

completed by suspending a concentrated aqueous solution of the salt, with catalyst added, in a hydrocarbon solvent, and heating at the desired temperature. In contrast to the bulk polymers, these suspension polymers showed an increase in capacity with decreasing swelling coefficient. The titration curves for two polymers prepared at different temperatures and having different swelling coefficients are shown in Fig. 4. Some additional physical characteristics of the polymers are shown in Table V.

For comparison, the titration curve for a typical polymer of tetraallylammonium bromide prepared by bulk polymerization at 40° is included. The swelling coefficient of this polymer is 1.26, and 36% of the theoretical capacity was available.

Effect of Initial Concentration of Chloride Ion on Capacities on Polymers.—As stated above, determination of capacities of the polymers was carried out by suspending the hydroxide form of the polymer in 0.01 *N* sodium chloride solution, and titrating with 1 *N* hydrochloric acid. In order to determine whether or not this initial anion concentration affected the ultimate capacity of the sample, a number of determinations were made in which varying initial concentrations of chloride ion were used. The titration curves for these determinations are shown in Fig. 5. These results indicate that the ultimate capacity of the resin is not affected, although the initial *pH* is higher. Previous work of this type has been done, using a different ion exchange resin.⁶

Rates of Ion Exchange.—The rapidity with which ion exchange reactions take place in the quaternary ammonium polymers makes rate determination rather difficult. Since the method employed for determination of capacities involved adding a known volume of hydrochloric acid, usually one

(6) R. Kunin and F. X. McCarvey, *Ind. Eng. Chem.*, **41**, 1265 (1949).

milliliter, waiting for a three-minute interval, then reading the *pH* value, we considered it rather important to determine whether or not this three-minute interval was sufficient to allow the reaction to proceed to completion. In order to check this, three samples of equal weight of a polymer were converted to the hydroxyl form and subjected to 0.01 molar potassium chloride and equivalent volumes of a known excess of standard hydrochloric acid for varying times. The results of this determination as recorded in Table VI appear to vary only within the limits of experimental error, and indicate that the reaction reached equilibrium in two minutes or less.

Throughout this work, it was obvious that the rate of exchange of hydroxyl for halide was much slower than the reverse reaction. As may be observed from a study of Fig. 6, the exchange reaction proceeded very rapidly during the passage of the first 150 ml. of potassium chloride solution, reaching a hydroxyl ion content of 0.0026 mole per liter. The conversion thereafter was much slower since the last sample collected (after 650 ml. had passed) showed a concentration of approximately 0.001 mole per liter. The dotted portion of the graph represents the effect of the dilution of the first sample of effluent by the small amount of water which did not drain from the resin.

As observed from curve B of Fig. 6, the rate of exchange of hydroxyl ion for chloride ion was slower than the reverse reaction. Approximately 500 ml. of alkali was necessary to bring the chloride ion concentration in the effluent to a reasonably constant value. The concentration of chloride ion in the effluent after 650 ml. had passed was about 0.006 mole per liter. After 1025 ml. had passed, the concentration was reduced to about 0.004 mole per liter.

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[CONTRIBUTION FROM THE WESTERN REGIONAL RESEARCH LABORATORY¹]

The Hydrolysis Rate of Betaine Amide and Ester Chlorides

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The acidic and alkaline hydrolysis rates of a typical betaine ester and betaine amide have been studied. These derivatives are hydrolyzed faster in alkali and slower in acid than similar uncharged compounds.

Betaine hydrochloride (carboxymethyltrimethylammonium chloride) can be readily obtained from sugar-beet processing liquors but, up to the present, large-scale recovery of this non-toxic compound for chemical purposes has not been considered worthwhile. Since betaine hydrochloride is both a quaternary salt and a carboxylic acid, its use for the preparation of stable, water-soluble derivatives of a large number of otherwise insoluble amines

(1) Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Report of a study made under the Research and Marketing Act of 1946. Article not copyrighted.

and alcohols appears attractive.² Hence, we have investigated the rate of hydrolysis of a typical betaine ester and an amide in acid and alkaline media. For this study betaine cyclohexyl ester chloride and betaine anilide chloride were chosen, because both can be purified satisfactorily and neither is excessively hygroscopic.

The hydrolysis of cationic esters or amides has not been investigated thoroughly. It is apparent that the presence of the positive center due to the quaternary nitrogen should facilitate the approach

(2) A. L. Linch, U. S. Patents 2,359,862, 2,359,863, and 2,359,864 (1944).

of hydroxide ion and hinder the approach of hydronium ion. Hence, as compared to sterically similar, uncharged esters or amides, the cationic derivatives should show very fast rates of alkaline hydrolysis and slow rates of acid hydrolysis. Nielsen³ estimated a rate for the alkaline hydrolysis of carbethoxymethyltriethylammonium iodide but indicated some doubt as to the accuracy of his result, because the reaction was extremely rapid. Bell and Waind⁴ also reported on the alkaline hydrolysis of the same ester, but derivatives of betaine itself apparently have not been investigated. Fairly large salt effects are exhibited by these cationic derivatives when subjected to alkaline or acid hydrolysis,^{3,4} so that presumably the rates we report are a function of ionic strength and cannot be extrapolated accurately to $\mu = 0$. Comparison of the rates obtained in this study with those for the hydrolysis of ordinary uncharged esters or amides are probably indicative of order of magnitude only.

Experimental

Methods.—The experimental difficulties encountered in the alkaline hydrolysis of the cyclohexyl ester were such that the accuracy of these results is not as good as that ordinarily reported for saponifications. Neither reduction of the temperature to 0° nor change of solvent to 80% ethanol effected a suitable slowing down of the rate for accurate determination by titration methods. Since the betaine ester chloride is ionic, conductivity measurements involve small differences between relatively large numbers. An estimate of the rate was obtained by following the hydrolysis in alkaline buffers. One set of experiments was run in sodium borate buffer and one set in the quinine-quinine sulfate, potassium sulfate system suggested by Bell and Prue⁵ for the determination of the rate of saponification of methyl chloroacetate. Unreacted ester in an aliquot was determined gravimetrically by precipitation as the reineckate when the borate system was used. In the quinine system, the method of analysis was essentially that of the English workers; an aliquot of reaction mixture was removed, filtered (to remove excess solid buffer) into a weighed solution containing excess sodium hydroxide, and the amount of hydroxide left after complete saponification of the weighed aliquot was determined by potentiometric titration to pH 5.7 with standard hydrochloric acid.

The alkaline hydrolysis of the anilide and the attempted acid hydrolysis of both the ester and the anilide were followed by conventional titration methods on aliquots in sealed tubes. For the acid hydrolysis of the ester, one run at $100.0 \pm 0.1^\circ$, 0.01 M in hydrochloric acid and 0.0099 M in ester was followed to about 80% completion over a period of slightly more than two weeks.

The acid hydrolysis of the betaine anilide chloride was attempted in 0.02 M hydrochloric acid at 100°, but as no reaction could be detected after several days, the run was abandoned. No runs were made in stronger acid solutions where hydrolysis could undoubtedly be effected more rapidly.

Compounds.—Betaine anilide chloride was synthesized by reaction of the acid chloride of betaine² with aniline. It was recrystallized from a mixture of isopropyl alcohol and isopropyl ether and dried *in vacuo*.

Anal. Calcd. for $C_{11}H_{17}ClN_2O$: Cl, 14.65; equiv. wt., 228.7. Found: Cl, 14.78; equiv. wt., 226.5, 229.3 (by saponification).

Betaine cyclohexyl ester chloride was synthesized according to the general directions of Linch,² recrystallized from a mixture of acetone and chloroform, and dried *in vacuo*.

Anal. Calcd. for $C_{11}H_{23}ClNO_2$: Cl, 15.06; equiv. wt., 235.8. Found: Cl, 14.90; equiv. wt., 233.5 (by saponification).

The ester reineckate was prepared by mixing an aqueous solution of ammonium reineckate and betaine cyclohexyl ester chloride. The insoluble reineckate was filtered and washed with ice-water until a colorless wash liquor was obtained.

*Anal.*⁶ Calcd. for $C_{11}H_{22}NO_2 \cdot C_6H_6CrN_6S_4 \cdot H_2O$: N, 18.25; H_2O , 0.35. Found: N, 18.0; H_2O , 0.4.

Results and Discussion

Alkaline Hydrolysis of Ester.—The rate constants for the alkaline hydrolysis of the ester run in buffer were calculated from the integrated form of the first order rate expression. The pH of the buffer solution was measured with a standardized glass electrode and (a_{OH^-}) calculated from the usual expression for pK_w . The k_2' obtained in this manner is not the same as the rate constant which would be obtained by titration methods, in which total hydroxide concentration (C_{OH^-}) is measured instead of (a_{OH^-}). For the quinine buffer system it has been shown that the (C_{OH^-}) (at 25° and μ 0.2) can be calculated from the expression⁵

$$C_{OH^-} = 4.70 \times 10^{-6} (SO_4^{2-})^{1/2} \quad (I)$$

so that a k_2 based on (C_{OH^-}) instead of (a_{OH^-}) in I can be obtained. We used the readily measured (a_{OH^-}) for the borate buffer and the quinine buffer at 32.1°, and have reported values for both k_2 and k_2' where possible.

The results of the saponification runs on the betaine cyclohexyl ester chloride in the quinine-quinine sulfate buffer ($pH \sim 8$) are presented in Table I. The k_2' values are uncertain to at least $\pm 5\%$ as the accuracy of the measurement of pH is probably no better than ± 0.02 pH unit. The k_2 rates are also not exact, however, as the numerical constant in I contains one factor uncertain¹ to about the same extent.⁵

TABLE I

SAPONIFICATION OF BETAINE CYCLOHEXYL ESTER CHLORIDE IN QUININE-QUININE SULFATE BUFFER

Normality K_2SO_4	μ^a	$T, ^\circ C.$	(a_{OH^-})	(C_{OH^-})	$k_2', l. mole^{-1} min.^{-1}$	$k_2, l. mole^{-1} min.^{-1}$
0.05	0.20	25.0	9.33×10^{-7b}	1.06×10^{-6}	905	795
.06	.20	25.0	9.77×10^{-7b}	1.16×10^{-6}	915	770
.06	.20	32.1	9.55×10^{-7c}	1370 ^d	...

^a Sufficient KCl added to ester salt to achieve this ionic strength. Reaction mixture contained 2 g. quinine and 0.5 g. quinine sulfate/70 ml. solution. ^b pK_w 14.00. ^c pK_w 13.77. ^d The activation energy calculated from k_2' at 25.0° and 32.1° is about 10,400 cal.

The quinine buffer system is well suited for this type of work, within a limited temperature range, as the excess of both solid quinine and quinine sulfate gives adequate buffering capacity. Measurements of pH stayed essentially constant throughout a run. The runs in borate buffer were not made at constant ionic strength and the capacity of the buffer was so low that only the first part of the reaction could be followed. At 25° the k_2' values obtained at pH 8.45, 8.61, 8.82 and 9.00 averaged 970 $l. mole^{-1} min.^{-1}$, but the agreement between successive points in each run was not sufficient to justify much confidence in the values obtained.

In view of the large negative salt effect which presumably applies to the hydrolysis of betaine cy-

(3) R. F. Nielsen, *THIS JOURNAL*, **58**, 206 (1936).

(4) R. P. Bell and G. M. Waind, *J. Chem. Soc.*, 1979 (1950).

(5) R. P. Bell and J. E. Prue, *Trans. Faraday Soc.*, **46**, 14 (1950).

(6) This analysis by H. M. Wright and E. A. McComb of this Laboratory.

clohexyl ester chloride, it is difficult to find any exact basis for comparison of the rates of the present study with values reported for other esters. The betaine ester saponifies about 125 times faster than ethyl acetate at comparable ionic strength.⁴ From data available in the literature⁷⁻⁹ it may be estimated that betaine ester chlorides at this ionic strength saponify at about the same rate as chloroacetic and formic esters.

The most recently reported rates for carbethoxymethyltriethylammonium iodide are at 0° in water.⁴ A value of about 750 l. mole⁻¹ min.⁻¹ at 25° at comparable μ can be calculated, although Nielsen⁸ estimated a rate of 1300 at 20° in the absence of salt. The difference in rate of saponification between this ester and the ethyl ester of betaine (estimated at 2300 l. mole⁻¹ min.⁻¹) is probably due to steric factors. The steric effect of β -substituents in the acid moiety of esters has not been investigated as thoroughly as that of α -substituents, but models indicate that three ethyl groups on the quaternary nitrogen offer more shielding for the carbonyl carbon than do three correspondingly placed methyl groups. Cason has noted a somewhat similar steric effect for a β -ethyl group as compared to a β -methyl group¹⁰ on the hydrolysis rates of branched chain fatty acid amides.

Alkaline Hydrolysis of Anilide.—The second-order rate constants for the alkaline hydrolysis of the betaine anilide chloride were calculated from the usual integrated second-order rate expression, and the results are summarized in Table II.

The Arrhenius activation energy for the hydrolysis calculated from the two runs at the same ionic strength is 15,900 cal., which is about the same as the value (15,200 cal.) reported for the hydrolysis of acetanilide in water with 0.1 N KOH.¹¹ Disregarding salt effects, the betaine anilide chloride is hydrolyzed by alkali about 6 times faster than

(7) L. P. Hammett, "Physical Organic Chemistry," 1st Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 211-213.

(8) B. E. Mirza and G. D. Advani, *J. Univ. Bombay*, **11A**, pt. 5, 63 (1943).

(9) D. P. Evans, J. J. Gordon and H. B. Watson, *J. Chem. Soc.*, 1439 (1938).

(10) J. Cason, personal communication.

(11) J. M. A. Hoeflake, F. E. C. Scheffer, J. R. H. van Nouhouys and J. C. Posthumus-Bruyn, *Rec. trav. chim.*, **51**, 673 (1932).

TABLE II
HYDROLYSIS OF BETAINE ANILIDE CHLORIDE (0.02 N) IN SODIUM HYDROXIDE

T, °C.	Solvent	Approx. ratio of OH ⁻ to anilide	k _s , l. mole ⁻¹ min. ⁻¹ × 10 ⁺²
64.90	Water	2:1	3.70
79.90	Water	2:1	10.1
79.90	Water	3:1	9.8
79.90	80% methanol (vol. %)	2:1	6.5

acetanilide,¹¹ and about 150 times faster than the sterically similar isovaleranilide.¹²

Acid Hydrolysis of Ester.—As might be anticipated, betaine cyclohexyl ester appears to be relatively stable in acid solution. Analysis of the data showed no clear-cut kinetic order, which is not surprising in view of the fairly large positive salt effect expected for the hydronium ion-catalyzed hydrolysis of a cationic ester. Considerably more work would be required to establish an accurate rate for this hydrolysis, but an average rate of $6.5 \pm 0.6 \times 10^{-3}$ l. mole⁻¹ min.⁻¹ for the first half of the reaction can be calculated from the data, irrespective of the assumed degree of ionization of the betaine hydrochloride ($pK \sim 2$)¹³ produced in the reaction.

From the rate constants for the acid hydrolysis of cyclohexyl acetate¹⁴ in water at 25 and 35°, it may be estimated that the betaine cyclohexyl ester chloride (neglecting salt effects) hydrolyzes about 1/80 as fast as the ordinary acetate. Inasmuch as the steric effect of the three methyl groups on the nitrogen is difficult to determine, and since such "proximity" effects are frequently important in acid hydrolyses,⁷ it is possible that the large decrease in rate for the betaine ester may not be due entirely to its cationic nature.

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