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The use of 2-deoxy-2-trichloroacetamido-D-glucopyranose derivatives in syntheses of oligosaccharides †

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Abstract

3,4,6-Tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranosyl trichloroacetimidate and its *O*-benzylated analogue were tested as glycosyl donors in the reaction with a set of sugar acceptors unsubstituted on O-3 and O-4, typically encountered in the synthesis of oligosaccharides. Glycosides were obtained in good to excellent yields with only a slight excess (1.1–1.2 equiv) of the donor, and with a high degree of 1,2-*trans* stereoselectivity. The corresponding 2-(trichloromethyl)oxazolinium ion was postulated to be the major reactive intermediate. The *N*-trichloroacetyl groups in the disaccharide products were easily transformed into *N*-acetyl under neutral conditions by reduction with tributylstannane.

1. Introduction

2-Acetamido-2-deoxy-β-D-glucopyranosides are widely distributed in living organisms where they constitute building blocks of peptidoglycan, proteoglycans (hyaluronic acid), glycoproteins (milk oligosaccharides), and glycolipids (blood-group substances) [1].

Numerous procedures for the 1,2-*trans*-glucosylation of D-glucosamine have been reported, but only two of them are widely used in oligosaccharide synthesis. The oxazoline procedure [2] and more recent developments [3] give good results only with reactive acceptors, but pure 2-acetamido-2-deoxy-β-D-glucosides are

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directly obtained. The phthalimido procedure [4] gives good yields with most aglycons, and with a high degree of stereoselectivity. Despite some recent improvement [5], the phthalimido cleavage still requires basic conditions, and this sequence cannot be applied to alkali-labile glycoconjugates (O-glycopeptides or structures containing uronic acid esters).

New approaches have emerged which are based on the use of other participating substituents. Promising seems to be the sulfonamidoglycosylation of glycals [6] and the azaglycosylation reaction [7]. *N*-Haloacetyl derivatives of 2-amino-2-deoxyhexoses have also been used in glycosylation reactions. *N*-Chloroacetyl [8], *N*-dichloroacetyl [9,10], and *N*-trifluoroacetyl [11] derivatives were prepared and tested in disaccharide synthesis. *N*-Trichloroacetylated species were also used in nucleoside synthesis [12] and in the reaction with methanol [13].

Trichloroacetimidates [14] are known to be powerful glycosylating agents, and are much more reactive than the corresponding nonhalogenated congeners [15]. Despite the inductive effect of the halogens, chloroacetamido [8] and trifluoroacetamido [11] derivatives give rise to the formation of intermediate oxazolinium ions. Thus, if an *N*-trichloroacetylated species could be transformed into the corresponding 2-(trichloromethyl)oxazoline, the latter could be considered as an intramolecular trichloroacetimidate, a potentially reactive glycosyl donor for the synthesis of 1,2-*trans*-2-amino-2-deoxyglycosides.

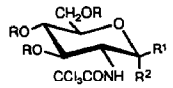
We now report on the behaviour of 2-deoxy-2-trichloroacetamido-D-glucopyranosyl derivatives in glycosylation reactions.

2. Results and discussion

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranose (**3**) has been prepared [12,13,16] in four steps from commercial D-glucosamine hydrochloride. Our value for the melting point of **3**, which is close to that reported by Osawa [16], is at variance with those given by others [12,13], probably because of the existence of another crystalline form. Anomeric deprotection of **3** with hydrazine acetate in *N*,*N*-dimethylformamide followed by treatment with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded the highly crystalline, stable trichloroacetimidate **4** (79%), the structure of which was evident from its ^{1}H NMR spectrum.

A shorter route to **4** was achieved as follows. D-Glucosamine hydrochloride was selectively *N*-substituted by treatment with trichloroacetyl chloride in buffered (pH 9) aqueous media to give crystalline **1** (65%). Acetylation of **1** (acetic anhydride–pyridine or acetic anhydride–sodium acetate at 100°C) gave an anomeric mixture of **2** and **3** in a ratio ~ 9 : 1, as determined by ^{1}H NMR. Pure α anomer **2** can be obtained by simple recrystallization. Treatment of the crude mixture of **2** and **3**, as described above, afforded **4** (76% from **1**).

Attempted preparation of the oxazoline **6** directly from **2** or **3** with trimethylsilyl triflate [17] failed. Treatment of **2** or **3** with boron trifluoride etherate, bromotrimethylsilane, and *sym*-collidine did not lead to the formation of the expected



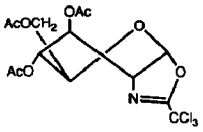
1 R = H, R^1, R^2 = H, OH

2 R = Ac, R^1 = H, R^2 = OAc

3 R = Ac, R^1 = OAc, R^2 = H

4 R = Ac, R^1 = H, R^2 = OC(NH)CCl_3

5 R = Ac, R^1 = H, R^2 = Br



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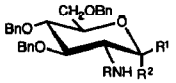


7 R = H, R^1, R^2 = H, OH

8 R = $COCCl_3$, R^1 = H, R^2 = OC(NH)CCl_3

oxazoline, as reported [18] for the *N*-acetylated analogues, but gave the α-bromide **5** (84%) with only traces (< 5%) of **6**. However, addition of tetrabutylammonium bromide (1 equiv) from the beginning of the reaction allowed the formation of **6** in excellent yield (90%). The *J* values for **6** strongly suggest a significant departure from the $^4C_1$ conformation in solution and are very close to those reported [19] for the corresponding 2-methyloxazoline which adopts a slightly modified $^OS_2$ conformation.

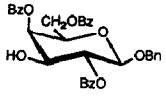
The *O*-benzylated analogue **8**, which was assumed to be more reactive, was prepared as follows. The amine **7**, derived from the corresponding known [20] hydrochloride, was *N*-acylated by treatment with trichloroacetyl chloride in dichloromethane, and the crude product was processed as described for the preparation of **4** to give the amorphous, unstable imidate **8**, the structure of which was evident from its ^{1}H NMR spectrum.

Compounds **4**, **6**, and **8** were tested as glycosyl donors in the reaction with a set of sugar acceptors unsubstituted on O-3 and O-4, typically encountered in the synthesis of oligosaccharides. Preliminary experiments with reactive acceptors (unsubstituted on O-6 and O-3, details not presented) showed that the best results were obtained with trimethylsilyl triflate as a promoter. Reactions were conducted with a moderate excess (1.1–1.2 equiv) of the donors in 1,2-dichloroethane, at various temperatures, mainly depending on the solubility of the acceptor. The results are reported in Table 1.

Table 1
Reactions of glucosyl donors **4**, **6**, and **8** with acceptors [a]

Donor	Acceptor						
	9	**10**	**11**	**12**	**13**	**14**	**15**
4	**16** (84)	**18** (82)	**20** (81)	**22** (84)	**25** (80)	**26** (42)	**29** (89)
6	**16** (85)			**22** (85)		**26** (43)	**29** (92)
8		**19** (72)	**21** (71)	**23** (75)		**27** (81)	

[a] Yields (%) are given, in parentheses, for products purified by column chromatography.



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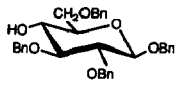

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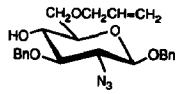

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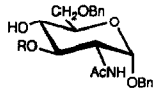
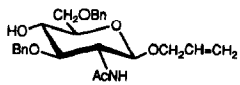


12 R = $CH_2CH{=}CH_2$

13 R = Bn



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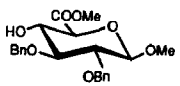
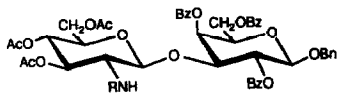


15

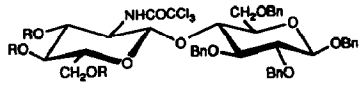
The present results show that compounds **4**, **6**, and **8** are effective reagents for incorporating 2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl units into disaccharides. The good yields obtained with acceptors of low reactivity (**12–15**) and the high degree of 1,2-*trans* stereoselectivity observed compare favourably with those obtained with 2-deoxy-2-phthalimido-D-glucopyranosyl derivatives which are currently the standard donors of β-D-glucosaminyl groups. The main advantage of the method reported is that the conversion *N*-trichloroacetyl → *N*-acetyl in the products can be achieved in a single step without affecting most of the protecting groups currently used in carbohydrate chemistry, thus allowing the preparation of structures containing uronic esters (i.e., the methyl uronate **30**). Among the methods tested for the reduction of the 2-trichloroacetamido group, that employing tributylstannane–azoisobutyronitrile (AIBN) [21] in refluxing benzene was found to be the most reliable. For compounds with a low solubility, addition of *N*,*N*-dimethylacetamide as cosolvent was beneficial. Thus, compounds **16**, **23**, **27**, **29**, and **33** were easily converted into the corresponding *N*-acetyl derivatives in $\geqslant 85\%$ yield.

As a general rule, very similar results were obtained starting from imidate **4** or oxazoline **6**. The greater reactivity (and instability) of the *O*-benzylated imidate **8** led to slightly lower yields, with the exception of glycosylation of **14**. Position 4 of glucose, glucosamine, and glucuronic acid derivatives was glycosylated in high yields (80–90%) either with imidate **4** or oxazoline **6**, with the exception of compound **14**. In this case, the coupling product was the pure β-linked disaccharide derivative **26** (42%), and no transglycosylation [8] was observed, since unreacted **14** was recovered. The use of a larger excess of **4** or **6** (2.5 equiv) obviously increased the yield up to ~ 75% (details not presented), but these conditions are not satisfactory, at least from a preparative point of view. However, coupling of **14** with the more reactive imidate **8** afforded **27** in 81% yield. Careful examination of the ^{1}H NMR spectra of **26** and **27** showed, for the "reducing unit", a significant departure from the $^4C_1$ conformation in solution ($J_{1,2}$ 6.0, $J_{2,3} = J_{3,4} = 6.5$ Hz).



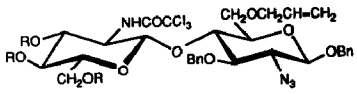
16 R = $COCCl_3$

17 R = $COCH_3$



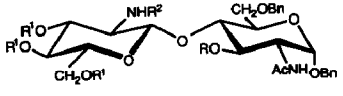
18 R = Ac

19 R = Bn



20 R = Ac

21 R = Bn



22 R = $CH_2CH{=}CH_2$, R^1 = Ac, R^2 = $COCCl_3$

23 R = $CH_2CH{=}CH_2$, R^1 = Bn, R^2 = $COCCl_3$

24 R = $CH_2CH{=}CH_2$, R^1 = Bn, R^2 = Ac

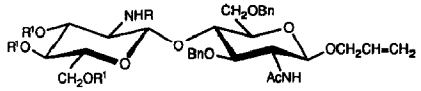
25 R = Bn, R^1 = Ac, R^2 = $COCCl_3$

Such a phenomenon was not observed for the (1 → 4)-linked disaccharide derivatives **22** and **25**, and was apparently not caused by the trichloroacetamido group, since a similar distortion was observed in the bis-acetamido disaccharide derivative **28**. Whether this phenomenon is general or not with 4-*O*-substituted 2-acetamido-2-deoxy-β-D-glucosides remains to be established.

Regarding the possible mechanism, its seems reasonable to suggest that glycosylations with **4** or **6** involve the same intermediary 2-(trichloromethyl)oxazolinium ion. Indeed, when imidate **4** was treated with trimethylsilyl triflate at −20°C, and when the reaction was rapidly quenched by addition of a base, the oxazoline **6** was isolated as the main product, with only traces of glycal-like species derived from the corresponding ring-opened oxocarbonium ion. The electron-withdrawing effect of the trichloromethyl group in the intermediary oxazolinium ion greatly increases the electrophilic character of the anomeric carbon, and could explain the much greater reactivity of **6**, compared to that of its *N*-acetyl congener [2].

To assess the influence of the 2-trichloroacetamido group on the reactivity at O-3, we prepared the acceptor **32** from the known [22] derivative **31**, by alkaline treatment followed by selective *N*-trichloroacetylation. Coupling of **32** with **4** (1.15 equiv), as described before, afforded **33** in good yield (87%). Thus, it appears that the 2-trichloroacetamido group has neither a pronounced steric nor an electronic deactivating effect on substitution reactions at the nearby 3-hydroxyl group. In **33**, both *N*-trichloroacetyl groups were easily reduced into *N*-acetyl, to give the known [2] disaccharide derivative **34**.

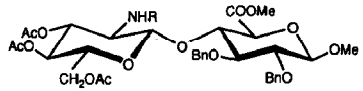
In conclusion, the use of *N*-trichloroacetyl derivatives of 2-amino-2-deoxy-D-glucose in glycosylation reactions complements the currently used procedures. The



26 R = $COCCl_3$, R^1 = Ac

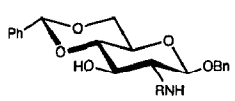
27 R = $COCCl_3$, R^1 = Bn

28 R = Ac, R^1 = Bn



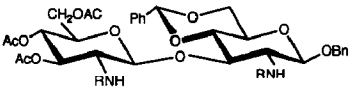
29 R = $COCCl_3$

30 R = Ac



31 R = Ac

32 R = $COCCl_3$



33 R = $COCCl_3$

34 R = Ac

crystalline imidate **4**, easy to prepare and to handle, gives good yields of β-glucosides with a high degree of 1,2-*trans* selectivity. The *N*-trichloroacetyl groups in the disaccharide products were easily transformed into *N*-acetyl under very mild conditions.

Application of this method to other sugars and for the synthesis of more complex oligosaccharides is currently being investigated in our group.

3. Experimental

General methods.—Melting points were determined in capillary tubes with a Büchi apparatus and are uncorrected. Optical rotations were measured at 20–25°C with a Perkin–Elmer Model 141 polarimeter. The ^{1}H NMR spectra were recorded at 300 MHz with a Bruker AM-300 WB spectrometer. Chemical shifts (δ) are given from the signal of internal Me_4Si unless otherwise stated. Unprimed numbers refer to the "reducing" unit and primed numbers to the "nonreducing" sugar unit. The purity of the products was determined by TLC on Silica Gel F_{254} (Merck) with detection by charring with H_2SO_4. Flash-column chromatography was performed on Silica Gel (Merck, 40–63 μm). Elemental analyses were performed by the Service Central de Microanalyses du Centre National de la Recherche Scientifique (Vernaison, France).

*2-Deoxy-2-trichloroacetamido-*D*-glucopyranose* (**1**).—Trichloroacetyl chloride (8.4 mL, 75 mmol) was added dropwise at room temperature within 1 h to a vigorously stirred solution of D-glucosamine hydrochloride (10.78 g, 50 mmol) and $NaHCO_3$ (12.6 g, 150 mmol) in water (100 mL). The mixture was stirred for 1 h, neutralized with M HCl, concentrated, and dried in vacuo. The residue was stirred for 2 h at 0°C with MeOH (100 mL), the salts were filtered off, and the filtrate was

concentrated. Crystallization of the residue from cold water (3 crops) afforded pure **1** (10.55 g, 65%); mp 163–165°C; $[\alpha]_D$ +50° (3 min) → +18° (*c* 1, equil., H_2O); ^1H NMR (Me_2SO-d_6): δ 8.60 (d, $J_{2,NH}$ 8.5 Hz, NHβ), 8.15 (d, $J_{2,NH}$ 8.0 Hz, NHα), 5.08 (dd, $J_{1,2}$ 3.5, $J_{1,OH}$ 4.0 Hz, H-1α), and 4.65 (dd, $J_{1,2}$ 8.0, $J_{1,OH}$ 6.0 Hz, H-1β). Anal. Calcd. for $C_8H_{12}Cl_3NO_6$: C, 29.61; H, 3.73; N, 4.31. Found: C, 29.42; H, 3.90; N, 4.11.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-α-* (**2**) *and -β-*D*-gluco-pyranose* (**3**).—(*a*) A solution of **1** (1 g) in pyridine (10 mL) and Ac_2O (5 mL) was stirred overnight at room temperature, then concentrated. A solution of the residue in toluene (20 mL) was filtered through Celite, then concentrated to give a mixture of **2** and **3** as a white solid (1.49 g, 98%). Recrystallization from EtOAc–hexane afforded pure **2** (1.1 g, 72%); mp 156–157°C; lit. [13] mp 159–160°C; $[\alpha]_D$ +72° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.80 (d, 1 H, *J* 8.5 Hz, NH), 6.31 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.36 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 9.5 Hz, H-3), 5.24 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.34 (m, 1 H, H-2), 4.28 (dd, 1 H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 13.0 Hz, H-6a), 4.08 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 4.04 (m, 1 H, H-5), and 2.18, 2.10, 2.04 (3s, 12 H, 4Ac).

The mother liquors from the crystallization of **2** were eluted from a column of silica gel (30 g) with 2:1 hexane–EtOAc to give, first, **3** (150 mg, 10%); mp 135–136°C (from EtOAc–hexane); $[\alpha]_D$ +3.5° (*c* 1, $CHCl_3$); lit. [16] mp 135–136°C; lit. [12] mp 159–160°C, $[\alpha]_D$ +7° ($CHCl_3$); lit. [13] mp 167.5–168.5°C, $[\alpha]_D$ +0.5° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.04 (d, 1 H, *J* 9.5 Hz, NH), 5.81 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 5.36 (dd, 1 H, $J_{2,3}$ 11.0, $J_{3,4}$ 9.5 Hz, H-3), 5.17 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.31 (m, 1H, H-2), 4.29 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.17 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.88 (m, 1 H, H-5), and 2.12, 2.11, 2.08, 2.06 (4s, 12 H, 4Ac).

Next eluted was **2** (220 mg, 14%).

(*b*) 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride [23] (5.57 g, 14.5 mmol) was dispersed in dry CH_2Cl_2 (80 mL). Et_3N (3.1 mL, 22 mmol) and trichloroacetyl chloride (1.91 mL, 17 mmol) were added successively at 0°C. The mixture was stirred for 30 min, then washed with cold water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Crystallization of the residue from EtOAc–hexane gave **3** (6.58 g, 92%); mp 135–136°C; $[\alpha]_D$ +4° (*c* 1, $CHCl_3$).

*3,4,6-Tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-α-*D*-glucopyranosyl trichloroacet-imidate* (**4**).—(*a*) A solution of the above-described crude mixture of **2** and **3** (1.97 g, 4 mmol) and hydrazine acetate (552 mg, 6 mmol) in DMF (20 mL) was stirred for 20 min at room temperature, then diluted with EtOAc (80 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. A mixture of the residue, trichloroacetonitrile (4 mL, 40 mmol), and DBU (0.15 mL, 1 mmol) in CH_2Cl_2 (12 mL) was stirred for 30 min at room temperature, then concentrated. The residue was eluted from a column of silica gel (80 g) with 2:1 hexane–EtOAc containing 0.1% of Et_3N, and crystallized from EtOAc–hexane to give **4** (1.83 g, 77%); mp 160–161°C; $[\alpha]_D$ +75° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.72 (s, 1 H, C=NH), 6.98 (d, 1 H, *J* 8.5 Hz, NH), 6.49 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.44 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 10.0 Hz, H-3), 5.29 (t, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.44 (m, 1 H, H-2), 4.29 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.26 (m, 1 H, $J_{5,6b}$ 2.5 Hz, H-5), 4.23 (dd,

1 H, H-6b), and 2.09, 2.07, 2.06 (3s, 9 H, 3Ac). Anal. Calcd for $C_{16}H_{18}Cl_6N_2O_9$: C, 32.29; H, 3.05; N, 4.71. Found: C, 32.25; H, 3.12; N, 4.62.

(*b*) A similar sequence starting from **3** (492 mg, 1 mmol) afforded **4** (470 mg, 79%).

3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranosyl bromide (**5**) *and 2-trichloromethyl-(3,4,6-tri-O-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-d]2-oxazoline* (**6**).—(*a*) $BF_3 \cdot OEt_2$ (0.37 mL, 3 mmol), freshly distilled bromotrimethylsilane (0.4 mL, 3 mmol), and *sym*-collidine (0.39 mL, 3 mmol) were added sequentially to a solution of the crude mixture of **2** and **3** (492 mg, 1 mmol) in dry 1,2-dichloroethane (5 mL). The mixture was stirred at room temperature under dry Ar for 36 h, then diluted with CH_2Cl_2 (20 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. The residue was eluted from a column of silica gel (30 g) with 2:1 hexane–EtOAc to give amorphous **5** (426 mg, 84%); $[\alpha]_D$ +129° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.02 (d, 1 H, *J* 8.5 Hz, NH), 6.57 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.44 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 10.0 Hz, H-3), 5.28 (dd, 1H, $J_{4,5}$ 10.0 Hz H-4), 4.34 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.28 (m, 1H, H-2), 4.15 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6b), and 2.12, 2.08, 2.06 (3s, 9 H, 3Ac). Anal. Calcd for $C_{14}H_{17}BrCl_3NO_8$: C, 32.74; H, 3.34; N, 2.73. Found: C, 32.58; H, 3.41; N, 2.58.

A solution of **5** (513 mg, 1 mmol), *n*-Bu_4NBr (322 mg, 1 mmol), and *sym*-collidine (0.19 mL, 1.5 mmol) in dry 1,2-dichloroethane (5 mL) was stirred at room temperature for 30 min, then diluted with CH_2Cl_2 (25 ml), washed with water, brine, and water, dried ($MgSO_4$), and concentrated. The residue was eluted from a column of silica gel (30 g) with 3:2 hexane–EtOAc containing 0.1% of Et_3N, to give syrupy **6** (397 mg, 92%); $[\alpha]_D$ +22.5° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.34 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1), 5.41 (t, 1 H, $J_{2,3} = J_{3,4} = 2.5$ Hz H-3), 4.95 (m, 1 H, $J_{4,5}$ 7.8, $J_{2,4}$ 1.5 Hz, H-4), 4.47 (m, 1 H, H-2), 4.28 (dd, 1 H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 11.0 Hz, H-6a), 4.19 (dd, 1 H, $J_{5,6b}$ 5.5 Hz, H-6b), 3.79 (m, 1 H, H-5), and 2.14, 2.10, 2.08 (3s, 9 H, 3Ac). Anal. Calcd for $C_{14}H_{16}Cl_3NO_8$: C, 38.87; H, 3.73; N, 3.24. Found: C, 38.80; H, 3.82; N, 3.11.

(*b*) A crude mixture of **2** and **3** (492 mg, 1 mmol) and *n*-Bu_4NBr (322 mg, 1 mmol) was treated for 8 h as described above in (*a*). The residue was eluted from a column of silica gel (30 g) with 3:2 hexane–EtOAc containing 0.1% of Et_3N, to give **6** (389 mg, 90%).

3,4,6-Tri-O-benzyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranosyl trichloroacetimidate (**8**).—2-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose hydrochloride [20] (**7**; 972 mg, 2 mmol) was dispersed in CH_2Cl_2 (20 mL). Et_3N (0.7 mL, 5 mmol) and trichloroacetyl chloride (0.3 mL, 2.6 mmol) were added successively at 0°C, and the mixture was stirred for 30 min, then diluted with CH_2Cl_2 (30 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. A mixture of the solid residue, trichloroacetonitrile (2 mL, 20 mmol) and DBU (0.1 mL, 0.7 mmol) in CH_2Cl_2 (12 mL) was stirred for 30 min at room temperature, then concentrated. The residue was eluted from a column of silica gel (60 g) with 3:1 hexane–EtOAc containing 0.2% of Et_3N, to give amorphous **8** (1.2 g, 81% from **7**); $[\alpha]_D$ +77° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.70 (s, 1 H, C=NH), 7.25

(m, 15 H, 3 Ph), 6.51 (d, 1 H, *J* 8.5 Hz, NH), 6.44 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.70 (3 ABq, 6 H, 3 OCH_2Ph), 4.38 (m, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 3.83 (dd, 1 H, $J_{5,6a}$ 2.8, $J_{6a,6b}$ 11.0 Hz, H-6a), and 3.70 (dd, 1 H, $J_{5,6b}$ 1.2 Hz, H-6b). Anal. Calcd for $C_{31}H_{30}Cl_6N_2O_6$: C, 50.36; H, 4.09; N, 3.79. Found: C, 50.21; H, 4.18; N, 3.61.

Benzyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**16**).—(*a*) A mixture of **4** (66 mg, 0.11 mmol), benzyl 2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside [24] (**9**; 58 mg, 0.1 mmol), and activated powdered 4A molecular sieves (100 mg) in anhyd 1,2-dichloroethane (1.5 mL) was stirred for 1 h at room temperature under dry Ar, then cooled to 0°C. Trimethylsilyl triflate in toluene (1.0 M; 22 μL, 0.2 equiv) was added, and the mixture was stirred at 0°C for 2 h. Et_3N (20 μL) was added, and the mixture was diluted with CH_2Cl_2 (20 mL), filtered, and concentrated. The residue was eluted from a column of silica gel (10 g) with 1:1 hexane–EtOAc to give **16** (85 mg, 84%); mp 193–194°C (from hexane–EtOAc); $[\alpha]_D$ +8° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.15–7.10 (m, 20 H, 4Ph), 6.41 (d, 1 H, *J* 8.0 Hz, NH), 5.82 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz H-4), 5.65 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, H-2), 5.28 (dd, 1 H, $J_{2',3'}$ 10.5, $J_{3',4'}$ 9.0 Hz, H-3'), 4.97 (t, 1 H, $J_{4',5'}$ 9.0 Hz, H-4'), 4.96 (d, 1 H, H-1'), 4.73 (ABq, 2 H, OCH_2Ph), 4.49 (d, 1 H, H-1), 4.18 (dd, 1 H, H-3), 3.58 (m, 1 H, H-2'), and 1.99, 1.96, 1.89 (3s, 9 H, 3Ac). Anal. Calcd for $C_{48}H_{46}Cl_3NO_{17}$: C, 56.79; H, 4.57; N, 1.38. Found: C, 56.89; H, 4.46; N, 1.44.

(*b*) Compound **6** (48 mg, 0.11 mmol) was treated as described in (*a*), to give **16** (87 mg, 85%); mp 193–194°C.

Benzyl O-*(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**17**).—A solution of **16** (76 mg, 75 μmol), tributylstannane (0.1 mL, 0.35 mmol), and AIBN (2 mg) in dry benzene (2.5 mL) was stirred for 20 min under a flow of dry Ar, then heated under reflux for 1 h, cooled, and concentrated. The solid residue was washed with hexane (3 × 2 mL), and recrystallized from EtOAc–hexane to give **17** (60 mg, 88%); mp 201–202°C; $[\alpha]_D$ +19.5° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.20–7.10 (m, 20 H, 4 Ph), 5.80 (dd, 1H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz, H-4), 5.67 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, H-2), 5.38 (dd, 1 H, $J_{2',3'}$ 10.5, $J_{3',4'}$ 9.0 Hz, H-3'), 5.16 (d, 1 H, *J* 8.0 Hz, NH), 5.08 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1'), 4.88 (t, 1 H, $J_{4',5'}$ 9.0 Hz, H-4'), 4.74 (ABq, 2 H, OCH_2Ph), 4.61 (d, 1 H, H-1), 4.07 (dd, 1 H, H-3), 3.21 (m, 1 H, H-2'), and 1.96, 1.95, 1.89, 1.25 (4s, 12 H, 4Ac). Anal. Calcd for $C_{48}H_{49}NO_{17}$: C, 63.22; H, 5.41; N, 1.54. Found: C, 63.15; H, 5.48; N, 1.46.

Benzyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**18**).—A mixture of **4** (66 mg, 0.11 mmol), and benzyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside [25] (**10**; 54 mg, 0.1 mmol) was treated as described for the preparation of **16**. The residue was eluted from a column of silica gel (10 g) with 4:1 hexane–EtOAc to give **18** (80 mg, 82%); mp 154–156°C (from hexane–EtOAc); $[\alpha]_D$ −26° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 20 H, 4 Ph), 6.32 (d, 1 H, *J* 9.0 Hz, NH), 4.51 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1'), 4.45 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.13 (dd, 1 H, $J_{5',6'a}$ 4.5, $J_{6'a,6'b}$ 12.0 Hz, H-6'a), 3.97 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.0 Hz, H-4), 3.93 (dd, 1 H, $J_{5',6'b}$ 2.5 Hz, H-6'b), 3.87 (m, 1 H, $J_{2',3'}$ 10.5 Hz, H-2'), 3.69 (dd, 1 H, $J_{5,6a}$ 3.0, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.64 (dd, 1 H,

$J_{5,6b}$ 2.5 Hz, H-6b), 3.55 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 3.45 (dd, 1 H, H-2), 3.37 (m, 1 H, H-5'), 3.32 (m, 1 H, H-5), and 2.03, 1.98, 1.94 (3s, 9 H, 3Ac). Anal. Calcd for $C_{48}H_{52}Cl_3NO_{14}$: C, 59.23; H, 5.38; N, 1.44. Found: C, 59.20; H, 5.43; N, 1.54.

Benzyl O-*(3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**19**).—A mixture of **8** (82 mg, 0.11 mmol) and **10** (54 mg, 0.1 mmol) was treated at −20°C as described for the preparation of **16**. The residue was eluted from a column of silica gel (10 g) with 8:1 toluene–EtOAc to give **19** (86 mg, 72%); mp 143–145°C (from EtOH); $[\alpha]_D$ −4.5° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.25 (m, 35 H, 7 Ph), 6.63 (d, 1 H, *J* 8.0 Hz, NH), 4.84 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1'), 4.47 (d, 1H, $J_{1,2}$ 7.5 Hz, H-1), 4.04 (t, 1H, $J_{3,4} = J_{4,5} = 9.0$ Hz, H-4), 3.64 (m, 1 H, $J_{2',3'}$ 10.0 Hz, H-2'), and 3.47 (dd, 1 H, H-2). Anal. Calcd for $C_{63}H_{64}Cl_3NO_{11}$: C, 67.71; H, 5.77; N, 1.25. Found: C, 67.48; H, 5.81; N, 1.31.

Benzyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-6-*O*-allyl-2-azido-3-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**20**).—A mixture of **4** (66 mg, 0.11 mmol) and benzyl 6-*O*-allyl-2-azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside [26] (**11**; 42 mg, 0.1 mmol) was treated at −20°C for 30 min as described for the preparation of **16**. The residue was eluted from a column of silica gel (10 g) with 2:1 hexane–EtOAc to give amorphous **20** (70 mg, 81%); $[\alpha]_D$ −34° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 10 H, 2 Ph), 6.83 (d, 1 H, *J* 9.0 Hz, NH), 5.96 (m, 1 H, $OCH_2CH{=}CH_2$), 5.19 (dd, 1 H, $J_{2',3'}$ 10.0, $J_{3',4'}$ 9.0 Hz, H-3'), 5.09 (t, 1H, $J_{4',5'}$ 9.0 Hz, H-4'), 4.84 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1'), 4.27 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.96 (m, 1 H, H-2'), 3.37 (dd, 1 H, $J_{2,3}$ 9.0 Hz, H-2), and 2.04, 2.03, 1.97 (3s, 9 H, 3Ac). Anal. Calcd for $C_{37}H_{43}Cl_3N_4O_{13}$: C, 51.79; H, 5.05; N, 6.53. Found: C, 51.78; H, 5.15; N, 6.33.

Benzyl O-*(3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-6-*O*-allyl-2-azido-3-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**21**).—A mixture of **8** (82 mg, 0.11 mmol) and **11** (42 mg, 0.1 mmol) was treated at −20°C as described for the preparation of **16**. The residue was eluted from a column of silica gel (10 g) with 3:1 hexane–EtOAc to give amorphous **21** (71 mg, 71%); $[\alpha]_D$ −2° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 25 H, 5Ph), 6.93 (d, 1 H, *J* 8.0 Hz, NH), 5.90 (m, 1 H, $OCH_2CH{=}CH_2$), 4.95 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1'), 4.26 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.72 (m, 1 H, H-2'), and 3.34 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2). Anal. Calcd for $C_{52}H_{55}Cl_3N_4O_{10}$: C, 62.31; H, 5.53; N, 5.59. Found: C, 62.11; H, 5.64; N, 5.41.

Benzyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-2-acetamido-3-*O*-allyl-6-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**22**).—(*a*) A mixture of **4** (137 mg, 0.23 mmol), benzyl 2-acetamido-3-*O*-allyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranoside [27] (**12**; 88 mg, 0.2 mmol) and activated powdered 4A molecular sieves (200 mg) in anhyd 1,2-dichloroethane (2.5 mL) was stirred for 1 h at room temperature under dry Ar. Trimethylsilyl triflate in toluene (1.0 M; 115 μL, 115 μmol) was added, and the mixture was stirred for 4 h. Et_3N (0.1 mL) was added, and the mixture was diluted with CH_2Cl_2 (25 mL), filtered, and concentrated. The residue was eluted from a column of silica gel (15 g) with 3:1 EtOAc–hexane to give **22** (147 mg, 84%); mp 204–205°C (from MeOH); $[\alpha]_D$ +38° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$); δ 7.40 (m 10 H, 2 Ph), 6.22 (d, 1 H, *J* 9.5 Hz,

NH′), 5.82 (m, 1 H, $OCH_2CH{=}CH_2$), 5.46 (d, 1 H, J 9.0 Hz, NH), 5.03 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.5$ Hz, H-4′), 4.94 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1) 4.87 (dd, 1 H, $J_{2',3'}$ 10.5 Hz, H-3′), 4.27 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.18 (m, 1 H, $J_{2,3}$ 10,0 Hz, H-2), 3.91 (m, 1 H, H-2′), and 2.06, 2.05, 2.00, 1.93 (4s, 12 H, 4Ac). Anal. Calcd for $C_{39}H_{47}Cl_3N_2O_{14}$: C, 53.58; H, 5.42; N, 3.20. Found: C, 53.51; H, 5.48; N, 3.11.

(*b*) A mixture of **6** (100 mg, 0.23 mmol) and **12** (88 mg, 0.2 mmol) was treated as described above, to give **22** (149 mg, 85%); mp 204–205°C.

Benzyl O-*(3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-2-acetamido-3-*O*-allyl-6-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**23**).—A mixture of **8** (81 mg, 0.11 mmol) and **12** (44 mg, 0.1 mmol) was treated as described for the preparation of **22**. The residue was eluted from a column of silica gel (10 g) with 3:2 EtOAc–hexane to give **23** (77 mg, 75%); mp 174–175°C (from EtOAc–hexane); $[\alpha]_D$ +47° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 25 H, 7Ph), 6.44 (d, 1 H, J 8.0 Hz, NH′), 5.80 (m, 1 H, $OCH_2CH{=}CH_2$), 5.48 (d, 1 H, J 9.0 Hz, NH), 4.96 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.56 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.20 (m, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.02 (t, 1 H, $J_{3,4} = J_{4,5} = 9.0$ Hz, H-4), 3.79 (m, 1 H, $J_{2',3'}$ 10.5 Hz, H-2′), and 1.95 (s, 3 H, Ac). Anal. Calcd for $C_{54}H_{59}Cl_3N_2O_{11}$: C, 63.68; H, 5.84; N, 2.75. Found: C, 63.71; H, 5.88; N, 2.62.

Benzyl O-*(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 4)-2-acetamido-3-*O*-allyl-6-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**24**).—Compound **23** (102 mg, 0.1 mmol) was treated as described for the preparation of **17**. The residue was crystallized from MeOH to give **24** (78 mg, 85%); mp 215–216°C; $[\alpha]_D$ +55.5° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 25 H, 5 Ph), 5.77 (m, 1 H, $OCH_2CH{=}CH_2$), 5.48 (d, 1 H, J 9.0 Hz, NH), 4.93 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.76 (d, 1 H, J 8.5 Hz, NH′), 4.53 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.19 (m, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 3.89 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.68 (m, 1 H, $J_{2',3'}$ 10.0 Hz, H-2′), and 1.93, 1.70 (2 s, 6 H, 2Ac). Anal. Calcd for $C_{54}H_{62}N_2O_{11}$: C, 70.88; H, 6.83; N, 3.06. Found: C, 70.75; H, 6.88; N, 2.97.

Benzyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-2-acetamido-3-6-di-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**25**).—A mixture of **4** (137 mg, 0.23 mmol) and benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside [28] (**13**; 98 mg, 0.2 mmol) was treated for 2 h as described for the preparation of **22**. The residue was eluted from a column of silica gel (15 g) with 5:2 toluene–acetone to give **25** (148 mg, 80%); mp 203–204°C (from MeOH); $[\alpha]_D$ +54° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 15 H, 3 Ph), 6.21 (d, 1 H, J 9.0 Hz, NH′), 5.07 (d, 1 H, J 9.0 Hz, NH), 5.00 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.5$ Hz, H-4′), 4.92 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.86 (dd, 1 H, $J_{2',3'}$ 10.5 Hz, H-3′), 4.29 (d, 1H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.14 (m, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.01 (t, 1 H, $J_{3,4} = J_{4,5} = 9.0$ Hz, H-4), 3.95 (m, 1 H, H-2), and 2.04, 2.00, 1.94, 1.71 (4 s, 12 H, 4Ac). Anal. Calcd for $C_{43}H_{49}Cl_3N_2O_{14}$: C, 55.88; H, 5.34; N, 3.03. Found: C, 55.79; H, 5.38; N, 2.91.

Allyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranosyl)-(1 → 4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**26**).—(*a*) A mixture of **4** (66 mg, 0.11 mmol) and allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside [29] (**14**; 44 mg, 0.1 mmol) was treated for 5 h as described for the preparation of **22**. The residue was eluted from a column of silica gel (8 g) with

2:1 EtOAc–hexane to give, first, **26** (37 mg, 42%); mp 135–136°C (from EtOAc–hexane); $[\alpha]_D$ −42° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 10 H, 2 Ph), 6.58 (d, 1 H, *J* 9.0 Hz, NH′), 5.85 (d, 1 H, *J* 8.5 Hz, NH), 5.84 (m, 1 H, $OCH_2CH{=}CH_2$), 5.08 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.5$ Hz, H-4′), 5.00 (dd, 1 H, $J_{2',3'}$ 10.5 Hz, H-3′), 4.67 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.44 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 3.98 (m, 1 H, H-2′), 3.84 (t, 1 H, $J_{2,3} = J_{3,4} = 6.5$ Hz, H-3), 3.78 (m, 1 H, H-2), and 2.06, 2.04, 2.03, 1.92 (4 s, 12 H, 4 Ac). Anal. Calcd for $C_{39}H_{47}Cl_3N_2O_{14}$: C, 53.58; H, 5.42; N, 3.20. Found: C, 53.51; H, 5.48; N, 3.08.

Next eluted was **14** (20 mg, 45%).

(*b*) Compound **6** (47 mg, 0.11 mmol) was treated as described above to give **26** (38 mg, 43%); mp 135–136°C.

Allyl O-(3,4,6-tri-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-(1 → 4)-2-acetamido-3-6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**27**).—A mixture of **8** (177 mg, 0.24 mmol) and **14** (88 mg, 0.2 mmol) was treated for 2 h as described for the preparation of **22**. The residue was eluted from a column of silica gel (15 g) with 1:1 EtOAc–hexane to give **27** (165 mg, 81%); mp 171–172°C (from EtOAc–hexane); $[\alpha]_D$ −24° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 25 H, 5 Ph), 6.59 (d, 1 H, *J* 8.5 Hz, NH′), 5.94 (d, 1 H, *J* 8.0 Hz, NH), 5.85 (m, 1 H, $OCH_2CH{=}CH_2$), 4.68 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.49 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.07 (t, 1 H, $J_{3,4} = J_{4,5} = 6.0$ Hz, H-4), 3.88 (m, 2 H, H-2,3), 3.80 (m, 1 H, $J_{2',3'}$ 10.0 Hz, H-2′), and 1.92 (s, 3 H, Ac). Anal. Calcd for $C_{54}H_{59}Cl_3N_2O_{11}$: C, 63.66; H, 5.84; N, 2.75. Found: C, 63.61; H, 5.92; N, 2.69.

Allyl O-(2-acetamido-3,4,6-tri-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-(1 → 4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**28**).—Compound **27** (102 mg, 0.1 mmol) was treated as described for the preparation of **17**. The residue was crystallized from MeOH to give **28** (80 mg, 87%); mp 200–201°C; $[\alpha]_D$ −33° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 25 H, 5 Ph), 6.44 (d, 1 H, *J* 9.0 Hz, NH), 5.84 (m, 1 H, $OCH_2CH{=}CH_2$), 4.83 (d, 1 H, *J* 8.5 Hz, NH′), 4.57 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 4.31 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.12 (m, 1 H, $J_{2,3}$ 5.0 Hz, H-2), 3.96 (t, 1 H, $J_{3,4} = J_{4,5} = 4.5$ Hz, H-4), 3.81 (m, 1 H, $J_{2',3'}$ 10.0 Hz, H-2′), 3.78 (dd, 1 H, H-3), 3.48 (dd, 1 H, $J_{3',4'}$ 8.5 Hz, H-3′), and 1.96, 1.74 (2 s, 6 H, 2 Ac). Anal. Calcd for $C_{54}H_{62}N_2O_{11}$: C, 70.88; H, 6.83; N, 3.06. Found: C, 70.79; H, 6.87; N, 2.91.

Methyl [methyl O-(3,4,6-tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-(1 → 4)-2,3-di-O-benzyl-β-D-glucopyranosid]uronate (**29**).—(*a*) A mixture of **4** (137 mg, 0.23 mmol) and methyl (methyl 2,3-di-*O*-benzyl-β-D-glucopyranosid)uronate [30] (**15**; 80 mg, 0.2 mmol) was treated for 1 h as described for the preparation of **16**. The residue was eluted from a column of silica gel (15 g) with 3:1 toluene–EtOAc to give **29** (148 mg, 89%); mp 150–151°C (from EtOAc–hexane); $[\alpha]_D$ −27° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 10 H, 2 Ph), 6.96 (d, 1 H, *J* 9.0 Hz, NH), 5.15 (m, 2 H, H-3′,4′), 4.91 (d, 1 H, $J_{1',2'}$ 8.0 Hz,H-1′), 4.34 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.19 (dd, 1 H, $J_{5',6'a}$ 4.2, $J_{6'a,6'b}$ 12.0 Hz, H-6′a),, 4.08 (m, 1 H, $J_{2',3'}$, 10.5 Hz, H-2′), 4.04 (dd, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.5 Hz, H-4), 3.93 (dd, 1 H, $J_{5',6'b}$ 2.5 Hz, H-6′b), 3.86 (d, 1 H, H-5), 3.84 (s, 3 H, COOMe), 3.63 (m, 1 H, H-5′), 3.59 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 3.54 (s, 3 H, OMe), 3.37 (dd, 1 H, H-2), and 2.02,

2.01, 1.94 (3 s, 9 H, 3Ac). Anal. Calcd for $C_{36}H_{42}Cl_3NO_{15}$: C, 51.78; H, 5.07; N, 1.68. Found: C, 51.70; H, 5.01; N, 1.51.

(*b*) Compound **6** (100 mg, 0.23 mmol) was treated as described above, to give **29** (154 mg, 92%); mp 150–151°C.

Methyl [methyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 4)-2,3-di-O-benzyl-β-D-glucopyranosid]uronate (**30**).—Compound **29** (125 mg, 0.15 mmol) was treated as described for the preparation of **17**. The residue was crystallized from MeOH to give **30** (98 mg, 89%); mp 218–219°C; ^{1}H NMR ($CDCl_3$): δ 7.25 (m, 10 H, 2 Ph), 5.58 (d, 1 H, *J* 9.0 Hz, NH), 5.07 (m, 2 H, H-3′,4′), 4.64 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.33 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.14 (dd, 1 H, $J_{5',6'a}$ 4.0, $J_{6'a,6'b}$ 12.5 Hz, H-6′a), 4.02 (m, 1 H, $J_{2',3'}$ 10.0 Hz, H-2′), 4.01 (dd, 1 H, $J_{3,4}$ 8.5, $J_{4,5}$ 9.5 Hz, H-4), 3.87 (m, 1 H, H-5), 3.86 (dd, 1 1 H, $J_{5',6'b}$ 2.5 Hz, H-6′b), 3.85 (s, 3 H, COOMe), 3.62 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 3.54 (s, 3 H, OMe), 3.39 (dd, 1 H, H-2), and 2.01, 1.98, 1.95, 1.93 (4 s, 12 H, 4 Ac). Anal. Calcd for $C_{36}H_{45}NO_{15}$: C, 59.09; H, 6.21; N, 1.91. Found: C, 59.01; H, 6.25; N, 1.79.

Benzyl 4,6-O-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**32**).—A mixture of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside [22] (**31**; 1.0 g, 2.5 mmol) and ethanolic KOH (4 M, 25 mL) was stirred overnight under reflux, then cooled. The pH of the solution was adjusted to ~ 8 with cold 1 M HCl, and the mixture was concentrated. Water (50 mL) was added, and the resulting slurry was extracted with $CHCl_3$ (5 × 20 mL). The organic extracts were washed with brine and water, dried (Na_2SO_4), and concentrated. The crude residue was dissolved at 0°C in anhyd CH_2Cl_2 (20 mL), and Et_3N (0.7 mL, 5 mmol) and trichloroacetyl chloride (0.34 mL, 3 mmol) were added successively. The mixture was stirred for 30 min, then diluted with CH_2Cl_2 (30 mL), washed with water, satd aq $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated. The residue was crystallized from EtOH to give **32** (968 mg, 81%); mp 215–216°C; $[\alpha]_D$ −65° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.40 (m, 10 H, 2 Ph), 6.86 (d, 1 H, *J* 7.0 Hz, NH), 5.57 (s, 1 H, PhC*H*), 4.95 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.76 (ABq, 2 H, OCH_2Ph), 4.39 (dd, 1 H, $J_{5,6eq}$ 5.0, $J_{6ax,6eq}$ 10.5 Hz, H-6*eq*), 4.31 (m, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 8.5, $J_{3,OH}$ 3.0 Hz, H-3), and 2.90 (d, 1 H, OH-3). Anal. Calcd for $C_{22}H_{22}Cl_3NO_6$: C, 52.55; H, 4.41; N, 2.78. Found: C, 52.75; H, 4.20; N, 2.83.

Benzyl O-(3,4,6-tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-(1 → 3)-4,6-O-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**33**).—A mixture of **4** (177 mg, 0.23 mmol) and **32** (105 mg, 0.2 mmol) was treated as described for the preparation of **16**. The residue was eluted from a column of silica gel (15 g) with 3 : 2 hexane–EtOAc to give **33** (163 mg, 87%); mp 185–186°C (from EtOAc–hexane); $[\alpha]_D$ −40° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.35 (m, 10 H, 2 Ph), 7.16 (d, 1 H, *J* 7.5 Hz, NH), 6.60 (d, 1 H, *J* 8.0 Hz, NH′), 5.55 (s, 1 H, PhC*H*), 5.37 (dd, 1 H, $J_{2',3'}$ 11.0, $J_{3',4'}$ 9.5 Hz, H-3′), 5.06 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-4′), 5.02 (d, 1 H, $J_{1',2'}$ 8.5 Hz, H-1′), 4.94 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.76 (ABq, 2 H, OCH_2Ph), 4.49 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 4.38 (dd, 1 H, $J_{5,6eq}$ 5.0, $J_{6ax,6eq}$ 10.5 Hz, H-6*eq*), and 2.02, 1.98, (3 s, 9 H, 3Ac). Anal. Calcd for $C_{36}H_{38}Cl_6N_2O_{14}$: C, 46.22; H, 4.09; N, 2.99. Found: C, 46.44; H, 3.94; N, 2.72.

Benzyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**34**).—A mixture of **33** (94 mg, 0.1 mmol), tributylstannane (0.24 mL, 0.9 mmol), and AIBN (5 mg) in dry benzene (3 mL) and dry *N,N*-dimethylacetamide (1 mL) was treated as described for the preparation of **17**. The residue was crystallized from MeOH to give **34** (60 mg, 82%); 296–298°C (dec); $[\alpha]_D$ −45° (*c* 1, $CHCl_3$); lit. [2] mp 297–298°C, $[\alpha]_D$ −43° (*c* 2.8, pyridine); ^{1}H NMR (Me_2SO-d_6): δ 7.80 (d, 1 H, *J* 9.0 Hz, NH), 7.62 (d, 1 H, *J* 9.0 Hz, NH'), 7.35 (m, 10 H, 2 Ph), 5.67 (s, 1 H, PhC*H*), 5.14 (t, 1 H, $J_{2',3'} = J_{3',4'} = 9.5$ Hz, H-3'), 4.87 (d, 1 H, $J_{1',2'}$ 8.5 Hz, H-1'), 4.75 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-4'), 4.67 (ABq, 2 H, OCH_2Ph), 4.64 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.23 (dd, 1 H, $J_{5,6eq}$ 5.0, $J_{6ax,6eq}$ 10.0 Hz, H-6*eq*), 4.06 (dd, 1 H, $J_{5',6'a}$ 4.0, $J_{6'a,6'b}$ 12.0 Hz, H-6'a), 3.93 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 3.82 (t, 1 H, $J_{5,6ax}$ 10.0 Hz, H-6*ax*), 3.81 (dd, 1 H, $J_{5',6'b}$ 2.5 Hz, H-6'b), 3.70 (m, 1 H, H-2), 3.66 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), and 1.94, 1.92, 1.90, 1.85, 1.72 (5 s, 15 H, 5 Ac).

References

[1] N. Sharon, in *Complex Carbohydrates*, Addison-Wesley, Reading, MA, 1975.
[2] S.E. Zurabyan, T.S. Antonenko, and A.Ya. Khorlin, *Carbohydr. Res.*, 15 (1970) 21–27.
[3] M. Kiso and L. Anderson, *Carbohydr. Res.*, 72 (1979) c15–c17.
[4] R.U. Lemieux, M.T. Takeda, and B.Y. Chung, *ACS Symp. Ser.*, 39 (1976) 90–115.
[5] O. Kanie, S.C. Crawley, M.M. Palcic, and O. Hindsgaul, *Carbohydr. Res.*, 243 (1993) 139–164.
[6] D.A. Griffith and S.J. Danishefsky, *J. Am. Chem. Soc.*, 112 (1990) 5811–5819.
[7] S.J. Danishefsky, K. Kosek, D.A. Griffith, J. Gervay, J.M. Peterson, F.E. McDonald, and T. Oriyama, *J. Am. Chem. Soc.*, 114 (1992) 8331–8333.
[8] F. Dasgupta and L. Anderson, *Carbohydr. Res.*, 202 (1990) 239–255.
[9] D. Shapiro, A.J. Acher, and E.S. Rachaman, *J. Org. Chem.*, 32 (1967) 3767–3771.
[10] A.J. Acher and D. Shapiro, *J. Org. Chem.*, 34 (1969) 2652–2654.
[11] W. Meyer zu Reckendorf and N. Wassiliadou-Micheli, *Chem. Ber.*, 103 (1970) 1792–1796.
[12] M.L. Wolfrom and H.B. Bhat, *J. Org. Chem.*, 32 (1967) 1821–1823.
[13] A.M. Dempsey and L. Hough, *Carbohydr. Res.*, 41 (1975) 63–76.
[14] R.R. Schmidt, *Angew. Chem. Int. Ed. Engl.*, 25 (1986) 212–235.
[15] J.R. Pougny, J.-C. Jacquinet, M. Nassr, D. Duchet, M.L. Milat, and P. Sinaÿ, *J. Am. Chem. Soc.*, 99 (1977) 6762–6763.
[16] T. Osawa, *Chem. Pharm. Bull.*, 8 (1960) 597–610.
[17] S. Nakabayashi, C.D. Warren, and R.W. Jeanloz, *Carbohydr. Res.*, 150 (1987) c7–c10.
[18] M. Colon, M.M. Staveski, and J.T. Davies, *Tetrahedron Lett.*, 32 (1991) 4447–4450.
[19] M.A. Nashed, C.W. Slife, M. Kiso, and L. Anderson, *Carbohydr. Res.*, 82 (1980) 237–252.
[20] R. Harrison and H.G. Fletcher, Jr., *J. Org. Chem.*, 30 (1965) 2317–2323.
[21] H.G. Kuivala, *Synthesis*, (1970) 499–509.
[22] P.H. Gross and R.W. Jeanloz, *J. Org. Chem.*, 32 (1967) 2759–2763.
[23] M. Bergmann and L. Zervas, *Ber.*, 64 (1931) 975–980.
[24] S. Rio, J.-M. Beau, and J.-C. Jacquinet, *Carbohydr. Res.*, 244 (1993) 295–313.
[25] J.-M. Petit, J.-C. Jacquinet, and P. Sinaÿ, *Carbohydr. Res.*, 82 (1980) 130–134.
[26] D. Tailler, J.-C. Jacquinet, and J.-M. Beau, *Abstr. Pap. Eurocarb VII*, Cracow, Poland, 1993, A-141.
[27] J.-C. Jacquinet and P. Sinaÿ, *J. Org. Chem.*, 42 (1977) 720–724.
[28] J.-C. Jacquinet and P. Sinaÿ, *Carbohydr. Res.*, 38 (1974) 305–311.
[29] P. Rollin and P. Sinaÿ, *J. Chem. Soc., Perkin Trans. 1*, (1977) 2513–2517.
[30] N.J. Davis and S.L. Flitsch, *Tetrahedron Lett.*, 34 (1993) 1181–1184.