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Derivatives of α- and β-*S*-Thiophosphates of 2-Bromo-2-deoxy-D-hexopyranose

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ABSTRACT: *The first examples of S-thiophosphate derivatives of 2-bromo-2-deoxy sugars* **7–12** *were synthesized by reacting alkyl ammonium salts* **1–4** *of thiophosphoric acids with α-1,2-cis (***5***) or α-1,2-trans dibromo sugars (***6***) and addition of free thiophosphoric acids* **1a** *or* **2a** *to 2-bromo-D-glucal (***13***). It was observed that the solvent determines formation of either the O- or S-glycosyl compound. β-Thiophosphates can be transformed to the α-configuration in the presence of acid in quantitative yield. The structures of the synthesized derivatives of* **7–12** *were confirmed by spectroscopic methods.* © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 465–470, 1999

INTRODUCTION

Phosphorylated sugars represent a class of derivatives of high biological importance; they participate in the metabolism of nucleotides [1] and are known as mediators of glycosyl transfer [2] and as regulators of the cellular metabolism of D-glucose [3]. Dithiophosphates of 2-deoxy-D-glucose and fully acetylated D-glucose are interesting compounds from both a biological and chemical point of view. These derivatives as glycosylating donors are valuable for the synthesis of other classes of sugars, for example, *O*-alkyl glycosides [4], *O*-aryl glycosides [5], disaccharides [6] and 1-*O*-acyl esters [7]. The reaction of salts of thio acids with α-bromides afforded *β-S*- and *β-O*-thiophosphates of fully acetylated sugars in high yields. The effect of a salt cation on forming either *S*- or *O*-thiophosphate has already been noted [8]. Also, the conditions of the reaction can determine the formation of either *S*- or *O*-glycosyl derivatives, as it was shown by means of glycosylation of an alkyl ammonium salt of a thio acid with 1-unprotected benzylated D-glucose. The use of $BF_3 \cdot Et_2O$ as a promoter leads to the *S*-glycosyl derivative [9]. If tetrabutyl-ammonium chloride is used as a catalyst in a phase transfer system, the reaction leads to the formation of the *O*-glycosyl derivative [10]. Only one example of a phosphate with a halogen atom bound to the C-2 of the sugar ring (α-2-deoxy-2-iodoglycosyl phosphate), as obtained in the N-iodosuccinimide procedure, is known [11].

This article presents two independent routes of the synthesis of α- and β-thiophosphates of 2-bromo-2-deoxy sugars.

RESULTS

The reaction of stoichiometric amounts of **1–4**, alkyl ammonium salts of thiophosphoric acid [12–14], with either 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranose bromide **(5)** [15] or 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-mannopyranose bromide **(6)** [16] in dichloromethane under reflux for several hours leads to either α- or β-thiophosphates, **7–12,** of the 2-bromo-2-deoxy sugars in quantitative yields (Scheme 1). The details of reaction conditions and the ratio of anomers observed by ^{31}P NMR are included in Table 1 (entries 1–6). When reacted with **5** or **6**, the alkyl ammonium salts of **1–4** (triethylammonium or dicyclohexylammonium), which have ambident anions of phosphorus thio acids gave *S*-

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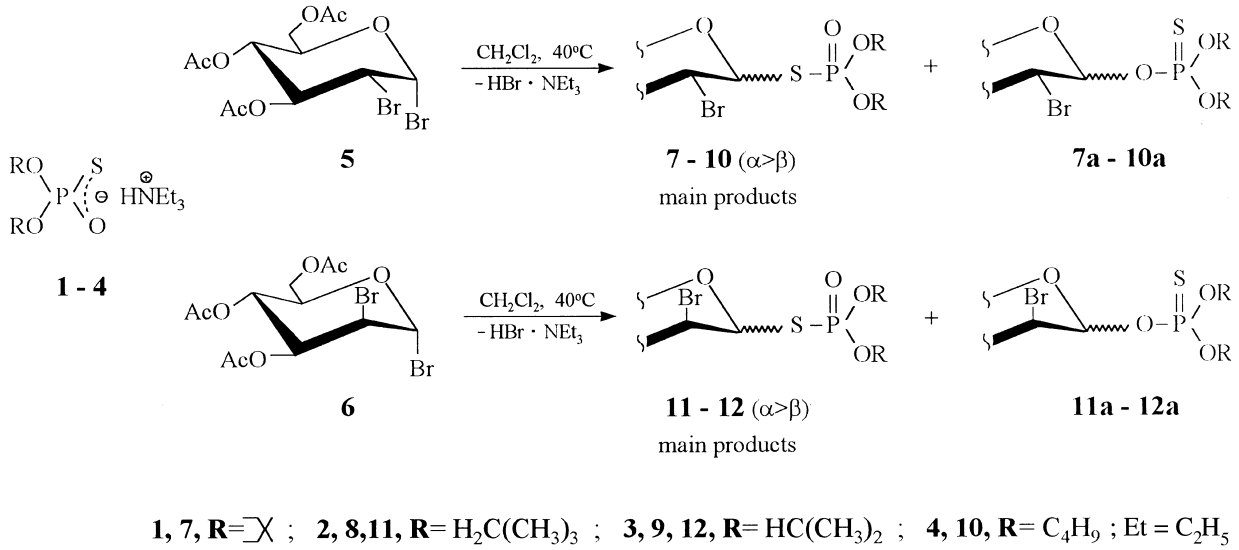


SCHEME 1 Glycosylation of alkyl ammonium salts **1–4** of thiophosphoro acids by α-1,2-dibromo sugar **5** or **6** in dichloromethane as a solvent.

TABLE 1 *S*- and *O*-Thiophosphates of 2-Bromo-2-deoxy-α/β-D)-hexopyranose **(7–12)**: Reaction Time and ^{31}P NMR Data

					^{31}P NMR ($CDCl_3$), δ (ppm)		
					S-Glycosyl		*O-Glycosyl*
Entry	*Salt*	*α-1,2- Dibromide*	*Glycosyl*	Reaction Time at Boiling *Point (in CH_2Cl_2)*	*α(%)*	*β(%)*	*α/β(%)*
1	**1**	**5**	**7**	10 h		14.97 (88)	58.41 (12)
2	**2**	**5**	**8**	12 h	23.13 (22)	22.10 (62)	59.10 (17)
3	**3**	**5**	**9**	25 h		19.58 (100)	
4	**4**	**5**	**10**	15 h	22.59 (15)	22.33 (70)	57.21 (15)
5	**2**	**6**	**11**	10 h	21.10 (100)		
6	**3**	**6**	**12**	12 h	19.42 (65)	19.10 (19)	57.17 (16)
7	**1**	**5**	**7a**	90 min[a]		14.97 (10)	59.02 (α) (27) 58.41 (β) (63)

[a]Reaction was performed at boiling point in butanone-2.

glycosyl derivatives of **7–12** in yields of 85–100%. These major products were accompanied by small amounts of the *O*-glucosyl derivatives (**7a,8a, 10a,12a**), as shown in Table 1 (entries 1, 2, 4, 6). The spectroscopic data (^{31}P NMR) show the highest stereoselectivity (100%) for forming the β-*S*-glycosyl derivative of **9** and the α-*S*-glycosyl of **11** (Table 1, entries 3, 5). Monitoring (^{31}P NMR) of the reaction revealed that the *O*-glycosyl derivative (δ = 57–59) as the initial product was rapidly converted to the more thermodynamically stable *S*-glycosyl derivative with the chemical shift the range of δ = 15–23 (rearrangement thiono → thiolo). Based on the data in the literature [8] and the results of the study presented previously (see Table 1, entries 1, 2, 4, 6), I expected to find compounds *O*–(**9,11a**) and *S*-glycosyl derivatives (**9,11**) in the reaction mixture (using ^{31}P NMR). The stereoselective course of the reaction toward *S*-glycosyl derivatives **9**β and **11**α was unexpected.

The ^{1}H NMR spectral analysis, chemical shift, and coupling constants (H-1/H-2, $J_{1,2} \approx 9.0$ Hz, and H-1/P, $^3J_{HP} \approx 10.0$ Hz) for the anomeric proton indicate the *β-gluco* configuration of **7–9** (Table 1, entries 1–4). The downfield signal of H-1 ($\delta = 6.43$, as *dd*) and the coupling constant with H-2 ($J_{1,2} \approx 1.0$ Hz) and P ($^3J_{HP} \approx 12.5$ Hz) show that the synthesis of **11** and **12** leads to the formation of α-anomers, which have the *manno* configuration at C-2 (Table 1, entries 5,6).

The reaction of salt **1** with **5** under reflux in butanone-2 gave the *O*-thiophosphate of **7a** as a mixture of α- and β-anomers in 90% yield (Scheme 2). Under the above-mentioned conditions, the *S*-glycosyl (7β) derivative was formed in as low as a 10% yield (Table 1, entry 7). By means of column chromatography on a silica gel, it was possible to separate pure **7a** (with 67% yield) as a mixture of α/β anomers in a ratio of 35%:65%. The same results were observed spectroscopically (^{31}P NMR) in an alternative reaction of the silver salt of thio acid **1a** with **5** performed in boiling benzene for 3 hours. The use of butanone-2 as a solvent in the reaction of **1** with **5** offers a better route for the synthesis of **7a**.

In the presence of a catalytic amount of acid, β-*S*-thiophosphate (**7*β***) in dichloromethane was transformed in a few hours into the α-anomer of **7**α in quantitative yield. This reaction led to a crystalline form of **7**α that was stable for several months at 5–10°C.

It was found that thiophosphates of 2-bromo-2-deoxy sugars can be obtained by the addition of a stoichiometric amount of free thiophosphoric acid **1a** or **2a** (separated from alkyl ammonium salts **1** or **2**) to 2-bromo-D-glucal **13** [15] under reflux in benzene, as shown in Scheme 3. Regioselective addition afforded the *S*-glycosyl derivatives of **7** and **8** as the main products. Spectroscopic data of **7** and **8** obtained by this route were the same as for glycosylation of salt **1** or **2** by dibromides **5** or **6**.

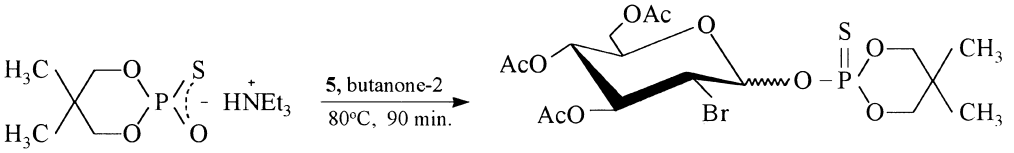
In conclusion, this work presents stereoselective syntheses of *β-S-gluco* and *α-S-manno* thiophosphates of 2-bromo-2-deoxy-D-hexopyranose, compounds which provide interesting models for investigations in sugar chemistry.

EXPERIMENTAL

Instruments and Starting Materials

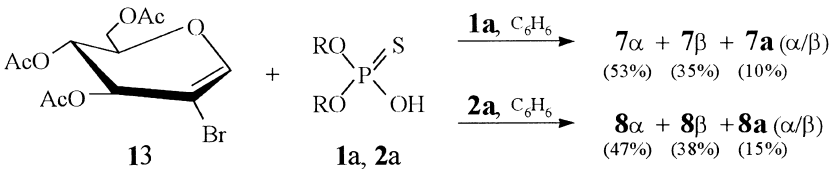
Melting points were determined with a Boetius PHMK 05 apparatus and are uncorrected. The ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded in $CDCl_3$ with a Bruker AC 200 spectrometer operating at 200.11 MHz, 50.33 MHz, and 81.01 MHz, respectively. The ^{1}H and ^{13}C chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane (1%) as an internal standard, while the ^{31}P chemical shifts are relative to external 85% H_3PO_4. Specific rotations were measured in chloroform (Polamat A polarimeter). With benzene/chloroform/acetone in the ratio of 3:1:1 as the developing solvent, thin-layer chromatography (TLC) was performed on silica plates (Kieselgel 60 F_{254}, Merck). The detection was done by exposure to iodine vapors. Column chromatography was performed on a silica gel (35–70 mesh, Merck). Elemental analyses were performed by the Microanalytical Laboratory, Institute of Chemistry, Medical University of Łódź, and the Microanalytical Laboratory of the Center of Molecular and Macromolecular Studies of the Polish Academy of Science, Łódź. All reactions were performed in dry solvents that were prepared by standard techniques.

All of the starting materials of the **1–4** salts, free acids **1a, 2a,** and α-1,2-dibromides **5** and **6** were prepared according to procedures described earlier. As phosphorylating agents, we have used the triethylammonium salt of 2-hydroxy-2-thio-5,5-dimethyl-1,3,2-dioxaphosphorinane **1** [12] and its free acid **1a** [12], the triethylammonium salt of acid *O,O*-dineopentyl-thiophosphate **2** [13] and its free acid **2a** [13], dicyclohexylammonium salts *O,O*-diisopropyl-thiophosphate **3** [14], and *O,O*-dibutyl-thiophosphate **4** [14]. 3,4,6-Tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide **5** and 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal **13**, were obtained from α-acetobromoglucose. 3,4,6-Tri-*O*-acetyl-2-bromo-2-deoxy-α-D-mannopyranosyl bromide **6** was synthesized by a method described by Descotes et al. [16].



1 **7a** (α<β)

SCHEME 2 Glycosylation of triethylammonium salt **1** by **5** in butanone-2 as a solvent.



1a, R= ; **2a, R=** $H_2C(CH_3)_3$

SCHEME 3 Addition of free thiophosphoro acids (**1a** or **2a**) to 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal.

*General Procedure for Syntheses of α/β Thiophosphates of 3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-*D*-gluco and Mannopyranose* **7–12**

Stoichiometric amounts of alkyl ammonium salts **1–4** and α-1,2-dibromide of either **5** or **6** were heated under reflux in dichloromethane (for duration see Table 1, entries 1–7). When the reaction had stopped (monitored by TLC and ^{31}P NMR), the amine hydrobromide was filtered off (yield was about 100%). The organic layer was washed three times with water and dried with $CaCl_2$. Concentration in vacuo gave syrupy residues of **7–12**. The ratio of anomers was confirmed spectroscopically (^{31}P, ^{1}H, and ^{13}C NMR). Pure thiophosphates of the 2-bromo sugars were separated from crude reaction mixtures by means of crystallization or column chromatography on a silica gel.

*S-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-β-*D*-gluco-pyranosyl)-thio-2-oxo-5,5-dimethyl-1,3,2-dioxophosphorinane* (**7β**). Salt **1** (0.28 g, 1 mmol) and **5** (0.43 g, 1 mmol), were reacted with the solvents and with the conditions shown in Table 1. Crystallization from carbon tetrachloride/petroleum ether and recrystallization from carbon tetrachloride afforded (0.34 g, 63%) of **7β** as colorless crystals, m.p. 152–154°C. $[\alpha]_{578}^{27} = +15$ (c = 0.1, $CHCl_3$). ^{31}P NMR see Table 1. ^{1}H NMR ($CDCl_3$) δ:0.89 and 1.29 (2s, 6 H, 2 CH_3), 2.04, 2.06, 2.08 (3s, 9 H, 3 CH_3CO), 3.78–3.96 (m, 4 H, 2 CH_2), 4.06–4.15 (m, 1 H, 5-H), 4.16–4.29 (m, 2 H, 6-H_a, 6-H_b), 4.31–4.38 (m, 1 H, 2-H), 5.08 (*dd*, $J_{3,4}$ = 10.3 Hz, $J_{4,5}$ = 9.7 Hz, 1 H, 4-H), 5.18 (*dd*, $J_{2,3}$ = 11.5 Hz, $J_{3,4}$ = 10.2 Hz, 1 H, 3-H), 5.54 (*dd*, $J_{1,2}$ = 9.2 Hz, $^{3}J_{HP}$ = 10.8 Hz, 1 H, 1-H). ^{13}C NMR ($CDCl_3$): δ: 20.03, 20.29, 20.37, (3s, *C*:H_3CO), 21.59 (s, CH_3CO), 21.59 (s, CH_3, eq), 21.72 (s, CH_3, ax), 32.08 [*d*, $^{3}J_{C,P}$ = 6.0 Hz, *C*$(CH_3)_3$], 49.27 (*d*, $^{3}J_{CP}$ = 9.6 Hz, C-2), 60.74 (s, C-6), 68.02 (s, C-4), 75.23 (s, C-5), 76.43 (s, C-3), 78.19 (dd, $^{2}J_{CP}$ = 9.8 Hz, CH_2O), 88.75 (*d*, $J_{CP} < 1$ Hz, C-1), 169.15, 170.11, 170.21 (3s, 3 CH_3CO). Anal. calcd. for $C_{17}H_{26}BrO_{10}PS$ (532.02): C, 38.34; H, 4.93. Found: C, 37.96; H, 4.69.

*S-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-*D*-gluco-pyranosyl)-thio-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane* (**7α**). Two drops of acetic acid were added to a solution of **7β** (0.53g 1 mmol) in CH_2Cl_2 (7 mL), and the mixture was heated at the boiling point of the solvent for 12 hours. The crude product was purified by crystallization from carbon tetrachloride/petroleum ether and recrystallized from carbon tetrachloride to afford (0.36 g, 68%) of pure **7α** as colorless crystals, m.p. 170–172°C. $[\alpha]_{578}^{26} = +16$ (c = 1.3, $CHCl_3$). ^{31}P NMR ($CDCl_3$): δ: 15.20. ^{1}H NMR ($CDCl_3$) δ; 0.91 and 1.29 (2s, 6 H, 2 CH_3), 2.01, 2.04, 2.06 (3s, 9 H, 3 CH_3CO), 3.83–3.99 (m, 4 H, 2 CH_2), 4.02–4.14 (m, 1 H, 5-H), 4.26–4.29 (m, 2H, 6-H_a, 6-H_b), 4.31–4.37 (m, 1 H, 2-H), 5.04 (*dd*, 1 H, $J_{3,4}$ = 10.2 Hz, $J_{4,5}$ = 10.2 Hz, 1 H, 4-H), 5.35 (*dd*, $J_{3,4}$ = 9.1 Hz, $J_{2,3}$ = 8.9 Hz, 1 H, 3-H), 6.07 (*dd*, $J_{1,2}$ = 4.9, $^{3}J_{HP}$ = 8.2 Hz, 1 H, 1-H). ^{13}C NMR ($CDCl_3$) δ: 20.60, 20.75, 20.85 (3s, *C*H_3CO), 22.11 (s, CH_3, eq), 22.50 (s, CH_3, ax), 32.69 [*d*, $^{3}J_{CP}$ = 6.4 Hz, *C*$(CH_3)_2$] 47.08 (*d*, $^{3}J_{C\text{-}2,P}$ = 8.7 Hz, C-2), 61.58 (s, C-6), 69.21 (s, C-4), 75.29 (s, C-5), 76.62 (s, C-3), 78.46 (*dd*, $^{2}J_{CP}$ = 8.4 Hz, OCH_2), 85.72 (*d*,$^{2}J_{CP} < 1$ Hz, C-1), 169.56, 169.87, 170.76, (3s, 3 CH_3CO). Anal. calcd for $C_{17}H_{26}BrO_{10}PS$ (532.02): C, 38.34; H, 4.93; P, 5.82. Found: C, 38.53; H, 5.20; P, 5.86.

*O-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α/β-*D*-glucopyranosyl)-oxo-2-thiono-5,5,-dimethyl-1,3,2-dioxaphosphorimnan* (**7a**). Salt **1** (0.35g, 1 mmol) and **5** (0.43 g, 1 mmol) were reacted with the solvents and with the conditions, shown in Table 1. The crude product was purified by chromatography on a silica gel (eluent:diethyl ether/hexane in the ratio of 1:1), and afforded **7a** (0.35 g, 67%) as a mixture of anomers, ^{31}P NMR δ: 58.41 and 59.02 in a ratio of 65% (β): 35% (α). $[\alpha]_{578}^{27}$-10 (c = 0.1, $CHCl_3$). ^{1}H NMR

($CDCl_3$) δ: 0.85 and 1.18 (2s, 6 H, 2 CH_3), 2.05 (s, 3 H, CH_3CO), 2.07 (s, 6 H, 2 CH_3CO), 3.40–3.51 (m, 4 H, 2 CH_3), 4.04–4.36 (m, 3 H, 5-H, 6-H_a, 6-H_b), 4.80–4.97 (m, 1 H, 2-H), 5.15–5.23 (m, 1 H, 4-H), 5.37–5.40 (m, 1 H, 3-H), 5.48 (*dd*, $J_{1,2}$ = 8.4 Hz, $^3J_{HP}$ = 11.2 Hz, 1 H, 1-Hβ), 6.45 (*dd*, $J_{1,2}$ = 3.3 Hz, J_{HP} = 11.2 Hz, 1 H, 1-Hα). ^{13}C NMR ($CDCl_3$) δ: 20.35 (s, 4 CH_3CO, α/β), 20.64 (s, 2 CH_3CO, α/β), 31.80 [*d*, $^3J_{CP}$ = 6.0 Hz, $C(CH_3)_2$], 61.03, 61.72 (2s, C-6, α/β), 95.29 (*d*, $^2J_{CP}$ < 1 Hz, C-1α), 98.62 (*d*, $^2J_{CP}$ < 1 Hz, C-1β), 168.97, 169.27, 169.55, 170.11, 170.28, 170.40 (6s, 6 CH_3CO, α/β). Anal. calcd. for $C_{17}H_{26}BrO_{10}PS$ (532.02): C, 38.34; H, 4.93. Found: C, 38.57; H, 5.18.

S-(*3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-β-*D-*glucopyranosyl*)-*O,O*-diisopropylthiophosphate (**9β**). Salt **3** (0.38 g, 1 mmol) and **5** (0.43 g, 1 mmol) were reacted with the solvents and with the conditions shown in Table 1. Chromatography was performed twice on a silica gel column with diethyl ether/hexane in the ratio of 1:1 as the eluent to afford (0.31 g, 58%) of **9β** as a light straw-colored oil. $[\alpha]_{578}^{26}$ = +19 (c = 0.2, $CHCl_3$). ^{31}P NMR, see Table 1. ^{1}H NMR ($CDCl_3$) δ: 1.36 (*dd*, $^3J_{HP}$ = 3.2 Hz, 12 H, 4 CH_3), 2.00, 2.05, 2.06 (3s, 9 H, 3 CH_3CO), 3.80–3.94 (m, 1H, 5-H), 4.08–4.38 (m, 3H, 2-H, 6-H_a, 6-H_b), 4.73–4.81 [m, 1 H, $CH(CH_3)_3$], 4.90 (*dd*, $J_{3,4}$ = 11.4 Hz, $J_{4,5}$ = 10.8 Hz, 1 H, 4-H), 5.15 (*dd*, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 10.7 Hz, 1 H, 3-H), 5.30 (dd, $J_{1,2}$ = 9.3 Hz, $^3J_{HP}$ = 9.5 Hz, 1 H, 1-H). ^{13}C NMR ($CDCl_3$) δ: 20.22 (s, 2 CH_3CO), 20.33 (s, CH_3CO), 23.14 (*d*, $^3J_{CP}$ = 4.6 Hz, CH_3), 23.42 (*d*, $^3J_{CP}$ = 4.5 Hz, CH_3), 49.09 (*d*, $^3J_{CP}$ = 10.3 Hz, C-2), 61.44 (s, C-6), 68.26 (s, C-4), 73.15 (s, C-5), 73.26 (s, C-3), 75.70 (*d*, $^2J_{CP}$ = 6.3 Hz, CH), 85.56 (*d*, $^2J_{CP}$ < 1 Hz, C-1), 169.11, 169.16, 170.07 (3s, CH_3CO). Anal. calcd. for $C_{18}H_{30}BrO_{10}PS$ (549.36): C, 39.41; H, 5.52; P, 5.65. Found: C, 39.19; H, 5.25; P, 5.32.

S-(*3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-*D-*mannopyranosyl*)-*O,O-dineopentylthiophosphate* (**11α**): Salt **2** (0.35 g, 1 mmol) and **6** (0.43 g, 1 mmol) were reacted with the solvents and with the conditions shown in Table 1. Crystallization from carbon tetrachloride/hexane afforded (0.40 g, 67%) of **11α** as colorless crystals, m.p. 182–184°C. $[\alpha]_{578}^{27}$ = +64 (c = 0.1, $CHCl_3$). ^{31}P NMR (see Table 1). ^{1}H NMR ($CDCl_3$) δ: 0.94 and 0.96 (2s, 18 H, 6 CH_3), 2.01, 2.05, 2.07 (3s, 9 H, 3 CH_3CO), 3.77–3.89 (m, 4 H, 2 CH_2O), 4.12–4.43 (m, 3 H, 5-H, 6-H_a, 6-H_b), 4.82 (*dd*, $J_{1,2}$ = 1.4 Hz, $^3J_{HP}$ = 13.2 Hz, 1 H, 2-H) 5.27–5.41 (m, 1 H, 3-H), 5.50 (*dd*, $J_{3,4}$ = 11.1 Hz, $J_{4,5}$ = 10.8 Hz, 1 H, 4-H), 6.43 (*dd*, $J_{1,2}$ = 1.2 Hz, $^3J_{HP}$ = 12.3 Hz, 1 H, 1-H). ^{13}C NMR ($CDCl_3$) δ: 20.40, 20.48, 20.59 (3s, CH_3CO), 25.86 (s, 6 CH_3), 32.33 [*d*, $^3J_{CP}$= 6.9 Hz, $C(CH_3)_3$], 51.63 (s, C-2), 61.13 (s, C-6), 64.95 (s, C-3), 67.23 (s, C-4), 73.61 (s, C-5), 77.66 (*d*, $^2J_{CP}$ = 6.9 Hz, CH_2O), 85.20 (*d*, $^2J_{CP}$ < 1 Hz, C-1), 168.97, 170.01, 170.12 (3s, CH_3CO). Anal. calcd. for $C_{22}H_{38}BrO_{10}PS$ (605.47): C, 43.64; H, 6.33; P, 5.12. Found: C; 43.35; H, 6.16; P 4.89.

General Procedure for the Addition of Thiophosphate acids (**1a, 2a**) *to 3,4,6-Tri-O-Acetyl-2-bromo-*D-*glucal* (**13**). Stoichiometric amounts of acid **1a** or **2a** dissolved in the smallest possible amount of benzene were added to the solution of **13** (1 mmol). The reaction mixtures were heated under reflux for several hours. After completion of the reaction (TLC and ^{31}P NMR monitored), the organic layer was washed with aqueous $NaHCO_3$ and water, and were dried ($CaCl_2$). The organic solvent was evaporated under reduced pressure. Syrupy residues contained the corresponding derivatives **7** or **8** in almost quantitative yields.

Addition of Acid **1a** *to* **13**. Acid **1a** (0.45 g, 2.5 mmol) and **13** (0.87 g, 2.5 mmol) in benzene (8 mL) were refluxed for 20 hours to afford (1.15 g, yield 90%) of adducts **7β**, **7α**, **7a** in the ratio of 35:55:10, ^{31}P NMR ($CDCl_3$) δ: 14.97, 15.10, and 58.18, respectively. Spectroscopic data (^{31}P, ^{1}H, ^{13}C NMR) were identical with those of derivatives of 7 (α/β) and **7a**.

Addition of Acid **2a** *to* **13**. Acid **2a** (0.63 g, 2.5 mmol) and **13** (0.87 g, 2.5 mmol) in benzene (8 mL) were refluxed for 25 hours to afford (1.32 g, yield 87%) of adducts **8α**, **8β**, **8a** in the ratio of 47:38:15, ^{31}P NMR ($CDCl_3$) δ: 22.10, 23.13, and 59.10, respectively. Spectroscopic data (^{31}P, ^{1}H, ^{13}C NMR) were identical with those of derivatives of **7** (α/β) and **7a**.

REFERENCES

[1] Bayer, T. A.; Sadler, J. E.; Rearick, J. J.; Paulsen, J. C.; Hill, R. J. Adv Enzymol Relat Arens Mol 1981, 52, 23.

[2] Singer, S. J. Annu Rev Biochem 1981, 50, 733, and references cited therein.

[3] (a) Kim, J. H.; Kim, S. H.; Hahn, E. W.; Song, C. W. Science 1978, 200, 206; (b) Ekstein, F. Annu Rev Biochem 1985, 54, 367.

[4] Michalska, M.; Borowiecka, J.; J Carbohydr Chem 1983, 2, 99.

[5] Bielawska, H.; Michalska, M. J Carbohydr Chem 1986, 5, 445.

[6] (a) Bielawska, H.; Michalska, M. J Carbohydr Chem 1991, 10, 107; (b) Laupichler, J.; Sajus, H.; Thiem, J. Synthesis 1992, 11, 1133.

[7] (a) Borowiecka, J.; Michalska, M. Synthesis 1994, 7, 709; (b) Borowiecka, J.; Michalska, M. Synthesis 1996, 7, 858; (c) Borowiecka, J. Liebigs Ann Rec 1997, 7, 2147.

[8] (a) Michalska, M.; Michalski, J.; Orlich, J. Bull Acad Polon Sci Ser Sci Chem 1974, 12, 1053; (b) Michalska, M.; Michalski, J.; Orlich, J. Tetrahedron 1978, 34, 617.
[9] Kudelska, W. Pol J Chem 1997, 71, 1548.
[10] Bogusiak, J.; Szeja, W. J Carbohydr Chem 1991, 10, 47.
[11] Niggermann, J.; Lindhorst, T. K.; Walfort, M.; Laupichler, L.; Sajus, A.; Thiem, J. Carbohydrate Res 1993, 246, 173.
[12] Edmundson, R. S.; Lambie, A. J. J Chem Soc 1967, 8, 577.
[13] Bluj, S.; Borecka, B.; Łopusiński, A.; Michalski, J. Roczniki Chemii 1974, 48, 329.
[14] Kabachnik, M. J.; Joffe, C. T.; Mastriukowa, T. A. J Gen Chem 1955, 25, 684.
[15] Fogh, A.; Lundt, J.; Pedersen, C.; Rasmussen, R. Acta Chem Scan 1977, B31, 768.
[16] Teichmann, M.; Descotes, G.; Lafont, D. Synthesis 1993, 7, 889.