349. *The Mechanism of Acylation by Carboxylic Anhydrides in Non-aqueous Media, catalysed by Mineral Acid.*

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Experiments, mainly kinetic, are reported on the acylation of β-naphthol by acetic, butyric, dichloroacetic, and benzoic anhydride in acetic, butyric, and dichloroacetic acid, catalysed by hydrofluoric, hydrochloric, hydrobromic, and perchloric acid. Some experiments on the acylation of water are also described.

The kinetic results and infrared spectra indicate that in these systems the acyl derivative of the catalysing acid, is formed as the result of a rapid equilibrium with the anhydride, and attacks the compound undergoing acylation in a slow, bimolecular step. For the three halogen acids the pre-equilibria lie well towards the acyl halide, but in perchloric acid catalysis only a small amount of the acyl perchlorate is present. Reaction in the presence of hydrogen fluoride is complicated by other features, among which is the powerful catalysis of the slow step by molecular hydrogen fluoride, to which the efficacy of hydrogen fluoride in Friedel–Crafts acylation by anhydrides may also be due.

The observed relative reactivites are, as expected, AcBr $>$ AcCl $\gg$ AcF and AcCl $>$ Pr·COCl $\gg$ BzCl.

In excess of acetic acid, and at ordinary temperatures, benzoyl and butyryl chloride can be made to act only as acetylating agents. Such reactions may form the basis of a general, one-step preparation of acyl derivatives from the parent acids.

The work now described is chiefly a kinetic investigation into the mechanism of acylation of hydroxylic compounds by acetic anhydride in acetic acid. Various mineral acid catalysts have been used, and other solvent–anhydride combinations. The main substance acylated has been β-naphthol, though water has also been studied.

Previous kinetic work in this general field has not been so extensive as might be supposed. No other hydroxylic compound appears to have been studied and no media other than acetic acid. The one previous study with β-naphthol, by Conant and Bramann,[1] is scarcely quantitative, and their mechanistic conclusions have been shown to be incorrect. Of the two previous studies of relevance on the acylation of water, the first is the early work of Orton and Jones,[2] whose conclusions are at variance with those drawn from Yvernault's more recent study.[3] Yvernault's presentation of his work makes it difficult to assess. He is led, however, to conclusions which are similar to those to be drawn from the present work, namely, that the acyl derivative of the catalysing acid is the active acylating agent in the systems under discussion.

Mackenzie and Winter [4] studied the acylation of quinones by acetic anhydride catalysed

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[1] Conant and Bramann, *J. Amer. Chem. Soc.*, 1928, **50**, 2305.

[2] Orton and Jones, *J.*, 1912, 1708.

[3] Yvernault, (*a*) *Compt. rend.*, 1951, **233**, 411; (*b*) *ibid.*, 1952, **235**, 167; (*c*) Thesis, Strasbourg, 1954; (*d*) *Compt. rend.*, 1955, **241**, 485.

[4] Mackenzie and Winter, *Trans. Faraday Soc.*, 1948, **44**, 159, 171, 243.

by perchloric acid (Thiele reaction). Their kinetic, and related indicator ionisation data, were complex, and their arguments for a mechanism involving both Ac_2OH^+ and $AcClO_4$ as acylating agents are therefore not compelling. Other relevant work on acylation catalysed by this acid has been undertaken by Burton and Praill,[5] but their arguments in favour of particular intermediates, based on changes in reaction yields, must also be regarded as reasonable rather than as unequivocal. These previous studies will be done fuller justice in the discussion below Their inconclusive nature prompted the present work, which was also intended to be complementary to that on the acid-catalysed decomposition of acetic anhydride in aqueous media.[6]

In aqueous media, it seems at present probable that carboxylic anhydrides decompose, under acid catalysis, by the route:

$$\begin{array}{rcll}
(R\cdot CO)_2O + H_3O^+ & \rightleftharpoons & (R\cdot CO)_2OH^+ + H_2O & \text{Fast}\\
(R\cdot CO)_2OH^+ & \longrightarrow & R\cdot CO^+ + R\cdot CO_2H & \text{Slow}\\
R\cdot CO^+ + H_2O & \longrightarrow & R\cdot CO_2H & \text{Fast}
\end{array}$$

The uncatalysed solvolysis[7] is considered to be bimolecular. In acetic acid, the uncatalysed reaction with water (studied more often than the catalysed reaction) is fairly certainly bimolecular also.[3a, 8] However, some modification of the mechanism of acid-catalysis found in aqueous media is to be expected in acetic acid, and other media of low dielectric constant, if only owing to the prevalence in them of ion association. The following schemes have *a priori* possibility, when hydrogen chloride is the catalyst:

$$\begin{array}{rcllll}
 & & & (1) & & \\
(R\cdot CO)_2O + HCl & \rightleftharpoons & (R\cdot CO)_2OH^+Cl^- & \text{Fast} & & \\
(R\cdot CO)_2OH^+Cl^- + H_2O & \longrightarrow & 2R\cdot CO_2H + HCl & \text{Slow} & & \\
 & & & & (2) & (3)\\
(R\cdot CO)_2O + HCl & \rightleftharpoons & (R\cdot CO)_2OH^+Cl^- & & \text{Fast} & \text{Fast}\\
(R\cdot CO)_2OH^+Cl^- & \longrightarrow & R\cdot COCl + R\cdot CO_2H & & \text{Slow} & \text{Fast}\\
R\cdot COCl + H_2O & \longrightarrow & R\cdot CO_2H + HCl & & \text{Fast} & \text{Slow}
\end{array}$$

The present work began with a study of the acylation of β-naphthol by acetic anhydride in acetic acid, with hydrogen chloride as catalyst. The initial results indicated rapid formation of acetyl chloride which then acylated the naphthol in a slow, bimolecular step, *i.e.*, scheme (3) above. The existence of similar mechanisms was then investigated for other mineral acids, in particular for hydrobromic, hydrofluoric, and perchloric acid (sulphuric and nitric acid present individual difficulties, see below). The reaction between other anhydrides and hydrogen chloride was examined also for butyric and dichloroacetic acid systems and, to some extent, for benzoic anhydride in acetic acid. Complementary studies of the acylation of water were also made in several of the above systems. The carboxylic acid solvents are not easy to obtain perfectly anhydrous, and in order to interpret the data on β-naphthol it was necessary to know the rate at which any water they contained was acylated. The kinetic results obtained concerning water were less accurate than those for β-naphthol, and therefore the experiments with the former were usually restricted to the establishment of the data essential for the interpretation of work with the latter, though enough was done in the acetic–hydrochloric system to show that the mechanisms of acylation are the same. With stronger acid catalysts than hydrogen chloride, kinetic complications occur in the water reaction.

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[5] Burton and Praill, *J.*, 1950, 1203, 2034.
[6] Gold and Hilton, *J.*, 1955, 843.
[7] Gold, Hilton, and Jefferson, *J.*, 1954, 2756.
[8] Janssen, Haydel, and Greathouse, *Ind. Eng. Chem.*, 1957, **49**, 197.

EXPERIMENTAL

Materials.—Acetic acid, purified as previously described,[9] had m. p. >16·6°. Butyric acid, purified as described by Vogel,[10] had b. p. 163°. Dichloroacetic acid was distilled at 1 mm. (b. p. 63°) to remove chloride. " AnalaR " acetic anhydride was refluxed over magnesium and fractionally distilled. Butyric anhydride was fractionally distilled, and a fraction, b. p. 197—200°, collected. Dichloroacetic anhydride (Chemicals Procurement Ltd., New York, U.S.A.) was fractionally distilled at 0·5 mm., and a fraction, b. p. 64—66°, m. p. 26°, collected. This compound has previously only been reported as a liquid. Its purity (>99%) was checked by hydrolysis and titration of the acid produced. " AnalaR " benzoic anhydride had m. p. 42°. Commercial [^{14}C]acetic anhydride was diluted to give a stock of activity about 0·1 mc/20 ml. " AnalaR " acetyl chloride was distilled from dimethylaniline, then having b. p. 52°. Butyryl chloride, redistilled, had b. p. 102°. Dichloroacetyl chloride was fractionally distilled at *ca.* 20 mm. (b. p. 44°). Acetyl bromide was redistilled (b. p. 77°). Acetyl fluoride was prepared by Mashentsev's method; [11] it was redistilled from sodium fluoride (b. p. 21°) and was stored, for short periods, under anhydrous conditions, in a refrigerator. " AnalaR " benzoyl chloride was redistilled (b. p. 197°). β-Naphthol had m. p. 122°. β-Naphthyl acetate and butyrate (for use as standard samples), prepared by Vogel's method,[12] had m. p. 69° and b. p. 122°/0·5 mm., respectively.

Solutions of acetyl perchlorate in acetic anhydride were prepared by dissolving known amounts of pure silver perchlorate (kindly supplied by Dr. I. R. Beattie) in this solvent and adding a calculated quantity of acetyl chloride. The vessels used were centrifuge tubes, fitted with ground-glass stoppers; and the resulting precipitates of silver chloride were centrifuged as rapidly as possible, for these solutions were not stable, becoming yellow and darkening with time.[4] Further details of their use are described below.

Nearly anhydrous solutions of the various mineral acids were prepared as follows. The hydrochloric acid solutions were made by bubbling in the dry gas, formed by addition of the concentrated aqueous acid to concentrated sulphuric acid and washed with the latter. Perchloric, hydrobromic, and some of the hydrofluoric acid solutions were made by the addition, to the solvent, of the purest available concentrated aqueous acid, followed by an appropriate amount of the relevant carboxylic acid anhydride. After a suitable interval, the amount of water present in the resulting solution was determined by Karl Fischer titration, and further anhydride added if necessary. Solutions of hydrogen fluoride in acetic acid were also made by passing the gas, quoted as 99% pure, from a cylinder kindly supplied by the National Smelting Co. Ltd. In some cases cooling was necessary. The hydrogen fluoride solutions were made up and stored in Polythene bottles. Stock perchloric acid solutions had concentrations $<10^{-2}$M. They were stable for at least one week.

Hydrogen chloride and bromide solutions were analysed by titration, after dilution with water, against silver nitrate. The hydrogen fluoride solutions were diluted with weak alkali and titrated by the thorium nitrate method. The perchloric acid solutions were made up, by weight, from an aqueous solution of known composition.

Stoicheiometry of Reactions Studied.—(1) *Acylation of water.* The method of following the rate of acylation of this substance was chemical, rather than physical, and hence for any run in any of the systems it was possible to determine directly whether the concentration of water was eventually reduced to negligible proportions, it being invariably used in deficit. This was done for at least one run, in each system studied. It seems unlikely that water is destroyed chemically in any way other than by acylation, in these systems, and the reaction must therefore be quantitative under the conditions used. This argument, of course, assumes that the Karl Fischer analytical method used is also quantitative for the solutions involved. This is very probably so, except perhaps for the hydrofluoric acid solutions (see below).

(2) *Acylation of β-naphthol.* For all the systems studied kinetically, independent preparative scale reactions, under similar conditions, showed >95% yield of the acylated material. Good physical constants indicated negligible rearrangement, and the absence of nuclear attack.

Details of Kinetic Experiments.—(1) *Analytical methods.* (i) β-Naphthol. β-Naphthol has a

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[9] Satchell, *J.*, 1956, 3911.
[10] Vogel, *J.*, 1948, 1814.
[11] Mashentsev, *J. Appl. Chem.* (*U.S.S.R.*), 1941, **14**, 816.
[12] Vogel, " Practical Organic Chemistry," Longmans, Green & Co., 1948.

moderately intense ultraviolet absorption band centred around 3300 Å, which is absent in spectra of its acetate and butyrate. Hence absorption measurements at this wavelength were used. Beer's law is obeyed in the solvents involved in the kinetic experiments, and there was no interference from other components of the reaction mixtures. The ultraviolet measurements were made with a Beckman spectrophotometer, and quartz cells, of 1 cm. path, fitted with ground stoppers.

(ii) Water. Water determinations, kinetic and otherwise, were made with a commercial Karl Fischer apparatus, fitted with a semimicro-burette. The titres were usually rather small (*ca.* 2 ml. or less), and in some instances the commercial Karl Fischer reagent (supplied by B.D.H.) was diluted with anhydrous methanol before use to increase the titre.

(2) *Catalysis by hydrogen chloride.* Kinetic runs involving catalysis by this acid were carried out at 40°, in graduated flasks, fitted with ground-glass stoppers. Mixtures were made up, by volume, from solvent, stock hydrogen chloride–solvent solution, and anhydride. The vessels were filled to just below the mark to allow for the liquid expansion on going from room temperature to 40°, and placed in the thermostat bath.

If β-naphthol was being acylated, a sufficient time was allowed to elapse before the run was started, for the small known amount (usually $\leqslant$M/50) of water in the solvent to be effectively destroyed. The correction of the initial concentration of anhydride for loss due to this reaction was usually small. Then solid β-naphthol (enough to give an approximately 0·01M-solution) was added. This quickly dissolved on shaking. Samples for analysis were withdrawn at appropriate intervals. Useful light absorption was provided by a 1 ml. sample run into reagent-grade glacial acetic acid, and made up to 25 ml. This dilution also effectively stops the reaction. The anhydride was always in excess (usually > ten-fold) over the naphthol, since this was found to reduce the kinetics to first-order. In many cases (see Discussion), the acid chloride was used together with, or instead of, hydrogen chloride or the anhydride. These reaction mixtures were prepared and treated in ways analogous to those described above.

It was shown that there was negligible loss of hydrogen chloride from the reaction vessels, whose stoppers were sealed with Apiezon Q compound.

When water was being acylated it was obviously not necessary for the solvent's water content to be destroyed. In these runs a small amount of water was added, from a micropipette, as soon as flask and contents had attained 40°. The total water concentration for these runs was *ca.* M/15 initially. Hence the anhydride had to be *ca.* M/1·5 to reduce the kinetics to first-order. The samples for analysis (usually 1 ml.) were run directly into the titration flask of the Karl Fischer apparatus, the dilution sufficing to arrest the reaction. The titration was accomplished as rapidly as possible.

Almost all the rate constants quoted in this paper are average values computed from two or more runs. The reproducibility for the β-naphthol was *ca.* ±3%, but for the water only *ca.* ±10%. (A given Karl Fischer determination was sometimes only reproducible to ±8%.)

(3) *Catalysis by hydrogen bromide and perchloric acid.* The procedures were similar to that for hydrogen chloride. These acids were only used with the acetic solvent system. Work on hydrogen bromide catalysis was done at 40°, and on perchlorate catalysis at 25°. Acetyl perchlorate was made when required in solution in acetic anhdride, as previously described. These solutions were not stable,[4] and it was found desirable to carry out a series of runs, for any given perchlorate concentration, starting them at different times after the preparation of the perchlorate. In this way an extrapolation giving the reactivity of the acetyl perchlorate immediately after formation could be constructed. The concentration of acetyl perchlorate in acetic anhydride was made such that useful samples of the stock solution could be taken which contained less anhydride than the total necessary for a run. Additional anhydride was, therefore, also added. The detailed procedure was as follows. The reaction mixture was completely made up, except for the acetyl perchlorate sample. (This mixture contained a little perchloric acid, to catalyse the acylation of solvent water, but the acetyl perchlorate sample was to contain the major perchlorate contribution.) It was then left at 25° until the solvent water had been reduced to well below the concentration of the perchlorate to be added; then the freshly made acetyl perchlorate was added, followed by β-naphthol to start the reaction. By this procedure, and by making up the acetyl perchlorate in acetic anhydride, it was attempted to ensure that none of this compound was converted into perchloric acid by reaction with water.

(4) *Catalysis by hydrogen fluoride.* The procedures with this catalyst, studied only in acetic acid, were similar to those used for hydrogen chloride, except that Polythene vessels were used.

These vessels comprised a bulb of stout Polythene, fitted with Polythene tubing to act as a neck. The neck was sealed with a reasonably gas-tight, hydrogen fluoride-resistant plastic stopper. Runs concerning fluoride catalysis were at 40°. Loss of fluoride from the reaction vessels was very slow, and negligible over the duration of most of the runs.

(5) *Indicator measurements.* Some measurements were made of the extent of ionisation of a Brønsted base indicator in the reaction mixtures used in the experiments on perchloric acid catalysis. The mixtures were made up as previously described except that, in place of β-naphthol, there was added a small volume of solvent containing the indicator (*NN*-dimethyl-2,4-dinitroaniline, a Brønsted base not very susceptible to acylation; kindly supplied by Mr. R. W. Lambert). The acetic acid solvent used for making up the indicator solutions was a specially dried sample made by adding of an appropriate amount of acetic anhydride, followed by prolonged storage at 60°. The determination of ionisation data in acetic acid has been discussed previously.[13]

(6) *Infrared measurements.* These were made with a Grubb–Parsons double-beam spectrometer, with a fixed quartz sample cell for liquids, and the Nujol mull technique for solids. Spectra were taken within 30 min. of making up the solution, often more quickly.

(7) *Experiments with* [^{14}C]*-labelled acetic anhydride.* A weighed sample (*ca.* 0·3 g.) of β-naphthol, added last, was acylated, at 40°, under conditions analogous to those of the kinetic experiments with hydrogen chloride, with a known (*ca.* 1 g.) excess of labelled anhydride, dissolved in a known (*ca.* 10 g.) amount of acetic acid molar with respect to hydrogen chloride. The product was isolated after 1 hr. and its activity compared with that of the anhydride. The counting was by a scintillation technique. There were no complications due to quenching.

RESULTS AND DISCUSSION

(a) *Acylation in the System* Ac_2O–HCl–AcOH.—(1) *Reaction with* β*-naphthol.* Preliminary experiments showed that, compared with the reaction rates obtained when they were both present, the rates obtained when either acetic anhydride or hydrogen chloride was absent, were negligible. Experiments, with both present, directed towards the determination of the reaction orders gave the following results. (i) With anhydride always in about ten-fold excess of the naphthol, then, for any given hydrogen chloride concentration the observed kinetics were first-order with respect to the naphthol (Fig. 1). (ii) Variation of the hydrogen chloride concentration, at fixed anhydride concentration, showed the order with respect to hydrogen chloride to vary from unity, when its concentration was much less than the anhydride's, to considerably less than unity when it was in excess of the anhydride. (iii) Similar results were found at fixed hydrogen chloride concentration, for the order with respect to anhydride. These data, collected in Table 1, are most easily explained, at the qualitative level, by the postulation of a rapid * equilibrium between anhydride and hydrogen chloride, producing the acylating agent, which then attacks the β-naphthol in a slow step. For the concentration ranges used, if, when either the anhydride or catalyst is in excess, the equilibrium is displaced well towards the maximum possible formation of acylating agent, then the approximately first-order behaviour under these conditions for the compound in deficit is explained.

The same values for the rate constants were obtained, whether one started with hydrogen chloride and acetic anhydride as reagents, or with acetyl chloride together with the appropriate amount of anhydride and/or hydrogen chloride. The rates depend, that is, only on the stoicheiometric chloride and acetyl concentrations (Table 2). For this reason the acylating agent is considered to be acetyl chloride rather than $Ac_2OH^+Cl^-$, because otherwise the improbable assumption would be necessary that acetyl chloride is converted largely into $Ac_2OH^+Cl^-$ in acetic acid under some conditions (*e.g.*, in the presence of excess of hydrogen chloride or anhydride). This conclusion is supported by the infrared spectra of the systems (see below).

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* Rapid in the sense that the equilibration is essentially complete before the addition of the naphthol. The period involved was at least 30 min., but usually less than an hour. The word "rapid" is used in this sense throughout the paper.

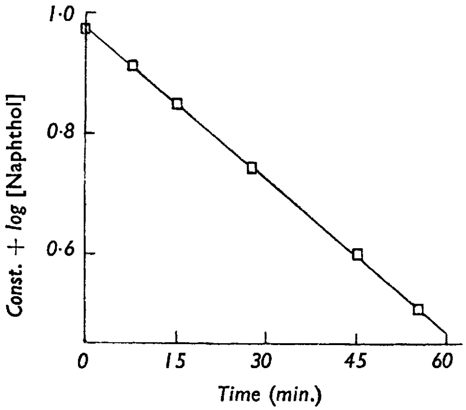
[13] Satchell, *J.*, 1958, 1916.

It is clear, from this purely qualitative discussion, that a mechanism analogous to the third of those quoted above operates in the present instance, *viz.*:

$$\text{(1)}\ Ac_2O + HCl \rightleftharpoons AcCl + AcOH \quad \text{Fast}$$
$$\text{(2)}\ AcCl + ROH \longrightarrow ROAc + HCl \quad \text{Slow, } k_2$$

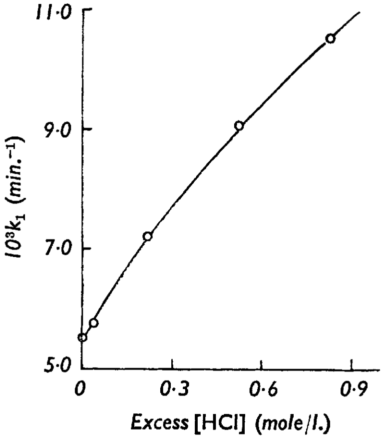
The second step is a bimolecular, nucleophilic substitution of a type often previously studied.[14] In solutions of low dielectric constant, such as acetic acid, it is likely to be subject to appreciable salt effects in the presence of dipolar solutes.[15] Hence those runs with excess of hydrogen chloride will be particularly likely to exhibit such an effect, while those with excess of anhydride (*i.e.* those in which most of the catalyst will be converted into acetyl chloride) will be much less subject to it. The evaluation of the equilibrium constant, $K = [AcCl]/[HCl][Ac_2O]$, for step 1, and the second-order constant, k_2, for step 2, is, therefore, best done from results obtained with hydrogen chloride in deficit. Tables 1 and 2 reveal that K is certainly fairly large. An approximate value, previously given,

FIG. 1. *First-order plot for acetylation of β-naphthol by acetic anhydride catalysed by hydrogen chloride.*



Initial [Naphthol] $\approx$0·008M. [HCl] = 0·6M. $[Ac_2O]$ = 0·18M.
k_1 = 19·2 × 10^{-3} min.$^{-1}$.

FIG. 2. *Salt-effect of hydrogen chloride on the rate of acetylation of β-naphthol by acetyl chloride.*



[AcCl] = 0·08M.

TABLE 1. *Acylation of* β-*naphthol by acetic anhydride in acetic acid catalysed by hydrogen chloride at* 40°.

Initial [β-Naphthol] ~0·008M. $[H_2O]$ = 0·02M.
k_1 = observed first-order rate constant (in min.$^{-1}$).

(a) *Order in hydrogen chloride.*

$[Ac_2O]_s$ *	[HCl]	10^3k_1
0·08	0·03	2·09
0·08	0·06	4·11
0·08	0·12	5·70
0·12	0·09	6·16
0·12	0·12	8·22
0·08	0·30	7·20
0·08	0·60	9·03
0·08	0·90	10·5

(b) *Order in acetic anhydride.*

$[Ac_2O]_s$ *	[HCl]	10^3k_1
0·08	0·60	9·03
0·12	0·60	13·5
0·18	0·60	19·2
0·18	0·18	12·6
0·38	0·18	12·8
0·68	0·18	13·0

* $[\ ]_s$ represents the stoicheiometric molarity, after appropriate correction for reaction with solvent water.

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[14] *E.g.*, Hudson and Savill, *J.*, 1958, 4121.
[15] Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Son Ltd., London, 1953.

is much too low.[16] The results may, indeed, be explained satisfactorily with $K = \infty$, *i.e.*, by assuming quantitative formation of acetyl chloride. Results referring to the addition of acetyl chloride only (Table 2) show that the rate of acylation of naphthol is closely proportional to the stoicheiometric concentration of acetyl chloride. If a significant quantity of the chloride was being converted into anhydride this proportionality would not have been observed. However, in view of the various experimental errors, K would have to be less than *ca.* 50 for this effect to be unequivocally detected. The same conclusions are to be drawn from the observed rates in the presence of added anhydride. Here, if $K = \infty$, the 0·02M-acetyl chloride lost as hydrogen chloride will be completely regenerated in the presence of added anhydride, leading to a predictable increase in rate. Also runs with different added excess of anhydride should all give the *same* rate (if the possibility of a solvent effect due to this compound is ignored). These expectations are reasonably fulfilled, and again significant discrepancies might have been expected if K were less than *ca.* 50. The fact that the rates with different excesses of anhydride are all very similar points to a small solvent effect for this compound. The addition of similar volumes of acetone also produces little effect on the rate. An average value for k_2 is $69 \cdot 8 \times 10^{-3}$ l. mol.$^{-1}$ min.$^{-1}$.

TABLE 2. *Acylation of* β-*naphthol by* AcCl–HCl–Ac_2O *in acetic acid at* 40°.

Initial [β-Naphthol] ~0·008M. $[H_2O] = 0 \cdot 02$M.

k_1 = observed first-order rate constant (in min.$^{-1}$).

$[AcCl]_s$	$[Ac_2O]_s$	$[HCl]_s$	10^3k_1	$[AcCl]_s$	$[Ac_2O]_s$	$[HCl]_s$	10^3k_1	$[AcCl]_s$	$[Ac_2O]_s$	$[HCl]_s$	10^3k_1
0·08	—	0·04	5·70	0·18	—	0·42	19·7	—	0·38	0·18	12·8
—	0·08	0·12	5·70	—	0·18	0·60	19·2	0·18 †	0·50 †	—	13·0
0·08	—	0·52	8·97	0·08	—	0·02 *	5·52	—	0·68	0·18	13·0
—	0·08	0·60	9·03	0·12	—	0·02 *	8·41	0·18	0·20	0·02 *	13·0
0·08	—	0·22	7·34	0·18	—	0·02 *	12·8	0·18	0·40	0·02 *	13·0
—	0·08	0·30	7·20	0·18 †	0·20 †	—	13·0				

* Arising from reaction with solvent water. † In these calculations allowance was made for reaction between acetic anhydride and hydrogen chloride, with K assumed to be infinity.

Thus, from the viewpoint of the kinetic experiments, the formation of acetyl chloride may be assumed to be quantitative. Consideration of the data in Table 1, with this in mind, reveals the magnitude of the salt effect operating in the presence of excess of hydrogen chloride. A plot of the rates, at 0·08M-anhydride, for increasing hydrogen chloride concentration is given in Fig. 2.

Although the kinetic results show that K is large, that it is not very large indeed is revealed by infrared spectra. Alone, or in solution in acetic acid, acetic anhydride shows, in particular, an absorption doublet at 12·5 μ, and a very strong band at 8·85 μ. Acetyl chloride alone has no bands at 12·5 or at 8·85 μ, but has a very strong band at 9·10 μ. However, acetyl chloride in 4—5M-solution in acetic acid has detectable absorption at 12·5 μ, and its 9·10 μ absorption possesses a definite shoulder in the 8·85 μ region. It seems difficult to attribute these changes to anything except the formation of a small amount of acetic anhydride. Unfortunately the small amount of anhydride, and the nature of the bands, make quantitative estimation difficult. A value for K between 50 and 100 is probably consistent with the observations.

It was mentioned previously that the infrared spectra did not favour a species $Ac_2OH^+Cl^-$ (rather than AcCl) as the acylating agent. This is because the spectrum of acetyl chloride in acetic acid (or of acetic anhydride plus hydrogen chloride in this solvent) is basically that expected for superposition of the spectra of acetic acid and acetyl chloride—apart from the minor modifications attributed to acetic anhydride. If acetyl chloride were present chiefly as $Ac_2OH^+Cl^-$, this close similarity would be very unexpected.

If the mechanistic interpretation of the kinetics, supported by the infrared spectra, is correct, and there exists a rapid equilibrium between anhydride, catalyst, acyl chloride, and

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[16] Satchell, *Chem. and Ind.*, **1958**, **1442**.

solvent, then addition of [^{14}C]anhydride to an acetic acid–hydrogen chloride mixture should result in the rapid dispersion of the isotope throughout the solvent. When β-naphthol was added, the resulting acetate had the activity expected from complete exchange of acetyl groups between the anhydride and solvent. While this is a necessary consequence of the proposed equilibrium, it does not support it in a positive sense because other mechanisms for the acetyl exchange are conceivable, *e.g.*:

$$\text{(1)}\quad {}^{14}\text{Ac}_2\text{O} + \text{HCl} \longrightarrow {}^{14}\text{AcCl} + \text{AcOH}$$
$$\text{(2)}\quad {}^{14}\text{AcCl} + \text{AcOH} \rightleftharpoons {}^{14}\text{AcOH} + \text{AcCl}$$

If the second step were fast, at ordinary temperatures, this mechanism could account for the observed exchange without invoking the existence of a rapid reversal of the first step. Brown [17] showed that reaction of benzoyl chloride with aliphatic acids can be used for the preparation of low-boiling acyl chlorides and favoured the scheme:

$$\text{(1)}\quad \text{BzCl} + \text{AcOH} \longrightarrow \text{BzOH} + \text{AcCl}\uparrow$$

rather than:

$$\text{(2)}\quad \text{BzCl} + \text{AcOH} \rightleftharpoons \text{BzOAc} + \text{HCl}$$
$$\text{BzOAc} + \text{HCl} \longrightarrow \text{BzOH} + \text{AcCl}\uparrow$$

because, while the reaction is carried out at the b. p., nevertheless high yields of acyl halide are obtained, which means that little halide is lost. Brown argued that much would be lost as hydrogen chloride if the scheme (2) operated predominantly, but this is no longer convincing since reaction between an anhydride and hydrogen chloride is now known to be fast, and will be especially so at high temperatures, so that the hydrogen chloride need not necessarily have time to be evolved as gas. However, the existence of reactions such as (1) is certainly possible. And they may be fast.

Another possible route for acetyl exchange is the uncatalysed process:

$${}^{14}\text{Ac}_2\text{O} + \text{AcOH} \rightleftharpoons \text{Ac}_2\text{O} + {}^{14}\text{AcOH}$$

which is probably rapid in the sense used in this paper.[18]

(2) *Reaction with water.* In this case preliminary experiments showed that the rate of reaction between anhydride and water, in the absence of the catalyst, although fairly slow, was not negligible compared with those of the catalysed reactions. All the quoted rate constants of catalysed reactions have, therefore, been appropriately corrected, it being assumed, as is well established, that the rate of the uncatalysed reaction is of the first order in both anhydride and water. The value of the second-order constant now obtained is $k_2 = 2{\cdot}47 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$. This is compatible with previous values, obtained at other temperatures.[3a,8]

The experiments to determine the reaction orders, for the catalysed reaction, produced the following results. (i) In the presence of excess of anhydride, at any given catalyst concentration, the kinetics were of first order in water. (ii) In the presence of anhydride, in an excess of both water and catalyst, the rate was closely proportional to the catalyst concentration. (Runs with hydrogen chloride concentrations comparable with, or in excess of, the anhydride, were not studied, being too rapid.) (iii) Increase in the anhydride concentration, at fixed catalyst concentration, increased the rate slightly. [A first-order plot is given in Fig. 3 and the findings (ii) and (iii) are illustrated by data in Table 3.] As with acylation of β-naphthol the same results were obtained whether the source of chloride was hydrogen chloride or acetyl chloride.

The general conclusion to be drawn from these results, and the previous discussion of

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[17] Brown, *J. Amer. Chem. Soc.*, 1938, **60**, 1325; see also Mashentsev, *J. Gen. Chem.* (*U.S.S.R.*), 1946, **16**, 203.

[18] Brown and Trotter, *J.*, 1951, 87.

the naphthol reaction, is that the mechanisms of the two reactions are essentially analogous. For acylation of water the scheme is:

$$\begin{aligned} \mathrm{Ac_2O + HCl} &\rightleftharpoons \mathrm{AcCl + AcOH} \\ \mathrm{AcCl + H_2O} &\longrightarrow \mathrm{AcOH + HCl} \end{aligned}$$

with the equilibrium for the first step far to the right. An average value for the second-order constant for the second step is $k_2 = 1{\cdot}7$ l. mole^{-1} min.$^{-1}$. Water is thus acylated by acetyl chloride about 24·5 times faster than β-naphthol.

Two points merit further discussion. (*a*) Finding (i), as well as establishing the first-order loss of water, implies that no appreciable quantity of the catalyst is lost in the water, as H_3O^+, in the concentration ranges studied. (This may, in fact, also be deduced from data given by Smith and Elliott [19].) If catalyst were lost as H_3O^+, then, as the reaction proceeded and less and less water remained available, more and more catalyst would be freed and be converted into acetyl chloride. The rate would thus increase and first-order plots would not be obtained. While this complication does not intrude for the present hydrogen chloride catalysis, it will do so for acids of sufficient strength (see below); it would also affect hydrogen chloride catalysis if the water content were sufficiently high, or in the event of an increase in the dielectric constant. (2) The increase in rate as the anhydride excess is raised, though small, is significantly greater than for the β-naphthol reaction. Perhaps acylation of water is a little more subject to changes in dielectric constant. However, a more probable reason for the small effect is mentioned below.

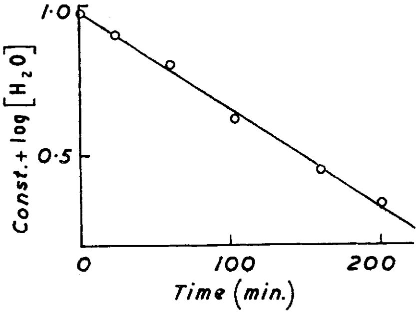

FIG. 3. *First-order acetylation of water by acetic anhydride catalysed by hydrogen chloride.*

Initial $[H_2O] \simeq 0{\cdot}07$M. $[Ac_2O] = 1{\cdot}05$M. [HCl] $= 0{\cdot}0024$M.
$k_1 = 4{\cdot}9 \times 10^{-3}$ min.$^{-1}$ (corr. for rate of uncatalysed reaction).

TABLE 3. *Acylation of water by acetic anhydride in acetic acid catalysed by hydrogen chloride at* 40°.

Initial $[H_2O] = 0{\cdot}07$—$0{\cdot}05$M. k_1 = First-order rate constant (in min.$^{-1}$).

(a) *Order in hydrogen chloride.*

$[Ac_2O]$	1·05	1·05	1·05	1·05	1·05	1·05
[HCl]	0·0024	0·0048	0·012	0·012 (AcCl)	0·024	0·048
10^3k_1 *	4·9	9·9	22	23	43	88

(b) *Order in acetic anhydride.*

$[Ac_2O]$	0·52	1·05	1·53
[HCl]	0·012	0·012	0·012
10^3k_1 *	20	22	26

* Rates for catalysed reactions have been corrected for the velocity in the absence of hydrogen chloride, for which the second-order rate constant $k_2 = 2{\cdot}47 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$.

(3) *Present mechanistic conclusions and previous work.* (i) The conclusion concerning the formation of acetyl chloride agrees well with Colson's results,[20] overlooked by previous

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[19] Smith and Elliott, *J. Amer. Chem. Soc.*, 1953, **75**, 3566.
[20] Colson, *Bull. Soc. chim. France*, 1897, **17**, 58.

workers. Colson found it possible to distil good yields of acetyl chloride from acetic anhydride saturated with hydrogen chloride; and there are a few similar reports in the older literature of the formation of acyl halides from anhydrides and hydrogen halides under various conditions. It is also possible to obtain some acetyl chloride by heating the anhydride with calcium chloride [21] (there are other similar reports here also). (ii) Conant and Bramann,[1] in their work on β-naphthol with various mineral acids as catalysts, concluded that the acylation rate was determined by the hydrogen-ion activity for the medium, as measured by the chloranil electrode. They suggested $AcOH_2^+$ as the catalytic species, which is inconsistent with the mechanism now proposed, and has been shown to be invalid by Russell and Cameron [22] who pointed out that the chloranil electrode does not permit measurements in the presence of acetic anhydride. When the latter authors overcame this difficulty by using a hydrogen electrode, they found very different activites, and moreover evidence of compound formation for sulphuric, and perhaps also for perchloric, acid solutions. They tentatively interpret the latter as due to mixed anhydrides. Their results are consistent with those of the present investigation. (iii) In their early study of the acylation of water Orton and Jones [2] used various acetic acid–water mixtures as solvent, and various mineral acids as catalyst, especially hydrochloric, sulphuric, and nitric acid. In fairly aqueous media (50%), where dissociation will be complete, they found that equivalent amounts of the different catalysts were equally effective. This is in agreement with the mechanism for aqueous solutions (see p. 1753) where, for low acid concentrations, the rate is dependent on the hydrogen-ion concentration. As the proportion of acetic acid in the medium was increased, Orton and Jones observed departure from this equivalence; in particular, nitric acid showed a marked loss of catalytic power, compared with both hydrochloric and sulphuric acids, which were claimed to approach equal effectiveness on a molar basis. There are few data to support the latter conclusion, and more recent knowledge about such sulphuric solutions (see below) makes it suspect. However, it led Orton and Jones to suggest that, in this region, the catalytic species was the molecular acid, though the mechanism by which it operated was not revealed. The loss of activity of nitric acid is doubtless real; it was tentatively explained by the authors as due to the formation of acetyl nitrate, which thus removed molecular nitric acid and so lowered the reaction rate compared with that for hydrochloric acid catalysis which did not suffer such removal. The results of the present study lead, of course, to a reinterpretation: both acetyl chloride and nitrate are formed, but the latter is a much less active acylating agent. Acylation in the presence of nitric acid is discussed more fully below.

(4) Yvernault [3] studied in detail the acylation of water, catalysed by both hydrochloric and perchloric acid. Only catalysis by the former will be discussed now. In general, for experimental reasons, he employed rather higher water and anhydride concentrations than were used in the present study. This somewhat complicated the kinetics, because of the changes in dielectric constant involved, and is, perhaps, the reason why he generally presented his data in terms of instantaneous velocities rather than rate constants. He first proposed [3a, b] a two-step consecutive scheme with acetyl chloride as intermediate, but finally [3c] reached conclusions similar to the present author's concerning the pre-equilibrium. The two sets of results are difficult to compare because Yvernault rarely simplified the kinetic behaviour by using an excess of acylating agent.

In the presence of appreciable anhydride Yvernault found an unexpected increase in rate (just beginning to be detected in our results, see Table 3) which he attibutes to an additional ionic mechanism. This seems very probable: the increased dielectric constant will favour the transference of a proton from the catalyst to water.

Summing up, it may be concluded that all the available experimental data are compatible with, indeed support, the mechanisms given on pp. 1757 and 1760. The foregoing material has been treated in some detail since it contains many points of relevance to

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[21] Gmunder, *Helv. Chim. Acta*, 1953, **36**, 2021.

[22] Russell and Cameron, *J. Amer. Chem. Soc.*, 1938, **60**, 1345.

catalysis in the other systems dealt with below. These points will be taken for granted in subsequent discussion. It was to test the generality of the proposed mechanism, and to demonstrate the ready formation of acyl chlorides, from anhydrides and hydrogen chloride in different systems, that the experiments discussed in sections (*b*), (*c*), and (*d*) below were conducted. Sections (*e*), (*f*), (*g*), and (*h*) deal with the extension to other mineral acids as catalysts.

(b) *Acylation in the System* $(\text{Pr·CO})_2\text{O}$–HCl–$\text{Pr·CO}_2\text{H}$.—For this system the experiments covered much the same ground as for the acetic system, except that the water acylation was restricted to establishing the rate at a single composition. The acylation of β-naphthol is reported in Tables 4 and 5. The main points emerging are the following: (1) The previous mechanism is satisfactory, and with butyric anhydride in excess of the catalyst, increasing the anhydride affects the rate negligibly, so that butyryl chloride is formed effectively quantitatively. This conclusion also follows from the rates in the presence of butyryl chloride alone. (2) A salt effect in the presence of excess of hydrogen chloride is comparable in magnitude with that found for acetic acid. (3) The second-order constant k_2 for acylation of β-naphthol by butyryl chloride in butyric acid is 8·86 l. mole^{-1} min.$^{-1}$, compared with $k_2 = 69{\cdot}8 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$ for acetyl chloride in acetic acid. Some of the difference is due to the change in dielectric constant (~3 to ~6), but it must be mostly due to the expected lower reactivity of butyryl chloride in reactions of the type under discussion (see p. 1763). (4) The second-order constant k_2 for the acylation of water is 0·162 l. mole^{-1} min.$^{-1}$ compared with 1·70 for the acetic system. The considerations of (3) apply again here.

TABLE 4. *Acylation of* β-*naphthol by butyryl chloride in butyric acid at* 40°.

Initial [β-Naphthol] ~0·01M. $[\text{H}_2\text{O}]$ = 0·03M.

k_1 = First-order rate constant (in min.$^{-1}$).

[Pr·COCl]$_s$	0·07	0·21	0·46	0·94	0·21
[HCl]$_s$	0·03	0·03	0·03	0·03	0·93
10^3k_1	0·614	1·89	4·32	8·97	5·85

TABLE 5. *Acylation of* β-*naphthol by* Pr·COCl–HCl–$\text{Pr·CO}_2\text{O}$ *in butyric acid at* 40°.

Initial [β-Naphthol] ≈0·01M. $[\text{H}_2\text{O}]$ = 0·03M.

k_1 = First-order rate constant (in min.$^{-1}$).

[$\text{Pr·CO}_2\text{O}$]$_s$	0·21	0·21	0·21	—	0·46	—	0·07	0·47
[Pr·COCl]$_s$	—	—	—	0·21	—	0·46	0·21	0·21
[HCl]$_s$	0·21	0·10	0·24	0·03	0·49	0·03	—	—
10^3k_1	1·86	0·91	1·94	1·89	4·46	4·32	1·86	1·89

No infrared study was made of this system.

(c) *The System* $(\text{CHCl}_2\text{·CO})_2\text{O}$–HCl–$\text{CHCl}_2\text{·CO}_2\text{H}$.—In this system it was impossible to undertake a kinetic study with β-naphthol whose solutions in this acid are unstable and become coloured. Also, as dichloroacetic is a fairly strong acid, much of any added water will probably be ionised. This will complicate its acylation, and, owing to the lower accuracy of the experiments with water, it was thought not profitable to study this reaction. However, infrared measurements with various mixtures of the system's components, and with dichloroacetyl chloride revealed little evidence for the existence of anhydride when the chloride was added to dichloroacetic acid or after hydrogen chloride had been bubbled into a solution of the anhydride in this solvent. It is clear that the equilibrium $(\text{CHCl}_2\text{·CO})_2\text{O} + \text{HCl} \rightleftharpoons \text{CHCl}_2\text{·COCl} + \text{CHCl}_2\text{·CO}_2\text{H}$ lies well to the right, as for the acetic system.

(d) *Miscellaneous Experiments.*—(1) *With benzoic anhydride and benzoyl chloride.* Preliminary study showed that benzoyl chloride acylates β-naphthol very slowly, at ordinary temperatures, in benzene. Attempts to use this solvent were abandoned. In acetic acid, however, the reaction rate was convenient. Preparative experiments, at room temperature, showed that the product, obtained in high yield, was essentially pure β-naphthyl acetate, rather than the benzoate. That some acetyl chloride would be formed, and hence that some acetylation would occur, follows from Brown's experiments [17] (see above). That no benzoylation occurs means that benzoyl chloride is very much less reactive towards β-naphthol than acetyl chloride. Thus both benzoyl and butyryl chloride have been found less reactive than acetyl chloride. This is to be expected since both phenyl and propyl groups lower any positive charge on the carbonyl-carbon atom more than the methyl group does, the first by conjugative relay, and the second by its greater $+I$ effect. Lowering the positive charge on the carbonyl-carbon atom hinders nucleophilic attack by the naphthol.

Infrared spectra showed that, in acetic acid, benzoic anhydride and hydrogen chloride rapidly form benzoyl chloride and benzoic acid, probably fairly quantitatively. The benzoyl chloride formed in this way does not change to acetyl chloride rapidly at ordinary temperatures. That quantitative conversion is eventually obtained, when acetyl components are in excess of benzoyl, can be shown kinetically.

If benzoyl chloride is added to acetic acid, the mixture brought to 40°, and β-naphthol immediately added, the observed acylation kinetics are autocatalytic in form. This is expected for two consecutive reactions, $\mathrm{BzCl} \longrightarrow \mathrm{AcCl} \longrightarrow$ Product, whose rate constants are not too different.[23] The autocatalytic behaviour would probably be capable of analysis, but this was not attempted here. Instead the reaction mixtures were set aside at 40° for 24 hr. before addition of naphthol. When this was done, excellent first-order plots were obtained. No change in rate resulted from leaving the mixtures for 48 hr. The observed rate constants (Table 6) were in reasonably good agreement with those obtained with acetyl chloride in acetic acid, if it was assumed that conversion of benzoyl into acetyl chloride was quantitative. The concomitant formation of ~0·2M-benzoic acid appears to have a rather small decelerative effect.

TABLE 6. *Acetylation of β-naphthol by benzoyl chloride and butyryl chloride in acetic acid at* 40°.

Initial [β-Naphthol] ~0·01M. $[H_2O] = 0{\cdot}02$M.

k_1 = First-order rate constant (in min.$^{-1}$).

(a) *Butyryl components as reagents.*

$[\mathrm{Pr{\cdot}COCl}]_s$	$[\mathrm{HCl}]_s$	10^3k_1	$[\mathrm{Pr{\cdot}CO_2O}]_s$	[HCl]	10^3k_1
0·18	0·02	12·8	0·18	0·20	12·6

(b) *Benzoyl components as reagents.*

$[\mathrm{BzCl}]_s$	$[\mathrm{HCl}]_s$	10^3k_1	$[\mathrm{Bz_2O}]_s$	[HCl]	10^3k_1
0·18	0·02	11·7	0·18	0·20	11·7
0·33	0·02	20·8			

(c) *Acetyl components as reagents.*

$[\mathrm{AcCl}]_s$	$[\mathrm{HCl}]_s$	10^3k_1
0·18	0·02	12·8

(2) *Experiments with butyryl chloride in acetic acid.* It appears from the foregoing that if butyryl chloride is used as acylating agent in acetic acid solvent and the mixture left for an appropriate time before the addition of the compound to be acylated, the acetate and not the butyrate will be formed. This was shown preparatively. It was also shown kinetically, in a way similar to that used for benzoyl chloride above, the mixture being left for 30 min. at 40°. The rate (Table 6) was identical with that appropriate for the equivalent amount of acetyl chloride. The reaction between butyryl chloride and acetic acid at 40° must thus be fairly fast, as the corresponding reaction for acetyl chloride has already been shown to be. In comparison, the benzoyl chloride reaction is measurably slow.

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[23] *E.g.*, Frost and Pearson, " Kinetics and Mechanism," John Wiley and Sons, Inc., 1953.

It is clear that Brown's method for preparation of volatile acyl halides from the parent acid and benzoyl chloride, might form the basis of a fairly general one-step method of acylation. Volatility is of no consequence, as the halide has not to be isolated, and a better source of halide would be the more reactive, and equally accessible, acetyl chloride. Solid acids could be dissolved in a suitable solvent.

(e) *Acylation in the System* Ac_2O–HBr–AcOH.—The rates in this system are much faster than in the corresponding one with hydrogen chloride, and no measurements were possible with bromide in excess of anhydride. Otherwise the experimental pattern was similar. Results on the reactions with water and β-naphthol are collected in Tables 7 and 8 respectively. The main points are the following:

TABLE 7. *Acylation of water by acetyl bromide in acetic acid at* 40°.

Initial $[H_2O]$ ~0·10—0·05M.

k_1 = First-order rate constant (in min.$^{-1}$).

$[Ac_2O]$	1·05	1·05	1·05	0·52
$10^3[AcBr]$	0·126	0·378	1·01	0·378
10^3k_1 *	5·52	17·2	46·0	16·8

* Corrected for rate of uncatalysed reaction (see Table 3).

TABLE 8. *Acylation of* β-*naphthol by* Ac_2O–HBr–AcBr *in acetic acid at* 40°.

Initial [β-Naphthol] ~0·01M. $[H_2O]$ = 0·018M.

k_1 = First-order rate constant (in min.$^{-1}$).

$[Ac_2O]_s$	[HBr]	10^3k_1	$[Ac_2O]_s$	[HBr]	10^3k_1	$[Ac_2O]_s$	[AcBr]	10^3k_1
0·18	0·051	53·1	0·18	0·013	13·4	0·13	0·051	53·1
0·18	0·026	27·6	0·10	0·051	49·0	0·35	0·026	26·8
0·38	0·026	27·9	0·38	0·051	53·0			

(1) The mechanism proposed for the hydrogen chloride catalysis is again required:

$$Ac_2O + HBr \longrightarrow AcBr + AcOH \quad \text{Fast}$$
$$AcBr + ROH \rightleftharpoons ROAc + HBr \quad \text{Slow}$$

With anhydride in excess of the catalyst, variation of the anhydride concentration affects the rate negligibly. The acetyl bromide must be formed effectively quantitatively.

(2) The second-order constant k_2 for acylation of β-naphthol by acetyl bromide in acetic acid is 1040×10^{-3} l. mole^{-1} min.$^{-1}$ in comparison with $69·8 \times 10^{-3}$ for acetyl chloride. The difference is in agreement with previous work on this sort of reaction [24,25] and is due to the greater polarity of the C–Br bond, which facilitates nucleophilic attack on the carbon.

(3) For acylation of water $k_2 = 46$ l. mole^{-1} min.$^{-1}$ compared with 1·7 for acetyl chloride. (There were no kinetic complications due to the protonation of water by hydrogen bromide.)

(f) *Acylation in the System* Ac_2O–HF–AcOH.—This system proved complicated. Infrared studies showed that solutions of hydrogen fluoride in acetic acid, made up from aqueous hydrogen fluoride and acetic anhydride, contained appreciable quantities of acetyl fluoride. It is not clear whether this was due to the inadequacy of the Karl Fischer method in these systems (leading to the addition of excess of anhydride). Water titres do fall to very close to zero in the presence of excess either of anhydride and catalyst or of acetyl fluoride. Catalyst solutions made by bubbling the gas into acetic acid gave no evidence of acetyl fluoride. These were used in the experiments described below.

Acetyl fluoride in acetic acid (after 1 hr.) gives no evidence of anhydride formation, and solutions of the anhydride and excess of hydrogen fluoride gave infrared spectra characteristic of acetyl fluoride, though with evidence for a little residual anhydride.

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[24] *E.g.*, Archer, Hudson, and Wardill, *J.*, 1953, 888.

[25] Bevan and Hudson, *J.*, 1953, 2187.

Fairly quantitative formation of acetyl fluoride must occur. Colson [20] has prepared this substance from the anhydride and gaseous hydrogen fluoride.

At 40°, acetyl fluoride in acetic acid attacks β-naphthol very slowly ($k_2 < 0{\cdot}01 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$), the reaction being autocatalytic. However, equivalent amounts (M) of anhydride and hydrogen fluoride react at a considerable speed, as does a similar solution containing a deficit of catalyst. This is very difficult to understand if the formation of acetyl fluoride is really quantitative. The rates (calculated from good first-order plots) are nearly as fast as at comparable concentrations of acetyl chloride.

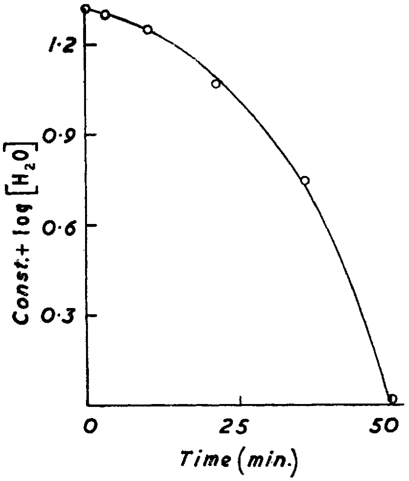

FIG. 4. *Acetylation of water by acetic anhydride catalysed by perchloric acid.*

Initial $[H_2O] \simeq 0{\cdot}25$M. $[Ac_2O] = 1{\cdot}05$M. $[HClO_4] = 1{\cdot}8 \times 10^{-4}$M.

Runs with acetyl fluoride and added hydrogen fluoride revealed catalysis by the added acid, as might have been expected from Bevan and Hudson's work.[25] Following Bernstein, Chapman, and others,[26] Bevan and Hudson showed that, in partially aqueous media, the hydrolysis of benzoyl fluoride is catalysed by hydrochloric acid and suggested a mechanism in which a hydronium ion assists the departing fluorine by hydrogen-bond formation (fluorine has greater hydrogen-bonding tendency than the other halide). The strongest known hydrogen bond with fluorine is that in the HF_2^- ion. The species HF might, therefore, be expected to catalyse powerfully the heterolysis of a carbon–fluorine bond. Higher molecular aggregates would not be expected to be so effective. The molecular state of hydrogen fluoride in acetic acid is not known, though it very probably undergoes aggregation of some kind, especially at high concentrations, as it is thought to do in the pure liquid and in water.[27] These considerations are consistent with the powerful catalysis, noted above, and the observation that, in the range above *ca.* 0·2M, increase in the hydrogen fluoride concentration decreases the reaction rate. The autocatalytic reaction of acetyl fluoride alone with β-naphthol is understandable. Perhaps the reaction in the presence of anhydride and deficit of catalyst is to be explained by the continued existence of a small quantity of the latter.

These qualitative conclusions will be made more precise when further work with this complex system is complete. The ability of anhydrous hydrogen fluoride to act as a Friedel–Crafts catalyst in acylation by anhydrides may be related to the phenomena discussed above.[28]

(g) *Acylation in the System* Ac_2O–$HClO_4$–AcOH.—(1) Acylation of water gave accelerative plots (Fig. 4). Perchloric acid is a strong acid and its concentration was much less

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[26] Miller and Bernstein, *J. Amer. Chem. Soc.*, 1948, **70**, 3602; Chapman and Levy, *J.*, 1952, 1677.
[27] Bell and McCoubrey, *Proc. Roy. Soc.*, 1946, *A*, **234**, 192.
[28] Gore, *Chem. Rev.*, 1955, **55**, 229.

than the water concentration throughout most of the reaction, so that it is largely ionised, to form $H_3O^+ClO_4^-$ (which is little dissociated in acetic acid):[29]

$$H_2O + HClO_4 \rightleftharpoons H_3O^+ClO_4^- \qquad K_{HClO_4}$$

As the free water is removed the amount of free perchloric acid * will increase. Since it is this species which is important for catalysis (see below), this accounts for the acceleration (see discussion on p. 1760). Calculation of K_{HClO_4} made by drawing tangents at different points on the curve in Fig. 4 gives a value in reasonable agreement with those given by Smith and Elliott[19] and by Kolthoff and Bruckenstein.[29]

Curved plots were avoided for the β-naphthol runs by leaving the reaction mixtures till the water was destroyed, before the naphthol was added; naphthol does not appear to pick up protons itself in the concentration range used (see below).

(2) The rate of acylation of β-naphthol was alway of the first order in β-naphthol. The results in Table 9 indicate that the rate is also probably of first order in both perchloric acid and acetic anhydride, if a small salt effect is assumed to operate, even at the low values here employed, when the perchloric concentration is changed. This is reasonable in view of the extensive ionisation probable for perchloric acid in acetic acid.[29] The above observations are consistent with two different mechanisms:

TABLE 9. *Acylation of β-naphthol by acetic anhydride in acetic acid catalysed by perchloric acid at 25°.*

Initial [β-Naphthol] ≈0·01M. $[H_2O]$ = 0·014M.

k_1 = First-order rate constant (in min.$^{-1}$).

$[Ac_2O]_s$	0·24	0·24	0·24	0·24	0·12	0·44
$10^4[HClO_4]$	11·0	5·50	2·80	1·1	1·1	1·1
10^3k_1	57·6	26·5	12·8	4·26	2·02	8·04

$$\begin{array}{llll} \text{(i)} & Ac_2O + HClO_4 & \rightleftharpoons Ac_2OH^+ClO_4^- & \text{Fast} \\ & Ac_2OH^+ClO_4^- + ROH & \longrightarrow ROAc + AcOH + HClO_4 & \text{Slow, } k \\ \text{(ii)} & Ac_2O + HClO_4 & \rightleftharpoons AcClO_4 + AcOH & \text{Fast} \\ & AcClO_4 + ROH & \longrightarrow ROAc + HClO_4 & \text{Slow, } k \end{array}$$

$Ac_2OH^+ClO_4^-$ and $AcClO_4$ being present only in low concentration.

(3) Runs with acetyl perchlorate showed that, with a reasonable extrapolation, the same rates were observed as with mixtures of anhydride and acid catalyst (Table 10).

TABLE 10. *Acylation of β-naphthol by acetic anhydride in acetic acid catalysed by acetyl perchlorate at 25°.*

Initial [β-Naphthol] ≈0·01M. $[H_2O]$ = 0·014M.

k_1 = First-order rate constant (in min.$^{-1}$).

$[Ac_2O]_s$	$10^4[AcClO_4]$	$10^4[HClO_4]$	10^3k_1	T *
0·24	4·4	1·1	18·2	50
0·24	4·4	1·1	20·2	40
0·24	4·4	1·1	22·3	30
0·24	4·4	1·1	23·8	20
0·24	4·4	1·1	26·3 †	0

* Period (in min.) elapsing between formation of acetyl perchlorate and its addition to reaction mixture. † Extrapolated value (cf. Table 9).

Thus acetyl perchlorate can be rapidly converted into perchloric acid in the reaction mixtures, either by reaction with the solvent or with naphthol.

(4) Some ionisation data are given in Table 11, together with the experimental second-order constants (k_2) obtained at the same acidities and solvent composition. If the correct mechanism is (i) above, then log k_2 might be expected to be correlated linearly with

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* The " free " perchloric acid probably exists largely as the ion pair $AcOH_2^+ClO_4^-$, but is written as $HClO_4$ in the equations for simplicity.

[29] Kolthoff and Bruckenstein, *J. Amer. Chem. Soc.*, 1956, **78**, 1; 1957, **79**, 1, 5915.

TABLE 11. *Ionisation of the Brønsted base* NN-*dimethyl*-2,4-*dinitroaniline* (B) *in* Ac_2O–$HClO_4$–AcOH *at* 25°.

I = [BH]/[B]. k_2 = Second-order rate constant (in l. mole^{-1} min.$^{-1}$) for acylation of β-naphthol.

10^5[B]	$[Ac_2O]_s$	$10^4[HClO_4]$	log I	log k_2 + Const.
1·0	0·24	1·1	−1·07	2·21
2·0	0·24	2·8	−0·30	1·73
2·0	0·24	5·5	0·10	1·42
4·0	0·24	11·0	0·39	1·08

log I ($I = [BH^+ClO_4^-]/[B]$ where B is a Brønsted base indicator) for the following reasons.

The experimental velocity, at a given acid concentration, is given by:

$$v = k_2[Ac_2O]_{\text{stoich}}[ROH] = k_2[A]_{\text{stoich}}[ROH]$$

where A represents anhydride. In the following AH^+ will represent $Ac_2OH^+ClO_4^-$ and BH^+ will represent $BH^+ClO_4^-$. Square brackets denote concentration, and parentheses activity. The velocity according to mechanism (i) is given by:

$$v = k[AH^+][ROH]f_{AH}f_{ROH}/f_x$$

where f_x is the activity coefficient for the transition state. Hence

$$k_2 = k[AH^+]f_{AH}f_{ROH}/[A]_{\text{stoich}}\,f_x$$

since $$K_{AH^+} = [AH^+]f_{AH^+}/[A](HClO_4)f_A = [AH^+]f_{AH}/[A]_{\text{stoich}}(HClO_4)f_A$$

when the ionisation is small, and

$$K_{BH^+} = [BH^+]f_{BH^+}/[B](HClO_4)f_B$$

hence $$k_2 = k\,\frac{[BH^+]}{[B]}\,\frac{f_{AH^+}f_{ROH}}{f_x}\cdot\frac{K_{AH^+}\,f_Af_{BH^+}}{K_{BH^+}\,f_Bf_{AH^+}}$$

If it is assumed that the two activity-coefficient ratios remain constant with alteration in medium, which is reasonable in view of their symmetry [30] then:

$$\log k_2 = \text{Const.} + \log[BH^+]/[B] = \text{Const.} + \log I$$

Table 12 shows that there is no linear relation between log k_2 and log I. Mechanism (ii), involving acetyl perchlorate as the intermediate, therefore seems more likely to be dominant, though the case cannot be argued more strongly. If the conclusions of Mackenzie and Winter [4] and of Burton and Praill [5] are correct, participation of $Ac_2OH^+ClO_4^-$ would have been expected to be prominent.

TABLE 12. *Collected second-order rate constants* (k_2, *in l. mole*$^{-1}$ *min.*$^{-1}$) *for acylation of water and* β-*naphthol in acetic acid* (*or butyric acid*) *at* 40°.

Acylation of water.	k_2	*Acylation of β-naphthol.*	k_2
Ac_2O	0·00247	AcF	<0·00001
AcCl	1·70	AcCl	0·0698
AcBr	46·0	AcBr	1·040
Pr·COCl (in $Pr{\cdot}CO_2H$)	0·162	Pr·COCl (in $Pr{\cdot}CO_2H$)	0·00886

Apart from their work the only other relevant study appears to be Yvernault's.[3d] As in his experiments with hydrogen chloride this author acylated water. In spite of the complexities involved for this substance, noted above, he deduced a mechanism identical with that proposed here on the basis of the acylation of β-nahthol. In doing this he used an argument, intended to be similar to ours and based on indicator measurements, but it is not convincing (*a*) because he expected a correlation between I and reaction velocity (rather than rate constant) and (*b*) because his indicator concentration was only about one-quarter of his acid concentration.

[30] Bethell and Gold, *J.*, 1958, 1905, 1930.

Yvernault's kinetic conclusions, so far as they are comparable, are in agreement with the present study.

(h) *Acylation Catalysed by* HNO_3 *and* H_2SO_4.—These two, seemingly obvious, catalysts were not used in the present work because both suffer from special complications. (1) Acetic anhydride and nitric acid very probably form acetyl nitrate, but systems containing these components also form nitrogen pentoxide, which acts as a nitrating agent.[31] In systems capable of nitration (*e.g.*, β-naphthol), this reaction has always been observed to occur in preference to acetylation.[32] Acetylation of water by acetyl nitrate, though perhaps a profitable study, was not attempted here. Savill and Lees [33] have shown that acetyl nitrite is solvolysed, without complication, in aqueous acetone. (2) Sulphuric acid and acetic anhydride in acetic acid probably form first acetyl sulphate which slowly rearranges to sulphoacetic acid.[34] This will complicate acylation. Further study of this system is planned.

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[31] *E.g.*, Gold, Hughes, and Ingold, *J.*, 1950, 2467.
[32] Burton and Praill, *J.*, 1955, 729; Bonner, *J.*, 1959, 3908.
[33] Savill and Lees, *J.*, 1958, 2262.
[34] Murray and Kenyon, *J. Amer. Chem. Soc.*, 1940, **62**, 1230