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CHEMISTRY OF N-CHLOROSACCHARIN

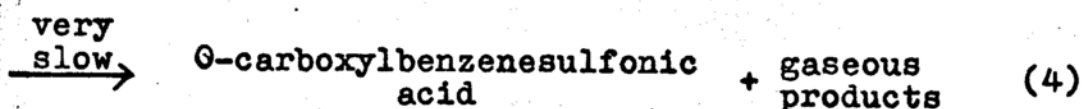
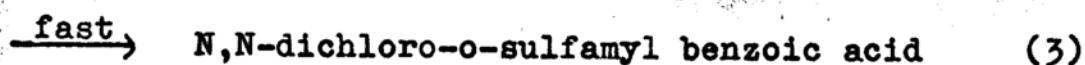
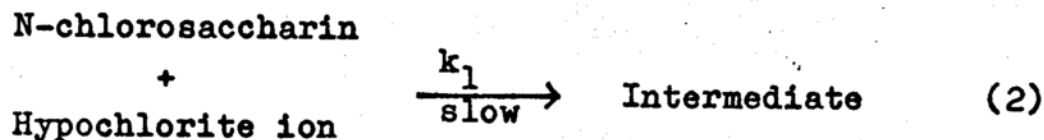
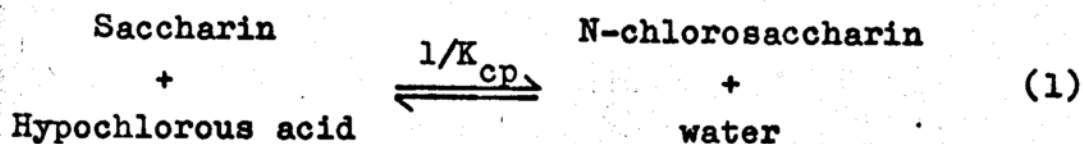
by HAN-SON DAWN

(Under the supervision of Professor Louis W. Busse)

Results of an investigation into the chemistry of N-chlorosaccharin and related positive chlorine species are described. Because of the strongly electron withdrawing nature of the groupings around the imide nitrogen in saccharin, its N-chloro derivative was expected to be extremely powerful chlorinating agent. Its chlorine potential in aqueous environment, its behavior in a variety of organic solvents, and its hydrolytic behavior in water have been studied as parts of this investigation.

In aqueous medium N-chlorosaccharin appears to be in dynamic equilibrium with saccharin and hypochlorous acid. The equilibrium constant for this reaction, K_{cp} , has been calculated from the equilibrium absorbance of the solution and the absorptivities of the species present in the solution. Its relatively high value ($K_{cp} = 1.4 \times 10^{-5}$ M) indicates that the positive chlorine on the chloroimide is readily available.

When excess amounts of hypochlorous acid were present the intact chloroimide was found to undergo successive hydrolytic cleavage. Based on reaction rate measurement and chromatographic identification of products the following reaction scheme was proposed.



The apparent rate constant, k_1 , for the cleavage of imide bond by hypochlorite ion was $1.8 \times 10^5 \text{ l mol}^{-1} \text{ sec}^{-1}$ over the pH range 4-6.

On the other hand, N-chlorosaccharin was found to be relatively stable in carbon tetrachloride, ethyl acetate, chloroform, acetone, and 1,4-dioxane to the extent that the ultraviolet spectra or positive chlorine content of the solution did not change for at least three hours after preparation. The solubilities in these solvents were 4.3, 85.1, 112.0, 173.0 and 287.0 gm/l, respectively. In methanol, however, N-chlorosaccharin rapidly converted to saccharin while the solution retained the same amount of positive chlorine. When water was added the rate of conversion increased linearly with respect to the amount

of water present. This is probably due to the occurrence of methanolysis and hydrolysis to form methylhypochlorite and hypochlorous acid, respectively, in aqueous methanol. The rate constants for methanolysis and hydrolysis estimated on this basis were $4.1 \times 10^{-3} \text{ sec}^{-1}$ and $1.1 \times 10^{-2} \text{ l mol}^{-1} \text{ sec}^{-1}$, respectively.

Covalent addition of N-chlorosaccharin to cyclohexene in carbon tetrachloride was observed. Rate measurement showed that the reaction was first order with respect to both reactants and the second order rate constant was $3.5 \times 10^{-2} \text{ l mol}^{-1} \text{ sec}^{-1}$. N-(2-chlorocyclohexyl)saccharin was identified to be the product.

A correlation has been shown between the equilibrium constants (K_T and K_L values) for reactions which involve a nitrogen containing base accepting a proton (K_T) and a positive chlorine ion (K_L), respectively, from aqueous hypochlorous acid solutions. Specifically, K_T and K_L are defined for different bases as shown in the table on p. 4. $K_{a,1}$, $K_{a,2}$, $K''_{a,1}$, and $K''_{a,3}$ are the acid dissociation constants for the amides or imides, hypochlorous acid, conjugate acid of the amine, and conjugate acid of the N-chloramine, respectively. Different linear correlations between $-\log_{10} K_T$ and $-\log_{10} K_L$ values were found for (A) anions of amides and imides and (B) amines. While those for amines fell on a line $(-\log_{10} K_T) = 0.39 (-\log_{10} K_L) - 2.50$, for imide and amide anions the values fell on the line $(-\log_{10} K_T) = 0.78 (-\log_{10} K_L) + 0.60$.

$$\frac{K_T}{K_L}$$

$$\frac{K_L}{K_T}$$

imides and
amides

$$\frac{[R_2NH][OCl^-]}{[R_2N^-][HOCl]} = \frac{K_{a,2}}{K_{a,1}} = \frac{[R_2NCl][OH^-]}{[R_2N^-][HOCl]} = \frac{K_W}{K_{a,1} K_{cp}}$$

tertiary
amines

$$\frac{[R_3NH^+][OCl^-]}{[R_3N][HOCl]} = \frac{K_{a,1}}{K''_{a,1}} = \frac{[R_3NCl^+][OH^-]}{[R_3N][HOCl]} = \frac{K_W}{K_{a,1} K_{cp}}$$

secondary
amines

$$\frac{[R_2NH_2^+][OCl^-]}{[R_2NH][HOCl]} = \frac{K_{a,1}}{K''_{a,1}} = \frac{[R_2NHC1^+][OH^-]}{[R_2NH][HOCl]} = \frac{K_W}{K''_{a,1} K_{cp}}$$

The failure of all data to appear on the same line was rationalized on the basis of the "principle of hard and soft acids and bases". This correlation permits the prediction of K_{cp} of other N-chlorinated molecules from a knowledge of its structure, its pK_a value and pK_a value of the non-chlorinated conjugate.

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DATE

January 6, 1969

CHEMISTRY OF N-CHLOROSACCHARIN

by

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A thesis submitted in partial fulfillment of the
requirements for the degree of

DOCTOR OF PHILOSOPHY

at the

UNIVERSITY OF WISCONSIN

1969

TO
my father
and
my wife Karen

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INTRODUCTION

Organochlorinating agents such as N-chlorosuccinimide, chloramine T and dichloramine T have been widely used as disinfectant, bleach and detoxifying agents. The search for new agents is, however, still going on. This leads to the twofold purposes of the present study: (1) to discover more effective organochlorinating agents, and (2) to obtain information that will provide a better understanding of mechanisms of reactions of these agents.

The chemistry of these compounds has attracted little attention aside from the classic work of Soper.¹⁻⁷ Not until recently has the relative oxidizing power of these agents been studied. Higuchi and coworkers⁸⁻¹⁰ undertook the task of classifying thirteen N-chlorospecies according to their "chlorine potential", a function related to the relative availability of positive chlorine in the form of hypochlorous acid. Although the authors did not attempt to correlate the chlorine potential with chemical structure, a trend can be found in their report that the positive chlorine is more readily available when it is attached to a less basic nitrogen. Based on this observation one would expect N-chlorosaccharin to be a particularly effective chlorinating agent since saccharin is a strong acid. Therefore, this investigation was specifically aimed at the chemistry of N-chlorosaccharin.

In addition, a quantitative free energy relationship was sought between the availability of positive chlorine from an N-chloro molecule and the acidity of its non-chlorinated conjugate. Such a relationship should be useful in predicting the chlorine potential of a molecule for which this value has not been determined.

The presentation has been divided into the following parts. In section I, the chemistry of N-chlorosaccharin determined in water as well as in organic solvents is reported. These studies included measurement of its chlorine potential, observations on its reactivity toward some organofunctional groups and elucidation of the mechanism responsible for the decomposition of the chloroimide in water. Section II deals more generally with the effect of structure of an N-chloro compound on its chlorine potential. The differences in free energy of formation for these compounds before and after they are N-chlorinated were calculated.

A Review of Chemistry of Positive Chlorine

Chlorine atoms that are attached to either oxygen or nitrogen in an organic molecule are generally considered to be in their oxidative state of +1 (positive chlorine) owing to their ability to (1) quantitatively oxidize iodide into iodine, and (2) replace hydrogen atoms in aromatic systems. Among the organic positive-chlorine-containing compounds, (or organochlorinating agent)

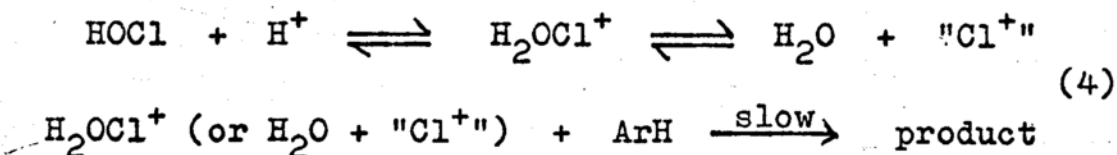
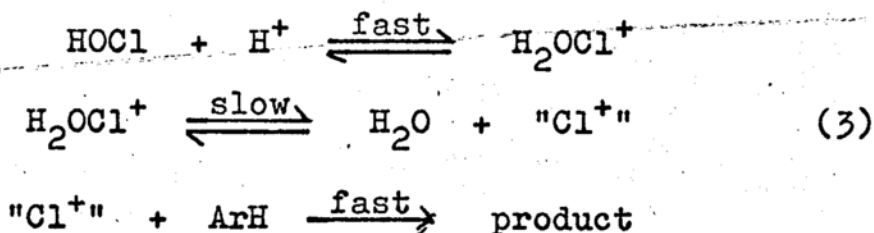
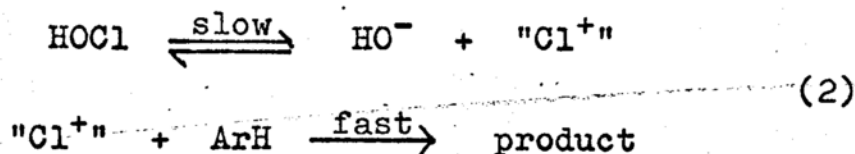
hypochlorous acid is by far the most widely used. N-chloro derivatives of imides and amides such as N-chlorosuccinimide and chloramine T have had their share of attention. Acyl hypochlorites and alkyl hypochlorites have been relatively neglected mainly due to their instability. References to the practical applications of organochlorinating agents can be found in the field of medicine as disinfectants or in the textile industry as bleaching agents.

For the sake of compactness only the chemistry of hypochlorous acid and of N-chloro species has been reviewed here. Emphasis has been placed on the mechanistic aspects of the reactions of positive chlorine. Reactions involving free radical intermediates have not been included. For this purpose the studies in the past have been categorized into two parts: (1) those dealing with mechanisms of aromatic chlorination, and (2) those concerned with mechanisms of exchange of positive chlorine among organochlorinating agents.

Mechanism of aromatic chlorination. When hypochlorous acid is used in aromatic chlorination, the general rate law¹¹ was found to be,

$$\begin{aligned} d[\text{HOCl}]/dt = & k[\text{HOCl}] + k'[\text{HOCl}][\text{H}^+] \\ & + k''[\text{HOCl}][\text{H}^+][\text{ArH}] \end{aligned} \quad (1)$$

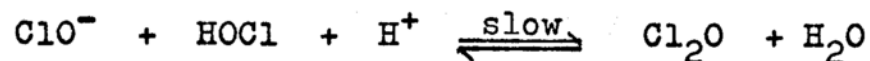
where ArH is the aromatic substrate. Not all of the three terms on the left side of the equation are necessarily observed in every case. For moderately reactive ArH's such as sodium benzylsulfonate,¹² benzene and toluene,¹³ only the third term appears in the rate equation. On the other hand, either the first two terms or all three terms have been found for strongly reactive ArH. For example, the rate equation for methyl p-tolylether¹⁴ and anisole¹⁵ shows the first two terms while that for methyl m-tolyl ether shows all three. The significance of each term has been interpreted as shown in equations (2), (3), and (4), respectively.



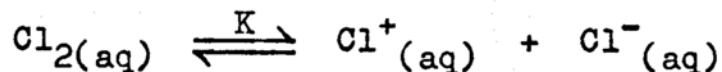
In all instances, either the chlorine cation, "Cl⁺", or H₂OCl⁺ has been postulated to be the chlorinating

species, which substitutes the hydrogen on the benzene ring electrophilically. This postulate is very attractive in view of the fact that Ingold and coworkers¹⁶ have shown that the nitronium ion, NO_2^+ , is the active agent in aromatic nitration.

To further establish this proposal de la Mare, et al.¹⁴ attempted to eliminate the presence of other possible chlorinating species that might account for the kinetic observation. For example, (1) silver perchlorate was added to precipitate any chloride ion which could form chlorine with hypochlorous acid in a slow step, and (2) the authors kept the acidity of the medium high and hypochlorous acid concentration low so that chlorine oxide, also a chlorinating agent, would not be formed according to the reaction



Nevertheless, the evidence at the present time is still not conclusive. Criticism of the " Cl^+ " postulate came mainly from the estimation of the equilibrium constant,¹⁷ K , of the reaction

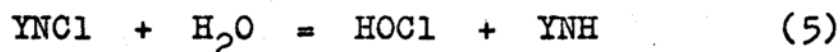


where K was found to be in the order of 10^{-60} M. By applying the concept that ligand yield stabilization

usually occurs to cations, Arotsky and Symon¹⁸ were able to increase K to the order of 10^{-40} M, but this is still too small to produce a significant quantity of Cl^+ in solution. This is further supported by the fact that no Cl^+ was detected in oleum in which I^+ was successfully prepared. Consequently the mechanisms represented by equations (2) and (3) are doubtful. Although definite proof has yet to be found, it has been generally accepted that H_2OCl^+ is the chlorinating species in equation (4).

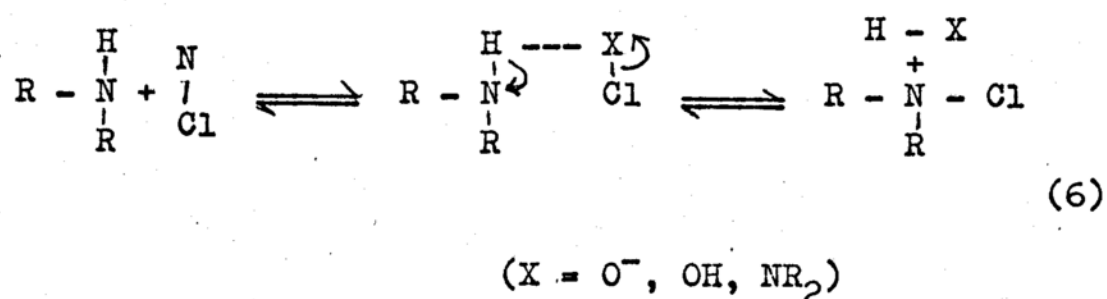
Aromatic chlorination with chloramine appears to be a bimolecular substitution reaction. Brown and Soper¹⁹ reported that kinetic evidence of the reaction between diethylchloramine and phenols can be interpreted in terms of interaction between the phenoxide ions and the diethylchlorammonium cations.

Mechanism of exchange of positive chlorine among organochlorinating agents. N-chloro compounds were first shown to undergo hydrolysis, in the following fashion



by Selivanov.²⁰ In this reaction the positive chlorine content of the system remains intact. Soper regarded this fact as definite proof for the positive nature of the N-chlorine atom. He later reported⁵ that direct exchange of positive chlorine also occurs between two nitrogen

containing compounds such as acetanilide and p-toluene-sulfonamide. Subsequently, the following reaction mechanism was suggested based mainly on the results obtained from N-chlorination of acetanilide with hypochlorous acid. These results were consistent with the interpretation that hypochlorite ion was the chlorinating species:



The processes were: (1) hydrogen bond formation by the aminohydrogen with the oxygen or nitrogen of the chlorinating molecule, (2) electron release by the chlorine atom of the chlorinating molecule, whereby the chlorine atom becomes a positive chlorine ion, and (3) new bond formed between chlorine ion and nitrogen which in the meantime releases the proton.

Weil and Morris²¹ studied the rates of formation of monochloramine, N-chlormethylamine and N-chlordimethylamine. They found that the pH profiles of observed second order rate constants exhibited bell-shaped curves with maximum rates in the region of pH 8. The authors attributed this observation to reaction occurring either between hypochlorous acid and ammonia, methylamine or

dimethylamine, or between hypochlorite ion and ammonium, methylammonium or dimethylammonium ions. These two alternative mechanisms are kinetically indistinguishable. They cannot be differentiated by means of primary salt effect, as shown in the discussion below.

For the nonionic mechanism

$$\text{rate} = k_1[\text{NH}_3][\text{HOCl}]f_{\text{NH}_3} f_{\text{HOCl}}/f_X \quad (7)$$

and the ionic mechanism

$$\text{rate} = k'_1[\text{NH}_4^+][\text{OCl}^-]f_{\text{NH}_4^+} f_{\text{OCl}^-}/f_X \quad (8)$$

where f 's are activity coefficients and the subscript "X" represents the activated complex. If the expressions for the dissociation constants of HOCl and NH_3

$$K_a = ([\text{H}^+][\text{OCl}^-]/[\text{HOCl}])f_{\text{H}^+} f_{\text{OCl}^-}/f_{\text{HOCl}} \quad (9)$$

and

$$K_b = ([\text{NH}_4^+][\text{OH}^-]/[\text{NH}_3])f_{\text{OH}^-} f_{\text{NH}_4^+}/f_{\text{NH}_3} \quad (10)$$

are substituted into equation (7), the equation,

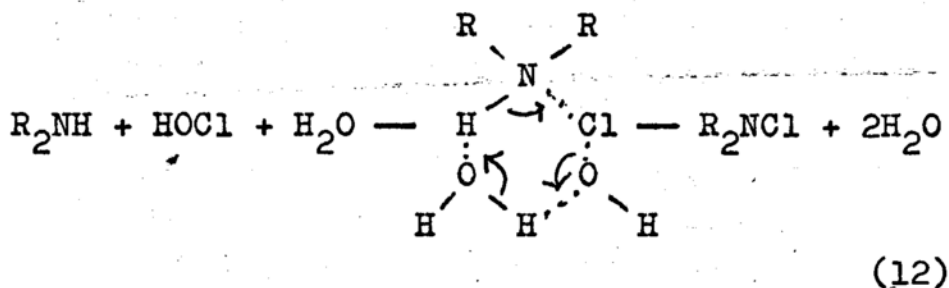
$$\text{rate} = (k_1 K_w / K_a K_b)[\text{NH}_4^+][\text{OCl}^-]f_{\text{NH}_4^+} f_{\text{OCl}^-}/f_X \quad (11)$$

results, where K_w is the activity product of water.

Equation (11) reduces to equation (8) for $k'_1 = k_1 K_w / K_a K_b$.

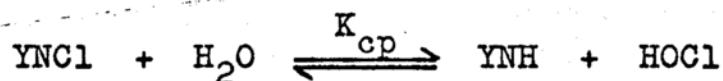
Hence, changes in ionic strength will have the same influence whichever mechanism is operative.

If the ionic mechanism (equation 6) operated, it would be expected that chlorination of ammonium ions would proceed more rapidly than chlorination of dimethylammonium ions because the former has more hydrogen atoms and hydrogen bond formation with hypochlorite ion would be expected to be a more favorable reaction. Results of Morris, et al. did not support this mechanism because the rate constant for formation of monochloramine was smaller than those for formation of dimethylchloramine. On the other hand, the rate constants of formation seemed to be proportional to the basic ionization constants of the amines. Based on this finding, Morris, et al. favored the nonionic mechanism with the free electron pair on the nitrogen attacking the positive chlorine. They also considered that it was not likely that these nitrogen bases would displace the more strongly basic hydroxyl group from the hypochlorous acid unless neutralization of the hydroxyl group occurred simultaneously. Therefore, a cyclic transition state was postulated in a concerted process in which combination of the hydrogen and hydroxyl proceeded at the same time as the displacement.



where R is H or CH₃.

Recently, Higuchi and coworkers^{8,10} classified thirteen N-chloro compounds according to their chlorine potentials, defined as $-\log_{10} K_{cp}$, in which K_{cp} is the equilibrium constant for the reaction of the following general formula,




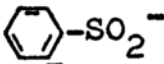
In their study, kinetic observation for eleven exchange reactions were reported. These are summarized in Table I.

Although in some cases in Table I the reactive species is still ambiguous, it appears that the positive chlorine acceptor must possess at least one pair of unshared electrons. Soper's mechanism apparently does not apply here because in most cases no amino hydrogen atoms are present on the acceptor molecule and consequently no preliminary hydrogen bonding can occur. The authors favored Morris' postulate (equation 12). It appears at this moment that sufficient data have not been collected to pinpoint the mechanism which is actually operative.

TABLE I

POSSIBLE REACTIVE SPECIES IN THE TRANSFERENCE OF POSITIVE CHLORINE AMONG NITROGEN CONTAINING MOLECULES

Reactants	Kinetic Evidence -pH Profile of Observed 2nd Order Rate Constant	Possible Reactive Species
$Q + HOCl$	linear with slope of +1 in pH range 3-5	$QH^+ + OCl^-$ or $Q + HOCl$
$Q + R_1R_2NCl$	linear with slope of +1 in pH range 3-4	$Q + R_1R_2NCl$
$Q^+Cl + R_1R_2NH$	linear with slope of +1 in pH range 3-4	$Q^+Cl + R_1R_2NCl$
$Q^+Cl + SI$	linear with slope of +1 in pH range 1-3	$Q^+Cl + SI^-$
$Q + NCS$	linear with slope of +1 in pH range 1-3	$Q + NCS$
$Q^+Cl + (R_2)_2NH$	linear with slope of +1 in pH range 1-3	$Q^+Cl + (R_2)_2NH$
$(R_2)_2NCl + Q$	horizontal line in pH range 2-4	$Q + (R_2)_2N^+HCl$ or $(R_2)_2NCl + Q^+H$
$R_1R_2NCl + (R_2)_2NH$	linear with slope of +1 in pH range 5-7	$R_1R_2NCl + (R_2)_2NH$
$R_1R_2NH + (R_2)_2NCl$	horizontal line in pH range 2-3	$R_1R_2N^- + (R_2)_2N^+(H)Cl$ or $R_1R_2NH + (R_2)_2NCl$
$NCS + R_1R_2NH$	linear with slope of +1 in pH range 4-6	$NCS + R_1R_2N^-$
$SI + R_1R_2NCl$	linear with slope of +1 in pH range 4-6	$SI^- + R_1R_2NCl$

Q = Quinuclidine, 
 R_1 = 
 R_2 = CH_3
 SI = Succinimide
 NCS = N-chlorosuccinimide

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SECTION I

CHEMISTRY OF N-CHLOROSACCHARIN

PART I

N-CHLOROSACCHARIN AS A CHLORINATING REAGENT. STRUCTURE, CHLORINE POTENTIAL, AND STABILITY IN WATER AND ORGANIC SOLVENTS

ABSTRACT

The structure of N-chlorosaccharin was confirmed by similarities of its ultraviolet and infrared spectra to those of N-methylsaccharin and differences from those of O-methylsaccharin. Its probable usefulness as a chlorinating agent was indicated by its low chlorine potential in water ($pK_{cp} = 4.85$ at 25°), and its solubility and stability in a wide variety of organic solvents. Cleavage of the imide bond of N-chlorosaccharin by hypochlorite ion in water and the reaction of N-chlorosaccharin with methanol were also investigated.

INTRODUCTION

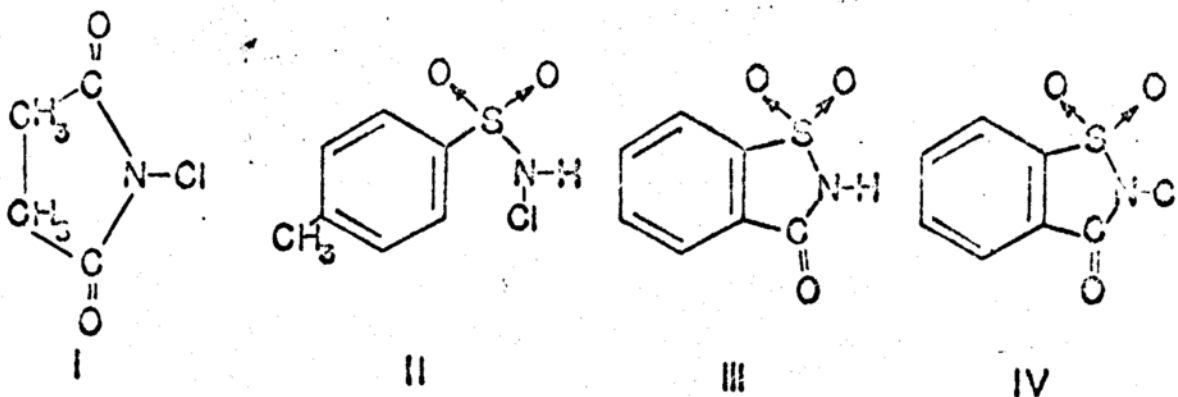
N-chloroimides (e.g., N-chlorosuccinimide (I))¹ and

¹F. L. Lambert, W. D. Ellis, and R. J. Parry, J. Org. Chem., **30**, 304 (1965); L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, N.Y., 1967.

sulfonamides (e.g., chloramine T (II))² are widely used as

²C. M. Suter, "The Organic Chemistry of Sulfur," Wiley, N.Y., 1944.

chlorinating and oxidizing reagents. The chlorinating



power of these molecules, expressed as their chlorine potential,³ pK_{cp} , has been shown⁴ to be related to the

³For a N-chloro compound, R_2NCl , $pK_{cp} = -\log_{10} K_{cp}$, where K_{cp} is the equilibrium constant for the reaction
 $R_2NCl + H_2O \rightleftharpoons R_2NH + HOCl$.

⁴See Section II, "Prediction of Chlorine Potential of N-chlorinated Organic Molecules" of this work.

acidity of their non-chlorinated conjugates, with the stronger chlorinating agent being derived from the stronger acid. Thus, because saccharin (III) is a stronger acid ($pK_a = 1.31$)⁵ than succinimide ($pK_a = 9.62$)⁶

⁵From this work.

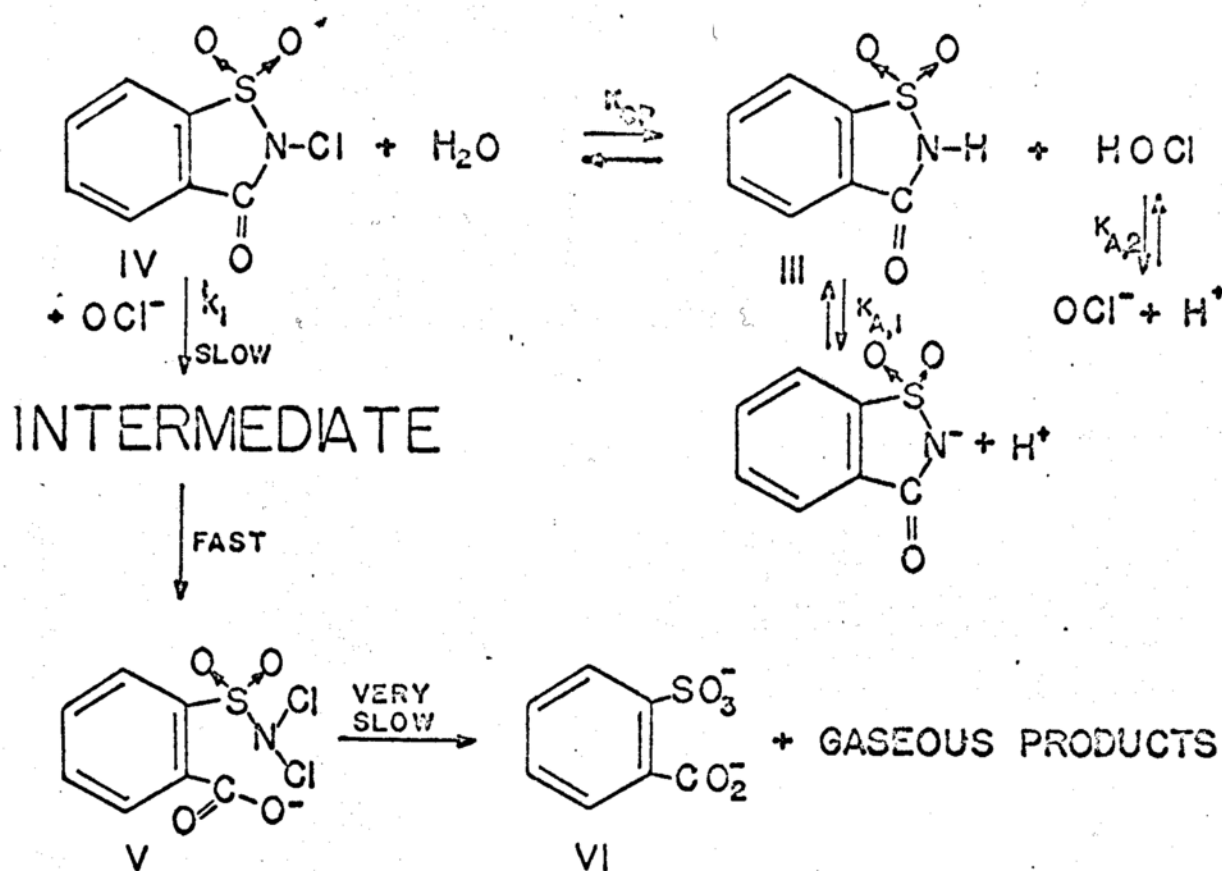
⁶H. H. Walton and A. A. Schilt, J. Amer. Chem. Soc., **74**, 4995 (1952).

or p-tolylsulfonamide ($\text{pK}_a = 10.3$),⁷ it was expected that

⁷T. Higuchi, K. Ikeda, and Hussein, A., J. Chem. Soc., (B) 546 (1967).

N-chlorosaccharin (IV) would be an even stronger chlorinating reagent than I or II.

When attempting to determine the K_{cp} value of IV it was found that other reactions were occurring besides transfer of positive chlorine between IV and water. These included acid dissociation of saccharin, cleavage of the imide of IV by hypochlorite ion, formation of N,N-dichloro-o-sulfamylbenzoic acid (V) and possibly the monochloro derivative, and slow decomposition of V to yield O-carboxylbenzenesulfonic acid (VI) and gaseous compounds. The overall reaction scheme is believed to be



In this communication we report evidence for this reaction scheme together with values of the equilibrium constant, K_{cp} , and second order rate constant, k_1 . Approximate values of the solubility of IV in carbon tetrachloride, ethyl acetate, acetone, 1,4-dioxane, and chloroform were also determined and the stability of its solutions in the above solvents and methanol was investigated.

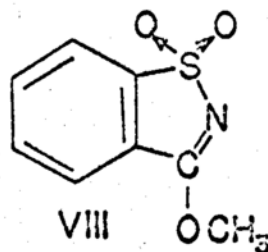
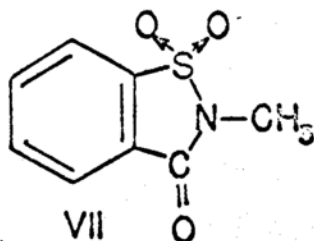
RESULTS AND DISCUSSION

Synthesis and Structure of N-Chlorosaccharin

A chlorinated derivative of saccharin was precipitated⁸ as a white crystalline powder (mp 148-150°)

⁸F. D. Chattaway, J. Chem. Soc., 87, 1882 (1905).

when chlorine gas was passed into cold aqueous solutions of sodium saccharin. Ultraviolet and infrared spectral features of this compound are shown in Figures I and II, respectively, together with those of N-methylsaccharin (VII) and O-methylsaccharin (VIII).



The chlorinated derivative of saccharin being discussed is believed to be N-chlorosaccharin (IV) and not the isomeric O-chlorosaccharin because of the similarities of its ultraviolet and infrared spectra to those of N-methylsaccharin and their differences from

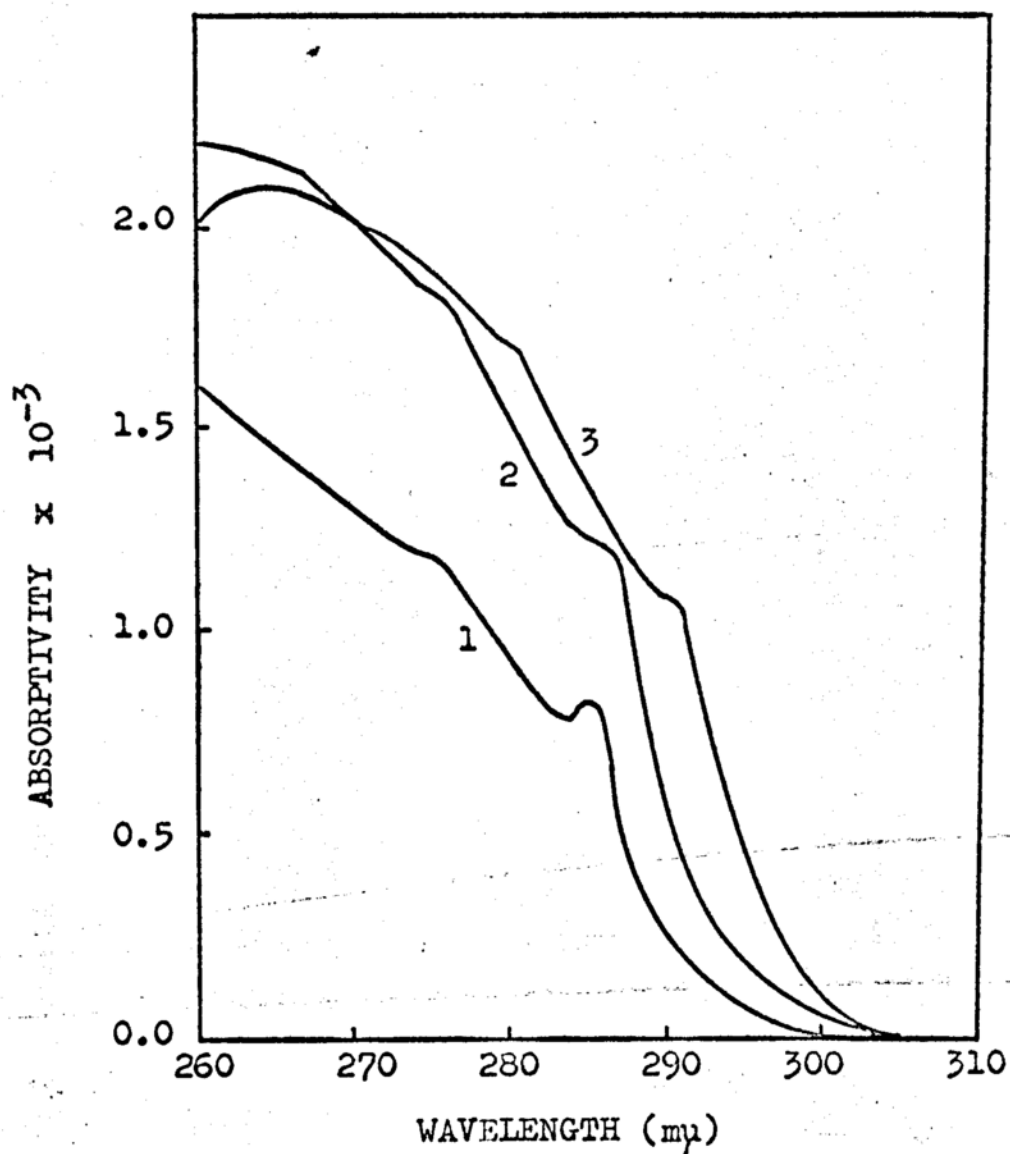


Figure I. Ultraviolet spectra of N-methylsaccharin (1), N-chlorosaccharin (2), and O-methylsaccharin (3), in ethyl acetate.

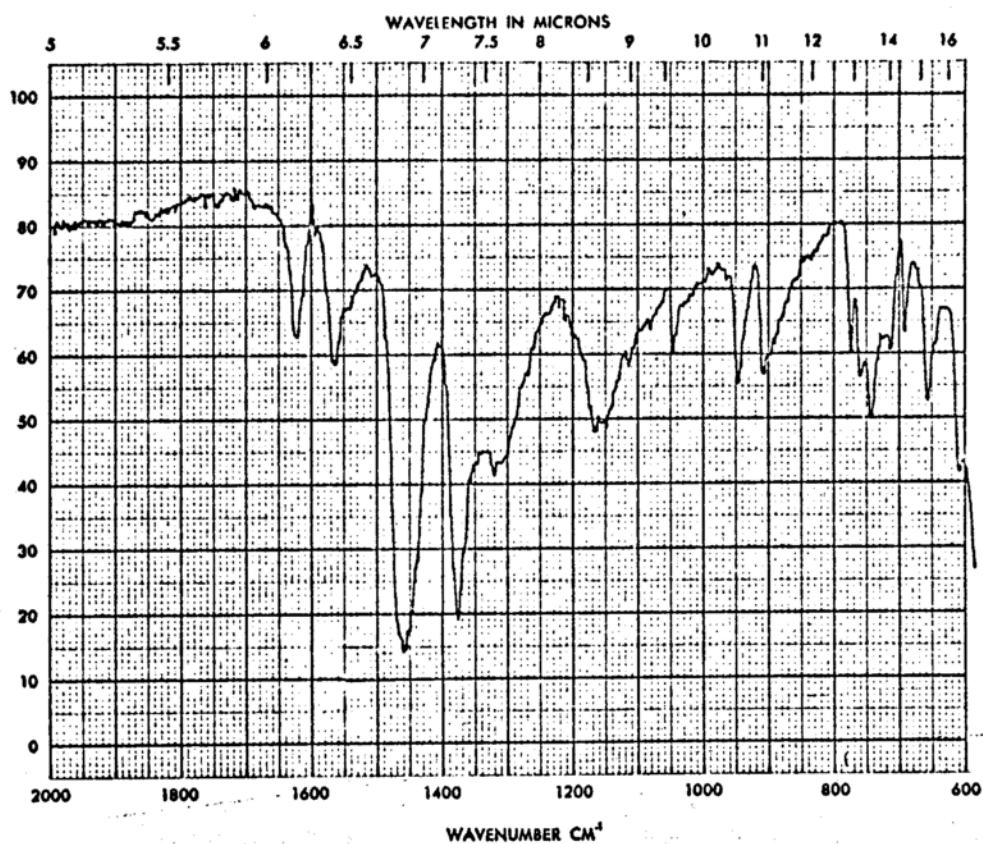


Figure IIa. The infrared spectrum of O-methylsaccharin. Sample was prepared into nujol mull and placed between salt plates for the measurement of spectrum.

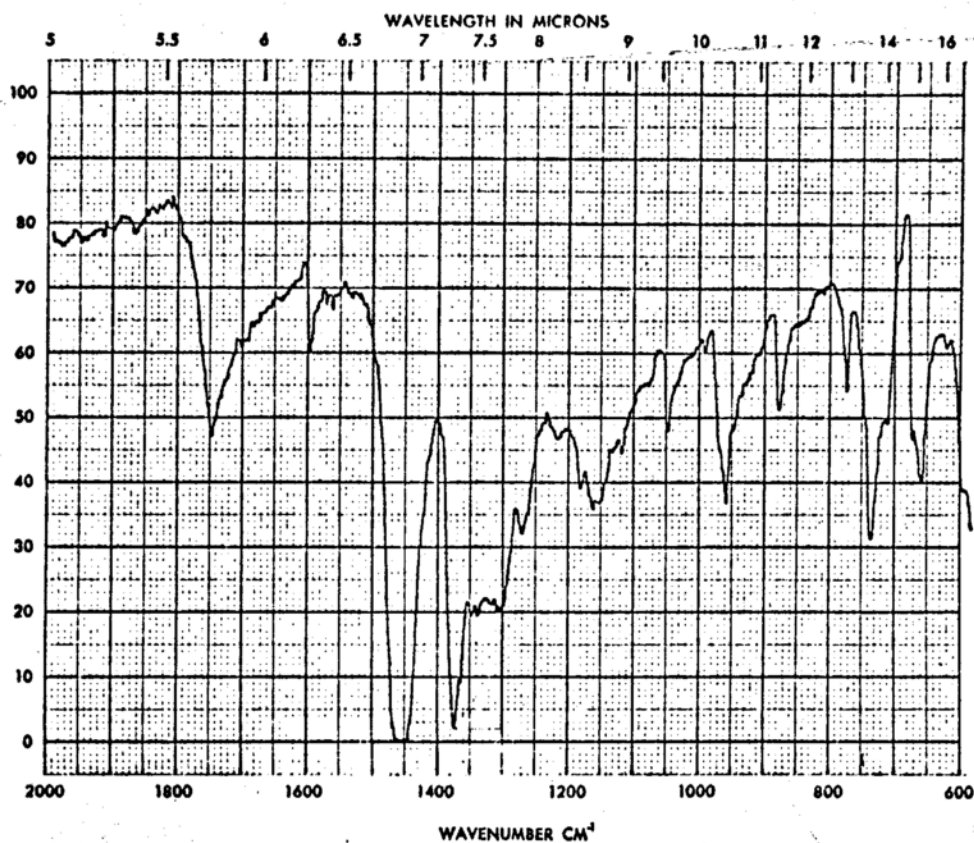


Figure IIb. The infrared spectrum of N-methylsaccharin. Nujol mull of sample was prepared and placed between salt plates for the measurement of spectrum.

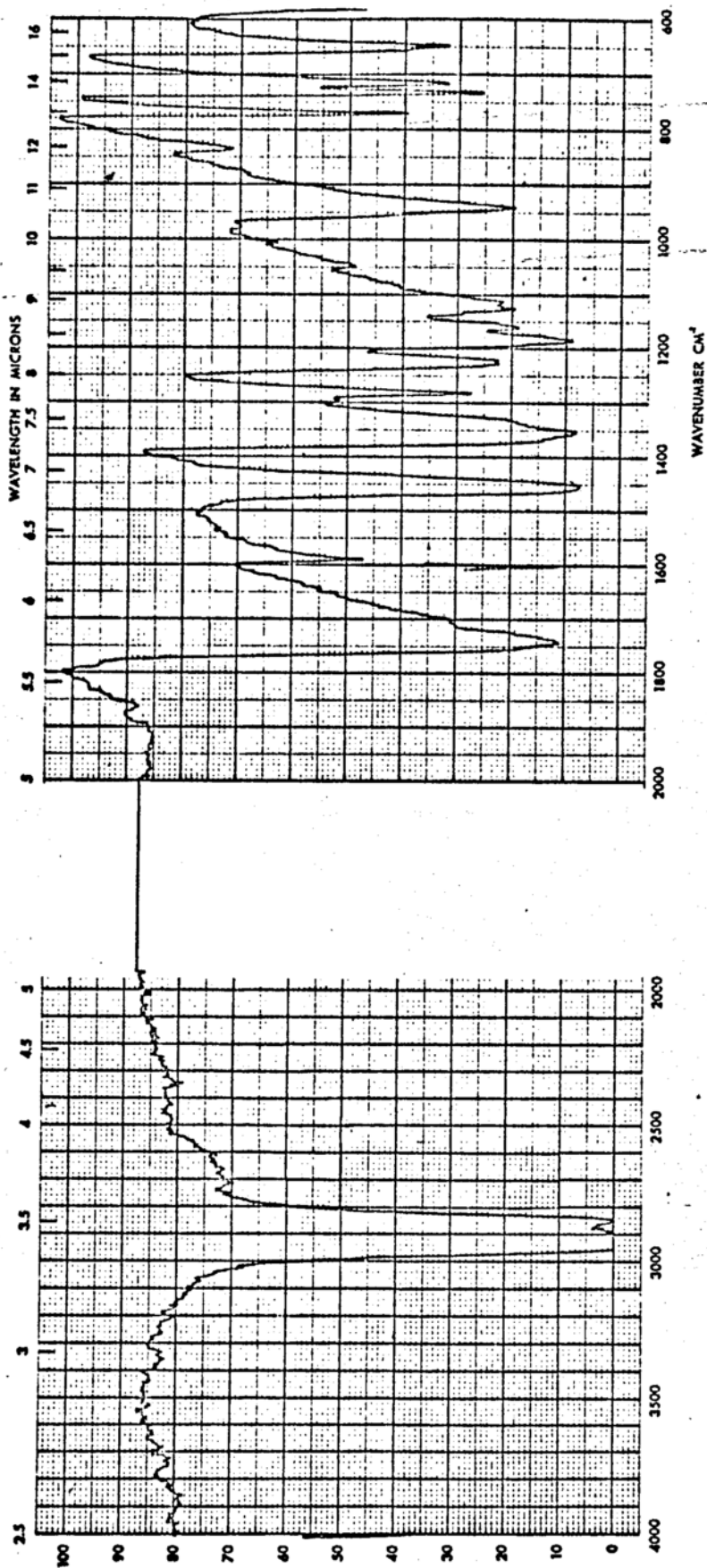


Figure IIc. Infrared spectrum of N-chlorosaccharin. Nujol mull of sample was prepared and placed between salt plates for the measurement of spectrum. Spectrum was calibrated at 6.238 μ .

those of O-methylsaccharin. The strongest piece of evidence in support of this conclusion is the presence of a strong band in the carbonyl stretching region of the infrared spectrum of N-methylsaccharin, and the chlorinated saccharin, and its absence from the spectrum of O-methylsaccharin.

Chlorine Potential of N-Chlorosaccharin

A substance with an ultraviolet spectrum⁹ closely

⁹Shown in Appendix I.

resembling that of N-chlorosaccharin was rapidly (complete within 30 sec) formed when a solution of saccharin (1.16×10^{-4} M) in 6.8 N sulfuric acid was mixed with an equal volume of aqueous hypochlorous acid (1.34×10^{-3} M). When similar mixtures were made at higher pH values (in monochloroacetic acid, sodium monochloroacetate buffers) the spectra which were rapidly generated resembled those of mixtures of saccharin, sodium saccharin, and N-chlorosaccharin.

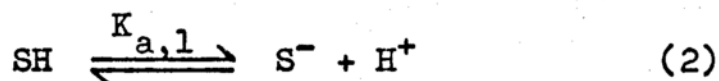
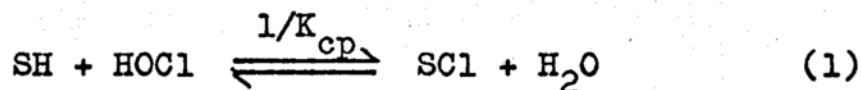
These rapidly generated spectra did not change more than three per cent during three minutes at pH values below 3.8. They did, however, change appreciably over longer time periods because of reactions which will be shown to involve cleavage of the imide bond of N-chlorosaccharin

followed by slow decomposition of the ring-opened intermediate. Similar spectral behavior¹⁰ was observed when 0.5 ml aliquots of a solution of N-chlorosaccharin

¹⁰Shown in Appendix II.

in ethyl acetate (9.72×10^{-3} M) were mixed with 20 ml of various buffer solutions. N-chlorosaccharin was added as its ethyl acetate solution because of its slow rate of dissolution in water.

These initial rapid reactions are believed to be due to the establishment of the equilibria



where SH and S⁻ are saccharin and saccharin anion, respectively; SCl is N-chlorosaccharin, and $K_{cp} = [\text{SH}][\text{HOCl}]/[\text{SCl}]$. The value of K_{cp} was calculated from spectrophotometric measurements of equilibrium concentrations of reactants and products following the mixing either of aqueous solutions of saccharin with buffered solutions of hypochlorous acid, or of ethyl acetate solutions of N-chlorosaccharin with buffer solutions. Results from several series of experiments are included in Table I.

TABLE I

HYDROLYTIC CONSTANT,^a K_{cp} , FOR N-CHLOROSACCHARIN AT 25°

Expt. No.	[HOCl] added $\times 10^4$ M	[SH] added $\times 10^4$ M	[SCl] added $\times 10^4$ M	$K_{cp} \times 10^5$ M
1	7.23	1.81	--	1.4
2	10.6	1.77	--	1.4
3	13.8	1.73	--	1.3
4	9.55	3.54	--	1.3
5	4.66	2.72	--	1.4
6 ^b	--	0.379	1.58	1.8
7 ^b	--	0.948	1.54	2.0

^aCalculated as described in Experimental section.^bSolutions contain 2.4 volume % ethyl acetate.

The mean value for K_{cp} in water is 1.4×10^{-5} M at 25° (excluding the K_{cp} values calculated from experiments 6 and 7 where 2.4 volume % ethyl acetate was present).

Thus, N-chlorosaccharin has a lower chlorine potential ($pK_{cp} = -\log_{10} K_{cp} = 4.85$) than N-chlorosuccinimide¹¹ ($pK_{cp} = 7.91$) and chloramine T¹¹.

¹¹T. Higuchi, A. A. Hussain, and I. H. Pitman, J. Chem. Soc., (B), in press.

($pK_{cp} = 7.77$). Its value is very close to that which would be predicted⁴ (5.27) on the basis that

N-chlorosaccharin is a complex between a soft base (S^-) and a hard acid (Cl^+). For such a case the chlorine potential would be expected to be related to the pK_a of saccharin by the identity $pK_{cp} = 0.28 pK_a + 4.90$.

Degradation of N-Chlorosaccharin in Aqueous Hypochlorite Solution

The previously mentioned changes in the ultraviolet spectrum of an equilibrium mixture of saccharin, saccharin anion and N-chlorosaccharin increase in rate when the pH of the solution is raised or when the concentration of hypochlorous acid is increased. These changes are believed to be due to a relatively fast cleavage of the imide bond of N-chlorosaccharin followed by a slower decomposition of the chlorinated O-sulfamylbenzoic acid. Results in Figure III show the change in ultraviolet absorbance at 282 m μ in a 2 cm cell plotted against time following the mixing of a solution of saccharin (5.60×10^{-4} M) in an acetic acid-sodium acetate buffer (3×10^{-2} M) at pH 3.9 with an equal volume of aqueous hypochlorous acid (1.50×10^{-2} M). After the reaction had proceeded for longer than 40 minutes unidentified gases were evolved. The ultraviolet spectrum, which was measured three minutes after mixing the reactants is shown in Figure IV to be almost identical to that obtained three minutes after mixing equal volumes of solutions of

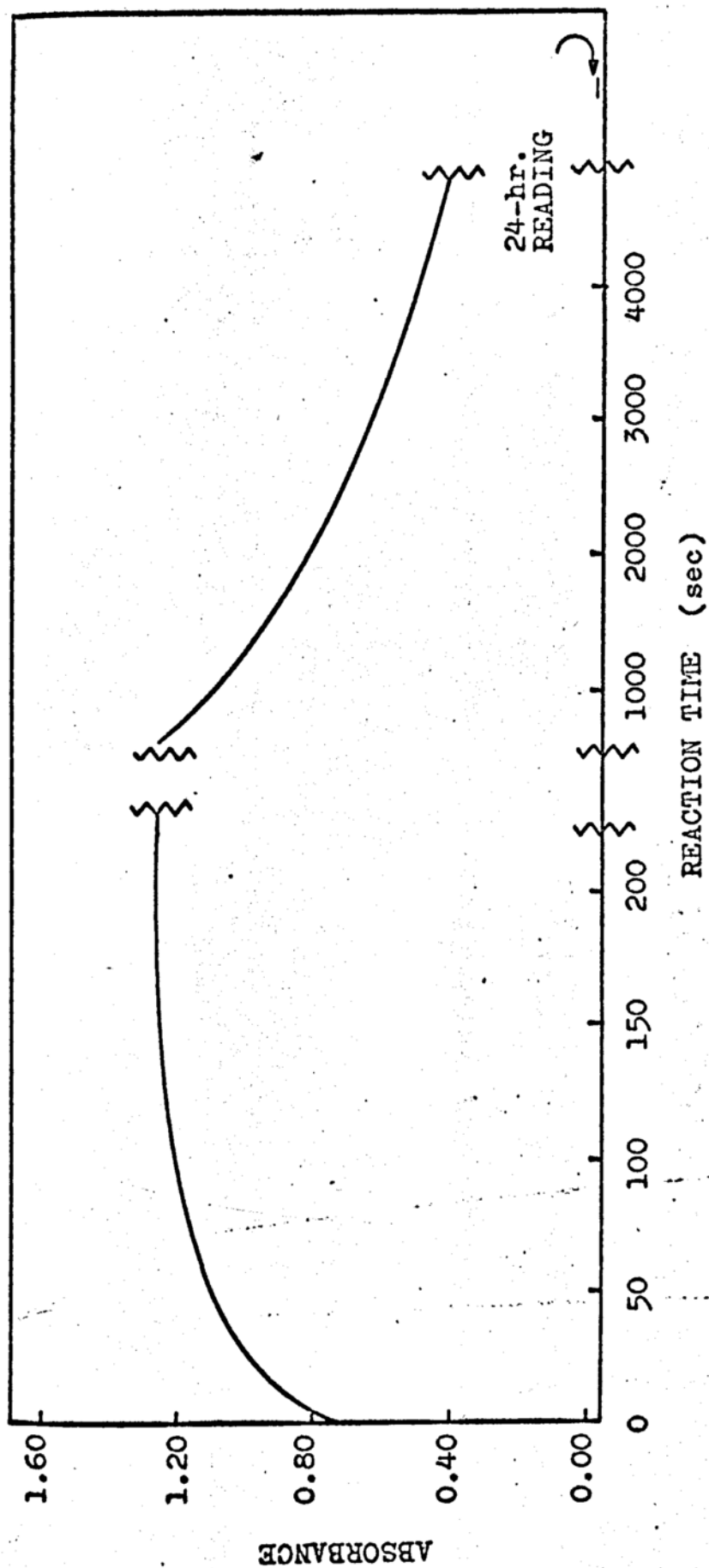
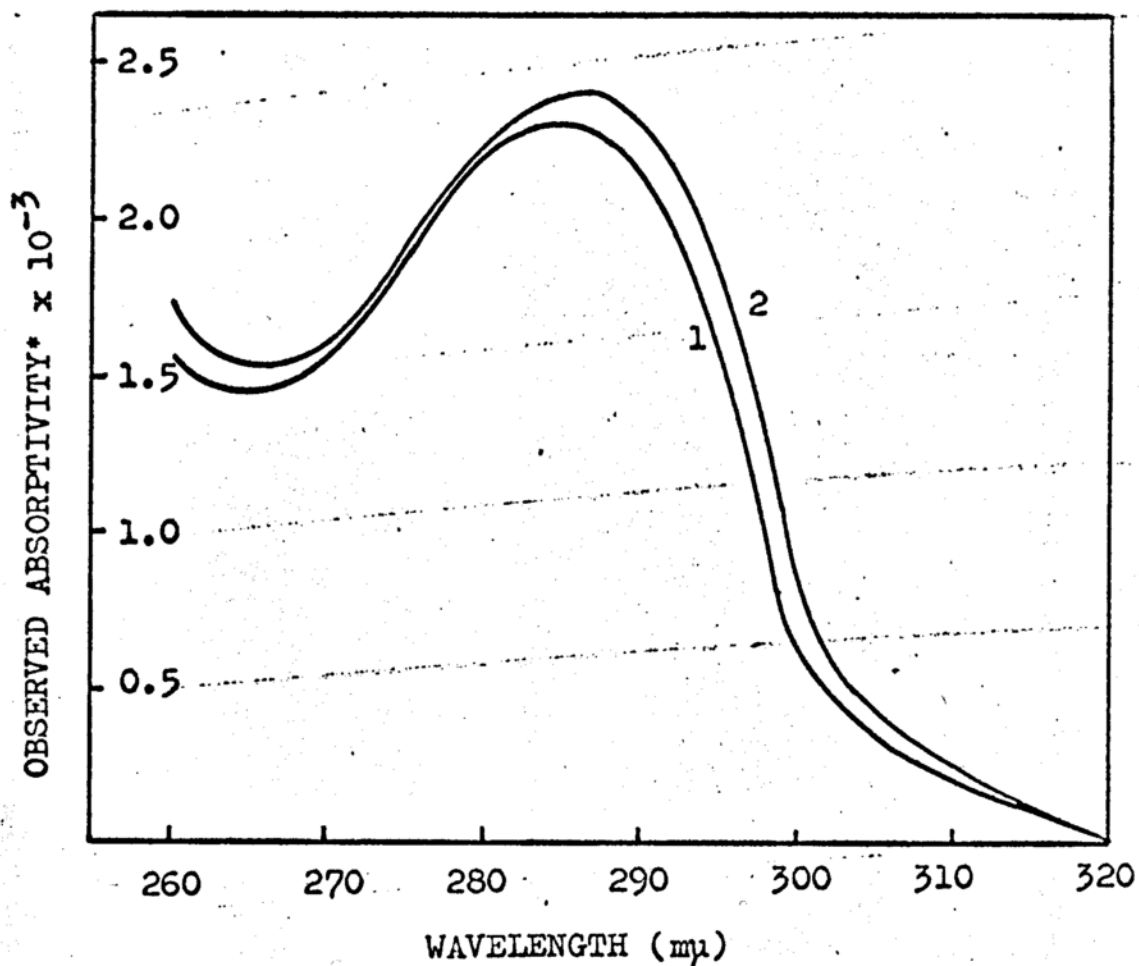


Figure III. Observed change in absorbance at 282 mμ in a 2 cm cell containing initially 5.25×10^{-3} M HOCl and 2.8×10^{-4} M saccharin in pH 3.9, 0.03 M acetate buffer at 25°.

Figure IV. The ultraviolet spectra for the following reaction mixtures after three minutes.



1. Mixture of 7.15×10^{-3} M HOCl and 2.14×10^{-4} M saccharin with same concentration of HOCl as reference (pH 4.9).
2. Mixture of 6.85×10^{-3} M HOCl and 3.00×10^{-4} M O-sulfamylbenzoic acid with same concentration of HOCl as reference (pH 3.30).

Acetate buffer 0.03 M, 2 cm, spectrophotometric cell.

*Observed absorptivities were calculated by dividing the absorbances with the added concentration of saccharin (in 1.) or O-sulfamylbenzoic acid (in 2.) and the pathlength of the cell.

O-sulfamylbenzoic acid (6.00×10^{-4} M) and hypochlorous acid (1.37×10^{-2} M).

The reactions occurring in the hypochlorous acid, saccharin system could be quenched by adding the drawn sample to excess sodium bisulfite to reduce the positive chlorine. When bisulfite was added at progressively longer time intervals after the reactants had been mixed, and the solution was placed on a silicic acid, 2N sulfuric acid column, saccharin and O-sulfamylbenzoic acid (identified by their ultraviolet spectra in chloroform) were eluted with chloroform. The amount of saccharin obtained decreased and the amount of O-sulfamylbenzoic acid increased initially and then decreased as the time elapsed before the addition of bisulfite increased. Results of the amounts of saccharin and O-sulfamylbenzoic acid obtained are plotted as a function of time before addition of bisulfite in Figure V. O-Carboxylbenzenesulfonic acid, which was also expected to be a product of the degradation of N-chlorosaccharin, could not be eluted from the column with chloroform because of its high acidity. It was, however, eluted with aqueous phosphate buffer after the saccharin and O-sulfamylbenzoic acid had been removed. It was identified by the similarity of its ultraviolet spectra in 1 M hydrochloric acid and 0.1 M sodium hydroxide to those of authentic material. Thus, the changes in ultraviolet absorbance,

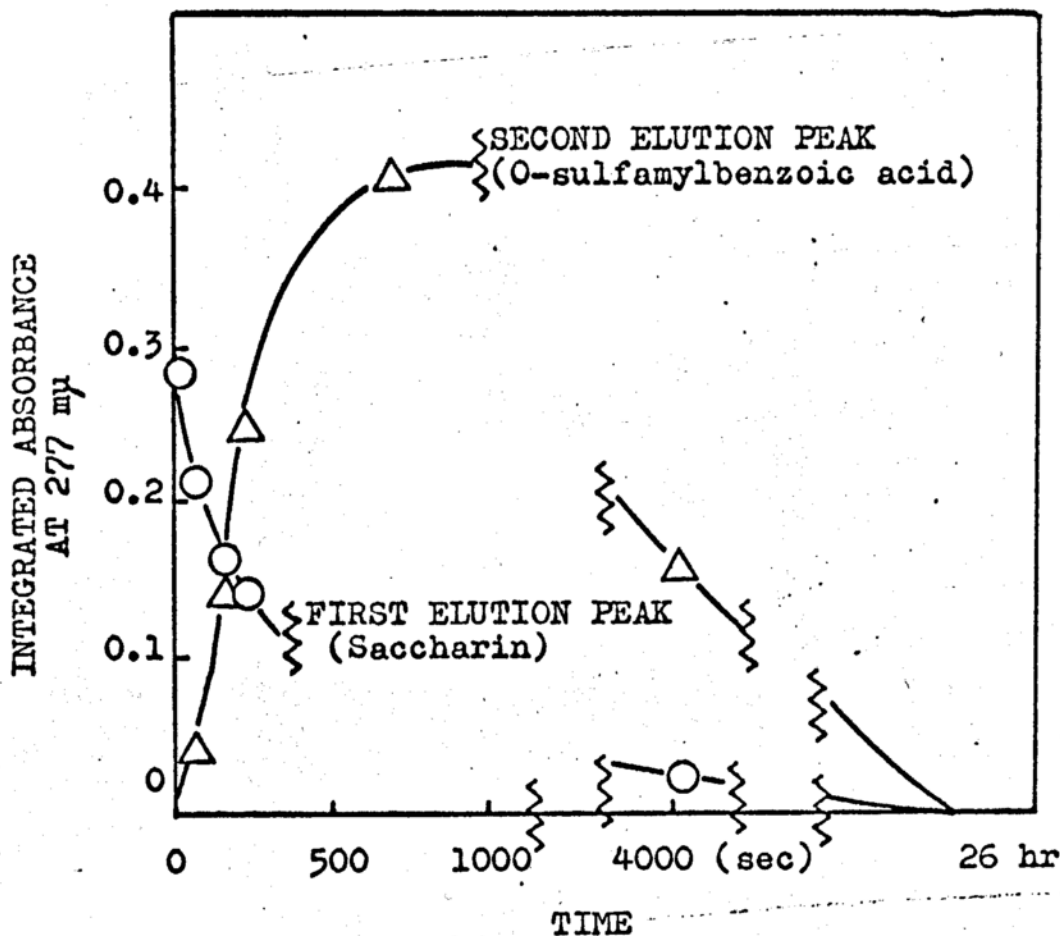


Figure V. Integrated absorbance areas under the first and the second elution peaks obtained at various reaction times for mixture of hypochlorous acid and saccharin killed with sodium bisulfite. The system initially contained 3.90×10^{-3} M HOCl and 4.85×10^{-4} M of saccharin (pH 3.4).

and product analysis are consistent with the proposed reaction scheme for degradation of N-chlorosaccharin.

Kinetic data for the ring cleavage reaction were obtained from measurements of changes in ultraviolet absorbance at 282 mμ following addition of 1 ml of solutions of saccharin ($1.74 - 2.18 \times 10^{-3}$ M) and 1 ml hypochlorous acid ($5.78 - 2.88 \times 10^{-2}$ M) to 4.6 ml acetate buffers of ionic strength (I) 0.5. Under these conditions (where the initial concentration of hypochlorous acid, $[\text{HOCl}]_{\text{added}}$, was greatly in excess of the added concentration of saccharin, $[\text{SH}]_{\text{added}}$), the ring cleavage reaction was pseudo first order and a pseudo first order rate constant, k_1' , was calculated by taking the maximum absorbance as the absorbance of the pure product. Because it is not known whether this product is N,N-dichloro-o-sulfamylbenzoic acid, N-chloro-o-sulfamylbenzoic acid or an isomer of these, an unspecified intermediate was included in the reaction scheme. However, it is believed that irreversible ring cleavage is the rate determining step in the reaction. On this basis, the rate equation¹² for consumption of

¹²Detailed derivation in Appendix III.

total saccharin species, SH_{total} ; ($[\text{SH}_{\text{total}}] = [\text{SH}] + [\text{S}^-] + [\text{SCl}]$) would be

$$\text{Rate} = \frac{k_1 K_{a,2} [\text{HOCl}]_{\text{added}}^2 [\text{SH}_{\text{total}}]}{[\text{H}^+][\text{HOCl}]_{\text{added}} + K_{a,1} K_{\text{cp}} + K_{\text{cp}}[\text{H}^+]} \quad (3)$$

where $K_{a,1}$ and $K_{a,2}$ are the acid dissociation constants of saccharin and hypochlorous acid ($K_{a,2} = 2.82 \times 10^{-8}$).¹¹ Thus the second order rate constant, k_1 , would be related to the pseudo first order rate constant, k_1' , at different pH values and added hypochlorous acid concentration by the identity

$$k_1 = k_1' \frac{[\text{H}^+][\text{HOCl}]_{\text{added}} + K_{a,1} K_{\text{cp}} + K_{\text{cp}}[\text{H}^+]}{K_{a,2} [\text{HOCl}]_{\text{added}}^2} \quad (4)$$

Values of k_1 calculated in this way are included in Table II, page 34.

The constancy of values of k_1 in Table III is strong evidence in support of the proposed reaction scheme. The kinetics of degradation of the chlorinated O-sulfamylbenzoic acid were not determined.

This overall reaction scheme is essentially the same as that proposed by Chattaway⁸ to account for the degradation of N-chlorosaccharin in solutions of caustic alkalis.

TABLE II

RATE CONSTANT, k_1 , FOR CLEAVAGE OF IMIDE BOND OF N-CHLOROSACCHARIN

pH	[Saccharin] added $\times 10^4$ M	[HOCl] added $\times 10^3$ M	$k_1' \times 10^2 \text{ sec}^{-1}$	$k_1 \times 10^{-5} \text{ M}^{-1} \text{ sec}^{-1}$
5.4	3.30	7.28	3.63	1.9
	3.30	5.82	2.32	1.8
	3.30	5.09	1.98	2.0
	3.30	4.36	1.52	2.1
4.9	3.30	7.28	3.30	1.6
	3.30	5.82	2.32	1.7
	3.30	4.36	1.35	1.8
	2.64	5.82	2.24	1.7
4.3	2.64	8.74	4.88	1.7
	3.30	7.28	2.77	1.6
	3.30	5.82	1.79	1.6
	3.30	5.09	1.63	1.8
	3.30	4.36	1.26	1.9
			Average:	1.8 ± 0.2

Solutions of N-Chlorosaccharin in Organic Solvents

N-chlorosaccharin is only slightly soluble in water (estimated solubility < 0.1 g/l at 25°) but is readily soluble in organic solvents as shown in Table III.

TABLE IIISOLUBILITY AND STABILITY OF N-CHLOROSACCHARIN AT 25°

Solvent	Solubility (g/l)	Stability ^a (hr)
Carbon tetrachloride	4.3	20
Ethyl acetate	85.1	3
Chloroform	112.0	3
Acetone	173.0	4
1,4-Dioxane	287.0	3

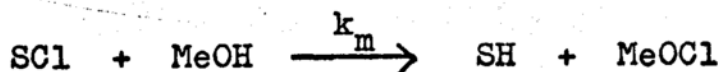
^aUltraviolet spectrum or positive chlorine content did not change more than 3% during these time periods.

Solubility was estimated by measuring the maximum concentration of N-chlorosaccharin that could be dissolved by stirring with the solvent in a sealed vessel at 25° . Samples of solution were removed every 15 minutes and analyzed by ultraviolet spectrophotometry, and iodometric titration, for N-chlorosaccharin and positive chlorine, respectively. When the concentration of the solution in the presence of undissolved crystals did not change during 45 minutes it was assumed to be saturated.

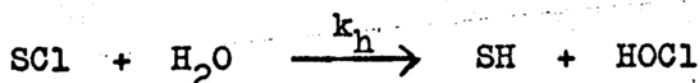
The solutions of N-chlorosaccharin shown in Table III were reasonably stable for at least three hours at 25°. However, fast spectral changes did occur in dry methanol and after ten minutes the solution had an identical spectrum to that of an equivalent concentration of saccharin in methanol. At this time, the titre of iodine against positive chlorine did not decrease more than 6% indicating that the reaction product (or products) were potential chlorinating agents. A possible reaction which would account for this behavior would be



The rate of consumption of N-chlorosaccharin and rate of formation of saccharin were pseudo first order reactions and, from measurements of changes in concentration with time, a pseudo first order rate constant k_m with a value $4.1 \times 10^{-3} \text{ sec}^{-1}$ at 25° was calculated. When known amounts of water were added to the methanol the rate of conversion of N-chlorosaccharin to saccharin increased and it seems likely that the reactions occurring were



and



(6)

Measurement of concentration changes as a function of time again yielded pseudo first order rate constant, k_{obs} , which according to the above scheme would be related to the individual rate constant by the identity

$$k_{\text{obs}} = k_m + k_h[\text{H}_2\text{O}] \quad (7)$$

Figure VI shows plots of k_{obs} against H_2O to be straight lines as required by the proposed reaction scheme. The fact that the value of k_m calculated from the plot in Figure VI ($4.1 \times 10^{-3} \text{ sec}^{-1}$) is the same as that calculated from experiments in dry methanol is consistent with the reaction scheme.

The chemical literature contains, what we believe to be erroneous, references^{2,13} to a reaction between

¹³S. M. Verma and R. C. Srivastava, Indian J. Chem., 4, 445 (1966).

N-chlorosaccharin and methanol to yield N-methylsaccharin. Although these references are apparently based on studies of Remse and Dohme,¹⁴ the original work makes no mention

¹⁴N. I. Remse and A. R. L. Dohme, Amer. Chem. J., 11, 345 (1890).

of this reaction and treats instead the reaction between methanol and the product formed by reaction of saccharin

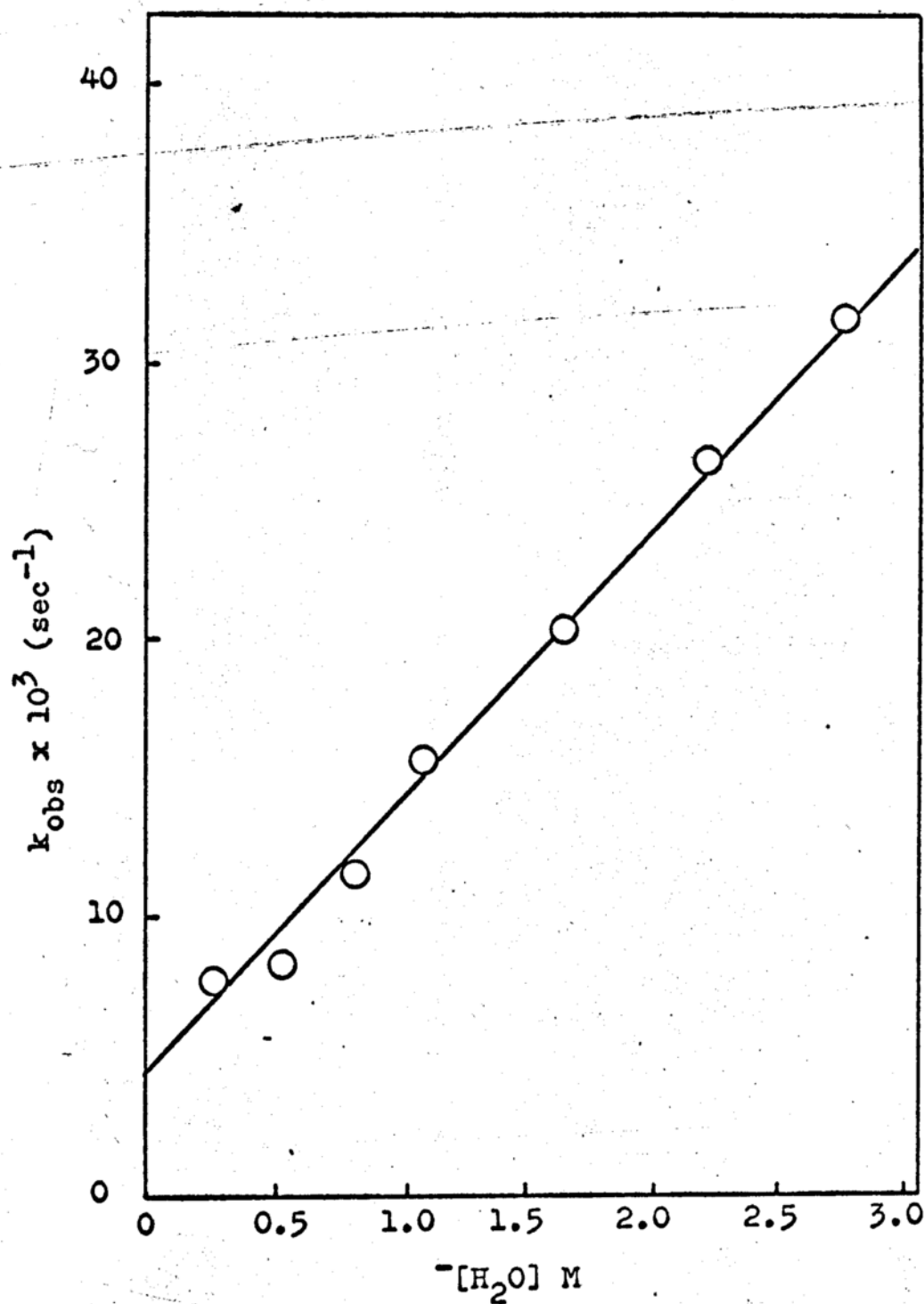


Figure VI. Plot of k_{obs} against concentration of water in methanol for reaction of N-chlorosaccharin in aqueous methanol.

and phosphorous pentachloride at 70-75°. This latter product is presumably pseudo-saccharin chloride^{15,16} and

¹⁵J. A. Jesurun, Ber., 26, 2286 (1893).

¹⁶J. R. Meadoc and E. E. Reid, J. Amer. Chem. Soc., 65, 457 (1943).

not N-chlorosaccharin.

Conclusion

N-chlorosaccharin is likely to have only limited usefulness as a chlorinating agent in water because of its poor solubility and slow rate of dissolution. On the other hand, it is readily soluble in several organic solvents and because it readily releases its positive chlorine in water it is expected to be a good chlorinating agent in these solvents. The reaction of N-chlorosaccharin with methanol does not reduce the availability of positive chlorine appreciably and these solutions also should be useful chlorinating systems.

EXPERIMENTAL

Reagents and Equipment

All reagents used were of the highest grade commonly available and were normally subjected to further purification before use. Saccharin (Aldrich) was recrystallized from acetone, (mp 228-229°). N-chloro-saccharin was prepared and purified according to Chattaway.⁸ The purity of the recrystallized product (mp 148-150°), determined iodometrically, was 98% based on active chlorine titration. Hypochlorous acid was prepared essentially according to Higuchi.¹⁷ Commercially

¹⁷T. Higuchi and J. Hasegawa, J. Phys. Chem., **69**, 796 (1965).

available bleaching solution (contains 5% sodium hypochlorite) was acidified with boric acid and distilled under vacuum at 50°C. The distillate was redistilled under vacuum at the same temperature. A diluted solution of the second distillate was used in the reactions. The diluted solutions usually fell in the concentration range of 2×10^{-2} - 4×10^{-2} M. Monochloroacetate acid (J. T. Baker, A. R. Grade) was recrystallized from benzene before use. Water used throughout this study was finally distilled from acid permanganate to remove possible

volatile nitrogenous contaminants. Succinimide (Aldrich) was recrystallized from acetone; mp 124-126°. Cyclohexene (Matheson Coleman and Bell), bp 82.5-83.5°, was used. Methanol (Allied Chemical, reagent grade) was dried according to Vogel.¹⁸ O-methylsaccharin was

¹⁸A. I. Vogel, "Practical Organic Chemistry," 3rd ed., John Wiley and Sons, Inc., New York, 1962.

prepared by following the procedure used by Meadon and Reid¹⁶ (mp 180-181°). N-methylsaccharin was synthesized according to Brackett¹⁹ (mp 131-132°). 1,4-Dioxane

¹⁹R. N. Brackett, Amer. Chem. J., 9, 407 (1887).

(Allied Chemical, reagent grade) was purified according to Vogel¹⁸ (bp 99-100°).

Cary 11, 14, or 15 recording spectrophotometers, which were thermostated at 25.0 \pm 0.2° by circulating water, were used to measure absorbances. pH values were measured using a Corning 12 research pH meter.

Calculations and Procedures

Acid dissociation constant and molar absorptivity of saccharin. Because saccharin is a strong acid the absorbance of the neutral molecule in water was difficult to measure and its acid dissociation constant, $k_{a,1}$,

could not be calculated directly by using the relationship²⁰

$$K_{a,1} = \frac{(A - A_{SH})[H^+]}{(A_{S^-} - A)} \quad (8)$$

²⁰Detailed derivation and calculation in Appendix IV.

where, A , is the absorbance of an equilibrium solution of saccharin and saccharin anion, and A_{SH} and A_{S^-} are the absorbances of the same solution at pH values where >99% of the saccharin was in the form of its neutral molecule and anion, respectively. Although the value of A_{SH} could not be measured, values of A_{S^-} , A , (both in a 5 cm cell at 270 mμ) and $[H^+]$ were measured for the equilibrium solutions formed when 1 ml aliquots of aqueous solutions of saccharin (3.80×10^{-3} M) were added to 20 ml of solutions of HCl and KCl (total concentration 2×10^{-1} M) at 25°. Plots of $(A_{S^-} - A)/[H^+]$ against A gave a straight line with slope of 20.4, and intercept on the Y-axis of -21.7. From the equation it can be seen that the slope of this line and the intercept on the Y-axis are related to $K_{a,1}$ and the molar absorptivity of saccharin, ϵ_{SH}^{270} by the identities $K_{a,1} = \frac{1}{\text{slope}}$ and

$$\epsilon_{SH}^{270} = - \frac{\text{Intercept}}{\text{slope}[\text{SH}]_{\text{added}}^b} \quad (9)$$

where b is the pathlength of the spectrophotometer cell. From results of the above experiment values of $K_{a,1} = 4.91 \times 10^{-2}$ (lit., 2.5×10^{-2} at 18°)²¹ and

²¹J. M. Kolthoff, Rec. Trav. Chim. Pays-Bas, 44, 629 (1925).

$\epsilon_{SH} = 1119$ in water at $25.0 \pm 0.2^\circ$ were calculated.

Determination of the hydrolytic constant, K_{cp} , for N-chlorosaccharin. The K_{cp} value was calculated from the absorbance, A , of an equilibrium solution of saccharin (SH), saccharin anion (S^-), N-chlorosaccharin (SCl), and hypochlorous acid by using the equation²²

$$\frac{(A - A_0)(K_{a,1} + [H^+])}{[H^+] \left\{ [HOCl]_{added} - \frac{A}{A_\infty - A_0} [SH]_{added} \right\}} = \frac{A}{K_{cp}} - \frac{A}{K_{cp}}$$

(10)

²²Detailed derivation and results in Appendix V.

A_0 and A_∞ were the absorbances of the solution under conditions where $> 99\%$ of the added saccharin was in the form of saccharin plus saccharin anion and N-chlorosaccharin, respectively, and $K_{a,1}$ was the acid dissociation constant of saccharin. Values of A_0 , A , and $[H^+]$ could be measured directly but values of A_∞

could not because of the difficulty of working at pH values where the saccharin would not be dissociated to an appreciable extent. Also, A_{∞} could not be calculated from the identity

$$A_{\infty} = \epsilon_{SCl} [SH]_{\text{added}} b + \epsilon_{HOCl} \{ [HOCl]_{\text{added}} - [SH]_{\text{added}} \} b \quad (11)$$

until a sufficiently accurate value of the molar absorptivity of N-chlorosaccharin, ϵ_{SCl} , was available.

Inspection of equation (10) shows that when $[HOCl]_{\text{added}}$ is much larger than $[SH]_{\text{added}}$, a plot of

$$\frac{(A - A_o)(K_{a,1} + [H^+])}{[H^+][HOCl]_{\text{added}}}$$

against A at different pH values should give a straight line from which values of K_{cp} ($= -\frac{1}{\text{slope}}$) and A_{∞} ($= -\frac{\text{Intercept}}{\text{slope}}$) could be calculated. A value of ϵ_{SCl} could then be calculated from this A_{∞} value and used to calculate A_{∞} values for subsequent experiments where $[HOCl]_{\text{added}}$ was not much greater than $[SH]_{\text{added}}$. This was the method used to compute K_{cp} values. Typical sets of results for experiments carried out under conditions where (A) $[HOCl]_{\text{added}} > [SH]_{\text{added}}$, and (B) $[HOCl]_{\text{added}}$ was not much greater than $[SH]_{\text{added}}$, and (C) N-chlorosaccharin was added to buffered solution of saccharin are shown in Tables IV, V and VI, respectively.

TABLE IV

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN WATERUNDER THE CONDITION WHERE $[HOCl]_{added}$ WAS MUCH GREATER THAN $[SH]_{added}^*$

pH	A_0	A	$L^{**} \times 10^{-3}$	Slope $\times 10^{-4}$	Intercept $\times 10^{-4}$	$K_{cp} \times 10^5$	\angle 270 SC1
2.303	0.611	0.950	3.47				
2.365	0.613	0.939	3.81				
2.480	0.616	0.925	4.62				
2.685	0.619	0.819	6.79	-7.22	7.19	1.38	2652
2.944	0.622	0.857	10.0				
3.344	0.624	0.774	15.5				
3.666	0.625	0.719	20.3				

* $[SH]_{added} = 1.77 \times 10^{-4}$ M, $[HOCl]_{added} = 1.06 \times 10^{-3}$ M. Buffer concentration = 0.04 M (monochloroacetate). Absorbance measured at 270 mμ with 2-cm cell.

$$**L = \frac{(A - A_0)(K_{a,1} + H^+)}{[H^+][HOCl]_{added}}$$

TABLE V

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN WATER
 UNDER THE CONDITION WHERE $[HOCl]_{added}$ WAS NOT MUCH GREATER THAN $[SH]_{added}$ *

pH	$[H^+] \times 10^3$ M	A_0	A	A_∞	$K_{cp} \times 10^5$ M
2.296	5.06	0.861	1.245	1.453	1.5
2.402	3.96	0.866	1.236	1.453	1.3
2.465	3.43	0.868	1.217	1.453	1.4
2.585	2.60	0.872	1.187	1.453	1.4
2.802	1.58	0.876	1.140	1.453	1.3
3.055	0.88	0.880	1.070	1.453	1.4
3.200	0.631	0.881	1.032	1.453	1.4
3.296	0.506	0.882	1.015	1.453	1.4
3.465	0.343	0.882	0.976	1.453	1.5
Average: 1.4 ± 0.1					

* $[SH]_{added} = 2.72 \times 10^{-4}$ M, $[HOCl]_{added} = 4.66 \times 10^{-4}$ M.
 Monochloroacetate buffer 0.04 M. Absorbances were measured at
 270 mμ with 2-cm cell.

TABLE VI

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN WATER

UNDER THE CONDITION WHERE N-CHLOROSACCHARIN WAS ADDED TO BUFFERED SOLUTIONS OF SACCHARIN*

pH	$[H^+] \times 10^3$	A_o	A	A_s	$K_{cp}^{**} \times 10^5$
2.290	5.13	0.604	0.760	1.028	1.9
2.330	4.68	0.606	0.753	1.028	2.0
2.466	3.42	0.611	0.751	1.028	1.6
2.700	2.00	2.617	0.707	1.028	2.1
3.020	0.955	0.621	0.683	1.028	1.8
3.298	0.504	0.623	0.671	1.028	1.4
3.455	0.351	0.624	0.658	1.028	1.5
3.565	0.272	0.624	0.656	1.028	2.0
Average: 1.8 ± 0.3					

* $[SCl]_{added} = 1.58 \times 10^{-4}$ M, $[SH]_{added} = 3.79 \times 10^{-5}$ M. Buffer (monochloroacetate) concentration = 0.05 M. All solutions contained 2.4 volume % of ethyl acetate. Absorbances were measured at 270 mμ with 2-cm cell.

**In using equations (10) and (11) to calculate K_{cp} the values 1.96×10^{-4} M (added concentration of SCl + added concentration of saccharin) and 1.58×10^{-4} M (added concentration of SCl) were used for the terms " $[SH]_{added}$ " and " $[HOC1]_{added}$ ", respectively, since the amount of N-chlorosaccharin added can be treated as adding an equal amount of HOCl and saccharin to the solution. K_{a1} determined in solution containing 2.4 volume % ethyl acetate was 0.0382 and was used in calculations here.

Results from several series of experiments at different ratios of $[\text{HOCl}]_{\text{added}}$ to $[\text{SH}]_{\text{added}}$ are collected in Table I. The procedures for typical experiments were

(1) For the case where saccharin and hypochlorous acid were mixed: Aqueous solutions of saccharin, hypochlorous acid, and monochloroacetate buffer, were prepared separately and brought to $25 \pm 0.2^\circ$. Exactly 1 ml of saccharin solution was added to exactly 20 ml of buffer solution in an Erlenmeyer flask, which was immersed in a water bath at $25 \pm 0.2^\circ$. Then 1 ml of hypochlorous acid was injected into this solution. Since the equilibrium was almost instantaneously established, the equilibrium absorbance was measured immediately after the injection in a 2-cm silica cell. In the meantime, the remaining portion of the reaction mixture was used for pH measurement. This process was repeated at different pH values and different hypochlorous acid concentrations.

(ii) For the case where N-chlorosaccharin in ethyl acetate was added to buffers: 0.5 Ml portion of aqueous saccharin stock solution was first added into 20 ml portion of 0.05 M monochloroacetate solution in Erlenmeyer flasks, which were immersed in water bath of $25 \pm 0.2^\circ$. Then, 0.5 ml portion of freshly prepared ethyl acetate stock solution of N-chlorosaccharin was injected into flasks. The equilibrium absorbance was measured in a 2-cm light-path silica cell at 270 m μ immediately after

a homogeneous solution had been obtained (in about 10 sec, with vigorous shaking). At the same time, the remaining portion of the reaction mixture was used for pH measurement. This process was repeated at several different pH values.

The concentrations of both stock solutions were varied in different experiments.

Determination of the rate constant for the cleavage of imide bond of N-chlorosaccharin. A saccharin stock solution, acetate buffer solutions (0.5 M with ionic strength adjusted to 0.5 by adding sodium sulfate) of different pH values and hypochlorous acid of various concentrations were prepared and brought to $25 \pm 0.2^\circ$. 4.6 ml of buffer solution of desired acidity was mixed with 1.0 ml of saccharin solution in a 2-cm cell. Into this cell 1.0 ml of hypochlorous acid of desired concentration was injected. The cell was quickly shaken and placed in a spectrophotometer. The change of absorbance at 282 m μ was then recorded. At the end of the fast reaction (after the maximum absorbance reading had passed) the pH of the mixture was determined.

Chromatographic separation of the components of the reaction mixture of saccharin and hypochlorous acid. A partition column was prepared as follows: 20 ml of 2 N sulfuric acid were added to 20 g of silicic acid, and

mixed well. A slurry was made with 40 ml of chloroform and packed into a glass column (50 cm long, 2 cm diameter) containing a plug of glass wool and having a teflon stopcock.

A ten ml portion of reaction mixture was added to two ml of 4 N sulfuric acid which contained sufficient sodium bisulfite to quench the reaction by reducing the positive chlorine to chloride ion and, consequently, N-chlorospecies were converted into their conjugate non-chlorinated derivatives. Five ml of the quenched reaction mixture were then chromatographed according to the procedure below: 5 g of silicic acid were added to the mixture and a slurry was made with 10 ml of chloroform. The slurry was then packed on the top of the column. This was topped with a filter paper disk.

Saccharin²³ was eluted with 100 ml of 2% butanol in

²³Chromatogram from separation of a known mixture of saccharin and O-sulfamylbenzoic acid is shown in Appendix VI.

chloroform and O-sulfamylbenzoic acid with 100 ml of 6% butanol in chloroform.

The integrated absorbances were obtained by adding the absorbances of all fractions (10 ml eluate in each fraction), that contain the same component, at 277 mμ.

Alcoholysis of N-chlorosaccharin to saccharin in methanol. A stock solution of N-chlorosaccharin was made up in ethyl acetate (4.00×10^{-2} M). 0.02 Ml of this solution was injected into a 1-cm stoppered cell containing 2.0 ml of desired aqueous methanol. The disappearance of N-chlorosaccharin was then followed at 276 m μ spectrophotometrically.

PART II

COVALENT ADDITION OF N-CHLOROSACCHARIN TO CYCLOHEXENE

It has recently been reported¹ that N-chloro-N-

¹T. Ohashi, M. Sugie, M. Okahara, and S. Kowori, Tetrahedron Letters, 4195 (1968).

methylthanesulfonamide will add covalently across the
>C=C< double bond 1-hexene under photoirradiation. In
similar, but apparently more facile, reactions,
N,N-dichlorobenzenesulfonamide² and N-aryl-N-halosulfona-

²W. Theilacker and H. Wessel, Liebigs Ann. Chem.,
703, 34 (1967).

mides³ will add covalently to cyclohexene. Because

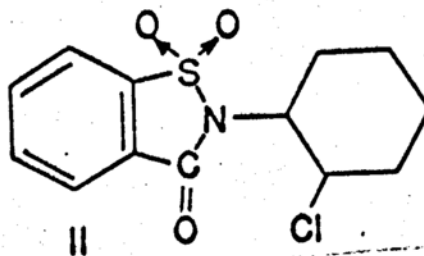
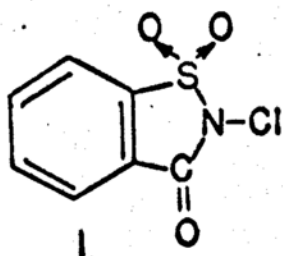
³M. S. Kharasch and H. M. Priestley, J. Amer. Chem. Soc., 61, 3425 (1939).

N-chloro compounds are used as chlorinating and oxidizing
agents for a wide variety of compounds, addition reactions
of the above type must be expected to occur if the
molecules to be chlorinated contain unsaturated groups.

We have recently discussed⁴ the possible usefulness

⁴H. Dawn, T. Higuchi and I. H. Pitman, Submitted
for publication.

of N-chlorosaccharin (I) as an organochlorinating agent on the basis of its low chlorine potential in water and its solubility and stability in a variety of organic solvents. However, we now present evidence that I will also covalently add to cyclohexene in a facile reaction



at room temperature to yield N-(2-chlorocyclohexyl)-saccharin (II).

When I (400 mg) was added to cyclohexene (15 ml) at 25° it gradually dissolved and simultaneously a white powder crystallized out of solution. After recrystallization from acetone-water, this powder had mp 171-172.5°, and the same elemental analysis as II (Found: C, 52.07; H, 4.86; N, 4.78; Cl, 11.94; S, 10.97. II, $C_{13}H_{14}NClSO_3$, requires C, 52.0; H, 4.67; N, 4.67; Cl, 11.85; S, 10.70). Its structure was confirmed by nmr and ir spectroscopy. Its nmr spectrum showed the presence of 4 benzene protons and 10 cyclohexene protons but no cyclohexene-ethylene protons were evident. The ir spectrum of the compound was consistent with that of structure II and contained a

strong band at the carbonyl stretching frequency region. This latter piece of evidence ruled out the possibility that an O-C bond existed between saccharin and cyclohexene. The product did not release iodine from aqueous solutions of potassium iodide thereby indicating that it was not in equilibrium with N-chlorosaccharin and that its chlorine was fixed and no longer "active".

The rate of formation of the adduct was determined by measuring changes in ultraviolet absorbance at 270 m μ after carbon tetrachloride solutions of I and cyclohexene (which had been equilibrated at $25.0 \pm 0.2^\circ$) were mixed in a 1 cm spectrophotometer cell. The rate of change of absorbance was first order when (cyclohexene)_{added} was much greater than (I)_{added} and pseudo first order rate constant, k_{obs} , values, were calculated. At two different cyclohexene concentrations the value of $k_{obs}/[\text{cyclohexene}]_{\text{added}} = k_1$ was constant and thus the reaction appeared to be first order in cyclohexene and I. Results of two experiments are presented in Table I.

TABLE I

RATE CONSTANTS FOR THE COVALENT ADDITION OF
N-CHLOROSACCHARIN TO CYCLOHEXENE IN
CARBON TETRACHLORIDE AT 25°

[Cyclo- hexene] added x 10 M	[N-chloro- saccharin] added x 10 ⁴ M	10 ² k _{obs} sec ⁻¹	10 ² k ₁ M ⁻¹ sec ⁻¹
4.96	6.30	1.69	3.4
3.22	10.00	1.16	3.6

SECTION II

PREDICTION OF CHLORINE POTENTIALS OF N-CHLORINATED ORGANIC MOLECULES

PREDICTION OF CHLORINE POTENTIALS OF N-CHLORINATED ORGANIC MOLECULES

ABSTRACT

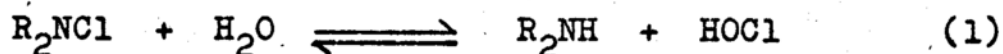
Different linear free energy correlations have been found between the tendencies of (a) the anions of imides and amides, and (b) secondary and tertiary amines, to accept a proton or to accept a positive chlorine ion to yield an N-chloro derivative. An attempt has been made to account for the two correlations by treating the N-protonated and N-chloro derivatives as Lewis acid-base complexes between "hard" (H^+) and "soft" (Cl^+) acids and "soft" (anions of amides and imides) and "hard" (amines) bases. From the relationships developed it should be possible to predict the chlorine potential of an N-chloro compound whose structure and relevant acid dissociation constants (of the N-chloro and N-protonated derivatives) are known.

RESULTS AND DISCUSSION

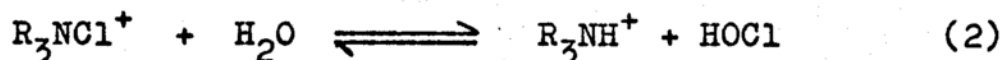
In a previous paper¹ we defined the chlorine

¹T. Higuchi, A. A. Hussain and I. H. Pitman, J. Chem. Soc., (B), in press.

potential, pK_{cp} , of an N-chlorinated molecule as $pK_{cp} = -\log_{10} K_{cp}$, where K_{cp} was the equilibrium constant for the reaction in which the N-chlorinated molecule was hydrolyzed to yield hypochlorous acid. For an N-chlorinated secondary amine, imide, or amide, the reference reaction would be,



For the N-chloro derivative of a tertiary amine the reference reaction would be,



Thus, for the case represented in equation (1)

$$pK_{cp} = (\Delta G_{R_2NH}^{\circ} - \Delta G_{R_2NCl}^{\circ}) + (\Delta G_{HOCl}^{\circ} - \Delta G_{H_2O}^{\circ}) / 2.303 RT$$

The free energy difference $(\Delta G_{HOCl}^{\circ} - \Delta G_{H_2O}^{\circ})$ was calculated to be $+37.7 \text{ kcal mol}^{-1}$ from the difference in standard free energies of formation of $HOCl_{aq}$ ($\Delta G_f^{298} = -19.0 \text{ kcal mol}^{-1}$)² and

²G. N. Lewis and M. Randall, "Thermodynamics and the Free Energy of Chemical Substances," McGraw-Hill Book Company, New York, 1923, p. 508.

$H_2O(\Delta G_f^{298} = 56.7 \text{ kcal mol}^{-1})$.³ Hence the differences in

³"Selected Values of Chemical Thermodynamic Properties," Natl. Bur. of Standards Circ. 500, U.S. Government Printing Office, Washington, D.C., 1952.

standard free energy between an amine, sulfonamide and imide, and its N-chloro conjugate at 25°C were calculated using the identity,

$$13.6 \text{ pK}_{cp} - 37.7 = \Delta G_{R_2NH}^{\circ} - \Delta G_{R_2NCl}^{\circ}$$

For N-chlorinated tertiary amines the difference in standard free energy

$$(\Delta G_{R_3NH^+}^{\circ} - \Delta G_{R_3NCl^+}^{\circ}) = 13.6 \text{ pK}_{cp} - 37.7$$

values of these standard free energy differences for fourteen compounds are listed in Table I together with the pK_a values of the various substrates.

From these results it is evident that there is a qualitative relationship between the acidity of the substrate and its stability relative to its N-chloro derivative. For example, saccharin (pK_a 1.30) is a strong acid and its standard free energy is 10.7 kcal less than that of its N-chloro derivative, whereas for the weakly acidic piperidine ($pK_a > 30$) the free

TABLE I

FREE ENERGY DIFFERENCES BETWEEN NITROGEN CONTAINING
MOLECULES AND THEIR N-CHLORO DERIVATIVES

Substrate	pK_a	pK_{cp}^f	$(\Delta G_{R_2NH}^\circ - \Delta G_{R_2NCl}^\circ)$ kcal mol ⁻¹
Saccharin	1.30 ^a	4.85 ^a	-30.7
Quinuclidinium ion	10.95 ^b	5.15	-30.3
N-Me-benzene-sulfonamide	11.35	7.96	-26.5
Succinimide	9.62 ^c	7.71	-26.8
p-Toluene-sulfonamide	10.30 ^d	7.77	-26.7
N-chloro-p-toluene-sulfonamide	4.55 ^d	6.55	-28.4
Me ₂ NH	> 30.0 ^e	14.93	-17.0
Et ₂ NH	> 30.0 ^e	15.23	-16.6
Pr ₂ NH	> 30.0 ^e	15.21	-16.6
i-Pr ₂ NH	> 30.0 ^e	13.10	-19.5
Bu ₂ NH	> 30.0 ^e	15.38	-16.4
BuMeNH	> 30.0 ^e	15.06	-16.8
Piperidine	> 30.0 ^e	16.19	-15.3
Morpholine	> 30.0 ^e	14.06	-18.2

^aSee Section I of this work.

^bSee reference 1.

^cH.F. Walton and A.A. Schilt, J. Amer. Chem. Soc., **74**, 4995 (1952).

^dT. Higuchi, K. Ikeda and A. A. Hussain, J. Chem. Soc., (B), 546 (1967).

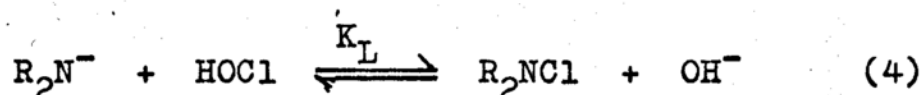
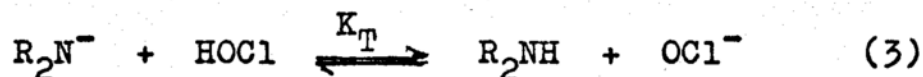
^eEstimated base on the acid dissociate constant of ammonia ($pK_a = 35$) by R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N.Y., 1959.

^fUnless otherwise stated values were taken from reference 1.

energy difference is only 15.3 kcal. Values for the other compounds fall roughly within this range.

However, ionization of a proton (pK_a) and substitution of a proton for a positive chlorine substituent (pK_{cp}) are vastly different processes and no linear free energy relationship between pK_a and pK_{cp} was evident.

A more useful approach appeared to be to compare equilibrium constants for competitive reactions in which bases extract either a proton or a positive chlorine ion out of aqueous hypochlorous acid. The substrates in these reference reactions are the anions of the imides and amides, and the neutral molecules of amines. The reference reactions for imides or amides are,



values of the equilibrium constants, K_T (for reaction (3)) and K_L for reaction (4)) can be obtained from the identities,

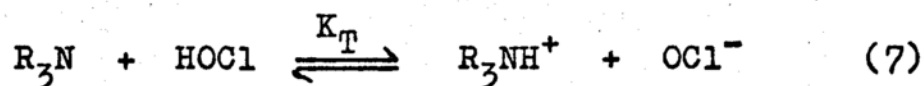
$$K_T = \frac{[R_2NH][OCl^-]}{[R_2N^-][HOCl]} = \frac{K_{a,2}}{K_{a,1}} \quad (5)$$

and

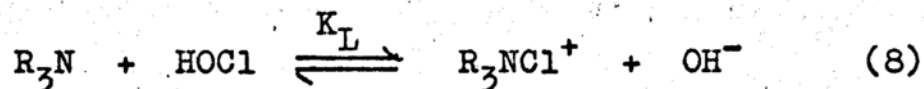
$$K_L = \frac{[R_2NCl][OH^-]}{[R_2N^-][HOCl]} = \frac{K_w}{K_{a,1} K_{cp}} \quad (6)$$

where $K_{a,1}$, $K_{a,2}$ and K_w , are the acid dissociation constants for the amides or imides, hypochlorous acid, and water, respectively, and K_{cp} is the equilibrium constant for hydrolysis of the N-chloro compound.

For a tertiary amine the reference reactions are



and



Thus, for tertiary amines

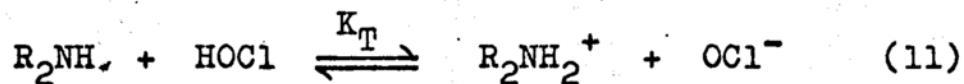
$$K_T = \frac{[R_3NH^+][OCl^-]}{[R_3N][HOCl]} = \frac{K_{a,2}}{K_{a,1}''} \quad (9)$$

and

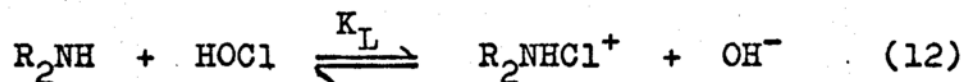
$$K_L = \frac{[R_3NCl^+][OH^-]}{[R_3N][HOCl]} = \frac{K_w}{K_{a,1} K_{cp}} \quad (10)$$

where $K_{a,1}''$ is the acid dissociation constant of the conjugate acid of the amine and the other equilibrium constants are as defined above.

For secondary amines the reference reactions are,



and



Therefore, for secondary amines

$$K_T = \frac{[R_2NH_2^+][OCl^-]}{[R_2NH][HOCl]} = \frac{K_{a,2}}{K_{a,1}} \quad (13)$$

and

$$K_L = \frac{[R_2NHC1^+][OH^-]}{[R_2NH][HOCl]} = \frac{K_w}{K_{a,3} K_{cp}} \quad (14)$$

where $K_{a,1}$, and $K_{a,3}$, are the acid dissociation constants for the conjugate acids of the amine and the N-chloroamine, respectively.

Values of $-\log_{10} K_T$ and $-\log_{10} K_L$ for the fourteen imides, amides and amines studied are included in Table II together with the values of the appropriate acid dissociation constants. Because the only chlorammonium acid dissociation constants ($pK_{a,3}$ values) available were those for dimethylchlorammonium ion and diethylchlorammonium ion, these values were plotted against the acid dissociation constants of the dimethylammonium and diethylammonium ions. The $pK_{a,3}$

TABLE II

ACID DISSOCIATION CONSTANTS AND $-\log_{10}K_T$ AND $-\log_{10}K_L$
VALUES FOR 14 ORGANIC NITROGEN CONTAINING MOLECULES

Substrate	$pK_{a,1}^a$	$pK_{a,1}^{b,c}$	$pK_{a,3}^{b,c}$	$-\log_{10}K_T$	$-\log_{10}K_L$
1. Saccharin	1.30			6.24	7.81
2. N-chloro-p-toluene-sulfonamide	4.55			3.00	2.90
3. p-Toluenesulfonamide	10.30			-2.75	-4.70
4. N-Me-benzenesulfonamide	11.35			-1.80	-5.31
5. Succinimide	9.62			-2.07	-3.33
6. Quinuclidine		10.95		-3.40	-2.10
7. Me ₂ NH		10.73	0.46 ^c	-3.18	-1.39
8. Et ₂ NH		10.98	1.02 ^c	-3.43	-2.25
9. Pr ₂ NH		11.00	1.07 ^d	-3.45	-2.28
10. i-Pr ₂ NH		11.05	1.19 ^d	-3.50	-0.29
11. Bu ₂ NH		11.25	1.64 ^d	-3.70	-3.02
12. BuMeNH		10.90	0.84 ^d	-3.35	-1.90
13. Piperidine		11.12	1.34 ^d	-3.57	-3.53
14. Morpholine		8.33	-4.80 ^d	-0.78	4.74

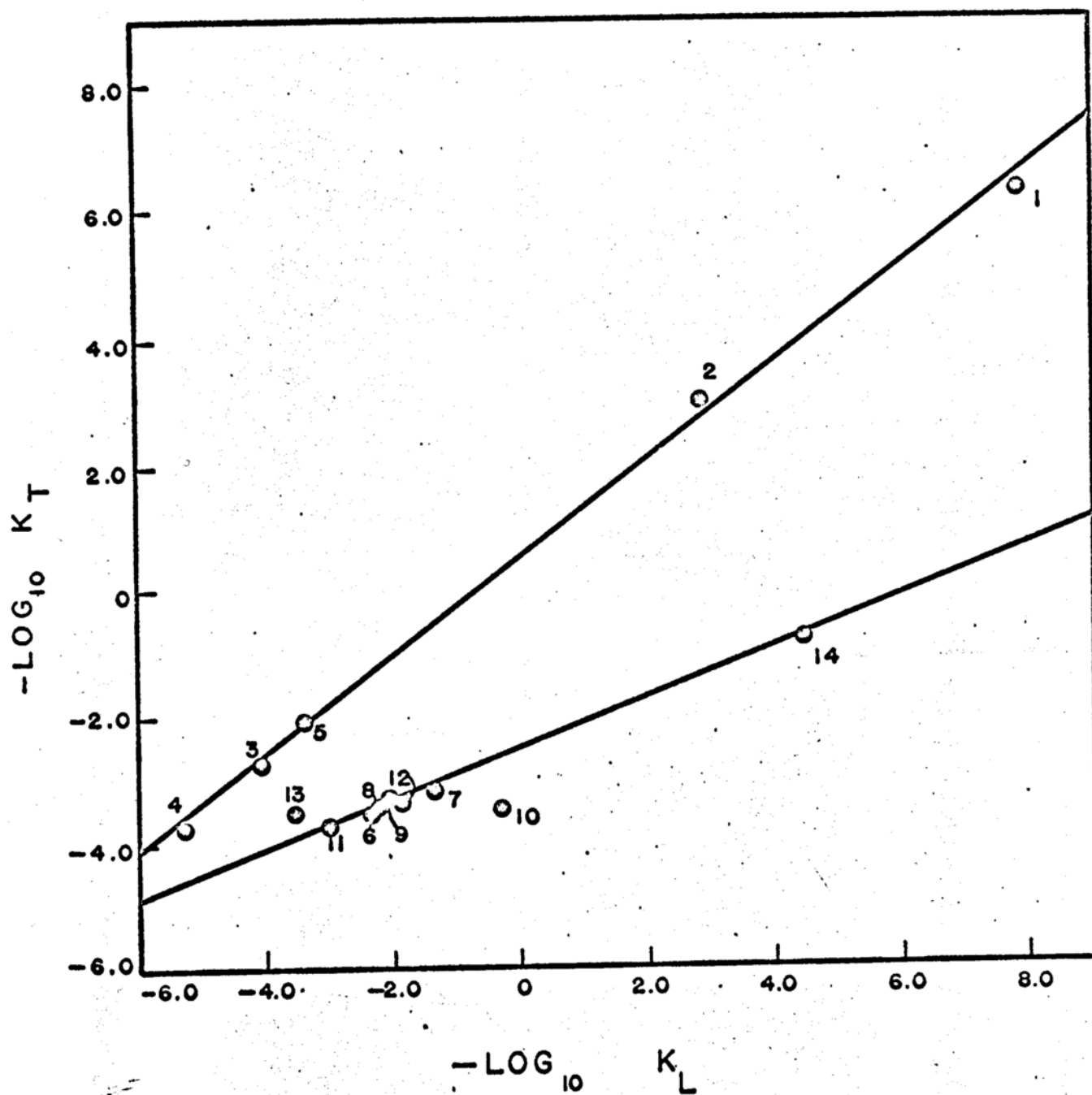
^aSee table for reference. ^bD. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworths, London, 1965. ^cI. Weil and J. C. Morris, J. Amer. Chem. Soc., 71, 3123 (1949). ^dEstimated as described in text.

values of the other chlorammonium species were extrapolated from the resulting linear free energy relationship. The values for all the chlorammonium ions except N-chloromorpholinium ion are expected to be reliable to within ± 0.5 of a pK_a unit because the ammonium ions all have similar acid strengths.

Morpholinium ion is considerably more acidic than the other ammonium ions and the estimate of the pK_3'' value of N-chloromorpholinium ion is probably less reliable because of the larger extrapolation required.

As seen from the plot of $-\log K_T$ against $-\log K_L$ in Figure I, the compounds investigated fall into two distinct groups. A reasonably good linear correlation exists between $-\log K_T$ and $-\log K_L$ values for the anions of imides and amides and another between the values for amines. The two lines appears to converge at $-\log K_T = -5.40$. Thus, the following discussion about possible reasons as to why a compound falls on the upper or lower line only applies to bases whose conjugate acids have pK_a values below 12.95 (see equations(5), (9), and (13)).

From the results in Figure I it can be seen that if an imide (or amide) anion and a secondary amine had similar tendencies to accept a proton (K_T) then the imide anion would have the greater tendencies to accept a positive chlorine ion (K_L). Conversely, if both types of compound had similar tendencies to accept a positive



chlorine ion then the amine would accept a proton more strongly than would the imide anion. These results suggest that N-chloro imides, and amides, are stabilized relative to imides and amides by some factors which do not contribute as strongly towards the stabilization of N-chloro secondary and tertiary ammonium ions relative to the ammonium ions. These factors⁴ may include

⁴R. G. Pearson, J. Amer. Chem. Soc., 85, 3533 (1963).

greater covalent character of the N-Cl bond, some form of π bonding, or electron correlation effects. A qualitative understanding⁵ of the differences between these two groups

⁵R. G. Pearson and J. Songstad, ibid., 89, 1827 (1967).

of compounds comes from treating the N-chloro and N-protonated derivatives as complexes formed between Lewis acids (H^+ , Cl^+) and bases. According to the principle of hard and soft acids and bases, complexes formed between acids and bases of similar degrees of hardness or softness will be the most stable. Hence, complexes formed between soft bases such as the highly polarizable anions of imides and amides and the soft acid, Cl^+ , (cf Br^+ , I^+)⁵ are expected to be more stabilized by the interactions of the chlorine than are the complexes

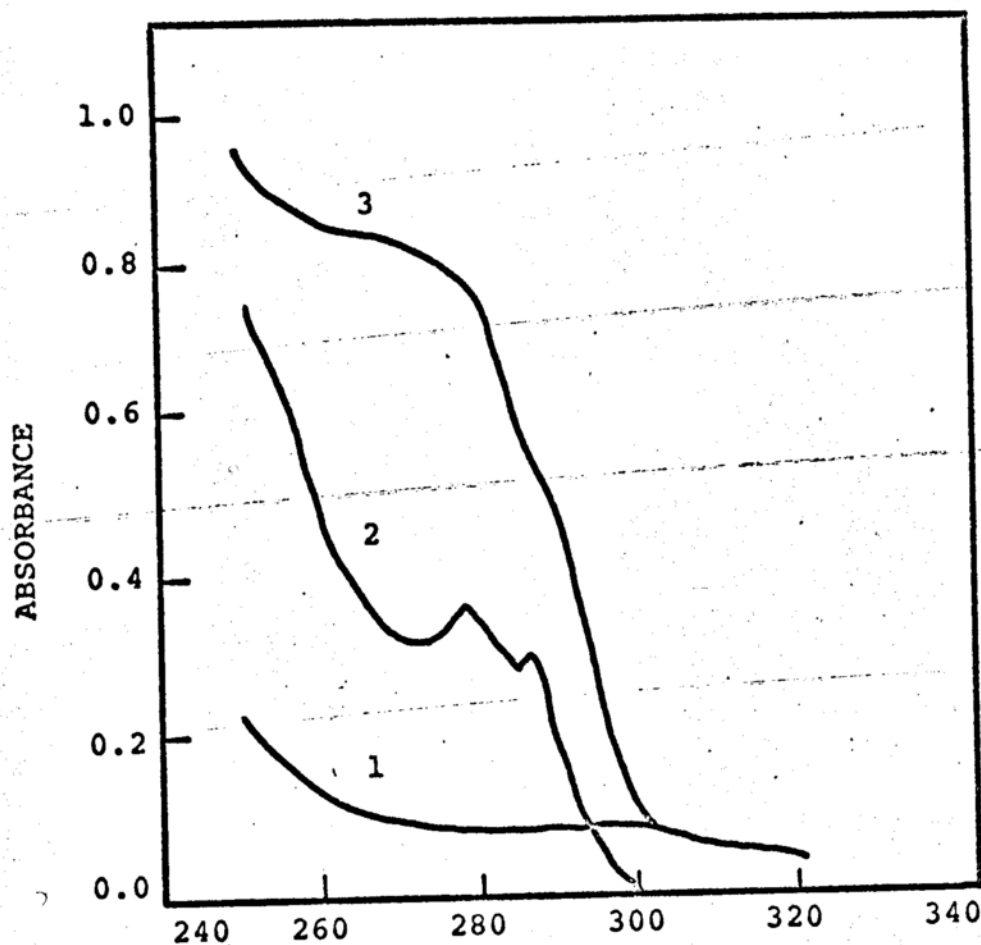
formed with the hard acid, H^+ . Similarly, complexes of hard bases such as secondary and tertiary amines (cf NH_3 , RNH_2)⁵ and the hard acid, H^+ , are expected to be more stable than those with the soft acid, Cl^+ .

Small displacements of compounds from their correlation lines are probably due to differences in the steric requirements of Cl and H substituents.

By using the correlation lines in Figure I and the relationships developed in this paper it should be possible to predict the chlorine potential of an N-chloro compound from a knowledge of its structure and the relevant acid dissociation constants.

APPENDIX I

SPECTRUM OF THE MIXTURE OF SACCHARIN AND HYPOCHLOROUS
ACID IN 6.8 N-SULFURIC ACID

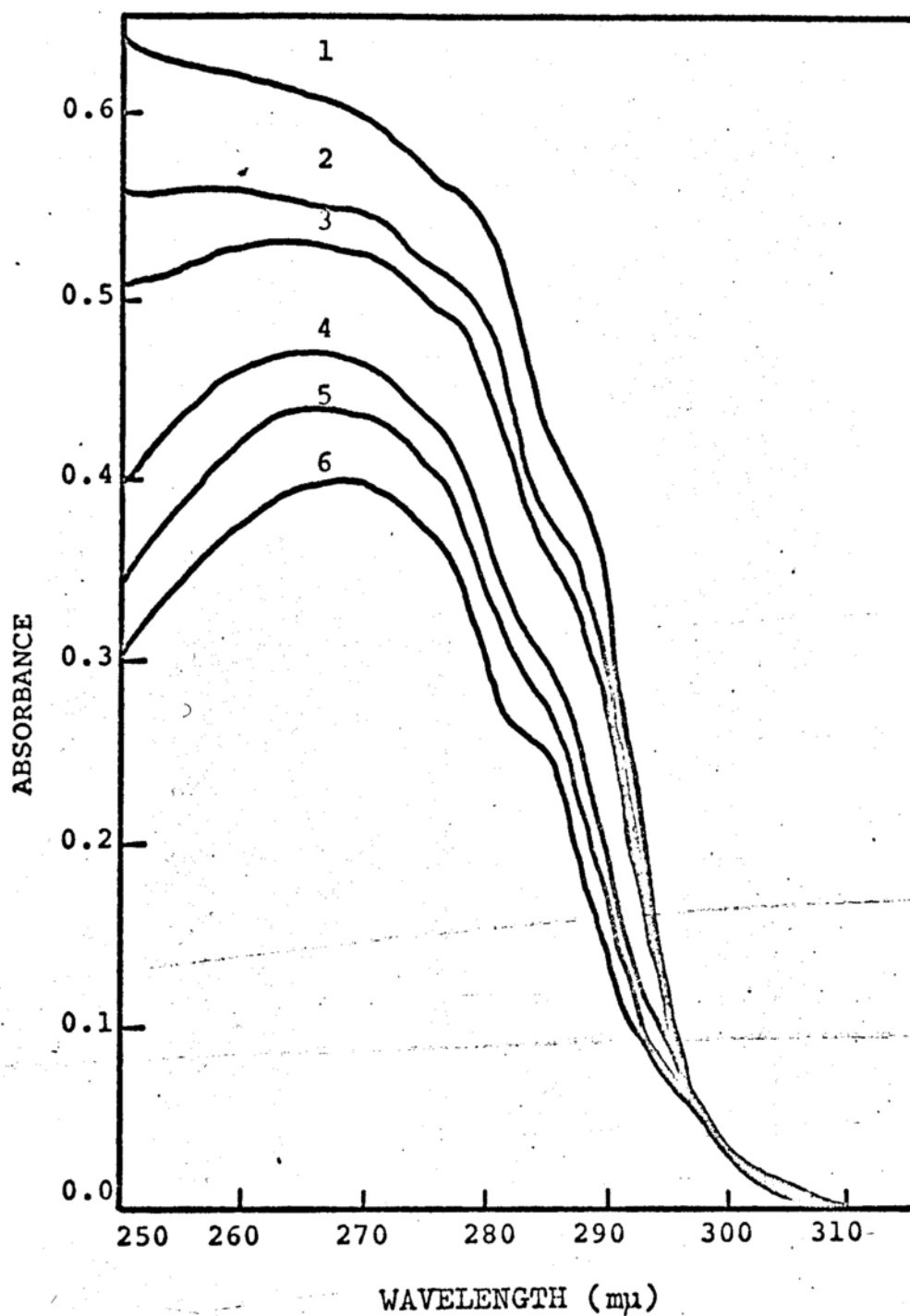


1. Solution of 6.18×10^{-4} M HOCl in 6.8 N H_2SO_4 .
2. Solution of 5.80×10^{-5} M Saccharin in 6.8 N H_2SO_4 .
3. Mixture of 6.18×10^{-4} M HOCl and 5.80×10^{-5} M saccharin in 6.8 N H_2SO_4 . Spectrum was taken immediately after mixing.

Measurements were made with 5 cm cell.

APPENDIX II

SPECTRA OF N-CHLOROSACCHARIN IN BUFFER SOLUTIONS OF VARIOUS ACIDITIES



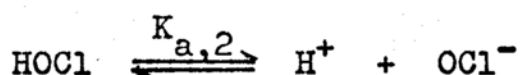
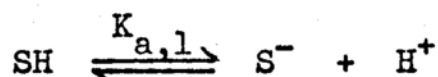
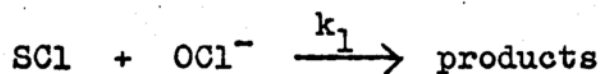
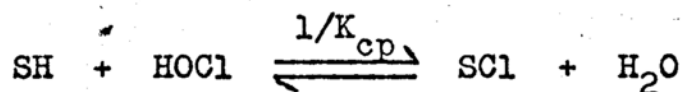
Initial concentration of N-chlorosaccharin:

2.43×10^{-4} M in (1) 2 N sulfuric acid, pH = 0.0; (2) 0.29 M sulfate buffer, pH = 1.20; (3) 0.29 M sulfate buffer, pH = 1.67; (4) 0.2 M phosphate buffer, pH = 2.58; (5) 0.2 M phosphate buffer, pH = 3.06; (6) 0.2 M acetate buffer of both pH 4.03 and 5.30. This spectrum is also identical to that of saccharin solution under the same conditions. 1 cm cells were used to measure the absorbances.

APPENDIX III

DERIVATION OF THE RATE EQUATION FOR THE DEGRADATION
OF N-CHLOROSACCHARIN IN AQUEOUS HYPOCHLORITE SOLUTION

The important reactions in the saccharin-hypochlorous acid mixture are the following,



where K_{cp} is the thermodynamic hydrolytic constant; k_1 is the second order rate constant for the cleavage of imide bond; $K_{a,1}$ and $K_{a,2}$ are the acid dissociation constants of saccharin and hypochlorous acid, respectively. And the rate of degradation is,

$$\text{Rate} = d[\text{products}]/dt = k_1[\text{SCl}][\text{OCl}^-] \quad (1)$$

Since at any time the concentration of N-chlorosaccharin, SCl , relates to total saccharin species, SH_{total} , by the identity,

$$[\text{SH}_{\text{total}}] = [\text{SCl}] + [\text{S}^-] + [\text{SH}] \quad (2)$$

and the relationships,

$$K_{a,1} = \frac{[\text{H}^+][\text{S}^-]}{[\text{SH}]} \quad \text{and} \quad K_{cp} = \frac{[\text{SH}][\text{HOCl}]}{[\text{SCl}]} \quad (3)$$

always hold, the combination of equations yields,

$$[SH_{total}] = [SCl] + \frac{K_{a,1}[SCl]K_{cp}}{[H^+][HOCl]} + \frac{K_{cp}[SCl]}{[HOCl]}$$

or

$$[SCl] = \frac{[SH_{total}][H^+][HOCl]}{[H^+][HOCl] + K_{a,1}K_{cp} + K_{cp}[H^+]} \quad (4)$$

When equation (4) and $[OCl^-] = (K_{a,2}[HOCl])/[H^+]$ are substituted into equation (1) the rate of degradation becomes

$$Rate = \frac{k_1 K_{a,2}[HOCl]^2[SH_{total}]}{[H^+][HOCl] + K_{a,1}K_{cp} + K_{cp}[H^+]} \quad (5)$$

under the conditions where $[HOCl]_{added} \gg [SH]_{added}$ and the pH of the solutions are buffered at two units below $pK_{a,2}$, $[HOCl] = [HOCl]_{added}$: Thus,

$$Rate = \frac{k_1 K_{a,2}[HOCl]_{added}^2 [SH_{total}]}{[H^+][HOCl]_{added} + K_{a,1}K_{cp} + K_{cp}[H^+]} \quad (6)$$

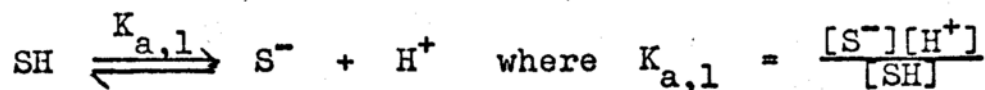
Hence, a pseudo first order reaction with respect to saccharin was observed and k_1 can be calculated from the pseudo first order rate constant, k'_1 , and other known quantities by using the following identity,

$$k_1 = k'_1 \frac{[H^+][HOCl]_{added} + K_{a,1}K_{cp} + K_{cp}[H^+]}{K_{a,2}[HOCl]_{added}^2} \quad (7)$$

APPENDIX IV

ACID DISSOCIATION CONSTANT AND MOLAR ABSORPTIVITY
OF SACCHARIN

Saccharin partially dissociates in water according to



Based on the law of conservation of mass and Beer's law we have the relationships,

$$[\text{SH}]_{\text{added}} \quad (\text{concentration of saccharin initially added}) = [\text{SH}] + [\text{S}^-] \quad (1)$$

and

$$A = \sum_{\text{SH}} [\text{SH}]b + \sum_{\text{S}^-} [\text{S}^-]b \quad (2)$$

where

A = the absorbance of an equilibrium solution of saccharin and saccharin anion

\sum_X = molar absorptivity of X; $\sum_{\text{S}^-}^{270} = 1570$

[X] = molarity of X

b = pathlength of cell

are derived, respectively.

Substituting [SH] in equation (2) with $[\text{SH}]_{\text{added}} - [\text{S}^-]$, we have,

$$A = \sum_{\text{SH}} [\text{SH}]_{\text{added}} b - \sum_{\text{SH}} [\text{S}^-]b + \sum_{\text{S}^-} [\text{S}^-]b \quad (3)$$

$$A = A_{\text{SH}} + (\sum_{\text{S}^-} - \sum_{\text{SH}}) [\text{S}^-]b$$

where

$A_{SH} = \epsilon_{SH}[SH]_{added} b$; the absorbance of the same solution at pH values where more than 99% of the saccharin is in the form of its neutral molecule.

Similarly, substituting $[S^-]$ with $[SH]_{added} - [SH]$

we have

$$A = \epsilon_{SH}[SH]b + \epsilon_{S^-}[SH]_{added} b - \epsilon_{S^-}[SH]b \quad (4)$$

$$A = (\epsilon_{SH} - \epsilon_{S^-})[SH]b + A_{S^-}$$

where

$A_{S^-} = \epsilon_{S^-}[SH]_{added} b$; the absorbance of the same solution at pH values where more than 99% of the saccharin is in the form of its anion.

Eliminating the term, $(\epsilon_{S^-} - \epsilon_{SH})$, by combination of equations (3) and (4) yields,

$$\frac{(A_{S^-} - A)}{(A - A_{SH})} = \frac{[SH]}{[S^-]}$$

Since

$$\frac{[SH]}{[S^-]} = \frac{[H^+]}{K_{a,1}}$$

thus,

$$\frac{(A_{S^-} - A)}{(A - A_{SH})} = \frac{[H^+]}{K_{a,1}}$$

or

$$\frac{A_{S^-} - A}{[H^+]} = \frac{A}{K_{a,1}} - \frac{A_{SH}}{K_{a,1}} \quad (5)$$

A plot of $(A_{SH} - A)/[H^+]$ against A would be linear and yield values of

$$K_a = \left(\frac{1}{\text{slope}} \right) \quad \text{and} \quad SH = \left(- \frac{\text{intercept}}{\text{slope } [SH]_{\text{added}} b} \right)$$

Figure I shows two determinations made in 0.2 M HCl-KCl buffer at 270 mμ in slightly different solvent systems. The results on line 2 are from solutions containing 2.5 volume % ethyl acetate while those on line 1 do not. The results are shown in Table I.

TABLE I
THE DISSOCIATION CONSTANT, $K_{a,1}$, AND MOLAR
ABSORPTIVITY, ϵ_{SH} , OF SACCHARIN ACID

$[SH]_{\text{added}} \times 10^4 \text{ M}$	Slope	Intercept	$K_{a,1}$	ϵ_{SH}
1. 1.90	20.4	-21.7	0.0491	1119
2.* 2.00	26.1	-29.3	0.0383	1120

*Solution containing 2.5 volume % ethyl acetate.

The slight difference between the two $K_{a,1}$ values is probably due to the change of the solvent system. An average value of 1120 for ϵ_{SH} is obtained. The value of $K_{a,1}$, 0.0491 or 0.0383 was selected according to the absence or presence of 2.4 volume % ethyl acetate in the solution.

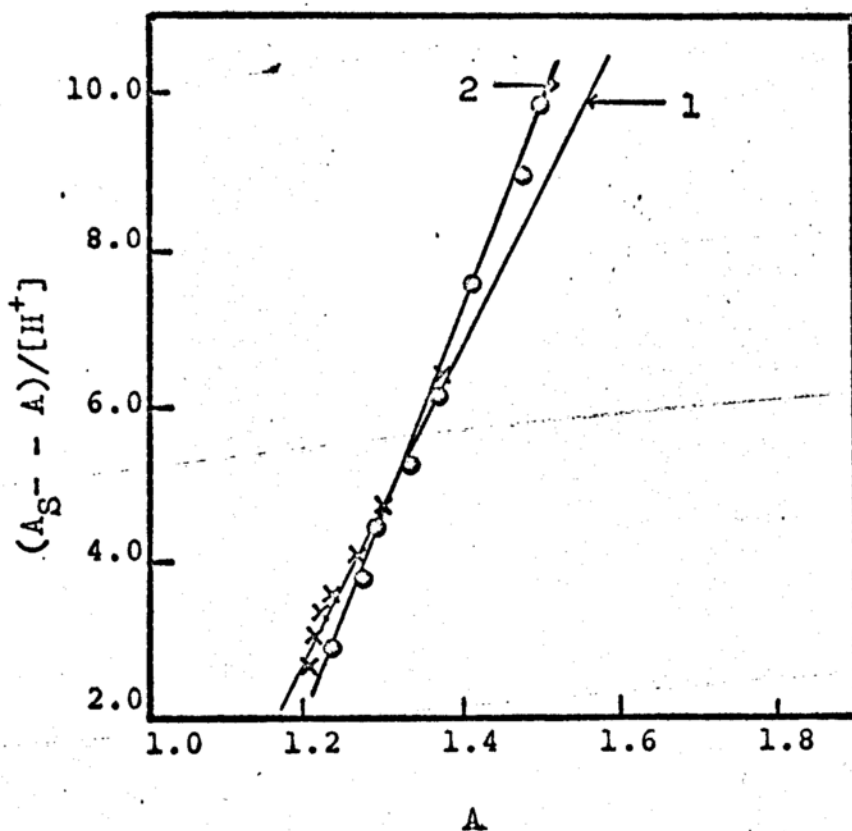


Figure I. Determination of $K_{a,1}$ and molar absorptivity of saccharin 0.2 M KCl-HCl buffer solution. Measurement of absorbance was made at 270 m μ with a 5-cm cell. Composition of the systems:

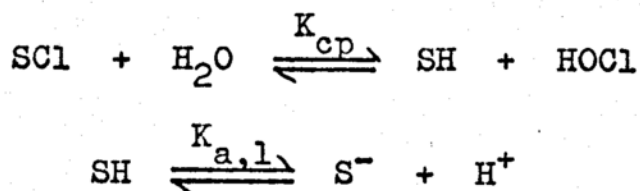
1. 1.90×10^{-4} M saccharin in aqueous buffer solution. Results are shown in Table I.
2. 2.00×10^{-4} M saccharin in aqueous buffer solution containing 2.4% ethyl acetate.

APPENDIX V

DETERMINATION OF THE HYDROLYTIC CONSTANT, K_{cp} ,
FOR N-CHLOROSACCHARIN

The hydrolytic constant, K_{cp} , as previously defined,¹ of N-chlorosaccharin (SCl) was expected to be extremely high. The dissociation constant of the parent acid, saccharin (SH) is 4.91×10^{-2} compared to 2.40×10^{-10} for succinimide, the parent acid for N-chlorosuccinimide. In this section results of an investigation designed to measure the hydrolytic constant are given in detail.

In the pH range of 0 to 4 the important reactions in the saccharin-hypochlorous acid mixture immediately after mixing are two related equilibria, viz:



(Hypochlorous acid is virtually unionized in this range, $pK_a = 7.55$) where $K_{a,1}$ is the dissociation constant of saccharin and S^- represents the anion form of saccharin.

Letting $[\text{SH}] + [\text{S}^-] = [\text{ST}]$, the total concentration of saccharin, then at any hydrogen ion concentration, $[\text{H}^+]$, and rearranging, we obtain

$$[\text{SH}] = \frac{[\text{ST}][\text{H}^+]}{K_a + [\text{H}^+]} \quad (1)$$

Substituting equation (1) into the expression,

$$K_{cp} = \frac{[\text{SH}][\text{HOCl}]}{[\text{SCl}]}$$

and rearranging, yields

$$\frac{[ST]}{[SCl]} = \frac{K_{cp}(K_{a,1} + [H^+])}{[H^+][HOCl]} \quad (2)$$

Also, according to Beer's law, the observed absorbance, A , of the solution at equilibrium,

$$A = \sum_{SH}[SH]b + \sum_S[S^-]b + \sum_{SCl}[SCl]b + \sum_{HOCl}[HOCl]b$$

$$A = \sum_{ST}[ST]b + \sum_{SCl}[SCl]b + \sum_{HOCl}[HOCl]b \quad (3)$$

where \sum_X is the absorptivity of "X" and

$$\sum_{ST} = \frac{\sum_S - K_{a,1} + \sum_{SH}[H^+]}{[H^+] + K_{a,1}}$$

and b is the pathlength of the cell.

Substituting $[ST] = [SH]_{\text{added}} - [SCl]$ and $[HOCl] = [HOCl]_{\text{added}} - [SCl]$, where $[SH]_{\text{added}}$ and $[HOCl]_{\text{added}}$ are the concentration of saccharin and hypochlorous acid initially added, into (3) yields

$$A = \sum_{ST}[SH]_{\text{added}}b - \sum_{ST}[SCl]b + \sum_{SCl}[SCl]b \\ - \sum_{HOCl}[HOCl]_{\text{added}}b + \sum_{HOCl}[SCl]b$$

$$A = A_0 + \Delta \sum [SCl]b \quad (4)$$

where

$A_0 = \sum_{ST} [SH]_{\text{added}} b + \sum_{HOCl} [HOCl]_{\text{added}} b$; the absorbance of the solution under conditions where more than 99% of the added saccharin was in the form of saccharin plus saccharin anion,

$$\Delta \epsilon = \sum_{SCl} - \sum_{ST} - \sum_{HOCl}$$

On the other hand, equation (3) can be reformulated by substitution of $[SCl] = [SH]_{\text{added}} - [ST]$ and $[HOCl] = [HOCl]_{\text{added}} - [SH]_{\text{added}} + [ST]$ which gives,

$$A = \sum_{ST} [ST] b + \sum_{SCl} [SH]_{\text{added}} b - \sum_{SCl} [ST] b + \sum_{HOCl} [HOCl]_{\text{added}} b - \sum_{HOCl} [SH]_{\text{added}} + \sum_{HOCl} [ST] b$$

$$A = A_{\infty} - \Delta \epsilon [ST] b \quad (5)$$

where

$A_{\infty} = \sum_{SCl} [SH]_{\text{added}} b + \sum_{HOCl} [HOCl]_{\text{added}} b - \sum_{HOCl} [SH]_{\text{added}} b$; the absorbance of the solution under conditions where more than 99% of the added saccharin was in the form of N-chlorosaccharin,

$$\frac{(5)}{(4)} \text{ gives } \frac{[ST]}{[SCl]} = \frac{A_{\infty} - A}{A - A_0} \quad (6)$$

Substitution of (6) into (2) yields,

$$\frac{K_{cp}(K_{a,1} + [H^+])}{[H^+][HOCl]} = \frac{A_{\infty} - A}{A - A_0} \quad (7)$$

or

$$\frac{K_{cp} (K_{a,1} + [H^+])}{[H^+][HOCl]_{added} - [SCl]} = \frac{A_{\infty} - A}{A - A_0} \quad (7)$$

From the definition of A and A_0 the following relationship can be derived,

$$A_{\infty} - A_0 = \Delta \sum [SH]_{added} \quad (8)$$

The combination of equations (8) and (4) gives

$$[SCl] = \frac{A - A_0}{A_{\infty} - A_0} [SH]_{added} \quad (9)$$

Substituting (9) into (7) and rearranging we have the final form of the equation,

$$\frac{(A - A_0)(K_{a,1} + [H^+])}{[H^+] \left\{ [HOCl]_{added} - \frac{A - A_0}{A_{\infty} - A_0} [SH]_{added} \right\}} = \frac{A_{\infty}}{K_{cp}} - \frac{A}{K_{cp}} \quad (10)$$

Under the conditions where $[HOCl]_{added} \gg [SH]_{added}$, the term,

$$[HOCl]_{added} - \frac{A - A_0}{A_{\infty} - A_0} [SH]_{added} = [HOCl]_{added}.$$

Since

$$\frac{A - A_0}{A_{\infty} - A_0}$$

is also less than unity, therefore a plot of

$$\frac{(A - A_0)(K_{a,1} + [H^+])}{[H^+][HOCl]_{\text{added}}}$$

against A would show a straight line (Figure I).

$$K_{cp} = \left(- \frac{1}{\text{slope}} \right) \quad \text{and} \quad A_{\infty} = \left(- \frac{\text{intercept}}{\text{slope}} \right)$$

were calculated and summarized in Table I.

The absorptivity of N-chlorosaccharin, ϵ_{SCl} , was then used in the calculations of K_{cp} under the conditions where (A) $[HOCl]_{\text{added}}$ was not much greater than $[SH]_{\text{added}}$, or (B) N-chlorosaccharin was added to the buffered solution of saccharin. Tables II and III summarize the values of K_{cp} obtained under conditions (A) and (B), respectively.

The K_{cp} values all agreed reasonably well. The mean values for K_{cp} in water is $1.3 \times 10^{-5} \text{ M}$ at 25° (excluding the K_{cp} values calculated from experiments where 2.4 volume % ethyl acetate was present).

¹Hussain, A. A., Ph.D. thesis, University of Wisconsin, Madison, Wisconsin, (1965).

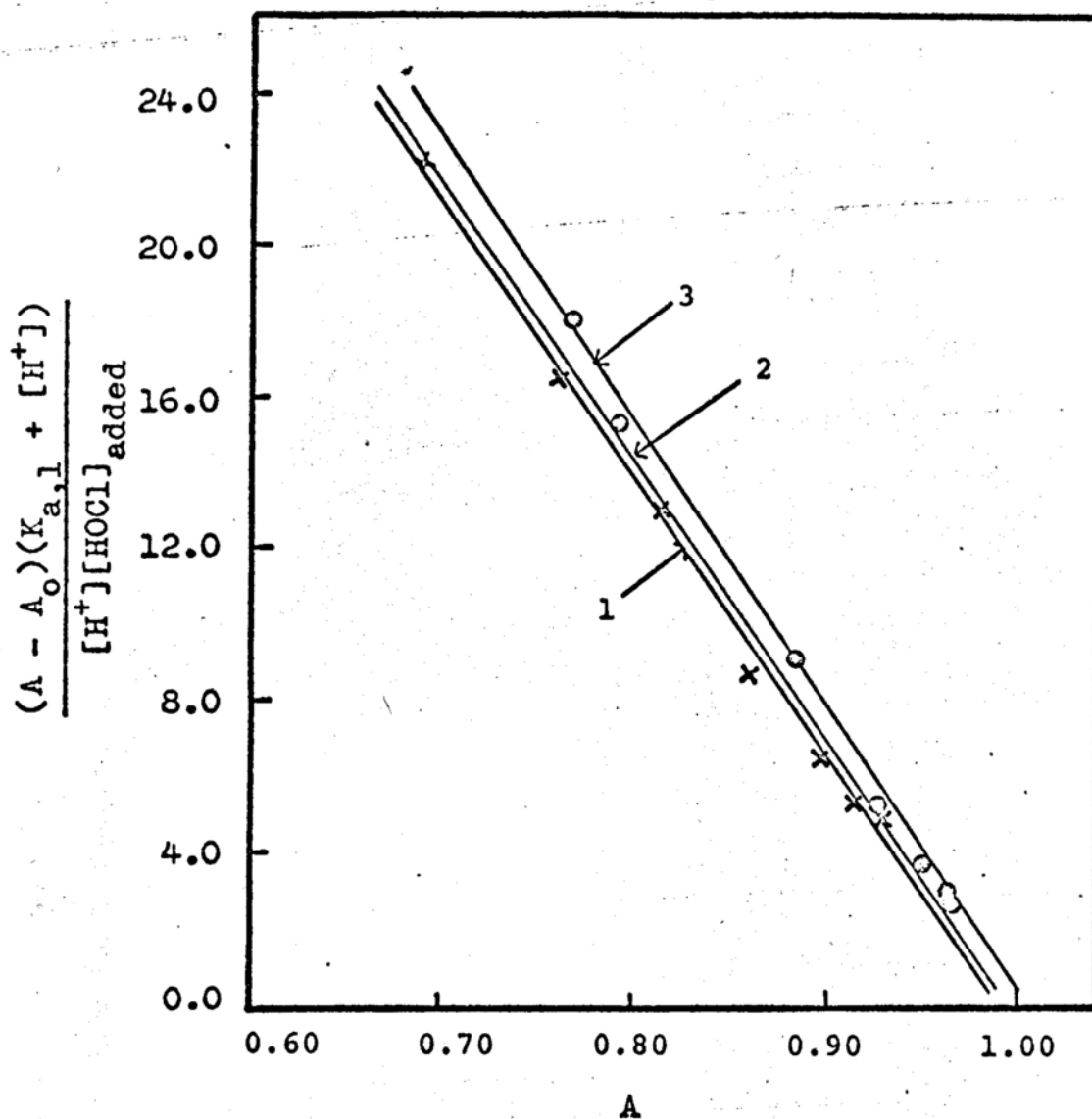


Figure I. Determination of K_{cp} and molar absorptivity of N-chlorosaccharin at three different initial concentrations. Buffer concentration = 0.045 M, absorbances measured at 270 m μ with 2-cm cell.

1. Initially contain saccharin 1.81×10^{-4} M and hypochlorous acid 7.23×10^{-4} M. (Data are marked with "X").
2. Initially contain saccharin 1.77×10^{-4} M and hypochlorous acid 1.06×10^{-3} M. (Data are not shown in this figure, but in Table IV, page 45).
3. Initially contain saccharin 1.73×10^{-4} M and hypochlorous acid 1.38×10^{-3} M. (Data are marked with "o").

TABLE I

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° UNDER THE CONDITION WHERE $[\text{HOCl}]_{\text{added}}$ WAS MUCH GREATER THAN $[\text{SH}]_{\text{added}}^*$

$[\text{SH}]_{\text{added}}$ $\times 10^4 \text{ M}$	$[\text{HOCl}]_{\text{added}}$ $\times 10^4 \text{ M}$	Slope $\times 10^{-4} \text{ M}$	Intercept $\times 10^{-4} \text{ M}$	K_{cp} $\times 10^{-5} \text{ M}$	A_{∞}	\sum_{SCL}^{**}
1.81	7.23	-7.11	7.05	1.40	0.991	2640
1.77	10.6	-7.22	7.19	1.38	0.995	2652
1.73	13.8	-7.63	7.64	1.31	1.001	2670
AVERAGE:						2654

*Constants used were $K_{a,1} = 0.0491$; $\sum_{\text{S}^-} = 1570$; and $\sum_{\text{SH}} = 1120$.

$$^{**}\sum_{\text{SCL}} = \frac{A - \sum_{\text{HOCl}}([\text{HOCl}]_{\text{added}} - [\text{SH}]_{\text{added}})^b}{[\text{SH}]_{\text{added}}^b}$$

TABLE IIa

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN
WATER UNDER THE CONDITION WHERE $[HOCl]_{added}$ WAS NOT MUCH
GREATER THAN $[SH]_{added}$ *

pH	$[H^+]$ $\times 10^3$ M	A_0	A	A_∞	K_{cp} $\times 10^5$ M
2.296	5.06	0.861	1.245	1.453	1.5
2.402	3.96	0.866	1.236	1.453	1.3
2.465	3.43	0.868	1.217	1.453	1.4
2.585	2.60	0.872	1.187	1.453	1.4
2.802	1.58	0.876	1.140	1.453	1.3
3.055	0.88	0.880	1.070	1.453	1.4
3.200	0.631	0.881	1.032	1.453	1.4
3.296	0.506	0.882	1.015	1.453	1.4
3.465	0.343	0.882	0.976	1.453	1.5
AVERAGE:					1.4 ± 0.1

* $[SH]_{added} = 2.72 \times 10^{-4}$ M; $[HOCl]_{added} = 4.66 \times 10^{-4}$ M.
Monochloroacetate buffer 0.04 M. Absorbances were
measured at 270 mμ with 2-cm cells.

TABLE IIb

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN
WATER UNDER THE CONDITION WHERE $[HOCl]_{added}$ WAS
NOT MUCH GREATER THAN $[SH]_{added}$ *

pH	$[H^+]$ $\times 10^3$ M	A_0	A	A_{∞}	K_{cp} $\times 10^5$ M
2.305	4.95	1.112	1.598	1.918	1.3
2.405	3.94	1.117	1.565	1.918	1.3
2.466	3.42	1.120	1.550	1.918	1.3
2.586	2.60	1.125	1.520	1.918	1.3
3.810	1.55	1.131	1.453	1.918	1.3
3.060	0.870	1.135	1.380	1.918	1.2
3.210	0.617	1.137	1.334	1.918	1.3
3.300	0.501	1.137	1.314	1.918	1.2
3.458	0.348	1.138	1.281	1.918	1.2
AVERAGE:					1.3

* $[SH]_{added} = 3.54 \times 10^{-4}$ M; $[HOCl]_{added} = 4.55 \times 10^{-4}$ M.
Buffer (monochloroacetate) concentration = 0.04 M.
Absorbances were measured at 270 m μ with a 2-cm cell.

TABLE IIIa

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN
WATER UNDER THE CONDITION WHERE N-CHLOROSACCHARIN
WAS ADDED TO BUFFERED SOLUTIONS OF SACCHARIN*

pH	$[H^+]$ $\times 10^3$ M	A_0	A	A_∞	K_{cp}^{**} $\times 10^5$ M
2.290	5.13	0.604	0.760	1.028	1.9
2.330	4.68	0.606	0.753	1.028	2.0
2.466	3.42	0.611	0.751	1.028	1.6
2.700	2.00	0.617	0.707	1.028	2.1
3.020	0.955	0.621	0.683	1.028	1.8
3.298	0.504	0.623	0.671	1.028	1.4
3.455	0.351	0.624	0.658	1.028	1.5
3.565	0.272	0.624	0.646	1.028	2.0
AVERAGE:					1.8 ± 0.3

*[SCl]_{added} = 1.58×10^{-4} M; [SH]_{added} = 1.79×10^{-5} M.
Buffer (monochloroacetate) concentration = 0.05 M. All
solutions contained 2.4 volume % of ethyl acetate.
Absorbances were measured at 270 mμ with a 2-cm cell.

**In using equations (10) and (11) to calculate K_{cp} , the
values 1.96×10^{-4} M (added concentration of SCl
+ added concentration of saccharin) and 1.58×10^{-4} M
(added concentration of SCl) were used for the terms
"[SH]_{added}" and "[HOC1]_{added}", respectively, since the
amount of N-chlorosaccharin added can be treated as
adding an equal amount of HOC1 and saccharin to the
solution. $K_{a,1}$, determined in solution containing
2.4 volume % ethyl acetate was 0.0382 and was used in
calculations here.

TABLE IIIb

DETERMINATION OF HYDROLYTIC CONSTANT, K_{cp} , AT 25° IN
WATER UNDER THE CONDITION WHERE N-CHLOROSACCHARIN
WAS ADDED TO BUFFERED SOLUTIONS OF SACCHARIN*

pH	$[H^+]$ $\times 10^3$ M	A_0	A	A_∞	K_{cp}^{**} $\times 10^5$ M
2.300	5.01	0.765	0.942	1.115	1.8
2.346	4.51	0.767	0.932	1.315	1.9
2.480	3.31	0.773	0.910	1.315	2.1
2.706	1.97	0.780	0.886	1.315	2.1
3.07	0.940	0.786	0.848	1.315	2.2
3.311	0.489	0.788	0.834	1.315	1.7
AVERAGE:					2.0

*[SCl]_{added} = 1.54×10^{-4} M; [SH]_{added} = 9.48×10^{-5} M.
Buffered (monochloroacetate) concentration = 0.05 M.
All solutions contained 2.4 volume % of ethyl acetate.
Absorbances were measured at 270 mμ with a 2-cm cell.

**Same method of calculation as in Table IIIa was used.

APPENDIX VI

CHROMATOGRAM OF SEPARATION OF A KNOWN MIXTURE OF
SACCHARIN AND O-SULFAMYL BENZOIC ACID FROM A
SILICIC ACID PARTITION COLUMN WITH 2 N SULFURIC
ACID AS STATIONARY PHASE

