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Note

Reactions of the ketone derived from (±)-3,4,5-tri-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol: preparation of racemic derivatives of *epi*-inositol and of 4-*C*-methyl-*epi*- [(±)-*iso*-laminitol] and 4-*C*-methyl-*myo*-inositol [(±)-laminitol] [1]

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Abstract

Oxidation of (±)-3,4,5-tri-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol with the pyridine–SO_3 complex in methyl sulfoxide gave the ketone which was reduced with sodium borohydride to give almost exclusively the corresponding *epi*-inositol derivative. Reaction of the ketone with diazomethane gave an epoxide which was reduced with lithium aluminium hydride to give a 4-*C*-methyl-*myo*-inositol derivative and reaction of the ketone with methyl magnesium iodide gave the isomeric 4-*C*-methyl-*epi*-inositol derivative.

Keywords: Inosose; *C*-Methyl derivatives of *myo*- and *epi*-inositol; Laminitol; *iso*-Laminitol; Oxirane; *epi*-Inositol

We have described previously [1] the preparations of the ketones **2** and **5** (from the alcohols **1** and **4**, respectively) and their reduction with sodium borohydride to give predominantly (ca. 75%) the starting *myo*-inositol derivatives **1** and **4** together with small proportions of the epimeric *chiro*- (**3**) and *scyllo*- (**6**) derivatives, respectively. This allowed [2] the preparation of tritium-labelled chiral 1D-*myo*-inositol 1,4,5-trisphosphate from the ketone **2** as we had also developed [1,3] an efficient resolution of the alcohol **1**.

For investigations on the biological properties [4] of 1D-*myo*-inositol 1,2,6-trisphosphate (**7**) we prepared [5] the protected *myo*-inositol derivative **12**. The diastereoisomeric (−)-ω-camphanates of **12** were readily separated [5], giving access to both of the enantiomers of **12**, and one of these enantiomers was

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[1] Dedicated to Professor Dr. Hans Paulsen on the occasion of his 75th birthday.

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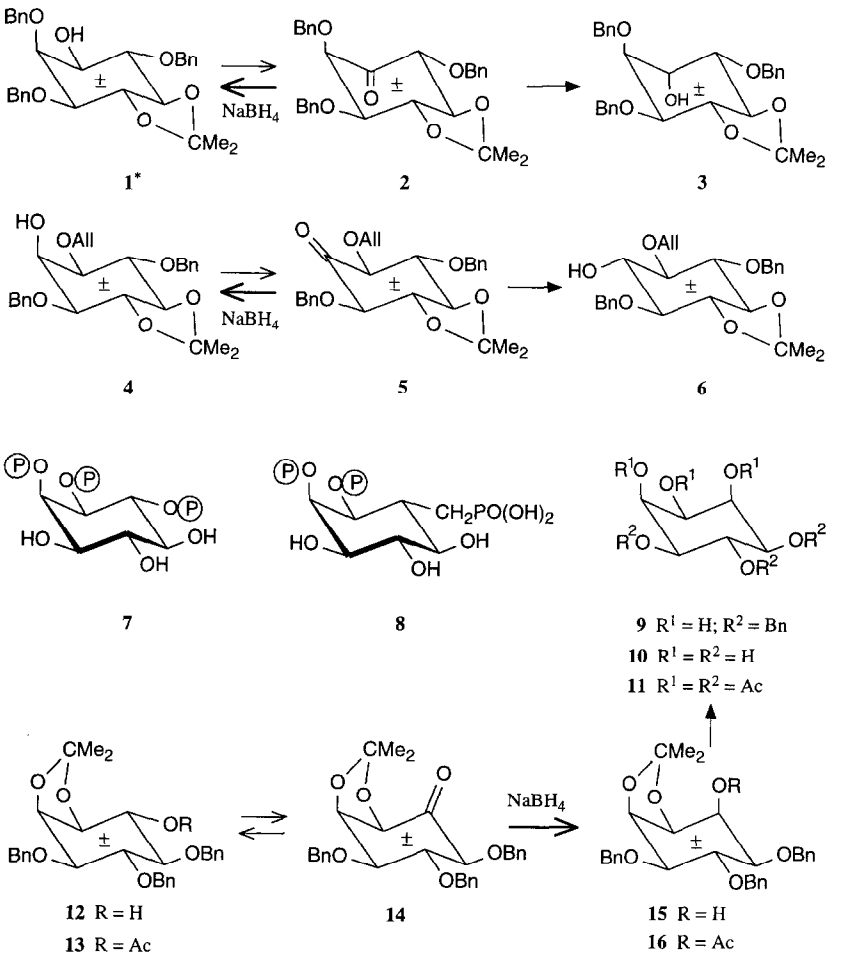
converted [6] into 1D-*myo*-inositol 1,2,6-trisphosphate (**7**). For labelling studies, **12** was oxidised with the sulfur trioxide–pyridine complex in dry methyl sulfoxide containing NEt_3 [7], to give the ketone **14** in good yield but, on reduction with sodium borohydride, this gave almost exclusively (see below) the *epi*-inositol derivative **15** (Scheme 1). Hence the readily available [5] enantiopure derivatives of **12** will give access to the enantiopure *epi*-inositol derivatives corresponding to **15**. The syrupy racemic *epi*-inositol derivative **15** gave a crystalline acetate **16** and both **15** and **16** could be separated from the corresponding *myo*-inositol derivatives **12** and **13** [5] on TLC, showing that the reduction of the ketone **14** by sodium borohydride gave only traces of the *myo*-inositol derivative **12**. Removal of the isopropylidene group from **15** gave the crystalline triol **9** and this on hydrogenolysis gave *epi*-inositol (**10**) which was characterised as the crystalline hexaacetate **11**. Compound **11** had a ^1H NMR spectrum identical with that reported [8] and a mp similar to that recorded [9,10].

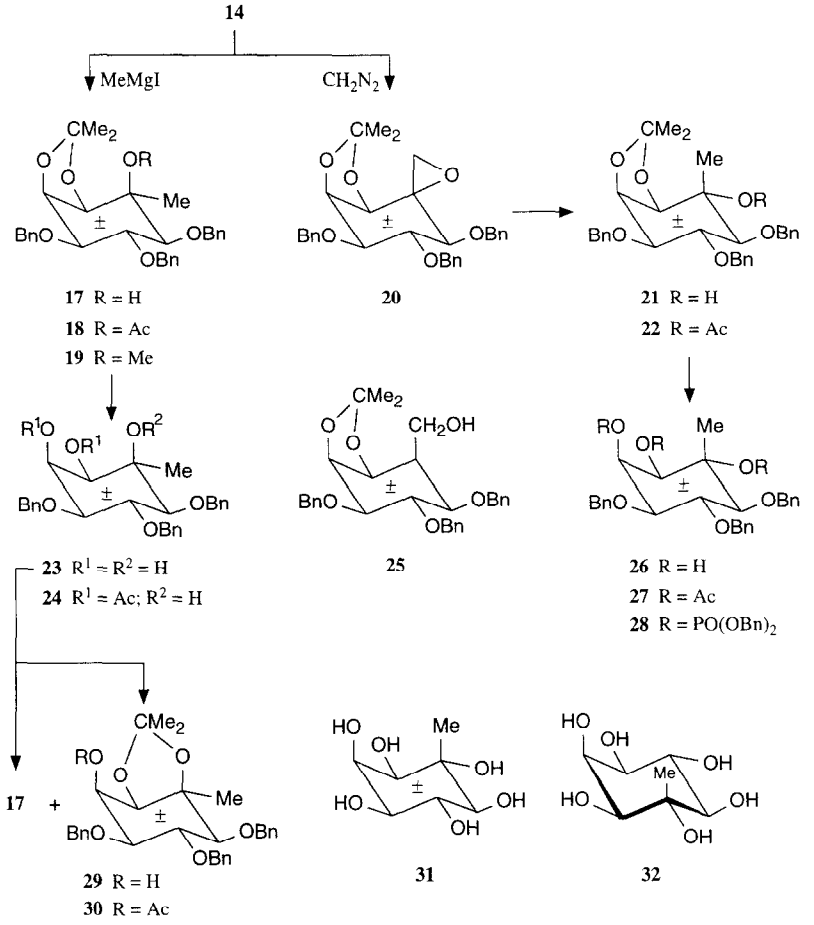
In order to prepare intermediates that might lead to a 6-phosphonate analogue **8** of 1D-*myo*-inositol 1,2,6-trisphosphate (**7**), the ketone **14** was treated with diazomethane to give an oxirane **20** (Scheme 2). Reduction of **20** with lithium aluminium hydride



All = CH_2-CH=CH_2; Bn = CH_2Ph; Ⓟ = $PO(OH)_2$

*In the formulae, racemic inositol derivatives are indicated with (±) in the ring; enantiomerically pure inositol derivatives, represented in their correct absolute configurations, are shown with thickened lines in the ring and *meso*-compounds are shown with neither of these modifications.

Scheme 1.



Scheme 2.

gave a 4-*C*-methylinositol derivative which we consider, from its reactions and from the NMR spectrum of the acetyl derivative **22**, to be the 4-*C*-methyl-*myo*-inositol derivative **21**. Compound **21** was treated with acetic anhydride and 4-dimethylaminopyridine [11] to give the syrupy acetate **22**; in the NOESY spectrum the cross-peaks between one of the isopropylidene CMe groups and the methyl group attached to the ring indicated the structure **22**. It has been established that reduction of such oxiranes as **20** with lithium aluminium hydride provides the *C*-methyl derivatives rather than the hydroxymethyl derivatives [12,13], which indicates that the oxirane formed was **20**, but the reverse situation has been shown to be true for reductions with zinc borohydride on silica gel [14]. Thus reduction of **20** with zinc borohydride should give a mixture [14] of **25** together with the isomeric hydroxymethyl derivative required for the preparation of a 6-phosphonate analogue **8** of 1D-*myo*-inositol 1,2,6-trisphosphate.

Hydrolysis of the isopropylidene group from **21** gave the crystalline triol **26** which was treated with acetic anhydride in the presence of 4-dimethylaminopyridine [11] to give the crystalline triacetate **27**. The triol **26** was also converted into the tris(dibenzyl phosphate) **28**. When the triol **26** was treated with 2,2-dimethoxypropane and an acid catalyst it gave a single product which was identical with alcohol **21**, thus again indicating the 4-*C*-methyl-*myo*-inositol structure **26** for the triol rather than the isomeric *epi*-inositol structure **23** (see below).

The triol **26** is a derivative of racemic laminitol (**31**). (−)-Laminitol (**32**, 4-*C*-methyl-1D-*myo*-inositol) was isolated from the brown alga *Laminaria cloustoni* [15] and the overall structure was established by Lindberg and Wickberg [16] whilst the absolute configuration was established by Posternak and Falbriard [17]. Three syntheses of (−)-laminitol [18–20] and two syntheses of racemic laminitol [18,21] have been described. As the enantiomers of the alcohol **12** are readily available [5] the route from **12** through **14**, **20**, **21**, and **26** should provide both enantiomers of laminitol.

When the ketone **14** was treated with methylmag-

nesium iodide in ether the isomeric *C*-methyl derivative **17** was obtained and this could not be converted into the acetate **18** under the conditions used for the conversion of **21** into **22** although it gave a crystalline methyl ether **19**. This difficulty in acetylation indicates a very hindered axial hydroxyl group as occurs in **17**. Hydrolysis of the isopropylidene group from **17** gave the crystalline triol **23** which was converted only into the diacetate **24** on acetylation with acetic anhydride–pyridine. When the triol **23** was treated with dimethoxypropane and an acid catalyst it gave a mixture of two *O*-isopropylidene derivatives **17** and **29** which were separable by TLC and which were formed by reaction on either of the *cis*-diol systems present in **23**. These two isopropylidene derivatives were best separated after acetylation so that **29** was converted into **30** whilst **17** remained unchanged. Thus the product **17** from the reaction of MeMgI with the ketone **14** is a derivative of (±)-4-*C*-methyl-*epi*-inositol (*iso*-laminitol). Two syntheses of racemic *iso*-laminitol [17,21] and one [17] of enantiopure *iso*-laminitol (1D-4-*C*-methyl-*epi*-inositol) have been described.

1. Experimental

General.—The general methods were as described [22].

(±)-(2,4,5,6/3)-2,3,4-Tri-O-benzyl-2,3,4,5,6-pentahydroxy-5,6-O-isopropylidenecyclohexanone (**14**) *derived from (±)-3,4,5-tri-O-benzyl-1,2-O-isopropylidene-myo-inositol* (**12**).—Pyridine–SO_3 complex (1.5 g) in dry Me_2SO (7.5 mL) was added dropwise with cooling to a solution of the alcohol **12** (1.5 g, 3 mmol) in dry Me_2SO (7.5 mL) and Et_3N (7.5 mL). The solution was kept at 20 °C and after 30 min TLC (19:1 $CHCl_3$–acetone) indicated that complete conversion of the alcohol (R_f 0.6) into the ketone (R_f 0.8) had occurred. The solution was poured into water and the product extracted with ether. The ether extract was washed successively with ice-cold M HCl, satd aq KCl, and satd aq $NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography on silica gel (1:2, 1:1, 2:1 ether–light petroleum) gave the ketone **14** (1.2 g, 80%) as an oil which analysed as the hydrate (gem diol); ^{1}H NMR data: δ 1.34, 1.46 (2 s, each 3 H, 2 × CMe), 3.90–4.03 (m, 3 H, ring protons with major peaks at 3.91, 3.94, 3.98, and 4.02), 4.27–4.54 (m, 2 H, with major peaks at 4.27, 4.34, and 4.45), 4.69 (ABq, 2 H, *J* 11.6 Hz, CH_2Ph), 4.71, 4.76 (2 s, each 2 H, 2 × CH_2Ph), 7.21–7.30 (m, 15 H, Ph). Anal. Calcd for $C_{30}H_{32}O_6 \cdot H_2O$: C, 71.13; H, 6.77. Found: C, 71.37; H, 6.48.

(±)-1,5,6-Tri-O-benzyl-2,3-O-isopropylidene-epi-inositol (**15**) *and the acetate* (**16**).—A mixture of **14** (650 mg, 1.33 mmol) and $NaBH_4$ (240 mg, 6.3 mmol) in EtOH (20 mL) was stirred at 0 °C for 10 min and then allowed to warm to 20 °C. After 1 h, TLC (2:1 ether–light petroleum) showed complete conversion of the ketone (R_f 0.55) into the alcohol (R_f 0.5). Water was added and the ethanol evaporated; the residue was extracted with ether, and the ether solution dried ($MgSO_4$) and concentrated to give the product **15** as an oil (620 mg, 95%). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found: C, 73.02; H, 6.87.

The alcohol **15** gave an acetate **16**; mp 92–94 °C (from light petroleum bp 60–80 °C); ^{1}H NMR data: δ 1.32, 1.55 (2 s, each 3 H, CMe_2), 2.13 (s, 3 H, Ac), 3.47–3.65 (m, 2 H, ring protons with major peaks at 3.47, 3.51, 3.55, 3.61, and 3.65), 4.07–4.39 (m, 3 H, ring protons with major peaks at 4.07, 4.15, 4.21, 4.26, 4.34, and 4.39), 4.45–5.10 (m, 6 H, 3 × CH_2Ph with major peaks at 4.58, 4.63, 4.75, and 4.80), 5.29 (t, 1 H, *J* 4.0 Hz, H-4 or H-2), 7.31 (s, 15 H, Ph). Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 71.99; H, 6.66.

On TLC (19:1 $CHCl_3$–acetone) the alcohol **15** (R_f 0.65) could be distinguished from **12** (R_f 0.6) whilst TLC (2:1 ether–light petroleum) showed good separation of the acetate **16** (R_f 0.6) from 4-*O*-acetyl-1,5,6-tri-*O*-benzyl-2,3-*O*-isopropylidene-*myo*-inositol [5] (**13**, R_f 0.8) and showed only traces of contamination of **15** by **12** or **16** by **13**, respectively, in the crude reactions products.

1,5,6-Tri-O-benzyl-epi-inositol (**9**).—A solution of the isopropylidene compound **15** (510 mg) in 1:9 M HCl–MeOH (20 mL) was heated under reflux for 45 min. The solution was diluted with water (20 mL) and the triol **9** (440 mg, 94%) which crystallised out on cooling was filtered off and washed with water; mp 182–184 °C; ^{1}H NMR data: δ 3.32–3.62 (m, 5 H, 2 ring protons and 3 × OH), 3.95–4.22 (m, 4 H, ring protons), 4.65 (s, 4 H, 2 × CH_2Ph), 4.76 (s, 2 H, CH_2Ph), 7.29, 7.32 (2 s, 15 H, Ph). Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.50; H, 6.56.

epi-*Inositol hexaacetate* (**11**).—A solution of the alcohol **9** (320 mg) in glacial HOAc (20 mL) and 10% Pd–C (200 mg) was stirred under hydrogen at room temperature and pressure for 24 h. The mixture was filtered through Celite and the Celite washed

with HOAc and water. Evaporation of the filtrate gave epi-inositol (**10**) as a solid which was treated with Ac_2O in pyridine at 50 °C for 24 h. Ice was added, the mixture was concentrated, the residue was taken into CH_2Cl_2, and the solution was washed with M HCl and satd aq $NaHCO_3$, dried ($MgSO_4$), and concentrated. Crystallisation of the product from toluene gave **11**; mp 185–188 °C, lit [9] 187–188 °C, lit [10] 186–190 °C; ^{1}H NMR data: δ 2.01 (s, 9 H, 3 × Ac), 2.04 (s, 3 H, Ac), 2.17 (s, 6 H, 2 × Ac), 5.01–5.16 (m, 3 H), 5.57–5.83 (m, 3 H) (cf. ^{1}H NMR spectrum in [8]).

*(±)-4,4′-Anhydro-1,5,6-tri-*O*-benzyl-4-*C*-hydroxymethyl-2,3-*O*-isopropylidene-*myo*-inositol* (**20**) *derived from the ketone* **14**.—A solution of CH_2N_2 in ether was added to a solution of **14** (1.2 g) in ether containing a trace of MeOH until a yellow colour persisted. The solution was left overnight at 20 °C, and TLC (2:1 ether–light petroleum) showed conversion of the ketone (R_f 0.6) into major (R_f 0.85) and minor (R_f 0.7) products. The solution was concentrated and toluene evaporated from the residue, and column chromatography (1:2 ether-light petroleum) then gave **20** (732 mg, 59%) as a syrup. The minor product (200 mg) was not further investigated. ^{1}H NMR data for **20**: δ 1.33, 1.51 (2 s, each 3 H, CMe_2), 3.03 (s, 2 H, oxirane CH_2), 3.35–4.17 (m, 4 H, ring protons with major peaks at 3.35, 3.47, 3.54, 3.65, 3.71, 3.75, 3.80, 3.84, 3.96, 4.04, and 4.12), 4.46–4.86 (m, 7 H, 3 × CH_2Ph and 1 ring proton with major peaks at 4.46, 4.50, 4.54, 4.57, 4.61, 4.65, 4.71, 4.74, and 4.77), 7.29, 7.30 (2 s, 15 H, Ph).

*(±)-1,5,6-Tri-*O*-benzyl-2,3-*O*-isopropylidene-4-*C*-methyl-*myo*-inositol* (**21**).—A solution of the epoxide **20** (460 mg, 0.9 mmol) in dry ether was added dropwise to a suspension of $LiAlH_4$ (200 mg, 5.3 mmol) in dry ether. TLC (2:1 ether–light petroleum) showed conversion of the epoxide (R_f 0.85) into the alcohol (R_f 0.65) together with some faster byproducts. After 30 min, EtOAc was added dropwise to decompose the excess of $LiAlH_4$ and the mixture was distributed between ether and water. The ether layer was washed (satd aq KCl), dried ($MgSO_4$), and concentrated. Column chromatography (1:1 ether–light petroleum) gave **21** as an oil (330 mg, 71%) which crystallised on standing; mp 82–84 °C (from EtOAc–light petroleum bp 60–80 °C); ^{1}H NMR data: δ 1.30, 1.35, 1.46 (3 s, each 3 H, 3 × CMe), 3.34 (d, 1 H, *J* 4.3 Hz), 3.89–4.19 (m, 3 H, with major peaks at 3.93, 3.99, 4.04, and 4.08), 4.42–4.96 (m, 8 H, 3 × CH_2Ph and 2 ring protons with major peaks at 4.45, 4.48, 4.55, 4.70, 4.77 and 4.83), 7.25–7.43 (m, 15 H, Ph with major peaks at 7.28 and 7.31). Anal. Calcd for $C_{31}H_{36}O_6$: C, 73.79; H, 7.19. Found: C, 73.76; H, 7.18.

A portion was acetylated using 4-dimethylaminopyridine and NEt_3 in Ac_2O to give the syrupy acetate **22** (R_f 0.6 in 1:1 ether–light petroleum); ^{1}H NMR data: δ 1.30, 1.44, 1.68 (3 s, each 3 H, 3 × CMe), 1.78 (s, 3 H, Ac), 3.77–4.10 (m, 2 H, ring protons with major peaks at 3.86, 3.90, 3.94, and 3.99), 4.30–4.52 (m, 3 H, ring protons with major peaks at 4.30, 4.37, 4.42, and 4.45), 4.64–4.79 (m, 6 H, 3 × CH_2Ph with major peaks at 4.64, 4.69, and 4.79), 7.30 (s, 15 H, Ph).

In the 500-MHz ^{1}H NMR spectrum of **21** the signals for the ring protons and benzylic methylene protons were resolved showing the following: δ 3.85 (dd, 1 H), 4.05 (dd, 1 H), and 4.67, 4.70, 4.80 (3 ABq, each 2 H). The NOESY spectrum of **22** showed cross-peaks between the CMe groups at δ 1.30 and 1.68, and between the CMe groups at δ 1.44 and 1.68 (of the isopropylidene group), indicating an axial CMe group at C-4 interacting with one of the CMe groups of the isopropylidene group.

*(±)-1,5,6-Tri-*O*-benzyl-4-*C*-methyl-*myo*-inositol* (**26**).—The isopropylidene compound **21** (185 mg) was heated under reflux with M HCl–MeOH (1:9, 10 mL) for 30 min. The solution was cooled, water was added, and most of the MeOH was evaporated. The product crystallised out and was extracted with CH_2Cl_2; the extract was washed with satd aq $NaHCO_3$, dried (K_2CO_3), and concentrated to give **26**; mp 99–101 °C (from EtOAc–light petroleum bp 60–80 °C); ^{1}H NMR data: δ 1.41 (s, 3 H, CMe), 2.71–2.87 (m, 3 H, 3 × OH), 3.32–4.28 (m, 5 H, ring protons with major peaks at 3.32, 3.41, 3.77, 3.86, 4.20, and 4.25), 4.60–4.95 (m, 6 H, 3 × CH_2Ph with major peaks at 4.65, 4.71, 4.73, and 4.76), 7.30 (s, 15 H, Ph). Anal. Calcd for $C_{28}H_{32}O_6 \cdot 0.5H_2O$: C, 71.01; H, 7.02. Found: C, 70.98; H, 6.94.

A portion of the product was converted into the isopropylidene derivative using 2,2-dimethoxypropane and toluene-*p*-sulfonic acid in acetone as described below for a similar reaction with the triol **23**. The single product (TLC) had a ^{1}H NMR spectrum identical with that of **21**.

*(±)-2,3,4-Tri-*O*-acetyl-1,5,6-tri-*O*-benzyl-4-*C*-methyl-myo-inositol* (**27**).—The triol **26** (50 mg) was treated with Ac_2O (1 mL) and 4-dimethylaminopyridine (20 mg) in CH_2Cl_2 (5 mL) and NEt_3 (1 mL) at room temperature for 18 h. The mixture was distributed between ether and water, and the ether layer was washed with M HCl, satd aq KCl, and satd aq

$NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography (1:1 ether–light petroleum) gave **27** which crystallised on standing; mp 117–119 °C (from EtOAc–light petroleum bp 60–80 °C); ^1H NMR data: δ 1.56 (s, 3 H, CMe), 1.81, 2.06, 2.14 (3 s, each 3 H, 3 × Ac), 3.70–3.88 (m, 2 H, ring protons with major peaks at 3.70, 3.73, and 3.79), 4.44–4.93 (m, 7 H, 3 × CH_2Ph and 1 ring proton with major peaks at 4.57, 4.63, 4.67, 4.79, and 4.82), 5.70 (t, 1 H, *J* 3.6 Hz, H-2), 5.97 (d, 1 H, *J* 3.7 Hz, H-3), 7.28 (s, 15 H, Ph). Anal. Calcd for $C_{34}H_{38}O_9$: C, 69.14; H, 6.48. Found: C, 68.66; H, 6.30.

(±)-1,5,6-Tri-O-benzyl-4-C-methyl-myo-*inositol 2,3,4-tris(dibenzyl phosphate)* (**28**).—Treatment of the triol **26** with dibenzyloxy(diisopropylamino)phosphine and tetrazole followed by oxidation of the intermediate phosphite to the phosphate with 3-chloroperoxybenzoic acid, as described [23] for similar phosphorylations of *myo*-inositol derivatives, gave the tris(dibenzyl phosphate) **28** which was purified by column chromatography (ether followed by 4:1 ether–EtOAc); ^{31}P NMR data: δ −6.66, −2.22, −1.28 (and +7.33 for a slight contaminant). Anal. Calcd for $C_{70}H_{71}O_{15}P_3$: C, 67.52; H, 5.75; P, 7.46. Found: C, 66.78; H, 5.59; P, 8.30.

(±)-1,5,6-Tri-O-benzyl-2,3-O-isopropylidene-4-C-methyl-epi-*inositol* (**17**).—Magnesium turnings (0.5 g) were stirred in dry ether, a solution of MeI (2.8 g) in dry ether was added at such a rate that the heat of reaction kept the mixture refluxing, and the mixture was then warmed until almost all the Mg had reacted. A solution of the ketone **14** (1.08 g) in dry ether was added slowly and the mixture was heated under reflux for 1 h. Acetone was added cautiously to decompose the excess of Grignard reagent, water was added, and the mixture was filtered through Celite to remove the $Mg(OH)_2$. The ether layer was separated, washed with satd aq KCl, dried ($MgSO_4$), and concentrated to give an oil (1.07 g). Column chromatography (1:2 ether–light petroleum, then 1:1) separated the faster byproducts (170 mg) from the major product **17** which was obtained as an oil (780 mg); ^1H NMR data: δ 1.23, 1.34, 1.54 (3 s, each 3 H, 3 × CMe), 3.20 (d, 1 H, *J* 6.7 Hz), 3.38 (s, 1 H), 3.66–4.41 (m, 4 H, with major peaks at 3.66, 3.71, 3.73, 3.77, 3.86, 3.94, 4.06, 4.13, 4.21, 4.29, 4.34, 4.37, and 4.41), 4.65 (s, 2 H, CH_2Ph), 4.72 (ABq, 2 H, *J* 11.6 Hz, CH_2Ph), 4.76 (s, 2 H, CH_2Ph), 7.30–7.35 (m, 15 H, Ph). Anal. Calcd for $C_{31}H_{36}O_6$: C, 73.79; H, 7.19. Found: C, 73.55; H, 7.28.

Compounds **21** and **17** had similar R_f values (0.65) on TLC in 2:1 ether–light petroleum but were readily distinguished in 19:1 $CHCl_3$–acetone (**21** R_f 0.6, **17** R_f 0.8). No acetate was formed from **17** under the conditions used for preparing **22**.

(±)-1,5,6-Tri-O-benzyl-4-C-methyl-epi-*inositol* (**23**).—The isopropylidene compound **17** was hydrolysed by heating with 1:9 M HCl–MeOH under reflux for 30 min. Sodium hydrogen carbonate was added and the solvents were evaporated. Toluene was evaporated from the residue which was extracted with $CHCl_3$. The extract was dried and concentrated to give **23**; mp 106–108 °C (from EtOAc–light petroleum bp 60–80 °C); ^1H NMR data: δ 1.27 (s, 3 H, CMe), 3.12–3.72 (m, 6 H, with major peaks at 3.12, 3.19, 3.34, 3.46, 3.50, 3.65, and 3.72), 3.94–4.20 (m, 2 H, with major peaks at 3.94, 4.05, and 4.16), 4.56–5.01 (m, 6 H, 3 × CH_2Ph with major peaks at 4.56, 4.69, 4.84, 4.90, and 5.01), 7.30 (s, 15 H, Ph). Anal. Calcd for $C_{28}H_{32}O_6 \cdot 0.5H_2O$: C, 71.01; H, 7.02. Found: C, 71.54; H, 6.77.

Conversion of the triol **23** *into a mixture of the isopropylidene derivatives* **17** *and* **29**.—A solution of the triol **23** (370 mg), acetone (5 mL), 2,2-dimethoxypropane (5 mL), and toluene-*p*-sulfonic acid (21 mg) was kept at 20 °C for 8 h. TLC (2:1 ether–light petroleum) then showed two major products (R_f 0.65 and 0.7) in approximately equal proportions. Triethylamine and $NaHCO_3$ were added, the mixture was concentrated, and the oily product was extracted from the residue with ether. The ^1H NMR spectrum of this mixture showed resonances due to the alcohol **17** (see above) together with those of **29** [δ 1.27, 1.38, 1.54 (3 s, each 3 H, 3 × CMe), 3.23 (d, 1 H, *J* 7.3 Hz)]. This mixture of **17** and **29** was acetylated with Ac_2O–pyridine at 50 °C for 12 h after which time TLC (19:1 $CHCl_3$–acetone) showed two products (R_f 0.7 and 0.85); the more polar product co-chromatographed with the alcohol **17**. Column chromatography (same solvent) gave the syrupy acetate **30** (150 mg); ^1H NMR data: δ 1.21, 1.38, 1.61 (3 s, each 3 H, 3 × CMe), 2.08 (s, 3 H, Ac), 3.18 (d, 1 H, *J* 10.4 Hz), 4.08–4.30 (m, 3 H, with major peaks at 4.08, 4.10, 4.16, and 4.24), 4.58–5.10 (m, 7 H, 3 × CH_2Ph and 1 ring proton with major peaks at 4.67, 4.71, 4.75, 4.86, and 4.89).

Eluted later was the alcohol **17** (150 mg) with a ^1H NMR spectrum identical with that described above.

(±)-2,3-Di-O-acetyl-1,5,6-tri-O-benzyl-4-C-methyl-epi-*inositol* (**24**).—The triol **23** was treated with Ac_2O–pyridine at 50 °C for 48 h and the acetate **24** isolated in the usual way; mp 153–155 °C (from EtOAc–light petroleum bp 60–80 °C); ^1H NMR data: δ 1.16 (s, 3 H, CMe), 2.11, 2.14 (2 s, each 3 H,

2 × Ac), 2.75 (bs, 1 H, OH), 3.23 (d, 1 H, *J* 9.8 Hz, H-5), 3.59 (dd, 1 H, *J* 3.1 and 9.7 Hz, H-1), 4.12 (t, 1 H, *J* 9.8 Hz, H-6), 4.43–5.08 (m, 7 H, 3 × CH_2Ph and H-3 with major peaks at 4.56, 4.59, 4.64, 4.69, 4.71, 4.84, 4.91, 4.96, and 5.08), 5.74 (t, 1 H, *J* 3.1 Hz, H-2), 7.30 (s, 15 H, Ph). Anal. Calcd for $C_{32}H_{36}O_8$: C, 70.06; H, 6.61. Found: C, 69.89; H, 6.61.

(±)-1,5,6-Tri-O-benzyl-2,3-O-isopropylidene-4-C-methyl-4-O-methyl-epi-*inositol* (**19**).—The alcohol **17** (70 mg) was treated with methyl iodide (0.1 mL) and NaH/oil (50 mg) in dry DMF in the usual way. Column chromatography (1:2 ether–light petroleum) of the crude product gave **19** as an oil which crystallised on standing; mp 117–119 °C (from light petroleum bp 60–80 °C); ^{1}H NMR data: δ 1.25, 1.34, 1.58 (3 s, each 3 H, 3 × CMe), 2.97 (d, 1 H, *J* 9.8 Hz, H-5), 3.43 (s, 3 H, OMe), 3.57–3.73 (m, 2 H, H-1 and H-3, with major peaks at 3.64, 3.67, 3.71, and 3.73), 4.17–4.37 (m, 2 H, H-2 and H-6 with major peaks at 4.17, 4.24, 4.28, 4.31, and 4.37), 4.74 (ABq, 2 H, *J* 11.6 Hz, CH_2Ph), 4.81 (s, 2 H, CH_2Ph), 4.84 (ABq, 2 H, CH_2Ph), 7.30 (s, 15 H, Ph). Anal. Calcd for $C_{32}H_{38}O_6$: C, 74.11; H, 7.39. Found: C, 74.00; H, 7.19.

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