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Note

Anionic intermediates in base-catalyzed reactions of monosaccharides

YUAN Z. LAI*
College of Forest Resources, University of Washington, Seattle, Washington 98105 (U. S. A.)
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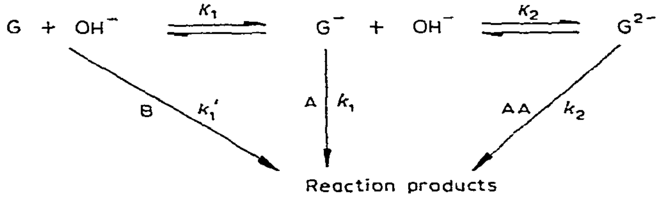
Recently, Garrett and Young[1] interpreted the kinetics of base-catalyzed transformations among D-glucose, D-mannose, and D-fructose in terms of an SN2 type of reaction (Path B in Scheme 1), where G is the undissociated species, and k'_1 is the bimolecular rate-constant.

Although their experimental data seem to conform with such an interpretation, it is, however, obviously inconsistent with the positive entropy changes (4.15 to 18.1 eu)[1] and with the enolization mechanism generally accepted[2,3] for these reactions. Furthermore, the proposed mechanism fails to account for two, distinct, kinetic patterns: (*a*) the rate of an aldose–ketose transformation increases initially with increasing concentration of hydroxyl ion and levels off to a constant value at a concentration of base that is ~0.15*N*; whereas (*b*) the rate of degradation of D-fructose increases continuously with the concentration of base up to the highest alkalinity used (0.6*N*). Surprisingly, the latter observation was regarded as showing that, under these conditions, according to Path B, only the uncharged species is present. This appears rather unlikely, because, under the experimental conditions (pH 13), most of the molecules of D-fructose should have been in the dissociated form, as its pK value has been determined[4] to be 12.27. In view of these discrepancies, the original data were restudied, and, as discussed in this communication, have been found to fit the alternative mechanism better, in terms of the formation of mono- and di-anionic intermediates (Paths A and AA in Scheme 1).



Scheme I

According to this approach, the rate-controlling steps of a reaction are those

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*Present address: Department of Chemistry, University of Montana, Missoula, Montana 59801 (U. S. A.)

governed by k_1 and k_2, specific rate-constants for spontaneous transformation of mono- and di-anionic intermediates, G^- and G^{2-}, respectively (see Scheme 1), and the observed first-order rate-constant for reaction at a given concentration of hydroxyl ion is:

$$k_{\mathrm{obs}} = \frac{K_1[\mathrm{OH}^-]\{k_1 + k_2 K_2[\mathrm{OH}^-]\}}{1 + K_1[\mathrm{OH}^-] + K_1 K_2[\mathrm{OH}^-]^2} \qquad (1)$$

For aldose–ketose transformation in a dilute solution of an alkali (less than 0.01*N*), equation *1* can be reduced to equation *2*, as the magnitude of K_2 is[5] in the order of 1.5 at 25°, and the term $K_2[\mathrm{OH}^-]$ is negligible.

$$k_{\mathrm{obs}} = \frac{K_1 k_1[\mathrm{OH}^-]}{1 + K_1[\mathrm{OH}^-]} \qquad (2)$$

From equation *2*, the following expression can be obtained.

$$1/k_{\mathrm{obs}} = 1/k_1 + 1/K_1 k_1[\mathrm{OH}^-] \qquad (3)$$

Fig. 1 shows plots of $1/k_{\mathrm{obs}}$ against $1/[\mathrm{OH}^-]$ for the aldose–ketose transformations, and these are straight lines. The kinetic parameters obtained from these plots are recorded in Table I. It should be mentioned that the rate equation *2* is practically identical to that used by Garrett and Young[1] for a bimolecular reaction, except that the term $k_1 K_1$ is replaced by k_1', and a good relationship between these two quantities has been obtained (see Table I).

Despite the fact that values of k_1 and K_1 were obtained for reactions at base

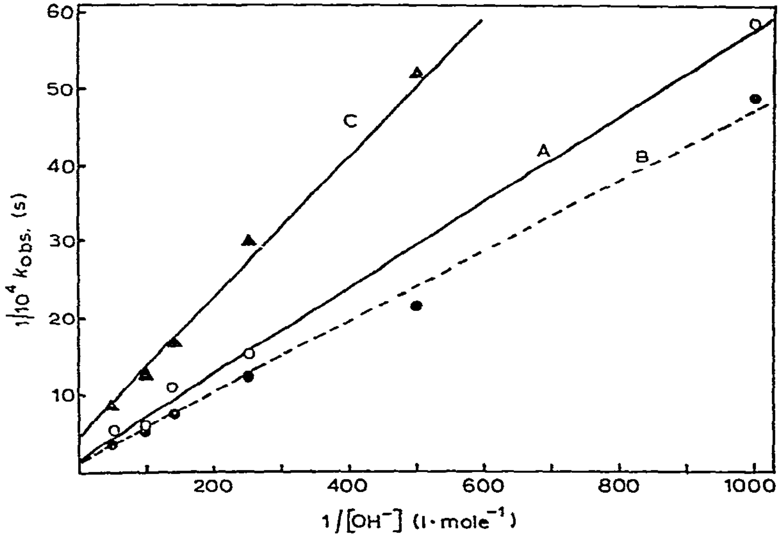

Fig. 1. Plot showing linear relationship between values of $1/k_{\mathrm{obs}}$ and $1/[\mathrm{OH}^-]$ for the transformation reactions of D-fructose (A), D-glucose (B), and D-mannose (C) at 35°.

TABLE I

OBSERVED EQUILIBRIUM CONSTANTS (K) AND SPECIFIC RATE CONSTANTS (k)[a] FOR THE ALKALINE TRANSFORMATION OF SOME HEXOSES[b] AT 35°

Reaction pathway	K_1	K_2	k_1	k_2	$K_1 k_1'$[c]	k_1'[d]
F → G	20.5		0.80		16.4	16.1
	20.5	0.4	0.64	2.20		
G → F	30.2		0.75		22.6	20.7
M → F	50.6		0.20		11.1	8.4
F → D	20.5	0.4	0.06	2.15	1.2	1.3

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[a] Unit of 10^{-4} s^{-1}. [b] Based on the model Glucose (G) ⇌ Fructose (F) → degradation products (D).
↖ ↗
Mannose (M)

[c] Products of k_1 and K_1 with units of 10^{-4} l·mol^{-1}·s^{-1}. [d] Bimolecular rate-constants reported by Garrett and Young[1] with the unit of 10^{-4} l·mol^{-1}·s^{-1}

concentrations below 0.01*N*, the theoretical curves of k_{obs} derived from these constants by use of equation *2* are in good agreement with experimental data up to the highest concentration used (0.6*N*) for the reactions of D-glucose and D-mannose. Thus, the rate constants k_1 and k_2 must be almost equal for these reactions, as values of k_{obs} reach their limiting values at 0.15*N* concentration of base, and presence of di-anionic species has practically no effect on the rate of reaction. However, the experimental point for the reaction of D-fructose at the concentration of 0.6*N* is about 15 per cent higher than the calculated value; assuming no errors in the data, this may indicate that the value of k_2 is slightly higher than that of k_1.

On the other hand, equation *2* is not applicable to the degradation reaction of D-fructose, as the rate of it is inappreciable in alkali solutions less than 0.01*N*, and it fails to reach a limiting value for the entire range of pH used. This behavior, in contrast to that of the transformation reactions, shows that di-anionic species play an important role in this type of reaction. The rate-constants of this reaction *via* mono- and di-anionic intermediates can be estimated by equation *4* (which is rearranged from equation *1*).

$$k_{obs}\left(\frac{1+K_1[OH^-]+K_1K_2[OH^-]^2}{K_1[OH^-]}\right) = k_1+k_2K_2[OH^-] \qquad (4)$$

For D-fructose, the value of K_1 has been determined to be 20.5 at 35° (see Table I), and the approximate magnitude of K_2 is assumed to be 0.4, if it is one-fiftieth of K_1, as generally believed[5].

The left-hand side of equation *4* was plotted against the concentration of hydroxyl ion (see Fig. 2), giving a straight line for the degradation, as well as for the transformation, of D-fructose. Constants k_1 and k_2 (given in Table I) were calculated from the slope ($k_2 \cdot K_2$) and the intercept (k_1); they indicate that the rate constant of the degradation reaction *via* a di-anionic intermediate is 36 times that *via* a mono-anionic intermediate; this ratio is lowered to 4 for the transformation reaction.

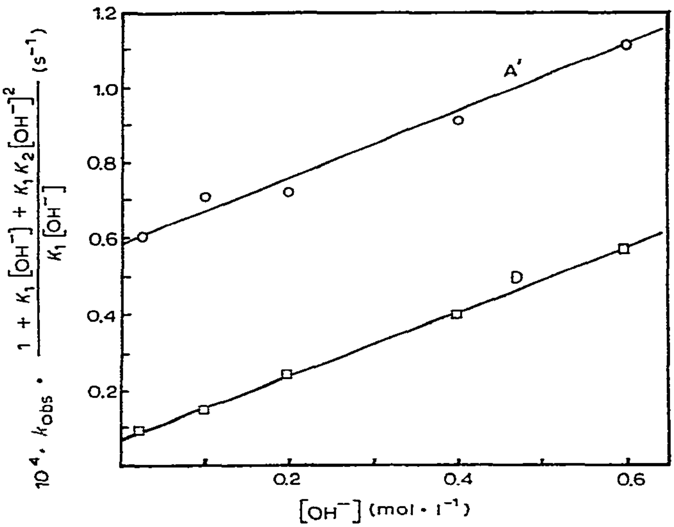

Fig. 2. Plot of the left-hand side of equation *4* *versus* the hydroxyl-ion concentration for the transformation (A') and degradation (D) of D-fructose at 35°.

The foregoing discussion clearly shows that base-catalyzed reactions of free sugars fit better the formation of anionic intermediates, in conformity with the results of base-catalyzed, endwise depolymerization of amylose[6] and β-D-(1→3)-glucan[7]. The rate-determining step of the latter reactions is the transformation of a reducing, D-glucose end-group to a D-fructose moiety, and thus there is an almost identical pattern, in that the rate of reaction becomes independent of the concentration of hydroxyl ion at about 0.15*N*, as has been found for all these reactions.

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