The Solvolysis of Acid Chlorides. A Presentation of the Problem and a Proposal for the Mechanism

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(Received August 28, 1963)

The nucleophilic substitution reactions of derivatives of carboxylic acids, especially the hydrolysis of esters, have been studied very thoroughly, and the mechanism is well understood.[1] However, the investigations of the kinetics of the hydrolysis and alcoholysis of acid chlorides have not led to completely concordant conclusions, and a reasonable explanation for all the data available seems to be lacking. Hudson and his co-workers,[2-10] Gold, Hilton and Jefferson,[11] and Kelly and Watson[12] have suggested that aromatic acid chlorides may be hydrolyzed by either the S_N1 or the S_N2 mechanism, and Newman,[13] Gould[14] and Hine[15] have agreed with them. The two paths they proposed are as follows:

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[1] For instance, M. L. Bender, *Chem. Revs.*, **60**, 53 (1960).

[2] R. F. Hudson and J. E. Wardill, *J. Chem. Soc.*, **1950**, 1729.

[3] B. L. Archer and R. F. Hudson, ibid., **1950**, 3259.

[4] D. A. Brown and R. F. Hudson, ibid., **1953**, 883.

[5] B. L. Archer, R. F. Hudson and J. E. Wardill, ibid., **1953**, 888.

[6] D. A. Brown and R. F. Hudson, ibid., **1953**, 3352.

[7] R. F. Hudson and B. Saville, ibid., **1955**, 4121.

[8] R. F. Hudson and B. Saville, ibid., **1955**, 4130.

[9] E. W. Crundon and R. F. Hudson, ibid., **1956**, 501.

[10] C. W. L. Bevan and R. F. Hudson, ibid., **1953**, 2187.

[11] V. Gold, J. Hilton and E. G. Jefferson, ibid., **1954**, 2756.

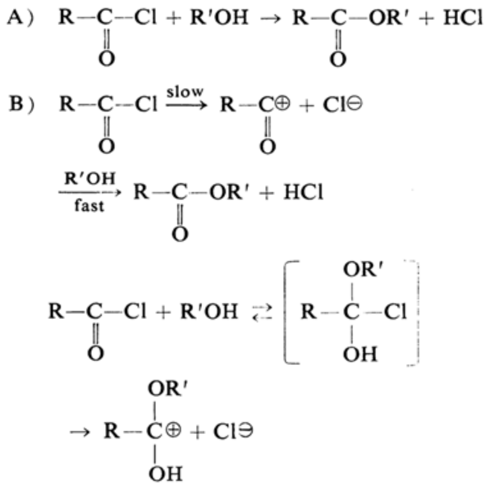
[12] M. J. Kelly and G. M. Watson, *J. Phys. Chem.*, **62**, 260 (1958).

[13] M. S. Newman in Newman (ed.), "Steric Effects in Organic Chemistry," John Wiley & Sons, Inc., New York (1956), p. 225.

[14] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt & Co., New York (1959), p. 332.

[15] J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York (1956), p. 300.

On the other hand, Bunton et al.[16,17] and Peeling[18] have suggested a two-stage process, excluding path B.



$$\text{A)}\quad R-\underset{\underset{O}{\|}}{C}-Cl + R'OH \rightarrow R-\underset{\underset{O}{\|}}{C}-OR' + HCl$$

$$\text{B)}\quad R-\underset{\underset{O}{\|}}{C}-Cl \xrightarrow{\text{slow}} R-\underset{\underset{O}{\|}}{C}\oplus + Cl^{\ominus}$$

$$\xrightarrow[\text{fast}]{R'OH} R-\underset{\underset{O}{\|}}{C}-OR' + HCl$$

$$R-\underset{\underset{O}{\|}}{C}-Cl + R'OH \rightleftarrows \left[R-\overset{\overset{OR'}{|}}{\underset{\underset{OH}{|}}{C}}-Cl \right]$$

$$\rightarrow R-\overset{\overset{OR'}{|}}{\underset{\underset{OH}{|}}{C}}\oplus + Cl^{\ominus}$$

In order to resolve these two divergent views and to find a reasonable mechanism for the hydrolysis of acid chlorides the present investigation was undertaken.

Evaluation of the Two Mechanisms

The mechanism of Hudson et al. differs from the addition-ionization mechanism in that it has a path B in addition to a path A, the latter being essentially similar to the addition-ionization mechanism.

The evidence which has led some workers to propose path B is as follows:

a) The relative rates of the solvolysis of the following *p*-substituted benzoyl chlorides suffer an almost complete reversal in order as the reaction is transferred from 40/60 ethanol-ether (dielectric constant 13) to 50/50 water-acetone (dielectric constant 53),[4] as Table I shows. In 50% water-acetone, the solvolysis of only the *p*-nitro compound appears to have retained its bimolecular character.

TABLE I. EFFECT OF SOLVENT CHANGES ON RELATIVE SOLVOLYSIS RATES OF *p*-SUBSTITUTED BENZOYL CHLORIDES

Medium	D	Relative solvolysis rate				
		p-NO$_2$	p-Br	H	p-Me	p-MeO
40% EtOH-ether	13	32	2.5	1	0.47	0.25
EtOH	22	22	2.1	1	0.70	0.81
50% H$_2$O-acetone	52	12	0.92	1	2.9	30

b) When the logarithms of the observed first-order rate constants of benzoyl chloride in water-acetone are plotted against the logarithms of water concentrations the "apparent order" in water varies from about 1.1～1.5 in 5～15% water to near 7 in 50% water.[3,11,12] The apparent order in water of the hydrolysis of 2, 4, 6-trinitrobenzoyl chloride in 10～30% water-90～70% acetone at 0°C is ca. 1. The apparent order in water of the hydrolysis of *p*-methoxybenzoyl chloride in 10～30% water -90～70% acetone at 0°C is ca. 3.5.[6]

c) The alcoholysis or hydrolysis of mesitoyl chloride is very fast, even faster than *p*-nitrobenzoyl chloride,[6,18,19] as Table II shows.

However, the following evidence seems to be against the path B):

a) Boehme[20] measured the hydrolysis of benzoyl chloride in 2～30% water-98～70% dioxane; his findings show that the apparent order in water at 2～5% water-dioxane is ca. 2.9. This cannot be explained by path B, which is considered to take place only at a higher water concentration, or at a higher dielectric constant.

b) Peeling[18] and Bunton et al.[17] found that the solvolysis of mesitoyl chloride is accelerated by the presence of alkali, as is shown in Table II. Although Brown and Hudson[6] reported that the hydrolysis rate of mesitoyl chloride in 5% water-acetone at 0.2°C did not change upon the addition of 0.001 M alkali, Bender and Chen[21] established that hydroxide ions do catalyze the hydrolysis of 4-substituted-2, 6-dimethylbenzoyl chlorides in 99% acetonitrile-water. This means that the solvolysis of mesitoyl chloride proceeds through a tetrahedral complex, at least in the presence of alkali.

TABLE II. ALCOHOLYSIS OF SUBSTITUTED BENZOYL CHLORIDES IN 80% ALCOHOLIC ACETONE AT -10.75°C

1) In the absence of alkali

Substituents	H	p-NO$_2$	p-Me	2, 4, 6-Trimethyl
$10^6 k_1$ (sec^{-1})	4.97	212	2.25	521

2) In the presence of alkali (0.2 M $\ominus$OEt)

	H	p-Nitro	2, 4, 6-Trimethyl
Second order rate constant k_2 (M^{-1} sec^{-1})	3	3	0.34

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[16] C. A. Bunton, T. A. Lewis and D. A. Llewellyn, *Chem. & Ind.*, **73**, 1154 (1954).

[17] C. A. Bunton and T. A. Lewis, ibid., **1956**, 180.

[18] E. R. A. Peeling, *J. Chem. Soc.*, **1959**, 2307.

[19] J. F. Norris and V. W. Ware, *J. Am. Chem. Soc.*, **61**, 1418 (1939).

[20] H. Boehme and W. Schuelhoff, *Ber.*, **84**, 28 (1951).

[21] M. L. Bender and M. C. Chen, *J. Am. Chem. Soc.*, **85**, 30 (1963).

c) In the reaction with diazomethane, benzoyl chloride is reactive, whereas mesitoyl chloride is inert.[22] If acylium ions are formed, mesitoyl chloride should react with diazomethane also.

d) Bunton et al.[17] found that the carbonyl oxygen of mesitoyl chloride suffers exchange with the oxygen of the solvent water. This indicates the existence of a tetrahedral intermediate of a finite life-time.[23] Their results are shown in Table III.

TABLE III. COMPARISON OF RATES OF EXCHANGE (k_e) AND HYDROLYSIS (k_h) OF SUBSTITUTED BENZOYL CHLORIDES AT 25°C

Substituents	% Water in the mixture with dioxane	$10^4 k_h$ sec^{-1}	$10^4 k_e$ sec^{-1}	k_h/k_e
H	5	1.2[20]	0	—
	25	7.57	0.30	25
	33	14.8	0.82	18
p-Me	5	0.346[4]	0	—
	25	6.22	0	—
	33	22.7	0.44	51
2, 4, 6-TriMe	5	33.5	1.1	31

e) The chlorine exchange between $Li^{36}Cl$ in dry acetone and mesitoyl chloride is much slower than with benzoyl chloride.[17] If acylium ions are formed, exchange should be faster with mesitoyl chloride. The slow exchange of chlorine atoms must be taking place through a tetrahedral intermediate.

f) Although mesitoyl chloride reacts with methanol or ethanol almost instantaneously at room temperature, it reacts with *t*-butyl alcohol or *t*-amyl alcohol much slower, and when mesitoyl chloride was mixed with a great excess of *t*-amyl alcohol at room temperature, about a 1 : 1 mixture of mesitoyl chloride and *t*-amyl mesitoate was observed by the infrared absorption method after 10 min.[24] The formation of *t*-butyl mesitoate from *t*-butyl alcohol and mesitoyl chloride is catalyzed by pyridine.[25] The reaction should not be catalyzed by pyridine if it proceeds via an acylium ion.

g) Although it is known that 2, 4, 6-trimethylbenzyl chloride ionizes in a liquid sulfur dioxide solution to a greater extent than does benzyl chloride,[26] conductance measurements on a solution of mesitoyl chloride in liquid sulfur dioxide indicated no appreciable ionization.[27]

h) The rate of the solvolysis of 2, 4, 6-trimethylbenzyl chloride and mesitoyl chloride are shown in Table IV. Table IV shows that 2, 4, 6-trimethylbenzyl chloride can not be solvolyzed by the S_N1 mechanism in 25% H_2O-acetone. In view of the evidence cited in g), it seems unlikely that mesitoyl chloride is solvolyzed by S_N1 in a poorer ionizing solvent than the solvent in which 2, 4, 6-trimethylbenzyl chloride failed to be solvolyzed by S_N1.

The evidence gathered above seems to indicate that the solvolysis of mesitoyl chloride does not proceed via an acylium ion but via a tetrahedral intermediate. If mesitoyl chloride is not solvolyzed by S_N1, it is reasonable to assume that other benzoyl chlorides are also solvolyzed by way of tetrahedral intermediates. A simple expression of an addition-ionization mechanism through a tetrahedral intermediate

TABLE IV. RATES OF SOLVOLYSIS OF 2, 4, 6-TRIMETHYLBENZYL AND MESITOYL CHLORIDES

Substance	Solvent	Temp.	Added material	$10^4 k_1$ sec^{-1}	$10^3 k_2$ M^{-1} sec^{-1}	Ref.
Trimethylbenzyl chloride	25%H_2O-acetone*	30	—	0.134	—	6
	25%H_2O-acetone	30	0.027 M $^{\ominus}$OH	—	4.306	6
	50%H_2O-acetone	20.4	—	103.2	—	6
	50%H_2O-acetone	20.4	0.027 M $^{\ominus}$OH	104.1	—	6
Trimethylbenzoyl chloride	5%H_2O-acetone	0.2	—	15.84	—	6
	5%H_2O-dioxane	25	—	33.5	—	17
	5%H_2O-dioxane	25	1 M $^{\ominus}$OH	—	2650	17

* x% A−B means x% A−$(100-x)$% B, (v/v)

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22) W. E. Bachman and J. Sheehan, unpublished results; cited from p. 227 of Ref. 13.

23) In 99% acetonitrile-water, which has a higher dielectric constant and a lower water content, Bender and Chen[20] observed no carbonyl oxygen exchange. The absence of exchange is, however, " not an infallible indication of an acylium ion intermediate," as Bender and Chen state. An explanation for their results is given later in the text.

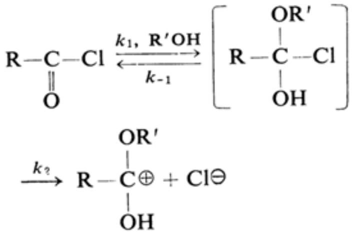
24) Mesitoyl chloride was dissolved in respective alcohols, and the carbonyl absorption of the solution was determined in calcium fluoride cells against the pure alcohols at room temperature. In the cases of methyl and ethyl alcohols, only the ester absorption was observed at 5.77 μ, even immediately after mixing, while in the case of *t*-amyl alcohol, the height of the peaks due to *t*-amyl mesitoate (5.77 μ) and mesitoyl chloride (5.57 μ) was about the same at 10 min. after mixing.

25) S. G. Cohen and A. Schneider, *J. Am. Chem. Soc.*, 63, 3382 (1941).

26) W. T. Nauta and J. W. Dienske, *Rec. trav. chim.*, **55**, 1000 (1936).

27) N. N. Lichtin, Boston Univ.; cited from p. 226 of Ref. 13.

is the following:



$$R-\underset{\underset{O}{\|}}{C}-Cl \underset{k_{-1}}{\overset{k_1,\ R'OH}{\rightleftarrows}} \left[R-\overset{\overset{OR'}{|}}{\underset{\underset{OH}{|}}{C}}-Cl \right] \xrightarrow{k_2} R-\overset{\overset{OR'}{|}}{\underset{\underset{OH}{|}}{C}}{}^{\oplus} + Cl^{\ominus}$$

The rate of solvolysis is expressed by:

$$-\frac{d(RCOCl)}{dt}=\frac{k_1k_2(RCOCl)(R'OH)}{k_2+k_{-1}} \qquad (1)$$

However, this simple mechanism fails to explain some of the data available. As is shown in Table III, the hydrolysis rate of *p*-toluyl chloride increases very much as the water concentration increases from 5% to 33%, yet k_h/k_e is very large, i.e., over 51. When k_h/k_e $(=k_2/k_{-1})$ is very large, Eq. 1 becomes

$$-\frac{d(RCOCl)}{dt}=k_1(RCOCl)(R'OH) \qquad (2)$$

The observed increase of rate upon the increase in water concentration from 25 to 33% gives a value of 4.4 as an apparent order in water by plotting $\log k_1$ versus $\log(H_2O)$.

$$-\frac{d(RCOCl)}{dt}=k_{obs}\,(RCOCl)$$

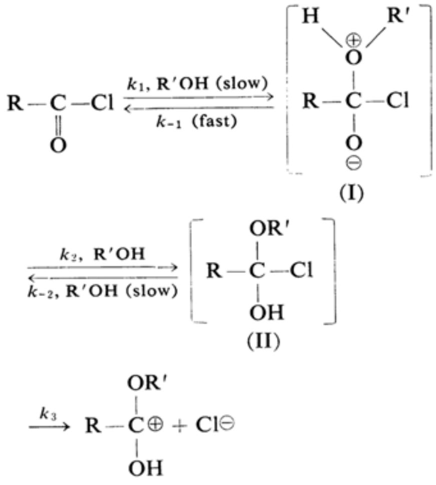
$$=\text{constant}\times(H_2O)^n(RCOCl)$$

$$n=\frac{\Delta(\log k_{obs})}{\Delta(\log(H_2O))}=\text{apparent order in }(H_2O)$$

However, k_1 should not be so much dependent upon the concentration of water. Generally the substituted benzoyl chlorides with electron-releasing groups show a greater dependence upon the concentration of water, and this is incompatible with Eq. 1 or 2.

A Refined Addition-Ionization Mechanism

The Solvolysis of Aroyl Chlorides.—Therefore, the following mechanism[28] is proposed in order to explain the available data on the solvolysis of substituted benzoyl chlorides:**



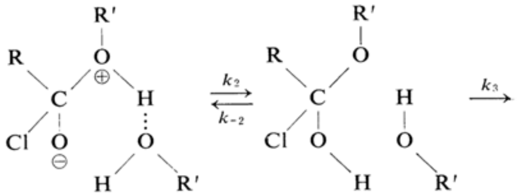
$$R-\underset{\underset{O}{\|}}{C}-Cl \underset{k_{-1}\ (fast)}{\overset{k_1,\ R'OH\ (slow)}{\rightleftarrows}} \left[R-\overset{\overset{H\ \overset{\oplus}{O}\ R'}{|}}{\underset{\underset{O^{\ominus}}{|}}{C}}-Cl \right]_{(I)} \underset{k_{-2},\ R'OH\ (slow)}{\overset{k_2,\ R'OH}{\rightleftarrows}} \left[R-\overset{\overset{OR'}{|}}{\underset{\underset{OH}{|}}{C}}-Cl \right]_{(II)} \xrightarrow{k_3} R-\overset{\overset{OR'}{|}}{\underset{\underset{OH}{|}}{C}}{}^{\oplus} + Cl^{\ominus}$$

With the usual steady-state assumptions for I and II, the rate of solvolysis is calculated as:

$$-\frac{d(RCOCl)}{dt}$$

$$=\frac{k_1k_2k_3(RCOCl)(R'OH)^2}{k_{-1}k_3+k_{-1}k_{-2}(R'OH)+k_2k_3(R'OH)} \qquad (3)$$

Although k_2 and k_{-2} could be an intramolecular proton transfer, it may be more plausible to go through a six-membered transition state with another solvent, since hydroxylic solvents exist as polymers.



Hudson and Saville[7)] found that the alcoholysis of acetyl chloride and *p*-nitrobenzoyl chloride is much faster in ethanol-carbon tetrachloride than in an ethanol-ether mixture at the same ethanol concentration. Their results are shown in Table V. While ethanol exists as a polymer in carbon tetrachloride, it probably exists in ether as a hydrogen-bonded form with ether molecules. In carbon tetrachloride, the attack of ethanol on the acid chloride, is

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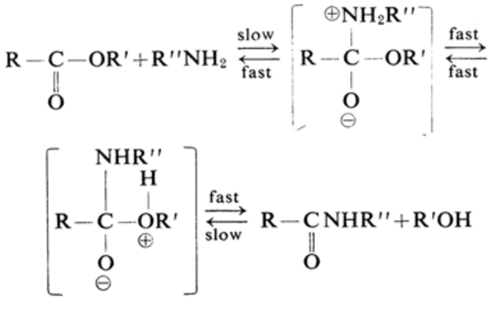
[28] This is somewhat analogous to the aminolysis of esters (Ref. 14, p. 330):



$$R-\underset{\underset{O}{\|}}{C}-OR'+R''NH_2 \underset{fast}{\overset{slow}{\rightleftarrows}} \left[R-\overset{\overset{\oplus NH_2R''}{|}}{\underset{\underset{O^{\ominus}}{|}}{C}}-OR' \right] \underset{fast}{\overset{fast}{\rightleftarrows}} \left[R-\overset{\overset{NHR''}{|}}{\underset{\underset{O^{\ominus}}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\oplus}{O}}R' \right] \underset{slow}{\overset{fast}{\rightleftarrows}} R-\underset{\underset{O}{\|}}{C}NHR''+R'OH$$

** A difficulty with this mechanism has been pointed out by a referee; that is, the mechanism proposed here may not be compatible with the linear relationship between σ^+ and ρ, or with the rather large negative ρ value observed for the hydrolysis of 4-substituted-2, 6-dimethylbenzoyl chlorides.[21)] However, the present author is not quite convinced by these results and the interpretations thereof, mainly because of the conditions employed for the kinetic and isotopic studies.

TABLE V. ETHANOLYSIS OF ACID CHLORIDES AT 20°C

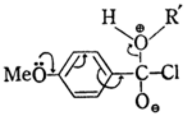
Substance	(EtOH) mol./l.	10^4k_1 (min^{-1}) in CCl_4	10^4k_1 (min^{-1}) in ether	k_{CCl_4}/k_{ether}
Acetyl chloride	0.172	369	4.8	77
	0.345	969	16.85	57.5
	0.69	2290	61.8	37.1
p-Nitrobenzoyl chloride	0.69	139	10.0	13.9

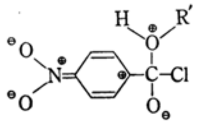
followed by a proton transfer through another ethanol molecule which is hydrogen-bonded to the reacting ethanol molecule. In ether, every ethanol molecule is linked to an ether molecule rather than to another ethanol molecule at low concentrations of ethanol, and thus the formation of intermediate I is not readily followed by a proton transfer; rather, it dissociates back to the starting materials. Since the dielectric constant of ether is even a little larger than that of carbon tetrachloride and since the mole fractions of ethanol in ether and carbon tetrachloride with the same concentration of ethanol are about the same, it is not at all possible to attribute the large difference in rate to the change in the dielectric constant of the medium. The hydrolysis rates of benzoyl chloride in 5% water-dioxane (dielectric constant 3.8) and 5% water-acetone (dielectric constant 22.2) are not very different (7.30×10^{-5} sec^{-1} and 5.45×10^{-5} sec^{-1}, respectively[4]). Thus, the data on the ethanolysis of acid chlorides in ether and in carbon tetrachloride seem to indicate the validity of the proposed intermediates, I and II.

As is shown in Table III, k_h/k_e is very large for benzoyl and *p*-toluyl chloride in 5~33% water-dioxane and for mesitoyl chloride in 5% water-dioxane at 25°C. When k_h/k_e is very large, i.e., $k_3 \gg k_{-2}[\mathrm{R'OH}]$, Eq. 3 becomes

$$-\frac{\mathrm{d(RCOCl)}}{\mathrm{d}t}=\frac{k_1k_2\mathrm{(RCOCl)(R'OH)}^2}{k_{-1}+k_2\mathrm{(R'OH)}} \qquad (4)$$

k_{-1} is large in a solvent of low polarity and small in a solvent of high polarity. k_1 is large for *p*-nitrobenzoyl chloride and small for *p*-anisoyl chloride. k_{-1} is small for the former and large for the latter, since an electron-releasing group helps R'OH leave from I and an electron-withdrawing group prevents its departure. When the polarity of the medium





is low and/or an electron-releasing substituent is present, $k_{-1} \gg k_2$ (R'OH) may be realized. Then, Eq. 4 becomes:

$$-\frac{\mathrm{d(RCOCl)}}{\mathrm{d}t}=\frac{k_1k_2}{k_{-1}}\mathrm{(RCOCl)(R'OH)}^2 \qquad (5)$$

Although k_1 and k_2 also depend upon the polarity of the medium or on the concentration of water, the dependence of k_{-1} on the polarity of the medium may be far greater. Thus, an apparent order in water of 2 or more may be realized in these cases. We recall that the apparent order in water, *n*, is ca. 2.9 for benzoyl chloride in 2~5% water-dioxane at 25°,[20] and *n* is ca. 3.2 for *p*-anisoyl chloride in 10~30% water-90~70% acetone at 0°C.[6]

When the polarity of the solvent is rather high and electron-withdrawing substituents are present, it is possible that $k_{-1} \ll k_2$ (R'OH) is realized. Then, Eq. 4 becomes

$$-\frac{\mathrm{d(RCOCl)}}{\mathrm{d}t}=k_1\mathrm{(RCOCl)(R'OH)} \qquad (6)$$

n is ca. 1.15 for benzoyl chloride in 5~15% water-acetone at 25°C, ca. 0.8 for *p*-nitrobenzoyl chloride in 5~25% water-acetone at 0°C, and ca. 1.06 for 2, 4, 6-trinitrobenzoyl chloride in 10~30% water-acetone at 0°C.[5]

When the concentration of water becomes very large, k_{-2} becomes appreciable; the trend may be seen in Table III. Therefore, we have to consider Eq. 3 rather than 4, 5 or 6. k_3 is an ionization step and highly dependent on the polarity of the medium, and it is probable that the apparent order in water, *n*, is rather great. The *n* for benzoyl chloride in 25~40% water-acetone at 25°C is ca. 2.72 and in 50~75% water-acetone at 0°C is ca. 6.85.[3] The fact that no carbonyl oxygen exchange was observed with mesitoyl chloride in 99% acetonitrile-water[21] can be explained by this mechanism. The conversion of intermediate II to I is helped by water, and at the very low concentration of water, k_{-2} may be inappreciably small; the trend may be seen in Table III. Thus, the findings of Bender and Chen[21] (no oxygen exchange) is understandable, while at the higher concentration of water the exchange of oxygen is expected, and it was really found to take place.[17]

Thus, all the data available on the hydrolysis of aroyl chlorides[29] can be explained very well in terms of intermediates I and II, and Eqs. 3, 4, 5 and 6.

The Solvolysis of Acyl Chlorides and Chloroformates.—It is not certain whether or not acetyl chloride and chloroformates are solvolyzed via a tetrahedral intermediate, and there are no data available on the exchange of the

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[29] The papers not so far cited include; J. F. Norris and H. H. Young, Jr., *J. Am. Chem. Soc.*, **57**, 1420 (1935); G. E. K. Branch and A. C. Nixon, ibid., **58**, 2499 (1936); C. G. Swain, R. B. Mosley and D. E. Bown, ibid., **77**, 3731 (1955).

TABLE VI. SOLVOLYSES OF VARIOUS ACID CHLORIDES AT 25°C

Substance	Solvent	$10^5 k_1$, sec^{-1}	Ref.
2,4,6-Trimethoxybenzoyl chloride	5% water-dioxane	830	16
2,4,6-Trimethylbenzoyl chloride	5% water-dioxane	335	16
2,6-Dimethoxybenzoyl chloride	5% water-dioxane	330	16
Acetyl chloride	5% water-acetone	668	29
p-Nitrobenzoyl chloride	5% water-acetone	169	3
Benzoyl chloride	5% water-acetone	7.71	3
p-Methoxybenzoyl chloride	5% water-acetone	3.0	3
Ethyl chloroformate	10% water-dioxane	0.39	19

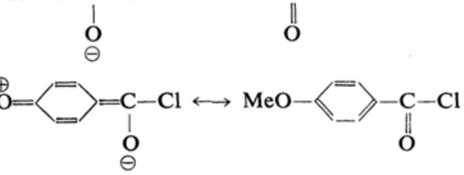
oxygen of these compounds with a solvent. However, it is very probable that these substances are also solvolyzed by a similar mechanism. The rates of the solvolysis of various acid chlorides are compared in Table VI.

There have been several papers reporting on the solvolysis of acyl chlorides[30-35] and chloroformates,[20,36-39] but none of them present clear evidence with which one can decide the mechanism unambiguously.

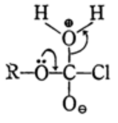
Some workers presuppose, without good evidence, the appearence of an acylium ion during the solvolysis of acyl chlorides and chloroformates. However, the absence of this species may be clearly understood if one compares their rates with the rate of benzoyl chlorides and also the rates of the solvolysis of ethyl chloride, benzyl chloride and methoxymethyl chloride. The rate of the alcoholysis of ethyl chloride at 25°C is extremely slow, that of benzyl chloride is fairly fast, and that of methoxymethyl chloride is extremely fast.[40] Thus, the order is $CH_3CH_2Cl \ll C_6H_5CH_2Cl \ll CH_3OCH_2Cl$. This rate sequence is what is expected for an S_N1 reaction, based on the stability of the carbonium ions formed. On the other hand, the rate sequence for the solvolysis of acetyl chloride, benzoyl chloride and alkyl chloroformates is completely the opposite, that is, $CH_3COCl \gg C_6H_5COCl \gg C_2H_5 \cdot OCOCl$, as Table VI shows. If an acylium ion is playing any significant role in the solvolysis of acyl chlorides or chloroformates, the rate sequence should be the opposite; that is, the chloroformates capable of forming the most stable acylium ion should be solvolyzed the most quickly and acetyl chloride should be solvolyzed the most slowly because of the unstabilized acetyl cation. Since what was found in various media by various workers is contrary to this, acyl chlorides and chloroformates must be solvolyzed, not via an acylium ion, but by way of the addition-ionization mechanism.

Acetyl chloride is more reactive than benzoyl chloride because of a lack of conjugation with the phenyl ring. If acetyl chloride follows the mechanism proposed for benzoyl chloride, k_1 is very large, k_{-1} is probably very large, and the rate may follow Eq. 5. The apparent order in water, n is found to be 2 in 1~5% water-acetone at 24.8°C,[30] 1.4 in 1~4% ethanol-carbon tetrachloride, and 2.0 in 1~40% ethanol-ether at 20°C.[7]

Chloroformates are less reactive than acetyl chloride because of resonance such as the following, and these compounds are somewhat analogous to *p*-anisoyl chloride.



If chloroformates follow the mechanism proposed for benzoyl chlorides, k_1 is rather small, k_{-1} may be very large, and the rate may follow Eq. 5:



The apparent order in water, n, is found to be 1.6~2.2 for ethyl chloroformate in 10~70%

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30) G. Zimmerman and C. Tuan, ibid., **77**, 332 (1955).

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37) M. Green and R. F. Hudson, *Proc. Chem. Soc.*, **1959**, 149.

38) E. W. Crunden and R. F. Hudson, *J. Chem. Soc.*, **1961**, 3748.

39) R. F. Hudson and M. Green, ibid., **1962**, 1055.

40) Extrapolation of the rates of the solvolysis of methoxymethyl chloride in a methanol-dioxane mixture[41] to pure methanol gives $k_1 = 2.2\,sec^{-1}$ at 25°C.[42] On the other hand, the rate constant of α, 2, 4, 6-tetramethylbenzyl chloride in pure ethanol at 25°C is only $3.27 \times 10^{-4}\,sec^{-1}$.[43]

41) P. Salomaa, *Ann. Acad. Turkuensis*, **1953**, A14.

42) P. D. Bartlett and B. T. Storey, *J. Am. Chem. Soc.*, **80**, 1398 (1958).

43) G. Baddeley and J. Chadwick, *J. Chem. Soc.*, **1951**, 368.

water-dioxane at 25°C, and 1.1∼1.4 for *t*-butylperoxy chloroformate in 20∼100% methanol-carbon tetrachloride.[44] Leimu studied the rate of the methanolysis of chloroformates and found that β-chloroethyl chloroformate is solvolyzed 12.5 times faster than isopropyl chloroformate.[45]

The Solvolysis of Aroyl Chlorides in the Presence of Alkali.—Although the solvolysis of acid chlorides in general is not catalyzed by the presence of acids, [2,31,46] it is much accelerated by the addition of alkali, as Table VII shows.

TABLE VII. EFFECT OF ALKALI ON THE SOLVOLYSES OF ACID CHLORIDES[6,18]

1) 80% alcoholic acetone at −10.75°C

	Benzoyl chloride	*p*-Nitrobenzoyl chloride	Mesitoyl chloride
$10^6 k_1$ (sec^{-1})	4.97	212	521
k_2* (M^{-1} sec^{-1})	3	2	0.34
k_2/k_1	6×10^5	6×10^5	650

* (OEt⊖) = 0.02 M

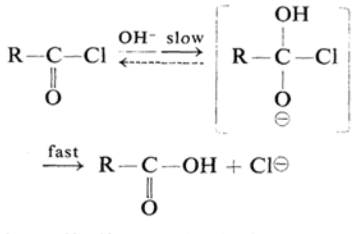
2) 25% water-acetone at 0.2°C

	p-Nitrobenzoyl chloride	*p*-Anisoyl chloride	$\dfrac{k_{\text{nitro}}}{k_{\text{anisoyl}}}$
$10^4 k_1$ (sec^{-1})	20.32	2.82	7.2
k_2* (M^{-1} sec^{-1})	6.82	0.405	16.8
k_2/k_1	3360	1430	

* 0.003 M OH⊖

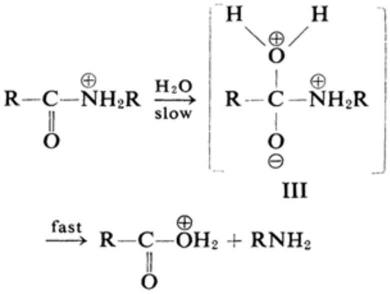
The relatively small increase of the rate on the addition of alkali to mesitoyl chloride is interesting. The slower rate of mesitoyl chloride than benzoyl and *p*-nitrobenzoyl chloride in alkali may be explained by the presence of steric hindrance and electron-releasing substituents.

When alkali is present, a probable mechanism may be the following:



If the alkaline solvolysis proceeds by this scheme, the rate increase upon the addition of alkali should be greater in a solvent of low polarity and greater for an acid chloride with electronegative substituents. Table VII is in agreement with this.

The basic hydrolysis of acid chlorides is somewhat analogous to the acid hydrolysis of amides:



III

In this case, an inappreciable oxygen exchange between solvent and amide is observed, and cation III seems to be an activated complex rather than an intermediate. There are no experimental data available on the isotope exchange in the alkaline solvolysis of acid chlorides, but the alkaline solvolysis of acid chlorides may possibly proceed through an activated complex, not an intermediate.

Mesitoyl Chloride.—The case of mesitoyl chloride is worthy of further comment. It is well known that mesitoic acid is resistant to esterification under ordinary conditions and that methyl mesitoate is saponified with difficulty.[47-48] However, Bender proved conclusively that the alkaline hydrolysis of methyl mesitoate proceeds through a tetrahedral intermediate, which goes to hydrolyzed acid 6.8 times faster than it goes back to the starting ester.[49] Acetomesitylene gives a 2, 4-dinitrophenylhydrazone[50] and reacts with hydroxylamine to give acetomesidide.[51] Although these examples show that it is not impossible to form a tetrahedral intermediate for mesitoic acid derivatives, the very fast solvolysis of mesitoyl chloride[52] is yet to be explained.

From dipole moments,[53-54] ultraviolet absorption[55] or infrared absorption,[56] it is known

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[44] H. Minato, Ph. D. thesis (Harvard University, 1961), p. 40.

[45] R. Leimu, *Ber.*, **70B**, 1040 (1937).

[46] The only exception reported is mesitoyl chloride.[21]

[47] H. L. Goering, T. Rubin and M. S. Newman, *J. Am. Chem. Soc.*, **76**, 787 (1954). In the alkaline hydrolysis of methyl mesitoate in 60% dioxane −40% water, $k_2 = 1.40\times10^{-3}$ M^{-1} sec^{-1} at 126°C.

[48] M. L. Bender, R. D. Ginger and J. P. Unik, ibid., **80**, 1044 (1958). In the alkaline hydrolysis of ethyl benzoate at 25°C, $k_2 = 8.4\times10^{-3}$M^{-1} sec^{-1}. By extrapolating the data of Refs. 47 and 48, k_2 (Ethyl benzoat)/k_2(Methyl mesitoate) = 44000 at 25°C and 1530 at 125°C.

[49] M. L. Bender and R. S. Dewey, ibid., **78**, 317 (1956).

[50] D. E. Pearson and F. Greer, ibid., **77**, 1294 (1955).

[51] E. Feith and S. H. Davies, *Ber.*, **24**. 3546 (1891).

[52] For the more recent papers on this compound, see Ref. 21 and I. Ugi and F. Beck, *Ber.*, **94**, 1839 (1961).

[53] J. B. Bentley, K. B. Everard, R. J. B. Marsden and L. E. Sutton, *J. Chem. Soc.*, **1949**, 2957.

[54] H. B. Keevans and J. R. Platt, *J. Am. Chem. Soc.*, **71**, 1741 (1949).

[55] E. A. Braude, F. Sondheimer and W. F. Forbes, *Nature*, **173**, 117 (1954).

[56] Methyl benzoate 5.80 μ, methyl mesitoate 5.77 μ, methyl acetate 5.73 μ; benzoyl chloride 5.64 μ, mesitoyl chloride 5.57 μ, acetyl chloride 5.55 μ.

Table VIII. Relative rates of solvolyses of some esters and acid chlorides

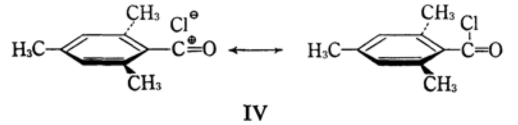
Condition	Ethyl acetate	Ethyl benzoate	Methyl mesitoate	Ref.
Acid[a]	173	1	too slow	57
Basic[a]	10	1	2.3×10^{-5}	47, 48

Condition	Acetyl chloride	Benzoyl chloride	Mesitoyl chloride	Ref.
Neutral or acid[b]	86.7	1	43.5	18
Basic[b]	too fast	more than 925[c]	1	18

a) Second order rate constants
b) First order rate constants
c) Too fast to measure accurately

that steric hindrance by *o*-substituents can decrease the extent of conjugation between a benzene ring and a carbonyl group by preventing these groups from becoming coplanar. Bunton and Lewis[17] attributed the fast solvolysis rate of mesitoyl chloride to the failure of the carbonyl group to conjugate with the benzene ring. The solvolyses of some esters and acid chlorides are compared in Table VIII. The resistance of mesitoic acid towards esterification or of mesitoate towards hydrolysis is usually explained by the blocking effect of *o*-substituents. If mesitoyl chloride is reactive only because of the lack of conjugation between a carbonyl group and a benzene ring, as Bunton and Lewis maintain, it is difficult to explain why methyl mesitoate is not solvolyzed more easily than benzoate in a weakly acid solution, and why methyl mesitoate is solvolyzed 10^5 times more slowly than ethyl benzoate in an alkaline solution. It seems that the explanation must depend upon a factor peculiar to acid chlorides.

It is conceivable that the structure of mesitoyl chloride differs from those of benzoyl chloride and of mesitoate esters. Although the ortho substituents prevent the chlorocarbonyl group from becoming coplanar with the ring, the carbonyl group may remain colinear with the bonding-ring carbon atom as in the mesitoyl cation. The molecule may then be described by the resonance structures (IV).



IV

The fact that mesitoyl chloride is a non-conductor in sulfur dioxide[27] need not void this hypothesis. An incoming hydroxylic solvent can attack the carbonyl carbon from the direction of the *p*-orbital perpendicular to the ring without steric hindrance. The solvolysis still proceeds not by the direct displacement of chloride but rather by addition-ionization, since the isotope exchange experiment showed the existence of a tetrahedral intermediate. The tetrahedral intermediate formed in the hydrolysis of mesitoate esters, on the other hand, is formed very much more sluggishly because, as we postulate, the alkoxy-carbonyl group does not depart from the usual trigonal structure.

Summary

A mechanism has been proposed which seems to be consistent with all the experimental results obtained by various workers on the solvolyses of acid chlorides.

The author wishes to thank Professor Paul D. Bartlett of Harvard University for his encouragement and valuable advice, the members of Professor Bartlett's research group in 1958—1961 for their stimulating discussions, and the Bell Telephone Laboratories for a research fellowship in 1959—1961.

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