Synthesis of D- and L-*myo*-Inositol 1,4,6-Trisphosphate, Regioisomers of a Ubiquitous Second Messenger

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A regioisomer of the second messenger D-*myo*-inositol 1,4,5-trisphosphate [D-Ins(1,4,5)P_3, **1**], DL-*myo*-inositol 1,4,6-trisphosphate [DL-Ins(1,4,6)P_3, **4ab**], together with the chiral antipodes D-Ins(1,4,6)P_3(**4a**) and L-Ins(1,4,6)P_3(**4b**), was synthesized from *myo*-inositol. The racemic diol **6**, after removal of the *trans*-ketal of fully protected **5** was *p*-methoxybenzylated to give the 6-*O*-alkylated derivative **9**, as the major product in 52% yield. Gentle acidic hydrolysis of **9**, followed by benzylation of the resulting triol, gave the fully protected compound **11ab**. Isomerization of the two allyl groups followed by acidic hydrolysis of the resulting *cis*-prop-1-enyl moieties and the *p*-methoxybenzyl group gave the triol **13ab**. Phosphorylation of **13ab** followed by deprotection of the resulting compound, **14ab**, with sodium in liquid ammonia and purification by ion exchange chromatography provided **4ab** in 60% yield. The intermediate **9** was converted into the *cis*-diol **16ab** in two steps. Selective acylation at the equatorial hydroxyl group using (*S*)-(+)-*O*-acetylmandelic acid in the presence of DCC and DMAP provided two diastereoisomers, **18** and **19**, which were separated by flash chromatography. Further transformations provided the corresponding D- and L-1,4,6 triols, **13a** and **13b**, respectively, and phosphorylation, followed by deprotection of the fully blocked products as for the racemic **4ab**, gave **4a** and **4b**, respectively. The absolute configuration of fully protected **11a** was determined by transformation to the known compound L-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (**22**). Compound **4a** was a full agonist at the platelet Ins(1,4,5)P_3 receptor for Ca^{2+} release, but **4b** was devoid of activity.

Introduction

In the polyphosphoinositide pathway of cellular signaling, the minor membrane lipid phosphatidylinositol 4,5-bisphosphate is cleaved to give the hydrophobic diacylglycerol and the hydrophilic D-*myo*-inositol 1,4,5-trisphosphate [Ins(1,4,5)P_3, Figure 1] in response to agonist occupation of cell surface receptors.[1,2] Ins(1,4,5)P_3 is a ubiquitous second messenger which releases calcium ions from intracellular stores.[1,2] Ins(1,4,5)P_3 acts through an intracellular endoplasmic reticular receptor, which has been isolated,[3] cloned, sequenced,[4,5] and reconstituted[6] and possesses several subtypes.

Ins(1,4,5)P_3 is metabolized by two known pathways once it has released Ca^{2+} ions.[7] First, an Ins(1,4,5)P_3 5-phosphatase removes the 5-phosphate group from the Ins(1,4,5)P_3 to give Ins(1,4)P_2, which is inactive in stimulating Ca^{2+}-release. Second, Ins(1,4,5)P_3 may also be phosphorylated by an Ins(1,4,5)P_3 3-kinase to give the tetrakisphosphate Ins(1,3,4,5)P_4. The function of the latter still remains unresolved; however, Ins(1,3,4,5)P_4 may gate a plasma membrane Ca^{2+} channel.[8] An Ins(1,3,4,5)P_4 binding protein has been purified from porcine platelets[9] and has found to be a GTPase activating protein-1 (GAP1) family member. This GTPase activating protein-1 site has been designated GAP1^{IP4BP}, and binding of Ins(1,3,4,5)P_4 at this location may have a pivotal role in cellular signaling.

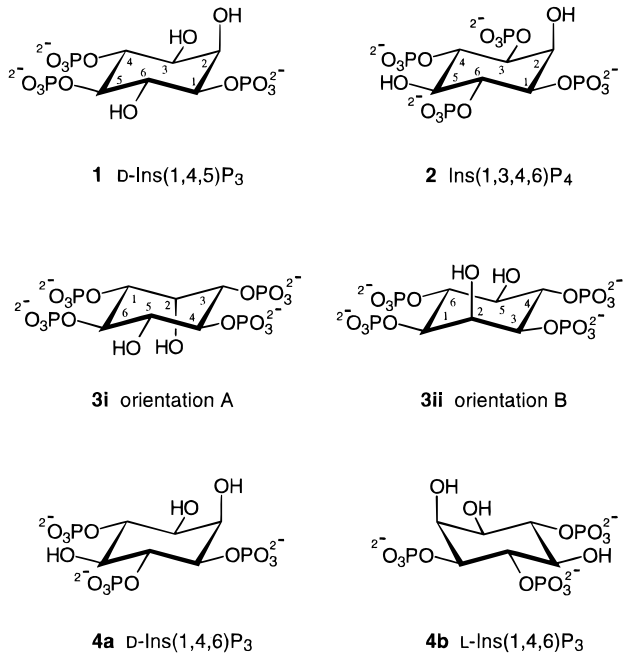

Figure 1.

We, and many other groups, have synthesized many inositol phosphates[10] and their corresponding phosphorothioate analogues in order to study structure−activity

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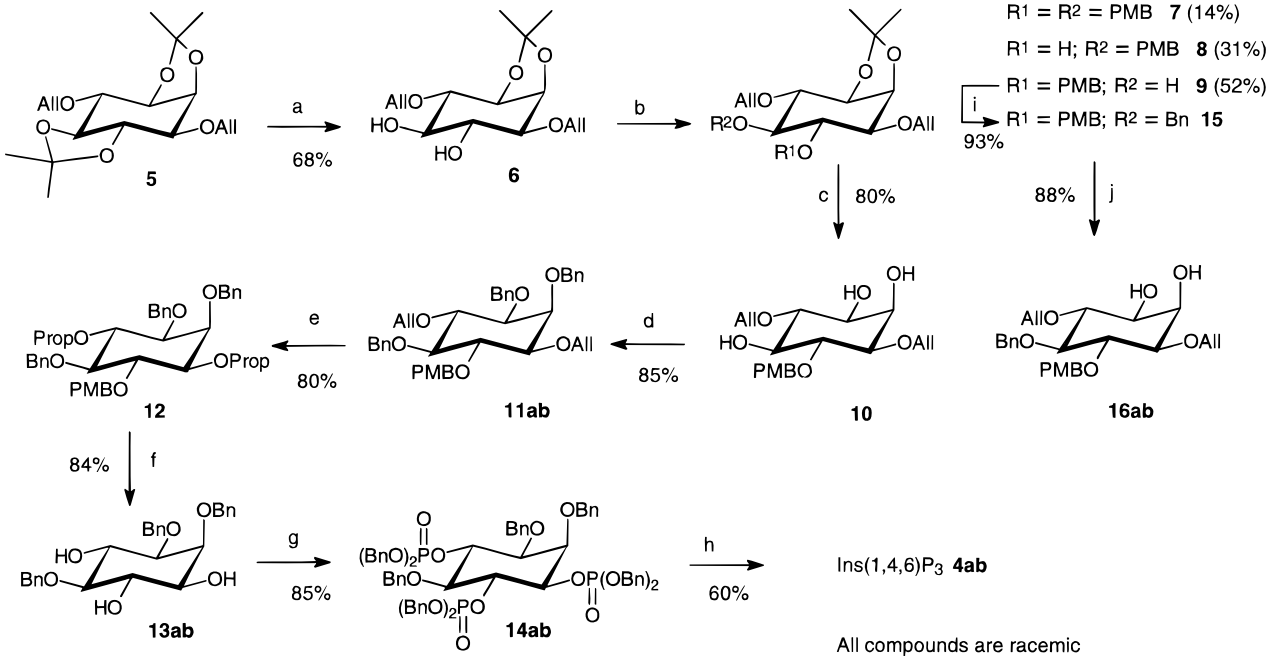
Scheme 1[a]



[a] (a) PTSA, CH_2Cl_2, 1 equiv $HOCH_2CH_2OH$, 0 °C to rt 40 min; (b) $Bu_2Sn{=}O$, CH_3CN, Bu_4NI, PMBCl, reflux, 48 h; (c) 1 M HCl (aq)−CH_3OH (1:9), 50 °C, 30 min; (d) BnBr, DMF, NaH, 2 h; (e) Bu^{t}OK, DMSO, 50 °C, 5 h; (f) C_2H_5OH−1 M HCl (aq), 4 h reflux; (g) bis(benzyloxy)(diisopropylamino)phosphine, 1*H*-tetrazole, CH_2Cl_2, 15 min, then Bu^{t}OOH, 30 min; (h) Na/NH_3, then ion exchange chromatography over Q-Sepharose; (i) BnBr, NaH, DMF, 2 h; (j) CH_3OH−1 M HCl (aq) (9:1), 50 °C, 45 min.

relationships for receptor recognition, as well as to establish the inhibition requirements for the enzymes 3-kinase and 5-phosphatase.[7,11,12] An important feature in all these structure−activity studies is the critical role of the diequatorial 4,5-bisphosphate motif for the release of Ca^{2+} from intracellular stores. The striking fact that *myo*-inositol 1,3,4,6-tetrakisphosphate [Ins(1,3,4,6)P_4, **2**] (a naturally occurring *myo*-inositol phosphate) is a partial agonist,[13] at least in SH-SY5Y cells, and possesses some Ca^{2+} mobilizing activity,[13,14] even nominally without a 4,5-bisphosphate motif, was an interesting observation. This unusual activity was the stimulus for our current studies, to modify and dissect Ins(1,3,4,6)P_4, in an attempt to design less efficacious partial agonists with good binding affinity. The activity of **2** may be rationalized by envisaging the molecule adopting one of two possible binding orientations (**3i** and **3ii** in Figure 1). The 1,6-bisphosphate of Ins(1,3,4,6)P_4 can mimic the crucial 4,5-bisphosphate of Ins(1,4,5)P_3, while the 3- or 4-phosphate of the 3,4-bisphosphate may mimic the 1-phosphate of Ins(1,4,5)P_3. The decreased potency and efficacy of Ins(1,3,4,6)P_4, in terms of Ca^{2+} mobilization, is probably due to a perturbing influence of the 2-hydroxyl group at the pseudo 3- or 6-positions in binding orientations, **3i** or **3ii**, since the symmetrical *scyllo*-Ins(1,2,4,5)P_4[15] is nearly as potent as Ins(1,4,5)P_3.

Since the 1-phosphate group and the equatorial 6-hydroxyl moiety are responsible for enhanced receptor binding, it appears likely that orientation **3i** is the active one, since inverting the 3-hydroxyl group of Ins(1,4,5)P_3 to give L-*chiro*-Ins(2,3,5)P_3 only results in a 10-fold decrease in Ca^{2+}-mobilizing activity.[16] Removing the 3-phosphate group from Ins(1,3,4,6)P_4 in orientation **3i** gives D-Ins(1,4,6)P_3 (**4a**), a molecule which has been described in racemic[17] and chiral[18] form and has been found naturally in intact avian erythrocytes,[19] where it is phosphorylated to give Ins(1,3,4,6)P_4. Ins(1,4,6)P_3 has also been identified in WRK rat mammary tumor cells, albeit in a concentration only 1/10 of Ins(1,4,5)P_3.[20]

It is desirable to develop an efficient synthetic route to the regioisomers of Ins(1,4,5)P_3 for structure−activity studies, and here we report the synthesis of racemic and chiral D-**4a** and its antipode, L-Ins(1,4,6)P_3 (**4b**), and an efficient method for resolving enantiomeric phosphorylation precursors using (*S*)-(+)-*O*-acetylmandelic acid (**17**). A preliminary report describing our route to racemic Ins(1,4,6)P_3 (**4ab**) has appeared.[17]

Results and Discussion

The di-*O*-allyl intermediate **5** was prepared according to the method of Gigg *et al.*[21] The less stable *trans*-isopropylidene acetal was removed selectively to afford **6** using a catalytic amount of toluene-*p*-sulfonic acid and 1 equiv of ethane-1,2-diol, in dichloromethane. It was

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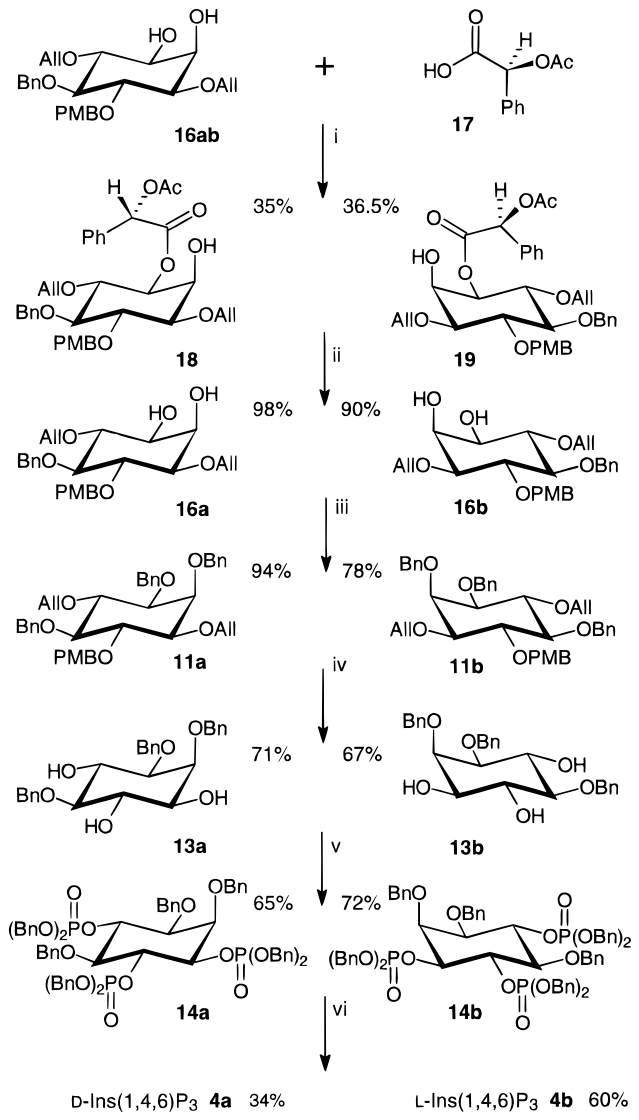
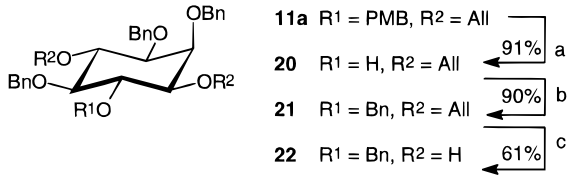
Scheme 2[a]



[a] (i) CH_2Cl_2, DMAP, DCC, −20 °C; (ii) NaOH, MeOH, reflux 30 min; (iii) BnBr, NaH, DMF, 2 h; (iv) Bu^{t}OK, DMSO, 50 °C, 5 h, then aq 1 M HCl−ethanol (1:2), reflux, 3 h; (v) bis(benzyloxy)(diisopropylamino)phosphine, 1*H*-tetrazole, CH_2Cl_2, rt 15 min, Bu^{t}OOH, −78 °C, 30 min; (vi) Na/NH_3, then ion exchange chromatography over Q-Sepharose.

Scheme 3[a]



[a] (a) 1 M aqueous HCl−ethanol (1:2), reflux, 4 h; (b) NaH, BnBr, DMF, rt 2 h; (c) 10% Pd/C, ethanol−water (6:1), reflux, 2 h.

found that the nature of the protective group at positions 3 and 6 influenced the rate of hydrolysis of the 4,5-*trans*-isopropylidene acetal. If ester groups were present, the rate of hydrolysis of the *trans*-acetal was slow. When positions 3 and 6 were blocked with benzyl groups, hydrolysis was smooth and complete within 45 min. However, to control the formation of **6**, cooling was necessary when allyl groups occupied these positions, in order to prevent the formation of the tetrol DL-1,4-di-*O*-allyl-*myo*-inositol.

The *trans*-5,6-diol of **6** was now exposed, and it was envisaged that the 6-position would be more reactive toward tin-mediated alkylation over the 5-position.[22] Thus, treatment of diol **6** with a mixture of dibutyltin oxide, tetrabutylammonium iodide, and *p*-methoxybenzyl chloride gave three products, with the required **9** as the major product. The ^{1}H NMR spectrum distinctly showed the 5-OH coupling to C-5-H, $\delta = 3.43$ (ddd), where upon D_2O exchange the ddd collapsed to a dd. C-5-H is further upfield than C-6-H; thus, C-6-OH has been *p*-methoxybenzylated. Also formed were **7** and **8** in lower yields. The ^{1}H NMR spectrum of **8** showed coupling of C-6-H to C-6-OH, at $\delta = 3.94$, as a dt, and upon D_2O exchange, the dt collapsed to a triplet; thus, C-5-OH was alkylated. Fully blocked **7** was isolated in 14% yield.

The 2,3-*O*-isopropylidene of **9** was hydrolyzed under mild acidic conditions to give triol **10**, and the three hydroxyl groups were alkylated with benzyl bromide to afford **11ab**. The allyl groups at the 1- and 4-positions were isomerized with potassium *tert*-butoxide to give the 1,4-di-*O*-(*cis*-prop-1-enyl) derivative **12**. The *cis*-prop-1-enyl and the *p*-methoxybenzyl ethers of **12** were hydrolyzed under acidic conditions to give DL-1,2,5-tri-*O*-benzyl-*myo*-inositol (**13ab**).

The treatment of bis(benzyloxy)(diisopropylamino)-phosphine[23] with 1*H*-tetrazole in dry dichloromethane gave a tetrazolide complex indicated in the ^{31}P NMR spectrum at $\delta = 126.7$ ppm. The addition of triol **13ab** to the P(III) complex produced a familiar AB spin−spin coupling pattern assigned to the phosphitylated 1,6-bisphosphite triester system ($\delta = 140.2$ and 142.3 ppm, $^5J_{PP} = 3.7$ Hz), together with a singlet at $\delta_P = 141.6$ ppm for the phosphitylated C-4-OH. Oxidation of the tris-phosphite triester gave the fully protected derivative DL-1,2,5-tri-*O*-benzyl-3,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (**14ab**). The compound was deprotected using sodium in liquid ammonia[17] and the crude product was purified by ion exchange chromatography on Q-Sepharose Fast Flow using a gradient of TEAB as eluent to give DL-Ins(1,4,6)P_3 (**4ab**) as its glassy triethylammonium salt.

Several methods have been used to resolve *myo*-inositol phosphate precursors.[10] Some of these rely on reacting the racemic mixture of the protected inositol with a chiral acid derivative to form a pair of diastereoisomeric esters that can then be separated by chromatography or crystallization. (1*S*)-(−)-*ω*-Camphanic acid chloride has been used successfully to resolve a number of *myo*-inositol phosphate precursors. For example, camphanic acid chloride was reacted with DL-1,2,4-tri-*O*-benzyl-5,6-*O*-isopropylidene-*myo*-inositol,[24] and a single crystalline diastereoisomer was isolated from the mixture. The other syrupy diastereoisomer was further transformed to give D-Ins(1,4,5)P_3.[25] Riley *et al.*[26] have used (1*S*)-(−)-*ω*-camphanic acid chloride to resolved DL-2,4,5-tri-*O*-benzyl-1-*O*-(*p*-methoxybenzyl)-*myo*-inositol *via* its easily separable 3,6-biscamphanates. The resulting enantiomers were used to synthesize D- and L-Ins(1,3,4)P_3.

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The commercially available reagent (*S*)-(+)-*O*-acetylmandelic acid has been used previously to resolve DL-1,4,5,6-tetra-*O*-benzyl-*myo*-inositol.[27] The two resulting 1-*O*-acylated diastereoisomers were easily separated and were used to synthesize unaccessible hexoses[27] and the β-glucosidase and α-mannosidase inhibitors (+)- and (−)-norjirimycin.[28] Another partially protected derivative, DL-3,4-di-*O*-benzyl-5,6-di-*O*-(*p*-methoxybenzyl)-*myo*-inositol, was selectively acylated at the 1-position with (*S*)-(+)-*O*-acetylmandelic acid.[29] Further elaboration of one of the diastereoisomers led to the total synthesis of (+)-polyoxin J. We pursued the resolution of a partially protected *myo*-inositol derivative using (*S*)-(+)-*O*-acetylmandelic acid, in order to deliver D- and L-Ins(1,4,6)P_3 (**4a** and **4b**).

DL-1,4-Di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**16ab**) was synthesized by benzylation of compound **9** to give fully blocked **15**, and removal of the isopropylidene acetal gave diol **16ab**. Coupling of **16ab** with (*S*)-(+)-*O*-acetylmandelic acid provided two equatorially substituted diastereoisomers, **18** and **19**. The simplicity of the resolution and easy separation of both diastereoisomers make this a powerful method for resolving *myo*-inositol phosphate precursors in high yield. D-1-*O*-[*S*-(+)-*O*-Acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**19**), was isolated as the less polar isomer as a syrup, and the more polar L-1-*O*-[*S*-(+)-*O*-acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**18**) was crystalline. The shape of the unit crystal and weak diffraction patterns for **18** unfortunately precluded a single X-ray analysis, so the structural determination was pursued by a chemical route.

The C-1-H resonance (δ = 4.77) of the less polar diastereoisomer **19** was shifted downfield, due to the carbonyl deshielding effect of the acetyl mandelate. Thus, selective acylation had occurred at the 1-position. The corresponding C-1-H resonance of the more polar diastereoisomer **18** could not be clearly identified by ^{1}H NMR due to overlap with other signals. However, C-2-H of **18** showed a broad singlet at δ = 4.29, indicating that C-2-OH was not acylated. Thus, C-1-OH was selectively esterified for both diastereoisomers.

The individual diastereoisomers were then deacylated with methanolic sodium hydroxide solution to give D-(**16a**) and L-1,4-di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**16b**). The hydroxyl groups at the *cis*-2,3-diol of each enantiomer were benzylated to give the fully protected compounds **11a** and **11b**. The allyl groups, for each enantiomer, were isomerized with potassium *tert*-butoxide in anhydrous DMSO,[21] rendering them acid sensitive. The *cis*-prop-1-enyl ethers and *p*-methoxybenzyl group were cleaved under acidic conditions to give L-2,3,5-tri-*O*-benzyl-*myo*-inositol (**13b**), used for the synthesis of L-Ins(1,4,6)P_3, and D-2,3,5-tri-*O*-benzyl-*myo*-inositol (**13a**), used for the synthesis of D-Ins(1,4,6)P_3. **13a** and **13b** were isolated and showed equal and opposite specific rotations.

To establish the absolute configuration for D-2,3,5-tri-*O*-benzyl-*myo*-inositol (**13a**) a search was carried out to find a related target compound that could be synthesized in a small number of steps. Since the enantiomers of D- and L-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol have been well characterized by Gigg and co-workers[30] by selective benzylation of the known derivatives D- and L-2,4,5-tri-*O*-benzyl-*myo*-inositol, respectively, we chose one of the former pair as a reference.

Thus, L-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (**22**) was synthesized from D-1,4-di-*O*-allyl-2,3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**11a**). The *p*-methoxybenzyl group was removed from **11a** by acidic hydrolysis to provide D-1,4-di-*O*-allyl-2,3,5-tri-*O*-benzyl-*myo*-inositol (**20**) as a syrup. The exposed 6-hydroxyl group was then benzylated to give D-1,4-di-*O*-allyl-2,3,5,6-tetra-*O*-benzyl-*myo*-inositol (**21**). Gigg *et al*.[30] prepared racemic **21** as a syrup; however, in our hands, chiral **21** was a low melting point solid. The allyl groups were then removed in a one-pot reaction using palladium on carbon in the presence of toluene-*p*-sulfonic acid to give D-2,3,5,6-tetra-*O*-benzyl-*myo*-inositol (**22**) (the same as L-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol). The specific rotation was found to be $[\alpha]_D$ = +4.0° and agreed well with the literature value,[30] as did the melting point.

The fully blocked trisphosphates **14a** and **14b** were essentially synthesized in the same way as for the racemic mixture. It was found that chloroform−acetone (10:1) easily separated phosphonate impurities from the fully protected product. Deprotection of the fully blocked enantiomers with sodium in liquid ammonia, followed by purification of the product on Q-Sepharose Fast Flow using a gradient of TEAB as buffer, gave D-Ins(1,4,6)P_3 (**4a**) and L-Ins(1,4,6)P_3 (**4b**). The rotations for the respective compounds at pH 8.6 in 1 M TEAB buffer were $[\alpha]_D$ = −29.1° and $[\alpha]_D$ = +25.0°. The size of the rotation in TEAB buffer was much larger than that in water. Recent literature values for D-Ins(1,4,6)P_3 and L-Ins(1,4,6)P_3 were $[\alpha]_D$ = −8.9° (*c* 0.90, H_2O) and $[\alpha]_D$ = +9.4° (*c* 0.85, H_2O), respectively, for material prepared by a different route.[18]

Both enantiomers of Ins(1,4,6)P_3 were examined for their ability to release Ca^{2+} from permeabilized rabbit platelets and to displace [^{3}H]Ins(1,4,5)P_3 from its specific rat cerebellar binding site.[31] D-Ins(1,4,6)P_3 was found to be a potent agonist at the Ins(1,4,5)P_3 receptor and only 2−3-fold less potent than Ins(1,4,5)P_3 for Ca^{2+} release. It was also some 32-fold weaker at displacing [^{3}H]Ins(1,4,5)P_3 than Ins(1,4,5)P_3 from rat cerebellar membranes. L-Ins(1,4,6)P_3 was essentially inactive at releasing Ca^{2+} or displacing [^{3}H]Ins(1,4,5)P_3 from its binding sites.[31] Thus, these results demonstrate that regioisomers of the natural messenger Ins(1,4,5)P_3 can also be highly potent agonists. We have discussed a route to the enantiomers of one such trisphosphate regioisomer, Ins(1,4,6)P_3, and have demonstrated that the use of (*S*)-(+)-*O*-acetylmandelic acid as a chiral auxilary is worthy of more widespread application in this field.

Experimental Section

General Information. Thin-layer chromatography (TLC) was performed on precoated plates (Merck TLC aluminium sheets silica 60 F_{254}): products were visualized by spraying with phosphomolybdic acid in methanol, followed by heating.

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Flash chromatography refers to the procedure developed by Still and co-workers[32] and was carried out on Sorbsil C60 silica gel.

The ^{31}P NMR shifts were measured in ppm relative to external 85% phosphoric acid and are negative when upfield from this reference. Melting points (uncorrected) were determined using a Kofler block. Low-resolution mass spectra were recorded by the University of Bath Mass Spectrometry Service. High-resolution accurate mass spectrometry was carried out by the EPSRC Mass Spectrometry Service in Swansea, UK. Optical rotations were measured at ambient temperature. Chemicals were purified according to standard procedures.[33]

Ion exchange chromatography was performed on an LKB-Pharmacia medium pressure ion exchange chromatograph using Q-Sepharose Fast Flow and gradients of triethylammonium bicarbonate (TEAB) as eluent. Fractions containing phosphate were assayed by a modification of the Briggs phosphate test.[34,35]

DL-1,4-Di-*O*-allyl-2,3-*O*-isopropylidene-*myo*-inositol (6). A mixture of DL-3,6-di-*O*-allyl-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (**5**) (10.7 g, 31.47 mmol) toluene-*p*-sulfonic acid (0.10 g, 0.5 mmol), and ethane-1,2-diol (1.75 mL, 31.47 mmol), in dichloromethane (100 mL), was stirred at 0 °C in an ice bath for 10 min. The ice bath was removed and the mixture was stirred for a further 30 min until the solution became slightly cloudy. Triethylamine (2 mL) was added to the cloudy solution followed by water (100 mL). The starting material and product were separated, leaving DL-1,4-di-*O*-allyl-*myo*-inositol in the water layer. The product **6**, $R_f = 0.30$ (ether), was separated and the organic layer was evaporated to give the title compound plus starting material. The mixture was recrystallized from ethyl acetate−hexane to give the pure title compound **6** (6.4 g, 68%): mp 130 −131 °C (lit.[21] mp 130−132 °C); ^1H NMR (270 MHz, $CDCl_3$) 1.37, 1.54 (2s, 6H), 3.10 (s, D_2O ex, 2H), 3.36 (t, $J = 9.5$ Hz, 1H), 3.49 (t, $J = 9.5$ Hz, 1H), 3.49 (dd, $J = 2.6$, 9.5 Hz, 1H), 3.89 (t, $J = 9.3$ Hz, 1H), 4.08 (dd, $J = 5.3$, 6.8 Hz, 1H), 4.17−4.39 (m, 4H), 4.43 (dd, $J = 4.0$, 5.3 Hz, 1H), 5.16−5.36 (m, 4H), 5.87−6.05 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.91, 27.99, 71.64, 72.29, 71.38, 72.94, 73.88, 76.80, 79.20, 81.63, 109.88, 117.38, 118.06, 134.60, 134.73 ppm.

Selective Alkylation of 1,4-Di-*O*-allyl-2,3-*O*-isopropylidene-*myo*-inositol (Using *p*-Methoxybenzyl Chloride) (7−9). A mixture of DL-1,4-di-*O*-allyl-2,3-*O*-isopropylidene-*myo*-inositol (**6**) (4.5 g, 15 mmol), acetonitrile (300 mL), dibutyltin oxide (5 g, 20 mmol), tetrabutylammonium iodide (7.38 g, 20 mmol), and *p*-methoxybenzyl chloride (5.42 mL, 40 mmol) was heated under reflux in a Soxhlet apparatus containing molecular sieves (4 Å, 30 g), for 48 h. The reaction mixture was cooled, the solvent was evaporated, and the orange residue was partitioned between water (250 mL) and ether (250 mL). The organic layer was separated and stirred with a saturated solution of sodium hydrogen carbonate (250 mL), for 1 h. The solid was removed by filtration through Celite and washed with ether, and the organic layer was dried over magnesium sulfate. TLC (ether−hexane, 3:2) showed five compounds, *p*-methoxybenzyl iodide, $R_f = 0.70$; *p*-methoxybenzyl chloride, $R_f = 0.60$; DL-1,4-di-*O*-allyl-2,3-*O*-isopropylidene-5,6-di-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**7**), $R_f = 0.50$; DL-1,4-di-*O*-allyl-2,3-*O*-isopropylidene-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**9**), $R_f = 0.40$; and DL-1,4-di-*O*-allyl-2,3-*O*-isopropylidene-5-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**8**), $R_f = 0.22$, which were separated by flash chromatography, to give the products as syrups. DL-1,4-Di-*O*-allyl-2,3-*O*-isopropylidene-5-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**8**) was then recrystallized from hexane: Yields, **7** (1.15 g, 14%), **8** (1.96 g, 31%), **9** (3.27 g, 52%).

7: ^1H NMR (270 MHz, $CDCl_3$) δ 1.37, 1.54 (2s, 6H), 3.34 (t, $J = 9.2$ Hz, 1H), 3.49 (dd, $J = 3.7$, 8.8 Hz, 1H), 3.65 (dd, $J = 7.0$, 9.5 Hz, 1H), 3.79 (s, 3H), 3.80 (s, 3H), 3.84 (t, $J = 8.8$ Hz, 1H), 4.07 (dd, $J = 5.7$, 6.8 Hz, 1H), 4.18−4.33 (m, 4H), 4.38 (dd, $J = 3.8$, 5.55 Hz, 1H), 4.70, 4.72 (AB, $J = 10.4$ Hz, 2H), 4.71, 4.77 (AB, $J = 10.4$ Hz, 2H), 5.15−5.36 (m, 4H), 5.89−6.03 (m, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.8$ Hz, 2H), 7.27 (d, $J = 8.6$ Hz, 2H), 7.28 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.68, 27.60, 55.07, 72.36, 72.78, 74.79, 74.80, 76.93, 78.91, 80.37, 81.73, 82.15, 109.66, 113.39, 113.58, 116.63, 117.41, 129.25, 129.51, 129.67, 130.64, 134.83, 135.05, 159.06 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 693 (M + NBA, 10), 555 (33), 525 (60), 379 (20), 137 (95), 121 (100). Anal. Calcd for $C_{31}H_{40}O_8$: C, 68.85; H, 7.46. Found: C, 69.0; H, 7.54.

8: mp 70−72 °C (from hexane); ^1H NMR (270 MHz, $CDCl_3$) δ 1.37, 1.52 (2s, 6H), 2.68 (d, $J = 1.5$, D_2O ex, 1H), 3.23 (t, $J = 9.2$ Hz, 1H), 3.50 (dd, $J = 3.8$, 9.7 Hz, 1H), 3.50 (dd, $J = 6.8$, 9.2 Hz, 1H), 3.79 (s, 3H), 3.94 (dt, $J = 1.5$, 9.7 Hz, D_2O ex, t, $J = 9.5$ Hz, 1H), 4.10 (dd, $J = 5.3$, 6.8 Hz, 1H), 4.17−4.37 (m, 4H), 4.41 (dd, $J = 3.85$, 5.3 Hz, 1H), 4.66, 4.81 (AB, $J = 10.8$ Hz, 2H), 5.15−5.34 (m, 4H), 5.87−6.03 (m, 2H), 6.86 (d, $J = 8.8$ Hz), 7.31 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.75, 27.75, 55.77, 71.74, 72.62, 74.63, 71.35, 73.75, 76.64, 79.14, 81.24, 82.09, 109.79, 113.78, 116.86, 117.86, 129.64, 130.45, 134.70, 134.92, 159.22 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 573 (M + NBA, 100), 419 (M − H, 18), 379 (15), 335 (20), 299 (100), 137 (72). Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.68; H, 7.67. Found: C, 65.7; H, 7.79.

9: ^1H NMR (270 MHz, $CDCl_3$) δ 1.37, 1.55 (2s, 6H), 2.72 (d, $J = 2.0$ Hz, D_2O ex, 1H), 3.43 (ddd, $J = 2.0$, 8.2, 8.2 Hz, D_2O ex, dd, $J = 8.2$, 8.2 Hz, 1H), 3.58 (m, 2H), 3.74 (t, $J = 8.2$ Hz, 1H), 3.79 (s, 3H), 4.07 (1H, dd, $J = 5.7$, 6.8 Hz, 1H), 4.17−4.36 (m, 4H), 4.39 (dd, $J = 3.85$, 5.5 Hz, 1H), 4.70, 4.82 (AB, $J = 10.8$ Hz, 2H), 5.15−5.34 (m, 4H), 5.87−6.03 (m, 2H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.31 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.62, 27.56, 55.07, 72.07, 72.13, 74.30, 73.43, 74.43, 77.00, 78.78, 79.98, 81.24, 109.72, 113.71, 117.09, 117.44, 128.48, 130.42, 134.63, 134.73, 159.12 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 573 (M + NBA, 50), 419 (M − H, 28), 379 (38), 299 (100), 258 (38), 137 (72), 121 (80). Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.68; H, 7.67. Found: C, 65.6; H, 7.61.

DL-1,4-Di-*O*-allyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (10). A mixture of DL-1,4-di-*O*-allyl-2,3-*O*-isopropylidene-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**9**) (2.72 g, 6.47 mmol), and 1 M HCl−methanol (90 mL, 1:9), was heated at 50 °C for 30 min. The reaction mixture was cooled and TLC showed consumption of starting material to give a new product of $R_f = 0.20$ (ether). Sodium hydrogen carbonate (5 g) was added, and the solvents were evaporated. The residue was partitioned between water (50 mL) and dichloromethane (50 mL), and the organic layer was separated, dried over magnesium sulfate, filtered, and evaporated to dryness. The remaining solid was recrystallized from ethyl acetate−hexane to give **10** (1.97 g, 80%): mp 120−120 °C (from ethyl acetate−hexane); ^1H NMR (270 MHz, $CDCl_3$) δ 2.66, 2.85 (2s, D_2O ex, 3H), 3.32 (dd, $J = 2.75$, 9.5 Hz, 1H), 3.44 (m, 2H), 3.59 (t, $J = 9.3$ Hz, 1H), 3.72 (t, $J = 9.3$ Hz, 1H), 3.80 (s, 3H), 4.17−4.36 (m, 5H), 4.64, 4.86 (AB, $J = 10.8$ Hz, 2H), 5.16−5.35 (m, 4H), 5.87−6.04 (m, 2H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.31 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.23, 71.38, 73.82, 75.15, 69.34, 71.51, 74.40, 79.59, 80.43, 80.60, 113.87, 117.15, 117.57, 129.61, 130.64, 134.41, 135.05, 159.25 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 533 (M + NBA, 65), 379 (M − H, 100), 303 (35), 272 (20), 182 (25), 167 (30). Anal. Calcd for $C_{20}H_{28}O_7$: C, 63.12; H, 7.42. Found: C, 62.9; H, 7.46.

DL-1,4-Di-*O*-allyl-2,3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (11ab). A mixture of DL-1,4-di-*O*-allyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**10**) (1.52 g, 4 mmol) and sodium hydride (0.86 g, 36 mmol) was stirred in dry DMF (40 mL). Benzyl bromide (1.78 mL, 15 mmol) was added dropwise and the solution was stirred for a further 2 h. TLC (ether−light petroleum, 1:1) showed a new product of $R_f = 0.50$. The excess sodium hydride was destroyed with methanol (10 mL), and the solvents were evaporated *in vacuo* to give a syrup. The syrup was partitioned between water (100 mL) and ether then washed with 0.1 M HCl (50 mL), a saturated aqueous solution of sodium hydrogen carbonate (100 mL), and water

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(100 mL). The organic layer was dried over magnesium sulfate and filtered and the solvent evaporated. The remaining syrup was purified by flash chromatography to give the title compound **11ab** (2.20 g, 85%): mp 53−54 °C (from hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.22 (dd, J = 2.2, 9.7 Hz, 1H), 3.29 (dd, J = 2.2, 9.9 Hz, 1H), 3.38 (t, J = 9.3 Hz, 1H), 3.77 (s, 3H), 3.92 (t, J = 9.5 Hz, 1H), 3.97 (t, J = 9.5 Hz, 1H), 3.99 (t, J = 2.2 Hz, 1H), 4.08−4.10 (m, 2H), 4.27−4.43 (m, 2H), 4.57−4.85 (m, 8H), 5.11−5.34 (m, 4H), 5.84−6.04 (m, 2H), 6.83 (d, J = 8.6 Hz, 2H), 7.22−7.42 (m, 17H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.20, 71.58, 72.82, 73.95, 74.53, 75.44, 75.83, 74.27, 80.60, 80.73, 81.25, 81.38, 83.58, 113.68, 116.57, 127.24, 127.44, 127.50, 127.73, 127.83, 128.05, 128.28, 129.74, 131.07, 134.89, 135.38, 138.49, 138.91, 159.09 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 803 (M + NBA, 100), 696 (35), 665 (55), 559 (25), 485 (40), 440 (35), 318 (68), 287 (60), 178 (30), 124 (25). Anal. Calcd for $C_{41}H_{46}O_7$: C, 75.65; H, 7.13. Found: C, 75.9; H, 7.19.

DL-2,3,5-Tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-1,4-di-*O*-*cis*-prop-1-enyl-*myo*-inositol (12). A mixture of DL-1,4-di-*O*-allyl-2,3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**11ab**) (1.5 g, 2.3 mmol) and freshly sublimed potassium *tert*-butoxide (3.66 g, 30 mmol) in dry DMSO (20 mL) was kept at 50 °C for 5 h under an atmosphere of nitrogen. TLC (ether−hexane, 1:1) showed conversion of stating material (R_f = 0.50) into a single product (R_f = 0.72). The dark mixture was cooled, a saturated solution of potassium chloride (50 mL) was added, and the product was extracted with ether (4 × 50 mL). The organic layer was dried over magnesium sulfate and evaporated to give a solid. The crude product was purified by flash chromatography (ether−hexane, 1:2) to give the title compound **12** (1.2 g, 80%): mp 89−91 °C (from hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.64 (dd, J = 1.65, 6.6 Hz, 3H), 1.67 (dd, J = 1.5, 6.4 Hz, 3H), 3.33 (dd, J = 2.4, 9.7 Hz, 1H), 3.42 (t, J = 9.3 Hz, 1H), 3.51 (dd, J = 2.2, 9.9 Hz, 1H), 3.76 (s, 3H), 4.02 (t, J = 2.2 Hz, 1H), 4.03 (t, J = 9.9 Hz, 1H), 4.17 (t, J = 9.3 Hz, 1H), 4.36 (dq, J = 6.8 Hz, 1H), 4.44 (dq, J = 6.8 Hz, 1H), 4.53−4.83 (m, 8H), 6.08 (dd, J = 1.65, 6.2 Hz, 1H), 6.26 (dd, J = 1.65, 6.4 Hz, 1H), 6.83 (d, J = 8.6 Hz, 2H), 7.23−7.41 (m, 17H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 9.27, 9.36, 55.16, 72.57, 74.45, 75.25, 75.69, 75.91, 78.75, 80.34, 82.53, 82.95, 84.36, 98.10, 100.50, 113.67, 127.34, 127.55, 127.78, 128.07, 128.17, 128.21, 128.26, 129.89, 130.81, 138.27, 138.58, 145.70, 147.68, 159.09 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 803 (M + NBA, 100), 696 (35), 665 (25), 559 (20), 485 (30), 322 (35), 273 (30), 118 (24). Anal. Calcd for $C_{41}H_{46}O_7$: C, 75.65; H, 7.13. Found: C, 75.6; H, 7.18.

DL-1,2,5-Tri-*O*-benzyl-*myo*-inositol (13ab). DL-2,3,5-Tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-1,4-di-*O*-*cis*-prop-1-enyl-*myo*-inositol (**12**) (0.95 g, 1.46 mmol) was suspended in ethanol−1 M HCl (60 mL, 2:1). The mixture was heated at reflux temperature for 4 h, after which TLC (ether) showed a product of R_f = 0.30. The solvents were evaporated and the solid was partitioned between water and dichloromethane (100 mL each) and washed with sodium hydrogen carbonate (100 mL) and water (100 mL). The organic layer was then dried over magnesium sulfate and then evaporated. The title compound **13ab** was purified by flash chromatography (dichloromethane−ethyl acetate, 1:1) (0.55 g, 84%): mp 161−162 °C (from ethyl acetate−hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.65−2.65 (br s, D_2O ex, 3H), 3.23 (t, J = 9.2 Hz, 1H), 3.30 (dd, J = 2.4, 9.7 Hz, 1H), 3.40 (dd, J = 2.75, 9.7 Hz, 1H), 3.82 (t, J = 9.5 Hz, 1H), 4.06 (t, J = 2.6 Hz, 1H), 4.12 (t, J = 9.5 Hz, 1H), 4.58−4.98 (m, 6H), 7.25−7.40 (m, 15H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 71.51, 74.01, 72.16, 72.42, 72.84, 78.42, 80.43, 84.29, 127.04, 127.14, 127.33, 127.56, 127.98, 128.08, 128.21, 139.20, 139.79, 139.92 ppm; MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 603 (M + NBA, 100), 379 (M − H, 85), 359 (20), 335 (10), 303 (20), 151 (20), 109 (5). Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.96; H, 6.49. Found: C, 71.9; H, 6.71.

DL-2,3,5-Tri-*O*-benzyl-1,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (14ab). A mixture of bis(benzyloxy)(diisopropylamino)phosphine[23] (0.69 g, 2 mmol) and 1*H*-tetrazole (0.21 g, 3 mmol) in dry dichloromethane was stirred for 15 min. DL-1,2,5-Tri-*O*-benzyl-*myo*-inositol (**13ab**) (0.2 g, 0.44 mmol) was then added and the reaction was stirred for a further 15 min. The solution was cooled to −78 °C and *tert*-butyl hydroperoxide (1 mL, 7 mmol) was added and the mixture was stirred for 30 min. The reaction mixture was partitioned between dichloromethane and a 10% solution of sodium metabisulfite (100 mL), and the organic layer was washed with brine and water (100 mL of each) and dried over magnesium sulfate. The remaining syrup was purified by flash chromatography (chloroform−acetone, 10:1), then ethyl acetate−pentane (2:1), to give **14ab** as a syrup (0.465 g, 85%): TLC, R_f = 0.30 (chloroform−acetone, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41 (dd, J = 2.0, 9.8 Hz, 1H), 3.56 (t, J = 9.2 Hz, 1H), 4.21 (dt, J = 2.0, 9.5 Hz, 1H), 4.42 (br s, 1H), 4.44−5.09 (m, 18H), 6.98−7.41 (m, 45H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.89, 69.21, 69.41, 69.77, 72.10, 73.53, 75.02, 74.57, 76.32, 77.49, 78.04, 78.78, 79.53, 127.05, 127.47, 127.66, 127.89, 127.96, 128.05, 128.18, 128.47, 128.57, 135.51, 135.77, 135.90, 137.10, 137.85, 137.98 ppm; ^{31}P NMR (162 MHz, $CDCl_3$) δ −1.56, −1.86, −1.99 ppm; MS (FAB$^+$, NBA) *m*/*z* (relative intensity) 1231 (M + H, 80), 1141 (80), 1051 (30), 91 (100). Anal. Calcd for $C_{69}H_{69}O_{15}P_3$: C, 67.31; H, 5.65. Found: C, 67.6; H, 5.60.

DL-*myo*-Inositol 1,4,6-Trisphosphate (4ab). Ammonia was condensed into a three-neck flask at −78 °C. Small slivers of freshly cut sodium were added to the liquid ammonia until the color remained blue. The ammonia was then distilled into a second flask and kept at −78 °C. Sodium was then added once again until the solution remained blue. DL-2,3,5-Tri-*O*-benzyl-1,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (**14ab**) (0.1 g, 81.3 μmol), in dry dioxane (1 mL), was then added to the sodium in liquid ammonia. The solution was stirred vigorously for 2 min during which time the sodium in liquid ammonia remained blue. The reaction was quenched with methanol, and the solvents were evaporated under a stream of nitrogen. The residue was dissolved in MilliQ water (250 mL) and purified by ion exchange chromatography on Q-Sepharose Fast Flow, eluting with a gradient of TEAB buffer (0−1000 mmol) at pH 8.6. The triethylammonium salt of **4ab** eluted at *ca*. 600 mmol buffer (48.8 μmol, 60%): ^{1}H NMR (270 MHz, D_2O) δ 3.61 (t, J = 9.2 Hz, 1H), 3.72 (dd, J = 2.4, 9.7 Hz, 1H), 4.07 (t, J = 9.5 Hz, 1H), 4.20 (br s, 1H), 4.21 (q, J = 9.3 Hz, 1H), 4.33 (q, J = 9.3 Hz, 1H); ^{31}P NMR (109 MHz, D_2O) δ 1.01 (d, J = 9.8 Hz, 1P), 1.44 (d, J = 9.8 Hz, 1P), 2.02 (d, J = 9.8 Hz, 1P); MS (FAB$^-$, NBA) *m*/*z* (relative intensity) 419 (M − H), (70), 354 (25), 291 (45), 266 (30), 201 (100), 188 (30), 113 (45); HRMS (FAB$^-$, NBA) calcd for $C_6H_{14}O_{15}P_3$ (M − H$^+$) *m*/*z* 418.9545, found 418.9534.

DL-1,4-Di-*O*-allyl-5-*O*-benzyl-2,3-*O*-isopropylidene-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (15). A mixture of DL-1,4-di-*O*-allyl-2,3-*O*-isopropylidene-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**9**) and sodium hydride (1.2 g, 50 mmol) was stirred in dry DMF (150 mL) at room temperature. Benzyl bromide (2.37 mL, 20 mmol) was added dropwise and the reaction was then stirred for 2 h, after which TLC (ether−hexane, 1:1) showed a product of R_f = 0.44. The excess sodium hydride was destroyed with methanol (10 mL), and the solvents were evaporated *in vacuo*. The residue was partitioned between ether (300 mL) and water (200 mL), and the organic layer was washed with brine and water (200 mL each). The organic layer was dried over magnesium sulfate, and the solvent was evaporated. Flash chromatography (ether−hexane, 1:1) of the crude product provided the title compound **15** as a syrup (7.1 g, 93%): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.38, 1.55 (2s, 6H), 3.36 (t, J = 9.2 Hz, 1H), 3.61 (dd, J = 3.8, 9.0 Hz, 1H), 3.67 (dd, J = 7.0, 9.5 Hz, 1H), 3.79 (s, 3H), 3.86 (t, J = 8.8 Hz, 1H), 4.08 (dd, J = 5.7, 6.8 Hz, 1H), 4.20−4.37 (m, 4H), 4.38 (dd, J = 3.85, 5.5 Hz, 1H), 4.68−4.83 (m, 4H), 5.15−5.34 (m, 4H), 5.88−6.02 (m, 2H), 6.85 (d, J = 8.8 Hz, 2H), 7.25−7.37 (m, 7H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.82, 27.75, 55.25, 72.51, 72.93, 74.91, 75.91, 74.60, 77.08, 77.55, 79.08, 80.52, 82.26, 109.84, 113.80, 116.80, 117.50, 127.58, 128.02, 128.31, 129.68, 130.83, 134.99, 135.21, 138.69, 159.12 ppm; MS (FAB$^+$, NBA) *m*/*z* (relative intensity) 419 (1.2), 389 (3.3), 121 (100), 91 (45). Anal. Calcd for $C_{30}H_{38}O_7$: C, 70.55; H, 7.51. Found: C, 70.4; H, 7.64.

DL-1,4-Di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (16ab). DL-1,4-Di-*O*-allyl-5-*O*-benzyl-2,3-*O*-isopropylidene-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**15**) (6.54 g,

12.82 mmol) was dissolved in methanol−1 M HCl (100 mL, 9:1), and the mixture was stirred at 50 °C for 45 min, after which TLC (ether) showed one product of R_f = 0.52. The reaction was cooled and 1 M TEAB (20 mL) was added. The solvents were evaporated to give a white solid. The solid was partitioned between dichloromethane (200 mL) and water (200 mL), and the organic layer was dried over magnesium sulfate, which was filtered, and the solvent was evaporated to give a solid, **16ab** (5.3 g, 88%): mp 87−88 °C (from ether−hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.76 (s, D_2O ex, 2H), 3.32 (dd, J = 2.9, 9.5 Hz, 1H), 3.38 (t, J = 9.3 Hz, 1H), 3.61 (br d, J = 9.5 Hz, D_2O ex, dd, J = 3.8, 9.5 Hz, 1H), 3.69 (t, J = 9.5 Hz, 1H), 3.78 (s, 3H), 3.87 (t, J = 9.5 Hz, 1H), 4.18−4.44 (m, 5H), 4.70−4.90 (m, 4H), 5.14−5.35 (m, 4H), 5.87−6.02 (m, 2H), 6.83 (d, J = 8.8 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.27−7.35 (m, 7H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.19, 71.71, 74.27, 75.52, 69.31, 71.65, 79.79, 80.89, 81.20, 83.10, 113.73, 117.09, 117.48, 127.50, 127.70, 128.30, 129.61, 130.84, 134.56, 134.99, 138.63, 159.16 ppm; MS (FAB$^-$, NBA) *m/z* (relative intensity) 623 (M + NBA, 80), 469 (M − H, 100), 429 (15), 273 (15), 124 (10). Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.9; H, 7.29. Found: C, 68.7; H, 7.27.

D- and L-1-*O*-[*S*-(+)-*O*-Acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (19 and 18). A mixture of DL-1,4-di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**16ab**) (4.068 g, 8.65 mmol), (*S*)-(+)-*O*-acetylmandelic acid (**17**) (1.75 g, 9 mmol), and DMAP (0.03 g, 0.25 mmol) in dry dichloromethane (10 mL) was stirred at −20 °C. A solution of DCC (1.96 g, 9.5 mmol), in dry dichloromethane (20 mL), was added dropwise over 1.5 h at −20 °C and stirring continued overnight. TLC (pentane−ethyl acetate, 2:1) showed two products of R_f = 0.40 and R_f = 0.28. The reaction mixture was filtered through Celite, which was washed thoroughly with dichloromethane (2 × 100 mL). The solvent was evaporated to give a syrup which was purified by flash chromatography using pentane−ethyl acetate (2:1), to provide pure D-1-*O*-[*S*-(+)-*O*-acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**19**) (2.04 g, 36.5%) as a syrup and L-1-*O*-[*S*-(+)-*O*-acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**18**) (1.96 g, 35%) as a solid.

19: TLC, R_f = 0.40; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.15 (s, 3H), 2.65 (s, D_2O ex, 1H), 3.31 (dd, J = 2.6, 9.7 Hz, 1H), 3.42 (t, J = 9.3 Hz, 1H), 3.71 (s, 3H), 3.85 (t, J = 9.3 Hz, 1H), 3.94 (t, J = 9.5 Hz, 1H), 4.08−4.29 (m, 5H), 4.77 (dd, J = 2.6, 10.3 Hz, 1H), 4.68−4.83 (m, 4H), 5.07−5.28 (m, 4H), 5.79−5.95 (m, 2H), 5.97 (s, 1H), 6.80 (d, J = 8.6 Hz, 2H), 7.21 (d, J = 8.6 Hz, 2H), 7.24−7.52 (m, 10H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.31, 54.88, 71.53, 74.11, 75.22, 75.52, 67.37, 74.58, 77.86, 79.10, 80.34, 82.66, 82.85, 113.47, 116.52, 117.20, 127.16, 127.22, 127.48, 128.02, 128.55, 128.98, 129.33, 130.63, 133.24, 138.48, 134.18, 134.48, 158.91, 168.00, 170.40 ppm; MS (FAB$^-$, NBA) *m/z* (relative intensity) 799 (M + NBA, 28), 645 (M − H, 65), 469 (31), 193 (50), 175 (50), 149 (100); $[\alpha]_D$ = −8° (*c* 4.6, CH_2Cl_2). Anal. Calcd for $C_{37}H_{42}O_{10}$: C, 68.7; H, 6.55. Found: C, 68.5; H, 6.55.

18: mp 103−105 °C (from ethanol); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.18 (s, 3H), 2.89 (s, D_2O ex, 1H), 3.36 (t, J = 9.3 Hz, 1H), 3.36 (dd, J = 2.6, 9.5 Hz, 1H), 3.52 (dd, J = 5.5, 11.9 Hz, 1H), 3.76 (s, 3H), 3.77−4.23 (m, 5H), 4.29 (br s, D_2O ex, J = 2.6 Hz, 1H), 4.68−4.91 (m, 7H), 5.18−5.40 (m, 3H), 5.86−6.01 (m, 1H), 5.97 (s, 1H), 6.82 (d, J = 8.8 Hz, 2H), 7.27−7.35 (m, 12H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.54, 55.12, 71.70, 73.87, 75.49, 75.75, 67.61, 74.73, 74.92, 77.89, 79.29, 80.53, 82.85, 113.67, 116.26, 117.53, 127.42, 127.66, 127.97, 128.18, 128.81, 129.38, 129.56, 130.84, 133.14, 138.53, 134.28, 134.64, 159.11, 168.37, 170.48 ppm; MS (FAB$^-$, NBA) *m/z* (relative intensity) 799 (M + NBA, 68), 645 (M − H, 95), 469 (42), 193 (55), 175 (40), 149 (100); $[\alpha]_D$ = +59° (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{37}H_{42}O_{10}$: C, 68.7; H, 6.55. Found: C, 68.4; H, 6.50.

L-1,4-Di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (16b). A mixture of D-1-*O*-[*S*-(+)-*O*-acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**19**) (2.04 g, 3.15 mmol) and sodium hydroxide (0.8 g, 20 mmol) in methanol was heated at reflux temperature for 30 min. The mixture was cooled and neutralized with carbon dioxide. The solid was diluted with water (50 mL) and evaporated to dryness *in vacuo*. The product was extracted with dichloromethane (5 × 100 mL) and the solvent was evaporated to give the product **16b** (1.34 g, 90%): mp 111−113 °C (from ethyl acetate−hexane); TLC R_f = 0.52 (ether); The mass spectrum and NMR data were the same as for the racemic mixture **16ab**; $[\alpha]_D$ = −51° (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.90; H, 7.29. Found: C, 69.0; H, 7.32.

D-1,4-Di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (16a). A mixture of L-1-*O*-[*S*-(+)-*O*-acetylmandelyl]-3,6-di-*O*-allyl-5-*O*-benzyl-4-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**18**) (1.96 g, 3.03 mmol) and sodium hydroxide (0.8 g, 20 mmol) in methanol was heated at reflux temperature for 30 min. Workup was carried out in the same way as for **16b** (1.40 g, 98%): mp 111−113 °C (from ethyl acetate−hexane); TLC, R_f = 0.52 (ether); The mass spectrum and NMR data were the same as for the racemic mixture **16ab**; $[\alpha]_D$ = +51° (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.90; H, 7.29. Found: C, 68.8; H, 7.31.

L-1,4-Di-*O*-allyl-2.3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (11b). A mixture of L-1,4-di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**16b**) (1.70 g, 3.6 mmol) and sodium hydride (0.48 g, 20 mmol) in dry DMF (20 mL) was stirred at room temperature. Benzyl bromide (1.07 mL, 9 mmol) was added to the mixture, which was then stirred for 2 h. The excess sodium hydride was destroyed with methanol (5 mL), and the solvents were evaporated *in vacuo*. The residue was partitioned between ether and water (100 mL of each), and the organic layer was separated and dried over magnesium sulfate. The title compound **11b** was purified by flash chromatography (1.82 g, 78%): mp 72−73 °C (from ethyl acetate−hexane); TLC, R_f = 0.50 (ether−pentane, 1:1); The mass spectrum and NMR data were the same as for the racemic mixture **11ab**; $[\alpha]_D$ = −19° (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{41}H_{46}O_7$: C, 75.6; H, 7.13. Found: C, 75.3; H, 7.05.

D-1,4-Di-*O*-allyl-2,3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (11a). A mixture of D-1,4-di-*O*-allyl-5-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**16a**) (1.60 g, 3.4 mmol) and sodium hydride (0.48 g, 20 mmol) in dry DMF (20 mL) was stirred at room temperature. Benzyl bromide (1.07 mL, 9 mmol) was added to the mixture, which was then stirred for a further 2 h. Workup and purification as for the L-enantiomer gave the pure title compound **11a** (2.08 g, 94%): mp 72−73 °C (from ethyl acetate−hexane); TLC, R_f = 0.50 (ether−pentane, 1:1); The mass spectrum and NMR data were the same as for the racemic mixture **11ab**; $[\alpha]_D$ = +19° (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{41}H_{46}O_7$: C, 75.6; H, 7.13. Found: C, 75.3; H, 6.96.

L-2,3,5-Tri-*O*-benzyl-*myo*-inositol (13b). A solution of L-1,4-di-*O*-allyl-2.3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**11b**) (1.55 g, 2.37 mmol) and freshly sublimed potassium *tert*-butoxide (3.66 g, 30 mmol) in anhydrous DMSO (30 mL) was kept at 50 °C for 5 h, after which TLC (ether−hexane, 1:1) showed complete conversion of starting material (R_f = 0.50) into a single product (R_f = 0.72). The dark mixture was cooled, water (50 mL) was added, and the product was extracted with ether (4 × 100 mL). The organic layer was dried over magnesium sulfate, and the solvent was evaporated to give an off-white solid. This product was not isolated but treated with 1 M aqueous HCl−ethanol (60 mL, 1:2) for 3 h, after which no starting material was left. The reaction was cooled, and the solvents were evaporated *in vacuo*. The remaining solid was partitioned between dichloromethane and water (100 mL of each) and the organic layer was dried over magnesium sulfate. The title compound **13b** was purified by flash chromatography (dichloromethane−ethyl acetate, 1:1) (0.71 g, 67%): mp 176−177 °C (from ethyl acetate−hexane); TLC, R_f = 0.40 (ether); The mass spectrum and NMR data were the same as for the racemic mixture **13ab**; $[\alpha]_D$ = −34° (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.96; H, 6.49. Found: C, 72.2; H, 6.72.

D-2,3,5-Tri-*O*-benzyl-*myo*-inositol (13a). A solution of D-1,4-di-*O*-allyl-2,3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**11a**) (1.2 g, 1.84 mmol) and freshly sublimed potassium *tert*-butoxide (3.66 g, 30 mmol) in anhydrous DMSO (30 mL) was kept at 50 °C for 5 h, after which TLC (ether−hexane, 1:1) showed complete conversion of starting material (R_f =

0.50) into a single product ($R_f = 0.72$). The intermediate was worked up, hydrolyzed, and purified in the same way for the L-enantiomer to give **13a** with the same $R_f = 0.40$ (ether) (0.59 g, 71%): mp 176−177 °C (from ethyl acetate−hexane); The mass spectrum and NMR data were the same as for the racemic mixture **13ab**; $[\alpha]_D = +34°$ (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.96; H, 6.49. Found: C, 71.9; H, 6.75.

D-2,3,5-Tri-*O*-benzyl-1,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (14a). A mixture of bis(benzyloxy)(diisopropylamino)phosphine[23] (1.036 g, 4 mmol) and 1*H*-tetrazole (0.42 g, 6 mmol) in dry dichloromethane (5 mL) was stirred for 15 min. D-2,3,5-Tri-*O*-benzyl-*myo*-inositol (**13a**) (0.15 g, 0.33 mmol) was then added and the reaction was stirred for a further 15 min. The solution was cooled to −78 °C and *tert*-butyl hydroperoxide (1 mL, 7 mmol) was added and the mixture was stirred for 30 min. The reaction mixture was partitioned between dichloromethane (100 mL) and a 10% solution of sodium metabisulfite (100 mL), and the organic layer was washed with brine and water (100 mL of each), dried over magnesium sulfate, and evaporated. The remaining syrup was purified by flash chromatography (chloroform−acetone, 10:1, then ethyl acetate−pentane 2:1), to give **14a** as a syrup (0.21 g, 65%): TLC, $R_f = 0.30$ (chloroform−acetone, 10:1); The mass spectrum and NMR data were the same as for the racemic mixture **14ab**; $[\alpha]_D = 0° \pm 1°$ (*c* 3.6, CH_2Cl_2). Anal. Calcd for $C_{69}H_{69}O_{15}P_3$: C, 67.31; H, 5.65. Found: C, 67.4; H, 5.42.

L-2,3,5-Tri-*O*-benzyl-1,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (14b). A mixture of bis(benzyloxy)(diisopropylamino)phosphine[23] (0.69 g, 2 mmol) and 1*H*-tetrazole (0.42 g, 6 mmol) in dry dichloromethane (5 mL) was stirred for 15 min. L-2,3,5-Tri-*O*-benzyl-*myo*-inositol (**13b**) (0.15 g, 0.33 mmol) was then added and the reaction was stirred for a further 15 min. The solution was cooled to −78 °C and *tert*-butyl hydroperoxide (1 mL, 7 mmol) was added and the mixture was stirred for 30 min. The mixture was worked up in the same way as the D-enantiomer in order to obtain the product **14b** as a syrup (0.24 g, 72%): TLC, $R_f = 0.30$ (chloroform−acetone, 10:1); The mass spectrum and NMR data were the same as for the racemic mixture **14ab**; $[\alpha]_D = 0° \pm 1°$ (*c* 4.1, CH_2Cl_2). Anal. Calcd for $C_{69}H_{69}O_{15}P_3$: C, 67.31; H, 5.65. Found: C, 67.2; H, 5.83.

D-*myo*-Inositol 1,4,6-Trisphosphate (4a). The deprotection of D-2,3,5-tri-*O*-benzyl-1,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (**14a**) (0.11 g, 89 μmol) was carried out in the same way as for the racemic compound, **14ab** → **4ab** (30.1 μmol, 34%); (The NMR spectra were slightly different from the racemic mixture due to different pH values of the compound in the NMR tube) ^{1}H NMR (400 MHz, D_2O) δ 3.49 (t, $J = 9.15$ Hz, 1H), 3.58 (dd, $J = 2.5$, 9.8 Hz, 1H), 3.93 (dt, $J = 2.5$, 9.5 Hz, 1H), 4.07 (br s, 1H), 4.07 (q, $J = 9.2$ Hz, 1H), 4.20 (q, $J = 9.2$ Hz, 1H); ^{31}P NMR (162 MHz, D_2O) δ 0.97 (d, $J = 8.3$ Hz, 1P), 0.39 (d, $J = 8.8$ Hz, 1P), −0.03 (d, $J = 9.5$ Hz, 1P); MS (FAB^-, NBA) *m*/*z* (relative intensity) 419 (M − H, 100), 339 (10), 159 (7), 97 (7); $[\alpha]_D = -29.1°$ (*c* 0.26, TEAB, pH = 8.6); HRMS (FAB^-, NBA) calcd for $C_6H_{14}O_{15}P_3$ (M − H^+) *m*/*z* 418.9545, found 418.9563.

L-*myo*-Inositol 1,4,6-Trisphosphate (4b). The deprotection of L-2,3,5-tri-*O*-benzyl-1,4,6-tris[bis(benzyloxy)phospho]-*myo*-inositol (**14b**) (0.11 g, 89 μmol) was carried out in the same way as for the racemic compound **14a** → **4a** (53.05 μmol, 60%): ^{1}H NMR (400 MHz, D_2O) δ 3.58 (t, $J = 9.2$ Hz, 1H), 3.68 (dd, $J = 2.5$, 9.7 Hz, 1H), 4.04 (dt, $J = 2.5$, 9.5 Hz, 1H), 4.17 (br s, 1H), 4.17 (q, $J = 9.2$ Hz, 1H), 4.29 (q, $J = 9.2$ Hz, 1H); ^{31}P NMR (162 MHz, D_2O) δ 2.11 (d, $J = 6.7$ Hz, 1P), 1.44 (d, $J = 6.7$ Hz, 1P), 1.04 (d, $J = 8.9$ Hz, 1P); MS (FAB^-, NBA) *m*/*z* (relative intensity) 419 (M − H, 100), 339 (10), 159 (7), 97 (7); $[\alpha]_D = +25.0°$ (*c* 0.88, TEAB, pH = 8.6); HRMS (FAB^-, NBA) calcd for $C_6H_{14}O_{15}P_3$ (M − H^+) *m*/*z* 418.9545, found 418.9523.

D-1,4-Di-*O*-allyl-2,3,5-tri-*O*-benzyl-*myo*-inositol (20). D-1,4-Di-*O*-allyl-2,3,5-tri-*O*-benzyl-6-*O*-(*p*-methoxybenzyl)-*myo*-inositol (**11a**) (0.60 g, 0.93 mmol) was suspended in 1 M HCl−ethanol (60 mL, 1:2). The mixture was heated at reflux temperature for 4 h, after which TLC (ether−petroleum ether, 1:1) showed the appearance of a major product of $R_f = 0.40$. The reaction was cooled, and the solvents were evaporated *in vacuo*. The remaining solid was taken up in dichloromethane (100 mL) and washed with water (100 mL). The organic layer was dried over magnesium sulfate and filtered, and the solvent was evaporated. The residue was purified by flash chromatography to give the title compound **20** as a syrup (0.45 g, 91%): ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.25 (s, D_2O ex, 1H), 3.09 (dd, $J = 2.2$, 9.9 Hz, 1H), 3.31 (t, $J = 9.15$ Hz, 1H), 3.32 (dd, $J = 2.2$, 9.8 Hz, 1H), 3.90 (t, $J = 9.5$ Hz, 1H), 3.93−4.10 (m, 4H), 4.28−4.44 (m, 2H), 4.62, 4.69 (AB $J = 11.9$ Hz, 2H), 4.85, 4.91 (AB $J = 11.1$ Hz, 2H), 5.12−5.30 (m, 4H), 5.80−6.05 (m, 2H), 7.21−7.41 (m, 15H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 71.06, 72.88, 73.91, 74.50, 75.28, 72.55, 73.49, 79.69, 80.92, 81.15, 83.29, 116.50, 127.30, 127.46, 127.56, 127.72, 127.85, 128.08, 128.34, 134.47, 135.31, 138.40, 138.75, 138.82 ppm; MS (FAB^-, NBA) *m*/*z* (relative intensity) 683 (M + NBA, 100), 576 (30), 529 (M − H, 8), 503 (35), 489 (18), 322 (12), 273 (10), 184 (10); $[\alpha]_D = -3°$ (*c* 9, CH_2Cl_2). Anal. Calcd for $C_{33}H_{38}O_6$: C, 74.67; H, 7.22. Found: C, 74.9; H, 7.41.

D-1,4-Di-*O*-allyl-2,3,5,6-tetra-*O*-benzyl-*myo*-inositol (21). A mixture of D-1,4-di-*O*-allyl-2,3,5-tri-*O*-benzyl-*myo*-inositol (**20**) (0.29 g, 0.55 mmol) and sodium hydride (0.12 g, 5 mmol) was stirred in dry DMF (10 mL) at room temperature. Benzyl bromide (0.12 mL, 1.0 mmol) was added and the reaction was stirred for a further 2 h, after which TLC (ether−pentane, 1:2) showed a product of $R_f = 0.60$. The excess sodium hydride was destroyed with methanol, and the solvents were evaporated *in vacuo*. The residue was partitioned between ether and water (50 mL of each), and the organic layer was then dried and evaporated to give a syrup. The residue was purified by flash chromatography (ether−pentane, 1:2) to give the title compound **21** (0.31 g, 90%): mp 63−65 °C (from pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.23 (dd, $J = 2.1$, 9.8 Hz, 1H), 3.30 (1H, dd, $J = 2.1$, 10.1 Hz, 1H), 3.40 (t, $J = 9.15$ Hz, 1H), 3.93 (t, $J = 9.8$ Hz, 1H), 3.98 (t, $J = 9.5$ Hz, 1H), 3.99 (t, $J = 2.45$ Hz, 1H), 4.04−4.12 (m, 2H), 4.29−4.42 (m, 2H), 4.60, 4.67 (AB, $J = 10.8$ Hz, 1H), 4.77−4.89 (m, 6H), 5.12−5.31 (m, 4H), 5.85−6.02 (m, 2H), 7.23−7.41 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.63, 72.84, 73.97, 74.32, 75.84, 75.95, 74.59, 80.65, 80.77, 81.43, 81.58, 83.63, 116.60, 116.66, 127.28, 127.48, 127.79, 127.94, 128.09, 128.31, 134.91, 135.42, 138.53, 138.86, 138.91, 138.95 ppm; MS (FAB^-, NBA) *m*/*z* (relative intensity) 773 (M + NBA, 100), 666 (50), 470 (30), 322 (38), 291 (30), 140 (30); $[\alpha]_D = +18°$ (*c* 1, CH_2Cl_2). Anal. Calcd for $C_{40}H_{44}O_6$: C, 77.39; H, 7.14. Found: C, 77.2; H, 7.15.

L-1,2,4,5-Tetra-*O*-benzyl-*myo*-inositol (22). A mixture of D-1,4-di-*O*-allyl-2,3,5,6-tri-*O*-benzyl-*myo*-inositol (**21**) (0.26 g, 1.78 mmol), toluene-*p*-sulfonic acid (0.15 g, 0.75 mmol), and 10% palladium on activated charcoal (Fluka, 0.25 g) was heated under reflux for 2 h in ethanol−water (35 mL, 6:1). TLC (ether) showed a new product of $R_f = 0.50$ and debenzylated products at the baseline. The palladium on activated charcoal was filtered through Celite to give a colorless solution, and the solvents were evaporated. The title compound **22** was purified by flash chromatography (dichloromethane−ethyl acetate, 1:1) (0.14 g, 61%): mp 103−105 °C (from ether) (lit.[30] mp 105−107 °C); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.35 (br s, D_2O ex, 1H), 2.61 (br s, D_2O ex, 1H), 3.28 (dd, $J = 2.2$, 9.9 Hz, 1H), 3.38 (t, $J = 9.15$ Hz, 1H), 3.51 (br d, $J = 9.5$ Hz, D_2O ex, dd, $J = 2.2$, 9.5 Hz, 1H), 3.79 (t, $J = 9.5$ Hz, 1H), 4.05 (t, $J = 2.2$ Hz, 1H), 4.15 (t, $J = 9.5$ Hz, 1H), 4.56−4.93 (m, 8H), 7.21−7.33 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 72.51, 74.63, 75.21, 75.46, 74.64, 73.25, 76.19, 80.39, 81.88, 83.28, 127.65, 127.75, 127.78, 127.91, 128.04, 128.35, 128.43, 128.48, 128.56, 137.85, 138.60, 138.71 ppm; MS (FAB^-, NBA) *m*/*z* (relative intensity) 692 (M + NBA, 100), 586 (40), 539 (55), 472 (15), 322 (25), 287 (20); $[\alpha]_D = +4°$ (*c* 1, CH_2Cl_2) [lit.[30] $[\alpha]_D = +3.9°$ (*c* 1, $CHCl_3$)]. Anal. Calcd for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 75.6; H, 6.94.

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