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GLYCOSYLATION OF ORGANIC THIO- AND SELENOACIDS OF PHOSPHORUS†

THE REACTION OF ORGANIC MONOTHIO ACIDS OF PHOSPHORUS WITH GLYCOSYL BROMIDES. THIONO–THIOLO REARRANGEMENT OF GLYCOSYL PHOSPHOROTHIOATES

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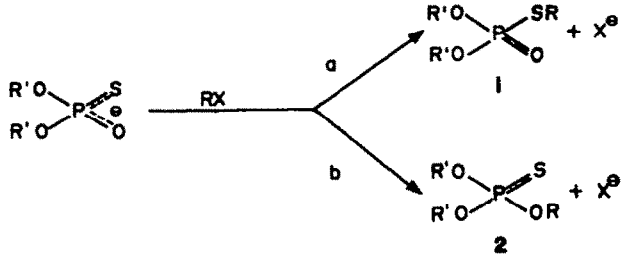
Abstract—Ambident anions derived from phosphorus monothio acids have been glycosylated by 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl-, 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl- and 2,3,4-tri-acetyl-α-D-xylopyranosyl bromides, yielding β-S-glycosyl- and β-O-glycosylthioates. The S/O ratio of the glycosylated phosphorothioates depends markedly on the salt used. Ammonium salts favour the formation of S-derivatives, whereas silver salts give mainly O-derivatives. O-Glucosyl phosphorothioate undergoes thermal isomerisation to S-glucosyl phosphorothioate, with retention of configuration at the glycosylic centre. The implications of this stereochemical result are briefly discussed.

The salts of the monothio acids of phosphorus are easily obtainable by the addition of elemental S to dialkyl phosphites, or their structural analogues, in the presence of amines.[1] The salts are typical ambident nucleophiles, the negative charge being distributed within the O–P–S triad between the "hard" oxygen and the "soft" polarisable S atom.

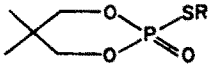
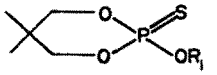
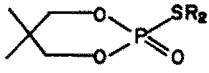
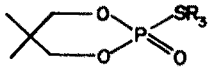
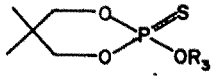


The reactions of monothio acids with electrophilic reagents R–X are markedly dependent on the nature of the electrophilic reagent. Other factors are of less importance. There is a qualitative consistency between the reaction course and the HSAB rule. The "soft" electrophiles such as alkyl halides react preferentially with the anions of phosphorus monothio acids with the formation of a C–S bond leading to thiolo derivatives 1. "Hard" reagents such as acylating and phosphorylating reagents react at the O atom giving thiono derivatives of type 2. Only a few examples are known of alkylating reagents which react in both directions a and b to give a mixture of derivatives 1 and 2. These include oxonium salts,[2] diazomethane[3] and certain types of diazonium salts.[4] Esters 1 and 2 are highly reactive towards both electrophilic and nucleophilic reagents. For example the phosphorus residue is readily split by hydrolysis or chlorinolysis yielding thiols[5] or sulphenyl chlorides,[6] respectively. These reactions may, therefore, be of potential use for introducing sulphur into sugars via esters 1. This paper deals with the glycosylation of ambident anions derived from monothio acids of phosphorus and describes a new class of electrophilic reagents, namely glycosyl halides, which may be made to react at either S or O depending on the conditions chosen. Several new types of derivatives of both classes 1 and 2 were obtained in the course of this study (R = peracetylated monosaccharide residues).

A dramatic difference in the course of glycosylation was observed when the triethylammonium or silver salts of the phosphorus monothio acids were used. Reaction with ammonium salts leads predominantly to thiolo derivatives 1. In the case of silver salts the proportions of the products formed can be reversed with derivatives of type 2 predominating. The present work is also concerned with the thiono–thiolo rearrangement 2→1.

†For a preliminary report see, M. Michalska, J. Michalski and I. Orlich, *Bull. de l'Acad. Polon. des Sciences, Ser. des Sci. Chim.* 22, 1053 (1974).

Table 1. ^{31}P NMR spectra of thiolo 1 and thiono 2 esters containing various sugar residues

Thioloesters	δ ppm	Thionoesters	δ ppm
	−13.5		−58.2
	−16.0	—	—
	−16.5		−60.5
$(NeopO)_2P(O)SR_1$	−23.0	$(NeopO)_2P(S)OR_1$	−66.9[a]
$(n\text{-}BuO)_2P(O)SR_1$	−21.0	$(n\text{-}BuO)_2P(S)OR_1$	−66.0[a]
$(EtO)_2P(O)SR_1$	−23.2	$(EtO)_2P(S)OR_1$	−66.3[a]

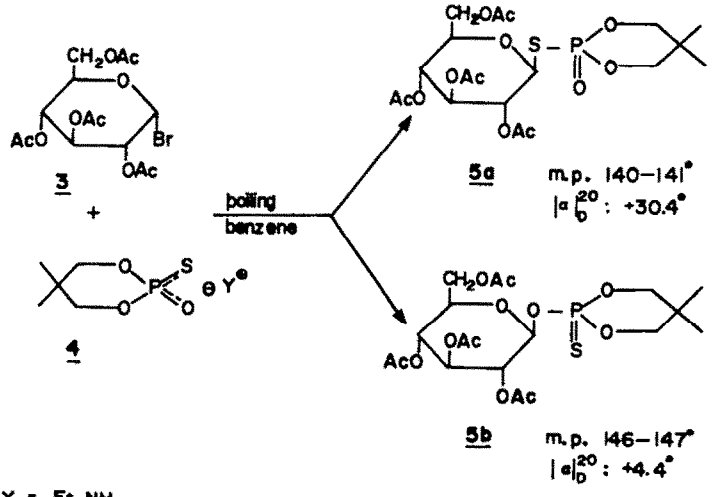
R_1 = 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl-.
R_2 = 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl-.
R_3 = 2,3,4-tri-O-acetyl-α-D-xylopyranosyl.
a—^{31}P NMR evidence only; compounds not isolated.

RESULTS AND DISCUSSION

Glycosylation of the ammonium salts of thiophosphorus acids in a neutral solvent like benzene, by means of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide **3**, is nearly quantitative (Method A). Special attention was given to glycosylation of the triethylammonium salt of monothiophosphoric acid **4** containing the 2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinyl ring system. These compounds are readily obtainable and tend to form crystalline derivatives readily. The main product in this case is the S-glucosyl derivative **5a**, accompanied by a small quantity of the O-glucosyl derivative **5b** which can be separated by means of TLC or fractional crystallisation.

In order to prove the configuration at the anomeric C atom, the S-glucosyl derivative **5a** was also obtained by two independent routes involving condensation of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl sulfenyl bromide **6**[8] with 2-hydro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinan **7**[9] (Method B) and reaction of the sodium salt of the 2,3,4,6-tetra-O-acetyl-β-D-thioglucose **8**[10] with 2-chloro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinan **9**[9] (Method C).

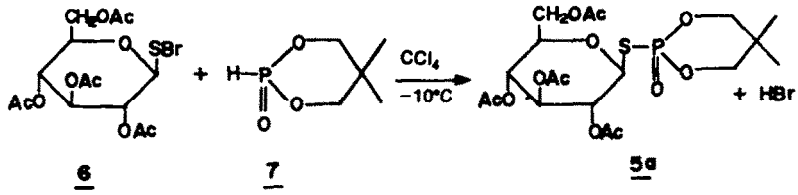
The properties of **5a** obtained by these two methods were identical with those of the compound obtained by glycosylation of the triethylammonium salt **4** with glucopyranosyl bromide. Since compounds **6** and **8** have the β-configuration at C_1[8,10] and the reactions described



do not involve rupture of the C_1–S bond, it is concluded that compound **5a** also has the β-configuration. Additional evidence for this assignment comes from the alkaline methanolysis of **5a** which leads to the known bis-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)disulphide.[11]

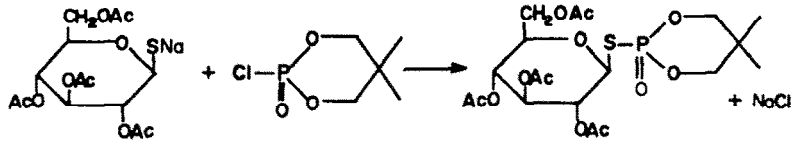
The structure of the S-glucosyl derivative **5a** is unambigously established by the presence in its IR spectrum of a band at 1280 cm^{-1}, characteristic of the P=O group. Confirmatory evidence is obtained from ^{31}P NMR spectrum which exhibits absorption characteristic for the P=O group, δ = −13.5 ppm (± 1.0 ppm). The O-isomer **5b** shows a P=S band in its IR spectrum at 680 cm^{-1} and the ^{31}P chemical shift observed δ = −58.2 ppm (± 1.0 ppm) is characteristic of thiono esters.[7]

When the glycosylation reaction was repeated with the silver salt in place of the triethylammonium salt a dramatic effect was observed. In this case the major product was the thionoester **5b** (61%).



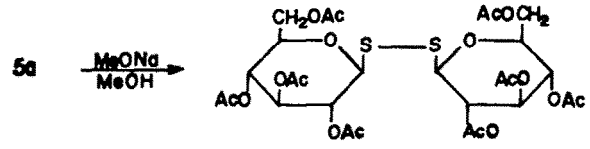
6 7 5a

$|\alpha|_D^{20}$ = +30.4°
m.p.: 140–14 f°

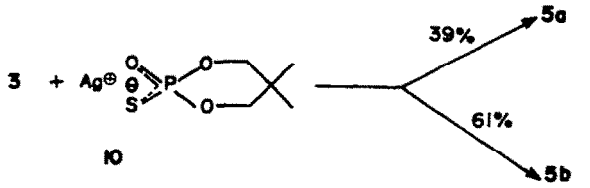


5a

$|\alpha|_D^{20}$ = +30.4°
m.p. 140–141°



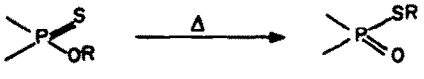
m.p. 143–144°
$|\alpha|_D^{20}$ = −158°



10

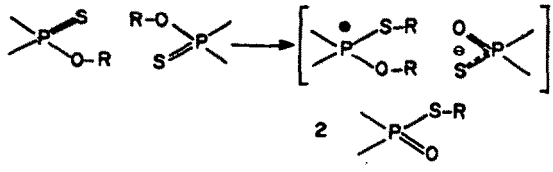
A similar effect was observed in the reaction between **10** and 2,3,4-tri-O-acetyl-α-D-xylopyranosyl bromide **11**. This is a novel observation in the alkylation of phosphorus monothio acids. An early report[12] described thiolo esters as the only product by treatment of alkyl halides with the silver salts of monothio acid. The pronounced difference between the silver and ammonium salts can be explained on the basis of two effects: an increase in the S_N1 character of the reaction by complexation of silver ion with the halide and shielding of the S atom through formation of a strong bond between the S and Ag atoms.

Because thiono esters of type **2** became readily obtainable via the silver salt it was of interest to study the steric course of the thermal thiono–thiolo isomerisation.



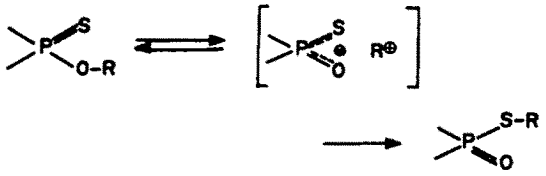
Heating **5b** at temperatures slightly above its m.p. for a few minutes gave **5a** in 95% yield. Since the ^{1}H NMR spectra of **5b** and **5a** establish unambigously that both have the β-configuration this result demonstrates that isomerisation takes place with full retention of configuration at the glycosylic C atom.

Such thiono–thiolo isomerisations which are closely related to the Pishchimuka reaction[13] were first described by Emmet and Jones.[14] Thermal isomerisations of this type are usually regarded as bi-molecular two-step processes.[15]

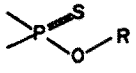


The stereochemical consequence of this mechanism is that the thiolo ester formed should have a configuration at carbon opposite to that in the thiono ester in view of the S_N2 type alkylation process involved. An ion pair mechanism is also possible.[16,17] This mechanism should

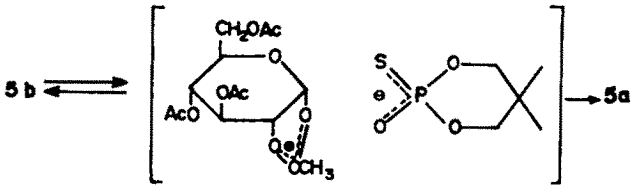
result either in retention of configuration at the C atom or racemisation.



An alternative mechanism involving a 4-center transition state has also been considered[18] and the stereochemical consequence of this concerted mechanism is that the thiolo ester configuration should be the same as that of the starting thiono ester. The retention of



configuration at the glycosylic C atom observed in the isomerisation of **5b** into **5a** leads us to favour a monomolecular mechanism with intermediate ion pair formation. Heterolytic cleavage of the C–O bond is facilitated by the conjugative influence of the sugar ring oxygen and anchimeric assistance of the acetoxy group in the C-2 position thus stabilizing the cation formed and preventing recombination to give the α-anomer.



Synchronous monomolecular or radical pair mechanisms are considered less likely although they cannot be completely excluded. Further stereochemical and kinetic studies on the isomerisation reaction are in progress.

Another observation of interest is that the rate of isomerisation leading to the thermodynamically more stable thiolo esters is distinctly less than that of the glycosylation reactions suggesting that the latter processes are kinetically controlled.

EXPERIMENTAL

M.ps (Kofler) are uncorrected. ^{31}P NMR spectra were recorded ($CHCl_3$, with 85% H_3PO_4 as external standard) on Jeol G-60 MHz operating at 24.3 MHz and Jeol-60 MHz FT. ^{1}H NMR spectra were recorded on Varian 60 MHz ($CDCl_3$, with TMS as internal standard). The chemical shifts are reported as δ values (±1 ppm). All IR spectra were recorded on Unicam SP-200 G (KBr tablets); all rotations were determined in $CHCl_3$ on a Perkin Elmer 141 photopolarimeter. All analyses were carried out at the Microanalytical Laboratory of the Centre of Molecular and Macromolecular Studies. TLC was performed on plates covered with Silica Gel G (Stahl), column chromatography on Silica Gel Serva (200–300 mesh). The mixture benzene–chloroform–acetone (3:1:1) was used as the developing solvent and eluent. The reaction course was monitored by tlc in parallel on two microscope slides. Spots were located with ammonium molybdate spray[19] and exposed to iodine vapours. The time of the reaction was indicated by the disappearance of the spot of the starting phosphorothioate salt. Light petroleum refers to the fraction of b.p. 60–80°.

Starting materials. Compound **3** and 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide were prepared according to Barczai-Martos and Körösy.[20] 2,3,4-Tri-O-acetyl-α-D-xylopyranosyl bromide was prepared according to Gakhokidze.[21] The triethylammonium and dicyclohexylammonium salts of the phosphorothioacids were obtained according to a standard procedure by adding sulphur to the appropriate hydrogen phosphite[22] in the presence of amine. The purity of the salts used was checked by ^{31}P NMR. The silver salt **10** was obtained from **4** and $AgNO_3$ in aqueous soln.

2 - S - (2,3,4,6 - *Tetra* - O - *acetyl* - β - D - *glucopyranosyl*) - 2 - *oxo* - 5,5 - *dimethyl* - 1,3,2 - *dioxaphosphorinan* (**5a**).

Method A. **4** (1.4 g; 4.8 mmole) and 2 g (4.8 mmole) of **3** were dissolved in benzene (20 ml) and heated under reflux for 8 hr. Triethylamine hydrobromide (0.8 g; 90%) was filtered off, the benzene soln washed twice with water and dried over $MgSO_4$. Benzene was evaporated under vacuum and the syrupy residue† purified (CCl_4–light petroleum). The product (2.3 g; 90%) crystallized as colourless needles, m.p. 140–141°; $|\alpha|_D^{20}$: +30.4° (c = 1.4). ^{31}P NMR: −13.5; ^{1}H NMR: 1.99, 2.02, 2.07 (4 × AcO, 3s); 0.9, 1.3 (5,5-di-Me, 2s), IR: $\gamma_{P=O}$ = 1280 cm^{-1}. (Found: C, 44.68; H, 5.66; P, 6.05. $C_{19}H_{29}O_{12}SP$ requires: C, 44.53; H, 5.70; P, 6.05%).

Method B. To a cooled (−10°) suspension of 1 g (2.5 mmole) of 2,3,4,6-tetra-O-acetyl-1-S-acetyl-β-D-glucopyranose in 10 ml of CCl_4 0.52 g (3.3 mmole) of Br_2 dissolved in 5 ml of CCl_4 were added. The mixture was left at −10° for 5 min. The excess Br_2 and the solvent were removed under vacuum (temp of the water bath did not exceed 30°). The resulting crude **6**[8] was dissolved in benzene (15 ml) and 0.37 g (2.5 mmole) of **7** in 10 ml benzene added dropwise at 0–5°. The mixture was kept 0.5 hr at ambient temp. and the solvent evaporated under vacuum. The oily residue was purified by crystallizing twice (CCl_4–light petroleum), giving 0.8 g (63.5%) of **5a**, m.p. 140–141°, as colourless needles; $|\alpha|_D^{20}$: +30.4° (c = 1.38).

Method C. To 3 g (8.2 mmole) of 2,3,4,6 - tetra - O - acetyl - β - D - thioglucose dissolved in benzene (15 ml) a soln of 0.10 g (8.2 mmole) of Na in abs EtOH was added. The solvents were evaporated under vacuum. The sodium salt (**8**) was suspended in benzene (15 ml), 1.5 g of **9** (8.2 mmole) in 10 ml benzene added and the mixture was heated under reflux for 15 hr. From the cooled mixture 0.35 g (73%) of NaCl was filtered off, the benzene soln washed twice with water and dried over $MgSO_4$. The solvent was evaporated under vacuum.

To the oily residue 15 ml of CCl_4 were added and the mixture left in a refrigerator at 0° for 18 hr. The colourless solidified product was crystallized (CCl_4–light petroleum) giving 2.2 g (52%) of **5a**, m.p. 140–41°; $|\alpha|_D^{20}$: +30.7° (c = 1.28).

Methanolysis of **5a**. *Bis*(2,3,4,6 - *tetra* - O - *acetyl* - β - D - *glucopyranosyl*)*disulphide*[11]

2 - *Methoxy* - 2 - *oxo* - 5,5 - *dimethyl* - 1,3,2 - *dioxaphosphorinan*.[9] To a cooled (−20°) soln of 2 g (3.9 mmole) of **5a** in abs. MeOH (20 ml) a cooled (−20°) soln of 0.18 g Na (7.8 mmole) in abs. MeOH was added and the mixture was kept at −20° for about 20 min until complete disappearance of **5a**

†^{31}P NMR of the crude product gave two signals: −13.5 and −58.5, integrated as 90 and 10%, respectively, and attributed to the thiolo (**5a**) and thiono (**5b**) isomers. The thiono isomer could be isolated (0.2 g) in a pure state (m.p. 144–46°) by fractional crystallization of 10 g of the crude product.

(TLC). The mixture was neutralized with 10% AcOH (phenolphtaleine) and left at room temp for 2 hr. The solvent was evaporated and the syrupy residue extracted with benzene (5× 10 ml), dried over $MgSO_4$, the benzene was evaporated and the semi-crystalline mass purified by crystallization (benzene–light petroleum). 2 - Methoxy - 2 - oxo - 5, 5 - dimethyl - 1,3,2 - dioxaphosphorinan crystallized in colourless plates, m.p. 93–93.5° (lit.,[9] m.p. 94°). ^{31}P NMR: −6.5 ppm; IR: $\gamma_{P=O} = 1280\ cm^{-1}$. The colourless oil obtained after the benzene extraction was left in a crystallizing dish for 18 hr at room temp., triturated twice with 30 ml benzene, which was then evaporated. The syrupy residue was dissolved in 3 ml dry pyridine, 2 ml Ac_2O was added and the mixture left at room temp for 24 hr and then poured onto crushed ice. The ppt was crystallized from MeOH, yield: 1 g (70%) of the disulphide, colourless needles m.p. 143–4°, $|\alpha|_D^{20} = -158°$ (lit.[11], m.p. 143–44°; $|\alpha|_D^{20} = -160°$).

S - (2,3,4,6 - *Tetra* - O - *acetyl* - *β* - D - *glucopyranosyl*) - O,O - *diethyl phosphorothioate.* 5 g (1.4 mmole) of the dicyclohexylammonium salt of O,O-diethylphosphorothioate and 5.7 g (1.4 mmole) of 3 were dissolved in 20 ml CH_2Cl_2 and refluxed for 10 hr. 3.1 g (90%) of dicyclohexylhydrobromide was filtered off, the filtrate washed with water and dried over Na_2SO_4.

The solvent was removed under vacuum and the residual light yellow syrup purified by column chromatography. The product (light yellow syrup, 5.3 g[72%]) crystallized after a few weeks as colourless needles, m.p. 42–45°; $|\alpha|_D^{20}$: +13.9° (*c* = 4.09). ^{31}P NMR: −23.2. ^1H NMR: 1.34 (2× $\underline{CH_3}CH_2O$, t); 1.97, 1.99, 2.03 (4× AcO, 3s). (Found: C, 43.36; H, 5.95; P, 5.95. $C_{18}H_{29}O_{12}SP$ requires: C, 43.24; H, 5.80; P, 6.20%).

S - (2,3,4,6 - *Tetra* - O - *acetyl* - *β* - D - *glucopyranosyl*) - O,O - *di* - *n*- *butyl phosphorothioate.* 3 (2 g; 4.8 mmole) and 2 g (4.8 mmole) of the dicyclohexylammonium salt of O,O - di - n - butyl - phosphorothioate were dissolved in 30 ml CH_2Cl_2 and the mixture refluxed for 12 hr, 1.1 g (86%) dicyclohexylamine hydrobromide were filtered off, the filtrate washed with water and dried over Na_2SO_4. The solvent was removed under vacuum, and the oily residue was purified by column chromatography on silica gel. The product was isolated as a colourless syrup, 2.2 g (81%); $|\alpha|_D^{20}$: +8.6° (*c* = 2.3); ^{31}P NMR: −21.0; ^1H NMR: 1.89, 2.00, 2.06 (4× AcO, 3s); 0.92, 1.02 (2× $\underline{CH_3}CH_2CH_2CH_2$, −2 s). (Found: C, 47.60; H, 6.65; P, 5.59. $C_{22}H_{37}O_{12}SP$ requires: C, 47.68; H, 6.65; P, 5.59%).

S - (2,3,4,6 - *Tetra* - O - *acetyl* - *β* - D - *glucopyranosyl*) - O,O - *di* - *neopentyl phosphorothioate.* 3 (2.6 g; 6.3 mmole) and 2.2 g (6.3 mmole) of the triethylammonium salt of O,O-di-neopentyl phosphorothioate were dissolved in 20 ml benzene and refluxed for 8 hr 0.92 (80%) of triethylamine hydrobromide was filtered off, the benzene layer washed with water and dried over Na_2SO_4. The solvent was evaporated under vacuum, the residual syrupy product triturated with light petroleum and left in a refrigerator for 12 hr. The solidified product (2.1 g, 49%) was crystallized twice (CCl_4–light petroleum) giving colourless needles, m.p. 116–17°; $|\alpha|_D^{20}$: +6.6° (*c* = 1.8); ^{31}P NMR: −23.0; ^1H NMR: 1.95, 2.00, 2.05, 2.10 (4× AcO, 4s); IR: $\gamma_{P-O} = 1278\ cm^{-1}$. (Found: C, 49.32; H, 7.20; P, 5.31. $C_{24}H_{41}O_{12}SP$ requires: C, 49.35; H, 7.17; P, 5.30%).

2 - *S* - (2,3,4,6 - *Tetra* - O - *acetyl* - *β* - D - *galactopyranosyl*) - 2 - *oxo* - 5,5 - *dimethyl* - 1,3,2 - *dioxaphosphorinan.* 2 g (4.8 mmole) of 2,3,4,6 - tetra - O - acetyl - *α* - D - galactopyranosyl bromide and 1.4 g (4.8 mmole) of 4 were heated in boiling benzene (25 ml) of 8 hr. 0.88 g (90%) triethylamine hydrobromide was filtered off, the filtrate washed twice with water and dried over $MgSO_4$. Benzene was evaporated under vacuum and the residual syrup refluxed in CCl_4–light petroleum to give 2.2 g (88%) of colourless needles, m.p. 166–68° (after two crystallizations); $|\alpha|_D^{20}$: +2.65° (*c* = 1.2); ^{31}P NMR: −15.2; ^1H NMR: 1.98, 2.04, 2.1 and 2.2 (4× AcO, 4s); 0.9, 1.35 (5,5-di-Me, 2s). (Found: C, 44.53; H, 5.82; P, 6.24. $C_{19}H_{29}O_{12}SP$ requires: C, 44.53; H, 5.70; P, 6.05%).

2 - *S* - (2,3,4 - *Tri* - O - *acetyl* - *β* - D - *xylopyranosyl*) - 2 - *oxo* - 5,5 - *dimethyl* - 1,3,2 - *dioxaphosphorinan* (12a). 2.2 g (6.5 mmole) of 11 and 1.8 g (6.5 mmole) of 4 were heated under reflux in benzene for 2 min. Triethylamine hydrobromide was filtered off (0.82 g, 84.5%). The benzene soln was washed with water, dried over $MgSO_4$ and concentrated. The oily residue was purified by crystallization from CCl_4–light petroleum giving 2.5 g (88%) of colourless needles, m.p. 130–32°; $|\alpha|_D^{20} = -23.7°$ (*c* = 1.6); ^{31}P NMR: −16.0; ^1H NMR: 1.96, 2.01, 2.2 (3× AcO, 3s). (Found: C, 43.89; H, 5.83; P, 7.09. $C_{16}H_{25}O_{10}SP$ requires: C, 43.63; H, 5.69; P, 7.04%).

Glycosylation of monothioacids silver salts

2 - (2,3,4,6 - *Tetra* - O - *acetyl* - *β* - D - *glucopyranosyl*) - 2 - *thiono* - 5,5 - *dimethyl* - 1,3,2 - *dioxaphosphorinan* 5b. 1.5 g (5.1 mmole) of 10 and 2.1 g (5.1 mmole) of 3 were refluxed in benzene (20 ml) for 6 hr. AgBr was filtered the filtrate concentrated under vacuum and the syrupy residue† subjected to chromatographic separation on a column (1 cm dia., 30 g Si gel). The eluent was divided into 3 main fractions: I–0.8 g (44%), $R_f = 0.75$; m.p. 144–46° (5b); ^{31}P NMR: −58.2; $|\alpha|_D^{20}$: +8.2° (*c* = 1.3); IR: $\gamma_{P=S} = 700\ cm^{-1}$; II—0.4 g (22%)—a mixture of 5a and 5b; III—0.6 g (33%) (5a) m.p. 140–41°, $R_f = 0.5$; ^{31}P NMR: −13.5. 5b was submitted to analysis after a second purification on the column. (Found: C, 44.35; H, 5.80; P, 6.30. $C_{19}H_{29}O_{12}SP$ requires: C, 44.53; H, 5.70; P, 6.05%).

2 - (2,3,4 - *Tri* - O - *acetyl* - *β* - D - *xylopyranosyl* - 2 - *thiono* - 5,5 - *dimethyl* - 1,3,2 - *dioxaphosphorinan* (12b). 1.6 g (5.5 mmole) of 10 and 1.84 g (5.5 mmole) of 11 were refluxed in benzene for 40 min. AgBr was filtered off and the benzene evaporated under vacuum. The oily residue was separated on a column (1 cm dia), packed with 30 g of silica gel, into 3 fractions: I—0.3 g (13%) (12b), $R_f = 0.8$; m.p. 146–47° (CCl_4–light petroleum ether); $|\alpha|_D^{20} = +4.4$ (*c* = 0.4); ^{31}P NMR = −60.5; IR: $\gamma_{P=S} = 670\ cm^{-1}$. (Found: C, 43.64; H, 5.80; P, 6.73. $C_{16}H_{25}O_{10}SP$ requires: C, 53.63; H, 5.69; P, 7.04%). II—0.8 g (34%) of a mixture of 12a and 12b ($R_f = 0.8$ and $R_f = 0.6$). III—0.4 g (17%) (12a); m.p. 130–32° (CCl_4–light petroleum); $|\alpha|_D^{20} = -23.7°$ (*c* = 0.5).‡ ^{31}P NMR of the crude oily product showed 2 signals: at −60.5 and −16.5 integrated as 61:39, respectively.

Isomerisation of 5b *in boiling benzene.* A soln of 5b (100 mg; 0.19 mmole) in benzene (10 ml) was refluxed for 8 hr. The solvent was evaporated under vacuum and the syrupy residue was subjected to ^{31}P NMR. The ^{31}P NMR spectrum showed two signals: −58.2 (5b) and −13.5 (5a) integrated as 67:33, respectively.

†^{31}P NMR of the crude syrup showed two signals: at −58.2 and −13.5 integrated as 60:40, respectively.

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