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The α- and β-Anomers of D-Xylopyranose 1-Phosphate[1,2]

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The phosphorylation of 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide with silver dibenzyl phosphate, followed by successive hydrogenolysis and alkaline hydrolysis, gave rise to a mixture of *ca.* 60% β- and 40% α-D-xylopyranose 1-phosphates. The anomers were separated by fractional crystallization of the strychnine salts. Experimental conditions have been observed, whereby with prolonged hydrogenolysis after the phosphorylation only the α-anomer is isolated. When the acetobromoxylose was phosphorylated with silver diphenyl phosphate, only the α-pentose 1-phosphate was isolated. The phosphorylation results are compared with those previously observed in the sugar pyranose series and the conclusion is drawn that, with silver dibenzyl phosphate, the steric course of the phosphorylation at C_1 is controlled not only by the C_2-neighboring-group effect but also by a second effect from the substituent at C_5. A mechanism is suggested to show that this latter effect may be the consequence of electrostatic interaction with the pyranose ring oxygen. Salts of the anomeric forms of D-xylopyranose 1-phosphate showed characteristic infrared absorption spectra.

Both the α- and β-anomers of D-xylopyranose 1-phosphate were required for studies of enzymic xylan synthesis. The α-anomer previously had been made by Meagher and Hassid,[4] but a synthesis of the β-anomer[5] had not been reported till after completion of this work.

In the earlier synthetic work[6,7] it was recognized that the phosphorylating agent exercised an important influence in determining the anomeric configuration of the sugar 1-phosphate obtained. Recently, Khorana, *et al.*,[8,9] showed that the same phosphorylating agent acting on tri-*O*-acyl-β-D-ribofuranosyl bromides (C_1C_2-*trans*)[10] gave rise predominantly to the β1-phosphate (C_1C_2-*trans*) when the C_2-acyloxy substituent was free to influence the substitution at C_1 or to the α1-phosphate (C_1C_2-*cis*)[10] when the neighboring C_2-group effect was absent. It thus became clear that both the phosphorylating agent and the neighboring C_2-group effect may control the steric course of the phosphorylation reaction at C_1.

Cori and associates[11] had shown that the action of trisilver phosphate on tetra-*O*-acetyl-α-D-gluco-, -galacto- or -mannopyranosyl bromides (C_1C_2-*cis* or *trans*) gave rise to the corresponding α-D-hexose 1-phosphate with retention of the original C_1C_2-configuration, and Hassid, *et al.*,[4,5] extending the Cori procedure to tri-*O*-acetyl-α-D xylo- and -β-L-arabino-pyranosyl bromides, similarly obtained α-D-xylose and β-L-arabinose 1-phosphates, respectively. However, this procedure is not satisfactory from a preparative standpoint, as more than two-thirds of the original sugar is lost in the acid hydrolysis step subsequent to the phosphorylation reaction and the yield of the sugar phosphate obtained is poor. Posternak[12-14] introduced the use of silver diphenyl phosphate and found that the phosphorylation took a course sterically analogous to that with trisilver phosphate, with the added advantage that the subsequent hydrogenolysis and alkaline hydrolysis of the protecting groups helped to circumvent the destructive acid hydrolysis step of the Cori procedure and the yields of the sugar phosphates obtained were reported to be five times better. Using monosilver phosphate, Reithel[15] observed that reaction with tetra-*O*-acetyl-α-D-hexopyranosyl bromides (C_1C_2-*cis*), followed by alkaline hydrolysis, gave rise to β-D-hexose 1-phosphates (C_1C_2-*trans*), and Putman and Hassid[5] used this method to prepare β-D-xylose and α-L-arabinose 1-phosphates. Low yields of the sugar phosphates were obtained and Wright and Khorana[8] failed to isolate any sugar phosphate from the reaction with tri-*O*-benzoyl-β-D-ribofuranosyl bromide. The use of silver dibenzyl phosphate, due to Wolfrom, *et al.*,[16] and Posternak, *et al.*,[14] showed that reaction with tetra-*O*-acetyl-α-D-hexopyranosyl halides, with C_1C_2 either *cis* (as in D-glucose) or *trans* related (as in D-mannose), gave rise entirely to the C_1C_2-*trans*-hexose 1-phosphates (β-D-glucose and α-D-mannose derivatives) in good over-all yields.

An examination of these conclusions reached by previous workers suggested that the phosphorylation reactions of tri-*O*-acetyl-α-D-xylopyranosyl bromide with silver diphenyl and dibenzyl phosphates may serve as the most satisfactory means for preparing the desired α- and β-anomers, respectively, of D-xylose 1-phosphate; accordingly we undertook to examine these reactions. The present paper reports the results of these phosphorylation studies. Preliminary notes[17,18] on this work have been published.

The phosphorylation reaction of acetobromoxylose with silver dibenzyl phosphate in benzene solution, either at room temperature or under reflux conditions, gave a product which failed to crystallize and which was directly submitted to hydrogen-

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(2) Issued as N.R.C. No. 4918.

(3) National Research Council Postdoctorate Fellow, 1955-1957.

(4) W. R. Meagher and W. Z. Hassid, THIS JOURNAL, **68**, 2135 (1946).

(5) E. W. Putman and W. Z. Hassid, *ibid.*, **79**, 5057 (1957).

(6) L. F. Leloir, "Sugar Phosphates" in L. Zechmeister, "Progress in the Chemistry of Organic Natural Products," Vol. 8, Springer Verlag, Vienna, 1951, p. 50.

(7) A. B. Foster and W. G. Overend, *Quart Revs.*, **11**, 61 (1957).

(8) R. S. Wright and H. G. Khorana, THIS JOURNAL, **78**, 811 (1956).

(9) G. M. Tener, R. S. Wright and H. G. Khorana, *ibid.*, **79**, 441 (1957).

(10) These abbreviated terms are used throughout this paper to denote the steric relationship between the bulkier substituents at the corresponding members of the sugar pyranose ring.

(11) C. F. Cori, S. P. Colowick and G. T. Cori, *J. Biol. Chem.*, **121**, 465 (1937); S. P. Colowick, *ibid.*, **124**, 557 (1938).

(12) T. Posternak, *ibid.*, **180**, 1269 (1949).

(13) T. Posternak, THIS JOURNAL, **72**, 4824 (1950).

(14) T. Posternak and J. P. Rosselet, *Helv. Chim. Acta*, **36**, 1614 (1953).

(15) F. J. Reithel, THIS JOURNAL, **67**, 1056 (1945).

(16) M. L. Wolfrom, C. S. Smith, D. E. Pletcher and A. E. Brown, *ibid.*, **64**, 23 (1942).

(17) N. J. Antia and R. W. Watson, *Chemistry & Industry*, 1143 (1956).

(18) N. J. Antia and R. W. Watson, *ibid.*, 600 (1957).

olysis with a palladium–charcoal catalyst, followed by an alkaline hydrolysis, to remove successively the protecting benzyl and acetyl groups. The xylose 1-phosphate, isolated as the barium salt in over-all yields of 65–75% of theory, proved to be a mixture of anomers which was fractionated from aqueous solution through the crystalline strychnine salts. The more soluble fraction A ($[\alpha]^{25}D$ +20.1°) was shown to be the anhydrous monostrychnine salt of α-D-xylopyranose 1-phosphate by reconversion to the barium salt found identical with that obtained by Meagher and Hassid.[4] This was further confirmed by preparation of the same strychnine salt from a sample of α-D-xylopyranose 1-phosphate, prepared by the procedure of Meagher and Hassid,[4] an attempted fractionation of which showed no contamination with the β-anomer. The less soluble strychnine salt fraction B ($[\alpha]^{25}D$ −30°) analyzed for the dihydrate of the distrychnine salt of D-xylose 1-phosphate and gave a *levorotatory* barium salt. It was concluded from the mode of synthesis and the optical rotation values that the salts of series B must belong to β-D-xylopyranose 1-phosphate. A quantitative separation of the mixture of anomers formed was not possible and the proportion of the anomers present in the mixture was estimated from the known $[\alpha]D$ values to be approximately 40% α, 60% β.

During one experimental run with silver dibenzyl phosphate, the phosphorylation product was inadvertently submitted to a prolonged hydrogenolysis and then worked up as usual. This procedure dephosphorylated the β-anomer and only α-D-xylopyranose 1-phosphate was isolated.

In investigating the action of silver diphenyl phosphate on acetobromoxylose, the phosphorylation reaction was carried out at room temperature and the product worked up as before, hydrogenolysis being effected with Adams catalyst. Without recourse to any fractionation procedure, the sugar phosphate, isolated in over-all yields of 32–35% of theory, was shown to be exclusively α-D-xylose 1-phosphate. It thus appeared that the phosphorylation reaction gave exclusively the C_1C_2-*cis* sugar 1-phosphate, a result found to be in good agreement with those of Posternak.[13] Although this reaction never gave any evidence of the formation of the β-anomer, there is some uncertainty on the absolute stereospecificity of this reaction, imposed by limitations of the experimental procedure used. For the hydrogenolysis reaction to be complete the minimum period required was three times that normally used for a Pd/C catalyst and the inorganic phosphate formed in the over-all reaction sequence amounted to 6–7 times that obtained in the silver dibenzyl phosphate reactions. In the light of a previous experience with silver dibenzyl phosphate, this inorganic phosphate may well have arisen from the prolonged hydrogenolysis[19] of a labile β-D-xylose 1-(diphenyl phosphate) intermediate. On the other hand, diphenyl phosphate esters would be expected to hydrolyze more rapidly than those of dibenzylphosphoric acid[20] and it is possible that an α-D-xylose 1-(diphenyl phosphate) intermediate might itself suffer a partial breakdown under hydrogenolysis conditions that an α-D-xylose 1-(dibenzyl phosphate) may survive better. In the absence of any experimental evidence of the formation of the β-anomer, this latter explanation accounts satisfactorily for the observed facts, and leads us to favor the view that the phosphorylation reaction is almost exclusively stereospecific.

In one experimental run with silver diphenyl phosphate, when the phosphorylation was effected in refluxing benzene, attempts to crystallize the intermediate tri-*O*-acetylxylose 1-(diphenyl phosphate) resulted in the isolation of a phosphorus-free compound, the structure of which is shown in an accompanying publication[21] to be 2,3,4-tri-*O*-acetyl-α-D-xylopyranose.

The infrared absorption spectra of the barium salts of the two anomers of D-xylose 1-phosphate showed three broad ill-defined bands at *ca.* 1100–1125, 1630–1650 and 3280–3350 $cm.^{-1}$, but the resolution in the 800–1050 $cm.^{-1}$ region was fair enough to serve the identification of each anomer. The most striking difference between the two anomers was noted at 935 $cm.^{-1}$. Whereas the α-anomer showed a markedly strong peak, the β-anomer gave only a weak inflection at this point in the curve of the recorded spectrum.

The strychnine salts of the two anomers also gave characteristically different infrared spectra. The crystalline dipotassium salt of the α-anomer showed a well-defined spectrum, but a comparison with the β-anomer was not possible as this failed to give a crystalline potassium salt.

Discussion of Results

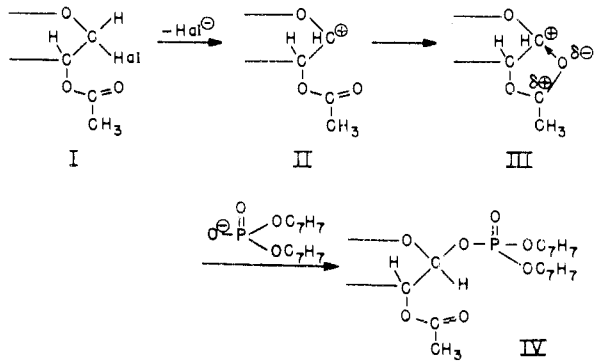
Silver dibenzyl phosphate had been shown by previous workers to react with tetra-*O*-acetyl-α-D-hexopyranosyl halides (C_1C_2-*cis* or *trans*) to form almost entirely the corresponding C_1C_2-*trans*-hexose 1-phosphates. That a strong C_2-neighboring-group effect controlled the steric course of these phosphorylations was evident from the nature of the products obtained. When the original halogenoacylglycoside has C_1C_2-*trans*, as in the mannose series, this effect may involve neighboring-group participation of the C_2-acetoxy group in dissociation of the C_1–halogen bond. Lemieux[22] has discussed the implications of these participation effects in the replacement reactions of polyacylglycosyl halides. In the reaction of a C_1C_2-*cis*-tetra-*O*-acetylhexosyl halide (I), as in the glucose–galactose series, such a participation is not possible and yet the manifestation of a strong C_2-neighboring-group effect suggests a reaction mechanism involving a carbonium ion (II), which may be stabilized through III to enforce substitution at C_1 with inversion (IV).

(19) Sugar monophosphates are known to be stronger acids than free phosphoric acid (see W. D. Kumler and J. J. Eiler, THIS JOURNAL, **65**, 2355 (1943)) and the acidic *p*H of the tri-*O*-acetylxylose 1-phosphate formed in the initial stages of the hydrogenolysis may bring about hydrolysis of the acetyl sugar dibenzyl or diphenyl phosphate intermediate to give rise to dibenzyl- or diphenylphosphoric acid, subsequently hydrogenolyzed to inorganic phosphate.

(20) The diphenyl phosphate ion would be stabilized by resonance unavailable to the dibenzyl phosphate ion and this would contribute a driving force to the hydrolytic reaction in favor of the formation of the former ion (*cf.* N. S. Corby, G. W. Kenner and A. R. Todd, *J. Chem. Soc.*, 1234 (1952)).

(21) N. J. Antia, THIS JOURNAL, **80**, 6138 (1958).

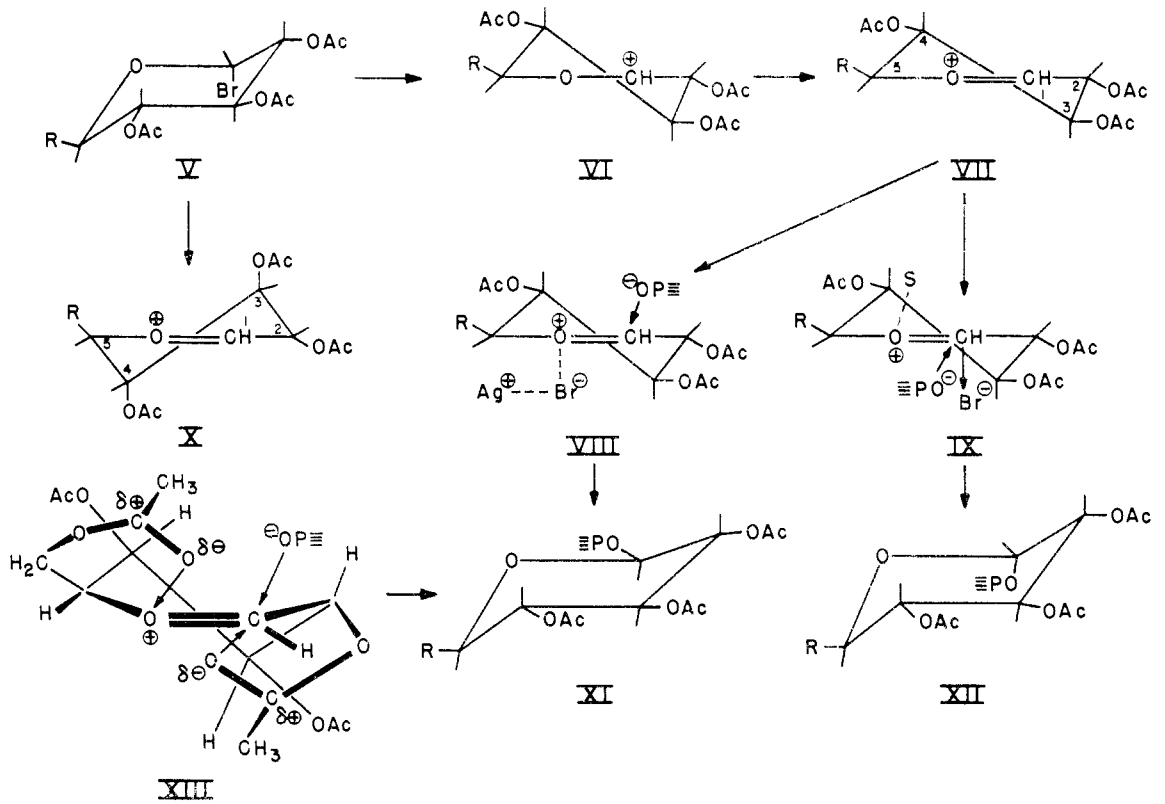
(22) R. U. Lemieux, *Adv. Carbohydrate Chem.*, **9**, 1 (1954).



The C_2-neighboring-group effect may thus involve a "shielding" of one side of the ring structure without participation in dissociation of the C_1–halogen bond.

That a mixture of *ca.* 60% C_1C_2-*trans* and 40% C_1C_2-*cis* products is formed from the C_1C_2-*cis*-acetobromoxylose clearly indicates that in this case the C_2-neighboring-group effect must operate in conjunction with another, probably opposing, effect. The pentose derivative differs from the hexoses in the lack of a C_5-acyloxymethyl substituent ing-group effect. Evidence obtained by Newth and Phillips[23] from comparative kinetic studies of the methanolysis rates of α-1-bromopolyacetyl derivatives of D-glucose, -galactose, -mannose and -xylose also points to a marked steric effect from the C_5 substituent on the reaction at C_1.

Huber[24] has put forward a mechanism of substitution at C_1 to explain a wide variety of reactions shown by anomeric sugar-pyranose forms. According to this mechanism, the acetobromoglucose or -xylose, in its preferred C1-chair conformation V (with maximum number of bulky substituents in equatorial position) would be expected to give the oxonium ion[25] VII (half-chair conformation analogous to that postulated by Barton, *et al.*,[26] for cyclohexenes), envisioned as forming through the carbonium ion VI. The oxonium ion VII may be stabilized by the formation of an ion-pair with the halogen ion moving from C_1 to the pyranose O atom on the same side of the ring structure to give VIII or the stabilization may be brought about by solvent action of the pyranose oxygen *trans* to the departing C_1-substituent of the incipient double bond, as shown at IX.



S = solvent, Ac = $COCH_3$, R = H or $-CH_2OAc$, OP ≡ denotes dibenzyl phosphate.

and it would appear that this structural difference is responsible for this second effect. If the effect of the C_5-substituent involved a "shielding" of ring structure or "neighboring-group participation" at C_1, then the tetra-*O*-acylglucosyl or galactosyl bromide would be expected to lead, at least in part, to the formation of the α1-phosphate with retention of configuration at C_1, which is not the case. The C_5 substituent effect appears then to be a structural influence different in nature from the C_2-neighbor-

trans-Addition of the incoming phosphate group to the double bond should then lead from the oxonium ion VIII to the β1-phosphate XI and from IX to the α1-phosphate XII. Having established pre-

(23) F. H. Newth and G. O. Phillips, *J. Chem. Soc.*, 2904 (1953).

(24) G. Huber, *Helv. Chim. Acta*, **38**, 1224 (1955).

(25) The alternative structure X for the oxonium ion would not be favored by the rules of conformational analysis, for it would have the bulkier substituents axial at C_3 and C_4.

(26) D. H. R. Barton, R. C. Cookson, W. Klyne and C. W. Shoppee, *Chemistry & Industry*, 21 (1954).

viously that the steric effect from the C_5-substituent did not act by a "shielding" mechanism at C_1, it is conceivable that this effect may arise from electrostatic interaction between the carbonyl oxygen of the C_5-substituent and the pyranose ring oxygen in an oxonium ion of type VII. The manner in which the C_2- and C_5-group effects may operate is shown at XIII. If the departing halide ion formed an ion-pair with the pyranose O atom of the oxonium ion (shown at VIII), then such ion-pair formation would be expected to be favored in xylose (no neutralization or diminution of charge on pyranose O atom from C_5-substituent) relative to glucose with the result that more rigid *trans*-addition at C_1 should obtain, favoring β1-phosphate formation, which is not the case. Considering the alternative of stabilization of the oxonium ion by solvent action, shown in IX, such a mechanism would be expected to operate freely in xylose (with no interference from the C_5-substituent) and to favor the reaction sequence (VII → IX → XII) leading to the α1-phosphate, while at the same time the C_2-neighboring group effect, operating as shown at XIII, would favor the direction XIII → XI leading to the β1-phosphate. In the case of glucose, however, the C_5-substituent would be expected to nullify the charge on the pyranose oxygen, as shown at XIII, and thereby to virtually eliminate solvent action, with the result that the reaction sequence XIII → XI (leading to the β1-phosphate) would be exclusively favored. The stabilization of the oxonium ion VII by solvent action or by electrostatic action from the C_5-substituent, leading to steric control of the incoming substituent, would thus appear to give a satisfactory explanation of the difference observed in the phosphorylation behavior of glucose and xylose.

Experimental

All melting points are uncorrected. The infrared spectra were determined in Nujol, using a Perkin-Elmer double-beam recording spectrophotometer.

(I) **Silver Dibenzyl Phosphate[27] Phosphorylations. (a) Refluxing Benzene, Normal Hydrogenolysis Conditions.**—The acetobromoxylose (1 g.) was dissolved in dry benzene (30 cc.) and powdered silver dibenzyl phosphate (1.5 g.) added. The suspension was agitated mechanically in the dark and the temperature slowly raised over 30 minutes to reflux. The mass was kept gently under reflux for 90 minutes with continuous agitation. On cooling, the separating silver salts were centrifuged off and washed once with benzene. The combined supernatant and washings were evaporated *in vacuo* to dryness and the sirupy residue was taken up in ether (30 cc.) and cooled overnight at 0–5°. Some excess silver dibenzyl phosphate separated which was centrifuged off and washed once with cold ether. The combined supernatant and washings were evaporated *in vacuo* to dryness and the sirupy residue taken up in 98% alcohol (15 cc.). The catalyst for the hydrogenolysis was freshly prepared by reducing $PdCl_2$–charcoal[28] (12% Pd) (1 g.) with H_2 in methanol and washing to neutral *p*H. To this catalyst, suspended in alcohol (35 cc.), was added the alcohol solution of the phosphorylation product and the hydrogenolysis carried out. The H_2 absorption was complete in *ca.* 20 minutes, when the catalyst was centrifuged off and washed with alcohol. The combined supernatant and washings were evaporated *in vacuo* to a small volume (*ca.* 5 cc.), water (50 cc.) was added and the *p*H adjusted to 11–11.5 with aqueous NaOH and maintained there for 2 hours at room temperature. The *p*H was next lowered to 8–8.5 with aqueous HCl and a solution of barium acetate (1.25 g.) in water (25 cc.) added. The mass was kept at 0–5° for *ca.* 1 hour. The separating inorganic phosphate (69 mg.) was centrifuged off and washed once with water (25 cc.). To the combined supernatant and washings was added 3 times the volume of alcohol and the mass cooled overnight at 0–5°. The separating barium salt of xylose 1-phosphate was centrifuged off and washed successively with (a) 60% alcohol (200 cc.), (b) 80% alcohol (100 cc.), (c) 98% alcohol (200 cc.) and (d) ether (100 cc.). The dried salt (0.863 g.) showed an $[\alpha]^{25}D$ +23.65° (*c* 1.48, 5% aqueous acetic acid) and the infrared spectrum corresponded to one for a mixture of α- and β-anomers identical with that obtained in procedure Ic below.

(b) **Refluxing Benzene, Prolonged Hydrogenolysis Conditions.**—The bromo compound (5 g.) was treated with silver dibenzyl phosphate (8.5 g.) and the silver salts were separated as described in procedure Ia above to give a sirupy product (7.5 g.). A part of this syrup (4 g.) was hydrogenolyzed with Pd/C in alcohol solution as before, the period of hydrogenolysis being prolonged to *ca.* 75 minutes. The hydrogenolyzed product was worked up in the usual manner to yield inorganic barium phosphate (1.165 g.) and the barium salt of α-D-xylose 1-phosphate (0.634 g.). Treatment of this barium salt in aqueous solution with the stoichiometric amount of K_2SO_4 gave a crystalline dipotassium salt, which showed $[\alpha]^{25}D$ +75.5° (*c* 2, water). The optical rotation, infrared and X-ray diffraction data were all identical with those from the potassium salt prepared by the procedure of Meagher and Hassid.[4]

(c) **Room Temperature Phosphorylation, Normal Hydrogenolysis Conditions.**—The suspension of silver dibenzyl phosphate (1.5 g.) in a solution of acetobromoxylose (1 g.) in dry benzene (30 cc.) was mechanically shaken with glass beads at room temperature in the dark for 2 hours and the product worked up as described in procedure Ia above to yield inorganic barium phosphate (0.053 g.) and the barium salt of xylose 1-phosphate (0.75–0.9 g.). After purification by reprecipitation from alcohol–water (3:1), the sugar phosphate barium salt showed $[\alpha]^{25}D$ +19.62° (*c* 1.47, 5% aqueous acetic acid). *Anal.* Calcd. for $C_5H_9O_8PBa \cdot 1.5\ H_2O$: P, 7.89. Found: total P, 7.72; acid-labile P,[29] 7.61.

To a solution of this barium salt (2.689 g.) in water (400 cc.) was added strychnine sulfate[30] (6.306 g.) and the mass mechanically shaken with glass beads for 16.5 hours at room temperature. After separating the barium sulfate formed, the supernatant was evaporated *in vacuo* to saturation and the mass cooled overnight at 0–5°. The first crop of crystals was filtered by suction and the procedure of concentration by evaporation to crystallization point was repeated with the mother liquors. In this manner 5 crops of crystals were taken, with $[\alpha]^{25}D$ values[31] ranging from −21.9 to −6.56° (*c* 0.6 water). The fractions (1.5 g.) with $[\alpha]^{25}D$ values equal to or more negative than −17° were combined and repeatedly recrystallized from water to constant rotation. The strychnine salt B (1.042 g.) so obtained showed $[\alpha]^{25}D$ −30.00° (*c* 0.58 water), m.p. 235° dec. (shrinks at 196°). *Anal.* Calcd. for the dehydrated salt, $C_{47}H_{55}O_{12}N_4P$: C, 62.81; H, 6.13; N, 6.24; P, 3.45; pentose, 16.7. Found: C, 62.75; H, 6.12; N, 6.27; P, 3.39; pentose,[32] 17.62. Calcd. for the hydrate, $C_{47}H_{55}O_{12}N_4P \cdot 2H_2O$: drying weight loss, 3.85. Found: drying[33] weight loss, 3.93.

The mother liquors from the 5 crystal crops mentioned above were evaporated *in vacuo* to near dryness, the residue taken up in the minimum quantity of water, and acetone slowly added to incipient turbidity. On cooling to 0–5°,

(27) Prepared by the procedure of F. Lynen, *Ber.*, **73**, 357 (1940).

(28) Prepared by the procedure of R. Mozingo, *Org. Syntheses*, **26**, 78 (1946).

(29) All acid-labile P determinations were made by heating the sample with *N* HCl at 100° for 7 minutes and estimating colorimetrically by the procedure of E. J. King (*Biochem. J.*, **26**, 292 (1932)).

(30) The commercial product with a molecular composition of $(C_{21}H_{22}O_2N_2)_2 \cdot H_2SO_4 \cdot 5H_2O$ was used.

(31) All [α]D determinations for the strychnine salts were made after drying for 2 hours over P_2O_5 at 56° (0.1–0.3 mm.).

(32) All pentose determinations were made by heating the sample at 100° for 20 minutes with the orcinol reagent of E. Volkin and W. E. Cohn (see D. Glick, "Methods of Biochemical Analysis," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1954, p. 298, and estimating colorimetrically by the procedure described by these authors.

(33) For 2 hours over P_2O_5 at 56° (0.1–0.3 mm).

crystals (0.855 g.) were obtained, $[\alpha]^{25}D$ +11.59° (*c* 1.61 water). Recrystallization of this material from aqueous acetone–alcohol gave the strychnine salt A (0.33 g.), $[\alpha]^{25}D$ +20.08° (*c* 0.6 water), m.p. 217–220° dec. *Anal.* Calcd. for $C_{26}H_{33}O_{10}N_2P$: C, 55.33; H, 5.85; N, 4.97; P, 5.50. Found: C, 55.23; H, 5.71; N, 4.70; P, 5.51. Drying of the salt showed absence of solvent of crystallization.

For reconversion to the barium salt, the strychnine salt B (1.042 g.) in aqueous solution (250 cc.) was treated with aqueous NaOH to raise the *p*H from 7 to 10 and the separating strychnine base extracted 5 times with chloroform (100 cc.) precooled to 0°. The clear aqueous solution of *p*H 8–8.5 was concentrated *in vacuo* to *ca.* 70 cc., treated with an aqueous solution (30 cc.) of barium acetate (0.625 g.) and, after separating the inorganic phosphate (27 mg.), the barium salt of β-D-xylose 1-phosphate (0.325 g.) was isolated in the usual manner. This salt, after purification by reprecipitation from alcohol–water (3:1, showed $[\alpha]^{25}D$ −13.30° (*c* 1.5, 5% aqueous acetic acid). *Anal.* Calcd. for the dehydrated salt $C_5H_9O_8PBa$: C, 16.43; H, 2.46. Found: C, 16.51; H, 2.54. Calcd. for the hydrate $C_5H_9O_8PBa \cdot 1.5H_2O$: P, 7.89; drying weight loss, 6.88. Found: total P, 7.64; acid-labile P, 7.45; drying weight loss, 6.33. An aqueous solution of this barium salt, treated with the stoichiometric amount of K_2SO_4, failed to give a crystalline potassium salt.

The strychnine salt A (0.256 g.) was similarly converted to the barium salt (0.142 g.) of α-D-xylose 1-phosphate. This barium salt showed an $[\alpha]^{25}D$ +70.88° (*c* 1.425, 5% aqueous acetic acid) and an infrared spectrum identical with that of the corresponding salt obtained by procedure Ib above.

(II) Silver Diphenyl Phosphate[34] Phosphorylations. (a) Room Temperature Reaction.—A benzene solution (70 cc.) of acetobromoxylose (1 g.) was treated with silver diphenyl phosphate (1.58 g.) at room temperature in the dark for 2 hours and the silver salts were separated in the usual manner. The sirupy product was hydrogenolyzed with Adams catalyst (0.2 g.) in alcohol solution (100 cc.). Gas absorption was complete in *ca.* 1 hour. The catalyst was filtered off and washed with alcohol. The combined filtrate and washings were concentrated *in vacuo*, the product deacetylated and worked up in the usual manner to give inorganic phosphate (0.398 g.) and the barium salt (0.396 g.) of α-D-xylose 1-phosphate (infrared spectral identity established). This salt, after purification by reprecipitation, showed $[\alpha]^{25}D$ +67.26° (*c* 1.56, 5% aqueous acetic acid). *Anal.* Calcd. for $C_5H_9O_8PBa \cdot 1.5H_2O$: P, 7.89. Found: total P, 7.71; acid-labile P, 7.71. The barium salt readily gave a crystalline dipotassium salt of α-D-xylose 1-phosphate (infrared spectral identity established) with $[\alpha]^{25}D$ +77.5° (*c* 1.6, water).

(b) Reaction in Refluxing Benzene.—The bromo compound (5 g.) was treated with silver diphenyl phosphate (7.91 g.) in refluxing benzene solution (50 cc.) as in procedure Ia and the silver salts separated in the usual manner. After precipitating off the excess phosphorylating agent with ether as before, the sirupy product gave a crystalline compound (0.6 g.) from CCl_4–ether. Recrystallized from ether–pentane, this compound showed a m.p. 129–131°, the absence of phosphorus and a pentose content of 50.9%. An infrared spectrum established the identity of this compound with 2,3,4-tri-*O*-acetyl-α-D-xylopyranose obtained by another procedure.[24] The rest of the phosphorylation product was not worked up any further, as it was found to have suffered extensive decomposition during the attempts made to crystallize the intermediate tri-*O*-acetyl-D-xylose 1-(diphenylphosphate).

(III) Trisilver Phosphate[35] Phosphorylation.—The barium salt of α-D-xylose 1-phosphate was prepared by interaction of acetobromoxylose with trisilver phosphate in the manner of Meagher and Hassid.[4] The entire quantity (0.393 g.) was converted to the strychnine salt and fractionally crystallized from aqueous dioxane. The first four crops of crystals with nearly constant $[\alpha]D$ values were combined (0.3 g.) and recrystallized from aqueous dioxane–acetone to give the strychnine salt (0.26 g.) of α-D-xylose 1-phosphate, $[\alpha]^{25}D$ +20° (*c* 0.475 water), m.p. 217–219° dec. *Anal.* Calcd. for $C_{26}H_{33}O_{10}N_2P$: C, 55.33; H, 5.85; N, 4.97; P, 5.50. Found: C, 55.45; H, 5.87; N, 5.00; P, 5.77. An infrared spectrum was identical with that of strychnine salt A obtained by procedure Ic above. No evidence of the formation of strychnine salt B was obtained from the attempted crystallization of the mother liquors from the four crystal crops taken above.

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(34) Prepared by the procedure of T. Posternak (ref. 12).

(35) Prepared by the procedure of C. F. Cori, S. P. Colowick and G. T. Cori (ref. 11).

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[CONTRIBUTION FROM THE DIVISION OF APPLIED BIOLOGY, NATIONAL RESEARCH LABORATORIES]

The Isomeric Xylopyranose Triacetates Produced by Solvolysis of 2,3,4-Tri-*O*-acetyl-α-D-xylopyranosyl Bromide[1]

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The action of aqueous acetone, with or without silver carbonate, on 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide gave rise to a mixture of three isomeric tri-*O*-acetyl-D-xylopyranoses. The ready mutarotation of isomers B and C showed that they must be the α- and β-anomers, respectively, of the pentose 2,3,4-triacetate. Isomer A failed to mutarotate in chloroform and was converted by the action of aqueous pyridine to isomer B, suggesting a $C_1 \rightarrow C_2$ acetyl migration. Quantitative infrared spectrometric measurements showed the presence of three carbonyl groups in isomer A, ruling out a possible C_1C_2-orthoacid structure and assigning the structure of 1,3,4-tri-*O*-acetyl-α-D-xylopyranose to this isomer. The mechanism of the formation and interconversion of the isomers is discussed. The $C_2 \rightarrow C_1$ acetyl migration, shown by 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide, appears to occur without C_2-neighboring-group participation in dissociation of the C_1–halogen bond.

In a previous paper,[3] it was reported that attempts to crystallize the product of a phosphorylation reaction of 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide with silver diphenyl phosphate led to the isolation of a phosphorus-free triacetylxylose. Wright and Khorana,[4] in attempting to crystallize the product of a phosphorylation reaction of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl bromide had similarly obtained a tribenzoylribose, which did not contain phosphorus and was shown by Ness and Fletcher,[5,6] to be 1,3,5-tri-*O*-benzoyl-α-D-ribofura-

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