[Contribution from the Walker Chemical Laboratory of the Rensselaer Polytechnic Institute]

γ-Chloropropyl Imidobenzoate Hydrochloride[1]

By John B. Cloke and Frederick A. Keniston

The work reported herein was undertaken in order to ascertain the stability of γ-chloropropyl imidobenzoate hydrochloride (I) in water as a part of a general study of imine stability. This compound (I) was prepared, following the general method of Pinner,[2] by the interaction of trimethylene chlorohydrin, benzonitrile and dry hydrogen chloride in dry ether

$$C_6H_5CN + HOCH_2CH_2CH_2Cl + HCl \longrightarrow$$
$$C_6H_5C(=NH_2Cl)OCH_2CH_2CH_2Cl \quad (1)$$
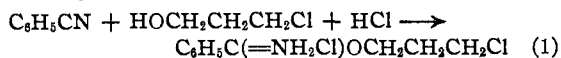
The dihydrochloride, which was also formed, was converted into the monohydrochloride by the exposure of the mixture to lime and soda lime in a vacuum desiccator.

The compound (I) reacts normally with water according to the monomolecular law to give ammonium chloride and γ-chloropropyl benzoate (II). Although other reactions also may occur, the isolation of (II) in a state of purity would indicate that these are unimportant. The data show that the immonium group of our compound (I) is decidedly more sensitive to saponification than is that of the propyl compound studied by Stieglitz and his associates[3] in their work on imido esters. The value of the affinity constant of the base is likewise in harmony with the Stieglitz generalization, namely, that the direction of such a reaction is that in which a weaker is converted into a stronger base.

When our hydrochloride (I) was heated it underwent pyrolysis according to the Pinner–Stieglitz reaction[4] to give benzamide and trimethylene chloride. Unfinished work indicates that γ-chloropropyl imidobenzoate (III) can be prepared by the usual method from the hydrochloride (I). However, (III) undergoes several reactions rather easily. Thus, it appears to rearrange to give γ-chloropropyl benzamide and μ-phenylpentoxazo-

line hydrochloride (IV), the latter of which in the presence of a base, such as (III), is converted into the base itself. Details of this work will be reported later.

Experimental Part

γ-Chloropropyl Imidobenzoate Hydrochloride.—Equimolar quantities of purified benzonitrile and trimethylene chlorohydrin[5] dissolved in dry ether were saturated with dry hydrogen chloride gas at 0° in a moisture-proof flask. When no more gas was being absorbed the inlet tube was connected to a drying tube and the solution allowed to stand overnight, whereby a hard crystalline mass separated. This was collected on a filter in a moisture-proof housing, washed with absolute ether and then transferred to a vacuum desiccator charged with lime and soda lime. At the end of a week under diminished pressure all of the excess hydrogen chloride was found to have been removed from the addition product. The compound was completely soluble in absolute alcohol, thus indicating freedom from ammonium chloride and therefore from water decomposition. The compound was also soluble in water, hot benzene, acetic acid and chloroform. It was insoluble in ether and only slightly soluble in carbon tetrachloride.

Anal. Calcd. for $C_{10}H_{13}ONCl_2$: N, 5.98. Found: N, 5.99, 5.97.

The compound melted at 116.2°. It decomposed to give trimethylene dichloride and benzamide, m. p. 127.5°.

Reaction Rate with Water.—The velocity with which the compound (I) reacted with water, $C_6H_5—C(=NH_2Cl)OCH_2CH_2CH_2Cl + H_2O = C_6H_5—CO—O—CH_2CH_2CH_2Cl + NH_4Cl$, was ascertained by the method of Stieglitz and Derby[6] for analogous compounds. This method is based upon the fact that an imido ester can be liberated from its hydrochloride by the action of sodium hydroxide and that the free ester is much more soluble in carbon tetrachloride than it is in water, whereas the reverse solubility behavior holds for ammonia. The reaction velocity constant, k, was calculated from the equation for a monomolecular reaction

$$k = \frac{2.303}{t_2 - t_1} \log \frac{v_1}{v_2}$$

where v_1 and v_2 represent the relative concentrations of the imido ester hydrochloride at times t_1 and t_2.

In the work which is recorded in the following tables, a 0.05 molar aqueous solution of the imido ester salt was prepared and maintained at a defin-

(1) This paper is an abstract of a thesis presented by Frederick A. Keniston to the Rensselaer Polytechnic Institute in June, 1927, as a part of the requirements for the degree of Chemical Engineer.

(2) Pinner, "Die Imidoäther und ihre Derivate," R. Oppenheim, Berlin, 1892.

(3) Stieglitz, *Rept. Int. Congress Arts Science, St. Louis*, **4**, 276 (1904); *Am. Chem. J.*, **39**, 29 (1908); Stieglitz with Derby, McCracken and Schlesinger, *ibid.*, **39**, 29, 166, 402, 437, 586, 719 (1908); Stieglitz, This Journal, **32**, 221 (1910); *ibid.*, **34**, 1687 (1912); *ibid.*, **35**, 1774 (1913); Carr, doctoral dissertation, University of Chicago, 1910.

(4) Pinner, *Ber.*, **16**, 355, 1654 (1883); Stieglitz, *Am. Chem. J.*, **21**, 101 (1899).

(5) Hultman, Davis and Clarke, This Journal, **43**, 369 (1921).

(6) Derby, *Am. Chem. J.*, **39**, 439–441 (1908).

ite temperature in a thermostat. Without delay a 25-cc. volume of the reacting solution was pipetted into a Squibb funnel which contained a carefully measured volume of 0.1 N sodium hydroxide and a suitable quantity of carefully purified carbon tetrachloride. At once the mixture was well shaken, the carbon tetrachloride layer was drawn off, and the extraction was repeated twice with fresh portions of this solvent. Finally the residual aqueous alkaline solution was titrated with 0.1 N hydrochloric acid. Table I gives the data for the first run.

TABLE I

Temp., 25°; t = time in minutes from moment of dissolving; v_b = volume of 0.1 N NaOH in cc.; v_a = volume of 0.1 N HCl.

t	v_b	v_a	$v_b - v_a$	k, min.$^{-1}$
5	8.28	3.73	4.55	...
22	8.28	4.13	4.15	(0.00541)
39	8.28	4.78	3.50	.00772
70	8.80	5.98	2.82	.00736
102	7.24	5.13	2.11	.00792
132	6.73	5.03	1.70	.00775
173	6.21	4.97	1.24	.00774

Av. k = 0.0077

Table II presents a summary of runs similar to that recorded in Table I. In those cases where the first value of the constant deviates significantly from the average, which also may be noted in the work of Stieglitz and his associates, this value has been excluded. Such values are enclosed in parentheses.

TABLE II

Run 2	3	4	5	6
Temp., °C. 25	25	0	0	0
Successive constants, $k \times 10^4$, min.$^{-1}$				
69.0	(116.0)	(5.95)	(9.74)	3.04
82.8	88.6	2.54	3.86	2.89
80.2	78.1	2.37	3.18	3.21
77.8	81.8	3.58	3.14	3.21
78.0	77.0	3.55	3.58	3.72
81.7	76.7	3.52	3.68	3.54
74.2		3.41		
		3.68		
Av. k 77.7	80.4	3.16	3.49	3.27

Grand average of 1, 2 and 3	0.00784
Grand average of 4, 5 and 6	0.000331

These data correspond to an activation energy of the order of 20,500 cal.

γ-Chloropropyl Benzoate.—The combined carbon tetrachloride solution obtained in the reaction velocity runs was extracted with dilute hydrochloric acid, dried over calcium chloride and distilled. The γ-chloropropyl benzoate distilled at

154–156° at 22 mm.: d^{22}_4 1.1672; n^{22}D 1.5136; MR_D (obsd.) 51.15; MR_D (calcd.) 51.30.

Anal. Calcd. for $C_{10}H_{11}O_2Cl$: Cl, 17.85; sap. equiv., 99.8. Found: Cl, 18.15; sap. equiv., 101.9.

After our work had been done, Kirner[7] described the preparation of this compound by another method.

Hydrolysis and Affinity Constants.—The Bredig conductivity method, which was used by Stieglitz and his associates in their work on the determination of the hydrolysis constants of the simpler imido ester salts, was contra-indicated in the case of our γ-chloropropyl imidobenzoate hydrochloride since the free ester is too unstable. Accordingly the hydrogen-ion concentration method was employed. For this purpose the quinhydrone electrode was found to be satisfactory. However, in order to use this method, it was necessary to take simultaneous time–potential readings and to extrapolate the practically linear values to the time of the preparation of the solution in order to get the pH of the undecomposed imido ester salt solution. A similar method had been used by Pring[8] for other bases.

In the present work the proper quantity of the imido ester salt was dissolved at a noted time in saturated quinhydrone solution at 25°. The solution was then poured into a special electrode vessel in a 25° bath, a saturated calomel cell was joined to the system, when the potential readings were taken on a Type K Leeds and Northrup potentiometer at regular intervals. The pH was calculated from the equation

$$pH = (0.4526 - E_c)/0.0591$$

Table III gives the significant data.

TABLE III

v = the volume of solution containing one mole of salt; E_c = extrapolated potential; K_h = hydrolysis constant.

v	E_c	pH	$C_H \times 10^4$	% Hydrolysis	$K_h \times 10^6$
32	0.2446	3.52	3.02	0.966	2.92
32	.2447	3.52	3.02	.966	2.92
32	.2447	3.52	3.02	.966	2.92
64	.2338	3.70	2.01	1.29	2.59
64	.2340	3.70	2.01	1.29	2.59
64	.2342	3.69	2.04	1.31	2.67
128	.2234	3.88	1.32	1.69	2.23
128	.2231	3.88	1.32	1.69	2.23
128	.2234	3.88	1.32	1.69	2.23
256	.2165	3.99	1.02	2.51	2.56
256	.2138	4.04	.912	2.33	2.12
256	.2149	4.02	.955	2.44	2.33

Av. K_h 2.53 × 10^{-6}

(7) Kirner, THIS JOURNAL, **48**, 2745 (1926).
(8) Pring, *Trans. Faraday Soc.*, **19**, 705–717 (1923).

The ionization constant of the base, K_b, may be computed from the well-known expression, $K_b = K_w/K_h$, whence we obtain $K_b = 1.02 \times 10^{-14}/2.53 \times 10^{-6} = 4.03 \times 10^{-9}$. This value is in harmony with the work of Stieglitz and his associates on related compounds.

Summary

γ-Chloropropyl imidobenzoate hydrochloride has been synthesized in order to compare its stability in water with that of the propyl compound studied by Stieglitz. The value of 0.00784 for the reaction velocity constant of our compound at 25° shows that γ-chlorosubstitution in the propyl group has an accelerating effect on the saponification of the imino group. The affinity constant of the base has also been ascertained. Work on a number of related compounds will be reported later.

TROY, N. Y.   RECEIVED OCTOBER 13, 1937

Alkylation of Reactive Methylene Groups with Alkyl Sulfates

BY EVERETT BOWDEN

The alkylation of compounds containing reactive methylene groups has almost always been carried out using alkyl halides; alkylations by methyl and ethyl sulfate have been very largely confined to phenols, amines, and acids. The practicability of effecting carbon to carbon alkylations by alkyl sulfates seems to have been largely overlooked. Thus, of the compounds mentioned below only benzoylacetone[1] and malonic ester[2] seem to have been alkylated by alkyl sulfates, and the yields were not reported. We have carried out a series of carbon to carbon alkylations and the results indicate that these reactions can be effected as satisfactorily with alkyl sulfates as with alkyl halides, and cheaper. (The higher boiling point of the alkyl sulfates is also advantageous, since it permits a higher reaction temperature.) Acetoacetic ester, camphor and cyanacetic ester were alkylated to the corresponding monoethyl derivative with yields of 87, 45, and 75% as compared to yields of 82,[3] 50,[4] and 74%[5] as reported in the literature.

Malonic ester was methylated in alcohol using sodium ethoxide and methyl sulfate. Malonic ester, acetoacetic ester, ethyl acetoacetic ester, benzoylacetone and cyanoacetic ester (two alkylations, mono- and dialkylated) were ethylated by diethyl sulfate and sodium ethoxide in alcohol. Phenylacetic ester was alkylated by ethyl sulfate using sodium in ether. Benzyl cyanide, butyl cyanide, acetophenone, isobutyl methyl ketone and camphor were alkylated using diethyl sulfate and sodamide in an inert solvent. For the sake of brevity only two preparations are described in this paper.

Alkylation of Benzyl Cyanide.—Eleven grams of sodamide was suspended in 125 ml. of dry ether. Twenty-nine grams of benzyl cyanide was added over a period of one hour. Ammonia was evolved and the mixture boiled gently under reflux. The flask was warmed for another fifteen minutes, then 38 g. (0.25 mole) of diethyl sulfate added drop by drop, each addition producing a violent reaction. The addition required one-half to three-quarters of an hour. Cooling was required and much ammonia was evolved. Fifty ml. of dry ether was added to the heavy sludge, and the mass allowed to stand overnight. Most of the ether was then distilled with stirring, the residue was dissolved in water, the oil separated and the aqueous layer extracted twice with ether. The combined oil and ether were washed once with water and fractionated: yield 33 g., b. p. 105–106° at 8 mm. (89% of calcd.) of α-phenylbutyronitrile.

Preparation of Diethyl Acetonitrile.—Eighty-one grams (1.00 mole) of ethyl cyanoacetate was dissolved in an equal volume of very dry ethanol; then 154 g. (1.00 mole) of diethyl sulfate was added. This was followed in the cold by 46 g. (2.00 mole) of sodium dissolved in 400 ml. of absolute alcohol. Another mole of diethyl sulfate was then added in portions.

The contents of the flask were next subjected to slow distillation, the last of the alcohol being removed *in vacuo*. The residue was dissolved as well as possible in a small quantity of water, the mixture stirred in the cold one to two hours, while a cold concentrated solution of 55 g. of sodium hydroxide in water was slowly dropped in, the volume of the mixture being maintained at 200–300 ml. When solution was practically complete, the mixture was extracted with benzene, acidified with excess hydrochloric acid, again extracted thoroughly with benzene. This benzene was distilled and the oily residue decarboxylated in the same apparatus, followed by fractionation: yield 60 g.; b. p. 142–146° (60% of the theoretical, over the entire reaction).

Conclusion

Alkylation of various representative compounds containing reactive methylene groups has been carried out satisfactorily using methyl and ethyl sulfates.

MADISON, WIS.   RECEIVED NOVEMBER 22, 1937

(1) Auwers, *Ber.*, **45**, 996 (1912).
(2) Nef, *Ann.*, **309**, 188 (1899).
(3) Conrad-Limpach, *ibid.*, **192**, 155 (1878).
(4) Haller and Louvier, *Ann. chim.*, [9] **9**, 190 (1918).
(5) Hessler, *Am. Chem. J.*, **22**, 170 (1899).