reaction proceeds through an initial attack on a hydroxyl group, the relative efficiencies of the phenols should be divided by the number of equivalent "most reactive" hydroxyl groups. In this case the reduced relative efficiencies of the quinols are lowered considerably.

Phloroglucinol is seen to be less reactive than resorcinol (even with no symmetry corrections). This is due presumably to the well-known tendency for phloroglucinol to exist in its tautomeric keto form.

The electron-withdrawing *p*-nitro group is seen to greatly deactivate phenol toward peroxy radical attack. The electron-donating *p*-methoxy group greatly activates phenol. These results infer that polar resonance forms in which electronic charge is transferred from the phenol to the peroxy radical are of importance in the transition state of the reaction.

Experimental

Materials.—Methyl methacrylate monomer was purified as described elsewhere.[10] 2,2′-Azobis-(isobutyronitrile) was recrystallized several times from methanol before use. Phenol, itself, was distilled using an air condenser. After a large fraction had been distilled, one drop (boiling at 178°) was collected in a weighed flask. The flask plus the phenol was reweighed and the solution used for the phenol experiments was then made up directly in the same flask.

Dilatometric Procedure.—A weighed amount of initiator and a weighed amount of phenol were added to a small flask. Twenty-five ml. of methyl methacrylate, previously saturated with air at room temperature, was pipetted into the flask and the temperature noted. The initiator and phenol were dissolved and mixed by shaking. A dilatometer of about 20 ml. capacity was then filled from the flask.

The dilatometer was then inserted into a constant-temperature bath held at 44.4° by an infrared lamp which was filtered by an added red-glass filter. The temperature of the bath was held constant to within 0.005°. The bath was located in a darkroom and the dilatometer was illuminated by a red safe-light during the run.

After the solution had come almost up to temperature, the dilatometer was removed briefly from the bath and the liquid in the capillary adjusted to the mark. The time necessary to make this adjustment was usually less than 15 sec. The zero time was taken to be the time of the initial insertion of the dilatometer into the bath. Periodic readings of the level of the liquid in the capillary were made with a cathetometer until about 30 min. after the easily-observed end of the inhibition period. Typical plots of the dilatometric measurements are shown in Fig. 5.

The procedure and necessary monomer constants for calculating polymerization rates are described elsewhere.[10]

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, DAVIS, CALIFORNIA]

The Amine Induced Chloroacetolysis of Trityl Chloride in Carbon Tetrachloride. A 2 : 1 Acid–Amine Adduct as a Reactant

BY L. J. ANDREWS AND R. M. KEEFER

RECEIVED JANUARY 19, 1962

The kinetics of reaction of chloroacetic acid with trityl chloride in carbon tetrachloride in the presence of β-bromoallyl-*n*-hexylamine have been investigated. When the acid to amine ratio is 2:1, the chloroacetolysis is first order with respect to the salt, $Am(HA)_2$. When the acid to amine ratio is between 2 and unity, the medium contains both $Am(HA)_2$ and $Am.HA$; apparently the latter is present predominantly in dimeric form and is a much less effective reactant than $Am(HA)_2$. When their total acid to total amine ratios are greater than 2, the media contain free acid, and the reactions then occur via a path which is rate dependent on the concentrations both of $Am(HA)_2$ and the free acid. There is some evidence that reactive aggregates, $Am(HA)_x$ (where $x > 2$), may also be present in solutions in which the acid is in large excess of the amine.

As part of an investigation of polar processes in non-polar media, the acetolysis and chloroacetolysis reactions of trityl chloride in carbon tetrachloride have been studied recently.[1,2] To prevent the accumulation of hydrogen chloride in the medium and thus insure that ester formation proceeds to completion one of two amines (β-bromoallyl-*n*-hexylamine or tri-*n*-butylamine), has been added to the initial reaction mixture as the carboxylic acid salt. Since these amines both form salts with carboxylic acids and hydrogen chloride which are appreciably soluble in carbon tetrachloride, it has proved feasible to conduct spectrophotometric studies of the kinetics of the amine induced reactions.

It has been convenient to study the acetolysis reaction at room temperature only with the acetic acid concentration relatively high (>0.5 *M*) and in large excess of that of the amine ($CH_2{=}CBrCH_2NHC_6H_{13}$-*n*). Under these conditions the reaction is first order with respect to the amine salt and of an apparent order higher than first with respect to the acid. The salt is presumed to function, in the form of an ion-pair,[3] as a nucleophile, in the rate determining step, while the acid must promote reaction through electrophilic solvation of the departing chloride of the trityl chloride molecule.

The chloroacetolysis reaction is relatively rapid around 25° even when the acid concentration is relatively low (0.2 *M* or less) and not much larger than that of the amine (either $CH_2{=}CBrCH_2NHC_6H_{13}$-*n* or $(n\text{-}C_4H_9)_3N$). Qualitatively the rate of the reaction is dependent both on the free acid and the amine salt concentration, but the variations in rate with changes in acid and amine concentration cannot satisfactorily be explained on the assumption that the salt which participates as a reactant is a 1:1 amine-acid adduct. Rather, kinetic evidence has been obtained that when sufficient acid is available, aggregates of the type $R_3N(RCOOH)_x$, where $x > 2$, must form. The formation of such association products of carboxylic acids and their 1:1 acid–amine salts in non-polar media has also

---

(1) L. J. Andrews and R. M. Keefer, *J. Am. Chem. Soc.*, **83**, 3708 (1961).

(2) R. M. Keefer and L. J. Andrews, *ibid.*, **84**, 941 (1962).

(3) R. M. Fuoss and C. A. Kraus, *ibid.*, **77**, 4474 (1955).

been detected experimentally by ultraviolet[2] and infrared[4,5,6] spectrophotometry.

It has been concluded on the basis of preliminary rate measurements made in connection with the earlier work on chloroacetolysis that the 2:1 chloroacetic acid-β-bromoallyl-*n*-hexylamine salt reacts with trityl chloride even in the absence of the free acid. A more detailed kinetic investigation has now been conducted to determine the relative importance of the 1:1 and 2:1 salts and of the free acid as reactants in the amine induced reaction in carbon tetrachloride.

Experimental

Materials.—The sources of the solvent, the amines, the chloroacetic acid and of the trityl chloride were the same as stated previously.[1,2]

The Rate Runs.—The chloroacetolysis reactions were followed spectrophotometrically at 278 mμ, a wave length at which trityl chloride absorbs much more strongly than does trityl chloroacetate, by the general procedure which was used in the earlier investigation.[2] The optical measurements were made using blanks which were identical with the rate samples except that they contained no trityl chloride. In general the acid and the amine were in large excess of the organic halide. Rate constants k, defined in eq. 1, were calculated from the slopes of plots of log $(d_t - d_f)$ *versus* time,

$$kt = 2.303 \log [(C_6H_5)_3CCl]_i/[(C_6H_5)_3CCl] = 2.303 \log (d_i - d_f)/(d_t - d_f) \quad (1)$$

where the subscripts i, f and t refer to initial time, reaction termination and to time t, respectively. The runs with β-bromoallyl-*n*-hexylamine could be followed spectrophotometrically even when the total acid to total amine ratio was as low as unity. The optical method could not, however, be used with rate mixtures in which the acid to tri-*n*-butylamine ratio was less than 2 because of the intense absorption of the saturated amine, even at very low concentration, in the 278 mμ region.

The Concentrations of 1:1 and 2:1 Salts in the Acid-Amine Solutions.—In solutions of amines and carboxylic acids in non-polar media, the 2:1 acid-amine adduct is sufficiently stable so that it may exist in appreciable concentration even when the total acid to amine concentration ratio is as low as 1:1.[2,4] When this ratio lies between 1:1 and 2:1 and the amine is tertiary, the solute composition is governed by the equilibrium

$$2\text{Am.HA} \rightleftarrows \text{Am(HA)}_2 + \text{Am}$$

$$K_2 = \frac{[\text{Am(HA)}_2][\text{Am}]}{[\text{Am.HA}]^2} \quad (2)$$

An ultraviolet spectrophotometric method was used in the previous investigation[2] to evaluate the equilibrium constant K_2 for the interaction of tri-*n*-butylamine and chloroacetic acid in carbon tetrachloride. A similar investigation using β-bromoallyl-*n*-hexylamine and chloroacetic acid in carbon tetrachloride has now been made to serve as a basis for the estimation of the concentrations of the several salt species present in the rate samples. The spectrophotometric data for the secondary amine cannot be interpreted satisfactorily using eq. 2 but may be reasonably well interpreted if it is assumed that the 1:1 salt is largely in dimeric[5] form (eq. 3). Yerger and Barrow[5] have previously presented evidence that

$$(\text{Am.HA})_2 \rightleftarrows \text{Am(HA)}_2 + \text{Am}$$

$$K_3 = \frac{[\text{Am(HA)}_2][\text{Am}]}{[(\text{Am.HA})_2]} \quad (3)$$

dimerization of the 1:1 salt of diethylamine and acetic acid takes place in carbon tetrachloride.

The optical densities (d) at 270 and 278 mμ of a series of carbon tetrachloride solutions in which the acid to secondary amine ratio was less than 2 were measured *versus* a carbon tetrachloride blank using 1 cm. absorption cells. Presumably these solutions contained no free acid. Equations 4–6 apply in this case, where $[\text{Am}]_t$ and $[\text{HA}]_t$ refer, respectively, to the total concentrations of amine and acid (calculated as the monomer); D and S_2 represent the concentrations of (Am.-HA)$_2$ and Am(HA)$_2$ respectively, and the terms in ϵ are the extinction coefficients of the several absorbing species.

$$d = [\text{Am}]\epsilon_{\text{Am}} + D\epsilon_{\text{D}} + S_2\epsilon_{\text{S}_2} \quad (4)$$

$$[\text{Am}]_t = [\text{Am}] + 2D + S_2 \quad (5)$$

$$[\text{HA}]_t = 2D + 2S_2 \quad (6)$$

Using these equations it can be shown that

$$[\text{Am}] = \frac{d - \frac{1}{2}[\text{HA}]_t\,\epsilon_{\text{D}} - ([\text{HA}]_t - [\text{Am}]_t)(\epsilon_{\text{S}_2} - \epsilon_{\text{D}})}{\epsilon_{\text{Am}} + \epsilon_{\text{S}_2} - \epsilon_{\text{D}}} \quad (7)$$

The value of ϵ_{S_2} was calculated from the optical densities of solutions in which $[\text{HA}]_t$ was from 2.5 to 5 times $[\text{Am}]_t$. The free acid does not absorb appreciably in the wave length region of these measurements. The direct evaluation of ϵ_{D} was not feasible since for the preparation of (Am.HA)$_2$ solutions free of appreciable amounts of Am.(HA)$_2$, such large concentrations of amine were required that the salt only made a small contribution to the total optical density. By optical investigation of solutions with $[\text{Am}]_t >> [\text{HA}]_t$ it was demonstrated qualitatively that ϵ_{D}, like ϵ_{S_2}, was much smaller than ϵ_{Am}.

Values of [Am] appearing in Table I were calculated from spectrophotometric data recorded at 270 and 278 mμ (eq. 7) on the assumption that $\epsilon_{\text{D}} = 2\epsilon_{\text{S}_2}$. It is implied in making this assumption that the extinction coefficients of the salt species, (Am.HA)$_2$ and Am(HA)$_2$, are directly proportional to the number of $\geqslant$N–H coördination sites which are present, two in the first case and one in the second. It is significant that the agreement in values of [Am] calculated on this basis (see Table I) from data taken at two wave lengths is relatively good. Various other relationships between ϵ_{D} and ϵ_{S_2} were tested, but none was as satisfactory in the correlation of the data as that which was finally used. The value of ϵ_{Am} required for these calculations was determined from the optical densities of solutions of pure amine. The average values of [Am] have been used (eqs. 5 and 6) to obtain the value of [Am(HA)$_2$], and [(Am.HA)$_2$]. These have been used in calculating the values of K_3 which appear in Table I. The average constant is somewhat smaller than that reported[5] for the corresponding reaction of diethylamine and acetic acid (K = 0.062).

TABLE I

EQUILIBRIUM CONSTANT FOR INTERCONVERSION OF (Am.HA)$_2$ AND Am(HA)$_2$ SALTS OF $CH_2{=}CBrCH_2NHC_6H_{13}$-*n* AND CHLOROACETIC ACID (CCl$_4$, 25.3 ± 0.1°)

	λ = 270 mμ[a]		λ = 278 mμ[b]		
$[\text{HA}]_t$, mole/l.	d	[Am] × 10^3, mole/l.	d	[Am] × 10^3, mole/l.	K_3 × 10^2 mole/l.
		$[\text{Am}]_t$ = 0.050 M			
0.0805	0.349	2.6	0.174	2.9	1.22
.0705	.492	4.9	.226	5.4	1.31
.0604	.698	8.1	.296	8.7	1.34
.0554	.840	10.4	.335	10.6	1.40
.0504	.975	12.5	.384	12.9	1.35
.0252	...	..	.729	29.2	1.57
		$[\text{Am}]_t$ = 0.100 M			
0.1610	0.593	3.5	0.304	3.7	1.42
.1409	.838	7.4	.389	7.8	1.63
.1208	1.22	13.6	.517	13.8	1.79
.1107	1.48	17.7	.600	17.7	1.86
.1007	...	..	.712	23.0	2.04
.0503	...	..	1.41	56.1	1.91
				Av.	1.57

[a] At 270 mμ ϵ_{Am} = 66.6 and ϵ_{S_2} = 3.7. [b] At 278 mμ ϵ_{Am} = 23.4 and ϵ_{S_2} = 2.25.

---

(4) G. M. Barrow and E. A. Yerger, *J. Am. Chem. Soc.*, **76**, 5211 (1954).

(5) E. A. Yerger and G. M. Barrow, *ibid.*, **77**, 4475, 6206 (1955).

(6) G. M. Barrow, *ibid.*, **78**, 5802 (1956).

Results[7]

Reaction When $[HA]_t/[Am]_t = 2$.—As a further test of the tentative conclusion[2] that the 2:1 acid–amine salt of $CH_2{=}CBrCH_2NHC_6H_{13}$-*n* may react with trityl chloride in the absence of excess acid, a comparison has been made of the rate constants k for a series of solutions in which $[HA]_t$ and $[Am]_t$ both vary appreciably but in which their ratio remains 2:1. For these rate runs $k/[Am]_t$ should closely approximate $k/[Am(HA)_2]$ since there is apparently very little free acid or free amine in such solutions.[2,4] Actually the values of $k/[Am]_t$ are essentially independent of changes in the total acid or amine concentrations. Typical pertinent results are presented in Table II. That is, the reaction rate is dependent on the 2:1 salt concentration, but there is no indication that it is also dependent on any traces of uncombined acid which may be present in the media.

TABLE II

THE DEPENDENCE OF RATE CONSTANT ON THE ACID–AMINE CONCENTRATION RATIO (CCl_4, 25.4°)

$10^3[(C_6H_5)_3CCl]_i$, mole/l.	$[CH_2{=}CBrCH_2NHC_6H_{13}\text{-}n]_t$, mole/l.	$[ClCH_2COOH]_t$, mole/l.	$10^3k/[Am]_t$, l. mole^{-1} sec.$^{-1}$
	$[HA]_t/[Am]_t = 2/1$		
5.93	0.105	0.201	16.8
5.93	.0525	.1004	15.7
5.93	.0263	.0502	14.9
3.67	.0806	.1534	13.8
3.67	.0403	.0767	13.1
3.67	.0202	.0384	12.5
	$[HA]_t/[Am]_t = 2.5/1$		
4.04	0.0804	0.2040	98.9
4.04	.0402	.1020	54.0
4.04	.0201	.0510	35.5
	$[HA]_t/[Am]_t = 3/1$		
3.72	0.0794	0.2395	262
3.72	.0397	.1197	122
3.72	.0199	.0598	69.4
	$[HA]_t/[Am]_t = 3.5/1$		
3.63	0.0400	0.1396	160
3.63	.0200	.0698	74.5
	$[HA]_t/[Am]_t = 4/1$		
3.67	0.0399	0.1603	360
3.67	.0199	.0801	165
	$[HA]_t/[Am]_t = 1.5/1$		
4.04	0.0800	0.1220	5.3
4.04	.0400	.0610	5.6
4.04	.0200	.0305	7.0
	$[HA]_t/[Am]_t = 1/1$		
3.67	0.0807	0.0826	2.0
3.67	.0404	.0413	2.9
3.67	.0202	.0207	3.0

On the other hand, the value of $k/[Am]_t$ for a series of solutions with a fixed ratio of $[HA]_t/[Am]_t$ which is greater than 2/1 varies with $[HA]_t$. This is illustrated in Table II for several different acid-amine ratios. Actually the variations in $k/[Am]_t$ at a particular ratio are approximately proportional to $[HA]_t$. This might be explained on the assumption that when the ratio is greater than 2, the rate constant k is related to the amine (presumed to be present as $Am(HA)_2$) and acid content of the medium as shown in eq. 8. A term involving the

$$\begin{aligned} k &= k_1[Am(HA)_2] + k_2[Am(HA)_2][HA] \\ &= k_1[Am]_t + k_2[Am]_t([HA]_t - 2[Am]_t) \qquad (8) \end{aligned}$$

free acid, but not the amine, has not been included in this equation since chloroacetolysis occurs very slowly in an amine-free medium relative to the reaction which occurs when amine salt is also present.[2] For the runs with $[HA]_t/[Am]_t > 2$ for which results are presented, the contribution of $k_1[Am]_t$ to the rate constant k is relatively small as compared to that of the free acid dependent term (eq. 8).

Reaction When $[HA]_t/[Am]_t < 2$.—The results for several runs in which the total acid to total amine ratio is 1/1 or 1.5/1 are included in Table II. It is presumed that all of the acid in these solutions should be contained in a mixture of the two salts, $(Am.HA)_2$ and $Am(HA)_2$. The amine in the latter form must be a considerably more effective reagent than it is in the dimeric salt, since the k values for reaction at fixed $[Am]_t$ drop quite markedly as $[HA]_t$ is reduced (see the last six runs of Table II). A direct study of the reactivity of $(Am.HA)_2$ as it exists in a solution free of the 2:1 salt could not be accomplished. To rid the solution of the 2:1 salt, a high enough concentration of free amine is required so that the trityl chloride concentration of the medium cannot be evaluated spectrophotometrically.

By assuming that, of the two salts, only $Am(HA)_2$ reacts at an appreciable rate with trityl chloride a set of rate constants has been predicted for those reaction mixtures (Table II) in which $[HA]_t/[Am]_t < 2$. These predictions have been made using the average value (14.5×10^{-3} l. mole^{-1} sec.$^{-1}$) of $k/[Am(HA)_2]$ obtained for runs in which $[HA]_t = 2[Am]_t$. To insure that it applies to solutions which contain no traces of free acid, this average value actually is based on the results of seven runs at an acid to amine ratio of slightly less than 2 (see the first six runs of Table II). By using a value of $K_3 = 0.016$ mole/l. (see Table I) the required $Am(HA)_2$ concentrations have been calculated from eq. 9, which is derived from equations 3, 5 and 6. The predicted rate constants

$$S_2^2 + S_2([Am]_t - [HA]_t + K_3) - K_3[HA]_t/2 = 0 \quad (9)$$

($k = 14.5 \times 10^{-3}S_2$ sec.$^{-1}$) are somewhat higher than the experimental values (Table III). This may be a reflection of errors in the values of K_3 and $k/[Am]_t$ used in these calculations. Actually if $(Am.HA)_2$ competed effectively with $Am(HA)_2$ as a reactant in chloroacetolysis, this order for the predicted and observed constants should have been reversed.

Reaction When $[HA]_t/[Am]_t > 2$.—It has been suggested that when the total acid to amine ratio is greater than 2, chloroacetolysis may occur by two processes, one of which is dependent in rate

---

(7) Throughout this discussion the chloroacetic acid concentration is calculated on the assumption that the acid is monomeric in nature; the free acid is undoubtedly almost completely in dimeric form in carbon tetrachloride.

TABLE III

PREDICTED RATE CONSTANTS FOR REACTION WHEN $[HA]_t/[Am]_t < 2$

[HA]t, mole/l.	[Am]t, mole/l.	S_2, mole/l.	D, mole/l.	10^3k, sec.$^{-1}$ Calcd.	10^3k, sec.$^{-1}$ Found
0.1220	0.0800	0.047	0.014	0.68	0.42
.0610	.0400	.025	$.005^5$	.36	.22
.0305	.0200	.013	$.002^3$	.19	.14
.0826	.0807	.020	.021	.29	.16
.0413	.0404	.012	$.008^7$	.17	.12
.0207	.0202	.0072	.0032	.10	.06

on $[Am(HA)_2]$ and the other of which is dependent on the concentrations both of this salt and of the free acid in the medium (see eq. 8). If this is actually the case, $k/[Am]_t$ values should be linear with respect to the free acid concentration of the medium (calculated as $[HA]_t - 2[Am]_t$). This relationship has been tested as shown in Fig. 1. The straight line of this figure applies to reactions in which the amine is $CH_2{=}CBrCH_2NHC_6H_{13}$-*n*. The points conform to this line as long as the free acid concentration is moderate (<0.6 *M*). The upward deviation of the points from the line in the high free acid concentration region might be explained in any of three ways; at (a) the higher acid levels the reaction may be subject to a medium effect[8]; (b) a contribution to k from terms of higher order than first with respect to the free acid may become important[9]; or (c) an appreciable fraction of $Am(HA)_2$ may be converted to a somewhat more reactive salt species,[10] such as $Am(HA)_3$. It is not possible on the basis of information now available to state with certainty how much of the deviation can be ascribed to alternative causes (a) or (b). There is, however, rather good reason to believe that some aggregates which incorporate more than two molecules of acid per molecule of amine may be present in solutions in which $[HA]_t/[Am]_t$ exceeds 2. The evidence is to be found in the results of a group of runs in which tri-*n*-butylamine has been substituted for the unsaturated secondary amine used in most of the rate work. The results for three series of runs with the saturated amine at three different concentrations are recorded in Fig. 1 in the upper set of three curves. As is the case for the plot of the data on the unsaturated amine, the plots of $k/[n\text{-}C_4H_9)_3N]_t$ *vs.* $[HA]_t - 2[Am]_t$ curve upward. However, the data for the saturated amine fall onto different curves depending on the total amine content of the medium; that is, the values of $k/[Am]_t$ at fixed values of $[HA]_t - 2[Am]_t$ diminish as $[Am]_t$ increases. This diminution can best be explained on the assumption that the free acid concentrations which are indicated by the points on Fig. 1 are higher than the actual values because of the interaction (eq. 10) where y may have a range of integral values. The resulting reduction in the free acid concentration below the level indicated in the points of Fig. 1 should be most pronounced for solutions with the highest total amine concentrations.

$$Am(HA)_2 + yHA \rightleftarrows Am(HA)_{2+y} \qquad (10)$$

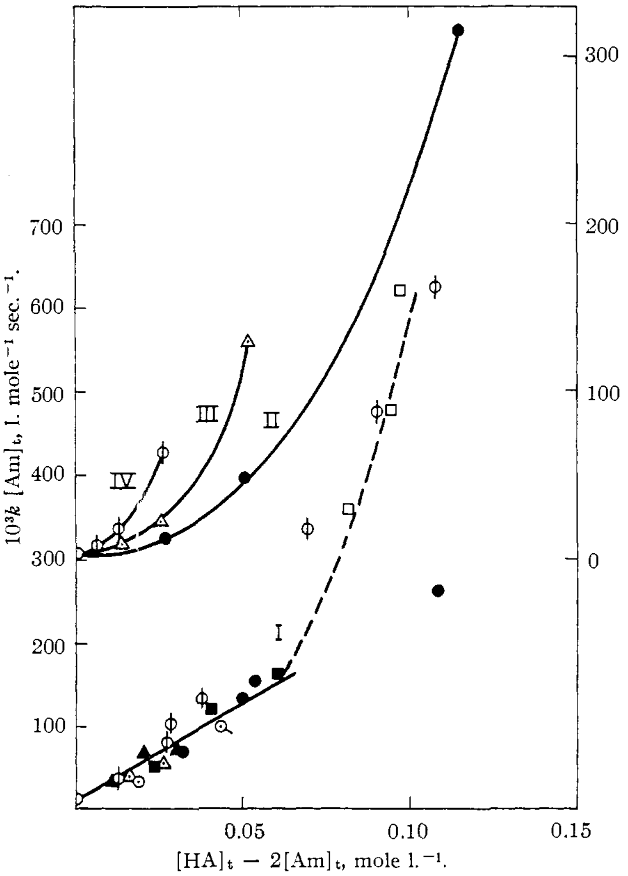

Fig. 1.—The variations in $k/[Am]_t$ with the apparent free acid concentration of the medium ($[HA]_t/[Am]_t > 2$). Curves II, III and IV apply to reaction mixtures containing tri-*n*-butylamine; these curves are referred to the right hand ordinate axis. All points which do not lie directly on curves II, III or IV apply to reaction mixtures containing β-bromoallyl-*n*-hexylamine and are referred to the left hand ordinate axis. The various symbols pertain to the total amine concentrations $[Am]_t$ of the reaction mixtures: ⊙, 0.10 *M*; ⊙, 0.08 *M*; ●, 0.05 *M*; ■, 0.04 *M*; △, 0.025 *M*; ▲, 0.02 *M*; ϕ, 0.0125 *M*; □, 0.0065 *M*. Some of the points for reactions with the unsaturated amine are based on data obtained previously.[2]

The unsaturated amine apparently has a considerably lower tendency to form aggregates $Am(HA)_x$, where $x > 2$, than the saturated amine. It should be noted that the points which fit the straight line of Fig. 1 apply to runs with $[CH_2{=}CBrCH_2NHC_6H_{13}\text{-}n]_t$ ranging in value from 0.012 *M* to 0.10 *M*. Only when $[HA]_t - 2[Am]_t$ (the apparent free acid concentration) reaches a relatively high level is there any indication that the $k/[Am]_t$ values are no longer accomodated by a single curve.

The Mechanism of Chloroacetolysis.—The relatively low reactivity of the 1:1 acid–amine salt in the chloroacetolysis reaction most likely should be attributed to its ineffectiveness as an electrophile in solvating the departing chloride of the trityl

---

[8] For related effects in other reactions of trityl chloride see, for example, R. F. Hudson and B. Saville, *J. Chem. Soc.*, 4130 (1955).

[9] *Cf.* H. Hart and F. A. Cassis, *J. Am. Chem. Soc.*, **76**, 1634 (1954).

[10] A 3:1 acid–amine ion-pair type aggregate of sulfuric acid and an indicator base has been observed to form in nitromethane; H. Van Looy and L. P. Hammett, *ibid.*, **81**, 3872 (1959).

chloride molecule. It is pertinent in this regard that the benzolysis of trityl chloride in a non-polar solvent is more sensitive in rate to the capacity of the medium to provide for electrophilic than for nucleophilic solvation.[11,12] It has been demonstrated in this and the previous[2] study of chloroacetolysis that when there is free acid in the medium (when $[HA]_t/[Am]_t > 2$), a term appears in the rate law which involves the product of the concentrations of the 2:1 salt and the acid. Presumably $Am(HA)_2$ and the free acid may function, respectively, as nucleophile and electrophile either in a concerted or a stepwise (eq. 11) attack on trityl chloride.

$$(C_6H_5)_3CCl + HOOCR \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} (C_6H_5)_3C^+Cl^- \text{---} HOOCR$$

$$\xrightarrow[k_2\text{ (slow)}]{R_1R_2N\overset{+}{H}_2\,\overset{-}{O}COR.RCOOH}$$

$$(C_6H_5)_3COCOR + R_1R_2NH_2{}^+Cl^- + RCOOH \quad (11)$$

The reaction which occurs when $[HA]_t/[Am]_t = 2$ is most interesting. Under these conditions a single 2:1 salt molecule must function both as the nucleophile and the electrophile which are required to accomplish displacement readily. The detailed course of the reaction which occurs under these circumstances cannot be formulated at this time.

Acknowledgment.—The authors are indebted to the National Science Foundation for a grant in support of this research.

---

(11) M. F. Hawthorne and D. J. Cram, *J. Am. Chem. Soc.*, **76**, 3451 (1954).

(12) See C. E. Boozer, J. D. Robinson, A. Soldatos, J. C. Trisler and C. Wiley, *ibid.*, **78**, 3428 (1956), for a discussion of the relative importance of these two types of solvation in solvolytic reactions of halides.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, NEW YORK]

Chromatography on Columns Packed with a Non-polar Material[1]

BY IZCHAK Z. STEINBERG[2] AND HAROLD A. SCHERAGA

RECEIVED FEBRUARY 14, 1962

A method is described for the preparation of polystyrene particles of high adsorptive surface area. The chromatography of several organic acids (in aqueous solution) on the polystyrene thus prepared illustrates the dependence of the strength of hydrophobic bonds on the nature and size of the interacting non-polar groups. The separation of mixtures of some organic acids could thus be accomplished by chromatography on the large-surface polystyrene. Urea seems to decrease the strength of the hydrophobic bonding to the non-polar surface. The general effect of urea on the adsorption process is shown, however, to be somewhat complicated.

Introduction

The thermodynamic parameters for the interactions of non-polar groups of proteins in aqueous solution (hydrophobic bonds) have recently been calculated by a statistical mechanical treatment,[3] based on earlier considerations of the properties of water and of aqueous solutions of hydrocarbons.[4-7] It is known from experiment[4-7] that the transfer of a non-polar substance from a non-polar phase into water is accompanied by a decrease in both enthalpy and entropy (near room temperature); the predominance of the entropy effect over that of the enthalpy makes the process endergonic, that is, unfavorable. Presumably, the non-polar group has an ordering effect on the water molecules near it,[4] thereby increasing the degree of hydrogen bonding among the water molecules. Non-polar groups in an aqueous medium tend to associate; this association minimizes their contact with water and is accompanied by a decrease in the degree of hydrogen bonding and an increase in the freedom of the water molecules which are thus liberated from the neighborhood of the non-polar groups. Near room temperature, the formation of a hydrophobic bond between a pair of side-chain groups in a protein is accompanied by a decrease in free energy and an increase in both enthalpy and entropy; the predominance of the entropy effect over that of the enthalpy makes the process exergonic. The actual numerical values[3] depend on the nature of the side-chain groups and on their extent of overlap.

Adsorption experiments on non-polar surfaces may provide useful information about the properties of hydrophobic bonds in aqueous solution which were predicted in the previous calculations.[3] Such experiments can be carried out by chromatographic methods. Rieman[8] has recently reviewed his work and that of his collaborators showing that mixtures of some organic substances can be separated on ion exchange resins; these experiments utilized the varying degree of binding of non-polar substances to the non-polar parts of the resins. However, it was reported[8,9] that no adsorption or separation could be effected on columns of polystyrene free of ionic groups because the surface area of the polystyrene particles was too small. For the purposes of the present

---

(1) This work was supported by a research grant (E-1473) from the National Institute of Allergy and Infectious Diseases of the National Institutes of Health, Public Health Service, and by a research grant (G-14792) from the National Science Foundation.

(2) On leave from the Department of Biophysics, Weizmann Institute of Science, Rehovoth, Israel, 1961–1962.

(3) G. Nemethy and H. A. Scheraga, *J. Phys. Chem.*, in press.

(4) H. S. Frank and M. W. Evans, *J. Chem. Phys.*, **13**, 507 (1945).

(5) H. S. Frank and W. Y. Wen, *Discussions Faraday Soc.*, **24**, 133 (1957).

(6) W. Kauzmann, *Adv. in Protein Chem.*, **14**, 1 (1959).

(7) G. Nemethy and H. A. Scheraga, *J. Chem. Phys.*, I and II, in press.

(8) W. Rieman, 111, *J. Chem. Ed.*, **38**, 338 (1961).

(9) G. D. Manalo, A. Breyer, J. Sherma and W. Rieman, III, *J. Phys. Chem.*, **63**, 1511 (1959).