The ketones are insoluble in water and concentrated sulfuric acid and soluble in ether, ethanol, benzene and bisnonafluorobutyl oxide.

2,4-Dinitrophenylhydrazone and semicarbazone derivatives were prepared, but all attempts to prepare bisulfite addition products were unsuccessful.

The yields of ketone found in the various preparations are listed in column 3 of Table II.

Derivatives

Preparation of 2,4-Dinitrophenylhydrazones.—A solution of 2,4-dinitrophenylhydrazine was prepared by adding 0.5 g. of 2,4-dinitrophenylhydrazine to 10 ml. of 50% sulfuric acid, followed by the addition of 10 ml. of 95% ethanol. To this solution, 0.5 g. of ketone was added and allowed to stand for one week instead of the usual few hours. The crystals were filtered and recrystallized three times from ethanol and water. The highest yields of the 2,4-dinitrophenylhydrazones were obtained when a solution of 50% sulfuric acid was used.

Preparation of Semicarbazone.—The semicarbazone was prepared by refluxing a solution of semicarbazide hydrochloride, water, ethanol and ketone for one hour, after which the solvents were removed under vacuum. The solution must be refluxed at least one hour to obtain an appreciable yield of semicarbazone. The semicarbazone was crystallized from ether after being decolorized with activated charcoal.

Degradation.—The ketones reacted vigorously with a solution of concentrated potassium hydroxide to give a haloform-type splitting reaction, yielding a monohydrofluorocarbon. Upon acidification, the sole organic product was an aromatic acid. In every case, benzoic acid, *p*-toluic acid or 2,4-dimethylbenzoic acid, was obtained and identified by its melting point and neutral equivalent. The monohydrofluorocarbons obtained were identified by their physical properties.

The authors wish to acknowledge the sponsorship of the Minnesota Mining and Manufacturing Company for part of the work reported in this paper.

GAINESVILLE, FLA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Hydrolysis of Ethyl Fluoroacetates[1]

BY GEORGE GORIN, OGDEN R. PIERCE AND EARL T. MCBEE

RECEIVED FEBRUARY 26, 1953

Ethyl monofluoroacetate is hydrolyzed more slowly than ethyl acetate in 70% aqueous acetone with 0.1 *M* hydrochloric acid as a catalyst. Ethyl difluoroacetate and ethyl trifluoroacetate, on the other hand, are hydrolyzed more rapidly than ethyl acetate, and are susceptible to fairly rapid hydrolysis even in initially neutral medium. The significance of these results is discussed. Reaction rate constants are given at 25° and two other temperatures, and energies of activation have been calculated.

Henne and Pelley[2] reported recently that the acetate esters of alcohols containing fluorine atoms in the β- or γ-positions are hydrolyzed more slowly than the corresponding unsubstituted esters in 50% acetone and 0.1 *M* hydrochloric acid, the decrease in rate being about tenfold or less. This paper reports the investigation of a series of compounds in which substitution is at the α-position of the acid, namely, the series ethyl monofluoroacetate, ethyl difluoroacetate and ethyl trifluoroacetate. The effect of this type of substitution is more varied and more profound.

Experimental

Materials.—In order to avoid systematic errors, several samples of each ester were prepared and used interchangeably, except in the case of ethyl monofluoroacetate, the toxicity of which made it advisable to keep manipulation at a minimum. Ethyl monofluoroacetate (Monsanto Chemical Co.) and ethyl difluoroacetate (Columbia Chemicals, Inc.) were purified by treatment with dilute aqueous sodium bicarbonate to remove excess acid and then with a large excess of anhydrous calcium chloride to remove water and alcohol. Ethyl trifluoroacetate was prepared from trifluoroacetic acid and ethyl alcohol. Each ester was rectified at least once through a 4-ft. helices-packed "Todd" distillation column, and the product collected for use was no more than the middle third of the fraction boiling over a 0.5° range. The saponification equivalent (sapn. equiv.) was determined by treatment with 1–2 *M* sodium hydroxide at room temperature for 2–12 hours.[3] These are representative properties: ethyl monofluoroacetate, b.p. 114° (750 mm.), $n^{24}\mathrm{D}$ 1.3737, sapn. equiv. 106.5 (calcd. 106.1); ethyl difluoroacetate, b.p. 98.8° at 740 mm., $n^{20}\mathrm{D}$ 1.34713,[4] sapn. equiv. 123.7 (calcd. 124.1); ethyl trifluoroacetate, b.p. 60.7° (740 mm.), $n^{20}\mathrm{D}$ 1.30735,[4] sapn. equiv. 142.1 (calcd. 142.1). The purification of acetone, ethyl acetate, trifluoroacetic acid and difluoroacetic acid has been described elsewhere.[5] All other reagents were C.P. or of analytical grade.

Composition and Properties of Reaction Medium.—The reaction medium contained in all cases 70.0 ml. (54.9 ± 0.1 g.) acetone; to this were added about 1 ml. of ethyl acetate and the catalyzing acid, and enough water to make 100 ml. To correct for changes in volume in experiments at temperatures other than 25°, the following densities were assumed: 0°, 0.916 g./ml.; 15°, 0.898; 25°, 0.888; 35°, 0.879; 50°, 0.864.[6]

Temperature Regulation.—Temperatures were checked with a thermometer calibrated by the Bureau of Standards, and maintained with the tolerances: 0.00 ± 0.02°; 15.0 ± 0.1°; 25.00 ± 0.05°; 35.00 ± 0.05°; 50.2 ± 0.1°.

Ethyl Acetate and Ethyl Monofluoroacetate.—The rates of reaction at 25° were determined essentially as described elsewhere,[5] except that in these experiments the solutions were approximately 0.1 *M* in ethyl acetate. Measurements at 35° were made as follows (procedure A): the reaction mixture was made up at 25°, and aliquot portions were immediately titrated; the mixture was then allowed to come to equilibrium at the higher temperature, and other aliquot portions were withdrawn and titrated at appropriate intervals; the ester concentration and zero-time titer were calculated by allowing for the expansion of the solvent. Measurements at 50° were made as follows (procedure B): all reagents except ethyl monofluoroacetate were mixed at 25°, diluted to 99.0 ml., and allowed to come to equilibrium at

---

[1] Presented before the Division of Organic Chemistry, 123rd National Meeting of the American Chemical Society, Los Angeles, Calif., March 15–19, 1953.

[2] A. H. Henne and R. L. Pelley, THIS JOURNAL, **74**, 1426 (1952).

[3] After each determination, the solution was tested with the zirconium-alizarin sulfonate reagent (F. P. Treadwell and W. T. Hall, "Analytical Chemistry," Vol. I, 9th ed., John Wiley and Sons, Inc., New York, N. Y., p. 439) and the fluorine present as fluoride ion amounted to less than 0.5%.

[4] Determined with a Bausch and Lomb Precision Refractometer by Mr. J. P. Wright.

[5] O. R. Pierce and G. Gorin, THIS JOURNAL, **75**, 1749 (1953).

[6] The values at 0–25° were calculated from the formula given in "International Critical Tables," Vol. III, p. 112, taking the percentage of acetone by weight as 62% (the weight of water required to make 100.0 ml. of solution with no other reagents added was 33.25 ± 0.15 g). The values at 35° and 50° were estimated by extrapolation.

the higher temperature; 1.00 ml. of ester was then added with a calibrated pipet (weight delivered reproducible within < 1%); aliquot samples were titrated soon after mixing and the zero-time titer was estimated by direct extrapolation, whereas the concentration of ester was calculated by allowing for expansion.

Ethyl Difluoroacetate.—The difluoroacetic acid liberated in the hydrolysis of this ester could not be determined satisfactorily by titration with alkali, due to the sensitivity of the unreacted ester toward alkaline reagents. The acid was therefore determined iodometrically by reaction with a mixture of potassium iodate and potassium iodide and titration of the liberated iodine to a starch end-point. Since the reaction of acids with iodate–iodide is not instantaneous, small variations in the stoichiometry of the titrations were observed, depending on the length of time taken for titration and other factors; however, satisfactory reproducibility could be obtained in any given set of conditions. The correct stoichiometry was secured by standardizing the thiosulfate solution against standard acid under the same conditions as obtained in the rate experiments; hydrochloric acid and difluoroacetic acid gave identical titers. In experiments 17–19, 0.01 *M* difluoroacetic acid was used as a catalyst; 5.00-ml. aliquot samples were withdrawn at intervals, diluted with 40 ml. of water (this was necessary to permit proper development of the starch–iodine color), treated with 1 ml. of 0.03 *M* potassium iodate–0.15 *M* potassium iodide, and titrated with 0.01 *N* sodium thiosulfate in the presence of 1 ml. 0.2% starch solution. In experiments 20–35, 0.05 *M* hydrochloric acid was used as a catalyst, with 3 ml. of iodate–iodide mixture. The solutions for measurements at 15 and 0° were mixed both by procedure A and procedure B, and the results were the same within experimental error.

Ethyl Trifluoroacetate by the Titration Method.—The trifluoroacetic acid liberated in the hydrolysis of this ester could also be determined iodometrically; however, the procedure had to be modified because ethyl trifluoroacetate was hydrolyzed rapidly by water in the absence of a catalyst. In the first place, solutions for measurements at all temperatures were mixed by procedure B. Secondly, since it was clearly not permissible to dilute the aliquot samples with a large volume of water before performing the titrations, starch was not used as an indicator. In experiments 36–40 and 48–54, in which no catalyst was employed, 5.00-ml. aliquot samples were diluted with 10 ml. of 80% aqueous acetone, treated with 1 ml. of potassium iodate–potassium iodide and titrated to the disappearance of the iodine color. In experiments 55–58, 30 ml. of 80% acetone and 3 ml. of iodate–iodide were used. For runs at 15 and 0°, the acetone–iodate–iodide mixture was chilled in ice before the sample was added.

Ethyl Trifluoroacetate by the Conductivity Method at 25° (Experiments 41–47).—The hydrolysis of ethyl trifluoroacetate in 70% aqueous acetone is accompanied by an increase in the specific conductance of the system, due to the conductivity of the liberated trifluoroacetic acid. The rate of reaction could accordingly be determined by performing the hydrolysis in a conductivity cell, and measuring the resistance as a function of time.

The conductivity cell consisted of a piece of 17-mm. glass tubing, in which were fused two platinum electrodes, about 1 cm.^{2} in area and 10 cm. apart. The piece of glass tubing was fused at one end to a 125-ml. erlenmeyer flask in nearly the same plane as the bottom of the flask, and at the other end to a filling tube, which was in the same plane as the erlenmeyer flask itself. This manner of construction made it possible to transfer liquid back and forth from flask to cell by tilting the apparatus through an appropriate angle, and to keep the cell immersed in a constant-temperature bath while the mouth of the flask and the tip of the filling tube remained above the surface of the thermostat liquid. The electrodes were connected to a Fisher–Serfass conductivity bridge (rated accuracy 1–2%). The cell constant was about 6 cm.$^{-1}$. Two different cells were used, with results identical within experimental error.

The cell was calibrated as follows. One hundred ml. of 70% acetone was placed in the cell and its resistance measured; in all cases it was $>10^6$ ohms. Trifluoroacetic acid was added in small portions with a 0.5-ml. microburet, and after each addition the solution was thoroughly mixed and its resistance measured. After about 1 ml. of acid had been added and the final resistance measured, the concentration of acid was determined by titration. The concentration of acid present after each addition was then computed by direct proportion to the total amount added and the resultant final normality, a small correction being applied for the change in volume due to the addition of acid. The results of five sets of such determinations were plotted on a graph, and a smoooth curve was drawn through the points. The specific resistances corresponding to integral concentrations of trifluoroacetic acid were:

M	0.0060	0.0100	0.0150	0.0200	0.0250
Ohm-cm.	1930	1220	862	688	584

The measurements at low concentrations were not precise, because of the difficulties inherent to the determination of high resistances (absolute value > 10,000 ohms); on the other hand, the curve flattened out rapidly with increasing concentrations of acid, so that the practical range of measurements was restricted to 0.006–0.025 *M* trifluoroacetic acid.

For the determination of reaction rates, 1.00 ml. of ester, 70.0 ml. of acetone, water, and, in experiments 45–47, difluoroacetic acid, were mixed to give 100 ml. of solution, which was transferred to the conductivity cell. The resistance was measured as a function of time, and the concentration of acid corresponding to each measurement was estimated from the calibration curve. Since the interval between measurements was short, k was not calculated from successive values of $(a - x)$, as the uncertainty in the value of $(t_2 - t_1)$ might be too large. Experiment 41 is typical.

Time $\times 10^{-1}$, sec.	$(a - x)$, mole/l.	$10^{-1} \times (t_2 - t_1)$ sec.	$10^5 k$ sec.$^{-1}$
0	(0.0832)		
426	.0744	426	2.62
474	.0735	474	2.61
528	.0725	102	2.54
594	.0713	120	2.53
642	.0705	168	2.48
708	.0695	180	2.34
774	.0684	132	2.29
924	.0658	150	2.58
990	.0646	216	2.65
1050	.0636	126	2.69
1115	.0626	125	2.51
		Average	2.53

Results

The results of this investigation are summarized in Table I.

In the case of ethyl acetate it has been shown that uncatalyzed ("spontaneous") hydrolysis by water is extremely slow,[7] that catalysis by the liberated acetic acid is negligible in comparison to that by 0.1 *M* hydrochloric acid, and that the reaction rate constant is closely proportional to the stoichiometric concentration of catalyst over a wide range of catalyst concentration.[8] The reaction rate constant in each experiment was measured by

$$k = \frac{2.303}{t_2 - t_1} \log \frac{(a - x_1)^{5}}{(a - x_2)} \qquad (1)$$

and its value, divided by the concentration of hydrochloric acid present in the medium, should therefore be a constant. The average of four determinations, in which the exact concentration of catalyst was varied between 0.09 and 0.11 *M*, is given in column six of Table I, together with the

---

[7] W. Poethke, *Ber.*, **68B**, 1031 (1935).

[8] For a study of the range 0.0002–0.2 *M* in water, see H. M. Dawson and W. Lowson, *J. Chem. Soc.*, 2146 (1928); for the range 0.025–0.1 *M* in 70% acetone, see Ref. 5.

TABLE I

REACTION RATE CONSTANTS

Expt.	Ester	Temp., °C.	Concn. catalyst, *M*	$10^6 k$ sec.$^{-1}$	$10^5 k_{cat.}$ l. mole^{-1} sec.$^{-1}$
1–4	CH_3CO_2Et	25.00	0.1 HCl		4.60 ± 0.04
5–8	CH_2FCO_2Et	25.00	.1 HCl		2.53 ± .02
9–12	CH_2FCO_2Et	35.00	.1 HCl		6.95 ± .03
13–16	CH_2FCO_2Et	50.2	.1 HCl		25.0 ± .3
17–19	CHF_2CO_2Et	25.00	.01 CHF_2CO_2H	0.6	
20–24	CHF_2CO_2Et	25.00	.05 HCl	5.35 ± 0.03	9.5
25–28	CHF_2CO_2Et	15.0	.05 HCl	2.40 ± .03	
29–35	CHF_2CO_2Et	0.00	.05 HCl	0.597 ± .013	
36–40	CF_3CO_2Et	25.00	......	24.0 ± .0	
41–44	CF_3CO_2Et	25.00	......	23.8 ± .4	
45–47	CF_3CO_2Et	25.00	.01 CF_3CO_2H	24.5 ± 1.0	
48–50	CF_3CO_2Et	15.0	......	12.6 ± 0.1	
51–54	CF_3CO_2Et	0.00	......	4.43 ± .08	
55–58	CF_3CO_2Et	0.00	.05 HCl	8.3 ± .4	

indeterminate error of the mean[9] as a measure of reproducibility. The result is in good agreement with that reported by Davies and Evans.[10]

In the case of ethyl monofluoroacetate, blank experiments demonstrated that the spontaneous hydrolysis by water could likewise be neglected, and agreement with the first-order rate law showed that catalysis by the liberated monofluoroacetic acid was negligible. The reaction rate constant was proportional to the concentration of hydrochloric acid added within the concentration range investigated (0.09–0.11 *M*), and the results are therefore reported as for ethyl acetate, but at three temperatures.

In the case of ethyl difluoroacetate, preliminary experiments showed that hydrolysis of the ester occurred at an appreciable rate in initially neutral medium. Unfortunately, the precision of the analytical method was poor at low concentrations of difluoroacetic acid, and the results were not satisfactorily reproducible; however, an upward trend in the value of *k* could be discerned clearly as the reaction proceeded, indicating catalysis by the liberated difluoroacetic acid. The relative importance of the spontaneous and catalyzed reactions was determined in experiments 17–19, in which the medium was made initially 0.01 *M* in difluoroacetic acid, and four or five measurements were made in the interval to 10% reaction, *i.e.*, while the ester concentration decreased from 0.1 to 0.09 *M* and the difluoroacetic acid concentration was doubled. The reaction rate constant calculated from the integrated first-order equation 1 remained constant within 25% and indicated within this accuracy the magnitude of the rate of the spontaneous reaction. The value is reported in column five of Table I to only one significant figure, because of the limited precision of the data.

In experiments 20–35, ethyl difluoroacetate was hydrolyzed in 0.05 *M* hydrochloric acid, and the analytical data were satisfactorily precise. The reaction was allowed to proceed to about 10% completion, within which range the effect of the liberated difluoroacetic acid can be neglected. The concentration of catalyst actually varied between 0.045 and 0.055 *M*, and the rate constants were converted to a common basis by assuming direct proportionality to the hydrochloric acid concentration; this assumption can be made because the spontaneous reaction only accounts for about 10% of the total rate, and the variation in catalyst concentrations is small. The rates adjusted to 0.0500 *M* catalyst concentration are reported in column five. These values are the sums of two rate constants: that of the spontaneous reaction, k_{H_2O}, and that of the acid-catalyzed reaction. If this is proportional to the stoichiometric concentration of catalyst, as is the case with ethyl acetate, one can then write that the experimental rate constant

$$k = k_{H_2O} + k_{HCl}C_{HCl} \qquad (2)$$

The value of k_{HCl} calculated on this basis appears in column six.

With ethyl trifluoroacetate, hydrolysis in initially neutral medium (experiments 36–40) was quite rapid, and no appreciable increase in rate could be observed in the interval 0–20% reaction, while the concentration of trifluoroacetic acid increased from 0 to 0.02 *M*: application of equation 1 to the data in this range gave consistent values of *k* with no apparent upward trend. The constant *k*, therefore, measures the rate of the spontaneous reaction; its values at three temperatures are reported in column five.[11]

In experiments 41–44, the rate of hydrolysis of ethyl trifluoroacetate was determined independently by a conductivity method, and the results are in excellent agreement with those of the titration method. In the conductivity experiments it was possible to make very frequent measurements and to obtain more values of *k* in each run: one of these is reported in detail (*cf.* Experimental section) to show how the values of *k* vary as the reaction proceeds. The results of experiments 45–47,

---

[9] F. Daniels, *et al.*, "Experimental Physical Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1949, p. 357.

[10] G. Davies and D. P. Evans, *J. Chem. Soc.*, 339 (1940), corrected to 25.0°. 4.55 × 10^{-5} liter mole^{-1} sec.$^{-1}$.

[11] In the experiments conducted at 15 and 0° the values of *k* calculated in the range 0.015–0.02 *M* trifluoroacetic acid began to show an upward drift, probably indicating that the acid-catalyzed reaction has the lower activation energy. At 15°, therefore, measurements were carried out to a final acid concentration of 0.015 *M*, and those at 0° to a concentration of 0.01 *M*. In these ranges, the values of *k* were constant within experimental error, and were averaged straightforwardly.

in which the medium was made initially 0.01 *M* in trifluoroacetic acid, confirm the finding that catalysis by trifluoroacetic acid at concentrations <0.02 *M* is negligible in comparison to the spontaneous hydrolysis.

The effect of acid catalysis becomes appreciable, however, when 0.05 *M* hydrochloric acid is added. Unfortunately, the conductivity method could not be applied in this case, and the titrations were very difficult to perform, because the reaction was so fast as to make the end-points extremely fleeting. A few experiments, 55–58, could, however, be carried out at 0°; the reaction medium was made 0.05 *M* in hydrochloric acid, and the reaction allowed to proceed to about 10% completion, in which range catalysis by the liberated trifluoroacetic acid could be neglected. Making the same assumptions as in the case of ethyl difluoroacetate, a value of the catalytic constant can be calculated by equation 2 and is given in column six.

For the reactions which were studied at three temperatures, the energy of activation can be calculated by means of the well-known Arrhenius equation

$$E = \frac{2.303\ RT_1T_2}{T_2 - T_1} \log \frac{k_2}{k_1}$$

where k_2 and k_1 are the reaction rate constants at temperatures T_2 and T_1, respectively. The results are reported in Table II. In the calculation of the activation energy for ethyl difluoroacetate, the values of *k* from column five were used directly, although, as has been remarked, they are really the sums of two rates. Since the spontaneous reaction makes only a small contribution to the total rate, and since the energies of activation for the spontaneous and catalyzed reactions cannot be greatly different, the calculated energy of activation is that of the catalyzed reaction to a good approximation.

TABLE II

ENERGIES OF ACTIVATION

System	Temp., °C.	*E*, kcal./mole
CH_3CO_2Et in 0.1 *M* HCl[10]		16.2
CH_2FCO_2Et in 0.1 *M* HCl	25–35	18.5
	35–50	16.7
CHF_2CO_2Et in 0.05 *M* HCl	0–15	14.5
	15–25	13.7
CF_3CO_2Et in water	0–15	10.9
	15–25	10.9

The results reported above can be rationalized in terms of the mechanism proposed for esters generally by Day and Ingold, according to which the hydrolysis reaction takes place in three steps

$$\text{(A)}\quad RCO_2R' + H_3O^+ \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} (RCO_2R'H)^+ + H_2O$$

$$\text{(B)}\quad (RCO_2R'H)^+ + H_2O \overset{k_2}{\rightleftarrows} (RCO_2H_2)^+ + R'OH$$

$$\text{(C)}\quad (RCO_2H_2)^+ + H_2O \rightleftarrows RCO_2H + H_3O^+$$

of which the proton transfers A and C are fast in comparison with B. Although all three reactions are reversible, the reversal of B and C can be neglected under the experimental conditions which obtain in this investigation, while equilibrium A, with equilibrium constant K_1, is quickly established and always maintained. The concentration of "esterium" ion is therefore given by

$$C_{(RCO_2R'H)^+} = K_1 \frac{C_{H_3O^+}C_{RCO_2R'}}{C_{H_2O}}$$

and the rate of reaction

$$v = k_2C_{H_2O}C_{(RCO_2R'H)^+} = k_2K_1C_{(H_3O)^+}C_{RCO_2R'} \quad (3)$$

which shows the proportionality to hydrogen ion concentration and first-order dependence on ester concentration required by experiment.[12]

The reaction rate constant therefore embodies the results of two processes, measured by K_1 and k_2, respectively, namely, the extent to which the ester will accept a proton at equilibrium and the rate at which the resultant complex is hydrolyzed by water. The equilibrium constant K_1 measures the basicity of the ester, and it is certainly to be expected from analogy with the fluorinated acids that progressive fluorine substitution will decrease the magnitude of this constant. On the other hand, it is apparent from the increasing susceptibility of ethyl difluoroacetate and ethyl trifluoroacetate to spontaneous hydrolysis that progressive fluorine substitution facilitates attack by water. This is because the water molecule is a nucleophilic reagent, and attack by such will be favored by inductive withdrawal of electrons from the carbethoxy carbon. In the case of ethyl difluoroacetate and ethyl trifluoroacetate, it appears that the increase in the magnitude of k_2 more than compensates for the decrease in the magnitude of K_1; in the case of ethyl monofluoroacetate, as well as the esters investigated by Henne and Pelley,[2] this is not the case.

Acknowledgment.—The authors wish to express their appreciation of the assistance rendered by Mr. Gene A. Brost, who performed most of the conductivity measurements. This work was sponsored by the Material Laboratory, Wright Air Development Center, Dayton, Ohio.

LAFAYETTE, INDIANA

---

[12] J. N. E. Day and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 686 (1941). In their formulation, these authors wrote H^+ as the catalyzing species

$$\text{(A')}\quad RCO_2R' + H^+ \rightleftarrows (RCO_2R'H)^+$$

and derived

$$v = k_2K_1C_{H^+}C_{H_2O}C_{RCO_2R'}$$

which differs from 3 in that it contains a C_{H_2O} term. For the purposes of this discussion, the difference is inconsequential, since all the data under consideration were determined in the same medium, and the effect of water is constant in all cases; but, for this very reason, the kinetic data can give no indication as to which formulation is the more nearly correct. Since a satisfactory body of independent evidence indicates, however, that the proton is hydrated in aqueous solution, it would seem preferable to consider H_3O^+ the catalyzing species, and to ascribe the undeniable effect of water concentration on the rate of reaction to a medium effect.