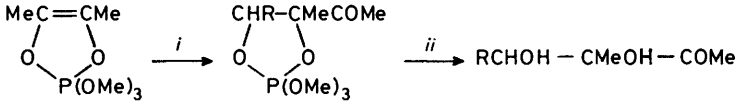
Preparation of Sugars with Branched Chains, a Methylene Bridge, or C-1-Phenyl Substituents by the Ramirez Dioxaphosphole Condensation

By **Serge David** * and **Marie-Christine Lépine**, Laboratoire de Chimie Organique Multifonctionnelle, Université Paris-Sud, 91405 Orsay Cedex, France

The products of condensation of 2,3-*O*-isopropylidene-D-glyceraldehyde with 4,5-dimethyl- and 4,5-tetramethylene-2,2,2-trimethoxy-1,3,2-dioxaphospholes, (1) and (2), were hydrolysed to the free sugars which were converted by acidified methanol into the corresponding mixture of glycosides. In this way were prepared the methyl pyranosides and furanosides of 1-deoxy-3-*C*-methyl-D-*ribo*-hexose [(7), (9), and (10)], and 1,2-*C*-tetramethylene-D-ribose [(11) and (13)]. Condensation of the same aldehyde with the 4-phenyldioxaphosphole (3) led to 1-*C*-phenyl-D-lyxose (15) which was further characterized as the tetra-*O*-benzoate (16) and tetra-*O*-acetate (17) of the α-D-pyranoside tautomer.

In 1965, Ramirez *et al.*[1,2] reported that aldehydes readily react with 2,2,2-trimethoxy-4,5-dimethyl-1,3,2-dioxaphosphole to give dioxaphospholans which can be hydrolysed to keto-diols (Scheme). The authors examined the course of the reaction with four simple aldehydes RCHO (R = Me, Pr^n, n-C_6H_{13}, and Ph). Two isomers might have been expected. Aliphatic aldehydes only gave phospholans with *cis* configuration of R and Ac but in the case of benzaldehyde, a weak ^1H n.m.r. signal in the spectrum of the crude condensation product was ascribed to the presence of 10% of the *trans* derivative.[2] No further synthetic applications have been reported. We now describe the condensation of 1,2-*O*-isopropylidene-D-glyceraldehyde with the dioxaphospholes (1), (2), and (3). Although the yields may be modest, the starting materials are readily available, and the reactions provide a quick access to structures, some of which [(7), (9), and (10)] belong to known types, while others [(11), (13), (15), (16), and (17)] are quite novel. The syntheses of compounds (7), (9), and (10) have been reported in a preliminary paper.[3]



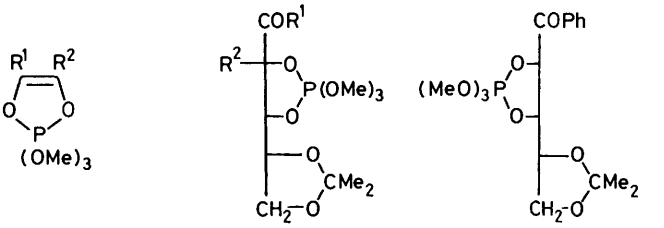
SCHEME Reagents: *i*, R–CHO; *ii*, H_2O

DISCUSSION

The dioxaphospholes (1) and (3) were already known.[4,5] Condensation of cyclohexane-1,2-dione with trimethyl phosphite at room temperature gave the new, bicyclic dioxaphosphole (2) as a distillable oil (59%). The protected triose, 2,3-*O*-isopropylidene-D-glyceraldehyde was first used as the pure liquid but later on, because of the losses inherent to its purification, we found it more convenient to start with the crude, filtered benzene solution obtained according to reference 6. This triose is a better electrophile than the simple aldehydes utilized by Ramirez *et al.*, and, accordingly, when pure reacted *ca.* four times faster with the dioxaphospholes (1), (2), and (3).

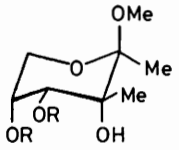
The sequence of operations leading to the crude, free sugar fraction was the same in each case, and only the reaction with (1) will be described in detail. Reaction of the neat liquids gave a distillable oil in 70% yield. Signals arising from two acetyl protons were seen in the n.m.r. spectrum, at δ 2.20 and 2.33, with a 9 : 1 intensity ratio, an indication that 10% of the product was possibly the *trans* isomer. On the other hand, condensation in benzene solution gave a product which appeared homogeneous by 60-MHz ^1H n.m.r. No resolution was attempted at this stage, but the following transformations indicated the presence of at least 31% of the phospholan (4) in the distilled oil.

The oil was hydrolysed with water as described for other 2,2,2-trimethoxy-1,3-dioxaphospholans.[1] These conditions involved a quick drop of the pH of *ca.* 0.8 at the beginning of the reaction, with consequent removal of the isopropylidene acetal protecting group. For this reason, this hydrolysis led to the free sugar(s), a state not very favourable for their isolation, so that an acid-stable protecting group on 2-OH of D-glyceraldehyde should be commended for preparative work. The aqueous hydrolysis mixture was freed from inorganic material by ion-exchange chromatography and evaporated to dryness to give a residue which will be subsequently referred to as the ' crude sugar fraction.'



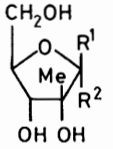
(1) $R^1 = R^2 = Me$
(2) $R^1, R^2 = [CH_2]_4$
(3) R = H, R = Ph
(4) $R^1 = R^2 = Me$
(5) $R^1, R^2 = [CH_2]_4$
(6)

Treatment of this fraction with methanol in the presence of acidic resin gave a mixture of glycosides which were separated by column chromatography to afford (7) (amorphous; 19%), (9) (traces), and (10) (m.p. 99 °C; 31%). Any one of these could be partially converted into the other two with acidic methanol. Thus we were able to prepare the crystalline glycoside (10) from its isomer (7) in 45% isolated yield showing that they are derivatives of the same free sugar.



(7) R = H

(8) R = Bz



(9) R^1 = Me, R^2 = OMe

(10) R^1 = OMe, R^2 = Me

The pyranose nature of the glycoside (7) was indicated by the presence in its ^{1}H n.m.r. spectrum of two doublets which disappear on addition of D_2O (Table). Further information was derived from the properties of the diester (8), the product of conventional benzoylation. In its ^{1}H n.m.r. spectrum (Table), a singlet of one exchangeable proton at δ 3.98 indicated the presence of a free tertiary hydroxy-group, in confirmation of the expected 4,5-dibenzoate structure. Irradiation at the frequency of the 4-H doublet left 5-H showing as an only slightly broadened singlet, with almost zero coupling to the methylene protons, an indication of equatorial orientation. As the configuration is D at C-5, the ring must be in the D$^1C_4$ chair conformation. The circular dichroism curve of the dibenzoate (8) indicated ' negative chirality ' in the sense used by Nakanishi [7] between the two benzoate groups. This is only possible for an equatorial benzoate at C-4, and an axial 4-H proton. Finally the configuration at C-3 was indicated by ^{13}C n.m.r. data on the glycoside (7) in $CDCl_3$. There is no detectable ^3J coupling between C-3′ and 4-H, so there must be a *gauche* relationship (*cf.* ref. 8).

These parameters could also be compatible [9] with either a D-*arabino* or a D-*lyxo* configuration, respectively in the $B_{1,4}$ or $^{2,5}B$ conformations. These, however, are improbable, since it is possible for derivatives with such configurations to adopt much less strained conformations.

We formulate the pyranoside as a β-anomer because its molecular rotation (−270°) is nearer to that calculated [10] for structure (7) (−175°) than to that calculated for its C-2 epimer (−70°). Structure (7) is no doubt that of the more stable pyranose anomer.

Furanose structures for the other two glycosides are indicated by the presence of a primary OH triplet in their ^{1}H n.m.r. spectra. We suggest that the more polar furanoside [m.p. 99 °C (from CH_2Cl_2); $[\alpha]_D^{20}$ −84° (*c* 1 in MeOH)] is the β-anomer (10), because of its lower optical rotation. The other furanoside (9), $[\alpha]_D^{20}$ +4.5° (*c* 0.5 in CH_2Cl_2), could only be isolated in small yield.

It is noteworthy that a single configuration, with three chiral centres, was formed in this condensation in at least 50% yield, starting from a precursor with only a single chiral centre.

Glycosidation of the ' crude sugar fraction ' prepared from the dioxaphosphole (2) gave three methyl glycosides as the main products, and possibly others in trace amounts. Two of the main glycosides were formulated as the derivatives (11) and (13) of a common

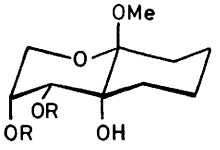
Comparison of the ^{1}H and ^{13}C n.m.r. spectra of the glycosides (7), (8), (11), and (12)

Methyl glycopyranoside (7)			Methyl glycopyranoside (11)		
(a) 250-MHz ^{1}H n.m.r. data * in $(CD_3)_2SO$					
1.03; 1.20	(2 s)	2 CMe	1.75—2.5		CH_2-bridge
3.07	(s)	OMe	3.66	(s)	OMe
3.44	(q, $J_{4.OH}$ 9, $J_{4.5}$ 3.2 Hz)	4-H	4.11	(q, $J_{3.OH}$ 8.2 Hz, $J_{3,4}$ 3.2 Hz)	3-H
3.49	(pseudo-d, spacing 2.5 Hz)	6a-H, 6b-H	4.10 4.18	(q, $J_{5a.5b}$ 17.6 Hz, $J_{4.5a}$ 1.3 Hz) (q, $J_{4.5b}$ 1.3 Hz)	5a-H 5b-H
3.64	(broad)	5-H	4.28	(m)	4-H
4.33	(d)	4-OH	4.97	(d)	3-OH
4.64	(s)	3-OH	5.40	(s)	2-OH
5.36	(d, $J_{5.OH}$ 5 Hz)	5-OH	6.27	(d, $J_{4.OH}$ 4 Hz)	4-OH
(b) 41.4-MHz ^{13}C n.m.r. data * in $CDCl_3$					
16.25; 19.17		C-1; C-3′	19.57; 21.72; 26.65; 29.53		CH_2-bridge
48.29		OMe	47.21		OMe
63.82		C-6	64.35		C-5
68.62; 69.86		C-4; C-5	68.30; 70.36		C-3; C-4
76.17		C-3	75.04		C-2
103.85		C-2	101.95		C-1
(c) 250-MHz ^{1}H n.m.r. data * in $(CD_3)_2SO$					
Dibenzoate (8)			Dibenzoate (12)		
1.13; 1.43	(2 s)	2 CMe	1.2—2.02		CH_2 bridge
3.29	(s)	OMe	3.20	(s)	OMe
3.87	(d, $J_{6a.6b}$ 13.2 Hz)	6a-H	3.84	(d, $J_{5a.5b}$ 13.0 Hz)	5a-H
3.99	(d)	6b-H	4.00	(q, $J_{4.5b}$ 2.0 Hz)	5b-H
4.76	(s)	OH	4.46	(s)	OH
5.43	(d, $J_{4.5}$ 3.0 Hz)	4-H	5.43	(d, $J_{3.4}$ 4.0 Hz)	3-H
5.49	br (s)	5-H	5.49	(br, s)	4-H
7.50—8.20		Ar-H	7.30—8.20		Ar-H

*All intensities agree with the given interpretations.

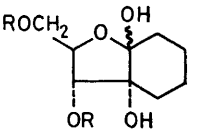
parent sugar, as any one of them could be partially converted into the other with acidified methanol. The suggested structure (11) rests on a close similarity of properties with (7), to the extent that the same accidental, near coincidences of resonance are observed (*Table*). In the 250-MHz ^{1}H n.m.r. spectrum of the methyl glycoside (7), the methylene protons appear as a pseudo-doublet which collapses to a singlet on irradiation at 5-H, so the difference between their frequencies is very small compared with their probably strong, geminal coupling. Such an ABX system is not amenable to first order analysis, and the observed spacing, 2.5 Hz, is only a rough and inferior, estimation of $J_{5,6}$. On the other hand, in the case of the methyl glycoside (11) the difference between the frequencies of the methylene protons is of the order of 20 Hz and a more reliable estimation of $J_{4,5}$ is possible. The c.d. spectra of the dibenzoates (8) and (12) are almost identical.

The presence in the ^{1}H n.m.r. spectrum of glycoside (13) of a triplet at δ 4.78 which vanished on addition of D_2O indicated its furanoside constitution. The $J_{3,4}$ coupling constant of the dibenzoate (14), 3.4 Hz, lies



(11) R = H

(12) R = Bz



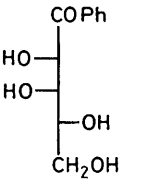
(13) R = H

(14) R = Bz

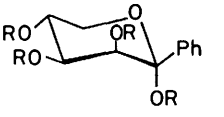
somewhat outside the usual range for *cis*-protons on furanose rings, in agreement which the proposed structure. The optical rotation of the furanoside (13) is positive, like that of the minor α-furanoside (9). However, present evidence affords no definitive proof of its anomeric configuration. Glycosides (11) and (13) are the first instances of derivatives of a novel type of branched chain sugar having a methylene bridge between two carbons of the ring. Although the overall yield from (2) is low (10—16%), these glycosides are prepared in very few steps from starting materials which are readily available in large quantities.

The third methyl glycoside did not equilibrate with derivatives (11) and (13) in acidic methanol. Its furanoside nature was proved by the presence of a triplet due to a primary alcoholic function in its ^{1}H n.m.r. spectrum but its constitution was not elucidated further.

The ' crude sugar fraction ' prepared from the dioxaphosphole (3) was purified by chromatography followed by crystallization. This gave in low yield the crystalline free sugar. No conclusion could be drawn from the ^{1}H n.m.r. spectrum in solution in $(CD_3)_2SO$, which obviously was that of a tautomeric mixture. Glycosidation also was unsuccessful, but much better yields were achieved by benzoylation of the crude sugar to give a crystalline tetrabenzoate (16), or acylation to an amorphous tetraacetate (17). Compound (15) should be an unbranched ketonic derivative, as no aldehyde signal was observed in the crude condensation products, which suggested that their structure was analogous to (6). Accordingly in the ^{1}H n.m.r. spectra of (16) and (17), there is no singlet which could be ascribed to 1-H of the alternative C-2 phenyl-substituted esters. The pyranose nature of compounds (16) and (17) is proved by the presence of two low-field signals due to ring methine protons while a methylene signal (J_{gem} 12.5 Hz) was observed at relatively



(15)

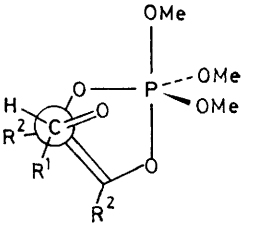


(16) R = Bz

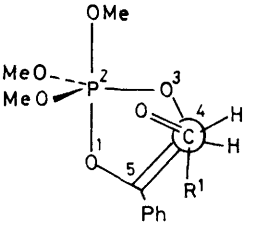
(17) R = Ac

higher field. The strong coupling between 3-H and 4-H [7.5 Hz in (16) and 9 Hz in (17)] indicates that both are axial. As the configuration is D at C-5, the conformation is $^4C_1$. The weak $J_{2,3}$ coupling indicates that the ester function at C-2 is axially oriented. As esters (16) and (17) have been prepared in yields of >50% from the partially purified sugar (15), they probably correspond to the more stable conformation in the acylation medium. They are accordingly formulated as the α-D anomer, a configuration with a favourable anomeric effect, with the bulky phenyl substituent equatorially oriented. The pyranose ester (16), prepared in 8% isolated yield from the dioxaphosphole (3), is representative of a new type of phenyl-substituted sugar, which is now easily available by the above synthesis.

Possible transition states, A and B, to the D-*ribo*-phospholans (4) and (5), and to the D-*lyxo*-phospholan (6) are depicted in the Figure, following the suggestions



A



B

of Ramirez *et al.*[5] The phosphole ring and apical P–O bonds are in the plane of the paper, while the aldehyde carbonyl group is drawn above this plane. Reaction then would proceed by severance of the apical P–O-1 bond. In these conformations of the phospholes, O-1 is less hindered by the methoxy-groups than O-3 because of the greater length of apical bonds, and the position of the phenyl substituent in the vicinity of O-1 is plausible. It is seen that in both transition states A and B, the bulky aldehyde side chain R^1 also avoids the vicinity of O-3, with the somewhat paradoxical result that, in state

A, it lies between the C-4 and C-5 substituents of the phosphole ring.

EXPERIMENTAL

Preparative chromatographic separations with the given eluants were performed on silica gel columns, with monitoring of the effluent by t.l.c. on silica gel. ^{1}H N.m.r. chemical shifts in the given solvent are reported as δ values with Me_4Si as internal standard.

4,5-Tetramethylene-2,2,2-trimethoxy-1,3,2-dioxaphosphole (3).—A mixture of cyclohexane-1,2-dione (50 g) and trimethyl phosphite (60 ml) was kept for 2 d at room temperature under nitrogen. Distillation then gave the *dioxaphosphole* (3) (62.3 g; 59%), b.p. 80 °C at 0.5 mmHg; δ (60 MHz, CCl_4) 1.63 (4 H, m, 7- and 8-H), 2.10 (4 H, m, 6- and 9-H), 3.41 (9 H, d, $J_{P,Me}$ 13.2 Hz, 3 MeO) (Found: C, 45.5; H, 7.5. $C_9H_{17}PO_5$ requires C, 45.8; H, 7.3%).

Preparation and Hydrolysis of 2,2,2-Trimethoxy-1,3,2-dioxaphospholan (4).—A slight molar excess of the dioxaphosphole (1) was added to 1,2-*O*-isopropylidene-D-glyceraldehyde, and the mixture was kept for 2 d at room temperature under nitrogen, when the ^{1}H n.m.r. signal of CHO at δ 9.65 (60 MHz, CCl_4) was absent from the spectrum. Distillation then gave a liquid (70%), b.p. 115 °C at 0.5 mmHg; δ (60 MHz, CCl_4) 1.25, 1.32, and 1.41 (9 H, 3 s, CMe_2 and 3′-Me), 2.20 (2.7 H, s, MeCO), 2.33 (0.3 H, s, MeCO), 3.48 [9 H, d, $J_{P,Me}$ 12.6 Hz, $(MeO)_3$], and 3.70—4.0 (4 H).

This liquid, which contained dioxaphospholan (4) was hydrolysed without further purification. When a mixture of this liquid (36 g) with water (30 ml) was vigorously stirred at room temperature, the pH dropped to 0.8 in 3 min. The pH was brought to 5.6 with 1M-aqueous NaOH, and the mixture heated at 110 °C for 8 h, the pH being kept at 5.6 by addition of 1M-NaOH (93 ml altogether). The cooled solution was passed through columns of sulphonic acid resin (H^+ form), and afterwards weakly basic resin (acetate form). The columns were washed with water, and the combined effluents were evaporated to dryness to give a semi-crystalline residue, the 'crude sugar' (11.5 g; 62%), in which t.l.c. ($CHCl_3$–MeOH, 8 : 2 v/v) indicated the presence of one major component.

The preparation of the 'crude sugars' from the dioxaphospholes (1), (2), and (3) was further simplified as follows. A solution of 1,2-*O*-isopropylidene-D-glyceraldehyde in benzene (400 ml) was prepared from 1,2:5,6-di-*O*-isopropylidenemannitol (50 g) as described in ref. 6 with the exclusion of the last distillation. To this solution, kept under nitrogen, was added the dioxaphosphole (35 g), and the course of the reaction was monitored as above. Evaporation of the benzene gave a residue which was hydrolysed with water, eventually adding enough methanol to keep the products in solution. Inorganic matter was removed as above, and the solution was evaporated to dryness to give the 'crude sugar fraction.' Weights of the residues were 28.3 g from the phosphole (1), 22.2 g from (2), and 20 g from (3).

Methyl 1-Deoxy-3-C-methyl-β-D-ribo-hexulopyranoside (7) *and Methyl 1-Deoxy-3-C-methyl-β-D-ribo-hexulofuranoside* (10).—A solution of the crude sugar from (1) (8.2 g) in methanol, in the presence of a sulphonic acid resin (H^+ form) was kept for 1 d at room temperature, when t.l.c. ($CHCl_3$–MeOH, 6 : 1 v/v) indicated the formation of two major and two minor components. The solution was filtered and evaporated to dryness. Chromatography ($CHCl_3$–MeOH, 6 : 1 v/v) of the residue first gave the *pyranoside* (7) as a syrup (1.6 g; 19%). A crystalline sample was obtained by the ammonolysis of the dibenzoate (8) (see later), m.p. 75—80 °C (from ether–hexane), $[\alpha]_D^{20}$ −16.7° (*c* 1 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 380br cm^{-1} (OH); ^{1}H and ^{13}C n.m.r. data in Table (Found: C, 50.0; H, 8.3; O, 41.8. $C_8H_{16}O_5$ requires C, 50.0; H, 8.4; O, 41.6%).

The next chromatographic fraction was considered to be methyl 1-deoxy-3-*C*-methyl-α-D-*ribo*-hexulofuranoside (9), amorphous (traces), $[\alpha]_D^{20}$ +4.5° (*c* 0.5 in CH_2Cl_2); δ[240 MHz, $(CD_3)_2SO$] 1.07 (3 H, s, CMe), 1.17 (3 H, s, CMe), 3.13 (3 H, s, OMe), 3.33 and 3.46 (ring H), 3.68 (1 H, s, 3-OH), 4.73 (1 H, t, $J_{6.OH}$ 5 Hz, 6-OH), and 4.90 (1 H, d, $J_{4.OH}$ 6 Hz, 4-OH).

Continued elution then gave the *methyl furanoside* (10) (2.6 g; 29%), m.p. 99° (from CH_2Cl_2); $[\alpha]_D^{20}$ −84° (*c* 1.3 in MeOH), $[\alpha]_D^{20}$ −62° (*c* 1, H_2O); $\nu_{max.}$ (Nujol) 3 430, 3 290, and 3 200 cm^{-1} (OH); δ[240 MHz, $(CD_3)_2CO$] 1.15 (3 H, s, CMe), 1.29 (3 H, s, CMe), 3.19 (3 H, s, OMe), 3.54 (1 H, m, 5-H), 3.57 (1 H, q, $J_{5,6a}$ 5.5, J_{gem} 11.8 Hz, 6a-H), 3.64 (1 H, q, $J_{5,6b}$ 2.4 Hz, 6b-H), 3.68 (1 H, s, 3-OH), 3.77 (1 H, m, 4-H), 3.88 (1 H, t, $J_{6.OH}$ 7.3 Hz, 6-OH), and 4.11 (1 H, d, $J_{4,OH}$ 7.3 Hz, 4-OH) (Found; C, 50.0; H, 8.4; O, 41.9. $C_8H_{16}O_5$ requires C, 50.0; H, 8.4; O, 41.6%).

Isomerizations.—A methanolic solution of the pyranoside (7) (200 mg) was kept overnight at 20 °C in the presence of acidic resin. T.l.c. then indicated the presence of the same components as in the mixture obtained above by glycosidation of the crude sugar. Column chromatography separated the pyranoside (7) (45 mg) from the furanoside (10) (90 mg; m.p. 96—98 °C). A similar treatment of the furanoside (10) (0.4 g) gave the pyranoside (7) as a syrup, identified by its ^{1}H n.m.r. spectrum, and some starting material (0.2 g).

Methyl 4,5-Di-O-benzoyl-1-deoxy-3-C-methyl-β-D-ribo-hexulopyranoside (8).—A solution of the pyranoside (7) (107 mg) and benzoyl chloride (0.2 ml) in pyridine (5 ml) was kept for 17 h at room temperature and then poured into water. The organic mixture was extracted with chloroform and the organic phase treated in the usual way, to give the *dibenzoate* (8) as needles (70%), m.p. 146—148 °C (hexane), $[\alpha]_D^{20}$ −24.5 °C (*c* 1 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 715 (CO), 2 930 (CH). 3 400 (shoulder, H-bonded OH), and 3 570 cm^{-1} (OH); c.d. (*c* 10^{-4} M in MeOH): $\Delta\varepsilon_{236}$ −16.10 and $\Delta\varepsilon_{222}$ +3.45; ^{1}H n.m.r. data in Table (Found: C, 66.4; H, 6.0. $C_{22}H_{24}O_7$ requires C, 66.0; H, 6.0%).

Ammonia was slowly bubbled during 2 h into a solution, cooled to −15 °C, of dibenzoate (8) in anhydrous methanol. The solution was then allowed to warm to room temperature and then evaporated to dryness. Chromatography of the residue ($CHCl_3$–MeOH, 8 : 1 v/v) gave the pyranose (7) (70%), m.p. 75—80 °C (from ether–hexane).

Methyl 1,2-C-tetramethylene-β-D-ribopyranoside (11) and *-α-D-ribofuranoside* (13).—The 'crude sugar fraction' (21.4 g) from the dioxaphosphole (3) was first purified by chromatography ($CHCl_3$–MeOH, 9 : 1 v/v) with collection of fractions having R_F *ca.* 0.2 on t.l.c. ($CHCl_3$–MeOH, 9 : 1 v/v). A second chromatography ($CHCl_3$–MeOH, 93–7 v/v) allowed the separation of the free sugar as a pure (1.3 g) and a slightly contaminated fraction (3.7 g). Glycosidation as above of the pure fraction gave four new products, which were separated by chromatography ($CHCl_3$–MeOH, 9 : 1 v/v) in the following order of increasing polarities: (i) the *methyl β-D-pyranoside* (11) as fine needles (0.40 g), m.p. 108—110 °C (from $CHCl_3$–Pr^i_2O), $[\alpha]_D^{20}$ −79° (*c* 0.7 in $CHCl_3$);

^{1}H n.m.r. data in Table (Found: C, 54.3; H, 8.3; O, 36.4. $C_{10}H_{18}O_5$ requires C, 55.0; H, 8.3; O, 36.7); (ii) an unidentified product (50 mg); (iii) the *methyl* D-*ribofuranoside* (13) (0.20 g amorphous) $[\alpha]_D^{20}$ +60° (*c* 0.5 in MeOH); δ [240 MHz, $(CD_3)_2SO$] 1.08—1.67 (7 H of the methylene bridge), 2.01 (1 H, d, *J* 12 Hz, 1 H of the methylene bridge), 3.10 (3 H, s, OMe), 3.22 (1 H, q, $J_{3.OH}$ 6, $J_{3.4}$ 3.3 Hz, 3-H), 3.52 (1 H, m, J_{gem} 5 Hz, 5-H), 3.56 (5′-H), 3.63 (4-H), 3.67 (1 H, s, 2-OH), 4.78 (superposition of d and t, 3-OH and 5-OH) [the composition was estimated from that of the dibenzoate (14)]; and (iv) a methyl 1,2-C-tetramethylene-D-pentafuranoside, (0.20 g), amorphous, $[\alpha]_D^{20}$ −40° (*c* 0.5 in MeOH); δ [240 MHz, $(CD_3)_2SO$] 1.00—1.79 (7 H of the methylene bridge), 1.99 (d, *J* 12 Hz, 1 H of the methylene bridge), 3.14 (3 H, s, OMe), 3.41—3.63 (3 H, m, 4-, 5-, and 5′-H), 3.84 (1 H, pseudo-t, $J_{3.4} = J_{3.OH}$ = 7 Hz, 3-H), 4.05 (1 H, s, 2-OH), 4.66 (1 H, t, *J* 6 Hz, 5-OH), and 4.91 (1 H, d, 3-OH). The composition was estimated from that of the dibenzoate prepared in the usual way (benzoyl chloride, pyridine) and purified by chromatography (ether–light petroleum, 1 : 2 v/v), amorphous, $[\alpha]_D^{20}$ −44° (*c* 0.7 in $CHCl_3$); δ (240 MHz, $CDCl_3$) 1.06—1.83 and 1.98—2.29 (8 H, CH_2-bridge), 3.06 (1 H, s, 2-OH), 3.36 (3 H, s, OMe), 4.34 (1 H, m, 4-H), 4.56 (2 H, m, 2 × 5-H), 5.72 (1 H, d, $J_{3.4}$ 7 Hz, 3-H), and 7.3—7.7 and 7.92—8.14 (ArH) (Found: C, 67.8; H, 6.3. $C_{24}H_{26}O_7$ requires C, 67.8; H, 6.2%).

On standing overnight in methanolic solution at 20 °C, in the presence of acidic resin, any one of the two glycosides (11) and (13) was partially converted into the other, but the more polar glycoside from fraction (iv) was isomerized to products different from (11) and (13) [t.l.c. ($CHCl_3$–MeOH, 95 : 5 v/v)].

Methyl 3,4-*Di*-O-*benzoyl*-1,2-C-*tetramethylene*-β-D-*ribopyranoside* (12).—Prepared from the glycoside (11) (0.13 g) in the usual way (benzoyl chloride, pyridine) and purified by chromatography (ether–light petroleum 1 : 2 v/v), the *glycoside* (12) was amorphous (0.15 g), $[\alpha]_D^{20}$ −155° (*c* 0.6 in $CHCl_3$); $\lambda_{max.}$ 236 nm (ε 20 700) *c* 10^{-4} M in MeOH); c.d. $\Delta\varepsilon_{236}$ −13.21; $\Delta\varepsilon_{222}$ 3.64 (*c* 10^{-4} M in MeOH); ^{1}H n.m.r. data in Table (Found: C, 68.1; H, 6.2. $C_{24}H_{26}O_7$ requires C, 67.6; H, 6.2%).

Methyl 3,5-*Di*-O-*benzoyl*-1,2-C-*tetramethylene*-D-*ribofuranoside* (14).—Prepared as above from fraction (iii) the *glycoside* (14) was amorphous, $[\alpha]_D^{20}$ +53.3° (*c* 0.9 in $CHCl_3$); δ (240 MHz, $CDCl_3$) 1.41—1.74 (6 H from the methylene bridge), 2.04 (1H, d, *J* 12 Hz, 1 H from the methylene bridge), 2.25 (1 H, d, *J* 12 Hz, 1 H from the methylene bridge), 3.36 (3 H, s, OMe), 4.33 (1 H, pseudo-q, $J_{4.5}$ 4.9, $J_{4.5'}$ 4.2, $J_{3.4}$ 3.4 4-H), 4.64 (1 H, q, J_{gem} 12.5 Hz, 5-H), 4.74 (1 H, q, 5′-H), 4.94 (1 H, d, 3-H), and 7.35—7.66 and 8.01—8.15 (ArH) (Found: C, 67.5; H, 6.3; O, 25.8. $C_{24}H_{26}O_7$ requires C, 67.6; H, 6.2; O, 26.3%).

1-C-*Phenyl*-D-*lyxose* (15).—Chromatography (ethyl acetate–propan-2-ol–water, 80 : 15 : 5 v/v/v) of the 'crude sugar' (20 g) from the phosphole (3) gave as the less polar fraction *the free sugar* (15) (3.5) g) which was directly esterified (see below). The sugar (15) was obtained crystalline in low yield, m.p. 150° (from ethyl acetate–methanol) (Found: C, 58.2; H, 6.2; O, 35.3. $C_{11}H_{14}O_5$ requires C, 58.4; H, 6.2; O, 35.4%).

1,2,3,4-*Tetra*-O-*benzoyl*-1-C-*phenyl*-α-D-*lyxopyranoside* (16).—The usual esterification with benzoyl chloride and pyridine, 17 h at 20 °C, followed by chromatography (chloroform) gave the *tetrabenzoate* (16) as crystals (71%), m.p. 122—123 °C (from chloroform–light petroleum), $[\alpha]_D^{21}$ +56° (*c* 0.6 in $CHCl_3$); δ (240 MHz, $CDCl_3$) 4.59 (q, 1 H, J_{gem} 12.5, $J_{4.5}$ 5.5 Hz, 5-H), 4.93 (q, 1 H, $J_{4.5'}$ 3 Hz, 5′-H), 6.00 (1 H, octet, $J_{3.4}$ 7.5 Hz, 4-H), 6.30 (1 H, q, $J_{2.3}$ 3 Hz, 3-H), 6.56 (1 H, d, 2-H), and 7.4 and 8.0 (ArH) (Found: C, 72.7; H, 4.7; O, 22.7. $C_{39}H_{30}O_9$ requires C, 72.8; H, 4.7; O, 22.4%).

1,2,3,4-*Tetra*-O-*acetyl*-1-C-*phenyl*-α-D-*lyxopyranoside* (17).—Prepared as usual (acetic anhydride–pyridine) and purified by chromatography ($CHCl_3$–MeOH, 98 : 2), *compound* (17) was amorphous (54%), $[\alpha]_D^{20}$ +69° (*c* 0.5 in $CHCl_3$); δ (240 MHz, $CDCl_3$) 2.00, 2.05, 2.12, and 2.20 (4 × 3 H, 4 s, 4 COMe), 4.17 (1 H, q, $J_{4.5}$ 5, J_{gem} 12.5 Hz, 5-H), 4.34 (1 H, q, $J_{4.5'}$ 2.5 Hz, 5′-H), 5.35 (1 H, octet, $J_{3.4}$ 9 Hz, 4-H), 5.66 (1 H, q, $J_{2.3}$ 2.5 Hz, 3-H), 6.11 (1 H, d, 2-H), and 7.54 and 7.9 (ArH) (Found: C, 57.7; H, 5.6; O, 36.2. $C_{19}H_{22}O_9$ requires C, 57.9; H, 5.6; O, 36.8%).

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