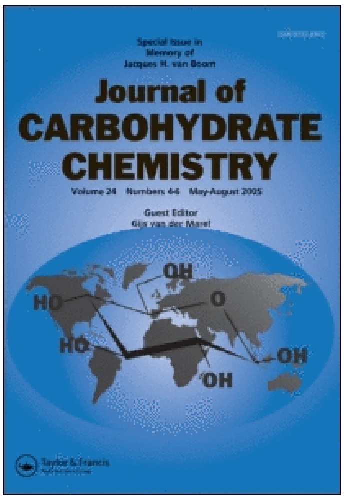

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KINETICS AND MECHANISM FOR THE EPIMERIZATION OF ALDOPENTONIC ACID POTASSIUM SALTS IN AQUEOUS ALKALI

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ABSTRACT

The epimerization of the potassium salts of L-arabinonic, D-ribonic, D-lyxonic and D-xylonic acids in aqueous alkali was followed kinetically by gas chromatographic analyses of the silylated samples. Mass spectrometric measurements indicated that the reaction proceeded by a complete proton exchange at C2, the kinetic deuterium isotope effect, $\underline{k}_H/\underline{k}_D$, being 4.2. Most probably the proton transfer from the C2 atom to hydroxide ion is the rate-limiting stage of the epimerization.

INTRODUCTION

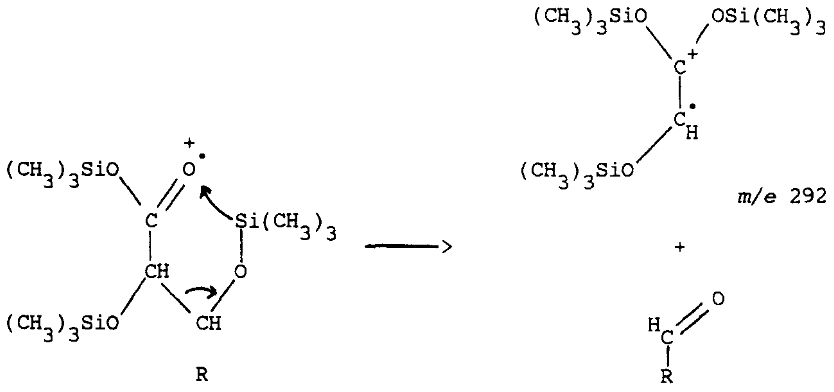
Epimerization plays an important role in the synthetic chemistry of sugars, both at the laboratory and industrial scale. For example, the generally known conversion of D-glucose to D-ribose[1-3] involves a hydroxide ion catalyzed epimerization of calcium D-arabinonate to D-ribonate.[2] Although this pathway has recently been simplified by epimerizing D-arabinose directly to D-ribose in the presence of molybdic acid loaded on anion exchange fiber,[4] the base-catalyzed epimerization of aldonic acid salts is still a process of considerable interest.[5,6]

Our present report deals with the kinetics of the epimerization of isomeric potassium aldopentonates in aqueous alkali. The mechanism was elucidated by studying mass spectroscopically the proton exchange at C2 during the epimerization, and by measuring the effect of the C2 deuteration on the rate of epimerization. Furthermore, the activation parameters were determined.

RESULTS AND DISCUSSION

Table 1 summarizes the kinetic data for the reversible epimerization of potassium arabinonate to ribonate and xylonate to lyxonate. The rate constants obtained by approaching the equilibrium composition from opposite directions were equal within the limits of experimental errors. No marked side reactions were detected. As seen from Table 1, the rate of epimerization is rather sensitive to the configuration of the starting material, the relative rate constants at 373.2 K being 1 for potassium ribonate, 0.60 for arabinonate, 0.25 for lyxonate and 0.13 for xylonate.

The proton exchange at C2 of the starting materials was studied by epimerizing L-(2-^{1}H)arabinonate in alkaline deuterium oxide ([KOD] = 0.047 mol dm^{-3}) and analyzing the isotopic composition of the silylated products by gas chromatography/mass spectrometry. Ions with *m/e* equal to 292 and 293, formed according to Scheme 1,[7] were selected as indicators of the isotopic composition at C2. After 19 h at 413.2 K the deuterium fraction at C2 of the starting material was 0.46, whereas the ribonate formed was quantitatively deuterated at C2. In other words, the epimerization appears to be accompanied with a complete proton exchange at C2. The fact that the C2 proton is really abstracted in the rate-limiting step was shown by measuring the rate constants for the epimerization of potassium



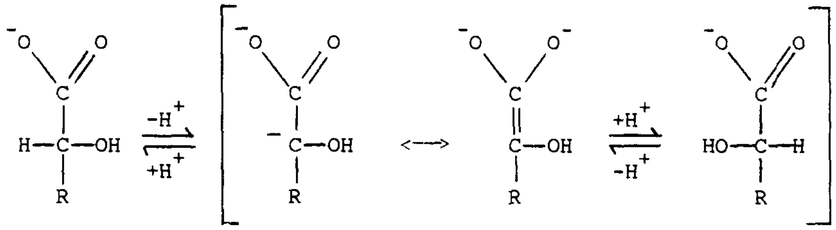
Scheme 1

TABLE 1

Second-order rate constants, and the entropies and enthalpies of activation for the epimerization of isomeric potassium aldopentonates in aqueous alkali.[a]

Reaction	T (K)	$10^5 k_3$ ($dm^3\ mol^{-1}\ s^{-1}$)		$10^5 k_{-3}$ ($dm^3\ mol^{-1}\ s^{-1}$)		$\Delta S^{\ddagger}$ [b] ($J\ K^{-1}\ mol^{-1}$)	$\Delta H^{\ddagger}$ ($kJ\ mol^{-1}$)
Arabinonate $\underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}}$ Ribonate	373.2	1.2	(1.2)[c]	1.9	(2.0)[c]	-18 ± 3[d]	121 ± 2[d]
	383.2	3.4		6.0		-21 ± 8[e]	181 ± 3[e]
	393.2	8.7	(9.0)	14			
	413.2	57	(56)	87			
Xylonate $\underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}}$ Lyxonate	373.2	0.28	(0.25)	0.53	(0.50)	-21 ± 18[d]	124 ± 7[d]
	383.2	0.61		1.4		- 8 ± 9[e]	127 ± 4[e]
	393.2	2.0		4.0			
	413.2	14		30			

a. The first-order rate constants measured at [KOH] = 0.048 mol dm^{-3}.
b. At 373.2 K.
c. The values in the parentheses were obtained by the Arrhenius equation.
d. For the forward reaction.
e. For the reverse reaction.



Scheme 2

D-(2-^{2}H)arabinonate to D-(2-^{1}H)ribonate in aqueous alkali. The values obtained for the second-order rate constants were 2.2 x 10^{-5} and 1.3 x 10^{-4} $dm^3\ mol^{-1}\ s^{-1}$ at 393.2 and 413.2 K, respectively. The kinetic deuterium isotope effect, $\underline{k}_H/\underline{k}_D$, is thus about 4.2. The value of this magnitude ($3 < \underline{k}_H/\underline{k}_D < 7$) is typical for reactions proceeding by a rate-limiting proton abstraction from an sp^3 hybridized carbon.[8] Most probably potassium aldopentonates are epimerized in aqueous alkali via a rate-limiting transfer of the C2 proton to hydroxide ion with concomitant formation of a resonance stabilized C2 carbanion (Scheme 2). A similar mechanism has been earlier suggested for the epimerization of aldonic acid lactones in the presence of amines.[9] The values for the entropy of activation of the epimerization reaction are listed in Table 1. They are all moderately negative, and may thus be considered to be consistent with the suggested bimolecular nature of the rate-limiting stage.

EXPERIMENTAL

Materials. The potassium salts of L-arabinonic and D-ribonic acids were obtained by treating the corresponding commercial γ-lactones (Koch-Light, Fluka) in aqueous solution with an equal amount of potassium hydroxide. Potassium D-lyxonate and D-xylonate were prepared by oxidizing D-lyxose and D-xylose (Fluka) with potassium hypoiodite in methanol.[10] Potassium D-(2-^{2}H)arabinonate was obtained similarly from D-(2-^{2}H)arabinose, synthesized as described previously.[11] The isotopic purity of the deuterated starting material, 2-*O*-benzyl-D-(2-^{2}H)arabinose, was checked by NMR spectroscopy in pyridine-$\underline{d}_5$ (a Tesla 100 MHz spectrometer).

Kinetic measurements. The epimerization reactions were carried out in sealed tubes immersed in a thermostated bath. Each tube contained 0.21 mL of the reaction solution, the initial substrate concentration being 1.6 x

10^{-3} mol dm^{-3}. At suitable intervals the tubes were transferred to an ice bath, and the solvent was removed with a nitrogen stream. The residues were dried over phosphorous pentoxide (24 h), and then silylated by adding 50 µl of anhydrous pyridine, 100 µl of bis(trimethylsilyl)trifluoroacetamidide and 50 µl of trimethylchlorosilane. The sealed tubes were immersed for several h in an ultrasonic bath and finally incubated for 10 min at 120 °C. The compositions of the silylated samples were determined by gas chromatography (Varian 1400) on a column (40 m x 0.27 mm) coated with the OV-1 phase of 0.1 µm film thickness. The method employed was similar to that described by Petersson.[12]

Mass spectroscopic study of proton exchange at C2 during epimerization. Potassium L-(2-^{2}H)arabinonate was epimerized in alkaline deuterium oxide, as described above. The silylated residues of the dried samples were analyzed by gas chromatography/mass spectrometry (Varian MAT 711 spectrometer) using an OV-17 packed column (1.8 m x 2 mm).

Calculation of the rate constants. The pseudo first-order rate constants $\underline{k}_1$ and $\underline{k}_{-1}$, for the reversible epimerization of AH to BH (eqn. 1) were calculated via eqn. (2) by applying the least-squares method.

$$\mathrm{AH} \underset{\underline{k}_{-1}}{\overset{\underline{k}_1}{\rightleftharpoons}} \mathrm{BH} \qquad (1)$$

$$\frac{[\mathrm{BH}]_t}{[\mathrm{AH}]_{\underline{t}}} = \frac{\underline{k}_1 - \underline{k}_1 e^{-(\underline{k}_1+\underline{k}_{-1})\underline{t}}}{\underline{k}_{-1} + \underline{k}_1 e^{-(\underline{k}_1+\underline{k}_{-1})\underline{t}}} \qquad (2)$$

The pseudo first-order rate constant, $\underline{k}_2$, for the epimerization of potassium (2-^{2}H)arabinonate to an equilibrium mixture of (2-^{1}H)arabinonate and (2-^{1}H)-ribonate (eqn. 3) was obtained by

$$\mathrm{AD} \xrightarrow{\underline{k}_2} \mathrm{BH} \underset{\underline{k}_1}{\overset{\underline{k}_{-1}}{\rightleftharpoons}} \mathrm{AH} \qquad (3)$$

substituting the known values of $\underline{k}_1$ and $\underline{k}_{-1}$ into eqns. (**4**) and (5)[13] and minimizing the differences between the observed and calculated values of $\underline{x}$(BH) by the least-squares method. The parameters γ_1 and γ_2

$$\underline{x}(\mathrm{BH}) = \underline{k}_2\left[\frac{\underline{k}_1}{\gamma_1\gamma_2} + \frac{\underline{k}_1-\gamma_1}{\gamma_1(\gamma_1-\gamma_2)}e^{-\gamma_1\underline{t}} + \frac{\underline{k}_1-\gamma_2}{\gamma_2(\gamma_2-\gamma_1)}e^{-\gamma_2\underline{t}}\right] \tag{4}$$

$$\gamma^2 + (\underline{k}_{-1}+\underline{k}_{-1}+\underline{k}_2)\gamma + \underline{k}_1\underline{k}_2 + \underline{k}_{-1}\underline{k}_2 = 0 \tag{5}$$

in eqn. (**4**) are the roots of eqn. (**5**) taken with the reverse signs, and $\underline{x}$(BH) is the mole fraction of BH. The second-order rate constants were obtained by dividing the first-order rate constants by the concentration of hydroxide ion. For examples $\underline{k}_3 = \underline{k}_1/[\mathrm{KOH}]$.

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