149. A Synthesis of 1D- and 1L-*myo*-Inositol 1,3,4,5-Tetraphosphate

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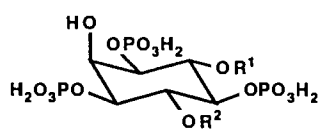
A synthesis of 1D- and 1L-*myo*-inositol 1,3,4,5-tetraphosphate (**1a** and **1b** resp.) is described. The dibenzylated *myo*-inositols **9a** and **9b**, which, by phosphorylation, gave **1a** and **1b**, respectively, were prepared *via* two routes. On the one hand, the racemate **3a**/**3b**, obtained from *myo*-inositol, was resolved by its transformation into the diastereoisomeric carbamates **5a** and **5b**. Benzylation and deprotection of **5a** and **5b** gave the enantiomers **9a** and **9b**, respectively. On the other hand, treatment of the diester **18** with *pig liver esterase* gave the ester **21a** with high enantiomeric excess. Benzylation and deprotection of **21a** yielded **9b**. The dibenzyl derivative **9a** was obtained using the same enzymatic hydrolysis followed by a protection-deprotection sequence.

Introduction. – *myo*-Inositol 1,4,5-triphosphate (IP_3) plays an important role as a cellular second messenger [1]. IP_3 is produced by the hydrolysis of phosphatidylinositol 4,5-diphosphate and it controls the liberation of Ca^{2+} from an intracellular store. The investigations of the mechanism of these two processes showed the role of other inositol phosphates [2] and among them of *myo*-inositol 1,3,4,5-tetraphosphate (IP_4) [3]. This phosphate appears to also be a second messenger and to be formed from IP_3 [4]. To the best of our knowledge, the absolute configuration of the biologically active IP_4 **1a** has been proved by correlation with 1D-*myo*-inositol 1,4,5-triphosphate.

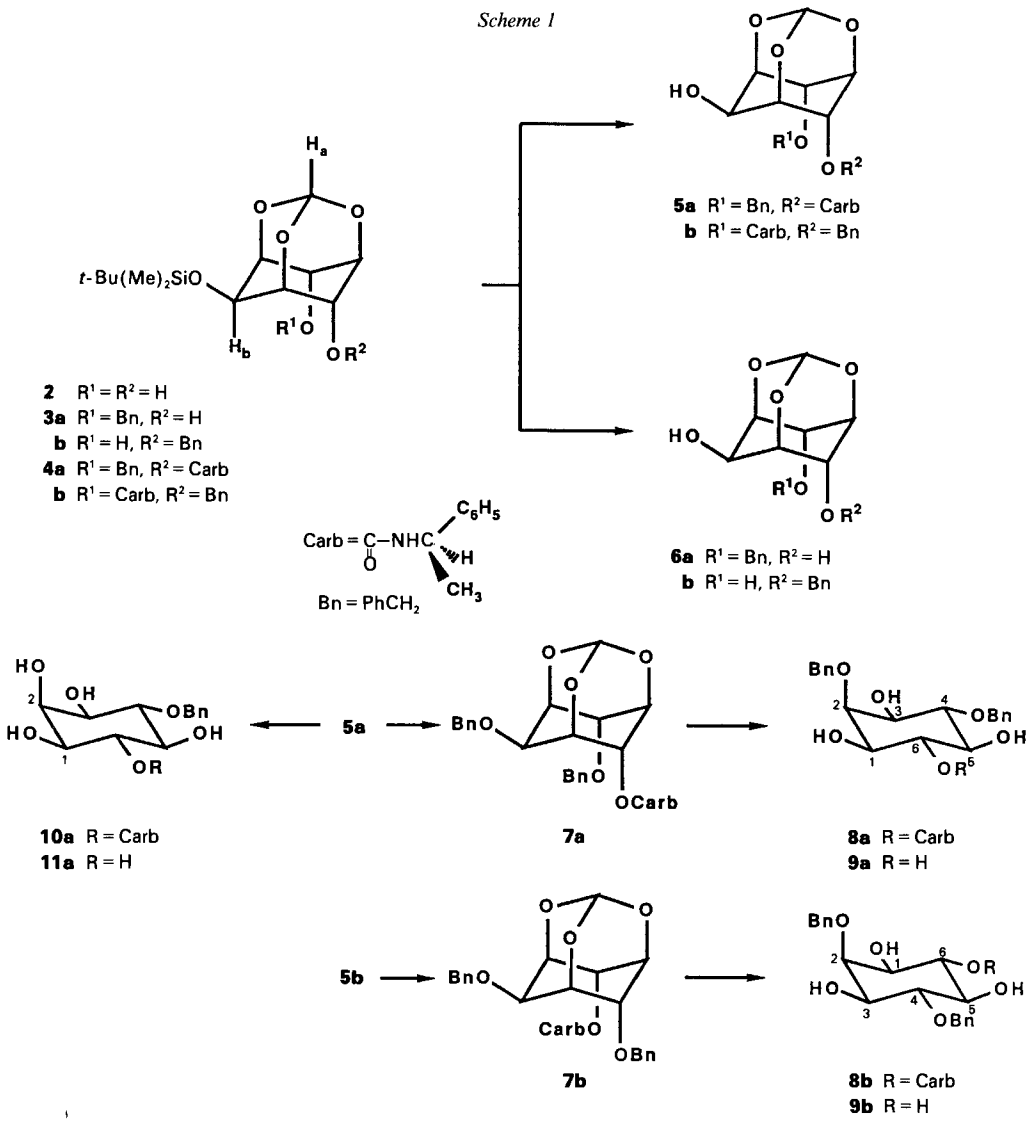


1a $R^1 = H$, $R^2 = PO_3H_2$
b $R^1 = PO_3H_2$, $R^2 = H$

Several syntheses of IP_3 [5] and of IP_4 [6] have been reported, including one of racemic IP_4 very close to our synthesis [6b]. We report here a full account of our synthesis of both enantiomers of IP_4.

Results and Discussion. – The first approach to the enantiomeric key dibenzyl ethers **9a** and **9b** *(Scheme 1)* [6b] [6c] used a resolution based upon the formation of diastereoisomeric carbamates. The silylated orthoformate **2**, described by *Lee* and *Kishi* [7], was formed in an optimised overall yield of 53% from *myo*-inositol. Treatment of **2** with 1.2 equiv. of $PhCH_2Br$ in the presence of K(*t*-BuO) gave the racemate **3a**/**3b** (99%; *Scheme 1*).

Scheme 1



A complete assignment of the ^{1}H-NMR spectra was possible only for the racemate **3a**/**3b**. In the other cases, the high symmetry of *myo*-inositol and of its derivatives possessing a trioxa-adamantane structure and the high multiplicity of the protons (due to several long-range couplings[1]) and to couplings of higher order) did not allow a full assignment of the signals. The assignment in the case of the racemate **3** is based upon two-dimensional spectra (COSY) and upon spectra simulation (program PANIC; see *Exper. Part*).

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[1]) As reported for a similar compound [8], a ^5J coupling constant (with a value between 1.2 Hz and 1.3 Hz) was found for H_a and H_b in **3a**/**3b** and in **2**, **6a**/**6b**, and **7a**.

Treatment of the racemate **3a**/**3b** with (+)-(*R*)-1-phenylethyl isocyanate in the presence of BuLi at −78° gave a mixture of the diastereoisomers **4a** and **4b** and some starting material. The ratio of starting material **3a**/**3b** to the products **4a** and **4b** in the crude mixture was estimated in the IR spectrum by the relative strength of the bands at 3500 (OH) and 3440 cm^{-1} (NH of the carbamate). For optimum results, the reaction mixture had to be neutralised at −78°; acidic workup gave back the starting material.

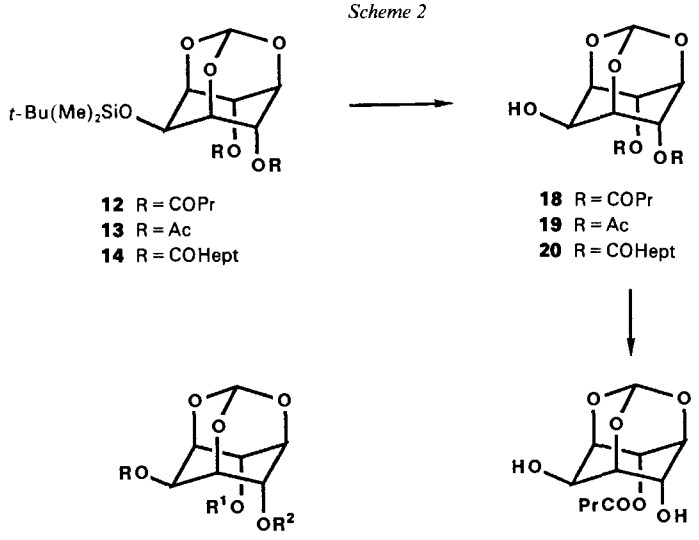
The racemate **3a**/**3b** could not be separated from the carbamates **4a** and **4b**. Desilylation of the mixture gave the diastereoisomers **5a** (33%) and **5b** (36.5%), and the racemate **6a**/**6b** (22%) which were separated by medium-pressure liquid chromatography (MPLC). The racemate **6a**/**6b** was recycled (→**3a**/**3b**).

Benzylation of **5a** with benzyl trichloroacetimidate in the presence of trifluoromethanesulfonic acid gave **7a** (72% yield) [9]. The orthoformate group of **7a** was readily hydrolysed by aqueous CF_3COOH to give **8a** (98%) which, by treatment with NaOEt at 80°, yielded the enantiomer **9a** (98%). Similar results were obtained from **5b** (→**7b**→**8b**→**9b**).

The absolute configuration of **9a** follows from the transformation of both its precursors **5a** and **6a** (obtained from **25a**, see below) into the known monobenzyl-*myo*-inositol **11a**. Thus, on the one hand, the monobenzylated carbamoyl orthoformate **5a** was hydrolysed to **10a** (aq. CF_3COOH) and then treated with NaOEt in EtOH to give **11a**, whose specific rotation was identical with the value reported for the L-enantiomer [10]. On the other hand, the monobenzylated orthoformate **6a** was hydrolysed (aq. CF_3COOH) to give the same enantiomer **11a**.

The second approach to **9a** and **9b** is based upon an enantioselective monodeacylation of *meso*-derivatives of *myo*-inositol *(Scheme 2)*. Neither the silylated diacyl orthofor-

Scheme 2



12 R = COPr
13 R = Ac
14 R = COHept

18 R = COPr
19 R = Ac
20 R = COHept

15 R = Trt, $R^1 = R^2$ = COPr
16 R = $R^1 = R^2$ = Ac
17 R = $R^1 = R^2$ = COPr

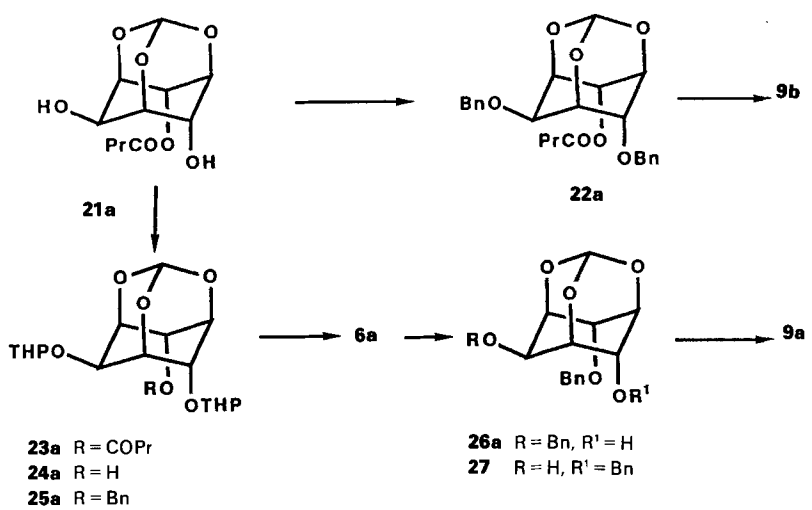
21a

mates **12**–**14** nor the corresponding tritylated (Trt) analog **15** were deacylated in the presence of a range of enzymes[2]) [11]. Also the triacyl orthoformates **16** and **17** proved resistant to enzymatic hydrolysis. Among the diacyl-alcohols **18**–**20**, obtained from the corresponding silyl ethers, the dioctanoate **20** proved again resistant to the enzymes[2]). The diacetate **19** was very slowly hydrolysed by PLE only (no enantioselectivity was observed), and the dibutyrate **18** was hydrolysed by six enzymes. Four of these (CC, WG, PPL, and PI) gave predominantly the (−)-monobutyrate **21a** (ee 30–40%). α-Chymotrypsin gave the desired (+)-monobutyrate **21b**, with moderate enantiomeric excess (ee 40%). Hydrolysis with PLE, finally, yielded the (−)-butyrate **21a** highly enantioselectively (ee > 95%) in high yields (83%).

To obtain this result, a pH value of 6.8 had to be maintained throughout the hydrolysis. Otherwise, the facile 1,3-acyl migration lowered the enantioselectivity. To obtain high reaction rates at pH 6.8, 400 units of PLE (optimum pH 8.0) per mmol of substrate were used. Although reactions on a larger scale led to a slightly poorer ee of the product, **21a** was still obtained enantiomerically pure after two recrystallisations (68%). The enantiomeric purity of the monobutyrate **21a** was determined by a shift experiment. While racemic **21** showed clear line splitting in the 400-MHz ^{1}H-NMR upon addition of [Eu(hfc)$_3$], no such line splitting was observed for **21a** under otherwise identical conditions.

Benzylation of **21a** using an excess of benzyl trichloroacetimidate gave **22a** (62%; *Scheme 3*). About 5% racemisation was observed (^{1}H-NMR in the presence of [Eu(hfc)$_3$])

Scheme 3



23a R = COPr
24a R = H
25a R = Bn

26a R = Bn, R¹ = H
27 R = H, R¹ = Bn

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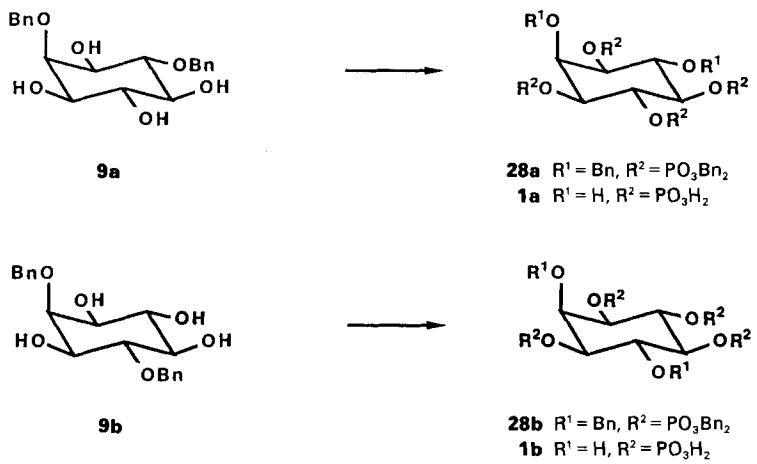
[2]) Enzymes used (abbreviation; source): Pig liver esterase (PLE; *Sigma*); lipases: *candida cylindracea* (CC; *Sigma*); porcine pancreas (type II; PPL; *Sigma*); wheat germ (type I; WG; *Sigma*); *rhizopus arrhizus* (type XI; *Sigma*); *chromobacterium viscosum* (*Sigma*); *rhizopus niveus* (*Amano*); *rhizopus javanicus* (*Amano*); *pseudomonas fluorescens* (*Amano*); *pseudomonas sp.* (*Amano*); *aspergillus niger* (*Amano*); *mucor javanicus* (*Amano*); lyophilized yeast (*Reininghaus*); proteases: papain (*Sigma*); α-chymotrypsin (CT; *Fluka*); *aspergillus oryzae* (PI; *Sigma*); *aspergillus sojae* (type XIX, *Sigma*); *rhizopus sp.* (type XVIII; *Sigma*).

after a reaction time of 30 min. Longer reaction times led to increasing racemisation. Acid hydrolysis of the orthoester **22a** followed by alkaline deacylation gave **9b** identical to the material obtained by the first approach.

To complete the synthesis of **1a**, **21a** was transformed [12] into a mixture **23a** of the diastereoisomeric 2,4-bis(tetrahydropyranyl) derivatives (91%; *Scheme 3*, THP = tetrahydro-2*H*-pyranyl). No racemisation was observed. Deacylation of **23a** with 5% NaOMe in MeOH yielded **24a** (96%), which was benzylated to **25a** (91%) [13]. Hydrolysis of **23a** with aq. AcOH selectively removed the THP groups, forming the monobenzyl orthoformate **6a** (87%) and only *ca.* 2–3% of **11a**. Regioselective benzylation of **6a** with benzyl trichloroacetimidate gave the dibenzyl ether **26a** (81%, accompanied by not more than 10% of the *meso*-dibenzyl ether **27**). Benzylation of **6a** under phase transfer conditions [14] gave 80% of **26a**/**27** in a ratio of 4:1 (HPLC). Hydrolysis of **26a** with aq. CF_3COOH, as described for **7**, gave **9a**.

Thus, **9a** was prepared from **2** *via* **4a** in 6 steps and 23% yield, while the preparation using the enantioselective enzymatic hydrolysis required 9 steps and gave **9a** in 28% yield. The enantiomer **9b** was prepared *via* **4b** in 6 steps and in 25% yield, while the alternative 'enzymatic' synthesis required 5 steps and gave **9b** in 32% yield.

Scheme 4



The tetrols **9a** and **9b** were phosphorylated with bis(benzyloxy)(diisopropylamino)-phosphine in the presence of tetrazole followed by oxidation with *m*-chloroperbenzoic acid [15], giving the protected tetraphosphate **28a** and **28b**, respectively, in good yields (98%; *Scheme 4*)[3]). The products **28a** and **28b** were rapidly chromatographed on silica gel pretreated with $NaHCO_3$ and then immediately deprotected. Hydrogenolysis under medium pressure in the presence of 10% Pd/C occurred in two stages, and the addition of fresh catalyst for each stage was required for complete deprotection. Compounds **1a** and **1b** were isolated as their cyclohexylammonium salts (76%). The ^{1}H-NMR, ^{13}C-NMR,

[3]) *Fraser-Reid* and coworkers recently reported [16] the use of the same reagent for the phosphorylation of similar compounds.

and ^{31}P-NMR spectra of the free acids **1a** and **1b** were in good agreement with the reported spectra [17].

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Experimental Part

General. M.p.: in an open capillary (not corrected) or under a hot-stage microscope. TLC: 0.25-mm precoated silica-gel plates *(Kieselgel 60 F_{254}, Merck)* or 0.1-mm precoated cellulose plates *(F_{254}, Merck)*; solvent systems: *A* = MeCN, *B* = AcOEt/hexane *x:y*, *C* = AcOEt, *D* = CH_2Cl_2/MeOH *x:y*, *E* = PrOH/NH_3 25%/H_2O *x:y:z*, *F* = AcOEt/MeOH *x:y*; detection by spraying with 0.02M soln. of I_2 in 10% aq. H_2SO_4 or with 5% soln. of vanillin in conc. H_2SO_4, or by dipping the plates in 10% phosphormolybdinic acid in EtOH followed by heating at *ca.* 200°, or, for P-containing compounds, by spraying with a 0.1% $FeCl_3$ soln. in 80% EtOH followed by a 0.8% soln. of sulfosalicylic acid in 80% EtOH according to *Desjobert* and *Petek* [18]. IR spectra: 3% solns. in $CHCl_3$, unless otherwise specified. ^{1}H-NMR, ^{13}C-NMR, and ^{31}P-NMR spectra: at 200 or 400 MHz (^{1}H), 50 or 100 MHz (^{13}C), 80 or 160 MHz (^{31}P), in $CDCl_3$, unless otherwise specified; δ in ppm relative to TMS as internal standard, or relative to H_3PO_4 for ^{31}P-NMR as external standard (uncorrected). FC = flash chromatography; MPLC = medium-pressure liquid chromatography.

*(1R,3s,5S,6R,7s,8S,9s)-9-[(*tert*-Butyl)dimethylsilyloxy]-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane-6,8-diol* (**2**). *a)* To a suspension of *myo*-inositol (50 g, 0.278 mol) and of TsOH · H_2O (13.83 g, 0.073 mol) in dry DMF (700 ml), triethyl orthoformate (83 ml, 0.5 mol) was added dropwise under Ar at 140°. The soln. was stirred for 3 h at 140°, then cooled to 100°, and DMF distilled off at reduced pressure at 70 to 80°. The residue was treated with 100 ml of 10% $NaHCO_3$ soln., stirred for 15 min at r.t., diluted with H_2O (1 l), and extracted 3× with 250 ml of $CHCl_3$. The aq. phase was lyophilised, the residue treated with MeOH (2 l) at 50°, and the suspension filtered. MeOH was evaporated under vacuum. FC (*A*; crude product dissolved in H_2O) gave 47.9 g (91%) of *(1R,3s,5S,6R,7s,8S,9s)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane-6,8,9-triol* as colourless crystals. Recrystallization from AcOEt and MeOH gave an anal. sample. R_f (*A*) 0.51. Spectral data (except ^{13}C-NMR): [7]. ^{13}C-NMR (CD_3OD): 61.00 (*d*); 68.94 (2 *d*); 70.47 (*d*); 75.85 (2 *d*); 103.84 (*d*).

b) 2,6-Dimethylpyridine (68.5 ml, 0.59 mol) was added dropwise under Ar to a soln. of *t*-BuMe_2SiCl (42.7 g, 0.283 mol) in dry DMF (300 ml) at 0°. A soln. of *(1R,3s,5S,6R,7s,8S,9s)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane-6,8,9-triol* (45 g, 0.236 mol) in DMF (170 ml) was then added dropwise. The mixture was stirred for 24 h at r.t., DMF removed at reduced pressure, and the residue dissolved in $CHCl_3$ (1.2 l) and washed with brine. Usual workup and FC (*B*, 4:6) afforded 41.64 g (58%) of **2** as colourless crystals. Recrystallisation from AcOEt/hexane gave an anal. sample of **2**. R_f (*B*, 1:2) 0.34. Spectral data: [7]. ^{13}C-NMR (CD_3OD): −4.57 (*q*); 19.16 (*s*); 26.36 (*q*); 62.36 (*d*); 69.25 (2 *d*); 70.80 (*d*); 76.44 (2 *d*); 103.82 (*d*).

*(1S,3R,5R,6S,7S,8R,9R)- and (1R,3S,5S,6R,7R,8S,9S)-8-(Benzyloxy)-9-[(*tert*-butyl)dimethylsilyloxy]-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decan-6-ol* (**3a** and **3b**). To K(*t*-BuO) (2.68 g, 23.88 mmol) in DMF (27 ml) under Ar, a soln. of **2** (6.67 g, 21.91 mmol) in DMF (67 ml) was added dropwise over 30 min at 0°. After stirring for 30 min at 0°, a soln. of $PhCH_2Br$ (3.85 ml, 32.41 mmol) in DMF (27 ml) was added within 1 h. The mixture was stirred for 4.5 h at 0°, DMF removed *i.v.*, and the residue in AcOEt washed with brine. Usual workup and FC (*B*, 1:8 to 1:5) afforded **3a**/**3b** as an oil. Crystallisation from hexane gave 8.53 g (99%) of **3a**/**3b** as white crystals. M.p. 51–53°. R_f (*B*, 1:2) 0.43. IR: 3500*m* (br.), 3088*w*, 3062*w*, 3025*w*, 2956*s*, 2930*s*, 2860*w*, 1730*w*, 1600*w*, 1500*w*, 1462*w*, 1454*w*, 1395*w*, 1370*w*, 1360*w*, 1316*w*, 1300 (sh), 1164*s*, 1140*s*, 1105*s*, 1070*s*, 1000*s*, 968*s*, 940*m*, 890*s*, 880*s*, 840*s*, 710*m*, 700*m*, 665*m*. ^{1}H-NMR: 0.15 (*s*, 3 H); 0.16 (*s*, 3 H); 0.95 (*s*, 9 H); 3.65 (*d*, *J* = 10.1, OH); 4.14 (*m*, 2 H); 4.22 (*m*, 1 H); 4.25 (*m*, 1 H); 4.39 (*m*, 1 H); 4.43 (*m*, 1 H); 5.49 (*d*, *J* = 1.27, 1 H); 7.35 (*m*, 5 arom. H). Simulated spectrum (program PANIC): 0.15 (*s*, CH_3Si); 0.16 (*s*, CH_3Si); 0.95 (*s*, *t*-BuSi); 3.65 (*d*, *J*(OH, 6) = 10.19, OH); 4.13 (*dddd* app. as *'dquint.'*, *J*(5,6) = 4.12, *J*(1,5) = 2.00, *J*(5,9) = 1.83, *J*(5,7) = 1.67, H–C(5)); 4.15 (*dddd* app. as *dquint.*, *J*(1,8) = 4.23, *J*(1,9) = 2.10, *J*(1,5) = 2.00, *J*(1,7) = 1.65, H–C(1)); 4.22 (*ddd* app. as ~ *dt*, *J*(1,9) = 2.10, *J*(5,9) = 1.83, ^5J(3,9) = 1.27, H–C(9)); 4.25 (*dddd* app. as ~ *sept.*, *J*(6,7) = 3.74, *J*(7,8) = 3.71, *J*(5,7) = 1.67, *J*(1,7) = 1.65, H–C(7)); 4.39 (*ddd*, *J*(1,8) = 4.23, *J*(7,8) = 3.71, *J*(6,8) = 2.04, H–C(8)); 4.43 (*dddd* app. as *ddt*, *J*(6,

OH) = 10.19, $J(5,6) = 4.12$, $J(6,7) = 3.74$, $J(6,8) = 2.04$, H–C(6)); 5.49 (*d*, $^5J(3,9) = 1.27$, H–C(3)); 7.35 (*m*, 5 arom. H). ^{13}C-NMR: –4.69 (*q*); –4.63 (*q*); 18.36 (*s*); 25.88 (*q*); 60.86 (*d*); 67.50 (*d*); 68.31 (*d*); 72.54 (*d*); 74.86 (*d*); 74.93 (*d*); 73.12 (*t*); 102.53 (*d*); 127.99 (*d*); 128.74 (*d*); 128.85 (*d*); 135.98 (*s*). MS: 397 (8), 396 (20), 395 (100), 197 (5), 91 (9). Anal. calc. for $C_{20}H_{30}O_6Si$ (394.52): C 60.91, H 7.61; found: C 61.05, H 7.82.

(1R,3S,5S,6R,7R,8S,9S)- and (1S,3R,5R,6S,7S,8R,9R)-8-(Benzyloxy)-9-hydroxy-2,4,10-trioxatricyclo-[3.3.1.1^{3,7}]dec-6-yl N-*[(R)-1-Phenylethyl]carbamate* (**5a** and **5b**). To BuLi (1.9 ml, 3.04 mmol) in dry THF (2 ml) at –78° under Ar, a soln. of **3a**/**3b** (1 g, 2.53 mmol) in THF (10 ml) was added dropwise. The mixture was stirred for 1 h. A soln. of (+)-(*R*)-(1-phenylethyl) isocyanate (1.6 ml, 12.67 mmol, from *Fluka* or synthesised from (+)-(*R*)-1-phenylethylamine and phosgen in toluene) in THF (2 ml) was then added within 1 h. The mixture was stirred for 90 min at –78°. To the cold mixture (–78°) were added conc. HCl (0.27 ml), MeOH (12 ml), 1M HCl (until the soln. reached pH 5–6), MeOH (15 ml), and a buffer soln. (15 ml of a soln. of 4.25 g KH_2PO_4 and 4.43 g Na_2HPO_4 in H_2O (100 ml)). The mixture was warmed to r.t. within 4 h and concentrated *i.v.* The residual soln. was diluted with AcOEt, washed with brine, dried ($MgSO_4$), and evaporated. To the residue in MeOH, silica gel was added, the suspension evaporated, and the residue deposited on a chromatography column. FC (*B*, 1:8 to 1:2) gave 1.55 g of partially purified **3a**/**3b**/**4a**/**4b**. $Bu_4NF \cdot 3\ H_2O$ (880 mg) was added to a soln. of this mixture in dry THF (33 ml). After 2 h at r.t., the soln. was diluted with AcOEt and washed with brine. After usual workup, the crude product was chromatographed (FC, *B*, 1:2 to 1:1). A mixture composed of **5a** (33%), **5b** (36.5%), and **6a**/**6b** (22.4%) was obtained (yields refer to **3a**/**3b**). The products were separated by MPLC (*B*, 35:65). The diastereoisomeric purity of **5a** and of **5b** was determined by HPLC (*Zorbax Sil; B*, 1:1): > 99%.

Data of **5a**: R_f (*B*, 1:1) 0.47. $[\alpha]_D^{24.5} = +25.8$ (*c* = 1, $CHCl_3$). IR: 3575*w*, 3463*w* 3095*w*, 3075*w*, 3040*w*, 3010*w*, 2979*w*, 2958*w*, 2878*w*, 1790 (sh), 1778*s*, 1773 (sh), 1607*w*, 1589*w*, 1580*w*, 1549*w*, 1539*w*, 1528*w*, 1513 (sh), 1498*s*, 1477 (sh), 1464*w*, 1453*m*, 1405*w*, 1380*m*, 1364 (sh), 1352*w*, 1327*w*, 1303*m*, 1282*w*, 1168*s*, 1149 (sh), 1134*m*, 1105*s*, 1082*s*, 1070*s*, 1016*s*, 998*s*, 962*s*, 945*m*, 916*w*, 897*m*, 699*w*, 668*w*. ^{1}H-NMR: 1.26 (*d*, *J* = 6.72, 3 H); 3.00 (br. *s*, OH); 4.09 (br. *s*, 1 H); 4.18 (br. *s*, 1 H); 4.26 (br. *s*, 1 H); 4.38 (br. *s*, 1 H); 4.70 (*m*, 6 H); 5.37 (*m*, 1 H); 5.49 (*s*, 1 H); 7.27 (*m*, 10 H). ^{13}C-NMR: 21.97 (*q*); 50.70 (*d*); 61.38 (*d*); 66.66 (*d*); 68.24 (*d*); 71.16 (*t*); 72.10 (*d*); 72.59 (*d*); 73.10 (*d*); 103.17 (*d*); 125.86 (*d*); 127.01 (*d*); 127.48 (*d*); 127.97 (*d*); 128.53 (*d*); 128.66 (*d*); 137.50 (*s*); 147.86 (*s*); 153.88 (*s*). MS: 428 (100), 282 (5), 281 (16). Anal. calc. for $C_{23}H_{25}O_7N$ (427.45): C 64.63, H 5.89, N 3.28; found: C 64.69, H 5.70, N 3.45.

Data of **5b**: R_f (*B*, 1:1) 0.39. $[\alpha]_D^{24.5} = +22.3$ (*c* = 1, $CHCl_3$). IR: 3570*w*, 3440*w*, 3088*w*, 3065*w*, 3033*w*, 3007*w*, 2975*w*, 2930*w*, 2875*w*, 1728*s*, 1510*m*, 1502*s*, 1499*s*, 1452*m*, 1403*w*, 1392*w*, 1378*w*, 1360*w*, 1349*w*, 1321*w*, 1300*w*, 1280*w*, 1162*s*, 1145*w*, 1130*w*, 1102*s*, 1080*m*, 1062*m*, 1010*s*, 982*s*, 958*s*, 940*w*, 800*w*, 717*w*, 712*w*, 700*s*, 673*w*, 668*w*, 662*w*. ^{1}H-NMR: 1.1 (br. *s*, 0.6 H); 1.45 (*d*, *J* = 6.6, 2.4 H); 3.15 (br. *s*, OH); 4.62–4.12 (*m*, 6 H); 4.78 (*m*, 1 H); 4.85 (*m*, 1 H); 5.4 (*m*, 2 H); 7.25 (*m*, 10 H). ^{13}C-NMR: 22.15 (*q*); 50.63 (*d*); 61.15 (*d*); 66.63 (*d*); 68.10 (*d*); 70.79 (*t*); 72.08 (*d*); 72.51 (*d*); 72.59 (*d*); 103.00 (*d*); 125.76 (*d*); 127.02 (*d*); 127.23 (*d*); 127.80 (*d*); 128.37 (*d*); 128.47 (*d*); 137.24 (*s*); 142.98 (*s*); 153.90 (*s*). MS: 429 (8), 428 (100), 324 (9). Anal. calc. for $C_{23}H_{25}O_7N$ (427.45): C 64.63, H 5.89, N 3.28; found: C 64.53, H 5.95, N 3.21.

Data of **6a**/**6b**: IR: 3615 (sh), 3590*w*, 3575*m*, 3570*w*, 3535*w*, 3510*w*, 3495*m*, 3465*w*, 3440*w*, 3380*w*, 1604*w*, 1496*w*, 1453*w*, 1410*m*, 1372*w*, 1350*w*, 1296*m*, 1280*w*, 1262*w*, 1238*m*, 1185*m*, 1162*s*, 1142*w*, 1124*w*, 1080*s*, 1066 (sh), 1053*s*, 1013*s*, 990*s*, 953*s*, 940*m*, 910*w*, 880*s*, 870 (sh). ^{1}H-NMR: 3.25 (*d*, *J* = 11.53, OH); 3.73 (*d*, *J* = 10.2, OH); 4.08 (*m*, 1 H); 4.25 (*m*, 3 H); 4.45 (*m*, 2 H); 4.63 (*d*, *J* = 11.6, 1 H); 4.70 (*d*, *J* = 11.6, 1 H); 5.44 (*d*, *J* = 1.27, 1 H); 7.34 (*m*, 5 H). ^{13}C-NMR: 61.34 (*d*); 69.02 (*d*); 69.98 (*d*); 72.84 (*t*); 73.98 (*d*); 75.42 (*d*); 76.04 (*d*); 104.25 (*d*); 129.13 (*d*); 129.54 (*d*); 138.91 (*s*). MS: 299 (14, $M^{+\cdot} + 2 + NH_3$), 298 (100, $M^{+\cdot} + 1 + NH_3$), 281 (23). Anal. calc. for $C_{14}H_{16}O_6$ (280.28): C 60.00, H 5.75; found: C 59.87, H 5.76.

Silylation of **6a**/**6b**. To a soln. of **6a**/**6b** (3.64 g, 12.99 mmol) in dry DMF (36 ml) under Ar, imidazole (1.15 g, 16.89 mmol) was added and then *t*-$BuMe_2SiCl$ (2.15 g, 14.26 mmol). The mixture was stirred for 1 day. After evaporation of DMF, the residue was dissolved in AcOEt and washed with brine. FC (*B*, 1:4) gave 4.63 g (90%) of **3a**/**3b**.

(1R,3S,5R,6R,7S,8R,9R)-8,9-Bis(benzyloxy)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]dec-6-yl N-*[(R)-1-Phenylethyl]carbamate* (**7b**). A soln. of **5b** (176 mg, 0.41 mmol) in dry CH_2Cl_2 (2.3 ml) and cyclohexane (4.6 ml) was treated under Ar at r.t. with benzyl trichloroacetimidate (3.39 g, 13.4 mmol) and trifluoromethanesulfonic acid (TfOH, 30 µl, 0.3 mmol). The soln. was stirred for 1 h, quenched with a buffer soln. (0.025 M KH_2PO_4 and 0.025 M Na_2HPO_4), cooled to 0°, and extracted with CH_2Cl_2. Washing with the buffer soln. following by normal workup gave a product which was chromatographed on 25 g of SiO_2 (FC with *B*, 1:8 to 1:5); then MPLC with (*B*, 1:4) to give 153 mg (72%) of **7b** as an oil.

Data of **7a**: R_f (*B*, 1:2) 0.295. $[\alpha]_D^{25} = +14.2$ (*c* = 1, $CHCl_3$). IR: 3440*w*, 3118*w*, 3090*w*, 3068*w*, 3038*w*, 3005*w*, 2977*w*, 2930*w*, 2900*w*, 2875*w*, 1952*w*, 1875*w*, 1810*w*, 1728*s*, 1605*w*, 1587*w*, 1496*m*, 1452*w*, 1400*w*, 1378*w*, 1362*w*,

1344*w*, 1328*w*, 1306*w*, 1278*w*, 1238*w*, 1195*w*, 1164*s*, 1131*m*, 1112 (sh), 1100*s*, 1080*s*, 1023 (sh), 1002*s*, 952*m*, 910*s*, 868*w*, 694*w*, 662*w*. ^{1}H-NMR: 1.22 (*d*, *J* = 6.7, 3 H); 3.91 (*d*, *J* = 0.9, 1 H); 4.78–4.30 (*m*, 10 H); 5.35 (*m*, 1 H); 5.55 (*d*, *J* = 1.2, 1 H); 7.30 (*m*, 15 H). ^{13}C-NMR: 21.9 (*q*); 50.6 (*d*); 67.0 (2 *d*); 68.5 (*d*); 69.6 (*d*); 70.1 (*d*); 70.8 (*t*); 71.2 (*t*); 73.3 (*d*); 103.1 (*d*); 125.8 (*d*); 126.9 (*d*); 127.1 (*d*); 127.2 (*d*); 127.3 (*d*); 127.5 (*d*); 127.7 (*d*); 127.9 (*d*); 128.1 (*d*); 128.2 (*d*); 128.5 (*d*); 128.6 (*d*); 128.8 (*d*); 128.9 (*d*); 137.6 (*s*); 142.9 (*s*); 153.8 (*s*). MS: 519 (14), 518 (33), 371 (31), 105 (100). Anal. calc. for $C_{30}H_{31}NO_7$ (517.58): C 69.62, H 6.04, N 2.71; found: C 69.33, H 6.07, N 2.82.

Data of **7b**: R_f (*B*, 1:2) 0.288. $[\alpha]_D^{24.5} = +13.3$ (*c* = 1, $CHCl_3$). IR: 3445*w*, 3090*w*, 3070*w*, 3035*w*, 3005*w*, 2970*w*, 2870*w*, 1728*s*, 1605*w*, 1509*m*, 1494*s*, 1450*m*, 1375*m*, 1362*m*, 1302*m*, 1278*m*, 1162*s*, 1130*m*, 1100*s*, 1079*s*, 1021*m*, 950*s*, 898*m*, 860*w*. ^{1}H-NMR: 1.05 (br. *d*, *J* = 5.3, 0.6 H); 1.41 (*d*, *J* = 6.3, 2.4 H); 3.65 (br. *s*, 0.3 H); 3.93 (br. *s*, 0.7 H); 4.00 (br. *s*, 0.2 H); 4.6–4.3 (*m*, 6.8 H); 4.75 (*m*, 3 H); 5.38 (br. *s*, 1 H); 5.54 (*s*, 1 H); 7.3 (*m*, 15 H). ^{13}C-NMR: 22.24 (*q*); 50.67 (*d*); 67.09 (*d*); 68.40 (*d*); 69.67 (*d*); 70.13 (2 *d*); 70.75 (*t*); 71.24 (2 *t*); 72.98 (*d*); 103.05 (*d*); 125.07 (*d*); 125.11 (*d*); 125.27 (*d*); 125.77 (*d*); 126.98 (*d*); 127.35 (*d*); 127.50 (*d*); 127.54 (*d*); 127.84 (*d*); 128.09 (*d*); 128.20 (*d*); 128.43 (*d*); 128.56 (*d*); 128.74 (*d*); 128.78 (*d*); 137.46 (*s*); 137.68 (*s*); 142.93 (*s*); 153.81 (*s*). MS: 520 (7), 519 (31), 518 (100), 414 (11), 371 (17). Anal. calc. for $C_{30}H_{31}NO_7$ (517.58): C 69.62, H 6.04, N 2.71; found: C 69.66, H 6.07, N 2.65.

*1*D*-2,4-Di-*O*-benzyl-6-*O*-{[(*R*)-1-phenylethyl]aminocarbonyl}-*myo*-inositol* (**8b**). A soln. of **7b** (451 mg, 0.873 mmol) in H_2O (2.5 ml) and CF_3COOH (8 ml) was stirred for 2.5 h at r.t. and then evaporated at 40–45°. The residue was twice dissolved in H_2O (6 ml) and evaporated. A soln. of the residue in MeOH (5.5 ml) and 25% NH_3 (1 ml) was stirred for 15 min at r.t. and evaporated at 40°. The residue was dissolved in MeOH and evaporated (3×). FC (*B*, 2:1) afforded 434.7 mg (98%) of **8b** as a foam.

Data of **8a**: R_f (*B*, 4:1) 0.65. $[\alpha]_D^{25} = +21.9$ (*c* = 1, $CHCl_3$). IR: 3560*m*, 3440*m*, 3680–3100 (br.), 3115*w*, 3088*w*, 3065*w*, 3038*w*, 3002*w*, 2978*w*, 2930*w*, 2880*w*, 1952*w*, 1875*w*, 1810*w*, 1722 (sh), 1710*s*, 1604*w*, 1587*w*, 1548*w*, 1510 (sh), 1497*s*, 1452*m*, 1395*m*, 1376*m*, 1348*m*, 1240*m*, 1200*m*, 1120*s*, 1092*s*, 1076*s*, 1058*s*, 1029*m*, 1010*s*, 940*w*, 915*w*, 692*w*, 662*w*. ^{1}H-NMR: 1.49 (*d*, *J* = 6.6, 3 H); 2.31 (br. *s*, OH); 2.86 (br. *s*, OH); 3.01 (br. *s*, OH); 3.64–3.44 (*m*, 3 H); 3.72 (*dd* app. as *t*, *J* = 10, 1 H); 3.99 (*s*, 1 H); 5.00–4.75 (*m*, 6 H); 5.27 (*d*, *J* = 6.6, 1 H); 7.35 (*m*, 15 H). ^{13}C-NMR: 22.08 (*q*); 50.83 (*d*); 71.08 (*d*); 71.91 (*d*); 73.47 (*d*); 74.93 (*t*); 75.33 (*t*); 77.64 (*d*); 79.49 (*d*); 81.62 (*d*); 125.81 (*d*); 127.25 (*d*); 127.64 (*d*); 127.75 (*d*); 128.03 (*d*); 128.32 (*d*); 128.39 (*d*); 128.53 (*d*); 138.27 (*s*); 138.35 (*s*); 142.93 (*s*); 157.09 (*s*). MS: 508 (3), 204 (6), 106 (9), 105 (100), 97 (4). Anal. calc. for $C_{29}H_{33}NO_7$ (507.58): C 68.62, H 6.55, N 2.76; found: C 68.87, H 6.68, N 2.71.

Data of **8b**: R_f (*B*, 4:1) 0.62. $[\alpha]_D^{24.5} = +39.8$ (*c* = 1, $CHCl_3$). IR: 3670*w*, 3555*w*, 3440*m*, 3640–3200 (br.), 3090*w*, 3065*w*, 3035*w*, 3000*w*, 2990*w*, 2935*w*, 2900*w*, 2875*w*, 1728*s*, 1709 (sh), 1604*w*, 1509 (sh), 1495*s*, 1450*m*, 1395*m*, 1372*m*, 1348*m*, 1300*w*, 1115*s*, 1075*s*, 1052*s*, 1028*m*, 1009*s*, 950*m*, 917*w*, 859*w*, 690*m*, 660*m*, 630*w*. ^{1}H-NMR: 1.5 (*d*, *J* = 6.6, 3 H); 2.3 (br. *s*, OH); 2.9 (br. *s*, OH); 3.35 (br. *s*, OH); 3.53 (*m*, 3 H); 3.70 (*t*, *J* = 9.2, 1 H); 4.02 (br. *s*, 1 H); 4.96–4.79 (*m*, 6 H); 5.25 (*d*, *J* = 6.6, 1 H); 7.34 (*m*, 15 H). ^{13}C-NMR: 22.15 (*q*); 50.88 (*d*); 71.10 (*d*); 71.96 (*d*); 73.57 (*d*); 74.99 (*t*); 75.37 (*t*); 77.82 (*d*); 79.45 (*d*); 81.62 (*d*); 125.80 (*d*); 127.30 (*d*); 127.69 (*d*); 127.80 (*d*); 128.06 (*d*); 128.38 (*d*); 128.44 (*d*); 128.58 (*d*); 138.29 (*s*); 138.36 (*s*); 143.00 (*s*); 157.04 (*s*). MS: 509 (0.5), 508 (1.5), 269 (9), 182 (8), 181 (100). Anal. calc. for $C_{29}H_{33}NO_7$ (507.58): C 68.62, H 6.55, N 2.76; found: C 68.44, H 6.75, N 2.66.

*1*D*-2,4-Di-*O*-benzyl-*myo*-inositol* (**9b**). To a soln. of Na (43.1 mg, 1.87 mmol) in dry EtOH (1.5 ml) under Ar at r.t., a soln. of **8b** (109 mg, 0.215 mmol) in EtOH (1.5 ml) was added. The mixture was kept for 1 h at 80°, then cooled to r.t., treated with 1M HCl until pH 2–3, and evaporated. Silica gel was added to the residue in MeOH, the suspension evaporated and the residue deposited on a chromatography column. FC (*C*) afforded 75.8 mg (98%) of **9b** as colourless crystals. Recrystallization from Et_2O gave an anal. sample.

Data of **9a**: M.p. 145.2–146.1°. R_f (*C*) 0.20. $[\alpha]_D^{25} = -29.2$ (*c* = 1, EtOH). IR (KBr): 3580*w*, 3440*s*, 3330*s*, 3085*w*, 3060*w*, 3030*w*, 2950*w*, 2920*m*, 2895*w*, 2870*w*, 2860*w*, 2850*w*, 2790*w*, 1495*w*, 1470*w*, 1455*w*, 1429*w*, 1420*w*, 1402*w*, 1376*w*, 1367*w*, 1349*w*, 1330*w*, 1321*w*, 1301*w*, 1283*w*, 1254*w*, 1243*w*, 1232*w*, 1218*w*, 1211*w*, 1190*w*, 1176*w*, 1149*m*, 1138*m*, 1112*s*, 1091*m*, 1079*m*, 1065 (sh), 1044*s*, 1028 (sh), 1007*s*, 942*w*, 924*w*, 918 (sh), 900*w*, 827*w*, 814*w*, 762 (sh), 753*m*, 698*s*. ^{1}H-NMR (CD_3OD): 3.35 (*m*, 1 H); 3.48 (*m*, 1 H); 3.60 (*m*, 2 H); 3.70 (*m*, 1 H); 3.72 (*m*, OH); 3.85 (*m*, OH); 3.94 (*m*, 1 H); 4.04 (*m*, 2 OH); 4.86 (*m*, 4 H); 7.33 (*m*, 10 H). ^{13}C-NMR (CD_3OD): 73.75 (*d*); 73.81 (*d*); 74.97 (*d*); 75.91 (*t*); 76.35 (*t*); 76.81 (*d*); 82.80 (*d*); 83.42 (*d*); 128.30 (*d*); 128.44 (*d*); 128.88 (*d*); 128.96 (*d*); 129.10 (*d*); 129.13 (*d*); 129.23 (*d*); 140.53 (*s*); 140.64 (*s*). MS: 360 (< 0.1); 269 (22); 109 (9); 107 (38); 92 (10); 91 (100); 65 (6). Anal. calc. for $C_{20}H_{24}O_6$ (360.41): C 66.65, H 6.71; found: C 66.87, H 6.46.

Data of **9b**: M.p. 145.8–146.1°. $[\alpha]_D^{25} = +29.7$ (*c* = 1, EtOH). Anal. calc. for $C_{20}H_{24}O_6$ (360.41): C 66.65, H 6.71; found: C 66.48, H 6.63.

*1*L*-4-O-Benzyl-6-O-{[(R)-1-phenylethyl]aminocarbonyl}-myo-inositol* (**10a**). A soln. of **5a** (114.9 mg, 0.281 mmol) in CF_3COOH (5.5 ml) and H_2O (1.7 ml) was stirred for 1.5 at r.t. The solvents were evaporated at 40–45°.

The residue was twice dissolved in H_2O and evaporated. A soln. of the residue in 25% NH_3 (0.7 ml) and MeOH (3.8 ml) was stirred for 15 min at r.t. and evaporated. The residue was dissolved in MeOH and evaporated again (3 ×). To the residue in MeOH, silica gel was added, the mixture evaporated, and the residue deposited on a column. FC (*F*, 98:2 to 90:10) gave 112.2 mg (100%) of **10a** as white crystals. M.p. 186–188°. R_f (*F*, 98:2) 0.3. $[\alpha]_D^{25} = +48.4$. IR (KBr): 3522*s*, 3424*s* (br.), 3390*s* (br.), 3302*s* (br.), 3082*m*, 3060*m*, 3032*m*, 2978*m*, 2955*m*, 2922*m*, 2897*m*, 1900*w*, 1875*w*, 1810*w*, 1738 (sh), 1721 (sh), 1710 (sh), 1705 (sh), 1700 (sh), 1694 (sh), 1689 (sh), 1680*s*, 1674*s*, 1652 (sh), 1648 (sh), 1604*w*, 1583*w*, 1562 (sh), 1543 (sh), 1538*s*, 1496*s*, 1453*s*, 1404*s*, 1368*s*, 1340*s*, 1330*s*, 1320*s*, 1300*s*, 1284*s*, 1274*s*, 1249*s*, 1216*s*, 1189*m*, 1159*m*, 1132*s*, 1119*s*, 1098*s*, 1084*s*, 1070*s*, 1058*s*, 1043 (sh), 1035 (sh), 1018*s*, 1003 (sh), 998*s*, 959*m*, 944*m*, 918*m*, 909*m*, 902*m*, 889*m*, 830*w*, 802*w*, 782*m*, 749*s*, 720*s*, 695*s*, 666*m*, 630*m*, 605*m*. ^{1}H-NMR (CD_3OD): 1.44 (*d*, *J* = 7.05, 3 H); 3.50 (*m*, 3 H); 3.68 (*m*, 1 H); 3.92 (*dd*, app. as *t*, *J* = 2.7, 2.7, 1 H); 4.88 (*m*, 5 H); 7.23 (*m*, 10 H). ^{13}C-NMR (CD_3OD): 22.92 (*q*); 51.90 (*d*); 71.84 (*d*); 73.06 (*d*); 74.35 (*d*); 74.64 (*d*); 76.09 (*t*); 77.65 (*d*); 83.22 (*d*); 126.95 (*d*); 127.83 (*d*); 128.38 (*d*); 129.09 (*d*); 129.35 (*d*); 140.43 (*s*); 145.56 (*s*); 158.69 (*s*). MS: 418 (< 1), 122.2 (13), 106 (10), 105 (100). Anal. calc. for $C_{22}H_{27}NO_7$ (417.46): C 63.30, H 6.52, N 3.35; found: C 63.27, H 6.40, N 3.52.

*1*L*-4-O-Benzyl-*myo*-inositol* (**11a**). To a soln. of Na (45.8 mg, 1.99 mmol) in dry EtOH (1.5 ml) at r.t. under Ar was added a soln. of **10a** (112.2 mg, 0.27 mmol) in EtOH (1.5 ml). The mixture was kept at 80° for 2.5 h, the cooled soln. (r.t.) acidified to pH 2–3 with 1M HCl, silica gel added, and the suspension evaporated. The residue was deposited on a chromatography column. FC (*F*, 9:1 to 8:2) gave 72.6 mg (100%) of **11a**. The product was recrystallised from MeOH and i-PrOH at r.t. M.p. 175.5–177.7° ([10]: 176–178°). R_f (*F*, 9:1) 0.08. $[\alpha]_D^{22} = -5.6$, $[\alpha]_{436}^{22} = -10.7$ (*c* = 1, MeOH; [10]: $[\alpha]_D^{22} = -6$, $[\alpha]_{436}^{22} = -11$). IR (KBr): 3900*s* (br.), 3800*s* (br.), 3083*w*, 3062*w*, 3028*m*, 2968*w*, 2930*m*, 2910*m*, 2895*m*, 2862*w*, 2780 (sh), 2738 (sh), 2660 (sh), 1945*w*, 1870*w*, 1800*w*, 1740*w*, 1704*w*, 1695*w*, 1688*w*, 1682*w*, 1675*w*, 1648*w*, 1636*w*, 1621*w*, 1604*w*, 1588*w*, 1575*w*, 1565*w*, 1552*w*, 1539*w*, 1511*w*, 1498*w*, 1475*w*, 1472*w*, 1469*w*, 1453*m*, 1441*m*, 1410 (sh), 1399*m*, 1371*m*, 1349*m*, 1330 (sh), 1303*m*, 1276*w*, 1265*m*, 1258 (sh), 1248 (sh), 1232*m*, 1217*w*, 1184*m*, 1140*s*, 1118*s*, 1058*s*, 1029*s*, 995*s*, 939*m*, 898*m*, 832*w*, 759*m*, 730*s*, 712*m*, 694*s*, 618*m*. ^{1}H-NMR ((D$_5$)pyridine): 4.09 (*dd*, *J* = 2.8, 9.6, 1 H); 4.15 (*dd* app. as *t*, *J* = 9.25, 9.35, 1 H); 4.20 (*dd*, *J* = 2.9, 9.6, 1 H); 4.51 (*dd* app. as *t*, *J* = 9.25, 9.50, 1 H); 4.71 (*t*, *J* = 9.35, 9.6, 1 H); 4.75 (*t*, *J* = 2.8, 2.9, 1 H); 5.34 (*d*, *J* = 11.50, 1 H); 5.41 (*d*, *J* = 11.50, 1 H); 6.5 (br. *s*, 5 OH); 7.31 (*m*, 3 H); 7.67 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 73.54 (*d*); 73.64 (*d*); 74.75 (2 *d*); 76.33 (*t*); 76.72 (*d*); 83.49 (*d*); 128.72 (*d*); 129.42 (*d*); 129.47 (*d*); 140.85 (*s*). MS: 541 (50, dimer), 271 (100). Anal. calc. for $C_{13}H_{18}O_6$ (270.28): C 57.77, H 6.71; found: C 57.78, H 6.90.

*(1*R*,3*s*,5*S*,6*R*,7*s*,8*S*,9*s*)-9-[(*tert*-Butyl)dimethylsilyloxy]-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane-6,8-diyl Dibutanoate* (**12**). To a suspension of **2** (25.0 g, 82.0 mmol) in dry CH_2Cl_2 (150 ml) and dry pyridine (26.5 ml, 328 mmol), butyric anhydride (29.5 ml, 180.4 mmol) and 4-(dimethylamino)pyridine (50 mg, 0.41 mmol) were added at 0° [19]. The soln. was stirred for 4 h at r.t. After dilution with dry MeOH (50 ml) and stirring for 30 min, the solvents were evaporated. A soln. of the residue in CH_2Cl_2 (100 ml) was washed twice (10 ml each) with sat. $NaHCO_3$ soln., 10% HCl soln., and H_2O. The org. layer was dried (Na_2SO_4) and evaporated. FC (*B*, 1:3) gave 35.0 g (96%) of **12** as a colourless oil. R_f (*B*, 1:3) 0.73. IR (film): 3500*w*, 2960*s*, 2940*s*, 2890*m*, 2860*m*, 1700*s*, 1470*m*, 1420*w*, 1380*m*, 1360*m*, 1350*w*, 1300*w*, 1280*w*, 1250*w*, 1160*s*, 1140*s*, 1120*m*, 1090*m*, 1060*w*, 1040*w*, 1000*s*. ^{1}H-NMR: 0.12 (*s*, 6 H); 0.93–1.0 (*m*, 15 H); 1.66 (*tq*, *J* = 7.2, 7.2, 4 H); 2.28 (*t*, *J* = 7.2, 4 H); 4.11–4.18 (*m*, 3 H); 4.49 (*m*, 1 H); 5.49 (*dd*, app. as *t*, 2 H); 5.57 (*d*, *J* = 1.2, 1 H). ^{13}C-NMR: –4.61 (*s*); 13.52 (*q*); 18.08 (*t*, *s*); 25.70 (*q*); 35.78 (*t*); 61.35 (*d*); 66.55 (*d*); 68.09 (d), 71.79 (*d*); 102.97 (*d*); 171.52 (*s*). CI-MS: 447 (7), 446 (29), 445 (100), 420 (4), 419 (12), 387 (5), 306 (12), 305 (63), 287 (4), 247 (5), 191 (33). Anal. calc. for $C_{21}H_{36}O_8Si$ (444.61): C 56.73, H 8.16; found: C 56.61, H 8.31.

*(1*S*,3*r*,5*R*,6*S*,7*r*,8*R*,9*r*)-9-Hydroxy-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane-6,8-diyl Dibutanoate* (**18**). $Bu_4NF \cdot 3H_2O$ (23.4 g, 74.2 mmol) was added to a soln. of **12** (30.0 g, 67.5 mmol) in dry THF (350 ml). After stirring for 10 h at r.t., evaporation and FC of the residue (*B*, 1:1) yielded 16.95 g (76%) of **18** as white crystals. An anal. sample was recrystallised from hexane/Et_2O. M.p. 59–60°. R_f (*B*, 1:1) 0.53. IR (KBr): 3500*s*, 2960*s*, 2940*m*, 2880*m*, 1740*s*, 1470*w*, 1420*m*, 1380*s*, 1300*s*, 1250*w*, 1200*s*, 1160*s*, 1120*m*, 1080*m*, 1040*m*, 1000*s*. ^{1}H-NMR: 0.89 (*t*, *J* = 7.4, 6 H); 1.59 (*tq*, *J* = 7.4, 7.4, 4 H); 2.17–2.26 (*m*, 4 H); 3.10 (br. *d*, *J* = 11.8, OH, exchangeable with D_2O); 3.89 (br. *d*, 1 H); 4.16 (*m*, 2 H); 4.47 (*ddd*, *J* = 1.6, 3.5, 5.2, 1 H); 5.46 (*dd* app. as *t*, *J* = 4.1, 3 H). ^{13}C-NMR: 13.57 (*q*); 18.16 (*t*); 35.82 (*t*); 61.17 (*d*); 66.37 (*d*), 67.49 (*d*); 71.58 (*d*); 103.21 (*d*); 171.76 (*s*). CI-MS: 333 (3), 332 (17), 331 (100). Anal. calc. for $C_{15}H_{22}O_8$ (330.34): C 54.54, H 6.71; found: C 54.83, H 6.98.

*(1*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-8,9-Dihydroxy-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]dec-6-yl Butanoate* (**21a**). Procedure for the hydrolysis with PLE: finely powdered **18** (1.65 g, 5 mmol) was suspended in 70 ml of a 0.1M phosphate-buffer soln. at pH 6.8, and 0.5 ml of PLE (2000 U) were added. The additon of 1M NaOH monitored by an autoburette (pH-stat) proceeded until 1 equiv. of base had been consumed. The mixture was extracted with

AcOEt (3 ×, 100 ml), dried (Na_2SO_4) and evaporated. FC (*B*, 1:1) gave 1.08 g (83%) of **21a**. M.p. 69–70°. $[\alpha]_D^{25} = -5.7$ ($c = 1.5$, $CHCl_3$). The ee value (> 95%) was determined in the 400-MHz ^{1}H-NMR by addition of Eu(hfc)$_3$ to **21a** in a molar ratio of 0.3:1.

For reactions on a larger scale, two recrystallisations from CH_2Cl_2/cyclohexane gave enantiomerically pure **21a** (68%). IR: 3580*m*, 3030*w*, 2970*m*, 2880*w*, 1740*s*, 1455*w*, 1410*m*, 1380*w*, 1350*w*, 1290*m*, 1240*m*, 1180*m*, 1160*s*, 1080*s*, 1060*m*, 1010*s*, 990*s*. ^{1}H-NMR: 0.96 (*t*, *J* = 7.4, 3 H); 1.70 (*tq*, *J* = 7.4, 7.4, 2 H); 2.33 (*t*, *J* = 7.4, 2 H); 2.50 (br. *d*, *J* = 6.0, OH); 3.22 (br. *d*, *J* = 11.4, OH); 3.97 (*dd*, *J* = 1.3, 3.8, 1 H); 4.15 (*ddd*, *J* = 3.8, 3.8, 1.8, 1 H); 4.17 (*ddd*, *J* = 1.8, 1.8, 3.8, 1 H); 4.34 (*ddd*, *J* = 6.0, 3.8, 1.8 1 H); 4.52 (*ddd*, *J* = 3.8, 3.8, 1.8, 1 H); 5.44 (*d*, *J* = 1.3, 1 H); 5.52 (*ddd*, *J* = 1.8, 3.8, 3.8, 1 H). ^{13}C-NMR: 13.50 (*q*); 18.10 (*t*); 35.85 (*t*); 60.69 (*d*); 67.27 (*d*); 67.79 (*d*); 68.29 (*d*); 71.69 (*d*); 74.23 (*d*); 102.87 (*d*); 171.76 (*s*). CI-MS: 262 (13), 261 (100), 191 (12), 73 (3). Anal. calc. for $C_{11}H_{16}O_7$ (260.25): C 50.77, H 6.20; found: C 50.71, H 6.47.

*(1*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-8,9-Bis(benzyloxy)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]dec-6-yl Butanoate* (**22a**). Benzyl trichloroacetimidate (8.13 g, 32.2 mmol) and TfOH (84 µl) were added at r.t. to a soln. of **21a** (0.3 g, 1.15 mmol) in dry CH_2Cl_2 (6 ml) and cyclohexane (8 ml, distilled over $LiAlH_4$). The mixture was stirred for 30 min, diluted with CH_2Cl_2 (10 ml) and pyridine (0.5 ml), stirred for 5 min, and then washed with H_2O (2 ×), dried (Na_2SO_4), and evaporated. FC (*B*, 1:10 to 1:3) gave 0.31 g (62%) of **22a** as a colourless oil. $[\alpha]_D^{25} = -22.1$ ($c = 1.1$, $CHCl_3$) for ee 90%. IR: 3020*m*, 2980*m*, 2880*w*, 1740*s*, 1500*w*, 1450*m*, 1380*m*, 1255*m*, 1170*s*, 1100*s*, 1000*s*. ^{1}H-NMR: 0.78 (*t*, *J* = 7.5, 3 H); 1.41 (*ddd*, *J* = 7.5, 7.5, 15.0, 2 H); 1.99, 2.04 (*t*/*AB*, *J* = 7.5, 7.5, 15.0, 2 H); 3.93 (br. *s*, 1 H); 4.29–4.30 (*m*, 1 H); 4.32–4.37 (br. *s*, 2 H); 4.45, 4.50 (*AB*, *J* = 11.5, 2 H); 4.58–4.60 (*m*, 1 H); 4.70, 4.74 (*AB*, *J* = 12.3, 2 H); 5.38 (*dd* app. as *t*, *J* = 3.8, 1 H); 5.57 (*d*, *J* = 1.2, 1 H); 7.17–7.42 (*m*, 10 H). ^{13}C-NMR: 13.49 (*q*); 17.89 (*t*); 35.81 (*t*); 66.62 (*d*); 68.20 (*d*); 69.52 (*d*); 70.10 (*d*); 71.34 (*t*); 71.69 (*t*); 73.61 (*d*); 103.17 (*d*); 127.38 (*d*); 127.98 (*d*); 128.08 (*d*); 128.41 (*d*); 128.48 (*d*); 137.25 (*s*); 137.53 (*s*); 172.24 (*s*). CI-MS (NH_3): 459 (5), 458 (16), 449 (5), 443 (5), 442 (28), 441 (100), 388 (9), 382 (5), 371 (3), 102 (4), 58 (3), 35 (17). Anal. calc. for $C_{25}H_{28}O_7$ (440.50): C 68.17, H 6.40; found: C 68.33, H 6.38.

*(1*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-8,9-Bis[(tetrahydro-2*H*-pyran-2-yl)oxy]-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]dec-6-yl Butanoate* (**23a**). To an ice-cooled soln. of **21a** (1.4 g, 5.38 mmol) and freshly distilled 3,4-dihydro-2*H*-pyran (2.6 ml, 26.9 mmol) in dry CH_2Cl_2 (20 ml) was added TsOH·H_2O (10 mg, 0.05 mmol). The mixture was stirred for 10 min at 0° and then for 15 min at r.t. The soln. was diluted with Et_2O (30 ml), extracted with brine (10 ml), sat. $NaHCO_3$ soln. (10 ml), H_2O (20 ml), dried ($MgSO_4$/K_2CO_3), and evaporated below 30°. FC (*B*, 1:3) afforded 2.1 g (91%) of **23a** as a colourless oil. R_f (*B*, 1:1) 0.65. $[\alpha]_D^{25} = -20.0$ ($c = 1.1$, $CHCl_3$). IR: 3090*w*, 3080*w*, 3040*m*, 3010*m*, 2950*s*, 2880*m*, 2860*m*, 1740*s*, 1490*w*, 1480*m*, 1470*m*, 1460*m*, 1440*m*, 1380*m*, 1355*m*, 1330*m*, 1305*m*, 1290*m*, 1270*m*, 1255*m*, 1180*s*, 1165*s*, 1130*s*, 1080*s*, 1040*s*, 1000*s*. ^{1}H-NMR: 0.95 (*dt*, *J* = 7.5, 7.5, 3 H); 1.43–1.90 (*m*, 14 H); 2.30 (*m*, 2 H); 3.45–3.60 (*m*, 2 H); 3.77–3.40 (*m*, 2 H); 4.15 (*m*, 1 H); 4.25 (*m*, 1 H); 4.39 (*m*, 1 H); 4.50 (*m*, 2 H); 4.70 (*m*, 1 H); 4.91 (*m*, 1 H); 5.42 (*m*, 1 H); 5.57 (*d*, *J* = 1.4, 1 H). ^{13}C-NMR: 13.62 (*q*); 13.66 (*q*); 18.09 (*t*); 19.33 (*t*); 19.47 (*t*); 19.76 (*t*); 20.99 (*t*); 25.15 (*t*); 25.35 (*t*); 30.64 (*t*); 30.72 (*t*); 30.77 (*t*); 35.92 (*t*); 35.95 (*t*); 62.27 (*t*); 62.33 (*t*); 62.61 (*t*); 62.64 (*t*); 62.83 (*t*); 65.31 (*d*); 65.51 (*d*); 67.18 (*d*); 68.11 (*d*); 68.37 (*d*); 68.43 (*d*); 69.40 (*d*); 71.17 (*d*); 71.60 (*d*); 71.68 (*d*); 71.94 (*d*); 72.92 (*d*); 72.98 (*d*); 97.98 (*d*); 99.39 (*d*); 103.11 (*d*); 172.17 (*s*); 172.21 (*s*); 172.25 (*s*). CI-MS (NH_3): 430 (22), 429 (91), 345 (10). Anal. calc. for $C_{21}H_{32}O_9$ (428.49): C 58.87, H 7.53; found: C 58.87, H 7.71.

*(1*R*,3*S*,5*S*,6*R*,7*R*,8*S*,9*S*)-8,9-Bis[(tetrahydro-2*H*-pyran-2-yl)oxy]-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decan-6-ol* (**24a**). To a soln. of dry MeOH (10 ml) and **23a** (2.0 g, 4.66 mmol), one drop of 1M NaOMe/MeOH was added. After stirring for 4 h at r.t., the soln. was neutralised with solid NH_4Cl, filtered, and evaporated. FC (*B*, 1:3) afforded 1.6 g (96%) of **24a** as a colourless oil. R_f (*B*, 1:1) 0.43. $[\alpha]_D^{25} = -8.9$ ($c = 1.4$, $CHCl_3$). IR: 3500*m*, 3000*w*, 2950*m*, 2850*w*, 1200*s*, 1160*s*, 1140*m*, 1120*m*, 1070*s*, 1040*s*, 1020*m*, 1000*m*. ^{1}H-NMR: 1.50–1.83 (*m*, 12 H); 3.49–3.63 (*m*, 3 H); 3.66–3.99 (*m*, 3 H); 4.26–4.32 (*m*, 2 H); 4.38–4.69 (*m*, 4 H); 4.80–4.90 (*m*, 1 H); 5.54 (*d*, *J* = 1.3, 1 H). ^{13}C-NMR: 19.07 (*t*); 19.34 (*t*); 19.41 (*t*); 19.47 (*t*); 25.27 (*t*); 30.57 (*t*); 30.63 (*t*); 30.67 (*t*); 62.41 (*t*); 62.47 (*t*); 62.58 (*t*); 63.29 (*t*); 64.04 (*d*); 64.07 (*d*); 64.93 (*d*); 67.76 (*d*); 67.82 (*d*); 67.99 (*d*); 68.06 (*d*); 68.13 (*d*); 68.21 (*d*); 68.83 (*d*); 70.60 (*d*); 72.19 (*d*); 72.71 (*d*); 73.71 (*d*); 73.92 (*d*); 74.08 (*d*); 74.20 (*d*); 97.41 (*d*); 98.30 (*d*); 100.10 (*d*); 100.74 (*d*); 102.52 (*d*); 102.60 (*d*). CI-MS (NH_3): 377 (19), 376 (100), 359 (11), 344 (9), 292 (13), 102 (36), 85 (4), 35 (4). Anal. calc. for $C_{17}H_{26}O_8$ (358.39): C 56.97, H 7.31; found: C 57.21, H 7.53.

*(1*R*,3*S*,5*S*,6*R*,7*R*,8*S*,9*S*)-6-(Benzyloxy)-8,9-bis[(tetrahydro-2*H*-pyran-2-yl)oxy]-2,4,10-trioxatricyclo-[3.3.1.1^{3,7}]decane* (**25a**). Hexane-washed NaH (0.180 g, 7.53 mmol) was added to a soln. of **24a** (1.4 g, 3.90 mmol) in dry THF (10 ml) and stirred for 30 min at r.t. After addition of Bu_4NI (15 mg, 0.039 mmol) and $PhCH_2Br$ (0.8 ml, 6.46 mmol) the mixture was stirred for 2 h at r.t., diluted with MeOH (5 ml), stirred for 5 min, evaporated, redissolved in AcOEt, and washed with brine (10 ml). The org. layer was dried (Na_2SO_4) and evaporated. FC (*B*, 1:3) gave 1.6 g (91%) of **25a** as a colourless oil. R_f (*B*, 1:3) 0.36. $[\alpha]_D^{25} = -14.5$ ($c = 1.5$, $CHCl_3$). IR: 3050*m*, 2950*s*,

2880*m*, 2870*m*, 1500*w*, 1460*w*, 1455*m*, 1440*m*, 1380*m*, 1350*w*, 1325*w*, 1305*w*, 1270*w*, 1200*w*, 1170*s*, 1125*s*, 1100*m*, 1080*s*, 1040*s*, 1000*s*. ^{1}H-NMR: 1.45–1.80 (*m*, 12 H); 3.45–3.58 (*m*, 2 H); 3.89–4.00 (*m*, 2 H); 4.20–4.86 (*m*, 10 H); 5.56 (*s*, 1 H); 7.26–7.36 (*m*, 5 H). ^{13}C-NMR: 19.03 (*t*); 19.48 (*t*); 19.54 (*t*); 19.68 (*t*); 25.27 (*t*); 25.34 (*t*); 30.37 (*t*); 30.77 (*t*); 61.96 (*t*); 62.45 (*t*); 62.75 (*t*); 62.99 (*t*); 65.96 (*d*); 66.12 (*d*); 66.18 (*d*); 67.94 (*d*); 67.99 (*d*); 69.52 (*d*); 70.61 (*d*); 70.95 (*t*); 71.03 (*t*); 71.54 (*d*); 72.02 (*d*); 72.46 (*d*); 72.53 (*d*); 72.72 (*d*); 73.81 (*d*); 73.87 (*d*); 73.94 (*d*); 98.40 (*d*); 98.59 (*d*); 98.64 (*d*); 103.15 (*d*); 127.35 (*d*); 127.39 (*d*); 127.68 (*d*); 127.78 (*d*); 128.23 (*d*); 128.29 (*d*); 128.34 (*d*); 137.75 (*s*). CI-MS (NH_3): 467 (27), 466 (100), 450 (23), 449 (92), 383 (9), 382 (43), 365 (19), 102 (24), 85 (9). Anal. calc. for $C_{24}H_{32}O_8$ (448.52): C 64.27, H 7.19; found: C 64.24, H 7.03.

(1S,3S,5R,6R,7R,8R,9R)-9-(Benzyloxy)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane-6,8-diol (**6a**). A soln. of **25a** (0.5 g, 1.14 mmol) in AcOH/H_2O/THF 2:2:1 (10 ml) was stirred for 24 h at r.t., neutralised with solid K_2CO_3, and extracted (3 ×) with Et_2O. The org. phase was dried (Na_2SO_4) and evaporated. FC (*B* 1:1) gave 0.28 g (87%) of **6a** as a colourless oil. R_f (*B*, 1:1) 0.24. $[\alpha]_D^{25} = -16.6$ (*c* = 1.0, EtOH). Anal. calc. for $C_{14}H_{16}O_6$ (280.28): C 60.00, H 5.75; found: C 59.79, H 6.00.

(1S,3R,5S,6S,7R,8R,9R)-8,9-Bis(benzyloxy)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decan-6-ol (**26a**). To a soln. of **6a** (0.20 g, 0.71 mmol) in dry CH_2Cl_2 (4 ml) and dry cyclohexane (5 ml), benzyl trichloroacetimidate (0.32 g, 1.28 mmol) and TfOH (50 µl) were added. After 30 min, the reaction was stopped by addition of pyridine (0.5 ml). HPLC (silica gel; *B*, 1:1) showed two peaks in a ratio of 10:1. Usual workup and FC (*B*, 1:3) afforded 0.21 g, (81%) of **26a** as a colourless oil and traces of **27**. **26a**: R_f (*B*, 1:1) 0.54. $[\alpha]_D^{25} = -8.4$ (*c* = 1.0, EtOH). IR: 3500*s*, 3090*m*, 3060*m*, 2960*s*, 2880*m*, 1130*s*, 1080*s*. ^{1}H-NMR: 3.75 (*d*, *J* = 10.0, OH); 3.88 (*d*, *J* = 1.4, 1 H); 4.23–4.29 (*m*, 2 H); 4.32–4.49 (*m*, 3 H); 4.47, 4.55 (*AB*, *J* = 11.5, 2 H); 4.64, 4.77 (*AB*, *J* = 12.3, 2 H); 5.51 (*d*, *J* = 1.4, 1 H); 7.15–7.45 (*m*, 10 H). ^{13}C-NMR: 66.12 (*d*); 67.65 (*d*); 67.96 (*d*); 69.92 (*d*); 71.33 (*t*); 72.12 (*d*); 72.89 (*t*); 74.50 (*d*); 102.59 (*d*); 127.99 (*d*); 128.53 (*d*); 128.72 (*d*); 128.81 (*d*); 135.87 (*s*); 137.52 (*s*). CI-MS (NH_3): 390 (4), 389 (24), 388 (100), 382 (9), 372 (13), 371 (57), 365 (4), 298 (8), 281 (10), 196 (8), 179 (4), 136 (7), 108 (4), 102 (8), 35 (10). Anal. calc. for $C_{21}H_{22}O_6$ (370.41): C 68.09, H 5.97; found: C 68.07, H 5.69.

Compounds **6a**, **22a**, and **26a** were deprotected, as described for **7**, to yield **11a**, **9b**, and **9a**, resp.

1L-4-O-Benzyl-myo-*inositol* (**11a**). From **6a** (0.4 g, 1.43 mmol), 0.35 g (91%) of **11a** were obtained. M.p. 176–177°. $[\alpha]_D^{22} = -5.8$ (*c* = 1.1, MeOH).

1D-2,4-Di-O-benzyl-myo-*inositol* (**9b**). Deprotection of **22a** (0.3 g, 0.68 mmol) followed by treatment of the crude product with 5% NaOMe/MeOH and recrystallisation from Et_2O gave 0.2 g (85%) of **9b**. M.p. 145–146°. $[\alpha]_D^{25} = 29.5$ (*c* = 1.1, EtOH).

1L-2,4-Di-O-benzyl-myo-*inositol* (**9a**). Deprotection of **26a** (0.2 g, 0.54 mmol) afforded, after crystallisation from Et_2O, 0.16 g (83%) of **9a**. M.p. 145–146°. $[\alpha]_D^{25} = -29.3$ (*c* = 1.3, EtOH).

1D-2,4-Di-O-benzyl-myo-*inositol 1,3,5,6-Tetrakis(dibenzyl phosphate)* (**28b**). To bis(benzyloxy)(diisopropylamino)phosphine (1.27 g, 3.68 mmol) [15] in dry MeCN (11.4 ml) at r.t. under Ar, tetrazole (349.8 mg, 4.99 mmol) was added and stirred for 30 min. A soln. of **9b** (75.8 mg, 0.21 mmol) in MeCN (3.8 ml) was added within 2 h and the mixture was stirred for 21 h at r.t. The cooled soln. (ice bath) was treated with *m*-chloroperbenzoic acid (719.3 mg, 4.17 mmol) and stirred again for 21 h at r.t. The mixture was dissolved with CH_2Cl_2 and washed with 10% aq. $NaHSO_3$ soln., the aq. phase reextracted with $CHCl_3$ (filtered through silica gel and basic *Alox*), and the combined org. layers were washed with aq. sat. $NaHCO_3$ soln. The aq. layer was reextracted with $CHCl_3$ and the combined org. layers were dried ($MgSO_4$) and evaporated. A rapid chromatography of the residue on silica gel containing 2% $NaHCO_3$ (freshly mixed; FC; *D*, 1:0 to 98:2) gave **28b** (289.5 mg, 98%) after drying *i.v.* for 1 h. It was used immediately for the next step.

Data of **28a**: R_f (*D*, 98:2) 0.04. ^{1}H-NMR: 4.07 (*t*, *J* = 9.3, 1 H); 4.25 (*dddd*, *J* = 2.4, 7.5, 9.5, 15, 2 H); 4.45 (*dd*, *J* = 9.3, 18.4, 1 H); 4.58–5.12 (*m*, 22 H); 7.3 (*m*, 50 H). ^{13}C-NMR: 69.13 (*t*); 69.19 (*t*); 69.23 (*t*); 69.30 (*t*); 69.40 (*t*); 69.51 (*t*); 69.58 (*t*); 69.75 (*t*); 74.57 (*t*); 75.30 (*d*); 75.37 (*d*); 75.42 (*d*); 75.78 (*t*); 75.88 (*d*); 75.98 (*d*); 77.11 (*d*); 77.19 (*d*); 77.96 (*d*); 127.23 (*d*); 127.33 (*d*); 127.70 (*d*); 127.79 (*d*); 127.85 (*d*); 127.91 (*d*); 128.04 (*d*); 128.18 (*d*); 128.44 (*d*); 135.37 (*s*); 135.49 (*s*); 135.63 (*s*); 135.79 (*s*); 135.93 (*s*); 136.06 (*s*); 138.00 (*s*); 138.07 (*s*). ^{31}P-NMR: −1.34; −1.01; −0.83; −0.60.

1D-myo-Inositol 1,3,4,5-Tetraphosphate (**1a**). A soln. of **28a** (283 mg, 0.2 mmol) in 80% EtOH (15 ml) was hydrogenolysed at r.t. under a H_2 pressure of 8 bar in the presence of 10% Pd/C (560 mg) for 2 h. TLC (cellulose plates; *E* 5:4:1) showed the presence of a single, UV-active product (R_f 0.22) which was identified as a monobenzylated compound by ^{1}H-NMR of its dicyclohexylammonium salt (^{1}H-NMR (D_2O): 1.1–2.05 (*m*, 20 H); 3.15 (*m*, 2 H); 3.91–4.24 (*m*, 4 H); 4.43 (*m*, 2 H); 7.4 (*m*, 3 H); 7.6 (*m*, 2 H)). The catalyst was removed by centrifugation and washed with EtOH and H_2O. The resulting soln. was evaporated and the residue diluted with 60% EtOH (15 ml) and treated with 10% Pd/C (560 mg). After hydrogenolysis at 8 bar for 2 h, UV-active spots had completely disappeared on TLC in favour of a spot corresponding to a new, UV-inactive, P-containing product (*E*, 5:5:2; R_f

0.31). The catalyst was removed by centrifugation. The soln. was evaporated and the residue taken up in a few ml of H_2O. Freshly distilled cyclohexylamine was added until the soln. reached pH 9.5–10. The soln. was lyophilised. The residue was dissolved in 1 ml of H_2O and treated with acetone to precipitate the cyclohexylammonium salt which was isolated by centrifugation, giving 145.4 mg (76%) of **1a**·4.5 cyclohexylamine.

Data of **1a**·*4.5 Cyclohexylamine:* M.p. 173.7–175.7°. R_f (*E*, 5:5:2) 0.31. $[\alpha]_D^{25} = -2.5$ ($c = 1$, H_2O). IR (KBr): 3420*m* (br.), 3200*m*, 3090*m*, 3020 (sh), 3005*s*, 2980 (sh), 2965*s*, 2955*s*, 2940*s*, 2915 (sh), 2880*m*, 2860*s*, 2825*m*, 2775*w*, 2720*w*, 2670*w*, 2610*w*, 2560*w*, 2505*w*, 2010*w*, 1648*w* (br.), 1610*w*, 1598*w*, 1499*w*, 1491*w*, 1470*w*, 1465*w*, 1456*w*, 1448*w*, 1390*w*, 1195*m* (br.), 1123*m*, 1050*s* (br.), 1020*m*, 975*w*, 924*m* (br.), 845*w*, 810*w*, 715*w*. ^{1}H-NMR (D_2O): 1.19–2.04 (*m*, 45 H); 3.2 (*m*, 4.5 H); 3.97 (*dd* app. as *t*, $J = 9.3, 9.3$, 1 H); 4.16 (*m*, 2 H); 4.19 (*ddd*, app. as *dt*, $J = 2, 10, 10$, 1 H); 4.46 (*m*, 2 H). ^{13}C-NMR (D_2O): 23.75 (*t*); 24.25 (*t*); 30.30 (*t*); 50.27 (*d*); 70.62 (*m*, 1 C); 71.03 (*m*, 1 C); 74.36 (*m*, 2 C); 75.98 (*m*, 1 C); 78.15 (*m*, 1 C). ^{31}P-NMR (D_2O): 1.48 (2 P); 1.99 (1 P); 2.3 (1 P). FAB-MS: 897, 798, 699, 600, 523, 501.

The enantiomer **1b** crystallised with 5 equiv. of cyclohexylamine. Data of **1b**·5 cyclohexylamine: M.p. 169.8–171.8°. $[\alpha]_D^{25} = +2.6$ ($c = 1$, H_2O).

REFERENCES

[1] See *e.g.* M.J. Berridge, R.F. Irvine, *Nature (London)* **1984,** *312,* 315; M.J. Berridge, *Biochem. J.* **1984,** *220,* 345; M.J. Berridge, *Scient. Am.* **1985,** *253,* 124; A.A. Abdel-Latif, *Pharmacol. Rev.* **1986,** *38,* 227, and ref. cit. therein.

[2] G.M. Burgess, R.F. Irvine, M.J. Berridge, J.S. McKinney, J.W. Putney, *Biochem. J.* **1984,** *224,* 741; R.F. Irvine, A.J. Letcher, D.J. Lander, M.J. Berridge, *ibid.* **1986,** *240,* 301; B. Michell, *Nature (London)* **1986,** *319,* 176; M.C. Sekat, J.F. Dixon, L.E. Hokin, *J. Biol. Chem.* **1987,** *262,* 340.

[3] I.R. Batty, S.R. Nahorsky, R.F. Irvine, *Biochem. J.* **1985,** *232,* 211; R.F. Irvine, A.J. Letcher, J.P. Heslop, M.J. Berridge, *Nature (London)* **1986,** *320,* 631; B. Michell, *ibid.* **1986,** *324,* 613.

[4] M.D. Housley, *Trends Biochem. Sci.* **1987,** *12,* 133; R.F. Irvine, R.M. Moor, *Biochem. J.* **1986,** *240,* 917.

[5] S. Osaki, Y. Watanabe, T. Ogasawara, Y. Kondo, N. Shiotani, H. Nishii, T. Matsuki, *Tetrahedron Lett.* **1986,** *27,* 3157; M. Cooke, V.L. Potter, R. Gigg, *ibid.* **1987,** *28,* 2305; J.P. Vacca, S.J. deSolms, J.R. Huff, *J. Am. Chem. Soc.* **1987,** *109,* 3478; C.B. Reese, J.G. Ward, *Tetrahedron Lett.* **1987,** *28,* 2309.

[6] a) S.J. deSolms, J.P. Vacca, J.R. Huff, *Tetrahedron Lett.* **1987,** *28,* 4503; b) D.C. Billington, R. Baker, *J. Chem. Soc., Chem. Commun.* **1987,** 1011; c) S. Osaki, Y. Kondo, H. Nakahira, S. Yamaoka, Y. Watanabe, *Tetrahedron Lett.* **1987,** *28,* 4691.

[7] H.W. Lee, Y. Kishi, *J. Org. Chem.* **1985,** *50,* 4402.

[8] S. Sternhell, *Rev. Pure Appl. Sci.* **1964,** *14,* 15.

[9] H.P. Wessel, T. Iversen, D.R. Bundle, *J. Chem. Soc., Perkin Trans. 1* **1985,** 2247.

[10] P.J. Garegg, B. Lindberg, *Carbohydr. Res.* **1985,** *139,* 209.

[11] J.B. Jones, *Tetrahedron* **1986,** *42,* 3351.

[12] K.F. Bernardy, M.B. Floyd, J.F. Poletto, M.J. Weiss, *J. Org. Chem.* **1978,** *44,* 1438.

[13] S. Czernecki, C. Georgoulis, C. Provelenghiou, *Tetrahedron Lett.* **1976,** 3535.

[14] P.J. Garegg, T. Iversen, S. Oscarsen, *Carbohydr. Res.* **1976,** *50,* C12.

[15] W. Bannwarth, A. Trzeciak, *Helv. Chim. Acta* **1987,** *70,* 175.

[16] K.-L. Yu, B. Fraser-Reid, P.M. Gross, *Tetrahedron Lett.* **1988,** 979.

[17] S. Cerdan, C.A. Hansen, R. Johanson, T. Inubushi, J.R. Williamson, *J. Biol. Chem.* **1986,** *261,* 14676; J.C. Lindon, D.J. Baker, J.M. Williams, R.F. Irvine, *Biochem. J.* **1987,** *244,* 591.

[18] A. Desjobert, F. Petek, *Bull. Soc. Chim. Biol.* **1956,** *38,* 871; H.E. Wade, D.M. Morgan, *Nature (London)* **1953,** *171,* 529.

[19] G. Höfle, W. Steglich, H. Vorbruggen, *Angew. Chem.* **1978,** *90,* 602.