[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, PURDUE UNIVERSITY]

Alkaline Stability of 2-*O*-D-Xylopyranosyl-L-arabinose[1]

BY ROY L. WHISTLER AND W. M. CORBETT

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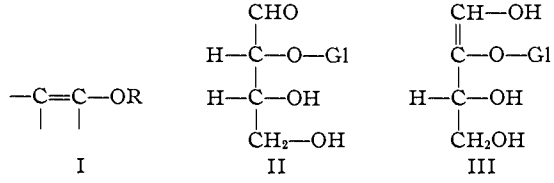
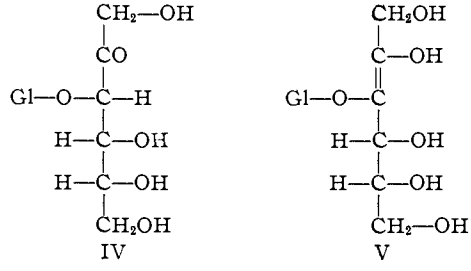
Stability of 2-*O*-D-xylopyranosyl-L-arabinose to alkali at 25° supports the view that degradation of alkaline solutions of reducing sugar derivatives at low temperatures takes place by elimination of an alkoxy group from a β-alkoxycarbonyl unit. Degradation of the disaccharide to acidic products occurs at 100°.

It is well known that certain glycosides and oligosaccharides are alkali sensitive.[2] The alkali sensitivity of oligosaccharides has been described by Evans and associates[3] as due to the presence of the structural unit I. Thus, it was postulated that maltose is degraded in alkaline solution to 2-*O*-α-D-glucopyranosyl-D-erythrose (II), the enediol III of which is then hydrolyzed to D-glucose and D-erythrose.



I II III

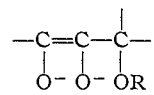
The alkaline degradation of turanose (IV) also has been explained as proceeding through the enediol



IV V

V with hydrolysis to D-glucose and D-fructose prior to the onset of further decomposition.[4]

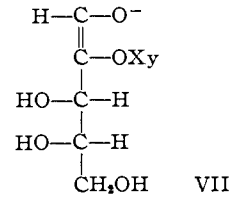
Recently a different explanation has been proposed[5] following new investigations of the rates and products of degradation of numerous hexose derivatives and disaccharides[5,6] by lime water at 25°. The results are best explained by the elimination of an alkoxy group from the di-ion VI of a β-alkoxycarbonyl unit. Thus, degradation of a substituted glycose is demonstrated to occur at 25° if it can form directly the di-ion VI, as is the case in 3-*O*-β-D-glucosyl-D-glucose[5] (laminaribiose), 3-*O*-α-D-glucosyl-D-fructose (turanose)[5] and 1-*O*-methyl-D-fructose,[6b] or if it can undergo a Lobry de Bruyn and Alberda van Ekenstein transformation to an isomer which can then form the di-ion, as in the transformation of a 4-*O*-D-glycosyl-D-glucose (maltose[6d] and lactose[6c]) to a 4-*O*-D-glycosyl-D-fructose (maltulose and lactulose).



VI

According to this mechanism a glycose substituted at carbon atom C2 will be stable toward mild alkali at 25°, whereas according to the previously described mechanism the 2-*O*-substituted glycoses would be unstable. Since a test of this point would lend considerable weight to one or the other theories, the stability of 2-*O*-D-xylopyranosyl-L-arabinose to dilute alkali has been examined. The disaccharide was recently isolated by Whistler and McGilvray[7] from the partial hydrolysis products of corn cob hemicellulose-B, and now has been obtained in a crystalline condition.

Although the ion of 2-*O*-D-xylopyranosyl-L-arabinose (VII) contains the structure I it is found to be quite stable in alkali at 25°. Its stability is



VII

shown by the absence throughout the reaction of reducing sugars other than the initial material, by the very slow production of acidic products, by the almost constant reducing value of the solution over a period of 72 hours and by the fact that the alkaline solution remains colorless. The very slow formation of acidic products demonstrates that the glycosyl group is stable to alkali at 25°, and also that the bond between carbon atoms C2 and C3 of the reducing sugar unit is cleaved less readily than the bond between carbon atoms C3 and C4 in D-fructose; cleavage of either bond results in the formation of lactic acid. The stability of the carbon–carbon bond in 2-*O*-D-xylopyranosyl-L-arabinose cannot be due to the presence of a glycosyl linkage in position alpha to a carbonyl group since the similar linkage in the D-fructose residue of turanose allows fission of the C3-C4 bond with formation of lactic acid.[5] This more ready fission of carbon bonds in ketoses over those in aldoses is in agreement with the accepted view that the alkaline degradation of D-glucose to lactic acid proceeds through D-fructose.

The above results demonstrate that 2-*O*-D-xylopyranosyl-L-arabinose is stable to alkali at 25° because it cannot form the di-ion VI. However, at 100° the disaccharide is readily degraded to acidic products (2.51 equivs. in 1 hour) accompanied by

(1) Journal Paper No. 849 of the Purdue Agricultural Experimental Station, Lafayette, Indiana.

(2) See C. E. Ballou, *Advances in Carbohydrate Chem.*, **9**, 59 (1954).

(3) See W. L. Evans, *Chem. Revs.*, **31**, 537 (1942).

(4) H. S. Isbell, *J. Research Natl. Bur. Standards*, **26**, 35 (1941).

(5) W. M. Corbett and J. Kenner, *J. Chem. Soc.*, 3274 (1954).

(6) (a) J. Kenner and G. N. Richards, *ibid.*, 278 (1954); (b) 1784 (1954); (c) W. M. Corbett and J. Kenner, *ibid.*, 2245 (1953); (d) 1789 (1954).

(7) R. L. Whistler and D. I. McGilvray, THIS JOURNAL, **77**, 1884 (1955).

the formation of a yellow color. Because of the limited amounts of disaccharide available, it was not possible to identify the products from degradation by hot alkaline solutions. The mechanism of the degradation under these drastic conditions is unknown.

Experimental

2-*O*-D-Xylopyranosyl-L-arabinose.—Hemicellulose-B, prepared from corn cobs, was partially hydrolyzed under conditions similar to those reported by Whistler and McGilvray.[7] After neutralization, the hydrolyzate was eluted from a charcoal–celite column in the usual way.[8] The 5% ethanol eluate was concentrated and chromatographed on a cellulose column, using butanol saturated with water. The first component to be eluted was 2-*O*-D-xylopyranosyl-L-arabinose which was obtained in a crystalline form by concentration of the eluent. Crystallinity was proved by X-ray diffraction. After recrystallization from aqueous ethanol the disaccharide had m.p. 167–168°, $[\alpha]^{25}D$ + 32.9 (*c* 0.97 in water).

Anal. Calcd. for $C_{10}H_{18}O_9$: C, 42.65; H, 6.44. Found: C, 42.85; H, 6.57.

When an aqueous ethanol solution of 2-*O*-D-xylopyranosyl-L-arabinose was allowed to evaporate rapidly in a vacuum desiccator, fine needles of the disaccharide hydrate were obtained, m.p. 80–81°. Recrystallization of this hydrate by seeding an aqueous ethanol solution with the higher melting form or heating the lower melting form at 45° over phosphorus pentoxide gave 2-*O*-D-xylopyranosyl-L-arabinose, m.p. 166–167°, $[\alpha]^{25}D$ + 47.0 → 32.5° (*c* 1.15, in water).

Anal. Calcd. for $C_{10}H_{18}O_9 \cdot 2H_2O$: C, 37.74; H, 6.98. Found: C, 37.86; H, 7.09.

Action of Lime Water upon 2-*O*-D-Xylopyranosyl-L-arabinose.—Sixty-four and eight-tenths mg. of 2-*O*-D-xylopyranosyl-L-arabinose was dissolved in 25 ml. of 0.033 *N* lime water and maintained at 25°. Periodically, 2-ml. aliquots were withdrawn and run into 10 ml. of 0.01 *N* sulfuric acid. After 1/4 hour, the solution was titrated with 0.01 *N* sodium hydroxide solution to the first semipermanent end-point with phenolphthalein. The solution was then diluted to 50-ml. and 2-ml. samples were taken to determine the reducing value by the method of Hagedorn and Jensen.[9] Samples of the solution were also examined by paper chromatography which revealed the presence of 2-*O*-D-xylopyranosyl-L-arabinose only.

Time (hr.)	Equiv. acid produced	Reducing value	Time (hr.)	Equiv. acid produced	Reducing value
0	0.000	1.000	10	0.038	...
1	.016	...	48	.044	0.962
3	.022	...	72	.044	.962

After the solution had been heated at 100° for 1 hour the acid produced was 2.51 equiv. The solution had attained a deep yellow color and chromatographic analysis indicated that most of the 2-*O*-D-xylopyranosyl-L-arabinose had undergone degradation. D-Xylose was detected in trace amounts.

(8) R. L. Whistler and D. F. Durso, THIS JOURNAL, **72**, 677 (1950).

(9) H. C. Hagedorn and B. N. Jensen, *Biochem. Z.*, **135**, 46 (1923).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

Synthetic Analogs of Cortical Hormones. II. 3-Substituted α-2,5-Trihydroxyacetophenone Derivatives

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The synthesis and some reactions of 3,5-diacetoxy-α-diazoacetophenone and of 3-acetoxy-, 3-nitro- and 3-bromo-2,5-diacetoxy-α-diazoacetophenone have been described. The diazo ketones yielded α-halo ketones by reaction with hydrogen halides, α-ketols by hydrolysis with hot dilute sulfuric acid, and (except for the 3-nitro diazo ketone) α-ketol acetates by reaction with hot acetic acid. The α-ketol acetates also were obtained by treatment of the respective α-bromo ketones with silver acetate in hot toluene or acetic acid. α,2,5-Triacetoxy-3-nitroacetophenone and 3-bromo-α,2,5-trihydroxyacetophenone produced appreciable eosinopenia in adrenalectomized mice. 2,5-Diacetoxy-3-acetylaminobenzoic acid, obtained by catalytic reduction of 3-nitrogentisic acid in acetic anhydride, also produced some eosinopenia in adrenalectomized mice.

Biological similarities between cortisone and salicylates,[2] and between salicylates and sodium gentisate,[3] have been reported recently. However, α,2,5-trihydroxyacetophenone (XXIII), a compound which appeared of interest because of superficial structural relationships to all of these active substances, was found to produce no lowering of the eosinophil count in adrenalectomized mice.[4]

Since it appeared likely that the biological activity of a compound such as α,2,5-trihydroxyacetophenone might be dependent, at least to some extent, upon the potential of its hydroquinone–quinone system, a series of α,2,5-trihydroxyacetophenone derivatives containing electron-attracting and electron-repelling substituents in the 3-position have been synthesized and submitted to pharmacological testing. The substances here described include two, α,2,5-triacetoxy-3-nitroacetophenone (XVIII) and 3-bromo-α,2,5-trihydroxyacetophenone (XXII), which showed appreciable activity in lowering the eosinophil count of adrenalectomized mice.

α,2,5-Triacetoxy-3-nitroacetophenone (XVIII), α,2,5-triacetoxy-3-bromoacetophenone (XIX) and α,2,3,5-tetraacetoxyacetophenone (XX), as well as α,3,5-triacetoxyacetophenone (XXIV), were obtained from the corresponding diazo ketones (VII, VIII, IX and XXV, respectively) by means of the general reaction sequence which has been described previously[4] for the preparation of α,2,5-triacetoxyacetophenone and which is illustrated in Fig. 1.

Hydrolysis of diazo ketone VIII with hot 15% sulfuric acid also yielded directly 3-bromo-α,2,5-trihydroxyacetophenone (XXII). However, under similar conditions, diazo ketone VII yielded a monoacetyl derivative of α,2,5-trihydroxy-3-nitroacetophenone (XXI).

When an attempt was made to prepare α,2,5-triacetoxy-3-nitroacetophenone (XVIII) by the action of boiling acetic acid on 2,5-diacetoxy-α-diazo-3-nitroacetophenone (VII), the only crys-

(1) Postdoctorate Research Fellow, 1951–1952.

(2) H. F. Hailman, *J. Clin. Endocrinol. and Metabolism*, **12**, 454 (1952).

(3) K. Meyer and C. Ragan, *Science*, **108**, 281 (1948).

(4) M. C. Kloetzel, R. P. Dayton and B. Y. Abadir, *J. Org. Chem.*, **20**, 38 (1955).