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Carbohydrate Research 290 (1996) 79–86

CARBOHYDRATE
RESEARCH

Note

Intermolecular aglycon transfer of a phenyl 1-thiogalactosaminide derivative under trichloroacetimidate glycosylation conditions

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Received 29 January 1996; accepted 10 April 1996

Keywords: Thioglycoside; Trichloroacetimidate glycosylation; Aglycon transfer; 2-Deoxy-2-trichloroacetamido-D-galactose

Thioglycosides are stable and versatile derivatives that allow flexible strategies for the syntheses of complex oligosaccharides [1]. The alkyl(aryl) 1-thio group can be considered as a temporary protection for the anomeric center, and is stable under a large set of reaction conditions, thus allowing manipulation of protective groups or chemical modifications elsewhere in the molecule. In addition, thioglycosides can be activated directly through the use of thiophilic promoters such as methyl triflate [2], dimethyl(methylthio)sulfonium triflate (DMTST) [3], and *N*-iodosuccinimide–catalytic triflic acid [4,5], the most frequently used among the numerous electrophilic entities that have been reported. Consequently, the 1-thioglycoside methodology constitutes an extraordinarily attractive choice for the block synthesis of oligosaccharides.

However, limitations in the applicability of thioglycosides are arising. Intramolecular 1,2-migration of the anomeric ethylthio group with concomitant inversion of configuration at the C-2 atom has been reported [6]. Intermolecular thioglycoside transfer has been observed as a side-reaction under Helferich or Koenigs–Knorr conditions of glycosylation [7]. A recent report [8] in which a nearly quantitative intermolecular aglycon transfer of ethyl 1-thiorhamnopyranoside derivatives under the same glycosylation conditions was described prompts us to disclose our own observations, now under trichloroacetimidate glycosylation conditions.

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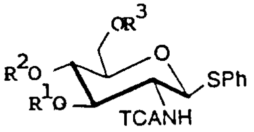
PII S0008-6215(96)00116-4

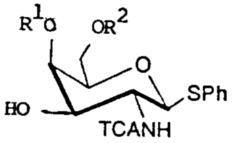
1. Results and discussion

During the course of a programme devoted to the synthesis of chondroitin sulfate oligosaccharides [9,10], we focused on the preparation of the suitably protected disaccharide building block **12**. This synthon possesses the basic sequence of the repeating units of chondroitins, and could be used for extension to higher oligosaccharides as an alternative to the previously reported synthesis [10], in which the D-galactosamine residue was obtained by selective inversion of configuration at C-4 of a D-glucosamine residue in a pre-constructed oligosaccharide. The *N*-trichloroacetyl protection was selected owing to its powerful β-directing effect in glycosylation reactions, and its ease of transformation into *N*-acetyl under neutral conditions [11].

For the synthesis of such a building block, two monosaccharide coupling synthons were designed, namely the acceptor **4**, the D-*galacto* analogue of the previously employed **8** [10], and the donor **7**.

Preparation of **4** was achieved as follows. *O*-Deacetylation of the known thioglycoside **1** [10] afforded quantitatively the corresponding triol, which was directly transformed into the crystalline 3,6-di-*O*-pivaloyl derivative **2** in 86% yield. It should be noted that attempted selective *O*-benzoylation (details not presented) afforded a mixture of 3,6- and 4,6-di-*O*-benzoyl derivatives that could not be easily separated. Treatment of **2** with trifluoromethanesulfonic anhydride and pyridine in 1,2-dichloroethane at − 15 °C gave the corresponding 4-*O*-triflyl derivative that was treated in situ with water [12], and heated at 80 °C to give the expected 4,6-di-*O*-pivaloyl-D-*galacto* intermediate, the structure of which was evident from its ^{1}H NMR spectrum. Direct *O*-deacetylation of this crude intermediate afforded the crystalline triol derivative **3** in 86% overall yield. Treatment of **3** with 2-methoxypropene in DMF under acid catalysis gave the 4,6-*O*-isopropylidene derivative **4** in 90% yield, the structure of which was deduced from its ^{1}H NMR spectrum.





	R¹	R²	R³
1	Ac	Ac	Ac
2	Piv	H	Piv

	R¹	R²
3	H	H
4	-CMe$_2$-	

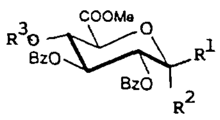
The D-glucuronic acid unit was prepared as follows. Methyl (4-methoxyphenyl 2,3-di-*O*-benzoyl-β-D-glucopyranosid)uronate (**5**), the synthesis of which was reported elsewhere [13], was chloroacetylated to give the crystalline derivative **6** in 88% yield.

Table 1
Formation of intermolecular aglycon transfer products [a]

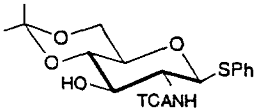
Entry	Reactants	Catalyst	Solvent	Products	
				Coupling (%)	Transfer (%)
1	**7**+**4**	TMSOTf	CH_2Cl_2	–	**11** (80)
2	**7**+**4**	$BF_3 \cdot Et_2O$	CH_2Cl_2	**12** (25)	**11** (60)
3	**7**+**4**	$BF_3 \cdot Et_2O$	toluene	**12** (50)	**11** (35)
4	**9**+**4**	$BF_3 \cdot Et_2O$	CH_2Cl_2	**14** (52)	**13** (32)
5	**10**+**4**	AgOTf	CH_2Cl_2	**14** (25)	**13** (60)
6	**7**+**8**	$BF_3 \cdot Et_2O$	CH_2Cl_2	**15** (83)	–
7	**9**+**8**	$BF_3 \cdot Et_2O$	CH_2Cl_2	**16** (85)	–

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

Introduction of the trichloroacetimidoyl group at C-1 was achieved by selective oxidative removal of the 4-methoxyphenyl group using ceric ammonium nitrate in toluene–acetonitrile–water [14], followed by treatment with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to afford the crystalline α-imidate **7** in 72% overall yield, the structure of which was evident from its ^{1}H NMR spectrum ($J_{1,2}$ 3.5 Hz).



	R^1	R^2	R^3
5	OMP	H	H
6	OMP	H	$COCH_2Cl$
7	H	$OC(NH)CCl_3$	$COCH_2Cl$



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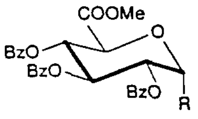
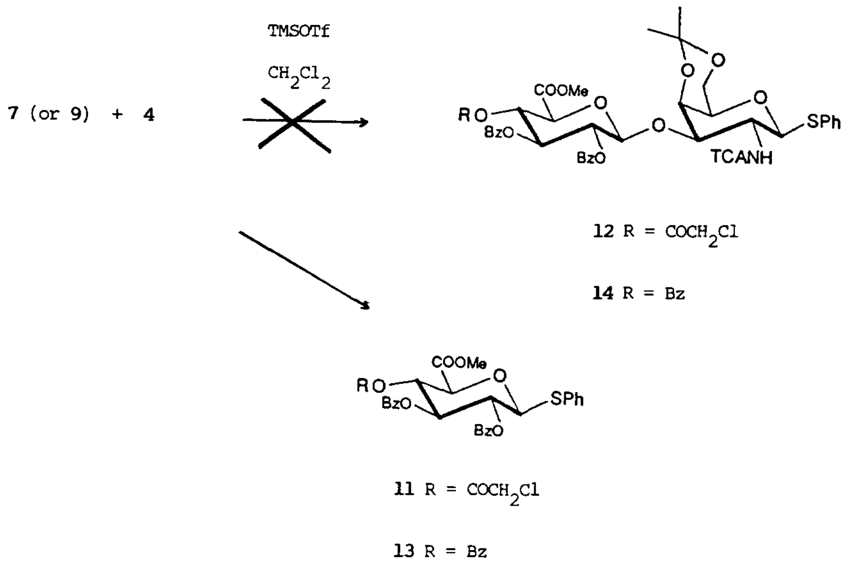


9 R = $OC(NH)CCl_3$

10 R = Br

The crucial coupling between donor **7** and acceptor **4** was then studied (Table 1). Condensation of the imidate **7** (1.2 equiv) with the alcohol **4** (1 equiv) in dry dichloromethane at room temperature in the presence of trimethylsilyl triflate (10% based on **7**) afforded the crystalline phenyl 1-thio-β-D-glycoside **11** (entry 1) in 80% yield as the sole isolable product (Scheme 1). Despite varying the nature of the catalyst (entry 2), or the solvent (entry 3), it was not possible to obtain the disaccharide derivative **12** in reasonable yield (i.e., acceptable for a multi-step synthesis), or to eliminate the aglycon transfer product **11**. Lowering the temperature did not significantly change the product distribution. Very similar results were obtained with the imidate **9** [10] (entry 4), or with the bromide **10** [10] (entry 5) using silver triflate as a promoter, thus excluding any effect of the substituent at O-4 of the donor, or of the mode of activation.



12 R = $COCH_2Cl$

14 R = Bz

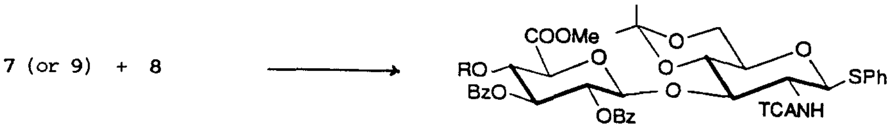
11 R = $COCH_2Cl$

13 R = Bz

Scheme 1.

To obtain an insight into the influence of the acceptor, we performed the condensations between the imidate **7** or **9** and the acceptor **8** [10] (entries 6 and 7), the D-*gluco* analogue of **4**, with $BF_3 \cdot Et_2O$ as a catalyst (Scheme 2). Both reactions proceeded smoothly, and the crystalline coupling products **15** and **16** were obtained in 83 and 85% yields, respectively. No formation of transfer product was observed in these reactions. Very similar results were obtained with the ethyl 1-thio analogues of **4** and **8** (details not presented). It has recently been postulated [8] that the use of 'less-reactive' thioglycosides (i.e., phenyl or 4-nitrophenyl instead of ethyl) might overcome the transfer reaction. This hypothesis does not seem to be valid.

The 3-OH group in a D-*galacto* structure is generally expected to be one of the most reactive secondary hydroxyl groups [15]. We also previously demonstrated [11] that the electron-withdrawing 2-trichloroacetamido group has neither steric nor electronic deactivating effect on substitution reactions at the nearby 3-OH group. Such a clear-cut



15 R = $COCH_2Cl$

16 R = Bz

Scheme 2.

difference in the behaviour of D-*gluco* and D-*galacto* analogues has not previously been reported, and is difficult to rationalize. One of the most plausible explanations may be that a mismatched pair was formed in the transition state of the β-coupling between **4** and **7**, but not in the β-coupling of **8** and **7**.

In conclusion, unfavourable interactions in the transition state between a glycosyl donor and an acceptor may lead to the formation of unexpected and undesired species, such as intermolecular aglycon transfer products. Moreover, one has to keep in mind that the sulfur atom in an alkyl(aryl) 1-thioglycoside can react readily not only with thiophilic reagents, but also with electrophilic centers such as glycosyl oxocarbenium ions.

2. 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 'non-reducing' 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).

*Phenyl 2-deoxy-3,6-di-*O*-pivaloyl-1-thio-2-trichloroacetamido-β-D-glucopyranoside* (**2**).—A solution of phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-2-trichloroacetamido-β-D-glucopyranoside (**1**) [10] (1.085 g, 2 mmol) in dry MeOH (15 mL) was treated with M methanolic NaOMe (0.5 mL) for 2 h at room temperature. The mixture was then deionized with Amberlite IR-120 (H^+) resin, filtered, concentrated, and dried in vacuo.

Pivaloyl chloride (0.79 mL, 6.4 mmol) was added dropwise at 0 °C to a solution of the residue in pyridine (6 mL) and CH_2Cl_2 (3 mL). The mixture was stirred for 1.5 h at 0 °C, and MeOH (1 mL) was added. The mixture was diluted with CH_2Cl_2 (30 mL), washed with cold aq 5% HCl, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. The residue was eluted from a column of silica gel (50 g) with 10:1 CH_2Cl_2–EtOAc to give **2** (1.01 g, 86%); mp 222–223 °C (from EtOAc–heptane); $[\alpha]_D$ $-28°$ (c 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.35 (m, 1 H, Ph), 7.21 (d, 1 H, J 9.5 Hz, NH), 5.44 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 10.5 Hz, H-3), 4.82 (d, 1 H, $J_{1,2}$ 10.5 Hz, H-1), 4.46 (dd, 1 H, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 13.0 Hz, H-6a), 4.36 (dd, 1 H, $J_{5,6b}$ 2.2 Hz, H-6b), 4.10 (m, 1 H, H-2), 3.65 (m, 1 H, $J_{4,5}$ 10.0 Hz, H-5), 3.46 (m, 1 H, $J_{4,OH}$ 6.5 Hz, H-4), 3.25 (d, 1 H, OH), and 1.23, 1.10 (2 s, 18 H, CMe_3). Anal. Calcd for $C_{24}H_{32}Cl_3NO_7S$: C, 49.28; H, 5.51; N, 2.39. Found: C, 49.21; H, 5.52; N, 2.31.

Phenyl 2-deoxy-1-thio-2-trichloroacetamido-β-D-galactopyranoside (**3**).—Trifluoromethanesulfonic anhydride (0.22 mL, 1.3 mmol) was added at -15 °C to a solution of **2** (585 mg, 1 mmol) in dry pyridine (0.5 mL) and 1,2-dichloroethane (8 mL), and the mixture was stirred for 3 h at this temperature. Water (0.5 mL) was then added, and the mixture was stirred for 2 h at 80 °C. Dichloromethane (25 mL) was added, and the mixture was washed with ice-cold aq 5% HCl, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. A solution of the residue in 1:1 EtOAc–heptane was filtered through a pad (2 × 3 cm) of silica gel, and concentrated to give the 4,6-di-*O*-pivaloyl-D-*galacto* analogue of **2** (520 mg, 89%); ^1H NMR ($CDCl_3$): δ 5.31 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz, H-4), 4.15 (m, 2 H, H-6a,6b), and 2.65 (d, 1 H, *J* 4.5 Hz, 3-OH).

A solution of the above isolated intermediate in MeOH (10 mL) was treated overnight at room temperature with M methanolic NaOMe (1 mL), then deionized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to give **3** (358 mg, 86% from **2**); mp 178–179 °C (from MeOH); $[\alpha]_D$ +31° (*c* 1, MeOH); ^1H NMR [$(CD_3)_2SO$]: δ 8.75 (d, 1 H, *J* 9.5 Hz, NH), 7.30 (m, 5 H, Ph), 4.94 (d, 1 H, $J_{1,2}$ 10.5 Hz, H-1), 4.85 (d, 1 H, *J* 7.0 Hz, 3-OH), 4.73 (d, 1 H, *J* 4.5 Hz, 4-OH), 4.69 (t, 1 H, *J* 6.0 Hz, 6-OH), 3.96 (m, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 3.75 (m, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz, H-4), 3.70 (m, 1 H, H-3), and 3.50 (m, 3 H, H-5,6a,6b). Anal. Calcd for $C_{14}H_{16}Cl_3NO_5S$: C, 40.35; H, 3.87; N, 3.36. Found: C, 40.51; H, 4.01; N, 3.23.

*Phenyl 2-deoxy-4,6-O-isopropylidene-1-thio-2-trichloroacetamido-β-*D*-galactopyranoside* (**4**).—2-Methoxypropene (0.2 mL, 2 mmol) was added to a solution of **3** (417 mg, 1 mmol) and (±)-camphor-10-sulfonic acid (CSA, 15 mg) in dry DMF (4 mL), and the mixture was stirred for 1 h at room temperature. Et_3N (50 μL) was added, and the mixture was concentrated. The residue was eluted from a column of silica gel (30 g) with 2:1 EtOAc–heptane containing 0.2% of Et_3N to give **4** (415 mg, 90%); $[\alpha]_D$ −13° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.40 (m, 5 H, Ph), 6.72 (d, 1 H, *J* 8.0 Hz, NH), 5.00 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1), 4.19 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz, H-4), 4.05 (m, 3 H, H-3,6a,6b), 3.76 (m, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 3.48 (m 1 H, H-5), 2.53 (d, 1 H, *J* 10.0 Hz, 3-OH), and 1.46, 1.44 (2 s, 6 H, CMe_2). Anal. Calcd for $C_{17}H_{20}Cl_3NO_5S$: C, 44.70; H, 4.41; N, 3.06. Found: C, 44.62; H, 4.55; N, 3.00.

*Methyl (4-methoxyphenyl 2,3-di-O-benzoyl-4-O-chloroacetyl-β-*D*-glucopyranosid)uronate* (**6**).—A mixture of methyl (4-methoxyphenyl 2,3-di-*O*-benzoyl-β-D-glucopyranosid)uronate (**5**) [13] (522 mg, 1 mmol) and chloroacetic anhydride (256 mg, 1.5 mmol) in dry pyridine (0.5 mL) and CH_2Cl_2 (5 mL) was stirred for 30 min at 0 °C. Ice-cold water (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (20 mL), washed with aq 5% $KHSO_4$, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. The residue was crystallized from heptane–EtOAc to give **6** (527 mg, 88%); mp 168–169 °C; $[\alpha]_D$ +58° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.95–7.30 (m, 10 H, Ph), 6.88 (m, 4 H, PhOMe), 5.80 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 5.70 (dd, 1 H, $J_{1,2}$ 7.5 Hz, H-2), 5.65 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 5.26 (d, 1 H, H-1), 4.37 (d, 1 H, H-5), 3.98 (ABq, 2 H, $COCH_2Cl$), and 3.76, 3.75 (2 s, 6 H, OMe). Anal. Calcd for $C_{30}H_{27}ClO_{11}$: C, 60.15; H, 4.54. Found: C, 60.17; H, 4.48.

*Methyl 2,3-di-O-benzoyl-4-O-chloroacetyl-1-O-trichloroacetimidoyl-α-*D*-glucopyranuronate* (**7**).—Water (16 mL) and ceric ammonium nitrate (3.65 g, 6.65 mmol) were added to a solution of **6** (800 mg, 1.33 mmol) in toluene (16 mL) and MeCN (20 mL), and the mixture was vigorously stirred for 2 h at room temperature. EtOAc (50 mL) was added, and the organic layer was washed with brine and water, dried ($MgSO_4$), and concentrated. The residue was eluted from a column of silica gel (40 g) with 3:2 heptane–EtOAc, and fractions containing the corresponding hemiacetal were pooled, and concentrated. A mixture of the residue, trichloroacetonitrile (1.2 mL, 12 mmol), and DBU (50 μL, 0.33 mmol) in CH_2Cl_2 (10 mL) was stirred for 30 min at room temperature, then concentrated. The residue was eluted from a column of silica gel (60 g) with 2:1 heptane–EtOAc containing 0.2% of Et_3N to give **7** (610 mg, 72% from **6**); mp 140–141 °C (from EtOAc–heptane); $[\alpha]_D$ +114° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.70 (s, 1 H, C=NH), 7.90–7.30 (m, 10 H, Ph), 6.85 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 6.13 (t, 1 H, $J_{2,3} = J_{3,4}$ = 10.0 Hz, H-3), 5.60 (t, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 5.55 (dd, 1 H, H-2), 4.68 (d, 1 H, H-5), 3.99 (ABq, 2 H, COCH_2Cl), and 3.80 (s, 3 H, COOMe). Anal. Calcd for $C_{25}H_{21}Cl_4NO_{10}$: C, 47.12; H, 3.32; N, 2.20. Found: C, 47.22; H, 3.34; N, 2.11.

Typical Lewis acid-catalyzed glycosyl transfer reactions with acceptor **4**.—A mixture of the donor (0.12 mmol), acceptor **4** (0.1 mmol), and activated powdered 4 Å molecular sieves (0.1 g) in anhyd CH_2Cl_2 (1.5 mL) was stirred for 30 min at room temperature under dry Ar. $BF_3 \cdot Et_2O$ in toluene (1.0 M, 24 μL) was added, and the mixture was stirred at room temperature for 30 min. Et_3N (28 μL) was added, and the mixture was diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. Column chromatography on silica gel (10 g) with 3:2 heptane–EtOAc containing 0.1% of Et_3N gave first the transfer products. Further elution afforded the coupled products.

Data for methyl (phenyl 2,3-di-*O*-benzoyl-4-*O*-chloroacetyl-1-thio-β-D-glucopyranosid)uronate (**11**): mp 160–161 °C (from EtOAc–heptane); $[\alpha]_D$ +80° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.95–7.25 (m, 15 H, Ph), 5.75 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.5 Hz, H-3), 5.48 (dd, 1 H, $J_{1,2}$ 10.0 Hz, H-2), 5.42 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.91 (d, 1 H, H-1), 4.28 (d, 1 H, H-5), 3.94 (ABq, 2 H, COCH_2Cl), and 3.82 (s, 3 H, COOMe). Anal. Calcd for $C_{29}H_{25}ClO_9S$: C, 59.54; H, 4.31. Found: C, 59.48; H, 4.34.

Data for phenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-chloroacetyl-β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-4,6-*O*-isopropylidene-1-thio-2-trichloroacetamido-β-D-galactopyranoside (**12**): mp 243–244 °C (from EtOAc–heptane); $[\alpha]_D$ +27° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.90–7.20 (m, 15 H, Ph), 6.92 (d, 1 H, *J* 7.0 Hz, NH), 5.64 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 9.5 Hz, H-3′), 5.47 (dd, 1 H, $J_{4',5'}$ 10.0 Hz, H-4′), 5.45 (dd, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′), 5.42 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1), 5.17 (d, 1 H, H-1′), 4.68 (dd, 1 H, $J_{2,3}$ 11.0, $J_{3,4}$ 3.5 Hz, H-3), 4.49 (dd, 1 H, $J_{4,5}$ 1.0 Hz, H-4), 4.16 (d, 1 H, H-5′), 4.02 (m, 2 H, H-6a,6b), 3.95 (ABq, 2 H, COCH_2Cl), 3.78 (s, 3 H, COOMe), 3.71 (m, 1 H, H-2), 3.43 (m, 1 H, H-5), and 1.48, 1.42 (2 s, 6 H, CMe_2). Anal. Calcd for $C_{40}H_{39}Cl_4NO_{14}S$: C, 51.57; H, 4.22; N, 1.50. Found: C, 51.53; H, 4.32; N, 1.50.

Data for methyl (phenyl 2,3,4-tri-*O*-benzoyl-1-thio-β-D-glucopyranosid)uronate (**13**): mp 194–195 °C (from EtOH); $[\alpha]_D$ +24° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$); δ 8.0–7.20 (m, 20 H, Ph), 5.92 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.5 Hz, H-3), 5.64 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 5.50 (dd, 1 H, $J_{1,2}$ 10.0 Hz, H-2), 5.06 (d, 1 H, H-1), 4.37 (d, 1 H, H-5), and 3.72 (s, 3 H, COOMe). Anal. Calcd for $C_{34}H_{28}0_9S$: C, 66.66; H, 4.61. Found: C, 66.59; H, 4.64.

Data for phenyl *O*-(methyl 2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-4,6-*O*-isopropylidene-1-thio-2-trichloroacetamido-β-D-galactopyranoside (**14**): mp 200–201 °C (from EtOAc–heptane); $[\alpha]_D$ −12° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.95–7.25 (m, 20 H, Ph), 6.97 (d, 1 H, *J* 7.0 Hz, NH), 5.81 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 9.5 Hz, H-3′), 5.62 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-4′), 5.52 (dd, 1 H, $J_{1',2'}$ 7.5 Hz, H-2′), 5.42 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1), 5.24 (d, 1 H, H-1′), 4.68 (dd, 1 H, $J_{2,3}$ 11.0, $J_{3,4}$ 3.2 Hz, H-3), 4.54 (dd, 1 H, $J_{4,5}$ 1.0 Hz, H-4), 4.24 (d, 1 H, H-5′), 4.02 (m, 2 H, H-6a,6b), 3.75 (m, 1 H, H-2), 3.66 (s, 3 H, COOMe), 3.47 (m, 1 H, H-5), and 1.48, 1.44 (2 s, 6 H, CMe_2). Anal. Calcd for $C_{45}H_{42}Cl_3NO_{14}S$: C, 56.34; H, 4.41; N, 1.46. Found: C, 56.28; H, 4.49; N, 1.38.

General procedure for the coupling with acceptor **8**.—A mixture of the donor (0.12 mmol) and acceptor **8** (0.1 mmol) was treated as described for the glycosyl transfer reactions. The products were eluted from a column of silica gel (10 g) with 5:1 toluene–EtOAc containing 0.1% of Et_3N.

Data for phenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-chloroacetyl-β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-4,6-*O*-isopropylidene-1-thio-2-trichloroacetamido-β-D-glucopyranoside (**15**): mp 194–195 °C (from EtOAc–heptane); $[\alpha]_D$ +44° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.95–7.25 (m, 15 H, Ph), 7.02 (d, 1 H, *J* 7.5 Hz, NH), 5.68 (t, 1 H, $J_{2',3'} = J_{3',4'} = 9.5$ Hz, H-3′), 5.48 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-4′), 5.38 (dd, 1 H, $J_{1',2'}$ 7.5 Hz, H-2′), 5.37 (d, 1 H, $J_{1,2}$ 10.5 Hz, H-1), 5.08 (d, 1 H, H-1′), 4.49 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 4.16 (d, 1 H, H-5′), 3.96 (dd, 1 H, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.95 (ABq, 2 H, $COCH_2Cl$), 3.80 (s, 3 H, COOMe), 3.77 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.42 (m, 2 H, H-2,6b), and 1.41, 1.26 (2 s, 6 H, CMe_2). Anal. Calcd for $C_{40}H_{39}Cl_4NO_{14}S$: C, 51.57; H, 4.22; N, 1.50. Found: C, 51.48; H, 4.28; N, 1.41.

Data for phenyl *O*-(methyl 2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-4,6-*O*-isopropylidene-1-thio-2-trichloroacetamido-β-D-glucopyranoside (**16**): mp 189–190 °C (from EtOAc–heptane); $[\alpha]_D$ +7° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.95–7.25 (m, 20 H, Ph), 7.08 (d, 1 H, *J* 7.0 Hz, NH), 5.86 (t, 1 H, $J_{2',4'} = J_{3',4'} = 9.5$ Hz, H-3′), 5.64 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-4′), 5.46 (dd, 1 H, $J_{1',2'}$ 7.5 Hz, H-2′), 5.40 (d, 1 H, $J_{1,2}$ 10.5 Hz, H-1), 5.17 (d, 1 H, H-1′), 4.53 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 4.24 (d, 1 H, H-5′), 3.96 (dd, 1 H, $J_{5,6a}$ 5.0, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.80 (m, 2 H, H-4,6b), 3.70 (s, 3 H, COOMe), 3.42 (m, 2 H, H-2,5), and 1.41, 1.26 (2 s, 6 H, CMe_2). Anal. Calcd for $C_{45}H_{42}Cl_3NO_{14}S$: C, 56.34; H, 4.41; N, 1.46. Found: C, 56.41; H, 4.38; N, 1.41.

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