328. *The Preparation of 7- and 9-Glucopyranosyl and -Xylopyranosyl Derivatives of 8-Azaxanthine (5 : 7-Dihydroxy-v-triazolo[d]pyrimidine).*

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N-Glycosyl derivatives of 8-azaxanthine and of triazoles have been prepared in the course of a study on purine antimetabolites.

Acetylglycosyl azides with dimethyl acetylenedicarboxylate readily give *N*-glycosyltriazoles (I; R = *O*-acetylglycosyl). These with ammonia yield the dicarboxyamides (II; R = glycosyl), which with hypobromite are converted into mixtures containing both 7- and 9-glycosyl derivatives of 8-azaxanthine (V and VI; R = glycosyl). The separation and orientation of these *N*-glycosyl derivatives has been achieved.

Interesting medical and biological properties are displayed by certain analogues of the naturally occurring purine bases. Under the stimulus of the antibacterial and carcinostatic behaviour encountered in this field, many such analogues have been prepared.[1] Purine bases, bearing a wide variety of functional groups, represent the bulk of compounds studied in this work, although recently more attention has been given to modification of the purine ring system itself. In the latter class the *v*-triazolo[*d*]-pyrimidines (8-azapurines) have been much studied, 5-amino-7-hydroxy-*v*-triazolo[*d*]-pyrimidine (8-azaguanine) being regarded as particularly promising from a chemotherapeutic point of view. The search for purine antagonists has mainly involved free bases. Since some of these are converted into nucleosides and nucleotides in bacteria and other living systems, it is clear that *N*-glycosyl derivatives of the appropriate bases also possess potential antimetabolite function. However, relatively few compounds of this sort are available for testing. For instance, the literature contains no chemical synthesis of an 8-azapurine nucleoside.* The present work arose from our studies on glycosyl azides, and particularly β-D-ribofuranosyl azide, as intermediates for the chemical synthesis of certain purine nucleotide precursors.[2,3] We wished to compare the behaviour of the sugar azides with that of alkyl and aryl azides towards unsaturated compounds. This has now led to syntheses of both the 7- and the 9-glycosyl derivative of 8-azaxanthine.

* Ribofuranosyl derivatives of 8-aza-adenine and 8-azahypoxanthine have been prepared by Davoll, (cf. Matthews, Ciba Foundation Symposium, "Chemistry and Biology of Purines," London, 1957, p. 270) but the method of synthesis has not yet been disclosed.

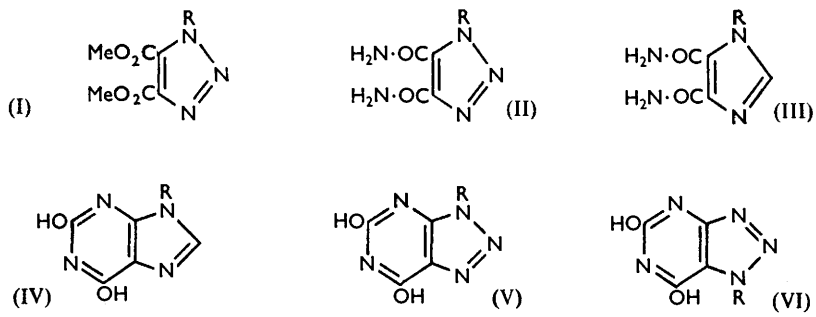
[1] Hitchings and Elion, 3rd Internat. Congr. Biochemistry, Brussels, 1955, p. 55.
[2] Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.
[3] Baddiley, Buchanan, Hodges, and Prescott, *J.*, 1957, 4767.

Xylopyranosyl and glucopyranosyl derivatives have been prepared in the first instance, although there are indications that the synthesis may be extended to ribofuranosyl derivatives.

Curtius and Raschig [4] have described the preparation of dimethyl 1-benzyl-1 : 2 : 3-triazole-4 : 5-dicarboxylate (I; R = CH_2·Ph) from benzyl azide and dimethyl acetylenedicarboxylate. In the present work an analogous reaction was used. Dimethyl 1-(2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1 : 2 : 3-triazole-4 : 5-dicarboxylate (I; R = tetra-*O*-acetyl-β-D-glucopyranosyl) was obtained in excellent yield by heating dimethyl acetylenedicarboxylate (1 or 2 mols.) with 2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-glucopyranosyl azide in benzene or acetone for several hours. Dimethyl 1-(2 : 3 : 4-tri-*O*-acetyl-β-D-xylopyranosyl)-1 : 2 : 3-triazole-4 : 5-dicarboxylate (I; R = tri-*O*-acetyl-β-D-xylopyranosyl) was obtained similarly. The acetylated glycosyltriazoles with methanolic ammonia at 0° overnight gave 1-β-D-glucopyranosyl- and 1-β-D-xylopyranosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide (II; R = β-D-glycopyranosyl).

The identity of these amides was confirmed when N-hydrochloric acid at 100° liberated the parent sugar (detected by paper chromatography) and a base, which was isolated and identified as 1 : 2 : 3-triazole-4 : 5-dicarboxyamide by conversion, *via* a presumed monoamide intermediate, into the dicarboxylic acid.

The preparation of xanthosine (IV; R = β-D-ribofuranosyl) and of 9-xylosylxanthine by the action of hypobromite on the corresponding glycosylglyoxaline-4 : 5-dicarboxyamides (III; R = glycosyl) has been reported by Spring and his collaborators.[5,6] In the same way, but under somewhat different reaction conditions, 1-xylosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide yielded cyclic products. After treatment with an excess of aqueous potassium hypobromite at 2° for 18 hr., then at 60° for 30 min., paper chromatograms revealed a major product which appeared in ultraviolet light as a bright blue, fluorescent spot, still visible after exposure to hydrochloric acid vapour. The reaction mixture was

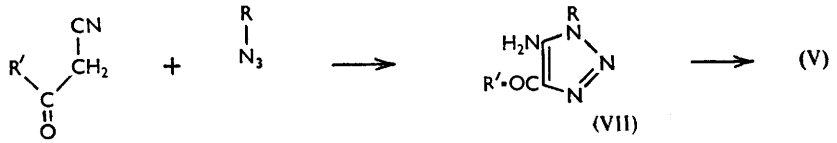


then diluted and percolated through a column of Dowex-2 resin in the formate form; elution with 0·1M- or 0·2M-ammonium formate removed two major components. The first of these (A) showed maximum ultraviolet absorption at 278 mμ in neutral, aqueous solution. The second (B) exhibited maxima at 250 and at 278 mμ. These fractions were concentrated and ammonium formate was sublimed from the solid residues; materials A and B remained as pale powders.

Acid hydrolysis of both A and B gave xylose and 8-azaxanthine (V; R = H) (detected on paper chromatograms). A and B had similar R_F values in the solvent systems used, but the resulting spots exhibited marked differences in fluorescent behaviour. Whereas A was detected in ultraviolet light as a bright blue fluorescence where basic solvent systems were used or after exposure of chromatograms to ammonia, B gave a similar blue fluorescence only under acid conditions.

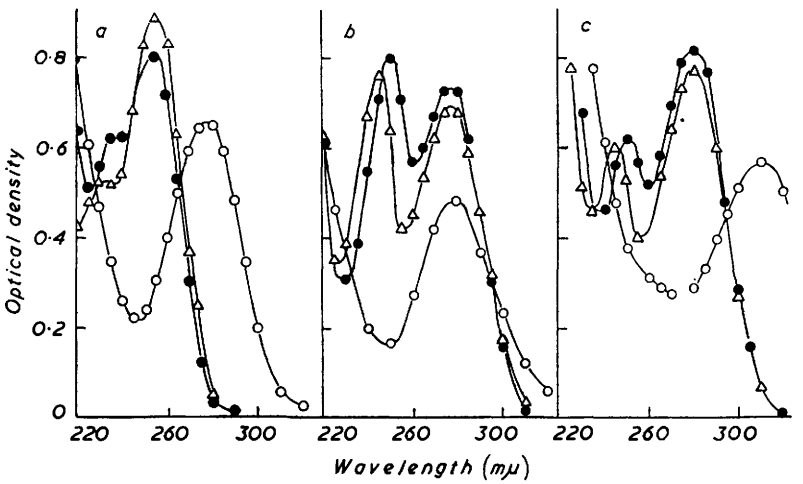
[4] Curtius and Raschig, *J. prakt. Chem.*, 1930, **125**, 466.
[5] Baxter and Spring, *J.*, 1947, 378.
[6] Howard, McLean, Newbold, Spring, and Todd, *J.*, 1949, 232.

Although Spring's work on the corresponding glyoxaline derivatives led to the isolation of only one isomer, 9-xylosylxanthine,[5] the presence of A and B above pointed to the formation of both 7- and 9-xylosyl-8-azaxanthine (VI and V; R = xylosyl) in the present case. Since the spectroscopic differences between A and B were considerable, comparison with the appropriate methylated bases appeared promising as a means of orientation. Since the Hofmann reaction can yield only 7- and 9-isomers in this case, only one reference compound, either 7- or 9-methyl-8-azaxanthine, was required. 9-Methyl-8-azaxanthine (V; R = Me) was synthesised: methyl azide and cyanoacetamide gave the aminotriazolecarboxyamide (VII; R = Me, R′ = NH_2) which was converted into the azaxanthine derivative (V; R = Me) by fusion with urea at 170—180°.



Dimroth [7,8] synthesised several derivatives of 1-phenyl-1 : 2 : 3-triazole by reaction between phenyl azide and malonic or cyanoacetic esters. He proved that phenyl azide and methyl cyanoacetate yield exclusively the 1-phenyl isomer (VII; R = Me, R′ = OMe). Recently Hoover and Day [9] prepared triazole derivatives (VII; R = CH_2Ph,

Absorption spectra of N-*xylosyl*-8-*azaxanthine and of* 9-*methyl*-8-*azaxanthine* (*a*) *at* pH 2·2, (*b*) *at* pH 7·0, *and* (*c*) *in* 0·1N-*sodium hydroxide* (*concns.* 10^{-4} *mole/l.*).



○ 7-*Xylosyl-* (*A*). ● 9-*Xylosyl-* (*B*). △ 9-*Methyl*-8-*azaxanthine.*

R′ = OMe or NH_2) from benzyl azide and malonic or cyanoacetic ester. It has been assumed by the American authors that phenyl and benzyl azide would react similarly, to give triazoles with identical orientation of substituents. In our synthesis of 9-methyl-8-azaxanthine as outlined above we have also made the reasonable assumption that phenyl azide and methyl azide would react similarly. We feel, however, that the analogy between phenyl azide and methyl or benzyl azide is not rigid and a more rigorous proof of the orientation of substituents in the *N*-methyltriazole (VII; R = Me, R′ = NH_2) is under investigation.

9-Methyl-8-azaxanthine (V; R = Me) and material B are very similar spectroscopically (see Figure). At pH 7 both displayed two peaks (maxima at 245 and 278 mμ, and 250

[7] Dimroth, *Ber.*, 1902, **35**, 4041.
[8] Dimroth, *Annalen*, 1909, **364**, 183.
[9] Hoover and Day, *J. Amer. Chem. Soc.*, 1956, **78**, 5832.

and 278 mμ, respectively), compared with a single peak (278 mμ) in the case of material A. At pH 2·2 both compounds gave a single peak (255 mμ) with a shoulder whereas the position of the peak of A remained unchanged (278 mμ). In 0·1N-sodium hydroxide solution, however, the maximum of A moved to 310 mμ, whereas the maxima of 9-methyl-8-aza-xanthine and B were substantially those recorded at pH 7. On this evidence, material A was formulated as the 7-xylosyl (VI) and B as the 9-xylosyl derivative (V). The fluorescence properties of B resemble those of 9-methyl-8-azaxanthine, in accordance with this formulation.

From 1-D-glucopyranosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide (III; R = glucosyl), glucopyranosyl derivatives similar to A and B in absorption and fluorescence were obtained and were formulated as the 7- and the 9-isomer, severally.

The configuration of the glycosidic linkage in the glucosyl-triazoles and -8-azaxanthines is certainly β, since they were prepared from 2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-glucopyranosyl azide by reactions which would not affect the glycosidic centre. It is reasonable to assume from its method of preparation that the xylopyranosyl azide is also a β-compound, and so the triazoles and 8-azaxanthine derivatives in the xylose series are β-glycosyl derivatives.

In a recent publication,[10] Smith and Matthews describe the isolation of a ribosyl-8-azaxanthine from *Bacillus cereus* grown in a medium containing 8-azaxanthine. The ultraviolet absorption maximum (257 mμ in 0·1N-hydrochloric acid) recorded by them closely resembles that of 9-methyl-8-azaxanthine and of B, and is thus consistent with the ribosyl derivative's being a 9-isomer.

It would be expected that the the Hofmann reaction on the *N*-glycosyltriazoledi-carboxyamides would lead to aminotriazolecarboxyamides, *e.g.*, (VII; R = glycosyl, R′ = NH_2). These are of interest in view of their structural similarity to the ribose 5-phosphate derivative of 5-aminoglyoxaline-4-carboxyamide, a natural nucleotide precursor. It has been shown by the Bratton–Marshall test on paper chromatograms that compounds of this type are present in the reaction mixture. Further work on their identification is in progress. Further, when the Hofmann reaction is carried out at 2° it is possible to detect the *N*-bromoamide intermediates by paper chromatography, little or no azaxanthine derivatives then being formed.

Experimental

Unless indicated otherwise, ascending paper chromatograms were run in the system, propan-1-ol–aqueous ammonia (*d* 0·880)–water (6 : 3 : 1), on Whatman No. 4 paper.

Dimethyl 1-(2 : 3 : 4 : 6-*Tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-1 : 2 : 3-*triazole*-4 : 5-*dicarboxylate*.—2 : 3 : 4 : 6-Tetra-*O*-acetyl-β-D-glucopyranosyl azide [11] (3·7 g., 1 mol.) was heated under reflux for 2½ hr. with freshly distilled dimethyl acetylenedicarboxylate [12] (1·8 g., 1·2 mol.) in dry benzene (30 c.c.). The yellow solution was poured into an excess of light petroleum (b. p. 40—60°); the precipitated oil rapidly crystallised. The *product* (4·7 g., 96%) had m. p. 153°, after recrystallisation from ethanol (Found: C, 46·6; H, 4·9; N, 7·8. $C_{20}H_{25}O_{13}N_3$ requires C, 46·9; H, 4·9; N, 8·1%). The yield was 85% when acetone was the solvent. When 2 mols. of the acetylene were used, reaction in benzene gave a 90% yield of the above product.

1-β-D-*Glucopyranosyl*-1 : 2 : 3-*triazole*-4 : 5-*dicarboxyamide*.—Dimethyl 1-(2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1 : 2 : 3-triazole-4 : 5-dicarboxylate (1·05 g.) was treated at 0° overnight with dry methanol (30 c.c.) saturated with ammonia. Evaporation of solvent to small volume, followed by the addition of ether, precipitated a white gum which hardened rapidly (0·54 g., 85%). Recrystallised from aqueous methanol the *diamide* formed colourless crystals of indeterminate m. p. (Found, in sample dried at 50°/1 mm. for 12 hr.: C, 36·8; H, 5·1; N, 21·4. $C_{10}H_{15}O_7N_5,\frac{1}{2}H_2O$ requires C, 36·8; H, 4·9; N, 21·5%).

Dimethyl 1-(2 : 3 : 4-*Tri*-O-*acetyl*-β-D-*xylopyranosyl*)-1 : 2 : 3-*triazole*-4 : 5-*dicarboxylate*.—2 : 3 : 4-Tri-*O*-acetyl-β-D-xylopyranosyl azide (3·0 g., 1 mol.) was heated under reflux for 5 hr. with dimethyl acetylenedicarboxylate (2·3 g., 1·55 mol.) in dry benzene (30 c.c.), then poured

[10] Smith and Matthews, *Biochem. J.*, 1957, **66**, 323.
[11] Bertho, *Ber.*, 1930, **63**, 836.
[12] Huntress, Lesslie, and Bornstein, *Org. Synth.*, 1952, **32**, 55.

into an excess of light petroleum (b. p. 40—60°). The precipitated oil crystallised on trituration with methanol. The colourless *ester* (3·4 g., 76%) had m. p. 114° after recrystallisation from ethanol (Found: C, 46·5; H, 4·8; N, 10·0. $C_{17}H_{21}O_{11}N_3$ requires C, 46·1; H, 4·7; N, 9·5%).

1-β-D-*Xylopyranosyl*-1 : 2 : 3-*triazole*-4 : 5-*dicarboxyamide*.—Dimethyl 1-(2 : 3 : 4-tri-*O*-acetyl-β-D-xylopyranosyl)-1 : 2 : 3-triazole-4 : 5-dicarboxylate (2·5 g.) was treated at 0° overnight with dry methanol (30 c.c.) saturated with ammonia. Concentration of the solution *in vacuo* led to the separation of colourless crystals (1·3 g., 88%). Addition of ether to the mother liquors gave a further small crop (0·05 g.). The *diamide* was purified by recrystallisation from aqueous methanol (Found, in sample dried at 50°/1 mm. for 12 hr.: C, 36·7; H, 5·1; N, 23·7. $C_9H_{13}O_6N_5,\frac{1}{2}H_2O$ requires C, 36·5; H, 4·7; N, 23·7%).

Acid Hydrolysis of Triazole Derivatives.—(*a*) 1-Glucosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide (69 mg.) in N-hydrochloric acid (5 ml.) was kept at 90° for 1 hr. The solid (18 mg.) which separated was filtered off. Treatment of this product with N-sodium hydroxide at 100° for 2 hr., followed by dilution of the resulting solution, passage down a Dowex-50 column (H^+ form), and concentration of the effluent, gave a white solid (5 mg.). This had m. p. 198°, alone or in admixture with 1 : 2 : 3-triazole-4 : 5-dicarboxylic acid prepared from 1-benzyl-1 : 2 : 3-triazole-4 : 5-dicarboxylic acid [14] by debenzylation. (*b*) Milligram quantities of 1-glucosyl- and 1-xylosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide in N-hydrochloric acid (0·2 ml.) were kept at room temperature for 20 min., then at 95°. Paper chromatography revealed considerable hydrolysis of the xylosyl derivative at room temperature. The glucosyl derivative appeared to be unaffected. Both xylosyl and glucosyl derivative were completely hydrolysed after 20 min. at 95°. Initial decomposition products were the parent sugars (detected by aniline phthalate spray) and a base, presumably 1 : 2 : 3-triazole-4 : 5-dicarboxyamide.

	R_F
1-Glucosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide	0·63
1-Xylosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide	0·66
1 : 2 : 3-Triazole-4 : 5-dicarboxyamide (by hydrolysis)	0·59

Further acid hydrolysis of 1 : 2 : 3-triazole-4 : 5-dicarboxyamide led to the appearance of a component with R_F 0·27, probably a monamide, and finally to 1 : 2 : 3-triazole-4 : 5-dicarboxylic acid, R_F 0·18.

All these substances were readily detected on paper chromatograms as opaque spots in ultraviolet light of 254 mμ wavelength. It should be noted that the actual ultraviolet absorption maxima of these compounds lie in the 220—230 mμ region. The two glycosyl derivatives slowly developed rather weak blue colours with the periodate–Schiff spray.

Action of Hypobromite on 1-β-D-*Xylopranosyl*-1 : 2 : 3-*triazole*-4 : 5-*dicarboxyamide*.—Freshly prepared potassium hypobromite [5] (15 ml.) at 2° was added to 1-xylopyranosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide (740 mg.), the mixture being maintained for 18 hr. at this temperature, then for 30 min. at 65°. After dilution with water (50 ml.) the solution was passed down a column of Dowex-2 (formate) (15 × 3 cm.; 200—400 mesh). The resin was washed with water and products were eluted with 0·1M-ammonium formate solution at pH 7 (fractions 1—180) and then with 0·2M-ammonium formate. Fractions 230—296 (each of 10 ml.) contained the component A; fractions 342—451 contained the component B.

7-β-D-*Xylopranosyl*-8-*azaxanthine*. The combined fractions 230—296 were evaporated to dryness at 35° (rotatory evaporator) and ammonium formate was removed by sublimation *in vacuo* at 60°. The residual white powder was recrystallised from water. The N-*glycosyl derivative* (59 mg.) was dried for 8 hr. at 85°/1 mm. (Found: C, 38·2; H, 4·3; N, 25·0. $C_9H_{11}O_6N_5$ requires C, 37·9; H, 3·9; N, 25·1%). The total 7-xylosyl derivative content of fractions 230—296, estimated spectrophotometrically, was 110 mg.

9-β-D-*Xylopyranosyl*-8-*azaxanthine*. Fractions 342—381 (which were halide-free) and fractions 382—451 (which contained a little ammonium bromide) were evaporated as two batches as before. Ammonium formate was removed by sublimation and the residual materials were dissolved in wet methanol and reprecipitated by ether. The hygroscopic, freshly precipitated 9-*xylosyl derivative* (15 mg.) from fractions 342—381 was dried at 60°/1 mm. for 12 hr. (Found: C, 33·2; H, 5·3; N, 20·9. $C_9H_{11}O_6N_5,2\frac{1}{2}H_2O$ requires C, 32·8; H, 5·3; N, 20·6%). The material from fractions 382—451 was difficult to purify. Ammonium bromide

[13] Bertho, *Annalen*, 1949, **562**, 229.
[14] Wiley, Hussing, and Moffatt, *J. Org. Chem.*, 1956, **21**, 190.

was finally removed by adsorption of the xylosyl derivative on charcoal, followed by elution with ethanol–ammonia–water, but losses were considerable. The 9-xylosyl derivative content of fractions 342—451, estimated spectrophotometrically, was 90 mg.

Action of Hypobromite on 1-β-D-*Glucopyranosyl*-1 : 2 : 3-*triazole*-4 : 5-*dicarboxyamide.*—Freshly prepared potassium hypobromite [5] (15 ml.) at 2° was added to 1-glucosyl-1 : 2 : 3-triazole-4 : 5-dicarboxyamide (750 mg.). After 18 hr. at this temperature the mixture was maintained at 65° for 30 min., diluted with water (50 ml.), and percolated through a Dowex-2 resin column in the formate form (200—400 mesh; 15 × 3 cm.). The resin was washed with water and with 0·1M-ammonium formate (1 l.) (pH 7), and the products were eluted with 0·2M-ammonium formate at pH 7, 10 ml. fractions being collected. Tubes 44—74 which exhibited a single absorption maximum at 278 mμ were combined. Tubes 141—200 which exhibited maxima at 250 and 278 mμ were also combined.

7-β-D-*Glucopyranosyl*-8-*azaxanthine.* The combined fractions 44—74 were evaporated to dryness at 35° (rotary evaporator) and ammonium formate was removed by sublimation *in vacuo* at 60°. The residual white powder (150 mg.) was recrystallised from water. The N-*glycosyl derivative* was dried for 12 hr. at 60°/1 mm. (Found: C, 36·9; H, 4·7; N, 21·7. $C_{10}H_{13}O_7N_5,\frac{1}{2}H_2O$ requires C, 37·1; H, 4·4; N, 21·6%).

9-β-D-*Glucopyranosyl*-8-*azaxanthine.* Combined fractions 141—200 were evaporated and ammonium formate was removed as before. The residue was dissolved in methanol and reprecipitated by the addition of ether. The material obtained in this way (68 mg.) contained a little inorganic halide. It was dissolved in a small volume of aqueous methanol and reprecipitated by the addition of ethanol. The *glycosyl derivative* was dried for 12 hr. at 80°/1 mm. (Found: C, 32·6; H, 4·8. $C_{10}H_{13}O_7N_5,3H_2O$ requires C, 32·8; H, 5·2%).

Hydrolysis of N-*Glycosyl*-8-*azaxanthines.*—N-Hydrochloric acid (0·2 ml.) was added to milligram quantities of the four glycosyl derivatives. Paper chromatograms revealed no decomposition after 30 min. at room temperature. After 1 hr. at 95° both 7-glycosyl

	R_F	Conditions for fluorescence
7-Glucopyranosyl-8-azaxanthine	0·38	Basic
9-Glycopyranosyl-8-azaxanthine	0·38	Acidic
7-Xylopyranosyl-8-azaxanthine	0·42	Basic
9-Xylopyranosyl-8-azaxanthine	0·41	Acidic
8-Azaxanthine	0·32	Acidic

derivatives were completely hydrolysed to the parent sugars (detected by benzidine spray [15]) and 8-azaxanthine. The 9-xylosyl derivative was also completely hydrolysed under these conditions, but hydrolysis of the 9-glucosyl derivative was not quite complete. After 2 hr. at 95° the 9-glucosyl derivative was completely hydrolysed.

Detection of these compounds by their fluorescence appears preferable to detection by their opacity under non-fluorescent conditions.

5-*Amino*-1-*methyl*-1 : 2 : 3-*triazole*-4-*carboxyamide.*—Cyanoacetamide (3·7 g., 1·0 mol.) and methyl azide (6·0 g., 2·4 mol.) were added to a stirred, freshly prepared solution from sodium (1 g.) in ethanol (100 ml.), and the mixture was then heated under reflux for 1 hr. After cooling, the crystalline product (1·45 g.) was filtered off and washed with cold water and cold ethanol. Recrystallised from ethanol the *triazole* formed white needles, m. p. 248° (Found: C, 33·9; H, 5·0. $C_4H_7ON_5$ requires C, 34·0; H, 5·0%).

The compound ran as a single spot, R_F 0·73, detected by ultraviolet absorption and by the purple colour produced with a modified Bratton–Marshall spray reagent.[16] When an ethanol solution of 5-amino-1-methyl-1 : 2 : 3-triazole-4-carboxyamide was saturated with hydrogen chloride the base hydrochloride separated readily.

9-*Methyl*-8-*azaxanthine.*—Finely powdered urea (500 mg.) was fused with 5-amino-1-methyl-1 : 2 : 3-triazole-4-carboxyamide hydrochloride (500 mg.) at 170—180° for 2½ hr. The product was dissolved in a little hot water and the solution diluted and passed down a Dowex-50 resin column (H^+ form). The effluent and washings were combined, adjusted to pH 10 (ammonium hydroxide), and percolated through a Dowex-2 resin column (10 × 1·5 cm.; formate form) which was then washed with water and eluted with 0·1N-formic acid (150 ml.). The eluate was evaporated to dryness at 35° (rotary evaporator) and the residual white solid recrystallised

[15] Horrocks, *Nature*, 1949, **164**, 444.
[16] Greenberg and Spilman, *J. Biol. Chem.*, 1956, **219**, 411.

from water. 9-*Methyl*-8-*azaxanthine* (63 mg.) formed white needles, m. p. 320° (decomp.) (Found: C, 35·9; H, 3·4; N, 41·9. $C_5H_5O_2N_5$ requires C, 36·1; H, 3·0; N, 41·7%). It was homogeneous (R_F 0·68) when examined by paper chromatography. The compound was detected on the paper by its brilliant blue fluorescence after exposure to hydrochloric acid vapour.

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