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Preliminary communication

Synthesis of *S*-(2-deoxy-α-D-glycosyl) phosphorodithioates by addition of dialkyl hydrogenphosphorodithioates to glycals: a potential route to 2-deoxy-1-thio-α-D sugars

JOANNA BOROWIECKA and MARIA MICHALSKA*

Department of Organic Chemistry, Faculty of Pharmacy, Medical Academy, 90-145 Lodz, Narutowicza 120A (Poland)

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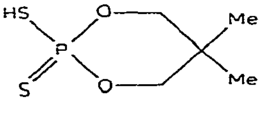
Carbohydrate thiophosphates are of potential interest as intermediates in the synthesis of biologically important derivatives of thio sugars, for example, antimetabolites and antibiotics. The phosphoryl group can readily be removed by nucleophilic displacement at phosphorus, for example, by alkaline hydrolysis[1].

$$RO_2P(S)SR' + HO^- \rightarrow (RO)_2P(S)O^- + HSR'$$

We now report a one-step synthesis of *S*-(2-deoxy-α-D-glycosyl) phosphorodithioates by the uncatalysed addition of *O,O*-dialkylphosphorodithioic acids to 1,2-unsaturated sugars.

3,4,6-Tri-*O*-acetyl-D-glucal[2] and 3,4,6-tri-*O*-acetyl-D-galactal[3] react smoothly with 2-mercapto-5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane[4] (**1**) in benzene at ambient temperature, giving 5,5-dimethyl-2-thioxo-2-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosylthio)-1,3,2-dioxaphosphorinane (**2**) and 5,5-dimethyl-2-thioxo-2-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*lyxo*-hexopyranosylthio)-1,3,2-dioxaphosphorinane (**3**), respectively. The addition is usually complete within 48 h and is kinetically controlled. Warming leads to a less-favourable ratio of α:β isomers.

Other dialkylphosphorodithioic acids (**4**), including commercially available dimethyl hydrogenphosphorodithioate, can also be employed in this type of addition to give products of type **5**.



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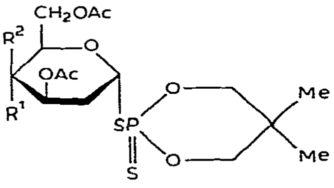
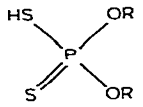


2 R^1 = OAc, R^2 = H
3 R^1 = H, R^2 = OAc



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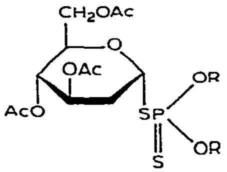

5

R = Me, Pr, Bu

The acid-catalyzed addition of monothioacetic acid to D-glucal takes a different course, because of subsequent, spontaneous elimination of acetic acid which leads to 1-*S*-substituted 2,3-unsaturated sugars[6].

The products obtained in the course of this investigation could easily be purified by recrystallization from ethyl ether and were pure α anomers. This was established by ^{31}P- and ^{1}H-n.m.r. spectroscopy, and confirmed by the high, positive $[\alpha]_D$ values characteristic of α-D-glycosides. The chemical shifts and the splittings of the anomeric proton signals in the 90-MHz n.m.r. spectra of the compounds listed in Table I are characteristic of equatorial protons coupled to vicinal axial and equatorial protons ($J_{1,2\,ax}$ ~5 Hz and $J_{1,2\,eq}$ ~1.5 Hz),

TABLE I

ANALYTICAL AND N.M.R. DATA

Compound	*M.p. (degrees)*	*Analysis*			^{31}P *(H_3PO_4) (±1 p.p.m.)*	^{1}H *(Me_4Si)*		$[\alpha]^{20}_D$ *(chloroform) (degrees)*
			Calc	*Found*				
		C	43.41	43.43		H-1	6.32 (dq)	
2	126–127	H	5.77	5.87	−82.42	H-2ax	1 98 (m)	
		P	6 59	6.78		H-2eq	2.25	+182
						3 × Ac	1 63	
							1.71 (s)	
							1.79	
		C	39.07	38 98		H-1	5 82 (dq)	
5 (R = Me)	90–92	H	5.34	5.48	−96.04	H-2ax	1 90 (m)	
		P	7.20	7 50		H-2eq	2 12	+222
						1 × Ac	1 63 (s)	
						2 × Ac	1 72 (s)	
						2 × Me	3 36 (s)	
							3 52 (s)	
		C	43 41	43.08		H-1	6.40 (dq)	
3	120–121	H	5.77	5.95	−83.23	H-2ax	1.88–2 55 (m)	
		P	6 59	7.22		H-2eq		+193
						3 × Ac	1.67	
							1.69 (s)	
							1.75	

and to phosphorus with J_{PSCH} ~10 Hz (cf. Ref. 7). The characteristic doublet of quartets for the anomeric proton collapsed after ^{31}P-decoupling to a quartet having the same H—H coupling constants.

The crude reaction mixtures also contained small proportions of the isomeric *S*-(2-deoxy-β-D-glycosyl) dialkyl phosphorodithioates. The yields of analytically pure α anomers were >60% in all cases. All compounds gave satisfactory elemental analyses, and the mass spectra agree with the assigned structures. The dipropyl and dibutyl esters (**5**, R = Pr, Bu) were obtained as syrups in equally high yields.

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