Studies on the Chemical Decomposition of Simple Sugars. XI. Acetol Formation from ^{14}C-Labeled Pentoses*

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In the preceding report⁽¹⁾, formation of acetol from labeled hexoses was examined, and the examination of the activity distribution revealed the origins of every carbon atom of acetol produced. The terminal carbons of hexoses were found to be converted into methyl carbon of acetol.

Moreover, some characteristic properties of

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1) R. Goto, J. Hayami, K. Kudo and S. Otani, This Bulletin, 34, 753 (1961).

the reaction suggested that on one of the steps of the reaction, a cleavage in the carbon chain of an intermediate occured between the C-3 and the C-4 of the original hexose, and that no skeletal rearrangement in the C_3-group was involved before and after the splitting of the chain.

In a series of papers of the same title, two different mechanisms of acetol formation were proposed[1], the one—Nodzu's mechanism[2a]—assumed an intermediate formation of acetylformoin from a hexose, and the other—Goto's mechanism—assumed an intramolecular oxidation reduction of 3-deoxyhexosone. Goto's challenge for Nodzu's mechanism[2b], had its starting point in the need of a general interpretation for the acetol formation from pentose and hexose. He inferred from Nodzu's mechanism that if it was applied to a pentose, it could not lead to the formation of acetol. However, a pentose as well as a hexose gives acetol. Therefore, for the establishment of a general mechanism of acetol formation, it is important to decide whether there is a common mode of reaction between the mode of acetol formation from pentose and that from hexose.

In the present work, D-xylose-1-^{14}C and D-arabinose-5-^{14}C were synthesized and these were decomposed in concentrated buffer solution of potassium hydrogen phosphate and acetol was isolated. The distribution of labeled positions was, then, determined.

Experimental

Labeled Sugars and Assay Method.—*D-Xylose-1-^{14}C.*—D-Xylose-1-^{14}C was synthesized from D-glucose-1-^{14}C by Sowden's method[3] with an improvement in the reduction procedure[*1]; that is, instead of the catalytic hydrogenation of 1,2-*O*-isopropylidene-D-*xylo*-dialdopentofuranose (I)[*2], reduction with lithium aluminum hydride was adopted as was the case with the synthesis of 3-*O*-methyl-D-xylose by Corbett[4].

I was prepared from 2.5 g. of D-glucose-1-^{14}C according to Sowden's method. Ethereal solution (70 ml.) of I was placed in a two-necked flask equipped with a dropping funnel and a reflux condenser. Lithium aluminum hydride (0.75 g.) in ether (75 ml.) was added dropwise in 30 min.; the mixture was refluxed for 30 min. Excess of lithium aluminum hydride was decomposed with ethyl acetate (2.5 ml.) and water (45 ml.); ether on the upper layer was removed by air current. Residual aqueous solution was neutralized with dilute sulfuric acid and filtered. The filtrate was concentrated under reduced pressure. The residual light syrup was dissolved in 60 ml. of 0.1 N sulfuric acid and heated in a boiling water bath for an hour. After cooling, the hydrolyzate was passed through an ion-exchange resin (10 ml. of Amberlite IR-120 and 25 ml. of Amberlite IR-45). The effluent and the washing were combined and concentrated under reduced pressure. D-Xylose-1-^{14}C often crystallized on concentration. However, if necessary, the solution was lyophilized after concentration to an appropriate volume, and the residue was crystallized from methanol-isopropanol in the usual way[5]. Yield; 1.5 g. or 72% (in typical run).

D-Arabinose-5-^{14}C. — D-Arabinose-5-^{14}C was synthesized by Ruff degradation according to Isbell[6].

Radioassay. — Every sample was converted into barium carbonate by Van Slyke-Folch wet combustion. Barium carbonate was collected on filter paper, and counted in an infinite thickness in a 2π-gas flow counter[*3]. Only iodoform was counted in a medium thickness and corrected for an infinite thickness by parallel counting of the parent sugar of about an equal thickness. Probable errors of the counting were all within 5%.

Decomposition of Labeled Pentose.—Ten grams of arabinose or xylose was dissolved into 200 ml. of concentrated solution of potassium hydrogen phosphate (40%, pH 6.7); the mixture was heated and distilled in the way described earlier[1,7].

TABLE I. RADIOASSAY DATA FOR ^{14}C-LABELED PENTOSES

	Sample	Carbon atom (s)	Radio-activity μc/mol.
	Radioacetol from D-xylose-1-^{14}C		
	Xylose-1-^{14}C		19.6
Acetol	Acetol semicarbazone	all	9.7
	Iodoform	CH_3	9.5
	Indirectly determined	CO	—*
	Formaldehyde dimedone	CH_2OH	almost 0
	Radioacetol from D-arabinose-5-^{14}C		
	Arabinose-5-^{14}C		257
Acetol	Acetol semicarbazone	all	136
	Iodoform	CH_3	125
	Indirectly determined	CO	—*
	Formaldehyde dimedone	CH_2OH	14

* Substantially free from radioactivity.

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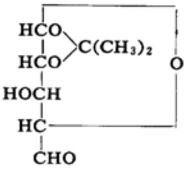
2) a) R. Nodzu et al., *Mem. Coll. Sci. Kyoto Imp. Univ.*, **A20**, 197 (1937).
b) R. Goto, *J. Chem. Soc. Japan* (*Nippon Kwagaku Kwaisi*), **64**, 999, 1054 (1943).

[*1] Isbell et al. also proposed an excellent method of reduction with $LiBH_4$ in tetrahydrofuran. (H. S. Isbell et al., *J. Research NBS*, **64A**, 359 (1960)).

[*2] 

(I) or its dimeric form.

3) J. C. Sowden, *J. Am. Chem. Soc.*, **73**, 5496 (1951).

4) W. M. Corbett, G. N. Richards and R. L. Whistler, *J. Chem. Soc.*, **1957**, 11.

5) Cf. H. S. Isbell et al., *J. Research NBS*, **48**, 163 (1952).

6) H. S. Isbell, N. B. Holt and H. L. Frush, ibid., **57**, 95 (1956).

[*3] A product of Metro Electronic Institute, Kyoto.

7) R. Nodzu, This Bulletin, **10**, 122 (1935).

Degradation was carried out in the same way as reported earlier[1], but degradation of the acetic acid was not undertaken. Radioactivity of the carbonyl carbon of acetol was determined indirectly from the total activity of acetol deducting the activities of methyl and carbinol carbon. These data are summarized in Table I.

Results and Discussion

The results from radioassay may be expressed in the following way.

1) In the case of D-xylose-1-^{14}C, radioacetol of about a half specific radioactivity of the parent xylose was obtained.

On the degradation, the methyl carbon of acetol was converted into iodoform which contains substantially all the activity of the acetol. The carbinol carbon of acetol was converted into formaldehyde by periodate oxidation and was captured as formaldehyde dimedone which was found almost free from activity. In consequence, xylose-1-^{14}C was proved to produce acetol-3-^{14}C (methyl-^{14}C).

2) D-Arabinose-5-^{14}C similarly yielded radioacetol of about a half specific activity of the original arabinose.

The degradation gave iodoform which containes almost all the radioactivity of parent acetol, however a slight degree of activity was observed for formaldehyde which was derived from carbinol carbon of acetol.

Therefore, it may be concluded that arbinose-5-^{14}C produces acetol-3-^{14}C.

The above results are in accord with the expectation from a tracer experiment of hexoses, that is, the terminal carbon of a pentose —C-1 and C-5— are converted into methyl carbon of acetol.

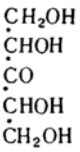
These facts suggest that a common mechanism operates in the formation of acetol from simple sugars.

From Table I, a similar behavior of D-arabinose-5-^{14}C and D-xylose-1-^{14}C in the formation of acetol is perceived. These facts constitute the characteristics of the acetol formation from a pentose.

Ignoring the effect of a difference in configuration between arabinose and xylose, also ignoring the slight randomization of a label, the contribution ratio of the upper C_3 and the lower C_3 of a pentose may be postulated as about 1 : 1[8]. Almost an equal contribution of upper and lower C_3 part of a pentose for formation of acetol, suggests participation of an intermediate of a good symmetrical structure. This means destruction of the configurational difference between arabinose and xylose to yield an intermediate of common or analogous nature through some transformation reaction of a pentose[*4].

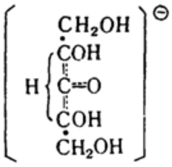
In such a reaction an isomerization of a sugar plays an important role on the essential pathway of the reaction, an effect of symmetrical natures of an intermediate may be often visualized[9].

An examination of the mechanism of acetol formation, which will be discussed in detail in a succeeding paper[10], suggests the above intermediate to be 3-ketopentose (II) or its enediolate[*5,11,12] (III), in which, the configurational difference between arabinose and xylose is destroyed.



$$\begin{array}{l} \dot{C}H_2OH \\ \dot{C}HOH \\ \dot{C}O \\ \dot{C}HOH \\ \dot{C}H_2OH \end{array}$$

(II)



$$\left[\begin{array}{l} \quad CH_2OH \\ H\left\{ \begin{array}{l} \dot{C}OH \\ \dot{C}{=}O \\ \dot{C}OH \end{array} \right. \\ \quad \dot{C}H_2OH \end{array} \right]^{\ominus}$$

(III)

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[*4] In addition, there is no essential difference between the acetol formation and a configuration of a monosaccharide. Also refer to R. Goto (loc. cit.)

8) H. F. Bauer and C. Teed, *Can. J. Chem.*, **33**, 1824 (1955). Also refer to M. Gibbs, *J. Am. Chem. Soc.*, **72**, 3964 (1950).

[*5] Or their equivalent compounds.

9) J. C. Sowden, M. G. Blair and D. J. Kuenne, *J. Am. Chem. Soc.*, **79**, 6450 (1957).

10) J. Hayami, This Bulletin, **34**, 927 (1961).

11) R. L. Whistler and J. N. BeMiller, "Advances in Carbohydrate Chem.", Vol. **13**, (1957), p. 289.

12) J. C. Sowden, ibid., Vol. **12**, (1957) p., 36.
J. C. Speck, Jr., ibid., Vol. **13**, (1958), p. 63.