168. *The Kinetics of the Alkaline Hydrolysis of the Halogen-substituted Acetates.*

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THE alkaline hydrolysis of sodium chloroacetate, represented stoicheiometrically by the equation $CH_2Cl{\cdot}CO_2Na + NaOH = CH_2OH{\cdot}CO_2Na + NaCl$, was one of the earliest reactions of the second order to be studied kinetically with reference to the applicability of the law of mass action. The results obtained by Schwab (Diss., Amsterdam, 1883; cf. van 't Hoff–Cohen, "Studien zur chemischen Dynamik," p. 15) in experiments at 100° with equivalent quantities of the reactants showed that the progress of the change could be represented with fairly close approximation by the bimolecular formula $k_{bi} = x/ta(a - x)$. The fact that k_{bi} increases considerably with the initial concentration of the reactants was confirmed by Senter (J., 1907, **91**, 460), but this is in all probability to be attributed to inert-salt effects which increase in magnitude as the total salt content of the solutions increases.

In more recent experiments (Dawson and Lowson, *Proc. Leeds Lit. Phil. Soc.*, 1934, **2**, 544) at 25° with the chloroacetate in considerable excess ($1{\cdot}0M$-$CH_2Cl{\cdot}CO_2Na$ + $0{\cdot}1M$-NaOH), it has been found by titration of the residual alkali that k_{bi} remains approximately constant until about 70% of the alkali has disappeared, but that this coefficient increases continuously in the later stages of the reaction.

As a result of the further investigation of the alkaline hydrolysis of solutions represented by the general formula aM-$CH_2Cl{\cdot}CO_2Na$ + bM-NaOH, it was found that the course of the reaction, expressed in terms of k_{bi}, depends on the relative values of a and b, and, in the case of equivalent solutions, on the absolute concentration.

When the concentration of the alkali is appreciably greater than that of the chloroacetate ($b > a$), k_{bi} remains sensibly constant throughout the entire course of the hydrolytic change. When, however, $a > b$ or $a = b$, the value of k_{bi} increases appreciably in the later stages of the reaction, although it remains nearly constant in the early stages. Furthermore, the data for dilute solutions containing equivalent quantities of the reactants show that the initial value of k_{bi} varies considerably with the concentration. It seemed probable that these variations in k_{bi} were due to concurrent hydrolytic processes in which the hydroxyl ion is not primarily involved, and this view is supported by the experiments now to be described.

According to the results obtained by Dawson and Dyson (J., 1933, 49, 1133) in the investigation of the mechanism of halogen elimination in neutral and acid solution, it would seem that the separation of halogen under the conditions afforded by alkaline hydrolysis is due to four simultaneous changes in which the primary reacting entities are the chloroacetate ion and (A) the hydroxyl ion, (B) the water molecule, (C) a second chloroacetate ion, or (D) the glycollate ion.

In the case of reactions (C) and (D) there is definite evidence to support the view that the complete reaction involves two consecutive stages corresponding with

$$CH_2Cl{\cdot}CO_2' + R' \longrightarrow R{\cdot}CH_2{\cdot}CO_2' + Cl',$$
$$R{\cdot}CH_2{\cdot}CO_2' + OH' \longrightarrow CH_2(OH){\cdot}CO_2' + R',$$

in which R' represents the chloroacetate or the glycollate ion. Since, however, there is no measurable difference between the rate of elimination of halogen in the first stage, and the rate of disappearance of hydroxyl ion in the second stage, it is apparent that the second stage keeps pace with the first, and that the velocity of alkaline hydrolysis can be followed by titration with standard silver or with standard acid.

On the above assumption, the actual rate of hydrolysis should be given by the sum of the velocities of the reactions (A), (B), (C), and (D), as represented by $v = v_A + v_B + v_C + v_D$. The reaction velocity, when x mols. of the products have been formed, should therefore be given by

$$dx/dt = k_A(a - x)(b - x) + k_B(a - x) + k_C(a - x)^2 + k_Dx(a - x) \quad . \quad . \quad (1)$$

in which k_A, k_B, k_C, and k_D are the velocity coefficients which characterise reactions (A), (B), (C), and (D) respectively.

Since k_B, k_C, and k_D are all less than $k_A/100$, it may be anticipated that the reactions (B), (C), and (D) will be almost negligible in comparison with (A) when the concentration of the alkali (b) is appreciably greater than that of the chloroacetate (a). In these circumstances, the entire course of the alkaline hydrolysis should conform closely to the requirements of the formula for a simple bimolecular reaction. On the other hand, when $a > b$ or $a = b$, the reactions (B), (C), and (D) may be expected to contribute appreciably to the observed velocity in the late stages of the reaction.

The contributions of (B), (C), and (D) relative to that of (A) are given at any stage of the reaction by v_B/v_A, v_C/v_A, and v_D/v_A. Since $v_B/v_A = k_B/k_A(b - x)$, it is evident that the relative effect of (B) is determined by the concentration of the residual alkali and is independent of that of the chloroacetate. From $v_C/v_A = (k_C/k_A)[(a - x)/(b - x)]$, it follows that the relative effect of (C) is determined by the ratio of the residual concentrations of the chloroacetate and alkali, whilst the relation $v_D/v_A = k_D x/k_A(b - x)$ indicates that the relative effect of (D) depends on the ratio of the concentrations of the glycollate and the alkali. In the particular case where $a = b$, the only difference to be noted is that the relative effect of (C) remains unchanged throughout the reaction, for in these circumstances $v_C/v_A = k_C/k_A$. By integration of equation (1), we obtain, when $a > b$,

$$k' = k_A(a - b) - k_B - k_D a = \frac{1}{t - t_0} \cdot \log_e \frac{k_A(b - x_0) + k_B + k_C(a - x_0) + k_D \cdot x_0}{k_A(b - x) + k_B + k_C(a - x) + k_D \cdot x} \cdot \frac{a - x}{a - x_0} \qquad (1a)$$

and, when $b > a$,

$$k'' = k_A(b - a) + k_B + k_D \cdot a = \frac{1}{t - t_0} \cdot \log_e \frac{k_A(b - x) + k_B + k_C(a - x) + k_D \cdot x}{k_A(b - x_0) + k_B + k_C(a - x_0) + k_D \cdot x_0} \cdot \frac{a - x_0}{a - x} \qquad (1b)$$

If $b = a$, the integration of (1) leads to

$$k''' = k_B + k_D a = \frac{1}{t - t_0} \log_e \frac{(k_A + k_C)(a - x) + k_B + k_D x}{(k_A + k_C)(a - x_0) + k_B + k_D \cdot x_0} \cdot \frac{a - x_0}{a - x} \quad . \qquad (1c)$$

Velocities in the Later Stages of Alkaline Hydrolysis.—The observations to be described in support of the validity of equation (1) as a general expression for the rate of alkaline hydrolysis are, in the first instance, concerned with the late stages of the reaction. When $a >$ or $= b$, the reactions (B), (C), and (D) may under these conditions be expected to contribute significantly to the reaction velocity. In these and in all other experiments, variations in reaction velocity which might be attributed to variations in the reaction medium (inert-salt effects) have been eliminated as far as possible by the use of solutions in which the total concentration of strong electrolyte is kept constant at 1 g.-equiv. per litre. This is effected by the addition of sodium nitrate, which does not interfere with the determination of the progress of the reaction by the use of standard silver solution. The initial composition of the solutions is therefore represented by the general formula $a\mathrm{CH_2Cl{\cdot}CO_2Na} + b\mathrm{NaOH} + (1 - a - b)\mathrm{NaNO_3}$.

The course of the reaction has been followed by titration of the halide formed with standard silver solution, the precision of which is distinctly greater than titration with standard acid. The accuracy attainable in the late stages of the reaction is, however, limited by the large amount of halide which is already present in the solution when the required stage has been reached. In these circumstances, the actual procedure was to conduct the experiments with synthetic solutions identical in composition with those produced by actual hydrolysis of the solution $a\mathrm{CH_2Cl{\cdot}CO_2Na} + b\mathrm{NaOH}$ [*e.g.*, $(a - x)\mathrm{CH_2Cl{\cdot}CO_2Na} + (b - x)\mathrm{NaOH} + x\mathrm{CH_2OH{\cdot}CO_2Na} + x\mathrm{NaCl}$] except for the fact that the halide was replaced by an equivalent amount of nitrate. By this means it has been found possible to study the course of the reaction in its later stages with much greater precision than could have been obtained otherwise.

The actual experimental data which are presented to illustrate the nature of the later stages of alkaline hydrolysis refer to solutions of the more readily hydrolysable bromoacetate, which affords convenient speeds of reaction at 45°. There can be no doubt, however, that the character of the relations which are involved is precisely the same for the chloroacetate.

For the bromoacetate at 45°, the values of the velocity coefficients for the reactions (A), (B), (C), and (D) are $k_A = 4{\cdot}0 \times 10^{-2}$, $k_B = 44 \times 10^{-6}$, $k_C = 210 \times 10^{-6}$, and $k_D = 370 \times 10^{-6}$. The fact that k_A varies somewhat with the concentration of the reactants (cf. p. 782) is not of any significance in these late-stage experiments.

Alkaline Hydrolysis of Sodium Bromoacetate.—(i) *When* (a > b). Table I shows, in the first instance, the results for $a = 0{\cdot}2$, $b = 0{\cdot}0495$. The synthetic solution, representing 50% hydrolysis, had the composition

$$0{\cdot}175CH_2Br{\cdot}CO_2Na + 0{\cdot}0245NaOH + 0{\cdot}025CH_2(OH){\cdot}CO_2Na + 0{\cdot}775NaNO_3.$$

The recorded numbers give the time in minutes, the volume of *ca.* 0·05*N*-silver solution required by 25 c.c. of reaction mixture, the bromide concentration [Br′] in equivs. per litre, the value of k_{bi}, *i.e.*,

$$k_{bi} = \frac{1}{t - t_0} \cdot \frac{1}{a - b} \cdot \log_e \frac{(a - x)(b - x_0)}{(b - x)(a - x_0)}$$

and the value of k' as given by equation (1*a*). At each stage in the reaction, $x = 0{\cdot}025 + [Br']$.

The second set of figures refers to an experiment with $a = 0{\cdot}50$ and $b = 0{\cdot}0500$, the synthetic solution again corresponding with 50% hydrolysis. The recorded numbers have the same significance as in the first experiment.

TABLE I.

$t - t_0$.	Ag, c.c.	$[Br'] . 10^2$.	$k_{bi} . 10^2$.	$k' . 10^3$.	$t - t_0$.	Ag, c.c.	$[Br'] . 10^2$.	$k_{bi} . 10^2$.	$k' . 10^3$.
$0{\cdot}2CH_2Br{\cdot}CO_2Na + 0{\cdot}0495NaOH + 0{\cdot}75NaNO_3$ (*At* 45°).									
0	1·70	0·338	—	—	145	8·96	1·781	4·87	5·97
23	3·42	0·680	4·52	5·98	164	9·44	1·877	4·91	5·93
47	4·92	0·978	4·57	5·96	186	10·00	1·988	5·07	5·98
69	6·10	1·213	4·65	6·00	211	10·47	2·082	5·17	5·93
93	7·14	1·420	4·67	5·95	233	10·88	2·164	5·38	5·97
105	7·61	1·513	4·70	5·94	286	11·59	2·305	5·94	5·94
119	8·15	1·621	4·79	5·99					
$0{\cdot}5CH_2Br{\cdot}CO_2Na + 0{\cdot}0500NaOH + 0{\cdot}45NaNO_3$ (*At* 45°).									
0	4·12	0·821	—	—	65	11·28	2·247	6·37	17·4
22	7·47	1·488	4·98	17·0	79	11·93	2·377	7·26	17·2
35	8·92	1·777	5·22	17·1	91	12·44	2·478	10·5	17·2
47	10·01	1·994	5·55	17·2					

In the first experiment $100k_{bi}$ increases continuously from 4·5 to 5·9, and in the second, for which the measurements extend to an appreciably later stage in the hydrolysis, $100k_{bi}$ increases from 5·0 to 10·5. On the other hand, both experiments show that k' remains constant throughout and afford thereby strong support for the view that the progress of the reaction is correctly represented by equation (1).

(ii) *When* (b > a). Table II gives the corresponding data for an experiment with alkali in excess ($a = 0{\cdot}05$, $b = 0{\cdot}20$). The synthetic solution in this case had the composition $0{\cdot}00990CH_2Br{\cdot}CO_2Na + 0{\cdot}160NaOH + 0{\cdot}040CH_2(OH){\cdot}CO_2Na + 0{\cdot}79NaNO_3$, corresponding with 80% hydrolysis. The volumes of silver solution refer in this experiment to 100 c.c. of the reaction mixture, and x is derived from [Br′] by the addition of 0·0400. Since the alkali is present in considerable excess, the values of

$$k_{bi} = \frac{1}{t - t_0} \cdot \frac{1}{b - a} \cdot \log_e \frac{b - x}{a - x} \cdot \frac{a - x_0}{b - x_0}$$

and of k'' as given by equation (1*b*) are both found to remain sensibly constant throughout the entire stage of the reaction which is covered by the observations. This result is also in complete accord with equation (1).

(iii) *When* a = b. The results in Table III are those for an experiment with $a = b = 0{\cdot}05$. The synthetic solution, corresponding with 80% hydrolysis, was represented by $0{\cdot}00990CH_2Br{\cdot}CO_2Na + 0{\cdot}00990NaOH + 0{\cdot}040CH_2(OH){\cdot}CO_2Na + 0{\cdot}94NaNO_3$. As the

TABLE II.

$0{\cdot}0499CH_2Br{\cdot}CO_2Na + 0{\cdot}2NaOH + 0{\cdot}75NaNO_3$ (*At* 45°).

$t - t_0$.	Ag, c.c.	$[Br'] . 10^3$.	$k_{bi} . 10^2$.	$k'' . 10^3$.	$t - t_0$.	Ag, c.c.	$[Br'] . 10^3$.	$k_{bi} . 10^2$.	$k'' . 10^3$.
0	1·84	0·916	—	—	256	16·38	8·16	4·15	6·23
57	7·47	3·72	4·16	6·25	299	17·34	8·63	4·26	6·39
91	9·90	4·93	4·14	6·23	353	18·06	8·99	4·23	6·35
138	12·66	6·30	4·25	6·39	413	18·60	9·26	4·18	6·28
174	14·18	7·06	4·26	6·39	498	19·10	9·51	4·12	6·19
208	15·24	7·59	4·21	6·31					

time values show, the rate of hydrolysis in this case is relatively slow. The silver-titration data refer to 100 c.c. of the reaction mixture, and x is given by $[Br'] + 0{\cdot}0400$. With equivalent quantities of the reactants, k_{bi} represents the value of

$$(x - x_0)/(t - t_0)(a - x_0)(a - x),$$

and k''' is the constant indicated by equation (1*c*).

TABLE III.

$0{\cdot}0499CH_2Br{\cdot}CO_2Na + 0{\cdot}0499NaOH + 0{\cdot}90NaNO_3$ (*At* 45°).

$t - t_0$.	Ag, c.c.	$[Br] . 10^3$.	$k_{bi} . 10^2$.	$k''' . 10^5$.	$t - t_0$.	Ag, c.c.	$[Br'] . 10^3$.	$k_{bi} . 10^2$.	$k''' . 10^5$.
0	0·22	0·11	—	—	4280	13·73	6·84	5·24	6·20
633	4·67	2·33	4·72	6·22	4750	14·28	7·11	5·40	6·26
1395	7·98	3·97	4·78	6·30	7140	15·98	7·96	5·77	6·20
1880	9·56	4·76	4·91	6·23	10780	17·30	8·61	6·27	6·02
2835	11·67	5·81	5·03	6·21	14660	18·12	9·02	7·07	5·99
3295	12·52	6·23	5·18	6·30					

The continuous increase of $100k_{bi}$ from 4·7 to 7·1 shows clearly that the alkaline hydrolysis in the late stages departs very considerably from the requirements of the simple bimolecular equation. On the other hand, the constancy of k''' indicates that the course of the reaction is satisfactorily represented by equation (1). It may be observed that the values of k_{bi} and of k''' are not of the same order of magnitude. This is, of course, due to the circumstance that k_{bi} is determined by the magnitude of k_A, whilst k''' is determined by k_B, k_D, and a.

Initial Velocities in Equivalent Solutions.—The further experiments to be described refer to the early stages of hydrolysis in solutions which contain equivalent quantities of the reactants. In these circumstances the effects of reaction (D) [and also of (C)] may be neglected.

In this connexion, it should be noted that preliminary observations with 0·1*M*-chloroacetate showed that k_{bi} increases steadily from 109 to 115×10^{-5} when the concentration of the alkali is increased from 0·1 to 0·5 mol. per litre. This increase occurs in spite of the fact that the total salt content (chloroacetate + hydroxide + nitrate) and the ionic strength remain the same, and that reactions (B), (C), and (D) play no significant part. It is probable that the increase is due to the greater inert-salt effect of the hydroxide than of the compensating nitrate. There is also some evidence that the inert-salt effects of the chloro- and bromo-acetate are not quite the same as that of the nitrate, and, in general, it may be anticipated that the replacement of chloro- or bromo-acetate and hydroxide by glycollate and halide as the hydrolysis proceeds, will be associated with a small drift in the value of k_{bi}.

Attention is directed to these differential salt effects for there can be no doubt that they play some part in the experiments with equivalent amounts of the reactants which will now be discussed. The results may be elucidated by a consideration of the relation between v/a^2 and a, where $v = \Delta x/\Delta t$ is the measured velocity of the reaction over the range $a + x$ to $a - x$ for values of $x = 0{\cdot}05a$. The curve obtained by plotting v/a^2 against a with the data for the chloroacetate at 45° is shown in the fig., and from this it is evident that v/a^2 decreases more or less linearly with the concentration, passes through a minimum, and then increases rapidly when the concentration of the reactants is further reduced. It may readily be shown that these relations are in agreement with the general equation for alkaline hydrolysis.

Since reaction (D) may be left out of account when the initial velocities only are under consideration, equation (1) takes the form

$$v = v_A + v_B^{\cdot} + v_C = k_A \,.\, a^2 + k_B^{\cdot} \,.\, a + k_C \,.\, a^2$$

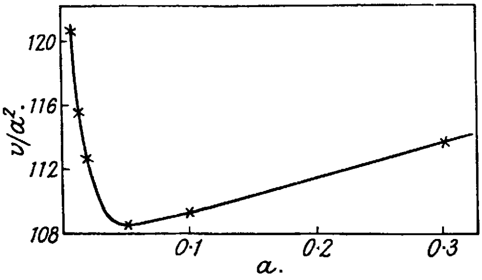
or

$$v/a^2 = k_A + k_C + k_B^{\cdot}/a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (3)$$

in which k_C may be neglected as a first approximation in that k_C/k_A for both the chloroacetate and the bromoacetate is of the order 1/200. Although the total salt concentration of the solutions is the same for all values of a, account must be taken of the variation of k_A with the nature of the salt constituents. It is probable that k_A varies linearly with the concentration of the reactants as expressed by the relation $k_A = k_A^0 + \gamma a$, where k_A^0 is the limiting value of k_A when $a = 0$ and γ is a measure of the differential inert-salt effect. On substitution in (3), this becomes

$$v/a^2 = k_A^0 + \gamma a + k_B^{\cdot}/a \quad . \quad . \quad . \qquad (3a)$$

from which it follows that v/a^2 should pass through a minimum when $a = \sqrt{k_B^{\cdot}/\gamma}$. By plotting $(v/a^2 - k_B^{\cdot}/a)$ against a, the values of k_A^0 and γ may be directly obtained from the experimental data for the chloroacetate at 45°. At this temperature, reaction (A) proceeds too rapidly to permit of measurements with the bromoacetate at higher concentrations, and in these circumstances it is assumed that the relative change in k_A produced by variations in a is the same for the bromo- and the chloro-acetate.



Alkaline hydrolysis of sodium chloroacetate at 45° with equivalent concentrations (a) *of alkali and chloroacetate. Plot of* v/a² *against* a.

Table IV affords a comparison of the observed values of v/a^2 with those calculated from

$$10^5 \,.\, v/a^2 = 104{\cdot}0 + 26a + 0{\cdot}165/a \text{ for the chloroacetate,}$$

and from

$$10^4 \,.\, v/a^2 = 395{\cdot}0 + 100a + 0{\cdot}44/a \text{ for the bromoacetate.}$$

Although the concentration for which v/a^2 has a minimum value cannot be determined directly from the experimental data with any considerable degree of accuracy, it may be noted that these equations lead to the value $a = 0{\cdot}08$ for the chloroacetate and $a = 0{\cdot}066$ for the bromoacetate.

Table IV.

Initial specific velocities for $aCH_2Cl{\cdot}CO_2Na + aNaOH$ (*At* 45°).

a	0·01	0·015	0·02	0·05	0·08	0·10	0·30	0·50
$v/a^2 . 10^5$, obs.	120·5	115·4	112·5	108·0	108·6	109·0	113·5	117·5
$v/a^2 . 10^5$, calc.	120·8	115·4	112·8	108·6	108·1	108·3	112·4	117·3

Initial specific velocities for $aCH_2Br{\cdot}CO_2Na + aNaOH$ (*At* 45°).

a	0·0045	0·01	0·02	0·05
$v/a^2 . 10^4$, obs.	485	448	418	403
$v/a^2 . 10^4$, calc.	493	440	419	409

The above observations show clearly that the rate of alkaline hydrolysis, even in the initial stages of the reaction, cannot be interpreted generally in terms of the assumption that the process is entirely due to bimolecular collisions between the chloro- or bromoacetate ions and hydroxyl ions. The rapid increase of v/a^2 at low concentrations is without doubt due to the increasing relative importance of the concurrent hydrolytic change in which the primary reactants are the halogen-substituted acetate ion and the water molecule, *i.e.*, reaction (B). In the case of the alkaline hydrolysis of the chloroacetate, it follows from the coefficients $k_A = 104 \times 10^{-5}$ and $k_B^{\cdot} = 0{\cdot}165 \times 10^{-5}$ that reaction (B) will in fact become the predominant reaction when the concentration $a(= b)$ is less than $0{\cdot}165/104 = 0{\cdot}0016$ mol. per litre.

EXPERIMENTAL.

The procedure followed in the determination of the bromide produced by hydrolysis of the bromoacetate has been previously described. On account of the greater solubility of silver chloride, the Volhard method can only be used for the precise determination of the rate of hydrolysis of the chloroacetate if the silver chloride is removed by filtration previous to the back titration with standard thiocyanate. The standardisation of the silver and the thiocyanate solution was based on carefully purified potassium chloride, and the titration conditions were maintained as constant as possible throughout.

SUMMARY.

The observations described lead to the conclusion that the alkaline hydrolysis of the halogen-substituted acetates is in general the result of four simultaneous reactions in which the halogenoacetate ion reacts with the hydroxyl ion, the water molecule, a second halogenoacetate ion, and the glycollate ion as represented by the equation

$$v = v_A + v_B + v_C + v_D$$
$$= k_A[CH_2X{\cdot}CO_2'][OH'] + k_B[CH_2X{\cdot}CO_2'][H_2O] + k_C[CH_2X{\cdot}CO_2']^2 + k_D[CH_2X{\cdot}CO_2'][CH_2(OH){\cdot}CO_2']$$

Since k_B, k_C, and k_D are all less than $k_A/100$ it follows that the rate of alkaline hydrolysis will be almost entirely determined by v_A so long as the concentration of the hydroxyl ions is not very small. If this is not the case, as, *e.g.*, when the initial concentrations of the reactants are small, or when the late stages of hydrolysis in the absence of excess alkali are in question, it is clear that the hydrolytic process is no longer a simple bimolecular reaction corresponding with (A), but that the reactions (B), (C), and (D) contribute very appreciably to the observed rate of hydrolysis.

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