diphenylethylene, styrene, methylphenylacety-
lene and trimethylphenylallene at temperatures

ranging from 130 to 300°.

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The Removal of Hydrogen and Acid Radicals from Organic Compounds by Means of Bases. I. The Removal of Hydrogen Chloride from Ald-chlorimines by Sodium Hydroxide. Rates of Reaction in Alcoholic Solution[1]

BY CHARLES R. HAUSER, JOHN W. LEMAISTRE AND A. E. RAINSFORD

Recently, several independent workers have suggested that in the removal of HX (where X is halogen, acetate, etc.) from certain organic compounds by means of bases, a proton is removed first, followed by the release of X with a complete octet of electrons. This mechanism has been proposed by Drake and McElvain[2] for the removal of hydrogen bromide from ethyl β-bromopropionate in the presence of piperidine, and by Mills[3] for the removal of acetic acid from β-aldoxime acetates in the presence of alkali. It has been suggested[4] that the removal of hydrogen chloride from ald-chlorimines by various bases also follows this course.

This mechanism appears to be a satisfactory hypothesis for classifying a number of reactions brought about by bases. The removal of HX from various compounds which may be regarded as belonging to the type $:\ddot{A}:\ddot{D}:$ or $:A::D:$, where $\ddot{H}:\ddot{X}:$ $\ddot{H}:\ddot{X}:$

A and D are carbon, nitrogen or oxygen, in the presence of a base B, might be represented by the general equation[5]

$$:\ddot{A}:\ddot{D}: + B \longrightarrow :\ddot{A}:\ddot{D}:^- + BH^+$$
$$\ddot{H}:\ddot{X}: \qquad\qquad :\ddot{X}:$$
$$\downarrow$$
$$:\ddot{A}::\ddot{D}: + :\ddot{X}:^-$$

Several examples have already been mentioned.[6] Alkali removes HX from compounds of the type RCH=NX, where X is halogen, acetate, 2,4-dinitro-,[7] or 2,4,6-trinitrophenoxy.[8]

In this paper are reported the results of a study of the rates of reaction of ald-chlorimines with sodium hydroxide in which the yields of nitriles are practically quantitative. Bimolecular velocity constants have been determined at 0° for seventeen chlorimines in 92.5% alcohol and for four chlorimines in a 50% dioxane–water mixture. Constants have been determined also at 30° for five chlorimines in 92.5% alcohol, and the temperature coefficients and heats of activation for the reactions calculated.

Experimental

Solvents.—Commercial ethyl alcohol (95% by volume) was distilled through a four-bulb fractionation column. The portion boiling at 78.1 ≠ 0.02° was used in this work. This solvent contained 92.5% ethyl alcohol by weight: d^{20}_4 0.8111.

Commercial dioxane was distilled through a four-bulb column. The fractions freezing below 11.0° were rejected. The distilled product (f. p. 11.0–11.2°) was mixed with an equal weight of water to give the 50% dioxane used in this work.
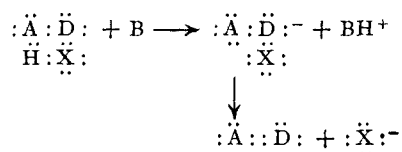
(1) This paper is in part from a thesis presented by J. W. LeMaistre in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Duke University.

(2) Drake and McElvain, THIS JOURNAL, **56**, 699, 1810 (1934). It is stated in a note of a paper by Noller and Dinsmore [*ibid.*, **54**, 1032 (1932)] that a referee suggested that the removal of hydrogen bromide from alkyl bromides by pyridine may consist of the incipient withdrawal of a hydrogen ion, which would promote the liberation of halide ion. Very recently, Olivier [*Rec. trav. chim.*, **53**, 1093 (1934)] has proposed a similar mechanism for the removal of hydrogen halide from ethylene dibromide and other aliphatic halides in the presence of alkali. See also, Michael, THIS JOURNAL, **42**, 818 (1920). A similar mechanism has been used to explain the alkaline hydrolysis of certain sulfonamides and the decomposition of quaternary ammonium hydroxides. See Ingold and co-workers, *J. Chem. Soc.*, 1305 (1926); 997 (1927); 526 (1933).

(3) Mills, *J. Soc. Chem. Ind.*, **51**, 750 (1932). For complete mechanism see original paper.

(4) Hauser and Moore, THIS JOURNAL, **55**, 4526 (1933), and A. G. Gillaspie, M.A. Thesis, Duke University, 1930.

(5) A similar concept may be applicable to the removal of HX from compounds of the type H   where A is carbon or nitrogen.
$:\ddot{A}:\ddot{X}:$

(6) Verhoek [THIS JOURNAL, **56**, 576 (1934)] has suggested that the trichloroacetate ion decomposes to form CO_2 and $(CCl_3)^-$, and that the latter reacts with water to form chloroform. On this basis, the reaction of trichloroacetic acid with a base might be regarded as involving the removal of HX, where X is CCl_3. Likewise, the removal of chloroform from compounds of the type $RC(CCl_3)=NH$ by potassium hydroxide [Houben and Fischer, *Ber.*, **66**, 339 (1933)] might be regarded as involving the removal of HX. (As suggested by a referee, however, CCl_3COOH might be hydrolyzed by NaOH to form $CHCl_3$ and $NaOCOONa$ just as CBr_4 is hydrolyzed to form $CHBr_3$ and NaOBr.)

(7) Brady and Truszkowski, *J. Chem. Soc.*, **125**, 1087 (1924).

(8) Brady and Klein, *ibid.*, **127**, 844 (1925).

Preparation of Solutions.—Ald-chlorimines were prepared and purified as described previously.[9] Alcoholic solutions (0.0015–0.03 M) of these compounds were made up at 0° in a 250-cc. volumetric flask. Two 25-cc. samples were then withdrawn by means of a pipet and each run into a mixture of 10 cc. of acetic acid and 10 cc. of 10% potassium iodide solution. After diluting with water to 200 cc. the solutions were titrated with standard sodium thiosulfate using starch as indicator.

A stock solution (approximately 0.2 molar) of sodium hydroxide was prepared by dissolving clean sodium in 92.5% alcohol.[10] Solutions of sodium hydroxide (0.003–0.06 M) were made up from this and 92.5% alcohol at 0° in a 250-cc. volumetric flask. Two 25-cc. samples, after diluting each with water to 150 cc., were titrated with standard hydrochloric acid using phenolphthalein as indicator.

Solutions of chlorimines and of c. p. sodium hydroxide in 50% dioxane were analyzed in similar manner.

General Procedure.—The pipets used in this work were kept in a refrigerator at approximately 0°. The solutions were kept in an ice-bath at 0 ± 0.05°. The sodium hydroxide solution (200 cc.) was added to the equal volume of chlorimine solution which had been transferred to a liter flask, and the mixture shaken in the ice-bath. At intervals 50-cc. samples were analyzed for active chlorine as described above. During the early part of this work 500 cc. each of chlorimine and of sodium hydroxide solutions were prepared, 100-cc. samples of each analyzed, and the remainders of the solutions mixed. Samples of 100 cc. were analyzed during the course of the reaction.

Results.—Although a slight excess of chlorimine was used in a few experiments, the concentration of the sodium hydroxide was usually about twice that of the chlorimine. In several cases after the completion of the reaction when tests for active chlorine were negative, the amount of base remaining was determined by titrating samples with standard acid. It was found in this manner that an amount of base equivalent to the chlorimine taken had been neutralized. It has been shown previously[11] that ald-chlorimines are decomposed by alkali to form nitriles in high yields. In this work 0.01 M alcoholic solutions of p-methoxy- and p-chloro-benzalchlorimines were decomposed by 0.02 M alkali at 0°, under conditions similar to those used in the rate measurements. The excess alkali was neutralized with carbon dioxide and the solvent evaporated. After drying, the residue was extracted with ether. The yields of the corresponding nitriles obtained were about 99% of the theoretical amounts.

Velocity constants have been calculated from the second order rate of reaction equation

$$K = \frac{1}{t(a - b)} \ln \frac{b(a - x)}{a(b - x)}$$

where k is the specific reaction rate constant in gram molecules per liter per minute.

(9) Hauser, Gillaspie and LeMaistre THIS JOURNAL, **57**, 567 (1935).

(10) Wegscheider has stated that the concentration of ethoxyl ion in alcoholic solutions containing over 5% of water is negligible [*Monatsh.*, **39**, 201 (1919)]. See also de Bruyn and Steger, *Rec. trav. chim.*, **18**, 41 (1899).

(11) Hauser and Gillaspie, THIS JOURNAL, **52**, 4518 (1930); see also Reference 4.

Two sets of measurements have been made with each chlorimine using different concentrations of reactants in each case. The data and velocity constants obtained with a representative chlorimine are given in Table I.

TABLE I

p-METHOXY-BENZALCHLORIMINE IN 92.5% ALCOHOL AT 0°

	Concn. NaOH, M	Concn. chlorimine, M	Initial HCl titer
Expt. 1	0.02868	0.0128	52.82 cc. (0.0543 N)
Expt. 2	.02313	.01212	48.00 cc. (.0482 N)

Time, min.	Expt. 1 0.0505 N Na$_2$S$_2$O$_3$, cc.	K	Time, min.	Expt. 2 0.0485 N Na$_2$S$_2$O$_3$, cc.	K
0	50.70	..	0	50.00	..
10	48.75	0.287	15	45.40	0.286
30	40.10	.286	45	37.95	.284
60	32.50	.284	75	32.00	.287
100	25.05	.279	105	27.80	.274
140	19.75	.281	135	24.10	.278
180	15.88	.280	165	20.90	.280
220	12.75	.279	195	18.50	.277
	Average	.282		Average	.282

Total average 0.282

Velocity constants have been determined also for the reactions of five chlorimines with sodium hydroxide in 92.5% alcohol at 30 ± 0.05°. The temperature coefficients and heats of activation Q have been calculated from the data obtained. The results are given in Table II. These heats of activation appear to be the same within the probable experimental error.

TABLE II

TEMPERATURE COEFFICIENTS AND HEATS OF ACTIVATION OF ALD-CHLORIMINES WITH SODIUM HYDROXIDE IN 92.5% ALCOHOL

Chlorimine	Q	K_{35}/K_{25}
Benzal-	20,000 cal.	2.99
4-Methoxybenzal-	20,060	3.01
4-Chlorobenzal	20,230	3.03
3,4-Methylenedioxybenzal-	20,550	3.09
Cinnamal-	19,940	2.97

The rates of reaction of four representative chlorimines with sodium hydroxide have been measured also in 50% dioxane at 0°. Since the end-points in this solvent were rather vague and difficult to determine precisely, the velocity constants obtained were reproducible to within only ± 2–5%. These constants and the ones obtained for the same chlorimines in 92.5% alcohol together with values obtained for two chlorimines in 80% alcohol, are arranged in ascending order in Table III. Although of different magnitudes these constants are in the same relative order in these three different solvents. This agreement of order

is all that was expected and strengthened the opinion that the rates of reaction in alcohol are comparable with one another, at least, when there is a significant difference between them.

TABLE III

BIMOLECULAR CONSTANTS FOR CHLORIMINES IN 92.5% ALCOHOL, IN 50% DIOXANE AND IN 80% ALCOHOL AT 0°

Substituted benzalchlorimine	K in 92.5% alc.	K in 50% dioxane	K in 80% alc.
2-Methoxy-	0.170	0.29	...
4-Methoxy-	.282	.30	0.240
4-Chloro-	2.80	1.70	2.36
2-Chloro-	7.70	3.70	...

The average values of the velocity constants, obtained for 17 chlorimines in 92.5% alcohol at 0°, are arranged in the order of their magnitudes in Table IV. In general, these constants were reproducible to within ±1-2%, except in a few cases where the rates were exceptionally high; the latter were reproducible to within about ±4-6%. The rates for benzal- and furfuralchlorimines, which have been obtained only 80–85% pure, were determined in the presence of 15–20% of the corresponding aldehydes. It is probable, however, that the presence of the impurity had no appreciable effect upon their rates of reaction with the base under the conditions employed, since p-methoxybenzalchlorimine, when mixed with an equivalent amount of the corresponding

TABLE IV

RATES OF REACTION OF R—CH=NCl WITH NaOH IN 92.5% ALCOHOL AT 0°

|	R	Bimolecular const. K	K_a of RCOOH × 10[5]	I. D. T.[a] °C.
1	2-Methoxyphenyl-	0.170	8.0	172
2	4-Methoxyphenyl-	.282	3.1	163
3	β-Phenylvinyl-	.348	3.8	120
4	3,4-Methylenedi-oxyphenyl-	.401	4.5	170
5	4-Methylphenyl-	.520	4.3	178
6	Phenyl-	1.00	6.1	170
7	3-Methoxyphenyl-	1.10	8.8	177
8	β-(2-Nitrophenyl)-vinyl-	1.31	...	124
9	2-Methylphenyl-	2.67	12.2	...
10	4-Chlorophenyl-	2.80	9.1	195
11	3-Nitro-4-methoxy-phenyl-	5.8	19.0	168
12	3-Chlorophenyl-	6.1	15.0	215
13	2-Chlorophenyl-	7.7	130.0	215
14	3-Nitrophenyl-	31.7	30.0	213
15	2-Furyl-	38.0	71.0	165
16	4-Nitrophenyl-	78.0	39.0	213
17	2-Nitrophenyl-	540.0	700.0	180–200

[a] Instantaneous decomposition temperature of chlorimines.[9]

aldehyde, gave a constant identical with the one obtained when the pure chlorimine was used.

Discussion

In addition to the velocity constants for the chlorimines, there are listed in Table IV the ionization constants of the corresponding acids, and the instantaneous decomposition temperatures of the chlorimines. It is considered that the latter values represent the approximate relative thermal stabilities of these compounds. Although hydrogen chloride can be removed from ald-chlorimines by heat alone[9] it can be seen from Table IV that their rates of reaction with sodium hydroxide are apparently independent of their thermal instabilities. In fact, several of the chlorimines which have relatively high instantaneous decomposition temperatures have also relatively high velocity constants, being decomposed by the base more rapidly than others which are thermally more unstable. Hence the reaction with the base evidently does not consist of the spontaneous (thermal) decomposition of the ald-chlorimines, followed by the neutralization of the hydrogen chloride that would be produced.

It has been suggested[4] that a proton is removed first from an ald-chlorimine by the action of the base, followed by the removal of chlorine with a complete octet of electrons. This might be represented as follows

$$RCH=NCl + B \xrightarrow{\ I\ } (RC=NCl)^- + BH^+$$
$$\downarrow II$$
$$RCN + Cl^-$$
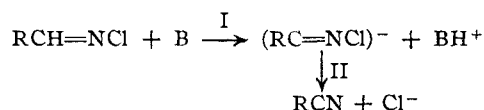
The fact that second order constants are obtained indicates that I is the rate-determining step[12] and that II is relatively fast. According to Brönsted's definition of an acid and base, it may be regarded that the ald-chlorimines function as extremely weak acids.[13]

Although there is no conclusive evidence in favor of this mechanism, it satisfactorily accounts for the following experimental facts. First, the rate of reaction of an ald-chlorimine with sodium hydroxide is proportional to the concentration of

(12) There seems to be a possibility that the reaction measured is the rate of formation of a coördination complex between the aldehydic hydrogen atom of the ald-chlorimine and the base, thus (Cl—N=CR—H ◄—— :OH⁻). In any event it would appear that the aldehydic hydrogen is primarily involved in the reaction.

(13) Conant and Wheland (THIS JOURNAL, 54, 1212 (1932)), have shown that the reaction (RH + R'K ——► RK + R'H) in which a hydrocarbon functions as an acid, requires as long as a month in certain cases for practical completion. They found, however, no real parallelism between the rates of reaction and the acidic strengths of the hydrocarbons.

the base as well as to that of chlorimine (second order reaction), and the decomposition of an ald-chlorimine with a series of bases[4] (amines) in benzene solution is more rapid the stronger the base used. Second, it can be seen from Table IV that, with the exceptions of the ortho compounds (Nos. 1, 9, 13, 15), the rates of reactions of the ald-chlorimines (RCH=NCl) with sodium hydroxide are, in general, in the same relative order as the ionization constants of the corresponding carboxylic acids (RCOOH). Because of the proximity of the ortho substituents to the aldehydic hydrogen atom of the ald-chlorimines the abnormally low constants obtained for the ortho compounds might be attributed to a so-called "steric hindrance" factor.

It would seem unlikely that chloride ion is removed first from the ald-chlorimines in the presence of cold alkali, since keto-chlorimines (RCR=NCl) as well as most other nitrogen–chlorine compounds which possess no active hydrogen, show practically no tendency to release chloride ion under similar conditions. On the contrary, these compounds[14] undergo hydrolysis to form hypochlorous acid, in which the halogen is removed presumably with only a sextet of electrons.[15] It has been shown that the rate of hydrolysis of a keto-chlorimine is very much slower than the rate of removal of hydrogen chloride

(14) Slosson [Am. Chem. J., **29**, 289 (1903)] showed that certain N-substituted halogen amides (RCONR–Hal) were hydrolyzed by alkali to form RCONRH.

(15) See Sidgwick, "Electronic Conception of Valence," 1927, p. 158.

from an ald-chlorimine.[4] In fact, the latter reaction probably takes place only because it is so much faster than the hydrolysis of the (N–Cl) bond. This seems best explained by the mechanism suggested, for the removal of chlorine from nitrogen with a complete octet of electrons should be considerably facilitated by the presence of a negative charge on the molecule to which the chlorine is attached. It is well known that halide ion is removed more readily from the sodium salt of a halogen amide, $(RCONHal)Na$, or from its negative ion, $(RCONHal)^-$, than from the corresponding halogen amide itself.

The writers wish to express their indebtedness to Dr. Douglas G. Hill for the valuable suggestions concerning the kinetics of the reactions studied.

Summary

1. Second order velocity constants have been determined for the reaction of sodium hydroxide with seventeen ald-chlorimines in 92.5% alcohol. The constants for four chlorimines have been determined also using as solvent a 50% mixture of dioxane and water.

2. The temperature coefficients and heats of activation of five ald-chlorimines with alcoholic sodium hydroxide have been determined.

3. A general mechanism has been discussed for the removal of HX from organic compounds in the presence of bases with special reference to the removal of hydrogen chloride from ald-chlorimines.

DURHAM, N. C.   RECEIVED DECEMBER 31, 1934

Some Organic Mercurials

BY MERRILL C. HART AND HANS P. ANDERSEN

Previous work on alkyl mercury derivatives[1] in which mercury is attached to oxygen has shown that variations in structure have a very limiting influence on the bacteriostatic properties of the resulting compounds. In the present investigation the study was extended to include compounds in which mercury is linked to the carbon of the benzene ring.

Variations in properties with different structures have been reported. Some authors[2] have

(1) Hart and Andersen, THIS JOURNAL, **56**, 2752 (1934).

(2) Caius, Kamat and Naidu, Indian J. Med. Res., **15**, 327 (1927).

tried to explain this on the basis of mercury percentage in the particular compounds. Others[3] have attributed the properties to substituents in the molecules and the positions in which they occur. For example, nitro, halogen and alkyl groups have been said to enhance the bacteriological properties. In this research these groups were not found to be particularly effective. A number of different types of compounds were prepared and our studies indicate that the euthera-

(3) Schoeller and Schrauth, Z. Hyg. Infektionskrankh., **70**, 24 (1911); Henry, Sharp and Brown, Biochem. J., **19**, 513 (1925); Raiziss and Severac, J. Lab. Clin. Med., **9**, 71 (1923).