propanol (**23a**). The second product was identified as 3-(1-hydroxycyclohexyl)propanol (**22a**): ir (CS_2) strong hydrogen bonding and little free OH absorption; nmr (CCl_4) τ 6.2 (t, 2), 5.0 (broad s, 2), 8.5 (m, 14). After 4 days, large crystals developed in the ethereal solution. They were found to be **22a**, mp 66–68° (lit.[19] mp 60°).

Anal. Calcd for $C_9H_{18}O_2$ (**23a**): C, 68.3; H, 11.4. Found: C, 68.0; H, 11.6.

1-Oxaspiro[4.5]decane (6).—The diol **22a** (1.0 g) was treated with 2 g of tosyl chloride in 10 ml of pyridine for 18 hr at 40–50°. The product was poured onto cracked ice and extracted with ether. The ethereal extract was washed with 6 *M* hydrochloric acid, water, 10% sodium bicarbonate solution, and water, dried ($MgSO_4$), and concentrated. The crude mixture (0.5 g) was shown to be homogeneous on gas chromatography (silicone rubber programmed from 50 to 100°): ir (CS_2) 1145, 1120, 1085, 1050, 925, 905 cm^{-1}. 1-Oxaspiro[4.5]decane (**6**) was previously prepared by the treatment of 3-(1-hydroxycyclohexyl)propyl *n*-pentyl ether with tosyl chloride in pyridine.[20]

1-(1-Hydroxycyclohexyl)-2-propanol (23a).—1-Allylcyclohexanol (1.4 g) was treated with 3.12 g of mercuric acetate in 20 ml of THF–water. The yellow suspension disappeared in 10 sec and the reaction was stirred at room temperature for 15 min. Sodium hydroxide (3 *M*, 10 ml) was added, followed by 0.5 g of sodium borohydride in 10 ml of 3 *M* sodium hydroxide. The product was extracted with ether (the water layer being saturated with sodium chloride). The ethereal extract was washed with water, dried ($MgSO_4$), and concentrated. Gas chromatography of the crude product showed one major peak: ir (CS_2) 3400 (strong hydrogen-bonded OH absorption), 2960, 2925, 2850 cm^{-1}; nmr (CCl_4) τ 4.3 (s, 2), 6.0 (m, 1), 8.5 (m, 10), 8.8 (d, 3).

1-Allylcyclopentanol (21b).—The reaction of allylmagnesium chloride (23 g of allyl chloride and 15 g of magnesium turnings) and cyclopentanone (25 g) gave 10.9 g (29%) of the alcohol **21b**, bp 71–73° (20 mm) [lit.[21] bp 63° (10 mm)].

3-(1-Hydroxycyclopentyl)propanol (22b).—1-Allylcyclopentanol (5.3 g) was treated with 1.5 g of sodium borohydride and 5.0 g of 47% boron trifluoride etherate in 200 ml of THF (dried over sodium) under a nitrogen atmosphere. The mixture was stirred at room temperature overnight. Unchanged diborane was destroyed with 10 ml of water; the mixture was treated with 30 ml of 3 *M* sodium hydroxide, followed by addition of 30% hydrogen peroxide. The product was extracted with ether. The ethereal extract was washed with 6 *M* sodium hydroxide and water, dried ($MgSO_4$), concentrated, and distilled, yielding 1.25 g (20%) of a viscous liquid, bp 122–130° (5 mm). Gas chromatography (silicone rubber programmed from 50 to 180°) showed two peaks. The first peak (28%) on the basis of its retention time, ir, and the analogous reaction in the preparation of **22a** was tentatively assigned as the diol **23b**. The second peak (72%) was assigned as the diol **22b**, mainly because of the nmr signal at τ 6.4 (triplet corresponding to the methylene hydrogens α to the primary hydroxyl group).

1-Oxaspiro[4.4]nonane (12).—A mixture of **22b** and **23b** (0.8 g) was treated with 2.0 g of tosyl chloride in pyridine for 18 hr at 50°. The product was poured onto cracked ice and extracted with ether. The ethereal extract was washed with water, 6 *M* hydrochloric acid, water, sodium bicarbonate solution, and water, dried ($MgSO_4$), and concentrated. Gas chromatography (diethylene glycol succinate) of the crude product showed only one major product: ir (CS_2) 1165, 1100, 1050, 970, 945, 920, 900 cm^{-1}; nmr (CCl_4) τ 6.3 (t, 2), 8.1–8.5 (m, 12).

Anal. Calcd for $C_8H_{14}O$: C, 76.2; H, 11.1. Found: C, 76.2; H, 11.2.

Registry No.—Lead tetraacetate, 546-67-8; **1**, 4442-79-9; **5**, 1124-63-6; **8**, 766-00-7; **9**, 18320-80-4; **11**, 767-05-5; **12**, 176-10-3; **21a**, 1123-34-8; **23a**, 18321-43-2; 1-cyclohexen-1-ylmorpholine, 670-80-4.

(19) J. Colonge, R. Falcotet, and R. Gaumont, *Bull. Soc. Chim. Fr.*, 211 (1958).

(20) W. B. Renfrow, D. Oakes, C. Lauer, and T. A. Walter, *J. Org. Chem.*, **26**, 935 (1961).

(21) G. Crane, C. E. Boord, and A. L. Henne, *J. Amer. Chem. Soc.*, **67**, 1237 (1945).

The Synthesis of Imidate Hydrochlorides by Reaction of Ethyl Chloroformate with Amides and Thionamides

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The scope of the reaction of ethyl chloroformate with amides as a preparation of ethyl imidate hydrochlorides has been investigated. The imidate salts have been prepared successfully in good yields from aliphatic amides containing from one to eight carbon atoms, both straight and branched chain. The N-methyl and N-ethyl derivatives of these aliphatic amides reacted in the same way to give N-substituted imidate hydrochlorides. Attempts to employ the reaction with aromatic amides or N-substituted amides in which the substituent is larger than ethyl were unsuccesful. In certain cases a side reaction occurred. Thus the hemihydrochlorides of acetamide and N-methylcaprylamide were obtained as a second product from acetamide and N-methylcaprylamide, respectively. N-Methylacetamide gave its hemihydrochloride as the only product of the reaction. Thionamides have been found to react with ethyl chloroformate in a similar way, giving the ethyl imidate hydrochloride and carbonyl sulfide as products. The hydrochloride salts of ethyl acetimidate, ethyl propionimidate, ethyl isobutyrimidate, ethyl benzimidate, and ethyl N-phenylacetimidate have been prepared from thioacetamide, thiopropionamide, thioisobutyramide, thiobenzamide, and thioacetanilide, respectively. The reactivity of thionamides is considerably greater than that of the analogous oxygen compounds. The rate curve for the reaction, using propionamide, shows it to be autocatalytic. A possible mechanism for the reaction is suggested.

Although imidates (imino ethers, imido esters) and their salts have been known for nearly a century,[2] and are useful intermediates for the synthesis of a variety of compounds,[3] there has been only one general direct method for their preparation, namely, the method of Pinner,[4] which involves synthesis of the imidate hydrochloride from the appropriate nitrile and alcohol with anhydrous hydrogen chloride (eq 1). The salt

$$RCN + R'OH + HCl \longrightarrow RC(=NH_2Cl)OR' \quad (1)$$

(1) National Science Foundation Undergraduate Research Participant, Grant No. GY-83.

(2) A. Pinner and F. Klein, *Ber.*, **10**, 1889 (1877).

(3) R. Roger and D. G. Neilson, *Chem. Rev.*, **61**, 179 (1961).

(4) A. Pinner, "Die Imidoaether and ihre Derivative," Oppenheim, Berlin, 1892, pp 1–85.

is then easily converted into the free imidate by treatment with potassium carbonate solution. Several other methods of synthesis of specific imidates have been reported, and these have been reviewed by Roger and Nielson.[3]

The Pinner synthesis suffers from some limitations. Long periods of time are often required to obtain the product, and yields are frequently poor. Its most serious limitation lies in the fact that it is not applicable to the preparation of N-substituted imidates. Indeed, very few compounds of this type have been reported, especially where the N substituent is alkyl.

In 1956, Hechelhammer[5] announced the preparation of ethyl formimidate hydrochloride, ethyl acetimidate hydrochloride, and O-ethylcaprolactim hydrochloride by the reaction of ethyl chloroformate with formamide, acetamide, and ϵ-caprolactam, respectively (eq 2). He suggested general applicability of the reaction, although little experimental detail was given.

$$RCONH_2 + EtOCOCl \longrightarrow RC(=NH_2Cl)OEt + CO_2 \quad (2)$$

This reaction was of interest to us, since it represented potentially another general method of preparation of imidate hydrochlorides, which might prove superior to the Pinner method in terms of convenience and yield. Of particular interest was the applicability of the reaction to the preparation of N-substituted imidate hydrochlorides, since no other direct method of synthesis of these compounds is known.

Accordingly, an investigation was undertaken to determine the extent to which this reaction has general applicability as a useful method of preparation of imidate hydrochlorides, and to learn something of the mechanism by which the reaction proceeds.

Results and Discussion

Reaction of Unsubstituted Amides.—Reactions of ethyl chloroformate with 13 different simple amides were attempted. Ten of these yielded the expected imidate hydrochlorides in reasonably good yields, by mixing the reactants without solvent at temperatures below 50°. The products (**1–10**) are listed in Table I together with their melting points and percentage yields. Each of these compounds was also prepared by the method of Pinner,[4] and the melting points and percentage yields by that method are given in Table I for comparison. For those imidate hydrochlorides which have been previously reported by the Pinner synthesis, the literature melting points are also included in the table.

Acetamide showed unique behavior, in that, in addition to ethyl acetimidate hydrochloride (**1**), a second product was formed—acetamide hemihydrochloride (**11**). The two compounds, which were

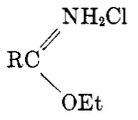
$$(CH_3CONH_2)_2HCl$$
11

formed in a ratio by weight of ~2:3 **1**:**11**, were easily separable, since **1** is readily soluble in chloroform and **11** is not. When the reaction was run in dioxane or in tetrahydrofuran as solvent, the only product formed was **11**, in essentially 100% yield.

(5) Hechelhammer, German Patent 948,973 (Sept 13, 1956).

TABLE I

IMIDATE HYDROCHLORIDES OF TYPE



Compd no.	R	$RCONH_2$ + EtOCOCl Mp, °C[a]	Yield, %	RCN + EtOH + HCl Mp, °C[a]	Yield, %	Lit. mp, °C
1	CH_3	113	32	112–113	54	98–100[b]
2	CH_3CH_2	92–93	65	93–94	36	90–92[b]
3	$CH_3(CH_2)_2$	64–65	83	56–58	48	64–65[b]
4	$(CH_3)_2CH$	89	68	83	85	76[c]
5	$CH_3(CH_2)_3$	Liq[d]	72	Liq[d]	62	
6	$(CH_3)_2CHCH_2$	88–89	75	89–90	47	90[c]
7	$CH_3(CH_2)_4$	Liq[d]	75	Liq[d]	63	Liq[c]
8	$(CH_3)_2CH(CH_2)_2$	Liq[d]	80	Liq[d]	67	Liq[e]
9	$CH_3(CH_2)_5$	Liq[d]	75	Liq[d]	45	67[f]
10	$CH_3(CH_2)_6$	Liq[d]	88	34	55	

[a] Really decomposition temperature; melting is accompanied by gas evolution. [b] See ref 4. [c] N. S. Drosdov and A. F. Bekhli, *J. Gen. Chem. USSR*, **14**, 280 (1944). [d] A viscous syrup at room temperature, which crystallized on storing at 0°, but remelted on return to room temperature. [e] A. Pinner, *Ber.*, **17**, 171 (1884). [f] A. Pinner, *ibid.*, **28**, 473 (1895).

The three amides which were used unsuccessfully in the reaction were benzamide, *p*-nitrobenzamide, and α-phenylacetamide. None of those showed any signs of reacting with ethyl chloroformate, even though a variety of reaction conditions were employed, including temperatures up to 80° for periods up to 60 hr. It should be noted that excessive temperatures must be avoided in this reaction since it is well known that imidate hydrochlorides are thermally unstable.[3,4]

One may cautiously conclude, on the basis of the small sample of amides used, that the reaction constitutes a general method for the preparation of unsubstituted imidate hydrochlorides from aliphatic amides (generally in higher yields than by the Pinner method), but is unsatisfactory for at least some aromatic ones.

Reaction of N-Substituted Amides.—Thirteen ethyl N-alkyl imidate hydrochlorides were prepared from N-alkylamides and ethyl chloroformate. These compounds (**12–24**) are listed in Table II. Reaction conditions were essentially the same as those employed for the unsubstituted amides.

N-Methylcaprylamide yielded two products, in approximately equal amounts by weight—the expected ethyl N-methylcaprylimidate hydrochloride (**23**) and another product identified as N-methylcaprylamide hemihydrochloride (**25**).

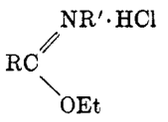
When the reaction was attempted with N-methylacetamide, no imidate hydrochloride was produced, but rather N-methylacetamide hemihydrochloride (**26**) was obtained in nearly quantitative yield.

$$(CH_3(CH_2)_6CONHCH_3)_2\cdot HCl \qquad (CH_3CONHCH_3)_2\cdot HCl$$
25 **26**

Attempts to carry out the reaction on two additional N-substituted amides were unsuccessful. Neither N-*n*-butylacetamide nor acetanilide (N-phenylacetamide) showed any signs of reaction when mixed with ethyl chloroformate at temperature up to 60° for periods up to 12 hr.

It appears that the reaction is generally applicable

TABLE II
IMIDATE HYDROCHLORIDES OF TYPE



Compd no.	R	R′	Yield, %	Analytical data[a] Calcd Neut equiv	Calcd % N	Calcd % Cl	Found Neut equiv	Found % N	Found % Cl
12	H	CH_3	88	123.5	11.34	28.69	122.3	11.20	28.50
13	H	CH_3CH_2	92	137.6	10.18	25.76	136.6	10.08	25.60
14	CH_3	CH_3CH_2	78	151.6	9.24	23.38	151.2	9.22	23.42
15	CH_3CH_2	CH_3	67	151.6	9.24	23.38	150.2	9.33	23.22
16	CH_3CH_2	CH_3CH_2	75	165.7	8.46	21.40	164.2	8.56	21.06
17	$CH_3(CH_2)_2$	CH_3	80	165.7	8.46	21.40	164.5	8.50	21.25
18	$CH_3(CH_2)_2$	CH_3CH_2	76	179.7	7.80	19.73	178.2	7.68	19.40
19	$CH_3(CH_2)_3$	CH_3CH_2	69	193.7	7.23	18.30	192.2	7.32	18.00
20	$CH_3(CH_2)_4$	CH_3	73	193.7	7.23	18.30	192.8	7.21	18.21
21	$CH_3(CH_2)_4$	CH_3CH_2	77	207.8	6.74	17.06	206.4	6.80	17.10
22	$CH_3(CH_2)_5$	CH_3CH_2	84	221.8	6.32	15.98	220.2	6.30	15.91
23	$CH_3(CH_2)_6$	CH_3	44	221.8	6.32	15.98	221.0	6.30	16.00
24	$CH_3(CH_2)_6$	CH_3CH_2	74	235.8	5.96	15.03	234.5	6.05	14.85

[a] Additional evidence for identification of the compounds was obtained by hydrolysis of each compound to the corresponding amine hydrochloride and ester, and comparison of their infrared spectra with those of authentic samples; see Experimental Section.

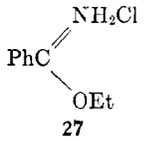
to the preparation of N-methyl- and N-ethylalkylimidate hydrochlorides. Whether it can be extended to N-substituted aryl compounds, or compounds in which the N substituent is larger than ethyl, requires further investigation.

Reaction of Thionamides.—It was found that thionamides undergo a reaction with ethyl chloroformate similar to that of the amides, the products being the ethyl imidate hydrochloride and carbonyl sulfide (eq 3). Thus the hydrochloride salts of ethyl acet-

$$RCSNH_2 + EtOCOCl \longrightarrow RC(NH_2Cl)OEt + COS \quad (3)$$

imidate (**1**), ethyl propionimidate (**2**), and ethyl isobutyrimidate (**4**) were prepared by the reaction of ethyl chloroformate with thioacetamide, thiopropionamide, and thioisobutyramide, respectively.

In addition, ethyl benzimidate hydrochloride (**27**) and ethyl N-phenylacetimidate hydrochloride (**28**) were prepared successfully from thiobenzamide and thioacetanilide, respectively, by this reaction. These



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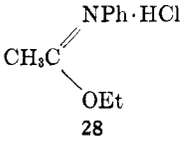


28

latter two preparations are of particular interest, since they represent successful reactions of thionamides, the oxygen analogs of which did not react with ethylchloroformate, as reported above.

The reactions of the thionamides proceeded at a considerably faster rate than those of the corresponding amides. For example, acetamide required 1.5 hr at 45° for complete reaction, whereas the reaction of thioacetamide was complete in 5 min at a temperature of 30°. (Furthermore, no side reaction occurred in the latter case as it did in the former.)

One may conclude that the use of thionamides in this reaction is probably a more satisfactory and more general method of preparing imidate hydrochlorides than is the use of amides. A serious limitation, of course, is the lack of availability of thionamides.

Kinetic Studies.—Throughout this investigation it was observed that reaction between ethyl chloroformate and an amide or thionamide did not begin immediately upon mixing. A short induction period was required, after which the reaction proceeded slowly at first and gradually increased in rate. In an effort to explain this phenomenon a study of the reaction rate was undertaken.

Propionamide was selected as the model amide for the rate study, since it is obtainable in high purity, does not undergo any side reactions (as does, for example, acetamide), and reacts at a rate convenient for study.

The reaction between propionamide and ethyl chloroformate was carried out at 30° and the progress of the reaction was followed by absorption of the liberated CO_2, the amount of which was determined at 15-min intervals by weighing the absorption tube. A plot of millimoles CO_2 liberated *vs.* time gave an S-shaped curve typical of autocatalytic reactions. The curve obtained from a typical run is shown in Figure 1. In order to establish that the reaction is indeed autocatalytic, it was repeated under identical conditions, but with small amounts of the product, ethyl propionimidate hydrochloride, added. The results, two of which are also shown in Figure 1, confirmed autocatalysis.

In view of the fact that the reaction is heterogenous, as well as autocatalytic, a detailed study of the kinetics would be extremely complex.

A possible mechanism which is consistent with the observations is shown in Scheme I. It involves nucleophilic attack of the oxygen of the amide (or of the sulfur of the thionamide) on the carbonyl carbon of the ethyl chloroformate, with elimination of the chloride ion. This is followed by nucleophilic attack of the ethoxy oxygen with elimination of carbon dioxide (or carbonyl sulfide).

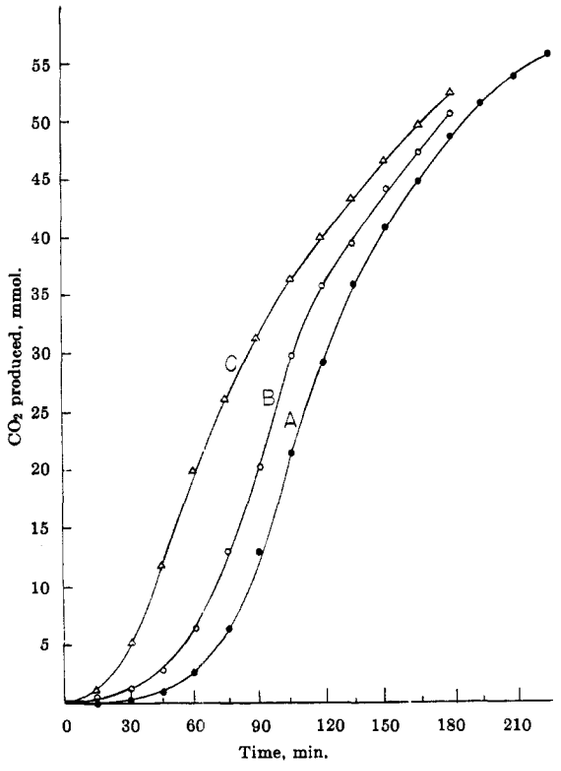
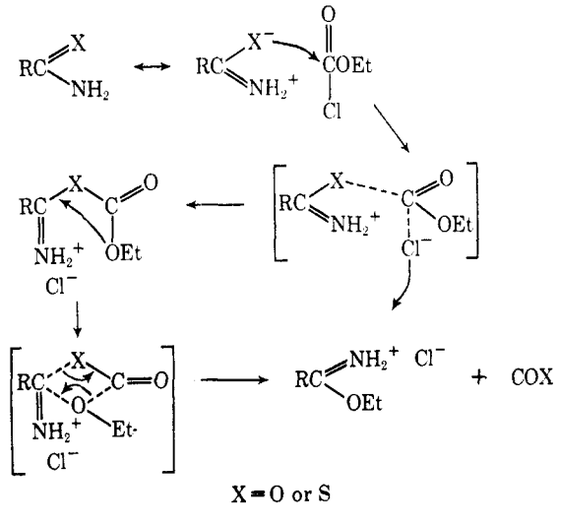


Figure 1.—Production of CO_2 from 105 mmol of propionamide + 105 mmol of ethyl chloroformate at 30°: A, no catalyst; B, 1 mmol of ethyl propionimidate hydrochloride added; C, 10 mmol of ethyl propionimidate hydrochloride added.

SCHEME I



While this postulated mechanism does not explain the autocatalysis of the reaction, it is consistent with the products formed and with the higher reactivity of the thionamides because of the greater nucleophilicity of sulfur than of oxygen.

Experimental Section

Melting points were taken in an open capillary and are corrected. Infrared spectra were recorded on a Perkin-Elmer Model 137B infrared spectrophotometer. Neutral equivalents were determined by potentiometric titration with standard 0.1 *N* NaOH solution using a Beckman zeromatic pH meter. Chloride analyses were by the modification of Caldwell and Moyer[6] of the Volhard method. Analyses for nitrogen were by a modification of the Kjeldahl method.[7]

Materials.—The ethyl chloroformate was obtained from Eastman Organic Chemicals. All nitriles, amides, and thionamides used as starting materials were obtained commercially, except the following, which were synthesized as indicated. Caproamide, isocaproamide, heptamide, and caprylamide were prepared from the acyl chlorides and ammonia by the method Philbrook;[8] α-phenylacetamide was prepared by hydrolysis of the nitrile according to the method of Wenner.[9] The N-methyl derivatives of butyramide, caproamide, and caprylamide, and the N-ethyl derivatives of propionamide, butyramide, valeramide, caproamide, heptamide, and caprylamide were obtained from the acyl chloride and the amine by the method of D'Alelio and Reid.[10] Thiopropionamide was prepared by the method of Pesina,[11] and thioisobutyramide by the method of Taylor and Zoltewicz.[12]

Synthesis of Unsubstituted Imidate Hydrochlorides (1–10).—The apparatus consisted of a 250-ml, three-necked, round-bottomed flask suspended in a water bath. The flask was fitted with a well-sealed stirrer, a dropping funnel, and a water-cooled condenser. A connecting tube at the top of the condenser was extended into a saturated solution of $Ba(OH)_2$, so that the evolution of CO_2 could be followed.

In a typical run 0.1 mol of amide was placed in the flask and 0.1 ml of ethyl chloroformate was added all at once from the dropping funnel. The temperature of the water bath was maintained at 40–45° and the mixture was stirred. After approximately 15 min the reaction began, as evidenced by the evolution of CO_2. Stirring was continued until CO_2 evolution ceased. (Reaction time varied between 1.5 and 5 hr.) The product was washed repeatedly with anhydrous ether and placed in a vacuum desiccator over H_2SO_4. The products, per cent yields, and melting points are shown in Table I.

Attempts to employ this procedure with benzamide, *p*-nitrobenzamide, and α-phenylacetamide gave no reactions.

Compounds **1–10** were also prepared from the appropriate nitriles, ethanol, and dry HCl by the method of Pinner.[4] Infrared spectra ($CHCl_3$) of the compounds prepared each of the two ways were identical. Table I shows yields and melting points of products.

Acetamide Hemihydrochloride (11).—In the preparation of ethyl acetimidate hydrochloride (**1**), as described above, 5.9 g (0.1 mol) of acetamide and 10.8 g (0.1 mol) of ethyl chloroformate yielded a solid crystalline mass weighing 9.1 g. This solid was extracted with dry chloroform. Evaporation of the chloroform solution gave 3.9 g of **1**. The residue from the extraction was 5.2 g of **11**, mp 124–125° (lit.[2] mp 125°).

Anal. Calcd for $C_4H_{11}ClN_2O_2$: neut equiv, 154.6; Cl, 22.93. Found: neut equiv, 154.0; Cl, 22.99.

The ir spectrum (KBr) was identical with that of **11** prepared by the method of Strecker.[13]

Synthesis of N-Substituted Imidate Hydrochlorides (12–24).—The apparatus and procedure were the same as described for the preparation of **1–10**, except that dry petroleum ether (bp 30–60°) was used for washing the products rather than ethyl ether, owing to higher solubility of the N-substituted imidate salts in the latter solvent. All the products were liquids. Attempts to distil them, even at very low pressures, resulted in decomposition. The products, per cent yields, and analytical data are presented in Table II.

Attempts to employ this procedure with N-*n*-butylacetamide and with acetanilide gave no reaction.

Compounds **12–24** were further characterized by identification of their hydrolysis products. To a sample of the imidate hydro-

(6) J. R. Caldwell and H. V. Moyer, *Ind. Eng. Chem., Anal. Ed.*, **7**, 38 (1935).

(7) W. Reiman, J. D. Neuss, and B. Naiman, "Quantitative Analysis," McGraw-Hill Book Co., Inc., New York, N. Y., 1951, p 161–163.

(8) G. E. Philbrook, *J. Org. Chem.*, **19**, 623 (1954).

(9) W. Wenner in "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley & Sons, Inc., New York, N. Y., 1963, p 760.

(10) G. F. D'Alelio and E. E. Reid, *J. Amer. Chem. Soc.*, **59**, 109 (1937).

(11) A. G. Pesina, *J. Gen. Chem. USSR*, **9**, 804 (1939).

(12) E. C. Taylor and J. A. Zoltewicz, *J. Amer. Chem. Soc.*, **82**, 2656 (1960).

(13) A. Strecker, *Ann.*, **103**, 321 (1857).

chloride was added an equimolar amount of H_2O. A reaction occurred immediately. The ethyl ester was distilled off; the amine hydrochloride remained as residue. These were identified by comparison with ir spectra of authentic samples.

N-Methylcaprylamide Hemihydrochloride (25).—In the preparation of N-methylcaprylimidate hydrochloride (**23**), described above, 4.0 g (0.025 mol) of N-methylcaprylamide and 2.7 g (0.025 mol) of ethyl chloroformate gave two products: one solid, one liquid. The mixture was extracted with anhydrous ethyl ether, which dissolved the liquid but not the solid. Evaporation of the ether from solution gave 2.44 g of **23**. The residue from the extraction was 2.33 g of **25**, mp 38° (lit.[10] mp 38–40°).

Anal. Calcd for $C_{18}H_{39}ClN_2O_2$: neut equiv, 351.0; Cl, 10.10. Found: neut equiv, 347.8, Cl, 10.30.

The ir spectrum was identical with that of **25** prepared by the method of Blicke and Burckhalter.[14]

N-Methylacetamide Hemihydrochloride (26).—In the apparatus described 14.6 g (0.2 mol) of N-methylacetamide and 21.7 g (0.2 mol) of ethyl chloroformate were stirred at 40°. After 30 min reaction was complete and the solid product was washed with anhydrous ethyl ether, giving 18.2 g of **26** (99.6% yield), mp 89–90° (lit.[14] mp 87–89°).

Anal. Calcd for $C_6H_{15}ClN_2O_2$: neut equiv, 182.6; Cl, 19.41. Found: neut equiv, 183.8; Cl, 19.51.

The ir spectrum was identical with that of **26** prepared by the method of Blicke and Burckhalter.[14]

Preparation of Imidate Hydrochlorides from Thionamides.—The apparatus and general procedure were the same as described above for the preparation of **1–10** and **12–24**.

A. Ethyl Acetimidate Hydrochloride (1).—Thioacetamide (5.0 g, 0.66 mol) and ethyl chloroformate (7.2 g, 0.066 mol) were mixed at 30°. The reaction was complete in 5 min. The resulting crystals were washed with ether and dried *in vacuo:* yield of **1**, 7.6 g (94%); mp 112–113°.

B. Ethyl Propionimidate Hydrochloride (2).—Thiopropionamide (5.8 g, 0.065 mol) and ethyl chloroformate (7.1 g, 0.065 mol) were mixed at 30°. The reaction was complete in 5 min. Anhydrous ether (50 ml) was added to the liquid and allowed to stand overnight at 0°. The white crystals were filtered, washed with ether, and dried *in vacuo:* yield of **2**, 7.9 g (88%); mp 92°.

C. Ethyl Isobutyrimidate Hydrochloride (4).—Thioisobutyramide (2.0 g, 0.02 mol) and ethyl chloroformate (2.2 g, 0.02 mol) were allowed to react at 30°, with the reaction being completed in 10 min. The white crystalline mass was washed with anhydrous ether and dried *in vacuo:* yield of **4**, 1.4 g (45%); mp 82°.

D. Ethyl Benzimidate Hydrochloride (27).—Thiobenzamide (3.0 g, 0.022 mol) and ethyl chloroformate (2.7 g, 0.022 mol) were mixed at 30°. The reaction was complete in 30 min, and the resulting crystals were washed and dried as above: yield of **27**, 2.7 g (66%); mp 128° (lit.[4] mp 125°).

The ir spectrum was identical with that of **27** prepared from benzonitrile and ethanol by the method of Pinner.[4]

E. Ethyl N-Phenylacetimidate Hydrochloride (28).—Thioacetanilide (7.6 g, 0.05 mol) and ethyl chloroformate (5.4 g, 0.05 mol) were mixed at 40°, and the reaction was complete in 45 min. The solid product was washed with anhydrous ether, then with dry dioxane, and stored *in vacuo:* yield of **28**, 6.0 g (60%); mp 92–93° (lit.[15] mp 100°).

Anal. Calcd for $C_{10}H_{14}ClNO$: neut equiv, 199.7; Cl, 17.75; N, 7.01. Found: neut equiv, 206.0; Cl, 17.32; N, 6.89.

The compound was further characterized by identification of its hydrolysis products. To a sample of **28** was added an equimolar amount of H_2O, and the mixture distilled. The distillate was identified as ethyl acetate and the residue as aniline hydrochloride by comparison of their ir spectra with those of authentic samples.

Rate Studies.—The apparatus was the same as that used in the preparation of the imidate hydrochlorides, modified as follows. The dropping funnel was mounted on top of a side-arm adapter, the side arm of which was fitted with a delivery tube from a nitrogen tank. The condenser was cooled by pumping through it acetone from a Dry Ice–acetone mixture. (This was found necessary in order to prevent ethyl chloroformate from being swept out of the system by the nitrogen stream.) The delivery tube from the top of the condenser was attached to one stem of a three-way stopcock. To each of the other stems was attached a 150-mm absorption tube packed with indicating CO_2 absorbent.[16] This stopcock arrangement permitted selective absorption into either of the tubes. The propionamide used was Eastman Organic Chemicals No. 675, recrystallized three times from benzene (mp 79.5–80°).

In a typical experiment, the propionamide was placed in the flask and the system was purged with nitrogen for 1 hr. The weighed absorption tubes were attached, and the stopcock was turned so that the exit gases could pass through tube no. 1. The ethyl chloroformate was added from the dropping funnel, and the timer started. Stirring was continued throughout, and the water bath was maintained at 30 ± 0.1°. Nitrogen was allowed to flow through the system continuously to sweep out the CO_2 as formed.

After 15 min the stopcock was turned to close absorption tube no. 1 and open no. 2. Tube no. 1 was disconnected, weighed, and reconnected. This procedure was repeated every 15 min, alternating the gas flow through the two absorption tubes.

Registry No.—**5**, 18542-63-7; **10**, 18542-64-8; **12**, 18542-65-9; **13**, 18542-66-0; **14**, 18542-67-1; **15**, 18542-68-2; **16**, 18542-69-3; **17**, 18542-70-6; **18**, 18542-71-7; **19**, 18559-84-7; **20**, 18559-85-8; **21**, 18559-86-9; **22**, 18559-87-0; **23**, 18598-45-3; **24**, 18559-88-1; ethyl chloroformate, 541-41-3.

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