Competition between Non-Classical Single and Double Epimerizations in Cyclitol Chemistry[‡]

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In memory of Prof. Dr. Christian Pedersen[‡‡]

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Two competitive regio- and stereoselective epimerization reactions were investigated in four cyclitols characterized by four contiguous OH groups with a *cis-trans-trans* sequence and by varied substituents (OMe, OBz, F, H) adjacent to this tetrol unit. The starting materials were synthesized from L-quebrachitol (compounds **5**–**7**) and *myo*-inositol (compound **8**). Their acetalization with the chloral/DCC reagent system gave cyclic acetals with one epimerized chiral ring atom and also with two epimerized chiral centres. The single epimerization takes place exclusively at the middle C-atom of the *cis-trans* triol unit in the tetrol sequence (products **15**, **17**, **19**/**20** and **24**–**27**), whereas the double epimerization occurs at both of the "*centrally located*" C-atoms in the *cis-trans-trans* tetrol unit (products **16**, **18**, **21** and **28**). The product ratios of singly to doubly inverted compounds change as follows: the lower the electron-withdrawing effect of the substituents adjacent to the tetrol unit, the higher the percentage of the corresponding doubly inverted product. However, the singly inverted products remain the major products in all cases. X-ray analyses are given for the starting material 1-fluoro-2-*O*-(methyl)cyclohexane-2,3,4,5,6-pentol (**5**) and for the products 1-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-5-*O*-(methyl)cyclohexane-1,2,3,4,5-pentol (**17**), 3-*O*-acetyl-1-*O*-benzoyl-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-4,5-*O*-(2,2,2-trichloroethylidene)-*muco*-inositol (**22**) and 2,3-di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (**24**).

Introduction

The biological relevance of inositols has always drawn a lot of attention to this multifunctional family.[1−5] However, the separation of inositol derivatives from natural sources is limited to a few representatives and so various compounds of this type are produced by chemical methods[1,2,6,7] (for the nomenclature of inositols see ref.[8]). We focused our efforts on selective epimerizations of easily accessible cyclitol derivatives with a three-component procedure used very successfully in pyranoside chemistry (review[9]). This method is based on a non-classical acetalization reaction requiring a cyclic triol with contiguous hydroxy groups in a *cis-trans* sequence as substrate and chloral/DCC as reagents. When these components are heated in dichloromethane or 1,2-dichloroethane, the reaction proceeds with clean inversion of the configuration at the middle C-atom of the contiguous *cis-trans* triol unit.[9,10] First studies with selected cyclitols such as quinic acid and shikimic acid esters gave the same results in terms of regio- and stereoselectivity.[10−13]

A corresponding acetalization experiment with a cyclitol derivative containing four unprotected contiguous OH groups with a *cis-trans-trans* sequence gave a surprising result. L-1-*O*-Benzyl-2-*O*-methyl-*chiro*-inositol (**1**), chloral and DCC yielded cyclitol derivatives that were selectively epimerized either at one (compounds **2** and **3**) or at two (product **4**) stereogenic centres[10,11] (Scheme 1). The singly epimerized compounds **2** and **3** had been expected in accord with the reaction pathway described for acetalizations/epimerizations of cyclic *cis-trans* triols[9,10] (ref.[9] refers to the review article, which describes the unconventional epimerization reaction, including the mechanism, in very detailed fashion).

In the case of the D-*chiro*-inositol **4** it is noteworthy that the inversion of the configuration at two stereogenic ring

[‡] For part 18 see ref.[10]

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[‡‡] To honor an excellent Danish carbohydrate chemist and person of high integrity

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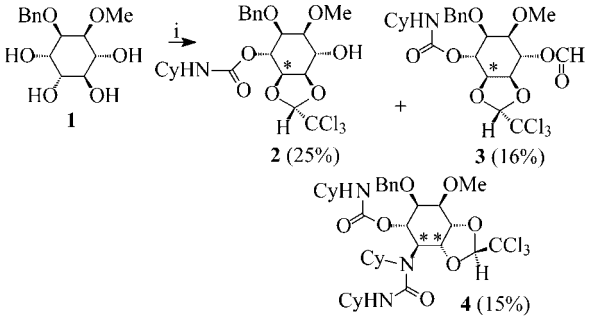
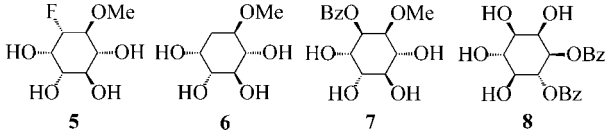


Scheme 1. Competing unconventional epimerizations first observed in the acetalization of L-1-*O*-benzyl-2-*O*-methyl-*chiro*-inositol (**1**);[10,11] i = chloral, DCC, CH_2Cl_2, reflux

atoms is accompanied by C−*N* bond formation, particularly as aminocyclitols are interesting species.[14]

In order to obtain preliminary information about the scope of the two competing epimerization reactions and to anticipate the synthetic potential of a novel double epimerization reaction, the substituent pattern of the starting material was varied as shown in Scheme 2. The starting materials **5**−**8** all contain the required four contiguous OH groups with *cis-trans-trans* sequence as well as varied substituents adjacent to the tetrol unit. The tetrols **5** and **6** in particular are highly comparable pairs of starting materials in terms of the similar steric neighbouring group effects of fluorine and hydrogen but significantly different in their electronic natures.

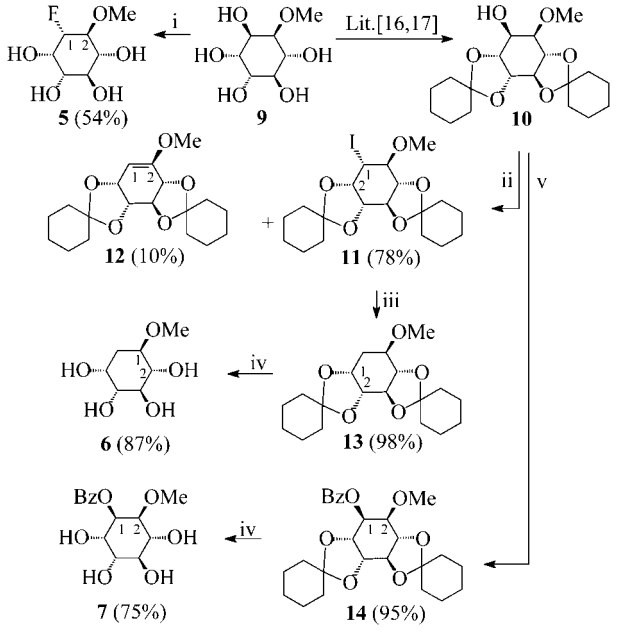


Scheme 2. Selected starting materials for comparative studies of single and double epimerization of cyclic *cis-trans-trans* tetrols

Results and Discussion

Synthesis of the Starting Materials

Kozikowski et al.[15] described in 1989 the fluorination of L-quebrachitol with *N*,*N*-diethylaminosulfur trifluoride (DAST) in the absence of solvent. The crude product from the reaction was subsequently treated with boron tribromide to obtain a stereochemically uniform product by methyl ether cleavage. We similarly fluorinated L-quebrachitol (**9**) with DAST in a one-pot procedure, although in a dichloromethane suspension. The product isolated after this procedure was exclusively the (1*S*,2*S*,3*R*,4*S*,5*S*,6*S*)-1-fluoro-2-*O*-(methyl)cyclohexane-2,3,4,5,6-pentol (**5**; Scheme 3, Figure 1).



Scheme 3. Synthesis of the 1-fluoroinositol **5** and the methylene derivative **6**; i = DAST, CH_2Cl_2, −30 °C to room temp.; ii = I_2, Ph_3P, imidazole, toluene, reflux; iii = Bu_3SnH, AIBN, toluene; iv = 80% TFA; v = BzCl, pyridine, CH_2Cl_2, room temp.

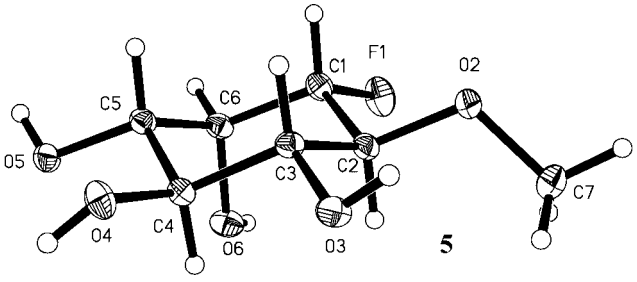


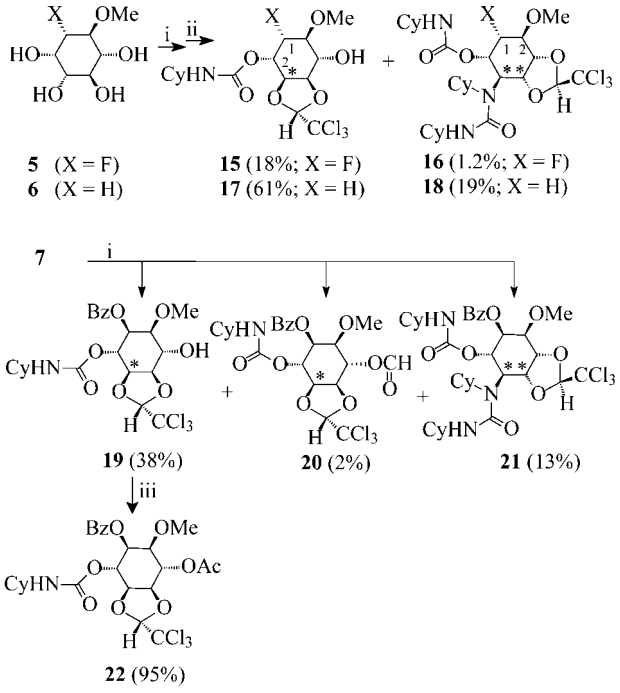
Figure 1. X-ray analysis of (1*S*,2*S*,3*R*,4*S*,5*S*,6*S*)-1-fluoro-2-methoxy-3,4,5,6-tetrahydroxycyclohexane (**5**)

The cyclitols **6** and **7** were similarly synthesized from L-quebrachitol (**9**) via the common key intermediate 3,4:5,6-di-*O*-cyclohexylidene-2-*O*-methyl-(−)-*chiro*-inositol (**10**).[16,17] Substitution of its free OH group by iodine or benzoylation resulted in the compounds **11** and **14**, respectively (Scheme 3). The iodination procedure was carried out analogously to that reported in ref.[18] Subsequently, the cyclohexylidene groups of **11** and **14** were cleaved by treatment with 80% aqueous trifluoroacetic acid (TFA; Scheme 3).

Methylidene derivative **6** (see also ref.[19]) was synthesized from 2,3:4,5-di-*O*-cyclohexylidene-1-iodo-6-*O*-(methyl)-cyclohexane-2,3,4,5,6-pentol (**11**) in two steps. Firstly, 1,2:3,4-di-*O*-cyclohexylidene-5-*O*-(methyl)cyclohexane-1,2,3,4,5-pentol (**13**) was generated by reductive deiodination of **11** with tributylstannane/AIBN, followed by deketalization with aqueous TFA (Scheme 3).

Epimerization of the Cyclitols

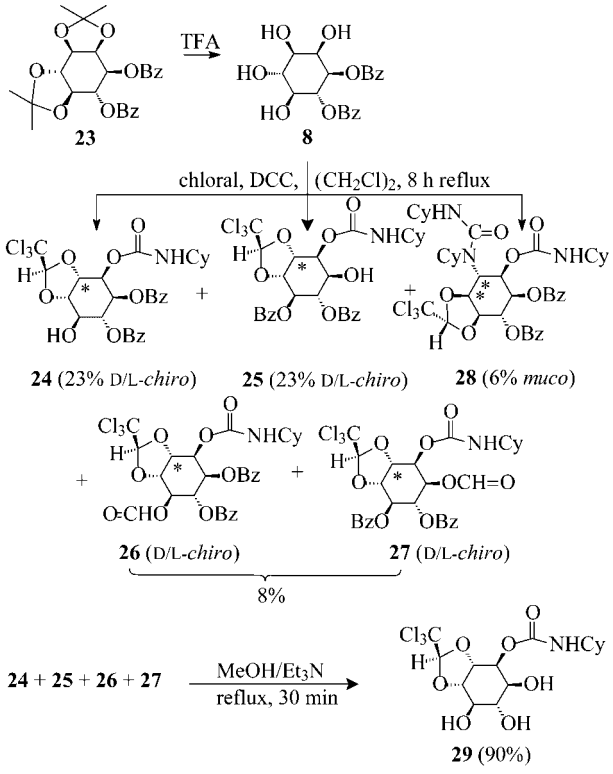
When the tetrols **5** and **6** were heated at reflux with chloral/DCC in dichloromethane for 8 h and the crude products subsequently treated with boiling methanolic triethylamine, the product pairs **15** (18%)/**16** (1.2%), and **17** (61%)/**18** (19%) were obtained (Scheme 4). The small amounts of formylated by-products result from a haloform cleavage of chloral stimulated by DCC.[9] They can be deformylated to give the corresponding major products **15** and **17**, respectively, by treatment with methanolic triethylamine.



Scheme 4. Unconventional epimerization of the cyclitols **5**, **6** and **7**; i = chloral, DCC, CH_2Cl_2, reflux; ii = MeOH, Et_3N, reflux; iii = acetic acid anhydride, pyridine, room temp.

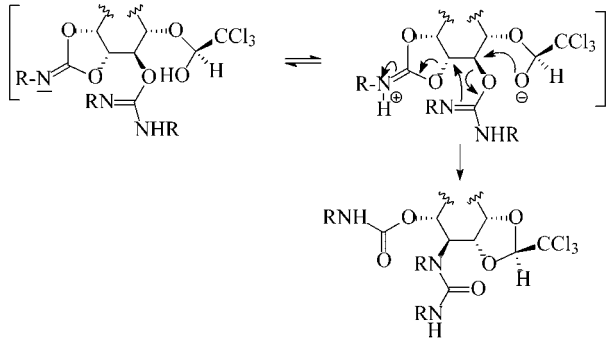
In the case of 1-*O*-benzoyl-2-*O*-methyl-(−)-*chiro*-inositol (**7**; Scheme 4) and 3,4-di-*O*-benzoyl-*myo*-inositol (**8**; Scheme 5), the triethylamine procedure was not used, because in this case the deformylation was accompanied by debenzoylation. The product mixture formed from compound **7** thus contained the singly inverted major product **19** (38%), its formyl derivative **20** (2%) and the doubly inverted compound **21** (13%) with a (+)-*chiro*-configuration (Scheme 4).

Starting material **8** (prepared from **23**[20]) surprisingly gave five products after treatment with chloral/DCC; four are singly inverted derivatives with *chiro* configurations (**24**−**27**) and the fifth is the doubly inverted derivative **28** with *muco* configuration (Scheme 5). The range of products is the result of a benzoyl group migration. Heating of the product mixture **24**−**27** at reflux with methanolic triethylamine solution allowed simultaneous complete deformylation and debenzoylation of the compounds, so that the *chiro* derivative **29** was obtained exclusively (Scheme 5).



Scheme 5. Synthesis and epimerization of dibenzoyl-*myo*-inositol (**8**)

The formation of the cyclitol derivatives **15**, **17**, **19**, **20** and **24**−**27** is consistent with the well investigated single epimerizations of cyclic *cis*-*trans*-triols (pyranosides) in carbohydrate chemistry.[9,10] Here, the middle chiral carbon atom of an original *cis*-*trans*-triol unit is selectively inverted (Schemes 4 and 5). In contrast, the doubly inverted products **16**, **18**, **21** and **28** are the results of a tandem mechanism outlined in Scheme 6 (see also Vowinkel and Gleichenhagen's isourea experiments[21]).



Scheme 6. Tandem mechanism of the double inversion proposed in ref.[10]

An useful side feature of the novel double epimerization reaction is a novel route to aminoinositol derivatives. The ratio of single inversion products to the doubly inverted products indicates that electron-withdrawing groups sup-

press the tandem course with two inversions. In other words, the lower the electron-withdrawing effect of the substituents adjacent to the tetrol unit, the higher is the percentage of the corresponding doubly inverted product (Table 2).

Methods for stepwise deprotection of chloral/DCC epimerization products are already described in various examples in carbohydrate chemistry[9] and for the inositol derivatives **2** and **4** in ref..[10] At present, we are investigating one-pot procedures for complete deprotection of the epimerization products. The results will be reported in a separate paper.

Structural Analysis of the Epimerization Products

The structures of the new products are supported by their NMR spectroscopic data and by X-ray analyses. Thus, a crystal of starting material **5** was investigated by X-ray diffraction. The compound adopts a $^1C_4$ chair conformation with an equatorial arrangement of the methoxy group at C-atom 2 (Figure 1). The length of the carbon−fluorine bond is 140.88 pm.

Moreover, 1-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-5-*O*-(methyl)cyclohexane-1,2,3,4,5-pentol (**17**) crystallized from methanol to give monoclinic crystals, which were also analysed by X-ray diffraction (Figure 2). Furthermore, the structures of *muco* derivative **22** and *chiro* product **24** could be confirmed in the same way (Figure 3 and 4). In the case of **24**, suitable crystals were only obtained by crystallization from 2-propanol, this solvent being incorporated into the crystal lattice.

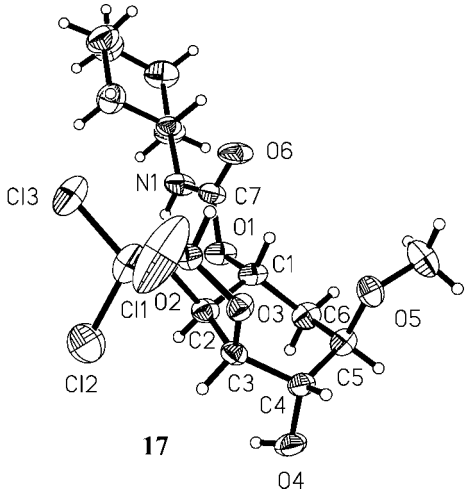


Figure 2. X-ray analysis of (1*R*,2*R*,3*R*,4*S*,5*R*)-1-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-5-*O*-(methyl)cyclohexane-1,2,3,4,5-pentol (**17**)

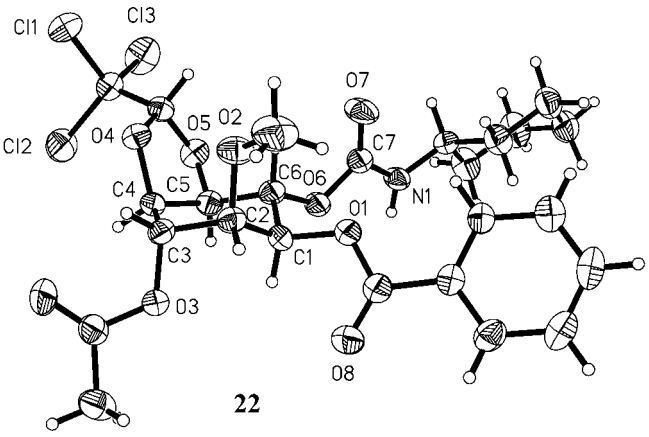


Figure 3. X-ray analysis of 3-*O*-acetyl-1-*O*-benzoyl-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-4,5-*O*-(2,2,2-trichloroethylidene)-*muco*-inositol (**22**)

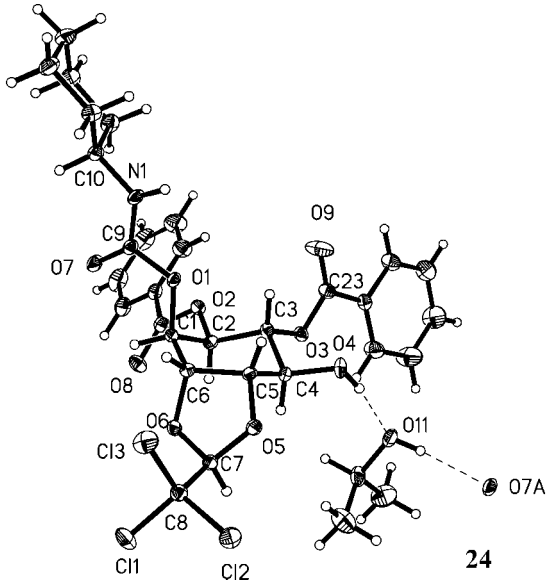


Figure 4. X-ray analysis of 2,3-di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (**24**) crystallized with a 2-propanol molecule

The assignment of signals in the ^1H and ^{13}C NMR spectra was performed by recording of DEPT and two-dimensional $^1H,^1H$ and $^{13}C,^1H$ correlation spectra (comparative ^{13}C NMR spectroscopic data see ref.[22]). Key signals attributable with confidence to a definite position were found out from typical correlations (e.g., coupling of a ring proton with fluorine, correlation of a ring proton over three bonds to the proton signal of OMe, correlation of a ring proton to the carbonyl function of a benzoyl group, or to the *C*ONH function of a carbamoyl group). On this basis the assignment of signals for the other ring atoms became possible. The atomic configurations of adjacent ring protons were assigned with the assistance of the Karplus relationship.[23] All spectra of the epimerized compounds show the characteristic signals of a carbamoyl group and of a trichloroethylidene group.

The latter is characterized by the singlet of the acetal proton (δ ≈ 5.38−5.94) and by the C signals of the acetal moiety (δ_{CCl3} ≈ 98.5−101.7 ppm; δ_{CH} ≈ 106.0−108.7 ppm). For the doubly inverted compounds **16**, **18**, **21** and **28**, the signal for the *N*-substituted ring C-atom is shifted to significantly higher field than the other ring-C-atom signals.

The puckering parameters[24] for the six-membered rings of **5**, **17**, **22** and **24** are listed in Table 1. CCDC-222987 and -222989 to -222991 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

Table 1. Puckering parameters of the compounds **5**, **17**, **22** and **24**

Compound	**5**	**17**	**22**	**24**
Puckering Amplitude (Q)/Å	0.626(1)	0.520(8)	0.555(4)	0.556(2)
Θ /°	3.9(1)	158.1(9)	153.7(4)	21.6(2)
φ /°	193.3(14)	119(2)	177.1(10)	107.6(7)

Table 2. Yield ratio of singly to doubly epimerized products with dependence on the starting material

Starting material	**1**	**6**	**7**	**5**
Molar ratio of the mono-to-the-double inverted products	2.7	3.1	9.0	15.0

Conclusions

(1) Cyclitols containing four contiguous hydroxy groups with a *cis*/*trans*/*trans* sequence can be effectively epimerized by an unconventional acetalization procedure with chloral/DCC but without the need for protecting group chemistry. One obtains two defined key products: a singly epimerized cyclitol acetal and an aminocyclitol derivative with two epimerized stereogenic ring C-atoms.

(2) The results of the three-component reactions reported in this paper allow the conclusion that electron-withdrawing moieties adjacent to the *cis*/*trans*/*trans* tetrol unit suppress the less favoured double epimerization reaction. This effect is reflected in comparisons of the molar ratios of singly inverted to doubly inverted products (Table 2).

(3) The results are not only of outstanding interest in terms of the substances isolated, but also for the assumed tandem mechanism.

Experimental Section

General Remarks: Melting points were obtained with a Leitz polarizing microscope (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90). ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker AC 250 (250.13 and 62.9 MHz, respectively), ARX 300 (300.13 and 75.5 MHz, respectively), and AVANCE 500 (500.13 and 125.8 MHz, respectively) spectrometers. Calibration of spectra was carried out with the aid of the solvent peaks ($CDCl_3$: ^{1}H: δ = 7.25 ppm, ^{13}C: δ = 77.0 ppm. CD_3OD: ^{1}H: δ = 3.30 ppm, ^{13}C: δ = 49.0 ppm; $(CD_3)_2CO$: ^{1}H: δ = 2.04 ppm, ^{13}C: δ = 29.8 ppm). ^{19}F NMR spectra were recorded at 235.2 MHz (AC 250 spectrometer, δ^{19}F values referenced to $CFCl_3$). Optical rotations were measured with a Polar Lμ P instrument (IBZ Meßtechnik). Infrared spectra were recorded with a Protegé Nicolet 460 IR spectrometer (Nujol). Column chromatography: E. Merck Silica Gel 60 (40−63 μ m); thin-layer chromatography (TLC): E. Merck Silica Gel 60 F_{254} foils.

For the X-ray structure determination of **17** and **22**, a Bruker P4 four-circle diffractometer with Mo-*Kα* radiation (λ = 0.71073 Å) and a graphite monochromator was used. The results for **5** were obtained on a SMART Apex with CCDC area detector and Mo-*Kα* radiation, while compound **24** was investigated both with a Bruker P4 and with a STOE IPDS, also with Mo-*Kα* radiation. The structures were solved by direct methods (Bruker SHELXTL, 1990, Bruker Analytical X-ray Inst. Inc. for **5**, **22**, **24**, SHELXS-86[25] for **17**). The refinement was carried out in all cases by the full-matrix, least-squares method of Bruker SHELXTL, Vers.5.10, Copyright 1997, Bruker Analytical X-ray Systems. All non-hydrogen atoms were refined anisotropically. For compound **5** the hydrogens of the OH groups were found from the difference map and refined while allowing the groups to rotate about the C−O bond. For compound **24** the hydrogen of the OH group of the solvent molecule could be found in the difference map. The refinement was carried out as above. All other hydrogens were placed in theoretical positions and refined by use of the riding model.

(1*S*,2*S*,3*R*,4*S*,5*S*,6*S*)-1-Fluoro-2-*O*-(methyl)cyclohexane-2,3,4,5,6-pentol (5): A suspension of L-quebrachitol (**9**, 2.5 g, 12.87 mmol) in dry CH_2Cl_2 (25 mL) was cooled to −30 °C with stirring under an argon atmosphere. Subsequently, DAST (5 mL, 38.15 mmol) was added in portions, and stirring was continued for 4 h at room temp. (TLC monitoring). After renewed cooling of the mixture to −30 °C, methanol (10−15 mL) was carefully added dropwise, and the dark solution was heated with charcoal. After filtration through kieselgur (diatomit, purchased from Riedel-de Haën) and washing of the filter cake with methanol, the combined organic phases were concentrated under reduced pressure and the residue was purified by column chromatography (**5**: R_f = 0.41; $CHCl_3$/MeOH, 4:1 v/v). Colourless crystals of **5** (1.36 g, 54%) were isolated, m.p. 176−177 °C (methanol). $[\alpha]_D^{24}$ = −1.5 (*c* = 1.10, MeOH). ^{1}H NMR (250 MHz, CD_3OD, D_2O): δ = 4.47 (ddd, $^2J_{F,1}$ = 47.8, $^3J_{1,2}$ = 9.7, $^3J_{1,6}$ = 2.9 Hz, 1 H, H-1), 4.21 (m, $^3J_{F,6}$ = 9.0, $^3J_{5,6}$ = 2.7 Hz, 1 H, H-6), 3.62−3.54 (m, $^3J_{4,5}$ = 9.9 Hz, 2 H, H-4, H-2), 3.58 (s, 3 H, OCH_3), 3.44 (ddd, $^3J_{5,6}$ = 2.7, $^4J_{F,5}$ = 1.4 Hz, 1 H, H-5), 3.29 (m, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.5 Hz, 1 H, H-3) ppm. ^{13}C{^{1}H} NMR (62.9 MHz, CD_3OD, D_2O): δ = 93.3 (d, $^1J_{C,F}$ = 182.1 Hz, C-1), 82.1 (d, $^2J_{C,F}$ = 17.6 Hz, C-2), 73.9 (d, $^3J_{C,F}$ = 13.4 Hz, C-3), 73.4 (d, $^4J_{C,F}$ = 16.9 Hz, C-4), 71.5 (d, $^2J_{C,F}$ = 11.0 Hz, C-6), 71.1 (d, $^3J_{C,F}$ = 1.9 Hz, C-5), 60.9 (s, OCH_3) ppm. ^{19}F{^{1}H} NMR (235 MHz, CD_3OD, D_2O): δ = −196.9 (s) ppm. X-ray structure see Figure 1. $C_8H_{16}FO_5$ (196.18): calcd. C 42.86, H 6.68; found C 42.61, H 6.73.

(1*R*,2*R*,3*S*,4*R*,5*R*)-1-*O*-(Methyl)cyclohexane-1,2,3,4,5-pentol (6)

(1*R*,2*S*,3*S*,4*R*,5*S*,6*S*)-2,3:4,5-Di-*O*-cyclohexylidene-1-iodo-6-*O*-(methyl)cyclohexane-2,3,4,5,6-pentol (11) and (3*S*,4*R*,5*R*,6*R*)-3,4:5,6-di-*O*-cyclohexylidene-2-*O*-(methyl)cyclohex-1-en-2,3,4,5,6-

pentol (12): Iodine (9.1 g, 35.8 mmol), triphenylphosphane (10 g, 38.1 mmol) and imidazole (4.0 g, 58.7 mmol) were added (under argon) to a solution of L-3,4:5,6-di-*O*-cyclohexylidene-2-*O*-methyl-*chiro*-inositol[16,17] (7.28 g, 20.6 mmol) in dry toluene (400 mL). After it had been heated at reflux for 3 h, the mixture was cooled down. The excess of iodine was reduced by treatment with aq. $NaHCO_3$ solution and aq. $Na_2S_2O_3$ solution. The organic phase was then separated, and the aqueous phase was washed with toluene. Finally, the combined organic phases were washed with saturated NaCl solution, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was column chromatographically purified [eluent gradient: 1 L of heptane → heptane/EtOAc, 20:1 v/v (2 L)]. The major product (**11**, 7.45 g, 78%, (R_f = 0.62, toluene/EtOAc, 8:1 v/v) and the by-product (**12**, 695 mg, 10%, R_f = 0.44 toluene/EtOAc, 8:1 v/v) were isolated. **11:** M.p. 125−126 °C. $[\alpha]_D^{23}$ = +36.6 (c = 1.17, $CHCl_3$). **12:** M.p. 152−153 °C. $[\alpha]_D^{23}$ = −25.25 (c = 1.19, $CHCl_3$).

Compound 11: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.31 ("t", 1 H, H-2), 4.19 (dd, $^3J_{2,3}$ = 5.0, $^3J_{3,4}$ = 9.0 Hz, 1 H, H-3), 3.97 (dd, $^3J_{1,2}$ = 4.8, $^3J_{1,6}$ = 9.0 Hz, 1 H, H-1), 3.76 (dd, $^3J_{4,5}$ = 10.1 Hz, 1 H, H-4), 3.72 ("t", $^3J_{5,6}$ = 9.2 Hz, 1 H, H-6), 3.60 (s, 3 H, OCH_3), 3.20 (dd, 1 H, H-5), 1.78−1.30 (m, 20 H, cyclohexylidene CH_2) ppm. $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ = 112.4, 110.1 (2 C, cyclohexylidene C_q), 82.9 (C-6), 78.9 (C-4), 78.1 (C-5), 77.6 (C-2), 75.3 (C-3), 59.3 (OCH_3), 25.3 (C-1), 38.0, 36.4, 36.3, 34.9, 24.9 (2 ×), 23.9, 23.7, 23.6 (2 ×) (10 C, cyclohexylidene CH_2) ppm. $C_{19}H_{29}IO_5$ (464.34): calcd. C 49.15, H 6.30; found C 49.33, H 6.35.

Compound 12: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.88 (ddd, $^3J_{5,6}$ = 7.0, $^3J_{1,6}$ = 3.5, J = 1.0 Hz, 1 H, H-6), 4.63 (dd, $^4J_{1,3}$ = 2.0 Hz, 1 H, H-1), 4.32 (dd, $^3J_{4,5}$ = 9.8 Hz, 1 H, H-5), 4.09 (ddd, $^3J_{3,4}$ = 9.0, J = 1.0 Hz, 1 H, H-3), 3.62 ("t", 1 H, H-4), 3.65 (s, 3 H, OCH_3), 1.75−1.28 (m, 20 H, cyclohexylidene CH_2) ppm. $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ = 156.2 (C-2), 114.2, 111.0 (2 C, cyclohexylidene C_q), 90.4 (C-1), 80.6 (C-4), 74.6 (C-5), 74.4 (C-6), 72.9 (C-3), 55.4 (OCH_3) 37.5, 36.4, 35.9, 34.5, 25.1, 24.9, 23.9, 23.6, 23.5, 23.4 (10 C, cyclohexylidene CH_2) ppm. $C_{19}H_{28}O_5$ (336.42): calcd. C 67.83, H 8.39; found C 67.77, H 8.61.

(1*R*,2*R*,3*R*,4*S*,5*R*)-1,2:3,4-Di-*O*-cyclohexylidene-5-*O*-(methyl)cyclohexane-1,2,3,4,5-pentol (13): A solution of **11** (3.69 g, 10.94 mmol), Bu_3SnH (3.5 mL, 13.12 mmol) and AIBN (179.6 mg, 1.094 mmol) in dry toluene (70 mL) was heated at reflux for about 3 h under argon. After completion of the reaction (TLC monitoring, toluene/EtOAc, 8:1 v/v), the mixture was cooled down, satd. aq. KF solution was added, and the mixture was vigorously stirred for 30 min. The precipitate (Bu_3SnF) was removed by filtration and washed with toluene. The organic phase was separated, and washed with water (twice, 10 mL) and satd. aq. NaCl solution (10 mL). After concentration of the dried (Na_2SO_4) solution under reduced pressure and flash chromatographic purification (R_f = 0.36 (toluene/EtOAc, 8:1 v/v), compound **13** (3.63 g, 98%) was isolated as a colourless syrup; $[\alpha]_D^{23}$ = −45.2 (c = 0.92, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.38 (ddd, 1 H, H-1), 4.18 (dd, $^3J_{1,2}$ = 5.8, $^3J_{2,3}$ = 8.5 Hz, 1 H, H-2), 3.64 (ddd, 1 H, H-5), 3.54 (dd, $^3J_{2,3}$ = 8.5 Hz, 1 H, H-3), 3.45 (s, 3 H, OCH_3), 3.33 (dd, $^3J_{3,4}$ = 10.1, $^3J_{4,5}$ = 8.8 Hz, 1 H, H-4), 2.40 (ddd, $^2J_{6eq,6ax}$ = 15.2, $^3J_{5,6eq}$ = 6.0, $^3J_{1,6eq}$ = 4.0 Hz, 1 H, H-6eq), 1.68 (ddd, $^3J_{5,6ax}$ = 7.8, $^3J_{1,6ax}$ = 5.2 Hz, 1 H, H-6ax) 1.65−1.30 (m, 20 H, cyclohexylidene CH_2) ppm. $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ = 112.0, 110.0 (2 C, cyclohexylidene C_q), 79.4 (C-3), 79.4 (C-4), 76.9 (C-2), 76.6 (C-5), 73.6 (C-1), 57.3 (OCH_3), 32.2 (C-6) 38.0, 36.5, 36.4, 34.8, 25.0 (2 ×), 23.9, 23.7, 23.6, 23.5 (10 C, cyclohexylidene CH_2) ppm. $C_{19}H_{30}O_5$ (338.44): calcd. C 67.43, H 8.93; found C 66.92, H 8.63.

(1*R*,2*R*,3*S*,4*R*,5*R*)-1-*O*-(Methyl)cyclohexane-1,2,3,4,5-pentol (6): A solution of cyclitol **13** (3.6 g, 10.64 mmol) in 80% aq. TFA (35 mL) was stirred overnight at room temp. The workup procedure was analogous to that used for **5**. After column chromatographic separation ($CHCl_3$/MeOH, 10:1 v/v), the colourless crystalline product **6** (1.65 g, 87%) was isolated, m.p. 145−146 °C (MeOH). $[\alpha]_D^{22}$ = −67.2 (c = 0.46, MeOH), R_f = 0.31 ($CHCl_3$/MeOH, 5:1 v/v). ^{1}H NMR (250 MHz, CD_3OD, D_2O): δ = 4.01 (ddd, $^3J_{5,6eq}$ = 5.0 Hz,$^3J_{4,5}$ = 3.0, $^3J_{5,6eq}$ = 2.5 Hz, 1 H, H-5), 3.59 ("t", $^3J_{2,3}$ = $^3J_{3,4}$ = 9.3 Hz, 1 H, H-3), 3.44 (ddd, $^3J_{1,2}$ = 9.3, $^3J_{1,6eq}$ = 4.4 Hz, 1 H, H-1), 3.42 (s, 3 H, OCH_3), 3.38 (dd, $^3J_{3,4}$ = 9.3 Hz, 1 H, H-4), 3.27 ("t", 1 H, H-2), 2.24 (m, $^2J_{6ax,6eq}$ = 13.8 Hz, 1 H, H-6eq), 1.32 (m, $^3J_{1,6ax}$ = 11.5, $^3J_{5,6ax}$ = 2.5 Hz, 1 H, H-6ax) ppm. $^{13}C\{^1H\}$ NMR (62.9 MHz, CD_3OD, D_2O): δ = 79.5 (C-1), 77.8 (C-2), 75.3 (C-4), 74.3 (C-3), 69.5 (C-5), 57.8 (OCH_3), 33.2 (C-6) ppm. $C_7H_{14}O_5$ (178.18): calcd. C 47.19, H 7.92; found C 47.49, H 8.29.

1-*O*-Benzoyl-2-*O*-methyl-(−)-*chiro*-inositol (7)

1-*O*-Benzoyl-3,4:5,6-di-*O*-cyclohexylidene-2-*O*-methyl-(−)-*chiro*-inositol (14): Benzoyl chloride (4.17 mL, 36.0 mmol) was added dropwise at 0 °C over 15 min to a stirred solution of 3,4:5,6-di-*O*-cyclohexylidene-2-*O*-methyl-(−)-*chiro*-inositol (**10**,[16,17] 8.50 g, 24.0 mmol) in pyridine (15 mL) and CH_2Cl_2 (15 mL). Stirring was continued at room temp. for 2 h (TLC monitoring). After filtration and washing of the precipitate with CH_2Cl_2, the combined filtrates were subsequently washed with water (60 mL), diluted aq. sulfuric acid (20 mL), satd. aq. $NaHCO_3$ solution (50 mL) and 5% aq. $NaHSO_4$ solution (40 mL). The solution was then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography (R_f = 0.44, toluene/EtOAc, 20:1 v/v) and the colourless syrup of **14** (10.48 g, 95%) was deketalized without further purification.

1-*O*-Benzoyl-2-*O*-methyl-(−)-*chiro*-inositol (7): A solution of compound **14** (13.6 g, 29.7 mmol) in 80% aq. TFA (90 mL) was stirred overnight at room temp. The workup procedure was analogous to that used for **5**. After column chromatographic separation of **7** (R_f = 0.28, $CHCl_3$/MeOH, 6:1 v/v), the crystalline product **7** (6.66 g, 75%) was isolated, m.p. 143−144 °C (EtOAc), R_f = 0.31, $CHCl_3$/MeOH, 5:1 v/v, $[\alpha]_D^{24}$ = +50.1 (c = 1.01, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.99 (m, 2 H, *o*-Ph), 7.61 (m, 1 H, *p*-Ph), 7.48 (m, 2 H, *m*-Ph), 5.64 (dd, $^3J_{1,2}$ = 3.1, $^3J_{1,6}$ = 4.1 Hz, 1 H, H-1), 4.01 (dd, $^3J_{1,6}$ = 4.1, $^3J_{5,6}$ = 2.4 Hz, 1 H, H-6), 3.75−3.63 (m, 3 H, H-3, H-4, H-5), 3.56 (dd, $^3J_{1,2}$ = 3.1, $^3J_{2,3}$ = 10.0 Hz, 1 H, H-2), 3.43 (s, 3 H, OMe) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, CD_3OD): δ = 166.7 (COC_6H_5), 134.5 (*p*-Ph), 131.1 (*i*-Ph), 130.6 (*o*-Ph), 129.7 (*m*-Ph), 80.9 (C-2), 74.5, 74.3, 72.8 (C-3, C-4, C-5), 71.0 (C-1), 70.9 (C-6), 58.3 (OCH_3) ppm. $C_{14}H_{18}O_7$ (298.28): calcd. C 56.37, H 6.08; found C 56.23, H 6.10.

3,4-Di-*O*-benzoyl-*myo*-inositol (8): A solution of 3,4-di-*O*-benzoyl-1,2:5,6-di-*O*-isopropylidene-*myo*-inositol (**23**,[20] 1.0 g, 2.1 mmol) in 80% aq. TFA (20 mL) was stirred at room temp. overnight. The workup procedure was analogous to that used for **5**. After column chromatographic separation (toluene/EtOAc/EtOH, 5:2:1 v/v/v) the colourless crystalline product **8** (0.60 g, 72%) was isolated, m.p. 101−103 °C (*i*PrOH), R_f = 0.33 (toluene/EtOAc/EtOH, 4:2:1 v/v/v); for the ^{1}H NMR spectroscopic data see also ref..[26] The crystals of inositol **8** obtained by crystallization from *i*PrOH contain one equivalent of the solvent. ^{1}H NMR (300 MHz, CD_3OD): δ = 7.96−7.91 (m, 4 H, *o*-Ph), 7.53−7.46 (m, 2 H, *p*-Ph), 7.39−7.32 (m, 4 H, *m*-Ph), 5.82 (dd, $^3J_{4,5}$ = 9.5 Hz, 1 H, H-4), 5.19 (dd, $^3J_{3,4}$ = 10.4, $^3J_{2,3}$ = 2.4 Hz, 1 H, H-3), 4.29 (dd, $^3J_{1,2}$ = 2.8, $^3J_{2,3}$ = 2.4 Hz, 1 H, H-2), 3.92 (sept, 1 H, CH-*i*PrOH), 3.85 (dd, $^3J_{1,6}$ =

9.8, $^3J_{5,6}$ = 9.5 Hz, 1 H, H-6), 3.67 (d, ^3J = 9.5 Hz, 1 H, H-5), 3.61 (dd, $^3J_{1,2}$ = 2.8, $^3J_{1,6}$ = 9.8 Hz, 1 H, H-1), 1.15 (d, J = 6.1 Hz, 6 H, CH_3-*i*PrOH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, CD_3OD): δ = 167.8 (COC_6H_5), 167.4 (COC_6H_5), 134.4 (*p*-Ph), 134.2 (*p*-Ph), 131.4 (*i*-Ph), 130.9 (*i*-Ph), 130.8 (*o*-Ph), 130.6 (*o*-Ph), 129.4 (2 ×) (2C, *m*-Ph), 74.7 (C-3), 74.5 (C-4), 74.4 (C-6), 74.3 (C-1), 73.0 (C-5), 71.7 (C-2), 64.8 (CH-*i*PrOH), 25.3 (CH_3-*i*PrOH) ppm. $C_{23}H_{28}O_9$ (448.46): calcd. C 61.60, H 6.29; found C 61.44, H 6.30.

(1*R*,2*S*,3*R*,4*R*,5*S*,6*S*)-2-*O*-Cyclohexylcarbamoyl-1-fluoro-6-*O*-methyl-3,4-*O*-(2,2,2-trichloroethylidene)cyclohexane-2,3,4,5,6-pentol (15) and (1*R*,2*S*,3*R*,4*R*,5*S*,6*S*)-2-*O*-Cyclohexylcarbamoyl-3-(*N*,*N*′-dicyclohexylureido)-1-fluoro-6-*O*-methyl-4,5-*O*-(2,2,2-trichlorethylidene)cyclohexane-2,4,5,6-tetrol (16): A suspension of the fluorocyclitol **5** (2.0 g, 10.20 mmol) and chloral (3.46 mL, 35.68 mmol) in CH_2Cl_2 (80 mL) was stirred for 1−2 h at room temp. A solution of DCC (6.31 g, 30.58 mmol) in CH_2Cl_2 (10 mL) was then added and the mixture was heated at reflux for 8 h (under argon). After the reaction mixture had been cooled to room temp. and subsequent addition of CH_2Cl_2 (100 mL) and 10% aqueous AcOH (150 mL), it was shaken for about 30 min to destroy excess DCC. The precipitated *N*,*N*′-dicyclohexylurea was removed by filtration, the organic phase was separated, and the aqueous phase was washed with $CHCl_3$ (3 × 50 mL). The combined extracts were washed with satd. aq. $NaHCO_3$ solution (50 mL) and water (2 × 40 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was treated with cold acetone (50 mL) to dissolve the cyclitol products; further crystalline *N*,*N*′-dicyclohexylurea remains undissolved. The filtrate was concentrated and the residue was dissolved in dry MeOH (15 mL) and triethylamine (1 mL). The formylated by-products were selectively deformylated by heating of this solution at reflux for 15 min. After concentration of the methanolic solution under reduced pressure and a second treatment of the residue with cold acetone, a solution of the crude product almost free of *N*,*N*′-dicyclohexylurea was obtained. Finally, the products **15** and **16** were separated by column chromatography (heptane/EtOAc, 3:1 v/v).

Compound 15: Yield (826 mg, 18%), colourless needles m.p. 145−146 °C (cyclohexane), R_f = 0.11 (heptane/EtOAc, 2:1 v/v). $[\alpha]_D^{22}$ = +7.1 (c = 0.53, $CHCl_3$).

Compound 16: Yield (80 mg (1.2%), foam-like solidified substance; m.p. 236 °C, R_f = 0.21 (heptane/EtOAc, 2:1 v/v), $[\alpha]_D^{23}$ = +1.9 (c = 0.93, $CHCl_3$).

Compound 15: ^1H NMR (500 MHz, $CDCl_3$): δ = 5.39 (s, 1 H, $CHCCl_3$), 5.17 (ddd, $^3J_{F,2}$ = 21.8, $^3J_{2,3}$ = 6.0, $^3J_{1,2}$ = 2.8 Hz, 1 H, H-2), 4.76 (ddd, $^2J_{F,1}$ = 48.2, $^3J_{1,6}$ = 5.0, $^3J_{1,2}$ = 2.8 Hz, 1 H, H-1), 4.68 (m, 2 H, H-3, NH), 4.56 (ddd, $^3J_{4,5}$ = 8.5, $^3J_{3,4}$ = 6.6, $^5J_{F,4}$ = 1.3 Hz, 1 H, H-4), 3.67 ("t", $^3J_{5,6}$ = 8.5 Hz, 1 H, H-5), 3.48 (s, 3 H, OCH_3), 3.40 (ddd, $^2J_{F,6}$ = 15.7, $^3J_{5,6}$ = 8.5, $^3J_{1,6}$ = 5.0 Hz, 1 H, H-6) 3.40 (m, 1 H, cyclohexyl CH), 2.78 (br., 1 H, OH), 1.88 (m, 2 H, cyclohexyl CH_2), 1.64 (m, 2 H, cyclohexyl CH_2), 1.53 (m, 1 H, cyclohexyl CH_2), 1.27 (m, 2 H, cyclohexyl CH_2), 1.09 (m, 3 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ = 153.8 (NHCOO), 107.3 (*C*HCCl$_3$), 99.3 (CCl_3), 90.6 (d, $^1J_{C,F}$ = 199.0 Hz, C-1), 81.0 (d, $^2J_{C,F}$ = 23.0 Hz, C-6), 80.5 (C-4), 76.7 (d, $^3J_{C,F}$ = 7.0 Hz, C-3), 72.0 (d, $^3J_{C,F}$ = 7.0 Hz, C-5), 69.8 (d, $^2J_{C,F}$ = 18.0 Hz, C-2), 59.4 (OCH_3), 50.3 (cyclohexyl CH), 33.2 (2 ×), 25.4, 24.7 (2 ×) (5 C, cyclohexyl CH_2) ppm. $^{19}F\{^1H\}$ NMR (235 MHz, $CDCl_3$): δ = −202.7 (s) ppm. IR: $\tilde{\nu}$ = 1721 cm^{-1} (C=O, carbamoyl), 3390 cm^{-1} (N−H). $C_{16}H_{23}Cl_3FNO_6$ (450.71): calcd. C 42.64, H 5.14, N 3.11; found C 42.83, H 5.23, N 3.10.

Compound 16: ^1H NMR (250 MHz, $CDCl_3$): δ = 5.55 (br. dd, $^3J_{F,2}$ = 22.5, $^3J_{2,3}$ = 7.0 Hz, 1 H, H-2), 5.38 (s, 1 H, $CHCCl_3$), 5.21 (br., 1 H, H-4), 5.09 (br. d, $^2J_{F,1}$ = 49.0 Hz, 1 H, H-1), 4.78 (br., 1 H, H-5), 4.55 (d, $^3J_{NH,CH}$ = 7.5 Hz, 1 H, NH), 4.22 (d, $^3J_{NH,CH}$ = 7.5 Hz, 1 H, NH), 3.87 (br. m, 1 H, H-6), 3.67−3.56 (br. m, 2 H, H-3, cyclohexyl C*H*NH), 3.52 (s, 3 H, OCH_3), 3.47 (m, 1 H, cyclohexyl C*H*NH), 3.14 (m, 1 H, cyclohexyl CHN), 2.00−1.00 (m, 30 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ = 156.4 (NHCON), 154.1 (NHCOO), 105.9 (*C*HCCl$_3$), 99.6 (CCl_3), 89.4 (d, $^1J_{C,F}$ = 182 Hz, C-1), 79.8 (2 C, C-4, C-5), 76.8 (d, $^2J_{C,F}$ = 29.5 Hz, C-6), 69.6 (d, $^2J_{C,F}$ = 16.3 Hz, C-2), 58.9 (OCH_3), 57.5 (cyclohexyl CHN), 54.0 (d, $^3J_{C,F}$ = 6.5 Hz, C-3), 49.9, 49.1 (2 C, cyclohexyl CHNH), 33.9, 33.8, 33.4, 33.1, 32.3 (2 ×), 26.3 (2 ×), 25.7 (2 ×), 25.4, 25.0 (2 ×), 24.7 (2 ×) (15 C, cyclohexyl CH_2) ppm. $^{19}F\{^1H\}$ NMR (235 MHz, $CDCl_3$): δ = −206.6 (s) ppm. IR: $\tilde{\nu}$ = 1722 cm^{-1} (C=O, carbamoyl), 1645 cm^{-1} (C=O, urea) 3326 and 3462 cm^{-1} (N−H). $C_{29}H_{45}Cl_3FN_3O_6$ (657.05): calcd. C 53.01, H 6.90, N 6.40; found C 52.71, H 6.91, N 6.37.

(1*R*,2*R*,3*R*,4*S*,5*R*)-1-*O*-Cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-5-*O*-(methyl)cyclohexane-1,2,3,4,5-pentol (17) and (1*R*,2*R*,3*R*,4*S*,5*R*)-1-*O*-Cyclohexylcarbamoyl-2-(*N*,*N*′-dicyclohexylureido)-5-*O*-methyl-3,4-*O*-(2,2,2-trichloroethylidene)cyclohexane-1,2,4,5-tetrol (18): Compound **6** (1.1 g, 6.17 mmol), chloral (2.1 mL, 21.61 mmol) and DCC (3.81 g, 18.51 mmol) were reacted in CH_2Cl_2 (40 mL); the procedure is analogous to that used for **5**. After column chromatographic separation (eluent gradient: heptane/EtOAc, 6:1 v/v, 2.0 L to 3:1 v/v, 1.0 L), of compound **17** (1.62 g, 61%) was isolated and crystallized from cyclohexane (yellowish needles). After recrystallization from MeOH, m.p. 176−177 °C, R_f = 0.36 (heptane/EtOAc, 1:1 v/v), $[\alpha]_D^{24}$ = +20.6 ($CHCl_3$, c = 1.06). The crystalline product **18** (750 mg, 19%) was also obtained, m.p. 126−128 °C (cyclohexane), R_f = 0.48 (heptane/EtOAc, 1:1 v/v), $[\alpha]_D^{23}$ = +5.1 ($CHCl_3$, c = 0.67).

Compound 17: ^1H NMR (500 MHz, $CDCl_3$): δ = 5.42 (s, 1 H, $CHCCl_3$), 5.29 (br. m, 1 H, H-1), 4.60 (d, $^3J_{NH,CH}$ = 7.5 Hz, 1 H, NH), 4.56−4.46 (m, 2 H, H-2, H-3), 3.60 (dd, $^3J_{4,5}$ = 9.0, $^3J_{3,4}$ = 6.4 Hz, 1 H, H-4), 3.46 (br. m, 1 H, cyclohexyl CH), 3.40 (s, 3 H, OCH_3), 3.30 (ddd, $^3J_{5,6ax}$ = 10.8, $^3J_{4,5}$ = 9.0, $^3J_{5,6eq}$ = 3.8 Hz, 1 H, H-5), 2.91 (br., 1 H, OH), 2.19 (d"t", $^2J_{6ax,6eq}$ = 14.2 Hz, 1 H, H-6eq), 1.92 (br. m, 2 H, cyclohexyl CH_2), 1.74−1.55 (m, 4 H, H-6ax, cyclohexyl CH_2), 1.39−1.04 (m, 5 H, cyclohexyl CH_2) ppm $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): δ = 153.8 (NHCOO), 106.3 (*C*HCCl$_3$), 99.1 (CCl_3), 82.0, 77.3 (C-2, C-3), 76.7 (C-5), 73.7 (C-4) 67.9 (C-1), 57.1 (OCH_3), 50.1 (cyclohexyl CH), 28.2 (C-6), 33.3 (2 ×), 25.4, 24.7 (2 ×) (5 C, cyclohexyl CH_2) ppm. X-ray structure see Figure 2. $C_{16}H_{24}Cl_3NO_6$ (432.73): calcd. C 44.41, H 5.59, N 3.24; found C 44.70, H 5.78, N 3.21.

Compound 18: ^1H NMR (500 MHz, $CDCl_3$): δ = 5.40 (s, 1 H, $CHCCl_3$), 5.27 (br., 1 H, H-1), 5.10 (br., 1 H, H-3), 4.61 (dd, J = 5.5, J = 4.0 Hz, 1 H, H-4), 4.52 (br., 1 H, NH), 4.34 (d, $^3J_{NH,CH}$ = 6.0 Hz, 1 H, NH), 3.78 (br. m, 1 H, H-5), 3.63 (m, 1 H, cyclohexyl C*H*NH), 3.48−3.39 (m, 2 H, cyclohexyl C*H*NH, H-2), 3.43 (s, 3 H, OCH_3), 3.15 (m, 1 H, cyclohexyl CHN), 2.28 (m, 1 H, H-6), 1.66 (m, 1 H, H-6), 1.85−0.96 (m, 30 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): δ = 156.8 (NHCON), 154.6 (NHCOO), 106.4 (*C*HCCl$_3$), 99.5 (CCl_3), 79.6 (C-4), 79.2 (C-3), 75.0 (C-5), 68.4 (br., C-1), 58.4 (OCH_3), 56.9 (cyclohexyl CHN), 56.7 (br., C-2), 49.7, 49.3 (2C, cyclohexyl CHNH), 30.3 (C-6), 33.91, 33.87, 33.5, 33.3, 32.5, 32.4, 26.5 (2 ×), 25.8, 25.6, 25.4, 25.0 (2 ×), 24.8, 24.7 (15C, cyclohexyl CH_2) ppm. $C_{29}H_{46}Cl_3N_3O_6$ (639.06): calcd. C 54.50, H 7.26, N 6.58; found C 54.71, H 6.91, N 6.37.

1-*O*-Benzoyl-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-4,5-*O*-(2,2,2-trichloroethylidene)-*muco*-inositol (19), 1-*O*-Benzoyl-6-*O*-cyclohexylcarbamoyl-3-*O*-formyl-2-*O*-methyl-4,5-*O*-(2,2,2-trichloroethylidene)-*muco*-inositol (20) and 2-*O*-Benzoyl-3-*O*-cyclohexylcarbamoyl-4-(*N*,*N*′-bis(cyclohexylureido)-4-deoxy-1-*O*-methyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+)-*chiro*-inositol (21): Compound **7** (2.26 g, 7.6 mmol), chloral (2.58 mL, 26.5 mmol) and DCC (3.91 g, 18.9 mmol) were reacted in $(CH_2Cl)_2$ (80 mL); the procedure was analogous to that used for **5**. After column chromatographic separation (heptane/EtOAc, 2:1 v/v), the first fraction (R_f = 0.33), besides formyl compound **20** (0.08 g, 2%), also contained small amounts of the corresponding 3-*O*-acetyl derivative **22**, and so formyl derivative **20** could not be obtained analytically pure. When the syrupy fraction of **21** (R_f = 0.23, 0.75 g, 13%) was allowed to stand, an amorphous solid deposited. This was washed with pentane and recrystallized from EtOAc, m.p. 110−112 °C, $[\alpha]_D^{25}$ = +42.8 ($CHCl_3$, *c* = 1.11). Compound **19** (R_f = 0.17, 4.36 g, 38%) was isolated as a foam-like amorphous solid, melting range 60−74 °C, $[\alpha]_D^{24}$ = +8.5 ($CHCl_3$, *c* = 1.04). The compound was quantitatively converted into its 3-*O*-acetyl derivative **22** by treatment with acetic acid anhydride/pyridine, giving crystals suitable for an X-ray analysis; analytical data see below. A further by-product (0.64 g, R_f = 0.11) could not be identified.

Compound 19: ^{1}H NMR [300 MHz, $(CD_3)_2CO$]: δ = 8.07−8.03 (m, 2 H, *o*-Ph), 7.69−7.62 (m, 1 H, *p*-Ph), 7.55−7.48 (m, 2 H, *m*-Ph), 6.25 (d, $^3J_{NH,CH}$ = 8.2 Hz, 1 H, NH), 5.57 (dd, $^3J_{1,6}$ = 8.5, $^3J_{5,6}$ = 2.8 Hz, 1 H, H-6), 5.56 (s, 1 H, $CHCCl_3$), 5.46 (dd, $^3J_{1,6}$ = 8.5, $^3J_{1,2}$ = 2.8 Hz, 1 H, H-1), 4.93 (d, *J* = 4.5 Hz, 1 H, OH), 4.73−4.68 (m, 2 H, H-4, H-5), 4.42 (m, 1 H, H-3), 3.76 (dd, $^3J_{1,2}$ = 2.8, $^3J_{2,3}$ = 5.2 Hz, 1 H, H-2), 3.45 (s, 3 H, OCH_3), 3.31 (br., 1 H, cyclohexyl CH), 1.82−1.46 (m, 5 H, cyclohexyl CH_2), 1.40−0.90 (m, 5 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR [75.5 MHz, $(CD_3)_2CO$]: δ = 166.0 (COC_6H_5), 155.3 (NHCOO), 134.1 (*p*-Ph), 130.8 (*i*-Ph), 130.5 (*o*-Ph), 129.4 (*m*-Ph), 106.9 ($CHCCl_3$), 100.4 (CCl_3), 82.1 (C-4), 80.9 (C-2), 80.2 (C-5), 70.8 (C-1), 69.2 (C-6), 67.5 (C-3), 59.0 (OCH_3), 50.9 (cyclohexyl CH), 33.5 (2 ×), 26.2, 25.6 (2 ×) (5 C, cyclohexyl CH_2) ppm. $C_{23}H_{28}Cl_3NO_8$ (552.83): calcd. C 49.97, H 5.11, N 2.53; found C 50.50, H 5.57, N 2.58.

Compound 21: ^{1}H NMR [500 MHz, $(CD_3)_2CO$]: δ = 8.06 (m, 2 H, *o*-Ph), 7.64 (m, 1 H, *p*-Ph), 7.51 (m, 2 H, *m*-Ph), 6.03 (br., 1 H, H-3), 5.93 (d, 1 H, $^3J_{NH,CH}$ = 7.8 Hz, NH), 5.68 (s, 1 H, $CHCCl_3$), 5.66 (m, 1 H, H-5), 5.31 (dd, $^3J_{1,2}$ = 2.8, $^3J_{2,3}$ = 8.2 Hz, 1 H, H-2), 5.25 (d, $^3J_{NH,CH}$ = 7.8 Hz, 1 H, NH), 4.76 (dd, $^3J_{1,6}$ = 3.8, $^3J_{5,6}$ = 5.5 Hz, 1 H, H-6), 4.09 (dd, 1 H, H-1), 3.58 (m, 1 H, cyclohexyl CH), 3.49 (s, 3 H, OCH_3), 3.49 (m, 1 H, cyclohexyl CH), 3.47 (m, 1 H, H-4), 3.28 (m, 1 H, cyclohexyl CH), 1.98−0.91 (m, 30 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR [125.8 MHz, $(CD_3)_2CO$]: δ = 166.1 (COC_6H_5), 157.3 (NHCON), 155.2 (NHCOO), 134.1 (*p*-Ph), 130.9 (*i*-Ph), 130.6 (*o*-Ph), 129.4 (*m*-Ph), 107.1 ($CHCCl_3$), 100.6 (CCl_3), 79.2, 79.1 (C-5, C-6), 77.9 (C-1), 74.0 (C-2), 68.7 (C-3), 59.7 (OCH_3), 58.3 (C-4), 57.0, 50.6, 50.1 (3 ×) (5 C, cyclohexyl CH), 34.3, 34.2, 33.8, 33.5, 33.4, 33.2, 27.2, 26.9, 26.6, 26.2 (3 ×), 26.1, 25.6 (2 ×) (15 C, cyclohexyl CH_2) ppm. $C_{36}H_{50}Cl_3N_3O_8$ (759.16): calcd. C 56.96, H 6.64, N 5.54; found C 56.57, H 6.64, N 5.06.

3-*O*-Acetyl-1-*O*-benzoyl-6-*O*-cyclohexylcarbamoyl-2-*O*-methyl-4,5-*O*-(2,2,2-trichloroethylidene)-*muco*-inositol (22): Colourless crystals, m.p. 205−207 °C (*i*PrOH), $[\alpha]_D^{25}$ = +8.1 ($CHCl_3$, *c* = 1.10); yield of **22** (95%) by acetylation of **19** with acetic acid anhydride/pyridine at room temp.

Compound 22: ^{1}H NMR [300 MHz, $(CD_3)_2CO$]: δ = 8.06−7.02 (m, 2 H, *o*-Ph), 7.69−7.62 (m, 1 H, *p*-Ph), 7.55−7.49 (m, 2 H, *m*-Ph), 6.27 (d, $^3J_{NH,CH}$ = 8.2 Hz, 1 H, NH), 5.60−5.53 (m, 2 H, H-3, H-6), 5.59 (s, 1 H, $CHCCl_3$), 5.42 (dd, $^3J_{1,2}$ = 2.5, $^3J_{1,6}$ = 8.4 Hz, 1 H, H-1), 4.80−4.71 (m, 2 H, H-4, H-5), 3.84 (dd, $^3J_{1,2}$ = 2.5, $^3J_{2,3}$ = 6.0 Hz, 1 H, H-2), 3.46 (s, 3 H, OCH_3), 3.34 (br., 1 H, cyclohexyl CH), 2.12 (s, 3 H, $COCH_3$), 1.85−1.46 (m, 5 H, cyclohexyl CH_2), 1.38−0.90 (m, 5 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR [75.5 MHz, $(CD_3)_2CO$]: δ = 169.5 (*C*OMe), 165.6 (COC_6H_5), 154.7 (NHCOO), 134.0 (*p*-Ph), 130.3 (*i*-Ph), 130.2 (*o*-Ph), 129.1 (*m*-Ph), 106.6 ($CHCCl_3$), 99.7 (CCl_3), 79.6, 79.3 (C-4, C-5), 77.8 (C-2), 70.3 (C-1), 68.2, 68.1 (C-3, C-6), 58.7 (OCH_3), 50.7 (cyclohexyl CH), 33.3, 33.2, 25.8, 25.3, 25.2 (5C, cyclohexyl CH_2), 20.5 ($COCH_3$) ppm. MS (70 eV): *m*/*z* = 595 [M], 476 [M − CCl_3]. MS (FAB): *m*/*z* = 618 [M + Na]; X-ray structure see Figure 3. $C_{25}H_{30}Cl_3NO_9$ (594.87): calcd. C 50.48, H 5.08, N 2.35; found C 50.80, H 5.11, N 2.21.

2,3-Di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (24), 3,4-Di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-4-*O*-formyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (25), 2,3-Di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (26), 3,4-Di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-2-*O*-formyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (27) and 2,3-Di-*O*-benzoyl-1-*O*-cyclohexylcarbamoyl-6-*N*,*N*′-bis(cyclohexylureido)-6-deoxy-5,6-*O*-(2,2,2-trichloroethylidene)-*muco*-inositol (28): DCC (9.96 g, 48.1 mmol) was added with stirring to a suspension of 3,4-di-*O*-benzoyl-*myo*-inositol (**8**, 7.49 g, 19.3 mmol) and chloral (6.59 mL, 67.7 mmol) in 1,2-dichloroethane (225 mL), and the mixture was heated at reflux for 8 h (under argon). The workup procedure was analogous to that used for **15/16**, except for the Et_3N/MeOH treatment for deformylation. Four UV-active spots were detected in the primary crude product mixture. Column chromatographic separation (heptane/EtOAc, 2:1 v/v) gave the two regioisomeric major products **24** (2.88 g, 23%), m.p. 196 °C (*i*PrOH), R_f = 0.31 and **25** (2.79 g, 23%), m.p. 175−176 °C ($MeNO_2$), R_f = 0.25 as well as a mixture of the regioisomers **26** and **27** (1.08 g, 8%), R_f = 0.38. The pure crystalline component **26** (mp, 210−215 °C) was obtained by fractional crystallization from *i*PrOH. The fourth spot (R_f = 0.43) corresponds to the doubly inverted cyclitol **28** (0.93 g, 6%), m.p. 146−148 °C (diethyl ether/petroleum ether).

Compound 24: ^{1}H NMR [500 MHz, $(CD_3)_2CO$]: δ = 7.97 (m, 2 H, *o*-Ph), 7.89 (m, 2 H, *o*-Ph), 7.55 (m, 2 H, *p*-Ph), 7.45−7.38 (m, 4 H, *m*-Ph), 6.74 (d, $^3J_{NH,CH}$ = 7.8 Hz, 1 H, NH), 5.82 (s, 1 H, $CHCCl_3$), 5.71 ("t", $^3J_{1,2}$ = $^3J_{1,6}$ = 3.3 Hz, 1 H, H-1), 5.66 ("t", $^3J_{2,3}$ = $^3J_{3,4}$ = 9.7 Hz, 1 H, H-3), 5.54 (dd, $^3J_{2,3}$ = 9.7, $^3J_{1,2}$ = 3.3 Hz, 1 H, H-2), 5.43 (d, $J_{OH,H-4}$ = 5.0 Hz, 1 H, OH), 4.75−4.72 (m, 2 H, H-5, H-6), 4.30 (m, 1 H, H-4), 3.88 (sept, 1 H, CH-*i*PrOH), 3.27 (br., 1 H, cyclohexyl CH), 2.89 (br., 1 H, OH-*i*PrOH), 1.85−1.51 (m, 5 H, cyclohexyl CH_2), 1.31−1.11 (m, 5 H, cyclohexyl CH_2), 1.09 (d, $J_{CH,CH3}$ = 6.0 Hz, 6 H, CH_3-*i*PrOH) ppm. $^{13}C\{^1H\}$ NMR [75.5 MHz, $(CD_3)_2CO$]: δ = 166.2 (COC_6H_5), 165.8 (COC_6H_5), 154.8 (NHCOO), 134.2 (*p*-Ph), 134.0 (*p*-Ph), 130.9 (*i*-Ph), 130.3 (*o*-Ph, 4C), 130.3 (*i*-Ph), 129.2 (*m*-Ph, 4 C), 107.0 ($CHCCl_3$), 100.2 (CCl_3), 83.4 (C-5), 77.7 (C-6), 72.3 (C-3), 72.0 (C-4), 71.0 (C-2), 68.0 (C-1), 63.7 (CH-*i*PrOH), 51.1 (cyclohexyl CH), 33.7, 33.5, 26.2 (3 C, cyclohexyl CH_2), 25.7 (CH_3-*i*PrOH), 25.6, 25.5 (2 C, cyclohexyl CH_2) ppm. X-ray structure see Figure 4. **24** (crystallized with one equivalent of *i*PrOH) 24+ *i*PrOH: $C_{32}H_{38}Cl_3NO_{10}$ (703.01): calcd. C 54.67, H 5.45, N 1.99; found C 55.09, H 5.85, N 1.72.

Compound 25: ^{1}H NMR [300 MHz, $(CD_3)_2CO$]: δ = 7.97 (m, 4 H, *o*-Ph), 7.59 (m, 2 H, *p*-Ph), 7.45 (m, 4 H, *m*-Ph), 6.57 (d, $^3J_{NH,CH}$ = 8.0 Hz, 1 H, NH), 5.81 (s, 1 H, $CHCCl_3$), 5.71 (dd, $^3J_{4,5}$ = 8.1,

$^3J_{3,4}$ = 9.0 Hz, 1 H, H-4), 5.56 (dd, $^3J_{2,3}$ = 7.7, $^3J_{3,4}$ = 9.0 Hz, 1 H, H-3) 5.43 (dd, $^3J_{1,2}$ = 3.0, $^3J_{1,6}$ = 4.1 Hz, 1 H, H-1), 5.08 (dd, $^3J_{5,6}$ = 5.5, $^3J_{4,5}$ = 8.1 Hz, 1 H, H-5), 4.97 (d, J = 6.0 Hz, 1 H, OH), 4.85 (dd, $^3J_{1,6}$ = 4.1, $^3J_{5,6}$ = 5.5 Hz, 1 H, H-6), 4.38 (m, 1 H, H-2), 3.41 (br., 1 H, cyclohexyl CH), 1.96−1.10 (m, 10 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR [75.5 MHz, $(CD_3)_2CO$]: δ = 166.2 (COC_6H_5), 166.0 (COC_6H_5), 155.3 (NHCOO), 134.3 (*p*-Ph), 134.1 (*p*-Ph), 130.7 (*i*-Ph), 130.4 (*o*-Ph), 130.3 (*o*-Ph), 130.3 (*i*-Ph), 129.4 (*m*-Ph), 129.3 (*m*-Ph), 107.5 ($CHCCl_3$), 100.1 (CCl_3), 80.3 (C-5), 78.4 (C-6), 73.7 (C-3), 73.3 (C-4), 71.8 (C-1), 69.3 (C-2), 51.0 (cyclohexyl CH), 33.7 (2 ×), 26.2, 25.7 (2 ×) (5 C, cyclohexyl CH_2) ppm. MS (70 eV): m/z = 643 [M]. $C_{29}H_{30}Cl_3NO_9$ (642.92): calcd. C 54.18, H 4.70, N 2.18; found C 53.88, H 4.76, N 2.43.

Compound 26: ^1H NMR [300 MHz, $(CD_3)_2CO$]: δ = 8.30 (s, 1 H, CHO), 7.95−7.88 (m, 4 H, *o*-Ph), 7.62−7.54 (m, 2 H, *p*-Ph), 7.48−7.38 (m, 4 H, *m*-Ph), 6.76 (d, $^3J_{NH,CH}$ = 7.8 Hz, 1 H, NH), 5.94 (s, 1 H, $CHCCl_3$), 5.86−5.62 (m, 4 H, H-1, H-2, H-3, H-4), 5.01, 4.85 (2 × m, 2 H, H-5, H-6), 3.28 (br., 1 H, cyclohexyl CH), 1.90−1.50 (m, 5 H, cyclohexyl CH_2), 1.34−1.13 (m, 5 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR [75.5 MHz, $(CD_3)_2CO$]: δ = 165.8 (COC_6H_5), 165.6 (COC_6H_5), 161.0 (CHO), 154.6 (NHCOO), 134.4 (*p*-Ph), 134.3 (*p*-Ph), 130.4 (*o*-Ph), 130.4 (*o*-Ph), 130.1 (*i*-Ph), 130.0 (*i*-Ph), 129.4 (*m*-Ph), 129.3 (*m*-Ph), 107.3 ($CHCCl_3$), 99.7 (CCl_3), 80.4, 77.9 (C-5, C-6), 72.1, 70.9, 69.8, 67.8 (C-1, C-2, C-3, C-4), 51.1 (cyclohexyl CH), 33.7, 33.5, 26.2, 25.6, 25.5 (5 C, cyclohexyl CH_2) ppm. $C_{30}H_{30}Cl_3NO_{10}$ (670.93): calcd. C 53.71, H 4.51, N 2.09; found C 54.25, H 4.95, N 1.89.

Compound 28: ^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (m, 2 H, *o*-Ph), 7.91 (m, 2 H, *o*-Ph), 7.47 (m, 2 H, *p*-Ph), 7.40−7.28 (m, 4 H, *m*-Ph), 5.99 (dd, $^3J_{2,3}$ = 9.0, $^3J_{1,2}$ = 3.5 Hz, 1 H, H-2), 5.82 (dd, $^3J_{2,3}$ = 9.0, $^3J_{3,4}$ = 6.4 Hz, 1 H, H-3), 5.57 ("t", $^3J_{1,6}$ = 3.8, $^3J_{1,2}$ = 3.5 Hz, 1 H, H-1), 5.53 (s, 1 H, $CHCCl_3$), 5.21 ("t", $^3J_{3,4}$ = 6.4, $^3J_{4,5}$ = 6.0 Hz, 1 H, H-4), 5.02 (dd, $^3J_{4,5}$ = 6.0, $^3J_{5,6}$ = 2.5 Hz, 1 H, H-5), 4.71 (d, $^3J_{NH,CH}$ = 8.0 Hz, 1 H, NH), 4.28 (d, $^3J_{NH,CH}$ = 8.0 Hz, 1 H, NH), 3.84 (br., 1 H, H-6), 3.63 (br. m, 1 H, cyclohexyl C*H*NH), 3.30 (br. m, 1 H, cyclohexyl C*H*NH), 3.19 (br. m, 1 H, cyclohexyl CHN), 2.14−0.90 (m, 30 H, cyclohexyl CH_2) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ = 165.8 (COC_6H_5), 165.1 (COC_6H_5), 156.5 (NHCON), 154.2 (NHCOO), 133.1 (*p*-Ph), 132.9 (*p*-Ph), 130.0 (*o*-Ph), 129.7 (*i*-Ph), 129.6 (*o*-Ph), 129.5 (*i*-Ph), 128.3 (*m*-Ph), 128.2 (*m*-Ph), 106.0 ($CHCCl_3$), 99.7 (CCl_3), 82.3 (C-5), 80.4 (C-4), 72.2 (C-1), 70.9 (C-2), 69.3 (C-3), 57.8 (cyclohexyl CH), 55.5 (C-6), 49.9, 49.5 (2 C, cyclohexyl CH), 33.9, 33.8, 33.2 (2 ×), 32.0, 31.8, 26.2, 26.1, 25.7, 25.4, 25.2, 25.1, 25.0, 24.7, 24.6 (15 C, cyclohexyl CH_2) ppm. $C_{42}H_{52}Cl_3N_3O_9$ (849.25): calcd. C 59.40, H 6.17, N 4.95; found C 59.16, H 6.21, N 4.61.

1-*O*-Cyclohexylcarbamoyl-5,6-*O*-(2,2,2-trichloroethylidene)-(+/-)-*chiro*-inositol (29): Heating of compounds **24**−**27** (0.15 mmol) at reflux in methanol (10 mL) and Et_3N (1.0 mL, 7.2 mmol) for 30 min exclusively gave the same compound **29**. The syrupy crude product crystallized from $CHCl_3$ (yield 90%), m.p. 186−188 °C. ^1H NMR (250 MHz, CD_3OD): δ = 5.53 (s, 1 H, $CHCCl_3$), 5.20 ("t", $^3J_{1,2}$ = $^3J_{1,6}$ = 2.8 Hz, 1 H, H-1), 4.60 (dd, 1 H, H-4), 4.49 (dd, $^3J_{2,3}$ = 7.0, $^3J_{3,4}$ = 6.2 Hz, 1 H, H-3), 3.76 (dd, $^3J_{1,2}$ = 2.8, $^3J_{2,3}$ = 7.0 Hz, 1 H, H-2), 3.64−3.52 (m, 2 H, H-5, H-6), 3.36 (br., 1 H, cyclohexyl CH), 1.91−1.60 (m, 5 H, cyclohexyl CH_2), 1.41−1.14 (m, 5 H, cyclohexyl CH_2) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 157.8 (NHCOO), 108.7 ($CHCCl_3$), 101.7 (CCl_3), 84.3, 79.4 (C-5, C-6), 75.6, 74.5, 73.3, 72.6 (C-1, C-2, C-3, C-4), 52.3 (cyclohexyl CH), 34.9 (2 ×), 27.5, 27.0 (2 ×) (5 C, cyclohexyl CH_2) ppm. $C_{15}H_{22}Cl_3NO_7$ (434.70): calcd. C 41.45, H 5.10, N 3.22; found C 41.26, H 5.10, N 3.10.

[1] T. Posternak, *Les Cyclitols*, Hermann, Paris, **1962**; Engl. Ed. Holden-Day, San Francisco, **1965**.
[2] T. Hudlicky, M. Cebulak, *Cyclitols and Their Derivatives. A Handbook of Physical, Spectral, and Synthetic Data*, Wiley-VCH Weinheim, New York, Cambridge, **1993**.
[3] Y. Takahashi, H. Nakayama, K. Katagiri, K. Ichikawa, N. Ito, T. Takita, T. Takeuchi, T. Miyake, *Tetrahedron Lett.* **2001**, *42*, 1053−1056 and papers cited therein.
[4] D. C. Billington, *Chem. Soc. Rev.* **1989**, *18*, 83−122.
[5] D. C. Billington, *The Inositol Phosphates−Chemical Synthesis and Biological Significance*, Wiley-VCH Weinheim, **1993**.
[6] Y. Takahashi, H. Nakayama, K. Katagiri, K. Ichikawa, N. Ito, T. Takita, T. Takeuchi, T. Miyake, *Tetrahedron Lett.* **2001**, *42*, 1053−1056 and papers cited therein.
[7] S. J. Angyal, L. Odier, *Carbohydr. Res.* **1980**, *80*, 203−206.
[8] [8a] IUPAC-IUB Commun. on Biochem. Nomencl., in *Tentative rules for cyclitol nomenclature, Biol. Chem.* **1968**, *243*, 5809−5819. [8b] *Nomenclature of Cyclitols*, Recommendations **1973**: S. J. Angyal, L. Anderson, R. S. Cahn, R. M. C. Dawson, O. Hoffmann-Ostenhof, W. Klyne, T. Posternak, *Pure Appl. Chem.* **1974**, *37*, 285−297.
[9] R. Miethchen, *J. Carbohydr. Chem.* **2003**, *22*, 801−825 (review).
[10] Part 18: R. Miethchen, Chr. Sowa, M. Frank, M. Michalik, H. Reinke, *Carbohydr. Res.* **2002**, *337*, 1−9.
[11] R. Miethchen, C. Sowa, M. Michalik, *Tetrahedron Lett.* **2001**, *42*, 8637−8639.
[12] M. Frank, R. Miethchen, *Carbohydr. Res.* **1998**, *313*, 49−53.
[13] M. Frank, R. Miethchen, H. Reinke, *Eur. J. Org. Chem.* **1999**, 1259−1263.
[14] [14a] G. I. Drummond, L. Anderson, *J. Am. Chem. Soc.* **1956**, *78*, 1750−1753. [14b] T. Naito, *J. Antibiotics, Series B* **1962**, *15*, 373−379. [14c] T. Suami, T. Machinami, *Bull. Chem. Soc., Japan* **1970**, *43*, 2953−2956. [14d] J. M. Heal, P. Fox, P. S. Schein, *Biochem. Pharmacology* **1979**, *28*, 1301−1306. [14e] B. J. Paul, J. Willis, T. A. Martinot, I. Ghiviriga, K. A. Abboud, T. Hudlicky, *J. Am. Chem. Soc.* **2002**, *124*, 10416−10426.
[15] A. P. Kozikowski, A. H. Fauq, J. M. Rusnak, *Tetrahedron Lett.* **1989**, *30*, 3365−3368.
[16] S. J. Angyal, G. C. Irving, D. Rutherford, M. E. Tate, *J. Chem. Soc.* **1965**, 6662−6664.
[17] S. D Gero, *Tetrahedron Lett.* **1966**, *6*, 591−595.
[18] P. J. Garegg, B. Samuelsson, *J. Chem. Soc., Perkin I* **1980**, 2866−2869.
[19] S. C. Johnson, J. Dahl, T. L. Shih, D. J. A. Schedler, L. Anderson, T. L. Benjamin, D. C. Baker, *J. Med. Chem.* **1993**, *36*, 3628−3635.
[20] S. M. Khersonsky, Y.-T. Chang, *Carbohydr. Res.* **2002**, *337*, 75−78.
[21] E. Vowinkel, P. Gleichenhagen, *Tetrahedron Lett.* **1974**, 139−142.
[22] S. J. Angyal, L. Odier, *Carbohydr. Res.* **1982**, *100*, 43−54.
[23] M. Karplus, *J. Chem. Phys.* **1959**, *30*, 11−15.
[24] D. Cremer, J. A. Pople, *J. Am. Chem. Soc.* **1975**, *97*, 1354−1358.
[25] G. M. Sheldrick, University of Göttingen, **1986**.
[26] S. K. Chung, Y. T. Chang, *J. Chem. Soc., Chem. Commun.* **1995**, 11−13.

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