88. *Acylation. Part IX.* Acylation by Acetyl Chloride in Nitromethane. Catalysis by Hydrogen Chloride and Reaction Paths* via *both Un-ionised and Dissociated Acetyl Chloride.*

By D. P. N. SATCHELL.

A kinetic study of acylation of β-naphthol by acetyl chloride in nitromethane is reported. The effects of added hydrogen chloride and tetraethylammonium chloride are described. The reaction is of the first-order in both naphthol and acylating agent. Hydrogen chloride provides what is probably electrophilic catalysis, and added chloride ions depress the rate markedly owing to a mass-law effect. The results are explained in terms of a reaction mechanism involving un-ionised and dissociated acetyl chloride. Various mechanisms for the acid catalysis are discussed. The reaction provides an unequivocal example of the participation of free acetylium ions in acylation.

WHILE examples of Brønsted-acid catalysis of alkylation by alkyl halides are fairly common,[1] similar catalysis of acylation by acyl halides is rare.† In aqueous media such catalysis has yet been detected only for the fluorides.[2] In non-aqueous systems, besides cases[3,4] concerning the fluorides for which catalysis, especially by molecular hydrogen fluoride, is very marked, few other examples exist.[4,5,6] Moreover, most of these may properly be interpreted either in terms of an exchange of anions between acid catalyst and acyl halide, leading to a new reagent (which may or may not be more reactive) or in terms of profound changes in the system's dielectric constant as acid is added. Two likely cases of specific electrophilic assistance of the separation of the halide ion from the acyl halide by a

Acylation of β-naphthol by acetyl chloride in nitromethane at 25°.

Initial [β-naphthol] ≈0·04M; k_{obs} = observed first-order rate constant.

[AcCl] *	[HCl]	[Et_4NCl]	10^2k_{obs} (min.$^{-1}$)	[AcCl] *	[HCl]	10^2k_{obs} (min.$^{-1}$)
	Order in AcCl				*Effect of* HCl	
0·40	0·01 †	—	0·68	0·81	0·030	1·50
0·47	,,	—	0·74	,,	0·055	1·57
0·60	,,	—	1·02	,,	0·115	1·73
0·81	,,	—	1·41	,,	0·175	1·94
				,,	0·245	2·27
	Effect of saline chloride			,,	0·340	2·98
0·40	0·01 †	0·05	0·28			
0·81	,,	0·07	0·58			
,,	,,	0·12	0·58			
,,	0·055	,,	0·58			
,,	0·115	,,	0·58			

* Corrected for water content of solvent. † Arising from the water content of solvent.

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* Part VIII, preceding paper.

† Examples of both reactions involving catalysis by Lewis acids are, of course, very familiar.

[1] *E.g.*, Hart and Cassis, *J. Amer. Chem. Soc.*, 1954, **76**, 1634; Gelles, Hughes, and Ingold, *J.*, 1954, 2918; Patai and Zabricky, *J.*, 1961, 5479; Hughes, Ingold, Mok, and Pocker, *J.*, 1957, 1238; Leimu and Salomaa, *Acta Chem. Scand.*, 1947, **1**, 353; Andrews and Keefer, *J. Amer. Chem. Soc.*, 1961, **83**, 3708; Swain and Pegues, *ibid.*, 1958, **80**, 812.

[2] Bevan and Hudson, *J.*, 1953, 2187; Satchell, preceding paper.

[3] Kopple and Katz, *J. Amer. Chem. Soc.*, 1956, **78**, 6199; Fieser, *J. Amer. Chem. Soc.*, 1939, **61**, 1272; Simons, " Fluorine Chemistry," Academic Press, New York, 1950.

[4] Satchell, *J.*, 1960, 1752.

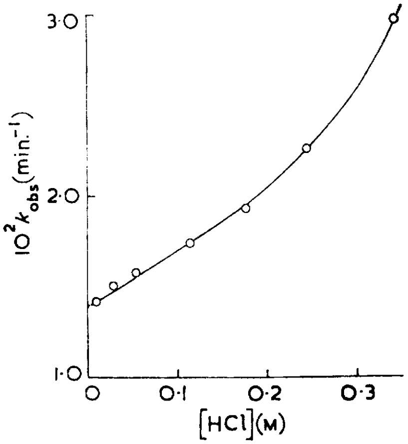
[5] *E.g.*, Hartough and Kosak, *J. Amer. Chem. Soc.*, 1946, **68**, 2639; Belton, Nowlan, and Wheeler, *Sci. Proc. Roy. Dublin Soc.*, 1949, **25**, 19.

[6] Litvinenko and Aleksandrove, *Doklady Akad. Nauk S.S.S.R.*, 1958, **118**, 321; Litvinenko, Aleksandrova, and Pilyuk, *Ukrain. Khem. Zhur.*, 1959, **25**, 81.

molecule of catalyst during, or as a prelude to, acylation do exist,[4,6] though one has previously received a different explanation.[4] These cases will be referred to below. We report now a further probable example, namely, the acetylation of β-naphthol by acetyl chloride in nitromethane.

RESULTS AND DISCUSSION

Kinetic Findings (see Table).—(i) In all cases β-naphthol was acylated by a large excess of acetyl chloride and the observed rate (k_{obs}) was that of first-order disappearance of naphthol (see Experimental section). (ii) At fixed acetyl chloride concentration, k_{obs} is increased by the addition of hydrogen chloride. Below *ca.* 0·15M-acid the acceleration is proportional to the amount of acid added and thereafter increases more steeply (see Figure). (iii) In the absence of *added* hydrogen chloride the reaction rate is (*a*) dependent on the first power of the acetyl chloride concentration and (*b*) reduced considerably by added chloride ions. (Even in the absence of added hydrogen chloride the reaction media always contain some of this acid—even before the acylation of naphthol begins—owing to the rapid acetylation of the residual water content of the " dried " solvent [see Experimental section].) (iv) The rate is also decreased by added chloride ions when added hydrogen chloride *is* present. In fact, for a given acetyl chloride concentration, the rate falls to the same value regardless of whether hydrogen chloride has been added or not, provided the chloride ions are present in excess of any added acid. Except at the highest hydrogen chloride concentrations studied, the removal, by chloride ions, of the rate enhancement due to the added acid constitutes only a small fraction of the total rate repression by the chloride ions. (v) Preliminary work (not detailed here) shows similar phenomena to be present in the corresponding system involving bromides.



Plot of k_{obs} against HCl concentration for the acetylation of β-naphthol.

Interpretation.—Our interpretation of the above facts is based on Pocker's explanation [7] of the results of Evans and others [8] concerning ionisation of *alkyl* halides in nitromethane. For instance, the extent of ionisation of triphenylmethyl chloride is dependent on the first power of its stoicheiometric concentration. This was interpreted by Evans in terms of ion-pair formation

$$Ph_3CCl \rightleftharpoons Ph_3C^+Cl^-$$

rather than straight-forward ionic dissociation

$$Ph_3CCl \rightleftharpoons Ph_3C^+ + Cl^-$$

because in the latter case the carbonium-ion concentration will not depend on the first power of the stoicheiometric substrate concentration. However, Pocker showed that

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[7] Pocker, *J.*, 1958, 240.

[8] Bentley, Evans, and Halpern, *Trans. Faraday Soc.*, 1951, **47**, 711.

free hydrogen chloride also existed in such systems and by considering additional equilibria involving this substance he demonstrated that, for the small amounts of ionisation expected for the systems concerned, the ions could be predominantly dissociated and yet the appropriate dependence on concentration retained. His experiments with added chloride ions (which depress ionisation) necessitated that ions be considered predominantly dissociated. And there is independent evidence on this point for the similar solvent nitrobenzene.[9]

Since the experimental conditions, and the nature of the data, concerning acylation by acetyl chloride noted above display marked similarities to those for the ionisation of alkyl halides studied by Pocker and Evans, it seems clear that a scheme basically similar to Pocker's should, or at least may, be used to explain them. Along these lines the equations (in which ROH = β-naphthol) are as follows:

$$(1)\ \mathrm{HCl} \rightleftharpoons (\mathrm{H^+})_{\mathrm{solv}} + \mathrm{Cl^-} \quad K_1 = [\mathrm{H^+}][\mathrm{Cl^-}]/[\mathrm{HCl}]$$

$$(2)\ \mathrm{HCl} + \mathrm{Cl^-} \rightleftharpoons \mathrm{HCl_2^-} \quad K_2 = [\mathrm{HCl_2^-}]/[\mathrm{Cl^-}][\mathrm{HCl}]$$

$$(3)\ \mathrm{CH{\cdot}COCl} \rightleftharpoons \mathrm{CH_3{\cdot}CO^+} + \mathrm{Cl^-} \quad K_3 = [\mathrm{CH_3{\cdot}CO^+}][\mathrm{Cl^-}]/[\mathrm{CH_3{\cdot}COCl}]$$

$$(4)\ \mathrm{CH_3{\cdot}COCl} + \mathrm{ROH} \xrightarrow{k_4} \mathrm{Products} \qquad \mathrm{Slow}$$

$$(5)\ \mathrm{CH_3{\cdot}CO^+} + \mathrm{ROH} \xrightarrow{k_5} \mathrm{Products} \qquad \mathrm{Slow}$$

In the absence of added chloride ions $[\mathrm{HCl_2^-}] > [\mathrm{Cl^-}]$ and if $[\mathrm{H^+}] > [\mathrm{CH_3{\cdot}CO^+}]$ (*i.e.*, if the extent of substrate ionisation is very small, for hydrogen chloride itself is probably little ionised [see below]), then $[\mathrm{H^+}] \approx [\mathrm{HCl_2^-}]$. It follows, for such conditions, that [7]

$$K_3 \approx [\mathrm{CH_3{\cdot}CO^+}]/[\mathrm{CH_3{\cdot}COCl}]\ \sqrt{(K_2/K_1)}$$

This means that the extent of ionisation of the acyl chloride is proportional to its stoicheiometric concentration. Also the ionisation will be largely depressed, by a mass-law effect, if chloride ion is added in excess of any hydrogen chloride present.

Since the reaction rate is given by:

$$-\mathrm{d}[\mathrm{ROH}]/\mathrm{d}t = \{k_4[\mathrm{AcCl}] + k_5[\mathrm{Ac^+}]\}[\mathrm{ROH}] = \{k_4 + k_5K_3\sqrt{(K_2/K_1)}\}[\mathrm{AcCl}][\mathrm{ROH}]$$

this scheme accounts for both the observed first-order dependence on acetyl chloride concentration and the type of rate depression produced by added chloride ions [step (5) is removed]. The appreciable reduction of the rate by chloride ions to a constant value, only dependent on the acetyl chloride concentration, argues strongly in favour of a dissociative mechanism, as above, rather than one based on a negative medium effect. The further possibility that chloride ions remove only catalysis of step (4) by hydrogen chloride may also be dismissed (see below).

These arguments are so reasonable that the main outlines of the mechanism appear established: both un-ionised and dissociated acetyl chloride participate in acetylation. However, so far the scheme does not account for the observed acceleration by *added* hydrogen chloride, for it is an essential part of Pocker's analysis that the ionisation ratio $[\mathrm{CH_3{\cdot}CO^+}]/[\mathrm{CH_3{\cdot}COCl}]$ will be independent of hydrogen chloride concentration. This is so even if further equilibria are written which formally represent electrophilic catalysis, *e.g.*:

$$\mathrm{R{\cdot}COCl} + \mathrm{HCl} \rightleftharpoons \mathrm{R{\cdot}CO^+} + \mathrm{HCl_2^-} \qquad (3a)$$

$$K_{3a} = [\mathrm{R{\cdot}CO^+}][\mathrm{HCl_2^-}]/[\mathrm{R{\cdot}COCl}][\mathrm{HCl}] \approx [\mathrm{R{\cdot}CO^+}]/[\mathrm{R{\cdot}COCl}]\sqrt{(K_1K_2)^{-1}}$$

Thus $[\mathrm{R{\cdot}CO^+}]$ is again independent of [HCl]. Moreover, that such equilibria may be written implies only that the hydrogen chloride controls the extent of ionisation, not that the ionisation step is necessarily mechanistically hydrogen chloride-assisted. However, it probably is (hydrogen chloride acting as a chloride acceptor), for to date all the other

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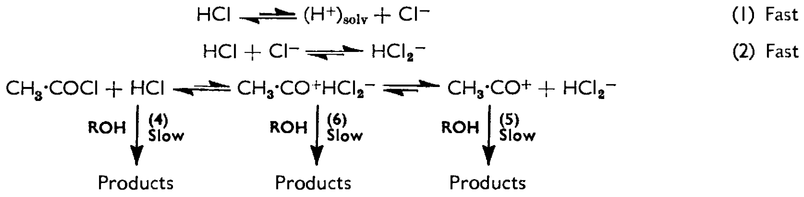
[9] Price and Lichtin, *Tetrahedron Letters*, 1960, **18**, 10.

convincing evidence for acetylium ion formation from acetyl chloride involves the presence of a Lewis acid to act as acceptor.[10] There appears no evidence for significant spontaneous ionisation. Thus, although in the present case the ionisation is independent of the *amount* of hydrogen chloride, it is probably dependent on the presence of this compound. The ionisation route, therefore, probably represents an acid catalysis.



Nevertheless, if we ignore for the present the possibility of a dielectric-constant effect, then some additional acid-catalysed pathway is required to account for the acceleration in rate as the hydrogen chloride concentration increases. We consider that the following modified scheme is perhaps the simplest which satisfactorily rationalises all the results. $K_6 = [CH_3{\cdot}CO^+HCl_2^-]/[CH_3{\cdot}COCl][HCl]$. Relatively few ion-pairs are considered to exist. The rate of acylation is given by:

$$-d[ROH]/dt = \{k_4[AcCl] + k_5[Ac^+] + k_6[Ac^+HCl_2^-]\}[ROH]$$

$$= \{k_4 + k_6K_6[HCl] + K_{3a}k_5\sqrt{(K_1K_2)^{-1}}\}[AcCl][ROH]$$

or

$$k_{obs} = \{k_4 + k_6K_6[HCl] + K_{3a}k_5\sqrt{(K_1K_2)^{-1}}\}[AcCl]$$

This mechanism provides for the first-order dependence on acetyl chloride, a catalytic rate-enhancement proportional to added hydrogen chloride, and the rate depression produced by added chloride ions. Both the ionic routes, (5) and (6), will be eliminated in the presence of an excess of chloride ion (since this largely removes free hydrogen chloride as HCl_2^-). The rate is then reduced to that of step (4). This is again in keeping with the result that an excess of chloride ion reduces the rate to a common value regardless of the stoicheiometric hydrogen chloride concentration. An important point is that, even in the absence of deliberately added hydrogen chloride, the addition of chloride ion reduces the rate considerably—in particular, much more than would be expected if only the linear catalytic effect of the residual hydrogen chloride in the solvent were then eliminated, for it may be seen from the data for added hydrogen chloride that such a small concentration as is formed in the " dried " solvent would exert only a very small effect. Thus in the absence of appreciable quantities of added hydrogen chloride the contribution from step (6) is to be regarded as small, and the rate repression by chloride ions as due to the removal of step (5), the contribution from which will otherwise be essentially constant (see above). The small contribution from step (6) is in keeping with the finding of predominant dissociation rather than pairing in nitromethane. Nevertheless, if the above scheme is essentially correct, the observed linear catalysis arises only from an increase in ion-pair formation. The departure from linearity at high concentration is discussed below.

The results show the contribution to the rate from steps (4) and (5) to be approximately equal. Since the overall ionisation must be small, it is clear that the acetylium ion must be much more reactive than the un-ionised acetyl chloride. This is a sensible conclusion. The value of k_4 may be calculated as $0{\cdot}72 \times 10^{-2}$ l. mole^{-1} min.$^{-1}$. It will be interesting to find the relative contributions from steps (4) and (5) for other acyl halides.

The formulation above of a catalytic path in terms of formal ion-pair intermediates is

[10] Burton and Praill, *J.*, 1951, 522, 726.

hardly to be distinguished chemically from formulations proposed (and perhaps preferred) by others for intermediates in hydrogen chloride-catalysed reactions of *alkyl* chlorides.[1] Species along the lines of $\mathrm{R{\cdot}\overset{\delta+}{CO}\cdots\overset{\delta-}{Cl}\cdots\overset{\delta+}{H}\cdots\overset{\delta-}{Cl}}$ have been suggested.

While the above scheme is neat and self-consistent, yet the basic mechanism [equations (1—5)] may be elaborated to include linear catalysis by hydrogen chloride in at least one other way which avoids assumption of ion-pairs.

This scheme involves a conventional protonation of the acylating agent:

$$\mathrm{R{\cdot}COCl} + (\mathrm{H^+})_{\mathrm{solv}} \rightleftharpoons (\mathrm{R{\cdot}COClH})^+ \qquad (7)$$

$$(\mathrm{R{\cdot}COClH})^+ + \mathrm{ROH} \longrightarrow \text{Products} \qquad (8)$$

Since $[(\mathrm{R{\cdot}COClH})^+] \approx K_7[\mathrm{HCl}][\mathrm{R{\cdot}COCl}]\sqrt{(K_1K_2)}$, it is easily shown that equations (1—5), together with (7) and (8), will also satisfy all the kinetic results. The position of the proton in the active intermediate could be either on oxygen or on chlorine. Our views on acid catalysis of reactions of acylating agents lead us to prefer the formulation on chlorine.

This mechanism is certainly possible and may contribute to some extent. Indeed, while we consider it likely that ionic species such as $\mathrm{CH_3{\cdot}CO^+HCl_2^-}$ will be more prominent than those such as $(\mathrm{CH_3{\cdot}COClH})^+$ and therefore perhaps contribute more to the reaction, nevertheless, as we now argue, the proton-transfer mechanism explains the departure from linear catalysis more satisfactorily. As the concentration of hydrogen chloride increases, this compound will perhaps show some tendency to aggregate even beyond $\mathrm{HCl^-_2}$ to, say, $\mathrm{H_2Cl_3^-}$. If we wish to attribute the extra rate enhancement to the presence of such species, as we do, then, since this process will tend to increase the availability of protons but to decrease that of species which can accept a chloride ion, some contribution from a proton transfer mechanism is indicated.

We have so far ignored more generalised medium effects. Nevertheless, the possibility must be considered that all the acceleration produced by added hydrogen chloride results from a generalised medium effect acting on one, or both, of the paths (4) and (5). We feel this to be unlikely for the following reasons. First, hydrogen chloride is very probably largely un-ionised in nitromethane, for the conductivity of such solutions is low.[11] It will therefore behave like a non-electrolyte of only moderate dielectric constant.[12] While it is impossible to predict its exact effect on the dielectric constant (35) of the solvent, it is difficult to believe it can raise it much. Indeed it may even lower it. Its presence will, in any event, have much less effect than, say, a comparable concentration of saline chloride. Secondly, of the two paths, (4) and (5), the former presumably involves an increase in charge on formation of the transition state and should therefore be affected by changes in dielectric constant. Yet this reaction, which predominates in the presence of added chloride and always constitutes about half the reaction, shows a negligible dependence on the salt concentration. The importance of this concentration must therefore be small in the present context, and that of the hydrogen chloride concentration is doubtless even smaller.

Route (5) remains. Here a rapid equilibrium forming acetylium ions and their subsequent rate-determining attack on the naphthol are involved. The effects of any change in dielectric constant on these two processes will be in opposite senses, and will therefore tend to cancel to some extent. The partial cancellation of what is, in any case, probably a very small effect seems to us to argue against an explanation of the rate enhancement by hydrogen chloride based on medium effects. One might expect that the rate, if changed at all, would decrease. We therefore tentatively favour an interpretation based on specific electrophilic catalysis. Independent evidence for such catalysis has been found in experiments with *alkyl* chlorides and bromides in nitromethane.[1]

[11] Janz and Danyluk, *Chem. Rev.*, 1960, **60**, 209.

[12] Mellor, " Comprehensive Treatise on Inorganic and Theoretical Chemistry," Supp. II, Part 1, 1956, p. 413, Longmans, Green and Co., Ltd., London.

Lastly, as noted earlier, there exist two other possible examples of electrophilic assistance, by Brønsted acids, of acylation by acyl chlorides. What appears to be the first, probably genuine case interpreted in this way is the catalytic effect of benzoic acid on the reaction between benzoyl chloride and aniline in benzene.[6] The formulation of a unique reaction path is, however, complicated by the strong affinity of the catalyst for the amine: an 8-membered, cyclic transition state is proposed. The other example, contained in some previous work of ours, was there interpreted as a general medium effect.[4] This case is discussed more fully, together with new results, in the following paper.

EXPERIMENTAL

Materials.—Nitromethane was refluxed over, and distilled successively from, phosphorus pentoxide and calcium hydride. It had b. p. 102°. A Karl Fischer estimation showed the product to contain *ca.* 0·01 mole of water per l. Acetyl chloride was distilled from isoquinoline and had b. p. 51°. β-Naphthol was a recrystallised sample, m. p. 122°. Anhydrous tetraethylammonium chloride was prepared by repeated recrystallisation of a commercial sample from a mixed organic solvent, followed by removal of solvent of crystallisation *in vacuo* (this required pumping for more than 48 hr.); the purity (found by estimation of chloride) was $>96\%$. Solutions of this compound in nitromethane were made up by weight. Gaseous hydrogen chloride was generated from the concentrated aqueous acid by concentrated sulphuric acid. The concentrations of stock nitromethane solutions of hydrogen chloride were estimated by titration.

Stoicheiometry.—The reaction was shown to yield β-naphthyl acetate in high yield by an experiment on the preparative scale.

Kinetic Arrangements.—All experiments were at 25°, but otherwise the general arrangements followed the pattern of previous work,[4] the loss of naphthol being followed by noting the fall in optical density at 3300 Å. Since the solvent has slight absorption in this region, only very small (0·1 ml.) samples of the reaction mixtures were taken and these were diluted by addition to sufficient glacial acetic acid (25 ml.) both to quench the reaction and to render negligible the absorption due to nitromethane. To retain, at the same time, reasonable absorption for the β-naphthol in the diluted solutions it was necessary to use an initial concentration of 0·04M. This therefore necessitated an acetyl chloride concentration of $\nless 0{\cdot}4$M to ensure accurate first-order removal of naphthol. Good first-order plots were always obtained. Data concerning the observed order in acetyl chloride, and the effects of added hydrogen chloride and saline chloride are in the Table. The quoted rates are all averages of at least two determinations. Each run was initiated by the addition of naphthol, and in every case the reaction mixture had previously been left long enough at the thermostat temperature for effectively all the residual water content to be destroyed.

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