Flexible Stereo- and Regioselective Synthesis of *myo*-Inositol Phosphates (Part 2): Via Nonsymmetrical Conduritol B Derivatives

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A practical route is described for the preparation of *myo*-inositol phosphates. Optically pure compounds can be prepared, in both forms, from *p*-benzoquinone by enzymatic resolution of a diacetoxyconduritol key intermediate. Monosubstituted inositol derivatives can be obtained by breaking the C_2 symmetry of conduritol B derivatives. A wide variety of *myo*-inositol phosphates can be synthesized by combining the previously reported symmetrical approach with this new nonsymmetrical approach.

Introduction

myo-Inositol phosphates are members of a large family of naturally occurring compounds that have been intensively studied in the last two decades because of their complex role in cell signaling and homoeostasis.[1–4] In particular, D-*myo*-inositol 1,4,5-trisphosphate, which is generated from the phospholipase C catalyzed cleavage of membrane-bound phosphatidylinositol bisphosphate (PIP_2), plays an essential role as a second messenger by inducing Ca^{2+} release from intracellular storage.[5,6]

Since *myo*-inositol phosphates are so important, a large number of chemical syntheses have been reported in the literature to date. Many of these start from achiral *myo*-inositol, use selective protection of the alcohol groups, and also involve enzymatic or chemical resolution for the preparation of enantiomerically pure compounds.[7,8] Recently, peptide-based asymmetric phosphorylation has been achieved.[9] Some de novo concepts have also been described, for instance based on microbial oxidation of benzene,[10] or starting from *p*-benzoquinone followed by enzymatic resolution,[11] or by dynamic kinetic asymmetric transformation of the conduritol B derivatives (all-*trans*-5-cyclohexene-1,2,3,4-tetraol).[12]. Several chiral pool approaches start with carbohydrates[13–15] or (–)-quinic acid,[16] and have been used to prepare conduritols that are suitable as intermediates for the syntheses of inositols.

Key intermediates for the synthesis of specific *myo*-inositol phosphates are the corresponding hydroxy group(s) protected derivatives with free hydroxy group(s) at the desired position for phosphorylation.[17] Our group has pioneered a concept for the synthesis of inositol phosphates that is based on C_2-symmetric conduritol B derivatives. We have also been able to demonstrate that regioselective enzymatic dephosphorylation expands the number of accessible derivatives,[11,18] but up until now this has been the only way to overcome the substitution pattern dictated by the choice of C_2-symmetric starting materials. In this paper, we present an extension to this concept that leads to even greater flexibility. As reported previously,[19] the syntheses of *myo*-inositol phosphates via C_2-symmetric conduritol B derivatives leads to pairwise protected (differentiated) *myo*-inositol intermediates, and this limits the number of possible *myo*-inositol phosphates. Breaking the C_2 symmetry of the conduritol B precursors makes additional substitution patterns available; we used this approach already to synthesize azido- and amino-*myo*-inositols.[20] In the work reported here, we describe its application to the synthesis of a number of inositol phosphates, substantially extending the scope of our approach. This new concept abolishes the C_2 symmetry of conduritol B derivatives by using a route analogous to the synthesis of monoazidoconduritol B. This route also starts from the enantiomeric building blocks **1** or **2** (see Scheme 1) and converts them, by monoepoxide formation and monoepoxide ring-opening (see Scheme 2), into monobenzylated conduritol B derivatives **3** or *ent*-**3**, respectively.

cis-Dihydroxylation leads only to the *myo* configuration of the resulting inositol derivatives; in contrast to the symmetrical route, however, in the case of nonsymmetric starting materials the attack of the hydroxylating agent leads to an isomeric mixture of **4** and **5**. Although at first glance this seems to be disadvantageous, it turns out to be a powerful alternative if an effective method for separating the two isomers is at hand.

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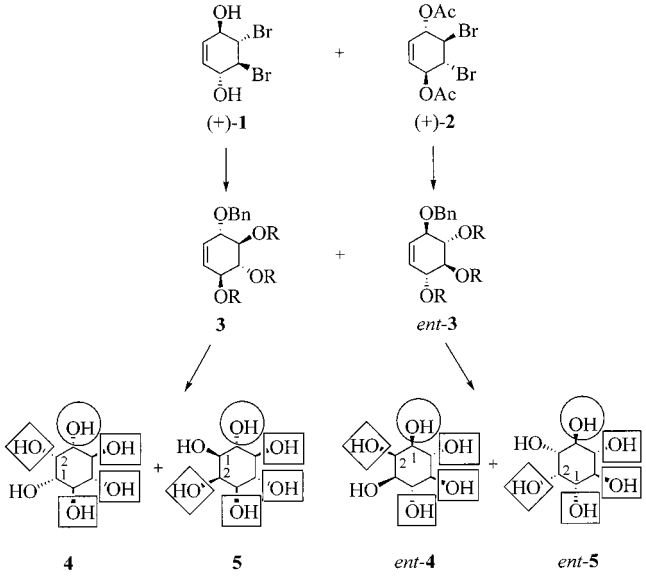
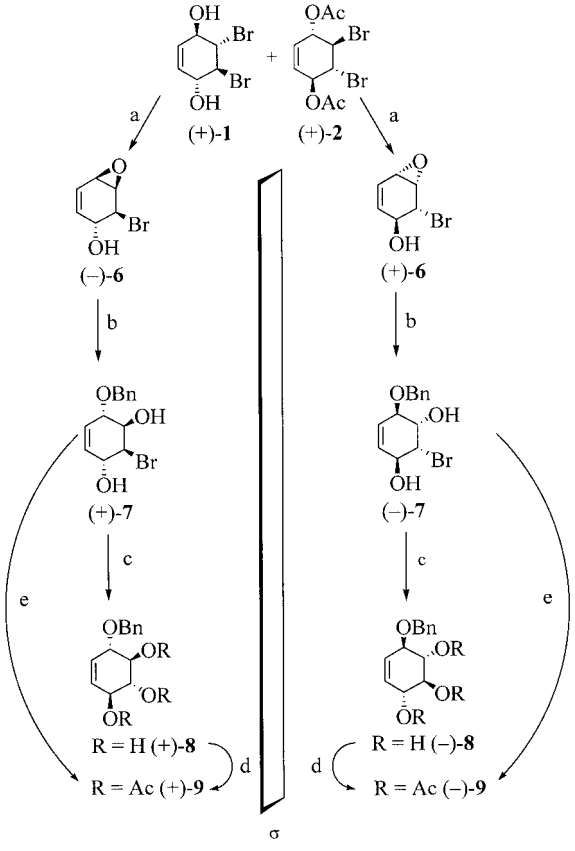


Scheme 1.



Scheme 2. Reagents and conditions: (a) LiOH, Et_2O/MeOH (92%). (b) BnOH, CH_2Cl_2, H_2SO_4 (cat.) (99%). (c) 1. LiOH, Et_2O/MeOH (99%); 2. *p*-TSA, H_2O (after crystallization <30%). (d) Ac_2O, pyridine (99%). (e) 1. Ac_2O, pyridine (100%); 2. KOAc, glacial AcOH/Ac_2O, 5 d, 125 °C (55%).

Results and Discussion

Diacetoxydibromocyclohex-5-ene (+)-**2** and (–)-**2** [or the corresponding diols (–)- and (+)-**1**] are again the enantiomeric building blocks[11,21] for the synthesis of *myo*-inositol derivatives. As we have described previously, they can easily be prepared from *p*-benzoquinone in four steps on a 100-g scale.

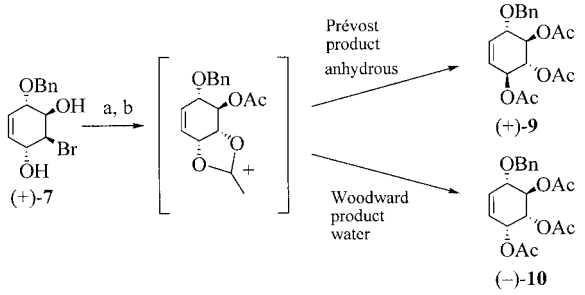
Preparation of Monobenzylconduritol B Derivatives

The monoepoxide (–)-**6** can be prepared in quantitative yield from diol (+)-**1** by treatment with lithium hydroxide as base in diethyl ether/methanol. Under the same conditions the diacetate (+)-**2** could be converted into the enantiomer (+)-**6** (see Scheme 2).[20] Treatment of the monoepoxide (–)-**6** with benzyl alcohol and a catalytic amount of concentrated sulfuric acid leads to (+)-**7** by ring-opening of the epoxide in the allylic position. No ring opening at the other position takes place; however, careful examination of the crude product shows that up to 10% of the S_N2' by-product is formed. For analytical purposes the products can be separated by chromatography, but it turned out to be easier to continue with the crude product as separation later, at the triol stage **8**, is very effective and opens up a fast, straightforward approach.

Reaction of the benzyl-protected (+)-**7** under the above-mentioned basic conditions transformed the bromohydrin into an epoxide intermediate which, on direct hydrolysis in water/tetrahydrofuran with catalytic amounts of *p*-toluenesulfonic acid, yielded a mixture of triols formed by S_N2 and S_N2' reactions. One by-product, for example, was determined to be 2-benzylconduritol B. Crystallization from ethyl acetate gave pure triol (+)-**8** in low yield (less than 30%), therefore this reaction is less effective than the route for the preparation of monoazidoconduritols.[20] The low tendency of (+)-**8** and (+)-**9** to crystallize forced us to search for alternatives. It should be mentioned that this route can be pursued more effectively for the synthesis of racemic compounds (**8** or **9**), since the racemic intermediates show an increased tendency to crystallize, so that purification is easy at the stage of the triol.

In view of the newly developed synthetic route to conduritol E and B derivatives,[22] it is possible to transform the bromohydrin derivative (+)-**7** into diacetates via acetoxonium intermediates. This avoids epoxide formation and epoxide opening and thus prevents formation of the by-products mentioned above (see Scheme 3). Therefore, diol (+)-**7** was first acetylated and then further converted under the conditions leading to either the *trans*- or the *cis*-diacetate product.

In the absence of water the acetoxonium intermediate undergoes ring opening by attack of acetate anions exclusively at the allylic centers to form the Prévost[23] product (+)-**9**, thus establishing the conduritol B stereochemistry, in 55% yield. In the presence of a sufficient amount of water the acetoxonium intermediate is transformed into the Woodward product (–)-**10**, with the conduritol F configuration, in 60% yield.[24,25] We performed this reaction by heating acetylated (+)-**7** in anhydrous or aqueous acetic acid with powdered KOAc. In the case of the Woodward pro-

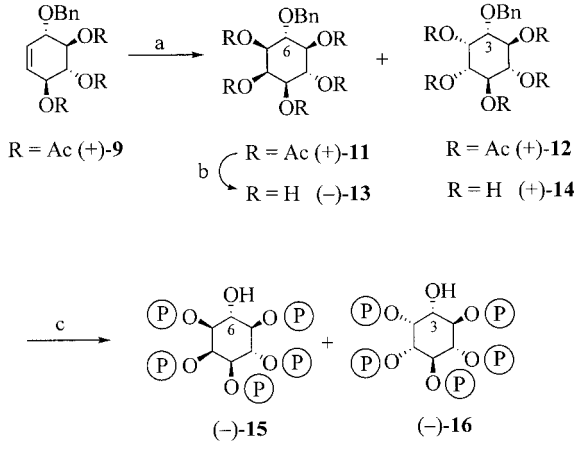


Scheme 3. Reagents and conditions: Preparation of the Prévost product (+)-**9**: (a) Ac_2O, pyridine (100%). (b) KOAc, glacial AcOH/Ac_2O, 5 d, 125 °C (55%). Preparation of the Woodward product (+)-**10**: (a) Ac_2O, pyridine (100%). (b) 1. KOAc, AcOH (95%), 5 d, 125 °C; 2. Ac_2O, CH_2Cl_2, DMAP (cat.) (60%).

duct, the crude reaction product had first to be acetylated. The triacetate (+)-**9** was purified by flash chromatography followed by recrystallization from diethyl ether/cyclohexane.

Synthesis of *myo*-Inositol Pentakisphosphates

cis-Dihydroxylation (see Scheme 4) of the conduritol B derivative (+)-**9** with ruthenium trichloride and sodium metaperiodate, followed by acetylation, gave a mixture of the *myo*-configured products (+)-**11** and (+)-**12** in high yields in a ratio of 6:4. The two products can be separated by fractional recrystallization, although it is more convenient to separate the two isomers at the stage of the protected *myo*-inositol phosphates.

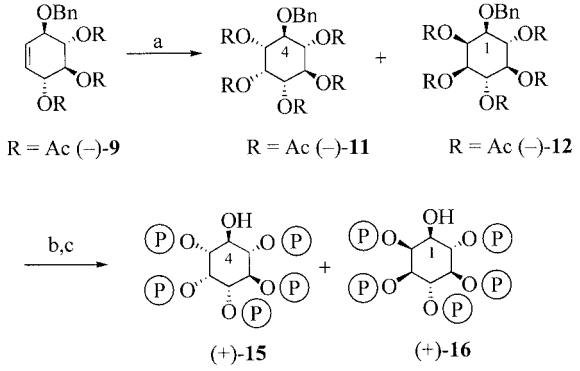


Scheme 4. Reagents and conditions: (a) 1. $RuCl_3$, $NaIO_4$, acetonitrile; 2. Ac_2O, pyridine (99%). (b) NaOMe, MeOH (99%). (c) 1. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (50%); 2. Pd/C, H_2, ethanol/water (99%).

Deprotection of the 6-benzyl-pentaacetate (+)-**11** and 3-benzyl-pentaacetate (+)-**12** with sodium methoxide in anhydrous methanol gave 6-benzyl-*myo*-inositol [(–)-**13**] and 3-benzyl-*myo*-inositol [(+)-**14**], respectively, in quantitative yield.

An isomeric mixture of the pentaols (–)-**13** and (+)-**14** was phosphorylated by treatment with (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine in the presence of 1*H*-tetrazole. Oxidation of the resulting phosphite with *m*-CPBA gave an isomeric mixture of the protected pentakisphosphates. To remove the excess of phosphorylating reagent, the crude product was purified by flash chromatography (CH_2Cl_2/MeOH, 95:5). The isomers can be separated easily by this method, and an earlier separation of the isomers is thus not needed. Pd/C-catalyzed hydrogenolysis led to the target compounds *myo*-Ins(1,2,3,4,5)P_5 [(–)-**15**] and *myo*-Ins(1,2,4,5,6)P_5 [(–)-**16**] in quantitative yield.

Since this route can start from either of two building blocks, as depicted in Scheme 1, both the D- and the L-series of *myo*-inositol polyphosphates are obtainable. In the case of *myo*-inositol derivatives this leads to different regioisomers, where the benzyl protecting group can easily be introduced in the 1-, 3-, 4-, and 6-position of the cyclitol ring, depending on the choice of starting material (see Scheme 5). For a deeper insight into *myo*-inositol nomenclature see refs.[1,2] Consequently, starting from the diacetate (+)-**2**, the enantiomers *myo*-Ins(1,2,3,5,6)P_5 [(+)-**15**] and *myo*-Ins(2,3,4,5,6)P_5 [(+)-**16**] are available.



Scheme 5. Reagents and conditions: (a) 1. $RuCl_3$, $NaIO_4$, acetonitrile; 2. Ac_2O, pyridine (99%). (b) NaOMe, MeOH (99%). (c) 1. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (50%); 2. Pd/C, H_2, ethanol/water (99%).

Separation of the resulting *myo*-inositol pentakisphosphates by HPLC ensures isomeric purity suitable for biological experiments. Under the chosen chromatographic purification conditions, the two isomers (–)-**15** and (–)-**16** or (+)-**15** and (+)-**16** differ in retention time by 6 min and can therefore also be separated easily at this stage.

The identity of (–)-**15** and (–)-**16** was confirmed by one- and two-dimensional NMR spectroscopy (see Figures 1 and 2), as it was possible to assign all the ^1H, ^{13}C, and ^{31}P resonances. The NMR spectra show no traces of the other inositol pentakisphosphate isomer. The chemical shifts of the inositol ring protons are highly dependent on the pH, and good resolution was achieved after adjustment of the pH to 6 with ND_4OD. The two nonphosphorylated CH groups in *myo*-Ins(1,2,3,4,5)P_5 [(–)-**15**] and *myo*-Ins(1,2,4,5,6)P_5 [(–)-**16**] can easily be recognized in the ^1H NMR spectra as

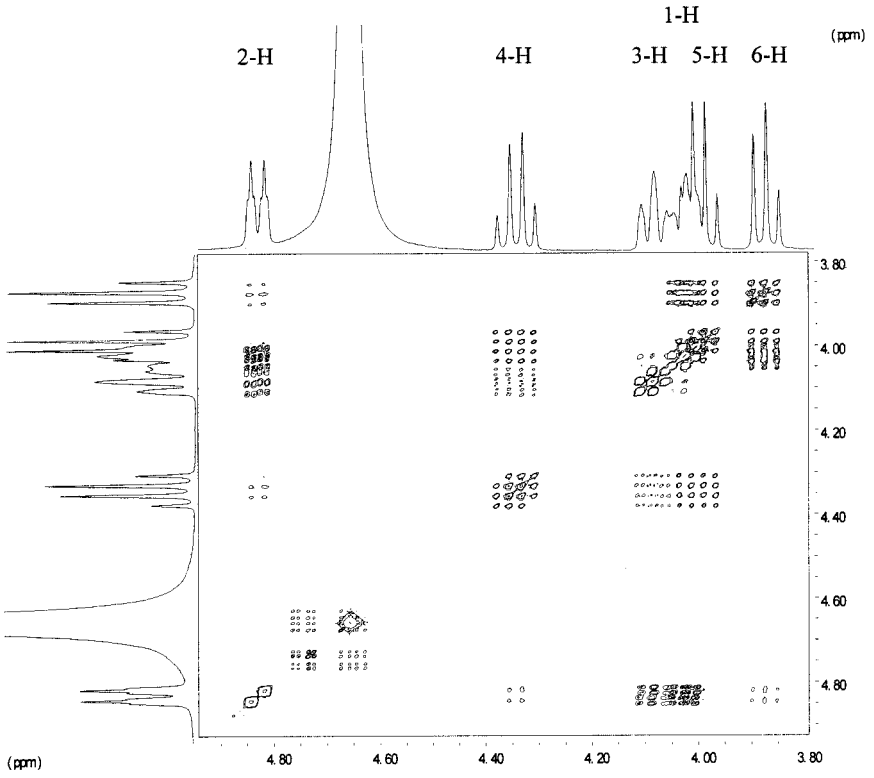


Figure 1. ^{1}H-^{1}H COSY spectrum of *myo*-Ins(1,2,3,4,5)P_5 (–)-**15**.

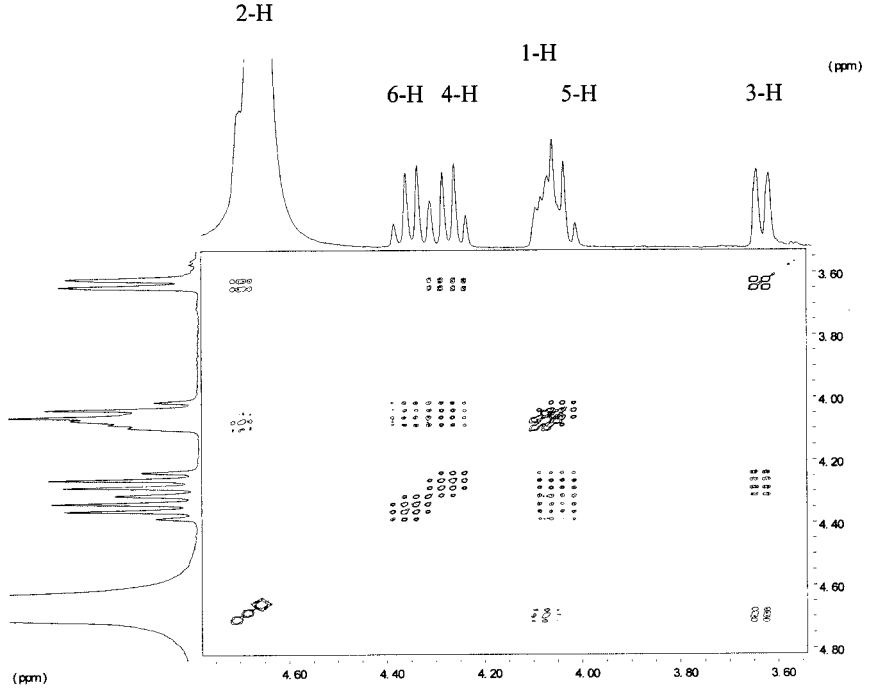


Figure 2. ^{1}H-^{1}H COSY spectrum of *myo*-Ins(1,2,4,5,6)P_5 [(–)-**16**].

they do not change multiplicity upon phosphorus decoupling and are the signals at highest field (**15**: δ = 3.87 ppm; **16**: δ = 3.64 ppm). They also show characteristic coupling patterns: 3-H in (–)-**16** exhibits a doublet (with the small $^3J_{2\text{-H},3\text{-H}}$ *cis* coupling not being resolved), while 6-H in (–)-**15** is characterized by a triplet signal resulting from two almost equivalent $^3J_{H,H}$ couplings. In the ^{1}H-^{1}H COSY spectrum of (–)-**16** the 2-H signal is hidden under that of HDO at δ = 4.70 ppm, but can be found by its cross-peaks to 1-H and 3-H.

myo-Ins(1,2,3,4,5)P_5 [(–)-**15**], *myo*-Ins(1,2,4,5,6)P_5 [(–)-**16**], and their enantiomers, were used as standards to assign the absolute configuration of enzymatic (phytases) degradation products of *myo*-InsP_6 by HPLC-MDD.[26]

Synthesis of *myo*-Inositol Tetrakisphosphates

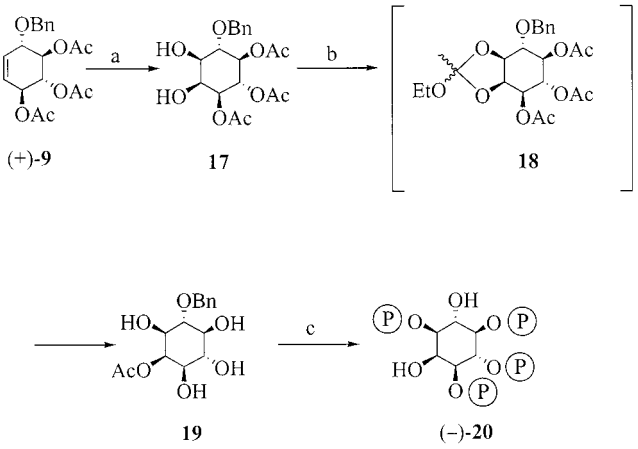
Selective protection of one of the free equatorial or axial hydroxy groups after *cis*-dihydroxylation of the unsymmetrical conduritol B derivative (+)-**9** allows access to different *myo*-inositol tetrakisphosphates.

Synthesis of myo-Ins(1,3,4,5)P_4 [(–)-20]

One of the most interesting targets that can be synthesized by this asymmetric route is *myo*-Ins(1,3,4,5)P_4 [(–)-**20**]. As mentioned above, *cis*-dihydroxylation of the conduritol B derivative (+)-**9** with ruthenium trichloride and sodium metaperiodate gave a mixture of the isomeric diols **17** (for a clearer view only the main isomer is shown in Scheme 6). Separation of the isomers was rendered counterproductive by protecting-group migration. This isomeric mixture was therefore further converted directly. For the synthesis of (–)-**20** there is the need for a suitable protected precursor with free hydroxy groups in the 1-, 3-, 4-, and 5-positions. Protection of the axial hydroxy group is therefore essential. The two hydroxy groups were differentiated by monofunctionalization of the axial hydroxy group of **17** by a previously reported method.[22] Treatment of **17** with triethyl orthoacetate in anhydrous tetrahydrofuran under acidic conditions (*p*-toluenesulfonic acid) resulted in the formation of an intermediate orthoester that can be converted directly, with acetic acid, into the axial acetate.[27] Regioselectivity in this reaction can be traced to stereoelectronic effects.[28] In this case the acetate groups in positions 3, 4, and 5 cannot be removed without removing the acetate group in the 2-position. The problem is thus that an orthogonal set of protecting groups is needed. Because we were searching for a fast and efficient route, a tedious multistep protection and deprotection route, for example via silylated **8**, was undesirable. One way to solve this problem is to use the intermediate orthoester as a protecting group for the diol. This orthoester **18** is stable towards base, therefore, after its formation, the acetate groups were removed with NaOMe in methanol. The orthoester was then directly converted with acetic acid into the axial acetate (see Scheme 6). This new method significantly shortens the route to the desired precursor **19**.

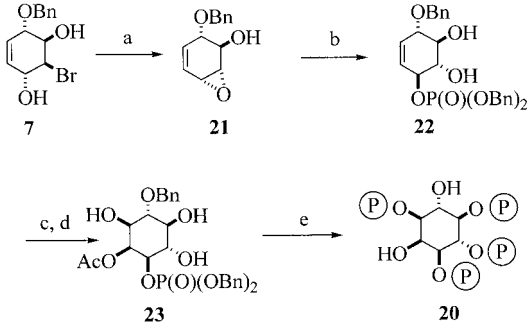
The success of this approach can be seen by monitoring the ^{1}H NMR spectra. The chemical shifts of the ring protons of the product are significantly different from those of the starting material. The resonances of all groups, except for the group in the 2-position, are strongly shifted upfield, indicating that the acetate groups in positions 3, 4, and 5 have been removed. In the ^{1}H NMR spectrum 2-H appears as a pseudotriplet ($^3J \approx 3$ Hz) with $\delta > 5$ ppm, demonstrating that an acetate group is at the 2-position.

Phosphorylation of the tetraol **19** by reaction with (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine in the presence of 1*H*-tetrazole, followed by oxidation with *m*-CPBA, gave the protected tetrakisphosphate, which, on deprotection by Pd/C-catalyzed hydrogenolysis and then cleavage of the acetate groups in aqueous NaOH, gave the target compound *myo*-Ins(1,3,4,5)P_4 [(–)-**20**] in 20% yield over all steps. Separation by preparative HPLC ensured a purity suitable for biological experiments.



Scheme 6. Reagents and conditions: (a) $RuCl_3$, $NaIO_4$, acetonitrile. (b) 1. $MeC(OEt)_3$, *p*-TSA; 2. NaOMe, MeOH; 3. 80% HOAc (99%). (c) 1. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA; 2. Pd/C, H_2, ethanol/water; 3. 0.25 N NaOH (over all steps 20%).

As an interesting alternative we tried opening epoxide **21** with dibenzyl phosphate (see Scheme 7). The racemic intermediate **22** was easy to purify by recrystallization. *cis*-Dihydroxylation and selective acetylation of the axial OH group gave **23**, the direct precursor for the synthesis of *myo*-Ins(1,3,4,5)P_4 (**20**). However, enantiomerically pure **22** turned out to be difficult to purify because of its drastically diminished tendency to crystallize. Therefore it is relatively tedious to synthesize larger amounts of starting material. Interestingly, *cis*-dihydroxylation proceeds preferably from the upper face, thus leading to a 2:1 ratio of the diols (for a better view only the main isomer is shown in Scheme 7).

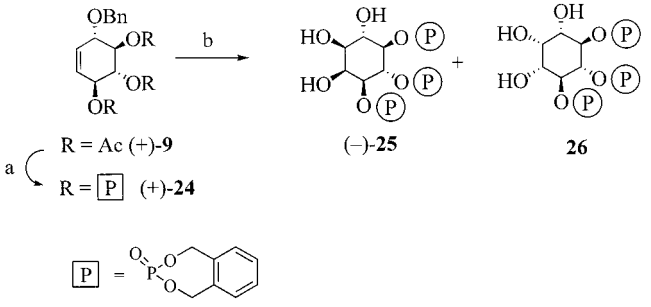


Scheme 7. Reagents and conditions: (a) LiOH, Et_2O/MeOH. (b) CH_2Cl_2, dibenzyl phosphate (40%). (c) $RuCl_3$, $NaIO_4$, CH_2Cl_2, acetonitrile. (99%). (d) 1. $MeC(OEt)_3$, *p*-TSA; 2. 80% HOAc (92%). (e) 1. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA.; 2. Pd/C, H_2, ethanol/water; 3. 0.25 N NaOH (40%).

This is thus a less useful route to enantiomerically pure *myo*-Ins(1,3,4,5)P_4 [(–)-**20**].

Synthesis of *myo*-Inositol Trisphosphates

As an alternative to the previously described chemoenzymatic synthesis[11] of *myo*-Ins(3,4,5)P_3 [(–)-**25**] and *myo*-Ins(4,5,6)P_3 (**26**), these *myo*-inositol trisphosphates can be synthesized in a few steps from (+)-**9,** as depicted in Scheme 8.

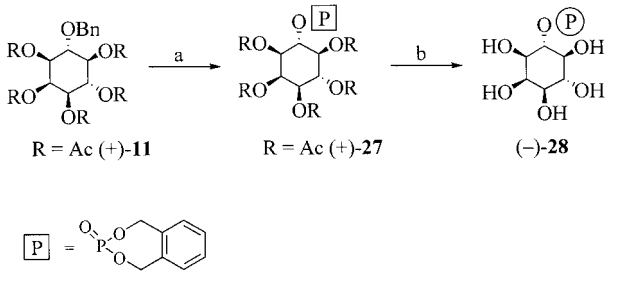


Scheme 8. Reagents and conditions: (a) 1. NaOMe, MeOH; 2. (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA. (b) 1. $RuCl_3$, $NaIO_4$, acetonitrile; 2. Pd/C, H_2, ethanol/water.

Synthesis of *myo*-Inositol Monophosphates

myo-Ins(6)P [(–)-28]

Because of the orthogonal set of protecting groups used in the synthesis of *myo*-inositol pentakisphosphates, it should be easy to synthesize *myo*-inositol monophosphates. Indeed, penta-*O*-acetyl-6-*O*-benzyl-D-*myo*-inositol [(+)-**11**] is a perfect precursor for the synthesis of *myo*-Ins(6)P [(–)-**28**]. The preparation started with Pd/C-catalyzed hydrogenolysis of (+)-**11** to deliver the free hydroxy group in the 6-position (see Scheme 9). Phosphorylation with (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine in the presence of 1*H*-tetrazole, followed by oxidation with *m*-CPBA, gave (+)-**27** in good yield. Pd/C-catalyzed hydrogenolysis followed by cleavage of the acetate groups in aqueous NaOH yielded (–)-**28** in quantitative yield.

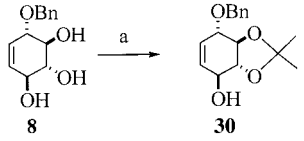


Scheme 9. Reagents and conditions: (a) 1. Pd/C, H_2, EtOAc (99%); 2. (1,5-dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine, 1*H*-tetrazole, CH_2Cl_2, then *m*-CPBA (51%). (b) 1. Pd/C, H_2, ethanol/water; 2. 0.25 N NaOH (99%).

The synthesis of *myo*-Ins(3)P (+)-**29** and its enantiomer *myo*-Ins(1)P (–)-**29** can also be accomplished by this route, but these isomers are prepared more effectively by the symmetric concept, as reported earlier.[19]

Outlook

It should be noted that this concept is not limited to the protecting pattern described above. It is possible to differentiate within the triol unit in monobenzylconduritol B (**8**) by isopropylidene protection: only the 2,3-*O*-isopropylidene-conduritol B derivative **30** is obtained, in 80% yield (Scheme 10). This opens the synthesis of further *myo*-inositol polyphosphates. The course of this reaction can be rationalized by the fact that the 3- and 4-positions are clearly disfavored. A similar result was previously reported by Trost[29] and by us[20] for other conduritol derivatives.



Scheme 10. Reagents and conditions: (a) 2,2-dimethoxypropane, anhydrous acetone, PPTSA, 3 d (80%).

As previously mentioned, all the products are available in both enantiomeric forms, which in the case of *myo*-inositol derivatives lead to different regioisomers in the D- or L-series. The concept of desymmetrization described in this paper greatly enhances the accessibility of regioisomers of *myo*-inositol phosphates.

Conclusions

In this part of the work, several *myo*-inositol phosphates have been synthesized by a nonsymmetrical approach. The new, very short and efficient, high-yielding routes described have allowed the synthesis of *myo*-Ins(1,2,3,4,5)P_5 [(–)-**15**], *myo*-Ins(1,2,4,5,6)P_5 [(–)-**16**], *myo*-Ins(2,3,4,5,6)P_5 [(+)-**16**], *myo*-Ins(1,2,3,5,6)P_5 [(+)-**15**], *myo*-Ins(6)P [(–)-**28**], *myo*-Ins(4)P [(+)-**28**], *myo*-Ins(3,4,5)P_3 [(–)-**25**], *myo*-Ins(4,5,6)P_3 (**26**), and *myo*-Ins(1,3,4,5)P_4 [(–)-**20**].

Experimental Section

General Remarks: All NMR spectra were recorded with a Bruker ARX 400 (400 MHz) spectrometer. Besides ^1H, ^{13}C, and ^{31}P experiments, 2D COSY (^1H-^1H, ^1H-^{13}C as well as ^1H-^{31}P) and DEPT spectra were recorded for the 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 standard. The multiplicity is inidcated 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 (+)-**1**, (–)-**1**, (–)-**2**, (+)-**2**,[11,21,22] (+)-**6**, (–)-**6**,[20,21] and their precursors, were prepared according to literature methods.

Purification and Analysis of Inositol Phosphates (HPLC-MDD): Inositol phosphates were purified and analyzed by the HPLC-MDD method described previously.[11,30] The compounds were separated by anion-exchange chromatography on a MonoQ HR10/10 column (Pharmacia). 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 impossible, 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*R*,2*S*,3*R*,6*S*)-6-Benzyloxy-2-bromocyclohex-4-ene-1,3-diol [(+)-7]: To remove all LiOH, the crude (1*R*,2*S*,3*R*,6*R*)-2-bromo-7-oxabicyclo[4.1.0]hept-4-en-3-ol [(–)-**6**] (18 g, 94 mmol; for the synthesis see refs.[20,21]) was taken up in CH_2Cl_2 (500 mL) and the organic solution washed twice with brine and dried with $MgSO_4$. The $MgSO_4$ was filtered off, and the filtrate was put in a 1-L round-bottomed flask. Benzyl alcohol (50 mL, 0.46 mol) and a catalytic amount of concentrated sulfuric acid (0.1 mL) were added to this solution and stirred at room temperature for 3 d. Saturated $NaHCO_3$ (20 mL) was added, and the aqueous solution was extracted twice with CH_2Cl_2. The combined organic layers were concentrated under reduced pressure to yield a brown oil (23 g), which, besides (+)-**7**, contained the S_N' by-product (approx. 10–15%). For an analytical sample the crude product was purified by flash chromatography (cyclohexane/ethyl acetate, 2:1) to yield pure (+)-**7**. R_f = 0.14 (cyclohexane/ethyl acetate, 2:1). $[\alpha]_D^{20}$ = +64.9 (*c* = 1.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$,): δ = 2.55, 2.65 (br. s, 1 H, OH), 4.06 (dd, *J* = 4.6, *J* = 2.0 Hz, 1 H, 6-H), 4.16 (dd, *J* = 4.3, *J* = 2.3 Hz, 1 H, 1-H), 4.39 (dd, *J* = 6.6, *J* = 2.0 Hz, 1 H, 2-H), 4.51 (d, *J* = 6.6 Hz, 1 H, 3-H), 4.66 (s, 2 H, CH_2), 5.88 (s, 2 H, 4-H, 5-H), 7.28–7.41 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 59.3 (C-2), 70.3 (C-3), 71.3 (C-1), 72.0 (CH_2Ph), 76.3 (C-6), 126.9 (C-4 or C-5), 127.8, 128.0, 128.5 (3×CH, C_{arom}), 129.8 (C-4 or C-5), 137.8 (C_{ipso}) ppm. MS (EI, 70 eV): *m*/*z* (%) = 298 (2) [M$^+$], 219 (8), 201 (61), 109 (4), 91 (100), 81, 79 (13, 34), 65 (76), 51 (19), 41 (22). IR (KBr): $\tilde{\nu}$ = 3390 (s, br), 3010 (w), 2860 (w), 1650 (w), 1490 (m,), 1470, 1380 (m), 1060 (s), 690 (s), 735 u. 695 (m) cm^{-1}. $C_{13}H_{15}BrO_3$ (299.2): calcd. C 52.19, H 5.05; found C 52.13, H, 5.07.

(1*S*,2*R*,3*S*,6*R*)-6-Benzyloxy-2-bromocyclohex-4-ene-1,3-diol [(–)-7]: A solution of (+)-**6** was allowed to react under the conditions described for the preparation of (+)-**7** to yield (–)-**7**. $[\alpha]_D^{20}$ = –55 (*c* = 2.0, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**7**.

(1*S*,2*R*,3*R*,4*S*)-1-*O*-Benzylconduritol B [(+)-8]: Powdered LiOH (4.0 g, 168 mmol) was added to a vigorously stirred solution of (+)-**7** (22 g, 74 mmol) in Et_2O (450 mL) and MeOH (220 mL) at 0 °C and the solution was stirred at 10 °C for 3 h. After the reaction was complete, water (300 mL) was added, and the aqueous layer was extracted with Et_2O (3×200 mL) and EtOAc (1×100 mL). The organic solution was washed twice with brine and concentrated under reduced pressure. To remove all LiOH, the residue was taken up in CH_2Cl_2 (200 mL) and the organic solution washed again twice with brine. Evaporation of the solvent yielded enantiopure **21** (17 g) as an oil. The resulting enantiopure monoepoxide **21** (16 g, 73 mmol) was dissolved in tetrahydrofuran (80 mL) and then water (200 mL); a trace of *p*-toluenesulfonic acid was added, and the solution was stirred at room temperature for 3 d. The filtrate was first reduced in volume under high vacuum and then lyophilized to yield a brown oil. Crystallization from EtOAc yielded (+)-**8** (6 g, 30%) as a colorless solid. R_f = 0.06 (cyclohexane/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +134 (*c* = 0.8, MeOH). ^{1}H NMR ([D$_6$]DMSO): δ = 3.20 (dψt, *J* = 4.5, *J* = 9.4 Hz, 1 H, 2-H or 3-H), 3.39 (m, 1 H, 2-H or 3-H), 3.90 (m, 2 H, 1-H, 4-H), 4.60, 4.65 (AB, *J* = 12 Hz, 2×1 H, Ph–CH_2), 4.86 (d, *J* = 4.1 Hz, 1 H, OH), 4.91 (d, *J* = 4.6 Hz, 1 H, OH), 4.93 (d, *J* = 5.6 Hz, 1 H, OH), 5.49 (d, *J* = 10.2 Hz, 1 H, $H_{olef.}$), 5.54 (d, *J* = 10.2 Hz, 1 H, $H_{olef.}$), 7.22–7.36 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$/MeOD, 6:1): δ = 70.9 ($PhCH_2$), 71.3, 79.81 (C-1, C-4), 74.8, 76.2 (C-2, C-3), 126.3, 131.6 (C-5, C-6), 127.2, 127.45, 128.1 ($C_{arom.}$), 139.1 (C_{ipso}) ppm. MS (EI, 70 eV): *m*/*z* (%) = 236 (56) [M$^+$], 107 (57), 91 (100), 41 (27). IR (KBr): $\tilde{\nu}$ = 3460 (m, br), 3020 (w), 1500 (w), 1450, 1370 (m), 1050 (s), 735 and 695 (m) cm^{-1}. $C_{13}H_{16}O_4$ (236.3): calcd. C 66.09, H 6.83; found C 65.88, H 6.43. HR-MS (ESI-neg., TOF): calcd. for $C_{13}H_{15}O_4$ [M – H]$^-$ 235.0981; found 235.0970.

(1*R*,2*S*,3*S*,4*R*)-1-*O*-Benzylconduritol B [(–)-8]: A solution of (–)-**7** was allowed to react to give (–)-**8** under the conditions described for the preparation of (+)-**8**. $[\alpha]_D^{20}$ = –130 (*c* = 1.0, MeOH). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**8**.

(1*S*,2*R*,3*R*,4*R*)-2,3,4-Tri-*O*-acetyl-1-*O*-benzylconduritol F [(–)-10]: The diol (+)-**7** (4.6 g, 15 mmol) was dissolved in a cooled mixture of pyridine (15 mL) and acetic anhydride (10 mL) and stirred overnight. Evaporation of the solvent yielded the diacetate (5.7 g, 99%) as a colorless oil. This residue was added to a hot solution of potassium acetate or sodium acetate (12 g) in acetic acid (100 mL) and water (5 mL). The mixture was stirred at 125 °C for 3 d. The solvent was then removed under reduced pressure, and the residue was dried under high vacuum. The residue was suspended in anhydrous dichloromethane, then acetic anhydride (25 mL) and 4-dimethylaminopyridine (DMAP, 100 mg) were added and the mixture was stirred overnight. For workup the mixture was added slowly to a vigorously stirred saturated solution of $NaHCO_3$ (200 mL water). The aqueous phase was extracted three times with ethyl acetate (3×100 mL). The combined organic phase was filtered through a small glass frit with silica gel, and the silica gel was washed with ethyl acetate. After evaporation of the solvent, the raw product was crystallized from ethanol to yield (–)-**10** (3.1 g, 54%) as a colorless solid. $[\alpha]_D^{20}$ = –10.2 (*c* = 1.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 2.01, 2.05, 2.11 (3×s, 3×3 H, 3×CH_3), 4.18 (dψt, *J* = 2.3, *J* = 7.6 Hz, 1 H, 1-H), 4.56, 4.68 (2×d, AB, *J* = 11.7 Hz, 2×1 H, $PhCH_2$), 5.05 (dd, *J* = 4.1, *J* = 10.7 Hz, 1 H, 3-H), 5.57–5.67 (m, 2 H, 4-H, 2-H), 5.85 (ddd, *J* = 2.0, *J* = 5.1, *J* = 10.2 Hz, 1 H, 5-H), 6.01 (dd, *J* = 2.5, *J* = 10.2 Hz, 1 H, 6-H), 7.26–7.40 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.6, 20.83, 20.85 (3×CH_3), 66.2 (C-4), 68.9 (C-3), 69.7 (C-2), 71.1 (CH_2Ph), 77.1 (C-1), 124.2 (C-5), 127.9, 128.4 ($C_{arom.}$), 132.5 (C-6), 137.7 (C_{ipso}), 169.8, 170.0, 170.3 (C=O) ppm. $C_{19}H_{22}O_7$ (362.4): calcd. C 62.98, H 6.12; found C 62.90, H 6.00.

(1*S*,2*R*,3*R*,4*S*)-2,3,4-Tri-*O*-acetyl-1-*O*-benzylconduritol B [(+)-9]. Route 1 [via (+)-8]: (1*S*,2*R*,3*R*,4*S*)-1-*O*-Benzylconduritol B [(+)-**8**, 1 g, 4.2 mmol] was dissolved in an ice-cooled mixture of pyridine (15 mL) and acetic anhydride (10 mL) and the mixture was stirred

overnight. Evaporation of the solvent gave pure (+)-**9** (1.5 g, 99%) as a colorless solid. **Route 2 [via (+)-7]:** (+)-**7** (10 g, 34 mmol) was dissolved in an ice-cooled mixture of pyridine (30 mL) and acetic anhydride (20 mL) and the mixture was stirred for 12 h. Evaporation of the solvent yielded a brown oil, which was taken up in ethyl acetate. The solution was then 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 the diacetate (13 g, 100%) as a brown oil. This diacetate was added to a hot solution of potassium acetate or sodium acetate (10 g) in anhydrous acetic acid (40 mL) and acetic anhydride (3 mL). The mixture was stirred at 130 °C for 5 d. The solvent was removed under high vacuum, and the residue was taken up in ethyl acetate. The solution was then filtered through a small glass frit with silica gel, and the silica gel was washed with ethyl acetate. After evaporation of the solvent, the raw product was purified by flash chromatography (cyclohexane/ethyl acetate, 3:2) to give a colorless oil (8.2 g). Crystallization from Et_2O/cyclohexane yielded (+)-**9** (6.5 g, 55%) as a colorless solid. R_f = 0.40 (cyclohexane/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +243 (c = 1.9, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.01 (s, 6 H, 2×CH_3), 2.03 (s, 3 H, CH_3), 4.28 (ddd, J = 7.8, J = 5.2, J = 2.4 Hz, 1 H, 1-H), 4.52, 4.66 (2×d, AB, J = 11.7 Hz, 2×1 H, CH_2), 5.24 (dd, J = 11.2, J = 8.1 Hz, 1 H, 3-H), 5.35 (dd, J = 11.3, J = 8.1 Hz, 1 H, 2-H), 5.57 (ddd, J = 7.6, J = 4.8, J = 2.5 Hz, 1 H, 4-H), 5.62 (dt, J = 10.3, J = 2.3 Hz, 1 H, $H_{olef.}$), 5.84 (dt, J = 10.7, J = 1.8 Hz, 1 H, $H_{olef.}$), 7.25–7.36 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.5; 20.6; 20.7 (CH_3), 71.2 (CH_2Ph), 71.7 (C-3), 71.8 (C-4), 72.1 (C-2), 76.5 (C-1), 126.1, 129.2 (C-5, C-6), 127.7, 127.8, 128.4 ($C_{arom.}$), 137.6 (C_{ipso}), 169.6, 170.0, 170.1 (C=O) ppm. $C_{19}H_{22}O_7$ (362.4): calcd. C 62.98, H 6.12; found C 62.63, H 5.60. HR-MS (ESI-pos., TOF): calcd. for $C_{19}H_{22}O_7Na$ $[M - H]^+$ 385.1299; found 385.1263.

(1*R*,2*S*,3*S*,4*R*)-2,3,4-Tri-*O*-acetyl-1-*O*-benzylconduritol B [(–)-9]: A solution of (–)-**8** was allowed to react under the conditions used for the preparation of (+)-**9** to give (–)-**9**. $[\alpha]_D^{20}$ = –229 (c = 1.5, $CHCl_3$). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**9**.

1,2,3,4,5-Penta-*O*-acetyl-6-*O*-benzyl-D-*myo*-inositol [(+)-11] and 1,2,4,5,6-Penta-*O*-acetyl-3-*O*-benzyl-*myo*-inositol [(+)-12]: A solution of sodium metaperiodate (2.1 g, 9.8 mmol, 1.5 equiv.) and ruthenium trichloride trihydrate (200 mg, 0.8 mmol) in water (24 mL) was added to a vigorously stirred ice-cooled solution of (+)-**9** (2.4 g, 6.6 mmol) in acetonitrile (120 mL). 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%, 100 mL). The aqueous layer was separated and extracted three times with EtOAc (3×100 mL). The combined organic layer was washed twice with brine and concentrated under reduced pressure to yield 2.4 g of an isomeric mixture of 3,4,5-tri-*O*-acetyl-6-*O*-benzyl-*myo*-inositol and 4,5,6-tri-*O*-acetyl-3-*O*-benzyl-*myo*-inositol as a colorless foam. Separation of the isomers was rendered counterproductive by protecting-group migration. The crude product was therefore dissolved in a cooled mixture of pyridine (15 mL) and acetic anhydride (15 mL) and stirred overnight. Evaporation of the solvent gave a colorless solid. The isomeric ratio of the two isomers (+)-**11** and (+)-**12** in the crude mixture was estimated by NMR spectroscopy to be 6:4. Recrystallization from ethanol yielded a pure isomeric mixture (1.9 g, 3.9 mmol, 60%). For analytical samples the isomers were separated by fractional crystallization from ethanol. **(+)-11:** R_f = 0.30 (ethyl acetate/cyclohexane, 3:2). $[\alpha]_D^{20}$ = +10.7 (c = 0.28, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 1.95, 1.96, 1.99, 2.01, 2.18 (s, 5×3 H, CH_3), 3.99 (ψt, J = 9.9 Hz, 1 H, 6-H), 4.62, 4.68 (2×d, AB, J = 11.7 Hz, 2×1 H, CH_2), 5.06 (dd, J = 9.9, J = 2.8 Hz, 1 H, 1-H), 5.09 (dd, J = 10.2, J = 3.0 Hz, 1 H, 3-H), 5.19 (ψt, J = 9.9 Hz, 1 H, 5-H), 5.41 (ψt, J = 10.2 Hz, 1 H, 4-H), 5.58 (ψt, J = 2.8 Hz, 1 H, 2-H), 7.20–7.36 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.4 (CH_3), 20.5 (2×CH_3), 20.6, 20.7 (CH_3), 68.5, 68.6 (C-2, C-3), 70.0 (C-4), 70.5 (C-1), 72.4 (C-5), 75.1 (CH_2Ph), 77.1 (C-6), 127.5, 127.8, 128.4 ($C_{arom.}$), 137.8 (C_{ipso}), 169.3(2×C=O), 169.5, 169.6, 170.0 (C=O) ppm. HR-MS (ESI-pos., TOF): calcd. for $C_{23}H_{29}O_{11}$ $[M + H]^+$ 481.1709; found 481.1710. **(+)-12:** R_f = 0.30 (ethyl acetate/cyclohexane, 3:2). $[\alpha]_D^{20}$ = +13.8 (c = 0.24, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 1.99, 2.00, 2.01, 2.02, 2.20 (s, 5×3 H, CH_3), 3.61 (dd, J = 10.2, J = 3.1 Hz, 1 H, 3-H), 4.41, 4.67 (2×d, AB, J = 12.2 Hz, 2×1 H, CH_2), 4.95 (dd, J = 2.8, J = 10.4 Hz, 1 H, 1-H), 5.09 (ψt, J = 9.9 Hz, 1 H, 5-H), 5.43 (ψt, J = 9.9 Hz, 1 H, 4-H), 5.49 (ψt, J = 10.4 Hz, 1 H, 6-H), 5.76 (ψt, J = 2.8 Hz, 1 H, 2-H), 7.21–7.37 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.5 (CH_3), 20.5 (2×CH_3), 20.6, 20.8 (CH_3), 66.7 (C-2), 69.2 (C-1), 69.5 (C-6), 70.9 (C-4), 71.2 (C-5), 71.8 (CH_2Ph), 74.5 (C-3), 127.8, 128.0, 128.5 ($C_{arom.}$), 136.9 (C_{ipso}), 169.56, 169.62, 169.8, 169.9, 170.0 (C=O) ppm. HR-MS (ESI-pos., TOF): calcd. for $C_{23}H_{29}O_{11}$ $[M + H]^+$ 481.1709; found 481.1710.

1,2,3,5,6-Penta-*O*-acetyl-4-*O*-benzyl-D-*myo*-inositol [(–)-11] and 2,3,4,5,6-Penta-*O*-acetyl-1-*O*-benzyl-*myo*-inositol [(–)-12]: The (–)-enantiomer **9** was *cis*-dihydroxylated and acetylated, as described for the conversion of (+)-**9**, to yield (–)-**11** {$[\alpha]_D^{20}$ = –9.8 (c = 0.30, $CHCl_3$)} and (–)-**12** {$[\alpha]_D^{20}$ = –15.1 (c = 0.29, $CHCl_3$)}. The R_f values and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**11** and (+)-**12**.

3-*O*-Benzyl-D-*myo*-inositol [(+)-14]: 1,2,4,5,6-Penta-*O*-acetyl-3-*O*-benzyl-*myo*-inositol [(+)-**12**; 30 mg, 0.06 mmol] was suspended in anhydrous methanol (5 mL) under argon and cooled to 4 °C. A 5.5 M sodium methoxide solution (10 μL, 0.05 mmol) was then added. The solution was allowed to warm to room temperature and stirred for 12 h. The solution was neutralized by addition of an ion exchanger (H^+ form, Dowex 50-X), then filtered; the resin was washed with water/methanol. The filtrate was first reduced in volume under high vacuum and then lyophilized to yield (+)-**14** (16 mg, 100%) as a colorless solid. $[\alpha]_D^{20}$ = +29 (c = 0.3, MeOH). Ref.[31] $[\alpha]_D^{20}$ = +25 (c = 0.5, MeOH). ^1H NMR ([D$_4$]MeOH): δ = 3.15 (ψt, J = 9.2 Hz, 1 H, 5-H), 3.22 (dd, J = 9.9, J = 2.8 Hz, 1 H, 3-H), 3.25 (dd, J = 8.1, J = 2.5 Hz, 1 H, 1-H), 3.60 (ψt, J = 9.7 Hz, 1 H, 6-H), 3.75 (ψt, J = 9.7 Hz, 1 H, 4-H), 4.11 (ψt, J = 2.8 Hz, 1 H, 2-H), 4.64, 4.71 (2×d, AB, J = 12.2 Hz, 2×1 H, CH_2), 7.20–7.45 (m, 5 H, Ph-H) ppm. ^{13}C NMR ([D$_4$]MeOH): δ = 70.9 (C-2), 73.0 (CH_2Ph),73.3 (C-1), 73.7 (C-4), 74.1 (C-6), 76.5 (C-5), 81.1 (C-3), 128.6, 129.1, 129.3 ($C_{arom.}$), 139.9 (C_{ipso}) ppm. HR-MS (ESI-neg., TOF): calcd. for $C_{13}H_{17}O_6$ $[M - H]^-$ 269.1033; found 269.1025.

1-*O*-Benzyl-D-*myo*-inositol [(–)-14]: A solution of (–)-**12** was allowed to react to give (–)-**14** under the conditions described for the preparation of (+)-**14**. $[\alpha]_D^{20}$ = –28 (c = 0.21, MeOH). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**14**.

6-*O*-Benzyl-D-*myo*-inositol [(–)-13]: The deprotection of 1,2,3,4,5-penta-*O*-acetyl-6-*O*-benzyl-*myo*-inositol [(+)-**11**; 120 mg, 0.25 mmol] was carried out as described for the preparation of (+)-**14** to yield 6-*O*-benzyl-*myo*-inositol (–)-**13** (70 mg, 100%) as a colorless solid. $[\alpha]_D^{20}$ = –8 (c = 0.25, MeOH). Ref.[8h] $[\alpha]_D^{20}$ = –5.9 (c = 1.1, MeOH). ^1H NMR ([D$_4$]MeOH): δ = 3.29 (ψt, J = 9.0 Hz, 1 H, 5-H), 3.33 (dd, J = 9.4, J = 2.3 Hz, 1 H, 1-H or 3-H), 3.49 (dd, J = 9.7, J = 3.1 Hz, 1 H, 1-H or 3-H), 3.61 (ψt, J = 10.2 Hz, 1 H, 4-H or 6-H), 3.63 (ψt, J = 9.7 Hz, 1 H, 4-H or 6-H), 3.94 (ψt, J =

2.8 Hz, 1 H, 2-H), 4.84 (s, 2 H, CH_2), 7.20–7.45 (m, 5 H, Ph-H) ppm. ^{13}C NMR ([D$_4$]MeOH): δ = 73.2, 73.3 (C-1, C-3), 74.4, 74.5 (C-2, C-6 or C-4), 76.0 (CH_2Ph), 76.4 (C-5), 83.2 (C-4 or C-6), 128.4, 129.1, 129.2 ($C_{arom.}$), 140.5 (C_{ipso}) ppm. HR-MS (ESI-neg., TOF): calcd. for $C_{13}H_{17}O_6$ [M – H]$^-$ 269.1033; found 269.1025.

4-*O*-Benzyl-D-*myo*-inositol [(+)-13]: A solution of (–)-**11** was allowed to react under the same conditions as those used for the preparation of (–)-**13** to give (+)-**13**. $[\alpha]_D^{20}$ = +9 (*c* = 0.25, MeOH). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**13**.

D-*myo*-Inositol 1,2,3,4,5-Pentakisphosphate [(–)-15] and D-*myo*-Inositol 1,2,4,5,6-Pentakisphosphate [(–)-16]: (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (1.25 g, 5.2 mmol) was added to a suspension of a isomeric mixture of 6-*O*-benzyl-*myo*-inositol [(–)-**13**] and 3-*O*-benzyl-*myo*-inositol [(+)-**14**] (235 mg, 0.87 mmol), obtained by saponification of a pure isomeric mixture of (+)-**11** and (+)-**12**, and 1*H*-tetrazole (610 mg, 8.7 mmol) in anhydrous dichloromethane (50 mL), and the solution was stirred at room temperature for 4 h. It was then cooled to –20 °C, and an anhydrous solution of *m*-CPBA (3.8 g, 15 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 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 brine. After evaporation of the solvent, the resulting colorless foam was purified by flash chromatography (CH_2Cl_2/MeOH, 95:5), whereby the isomeric products were separated to yield 3-*O*-benzyl-1,2,4,5,6-penta-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol [200 mg, 20%, R_f = 0.34 (CH_2Cl_2/MeOH, 95:5)] and 6-*O*-benzyl-1,2,3,4,5-penta-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol [350 mg, 35%, R_f = 0.27 (CH_2Cl_2/MeOH, 95:5)] as a colorless foam.

6-*O*-Benzyl-1,2,3,4,5-penta-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol: ^1H NMR ($CDCl_3$): δ = 4.00 (ψt, *J* = 9.4 Hz, 1 H, 6-H), 4.76–5.76 [m, 27 H, Ph-CH_2, 1-H, 2-H, 3-H, 4-H, 5-H, 5×$(CH_2)_2C_6H_4$], 7.06–7.50 (m, 25 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 67.8–69.6 [m, 5×$(CH_2)_2C_6H_4$], 73.6 (m, CH), 74.3 (Ph-CH_2), 74.8 (m, CH), 76.6 (m, CH), 77.3 (m, CH), 77.4 (m, CH), 77.8 (m, CH), 127.2–129.5 ($C_{arom.}$), 134.5–137.5 (C_{ipso}) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = +1.37, +0.12,–0.83, –1.65,–2.63 (PC-1, PC-2, PC-3, PC-4, PC-5) ppm.

3-*O*-Benzyl-1,2,4,5,6-penta-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol: ^1H NMR ($CDCl_3$): δ = 3.85 (d, *J* = 9.2 Hz, 1 H, 3-H), 4.53–5.80 [m, 27 H, Ph-CH_2, 1-H to 5-H, 5×$(CH_2)_2C_6H_4$], 7.06–7.57 (m, 25 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 68.0–69.7 [m, 5×$(CH_2)_2C_6H_4$], 72.5 (Ph-CH_2), 74.2 (m, CH), 75.9 (CH), 76.7 (m, CH), 77.3 (m, CH), 77.6 (m, CH), 127.6–129.6 ($C_{arom.}$), 134.4–137.0 (C_{ipso}) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = +0.10, –1.03, –2.51, –3.05, –3.23 (PC-1, PC-2, PC-4, PC-5, PC-6) ppm.

Deprotection/Hydrogenolysis: Preactivated Pd/C (150 mg, Degussa RW 10) in ethanol/water, (1:2, 30 mL) was added to a suspension of 6-*O*-benzyl-1,2,4,5,6-penta-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol or 3-*O*-benzyl-1,2,4,5,6-penta-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol (350 mg, 0.27 mmol) in ethanol (10 mL) and the mixture was stirred at room temperature under H_2 overnight. After the catalyst had been filtered off, the filtrate was concentrated under high vacuum and then lyophilized to give (–)-**15** or (–)-**16**, respectively, (150 mg, 96%) as a colorless, very hygroscopic foam. Separation by HPLC assured a purity >99%. **(–)-15:** $[\alpha]_D^{20}$ = –6.2 [*c* = 1.29, H_2O, pH adjusted to 6 (NH_4OH)]. Ref.[8h] $[\alpha]_D^{20}$ = –4.0 (*c* = 0.23, H_2O, free acid, pH = 1.6) ^1H NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.87 (ψt, *J* = 9.7 Hz, 1 H, H-6), 4.00 (ψq, *J* = 9.0 Hz, 1 H, 5-H), 4.03 (dψt, *J* = 2.5, *J* = 9.7 Hz, 1 H, 1-H), 4.08 (dψt, *J* = 2.5, *J* = 9.7 Hz, 1 H, 3-H), 4.34 (ψq, *J* = 9.4 Hz, 1 H, 4-H), 4.83 (dψt, *J* = 2.3, *J* = 9.7 Hz, 1 H, 2-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 71.3 (dd, *J* = 2.2, *J* = 6.7 Hz, C-6), 73.7 (m, C-3), 74.3 (dd, *J* = 2.3, *J* = 5.4 Hz, C-1), 74.8 (d, *J* = 6.4 Hz, C-2), 76.1 (m, C-4), 78.16 (m, C-5) ppm. $^{31}P\{^1H\}$ NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 1.96 (PC-1, PC-2), 2.21 (PC-3), 2.74 (PC-4), 2.87 (PC-5) ppm. HR-MS (ESI-neg., phosphoric acid, Q-TOF): calcd. for $C_6H_{16}O_{21}P_5$ [M – H]$^-$ 578.8844; found 578.8873. **(–)-16:** $[\alpha]_D^{20}$ = –7.8 [*c* = 1.3, H_2O, pH adjusted to 6 (NH_4OH)]. Ref.[8h] $[\alpha]_D^{20}$ = –7.1 (*c* = 0.86, H_2O, free acid, pH = 1.6). ^1H NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.64 (dd, *J* = 2.3, *J* = 9.9 Hz, 1 H, 3-H), 4.06 (ψq, *J* = 9.5 Hz, 51 H, 5-H), 4.08 (dψt, *J* = 2.5, *J* = 9.6 Hz, 1 H, 1-H), 4.27 (ψq, *J* = 9.8 Hz, 1 H, 4-H), 4.35 (ψq, *J* = 9.8 Hz, 1 H, 6-H), 4.76 (under HDO, 2-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 72.6 (s, C-3), 75.8 (m, C-1), 77.4 (d, *J* = 5.1 Hz, C-2), 78.6 (ψt, C-6), 79.5 (dd, *J* = 2.5, *J* = 6.6 Hz, C-4), 79.8 (m, C-5) ppm. $^{31}P\{^1H\}$ NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 1.96 (PC-1), 2.37 (PC-4), 2.61 (PC-6), 3.16 (PC-5), 3.78 (PC-2) ppm. HR-MS (ESI-neg., phosphoric acid, Q-TOF): calcd. for $C_6H_{16}O_{21}P_5$ [M – H]$^-$ 578.8845; found 578.8873.

D-*myo*-Inositol 2,3,4,5,6-Pentakisphosphate [(+)-16] and D-*myo*-Inositol 1,2,3,5,6-Pentakisphosphate [(+)-15]: A solution of an isomeric mixture of 1-*O*-benzyl-*myo*-inositol [(–)-**14**] and 4-*O*-benzyl-*myo*-inositol [(+)-**13**] was allowed to react under the conditions described for the preparation of (–)-**15** and (–)-**16** to give (+)-**15** and (+)-**16**. **(+)-15:** $[\alpha]_D^{20}$ = +6.0 (*c* = 1.0, H_2O). **(+)-16:** $[\alpha]_D^{20}$ = +8.2 (*c* = 1.5, H_2O). The ^1H NMR and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**15** and (–)-**16**, respectively.

D-*myo*-Inositol 1,3,4,5-Tetrakisphosphate [(–)-20]: (1*S*,2*R*,3*R*,4*S*)-2,3,4-Tri-*O*-acetyl-1-*O*-benzyl-conduritol B [(+)-**9**] was *cis*-dihydroxylated as described for the preparation of (+)-**11** and (+)-**12**. *p*-Toluenesulfonic acid monohydrate (6 mg) and triethyl orthoacetate (60 mg, 0.37 mmol) were added to a solution of the mixture of diols 3,4,5-tri-*O*-acetyl-6-*O*-benzyl-*myo*-inositol and 4,5,6-tri-*O*-acetyl-3-*O*-benzyl-*myo*-inositol (50 mg, 0.11 mmol) in anhydrous tetrahydrofuran (50 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 anhydrous methanol (15 mL) under argon and cooled to 4 °C. A 5.5 M sodium methoxide solution (18 μL, 0.1 mmol) was added. When the solution had come to room temperature and had been stirred for 2 h, it was neutralized by addition of an ion exchanger (H^+ form, Dowex 50-X), then filtered; the resin was washed with methanol. The filtrate was concentrated under reduced pressure, and the residue was dissolved in aqueous acetic acid (30 mL, 80%) and stirred at room temperature for 1 h. The organic phase was concentrated to yield a brown oil (30 mg), which contained only a mixture of 2-*O*-acetyl-6-*O*-benzyl-*myo*-inositol (**19**) and 2-*O*-acetyl-3-*O*-benzyl-*myo*-inositol. ^1H NMR ($CDCl_3$/[D$_4$]MeOH, 6:1): δ = 1.93, 2.04 (2×s, 0.65×3 H, 0.35×3 H, CH_3), 3.17-3.65 (m, 5 H, CH), 4.37, 4.64 (2×d, AB, *J* = 11.2 Hz, 2×0.35 H, Ph–CH_2), 4.74, 4.80 (2×d, AB, *J* = 11.2 Hz, 2×0.65 H, Ph-CH_2), 5.32 (ψt, *J* = 3.1 Hz, 0.65 H, 2-H), 5.55 (ψt, *J* = 2.8 Hz, 0.35 H, 2-H), 7.13–7.35 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$/[D$_4$]-MeOH, 6:1): δ = 20.7, 20.8 (2×CH_3), 70.1, 70.2, 72.3, 73.00, 73.4, 74.2, 74.4, 74.7, 77.9, 81.7 (C-ring), 72.0, 75.2 (Ph-CH_2), 127.6, 127.79, 127.81, 127.9, 128.16, 128.22, 128.3, 128.4, 129.9 ($C_{arom.}$), 134.6, 134.7 (C_{ipso}), 170.2, 171.9 (C=O) ppm. (1,5-Ddihydro-2,4,3-

benzodioxaphosphepin-3-yl)diethylamine (174 mg, 0.8 mmol) was added to a solution of 2-*O*-acetyl-6-*O*-benzyl-*myo*-inositol and 2-*O*-acetyl-3-*O*-benzyl-*myo*-inositol (30 mg, 0.11 mmol) and 1*H*-tetrazole (96 mg, 1.28 mmol) in dichloromethane (20 mL), and the solution was stirred at room temperature for 5 h. The solution was then cooled to –40 °C, and an anhydrous solution of *m*-CPBA (730 mg, 3 mmol) in dichloromethane (15 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 (30 mL) and washed consecutively with aqueous sodium sulfite (20%, 2 × 50 mL), saturated $NaHCO_3$ (3 × 50 mL), and brine. After evaporation of the solvent, the resulting colorless foam was purified by flash chromatography (CH_2Cl_2/MeOH, 95:5, R_f = 0.1) to yield a colorless foam (30 mg, 0.03 mmol, 30%), which contained 2-*O*-acetyl-6-*O*-benzyl-1,3,4,5-tetra-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-*myo*-inositol (purity >80%). This protected inositol (30 mg, 30 μmol) was deprotected, as described for the preparation of (–)-**28**, to give (–)-**20** as a colorless, very hygroscopic foam. Separation by preparative HPLC provided a sample (10 mg, 0.02 mmol) suitably pure for biological experiments. $[\alpha]_D^{20}$ = –4.7 [*c* = 0.67, H_2O, pH adjusted to 6 (NH_4OH)]. Ref.[8e] $[\alpha]_D^{20}$ = –4.08 (*c* = 2.02, H_2O, sodium salt, pH = 9.7). ^{1}H NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.86 (ψt, *J* = 10.2 Hz, 1 H, 6-H), 3.99 (ψq, *J* = 9.2 Hz, 1 H, 5-H), 4.00 (ψt, *J* = 9.7 Hz, 1 H, 1-H), 4.06 (dψt, *J* = 1.5, *J* = 9.7 Hz, 1 H, 3-H), 4.33 (ψs, 1 H, 2-H), 4.35 (ψq, *J* = 9.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 72.9 (s), 73.4 (m), 76.6 (m, 2 × C), 78.3 (m), 80.5 (m) ppm. ^{31}P{^{1}H} NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 2.11, 2.26, 2.65 (PC-1, PC-3, PC-5), 2.95 (PC-4) ppm. HR-MS (ESI-neg., phosphoric acid, Q-TOF): calcd. for $C_6H_{15}O_{18}P_4$ [M – H]$^-$ 498.9159; found 498.9209.

1-*O*-Benzyl-4-*O*-(di-*O*-benzylphospho)conduritol B (22): Dibenzyl phosphate (4.7 g, 16.9 mmol) was added to a solution of racemic monoepoxide **21** (3.1 g, 14.1 mmol) [for the preparation see the synthesis of (+)-**8**] in anhydrous dichloromethane (100 mL) and the solution was stirred at room temperature overnight. The solvent was then removed under reduced pressure. Recrystallization from ethyl acetate yielded **22** (2.8 g, 40%) as a voluminous, colorless solid. ^{1}H NMR ($CDCl_3$): δ = 3.71 (m, 2 H, 2-H, 3-H), 4.05 (m, 1 H, 1-H), 4.39 (br. s, 2 H, OH), 4.69 and 4.79 (2 × d, AB, *J* = 11.7 Hz, 2 H, $PhCH_2$), 4.78 (m, 1 H, 4-H), 4.97–5.11 (m, 4 H, CH_2-OP), 5.47 (dt, *J* = 10.7, *J* = 2.0 Hz, 1 H, 6-H), 5.72 (dt, *J* = 10.7, *J* = 2.0 Hz, 1 H, 5-H), 7.23 (m, 15 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 69.9 (ψt, *J* = 5.6 Hz, $CH_2C_6H_4$), 72.5 ($PhCH_2$), 74.5 (d, *J* = 3.0 Hz, C-3), 74.9 (s, C-2), 78.4 (s, C-1), 79.7 (d, CH, *J* = 5.1 Hz, C-4), 127.8 (d, *J* = 7.1 Hz, C-5), 127.7, 127.77, 127.83, 128.0, 128.1, 128.3, 128.4, 128.45, 128.56, 128.65, 128.73 ($C_{arom.}$), 130.3 (s, C-6), 135.4, 135.5 (C_{ipso}-CH_2P), 138.3 (C_{ipso}) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 0.95 ppm. ^{31}P NMR ($CDCl_3$): δ = 0.95 (ψsext, $J_{P,H}$ = 8.0 Hz) ppm.

(1*S*,2*R*,3*R*,4*S*)-1-*O*-Benzyl-2,3,4-tris-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)conduritol B [(+)-24]: Triacetate (+)-**9** (0.55 g, 1.3 mmol) was suspended in anhydrous methanol (10 mL) under argon and cooled to 4 °C. A 5.5 M sodium methoxide solution (0.1 mL, 0.55 mmol) was then added, the solution was allowed to warm to room temperature, and stirred for 12 h. The solution was neutralized by addition of an ion exchanger (H^+ form, Dowex 50-X) and filtered; the resin was washed with methanol. The filtrate was first reduced in volume under high vacuum to yield (+)-**8** (350 mg, 100%) as a colorless solid. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (1.1 g, 4.7 mmol) was added to a suspension of this triol (+)-**8** (260 mg, 1.1 mmol) and 1*H*-tetrazole (550 mg, 7.8 mmol) in anhydrous dichloromethane (40 mL), and the solution was stirred at room temperature for 4 h. It was then cooled to –20 °C, and an anhydrous solution of *m*-CPBA (3.3 g, 13 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 reaction mixture was diluted with dichloromethane (100 mL) and washed consecutively with aqueous sodium sulfite (20%, 2 × 100 mL), saturated $NaHCO_3$ (3 × 150 mL), and brine. After evaporation of the solvent, the resulting colorless foam was purified by flash chromatography (cyclohexane/ethyl acetate, 1:3) to yield (+)-**24** (500 mg 58%) as a colorless foam. R_f = 0.38 (ethyl acetate/cyclohexane, 3:1). $[\alpha]_D^{20}$ = +28.5 (*c* = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 4.42 (m, 1 H, 1-H), 4.67–5.64 [m, 15 H, 2-H, 3-H, 4-H, 3 × $(CH_2)_2C_6H_4$], 5.89 (dψt, *J* = 10.7, *J* = 1.8 Hz, 1 H, 5-H or 6-H), 6.03 (dψt, *J* = 10.2, *J* = 2.0 Hz, 1 H, 5-H or 6-H), 7.16–7.46 (m, 17 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 67.1 (d, *J* = 6.3 Hz), 68.6 (d, *J* = 7.0 Hz), 68.9 (d, *J* = 7.0 Hz), 69.1–69.4 (m), 69.5 (d, *J* = 8.3 Hz) ($CH_2)_2C_6H_4$], 71.5 ($PhCH_2$), 77.5 (m), 77.9 (m), 78.7 (m) (C-1, C-2, C-3, C-4), 126.25 (C-5 or C-6), 128.1–129.5 (C-5 or C-6, $C_{arom.}$), 134.9, 135.0, 135.2, 135.3, 135.4, 135.5, 137.0, 137.5 (C_{ipso}) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = –2.03, –1.20, 0.04 (PC-2, PC-3, PC-4) ppm. $C_{37}H_{37}O_{13}P_3$ (782.6): calcd. C 56.78, H 4.77; found C 56.51, H 5.01.

(1*R*,2*S*,3*S*,4*R*)-1-*O*-Benzyl-2,3,4-tri-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)conduritol B [(–)-24]: A solution of (–)-**9** was allowed to react under the conditions described for the preparation of (+)-**24** to give (–)-**24**. $[\alpha]_D^{20}$ = –31.6 (*c* = 0.5, $CHCl_3$). The R_f value and ^{1}H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**24**.

D-*myo*-Inositol 3,4,5-Trisphosphate [(–)-25] and *myo*-Inositol 4,5,6-Trisphosphate (26): A solution of sodium metaperiodate (140 mg, 0.65 mmol, 1.5 equiv.) and ruthenium trichloride trihydrate (13 mg, 0.04 mmol) in water (2 mL) was added to a vigorously stirred ice-cooled solution of (+)-**24** (350 mg, 0.44 mmol) in acetonitrile (120 mL). 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) and the aqueous layer was separated and extracted with EtOAc (3 × 500 mL). The combined organic layers were washed with brine and concentrated under reduced pressure to yield an isomeric mixture of diols (290 mg, 80%) as a colorless solid. Preactivated Pd/C (100 mg, Degussa RW 10) in ethanol/water (1:2, 30 mL) was added to a suspension of the crude product (200 mg, 0.24 mmol) in ethanol (10 mL), and 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. At this stage the isomers were separated by preparative HPLC to give (–)-**25** (50 mg, 12 μmol, 50%) and **26** (30 mg, 7 μmol, 30%) with purity >99% as colorless, very hygroscopic foam. The analytical data for *myo*-inositol 3,4,5-trisphosphate [(–)-**25**] are in agreement with previously published results.[11] **26:** ^{1}H NMR [D_2O, pH adjusted to 8.5 (ND_4OD)]: δ = 3.64 (dd, *J* = 2.0, *J* = 9.7 Hz, 2 H, 1-H and 3-H), 3.98 (ψs, 1 H, 2-H), 4.00 (ψq, *J* = 9.2 Hz, 1 H, 5-H), 4.19 (ψq, *J* = 9.0 Hz, 2 H, 4-H and 6-H) ppm. ^{13}C NMR [D_2O, pH adjusted to 8.5 (ND_4OD)]: δ = 71.3 (s, C-2), 71.7 (s, C-1 and C-3), 75.9 (m, C-4 and C-6), 78.0 (m, C-5) ppm. ^{31}P{^{1}H} NMR [D_2O, pH adjusted to 8.5 (ND_4OD)]: δ = 2.07 (PC-5), 5.67 (PC-4 and PC-6) ppm. ^{31}P NMR [D_2O, pH adjusted to 8.5 (ND_4OD)]: δ = 2.07 (d, *J* = 9.4 Hz, 1 P, PC-5), 5.67 (d, *J* = 8.3 Hz, 2 P, PC-4 and PC-6) ppm. For further analytical data see ref.[32]

D-*myo*-Inositol 1,5,6-Trisphosphate [(+)-25] and *myo*-Inositol-4,5,6-Trisphosphate (26): A solution of (–)-**24** was allowed to react under

the conditions used for the preparation of (–)-**25** and **26** to give (+)-**25** and **26**. $[\alpha]_D^{20}$ = +2.2 (*c* = 2.3, H_2O, free acid). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**25** and **26**.

1,2,3,4,5-Penta-*O*-acetyl-6-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(+)-27]: Pd/C (20 mg) was added to a suspension of (+)-**11** (80 mg, 0.17 mmol) in ethyl acetate (20 mL). After the mixture had been stirred at room temperature for 4 h, the catalyst was filtered off and washed with ethyl acetate. The filtrate was concentrated under reduced pressure to give the monoalcohol (66 mg, 100%) as a colorless foam. (1,5-Dihydro-2,4,3-benzodioxaphosphepin-3-yl)diethylamine (50 mg, 0.21 mmol) was added to a suspension of the 1,2,3,4,5-penta-*O*-acetyl-D-*myo*-inositol (66 mg, 0.17 mmol) and 1*H*-tetrazole (36 mg, 0.5 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 (190 mg, 0.8 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 (40 mL) and washed consecutively with aqueous sodium sulfite (20%, 2×30 mL), saturated $NaHCO_3$ (3×50 mL), and brine. After evaporation of the solvent, the resulting colorless foam was purified by flash chromatography (ethyl acetate) to yield (+)-**27** (50 mg, 51%) as a colorless foam. R_f = 0.45 (ethyl acetate). $[\alpha]_D^{20}$ = +16.4 (*c* = 0.24, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.00, 2.02, 2.12, 2.14, 2.21 (5×s, 5×3 H, CH_3), 4.95-5.22 [m, 5 H, $(CH_2)_2$-C_6H_4, 6-H], 5.11 (dd, *J* = 3.1, *J* = 10.7 Hz, 1 H, 3-H), 5.27 (dd, *J* = 2.8, *J* = 10.4 Hz, 1 H, 1-H), 5.31 (ψt, *J* = 9.7 Hz, 1 H, 5-H), 5.49 (ψt, *J* = 10.2 Hz, 1 H, 4-H), 5.60 (ψt, *J* = 2.8 Hz, 1 H, 2-H), 7.21–7.38 (m, 4 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.4, 20.5, 20.57, 20.60, 20.7 (5×CH_3), 68.2 (C-2), 68.4 (t, *J* = 3.8 Hz), 67.8 (s) (C-1, C-3), 68.6-68.9 [$(CH_2)_2C_6H_4$], 69.1 (C-4), 71.0 (d, *J* = 2.9 Hz, C-5), 76.3 (d, *J* = 5.7 Hz, C-6), 128.6, 128.7, 129.1 ($C_{arom.}$), 134.6, 134.7 (C_{ipso}), 169.5, 169.7, 169.8, 170.1 (C=O) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = –0.63 (PC-6) ppm. HR-MS (ESI-pos.): calcd. for $C_{24}H_{29}O_{14}PNa$ $[M + Na]^+$ 595.119; found 595.1193.

1,2,3,5,6-Penta-*O*-acetyl-4-*O*-(3-oxo-1,5-dihydro-3λ^5-2,4,3-benzodioxaphosphepin-3-yl)-D-*myo*-inositol [(–)-27]: A solution of (–)-**11** was allowed to react under the conditions described for the preparation of (+)-**27** to give (–)-**27**. $[\alpha]_D^{20}$ = –15.9 (*c* = 0.40, $CHCl_3$). The R_f value and ^1H and ^{13}C NMR spectroscopic data are identical with those obtained for (+)-**27**.

D-*myo*-Inositol 6-Phosphate [(–)-28]: Preactivated Pd/C (30 mg, Degussa RW 10) was added to a suspension of (+)-**27** (20 mg, 34 μmol) in ethanol/water (1:1, 30 mL) and the mixture was stirred at room temperature under hydrogen 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 addition of an ion exchanger (H^+ form, DOWEX 50-X) and filtered; the resin was washed with water. The filtrate was lyophilized to give (–)-**28** (10 mg, 99%) as a colorless, very hygroscopic foam. $[\alpha]_D^{20}$ = –2.5 [*c* = 0.5, H_2O, pH adjusted to 6 (NH_4OH)]. Ref.[8i,8j] $[\alpha]_D^{20}$ = –1.1 (*c* = 5, H_2O, biscyclohexylammonium salt). ^1H NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 3.38 (ψt, *J* = 9.2 Hz, 1 H, 5-H), 3.52 (dd, *J* = 2.8, *J* = 9.9 Hz, 1 H, 3-H), 3.61 (dd, *J* = 3.0, *J* = 9.7 Hz, 1 H, 1-H), 3.65 (ψt, *J* = 9.9 Hz, 1 H, 4-H), 4.03 (ψt, *J* = 2.8 Hz, 1 H, 2-H), 4.08 (ψq, *J* = 8.7 Hz, 1 H, 6-H) ppm. ^{13}C NMR [D_2O, 101 MHz, pH adjusted to 6 (ND_4OD)]: δ = 71.2 (s, C-3), 71.3 (d, *J* = 3.2 Hz, C-1), 72.1 (s, C-2), 72.5 (s, C-4), 74.1 (d, *J* = 3.8 Hz, C-5), 77.1 (d, *J* = 5.7 Hz, C-6) ppm. $^{31}P\{^1H\}$ NMR [D_2O, pH adjusted to 6 (ND_4OD)]: δ = 4.55 (PC-6) ppm. HR-MS (ESI-neg., phosphoric acid, Q-TOF): calcd. for $C_6H_{12}O_9P$ $[M - H]^-$ 259.0246; found 259.0219.

D-*myo*-Inositol 4-Phosphate [(+)-28]: A solution of (–)-**27** was allowed to react under the conditions used for the preparation of (–)-**28** to give (+)-**28**. $[\alpha]_D^{20}$ = +3.3 [*c* = 0.4, H_2O, pH adjusted to 6 (NH_4OH)]. The ^1H NMR and ^{13}C NMR spectroscopic data are identical with those obtained for (–)-**28**.

1-*O*-Benzyl-2,3-*O*-isopropylideneconduritol B (30): 1-*O*-Benzyl-conduritol B (**8**; 0.97 g, 4.2 mmol) was dissolved in 2,2-dimethoxypropane (20 mL) and anhydrous acetone (20 mL). Pyridinium *p*-toluenesulfonic acid (PPTSA; 40 mg) was then added, and the solution was stirred for 3 d. The solution was then diluted with diethyl ether (30 mL), and 2 N aqueous NaOH (20 mL) and brine (20 mL) were added. The aqueous layer was separated and extracted with diethyl ether (3×30 mL). The combined organic layers were concentrated under reduced pressure to yield **30** (1.0 g, 81%) as a yellowish oil. R_f = 0.30 (cyclohexane/ethyl acetate, 1:1). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.48 (s, 6 H, CH_3), 3.08 (br. s, 1 H, OH), 3.51 (dd, *J* = 9.9, *J* = 8.4 Hz, 1 H, 2-H or 3-H), 3.66 (dd, *J* = 9.7, *J* = 8.1 Hz, 1 H, 2-H or 3-H), 4.26 (ddd, *J* = 3.1, *J* = 8.1, *J* = 1.5 Hz, 1 H, 1-H or 4-H), 4.45 (dψt, *J* = 8.0, *J* = 1.4 Hz, 1 H, 1-H or 4-H), 4.67 and 4.84 (2×d, AB system, *J* = 12.2 Hz, 2×1 H, Ph-CH_2), 5.65 and 5.69 (2×d, *J* = 10.2 Hz, 2×1 H, 5-H and 6-H), 7.27–7.40 (m, 5 H, PhH) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.0 (2×CH_3), 70.6 (C-4), 77.3 (C-1), 80.1, 80.9 (C-2 and C-3), 111.03 [$C(CH_3)_2$], 126.8 (C-5 or C-6), 127.7, 128.3, 128.7 (C_6H_5), 130.8 (C-5 or C-6), 138.2 (C_{ipso}) ppm. MS (EI, 70 eV): *m/z* (%) = 276 (3) [M^+], 170 (2) [M^+ + H – OBn], 107 (19), 91 (100), 43 (54), 41 (35). IR (KBr): $\tilde{\nu}$ = 3400 (br. m), 3040 (w), 2900, 2860 (w), 1500 (w), 1450, 1370, 1050 (m), 735 (m), 695 (m) cm^{-1}. HR-MS (ESI-pos.): calcd. for $C_{16}H_{20}O_4$ $[M^+]$ 276.1346; found 276.1362.

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