

The Kinetics of the Cannizzaro Reaction of Glyoxal

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The kinetics of the Cannizzaro reaction of glyoxal have been investigated in water solution at different temperatures. The reaction is very rapid and is of the third order, the rate being proportional to the first power of the glyoxal concentration and to the square of hydroxyl ion concentration. The reaction is characterized by a very strong positive salt effect. The observed kinetics and salt effect have been discussed and a reaction mechanism has been suggested in which the slow and rate-determining reaction is a reaction between hydroxyl ion and a univalent negative ion which is formed from glyoxal and hydroxyl ion in a primary rapid reaction.

The kinetics of the Cannizzaro reaction of monoaldehydes have been extensively investigated as compared with those of α -dicarbonyl compounds, glyoxal and some of its derivatives, which are known to undergo the Cannizzaro reaction in the presence of alkali. The only observations thus far made, which are to be found in the literature, are those of Ariyama¹ and Alexander². When developing a colorimetric method for the determination of glyoxal Ariyama found that the rate of the Cannizzaro reaction of glyoxal increases more rapidly than the hydroxyl ion concentration of the solution. Alexander found that the conversion of phenyl glyoxal into mandelic acid under the influence of alkali is a first order reaction with respect to both reactants.

It seemed of interest to investigate the kinetics of the Cannizzaro reaction of glyoxal



more extensively in order to elucidate the reaction mechanism, particularly because, owing to the two carbonyl groups in glyoxal, the reaction involves formally only two reacting molecules, whereas three reacting molecules participate in the Cannizzaro reaction of monoaldehydes. This was expected to give rise to differences in the reaction mechanism.

The order of the reaction

The progress of reaction (A) could be followed by determining both the hydroxyl ion concentration and glyoxal concentration remaining in the reaction solution at different times by methods described in the experimental

part. Both methods gave nearly identical results, but owing to the rapidity of the reaction, relatively low concentrations had to be used in which case the determination of glyoxal concentration was found to give more accurate results^{cf. 3}). Therefore, the latter results were used in the calculation of specific rates.

The results obtained indicate that the rate of reaction (A) is proportional to the first power of glyoxal concentration and to the square of hydroxyl ion concentration. The specific rates were calculated from the integrated form (2) of the differential equation (1)

$$\frac{dx}{dt} = k (a - x) (b - x)^2 \quad (1)$$

$$k = \frac{1}{t(a-b)} \left[\frac{1}{b-x} - \frac{1}{b} - \frac{1}{a-b} \ln \frac{b(a-x)}{a(b-x)} \right] \quad (2)$$

by applying the initial condition $x = 0$, when $t = 0$. In these equations a and b are the initial concentrations of glyoxal and hydroxyl ion, respectively, and x the concentration of glyoxal reacted at time t , and k is the specific rate. In the experiments, in which equimolar concentrations were employed, *i.e.* $a = b$, eqns. (1) and (2) were replaced by eqns. (1a) and (2a)

$$\frac{dx}{dt} = k (a - x)^3 \quad (1a)$$

$$k = \frac{1}{2t} \left[\frac{1}{(a-x)^2} - \frac{1}{a^2} \right] \quad (2a)$$

Table 1 contains results obtained in experiments in which the order of the reaction was determined by using various initial concentrations of the reactants. The values obtained for the specific rate k are nearly the same; the small deviations may be due to experimental errors. The slight increase in the values with increasing hydroxyl ion concentration is probably due to the heat of the reaction which effects a small increase in the temperature of the reaction solution, but this source of error is eliminated when relatively low alkali concentrations are used in which case the reaction is slower and the temperature can be kept constant during the reaction. Tables 2 and 3 give details of two typical runs.

Table 1. Determination of the order of the Cannizzaro reaction of glyoxal in water solution at 25° C using different initial concentrations. Third order specific rates calculated from eqns. (2) and (2a).

a	b	$k \text{ l}^2 \text{ mole}^{-2} \text{ sec}^{-1}$
0.00195	0.01368	169
0.00364	0.01045	170
0.00569	0.00569	170
0.00585	0.00731	164
0.01057	0.00612	162
0.01186	0.00505	161

Table 2. The Cannizzaro reaction of glyoxal in water at 25° C. $a = b = 0.00569$. Specific rates calculated from eqn. (2a).

t (in minutes)	1	2	4	6	9	12	15
$10^3 \times (a - x)$	4.43	3.73	3.03	2.52	2.14	1.90	1.74
k	167	171	163	176	174	171	166
Average $k = 170 \text{ l}^2 \text{ mole}^{-2} \text{ sec}^{-1}$							

Table 3. The Cannizzaro reaction of glyoxal in water at 25° C. $a = 0.01186$, $b = 0.00505$. Specific rates calculated from eqn. (2).

t (in minutes)	0.5	1	1.5	2	2.5	3	3.5
$10^3 \times (a - x)$	10.82	10.09	9.67	9.31	9.11	8.83	8.69
$10^3 \times (b - x)$	4.01	3.28	2.86	2.50	2.30	2.02	1.88
k	152	164	160	164	157	168	164
Average $k = 161 \text{ l}^2 \text{ mole}^{-2} \text{ sec}^{-1}$							

The effect of temperature

The specific rates measured at different temperatures are given in Table 4. In all of these experiments the initial hydroxyl ion concentration was relatively low, about 0.005 N, in order that the reactions would proceed at a measurable rate and to avoid the influence of the heat of reaction. The table contains also the values of the activation energy E and the logarithm of the frequency

Table 4. The effect of temperature on the Cannizzaro reaction of glyoxal in water solution.

° C	0	15	25	35
$k \text{ l}^2 \text{ mole}^{-2} \text{ sec}^{-1}$	9.28	45.1	161	398
$E = 18\,200 \text{ cal/mole}$, $\log A = 15.52$				

factor A calculated according to the Arrhenius equation from the values of $\log k$ at different temperatures by the method of least squares.

The value of the activation energy, 18 200 cal per mole, is considerably lower than the activation energy of the Cannizzaro reaction of formaldehyde in water solution, 22 300 cal per mole, determined by Pajunen⁴. Similarly, the value of $\log A$, 15.52, is considerably higher than the corresponding value for formaldehyde, 11.90, both of which factors effect an enhanced reactivity of glyoxal as compared with formaldehyde.

Salt effect

Table 5 contains results obtained in experiments in which the effect of increase in electrolyte concentration on the reaction rate was investigated in solutions containing added sodium chloride. Table 6 gives details for one of the individual runs. As it is seen from Table 5, the Cannizzaro reaction of glyoxal is characterized by a very pronounced positive salt effect, the specific rate increasing rapidly with increasing electrolyte concentration. The magnitude of the salt effect is of a much higher order of magnitude than that generally observed in reactions between ions and neutral molecules taking place in water solution⁵.

Table 5. The effect of added sodium chloride on the rate of the Cannizzaro reaction of glyoxal in water at 25° C.

[NaCl]	—	0.084	0.263	0.572	0.789	1.034	1.316	1.545	1.842
k l ² mole ⁻² sec ⁻¹	161	187	212	249	266	295	309	349	377

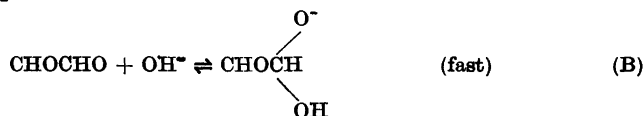
Table 6. The Cannizzaro reaction of glyoxal in water at 25° C in the presence of added sodium chloride. [NaCl] = 1.545, $a = 0.01099$, $b = 0.00418$.

t (in seconds)	22.3	41.2	62.3	98.6	113.8	149.1	167.9
$10^3 \times (a - x)$	9.95	9.44	9.00	8.55	8.46	8.21	8.13
$10^3 \times (b - x)$	3.14	2.63	2.19	1.74	1.65	1.40	1.32
k	341	340	358	363	347	352	344
Average $k = 349$ l ² mole ⁻² sec ⁻¹							

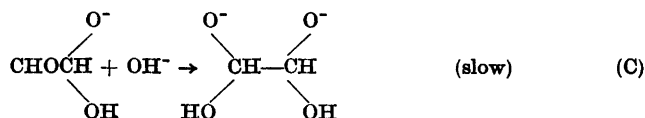
DISCUSSION

On the basis of the results presented above, a more detailed picture of the Cannizzaro reaction of glyoxal may be attempted. Although the reaction is of the third order, it is highly improbable that an actual termolecular reaction mechanism is involved. Using a method of calculation described by Tommila ⁶, a value of the order of 2×10^{10} l² mole⁻² sec⁻¹ is obtained for the frequency of a ternary collision between two hydroxyl ions and a glyoxal molecule at 25° C. If every collision between activated molecules were to lead to a reaction the frequency factor A should be of this order of magnitude in the case of a termolecular reaction, but actually a lower value for the frequency factor would be expected, because it is improbable that every collision between activated molecules will effect a reaction. The measured value of the frequency factor A is 3.3×10^{15} l² mole⁻² sec⁻¹, which is of a much higher order of magnitude than that evaluated for a ternary collision.

It is thus very probable that the reaction takes place in several successive steps, of which the first (B) involves a rapid equilibrium reaction between glyoxal and hydroxyl ion



The negatively charged addition product then reacts with another hydroxyl ion in a second step (C), which is slow and rate-determining



In the subsequent steps, discussed below, the reactive divalent anion formed in reaction (C) reacts rapidly to yield the final product, the anion of glycolic acid, but these rapid steps do not affect the kinetics of the reaction and cannot be kinetically distinguished.

The reactions (B) and (C) are in good accord with the observed reaction order. For the rate v of the reaction we have

$$v = k' [\text{OH}^-] [\text{CHOCH}(\text{OH})\text{O}^-] \quad (3)$$

in which k' is the specific rate of the rate-determining step (C). For the equilibrium (B) we obtain

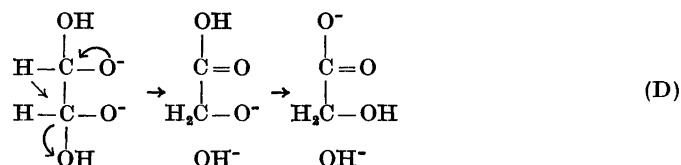
$$\frac{[\text{CHOCH}(\text{OH})\text{O}^-]}{[\text{CHOCHO}][\text{OH}^-]} = K \quad (4)$$

in which K denotes the equilibrium constant. From eqns. (3) and (4) we obtain for the reaction rate the expression

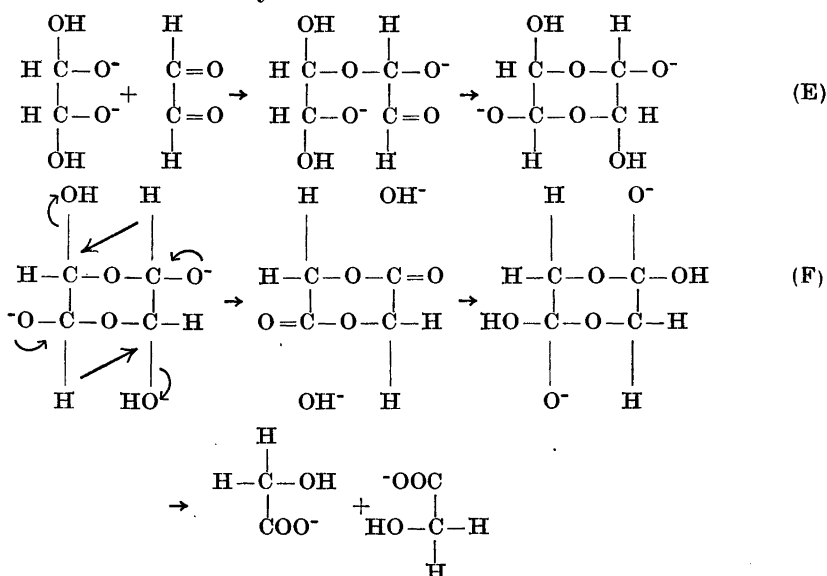
$$v = k'K[\text{CHOCHO}][\text{OH}^-]^2 \quad (5)$$

which is the same as that found experimentally if the experimental third order specific rate k is substituted for $k'K$.

The rapid subsequent reaction steps which follow reactions (B) and (C) are probably complicated as in the case of the Cannizzaro reaction of monoaldehydes⁶⁻⁹. The subsequent reaction of the anion formed in (C) may take place by an intramolecular hydrogen shift

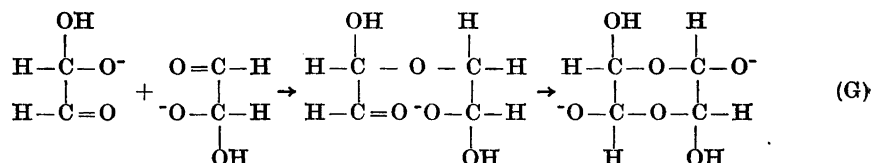


or, the anion may react first with another glyoxal molecule according to (E), after which the symmetrical product formed is converted to the final product by a mechanism (F) essentially similar to that suggested by Ingold, Wilson and Tommila⁶⁻⁹ for monoaldehydes



The mechanism (D) is in the present case the most probable. In the formation of the symmetrical product in (E) the attainment of the transition state involves a large increase in order, *i.e.* the activation entropy is negative and the frequency factor relatively low as compared with reaction (D). Similarly, the activation energy of the reaction path (D) has probably a much lower value than that of (E), since the latter involves typical carbonyl addition reactions that take place at a measurable speed, whereas in (D) as well as in (F), intramolecular hydrogen shifts take place in which much lower values of the activation energy are to be expected. The rapidity of the subsequent steps following the rate-determining reaction (C) are thus not as readily understood on the basis of mechanism (E) as in the case of the intramolecular mechanism (D). Also Alexander² assumed an intramolecular hydrogen shift to take place in the conversion of phenyl glyoxal to mandelic acid under the influence of alkali. The latter reaction was found to be of the second order, the rate being proportional to the first powers of hydroxyl ion and phenyl glyoxal concentrations. In this case the hydrogen shift was assumed to take place directly in the univalent anion corresponding to that formed in reaction (B), in accordance with the observed reaction order. The difference between the reaction mechanisms of glyoxal and phenyl glyoxal can be ascribed to the — *M* effect of the phenyl group¹⁰ which greatly facilitates the hydrogen shift to the adjacent carbon atom, as a result of which the reaction corresponding to (B) becomes the slowest and hence rate-determining.

If the Cannizzaro reaction of glyoxal were to take place formally similarly as in the case of monoaldehydes⁶⁻⁹, the rate-determining reaction following (B) would take place between two anions formed in (B) and would lead to a symmetrical product



The subsequent reactions could be presented by eqn. (F). This type of mechanism is in principle similar to that suggested by Karrer¹¹ for the Cannizzaro reaction of glyoxal and would lead to fourth order kinetics. If it is taken into account that in the Cannizzaro reaction the step corresponding to (B) generally takes place very rapidly, one must assume that in the case of glyoxal the reaction takes place by an easier and more rapid way than (G). Owing to the presence of two carbonyl groups in glyoxal, there is the possibility that another relatively rapid reaction (C), which in principle is similar to (B), occurs. This would explain the low value of the activation energy for the glyoxal reaction, 18 200 cal per mole, as compared with the formaldehyde reaction, the activation energy of which is 22 300 cal per mole⁴. The fact that reaction (C) is slower than (B) conforms with the mesomeric effect of substituents¹⁰. The — *M* influence of the second carbonyl group, which facilitates the addition of hydroxyl ion to the first carbonyl, no longer remains after reaction (B) has occurred.

From the value of $\log A$ (Table 4), 15.52, the activation entropy can be calculated according to the theory of absolute reaction rates¹². From the formula

$$\Delta S^* = R \ln \frac{A h}{e k T} \quad (6)$$

one obtains for the activation entropy, ΔS^* , of the Cannizzaro reaction of glyoxal the value $37.9 \text{ cal} \times \text{deg}^{-1} \text{ mole}^{-1}$ at 25°C . A is here expressed in $\text{cm}^6 \text{ mole}^{-2} \text{ sec}^{-1}$. Similarly as in the case of formaldehyde⁴, the reaction is characterized by a very high positive activation entropy. The corresponding value for formaldehyde is $21.2 \text{ cal} \times \text{deg}^{-1} \text{ mole}^{-1}$. A large positive activation entropy corresponds to a large decrease in order in the attainment of the transition state. Pajunen⁴ explained the large positive activation entropy of formaldehyde as being due to the hydration of the carbonyl group, which is not possible in the critical complex; this leads to a decrease in order. This may also be one of the main reason for the large activation entropy of the glyoxal reaction, and its high value as compared with that of the formaldehyde reaction may be ascribed to the presence of two hydrated carbonyl groups in the case of glyoxal.

The fact that in the glyoxal reaction the rate determining stage (C) takes place between two ions is in good accord with the strong positive salt effect observed. In the case of monoaldehydes, as with formaldehyde⁴, the influence of electrolytes on the reaction rate is very slight since the rate-determining stage takes place between an ion and a neutral molecule. In Fig. 1 values of $\log k$ for the Cannizzaro reaction of glyoxal in sodium chloride solutions are plotted against the ionic strength and against the square root of the ionic strength.

Although the observed salt effect is of nearly the same order of magnitude as is to be expected for reactions between ions, the application of Debye-

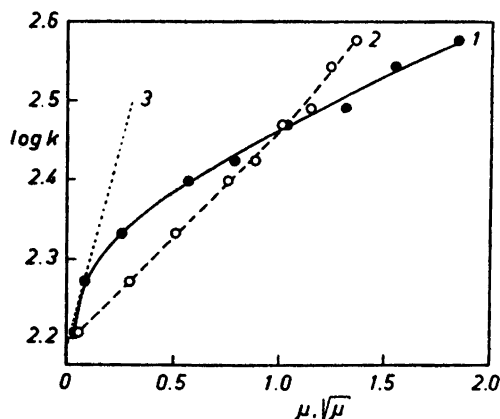


Figure 1. The Cannizzaro reaction of glyoxal in sodium chloride solutions at 25°C . 1. Plot of $\log k$ versus the ionic strength. 2. Plot of $\log k$ versus the square root of the ionic strength. 3. Debye-Hückel limiting law.

Hückel theory does not give satisfactory results when the activity coefficient of the critical complex of reaction (C) is taken to be equal to that of a divalent ion. If a_{GI} , a_{GIOH^-} , a_{OH^-} and a_{x} denote the activity coefficients of glyoxal, the ion formed in reaction (B), hydroxyl ion, and the critical complex of reaction (C), respectively, we obtain for the specific rate of reaction (C) from the Brönsted rate equation the expression:

$$k' = k_0' \frac{a_{\text{GIOH}^-} a_{\text{OH}^-}}{a_{\text{x}}} \quad (7)$$

and for the equilibrium constant of the reaction (B):

$$K = K_0 \frac{a_{\text{GI}} a_{\text{OH}^-}}{a_{\text{GIOH}^-}} \quad (8)$$

in which K_0 is the thermodynamic equilibrium constant. When $k_0' K_0$ is denoted by k_0 , and it is taken into account that the measured specific rate k is equal to $k'K$, it follows from eqns. (7) and (8)

$$\log k = \log k_0 + \log a_{\text{GI}} + 2 \log a_{\text{OH}^-} - \log a_{\text{x}} \quad (9)$$

If the changes in a_{GI} effected by changes in the ionic strength are neglected, and the activity coefficients of hydroxyl ion and the critical complex are calculated from the Debye-Hückel theory by considering the critical complex a divalent negative ion, the expression (10) is obtained for the influence of ionic strength on the specific rate at 25° C

$$\log k = \log k_0 + \frac{1.02 \sqrt{\mu}}{1 + a \sqrt{\mu}} - B \mu \quad (10)$$

a and B are constants. Eqn. (10) predicts that in the plot of $\log k$ versus the square root of the ionic strength the initial slope should be 1.02. From Fig. 1 it is seen that experimentally determined initial slope is considerably smaller, about 0.25, and the curve shows a slight drift upwards with increasing ionic strength. In many other reactions involving ions of greater charge than one, large deviations from the Debye-Hückel theory have been observed¹³. The Debye-Hückel derivation involves the assumption of a spherical symmetry of the potential field around the ion, which assumption is not justified in the present calculation of the activity coefficient of the doubly charged critical complex of the reaction (C), since in the transition state the two univalent negative charges are situated relatively far apart. Assuming that, as a limiting case, the logarithm of the activity coefficient of the critical complex is the same as that of two univalent ions, the plot of $\log k$ versus the ionic strength would be approximately linear owing to the cancellation of the terms containing the square root of the ionic strength. In view of the plot of $\log k$ versus the ionic strength shown in Fig. 1, it is also possible that an intermediate case is involved, in which the value of the activity coefficient of the critical complex is somewhere between the values calculated from the Debye-Hückel theory for a divalent ion and for two univalent ions.

EXPERIMENTAL

The solution of glyoxal in water was prepared and purified according to Ronzio and Waugh¹⁴. For the kinetic experiments, about 0.25 M stock solutions of glyoxal and sodium hydroxide were prepared. All water used in the experiments was distilled water freed from carbon dioxide by boiling.

The kinetic measurements were carried out in electrically heated water thermostats, the temperature of which was kept constant within $\pm 0.02^\circ\text{C}$ by a mercury contact regulator. A well stirred ice-water mixture was used as a thermostat at 0°C . All-glass reaction vessels were employed. When the reaction solution, which contained usually about 0.01 mole of glyoxal per liter, had attained the temperature of the thermostat, a volume of sodium hydroxide stock solution was added with vigorous shaking. Except in the experiments in which the order of the reaction was determined, the initial concentration of sodium hydroxide used was relatively low, about 0.005 M, because the rapidity of the reactions at higher sodium hydroxide concentrations did not permit the determination of the specific rates as accurately as when lower concentrations were employed. After the components were mixed, the progress of the reaction was followed by taking 8–11 samples of the reaction mixture with a 20 ml semiautomatic pipette during the course of the reaction. Zero time was the time of taking of the first sample. The samples were run into conical flasks which contained an excess of approximately 0.025 N standard hydrochloric acid solution, and the excess acid was titrated with approximately 0.025 N standard sodium hydroxide solution using phenol red as indicator. This titration gave the hydroxyl ion concentration of the reaction solution at the time of taking of the sample. After this titration, the glyoxal present in the sample was determined by the bisulphite method described in the preceding paper³ using an approximately 0.05 N standard iodine solution and an approximately 0.05 M bisulphite solution. Both methods, the determination of the hydroxyl ion concentration and the glyoxal concentration gave nearly identical results when applied to the calculation of the specific rates, but owing to the relatively low concentrations used in the experiments, the determination of glyoxal was found to be more accurate *cf.*³. For this reason, the results of the latter determination were generally employed in the calculation of the specific rates.

The author wishes to thank Prof. A. Meretoja and Prof. R. Leimu for their interest in this work and for many helpful discussions. The author is also indebted to the authorities of the *University of Turku* for a grant awarded to young scientists by the *Finnish Government*.

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Received November 8, 1955.