2. A new rearrangement leading to hydantoin derivatives substituted in the 4-position with an amino group has been described.

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THE MECHANISM OF CARBOHYDRATE OXIDATION. XII. THE ACTION OF POTASSIUM HYDROXIDE ON *l*-ARABINOSE AND *d*-XYLOSE

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When the hexose sugars, glucose, mannose, fructose and galactose are treated with aqueous solutions of potassium hydroxide, it is found that the amounts of certain reaction products are definitely dependent upon the normality of the solutions used and also upon the temperature employed. In a recent report, Shaffer and Friedman[1] have shown that the concentration of the sugar is also an important factor in the reaction of the hexose sugar under these conditions.

Since it is conceivable that pentose sugars may be formed as intermediate compounds in reactions involving the decomposition of hexose sugars in alkaline solutions, it becomes of much interest to know whether the products formed in a similar decomposition of the pentoses will show the same general relationship to the experimental conditions used as the hexose sugars do under similar circumstances. To obtain data with reference to this point was the principal objective in these experiments. For our experimental purposes we used the two easily accessible five-carbon atom sugars, *l*-arabinose and *d*-xylose. A similar·study concerning the theoretically possible intermediate trioses has been made in this Laboratory previously.[2]

Experimental

(a) **Materials.**—All materials used in these experiments were examined for their purity by well-known laboratory methods.

(b) **Manipulation. Lactic, Acetic and Formic Acids.**—A 100-cc. round-bottomed pyrex flask containing 25 cc. of potassium hydroxide of the desired normality was attached to a mechanical agitator placed in a thermostat. After sufficient time had elapsed for the flask and its contents to come to the desired temperature (25, 50 or 75°), 1.875 g. (0.5*M*) of the crystalline *l*-arabinose or *d*-xylose was added through a large funnel whose stem had been shortened. Usually ten samples, including different normalities and duplicates, were started within the period of an hour. As in all the previous studies in this series, the agitation of these solutions was continued for forty-eight hours. Owing to the difficulties arising from the deposition of moisture during the preparation of the reacting systems at 75°, it was found more convenient to place the sugar in the flask first and then add the standard alkali solution. The general procedure from this

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[1] Shaffer and Friedman, *J. Biol. Chem.*, **86**, 345 (1930).

[2] (a) Evans and Hass, THIS JOURNAL, **48**, 2703 (1926); (b) Evans and Cornthwaite, *ibid.*, **50**, 486 (1928).

point on for the determination of lactic, acetic and formic acids has been described previously. It was found that the difficulties attending the determination of zinc lactate due to the presence of large amounts of gum (probably a mixture of the zinc salts of saccharinic acids) could in some measure be overcome by boiling the aqueous solution with a little norite before removing the insoluble zinc carbonate. Obviously, this also introduces a possible error for zinc lactate.

In the determination of formic acid it was found best to attach a Kjeldahl bulb to the distilling column in order to prevent any of the solution from bumping over into the distillate. The receiver, a 250-cc. distilling flask, was completely immersed in a freezing mixture of salt and ice. A piece of glass tubing was sealed to the end of the condenser, in order that the condenser tube might extend down into the bulb part of the receiver. This was done for the purpose of diminishing, as far as possible, the loss of vapors from the receiver.

The distillations were carried to dryness, after which about 10 cc. of distilled water was added to the dry salt residue and the distillation again carried to dryness. It was found that much better results could be obtained in the formic acid determination by thus distilling the residues to dryness three or four times.

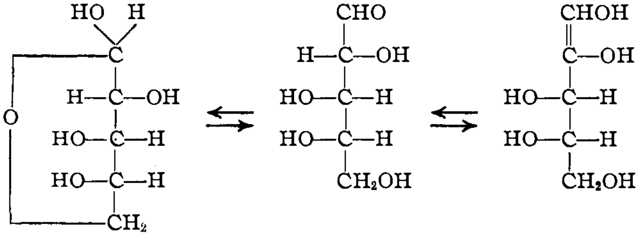
After the distillation was complete, the stem of the Kjeldahl bulb which extended into the flask was rinsed into the salt residue, while the remainder of the bulb and the condenser was rinsed with distilled water into the distillate. The distillate was then carefully transferred to a 100-cc. calibrated flask. After the temperature of the distillate had adjusted itself to that of the room, enough distilled water was added to make a volume of 100 cc.

Pyruvic Aldehyde Osazone.—In this determination, 25 cc. of the standard potassium hydroxide solution was placed in a 100-cc. round-bottomed flask, together with 17.5 cc. of 95% ethyl alcohol and 1.875 g. of the pentose sugars. After being agitated for forty-eight hours at the desired temperature, the pyruvic aldehyde osazone was determined as previously described.

Theoretical Discussion and Summary

When the behavior of *l*-arabinose and *d*-xylose in alkaline solutions is examined from the standpoint of their ability to form enediols in the same manner as has been repeatedly discussed for the hexose sugars, then it is possible to predict that the pentose sugars will form certain compounds which are also formed in the alkaline decomposition of the hexose sugars. Nef[3] made an exhaustive study of the behavior of these two pentose sugars in 8 N potassium hydroxide solution, and in an earlier report he gave an account of the behavior of *l*-arabinose in an alkaline cupric hydroxide system.

***l*-Arabinose 1,2-Enediol.**—The behavior of *l*-arabinose under our experimental conditions is shown in the equations



l-Arabinose *l*-Arabinose, aldehyde form *l*-Arabinose 1,2-enediol

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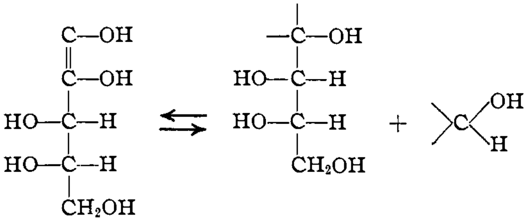
[3] Nef, (a) *Ann.*, **376**, 1 (1910); (b) **357**, 214 (1907).

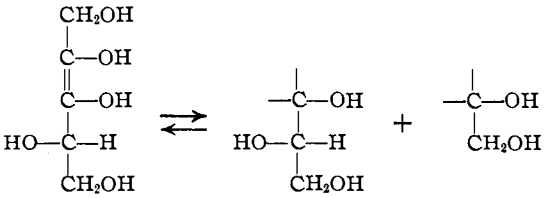
If the *l*-arabinose 1,2-enediol should undergo cleavage at the double bond, erythrose and formaldehyde would be formed according to the reaction


l-Arabinose 1,2-enediol — Erythrose, active form — Formaldehyde, active form

In these experiments the formaldehyde may be regarded as one of the sources of formic acid. Nef[3a] found that 8 *N* alkaline solutions of glycol aldehyde gave *traces* only of formic acid and no lactic acid. It has been shown in this Laboratory[4] that alkaline solutions of glycol aldehyde extending over 0.1–10 *N* give no trace of lactic acid under the experimental conditions which are employed in these experiments. However, such solutions gave rise principally to C_4 saccharins, which must have arisen from the tetroses formed.[5]

Therefore it follows that the lactic acid found in our experiments must have arisen through some other possible decomposition of the pentose sugars than through the intermediate formation of a tetrose sugar. Obviously, the same general structural relations and conclusions are equally true for *d*-xylose.

***l*-Arabinose 2,3-Enediol.**—As the concentration of the alkali is increased, the pentose sugars should give rise in each case to 2,3-enediols, which in turn may undergo a cleavage at the double bond, thus giving rise to glyceric aldehyde and glycol aldehyde. These changes are shown in the equation


l-Arabinose 2,3-enediol — Glyceric aldehyde active form — Glycol aldehyde active form

(a) **Lactic Acid.**—In the absence of an oxidizing agent, glyceric aldehyde becomes the source of lactic acid, through the intermediate formation of pyruvic aldehyde. If the alkaline solutions of these pentose sugars contain equilibrated systems,[6] similar to those which have been thought to

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[4] To be published.

[5] *Cf.* Fischer and Landsteiner, *Ber.*, **25**, 2549 (1892).

[6] *Cf.* Spoehr and Strain, *J. Biol. Chem.*, **85**, 365 (1929).

exist in alkaline solutions of the hexose sugars under the same conditions, then it would follow that the quantity of lactic acid formed should increase with an increase in the alkali normality. That this general relationship holds true may be seen in Fig. 1. Thus we see that the same general temperature relationships are also found to exist in the formation of lactic acid from the alkaline pentoses as were observed in the solutions of the hexoses. As the temperature rises, it is seen that the rate of formation of lactic acid at 75° becomes less than that at 50°. This same observation

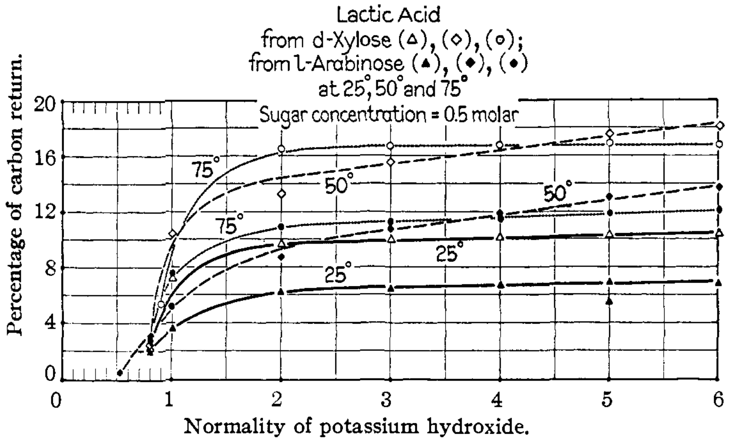


Fig. 1.

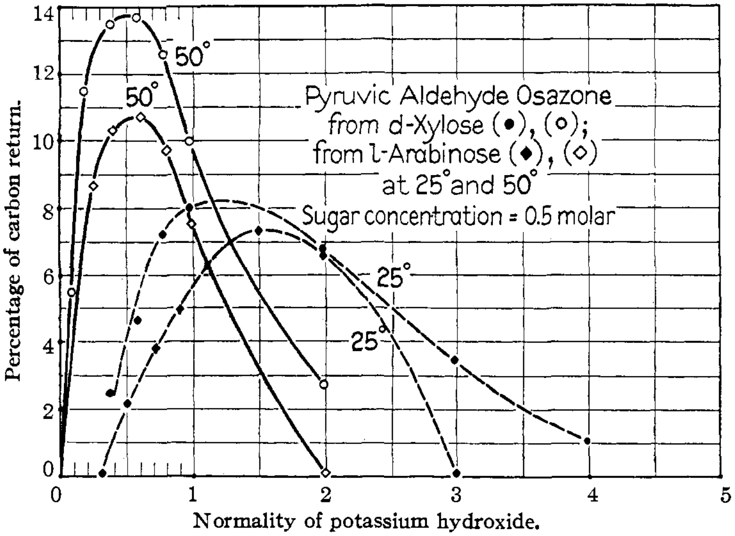
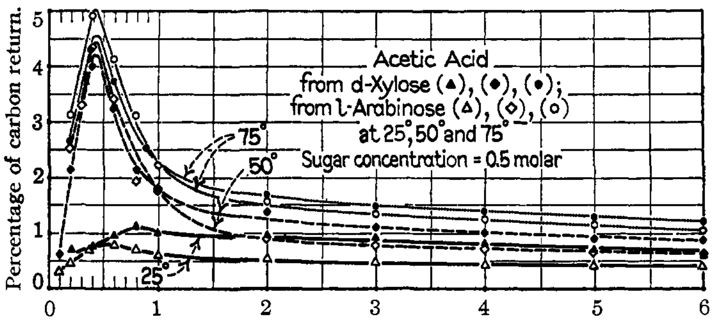


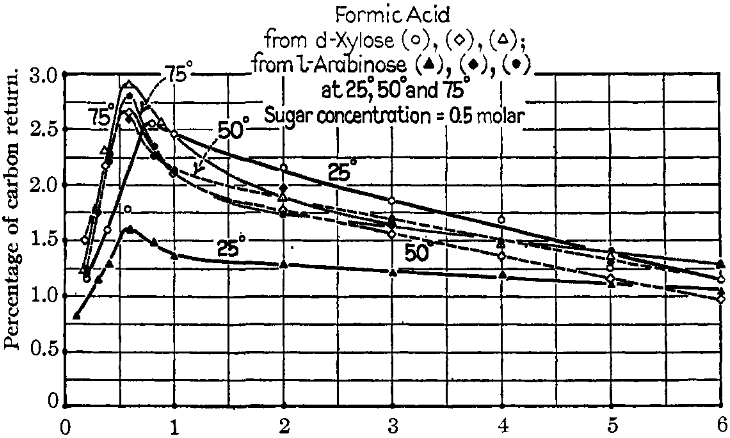
Fig. 2.

has also been made previously with mannose,[7] glucose,[7] fructose[8] and the trioses.[2] Although the cause of this difference has not been systematically investigated, yet this change may be due to an increasing rate of formation of the saccharinic acids arising from an increasing temperature, a condition which obviously would result in a corresponding decrease of the alkali normality of the reacting system due to neutralization. In time this would tend to diminish the pentose 2,3-enediol formation.



Normality of potassium hydroxide.

Fig. 3.



Normality of potassium hydroxide.

Fig 4.

(b) **Pyruvic Aldehyde.**—It is generally accepted that pyruvic aldehyde formation is the forerunner of lactic acid in the alkaline decomposition of the sugars. Since this acid was found in these reactions with the pentoses an examination was made for the presence of pyruvic aldehyde.

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[7] Evans and O'Donnell, This Journal, **50**, 2550 (1928).

[8] Evans and Hutchman, *ibid.*, **50**, 1497 (1928).

Our results are shown in Fig. 2. The temperature and alkali effects are practically the same as those which have been observed in this Laboratory with the trioses,[2] certain hexoses[7,8] and maltose.[9]

(c) **Acetic and Formic Acids.**—Previously it has been thought that the presence of acetic acid in these reactions might be due to a decomposition of pyruvic aldehyde into acetaldehyde and carbon monoxide, which, in turn, would yield acetic and formic acids, respectively. If this were true, then these acids should also show maximum yields, because the tendency of the pyruvic aldehyde toward a minimum after the maximum, has been thought to be due to the increasing rate of lactic acid formation with the increasing normality of the alkali. That these general considerations are also true in the alkaline decomposition of the pentoses may be seen in Figs. 3 and 4. It is also conceivable that the glycol aldehyde which is formed in the decomposition of the 2,3-pentose enediols as well as the 1,2-triose and 2,3-hexose enediols may also give rise to acetic acid formation.[10]

From the data presented in this report it is clear that any pentoses which might possibly form in the alkaline decomposition of the hexose sugars are to be considered as possible sources of pyruvic aldehyde, lactic, acetic and formic acids.

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A MODIFICATION OF THE SKRAUP SYNTHESIS OF QUINOLINE

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The Skraup synthesis is widely used as a method for the preparation of quinoline and its derivatives. The synthesis, when performed in the manner advocated by Skraup, is often accompanied by a violent reaction. In addition, the yields obtained are variable and often low. To overcome the disadvantages of the original Skraup method, various improvements have been published from time to time.

To date the most important of the improvements made have been the ferrous sulfate modification of Clarke and Davis,[1] the acetic acid modification of Cohn and Gustavson[2] and a thorium–vanadium oxide method of Darzens, Delaby and Hiron.[3] The ferrous sulfate modification gives a very much better yield than does the original Skraup method. The re-

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[9] Evans and Benoy, THIS JOURNAL, **52**, 294 (1930).

[10] (a) R. C. Hockett, Master's Thesis, The Ohio State University, **1928**; (b) G. P. Hoff, Doctor's Dissertation, **1925**; (c) *cf.* Evans, *Chemical Reviews*, **6**, 306 (1929).

[1] Clarke and Davis, "Organic Syntheses," John Wiley and Sons, Inc., New York, **1922**, Vol. II, p. 79.

[2] Cohn and Gustavson, THIS JOURNAL, **50**, 2709 (1928).

[3] Darzens, Delaby and Hiron, *Bull. soc. chim.*, **47**, 227 (1930).