reflushed with argon and the mixture filtered through a pad of celite which was washed copiously with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (30) (38 mg, 100%) as an amorphous white solid, ν_{max} (film) 3431, 1380, 1242, 1219 and 1052 cm^{-1}; δ (500 MHz) 4.32 (1H, dd, J 5.6 and 4.1 Hz, 7a-H), 4.02 (1H, ddt, J 9.9, 7.4 and 4.4 Hz, 7-H), 3.97 (1H, dd, J 7.5 and 5.8 Hz, 3a-H), 3.70 (1H, dd, J 9.4 and 7.5 Hz, 4-H), 3.49 (1H, m, 5-H), 2.51 (1H, br d, J 2.6 Hz, -OH), 2.34 (1H, br d, J 3.2 Hz, -OH), 2.16 (1H, d, J 7.7 Hz, 7-OH), 2.16 (1H, dt, J 12.9 and 4.6 Hz, 6 eq-H), 1.84 (1H, dt, J 13.0 and 9.9 Hz, 6 ax-H), 1.55 (3H, s, Me), 1.40 (3H, s, Me); m/z 205 (MH^+) and 189 (M^+-Me); Found: M^+-Me, 189.0763. $C_8H_{13}O_5$ requires M-Me, 189.0763.

***(1α,2α,3α,4β,5α)-1,2,3,4,5-Cyclohexanepentol* (31)**.- Acetonide (30) (50 mg, 0.25 mmol) was stirred in 80% aqueous trifluoroacetic acid (5 ml) at RT for 4h. After removing the volatiles *in vacuo*, the residue was freeze-dried, and the crude product purified by column chromatography (33% $CHCl_3$-IPA) to afford the *pentol* (31) (39 mg, 97%) as a white solid, m.p. >220°C; δ (500 MHz, D_2O) 3.86 (1H, dt, J 2.7 and 1.3 Hz, 2-H), 3.66 (1H, ddd, J 12.3, 4.5 and 2.7 Hz, 1-H), 3.41-3.33 (2H, m, 4-H and 5-H), 3.29 (1H, dd, J 9.7 and 2.9 Hz, 3-H), 1.85 (1H, dtd, J 11.9, 4.4 and 1.3 Hz, 6 eq-H), 1.63 (1H, q, J 11.9 Hz, 6 ax-H); m/z (FAB+ve) 165 (MH^+), 131 (MH^+-2(OH)), 109 and 57; Found: MH^+, 165.0685. $C_6H_{13}O_5$ requires MH, 165.0607.

***(3aα,4α,5β,7β,7aα)-Hexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-4,5,7-triol tris(dibenzylphosphate)* (32)**.- n-Butyllithium (0.144 ml of a 2.5 M solution in hexanes, 0.36 mmol) was added dropwise to a solution of the triol (30) (21 mg, 0.10 mmol) in THF (4 ml) at -32°C under argon. Diisopropylamine (0.061 ml, 0.44 mmol) was immediately added and the mixture stirred at -29 - -25°C for 15 min. Tetrabenzylpyrophosphate (200 mg, 0.37 mmol) was added in one portion and the reaction allowed to warm up gradually over 80 min and then stirred at +2°C for a further 210 min. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (30-100% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (32) (57 mg, 56% over 2 steps) as a thick oil, ν_{max} (film) 1273, 1013, 738 and 697 cm^{-1}; ^{1}H nmr δ (500 MHz) 7.40-7.16 (30H, m, Ph), 5.10-4.93 (12H, m, PhC$\underline{H}_2$O-), 4.57 (1H, td, J 9.3 and 7.2 Hz, 4-H), 4.52 (1H, ddt, J 12.2, 8.0 and 4.1 Hz, 7-H), 4.36 (1H, t, J 4.1 Hz, 7a-H), 4.18 (1H, m, 5-H), 4.00 (1H, dd, J 7.1 and 4.9 Hz, 3a-H), 2.43 (1H, dt, J 12.5 and 4.4 Hz, 6 eq-H), 2.19 (1H, q, J 12.0 Hz, 6 ax-H), 1.55 (3H, s, Me), 1.24 (3H, s, Me); ^{1}H-decoupled ^{31}P nmr δ (101 MHz) -1.91(s), -1.24 (s), -1.40 (s); m/z (FAB+ve) 985 (MH$^+$), 895 (M$^+$+2H-PhCH$_2$) and 91 (PhCH$_2$$^+$); Found: MH$^+$, 985.2824. $C_{51}H_{56}O_{14}P_3$ requires MH, 985.2754; Found: C, 62.23; H, 5.77. $C_{51}H_{55}O_{14}P_3$ requires C, 62.19; H, 5.63%.

(1α,2β,3α,4α,5α)-1,2,3,4,5-Cyclohexanepentol 1,2,5-trisphosphate (33).- Bromotrimethylsilane (0.028 ml, 0.21 mmol) was added dropwise to a stirred solution of the trisphosphate (32) (22 mg, 0.022 mmol) in DCM (1 ml) at RT under argon. After 65 min the volatiles were removed *in vacuo*, and the residue stirred with water (3 ml) for 80 min and then freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 4.6 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 1 ml min^{-1}) afforded the *trisphosphate* (33) (7.1 mg, 79%), retention time 5 min ; ^{1}H nmr δ (500 MHz, D_2O, pH 9.4) 4.01 (1H, s, 4-H), 3.91 (2H, br s, (-C$\underline{H}$OP(O)(OH)$_2$)$_2$), 3.76 (1H, br s, -C$\underline{H}$OP(O)(OH)$_2$), 3.47 (1H, d, J 6.9 Hz, 3-H), 2.17 (1H, d, J 10.5 Hz, 6 eq-H), 1.74 (1H, q, J 10.5 Hz, 6 ax-H); ^{31}P nmr δ (101 MHz), 5.93 (br s); m/z (FAB+ve) 427 (MNa$^+$), 405 (MH$^+$), 126 ($C_6H_6O_3{}^+$) and 109 ($C_6H_5O_2{}^+$); Found: MH$^+$, 404.9787. $C_6H_{16}O_{14}P_3$ requires MH, 404.9753.

(3aα,4β,5α,6β,7α,7aα)-6,7-Bis(benzyloxy)-5-fluorohexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-4-ol (34) ***and (3aα,4α,5β,6β,7α,7aα)-6,7-Bis(benzyloxy)-4-fluorohexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-5-ol*** (35).- Tris(dimethylamino)sulphur (trimethylsilyl)difluoride (TASF) (358 mg, 1.3 mmol) was dried in a flask fitted with a reflux condensor under argon. A solution of the epoxide (12) (50 mg, 0.13 mmol) in anhydrous THF (10 ml) was added dropwise and the mixture heated at reflux for 5 days. After cooling to RT water was added to quench the reaction, and the mixture extracted with ether. The organic extracts were washed with water (x 1), and the aqueous layer re-extracted with ether (x 1). The combined organic phase was dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (20-50% ether-petrol, gradient elution) of the residue afforded the *alcohols* (35) (5 mg, 10%) and (34) (20 mg, 38%) as oils, and starting *epoxide* (12) (18 mg, 36%). Less polar (35), ν_{max} (film) 3452, 1370, 1219, 1073 and 1026 cm^{-1}; ^{1}H nmr δ (500MHz) 7.38-7.28 (10H, m, Ph), 4.81 (1H, ddd, J 50.5, 8.4 and 5.2 Hz, 4-H), 4.73 (1H, d, J 11.7 Hz, PhC$\underline{H}_2$O-), 4.71 (1H, d, J 11.4 Hz, PhC$\underline{H}_2$O-), 4.64 (1H, d, J 11.7 Hz, PhC$\underline{H}_2$O-), 4.52 (1H, d, J 11.5 Hz, PhC$\underline{H}_2$O-), 4.36-4.29 (2H, m, 3a-H and 7a-H), 4.07-4.01 (2H, m, 5-H and 7-H), 3.84 (1H , m, 6-H), 2.39 (1H, d, J 6.9 Hz, -OH), 1.49 (3H, s, Me), 1.38 (3H, s, Me); ^{19}F nmr δ (84 MHz) -199 (ddd, J 49, 20 and 10 Hz); m/z 402 (M$^+$), 387 (M$^+$-Me), 311 (M$^+$-HF-PhCH$_2$) and 91 (PhCH$_2$$^+$); Found: M$^+$-Me, 387.1604. $C_{22}H_{24}O_5F$ requires M-Me, 387.1608.

More polar (34), ν_{max} (film) 3436 and 1047 cm^{-1}; ^{1}H nmr δ (500 MHz) 7.39-7.26 (10H, m, Ph), 4.80 (1H, ddd, J 51.5, 8.6 and 7.1 Hz, 5-H), 4.79 (1H, d, J 11.5 Hz, PhC$\underline{H}_2$O-), 4.72 (2H, d, J 12.7 Hz, PhC$\underline{H}_2$O-), 4.66 (1H, d, J 11.5 Hz, PhC$\underline{H}_2$O-), 4.46 (1H, dt, J 6.3 and 4.1 Hz, 3a-H), 4.30 (1H, t, J 6.1 Hz, 7a-H), 4.04 (1H, m, 4-H), 3.82 (1H, dd, J 7.3 and 6.0 Hz, 7-H), 3.64 (1H, dt, J 18.4 and 7.1 Hz, 6-H), 2.42 (1H, d, J 6.1 Hz, -OH), 1.49 (3H, s, Me), 1.37 (3H, s, Me); ^{19}F nmr δ (84 MHz) -196 (dddd, J 51, 18, 12 and 4 Hz); m/z 402 (M$^+$), 387 (M$^+$-Me), 311 (M$^+$-PhCH$_2$), 291 (M$^+$-PhCH$_2$-HF), 279 (M$^+$-Me-PhCH$_2$OH) and 91

($PhCH_2^+$); Found: M^+-Me, 387.1604. $C_{22}H_{24}O_5F$ requires M-Me, 387.1608; Found: C, 68.49; H, 6.83. $C_{23}H_{27}O_5F$ requires C, 68.64; H, 6.76%.

***(3aα,4α,5β,6α,7β,7aα)-6-Fluorohexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-4,5,7-triol* (36)**.- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the dibenzyl ether (34) (62 mg, 0.15 mmol) in ethanol (5 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 17h, the flask was reflushed with argon the mixture filtered through a pad of celite, which was washed copiously with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (36) (35 mg, 100%) as a thick oil, ν_{max} (film) 3521, 1369, 1119 and 1006 cm^{-1}; δ (500 MHz) 4.61 (1H, dt, J 51.6 and 8.1 Hz, 6-H), 4.48 (1H, m, 7a-H), 4.10 (1H, dd, J 7.1 and 5.9 Hz, 3a-H), 4.05 (1H, ddd, J 12.8, 7.8 and 4.2 Hz, 7-H), 3.81 (1H, dd, J 9.7 and 7.7 Hz, 4-H), 3.60 (1H, dt, J 14.1 and 9.2 Hz, 5-H), 1.55 (3H, s, Me), 1.40 (3H, s, Me); m/z 207 (M^+-Me) and 189 (M^+-Me-H_2O); Found: M^+-Me, 207.0670. $C_8H_{12}O_5F$ requires M-Me, 207.0669.

(1α,2α,3α,4β,5α,6β)-6-Fluoro-1,2,3,4,5-cyclohexanepentol (37).- Acetonide (36) (22 mg, 0.10 mmol) was stirred in 80% aqueous trifluoroacetic acid (3 ml) at RT for 4h. After removing the volatiles *in vacuo*, the residue was freeze-dried, and the crude product purified by column chromatography (33% $CHCl_3$-IPA) to afford the *pentol* (37) (18 mg, 100%) as a white powder, ^1H nmr δ (500 MHz, D_2O) 4.69 (1H, dt, J 53.0 and 9.3 Hz, 6-H), 3.95-3.92 (1H, m, 2-H), 3.69 (1H, ddd, J 12.5, 9.7 and 3.0 Hz, 1-H), 3.52 (1H, t, J 9.7 Hz, 4-H), 3.48-3.44 (1H, m, 5-H), 3.43 (1H, dd, J 9.8 and 2.9 Hz, 3-H); ^{19}F nmr δ (84 MHz) -200.6 (dt, J 53.7 and 12.5 Hz); m/z (FAB+ve) 183 (MH^+), 164 (M^+-H_2O) and 131 (M^+-3(OH)); Found: MH^+, 183.0669. $C_6H_{11}O_5F$ requires MH, 183.0669.

(3aα,4α,5β,6α,7β,7aα)-6-Fluorohexahydro-2,2-dimethylbenzo[d]-1,3(2H)-dioxol-4,5,7-triol tris(dibenzylphosphate) (38).- n-Butyllithium (0.21 ml of a 2.5 M solution in hexanes, 0.53 mmol) was added dropwise to a solution of the triol (36) (33 mg, 0.15 mmol) in THF at -30°C under argon. Diisopropylamine (0.088 ml, 0.63 mmol) was immediately added and the mixture stirred at -30 - -25°C for 15 min. Tetrabenzylpyrophosphate (291 mg, 0.54 mmol) was added in one portion, and the reaction allowed to warm gradually to -2°C over 4h, and then stirred at 0-10°C for a further 90 min. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (30-100% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (38) (116 mg, 77% over 2 steps) as a thick oil, ν_{max} (film) 1274 and 1019 cm^{-1}; ^1H nmr δ (500 MHz) 7.39-7.18 (30H, m, Ph), 5.12-4.95 (12H, m, $PhC\underline{H_2}O$-), 4.84 (1H, ddd, J 51.0, 9.5 and 7.4 Hz, 6-H), 4.81-4.61 (3H, m, 4-H, 5-H and 7-H), 4.52 (1H, dt, J 5.5 and 4.2 Hz, 7a-H), 4.19 (1H, t, J 5.8 Hz, 3a-H), 1.50 (3H, s, Me), 1.22 (3H, s, Me); ^1H decoupled ^{31}P nmr δ (101 MHz) -1.37 (d, J 0.9 Hz), -1.45 (s), -1.47 (s); ^{19}F nmr δ (84 MHz) -196 (d, J 54 Hz); m/z 1003 (MH^+), 913 (MH^++H-$PhCH_2$) and 91 ($PhCH_2^+$); Found: MH^+, 1003.2816. $C_{51}H_{55}O_{14}P_3F$ requires MH, 1003.2789.

(1α,2β,3α,4α,5α,6β)-6-Fluoro-1,2,3,4,5-cyclohexanepentol 1,2,5-trisphosphate (39).- Bromotrimethylsilane (0.070 ml, 0.53 mmol) was added dropwise to a stirred solution of the trisphosphate (38) (51 mg, 0.051 mmol) in DCM (1 ml) at RT under argon. After 65 min, the volatiles were removed *in vacuo*, the residue stirred with water (2 ml) for 80 min and then freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 4.6 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 1 ml min^{-1}) afforded the *trisphosphate* (39) (20 mg, 93%), retention time 9 min ; ^{1}H nmr δ (500 MHz, D_2O, pH 9.0) 4.44 (1H, dt, J 52.1 and 7.7 Hz, 6-H), 4.09 (1H, br s, 4-H), 3.99-3.95 (3H, m, -C<u>H</u>OP(O)$(OH)_3$), 3.59 (1H, d, J 5.8 Hz, 3-H); ^{31}P nmr δ (101 MHz) 6.85 (1P, br s), 5.86 (1P, s), 5.27 (1P, br s); ^{19}F nmr δ (84 MHz) -196.4 (d, J 53.7 Hz); m/z (FAB+ve) 445 (MNa^+), 423 (MH^+) and 109 ($C_6H_5O_2^+$); Found: MH^+, 422.96587. $C_6H_{16}O_{14}P_3$ requires MH, 422.96586.

***(3aα,4β,5α,6β,7α,7aα)-6,7-Bis(benzyloxy)hexahydro-2,2,5-trimethylbenzo[d]-1,3(2H)-dioxol-4-ol* (40) *and* *(3aα,4α,5β,6β,7α,7aα)-6,7-Bis(benzyloxy)hexahydro-2,2,4-trimethylbenzo[d]-1,3(2H)-dioxol-5-ol* (41)**.- Methyllithium (22.3 ml of a solution in ether, 31.4 mmol) was added dropwise to a stirred solution of copper (I) cyanide (1.4 mg, 16 mmol) in THF (15 ml) at -78°C under argon. The reaction was allowed to warm gradually to -30°C, then a solution of the epoxide (12) (300 mg, 0.78 mmol) in THF (10 ml) was added. After 22h at -30°C , saturated aqueous ammonium chloride solution (60 ml) was added, and the mixture stirred at RT for a further 2h. The mixture was then extracted with ether, dried ($MgSO_4$) and evaporated *in vacuo* . Column chromatography (15% ether- petrol) of the residue afforded the *alcohols* (41) (10 mg, 3%) and (40) (219 mg, 71%), as an oil and white solid respectively, and starting *epoxide* (12) (6 mg, 2%). Less polar (41), ν_{max} (film) 3483, 2923, 1452, 1378, 1217,1027, 736 and 698 cm^{-1}; δ (270 MHz) 7.45-7.30 (10H, m, Ph), 4.86 (1H, d, J 11.5 Hz, PhC<u>H</u>$_2$O-), 4.77 (1H, d, J 11.7 Hz, PhC<u>H</u>$_2$O-), 4.75 (1H, d, J 11.5 Hz, PhC<u>H</u>$_2$O-), 4.60 (1H, d, J 11.5 Hz, PhC<u>H</u>$_2$O-), 4.21 (1H, t, J 5.6 Hz, 7a-H), 4.04 (1H, dd, J 7.8 and 5.9 Hz, 7-H), 3.98 (1H, t, J 5.2 Hz, 3a-H), 3.69 (1H, m, 5-H), 3.58 (1H, dd, J 7.8 and 3.4 Hz, 6-H), 2.64 (1H, br d, J 8.1 Hz, -OH), 2.31 (1H, m, 4-H), 1.50 (3H, s, Me_2C-), 1.36 (3H, s, Me_2C-), 1.03 (3H, d, J 7.3 Hz, Me); m/z 398 (M^+), 383 (M^+-Me), 307 (M^+-$PhCH_2$), 216 (M^+-2($PhCH_2$)), 201 (M^+-Me-2($PhCH_2$)) and 91 ($PhCH_2^+$); Found: C, 72.28; H, 7.64. $C_{24}H_{30}O_5$ requires C, 72.34; H, 7.59%.

More polar (40), m.p. 92-94°C; ν_{max} (film) 3440, 1460, 1380, 1220, 1090, 1070, 1033, 748 and 697 cm^{-1}; δ (270 MHz) 7.45-7.25 (10H, m, Ph), 4.90 (1H, d, J 10.8 Hz, PhC<u>H</u>$_2$O-), 4.85 (1H, d, J 10.8Hz, PhC<u>H</u>$_2$O-), 4.72 (1H, d, J 11.5 Hz, PhC<u>H</u>$_2$O-), 4.54 (1H, d, J 10.8 Hz, PhC<u>H</u>$_2$O-), 4.36 (1H, dd, J 5.6 and 3.7 Hz, 3a-H), 4.20 (1H, t, J 6.0 Hz, 7a-H), 3.72 (1H, dd, J 9.0 and 6.6 Hz, 7-H), 3.48 (1H, ddd, J 5.6, 5.6 and 3.9 Hz, 4-H), 2.99 (1H, t, J 9.0 Hz, 6-H), 1.95 (1H, m, 5-H), 1.58 (1H, d, -OH), 1.48 (3H, s, Me_2C-), 1.39 (3H, s, Me_2C-), 1.17 (3H, d, J 6.6 Hz, Me); m/z 398 (M^+), 383 (M^+-Me), 307 (M^+-$PhCH_2$), 201 (M^+-Me-2($PhCH_2$)) and 91 ($PhCH_2^+$); Found: C, 72.47; H, 7.35. $C_{24}H_{30}O_5$ requires C, 72.34; H, 7.59%.

***(3aα,4α,5β,6α,7β,7aα)-Hexahydro-2,2,6-trimethylbenzo[d]-1,3(2H)-dioxol-4,5,7-triol* (42)**.- 10% Palladium on activated charcoal (Lancaster) (catalytic amount) was added to a solution of the dibenzyl ether (42) (109 mg, 0.28 mmol) in ethanol (10 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 16h, the flask was reflushed with argon the mixture filtered through a pad of celite, which was washed copiously with ether . Evaporation of the solvents *in vacuo* afforded the *triol* (42) (116 mg, 97%) as a white solid, m.p. 118-120°C; ν_{max} (film) 3446, 1369, 1242, 1082, 1032 and 876 cm^{-1}; δ (270 MHz) 4.36 (1H, dd, J 5.3 and 5.2 Hz, 7a-H), 3.96 (1H, dd, J 7.6 and 5.4 Hz, 3a-H), 3.64 (1H, dd, J 9.5 and 7.7 Hz, 4-H), 3.49 (1H, br dd, J 9.9 and 3.7 Hz, 7-H), 3.01 (1H, t, J 10.0 Hz, 5-H), 2.69 (1H, br s, -OH), 2.43 (1H, br s, -OH), 2.01 (1H, br d, J 8.8 Hz, -OH), 1.83 (1H, m, 6-H), 1.53 (3H, s, Me_2C-), 1.39 (3H, s, Me_2C-), 1.19 (3H, d, J 6.6 Hz, Me); m/z 203 (M^+-Me), 185 (M^+-Me-H_2O), 167 (M^+-Me-2(H_2O)) and 149 (M^+-Me-3(H_2O)); Found: C, 55.06; H, 8.41. $C_{10}H_{18}O_5$ requires C, 55.04; H, 8.31%.

(1α,2α,3α,4β,5α,6β)-6-Methyl-1,2,3,4,5-cyclohexanepentol **(43)**.- Acetonide (42) (20 mg, 0.09 mmol) was stirred in 80% aqueous trifluoroacetic acid (7 ml) at RT for 5h. After removing the volatiles *in vacuo*, the residue was freeze-dried, and the crude product purified by column chromatography (50-60% IPA-$CHCl_3$, gradient elution) to afford the *pentol* (43) (13 mg, 79%) as an oil, ν_{max} (film) 3358, 2918, 1670, 1462, 1201, 1139, 1088, 1040, 1018 and 908 cm^{-1}; δ (500 MHz, D_2O) 3.86 (1H, t, J 2.8 Hz, 2-H), 3.41 (1H, t, J 9.5 Hz, 4-H), 3.31 (1H, dd, J 10.1 and 3.0 Hz, 3-H), 3.20 (1H, dd, J 11.3 and 2.4 Hz, 1-H), 2.90 (1H, dd, J 10.5 and 9.2 Hz, 5-H), 1.65 (1H, m, 6-H), 0.94 (3H, d, J 6.5 Hz, Me); m/z 178 (M^+), 160 (M^+-H_2O), 142 (M^+-2(H_2O)), 124 (M^+-3(H_2O)), 88 (M^+-5(H_2O)) and 73 (M^+-5(H_2O)-Me); Found: MNH_4^+, 196.1185. $C_7H_{18}NO_5$ requires MNH_4, 196.1185.

(3aα,4α,5β,6α,7β,7aα)-Hexahydro-2,2,6-trimethylbenzo[d]-1,3(2H)-dioxol-4,5,7-triol tris(dibenzylphosphate) **(44)**.- n-Butyllithium (0.32 ml of a 1.6 M solution in hexanes, 0.50 mmol) was added dropwise to a solution of the triol (42) (31 mg, 0.14 mmol) in THF (2 ml) at -30°C under argon. Diisopropylamine (0.08 ml, 0.59 mmol) was added after 1h and the mixture stirred at -30 - -25°C for 15 min. Tetrabenzylpyrophosphate (266 mg, 0.53 mmol) was added in one portion and the reaction allowed to warm up gradually over 90 min and then stirred at 0°C for a further 3h. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (40-100% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (44) (57 mg, 41%) as a thick oil, ν_{max} (film) 3032, 2957, 2894, 1587, 1495, 1381, 1274, 1022, 738 and 697 cm^{-1}; δ (270 MHz) 7.34-7.20 (30H, m, Ph), 5.18-4.95 (12H, m, $PhC\underline{H_2}O$-), 4.64 (1H, dt, J 8.6 and 6.8 Hz, 4-H), 4.51 (1H, dd, J 5.4 and 3.7 Hz, 7a-H), 4.29 (1H, ddd, J 11.8 and 3.7 Hz, 7-H), 4.16-4.06 (2H, m, 3a-H and 5-H), 2.38 (1H, m, 6-H), 1.52 (3H, s, Me_2C-), 1.22 (3H, s, Me_2C-), 1.16 (3H, d, J 6.8 Hz, Me); m/z 615 (M^+-PO_4Bn_2-OBn), 453 (M^+-6(OBn)), 277 ($PO_4Bn_2^+$), 107 (BnO^+) and 91 ($PhCH_2^+$) ; Found: C, 62.42; H, 5.91. $C_{52}H_{57}O_{14}P_3$ requires C, 62.52; H, 5.75%.

(1α,2β,3α,4α,5α,6β)-6-Methyl-1,2,3,4,5-cyclohexanepentol 1,2,5-trisphosphate **(45)**.- Bromotrimethylsilane (0.070 ml, 0.53 mmol) was added dropwise to a stirred solution of the trisphosphate (44) (56 mg, 0.056 mmol) in DCM (3 ml) at RT under argon. After 65 min, the volatiles were removed *in vacuo*, the residue stirred with water (9 ml) for 80 min and then freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 4.6 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 1 ml min^{-1}) afforded the *trisphosphate* (45) (19 mg, 82%), retention time 9 min ; ^1H nmr δ (500 MHz, D_2O, pH 7.0) 4.08 (2H, br s, 2-H and 4-H), 3.66 (2H, m, 1-H and 5-H), 3.48 (1H, d, J 7.0 Hz, 3-H), 1.91 (1H, br d, J 6.0 Hz, 6-H), 0.96 (3H, d, J 6.2 Hz, Me); ^{31}P nmr δ (101 MHz) 6.74 (1P, br s), 5.47 (1P, s), 3.90 (1P, br s); m/z (FAB+ve) 441 (MNa^+), 419 (MH^+) and 207 (M^+-2(PO_4H_3)-Me).

(R)-(+)-sec-Phenethyl alcohol **(46)**.- Borane-methyl sulphide complex (68 ml, 0.71 mol) was added dropwise to a solution of (S)-(+)-mandelic acid (98.5 g, 0.65 mol) in THF (900 ml) at RT under a flow of argon over 3h. The reaction was stirred for 6h, then methanol was added dropwise and stirring continued for a further 13h. The volatiles were then removed *in vacuo*, the residue stirred in methanol, and the process repeated (x 3). Column chromatography (MeOH-ethyl acetate-petrol, gradient elution) of the residue afforded the *diol* (57.3 g, 64%). *p*-Toluenesulphonyl chloride (80 g, 98%, 0.41 mol) was then added portionwise to a solution of the *diol* in pyridine (700 ml) at 0°C over 8h. The reaction was stirred at RT for 13h, then the volatiles removed *in vacuo*. The residue was washed with water (x 3), dried ($MgSO_4$), and the residual pyridine removed *in vacuo* to afford the *tosylate* as an orange oil. A solution of the tosylate in ether/THF (500 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (15.6 g, 0.41 mol) in ether (500 ml) at RT under argon. The reaction was stirred for 16h, then water (15.6 ml), aqueous sodium hydroxide solution (15.6 ml), and water (46.8 ml) were successively added dropwise. After 4h, sodium sulphate was added and stirring continued. The mixture was filtered through a pad of celite, washed with DCM, and the solvents evaporated *in vacuo*. Column chromatography (0-100% ether-petrol, gradient elution) followed by distillation (b.p. 96°C/ ~20mmHg) afforded the *alcohol* (46) (24.1g, 48% over 2 steps) as a colourless liquid, $[\alpha]_D^{27}$ +41.48° (neat) (lit.$[\alpha]_D^{22}$ +44.16°(neat)); ν_{max} (film) 3354, 2972, 1490, 1449, 1077, 900, 760 and 699 cm $^{-1}$; δ (500 MHz) 7.39 (5H, m, Ph), 4.88 (1H, dq, J 6.7 and 4.0 Hz, CHMe), 2.09 (1H, d, J 4.0 Hz, -OH), 1.50 (3H, d, J 6.7 Hz, CHMe); m/z 122 (M^+), 107 (M^+-Me), 79 and 77; Found: C, 73.38; H, 8.40. $C_8H_{10}O$ requires C, 78.65; H, 8.25%. Preparation of Mosher's ester indicated single diastereomer.

***[3aR-[3aα,4α,5β(R),7aα]-3a,4,5,7a-Tetrahydro-4-hydroxy-5-(1-phenylethoxy)benzo[d]-1,3-dioxol-2-one* (47) *and [3aS-[3aα,4α,5β(R),7aα]-3a,4,5,7a-Tetrahydro-4-hydroxy-5-(1-phenylethoxy)benzo[d]-1,3-dioxol-2-one* (48)**.- Tetrafluoroboric acid-diethyl ether complex (catalytic amount) was added to a stirred solution of epoxide (±)-(4) (32 mg, 0.2 mmol) and (R)-(+)-*sec*-phenethyl alcohol (46) (0.048 ml, 0.4 mmol) in DCM at RT under argon. After 30 min, water was added and the mixture extracted with DCM (x 3). The combined organic phase was dried ($MgSO_4$) and evaporated *in vacuo* . Column chromatography (30-75% ether-petrol, gradient elution) of the residue afforded the *alcohols* (47) and (48) (37 mg, 67%) as a thick oil and a 1:1 mixture of diastereomers. Subsequent HPLC (1" Dynamax 83,123-6 column; 6% IPA-petrol, 15 ml min^{-1}) effected separation of the diastereomers. Less polar (47), retention time 16.3 min; $[\alpha]_D^{20}$ +90.1° (c 1.1, $CHCl_3$); ν_{max} (film) 3452, 3030, 1797, 1356, 1169, 1050, 763 and 703 cm $^{-1}$; δ (500 MHz) 7.36-7.23 (5H, m, Ph), 5.80 (1H, br d, J 10.2 Hz, 6-H), 5.68 (1H, ddd, J 10.3, 3.5 and 1.5 Hz, 7-H), 4.99 (1H, dd, J 7.7 and 3.4 Hz, 7a-H), 4.86 (1H, q, J 6.4 Hz, PhCH(Me)O-), 4.57 (1H, m, 3a-H), 3.80 (2H, m, 4-H and 5-H), 2.65 (1H, br s, -OH), 1.47 (3H, d, J 6.5 Hz, Me); m/z 276 (M^+), 261 (M^+-Me), 190 (M^+-CO_2-C_2H_3O), 121 ($PhCH(Me)O^+$) and 105 ($PhCHMe^+$); Found: MNH_4^+, 294.1341. $C_{15}H_{20}NO_5$ requires MNH_4, 294.1341; Found: C, 64.96; H, 6.08. $C_{15}H_{16}O_5$ requires C, 65.21; H, 5.84%.

More polar (48), retention time 19 min; $[\alpha]_D^{20}$ +36.1° (c 1.73, $CHCl_3$); ν_{max} (film) 3462, 3061, 1797, 1355, 1170, 1050, 762 and 703 cm $^{-1}$; δ (500 MHz) 7.35-7.27 (5H, m, Ph), 6.16 (1H, br d, J 10.3 Hz, 6-H), 5.88 (1H, br dd, J 10.2 and 1.2Hz, 7-H), 5.01 (1H, br d, J 8.1Hz, 7a-H), 4.69 (1H, q, J 6.8 Hz, PhCH(Me)O-), 4.49 (1H, dd, J 8.1 and 7.9 Hz, 3a-H), 3.70 (2H, m, 4-H and 5-H), 3.21 (1H, br s, -OH), 1.49 (3H, d, J 6.6 Hz, Me); m/z 276 (M^+), 261 (M^+-Me), 190 (M^+-CO_2-C_2H_3O), 121 ($PhCH(Me)O^+$) and 105 ($PhCHMe^+$); Found: MNH_4^+, 294.1341. $C_{15}H_{20}NO_5$ requires MNH_4, 294.1341; Found: C, 65.11; H, 5.79. $C_{15}H_{16}O_5$ requires C, 65.21; H, 5.84%.

***[3aS-[3aα,6β(R),7α,7aα]-7-Benzyloxy-3a,6,7,7a-tetrahydro-6-(1-phenylethoxy)benzo[d]-1,3-dioxol-2-one* (49)**.- Freshly prepared silver (I) oxide (88 mg, 0.38 mmol) was added to a stirred solution of the alcohol (47) (53 mg, 0.19 mmol) and benzyl bromide (0.080 ml, 0.67 mmol) in DMF (2 ml) at RT under argon and the mixture stirred vigorously in the dark for 64h. The mixture was diluted with ether, filtered through a pad of silica which was then washed copiously with ether and DCM, and the filtrate evaporated *in vacuo*. The residue was dissolved in ether, washed with water (x 5) and brine (x 1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (30-100% ether-petrol, gradient elution) of the residue afforded the *benzyl ether* (49) (70 mg, 100%) as needles, m.p. 97-99°C; $[\alpha]_D^{20}$ +102.9° (c 1.0, $CHCl_3$); ν_{max} (film)

1810, 1175, 1110 and 1050 cm^{-1}; δ (500 MHz) 7.45-7.27 (10H, m, Ph), 5.82 (1H, dt, J 10.3 and 1.5 Hz, 5-H), 5.72 (1H, ddd, J 10.2, 3.4 and 2.3 Hz, 4-H), 5.01 (1H, dt, J 8.0 and 1.7 Hz, 3a-H), 4.92 (1H, d, J 11.1 Hz, $PhC\underline{H}_2O$-), 4.86 (1H, d, J 11.1 Hz, $PhC\underline{H}_2O$-), 4.82 (1H, q, J 6.5 Hz, $PhC\underline{H}Me$), 4.68 (1H, t, J 8.2 Hz, 7a-H), 3.86 (1H, ddd, J 10.0, 3.8 and 1.8 Hz, 6-H), 3.73 (1H, t, J 8.3 Hz, 7-H), 1.48 (3H, d, J 6.5 Hz, Me); m/z 275 (M^+-$PhCH_2$), 261 (M^+-PhCH(Me)), 121 (PhCH(Me)O^+), 105 ($PhCHMe^+$) and 91 ($PhCH_2^+$); Found: C, 72.33; H, 6.06. $C_{22}H_{22}O_5$ requires C, 72.11; H, 6.05%.

[1S-[1α,2α,5α(R),6β]]-6-Benzyloxy-5-(1-phenylethoxy)-3-cyclohexene-1,2-diol **(50)**.- The carbonate (49) (0.459 g, 1.25 mmol) was stirred in 1:5:1 triethylamine/methanol/water (12 ml) at RT. After 72h, the volatiles were removed *in vacuo* and the residue freeze-dried. The crude product was purified by column chromatography (50-100% ethyl acetate-petrol, gradient elution) to afford the *diol* (50) (0.421 g, 99%) as a white solid, m.p. 46-47°C; $[\alpha]_D^{20}$ +82.4° (c 2.5, $CHCl_3$); ν_{max} (film) 3408, 3060, 3030, 2972, 1491, 1449, 1110, 1082, 748 and 700 cm^{-1}; δ (500 MHz) 7.41-7.26 (10H, m, Ph), 5.73 (1H, ddd, J 10.2, 3.9 and 1.3 Hz, 3-H or 4-H), 5.52 (1H, dd, J 10.3 and 2.5 Hz, 3-H or 4-H), 4.88 (1H, d, J 11.6 Hz, $PhC\underline{H}_2O$-), 4.73 (1H, d, J 11.6 Hz, $PhC\underline{H}_2O$-), 4.66 (1H, q, J 6.5 Hz, $PhC\underline{H}$(Me)), 4.26 (1H, dd, J 4.4 and 4.3 Hz, 2-H), 3.88 (2H, m, 5-H and 6-H), 3.75 (1H, dt, J 7.1 and 5.0 Hz, 1-H), 3.06 (1H, d, J 5.5 Hz, 1-OH), 2.59 (1H, d, J 5.8 Hz, 2-OH), 1.47 (3H, d, J 6.4 Hz, $PhCH\underline{Me}$); m/z 325 (M-Me^+), 249 (M^+-$PhCH_2$), 190 (PhCH(Me)OCH=CH-CH_2-CHO^+), 121 (PhCH(Me)O^+), 105 ($PhCHMe^+$) and 91 ($PhCH_2^+$); Found: C, 74.20; H, 7.35. $C_{21}H_{24}O_4$ requires C, 74.09; H, 7.11%.

[1R-[1α,2α,3β,4α(R),5α,6α)-3-Benzyloxy-5,6-epoxy-4-(1-phenylethoxy)cyclohexane-1,2-diol (51).- mCPBA (2.68 g, 80%, 12.4 mmol) was added to a stirred solution of olefin (50) (2.111 g, 6.2 mmol) in DCM (30 ml) at RT under argon. After stirring for 48h, cyclohexene was added dropwise (excess) and the mixture stirred for 90 min. The solvents were removed *in vacuo* to afford the *epoxy diol* (51) (1.93 g, 92%) as a foam and a 17:1 mixture of epoxide stereoisomers. Column chromatography (10-50% ethyl acetate-petrol, gradient elution) yielded the major *epoxide* (51) (1.928 g, 87%) as a foam, $[\alpha]_D^{20}$ +98.9° (c 0.92, $CHCl_3$); ν_{max} (film) 3422, 3028, 2975, 2926, 1491, 1449, 1120, 1085, 890, 735 and 702 cm^{-1}; δ (500 MHz) 7.40-7.28 (10H, m, Ph), 4.71-4.66 (3H, m, $PhC\underline{H}$(Me)O- and $PhC\underline{H}_2O$-), 4.14 (1H, dd, J 4.4 and 3.1 Hz, 1-H), 3.79 (1H, dd, J 7.1 and 5.0 Hz, 3-H), 3.71 (1H, dd, J 4.7 and 3.2 Hz, 4-H), 3.69 (1H, dd, J 7.1 and 4.8 Hz, 2-H), 3.50 (2H, br s, -OH), 3.36 (1H, t, J 3.6 Hz, 5-H), 3.13 (1H, t, J 3.4 Hz, 6-H), 1.48 (3H, d, J 6.5 Hz, $PhCH\underline{Me}$); m/z 356 (M^+), 341 (M^+-Me), 265 (M^+-$PhCH_2$), 251 (M^+-PhCHMe), 156, 139, 121 (PhCH(Me)O^+), 105 ($PhCHMe^+$) and 91 ($PhCH_2^+$) ; Found: C, 70.77; H, 6.73. $C_{21}H_{24}O_5$ requires C, 70.77; H, 6.79%.

[3aR-[3aα,4α,5β(R),6β,7β,7aα)-4-Benzyloxy-6,7-epoxy-5-(1-phenylethoxy)hexahydro-2,2-dimethylbenzo[d]-1,3-dioxole (52).- Camphorsulphonic acid monohydrate (catalytic amount) was added to a stirred solution of epoxy diol (51) (0.321 g, 0.9 mmol) in 2,2-dimethoxypropane (10 ml) at RT under argon. After 16h, the mixture was poured into DCM and washed with aqueous sodium bicarbonate solution (x 1) and water (x 1). The aqueous layers were re-extracted with DCM (x 1) and the combined organic extracts dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (50% ether-petrol) of the residue afforded the *epoxy acetonide* (52) (0.317 g, 89%) as needles, m.p. 114-115°C (recrystallised from ether-petrol); $[\alpha]_D^{20}$ +134.1° (c 1.00, $CHCl_3$); ν_{max} (film) 2978, 2931, 1450, 1379, 1213, 1082, 1026, 704 and 663 cm^{-1}; δ (500 MHz) 7.45-7.27 (10H, m, Ph), 4.89 (1H, d, J 11.3 Hz, $PhC\underline{H}_2O$-), 4.82 (1H, q, J 6.5 Hz, $PhC\underline{H}Me$-), 4.77 (1H, d, J

11.3 Hz, PhC$\underline{H}_2$O-), 4.43 (1H, dd, J 8.1 and 2.8 Hz, 7a-H), 4.05 (1H, t, J 7.8 Hz, 3a-H), 3.85 (1H, dd, J 9.3 and 7.7 Hz, 4-H), 3.59 (1H, dd, J 9.3 and 0.6 Hz, 5-H), 3.25 (1H, dd, J 4.2 and 2.7 Hz, 7-H), 3.05 (1H, dd, J 4.1 and 0.6 Hz, 6-H), 1.51 (3H, s, Me), 1.48 (3H, d, J 6.5 Hz, PhCH$\underline{Me}$), 1.34 (3H, s, Me); m/z 381 (M^+-Me), 305 (M^+-PhCH$_2$), 291 (M^+-PhCHMe), 185, 121 (PhCH(Me)O^+), 105 (PhCHMe$^+$) and 91 (PhCH$_2^+$); Found: C, 73.02; H 7.27. $C_{24}H_{28}O_5$ requires C, 72.70; H, 7.12%.

***[2(R)]-L-3-O-Benzyl-4,5-O-isopropylidene-6-O-[2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl]-2-O-(phenylethyl)-muco-inositol* (53) *and* *[5(R)]-D-4-O-Benzyl-2,3-O-isopropylidene-6-O-[2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl]-5-O-(phenylethyl)-myo-inositol* (54).**- The dioxane alcohol (13) (2 ml) was added dropwise to sodium hydride (396 mg of 60% dispersion, 10 mmol) at RT under argon. When the effervescence had ceased, TMEDA (1 ml) was added, the mixture stirred for a further 4h and then a solution of the epoxide (52) (396 mg, 1.0 mmol) in TMEDA (1.0 ml) was added dropwise. The mixture was stirred at 100-110°C for 3 days and then allowed to cool to RT. Water was added and, after 5 min, the mixture extracted with ether. The extract was washed with water (x 2) and the aqueous phase re-extracted with ether. The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (4% MeOH-10% ether-86% petrol) of the residue afforded the *alcohols* (53) (176 mg, 31%) and (54) (273 mg, 48%), as a thick oil and a white solid respectively, and *starting epoxide* (65 mg, 16%). Less polar (53), $[\alpha]_D^{20}$ +63.4° (c 1.4, $CHCl_3$); ν_{max} (film) 3474, 2932, 1450, 1369, 1219, 1097, 1027 and 700 cm^{-1}; δ (500 MHz) 7.38- 7.24 (10H, m, Ph), 4.77 (1H, d, J 11.7 Hz, PhC$\underline{H}_2$O-), 4.70 (1H, q, J 6.5 Hz, PhC$\underline{H}$Me), 4.69 (1H, d, J 11.6 Hz, PhC$\underline{H}_2$O-), 4.46 (1H, t, J 5.1 Hz, 2"-H), 4.24 (1H, t, J 5.3 Hz, 4-H), 4.13 (1H, t, J 5.3 Hz, 5-H), 3.98 (1H, dd, J 7.2 and 4.9 Hz, 3-H), 3.72 (1H, dd, J 6.5 and 4.8 Hz, 6-H), 3.70-3.65 (2H, m, 1-H and 1'-H), 3.62 (1H, dd, J 7.2 and 2.8 Hz, 2-H), 3.58 (2H, d, J 11.1 Hz, 4"-H and 6"-H), 3.44 (1H, dt, J 9.6 and 6.2 Hz, 1'-H), 3.39 (2H, d, J 11.2 Hz, 4"-H and 6"-H), 2.82 (1H, br s, -OH), 1.77 (2H, m, 2'-H), 1.50 (3H, s, $\underline{Me}_2$CO), 1.45 (3H, d, J 6.5 Hz, PhCH$\underline{Me}$), 1.35 (3H, s, $\underline{Me}_2$CO), 1.17 (3H, s, Me), 0.71 (3H, s, Me); m/z 556 (M^+), 541 (M^+-Me), 465 (M^+-PhCH$_2$), 451 (M^+-PhCHMe), 115 ($C_6H_{11}O_2^+$), 105 (PhCHMe$^+$) and 91 (PhCH$_2^+$). More polar (54), m.p. 108-110°C; $[\alpha]_D^{20}$ +29.3° (c 0.76, $CHCl_3$); ν_{max} (film) 3437, 2954, 1451, 1378, 1212, 1094, 911 and 734 cm^{-1}; δ (500 MHz) 7.44- 7.24 (10H, m, Ph), 4.91 (1H, d, J 11.4 Hz, PhC$\underline{H}_2$O-), 4.88 (1H, q, J 6.4 Hz, PhC$\underline{H}$Me), 4.77 (1H, d, J 11.4 Hz, PhC$\underline{H}_2$O-), 4.52 (1H, t, J 5.2 Hz, 2"-H), 4.39 (1H, dd, J 5.6 and 3.9 Hz, 2-H), 4.15 (1H, dd, J 6.5 and 5.9 Hz, 3-H), 3.91 (1H, d, J 1.6 Hz, -OH), 3.79 (1H, ddd, J 14.6, 5.9 and 4.3 Hz, 1'-H), 3.74 (1H, dd, J 8.9 and 6.8 Hz, 4-H), 3.68 (1H, ddd, J 9.0, 3.8 and 1.6 Hz, 1-H), 3.60-3.55 (3H, m, 1"-H, 4"-H and 6"-H), 3.50 (1H, t, J 8.6 Hz, 6-H), 3.40 (1H, d, J 11.1 Hz, 4"-H or 6"-H), 3.39 (1H, d, J 11.2 Hz, 6"-H or 4"-H), 3.31 (1H, t, J 8.6 Hz, 5-H), 1.78 (2H, m, 2'-H), 1.52 (3H, s, $\underline{Me}_2$CO), 1.42 (3H, d, J 6.4 Hz, PhCH$\underline{Me}$), 1.38 (3H, s, $\underline{Me}_2$CO), 1.17 (3H, s, Me), 0.69 (3H, s, Me); m/z 541 (M^+-Me), 451 (M^+-PhCHMe), 345, 241, 176, 105 (PhCHMe$^+$) and 91 (PhCH$_2^+$); Found: C, 69.03; H 8.16. $C_{32}H_{44}O_8$ requires C, 69.04; H, 7.97%.

***D-6-O-[2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol* (55).**- 10% Palladium on activated charcoal (Fluka) (catalytic amount) was added to a solution of the dibenzyl ether (54) (105 mg, 0.18 mmol) in ethanol (10 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 16h, the flask was reflushed with argon and the mixture filtered through a pad of celite, which was washed copiously with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (55) (65 mg, 100%) as a white solid, m.p. 96.5-97.5°C; $[\alpha]_D^{20}$ +24.7° (c 0.45, $CHCl_3$); spectral data identical to previously prepared racemic material (15).

D-6-O-[2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol 1,4,5-tris(dibenzylphosphate) **(56)**.- n-Butyllithium (0.172 ml of a 2.5 M solution in hexanes, 0.43 mmol) was added dropwise to a solution of the triol (55) (45 mg, 0.12 mmol) in THF (4 ml) at -30°C under argon. Diisopropylamine (0.073 ml, 0.52 mmol) was then added and the mixture stirred at -30 - -25°C for 20 min. Tetrabenzylpyrophosphate (242 mg, 0.45 mmol) was added in one portion and the reaction allowed to warm gradually to + 2°C over 4h. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (30-100% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (56) (95 mg, 67%) as a thick oil, $[\alpha]_D^{20}$ -4.5° (c 1.13, $CHCl_3$); spectral data identical to previously prepared racemic material (16).

D-(-)-myo-Inositol 1,4,5-trisphosphate **(-)-(1)**.- 10% Palladium on activated charcoal (Fluka) (catalytic amount) was added to a solution of the protected trisphosphate (56) (243 mg, 0.21 mmol) in ethanol (10 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 48h, the flask was reflushed with argon, the mixture filtered and washed with ethanol. The volatiles were removed *in vacuo* and the residue freeze-dried to afford fully debenzylated material. This was stirred in 80% aqueous trifluoroacetic acid (*ca.* 6 ml) at RT for 4h. After removing the volatiles *in vacuo*, the residue was again freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 202 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 12 ml min^{-1}) afforded 1,4,5-IP_3 (-)-(1) (64 mg, 88%), retention time 42 min, $[\alpha]_D^{22}$ -24° (c 0.15, H_2O, pH 6.9); spectral data identical to previously prepared racemic material (±)-(1).

[3aR-[3aα,6α(R),7β,7aα]-7-Benzyloxy-3a,6,7,7a-tetrahydro-6-(1-phenylethoxy)benzo[d]-1,3-dioxol-2-one **(57)**.- Freshly prepared silver (I) oxide (0.79 g, 3.4 mmol) was added to a stirred solution of the alcohol (48) (0.476 g, 1.7 mmol) and benzyl bromide (0.717 ml, 6.0 mmol) in DMF (15 ml) at RT under argon and the mixture stirred vigorously in the dark for 3 days. The mixture was diluted with ether, filtered through a pad of silica which was then washed copiously with ether and DCM, and the filtrate evaporated *in vacuo*. The residue was dissolved in ether, washed with water (x 5) and brine (x 1), dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (30% ether-petrol) of the residue afforded the *benzyl ether* (57) (0.509g, 81%) as granules, m.p. 91-92°C; $[\alpha]_D^{20}$ -30.7° (c 0.90, $CHCl_3$); ν_{max} (film) 3029, 2973, 2926, 2881, 1811, 1353, 1177, 1114, 1052, 762, 739 and 700 cm^{-1}; δ (500 MHz) 7.38-7.26 (10H, m, Ph), 6.20 (1H, dt, J 10.3 and 1.5 Hz, 5-H), 5.90 (1H, ddd, J 10.2, 3.4 and 1.9 Hz, 4-H), 5.05 (1H, ddd, J 6.8, 3.3 and 1.4 Hz, 3a-H), 4.81 (2H, s, $PhC\underline{H_2}O$-), 4.72 (1H, q, J 6.5 Hz, $PhC\underline{H}Me$), 4.64 (1H, t, J 8.1 Hz, 7a-H), 3.90 (1H, ddd, J 7.9, 3.4 and 1.8 Hz, 6-H), 3.67 (1H, t, J 8.1 Hz, 7-H), 1.49 (3H, d, J 6.5 Hz, Me); m/z 351 (M^+-Me), 275 (M^+-$PhCH_2$), 261 (M^+-PhCH(Me)), 121 ($PhCH(Me)O^+$), 105 ($PhCHMe^+$) , 91 ($PhCH_2^+$) and 77 (Ph^+); Found: C, 72.33; H, 6.06. $C_{22}H_{22}O_5$ requires C, 72.11; H, 6.05%.

[1R-[1α,2α,5α(R),6β]]-6-Benzyloxy-5-(1-phenylethoxy)-3-cyclohexene-1,2-diol **(58)**.- The carbonate (57) (0.509 g, 1.39 mmol) was stirred in 1:5:1 triethylamine/methanol/water (14 ml) at RT. After 70h, the volatiles were removed *in vacuo* and the residue freeze-dried. The crude product was purified by column chromatography (50% ethyl acetate-petrol) to afford the *diol* (58) (0.459g, 97%) as a colourless oil, $[\alpha]_D^{20}$ +19.5° (c 1.7, $CHCl_3$); ν_{max} (film) 3404, 3030, 2971, 2919, 1490, 1449, 1081, 1030, 746 and 699 cm^{-1}; δ (500 MHz) 7.36-7.24 (10H, m, Ph), 5.96 (1H, dd, J 10.3 and 2.6 Hz, 5-H), 5.87 (1H, ddd, J 10.2, 3.9 and

1.3 Hz, 6-H), 4.79 (1H, d, J 11.6 Hz, PhC<u>H</u>$_2$O-), 4.70 (1H, q, J 6.5 Hz, PhC<u>H</u>(Me)), 4.56 (1H, d, J 11.6 Hz, PhC<u>H</u>$_2$O-), 4.29 (1H, br d, J 3.9 Hz, 1-H), 3.88 (1H, ddd, J 5.9, 2.6 and 1.3 Hz, 4-H), 3.78 (1H, dd, J 8.3 and 5.9 Hz, 3-H), 3.66 (1H, dt, J 8.4 and 4.2 Hz, 2-H), 3.05 (1H, d, J 4.7 Hz, -OH), 2.67 (1H, d, J 5.1 Hz, -OH), 1.47 (3H, d, J 6.8 Hz, PhCH<u>Me</u>); m/z 249 (M^+-PhCH$_2$), 235 (M^+-PhCHMe), 190 (PhCH(Me)OCH=CH-CH$_2$-CHO$^+$), 121 (PhCH(Me)O$^+$), 105 (PhCHMe$^+$) and 91 (PhCH$_2^+$); Found: MNH$_4^+$, 358.2018. $C_{21}H_{28}NO_4$ requires MNH$_4$, 358.2018; Found: C, 74.15; H, 7.05. $C_{21}H_{24}O_4$ requires C, 74.09; H, 7.11%.

***1S-[1α,2α,3β,4α(R),5α,6α)-3-Benzyloxy-5,6-epoxy-4-(1-phenylethoxy)cyclohexane-1,2-diol* (59)**.- mCPBA (6.80 g, 80%, 19.7 mmol) was added to a stirred solution of olefin (58) (3.778 g, 11.1 mmol) in DCM (40 ml) at RT under argon. After stirring for 48h, cyclohexene was added dropwise (excess) and the mixture stirred for 14h. The solvents were removed *in vacuo* to afford the *epoxy diol* (59) (3.01 g, 76%) as a foam and a 19:1 mixture of epoxide stereoisomers. Column chromatography (10-50% ethyl acetate-petrol, gradient elution) yielded the major *epoxide* (59) (72%) as a gum, $[\alpha]_D^{20}$ +43.8° (c 1.04, CHCl$_3$); ν_{max} (film) 3446, 2926, 1449, 1076, 901, 736 and 700 cm^{-1}; δ (500 MHz) 7.40-7.16 (10H, m, Ph), 4.81 (1H, q, J 6.4 Hz, PhC<u>H</u>Me), 4.44 (1H, d, J 11.8 Hz, PhC<u>H</u>$_2$O-), 4.37 (1H, d, J 11.8 Hz, PhC<u>H</u>$_2$O-), 4.13 (1H, dd, J 4.5 and 1.9 Hz, 1-H), 3.78 (2H, m, 2-H and 3-H or 4-H), 3.71 (1H, dd, J 5.8 and 2.6 Hz, 4-H or 3-H), 3.53 (2H, m, 5-H and 6-H), 2.90 (2H, br s, -OH), 1.49 (3H, d, J 6.4 Hz, PhCH<u>Me</u>); m/z 356 (M^+), 265 (M^+-PhCH$_2$), 251 (M^+-PhCHMe), 121 (PhCH(Me)O$^+$), 105 (PhCHMe$^+$) and 91 (PhCH$_2^+$); Found: C, 70.75; H, 6.90. $C_{21}H_{24}O_5$ requires C, 70.77; H, 6.79%.

***[3aS-[3aα,4α,5β(R),6β,7β,7aα)-4-Benzyloxy-6,7-epoxy-5-(1-phenylethoxy)-hexahydro-2,2-dimethylbenzo[d]-1,3-dioxole* (60)**.- Camphorsulphonic acid monohydrate (catalytic amount) was added to a stirred solution of epoxy diol (59) (0.314 g, 0.88 mmol) in 2,2-dimethoxypropane (10 ml) at RT under argon. After 4h, the mixture was poured into DCM and washed with aqueous sodium bicarbonate solution (x 1) and water (x 1). The aqueous layers were re-extracted with DCM (x 1) and the combined organic extracts dried (MgSO$_4$) and evaporated *in vacuo*. Column chromatography (50% ether-petrol) of the residue afforded the *epoxy acetonide* (60) (0.319 g, 91%) as a thick oil, $[\alpha]_D^{20}$ -2.5° (c 1.0, CHCl$_3$); ν_{max} (film) 2982, 2927, 1452, 1373, 1210, 1085, 1033, 912, 734 and 699 cm^{-1}; δ (500 MHz) 7.36-7.24 (10H, m, Ph), 4.83 (1H, q, J 6.2 Hz, PhC<u>H</u>Me-), 4.82 (1H, d, J 11.8 Hz, PhC<u>H</u>$_2$O-), 4.72 (1H, d, J 11.3 Hz, PhC<u>H</u>$_2$O-), 4.47 (1H, dd, J 8.1 and 2.7 Hz, 7a-H), 4.04 (1H, t, J 7.6 Hz, 3a-H), 3.81 (1H, dd, J 9.2 and 7.6 Hz, 4-H), 3.68 (1H, d, J 9.2 Hz, 5-H), 3.52 (1H, d, J 4.3 Hz, 6-H), 3.43 (1H, dd, J 4.2 and 2.7 Hz, 7-H), 1.51 (3H, s, Me), 1.50 (3H, d, J 6.0 Hz, PhCH<u>Me</u>), 1.33 (3H, s, Me); m/z 381 (M^+- Me), 305 (M^+-PhCH$_2$), 291 (M^+-PhCHMe), 185, 121 (PhCH(Me)O$^+$), 105 (PhCHMe$^+$) and 91 (PhCH$_2^+$); Found MNH$_4^+$, 414.2280. $C_{24}H_{32}NO_5$ requires MNH$_4$, 411.2280.

***[5(R)]-L-4-O-Benzyl-2,3-O-isopropylidene-6-O-[2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl]-5-O-[phenylethyl]-myo-inositol* (61)**.- The dioxane alcohol (13) (2 ml) was added dropwise to sodium hydride (396 mg of 60% dispersion, 10 mmol) at RT under argon. When the effervescence had ceased, TMEDA (1 ml) was added, the mixture stirred for a further 4h, and then a solution of the epoxide (60) (396 mg, 1.0 mmol) in TMEDA (1.0 ml) was added dropwise. The mixture was stirred at 100-110°C for 3 days and then allowed to cool to RT. Water was added and, after 5 min, the mixture extracted with ether. The extract was washed with water (x 2) and the aqueous phase re-extracted with ether. The combined organic extracts were dried (MgSO$_4$)

and evaporated *in vacuo*. Column chromatography (1% MeOH-10% ethyl acetate-89% petrol) of the residue afforded the *starting epoxide* (181 mg, 46%) and the *alcohol* (61) (236 mg, 42%) as a thick oil, $[\alpha]_D^{20}$ +7.2° (c 0.72, $CHCl_3$); ν_{max} (film) 3462, 2963, 1460, 1369, 1213, 1097, 1028, 918 and 734 cm^{-1}; δ (500 MHz) 7.31-7.17 (10H, m, Ph), 4.85 (1H, q, J 6.4 Hz, PhCHMe), 4.70 (1H, d, J 11.2 Hz, $PhCH_2O$-), 4.66 (1H, t, J 5.2 Hz, 2"-H), 4.48 (1H, d, J 11.2 Hz, $PhCH_2O$-), 4.42 (1H, dd, J 5.7 and 3.9 Hz, 2-H), 4.15 (1H, ddd, J 10.5, 6.5 and 4.0 Hz, 1'-H), 4.13 (1H, dd, J 6.5 and 5.9 Hz, 3-H), 3.91 (1H, d, J 1.9 Hz, -OH), 3.85 (1H, ddd, J 10.3, 7.5 and 4.1 H z, 1'-H), 3.79 (1H, ddd, J 8.9, 3.8 and 2.0 Hz, 1-H), 3.66 (1H, dd, J 8.8 and 6.8 Hz, 6-H), 3.62 (3H, m, 4-H, 4"-H and 6"-H), 3.37 (1H, t, J 8.5 Hz, 5-H), 2.00 (2H, m, 2'-H), 1.50 (3H, s, Me_2CO), 1.45 (3H, d, J 6.4 Hz, PhCHMe), 1.37 (3H, s, Me_2CO), 1.20 (3H, s, Me), 0.72 (3H, s, Me); m/z 541 (M^+-Me), 465 (M^+-$PhCH_2$), 451 (M^+-PhCHMe), 345, 241, 176, 143, 115 ($C_6H_{11}O_2^+$), 105 ($PhCHMe^+$) and 91 ($PhCH_2^+$).

L-6-O-[2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol **(62)**.- 10% Palladium on activated charcoal (Fluka) (catalytic amount) was added to a solution of the dibenzyl ether (61) (189 mg, 0.33 mmol) in ethanol (7 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 16h the flask was reflushed with argon, and the mixture filtered, and washed with ether and then DCM. Evaporation of the solvents *in vacuo* afforded the *triol* (62) (122 mg, 100%) as a white solid, m.p. 96-97°C; $[\alpha]_D^{20}$ -24.2° (c 0.57, $CHCl_3$); spectral data identical to previously prepared racemic material (15).

L-6-O-[2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethyl]-2,3-O-isopropylidene-myo-inositol 1,4,5-tris(dibenzylphosphate) **(63)**.- n-Butyllithium (0.480 ml of a 2.5 M solution in hexanes, 1.2 mmol) was added dropwise to a solution of the triol (62) (120 mg, 0.33 mmol) in THF (5 ml) at -30°C under argon. Diisopropylamine (0.196 ml, 1.4mmol) was then added and the mixture stirred at -30 - -25°C for 20 min. Tetrabenzylpyrophosphate (646 mg, 1.2 mmol) was added in one portion and the reaction allowed to warm gradually to + 4°C over 4h. The precipitated lithium dibenzylphosphate was filtered off, the cake washed with THF and the solvent evaporated *in vacuo*. Column chromatography (40-100% ethyl acetate-petrol, gradient elution) of the residue afforded the *trisphosphate* (63) (247 mg, 65%) as a gum, $[\alpha]_D^{20}$ +4.3° (c 0.37, $CHCl_3$); spectral data identical to previously prepared racemic material (16).

L-(+)-myo-Inositol 1,4,5-trisphosphate **(+)-(1)**.- 10% Palladium on activated charcoal (Fluka) (catalytic amount) was added to a solution of the protected trisphosphate (63) (243 mg, 0.21 mmol) in ethanol (10 ml) at RT under argon. The flask was flushed through with hydrogen and the mixture stirred vigorously under a hydrogen atmosphere. After 40h, the flask was reflushed with argon, and the mixture filtered and washed with ethanol. The volatiles were removed *in vacuo* and the residue freeze-dried to afford fully debenzylated material. This was stirred in 80% aqueous trifluoroacetic acid (*ca*. 5 ml) at RT for 6h. After removing the volatiles *in vacuo*, the residue was again freeze-dried. Purification of the crude product by HPLC (Spherisorb S5SAX column, 202 mm x 250 mm; 0.2M ammonium formate buffer at pH 4, 12 ml min^{-1}) afforded 1,4,5-IP_3 (+)-(1) (60 mg, 80%), retention time 35 min, $[\alpha]_D^{22}$ +27° (c 0.15, H_2O, pH 6.4); spectral data identical to previously prepared racemic material (±)-(1).

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