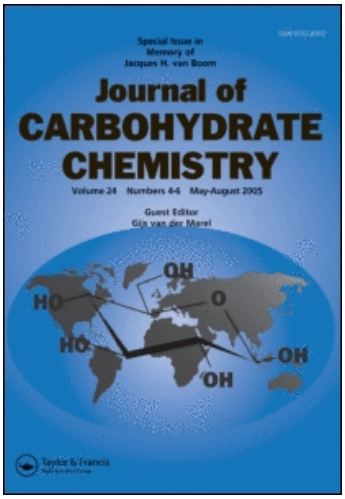

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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Christian Sowa[a]; Ralf Miethchen[a]; Helmut Reinke[a]
[a] Universität Rostock, Rostock, Germany

Online publication date: 21 August 2002

To cite this Article Sowa, Christian , Miethchen, Ralf and Reinke, Helmut(2002) 'NON-ANOMERIC SUGAR ISOUREAS', Journal of Carbohydrate Chemistry, 21: 4, 293 — 303
To link to this Article: DOI: 10.1081/CAR-120013497
URL: http://dx.doi.org/10.1081/CAR-120013497

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JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 21, No. 4, pp. 293–303, 2002

NON-ANOMERIC SUGAR ISOUREAS

Christian Sowa, Ralf Miethchen,* and Helmut Reinke

Universität Rostock, Fachbereich Chemie, Albert-Einstein-Strasse 3a,
D-18051, Rostock, Germany

ABSTRACT

Six non-anomeric isourea derivatives of D-fructose (**7**, **8**), D-glucose (**9**, **10**), 6-deoxy-L-altrose (**11**) and L-rhamnose (**12**) were synthesized from the precursors **1**–**6** by a CuCl-catalyzed addition of a non-glycosidic OH-group to DCC and DIPC, respectively. Subsequently, the isoureido group of phenyl 2,3,4-tri-*O*-benzyl-6-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-glucopyranoside (**10**) was replaced by an azido and a thioacetyl group, respectively, yielding the corresponding 6-deoxy-6-azido-D-glucopyranoside (**13**) and 6-deoxy-6-thioacetyl-D-glucopyranoside (**14**) in moderate to good yields.

INTRODUCTION

Hydroxyl groups can be activated for nucleophilic substitutions via isourea derivatives as leaving groups and various methods have been reported in the literature for the synthesis of *O*-alkyl and *O*-acyl-isoureas.[1–5] Aliphatic isourea derivatives are assumed to be suitable intermediates in epimerisation reactions.[6] The well known peptide coupling procedure employing dicyclohexylcarbodiimide (DCC) runs via an *O*-acylisourea[5] which is formed by addition of carboxylic acid to DCC. The acidity of alcohols is not strong enough for addition to DCC and requires catalysis. Vowinkel and Gleichenhagen[1] catalysed an addition of cyclohexanediols to DCC by CuCl and described reactions of the isoureas formed with proton acidic reagents like carboxylic acids, phenols or thiols. Mechanistic studies have shown that the nucleophilic reaction

*Corresponding author. E-mail: ralf.miethchen@chemie.uni-rostock.de

DOI: 10.1081/CAR-120013497 0732-8303 (Print); 1532-2327 (Online)

at the isourea moiety usually follows an S_N2 mechanism;[2] for comparisons with the Mitsunobu procedure see Refs. [2,3].

We are interested in sugar-isoureas in context with investigations of the reaction sequence of a non-conventional epimerisation reaction using the chloral/DCC reagent system.[6] Isourea moieties connected to non-anomeric positions of sugars were not described as far as we know. However, Tsutsumi et al.[7,8] described some reactions via 1-*O*-isourea sugar derivatives, i.e., reactions with phenols and thiophenols to furnish glycosides and thioglycosides, respectively. Horvat et al.[9] reported syntheses of glycopeptides and a $(1 \rightarrow 6)$-disaccharide via anomeric isourea sugars as glycosyl donors. Neither research group isolated these key intermediates.

RESULTS AND DISCUSSION

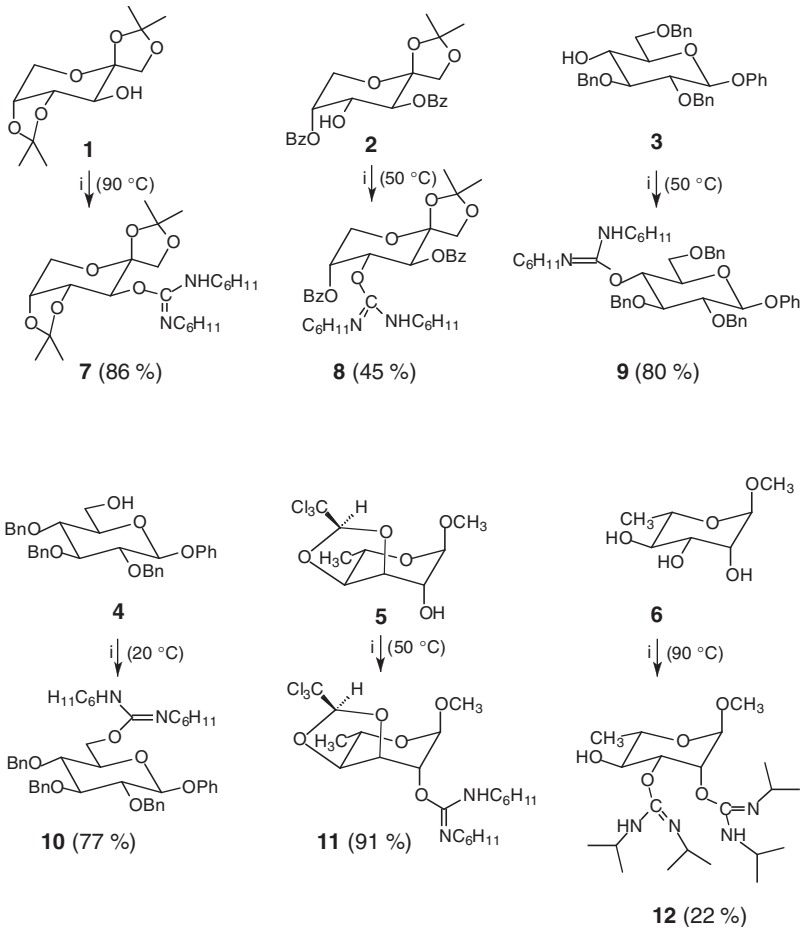
The non-glycosidic sugar isoureas **7**–**12** were prepared from the monosaccharides **1**–**6** and carbodiimides in the presence of catalytic amounts of anhydrous copper-(I)-chloride; Scheme 1. The method of CuCl-catalyzed introduction of isourea moieties using carbodiimide is based on a communication of Vowinkel and Gleichenhagen.[1] The authors describe corresponding reactions with cyclohexane-1,2-diols.

The experimental procedure, described for the fructose derivative **7**, is universally applicable for isourea preparations. However, different reaction temperatures (20, 50 and 90°C, respectively) proved to be of advantage for other starting materials. Methyl 2,3-di-*O*-(*N*,*N*′-diisopropylisoureido)-α-L-rhamnopyranoside (**12**), generated from methyl α-L-rhamnopyranoside (**6**) and diisopropylcarbodiimide (DIPC) was only obtained in low yield, because the three unprotected OH-groups of the starting material allowed the formation of further isourea derivatives. Compound **12** and the monoisourea derivatives **7**–**11** were easily soluble in all common organic solvents. Only the D-fructose derivative **7** and L-rhamnose derivative **12** could be crystallized. Whereas compound **12** crystallized from heptane, compound **7** did not crystallize from any concd soln. It became solid after removal of the solvent and showed a melting point at 109–110°C.

The chromatographic detection and separation of the isoureas is difficult, because the basicity of this group causes tailing. The latter can be suppressed by addition of triethylamine, however, the separation effect is reduced. Therefore, a high conversion was the stated objective. Furthermore, it is noteworthy, that the isourea derivatives already show lower R_f-values than the corresponding precursors with the free OH-group.

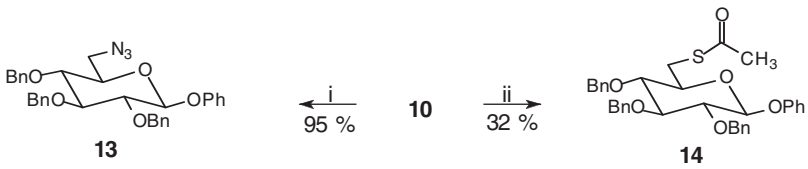
To obtain information about the reactivity of non-glycosidic isoureido groups model experiments were first carried out. The isoureido group of **10** was replaced by treatment with sodium azide or thioacetic acid, yielding the azide **13** (95%) and the thioacetic ester **14** (32%), respectively, Scheme 2. An isourea group connected to a secondary C-atom was less reactive compared to the 6-*O*-isoureido sugar **10**.[10a]

In connection with mechanistic studies of a non-conventional epimerisation reaction using the chloral/DCC reagent,[6] the reactivities of 1,2-*O*-isopropylidene-3-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-fructopyranose and 1,2-*O*-isopropylidene-4-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-fructopyranose to chloral were compared.[10a] 1,2-*O*-Isopropylidene-4-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-fructopyranose was prepared by

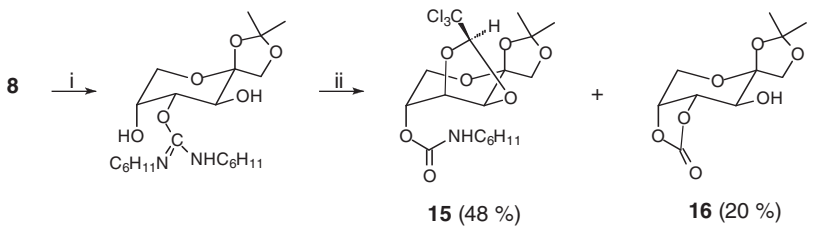


Scheme 1. i = DCC, DMF, CuCl, 24 h.

debenzoylation of **8** with 2% methanolic sodium methoxide (1 h, rt). The separated crude product was dissolved in 1,2-dichloroethane and treated with anhydrous chloral for 6 h under reflux yielding 1,2-*O*-isopropylidene-5-*O*-cyclohexylcarbamoyl-3,4-*O*-trichloroethylidene-β-D-tagatopyranose (**15**)[11] (48%) and the cyclic carbonic acid ester derivative **16** (20%); Scheme 3. The regioisomeric 1,2-*O*-isopropylidene-3-*O*-(*N*,*N*′-



Scheme 2. i = NaN_3, *p*-TsOH, DMF, 110°C, 19 h; ii = CH_3COSH, toluene, 110°C, 19 h.



Scheme 3. i = NaOMe/MeOH, rt, 1 h; ii = $Cl_3C-CH=O$, 1,2-DCE, reflux, 6 h.

dicyclohexylisoureido)-β-D-fructopyranose, analogously treated with chloral, did not generate any trichloroethylidene derivative.[10a,b]

The formation of **15** from 1,2-*O*-isopropylidene-4-*O*-(*N*,*N*′-dicyclohexyl-isoureido)-β-D-fructopyranose supports our hypothesis[6] that isoureas are intermediates in non-conventional epimerisations with the chloral/DCC reagent. However, the different reaction course of the two regioisomeric starting materials confirms also that the reaction of the isourea only progresses via a cyclic imidocarbonic ester to a cyclic acetal[6] when the isourea group is neighbour to a *cis*-arranged OH-group. 1,2-*O*-Isopropylidene-3-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-fructopyranose does not meet this prerequisite.

The structures of the compounds **7**–**14** are supported by their ^{1}H and ^{13}C NMR spectra. The ^{13}C NMR signal (N–*C*(N)–O) of an isourea moiety is found between 148 and 150 ppm. Furthermore, a strong IR-band between 1667 and 1674 cm^{-1} is characteristic for this group. The crystals of **12** were suitable for an X-ray analysis, Figure 1. A single crystal of **12** was tested by a rotational photograph on a Bruker P4

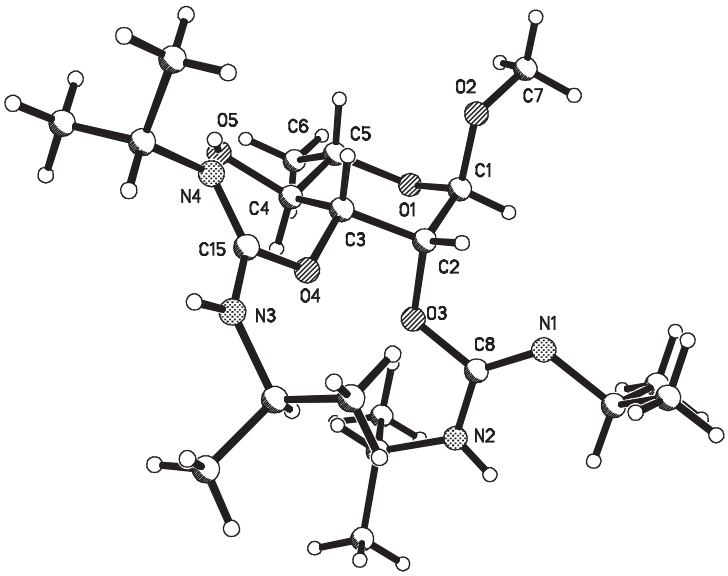


Figure 1. X-ray structure of methyl 2,3-di-*O*-(*N*,*N*′-diisopropylisoureido)-α-L-rhamnopyranoside (**12**).

four circle diffractometer equipped with a Mo–K_α sealed tube and a graphite monochromator. The reduced cell was found by the automatic cell determination routine of the Bruker SHELXTL software. The data collection was performed in routine ω-scan and the structure was solved by direct methods (Bruker SHELXTL) and refined by the full-matrix least-squares methods of SHELXL-97 (G. M. Sheldrick, Universität Göttingen, 1997). All non-hydrogen atoms were refined anisotropically while the hydrogens were put into theoretical positions and refined according to the riding model. There is a disorder phenomenon in both *O*-(*N*,*N*′-diisopropylisoureido) moieties. Each one of the two isopropyl groups takes different positions. Of course one can observe hydrogen bonding in the solid due to the different donating and accepting functionalities. Beside an intramolecular hydrogen bridge O(5)–H···N(4) with an O–N distance of 2.741 Å, there are infinite chains of molecules along the crystallographic a-axis via intermolecular H-bridges between N(2)–H and O(5) of the next molecule with an N–O distance of 3.296 Å. Thus, the O(5)–H group is both a donating and accepting site.

The puckering parameters[12] of **12** (puckering amplitude Q = 0.518 Å, magnitude of the distortion θ = 174.5°, φ-value 253°) indicate an almost undisturbed $^1C_4$ chair conformation of the pyranose ring.

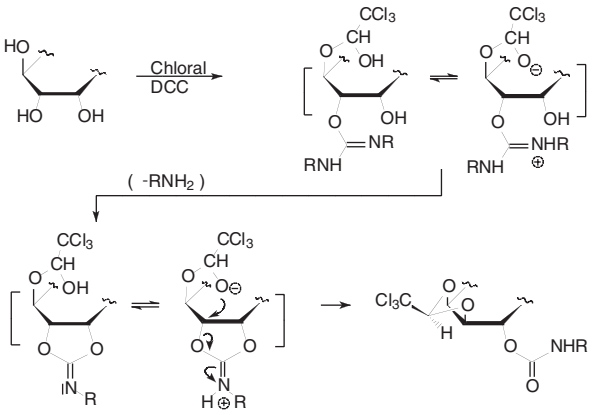
Further details of the data collection: Diffractometer: Bruker P4; radiation: λ = 0.71073 Å (Mo–K_α) with graphite monochromator; crystal size: 0.6 × 0.34 × 0.28 mm^3; formula: $C_{21}H_{42}N_4O_5$; formula weight: 430.59; temperature 293 (2) K; crystal system: monoclinic; space group: $P2_1$; unit cell dimensions: a = 9.5130 (10) Å, b = 14.147 (2) Å, c = 9.965 (2) Å; β = 95.510 (10)°; volume: 1334.9 (4) $Å^3$; Z = 2; density (calcd): 1.071 Mg/m^3; absorption coefficient: 0.076 mm^{-1}; F(000): 472; Θ range for data collection: 2.05 to 22.00°; index ranges: $-10 \le h \le 10$, $-14 \le k \le 14$, $-10 \le l \le 10$; reflections collected: 3655; independent reflections: 3269 [R(int) = 0.0212], 2754 reflections with $I > 2\sigma(I)$, completeness to Θ = 22.00°, 100%; data/restraints/parameters: 3269/1/320; goodness-of-fit on F^2: 1.044; final R indices [$I > 2\sigma(I)$]: R1 = 0.0498, *w*R2 = 0.1284; R indices (all data): R1 = 0.0606, *w*R2 = 0.1391; absolute structure parameter: −0.1 (17); largest diff. peak/ hole: 0.113/−0.137 e.$Å^{-3}$. The weighting scheme was calculated according to $w^{-1} = \sigma^2 (F_o^2) + (0.0716P)^2 + 0.0601P$ with $P = (F_o^2 + 2F_c^2)/3$.

Full crystallographic details, excluding structure factors, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-175568 These data may be obtained, on request, from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Tel.: +44-1223-336408, fax: +44-1223-336033, E-mail: deposit@ccdc.cam.ac.uk.

CONCLUSION

In this paper, we have shown that isourea groups can be easily introduced into any one non-glycosidic position of carbohydrates with carbodiimides catalysed by CuCl. The isourea moieties are potential leaving groups.

Moreover, it could be confirmed that isoureas are intermediates in non-conventional acetalation/epimerisation reactions with the chloral/carbodiimide reagent as reported in Ref. [6]; Scheme 4. Whereas 1,2-*O*-isopropylidene-4-*O*-(*N*,*N*′-dicyclohex-



Scheme 4. Mechanism of the non-conventional epimerisation of carbohydrates and inositols reported in Ref. [6].

ylisoureido)-β-D-fructopyranose yielded 5-*O*-cyclohexylcarbamoyl-1,2-*O*-isopropylidene-3,4-*O*-trichloroethylidene-β-D-tagatopyranose (**15**)[11] on heating with chloral (Scheme 3), the regioisomeric 1,2-*O*-isopropylidene-3-*O*-(*N*,*N'*-dicyclohexylisoureido)-β-D-fructopyranose did not form a chloral acetal. It follows from this also that one of the OH-groups neighboured to the isoureido moiety has to be *cis*-arranged allowing the subsequent formation of the cyclic imidocarbonic ester intermediate as postulated in previous papers, e.g. Ref. [6,13].

EXPERIMENTAL

General procedures. Melting points were obtained on a polarizing microscope Leitz (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-250 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 Meβtechnik). 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.

3-*O*-(*N*,*N'*-Dicyclohexylisoureido)-1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (7). To a soln of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**1**)[14] (4.97 g, 19.1 mmol) and DCC (5.47 g, 26.5 mmol) in anhydrous DMF (10 mL) copper-(I)-chloride (10 mg, 0.1 mmol) was added under stirring at 25°C (argon atmosphere). After roughly ten minutes the colour of the suspension turned to green. Now the mixture was warmed to 90°C and stirring was continued for 24 h. Then, the suspension was cooled down and filtered from precipitated dicyclohexylurea. Ethyl acetate (40 mL) was added to the filtrate before the soln was subsequently washed with sat. Na_2–EDTA-soln (twice 5 mL), water (10 mL) and brine (10 mL) and was dried (Na_2SO_4). After filtration and

evaporation of the solvents the residue was purified by column chromatography (heptane/EtOAc 5:1) yielding 7.71 g (86%) of **7**, which crystallized overnight after several hours under fine vacuum; mp 109–110°C, $[\alpha]_D^{24} = -123$ (*c* 1.2, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 5.47$ (br, 1 H, $J_{W/2} = 9$ Hz, H-3), 4.24 (dd, 1H, $J_{3,4} = 8.5$ Hz, H-4), 4.13 (dd, 1H, $J_{4,5} = 5.2$ Hz, H-5), 4.06 (dd, 1H, $J_{5,6b} = 2.4$ Hz, H-6b), 3.98 (d, 1H, $J_{6a,6b} = 13.3$ Hz, H-6a), 3.97 (d, 1H, H-1b), 3.82 (d, 1H, $J_{1a,1b} = 9.2$ Hz, H-1a), 3.39 (br, 2H, cyclohexyl-CH, NH), 2.73, (br, 1H, cyclohexyl-CH), 1.29, 1.33, 1.42, 1.51 (4 s, 12H, CH_3), 0.97–1.70 (m, 20H, cyclohexyl-CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 150.1$ (imino-C), 109.2, 111.2 ($C(CH_3)_2$), 104.9, (C-2), 60.3, (C-6), 68.8, 71.7, 74.0, 75.6 (C-1, C-3, C-4, C-5), 50.7, 53.8 (cyclohexyl-CH), 34.4 (cyclohexyl-CH_2), 25.0–27.8 (CH_3, cyclohexyl-CH_2). IR (KBr): 1672 cm^{-1} (C═N).

Anal. Calcd for $C_{25}H_{42}N_2O_6$ (466.6): C, 64.35; H, 9.07; N, 6.00. Found: C, 64.61; H, 9.13; N, 5.97.

3,5-Di-*O*-benzoyl-4-*O*-(*N*,*N*′-dicyclohexylisoureido)-1,2-*O*-isopropylidene-β-D-fructopyranose (8). From 1,2-*O*-isopropylidene-3,5-di-*O*-benzoyl-β-D-fructopyranose (**2**) (200 mg, 0.46 mmol),[10a,c] DCC (150 mg, 0.73 mmol) and CuCl (10 mg, 0.1 mmol) in anhydrous DMF for 1.5 h at 50°C. The work up procedure is analogous to that for **7**. Column chromatographic separation (R_f 0.38, toluene/EtOAc 9:1). Yield of **8**: 132 mg (45%) yellowish syrup, $[\alpha]_D^{24} = -168$ (*c* 1.4, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.12$ (m, 2H, *Ph*-H), 7.85 (m, 2H, *Ph*-H), 7.12–7.62 (m, 6H, *Ph*-H), 6.26 (d, 1H, H-3), 5.71 (dd, 1H, $J_{4,5} = 3.4$ Hz, $J_{3,4} = 10.8$ Hz, H-4), 5.65 (m, 1H, H-5), 4.26 (d, 1H, H-6a), 4.23 (d, 1H, H-1a), 4.02 (d, 1H, $J_{1\ gem.} = 9.0$ Hz, H-1b), 3.99 (dd, 1H, $J_{5,6a} = 1.8$ Hz, $J_{6a,6b} = 13.3$ Hz, H-6b), 3.30 (br, 1H, cyclohexyl-CH), 2.83 (br, 1H, cyclohexyl-CH), 1.54 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.18–1.90 (m, 20H, cyclohexyl-CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 165.7$, 166.0 (Bz—*C*═O), 150.1 (imino-C), 133.0, 133.2 (ipso-Ar–C), 128.1, 128.2, 128.4, 129.1, 129.8, 130.0 (Ar–C), 111.7 (ketal-C), 105.8 (C-2), 71.7 (C-1), 66.2, 70.6, 70.9 (C-3, C-4, C-5), 62.3 (C-6), 50.1, 53.5 (cyclohexyl-CH), 34.2, 34.5 (cyclohexyl-CH_2) 26.3, 26.7 (CH_3), 24.5, 24.8, 24.9, 25.5 (cyclohexyl-CH_2). IR (KBr): 1669 cm^{-1} (C═N), 1728 cm^{-1} (C═O), 3405 cm^{-1} (NH).

Anal. Calcd for $C_{36}H_{46}N_2O_8$ (634.8): C, 68.12 H, 7.30; N, 4.41. Found: C, 68.05; H, 7.46; N, 4.12.

Phenyl 2,3,6-tri-*O*-benzyl-4-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-glucopyranoside (9). From phenyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**3**) (300 mg, 0.57 mmol), DCC (210 mg, 1.0 mmol) and CuCl (10 mg, 0.1 mmol) in anhydrous DMF for 24 h at 50°C. The work up procedure is analogous to that for **7**. Column chromatographic separation (R_f 0.13, toluene/EtOAc/EtOH 4:2:1 v/v/v). Yield of **9**: 343 mg (80%) syrup, $[\alpha]_D^{24} = -8$ (*c* 0.99, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 5.06$ (d, 1H, $J_{1,2} = 6.4$ Hz, H-1), 5.05 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.99$ Hz, Bn–CH_2), 4.87 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.99$ Hz, Bn–CH_2), 4.81 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.99$ Hz, Bn–CH_2), 4.68 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.99$ Hz, Bn–CH_2), 4.59 (d, 1H, $J_{gem.,\ Bn-CH_2} = 11.75$ Hz, Bn–CH_2), 4.49 (d, 1H, $J_{gem.,\ Bn-CH_2} = 11.75$ Hz, Bn–CH_2), 3.72–3.85 (m, 4H, H-2, H-3, H-5, H-6), 3.65 (d, 1H, $J_{6a,6b} = 10.2$ Hz , H-6a), 3.46 (m, 1H, cyclohexyl-CH), 3.30 (m, 1H, cyclohexyl-CH), 1.45–1.79 (m, 10H, cyclohexyl-CH_2), 1.01–1.34 (m, 10H, cyclohexyl-CH_2). ^{13}C NMR (62 MHz,

$CDCl_3$): δ = 157.4 (ipso-Ph), 149.1 (imino-C), 138.4 (3 quat. Bn–C), 127.6–129.6 (Ar–C), 116.8 (*p*-Ph), 101.5 (C-1), 70.5, 73.7, 75.0, 81.6, 82.7 (C-2, C-3, C-4, C-5, C-6), 54.2 (cyclohexyl-CH), 50.3 (cyclohexyl-CH), 34.4 (cyclohexyl-CH_2), 24.8–25.6 (cyclohexyl-CH_2). IR (KBr): 1669 cm^{-1} (C═N).

Anal. Calcd for $C_{46}H_{56}N_2O_6$ (733.0): C, 75.38 H, 7.70; N, 3.82. Found: C, 75.17; H, 7.58; N, 3.73.

Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-(*N*,*N*′-dicyclohexylisoureido)-β-D-glucopyranoside (10). From phenyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (**4**) (240 mg, 0.45 mmol), DCC (200 mg, 0.9 mmol) and CuCl (10 mg, 0.1 mmol) in anhydrous DMF for 24 h at rt. The work up procedure is analogous to that for **7**. Column chromatographic separation (R_f 0.21, toluene/EtOAc/EtOH 4:2:1 v/v/v). Yield of **10**: 254 mg (77%) colourless syrup, $[\alpha]_D^{23} = -10$ (*c* 1.0, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.28–7.42 (m, 20H, *Ph*-H), 5.10 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.8$ Hz, Bn–CH_2), 5.07 (d, 1H, $J_{1,2} = 6.6$ Hz, H-1), 5.01 (d, 1H, $J_{gem.,\ Bn-CH_2} = 11.0$ Hz, Bn–CH_2), 4.93 (d, 2H, $J_{gem.,\ Bn-CH_2} = 11.0$ Hz, Bn–CH_2), 4.88 (d, 1H, $J_{gem.,\ Bn-CH_2} = 11.4$ Hz, Bn–CH_2), 4.70 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.6$ Hz, Bn–CH_2), 4.63 (d, 1H, $J_{6a,6b} = 11.9$ Hz, H-6a), 4.29 (dd, 1H, $J_{5,6} = 5.3$ Hz, H-6b), 3.60–3.82 (m, 4H, H-2, H-3, H-4, H-5), 3.49 (m, 1H, cyclohexyl-CH), 3.30 (m, 1H, cyclohexyl-CH), 1.08–2.03 (m, 20H, cyclohexyl-CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 157.4 (ipso-Ph), 148.5 (imino-C), 138.5, 138.3, 137.9 (3 quat. *Bn*–C), 127.6–129.6 (Ar–C), 116.7 (*p*-Ph), 101.6 (C-1), 74.0, 77.4, 82.1, 84.5 (C-2, C-3, C-4, C-5), 54.2 (cyclohexyl-CH), 64.5 (C-6), 55.8, 49.0 (cyclohexyl-CH), 34.9, 34.3, 34.0, 34.0 (cyclohexyl-CH_2), 24.8–25.6 (cyclohexyl-CH_2. IR (KBr): 1667 cm^{-1} (C═N).

Anal. Calcd for $C_{46}H_{56}N_2O_6$ (733.0): C, 75.38 H, 7.70; N, 3.82. Found: C, 75.21; H, 7.56; N, 4.09.

Methyl 2-*O*-(*N*,*N*′-dicyclohexylisoureido)-3,4-*O*-trichloroethylidene-6-deoxy-α-L-altropyranoside (11). From methyl 3,4-*O*-trichloroethylidene-6-deoxy-α-L-altropyranoside (**5**)[15] (1.0 g, 3.2 mmol), DCC (1.0 g, 4.8 mmol) and CuCl (10 mg, 0.1 mmol) in anhydrous DMF for 18 h at 50°C. The work up procedure is analogous to that for **7**. Column chromatographic separation (R_f 0.19, toluene/EtOAc 3:1 v/v). Yield of **11**: 1.52 g (91%) colourless syrup, $[\alpha]_D^{23} = -46$ (*c* 1.15, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.45 (s, 1H, acetal-H), 5.27 (br, 1H, H-1), 4.72 (br, 1H, $J_{W/2} = 3.0$ Hz, H-2), 4.67 (dd, 1H, $J_{2,3} = 3.1$ Hz, H-3), 4.17 (dd, 1H, $J_{3,4} = 5.7$ Hz, H-4), 3.82 (dd, 1H, $J_{4,5} = 9.2$ Hz, H-5), 3.38 (s, 3H, OMe), 3.38 (br, 2H, cyclohexyl-CH, NH), 2.83 (br, 1H, cyclohexyl-CH), 0.96–1.99 (m, 20H, cyclohexyl-CH_2), 1.37 (d, 3H, $J_{5,6} = 6.3$ Hz, H-6). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 148.4 (imino-C), 106.6 (acetal-C), 99.7 (C-1), 98.8 (CCl_3), 61.9, 67.9, 76.8, 78.3 (C-2, C-3, C-4, C-5), 55.7 (OMe), 50.6, 53.8 (cyclohexyl-CH), 34.1 (cyclohexyl-CH_2), 24.5–26.0 (cyclohexyl-CH_2), 18.7 (C-6). IR (KBr): 1674 cm^{-1} (C═N).

Anal. Calcd for $C_{22}H_{37}Cl_3N_2O_6$ (531.9): C, 49.68 H, 7.01; N, 5.27. Found: C, 49.97; H, 6.78; N, 5.14.

Methyl 2,3-di-*O*-(*N*,*N*′-diisopropylisoureido)-α-L-rhamnopyranoside (12). From methyl α-L-rhamnopyranoside (**6**)[16] (1.0 g, 5.6 mmol), DIPC (1.4 g, 11.2 mmol) and CuCl (10 mg, 0.1 mmol) in anhydrous DMF (10 mL) for 8 h at 90°C. The

work up procedure is analogous to that for **7**. Column chromatographic separation (R_f 0.11, heptane/EtOAc/Et_3N 12:4:1 v/v/v). Yield of **12**: 550 mg (22%) colourless crystals, mp 160–161°C (heptane), $[\alpha]_D^{24} = -122$ (*c* 1.4, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 5.35$ (dd, 1H, H-2), 4.77 (dd, 1H, $J_{2,3} = 3.5$ Hz, $J_{3,4} = 9.1$ Hz, H-3), 4.74 (d, 1H, $J_{1,2} = 1.8$ Hz, H-1), 3.64–3.91 (br, 4H, NH), 3.58 (m, 2H, H-4, H-5), 3.39 (br, 1H, CH), 3.36 (s, 3H, OMe), 3.11 (br, 1H, CH), 1.35 (d, 3H, $J_{5,6} = 5.9$ Hz, H-6), 0.97–1.18 (m, 24H, 8 CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 148.2$, 152.9 (2 imino-C), 96.7 (C-1), 67.4, 68.2, 68.6, 71.1 (C-2, C-3, C-4, C-5), 52.8 (OMe), 41.7, 42.1, 43.9, 44.2 (4 *C*H(CH_3)$_2$) 22.0 (4 CH(*C*H_3)$_2$), 16.5 (C-6). IR (KBr): 1652 cm^{-1}, 1668 cm^{-1} (C═N).

Anal. Calcd for $C_{21}H_{42}N_4O_5$ (430.6): C, 58.58 H, 9.83; N, 13.01. Found: C, 58.62; H, 9.94; N, 13.00.

Phenyl 6-azido-6-deoxy-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (13). A soln of **10** (250 mg, 0.38 mmol), *p*-toluenesulfonic acid monohydrate (10 mg) and sodium azide (65 mg, 1.0 mmol) in dry DMF was heated with stirring at 110°C for 19 h. Then DMF was removed under reduced pressure and the residue was treated with acetone (10 mL) without heating. After filtration to remove the precipitated dicyclohexylurea, the filtrate was concd and the residue was purified by flash chromatography (R_f 0.19; heptane/EtOAc 8:1 v/v). The cryst compd **13** (199 mg, 95%) was isolated; colourless crystals mp 74–76°C (heptane/EtOAc); $[\alpha]_D^{24} = -26$ (*c* 1.0, $CHCl_3$).

^{1}H NMR (250 MHz, acetone-d^6): $\delta = 7.19$–7.40 (m, 1H, *Ph*-H), 5.24 (d, 1H, $J_{1,2} = 7.6$ Hz, H-1), 5.09 (d, 1H, $J_{Bn-CH_2} = 11.3$ Hz, Bn–CH_2), 5.00 (d, 1H, $J_{Bn-CH_2} = 11.1$ Hz, Bn–CH_2), 4.93 (d, 1H, $J_{Bn-CH_2} = 11.4$ Hz, Bn–CH_2), 4.87 (d, 1H, $J_{Bn-CH_2} = 11.3$ Hz, Bn–CH_2), 4.84 (d, 1H, $J_{Bn-CH_2} = 11.3$ Hz, Bn–CH_2), 4.68 (d, 1H, $J_{Bn-CH_2} = 11.1$ Hz, Bn–CH_2), 3.55–3.88 (m, 5H, H-2, H-3, H-4, H-5, H-6b), 3.48 (dd, 1H, $J_{6a,6b} = 13.3$ Hz, $J_{6a,5} = 6.4$ Hz, H-6a). ^{13}C NMR (62 MHz, acetone-d^6): $\delta = 158.6$ (quat. Ar–C; Ph), 139.6, 139.9, 140.1 (quat. Ar–C; Bn), 128.3, 128.5, 128.6, 128.8, 128.8, 129.0, 129.1, 129.2, 129.3, 129.4, 129.9, 130.6 (Ar–C), 123.6 (*p*-Ph), 117.7 (*o*-Ph), 102.2 (C-1), 75.3, 79.5, 83.1, 85.3 (C-2, C-3, C-4, C-5), 75.6, 75.7, 76.3 (3 Bn–CH_2), 52.6 (C-6). IR (KBr): 2100 cm^{-1} (azide).

Anal. Calcd for $C_{33}H_{33}N_3O_5$ (551.6): C, 71.85 H, 6.03; N, 7.62. Found: C, 71.80; H, 6.24; N, 7.39.

Phenyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-thioacetyl-β-D-glucopyranoside (14). A soln of **10** (240 mg, 0.3 mmol) and thioacetic acid (0.5 mL) in dry toluene (5 mL) was refluxed for 14 h. Then the mixture was concd under reduced pressure and the residue was purified by flash chromatography (R_f 0.14; heptane/EtOAc 8:1 v/v). **14** (60 mg, 32%) was isolated as colourless cryst substance from a heptane–toluene mixture; mp 126–127°C (toluene/EtOAc); $[\alpha]_D^{24} = -10$ (*c* 1.02, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.28$–7.42 (m, 17H, Ar–H), 7.04–7.12 (m, 3H, Ar–H), 5.06 (d, 1H, $J_{gem.,\ Bn-CH_2} = 11.3$ Hz, Bn–CH_2), 4.97 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.9$ Hz, Bn–CH_2), 4.97 (d, 1H, $J_{1,2} = 7.7$ Hz, H-1), 4.93 (d, 1H, $J_{gem.,\ Bn-CH_2} = 10.9$ Hz, Bn–CH_2), 4.83 (d, 2H, $J_{gem.,\ Bn-CH_2} = 10.9$ Hz, 2 Bn–CH_2), 4.69 (d, 1H, $J_{gem.,\ Bn-CH_2} = 11.3$ Hz, Bn–CH_2), 3.43–3.62 (m, 5H, H-2, H-3, H-4, H-5, H-6), 2.35 (s, 3H, Me), 3.00 (dd, 1H, $J_{5,6a} = 8.6$ Hz, $J_{6a,6b} = 14.4$, H-6). ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 194.7$

(C═O), 128.6, 129.6, 157.2 (quat. Ph–C), 127,8, 127.8, 127.9, 128.0, 128.3, 128.5 (Ar–C), 122.8 (*p*-Ph–C), 116.9 (*o*-Ph–C), 101.6 (C-1), 75.1, 75.3, 75.8 (Bn–CH_2), 74.5, 80.3, 82.0, 84.4 (C-2, C-3, C-4, C-5), 30.9 (C-6), 30.5 (Me). IR (KBr): 1691 cm^{-1} (C═O).

Anal. Calcd for $C_{35}H_{36}O_6S$ (584.7): C, 71.89 H, 6.21; S, 5.48. Found: C, 71.72; H, 6.38; S, 5.46.

(*R*)-5-*O*-Cyclohexylcarbamoyl-1,2-*O*-isopropylidene-3,4-*O*-trichloroethylidene-β-D-tagatopyranose (15) and 4,5-*O*-carbonyl-1,2-*O*-isopropylidene-β-D-fructopyranose (16). To a soln of **8** (130 mg, 0.2 mmol) in anhyd methanol (10 mL) sodium (about 70 mg) was added with stirring at rt. After the sodium had disappeared, stirring was continued for 1 h. Then the soln was immediately neutralized with the acidic ion exchange resin Amberlite IR 120 (about 7.0 g), filtered and concd under reduced pressure at a temperature below 40°C. The syrupy residue of 4-*O*-(*N*,*N*′-dicyclohexylisoureido)-1,2-*O*-isopropylidene-β-D-fructopyranose was dissolved in 1,2-dichloroethane (10 mL). After addition of chloral (0.5 mL), the mixture was refluxed for 6 h, cooled down and subsequently washed with sat. Na_2–EDTA-soln (twice 5 mL), water (10 mL) and brine (10 mL). The TLC (toluene/EtOAc 6:1 v/v) showed two main spots (**15**: R_f 0.57; **16**: R_f 0.15). After drying (Na_2SO_4), filtration and evaporation of the solvents, the residue was purified by column chromatography (toluene/EtOAc 10:1 v/v) yielding 46 mg (48%) of **15**, mp 198–200°C (Lit.: 198.5–201°C[11]; ^1H and ^{13}C NMR data are identical with those of Ref. [11]), and 10 mg (20%) of **16**, mp 112–113°C (toluene/EtOAc/EtOH).

16: ^1H NMR (250 MHz, $CDCl_3$): δ = 4.81 (dd, 1H, $J_{3,4}$ = 5.1 Hz, $J_{4,5}$ = 7.4 Hz, H-4), 4.77 (dd, 1H, $J_{5,6}$ = 2.0 Hz, H-5), 4.17 (dd, 1H. $J_{6\ gem.}$ = 14.1 Hz, H-6a), 4.14 (d, 1H, $J_{1\ gem.}$ = 9.3 Hz, H-1a), 4.06 (d, 1H, H-6b), 3.99 (d, 1H, H-1b), 3.89 (d, 1H, H-3), 3.00 (br, 1H, OH), 1.50 (s, 3H, CH_3), 1.44 (s, 3H, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 154.3 (C═O), 112.5 ($C(CH_3)_2$), 103.3 (C-2), 76.8, 74.9, 72.6, 68.7 (C-1, C-3, C-4, C-5), 60.1 (C-6), 26.3, 25.9 ($C(CH_3)_2$). IR (KBr): 1829 cm^{-1} (C═O).

Anal. Calcd for $C_{10}H_{14}O_7$ (246.2): C, 48.78 H, 5.73. Found: C, 48.92; H, 5.81.

ACKNOWLEDGMENTS

C.S. is grateful for a grant by the *Studienstiftung des deutschen Volkes*. The *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* promoted our research by financial support.

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Received February 22, 2002
Accepted April 2, 2002