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Selective epimerization of L-*chiro*-inositol to L-*muco*- and D-*chiro*-inositol derivatives☆

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Dedicated to Professor Joachim Thiem on the occasion of his 60th birthday

Abstract

In a one step procedure, L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**) was acetalized to the L-*muco*-inositol derivatives **2**, **3** and D-2-*O*-benzyl-3-*O*-cyclohexylcarbamoyl-4-deoxy-4-(*N*,*N*′-dicyclohexylureido)-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**4**). Complete conversion of L-1-*O*-benzyl-6-*O*-cyclohexylcarbamoyl-3-*O*-formyl-2-*O*-methyl-4,5-*O*-trichloroethylidene-*muco*-inositol (**3**) into L-1-*O*-benzyl-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-4,5-*O*-trichloroethylidene-*muco*-inositol (**2**) is feasible by deformylation in boiling methanolic triethylamine. Furthermore, stepwise deprotection of **2** and **4** is described. Thus, compounds **5**, **10**, and **7** were obtained by decarbamoylation of **2**, **4**, and **6**, respectively, with boiling methanolic sodium methoxide. The trichloroethylidene group of L-1-*O*-benzyl-2-*O*-methyl-4,5-*O*-trichloroethylidene-*muco*-inositol (**5**) was removed in a two step procedure (hydrodechlorination–deacetalization) via the ethylidene acetal **7** to give L-1-*O*-benzyl-2-*O*-methyl-*muco*-inositol (**9**). On refluxing D-*chiro*-inositol derivative **4** with 99% acetic acid, the ureido moiety was cleaved generating D-2-*O*-benzyl-4-cyclohexylamino-3-*O*-cyclohexylcarbamoyl-4-deoxy-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**11**). By contrast, cleavage of the ureido moiety of **10** was relatively difficult. The corresponding D-2-*O*-benzyl-4-cyclohexylamino-4-deoxy-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**12**) was only formed in small amounts. The structures of **1**, **3** and **10** were confirmed by X-ray analysis.

Keywords: Inositols; Epimerization; Acetals; Deprotection; X-ray analysis

1. Introduction and scope

The biological relevance of inositols is well known.[2–4] Partly phosphorylated derivatives take part in fundamental biological processes, e.g., as second messengers.[5,6] Inositols and related polyhydroxycyclohexanes are also used as chiral auxiliaries in stereoselective synthesis.[7,8] However, the separation of inositol derivatives from natural sources is limited to a few representatives, so that various compounds of this type were prepared by chemical methods.[2–4,9] We focused our efforts on opening a new short way to these stereoisomers by epimerization from well accessible precursors.†

In former papers we reported about a one-pot procedure for selective epimerizations of various pyranosides using a chloral–DCC reagent combination.[1,11] For this reaction a cis–trans-sequence of three contiguous hydroxyl groups in the starting molecule is required. First attempts to apply the method to inositols like L-quebrachitol and *myo*-inositol with five or six unprotected OH-groups failed. Only (1*S*,2*S*,3*S*,4*R*,5*R*)-1-*O*-methylcyclohexane-1,2,3,4,5-pentol was successfully epimerized.[12]

☆ Epimerization of carbohydrates and cyclitols, Part 18. For Part 17, see Ref. 1.

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† The nomenclature used in this paper is in agreement with the IUPAC-IUB rules for cyclitols.[10]

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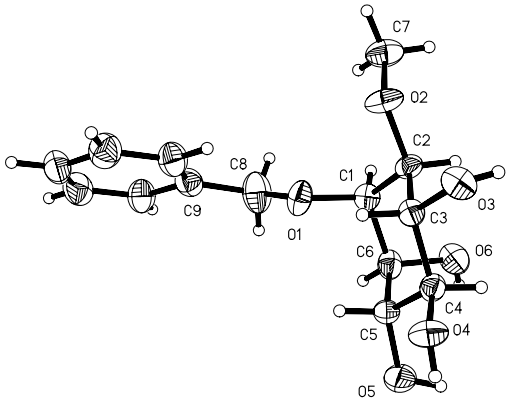


Fig. 1. Stereo drawing of L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**) with 50% probability of the thermal ellipsoids.

2. Synthesis and characterization

For the following reaction, we used L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**) synthesized from L-quebrachitol (Fig. 1).[13‡] The molecular structure of the compound is shown in Fig. 1.

On refluxing of **1** and chloral–DCC in 1,2-dichloroethane for 8 h, three products were formed, the L-*muco*-inositol derivatives **2**, **3** and the D-*chiro*-inositol derivative **4** (Scheme 1). Due to the pro-chirality of chloral, diastereomeric mixtures of the endo-H and exo-H forms of the cyclic acetals were expected. However, only the corresponding endo-H isomers were found after column chromatographic separation by yields of 25% (**2**), 16% (**3**) and 15% (**4**).

Formation of the L-*muco*-inositol derivatives **2** and **3** is in conformity with the mechanism of epimerizations described for chloral–DCC acetalizations of pyranoses.[11,16,17] As expected, the middle carbon atom of the triol unit of **1** with cis–trans-sequence (C-4/C-5/C-6) was inverted (Schemes 1 and 2).

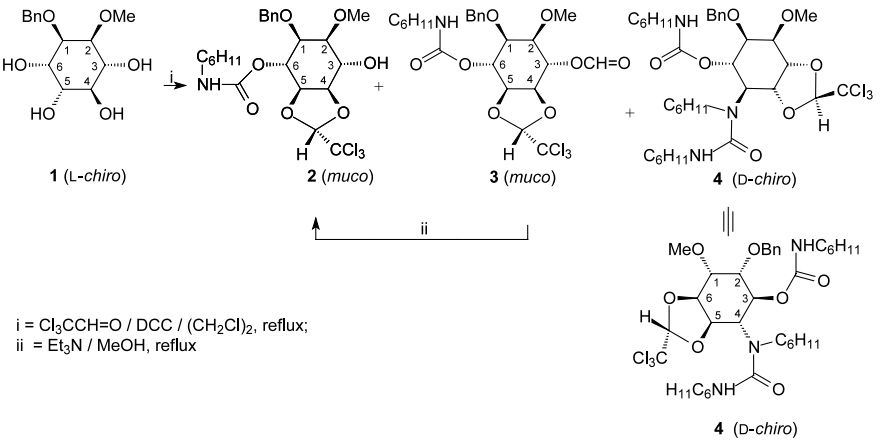
‡ Compound **1** was synthesized from L-quebrachitol via L-3,4:5,6-di-*O*-cyclohexylidene-2-*O*-methyl-*chiro*-inositol.[14,15]

The formyl group at C-3 of **3** results from a haloform reaction of the chloral (see also Ref. 11). Compound **3** crystallized from diethyl ether–light petroleum ether giving orthorhombic crystals which were suitable for an X-ray analysis (Fig. 2). Boiling methanolic triethylamine allows a selective removal of formyl groups. By this procedure, compound **3** was quantitatively converted into **2** within 15 min. Application of this deformylation procedure to the crude mixture of **2**, **3**, and **4** simplifies the chromatographic separation of the D-chiro derivative **4**, because formyl derivative **3** eluted closely to **4**.

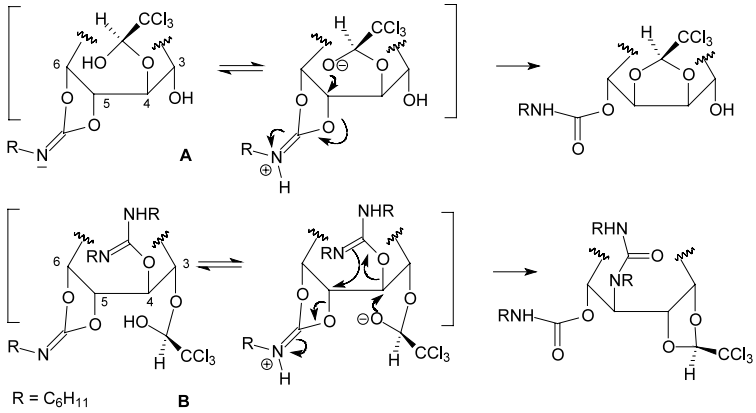
The formation of D-*chiro*-inositol derivative **4** came as a surprise. Related to **1**, the configuration at C-4 and C-5 was inverted. It seems possible that the compound results from a reaction sequence via the key intermediate B (Scheme 2). The latter may be formed via intermediate A (addition of 4-OH to DCC after hemiacetal displacement to 3-OH). Intermediate B allows a tandem-sequence as marked by arrows (Scheme 2). That would explain the regioselective introduction of a carbamoyl group into the 6-position of compound **4**, as well as the formation of the C–N-bond at C-atom 5. The C–N-bond formation corresponds to results published by Vowinkel and Gleichenhagen.[18]

The configuration of **4** is identified as one of D-*chiro*-inositol derivatives. Therefore, the numbering of **4** was changed, i.e., adapted following the rules.[10] The lower constitutional formula of **4** in Scheme 1 shows the upper one from the rear.

The stepwise deprotection of **2** is described in Scheme 3. Procedures to deprotect carbamoyl and trichloroethylidene functions were already reported in former papers.[1,11,12] Thus, decarbamoylation of **2** was carried out by refluxing in methanolic sodium methoxide giving **5** in 82% yield. Hydrodechlorination of **2** using tributylstannane–AIBN[19] was achieved in boiling toluene. After 12 h two ethylidene derivatives, **6** (54%) and **7**



Scheme 1. Epimerization of L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**).



Scheme 2. Proposed mechanisms for the epimerization of L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**).

(28%), were formed, because the reagent caused not only hydrodechlorination, but also decarbamoylation. The latter reaction gains importance with increasing reaction time. Compound **6** was contaminated with L-1-*O*-benzyl-4,5-*O*-chloroethylidene-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-*muco*-inositol (about 2.5%). Because the separation of the monochloroethylidene byproduct was difficult at this stage, the mixture of **6**/**7** containing this monochloro derivative was treated with methanolic sodium methoxide (decarbamoylation) followed by treatment with 80% aqueous trifluoroacetic acid (deacetalization) at room temperature. The latter reagent cleaves only the ethylidene group in L-1-*O*-benzyl-4,5-*O*-ethylidene-2-*O*-methyl-*muco*-inositol (**7**) forming L-1-*O*-benzyl-2-*O*-methyl-*muco*-inositol (**9**) which can be easily separated from the byproduct L-1-*O*-benzyl-4,5-*O*-chloroethylidene-2-*O*-methyl-*muco*-inositol (**8**) by column chromatography (Scheme 3). Hydrodechlorination of **5** with tributylstannane–AIBN yielded a mixture of **7** and **8** (ratio about 18–20:1).

Reactions of the D-*chiro*-inositol derivative **4** are shown in Scheme 4. On heating **4** with methanolic sodium methoxide for 24 h decarbamoylation to compound **10** was achieved. The structure of this D-chiro derivative was confirmed by X-ray measurements (Fig. 3).

Treatment of **4** with boiling 99% acetic acid resulted likewise in a lost of a carbamoyl moiety. However, in this case the ureido moiety was cleaved generating D-2-*O*-benzyl-4-cyclohexylamino-3-*O*-cyclohexylcarbamoyl-4-deoxy-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**11**), i.e., the carbamoyl group at C-3 still exists. Cleavage of the latter by refluxing with 2% methanolic sodium methoxide was even more difficult. On heating for 16 h, only 13% of the starting material **11** was converted into D-2-*O*-benzyl-4-cyclohexylamino-4-deoxy-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**12**) (Scheme 4).

Structure assignment based on NMR and X-ray data.—The assignment of signals in the ^{1}H and ^{13}C NMR spectra was performed by recording DEPT and two-dimensional $^{1}H,^{1}H$ and $^{13}C,^{1}H$ correlation spectra (comparative ^{13}C NMR data see Ref. 20). Thus, the signals for C-1 and C-2 could be confirmed by the correlation over three bonds to the proton signals OBn and OMe, respectively. On this basis, the assignment of signals for the other ring atoms became possible. All spectra show the characteristic signals of a carbamoyl group and a trichloroethylidene group. The latter is characterized by the singlet of the acetal proton (**2**–**5**, **10**–**12**: $\delta \approx 5.36$–5.46) and by the C signals of the acetal moiety ($\delta_{CCl_3} \approx 98.9$–$99.8$; $\delta_{CH} \approx 105.9$–$107.2$). For compounds **4** and **10**–**12**, the signal for C-4 is significantly shifted to a higher field due to the N-substituent compared to the other ring-C-atom signals. In the ^{1}H spectrum of **4**, recorded at room temperature, some signals were displayed as broad signals which were sharpened at a higher temperature indicating a dynamic process due to the flexibility of the molecule.

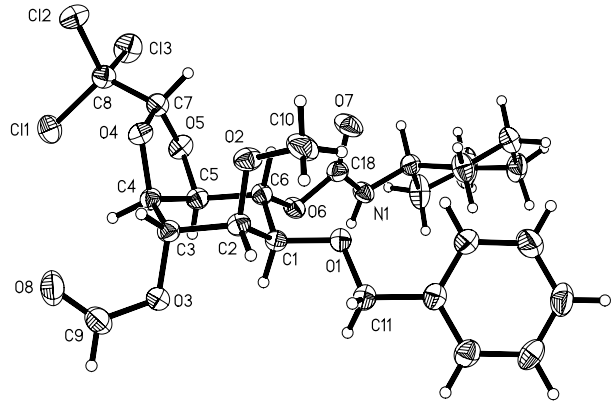
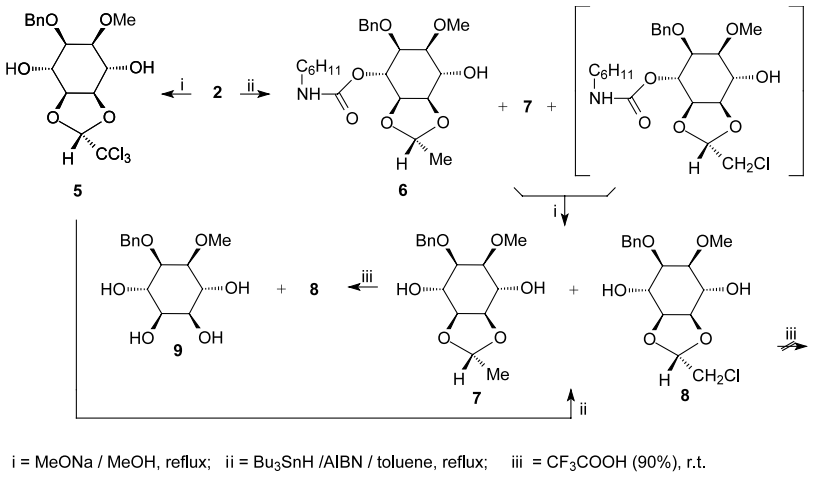


Fig. 2. Stereo drawing of L-1-*O*-benzyl-6-*O*-cyclohexylcarbamoyl-3-*O*-formyl-2-*O*-methyl-4,5-*O*-trichloroethylidene-*muco*-inositol (**3**) with 50% probability of the thermal ellipsoids.



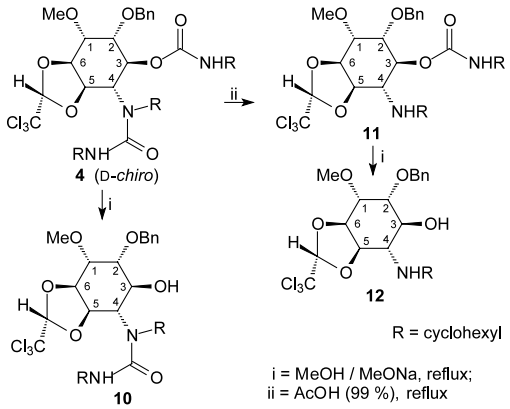
Scheme 3. Deprotection of L-1-*O*-benzyl-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-4,5-*O*-trichloroethylidene-*muco*-inositol (**2**).

The ethylidene acetal group in compounds **6** and **7** is represented by a quadruplet of the acetal proton ($\delta \approx 5.28-5.30$) and a doublet ($\delta \approx 1.32-1.34$, $J \approx 5.0$ Hz) of the methyl group. The location of these groups is detectable by the upfield shifts of the nearest ring protons compared to the spectra of the corresponding trichloroethylidene derivatives **2** and **5**.

The X-ray analyses of compounds **1** and **3** show that **1** adopts a distorted $^1C_4$ chair conformation in the crystal lattice whereas the muco-derivative **3** adopts a distorted $^4C_1$ conformation. However, ring flip seems to occur when compound **3** was dissolved in chloroform. This behavior is indicated by the fact that long range coupling of H-1 and H-5 ($^4J \approx 1.0$ Hz) was found in the corresponding ^{1}H NMR spectrum. Such a coupling requires a W-arrangement of these two protons which is only present in the case of a $^1C_4$ conformation. A $^1C_4$ chair conformation was also observed for L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**) in methanolic solution. This is indicated by 1,3-diaxial interactions of H-2 and H-4 (NOE). Because H-2 and H-4 interactions were also found for the epimeric L-1-*O*-benzyl-2-*O*-methyl-*muco*-inositol (**9**) in methanolic solution, a similar $^1C_4$ chair conformation can also be assumed for this compound.

The puckering parameters[21] for the six-membered rings of **1**, **3** and **10** are as follows: $Q = 0.573(3)$ Å (puckering amplitude), $\Theta = 4.3(3)°$, $\phi = 274(4)°$ for **1**, $Q = 0.543(2)$ Å (puckering amplitude), $\Theta = 154.7(2)°$, $\phi = 181.1(5)°$ for **3**, $Q = 0.765(5)$ Å (puckering amplitude), $\Theta = 85.0(4)°$, $\phi = 32.2(4)°$ for **10**.

Single crystals of **1** and **10** were tested by rotational photographs on a Bruker P4 four circle diffractometer equipped with a Mo K_α sealed tube and a graphite monochromator. Suitable reduced cells were found by the automatic cell-determination routine of the Bruker SHELXTL software. The data collections were performed in routine ω-scans. For **3**, the data collection was done on a Bruker SMART area detector system.



Scheme 4. Reactions of D-2-*O*-benzyl-3-*O*-cyclohexylcarbamoyl-4-deoxy-4-(*N*,*N*′-dicyclohexylureido)-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**4**).

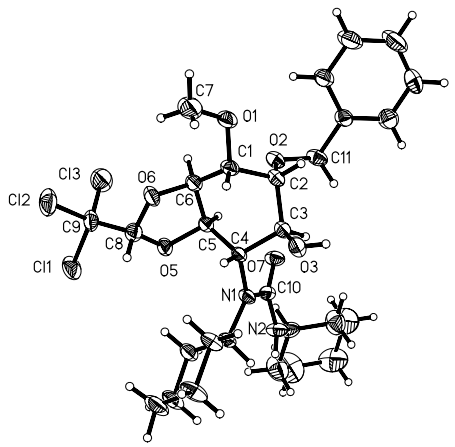


Fig. 3. Stereo drawing of D-2-*O*-benzyl-4-deoxy-4-(*N*,*N*′-dicyclohexylureido)-1-*O*-methyl-5,6-*O*-trichloroethylidene-*chiro*-inositol (**10**) with 30% probability of the thermal ellipsoids.

The structures were solved by direct methods (Bruker SHELXTL) and refined by the full-matrix least-squares methods of SHELXL-97.§ All non-hydrogen atoms were refined anisotropically while the hydrogens were put into theoretical positions and refined according to the 'riding model'.¶ However, the OH-groups were allowed to rotate and this special refinement procedure resulted in an improvement of the hydrogen bond directionality. Although hydrogen bonding occurs in all three investigated solids, the most interesting network of hydrogen bonds can be observed in the crystals of **1**. In this compound, the dominating motif is formed by four molecules. In the direction of the *b*-axis, two molecules are linked together by a hydrogen bridge between O-2 in the first and O-6 in the second molecule, the distance between the oxygens being 2.699 Å. This pair of molecules is in turn connected with another pair of two molecules in the *a*-axis direction. There are links between the OH-groups of O-3–O-4 (2.711 Å), O-3–O-6 (2.806 Å) and O-4–O-5 (2.811 Å). Hence the three groups O-3–H, O-4–H and O-6–H show both donating and accepting features.

In the crystal of **3**, there are hydrogen bridges only in the direction of the *a*-axis, between the NH as donating and the ring O-4 as accepting group, the distance being 3.183 Å.

In the solid of **10**, infinite chains of molecules can be observed which are made up of hydrogen links between the O-3–H and the carbonyl oxygen of O-7, the O···O distance being 2.775 Å.

The weighting scheme was calculated as follows, for **1** $w^{-1} = \sigma^2(F_o^2) + (0.0608P)^2 + 0.0119P$, for **3** $w^{-1} = \sigma^2(F_o^2) + (0.0510P)^2 + 0.0000P$ and for **10** $w^{-1} = \sigma^2(F_o^2) + (0.0679P)^2 + 0.1457P$ with $P = (F_o^2 + 2F_c^2)/3$ in all cases.

3. Conclusions

An inositol derivative containing four contiguous hydroxyl groups with cis–trans–trans sequence turn out to be precursors for two competing epimerization reactions achieved in a facile one-pot procedure with chloral–DCC. The results are not only of outstanding interest with regard to the compounds obtained, but also for the assumed tandem mechanism. Various opportunities for subsequent synthetic steps at each of the new inositol's chiral centers are offered by the diversity of the protecting group pattern.

§ G.M. Sheldrick, Universität Göttingen, 1997.

¶ See web pages: http://util.ucsf.edu/local/programs/shelxl/ch_04.html # 4.5 for further information on this terminology.

4. Experimental

General.—Melting points were obtained on a polarizing microscope Leitz (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-300 spectrometer (300.13 and 75.5 MHz, respectively). Calibration of spectra was carried out by means of solvent peaks. ($CDCl_3$: δ ^{1}H 7.25; δ ^{13}C 77.0; CD_3OD: δ ^{1}H 3.30; δ ^{13}C 49.0). Optical rotations were measured on a Polar LμP (IBZ Meßtechnik). Infrared spectra were recorded on a Protegé Nicolet 460 IR-spectrometer (Nujol). Column chromatography: E. Merck Silica Gel 60 (40–63 μm); thin-layer chromatography (TLC): E. Merck Silica Gel 60 F_{254} foils.

L-*1*-O-*Benzyl*-*2*-O-*methyl*-chiro-*inositol* (**1**).—To a stirred solution of 80% aq trifluoroacetic acid (60 mL), L-1-*O*-benzyl-3,4:5,6-di-*O*-cyclohexylidene-2-*O*-methyl-*chiro*-inositol[13] (7.20 g, 16.1 mmol) was added at rt and stirring continued overnight. After concentration of the solution under reduced pressure, the crude product was purified by column chromatography (R_f 0.24, 5:1 $CHCl_3$–MeOH); colorless crystals 4.46 g, 97%: mp 153–154 °C (acetone–EtOH); $[\alpha]_D^{24}$ −54.2° (*c* 1.0, MeOH).

^{1}H NMR (300.13 MHz, CD_3OD): δ 7.38–7.22 (m, 5 H, Ph), 4.70, 4.61 (AB, 2 H, $J_{AB} \approx 12.0$ Hz, C*H*$_2$–Ph), 4.02 (dd, 1 H, $J_{1,6} \approx 4.0$, $J_{5,6} \approx 3.0$ Hz, H-6), 3.92 (dd, 1 H, $J_{1,2} \approx 3.0$ Hz, H-1), 3.66 (dd, 1 H, $J_{4,5} \approx 9.5$ Hz, H-5), 3.66 (dd, 1 H, $J_{3,4} \approx 9.1$ Hz, H-3), 3.53 (dd, 1 H, H-4), 3.39 (dd, 1 H, $J_{2,3} \approx 10.0$ Hz, H-2), 3.39 (s, 3 H, OMe); ^{13}C NMR (75.5 MHz, CD_3OD): δ 139.9 (*i*-Ph), 129.3 (*m*-Ph), 128.9 (*o*-Ph), 128.7 (*p*-Ph), 82.5 (C-2), 76.6 (C-1), 74.9 (C-4), 74.1 (*C*H$_2$–Ph), 74.0, 72.6 (C-3, 5), 71.0 (C-6), 58.3 (OMe). Anal. Calcd for $C_{14}H_{20}O_6$ (284.3): C, 59.14; H, 7.09. Found: C, 58.87; H, 6.91.

L-*1*-O-*Benzyl*-*6*-O-*cyclohexylcarbamoyl*-*2*-O-*methyl*-*4,5*-O-*trichloroethylidene*-muco-*inositol* (**2**), L-*1*-O-*benzyl*-*6*-O-*cyclohexylcarbamoyl*-*3*-O-*formyl*-*2*-O-*methyl*-*4,5*-O-*trichloroethylidene*-muco-*inositol* (**3**) *and* D-*2*-O-*benzyl*-*3*-O-*cyclohexylcarbamoyl*-*4*-*deoxy*-*4*-*(*N,N′-*dicyclohexylureido)*-*1*-O-*methyl*-*5,6*-O-*trichloroethylidene*-chiro-*inositol* (**4**).—Compound **1** (2.80 g, 9.85 mmol), DCC (5.0 g, 24.2 mmol) and chloral (5.0 g, 33.9 mmol) in 1,2-dichloroethane (100 mL) were refluxed for 8 h. After cooling to rt and addition of CH_2Cl_2 (150 mL) and 10% aq AcOH (200 mL), the reaction mixture was shaken for about 30 min to destroy excess DCC. The precipitated *N*,*N*′-dicyclohexyl urea was removed by filtration, the organic phase was separated, and the aqueous phase was washed with $CHCl_3$ (3 × 70 mL). The combined extracts were washed with satd aq $NaHCO_3$ (100 mL) and water (2 × 70 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was treated with acetone (50 mL) to dissolve the products **2**, **3** and **4**; further crystalline

N,*N*′-dicyclohexyl urea remains undissolved. The filtrate was concentrated. The TLC (2:1 heptane–EtOAc) of the residue showed four spots. Compounds **2** (R_f 0.11), **3** (R_f 0.40) and **4** (R_f 0.28) were isolated from the mixture by column chromatography. The syrupy product **2** (1.32 g, 25%) crystallized from heptane colorless needles: mp 124–124.5 °C, $[\alpha]_D^{29}$ −12.9° (*c* 1.34, $CHCl_3$). The formyl derivative **3** (0.90 g, 16%) crystallized from 2:1 light petroleum ether–Et_2O: mp 142–143 °C (143–144 °C; DSC measurement); $[\alpha]_D^{29}$ −7.7° (*c* 1.37, $CHCl_3$); 1.1 g (15%) of compound **4** was isolated $[\alpha]_D^{22}$ +7.4° (*c* 1.07, $CHCl_3$). The latter is easily soluble in light petroleum ether and numerous other organic solvents like acetone, EtOAc, and $CHCl_3$. However, **4** did not crystallize. Only a porous-amorphous solid (melting range 85–90 °C) was obtained by concentration of its light petroleum solution under reduced pressure.

Moreover, *N*-acetyl-*N*,*N*′-dicyclohexyl-urea (R_f 0.20) was isolated as crystalline byproduct, mp 126–127 °C (heptane). It was characterized by X-ray, NMR and MS analyses.

2: ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 7.40–7.22 (m, 5 H, Ph), 5.52 (dd, 1 H, $J_{1,6} \approx 3.7$, $J_{5,6} \approx 2.0$ Hz, H-6), 5.39 (s, 1 H, C*H*–CCl_3), 4.79 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.67 (d, 1 H, $J_{NH,CH} \approx 8.0$ Hz, NH), 4.59 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.58 (dd overlapped to CH_2, 1 H, H-5), 4.54 (dd, 1 H, $J_{4,5} \approx 6.3$ Hz, H-4), 4.16 (dd, 1 H, $J_{3,4} \approx 6.3$ Hz, H-3), 3.93 (ddd, 1 H, $J_{1,2} \approx 2.6$, $^4J_{1,5} \approx 1.0$ Hz, H-1), 3.47 (m, 1 H, cyclohexyl-CH), 3.30 (s, 3 H, OMe), 3.22 (dd, 1 H, $J_{2,3} \approx 9.8$ Hz, H-2), 2.88 (br, 1 H, OH), 2.00–1.05 (m, 10 H, cyclohexyl-CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 153.5 (C(O)NH), 137.7 (*i*-Ph), 128.3 (*m*-Ph), 127.9 (*o*-Ph), 127.6 (*p*-Ph), 105.9 (*C*H–CCl_3), 99.2 (CCl_3), 81.7 (C-4), 78.9 (C-2), 77.8 (C-5), 72.4 (C-1), 71.8 (*C*H_2–Ph), 68.6 (C-3), 67.0 (C-6), 57.5 (OMe), 50.2 (cyclohexyl-CH), 33.2, 25.3, 24.7 (cyclohexyl-CH_2). Anal. Calcd for $C_{23}H_{30}Cl_3NO_7$ (538.8): C, 51.27; H, 5.61; N, 2.60. Found: C, 51.32; H, 5.63; N, 2.74.

3: ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 8.14 (d, 1 H, $J \approx 1.0$ Hz, CH=O), 7.40–7.24 (m, 5 H, Ph), 5.54–5.45 (m, 2 H, H-3, H-6), 5.46 (s, 1 H, C*H*–CCl_3), 4.76 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.64 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.65–4.59 (m, 2 H, H-4, H-5), 4.61 (br, 1 H, NH), 3.91 (ddd, 1 H, $J_{1,6} \approx 4.8$, $J_{1,2} \approx 2.5$, $^4J \approx 1.0$ Hz, H-1), 3.48 (m, 1 H, cyclohexyl-CH), 3.42 (dd, 1 H, $J_{2,3} \approx 9.1$ Hz, H-2), 3.34 (s, 3 H, OMe), 2.00–1.05 (m, 10 H, cyclohexyl-CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 160.2 (CH=O), 153.6 (C(O)NH), 137.6 (i-*Ph*), 128.3 (*m*-Ph), 127.9 (*o*-Ph), 127.8 (*p*-Ph), 106.0 (*C*H–CCl_3), 98.9 (CCl_3), 79.4, 78.4 (C-4, C-5), 76.9 (C-2), 73.7 (C-1), 72.3 (*C*H_2–Ph), 70.2 (C-3), 67.3 (C-6), 58.2 (OMe), 50.3 (cyclohexyl-CH), 33.3, 25.4, 24.7 (cyclohexyl-CH_2). Anal. Calcd for $C_{24}H_{30}Cl_3NO_8$ (566.9): C, 50.85; H, 5.33; N, 2.47. Found: C, 50.68; H, 5.19; N, 2.47.

4: ^{1}H NMR (300.13 MHz, $CDCl_3$, 55 °C): δ 7.39–7.22 (m, 5 H, Ph), 5.30 (dd, 1 H, $J_{3,4} \approx 8.2$ Hz, H-3), 5.45 (s, 1 H, C*H*–CCl_3), 5.14 (dd, 1 H, $J_{5,6} \approx 6.7$, $J_{4,5} \approx 9.8$ Hz, H-5), 4.80 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.79 (dd, 1 H, $J_{1,6} \approx 5.5$ Hz, H-6), 4.71 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.89 (br, 1 H, H-4), 4.54 (d, 1 H, $J \approx 7.5$ Hz, NH), 4.41 (d, 1 H, $J \approx 7.5$ Hz, NH), 3.79 (dd, 1 H, $J_{2,3} \approx 3.5$ Hz, H-2), 3.70 (dd, 1 H, $J_{1,2} \approx 2.0$ Hz, H-1), 3.67 (m, 1 H, cyclohexyl-CH), 3.48 (m, 1 H, cyclohexyl-CH), 3.44 (s, 3 H, OMe), 3.24 (br, 1 H, cyclohexyl-CH), 2.04–0.99 (m, 30 H, cyclohexyl-CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 156.7 (NHC(O)N), 154.4 (NHC(O)O), 137.9 (*i*-Ph), 128.3 (*m*-Ph), 127.7 (*o*-Ph), 127.6 (*p*-Ph), 107.2 (*C*H–CCl_3), 99.7 (CCl_3), 80.3 (C-6), 78.8 (C-1), 77.6 (C-2), 76.9 (C-5), 72.1 (*C*H_2–Ph), 70.7 (C-3), 58.0 (OMe), 56.3 (C-4), 55.9 (cyclohexyl-CH), 49.9, 49.4 (cyclohexyl-CH), 33.8, 33.7, 33.3, 33.2, 32.7, 32.1, 26.6, 26.5, 25.6, 25.6, 25.4, 25.0, 25.0, 24.71, 24.66 (cyclohexyl-CH_2); IR (Nujol): 1631 cm^{-1} (C=O, urea moiety), 1722 cm^{-1} (C=O, carbamoyl moiety), 3330, 3381 cm^{-1} (NH). Anal. Calcd for $C_{36}H_{52}Cl_3N_3O_7$ (745.2): C, 58.03; H, 7.03; N, 5.64. Found: C, 57.69; H, 7.03; N, 5.51.

L-*1*-O-*Benzyl*-*6*-O-*cyclohexylcarbamoyl*-*2*-O-*methyl*-*4,5*-O-*trichloroethylidene*-muco-*inositol* (**2**).—A solution of *muco*-inositol **3** (300 mg, 0.5 mmol) in dry MeOH (10 mL) and Et_3N (0.5 mL) was refluxed for 15 min and concentrated under reduced pressure yielding 285 mg (100%) of **2**; mp 124 °C (heptane).

L-*1*-O-*Benzyl*-*2*-O-*methyl*-*4,5*-O-*trichloroethylidene*-muco-*inositol* (**5**).—Compound **2** (446 mg, 1.0 mmol) was dissolved in 2% methanolic NaOMe (20 mL) and was refluxed for about 16 h (TLC control). Subsequently, the reaction mixture was cooled and neutralized with an acidic ion-exchanger resin (Amberlite IR-120). After evaporation of the solvent under reduced pressure and column chromatographic purification (R_f 0.13, 1:2 toluene–EtOAc) 300 mg (85%) of syrupy **5** was isolated. The product is easily soluble in Et_2O and less soluble in light petroleum, however, it did not crystallize. Concentration of the ethereal solution of **5** under reduced pressure yielded an amorphous solid (melting range 52–60 °C); $[\alpha]_D^{29}$ −25.8° (*c* 0.9, $CHCl_3$).

^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.41–7.26 (m, 5 H, Ph), 5.40 (s, 1 H, C*H*–CCl_3), 4.67 (s, 2 H, CH_2–Ph), 4.59 (m, 2 H, H-4, H-5), 4.32 (ddd, 1 H, $J_{1,6} \approx 6.5$, $J_{5,6} \approx 3.2$, $^4J \approx 1.0$ Hz, H-6), 4.28 (ddd, 1 H, $J_{3,4} \approx 3.3$, $^4J \approx 1.3$ Hz, H-3), 3.77 (dd, 1 H, $J_{1,2} \approx 2.8$ Hz, H-1), 3.48 (dd, 1 H, $J_{2,3} \approx 7.0$ Hz, H-2), 3.42 (s, 3 H, OMe), 2.53 (br, 2 H, 2OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 137.9 (*i*-Ph), 128.5 (*m*-Ph), 127.9 (*p*-Ph), 127.8 (*o*-Ph), 106.3 (*C*H–CCl_3), 99.6 (CCl_3), 81.1, 80.9 (C-4, 5), 78.7 (C-2), 75.9 (C-1), 68.2 (C-3), 68.0 (C-6), 72.4 (*C*H_2–Ph), 58.2 (OMe). Anal. Calcd for $C_{16}H_{19}Cl_3O_6$ (413.6): C, 46.46; H, 4.63. Found: C, 46.55; H, 4.60.

L-*1*-O-*Benzyl*-*6*-O-*cyclohexylcarbamoyl*-*4,5*-O-*ethylidene*-*2*-O-*methyl*-muco-*inositol* (**6**) *and* L-*1*-O-*benzyl*-*4,5*-O-*ethylidene*-*2*-O-*methyl*-muco-*inositol* (**7**).—To a stirred solution of **2** (540 mg, 1.0 mmol) in dry toluene (20 mL), Bu_3SnH (1.1 g, 3.75 mmol) and AIBN (20 mg, 0.12 mmol) were added (Ar atmosphere). After 16 h heating under reflux (TLC control) the mixture was shaken with satd aq KF (10 mL) for 2 h and filtered through kieselguhr to remove Bu_3SnF. Then the organic phase was separated, washed with water (2×5 mL), and dried ($MgSO_4$). On cooling the solution overnight (refrigerator) 160 mg of pure **6** crystallized. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (**6**: R_f 0.15, 7: R_f 0.10, 1:1 toluene–EtOAc) yielding further 74 mg of **6** (over all yield 54%) and 88 mg (28%) of L-1-*O*-benzyl-2-*O*-methyl-4,5-*O*-ethylidene-*muco*-inositol (**7**); for the physical data of compound **7** see the following procedure. Compound **6** crystallized from Et_2O, mp 112–113 °C (colorless needles); $[\alpha]_D^{29}$ −25.8° (*c* 0.88, $CHCl_3$).

6: ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.38–7.22 (m, 5 H, Ph), 5.45 (dd, $J_{1,6} \approx 3.6$, $J_{5,6} \approx 2.2$ Hz, 1 H, H-6), 5.30 (q, 1 H, C*H*–CH_3), 4.77 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.58 (d, 1 H, $J_{AB} \approx 12.0$ Hz, CH_2–Ph), 4.63 (d, 1 H, $J_{NH,CH} \approx 8.0$ Hz, NH), 4.24 (dd, 1 H, $J_{3,4} \approx 6.8$, $J_{4,5} \approx 6.0$ Hz, H-4), 4.18–4.10 (m, 2 H, H-3, H-5), 3.90 (ddd, 1 H, $J_{1,2} \approx 2.6$, $^4J_{1,5} \approx 1.0$ Hz, H-1), 3.46 (m, 1 H, cyclohexyl-CH), 3.19 (dd, 1 H, $J_{2,3} \approx 9.8$ Hz, H-2), 3.28 (s, 3 H, OMe), 2.53 (br, 1 H, OH), 1.98–1.05 (m, 10 H, cyclohexyl-CH_2), 1.34 (d, 3 H, $J_{CH_3,CH} \approx 5.0$ Hz, CH–CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 153.8 (C(O)NH), 137.8 (*i*-Ph), 128.2 (*m*-Ph), 127.8 (*o*-Ph), 127.6 (*p*-Ph), 100.5 (*C*H–CH_3), 79.8 (C-4), 79.5 (C-2), 75.7 (C-5), 72.4 (C-1), 71.7 (*C*H_2–Ph), 68.1 (C-3), 67.8 (C-6), 57.4 (OMe), 50.2 (cyclohexyl-CH), 33.3, 25.4, 24.7 (cyclohexyl-CH_2), 20.4 (CH–*C*H_3). Anal. Calcd for $C_{23}H_{33}NO_7$ (435.5): C, 63.43; H, 7.64; N, 3.22. Found: C, 62.53; H, 7.77; N, 3.25.

L-*1*-O-*Benzyl*-*4,5*-O-*ethylidene*-*2*-O-*methyl*-muco-*inositol* (**7**).—To a solution of **6** (479 mg, 1.1 mmol) in MeOH (20 mL), sodium (240 mg) was added forming sodium methoxide. Subsequently, the mixture was refluxed for 16 h, cooled to rt, neutralized using an acidic ion-exchange resin (Amberlite IR120), filtered and concentrated under reduced pressure. The residue was purified by column chromatography (eluent: 1:2 toluene–EtOAc, R_f 0.13) yielding 301 mg (88%) of **7** as colorless syrup.

7: ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.36–7.24 (m, 5 H, Ph), 5.28 (q, C*H*–CH_3), 4.65 (s, 2 H, CH_2–Ph), 4.26–4.15 (m, 4 H, H-3, 4, 5, 6), 3.72 (m, 1 H, $J_{1,2} \approx 3.0$, $J_{1,6} \approx 6.8$ Hz, H-1), 3.47 (m, 1 H, $J_{2,3} \approx 6.8$ Hz, H-2), 3.39 (s, 3 H, OMe), 2.81, 2.81 (2d, 2 H, $J \approx 6.0$ Hz, 2 OH), 1.32 (d, 3 H, $J \approx 5.0$ Hz, CH–CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 137.9 (*i*-Ph), 128.4 (*m*-Ph), 127.8 (*o*-Ph), 127.8 (*p*-Ph), 100.4 (*C*H–CH_3), 78.8 (C-4), 78.8 (C-5), 78.7 (C-2), 76.0 (C-1), 67.9, 67.8 (C-3, 6), 72.1 (*C*H_2–Ph), 58.2 (OMe), 20.4 (CH–*C*H_3). Anal. Calcd for $C_{16}H_{22}O_6$ (310.4): C, 61.92; H, 7.15. Found: C, 61.78; H, 7.11.

L-*1*-O-*Benzyl*-*2*-O-*methyl*-muco-*inositol* (**9**).—A solution of **7** (211 mg, 0.68 mmol) in 80% TFA (10 mL) was stirred for about 22 h at rt (TLC control). Then toluene (10 mL) was added and the mixture was concentrated at 40 °C under reduced pressure. After a second co-distillation of the residue with toluene (10 mL), the brownish syrupy crude product was purified by column chromatography (R_f 0.16, 6:1 $CHCl_3$–MeOH) yielding 180 mg (93%) of colorless syrupy **9**; $[\alpha]_D^{24}$ −5.5° (*c* 1.0, MeOH).

^{1}H NMR (250.13 MHz, CD_3OD): δ 7.43–7.23 (m, 5 H, Ph), 4.70 (s, 2 H, CH_2–Ph), 4.04 (t, 1 H, $J_{1,6} \approx J_{5,6} \approx$ 6.3 Hz, H-6), 3.99 (t, 1 H, $J_{2,3} \approx J_{3,4} \approx 7.0$ Hz, H-3), 3.84 (dd, 1 H, $J_{1,2} \approx 3.2$ Hz, H-1), 3.78–3.69 (m, 2 H, H-4, 5), 3.52 (dd, 1 H, $J_{2,3} \approx 7.0$ Hz, H-2), 3.42 (s, 3 H, OMe); ^{13}C NMR (75.5 MHz, CD_3OD): δ 139.6 (*i*-Ph), 129.4 (*m*-Ph), 129.2 (*o*-Ph), 128.8 (*p*-Ph), 82.9 (C-2), 79.8 (C-1), 74.3 (*C*H_2–Ph), 74.6, 74.4 (C-4, 5), 70.3 (C-3), 70.3 (C-6), 59.1 (OMe). Anal. Calcd for $C_{14}H_{20}O_6$ (284.3): C, 59.14; H, 7.09. Found: C, 58.01; H, 7.09.

L-*1*-O-*Benzyl*-*6*-O-*cyclohexylcarbamoyl*-*4,5*-O-*ethylidene*-*2*-O-*methyl*-muco-*inositol* (**6**), L-*1*-O-*benzyl*-*2*-O-*methyl*-muco-*inositol* (**9**) *and* L-*1*-O-*benzyl*-*4,5*-O-*chloroethylidene*-*2*-O-*methyl*-muco-*inositol* (**8**).—To a solution of **2** (0.57 g, 1.06 mmol) in dry toluene (25 mL) Bu_3SnH (1.1 g, 3.75 mmol) and AIBN (20 mg, 0.12 mmol) were added under stirring (Ar atmosphere). After 8 h heating under reflux (TLC control) the mixture was shaken with satd aq KF (10 mL) for 2 h and filtered through kieselguhr to remove Bu_3SnF. Then the organic phase was separated, washed with water (2×5 mL) and dried ($MgSO_4$). On cooling the solution overnight (refrigerator), 300 mg (65%) of pure **6** crystallized. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (1:1 toluene–EtOAc) and the fraction with $R_f \approx 0.18$ was concentrated, the residue (94 mg) was dissolved in 2% methanolic sodium methoxide (5 mL), and the mixture was refluxed for 16 h. After neutralization using Amberlite IR120, filtration and concentration under reduced pressure, the residue was treated with 80% TFA (5 mL) for 22 h at rt. Subsequently, the solution was worked-up as described for compound **9**. Column chromatographic separation gave 178 mg of **9** (59% related to **2**) and 80 mg of the monochloro acetal **8** (syrup, 22% related to **2**).

8: ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.36–7.25 (m, 5 H, Ph), 5.34 (t, 1 H, $J \approx 3.5$ Hz, C*H*–CH_2Cl), 4.67 (s, 2 H, CH_2–Ph), 4.31–4.23 (m, 4 H, H-3, 4, 5, 6), 3.75 (m, 1 H, $J_{1,2} \approx 2.8$, $J_{1,6} \approx 6.5$ Hz, H-1), 3.54 (d, $J \approx 3.5$ Hz,

CH–CH_2Cl), 3.49 (m, 1 H, $J_{2,3} \approx 6.5$ Hz, H-2), 3.41 (s, 3 H, OMe), 2.51 (br, 2 H, 2 OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 138.0 (*i*-Ph), 128.4 (*m*-Ph), 127.9 (*p*-Ph), 127.8 (*o*-Ph), 101.2 (*C*H–CH_2Cl), 79.5 (C-4), 79.5 (C-5), 78.9 (C-2), 76.1 (C-1), 72.3 (*C*H_2–Ph), 67.9, 67.8 (C-3, 6), 58.3 (OMe), 44.9 (CH–*C*H_2Cl). Anal. Calcd for $C_{16}H_{21}ClO_6$ (344.8): C, 55.74; H, 6.14. Found: C, 55.49; H, 6.20.

D-*2*-O-*Benzyl*-*4*-*deoxy*-*4*-*(*N,N′-*dicyclohexylureido)*-*1*-O-*methyl*-*5,6*-O-*trichloroethylidene*-chiro-*inositol* (**10**).—Compound **4** (300 mg, 0.40 mmol) in anhyd MeOH (10 mL)–sodium methoxide (0.13 g, 2.4 mmol) was decarbamoylated by refluxing the solution for about 14 h (TLC control). The reaction mixture was worked-up as described for **5**. After column chromatographic purification (R_f 0.30, 2:1 heptane–EtOAc), 204 mg (82%) of syrupy **10** was obtained. The compound crystallized from cyclohexane or 10:1 light petroleum ether–Et_2O in fine needles, mp 167–168 °C, $[\alpha]_D^{25}$ + 62.0° (*c* 1.0, $CHCl_3$). Crystals suitable for an X-ray measurement resulted from crystallization from 20:1 light petroleum ether–EtOAc, mp 165–166 °C.

10: ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.36–7.26 (m, 5 H, Ph), 5.39 (s, 1 H, C*H*–CCl_3), 5.00 (dd, 1 H, $J_{4,5} \approx 9.3$ Hz, H-5), 4.74 (d, 1 H, $J \approx 11.8$ Hz, CH_2–Ph), 4.73 (dd, $J_{1,6} \approx 4.3$, $J_{5,6} \approx 6.0$ Hz, H-6), 4.68 (d, 1 H, $J \approx 11.8$ Hz, CH_2–Ph), 4.50 (d, 1 H, $J \approx 7.5$ Hz, NH), 4.19 (dd, 1 H, $J_{3,4} \approx 9.0$ Hz, H-3), 3.88 (dd, 1 H, $J_{1,2} \approx 2.4$ Hz, H-1), 3.73–3.54 (m, 2 H, H-4, cyclohexyl-CH), 3.63 (dd, 1 H, $J_{2,3} \approx 6.5$ Hz, H-2), 3.49 (s, 3 H, OMe), 3.26 (br, 1 H, OH), 3.10 (m, 1 H, cyclohexyl-CH), 2.07–0.99 (m, 20 H, cyclohexyl-CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 138.1 (*i*-Ph), 128.5 (*m*-Ph), 127.6 (*o*-Ph), 127.8 (*p*-Ph), 158.3 (N=C(O)NH), 106.7 (*C*H–CCl_3), 99.6 (CCl_3), 80.7 (C-2), 78.8 (C-6), 77.8 (C-5), 77.2 (C-1), 72.8 (*C*H_2–Ph), 68.7 (C-3), 60.5 (C-4), 59.3 (OMe), 56.5, 49.4 (cyclohexyl-CH), 33.8, 33.8, 33.1, 32.2, 26.7, 26.7, 25.7, 25.7, 25.0, 25.0 (cyclohexyl-CH_2); IR (Nujol): 1622 cm^{-1} (C=N), 3354 cm^{-1} (NH), 3463 cm^{-1} (OH); MS (CI-isobutane): $m/z = 621$ [M + 1]. Anal. Calcd for $C_{29}H_{41}Cl_3N_2O_6$ (620.0): C, 56.18; H, 6.67; N, 4.52. Found: C, 56.50; H, 6.61; N, 4.42.

D-*2*-O-*Benzyl*-*4*-*cyclohexylamino*-*3*-O-*cyclohexylcarbamoyl*-*4*-*deoxy*-*1*-O-*methyl*-*5,6*-O-*trichloroethylidene*-chiro-*inositol* (**11**).—A solution of **4** (586 mg, 0.78 mmol) in 99% AcOH (20 mL) was refluxed for about 7 h (TLC control). Subsequently, the solution was concentrated under reduced pressure and purified by column chromatography (R_f 0.23; 2:1 heptane–EtOAc) yielding 390 mg (80%) of syrupy **11**. The compound crystallized from a 3:1 light petroleum ether–Et_2O mixture; colorless needles mp 109–110 °C; $[\alpha]_D^{25}$ + 13.2° (*c* 1.1, $CHCl_3$).

^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.37–7.22 (m, 5 H, Ph), 5.39 (s, 1 H, C*H*–CCl_3), 4.90 (dd, 1 H, $J_{3,4} \approx$ 6.5 Hz, H-3), 4.76 (dd, 1 H, $J_{1,6} \approx 5.6$ Hz, H-6), 4.74 (d, 1 H, $J \approx 12.1$ Hz, CH_2–Ph), 4.68 (d, 1 H, $J \approx 12.1$ Hz, CH_2–Ph), 4.66 (dd, 1 H, $J_{5,6} \approx 6.3$ Hz, H-5), 4.55 (d, 1 H, $J \approx 8.0$ Hz, NH), 3.73 (dd, 1 H, $J_{2,3} \approx 3.8$ Hz, H-2), 3.62 (dd, 1 H, $J_{1,2} \approx 2.3$ Hz, H-1), 3.50 (br, 1 H, cyclohexyl-CH), 3.40 (s, 3 H, OMe), 2.98 (dd, 1 H, $J_{4,5} \approx 8.5$ Hz, H-4), 2.57 (m, 1 H, cyclohexyl-CH), 2.00–0.80 (m, 21 H, cyclohexyl-CH_2, NH).; ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 154.6 (C=O), 138.0 (*i*-Ph), 128.2 (*m*-Ph), 127.7 (*o*-Ph), 127.6 (*p*-Ph), 107.1 (*C*H–CCl_3), 99.8 (CCl_3), 81.5 (C-5), 79.7 (C-6), 78.4 (C-1), 77.4 (C-2), 74.7 (C-3), 72.2 (*C*H_2–Ph), 58.1 (OMe), 55.8 (C-4), 54.8 (cyclohexyl-CH), 50.0, (cyclohexyl-CH), 34.3, 33.6, 33.5, 33.4, 26.1, 25.4, 25.1, 24.9, 24.8, 24.7 (cyclohexyl-CH_2); IR (Nujol): 1719 cm^{-1} (C=O), 3270, 3330 cm^{-1} (NH), 3444 cm^{-1} (OH); MS (70 eV): $m/z = 620$ [M]. Anal. Calcd for $C_{29}H_{41}Cl_3N_2O_6$ (620.0): C, 56.18; H, 6.67; N, 4.52. Found: C, 56.15; H, 6.69; N, 4.27.

D-*2*-O-*Benzyl*-*4*-*cyclohexylamino*-*4*-*deoxy*-*1*-O-*methyl*-*5,6*-O-*trichloroethylidene*-chiro-*inositol* (**12**).—A solution of **11** (290 mg, 0.46 mmol) was refluxed in 2% methanolic MeONa (10 mL). Gradually, the spot of **12** was detectable by TLC (R_f 0.48; 4:2:1 toluene–EtOAc–EtOH). After 16 h refluxing, the reaction was interrupted and the mixture was worked-up as described for **5**. Compound **12** (30 mg, 13%) and unreacted starting material **11** were isolated after column chromatographic separation. Yellowish syrup, $[\alpha]_D^{29}$ + 22.4° (*c* 0.9, $CHCl_3$); ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.39–7.26 (m, 5 H, Ph), 5.36 (s, 1 H, C*H*–CCl_3), 4.72 (s, 2 H, CH_2–Ph), 4.62 (dd, 1 H, $J_{1,6} \approx 3.8$ Hz, H-6), 4.52 (dd, 1 H, $J_{5,6} \approx 5.5$ Hz, H-5), 3.89 (dd, 1 H, $J_{1,2} \approx 2.8$ Hz, H-1), 3.71 (dd, 1 H, $J_{3,4} \approx 9.2$ Hz, H-3), 3.63 (dd, 1 H, $J_{2,3} \approx 8.2$ Hz, H-2), 3.48 (s, 3 H, OMe), 2.85 (m, 1 H, cyclohexyl-CH), 2.78 (dd, 1 H, $J_{4,5} \approx 8.1$ Hz, H-4), 2.26 (br, 2 H, NH, OH), 2.04–0.76 (m, 10 H, cyclohexyl-CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 138.1 (*i*-Ph), 128.5 (*m*-Ph), 127.8 (*p*-Ph), 127.7 (*o*-Ph), 106.4 (*C*H–CCl_3), 99.4 (CCl_3), 83.0 (C-5), 79.6 (C-2), 77.8 (C-6), 76.3 (C-1), 72.8 (*C*H_2–Ph), 70.0 (C-3), 59.6 (OMe), 57.9 (C-4), 54.1 (cyclohexyl-CH), 34.9, 33.4, 26.1, 25.1, 24.9 (cyclohexyl-CH_2). Anal. Calcd for $C_{22}H_{30}Cl_3NO_5$ (494.8): C, 53.40; H, 6.11; N, 2.83. Found: C, 53.36; H, 6.59; N, 2.87.

5. Supplementary material

Full crystallographic details (excluding structure factors) for the structures in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 167747 (**1**), CCDC 167748 (**3**) and CCDC 167749 (**10**) Copies of the data can be obtained, free of charge, on application to The Director, CCDC, 12 Union Road, Cambridge

CB2 1EZ, UK (Tel.: +44-1223-336408; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http.//www.ccdc.cam.ac.uk).

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References

1. Hager, Chr.; Miethchen, R.; Reinke, H. *Synthesis* **2000**, 226–232.
2. Posternak, T. *Les Cyclitols*; Hermann: Paris, 1962 Engl. Transl.: Holden-Day, San Francisco, 1965.
3. Hudlicky, T.; Cebulak, M. *Cyclitols and Their Derivatives. A Handbook of Physical, Spectral and Synthetic Data*; VCH Weinheim: New York, Cambridge, 1993.
4. Takahashi, Y.; Nakayama, H.; Katagiri, K.; Ichikawa, K.; Ito, N.; Takita, T.; Takeuchi, T.; Miyake, T. *Tetrahedron Lett*. **2001**, *42*, 1053–1056 and papers cited therein.
5. Billington, D. C. *Chem. Soc. Rev*. **1989**, *18*, 83–122.
6. Billington, D. C. *The Inositol Phosphates–Chemical Synthesis and Biological Significance*; VCH: Weinheim, 1993.
7. Chida, N.; Tobe, T.; Suwama, M.; Ohtsuka, M.; Ogawa, S. *J. Chem. Soc., Chem. Commun*. **1990**, 994–995.
8. Akiyama, T.; Nishimoto, H.; Kuwata, T.; Ozaki, S. *Bull. Chem. Soc. Jpn*. **1994**, *67*, 180–188.
9. Angyal, S. J.; Odier, L. *Carbohydr. Res*. **1980**, *80*, 203–206.
10. (a) IUPAC-IUB Communications on Biochemistry Nomenclature. *Biol. Chem*. **1968**, *243*, 5809–5819;;
(b) Angyal, S. J.; Anderson, L.; Cahn, R. S.; Dawson, R. M. C.; Hoffmann-Ostenhof, O.; Klyne, W.; Posternak, T. *Pure Appl. Chem*. **1974**, *37*, 285–297.
11. Miethchen, R.; Rentsch, D.; Frank, M. *J. Carbohydr. Chem*. **1996**, *15*, 15–31.
12. Frank, M.; Miethchen, R.; Reinke, H. *Eur. J. Org. Chem*. **1999**, 1259–1263.
13. Miethchen, R.; Sowa, Chr.; Michalik, M. unpublished results.
14. Angyal, S. J.; Irving, G. C.; Rutherford, D.; Tate, M. E. *J. Chem. Soc*. **1965**, 6662–6664.
15. Gero, S. D. *Tetrahedron Lett*. **1966**, *6*, 591–595.
16. Miethchen, R.; Rentsch, D. *Liebigs Ann. Chem*. **1994**, 1191–1197.
17. Zur, C.; Miller, A. O.; Miethchen, R. *J. Fluorine Chem*. **1998**, *90*, 67–76.
18. Vowinkel, E.; Gleichenhagen, P. *Tetrahedron Lett*. **1974**, 139–142.
19. Jacobsen, S.; Sløk, F. *Acta Chem. Scand*. **1993**, *47*, 1012–1018.
20. Angyal, S. J.; Odier, L. *Carbohydr. Res*. **1982**, *100*, 43–54.
21. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc*. **1975**, *97*, 1354–1358.