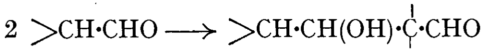
343. *The Kinetics of the Aldol Condensation.*

By R. P. Bell.

The condensation of acetaldehyde to aldol has been investigated in dilute aqueous solutions of sodium hydroxide (0·0005—0·03N), a dilatometric method being used. After correction for the slow further condensation of the aldol, the reaction is of the first order with respect to acetaldehyde. It is suggested that the slow rate-determining step is the formation of free acetaldehyde from the hydrate $CH_3{\cdot}CH(OH)_2$, this reaction being catalysed both by hydroxyl ions and by water molecules. The dependence of the reaction velocity on the hydroxyl-ion concentration agrees with this hypothesis. Experiments with solutions of sodium carbonate show that the catalytic power of these solutions is due to their content of hydroxyl ions.

All aliphatic aldehydes with a hydrogen atom on the α-carbon atom will undergo the aldol condensation according to the scheme



$$2 >CH{\cdot}CHO \longrightarrow >CH{\cdot}CH(OH){\cdot}\overset{|}{\underset{|}{C}}{\cdot}CHO$$

The reagents used to bring about this condensation are all basic, but no work has been done on the kinetics of the catalytic reaction involved, although Usherwood (J., 1923, **123**, 1717) has shown that condensation of *iso*butaldehyde takes place at a measurable rate in saturated sodium carbonate solution.

The present work deals chiefly with the condensation of acetaldehyde in solutions of sodium hydroxide between 0·0005 and 0·03N. It was therefore necessary to prepare solutions of acetaldehyde as far as possible free from acetic acid, and to protect them against oxidation by atmospheric oxygen. In the procedure finally adopted, freshly distilled acetaldehyde was mixed with an equal volume of air-free water, and a current of nitrogen passed first through this solution and then through a cooled flask containing air-free water. The solution obtained in the second flask contained only 1×10^{-4}—1×10^{-3} equiv. of acid per equiv. of acetaldehyde. These solutions were stored under nitrogen, and all transfers were carried out in a current of that gas. The acid concentration of the acetaldehyde solution used was determined before each experiment, and the necessary correction applied to the hydroxyl-ion concentrations.

The aldehyde content of the solutions was determined through the bisulphite compound by the method of Friedman, Cotonio, and Shaffer (*J. Biol. Chem.*, 1927, **73**, 342). This titration should serve in principle as a method for following the kinetics of the aldol condensation, in which the number of aldehyde groups present is halved. It was not, however, found convenient as an accurate method, partly because the reactions are too fast, and partly because elaborate precautions are required to prevent loss of acetaldehyde through the vapour phase and formation of acid by oxidation. The titration method was therefore used only to establish the fact that the main reaction taking place does, in fact, involve the disappearance of half the number of aldehyde groups present, and as a rough confirmation of the reaction velocity derived from the more accurate dilatometric measurements. This is illustrated by Table I, which compares the observed titres with those calculated from the dilatometric curve.

Density determinations with dilute solutions showed that the conversion of acetaldehyde into aldol in aqueous solution results in a contraction of about 50 c. mm. per g., so the reaction may be conveniently followed dilatometrically. (The conversion of acetaldehyde into either crotonaldehyde or paraldehyde is accompanied by an *expansion* in aqueous solution, and could thus be readily distinguished from the aldol condensation.) The dilatometer used had a volume of 31 c.c. and a capillary of 0·233 sq. mm. cross section. The thermostat temperature was 25° ± 0·005°. In carrying out an experiment, a mixture of acetaldehyde solution and air-free water was brought to thermostat temperature, and the reaction started by adding a small quantity of N/10-sodium hydroxide solution from a micro-burette. The reaction mixture was then immediately transferred to the dilatometer (previously filled with nitrogen) and forced up into the capillary by nitrogen under pressure. Reliable readings could be obtained 2—3 minutes after mixing. Since the acetaldehyde solution was saturated with nitrogen, the water used was de-aerated shortly before use in order to avoid the formation of bubbles during the experiment. The height of the meniscus was read to the nearest 0·1 mm., and 30—50 readings were taken in each experiment.

TABLE I.

0·337M-Acetaldehyde; 0·0071N-sodium hydroxide.

Time, mins.		0	0·5	1·5	3·0	5·0	7·0	9·0	11·0	13·0	15·0	20·0	30·0
Titre, c.c. of N/10-iodine	obs.	13·5	13·05	12·8	12·45	11·45	11·5	10·55	10·0	9·75	9·45	8·45	7·9
	calc.	—	13·05	12·9	12·3	11·7	11·2	10·8	10·15	9·7	9·35	8·7	7·8

It was found that the course of each experiment corresponded very nearly to that of a first-order reaction, and that the change of volume with time could be expressed within the experimental error by an equation of the form (1), where V_0 is the volume at time $t = 0$, k_1^* the

$$V_0 - V = A(1 - e^{-k_1^* t} + \beta t) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

velocity constant of the first-order reaction, and βt a correction term; β was throughout about 3% of k_1^*, so that for values of t greater than about 10 times the half-time of the first-order change the volume change was linear with time. This linearity persisted up to at least 20 times $t_{\frac{1}{2}}$, so the value of βA could be determined directly from this linear portion. The observed readings for the earlier stages of the reaction were then corrected by an amount $-\beta At$, and the first-order constant obtained by treating the corrected values according to the method of Guggenheim (*Phil. Mag.*, 1926, **2**, 540); A, the total volume change of the first-order reaction, was obtained by extrapolation to zero time. Table II compares the observed and calculated values for a typical experiment, the latter being given by equation (1) with $A = 106·4$ (expressed in mm. of the dilatometer scale), $k_1^* = 0·0611$, $\beta = 0·00173$.

TABLE II.†

0·0351M-Acetaldehyde; 0·0069N-sodium hydroxide.

Time (mins.).	$V_0 - V$ (mm.).		Time (mins.).	$V_0 - V$ (mm.).		Time (mins.).	$V_0 - V$ (mm.).		Time (mins.).	$V_0 - V$ (mm.).	
	Obs.	Calc.		Obs.	Calc.		Obs.	Calc.		Obs.	Calc.
4	23·3	23·7	16	69·5	69·3	28	92·0	92·3	40	104·8	104·6
6	33·1	33·7	18	74·2	74·2	30	94·8	95·0	60	116·8	117·2
8	42·4	42·6	20	78·7	78·7	32	97·1	97·2	80	123·8	123·8
10	50·6	50·5	22	82·5	82·5	34	99·2	99·4	100	127·5	128·2
12	57·7	57·4	24	86·0	86·4	36	101·2	101·3	120	131·9	131·9
14	64·0	63·7	26	89·1	89·5	38	103·1	102·9	140	135·9	135·9

† For the sake of brevity this table contains only alternate observed readings.

TABLE III.

[Me·CHO].	[NaOH].	10^3k.	$10^3\beta$.	A.	ΔV.	[Me·CHO].	[NaOH].	10^3k.	$10^3\beta$.	A.	ΔV.
0·176	0·0069	24·7	1·19	55	55	0·362	0·00310	14·5	0·80	102	55
0·351	0·0069	26·5	1·85	106	53	0·362	0·0047	18·6	1·20	101	55
0·528	0·0068	26·6	2·45	167	56	0·351	0·0069	26·5	1·74	106	53
0·703	0·0067	26·0	3·60	222	55	0·351	0·0108	38·3	2·56	102	52
						0·351	0·0134	44·6	2·84	111	55
0·362	0·00047	§2·47	—	—	—	0·337	0·0171	55·7	4·13	97	52
0·362	0·00135	§6·70	—	—	—	0·351	0·0206	65·8	5·04	104	53
0·362	0·00140	§7·68	—	—	—	0·343	0·0280	87·5	6·26	96	51

§ See p. 1640.

The results obtained with different concentrations of acetaldehyde and sodium hydroxide are in Table III. The values of k refer to decadic logarithms and are therefore related to k_1^* by the equation $k = 0{\cdot}434k_1^*$, the time being measured in minutes. In the three slowest experiments it was not convenient to measure β directly, and in calculating k the observed readings were corrected on the assumption that the value of the ratio k/β is the mean of the values for the other experiments; A is in mm. of the dilatometer scale, and ΔV represents the same volume converted into c. mm. and referred to 1 g. of acetaldehyde.

The form of equation (1) probably represents two consecutive irreversible first-order reactions, the second being much slower than the first. This may be shown by reference to the general case

$$M_1 \xrightarrow[k_1]{} M_2 \xrightarrow[k_2]{} M_3$$

the total volume of the solution being given by

$$V = A_1[M_1] + A_2[M_2] + A_3[M_3] + B$$

where A_1, A_2, A_3, and B are constants. If a_1 is the initial concentration of M_1, and V_0 the initial volume, the change of volume with time is given exactly by

$$V_0 - V = a_1 \left\{A_1 - A_3 - e^{-k_1 t}\left(A_1 - \frac{A_2k_1 - A_3k_2}{k_1 - k_2}\right) - e^{-k_2 t}\,\frac{k_1\,(A_2 - A_3)}{k_1 - k_2}\right\} \quad . \quad (2)$$

If $k_1 \gg k_2$ and $t \ll 1/k_2$, this reduces to

$$V_0 - V = a_1\,\{(A_1 - A_2)(1 - e^{-k_1 t}) + k_2 t\,(A_2 - A_3)\} \quad . \quad . \quad . \quad . \quad (3)$$

identical in form with (1).

Apart from the exact significance of the linear correction term in (1), it is clear that the main reaction taking place is a first-order change characterised by the velocity constant k_1^* (or k in Table III) and the total volume change A. The order of this reaction is further confirmed by the first four experiments in Table III, which show that for a constant hydroxyl-ion concentration the value of k is independent of the acetaldehyde concentration. Comparison with the titration results (cf. Table I) serves to identify this main reaction with the formation of aldol, and the contraction per g. of aldehyde (col. 6 in Table III) agrees well with that calculated from the densities of solutions of acetaldehyde and aldol. The subsequent slow contraction is probably due to further condensation of the aldol to give dialdan or similar products, since the formation of crotonaldehyde (or paraldehyde) would be accompanied by an *increase* of volume. This agrees with the fact that the aldehyde titre falls slightly below 50% of the initial value during the second slow stage of the reaction. It may be mentioned that the solutions remained colourless during the period covered by the measurements, but were slightly yellow on the following day.

It is surprising that the condensation of two acetaldehyde molecules to one of aldol should be kinetically of the first order. This can be accounted for by the scheme

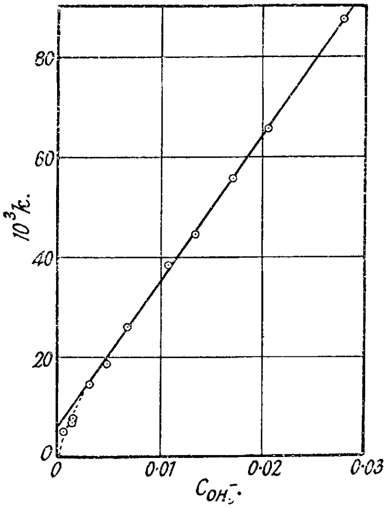
$$\left.\begin{array}{lll} (a) & CH_3{\cdot}CHO \rightleftarrows X & (slow) \\ (b) & X + CH_3{\cdot}CHO \searrow & \\ & \qquad CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}CHO & (fast) \\ \text{or} & 2CH_3{\cdot}CHO \nearrow & \end{array}\right\} \quad (4)$$

where X is any product formed from one molecule of acetaldehyde. It is suggested that the slow unimolecular process (*a*) may be the dehydration of hydrated acetaldehyde (ethylidene glycol), the reaction scheme then becoming

$$\left.\begin{array}{lll} (a) & CH_3{\cdot}CH(OH)_2 \rightleftarrows CH_3{\cdot}CHO + H_2O & (slow) \\ (b) & CH_3{\cdot}CH(OH)_2 + CH_3{\cdot}CHO \longrightarrow CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}CHO + H_2O & (fast) \end{array}\right\} \quad (5)$$

There is much evidence to show that in dilute aqueous solutions of aldehyde the equilibrium (*a*) is far over on the left-hand side, the amount of free aldehyde present being very small. Moreover, both density measurements (Perkin, J., 1887, **61**, 808) and calorimetric measurements (Brown and Pickering, J., 1897, **81**, 756) show that this equilibrium is not set up instantaneously, and in the latter case it was also established that the change is accelerated by hydroxyl ions. The second stage (*b*) might involve two unhydrated acetaldehyde molecules, but the scheme given above seems more probable in view of the fact that the aldol condensation appears to require the presence of water.

The figure shows the dependence of the velocity constant *k* upon the hydroxyl-ion concentration. With the exception of the three lowest points, the results are well represented by a straight line cutting the velocity axis above the origin. This indicates that the rate-determining process is catalysed not only by hydroxyl ions but also by water molecules; *i.e.*, there is a "spontaneous" reaction. This accords with the known facts about the hydration equilibrium of acetaldehyde. The straight line cannot, however, represent the velocity of the actual aldol condensation right down to $C_{OH'} = 0$, since the velocity becomes zero at zero hydroxyl-ion concentration. (Slightly acid solutions of acetaldehyde can be kept for several months at room temperature without any detectable change in aldehyde titre.) The three lowest points lie below the straight line, and the complete velocity–concentration curve must follow the course indicated roughly by the broken line. This behaviour can be accounted for on the basis of the above scheme if it is assumed that the second stage (*b*) is catalysed by hydroxyl ions only, its velocity becoming zero when $C_{OH'} = 0$. With decreasing hydroxyl-ion concentration a point will be reached at which the velocity of (*b*) is no longer great compared with that of (*a*), and in sufficiently dilute solutions the second-order reaction (*b*) will eventually become the rate-determining step. This explanation is supported by the fact that the three slowest reactions (marked with a section in Table III) are not strictly unimolecular, the velocity falling off too rapidly with time.



The above interpretation assumes the reaction scheme (5), but it will apply equally well to any other assumption about the unimolecular change (*a*); *e.g.*, (*a*) might be the enolisation of the acetaldehyde.

Since the first-order change is catalysed by both hydroxyl-ions and water molecules, other basic species (*e.g.*, the anions of weak acids) might be expected to exert a catalytic effect. However, it is clear from the above that the first-order change can only be investigated in solutions of fairly high hydroxyl-ion concentration, and in these circumstances it will be difficult to detect catalysis by other species. A few experiments were done in solutions of sodium carbonate (which is commonly used as a reagent for effecting the aldol condensation), and it was found that the velocity was indistinguishable from the value in sodium hydroxide solutions of the same hydroxyl-ion concentration. An experiment was also carried out using an 0·5M-acetate buffer of p_H 5·5, but no change could be detected in spite of the high concentration of basic acetate ions: this is accounted for by the absence of hydroxyl ions to catalyse the second stage of the reaction.

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