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Synthesis of Glycosyl Esters from Phosphoroates Derivatives of 2-Bromosugars

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ABSTRACT: *This work presents the synthesis of glycosyl esters of 2-bromo-2-deoxy-D-hexopyranose, having the α-D-manno (***10a–cα***), β-D-gluco (***11a–dβ***) and α-D-gluco (***11a,bα***) configuration, by a stereoselective reaction between phosphoroates* **3–8** *and carboxylic acids* **9a–d.** *Derivatives of* **10a–c** *and* **11a–d** *are formed in an overall quantitative yield, in an aprotic solvent in the presence of silver salts as a leaving group activator. The phosphoroselenoate of* **3** *was obtained by the condensation reaction of the triethylammonium salt of phosphoroseleno acid* **2** *with α-1,2-D-manno-pyranosyl dibromide* **1** *with high stereoselectivity. The structures of the compounds* **3,10a–c** *and* **11a–d** *were established by* ^{1}H *and* ^{13}C *NMR spectra and by elemental analyses*. © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:292–298, 2000

INTRODUCTION

The sugars of 1-*O*-acylates play an important role in numerous biological processes. For example, they inhibit the growth of plants [1] and cellular growth in leukemia [2] and have an inhibitory effect on some enzymes [3]. Glycosyl derivatives of medicaments with a carboxylic acid group are potential prodrugs [4]. Our recent investigation concentrates on glycosyl *o*-(2,6-dichloroanilino)phenylacetic acid (diclofenac) derivatives as potential prodrugs [5]. The esters of 2-bromosugars have been used as precursors to create the 2-deoxy function. This function was obtained by the removal of a bromine atom positioned at C-2 in the sugar ring, by use of reducing agents [6], or by photolysis [7]. At present, few ways of synthesis of 1-*O*-acetyl 2-bromo-2-deoxy-D-hexopyranose are known. The condensation of an acetoxymercury compound with a 1,2-dibromo sugar [6,8] or the substitution of a free anomeric hydroxyl group by acetoxyl in 2-bromo-2-deoxy-D-glucose are the main pathways [7,9]. The reaction of 3,4,6-tri-*O*-acetyl-D-glucal with *N*-bromosuccinimide in the presence of acetic acid can be used as a regioselective introduction of the acetoxyl group at an anomeric center and a bromine atom at a secondary position [10].

RESULTS AND DISCUSSION

Recently we have demonstrated that glycosyl phosphorothioates, phosphoroselenoates, and phosphorodithioates with a 2-deoxy function and an acetate residue in the secondary position of the sugar ring can be used as efficient glycosyl donors for carboxylic acids [11].

In continuation of this work, we have studied the influence of the bromine atom on the C-2 position of phosphoroate derivatives of 2-bromo-2-deoxy-pyranoses with the *α*-D-*manno* **3–5** and *β*-D-*gluco* configuration **6–8** on the stereoselective course of reaction with carboxylic acids **9a–d.** The derivatives of **4–8** were prepared according to the procedure recently elaborated by us [12,13]. At present, the Se-phosphoroate **3** is obtained by the condensation reaction of an equimolar amount of the triethylammonium

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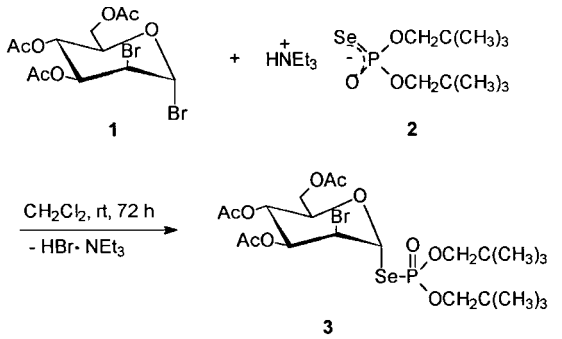
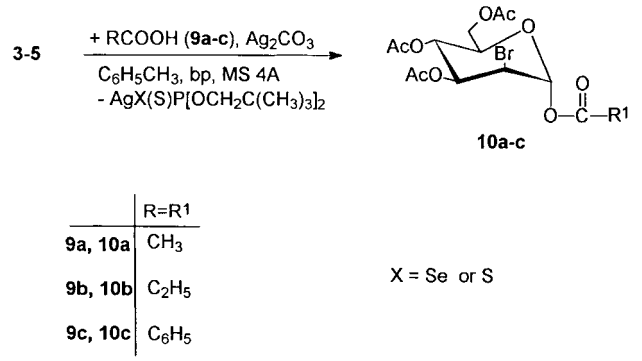
salt of the ambident anion derived from phosphorus monoseleno acid **2** [14] with 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*manno*-pyranose bromide **1** [15] in boiling dichloromethane (Scheme 1). After completion of the reaction, ammonium bromide was separated by filtration and obtained in about 95% yield. The ^{31}P-NMR spectral data for one signal with a chemical shift at δ = 11.73 with the value of the coupling constant, $J_{P,Se}$ = 495 Hz, which is characteristic for the isomer R-Se(O)P [16], indicate that, after full isomerization (selenono → selenolo), the thermodynamically more stable Se-glycosyl derivative **3** was formed. The anomeric configuration of derivative **3** by the ^{1}H-NMR spectrum, was designated. The signal of an anomeric proton (doublet of doublets) in lower field with a chemical shift at δ = 6.43 showed typical values of coupling constants for *manno*-glycosyl phosphate: $J_{1,2}$ = 1.3 Hz and $^{3}J_{H,P}$ = 12.3 Hz. By crystallization from petroleum ether, a 67% yield of the pure derivative of **3** was obtained.

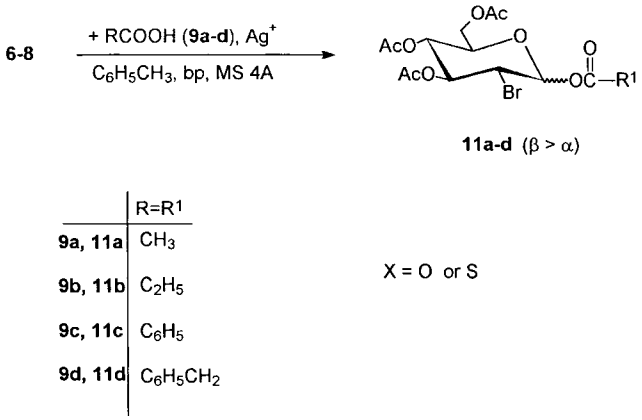
In the reaction of stoichiometric amounts of phosphoroates **3–8** with carboxylic acids **9a–d** in aprotic solvents (benzene, toluene, dichloromethane), activated by silver salts, esters of 2-bromosugar having the α-D-*manno* **10a–c** (Scheme 2) and the β-D-*gluco* configuration **11a–d** (Scheme 3) were obtained by method A (see Experimental). The following silver salts: silver carbonate, silver fluoride, and silver trifluoromethanesulfonate in the presence of molecular sieves (4A) were used as activators of the phosphoroate leaving group and for the generation of the carboxylate anion. The reactivity of the phosphoroates, with the configuration of α-D-*manno* **3–5** and β-D-*gluco* **6–8,** was not dependent on the presence of the phosphorus ligands. However, Se-phosphoroate **3** exemplified slightly higher reactivity (Table 2, entries 1,4,5) than phosphorodithioates and thioates **4–8** (Table 3, entries 1–17). Generally, boil-



SCHEME 1 Glycosylation of triethylammonium salt of O,O-dineopentylselenophosphate acid (**2**) by 2-bromo-2-deoxy-α-D-*manno*-pyranose bromide (**1**) in dichloromethane as a solvent.



SCHEME 2 Synthesis of 1-O-acyl derivatives of 2-bromo-2-deoxy-α-D-mannopyranose (**10a–c**).



SCHEME 3 Synthesis of 1-O-acyl derivatives of 2-bromo-2-deoxy-α,β-D-gluco-pyranose (**11a–d**).

TABLE 1 Glycosyl Donors

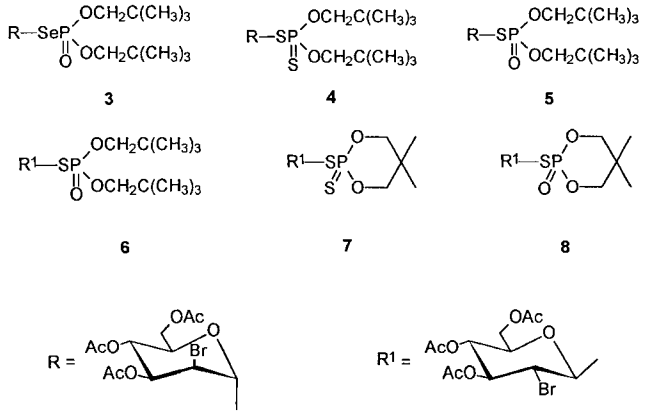


TABLE 2 Glycosyl Esters of 2-Bromo-2-deoxy-α,β-D-*manno*-pyranose **10a–c** Obtained in the Presence of Silver Carbonate as Activator by Method A

Entry	Glycosyl Donor	Carboxylic Acid	Ester $\alpha + \beta$	Solvent	Time[a] (*h*)	Ratio[b] α/β (%)
1	**3**	**9a**	**10a**	C_6H_6	5	100:0
2	**4**	**9a**	**10a**	$C_6H_5CH_3$	8	100:0
3	**5**	**9a**	**10a**	$C_6H_5CH_3$	7	100:0
4	**3**	**9b**	**10b**	C_6H_6	6	95:5
5	**3**	**9c**	**10c**	C_6H_6	5	95:5
6	**4**	**9c**	**10c**	$C_6H_5CH_3$	8	96:4
7	**5**	**9c**	**10c**	$C_6H_5CH_3$	7	94:6

[a]Time measured for the reaction performed at boiling points of the respective solvent.
[b]α/β Ratio determined by ^{13}C-NMR spectroscopy of the crude product.

ing of the solutions for several hours was sufficient to complete the glycosylation reactions of acids **9a–d** by **3–8;** special conditions are shown in Tables 2 and 3. After the reaction had been completed, the salt of phosphoric acid was separated (by filtration through Celite), and the filtrate was evaporated in vacuo. Syrupy or semicrystalline residues were obtained in 90–95% yields and examined by spectroscopy (^{1}H and ^{13}C NMR). The data in each case indicated overall quantitative formation of the esters of **10a–c** and **11a–d.** The reactions of phosphoroates **3–5** with the following acids: acetic **9a,** propionic **9b,** and benzoic **9c** in boiling benzene and toluene in the presence of silver carbonate as activator led to glycosyl esters of **10a–c** with α-D-*manno* stereoselectivity (Table 2, entries 1–3). In the reaction between acid **9a** and **3–5,** 2-bromo-2-deoxy-α-D-*manno*-pyranose acetate **10a**α, with 100% stereoselectivity, was formed (Table 2, entries 1–3). Glycosyl esters **10b**α and **10c**α were obtained from acid **9b** in reaction with **3** and acid **9c** with **3–5,** respectively, as major products (94–96%) in the mixture of anomers (Table 2, entries 4–7). The use of phosphoroates of 2-bromo-2-deoxy-α-D-*manno*-pyranoses **3–5** as glycosyl donors for carboxylic acids **9a–c** led to a stereoselective pathway of synthesis of 1-*O*-acyl derivatives with the α-D-*manno* configuration. The stereoselective course of the reaction of phosphorothioates and dithioates **6–8** (having the β-D-*gluco* configuration) with acids **9a–d** (Scheme 3) was influenced by the nature of the silver salts used as the activator. When reaction of glycosylation of acids **9a–d** by **6–8** in boiling toluene, was activated by silver carbonate, esters of 2-bromo-2-deoxy-D-*gluco*pyranose **11a–d** were obtained with high β-stereoselectivity 88–100% (Table 3, entries 1–3,5,6,10,11,14,15). Such a course of reaction enables us to use β-D-*gluco* phosphoroates **6–8** as effective glycosyl donors for carboxylic acids in the synthesis β-1-*O*-acyl derivatives.

However, with silver fluoride as the activator in a 3 molar ratio, glycosyl esters of **11b–d** were obtained in a mixture of anomers (α to β in the ratio of 28:72, 23:77, and 15:85, respectively), with β-anomers predominating (Table 3, entries 8,12,16). The reactions of phosphorodithioate **7** with acids **9b–d** in dichloromethane, in the presence of silver trifluoromethanesulfonate/Drierite, were completed at ambient temperature. Glycosyl esters **11b–d** were formed as a mixture of anomers in an almost equal ratio (Table 3, entries 9,13,17). The solvent can influence the stereochemical course of the reaction of liquid acids: acetic acid **9a** and propionic acid **9b** with phosphorodithioate **7** (Table 3, entries 4,7). When the reaction was performed under solvolytic conditions in the presence of silver carbonate at ambient temperature (method B, see Experimental) the stereochemical course was reversed in comparison with the results from the same reaction in toluene (Table 3, entries 1–3,5,6). The thermodynamically more stable 1-*O*-acyl-2-bromo-2-deoxy-α-D-*gluco*-pyranoses **11a**α and **11b**α were formed in 100% and 90% yields, respectively.

Esters **11a** and **11c** were observed by spectroscopy in an alternative reaction of 2-bromo-2-deoxy-α-D-*gluco*-pyranosyl bromide, and **12** [17] was observed with the silver salts of acids **9a** and **9c** in a 3 molar ratio in boiling toluene. In these reactions, both esters **11a** and **11c** were formed with lower stereoselectivity (α to β in the ratio of 23:77) than in the reactions of acid **9a** with **6–8** (Table 3, entries 1–3) and glycosylation of acid **9c** by **7,8** (Table 3, entries 10,11) in toluene, activated by silver carbonate.

Pure 1-*O*-acyl derivatives of 2-bromosugars **10a**α**, 11b**α**, 11b**β**,** and **11d**β were isolated by column chromatography on silica gel in 65–77% yields as light yellow syrups. Crystallization from ethanol afforded glycosyl esters **10c**α**, 11a**α**, 11a**β**,** and **11c**β as stable products at room temperature in 65–77% yields. The structures of the synthetized esters **10a–c** and **11a–d** were determined by ^{1}H and ^{13}C-NMR spectroscopy. The data from these spectra, that is, the chemical shift of the anomeric proton as a doublet, and typical values of vicinal coupling constants ($\delta = 6.57, J_{1,2e} \approx 1.7$ Hz; $\delta = 5.81, J_{1,2a} \approx 9.1$ Hz; $\delta = 6.42, J_{1,2a} \approx 3.3$ Hz) indicated that the esters of 2-bromosugars **10a–c** and **11a–d** had the configuration of α-D-*manno* (**10a–c**α), β-D-*gluco* (**11a–d**β), and α-D-*gluco* (**11a,b**α).

In summary, this work demonstrates that the reaction of nucleophilic substitution of phosphorothio, seleno, and dithio groups at the anomeric center of 2-bromosugars with acetate anions in aprotic solvents, activated by silver salts, led to a new form of synthesis of glycosyl esters. In this way, several not

TABLE 3 Glycosyl Esters of 2-Bromo-2-deoxy-α,β-D-*gluco*-pyranose **11a–d** Obtained by Method A

Entry	*Glycosyl Donor*	*Carboxylic Acid*	*Ester* $\alpha + \beta$	*Activator*	*Solvent*	*Time*[a] (*h*)	Ratio[b] α/β (%)
1	**6**	**9a**	**11a**	Ag_2CO_3	$C_6H_5CH_3$	10	0:100
2	**7**	**9a**	**11a**	Ag_2CO_3	$C_6H_5CH_3$	10	0:100
3	**8**	**9a**	**11a**	Ag_2CO_3	$C_6H_5CH_3$	11	0:100
4	**7**	**9a**	**11a**[c]	Ag_2CO_3	CH_3COOH	9[d]	100:0
5	**7**	**9b**	**11b**	Ag_2CO_3	$C_6H_5CH_3$	10	12:88
6	**8**	**9b**	**11b**	Ag_2CO_3	$C_6H_5CH_3$	11	10:90
7	**7**	**9b**	**11b**[c]	Ag_2CO_3	C_2H_5COOH	9[d]	90:10
8	**7**	**9b**	**11b**	AgF[e]	$C_6H_5CH_3$	12	28:72
9	**7**	**9b**	**11b**	AgOTf	CH_2Cl_2	120[d]	52:48
10	**7**	**9c**	**11c**	Ag_2CO_3	$C_6H_5CH_3$	10	0:100
11	**8**	**9c**	**11c**	Ag_2CO_3	$C_6H_5CH_3$	10	0:100
12	**7**	**9c**	**11c**	AgF[e]	$C_6H_5CH_3$	11	23:77
13	**7**	**9c**	**11c**	AgOTf	CH_2Cl_2	96[d]	53:47
14	**7**	**9d**	**11d**	Ag_2CO_3	$C_6H_5CH_3$	13	0:100
15	**8**	**9d**	**11d**	Ag_2CO_3	$C_6H_5CH_3$	12	0:100
16	**7**	**9d**	**11d**	AgF[e]	$C_6H_5CH_3$	13	15:85
17	**7**	**9d**	**11d**	AgOTf	CH_2Cl_2	96[d]	55:45

[a]Time measured for the reaction performed at boiling points of the respective solvent.
[b]α/β Ratio determined by ^{13}C-NMR spectroscopy of the crude product.
[c]Obtained by method B.
[d]Time measured for the reaction performed at ambient temperature.
[e]Silver fluoride was used in 3 molar ratio.

previously described 1-*O*-acyl glycosyl derivatives of 2-bromosugars with the α-D-*manno*, α-D-*gluco*, and β-D-*gluco* configuration were obtained in satisfactory yields. This approach enables the use of the 2-bromo-2-deoxy-hexopyranose acylates as precursors in the stereoselective synthesis of α and β-1-*O*-acyl-2-deoxy sugars. Further investigation of the properties of new synthetized glycosyl esters is currently in progress.

EXPERIMENTAL

Instruments and Starting Materials

Melting points were determined with the Boethius PHMK 05 apparatus and are uncorrected. The ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded in $CDCl_3$ with the use of the Bruker AC 200 spectrometer operating at 200.11 MHz, 50.33 MHz, and 81.01 MHz, respectively. The ^{1}H and ^{13}C chemical shifts are reported in parts per million (δ) downfield from trimethylsilane (TMS) (1% solution) as an internal standard, and the ^{31}P chemical shifts are relative to external 85% H_3PO_4. Specific rotations were measured in chloroform (Polamat A polarimeter). Thin-layer chromatography (TLC) was run on silica gel plates (Kieselgel 60 F_{254} Merck) with benzene:chloroform:acetone in the ratio of 3:1:1 as the developing solvent; detection was affected by exposure to iodine vapors. Column chromatography was performed on silica gel (35–70 mesh, Merck). The Glycosyl donors *S*-(3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*manno*-pyranosyl)-*O,O*-dineopentyldithiophosphate (**4**) [12], *S*-(3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*manno*-pyranosyl)-*O,O*-dineopentylthiophosphate (**5**) [13], *S*-(3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-D-*gluco*-pyranosyl]-*O,O*-diisopropylthiophosphate (**6**) [13], 2-(3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-D-*gluco*-pyranosyl)-thio-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinane (**7**) [12], *S*-(3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-D-*gluco*-pyranosyl)-thio-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (**8**) [13] were prepared according to stereoselective procedure recently described by us. The triethylammonium salt of *O,O*-dineopentyl-selenophosphate acid **2** was prepared by a published procedure [14]. 3,4,6-Tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*manno*-pyranosyl bromide (**1**) [15] and 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*gluco*-pyranose bromide **12** [17] were obtained by known methods. Aliphatic and aromatic anhydrous carboxylic acids **9a–d** were used as glycosyl acceptors. Silver carbonate as activator was freshly prepared. The solvents were dried by standard procedures before use.

Se-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-D-manno-pyranosyl)-O,O-dineopentyl selenolophosphate (**3**). A solution of 3,4-6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*manno*-pyranosyl bromide **1** (432 mg, 1 mmol) in dichloromethane (4 mL) was added to a solution of the triethylammonium salt of phosphoroseleno acid **2** (405 mg, 1 mmol) in dry dichloro-

methane (5 mL), and the mixture was stirred for 72 hours at room temperature. When the reaction had stopped (monitored by TLC and ^{31}P NMR), the amine hydrobromide was filtered off (yield 95%). The organic layer was then washed three times with water, dried over calcium chloride, and concentrated in vacuo. The semicrystalline residue was examined by ^{31}P-NMR spectroscopy and appeared to have only one signal (δ = 11.73). Pure compound **3** (430 mg, 67%) was obtained by crystallization from petroleum ether as colorless crystals. ^{31}P NMR: δ = 11.73, $J_{P,Se}$ = 495 Hz, m.p. 69–71°C, $[\alpha]_{578}^{27}$ = +3.5° (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 0.96, 0.97 (2s, 18H, CH_3), 2.08, 2.09 (2s, 9H, OAc), 3.88–3.82 (m, 4H, CH_2O), 4.17–4.43 (m., 3H, H-5, H-6a, H-6b), 4.83 (dd, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 3.4 Hz, 1H, H-2), 5.17–5.37 (m, 1H, H-3), 5.42 (dd, $J_{3,4}$ = $J_{4,5}$ = 7.6 Hz, 1H, H-4), 6.46 (dd, $J_{1,2}$ = 1.3 Hz, $^3J_{H,P}$ = 12.3 Hz, 1H, H-1); ^{13}C NMR ($CDCl_3$) δ: 20.59, 20.85 (2s, CH_3CO), 25.98 (6 CH_3), 32.06 (d, $^3J_{C,P}$ = 7.6 Hz, $C(CH_3)_2$), 51.58 (d, $^3J_{C,P}$ = 8.8 Hz, C-2), 61.25 (C-6), 65.04 (C-3), 69.40 (C-4), 73.81 (C-5), 76.67 (d, $^2J_{C,P}$ = 6.8 Hz, CH_2O), 85.07 (d, $^2J_{C,P}$ < 1 Hz, C-1), 169.13, 169.71, 170.25 (CH_3CO).

Anal. Calcd for $C_{22}H_{38}BrO_{16}Se$ (652.38): C, 40.50; H, 5.87; P, 4.75. Found: C, 40.67; H, 5.99; P, 4.85.

General Procedure for the Synthesis of 1-O-Acyl 2-Bromosugars (**10a–c** *and* **11a–d**)

Method A for **10a–c**α and **11a–d**β: A solution of stoichiometric amounts of phosphoroate **3–8,** carboxylic acid **9a–d**, and silver salt in anhydrous solvent (benzene, toluene, dichloromethane) in the presence of molecular sieves (MS, 4A) was heated under reflux (for specific conditions see Tables 2 and 3). The reaction was monitored by TLC_t, and ^{1}H and ^{13}C NMR spectroscopy. When the reaction had been completed, the precipitated silver phosphoro acid salt and the molecular sieves were removed by filtration through Celite 535, and the filtrate was washed with aq Na_2CO_3 and water. The dried ($MgSO_4$) organic layer, which was concentrated under reduced pressure, provided glycosyl esters **10a–c** and **11a–d** in quantitative yield confirmed by ^{1}H and ^{13}C-NMR spectroscopy. Purification by crystallization or column chromatography with the use of ethyl acetate/petroleum ether in the ratio of 1:3 as eluent led to the pure 1-*O*-acyl of 2-bromo-2-deoxy sugars (**10a–c** and **11a–d**).

1,3,4,6-Tetra-O-acetyl-2-bromo-2-deoxy-α-D-manno-pyranose (**10a**α). Phosphoroates **3–5** (1 mmol), acetic acid **9a** (60 mg, 1 mmol), and silver carbonate (137 mg, 0.5 mmol) were caused to react. For reaction conditions, see Table 2 (entries 1–3). Column chromatography performed twice (for eluent, see general procedure) resulted in obtaining 290 mg (72%, 0.7 mmol) of the **10a**α compound as a light straw-colored oil; $[\alpha]_{578}^{27}$ = +23° (c = 2.0, $CHCl_3$). Spectroscopic and physical data for this derivative **10a**α were comparable with values in the literature [10].

1-O-Propionyl-3,4,6-tri-O-acetyl-2-bromo-2-deoxy-α-D-manno-pyranose (**10b**α). Phosphoroselenoate **3** (652 mg, 1 mmol), propionic acid **9b** (74 mg, 1 mmol), and silver carbonate (136 mg, 0.5 mmol) were caused to react. For reaction conditions, see Table 2 (entry 4). Column chromatography performed twice (for eluent, see general procedure) gave 290 mg (68%) of the **10b**α compound as a light straw-colored oil; $[\alpha]_{578}^{27}$ = +25°C (c = 2.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 1.15 (t, 3H, CH_3), 1.99, 2.01, 2.02 (3s, 12H, OAc), 2.37 (q, 2H, CH_2CH_3), 3.98–4.31 (m, 3H, H-5, H-6a, H-6b), 4.37 (dd, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3.2 Hz, 1H, H-2), 4.97 (dd, $J_{3,4}$ = $J_{4,5}$ = 9 Hz, 1H, H-4), 5.11 (dd, $J_{2,3}$ = 4.2 Hz, $J_{3,4}$ = 9.6 Hz, 1H, H-3), 6.64 (d, $J_{1,2}$ = 1.7 Hz, 1H, H-1), ^{13}C NMR ($CDCl_3$), δ: 8.45 (CH_3CH_2), 20.26 (CH_3CO), 27.02 (CH_3CH_2), 47.75 (C-2), 61.47 (C-6), 65.21 (C-4), 68.41 (C-5), 70.85 (C-3), 92.88 (C-1), 165.31 [$OC(O)C_2H_5$], 168.91, 169.03 169.56 (CH_3CO). Anal. Calcd. for $C_{15}H_{21}BrO_9$ (425.23): C, 42.37; H, 4.98. Found: C, 42.57; H, 5.13.

1-O-Benzoyl-3,4,6-tri-O-acetyl-2-bromo-2-deoxy-α-D-manno-pyranose (**10c**α). Phosphorothioate **5** (585 mg; 1 mmol), benzoic acid **9c** (244 mg, 1 mmol), and silver carbonate (136 mg, 0.5 mmol) were caused to react. For reaction conditions, see Table 2 (entry 7). Crystallization gave 320 mg, 68% (from ethanol) of this derivative of **10c**α**;** m.p. 72–74°C; $[\alpha]_{578}^{27}$ = +43° (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$); δ: 2.07, 2.08, 2.12 (3s, 12H, OAc), 3.93–4.16 (m, 1H, H-5), 4.17–4.24 (m, 2H, H-6a, H-6b), 4.59 (q, $J_{2,1}$ = $J_{2,3}$ = 1.7 Hz, 1H, H-2), 5.33 (dd, $J_{3,4}$ = 8.0 Hz, $J_{4,5}$ = 7.8 Hz, 1H, H-4), 5.55 (dd, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 9.5 Hz, 1H, H-3), 6.57 (d, $J_{1,2}$ = 1.7 Hz, 1H, H-1), 7.49–7.53 (m, 2H, arom.), 7.60–7.64 (m, 1H, arom.), 8.03–8.08 (m, 2H, arom.); ^{13}C NMR ($CDCl_3$), δ 20:43 (CH_3CO), 47.82 (C-2), 61.58 (C-6), 65.37 (C-4), 68.74 (C-5), 71.31 (C-3), 93.42 (C-1), 128.55, 129.74, 133.84 (C-arom.) 163.40 [OC(O)Ph], 169.06, 169.80, 170.39 (CH_3CO). Anal. Calcd. for $C_{19}H_{21}BrO_9$ (473.27): C, 48,22; H, 4.47. Found: C, 48.49; H, 4.56.

1,3,4,6-Tetra-O-acetyl-2-bromo-2-deoxy-β-D-gluco-pyranose (**11a**β). Phosphorothioates **6** or **8** (1 mmol), acetic acid **9a** (60 mg, 1 mmol), and silver carbonate (137 mg, 0,5 mmol) were caused to react. For reaction conditions, see Table 3 (entries 1–3).

Crystallization gave 320 mg (77%, 0.78 mmol) of the **11aβ** compound as colorless crystals m.p. 94–96°C (from ethanol); $[\alpha]_{578}^{27} = +59°$ (c = 1.0, $CHCl_3$). ^1H NMR spectroscopic data correlated with the data described in the literature [9b, 10].

1-O-Propionyl-3,4,6-tri-O-acetyl-2-bromo-2-deoxy-β-D-gluco-pyranose (**11bβ**). Phosphorothioate **8** (700 mg, 1.5 mmol), propionic acid **9b** (110 mg, 1.5 mmol), and silver carbonate (205 mg, 0.75 mmol) were caused to react. For reaction conditions, see Table 3 (entry 6). The derivative **11bβ** (465 mg, 63%) was obtained by column chromatography as a syrup (for eluent, see general procedure); $[\alpha]_{578}^{27} = +58°$ (c = 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$) δ: 1.18 (t, J = 6.3 Hz, 3H, CH_2CH_3), 2.00, 2.05, 2.07 (3s, 12H, OAc), 2.43 (q, J = 7.4 Hz, 2H, CH_2CH_3), 3.88 (ddd, $J_{4,5}$ = 9.0 Hz, $J_{5,6a}$ = 2.7 Hz, $J_{5,6b}$ = 1.5 Hz, 1H, H-5), 4.09–4.14 (m, 1H, H-6a, H-6b), 4.30 (dd, $J_{2,3} = J_{2,1}$ = 6.4 Hz, 1H, H-2), 5.33 (dd, $J_{2,3} = J_{3,4}$ = 9.2 Hz, 1H, H-3), 5.77 (d, $J_{1,2}$ = 9.1 Hz, 1H, H-1). ^{13}C-NMR ($CDCl_3$) δ: 8.30 (CH_3CH_2), 20.14, 20.27, 20.61 (CH_3CO), 26.86 (CH_3CH_2), 47.53 (C-2), 61.09 (C-6), 68.28 (C-4), 72.36 (C-5), 73.98 (C-3), 92.63 (C-1), 169.07 [$OC(O)C_2H_5$], 169.13, 170.07, 171.64 (CH_3CO). Anal. Calcd. for $C_{15}H_{21}BrO_9$ (425.23): C, 42.37; H, 4.98. Found: C, 42.52; H, 5.11.

1-O-Benzoyl-3,4,6-tri-O-acetyl-2-bromo-2-deoxy-β-D-gluco-pyranose (**11cβ**). Phosphorodithioate **7** (518 mg, 1 mmol), benzoic acid **9c** (244 mg, 1 mmol), and silver carbonate (136 mg, 0.5 mmol) were caused to react. For reaction conditions, see Table 3 (entry 10). Crystallization from ethanol afforded 300 mg (65%) of the derivative **11c**β as colorless crystals; m.p. 65–67°C; $[\alpha]_{578}^{27} = +42°$ (c = 1.6, $CHCl_3$). ^1H-NMR ($CDCl_3$) δ: 2.03, 2.04, 2.11 (3s, 12H, OAc), 3.99–4.13 (m, 1H, H-5), 4.14–4.23 (m, 2H, H-6a, H-6b), 4.34 (dd, $J_{2,1} = J_{2,3}$ = 12.5 Hz, 1H, H-2), 5.09 (t, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 9.3 Hz, 1H, H-4), 5.41 (dd, $J_{2,3}$ = 9.1 Hz, $J_{3,4}$ = 9.2 Hz, 1H, H-3), 6.05 (d, $J_{1,2}$ = 9.1 Hz, 1H, H-1), 7.47–7.50 (m, 2H, arom.), 7.55–7.63 (m, 1H, arom.), 8.10–8.13 (m, 2H, arom.). ^{13}C NMR ($CDCl_3$) δ: 20.45, 20.55, 20.92 (CH_3CO), 47.57 (C-2), 61.33 (C-6), 69.96 (C-4), 72.83 (C-5), 74.37 (C-3), 93.66 (C-1), 128.47, 130.10, 133.88 (C-arom.), 164.12 [O*C*(O)Ph], 169.38, 169.50, 169.76 (CH_3CO). Anal. Calcd. for $C_{19}H_{21}BrO_9$ (473.27): C, 48.22; H, 4.47. Found: C, 48.39; H, 4.62.

1-O-Benzylcarbonyl-3,4-6-tri-O-acetyl-2-bromo-2-deoxy-β-D-gluco-pyranose (**11dβ**). Phosphorodithioate **7** (518 mg, 1 mmol), phenylacetic acid **9d** (136 mg, 1 mmol), and silver fluoride (651 mg, 3 mmol) were caused to react. For reaction conditions, see Table 3 (entry 16). Column chromatography (for eluent see general procedure) afforded 300 mg (62%) of the derivative **11d**β as a syrup; $[\alpha]_{578}^{27} = +46°$ (c = 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$) δ: 2.20, 2.23, 2.27 (3s, 12H, OAc), 3.64–3.74 (s, 2H, CH_2Ph), 3.80–3.93 (m, 1H, H-5), 4.00–4.19 (m, 2H, H-6a, H-6b), 4.37 (dd, $J_{2,1}$ = 11.5 Hz, $J_{2,3}$ = 11.2 Hz, 1H, H-2), 5.03 (dd, $J_{3,4}$ = 9.1 Hz, $J_{4,5}$ = 9.2 Hz, 1H, H-4), 5.32 (dd, $J_{2,3} = J_{3,4}$ = 9.2 Hz, 1H, H-3), 5.81 (d, $J_{1,2}$ = 9.1 Hz, 1H, H-1), 7.29 (s, 5H, arom.). ^{13}C NMR ($CDCl_3$) δ: 19.96, 20.09, 20.44 (CH_3CO), 40.10 (CH_2), 47.30 (C-2), 60.93 (C-6), 68.13 (C-4), 69.36 (C-5), 71.46 (C-3), 92.83 (C-1), 126.88, 128.24, 128.97, 132.37 (C-arom.), 168.48 [$OC(O)CH_2$], 169.14, 169.42, 169.90 (CH_3CO). Anal. Calcd for $C_{20}H_{23}BrO_9$ (487.30): C, 49.30; H, 4.76. Found: C, 49.11; H, 4.63.

Method B for esters of **11a**α *and* **11b**α**.** To the solution of phosphorodithioate **7** (1 mmol) in glacial acetic acid **9a** (30 mL) or propionic acid **9b** (30 mL), respectively, in the presence of molecular sieves (4A), a stoichiometric amount of silver carbonate (5 mmol) was added. The mixture was stirred at ambient temperature and in the dark. For time, see Table 3 (entries 4 and 7). After the reaction had been completed, 30 mL of dichloromethane was added and the precipitated silver salt of phosphorothio acid and molecular sieves were removed by filtration (Celite 535). The filtrate was evaporated in vacuo. The syrupy residue was dissolved in dichloromethane (20 mL), and the solution was washed with aq Na_2CO_3 and water. The dried ($CaCl_2$) organic solvent was evaporated in vacuo and the syrupy residue, which contained esters **11a**α and **11b**α, respectively, was purified.

1,3,4,6-Tetra-O-acetyl-2-bromo-2-deoxy-α-D-gluco-pyranose (**11a**α). Phosphorodithioate **7** (505 mg, 1 mmol) was dissolved in acid **9a** (30 mL) and silver carbonate (136 mg, 0.5 mmol) was added to react. For reaction conditions, see Table 3 (entry 4). Crystallization from ethanol gave 285 mg (68%) of **11a**α as colorless crystals, m.p. 80–81°C. ^1H NMR spectroscopic data correlated with the data described in the literature [10].

1-O-Propionyl-3,4,6-tri-O-acetyl-2-bromo-2-deoxy-α-D-gluco-pyranose (**11b**α). Phosphorodithioate **7** (505 mg, 1 mmol), was dissolved in acid **9b** (30 mL) and silver carbonate (136 mg, 1 mmol) was added to react. For reaction conditions see Table 3 (entry 7). The crude product was purified by column chromatography with the use of ethyl acetate/hexane

in the ratio of 1:3 as eluent and gave **11b**α (600 mg, 70%) as light straw-colored oil; $[\alpha]_{578}^{27} = +95°$ (c = 2.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 1.11 (t, 3H, CH_3CH_2), 2.03, 2.07, 2.10 (3s, 12H, OAc), 2.45 (q, 2H, CH_3CH_2), 4.05–4.37 (m, 3H, H-5, H-6a, H-6b), 4.49 (dd, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.0 Hz, 1H, H-2), 5.31 (t, $J_{3,4} = J_{4,5}$ = 9.5 Hz, 1H, H-4), 5.49–5.81 (m, 1H, H-3), 6.42 (d, $J_{1,2}$ = 3.3 Hz, 1H, H-1). ^{13}C-NMR ($CDCl_3$); δ: 9.32 (CH_3CH_2), 20.28 (CH_3CO), 29.32 (CH_3CH_2), 48.65 (C-2), 61.42 (C-6), 66.02 (C-4), 68.95 (C-5), 71.02 (C-3), 92.65 (C-1), 164.28 [$OC(O)C_2H_5$], 168.87, 169.09, 169.15 (CH_3CO). Anal. Calcd. for $C_{15}H_{21}BrO_9$ (425.23): C, 42.37; H, 4.98. Found: C, 42.59; H, 5.07.

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