178. *Experiments on the Synthesis of Purine Nucleosides. Part IX. A Synthesis of* 9-d-*Xylopyranosidoadenine.*

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Condensation of 4 : 6-diaminopyrimidine with *d*-xylose appears to give two glycosidic products. The first, obtained in low yield, is a crystalline 6-*amino*-4-d-*xylosidaminopyrimidine*, and the second and major product is an intractable syrup. Coupled with diazotised 2 : 5-dichloroaniline, these products give two isomeric azo-xylosides, each giving a distinct crystalline triacetyl derivative. Reductive fission of the azo-linkage in each of these isomeric triacetates gives one and the same 5 : 6-*diamino*-4-*triacetyl*-d-*xylosidaminopyrimidine*. The significance of this remarkable sequence of reactions is discussed.

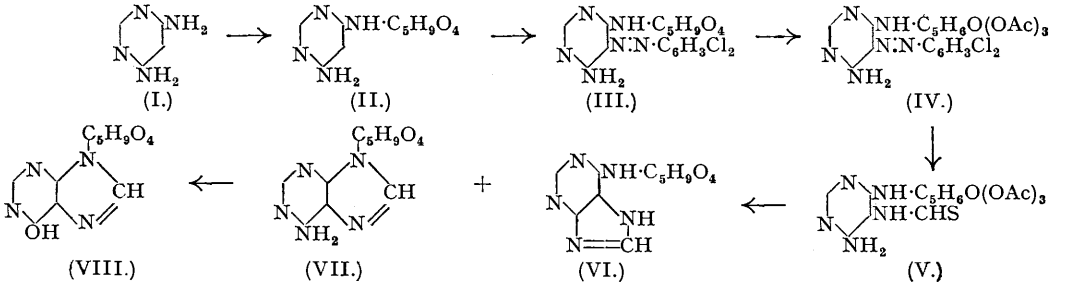
Thioformylation of 5 : 6-diamino-4-triacetyl-*d*-xylosidaminopyrimidine, followed by cyclisation and deacetylation, gives a mixture of 9-d-*xylopyranosidoadenine* and 6-d-*xylosidaminopurine*. The former is readily deaminated to 9-d-*xylopyranosidohypoxanthine* and is shown to be a pyranoside by periodate oxidation.

Following the discovery of a convenient method for the preparation of 4 : 6-diaminopyrimidine (Part IV; Kenner, Lythgoe, Todd, and Topham, J., 1943, 574), it was decided to proceed to the synthesis of 9-*d*-xylosidoadenine, using a route analogous to that described for 9-*d*-xylopyranosido-2-methyladenine (Part VI; Baddiley, Lythgoe, and Todd, this vol., p. 318). In undertaking this synthesis we had two objects in view, first to establish a route to the ribosides of adenine (including adenosine) on the closest analogous case, using the more readily available *d*-xylose as sugar component, and second to extend our range of synthetic purine *d*-xylosides in order to examine a series of these compounds bearing a variety of substituents in the purine nucleus.

Condensation of 4 : 6-diaminopyrimidine (I) with *d*-xylose under conditions similar to those used in the analogous condensation of 4 : 6-diamino-2-methylpyrimidine (Part III; Baddiley, Lythgoe, and Todd, J., 1943, 571) gave in low yield (*ca.* 10%) a crystalline glycoside which we designate 6-*amino*-4-d-*xylosidaminopyrimidine-I* (II), together with a considerably larger amount of resinous glycosidic material which could not

be crystallised. Despite an extended series of experiments we were unable to determine reaction conditions leading with certainty to an increased, or even constant, yield of crystalline material. A rather similar case had already been encountered in the preparation of 6-amino-4-*d*-xylosidamino-2-methylthiopyrimidine. There it was known that the resinous fraction of the crude xyloside contained considerable quantities of crystalline material (Part III, *loc. cit.*) as well as an isomeric xyloside (unpublished observations; cf. Baddiley, Kenner, Lythgoe, McNeil, Todd, and Topham, *Chem. Ind.*, 1943, **62**, 433). The possibility that the same might hold for the resinous glycosidic product from 4 : 6-diaminopyrimidine had therefore to be borne in mind.

The crystalline 6-amino-4-*d*-xylosidaminopyrimidine-I coupled readily with diazotised 2 : 5-dichloroaniline, giving 6-*amino*-4-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-I* (III), m. p. 166°. When the same coupling procedure was applied to the resinous material remaining after the crystalline xyloside had been separated from the xylosidisation mixture, a product was obtained which, after several recrystallisations, gave an isomeric 6-*amino*-4-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-II* (III), m. p. 250°. It thus seemed probable that the condensation of 4 : 6-diaminopyrimidine with *d*-xylose had given rise to two isomeric *d*-xylosides, and that in carrying out the projected nucleoside synthesis two series of isomeric intermediates and final products might be expected. For convenience we describe them for the present as Series I and Series II, the individual members being distinguished by adding to their systematic names the suffix I or II. The synthetic route to the purine glycosides employed in both series was similar to that used in Part VI (*loc. cit.*). Acetylation of the azo-compounds (III) before reduction was adopted, since preliminary experiments in Series I showed that reductive fission of (III), followed by thioformylation, gave a product difficult to isolate in a pure state. It was found by experience that the only satisfactory way to separate Series I from Series II was by direct crystallisation of the 6-amino-4-*d*-xylosidaminopyrimidine-I from the crude condensation product of *d*-xylose and 4 : 6-diaminopyrimidine; the resinous residue then consisted mainly of the Series II isomer. In the hope of simplifying the separation several experiments were carried out in which the crude xylosidisation product was coupled with diazotised 2 : 5-dichloroaniline, and the product acetylated and submitted to chromatographic analysis; possibly owing to the preponderance of the Series II compound in the mixture, no ready isolation of the Series I isomer could be effected in this way.



Because of the greater availability of the starting material the nucleoside synthesis was first carried out from 6-amino-4-*d*-xylosidamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine-II. Treatment with acetic anhydride in pyridine solution yielded 6-*amino*-4-*triacetyl*-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-II* (IV), which was reduced smoothly with Raney nickel and hydrogen to 5 : 6-*diamino*-4-*triacetyl*-d-*xylosidamino-pyrimidine*. (The Series II suffix is omitted from this intermediate and from the products obtained from it for reasons which will be made clear later.)

6-*Amino*-4-*triacetyl*-d-*xylosidamino*-5-*thioformamidopyrimidine* (V), prepared from this diamine by heating with dithioformic acid, was cyclised by heating in pyridine solution. The mixture of acetylated purine xylosides thus obtained did not crystallise readily and was accordingly deacetylated; from the product, two crystalline *d*-xylosides were isolated. One of these was evidently 9-d-*xylosidoadenine* (VII), since it could be hydrolysed to adenine and *d*-xylose, was insoluble in alkali, and was readily deaminated to 9-d-*xylosidohypoxanthine* (VIII). The other also yielded adenine and *d*-xylose on hydrolysis, but was readily soluble in alkali. From this and by analogy with the analogous 2-methyladenine xylosides (Part VI, *loc. cit.*) we regard this substance as 6-d-*xylosidaminopurine* (VI).

The size of the lactol ring in (VII) was determined by periodate titration by the method described in Part VIII (Lythgoe and Todd, this vol., p. 592). The xyloside reacted with 2 mols. of the reagent, liberating 1 mol. of formic acid; it is therefore more accurately described as 9-d-*xylopyranosidoadenine* and it would follow that (VIII) and presumably (V) also are *d*-xylopyranosides. 9-*d*-Xylopyranosidoadenine is very similar in ease of hydrolysis and optical rotation to 9-*d*-xylopyranosido-2-methyladenine (Part VI, *loc. cit.*), suggesting that both have the same stereochemical configuration; its absorption spectrum is, as anticipated, closely similar to that of adenosine.

The same synthetic scheme was now applied to the less accessible 6-amino-4-*d*-xylosidamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine-I in the expectation that a second pair of adenine xylosides would be obtained isomeric with those above described. 6-*Amino*-4-*triacetyl*-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-I* was readily obtained and the series of reactions used in the case of the Series II compound was applied. In this case the hydrogenation product was in the first experiment thioformylated without isolation, and owing

to the small amount available the thioformamido-compound (V) was not purified before cyclisation. Only one crystalline purine xyloside was isolated, probably owing to the use of impure thioformamido-compound; we had already observed in work on Series II that unless the pure thioformamido-compound were used crystallisation of the 6-*d*-xylosidaminopurine was barely possible. The crystalline product, although of slightly higher m. p. (298°) than the 9-*d*-xylosidoadenine (m. p. 292°) obtained from the Series II azo-glycoside, was otherwise identical in properties and a mixed m. p. showed no definite depression. Further evidence of identity was obtained by periodate titration, which showed the xyloside to have a pyranoside structure and to give a scission product with this reagent whose optical rotation was identical with that of the scission product of the Series II compound. Had the xylosides obtained in the two series been respectively α- and β-glycosides, the scission products would have been enantiomorphous (cf. Part VIII, *loc. cit.*). Finally, specimens of the two products were submitted to *X*-ray examination by Dr. I. G. Edmunds of the Manchester College of Technology; to him we are deeply indebted. Careful comparison of their *X*-ray powder photographs, which showed a large number of reflections, confirmed that the two materials were identical.

The identity of the 9-*d*-xylosidoadenine from the two isomeric azo-glycosides being established, the reduction of 6-amino-4-triacetyl-*d*-xylosidamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine-I with Raney nickel and hydrogen was repeated and this time the hydrogenation product was isolated before thioformylation. It proved to be identical (mixed m. p. and, within the limits of experimental error, optical rotation) with 5 : 6-diamino-4-triacetyl-*d*-xylosidaminopyrimidine already obtained by similar hydrogenation of 6-amino-4-triacetyl-*d*-xylosidamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine-II. Evidently the two series become one during the hydrogenation process.

What, then, is the nature of the isomerism shown by the azoglycosides of Series I and Series II? On the evidence so far presented and in view of our failure to isolate two crystalline homogeneous xylosides from the reaction between 4 : 6-diaminopyrimidine and *d*-xylose, it might be suggested that the two azo-glycosides are simply *cis*- and *trans*-azo-compounds. This seems most improbable, since coupling conditions are the same in their formation and since acid hydrolysis of both the Series I and the Series II compound yields one and the same 4 : 6-*diamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine*, and we conclude that isomers belonging to the two series are produced in the original xylosidisation. Although it is known that in some cases pyrimidine rings can be opened to give isomeric open-chain compounds [*e.g.*, acetylation of 4-amino-5-cyanopyrimidine (Part II; J., 1943, 386)], the subsequent course of reactions in the two series seems to preclude this being the reason for the formation of two xylosides. The conclusion seems inevitable that the isomerism concerns the sugar residue, *i.e.*, that they are α- and β-xylosides or furanoside and pyranoside. Evidence to decide between these alternatives should be obtainable by periodate oxidation, assuming that this method of attack can be extended to the case of xylosidaminopyrimidines (cf. Part VIII, *loc. cit.*). Experiments to this end are in progress and will shortly be reported. Meanwhile it may be observed that the procedure used for condensing 4 : 6-diaminopyrimidine with *d*-xylose is strictly analogous to the classical method of Fischer for the preparation of *O*-glycosides, a method which is known to yield a mixture of α- and β-glycosides. Whether the difference between our isomeric xylosides be of the α–β or furanose–pyranose type, it is clear that rearrangement of one isomer must occur during hydrogenation in ethyl acetate solution with a Raney nickel catalyst. As far as we are aware, no rearrangement of either type under such conditions has so far been described in the literature, and, if established, the observation might lead to developments of some significance in the chemistry of *N*-glycosides in general.

A feature of interest in the synthesis of the xylosides of adenine and 2-methyladenine (Part VI, *loc. cit.*) is the simultaneous production of acetylated 9-xylosido- and 6-xylosidamino-purines, cyclisation of the appropriate thioformamido-compounds proceeding in two directions. This was unexpected, since we had assumed by analogy with the behaviour of 6-amino-4-methylamino-5-thioformamido-2-methylthiopyrimidine (Part I; Baddiley, Lythgoe, McNeil, and Todd, J., 1943, 383) that the cyclisation would lead exclusively to the 9-substituted purine. It is impossible on present evidence to give a precise explanation of this apparent anomaly. It might be argued that substitution of a sugar residue for the 4-amino-group in the pyrimidine is not strictly analogous to substitution of an alkyl group or that steric hindrance makes ring closure in the desired direction more difficult. Another possibility is that production of the 6- and the 9-substituted purines is bound up with the fact that in the cases examined so far the sugar residue has been acetylated. In such cases one cannot exclude the possibility of chelation involving the glycosidic NH group and the carbonyl of the acetyl residue at C_2 in the sugar chain. The effect of such chelation would be indirectly to increase the electron density at the nitrogen atom in the imino-group at C_6, so enabling that group to take part in the cyclisation process.

Experimental.

The activated aluminium oxide used in these experiments was prepared by heating "alumina hydrate" (British Aluminium Co. Ltd.) from room temperature to 360° during 5 hours.

Condensation of 4 : 6-*Diaminopyrimidine with* d-*Xylose*.—To 4 : 6-diaminopyrimidine (40 g.) and *d*-xylose (20 g.) in absolute alcohol (1 l.), saturated alcoholic hydrogen chloride (8 c.c.) was added, and the mixture refluxed for a total of 22 hours spread over 3 successive days. Dry benzene was added at intervals during the operation, and water removed azeotropically through a 50 cm. Fenske column with a total reflux variable take-off head. The resulting solution was passed through a column of activated alumina (1600 g.), and the column was washed with absolute alcohol (8 l.) until no more 4 : 6-diaminopyrimidine came through. Elution of the column was effected by washing with water (9 l.) until the washings gave only a faint Molisch reaction, and the eluate was evaporated under reduced pressure at 30° to small

bulk (*ca.* 100 c.c.) and set aside overnight. 6-*Amino*-4-d-*xylosidaminopyrimidine-I* (*ca.* 3·5 g.) separated in colourless prisms; recrystallised from water, it had m. p. 207° (decomp.) and $[\alpha]_D^{19°}$ + 154° (*c*, 0·12 in water) (Found in material dried at 100°: C, 44·7; H, 6·0; N, 23·5. $C_9H_{14}O_4N_4$ requires C, 44·6; H, 5·8; N, 23·2%).

Hydrolysis. The xyloside (0·25 g.) was refluxed for 30 mins. with N/10-hydrochloric acid (15 c.c.). The resulting solution was made up to 20 c.c. and divided into 2 equal portions (*a*) and (*b*). (*a*) When saturated aqueous picric acid (10 c.c.) was added, 4 : 6-diaminopyrimidine picrate (0·15 g.) separated; recrystallised from water, it had m. p. 297° (decomp.), undepressed by an authentic specimen. (*b*) A solution of phenylhydrazine in aqueous acetic acid was added, and the mixture heated in a boiling water-bath. After 18 mins. *d*-xylosazone began to separate; it had m. p. 163°, undepressed in admixture with a specimen prepared under precisely similar conditions from authentic *d*-xylose.

The aqueous mother-liquors left after separation of 6-amino-4-*d*-xylosidaminopyrimidine-I gave on further concentration only a brownish resin, which would not crystallise and served as starting material for compounds of Series II.

Series II.

6-*Amino*-4-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-II.*—2 : 5-Dichloroaniline (32·4 g.), dissolved in dilute hydrochloric acid (200 c.c. of concentrated acid + 1 l. of water), was diazotised in the usual way. The diazo-solution, neutralised with excess of sodium bicarbonate, was added to the aqueous mother-liquor remaining after the separation of the crystalline 6-amino-4-*d*-xylosidaminopyrimidine-I (prepared from 40 g. of 4 : 6-diaminopyrimidine as described above). After standing overnight, the yellow solid was collected, washed with water, dried, ground up with ether to remove impurities, and again dried. (Yield, 28 g.) The *azo-glycoside*, recrystallised from pyridine–alcohol, formed orange-yellow plates, m. p. 250° (decomp.). Dried at 100°/0·5 mm., the crystals still contained pyridine (Found in material dried at 140°/0·5 mm.: C, 43·6; H, 4·3; N, 20·3. $C_{15}H_{16}O_4N_6Cl_2$ requires C, 43·4; H, 3·9; N, 20·2%). It showed $[\alpha]^{20°}$ + 11° (*c*, 0·24 in pyridine; Wratten No. 29 light filter).

6-*Amino*-4-*triacetyl*-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-II.*—*Method* 1. The above crude azo-glycoside (28 g.) was kept overnight with acetic anhydride (150 c.c.) in pyridine (500 c.c.). Alcohol (200 c.c.) was added cautiously and after 2 hours the solution was evaporated, and the residue taken up in ethyl acetate and passed through a column (40 cm. × 6 cm.) of activated alumina. When the column was washed with ethyl acetate, the bulk of the material was eluted as a uniform yellow band. The eluate was evaporated, and the residue recrystallised from benzene, giving yellow needles, m. p. 138—139° (Found in material dried at 100°: C, 46·3; H, 4·3; N, 15·5. $C_{21}H_{22}O_7N_6Cl_2$ requires C, 46·6; H, 4·1; N, 15·5%). Yield, 8 g. (11% calculated on original *d*-xylose used) $[\alpha]^{19°}$ — 306° (*c*, 0·37 in chloroform; Wratten No. 29 light filter).

Method 2. 4 : 6-Diaminopyrimidine (2·2 g.; 1 mol.) was condensed with *d*-xylose (3·0 g.; 1 mol.) in the normal manner (see above), refluxing being continued for 60 hours. The resulting alcoholic solution was evaporated in a vacuum, and the residue dissolved in water and coupled with diazotised 2 : 5-dichloroaniline (from 3·5 g. of the amine) in presence of excess of sodium bicarbonate. The precipitate of mixed azo-compounds (3·25 g.) was collected, dried, and acetylated at room temperature with acetic anhydride (15 c.c.) in pyridine (75 c.c.). The crude acetylated material was dissolved in ethyl acetate and passed through a column of activated aluminium oxide (30 × 2·5 cm.). On development with ethyl acetate three distinct bands were visible, an upper dark band containing much tarry material, a middle yellow band of sugar-free azopyrimidine derivative, and a lower yellow band of acetylated azo-glycosides. The lower yellow band was eluted with ethyl acetate, the eluate evaporated, and the residue recrystallised from benzene. 6-Amino-4-triacetyl-*d*-xylosidamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine-II was obtained in yellow needles, m. p. 138—139°, undepressed in admixture with the product obtained by Method 1 above (yield, 0·56 g.; 5·2% calculated on *d*-xylose). A sample, dissolved in chloroform and hydrolysed by addition of methanolic sodium methoxide (1 atom of sodium) and leaving overnight, gave orange-yellow plates of 6-amino-4-*d*-xylosidamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine-II, m. p. and mixed m. p. 249—250° (decomp.).

5 : 6-*Diamino*-4-*triacetyl*-d-*xylosidaminopyrimidine.*—The above acetyl-azo-compound (8 g.) was hydrogenated in ethyl acetate (100 c.c.) at 80°/100 atms. for 7 hours, a Raney nickel catalyst being used. The product which separated on cooling was dissolved in alcohol, and the solution filtered from nickel and evaporated. Trituration with light petroleum, followed by recrystallisation from ethyl acetate–alcohol, gave colourless needles (5·3 g.; 93%), m. p. 200°, $[\alpha]_D^{20°}$ + 6° (± 4°) (*c*, 0·34 in chloroform) (Found: C, 46·8; H, 5·6; N, 17·7. $C_{15}H_{21}O_7N_5$ requires C, 47·0; H, 5·5; N, 18·3%).

6-*Amino*-4-*triacetyl*-d-*xylosidamino*-5-*thioformamidopyrimidine.*—5 : 6-Diamino-4-triacetyl-*d*-xylosidaminopyrimidine-II (4 g.) was refluxed for 3 hours in alcohol (100 c.c.) with dithioformic acid (from 36 g. of the sodium salt). A second equal amount of dithioformic acid was added, heating continued for 3 hours, and the mixture left overnight. The liquid was filtered, the residue washed with hot alcohol, and the combined filtrate and washings evaporated to small bulk (30 c.c.). The *thioformyl* derivative which separated was recrystallised from alcohol, forming rosettes of colourless needles (1·8 g.; 40%), m. p. 187° (decomp.), which appeared to be hydrated (Found: C, 42·8; H, 5·2; N, 15·9. $C_{16}H_{21}O_7N_5S,H_2O$ requires C, 43·2; H, 5·2; N, 15·7%). Resinous material which remained in the mother-liquors could be used successfully for the preparation of 9-*d*-xylopyranosidoadenine.

9-d-*Xylopyranosidoadenine and* 6-d-*Xylosidaminopurine.*—The above thioformyl compound (1·5 g.) was refluxed in pyridine (10 c.c.) in a slow stream of nitrogen for 16 hours, by which time evolution of hydrogen sulphide had ceased. Solvent was removed in a vacuum, and the residue dissolved in dry chloroform (20 c.c.) and, after addition of methanolic sodium methoxide (0·08 g. of sodium in 20 c.c. of methanol), kept overnight. The solution was now evaporated in a vacuum, chloroform (20 c.c.) added, and the precipitate collected and dissolved in hot water (10 c.c.). On cooling, a crystalline solid (0·14 g.) (A) separated, leaving an alkaline mother-liquor (B).

(A) Recrystallisation from water gave 9-d-*xylopyranosidoadenine* in colourless plates, m. p. 292° (decomp.) (Found in material dried at 140°: C, 44·8; H, 5·0; N, 26·2. $C_{10}H_{13}O_4N_5$ requires C, 45·0; H, 4·9; N, 26·2%). The substance had $[\alpha]_D^{18°}$ — 26° (*c*, 0·28 in water) and its absorption spectrum showed a maximum at 2585 A. (ε, 15,000) in N/20-hydrochloric acid and at 2605 A. (ε, 12,400) in N/20-sodium hydroxide.

Periodate titration. Amount used, 0·094 g. Mols. of sodium periodate used per mol. of xyloside, 2·00; mol. of formic acid liberated per mol. of xyloside, 0·93. Rotation of final solution + 0·08° (*c*, 0·094; *l* = 2 dcm.).

Hydrolysis. The xyloside (50 mg.) (unaffected by boiling with N/10-sulphuric acid for 1 hour) was heated for 5 hours with N-acid (5 c.c.) and then exactly neutralised with sodium hydroxide. The solution was evaporated, and the residue extracted with alcohol. The undissolved material, dissolved in water and treated with picric acid, gave adenine picrate, m. p. and mixed m. p. 294—295°. The alcoholic extract was evaporated to dryness, and the product heated with acetic anhydride (2 c.c.) and fused sodium acetate (20 mg.) for 1 hour at 100°. On working up in the usual way, β-tetra-acetyl-*d*-xylose was obtained, m. p. and mixed m. p. 125—126°.

(B) The mother-liquors and washings from (A) were exactly neutralised with hydrochloric acid and evaporated in a vacuum. The residue was recrystallised from water. 6-d-*Xylosidaminopurine* was obtained in colourless needles (0·12 g.), m. p. 219° (decomp.) (Found in material dried at 140°: C, 44·8; H, 4·8; N, 25·9. $C_{10}H_{13}O_4N_5$ requires C, 45·0; H, 4·9; N, 26·2%). $[\alpha]_D^{22°}$ — 7° (*c*, 0·14 in water). Hydrolysis was readily effected with N/10-hydrochloric acid

and in the hydrolysis solution adenine and *d*-xylose were identified in the usual way as adenine picrate, m. p. 294—295°, and β-tetra-acetyl *d*-xylose, m. p. 124—125°.

9-d-*Xylopyranosidohypoxanthine*.—9-*d*-Xylopyranosidoadenine (0·1 g.) was dissolved in hot water (10 c.c.) and cooled to 65°, and sodium nitrite (0·257 g.; 10 mols.) added, followed by N-hydrochloric acid (5 c.c.). The temperature was maintained at 65° and evolution of nitrogen ceased in 30 mins.; the solution was then exactly neutralised with sodium hydroxide and concentrated. As no crystalline material had separated after 3 days, the solution was evaporated to dryness, and the residue kept overnight with acetic anhydride (1·5 c.c.) in pyridine (3·5 c.c.). The solution was evaporated in a vacuum, the residue thoroughly extracted with boiling chloroform (15 c.c. in all), and the chloroform evaporated, giving the acetylated material in the form of a resin. This product was dissolved in saturated methanolic ammonia (15 c.c.), and the solution set aside for 2 days and evaporated in a vacuum. On recrystallisation of the residue from methanol 9-d-*xylopyranosidohypoxanthine* was obtained in colourless prisms (10 mg.), m. p. 222°; the crystals appeared to be hydrated and held their water of crystallisation tenaciously even on heating at 140° for 5 hours (Found: C, 41·9; H, 5·1; N, 19·6. $C_{10}H_{12}O_5N_4,H_2O$ requires C, 42·0; H, 4·9; N, 19·6%).

Series I.

6-*Amino*-4-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-I*.—2 : 5-Dichloroaniline (0·4 g.) was dissolved in boiling water (12 c.c.), concentrated hydrochloric acid (2·5 c.c.) added, and the solution cooled to 0° and diazotised with sodium nitrite (0·18 g.). The filtered diazo-solution was added to a suspension of powdered 6-amino-4-*d*-xylosidaminopyrimidine-I (0·6 g.) in a little water, and excess of sodium bicarbonate (2·5 g. in 30 c.c. of water) added at once. After 3 hours the solid product was collected, dried, and recrystallised from pyridine–alcohol. The *azo* compound (0·58 g.; 56%) formed clusters of yellow needles, m. p. 166° (decomp.), which appeared to be hydrated (Found in material dried at 75°: C, 41·0; H, 4·8; N, 19·2; loss at 100°, 6·1. $C_{15}H_{16}O_4N_6Cl_2,1\frac{1}{2}H_2O$ requires C, 40·8; H, 4·3; N, 19·0; H_2O, 6·1%). A Wratten No. 29 filter and a source of white light being used, it had $[\alpha]^{20°}$ — 19° (*c*, 0·24 in pyridine).

6-*Amino*-4-*triacetyl*-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidine-I*.—The above azo-compound (4·0 g.) was kept overnight with acetic anhydride (20 c.c.) in pyridine (100 c.c.). Alcohol (20 c.c.) was now added and after 3 hours the solution was evaporated. The residue crystallised from benzene or ethyl acetate–alcohol in yellow needles (2·05 g.; 38%), m. p. 219—220° (Found in material dried at 100°: C, 46·1; H, 4·1; N, 15·5. $C_{21}H_{22}O_7N_6Cl_2$ requires C, 46·6; H, 4·1; N, 15·5%). With white light and a Wratten No. 29 filter it showed $[\alpha]^{19°}$ + 21° (*c*, 0·24 in chloroform).

5 : 6-*Diamino*-4-*triacetyl*-d-*xylosidaminopyrimidine*.—The above triacetyl-azo-compound (1·8 g.) in ethyl acetate (100 c.c.) was hydrogenated under pressure (80 atm.) at 100° for 4 hours, a Raney nickel catalyst being used. The catalyst was filtered off and washed with alcohol, and the combined filtrate and washings evaporated. The residue crystallised on trituration with light petroleum and was used directly for the next stage. In a second experiment it was recrystallised from ethyl acetate–alcohol and then had m. p. 198°, undepressed in admixture with the diamine prepared from the Series II azo-glycoside. It had $[\alpha]_D^{18°}$ + 10° (± 7°) (*c*, 0·17 in chloroform).

9-d-*Xylopyranosidoadenine*.—To the above crude diamine, dissolved in hot alcohol (100 c.c.), dithioformic acid (from 12 g. of the hydrated sodium salt) was added, and the mixture refluxed for 2 hours. A second similar quantity of dithioformic acid was now added, refluxing continued for a further 2 hours, and the whole kept overnight. The mixture was now heated to boiling, filtered, and the residue of dithioformic acid washed thoroughly with boiling alcohol (300 c.c.). Filtrate and washings were evaporated under reduced pressure, giving a crude resinous thioformyl-compound which did not crystallise readily and was not further purified.

The crude thioformyl derivative was freed from alcohol by heating at 100°/0·5 mm. for 4 hours, then refluxed in dry pyridine (10 c.c.) in a stream of nitrogen; after 16 hours evolution of hydrogen sulphide had ceased. The solution was evaporated under reduced pressure, but the residue could not be crystallised directly. It was accordingly dissolved in dry chloroform (25 c.c.) and after addition of a solution of sodium methoxide (0·1 g. of sodium in 25 c.c. of methanol) kept overnight. The resulting solution was evaporated in a vacuum, and the brownish residue recrystallised twice from water (charcoal). 9-d-*Xylopyranosidoadenine* was obtained in colourless prisms, m. p. 298° (decomp.) (Found in material dried at 140°/0·5 mm.: C, 45·2; H, 5·1; N, 26·0. $C_{10}H_{13}O_4N_5$ requires C, 45·0; H, 4·9; N, 26·2%). Yield of pure material, 82 mg. The solubility of the substance in water was not increased by adding alkali. *Light absorption*. (*a*) In N/20-hydrochloric acid: maximum at 2590 A. (ε, 13,000). (*b*) In N/20-sodium hydroxide: maximum at 2605 A. (ε, 14,000).

Periodate titration. Amount of xyloside used 0·0515 g. Periodate absorbed, 1·96 mols./mol.; formic acid liberated, 0·99 mol./mol. Rotation of final solution + 0·08° (*c*, 0·103; *l* = 2 dcm.)

The mother-liquors from the crystallisation of the 9-*d*-xylopyranosidoadenine-I were carefully neutralised with hydrochloric acid (N/10); only gummy material separated and no crystalline 6-xylosidaminopurine could be isolated from it.

4 : 6-*Diamino*-5-(2′ - 5′-*dichlorobenzeneazo*)*pyrimidine*, prepared in 90% yield by coupling 4 : 6-diaminopyrimidine with diazotised 2 : 5-dichloroaniline in presence of sodium hydrogen carbonate in the usual manner, formed yellow needles from pyridine, m. p. 281° (Found in material dried at 140°: N, 29·2. $C_{10}H_8N_6Cl_2$ requires N, 29·7%).

Hydrolysis of the Isomeric 6-*Amino*-4-d-*xylosidamino*-5-(2′ : 5′-*dichlorobenzeneazo*)*pyrimidines*.—The following procedure was applied in each case: The glycoside (30 mg.) was refluxed in a mixture of alcohol (3 c.c.) and N-sulphuric acid (5 c.c.) for 3 hours, and the solution cooled, neutralised with N-sodium hydroxide (5 c.c.), and evaporated. Water was added, and the yellow solid collected, dissolved in hot alcohol (5 c.c.), and purified by passing through a column of activated alumina, washing with alcohol being continued till the yellow band was eluted. The alcoholic washings were concentrated, and the azopyrimidine allowed to crystallise. The Series I isomer gave a product, m. p. 278—279°, undepressed in admixture with authentic 4 : 6-diamino-5-(2′ : 5′-dichlorobenzeneazo)pyrimidine (m. p. 278°). The Series II glycoside gave a product, m. p. 277—278°, undepressed by an authentic specimen or by the product from the Series I isomer.

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