[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

Activation Energies of the Hydrolysis of Esters and Amides Involving Carbonyl Oxygen Exchange[1]

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RECEIVED AUGUST 29, 1957

The effect of temperature on the relative rates of the concurrent alkaline hydrolysis and carbonyl oxygen exchange of benzamide and ethyl benzoate has been determined. In each case, an increase in temperature leads to a decrease in the ratio $k_{\text{hydrolysis}}/k_{\text{exchange}}$. Activation parameters have been calculated for the step involving the formation of the postulated tetrahedral intermediate and for the difference of the two steps in which the intermediate is partitioned. The results are consistent with the formation of a tetrahedral intermediate and substantiate the hypothesis that the formation of the intermediate is the slow step of the reaction. An analysis is made to indicate how this and other multiple step reactions can lead to an over-all activation energy which is not appreciably temperature dependent. Certain examples of the hydrolysis of carboxylic acid derivatives which exhibit a temperature variant activation energy can be accounted for in terms of the analysis of the temperature dependence of the kinetics of the concurrent hydrolysis and oxygen exchange reactions. The acidic and basic hydrolysis of ethyl benzoate under identical conditions of temperature and solvent show ratios of k_h/k_e that differ by a factor of about two while their rates of hydrolysis differ by a factor of about 10^4.

Introduction

Concurrent carbonyl oxygen exchange and hydrolysis have been demonstrated for the hydrolyses of a number of benzoate esters and benzamide. This concurrent hydrolysis and exchange has been interpreted to occur through the partitioning of an unstable tetrahedral addition intermediate of the form $RC(OH)_2X$, where X corresponds to an alkoxyl group in the case of an ester or an amido group in the case of an acid amide.[3,4] The determination of the magnitude of the carbonyl oxygen exchange which accompanies various hydrolytic reactions of carboxylic acid derivatives permits a more precise specification of the mechanism of the reaction and, in particular, permits a description of the relative breakdown of the addition intermediate into reactants and products. In order to elucidate the stepwise path of these hydrolytic reactions more precisely, we have investigated the effect of temperature on the isotopic oxygen exchange accompanying the hydrolysis of benzamide and ethyl benzoate.

Experimental

Materials.—A description has been given previously for the preparation of ethyl benzoate-*carbonyl*-O^{18} [3a] and benzamide-O^{18} [3c] used in these experiments. 1,4-Dioxane, which was stored under nitrogen, was purified according to the method described by Fieser,[5] $n^{20}\text{D}$ 1.4219.

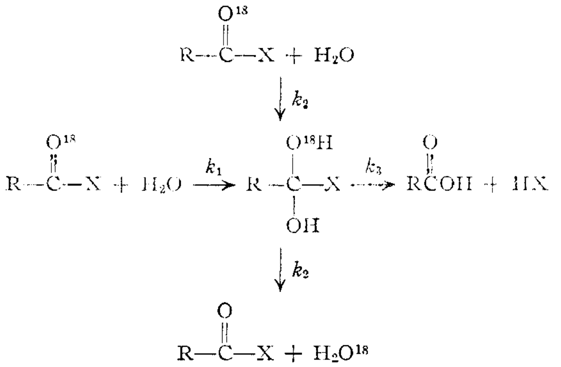
Kinetics of Hydrolysis.—For the hydrolysis of benzamide, the extent of reaction as a function of time was obtained by analysis of ammonia with Nessler reagent as previously described.[3c] The kinetics of the hydrolysis of ethyl benzoate were obtained by titration with standard sodium hydroxide or hydrochloric acid using phenolphthalein as indicator.[3a]

Oxygen Exchange Studies.—Samples of the ester or amide, enriched in carbonyl-O^{18}, were partially hydrolyzed under the desired reaction conditions and the remaining substrate was then isolated by solvent extraction, using ethyl acetate in the case of benzamide[3c] or methylene chloride in the case of ethyl benzoate.[3a] The recovered benzamide was purified by recrystallization; the recovered ethyl benzoate was purified by vacuum distillation in a micro distillation apparatus.[3e] Samples were thus obtained for the determination of the oxygen-18 content of the reactant as a function of the extent of hydrolysis. Oxygen-18 was determined as carbon dioxide in a Consolidated-Nier model 21-201 isotope ratio mass spectrometer. The oxygen atoms in the organic compounds were converted to carbon dioxide by pyrolysis over carbon at 1100° followed by oxidation of the carbon monoxide so produced to carbon dioxide by iodine pentoxide at 110° following the procedure of Doering and Dorfman.[6]

Results

Kinetics of the Concurrent Hydrolysis and Oxygen Exchange of $R{-}\underset{O}{\underset{\|}{C}}{-}X$.—The organic grouping

$R{-}\overset{O}{\overset{\|}{C}}{-}X$, representing any carboxylic acid derivative, is hydrolyzed in aqueous solution to produce a carboxylic acid or its anion and HX or its anion. Concurrently with the hydrolysis, an oxygen exchange reaction may take place between the carbonyl oxygen atom of the carboxylic acid derivative and water in the reaction medium. These two concurrent transformations can be accounted for by the reversible formation of a reaction intermediate which has two structurally equivalent carbon to oxygen bonds. An idealized reaction mechanism which describes the fate of a molecule which contains an oxygen-18 atom in the carbonyl position is



$$\begin{tikzcd} & R{-}\overset{O^{18}}{\overset{\|}{C}}{-}X + H_2O \arrow[d, "k_2"] & \\ R{-}\overset{O^{18}}{\overset{\|}{C}}{-}X + H_2O \arrow[r, "k_1"] & R{-}\underset{OH}{\overset{O^{18}H}{C}}{-}X \arrow[r, "k_3"] \arrow[d, "k_2"] & R\overset{O}{\overset{\|}{C}}OH + HX \\ & R{-}\overset{O}{\overset{\|}{C}}{-}X + H_2O^{18} & \end{tikzcd}$$

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[1] VII in the Series, Intermediates in the Reactions of Carboxylic Acid Derivatives. Previous paper, M. L. Bender, R. R. Stone and R. S. Dewey, THIS JOURNAL, **78**, 319 (1956). This research was supported by a F. G. Cottrell grant from the Research Corporation and in part by Grant H-2416 of the National Institutes of Health.

[2] From the Ph.D. thesis of R. D. G.

[3] (a) M. L. Bender, THIS JOURNAL, **73**, 1626 (1951); (b) M. L. Bender, R. D. Ginger and K. C. Kemp, *ibid.*, **76**, 3350 (1954); (c) M. L. Bender and R. D. Ginger, *ibid.*, **77**, 348 (1955); (d) M. L. Bender and R. S. Dewey, *ibid.*, **78**, 317 (1956); (e) M. L. Bender and K. C. Kemp, *ibid.*, **79**, 111 (1957).

[4] C. A. Bunton, T. A. Lewis and D. R. Llewellyn, *Chem. and Ind.*, 1154 (1954).

[5] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 381.

[6] W. E. Doering and E. Dorfman, THIS JOURNAL, **75**, 5595 (1953); *cf.* M. L. Bender and K. C. Kemp, *ibid.*, **79**, 116 (1957).

By the application of the principle of the stationary state to the scheme outlined above, it is possible to demonstrate eq. 1.[3a]

$$k_h/k_e \ln r/r_0 = \ln (S)/(S_0) \qquad (1)$$

where k_h, the specific rate constant for hydrolysis, is defined as $k_1k_3/(k_2 + k_3)$; k_e, the specific rate constant for exchange, is defined as $k_1k_2/2(k_2 + k_3)$; r is the excess atom fraction of carbonyl oxygen-18 in the reactant and (S) is the concentration of the reactant. It may then readily be verified that $k_h/k_e = 2k_3/k_2$ and that $k_1 = 2k_e + k_h$.[7] Thus from a measurement of k_h and k_h/k_e, it is possible to calculate k_e, k_3/k_2 and k_1.

Analysis of the Temperature Dependence of the Kinetics of the Concurrent Hydrolysis and Oxygen Exchange Reactions of R–CO–X.[7]—For a hydrolysis reaction such as that illustrated above for which the rate constant, k_h, is defined as $k_1k_3/(k_2 + k_3)$, it can be shown by application of the appropriate Arrhenius[8] equations in their usual integrated form for k_1, k_2 and k_3 that the temperature dependence of the hydrolytic rate constant k_h may be expressed as

$$\ln k_h = \ln B_1 - E_1/RT - \ln [B_2/B_3\, e^{(E_3-E_2)/RT} + 1] \quad (2)$$

Only if the bracketed term in eq. 2 is sufficiently small compared with the other terms or if it is approximately constant over the temperature range considered, can a plot of $\ln k_h$ *versus* $1/T$ be linear.

Similarly, from the expression for k_e, an expression can be calculated for the temperature dependence of the oxygen exchange rate constant

$$\ln k_e = \ln B_1 - E_1/RT - \ln [2 + 2B_3/B_2\, e^{(E_2-E_3)/RT}] \quad (3)$$

Again a linear plot of $\ln k_e$ *versus* $1/T$ may be obtained only if the bracketed term is comparatively small or approximately constant over the temperature range considered. Analysis of the importance of the logarithm terms in eq. 2 and 3 which are explicitly temperature dependent, requires the evaluation of $(E_2 - E_3)$ and B_2/B_3. From the application of the Arrhenius equation to k_2 and k_3 it readily follows that

$$\ln (k_2/k_3) = \ln (B_2/B_3) + (E_3 - E_2)/RT \qquad (4)$$

and in a similar manner it follows that

$$\ln k_1 = \ln B_1 - E_1/RT \qquad (5)$$

The Effect of Temperature on the Rates of Hydrolysis and Oxygen Exchange during the Alkaline Hydrolysis of Benzamide.—The alkaline hydrolysis of benzamide in water has been studied by Reid,[9] Bolin,[10] Packer, Thomson and Vaughan[11] and Bunton, Lewis and Llewellyn,[4] as well as in the present investigation. The kinetic results illustrated graphically in Fig. 1 are mutually consistent with the exception of those of Bolin and indicate that the Arrhenius activation energy (E_h = 14.8 kcal./mole) for the alkaline hydrolysis of benzamide in water is not sensibly temperature independent, implying that the bracketed term in eq. 2 may be neglected over the range from 25–109°.

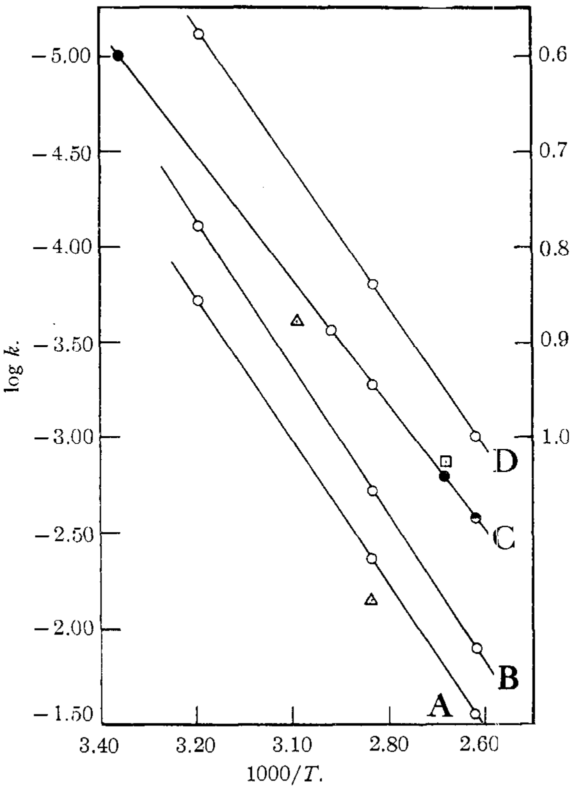

Fig. 1.—Temperature dependence of the velocity constants in the alkaline hydrolysis and oxygen exchange of benzamide in water: A, log k_1; B, log k_e; C, log k_h (●, Reid; ○, Packer; ◓, this investigation; △, Bolin; ⊡, Bunton); D, log k_2/k_3 (right-hand scale).

Data for the oxygen exchange of benzamide-O^{18} occurring during hydrolysis in aqueous sodium hydroxide at three temperatures are summarized in Fig. 2. The values of the ratio k_h/k_e, obtained according to eq. 1 for these systems are shown in Table I together with the values of k_1 and k_3/k_2 which may be computed from the former values.

TABLE I

THE VELOCITY CONSTANTS OF THE CONCURRENT ALKALINE HYDROLYSIS AND OXYGEN EXCHANGE OF BENZAMIDE AND ETHYL BENZOATE

Temp., °C.	k_h/k_e	$k_h \times 10^4$, l./mole sec.	$k_e \times 10^4$, l./mole sec.	k_3/k_2	$k_1 \times 10^4$, l./mole sec.
		Benzamide[a]			
109	0.208	26.3	126	0.104	279
80	.29	5.4	18.7	.145	42.6
40.7	.53	0.40	0.76	.263	1.92
		Ethyl benzoate[b]			
40.2	10.1	258	2.55	5.05	310
25.0	11.3	84[c]	0.74	5.65	98.3
9.0	14.7	26.5	0.18	7.35	30.2

[a] Initial amide and sodium hydroxide concentrations were approximately 0.1 *N*. [b] Initial ester and sodium hydroxide concentrations were approximately 0.01 *N*. [c] This value agrees with the value of 87 × 10^{-4} determined previously.[3a]

Arrhenius plots were also constructed for k_e, k_1 and k_3/k_2 as shown in Fig. 1. From the slopes of the lines the following values were obtained:

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[7] For a derivation of these points, see the Ph.D. thesis of R. D. Ginger, Illinois Institute of Technology, 1958.

[8] S. Arrhenius, *Z. physik. Chem.*, **4**, 222 (1889).

[9] E. E. Reid, *Am. Chem. J.*, **21**, 284 (1899); **24**, 397 (1900); **46**, 327 (1911).

[10] I. Bolin, *Z. anorg. allgem. Chem.*, **143**, 201 (1925).

[11] J. Packer, A. L. Thomson and J. Vaughan, *J. Chem. Soc.*, 2601, (1955).

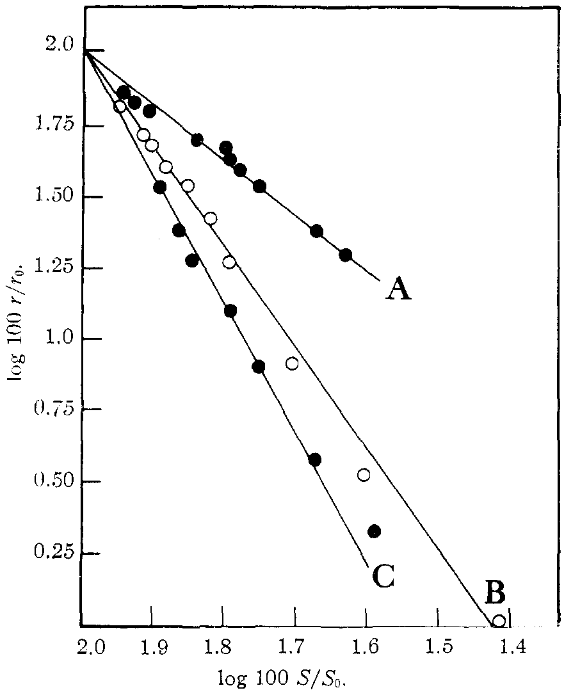

Fig. 2.—Oxygen exchange *vs.* hydrolysis in the alkaline hydrolysis of benzamide in water: A, 40.7°; B, 80°; C, 109°.

E_e = 17.5 kcal./mole, E_l = 17.2 kcal./mole and $(E_3 - E_2) = -3.2$ kcal./mole. Substitution of these values into equations 2 and 3 leads to log B_l = 8.25 and log (B_2/B_3) = 2.82.

The Temperature Dependence of the Rates of Hydrolysis and Oxygen Exchange during the Alkaline Hydrolysis of Ethyl Benzoate.—The rate of the alkaline hydrolysis of ethyl benzoate in 33% dioxane–water was studied previously by Bender.[3a] In this investigation the hydrolysis was studied at three temperatures. The oxygen exchange accompanying the hydrolysis determined at these temperatures is shown in Fig. 3. The values of the various rate constants obtained are presented in Table I. Figure 4 shows the Arrhenius plots constructed for k_e, k_l, k_h and k_3/k_2. From these plots, these several values were obtained: E_h = 12.9 kcal./mole; E_e = 14.9 kcal./mole; E_l = 13.2 kcal./mole; and $(E_3 - E_2) = -2.1$ kcal./mole. Substitution of these values into equations 2 and 3 leads to log B_l = 9.32 and log $(B_2/B_3) = -0.74$.

Discussion

The Significance of the Temperature Dependence of Oxygen Exchange During Hydrolysis.—An important consequence of the analysis of the hydrolysis of carboxylic acid derivatives by a carbonyl addition mechanism involving a tetrahedral intermediate is the consideration that the partitioning of the intermediate to hydrolysis or exchange might be a function of the temperature. This has indeed been shown to be the case in the two examples cited. The temperature variation of the partitioning of the intermediate (k_2/k_3) of the order of 50% over a 30° temperature range in ester hydrolysis and 150% over a 70° temperature range in amide hydrolysis is consistent with the formation of a tetrahedral intermediate.

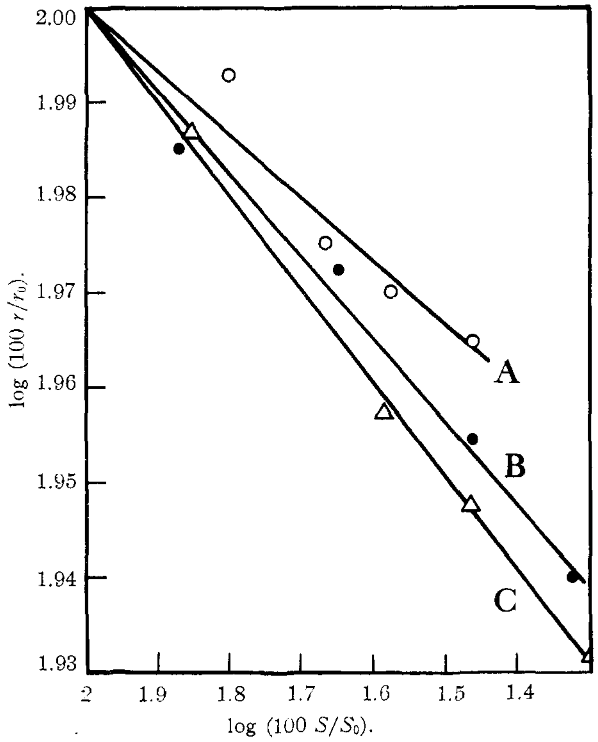

Fig. 3.—Oxygen exchange *vs.* hydrolysis in the alkaline hydrolysis of ethyl benzoate in 33% dioxane–water: A, 9.0°; B, 25.0°; C, 40.2°.

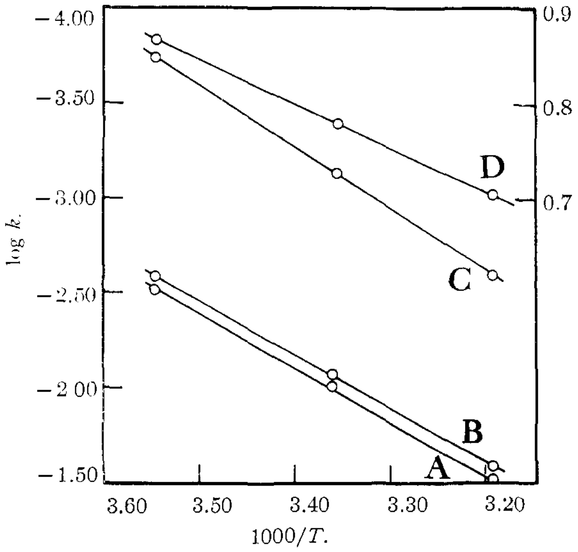

Fig. 4.—Temperature dependence of the velocity constants in the alkaline hydrolysis and oxygen exchange of ethyl benzoate in 33% dioxane–water: A, log k_l; B, log k_h; C, log k_e; D, log k_3/k_2 (right-hand scale).

The values of $E_2 - E_3$ for ester and for amide hydrolysis are of the same sign and are very similar in magnitude. However, the values of log B_2/B_3 for the two cases are quite different, leading to the result that $k_h > k_e$ in ester hydrolysis whereas $k_e > k_h$ in amide hydrolysis. The difference in the log B_2/B_3 terms may be due to a difference in solvation properties of the respective transition states. In the consideration of different families of compounds, therefore, the partitioning of the intermediate must be ascribed not only to electronic factors (which are reflected in the energy of activation)[3a,4] but also to the entropies of the processes.

It has been suggested by Bunton[12] that carbonyl oxygen exchange accompanying the hydrolysis of various carboxylic acid derivatives can also be explained by the partitioning of a suitably constituted transition state to reactants (producing oxygen exchange) or to products (producing hydrolysis). In designating the structure of such a transition state in the reaction of hydroxide ion and an ester, the position (or positions) of the proton becomes extremely crucial and difficult to assess. At present, it appears that all experimental evidence, including the data on the temperature dependence of oxygen exchange during hydrolysis, can be interpreted in terms of the mechanism involving an unstable, tetrahedral intermediate.

From the data presented earlier it is possible to evaluate the magnitude and the variation with temperature of the bracketed terms in eq. 2 and 3, respectively. The results of such calculations for the alkaline hydrolyses of benzamide and ethyl benzoate are summarized in Table II, which also includes values for the term E_1/RT for comparison.

TABLE II

VALUES OF EXPLICITLY TEMPERATURE-DEPENDENT TERMS IN EQUATION 2 AND 3 FOR THE ALKALINE HYDROLYSES OF BENZAMIDE AND ETHYL BENZOATE

Temp., °K.	E_1/RT	$\ln [B_2/B_3 e^{(E_3-E_2)/RT} + 1]^a$	$\ln [1 + B_3/B_2 e^{(E_2-E_3)/RT}]^b$
		Benzamide	
382	22.5	2.37	0.11
253	24.3	2.07	.13
313	27.5	1.58	.23
		Ethyl benzoate	
313	21.1	0.18	1.83
298	22.2	.15	1.97
282	24.3	.13	2.14

[a] This term refers to eq. 2 for k_h. [b] This term refers to eq. 3 for k_e.

From Table II, it may be noted that the bracketed terms are sufficiently small and constant so that it is not surprising or unusual that the Arrhenius plots for k_h and k_e are linear. Especially careful and refined experimental measurements would be required to demonstrate deviations from linearity. It has been demonstrated that even though the hydrolyses of benzamide and of ethyl benzoate, two typical carboxylic acid derivatives, may occur by a complex mechanism involving an addition intermediate, it does not necessarily follow that E_h is appreciably temperature dependent. This argument may be extended to suggest that there may be other reactions occurring in several steps and involving intermediates of similar instability which result in an over-all activation energy which is temperature independent.

As shown by the above analysis, the apparent absence of a temperature dependence of the Arrhenius activation energy is not necessarily inconsistent with the two-step mechanism for the hydrolysis of carboxylic acid derivatives. That is, the apparent temperature independence of the Arrhenius activation energy would be necessary but not sufficient evidence against the two-step mechanism that has been described previously.

However, it might be anticipated that an Arrhenius plot for the temperature dependency of k_h in the hydrolysis of some carboxylic acid derivatives might be non-linear if a two-step mechanism is operative. An inspection and recalculation of much of the literature data available up to the time of this investigation yielded no unequivocal evidence to indicate a temperature dependency of the Arrhenius activation energy for the hydrolysis of any carboxylic esters or amides. In addition, the two cases studied in this investigation yielded no evidence for such a temperature dependency. Semerano[13] reported a variation of the Arrhenius activation energy with temperature for the alkaline hydrolysis of acetanilide and the various acetotoluidides and acetxylidides in aqueous ethanol. However, the variations were variable in direction and often could be attributed to a probable experimental uncertainty in the kinetic measurements. Gold[14] has found that the hydrolysis of acetic anhydride exhibits a distinct departure from the Arrhenius law in a number of solvents including pure water. The decrease in the activation energy with increase in temperature is "in the opposite direction to that which would take place if it were caused by the incursion of a side reaction or second mechanism, so that this most frequent cause of breakdowns of the Arrhenius law can be ruled out as an explanation."[14] During the course of this investigation, Tommila[15] reported the results of a set of highly refined experiments in which the Arrhenius activation energy for a particular hydrolysis of a carboxylic ester is a function of the temperature. The results which were obtained for the hydrolysis of ethyl acetate in 21.6% *t*-butyl alcohol–water mixtures, for example, show a variation in the apparent activation energy from 7.50 to 9.20 kcal./mole corresponding to the temperature interval of 0–10° to that of 40–50°. In a more recent paper by Tommila,[16] the activation energies of the hydrochloric acid hydrolysis of simple aliphatic carboxylic acid esters, such as ethyl acetate, in various acetone–water solutions were found to have a similar temperature dependence. These temperature dependencies, however, are in the opposite direction to what one would expect for a two-step mechanism; that is, the activation energy should decrease with an increase of temperature for a two-step mechanism. Furthermore, interpretation of these results is complicated by the fact that these reactions were carried out in mixed solvents.

The temperature-dependent activation energy found by Gold for acetic anhydride is at least consistent with the hydrolytic two-step mechanism, involving the formation of an addition intermediate. It would, of course, be of considerable

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(12) C. A. Bunton, personal communication.

(13) G. Semerano, *Gazz. chim. ital.*, **61**, 921 (1931).

(14) V. Gold, *Trans. Faraday Soc.*, **44**, 506 (1948).

(15) E. Tommila, A. Koivisto, J. P. Lyyra, K. Antell and S. Heimo, *Ann. Acad. Sci. Fennicae*, **47A**, 1 (1952).

(16) E. Tommila and A. Hella, *ibid.*, **53A**, 3 (1954).

interest to carry out a complete oxygen exchange study for a carboxylic acid derivative in which the Arrhenius activation energy for hydrolysis and/or oxygen exchange is a sufficiently sensitive function of temperature to allow an experimental test of the theory that the temperature variation of the hydrolytic activation energy can be quantitatively accounted for on the basis of the mechanism proposed.

The Equivalence of the Intermediate in the Acidic and Alkaline Hydrolysis of Ethyl Benzoate.—In a previous investigation it was pointed out that the ratio k_h/k_e was identical for the hydrolysis of ethyl benzoate in either acidic or basic solution.[3a] The equivalence of this ratio has been cited by Taft[17] to indicate the existence of a common intermediate in acid and base-catalyzed ester hydrolysis. The previously reported values k_h/k_e for acidic and alkaline hydrolysis of ethyl benzoate were not performed at the same temperature. Therefore it was thought desirable to redetermine these values under exactly identical conditions of temperature and solvent composition. The results are given in Table III.

TABLE III

THE HYDROLYSIS AND OXYGEN EXCHANGE OF ETHYL BENZOATE IN ACIDIC AND ALKALINE SOLUTION[a]

Catalysis	k_h, l./mole sec.	k_h/k_e
Acidic	3.3×10^{-7}	5.3
Basic	8.4×10^{-3}	11.3

[a] 25.0°, 33% dioxane–water solution, initial concentrations of ester and catalyst were approximately 0.01 N.

It is seen that the values of k_h/k_e for acidic and basic catalysis differ by a factor of approximately two. However, in view of the fact that the rates of hydrolysis differ by a factor of roughly 10^4, the difference in the values of k_h/k_e is relatively insignificant. It therefore can be affirmed with substantial probability that in both the basic and acidic catalyses, a similar intermediate is formed, the most likely possibility in both cases being the unionized hydrate of the ester.

Acknowledgment.—The authors wish to express their appreciation to Drs. C. A. Bunton and V. Gold for valuable discussions and to Dr. H. Taube of the University of Chicago through whose courtesy the mass spectrometer under AEC Contract AT(11-1)-92 was made available.

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[17] R. W. Taft, Jr., THIS JOURNAL, **74**, 3120 (1952); R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 588.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

The Effect of Solvent on the Catalytic Activity of Aliphatic Amines in Elimination Reactions[1]

BY R. G. PEARSON AND D. C. VOGELSONG[2]

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Triethylamine, di-*n*-butylamine and *n*-hexylamine have been used as catalysts to study the rate of elimination of *p*-toluenesulfonic acid from 1-(*p*-toluenesulfonyl)-2-propyl *p*-toluenesulfonate in several non-aqueous solvents. By changing the solvent one can make either the primary, secondary or tertiary amine the strongest catalytic base.

Weinstock, Pearson and Bordwell[3] have shown that the elimination of *p*-toluenesulfonic acid from 1-(*p*-toluenesulfonyl)-2-propyl *p*-toluenesulfonate (hereafter called tosylate compound) is general base catalyzed in 50% dioxane–water mixtures. The kinetics indicate that the reaction follows the simple bimolecular mechanism

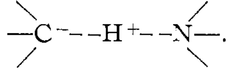
$$\begin{aligned} &CH_3CH(OTs)CH_2SO_2C_7H_7 + B \longrightarrow \\ &\qquad CH_3CH{=}CHSO_2C_7H_7 + BH^+ + OTs^- \quad (1) \end{aligned}$$

where B is the base, and OTs^- the *p*-toluenesulfonate anion. Because of this, it was thought that this reaction might be used in the study of the effects of solvents on the relative base strengths of primary, secondary and tertiary amines. Triethylamine, di-*n*-butylamine and *n*-hexylamine were chosen as representative amines because of the ease of purification. In previous studies[4] the equilibrium constants for the reactions of these three bases with the reference acid 2,4-dinitrophenol have been determined in several solvents.

The observed reaction in solvents of low dielectric constant was the formation of an ion-pair

$$B + HA \rightleftarrows BH^+,A^- \quad (2)$$

where HA is 2,4-dinitrophenol. A possible complication in the case of a primary or secondary amine compared to a tertiary amine, is that a double or triple hydrogen bond might hold the ion-pair together in the first two cases. This would cause these amines to appear stronger than the tertiary amine. In a kinetic process involving a proton removal, the transition state should be similar for all three classes of amines, resembling a single hydrogen bond, *e.g.*,



$$\diagdown\!\!\!\!\!\diagup\!\!C^- - - H^+ - - N\!\diagup\!\!\!\!\!\diagdown$$

In studies of the rate of proton abstraction from nitroethane in water by various alkylamines,[5] it was found that tertiary amines reacted more rapidly than their basic ionization constants in water would have predicted. This was considered evidence for a high electron density, or potential basicity, on nitrogen for these amines. It is of in-

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[1] Taken in part from a dissertation submitted by D. C. Vogelsong to the graduate school of Northwestern University in partial fulfillment of the requirements for the Ph.D. degree, August, 1956.

[2] Predoctoral fellow, E. I. du Pont de Nemours and Co., 1955-1956.

[3] J. Weinstock, R. G. Pearson and F. G. Bordwell, THIS JOURNAL, **78**, 3473 (1956).

[4] R. G. Pearson and D. C. Vogelsong, *ibid.*, **80**, 1038 (1958).

[5] R. G. Pearson and F. V. Williams, *ibid.*, **76**, 258 (1954).