thermal decomposition of these organic compounds leads to radical production. The experiments of Rice and collaborators suggest that they are formed. If this is so, the present experiments support the chain mechanism of the thermal decomposition of dimethyl ether.

One thing further might be deduced from the present study and from the work on acetaldehyde.[2] Norrish[7] has expressed the opinion that the primary act in the photolysis of aldehydes is of a different type than that which occurs with ketones. The work on acetaldehyde definitely disproves this. Norrish also considers that the fractional quantum yields found for ketones are due to a new type of predissociation. This explanation is not necessary, although it may be correct. The facts can be satisfactorily accounted for by assuming a simple recombination of the radicals liberated on the absorption of light.

Acknowledgment.—I wish to express my thanks to the National Research Council for the Fellowship which has enabled me to carry on the researches undertaken the past two years, and to the Chemical Laboratory of Harvard University for the facilities which have been extended to me during this time.

I am much indebted to Professor G. B. Kistiakowsky for the advice, help and time he has given me during my stay at Harvard.

Summary

1. Studies of the high-temperature photolysis of acetone have shown that methyl radicals do not initiate a chain decomposition of the acetone at temperatures below 400°.

2. The acetone-sensitized photo-decomposition of dimethyl ether has been investigated over a range of pressures, temperatures and light intensities. The rate of decomposition of the ether was proportional to the square root of the absorbed light and to the first power of the ether concentration; it was inversely proportional to the square root of the acetone concentration. The rate constant was found to be $10^4\ e^{-16,000/RT}$, moles$^{1/2}$, einsteins$^{-1/2}$, sec.$^{-1/2}$. Chain lengths of the ether decomposition were as great as 230 molecules decomposed per quantum of light absorbed.

3. Possible mechanisms of the acetone and of the ether decomposition have been discussed.

4. Diethyl ether was found to decompose in the presence of methyl radicals, with chains about one-tenth as great as those observed for dimethyl ether resulting.

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Velocity of Hydrolysis of Stereoisomeric Hydrazones and Oximes

BY RAYMOND WRIGHT JOHNSON[1] AND JULIUS STIEGLITZ

Although some data have been obtained on the rates of formation of hydrazones and oximes by the reaction of ketones with hydrazine and hydroxylamine, respectively, no information has been available concerning the rates with which the hydrolysis of these compounds proceeds.

The present investigation is the first of a series in which a study is being made to determine whether any essential differences in the rates of hydrolysis of the respective members of pairs of stereoisomeric hydrazones and oximes can be detected. It includes the search for possible differences in rates of hydrolysis due to other types of stereochemical influences. It is hoped that by such studies a deeper insight into the mechanism of hydrolytic decompositions may be obtained than has thus far been developed.

The purpose of this first of the series of studies was to obtain a method for the determination of such rates and to apply it to the determination of the relative rates of hydrolysis of benzophenone hydrazone and oxime and the individual pairs of stereoisomeric hydrazones and oximes of *p*-methoxybenzophenone. The method described, although empirical, yielded this information.

Preparation of Materials

Benzophenone Hydrazone.—This compound was prepared from benzophenone and hydrazine hydrate by the method of Curtius and Rauterberg;[2] m. p. 98–99°.

***p*-Methoxybenzophenone.**—This compound was prepared by the Friedel–Craft reaction according to the method of Gattermann, Ehrhardt and Maisch;[3] m. p. 62°.

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[1] From the dissertation of R. W. Johnson, presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy, August, 1932.

[2] Curtius and Rauterberg, *J. prakt. Chem.*, **44**, 194 (1891).

[3] Gattermann, Ehrhardt and Maisch, *Ber.*, **23**, 1204 (1890).

α- and β-*p*-Methoxybenzophenone Hydrazones.—A mixture of these two stereoisomeric compounds was prepared and separated by a modification of the method of Stieglitz and Chuang.[4] A solution of *p*-methoxybenzophenone (40 g.) in absolute ethyl alcohol (40 cc.) was added slowly, with stirring, to a mixture which consisted of barium oxide (28 g.), hydrazine hydrate (45 cc. of 50%, Kahlbaum) and absolute ethyl alcohol (14 cc.). After the first vigorous reaction had subsided, the mixture was refluxed on a steam-bath, with stirring, for forty-three hours. The mixture was diluted with ether and filtered. Evaporation of the ether and alcohol produced 39.1 g. of a yellow solid mixture of the two stereoisomeric compounds; m. p. 55–65°. The two pure forms were separated by the slow fractional crystallization of the crude mixture from xylene–ligroin (b. p. 40–50°) solutions. The α form was always present in much the larger amounts. The α form melted at 95–96°.

Anal. Calcd. for $C_{14}H_{14}ON_2$: N, 12.39. Found: N, 12.34, 12.46.

The β form melted at 84–85°.

Anal. Calcd. for $C_{14}H_{14}ON_2$: N, 12.39. Found: N, 12.51, 12.50.

Benzophenone Oxime.—This compound was prepared by the method of Fischer.[5]

α- and β-*p*-Methoxybenzophenone Oximes.—A mixture of the two stereoisomeric forms of this compound was prepared by the method of Hantzsch.[6] The melting point of the mixture was 116–120°. The two forms were separated by the slow fractional crystallization of acetic acid–water solutions of the mixture. The final purification of each form was effected by recrystallization from carbon tetrachloride–ligroin solutions. The α form had a melting point of 137–138°. The β form melted at 116.5°.

Anal. Calcd. for $C_{14}H_{13}O_2N$: N, 6.17. Found: N, (α form), 6.20, (β form), 6.26.

Methods

Choice of Solvent for Hydrazone Rate Work.—Experiments with benzophenone hydrazone showed that in alcohol–hydrochloric acid solutions the hydrazone is in part converted into diphenylketazine, $(C_6H_5)_2C{=}N{-}N{=}C(C_6H_5)_2$. The extent of the ketazine formation was found to be roughly inversely proportional to both the acidity and the temperature of the solution. Of the group of alcohols, methyl, ethyl, propyl, isopropyl and tertiary butyl alcohol, the ketazine formation was retarded most when propyl alcohol was used. However, it was found that ketazine formation could best be avoided by the use of an approximately 0.0255 *M* solution of the hydrazone in a mixture of equal volumes of glacial acetic acid and hydrochloric acid (0.6344 *N* or more concentrated). This was the solvent used in all of the rate work on hydrazones.

Analytical Determination of Hydrazine.—The method used for the determination of the rates of hydrolysis of the hydrazones involved the determination of the amount of hydrazine present in samples of the hydrolyzing mixture. For this determination the method described by Jamieson,[7] and tested by Kolthoff[8] was used. This method involves the titration of the hydrazine by means of standard potassium iodate solution in the presence of hydrochloric acid and a little chloroform. Tests showed that with 25-cc. samples of a solution of hydrazine in acetic acid–hydrochloric acid (mixtures such as were used in the rate work) a volume of concentrated hydrochloric acid of between 26 and 30 cc. when used in the determination of the hydrazine produced quantitative results.

Extraction Method for Hydrazone Work.—In the method decided upon for the determination of the rates of hydrolysis of hydrazones the unhydrolyzed hydrazone and the ketone present in a sample of a hydrolyzing mixture were to be extracted by means of chloroform, followed by the titration of the hydrazine in the aqueous layer. Therefore it was necessary to investigate the extent of the extraction of hydrazine by the chloroform. Samples (25 cc.) of a hydrazine solution (0.0255 *M*), composed of hydrazine hydrochloride dissolved in a mixture of equal volumes of glacial acetic acid and hydrochloric acid (0.6344 *N*), were used. These were extracted with 8 cc. and 6 cc. of chloroform, and, after the addition of 25 cc. of water, with two further 6-cc. portions of chloroform. The aqueous layer was rinsed into a glass-stoppered Erlenmeyer flask with 10 cc. of water, and, after the addition of 26 cc. of concentrated hydrochloric acid and 6 cc. of chloroform, was titrated with 0.018 *M* potassium iodate solution. The volume of the potassium iodate which should have been required if no hydrazone was extracted by the chloroform was 35.45 cc. The volumes required for two different samples were 35.35 and 35.34 cc. This proved that the error introduced by the extraction of hydrazine in this manner is not greater than 0.31%.

To test the quantitative efficiency of the extraction method with regard to the removal of the hydrazone the molar concentration of benzophenone hydrazone in a hydrolyzing mixture was determined as described above. The values of the term $\log A/(A - X)$ (in which A is the original concentration of the hydrazone and $A - X$ is the concentration at the end of a definite interval of time, ΔT) were plotted against time, ΔT. The straight line obtained was extrapolated back to zero time and the experimentally determined zero time concentration was compared with the known initial hydrazone concentration. The error in the determination was found to be 0.19%.

Method Used for Determination of Rates of Hydrolysis of Hydrazones.—The procedure followed in each of the runs summarized below was identical. The empirical nature of the method required that this be rigorously adhered to. A weighed quantity of hydrazone was dissolved in 235 cc. of glacial acetic acid (at exactly 25°) in a 500-cc. graduated flask. At a definite noted time exactly 250 cc. of hydrochloric acid (of known concentration and at exactly 25°) was added. The volume of the solution was quickly made up to 500 cc. by the addi-

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[4] C. Chuang, Abstracts of Theses, The University of Chicago, Science Series, Vol. III, 1924–1925, pp. 111–118.

[5] Fischer, "Anleitung zur Darstellung organ. Preparate," Braunschweig, 1908, p. 68.

[6] Hantzsch, *Ber.*, **24**, 54 (1891).

[7] Jamieson, *Am. J. Sci.*, **33**, 352 (1912).

[8] Kolthoff, THIS JOURNAL, **46**, 2009 (1924).

tion of glacial acetic acid. After it was thoroughly mixed, the solution was transferred to a dry 500-cc. Erlenmeyer flask which was placed in a thermostat at 25 ± 0.02°. From time to time a sample (25 cc.) of the solution was pipetted into a 150-cc. Squibb funnel (the stem of which had been ground off diagonally very close to the stopcock). Each sample was extracted with 8 cc. and then 6 cc. of chloroform, and this was followed by the addition of 25 cc. of water. The mixture was then further extracted with two 6-cc. portions of chloroform. Exactly two minutes was allowed between each of the extractions made on an individual sample. The aqueous layer, after the last extraction, was rinsed with 10 cc. of water into a 250-cc. glass-stoppered Erlenmeyer flask and 27 cc. of hydrochloric acid (*d* 1.19) and 6 cc. of chloroform were added to the mixture. The hydrazine in the solution was then titrated with potassium iodate solution. The time, ΔT, for each sample was taken as the interval between the time of the addition of the hydrochloric acid to the glacial acetic acid solution of the hydrazone (when the reaction mixture was prepared) and the time of the addition of the third portion of chloroform in the extraction of the particular sample. Values for K, the velocity constant, were obtained by the use of the equation for a first order reaction

$$K = \frac{2.303}{\Delta T} \log \frac{A}{(A - X)}$$

in which A is the calculated volume of standard potassium iodate solution, expressed in cc., required to titrate the hydrazine which would be liberated upon complete hydrolysis of 25 cc. of the hydrazone solution, and X is the volume, in cc., of the solution actually required to titrate a given sample withdrawn, etc., at the end of the interval of time, ΔT.

A typical set of data is given in Table I. The concentration of benzophenone hydrazone was 0.018 *M*. The concentration of hydrochloric acid in the reaction mixture was 0.4010 *N*. The concentration of the potassium iodate solution used was 0.01811 *M*.

TABLE I

VELOCITY OF HYDROLYSIS OF BENZOPHENONE HYDRAZONE

A = 24.85; temp., 25 ± 0.02°

ΔT, min.	X	$A - X$	% hydrolyzed	$K \times 10^4$
22	2.09	22.76	8.41	(39.95)
54	5.08	19.77	20.44	42.36
86	7.50	17.35	30.18	41.78
119	9.63	15.22	38.76	41.21
145	11.64	13.21	46.84	(43.59)
176	13.00	11.85	52.31	42.08
202	14.40	10.45	57.95	42.89
230	15.01	9.84	60.40	40.28

Order of the Reaction.—The hydrolysis of hydrazones proved to be a first order reaction by the following experiments. The rates of hydrolysis were determined for two solutions of benzophenone hydrazone of 0.015 and 0.03 *M* concentration, respectively, in glacial acetic–hydrochloric acid solution (0.3466 *N* with respect to hydrochloric acid). The average rates of hydrolysis for each (up to 60% of hydrolysis) were 39.05 × 10^4 and 39.17 × 10^4.

Analytical Determination of Hydroxylamine.—The method used for the determination of the rates of hydrolysis of the oximes involved the determination of the amount of hydroxylamine present in a sample of the hydrolyzing mixture. For this determination a modified form of the method described by Bray, Simpson and McKenzie[9] was used. The procedure adopted for this work was as follows. The hydroxylamine solution was boiled for ten minutes with a mixture consisting of 15 cc. of sulfuric acid (12 *N*) and 25 cc. of a ferric sulfate solution (57 g. $Fe_2(SO_4)_3 \cdot 9H_2O$ per liter of water to which 30 cc. of concentrated sulfuric acid is added). The boiled solution was cooled and made up to 200 cc. with water. The ferrous iron was then titrated with standard potassium permanganate solution. A blank was always run on a similar solution containing everything except the hydroxylamine. This was applied as a correction to all of the titration values. Tests showed that this procedure yielded quantitative results with acetic–hydrochloric acid solutions of hydroxylamine such as were used in the rate work.

Extraction Method for Oxime Work.—In the method used for the determination of the rates of hydrolysis of oximes the unhydrolyzed oxime and the ketone in a sample of a hydrolyzing mixture were extracted with chloroform, followed by the determination of the amount of hydroxylamine present in the aqueous layer. Tests showed that the error introduced by the extraction of hydroxylamine by the chloroform was not greater than 0.33%.

Method Used for the Determination of the Rates of Hydrolysis of Oximes.—The method as to solvent, procedure, etc., was identical with that described for the hydrazones up to the completion of the extraction of the undecomposed oxime and the ketone in a given 25-cc. sample. At this point the aqueous layer, which contained the hydroxylamine, was rinsed with 10 cc. of water into a wide-mouthed Erlenmeyer flask and the hydroxylamine was quantitatively determined by the method described above. The time, ΔT, for each sample was taken as the interval between the time of the addition of the hydrochloric acid to the glacial acetic acid solution of the oxime (when the reaction mixture was prepared) and the time of the addition of the third portion of chloroform in the extraction of the particular sample.

Values for K, the velocity constant, were obtained by substitution in the equation

$$K = \frac{2.303}{\Delta T} \log \frac{A}{(A - X)}$$

A is the calculated volume of the standard potassium permanganate solution which would be required to titrate the hydroxylamine which would be liberated upon complete hydrolysis of 25 cc. of the oxime solution. X is the volume of potassium permanganate solution (minus the blank) required for the titration of a given sample withdrawn at the end of the interval of time, ΔT. Typical data for one run are given in Table II. The concentration of benzophenone oxime was 0.04501 *N* (2.2178 g. per 500 cc.). The concentration of hydrochloric acid in the reaction mixture was 0.5880 *N*. The concentration of the potassium permanganate solution was 0.05323 *N*.

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[9] Bray, Simpson and McKenzie, THIS JOURNAL, **41**, 1366 (1919).

TABLE II

VELOCITY OF HYDROLYSIS OF BENZOPHENONE OXIME

$A = 21.14$; temp., 25 ± 0.02°

ΔT, min.	X	$A - X$	% hydrolyzed	$K \times 10^4$
134	2.84	18.30	13.43	10.77
193	3.97	17.17	18.78	10.78
248	4.91	16.23	23.23	10.66
297	5.78	15.36	27.34	10.68
339	6.45	14.69	30.51	10.74
380	7.09	14.05	35.54	10.75
574	9.70	11.44	45.88	10.70
626	10.28	10.86	48.63	10.64
683	10.94	10.20	51.75	10.67
1473	16.76	4.38	79.28	10.69

The fact that the reaction yields only the ketone and hydroxylamine was proved when the examination of the contents of completely hydrolyzed solutions yielded only these two substances.

Examination of Hydrolyzing Solution of the α-Form (Labile) of *p*-Methoxybenzophenone Oxime for the Presence of the β-Form (Stable).—The possibility that the labile form of the oxime might be converted to the stable form by the hydrochloric acid in the solvent mixture was recognized. The following experiment was performed in an attempt to find out whether or not such a change does occur. α-*p*-Methoxybenzophenone oxime (1.7 g.) was dissolved in 500 cc. of a mixture which consisted of equal volumes of glacial acetic acid and hydrochloric acid (0.9494 *N*). The temperature of the solution was held at 25° for seven hours. Hydrolysis of the oxime was approximately 20% complete at that time. Water (550 cc.) was added to the mixture. A previous test had shown that the addition of 500 cc. of water to 500 cc. of a completely hydrolyzed solution of this same original oxime concentration would just cause a faint milkiness due to the precipitation of the ketone. The crystalline solid which soon settled out was brought on a filter and dried; m. p. 133–134°. Inasmuch as the oximes are only slightly soluble in dilute acetic–hydrochloric acid mixtures, this precipitate must have been the α-form (m. p. 137–138°) contaminated with a little ketone or a very small amount of the β-form (m. p. 116.5°). An attempted fractional crystallization of the material only yielded the pure α-form.

Results

The average rates of hydrolysis for the hydrazones and oximes studied are given in Table III.

Discussion

The very small difference between the experimentally determined rates of hydrolysis of the two stereoisomeric forms of *p*-methoxybenzophenone hydrazone is rather surprising when compared with the much greater difference in the rates as found for the stereoisomeric *p*-methoxybenzophenone oximes. Further work will be done in this Laboratory on the rates of hydrolysis of hydrazones.

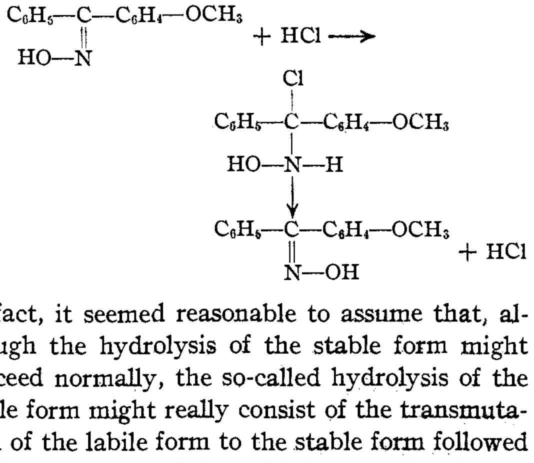
TABLE III

VELOCITY OF HYDROLYSIS OF HYDRAZONES AND OXIMES (25°C.)

Compound	Concn. of HCl in hydrolyzing solution, *N*	$K \times 10^4$
Benzophenone hydrazone	0.3010	33.69
Benzophenone hydrazone	.4010	42.68
α-*p*-Methoxybenzophenone hydrazone	.3010	25.98
β-*p*-Methoxybenzophenone hydrazone	.3010	25.13
α-*p*-Methoxybenzophenone hydrazone	.4010	34.26
β-*p*-Methoxybenzophenone hydrazone	.4010	33.00
Benzophenone oxime	.4747	9.34
α-*p*-Methoxybenzophenone oxime	.4747	6.28
β-*p*-Methoxybenzophenone oxime	.4747	8.25

In view of the fact that hydrochloric acid has been known to effect a transmutation of the labile form of a stereoisomeric oxime to the stable form of the same oxime, it was anticipated that such a transmutation might occur in the hydrochloric acid solutions used in this work. Such a transmutation might be represented as follows.

(1)



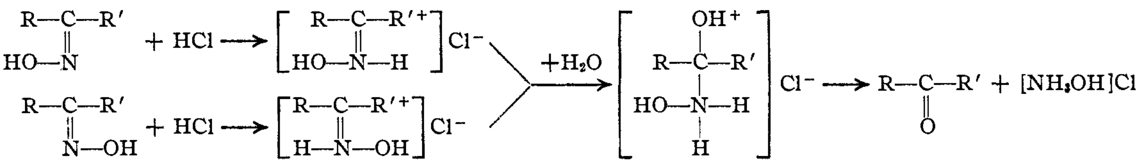
$$\begin{array}{l} C_6H_5-\underset{\underset{\displaystyle HO-N}{\|}}{C}-C_6H_4-OCH_3 + HCl \longrightarrow \\ C_6H_5-\overset{\overset{\displaystyle Cl}{|}}{\underset{\underset{\displaystyle HO-N-H}{|}}{C}}-C_6H_4-OCH_3 \\ \downarrow \\ C_6H_5-\underset{\underset{\displaystyle N-OH}{\|}}{C}-C_6H_4-OCH_3 + HCl \end{array}$$

In fact, it seemed reasonable to assume that, although the hydrolysis of the stable form might proceed normally, the so-called hydrolysis of the labile form might really consist of the transmutation of the labile form to the stable form followed by the hydrolysis of the stable form. If such were the case and if the transmutation were a very rapid reaction as compared with the hydrolysis of the stable form, the experimentally determined velocity constants for the two forms might be identical.

The fact that the experimentally determined rates of hydrolysis of the two forms of *p*-methoxybenzophenone oxime are distinctly different seems to be conclusive evidence that the reaction represented by (1) does not occur to any considerable extent. Additional evidence for the non-occurrence of (1) was found in the negative tests for the presence of the stable form in a partially hydrolyzed solution of the labile form. A consideration of the relative rates of hydrolysis of the two forms would indicate that if reaction (1) does occur there should be a considerable amount of the stable form, as compared with the amount of the labile form, present at any moment after zero time.

It was also recognized that a possible mechanism for the hydrolysis of the oximes might well consist of the addition of a molecule of hydrogen chloride and a molecule of water to each of the stereoisomeric forms of the oxime to form one and the same addition compound, followed by the breakdown of the intermediate with the production of a molecule of the ketone and one of hydroxylamine hydrochloride. This might be represented as in (2).

(2)



$$\underset{\mathrm{HO-N}}{\mathrm{R-\underset{\|}{C}-R'}} + \mathrm{HCl} \longrightarrow \left[\underset{\mathrm{HO-N-H}}{\mathrm{R-\underset{\|}{C}-R'^{+}}}\right]\mathrm{Cl^-}$$

$$\underset{\mathrm{N-OH}}{\mathrm{R-\underset{\|}{C}-R'}} + \mathrm{HCl} \longrightarrow \left[\underset{\mathrm{H-N-OH}}{\mathrm{R-\underset{\|}{C}-R'^{+}}}\right]\mathrm{Cl^-}$$

$$\xrightarrow{+\mathrm{H_2O}} \left[\begin{array}{c}\mathrm{OH^+}\\ |\\ \mathrm{R-C-R'}\\ |\\ \mathrm{HO-N-H}\\ |\\ \mathrm{H}\end{array}\right]\mathrm{Cl^-} \longrightarrow \mathrm{R-\underset{\underset{\displaystyle O}{\|}}{C}-R'} + [\mathrm{NH_3OH}]\mathrm{Cl}$$

In the event that this mechanism (2) were the true mechanism for the reactions, and in case the rates of the addition reactions were very rapid as compared with the rates of the breakdown of the intermediate, the rate of the breakdown would determine the rate of the reaction and the experimentally determined rates of hydrolysis of the two stereoisomeric forms of the oxime would be identical. The experimentally determined fact is that there is a difference in the rate of hydrolysis of the two forms of *p*-methoxybenzophenone oxime. This would indicate that the logical interpretation of the reaction would be that mechanism (2) is correct, but that the rate-determining step or slow reaction in the hydrolysis is the formation of the intermediate absorption compound by the addition of water and not the breakdown of this compound. If this conclusion is supported by the results of the studies of the rates of hydrolysis of other pairs of stereoisomeric oximes, it would represent an important contribution to the problem of hydrolytic decompositions of organic compounds. For many years the problem of whether the measurably slow reaction in such hydrolyses consists in the slow addition of water or in the slow breakdown of the addition product, or of both, has made little progress.[10] The hydrolysis of the stereoisomeric oximes may conform to the one type while the hydrolysis of the stereoisomeric hydrazones may conform to the other type. However, we have as yet no experimental evidence in the case of the hydrazones that the labile form does not pass over to the stable form prior to the hydrolysis. Critical evidence demands an extension of the present investigation over further pairs of stereoisomers both of the oximes and the hydrazones. This work is under way in this Laboratory.

Summary

1. Methods have been described whereby the kinetics of the hydrolysis of hydrazones and of oximes may be investigated.

2. A side reaction which produces a ketazine (R,R=C=N—N=C=R,R) was found to take place during the hydrolysis of hydrazones. It was found that this reaction may be held in check by an increase in the acidity of the hydrolyzing mixture.

3. Both the hydrolysis of hydrazones and that of oximes were found to be "pseudo" unimolecular reactions.

4. The velocity of hydrolysis of benzophenone hydrazone, of the stereoisomeric α- and β-*p*-methoxybenzophenone hydrazones, benzophenone oxime and of the stereoisomeric α- and β-*p*-methoxybenzophenone oximes were determined. Only a slight difference was found between the velocities of hydrolysis of the stereoisomeric *p*-methoxybenzophenone hydrazones. A considerable difference in the velocities was found to exist in the case of the stereoisomeric *p*-methoxybenzophenone oximes.

5. An examination of the contents of a hydrolyzing mixture which contained the labile form of *p*-methoxybenzophenone oxime yielded no evidence for the presence of the stable form of the oxime.

6. A theoretical interpretation of these relations is given, which, if substantiated by results extended over sufficient numbers of pairs of stereoisomers, may be expected to give critical evidence on moot questions in the problem of hydrolysis of organic compounds.

CHICAGO, ILLINOIS RECEIVED JULY 5, 1934

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[10] *Cf.* Stieglitz, *Am. Chem. J.*, **39**, 59 (1908).