1065. *Acylation. Part II.* Friedel–Crafts Acylation, with Stannic Chloride as Catalyst, in Solvents of Low Dielectric Constant.*

By D. P. N. Satchell.

At 25°, in carbon tetrachloride, with stannic chloride as catalyst, β-naphthol, *p*-methoxyphenol, and *m*-nitrophenol are acylated by both aromatic and aliphatic acid chlorides at the hydroxylic oxygen atom to give esters, rather than in the ring to give ketones. In ethylene dichloride some nuclear attack may occur, though the predominant product remains the ester.

Kinetic experiments with either carbon tetrachloride or ethylene dichloride as solvent show an order of unity for the phenol, one of close to unity for stannic chloride, and an order variable from unity to *ca.* 1·7 for the acid chloride, whether aliphatic or aromatic. The products do not appreciably retard the reaction.

The effect of changes in dielectric constant and in solvent structure have also been examined. Co-ordinating additives either increase or decrease the reaction rate according to their concentration.

The essential differences from the behaviour with aluminium chloride as catalyst are discussed, and the likely mechanisms for catalysis by stannic chloride and aluminium chloride are compared. It is shown that, with stannic chloride, intermediate complexes containing two mol. of acid chloride are involved as well as those containing only one. With stannic chloride, acetyl chloride is a more reactive acylating agent than benzoyl chloride, and within both the aliphatic and aromatic series electron-repelling substituents in the acid halide facilitate reaction, and electron-withdrawing substituents retard it. Similar effects are not necessarily to be expected for catalysis by aluminium chloride.

There has been little advance in the understanding of Friedel–Crafts acylation by acid chlorides since the first quarter of the century. By then it was realised [1] (*a*) that alkylated benzenes were attacked more readily than benzene itself, *i.e.*, that the reaction involved what is now termed an electrophilic substitution, (*b*) that complexes of some kind between the catalyst and acylating agent were involved, and (*c*) that reaction was often retarded by complex formation between the catalyst and the products. The two main advances since that time might be considered to be (1) the explicit realisation [2] that the reaction is really diverse in its manifestations and that no single mechanism is likely to embrace them all, and (2) a kinetic study of, among other things, the effects of different catalysts, which clearly illustrates this very point. In this study [3] the catalytic effects of different Lewis acids were revealed as subtly related to their co-ordinating powers.

In view of the specificity of the mechanistic detail to particular sets of reagents there are inevitably several aspects of the reaction which remain largely unclarified. These are: (i) The effect on reactivity of changing the halide in the acyl halide along the series F, Cl, Br, I. (The generality of the Calloway series [4] is now in doubt.[5] To mention one point only, it seems obvious that the stereochemical requirements of the particular catalyst will influence the order.) (ii) The nature of the active complex between acylating agent and catalyst. (It seems clear that both oxonium and acyl cation complexes will be formed in many cases. Whether or not the oxonium species can lead to significant acylation is

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* *J.*, 1960, 1752, is considered as Part I.

[1] Steele, *J.*, 1903, **83**, 1470; Perrier, *Ber.*, 1900, **33**, 815; Boeseken, *Rec. Trav. chim.*, 1901, **20**, 102; Meerwien, *Annalen*, 1927, **455**, 227; Olivier, *Rec. Trav. chim.*, 1914, **33**, 244.

[2] Burton and Praill, *Chem. and Ind.*, 1954, 90.

[3] Jensen and Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 2291, 3039; see also Ahmad, Baddeley, and Topping, *Chem. and Ind.*, 1958, 1327.

[4] Calloway, *J. Amer. Chem. Soc.*, 1937, **59**, 1474.

[5] Yamase and Goto, *J. Chem. Soc. Japan*, 1960, **81**, 1906.

not definitely decided.[3,6]) (iii) The effect on reactivity of changes in structure in the acyl group. (The few available data[6,7] do not permit any decision.) (iv) The effect of changes of solvent. (Complex effects are observed[8] and this topic promises to be most involved.) (v) The effect of a change in catalyst.

Jensen and Brown's systematic kinetic work[3] is an important start on the last subject, and indeed kinetic studies provide the main hope of resolving all the above problems. So far, however, such studies have been few, and recent papers by Brown and his colleagues[9] essentially confirm and considerably augment previous kinetic investigations. The earlier work[10] was largely concerned with catalysis by aluminium chloride in solvents of low polarity. Brown and his colleagues have also examined catalysis by aluminium chloride in nitrobenzene[8a] and catalysis by various Lewis acids[3] in benzoyl chloride as solvent-reactant. As noted, significant differences were observed for the different types of system. These are discussed below in so far as they relate to the results of the present study which concerns catalysis by stannic chloride in solvents of low polarity. The effect on the reaction of structural changes in the acid halide has been examined.

The reactions to be described are somewhat unusual in that, while previous kinetic investigations all involved the nuclear acylation of an aromatic compound to give a ketone, the present work involves acylation of phenolic compounds under conditions where acylation of the hydroxyl group predominates over ketone formation.

EXPERIMENTAL

Materials.—" AnalaR " carbon tetrachloride was refluxed over phosphorus pentoxide, and reagent-grade ethylene dichloride over calcium hydride for several hours, before fractional distillation; they had b. p. 76° and 83·4°, respectively. Dry acetic acid was prepared as previously described.[11] Ether was refluxed over sodium and then fractionally distilled (b. p. 34—35°). Stannic chloride and titanic chloride were purified by a method described previously.[12] Germanium tetrachloride (Johnson Matthey) was used without purification. Acetyl, propionyl, and n-butyryl chloride were refluxed over isoquinoline (to remove free acid), then fractionally distilled; they had b. p. 51°, 79°, and 102—103° respectively. Samples of acetyl chloride purified by use of dimethylaniline rather than isoquinoline gave essentially identical kinetics. Chloroacetyl chloride was fractionated and a sample of b. p. 105° collected. Benzoyl and *p*-toluoyl chloride were also fractionally distilled; they had b. p. 197° and 220°, respectively. β-Naphthol, *m*-nitrophenol, and *p*-methoxyphenol were recrystallised samples of m. p. 122°, 97°, and 56°, respectively. Standard samples of β-naphthyl acetate, propionate, butyrate, and benzoate, *m*-nitrophenyl acetate, and *p*-methoxyphenyl acetate, prepared by Vogel's method,[13] had m. p. 69°, m. p. 51°, b. p. 122°/0·5 mm., m. p. 106°, 53°, and 31° respectively.

Reaction Mixtures.—Contamination of reagents and reaction mixtures by atmospheric moisture was kept at a low level. The dried reagents (see above) were stored in a dry box, where the reaction mixtures were also made up. This procedure especially facilitates the handling of stannic and titanic chloride.

The reaction mixtures were made up in 10 (or 25) ml. volumetric flasks with ground-glass stoppers. When β-naphthol and *p*-methoxyphenol were being acylated these compounds were added as solids: they dissolved in the solvents involved fairly rapidly. *m*-Nitrophenol dissolves rather slowly and was therefore added as a solution in the appropriate solvent. All other components were also added as measured volumes, sometimes (*e.g.*, for stannic chloride) as volumes of stock solutions in the appropriate solvent.

Kinetic Arrangements.—The stoppered reaction flasks were removed from the dry box and

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[6] (*a*) Jensen, Marino, and Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3303; (*b*) Brown, Marino, and Stock, *ibid.*, p. 3310; (*c*) Jensen, *ibid.*, 1957, **89**, 1226.

[7] Cullinane, Chard, and Leyston, *J.*, 1952, 376; Man and Hauser, *J. Org. Chem.*, 1952, **17**, 397.

[8] (*a*) Brown and Young, *J. Org. Chem.*, 1957, **22**, 719; (*b*) Gore, *Chem. Rev.*, 1955, **55**, 229.

[9] Refs. 3, 6, and 8, and associated papers.

[10] Ref. 6(*a*) contains a summary of previous work.

[11] Satchell, *J.*, 1956, 3911.

[12] Satchell, *J.* 1960, 4388.

[13] Vogel, " Practical Organic Chemistry," Longmans, Green and Co., London, 1948.

additionally sealed with Apiezon Q compound to help exclude atmospheric moisture. They were then kept at 25° by partial immersion in a thermostat bath. At intervals 1 (or 2) ml. samples were quickly withdrawn and run into sufficient glacial acetic acid effectively to stop the reaction. The resulting solution was made up to 25 ml. The extent of acylation was followed by measurements of the intensity of the light absorption at 3300 Å (3000 Å for *p*-methoxyphenol) where absorption due to the unacylated phenol predominates.[14] (For *m*-nitrophenol allowance was made for the small but significant absorption of the ester produced.) There was no interference from the other reaction components. Spectral measurements were made with a Unicam S.P. 500 spectrophotometer.

The concentration of phenol in the reaction mixtures was usually *ca.* 5×10^{-3}M though for some experiments it was reduced to *ca.* $2{\cdot}5 \times 10^{-3}$M. The acid chloride was kept in at least *ca.* 10-fold excess over the phenol, a procedure which helped to simplify the kinetic behaviour. Except for acylation in ethylene dichloride (see below) good first-order plots for the loss of phenol were obtained. Reproducibility with different samples of reagents and on different occasions was satisfactory.

Stoicheiometry of Reactions.—Indepedent preparative-scale experiments were conducted for most of the reactions studied kinetically. These preparations were carried out at concentrations and temperatures similar to those obtaining in the kinetic experiments.

RESULTS AND DISCUSSION

Reaction Products: *Oxygen* versus *Nuclear Acylation.*—Phenolic compounds may be acylated at the hydroxyl group or at an aromatic carbon atom, or both. Previous evidence,[15] which chiefly concerns catalysis by aluminium chloride, indicates the effect of the solvent. Use of solvents of high polarity, such as nitrobenzene, usually results in nuclear acylation only, probably because the phenolic oxygen atom is largely engaged by the catalyst and so protected. With solvents of low dielectric constant we may presume that engagement is less complete and that reaction can result in a mixture in which the ester may even predominate. This appears the case, for example, for the reactions of phenol with dichloroacetyl chloride in carbon disulphide, and of *p*-chlorophenol with benzoyl and *p*-toluoyl chloride, when the solvent is *s*-tetrachloroethane.[16]

Preferential formation of the ester—the easier reaction when possible, because the free hydroxyl group will be much more readily acylated than a ring position—is likely to be the more pronounced the lower the activity of the catalyst. For instance, in the same solvent, stannic chloride seems likely to impede esterification less than aluminium chloride.

The present work involved the use of stannic chloride in carbon tetrachloride and ethylene dichloride in the acylation of β-naphthol, *p*-methoxyphenol, and *m*-nitrophenol by both aliphatic and aromatic acid chlorides. From the considerations noted above we expected that the primary products would in all cases be largely the result of attack on oxygen, and that by proper choice of conditions it would be possible to eliminate, or render negligible, any subsequent nuclear acylation. Independent preparative-scale reactions were conducted for most of the phenol–acyl halide combinations studied kinetically, conditions similar to those found useful for the rate measurements being used. With carbon tetrachloride as solvent these preparations provided products in >87% yield in all cases. The m. p.s and infrared spectra of the products showed them to be essentially uncontaminated samples of the expected esters. These results show that at most only very small amounts of nuclear acylation could have taken place under the kinetic conditions in carbon tetrachloride, and that the reaction is probably essentially quantitative. Similar conclusions are drawn from the light-absorption measurements, for the absorption always eventually fell to that characteristic of the *O*-acylated product. For carbon tetrachloride, therefore, our expectations were realised.

In ethylene dichloride, which has a dielectric constant of 10·36 compared with 2·3 for

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

[15] Thomas, " Anhydrous Aluminium Chloride," Reinhold Publ. Corp., New York, 1941.

[16] Hayashi, *J. prakt. Chem.*, 1929, **123**, 289; Kunckell and Johannssen, *Ber.*, 1898, **31**, 169.

carbon tetrachloride, some complications were found. With β-naphthol, which was the phenol most extensively studied in carbon tetrachloride, solutions in ethylene dichloride containing also stannic chloride and acetyl chloride quickly became yellow-orange and darkened further with time. The yellow colour is discharged when a sample is run into glacial acetic acid, so that the loss of the hydroxyl band at 3300 Å may still be followed. When this is done the simple first-order behaviour found in carbon tetrachloride is not observed.

When *m*-nitrophenol—a compound likely to be less susceptible to nuclear electrophilic attack—was used rather than β-naphthol, the reaction mixtures were initially colourless, became pale yellow only after about a reaction half-life, and thereafter darkened quite slowly. Light absorption at 3300 Å again indicated slight deviation from simple first-order behaviour, and the optical densities at infinite time were somewhat greater than those expected on the assumption that *m*-nitrophenyl acetate was the only product. A preparative-scale reaction (during which any free phenols, and perhaps some of any esters present, would probably have been lost during the working-up) gave a $>70\%$ yield of *m*-nitrophenyl acetate of good m. p. (after one recrystallisation). This is clearly the main product. The deviation of the rate data from first-order behaviour begins to be significant only after $1\frac{1}{2}$—2 half-lives, so a limited amount of kinetic work with this system seemed worth while. Some nuclear acylation (or other side reaction) probably occurs in this solvent, the product of which affects the light absorption. Whatever the nature of this product (unless it is a phenol, which is unlikely) it is presumably formed in rather small amounts, for otherwise an appreciable effect on the m. p. would be probable.

Kinetics of the Reaction in Carbon Tetrachloride.—(i) *Acylation of* β-*naphthol by acetyl chloride catalysed by stannic chloride.* In the main set of runs the β-naphthol concentration was *ca.* 5×10^{-3}M. The acetyl chloride concentration was varied between 0·07M and 0·56M, and the stannic chloride concentration between $0{\cdot}35 \times 10^{-3}$ and $10{\cdot}5 \times 10^{-3}$M. In the absence of stannic chloride the reaction rate was negligibly slow. For any run in the presence of the catalyst the observed loss of β-naphthol was an accurately first-order process for several half-lives. The first-order constants are collected in Table 1.

TABLE 1.

Acylation of β-naphthol by acetyl chloride in carbon tetrachloride solution at 25°.

With an excess of acetyl chloride. Initial [β-naphthol] ≈ 5×10^{-3}M.

(*a*) Order in stannic chloride.

[AcCl]	0·14	0·14	0·14	0·14	0·14	0·14	0·14
$10^3[SnCl_4]$	0·35	0·70	1·05	1·75	2·10	4·20	10·5
10^3k (min.$^{-1}$)	1·77	3·29	4·76	7·69	9·20	17·3	38·4

(*b*) Order in acetyl chloride.

[AcCl]	0·07	0·14	0·28	0·42	0·56
$10^3[SnCl_4]$	0·70	0·70	0·70	0·70	0·70
10^3k (min.$^{-1}$)	1·19	3·29	8·65	16·90	27·6

With an excess of stannic chloride. Initial [β-naphthol] ≈ $2{\cdot}5 \times 10^{-3}$M.

[AcCl]	0·028	0·028	0·056
$10^2[SnCl_4]$	8·6	17·2	17·2
10^3k (min.$^{-1}$)	5·31	9·33	19·7

k = First-order constant. In all Tables square brackets represent molarity.

It will be seen that in the concentration ranges involved (*i.e.*, with acetyl chloride in excess of stannic chloride) the rate is of rather more than first-order in acetyl chloride and appears to increase with increasing acetyl chloride concentration (though without reaching second-order). On the other hand, the order in stannic chloride is slightly less than first (*ca.* 0·9). To test if these orders were maintained when the stannic chloride was in excess of the acetyl chloride (rather than the reverse) some experiments were carried out with *ca.* 2×10^{-3}M-naphthol (to achieve the necessary deficit compared with acetyl chloride).

The results are also in Table 1. Under such conditions the order in acetyl chloride falls too close to unity, while that in stannic chloride remains at about 0·9, perhaps falling slightly.

A number of conclusions may be drawn from these results.

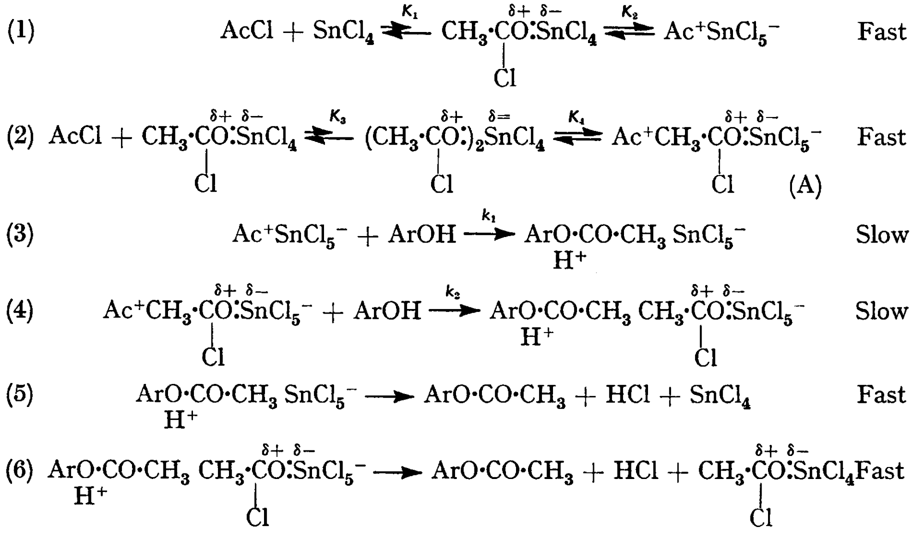
(*a*) The good first-order loss of naphthol indicates that the products (hydrogen chloride and ester) do not significantly disturb the reaction. At the naphthol concentrations used this compound will be essentially unassociated, and the good first-order behaviour also indicates that reaction is with the monomers rather than with any small concentration of associated forms.[17]

(*b*) The varying order for acetyl chloride, from close to unity when in low concentration to approaching 1·7 in the most concentrated solutions studied, could imply the existence of both unimolecular and bimolecular contributions to the reaction.

(*c*) The order of slightly less than unity for stannic chloride presumably implies an essentially unimolecular engagement in the reaction, together with some other small, and at present, inexplicable effect. [In ethylene dichloride (see below) the order is effectively unity.]

Additional information was provided by a spectral study of the addition of increasing amounts of stannic chloride to a solution of β-naphthol in carbon tetrachloride. In the concentration conditions obtaining in the kinetic experiments the Lewis acid had no detectable effect on the naphthol spectrum. Therefore there is presumably little complex formation between these components in the reaction mixtures.

A mechanism compatible with the above conclusions, and also with current views concerning the Friedel–Crafts acylation and the co-ordinating ability of tin, is as shown (1—6).



$$\text{(1)}\quad \mathrm{AcCl + SnCl_4} \underset{}{\overset{K_1}{\rightleftharpoons}} \mathrm{CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_4} \overset{K_2}{\rightleftharpoons} \mathrm{Ac^+SnCl_5^-} \qquad \text{Fast}$$

$$\text{(2)}\quad \mathrm{AcCl} + \mathrm{CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_4} \overset{K_3}{\rightleftharpoons} \mathrm{(CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta=}{\mathrm{O}}\mathrm{{:})_2SnCl_4} \overset{K_4}{\rightleftharpoons} \mathrm{Ac^+CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_5^-}\ \ (\mathrm{A}) \qquad \text{Fast}$$

$$\text{(3)}\quad \mathrm{Ac^+SnCl_5^- + ArOH} \xrightarrow{k_1} \underset{\mathrm{H^+}}{\mathrm{ArO}}\mathrm{{\cdot}CO{\cdot}CH_3\ SnCl_5^-} \qquad \text{Slow}$$

$$\text{(4)}\quad \mathrm{Ac^+CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_5^-} + \mathrm{ArOH} \xrightarrow{k_2} \mathrm{ArO{\cdot}CO{\cdot}}\underset{\mathrm{H^+}}{\mathrm{CH_3}}\ \mathrm{CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_5^-} \qquad \text{Slow}$$

$$\text{(5)}\quad \underset{\mathrm{H^+}}{\mathrm{ArO}}\mathrm{{\cdot}CO{\cdot}CH_3\ SnCl_5^-} \longrightarrow \mathrm{ArO{\cdot}CO{\cdot}CH_3 + HCl + SnCl_4} \qquad \text{Fast}$$

$$\text{(6)}\quad \underset{\mathrm{H^+}}{\mathrm{ArO}}\mathrm{{\cdot}CO{\cdot}CH_3\ CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_5^-} \longrightarrow \mathrm{ArO{\cdot}CO{\cdot}CH_3 + HCl + CH_3{\cdot}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{\delta+}{\mathrm{C}}}\overset{\delta-}{\mathrm{O}}\mathrm{{:}SnCl_4} \text{Fast}$$

The highly charged species $(Ac^+)_2SnCl_6^{=}$ has been omitted from the scheme but its inclusion makes no essential difference to the subsequent argument. Dissociation of the ion pairs is unlikely to be appreciable in carbon tetrachloride and in any case the observed kinetic orders, to be compatible with the predominant participation of free ions, would require processes (5) and/or (6) (hydrogen detachment) to be rate-determining.[3] This seems unlikely. Dissociation equilibria have therefore not been included in the reaction scheme.

Oxonium and acetylium complexes have been included,[3] for both will presumably always

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[17] Hudson and Stelzer, *Trans. Faraday Soc.*, 1958, **54**, 213.

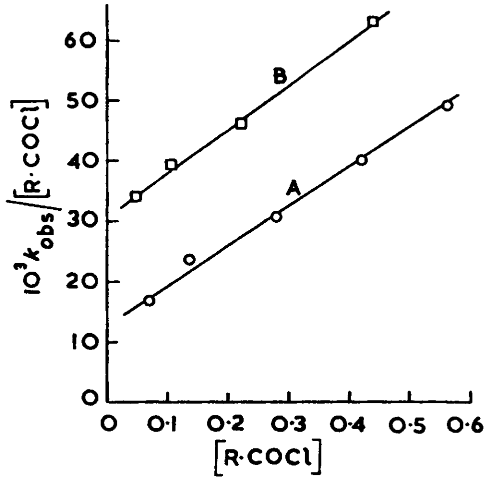
be formed to *some* extent, even though one may largely predominate.[6b] They are both postulated as intermediates of low concentration in the present system. In the mechanism written above, only the acetylium ions are responsible for acylation. However, the concentrations of these species are simply related to those of the corresponding oxonium version by an equilibrium constant, so that the circumstance whether or not both types acts as the acetylating agent,[3,6,18] while it will affect the value of the rate constant, does not affect the essential kinetic form predicted by the proposed mechanism. This is:

$$
\begin{aligned}
-\mathrm{d}[\mathrm{ArOH}]/\mathrm{d}t &= (k_1[\mathrm{Ac^+SnCl_5^-}] + k_2[\mathrm{A}])[\mathrm{ArOH}]\ * \\
&= (k_1K_1K_2[\mathrm{AcCl}][\mathrm{SnCl_4}] + k_2K_1K_3K_4[\mathrm{AcCl}]^2[\mathrm{SnCl_4}])[\mathrm{ArOH}] \\
&= K_1[\mathrm{AcCl}][\mathrm{SnCl_4}][\mathrm{ArOH}](k_1K_2 + k_2K_3K_4[\mathrm{AcCl}])
\end{aligned}
$$

or

$$k_{\mathrm{obs}} = K_1[\mathrm{AcCl}][\mathrm{SnCl_4}](a + b[\mathrm{AcCl}])$$

In these equations square brackets represent concentration, a and b are constants, and k_{obs} is the observed first-order rate constant. The mechanism predicts an increasing contribution to the rate from acetyl chloride as its concentration increases. At low concentrations, when b[AcCl] is small compared with a, the rate will be of the first-order in acetyl chloride; at higher concentrations the order will appear to increase, as found. The scheme may be tested by plotting k_{obs}/[AcCl] against [AcCl] at constant stannic chloride concentration: the Figure shows that a good straight line is obtained, as required. The data are perhaps somewhat limited, but the mechanism appears reasonable. The intermediate complexes are discussed more fully below.



Plot of k_{obs}/[R·COCl] against [R·COCl] for (A) acetyl and (B) propionyl chloride, with 0·70M-stannic chloride.

Kinetic results essentially similar to those found with acetyl chloride were obtained with propionyl chloride. They are given in Table 2. A graph of k_{obs}/[Et·COCl] against [Et·COCl] is also given in the Figure. A rectilinear plot is again obtained.

The explanation of the rising order in acetyl chloride in terms of a specific co-ordination effect, as given above, is more satisfactory than an explanation along the lines of a general solvation effect, which increases the amount of complex formation by stabilisation, though such a view is also tenable. Our preference is partly because of some results of Brown's and the effects of co-ordinating additives (both discussed below), and partly because the free stannic chloride would also be expected to participate in general solvation [12] and there is no evidence for this in the present systems.

* For A see reaction (2).

[18] Baddeley, *Quart. Rev.*, 1954, **8**, 355.

There are opportunities for various solvent effects in the above scheme. There will be the dielectric-constant effect on the equilibrium positions. The right-hand side will be favoured by increased polarity in the system. The rate-determining step, (3) and/or (4), which perhaps involves a slight dispersal of charge in the transition state (though this is not certain), will probably be rather less sensitive to increases in polarity. In practice (see below) a change to a medium of higher dielectric constant results in an appreciable increase in rate. The main influence seems likely to be on the equilibrium step. Some further effects of change in solvent composition are discussed below.

TABLE 2.

Acylation of β-naphthol by propionyl chloride in carbon tetrachloride solution at 25°.

With an excess of propionyl chloride. Initial [β-naphthol] ≈ 5 × 10^{-3}M.

[Et·COCl]	0·05	0·11	0·22	0·44	0·11
10^3[SnCl$_4$]	0·70	0·70	0·70	0·70	1·75
10^3k (min.$^{-1}$)	1·70	4·31	10·2	27·6	9·34

With an excess of stannic chloride. Initial [β-naphthol] ≈ 2·5 × 10^{-3}M.

[Et·COCl]	0·022	0·022	0·044
10^3[SnCl$_4$]	86·0	172	172
10^3k (min.$^{-1}$)	9·22	16·0	36·3

(ii) *Other Lewis acids as catalysts.* Attempts were made to use germanium tetrachloride and titanium tetrachloride as catalysts for the reaction, without success. The germanium compound proved too feeble a catalyst, and the titanium compound formed insoluble complexes with the acid halide.

(iii) *Effect of variation in structure of the phenol.* In an effort to obtain a more reactive compound than β-naphthol for use with germanium tetrachloride the behaviour of *p*-methoxyphenol was studied. This compound did prove somewhat, though not markedly, more reactive than β-naphthol. *m*-Nitrophenol was also studied, and proved *ca.* 20-fold less reactive than the *p*-methoxy-compound under the same conditions (see Table 3).

TABLE 3.

Comparison of reactivities of different phenols towards acylation by acetyl chloride in carbon tetrachloride, at 25°.

[SnCl$_4$] = 1·75 × 10^{-3}M; [AcCl] = 0·14M; initial [phenol] ≈ 5 × 10^{-3}M.

Phenol	β-$C_{10}H_7$·OH	*p*-MeO·C_6H_4·OH	*m*-NO_2·C_6H_4·OH
10^3k (min.$^{-1}$)	7·69	20·3	0·96

Since the slow step involves nucleophilic attack by the phenolic oxygen atom, a process which will be facilitated by electron accumulation on this atom, the rate factor is in the appropriate direction. Its comparatively small size perhaps confounds *a priori* expectations.

(iv) *Effect of variation in the structure of the acid chloride.* (1) Mechanism and a change from aliphatic to aromatic acid chloride. The results in Table 4 show that the kinetic pattern for acylation with benzoyl chloride has all the features found for acetyl chloride. We conclude that the mechanisms of acylation for these two compounds are basically the

TABLE 4.

Acylation of β-naphthol by benzoyl chloride in carbon tetrachloride solution at 25°.

Initial [β-naphthol] ≈ 5 × 10^{-3}M.

[BzCl]	0·43	0·43	0·43	0·22	0·086	0·086	0·043
10^2[SnCl$_4$]	0·86	2·58	8·60	2·58	17·2	8·60	17·2
10^3k (min.$^{-1}$)	3·97	10·6	30·0	3·90	4·90	2·65	2·46

same, and that minor structural modifications in either will not alter the general mechanistic outline.

(2) Effect of substituents. The following two series of acylating agents were studied. (*a*) Benzoyl and *p*-toluoyl chloride, and (*b*) chloroacetyl, acetyl, propionyl, and butyryl chloride. Comparative results are given in Table 5. For similar catalyst concentrations the order of reactivity is chloroacetyl < benzoyl < *p*-toluoyl < acetyl < propionyl < butyryl. Chloroacetyl chloride was, in fact, too unreactive to give measurable rates in the present work. The obvious conclusion from the above sequence is that, within the aliphatic and probably within the aromatic series, electron-repelling substituents enhance reactivity and electron-withdrawing substituents reduce it. There is the additional fact that benzoyl chloride is less reactive than acetyl chloride. Here the structural change involved is significantly different.

TABLE 5.

Comparison of reactivities of acid chlorides as acylating agents for β-naphthol in carbon tetrachloride solution.*

(*a*) $[\text{R·COCl}] = 0{\cdot}28\,\text{M}$; $[\text{SnCl}_4] = 0{\cdot}70 \times 10^{-3}\,\text{M}$.

Acid chloride	10^3k (min.$^{-1}$)
Acetyl	8·65
Propionyl	13·8
Butyryl	34·5
Chloroacetyl	V. slow

(*b*) $[\text{R·COCl}] = 0{\cdot}086\,\text{M}$; $[\text{SnCl}_4] = 8{\cdot}60 \times 10^{-2}\,\text{M}$.

Acid chloride	10^3k (min.$^{-1}$)
Acetyl	138
p-Toluoyl	21·6
Benzoyl	2·65

* Small interpolations between data have been made to obtain the comparisons in this Table, which are for equivalent molarities of acylating agent.

There are two main ways in which substituents may affect the reaction rate, namely, by altering the position of the equilibria producing the complex intermediates, and by affecting the rate of steps (3) and/or (4).

The effect that substituents within each structurally related series are likely to have on steps (3) and (4) seems clear. Increased electron repulsion will lower the charge density on the carbonyl-carbon atom of the acyl cation, and so will hinder nucleophilic attack by the phenol and reduce the rate. Electron withdrawal will have the opposite effect. (The argument holds whichever complex is the main acylating agent.)

As regards the equilibria, electron repulsion will facilitate complex formation, and the concomitant stabilisation of the positive pole produced will retard decomposition. Hence the equilibria will shift to the right for electron-repelling substituents, and the reaction rate will be increased.

In view of the observed reactivity sequences, it is plain that in the present systems the dominant effects of substitution in benzoyl or acetyl chloride must be on the position of the equilibria (1), rather than on the slow steps.

In comparing benzoyl chloride with acetyl chloride it is difficult to predict *a priori* whether benzoyl or acetyl chloride will have the greater tendency to form complexes with a catalyst. Recent work[19] on the infrared specta for their complexes with aluminium chloride indicates that in solvents of low polarity both halides give predominantly the oxonium complex. However, acetyl chloride shows the greater tendency to give some of the acylium complex that will doubtless be the more powerful acylating agent.

If similar trends in behaviour obtain with the weaker stannic chloride, then the circumstance that benzoyl is 50 times less reactive than acetyl chloride (Table 5) can arise from a variety of factors. (*A*) Even if the acylating complex is of the same type, and formed to the same extent, for both benzoyl and acetyl chloride the substitution of phenyl for methyl will reduce the charge on the carbonyl-carbon atom, by introducing conjugative relay. This will reduce the rate of step (3) or (4) for benzoylation. (*B*) The (small)

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[19] Cook, *Canad. J. Chem.*, 1959, **37**, 48; Cooke, Susz, and Herschmann, *Helv. Chim. Acta*, 1954, **37**, 1280; Susz and Wuhrmann, *ibid.*, 1957, **40**, 971.

amount of complex formation with stannic chloride may be greater for acetyl than for benzoyl chloride. (*C*) Acylation for the benzoyl compound might proceed largely *via* the oxonium complex, while an appreciable contribution from the acylium version might exist with acetyl chloride. As for the comparisons within the aromatic and the aliphatic series (see above), the resulting changes in the positions of the equilibria [effects (*B*) and (*C*)] are probably the dominant influence of the structural change. There exists a previous comparison of the reactivities of benzoyl and acetyl chlorides in a rather similar reaction:[6b] in ethylene dichloride as solvent, with aluminium chloride as catalyst, acetyl chloride is *ca.* 500 times more reactive in the acylation of toluene. However, detailed discussion of this comparison is deferred.

(v) *Kinetic consequences of changes in solvent composition.* (1) The addition of co-ordinating agents. At constant concentrations of acetyl chloride and stannic chloride,

TABLE 6.

Effect of added co-ordinating agents on the stannic chloride-catalysed rate of acylation of β-naphthol by acetyl chloride in carbon tetrachloride.

(*a*) Ethyl ether.

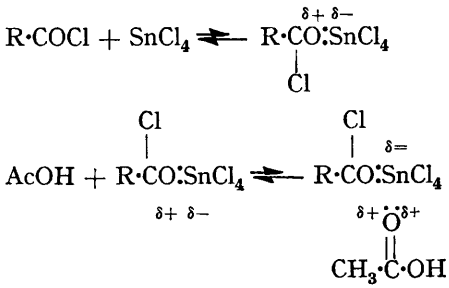
[AcCl]	10^3[SnCl$_4$]	[Et$_2$O]	10^3k (min.$^{-1}$)
0·14	1·75	0·00	7·69
0·14	1·75	0·048	11·1
0·14	1·75	0·19	17·3
0·14	1·75	0·48	15·0
0·14	1·75	0·96	10·5

(*b*) Acetic acid.

[AcCl]	10^3[SnCl$_4$]	[AcOH]	10^3k (min.$^{-1}$)
0·14	0·35	0·00	1·77
0·14	0·35	0·55	19·2
0·14	0·35	0·88	19·2
0·14	0·35	1·75	16·4
0·14	0·00	1·75	V. slow

the addition of increasing quantities of ethyl ether or of anhydrous acetic acid at first increases the reaction rate, but eventually reduces it. The concentration at which the rate is a maximum is approximately the same for ether and acetic acid, though the enhancement is more marked for the latter. Some experimental results are given in Table 6.

Since, even in the presence of additives, the rate without catalyst remains negligibly small, the rate enhancements are not to be explained as uncatalysed contributions. However, by bearing in mind the essentials of the proposed mechanism (p. 5408) and the well-established ability of stannic chloride to form complexes with oxygen-containing compounds, it seems possible to rationalise the observations. Stannic chloride forms particularly stable compounds with both ether[20] and acetic acid,[21] and their addition to the solvent therefore provides species which compete with the acetyl chloride for the catalyst. Eventually the additives will tend to monopolise the catalyst, and the rate will fall. Initially, however, they may increase the formation of an active complex by taking the part played by the second molecule of acid chloride in the doubly co-ordinated complexes. This process will increase the number of acylating complexes until such a



$$\mathrm{R{\cdot}COCl + SnCl_4 \rightleftharpoons \underset{\textstyle Cl}{\overset{\delta+\ \delta-}{R{\cdot}CO{:}SnCl_4}}}$$

$$\mathrm{AcOH + \underset{\delta+\ \delta-}{\overset{Cl}{R{\cdot}CO{:}SnCl_4}} \rightleftharpoons \underset{\overset{\delta+\,\ddot{O}\,\delta+}{\overset{\|}{CH_3{\cdot}C{\cdot}OH}}}{\overset{Cl\ \ \delta=}{R{\cdot}CO{:}SnCl_4}}}$$

time as the strongly co-ordinating additives seriously displace the acid chloride molecules from contact with the catalyst. The details of the effect will vary with the additive, the

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[20] See, *e.g.*, Bell and Skinner, *J.*, 1952, 2955.

[21] Satchell, *J.*, 1958, 3910, and references therein.

solvent, and other conditions. (This interpretation of the effect of co-ordinating agents is superficially at variance with Baddeley's.[18] This author sees additives as reducing the electrophilic character of any cations involved, by partial satisfaction of their electron demand, thus causing a fall in reaction rate. While a loss of electrophilicity is no doubt incurred, nevertheless it seems that in the present system the beneficial effect on the displacement of the complex-forming equilibria outweighs this loss. For systems where complex formation is quantitative the loss of electrophilicity must be a factor in the inhibition produced by additives, but we agree with Jensen and Brown [3] in thinking the most important effect, even then, to be competition for the catalyst.)

If a prominent effect of the additives is the extra co-ordination provided for the acetyl chloride complexes, as suggested above, and if the interpretation of the high and fractional orders in acetyl chloride is correct, then, with sufficient ether or acetic acid present, the order in acetyl chloride should be noticeably reduced, eventually falling to unity. This is the case. Results in Tables 7 and 8 indicate a less pronounced dependence on acetyl chloride concentration in the presence of 0·48M-ether, and an essentially first-order dependence in the presence of 1·75M-acetic acid. The latter compound has already been noted as producing the more marked effects. These results help to produce confidence in the overall mechanistic picture.

TABLE 7.

Order in acetyl chloride in presence of added ethyl ether.

[AcCl]	10^3[SnCl$_4$]	[Et$_2$O]	10^3k (min.$^{-1}$)	[AcCl]	10^3[SnCl$_4$]	[Et$_2$O]	10^3k (min.$^{-1}$)
0·035	1·75	0·48	2·88	0·14	1·75	0·48	15·0
0·07	1·75	0·48	6·17	0·28	1·75	0·48	36·1

TABLE 8.

Order in acetyl chloride in presence of added acetic acid.

[AcCl]	10^3[SnCl$_4$]	[AcOH]	10^3k (min.$^{-1}$)	[AcCl]	10^3[SnCl$_4$]	[AcOH]	10^3k (min.$^{-1}$)
0·07	0·35	1·75	8·13	0·28	0·35	1·75	34·4
0·14	0·35	1·75	16·4	0·56	0·35	1·75	76·7

(2) *Change in dielectric constant.* As previously argued, a general increase in polarity of the solvent, without necessarily an increase in specific co-ordinating ability, could affect the reaction rate in two ways. The equilibria forming the ionic complexes will be favoured, and this will tend to increase the rate. On the other hand, the effect on the rate-determining step is somewhat ambiguous, but, in any case, likely to be less important. In practice a change from carbon tetrachloride (dielectric constant ≈ 2·3) to ethylene dichloride (dielectric constant ≈ 10·4) increases the rate of reaction between *m*-nitrophenol and acetyl chloride *ca.* 20-fold.

TABLE 9.

Acylation of *m*-nitrophenol in ethylene dichloride solution catalysed by stannic chloride at 25°.

Initial [*m*-nitrophenol] ≈ 5 × 10^{-3}M.

(a) *Acylation by acetyl chloride.*

[AcCl]	10^3[SnCl$_4$]	10^3k (min.$^{-1}$)
0·07	0·88	3·56
0·14	0·88	9·86
0·28	0·88	25·6
0·14	1·76	20·3
0·14	2·64	28·8

(b) *Acylation by benzoyl chloride.*

[BzCl]	10^2[SnCl$_4$]	10^3k (min.$^{-1}$)
0·086	8·6	19·1

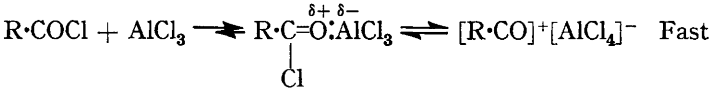
Because of the somewhat unsatisfactory nature of the reaction in ethylene dichloride (see above) rather little work was performed with this solvent. The results in Table 9 reveal, however, that the kinetic pattern must be very similar to that obtaining in carbon tetrachloride. It is interesting that the order in stannic chloride seems essentially unity in this medium. The order in acyl halide is still greater than unity in spite of the increase in polarity. This is presumably because the medium has not the *specific* solvating power of the acyl halide—indeed specific co-ordination effects could well be enhanced by the raised dielectric constant. In the concentration ranges studied, stannic chloride and *m*-nitrophenol did not appear to interact (as judged by measurements of ultraviolet absorption), so this possible complication was still absent.

In a single experiment, acetyl chloride proved *ca.* 25-fold more reactive than benzoyl chloride in this system. This value compares with a factor of about 50 obtained in carbon tetrachloride (though with a different phenol—β-naphthol).

Previous Mechanistic Conclusions and the Present Work.—Previous kinetic work on the acylation of aromatic compounds in solvents of low polarity has largely concerned aluminium chloride. This catalyst forms, even in ethylene dichloride, stable 1 : 1 complexes with, for example, benzoyl chloride and acetyl chloride,[6] in which the equilibrium position lies towards the complex side. Indeed it is common to pre-form the complex and add it as such. The ketone product also engages the catalyst, and so largely removes it from its useful sphere of influence. Thus reactions under such conditions[6] are usually of the first order in catalyst–acyl halide complex and of the first order in aromatic substrate. Reasonable excesses of acyl halide over catalyst have generally little effect on the reaction rate, the catalyst being already fully co-ordinated (the usual co-ordination number for aluminium is four). An excess of catalyst over acyl halide enhances the rate because it enables 1 : 2 complexes (*i.e.*, those containing the very active Al_2Cl_6 combination) to increase in number. The effect of changes in dielectric constant are not clear cut.[6a]

These results are in harmony with the traditional conception of the reaction; those now obtained with stannic chloride as catalyst do not fit it so well. This Lewis acid does not give quantitative formation of complexes with common acyl halides[3] nor, in the present case, does it form complexes appreciably with the products. The kinetics are therefore different from those with aluminium chloride. There will be free stannic chloride and free acyl halide at all relative concentrations of these substances, and the small extent of interaction between them involves complexes containing both one and two molecules of acyl halide. The reaction does not suffer the usual eventual marked reduction in rate owing to engagement of catalyst by products, though it might do so if the products were in great excess over the catalyst.

The effect of an increase in dielectric constant is to facilitate the reaction considerably. The essentials of the mechanism for aluminium chloride catalysis can be written as:



$$R\cdot COCl + AlCl_3 \longrightarrow R\cdot\underset{\substack{|\\ Cl}}{\overset{\delta+}{C}}{=}\overset{\delta-}{O}{:}AlCl_3 \rightleftharpoons [R\cdot CO]^+[AlCl_4]^- \quad \text{Fast}$$

$$[R\cdot CO]^+[AlCl_4]^- + ArH \longrightarrow \text{Products} \qquad \text{Slow}$$

where $R\cdot CO^+AlCl_4^-$ is probably present in greater amounts for acetyl than for benzoyl chloride[19] but where oxonium complex formation is probably essentially quantitative for both.[6] Quite how much acylium complex is likely to be present is not clear. If the oxonium complex is chiefly responsible for acylation in either the aliphatic or the aromatic series, then electron-repelling substituents should reduce the reaction rate owing to their reduction of the positive charge carried by the carbonyl carbon atom of the stoicheiometrically formed acylating agent. However, if the rate were increased, this would imply that the acylium complexes are playing a significant rôle, for their concentrations will be increased by such substituents. Brown's promised data on substituted benzoyl chlorides are therefore awaited with interest.[6a]

Finally, the above considerations of the differences of mechanistic detail make it clear that the relative reactivities of any two acyl halides may well be different when used with stannic chloride and when used with aluminium chloride. The only comparison available is that concerning benzoyl and acetyl chloride, which is particularly complicated from the interpretative viewpoint (see above). For stannic chloride we find a reactivity ratio of *ca.* 25; Brown and his collaborators [6b] found one of *ca.* 500 for aluminium chloride. Thus a notable difference in reactivity is indeed found for this case.

On the whole, available studies indicate that further progress in the understanding of the complexities of Friedel–Crafts acylation are now most likely to come from detailed work with individual catalysts, and that generalities embracing several catalysts are likely to prove invalid. From this viewpoint reviews dealing with the properties of particular Lewis acids are especially welcome.[22]

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, June 5th,* 1961.]

[22] Shiihara, Swartz, and Post, *Chem. Rev.*, **1961**, **61**, 1; Topchiev, Zavgorodnii, and Paushkin, "Boron Trifluoride and its Compounds as Catalysts in Organic Chemistry," Pergamon Press, London, 1959.