

Kinetics and Equilibria for the Solvolysis of Lactaldehyde in Aqueous Solution

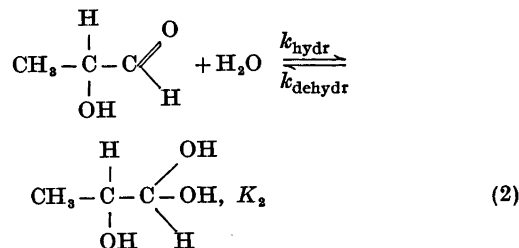
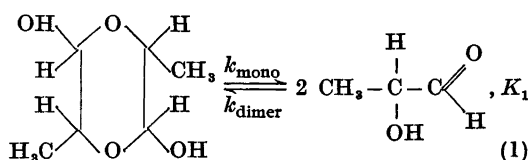
H. NIELSEN and P. E. SØRENSEN

Chemistry Department A, The Technical University of Denmark, Building 207, DK-2800 Lyngby, Denmark

Kinetics and equilibria have been studied for aqueous solutions of lactaldehyde (2-hydroxypropionaldehyde) at 298.2 K by UV spectrophotometry, a pH-stat technique and NMR spectroscopy. Rate constants for the water-, H^+ - and HO^- -catalysed hydration/dehydration reaction are reported as well as kinetic data for the H^+ -catalysed monomerization of the dimeric compound. An equilibrated solution of lactaldehyde in water contains largely the dimer and the hydrated monomer. The monomer is found to be approximately 96 % hydrated at equilibrium.

Simple sugars such as glycolaldehyde (2-hydroxyacetaldehyde), lactaldehyde (2-hydroxypropionaldehyde) and 1,3-dihydroxyacetone may be important intermediates in many metabolic reactions in biological systems. Thus, it was suggested and shown by Hough and Jones¹ that the methyl pentose sugars which are common in nature can be obtained from aldol condensation of two triose units, lactaldehyde and dihydroxyacetone, particularly in the presence of an enzyme such as aldolase. As each of these sugars can undergo various types of spontaneous as well as acid-base catalysed reactions, *e.g.* dimerization, keto-enol conversion and hydration, in aqueous solution, it is of considerable interest to study the kinetic and thermodynamic behaviour of such compounds for a better understanding of their biological role. Such investigations were carried out recently for glycolaldehyde² and the present paper presents results from a similar study of lactaldehyde. The equilibria between the three dominating forms of lactaldehyde in aqueous solution, the dimer, the monomer, and the

hydrated monomer, are presented in eqns. (1) and (2).



where k and K denote rate and equilibrium constants, respectively.

EXPERIMENTAL

DL-Lactaldehyde was synthesised according to the procedure described by Hough and Jones¹ with the only modification that pyruvaldehyde dimethyl acetal (FLUKA, 'pract.') was used as starting material instead of the butyl compound, which is not commercially available. Lactaldehyde is a white crystalline compound, the kinetic behaviour of which is very similar in nature to that of glycolaldehyde² and of dihydroxyacetone,³ and therefore appears in its dimeric form. Elemental analysis gave 48.7 % C and 8.1 % H (theoretical: 48.6 and 8.2 %).

Semicarbazide hydrochloride or hydroxylammonium chloride (both BDH, AnalaR) were used as scavengers for determining dehydration rate constants for the hydrate at selected pH-

values below 6.5. These experiments were carried out spectrophotometrically on a Beckman M24 instrument by following the reaction products (Schiff bases) at 225 and 214 nm, respectively, as described earlier.² At pH-values above 6.5 sulfite buffers ($\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$, BDH, AnalaR and $\text{Na}_2\text{S}_2\text{O}_5$, Riedel-de Haën, 'für Analyse') were efficient scavengers in connection with a pH-stat technique (Radiometer).³

NMR spectra for solutions of lactaldehyde in D_2O (Stohler, 99.8 %) and in dioxane (Merck, reinst) were recorded on a Varian A-60D instrument. To obtain appreciable amounts of lactaldehyde monomer for investigation of rates of hydration of this compound a 1 M solution in dioxane was heated under reflux for approximately 4 h.² Small samples of this solution (rapidly cooled) were injected by a microsyringe into aqueous acetate buffer (glacial acetic acid, BDH, lab. reagent, distilled and $\text{CH}_3\text{COONa} \cdot 3\text{H}_2\text{O}$, Riedel-de Haën, 'für Analyse'), equimolar solution, and the decrease in absorption, due to the disappearance of the free carbonyl group, was followed spectrophotometrically at 275 nm. Complete mixing took 5–10 s and this technique was sufficiently rapid despite the fact that the reaction is rather fast ($t_{1/2} \approx 5$ s) and the total change in absorbance only about 0.25. The H^+ -catalysed monomerization of dimeric lactaldehyde in freshly prepared 0.1 M aqueous solution was also followed at this wavelength (hydrochloric acid, Merck, Titrisol). This procedure is possible because a small proportion (≈ 4 %, see later) of the monomer is still present in its unhydrated form at equilibrium.

NaCl (Riedel-de Haën, 'für Analyse') was used for adjusting ionic strength and redistilled water was used throughout. For the experiments where sulfite was used as a scavenger the solutions were kept free from carbon dioxide and oxygen by a stream of O_2 -free nitrogen. All kinetic experiments were carried out at 298.2 ± 0.2 K.

RESULTS AND DISCUSSION

NMR Measurements. Spectra of an equilibrated solution (5 %, 298.2 K) of lactaldehyde in D_2O gave two doublets at δ 1.14–1.25 and 1.11–1.22 deriving from the methyl group in the dimer and the hydrated monomer, respectively. The intensity of the signals indicated a 45/55 % mixture of these two species and they undoubtedly represent almost 100 % (see later) of the total concentration of the compound as no low field signal, deriving from the carbonyl proton of the free aldehyde, was observed with certainty. However, after heat-

ing of lactaldehyde in dioxane as described in the experimental section the NMR spectrum shows a pronounced peak at δ 8.79 indicating the presence of a considerable amount of the monomeric unhydrated species in this solution.

Hydration experiments. Injection of 25, 50, and 75 mm³, respectively, of this solution in 1 cm³ of a 10^{-2} M (total) solution of acetate buffer ($I=0.1$, pH=4.60) in 1 cm silica cells gave first order kinetic curves when the decrease of the carbonyl absorption was followed at 275 nm and the following rate constants [$k_{\text{hydr}} + k_{\text{dehydr}}$ in eqn. (2)] were obtained (mean values of two experiments): 0.146, 0.138 and 0.130 s⁻¹. A simple extrapolation to pure aqueous solution gives a value of 0.150 ± 0.005 s⁻¹ for this constant. Because of the rather low concentration of the buffer, catalytic effects have been ignored and it was observed that no measurable pH-change took place as a result of the injections. The fact that first order kinetics was observed in the present case indicates that only the hydration reaction is followed and not the dimerization, the rate of which would show a second order dependence on carbonyl concentration.

Dehydration experiments. As found from NMR measurements an equilibrated solution of lactaldehyde in water contains both hydrated monomer and the dimer and the kinetic curves obtained from scavenger experiments therefore reflect two parallel reactions, the dehydration and the monomerization, leading to the same reaction product. We have analysed the kinetic data by fitting these (least squares computer program) to an expression of the type $Y = X_1(1 - e^{-k_1 t} - e^{-k_2 t}) + X_2$, where Y represents some linear function of concentration of the reaction products followed, X_1 and X_2 are constants and k_1 and k_2 denote the observed first order rate constants for dehydration and monomerization, respectively. From this analysis it becomes clear that one of these rate constants is only a few per cent of the other, and that the kinetic curves therefore deviate only slightly from first order behaviour. The smaller value can clearly be ascribed to the less mobile monomerization process and is therefore k_2 . It could only be determined with little accuracy but it was found to be of the same order of magnitude as a value determined from a separate investigation of the mono-

merization reaction (see below). Throughout the pH-range investigated good linearity was observed when $k_1 = k_{\text{dehydr}}^{\text{obs}}$ was plotted against total scavenger concentration, *i.e.* $k_{\text{dehydr}}^{\text{obs}} = k_{\text{dehydr}}^{\circ} + k_{\text{scavenger}} [\text{scavenger}]$. Such simple behaviour may prove the efficiency of the applied scavenger substances. Values of $k_{\text{dehydr}}^{\circ}$ as a function of pH are given in Table 1. The catalytic activity of the various scavenger substances was not studied in detail but general acid-base catalysis was observed in all cases in agreement with results from studies of

similar systems.^{2,4} Quantitative information about specific catalysis by H^+ and HO^- ions is obtained from the data in Table 1 if $k_{\text{dehydr}}^{\circ}$ is plotted against the concentrations of these two species, respectively. These plots show good linearity and $k_{\text{dehydr}}^{\text{H}}$ and $k_{\text{dehydr}}^{\text{HO}}$ are found to be 3.4 and $7.5 \times 10^3 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$, respectively, which values seem reasonable compared to 8.3 and $6 \times 10^3 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ found for glycolaldehyde.² It appears that $k_{\text{dehydr}}^{\circ}$ is practically independent of pH in the range 4–7 and equal to $(6.3 \pm 0.5) \times 10^{-3} \text{ s}^{-1}$ (mean

Table 1. Rate constants for the dehydration ($k_{\text{dehydr}}^{\circ}$) of lactaldehyde in aqueous solution as a function of pH ($I=0.10$, 298.2 K). Concentrations in mol dm^{-3} , rate constants in s^{-1} .

pH measured	Scavenger (conc. range) ^b	$[\text{H}^+] \times 10^3$ ^c	$[\text{HO}^-] \times 10^7$ ^d	$k_{\text{dehydr}}^{\circ} \times 10^3$
2.00 ^a	semicarbazide (0.05–0.25)	12.7		51(2)
2.90	semicarbazide (0.02–0.10)	1.52		10(2)
3.65	semicarbazide (0.02–0.10)	0.270		8.9(3)
4.20	semicarbazide (0.02–0.10)	0.0760		7.2(2)
5.00	semicarbazide (0.02–0.10)	0.0121		6.8(2)
6.00	hydroxylamine (0.01–0.04)	—	—	6.3(2)
6.65	sulfite (0.005–0.025)		0.588	4.3(9)
7.38	sulfite (0.005–0.025)		3.09	6.8(6)
7.58	sulfite (0.005–0.025)		5.00	8.4(3)
7.75	sulfite (0.005–0.025)		7.00	10.4(2)
8.02	sulfite (0.005–0.030)		13.8	14.5(5)
8.33	sulfite (0.005–0.035)		28.1	26(1)

^a $I=0.25$. ^b Total concentrations. ^c $[\text{H}^+] = \frac{10^{-\text{pH}}}{f_{\text{H}^+}}$, $f_{\text{H}^+}=0.83$ ($I=0.10$), $f_{\text{H}^+}=0.79$ ($I=0.25$) (Ref. 7).

^d $[\text{HO}^-] = \frac{10^{\text{pH}-\text{p}K_{\text{H}_2\text{O}}}}{f_{\text{HO}^-}}$, $f_{\text{HO}^-}=0.76$ ($I=0.10$) (Ref. 7).

Table 2. Rate constants for the monomerization of lactaldehyde in aqueous solution as a function of $[H^+]$ ($I = 0.10$, 298.2 K). Concentrations in mol dm^{-3} , rate constants in s^{-1} .

$C_{\text{HCl}}([H^+])$	$k_{\text{mono}}^{\text{obs}} \times 10^4$
0.02	2.17(2)
0.04	4.00(1)
0.06	4.42(3)
0.08	7.53(1)
0.10	9.25(1)
0.12 ^a	11.10(5)

^a $I = 0.12$.

value). This value can be ascribed to the pure water catalysed reaction and is comparable with, e.g., $9.6 \times 10^{-3} \text{ s}^{-1}$ for glycolaldehyde and with values for a series of aliphatic carbonyl compounds, the dehydration of which is not subject to intramolecular catalysis.⁴

Monomerization. Kinetic results from the H^+ -catalysed monomerization of the dimer of lactaldehyde are given in Table 2. The kinetic curves obtained as described in the experimental section were of first order ($\ln|A_{\text{eq}} - A|$ against time) and $k_{\text{mono}}^{\text{H}}$ and k_{mono}° were found to be $(9.0 \pm 0.2) \times 10^{-3} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ and $(2.7 \pm 0.9) \times 10^{-5} \text{ s}^{-1}$ from the slope and intersection respectively, of a plot of $k_{\text{mono}}^{\text{obs}}$ against $[H^+]$. These rate constants are seen to be considerably smaller than the corresponding values for the dehydration reaction but of a similar order of magnitude as found by Bell and Baughan for the monomerization of dihydroxyacetone.⁵ Each value observed for $k_{\text{mono}}^{\text{obs}}$ is actually a sum of the forward and backward reaction rate constants in eqn. (1) (the hydration reaction assumed to be much faster than the dimerization) but as we have observed good agreement between k_{mono}° determined by the method above and values for this constant estimated from the scavenger experiments (see previous paragraph) the contribution from dimerization is presumably small and water itself operates as a sufficiently good scavenger for the monomerization process.

Equilibrium constants. K_2 for eqn. (2) is obtained by combining $k_{\text{hydr}}^{\text{obs}} = k_{\text{hydr}}^{\circ} + k_{\text{dehydr}}^{\circ} = 0.150 \text{ s}^{-1}$ and $k_{\text{dehydr}}^{\circ} = 6.3 \times 10^{-3} \text{ s}^{-1}$, i.e., $K_2 = k_{\text{hydr}}^{\circ}/k_{\text{dehydr}}^{\circ}$ is found to be 23 corre-

sponding to approximately 96 % hydration of lactaldehyde in aqueous solution. This relatively high degree of hydration explains why no signals from the free carbonyl group is observed in the NMR spectrum of lactaldehyde in aqueous solutions of moderate concentrations.

The corresponding equilibrium constant for glycolaldehyde reported earlier,² indicating 90 % hydration of this compound, is probably too low. A large extrapolation from a 50 % water/dioxane mixture was used to obtain $k_{\text{hydr}}^{\text{obs}}$ in pure water and this may not be well justified because it relies on constant reaction orders with respect to water over a large range of water concentrations. These reaction orders have recently been shown to vary considerably with water concentration⁶ and we have shown that application of the procedure for obtaining $k_{\text{hydr}}^{\text{obs}}$ as described in the present paper, to glycolaldehyde leads to higher values for the degree of hydration of this compound in agreement with the result found by applying an empirical expression correlating equilibrium constants with Tafts polar and steric substituent parameters.³

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