Efficient and Systematic Syntheses of Enantiomerically Pure and Regiospecifically Protected *myo*-Inositols

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Abstract: Efficient and systematic syntheses of a variety of enantiomerically pure and regiospecifically protected *myo*-inositols, which can be readily used as precursors for most natural and unnatural derivatives of *myo*-inositol, have been developed. The key strategies are the use of camphor as a protecting group *and* a chiral auxiliary and the development of regiospecific control in various steps. The diastereomerically pure 1D-2,3-*O*-(1′*R*,2′*R*,4′*R*-1′,7′,7′-trimethyl[2.2.1]bicycloheptyl-2′-ylidene)-*myo*-inositol (**1a**) was obtained in 31% yield via acetalization of *myo*-inositol with D-camphor dimethyl acetal followed by crystallization from methanol. In route A, silylation of tetrol **1a** with *tert*-butyldiphenylsilyl chloride (TBDPS-Cl) afforded 1-*O*-TBDPS-4,5,6-triol **7** exclusively, which served as a key intermediate. Further protection with other reagents, exhaustively or regiospecifically, combined with selective deprotecting steps, led to protected *myo*-inositols with free hydroxyls at 1-, 5-, 6-, 1,4-, 4,5-, 5,6-, 1,4,5-, and 1,4,6-positions. In route B, the diastereomeric camphor-protected tetrols **1** were protected with a bifunctional silylating agent, 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (TIPDS-Cl_2), to give diol **31**. Subsequent protections/deprotections led to *myo*-inositols derivatives with free hydroxyls at 2-, 1,2-, 2,3-, 4,5-, 5,6-, 1,2,6-, and 1,3,4-positions. In route C the 4,5,6-triol **7** (from route A) was deacetalized to afford 1-TBDPS-inositol. 1-TBDPS-inositol after selective trisbenzoylation and alkylation followed by debenzoylation afforded 1,2,6-protected inositol (free hydroxyls at 3,4,5-positions). In route D the 4,5-diol **31** (from route B) was deacetalized to give 1,6-TIPDS-inositol. Alkylation or benzoylation of 1,6-TIPDS-inositol and subsequent desilylation afforded 1,6-diols (protected at 2,3,4,5-positions). Overall, the various precursors of phosphoinositides were obtained in 4-8 steps from inositol in 5-25% yields.

The various inositol phosphates and inositol phospholipids, including phosphatidylinositol (PI),[1] PI-4-phosphate (PI-4-P), PI-4,5-bisphosphate (PI-4,5-P_2), PI-3,4-bisphosphate (PI-3,4-P_2), PI-3,4,5-trisphosphate (PI-3,4,5-P_3), inositol 1-phosphate (IP), inositol 1,4-bisphosphate (1,4-IP_2), inositol 1,4,5-trisphosphate (1,4,5-IP_3), inositol 1,3,4-trisphosphate (1,3,4-IP_3), inositol 1,3,4,5-tetrakisphosphate (1,3,4,5-IP_4), and the corresponding inositol 1,2-cyclic phosphates (IcP, IcP-4-P, and IcP-4,5-P_2) have been found to trigger many important biological processes, through very complex pathways.[2a-g] In addition, membrane protein anchors contain a glucosylphosphatidylinositol (GPI) moiety[2h-k] and glucosylinositol phosphate (GIP) is a partial structure of putative modulators involved in the cellular response to insulin.[2k-m] Apart from heterogeneity of fatty acids and carbohydrates in inositol phospholipids and inositol phosphoglycans, more than 20 different inositol phosphates have been identified in different cells.[2e,g] Interconversion between phosphoinositides is carried out by the large number of highly specific phospholipases, kinases, and phosphatases.[2g] Most of these processes have been discovered in the past few years, and more are still forthcoming. Investigation of the chemical mechanism of these processes have been hampered by the difficulty in the synthesis of various substrates, substrate analogues, and inhibitors. Although the synthesis of these compounds has received extensive attention in recent years, many of the inositol derivatives and their analogues are not yet readily available. 1D-*myo*-Inositol-1,5,6-triphosphate, for example, is one of the most expensive compounds ($89/10 μg) in the 1992 Sigma catalogue. The prices for one milligram of other inositol polyphosphates range from $100 to $5000.

The main problem in such syntheses lies in the availability of properly protected and enantiomerically pure *myo*-inositol derivatives. Numerous syntheses of such phosphoinositide precursors have been reported to date.[3] However, most of these procedures involve numerous protecting and optical resolution steps, which lead to low overall yields. In addition, many of the reported syntheses are aimed at specific phosphoinositides utilizing a specific starting material. The isomers of di-*O*-cyclohexylidene-[4] and di-*O*-isopropylidene-*myo*-inositol[5] have found a widespread application as convenient starting derivatives. However, these compounds are synthesized from *myo*-inositol as a mixture of three positional isomers and separated by a combination of crystallization and chromatography.[4,5] The separated positional isomers are mixtures of enantiomers, which are generally resolved by further derivatization with a chiral auxiliary.[3d] This procedure lengthens the total synthesis by three steps: (i) derivatization of a racemic inositol derivative with a chiral auxiliary, (ii) separation

(1) Abbreviations: GIP, 6-*O*-(2-amino-2-deoxy-α-D-glucopyranosyl)-inositol 1-phosphate; GPI, 6-*O*-(2-amino-2-deoxy-α-D-glucopyranosyl)phosphatidylinositol; IP, inositol 1-phosphate; 1,4-IP_2, inositol 1,4-bisphosphate; 1,4,5-IP_3, inositol 1,4,5-trisphosphate; 1,3,4-IP_3, inositol 1,3,4-trisphosphate; 1,2,6-IP_3, inositol 1,2,6-trisphosphate; 1,3,4,5-IP_4, inositol 1,3,4,5-tetrakisphosphate; IcP, inositol 1,2-cyclic phosphate; IcP-4-P, inositol 1,2-cyclic phosphate-4-phosphate; IcP-4,5-P_2, inosltol 1,2-cyclic phosphate-4,5-bisphosphate; MOM-Cl, methoxymethylene chloride; PI, phosphatidylinositol; PI-4-P, phosphatidylinositol 4-phosphate; PI-3,4-P_2, phosphatidylinositol 3,4-bisphosphate; PI-4,5-P_2, phosphatidylinositol 4,5-bisphosphate; PI-3,4,5-P_3, phosphatidylinositol 3,4,5-trisphosphate; TBDMS-Cl, *tert*-butyldimethylsilyl chloride; TBDPS-Cl, *tert*-butyldiphenylsilyl chloride; TIPDS-Cl_2, 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane; TMS-DEA, (diethylamino)trimethylsilane; TMSOTf, trimethylsilyl triflate.

(2) Recent reviews on phosphoinositide metabolism: (a) Berridge, M. J.; Irvine, R. F. *Nature* **1984**, *312*, 315-321. (b) Berridge, M. J. *Biochem. J.* **1984**, *220*, 345-360. (c) Hokin, R. H. *Ann. Rev. Biochem.* **1985**, *54*, 205-235. (d) Michell, R. H. *Nature* **1986**, *319*, 176-177. (e) Majerus, P. W.; Conolly, T. M.; Bansal, V. S.; Inhorn, R. C.; Ross, T. S.; Lips, D. L. *J. Biol. Chem.* **1988**, *263*, 3051-3054. (f) Berridge, M. J. *Ann. Rev. Biochem.* **1987**, *56*, 159-193. (g) Berridge, M. J.; Irvine, R. F. *Nature* **1989**, *341*, 197-205. GPI as membrane protein anchors: (h) Ferguson, M. A. J.; Williams, A. F. *Ann. Rev. Biochem.* **1988**, *57*, 285-320. (i) Low, M. G. *Biochem. J.* **1987**, *244*, 1-13. (j) Low, M. G. *FASEB J.* **1989**, *3*, 1600-1608. (k) Special Issue *Cell. Biol. Int. Rep.* **1991**, *15*, 739-1166. Insulin mimetics: (l) Romero, G.; Luttrell, L.; Rogol, A.; Zeller, K.; Hewlett, E.; Larner, J. *Science* **1988**, *240*, 509-511. (m) Saltiel, A. R.; Cuatrecasas, P. *Am. J. Physiol.* **1988**, *255*, c1-c11. (n) Farese, R. V. *Proc. Soc. Exp. Biol. Med.* **1990**, 312-324. See, also: ref 2k.

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(4) (a) Garegg, P. J.; Lindberg, B.; Kvarnstroem, I.; Svensson, S. C. T. *Carbohydr. Res.* **1985**, *139*, 209-215. (b) Garegg, P. J.; Iversen, T.; Johansson, R.; Lindberg, B. *Carbohydr. Res.* **1984**, *130*, 322-326. (c) Garegg, P. J.; Lindberg, B.; Kvarnstroem, I.; Svensson, S. C. T. *Carbohydr. Res.* **1988**, *173*, 205-216.

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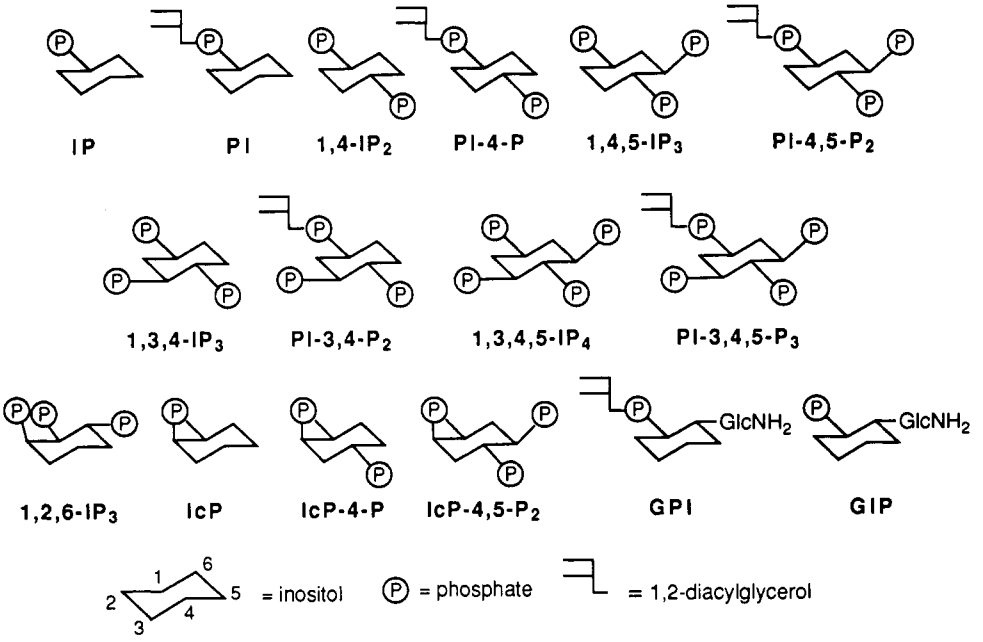
Chart I



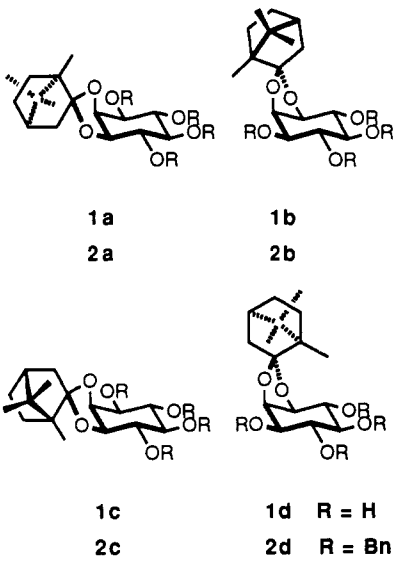
of diastereomers, and (iii) removal of the chiral auxiliary. Alternatively, optically active precursors of phosphoinositides may be synthesized from chiral natural derivatives of inositol[6] and carbohydrates,[7] via asymmetric acylation of prochiral inositol derivative with chiral acylating reagents[8] and using enzymatically[9] promoted asymmetric induction.

In this paper we report efficient and systematic syntheses of most of the possible enantiomerically pure isomers of protected *myo*-inositols starting from a common precursor, camphor-protected inositol. Uniform or selective derivatization of the free hydroxyl groups of these intermediates, followed by deprotection, can lead to all possible naturally occurring inositol derivatives as well as some unnatural derivatives. Some of the synthetic approaches can also be applied to synthesis of the analogues of *myo*-inositol derivatives including potential enzyme inhibitors.

Results

Overall Goals and Strategies. Our main goals are to devise the synthetic scheme such that a common intermediate can lead to several derivatives and to improve the yields of syntheses by reducing the number of steps. The target compounds are enantiomerically pure *myo*-inositol derivatives with all but the following hydroxyl groups protected:[10] 1 (for the synthesis of PI and IP), 1,4 (for PI-4-P and 1,4-IP_2), 1,3,4 (for PI-3,4-P_2 and 1,3,4-IP_3), 1,4,5 (for PI-4,5-P_2 and 1,4,5-IP_3), 1,2,6 (for 1,2,6-IP_3), 1,3,4,5 (for PI-3,4,5-P_3 and 1,3,4,5-IP_4), 1,6 (for GPI), and 1,2 (for IcP). In addition to above phosphates it should be also possible to synthesize other types of compounds such as unnatural polyphosphates and their phosphorothioate and methanophosphonate analogues.

Chart II



The first key strategy in our synthesis is to use D-camphor instead of cyclohexanone as the first protecting agent. Simultaneously, camphor also serves as a chiral auxiliary and eliminates the need for optical resolution at the later stage of synthesis. The second key strategy is to develop regiospecificity in the introduction of protecting groups. Thus, the first protecting group (camphor) is introduced regiospecifically at the 2,3-positions to give tetrol **1a**; the second protecting group is introduced regiospecifically at the 1-position to give triol **7** (Route A) or at the 1,6-positions to give diol **31** (Route B). Further regiospecific or exhaustive protections of **7** and **31**, combined with regiospecific deprotections, lead to a variety of useful derivatives. Two major branches of routes A and B are designated as Route C and Route D, respectively. Protective groups cleavable under hydrogenolytic conditions utilized in a number of the reported syntheses have been precluded since they are less suitable for the synthesis of natural inositol phospholipids with unsaturated acyl chains or phosphorothioate derivatives of inositol. Details of the synthetic schemes are described in the following sections.

Regiospecific Protection of *myo*-Inositol with Bornanediyl Group. It has been shown previously that acetalization of *myo*-

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(10) A counterclockwise numbering of inositol (equivalent to D-configuration) is used throughout this paper as recently suggested: IUB Nomenclature Committee, *Biochem. J.* **1989**, *258*, 1–2.

Table I. Positional Specificity of the Protection of 2,3-*O*-Cyclohexylidene-*myo*-inositol (**3**)

reagent[a]	conditions[b]	products	ratio[c] **4/5**	yields **4 + 5** [%]
TBDPS-Cl	DMF, imidazole, −10 °C → 4 °C	**4**, **5**[d]	20	75
	pyridine, imidazole, −10 °C → 4 °C	**4**, **5**[d]	>20	
TBDMS-Cl	DMF, imidazole, 4 °C	**4**, **5**[e]	3.6	31
$TIPDS-Cl_2$	DMF, imidazole, −10 °C → 4 °C	**4**[f]		75
TMS-DEA	pyridine, −20 °C	**4**, **5**[g]	0.5	68
PhCH(OTBDMS)COCl	pyridine, −40 °C–30 °C	**4**[h]	>20	55

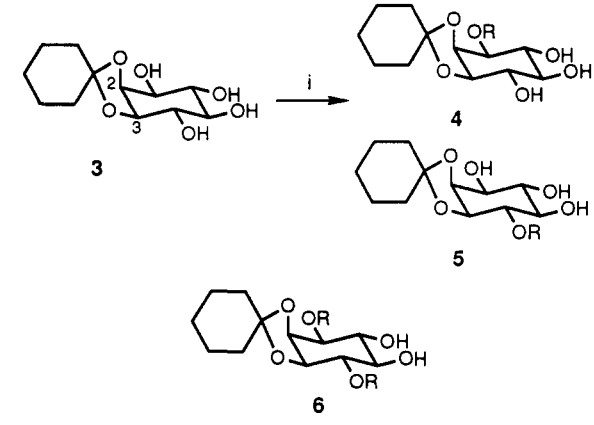
[a] Alkylation reactions with MOM-Cl and 2-(ethoxycarbonyl)benzyl bromide proceeded with low regioselectivity and low yields of **4** + **5**. [b] 10% excess of protecting reagents was applied in each case. [c] Due to difficulties in the quantitative spectroscopic analysis of complex mixtures containing several positional isomers, and bis- and higher protected compounds, the regioselectivity of the protection is expressed as yields and ratios of major isolated products. [d] 1,4-Bissilyl derivative is obtained with 2 equiv of TBDPS-Cl. [e] With 2.2 equiv of TBDMS-Cl 1,4,6-trissilyl ether (45%) and 1,4,5-trissilyl ether (14%) were obtained in addition to mono- and bissilyl ethers. [f] Cyclic 1,6-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl) bisether was the only isolated product. [g] Isomers **4** and **5** were not separated; the ratio was determined from ^1H NMR spectrum; the reaction affords a number of more highly protected isomers, which were not analyzed. [h] Only 1-protected derivative was isolated.

inositol with cyclohexanone, 1,1-dimethoxycyclohexane or 2,2-dimethoxypropane followed by hydrolysis of *trans*-acetal groups afforded 1,2-*O*-acetals of *myo*-inositol in up to 85% yield.[7e,11] Monoacetalization is thus the most efficient process of several known regioselective protections of inositol. Camphor dimethyl acetal served as our monoacetalization reagent since D-camphor is the best available chiral ketone with a quaternary (and thus nonenolizable) chiral center in a close vicinity to the carbonyl group. Acetalization of inositol with D-camphor dimethyl acetal afforded a mixture containing numerous mono- and bisacetals, initially. Removal of *trans*-acetal groups by alcoholysis gave a mixture of four diastereomers **1a–d** differing in their configurations of *myo*-inositol (1D-2,3- or 1D-1,2-acetal) and at the quaternary carbon atom C-2 of the camphor residue (*O*-3-exo or *O*-3-endo).[12] Crystallization of the mixture from methanol afforded pure diastereomer **1a** in 31% yield.

Configurational assignment of **1a** was carried out by converting it into the corresponding tetrabenzyl ether **2a**, followed by spectroscopic and chromatographic comparison of the latter with stereoisomers **2a–d** obtained earlier.[12] The configuration of **1a** was assigned as 1D-2-*O*-*exo*-3-*O*-*endo*.[12,13]

Route A: Regiospecific Monoprotection of Tetrol 1a To Give Triol 7a. To select reagents with which to carry out further regioselective single protection of **1a**, we used 2,3-*O*-cyclohexylidene-*myo*-inositol (**3**) as a model substrate (Scheme I). The results indicate that in most cases 1- and 4-hydroxyl groups were the preferred sites of the protection. The yields of protected products **4** and **5** and reaction conditions are summarized in Table I. From a preparative standpoint, sufficiently good distinction between these hydroxyl groups was achieved with sterically bulky silyl and acyl reagents such as *tert*-butyldiphenylsilyl chloride (TBDPS-Cl) and (*tert*-butyldimethylsilyloxy)phenylacetyl chloride.[14] With smaller groups such as *tert*-butyldimethylsilyl (TBDMS) and trimethylsilyl selectivity was generally low, both in terms of the position of the protected hydroxyl groups and the yields of monoprotected compounds. The formation of bis-1,4-protected derivatives **6** and various tris-protected compounds was usually observed at the cost of the yield of monoprotected products **4** and **5**. In the case of bulky reagents such as TBDPS-Cl the 1-hydroxyl function was the most reactive. The reaction of **3** with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane ($TIPDS-Cl_2$) afforded exclusively 1,6-bissilyl derivative in agreement with recent report.[15] With a less bulky TMS-DEA the 4-hydroxyl was preferentially silylated over 1-hydroxyl group, but the difference in the reactivity was small.

Scheme I.[a] Regioselectivity of Protection of 2,3-Cyclohexylidene-*myo*-inositol (**3**)



[a] (i) TBDPS-Cl, TBDMS-Cl, TMS-DEA, PhCH(TBDMS-O)COCl.

Identification of positional isomers of O-substituted cyclohexylidene-*myo*-inositols was based on ^1H–^1H COSY spectra in DMSO-d_6 and pyridine-d_5 and the spin–spin couplings of hydroxyl protons to inositol ring protons in isolated products. In the case of acylation reactions the downfield shift of inositol ring proton at the derivatized position was also used to further verify the structural analysis. In most cases we have used a downfield position and small vicinal couplings of the equatorial H-2 proton as a starting point for our assignments of ^1H NMR spectra. However, increasing the number of protecting groups causes the inositol ring to adopt nonchair conformations, thus making spectral analyses and signal assignments less certain. In such cases the structure of intermediates was deduced from NMR spectra of an ultimate inositol product having fewer protective groups and existing predominantly in a chair conformation.

On the basis of the above results, TBDPS-Cl was chosen as the reagent for regiospecific reaction with the camphor-protected inositol **1a**. Reaction of **1a** with 1.1 equiv of TBDPS-Cl in pyridine or DMF in the presence of imidazole at 4 °C afforded 1-TBDPS-ether **7** in 88% yield (Scheme II). The amount of the 4-silylated isomer in isolated product was less than 5%.

Route A1: Further Exhaustive Protection of 7. The triol **7** was subsequently exhaustively reacted with methoxymethylene chloride (MOM-Cl) in the presence of diisopropylethylamine to give 4,5,6-*O*-tris-MOM derivative **8** (69%). The cleavage of TBDPS group in **8** with tetra-*n*-butylammonium fluoride afforded 1-alcohol **9** in 88% yield. The above scheme could be also carried out without isolation of intermediate **8** with some improvement of the total yield (58% in three steps starting from **1a**) or without isolation of any intermediate (52%).

Route A2: Regiospecific Monoprotection of 7 with TBDPS-Cl. Silylation of **7** with 1.1 equiv of TBDPS-Cl/imidazole in pyridine

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(12) Bruzik, K. S.; Salamonczyk, G. M. *Carbohydr. Res.* **1989**, *195*, 67–73.

(13) The configuration of **1a** was confirmed by X-ray crystallography, Salamonczyk, G. M.; Pietrusiewicz, M.; Bruzik, K. S., Wieczorek, W., to be published.

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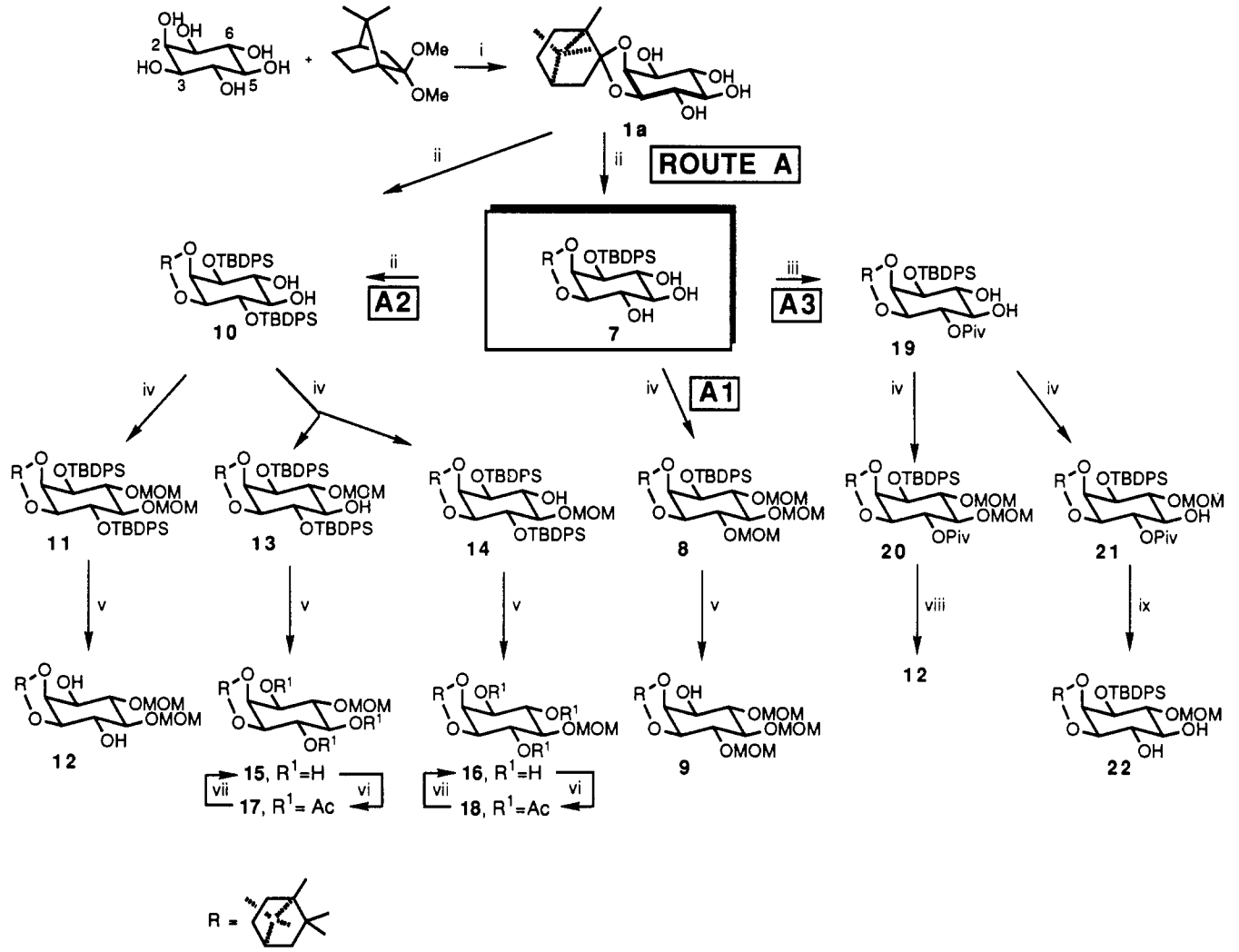
Scheme II.[a] Synthesis of Inositol Derivatives from **1a** Using Monofunctional Protecting Reagents



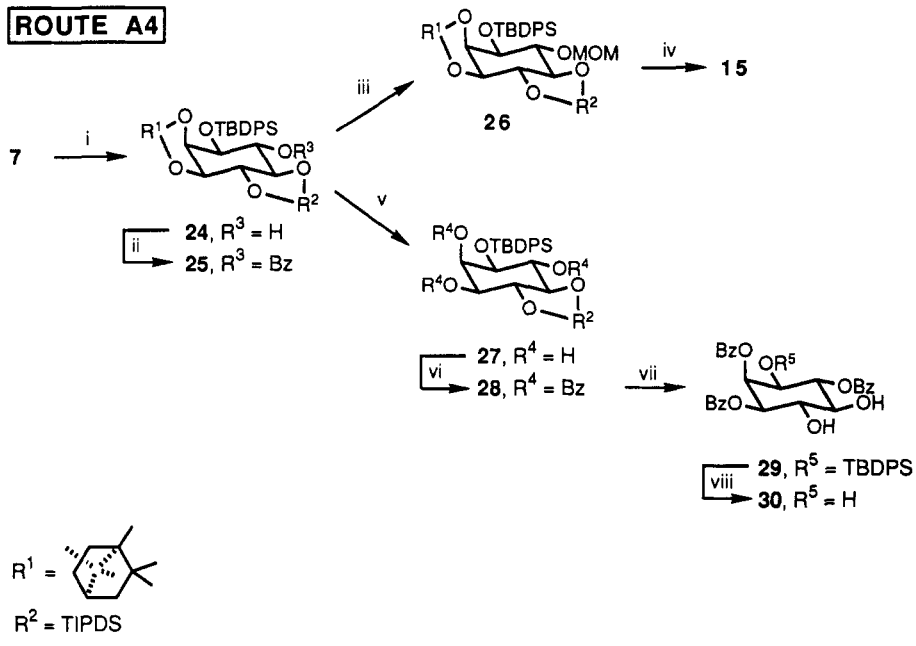
[a] (i) TMSOTf, (ii) TBDPS-Cl/imidazole/Py, (iii) Me_3COCl/Py, (iv) $ClCH_2OMe/iPr_2EtN$, (v) Bu_4N^+, F^-, (vi) Ac_2O/Py, (vii) K_2CO_3/MeOH, (viii) KOH/EtOH, (ix) MeONa/MeOH.

at 4 °C afforded the bissilyl ether **10** in 73% yield. Alternatively, **10** may be obtained in one step from **1a** in 84% yield using 2.1 equiv of TBDPS-Cl/imidazole. The bissilyl ether **10** upon further exhaustive alkylation with MOM-Cl at 50 °C gave fully protected derivative **11**. Subsequent cleavage of the silyl ether groups as above afforded 1,4-diol **12** (54% in three steps). The synthesis of **12** could also be carried out without isolation of intermediates **10** and **11**. Alkylation of **10** with 1 equiv of MOM-Cl at room temperature produced a mixture of 6-MOM ether **13** and 5-MOM ether **14** (2.5:1, 46% overall yield of mono-MOM ethers from **1a**). Separation of **13** and **14** at this stage or after their desilylation proved difficult. The mixture was treated with tetra-*n*-butylammonium fluoride to give a mixture of 1,4,5- and 1,4,6-triols (**15** and **16**, respectively). Acetylation of this mixture with acetic anhydride in pyridine afforded a mixture of triacetates **17** and **18**, which was easily separated by chromatography on silica gel. Saponification of acetate groups in **17** and **18** with potassium carbonate in methanol afforded the highly desirable 1,4,5-triol **15** and 1,4,6-triol **16**, respectively (80% yield in the last two steps).

Route A3: Regiospecific Monoprotection of 7 with Pivaloyl Chloride. Alternatively, the crude 1-TBDPS ether **7** was acylated with pivaloyl chloride in pyridine at −10 °C yielding the 4-ester **19** (78% in two steps from **1a**). Reaction of **19** with MOM-Cl at 50 °C afforded 5,6-bis-MOM derivative **20** (69%) and 6-MOM ether **21** (24%). Attempts to deacylate **20** with mild acyl-cleaving reagents such as methylamine/THF and aqueous ammonia/ethanol were unsuccessful. Deacylation could finally be achieved with potassium hydroxide/ethanol; however, the latter conditions were found to also cleave off the TBDPS group to give diol **12** (89%). Higher yields of **21** could be obtained when alkylation of **19** was carried out at room temperature (**21**/**20**, 2.5:1). After separating the mixture alcohol **21** was methanolyzed with sodium methoxide/methanol to give 6-MOM-diol **22**. Analogous treatment of the crude mixture from alkylation gave **22** (18%), unreacted **20** (63%), and 4-MOM isomer **23** (8%, not shown). The formation of another product with MOM group at 5-position was not observed. The isomer **23** most likely arises from the formation of 5- or 6-pivaloyl derivative during acylation of **7** (see Experimental Section) followed by methoxymethylation of 4-hydroxyl group.

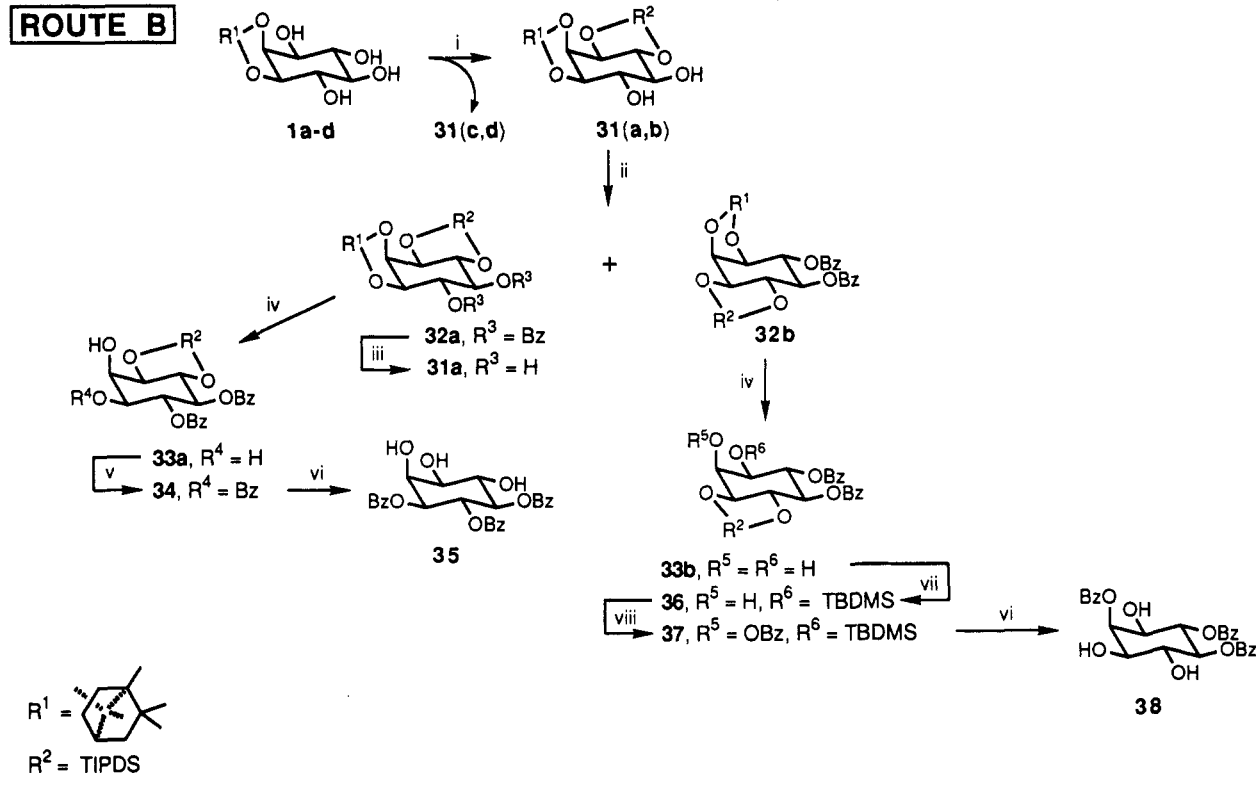
Route A4: Regiospecific Bisprotection of 7 with TIPDS-Cl_2. In order to improve selectivity of the protection of the 6-hydroxyl group we utilized a bifunctional reagent 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (TIPDS-Cl_2) to simultaneously derivatize the 4,5-diol grouping in the triol **7**. Reaction of **7** with TIPDS-Cl_2 in pyridine in the presence of imidazole afforded the corresponding 6-hydroxy derivative **24** (Scheme III) (81% yield from **1a**). The potassium alkoxide generated from **24** with potassium hydride was treated with benzoyl chloride to afford the 6-benzoyl derivative **25** (66%). Reaction of the above alkoxide with MOM-Cl afforded 6-MOM derivative **26**, which was subsequently desilylated to give **15** in low yield (25% from **24**, 6% from inositol). Deacetalization of **24** with trifluoroacetic acid (TFA) afforded the 2,3,6-triol **27** in 70% yield. The triol **27** was further reacted with benzoyl chloride/DMAP in boiling pyridine to give the tribenzoyl derivative **28** (70%). Fully protected compound **28** was partially de-

Scheme III.[a] Synthesis of 1,4,5-Triol from **7** Using Regioselective Simultaneous Protection at 4- and 5-Positions



[a] (i) TIPDS-Cl_2/imidazole/Py, (ii) KH/BzCl, (iii) KH/MOM-Cl, (iv) Bu_4N^+, F^-, (v) TFA/$CHCl_3$, (vi) BzCl/DMAP/Py, (vii) 5% HF/MeCN, (viii) 25% HF/MeCN, 50 °C.

Scheme IV.[a] Synthesis of 1,2,6- and 1,3,4-Triols from **1a** + **1b** Using Simultaneous Protection at 1,6 or 3,4-Positions



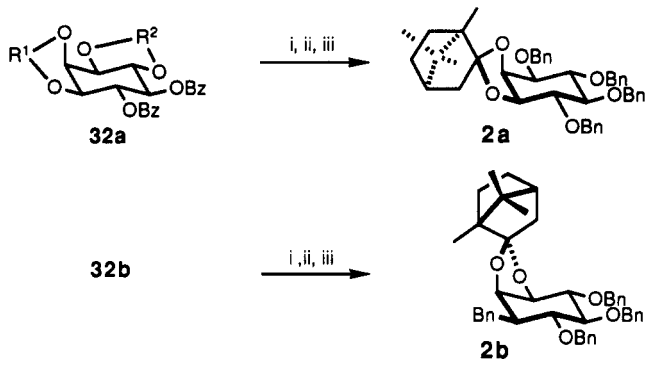
[a] (i) TIPDS-Cl_2/imidazole/Py, separation, (ii) BzCl/Py, separation, (iii) $MeNH_2$, (iv) TFA/chloroform, (v) BzCl/Py, (vi) 5% HF/MeCN, (vii) TBDMS-Cl/imidazole/Py, (viii) BzCl/DMAP/Py.

silylated with 5% HF in acetonitrile to give the 4,5-diol **29** (72%, 8.7% from inositol in six steps), which could be further deprotected with 25% HF/MeCN at 50 °C to afford 1D-2,3,6-tribenzoyl-*myo*-inositol (**30**).

Route B: Regiospecific Bisprotection of 1 with TIPDS-Cl_2. Reaction of a mixture of tetrols containing predominantly isomers **1a** and **1b** (ca. 1:1 ratio) and small quantity of **1c,d** isomers (10%, as judged by ^{13}C NMR), which is a byproduct from recrystallization of **1a**, with TIPDS-Cl_2 produced a mixture of diols **31a–d** (95%), from which the mixture of two major isomers **31a,b** was readily isolated by chromatography (Scheme IV).[16] The mixture of diols **31a,b** was further reacted with benzoyl chloride in pyridine

(16) Compounds **31a** and **31b** (and **31c** and **31d**) are not distinguished by their chromatographic mobilities, and thus separation of the mixture of four isomers **31a–d** gives two fractions **31a,b** and **31c,d**.

Scheme V.[a] Configurational Assignment of **32a** and **32b**



[a] (i) Bu_4N^+, F^-, (ii) $MeNH_2$, (iii) NaH, BnBr.

to give fully protected derivatives **32a,b**. This mixture was easily separated by chromatography on silica gel (toluene–hexane–ether, 1:1:0.02) into individual isomers **32a** (39%, R_f 0.28) and **32b** (51%, R_f 0.42). The configurations of the separated isomers **32a** and **32b** were determined by their sequential deprotection with tetra-*n*-butylammonium fluoride and methylamine (Scheme V), followed by exhaustive benzylation to give **2a** and **2b**, respectively. The identity of tetrabenzyl ethers **2** was then established based on their ^1H NMR spectra. The lower mobility isomer **32a** was found to have the same inositol configuration as **2a**, and **32b** that of **2b**. Selective deprotection of the acetal group of the isomers **32a** and **32b** separately with 10% TFA in chloroform gave the 2,3-diol **33a** and the 1,2-diol **33b**, respectively. The diol **33a** was benzoylated at the 3-position, and the product **34** was desilylated with 5% HF in acetonitrile to produce 1D-3,4,5-tribenzoyl-*myo*-inositol (**35**) in 94% yield. The diol **33b** was silylated regiospecifically with TBDMS-Cl/imidazole in pyridine at room temperature to produce 1-TBDMS-ether **36** (98%). Subsequent benzoylation of the 2-hydroxyl in **36** with benzoyl chloride/DMAP in pyridine afforded the fully protected derivative **37**, which after desilylation with TFA produced 1D-2,5,6-tribenzoyl-*myo*-inositol (**38**, 90%). In a separate synthesis silylation of pure **1a** afforded quantitatively **31a**; however, the application of the mixture **1a–d** for this reaction allows not only utilization of the byproduct but also the synthesis of the stereoisomer **31b**.

Route C: Deacetalization of 7 To Deprotect 2,3-Hydroxyl Groups. In routes A and B the 2,3-positions remain protected with camphor until later stages. In order to increase the versatility of our synthetic schemes, we developed another pathway starting with deprotection of the bornanediyl group in **7** and **31** to release 2,3-hydroxyl groups. Deacetalization of **7** with BF_3-etherate/mercaptoethanol produced 1-TBDPS-ether **39** (79%) (Scheme VI), which after treatment with TIPDS-Cl_2/imidazole gave the 2,5,6-triol **40** (80%). Reversal of the protection pattern by alkylation with MOM-Cl to tris-MOM derivative **41** and its subsequent desilylation with tetra-*n*-butylammonium fluoride afforded the 1D-2,5,6-trisMOM-*myo*-inositol **42** (78%). The pentol **39** was selectively trisprotected at 3-, 4-, and 5-positions with benzoyl chloride/pyridine to give **43** in 88% yield. The 2,6-diol **43** was further alkylated with MOM-Cl/*i*-Pr_2EtN to give the fully protected compound **44** (75%). Debenzoylation of **44** with methylamine afforded the 1-TBDPS-2,6-bis-MOM-*myo*-inositol **45** (95%).

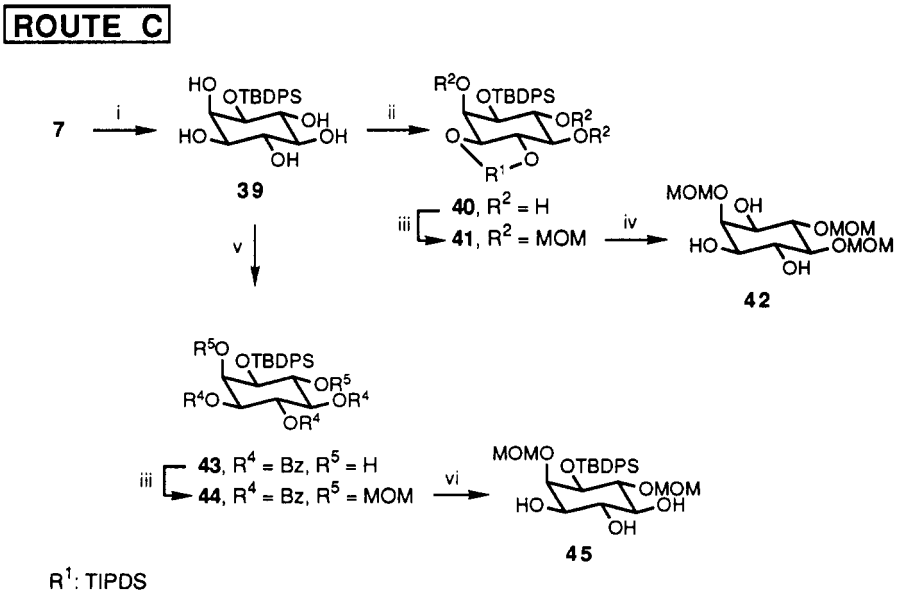
Route D: Deacetalization of 31a. Route D parallels route C, except that the starting compound is **31a**. Deacetalization of **31a** with TFA/chloroform produced the 2,3,4,5-tetrol **46** (84%) (Scheme VII), which after treatment with MOM-Cl/*i*-Pr_2EtN gave the fully protected compound **47** (88%). Desilylation of **47** with tetra-*n*-butylammonium fluoride produced the 1,6-diol **48** (97%). Analogously, benzoylation of the tetrol **46** to the fully protected compound **49** and its subsequent desilylation (without isolation) with 5% HF in acetonitrile produced the 1,6-diol **50** (83% from **46**).

Discussion

In spite of recent advances, the available synthetic procedures leading to optically active precursors of inositol phosphates and phospholipids starting from *myo*-inositol remain lengthy and relatively inefficient. A cause of this inefficiency lies in low yields of the synthesis of the racemic dicyclohexylidene-*myo*-inositols and in the large number of steps required to achieve a proper protection pattern and the resolution of racemic derivatives into optical antipodes. In most cases separation requires chromatography of diastereomeric esters imposing a scale limitation of such methods. Most of the reported methods have a narrow scope of application allowing synthesis of only a single or a small number of phosphoinositide precursors. In addition, some of the most efficient recent methods utilize expensive camphanic chloride as a resolving agent. The currently available methods starting from *myo*-inositol are summarized in Table II.

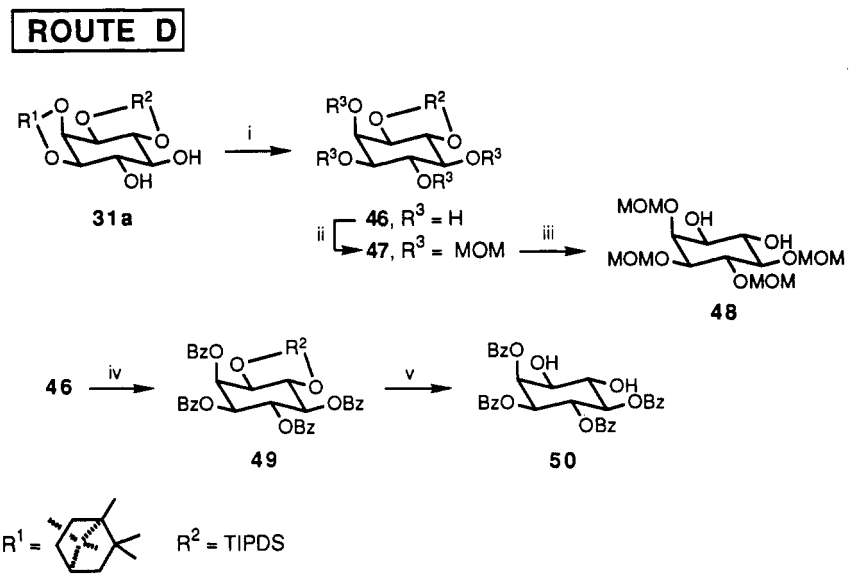
Our synthetic routes start with readily available key compounds such as **1a**, **7**, **39**, and **46**. Synthesis of 1-alcohol and 1,4-diol is conveniently achieved using monofunctional protecting reagents such as TBDPS-Cl and acyl chlorides. Synthesis of 1,4,5-triols,

Scheme VI.[a] Synthesis of 1,3,4- and 3,4,5-Triols from 1-TBDPS-inositol **39**



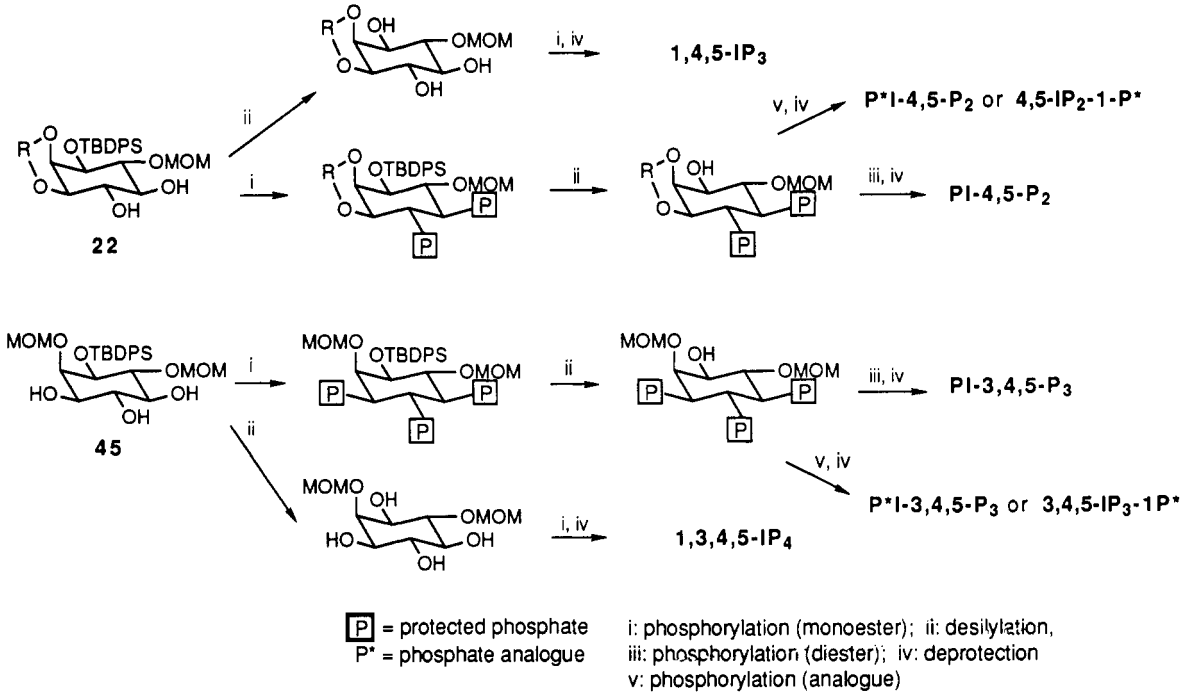
[a] (i) $HSCH_2CH_2OH$, BF_3/Et_2O, (ii) TIPDS-Cl_2/imidazole/Py, (iii) MOM-Cl/*i*-Pr_2EtN/DMF, (iv) Bu_4N^+, F^-, (v) BzCl/Py, (vi) $MeNH_2$.

Scheme VII.[a] Synthesis of 1,6-Diols from 1,6-TIPDS-inositol **46**



[a] (i) TFA/$CHCl_3$, (ii) MOM-Cl/*i*-Pr_2EtN, (iii) Bu_4N^+, F^-, (iv) BzCl/Py; (v) 5% HF/MeCN.

Scheme VIII. Strategy of Synthesis of PIP_2 and PIP_3 and Their Analogs from the Diol **22** and the Triol **45**



although possible with the use of these monofunctional reagents, requires separations of positional isomers and is therefore more difficult. Triols with hydroxy groups at 1,4,5-, 1,3,4-, and 1,2,6-positions can be more conveniently synthesized using bifunctional TIPDS-Cl_2 as the protecting agent. Triols with hydroxy groups at 2,3,6- and 2,5,6-positions are also synthesized as intermediates. The potential utility of some of our precursors to synthesis of phosphoinositides is outlined in Scheme VIII for the diol **22** and the triol **45**. In these cases phosphorylation of 4- and 5-hydroxyls (**22**) or 3-, 4-, and 5-hydroxyls (**45**) with a phosphomonoester synthon is followed by the desilylation at 1-position and further phosphorylation with a phosphodiester or modified phosphomonoester equivalents. This procedure should allow synthesis of natural PI-4,5-P_2 and PI-3,4,5-P_3 and their phosphorothioate and phosphonate analogs as well as analogs of 1,4,5-IP_3 and 1,3,4,5-IP_4, in which phosphates at 1- and the remaining positions are modified in a different way. Alternatively, desilylation at 1-position in **22** and **45**, followed by uniform phosphorylation with a phosphomonoester synthon, should produce natural 1,4,5-IP_3 and 1,3,4,5-IP_4, respectively. In the following section we comment on the advantages and disadvantages of our synthetic procedures for specific derivatives and on the potential significance of these derivatives and their applications.

1-Alcohol 9. This PI and IP precursor is synthesized in diastereomerically pure form in only four steps from *myo*-inositol in 16% total yield. We have recently demonstrated the utility of this compound for the synthesis of P-chiral oxygen isotope labeled PI and diastereomerically pure phosphorothioate analogs of PI,[38a]

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Table II. Synthetic Methods of Optically Pure Phosphoinositide Precursurs Starting From *myo*-Inositol

precursor	no. of steps[a]	yield [%][b]	ref	precursor	no. of steps[a]	yield [%][b]	ref
			PI, IP				
2,3,4,5,6-pentamethyl-*myo*-inositol	8	2.5	4b,c	2,3:5,6-dicyclohexylidene-4-MOM-*myo*-inositol	7	3.5	20
2,3,4,5,6-pentabenzyl-*myo*-inositol	9	*c*	17	2,3,4,5,6-pentaacetyl-*myo*-inositol	8	3	21a–d
	16	*c*	5a,18	2,3:5,6-diisopropylidene-4-THP-*myo*-inositol	7	4.2	22
	6	20[d]	19	2,3:4,5-diisopropylidene-6-benzyl-*myo*-inositol	4	12.5	23
2,3,6-tribenzyl-4,5-isopropylidene-*myo*-inositol	11	1.5	5a,18	**9**	4	16.5[d]	this work
			1,4-IP_2				
2,3:5,6-dicyclohexylidene-*myo*-inositol	4	6	24	5,6-isopropylidene derivative of **1a**	4	14	27a
		c	25	2,3,5,6-tetrabenzyl-*myo*-inositol	8	*c*	18e
2,3,5,6-tetrabenzyl-4-(*p*-methoxybenzyl)-*myo*-inositol[e]	12	6	26	**12**	4	17[d]	this work
			PI-4,5-P_2				
4,5-diallyl-2,3,6-tribenzyl-*myo*-inositol	11	3	28	2,3:4,5-diisopropylidene-6-benzyl-*myo*-inositol	4	12.5	23
4,5-propenyl-2,3,6-tribenzyl-*myo*-inositol	12	3.4	28	**22**	5	5	this work
1-camphanoyl-2,3-cyclohexylidene-6-benzyl-*myo*-inositol	4	4	24				
			1,4,5-IP_3				
2,3,6-tribenzyl-*myo*-inositol	11	2.9[f]	28	6-benzyl ether of **1a**	4	14	27a
	12	1.8[f]	18	2,3-isopropylidene-6-benzyl-*myo*-inositol	5	10.5	23
	6	6.5	24	**15**	6	10	this work
	12	*c*	18e	**15**	5	6.3	this work
2,3-cyclohexylidene-6-benzyl-*myo*-inositol	5[g]	3.4	24a	**30**	6	11	this work
	7[h]	7	9a				
2,3-cyclopentylidene-6-(2,7-dibromo-9-phenyl-9-yl)-*myo*-inositol	11	*c*	29				
			1,2,6-IP_3				
3,4,5-tribenzyl-*myo*-inositol	11	*c*	30	**35**	6	25[i]	this work
			1,3,4-IP_3				
2,5,6-tribenzyl-*myo*-inositol	11[j]	2.1 (4)[k]	31	2,5,6-tribenzoyl-*myo*-inositol	9	12[f,l]	15
	10	8.4	9b	**38**	8	23[j]	this work
	10	*c*	18d,e	**42**	6	13.5	this work
			1,3,4,5-IP_4				
2,6-dibenzyl-*myo*-inositol	8 (11)	12 (15)[m]	32	2,6-dibenzoyl-*myo*-inositol	4	4.3	8
	10	2.7	33		4	8.3[f,n]	35
	13	*c*	34	2,6-dimethyl-*myo*-inositol	8	*c*	18d
	11	5.3	9b				
			PI-3,4,5-P_3				
1-allyl-2,6-dibenzyl-*myo*-inositol	12	*c*	34	**45**	6	14	this work
			GIP				
1-*p*-MeO-benzyl-2,3,4,5-tetrabenzyl-*myo*-inositol	13	7.8	36	**48**	5[o]	18	this work
1-TBDMS-2,3:4,5-dicyclohexylidene-*myo*-inositol	7	1.6	37	**50**	5[o]	15	this work

[a] Chromatographic separation of diastereomers is counted as one step. [b] The values given refer to the yield of the single D-enantiomer of the final phosphoinositide precursor. [c] Yields in some steps were not given. [d] Based on the yield of the predominant diastereomer. [e] This precursor would be also applicable toward synthesis of PIP. [f] Yields in some steps were not reported; it was assumed they were quantitative. [g] Separation of diastereomers by crystallization was not counted as a step. [h] Chemical-enzymatic method. [i] Calculated assuming that the synthesis proceeded from pure **1a**. [j] Calculated assuming that the synthesis proceeded starting from the enantiomer of **1a** obtained with L-camphor. [k] Two procedures starting from different isomers of biscyclohexylidene-*myo*-inositol; separation of enantiomers was achieved by using chiral HPLC column. [l] Calculated using 70% yield in the synthesis of 2,3-cyclohexylidene-*myo*-inositol. [m] Values in parentheses refer to a longer chemoenzymatic process. [n] Separation of enantiomers was achieved using chiral HPLC column. [o] The synthesis of the actual precursor for glycosylation (i.e., 1-protected **48** or **50**) would require 1–3 more steps.

substrates used to study the mechanism of phosphoinositide-specific phospholipase C. Synthesis of IP has also been accomplished starting from **9**[38b] and by regioselective phosphitylation of partially purified **1a**.[27b] Since the deprotection of acetal and MOM groups

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requires only weakly acidic conditions, the above precursor should also be applicable to the synthesis of unsaturated phosphatidylinositols.

1,4-Diol 12. Protection of the hydroxyl group at 4-position in triol **7** with TBDPS-Cl is regioselective, and no separations of isomers are necessary. The final diol **12**, which is a precursor of 1,4-IP_2,[39] is produced in four steps from inositol in 17% overall yield. An analogous but less efficient way to optically pure 1,4-diol starting from the partially purified **1a** has been reported recently.[27a] Preparation of 1,4-*O*-bis-TBDPS-inositol should be possible from **10** (see synthesis of **39**). Such tetrol might serve as a substrate for the synthesis of 1L-1,4,5-IP_3[40] and unnatural 2,3,5,6-IP_4.

1,4,5-Triol 15. The synthesis of this precursor of 1,4,5-IP_3 via route A2 depends on the regioselective alkylation of 5,6-diol **10**. With MOM-Cl as the alkylating reagent the preference between alkylation of 5- and 4-hydroxyl groups was low, and large amounts of bisether **11** were also produced. Thus, **15** was obtained in six steps from inositol in a relatively low overall yield (7.5%). Attempts to improve regioselectivity of derivatization of **10** by employing activation with dibutyltin oxide, and by using MOM-Cl and benzyl bromide as alkylating reagents, were unsuccessful (data not presented). An alternative route to **15** is A4. The regioselectivity of the protection was greatly improved with TIPDS-Cl_2 to simultaneously protect 4- and 5-hydroxyl groups in the triol **7**. Due to steric hindrance the protection of the 6-hydroxyl group in the product **24** could be only achieved with some difficulty[41] and with moderate yield. The synthesis of **15** was, however, shortened to five steps with 6% overall yield.

4,5-Diol 22. The synthesis of PI-4,5-P_2 requires different protective groups at 1- and 2,3,6-positions. The diol **22** which features such a protection pattern is obtained in only five steps from *myo*-inositol in 5% overall yield (route A3). Protection of 4-hydroxyl function with pivaloyl group in triol **7** was less regioselective than it was with TBDPS. The intermediates **19** and **21** had to be rigorously purified, and thus this scheme is more laborious as compared to the synthesis of other precursors.

4,5-Diol 29 and 1,4,5-Triol 30. The 1,4,5-protected derivative **27** is formed in four steps from inositol with excellent positional selectivity. Reversal of the protection pattern leads to **29** (8.7%, six steps) and to **30** (6%, seven steps). The triol **30** has been recently used for the synthesis of 1,4,5-IP_3.[6b] The yield in the deacetalization of **24** is likely to be improved with mercaptoethanol/BF_3 as described for triol **7**, although such a possibility was not tested. The benzoylation step can possibly be replaced by methoxymethylation as described for triol **40**. MOM groups would allow a more facile deprotection of silyl groups.

1,3,4-Triols 38 and 42. Two routes are possible to the precursor of 1,3,4-IP_3. In route C, deacetalization of **7** followed by bissilylation leads to 2,5,6-triol **40**. Reversal of the protection pattern gives the 1,3,4-triol **42** in six steps from inositol (13%). Benzoylation instead of alkylation is possible; however, the complete desilylation in a fully protected compound became a problem (data not presented). Route B, although slightly more laborious, makes use of a mixture of tetrols **1b** and **1a**, which is a side product in the purification of **1a**. Regioselectivity and chemical yield in this process are excellent. The 1,3,4-triol **38** is obtained in eight steps. The synthesis of precursors of PI-3-P and PI-3,4-P_2 should also be possible from **39**, but we have not explored such a possibility.

1,2,6-Triol 35. The synthesis of this compound was achieved starting from the mixture of tetrols **1**. However, the procedure could be simplified with utilization of pure **1a**. This precursor of 1,2,6-IP_3 may thus be synthesized in six steps from inositol via **1a**. 1,2,6-IP_3, known under its pharmaceutical code PP56, has been found recently to possess interesting antiinflammatory and antidiabetic properties and is now in phase 1 clinical trials.[42]

3,4,5-Triol 45. This synthesis uses 1-TBDPS-inositol **39** as a key intermediate synthesized from inositol in three steps (22%). We believe the pentol **39** is more useful an intermediate than recently reported racemic 1-*O*-allyl- and 1-*O*-benzoyl-*myo*-inositols[43] due to the high regioselectivity of protection possible to obtain with **39**. The racemic 1-*O*-trityl-*myo*-inositol, which we have synthesized recently by direct tritylation of inositol (50%),[44] should display properties similar to those of **39**. Tris-benzoylation of **39** occurs exclusively at 3-, 4-, and 5-positions. The high regioselectivity of this process is most likely due to an inherent low reactivity of 2-hydroxyl group[3e] and the steric hindrance imposed on 2- and 6-hydroxyl groups by the bulky TBDPS group at 1-position. While the triol **45** may be used as a precursor of PI-3,4,5-P_3 (Scheme VIII), desilylation of **45** should afford 2,6-bis-MOM-inositol, a precursor of 1,3,4,5-IP_4. The two phosphoinositides are biologically produced by the action of 1,4,5-IP_3-3-kinase and PI-4,5-P_2-3-kinase on 1,4,5-IP_3 and PI-4,5-P_2, respectively.[2g] PI-3,4,5-P_3, however, is not a substrate for PI-PLC and its cellular function is unclear.

1,6-Diols 48 and 50. The high regioselectivity obtained in the 1,6-bisprotection of **1a** with TIPDS-Cl_2 (to give **31a**) allows expedient synthesis of the 1,6-diols **48** and **50** in 5 steps from inositol in 18% and 15% yield, respectively (route D). Compounds **48** and **50** should be useful precursors of GPI protein anchors and insulin mimetics.

1,4,5,6-Tetrol 1a. Apart from its synthetic utility exploited in this report **1a** should be a useful precursor of 1,4,5,6-IP_4, a phosphoinositide found in avian erythrocytes.[45]

Synthetic intermediates described here may also serve as precursors of a handful of natural and unnatural phosphoinositides such as 5-IP (**13**, **21**), 6-IP (**14**, **24**), IcP (**33b**), 1L-IcP (**33a**), 4,5-IP_2 (**31a**, **29**), 5,6-IP_2 (**32b**), 2,6-IP_2 (**43**), 1,6-IP_2 (**48**, **50**), 1,4,6-IP_3 (**16**), 2,3,6-IP_3 (**27**), 3,4,5-IP_3 (**35**, **45**), 2,5,6-IP_3 (**40**), 2,3,4,5-IP_4 (**46**), and 2,3,4,5,6-IP_5 (**39**). A large number potentially useful derivatives may be obtained from L-camphor-derived intermediates such as 1,2-diol (from L analogue of **1a**),[12] 2,3,4-triol (L analogue of **35**), 1,3,6-triol (L analogue of **38**), 1,5,6-triol (L analogue of **45**), and 2,4,5-triol (L analogue of **40**).

Finally, inversion of configuration at C-1 in **7** should provide a useful route to 1D-1-deoxy-1-substituted-*chiro*-inositols, precursors in the synthesis of *chiro*-inositol-containing phosphoinositides.

Conclusions

We have demonstrated that a large number of precursors of biologically important inositol phosphates and phospholipids can be prepared starting from the common intermediates: tetrol **1a** and triol **7**. Our synthetic approach offers the following advantages: (i) the starting compound **1a** is readily accessible in the optically pure form; (ii) the regioselectivity of the protection of the hydroxyl groups at 1-, 4-, 1,6-, and 4,5-positions in **1a** or **7** with TBDPS-Cl and TIPDS-Cl_2 is high enough to make separations of positional isomers of protected inositols unnecessary; (iii) selective derivatization of **1a** affords other key compounds such as triol **7**, diol **10**, pentol **39**, and tetrol **46** (in two to three steps from inositol), from which almost every protection pattern is possible; (iv) due to the presence of the chiral camphor auxiliary in some intermediates, their diastereomeric purity can be conveniently monitored by ^1H NMR; (v) the presence of camphor protective group in some of the final precursors enables easier separations of the diastereomeric P-chiral analogs of inositol

(38) (a) Synthesis of PI and its P-chiral analogs starting from **9** is published separately: Bruzik, K. S.; Morocho, A.; Jhon, D.-Y.; Rhee, S. G.; Tsai, M.-D. *Biochemistry* **1992**, *31*, 5183–5193. (b) The synthesis of other inositol phospholipids and phosphates will be published elsewhere.

(39) The protection of diol **12** with TBDMS-Cl is not selective and produces a mixture of 1- and 4-TBDMS ethers, which are difficult to be separated. We have not tested other possibilities of the protection of **7** at 4-position, which would in principle lead to 1-TBDPS-4-alcohol applicable toward the synthesis of PI-4-P.

(40) Meek, J. L.; Davidson, F.; Hobbs, F. W. *J. Am. Chem. Soc.* **1988**, *110*, 2317–2318.

(41) The protection of the 6-hydroxyl group in **24** could not be achieved with benzoyl chloride/pyridine/DMAP, with benzoyl chloride/NaH in THF and with MOM-Cl/*i*-Pr_2EtN.

(42) Siren, M.; Linne, L.; Persson, L. ref 3d, pp 103–110.

(43) Zapata, A.; de la Pradilla, R. F.; Martin-Lomas, M.; Penades, S. *J. Org. Chem.* **1991**, *56*, 444–447.

(44) Bruzik, K. S.; Tsai, M.-D., unpublished results.

(45) Mayr, G. W.; Dietrich, W. *FEBS Lett.* **1987**, *213*, 278–282.

(46) MacKenzie, C. A.; Stockter, J. H. *J. Org. Chem.* **1955**, *20*, 1695–1700.

phospholipids;[38a] (vi) use of MOM protective groups enables complete deprotection of inositol (acetal and MOM protective groups) under weakly acidic conditions in one step; (vii) D-camphor is among the least expensive chiral compounds.

In summary, good accessibility of optically pure tetrol **1a** and high regioselectivity in the various protection and deprotection steps results in a comprehensive synthetic scheme applicable toward the synthesis of most, if not all, of natural phosphoinositides. The methods can be readily adapted to the synthesis of unnatural analogs of phosphoinositides.

Experimental Section

General Methods and Reagents. 1,1-Dimethoxycyclohexane and D-camphor dimethyl acetal were obtained as described.[12,46] Racemic 2,3-cyclohexylidene-*myo*-inositol (**3**) was obtained by the modification of the existing procedures[7e,11] analogously to the synthesis of **1a** described below. Commercially available anhydrous pyridine, DMSO, and DMF were used as solvents without further purification or drying. All other reagents were obtained from commercial sources unless otherwise specified. ^{1}H NMR spectra were obtained with NMR spectrometers operating at 250, 300, and 500 MHz frequency, depending on the spectral complexity. ^{13}C NMR spectra were obtained at 62.9 and 75.5 MHz. Chemical shifts are referenced indirectly to tetramethylsilane. Splitting patterns are designated as follows: s, singlet; d, doublet; tr, triplet; m, multiplet; br, broad. Optical rotations were measured with a Perkin-Elmer 241 MC polarimeter at ambient temperatures (22 ± 2 °C). Mass spectra were recorded with VG 70-250S spectrometer. Melting points are uncorrected. TLC was performed on precoated plates of silica gel (60 F_{254}, Merck) using phosphomolybdic acid/ethanol reagent to visualize spots. R_f values are chromatographic mobilities of compounds. Column chromatography was performed on silica gel 60 (40–63 μm, Merck).

General Procedures. Except where otherwise stated the reaction mixtures resulting from acylation and silylations in pyridine or DMF were diluted with 3-fold volume of ethyl acetate and washed three times with water. Small scale procedures were typically performed in a pear shaped flask, and phases were separated using a syringe. The organic phase was dried by azeotropic evaporation of anhydrous toluene, dioxane, or ethyl acetate. This procedure is referred to as the aqueous workup.

1D-2,3-*O*-(D-1′,7′,7′-Trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (1a). (a) *myo*-Inositol (18.1 g, 0.1 mol) was solubilized in DMSO (150 mL) by heating the suspension at 110 °C. Such solutions (with inositol concentration up to 15%) may be cooled down to room temperature without inositol precipitation. The above solution was treated with D-camphor dimethyl acetal (31.3 g, 0.158 mol) and TMS-triflate (0.3 mL). The mixture was heated at 90 °C during 3 h. Ethylene glycol (3.2 g) and chloroform (350 mL) were added, and the mixture was heated at 50 °C for 2 h. The mixture was concentrated under vacuum, redissolved in chloroform–ether (1:2, 1 L), and stirred at 4 °C for 24 h. Solid, white precipitate was separated by centrifugation. The clear supernatant was concentrated and added with chloroform–methanol (9:1, 300 mL) and *p*-toluenesulfonic acid (1 g), and the mixture was stirred at room temperature for 12 h. The solid product was filtered off, and both batches of the solid product were pooled and recrystallized from minimal amount of methanol. Second crystallization from methanol gave **1a** (8.0 g, 25%) essentially free from other isomers. Three times recrystallization of the mother liquor from methanol afforded another crop of **1a** (1.8 g, 6%). To prevent acetal group migration or deprotection triethylamine was added to methanol used for recrystallization, and pure tetrol **1a** was stored at −10 °C. As byproducts a mixture of other three diastereomers was obtained after recrystallization of the mother liquor (11.06 g, 66% total yield of **1a–d**). (b) The mixture of tetrols **1** obtained from the synthesis containing ca. 30% of **1a** was treated with excess benzoyl chloride in pyridine at room temperature. The attempts at separation of isomers by crystallization were unsuccessful due to a tendency of the product to form a colloidal solid in several solvent systems tested. Chromatography of the mixture on silica gel (toluene–hexane–ether, 80:40:1) afforded the pure isomer having the lowest chromatographic mobility. Its subsequent deprotection with methylamine in chloroform–methanol (2:1) (room temperature, 48 h) afforded **1a** having essentially identical ^{1}H NMR spectrum (pyridine-d_5) to this one of a sample prepared by the crystallization route: mp 231–232 °C; $[\alpha]_D$ +44.3° (*c* 1.9, pyridine), R_f 0.25 (chloroform–methanol, 4:1); ^{1}H NMR (CD_3OD) δ 4.27 (dd, H-2, $J_{1,2}$ = 4.3, $J_{2,3}$ = 5.5 Hz, 1 H), 3.77 (dd, H-3, $J_{3,4}$ = 7.2 Hz, 1 H), 3.68 (dd, H-1, $J_{1,6}$ = 9.6 Hz, 1 H), 3.51 (tr, H-6, $J_{5,6}$ = 9.3 Hz, 1 H), 3.44 (dd, H-4, $J_{4,5}$ = 10.1 Hz, 1 H), 3.12 (dd, H-5, 1 H), 2.03 (m, 2 H), 1.70 (m, 2 H), 1.49 (d, *J* = 13.0, 1 H), 1.38 (m, 1 H), 1.21 (m, 1 H), 1.03 (s, Me), 0.87 (s, Me), 0.85 (s, Me); ^{13}C NMR (pyridine-d_5) δ 117.5 (C-2′), 78.0, 77.8, 77.1, 75.9, 74.0, 71.9 (inositol), 51.9, 48.2, 46.0, 45.7, 30.0, 27.6, 21.0, 20.6, 10.2 (camphor). Anal. Calcd for $C_{15}H_{26}O_6$: C, 61.1; H, 8.33. Found: C, 60.94; H, 8.56.

1D-1,4,5,6-*O*-Tetrabenzyl-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositols (2a and 2b).[12] Dibenzoyl derivatives **32a** and **32b** (64 mg, 82 μmol) obtained as described later were separately treated with tetra-*n*-butylammonium fluoride (1.5 equiv, 1 h), followed by methylamine (room temperature, 48 h). Both products were dissolved in DMF and were treated with benzyl bromide in the presence of sodium hydride. The product **2a** derived from **32a** had R_f 0.19 (benzene–diisopropyl ether, 100:2), and **2b** from **32b** had R_f 0.29. **2a**: ^{1}H NMR ($CDCl_3$) δ 7.45–7.25 (m, Ph, 20 H), 4.95–4.7 (m, CH_2, 8 H), 4.31 (dd, *J* = 3.9, 6.1 Hz, 1 H), 3.97 (dd, *J* = 6.2, 6.9 Hz, 1 H), 3.94–3.71 (m, 3 H), 3.44 (dd, *J* = 7.7, 9.6 Hz, 1 H), 1.97 (m, 2 H), 1.75 (m, 2 H), 1.48 (d, H), 1.45–1.24 (m, 3 H), 1.08, 0.88, 0.85 (each s, 3 H). **2b**: ^{1}H NMR ($CDCl_3$) δ 7.45–7.25 (m, Ph, 20 H), 4.95–4.65 (m, CH_2, 8 H), 4.27 (dd, *J* = 3.9, 5.4 Hz, 1 H), 4.07 (dd, *J* = 5.4, 7.3 Hz, 1 H), 3.86 (tr, *J* = 8.7 Hz, 1 H), 3.74 (dd, *J* = 7.3, 10.0 Hz, 1 H), 3.66 (dd, *J* = 3.8, 8.5 Hz, 1 H), 3.39 (dd, *J* = 8.8, 10.0 Hz, 1 H), 2.14 (d tr, 1 H), 1.94 (ddd, 1 H), 1.67 (m, 2 H), 1.45 (d, 1 H), 1.38–1.1 (m, 2 H), 1.06 (s, 3 H), 0.83 (s, 6 H).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (7). A solution of tetrol **1a** (3.35 g, 10.15 mmol) and imidazole (1.04 g, 1.5 equiv) in pyridine (35 mL) was treated with TBDPS-Cl (2.82 g, 10.3 mmol) at −10 °C. The progress of the reaction was monitored by TLC (chloroform/methanol, 4:1). After 24 h the mixture was concentrated and subjected to the aqueous workup. Organic phase was concentrated, and the residue was chromatographed on silica gel (chloroform/methanol, 15:1) giving pure product (5.06 g, 88%) as a colorless glassy solid: $[\alpha]_{578}$ −24.7° (*c* 4.4, $CDCl_3$); R_f 0.42 (chloroform–methanol, 15:1); ^{1}H NMR ($CDCl_3$) δ 7.7 (m, Ph, 4 H), 7.5–7.3 (m, Ph, 6 H), 3.87 (dd, H-2, *J* = 3.7, 5.3 Hz), 3.78 (m, H-3, H-4, 2 H), 3.56 (dd, H-1, *J* = 7.0 Hz), 3.49 (dd, H-6, *J* = 9.0 Hz, 1 H), 3.10 (br tr, H-5, 1 H), 1.93 (m, 2 H), 1.67 (m, 4 H), 1.29 (m, 3 H), 1.08 (s, Me, 9 H), 1.04 (s, Me, 3 H), 0.85 (s, Me, 3 H), 0.82 (s, Me, 3 H); ^{13}C NMR ($CDCl_3$) δ 136.0, 135.8, 133.5, 133.4, 129.9, 128.8, 127.8, 127.7 (Ph), 118.06 (C-2′), 76.3, 76.1, 75.8, 73.0, 72.6, 72.6 (CH-inositol), 51.5, 48.0, 45.2, 45.0, 29.5, 27.0, 20.5, 20.4, 19.3 (camphor), 26.9, 19.3 (*t*-Bu). Anal. Calcd for $C_{32}H_{44}O_6Si$: C, 69.53; H, 8.02. Found: C, 69.57; H, 8.39.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-4,5,6-*O*-tris(methoxymethylene)-*myo*-inositol (8). The solution of triol **7** (4.96 g, 8.7 mmol) and diisopropylethylamine (6.8 g, 53 mmol) in THF (50 mL) was treated with MOM-Cl (4.3 g, 53 mmol). The resulting mixture was heated at 50 °C for 24 h. Solvents and excess reagents were evaporated, and residue was dissolved in ether (200 mL) and washed twice with phosphate buffer (1 M, pH 7.0). Ether layer was dried, concentrated and the residue was chromatographed on silica gel (ether–hexane, 1:1) yielding pure product (oil, 4.3 g, 69%): TLC R_f 0.4 (hexane–ether, 1:1); ^{1}H NMR ($CDCl_3$, 70 °C, broad lines are observed at ambient temperature) δ 7.8 (m, Ph, 4 H), 7.35 (m, Ph, 6 H), 4.78 (m, CH_2, 2 H), 4.67 (m, CH_2, 2 H), 4.47 (m, CH_2, 2 H), 4.24 (dd, *J* = 4.2, 6.7 Hz, 1 H), 4.13 (tr, *J* = 7.4 Hz, 1 H), 4.02 (dd, *J* = 4.0, 7.7 Hz), 3.78 (tr, *J* = 7.5 Hz, 1 H), 3.60 (dd, *J* = 4.1, 6.6 Hz, 1 H), 3.51 (dd, *J* = 4.3, 7.6 Hz, 1 H), 3.37, 3.34, 3.19 (s, Me, 3 H), 1.8 (m, 4 H), 1.35 (m, 3 H), 1.10 (s, Bu, 9 H), 1.09 (each s, Me, 3 H), 0.94 (s, Me, 3 H), 0.88 (s, Me, 3 H); ^{13}C NMR ($CDCl_3$, 30 °C) δ 136.1, 133.9, 133.6, 129.9, 129.6, 127.6, 127.5 (Ph), 117.3 (C-2′), 96.5, 96.0 (br, CH_2OMe), 79.0, 77.8, 77.0, 74.3, 74.1, 69.9 (CH, inositol), 55.65, 55.57, 51.4 (OMe), 47.8, 45.1, 43.2, 29.9, 27.2, 27.0, 20.6, 20.3, 18.8, 10.2 (camphor, Bu).

1D-2,3-*O*-(D-1′,7′,7′-Trimethyl[2.2.1]bicyclohept-2′-ylidene)-4,5,6-*O*-tris(methoxymethylene)-*myo*-inositol (9). Compound **8** (0.87 g, 1.25 mmol) was dissolved in a 1.0 M solution of tetra-*n*-butylammonium fluoride in THF (2.5 mL). After 0.5 h at room temperature all substrate has been converted into alcohol **9** (TLC, ether–hexane, 2:1). After aqueous workup the crude product was purified by chromatography on silica gel (hexane–ether, 1:2) giving 0.51 g of **9** (oil, 88%): $[\alpha]_D$ −4.1° (*c* 2.5, $CHCl_3$); TLC R_f 0.13 (hexane–ether, 1:2); ^{1}H NMR (benzene-d_6, 24 °C, all resonances in NMR spectra are duplicated due to two conformers existing in a slow exchange) δ 5.53 (m, 1 H), 4.83 (dd, 1 H), 4.76 (m, 2 H), 4.64 (dd, 1 H), 4.56 (dd, 1 H), 4.19 (dd, 0.5 H), 4.16 (dd, 0.5 H), 4.14 (dd, 0.5 H), 4.08 (dd, 0.5 H), 4.00 (tr, 0.5 H), 3.96 (d tr, 1 H), 3.87 (m, 1.5 H), 3.64 (ddd, 1 H), 3.30 (s, Me, 3 H), 3.27, 3.26, 3.15, 3.14 (each s, Me, 1.5 H), 2.08 (m, 1 H), 1.94 (m, 1 H), 1.61 (m, 1 H), 1.38 (s, 1.5 H), 1.37 (s, 1.5 H), 1.19 (m, 1.5 H), 1.05 (s, Me, 3 H), 0.96, 0.95, 0.75, 0.74 (each s, Me, 1.5 H); ^{1}H NMR (DMSO-d_6, 60 °C) δ 4.72 (m, CH_2, 6 H), 4.68 (d, OH, *J* = 3.6 Hz), 4.16 (dd, H-2, $J_{1,2}$ = 4.0 Hz), 3.91 (tr, H-3, $J_{2,3}$ = 6.7 Hz, 1 H), 3.82 (m, H-1, 1 H), 3.70 (dd, H-4, $J_{4,5}$ = 8.9 Hz, 1 H), 3.63 (dd, H-6, $J_{5,6}$ = 7.1 Hz, 1 H), 3.44 (dd, H-5, 1 H), 1.90 (m, 2 H), 1.70 (m, 2 H), 1.41 (d, *J* = 12.9 Hz), 1.3 (m, 2 H), 0.99 (s, Me, 3 H), 0.84 (s, Me, 6 H); ^{13}C NMR (benzene-d_6, 24 °C, reso-

nances are duplicated due to two conformers existing in a slow exchange) δ 118.0, 117.7 (C-2′), 103.6, 97.6, 97.5, 97.4, 96.5, 96.4 (*C*H$_2$OMe), 80.8, 80.6, 79.4, 79.2, 78.5, 78.2, 77.7, 75.8, 75.3, 73.8, 69.8, 69.7 (CH, inositol), 55.7, 55.6, 55.5, 55.4, 51.8, 51.6 (OMe), 48.2, 48.0, 45.5, 45.4, 44.4, 30.2, 30.1, 27.3, 27.1, 20.7, 20.6, 20.4, 20.3, 18.7, 18.4, 10.6, 9.9 (camphor, *t*-Bu); MW for $C_{22}H_{38}O_9$ 446.2516, found 446.2530.

1D-1,4-*O*-Bis(*tert*-butyldiphenylsilyl)-2,3-*O*-(D-1′,7′,7′-trimethyl-[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (10). To the solution of tetrol **1a** (0.82 g, 2.49 mmol) in pyridine was added TBDPS-Cl (1.5 g, 2.1 equiv) at −30 °C. The reaction was carried out at −10 °C during 24 h. After the aqueous workup and purification by chromatography (hexane–acetone, 10:0.7) 1.72 g of diol **10** was obtained (86%): $[\alpha]_D$ −30.5° (*c* 2.3, $CHCl_3$); TLC R_f 0.32 (hexane–acetone, 10:1.5); ^{1}H NMR (C_6D_6) δ 7.9 (m, Ph, 6 H), 7.85 (m, Ph, 2 H), 7.25 (m, Ph, 12 H), 3.94 (dd, H-1, *J* = 4.2, 9.7 Hz, 1 H), 3.82 (dd, H-2, *J* = 4.3, 5.7 Hz, 1 H), 3.71 (d tr, *J* = 2.4, 10.0 Hz, 1 H), 3.70 (dd, *J* = 6.0 Hz, 9.1 Hz, 1 H), 3.49 (tr, *J* = 6.1 Hz, 1 H), 3.15 (d tr, *J* = 2.2, 9.1 Hz, 1 H), 2.12 (d, *J* = 2.2 Hz, 1 H), 2.06 (d, *J* = 2.4 Hz, 1 H), 1.86–1.56 (m, 5 H), 1.22, 1.20 (each s, Bu, 9 H), 1.11, 0.77, 0.38 (each s, Me, 3 H); ^{13}C NMR (CD_3OD) δ 137.4, 137.3, 137.2, 137.1, 137.0, 135.8, 135.6, 135.4, 135.2, 134.7, 134.6, 130.76, 130.69, 130.5, 130.4, 130.3, 128.5, 128.4, 128.34, 128.29 (Ph), 118.3 (C-2′), 79.2, 77.7, 77.1, 77.0, 73.6, 73.3 (CH, inositol), 52.5, 48.8, 46.2, 45.2, 30.3, 27.9, 27.8, 27.7, 20.9, 20.3, 20.2, 19.8, 9.9.

1D-5,6-*O*-Bis(methoxymethylene)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]-bicyclohept-2′-ylidene)-*myo*-inositol (12). (a) The crude diol **10** obtained from tetrol **1a** (678 mg, 2.05 mmol) was dissolved in THF (5 mL) and *i*-Pr$_2$EtN (2.0 mL) and MOM-Cl (2.0 mL) were added. The mixture was heated at 50 °C for 12 h and was subsequently subjected to the aqueous workup. The resulting crude, anhydrous product **11** was dissolved in 1.0 M solution of tetra-*n*-butylammonium fluoride in THF, and reaction was continued at room temperature for 72 h. The mixture was concentrated, and the residue was chromatographed (hexane–acetone, 10:2.5) to give diol **12** (0.46 g, 54% from **1a**). (b) Fully protected derivative **20** (vide infra, 607 mg, 0.82 mmol) in ethanol (10 mL) was treated with aqueous potassium hydroxide (40%, 2 mL) at 70 °C during 7 h. The mixture was neutralized, subjected to aqueous workup, and chromatographed as described above to give **12** (0.305 g, 89%). The analogous reaction carried out with tetra-*n*-butylammonium hydroxide in methanol at 50 °C during 96 h afforded **12** in 84% yield: mp 96–97 °C; $[\alpha]_D$ −6.1° (*c* 2.5, $CHCl_3$); TLC R_f 0.15 (hexane–acetone, 10:3); ^{1}H NMR (CD_3OD) δ 4.82 (m, CH_2, 4 H), 4.25 (dd, H-2, $J_{1,2}$ = 4.2 Hz, $J_{2,3}$ = 5.7 Hz, 1 H), 3.89 (dd, H-3, $J_{3,4}$ = 7.0 Hz, 1 H), 3.79 (dd, H-1, $J_{1,6}$ = 9.0 Hz, 1 H), 3.62 (dd, H-4, $J_{4,5}$ = 9.9 Hz, 1 H), 3.57 (tr, H-6, $J_{5,6}$ = 8.9 Hz, 1 H), 3.44, 3.40 (each s, Me, 3 H), 3.55 (dd, H-5, 1 H), 2.04 (m, 2 H), 1.71 (m, 2 H), 1.48 (d, *J* = 13.0 Hz, 1 H), 1.40 (m, 1 H), 1.20 (m, 1 H), 1.04, 0.91, 0.88 (each s, Me, 3 H); ^{13}C NMR (CD_3OD) δ 119.0 (C-2′), 98.8, 97.5 (*C*H$_2$OMe) 81.7, 81.5, 77.7, 76.8, 74.3, 70.7 (inositol), 56.2, 55.9 (OMe), 52.6, 48.9, 46.5, 46.2, 30.7, 27.9, 21.2, 20.9, 10.3; MW for $C_{20}H_{34}O_8$ 402.2254, found 402.2251.

1D-6-*O*- and 5-*O*-(Methoxymethylene)-2,3-*O*-(D-1′,7′,7′-trimethyl-[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositols (15 and 16, Respectively). (a) Into the solution of diol **10** (1.44 g, 1.78 mmol) and *i*-Pr$_2$EtN (1.0 mL) in THF (5 mL) was added MOM-Cl (0.3 mL), and the mixture was heated at 50 °C during 6.5 h. After the aqueous workup chromatography on silica gel (hexane–acetone, 100:4) afforded the mixture of **13** and **14** (690 mg, 46%). The foregoing mixture (635 mg, 0.75 mmol) was dissolved in 1.0 M solution of tetra-*n*-butylammonium fluoride in THF, and the reaction was continued at room temperature for 24 h. Product was purified by chromatography on silica gel (chloroform–methanol, 20:1) giving 256 mg of the mixture of **15** and **16**, respectively (91%). This mixture (88 mg, 0.245 mmol) was reacted with acetic anhydride (0.1 mL) in pyridine (0.5 mL) at room temperature during 12 h. Chromatography of the resulting product (hexane–ether, 1:1) afforded 1,4,5-triacetate **17** (74.2 mg, R_f 0.13) and 1,4,6-triacetate **18** (33.2 mg, R_f 0.08, total yield 90%). Triacetates **17** and **18** were separately treated with K_2CO_3 in MeOH (100 mg in 1 mL) during 10 h. Triols **15** (51 mg) and **16** (20 mg, overall yield 80% in two steps) were isolated after chromatography as colorless noncrystalline solids. **15**: $[\alpha]_D$ +14.5° (*c* 4.5, CD_3OD); ^{1}H NMR (CD_3OD) δ 4.83 (s, C*H*$_2$OMe, 2 H), 4.27 (dd, H-2, *J* = 4.2, 5.7 Hz, 1 H), 3.81 (dd, H-1, *J* = 4.2, 9.1 Hz, 1 H), 3.78 (dd, H-3, *J* = 5.7, 7.2 Hz, 1 H), 3.53 (tr, H-6, *J* = 9.0 Hz, 1 H), 3.50 (dd, H-4, *J* = 7.2, 9.9 Hz, 1 H), 3.34 (s, OMe, 3 H), 3.25 (dd, *J* = 9.0, 9.9 Hz, 1 H), 2.07 (m, 2 H), 1.70 (m, 2 H), 1.48 (d, 1 H), 1.40 (m, 1 H), 1.20 (m, 1 H), 1.04, 0.88, 0.87 (each s, Me, 3 H); ^{13}C NMR (CD_3OD) δ 118.9 (C-2′), 98.8 (*C*H$_2$OMe), 81.6, 77.7, 77.4, 76.9, 74.4, 71.6 (CH, inositol), 56.2 (OMe), 52.6, 49.8, 46.6, 46.3, 30.6, 27.9, 21.2, 20.9, 10.4; MW for $C_{18}H_{30}O_7$ 358.1992, found 358.1998. **16**: $[\alpha]_D$ +19.1° (*c* 1.4, CD_3OD); ^{1}H NMR (CD_3OD) δ 4.82, 4.79 (each d, C*H*$_2$OMe), 4.27 (dd, H-2, *J* = 4.0, 5.7 Hz, 1 H), 3.81 (dd, H-3, *J* = 5.7, 7.0 Hz, 1 H), 3.72 (dd, H-1, *J* = 4.0, 9.5 Hz, 1 H), 3.62 (dd, H-6, *J* = 8.5, 9.5 Hz, 1 H), 3.56 (dd, H-4, *J* = 7.0, 9.5 Hz, 1 H), 3.43 (dd, H-5, *J* = 8.5, 9.5 Hz, 1 H), 3.30 (s, OMe, 3 H), 2.05 (m, 2 H), 1.70 (m, 2 H), 1.48 (d, 1 H), 1.37 (m, 1 H), 1.20 (m, 1 H), 1.03, 0.87, 0.84 (each s, Me, 3 H); ^{13}C NMR (CD_3OD) δ 118.9 (C-2′), 98.9 (*C*H$_2$OMe), 83.0, 77.54, 77.48, 76.4, 73.3, 71.6 (inositol), 56.2 (OMe), 52.4, 48.8, 46.4, 46.1, 30.5, 27.8, 21.1, 20.8, 10.3 (camphor); MW for $C_{18}H_{30}O_7$ 358.1991, found 358.2016. (b) 6-Alcohol **24** described below (505 mg, 0.64 mmol) was reacted with MOM-Cl (analogously as described later for the synthesis of 6-benzoyl derivative **25**) to give **26**. After aqueous workup the crude product was dried by evaporation with dry dioxane and treated with tetra-*n*-butylammonium fluoride in THF. Chromatography of the reaction mixture as above afforded pure **15** (58 mg, 25%), $[\alpha]_D^{20}$ +16.8° (*c* 1.2, CH_3OH).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-4-*O*-(trimethylacetyl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (19). Crude triol **7** (from 3.64 mmol of tetrol **1a**) was dissolved in pyridine (5 mL), and pivaloyl chloride (480 mg, 1.1 equiv) was added at −10 °C. After 3 h the mixture was concentrated, redissolved in hexane–ether (1:1), and washed three times with water, and the organic phase was concentrated. The residue was chromatographed on silica gel (hexane–acetone, 10:1.5) giving 1.85 g of diol (78% in two steps from **1a**). The product was contaminated with ca. 15% of an unidentified isomer which was not separated prior to the next stages: TLC R_f 0.27 (hexane–acetone, 10:2.5); ^{1}H NMR (DMSO-d_6, major isomer) δ 7.75 (m, Ph, 4 H), 7.5–7.3 (m, Ph, 6 H), 5.15 (d, OH, *J* = 5.6 Hz, 1 H), 5.07 (d, OH, *J* = 6 Hz, 1 H), 4.50 (tr, H-4, *J* = 8.0 Hz, 1 H), 4.05 (dd, H-3, *J* = 4.0 Hz, 9.0 Hz, 1 H), 3.80 (dd, H-2, *J* = 3.8, 6.6 Hz, 1 H), 3.70 (m, H-5, 1 H), 3.63 (tr, H-1, *J* = 6.5 Hz, 1 H), 3.46 (m, H-6, 1 H), 1.89 (m, 1 H), 1.63 (m, 3 H), 1.25 (m, 3 H), 1.13, 1.02 (each s, Bu, 9 H), 1.00, 0.84, 0.82 (each s, Me, 3 H); ^{13}C NMR (CD_3OD, major isomer) δ 179.8 (C=O), 137.5, 137.4, 135.6, 134.7, 130.9, 130.9, 128.6, 128.5 (Ph), 118.6 (C-2′), 77.7, 77.0, 74.4, 73.4, 72.3 (inositol), 52.5, 46.5, 45.2, 39.8, 30.6, 27.9, 27.7, 21.4, 20.9, 20.2, 10.6 (Bu, camphor); MW for $C_{37}H_{52}O_7Si$ 636.3482, found 636.3494.

1D-5,6-*O*-Bis(methoxymethylene)-1-*O*-(*tert*-butyldiphenylsilyl)-4-*O*-(trimethylacetyl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (20). Diol **19** (0.72 g, 1.04 mmol), *i*-Pr$_2$EtN (1.0 mL), and MOM-Cl (0.35 mL) in THF (3 mL) were heated at 50 °C during 24 h. TLC analysis after this time showed that no substrate was present. Usual aqueous workup and chromatography on silica gel (hexane–acetone, 10:0.7) afforded pure **20** (0.55 g, 69%) and **21** (0.19 g, 24%). Ether **21** was slightly contaminated (10% based on ^{13}C NMR) with an unidentified isomer: TLC R_f 0.39 (hexane–acetone, 10:1.25); ^{1}H NMR (DMSO-d_6) δ 7.7 (m, Ph, 4 H), 7.4 (m, Ph, 6 H), 4.80 (tr, *J* = 4.9 Hz, 1 H), 4.58 (s, 2 H), 4.54 (br m, 1 H), 4.46 (br m, 1 H), 4.26 (dd, *J* = 3.5, 8.8 Hz, 1 H), 3.90 (m, 2 H), 3.75 (m, 1 H), 3.27, 3.13 (each s, Me, 3 H), 1.84 (m, 1 H), 1.72 (m, 2 H), 1.35 (m, 1 H), 1.24 (m, 2 H), 1.12, 1.02 (each s, Bu, 9 H), 1.07, 0.95, 0.84 (each s, Me, 3 H); ^{13}C NMR ($CDCl_3$) δ 177.7 (C=O), 136.1, 135.9, 134.4, 133.6, 129.62, 129.60, 127.6, 127.4 (Ph), 117.0 (C-2′), 97.7, 96.1 (*C*H$_2$OMe), 77.4, 75.3, 74.0, 73.4, 70.2 (inositol), 55.6, 55.5 (OMe), 51.4, 47.8, 45.1, 42.4, 38.6, 29.8, 27.2, 27.1, 27.0, 20.5, 20.2, 19.1, 10.2 (camphor, Bu).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-6-*O*-(methoxymethylene)-4-*O*-(trimethylacetyl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2-ylidene)-*myo*-inositol (21). TLC R_f 0.27 (hexane–acetone, 10:1.25); ^{13}C NMR (CD_3OD) δ 179.5 (C=O), 137.4, 137.2, 135.6, 134.6, 130.9, 130.8, 128.65, 128.61 (Ph), 118.6 (C-2′), 97.1 (*C*H$_2$OMe), 78.6, 77.4, 76.9, 76.0, 73.0, 72.1 (CH, inositol), 56.0 (OMe), 52.6, 46.4, 44.9, 39.8, 30.7, 27.92, 27.7, 27.6, 21.4, 20.8, 20.2, 10.6.

1D-1-*O*-(*tert*-Butyldimethylsilyl)-6-*O*-(methoxymethylene)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (22). The foregoing derivative **21** (282 mg, 0.4 mmol) was dissolved in MeOH (3 mL), and 1 mL of 1.0 M potassium *tert*-butoxide was added. After 5 h at 50 °C substrate has disappeared (TLC). After the aqueous workup the crude product was chromatographed on silica gel (hexane–acetone, 8:1) yielding pure **22** (208 mg, 85%): $[\alpha]_D$ −39.5° (*c* 4.2, chloroform); ^{1}H NMR (CD_3OD) δ 7.75 (m, Ph, 4 H), 7.45–7.25 (m, Ph, 6 H), 4.77 (m, CH_2, 2 H), 3.91 (H-3, dd, *J* = 4.1, 9.5 Hz, 1 H), 3.80 (dd, H-2, *J* = 4.3, 5.2 Hz, 1 H), 3.70 (tr, H-4, *J* = 9.4 Hz, 1 H), 3.59 (dd, H-1, *J* = 5.3, 7.0 Hz, 1 H), 3.51 (dd, H-6, *J* = 7.1, 9.8 Hz, 1 H), 3.35 (s, Me, 3 H), 3.10 (tr, H-5, *J* = 9.6 Hz, 1 H), 1.91 (m, 1 H), 1.7–1.5 (m, 3 H), 1.30 (m, 2 H), 1.15 (d, *J* = 12.3 Hz, 1 H), 1.08 (s, Bu, 9 H), 1.04, 0.90, 0.86 (each s, Me, 3 H); ^{13}C NMR (CD_3OD) δ 137.3, 137.1, 135.6, 134.5, 130.7, 130.6, 128.5, 128.4 (Ph) 118.6 (C2′), 97.2 (*C*H$_2$OMe), 81.7, 77.8, 76.7, 74.3, 73.50, 73.47 (inositol), 55.8 (OMe), 52.6, 46.3, 45.9, 30.4, 27.9, 27.6, 21.3, 21.0, 20.1, 10.3; MW for $C_{34}H_{48}O_7Si$ 596.3169, found 596.3177. Anal. Calcd for $C_{34}H_{48}O_7Si$: C, 68.40; H, 8.11. Found: C, 68.43; H, 8.40.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-4-*O*-(methoxymethylene)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (23). The

crude mixture from the alkylation reaction above containing mono- and bis-MOM derivatives (1.58 g, 2.32 mmol) in THF was treated as described for **22** giving **20** (1.06 g, 63%) **22** (245 mg, 18%), and **23** (106 mg, 8%). All products were noncrystalline solids. **23**: ^{1}H NMR (DMSO-d_6) δ 7.67 (m, 4 H), 7.40 (m, 6 H), 4.85 (d, J = 4.7 Hz, OH), 4.80 (d, J = 4.7 Hz, OH), 4.73 (d, CH_2, J = 6.3 Hz, 1 H), 4.62 (d, CH_2, J = 6.3 Hz, 1 H), 4.15 (dd, H-3, J = 4.1, 9.2 Hz, 1 H), 3.67 (dd, H-2, J = 4.1, 6.0 Hz, 1 H), 3.54 (tr, H-4, J = 8.3 Hz, 1 H), 3.49 (tr, H-1, J = 6.4 Hz), 3.32 (m, H-6, 1 H), 3.27 (s, Me), 3.11 (m, H-5, 1 H), 1.86 (m, 1 H), 1.59 (m, 2 H), 1.39 (m, 1 H), 1.25 (m, 2 H), 1.02 (s, Bu, 9 H), 0.97, 0.80, 0.79 (each s, Me). Anal. Calcd for $C_{34}H_{48}O_7Si$: C, 68.40; H, 8.11. Found: C, 68.08; H, 8.39.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (24). Tetrol **1a** (1.0 g, 3.19 mmol) was treated with TBDPS-Cl in pyridine in the presence of imidazole as described above. The reaction mixture was treated subsequently with TIPDS-Cl_2 (1.1 g, 10% excess) at 0 °C. The mixture was then stored at room temperature for 12 h and was subjected to aqueous workup. The product was purified by chromatography on silica gel (hexane–ether, 20:1) giving **24** (2.05 g, 81%): TLC R_f 0.64 (hexane–acetone, 10:1); ^{1}H NMR (C_6D_6) δ 7.9 (m, Ph, 4 H), 7.25 (m, Ph, 6 H), 4.09 (tr, H-6, J = 9.5 Hz, 1 H), 4.00 (dd, H-1, J = 3.7, 9.5 Hz, 1 H), 3.87 (dd, H-2, J = 3.7, 5.7 Hz, 1 H), 3.84 (dd, H-4, J = 6.3, 9.3 Hz, 1 H), 3.47 (dd, H-3, J = 5.9, 6.1 Hz, 1 H), 3.25 (tr, H-5, J = 9.1, H-1), 2.50 (br s, OH, 1 H), 2.28 (m, 1 H), 1.80 (m, 1 H), 1.66 (m, 2 H), 1.4–1.05 (m, 44 H), 0.97, 0.82 (each s, Me, 3 H); ^{13}C NMR ($CDCl_3$) δ 136.3, 136.1, 134.3, 133.4, 129.7, 129.6, 127.5, 127.4 (Ph), 117.7 (C-2′), 79.7, 77.8, 77.1, 76.5, 71.2 (CH, inositol), 51.6, 48.0, 45.2, 44.7, 29.2, 27.1, 20.5, 20.4, 19.4, 9.8 (camphor), 26.8 (*Me*C), 14.1 (Me*C*), 17.4–17.1 (*Me*CH, six peaks), 12.9, 12.5, 12.2, 11.8 (Me*CH*); MS (FAB) m/z 796 (M + 2, 10), 795 (M + 1, 17), 794 (M, 11), 738 (M − Bu, 6), 603 (5), 547 (19), 459 (21).

1D-6-*O*-Benzoyl-1-*O*-(*tert*-butyldiphenylsilyl)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (25). 6-Alcohol **24** (0.555 g, 0.7 mmol) was treated with potassium hydride (140 mg) in THF (5 mL) at room temperature and after evolution of the hydrogen gas had ceased benzoyl chloride (161 μL, 2-fold excess) was added. The mixture was kept at room temperature for 1 h, and was subjected to aqueous workup. Product was purified by chromatography on silica gel (hexane–ether, 20:1) to give pure **25** (noncrystalline solid, 418 mg, 66%): TLC R_f 0.2 (hexane–ether, 20:1); $[\alpha]_D$ +26.2° (c 2.6, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 8.1–7.75 (m, Ph, 6 H), 7.35–7.0 (m, Ph), 5.62 (dd, H-6, J = 4.5, 5.8 Hz, 1 H), 4.70 (dd, H-1(5), J = 7.5, 4.5 Hz, 1 H), 4.54 (dd, H-5(1), J = 4.0, 6.0 Hz, 1 H), 4.34 (tr, H-3, J = 7.9 Hz, 1 H), 4.17 (tr, H-2(4), J = 7.6 Hz, 1 H), 4.10 (dd, H-4(2), J = 4.0, 8.1 Hz, 1 H), 2.22, 1.78, 1.6, 1.45–0.9, 0.87, 0.73, 0.67; ^{13}C NMR (C_6D_6) δ 165.2 (C=O), 136.3, 135.9, 135.7, 133.4, 133.2, 132.7, 130.6, 130.2, 130.1, 130.0 (Ph), 117.4 (C-2′), 81.2, 80.0, 76.0, 75.5, 72.4, 71.5 (CH, inositol), 51.6, 48.0, 45.5, 43.7, 29.9, 27.3, 27.1, 20.6, 20.3, 19.6, 18.0–17.4 (eight peaks) 13.5, 13.4, 12.9, 12.6, 9.9.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (27). Alcohol **24** (2.0 g) was treated with trifluoroacetic acid (1 mL) in chloroform (8 mL) at room temperature during 24 h. Neutralization with phosphate buffer followed by the aqueous workup and chromatography (hexane–acetone, 20:1) gave pure product **27** (1.1 g, 70%): TLC R_f 0.4 (hexane–acetone, 4:1); ^{1}H NMR (CD_3OD) δ 7.4 (m, Ph, 4 H), 7.4 (m, Ph, 6 H), 3.88 (m, H-4, H-6, 2 H), 3.70 (tr, H-2, J = 2.7 Hz, 1 H), 3.53 (dd, H-1(3), J = 2.8, 9.8 Hz), 3.29 (tr, H-5, 8.6 Hz, 1 H), 3.03 (dd, H-3(1), J = 2.5, 9.3 Hz, 1 H), 1.2–0.9 (m, *i*-Pr, *t*-Bu, 37 H); ^{13}C NMR (CD_3OD) δ 137.4, 137.1, 135.5, 134.8, 130.75, 130.7, 128.6, 128.5 (Ph), 80.4, 77.9, 75.3, 74.7, 74.1, 73.2 (inositol), 27.6 (*Me*C), 20.3 (Me*C*), 17.9, 17.8, 17.7 (*Me*CH), 14.0, 13.4, 13.3 (Me*CH*).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-2,3,6-*O*-tribenzoyl-*myo*-inositol (28). The foregoing triol (**27**, 695 mg, 1.14 mmol), benzoyl chloride (0.9 mL), and DMAP (50 mg) in pyridine (2.5 mL) were refluxed during 20 h. After the aqueous workup and chromatography (hexane–ether, 20:1) 2,3,6-tribenzoyl derivative **28** was obtained (730 mg, 70%): TLC R_f 0.2 (hexane–acetone, 20:1); ^{1}H NMR (C_6D_6) δ 8.3, 8.17, 8.07 (each m, Ph, 2 H), 7.70 (m, Ph), 7.15 (m, Ph, 9 H), 6.90 (m, Ph, 6 H), 6.54 (tr, H-6, J = 9.7 Hz, 1 H), 6.04 (tr, H-2, J = 2.8 Hz, 1 H), 5.39 (dd, H-3, J = 2.7, 10.0 Hz, 1 H), 4.65 (dd, H-4, J = 8.6 Hz, 10.0 Hz, 1 H), 4.37 (dd, H-1, J = 2.9, 10.1 Hz, 1 H), 3.76 (tr, H-5, J = 9.1 Hz, 1 H), 1.35–0.80 (m, 37 H); MS (FAB) m/z 916 (M − C_4H_8, 21), 895 (M − Ph, 9), 852 (4), 796 (2), 730 (2), 672 (3), 593 (9), 473 (16).

1D-*O*-(*tert*-Butyldiphenylsilyl)-2,3,6-*O*-tribenzoyl-*myo*-inositol (29). Derivative **28** (0.7 g, 0.72 mmol) was dissolved in acetonitrile–chloroform (7:1, v/v, 8 mL) and added with 5% aqueous HF (1.1 mL). After 12 h at room temperature the mixture was neutralized with aqueous sodium bicarbonate, and the product was chromatographed on silica gel (chloroform–methanol, 40:1) to give **29** (72%): TLC R_f 0.3 (chloroform–methanol, 40:1); $[\alpha]_D$ −1.5° (c 2, CH_3OH); ^{1}H NMR (DMSO-d_6) δ 8.1–7.15 (m, Ph, 25 H), 5.73 (tr, H-6, J = 9.8 Hz, 1 H), 5.53 (tr, H-2, J = 2.7 Hz, 1 H), 5.44 (d, OH, J = 7.3 Hz), 5.43 (d, OH, 5.2 Hz), 5.03 (dd, H-1, J = 2.7, 10.0 Hz, 1 H), 4.59 (dd, H-3, J = 2.7 Hz, 10.0 Hz, 1 H), 3.86 (m, H-4, 1 H), 3.57 (m, H-5, 1 H), 0.73 (s, Bu, 9 H); ^{13}C NMR ($CDCl_3$) δ 166.6, 165.8, 165.4 (C=O, benzoyl), 135.9–127.4 (19 signals, Ph), 74.9, 73.5, 72.2, 71.9, 71.7, 70.1 (CH, inositol), 26.4 (C*Me*), 19.0 (*C*Me); MS (FAB) m/z 674 (M − C_4H_8, 28), 653 (M − Ph, 23), 610 (11), 531 (5).

1D-2,3,6-*O*-Tribenzoyl-*myo*-inositol (30). Diol **29** was dissolved in acetonitrile (1 mL), and 50% aqueous HF (1 mL) was added. The precipitation was solubilized by adding chloroform. The mixture was maintained at 50 °C during 24 h. The mixture was neutralized with sodium bicarbonate, and the precipitated solid product was centrifuged off, washed with ether, and briefly chromatographed on silica gel (chloroform–methanol, 50:1) to give pure **30** (70%): TLC R_f 0.24 (chloroform–methanol, 20:1); $[\alpha]_{546}^{20}$ +5.9° (c 2.5, THF), lit. +5.4°;[6b] ^{1}H NMR (CD_3OD) δ 8.15–7.3 (m, Ph, 15 H), 5.93 (tr, H-2, J = 2.8 Hz, 1 H), 5.66 (tr, H-6, J = 9.9 Hz, 1 H), 5.21 (dd, H-3, J = 2.9, 10.1 Hz, 1 H), 4.19 (dd, H-1, J = 2.9, 10.2 Hz, 1 H), 4.17 (tr, H-4, J = 10.2 Hz, 1 H), 3.77 (tr, H-5, J = 9.5 Hz, 1 H). Anal. Calcd for $C_{27}H_{24}O_9$: C, 65.84; H, 4.91. Found: C, 65.44; H, 5.00.

Reaction of the Mixture 1a–d with 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane. The mixture containing all four isomers **1** (3.14 g, 10 mmol) was dissolved in pyridine (20 mL), and the solution was treated with TIPDS-Cl_2 (1.1 equiv) at −30 °C. The mixture was warmed up to room temperature in the course of 0.5 h and was stirred for 3 h. After the aqueous workup the product was chromatographed (hexane–acetone, 10:1.5). Two fractions both containing two isomers **31a,b** (R_f 0.33) and **31c,d** (R_f 0.40) were isolated: total yield 5.52 g (96%). **31a,b**: ^{13}C NMR (CD_3OD) δ 118.1, 118.0 (C-2′), 78.9, 78.7, 77.5, 76.8, 76.75, 76.69, 76.4, 74.7, 74.4, 74.3, 73.9 (CH-inositol), 54.2, 52.1, 47.4, 46.1, 46.0, 45.9, 32.3, 30.0, 29.0, 27.8, 27.4, 23.3, 20.9, 20.8, 20.7, 18.0, 17.8, 17.7, 17.67, 17.6, 14.4, 13.8, 13.5, 13.0, 12.8, 10.2.

1D-1,6-*O*-(1,1,3,3-Tetraisopropyldisiloxanedi-1,3-yl)-2,3-*O*-(D-1′,7′,7′-trimethyl[2.2.1]bicyclohept-2′-ylidene)-*myo*-inositol (31a). (a) Pure diol **31a** was obtained analogously as described above for the mixture **31a,b** except pure tetrol **1a** was used as a substrate. Diol **31a** was also obtained in 91% yield by debenzoylation of **32a** with methylamine/toluene at 50 °C during 48 h: TLC R_f 0.33 (hexane–acetone, 10:1.5); $[\alpha]_D^{20}$ + 9.3° (c 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.21 (dd, H-2, J = 4.3, 5.2, 1 H), 3.92 (dd, H-1, J = 4.3, 9.2 Hz, 1 H), 3.83 (tr, H-3, J = 5.4, 7.0 Hz), 3.80 (tr, H-6, J = 9.2 Hz, 1 H), 3.57 (dd, H-4, J = 7.0, 10.2 Hz, 1 H), 3.26 (dd, H-5, J = 9.2, 10.1 Hz, 1 H), 2.86 (br, s, OH), 2.70 (br s, OH), 1.97 (m, 2 H), 1.70 (m, 2 H), 1.48 (d, 1 H), 1.38 (m, 1 H), 1.22 (m, 1 H), 1.12–0.98 (m, 31 H), 0.84 (s, 3 H), 0.81 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 117.5 (C-2′), 76.6, 75.7, 75.5, 73.7, 73.4 (CH, inositol), 51.4, 48.0, 45.3, 45.2, 20.4, 20.2 (camphor), 17.5–17.0 (seven peaks, CH*Me*), 12.9, 12.7, 12.2, 12.0 (*C*HMe), 9.8 (Me). Anal. Calcd for $C_{28}H_{52}O_7Si_2$: C, 60.39; H, 9.41. Found: C, 59.95; H, 9.38.

Benzoylation of Diols 31a,b. The mixture of diols **31a,b** (1.69 g, 2.9 mmol) was treated with benzoyl chloride (1.0 g, 20% excess) in pyridine (10 mL) first at room temperature (4 h) and then at 60 °C (1 h). The product was chromatographed on silica gel (toluene–hexane–ether, 1:1:0.02) giving two fractions **32a** (R_f 0.32, 0.9 g, 39%) and **32b** (R_f 0.47, 1.16 g, 51%). **32a** (noncrystalline solid): ^{1}H NMR ($CDCl_3$) δ 7.95 (m, Ph, 4 H), 7.4 (m, Ph, 2 H), 7.3 (m, Ph, 4 H), 5.58 (dd, H-6(5), J = 7.1, 10.7 Hz, 1 H), 5.38 (dd, H-5(6), J = 9.1, 10.7 Hz, 1 H), 4.38 (dd, H-2, J = 4.1, 5.3 Hz, 1 H), 4.19 (m, 3 H), 2.03 (m, 1 H), 1.91 (m, 1 H), 1.72 (m, 2 H), 1.49 (d, 1 H), 1.41 (m, 1 H), 1.17 (m, 1 H), 1.11–0.82 (numerous singlets, 36 H); ^{13}NMR ($CDCl_3$) δ 165.6, 165.5 (C=O), 132.8, 132.7, 129.7, 129.6, 129.0, 128.1, 128.0, 125.3 (Ph), 118.2 (C-2′), 76.7, 75.0, 73.79, 73.73, 73.67, 72.4 (CH, inositol), 51.7, 48.1, 45.4, 45.2, 29.2, 27.1, 20.5, 20.2 (camphor), 17.6, 17.2, 17.1, 17.0, 16.9 (CH*Me*), 13.0, 12.6, 12.1, 12.0 (*C*HMe), 9.5 (C*Me*). **32b**: mp 125.5–127 °C; ^{1}H NMR ($CDCl_3$) δ 7.95 (m, Ph, 4 H), 7.4 (m, Ph, 2 H), 7.3 (m, Ph, 4 H), 5.63 (dd, H-6(5), J = 7.2, 10.9, 1 H), 4.36 (dd, H-5(6), J = 9.6, 10.9 Hz, 1 H), 4.28 (m, 3 H), 4.07 (dd, J = 3.7, 9.0 Hz, 1 H), 2.34 (m, 1 H), 1.96 (d, 1 H), 1.85–1.6 (m, 3 H), 1.35–1.13 (m, 2 H), 1.1–0.8 (numerous singlets, 37 H); ^{13}C NMR ($CDCl_3$) δ 165.7, 165.6 (C=O), 132.9, 132.7, 129.7, 129.6, 129.0, 128.2, 128.0, 125.3 (Ph), 118.2 (C-2′), 77.7, 75.5, 73.9, 73.7, 72.7, 72.4 (CH, inositol), 53.6, 47.9, 46.0, 45.1, 28.3, 26.7, 20.4, 20.1 (camphor), 17.56, 17.1, 16.9 (CH*Me*), 13.0, 12.6, 12.1 (*C*HMe), 9.8 (Me).

1D-4,5-*O*-Dibenzoyl-1,6-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (33a). Fully protected derivative **32a** (0.799 g, 1.02 mmol) was treated with 20% (v/v) solution of TFA in chloroform during

24 h at room temperature. The mixture was concentrated to dryness, the residual acid was neutralized with pyridine/chloroform, and the mixture was concentrated under vacuum. The crude product was chromatographed (hexane–acetone, 10:1) giving pure **33a** (0.638 g, 99%). Recrystallization from pentane afforded regular cubic crystals. This product (and its enantiomer **33b**) displayed complicated melting behavior with initial melting at 110 °C, partial solidification at higher temperature, and second melting point at 147–148 °C: $[\alpha]_D$ −17.4° (*c* 5.0, $CHCl_3$); TLC R_f 0.21 (hexane–acetone, 4:1); ^{1}H NMR (CD_3OD) δ 7.9 (m, Ph, 4 H), 7.45 (m, Ph, 2 H), 7.25 (m, Ph, 4 H), 5.78 (tr, H-5(6), *J* = 10.1, Hz, 1 H), 5.48 (tr, H-6(5), *J* = 9.5 Hz, 1 H), 4.36 (tr, H-4, *J* = 9.2 Hz, 1 H), 4.12 (tr, H-2, *J* = 2.7 Hz, 1 H), 3.94 (m, 2 H), 1.15–0.75 (m, 32 H); ^{13}C NMR (CD_3OD) δ 167.7, 167.1 (C=O), 134.15, 134.09, 131.1, 130.9, 130.54, 130.50, 129.3 (Ph), 76.6, 75.7, 75.4, 74.5, 74.4, 71.2 (CH, inositol), 17.9, 17.8, 17.73, 17.69, 17.65, 17.63, 17.58 (CH*Me*), 13.96, 13.91, 13.5, 13.3 (*C*HMe); MS (EI) *m/z* 587 (M − C_3H_7, 2), 465 (2), 343 (31), 105 (BP), 77 (23). Anal. Calcd for $C_{32}H_{46}O_9Si_2$: C, 60.19; H, 7.34. Found: C, 60.19; H, 7.32.

1D-5,6-*O*-Dibenzoyl-3,4-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (33b). Diol **33b** was obtained analogously from **32b** in 97.5% yield: $[\alpha]_D$ +17.6° (*c* 5.0, $CHCl_3$); mp 148 °C (same melting behavior as of **33a**). ^{1}H, ^{13}C NMR, and MS spectra were identical to those of **33a**.

1D-3,4,5-*O*-Tribenzoyl-*myo*-inositol (35). Diol **33a** (490 mg, 0.78 mmol) in pyridine (3 mL) was treated with benzoyl chloride (120 mg, 1.1 equiv) at −30 °C and warmed to room temperature within 1 h. TLC (acetone–hexane, 10:2) showed completion of the reaction. The mixture was subjected to aqueous workup, and the product was concentrated under vacuum and dissolved in acetonitrile (10 mL) containing 10% aqueous HF (polyethylene vial). Chloroform (2 mL) was added to facilitate solubilization. After 6 h TLC (chloroform–methanol, 10:1) showed complete disappearance of the substrate. The mixture was diluted with chloroform and washed subsequently with saturated aqueous sodium bicarbonate and water. Crude product was chromatographed on silica gel (chloroform–methanol, 20:1) giving **35** (360 mg, 94%) as a noncrystalline solid: TLC R_f 0.31 (chloroform–methanol, 10:1); $[\alpha]_D$ +10.2° (*c* 2.8, $CHCl_3$); ^{1}H NMR (CD_3OD) δ 7.93 (m, Ph, 4 H), 7.75 (d, Ph, 2 H), 7.45 (tr, Ph, 2 H), 7.31 (m, Ph, 5 H), 7.17 (tr, Ph, 2 H), 6.14 (tr, H-4, *J* = 10.2 Hz, 1 H), 5.59 (tr, H-5, *J* = 9.8 Hz, 1 H), 5.45 (dd, H-3, *J* = 2.5 Hz, 10.4 Hz, 1 H), 4.43 (b tr, H-2, *J* = 2.3 Hz, 1 H), 4.20 (tr, H-6, *J* = 9.7 Hz, 1 H), 3.85 (dd, H-1, *J* = 2.6 Hz, 9.7 Hz, 1 H); ^{13}C NMR (CD_3OD) δ 167.5, 167.3, 167.2, 134.3, 134.2, 134.1, 131.0, 130.7, 130.6, 130.4, 130.3, 129.4, 129.3, 75.6, 74.2, 72.9, 72.3, 71.5.

1D-1-*O*-(*tert*-Butyldimethylsilyl)-2,5,6-*O*-tribenzoyl-3,4-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (37). Diol **33b** (400 mg, 0.63 mmol) in pyridine (3 mL) was treated with the solution of TBDMS-Cl (114 mg, 1.2 equiv) in pyridine (0.5 mL) in the presence of imidazole (1.5 equiv) at ambient temperature during 24 h. After aqueous workup and chromatography (hexane–ether, 4:1) the alcohol **36** (472 mg, 98%) was obtained. The 2-alcohol **36** (460 mg, 0.61 mmol), benzoyl chloride (450 mg), and DMAP (80 mg) in pyridine (2 mL) were heated at 70 °C during 24 h. After routine workup and chromatography (hexane–ether, 15:1) fully protected derivative **37** (535 mg, quantitative yield) was obtained: TLC R_f 0.44 (hexane–ether, 6:1): ^{1}H NMR ($CDCl_3$) δ 8.15–7.85 (m, Ph), 7.6–7.3 (m, Ph), 5.91 (tr, H-6, *J* = 10.0 Hz, 1 H), 5.81 (tr, H-2, *J* = 3.1 Hz, 1 H), 5.56 (dd, H-5, *J* = 9.5, 10.4 Hz), 4.37 (tr, H-4, *J* = 9.3 Hz), 4.14 (dd, H-1, *J* = 3.1, 9.8 Hz, 1 H), 4.07 (dd, H-3, *J* = 3.2, 10.0 Hz, 1 H), 0.92–0.80 (m, Me, 28 H), 0.64 (s, Bu, 9 H), 0.09 (s, Me, 3 H), −0.15 (s, Me, 3 H).

1D-2,5,6-*O*-Tribenzoyl-*myo*-inositol (38). The solution of the foregoing derivative **37** (520 mg, 0.61 mmol) in chloroform (5 mL) containing TFA (1 mL) was heated at 50 °C during 12 h. After the reaction had been completed as judged by TLC (ether–hexane, 6:1) the usual aqueous workup and chromatography on silica gel (analogously to purification of **35**) afforded pure **38** (279 mg, 90%): $[\alpha]_D$ −8.6° (*c* 2.5, $CHCl_3$); TLC R_f 0.35 (chloroform–methanol, 9:1); ^{1}H NMR (CD_3OD) δ 8.2 (m, Ph, 2 H), 7.9 (m, Ph, 4 H), 7.7–7.45 (m, Ph, 5 H), 7.35 (m, Ph, 4 H), 5.85 (tr, H-2, *J* = 2.9 Hz, 1 H), 5.79 (tr, H-6, *J* = 10.1 Hz, 1 H), 5.45 (tr, H-5, *J* = 9.9 Hz), 4.21 (dd, H-1, *J* = 10.1 Hz, 1 H), 4.14 (tr, H-4, *J* = 9.7 Hz, 1 H), 3.92 (dd, H-3, *J* = 9.9 Hz, 1 H); ^{13}C NMR (CD_3OD) δ 167.8, 167.64, 167.62 (C=O), 134.1, 131.5, 130.93, 130.88, 130.7, 130.55, 130.53, 129.31, 129.28 (Ph), 76.2, 75.8, 74.8, 72.8, 71.7, 69.8 (CH, inositol); MW for $C_{27}H_{25}O_9$ (MI + 1 H) 493.1498, found 493.1491.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-*myo*-inositol (39). Triol **7** (1.0 g, 1.81 mmol) in $CHCl_3$ (2 mL) was treated with mercaptoethanol (1.5 mL) and BF_3–etherate (0.3 mL) at room temperature during 2.5 h. The mixture was concentrated, and the crude product was chromatographed on silica gel (gradient: chloroform–methanol, 60:1 to 9:1) giving pure **39** (600 mg, 80%) as a glassy solid. The typical deprotection conditions for acetal group cleavage such as 0.2 N HCl/methanol, glacial acetic acid/Zn, TFA, and TFA–$CHCl_3$ resulted in the isomerization and/or TBDPS group cleavage. Product **39** isomerizes to 2-TBDPS-inositol with traces of acidic catalysts: TLC R_f 0.5 (chloroform–methanol, 4:1); $[\alpha]_D$ −6.4° (*c* 3.5, MeOH); ^{1}H NMR (DMSO-d_6) δ 7.7 (m, Ph, 4 H), 7.35 (m, Ph, 6 H), 4.56 (d, OH), 4.53 (d, OH), 4.42 (d, OH), 4.39 (d, OH), 4.35 (d, OH), 3.62 (d tr, H-6, *J* = 9.4, 4.9 Hz), 3.51 (m, H-2, 1 H), 3.41 (dd, H-1, *J* = 2.6, 9.6 Hz, 1 H), 3.35 (d tr, H-4, *J* = 9.4, 4.9 Hz, 1 H), 2.80 (m, H-3, H-5, 2 H), 1.00 (s, Me, 9 H); ^{13}C NMR (CD_3CN) δ 137.0, 136.8, 135.1, 134.7, 130.7, 130.6, 128.6, 128.5 (Ph), 75.6, 75.2, 74.0, 73.7, 73.6, 72.6 (CH, inositol), 27.5 (Me), 20.2 (*C*Me).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3,4-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (40). Pentol **39** (147 mg, 0.35 mmol) in pyridine (1 mL) was treated with TIPDS-Cl_2 (143 mg, 30% excess) and imidazole (142 mg, 3-fold excess) at 0 °C during 12 h. Aqueous workup of the mixture followed by chromatography (hexane–acetone, 10:1) gave pure **40** (184 mg, 80%): TLC R_f 0.33 (hexane–acetone, 4:1); ^{1}H NMR (DMSO-d_6) δ 7.75 (m, Ph, 4 H), 7.35 (m, Ph, 6 H), 4.68 (d, OH), 4.65 (d, OH), 4.41 (d, OH), 3.70 (m, H-6, H-4, 2 H), 3.51 (dd, H-1(3), *J* = 2.3, 9.7 Hz, 1 H), 3.38 (m, H-2, 1 H), 3.14 (dd, H-3(1), *J* = 2.5, 8.9 Hz, 1 H), 2.94 (m, H-5, 1 H), 1.05–0.75 (m, *i*-Pr, Bu, 37 H); ^{13}C NMR ($CDCl_3$) δ 135.9, 135.8, 134.0, 139.6, 129.9, 127.7, 127.6 (Ph), 76.3, 74.7, 74.2, 73.1, 72.1 (CH, inositol), 27.0 (C*Me*), 19.5 (*C*Me), 17.5, 17.3, 17.2, 17.0 (CH*Me*), 12.8, 12.7, 12.1, 12.0 (*CH*Me).

1D-2,5,6-Tris(methoxymethylene)-*myo*-inositol (42). Triol **40** (34 mg, 50 μmol) in DMF (0.5 mL) was treated with *i*-Pr_2EtN (0.1 mL) and MOM-Cl (75 μL). The mixture was stored at room temperature for 24 h. After aqueous workup (hexane, water) the product **41** was dried by azeotropic evaporation of dioxane and was further treated with tetra-*n*-butylammonium fluoride (0.3 mL, 1.0 M solution in THF). After 12 h the mixture was chromatographed on silica gel (hexane–acetone, 3:1, then 1:1) giving pure **42** (12.5 mg, 78%) as white crystals: mp 75.5–76.5 °C; TLC R_f 0.14 (hexane–acetone, 1:1); $[\alpha]_D$ −15.4° (*c* 0.6, MeOH); ^{1}H NMR (CD_3CN) δ 4.82–4.71 (m, CH_2OMe, 6 H), 3.87 (tr, H-2, *J* = 2.6 Hz, 1 H), 3.60–3.39 (m, 5 H), 3.39, 3.38, 3.37 (each s, Me, 3 H), 3.37–3.21 (m, 3 H); ^{13}C NMR (CD_3CN) δ 99.3, 99.0, 98.9 (*C*H_2OMe), 83.0, 81.8, 81.6, 74.1, 72.3, 72.0 (CH, inositol), 56.2 (OMe); MS (EI) *m/z* 267 (MI − C_2H_5O), 250, 249 (MI − C_2H_5O, −H_2O), 235 (MI − C_2H_5O, −CH_4O), 217, 175, 143, 117, 99, 86, 73, 45 (BP).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3,4,5-*O*-tribenzoyl-*myo*-inositol (43). The solution of pentol **39** (199 mg, 0.47 mmol) in pyridine (1.3 mL) was treated with benzoyl chloride (205 mg, 3.1 equiv) at −10 °C during 2 h. After aqueous workup the mixture was chromatographed on silica gel (hexane–acetone, 4:1) giving **43** (307 mg, 89%, glassy solid): ^{1}H NMR ($CDCl_3$) δ 8.0–7.25 (m, Ph, 25 H), 6.20 (tr, H-4, *J* = 10.3 Hz, 1 H), 5.38 (tr, H-5, *J* = 9.9 Hz, 1 H), 5.16 (dd, H-3, *J* = 2.7, 10.4 Hz, 1 H), 4.41 (d tr, H-6, *J* = 9.5, 4.0 Hz, 1 H), 4.23 (tr, H-2, *J* = 2.7 Hz, 1 H), 3.90 (dd, H-1, *J* = 2.7, 9.2 Hz, 1 H), 1.13 (9 H, Me); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.6, 165.4 (C=O), 135.8, 135.5, 133.1, 133.0, 132.8, 132.2, 130.1, 129.7, 129.4, 129.2, 129.1, 129.0, 128.3, 128.2, 128.0, 127.9 (Ph), 74.5, 73.3, 72.2, 71.7, 70.5, 69.9 (CH, inositol), 26.9 (C*Me*), 19.2 (*C*Me).

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-2,6-*O*-bis(methoxymethylene)-3,4,5-*O*-tribenzoyl-*myo*-inositol (44). 2,6-Diol **43** (134 mg, 0.183 mmol) in DMF-*i*-Pr_2EtN (1 mL, 1:1 v/v) containing MOM-Cl (0.2 mL) was heated at 50 °C during 12 h. The reaction mixture was worked up in a usual manner and chromatographed (hexane–acetone, 8:1) to give pure **44** (113 mg, 75%) as a noncrystalline solid: $[\alpha]_D$ +41° (*c* 1.6, chloroform); TLC R_f 0.33 (hexane–acetone, 3:1); ^{1}H NMR ($CDCl_3$) δ 8.1–7.1 (m, Ph, 25 H), 6.12 (dd, H-4, *J* = 9.9, 10.5 Hz, 1 H), 5.56 (tr, H-5, *J* = 9.5 Hz, 1 H), 4.98 (dd, H-3, *J* = 2.3, 10.7 Hz, 1 H), 4.85 (d, CH_2, *J* = 6.9 Hz, 1 H), 4.64 (d, CH_2, *J* = 6.4 Hz, 1 H), 4.61 (dd, CH_2, *J* = 6.4 Hz, 1 H), 4.40 (tr, H-6, 9.9 Hz, 1 H), 4.38 (d, CH_2, *J* = 6.9 Hz, 1 H), 4.24 (dd, H-1, *J* = 2.1, 9.6 Hz, 1 H), 3.96 (tr, H-2, *J* = 2.4 Hz, 1 H), 3.23 (s, Me, 3 H), 2.97 (s, Me, 3 H), 1.16 (s, Bu, 9 H); ^{13}C NMR ($CDCl_3$) δ 165.76, 165.73, 165.3 (C=O), 135.8, 133.2, 132.95, 132.89, 132.83, 132.79, 130.1, 129.94, 129.87, 129.6, 129.5, 129.30, 129.29, 128.15, 128.12, 128.0, 127.8 (Ph), 98.6, 98.05 (*C*H_2OMe), 79.1, 76.7, 73.9, 72.4, 71.7, 70.9 (CH, inositol), 55.84, 55.76 (OMe), 27.1 (C*Me*), 19.2 (*C*Me).

1D-2,6-*O*-Bis(methoxymethylene)-1-*O*-(*tert*-butyldiphenylsilyl)-*myo*-inositol (45). The solution of foregoing fully protected *myo*-inositol **44** in toluene containing 20% methylamine was heated at 50 °C during 12 h. Pure product (95%) was obtained after chromatography (hexane–acetone, 2:1) as a viscous oil: TLC R_f 0.09 (hexane–acetone, 2:1); $[\alpha]_D$ +46° (*c* 1.8, MeOH); ^{1}H NMR (CD_3CN) δ 7.75, 7.35 (m, Ph, 10 H), 4.65 (m, CH_2, 2 H), 4.54 (m, CH_2, 2 H), 3.86 (tr, H-2, *J* = 2.5 Hz, 1 H), 3.83 (d, OH), 3.61 (tr, H-6, *J* = 9.1 Hz, 1 H), 3.40 (m, 2 H), 3.31 (s, Me, 3 H), 3.29 (s, Me, 3 H), 3.18 (d, OH), 3.05 (m, 2 H), 1.05 (s, Bu, 9 H); ^{13}C NMR (CD_3OD) δ 137.1, 137.0, 134.9, 134.7, 131.2, 130.9,

128.8, 128.6 (Ph), 99.4, 99.1 (CH_2OMe), 83.5, 81.8, 75.5, 74.7, 74.6, 72.3 (CH, inositol), 56.4, 56.3 (OMe), 27.7 (*CMe*), 20.1 (*CMe*).

1D-1,6-*O*-(1,1,3,3-Tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (46). (a) The deprotection of crude **31a** obtained from **1a** (20.0 g, 63.7 mmol) with chloroform-TFA (330 mL, 10:1 v/v) at room temperature was complete within 4 h at room temperature with only little isomerization observed. Chromatography on silica gel (chloroform-methanol, 9:1) afforded **46** (22.6 g, 84%) as a glassy solid. (b) The diol **31a** (487 mg, 0.87 mmol) was deprotected analogously as described above for triol **7**. The product was purified by silica gel chromatography as above giving **46** (225 mg, 61%): TLC R_f 0.22 (chloroform-methanol, 9:1); $[\alpha]_D$ +8.5° (*c* 3.4, MeOH); ^{1}H NMR (DMSO-d_6) δ 4.58, 4.51, 4.45, 4.39 (each d, OH), 3.72 (m, H-2, H-6, 2 H), 3.51 (dd, H-1, J = 2.8, 9.1 Hz, 1 H), 3.41 (d tr, H-4, J = 4.6, 9.4 Hz, 1 H), 3.19 (ddd, H-3, J = 5.3, 2.5, 9.7 Hz, 1 H), 3.03 (d tr, H-5, J = 4.6, 8.9 Hz, 1 H), 1.07-0.9 (m, *i*-Pr, 28 H); ^{13}C NMR ($CDCl_3$) δ 76.2, 74.5, 74.1, 72.8, 71.8, 71.4 (broad signals, CH, inositol), 17.22, 17.17 (CH*Me*), 12.7, 12.05 (*C*HMe).

1D-1,6-*O*-(1,1,3,3-Tetraisopropyldisiloxanedi-1,3-yl)-2,3,4,5-*O*-tetrakis(methoxymethylene)-*myo*-inositol (47). Tetrol **46** (10.0 g, 23.7 mmol) was alkylated with MOM-Cl (9.5 mL) in DMF (50 mL) in the presence of *i*-Pr_2EtN (15.9 g, 20% excess). The mixture was stored at room temperature during 12 h and next heated at 60 °C during 5 h. The product was purified by silica gel chromatography (hexane-acetone, 10:1) giving **47** as a thick oil (12.04 g, 85%): TLC R_f 0.26 (hexane-acetone, 5:1); $[\alpha]_D$ +30.3° (*c* 3.5, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 5.03 (m, CH_2OMe, 5 H), 4.70 (m, CH_2OMe, 3 H), 4.26 (tr, H-6(4), J = 9.0 Hz, 1 H), 4.24 (tr, H-4(6), J = 9.8 Hz, 1 H), 4.14 (tr, H-2, 2.5 Hz, 1 H), 3.47 (m, H-5, H-3, H-1, 3 H), 3.40, 3.39, 3.33, 3.29 (each s, Me, 3 H), 1.18-0.94 (m, *i*-Pr, 28 H); ^{13}C NMR (C_6D_6) δ 98.8, 98.7, 97.8, 96.0 (CH_2OMe), 80.4, 77.8, 76.9, 76.3, 76.0, 75.9 (CH, inositol), 56.4, 56.2, 55.4, 55.3 (OMe), 17.68-17.29 (seven signals, CH*Me*), 13.2, 13.0, 12.6, 12.4 (*C*HMe); MS (EI) 491 (MI - $2C_2H_5O$, -OH), 387 (5), 357 (5), 303 (2), 277 (6), 263 (9), 249 (11), 109 (3), 45 (BP).

1D-2,3,4,5-*O*-Tetrakis(methoxymethylene)-*myo*-inositol (48). Fully protected derivative **47** (11.6 g, 19.4 mmol) was treated with tetra-*n*-butylammonium fluoride in THF (43 mL, 1.0 M). After 0.5 h the mixture was concentrated and chromatographed on silica gel (hexane-acetone, 3:1, then 1:1) to give pure **48** (6.7 g, 97%): $[\alpha]_D$ +3.6° (*c* 1.2, $CHCl_3$); TLC R_f 0.23 (hexane-acetone, 1:1); ^{1}H NMR (C_6D_6) δ 4.92-4.56 (m, CH_2, 8 H), 4.19 (dd, H-4(5), J = 9.3, 10.0 Hz, 1 H), 4.14 (tr, H-2, J = 2.5 Hz, 1 H), 3.93 (tr, H-5(4), J = 9.5 Hz, 1 H), 3.47 (dd, H-3, J = 2.6, 10.1 Hz, 1 H), 3.31, 3.23, 3.22, 3.10 (each s, Me, 3 H), 3.3-3.2 (m, H-1, H-6, 2 H); ^{13}C NMR (C_6D_6) δ 98.5, 98.3, 97.9, 96.2 (CH_2OMe), 85.3, 77.4, 76.9, 76.5, 73.3, 72.3 (CH, inositol), 55.8, 55.5, 55.4 (OMe); MS (EI) m/z 311 (MI - C_2H_5O), 279 (MI - C_2H_5O, $-CH_4O$), 261 (MI - C_2H_5O, $-CH_4O$, $-H_2O$), 217, 187, 161, 130, 109, 73, 45 (BP).

1D-2,3,4,5-*O*-Tetrabenzoyl-*myo*-inositol (50). Tetrol **46** (202 mg, 0.48 mmol) was refluxed in pyridine with benzoyl chloride/DMAP during 24 h. After the aqueous workup the residue was dissolved in acetonitrile containing 10% aqueous HF (50%), and the solution was kept at 45 °C during 12 h. The mixture was neutralized with aqueous potassium bicarbonate and concentrated, and the residue was chromatographed to give **50** (237 mg, 83%, noncrystalline solid): TLC R_f 0.56 (chloroform-methanol, 9:1); $[\alpha]_D$ +75° (*c* 1.2, MeOH); ^{1}H NMR ($CDCl_3$) δ 8.05 (m, Ph, 4 H), 7.85 (m, Ph, 2 H), 7.55-7.2 (m, 12 H), 6.22 (tr, H-4, J = 10.2 Hz, 1 H), 6.12 (tr, H-2, J = 2.8 Hz, 1 H), 5.81 (tr, H-5, J = 9.8 Hz, 1 H), 5.68 (dd, H-3, J = 2.8, 10.5 Hz, 1 H), 4.40 (tr, H-6, J = 9.7 Hz, 1 H), 4.22 (dd, H-1, J = 2.8, 9.8 Hz, 1 H), 4.05 (br s, OH); ^{13}C NMR ($CDCl_3$) δ 166.6, 166.2, 165.7, 165.5 (each C=O), 133.3, 133.2, 133.1, 133.0, 129.9, 129.7, 129.5, 129.3, 129.2, 128.5, 128.3, 128.2 (Ph), 73.6, 72.2, 71.4, 70.6, 70.5, 70.3 (CH, inositol). Anal. Calcd for $C_{34}H_{28}O_{10}$: C, 68.38; H, 4.73. Found: C, 68.42; H, 4.95.

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Intramolecular Palladium-Catalyzed 1,4-Addition to Conjugated Dienes. Stereoselective Synthesis of Fused Tetrahydrofurans and Tetrahydropyrans

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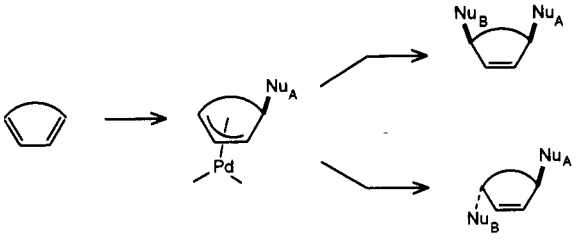
Abstract: Palladium-catalyzed oxidation of diene alcohols **2a**, **2b**, **4a**, **4b**, **5**, and **6** led to an intramolecular 1,4-addition to the conjugated diene to yield fused tetrahydrofurans or tetrahydropyrans. The reactions were run in acetone-acetic acid (4:1) or in an alcohol as the solvent, and the oxidant employed was *p*-benzoquinone. The catalyst used was palladium acetate. The reactions proceed via a heterocyclic (π-allyl)palladium complex, which is formed by intramolecular attack of the alcohol function on a (π-diene)palladium complex. Attack by acetate, chloride, or an alcohol on the π-allyl intermediate leads to an overall 1,4-oxyacetoxylation, 1,4-oxychlorination, or 1,4-oxyalkoxylation, respectively. In the intramolecular 1,4-oxyacetoxylation it was possible to obtain dual stereocontrol in most cases, i.e., the reaction can be directed toward either a cis or trans oxyacetoxylation across the diene. These new procedures allow the preparation of fused [6,5], [7,5], [6,6], and [7,6] tetrahydrofurans and tetrahydropyrans.

Nucleophilic additions to unsaturated hydrocarbons coordinated to a transition metal are important in organic synthesis.[1-3] In many cases these reactions are part of a catalytic process. The stereochemistry of the nucleophilic addition is of great interest, and the nucleophile may attack the hydrocarbon ligand from the same face as the metal or the opposite face. It is of particular

Scheme I



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