603. *Kinetics of the Aldol Condensation of Acetaldehyde.*

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Measurements are reported on the initial reaction rates of the aldol condensation of acetaldehyde and of the reaction of acetaldehyde with formaldehyde, in sodium hydroxide solutions and in borate and carbonate buffers. The acidic properties of acetaldehyde and formaldehyde have been investigated, and the results are used to correct the hydroxide-ion concentrations in the kinetic experiments. The corrected results show that the aldol condensation is almost of the second order with respect to aldehyde, though the apparent order decreases slightly with increasing aldehyde concentration. The aldol condensation in buffer solutions exhibits general base catalysis, but does not obey the usual quantitative laws.

The results are interpreted by assuming that the ionization and condensation steps of the aldol condensation have comparable rates, the former being the faster under most conditions. A similar interpretation applies to the previously unexplained kinetics of the acid-catalysed decomposition of the diazoacetate ion.[19] The rate of reaction between acetaldehyde and formaldehyde is proportional to the first power of the acetaldehyde concentration, but independent of formaldehyde concentration, and is therefore governed by the rate of ionization of acetaldehyde. The value thus found for the rate of ionization is similar to that for acetone, and is consistent with the observed kinetics of the aldol condensation.

It is generally accepted that the base-catalysed aldol condensation of acetaldehyde takes place in two steps. In the first of these the anion $CH_2{\cdot}CHO^-$ is formed by the reaction of one molecule of aldehyde with a base, and in the second this anion combines with a second molecule of aldehyde to form the anion of aldol, $CHO{\cdot}CH_2{\cdot}CHMe{\cdot}O^-$. The first investigation of the kinetics of this reaction in dilute sodium hydroxide [1] suggested that it is of the first order with respect to aldehyde, indicating that the first of the above steps is rate-determining. The same conclusion follows from the observation [2] that in the aldol condensation of a concentrated solution of acetaldehyde in deuterium oxide no deuterium becomes attached to the carbon atoms of the aldol. More recent kinetic work [3,4] led to a reaction order between the first and the second, varying with the aldehyde concentration, suggesting that the first and the second step of the reaction are of comparable velocities.

[1] Bell, *J.*, 1937, 1637.

[2] Bonhoeffer and Walters, *Z. phys. Chem.*, 1938, *A*, **181**, 441.

[3] Broche, " Colloque National de Cinétique," Strasbourg, 1953.

[4] Broche and Gibert, *Bull. Soc. chim. France*, 1955, 131.

This view was supported by measurements on deuterium exchange in buffer solutions over a wide range of aldehyde concentrations.[5] The amount of deuterium introduced into the unchanged acetaldehyde increased as the reaction progressed, but decreased with increasing aldehyde concentration, becoming negligible at very high concentrations. The results were consistent with the mixed kinetics previously reported,[3,4] but a quantitative comparison was not possible without further knowledge of the reaction kinetics in buffer solutions and the magnitude of the kinetic isotope effects involved. Some information on the latter point has been given recently by Pocker,[6] but our quantitative understanding of the reaction is still far from complete.

The present paper deals with three aspects of the reaction. The first combines kinetic work in sodium hydroxide solutions with measurements of the acidic properties of acetaldehyde in alkaline solutions, where it is converted partly into the ion $Me{\cdot}CH(OH){\cdot}O^-$. Under the conditions used in kinetic experiments this produces a considerable reduction in the hydroxyl-ion concentration and affects the apparent order of the reaction. The second aspect concerns kinetic measurements in buffer solutions, in which general base catalysis should be detectable if the formation of the ion $CH_2{\cdot}CHO^-$ is wholly or partly rate-determining. Finally, the rapid addition of the ion $CH_2{\cdot}CHO^-$ to formaldehyde has been used to obtain an independent measure of the rate of ionization of acetaldehyde.

The overall chemistry of the aldol condensation is complicated, since the aldol originally formed can undergo a variety of changes, *e.g.*, dehydration to crotonaldehyde, dimerization to paraldol, addition to a further molecule of acetaldehyde to give 6-hydroxy-2,4-dimethyl-1,3-dioxan, and ultimately condensation to products of high molecular weight.[7] It is therefore necessary to consider only initial reaction rates, and almost all the kinetic measurements described here refer to the initial rates of volume change measured dilatometrically. These can be used directly for determining the effect upon the reaction velocity of aldehyde concentration and of the nature and concentration of the catalyst solution. Attempts were made to convert these dilatometric rates into true velocity constants by means of spectrophotometric measurements, but with only partial success.

EXPERIMENTAL

Acetaldehyde was distilled in a current of oxygen-free nitrogen, condensed in a dry-ice trap, and stored in sealed bulbs containing 0·5—2 g. Titration of aqueous solutions showed that it contained 0·1—0·2 mol. % of an acid of p*K* about 5, presumably acetic acid, and this was estimated in each batch and allowed for in calculating the composition of solutions. A 40% aqueous solution of formaldehyde was used: it contained about 0·05 mol. % of acid, presumably formic. Acetaldehyde solutions were analysed by Friedman, Cotonio, and Schaeffer's method,[8] and formaldehyde solutions by treatment with an excess of sodium sulphite and titrating with standard acid the alkali released according to the equation $CH_2(OH)_2 + SO_3^{2-} \longrightarrow CH_2(OH){\cdot}SO_3^- + OH^-$. Inorganic materials were of " AnalaR " grade, and solutions were made with boiled-out distilled water. Special care was taken to exclude carbon dioxide in preparing and handling dilute sodium hydroxide solutions.

Conductivities were measured with a Cambridge bridge, with a telephone detector and a cell with platinized electrodes having a cell constant of about 0·3. Spectrophotometric measurements were made either with a Perkin-Elmer recording Spectracord 3000A, or with a Unicam S.P. 500 spectrophotometer having a cell compartment controlled to 25° ± 0·2°.

Conventional Pyrex dilatometers were used, having volumes of about 30 c.c. and capillaries of about 0·2 mm.² cross-section. The initial rates of volume change were calculated by a method developed by Broche and Gibert,[3,4] which has the advantage that no subjective drawing of initial tangents is involved. If the dilatometer readings at times t and $t + \delta t$ are respectively $x(t)$ and $x(t + \delta t) = x(t) + \delta x$, then Taylor's theorem leads to the expression

$$\delta x/\delta t = x'(t) + \tfrac{1}{2}x'(t)x''(t)\delta t + \ldots\ldots$$

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[5] Bell and Smith, *J.*, 1958, 1691.

[6] Pocker, *Chem. and Ind.*, 1959, 599.

[7] Owen, *Ann. Reports*, 1944, **41**, 139.

[8] Friedman, Cotonio, and Schaeffer, *J. Biol. Chem.*, 1927, **73**, 341.

If $x''(t)$ can be taken as constant over a limited period, then a plot of $\delta x/\delta t$ against δt for a given value of t will give $x'(t)$ by extrapolation: similarly, the initial slope $x'(0)$ can be obtained by extrapolation from the values of $x'(t)$ at different times. If $(\mathrm{d}V/\mathrm{d}t)_0$ is the initial rate of change of volume thus determined we can define a *dilatometric reaction velocity* by $v^* = (\mathrm{d}V/\mathrm{d}t)_0/V$: this is independent of the size of the dilatometer and the bore of its capillary. All the rates given in Tables 3—8 represent v^* in units of sec.^{-1}. The chemical rate in mole l.^{-1} sec.^{-1} can be obtained from v^* by dividing by the volume change of the reaction in l. mole^{-1}, if this is known.

All dilatometric and other measurements were carried out at 25°.

The Acidity of Solutions of Formaldehyde and Acetaldehyde.—An aldehyde, R·CHO, can behave as a weak acid in aqueous solution by adding on hydroxyl ions to give R·CH(OH)·O^-, the conjugate base of the hydrated form R·CH(OH)_2. Thus chloral hydrate has a pK of about 11,[9] and values between 12 and 14 have been reported [10] for $\text{CH}_2\text{(OH)}_2$ at different temperatures; both chloral and formaldehyde exist almost entirely in the hydrated form in aqueous solution. The results for formaldehyde involved the use of glass electrodes in strongly alkaline solutions, and are of doubtful accuracy.

Our own measurements were made by the method developed by Ballinger and Long,[11] based on the change of conductivity produced when a large excess of a very weak acid is added to a dilute solution of sodium hydroxide. If a represents the total aldehyde concentration (including both hydrated and unhydrated species) and x the concentration of anion formed, we can define an equilibrium constant by $K' = x/(a - x)[\text{OH}^-]$, where the activity coefficients of the two anions will cancel out to a good approximation. Provided that $a \gg [\text{OH}^-]$ it is easily shown that

$$\lambda_0/(\lambda_0 - \lambda) = \alpha(1 + 1/K'a),\ \alpha = (l_{\text{OH}} + l_{\text{Na}})/(l_{\text{OH}} - l_{\text{A}}) \quad . \quad . \quad . \quad . \quad (1)$$

where λ_0 and λ are the conductivities with and without the addition of aldehyde and l represents ionic mobility. In principle, it should be possible to determine both K' and α from the slope and intercept of a plot of $\lambda_0/(\lambda_0 - \lambda)$ against $1/a$, but in practice it is necessary to estimate α separately by assuming a value for l_{A}, the mobility of the anion, and then to obtain K' from the slope of the plot. We have taken the anion mobilities as equal to those of formate and acetate for formaldehyde and acetaldehyde respectively, leading to 1·73 and 1·58 for the corresponding values of α.

Because of the progress of the aldol condensation it is necessary to extrapolate the conductivity to zero time in the experiments with acetaldehyde. The small acid content of both aldehydes (0·05—0·02 mol. %) must be allowed for. This is most conveniently done by neutralizing the formic or acetic acid before adding the aldehyde to the sodium hydroxide solution, and adding a correction to the observed value of λ_0–λ to allow for the sodium formate or acetate thus introduced. At the same time a much smaller correction is made to allow for the effect of the increased ionic strength on the ionic mobilities: this was calculated from the Onsager conductivity equation. For acetaldehyde the total correction is large, the observed conductivity change being usually an increase rather than a decrease, and this constitutes the chief source of error in applying the method to this substance.

The results obtained are given in Tables 1 and 2. Fig. 1 shows the plots of the corrected values of $\lambda_0/(\lambda_0 - \lambda) - \alpha$ against $1/a$, and the slopes of the straight lines lead to K' (formaldehyde) = 5·1, K' (acetaldehyde) = 1·8. Since formaldehyde exists in aqueous solution almost entirely as the hydrate $\text{CH}_2\text{(OH)}_2$,[12] the acid dissociation constant of this species is given by $K_a = K'K_w = 5{\cdot}1 \times 10^{-14}$. Acetaldehyde, on the other hand, is about 55% hydrated at 25°,[13] so that the acid strength of Me·CH(OH)_2 is $K_a = K'K_w/0{\cdot}55 = 3{\cdot}3 \times 10^{-14}$.

TABLE 1. *Acidity of formaldehyde.*

λ = reciprocal of cell resistance (ohms); $\lambda_0 = 8{\cdot}66 \times 10^{-4}$ mho throughout; [NaOH] = $1{\cdot}22 \times 10^{-3}$ throughout; $[\text{H·CO}_2\text{Na}] = 5 \times 10^{-4}a$ throughout.

a	0·0315	0·0442	0·0629	0·126	0·252	1·26
$10^4(\lambda_0 - \lambda)$, obs	0·71	1·06	1·23	2·10	2·64	3·04
,, corr.	0·71	1·07	1·24	2·12	2·68	3·22

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[9] Euler, *Ber.*, 1903, **36**, 4255.

[10] Martin, *Austral. J. Chem.*, 1954, **7**, 400.

[11] Ballinger and Long, *J. Amer. Chem. Soc.*, 1959, **81**, 1050.

[12] Bieber and Trümpler, *Helv. Chim. Acta*, 1947, **30**, 1860.

TABLE 2. *Acidity of acetaldehyde.*

10^3[NaOH]	$10^4\lambda_0$	a	10^3[Me·CO$_2$Na]	$10^4(\lambda_0 - \lambda)$ obs.	$10^4(\lambda_0 - \lambda)$ corr.
1·00	7·58	0·047	0·72	−1·72	0·40
1·00	7·58	0·101	1·46	−3·32	0·69
1·00	7·58	0·200	2·71	−6·13	1·26
1·00	7·58	0·290	1·43	−2·48	1·45
1·00	7·58	0·475	2·23	−3·52	2·60
2·00	15·13	0·197	2·64	−4·35	2·87
2·00	15·13	0·390	1·54	−0·25	3·97
3·00	22·90	0·047	0·77	−1·05	1·05
3·00	22·90	0·101	1·46	−1·68	2·12
5·00	38·60	0·101	1·46	−0·50	4·27

The pK found for CH$_2$(OH)$_2$ is in reasonable agreement with previous values,[10] but is probably more accurate than these. The lower acidity found for Me·CH(OH)$_2$ shows the expected effect of the methyl group, though the effect is considerably smaller than that shown in the pair H·CO$_2$H (pK 3·75) and Me·CO$_2$H (pK 4·75).

Kinetics of the Aldol Condensation in Sodium Hydroxide Solutions.—The reaction takes place at a convenient rate in 10^{-3}—10^{-2}M-sodium hydroxide, and the initial dilatometric rates are given in Table 3. In calculating the hydroxide-ion concentrations allowance has been made for the acetic acid contained in the acetaldehyde, and also for the removal of hydroxide ions by the reaction Me·CHO + OH$^-$ $\rightleftharpoons$ Me·CH(OH)·O$^-$, the value of K' obtained in the last section being used. The second effect is important, and the true values of [OH$^-$] differ considerably from the stoicheiometric concentration of sodium hydroxide.

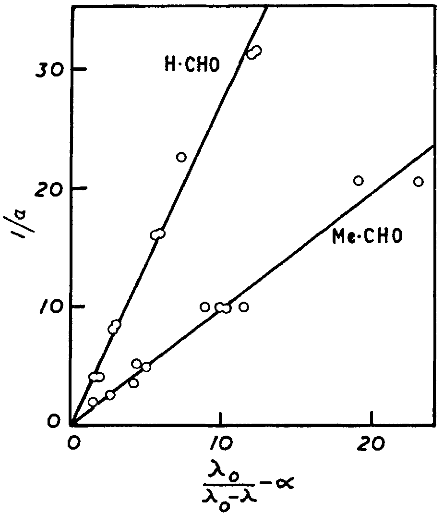

FIG. 1. *Effect of formaldehyde and acetaldehyde on the conductivity of sodium hydroxide solutions.*

The reaction in sodium hydroxide solutions was also studied spectrophotometrically. Spectra taken with the Spectracord showed a complicated series of changes. The broad band of acetaldehyde at 2800 Å decreases slightly in intensity during the first few per cent of the reaction, but subsequently absorption in this region increases, and a strong band appears at 2250 Å, probably due to crotonaldehyde. (The absorption spectrum of aldol itself is not known, since the material usually obtained as acetaldol probably consists mainly of 6-hydroxy-2,4-dimethyl-1,3-dioxan,[7,14] and is also usually contaminated with crotonaldehyde and other products.) As the reaction progresses new bands appear at longer wavelengths, notably one at 2780 Å, and for long reaction times the absorption extends into the visible, with a maximum at about 3100 Å.

The growth of the peak at 2780 Å has been used to obtain relative reaction rates for concentrations of sodium hydroxide in the range 0·1—4M, where the velocities are too high for the dilatometric method. Measurements were made at 25° with the Unicam instrument. After a

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[13] Bell and Clunie, *Trans. Faraday Soc.*, 1952, **48**, 439.

[14] Saunders, Murray, and Cleveland, *J. Amer. Chem. Soc.*, 1943, **65**, 1309, 1714.

TABLE 3. *The aldol condensation in dilute sodium hydroxide.*

a = Acetaldehyde concentration; v^* = initial dilatometric rate (sec.$^{-1}$).

10^5[NaOH]	10^5[OH$^-$]	10^9v^*	$10^5v^*/a^2$[OH$^-$]	10^5[NaOH]	10^5[OH$^-$]	10^9v^*	$10^5v^*/a^2$[OH$^-$]
	a = 0·100				a = 0·300		
100	85	25	292	100	65	132	232
200	169	34	199	200	130	256	219
300	254	72	285	300	200	331	183
500	424	82	193	500	332	621	208
1000	848	148	174				
		Mean	239			Mean	211
	a = 0·200				a = 0·400		
100	74	76	259	100	58	214	229
200	147	145	248	200	116	379	202
500	368	296	202	300	174	572	205
1000	740	528	180				
		Mean	230			Mean	209

short induction period the optical density D increases linearly with time; moreover, for a fixed concentration of sodium hydroxide the rate of increase is proportional to the square of the aldehyde concentration, thus resembling the dilatometric rates in Table 3. For example, with [NaOH] constant at 1·97M, the value of dD/dt for a = 0·01, 0·02, and 0·03 are 0·49 × 10^{-3}, 1·9 × 10^{-3}, and 4·4 × 10^{-3} sec.$^{-1}$, corresponding to (dD/dt)/a^2 = 4·9, 4·8, and 4·9. It thus seems justifiable to take dD/dt as an approximate measure of the relative rates of the aldol condensation, though the results cannot be compared exactly with the dilatometric rates. The results obtained with a fixed aldehyde concentration are given in Table 4, which shows that the velocity passes through a maximum at a sodium hydroxide concentration of between 0·5 and 1·0M.

TABLE 4. *The aldol condensation in concentrated sodium hydroxide.*

a = 0·02 throughout; dD/dt = rate of increase of optical density at 2780 Å (sec.$^{-1}$)

[NaOH]	0·10	0·30	0·50	1·00	1·50	1·93	1·97	4·02
10^4dD/dt	11·4	22·1	24·6	26·6	23·7	20·2	19·0	16·3

Kinetics of the Aldol Condensation in Buffer Solutions.—Most of these measurements were made dilatometrically in borate or carbonate buffers. In these solutions only small corrections are necessary for the presence of acetic acid and none for the acidity of acetaldehyde. The experiments were designed to determine the dependence of the rate both on the buffer composition and on the aldehyde concentration. The results are given in Tables 5 and 6. In

TABLE 5. *The aldol condensation in borate buffers.*

R = [H_3BO_3]/[$H_2BO_3^-$].

I = 0·1, a = 0·235, R = 1·00, 10^5[OH$^-$] = 1·72

[$H_2BO_3^-$]	0·10	0·08	0·06	0·04	0·02	0·01	0
10^9v^*	2·83	2·14	2·14	1·80	1·57	1·63	1·50 (extrap.)

I = 0·1, a = 0·235, R = 0·285, 10^5[OH$^-$] = 6·04

[$H_2BO_3^-$]	0·10	0·08	0·04	0·01	0
10^9v^*	8·36	7·55	6·85	5·93	5·5 (extrap.)

I = 0·1, a = 0·235, R = 0·168, 10^5[OH$^-$] = 10·3

[$H_2BO_3^-$]	0·10	0·08	0·06	0·04	0·02	0·01	0
10^9v^*	14·7	12·7	12·5	12·0	9·4	8·8	8·1 (extrap.)

I = 0·2 (0·1 for italicized figures), R = 0·25, 10^5[OH$^-$] = 6·90

Values of 10^9v^*

a =	0·48	0·40	0·30	0·20	a =	0·48	0·40	0·30	0·20
[$H_2BO_3^-$]					[$H_2BO_3^-$]				
0·20	50·2	36·5	18·6	9·22	0·06	*35·0*	*26·0*	—	—
0·16	47·7	29·7	19·6	—	0·04	33·5, *36·5*	21·4, *23·5*	13·5	5·90
0·12	44·0	26·6	15·4	6·88	0·02	*30·5*	*20·8*	—	—
0·10	*44·2*	*28·1*	—	—	0 (extrap.)	29	19·5	12·5	5·5
0·08	40·2, 39·7	23·9, *26·4*	14·7	6·75					

calculating the hydroxide-ion concentrations in the borate buffers the activity coefficients cancel out to a first approximation: in the carbonate buffers they were calculated from the expression $\log f_z = 0{\cdot}5z^2I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}})$, where I is the ionic strength.

Some dilatometric and spectrophotometric measurements were also made in carbonate and phosphate buffers. It was hoped that the initial decrease in the absorption at 2800 Å would give the absolute rate of disappearance of acetaldehyde, and that by comparing this with the initial dilatometric rate the specific volume change could be determined, thus making it possible to convert all the dilatometric rates into absolute rates. However, this was only partly successful, since (as in the experiments in sodium hydroxide solutions, described in the last section) the decrease of absorption was soon replaced by an increase, and by the appearance of absorption bands at lower wavelengths. It is thus probably an over-simplification to attribute the initial decrease of absorption at 2800 Å solely to a decrease in acetaldehyde concentration. The simple assumption leads to the following values:

TABLE 6. *The aldol condensation in carbonate buffers.*

$I = 0{\cdot}2$ throughout, $R = [H{\cdot}CO_3^-]/[CO_3^{2-}]$

$a = 0{\cdot}235$, $R = 1{\cdot}00$, $10^5[OH^-] = 10{\cdot}7$

$[CO_3^{2-}]$ ………………	0·05	0·04	0·03	0·02	0·01	0
10^9v^* …………………	13·4	12·8	12·0	11·7	11·0	10·3 (extrap.)

$a = 0{\cdot}235$, $R = 0{\cdot}50$, $10^5[OH^-] = 21{\cdot}5$

$[CO_3^{2-}]$ ………………	0·04	0·03	0·02	0·01	0
10^9v^* …………………	22·3	21·7	20·2	19·8	19·0 (extrap.)

$a = 0{\cdot}235$, $R = 0{\cdot}33$, $10^5[OH^-] = 32{\cdot}2$

$[CO_3^{2-}]$ ………………	0·05	0·04	0·03	0·02	0·01	0
10^9v^* …………………	35·0	32·5	30·7	29·4	27·3	25·5 (extrap.)

$R = 1{\cdot}00$, $10^5[OH^-] = 10{\cdot}7$. Values of 10^9v^*.

$a =$	0·12	0·235	0·46	0·67	0·80
$[CO_3^{2-}]$					
0·05	3·12	13·4	50·8	110	173
0·04	3·00	12·8	49·3	103	—
0·03	2·90	12·0	41·2	97	—
0·02	—	11·7	39·2	—	—
0·01	2·60	11·0	40·5	86	140
0 (extrap.)	2·5	10·3	39	80	132

$R = 0{\cdot}50$, $10^5[OH^-] = 21{\cdot}5$. Values of 10^9v^*.

$a =$	0·235	0·46	0·67
$[CO_3^{2-}]$			
0·05	—	88	198
0·04	22·3	87	183
0·03	21·7	82	173
0·02	20·2	78	173
0·01	19·8	73	171
0 (extrap.)	19	69	170

Carbonate buffer, $[HCO_3^-] = [CO_3^{2-}] = 0{\cdot}1$, $[Me{\cdot}CHO] = 0{\cdot}1$

Dilatometric rate, $v^* = 2{\cdot}2 \times 10^{-9}$ sec.$^{-1}$
Spectrophotometric rate $= 3{\cdot}0 \times 10^{-7}$ mole l.$^{-1}$ sec.$^{-1}$
Specific volume change $= 7{\cdot}3 \times 10^{-3}$ l. per mole of Me·CHO

Phosphate buffer, $[HPO_4^{2-}] = [PO_4^{3-}] = 0{\cdot}1$, $[Me{\cdot}CHO] = 0{\cdot}1$

Dilatometric rate, $v^* = 9{\cdot}1 \times 10^{-8}$ sec.$^{-1}$
Spectrophotometric rate $= 1{\cdot}3 \times 10^{-5}$ mole l.$^{-1}$ sec.$^{-1}$
Specific volume change $= 7{\cdot}0 \times 10^{-3}$ l. per mole of Me·CHO

The specific volume change, 7×10^{-3} l. mole^{-1}, is substantially greater than the value $2{\cdot}5 \times 10^{-3}$ given by Bell,[1] who compared the volume change with the decrease in titratable aldehyde groups. However, he assumed that the product was aldol, containing one titratable –CHO group: if, as is more likely, it is 6-hydroxy-2,4-dimethyl-1,3-dioxan, containing no aldehyde groups, the volume change would be 5×10^{-3}. This is not very different from our present value, considering the uncertainty in interpreting the optical data and the fact that Bell's observations were not confined to the initial stages of the reaction.

Kinetics of the Reaction between Acetaldehyde and Formaldehyde.—In alkaline solutions these two substances eventually yield pentaerythritol, presumably by three successive aldol condensations followed by a Cannizzaro reaction. However, the kinetic and spectrophotometric measurements described here show that the early stages of the reaction can be described by $\mathrm{Me{\cdot}CHO} + \mathrm{CH_2O} \longrightarrow \mathrm{CH_2(OH){\cdot}CH_2{\cdot}CHO} \rightleftharpoons \mathrm{CH_2{:}CH{\cdot}CHO}$. When acetaldehyde is mixed with a large excess of formaldehyde in an alkaline buffer, the carbonyl absorption at 2800 Å decreases steadily, and is replaced by strong absorption at 2240 Å, probably due to acraldehyde. For about the first 25% of the reaction there is a well-defined isosbestic point at 2520 Å. The decrease at 2800 Å is much faster than for the aldol condensation of acetaldehyde alone in the same buffer solution, and can reasonably be used to measure the initial rate of disappearance of acetaldehyde, since the reaction with formaldehyde appears to be simpler than with acetaldehyde alone. There is no detectable absorption at 2800 Å due to formaldehyde, which is almost completely hydrated to $\mathrm{CH_2(OH)_2}$ in aqueous solution.

A comparison of dilatometric and spectrophotometric observations was used to determine the specific volume change of the acetaldehyde–formaldehyde reaction. Initial rates were measured in each case, and several determinations with $[\mathrm{PO_4^{3-}}] = [\mathrm{HPO_4^{2-}}] = 0{\cdot}1$, $[\mathrm{Me{\cdot}CHO}] = 0{\cdot}1$, $[\mathrm{CH_2O}] = 4{\cdot}8$ gave concordant values of $1{\cdot}7 \times 10^{-2}$ l. per mole of Me·CHO for the volume change.

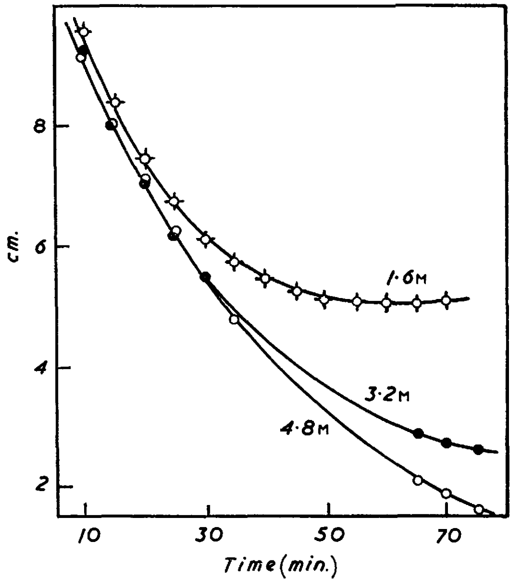

FIG. 2. *Dilatometric curves for the reaction of acetaldehyde with varying concentrations of formaldehyde.*

Most of the kinetic information about this reaction was obtained from dilatometric measurements. The volume decrease in presence of an excess of formaldehyde was much faster than with acetaldehyde alone, and no volume change was detectable with formaldehyde alone. Fig. 2 shows the dilatometric readings for the reaction in a phosphate buffer ($[\mathrm{PO_4^{3-}}] = [\mathrm{HPO_4^{2-}}] = 0{\cdot}1$) with a constant acetaldehyde concentration of 0·1M and varying formaldehyde concentrations. The initial rate is independent of formaldehyde concentration, though this is not true of the later stages of the reaction. The initial rates given in the tables were calculated by the procedure already described.

The order of the reaction with respect to acetaldehyde and hydroxyl ions was investigated in dilute solutions of sodium hydroxide, as shown in Table 7. On account of the acidity of formaldehyde the true hydroxyl-ion concentration was much smaller than that of the sodium hydroxide added: it was estimated from the value already given for the equilibrium constant of the reaction $\mathrm{CH_2(OH)_2} + \mathrm{OH^-} \rightleftharpoons \mathrm{CH_2(OH){\cdot}O^-} + \mathrm{H_2O}$. A correction was also made for the proportion of formaldehyde present as polymer, data quoted by Walker [15] being used.

The order of the reaction with respect to acetaldehyde was also studied in carbonate buffers as shown in Table 8. Similar results were obtained in phosphate buffers.

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[15] Walker, " Formaldehyde," Amer. Chem. Soc. Monograph, Reinhold, 1944.

TABLE 7. *Reaction of acetaldehyde with formaldehyde in dilute sodium hydroxide.*

[Me·CHO]	$[CH_2O]$	10^4[NaOH]	$10^4[OH^-]$	10^9v^*	$10^3v^*/[OH^-]$[Me·CHO]
0·02	3·22	100	7·4	22	1·5
0·10	3·22	106	7·8	120	1·5
0·10	1·61	100	11·7	173	1·4
0·10	3·22	200	14·8	250	1·7
0·10	3·22	522	38·6	630	1·6
0·20	3·22	100	7·4	220	1·5
0·20	3·22	10	0·74	18	1·2

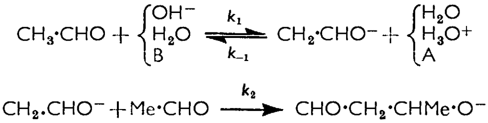
TABLE 8. *Reaction of acetaldehyde with formaldehyde in carbonate buffers.*

$[CO_3^{2-}] = [HCO_3^-] = 0{\cdot}1$; $[OH^-] = 1{\cdot}06 \times 10^{-4}$; $[CH_2O] = 4{\cdot}8$

[Me·CHO]	0·02	0·04	0·06	0·08	0·10
10^9v^*	6·5	13·5	20·7	25·1	35·5
$10^3v^*/[OH^-]$[Me·CHO]	3·1	3·2	3·2	3·0	3·3

DISCUSSION

It is convenient first to consider the kinetic scheme for the aldol condensation of acetaldehyde in a simple buffer solution A–B. The kinetically important part of the reaction can be written



$$CH_3\cdot CHO + \left\{\begin{matrix}OH^-\\ H_2O\\ B\end{matrix}\right. \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CH_2\cdot CHO^- + \left\{\begin{matrix}H_2O\\ H_3O^+\\ A\end{matrix}\right. \quad . \; . \; . \; . \; . \; . \; . \; . \quad (2)$$

$$CH_2\cdot CHO^- + Me\cdot CHO \xrightarrow{k_2} CHO\cdot CH_2\cdot CHMe\cdot O^-$$

where k_1 and k_{-1} are first-order constants whose values depend upon the composition of the buffer solution, and k_2 is a second-order constant. The ion $CHO\cdot CH_2\cdot CHMe\cdot O^-$ probably reacts rapidly with a further molecule of acetaldehyde to give 6-hydroxy-2,4-dimethyl-1,3-dioxan, and if this is so the reaction scheme (2) corresponds to the disappearance of three molecules of acetaldehyde. Our experiments give initial rates, and since there is good evidence [16,17] that the hydration equilibrium of acetaldehyde is established very much more rapidly than the reactions in scheme (2), the observed rates can be expressed in terms of a, the initial stoicheiometric aldehyde concentration, giving

$$-\frac{3}{\mathrm{d}a/\mathrm{d}t} = \frac{1}{ak_1} + \frac{k_{-1}}{a^2k_1k_2} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (3)$$

Equation (3) shows how the order of the reaction should vary between one and two with varying aldehyde concentration. The constants k_1 and k_{-1} are functions of the concentrations of the acidic and basic species present, *i.e.*,

$$\begin{aligned} k_1 &= k_{\mathrm{OH}}[OH^-] + k_0 + k_{\mathrm{B}}[B] \\ k_{-1} &= k_0' + k_{\mathrm{H}}[H^+] + k_{\mathrm{A}}[A] \end{aligned} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (4)$$

However, the various constants in scheme (4) are not all independent, since they are related through the equilibrium constant $[CH_2\cdot CHO^-]/[CH_3\cdot CHO][OH^-] = K$; applying the principle of detailed balancing to each acid–base pair separately, we obtain

$$k_1/k_{-1} = k_{\mathrm{OH}}[OH^-]/k_0' = k_0/k_{\mathrm{H}}[H^+] = k_{\mathrm{B}}[B]/k_{\mathrm{A}}[A] = K[OH^-] \quad . \; . \; . \quad (5)$$

so that equation (3) becomes

$$-\frac{3}{\mathrm{d}a/\mathrm{d}t} = \frac{1}{a\{k_{\mathrm{OH}}[OH^-] + k_0 + k_{\mathrm{B}}[B]\}} + \frac{1}{a^2k_2K[OH^-]} \quad . \; . \; . \quad (6)$$

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[16] Bell and Darwent, *Trans. Faraday Soc.*, 1950, **46**, 34.

[17] Bell, Rand, and Wynne-Jones, *Trans. Faraday Soc.*, 1956, **52**, 1093.

Further, since the buffer equilibrium can be written $[A][OH^-]/[B] = K_B$, an alternative form for equation (6) is

$$-\frac{3}{da/dt} = \frac{1}{a\{k_0 + [B][k_B + K_Bk_{OH}/[A]\}} + \frac{[A]}{a^2k_2KK_B[B]} \quad . \quad . \quad . \quad (7)$$

For solutions of sodium hydroxide the term in [B] disappears from equation (6), and if also $k_0 \ll k_{OH}[OH^-]$, we have

$$-\frac{3[OH^-]}{da/dt} = \frac{1}{ak_{OH}} + \frac{1}{a^2k_2K} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

In all the above equations no account has been taken of salt effects, so that some of the equilibrium and velocity constants will vary appreciably with salt concentration.

The last column of Table 3 shows that in sodium hydroxide solutions the aldol condensation is approximately of the second order in aldehyde, though there is some decrease of $v^*/a^2[OH^-]$ with increasing a: this indicates that the second term in equation (3) or (8) is the more important even at the highest aldehyde concentration studied. This conclusion differs from the previous finding [3,4] that the first-order term is considerable in the range $a = 0{\cdot}1$—$0{\cdot}4$, the difference being due to the fact that in earlier work no correction was made for the decrease in $[OH^-]$ caused by the formation of the ion $Me{\cdot}CH(OH){\cdot}O^-$. However, there is a further complication, which makes it difficult to give a quantitative interpretation. The ion $Me{\cdot}CH(OH){\cdot}O^-$ is present in concentrations comparable with $[OH^-]$, and may well contribute appreciably to k_1, since, although it is a considerably weaker base than OH^- (pK 13·5, compared with 15·7), there is much evidence [18] that proton transfers to OH^- are slower than would be expected. Examination of equation (6) shows that this would have the effect of increasing the apparent order with respect to aldehyde: hence the first-order term in equation (8) is probably more important than appears from Table 3.

The variation of reaction velocity with alkali concentration in concentrated sodium hydroxide solutions (Table 4) can be accounted for if we make the reasonable assumption that the ion $Me{\cdot}CH(OH){\cdot}O^-$ does not take part in the condensation. In these experiments the aldehyde concentration was low (0·02M) and it will be a good approximation to take only the second term of equation (8). If $x = [Me{\cdot}CH(OH){\cdot}O^-]$ the velocity is given by

$$-da/dt = (a - x)^2k_2K[OH^-] = k_2Ka^2[OH^-]/(1 + K'[OH^-])^2 \quad . \quad . \quad (9)$$

where K' is the equilibrium constant $x/(a - x)[OH^-]$, found experimentally to equal 1·8. Equation (9) predicts a maximum velocity at $K'[OH^-] = 1$, *i.e.*, $[OH^-] = 0{\cdot}6$. This is consistent with the values in Table 4, and the form of the velocity–concentration curve is well represented by equation (9).

Further information on the velocity in presence of hydroxide ions can be obtained from the measurements in buffer solutions (Tables 5 and 6), using the velocities extrapolated to zero buffer concentration. These values are collected in Table 8, which shows that the quantity $v^*/a^2[OH^-]$ exhibits no systematic variations over a considerable range of $[OH^-]$ and a; *i.e.*, the reaction is again close to the second order in acetaldehyde. The mean value of $v^*/a^2[OH^-]$ is somewhat smaller than that found from measurements in sodium hydroxide solutions (Table 3), but the difference is probably not greater than can be accounted for by the uncertainties of correcting for the formation of $Me{\cdot}CH(OH){\cdot}O^-$ in sodium hydroxide solution and of calculating $[OH^-]$ in the buffer solutions. Equation (6) predicts that for a given aldehyde concentration the reaction will be closer to the second order in a buffer solution than in a sodium hydroxide solution.

The results in Tables 5 and 6 demonstrate clearly the presence of general base catalysis since in every case the velocity increases with increase of buffer concentration at constant

[18] Bell, " Acid-Base Catalysis," Oxford, 1941, p. 92.

TABLE 8. *Hydroxide-ion catalysis from measurements in buffer solutions.*

$10^5[OH^-]$	a	10^9v^* (extr.)	$10^5v^*/a^2[OH^-]$	$10^5[OH^-]$	a	10^9v^* (extr.)	$10^5v^*/a^2[OH^-]$
	Borate buffers				*Carbonate buffers*		
1·72	0·235	1·50	160	10·7	0·12	2·5	164
6·04	0·235	5·5	165	10·7	0·235	10·3	174
6·90	0·20	5·5	197	10·7	0·46	39	174
6·90	0·30	12·5	201	10·7	0·67	80	169
6·90	0·40	19·5	177	10·7	0·80	132	194
6·90	0·485	29	180	21·5	0·235	19·0	160
10·3	0·235	8·1	144	21·5	0·46	69	153
				21·5	0·67	79	178
				32·2	0·235	25·5	144

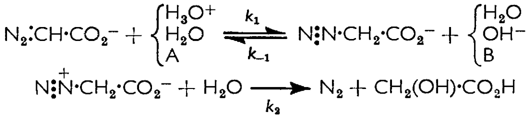
buffer ratio (and therefore constant $[OH^-]$). However, the quantitative laws obeyed are not those usually encountered, but show the following abnormalities:

(*a*) For a given buffer system the apparent catalytic effect of the basic constituent decreases with an increase in the concentration of the acidic constituent, *i.e.*, with decrease in $[OH^-]$.

(*b*) At a constant buffer ratio the effect of the basic buffer constituent relative to that of $[OH^-]$ decreases with increasing aldehyde concentration.

Both of these effects are in accordance with equations (6) and (7). These equations also predict that a plot of velocity against [B] at constant $[OH^-]$ should be concave to the concentration axis, but the part played by general base catalysis in this reaction is too small to establish this curvature or to attempt a quantitative test of the equations.

It is therefore of interest that published work by King and Bolinger [19] on quite a different reaction shows quantitative agreement with closely analogous equations.[20] The decomposition of the diazoacetate ion exhibits general acid catalysis, but shows anomalies which were left unexplained by the authors: in particular, the catalytic effect of an acid depends on the concentration of the corresponding base. If we postulate a two-stage reaction scheme,



$$N_2{:}CH{\cdot}CO_2^- + \left\{\begin{matrix} H_3O^+ \\ H_2O \\ A \end{matrix}\right. \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} N{:}\overset{+}{N}{\cdot}CH_2{\cdot}CO_2^- + \left\{\begin{matrix} H_2O \\ OH^- \\ B \end{matrix}\right.$$

$$N{:}\overset{+}{N}{\cdot}CH_2{\cdot}CO_2^- + H_2O \xrightarrow[k_2]{} N_2 + CH_2(OH){\cdot}CO_2H$$

with $k_1 = k_H[H^+] + k_0 + k_A[A]$, then a steady-state treatment gives for the observed first-order velocity constant k,

$$\frac{1}{k} = \frac{1}{k_0 + k_H[H^+] + k_A[A]} + \frac{K}{k_2[H^+]} \quad \cdots\cdots \quad (10)$$

where K is the equilibrium constant $[H^+][N_2{:}CH{\cdot}CO_2^-]/[N{:}\overset{+}{N}{\cdot}CH_2{\cdot}CO_2^-]$. This is closely analogous to equation (6) for the aldol condensation, except that there is no variation of reaction order with concentration, since the second step does not involve another molecule of substrate. In fact, all the velocity constants of King and Bolinger for reactions in sodium hydroxide solution and in buffers of phenol, ammonia, and piperidine (about 100 in all) can be represented by the following choice of constants:

$k_0 = 3{\cdot}0 \times 10^{-3}$ min.$^{-1}$
$k_H = 7{\cdot}0 \times 10^6$, $k(NH_4^+) = 1{\cdot}2$, $k_2/K = 5{\cdot}0 \times 10^8$;
$k\ (C_6H_5{\cdot}OH) = 4{\cdot}0$, k (piperidinium) $= 0{\cdot}014$ l. mole^{-1} min.$^{-1}$

Figs. 3 and 4 show a comparison between the experimental points and the calculated curves for phenol and ammonia buffers: the agreement is equally good for piperidine buffers and sodium hydroxide solutions.

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[19] King and Bolinger, *J. Amer. Chem. Soc.*, 1936, **58**, 1533.

[20] Bell, " The Proton in Chemistry," Cornell, 1959, p. 135.

Equations (4)—(8) for the aldol condensation contain the velocity constants k_0, k_{OH}, and k_B which represent the velocity of ionization of acetaldehyde in presence of the bases H_2O, OH^-, and B, and it would be valuable to have an independent measure of these velocities. For many carbonyl compounds these are equal to the rates of zero-order halogenation, but this method is not directly applicable to acetaldehyde, since oxidation preponderates in its reaction with halogens.[21] However, a good estimate of its rate of ionization can be obtained from the initial rate of reaction with formaldehyde. Fig. 4 and Tables 7 and 8 show that at high formaldehyde concentrations this reaction is of zero order with respect to formaldehyde, but of the first order in both acetaldehyde and hydroxyl ions, so that the rate-determining step is presumably $CH_3{\cdot}CHO + OH^- \longrightarrow CH_2{\cdot}CHO^- + H_2O$, followed by a rapid reaction of the anion with formaldehyde. Moreover, the comparison of dilatometric and spectrophotometric observations gave $1{\cdot}7 \times 10^{-2}$ l. per mole of acetaldehyde for the volume change of the reaction, so that the dilatometric constants in the last column of Table 7 give $k_{OH} = 1{\cdot}5 \times 10^{-3}/1{\cdot}7 \times 10^{-2} = 9 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ for the velocity constant of $CH_3{\cdot}CHO + OH^-$. This is quite close to the value $1{\cdot}7 \times 10^{-1}$ for the corresponding reaction of acetone [22] (from rates of halogenation), and the agreement is even closer if we multiply the acetaldehyde value by 2·2 to allow for its partial hydration in solution,[13] and divide the acetone value by 2 to allow for the presence of two equivalent methyl groups. The rate of ionization of acetaldehyde in carbonate buffers (Table 8) is about twice as great as can be accounted for by the concentration of hydroxyl ions, showing that the reaction $CH_3{\cdot}CHO + CO_3{}^{2-} \longrightarrow CH_2{\cdot}CHO^- + HCO_3{}^-$ is contributing appreciably. It is therefore probable that the

FIG. 3. *Decomposition of the diazoacetate ion in phenol buffers.*

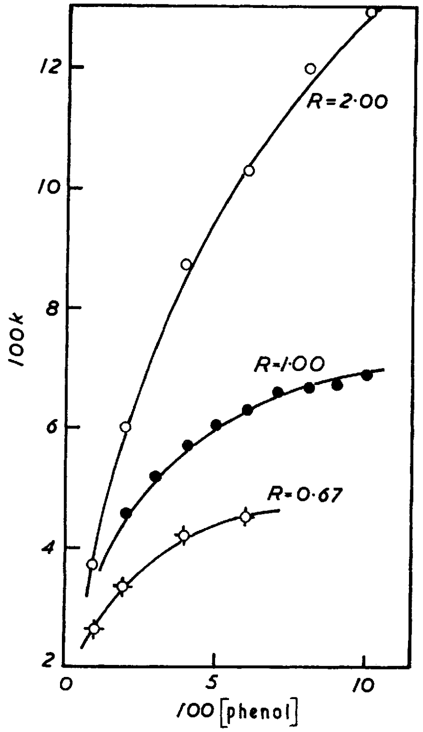
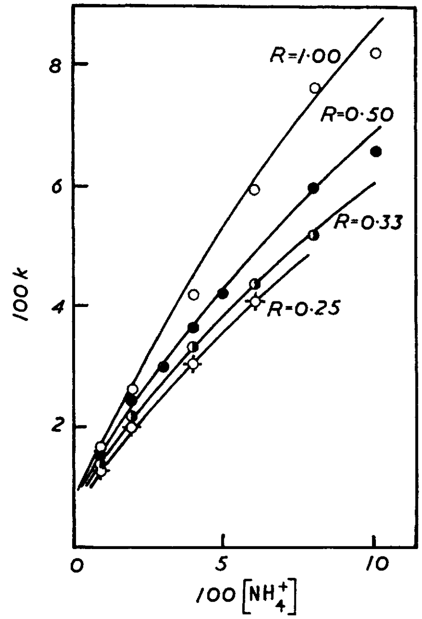


FIG. 4. *Decomposition of the diazoacetate ion in ammonia buffers.*



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[21] Bell and Ford-Smith, to be published.

[22] Bell and Longuet-Higgins, *J.*, 1946, 636.

reaction $CH_3{\cdot}CHO + CH_2(OH){\cdot}O^- \longrightarrow CH_2{\cdot}CHO^- + CH_2(OH)_2$ contributes something to the observed velocities in sodium hydroxide solutions, so that the velocity attributed to $CH_3{\cdot}CHO + OH^-$ may be rather too high.

Unfortunately, it is not possible to apply these rates of ionization quantitatively to the kinetics of the aldol condensation, since we lack the information necessary to convert the dilatometric constants in Table 3 into absolute rate constants. However, any reasonable choice for the specific volume change of the aldol condensation leads to the conclusion that in sodium hydroxide solutions the rate at which the ion $CH_2{\cdot}CHO^-$ undergoes further condensation is less than the rate at which it is formed by a factor of 3—6. This is consistent with an observed order of reaction close to 2, and also with the presence of modified general base catalysis, and the partial isotopic exchange previously found when the reaction is carried out in deuterium oxide.[5]

It has recently been reported [6] that trideuteroacetaldehyde undergoes the aldol condensation about 7 times as slowly as acetaldehyde in solutions of sodium hydroxide. The aldehyde concentration in these experiments is not given, but our experiments show that the ionization step is only partially rate-determining even at high concentrations. Since the condensation step will be little affected by isotopic substitution, the isotope effect on the rate of ionization should be considerably greater than 7. It is therefore surprising that Pocker [23] finds closely the same value for the isotope effect in the bromination of acetone and hexadeuteroacetone in alkaline solution, in which the ionization of the ketone is rate-determining.[22] Measurements in this laboratory [21] on the same reaction give an isotope effect of 10, which seems more probable, and agrees with the value reported by Wynne-Jones [24] for the neutralization of nitroethane and dideuteronitroethane by hydroxide ions. The discrepancy for acetone remains unexplained.

One of us (P. T. McT.) thanks Magdalen College, Oxford, for the award of a Perkin Research Scholarship, during the tenure of which this work was carried out.

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AUSTRALIA.] [*Received, February 22nd*, 1960.]

[23] Pocker, *Chem. and Ind.*, 1959, 1383.
[24] Wynne-Jones, *J. Chem. Phys.*, 1934, **2**, 381.