Flexible Stereo- and Regioselective Synthesis of *myo*-Inositol Phosphates (Part 1): Via Symmetrical Conduritol B Derivatives

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A practical route is described for the preparation of *myo*-inositol polyphosphates. Optically pure *myo*-inositol derivatives can be prepared from *p*-benzoquinone in both forms by enzymatic resolution of a C_2-symmetric diacetoxyconduritol B key intermediate, followed by *cis*-dihydroxylation. Selective functionalization of axial and equatorial hydroxy groups allows the synthesis of symmetric inositol phosphates as well as unsymmetrical, enantiomerically pure inositol phosphates. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2005)

Introduction

Inositol phosphates play key functions in biological systems as single compounds[1–3] or as part of more complex structures, for example glycosyl phosphatidyl inositol systems[4,5] and phosphatidylinositol phosphates.[6] A new level of attention has been focused on inositol phosphates, especially over the last two decades, after the discovery in 1983 that *myo*-inositol 1,4,5-trisphosphate [**1**; *myo*-Ins(1,4,5)P_3] is a Ca^{2+}-mobilizing second messenger.[7,8] Since then quite a large number of inositol phosphates, from Ins-P_1 to Ins-P_6 and even more highly phosphorylated systems with pyrophosphate groups, have been found in nature, establishing a complex inositol phosphate cascade in their metabolism, although their specific role has not been elucidated in each case. For biochemical studies the availability of inositol phosphates of defined structure is essential, and a method for their synthesis is urgently needed.

Key intermediates for the synthesis of *myo*-inositol polyphosphates are the corresponding hydroxy group(s) protected derivatives in enantiomerically pure form with free hydroxy group(s) at the desired phosphorylation position. Such protected inositol derivatives have been synthesized by various methods, such as from achiral *myo*-inositol by stereoselective protection and resolution, or from synthetic intermediates prepared from chiral building blocks either from the chiral pool or by de novo synthesis.[9]

In the present work a de novo strategy for the preparation of inositol derivatives is applied. Optically pure compounds in both forms can easily be prepared from *p*-benzoquinone by enzymatic resolution of diacetoxyconduritol B (**3**) to yield the building blocks for this procedure. Conduritol B derivatives seemed to be ideal intermediates for the synthesis of *myo*-inositol systems for two main reasons: first, conduritol B systems are C_2-symmetric, which means that *cis*-dihydroxylation of the double bond gives only one diastereoisomeric product, and second, several conduritol B systems are readily available synthetically in both enantiomeric forms by epoxide formation and nucleophilic ring opening. Protected *myo*-inositol systems **5** and *ent*-**5**, which have pairwise differentiated (orthogonal protection) hydroxy groups, are obtained from C_2-symmetric conduritol B systems **4** and *ent*-**4** (see Scheme 1), respectively. Because of the structural peculiarity of *myo*-inositol systems, the enantiomeric systems **5** and *ent*-**5** can lead to different regioisomeric *myo*-inositol bis- and tetrakisphosphates, namely bisphosphates D-*myo*-Ins(1,2)P_2 [(–)-**8**], D-*myo*-Ins(2,3)P_2 [(+)-**8**] (it is clear that D-2,3- corresponds to L-1,2-bisphosphate and likewise in the other cases), D-*myo*-Ins(4,5)P_2 [(–)-**9**], D-*myo*-Ins(5,6)P_2 [(+)-**9**], D-*myo*-Ins(3,6)-P_2 [(–)-**10**], and D-*myo*-Ins(1,4)P_2 [(+)-**10**], and tetrakisphosphates D-*myo*-Ins(1,2,4,5)P_4 [(–)-**11**], D-*myo*-Ins(2,3,5,6)P_4 [(+)-**11**], D-*myo*-Ins(1,2,3,6)P_4 [(+)-**12**], D-*myo*-Ins(1,2,3,4)P_4 [(–)-**12**], D-*myo*-Ins(3,4,5,6)P_4 [(+)-**13**], and D-*myo*-Ins(1,4,5,6)P_4[(–)-**13**].

Regioselective manipulation within the *cis*-diol group after dihydroxylation, by selective protection of the equatorial hydroxy group (see compound **6**) or the axial group (see compound **7**), gives appropriate precursors for the synthesis of *myo*-inositol mono-, tris-, and pentakisphosphates. Such a desymmetrization increases the potential of this symmetrical approach significantly. In this article we will demonstrate the utility of this approach.

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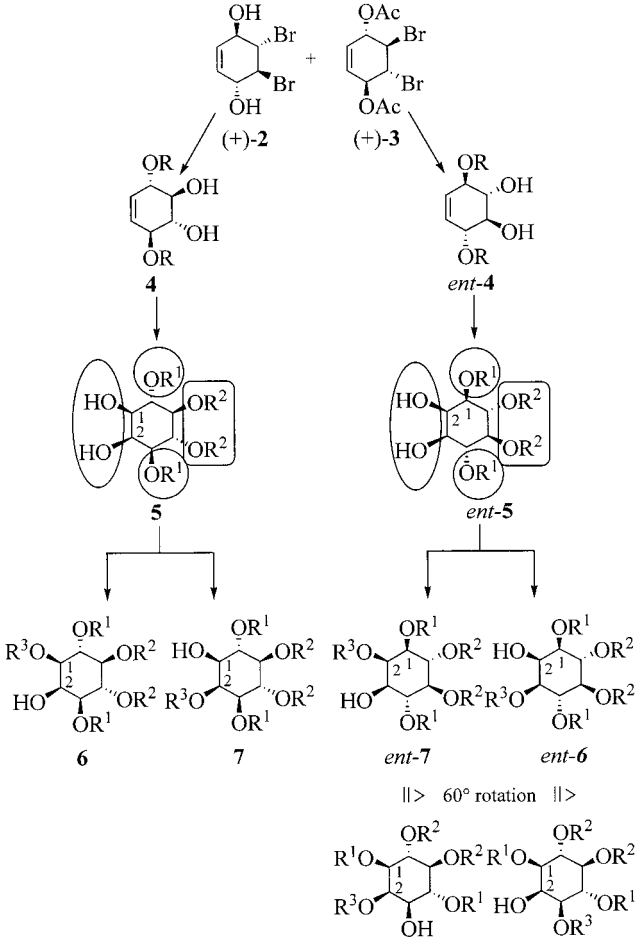


Scheme 1.

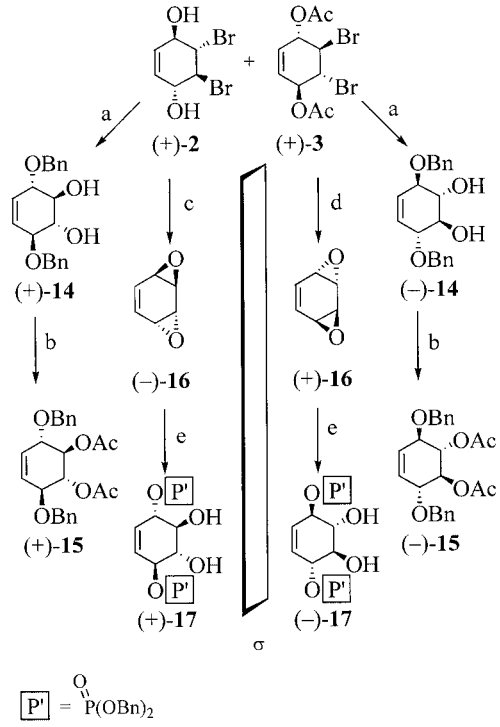
Results and Discussion

Synthesis of Symmetrical Conduritol B Building Blocks

The known diacetoxydibromocyclohex-5-enes (+)-**3** and (–)-**3** [or the corresponding diols (–)- and (+)-**2**] were used as the enantiomerically pure building blocks[10,11] for the synthesis of all the *myo*-inositol derivatives described. Racemic **3** can easily be prepared from *p*-benzoquinone in three steps and 70% overall yield. Enantiopure compounds were obtained by hydrolysis of racemic diacetate **3** with PPL (pig pancreas lipase, type II from Sigma–Aldrich Chemie GmbH) in Et_2O/phosphate buffer at pH = 7.0. The hydrolysis stops after 50% conversion of the starting material and proceeds with excellent enantioselectivity (>99% *ee*) for both the remaining diacetate (+)-**3** and the resulting diol (+)-**2**. The products can easily be separated on a 100-g scale due to their different solubilities in dichloromethane.

To avoid confusion, it should be mentioned that for the synthesis of *meso* or racemic compounds all routes can be carried out employing either racemic **2** or **3**. Besides the benefits of a shortened synthetic route, this facilitates purification by recrystallization, since the racemic intermediates show an increased tendency to crystallize. The presented intermediates can be used as valuable inositol building blocks, as their hydroxy groups are protected in an orthogonal way. However, this concept is certainly not limited to the given examples and should prove valuable for the preparation of further compounds.

It is well known that diol (+)-**2** can be used for the preparation of 1,4-di-*O*-benzylconduritol B [(+)-**14**]. To this end (+)-**14** was synthesized in a one-pot procedure in 70% yield from diol (+)-**2**, as reported previously.[12] Subsequent acetylation of the free hydroxy groups gave (+)-**15** (see Scheme 2). The diacetate (+)-**3** could be converted in the same way into the enantiomer (–)-**14**.



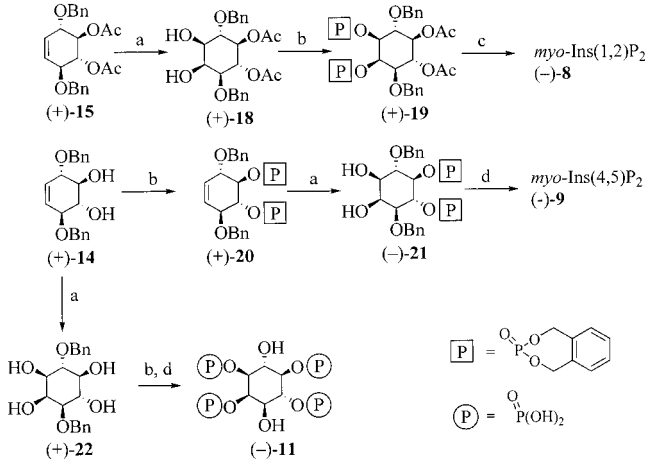
Scheme 2. Reagents and conditions: (a) BnOH, THF, NaOBn (70%). (b) Ac_2O, pyridine (76%). (c) THF, powdered molecular sieves, KOH (77%). (d) THF, powdered molecular sieves, KOH then MeOH (70%). (e) CH_2Cl_2, dibenzyl phosphate (55%).

The diphosphorylated conduritol B derivative (+)-**17** was synthesized[11] by double allylic opening with dibenzyl phosphate of *anti*-benzene dioxide (–)-**16**, which was synthesized in one step from the enantiomeric building blocks (Scheme 2).

These C_2-symmetric conduritol B systems are the starting points for the syntheses of a number of *myo*-inositol polyphosphates.

Synthesis of *myo*-Inositol Polyphosphates from Di-*O*-benzylconduritol B Derivatives

The intermediates obtained by the above-mentioned routes were used for the preparation of *myo*-Ins(1,2)P_2 [(–)-**8**], *myo*-Ins(4,5)P_2 [(–)-**9**], *myo*-Ins(1,2,4,5)P_4 [(–)-**11**], and their enantiomers (see Scheme 3).



Scheme 3. Reagents and conditions: (a) $RuCl_3$, $NaIO_4$, acetonitrile (99%). (b) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (60–65%). (c) 1. Pd/C, H_2, ethyl acetate/ethanol; 2. 0.25 N NaOH (99%). (d) Pd/C, H_2, ethanol/water (99%).

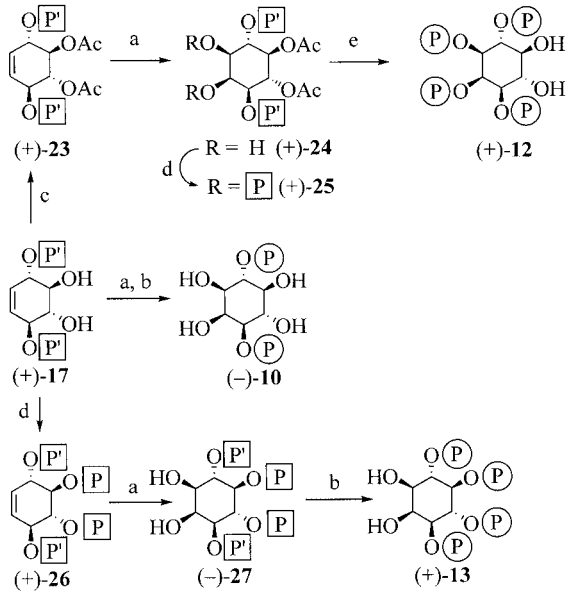
Flash *cis*-dihydroxylation of the conduritol B derivative (+)-**15** with ruthenium trichloride and sodium metaperiodate gave the protected and phosphorylated *myo*-inositol derivative (+)-**18** in high yield (see Scheme 3). In the case of the symmetrical approach, *cis*-dihydroxylation of the conduritol B derivatives led to only one product, with a *myo* configuration of the resulting inositol. The direct phosphorylation of the free hydroxy groups of (+)-**18** with (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine and subsequent oxidation with *m*-CPBA gave (+)-**19**. Hydrogenation of (+)-**19** followed by saponification of the acetate protecting groups furnished *myo*-Ins(1,2)P_2 [(–)-**8**] in quantitative yield.

In the case of the synthesis of *myo*-Ins(4,5)P_2 [(–)-**9**], the precursor (+)-**14** was first phosphorylated to form the protected conduritol B (+)-**20**, which was then *cis*-dihydroxylated under the conditions described above. Hydrogenation gave the target compound *myo*-Ins(4,5)P_2 [(–)-**9**].

It should also be noted that the intermediate tetraol (+)-**22**, which was obtained by flash *cis*-dihydroxylation of (+)-**14**, is a useful intermediate for the synthesis of *myo*-Ins(1,2,4,5)P_4 [(–)-**11**], as reported earlier by our group.[13] Phosphorylation of (+)-**22** and deprotection by Pd/C-catalyzed hydrogenation gave *myo*-Ins(1,2,4,5)P_4 [(–)-**11**] in 70% yield over two steps.

Synthesis of *myo*-Inositol Polyphosphates from 1,4-Diphosphorylated Conduritol B Derivative (+)-17

cis-Dihydroxylation of (+)-**17** with $RuCl_3/NaIO_4$ and subsequent Pd/C-catalyzed deprotection by hydrogenolysis gave *myo*-Ins(3,6)P_2 [(–)-**10**] in excellent yield (see Scheme 4). The enantiomer (–)-**17** gives *myo*-Ins(1,4)P_2 [(+)-**10**] in a similar manner.



Scheme 4. Reagents and conditions: (a) $RuCl_3$, $NaIO_4$, acetonitrile (99%). (b) Pd/C, H_2, ethanol/water (99%). (c) Ac_2O, pyridine (99%). (d) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (80%). (e) 1. Pd/C, H_2, ethyl acetate/ethanol; 2. 0.25 N NaOH (99%).

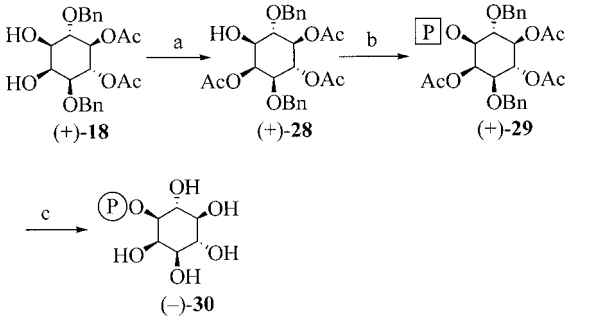
As previously described, it is possible to synthesize the tetrakisphosphate isomers *myo*-Ins(1,2,3,6)P_4 [(+)-**12**][13,14] and *myo*-Ins(3,4,5,6)P_4 [(+)-**13**][11] from the precursor (+)-**17**.

Differentiation within the *cis*-Diol Moiety for the Synthesis of *myo*-Inositol Mono-, Tris-, and Pentakisphosphates

Synthesis of myo-Ins(1)P_1 [(–)-30]

For the synthesis of *myo*-Ins(1)P_1 [(–)-**30**], the axial hydroxy group of the *cis*-diol moiety of (+)-**18** has to be regioselectively protected. Such desymmetrization yielded the appropriate precursor for the synthesis of monophosphates. The regioselective protection of the axial 2-OH group for the synthesis of (–)-**30** did not involve the previously reported tedious, multistep method involving temporary protection of the equatorial 1-OH with dibutyltin.[15] Instead, the two hydroxy groups were differentiated by monofunctionalization of the axial hydroxy group of (+)-**18**. Thus, treatment of (+)-**18** with triethyl orthoacetate under acidic conditions in anhydrous THF resulted in the formation of an intermediate orthoester, which was directly converted with acetic acid into the axial acetate (+)-**28** (see Scheme 5).[16] The regioselectivity in this reaction can be traced back to stereoelectronic effects.[17]

The phosphorylation was performed by treatment with (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine in the presence of 1*H*-tetrazole and subsequent oxidation of the resulting phosphite with *m*-CPBA to give (+)-**29**. Deprotection, carried out by hydrogenation followed by cleavage of the acetate groups in aqueous NaOH, delivered the

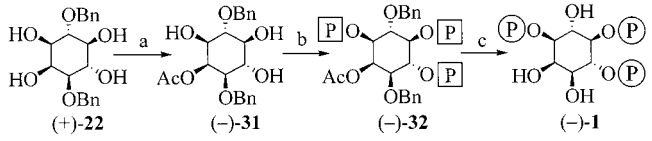


Scheme 5. Reagents and conditions: (a) 1. $MeC(OEt)_3$, *p*-TSA; 2. 80% HOAc (99%). (b) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (60%). (c) 1. Pd/C, H_2, ethanol/water; 2. 0.25 N NaOH (99%).

target compound *myo*-Ins(1)P_1 [(–)-**30**] in quantitative yield. The optical rotation value of *myo*-Ins(1)P_1 [(–)-**30**] was found to be –2.6 (pH adjusted to 6 with NH_4OH), which differs greatly from the previously reported value of Billington et al.[18] (+3.55, pH = 9, as the dicyclohexylammonium salt). The main reason for this is that the optical rotation is strongly dependent on the chosen pH value. Pizer et al.[19] have pointed out that the optical rotation of *myo*-Ins(1)P_1 [(–)-**30**] changes in sign when the pH value of the solution is adjusted from basic (+3.4, pH adjusted to 9 with cyclohexylamine) to acidic (–9.8, pH = 2) conditions. Our obtained values are +4.4 (pH adjusted to 9 with NH_4OH), and –6.1 [pH = 2 (free acid)], thus confirming the synthesis of (–)-**30**.

Synthesis of myo-Ins(1,4,5)P_3 [(–)-1]

For the synthesis of *myo*-Ins(1,4,5)P_3 [(–)-**1**] the tetraol (+)-**22** was monofunctionalized under the above-mentioned conditions for the selective functionalization of an axial hydroxy group to give the direct precursor (–)-**31** (see Scheme 6). This easy and effective procedure allows the selective protection of the single axial OH group in **22**.

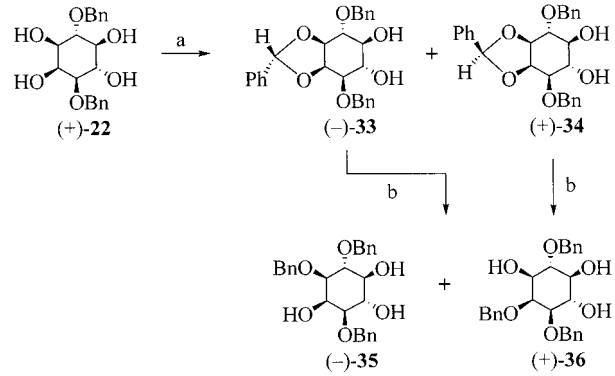


Scheme 6. Reagents and conditions: (a) 1. $MeC(OEt)_3$, *p*-TSA; 2. 80% HOAc (95%). (b) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (87%). (c) 1. Pd/C, H_2, ethanol/water; 2. 0.25 N NaOH (98%).

Phosphorylation under the conditions described above gave (–)-**32** in excellent yield. Hydrogenolysis and cleavage of the acetate group in aqueous NaOH delivered the target compound *myo*-Ins(1,4,5)P_3 [(–)-**1**] by a short and highly efficient reaction sequence.

Synthesis of *myo*-Ins(2)P (39), *myo*-Ins(2,3,6)P_3 [(+)-42], and *myo*-Ins(2,4,5)P_3 [(–)-44] by a Forced Protecting-Group Migration

We also tried to use **22** for the synthesis of a tribenzylated derivative. Employing racemic material, we were able to synthesize the cyclic acetal by a simple zinc chloride catalyzed reaction in benzaldehyde (see Scheme 7). The resulting *exo* product **33** (*exo*-phenyl) is almost insoluble in benzaldehyde and precipitates from the reaction mixture, thereby driving the equilibrium to this product. The isolated product is pure enough to be used in the ensuing reactions without purification; its conformation was unambiguously assigned by NOE experiments on the acetylated derivative **49** (structure not illustrated; see Exp. Sect.). Reduction of this acetal with borane–tetrahydrofuran complex in the presence of dibutylboryl triflate,[20] as described for other acetals of carbohydrates, led to the tribenzylated isomers in a ratio of 3:1, which were easily separable by column chromatography.



Scheme 7. Reagents and conditions: (a) benzaldehyde dimethylacetal, *p*-TSA, THF (69%). (b) 1 M BH_3 in THF, 1 M Bu_2BOTf in CH_2Cl_2, NEt_3 (87%).

However, when we employed the enantiomerically pure starting material (+)-**22** for acetalization under various reaction conditions (zinc chloride in benzaldehyde, as mentioned above, or benzaldehyde dimethyl acetal and *p*-toluenesulfonic acid as catalyst), the lower tendency of the product to crystallize prevented formation of a single reaction product. We have frequently observed in our work with conduritol and inositol derivatives that enantiomerically pure materials are less likely to crystallize than the corresponding racemates. Although the *exo* isomer (–)-**33** is still the less soluble one, its solubility is high enough to prevent precipitation of one diastereoisomer from the reaction mixture so the reaction leads to a 1:1 mixture of the *exo* and *endo* isomers (–)-**33** and (+)-**34** (*endo*-phenyl). The two isomers can be separated by careful column chromatography, however. The *endo* diastereoisomer (+)-**34** was unambiguously assigned by NOE experiments, where a strong cross peak between 2-H and the acetal-H can be observed.

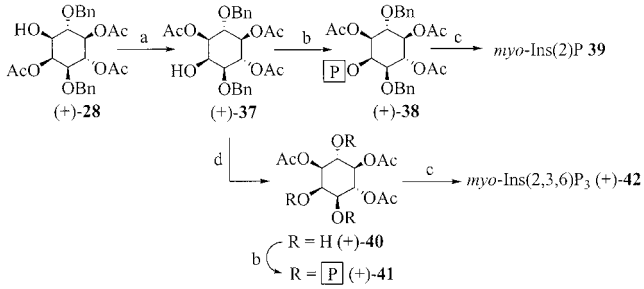
Reduction of the *exo* diastereoisomer under the above-mentioned conditions led to formation of the 1- and 2-benzylated triols (–)-**35** and (+)-**36** in a 46:54 ratio. The *endo* diastereoisomer delivers the 2-benzyl product (+)-**36** in 75%

isolated yield with no detectable amounts of the 1-benzyl product. Thus, this route, although it opens access to two interesting enantiopure tribenzylated triol building blocks, is not suitable for the synthesis of the desired *myo*-Ins(2,4,5)P_3 [(–)-**44**]. We therefore looked for a different strategy to deliver a suitably protected building block in high yields.

One problem associated with the use of esters as protecting groups in polyhydroxylated systems is the tendency for intramolecular transesterification, which leads to migration of the acyl function to a neighboring alcohol.[21] Protecting-group migration can be observed under mild basic or acidic conditions. However, one might be able to exploit this usually unwanted side-reaction for synthetic purposes if the equilibrium can be shifted to one product or the other.

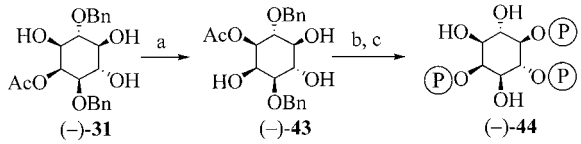
In the case of the acetylated (+)-**28**, we hoped that we could exploit the greater stability of an equatorial acetate over the thermodynamically less favorable axial acetate in (+)-**28** to obtain (+)-**37**. Whereas there was no migration of the axial acetate in position 2 to the equatorial position 1 on treatment of (+)-**28** under mildly basic conditions with K_2CO_3 in CH_2Cl_2 or under mildly acidic conditions with acetic acid, the treatment of (+)-**28** under more forcing conditions with trimethylsilyl trifluoromethanesulfonate in anhydrous diethyl ether led to the desired product with a free axial hydroxy group (see Scheme 8). The success of this conversion can easily be observed by NMR spectroscopy (see Figure 1). The signal of 2-H is strongly shifted upfield, from δ = 5.70 ppm to δ = 4.34 ppm, while that for 1-H is shifted downfield from δ = 3.68 ppm to δ = 4.88 ppm.

This useful intermediate (+)-**37** was also employed in the synthesis of more inositol-phosphates. Further conversion of the protecting groups, phosphorylation, and deprotection yielded *myo*-Ins(2)P (**39**) and *myo*-Ins(2,3,6)P_3 [(+)-**42**] (see Scheme 8).



Scheme 8. Reagents and conditions: (a) TMS–OTf, CH_2Cl_2 (100%). (b) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (60%). (c) 1. Pd/C, H_2, ethanol/water; 2. 0.25 N NaOH (98%). (d) Pd/C, H_2, ethyl acetate/ethanol (99%).

As a further example of the opportunities provided by this concept of forced protecting-group migration for the synthesis of enantiomerically pure *myo*-inositol polyphosphates, the synthesis of *myo*-Ins(2,4,5)P_3 (–)-**44** is described (see Scheme 9).



Scheme 9. Reagents and conditions: (a) THF, 2 N HCl (60%). (b) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA. (c) 1. Pd/C, H_2, ethanol/water; 2. 0.25 N NaOH (50%).

Previous work led us to propose that enantiopure (–)-**31** would be an ideal starting material for the synthesis of *myo*-Ins(2,4,5)P_3 [(–)-**44**] if the axial acetate group could be induced to migrate analogously. Initial attempts, in anhydrous

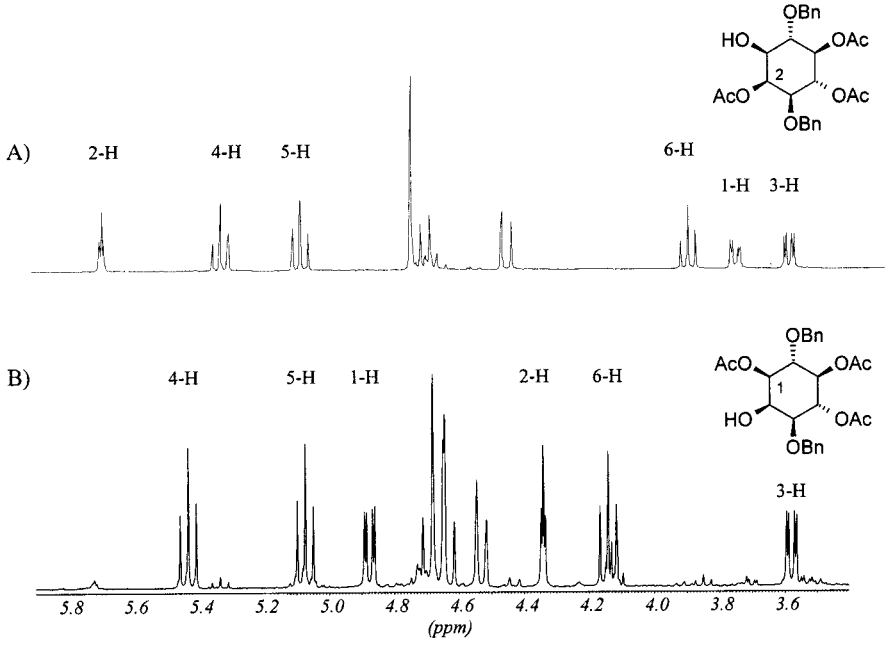
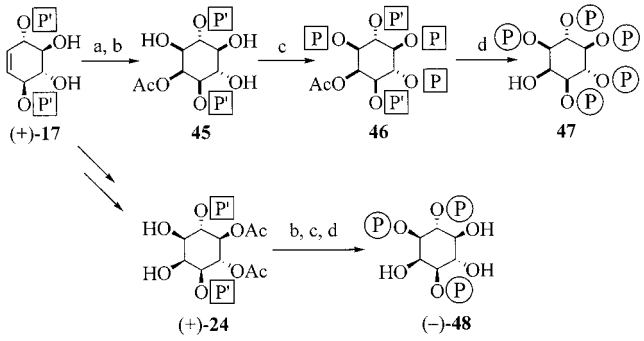


Figure 1. Comparison of the ^{1}H NMR spectra of **28** (A) and **37** (B).

diethyl ether with TMS–OTf, were unsuccessful. It was found in the end that migration does take place in tetrahydrofuran on addition of 2 N HCl and stirring at 80 °C for 36 h. The crude product contains, besides the product (–)-**43**, the starting material (–)-**31** and the de-*O*-acetylated product (+)-**22** in a 3:5:2 ratio. Longer reaction times resulted in a higher proportion of the saponification product. The desired compound (–)-**43** was isolated by flash chromatography in 30% yield; the starting material was also re-isolated in 50% yield, which corresponds to a product yield of 60% based on converted material. Phosphorylation with (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine in the presence of 1*H*-tetrazole, with subsequent oxidation with *m*-CPBA and then deprotection, delivered the desired product *myo*-Ins(2,4,5)P_3 [(–)-**44**] in excellent yield.

Synthesis of *myo*-Ins(1,3,6)P_3 [(–)-48] and the *meso* Compound *myo*-Ins (1,3,4,5,6)P_5 (47)

The versatile precursor (+)-**17** can easily be transformed in short reaction sequences into various other *myo*-inositol polyphosphates by the methods described above. Thus, both enantiomers of *myo*-Ins(1,3,6)P_3 [(–)-**48**] and the *meso* compound *myo*-Ins (1,3,4,5,6)P_5 (**47**) were accessible. The other enantiomer *myo*-Ins(1,3,4)P_3 [(+)-**48**] was synthesized analogously from (–)-**24** (see Scheme 10).



Scheme 10. Reagents and conditions: (a) $RuCl_3$, $NaIO_4$, acetonitrile/EtOAc (98%). (b) 1. $MeC(OEt)_3$, *p*-TSA; 2. 80% HOAc (98%). (c) (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (82%). (d) 1. Pd/C, H_2, ethanol/water; 2. 0.25 N NaOH (92%).

Outlook

As mentioned above, all products are available in both enantiomeric forms. The "symmetric concept", based on the use of C_2-symmetrical building blocks, allows the synthesis of a wide variety of inositol phosphate isomers. However, it is based on pairwise differentiation (orthogonal protection) of the hydroxy groups, which certainly limits the number of accessible building blocks. In the following article in this issue we will present a scheme to overcome this limitation and to complete this concept for the synthesis of *myo*-inositol polyphosphates.

Conclusions

The present work further emphasizes the potential of (+)- and (–)-**3** as versatile building blocks in the construction of nonracemic inositol polyphosphates. The efficient, high-yielding routes described allowed the synthesis of several *myo*-inositol polyphosphates in both enantiomeric forms, namely *myo*-Ins(1)P [(–)-**30**], *myo*-Ins(2)P (**39**), *myo*-Ins(1,2)P_2 [(–)-**8**], *myo*-Ins(4,5)P_2 [(–)-**9**], *myo*-Ins(3,6)P_2 [(–)-**10**], *myo*-Ins(1,4,5)P_3 [(–)-**1**], *myo*-Ins(2,4,5)P_3 [(–)-**44**], *myo*-Ins(1,3,6)P_3 [(–)-**48**], *myo*-Ins(2,3,6)P_3 [(+)-**42**], *myo*-Ins(1,2,4,5)P_4 [(–)-**11**], *myo*-Ins(1,2,3,6)P_4 [(+)-**12**], *myo*-Ins(3,4,5,6)P_4 [(+)-**13**], and *myo*-Ins (1,3,4,5,6)P_5 (**47**), as well as their enantiomers *myo*-Ins(3)P [(+)-**30**], *myo*-Ins-(2,3)P_2 [(+)-**8**], *myo*-Ins(5,6)P_2 [(+)-**9**], *myo*-Ins(1,4)P_2 [(+)-**10**], *myo*-Ins(3,5,6)P_3 [(+)-**1**], *myo*-Ins(2,5,6)P_3 [(+)-**44**], *myo*-Ins(1,3,4)P_3 [(+)-**48**], *myo*-Ins(1,2,4)P_3 [(–)-**42**], *myo*-Ins(2,3,5,6)P_4 [(+)-**11**], *myo*-Ins(1,2,3,4)P_4 [(–)-**12**], and *myo*-Ins(1,4,5,6)P_4 [(–)-**13**].

Experimental Section

General Remarks: All NMR spectra were recorded with a Bruker ARX 400 (400 MHz) spectrometer. In addition to ^1H, ^{13}C, and ^{31}P experiments, 2D COSY (^1H-^1H, ^1H-^{13}C, and ^1H-^{31}P) and DEPT spectra were recorded for unequivocal correlation of the hydrogen, carbon, and phosphorus atoms. The chemical shifts are given in ppm relative to TMS, although in practice the solvents were taken as internal standards. The multiplicity is given by the following symbols: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), ψt (pseudotriplet for unresolved dd), ur (unresolved) and br (broad). Melting points (not corrected) were recorded with a Büchi 510 heating block. IR spectra were obtained in pressed KBr, and only noteworthy absorptions (cm^{-1}) are listed. All optical rotations of the *myo*-inositol phosphates are given after adjusting to pH = 6 with NH_4OH or as free acids. TLC analyses were carried out on Merck (Darmstadt, Germany) aluminum-backed silica gel 60 F254 0.25 mm plates and were visualized by UV illumination at 254 nm before being sprayed with phosphomolybdic acid (10% in MeOH) and heated. For column chromatography, Merck silica gels 60 (40–63 μm, flash) and 60H (dry) were used. All organic extracts were dried with $MgSO_4$, filtered, and concentrated in a rotary evaporator. Only distilled solvents were used. The building blocks (+)- and (–)-**2**, (–)- and (+)-**3**, and their precursors were prepared according to literature methods,[10,11] as were 1,4-di-*O*-benzylconduritol B (**14**)[12] and 1,4-bis(di-*O*-benzylphospho)conduritol B (**17**).[11]

Purification and Analysis of Inositol Tris- and Tetrakisphosphates (HPLC-MDD): Inositol phosphates were purified and analyzed by the HPLC-MDD method described previously.[11,22] The compounds were separated by anion-exchange chromatography on a MonoQ HR10/10 column (Pharmacia). To purify inositol phosphates, a linear gradient of HCl was applied (0 min 0.2 mM HCl; 70 min 0.5 M HCl; flow rate 1.5 mL min^{-1}). In analytical runs, photometric detection at 546 nm was achieved with a metal-dye reagent [2 M Tris/HCl (pH = 9.1), 200 μM 4-(2-pyridylazo)resorcinol (PAR), 30 μM YCl_3, 10% (v/v) MeOH; flow rate 0.75 mL min^{-1}]. In purification steps, where on-line detection was not possible, an analogous experiment was carried out on a microplate. In brief, a 0.2–2-μL portion of the collected fraction was mixed with 100 μL of metal-dye reagent, and the absorbance at 540 nm was measured.

(1*S*,2*R*,3*R*,4*S*)-2,3-Di-*O*-acetyl-1,4-di-*O*-benzylconduritol B [(+)-15]: (1*S*,2*R*,3*R*,4*S*)-1,4-Di-*O*-benzylconduritol B [(+)-**14**; 64 g, 0.20 mol] was dissolved in a cooled mixture of pyridine (250 mL) and acetic anhydride (200 mL) and the solution was stirred at room temperature for 12 h. For workup the solution was added to a mixture of ice (350 g) and CH_2Cl_2 (350 mL). The aqueous solution was extracted with CH_2Cl_2 (3×150 mL). The combined organic layers were extracted with 15% aqueous HCl (3×150 mL), saturated $NaHCO_3$ (3×100 mL), and brine (100 mL). After evaporation of the solvent, the resulting solid was crystallized from ethyl acetate or ethanol to yield (+)-**15** (61 g, 76%) as a colorless solid. R_f = 0.48 (cyclohexane/ethyl acetate, 3:2). $[\alpha]_D^{20}$ = +192.2 (*c* = 1.25, $CHCl_3$). M.p. 116 °C. ^{1}H NMR ($CDCl_3$): δ = 2.06 (s, 6 H, CH_3), 4.30 (AA′XX′, 2 H, 1-H, 4-H), 4.54, 4.64 (2×d, AB, *J* = 11.81 Hz, 2×2 H, Ph-CH_2), 5.29 (AA′XX′, 2 H, 2-H, 3-H), 5.82 (s, 2 H, 5-H, 6-H), 7.33 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.7 (CH_3), 71.3 (Ph-CH_2), 72.7 (C-2, C-3), 76.9 (C-1, C-4), 127.7, 127.8, 128.4 ($C_{arom.}$), 127.9 (C-5, C-6), 137.8 (C_{ipso}), 169.9 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 395 (2), 244 (8), 196 (6), 153 (5), 111 (25), 91 (100), 43 (57) ppm. IR (KBr): $\tilde{\nu}$ = 3060, 3020 (m), 1750, 1730 (s), 1370 (m), 1240, 1220 (s), 1050 (m), 775, 695 (m) cm^{-1}. $C_{24}H_{26}O_6$ (410.5): calcd. C 70.23, H 6.38; found C 70.27, H 6.54.

(1*R*,2*S*,3*S*,4*R*)-2,3-Di-*O*-acetyl-1,4-di-*O*-benzylconduritol B [(–)-15]: A solution of (–)-**14** was allowed to react to give (–)-**15** under the conditions described for the preparation of (+)-**15**. $[\alpha]_D^{20}$ = –194.7 (*c* = 1.25 in chloroform). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical to those obtained for (+)-**15**.

4,5-Di-*O*-acetyl-3,6-di-*O*-benzyl-D-*myo*-inositol [(+)-18]: A solution of sodium metaperiodate (4.7 g, 22 mmol, 1.5 equiv.) and ruthenium trichloride trihydrate (280 mg, 1 mmol) in water (60 mL) was added to a vigorously stirred ice-cooled solution of (+)-**15** (5.2 g, 12.8 mol) in acetonitrile/ethyl acetate (1:1, 350 mL). The stirring was continued until TLC no longer showed any starting material (approx. 10 min). After the reaction had been quenched by addition of aqueous $Na_2S_2O_3$ (20%, 200 mL), the aqueous layer was separated and extracted with EtOAc (3×200 mL). The combined organic layers were washed twice with brine and concentrated under reduced pressure to yield (+)-**18** (4.9 g, 87%) as a grey solid. For an analytical sample, the solid was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate, 3:2) to yield pure (+)-**18** as a colorless solid. R_f = 0.09 (cyclohexane/ethyl acetate, 3:2). $[\alpha]_D^{20}$ = +34.7 (*c* = 0.9, $CHCl_3$). M.p. 129 °C. ^{1}H NMR ($CDCl_3$): δ = 1.95, 1.99 (s, 2×3 H, CH_3), 2.70, 2.90 (2×s, br, 2 H, OH), 3.48 (dd, *J* = 2.7, *J* = 9.84 Hz, 1 H, 3-H), 3.58 (dd, *J* = 2.5, *J* = 9.5 Hz, 1 H, 1-H), 3.90 (ψt, *J* = 9.6 Hz, 1 H, 6-H), 4.21 (ψt, *J* = 2.9, 1 H, 2-H), 4.55, 4.66 (2×d, AB, *J* = 12.05 Hz, 2×1 H, Ph-CH_2), 4.69, 4.77 (2×d, AB, *J* = 11.6 Hz, 2×1 H, Ph-CH_2), 5.04 (ψt, *J* = 9.84 Hz, 1 H, 5-H), 5.44 (ψt, *J* = 9.84 Hz, 1 H, 4-H), 7.33 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.68, 20.72 (CH_3), 69.1 (C-2), 71.7 (C-1), 71.7 (C-4), 72.8 (C-5), 72.4, 75.1 (Ph-CH_2), 77.1 (C-3), 79.3 (C-6), 127.6, 127.7, 127.8, 128.1, 128.5, 128.6 ($C_{arom.}$), 137.3, 138.1 (C_{ipso}), 170.03, 170.05 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 353 (6), 247 (10), 91 (100), 43 (72). IR (KBr): $\tilde{\nu}$ = 3450 (s, br), 3060, 3040 (m), 2960, 2900, 2890 (s), 1730 (s), 1370 (m), 1240 (s), 1060 (m), 740, 690 (m) cm^{-1}. $C_{24}H_{28}O_8$ (444.5): calcd. C 64.85, H 6.35; found C 64.60, H 6.28.

5,6-Di-*O*-acetyl-1,4-di-*O*-benzyl-D-*myo*-inositol [(–)-18]: A solution of (–)-**15** was allowed to react to give (–)-**18** under the conditions described for the preparation of (+)-**18**. $[\alpha]_D^{20}$ = –34.1 (*c* = 0.8 in $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**18**.

4,5-Di-*O*-acetyl-3,6-di-*O*-benzyl-1,2-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-19]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (195 mg, 0.82 mmol) was added to a suspension of (+)-**18** (150 mg, 0.34 mmol) and 1*H*-tetrazole (95 mg, 1.4 mmol) in anhydrous dichloromethane (20 mL), and the solution was stirred at room temperature for 12 h. The solution was then cooled to –40 °C and an anhydrous solution of *m*-CPBA (690 mg, 2.8 mmol) in dichloromethane (10 mL, dried with Na_2SO_4) was added. The solution was stirred at –20 °C for 30 min, then it was allowed to warm to room temperature, and the stirring was continued for 1 h. The product was worked up as described for (+)-**29**. Purification by flash chromatography (ethyl acetate/cyclohexane, 2:1) gave (+)-**19** (160 mg, 58%) as a colorless foam. R_f = 0.07 (ethyl acetate/cyclohexane, 1:1). $[\alpha]_D^{20}$ = +26 (*c* = 0.36, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.88, 1.99 (2×s, 2×3 H, CH_3), 3.65 (d, *J* = 10.2 Hz, 1 H, 3-H), 3.95 (ψt, *J* = 9.7 Hz, 1 H, 6-H), 4.48, 4.83 (2×d, AB, *J* = 11.7 Hz, 2×1 H, Ph-CH_2), 4.60, 4.83 (2×d, AB, *J* = 11.2 Hz, 2×1 H, Ph-CH_2), 4.67 (ψt, *J* = 9.7 Hz, 1 H, 1-H), 4.95–5.60 [m, 8 H, $(CH_2)_2$-C_6H_4], 5.10 (ψt, *J* = 9.7 Hz, 1 H, 5-H), 5.37 (ψt, *J* = 10.2 Hz, 1 H, 4-H), 5.41 (dψt, *J* = 10.1, *J* = 2.3 Hz, 1 H, 2-H), 7.18–7.39 (m, 18 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.5, 20.7 (2×CH_3), 68.5–69.0 [m, 2×$(CH_2)_2C_6H_4$], 70.9 (C-4), 72.0 (C-5), 72.1 ($PhCH_2$), 74.9 (d, *J* = 2.9 Hz, C-3), 75.0 ($PhCH_2$), 75.1 (dd, *J* = 1.9, *J* = 5.9 Hz, C-2), 75.9 (ψt, *J* = 4.8 Hz, C-1), 77.3 (d, *J* = 4.8 Hz, C-6), 127.7, 127.85, 127.91, 128.3, 128.4, 128.56, 128.63, 128.7, 128.8, 128.9, 129.0, 129.1 ($C_{arom.}$), 134.6, 135.0, 135.3, 135.4, 136.9, 137.7 (C_{ipso}), 169.5, 170.0 (C=O) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$,): δ = –0.21 (PC-2), 0.14 (PC-1) ppm. HR-MS (ESI-pos.): calcd. for $C_{40}H_{42}O_{14}P_2Na$ $[M + Na]^+$ 831.1948; found 831.194

5,6-Di-*O*-acetyl-1,4-di-*O*-benzyl-2,3-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-19]: A solution of (–)-**18** was allowed to react to give (–)-**19** under the same conditions as those described for the preparation of (+)-**19**. $[\alpha]_D^{20}$ = –30 (*c* = 0.76, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**19**.

D-*myo*-Inositol 1,2-Bisphosphate [(–)-8]: Deprotection (hydrogenolysis and deacetylation) of (+)-**19** (50 mg, 60 μmol) was carried out as described for the preparation of (–)-**30** to give (–)-**8** (20 mg, 100%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –12.1 [*c* = 1.2, H_2O, pH = 1.5 (free acid)]. $[\alpha]_D^{20}$ = –13.9 [*c* = 0.8, H_2O, pH adjusted to 6 (NH_4OH)]. Ref.[23,24] (bisphosphate isolated from *myo*-InsP_6; dephosphorylation catalyzed by phytase from wheat germ or bran) $[\alpha]_D^{20}$ = –10.5 (*c* = 2, H_2O, sodium salt, pH = 7). Ref.[23,24] $[\alpha]_D^{20}$ = –6 (*c* = 4, H_2O, free acid). ^{1}H NMR (D_2O, free acid): δ = 3.30 (ψt, *J* = 9.2 Hz, 1 H, 5-H), 3.58 (d, *J* = 10.2 Hz, 1 H, 3-H), 3.63 (ψt, *J* = 9.4 Hz, 1 H, 4-H), 3.74 (ψt, *J* = 9.4 Hz, 1 H, 6-H), 4.05 (dψt, *J* = 2.1, *J* = 8.9 Hz, 1 H, 1-H), 4.73 (d, *J* = 9.2 Hz, 1 H, 2-H) ppm. ^{13}C NMR (D_2O, free acid): δ = 72.4 (d, *J* = 3.1 Hz, C-3), 73.5 (d, *J* = 6.1 Hz, C-6), 74.5 (s, C-4), 76.5 (s, C-5), 77.4 (m, C-1), 79.4 (d, *J* = 6.1 Hz, C-2) ppm. ^{31}P{^{1}H} NMR (D_2O, free acid): δ = 1.11 (sh), 1.25 (PC-1, PC-2) ppm. HR-MS (ESI-neg, phosphoric acid 0.002%, Q-TOF): calcd. for $C_6H_{13}O_{12}P_2$ $[M - H]^-$ 338.9883; found 338.9841.

D-*myo*-Inositol 2,3-Bisphosphate [(+)-8]: A solution of (–)-**19** was allowed to react under the conditions described for the preparation of (–)-**8** to give (+)-**8**. $[\alpha]_D^{20}$ = +11.2 (*c* = 0.8, H_2O, free acid). The ^{1}H NMR and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**8**.

(1*S*,2*R*,3*R*,4*S*)-1,4-Di-*O*-benzyl-2,3-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)conduritol B [(+)-20]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (700 mg,

3 mmol) was added to a suspension of (+)-**14** (400 mg, 1.22 mmol) and 1*H*-tetrazole (350 mg, 5 mmol) in anhydrous dichloromethane (20 mL), and the solution was stirred at room temperature for 4 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (2.1 g, 9 mmol) in dichloromethane (20 mL, dried with Na_2SO_4) was added. The solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The product was worked up as described for (+)-**29**. Purification by flash chromatography (ethyl acetate/cyclohexane, 3:1) yielded pure (+)-**20** (500 mg, 65%) as a colorless foam. R_f = 0.32 (ethyl acetate/cyclohexane, 3:1). $[\alpha]_D^{20}$ = +21.5 (*c* = 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 4.40 (m, AA′XX′, 2 H, 1-H, 4-H), 4.71 (s, 4 H, Ph-CH_2), 4.95–5.00 (m, AA′XX′, 2 H, 2-H, 3-H), 5.02–5.25, 5.48–5.58 [m, 8 H, $(CH_2)_2C_6H_4$], 5.80 (s, 2 H, 5-H, 6-H), 7.17–7.46 (m, 18 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 68.3 [d, *J* = 7.1 Hz, $(CH_2)_2C_6H_4$], 69.0 [d, *J* = 7.1 Hz, $(CH_2)_2C_6H_4$], 71.2 (Ph-CH_2), 78.0 (d, *J* = 2.0 Hz, C-1, C-4), 78.4 (ψt, *J* = 4.6 Hz, C-2, C-3), 127.5 (C-5, C-6), 127.8, 127.9, 128.4, 128.5, 128.6, 128.8, 128.9 ($C_{arom.}$), 135.0, 135.3, 137.7 (C_{ipso}) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = –0.12 (PC-2, PC-3) ppm. MS (EI, 70 eV): *m*/*z* (%) = 571 (2), 477 (3), 277 (48), 201 (40.3), 200 (33), 184 (27), 119 (69), 104 (100), 102 (75), 65 (73). IR (film): $\tilde{\nu}$ = 3064 (m), 3029 (m), 3005 (m), 2934 (m), 2891 (m), 1498 (m), 1455 (m), 1384 (m), 1290 (s, br), 1223 (m), 1024 (s, br), 850 (s, br), 750 (s, br), 698 (m), 624 (m) cm^{-1}. HR-MS (ESI-pos.): calcd. for $C_{36}H_{36}O_{10}P_2Na$ [M + Na] 713.168; found 713.1682.

(1*R*,2*S*,3*S*,4*R*)-1,4-Di-*O*-benzyl-2,3-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)conduritol B [(–)-20]: A solution of (–)-**14** was allowed to react to give (–)-**20** under the conditions described for the preparation of (+)-**20**. $[\alpha]_D^{20}$ = –21.3 (*c* = 1.55, $CHCl_3$). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**20**.

3,6-Di-*O*-benzyl-4,5-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-21]: A solution of sodium metaperiodate (89 mg, 0.41 mmol, 1.5 equiv.) and ruthenium trichloride trihydrate (30 mg, 0.1 mmol) in water (1 mL) was added to a vigorously stirred ice-cooled solution of (+)-**20** (200 mg, 0.29 mmol) in acetonitrile (5 mL). The stirring was continued until TLC showed the complete absence of starting material (approx. 8 min). The reaction was then quenched by addition of aqueous $Na_2S_2O_3$ (20%, 10 mL). The aqueous layer was separated and extracted with EtOAc (3×20 mL). The combined organic layers were washed twice with brine and concentrated under reduced pressure to yield (–)-**21** (220 mg, 99%) as a colorless foam. $[\alpha]_D^{20}$ = –32.0 (*c* = 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 3.51 (dd, *J* = 2.3, *J* = 9.4 Hz, 1 H, 3-H), 3.61 (dd, *J* = 3.0, *J* = 9.7 Hz, 1 H, 1-H), 3.92 (ψt, *J* = 9.7 Hz, 1 H, 6-H), 4.17 (ψt, *J* = 2.6 Hz, 1 H, 2-H), 4.69 (m, AB, 2 H, Ph-CH_2), 4.72 (ψq, *J* = 9.0 Hz, 1 H, 5-H), 4.84 (s, 2 H, Ph-CH_2), 4.91–5.56 [m, 8 H, 2×$(CH_2)_2C_6H_4$], 5.13 (m, 1 H, 4-H), 7.07–7.50 (m, 18 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 68.1 [dd, *J* = 6.6, *J* = 10.7 Hz, $(CH_2)_2C_6H_4$], 68.7 (C-2), 68.8 [ψt, *J* = 7.6 Hz, $(CH_2)_2C_6H_4$], 71.6 (C-1), 72.5, 74.8 (2×Ph-CH_2), 77.9 (C-3), 78.4 (m, C-4), 79.3 (ψt, *J* = 5.7 Hz, C-5), 79.7 (C-6), 127.5–129.2 ($C_{arom.}$), 134.8, 134.9, 135.2, 135.3, 137.4, 138.4 (C_{ipso}) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 0.36 (PC-4), 0.83 (PC-5) ppm. MS (EI, 70 eV): *m*/*z* (%) = 322 (1), 200 (6), 192 (9), 104 (40), 91 (100). IR (KBr): $\tilde{\nu}$ = 3417 (m) 3055 (w), 3029 (w), 2934 (w), 2886 (w), 1283 (m), 1026 (s, br), 859 (m), 734 (m) cm^{-1}. HR-MS (ESI-pos.): calcd. for $C_{36}H_{38}O_{12}P_2Na$ $[M + Na]^+$ 747.1736; found 747.174.

1,4-Di-*O*-benzyl-5,6-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-21]: A solution of (–)-**20** was allowed to react to give (+)-**21** under the conditions used for the preparation of (–)-**21**. $[\alpha]_D^{20}$ = +28.8 (*c* = 0.65, $CHCl_3$). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**21**.

D-*myo*-Inositol 4,5-Bisphosphate [(–)-9]: Preactivated Pd/C (70 mg, Degussa RW 10) was added to a suspension of (–)-**21** (110 mg, 0.15 mmol) in ethanol/water (1:1, 40 mL), and the mixture was stirred at room temperature under H_2 for 12 h. The catalyst was filtered off, and the filtrate was lyophilized to give (–)-**9** (51 mg, 99%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –4.4 [*c* = 0.3, H_2O, pH adjusted to 6 (NH_4OH)]. $[\alpha]_D^{20}$ = +7.9 [*c* = 1.2, H_2O, pH = 1.4 (free acid)]. Ref.[25] $[\alpha]_D^{20}$ = –10 (*c* = 1, H_2O, tetrapotassium salt). ^1H NMR (D_2O, free acid): δ = 3.55 (dd, *J* = 2.5, *J* = 10.2 Hz, 1 H, 1-H), 3.67 (dd, *J* = 2.0, *J* = 9.7 Hz, 1 H, 3-H), 3.74 (ψt, *J* = 9.7 Hz, 1 H, 6-H), 3.99 (ψq, *J* = 9.2 Hz, 1 H, 5-H), 3.99 (ψs, 1 H, 2-H), 4.28 (ψq, *J* = 9.2 Hz, 1 H, 4-H) ppm. ^{13}C NMR (D_2O, free acid): δ = 70.5 (d, *J* = 2.5 Hz, C-3), 70.8 (C-1), 71.7 (d, *J* = 2.5 Hz, C-6), 72.1 (C-2), 78.3 (ψq, *J* = 3.2 Hz, C-4), 79.7 (ψq, *J* = 3.2 Hz, C-5) ppm. $^{31}P\{^1H\}$ NMR (D_2O, 161 MHz, free acid): δ = 1.21 (PC-5), 1.55 (sh, PC-4) ppm. HR-MS (ESI-neg, phosphoric acid, Q-TOF): calcd. for $C_6H_{13}O_{12}P_2$ [M – H] 338.9842; found 338.9883.

D-*myo*-Inositol 5,6-Bisphosphate P_2 [(+)-9]: A solution of (+)-**21** was allowed to react under the conditions described for the preparation of (–)-**9** to give (+)-**9**. $[\alpha]_D^{20}$ = +8.1 (*c* = 1.0, H_2O, free acid). The ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**9**.

3,6-Di-*O*-benzyl-D-*myo*-inositol [(+)-22]: A solution of sodium metaperiodate (2 g, 9.5 mmol) and ruthenium trichloride trihydrate (165 mg, 0.63 mmol) in water (15 mL) was added to a vigorously stirred ice-cooled solution of (+)-**14** (2.1 g, 6.4 mmol) in acetonitrile (60 mL). The stirring was continued until TLC showed complete absence of starting material (approx. 10 min). The reaction was then quenched by addition of aqueous $Na_2S_2O_3$ (20%, 150 mL). The aqueous layer was separated and extracted five times with EtOAc (5×150 mL). The combined organic layers were washed twice with brine and concentrated under reduced pressure to yield (+)-**22** (1.9 g, 82%) as a colorless solid. For an analytical sample, the residue was crystallized from ethyl acetate. M.p. 170 °C (ref.[26] 172 °C). R_f = 0.25 (ethyl acetate/cyclohexane, 1:1). $[\alpha]_D^{20}$ = +17.2 (*c* = 1.8, MeOH). Ref.[26] $[\alpha]_D^{20}$ = +16 (*c* = 1, MeOH). ^1H NMR ($CDCl_3$/[D$_4$]MeOH, 6:1): δ = 3.16 (dd, *J* = 9.7, *J* = 2.0 Hz, 1 H, 3-H or 1-H), 3.31 (ψt, *J* = 9.4 Hz, 1 H, 4-H or 6-H), 3.38 (dd, *J* = 9.7, *J* = 2.5 Hz, 1 H, 1-H or 3-H), 3.58 (ψt, *J* = 9.4 Hz, 1 H, 5-H), 3.78 (ψt, *J* = 9.4 Hz, 1 H, 4-H or 6-H), 4.07 (ψt, *J* = 2.0 Hz, 1 H, 2-H), 4.61 (AB, 2 H, Ph-CH_2), 4.79 (AB, 2 H, Ph-CH_2), 7.16–7.38 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$/[D$_4$]MeOH, 6:1): δ = 65.5 (C-2), 67.9 (C-1 or C-3), 68.3 (Ph-CH_2), 68.5 (C-5), 70.8 (C-4 or C-6), 71.1 (Ph-CH_2), 75.5 (C-1 or C-3), 77.5 (C-4 or C-6), 127.8, 127.9, 128.0, 128.1, 128.4, 128.5 ($C_{arom.}$), 137.9, 138.7 (C_{ipso}) ppm. MS (70 eV): *m*/*z* (%) = 360 (1) [M^+], 270 (5), 269 (14) [M^+ – Bn], 108 (26), 107 (50), 92 (36), 91 (100), 79 (32). $C_{20}H_{24}O_6$ (360.4): calcd. C 66.65, H 6.71; found C 66.93, H 6.71.

1,4-Di-*O*-benzyl-D-*myo*-inositol [(–)-22]: A solution of (–)-**14** was allowed to react to give (–)-**22** under the conditions described for the preparation of (+)-**22**. $[\alpha]_D^{20}$ = –18.3 (*c* = 2, MeOH). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**22**.

D-*myo*-Inositol 1,2,4,5-Tetrakisphosphate [(–)-11]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (830 mg, 3.5 mmol) was added to a suspension of (+)-**22** (290 mg, 0.7 mmol) and 1*H*-tetrazole (290 mg, 4.1 mmol) in anhydrous dichloromethane (30 mL), and the solution was stirred at room temperature for 12 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (4.1 g, 16.6 mmol) in dichloromethane (30 mL, dried

with Na_2SO_4) was added. The solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The product was worked up as described for (+)-**29**. Purification by flash chromatography (ethyl acetate/cyclohexane, 5:1) yielded 3,6-di-*O*-benzyl-1,2,4,5-tetra-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol (595 mg, 78%, purity >90%) as a colorless foam. ^{1}H NMR ($CDCl_3$): δ = 3.68 (d, J = 9.7 Hz, 1 H, 3-H), 3.97 (ψt, J = 9.9 Hz, 1 H, 6-H), 4.56 (d, AB, J = 11.2 Hz, 1 H, Ph-CH_2), 4.66–5.20 (m, 18 H, CH_2 and ring protons), 5.27–5.48 (m, 5 H, CH_2 and other ring protons), 7.06–7.50 (m, 26 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 68.1 [m, $(CH_2)_2C_6H_4$], 68.5 [m, $(CH_2)_2C_6H_4$], 68.7–69.0 [m, $(CH_2)_2C_6H_4$], 72.5 (s, CH_2, $PhCH_2$), 74.5 (s, CH), 74.6 (s, $PhCH_2$), (dd, J = 5.1, J = 1.6 Hz, CH), 75.8 (s, CH), 73.4 (m, 2×CH), 78.44 (m, CH), 127.36–129.18 (C_{arom}), 134.2–135.3, 136.8, 137.0, 137.7 (C_{ipso}) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = –0.70, 0.11, 0.24, 1.17 ppm.

Hydrogenolysis: Preactivated Pd/C (100 mg, Degussa RW 10) in ethanol/water (1:2, 30 mL) was added to a suspension of 3,6-di-*O*-benzyl-1,2,4,5-tetra-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol (200 mg, 0.18 mmol), as obtained above, in ethanol (20 mL). The mixture was stirred at room temperature under H_2 overnight. The catalyst was filtered off, and the filtrate was concentrated under high vacuum and then lyophilized to give 90 mg of a colorless, very hygroscopic foam. Purification by HPLC yielded pure (–)-**11** (80 mg, purity >99%). $[\alpha]_D^{20}$ = –26.3 (c = 0.7, H_2O, free acid). Ref.[26] $[\alpha]_D^{20}$ = –27.2 (c = 0.5, TEAB buffer pH = 8.6). ^{31}P{^{1}H} NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 1.93, 3.12, 3.58, 3.63 ppm. For more spectroscopic data see refs.[13,26]

(1*S*,2*R*,3*R*,4*S*)-2,3-Di-*O*-acetyl-1,4-bis-*O*-(di-*O*-benzylphospho)conduritol B [(+)-23]: A solution of (1*S*,2*R*,3*R*,4*S*)-1,4-bis-*O*-(di-*O*-benzylphospho)conduritol B [(+)-**17**; 2 g, 3 mmol] in a cooled mixture of pyridine and acetic anhydride (30 mL, 1:1) was stirred for 12 h at room temperature. For workup the solution was added to a mixture of ice (300 g) and CH_2Cl_2 (100 mL). The aqueous phase was extracted five times with CH_2Cl_2 (5×100 mL). The combined organic layers were extracted four times with 15% aqueous HCl (4×150 mL), saturated $NaHCO_3$ (4×150 mL), and brine (100 mL). Evaporation of the solvent yielded (+)-**23** (1.8 g, 86%) as a yellowish oil that crystallized after 1 d. R_f = 0.46 (dichloromethane/methanol, 95:5). $[\alpha]_D^{20}$ = +92.3 (c = 1.28, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.66 (s, 6 H, CH_3), 5.03 (m, 8 H, Ph-CH_2), 5.12 (m, 2 H, 1-H, 4-H), 5.30 (m, 2 H, 2-H, 3-H), 5.73 (s, 2 H, 5-H, 6-H), 7.35 (m, 20 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.4 (2×CH_3), 69.6 (m, 4×CH_2, Ph-CH_2), 71.6 (d, J = 4.9 Hz, 2×C, C-1, C-4), 75.5 (d, J = 5.0 Hz, 2×C, C-2, C-3), 127.5–129.6 ($C_{arom.}$ and $C_{olef.}$), 135.4–135.5 (C_{ipso}), 169.7 (C=O) ppm. ^{31}P NMR ($CDCl_3$): δ = –0.35 (sext, J = 8.5 Hz) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = –0.35 ppm. MS (EI, 70 eV): m/z (%) = 751 [M + H]$^+$, 473, 400, 386, 212. $C_{38}H_{40}O_{12}P_2$ (750.7): calcd. C 60.80, H 5.37; found C 60.85, H 5.45.

(1*R*,2*S*,3*S*,4*R*)-2,3-Di-*O*-acetyl-1,4-bis-*O*-(di-*O*-benzylphospho)conduritol B [(–)-23]: A solution of (–)-**17** was allowed to react under the conditions described for the preparation of (+)-**23** to give (–)-**23**. $[\alpha]_D^{20}$ = –90.4 (c = 1.28, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**23**.

4,5-Di-*O*-acetyl-3,6-bis-*O*-(di-*O*-benzylphospho)-D-*myo*-inositol [(+)-24]: A solution of sodium metaperiodate (820 mg, 3.9 mmol, 1.5 equiv.) and ruthenium trichloride trihydrate (70 mg, 0.3 mmol) in water (6 mL) was added to a vigorously stirred ice-cooled solution of (+)-**23** (1.9 g, 2.6 mmol) in acetonitrile (40 mL). The stirring was continued until TLC showed the complete absence of starting material (approx. 7 min). The reaction was then quenched by addition of aqueous $Na_2S_2O_3$ (20%, 100 mL). The aqueous layer was separated and extracted with EtOAc (3×100 mL). The combined organic layers were washed twice with brine and concentrated under reduced pressure to yield (+)-**24** (1.6 g, 77%) as a colorless solid. R_f = 0.16 (CH_2Cl_2/MeOH, 95:5). $[\alpha]_D^{20}$ = +33.8 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.80 (s, 3 H, CH_3), 1.86 (s, 3 H, CH_3), 3.66 (dd, J = 2.4, J = 9.2 Hz, 1 H, 1-H), 4.34 (ψs, 1 H, 2-H), 4.39 (dψt, J = 2.5, J = 9.3 Hz, 1 H, 3-H), 4.72 (ψq, J = 9.2 Hz, 1 H, 6-H), 4.88–5.20 (m, 9 H, 4×Ph-CH_2, 5-H), 5.57 (ψt, J = 9.9 Hz, 1 H, 4-H), 7.33 (m, 20 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.5 (CH_3), 20.7 (CH_3), 69.9, 70.1, 71.0 (5×C, Ph-CH_2, C-5), 70.3 (d, C-4), 70.7 (C-1), 71.9 (d, C-2), 76.0 (d, C-3), 78.8 (d, C-6), 128.0, 128.1, 128.57, 128.62, 128.7 ($C_{arom.}$), 135.5 (m, C_{ipso}), 169.7, 169.9 (C=O) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 0.80, 0.72 ppm. MS (EI, 70 eV): m/z (%) = 785 [M + H]$^+$, 707 [M – C_6H_5], 729, 454, 429, 391. IR (KBr): $\tilde{\nu}$ = 3410 (w), 3070 (w), 3030 (w), 2950 (w), 1755 (s), 1240 (s), 1040 (s), 1020 (s), 755 m), 705 (m) cm^{-1}. $C_{38}H_{42}O_{14}P_2$ (784.7): calcd. C 58.16, H 5.40; found C 58.00, H 5.49.

5,6-Di-*O*-acetyl-1,4-bis-*O*-(di-*O*-benzylphospho)-D-*myo*-inositol [(–)-24]: A solution of (–)-**23** was allowed to react under the conditions described for the preparation of (+)-**24** to give (–)-**24**. $[\alpha]_D^{20}$ = –34.8 (c = 1.2, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**24**.

4,5-Di-*O*-acetyl-3,6-bis-*O*-(di-*O*-benzylphospho)-1,2-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-25]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (520 mg, 2.2 mmol) was added to a suspension of (+)-**24** (250 mg, 0.32 mmol) and 1*H*-tetrazole (100 mg, 2.5 mmol) in anhydrous dichloromethane (20 mL), and the solution was stirred at room temperature for 12 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (2.1 g, 6 mmol) in dichloromethane (25 mL, dried with Na_2SO_4) was added. The solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The product was worked up as described for (+)-**29**. Purification by flash chromatography (dichloromethane/methanol, 3:1) yielded pure (+)-**25** (300 mg, 80%) as a colorless foam. R_f = 0.51 (dichloromethane/methanol, 95:5). $[\alpha]_D^{20}$ = +2.5 (c = 1.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.83 (s, 3 H, CH_3), 1.88 (s, 3 H, CH_3), 4.58 (ψt, J = 9.9 Hz, 1 H, 1-H or 3-H), 5.14 (m, 19 H, CH_2 and remaining CH-ring), 5.46 (ψt, J = 9.9 Hz, 2 H,), 7.31 (m, 28 H, C_6H_5 and C_6H_4) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.33 (CH_3), 20.34 (CH_3), 68.8 [m, Ph-CH_2 and $(CH_2)_2C_6H_4$], 69.8 [m, Ph-CH_2 and $(CH_2)_2C_6H_4$], 69.5 (d, J = 3.8 Hz, C-4 or C-5), 70.0 [m, Ph-CH_2 and $(CH_2)_2C_6H_4$], 70.1 (m, CH), 73.0 (d, J = 2.9 Hz, C-4 or C-5), 73.6 (m, CH), 75.2 (ψt, J = 5.3 Hz, CH), 76.9 (m, CH), 127.9–129.9 ($C_{arom.}$), 134.4–135.9 (C_{ipso}); 169. 7, 169. 9 (C=O) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = –0.65, –0.71 (PC-3 PC-6), –1.02, –1.74 (PC-2, PC-1) ppm. MS (FAB): m/z = 1149 [M + H]$^+$. $C_{54}H_{56}O_{20}P_4$ (1148.9): calcd. C 56.45, H 4.91; found C 56.35, H 5.00.

5,6-Di-*O*-acetyl-1,4-bis-*O*-(di-*O*-benzylphospho)-2,3-bis-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-25]: A solution of (–)-**24** was allowed to react under the conditions described for the preparation of (+)-**25** to give (–)-**25**. $[\alpha]_D^{20}$ = –1.7 (c = 1.3, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-25.

D-*myo*-Inositol 1,2,3,6-Tetrakisphosphate [(+)-12]: Deprotection (hydrogenolysis and deacetylation) of (+)-**25** (300 mg, 0.22 mmol) was carried out as described for the preparation of (–)-**30** to give (+)-**12** (100 mg, 95%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ =

+4.8 (c = 1.7, H_2O, free acid). Ref.[33] $[\alpha]_D^{20}$ = –19.9 (c = 2.6, H_2O, pH 10, sodium salt). Ref.[27] $[\alpha]_D^{20}$ = +1.5 (H_2O). ^{1}H NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.51 (ψt, J = 9.2 Hz, 1 H, 5-H), 3.80 (ψt, J = 9.6 Hz, 1 H, 4-H), 3.98 (dψt, J = 2.1, J = 8.5 Hz, 1 H, 3-H), 4.05 (dψt, J = 2.1, J = 9.5 Hz, 1 H, 1-H), 4.21 (ψq, J = 9.1 Hz, 1 H, 6-H), 4.81 (dψt, J = 10, J = 2.1 Hz, 1 H, 2-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 73.6 (d, J = 6.1 Hz, C-4), 75.7 (m, C-1), 75.9 (s, C-5), 76.5 (dd, J = 5.6, J = 2.5 Hz, C-3), 77.0 (d, J = 6.1 Hz, C-2), 78.7 (ψt, J = 6.1 Hz, C-6) ppm. ^{31}P{^{1}H} NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 2.06 (PC-2), 2.44 (PC-3), 2.49 (PC-1), 3.49 (PC-6) ppm. HR-MS (ESI-neg, phosphoric acid 0.002%, Q-TOF): calcd. for $C_6H_{15}O_{18}P_4$ [M – H]$^+$ 498.9158; found 498.9209.

D-*myo*-Inositol 1,2,3,4-Tetrakisphosphate [(–)-12]: A solution of (–)-**25** was allowed to react under the conditions described for the preparation of (+)-**12** to give (–)-**12**. $[\alpha]_D^{20}$ = –6.6 (c = 3.95, H_2O, free acid). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**12**.

D-*myo*-Inositol 3,6-Bisphosphate [(–)-10]: A solution of sodium metaperiodate (110 mg, 0.75 mmol) and ruthenium trichloride trihydrate (10 mg, 0.03 mmol) in water (1.5 mL) was added to a vigorously stirred ice-cooled solution of (+)-**17** (200 mg, 0.3 mmol) in acetonitrile/dichloromethane (20 mL, 1:1). The stirring was continued until TLC showed the complete absence of starting material (approx. 10 min). The reaction was then quenched by addition of aqueous $Na_2S_2O_3$ (20%, 20 mL). The aqueous layer was separated and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed twice with brine and concentrated under reduced pressure to yield 3,6-bis-*O*-(di-*O*-benzylphospho)-*myo*-inositol bisphosphate (210 mg, 98%) as a colorless solid. M.p. 158 °C (racemic). ^{1}H NMR ([D$_6$]DMSO): δ = 3.37 (dψt, J = 9.2, J = 5.6 Hz, 1 H, 5-H), 3.59 (ddd, J = 2.2, J = 9.2, J = 6.6 Hz, 1 H, 4-H), 4.08 (ψs, 1 H, 2-H), 4.15 (dψt, J = 2.2, J = 9.1 Hz, 1 H, 3-H), 4.44 (ψq, J = 9.2 Hz, 1 H, 6-H), 5.20 (m, 8 H, Ph-CH_2), 5.39 (m, 4 H, OH), 7.35 (m, 20 H, Ph-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 68.1–68.4 (4 C, Ph-CH_2), 69.6 (CH), 70.9 (CH), 81.34 (CH), 71.2 (CH), 72.8 (CH), 78.4 (CH), 127.6–128.3 ($C_{arom.}$), 136.2–136.6 (C_{ipso}) ppm. ^{31}P{^{1}H} NMR ([D$_6$]DMSO): δ = 0.30, –0.63 ppm. Preactivated Pd/C (50 mg, Degussa RW 10) in ethanol/water (1:2, 30 mL) was added to a suspension of 3,6-bis-*O*-(di-*O*-benzylphospho)-*myo*-inositol (130 mg, 0.2 mmol) in ethanol (15 mL). The mixture was stirred at room temperature under H_2 overnight. The catalyst was filtered off, and the filtrate was concentrated under high vacuum and then lyophilized to give 60 mg (95%) of a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –1.4 (c = 1.8, H_2O, free acid). Ref.[28] $[\alpha]_D^{20}$ = –0.12 (c = 4, H_2O, tetracyclohexylammonium salt). ^{1}H NMR (D_2O, free acid): δ = 3.40 (ψt, J = 9.4 Hz, 1 H, 5-H), 3.62 (dd, J = 3.0, J = 9.7 Hz, 1 H, 1-H), 3.71 (ψt, J = 9.7 Hz, 1 H, 4-H), 3.98 (dψt, J = 2.8, J = 9.6 Hz, 1 H, 3-H), 4.14 (ψq, J = 9.3 Hz, 1 H, 6-H), 4.16 (ψs, 1 H, 2-H) ppm. ^{13}C NMR (D_2O): δ = 71.94 (d, J = 3.0 Hz, CH), 73.04 (2 C, CH), 74.79 (d, J = 2.0 Hz, CH), 78.72 (d, J = 6.1 Hz, CH), 81.02 (d, J = 7.1 Hz, CH) ppm. ^{31}P{^{1}H} NMR (D_2O, free acid): δ = 1.12, 0.37 ppm. HR-MS (ESI-neg., phosphoric acid 0.002%, H_2O/acetonitrile, Q-TOF): calcd. for $C_6H_{13}O_{12}P_2$ [M – H]$^-$ 338.9841; found 338.9883.

D-*myo*-Inositol 1,4-Bisphosphate [(+)-10]: A solution of (–)-**17** was allowed to react to give (+)-**10** under the conditions described for the preparation of (–)-**10**. $[\alpha]_D^{20}$ = +1.6 (c = 1.3, H_2O, free acid). Ref.[25] $[\alpha]_D^{20}$ = +3.6 (c = 0.5, H_2O, tetrapotassium salt). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**10**.

2,4,5-Tri-*O*-acetyl-3,6-di-*O*-benzyl-D-*myo*-inositol [(+)-28]: *p*-Toluenesulfonic acid monohydrate (0.34 g, 1.79 mmol) and triethyl orthoacetate (11.2 mL, 60 mmol) were added to a solution of (+)-**18** (5.0 g, 11.5 mmol) in anhydrous tetrahydrofuran (140 mL) under argon. The mixture was stirred vigorously for 24 h. The solvent was then removed under reduced pressure, and the residue was dried under high vacuum. The residue was dissolved in aqueous acetic acid (130 mL, 80%) and stirred at room temperature for 1 h. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2 (300 mL). The solution was washed with saturated aqueous $NaHCO_3$ (2 × 150 mL) and then with brine (50 mL). After evaporation of the dichloromethane, the crude product was purified by flash chromatography (cyclohexane/ethyl acetate, 3:2) to yield (+)-**28** (4.8 g, 85%) as a colorless solid. R_f = 0.18 (ethyl acetate/cyclohexane, 3:2). $[\alpha]_D^{20}$ = +52.0 (c = 1.44, $CHCl_3$). M.p. 55 °C. ^{1}H NMR ($CDCl_3$): δ = 1.97, 1.99, 2.17 (s, 3 × 3 H, CH_3), 2.65 (br. s, 1 H, OH), 3.52 (dd, J = 2.7, J = 9.7 Hz, 1 H, 3-H), 3.68 (dd, J = 2.7, J = 9.7 Hz, 1 H, 1-H), 3.84 (ψt, J = 9.7 Hz, 1 H, 6-H), 4.42 and 4.68 (2 × d, AB, J = 12.15 Hz, 2 × 1 H, Ph-CH_2), 4.72 [AB (ur), 2 H, Ph-CH_2], 5.08 (ψt, J = 9.7 Hz, 1 H, 5-H), 5.33 (ψt, J = 9.7, 1 H, 4-H), 5.70 (ψt, J = 2.70 Hz, 1 H, 2-H), 7.33 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.6, 20.7, 20.9 (CH_3), 68.9 (C-2), 70.1 (C-1), 71.8 (C-4), 73.0 (C-5), 71.7, 75.1 (Ph-CH_2), 74.8 (C-3), 79.4 (C-6), 127.6, 127.7, 127.8, 127.9, 128.3, 128.5 ($C_{arom.}$), 137.2, 137.9 (C_{ipso}), 169.9, 170.0, 170.4 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 486 (3) [M$^+$], 443 (2), 395 (46), 289 (67), 229 (13), 109 (50), 91 (100), 43 (83.85). IR (KBr): $\tilde{\nu}$ = 3500 (m), 3060, 3040 (m), 2930, 2890 (m), 1750 (s), 1370 (m), 1230 (s), 1070 (m), 750, 700 (m) cm^{-1}. $C_{26}H_{30}O_9$ (486.5): calcd. C 64.19; H 6.22; found C 64.31, H 6.20.

2,5,6-Tri-*O*-acetyl-1,4-di-*O*-benzyl-D-*myo*-inositol [(–)-28]: A solution of (–)-**18** was allowed to react under the conditions used for the preparation of (+)-**28** to give (–)-**28**. $[\alpha]_D^{20}$ = –53.3 (c = 1.74 in $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**28**.

2,4,5-Tri-*O*-acetyl-3,6-di-*O*-benzyl-1-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-29]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (180 mg, 0.7 mmol) was added to a suspension of (+)-**28** (300 mg, 0.62 mmol) and 1*H*-tetrazole (130 mg, 1.8 mmol) in anhydrous dichloromethane (20 mL), and the solution was stirred at room temperature for 12 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (690 mg, 2.8 mmol) in dichloromethane (10 mL, dried with Na_2SO_4) was added. The solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The reaction mixture was diluted with dichloromethane (50 mL) and washed consecutively with aqueous sodium sulfite (20%, 2 × 50 mL), saturated $NaHCO_3$ (3 × 50 mL), and then with brine. After evaporation of the solvent, the resulting colorless foam was purified by flash chromatography (ethyl acetate/cyclohexane, 1:1) to yield (+)-**29** (250 mg, 60%) as a colorless foam. R_f = 0.20 (ethyl acetate/cyclohexane, 1:1). $[\alpha]_D^{20}$ = +44.9 (c = 0.78, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.91, 1.97, 2.20 (3 × s, 3 × 3 H, CH_3), 3.56 (dd, J = 2.8, J = 9.9 Hz, 1 H, 3-H), 4.03 (ψt, J = 9.9 Hz, 1 H, 6-H), 4.40 (d, AB, J = 12.2 Hz, 1 H, Ph-CH_2), 4.63 (d, AB, J = 11.2 Hz, 1 H, Ph-CH_2), 4.62 (dψt, J = 3.0, J = 9.0 Hz, 1 H, 1-H), 4.71 (d, AB, J = 12.2 Hz, 1 H, Ph-CH_2), 4.82 (d, AB, J = 12.2 Hz, 1 H, Ph-CH_2), 4.99–5.28 [m, 4 H, $(CH_2)_2C_6H_4$], 5.09 (ψt, J = 9.9 Hz, 1 H, 5-H), 5.30 (ψt, J = 9.9 Hz, 1 H, 4-H), 5.96 (ψt, J = 2.8 Hz, 1 H, 2-H), 7.17–7.28 (m, 14 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.5, 20.6, 20.9 (3 × CH_3), 68.1 (C-2), 68.4 [ψt, J = 6.5 Hz, $(CH_2)_2C_6H_4$], 71.0 (C-4), 71.6 ($PhCH_2$), 72.2 (C-5), 74.6 (C-3), 75.2 ($PhCH_2$), 76.0 (d, J = 5.7 Hz, C-1), 77.9 (d, J = 5.7 Hz, C-6), 127.7, 127.85, 127.91, 128.3, 128.4, 128.7, 128.8, 129.0, 129.1 ($C_{arom.}$), 134.97, 135.01, 137.1, 137.8 (C_{ipso}), 169.4, 169.6, 170.0 (C=O) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 1.05 (PC-1) ppm. MS

(EI, 70 eV): *m/z* (%) = 668 (2) [M^+], 577 (2), 535 (3), 471 (6.1) [M^+ + H – Bn – BnO], 291 (21), 243 (30), 201 (72.9), 199 (39.4), 183 (37), 136 (41), 109 (37), 104 (100), 43 (79). IR (KBr): $\tilde{\nu}$ = 3064 (w), 3031 (w), 2934 (w), 1751 (s), 1371 (s), 1223 (s, br), 1016 (s, br), 947 (m), 869 (m), 753 (m), 735 (m), 698 (m) cm^{-1}. HR-MS (ESI-pos.): calcd. for $C_{34}H_{37}O_{12}PNa$ [M + Na]$^+$ 691.192; found 691.192.

2,5,6-Tri-*O*-acetyl-1,4-di-*O*-benzyl-3-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-29]: A solution of (–)-**28** was allowed to react under the conditions described for the preparation of (+)-**29** to give (–)-**29**. $[\alpha]_D^{20}$ = –49.7 (*c* = 0.6, $CHCl_3$). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**29**.

D-*myo*-Inositol 1-Phosphate [(–)-30]: Pd/C (30 mg) was added to a suspension of (+)-**29** (50 mg, 74 μmol) in ethanol/water (1:1, 30 mL) and the mixture was stirred at room temperature under H_2 overnight. The catalyst was then filtered off and the filtrate was concentrated under high vacuum. The residue was dissolved in ice-cooled 0.25 M aqueous NaOH (10 mL) and stirred at 0 °C for 4 h. The solution was neutralized by addition of ion exchanger (H^+ form, Dowex 50-X), filtered, and the resin washed with water. The filtrate was lyophilized to yield 20 mg (99%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –6.1 [*c* = 1.4, H_2O, pH = 2 (free acid)]. Ref.[19] $[\alpha]_D^{20}$ = –9.8 (*c* = 3, H_2O, pH = 2), $[\alpha]_D^{20}$ = –2.6 [*c* = 1.2, H_2O, pH adjusted to 6 (NH_4OH)], $[\alpha]_D^{20}$ = +4.4 [*c* = 1.2, H_2O, pH adjusted to 9 (NH_4OH)]. Ref.[19] $[\alpha]_D^{20}$ = +3.4 [*c* = 3, H_2O, pH adjusted to 9 (cyclohexylamine)]. Ref.[29] $[\alpha]_D^{20}$ = +3.5 (*c* = 1, H_2O, sodium salt, pH = 9). ^1H NMR (D_2O, free acid): δ = 3.28 (ψt, *J* = 8.1 Hz, 1 H, 5-H), 3.51 (dd, *J* = 2.8, *J* = 10.2 Hz, 1 H, 3-H), 3.60 (ψt, *J* = 9.9 Hz, 1 H, 4-H), 3.71 (ψt, *J* = 9.2 Hz, 1 H, 6-H), 3.95 (dψt, *J* = 2.8, *J* = 9.4 Hz, 1 H, 1-H), 4.21 (ψt, *J* = 2.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR (D_2O, free acid): δ = 73.0 (s, C-3), 73.4 (s, C-2), 73.6 (d, *J* = 6.1 Hz, C-6), 74.5 (s, C-4), 76.1 (s, C-5), 78.5 (d, *J* = 5.1 Hz, C-1) ppm. $^{31}P\{^1H\}$ NMR (D_2O, free acid): δ = 0.96 (PC-1) ppm. HR-MS (ESI-neg, phosphoric acid, Q-TOF): calcd. for $C_6H_{12}O_9P$ [M – H]$^-$ 259.0249; found 259.0219.

D-*myo*-Inositol 3-Phosphate [(+)-30]: A solution of (–)-**29** was allowed to react under the conditions described for the preparation of (–)-**30** to give (+)-**30**. $[\alpha]_D^{20}$ = +3.4 [*c* = 1.1, H_2O, pH adjusted to 6 (NH_4OH)]. $[\alpha]_D^{20}$ = –4.5 [*c* = 0.6, H_2O, pH adjusted to 9 (NH_4OH)]. Ref.[30] $[\alpha]_D^{20}$ = –3.5° (H_2O, sodium salt, pH = 9). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**30**.

2-*O*-Acetyl-3,6-di-*O*-benzyl-D-*myo*-inositol [(–)-31]: *p*-Toluenesulfonic acid monohydrate (15 mg) and triethyl orthoacetate (0.3 mL, 1.6 mmol) were added to a solution of the tetraol (+)-**22** (300 mg, 0.83 mmol) in anhydrous tetrahydrofuran (20 mL) under argon and the mixture was stirred vigorously for 24 h. The solvent was removed under reduced pressure, and the residue was dried under high vacuum. The residue was dissolved in aqueous acetic acid (10 mL, 80%) and stirred at room temperature for 1 h. The organic phase was evaporated, and the residue was dissolved in ethyl acetate (100 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (2×20 mL) and then with brine (20 mL). Evaporation of the solvent yielded (–)-**31** (320 mg, 95%) as a colorless solid. $[\alpha]_D^{20}$ = –20.5 (*c* = 4.5, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 2.99 (br., 1 H, OH), 2.58 (br., 1 H, OH), 3.30 (dd, *J* = 9.9, *J* = 2.8 Hz, 1 H, 3-H), 3.50 (ψt, *J* = 9.2 Hz, 1 H, 5-H), 3.60 (dd, *J* = 9.7, *J* = 3.1 Hz, 1 H, 1-H), 3.65 (ψt, *J* = 8.9 Hz, 1 H, 6-H), 3.81 (ψt, *J* = 9.7 Hz, 1 H, 4-H), 4.43 and 4.78 (2×d, AB, *J* = 10.7 Hz, 2×1 H, Ph-CH_2), 4.80 and 5.00 (2×d, AB, *J* = 11.7 Hz, 2×1 H, Ph-CH_2), 5.70 (ψt, *J* = 2.5 Hz, 1 H, 2-H), 7.26–7.40 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.9 (CH_3), 69.0 (C-2), 70.2 (C-1), 71.8 (Ph-CH_2), 72.7 (C-4), 74.7 (C-5), 75.1 (Ph-CH_2), 77.5 (C-3), 81.1 (C-6), 127.9, 128.0, 128.1, 128.1, 128.5 (C_{arom}), 137.2, 138.4 (C_{ipso}), 170.6 (C=O) ppm. MS (70 eV): *m/z* (%) = 402 (2), [M^+], 311 (45) [M^+ – Bn], 310 (29), 205 (47), 127 (12), 109 (27), 107 (31), 99 (15), 92 (33), 91 (100), 86 (25), 81 (10), 73 (12), 65 (15), 43 (88). HR-MS (ESI-pos): calcd. for $C_{22}H_{27}O_7$ [M + H]$^+$ 403.1752; found 403.1756.

2-*O*-Acetyl-1,4-di-*O*-benzyl-D-*myo*-inositol [(+)-31]: A solution of (–)-**22** was allowed to react to give (+)-**31** under the conditions described for the preparation of (–)-**31**. $[\alpha]_D^{20}$ = +19.8 (*c* = 5.5, $CHCl_3$). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**31**.

2-*O*-Acetyl-3,6-di-*O*-benzyl-1,4,5-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-32]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (1.13 g, 4.7 mmol) was added to a suspension of 2-*O*-acetyl-3,6-di-*O*-benzyl-*myo*-inositol [(–)-**31**] (315 mg, 0.8 mmol) and 1*H*-tetrazole (660 mg, 9.4 mmol) in anhydrous dichloromethane (30 mL), and the solution was stirred at room temperature for 12 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (2.3 g, 9.4 mmol) in dichloromethane (20 mL, dried with Na_2SO_4) was added. The solution was allowed to warm to room temperature and the stirring was continued for 1 h. The reaction mixture was diluted with dichloromethane (200 mL) and washed consecutively with aqueous sodium sulfite (20%, 2×100 mL), saturated $NaHCO_3$ (3×150 mL), and then with brine. After evaporation of the solvent, the residue was purified by flash chromatography (ethyl acetate/cyclohexane, 5:1) to yield (–)-**32** (646 mg, 87%) as a colorless foam. $[\alpha]_D^{20}$ = –5.3 (*c* = 1.8, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 2.16 (s, 3 H, CH_3), 3.69 (dd, *J* = 2.8, *J* = 9.9 Hz, 1 H, 3-H), 4.07 (ψt, *J* = 9.7 Hz, 1 H, 6-H), 4.48 (d, AB, *J* = 11.4 Hz, 1 H, Ph-CH_2), 4.71 (m, 1 H, 1-H), 4.80–5.27 [m, 15 H, CH_2, $(CH_2)_2C_6H_4$, and other ring protons], 5.45–5.57 (m, 2 H, CH_2), 6.02 (ψt, *J* = 2.5 Hz, 1 H, 2-H), 7.06–7.49 (m, 22 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.7 (CH_3), 67.6 (CH), 68.0 (d, *J* = 6.7 Hz, CH_2OP), 68.4 (dd, *J* = 5.6, *J* = 10.0 Hz, 2×C, CH_2, CH_2OP), 68.8 (dd, *J* = 7.5, *J* = 1.5 Hz, CH_2, CH_2OP), 72.0 (Ph-CH_2), 74.8 (Ph-CH_2), 75.39 (CH), 75.43 (CH), 77.6 (t, *J* = 4.3 Hz, CH), 77.9 (dd, *J* = 6.2, *J* = 2.1 Hz, CH), 78.8 (m, CH), 126.9–129.8 ($C_{arom.}$), 132.2–137.6 (C_{ipso}), 169.2 (C=O) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 0.00, 0.79, 1.20 ppm. $C_{46}H_{47}O_{16}P_3$ (948.8): calcd. C 58.23, H 4.99; found C 57.92, H 4.95.

2-*O*-Acetyl-1,4-di-*O*-benzyl-3,5,6-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-32]: A solution of (+)-**31** was allowed to react under the conditions described for the preparation of (–)-**32** to give (+)-**32**. $[\alpha]_D^{20}$ = +5.0 (*c* = 1.6, CH_2Cl_2). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**32**.

D-*myo*-Inositol 1,4,5-Trisphosphate [(–)-1]: Deprotection (hydrogenolysis and deacetylation) of (–)-**32** (150 mg, 0.16 mmol) was carried out as described for the preparation of (–)-**30** to give (–)-**1** (66 mg, 98%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –9.2 (*c* = 1.4, H_2O, free acid). Ref.[31] $[\alpha]_D^{20}$ = –13.3 (*c* = 1, H_2O). Ref.[32] $[\alpha]_D^{20}$ = –10.3 (*c* = 1.8, H_2O, ammonium salt, pH = 6.73). ^1H NMR [D_2O, pH adjusted to 8.0 (ND_4OD)]: δ = 3.66 (dd, *J* = 9.7, *J* = 2.5 Hz, 1 H, 3-H), 3.87 (m, 3 H, 1-H, 6-H, 5-H), 4.12 (ψq, *J* = 8.7 Hz, 1 H, 4-H), 4.31 (ψt, *J* = 2.1 Hz, 1 H, 2-H) ppm. ^{13}C NMR [$CDCl_3$, pH adjusted to 8.0 (ND_4OD)]: δ = 72.8 (s, C-2), 73.8 (s, C-3), 74.6 (d, *J* = 7.0 Hz, CH), 76.7 (d, *J* = 5.7 Hz, CH), 77.3 (t, *J* = 5.4 Hz, C-4), 79.5 (t, *J* = 6.4 Hz, CH) ppm. $^{31}P\{^1H\}$ NMR [$CDCl_3$, pH adjusted to 8.0 (ND_4OD)]: δ = 4.16 + 5.55 (PC-1 and PC-5), 5.88 (PC-4) ppm. HR-MS (ESI-neg., phosphoric acid

0.002%, H_2O/acetonitrile, Q-TOF): calcd. for $C_6H_{14}O_{15}P_3$ $[M - H]^-$ 418.9535; 418.9546.

D-*myo*-Inositol 3,5,6-Trisphosphate [(+)-1]: A solution of (+)-**32** was allowed to react under the conditions described for the preparation of (–)-**1** to give (+)-**1**. $[\alpha]_D^{20}$ = +9.4 (*c* = 1.3, H_2O, free acid). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**1**.

***exo*-3,6-Di-*O*-benzyl-1,2-benzylidene-D-*myo*-inositol [(–)-33] and *endo*-3,6-Di-*O*-benzyl-1,2-benzylidene-D-*myo*-inositol [(+)-34]:** 3,6-Di-*O*-benzyl-*myo*-inositol [(+)-**22**; 1 g] and a catalytic amount of *p*-toluenesulfonic acid were suspended in 20 mL of dry tetrahydrofuran. Benzaldehyde dimethylacetal (0.63 mL, 1.5 equiv.) was added and the reaction mixture was stirred overnight. The mixture was diluted with diethyl ether, extracted with sodium hydrogencarbonate and brine, dried with sodium sulfate, and the solvents were evaporated. The crude product was purified by column chromatography (hexane/ethyl acetate) to give *exo*-3,6-di-*O*-benzyl-1,2-benzylidene-*myo*-inositol [(–)-**33**; 450 mg, 36%] and *endo*-3,6-di-*O*-benzyl-1,2-benzylidene-*myo*-inositol [(+)-**34**; 410 mg, 33%] along with unconverted starting material (240 mg). **(–)-33:** $[\alpha]_D^{20}$ = –15.8 (*c* = 0.4, acetone). ^1H NMR ([D$_6$]DMSO): δ = 3.28 (m, 1 H, under H_2O), 3.58 (m, 3 H), 4.33 (dd, *J* = 7.1, *J* = 5.1 Hz, 1 H), 4.38 (dd, *J* = 5.6, *J* = 3.1 Hz, 1 H), 4.60 and 4.68 (2×d, AB, *J* = 12.2 Hz, 2×1 H, $PhCH_2$), 4.77 and 4.80 (2×d, AB, *J* = 12.0 Hz, 2×1 H, CH_2Ph), 5.05 (d, *J* = 5.1 Hz, 1 H, OH), 5.07 (d, *J* = 4.6 Hz, 1 H, OH), 5.99 (s, 1 H, acetal-H) 7.19–7.40 (m, 15 H, Ph-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 71.4 (CH_2), 71.9 (CH), 72.7 (CH_2), 73.5 (CH), 74.2 (CH), 78.2 (CH), 79.4 (CH), 79.7 (CH), 102.2 (acetal-CH), 126.2-128.8 ($C_{arom.}$), 138.9, 139.1, 139.3 (C_{ipso}) ppm. IR (KBr): $\tilde{\nu}$ = 3484 (s), 3062 (m), 3030 (m), 2897 (m), 1453 (m), 1115 (s), 1075 (s), 1039 (s), 1025 (s), 1000 (s), 734 (m), 695 (s), 631 (s) cm^{-1}. $C_{27}H_{28}O_6$ (448.5): calcd. C 72.30, H 6.29; found C 72.31, H 6.10. **(+)-34:** $[\alpha]_D^{20}$ = +8.2 (*c* = 0.36, acetone). ^1H NMR ([D$_6$]-DMSO): δ = 3.28 (m, 1 H, under H_2O, 5-H), 3.49 (dd, *J* = 6.6, *J* = 9.7 Hz, 1 H, 6-H), 3.64 (m, 2 H, 4-H, 3-H), 4.21 (ψt, *J* = 6.6 Hz, 1 H, 1-H), 4.47 (dd, *J* = 6.1, *J* = 3.05 Hz, 1 H, 2-H), 4.61–4.72 (m, 2×2 H, 2×$PhCH_2$), 4.99 (d, *J* = 5.1 Hz, 1 H, OH), 5.07 (d, *J* = 4.1 Hz, 1 H, OH), 5.82 (s, 1 H, acetal-H) 7.18–7.44 (m, 15 H, Ph-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 71.5 (CH_2), 72.0 (C-4), 72.3 (CH_2), 73.8 (C-5), 76.2 (C-2), 77.5 (C-3), 78.2 (C-1), 83.0 (C-6), 103.2 (acetal-CH), 126.7, 127.0, 127.2, 127.4, 127.9, 128.0, 128.1, 129.1 ($C_{arom.}$), 137.6, 138.8, 139.9 (C_{ipso}) ppm. IR (KBr): $\tilde{\nu}$ = 3423 (s), 3063 (m), 3031 (m), 2880 (m), 1454 (m), 1089 (s), 1066 (s), 1000 (s), 739 (m), 698 (s) cm^{-1}. $C_{27}H_{28}O_6$ (448.5): calcd. C 72.30, H 6.29; found C 72.50, H 6.16.

***exo*-4,5-Di-*O*-acetyl-3,6-di-*O*-benzyl-1,2-benzylidene-D-*myo*-inositol (49):** For an unambiguous assignment of the new stereogenic center of (–)-**33**, it was acetylated and the product was analyzed by NMR spectroscopy. Thus, (–)-**33** (100 mg, 0.22 mmol) was dissolved in a cooled mixture of pyridine (7 mL) and acetic anhydride (7 mL) and the mixture was stirred at room temperature for 12 h. Evaporation of the solvent under high vacuum yielded **49** (120 g, 100%) as a colorless solid. The relative configuration at the new stereogenic center was confirmed by NOESY NMR, which showed only one strong cross-peak between the acetal-H and 6-H. ^1H NMR ($CDCl_3$): δ = 2.05, 2.06 (2×s, 2×3 H, CH_3), 3.85 (dd, *J* = 7.6, *J* = 3.0 Hz, 1 H, 3-H), 4.03 (dd, *J* = 9.3, *J* = 6.4 Hz, 1 H, 6-H), 4.67 (m, 2 H, 2-H, 1-H), 4.73 (s, 2 H, $PhCH_2$), 4.76, 4.89 (2×d, AB, *J* = 12.0 Hz, 2×1 H, $PhCH_2$), 5.08 (dd, *J* = 9.2, *J* = 7.6 Hz, 1 H, 5-H), 5.70 (ψt, *J* = 7.6 Hz, 1 H, 4-H), 6.21 (s, 1 H, acetal-H), 7.26–7.48 (m, 15 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.7, 20.7 (CH_3), 71.6 (C-4), 72.5 (C-5 and $PhCH_2$), 73.1 ($PhCH_2$), 73.9 (C-2 or C-1), 75.7 (C-3), 77.03 (C-6), 79.2 (C-2 or C-1), 103.9 (acetal-CH), 126.1, 127.5, 127.6, 127.7, 127.8, 128.2, 128.3, 128.35, 129.0 ($C_{arom.}$), 137.6, 137.9, 138.4 (C_{ipso}), 169.6, 169.9 (CO) ppm.

1,3,6-Tri-*O*-benzyl-D-*myo*-inositol [(–)-35] and 2,3,6-Tri-*O*-benzyl-D-*myo*-inositol [(+)-36]: A solution of 1 M BH_3 in THF (7 mL) was added to a dry flask containing (–)-**33** (240 mg, 0.53 mmol). The mixture was stirred for 10 min, then a solution of 1 M Bu_2BOTf in dichloromethane (0.5 mL) was added dropwise. The reaction mixture was stirred for 2 h, then triethylamine (0.3 mL) was added to the reaction flask, followed by careful addition of methanol until formation of hydrogen had ceased. The mixture was co-distilled with methanol three times and then subjected to column chromatography (cyclohexane/ethyl acetate, 1:2) to give 114 mg (47%) of 2,3,6-tri-*O*-benzyl-D-*myo*-inositol [(+)-**36**] and 98 mg (40%) of 1,3,6-tri-*O*-benzyl-*myo*-inositol [(–)-**35**]. The use of (+)-**34** (240 mg) gave exclusively 2,3,6-tri-*O*-benzyl-*myo*-inositol [(+)-**36**] (180 mg, 75%). **(–)-35:** $[\alpha]_D^{20}$ = –11.0 (*c* = 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.49 (br. s, 1 H, OH), 2.64 (br. s, 2 H, OH), 3.24 (dd, *J* = 9.4, *J* = 2.8 Hz, 1 H, 3-H), 3.38 (dd, *J* = 9.4, *J* = 2.8 Hz, 1 H, 1-H), 3.42 (ψt, *J* = 9.4, 1 H, 5-H), 3.84 (ψt, *J* = 9.4, 1 H, 6-H), 3.98 (ψt, *J* = 9.4, 1 H, 4-H), 4.25 (ψt, *J* = 2.8, 1 H, 2-H), 4.68 (m, 4 H, $PhCH_2$), 4.81 and 4.94 (2×d, AB, *J* = 11.2 Hz, 2×1 H, CH_2Ph), 7.27–7.40 (m, 15 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 67.0 (C-2), 71.9 (C-4), 72.2 ($PhCH_2$), 72.4 ($PhCH_2$), 74.3 (C-5), 75.4 ($PhCH_2$), 79.0 (C-3), 79.7 (C-1), 80.4 (C-6), 127.7, 127.8, 127.9, 127.91, 127.96, 128.4, 128.4, 128.5 ($C_{arom.}$), 137.7, 137.8, 138.7 (C_{ipso}) ppm. IR (KBr): $\tilde{\nu}$ = 3404 (s), 3064 (m), 3028 (m), 2938 (m), 2867 (m), 1496 (m), 1454 (s), 1370 (s), 1093 (s), 1057 (s), 740 (s), 697 (m) cm^{-1}. $C_{27}H_{30}O_6$ (450.5); calcd. C 71.98, H 6.71; found C 72.13, H 6.75. **(+)-36:** $[\alpha]_D^{20}$ = +7.2 (*c* = 0.9, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.35 (br. s, 1 H, OH), 2.66 (br. s, 2 H, OH), 3.30 (dd, *J* = 9.7, *J* = 2.0 Hz, 1 H, 3-H), 3.48 (ψt, *J* = 9.2, 1 H, 5-H), 3.54 (d, *J* = 9.2 Hz, 1 H, 1-H), 3.69 (ψt, *J* = 9.2, 1 H, 6-H), 4.02 (ψt, *J* = 9.4, 1 H, 4-H), 4.09 (ψt, *J* = 2.3, 1 H, 2-H), 4.60 and 4.73 (2×d, AB, *J* = 11.7 Hz, 2×1 H, CH_2Ph), 4.70 and 4.90 (2×d, AB, *J* = 11.7 Hz, 2×1 H, CH_2Ph), 4.84 and 4.94 (2×d, AB, *J* = 11.2 Hz, 2×1 H, CH_2Ph), 7.25–7.42 (m, 15 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 70.6 ($PhCH_2$), 72.5 (C-1 or C-4), 72.6 (C-4 or C-1), 74.8 ($PhCH_2$), 74.9 (C-5), 75.0 ($PhCH_2$), 76.4 (C-2), 80.2 (C-3), 81.7 (C-6), 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 128.6 ($C_{arom.}$), 137.7, 138.5, 138.6 (C_{ipso}) ppm. IR (KBr): $\tilde{\nu}$ = 3437 (s), 3061 (m), 3029 (m), 2951 (m), 2865 (m), 1452 (m), 1363 (s), 1114 (s), 1066 (s), 1027 (s), 756 (s), 701 (m) cm^{-1}. $C_{27}H_{30}O_6$ (450.5): calcd. C 71.98, H 6.71; found C 72.08, H 6.82.

1,4,5-Tri-*O*-acetyl-3,6-di-*O*-benzyl-D-*myo*-inositol [(+)-37]: (+)-**28** (500 mg, 1 mmol) and powdered molecular sieves (3 Å) (200 mg) were dissolved/suspended (20 mL) in anhydrous diethyl ether. A freshly prepared solution of 0.2 M trimethylsilyl triflate (0.5 mL) in anhydrous diethyl ether (with powdered molecular sieves) was added dropwise from a syringe. The mixture was stirred at room temperature for 24 h, then a second, freshly prepared solution of 0.2 M trimethylsilyl triflate (0.5 mL) in anhydrous diethyl ether (with powdered molecular sieves) was added dropwise, and stirring was continued for another 24 h. For workup, $NaHCO_3$ (500 mg) was added, the reaction solution was filtered through a small glass frit with silica gel, and the silica gel was washed with ethyl acetate. The filtrate was concentrated under reduced pressure to give (+)-**37** (500 mg, 100%) as a colorless solid. $[\alpha]_D^{20}$ = +56.7 (*c* = 3.05, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 1.92, 1.98, 2.07 (3×s, 3×3 H, CH_3), 3.58 (dd, *J* = 2.5, *J* = 9.7 Hz, 1 H, 3-H), 4.14 (ψt, *J* = 9.9 Hz, 1 H, 6-H), 4.34 (ψt, *J* = 2.5 Hz, 1 H, 2-H), 4.53, 4.67 (2×d, AB, *J* = 12.2 Hz, 2×1 H, Ph-CH_2), 4.63, 4.70 (2×d, AB, *J* = 12.1 Hz, 2×1 H, Ph-CH_2), 4.88 (dd, *J* = 3.1, *J* = 10.2 Hz, 1 H, 1-H), 5.07

(ψt, *J* = 9.9 Hz, 1 H, 5-H), 5.43 (ψt, *J* = 9.9 Hz, 1 H, 4-H), 7.2–7.4 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.6, 20.7, 20.9 (3×CH_3), 67.4 (C-2), 71.4 (C-4), 72.6 ($PhCH_2$), 72.6 (C-5), 73.0 (C-1), 75.3 ($PhCH_2$), 76.8 (C-6), 77.1 (C-3), 127.5, 127.7, 127.72, 127.8, 128.2, 128.4, 128.6 ($C_{arom.}$), 137.0, 138.1 (C_{ipso}), 169.9, 170.0, 170.2 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 443 (3), 395 (60), 289 (100), 229 (25), 169 (26), 127 (60), 109 (99), 91 (100), 43 (99). IR (KBr): ṽ = 3461 (m), 3068, 3032 (w), 2979, 2941, 2900 (w), 1748 (s), 1367 (m), 1226 (s), 1058 (s), 1030 (s), 929 (m), 741 (m) cm^{-1}. $C_{26}H_{30}O_9$ (486.5): calcd. C 64.19, H 6.22; found C 64.31, H 6.20.

3,5,6-Tri-*O*-acetyl-1,4-di-*O*-benzyl-D-*myo*-inositol [(–)-37]: A solution of (–)-**28** was allowed to react under the conditions used for the preparation of (+)-**37** to give (–)-**37**. $[\alpha]_D^{20}$ = –61.3 (*c* = 3.1, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**37**.

1,4,5-Tri-*O*-acetyl-3,6-di-*O*-benzyl-2-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-38]: The alcohol (+)-**37** (300 mg, 0.62 mmol) was phosphorylated as described for the preparation of (+)-**29** to give (+)-**38** (250 mg, 60%) as a colorless foam. R_f = 0.22 (ethyl acetate/cyclohexane, 1:1). $[\alpha]_D^{20}$ = +40.8 (*c* = 0. 9, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.94, 2.02, 2.14 (3×s, 3×3 H, CH_3), 3.65 (dψt, *J* = 10.0, *J* = 2.4 Hz, 1 H, 3-H), 4.00 (ψt, *J* = 9.7 Hz, 1 H, 6-H), 4.50, 4.63, 4.73, 4.79 (4×d, AB, *J* = 11.7 Hz, 4×1 H, Ph-CH_2), 4.74–4.84 [m, 1 H, $(CH_2)_2$-C_6H_4], 4.88 (dψt, *J* = 10.3, *J* = 2.3 Hz, 1 H, 1-H), 5.12 (ψt, *J* = 9.9 Hz, 1 H, 5-H), 5.21 [d, AB, *J* = 15.7 Hz, 2 H, $(CH_2)_2C_6H_4$], 5.28–5.36 [m, 1 H, $(CH_2)_2C_6H_4$], 5.28 (dψt, *J* = 9.5 *J* = 2.5 Hz, 1 H, 2-H), 5.39 (ψt, *J* = 10.2 Hz, 1 H, 4-H), 7.15–7.37 (m, 14 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.6, 20.7, 20.8 (3×CH_3), 68.8 [dd, *J* = 6.6, *J* = 14.7 Hz, $(CH_2)_2C_6H_4$], 70.8 (C-4), 71.5 (d, *J* = 3.0 Hz, C-1), 72.1 ($PhCH_2$), 72.4 (C-5), 73.0 (d, *J* = 6.1 Hz, C-2), 75.0 (d, *J* = 3.1 Hz, C-3), 75.1 ($PhCH_2$), 76.5 (C-6), 127.6, 127.79, 127.82, 128.0, 128.37, 128.43, 128.6, 128.7, 128.8, 129.0, 129.1 ($C_{arom.}$), 134.6, 135.3, 136.9, 137.8 (C_{ipso}), 169.7, 170.0, 170.2 (C=O) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 0.33 (PC-2) ppm. MS (EI, 70 eV): *m*/*z* (%) = 668 (2) [M$^+$], 471 (9), 291 (25), 243 (34), 201 (100), 104 (97), 43 (78). IR (KBr): ṽ = 3075 (w), 3031 (w), 2941, 2900 (w), 1748 (s), 1367 (m), 1288 (m), 1225 (s), 1058 (s), 1031 (s, br), 854 (w), 829 (w), 735 (w), 697 (w) cm^{-1}. HR-MS (ESI-pos.): calcd. for $C_{34}H_{37}O_{12}PNa$ [M + Na]$^+$ 691.193; found 691.192.

***myo*-Inositol 2-Phosphate (39):** Deprotection (hydrogenolysis and deacetylation) of (+)-**38** (50 mg, 74 μmol) was carried out as described for the preparation of (–)-**30**. ^{1}H NMR (D_2O, pH = 3): δ = 3.24 (ψt, *J* = 9.2 Hz, 1 H, 5-H), 3.53 (dd, *J* = 2.3, *J* = 9.2 Hz, 2 H, 1-H, 3-H), 3.63 (ψt, *J* = 9.7 Hz, 2 H, 4-H, 6-H), 4.55 (dψt, *J* = 2.3, *J* = 8.1 Hz, 1 H, 2-H) ppm. ^{13}C NMR (D_2O, pH = 3): δ = 73.0 (d, *J* = 2.9 Hz, C-1, C-3), 74.8 (s, C-4, C-6), 76.6 (s, C-5), 80.3 (d, *J* = 5.7 Hz, C-2) ppm. ^{31}P{^{1}H} NMR (D_2O, pH = 3): δ = 1.96 (PC-2) ppm. HR-MS (ESI-neg, phosphoric acid, Q-TOF): calcd. for $C_6H_{12}O_9P$ [M – H]$^-$ 259.0242; found 259.0219.

1,4,5-Tri-*O*-acetyl-D-*myo*-inositol [(+)-40]: Preactivated Pd/C (100 mg, Degussa RW 10) was added to a suspension of (+)-**37** (400 mg, 0.82 mmol) in ethyl acetate/ethanol (2:1, 20 mL) and the mixture was stirred at room temperature under H_2 for 4 h (TLC control). The catalyst was filtered off and washed with ethyl acetate/ethanol. Concentration of the filtrate under reduced pressure gave (+)-**40** (250 mg, 99%) as an oily solid. $[\alpha]_D^{20}$ = +13.5 (*c* = 0.5, acetone). ^{1}H NMR ($CDCl_3$/[D_4]MeOH, 6:1): δ = 2.02 (s, 6 H, 2×CH_3), 2.10 (s, 3 H, CH_3), 3.64 (dd, *J* = 2.5, *J* = 10.2 Hz, 1 H, 3-H), 3.96–4.04 (m, 4 H, 3×OH, 6-H), 4.08 (ψt, *J* = 2.8 Hz, 1 H, 2-H), 4.69 (dd, *J* = 2.8, *J* = 10.4 Hz, 1 H, 1-H), 4.90 (ψt, *J* = 9.7 Hz, 1 H, 5-H), 5.22 (ψt, *J* = 9.9 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$/[D_4]MeOH, 6:1): δ = 20.6 (CH_3), 20.7 (2×CH_3), 68.7 (C-6), 70.09 (C-3), 70.10 (C-2), 72.8 (C-4), 73.6 (C-5), 73.8 (C-1), 171.1, 171.3, 171.4 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 289 (2) [M$^+$ – OH], 168 (8), 144 (11), 126 (37), 115 (62), 73 (74), 43 (100). IR (KBr): ṽ = 3426 (s, br), 2938 (w), 1731 (s), 1369 (s), 1243 (s, br), 1043 (s), 919 (m), 734 (m), 710 (m) cm^{-1}. $C_{12}H_{18}O_9$ (306.3): calcd. C 47.06, H 5.92; found C 47.00, H 5.79.

3,5,6-Tri-*O*-acetyl-D-*myo*-inositol [(–)-40]: A solution of (–)-**37** was allowed to react under the conditions described for the preparation of (+)-**40** to give (–)-**40**. $[\alpha]_D^{20}$ = –10.5 (*c* = 0.41, acetone). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**40**.

1,4,5-Tri-*O*-acetyl-2,3,6-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-41]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (300 mg, 1.2 mmol) was added to a suspension of (+)-**40** (100 mg, 0.33 mmol) and 1*H*-tetrazole (140 mg, 2 mmol) in anhydrous dichloromethane (10 mL), and the solution was stirred at room temperature for 12 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (800 mg, 3.3 mmol) in dichloromethane (10 mL, dried with Na_2SO_4) was added. The solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The product was worked up as described for (+)-**29**. Purification by flash chromatography (ethyl acetate) yielded pure (+)-**41** (140 mg, 53%) as a colorless foam. R_f = 0.20 (ethyl acetate). $[\alpha]_D^{20}$ = +14.2 (*c* = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 2.14, 2.16, 2.24 (3×s, 3×3 H, CH_3), 4.88 (ψtψt, *J* = 2.3, *J* = 9.9 Hz, 1 H, 3-H), 5.28 (dψt, *J* = 9.7, *J* = 2.5 Hz, 1 H, 2-H), 5.50 (ψt, *J* = 10.2 Hz, 1 H, 4-H), 4.94–5.62 [m, 15 H, 3×$(CH_2)_2C_6H_4$, 1-H, 5-H, 6-H], 7.22–7.40 (m, 12 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 68.7–69.2 [m, 3×$(CH_2)_2$-C_6H_4], 68.6, 69.3, 70.2, 73.6, 75.9, 75.9 (C-1 to C-6), 128.6–129.4 ($C_{arom.}$), 134.5, 134.6, 134.6, 134.8, 135.0, 135.5, 137.1 (C_{ipso}), 169.7, 170.1 (C=O) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = –2.06, –0.67, –0.53 (PC-2, PC-3, PC-6) ppm. HR-MS (ESI-pos.): calcd. for $C_{36}H_{39}O_{18}P_3Na$ [M + Na]$^+$ 875.124; found 875.1246.

3,5,6-Tri-*O*-acetyl-1,2,4-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-41]: A solution of (–)-**40** was allowed to react under the conditions described for the preparation of (+)-**41** to give (–)-**41**. $[\alpha]_D^{20}$ = –18.0 (*c* = 0.4, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**41**.

D-*myo*-Inositol 2,3,6-Trisphosphate [(+)-42]: Preactivated Pd/C (100 mg, Degussa RW 10) was added to a suspension of (+)-**41** (80 mg, 0.09 mmol) in ethanol/water (1:2, 30 mL) and the mixture was stirred at room temperature under H_2 for 12 h. The catalyst was filtered off, and the filtrate was concentrated under reduced pressure. The residue was taken up in ice-cooled 0.25 N NaOH (10 mL) and stirred at this temperature for 5 h. The solution was neutralized by ion exchange (H^+ form, DOWEX 50-X) and filtered; the resin was washed with water. The filtrate was lyophilized to give (+)-**42** (40 mg, 100%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = +19.6 (*c* = 1.2, H_2O, free acid). Ref.[33] $[\alpha]_D^{20}$ = –13.7 (*c* = 0.75, H_2O, pH = 10, sodium salt). ^{1}H NMR (D_2O, free acid): δ = 3.48 (ψt, *J* = 9.2 Hz, 1 H, 5-H), 3.73 (d, *J* = 9.7 Hz, 1 H, 1-H), 3.79 (ψt, *J* = 9.7 Hz, 1 H, 4-H), 4.05 (ψt, *J* = 8.9 Hz, 1 H, 3-H), 4.19 (ψq, *J* = 9.2 Hz, 1 H, 6-H), 4.74 (d, *J* = 9.2 Hz, 1 H, 2-H) ppm. ^{13}C NMR (D_2O, free acid): δ = 69.8 (d, *J* = 3.2 Hz, C-1), 71.3 (d, *J* = 6.4 Hz, C-4), 74.1 (d, *J* = 3.2 Hz, C-5), 75.1 (m, C-3), 76.9 (d, *J* = 6.4 Hz, C-2), 78.5 (d, *J* = 6.4 Hz, C-6) ppm. ^{31}P{^{1}H} NMR (D_2O, free acid): δ = 1.08, 1.24, 1.90 (PC-2, PC-3, PC-6) ppm. HR-MS: calcd. for $C_6H_{16}O_{15}P_3$ [M + H]$^+$ 420.967; found 420.9702.

D-*myo*-Inositol 1,2,4-Trisphosphate [(–)-42]: A solution of (–)-**41** was allowed to react under the same conditions used for the preparation of (+)-**42** to give (–)-**42**. $[\alpha]_D^{20}$ = –15.2 (*c* = 1.1, H_2O, free acid). The ^1H NMR and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**42**.

1-*O*-Acetyl-3,6-di-*O*-benzyl-D-*myo*–inositol [(–)-43]: 2 N HCl (0.2 mL) was added to a solution of (–)-**31** (200 mg, 0.5 mmol) in tetrahydrofuran (20 mL, HPLC grade). After the solution had been stirred at 80 °C for 3 d, it was diluted with ethyl acetate (50 mL) and neutralized with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ethyl acetate (3 × 40 mL), and the combined organic layers were washed with brine (25 mL). After evaporation of the solvent, the resulting colorless oil was purified by flash chromatography with silica gel (ethyl acetate/cyclohexane, 1:1) to yield (–)-**43** (60 mg, 30%) as a colorless solid. About 50% of the starting material (–)-**31** [100 mg, R_f = 0.08 (ethyl acetate/cyclohexane, 1:1)] could also be re-isolated by chromatography. R_f = 0.08 (ethyl acetate/cyclohexane, 1:1), $[\alpha]_D^{20}$ = –1.9 (*c* = 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.08 (s, 3 H, CH_3), 3.40 (dd, *J* = 2.8, *J* = 9.4 Hz, 1 H, 3-H), 3.49 (ψt, *J* = 9.4 Hz, 1 H, 5-H), 3.92 (ψt, *J* = 9.9 Hz, 1 H, 6-H or 4-H), 3.93 (ψt, *J* = 9.4 Hz, 1 H, 4-H or 6-H), 4.31 (ψt, *J* = 2.5 Hz, 1 H, 2-H), 4.65 –4.74 (m, AB, 2 H, Ph-CH_2), 4.79 (s, AB, 2 H, Ph-CH_2), 4.85 (dd, *J* = 3.1, *J* = 10.2 Hz, 1 H, 1-H), 7.25–7.41 (m, 10 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2 (CH_3), 67.9 (C-2), 72.3 (C-4), 72.8 ($PhCH_2$), 73.6 (C-1), 74.5 (C-5), 75.4 ($PhCH_2$), 78.8 (C-6), 79.4 (C-3), 127.4–128.6 ($C_{arom.}$), 137.4, 138.5 (C_{ipso}), 170.4 (C=O) ppm. $C_{22}H_{26}O_7$ (402.4): calcd. C 65.66, H 6.51; found C 65.60, H 6.31.

D-*myo*–Inositol 2,4,5-Trisphosphate [(–)-44]: (–)-**43** (30 mg, 0.075 mmol) was dissolved in anhydrous dichloromethane (10 mL), and a solution of 1*H*-tetrazole (0.45 M in acetonitrile, 1 mL, 0.45 mmol) was added. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (81 mg, 0.34 mmol) was then added dropwise at ambient temperature, and the solution was stirred for 12 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (240 mg, 1 mmol) in dichloromethane (30 mL, dried with Na_2SO_4) was added. The solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The product was worked up as described for (+)-**29**. Purification by flash chromatography (ethyl acetate, R_f = 0.45) yielded 1-*O*-acetyl-3,6-di-*O*-benzyl-2,4,5-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol (40 mg) as a colorless foam. Preactivated Pd/C (40 mg, Degussa RW 10) ethanol/water (in 20 mL, 1:2) was added to a suspension of this compound (40 mg, 74 μmol) in ethanol (10 mL). The mixture was stirred at room temperature under H_2 for 12 h. The catalyst was then filtered off, and the filtrate was concentrated under reduced pressure. The residue was taken up in ice-cooled 0.25 N NaOH (10 mL) and stirred at this temperature for 3 h. The solution was neutralized by ion exchange (H^+ form, DOWEX 50-X) and filtered; the resin was washed with water. The filtrate was lyophilized to give (–)-**44** (15 mg, 50%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –2.1 [*c* = 0.5, H_2O, pH adjusted to 6 (NH_4OH)]. Ref.[34] $[\alpha]_D^{20}$ = –8.05 (H_2O, cyclohexylammonium salt). ^1H NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.55 (d, *J* = 9.7 Hz, 1 H, 1-H), 3.67 (d, *J* = 9.7 Hz, 1 H, 3-H), 3.83 (ψt, *J* = 9.4 Hz, 1 H, 6-H), 3.92 (ψq, *J* = 9.0 Hz, 1 H, 5-H), 4.27 (ψq, *J* = 9.2 Hz, 1 H, 4-H), 4.55 (d, *J* = 7.6 Hz, 1 H, 2-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 71.0 (m, C-3), 71.2 (d, *J* = 1.9 Hz, C-1), 72.9 (d, *J* = 1.9 Hz, C-6), 76.2 (d, *J* = 5.1 Hz, C-2), 77.2 (m, C-4), 78.6 (m, C-5) ppm. $^{31}P\{^1H\}$ NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.27 (PC-4), 3.58 (PC-5), 4.10 (PC-2) ppm. For more analytical data see ref.[33]

D-*myo*–Inositol 2,5,6-Trisphosphate [(+)-44]: A solution of (+)-**43** was allowed to react under the conditions described for the preparation of (–)-**44** to give (+)-**44**. $[\alpha]_D^{20}$ = +1.8 [*c* = 0.5, H_2O, pH adjusted to 6 (NH_4OH)]. The ^1H NMR and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**44**.

2-*O*-Acetyl-3,6-bis-*O*-(di-*O*-benzylphospho)-D-*myo*-inositol (45): Triethyl orthoacetate (0.15 mL, 0.82 mmol) was added to a solution of racemic 3,6-bis-*O*-(di-*O*-benzylphospho)-*myo*-inositol (250 mg, 0.36 mmol) [for the preparation, see the synthesis instructions for (–)-**10**] and *p*-toluenesulfonic acid monohydrate (30 mg, 0.16 mmol) in anhydrous tetrahydrofuran (50 mL). After the mixture had been stirred vigorously for 2 d, the solvent was removed under reduced pressure, and the residue was dried under high vacuum. The residue was dissolved in aqueous acetic acid (15 mL, 80%) and stirred for 1.5 h at room temperature. The solvent was evaporated and the residue was dissolved in dichloromethane (70 mL). The solution was washed twice with saturated aqueous $NaHCO_3$ (2 × 50 mL) and then with brine (50 mL). Evaporation of the dichloromethane gave a colorless solid (260 mg, 98%). ^1H NMR ($CDCl_3$/[D_4]-MeOH): δ = 2.04 (s, 3 H, CH_3), 3.31 (m, 1 H, OH), 3.44 (ψt, *J* = 9.4 Hz, 1 H, 5-H or 4-H), 3.68 (dd, *J* = 2.5, *J* = 9.7 Hz, 1 H, 1-H), 3.79 (ψt, *J* = 9.7 Hz, 1 H, 5-H or 4-H), 4.25 (dψt, *J* = 2.8, *J* = 9.4 Hz, 1 H, 3-H), 4.39 (ψq, *J* = 9.2 Hz, 1 H, 6-H), 4.97–5.12 (m, 8 H, $PhCH_2$), 5.60 (ψt, *J* = 2.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$/[D_4]MeOH, 6:1): δ = 20.3 (CH_3), 68.6 (d, *J* = 3.8 Hz, CH), 69.3 (d, *J* = 5.2 Hz, CH_2), 69.5 (d, *J* = 5.7 Hz, CH_2), 69.5 (d, *J* = 6.7 Hz, CH_2), 69.7 (d, *J* = 5.6 Hz, CH_2), 71.5 (d, *J* = 4.8 Hz, CH), 72.0 (d, *J* = 1.9 Hz, CH), 72.9 (d, *J* = 2.9 Hz, CH), 76.2 (d, *J* = 6.7 Hz, CH), 81.0 (d, *J* = 6.87 Hz, CH), 127.5-135.5 ($C_{arom.}$, C_{ipso}), 170.2 (CO) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$/[D_4]MeOH, 6:1): δ = 2.70, 3.33 ppm. HR-MS (ESI-pos.): calcd. for $C_{36}H_{41}O_{13}P_2$ $[M + H]^+$ 743.2016; found 743.2022.

2-*O*-Acetyl-3,6-bis-*O*-(di-*O*-benzylphospho)-1,4,5-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol (46): (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (380 mg, 1.6 mmol) was added to a solution of racemic **45** (250 mg, 0.34 mmol) and 1*H*-tetrazole (230 mg, 3.2 mmol) in anhydrous dichloromethane (30 mL); the mixture was stirred at room temperature for 12 h. After workup as described for the preparation of (–)-**32** [*m*-CPBA (1.5 g, 6.1 mmol) in dichloromethane (20 mL, dried with Na_2SO_4)] and purification by flash chromatography (dichloromethane/methanol, 95:5), pure **46** (360 mg, 82%) was isolated as a colorless foam. ^1H NMR ($CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 4.56 (ψt, *J* = 8.1 Hz, 1 H, 1-H or 3-H), 4.71 (ψt, *J* = 8.7 Hz, 1 H, 1-H or 3-H), 4.81–5.56 (m, 23 H, 4-H, 5-H, 6-H, 10 × CH_2), 6.16 (ψs, 1 H, 2-H), 7.20–7.39 (m, 32 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.6 (CH_3), 68.5 (d, *J* = 7.1 Hz, CH_2), 69.0 (d, *J* = 6.1 Hz, CH_2), 69.3 (s, CH), 69.5 (d, *J* = 6.1 Hz, CH_2), 69.8 (d, *J* = 6.1 Hz, CH_2), 70.2 (d, *J* = 6.1 Hz, CH_2), 73.1 (d, *J* = 3.8 Hz, CH), 73.4 (ψs, CH), 75.7 (m, CH), 76.7 (ψt, *J* = 5.3 Hz, CH), 77.2 (m, CH), 127.9–129.0 ($C_{arom.}$), 134.8, 134.9, 135.2, 135.4, 135.4, 135.5 (C_{ipso}), 135.6 (d, *J* = 7.1 Hz, C_{ipso}), 135.9 (d, *J* = 7.1 Hz, C_{ipso}), 168.7 (CO) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = –0.74, –1.04 (PC-3 and PC-6), –0.07, –1.75, –2.19 (PC-1, PC-5, PC-4) ppm. HR-MS (ESI-pos.): calcd. for $C_{60}H_{62}O_{22}P_5$ $[M + H]^+$ 1289.2421; found 1289.2450.

***myo*-Inositol 1,3,4,5,6-Pentakisphosphate (47):** Compound **46** (300 mg, 0.24 mmol) was hydrogenated [in ethanol/water, 1:1, 50 mg Pd/C (Degussa RW 10)] and de-*O*-acetylated (10 mL 0.25 N NaOH) as described for the preparation of (–)-**30** to give **47** (132 mg, 92%) as a colorless, very hygroscopic foam. Separation by HPLC assured purity >99%. ^1H NMR [D_2O, pH adjusted to 9

(ND_4OD)]: δ = 3.39 (dψt, J = 2.7, J = 9.6 Hz, 2 H, 1-H and 3-H), 4.03 (ψq, J = 9.5 Hz, 1 H, 5-H), 4.30 (ψq, J = 9.6 Hz, 2 H, 4-H and 6-H), 4.51 (ψt, J = 2.7, 1 H, 2-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 9 (ND_4OD)]: δ = 70.9 (s), 74.3 (m), 76.2 (m), 77.7 (m) ppm. $^{31}P\{^1H\}$ NMR [D_2O, pH adjusted to 9 (ND_4OD)]: δ = 3.05, 3.84, 4.60 ppm. The other analytical data are in agreement with those in ref.[15a]

D-*myo*-Inositol 1,3,6-Trisphosphate [(–)-48]: Triethyl orthoacetate (0.35 mL, 1.9 mmol) was added to a solution of (+)-**24** (500 mg, 0.64 mmol) and *p*-toluenesulfonic acid monohydrate (20 mg) in anhydrous tetrahydrofuran (15 mL); the mixture was stirred at room temperature for 24 h. Workup as described for the preparation of **45** yielded 2,4,5-tris-*O*-acetyl-3,6-bis-*O*-(di-*O*-benzylphospho)-D-*myo*-inositol as a colorless foam (470 mg, 83%). ^1H NMR ($CDCl_3$): δ = 1.78 (s, 6 H, CH_3), 2.11 (s, 3 H, CH_3), 3.89 (dd, J = 2.8, J = 9.9, 1 H, 1-H), 4.65 (dψt, J = 3.1, J = 9.9 Hz, 1 H, 3-H), 4.69 (ψq, J = 9.3 Hz, 1 H, 6-H), 4.89–5.11 (m, 8 H, $PhCH_2$), 5.18 (ψt, J = 9.7 Hz, 1 H, 5-H), 5.41 (ψt, J = 9.9 Hz, 1 H, 4-H), 5.77 (ψt, J = 2.8 Hz, 1 H, 2-H), 7.25–7.38 (m, 20 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.1, 20.2, 21.4 ($3\times CH_3$), 69.5, 69.6, 69.7, 69.75, 69.81 ($5\times CH_2$, $PhCH_2$), 69.8 (d, J = 2.9 Hz, C-1), 70.1 (d, J = 4.8 Hz, C-4), 70.7 (d, J = 4.8 Hz, C-5), 71.3 (d, J = 2.9 Hz, C-2), 73.6 (d, J = 5.7 Hz, C-3), 78.6 (d, J = 6.7 Hz, C-6), 127.7, 127.82, 127.85, 127.87, 128.5, 128.6, 129.7 ($C_{arom.}$), 135.1 (d, J = 2.0 Hz, C_{ipso}), 135.2 (d, J = 3.1 Hz, C_{ipso}), 135.3 (d, J = 3.1 Hz, C_{ipso}), 135.4 (d, J = 2.0 Hz, C_{ipso}), 169.7, 169.81, 169.84 (CO) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = –0.56, –0.24 ppm. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (175 mg, 0.8 mmol) was added to an anhydrous dichloromethane solution (15 mL) of this compound (300 mg, 0.38 mmol) and 1*H*-tetrazole (100 mg, 1.4 mmol); the mixture was stirred at room temperature for 12 h. Workup as described for the preparation of (+)-**29** [*m*-CPBA (0.5 g, 2.0 mmol) in dichloromethane (10 mL, dried with Na_2SO_4)] yielded a colorless foam (570 mg, 92%). The crude product thus obtained (200 mg, 0.21 mmol) was hydrogenated [in ethanol/water, 1:1, 200 mg Pd/C (Degussa RW 10)] and de-*O*-acetylated (20 mL 0.25 N NaOH) as described for the preparation of (–)-**30** to give (–)-**48** (150 mg, 93%) as a colorless, very hygroscopic foam. Separation by HPLC assured purity >99% (120 mg, 75%). The analytical data are in agreement with the previously published results.[33]

D-*myo*-Inositol 1,3,4-Trisphosphate [(+)-48]: The (–)-enantiomer **24** was converted as described for the preparation of *myo*-Ins(1,3,6)P_3 [(–)-**48**] to give D-*myo*-inositol 1,3,4-trisphosphate **[**(+)-**48**]. The ^1H, ^{13}C and ^{31}P NMR spectroscopic data are identical with those obtained for (–)-**48**.

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