

The Ionization Mechanism for the Hydrolysis of Acyl Chlorides

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Acyl chlorides fell in two classes with regard to their reactivity in water solution toward mercuric perchlorate, a powerful electrophilic reagent. Dimethylcarbamyl chloride, dimethylsulfamyl chloride, tetramethyldiamidophosphorochloridate, and benzoyl chloride reacted rapidly to form the corresponding acylium ions. Benzenesulfonfyl chloride, diethylphosphorochloridate, and *n*-butyl chloroformate were completely inert toward the mercuric ion, showing that they are extremely resistant to ionizing. The dimethylcarbamyl cation, $(\text{CH}_3)_2\text{NCO}^+$, was trapped in low yield by azide ion. Attempts to trap the corresponding sulfur and phosphorus cations by various nucleophilic reagents were unsuccessful.

Two mechanisms¹ have been considered for the reactions of acyl chlorides² in water solution. The reactions of alkyl-, aryl-, and alkoxy-substituted acyl chlorides with various anions and amines^{3,4} are usually fast and bimolecular. The ionization mechanism has been encountered less often. It was invoked for mesitoyl chloride,^{5,6} benzoyl chloride,⁷ dimethylcarbamyl chloride,⁸ dimethylsulfamyl chloride,⁹ and tetramethyldiamidophosphorochloridate.¹⁰ We have examined this mechanism further in two ways: (1) promoting the ionization mechanism by use of a strongly electrophilic reagent and (2) attempting to trap the unstable intermediate acylium ions.

Results and Discussion

Acylium Ions from the Mercuric Ion-Promoted Reaction.—Mercuric perchlorate abstracts bromide ion from alkyl bromides to generate the corresponding alkyl cations.^{11–14} The rates of the reactions of mercuric perchlorate in water solution with benzoyl chloride and benzenesulfonyl chloride, *n*-butyl chloroformate and dimethylphosphorochloridate, and dimethylcarbamyl chloride (1), dimethylsulfamyl chloride (2), and tetramethyldiamidophosphorochloridate (3) were measured. The rate constants for these reactions, found in Table I, show that the acyl chlorides carrying dimethylamino groups at the central atom reacted rapidly with mercuric perchlorate. Chloride 3 reacted more slowly than 1 and 2. Benzoyl chloride also reacted rapidly. Our interpretation is that the powerful electrophilic activity of mercuric perchlorate forms the acylium ions.

(1) For good reviews, see (a) I. Ugi and F. Beck, *Chem. Ber.*, **94**, 1839 (1961); (b) R. F. Hudson, *Chimia*, **15**, 394 (1961).

(2) We shall use the expression "acyl chloride" to describe compounds containing the group $\text{O}=\text{Z}-\text{Cl}$, where Z, the "central atom," is one whose other valences carry conventional organic substituents among which may be another oxygen atom. The corresponding acylium ions are then $\text{Z}^+=\text{O}$. The similarities of rates and mechanisms among the carbonyl, sulfonyl, and phosphonyl halides make it convenient to discuss them as a class.

(3) Acetyl, benzoyl and benzenesulfonyl chlorides and fluorides: C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75**, 141, 246 (1953).

(4) Ethyl chloroformate: (a) H. K. Hall, Jr., *ibid.*, **79**, 5439 (1957); (b) R. F. Hudson and M. Green, *J. Chem. Soc.*, 1055 (1961).

(5) R. F. Hudson and J. E. Wardill, *ibid.*, 1729 (1950).

(6) M. L. Bender and M. C. Chen, *J. Am. Chem. Soc.*, **85**, 37 (1963).

(7) V. Gold, J. Hilton, and E. G. Jefferson, *J. Chem. Soc.*, 2756 (1954).

(8) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **77**, 5993 (1955).

(9) H. K. Hall, Jr., *ibid.*, **78**, 1450 (1956).

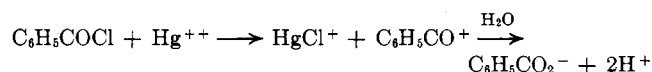
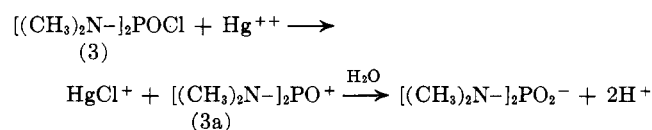
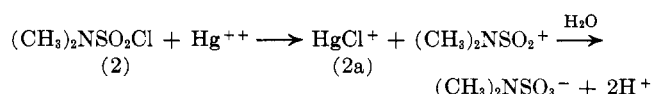
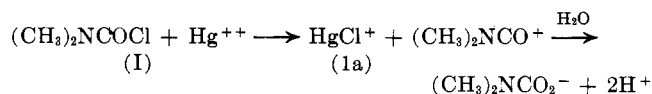
(10) H. K. Hall, Jr., *J. Org. Chem.*, **21**, 248 (1956).

(11) I. Roberts and L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 1063 (1957).

(12) O. T. Benfey, *ibid.*, **70**, 2163 (1948).

(13) S. Oae and C. A. Vander Werf, *ibid.*, **75**, 5037 (1953).

(14) S. Oae, *ibid.*, **78**, 4030 (1956).



(The ion 3a is analogous electronically to the PO_3^- ion intermediate in the hydrolysis of phosphate esters.)

Coordination of the mercuric ion at the oxygen atoms of these molecules, followed by hydrolysis, cannot be excluded by the present results. Coordination at nitrogen seems less likely since amides coordinate with metal ions at the oxygen atom. Because of the known tendency of mercuric ion to abstract halide ion, we prefer the simple acylium ion interpretation.

On the other hand, hydrolysis rates of the phenyl- or ethoxyl-substituted acyl chlorides, other than benzoyl chloride, were not affected significantly by mercuric perchlorate.¹⁵ There is a clear distinction between the two groups in this respect. The lack of reactivity of the phenyl and ethoxyl derivatives is surprising since all alkyl bromides studied react with mercuric perchlorate to form carbonium ions. Acyl chlorides of this class must be very reluctant to yield acylium ions and the mercuric ion must not be able to assist a bimolecular hydrolysis.

Acylium Ions from Electrophilic Action of Water.

Do the acylium ions form by ionization of the acyl chlorides in water solution in the absence of mercuric salts? Only dimethylaminoacyl chlorides and benzoyl chloride need be considered, since the other acyl chlorides did not ionize under more severe conditions.

The most satisfactory evidence for such ionization would be in trapping the intermediate acylium ion. The dimethylcarbamyl cation (1a) formed during the hydrolysis of chloride 1 in predominantly aqueous solvents, reacted with azide ion to form dimethylcarbamyl azide in 18% yield, as shown by the data in Table II. The parent carbamyl cation, H_2NCO^+ , has recently

(15) I. Dostrovsky and M. Halmann, *J. Chem. Soc.*, 516 (1953), found that silver nitrate did not react with diisopropylphosphorochloridate.

TABLE I
 RATES OF HYDROLYSIS OF ACYL CHLORIDES IN THE PRESENCE OF MERCURIC ION

Chloride	Solvent	Initial chloride concentration, $M \times 10^3$	Reagent	Concentration, M	Temperature, °C.	$k \times 10^4$, sec. ⁻¹
Tetramethyldiamidophosphorochloridate	Water	1.1	Sodium perchlorate	0.046	0.6	0.51
Tetramethyldiamidophosphorochloridate	Water	2.2	Mercuric perchlorate	.010	0.1	5.2
			Perchloric acid	.001		
Tetramethyldiamidophosphorochloridate	Water	1.1	Sodium perchlorate	.046	20.0	5.2
Tetramethyldiamidophosphorochloridate	Water	14.6	Mercuric chloride	Satd.	20.0	6.3
Tetramethyldiamidophosphorochloridate	Water	14.6	Perchloric acid	0.015	20.0	5.2
Tetramethyldiamidophosphorochloridate	Water	6.27	Mercuric perchlorate	.0075	20.0	26, 27
			Perchloric acid	.0075		
Tetramethyldiamidophosphorochloridate	Water	6.27	Mercuric perchlorate	.015	20.0	34, 35
			Perchloric acid	.015		
Diethylphosphorochloridate	Water	11.5	None		20.0	11
Diethylphosphorochloridate	Water	11.5	Mercuric perchlorate	.010	20.0	11
			Perchloric acid	.001		
Diethylphosphorochloridate	Water		Mercuric perchlorate	.50	20.0	5.6
			Perchloric acid	.05		
Dimethylsulfamyl chloride	86% Water- 14% dioxane (by volume)	20	None		25.0	2.4
Dimethylsulfamyl chloride	86% Water- 14% dioxane (by volume)	15.4	Perchloric acid	.001	25.0	2.2
Dimethylsulfamyl chloride	86% Water- 14% dioxane (by volume)	3.1	Mercuric perchlorate	.025	25.0	>30
			Perchloric acid	.0025		
Benzenesulfonyl chloride	66% Water- 33% dioxane (by volume)	29.3	Perchloric acid	.01	50.0	5.0
Benzenesulfonyl chloride	66% Water- 33% dioxane (by volume)	20.3	Mercuric perchlorate	.010	50.0	5.6
			Perchloric acid	.01		
Dimethylcarbamyl chloride	Water	11.0	None		0.1	1.6
Dimethylcarbamyl chloride	Water	11.0	Mercuric perchlorate	.015	0.1	>30, >30, >30
			Perchloric acid	.015		
Benzoyl chloride	33% Water- 66% dioxane (by volume)	25.8	None		25	1.8 ^a
Benzoyl chloride	33% Water- 66% dioxane (by volume)	25.8	Mercuric perchlorate	.005	25	>30
			Perchloric acid	.01		
<i>n</i> -Butyl chloroformate	50% Water- 50% dioxane (by volume)	63.7	Perchloric acid	.0046	30.0	0.150
<i>n</i> -Butyl chloroformate	50% Water 50% dioxane (by volume)	61.6	Mercuric perchlorate	.015	30.0	0.193 ^b
			Perchloric acid	.0191		

^a D. A. Brown and R. F. Hudson, *J. Chem. Soc.*, 3352 (1953) give 1.44×10^{-3} sec.⁻¹. ^b Initial value from slope of first-order plot. After 25% reaction, the plot becomes linear with $k_1 = 0.15 \times 10^{-3}$ sec.⁻¹.

been trapped using azide ion in a similar way.¹⁶ Azide ion reacted bimolecularly with dimethylsulfamyl chloride (2) and tetramethyldiamidophosphorochloridate (3).¹⁷ In these experiments, the yield of acyl azide found was in agreement with that calculated from the rate of the bimolecular reaction and no additional acyl azide formed by trapping an acylium ion was found. In a further search, the three acyl chlorides with dimethylamino groups at the central atom were allowed to react with nucleophilic compounds such as amines, oximes, azide, and sulfide ions in water or mixtures of water and dioxane at temperatures from 0–60°. These

compounds have been characterized^{18–21} as powerful nucleophiles toward other acylating agents, but it was hoped that they would be even more reactive toward acylium ions. The product data are given in Table III and the rate data are found in Table IV. In several cases, the nucleophilic reagents reacted bimolecularly with the acyl chlorides,²² while other nucleophilic

(18) W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 675 (1960).

(19) R. Swidler and R. E. Plapinger, *ibid.*, **78**, 3594 (1956).

(20) J. W. Churchill, M. Lapkin, F. Martinez, and J. A. Zaslowsky, *ibid.*, **80**, 1944 (1958); **81**, 2110 (1959).

(21) A. L. Green, G. L. Sainsbury, B. Saville, and M. Stansfield, *J. Chem. Soc.*, 1583 (1958).

(22) Finding second-order reactions of cyclic amines with 1 and 2 invalidates earlier evidence (see ref. 8 and 9) for trapping the corresponding acyl cations. The error occurred because higher concentrations were used in the product isolation experiments than in the kinetics experiments.

(16) M. Halmann, A. Lapidot, and D. Samuel, *J. Chem. Soc.*, 1944 (1962).

(17) D. Samuel and F. H. Westheimer, *Chem. Ind. (London)*, 51 (1959).

TABLE II
AZIDE ION AS A TRAP FOR THE DIMETHYLCARBAMYL CATION

Initial concn. of dimethylcarbamyl chloride, $M \times 10^3$	Solvent	Reagent	Concentration, M	Temp., °C.	$k_1 \times 10^3$, sec.^{-1}	Product	% Yield	
							Calcd.	Found
25	Water	NaCl	0.5	8.5	6.2			
25	Water	NaN ₃	.5	8.5	6.0	Dimethylcarbamylazide	0	9.3
25	Water	NaN ₃ then pyrrolidine	.5 .70	8.5	6.0	Dimethylcarbamylpyrrolidine ^a	0	10.1
25	Water-dioxane (20:3 by wt.)	NaN ₃	.5	20		Dimethylcarbamylazide	0	12.1
25	Water-dioxane (2:1 by wt.)	NaClO ₄	.5	20	4.3			
25	Water-dioxane (2:1 by wt.)	NaN ₃ then pyrrolidine	.5 .70	20	4.3	Dimethylcarbamylpyrrolidine ^a	0	18.4
22	Water-dioxane (1:2 by wt.)	NaClO ₄	.5	45	2.5			
22	Water-dioxane (1:2 by wt.)	NaN ₃ then pyrrolidine	.5 .	45	4.0	Dimethylcarbamylpyrrolidine ^a	38.2	44.8

^a Pyrrolidine was added after completion of the reaction (ten half-lives) to convert dimethylcarbamylazide to the more easily isolated dimethylcarbamylpyrrolidine. The agreement in yields of product isolated as pyrrolidine or as azide shows that dimethylcarbamylazide reacts completely with pyrrolidine and is not partly destroyed by hydrolysis during the work-up.

reagents did not react with the acyl chlorides. However, in no case was the yield of product higher than that calculated from the bimolecular reaction; thus no reaction of these nucleophiles with cations 2a and 3a was accomplished. Table V presents a summary of these results and a comparison with literature data on other organic halides.

A thorough recent study by Crunden and Hudson²³ described the effects of varying the structure and the solvent on the rates of hydrolysis of phosphoramidochloridates. Their interpretation was that tetramethyldiamidophosphorochloridate (3) "solvolyses by a predominantly bimolecular mechanism, although bond-breaking is probably more important than in the solvolysis of the phosphorochloridates". Our results could be accommodated by this interpretation, although we believe that bond breaking is of predominant importance. Even though the trapping of ion 3a was unsuccessful, the high sensitivity of chloride 3 to mercuric ion and insensitivity to powerful nucleophiles argue for an ionization mechanism.

Finally, the present results bear on a criterion of reaction mechanism which has been applied to acyl chlorides. The classical criterion of an ionization reaction of an organic halide, namely, that addition of alkali does not increase the solvolysis rate, was extended by Samuel and Westheimer^{17,24} and by Crunden and Hudson.²⁵ Because bimolecular reactions of tetramethyldiamidophosphorochloridate (3) with azide ion or other reactive nucleophiles at high concentration could be detected, they concluded that the neutral hydrolysis of 3 was also a bimolecular reaction. However, the behavior of dimethylcarbamyl chloride cannot be explained on this basis. It definitely ionizes, as shown by the azide trapping work, yet gives bimolecular reactions with reactive nucleophiles such as cyclic amines. Similarly, mesitoyl chloride ionizes during solvolysis, yet reacts with hydroxide ion.⁶ Probably only a large ratio k nucleophile/ k water is a satisfactory indication of a bimolecular hydrolysis.

(23) E. W. Crunden and R. F. Hudson, *J. Chem. Soc.*, 3591 (1962).

(24) In a private communication dated June 8, 1960, Professor Westheimer has indicated that he no longer holds this view.

(25) E. W. Crunden and R. F. Hudson, *J. Chem. Soc.*, 748 (1959).

Experimental

Materials. The acyl chlorides were obtained as described earlier.⁸⁻¹⁰ Diethylphosphorochloridate was obtained from Victor Chemical Works and mercuric perchlorate from the G. F. Smith Co. The chlorides dissolved rapidly and completely in the aqueous solutions at the highest concentrations used.

Methods of Rate Measurement. Differential Calorimetric Method.—Most of the rate constants were measured by a calorimetric method²⁶ which can be used with many reagents such as amines, alkali and mercuric ions which would interfere with potentiometric or conductimetric methods. The method was most effective for pseudo-first-order reactions with half-lives of 0.5-10.0 min. The added reagent was almost always present in sufficient excess to ensure first-order disappearance of acyl halide. The bimolecular rate constants, k_2 , required for the calculation of yields were calculated from the following equation

$$\frac{k_1 - k_1^0}{b} = k_2$$

where k_1^0 is the first-order hydrolysis rate in the presence of inert salts such as sodium perchlorate, k_1 is the observed first-order rate constant, and b is the concentration of nucleophile. The per cent yield, y , of product arising from bimolecular reaction of acyl halide with nucleophile is given by

$$y = \frac{100 x_{00}}{a_0} = \frac{100 k_2 b}{k_1^0 + k_2 b}$$

where x_{00} is the final concentration of acylation product and a_0 is the initial concentration of acyl chloride.

pH Method.—The "half-life" method mentioned earlier⁹ was also used. The amine and acyl chloride were mixed in equal concentrations with good stirring in a thermostated creased flask. A plot of pH, as measured with a pH meter, *vs.* time resembled a potentiometric titration curve. The time at which the solution changed from basic to acidic was taken as the half-life of the reaction. If this result agreed with the independently determined half life for the hydrolysis reaction in the absence of amine, the bimolecular contribution was concluded to be negligibly small. If the half-life was appreciably smaller, an appreciable bimolecular contribution was occurring. The bimolecular rate constant, k_2 if not zero, was calculated from the equation where a_0 is the

$$\log \frac{2k_1^0}{k_1^0 + k_2 a_0} = 0.434 t_{0.5} (k_1^0 - k_2 a_0)$$

initial concentration of acid chloride and of amine. The correct value of k_2 was found by trial and error. (The equation was satisfactorily sensitive to changes in the trial value of k_2 .) The following equation relates the per cent yield of bimolecular reaction product to the rate constants

(26) C. H. Lueck, L. F. Beste, and H. K. Hall, Jr., *J. Phys. Chem.*, **67** 972 (1963).

TABLE III.—PRODUCT YIELDS FROM ATTEMPTED TRAPPING EXPERIMENTS WITH NUCLEOPHILES OTHER THAN AZIDE ION^a

Halide	Initial concn., $M \times 10^4$	Solvent	Reagent	Concn., M	Analytical method	Product	Yield	
							Calcd.	Obsvd.
Tetramethyldiamidophosphorochloridate	16	Water	Sodium azide	0.50	Titration	Tetramethyldiamidophosphoryl azide	46.3	41.5
Tetramethyldiamidophosphorochloridate	16	Water	Sodium benzohydroxamate	.50	Isolation	<i>o</i> -Phenylcarbamyloxyhydroxamate	52.7	30.9
Tetramethyldiamidophosphorochloridate	16	Water	Sodium <i>m</i> -cresoxide	.50	Infrared	Tetramethyldiamidophosphoryl <i>m</i> -cresoxide	22.3	0
Tetramethyldiamidophosphorochloridate	16	Water	Pyrrolidine	.50	Infrared	Tetramethyldiamidophosphorylpyrrolidine	24.6	0
Tetramethyldiamidophosphorochloridate	16	Water	Sodium acetone oxime	.50	Infrared	N-methylacetamide	17.5	0
Tetramethyldiamidophosphorochloridate	14	Water	Sodium cyclohexanone oxime	.50	Isolation	Caprolactam	8.8	0
Dimethylcarbonyl chloride	46.7	Water	Pyrrolidine	.103	Isolation (Ref. 8)	Dimethylcarbonylpyrrolidine	55.0	52.3
Dimethylcarbonyl chloride	50	Water	2-Methylpiperidine	.050	Isolation	Dimethylcarbonyl-2-methylpiperidine	0	0
Dimethylsulfonyl chloride	38.5	86% Water-14% dioxane (by volume)	Piperidine	.087	Isolation (Ref. 9)	Dimethylsulfonylpiperidine	61.7	65.2
Dimethylsulfonyl chloride	26	86% Water-14% dioxane (by volume)	Sodium azide	.435	Titration	Dimethylsulfonyl azide	62.7	67.6
Dimethylsulfonyl chloride	26	86% Water-14% dioxane (by volume)	2-Methylpiperidine	.026	Isolation	Dimethylsulfonyl-2-methylpiperidine	0	0

^a All experiments run at 20°C.

$$y = \frac{100 x_{00}}{a_0} = 100 + \frac{115 k_1^0}{k_2 a_0} \log \left(1 - \frac{2a_0}{b_0 + k_1^0/k_2} \right)$$

where y is the per cent yield and b_0 is the initial amine concentration.

Potentiometric Millivolt Method.—Another method was applied to several of the kinetic runs. The rate of formation of chloride ion was measured by means of a silver-silver chloride electrode and a glass electrode in the reaction solution. The final value was determined carefully. The millivoltage readings were plotted against time. At infinite time and at the half-life, respectively,

$$E_{\infty} = E_0 - \frac{RT}{nf} \ln (\text{Cl}^-)_{\infty}$$

$$E_{0.5} = E_0 - \frac{RT}{nf} \ln (\text{Cl}^-)_{0.5}$$

subtracting,

$$E_{\infty} - E_{0.5} = \frac{RT}{nf} \ln 2 = 17.5 \text{ mv.}$$

To determine the half-life of the reaction, 17.5 mv. was subtracted from the final reading and the corresponding time was read from the graph. The rate constant was then calculated from the equation: $k_1 = 0.693/t_{0.5}$. The rate constant can be calculated analogously from other fractions of reaction. The method was not very accurate and many nucleophiles attacked the electrodes. It was useful particularly for the reaction of tetramethyldiamidophosphorochloridate with sodium benzohydroxamate where the succeeding Lossen rearrangement made the thermal method unsuitable.

The reaction of *n*-butyl chloroformate with mercuric perchlorate was followed titrimetrically by the method of Roberts.²⁷ Samples of the reacting solution were removed by a 30-ml. pipet and run into a small separatory funnel containing 50 ml. of chloroform and 10 ml. of 10% aqueous sodium perchlorate solution. The funnel was shaken and the lower layer was discarded. The aqueous layer was extracted again with 35 ml. of chloroform and was run into a 50-ml. volumetric flask and diluted to the mark with water. Hydrochloric acid, 5 ml. of 0.1000 *N*, was added to 10-ml. aliquots, which were adjusted to pH 2 and titrated with 0.025 *N* mercuric nitrate solution.

Product Yield Experiments.—The products from the reactions of dimethylamino-substituted acyl chlorides with strongly nucleophilic compounds were examined. Trapping of cationic intermediates would be indicated by a greater yield than that calculated from the observed rate constants. The results are given in Table III and those for the reaction of dimethylcarbonyl chloride with sodium azide are given separately in Table II. All the new product isolation experiments were performed at the same concentrations as the corresponding kinetics experiment. In addition, the results of the isolation experiments reported earlier^{8,9} were compared with rate data obtained here at comparable, though not quite identical, concentrations to show that those products arose from bimolecular reactions and not by trapping.

Product Isolation in the Reaction of Dimethylcarbonyl Chloride with Azide Ion.—In a typical run, dimethylcarbonyl chloride, 7.0 ml., was added with stirring to a solution of 97.6 g. of sodium azide in 3.0 l. of 66% water-33% dioxane held at 20.0°. After 20 min., the solution was cooled somewhat and 150 g. of purified pyrrolidine was added. After 1 week at 27°, the solution was acidified, using a pH meter, to pH 7 with *ca.* 150 ml. of sulfuric acid-water (1:2). It was extracted with one 5-l. and one 3-l. portion of chloroform. The aqueous layer was extracted continuously overnight with chloroform. The organic layers were concentrated to a very small volume with a rotating evaporator. The somewhat darkened product was taken up in ether, filtered through "Darco",²⁸ "Celite",²⁹ and magnesium sulfate and distilled to give 1.99 g. (18.4%) of dimethylcarbonylpyrrolidine, b.p. 65° (0.40 mm.), n_D^{20} 1.4848 (lit.⁸ b.p. 104° (9 mm.),

(27) I. Roberts, *Ind. Eng. Chem., Anal. Ed.*, **8**, 365 (1936).

(28) Trade-mark for Atlas Powder Co.'s activated carbon.

(29) Trade-mark for Johns Manville's diatomite products, filter aids, inerals, fillers, and catalyst carriers.

TABLE IV
RATES OF REACTION OF ACYL CHLORIDES TOWARD NUCLEOPHILIC COMPOUNDS

Halide	Solvent	Initial halide concn., $M \times 10^3$	Reagent	Concn., M	Method ^a	Temp., °C.	Half-life, min.	$k_1 \times 10^4$, sec. ⁻¹
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16, 16	None		A	20		5.2, 5.4
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium perchlorate	0.50	A	20		4.8, 4.9
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	N-Methylpiperazine	.50	A	20		4.5, 5.0
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium nitrate	.50	A	20		5.2
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium iodide	.50	A	20		5.4
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	14	Sodium cyclohexanone oxime	.50	A	20		5.7
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	11	Acetoxime	.05	A	20		6.0
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium acetone oxime	.50	A	20		6.3
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	9	Monosodium catecholates	.50	A	20		6.5
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium <i>m</i> -cresoxide	.50	A	20		6.7
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Pyrrolidine	.50	A	20		6.9
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16, 11	Sodium hydroxide	.50	A	20		7.2, 7.8
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16, 11	Pyridine	.50	A	20		7.9, 9.0
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	4.5	Sodium sulfide	.50	A	20		8.7
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium azide	.50	A	20		9.7
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium benzohydroxamate	.50	D	20		11
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	16	Sodium benzohydroxamate	.50	C	20		11.3
Tetramethyldiamidophosphorochloridate, $[(CH_3)_2N-]_2POCl$	Water	9	Acetoxime	.50	A	20		18
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	25	None	.50	A	8.5	1.70	5.6
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	25	Sodium azide	.50	A	8.5		6.0
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	25	Sodium chloride	.50	A	8.5		6.2
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	0.70	Sodium sulfate	.25	^b	8.5	1.74	6.6
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	50	Sodium hydroxide	.050	B	8.5	1.84	6.3
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	3.6	Pyrrolidine	.15	A	8.5		29
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	3.85	Pyrrolidine	.00385	B	8.5	1.29	Mixed order kinetics
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	50	Pyrrolidine	.0500	B	8.5	1.08	Mixed order kinetics
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	50	Morpholine	.0500	B	8.5	1.40	Mixed order kinetics
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	Water	50	2-Methylpiperidine	.0500	B	8.5	1.79	6.5
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	66% Water-33% dioxane (by volume)	25	None		A	20		3.9
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	66% Water-33% dioxane (by volume)	25	Sodium nitrate	.50	A	20		3.8
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	66% Water-33% dioxane (by volume)	25	Sodium perchlorate	.50	A	20		4.3
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	66% Water-33% dioxane (by volume)	25	Sodium azide	.50	A	20		4.3
Dimethylcarbonyl chloride, $(CH_3)_2NCOC$	66% Water-33% dioxane (by volume)	11	Sodium cyclohexanone oxime	.50	A	20		5.2

TABLE IV (Continued)

Halide	Solvent	Initial halide concn., $M \times 10^4$	Reagent	Concn., M	Method ^a	Temp., °C.	Half-life, minutes	$k_1 \times 10^4$, sec. ⁻¹
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	66% Water-33% dioxane (by volume)	7.2	Sodium sulfide	0.50	A	20		6.3
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	66% Water-33% dioxane (by volume)	25	Sodium hydroxide	.50	A	20		6.5
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	66% Water-33% dioxane (by volume)	2.2	<i>n</i> -Butylamine	.15	A	20		6.5
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	66% Water-33% dioxane (by volume)	11	Sodium acetone oxime	.50	A	20		8.0
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	66% Water-33% dioxane (by volume)	15	Piperidine	.15	A	20		27
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	66% Water-33% dioxane (by volume)	2.8	Pyrrrolidine	.15	A	20		76
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	33% Water-66% dioxane (by volume)	22	Sodium perchlorate	.50	A	45		2.5
Dimethylcarbonyl chloride, $(CH_3)_2NCOCl$	33% Water-66% dioxane (by volume)	22	Sodium azide	.50	A	45		4.0
Dimethylsulfonyl chloride, $(CH_3)_2NSO_2Cl$	86% Water-14% dioxane (by volume)	1	Sodium perchlorate	.054	c	8.5	25.7	0.444
Dimethylsulfonyl chloride, $(CH_3)_2NSO_2Cl$	86% Water-14% dioxane (by volume)	26	Sodium hydroxide	.0260	B	8.5	26.8	.431
Dimethylsulfonyl chloride, $(CH_2)_2NSO_2Cl$	86% Water-14% dioxane (by volume)	26	2-Methylpiperidine	.0260	B	8.5	27.0	.428
Dimethylsulfonyl chloride, $(CH_2)_2NSO_2Cl$	86% Water-14% dioxane (by volume)	26	Morpholine	.0260	B	8.5	21.2	Mixed order kinetics
Dimethylsulfonyl chloride, $(CH_2)_2NSO_2Cl$	86% Water-14% dioxane (by volume)	26	Piperidine	.0260	B	8.5	17.2	Mixed order kinetics
Dimethylsulfonyl chloride, $(CH_2)_2NSO_2Cl$	86% Water-14% dioxane (by volume)	26	Sodium azide	.435	C	8.5		1.19
Dimethylsulfonyl chloride, $(CH_2)_2NSO_2Cl$	66% Water-33% dioxane (by volume)	21.6	Sodium perchlorate	.5	A	50		4.8

TABLE IV (Continued)

Halide	Solvent	Initial halide concn., $M \times 10^2$	Reagent	Concn., M	Method ^a	Temp., °C.	Half-life, minutes	$k_1 \times 10^3$, sec. ⁻¹
Dimethylsulfanyl chloride, $(CH_3)_2NSO_2Cl$	66% Water-33% dioxane (by volume)	9.3	Sodium hydroxide	0.15	A	50	15	15
Dimethylsulfanyl chloride, $(CH_3)_2NSO_2Cl$	66% Water-33% dioxane (by volume)	21.6	Sodium azide	.50	A	50	26	26
Dimethylsulfanyl chloride, $(CH_3)_2NSO_2Cl$	66% Water-33% dioxane (by volume)	15.5	Sodium acetone oxime	.15	A	50	32	32
Dimethylsulfanyl chloride, $(CH_3)_2NSO_2Cl$	66% Water-33% dioxane (by volume)	6.2	Piperidine	.15	A	50	88	88

^a Methods.—A, differential calorimetric; B, half-life pH change; C, intermittent alkalimetric titration at constant pH; D, potentiometric. ^b See ref. 8. ^c See ref. 9.

TABLE V
REACTIVITY OF ORGANIC HALIDES UNDER S_N1 CONDITIONS

Halide	Hg(ClO ₄) ₂ or Hg(NO ₃) ₂ , k_2 , M^{-1} sec. ⁻¹	HgCl ₂ or HgBr ₂ , k_2 , M^{-1} sec. ⁻¹	% Yield of product from trapping an intermediate during solvolysis
$(C_6H_5)_3C-Cl$	> 6 ^c 33% water-66% dioxane (v:v), 25°		90 ^a 15% water-85% acetone (v:v), 34°
C_6H_5COCl			86 ^d 50% water-50% acetone (w:w), 30°
$CH_2=CHCH(C_6H_5)OCC_6H_4NO_2(p)$			52 ^e 60% water-40% dioxane (v:v), 25°
$p-CH_3OC_6H_4CH_2Cl$			35 ^e 30% water-70% acetone (v:v), 20°
$(C_6H_5)_2CHCl$	> 2 ^c water, 0°		34 ^b 10% water-90% acetone (v:v), 50°
$(CH_3)_2NCOCI$			18 ^e 66% water-33% dioxane, 20°
$(CH_3)_3CCl$, $(CH_3)_3CBr$	> 1.2 ^c 86% water-14% dioxane (v:v), 25°		13 ^e 25% water-75% methanol (v:v), 35°
$(CH_3)_2NSO_2Cl$	~3 ^c water, 20°		0 ^e 86% water-14% dioxane (v:v), 20°
$[(CH_3)_2N-]_2POCl$	0.0066 ^b 25% water-75% dioxane (v:v), 25°		0 ^e water, 10°
$C_6H_5CH_2Cl$	0.0035 ^b 30% water-70% dioxane (v:v), 25°		0 ^e 50% water-50% acetone (v:v), 80°
C_2H_5Br	~0 ^c 50% water-50% dioxane (v:v), 30°		0 ^m 50% water-50% acetone, 0°
C_2H_5OCOCI , $n-C_4H_9OCOCI$	~0 ^c 66% water-33% dioxane (v:v), 50°		0 ^m 85% water-15% acetone, 0°
$C_6H_5SO_2Cl$	~0 ^c water, 20°		0 ^m 50% water-50% acetone, 0°
$(C_2H_5)_2POCl$			0 ^e ethanol, 25°
		4.3×10^{-4} 84% water, 91.6% ethanol, 25°	
		4.3×10^{-2} water, 20°	
		1.5×10^{-4} 40% water-60% acetone (v:v), 71.5°	

^a C. G. Swain, D. C. Dittmer, and K. Lohmann, *J. Am. Chem. Soc.*, **75**, 136 (1953); D. Golomb, *J. Chem. Soc.*, 1334 (1959). ^b M. G. Church, E. D. Hughes, and C. K. Ingold, *ibid.*, 966 (1940). ^c Present work. ^d V. Gold, J. Hilton, and E. G. Jefferson, *J. Chem. Soc.*, 2756 (1954). ^e G. Kohnstam, A. Queen, and B. Shillaker, *Proc. Chem. Soc.*, 157 (1959). ^f L. Wilpulte-Steinert and P. J. C. Fierens, *Bull. soc. chim., Edges*, **64**, 277 (1955). ^g C. A. Buntam and B. Nayak, *J. Chem. Soc.*, 3854 (1959). ^h I. Roberts and L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 1063 (1937). ⁱ S. Koshi and R. Anantaraman, *ibid.*, **82**, 1574 (1960). ^j B. Bensley and G. Kohnstam, *J. Chem. Soc.*, 4747 (1957). ^k O. T. Benfey, *J. Am. Chem. Soc.*, **70**, 2163 (1948). ^l R. A. Sneed and A. M. Rosenberg, *J. Am. Chem. Soc.*, **83**, 900 (1961). ^m C. G. Swain and C. B. Scott, *ibid.*, **75**, 141 (1953). ⁿ R. F. Hudson and M. Green, *J. Chem. Soc.*, 1055 (1961). ^o I. Dostrovsky and M. Halman, *ibid.*, 516 (1953). ^p F. H. Westheimer and D. Samuel, *Chem. Ind. (London)*, 51 (1959).

n_D^{20} 1.4852). In other experiments, dimethylcarbamyl azide was isolated as a colorless liquid, b.p. 72–74° (30 mm.).²⁸

Anal. Calcd. for $C_3H_6ON_4$: C, 31.59; H, 5.30; O, 14.02; N, 49.10; Cl, 0. Found: C, 31.83, 31.77; H, 5.27, 5.21; O, 14.2, 14.6; N, 45.3, 45.6; Cl, 0.4. No explanation for the low nitrogen analysis can be given. The infrared spectrum was com-

(30) R. Stollé, *J. prakt. Chem.*, (2) **117**, 201 (1927), gives b.p. 59° (15 mm.).

pletely consistent with the assigned structure, showing frequencies characteristic of dimethylamino, carbonyl and azide groups.

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The Kinetics of the Acidic and Alkaline Hydrolysis of Ethyl Thionbenzoate

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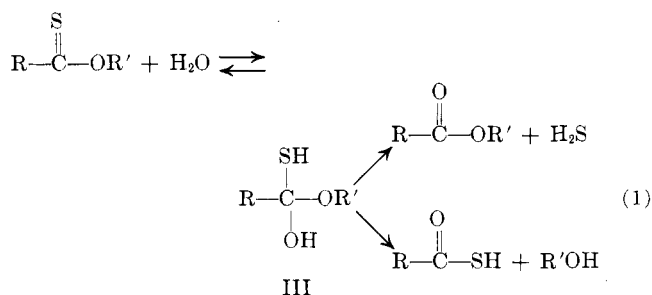
The hydrolysis of ethyl thionbenzoate in 40% aqueous acetone, in the presence of sodium hydroxide at 25.0° and in the presence of hydrochloric acid at 125°, has been shown to yield thiobenzoic acid and ethyl benzoate which is hydrolyzed to benzoic acid. The rate constants for the various steps in this reaction scheme are reported, and a possible mechanism for the reaction is discussed in the light of these data.

The hydrolysis of thiol esters I has been the subject of a number of studies because of interest in their reactivity compared to their oxygen analogs. In basic solution the rates of hydrolysis of analogous thiol and



oxygen esters are generally within a factor of two, but in acid solution most oxygen esters hydrolyze more rapidly than the corresponding thiol esters by at least a factor of ten.² However, the isomeric thion esters II have received relatively little attention aside from their conversion to oxygen esters with aqueous silver nitrate^{3,4} and their rearrangement to the isomeric thiol esters.⁴⁻⁶

A detailed study of the hydrolysis of thion esters II is of interest because it provides a particularly illuminating example of the carbonyl-addition mechanism⁷ of hydrolysis. An intermediate III resulting from addition of water to the thiocarbonyl group of the thion ester could give rise to either an oxygen ester and hydrogen sulfide or a thio acid and an alcohol (equation 1).



(1) Participant in the National Science Foundation Undergraduate Science Education Program.

(2) (a) L. H. Noda, S. A. Kuby, and H. A. Lardy, *J. Am. Chem. Soc.*, **75**, 913 (1953); (b) J. R. Schaeffgen, *ibid.*, **70**, 1308 (1948); (c) B. K. Morse and D. S. Tarbell, *ibid.*, **74**, 416 (1952); (d) P. N. Rylander and D. S. Tarbell, *ibid.*, **72**, 3021 (1950); (e) J. G. Overbeek and V. V. Koningsberger, *Koninkl. Ned. Akad. Wetenschap Proc.*, **58B**, 266 (1955); (f) Y. Iskander, *Nature*, **155**, 141 (1945); (g) K. A. Connors and M. L. Bender, *J. Org. Chem.*, **26**, 2498 (1961).

(3) M. Matsui, *Mem. Coll. Sci. Eng. Kyoto Imp. Univ.*, **3**, 247 (1909).

(4) S. A. Karjala and S. M. McElvain, *J. Am. Chem. Soc.*, **55**, 2966 (1933).

(5) S. G. Smith, *ibid.*, **83**, 4285 (1961).

(6) S. G. Smith, *Tetrahedron Letters*, **21**, 979 (1962).

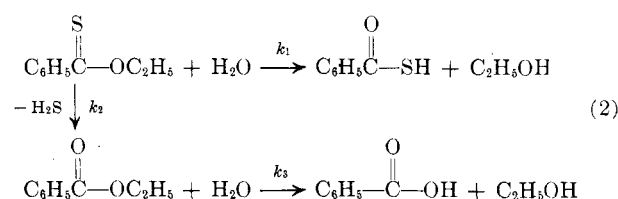
(7) M. L. Bender, *Chem. Rev.*, **60**, 53 (1960).

In addition, the rate level for this hydrolysis is important in connection with the recent application of thionbenzoate as an ambident leaving group in studies of ionization and ion-pair return.⁶

In the present work the kinetics of hydrolysis of ethyl thionbenzoate were studied under acid and alkaline conditions in 40% aqueous acetone.

Results

Alkaline Hydrolysis.—The hydrolysis of ethyl thionbenzoate in 40% aqueous acetone in the presence of sodium hydroxide at 25.0° was followed by analysis for ethyl thionbenzoate and ethyl benzoate by vapor phase chromatography. As illustrated in Fig. 1, ethyl benzoate is formed early in the reaction and subsequently disappears, the maximum concentration of ethyl benzoate being 9.3% of the initial thion ester concentration. This formation and disappearance of ethyl benzoate indicates that the rate constants k_1 , k_2 , and k_3 as defined in equation 2 are all of the same order of magnitude.



Determination of Rate Constant ($k_1 + k_2$).—In addition to the v.p.c. analysis, the disappearance of ethyl thionbenzoate in 40% aqueous acetone at 25.0° in the presence of 0.06 to 0.2 *M* sodium hydroxide was followed spectrophotometrically at 414 μ . The absorption data for runs with *ca.* 0.01 *M* ester and 0.06 to 0.08 *M* base were treated with the aid of the usual integrated second-order rate equation, a good fit being obtained, as illustrated in Table I. The second-order rate equation is actually an approximation in this case because of loss of base due to the concurrent hydrolysis of ethyl benzoate, but with the concentrations employed the error thus introduced is less than 1% at 50% reaction. At the higher base concentrations pseudo-first-order kinetics were observed. The calculated pseudo-second-order rate constants are summarized in Table II. In terms of the reaction scheme given in