Carbohydrate Phosphates. Part I. Synthesis of Derivatives of Some aldehydo-*Sugar Phosphates.*

By J. L. BARCLAY, A. B. FOSTER, and W. G. OVEREND.

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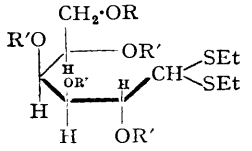
The synthesis is described of some phosphorylated derivatives of *aldehydo*-D-galactose and its 2-deoxy-analogue and of *aldehydo*-2-deoxy-D-glucose. The action of hydrogen bromide in acetic acid on 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XIII) and 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-glucose diethyl mercaptal (XVII) did not give the expected replacement of the triphenylmethyloxy-group by bromine; instead, a simultaneous fission occurred, which resulted, in the case of (XIII), in the formation of ethyl triphenylmethyl sulphide.

THERE are two main approaches which can be made to the synthesis of simple nucleotides. One involves the *initial* formation of glycosylamine (*i.e.*, nucleoside synthesis) and subsequent phosphorylation of the carbohydrate moiety, a method which has been extensively and successfully used by Todd and his colleagues (*e.g.*, *J.*, 1946, 647). For several reasons

it may prove more difficult to use this reaction sequence to synthesise deoxy-sugar nucleotides [Foster, *Farmakoterapi* (Oslo), 1951, No. 3, 1], especially those of the purine type. The alternative route, which has not been investigated, requires the formation of a phosphorylated *aldehydo*-sugar and condensation of this with a base to form finally the glycosylamine grouping. As a contribution to the latter approach we describe in this paper the synthesis of some phosphorylated *aldehydo*-sugars. Observations on the condensation reaction will form the subject of a separate communication.

Various intermediates may be utilised for the synthesis of *aldehydo*-sugar phosphates, *e.g.*, mercaptals (Wolfrom, *J. Amer. Chem. Soc.*, 1929, **51**, 2188), semicarbazones (Major and Cook, *J. Amer. Chem. Soc.*, 1936, **58**, 2474), or thiol esters (Wolfrom and Karabinos, *J. Amer. Chem. Soc.*, 1946, **68**, 724) and glyconic amides (Haworth, Peat, and Whetstone, *J.*, 1938, 1975), and certain cyclic acetals of some polyalcohols (Bourne, Corbett, and Stacey, *J.*, 1952, 2810; Foster and Overend, *J.*, 1951, 680). In this work sugar diethyl mercaptals have been used as intermediates.

Reaction of D-galactose diethyl mercaptal (I) with carefully purified triphenylmethyl chloride (1 mol.) in pyridine and then with acetic anhydride in the same solvent gives 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (II) in good



	R	R′
(I)	H	H
(II)	CPh_3	Ac
(III)	H	Ac
(IV)	$(PhO)_2PO$	Ac

	R	R′
(V)	CPh_3	Bz
(VI)	H	Bz
(VII)	$(PhO)_2PO$	Bz
(VIII)	Ac	Ac

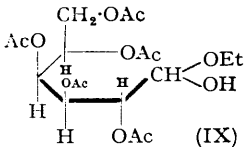
yield. Elimination of the triphenylmethyl group from (II) as triphenylmethyl bromide is achieved by careful treatment at 0° with acetic acid containing the theoretical amount of hydrogen bromide (cf. Wolfrom, Quinn, and Christman, *J. Amer. Chem. Soc.*, 1935, **57**, 713), and 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (III) is obtained. The possibility of hydrolysis and catalyst poisoning precludes the use of either aqueous acid (Kuhn, Rudy, and Weygand, *Ber.*, 1936, **69**, 1543) or hydrogenation (Micheel, *Ber.*, 1932, **65**, 262) to effect this conversion. In similar manner D-galactose diethyl mercaptal (I) was converted *via* (V) into 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (VI).

Phosphorylation of 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (III) with diphenyl phosphorochloridate in pyridine proceeded readily at 0°, to yield crystalline 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal 6-(diphenyl phosphate) (IV) in 93% yield. Under comparable conditions phosphorylation of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (VI) does not proceed and prolonged reaction (48 hours at 35°, followed by 0·5 hour at 60°) is necessary to give the difficultly crystalline phosphate (VII) in moderate yield (56%). This derivative was not studied further.

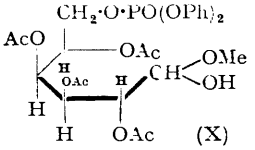
A general procedure for fission of thio-groups has been reported by Wolfrom (*J. Amer. Chem. Soc.*, 1930, **52**, 2464), involving the use of mercuric chloride in the presence of cadmium carbonate. A detailed study of the reaction led to the conditions described in the Experimental section. In model experiments 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-D-galactose diethyl mercaptal (VIII) gave 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-*aldehydo*-D-galactose. This crystallised with a molecule of ethanol which could be removed only with difficulty, by repeated crystallisation from dry toluene, and the ethanol may be present in a hemiacetal linkage as in (IX) (cf. Wolfrom, *loc. cit.*). This point, together with other related observations will be discussed in a future publication. A crystalline semicarbazone was easily prepared from 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-*aldehydo*-D-galactose monoethanolate.

Under the same conditions, 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal 6-(diphenyl phosphate) (IV) afforded 2 : 3 : 4 : 5-tetra-*O*-acetyl-*aldehydo*-D-galactose 6-(diphenyl phosphate) monomethanolate [represented as a hemiacetal (X)] (after crystallisation from methanol), from which a crystalline semicarbazone (XI) was prepared. It is clear that with the reaction sequence adopted, crystalline phosphorylated *aldehydo*-sugar derivatives can be obtained and that the aldehydo-group behaves normally with a usual reagent employed for characterisation.

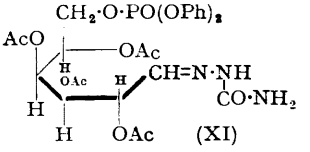
Although extension of the reaction sequence I ⟶ II ⟶ III ⟶ IV ⟶ X to the 2-deoxy-sugar series gave the desired products, from our viewpoint it was not completely successful since we did not obtain all the intermediates in crystalline form.



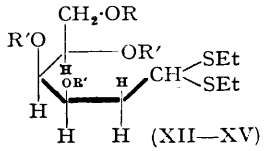
(IX)



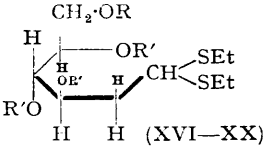
(X)



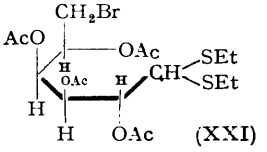
(XI)



(XII—XV)



(XVI—XX)



(XXI)

	R	R′
(XII)	CPh_3	H
(XIII)	CPh_3	Ac
(XIV)	H	Ac
(XV)	$(PhO)_2PO$	Ac
(XVI)	H	H

	R	R′
(XVII)	CPh_3	Ac
(XVIII)	H	Ac
(XIX)	Ac	Ac
(XX)	$(PhO)_2PO$	Ac

2-Deoxy-D-galactose diethyl mercaptal was converted successively into crystalline 2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XII) and thence into crystalline 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XIII). Cleavage of the triphenylmethyl group from (XIII) occurred on careful treatment at 0° with hydrogen bromide (1 mol.) in dry acetic acid but the product was syrupy. Elemental analysis agreed with that for 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-galactose diethyl mercaptal (XIV) but crystalline derivatives could not be obtained. The syrupy methanesulphonyl derivative of (XIV) readily underwent an exchange reaction with sodium iodide in dry acetone, providing some indication that the methanesulphonyloxy-residue was located at position 6, and that cleavage of the triphenylmethyl group from (XIII) was not accompanied by concomitant acetyl migration.

In like manner 2-deoxy-D-glucose diethyl mercaptal (XVI) was converted *via* (XVII) into 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (XVIII) which was obtained crystalline only with difficulty. On acetylation this gave authentic 3 : 4 : 5 : 6-tetra-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (XIX).

Reaction of the tri-acetates (XIV) or (XVIII) with diphenyl phosphorochloridate in pyridine gave syrupy diphenyl phosphates, probably (XV) and (XX) respectively, and removal of the ethylthio-groups then yielded syrupy products which were sulphur-free but could not be characterised as crystalline derivatives.

It is worthy of comment that reaction of 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (II) with hydrogen bromide in acetic acid may proceed in two stages (cf. Wolfrom, Quinn, and Christman, *loc. cit.*). As mentioned, treatment with 1·0 mol. (or preferably slightly less than 1·0 mol.) of hydrogen bromide in dry acetic acid at 0° for a very few minutes led to cleavage of the triphenylmethyl group to give 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (III). The use of more hydrogen bromide gave 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-bromo-6-deoxy-D-galactose diethyl mercaptal (XXI). Presumably the two reactions are consecutive.

Replacement of the acetate groups by benzoate groups, as in 2 : 3 : 4 : 5-tetra-*O*-benzoyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal, confers considerable stability on the molecule since treatment with excess of hydrogen bromide in acetic acid gave a good yield (67%) of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal with insignificant formation of the 6-bromo-6-deoxy-derivative. This may be due to a shielding effect by the benzoate groups. In this connection it is interesting that attempts to triphenylmethylate the alcohols (XIV) or (XVIII) were unsuccessful and it is possible that the

converse effect of the presence of the acetate groups might sterically hinder the approach of the large chlorotriphenylmethane molecule.

Alkyl bromides such as (XXI) have some value as intermediates in phosphate and polyphosphate synthesis (cf. *e.g.*, Clark, Todd, and Zussman, *J.*, 1951, 2952) and it was with this in mind that the action of excess of hydrogen bromide in acetic acid on 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XIII) and its 2-deoxy-D-glucose analogue (XVII) was examined. Treatment of the former at room temperature with 2 mols. of hydrogen bromide in acetic acid for 5 minutes led to extensive decomposition of the carbohydrate moiety. The rapid formation of insoluble triphenylmethyl bromide which normally occurs in reactions of the hexose derivatives such as (II) under the same conditions, did not occur in this case. Ethyl triphenylmethyl sulphide was subsequently isolated in 68% yield. It is possible that this product arose by the interaction of triphenylmethyl bromide, normally formed in the reaction, and ethanethiol which could result from demercaptolation. This type of behaviour does not appear to have been observed with the hexose derivatives such as (II) in which the mercaptal group is relatively stable. An increased lability towards acidic reagents, of the 1-substituents in (XIII) and (XVII), is to be expected because of the presence of the 2-methylene group (see Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433, and papers in the same series).

The action of excess of hydrogen bromide on 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-glucose diethyl mercaptal (XVII) did not yield ethyl triphenylmethyl sulphide but an unidentified product. Thus the action of hydrogen bromide in acetic acid on the 2-deoxy-hexose derivatives (XIII) and (XVII) is more complex than in the case of the hexose analogue (II) and does not give rise to the expected halogeno-derivatives.

Experimental

[α] refers to solutions in $CHCl_3$ unless otherwise stated.

Fission of 2 : 3 : 4 : 5 : 6-*Penta*-O-*acetyl*-D-*galactose Diethyl Mercaptal* (VIII).—A solution of the mercaptal (20 g.) in aqueous acetone was treated with mercuric chloride (3·6 mol.) and excess of cadmium carbonate as described by Wolfrom (*loc. cit.*). The charcoal treatment of the reaction mixture recommended by this author was omitted since it considerably reduced the yield. 2 : 3 : 4 : 5 : 6-Penta-*O*-acetyl-*aldehydo*-D-galactose monoethanolate (IX) (13·2 g., 75%) was isolated, with m. p. 126—128°. From (IX), 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-*aldehydo*-D-galactose (m. p. 118°) and its semicarbazone (m. p. 200°) were obtained as described by Wolfrom (*loc. cit.*).

2 : 3 : 4 : 5-*Tetra*-O-*acetyl*-D-*galactose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (IV).—A solution of 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (3 g., 1 mol.), prepared from 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal by the method of Wolfrom, Quinn, and Christman (*loc. cit.*), in dry pyridine (12 ml.) was treated with diphenyl phosphorochloridate (2 g., 1·1 mol.) at 0° for 12 hr. Pouring the mixture into ice water (200 ml.) gave a syrup which soon solidified. Recrystallisation from methanol afforded the *phosphate* as needles (4·2 g., 93%), m. p. 82°, $[\alpha]_D^{18}$ −6° (*c*, 2·0) (Found : C, 52·5; H, 5·7; S, 9·1; P, 4·7. $C_{30}H_{39}O_{12}S_2P$ requires C, 52·5; H, 5·7; S, 9·3; P, 4·5%).

2 : 3 : 4 : 5-*Tetra*-O-*acetyl*-aldehydo-D-*galactose* 6-(*Diphenyl Phosphate*) (X).—The preceding mercaptal (IV) (11·6 g.) was dissolved in acetone (50 ml.) and water (17 ml.) in which was suspended finely powdered cadmium carbonate (17 g.). The mixture was stirred vigorously and a solution of mercuric chloride (15 g.) in acetone (45 ml.) was added gradually during 1 hr. The mixture was stirred vigorously for a further 20 hr. with frequent additions of fresh cadmium carbonate, then filtered, the residue was washed with acetone, and the combined filtrate and washings were evaporated under reduced pressure at 35°. Final traces of water were removed by storage *in vacuo* over phosphoric oxide. The solid residue was extracted with warm chloroform (4 × 50 ml.), and the combined extracts were washed successively with water, aqueous potassium iodide (10%), and water, and then dried ($MgSO_4$). Concentration of the chloroform solution gave a pale yellow syrup which crystallised from methanol. Recrystallisation from acetone–ether–light petroleum (b. p. 60—80°) gave the *phosphate* (5·1 g., 49%) as needles, m. p. 97°, $[\alpha]_D^{18}$ +24° (*c*, 2·0) (Found : C, 52·95; H, 5·3; P, 5·05. $C_{26}H_{29}O_{13}P,CH_3{\cdot}OH$ requires C, 52·9; H, 5·4; P, 5·1%). It slowly restored the colour to Schiff's reagent.

Treatment of this product (0·1 g.) in 60% aqueous ethanol (3 ml.) containing sodium acetate

(0·02 g.) with semicarbazide hydrochloride (0·03 g.) at 0° for 12 hr. gave the *semicarbazone* (40 mg., 39%), m. p. 152° (from methanol) (Found: C, 50·4; H, 5·3; N, 6·5; P, 4·9. $C_{27}H_{32}O_{13}N_3P$ requires C, 50·9; H, 5·0; N, 6·6; P, 4·9%).

2 : 3 : 4 : 5-*Tetra*-O-*benzoyl*-D-*galactose Diethyl Mercaptal* (VI).—Treatment of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (m. p. 141°, $[\alpha]_D^{20}$ −24°) by essentially the method of Wolfrom *et al.* (*loc. cit.*) gave 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (67%), m. p. 96°, $[\alpha]_D^{20}$ −6·0° (*c*, 2·0). Wolfrom *et al.* record m. p. 96—97°, $[\alpha]_D^{20}$ −6·8°.

2 : 3 : 4 : 5-*Tetra*-O-*benzoyl*-D-*galactose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (VII).—A solution of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (2 g., 1 mol.) in dry pyridine (10 ml.) was treated with diphenyl phosphorochloridate (1 g., 1·25 mol.) for 48 hr. at 35° and then at 60° for 30 min., then poured into ice–water (100 ml.), and the resultant solution extracted with chloroform (4 × 25 ml.). The combined extracts were washed successively with aqueous potassium hydrogen sulphate, water, aqueous potassium hydrogen carbonate, and water, and then dried ($MgSO_4$). Evaporation under diminished pressure yielded a syrup which separated from ethanol as an amorphous solid. Recrystallisation from ethanol–*n*-pentyl alcohol gave the *product* (1·6 g., 56%), m. p. 60—62°, $[\alpha]_D^{17}$ −4° (*c*, 2·0) (Found: C, 64·2; H, 5·15; S, 6·7; P, 3·5. $C_{50}H_{47}O_{12}S_2P$ requires C, 64·2; H, 5·0; S, 6·8; P, 3·3%).

2-*Deoxy*-D-*galactose Diethyl Mercaptal.*—Prepared according to the method of Overend, Shafizadeh, and Stacey (*J.*, 1950, 671) the compound had m. p. 106—107°, $[\alpha]_D^{18}$ +45° (*c*, 0·8 in EtOH). Overend *et al.* give m. p. 107—108°, $[\alpha]_D^{20}$ +40° in MeOH.

2-*Deoxy*-6-O-*triphenylmethyl*-D-*galactose Diethyl Mercaptal* (XII).—A solution of 2-deoxy-D-galactose diethyl mercaptal (1·0 g.) in dry pyridine (8 ml.) was treated with triphenylmethyl chloride (1·03 g.) for 30 hr. at room temperature, then diluted with ice-water (100 ml.), and the syrup which separated was washed with water by decantation. The *mercaptal* (0·87 g., 46%), crystallised from methanol, had m. p. 92°, $[\alpha]_D^{17}$ +24·8° (*c*, 1·29) (Found: C, 67·6; H, 7·0; S, 12·6. $C_{29}H_{36}O_4S_2$ requires, C, 68·0; H, 7·0; S, 12·5%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*galactose Diethyl Mercaptal* (XIII).—A solution of 2-deoxy-D-galactose diethyl mercaptal (19 g.) in dry pyridine (*ca.* 80 ml.) was treated with triphenylmethyl chloride (19·6 g.) for 30 hr. at 35°. Acetic anhydride (106 ml.) was then added slowly to the cooled solution, with stirring during 1 hr. The mixture was set aside at 35° for a further 30 hr. and then poured into ice–water (3 l.) containing acetic acid (50 ml.). The syrup which separated solidified during 12 hr. and the product was then collected and washed with water. Recrystallisation from methanol afforded needles of the *product* (30 g., 66%), m. p. 91°, $[\alpha]_D^{18}$ −10·7° (*c*, 3·0) (Found: C, 65·8; H, 6·8; S, 9·8. $C_{35}H_{42}O_7S_2$ requires C, 65·8; H, 6·6; S, 10·0%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*galactose Diethyl Mercaptal* (XIV).—To a chilled solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (10 g. in the minimum amount of glacial acetic acid) a 10% solution of hydrogen bromide in glacial acetic acid (0·95 mol.) was added accurately from a microburette. The resultant mixture was filtered after 1 min. and the filtrate immediately poured on a mixture of ice and sodium hydrogen carbonate. Water was then added and the solution extracted with chloroform (6 × 25 ml.). The combined extracts were washed successively with water, aqueous sodium hydrogen carbonate, and water and dried ($CaCl_2$). Evaporation of the solution under diminished pressure at 35° (bath) gave a syrup which partly crystallised on treatment with methanol and water. The crystals (0·2 g.) had m. p. 90—91° alone and in admixture with starting material. Concentration of the mother-liquors and distillation of the residue afforded 3 : 4 : 5-*tri*-O-*acetyl*-2-*deoxy*-D-*galactose diethyl mercaptal* (4·9 g., 79%) as a pale yellow syrup, b. p. 200—205° (bath)/0·1 mm., n^{18} 1·5004, $[\alpha]_D^{20}$ +23·3° (*c*, 3·18) (Found: C, 48·7; H, 7·2; S, 16·4. $C_{16}H_{28}O_7S_2$ requires C, 48·4; H, 7·1; S, 16·2%).

Attempts to prepare a crystalline benzoate, 3 : 5-dinitrobenzoate, carbanilate, triphenylmethyl ether, toluene-*p*-sulphonate, or methanesulphonate were unsuccessful. Oxidation with perphthalic acid did not afford a crystalline derivative.

Action of Excess of Hydrogen Bromide on 3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*galactose Diethyl Mercaptal* (XIII).—An ice-cold solution of the mercaptal (2·5 g.) in glacial acetic acid (15 ml.) was treated with a 20% solution of hydrogen bromide in glacial acetic acid (2 mol.) for 5 min. at room temperature. The mixture was then filtered and the filtrate poured on a mixture of ice and sodium hydrogen carbonate. After dilution with water the solution was extracted with chloroform (4 × 15 ml.), and the combined extracts were washed with aqueous sodium hydrogen carbonate and water and dried ($CaCl_2$). Evaporation left a syrup which

crystallised on trituration with methanol. Recrystallisation from methanol gave colourless needles (0·9 g.) of ethyl triphenylmethyl sulphide, m. p. 127° (Found: C, 82·8; H, 6·3; S, 10·5. Calc. for $C_{21}H_{20}S$: C, 82·9; H, 6·6; S, 10·5%). Meyer and Fischer (*J. prakt. Chem.*, 1910, **82**, 525) cite m. p. 126°.

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*galactose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (XV).—Diphenyl phosphorochloridate (6·8 g.) was added to a chilled solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-galactose diethyl mercaptal (10 g.) in dry pyridine (40 ml.), and the mixture set aside at 0° overnight and then poured into ice–water (300 ml.). The aqueous solution was extracted with chloroform (4 × 50 ml.), and the combined extracts were washed, dried, and evaporated under diminished pressure. The residual syrup was dried at 30° for 4 hr. *in vacuo* to give the *product* (12·6 g., 79%) as a pale yellow syrup, n^{15} 1·5196, $[\alpha]_D^{15}$ +12° (*c*, 2·0) (Found: C, 52·4; H, 6·2; S, 10·4. $C_{28}H_{37}O_{10}S_2P$ requires C, 53·5; H, 5·9; S, 10·2%).

Attempted removal of the ethylthio-groups as previously described gave a product which contained phosphorus but not sulphur, but it was not crystalline. It restored the colour to Schiff's reagent.

2-*Deoxy*-D-*glucose Diethyl Mercaptal* (XVI).—Prepared according to the method of Hughes, Overend, and Stacey (*J.*, 1949, 2846) this compound had m. p. 134°, $[\alpha]_D^{19}$ +10° (*c*, 1·0 in EtOH).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*glucose Diethyl Mercaptal* (XVII).—A solution of 2-deoxy-D-glucose diethyl mercaptal (10 g.) in dry pyridine (63 ml.) was treated with triphenylmethyl chloride (10·4 g.) for 30 hr. at 35°, then cooled to 0°, and acetic anhydride (56 ml.) was slowly added during 30 min. After a further 30 hr. at 35° the mixture was diluted with ice–water (2 l.) containing glacial acetic acid (30 ml.). The syrup which separated had crystallised after 4 hr. It was collected, washed with water, and recrystallised from aqueous methanol. The *product* (18·7 g., 78%) was obtained as stout needles, m. p. 104°, $[\alpha]_D^{18}$ +43·3° (*c*, 3·0) (Found: C, 65·7; H, 6·3; S, 9·8. $C_{35}H_{42}O_7S_2$ requires C, 65·8; H, 6·6; S, 10·0%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*glucose Diethyl Mercaptal* (XVIII).—To a chilled solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-glucose diethyl mercaptal (10 g.) in glacial acetic acid a 10% solution of hydrogen bromide in glacial acetic acid (0·95 mol.) was added accurately. After 1 min. the precipitated triphenylmethyl bromide was removed and the filtrate poured on ice and sodium hydrogen carbonate. The mixture was worked up as described in the preparation of (XIV). The syrup obtained was dissolved in aqueous methanol, from which unchanged starting material (0·63 g.) separated. Concentration of the mother-liquors gave a syrup which was distilled, to give a pale yellow viscous syrup (4·3 g., 62%), b. p. 190—200° (bath-temperature)/0·01 mm., n^{17} 1·5159. The distillate partly crystallised on trituration with methanol and on recrystallisation from aqueous methanol the *product* (0·63 g.) was obtained as hexagonal prisms, m. p. 73°, $[\alpha]_D^{21}$ +38·7° (*c*, 3·0) (Found: C, 48·1; H, 6·9; S, 15·8. $C_{16}H_{28}O_7S_2$ requires C, 48·4; H, 7·1; S, 16·2%).

The crystalline material was very soluble in methanol and was difficult to free completely from adhering syrup: in subsequent reactions the syrup was used directly.

Acetylation of the syrup (0·6 g.) with pyridine (5 ml.) and acetic anhydride (3 ml.) by the usual method gave 3 : 4 : 5 : 6-tetra-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (0·48 g.), m. p. and mixed m. p. 76°, $[\alpha]_D^{18}$ +35° (*c*, 2·0 in MeOH) (Found: C, 49·3; H, 6·7; S, 14·9. Calc. for $C_{18}H_{30}O_8S_2$: C, 49·3; H, 6·8; S, 14·6%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*methanesulphonyl*-D-*glucose Diethyl Mercaptal*.—Methanesulphonyl chloride (300 mg.) was added to a cold solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (900 mg.) in dry pyridine (5 ml.), and the mixture set aside at 0°. Thereafter it was poured into ice–water (50 ml.) and extracted with chloroform (3 × 20 ml.). The combined extracts were worked up in the usual way and the resultant syrup dissolved in methanol and treated with charcoal. Concentration of the solution after removal of the charcoal gave the *product* (630 mg.) as a colourless syrup, $[\alpha]_D^{17}$ +36° (*c*, 1·82) (Found: C, 44·3; H, 6·5; S, 20·4. $C_{17}H_{30}O_9S_3$ requires C, 43·0; H, 6·3; S, 20·25%).

Action of Excess of Hydrogen Bromide on 3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*glucose Diethyl Mercaptal* (XVII).—A solution of (XVII) (2·5 g.) in dry glacial acetic acid (15 ml.) was treated with a solution of hydrogen bromide (2 mol.) in dry glacial acetic acid. After 5 min. the mixture was filtered and the filtrate poured on ice and sodium hydrogen carbonate. Water was added, the solution was extracted with chloroform, and the combined extracts were worked up as described for the 2-deoxy-D-galactose analogue. A brown syrup was thereby obtained which on distillation gave a pale yellow syrup (0·5 g.), b. p. 170—175° (bath-temperature)/0·01 mm. Trituration with methanol and recrystallisation from the same solvent gave an unidentified product (0·35 g.), m. p. 73° (Found: C, 88·0; H, 7·2; S, 5·7%). Redistillation of the

compound resulted in some decomposition and yielded a syrup which crystallised from methanol. The crystals (0·05 g.) had m. p. 69—70° (Found : C, 90·9; H, 9·6%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*glucose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (XX).—Diphenyl phosphorochloridate (1·23 g.) was added to a chilled solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (3·2 g.) in dry pyridine (15 ml.), and the mixture set aside overnight at 0°. Thereafter it was poured into ice–water and worked up in the usual way. The *product* (4·4 g., 80%) was obtained as a colourless viscous syrup, n^{18} 1·5195, $[\alpha]_D^{17}$ +32° (*c*, 1·1) (Found : C, 53·3; H, 6·2; S, 10·5. $C_{28}H_{37}O_{10}PS_2$ requires C, 53·5; H, 5·9; S, 10·2%).

Attempts to remove the thio-groups from the foregoing compound gave a product which was not crystalline, contained phosphorus, but no sulphur, and restored the colour to Schiff's reagent.

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CHEMISTRY DEPARTMENT,
THE UNIVERSITY, BIRMINGHAM, 15. [*Received, March 14th*, 1955.]