Use of Carbohydrate Derivatives for Studies of Phosphorus Stereochemistry. Part II.[1] Synthesis and Configurational Assignments of 1,3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones

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Methyl 2,3-di-*O*-methyl-4(or 6)-thio-α-D-glucopyranoside (*R*)- and (*S*)-4,6-methylphosphonothioates and methyl 2,3-di-*O*-methyl-α-D-glucopyranoside (*R*)- and (*S*)-4,6-methyl-(and phenyl)-phosphonothioates have been prepared by conventional procedures. The corresponding ethyl phosphorothioates are also described. The configuration at phosphorus in the thiolates has been assigned on the basis of n.m.r. and i.r. data. The thioxo-compounds have been correlated chemically with the corresponding phosphates of previously determined configuration. The preparation of methyl 2,3-di-*O*-methyl-4(and 6)-thio-α-D-glucopyranosides is described.

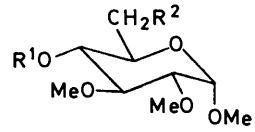
In the previous paper [1] it was shown that many aspects of the stereochemistry of 1,3,2-dioxaphosphorinan-2-ones may be studied conveniently within the asymmetric environment provided by a carbohydrate framework. Similar studies of other phosphorus-containing heterocycles are clearly possible and in this paper, as a prelude to some mechanistic studies, the preparation and configurational assignments of some 1,3,2-oxathiaphosphorinan-2-ones and 1,3,2-dioxaphosphorinan-2-thiones are described.

Preparation of Carbohydrate Precursors.—Methyl 2,3-di-*O*-methyl-6-thio-α-D-glucopyranoside (5) was prepared from the diol (1) by sequential tosylation [to give (2)], acetylation [to give (3)], displacement of tosyl by thioacetate [to give (4)], and reduction with lithium aluminium hydride. An attempt to convert (4) into (5) by deacetylation with sodium methoxide in methanol resulted in the preponderant formation of the disulphide (5′) from (5).

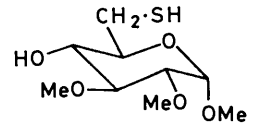
Methyl 2,3-di-*O*-methyl-4-thio-α-D-glucopyranoside (12) was formed from the galactopyranoside derivative (8) by sequential benzoylation [to give (9)], tosylation [to give (10)], displacement of tosyl by thioacetate [to give (11)], and reduction with lithium aluminium hydride. In both reaction sequences conventional procedures were used, product yields were adequate, and the thiols (5) and (12) were easily purified by chromatography over silica.

1,3,2-Oxathiaphosphorinan-2-ones.—There is little information available concerning the synthesis and conformations of 1,3,2-oxathiaphosphorinan-2-ones. We report here that the syntheses of these compounds and their configurational assignments can be accomplished in an analogous manner to that used for the corresponding 1,3,2-dioxaphosphorinan-2-ones.[1]

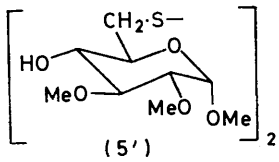
The 2-methyl-1,3,2-oxathiaphosphorinan-2-ones (6*eq*) and (6*ax*) were prepared in good yield, following chromatographic separation over silica, by treatment of the hydroxy-thiol (5) with methylphosphonic dichloride and triethylamine in ether or dichloromethane. Similarly the 2-ethoxy-derivatives (7*ax*) and (7*eq*) were prepared from (5) and ethyl phosphorodichloridate. However, whereas these four products were stable when chromatographed over silica in solvents containing an alcoholic component, greater care was required to separate the methylphosphonothioates (13*ax*) and (13*eq*) since the former appeared to decompose under such conditions. Compounds (13*ax*) and (13*eq*) were separable, however,



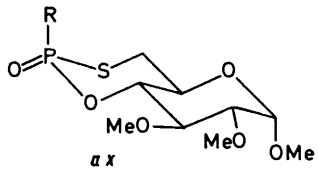
(1) R^1 = H, R^2 = OH
(2) R^1 = H, R^2 = OTs
(3) R^1 = Ac, R^2 = OTs
(4) R^1 = Ac, R^2 = SAc



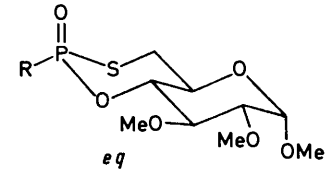
(5)



(5′)

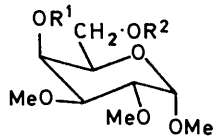


ax

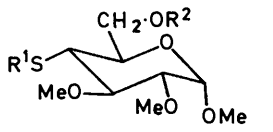


eq

(6) R = Me
(7) R = OEt



(8) R^1 = R^2 = H
(9) R^1 = H, R^2 = Bz
(10) R^1 = Ts, R^2 = Bz



(11) R^1 = Ac, R^2 = Bz
(12) R^1 = R^2 = H

when dry ether was used as the solvent for chromatography. The 2-ethoxy-derivatives (14*ax*) and (14*eq*) were also prepared. Tentative structural assignments were based primarily on evidence that in 1,3,2-dioxaphosphorinan-2-ones the compounds in which the P=O group is orientated equatorially have a P=O i.r. stretching frequency at higher wavelength and a ^{31}P n.m.r. chemical shift at higher field than when the P=O group is orientated axially.[1,2] The relevant data for compounds (6), (7),

[1] Part I, D. B. Cooper, T. D. Inch, and G. J. Lewis, preceding paper.

[2] J.-P. Majoral and J. Navech, *Bull. Soc. chim. France*, 1971, 95, 1331, 2609.

(13), and (14) are given in Table 1. There is no reason to suppose that the oxathiaphosphorinan-2-ones should not exhibit spectroscopic characteristics similar to those of the corresponding 1,3,2-dioxaphosphorinan-2-ones,

TABLE 1

^{31}P Chemical shifts and P=O i.r. frequencies of 1,3,2-oxathiaphosphorinan-2-ones

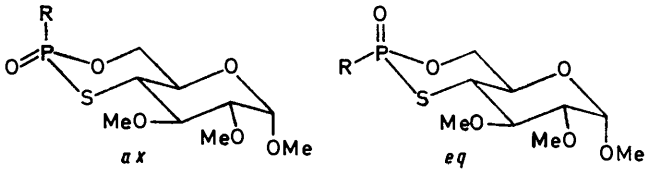
Compound	$\nu_{P=O}$ (cm^{-1})	^{31}P δ(p.p.m.)
(6*ax*)	1238 ($CDCl_3$)	−43·5
(6*eq*)	1215 ($CDCl_3$)	−46
(7*ax*)	1333 ($CDCl_3$)	−15
(7*eq*)	1318 ($CDCl_3$)	−19
(13*ax*)	1220 ($CDCl_3$), 1428 (KBr)	
(13*eq*)	1215 ($CDCl_3$), 1220 (KBr)	
(14*ax*)	1277 (KBr), 1264 ($CDCl_3$)	
(14*eq*)	1256 (liq. film), 1249 ($CDCl_3$)	

particularly since available proton chemical shift data are consistent with the foregoing assignments. Thus H-4*ax* and H-6*ax* in (6*eq*), which experience strong 2,4-diaxial deshielding by the axial P=O group, resonate at lower field than the corresponding protons in (6*ax*). Similarly the H-4 signal in (13*eq*) was at lower field than the corresponding signal in (13*ax*).

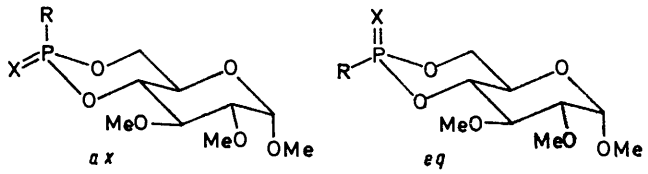
The available n.m.r. data are also consistent with similar chair conformations for (6), (7), and (13). For (6*eq*) an almost complete first-order proton analysis was available which provided unequivocal proof of conformation. Thus a large *trans* vicinal $J_{P-S-C-H-6eq}$ value of 19·6 Hz and small *gauche* vicinal $J_{P-S-C-H-4}$ and $J_{P-S-CH-H-6ax}$ values of 3·8 and 4·2 Hz, respectively, were consistent only with a chair conformation.[3] These couplings, together with a $J_{P,Me}$ value of 15·8 Hz, were also evident in the ^{31}P resonance which appeared as a broad quintet (1 : 4 : 6 : 4 : 1) with line separations of 15—20 Hz. Although the ^{1}H n.m.r. spectrum of (6*ax*) was not easily analysed, a similar ^{31}P quintet was indicative of a similar value for $J_{P,6eq}$, $J_{P,6ax}$, and $J_{P,4}$, since the ^{1}H n.m.r. spectra showed a $J_{P,Me}$ value of 14·8 Hz. The ^{31}P signals of (7) and (13) were also consistent with a chair conformation.

1,3,2-*Dioxaphosphorinan-2-thiones*.—Two general procedures for the synthesis of 1,3,2-dioxaphosphorinan-2-thiones are available. The first [4] involves the reaction of diols with $RP(S)Cl_2$. The second, which has been used more frequently,[5] involves the addition of sulphur to the trivalent phosphorus of 1,3,2-dioxaphosphorinans. In this laboratory the methylphosphonothioates (15*ax*) and (15*eq*) were prepared, in yields of 46 and 19% after chromatographic separation, by the reaction of (1) with methylphosphonothioic dichloride. It was found to be experimentally easier to use the second procedure to prepare the phenylphosphonothioates [(16*ax*) (29%) and (16*eq*) (21%)] and the ethylphosphorothioates [(17*ax*) (39%) and (17*eq*) (21%)]. In each case the isomer with the P=S bond equatorial preponderated.

Configurational assignments to the 2-thiones were achieved by chemical correlations with the corresponding 1,3,2-dioxaphosphorinan-2-ones. Thus oxidation of (15*ax*) and (15*eq*) with *m*-chloroperbenzoic acid under



(13) R = Me
(14) R = OEt



(15) R = Me, X = S
(16) R = Ph, X = S
(17) R = OEt, X = S
(18) R = Me, X = O
(19) R = Ph, X = O
(20) R = OEt, X = O

conditions known to give preponderantly retention of configuration [6] gave essentially only (18*ax*) and (18*eq*), respectively. Similar high stereoselectivity was observed for the conversions of (16*ax*) and (16*eq*) into (19*ax*) and (19*eq*), respectively. However, the stereoselectivity observed for the oxidations of the phosphorothioates (17) to give (20) was much lower, although retention of configuration was still strongly favoured.

Some of these assignments were confirmed by chromatographic experiments in which phosphorus(v) sulphide in pyridine was used to convert 1,3,2-dioxaphosphorinan-2-ones into the corresponding 2-thiones. Such reactions have been shown to take place with retention of configuration.[7] Thus the phosphonates (18) and (19) were converted, in part, into the corresponding 2-thiones by prolonged (up to 24 h) treatment with an excess of sulphide in boiling pyridine. However, the ethyl phosphates (20) were not easily converted into (17) under these conditions.

The ^{31}P n.m.r. chemical shifts of the thioxo-compounds showed the same pattern as observed in 1,3,2-dioxaphosphorinan-2-ones and related compounds in that the ^{31}P chemical shift is at higher field when the phosphorus substituent is axial than when it is equatorial (see Table 2). The use of ^{31}P chemical shifts for configurational assignments of six-membered phosphorus heterocycles thus appears to be of general applicability.[8]

[3] L. D. Hall and R. B. Malcolm, *Canad. J. Chem.*, 1972, **50**, 2092, 2102; B. Donaldson and L. D. Hall, *ibid.*, p. 2111.
[4] N. J. Ziemlanski and W. P. Kalaschnikov, *Zhur. obshchei Chim.*, 1967, **37**, 1141.
[5] C. L. Bodkin and P. Simpson, *J. Chem. Soc.* (*B*), 1971, 1136; W. G. Bentrude and J. H. Hargis, *Chem. Comm.*, 1969, 1113; W. Stec and A. Lopusinsky, *Tetrahedron*, 1973, **29**, 547.
[6] A. W. Herriott, *J. Amer. Chem. Soc.*, 1971, **93**, 3304.
[7] H. S. Aaron, *Chem. Comm.*, 1971, 366; J. Omelanczuk and M. Mikolajczyk, *Tetrahedron*, 1971, **27**, 5587.
[8] W. G. Bentrude and H.-W. Tan, *J. Amer. Chem. Soc.*, 1973, **95**, 4666.

The aromatic region in the n.m.r. spectrum of 2-phenyl-1,3,2-dioxaphosphorinans also appears to be characteristic of the configuration at phosphorus. In

TABLE 2

^{31}P Chemical shifts in 1,3,2-dioxaphosphorinan-2-thiones

Compd.	^{31}P δ (p.p.m.)	Comments (J values in Hz)
		J_{P,CH_3} 15·2 *
(15*ax*)	−90·5	^{31}P signal 1 : 3 : 4 : 4 : 3 : 1 sextet consistent with J_{P,CH_3} 15, $J_{P,6eq}$ 26—30, $J_{P,4ax}$ = $J_{P,6ax}$ = 2—4
		J_{P,CH_3} 16·5 *
(15*eq*)	−100	^{31}P signal 1 : 3 : 8 : 3 : 1 quintet consistent with J_{P,CH_3} 16·5, $J_{P,6eq}$ 24—26, $J_{P,6ax}$ = $J_{P,4ax}$ = 2—4
(16*ax*)	−79	Broad complex ^{31}P signal
(16*eq*)	−89	Broad complex ^{31}P signal
(17*ax*)	−60·5	^{31}P signal 1 : 2 : 1 : 1 : 2 : 1 sextet consistent with $J_{P,6eq}$ 26, J_{P-O-CH_3} 9—10, $J_{P,4}$ = $J_{P,6ax}$ = 2—4
(17*eq*)	−66·6	^{31}P signal 1 : 2 : 1 : 1 : 2 : 1 sextet consistent with $J_{P,6eq}$ 26, J_{P-O-CH_3} 9—10, $J_{P,4}$ = $J_{P,6ax}$ = 2—4

* Measured from proton spectra.

the compounds (16*ax*) and (19*ax*), where the phenyl substituent is axial, the five aromatic protons afford a complex signal between δ 7·4 and 7·9. In contrast, (16*eq*) and (19*eq*), where the phenyl substituent is equatorial, show a two-proton aromatic signal between δ 7·9 and 8·25 and a three-proton signal between 7·4 and 7·7.

EXPERIMENTAL

General experimental conditions are described in Part I.[1]

Methyl 4-O-*Acetyl*-6-S-*acetyl*-2,3-*di*-O-*methyl*-6-*thio*-α-D-*glucopyranoside* (4).—A solution of the diol (1) (15 g) and tosyl chloride (15 g) in pyridine was stored overnight at room temperature, then poured into water and extracted with chloroform. The extract was dried, concentrated, and stored overnight with acetic anhydride (20 ml) in pyridine (50 ml). The solution was concentrated, and the residue and potassium thioacetate (10 g) in dimethylformamide (100 ml) were heated at 60° for 1 h. The solution was poured into water (800 ml) and repeatedly extracted with ether; the extracts were dried and concentrated. The residue was recrystallised from light petroleum (b.p. 40—60°) to afford the *diacetate* (4) (10 g, 45%), m.p. 66—68°, $[\alpha]_D$ +109° (*c* 1·6) (Found: C, 48·5; H, 6·8. $C_{13}H_{22}O_7S$ requires C, 48·4; H, 6·9%).

Treatment of the Diacetate (4) *with Lithium Aluminium Hydride*.—A solution of (4) (2·5 g) in ether was added dropwise to a stirred suspension of lithium aluminium hydride in ether. The excess of hydride was destroyed with ethyl acetate in the usual way and inorganic complexes were dissolved in dilute sulphuric acid. The aqueous acidic solution was extracted with ether and the extracts were dried and concentrated to afford the thiol (5) (1·6 g, 87%). On storage (5) was slowly oxidised to the disulphide (5′) [t.l.c. in benzene–acetone–methanol (7 : 3 : 1): (5), R_F 0·5; (5′), R_F 0·3]. The *disulphide* (5′), m.p. 125—127° (from di-isopropyl ether), $[\alpha]_D$ +307° (*c* 2·1) (Found: C, 45·5; H, 7·0. $C_{18}H_{34}O_{10}S_2$ requires C, 45·5; H, 7·2%), was the major product when (4) was treated with sodium methoxide in methanol.

Methyl 6-O-*Benzoyl*-2,3-*di*-O-*methyl*-α-D-*galactopyranoside* (9).—A solution of the diol (8) [9] (16·2 g; prepared from methyl α-D-galactopyranoside [10] by benzylidenation, methylation, and catalytic hydrogenolysis) in dry pyridine was treated, dropwise, with benzoyl chloride (9 ml). The solution was stored overnight at room temperature, poured into water, and extracted with chloroform; the extract was dried and concentrated. The product was recrystallised from light petroleum–ethanol (10 : 1) to afford the *benzoate* (19) (13·5 g, 55%), m.p. 109°, $[\alpha]_D$ +110° (*c* 2·2) (Found: C, 58·3; H, 6·7. $C_{16}H_{22}O_7$ requires C, 58·9; H, 6·8%).

Methyl 6-O-*Benzoyl*-2,3-*di*-O-*methyl*-4-O-*tosyl*-α-D-*galactopyranoside* (10).—A solution of (9) (13 g) and tosyl chloride (25 g) in pyridine (40 ml) was heated at 60—70° for 5 h and stored overnight at room temperature. Conventional processing of the mixture afforded the *tosylate* (10) (14·6 g, 76%), m.p. 145—150° (from ethanol), $[\alpha]_D$ +87·5° (*c* 2·4) (Found: C, 57·5; H, 5·8. $C_{23}H_{28}O_9S$ requires C, 57·5; H, 5·9%).

Methyl 2,3-*Di*-O-*methyl*-4-*thio*-α-D-*glucopyranoside* (12).—A solution of (10) (14·6 g) and potassium thioacetate (18·5 g; 5-fold excess) in dimethylformamide (50 ml) was boiled under reflux for 5 h, cooled, diluted with water, and extracted with ether. The extract was dried and concentrated to afford a yellow syrup (11·6 g) [R_F 0·5 in light petroleum–acetone (7 : 3); in this solvent (10) had R_F 0·35] with n.m.r. spectral characteristics consistent with the glucopyranoside derivative (11). A solution of (11) (4 g) in ether was added dropwise to lithium aluminium hydride (1·5 g) in ether and the mixture was stored at room temperature for 1 h. The excess of hydride was destroyed with ethyl acetate and all inorganic material was dissolved in dilute hydrochloric acid. The aqueous solution was extracted with ether and the extracts were dried and concentrated. The residue was passed over silica in light petroleum–acetone (4 : 1) to afford (12) (2 g, 81%) as a chromatographically homogeneous syrup, $[\alpha]_D$ +113° (*c* 2).

Methyl 2,3-*Di*-O-*methyl*-6-*thio*-α-D-*glucopyranoside* (S)- and (R)-4,6-*Methylphosphonothioate* [(6*eq*) *and* (6*ax*)].—A solution of (5) (6·4 g), methylphosphonic dichloride (3·5 g), and triethylamine (7 g) in ether (100 ml) was boiled under reflux for 2 h. The solution was diluted with chloroform (400 ml), washed with water, dried, and concentrated. The residue was passed over silica in benzene–acetone–methanol (7 : 1 : 1) to give (i) unchanged (5) (1·5 g), R_F 0·5; (ii) the (S)-*phosphonothioate* (6*eq*) (1·6 g, 27%), R_F 0·4, m.p. 159—161° (from di-isopropyl ether), $[\alpha]_D$ +190° (*c* 1·7) (Found: C, 40·2; H, 6·3. $C_{10}H_{19}O_6PS$ requires C, 40·3; H, 6·4%,) δ_H 4·83 (H-1, $J_{1,2}$ 3·6 Hz), 3·26 (H-2, $J_{2,3}$ 9·2 Hz), 4·34 (H-4 $J_{3,4}$ = $J_{4,5}$ = 9—10, $J_{4,P}$ 3·8 Hz), 3·93 (H-5), 3·38 (H-6*ax*, $J_{5,6ax}$ 10·5, $J_{6ax,6eq}$ 13, $J_{6ax,P}$ 4·2 Hz), 2·91 (H-6*eq*, $J_{5,6eq}$ 3·9, $J_{6eq,P}$ 19·6 Hz), 1·87 (PMe, $J_{P,Me}$ 15·8 Hz), and 3·46, 3·53, and 3·57 (3 OMe); and (iii) the (R)-*phosphonothioate* (6*ax*) (2·5 g, 42%), R_F 0·34), m.p. 203—207° (from di-isopropyl ether), $[\alpha]_D$ +160° (*c* 2) (Found: C, 39·9; H, 6·1%), δ 4·83 (H-1, $J_{1,2}$ 3·6 Hz), 3·18 (H-2), 4·15—3·7 (H-4 and -5), 2·88 (H-6*eq*), 3·10 (H-6*ax*), 2·02 (PMe, J 14·8 Hz), and 3·47, 3·54, and 3·62 (3 OMe).

In another experiment (5) (0·7 g) in ether at room temperature was treated with methylphosphonic dichloride and triethylamine in ether in small quantities until no (5) remained. The solution was then stored at room temperature for 96 h. Conventional work-up gave (6*eq*) (0·25 g, 27%) and (6*ax*) (0·24 g, 25%).

[9] D. J. Bell and G. D. Greville, *J. Chem. Soc.*, 1955, 1136.
[10] J. L. Frahn and J. A. Mills, *Austral. J. Chem.*, 1965, **18**, 1303.

Methyl 2,3-*Di*-O-*methyl*-6-*thio*-α-D-*glucopyranoside* (R)- *and* (S)-4,6-(*Ethyl Phosphate*) [(7*ax*) *and* (7*eq*)].—A solution of (5) (0·7 g), ethyl phosphorodichloridate (3 g), and an excess of triethylamine in ether was stored at room temperature for 96 h. The solution was poured into water and extracted with chloroform, and the extracts were dried and concentrated. The product was passed over silica in benzene–acetone (7 : 1) to afford (i) the (R)-*phosphate* (7*ax*) (0·18 g, 19%), R_F 0·4, m.p. 135—138° (from di-isopropyl ether), $[\alpha]_D$ +207° (*c* 0·8) (Found: C, 40·1; H, 6·3. $C_{11}H_{21}O_7PS$ requires C, 40·2; H, 6·5%); and (ii) the (*S*)-phosphate (7*eq*) (0·2 g, 21%), $[\alpha]_D$ +88° (*c* 0·7), R_F 0·35 in benzene–acetone (7 : 1), as a chromatographically homogeneous syrup.

The proton spectra for (7*ax*) and (7*eq*) were not distinctive but were consistent with the assigned structures.

Methyl 2,3-*Di*-O-*methyl*-4-*thio*-α-D-*glucopyranoside* (R)- *and* (S)-4,6-*Methylphosphonothioate* [(13*eq*) *and* (13*ax*)].—A solution of (12) (2·6 g), methylphosphonic dichloride (1·6 g), and triethylamine (2·65 g) in ether (50 ml) was stored overnight at room temperature. The solution was filtered and the filtrate and residue processed separately. The filtrate was concentrated and passed over silica in dry ether to afford the (R)-*phosphonothioate* (0·9 g, 29%), m.p. 124° (from light petroleum–ether), $[\alpha]_D$ +42·5° (*c* 1·2), R_F 0·6 in light petroleum–acetone–methanol (7 : 3 : 1) (Found: C, 40·3; H, 6·3. $C_{10}H_{19}O_6PS$ requires C, 40·3; H, 6·4%), δ_H 1·86 (PMe, $J_{P,Me}$ 16 Hz), 3·49 (OMe), and 3·57 (2 OMe). The residue was partitioned between water and chloroform and the chloroform extract dried and concentrated to afford the (S)-*phosphonothioate* (13*ax*) (0·59 g, 13%), m.p. 183° (from ethanol), $[\alpha]_D$ +73° (*c* 1), R_F 0·5 in light petroleum–acetone–methanol (7 : 3 : 1) (Found: C, 40·0; H, 6·3%), δ_H 3·04 (H-4, $J_{3,4} = J_{4,5} = 9$—10, $J_{P,4} = 2$ Hz), 1·95 (PMe, $J_{P,Me}$ 16 Hz), and 3·46, 3·54, and 3·59 (3 OMe).

Methyl 2,3-*Di*-O-*methyl*-4-*thio*-α-D-*glucopyranoside* (S)- *and* (R)-4,6-(*Ethyl Phosphorothioate*) [(14*ax*) *and* (14*eq*)].—A solution of (12) (1·2 g), ethyl phosphorodichloridate (0·9 g), and triethylamine (1·4 g) in ether was stored overnight at room temperature [t.l.c. in benzene–acetone (4 : 1) : (12), R_F 0·6; (14-*ax*), R_F 0·4; (14*eq*), R_F 0·3]. Water was added and the ether layer was dried and concentrated. The product was resolved chromatographically over silica to afford (i) the (S)-*phosphorothioate* (14*ax*) (0·24 g, 14·5%), m.p. 98°, $[\alpha]_D$ +7° (*c* 1) (Found: C, 40·8; H, 6·5. $C_{11}H_{21}O_7PS$ requires C, 40·3; H, 6·5%); and (ii) the (*R*)-phosphorothioate (14*eq*) (0·27 g, 16%), $[\alpha]_D$ +46° (*c* 2).

Methyl 2,3-*Di*-O-*methyl*-α-D-*glucopyranoside* (S)- *and* (R)-4,6-*Methylphosphonothioate* [(15*eq*) *and* (15*ax*)].—A solution of the diol (1) (2·22 g), triethylamine (2·5 g), and methylphosphonothioic dichloride (1·6 g) in dry benzene (40 ml) was boiled under reflux for 2 h. The solution was cooled and partitioned with water, and the benzene portion was dried and concentrated. The residue was passed over silica in acetone–light petroleum (3 : 7) to give, in order of elution: (i) the (S)-*methylphosphonothioate* (15*eq*) (0·57 g, 19%), $[\alpha]_D$ +135° (*c* 1·0) (Found: C, 39·9; H, 6·4. $C_{10}H_{19}O_6PS$ requires C, 40·2; H, 6·4%); and (ii) the (R)-*methylphosphonothioate* (15*ax*) (1·37 g, 46%), m.p. 167—168° (from acetone–cyclohexane), $[\alpha]_D$ +75° (*c* 1·0) (Found: C, 40·0; H, 6·4%).

Oxidation of the Phosphonothioates (15).—A solution of *m*-chloroperbenzoic acid (0·086 g) in methylene chloride (2 ml) was added to a solution of (15*eq*) (0·12 g) in methylene chloride (30 ml) at 0° and the mixture was stored at 0° for 1 h. The solution was washed with concentrated aqueous sodium carbonate, dried, and concentrated. The residue was purified by chromatography over silica in benzene–acetone–methanol (7 : 3 : 1) to afford the (*S*)-methylphosphonate (18*eq*) (0·099 g, 88%).

Similarly (15*ax*) (0·12 g) was converted into (18*ax*) (0·09 g, 80%). Both reactions were highly stereoselective, only traces of (18*eq*) and (18*ax*) being detected by t.l.c. from the oxidations of (15*ax*) and (15*eq*), respectively.

Methyl 2,3-*Di*-O-*methyl*-α-D-*glucopyranoside* (S)- *and* (R)-4,6-*Phenylphosphonothioate* [(16*eq*) *and* (16*ax*)].—Dichloro(phenyl)phosphine (1·8 g) was added dropwise to a stirred solution of the diol (1) (2·22 g) and triethylamine (2·5 g) in dry benzene under nitrogen. The mixture was boiled under reflux for 30 min, then cooled, sulphur (0·4 g) was added, and the mixture was stirred for 1 h. The mixture was processed conventionally and the product passed over silica in acetone–light petroleum (1 : 4) to afford, in order of elution: (i) the (S)-*phenylphosphonothioate* (16*eq*) (0·75 g, 21%), m.p. 116—117° (from cyclohexane), $[\alpha]_D$ +98° (*c* 1·0) (Found: C, 49·9; H, 5·9. $C_{15}H_{21}O_6PS$ requires C, 50·0; H, 5·9%); and (ii) the (R)-*phenylphosphonothioate* (16*ax*) (1·05 g, 29%), m.p. 158—161° (from cyclohexane–acetone), $[\alpha]_D$ +126° (*c* 1·0) (Found: C, 50·3; H, 6·0%).

Oxidation of the Phosphonothioates (16).—The procedure described for the oxidation of (15*eq*) was used: (16*eq*) (0·09 g) afforded (19*eq*) (0·072 g, 86%) after chromatography in acetone–benzene (3 : 7); and (16*ax*) (0·18 g) afforded (19*ax*) (0·16 g, 94%), under similar conditions.

Methyl 2,3-*Di*-O-*methyl*-α-D-*glucopyranoside* (S)- *and* (R)-4,6-(*Ethyl Phosphorothioate*) [(17*eq*) *and* (17*ax*)].—Dichloro(ethoxy)phosphine (1·5 g) was added dropwise to a stirred solution of the diol (1) (2·22 g) and triethylamine (2·5 g) in warm dry benzene (60 ml) under nitrogen. After 30 min, sulphur (0·4 g) was added and the mixture was stored at room temperature for 30 h. The mixture was processed in the usual way and the crude product was passed over silica in ethyl acetate–light petroleum (2 : 3) to afford, in order of elution: (i) the (S)-*ethyl phosphorothioate* (17*ax*) (0·68 g, 21%), m.p. 81—82° (from cyclohexane–ethyl acetate), $[\alpha]_D$ +136° (*c* 1·0) (Found: C, 40·5; H, 6·5. $C_{11}H_{12}O_7PS$ requires C, 40·2; H, 6·5%); and (ii) the (R)-*ethyl phosphorothioate* (17*eq*) (1·29 g, 39%), m.p. 140—141° (from ethyl acetate–light petroleum), $[\alpha]_D$ +89° (*c* 0·1) (Found: C, 40·2; H, 6·5%).

Oxidation of the Phosphorothioates (17).—Compound (17*ax*) (0·098 g) was treated for 3 h in the usual way to give (20*ax*) (0·066 g, 70%) and (20*eq*) (0·019 g, 20%), which were separated over silica in benzene–acetone (7 : 3).

Similarly (17*eq*) (0·098 g) afforded (20*eq*) (0·07 g, 74%) and (20*ax*) (0·01 g, 11%).

Methyl 2,3-*Di*-O-*methyl*-α-D-*glucopyranoside* (R)- *and* (S)-4,6-*Phenylphosphonate* [(19*ax*) *and* (19*eq*)].—A solution of the diol (1) (1 g), triethylamine (0·5 g), and phenylphosphonic dichloride (0·9 g) in dichloromethane was stored at room temperature overnight and processed in the usual way. Separation by t.l.c. of (19*ax*) and (19*eq*) was achieved by double irrigation with benzene–acetone (7 : 3). Pure samples of the (R)-*phosphonate*, m.p. 173° (from di-isopropyl ether), $[\alpha]_D$ +156° (*c* 1) (Found: C, 52·1; H, 6·1. $C_{15}H_{21}O_7P$ requires C, 52·3; H, 6·2%), $\nu_{P=O}$ 1282 cm^{-1} (KBr); and the (S)-*phosphonate* (19*eq*), m.p. 107—109° (from di-isopropyl ether), $[\alpha]_D$ +18° (*c* 0·5) (Found: C, 51·9; H, 6·3%), $\nu_{P=O}$ 1256 cm^{-1} (KBr), were obtained by repeated column chromatography.

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