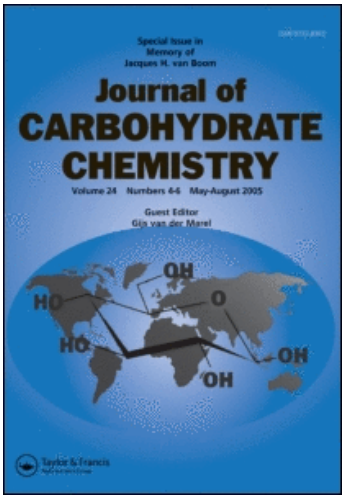

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O-(α-D-Glucopyranosyl)trichloroacetimidate as a Glucosyl Donor

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O-(α-D-GLUCOPYRANOSYL)TRICHLOROACETIMIDATE AS A GLUCOSYL DONOR [1]

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ABSTRACT

Model reactions of O-(α-D-glucopyranosyl)trichloroacetimidate 2α with methanol and cholesterol under various conditions demonstrated that stereocontrolled glucosyl transfer with inversion of configuration at the anomeric center is best carried out in dichloromethane at low temperatures with boron trifluoride-ether as a catalyst. Under these conditions β-glucoside 4β and β-disaccharides 5β - 9β were obtained in good to excellent yields.

With Brønsted acids, fast glucosyl transfer to the acid anion was mainly observed and required no further acidic catalysis. With strong acids formation of the thermodynamically more stable product dominated. However, with the weaker carboxylic acids highly diastereoselective inversion of configuration at the anomeric center led, for instance, to β-1-O-acyl derivatives 11β - 18β, revealing a convenient method for the synthesis of O-glycosyl-carboxylates. This method was also applied to resolution of racemic carboxylic acids.

Similar results were obtained with N-nucleophiles. Hydrazoic acid gave exclusively α-azide 19α. Nitrogen heterocycles gave with boron trifluoride-ether catalysis mainly β-nucleosides 20β - 23β. Reaction of trichloroacetimidate 2α with O-nucleophiles in acetonitrile as solvent led to different products due to competition

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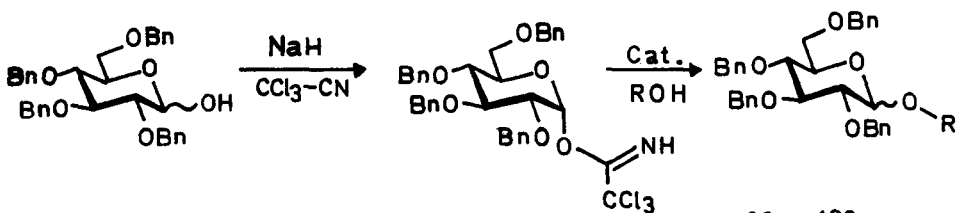
of the acetonitrile nitrogen-atom in the reaction course. The results were compared with an analogous reaction of the corresponding O-glucosyl-N-methyl-acetimidate.

INTRODUCTION

Glycoside bond formation via O-glycosyl trichloroacetimidates has proven quite successful concerning yield and diastereoselectivity. [2,3] Application of neighboring group participation for stereoselective control of the reaction gave 1,2-trans glycosides exclusively. [4,5] Nonparticipating neighboring protective groups led mainly to inversion products when the reaction was carried out with boron trifluoride catalysis at low temperatures. [2, 6-8] The stronger catalyst system trimethylsilyl triflate ($CF_3SO_3SiMe_3$) favored formation of the thermodynamically more stable product. [9]

Trichloroacetimidate activated β-glucopyranoside formation with nonparticipating groups at the 2-position was successfully demonstrated in a synthesis of cellotetraose and derivatives. [10] We have now investigated the influence of different reaction parameters (catalyst, solvent, temperature) on the reaction of O-benzylated O-(α-D-glucopyranosyl)trichloroacetimidate 2α with different O- and N-nucleophiles leading to a more detailed picture of this glycosylation method. Compound 2α is easily obtained from the corresponding 1-OH unprotected glucose 1 (Scheme 1). [2,3,11]

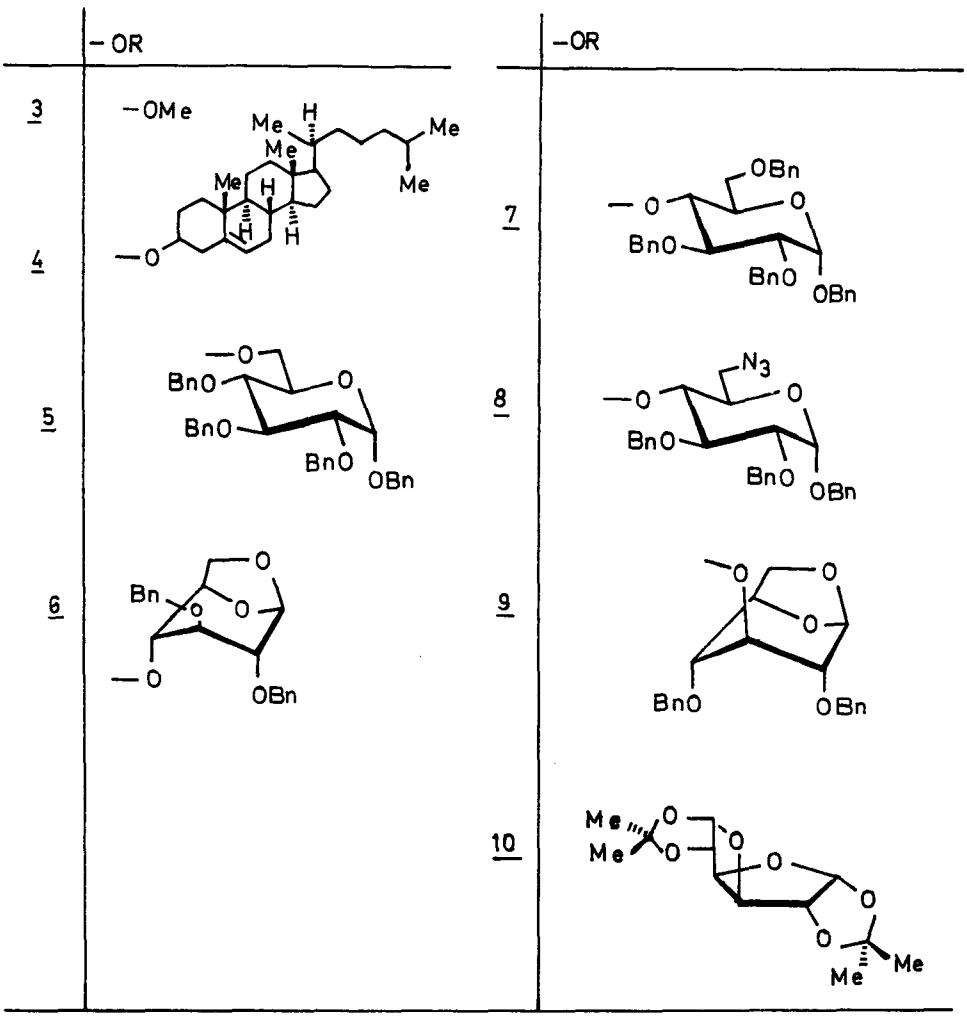
Scheme 1



1 2α 3β – 10β

3α – 8α, 10α

Scheme 1 cont.



RESULTS AND DISCUSSION

A. Reaction of Trichloroacetimidate 2α with Methanol, Cholesterol and Other Alcoholic O-Nucleophiles.

Catalytic activation of O-glycosyl-N-methyl-acetimidates with p-toluenesulfonic acid was reported by Sinaÿ and coworkers.[12] Here we report the results of experiments with O-glycosyl-tri-

Table 1. Reaction of 2α with methanol under various conditions. Formation of glycosides 3α and 3β.

Experiment	[2α]:[MeOH]:[TsOH]			Solvent	Temp. [°C]	Time [h]	Yield [%]	Ratio 3α : 3β
1	1	1	0	CH_2Cl_2	20	24	0	[a]
2	1	[b]	0	MeOH	60	5	100	<1:20
3	1	1	1	CH_2Cl_2	20	24	100	3: 7
4	1	1	1	CH_2Cl_2	20	1.5	90	1: 4
5	1	1	0.25	CH_2Cl_2	-12	8	70 [c]	1:10
6	1	0	1	CH_2Cl_2	20	0.03	[d]	

[a] No reaction; 2α was recovered.
[b] MeOH as reactant and solvent.
[c] In addition 20 % 1 was obtained.
[d] Reaction product was α-D-glucosyl tosylate (see text).

chloroacetimidate 2α as a glucosyl donor, methanol as an acceptor, with and without p-toluenesulfonic acid catalysis (Table 1). Experiments 1 and 2, where no catalyst was added, are borderline cases: reaction with one equivalent of methanol at room temperature gave no glycoside 3; however, reaction in methanol as solvent and reactant at elevated temperature led exclusively to β-glucoside 3β, a result not obtained with other alcoholic nucleophiles. Therefore acidic catalysis of the trichloroacetimidates is commonly required for glycosyl transfer.

Catalysis with p-toluenesulfonic acid at room temperature gave quantitatively methyl glucoside 3α,β (α:β - ratio~3:7; Exp. 3). More β-anomer 3β is obtained by shorter reaction time (Exp. 4) indicating anomerisation under the reaction conditions. Therefore, decreasing the amount of catalyst and lowering the reaction temperature (Exp. 5), led to preferred β-glucoside formation.

Reaction of trichloroacetimidate 2α with equivalent amounts of p-toluenesulfonic acid (Exp. 6) without any other nucleophile present yielded instantaneously O-(α-D-glucopyranosyl)tosylate. The structure of this compound was assigned from ^{1}H NMR data and comparison with literature values. [13] The β- anomer was not detected. This result clearly indicates at least partial intermediacy of O-glycosyl tosylates in glycoside bond formation with p-toluenesulfonic acid catalysis. [14] Because earlier glycosidation reactions with O-benzylated 1-O-tosyl-glucopyranose derivatives synthesized from appropriate glycosyl halides gave only modest results [13,15], p-toluenesulfonic acid and presumably Brønsted acids in general seemed not to be the most promising catalysts. This finding might be also pertinent to the glycosylation with O-glycosyl-N-methyl-acetimidates. [12,16]

Investigations with trichloroacetimidate 2α and cholesterol in different solvents and with different Brønsted acid catalysts confirmed this observation (Table 2). Acceptable yields of glycoside 4 but with low diastereoselectivities were obtained (Exp. 1-9).

Again, lowering the temperature (Exp. 10, 11) led to preferential inversion of the trichloroacetimidate configuration; β-anomer 4β was mainly obtained. This effect was quite dramatic when boron trifluoride-ether was chosen as the catalyst (Exp. 14, 15), this catalyst being favored for stereocontrolled β-glucosylation. Other Lewis acid catalysts like zinc chloride (Exp. 13) or an alkylating agent (Exp. 12) did not show any advantage.

The efficiency of β-glucoside bond formation with trichloroacetimidate 2α dissolved in dichloromethane at low temperatures with boron trifluoride-ether as the catalyst [10] was demonstrated in disaccharide formation with carbohydrate hydroxylic group donors (Scheme 1, Table 3). Under these reaction conditions gentiobiose derivative 5β and cellobiose derivatives 6β and 7β were clearly the preferred products over the corresponding maltose and isomaltose derivatives 5α, 6α and 7α, respectively (Exp. 1-4). The

Table 2. Reaction of 2α with cholesterol [a] under various conditions. Formation of glycosides 4α and 4β.

Exp.	Solvent	Catalyst	[2α]:[ROH][a]:[Cat.]			Temp. [°C]	Time [h]	Yield [%]	Ratio 4α : 4β
1	CH_2Cl_2	TsOH	1.5	1	1	20	24	80	1 : 1
2	Et_2O	TsOH	1.4	1	0.75	20	72	75	2 : 1
3	C_6H_6	TsOH	1	1	0.1	20	2	75	1 : 1
4	THF	TsOH	1	1	1	20	2	70	2 : 1
5	CH_2Cl_2	HBF_4	1	1	0.01	20	24	low	-
6	CH_2Cl_2	HBF_4	1	1	0.03	20	72	70	1 : 1
7	CH_2Cl_2	HBF_4	1	1	0.10	20	0.5	80	1 : 1
8	CH_2Cl_2	CF_3SO_3H	1	1	0.10	20	1	80	1 : 1
9	Et_2O	IR120,$H^{\oplus}$	1.4	1	2	20	72	45	1 : 1
10	CH_2Cl_2	TsOH	1	1	0.25	-10	48	80	1 : 1
11	CH_2Cl_2	TsOH	1.3	1	1	-40	36	61	1 : 5
12	CH_2Cl_2	$Et_3O^+BF_4^-$	1	1	1	20	1	55	1 : 1
13	CH_2Cl_2	$ZnCl_2$	1	1	6	20	20	80	2 : 3
14	CH_2Cl_2	$BF_3 \cdot OEt_2$	1	1	3	20	20	70	2 : 3
15	CH_2Cl_2	$BF_3 \cdot OEt_2$	1.3	1	1	-18	2.5	78	1 :13

[a] Cholesterol = ROH

β-disaccharides 5β and 6β were obtained in excellent yields (Exp. 2, 3). Satisfactory results were also obtained in the formation of 6-azido-6-deoxy-cellobioside derivative 8β against the corresponding maltoside 8α (Exp. 5). Applying similar reaction conditions to 3-O-unprotected 1,6-anhydroglucopyranose gave exclusively the β-anomer 9β, though in modest chemical yield (Exp. 6); the α-anomer was not detected. 1,2:5,6-Di-O-isopropylidene-α-D-glucopyranose is an interesting model case due to the low reactivity of the hydroxylic group in 3-position. Reaction

Table 3. Reaction of 2α with different alcohols ROH[a] in CH_2Cl_2 and $BF_3 \cdot OEt_2$ as catalyst. Formation of compounds 5β-10β, 5α-8α, 10α.

Exp.	[2α]:[ROH][a]		[Cat.]	Temp. [°C]	Time [h]	Yield [%]	Product Ratio
1	1.33	1	1	-18	2.5	90	5α : 5β = 1 : 16
2	1.30	1	0.035	-40	2	85	5α : 5β = 1 : 19
3	1.16	1	0.12	-38	1.5	90	6α : 6β = 1 : 10
4	1.50	1	0.8	-30	2.5	81	7α : 7β = 1 : 4
5	1.25	1	0.62	-30	2.5	63	8α : 8β = 1 : 4
6[b]	1.20	1	0.12	-35	3.5	32	9β
7	1	1	1	-40	2.5	30	10α :10β = 4 : 1

[a] For ROH see Scheme 1.

[b] First run result; the α-anomer was not detected; for yield: see Experimentel.

with compound 2α gave disaccharides 10 in a 4:1 10α/10β-ratio (Exp. 7). This result clearly indicates anomerisation in the catalyst activated trichloroacetimidate intermediate or even carbocation formation before attack of the poor nucleophile takes place. Formation of some α-D-glucopyranosyl fluoride as a by-product in this reaction favors the intermediacy of species with strong carbocation character. [17]

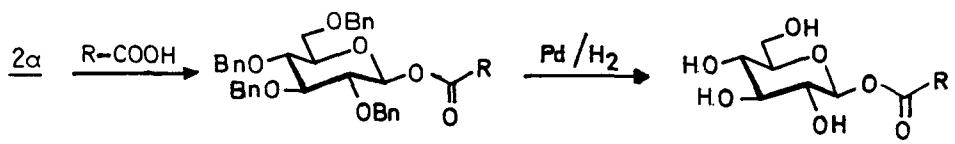
B. Reaction of Trichloroacetimidate 2α with Carboxylic Acids. Racemate Resolution.

The direct uncatalysed glycosylation of Brønsted acids by O-glycosyl trichloroacetimidates is a favorable property of these newly developed glycosyl donors. [2,11,18] Reaction of trichloroacetimidate 2α with phosphorous acid esters demonstrated the ease of glycosyl phosphate formation. [18] Depending on the acidity of the system used, either β- or α-products were formed. Therefore

O-(α-D-glucopyranosyl)tosylate formation (see above), presumably via intermediacy of the corresponding β-tosylate, is not surprising.

Carboxylic acids, being weaker acids, gave with O-α-glucosyl trichloroacetimidate 2α via inversion of trichloroacetimidate configuration mainly or exclusively β-O-acyl compounds (Scheme 2).[19] The reactions were carried out at room temperature with equimolar amounts of acid without addition of any other acidic catalyst. Compounds 11β - 18β were obtained in high yields. The examples in Scheme 2 demonstrate the versatility of this convenient method for O-1 acylation of carbohydrate molecules, which might be also

Scheme 2



11β - 18β-(R),(S) 15A-β 16A-β

	-O2C-R
11	-O2C-CH3
12	-O2C-H
13	-O2C-C6H5
14	-O2C-C6H4-Cl
15	-O2C-C6H4-OAc

	-O2C-R
16	-O2C-CH2-indole
17	-O2C-dioxolane(OMe, Me, Me)
18	-O2C-CH(OMe)-C6H5

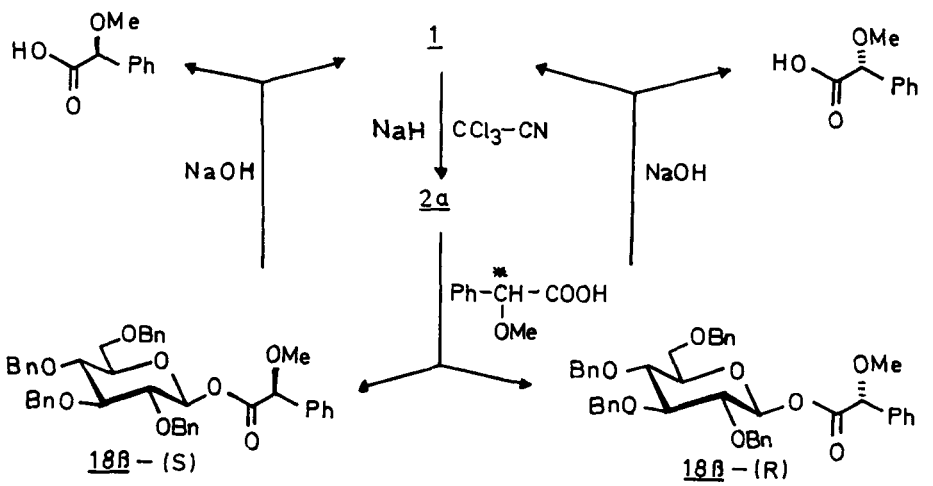
of use for pharmacological drug modification. [20] The method is competing with the different methods published for 1-O-acylation of carbohydrates. [21] It is related to the trichloroacetonitrile activated esterification of carboxylic acids by Cramer and coworkers. [22] It is less cumbersome than using glycosyl halide derived O-glycosyl-N-methylacetimidates as intermediates in this reaction. [23] Hydrogenolytic debenzylation of compounds 15β and 16β gave cleanly the corresponding unprotected β-D-glucopyranosyl carboxylates 15A-β and 16A-β, respectively.

Racemic α-methoxyphenylacetic acid was used in these experiments and led cleanly to the diastereoisomers 18β-(R) and 18β-(S) (Scheme 3), which were completely separated by column chromatography. Treatment of these compounds with sodium hydroxide liberated the enantiomeric acids and starting material 1, which is ready for further transformation into trichloroacetimidate 2α. This sequence demonstrates a new method for the resolution of racemic carboxylic acids.

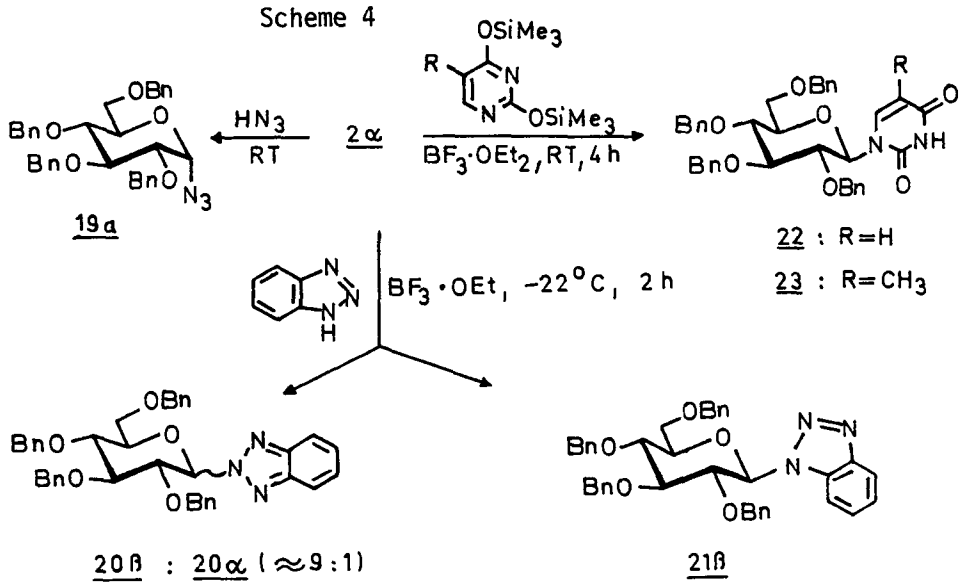
C. Reaction of Trichloroacetimidate 2α with N-Nucleophiles

Hydrazoic acid is a strong acid; therefore it is not surprising that via direct uncatalysed reaction with trichloroacetimidate 2α

Scheme 3



Scheme 4

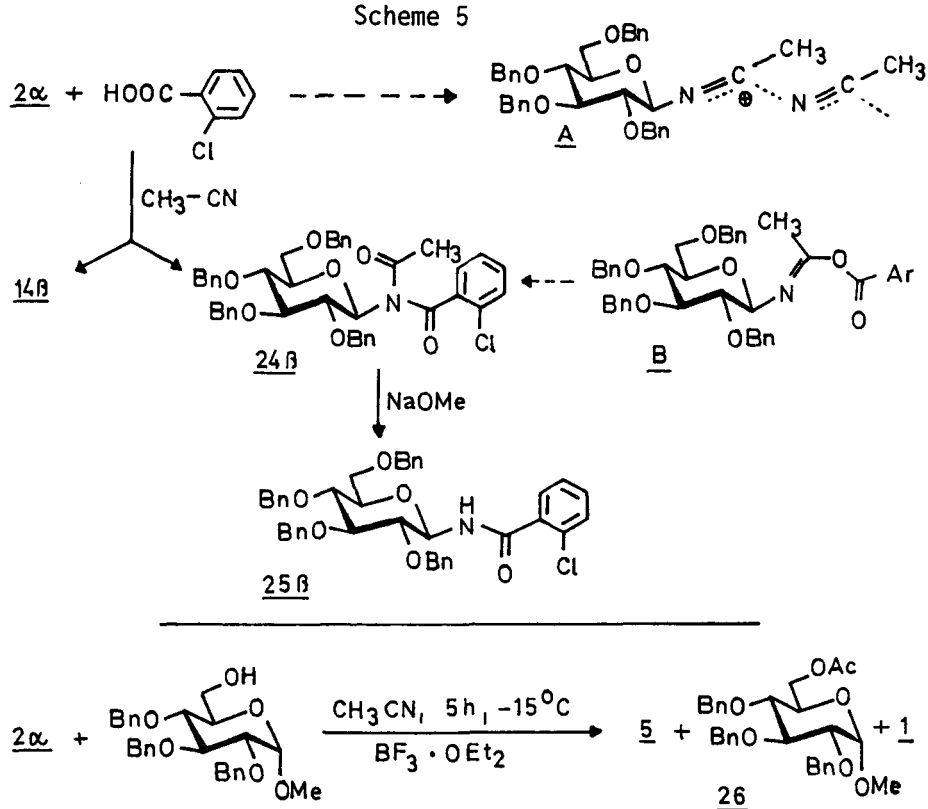


the α-D-glucopyranosyl azide 19α was obtained (Scheme 4). However, nitrogen heterocycles required acidic catalysis for reaction to take place. Benzotriazole gave with boron trifluoride-ether as a catalyst at low temperature again β-connection to the nitrogen -atom at position 2 (51 %, ratio of compounds 20β:20α∼9:1) and to the nitrogen-atom at position 1 (24 %, 21β; the corresponding α-anomer was not detected). The structures of compounds 20α, 20β, and 21β were assigned from ^{1}H NMR data and by comparison of UV data with UV data of 1-methyl- and 2-methylbenzotriazole. [24] The UV data from the latter benzotriazole were in good agreement with those observed for 21β and 20α,β, respectively. Similarly, reaction of trichloroacetimidate 2α with bistrimethylsilylated uracil and thymine and boron trifluoride-ether catalysis gave even at room temperature exclusively the β-connected nucleosides 22β and 23β, respectively. [25] The β-configuration and the C-1 to N-1 connection in these compounds was assigned from ^{1}H NMR data.

D. Reaction of Trichloroacetimidate 2α in Acetonitrile.

Previous successful α-glucoside bond formation by double inversion of configuration via intermediate nitrilium salts [26] led us

Scheme 5



to investigate the reaction of trichloroacetimidate 2α with o-chlorobenzoic acid. Products were the 1-O-acyl compound 14β and the N-bisacylated N-glucoside 24β, which gave with sodium methoxide the N-monoacylated N-glucoside 25β (Scheme 5). Compounds 24β and 25β were obtained exclusively when O-glucosyl-N-methyl acetimidate was used instead of trichloroacetimidate 2α.[12] The assumed reaction course is initiated by proton assisted carbocation formation, then reaction to a nitrilium salt (structure A[26]) which leads to O-aroyl acetimidate B.[12] Compound B then rearranges to reaction product 24β.

The higher reactivity of trichloroacetimidate 2α compared with O-glucosyl-N-methyl-acetimidate is again demonstrated by this difference in results. Proton transfer from o-chlorobenzoic acid to the trichloroacetimidate group generates o-chlorobenzoate and

subsequently fast formation of compound 14β, presumably via a tight ion pair. Competing nucleophilic attack of the nitrile nitrogen-atom to give nitrilium salt A is favored by ion separation, which is more probable for more stable protonated imidate species.

Comparable results were obtained when trichloroacetimidate 2α and methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside were treated with boron trifluoride-ether in acetonitrile. Competition between the nucleophilic 6-hydroxylic group and the acetonitrile nitrogen-atom gave β-disaccharide 5β (43 %), O-acetylated compound 26 (21 %), and hydrolysis product 1 (35 %). Formation of compound 26 is assumed to take place by reaction of the 6-hydroxylic group with intermediate A and subsequent hydrolysis. Attack of the hydroxylic group at C-1 of intermediate A which would give rise to the corresponding α-disaccharide was not observed.

EXPERIMENTAL

General Procedures. Melting points are uncorrected. ^{1}H NMR spectra were recorded in the solvents noted (Me_4Si, 0.00 ppm) with a Bruker CP 80 CW and a Bruker WM 250 Cryospec. R_F values refer to TLC performed on silica gel (Merck) with the solvent systems noted. Column chromatography was performed under normal pressure with silica gel (Merck, 70-325 mesh) and under medium pressure with silica gel (Merck, "LiChroprep" Si 60, 40-60 μm) with the solvent systems noted. Preparative thin-layer chromatography was done using glass plates (20 cm x 20 cm) coated with silica gel (PF-254, Merck) with the solvent systems noted. Optical rotation was determined with a Perkin-Elmer 241 MC.
IR-spectra were recorded with a Perkin Elmer Model 621 and UV spectra with a Cary 118.

O-(2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl)trichloroacetimidate (2α). Compound 2α was prepared from 2,3,4,6-tetra-O-benzyl-D-glucose according to ref. 11.

Methyl 2,3,4,6-Tetra-O-benzyl-α- and -β-D-glucopyranoside (3α and 3β). All experiments of Table 1 were carried out with 1 mmol compound 2α in 10 ml solvent. After the reaction times indicated in Table 1 the reaction mixtures were treated with solid sodium hydrogen carbonate and then extracted with dichloromethane/sodium hydrogen carbonate solution in water. The dichloromethane extracts were concentrated and the anomers separated by chromatography on silica gel (petroleum ether/ethyl acetate = 1:1, normal pressure): yields and α/β-ratios are summarized in Table 1; TLC (petroleum ether/ethylacetate = 1:1) 3α: R_F = 0.43, 3β: R_F = 0.62.

Compounds 3α and 3β gave ^{1}H-NMR spectral and optical rotation data identical with that reported for authentic material. [27]

Cholesteryl 2,3,4,6-Tetra-O-benzyl-α- and -β-D-glucopyranoside (4α and 4β). Experiment 10 in Table 2: Compound 2α (1.61 g, 2.35 mmol) and cholesterol (909 mg, 2.35 mmol) were dissolved in 25 mL of dry dichloromethane, the solution cooled to -10 °C, and then p-toluenesulfonic acid (101 mg, 0.59 mmol) added. After 48 h at -10 °C excess solid sodium hydrogen carbonate was added to the reaction mixture and then extracted with dichloromethane/sodium hydrogen carbonate solution in water. The dichloromethane extract was washed with water, dried with sodium sulfate, and then concentrated. The oily residue was separated by chromatography on silica gel (chloroform/petroleum ether = 10:1, medium pressure): yield 855 mg (40 %) of compound 4α; $[\alpha]_{589}^{20}$ = +46.0° (c = 1.5, $CHCl_3$) [lit. [28] $[\alpha]_{589}^{23}$ = + 44° (c = 1.2, $CHCl_3$)]; TLC R_F = 0.53 (chloroform/petroleum ether = 1:1); mp 140-142 °C from ethanol (lit. [28] mp. 142 °C); yield 855 mg (40 %) of compound 4α; $[\alpha]_{589}^{20}$ = +0.2° (c = 1.6, $CHCl_3$) [lit. [28] $[\alpha]_{589}^{23}$ = -0.4° (c = 1.2, $CHCl_3$)]; TLC R_F = 0.41 (chloroform/petroleum ether = 1:1); mp. 108-109 °C from chloroform/ethanol = 1:10 (lit. [28] mp. 96-97 °C from ethanol).

Anal. Calcd for $C_{61}H_{80}O_6$ (909.3): C, 80.57. H, 8.87. Found: 4α: C, 80.09, H. 8.87. 4β: C, 80.40; H, 8.79.

Experiments 1-9 and 11-13 in Table 2 were carried out as described above.

Experiments 14 and 15 in Table 2: The reactions were carried out as described above. Boron trifluoride-ether was added as 0.4 molar solution in dichloromethane within 45 min.

Methyl 6-O-(2,3,4,6-Tetra-O-benzyl-α- and -β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (5α and 5β). Experiment 1 in Table 3. Compound 2α (1.10 g, 1.60 mmol) and methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside [29] (558 mg, 1.2 mmol) were dissolved in 20 mL of dry dichloromethane, the solution cooled to -18 °C, and then boron trifluoride-ether (3 mL of a 0.4 molar solution) added during 45 min. After 2 h at -18 °C the reaction mixture was treated with excess solid sodium carbonate and then with dichloromethane/sodium hydrogen carbonate solution in water. The dichloromethane extract was washed with water, dried with sodium sulfate, and then concentrated. The oily residue was filtered through silica gel (chloroform/ethyl ether = 20:1): yield 1.07 g (90 %) pure mixture of compounds 5α and 5β; this material was chromatographed on silica gel (chloroform/petroleum ether/ethyl ether = 20:8:1, normal pressure): yield 62 mg (5 %) of sirupy 5α; $[\alpha]_{589}^{20}$ = +57° (c = 1.2, $CHCl_3$); TLC R_F = 0.46 (chloroform/ethyl ether = 20:1); yield 1005 mg (85 %) colourless crystals of 5β; $[\alpha]_{578}^{20}$ = +17.9° (c = 1, $CHCl_3$); TLC R_F = 0.43 (chloroform/ethyl ether = 20:1); mp. 133-134 °C from chloroform/ethanol = 1:15 (lit. [30] mp. 131-133 °C).

Compounds 5α and 5β gave ^{1}H-NMR spectral and optical rotation data identical with that reported for authentical material. [13, 27, 30]

Experiment 2 in Table 3 was carried out as described above.

1,6-Anhydro-4-O-(2,3,4,6-tetra-O-benzyl-α and -β-D-glucopyranosyl)-2,3-di-O-benzyl-β-D-glucopyranose (6α and 6β). Experiment 3 in Table 3: Compound 2α (9.59 g, 14.0 mmol) and 1,6-anhydro-2,3-di-O-benzyl-β-D-glucopyranose [31] (4.11 g, 12.0 mmol) were dis-

solved in 150 mL of dry dichloromethane and the reaction carried out as described for compounds 5α and 5β. The oily residue obtained was chromatographed on silica gel (chloroform/ethyl ether = 20:1, normal pressure): yield 0.85 g (8.2 %) of compound 6α as colourless oil $[\alpha]_{578}^{20}$ = +9.6° (c = 1, $CHCl_3$) [lit. [32] $[\alpha]_{589}^{22}$ = 7.7° (c = 2, $CHCl_3$) ; TLC R_F = 0.53 (chloroform/ethyl ether = 20:1); ^{13}C NMR (62.97 MHz, $CDCl_3$) δ 100.74 (C-1); 97.91 (C-1'). - Yield 8.5 g (81.8 %) of compound 6β; $[\alpha]_{578}^{20}$ = -18.5° (c = 1, $CHCl_3$) [lit. [33] $[\alpha]_{589}^{25}$ = -19.7° (c = 2.5, $CHCl_3$); TLC R_F = 0.38 (chloroform/ethyl ether = 20:1); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 102.59 (C-1'), 100.89 (C-1); mp. 88-89 °C from methanol (lit. [34] 86-87 °C from ethyl ether/petroleum ether).

Anal. Calcd for $C_{54}H_{56}O_{10}$ (865.0): C, 74.98; H, 6.53.
Found: 6α: C, 74.79; H, 6.43. 6β: C, 74.33; H, 6.71.

Methyl 4-O-(2,3,4,6-Tetra-O-benzyl-α- and -β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (7α and 7β). Experiment 4 in Table 3: Compound 2α (1.54 g, 2.25 mmol) and methyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside [34] (697 mg, 1.50 mmol) were dissolved in 25 mL of dry dichloromethane and the reaction carried out as described for compounds 5α and 5β. The oily residue obtained was chromatographed on silica gel (chloroform/ethyl ether = 20:1, normal pressure); yield 290 mg (19 %) of compound 7α as an oil; $[\alpha]_{578}^{20}$ = +39.5° (c = 1, $CHCl_3$) [lit. [12] $[\alpha]_{589}^{20}$ = +48° (c = 1.05, $CHCL_3$; TLC R_F = 0.64 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 5.72 (d, 1H, H-1'; $J_{1',2'}$ = 3 Hz), 3.40 (s, 3H, OCH_3). - Yield 910 mg (62 %) colourless crystals of compound 7β; $[\alpha]_{578}^{20}$ = +25.3° (c = 1, $CHCl_3$); TLC R_F = 0.55 (chloroform/ethyl ether = 20:1); mp. 85-88 °C from methanol.

Anal. Calcd for $C_{62}H_{66}O_{11}$ (987.2): C, 75.43; H, 6.74
Found: 7α: C, 75,54; H, 6.64. 7β: C, 75.34; H, 6.77.

Benzyl 6-Azido-4-O-(2,3,4,6-tetra-O-benzyl-α- and -β-D-glucopyranosyl)-2,3-di-O-benzyl-6-deoxy-α-D-glucopyranoside (8α and 8β).

Experiment 5 in Table 3: Compound 2α (627 mg, 0.90 mmol) and benzyl-6-azido-2,3-di-O-benzyl-α-D-glucopyranoside [29] (380 mg, 0.80 mmol) were dissolved in 20 mL of dry dichlormethane and the reaction carried out as described for compounds 5α and 5β. The oily residue obtained was chromatographed on silica gel; petroleum ether/ethyl ether = 3:2 (medium pressure); yield 90 mg (11 %) of compound 8α as an oil; $[\alpha]_{578}^{20}$ = +91.7° (c = 1.6, $CHCl_3$); TLC R_F = 0.87 (chloroform/ethyl ether = 20:1); IR (NaCl) 2090 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 5.59 (d, 1H, H-1'; $J_{1',2'}$ = 3.7 Hz). - Yield 420 mg (53 %) of compound 8β as an oil; $[\alpha]_{578}^{20}$ = 58.6° (c = 1, $CHCl_3$); TLC R_F = 0.71 (chloroform/ethyl ether = 20:1); IR (NaCl) 2090 cm^{-1} (N_3).

Anal. Calcd for $C_{61}H_{63}N_3O_{10}$ (989.2): C, 73.40; H, 6.36; N 4.21. Found: 8α C, 73.25; H, 6.36; N, 4.09. 8β C, 73.78; H, 6.59; N, 4.57.

1,6-Anhydro-3-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2,4-di-O-benzyl-β-D-glucopyranose (9β). Experiment 6 in Table 3: Compound 2α (1.32 g, 1.93 mmol) and 1,6-anhydro-2,4-di-O-benzyl-β-D-glucopyranose [31, 35] (550 mg, 1.61 mmol) were dissolved in 20 mL of dry dichloromethane and the reaction carried out as described for compounds 5α and 5β. The oily residue obtained was chromatographed on silica gel (toluene/acetone = 9:1, normal pressure): yield 500 mg 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl fluoride [17]; TLC R_F = 0.77 (toluene/acetone = 9:1); ^1H NMR ($CDCl_3$) δ 5.59 (dd, 1H, H-1; $J_{1,2}$ = 2.5 Hz; $J_{1,F}$ = 53.5 Hz); - yield 280 mg (51 %) of 1,6-anhydro-2,4-di-O-benzyl-β-D-glucopyranose; TLC R_F = 0.22 (toluene/acetone = 9:1). - Yield 220 mg (32 %, based on used 1,6-anhydro-2,3-di-O-benzyl-β-D-glucopyranose) of compound 9β as an oil; $[\alpha]_{578}^{20}$ = +17.1° (c = 1, $CHCl_3$); TLC R_F = 0.54 (toluene/acetone = 9:1); ^1H NMR ($CDCl_3$) δ 7.4-7.1 (m, 30 H, $6C_6H_5$), 5.50 (s, 1H, H-1), 5.0-3.2 (m, 25 H).

Anal. Calcd for $C_{54}H_{56}O_{10}$ (865.0): C, 74.98; H, 6.53. Found: C, 74.44, H, 6.55.

3-O-(2,3,4,6-Tetra-O-benzyl-α- and β-D-glucopyranosyl)-1:2,5:6-di-O-isopropylidene-α-D-glucofuranose (10α and 10β). Experiment 7 in Table 3: Compound 2α (342 mg, 0.50 mmol) and 1:2,5:6-di-O-isopropylidene-α-D-glucofuranose (130 mg, 0.5 mmol) were dissolved in 10 mL of dry dichloromethane and the reaction carried out as described for compounds 5α and 5β. The oily residue obtained was chromatographed on silica gel (petroleum ether/ethyl ether = 2:1, medium pressure): yield 95 mg (24 %) of compound 10α as an oil; $[\alpha]_{589}^{20}$ = +40.4° (c = 2, $CHCl_3$) [lit.[26] $[\alpha]_{589}^{20}$ = +43° (c = 2, $CHCl_3$)]; TLC R_F = 0.50 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 7.6-7.2 (m, 20H, $4C_6H_5$), 6.03 (d, 1H, H-1; $J_{1,2}$ = 3.7 Hz), 5.38 (d, 1H, H-1'; $J_{1',2'}$ = 3.6 Hz), 5.25-3.43 (m, 20 H), 1.50, 1.45 (2s, 6H, $2CH_3$), 1.33 (s, 6H, $2CH_3$). - Yield 22 mg (6 %) of compound 10β as colourless crystals; $[\alpha]_{589}^{20}$ = +11° (c = 1, $CHCl_3$); TLC R_F = 0.30 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 7.6-7.2 (m, 20 H, 4 C_6H_5), 5.88 (d, 1H, H-1; $J_{1,2}$ = 3.7 Hz), 5.05-4.38 (m, 13 H), 4.15 (d, 1 H, H-1', $J_{1',2'}$ = 7.4 Hz), 3.9-3.3 (m, 7 H), 1.50, 1.44, 1.34, 1.25 (4s, 12 H, 4 CH_3). - Yield 25 mg (9 %) 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl fluoride (see procedure for compound 9β).

Anal. Calcd for $C_{46}H_{54}O_{11}$ (782.9): C, 70,57; H, 6.95
Found: 10α C, 70.35; H, 6.80. 10β C, 70.44; H, 6.81.

1-O-Acetyl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranose (11). A solution of compound 2α (380 mg, 0.55 mmol) in 8 mL of dry dichloromethane was treated at room temperature with acetic acid (115 mg, 1.92 mmol). The reaction mixture was concentrated after 2 h and excess acetic acid was removed by azeotropic distillation with toluene under reduced pressure (10 torr). The oily residue obtained was chromatographed on silica gel (chloroform/ethyl ether = 20:1, normal pressure): Yield 270 mg (84 %). $[\alpha]_{578}^{20}$ = +13.1° (c = 1.h, $CHCl_3$); IR (NACl) 1750 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 5.61 (d, 1 H, H-1; $J_{1,2}$ = 7.2 Hz), 2.00 (s, 3 H, $COCH_3$).

The compound 11β gave ^1H NMR spectral and optical rotation data identical with that reported for authentic material.[37]

1-O-Formyl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranose (12). A solution of compound 2α (650 mg, 0.95 mmol) in 5 mL of dry dichloromethane was treated at room temperature with formic acid (175 mg, 3.80 mmol). As described for 11β, 380 mg (70 %) of compound 12β were obtained as an oil. $[\alpha]_{578}^{20}$ = +23.7° (c = 1.4, $CHCl_3$); TLC R_F = 0.62 (chloroform/ethyl ether = 20:1); IR (NaCl) 1738 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 8.0 (s, 1 H, CHO), 6.56 (d, 1 H, H-1; $J_{1,2}$ = 7.0 Hz).

Anal. Calcd for $C_{35}H_{36}O_7$ (568.7): C, 73.93; H. 6.38. Found: C, 74.07; H, 6.24.

1-O-Benzoyl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranose (13β). To a solution of compound 2α (1.07 g, 1.56 mmol) in 6 mL of dry dichloromethane was added at room temperature benzoic acid (210 mg, 1.72 mmol). After 5 h excess acid was removed by washing the reaction mixture with aqueous hydrogen carbonate solution. The dichloromethane extract was concentrated and the residue crystallized from methanol. Yield 824 mg (82 %) of compound 13β as colourless needles; mp. 91-92 °C; $[\alpha]_{578}^{20}$ = -24.2° (c = 2.0, $CHCl_3$); TLC R_F = 0.66 (chloroform/ethyl ether = 20:1); IR (NaCl) 1735 cm^{-1} (CO); ^1H-NMR ($CDCl_3$) δ 5.92 (d, 1 H, H-1; $J_{1,2}$ = 7.0 Hz).

Anal. Calcd for $C_{41}H_{40}O_7$ (644.8): C, 76.38; H, 6.25. Found: C, 76.07; H, 6.45.

2,3,4,6-Tetra-O-benzyl-1-O-(2-chlorobenzoyl)-β-D-glucopyranose (14β). To a solution of compound 2α (750 mg, 1.095 mmol) in 5 mL of dry dichloromethane was added at room temperature 2-chlorobenzoic acid (172 mg, 1.095 mmol). As described for 13β a solid residue was obtained, which was recrystallized from ethyl ether/petroleum ether. Yield 595 mg (80 %) colourless crystals of compound 14β; mp 107-108 °C; $[\alpha]_{578}^{20}$ = -16.0 ° (c = 1.0, $CHCl_3$); IR (NaCl) 1740 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 5.92 (d, 1 H, H-1, $J_{1,2}$ = 7 Hz).

Anal. Calcd for $C_{41}H_{39}ClO_7$ (679.2): C, 72.50; H, 5.79. Found: C, 72.60; H, 5.91.

1-O-(2-Acetoxybenzoyl)-2,3,4,6-tetra-O-benzyl-β-D-glucopyranose (15β). To a solution of compound 2α (3.0 g, 4.38 mmol) in 30 mL of dry dichloromethane was added at room temperature 2-acetoxybenzoic acid (790 mg, 4.38 mmol). After 3 h the reaction mixture was concentrated and the solid residue recrystallized from methanol: Yield 2.41 g (78 %) colourless needles of compound 15β; mp 85-86 °C; $[\alpha]_{578}^{20}$ = -11.0 ° (c = 1.0, $CHCl_3$); TLC R_F = 0.69 (chloroform/ethyl ether = 20:1); IR (NaCl) 1765 cm^{-1} (CO), 1730 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 5.95 (d, 1 H, H-1; $J_{1,2}$ = 7 Hz).

Anal. Calcd for $C_{43}H_{42}O_5$ (702.8): C, 73.49; H, 6.02. Found: C, 73.30; H, 5.98.

When the mother liquor from the recrystallization was concentrated, an oily residue was obtained, which was chromatographed on silica gel (chloroform/ethyl ether = 20:1; medium pressure): yield 200 mg (7 %) of compound 15β and 200 mg (7 %) of the corresponding α-anomer; TLC R_F = 0.62 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 6.59 (d, 1 H, H-1; $J_{1,2}$ = 3.0 Hz), 2.34 (s, 3 H, CH_3CO).

1-O-(2-Acetoxybenzoyl)-β-D-glucopyranose (15A-β) Compound 15β (300 mg, 0.43 mmol) was dissolved in a mixture of 15 mL of methanol, 10 mL of ethyl acetate, and 10 mL of acetic acid. After addition of 200 mg of palladium black catalyst [38] hydrogenation was monitored by TLC (chloroform/methanol = 3:1). After complete formation of a single product with R_F = 0.52 the reaction mixture was filtered and then the filtrate several times concentrated with toluene: yield 135 mg (96 %) of compound 15A-β as a colourless foam; $[\alpha]_{578}^{20}$ = -22.6° (c = 1.0, methanol); ^1H NMR (CD_3OD) δ 5.75 (br.d, 1 H, H-1), 2.37 (s, 3 H, CH_3CO).

2,3,4,6-Tetra-O-benzyl-1-O-[2-indolyl-(3)-acetyl]-β-D-glucopyranose (16β). Compound 2α (3.0 g, 4.38 mmol) and indolyl-3-acetic acid (767 mg, 4.38 mmol) were added to 50 mL of dry dichloromethane at room temperature. The suspension obtained became clear. The reaction mixture was concentrated after 6 h and

the residue obtained filtered through silica gel (chloroform/ethyl ether = 20:1). The filtrate was concentrated and the solid recrystallized from methanol: yield 2.4 g (77 %) colourless crystals of compound 16β; mp 104-105 °C; $[\alpha]_{578}^{20}$ = +0.4° (c = 1.0, $CHCl_3$); TLC R_F = 0.47 (chloroform/ethyl ether = 20:1); IR (NaCl) 3400 cm^{-1} (NH), 1750 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 8.04 (s, 1 H, NH), 5.71 (d, 1 H, H-1; $J_{1,2}$ = 7.6 Hz).

Anal. Calcd for $C_{44}H_{43}NO_7$ (697.8): C, 75.73; H, 6.21; N, 2.01. Found: C, 75.87; H, 6.32; N, 1.96.

When the mother liquor from the recrystallization was concentrated an oily residue was obtained, which was chromatographed on silica gel (chloroform/ethyl ether = 20.1, medium pressure), yield 150 mg (5 %) of compound 16β and 190 mg of a compound which seemed to be the α-anomer; TLC R_F = 0.53 (chloroform/ethyl ether = 20.1).

1-O-[2-Indolyl-(3)-acetyl]-β-D-glucopyranose (16A-β). Compound 16β (440 mg, 0.63 mmol) was hydrogenated as described for 15A-β. The product obtained was chromatographed on silica gel (chloroform/methanol = 3:1, medium pressure): yield 150 mg (71 %) of compound 16A-β as a colourless foam; $[\alpha]_{578}^{20}$ = +2.8 ° (c = 1.0, methanol), TLC R_F = 0.43 (chloroform/methanol = 3:1); ^1H NMR (CD_3CD) δ 7.6 - 6.9 (m, 6 H), 5.53 (d, 1 H, H-1, $J_{1,2}$ = 7.6 Hz), 3.9-3.2 (m, 8 H).

Methyl 5-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-β-D-ribofuranosiduronate (17β). To a solution of compound 2α (510 mg, 0.74 mmol) in 6 mL of dry dichloromethane was added methyl 2,3-O-isopropylidene-β-D-ribofuranosiduronic acid [37, 39] (162 mg, 0.74 mmol) at room temperature. After 4 h the reaction mixture was concentrated and the oily residue chromatographed on silica gel (chloroform/ethyl ether = 20:1, normal pressure): yield 420 mg (76 %) of compound 17β as a colourless oil; $[\alpha]_{578}^{20}$ = 9.2 ° (c = 1.5, $CHCl_3$); TLC R_F = 0.48 (chloroform/

ethyl ether 20:1); IR (NaCl) 1774 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 7.4-7.1 (m, 20 H, 4 C_6H_5), 5.63 (d, 1 H, H-1; $J_{1,2}$ = 7.0 Hz), 5.2-4.4 and 3.9-3.5 (2 m), 3.32 (s, 3 H, OCH_3), 1.48 and 1.30 (2 s, 6 H, 2 CH_3).

Anal. Calcd for $C_{43}H_{48}O_{11}$ (740.8): C, 69.72; H, 6.53. Found: C, 69.45; H, 6.44.

According to TLC of the reaction mixture there was a trace (>5 %) of the α-anomer with R_F = 0.57 (chloroform/ethyl ether = 20:1) present. Identification of the α-anomer was possible by an authentical example.[40]

2,3,4,6-Tetra-O-benzyl-1-O-[(R)-2-methoxy-2-phenylacetyl]-β-D-glucopyranose [18β-(R)] and 2,3,4,6-Tetra-O-benzyl-1-O-[(S)-2-methoxy-2-phenylacetyl]-β-D-glucopyranose [18β-(S)].

a) Synthesis and Diastereoisomer separation. To a solution of compound 2α (2.60 g, 3.80 mmol) in 15 mL of dry dichloromethane was added (R,S)-2-methoxy-2-phenylacetic acid (631 mg, 3.80 mmol) at room temperature. After 2 h the reaction was complete as indicated by TLC. The reaction mixture was concentrated and chromatographed on silica gel (chloroform/ethyl acetate = 20:1, normal pressure). The resulting mixture of diastereoisomers was separated by chromatography on silica gel (petroleum ether/ethyl ether = 2:1; medium pressure): yield 1.17 g (45 %) of compound 18β-(S) and 1.18 g (45 %) of compound 18β-(R); both compounds were obtained as colourless crystals from petroleum ether/ethyl ether; mp 18β-(R): 87-88 °C, 18β-(S): 78-79 °C; $[\alpha]_{578}^{20}$ 18β-(R) = -27.1 ° (c = 1.0, $CHCl_3$), 18β-(S) = +18.3 ° (c = 1, $CHCl_3$); TLC 18β-(R): R_F = 0.33, 18β-(S): R_F = 0.41 (petroleum ether/ethyl ether = 2:1); ^1H-NMR ($CDCl_3$) δ 18β-(R): 5.67 (d, 1 H, H-1; $J_{1,2}$ = 7.93 Hz), 3.40 (s, 3 H, OCH_3); 18β (S): 5.67 (d, 1 H, H-1; $J_{1,2}$ = 7.78 Hz), 3.40 (s, 3 H, OCH_3).

Anal. Calcd for $C_{43}H_{44}O_8$ (688.8): C, 74.98; H, 6.44. Found: 18β-(R): C, 75,13; H, 6.30. 18β-(S): C, 74.85; H, 6.60.

b) Cleavage of Compound 18β-(R) into Compound 1 and (R)-2-Methoxy-2-phenylacetic Acid. To a solution of compound 18β-(R) (650 mg, 0.94 mmol) in 15 mL of dioxane was added a solution of 5 mL 3 N sodium hydroxide in water at 10 °C. After 2.5 h quantitative cleavage was indicated by TLC. The organic solvent was evaporated under reduced pressure (10 torr). The residue was treated with ethyl ether/water and the phases separated. The aqueous phase was washed with ethyl ether (50 mL) and then the combined ether extracts were washed with 2 N sodium hydroxide (20 mL). The ether phase gave after concentration and filtration through silica gel (ethyl ether) 482 mg (95 %) of compound 1. The aqueous phases were acidified with 1 N hydrochloric acid to pH 1.5 and extracted with ethyl ether (5 x 40 mL). The extract was dried with sodium sulfate and concentrated: yield 151 mg (96 %) (R)-2-methoxy-2-phenylacetic acid as slightly yellow oil, which contained no impurities according to TLC. Treatment with ethanol gave colourless crystals; mp 62-64 °C (lit.[41] 65-66 °C); $[\alpha]_{589}^{20}$ = -145° (c = 0.57, ethanol) [lit.[41] = -146 ° (c = 0.5, ethanol)]; TLC R_F = 0.38 (chloroform/methanol = 6:1).

c) Cleavage of Compound 18β-(S) into Compound 1 and (S) 2-Methoxy-2-phenylacetic Acid. As described for 18β-(R) from 18β-(S) (750 mg, 1.09 mmol) 176 mg (97 %) (S)-2-methoxy-2-phenylacetic acid were obtained as slightly yellow oil, which gave after ethanol treatment colourless crystals; mp 62-64 °C (lit.[41] 64-65 °C); $[\alpha]_{589}^{20}$ = +144 ° (c = 0.57, ethanol) [lit.[41] = +146 ° (c = 0.5, ethanol)]; TLC R_F = 0.53 (chloroform/methanol = 3:1).

1-Azido-2,3,4,6-tetra-O-benzyl-α-D-glucopyranose (19α). To a solution of compound 2α (340 mg, 0.5 mmol) in 5 mL of dry dichloromethane 0.5 ml hydrazoic acid in ethyl ether[42] (1 N solution) was added at room temperature. After 10 h again 1 mL of this hydrazoic acid solution was added. After 3 h the reaction mixture was concentrated under reduced pressure (10 torr) and the residue chromatographed on silica gel (petroleum ether/ethyl ether = 1:1): yield 170 mg (61 %) of compound 19α as colourless oil; $[\alpha]_{578}^{20}$ =

+68.3 ^{o} (c = 1.5, $CHCl_3$); TLC R_F = 0.62 (petroleum ether/ethyl ether = 0.70); IR (NaCl) 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 7.5-7.0 (m, 20 H, 4 C_6H_5), 5.22 (d, 1 H, H-1; $J_{1,2}$ = 3.7 Hz), 5.0-4.3, 4.0-3.4 (2 m).

Anal. Calcd for $C_{34}H_{35}N_3O_5$ (565.7): C, 72.19; H, 6.24; N, 7.43. Found: C, 72.03; H, 6.28; N, 7.29.

2-(2,3,4,6-Tetra-O-benzyl-α- and -β-D-glucopyranosyl)-1,2,3-benzotriazole (20α and 20β) and 1-(2,3,4,6-Tetra-O-benzyl)-β-D-glucopyranosyl-1,2,3-benzotriazole (21β). Compound 2α (1.27 g, 1.85 mmol) and 1,2,3-benzotriazole (220 mg, 1.85 mmol) were dissolved in 25 mL of dry dichloromethane, the solution cooled to -22 ^{o}C, and then boron trifluoride - ether (1.25 mL of a 0.4 molar solution in dichloromethane) added. After 2 h the reaction mixture was treated with solid sodium carbonate and then with dichloromethane/aqueous sodium hydrogen carbonate solution. The dichloromethane extract was washed with water, dried with sodium sulfate, and concentrated. The oily residue was chromatographed on silica gel (chloroform/ethyl ether = 20:1, normal pressure) which gave 280 mg (24 %) of compound 21β as a colourless oil and 730 mg (61 %) of a mixture of compounds 20α and 20β. Treatment with 60 mL of methanol gave 420 mg (35 %) of compound 20β as colourless crystals. The mother liquor was concentrated and chromatographed on silica gel (petroleum ether/ethyl ether = 3:2; medium pressure): yield: 180 mg (16 %) of compound 20β and 70 mg (6 %) of compound 20α as colourless oil.

20α: $[\alpha]_{578}^{20}$ = +93.0 ^{o} (c = 0.5, $CHCl_3$); TLC R_F = 0.81 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 8.1-7.8 (m, 2 H), 7.6-7.1 (m, 22 H), 6.64 (d, 1 H, H-1'; $J_{1',2'}$ = 6.0 Hz), 5.2-3.5 (m, 14 H); UV (nm in methanol, lgε) 282.5 (4.01), 278.6 (4.07), 273 (4.04).

20β: mp 108-109 ^{o}C from methanol; $[\alpha]_{578}^{20}$ = -34.6 ^{o} (c = 1, $CHCl_3$); TLC R_F = 0.74 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 8.1-8.2 (m, 2 H), 7.5-6.7 (m, 22 H), 5.96 (d, 1 H, H-1';

$J_{1',2'}$ = 9.0 Hz), 5.0-3.7 (m, 14 H); UV (nm in methanol, lgε) 285.5 (4.01), 281.3 (4.11), 273.6 (4.01).

21β: $[\alpha]_{578}^{20}$ = -22.8 ° (c = 1, $CHCl_3$); TLC R_F = 0.51 (chloroform/ethyl ether = 20:1); ^1H NMR ($CDCl_3$) δ 8.3-8.0 (m, 2 H), 7.8-6.6 (m, 22 H), 6.02 (d, 1 H, H-1', $J_{1',2'}$ = 9.0 Hz), 5.1-3.6 (m, 14 H); UV (nm in methanol, lgε) 283 (3.68), 255 (3.92).

Anal. Calcd for $C_{40}H_{39}N_3O_5$ (641.8): C, 74.86; H, 6.13; N, 6.55. Found 20α: C, 74.37; H, 6.28; N, 6.57. 20β: C, 74.85; H, 6.12; N, 6.56. 21β: C, 74.81; H, 6.12; N, 6.58.

1-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)uracil (22β). Compound 2α (0.50 g, 0.73 mmol) and 2,4-bis (trimethylsilyloxy) pyrimidine [43] (0.50 g, 1.9 mmol) were dissolved in 25 mL of dry dichloromethane and then at room temperature boron trifluoride-ether (1.5 mL of a 0.5 molar solution in dichloromethane) added. After 2 h the reaction mixture was treated with a concentrated aqueous solution of sodium hydrogen carbonate. The dichloromethane extract was dried with sodium sulfate and the oily residue chromatographed on silica gel (toluene/acetone = 2:1, medium pressure). Yield 0.30 g (62 %) of compound 22β as colourless oil; $[\alpha]_{578}^{20}$ = -14.8° (c = 1, $CHCl_3$); TLC R_F = 0.41 (toluene/acetone = 2:1); ^1H NMR ($CODCl_3$) δ 9.7 (br.s, 1 H, NH), 7.5-7.0 (m, 20 H, 4 C_6H_5), 6.95 (d, 1 H, H-6; $J_{5,6}$ = 8.0 Hz), 5.90 (d, 1 H, H-5), 5.70 (d, 1 H, H-1'), 5.0-4.3 and 4.0-3.3 (2 m).

Anal. Calcd for $C_{38}H_{38}N_2O_7$ (652.7): C, 71.89; H, 6.04; H, 4.41. Found: C, 71.69; H, 5.96; N, 4.39.

1-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)thymine (23β). Compound 2α (0.5 g, 0.173 mmol) and 5-methyl-2,4-bis (trimethylsilyloxy)pyrimidine [45] (0.5 g, 1.8 mmol) were dissolved in 25 mL of dry dichloromethane and treated with boron trifluoride-ether (0.75 mmol) and worked up as described for compound 22β. Yield 0.31 g (61 %) of compound 23β as a colourless oil; $[\alpha]_{578}^{20}$ = -43.3° (c = 1, $CHCl_3$); TLC R_F = 0.44 (toluene/acetone = 2:1); ^1H NMR

($CDCl_3$) δ 8.9 (br.s, 1 H, NH), 7.6-7.1 (m, 20 H, 4 C_6H_5), 6.75 (s, 1 H, H-6), 5.65 (d, 1 H, H-1'; $J_{1',2'}$ = 8 Hz), 5.05-4.3 and 4.0-3.3 (2 m), 1.70 (s, 3 H, CH_3).

Anal. Calcd for $C_{39}H_{40}N_2O_7$ (666.7): C, 70.25; H, 6.04; N, 4.20. Found: C, 70.03; H, 6.16; N, 4.24.

N-Acetyl-N-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2-chlorobenzamide (24β) and compound 14β. To a solution of compound 2α (1.23 g, 1.80 mmol) in 15 mL of dry acetonitrile was added 2-chlorobenzoic acid (282 mg, 1.80 mmol) at room temperature. After 20 h according to TLC, complete formation of two new products had occurred. The reaction mixture was concentrated under reduced pressure and chromatographed on silica gel (toluene/ethyl acetate = 14:1, medium pressure): yield 720 mg (56 %) of compound 24β as a colourless oil and 290 mg (24 %) of compound 14β (see above); 24β: $[\alpha]_{578}^{20}$ = -3.8° (c = 1, $CHCl_3$) [lit.[12] $[\alpha]_{578}^{20}$ = -3.4° (c = 6.26, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 6.09 (d, 1 H, H-1'; $J_{1',2'}$ = 7.0 Hz) [lit.[46] (C_6D_6) δ 6.18 (d, 1 H, H-1'; $J_{1',2'}$ = 7.2 Hz]; IR (NaCl) 1725 cm^{-1} (CO), 1688 cm^{-1} (CO) (lit.[46] 1730 and 1675 cm^{-1}).

N-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2-chlorobenzamide (25β). To a solution of compound 24β (540 mg, 0.75 mmol) in 10 mL or dry dichloromethane was added 1 mL of a 1 N sodium methoxide/methanol solution at room temperature. After 1.5 h compound 24β had reacted completely (TLC-analysis). Then 50 mL of dichloromethane were added to the reaction mixture and two washings with 20 mL water were carried out. The dichloromethane extract was dried with sodium sulfate, concentrated and the oily residue filtered through silica gel (chloroform/ethyl ether = 20:1): yield 430 mg (84 %) of compound 25β as a colourless oil; $[\alpha]_{578}^{20}$ = +65° (c = 1, $CHCl_3$); TLC R_F = 0.56 (chloroform/ethyl ether = 20:1); IR (NaCl) 1660 cm^{-1} and 1525 cm^{-1} (CONH); ^{1}H NMR ($CDCl_3$) δ 6.04 (dd, 1 H, H-1'; $J_{NH,1'}$ = 9 Hz, $J_{1',2'}$ = 4.50 Hz).

Compound 25β gave ^{1}H NMR spectral data identical with authentic material.[12]

Methyl 6-O-Acetyl-2,3,4-tri-O-benzyl-α-D-glucopyranoside (26) and compound 1 and 5. To a solution of compound 2α (1.20 g, 1.75 mmol) in 10 mL of dry acetonitrile was added boron trifluoride-ether (3.6 mL of a 0.4 molar solution in acetonitrile, 1.44 mmol) at -15 °C. After 15 min methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside [29] (650 mg, 1.40 mmol) dissolved in 5 mL of dry acetonitrile was added during 10 min. After 20 h the reaction mixture was worked up as described for compound 11β. The oily residue obtained was chromatographed on silica gel (toluene/ethyl acetate = 9:1, medium pressure and petroleum ether/ethyl ether = 1:1, medium pressure): yield 590 mg (43 %) of compound 5β, 150 mg (21 %) of compound 26 and 265 mg (35 %) of compound 1.

26: $[\alpha]_{578}^{20}$ = +29° (c = 1.2, $CHCl_3$); IR (NaCl) 1740 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 7.5-7.2 (m, 15 H, 3 C_6H_5), 5.1-3.5 (m, 13 H), 3.36 (s, 3 H, OCH_3), 2.00 (s, 3 H, CH_3CO).

Compound 26 gave ^1H NMR spectral and optical rotation data identical with that from a compound obtained by acetylation of methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside. [29]

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