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The preparation of intermediates for the synthesis of 1D-*myo*-inositol 1,4,5- and 2,4,5-trisphosphates, 1,4-bisphosphate 5-phosphorothioate, and 4,5-bisphosphate 1-phosphorothioate from 1D-3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol ☆,†

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Abstract

The preparation of 1D-1,6-di-*O*-benzyl-2,5-di-*O*-*p*-methoxybenzyl-*myo*-inositol is described. This compound and 1D-3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol were converted into 1D-1,3,6-tri-*O*-benzyl-*myo*-inositol which was phosphorylated to give an intermediate for the synthesis of 1D-*myo*-inositol 2,4,5-trisphosphate. 1D-3,6-Di-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol was converted into 1D-2,3,6-tri-*O*-benzyl-*myo*-inositol (an intermediate for the synthesis of 1D-*myo*-inositol 1,4,5-trisphosphate) and 1D-2,3,6-tri-*O*-benzyl-1-*O*-*p*-methoxybenzyl-*myo*-inositol (an intermediate for the synthesis of the 1-phosphorothioate analogue of 1D-*myo*-inositol 1,4,5-trisphosphate). 1D-3,6-Di-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol was also converted into 1D-2,3,6-tri-*O*-benzyl-5-*O*-*p*-methoxybenzyl[and -5-*O*(*cis*-prop-1-enyl)]-*myo*-inositol both of which are intermediates for the synthesis of the 5-phosphorothioate analogue of 1D-*myo*-inositol 1,4,5-trisphosphate. The synthesis of 1D-2,3,6-tri-*O*-benzyl-*myo*-inositol 1,4-bis(dibenzyl phosphate) 5-(dibenzyl phosphorothioate) from 1D-2,3,6-tri-*O*-benzyl-*myo*-inositol 1,4-bis(dibenzyl phosphate) is described.

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† Dedicated to Professor Antonio Gómez-Sánchez.

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1. Introduction

1D-*myo*-Inositol 2,4,5-trisphosphate [Ins(2,4,5)P_3] is a product [3,4] of the chemical hydrolysis of phosphatidylinositol 4,5-bisphosphate. Unlike [4] the other product of this hydrolysis {1D-*myo*-inositol 1,4,5-trisphosphate, [Ins(1,4,5)P_3]}, it is poorly metabolised and is less effective in mobilising calcium ions. For this reason, it is often used [5] in biological experiments to explore the mechanism of calcium signalling in the phosphatidylinositol cycle. As the preparation of Ins(2,4,5)P_3 from phosphatidylinositol 4,5-bisphosphate requires a tedious chromatographic separation, synthetic methods have been investigated for the preparation of the chiral material [6] and its 3-azido-3-deoxy analogue [7].

We describe here two routes for the preparation of 1D-1,3,6-tri-*O*-benzyl-*myo*-inositol (**18**) which is a suitable intermediate for the synthesis of Ins(2,4,5)P_3. The more practical route starts from the recently described [8] 1D-3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol (**25**). The latter was also used as an intermediate for a new synthesis of 1D-2,3,6-tri-*O*-benzyl-*myo*-inositol (**37**) which has been used previously [9] as an intermediate for the synthesis of Ins(1,4,5)P_3. Compound **25** was also used to prepare intermediates suitable for the synthesis of the 1- and 5-phosphorothioate analogues of Ins(1,4,5)P_3. Since the phosphorothioate groups are poorly metabolised by phosphatases, these phosphorothioate analogues are useful compounds for biological studies.

2. Results and discussion

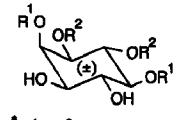
Previously [10], it was found that 1,2,5,6-tetra-*O*-benzyl-*myo*-inositol (**1**) was resolved via the bis-(−)-ω-camphanates **4** to give the diasteroisomer **6** by **crystallisation** and this allowed the preparation of the chiral diol **11**. Similar behaviour was observed [11,12] with the (−)-ω-camphanates of analogues of **1** in which *p*-methoxybenzyl groups replace some of the benzyl groups.

The discovery [12] of a simple route to the bis-*p*-methoxybenzyl ether **2** and its conversion [12] into the mono-*O*-isopropylidene derivative **13** allowed access to the diol **3**, which is an analogue of **1**. Thus, benzylation of **13** [12] and subsequent acid hydrolysis of the product **14** gave **3**. This was converted into the diastereoisomeric mixture of bis-(−)-ω-camphanates **5** and these behaved in the same way as **4**, allowing the separation of the pure diastereoisomer **7** by crystallisation. Saponification of **7** gave the chiral diol **12**, the absolute configuration of which was established as described below. Recrystallisation of the product remaining in the mother liquors after the removal of **7** also gave a pure sample of the diastereoisomer **8**.

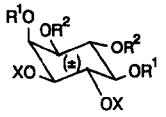
Tin-mediated benzylation of the diol **12** gave predominantly the alcohol **15** (with a little of **16**) as was established by examination of the ^{1}H NMR spectrum of the

corresponding acetate **17**. De-*p*-methoxybenzylation of **15**, using cerium(IV) ammonium nitrate [13], gave the chiral triol **18** required as an intermediate for the synthesis of Ins(2,4,5)P_3. To establish the absolute configuration of the triol **18**, it was converted into the *O*-isopropylidene derivative **23** and this on benzylation gave **24** with physical properties similar to those of its enantiomer [11] but with an opposite rotation. Although this route had been successful for the preparation of the required chiral triol **18**, it was lengthy. At this stage, we discovered [8,14a] the easy resolution of (±)-3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-*myo*-inositol to give the chiral diol **25**, and this indicated [14b] a simple route to the chiral triol **18**.

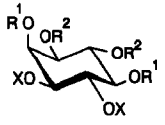
Crotylation of the diol **25** gave **26** which was hydrolysed to give the diol **27**. Tin-mediated benzylation of **27** gave the alcohol **28** and this on decrotylation with



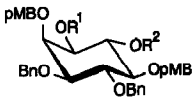
1* $R^1 = R^2 = Bn$
2 $R^1 = pMB, R^2 = H$ (*meso*)
3 $R^1 = pMB, R^2 = Bn$



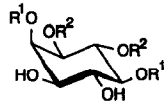
4 $R^1 = R^2 = Bn$
5 $R^1 = pMB, R^2 = Bn$



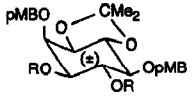
6 $R^1 = R^2 = Bn$
7 $R^1 = pMB, R^2 = Bn$



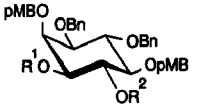
8 $R^1 = R^2 = X$
9 $R^1 = R^2 = H$
10 $R^1 = Bn, R^2 = Ac$



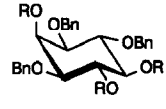
11 $R^1 = R^2 = Bn$
12 $R^1 = pMB, R^2 = Bn$



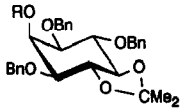
13 R = H
14 R = Bn



15 $R^1 = Bn, R^2 = H$
16 $R^1 = H, R^2 = Bn$
17 $R^1 = Bn, R^2 = Ac$



18 R = H
19 R = Ac
20 R = $P(OBn)_2$
21 R = $PO(OBn)_2$
22 R = PO(OBn)(ONa)

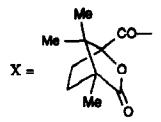


23 R = H
24 R = Bn

*In the formulae, racemic inositol derivatives are indicated with (±) in the ring and chiral inositol derivatives, represented in their correct absolute configurations, are shown with thickened lines in the ring.

Bn = CH_2Ph pMB = $CH_2Ph(pOMe)$

All = CH_2-CH=CH_2 Crot = CH_2-CH=CHMe

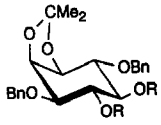
X = 

(-)-ω-camphanoyl

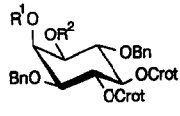
potassium *tert*-butoxide in Me_2SO [15] gave the triol **18** identical with the material prepared by the route described above. Phosphitylation of **18** with bis(benzyloxy)diisopropylaminophosphine [12] (**88**), to give **20**, followed by oxidation of the latter compound gave syrupy **21** which on treatment with sodium iodide in acetone [11] gave crystalline **22**. Compounds **21** and **22** are suitable for debenzylation to give 1D-*myo*-inositol 2,4,5-trisphosphate.

The availability of the diol **27** also suggested a new route to the chiral triol **37** [11], which is a useful intermediate for the synthesis of D-*myo*-inositol 1,4,5-trisphosphate [9]. Tin-mediated *p*-methoxybenzylation of **27** gave the alcohol **29** which was benzylated to give **30**. Decrotylation [15] of **30** gave the diol **35**, which has been prepared previously [16] and is a suitable [9] intermediate for the preparation of 1D-*myo*-inositol 4,5-bisphosphate 1-phosphorothioate. De-*p*-methoxybenzylation of **35** to give the triol **37** has been described previously [16]. Phosphorylation of the diol **35**, using the phosphoramidite reagent **88**, gave **40** and removal of the *p*-methoxybenzyl group with cerium(IV) ammonium nitrate [13] gave the alcohol **41** suitable for conversion into a chiral phosphorothioate.

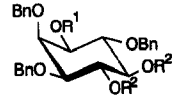
In another approach to the chiral triol **37**, the dicrotyl ether **27** was converted by tin-mediated crotylation into the alcohol **31** which was benzylated to give **32**.



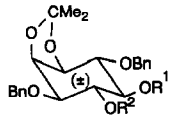
25 R = H
26 R = Crot



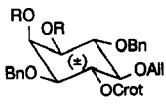
27 $R^1 = R^2 = H$
28 $R^1 = H$, $R^2 = Bn$
29 $R^1 = H$, $R^2 = pMB$
30 $R^1 = Bn$, $R^2 = pMB$
31 $R^1 = H$, $R^2 = Crot$
32 $R^1 = Bn$, $R^2 = Crot$
33 $R^1 = H$, $R^2 = All$
34 $R^1 = Bn$, $R^2 = All$



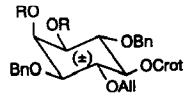
35 $R^1 = pMB$, $R^2 = H$
36 $R^1 = pMB$, $R^2 = Ac$
37 $R^1 = R^2 = H$
38 $R^1 = R^2 = Ac$
39 $R^1 = pMB$, $R^2 = P(OBn)_2$
40 $R^1 = pMB$, $R^2 = PO(OBn)_2$
41 $R^1 = H$, $R^2 = PO(OBn)_2$
42 $R^1 = CH{=}CHMe$, $R^2 = H$
43 $R^1 = CH{=}CHMe$, $R^2 = Ac$



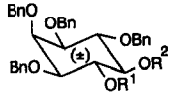
44 $R^1 = R^2 = H$
45 $R^1 = All$, $R^2 = H$
46 $R^1 = H$, $R^2 = All$
47 $R^1 = Crot$, $R^2 = H$
48 $R^1 = H$, $R^2 = Crot$
49 $R^1 = All$, $R^2 = Crot$
50 $R^1 = Crot$, $R^2 = All$



51 R = H
52 R = Bn



53 R = H
54 R = Bn

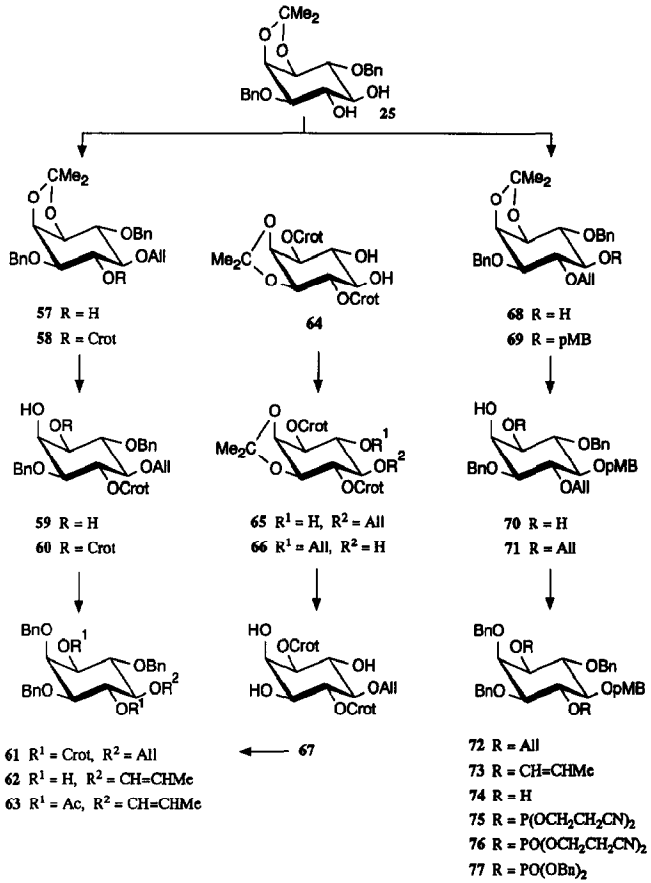


55 $R^1 = H$, $R^2 = CH{=}CHMe$
56 $R^1 = CH{=}CHMe$, $R^2 = H$

Decrotylation of **32** gave the chiral triol **37**, identical with the material described previously [16].

Tin-mediated allylation of the dicrotyl ether **27** gave the alcohol **33** which was benzylated to give **34**. Treatment of **34** with potassium *tert*-butoxide in Me_2SO removed [15] the crotyl groups and isomerised [17] the allyl group to a *cis*-prop-1-enyl group, to give the chiral diol **42** which has been prepared [16,18] previously and converted [16,18] into **37** by acid hydrolysis. Compound **42** has been used [18] as an intermediate for the synthesis of 1D-*myo*-inositol 4,5-bisphosphate 1-phosphorothioate.

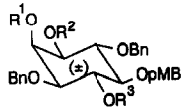
In order to investigate the uses of the chiral diol **25** for the preparation of intermediates suitable for the synthesis of the 5-phosphorothioate analogue of $Ins(1,4,5)P_3$, investigative experiments were first carried out with the racemic material [8] **44**. Tin-mediated allylation or crotylation of racemic **44** gave a readily separable mixture of approximately equal quantities of the monoallyl derivatives **45** and **46**, or the monocrotyl derivatives **47** and **48**, respectively. The separated



isomers **45** and **46** were crotylated to give **49** and **50**, and likewise allylation of the separated isomers **47** and **48** also gave **50** and **49**, respectively. In order to distinguish between **49** and **50**, the isomers were hydrolysed individually with acid to give **51** and **53**, and these diols were benzylated to give **52** and **54**, respectively. Treatment of these isomers with potassium *tert*-butoxide in Me_2SO resulted in removal of the crotyl group and isomerisation of the allyl group to a *cis*-prop-1-enyl group; in this way, **52** gave **55** and **54** gave **56**. As the prop-1-enyl derivatives **55** and **56** have been characterised previously [19], the structures of compounds **45–54** were established.

With the structures of the racemates **45** and **46** (and hence also those of the corresponding chiral monoallyl ethers **57** and **68**) established, routes became apparent for the synthesis from **57** and **68** of the chiral derivatives **62** and **74**, both of which would be useful in the preparation of intermediates suitable for the synthesis of 1D-*myo*-inositol 1,4-bisphosphate 5-phosphorothioate (**85**). Thus, the chiral allyl ether **57** was converted into **59** as described above for the racemate. Tin-mediated crotylation of **59** gave **60** which was benzylated to give **61** and this on treatment with potassium *tert*-butoxide in Me_2SO gave chiral 1D-2,3,6-tri-*O*-benzyl-5-*O*-(*cis*-prop-1-enyl)-*myo*-inositol (**62**) suitable, as an alternative to **74**, for phosphorylation as described previously [9] for the racemate of **62**.

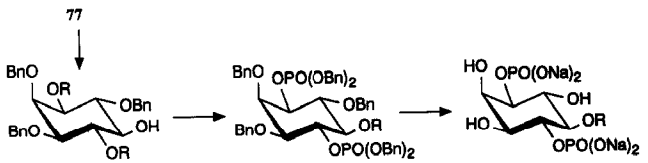
An alternative route to **61** (and hence **62**) was established by tin-mediated allylation of 1D-1,4-di-*O*-crotyl-2,3-*O*-isopropylidene-*myo*-inositol [8] (**64**), to give a



78 $R^1 = R^2 = H$, $R^3 = All$

79 $R^1 = Bn$, $R^2 = R^3 = CH{=}CHMe$

80 $R^1 = Bn$, $R^2 = R^3 = H$



81 $R = PO(OCH_2CH_2CN)_2$

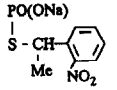
82 $R = PO(OBn)_2$

83 $R = P(OBn)_2$

84 $R = PS(OBn)_2$

85 $R = PS(ONa)_2$

86 R = PO(ONa)



$(RO)_2PN(CHMe_2)_2$

87 $R = CH_2CH_2CN$

88 R = Bn

mixture of **65** and its regioisomer **66**. These were separated by chromatography, and acid hydrolysis of **65** gave **67** which was benzylated to give **61**.

p-Methoxybenzylation of **68** gave **69** which gave **70** on acid hydrolysis. Tin-mediated allylation of **70** gave **71** which was benzylated to give **72**. This was treated with potassium *tert*-butoxide in Me_2SO to give the bis(*cis*-prop-1-enyl) ether **73**, and the prop-1-enyl groups were hydrolysed to give the diol **74** identical with the material described previously [9]. The racemic materials (**78**, **79**, and **80**) corresponding to the chiral compounds **70**, **73**, and **74** were also characterised, being prepared in the same way from the racemate **46**.

Phosphitylation of **74**, using [12] the phosphoramidite reagent **87**, followed by oxidation of the intermediate phosphite **75** gave crystalline **76** and this on treatment with cerium(IV) ammonium nitrate gave the syrupy alcohol **81**. We have previously [9] described the preparation of the bisphosphates **77** and **82**, and we now describe the conversion of **82** into the protected 5-phosphorothioate **84**. Compound **84** has been deprotected, using sodium in liquid ammonia, by our colleagues [20] in the Division of Physical Biochemistry, NIMR, and the phosphorothioate group of the product **85** has been "caged" by them with a 1-(2-nitrophenyl)ethyl group. The "caged" product **86** is being used [20] for physiological studies.

3. Experimental

General.—The general methods were as described [11,12].

(±)-3,4-Di-O-benzyl-1,6-O-isopropylidene-2,5-di-O-p-methoxybenzyl-myo-inositol (**14**).—The diol [12] **13** was treated with an excess of benzyl bromide and NaH/oil in DMF at 20°C. After 1 h, TLC (1:1 CH_2Cl_2–ether) showed complete conversion of **13** (R_f 0.5) into a product (R_f 1.0). The product was isolated in the usual way to give crude **14**, contaminated with benzylation byproducts. For analysis, a portion was crystallised from light petroleum to give **14**; mp 119–121°C. ^1H NMR data: δ 1.43, 1.48 (2 s, each 3 H, 2 CMe), 3.27–3.57 (m, 2 H, H-1,5), 3.78, 3.79 (2 s, each 3 H, 2 OMe), 4.48–4.53 (m, 8 H, 4 CH_2Ph), 6.79–7.28 (m, 18 H, aromatic). (Calcd for $C_{39}H_{44}O_8$: C, 73.10; H, 6.92%. Found: C, 73.08; H, 6.83%.

(±)-1,6-Di-O-benzyl-2,5-di-O-p-methoxybenzyl-myo-inositol (**3**).—A solution of the major portion of the crude **14**, described above, in 1:7:3 M HCl–MeOH–acetone was kept at 20°C until TLC (1:1 ether–light petroleum) showed complete conversion of **14** (R_f 0.7) into a product (R_f 0). After this time, crystals had separated from the solution. An excess of NEt_3 was added, the mixture was concentrated, and the crystalline **3** was washed with water and light petroleum (to remove benzylation byproducts); mp 155–157°C (from EtOH). ^1H NMR data: δ 2.38 (d, 1 H, *J* 1.53 Hz, OH), 2.47 (d, 1 H, *J* 7.93 Hz, OH), 3.79 (s, 6 H, 2 OMe), 4.52–5.03 (m, 8 H, 4 CH_2Ph), 6.79–7.31 (m, 18 H, aromatic). Calcd for $C_{36}H_{40}O_8$: C, 71.98; H, 6.71%. Found: C, 72.18; H, 6.42%.

Bis-(−)-ω-camphanates (**7** *and* **8**) *of 1,6-di-O-benzyl-2,5-di-O-p-methoxybenzyl-myo-inositol.*—A solution of the racemic diol **3** (3.01 g) and (−)-ω-camphanic acid

chloride (5 g) in dry pyridine (20 mL) was kept at 20°C for 18 h. The solution was cooled in ice and water (2 mL) was added. After 1 h, the solution was diluted with water (100 mL), the mixture of diastereoisomers **5** (4.85 g) crystallised out, and these were filtered off, washed with water, and dried. ^{1}H NMR data: δ 0.81 (3 H), 0.85 (3 H), 0.93 (9 H), 0.98 (6 H), 1.00 (3 H), 1.05 (6 H), 1.08 (6 H) (7 s, 12 CMe of the camphanate portions), 3.77, 3.80 (2 s, 12 H, 4 OMe). Crystallisation of the mixture of diastereoisomers **5** from 2:1 EtOAc–light petroleum gave the pure diastereoisomer **7** (1.63 g); mp 176–177°C; $[\alpha]_D^{25}$ −1.2° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 0.81 (3 H), 0.93 (6 H), 1.00 (3 H), 1.04 (3 H), 1.08 (3 H) (5 s, 6 CMe of the camphanate portion). Calcd for $C_{56}H_{64}O_{14}$: C, 69.98; H, 6.71%. Found: C, 70.21; H, 6.71%.

The contents of the mother liquors were recrystallised (×2) from EtOAc–light petroleum to give a pure sample of the diastereoisomer **8** (1.3 g); mp 114–116°C; $[\alpha]_D^{25}$ −14.4° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 0.85 (3 H), 0.93 (3 H), 0.98 (6 H), 1.05 (3 H), 1.08 (3 H) (5 s, 6 CMe of the camphanate portion). Found: C, 69.80; H, 6.56%.

1D-1,3,6-Tri-O-*benzyl-2,5-di*-O-p-*methoxybenzyl*-myo-*inositol* (**15**).—The bis-(−)-ω-camphanate **7** was saponified with NaOH in MeOH in the usual way, to give the chiral diol **12** as a syrup. A mixture of **12** (900 mg, 1.5 mmol), dibutyltin oxide (558 mg, 2.2 mmol), tetrabutylammonium bromide (722 mg, 2.2 mmol), benzyl bromide (0.5 mL, 4.5 mmol), and MeCN (50 mL) was heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 4 days when TLC (1:1 ether–light petroleum) showed complete conversion of **12** (R_f 0) into major (**15**, R_f 0.25) and minor (**16**, R_f 0.3) products. The products were isolated in the usual way [11] and acetylated with Ac_2O–pyridine. Crystallisation from EtOAc–light petroleum gave the acetate **17**; mp 137–138°C; $[\alpha]_D^{25}$ +6.0° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 1.94 (s, 3 H, Ac), 3.17–3.51 (m, 3 H, H-1,3,5), 3.76, 3.77 (2 s, 2 OMe), 4.01–4.23 (m, 2 H, H-2,6), 4.45 (ABq, 2 H, CH_2Ph), 4.60 (s, 2 H, CH_2Ph), 4.64 (ABq, 2 H, CH_2Ph), 4.77 (s, 2 H, CH_2Ph), 4.84 (ABq, 2 H, CH_2Ph), 5.61 (t, 1 H, *J* 9.77 Hz, H-4), 6.73–7.31 (m, 23 H, aromatic). Calcd for $C_{45}H_{48}O_9$: C, 73.5; H, 6.60%. Found: C, 73.65; H, 6.29%.

The acetate was saponified with NaOH in MeOH in the usual way, to give the alcohol **15**; mp 77–79°C (from EtOH); $[\alpha]_D^{25}$ +10.5° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 2.43 (s, OH), 3.09–3.42 (m, 3 H, H-1,3,5), 3.7 (s, 6 H, 2 OMe), 3.93–4.13 (m, 3 H, H-2,4,6), 4.54, 4.62, 4.74, 4.78 (4 s, each 2 H, 4 CH_2Ph), 4.86 (ABq, 2 H, CH_2Ph), 6.74–7.31 (m, 23 H, aromatic). Calcd for $C_{43}H_{46}O_8$: C, 74.76; H, 6.71%. Found: C, 74.35; H, 6.68%. This product co-chromatographed with the major product (R_f 0.25) described above.

1D-6-O-*Acetyl-1,3,4-tri*-O-*benzyl-2,5-di*-O-p-*methoxybenzyl*-myo-*inositol* (**10**).—Saponification of the bis-(−)-ω-camphanate **8** gave the diol **9** as a syrup which was subjected to tin-mediated benzylation as described above for the enantiomer **12**. Acetylation of the mixed products gave the acetate **10**; mp 138–139°C; $[\alpha[_D^{25}$ −8.0° (*c* 1, $CHCl_3$); with ^{1}H NMR spectrum identical with that of the enantiomer **17**. Calcd for $C_{45}H_{48}O_9$: C, 73.75; H, 6.60%. Found: C, 73.59; H, 6.54%.

1D-3,6-Di-O-*benzyl-4,5-di*-O-*(but-2-enyl)*-myo-*inositol* (**27**).—The chiral diol [8]

25 was treated with an excess of crotyl bromide and NaH in DMF, and the product **26** was isolated in the usual way and heated under reflux with 1:9 M HCl–MeOH for 30 min. An excess of $NaHCO_3$ was added and the solution was concentrated. Extraction of the residue with CH_2Cl_2 gave the diol **27**; mp 83–85°C (from light petroleum); $[\alpha]_D^{26}$ −8.8° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.69, 1.74 (2 s, 6 H, =CH*Me*), 2.45, 2.51 (2 s, 2 H, 2 OH), 3.13–3.84 (m, 5 H, ring protons), 4.13–4.45 (m, 5 H, H-2 and 2 OCH_2–CH=), 4.70 (s, CH_2Ph), 4.85 (ABq, CH_2Ph), 5.65–5.79 (m, 4 H, 2 CH=CH), 7.35 (s, 10 H, aromatic). Calcd for $C_{28}H_{36}O_6$: C, 71.79; H, 7.74%. Found: C, 71.75; H, 7.64%.

*1*D-*1,3,6-Tri*-O-*benzyl-4,5-di*-O-*(but-2-enyl)*-myo-*inositol* (**28**).—A mixture of the diol **27** (530 mg, 1.1 mmol), dibutyltin oxide (422 mg, 1.7 mmol), tetrabutylammonium bromide (546 mg, 1.7 mmol), and benzyl bromide (0.5 mL, 4.2 mmol) in MeCN (45 mL) was heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 7 h when TLC (4:1 ether–light petroleum) showed complete conversion of **27** (R_f 0.4) into major (R_f 0.85) and minor (R_f 0.8) products. The Soxhlet apparatus was removed, Et_3N (2 mL) was added, and the solution was heated under reflux for 1 h to destroy the excess of benzyl bromide. The product was isolated in the usual way [11] and recrystallised from light petroleum to give **28** (588 mg, 93%); mp 85–87°C; $[\alpha]_D^{25}$ +3.4° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.68–1.73 (m, 6 H, 2 =CH*Me*), 2.42 (s, OH), 3.11–3.37 (m, 3 H, ring protons), 3.66–3.98 (m, 2 H, ring protons), 4.17–4.41 (m, 5 H, H-2 and 2 OCH_2–CH=), 4.68 (s, 4 H, 2 CH_2Ph), 4.84 (s, 2 H, CH_2Ph), 5.65–5.72 (m, 4 H, 2 CH=CH), 7.31, 7.34 (2 s, 15 H, aromatic). Calcd for $C_{35}H_{42}O_6$: C, 75.24; H, 7.58%. Found: C, 75.20; H, 7.49%.

*1*D-*1,3,6-Tri*-O-*benzyl*-myo-*inositol* (**18**) *and 1*D-*2,4,5-tri*-O-*acetyl-1,3,6-tri*-O-*benzyl*-myo-*inositol* (**19**).—(*a*) Cerium(IV) ammonium nitrate (1.43 g) in 9:1 MeCN–water (10 mL) was added dropwise to a solution of the chiral alcohol **15** (450 mg) in 9:1 MeCN–water (10 mL). During 2 h, TLC (2:1 ether–light petroleum) showed conversion of **15** (R_f 0.7) through intermediate products (R_f 0.2 and 0.1) into a product (R_f 0). Water (25 mL) was added and the mixture was concentrated to remove the MeCN. The product was extracted with ether, and the extract washed with satd aq $NaHCO_3$, dried (K_2CO_3), and concentrated to give the crude product which was purified by column chromatography (ether) to give **18** (190 mg) with liquid crystalline properties, melting at 112°C and giving a clear liquid at 127°C (from light petroleum–ether); $[\alpha]_D^{25}$ +16.2° (*c* 1, $CHCl_3$). ^1H NMR data: δ 2.47, 2.62, 2.64 (3 s, 3 OH), 3.15–4.23 (m, 6 H, ring protons), 4.69 (s, 4 H, 2 CH_2Ph), 4.86 (ABq, 2 H, CH_2Ph), 7.32 (s, 15 H, aromatic). Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71%. Found: C, 71.88; H, 6.49%. This gave a crystalline triacetate **19**; mp 154–155°C (from light petroleum–ether); $[\alpha]_D^{25}$ +52.6° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.91, 1.98, 2.18 (3 s, 3 Ac), 3.37, 3.41, 3.43, 3.46, 3.48, 3.52, 3.54, 3.57 (8 s, 2 H, H-1,3), 3.88 (t, *J* 9.44 Hz, H-6), 3.33–4.90 (m, 6 H, 3 CH_2Ph), 5.01 (t, *J* 9.16 Hz, H-5), 5.34 (t, *J* 9.77 Hz, H-4), 5.83 (t, *J* 2.44 Hz, H-2), 7.27, 7.30 (2 s, 15 H, aromatic). Calcd for $C_{33}H_{36}O_9$: C, 68.73; H, 6.29%. Found: C, 68.63; H, 6.36%.

(*b*) A solution of the di(but-2-enyl) ether **28** (500 mg) and potassium *tert*-butoxide (1 g) in dry Me_2SO (25 mL) was kept at 50°C for 8 h when TLC (ether) showed complete conversion of **28** (R_f 0.85) into a product (R_f 0.3). The solution

was cooled and diluted with satd aq KCl (25 mL), and the product was extracted with ether. Column chromatography (ether) gave the triol **18** (250 mg) which was acetylated to give **19**; mp 155–157°C (from light petroleum–ether); $[\alpha]_D^{25}$ +51.5° (*c* 1, $CHCl_3$); with a ^1H NMR spectrum identical with that in (*a*).

*1D-1,2,3,6-Tetra-O-benzyl-4,5-O-isopropylidene-*myo*-inositol* (**24**).—A mixture of the chiral triol **18** [80 mg, regenerated by saponification of the triacetate **19** described in (*a*) above], toluene *p*-sulphonic acid (10 mg), 2,2-dimethoxypropane (2 mL), and acetone (5 mL) was stirred at 20°C for 2 h, after which time TLC (1:1 ether–light petroleum) showed conversion of **18** (R_f 0) into a product (R_f 0.5). NEt_3 and $NaHCO_3$ were added and the mixture was concentrated. The product was extracted from the residue with ether and the extract dried (K_2CO_3). Column chromatography (1:1 ether–light petroleum) gave pure **23** which was treated with benzyl bromide and NaH in DMF. The product was isolated in the usual way and column chromatography (1:3 ether–light petroleum) gave **24** (80 mg); mp 82–83°C (from light petroleum); $[\alpha]_D^{25}$ −34.2° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.45 (s, 6 H, CMe_2), 3.26–4.27 (m, 6 H, ring protons), 4.50, 4.64, 4.67, 4.74, 4.81, 4.86, 4.99 (m, 8 H, 4 CH_2Ph), 7.29, 7.30 (2 s, 20 H, aromatic), identical with those of the enantiomer [11] {lit. [11] mp 83–84°C, $[\alpha]_D^{27}$ +31° (*c* 1, $CHCl_3$), for the enantiomer}. Calcd for $C_{37}H_{40}O_6$: C, 76.52; H, 6.94%. Found: C, 76.72; H, 7.46%.

*1D-1,3,6-Tri-O-benzyl-*myo*-inositol 2,4,5-tris(dibenzyl phosphate)* (**21**).—The chiral triol **18** (100 mg) was treated with bis(benzyloxy)diisopropylaminophosphine (**88**) in the usual way [12] and TLC (ether) showed conversion of **18** (R_f 0.3) into the trisphosphite **20** (R_f 1.0) which was oxidised [12] with *m*-chloroperoxybenzoic acid to give crude **21** (R_f 0.4). Column chromatography (ether followed by EtOAc) gave the trisphosphate **21** (120 mg) as a syrup; $[\alpha]_D^{26}$ −9.0° (*c* 1, $CHCl_3$). ^{31}P NMR data: δ −1.48 (2 P), −1.75 (1 P). Calcd for $C_{69}H_{69}O_{15}P_3$: C, 67.31; H, 5.65; P, 7.55%. Found: C, 67.17; H, 5.69; P, 7.69%.

The trisphosphate **21** (78 mg) was treated with NaI (133 mg) in acetone (15 mL) under reflux for 6 h. TLC (90:10:1 $CHCl_3$–MeOH–HOAc) of acidified samples, during this time, showed conversion of **21** (R_f 0.6) through intermediate products (R_f 0.5 and 0.45) into a product (R_f 0); after this time, the product crystallised from the hot solution. The mixture was cooled and the product was filtered and washed with cold acetone to give **22** (30 mg); mp 269–271°C; $[\alpha]_D^{25}$ −5.0° (*c* 1, $CHCl_3$). ^{31}P NMR data (D_2O): δ −0.40 (1 P), −0.61 (2 P).

*1D-3,6-Di-O-benzyl-4,5-di-O-(but-2-enyl)-1-*O*-p-methoxybenzyl-*myo*-inositol* (**29**).—The diol **27** was subjected to tin-mediated *p*-methoxybenzylation (using *p*-methoxybenzyl chloride) as described for the tin-mediated benzylation used to produce **28**. TLC (4:1 ether–light petroleum) showed conversion of **27** (R_f 0.3) into a major product (R_f 0.75). Column chromatography (ether–light petroleum followed by ether) of the crude product gave **29** (82%); mp 85–87°C (from light petroleum–ether); $[\alpha]_D^{25}$ +1.2° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.68–1.72 (m, 6 H, 2 =CH*Me*), 2.40 (s, OH), 3.10–3.96 (m, 5 H, ring protons), 3.79 (s, OMe), 4.14–4.41 (m, 5 H, H-2 and 2 OCH_2–CH=), 4.60, 4.69, 4.83 (3 s, each 2 H, 3 CH_2Ph), 5.60–5.72 (m, 4 H, 2 CH=CH), 6.78–7.34 (m, 14 H, aromatic). Calcd for $C_{36}H_{44}O_7$: C, 73.44; H, 7.53%. Found: C, 73.29; H, 7.42%.

1D-2,3,6-Tri-O-benzyl-4,5-di-O-(but-2-enyl)-1-O-p-methoxybenzyl-myo-inositol (**30**).—The alcohol **29** was treated with an excess of benzyl bromide and NaH in DMF and the product was isolated in the usual way. Column chromatography (1:2 ether–light petroleum) gave **30** (90%); mp 62–64°C (from light petroleum); $[\alpha]_D^{25}$ −3.7° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.67–1.72 (m, 6 H, 2 =CH*Me*), 3.10–3.32 (m, 3 H, ring protons), 3.79 (s, 3 H, OMe), 3.75–4.05 (m, 3 H, ring protons), 4.24–4.44 (m, 4 H, 2 OCH_2–CH=), 4.53 (s, 2 H, CH_2Ph), 4.61 (ABq, 2 H, CH_2Ph), 4.83 (s, 4 H, 2 CH_2Ph), 5.63–5.70 (m, 4 H, 2 CH=CH), 6.77–7.32 (m, 19 H, aromatic). Calcd for $C_{43}H_{50}O_7$: C, 76.08; H, 7.43%. Found: C, 76.19; H, 7.61%.

1D-2,3,6-Tri-O-benzyl-1-O-p-methoxybenzyl-myo-inositol [16] (**35**).—A solution of the di(but-2-enyl) ether **30** (643 mg) and potassium *tert*-butoxide (1 g) in dry Me_2SO (25 mL) was kept at 50°C for 2 h during which time TLC (1:1 ether–light petroleum) showed conversion of **30** (R_f 0.85) through two mono(but-2-enyl) ethers (R_f 0.4 and 0.3) into the diol **35** (R_f 0). The solution was cooled, then diluted with satd aq KCl (25 mL), and the product was extracted with ether. The extract was dried (K_2CO_3) and concentrated to give **35** (276 mg); mp 104–106°C (from 10:1 light petroleum–EtOAc); $[\alpha]_D^{25}$ +12.8° (*c* 1, $CHCl_3$). ^1H NMR data: δ 2.62 (s, 2 OH), 3.11–3.51 (m, 3 H, H-1,3,5), 3.81 (s, 3 H, OMe), 3.90–4.16 (m, 3 H, H-2,4,6), 4.56 (s, 4 H, 2 CH_2Ph), 4.81 (ABq, 2 H, CH_2Ph), 6.81–7.32 (m, 19 H, aromatic), identical with those of the product described previously [16] {lit. [16] mp 105–106°C, $[\alpha]_D^{25}$ +15.5° (*c* 1, $CHCl_3$)}. This gave a diacetate **36**; mp 125–127°C; $[\alpha]_D^{25}$ +34.6° (*c* 1, $CHCl_3$) {lit. [16] mp 125–126°C, $[\alpha]_D^{25}$ +34.7° (*c* 1, $CHCl_3$)}; with a ^1H NMR spectrum identical with that described [16].

1D-2,3,6-Tri-O-benzyl-1-O-p-methoxybenzyl-myo-inositol 4,5-bis(dibenzyl phosphate) (**40**).—The chiral alcohol **35** (200 mg) was treated with bis(benzyloxy)diisopropylaminophosphine (**88**) in the usual way [12] and TLC (3:1 ether–light petroleum) showed conversion of **35** (R_f 0.3) into the bisphosphite (**39**) (R_f 1.0) which was oxidised [12] with *m*-chloroperoxybenzoic acid to give crude **40** (R_f 0.3). Column chromatography (3:1 ether–light petroleum followed by ether) gave **40** (73%); mp 95–97°C (from ether containing a trace of EtOH); $[\alpha]_D^{27}$ −10.2° (*c* 1, $CHCl_3$). ^{31}P NMR data: δ −1.75, −2.15. Calcd for $C_{63}H_{64}O_{13}P_2$: C, 69.35; H, 5.91; P, 5.68%. Found: C, 69.44; H, 5.79; P, 5.33%.

1D-2,3,6-Tri-O-benzyl-myo-inositol 4,5-bis(dibenzyl phosphate) (**41**).—A solution of cerium(IV) ammonium nitrate (460 mg) in 9:1 MeCN–water (3 mL) was added dropwise to a stirred solution of the bisphosphate **40** (230 mg) in 9:1 MeCN–water (5 mL) during 30 min when TLC (ether) showed complete conversion of **40** (R_f 0.5) into a product (R_f 0.25). Water (10 mL) was added, the solution was concentrated to remove MeCN, and the product was extracted with CH_2Cl_2. The extract was washed with satd aq $NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography (ether followed by EtOAc) gave **41** (129 mg, 63%); mp 90–91°C (from ether–light petroleum); $[\alpha]_D^{25}$ −15.6° (*c* 1, $CHCl_3$). ^{31}P NMR data: δ −1.55, −1.82. Calcd for $C_{55}H_{56}O_{12}P_2$: C, 68.03; H, 5.81; P, 6.38%. Found: C, 67.73; H, 5.78; P, 6.42%.

1D-3,6-Di-O-benzyl-1,4,5-tri-O-(but-2-enyl)-myo-inositol (**31**).—The diol **27** was subjected to tin-mediated crotylation (using crotyl bromide) as described for the

tin-mediated benzylation used to produce **28**. TLC (2:1 ether–light petroleum) showed conversion of **27** (R_f 0.2) into a product (R_f 0.6). Column chromatography (2:1 ether–light petroleum) gave **31** (358 mg, 98%); mp 56–57°C (from light petroleum); $[\alpha]_D^{27}$ −2.6° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.63–1.72 (m, 9 H, 3 =CH*Me*), 2.40 (s, OH), 3.09–3.34 (m, 3 H, ring protons), 3.65–3.92 (m, 2 H, ring protons), 4.05–4.43 (m, 7 H, H-2 and 3 OCH_2–CH=), 4.72, 4.81 (2 s, 4 H, 2 CH_2Ph), 5.56–5.73 (m, 6 H, 3 CH=CH), 7.35 (s, 10 H, aromatic). Calcd for: $C_{32}H_{42}O_6$: C, 73.53; H, 8.10%. Found: C, 73.53; H, 8.03%.

*1*D-*2,3,6-Tri*-O-*benzyl*-myo-*inositol [16,18]* (**37**).—The alcohol **31** was treated with benzyl bromide and NaH in DMF, and the product isolated in the usual way. Column chromatography (1:2 ether–light petroleum) gave the tribenzyl ether **32** as a syrup. ^1H NMR data: δ 1.58–1.71 (m, 9 H, 3 =CH*Me*), 3.10–3.30 (m, 3 H, ring protons), 3.74–4.80 (m, 3 H, ring protons), 4.23–4.43 (m, 6 H, 3 OCH_2–CH=), 4.61, 4.64, 4.82, 4.84 (m, 6 H, 3 CH_2Ph), 5.53–5.76 (m, 6 H, 3 CH=CH), 7.32 (s, 15 H, aromatic). Compound **32** (300 mg) and potassium *tert*-butoxide (1 g) in dry Me_2SO (25 mL) was kept at 50°C for 2 h when TLC (ether) showed complete conversion of **32** (R_f 1.0) into a product (R_f 0.5) which co-chromatographed with **37** which had been prepared previously [16]. The solution was diluted with satd aq KCl (25 mL) and the product was extracted with ether. Column chromatography (ether) gave **37** (115 mg); mp 120–122°C; $[\alpha]_D^{25}$ +7° (*c* 1, $CHCl_3$); with a ^1H NMR spectrum identical with that described [11] {lit. [16] mp 122–123°C, $[\alpha]_D^{25}$ +10° (*c* 1, $CHCl_3$)}.

*1*D-*1*-O-*Allyl-3,6-di*-O-*benzyl-4,5-di*-O-*(but-2-enyl)*-myo-*inositol* (**33**).—The diol **27** was subjected to tin-mediated allylation (using allyl bromide) as described for the tin-mediated benzylation used to produce **28**. TLC (2:1 ether–light petroleum) showed conversion of **27** (R_f 0.2) into a product (R_f 0.6). Column chromatography (2:1 ether–light petroleum) gave **33** (90%); mp 50–52°C (from light petroleum); $[\alpha]_D^{26}$ +0.5° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.64–1.74 (m, 6 H, 2 =CH*Me*), 2.43 (s, OH), 3.09–3.34 (m, 3 H, ring protons), 3.65–3.94 (m, 2 H, ring protons), 4.14–4.44 (m, 7 H, H-2 and 3 OCH_2–CH=), 4.72, 4.81 (2 s, 4 H, 2 CH_2Ph), 5.10–5.35 (m, 2 H, =CH_2), 5.65–6.15 (m, 5 H, 2 CH=CH and C*H*=CH_2), 7.34 (s, 10 H, aromatic). Calcd for $C_{31}H_{40}O_6$: C, 73.20; H, 7.93%. Found: C, 73.29; H, 7.94%.

*1*D-*2,3,6-Tri*-O-*benzyl-1*-O-*(*cis-*prop-1-enyl)*-myo-*inositol [16,18]* (**42**).—The alcohol **33** was treated with benzyl bromide and NaH in DMF, and the product was isolated in the usual way and purified by column chromatography (1:2 ether–light petroleum) to give the tribenzyl ether **34** as a syrup. ^1H NMR data: δ 1.57–1.71 (m, 6 H, 2 =CH*Me*), 3.11–3.31 (m, 3 H, ring protons), 3.69–4.48 (m, 9 H, 3 OCH_2–CH= and 3 ring protons), 4.63 (ABq, 2 H, CH_2Ph) 4.81, 4.84 (2 s, each 2 H, 2 CH_2Ph), 5.07–5.35 (m, 2 H, =CH_2), 5.62–6.12 (m, 5 H, 2 CH=CH and C*H*=CH_2), 7.32 (s, 15 H, aromatic). A solution of **34** (370 mg) and potassium *tert*-butoxide (1 g) in dry Me_2SO (25 mL) was kept at 50°C for 4 h when TLC (1:1 ether–light petroleum) showed complete conversion of **34** (R_f 0.8) into a product (R_f 0). The solution was diluted with satd aq KCl (25 mL) and the product was extracted with ether. Column chromatography (ether) gave **42** (50%); mp 113–115°C (from light petroleum–EtOAc); $[\alpha]_D^{25}$ +34.5° (*c* 1, $CHCl_3$); with ^1H NMR spectrum as described [16] {lit. [16] mp 114–115°C, $[\alpha]_D^{25}$ +33.0° (*c* 1, $CHCl_3$); lit. [18] mp

116–118°C, $[\alpha]_D^{11}$ +40.6° (*c* 4, $CHCl_3$)}. This gave a diacetate **43**; mp 153–155°C; $[\alpha]_D^{25}$ +48.7° (*c* 1, $CHCl_3$); $[\alpha]_D^{25}$ +41.7° (*c* 1, pyridine); with a ^1H NMR spectrum as described [16] {lit. [16] mp 154–155°C, $[\alpha]_D^{25}$ +49° (*c* 1, $CHCl_3$)}.

(±)-5-O-Allyl-1,4-di-O-benzyl-6-O-(but-2-enyl)-myo-*inositol* (**51**) *and (±)-6-O-allyl-1,4-di-O-benzyl-5-O-(but-2-enyl)*-myo-*inositol* (**53**).—(*a*) A mixture of (±)-1,4-di-*O*-benzyl-2,3-*O*-isopropylidene-*myo*-inositol [8] (**44**) (0.675 g, 1.7 mmol), dibutyltin oxide (0.550 g, 2.21 mmol), tetrabutylammonium bromide (0.550 g, 1.7 mmol), and allyl bromide (40 mL) was stirred and heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 7 h. TLC (3:1 ether–light petroleum) of the solution showed complete conversion of **44** (R_f 0.1) into two products (R_f 0.75 and 0.85). The solution was cooled, the solvent evaporated off, and the residue distributed between ether (40 mL) and water (40 mL). The ether layer was stirred with satd aq $NaHCO_3$ (40 mL) for 1 h, and the mixture was filtered through Celite. The separated ether layer was dried (K_2CO_3) and concentrated. Column chromatography (2:1 ether–light petroleum) gave **46** (R_f 0.7, 0.346 g, 47%) and **45** (R_f 0.6, 0.251 g, 34%).

Both alcohols (**45** and **46**) were treated separately with an excess of crotyl bromide and NaH in DMF at 20°C in the usual way until TLC showed complete conversion of starting material into new products. The new products (**49** from **45** and **50** from **46**) were isolated and purified by column chromatography to give **49** and **50** as syrups. ^1H NMR data for **49**: δ 1.34, 1.48 (2 s, 6 H, CMe_2), 1.72 (d, 3 H, *J* 4.3 Hz, =CH*Me*), 3.10–4.30 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.77 (m, 4 H, 2 CH_2Ph), 5.09–5.35 (m, 2 H, $=CH_2$), 5.64–6.12 (m, 3 H, CH=CH and C*H*=CH_2), 7.34 (m, 10 H, aromatic). ^1H NMR data for **50**: δ 1.34, 1.48 (2 s, 6 H, CMe_2), 1.70 (d, 3 H, *J* 3.7 Hz, =CH*Me*), 3.08–4.35 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.77 (s, 4 H, 2 CH_2Ph), 5.10–5.40 (m, 2 H, $=CH_2$), 5.61–6.16 (m, 3 H, CH=CH and C*H*=CH_2), 7.34 (m, 10 H, aromatic).

Compounds **49** and **50** were treated separately with 9:1 acetone–M HCl for 30 min. An excess of $NaHCO_3$ was added and the solution was concentrated. Extraction of each residue with CH_2Cl_2 gave the diols **51** (from **49**); mp 88–91°C (from ether–light petroleum); ^1H NMR data: δ 1.71 (d, 3 H, *J* 4.3 Hz, =CH*Me*), 2.40, 2.44 (2 s, 2 H, 2 OH), 3.15–4.38 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.71 (m, 4 H, 2 CH_2Ph), 5.03–5.39 (m, 2 H, $=CH_2$), 5.64–6.16 (m, 3 H, CH=CH and C*H*=CH_2), 7.34 (s, 10 H, aromatic). Calcd for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54%. Found: C, 71.54; H, 7.63%; and **53** (from **50**); mp 98–100°C (from ether–light petroleum); ^1H NMR data: δ 1.69 (d, 3 H, *J* 4.9 Hz, =CH*Me*), 2.39, 2.44 (2 s, 2 H, 2 OH), 3.23–4.37 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.70 (m, 4 H, 2 CH_2Ph), 5.05–5.37 (m, 2 H, $=CH_2$), 5.67–6.15 (m, 3 H, CH=CH and C*H*=CH_2), 7.34 (m, 10 H, aromatic). Calcd for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54%. Found: C, 71.09; H, 7.54%.

(*b*) A mixture of the diol **44** (0.395 g, 0.986 mmol), dibutyltin oxide (0.491 g, 1.97 mmol), tetrabutylammonium bromide (0.636 g, 1.97 mmol), crotyl bromide (0.2 mL), and MeCN (40 mL) was stirred and heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 24 h. TLC (1:1 ether–light petroleum) showed conversion of **44** (R_f 0) into two products (R_f 0.4 and 0.5)

which were isolated in the usual way. Column chromatography (1:1 ether–light petroleum) gave **48** (R_f 0.5, 0.189 g) and **47** (R_f 0.4, 0.1 g). ^{1}H NMR data for **47**: δ 1.33, 1.46 (2 s, 6 H, CMe_2), 1.70 (d, 3 H, J 4.3 Hz, =CH*Me*), 2.68 (s, OH), 3.12 (t, J 9.2 Hz, H-5), 3.45–4.33 (m, 7 H, 5 ring protons and OCH_2–CH=), 4.80 (m, 4 H, 2 CH_2Ph), 5.60–5.77 (m, 2 H, CH=CH), 7.34 (m, 10 H, aromatic). ^{1}H NMR data for **48**: δ 1.35, 1.50 (2 s, 6 H, CMe_2), 1.72 (d, 3 H, J 4.9 Hz, =CH*Me*), 2.67 (d, J 1.8 Hz, OH), 3.49–4.32 (m, 8 H, 6 ring protons and OCH_2–CH=), 4.76 (m, 4 H, 2 CH_2Ph), 5.63–5.74 (m, 2 H, CH=CH), 7.34 (s, 10 H, aromatic).

Both alcohols (**47** and **48**) were treated separately with allyl bromide and NaH in DMF at 20°C in the usual way. The products were isolated and purified to give **49** (from **48**) and **50** (from **47**) with ^{1}H NMR spectra identical with those described in (*a*). Compounds **49** and **50** were hydrolysed as above with 9:1 acetone–M HCl to give, respectively, **51** and **53** identical with the materials described in (*a*).

(±)-1,2,3,4-Tetra-O-*benzyl-5*-O-*(*cis*-prop-1-enyl)*-myo-*inositol [19]* (**55**).—The diol **51** was treated with an excess of benzyl bromide and NaH in DMF at 20°C until TLC (1:1 ether–light petroleum) showed complete conversion of **51** (R_f 0) into a product (R_f 0.8). The product was isolated in the usual way and column chromatography (1:4 ether–light petroleum) gave **52** as a syrup. ^{1}H NMR data: δ 1.70 (d, 3 H, J 4.3 Hz, =CH*Me*), 3.15–4.48 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.61 (ABq, 4 H, 2 CH_2Ph), 4.84 (s, 4 H, 2 CH_2Ph), 5.10–5.36 (m, 2 H, $=CH_2$), 5.66–6.16 (m, 3 H, CH=CH and CH=CH_2), 7.30 (s, 20 H, aromatic).

A solution of **52** (0.202 g) and potassium *tert*-butoxide (0.150 g) in dry Me_2SO (15 mL) was kept at 50°C for 2 h when TLC (1:1 ether–light petroleum) showed complete conversion of **52** (R_f 0.8) into a product (R_f 0.5). The solution was diluted with satd aq KCl (15 mL) and the product was extracted with ether. Column chromatography (1:1 ether–light petroleum) gave **55** (158 mg, 85%); mp 96–97°C (from light petroleum); identical with the material described [19] (lit. [19] mp 95–96°C). ^{1}H NMR data: δ 1.63 (dd, 3 H, J 1.8 and 6.7 Hz, =CH*Me*), 2.48 (d, J 2.4 Hz, OH), 3.11–3.57 (m, 3 H, H-1,3,5), 3.91–4.45 (m, 4 H, 3 ring protons and =C*H*Me), 4.76 (m, 8 H, 4 CH_2Ph), 6.22 (dd, 1 H, J 1.8 and 6.1 Hz, OCH=), 7.31 (s, 20 H, aromatic).

(±)-1,2,3,4-Tetra-O-*benzyl-6*-O-*(*cis*-prop-1-enyl)*-myo-*inositol [19]* (**56**).—The diol **53** was benzylated as described for the preparation of **52**. TLC (1:1 ether–light petroleum) showed conversion of **53** (R_f 0) into a product (R_f 0.7). The product was isolated in the usual way and column chromatography (1:4 ether–light petroleum) gave **54** as a syrup. ^{1}H NMR data: δ 1.69 (d, 3 H, J 4.9 Hz, =CH*Me*), 3.14–4.37 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.60, 4.84 (2 s, 8 H, 4 CH_2Ph), 5.10–5.35 (m, 2 H, $=CH_2$), 5.62–6.15 (m, 3 H, CH=CH and CH=CH_2), 7.32 (s, 20 H, aromatic).

Compound **54** was treated with potassium *tert*-butoxide as described above for the preparation of compound **55**. Column chromatography (1:2 ether–light petroleum) gave **56** (31 mg, 42%); mp 140–142°C (from light petroleum); identical with the material described [19] (lit. [19] mp 142–143°C). ^{1}H NMR data: δ 1.61 (dd, 3 H, J 1.8 and 6.7 Hz, =CH*Me*), 2.42 (d, J 2.4 Hz, OH), 3.22–4.42 (m, 7 H, 6 ring protons and =C*H*Me), 4.60 (ABq, 4 H, 2 CH_2Ph), 4.84 (ABq, 4 H, 2 CH_2Ph), 6.23 (dd, J 1.8 and 6.1 Hz, OCH=), 7.31 (s, 20 H, aromatic).

1D-5-O-Allyl-3,6-di-O-benzyl-4-O-(but-2-enyl)-myo-*inositol* (**59**), *1D-4-O-allyl-3,6-di-O-benzyl-5-O-p-methoxybenzyl*-myo-*inositol* (**70**), *and the racemate* (**78**).—The chiral diol [8] **25** (3.2 g) was treated with dibutyltin oxide (2.6 g), tetrabutylammonium bromide (2.6 g), and allyl bromide (60 mL) as described above for the corresponding racemate **44**, and the products **68** (1.77 g, 50%) and **57** (1.58 g, 42%) were isolated as described for the corresponding racemates **46** and **45**.

The alcohol **57** (1.58 g) was treated with crotyl bromide (1.5 mL) and NaH (0.5 g) in DMF (30 mL) in the usual way until TLC (1:1 ether–light petroleum) showed complete conversion of **57** (R_f 0.3) into a product **58** (R_f 0.75). This was isolated in the usual way and treated with 9:1 acetone–M HCl at reflux for 1 h when TLC (1:2 ether–light petroleum) showed conversion of **58** (R_f 0.5) into a product **59** (R_f 0). Column chromatography (2:1 ether–light petroleum) gave the diol **59** (1.2 g, 73% from **57**); mp 92–94°C (from light petroleum); $[\alpha]_D^{25}$ −10.2° (*c* 1, $CHCl_3$). ^1H NMR data: δ 1.70 (d, 3 H, *J* 4.9 Hz, =CH*Me*), 2.40 (broad signal, 2 OH), 3.25–4.38 (m, 10 H, 6 ring protons and 2 OCH_2–CH= of the crotyl and allyl groups), 4.77 (m, 4 H, 2 CH_2Ph with major peaks at 4.64, 4.70, 4.76, and 4.90), 5.10–5.37 (m, 2 H, =CH_2), 5.64–6.16 (m, 3 H, CH=CH and C*H*=CH_2), 7.34 (s, 10 H, aromatic). Calcd for $C_{27}H_{34}O_6 \cdot 0.5\ H_2O$: C, 69.95, H, 7.61% Found: C, 69.92; H, 7.30%.

The alcohol **68** (1.77 g) was treated with *p*-methoxybenzyl chloride (1.5 mL) and NaH in DMF (30 mL) in the usual way until TLC (1:1 ether–light petroleum) showed complete conversion of **68** (R_f 0.4) into a product **69** (R_f 0.65). This was isolated in the usual way and column chromatography (1:1 ether–light petroleum) gave **69** as a syrup (1.79 g, 79%) which was treated with 3:7:1 acetone–MeOH–M HCl at 50°C until TLC (1:1 ether–light petroleum) showed conversion into a product (R_f 0). Column chromatography (5:1 ether–light petroleum) gave the diol **70** (1.46 g, 88%); mp 116–117°C (from EtOAc–light petroleum); $[\alpha]_D^{24}$ −6.7° (*c* 1, $CHCl_3$). ^1H NMR data: δ 2.40, 2.47 (2 s, 2 H, 2 OH), 3.78 (s, 3 H, OMe), 3.28–4.39 (m, 8 H, 6 ring protons and OCH_2–CH=), 4.83 (m, 6 H, 3 CH_2Ph with major peaks at 4.70, 4.76, 4.79, and 4.89), 5.12–5.37 (m, 2 H, =CH_2), 5.80–6.17 (m, 1 H, C*H*=CH_2), 6.79–7.34 (m, 14 H, aromatic). Calcd for $C_{31}H_{36}O_7$: C, 71.52; H, 6.97%. Found: C, 71.57; H, 6.99%.

The racemic diol **78** (prepared in the same way from the racemate **46**) had mp 110–111°C (from light petroleum–EtOAc) and a ^1H NMR spectrum identical with that described for the chiral diol **70**. Found: C, 71.42; H, 7.08%.

1D-5-O-Allyl-1,4-di-O-(but-2-enyl)-myo-*inositol* (**67**).—A mixture of the chiral diol [8] **64** (2 g, 6 mmol), dibutyltin oxide (2.32 g, 9.3 mmol), tetrabutylammonium bromide (2.61 g, 8.1 mmol), and allyl bromide (40 mL) was stirred and heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 5 h. TLC (1:2 EtOAc–light petroleum) of the solution showed complete conversion of **64** (R_f 0.1) into two products (R_f 0.8 and 0.9) which were isolated in the usual way [11]. Column chromatography (1:3 EtOAc–light petroleum) gave **66** (R_f 0.9, 1.04 g, 46%) and **65** (R_f 0.8, 0.98 g, 43%).

The alcohol **65** (0.98 g) was treated with 9:1 acetone–M HCl at reflux for 1 h when TLC (1:3 EtOAc–light petroleum) showed conversion of **65** into a product

(R_f 0). Column chromatography (4:1 EtOAc–light petroleum) gave the triol **67** (0.79 g, 91%); mp 128–129°C (from EtOAc–light petroleum); $[\alpha]_D^{25}$ +6.7° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 1.69, 1.74 (2 s, 6 H, 2 =CH*Me*), 2.55, 2.60, 2.64 (3 s, 3 H, 3 OH), 3.12–4.36 (m, 12 H, 6 ring protons and 3 OCH_2–CH=), 5.10–5.37 (m, 2 H, =CH_2), 5.58–6.15 (m, 5 H, 2 CH=CH and C*H*=CH_2). Calcd for $C_{17}H_{28}O_6$: C, 62.17; H, 8.60%. Found: C, 62.27; H, 8.59%.

*1*D*-2,3,6-Tri*-O*-benzyl-5*-O*-(*cis*-prop-1-enyl)*-myo-*inositol* (**62**).—(*a*) The triol **67** (0.7 g, 2.13 mmol) was treated with benzyl bromide (2.5 mL) and NaH (1 g) in DMF (30 mL) in the usual way until TLC (1:2 ether–light petroleum) showed conversion of **67** (R_f 0) into a product (R_f 0.8). This was isolated in the usual way and column chromatography (1:3 ether–light petroleum) gave the tribenzyl ether **61** (0.97 g, 76%) as a syrup. ^{1}H NMR data: δ 1.67, 1.72 (2 s, 6 H, 2 =CH*Me*), 3.09–4.42 (m, 12 H, 6 ring protons and 3 OCH_2–CH=), 4.62, 4.65, 4.80, 4.82, 4.85 (m, 6 H, 3CH_2Ph), 5.08–5.35 (m, 2 H, =CH_2), 5.59–6.15 (m, 5 H, 2 CH=CH and C*H*=CH_2), 7.32 (s, 15 H, aromatic). Compound **61** (0.95 g, 1.58 mmol) was treated with potassium *tert*-butoxide (1.16 g) in dry Me_2SO (40 mL) at 50°C for 2 h when TLC (1:3 ether–light petroleum) showed conversion of **61** (R_f 0.5) into a product (R_f 0). The solution was diluted with satd aq KCl (40 mL) and the product was extracted with ether. Column chromatography (2:1 ether–light petroleum) gave **62** (0.68 g, 87%); mp 78–80°C (from light petroleum); $[\alpha]_D^{25}$ +14.2° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 1.53 (dd, 3 H, *J* 1.2 and 6.7 Hz, =CH*Me*), 2.31, 2.53 (2 s, 2 H, 2 OH), 3.27 (dd, 1 H, *J* 2.4 and 9.8 Hz, H-3), 3.46–4.46 (m, 6 H, 5 ring protons and =C*H*Me), 4.78 (m, 6 H, 3 CH_2Ph with major peaks at 4.63, 4.64, 4.67, 4.80, and 4.86), 6.20 (dd, 1 H, *J* 1.8 and 6.1 Hz, OCH=), 7.25 (m, 15 H, aromatic). Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99%. Found: C, 73.04; H, 6.80%.

The diacetate, 1D-1,4-di-*O*-acetyl-2,3,6-tri-*O*-benzyl-5-*O*-(*cis*-prop-1-enyl)-*myo*-inositol (**63**) had mp 127–128°C (from light petroleum); $[\alpha]_D^{25}$ −22.9° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 1.55 (dd, 3 H, *J* 1.2 and 6.7 Hz, =CH*Me*), 1.92, 2.01 (2 s, 6 H, 2 Ac), 3.43 (dd, 1 H, *J* 2.4 and 10.4 Hz, H-3), 3.53 (t, 1 H, *J* 9.8 Hz, H-5), 4.09 (t, 1 H, *J* 2.4 Hz, H-2), 4.09 (t, 1 H, *J* 9.8 Hz, H-6), 4.25–4.94 (m, with major peaks at 4.51, 4.57, 4.63, 4.68, 4.72, and 4.80, 8 H, 3 CH_2Ph, =C*H*Me, and H-1), 5.66 (t, 1 H, *J* 10.4 Hz, H-4), 6.03 (dd, 1 H, *J* 1.8 and 6.1 Hz, OCH=), 7.28, 7.30 (2 s, 15 H, aromatic). Calcd for $C_{34}H_{38}O_8$: C, 71.46; H, 6.67%. Found: C, 71.05; H, 6.66%.

(*b*) A mixture of the diol **59** (0.68 g, 1.5 mmol), dibutyltin oxide (0.684 g, 2.7 mmol), tetrabutylammonium bromide (0.886 g, 2.7 mmol), crotyl bromide (0.6 mL), and MeCN (40 mL) was stirred and heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 2 h. TLC (2:1 ether–light petroleum) showed conversion of **59** (R_f 0.2) into a product (R_f 0.9) which was isolated in the usual way [11], and column chromatography (2:1 ether–light petroleum) gave **60** (0.64 g, 84%) as a syrup. ^{1}H NMR data: δ 1.66, 1.72 (2 s, 6 H, 2 =CH*Me*), 2.42 (s, OH), 3.10–4.43 (m, 12 H, 6 ring protons and 3 OCH_2–CH=), 4.72, 4.79 (2 s, 4 H, 2 CH_2Ph), 5.08–5.35 (m, 2 H, =CH_2), 5.55–6.15 (m, 5 H, 2 CH=CH and C*H*=CH_2), 7.34 (s, 10 H, aromatic). Compound **60** (0.2 g) was treated with benzyl bromide and NaH in DMF and the product was isolated in the usual way. Column chromatography (1:2 ether–light petroleum) gave the tribenzyl ether **61** (0.16 g, 67%) as a

syrup with a ^{1}H NMR spectrum identical with that described in (*a*). Compound **61** (0.16 g) and potassium *tert*-butoxide (0.2 g) in dry Me_2SO (15 mL) was kept at 50°C for 2 h as described in (*a*), to give **62** identical with the material described in (*a*).

*1*D-*1,4-Di*-O-*allyl*-*3,6-di*-O-*benzyl*-*5*-O-p-*methoxybenzyl*-myo-*inositol* (**71**).—A mixture of the diol **70** (1.44 g, 2.77 mmol), dibutyltin oxide (1.38 g, 5.54 mmol), tetrabutylammonium bromide (1.79 g, 5.54 mmol), allyl bromide (1 mL), and MeCN (50 mL) was stirred and heated under reflux with a Soxhlet apparatus containing 3A molecular sieves for 6 h. TLC (3:1 ether–light petroleum) of the solution showed complete conversion of **70** (R_f 0.4) into a product (R_f 0.9) which was isolated in the usual way [11]. Column chromatography (2:1 ether–light petroleum) gave **71** (1.29 g, 83%); mp 110–112°C (from light petroleum); $[\alpha]_D^{25}$ +17.0° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 2.40 (s, 1 H, OH), 3.78 (s, 3 H, OMe), 3.19–4.39 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 4.72, 4.76, 4.82 (3 s, 6 H, CH_2Ph), 5.11–5.36 (m, 4 H, 2 =CH_2), 5.75–6.16 (m, 2 H, 2 CH=CH_2) 6.78–7.35 (m, 14 H, aromatic). Calcd for $C_{34}H_{40}O_7 \cdot 0.5\ H_2O$: C, 71.68; H, 7.25%. Found: C, 71.77; H, 7.09%.

*1*D-*1,4-Di*-O-*allyl*-*2,3,6-tri*-O-*benzyl*-*5*-O-p-*methoxybenzyl*-myo-*inositol* (**72**).—The alcohol **71** (1.2 g, 2.14 mmol) was treated with benzyl bromide (1 mL) and NaH (0.3 g) in DMF (40 mL), and the product isolated in the usual way. Column chromatography (1:2 ether–light petroleum) gave **72** (1.31 g, 94%); mp 56–57°C; $[\alpha]_D^{25}$ +12.6° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 3.15–4.38 (m, 10 H, 6 ring protons and 2 OCH_2–CH=), 3.78 (s, 3 H, OMe), 4.62, 4.64, 4.77, 4.84 (4 s, 8 H, 4 CH_2Ph), 5.09–5.34 (m, 4 H, 2 =CH_2), 5.69–6.21 (m, 2 H, 2 CH=CH_2), 6.77–7.32 (m, 19 H, aromatic). Calcd for $C_{41}H_{46}O_7$: C, 75.67; H, 7.13%. Found: C, 75.77; H, 7.21%.

*1*D-*2,3,6-Tri*-O-*benzyl*-*5*-O-p-*methoxybenzyl*-*1,4-di*-O-(cis-*prop*-*1*-*enyl*)-myo-*inositol* (**73**) *and the racemate* **79**.—A solution of the diallyl ether **72** (1.20 g, 1.84 mmol) and potassium *tert*-butoxide (1.35 g) in dry Me_2SO (50 mL) was kept at 50°C for 9 h. A portion of the solution was diluted with semi-satd aq KCl, and the product was extracted with ether and treated with 9:1 acetone–M HCl at reflux for 20 min. TLC (1:2 ether–light petroleum) showed complete conversion of **72** (R_f 0.5) into a product (R_f 0), indicating that the isomerisation of the allyl groups to prop-1-enyl groups was complete. The mixture was diluted with satd aq KCl (50 mL) and the product was extracted with ether. Column chromatography (1:2 ether–light petroleum) gave **73** (0.99 g, 83%); mp 76–77°C (from light petroleum); $[\alpha]_D^{26}$ −8.6° (*c* 1, $CHCl_3$). ^{1}H NMR data: δ 1.65 (dd, 6 H, *J* 1.8 and 6.7 Hz, 2 =CH*Me*), 3.27–3.58 (m, 3 H, H-1,3,5), 3.78 (s, 3 H, OMe), 3.92–4.50 (m, 5 H, 3 ring protons and 2 =C*H*Me), 4.60–4.82 (m, 8 H, 4 CH_2Ph), 6.07, 6.26 (2 m, 2 H, 2 OCH=), 6.77–7.31 (m, 19 H, aromatic). Calcd for $C_{41}H_{46}O_7$: C, 75.67; H, 7.13%. Found: C, 75.46; H, 7.21%. A preparation of impure and uncharacterised **73** has been described [9].

The racemic material **79** (prepared in the same way from **78**) had mp 78–79°C (from light petroleum) and a ^{1}H NMR spectrum identical with that described for **73**. Found: C, 75.40; H, 7.17%.

*1*D-*2,3,6-Tri*-O-*benzyl*-*5*-O-p-*methoxybenzyl*-myo-*inositol* [*9*] (**74**) *and the racemate* **80**.—A solution of the diprop-1-enyl ether **73** (0.82 g, 1.26 mmol) in 3:7:1

acetone–MeOH–M HCl (30 mL) was kept at 50°C for 30 min. $NaHCO_3$ (1 g) and Et_3N (1 mL) were added, the mixture was concentrated, and the residue extracted with CH_2Cl_2. The extract was dried (K_2CO_3) and concentrated to give **74** (0.692 g, 96%); mp 100–102°C (from light petroleum–ether); $[\alpha]_D^{25}$ +6.6° (*c* 1, $CHCl_3$); with a ^1H NMR spectrum as described [9] {lit. [9] mp 100–102°C, $[\alpha]_D^{25}$ +5.9° (*c* 1, $CHCl_3$)}.

The racemic diol **80** (prepared in the same way from **79**) had mp 103–104°C (from light petroleum–ether) and a ^1H NMR spectrum identical with that described [9] for the chiral diol **74**. Calcd for $C_{35}H_{38}O_7$: C, 73.66; H, 6.71%. Found: C, 73.65; H, 6.82%.

*1D-2,3,6-Tri-*O*-benzyl-5-*O*-p-methoxybenzyl-*myo*-inositol 1,4-bis[di-(2-cyanoethyl) phosphate]* (**76**).—The chiral diol **74** (200 mg) was treated with bis(2-cyanoethoxy)diisopropylaminophosphine (**87**) in the usual way [12], to give the bisphosphite **75** which was oxidised [12] with *m*-chloroperoxybenzoic acid. Column chromatography (EtOAc) gave **76** (0.264 g, 80%); mp 118–119°C (from EtOAc–light petroleum); $[\alpha]_D^{27}$ +8.1° (*c* 1, $CHCl_3$). ^1H NMR data: δ 2.17–2.58 (m, 8 H, 4 CH_2CN), 3.76 (s, 3 H, OMe), 3.49–5.02 (m, 22 H, 4 CH_2Ph, 4 OCH_2CH_2CN, and 6 ring protons), 6.77–7.35 (m, 19 H, aromatic). ^{31}P NMR data: δ −2.62, −3.16. Calcd for $C_{47}H_{52}N_4O_{13}P_2$: C, 59.87; H, 5.56; N, 5.94; P, 6.57%. Found: C, 60.42; H, 5.51; N, 5.99; P, 6.33%.

*1D-2,3,6-Tri-*O*-benzyl-*myo*-inositol 1,4-bis[di-(2-cyanoethyl) phosphate]* (**81**).—A solution of cerium(IV) ammonium nitrate (0.380 g) in 9:1 MeCN–water (5 mL) was added dropwise to a stirred solution of the bisphosphate **76** (0.165 g) in 9:1 MeCN–water (5 mL) during 30 min, when TLC (EtOAc) showed complete conversion of **76** (R_f 0.6) into a product (R_f 0.4). Water (15 mL) was added, the solution was concentrated to remove MeCN, and the product was extracted with CH_2Cl_2. The extract was washed with satd aq $NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography (EtOAc) gave **81** (95 mg, 66%) as a syrup; $[\alpha]_D^{25}$ −4.3° (*c* 1, $CHCl_3$). ^{31}P NMR data: δ −1.75, −3.30. Calcd for $C_{39}H_{44}N_4O_{12}P_2$: C, 56.93; H, 5.39; N, 6.81%. Found: C, 56.94; H, 5.57; N, 6.58%.

*1D-2,3,6-Tri-*O*-benzyl-*myo*-inositol 1,4-bis(dibenzyl phosphate) 5-(dibenzyl phosphorothioate)* (**84**).—A solution of tetrazole (136 mg) in dry MeCN (4 mL) was added to a stirred solution of the bisphosphate [9] **82** (330 mg) and bis(benzyloxy)diisopropylaminophosphine (**88**, 250 mg) in dry CH_2Cl_2 (4 mL) under N_2. After 2 h, TLC (30:1 $CHCl_3$–MeOH) showed complete conversion of **82** (R_f 0.4) into the phosphite **83** (R_f 0.5). The mixture was concentrated and the residue was extracted with 2:1 ether–CH_2Cl_2 (10 mL). The extract was washed with satd aq KCl, dried ($MgSO_4$), and concentrated to give the crude phosphite **83** as an oil. ^{31}P NMR data: δ 142, −1.68, −2.09. Sulphur (130 mg) was added to a stirred solution of **83** in pyridine (3 mL) under N_2. After 12 h, the mixture was concentrated and the residue diluted with water (5 mL). The product was extracted with 2:1 ether–CH_2Cl_2, the extract was washed successively with M HCl, satd aq KCl, and satd aq $NaHCO_3$, then dried ($MgSO_4$), and the solvent evaporated. TLC (as above) showed no separation of the phosphite **83** from the phosphorothioate **84**. Column chromatography (1:1:3 CH_2Cl_2–ether–light

petroleum followed by 1:1 CH_2Cl_2–ether) gave the phosphorothioate **84** (260 mg, 61%) as a syrup; $[\alpha]_D^{25}$ −4.7° (*c* 1.1, $CHCl_3$). ^{31}P NMR data: δ 68.77 (P=S), −1.88, −2.28. Calcd for $C_{69}H_{69}O_{14}P_3S$: C, 66.44; H, 5.88; P, 7.45; S, 2.57%. Found: C, 66.33; H, 5.65; P, 7.83; S, 2.68%.

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References

[1] J. Gigg, R. Gigg, and E. Martin-Zamora, *Tetrahedron Lett.*, 34 (1993) 2827–2830.
[2] T. Desai, *The Chemistry of Inositol Compounds of Biological Interest*, Ph.D. Thesis, C.N.A.A., 1991.
[3] C. Grado and C.E. Ballou, *J. Biol. Chem.*, 236 (1961) 54–60; R.V. Tomlinson and C.E. Ballou, *ibid.*, 236 (1961) 1902–1911.
[4] R.F. Irvine, K.D. Brown, and M.J. Berridge, *Biochem. J.*, 221 (1984) 269–272.
[5] R.F. Irvine and R.M. Moor, *Biochem. J.*, 240 (1986) 917–920; G.St.J. Bird, M.F. Rossier, A.R. Hughes, S.B. Shears, D.L. Armstrong, and J.W. Putney, *Nature (London)*, 352 (1991) 162–165; P.M. Smith, *Biochem. J.*, 283 (1992) 27–30; M.S. Islam, P. Rorsman, and P.O. Bergaren, *FEBS Lett.*, 296 (1992) 287–291; D.L.Kalinoski, S.B. Aldinger, A.G. Boyle, T. Huque, J.F. Maracek, G.D. Prestwich, and D. Restrepo, *Biochem. J.*, 281 (1992) 449–456; P.J. Cullen, R.F. Irvine, and A.P. Dawson, *ibid.*, 271 (1990) 549–553; C.C.H. Petersen, O.H. Petersen, and M.J. Berridge, *J. Biol. Chem.*, 268 (1993) 22262–22264.
[6] Y. Watanabe, T. Ogasawara, N. Shiotami, and S. Ozaki, *Tetrahedron Lett.*, 28 (1987) 2607–2610; W. Tegge, G.V. Denis, and C.E. Ballou, *Carbohydr. Res.*, 217 (1991) 107–116.
[7] A.P. Kozikowski, A.H. Fauq, G. Powis, P. Kurian, and F.T. Crews, *J. Chem. Soc., Chem. Commun.*, (1992) 362–364.
[8] T. Desai, J. Gigg, R. Gigg, and E. Martin-Zamora, *Carbohydr. Res.*, 258 (1994) 135–144.
[9] T. Desai, A. Fernandez-Mayoralas, J. Gigg, R. Gigg, and S. Payne, *Carbohydr. Res.*, 234 (1992) 157–175.
[10] T. Desai, A. Fernandez-Mayoralas, J. Gigg, R. Gigg, and S. Payne, *Carbohydr. Res.*, 205 (1990) 105–123.
[11] T. Desai, J. Gigg, R. Gigg, and S. Payne, *Carbohydr. Res.*, 225 (1992) 209–228.
[12] T. Desai, J. Gigg, R. Gigg, and S. Payne, *Carbohydr. Res.*, 228 (1992) 65–79.
[13] R. Johansson and B. Samuelsson, *J. Chem. Soc., Perkin Trans. 1*, (1984) 2371–2374; B. Classon, P.J. Garegg, and B. Samuelsson, *Acta Chem. Scand., Ser. B*, 38 (1984) 419–422.
[14] T. Desai, J. Gigg, R. Gigg, and E. Martin-Zamora, *Abstr. Int. Carbohydr. Symp. XVIth, Paris, France, 1992*, (a) A 150, (b) A 151.
[15] R. Gigg and C.D. Warren, *J. Chem. Soc., C*, (1968) 1903–1911; P.A. Gent, R. Gigg, and R. Conant, *J. Chem. Soc., Perkin Trans., 1* (1972) 1535–1542; R. Gigg, *ACS Symp. Ser.*, 39 (1977) 253–278.
[16] T. Desai, J. Gigg, R. Gigg, S. Payne, and S. Penades, *Carbohydr. Res.*, 234 (1992) 1–21.
[17] J. Cunningham, R. Gigg, and C.D. Warren, *Tetrahedron Lett.*, (1964) 1191–1196; J. Gigg and R. Gigg, *J. Chem. Soc., C*, (1966) 82–86.
[18] D. Lampe, S.J. Mills, and B.V.L. Potter, *J. Chem. Soc., Perkin Trans. 1*, (1992) 2899–2906.
[19] J. Gigg, R. Gigg, S. Payne, and R. Conant, *J. Chem. Soc., Perkin Trans. 1*, (1987) 423–429.
[20] D.R. Trentham, N. Bettache, J.E.T. Corrie, T. Desai, R.H. Gigg, G.P. Reid, and J.F. Wooton, *Abstr.*, Int. Union Physiol. Soc., Glasgow, August 1–6, 1993.