

993. *The Mechanism of Hydrolysis of Acid Chlorides. Part IX.*
Acetyl Chloride.*

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A convenient stopped-flow apparatus for the measurement of rapid solvolyses is described. It is used to measure the rates of hydrolysis of acetyl chloride in dioxan-water mixtures, and the effect of aniline thereon. These results are compared with similar ones for acetone-water mixtures and with the corresponding hydrolysis rates for benzoyl chloride. The mechanism of solvolysis of acid chlorides is briefly reviewed.

THE hydrolysis of acetyl chloride is so fast that a flow method has to be used to follow it. Although flow techniques were first introduced¹ by Hartridge and Roughton in 1923 and have subsequently undergone considerable modification and refinement,² their use has been restricted mainly to the study of biochemical reactions.² The introduction of the stopped-flow principle³ and of methods for recording rapid changes in physical properties have simplified and improved such methods considerably.

The present apparatus, which measures the change of electrical conductivity with time, is based on a version described by Prince.⁴ Particular attention is paid to variation in solvent composition, storage of reactants, simplification of the conductivity apparatus, and analysis of the photographic records. A brief introduction to the method is here followed by a description of its special features and method of operation. We then record its use for measuring the effect of solvent composition on the rate of hydrolysis of acetyl chloride in dioxan-water mixtures, for comparison with similar results, already available, for the hydrolysis of benzoyl chloride.

EXPERIMENTAL

Description of the Apparatus.—A conventional type of stopped-flow apparatus⁴ (see Fig. 1), made of glass, was used. Various modifications enabled hydrolyses to be followed conveniently over a wide range of solvent composition. Three interchangeable glass syringes (Chance), A, connected to reservoirs containing dioxan, water, and a solution of acetyl chloride in dioxan, respectively, were driven manually by a heavy brass plate, B. By various combinations of syringes of different sizes, a wide range of solvent composition could be attained. The syringes were connected to the glass tubes leading to the mixer, C, by short lengths of Polythene tubing into which the tapered Luer nozzles fitted closely.

Close-fitting floats in the form of Polythene cylinders, 2 cm. high, with slightly convex surfaces, reduced the rate of dissolution of air at the surface of the liquids, all of which were previously degassed. In this way, the solutions could be used for periods up to 12 hr. without serious interference from bubble formation during the compression.

* Part VIII, *J.*, 1962, 1076.

¹ Hartridge and Roughton, *Proc. Roy. Soc.*, 1923, *A*, **104**, 376.

² See Roughton, *Discuss. Faraday Soc.*, 1954, **17**, 114.

³ Chance, "Techniques of Organic Chemistry," Interscience Publ., Inc., New York, 1953, Vol. VIII, p. 690.

⁴ Prince, *Trans. Faraday Soc.*, 1958, **54**, 838.

The liquids from the syringes were forced into the mixer through 4 semi-tangential jets, 1 mm. in diameter, drilled in the tapered end of the observation tube, D, which was 3 mm. in diameter. Two pairs of electrodes, E (1.5 cm. lengths of platinum wire of 0.03" diam.), were sealed in the side of the observation tube by means of "Araldite" cement at distances of 5 and 27 mm. from the mixer.

The efficiency of mixing was estimated by following the conductance of the first cell during and immediately after the mixing of dioxan with aqueous hydrochloric acid. Visual tests were made by mixing a solution of hydrogen chloride in dioxan with aqueous sodium hydroxide

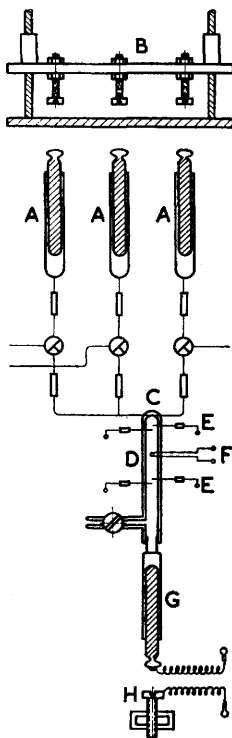


FIG. 1. Stopped-flow apparatus.

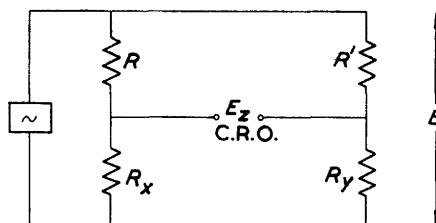


FIG. 2. Conductivity circuit.

containing phenolphthalein. These tests showed the mixing to be essentially complete within 4 milliseconds. Moreover, when trichloroacetyl chloride and methylchlorophosphine, which are both very reactive, were used, the final conductivity was reached immediately.

A small copper-constantan thermocouple, F, was made from flattened enamelled wires, 0.002" in diameter, contained in an elliptically cross-sectioned thin-walled glass tube. This was sealed midway between the two pairs of electrodes along the direction of the liquid flow. This is necessary to measure the temperature in the reaction zone owing to the high heat of mixing of water and dioxan.

The conductivity was measured by means of a simple bridge circuit (Fig. 2), with a Tinsley conductivity bridge of type 4896. The potential difference across the two centre points is given by

$$E_z = E \left(\frac{R_x}{R + R_x} - \frac{R_y}{R' + R_y} \right)$$

This can be made zero for any value of R and R_x . Thus, by suitable variation of R' and R_y , the signal displayed can be made to reach zero at the end of the reaction and hence the whole of the C.R.O. screen is used.

A sinusoidal input of 7 kc./sec. was supplied by an Advance audio-oscillator, type H 1, the input of which was isolated by a 1:1 transformer. The oscilloscope (Cossor 1049 double-beam) was connected directly to the bridge so that one point was permanently earthed.

At this frequency, errors in the derived values of conductances due to variations in the stray capacitances and cell capacitance (total admittance $\sim 10^{-5} \Omega^{-1}$) were within 2%. The Wheatstone bridge network and oscilloscope amplifier provided the necessary flat response over the band-width of ~ 2 kc./sec. produced by the highest modulation rate.

The oscilloscope was used under single-stroke conditions, with the beam suppressed, except when the stroke operated. The arrangement for stopping the liquid flow and triggering the oscilloscope time base was as described by Prince.⁴ A circuit to trigger the time base was completed through a contact made between a brass hemisphere attached to the outer end of the plunger of the receiving syringe (G, Fig. 1) and a brass stop bolt (H, Fig. 1). Thus the oscilloscope sweep commenced when the liquid in the flow system was brought to rest, and the change in resistance of the stationary solution between the selected electrode pair was displayed from that time by one beam.

The second beam was used to provide regular pulses of known frequency to give a time scale to the trace. For most of the reactions studied, the A.C. mains-supply frequency was a useful standard, but for slower runs the output from a decatron scaler,⁴ energised by the A.C. mains, was used. For the fastest reactions the frequency of the power-supply oscillator was used, and calibrated by using a decatron scaler.

Procedure for Measurements.—Before a rate measurement was made, the apparatus was filled with the reaction mixture, extreme care being taken to exclude air bubbles. This was done by filling and discharging the syringes repeatedly, and finally recharging them. The Wheatstone bridge was balanced with the fully reacted solution in the observation tube. The cell close to the mixer, used for the fastest reactions, was affected by diffusion from the mixer jets after about 15 sec., so that balancing had to be done in stages. A method has been described⁵ to overcome this difficulty, but it was not used in the present apparatus as the electrodes were too close to the mixer. The resistance in the balance arm of the Wheatstone bridge was then made slightly lower than that necessary for the balance. With this bridge setting, the power-supply voltage and oscilloscope amplifier were adjusted to give a trace which used the screen fully. The reaction was then carried out by a firm, sharp stroke of the push bar, and the thermocouple galvanometer reading was taken. The solution was then ejected, the film of the camera advanced, and the cycle of operations repeated about ten times.

The calibration resistances were inserted into the bridge circuit, and 8–10 calibrations were made before and after each series of experiments.

Analysis of the Photographic Records.—The traces were enlarged by Xerography and the widths of the traces at points along the time axis measured with a rule. Owing to the construction of the cathode ray tube, the axes were inclined at $\sim 5^\circ$ to the normal, and a special kind of drawing board was constructed to normalise the readings. From the readings a graph was constructed relating time to trace width, which was then converted into a second graph relating time and conductivity by means of the calibrations. Since these calibrations showed

TABLE I.
A typical run.

Concn. of acetyl chloride = $4 \times 10^{-3}M$. Vol. of water (before mixing) = 50%. Temp. = 27.5°.

Time axis (cm.) *	Time (10^{-3} sec.)	Trace width (cm.)	Conductance ($10^4\Omega^{-1}$)	Time axis (cm.)	Time (10^{-3} sec.)	Trace width (cm.)	Conductance ($10^4\Omega^{-1}$)
1.0	2.84	14.95	1.250	8.0	22.68	5.82	2.827
1.5	4.25	13.58	1.425	10.0	28.35	4.72	3.136
2.0	5.67	12.65	1.542	12.0	30.40	3.83	3.425
3.0	8.50	10.94	1.786	14.0	39.63	3.22	3.640
4.0	11.34	9.50	2.025	16.0	45.36	2.65	3.819
5.0	14.17	8.25	2.257	18	51.03	2.32	3.995
6.0	17.01	7.27	2.462	20	56.70	1.96	4.155
7.0	19.04	6.48	2.652	22	62.37	1.62	4.313

* 1 cm. = 2.835×10^{-3} sec.

⁵ Prince, *Z. Elektrochem.*, 1960, **64**, 13.

that the conductivity was proportional to concentration over the range of reaction considered, the rate constants were derived directly from the conductances by Guggenheim's method.⁶ A typical example of this method is given in Table 1.

The rate constant was calculated by the Guggenheim method for a time interval $T = 36.85 \times 10^{-3}$ sec.⁻¹. The values in Table 2 were taken from a progress curve of t against conductivity κ .

TABLE 2.

Calculation of a rate constant.

$t + T$ (cm.)	t (cm.)	$\kappa(t + T)$ (10^4 ohm ⁻¹)	$\kappa(t)$ (10^4 ohm ⁻¹)	$\Delta\kappa$ (10^4 ohm ⁻¹)	$4 + \log \Delta\kappa$	k_1
15	2	3.73	1.53	2.20	0.3424	—
16	3	3.82	1.79	2.03	0.3075	25.3
17	4	3.92	2.03	1.89	0.2765	24.8
18	5	4.01	2.26	1.75	0.2430	24.8
19	6	4.08	2.46	1.62	0.2095	25.4
20	7	4.16	2.65	1.51	0.1790	25.7
21	8	4.23	2.82	1.41	0.1492	25.7
22	9	4.30	2.98	1.32	0.1206	26.0

Mean $k_1 = 25.4$ sec.⁻¹. Graphically $k_1 = 25.7$ sec.⁻¹.

RESULTS AND DISCUSSION

The results recorded in Table 3 show that the rate of hydrolysis of acetyl chloride in dioxan-water mixtures changes rapidly with their composition.

This variation gives a value of 0.81 for the parameter m in the Grunwald-Winstein equation,⁷ $\log k_1/k_0 = mY$ obtained graphically (Fig. 3), which is similar to the values ($m \sim 1.0$) frequently observed in S_N1 ionisations. Cairns and Prausnitz⁸ recently obtained

TABLE 3.

Hydrolysis of acetyl chloride in aqueous dioxan.

$[\text{CH}_3\text{COCl}]$ (10^3M)	H_2O (% v/v) in dioxan	Temp.	k_1 (sec. ⁻¹)	k_1 (mean) (sec. ⁻¹)	k (mean) at 27° *
4.9	19.6	26.5°	0.330	0.306	0.318
		26.5	0.282		
2.7	33.3	25.4	2.93	2.95	3.33
		25.4	3.04		
"	"	25.4	2.87	2.95	3.33
		27.4	24.3		
4.0	50.0	27.5	25.7	23.4	22.5
		27.4	20.1		
1.7	"	27.7	23.4	23.4	22.5
		27.9	23.6		
1.8	75.6	27.5	271	292	292
		26.0	285		
0.81	"	27.0	326	292	292
		27.2	299		
"	"	27.2	278		

* Corr. to 27° by using the activation energy $E = 14$ kcal./mole (Cairns and Prausnitz, *J. Chem. Phys.*, 1960, **32**, 169).

rate constants for the hydrolysis in acetone-water (15–35% v/v of water) at low temperatures, thus extending considerably the solvent range over previous measurements.⁹ When their values of the activation energies are used to afford rate values at 27°, the rates in dioxan-water are found to be significantly greater (*ca.* 3.5 times) than the rates in acetone-water for equal water concentrations. The values of m in the two solvents are seen to be very close.

⁶ Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

⁷ Grunwald and Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 846.

⁸ Cairns and Prausnitz, *J. Chem. Phys.*, 1960, **32**, 169.

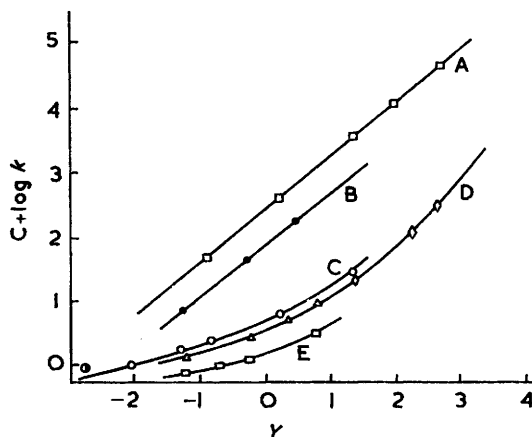
⁹ (a) Zimmerman and Yuan, *J. Amer. Chem. Soc.*, 1955, **77**, 332; (b) Swain and Scott, *ibid.*, 1953, **75**, 246.

Cairns and Prausnitz⁸ attributed the increase in rate with water concentration to the increase in the dielectric constant of the medium, assuming a bimolecular mechanism, and obtained a linear logarithmic relation between the second-order rate constant and the Kirkwood function, $D - 1/(2D + 1)$.

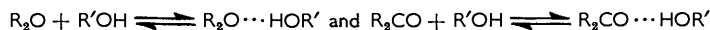
In view of the greater rates in dioxan, this explanation is inadequate, and specific solvation by water molecules must be involved. Qualitatively, the similar rates in the two solvents of the same water concentration and different dielectric constants may be

FIG. 3. Dependence of the rate of hydrolysis of $R\cdot COCl$ on the solvating power of the solvent mixture.

$R = Me$ ($C = 2.15M$); A, in dioxan at 27° ; B, in acetone at 27° . $R = Ph$; C, in acetone at 0° ($C = 4.48M$); D, in dioxan at 15° ($C = 4.02M$). $R = p\text{-NO}_2\cdot C_6H_4$ in acetone at 0° ($C = 2.80M$) (E).



explained by the similar hydrogen-bonding energies of acetone and dioxan. Measurements¹⁰ have shown that the equilibrium constants for the two equilibria are similar:



Further association in solvolytic media may be represented¹¹ by similar equilibria, viz.: $S + (H_2O)_n \rightleftharpoons S \cdots (H_2O)_n$ ($S = \text{solvent mol.}$), leading to comparable molecular distributions, in view of the similar interaction energies between R_2O and $R'OH$ and R_2CO and $R'OH$.

Specific association of solvent molecules around a polar transition state is determined primarily by these association equilibria,¹¹ so that the rate is related approximately to the water concentration and not to the dielectric constant.

TABLE 4.

Solvolysis of acetyl chloride and benzoyl chloride containing aniline in 50% v/v aqueous dioxan.*

[Ph·NH ₂] (M)	k_1 (sec. ⁻¹)		$\frac{k_2(\text{Ph}\cdot\text{NH}_2)}{k_2(\text{H}_2\text{O})}$	[Ph·NH ₂] (M)	k_1 (sec. ⁻¹)		$\frac{k_2(\text{Ph}\cdot\text{NH}_2)}{k_2(\text{H}_2\text{O})}$
	obs.	mean			obs.	mean	
Acetyl chloride at 26.0°				Benzoyl chloride at 25.0°			
0.295	530, 469, 502	500	1.93×10^3	0.284	61.1, 57.2	59.2	9.6×10^5

* k_2 (N) is the second order rate constant for reagent N.

For comparison, the effect of solvent composition on the rates of hydrolysis of benzoyl and *p*-nitrobenzoyl chloride is included in Fig. 3. For benzoyl chloride¹² m increases with water concentration from ca. 0.25 to ca. 1 over the range where $m = 0.81$ for acetyl

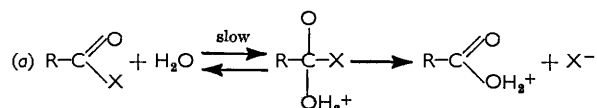
¹⁰ Prigogine, *J. Chim. phys.*, 1948, **45**, 19; Coggeshall and Saier, *J. Amer. Chem. Soc.*, 1951, **73**, 5414.

¹¹ Hudson and Stelzer, *Trans. Faraday Soc.*, 1958, **54**, 213.

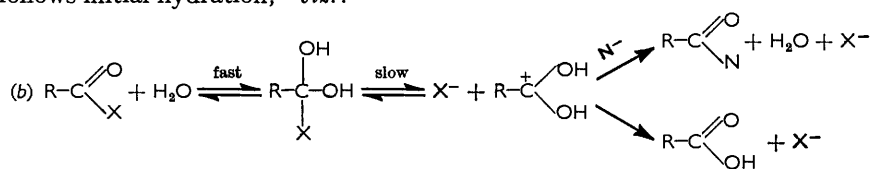
¹² Brown and Hudson, *J.*, 1953, 3352; Archer and Hudson, *J.*, 1950, 3259.

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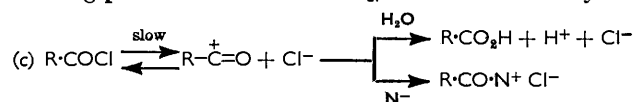
chloride. In the more aqueous solvents, a highly electrophilic intermediate, produced in an ionisation stage, has been detected kinetically in the hydrolysis of benzoyl chloride whereas no such intermediate is formed in the less aqueous solvents.¹³ These observations, and the effect of substituents on the reactivity,¹² have led to the postulate of two mechanisms,¹⁴ (a) a bimolecular displacement in the more nucleophilic and less aqueous solvents and (b) a rate-determining ionisation characterised by a large solvent effect. The bimolecular process is now considered to proceed through a tetrahedral sp^3 -hybridised transition state but the exact nature of the ionisation process is in some doubt.



The sensitivity of the rate to certain nucleophilic reagents,^{9b} in particular amines (Table 4), and the observation that ^{18}O exchange of the carbonyl group increases with water content in the 5–33% water-concentration range in dioxan,¹⁵ suggest that ionisation follows initial hydration,¹⁶ viz.:



Alternatively, a direct rate-determining ionisation has been postulated^{13,17} in view of the similar reactivities of benzoyl chloride in formic acid and in 65% v/v aqueous acetone, solvents of equal ionising power Y towards the S_N1 ionisation of alkyl halides:



This observation does not support the alternative mechanism which involves preliminary addition, because the $\text{H}\cdot\text{CO}$ group in the addition intermediate $[\text{R}\cdot\text{C}(\text{O})\cdot\text{O}\cdot\text{CHO}]$ formed in formic acid would reduce the rate of ionisation of this intermediate (reaction *b*).

The linearity of the $\log k$ - Y relationship for acetyl chloride over a wide range of water concentration suggests that a single mechanism operates, with a transition state similar to that of benzoyl chloride in the more aqueous solvents. The large rate increases produced by aniline in both cases show that bond formation is probably important in the hydrolysis. This inference is also supported by the observation that the rate of hydrolysis of trichloroacetyl chloride was too fast to be measured by the stopped-flow technique.

Thus most of the evidence at present is in favour of mechanism (*b*) for the ionisation, in which case the similar rates in formic acid and in 65% aqueous acetone would be coincidental.

It is noted that the activation energy observed for the hydrolysis of acetyl chloride in acetone containing less than 5% of water⁹ (7.5 kcal./mole) is considerably less than the values for the more aqueous solvents⁸ (13.15–14.26). Benzoyl chloride exhibits a similar behaviour, which is explained by the incursion of the bimolecular process (*a*) in solvents of low water content. This mechanism is similar to the alcoholysis in solvents of low polarity, which has already been investigated in detail.¹¹

¹³ Gold, Hilton, and Jefferson, *J.*, 1954, 2756.

¹⁴ Hudson, *Chimia*, 1961, 15, 394.

¹⁵ Bunton, Lewis, and Llewellyn, *Chem. and Ind.*, 1954, 1154.

¹⁶ Hall, *J. Amer. Chem. Soc.*, 1955, 77, 5993.

¹⁷ Crunden and Hudson, *J.*, 1956, 501.

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