1-(*o*-Carbethoxyphenyl)-2-mercaptoimidazole.—1-(*o*-Carbethoxyphenyl)-2-mercaptoimidazole was prepared by condensation of *o*-carbethoxyphenyl isothiocyanate with aminoacetal in the presence of acid according to the method of Wohl and Marckwald[22] for the preparation of 1-aryl- or 1-alkylimidazole-2-thiols. The *o*-carbethoxyphenyl isothiocyanate was prepared according to the procedure of Dyson and George[24] by the condensation of thiophosgene with aromatic primary amines. The over-all yield of the product, m.p. 123–124.5°, was 23%.

Anal. Calcd. for $C_{12}H_{12}N_2O_2S$: C, 58.04; H, 4.87; N, 11.29. Found: C, 58.15, 58.03; H, 4.93, 4.71; N, 11.00, 11.20.

Hydrazide of 1-(*o*-Carboxyphenyl)-imidazole (XI).—1-(*o*-Carbethoxyphenyl)-2-mercaptoimidazole (0.9 g. or 0.0036 mole) was heated to reflux in 45 ml. of ethanol with excess Raney nickel for 45 minutes according to the procedure of Cook, Downer and Heilbron[25] for the desulfurization of 5-amino-2-mercapto-1-methylimidazole. The Raney nickel was removed by filtration and the ethanol filtrate evaporated on the water-bath. The oily residue was heated on the steam-bath with 4 ml. of 99–100% hydrazine hydrate and 3 ml. of ethanol for 3 hr. After adding 3 ml. of water to the solution, the ethanol was removed *in vacuo* and white solid slowly formed. It was collected by filtration and recrystallized from ethanol yielding 0.10 g. (14%) of product, m.p. 209–210°.

Anal. Calcd. for $C_{10}H_{10}N_4O$: C, 59.39; H, 4.98; N, 27.71. Found: C, 59.45, 59.45; H, 4.47, 4.43; N, 27.6, 27.8.

A mixture of this product with the hydrazide prepared from ethyl 1-phenyl-2-imidazolecarboxylate, m.p. 210–211°, melted in the range 179 to 190°.

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[24] G. M. Dyson and H. J. George, *J. Chem. Soc.*, **125**, 1702 (1924).

[25] A. H. Cook, J. D. Downer and I. Heilbron, *ibid.*, 2028 (1948)

[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

The Effect of Structure on Kinetics and Mechanism of the Alkaline Hydrolysis of Anilides[1]

BY SYDNEY S. BIECHLER[2] AND ROBERT W. TAFT, JR.

RECEIVED APRIL 8, 1957

The rates of aqueous alkaline hydrolysis of trifluoroacetanilide and a series of N-methylanilides, $ROCN(CH_3)C_6H_5$, have been determined at 25.5° spectrophotometrically. The reactions have been carried out with large excesses of hydroxide ion, and pseudo first-order kinetics are obtained. The rate law followed by trifluoroacetanilide is $k_1 = k_2(OH^-)/1 + (OH^-)K$ and by the N-methylanilides is $k_1 = k_2(OH^-) + k_3(OH^-)^2$. The observed rate equations are explained in terms of a reaction sequence involving two reactive intermediates and the reversible formation of the conjugate base of trifluoroacetanilide as an unreactive side product. The divalent anion intermediate which leads to third-order kinetics is an analog of the intermediates proposed for the aqueous alkaline cleavage of acetylacetone and for the Cannizzaro reaction. The ratio of third to second-order constants, k_3/k_2, for the N-methylanilides increases with increasing electron-withdrawal and decreasing steric requirements of the substituent, R, as shown by the correlation equation: $\log (k_3/k_2) = \sigma^*\rho^* + \delta E_s +$ const. Contribution of two types of steric effects to the rate is indicated, one of which closely parallels steric effects in ester hydrolysis rates. It is suggested that the second steric component results from an inhibition of resonance in the anilide. The second-order hydrolysis constant for trifluoro-N-methylacetanilide is twenty-five times greater than that of trifluoroacetanilide in accord with this proposal.

The kinetics of the alkaline saponification of esters has been extensively investigated, but relatively little work has been done on the kinetics of the alkaline hydrolysis of amides and anilides.

Meloche and Laidler have studied *p*-substituted benzamides[3]; Cason and co-workers, several branched-chain amides[4]; Bruylants and co-workers, straight-chain aliphatic amides.[5] The alkaline alcoholysis of phenyl-substituted acetanilides has been studied by Verkade, Wepster and co-workers.[6] Oxygen exchange in the alkaline hydrolysis of benzamide has been investigated by Bender and co-workers.[7] All of these investigators carried out the hydrolysis rates using equivalent concentrations of base and of amide, with the exception of Wepster, *et al.*, who employed an excess of base. Satisfactory fit to a rate equation first order in amide and in hydroxide ion was reported in each case. These results are analogous to the kinetics obtained for the alkaline saponification of normal esters.

The present investigation was undertaken to determine the effect of structure in the acyl component of an amide on its hydrolysis rate. It was further desired to attempt a quantitative separation of the observed effects on the free energy of activation to contributing polar, steric and resonance effects and, in turn, correlation of these effects with corresponding ones from other reactions. Taft has carried out this kind of analysis for the effects of structure on the rates of alkaline saponification of esters.[8]

While Laidler and Meloche have carried out limited work of this general nature in the aromatic series, the data available in the aliphatic series do not include nearly enough variation of structure to permit conclusions of a quantitative nature.

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[1] This work was supported in part by the Office of Naval Research, Project NR055-328. Reproduction in whole or in part is permitted for any purpose of the United States Government.

[2] (a) Taken from the Ph.D. Thesis of Sydney S. Biechler, The Pennsylvania State University, August, 1956; (b) Shell Oil Co. Fellow for 1955–1956.

[3] I. Meloche and K. J. Laidler, THIS JOURNAL, **73**, 1712 (1951).

[4] (a) J. Cason, C. Gastaldo, D. L. Glusker, J. Allinger and L. B. Ash, *J. Org. Chem.*, **18**, 1129 (1953); (b) J. Cason and H. Wolfhagen, *ibid.*, **14**, 155 (1949).

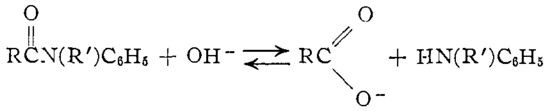
[5] (a) Mlle. De Roo and A. Bruylants, *Bull. soc. chim. Belges*, **63**, 140 (1954); (b) M. Willems and A. Bruylants, *ibid.*, **60**, 191 (1951).

[6] (a) P. E. Verkade and P. H. Witjens, *Rec. trav. chim.*, **62**, 201 (1943); (b) B. M. Wepster and P. E. Verkade, *ibid.*, **67**, 411, 425 (1948); **68**, 77, 88 (1949); **69**, 1393 (1950); (c) H. J. Biekart, H. B. Dessens, P. E. Verkade and B. M. Wepster, *ibid.*, **71**, 1245 (1952).

[7] (a) M. L. Bender and R. D. Ginger, THIS JOURNAL, **77**, 348 (1955); (b) M. L. Bender, R. D. Ginger and K. G. Kemp, *ibid.*, **76**, 3350 (1954); (c) for spectral evidence supporting the formation of intermediate II, *cf.* M. L. Bender, *ibid.*, **75**, 5986 (1953).

[8] R. W. Taft, Jr., *ibid.*, **74**, 3120 (1952); **75**, 4231 (1953); *cf.* Chapt. 13, in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956.

The work described herein is an investigation of the kinetics of the alkaline hydrolysis of substituted anilides, $RCON(R')C_6H_5$, in water or 50% (volume) dioxane-water at 25.5°. The stoichiometric reaction is shown by the equation



$$RC(=O)N(R')C_6H_5 + OH^- \rightleftharpoons RCO_2^- + HN(R')C_6H_5$$

The hydrolysis of anilides was selected for study because the reaction rates are determined conveniently by a spectrophotometric method (*cf.* Experimental). A mechanism for the reaction has been proposed, and an examination and correlation of the variation of rate with structure has been made.

Experimental

Materials.—Trifluoroacetanilide was obtained from the Caribou Chemical Co. and purified by sublimation, m.p. 84-85°.

Trifluoro-N-methylacetanilide was prepared by the method of Pachter and Kloetzel.[9] To trifluoroacetanilide, 3.5 g. in 66 ml. of dry acetone, was added 3.7 g. of powdered potassium hydroxide and 1.7 ml. of methyl iodide in 10 ml. of dry acetone. The mixture was heated under reflux for 30 minutes, after which the potassium iodide was filtered off. The solution was concentrated, water was added and the resulting oil was extracted with ether. Evaporation of the ether layer gave a yellow solid, which was recrystallized twice from ethanol-water to give a white solid, m.p. 25-26° (reported[10] 26-27°).

N-Methylformanilide was prepared by the method of Fieser and Jones.[11] Methylaniline, 6.4 g. of 85% formic acid and 20 ml. of toluene were heated at reflux and the toluene-water azeotrope was removed at 87-90° and toluene at 108-110°. The residue was distilled under vacuum. The fraction b.p. 130° (15 mm.) and $n^{25}D$ = 1.552 (reported 1.553) was used.

Difluoroacetanilide was prepared in the following manner: aniline, 5 g., a pinch of powdered potassium hydroxide and 4 g. of ethyl difluoroacetate (from Caribou Chemical Co.) were heated under reflux for two days. The flask was cooled and a solid crystallized from the solution. The solid had a melting point of 58° on recrystallization from ethanol-water (reported[12] m.p. 58°).

Difluoro-N-methylacetanilide was prepared in the same manner as trifluoro-N-methylacetanilide. The product was distilled, and the fraction boiling at 120-126° and having $n^{25}D$ 1.5020 was collected (reported[13] 1.5039).

Phenoxy-N-methylacetanilide was prepared from phenoxyacetyl chloride, 5 g., which was dissolved in 25 ml. of anhydrous ether. Methylaniline was added dropwise to the solution until reaction ceased. The methylaniline hydrochloride was filtered out and the ether solution extracted with water. The ether layer was evaporated, and white crystals were obtained upon recrystallization from ethanol-water, m.p. 92-93° (reported[14] 94°).

Chloro-N-methylacetanilide was prepared in the same manner as phenoxy-N-methylacetanilide. The product was recrystallized from ethanol-water, m.p. 68-69° (reported[14] 70°).

Betaine-N-methylanilide was prepared by heating 7.7 g. of chloro-N-methylacetanilide and 10 ml. of trimethylamine for 3 hr. in 20 ml. of absolute ethanol. The compound was obtained as a viscous liquid. The liquid was placed in a drying pistol over refluxing xylene, and an extremely hygroscopic solid was obtained. Although the sample gave satisfactory kinetics, analysis was low in carbon and nitrogen, a result reasonably attributed to the hygroscopic properties.

Anal. Calcd. for $C_{12}H_{19}N_2OCl$: C, 59.38; H, 7.83; N, 11.55. Found: C, 54.01; H, 8.16; N, 10.47.[15]

Ethyl dimethylcyanoacetate was prepared by adding 20 g. of ethyl cyanoacetate to a solution of 10 g. of sodium in 100 g. of absolute ethanol. A solution of 50 ml. of methyl iodide in 20 ml. of ethanol was added with cooling. The resulting solution was warmed and finally heated under reflux for 4 hr. The ethanol was removed by distillation, and water was added to the residue. The aqueous solution was extracted with ether and the ether extracts washed with three 10-ml. portions of 10% sodium hydroxide. The ether layer was dried over sodium sulfate and distilled. The ester was collected at b.p. 75° (15 mm.) and had $n^{25}D$ 1.4098.[16]

Dimethylcyano-N-methylacetanilide was obtained from the reaction of the acid chloride with methylaniline. The acid chloride was prepared from dimethylcyanoacetic acid (m.p. 54-55°[16,17] obtained from saponification of the ethyl ester). The acid chloride (b.p. 58°) (13 mm.)[16,17] was dissolved in ether and methylaniline was added until reaction ceased. The methylaniline hydrochloride was filtered off and the ether solution evaporated. A white solid was obtained, m.p. of 55-56°, after recrystallization from ethanol-water.

Anal. Calcd. for $C_{12}H_{14}ON_2$: C, 71.29; H, 6.93; N, 13.86. Found[18]: C, 71.20; H, 6.93.

Apparatus.—A Beckman DU spectrophotometer with jacketed cell compartment was used for the kinetic measurements; 1-cm. or 5-cm. fused silica absorption cells with ground glass stoppered tops were used. Water at 25.5 ± 0.05° was circulated through coils in the compartment by means of a circulating pump. The cover for the 5-cm. cell compartment was fitted with an additional circulation coil to provide more effective temperature control. A small thermometer placed in the cell compartment showed that the temperature remained constant at 25.5 ± 0.05°.

Kinetic Procedure.—For the trifluoroacetanilide in 50% (volume) dioxane-water, a solution 1.0×10^{-4} M of the anilide in dioxane was prepared. The reactions were carried out in 1-cm. absorption cells, by first adding 1.5 ml. of the anilide solution to the cell and then adding 1.5 ml. of a thermostated base solution of the appropriate concentration. Readings of optical density were taken at convenient intervals. The complete ultraviolet spectrum at the end of an experiment was identical with that of a known solution of aniline of the same concentration, showing a quantitative conversion of the anilide to aniline. This reaction was studied by the rate of disappearance of the anilide, at 265 mμ, the minimum on the aniline absorption curve. The anilide itself has no maximum or minimum in the region 250-300 mμ.

The experiments on the hydrolysis of trifluoroacetanilide in water were carried out in the same manner.

For the N-methylanilides, a solution of the anilide in water, usually about 1×10^{-4} M, was made up. In most cases, the compounds were relatively insoluble in water, so that a saturated solution was made, filtered and either used full strength or diluted to give a convenient reading on the spectrophotometer. The concentration was determined by the optical density produced by the methylaniline at the end of the reaction. The rates of these reactions were followed by the rate of appearance of N-methylaniline at wave lengths of 285 or 295 mμ.

For experiments that could be completed in a day, the reactions were carried to completion in the absorption cells. For slower ones, the reactions were begun in 50-ml. volumetric flasks, a sample immediately removed and placed in a cell in the instrument and the flask returned to the bath. The cell was allowed to remain in the instrument for the first day, frequent readings being taken. The solution in the cell was discarded and aliquots were removed from the flask for all subsequent points. For some of these slower runs, theoretical infinity points, based on faster runs,

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[9] I. J. Pachter and M. C. Kloetzel, THIS JOURNAL, **74**, 1321 (1952).

[10] E. J. Bourne, S. H. Henry, C. E. M. Tatlow and J. C. Tatlow, *J. Chem. Soc.*, 4014 (1952).

[11] L. F. Fieser and J. E. Jones, *Org. Syntheses*, **20**, 66 (1940).

[12] F. Swarts, *Rec. trav. chim.*, **28**, 143 (1909).

[13] D. D. Coffman, M. S. Raasch, G. W. Rigby, P. L. Barrick and W. E. Hanford, *J. Org. Chem.*, **14**, 747 (1949).

[14] C. A. Bischoff, *Ber.*, **34**, 2125 (1901).

[15] Analysis by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

[16] J. C. Hessler, THIS JOURNAL, **35**, 990 (1913); **38**, 909 (1916).

[17] G. Schroeter, C. Seidler, M. Sulzbacher and R. Kanitz, *Ber.*, **65B**, 432 (1932).

[18] Analysis by Clark Microanalytical Laboratory, Urbana, Ill.

were used. The final optical densities were consistent within 0.005 optical density unit.

In all experiments, at least a tenfold excess of base over anilide was used in order to obtain pseudo first-order kinetics.

Some difficulty was encountered with the trifluoro-N-methylacetanilide. A set of data made with a freshly prepared sample of the compound showed excellent first-order plots at all base concentrations, while some experiments repeated later showed serious curvature for experiments at low base concentrations. About four months had elapsed between these two sets of experiments. It seemed possible that the sample on standing had been partially converted to a substance that slowly consumes base. The compound was recrystallized several times in an attempt to remove any such impurity, but the same results were obtained. It is possible that the impurity was not removed by the recrystallization, but the actual cause of the curvature is unknown.

The alkaline saponification of ethyl dimethylcyanoacetate was followed by titration. Equivalent concentrations of ester and of base were used, and two runs, one at 0.01 *M* and one at 0.03 *M*, were carried out, in 86.91% (weight) ethanol-water.

Several N-methylanilides were prepared but found to be unsuitable for kinetic measurements. The rate of hydrolysis of N-methylacetanilide was too slow to measure at 25.5°. Cyano-N-methylacetanilide was found to be appreciably converted to its conjugate base in alkaline solution.

Isolation of Products.—Trifluoroacetanilide, 0.328 g., was allowed to react with 0.679 *M* sodium hydroxide, in dioxane–water, for two days. The solution was extracted with ether and the ether extracts dried over sodium sulfate. Aniline hydrochloride, 54.4% of the theoretical amount, was isolated by passing dry hydrogen chloride through the ether solution.

The aqueous layer was treated with 10 ml. of concentrated hydrochloric acid and extracted with ether. The ether was distilled at 33°, and a constant-boiling liquid, boiling at 102°, which contained ether and trifluoroacetic acid,[19] was obtained. This was titrated with 1.4935 *N* sodium hydroxide, which showed 59.6% recovery of trifluoroacetic acid.

Spectra.—At the aniline peak (~280 mμ) trifluoroacetanilide absorbs quite strongly. The rates of hydrolysis of trifluoroacetanilide were therefore followed at 265 mμ, the minimum on the aniline absorption curve, by the rate of disappearance of trifluoroacetanilide. The extinction coefficient at 265 mμ for the trifluoroacetanilide in water and aqueous hydroxide solutions is about five times that of aniline.

The N-methylanilides have no peaks in the 240 to 300 mμ region but absorb quite strongly at the low wave length region and gradually decrease so as to be very small or zero near the peak of N-methylaniline (~285 mμ). Hence most of the rates were followed at 285 mμ, by the rate of appearance of the N-methylaniline. A few of the N-methylanilides, however, do absorb slightly at this wave length, so that 295 mμ was used.

Complete spectra taken of several of the solutions at the end of the reaction corresponded to the spectrum of N-methylaniline. Beer's law was found to be obeyed within the concentration and wave length range employed.

Results

All experiments were carried out with at least a tenfold excess (generally much larger) of hydroxide ion over anilide or N-methylanilide. Under these conditions pseudo first-order kinetics are obtained.

Since the optical density is proportional to the concentration of the absorbing substance, the first order rate becomes

for absorbing reactant:

$$\ln (D_t - D_\infty) = -k_1t + \ln (D_o - D_\infty)$$

for absorbing product:

$$\ln (D_\infty - D_t) = -k_1t + \ln (D_\infty)$$

where D is optical density and k_1 is the observed pseudo first-order rate constant. The subscripts o, t and ∞ refer to zero time, time t, and time greater than ten half-times, respectively.

The precision of the first-order constants obtained from duplicate experiments is ±5% or less. The total change in optical density in most experiments was on the order of 0.5 optical density unit. The reactions were followed from 75 to 95% of complete reaction. A typical plot of log $(D_\infty - D_t)$ is shown in Fig. 1.

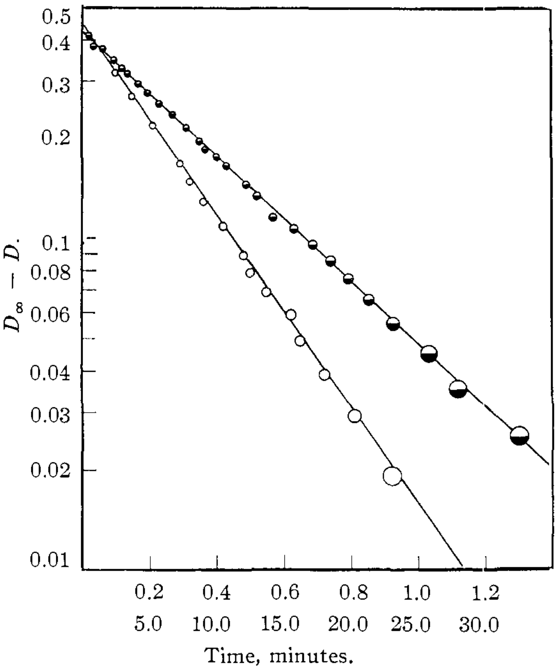

Fig. 1.—Typical alkaline hydrolysis of difluoro-N-methylacetanilide, $CHF_2CON(CH_3)C_6H_5$: ◒, 0.011 *M* NaOH; ○, 0.113 *M* NaOH.

Trifluoroacetanilide.—The observed pseudo first-order rate constants, k_1, are not directly proportional to the hydroxide ion concentration (*cf.* third column, $k_1/(OH^-)$, of Table I) but tend toward a limiting value at high hydroxide ion concentrations. The observed rate equation therefore differs from that found for the alkaline saponification of esters and amides. The experimental data fit the empirical relationship

$$1/k_1 = a + b/(OH^-) \qquad (2)$$

a and b are the intercept and slope, respectively, in a plot of $1/k_1$ *vs.* $1/(OH^-)$.

The fit of the data to this equation can be seen by a comparison of the calculated and the observed first-order rate constants shown in Table I. The mean deviation between calculated and observed constants is ±5%, which is on the order of the precision of the observed values. Within this precision no salt effect could be detected in aqueous solutions up to 0.557 *M* ionic strength. In dioxane–water (50% by volume) all experiments were carried out at a constant ionic strength of 0.500 *M*.

N-Methylanilides.—Pseudo first-order rate constants, k_1, were obtained in aqueous solutions at 25.5° and are shown in Table II.

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[19] M. Hauptschein and A. V. Grosse, THIS JOURNAL, **73**, 5139 (1951).

TABLE I

RATE CONSTANTS FOR THE ALKALINE HYDROLYSIS OF TRIFLUOROACETANILIDE AT 25.5°

In 50% (volume) aqueous dioxane and constant ionic strength (0.500 *M*)

(OH^-) concn., M_0	k_1, min.$^{-1}$ × 10^3	$k_1/(OH^-)$	k_1, calcd., eq. 2 × 10^3
0.0100	4.37	0.437	4.48
.0100	4.44	.444	4.48
.0250	8.64	.346	8.00
.0500	11.4	.228	10.8
.250	14.1	.056	15.0
.250	13.8	.055	15.0
.500	15.1	.030	15.8
.500	14.8	.030	15.8
Best values: $a = 60.0 \pm 2.0$; $b = 1.63 \pm 0.04$ (added salt Na_2SO_4)			
In water at 25.5°; no salt added except where indicated			
0.0060	1.75	3.14	1.92
.011	2.53	3.27	2.60
.011	2.38	2.14	2.60
.056	3.66	0.657	3.97
.056[a]	3.70	.664	3.97
.056	3.85	.691	3.97
.056[a]	3.99	.716	3.97
.278[a]	4.23	.152	4.42
.278	4.73	.170	4.42
.557	4.52	.081	4.48
Best values: $a = 22.0 \pm 0.5$; $b = 0.18 \pm 0.02$ (added salt Na_2SO_4)			

[a] Salt added to make ionic strength 0.557 *M*.

TABLE II

RATE CONSTANTS FOR N-METHYLANILIDES, $RCON(CH_3)C_6H_5$, IN WATER AT 25.5°

(OH^-) concn., *M*	Added salt	Ionic strength	k_1, min.$^{-1}$	$k_1/(OH^-)$	k_1 calcd.
$R = CF_3$					
0.0011	NaCl	0.011	0.189	172	0.195
.0011	NaCl	.011	.198	180	.195
.0011	None	.001	.192	175	.195
.0011	Na_2SO_4	.557	.204	185	.195
.0022	NaCl	.011	.507	230	.458
.0063	NaCl	.011	1.69	268	2.03
.0063	None	.006	1.79	284	2.03
.0111	None	.011	5.00	450	5.07
.0111	None	.011	5.16	465	5.07
.0111	Na_2SO_4	.557	5.08	458	5.07
.0111	Na_2SO_4	.557	5.05	455	5.07
$R = CHF_2$					
0.0056	None	0.006	0.042	7.50	0.042
.0056	None	.006	.043	7.68	.042
.0056	Na_2SO_4	.557	.042	7.50	.042
.0111	None	.011	.103	9.18	.098
.0111	None	.011	.109	9.82	.098
.0111	Na_2SO_4	.557	.089	8.00	.098
.0557	Na_2SO_4	.557	1.22	21.9	1.04
.0557	None	.056	1.07	19.2	1.04
.0557	None	.056	1.03	18.5	1.04
.0557	None	.056	1.08	19.4	1.04
.0860	None	.086	2.24	26.0	2.18
.0860	None	.086	2.28	26.5	2.18
.1113	None	.111	3.26	29.3	3.44
.1113	None	.111	3.01	27.0	3.44
.1113	None	.111	3.13	28.1	3.44
.1113	None	.111	3.11	27.9	3.44
.1113	Na_2SO_4	.557	3.35	30.1	3.44
.1113	Na_2SO_4	.557	3.46	31.1	3.44
.1113	Na_2SO_4	.557	3.37	30.3	3.44
$R = CH_2Cl$					
0.0557	Na_2SO_4	0.557	0.00310	0.0557	0.00326
.1113	Na_2SO_4	.557	.00710	.0638	.00726
.2236	Na_2SO_4	.557	.0172	.0769	.0174
.5570	Na_2SO_4	.557	.0638	.115	.0636
$R = CH_2\overset{+}{N}(CH_3)_3$					
0.0557	Na_2SO_4	0.557	0.000540	0.0097	0.000545
.1113	Na_2SO_4	.557	.00113	.0102	.00132
.2226	Na_2SO_4	.557	.00380	.0171	.00365
.5570	Na_2SO_4	.557	.0161	.0289	.0168
$R = C(CH_3)_2CN$					
0.0111	Na_2SO_4	0.557	0.00041	0.0370	0.00043
.0111	Na_2SO_4	.557	.00040	.0360	.00043
.0111	None	.011	.00041	.0370	.00043
.0111	None	.011	.00040	.0370	.00043
.1113	Na_2SO_4	.557	.00530	.0480	.00435
.1113	Na_2SO_4	.557	.00470	.0420	.00435
.2226	Na_2SO_4	.557	.00940	.0420	.0092
.2226	Na_2SO_4	2.597	.0115	.0520	.0120
.2226	Na_2SO_4	2.597	.0110	.0494	.0120
.5200	Na_2SO_4	2.597	.0387	.0744	.0358
.5200	Na_2SO_4	2.597	.0371	.0713	.0358
.5200	None	0.520	.0219	.0420	.0247
.5200	None	.520	.0233	.0450	.0247
.5570	None	.557	.0270	.0485	.0268
.5570	None	.557	.0282	.0506	.0268
1.298	Na_2SO_4	2.597	.143	.110	.146
1.298	Na_2SO_4	2.597	.136	.105	.146
2.597	None	2.597	.463	.178	.474
2.597	None	2.597	.468	.180	.474
$R = CH_2OC_6H_5$					
0.0557	Na_2SO_4	0.557	0.000890	0.0160	0.00114
.1113	None	.111	.00183	.0164	.00179
.1113	None	.111	.00181	.0162	.00179
.1113	Na_2SO_4	1.113	.00171	.0153	.00179
.2226	Na_2SO_4	0.557	.00370	.0166	.00383
.5570	None	0.557	.0110	.0197	.0114
$R = H$					
0.111	None	0.111	0.00211	0.0190	0.00214
.111	None	0.111	.00207	.0186	.00214
.283	Na_2SO_4	1.060	.00802	.0283	.00780
.283	None	0.283	.00797	.0283	.00780
.477	Na_2SO_4	1.060	.0171	.0358	.0176
.477	Na_2SO_4	1.060	.0177	.0371	.0176
.804	None	0.804	.0389	.0484	.0422
.804	None	0.804	.0382	.0475	.0422
1.060	None	1.060	.0730	.0689	.0688
1.060	None	1.060	.0700	.0660	.0688

The first-order rate constants were obtained over at least one power of ten in the hydroxide ion concentration for seven N-methylanilides. In each instance the first-order constants are not proportional to hydroxide ion concentration, but instead the quantity $k_1/(OH^-)$ increases markedly with increasing (OH^-)—*cf.* Table II and contrast with the behavior shown by trifluoroacetanilide. The first-order constants fit satisfactorily the rate equation

$$k_1 = k_2(OH^-) + k_3(OH^-)^2 \qquad (3)$$

dividing through by (OH^-).

$$\frac{k_1}{(OH^-)} = k_2 + k_3(OH^-)$$

A plot of $k_1/(OH^-)$ against (OH^-) gives a straight line of slope k_3 and intercept k_2. The fit of the data to equation 3 is shown in Table II by a comparison of observed and calculated values of k_1. Table III shows the values of k_2 and k_3 which give the best fit of observed values of k_1 to equation 3.

The mean deviation between calculated and observed values of k_1 is about ± 5% for each anilide studied. Within this precision the data show no indication of a measurable salt effect for ionic strengths up to 0.557 *M*. Using dimethylcyanomethyl-N-methylacetanilide, the kinetics were investigated at an ionic strength of 2.60 *M*. The third-order rate constant, k_3, is facilitated more by increasing the ionic strength from 0.577 to 2.60 *M* than is the second-order constant, k_2. The values of k_2 and k_3 obtained from experiments carried out at ionic strengths of 2.60 *M* are 0.042 l.-mole^{-1}-min.$^{-1}$ and 0.054 l.^{2}-mole^{-2}-min.$^{-1}$, respectively. These values are to be compared with k_2 = 0.037 and k_3 = 0.020 obtained at ionic strength 0.577 *M*.

TABLE III

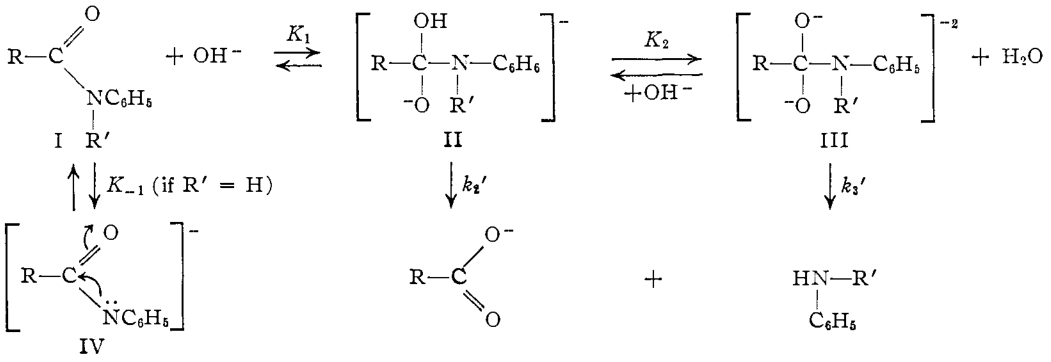
SECOND- AND THIRD-ORDER RATE CONSTANTS FOR HYDROLYSIS OF N-METHYLACETANILIDES, $RCON(CH_3)C_6H_5$, IN WATER AT 25.5°, IONIC STRENGTH 0.6 *M*

R	k_2, l.-m.$^{-1}$-min.$^{-1}$	k_3, l.^{2}-m.$^{-2}$-min.$^{-1}$	k_3/k_2
CF_3	147	2.8×10^4	190
CHF_2	6.4	2.2×10^2	34
$C(CH_3)_2CN$	0.037	0.020	0.5
$CH_2OC_6H_5$	.0150	.010	0.7
H	.0140	.048	3.4
CH_2Cl	.053	.110	2.0
$CH_2\overset{+}{N}(CH_3)_2$	.0073	.041	5.6

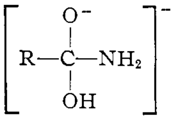
The rate of alkaline saponification of ethyl dimethylcyanoacetate in 86.91% (weight) ethanol-water at 25° has been determined in order to obtain a value of the steric substituent constant, E_s, for the dimethylcyanomethyl group. Two experiments were carried out using initial concentrations of ester and hydroxide ion of 0.030 and 0.010 *M*. Second-order rate constants of 39.8 and 37.2 l.-mole^{-1}-min.$^{-1}$ were obtained. Using the mean value, 38.5, the rate constant for ethyl acetate under these conditions[20] and a σ^* value of +1.10 (obtained by the additivity principle,[8] a steric substituent constant of −0.76) was obtained for the dimethylcyanomethyl group from the relationship $E_s \equiv \log(k/k_0) - (2.48)\,\sigma^*$.[8]

Reaction Mechanism

The following scheme satisfactorily explains the "non-classical" kinetics established in this work for the alkaline hydrolysis of trifluoroacetanilide and for the N-methylanilides



Bender[7] has obtained convincing evidence from the relative rates of oxygen isotope exchange and hydrolysis that the alkaline hydrolysis of amides, like that of esters, proceeds through an intermediate hydroxide ion addition complex



$$\left[R-\overset{O^-}{\underset{OH}{C}}-NH_2\right]^-$$

The activation energy for decomposition of the amide addition complex is apparently appreciably greater than that of the ester. It is therefore reasonable that the anilide hydrolysis should proceed through the intermediate II and it is conceivable that the reaction could also proceed *via* the intermediate III which is formed by the reaction of II with a second hydroxide ion.

If the anilide I were nearly completely converted at relatively high hydroxide ion concentration to either II or IV, with the entire hydrolysis process proceeding through step k_2', the observed pseudo first-order constants would become independent of the hydroxide ion concentration (as observed for trifluoroacetanilide). This relationship is shown in the rate equation derived below.

We strongly favor the formation of the conjugated base IV as the explanation of the kinetics observed for trifluoroacetanilide. The dianion intermediate, III, is required to explain the third-order kinetics observed with the N-methylanilides. If trifluoroacetanilide could be converted completely to II but yet involve no reaction proceeding through the dianion intermediate III, then there is no reasonable explanation for why, in contrast, the reaction with the N-methylanilides should be able to proceed (in part) through III. On the other hand, it is obvious that the conjugate base IV can be formed only with the anilide.

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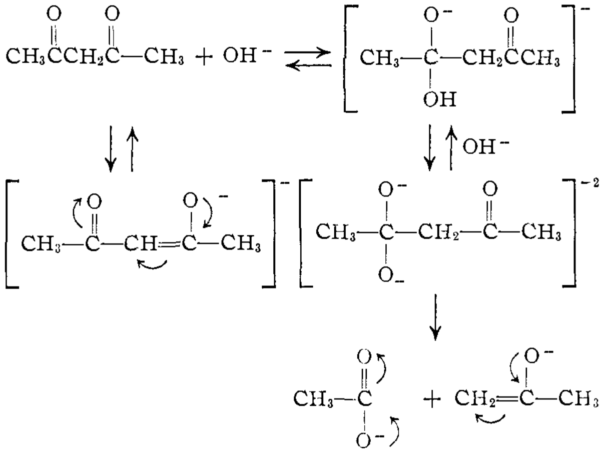
(20) H. A. Smith and H. S. Levenson, THIS JOURNAL, **61**, 1172 (1939).

The formation of the conjugate base of N-phenyl-4-bromobutanamide as a reactive intermediate in the alkaline cyclization reaction to give the pyrrolidone has been proposed.[21]

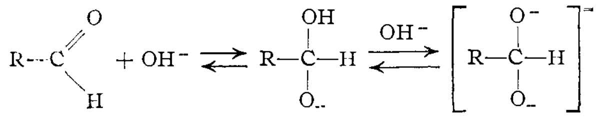
In the above scheme the conjugate base IV is formed as an unreactive side product, *i.e.*, the assumption is made that IV does not decompose directly to the reaction products. This seems likely for two reasons: (1) In amide hydrolysis where the hydrogen on nitrogen is not generally acidic enough to make equilibrium K_{-1} important, and in the N-methylanilide hydrolysis where this step is excluded, hydrolysis takes place readily (for example, k_2 values for trifluoroacetanilide and trifluoro-N-methylacetanilide are 5.56 and 140 l.-mole^{-1}-min.$^{-1}$, respectively). Thus the formation of IV is not necessary for hydrolysis; and (2) Resonance in the anion IV is expected to increase the double bond character of the C–N bond compared to that in the anilide and thereby stabilize IV against cleavage.

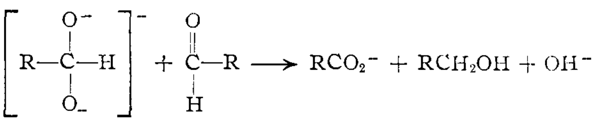
Our argument follows that used by Pearson and Mayerle to explain the kinetics of the alkaline cleavage of acetylacetone.[22] Pearson and Mayerle propose that the β-diketone but not its conjugate base, enolate ion, is the reactive species leading to cleavage products.

There is an additional parallel with the work of Pearson and Mayerle. The rate equation for the hydrolysis of the β-diketone is first order in acetylacetone and second order in hydroxide ion. A dianion intermediate similar to III was proposed to account for the observed rate equation.



A further analogy is provided by the Cannizzaro reaction. Under certain conditions, this reaction has been found to be second order in aldehyde and second order in hydroxide ion. Hammett has suggested the mechanism[23]

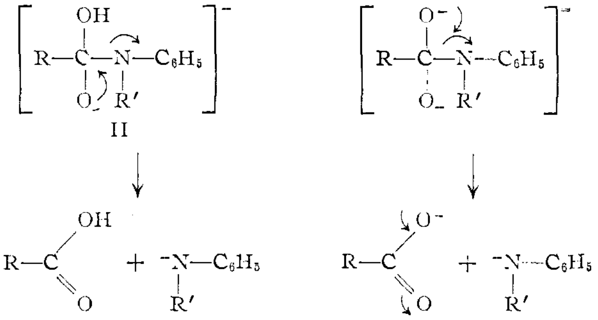




In terms of the proposed scheme, the rate equation 2 established for the hydrolysis of trifluoroacetanilide is explained by the formation of IV which lowers sufficiently (compared to the N-methylanilide case) the concentrations of the intermediates II and III so that at the accessible hydroxide ion concentrations the reaction proceeding through III is of no practical importance.

When the side equilibrium, K_{-1}, does not compete (as in N-methylanilide hydrolysis), the concentrations of intermediates II and III may be sufficient to allow a measurable amount of the hydrolysis reaction to proceed through both intermediates. In order for III, which must be at smaller concentrations, to compete favorably with II, its rate of decomposition must be favored.

A factor which may contribute to the required relationship is suggested by proposing that the following are the immediate products of cleavage of II and III



The extra resonance stabilization of the carboxylate ion compared to the carboxylic acid may act to lower the activation energy for the decomposition of III relative to II. It is further shown in subsequent discussion that inductive electron-withdrawal by the acyl group, R, increases the ratio of rate constants, k_3/k_2.

The following rate equations are derived on the basis of the proposed reaction scheme:

For trifluoroacetanilide hydrolysis:

let a = initial stoichiometric concentration of anilide
(OH^-) = hydroxide ion concentration $(OH^- \gg a)$
x = fraction of anilide hydrolyzed at time, t
(I) = concentration of species I at time, t
(IV) = concentration of species IV at time, t

then

$$a - x = (I) + (IV)$$

and

$$K_{-1} = \frac{(IV)}{(OH^-)(I)}$$

so that

$$(I) = \frac{a - x}{1 + K_{-1}(OH^-)}$$

assuming that hydrolysis takes place through step k_2'

$$\frac{-d(I)}{dt} = k_2(OH^-)(I) = \frac{(k_2)(OH^-)(a - x)}{[1 + (K_{-1})(OH^-)]}$$

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[21] H. W. Heine, P. Love and J. L. Bove, THIS JOURNAL, **77**, 5420 (1955).

[22] R. G. Pearson and E. A. Mayerle, *ibid.*, **73**, 926 (1951); *cf.* also R. G. Pearson, D. H. Anderson and L. L. Alt, *ibid.*, **77**, 527 (1955).

[23] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 350.

TABLE IV

FAILURE OF EQUATION (5) TO CORRELATE THE EFFECTS OF STRUCTURE ON THE SECOND- AND THIRD-ORDER RATES OF ALKALINE HYDROLYSIS OF N-METHYLANILIDES, $RCON(CH_3)C_6H_5$

	"Adjusted" substituent constants		Second-order rates			Third-order rates		
Substituent, R	σ^*	Es	$\rho_2^* = +2.633$ log $(k/k_0)_2$ calcd. eq. 5	$\delta_2 = +1.233$ log $(k/k_0)_2$ exptl.	d	$\rho_3^* = +4\text{-}265$ log $(k/k_0)_3$ calcd. eq. 5	$\delta_3 = +2.020$ log $(k/k_0)_1$ exptl.	d
CF_3	+2.31[a]	−2.40	+3.78	+4.02	−0.24	+5.59	+5.77	−0.18
CHF_2	+1.56	−1.90	+2.41	+2.66	− .25	+3.40	+3.66	−0.26
$CH_2N^+(CH_3)_3$	+1.41	−2.8[c]	+0.91	−0.29	+1.20	+0.94	−0.07	+1.01
$C(CH_3)_2CN$	+0.61[b]	−2.00[d]	− .22	+ .42	−0.64	−0.85	− .38	−0.47
CH_2Cl	+ .56	−1.48	+ .28	+ .58	− .30	−0.01	+ .36	− .37
$CH_2OC_6H_5$	+ .360	−1.57	− .35	+ .03	− .38	−1.04	− .68	− .36
H	.000	0.00	+ .62	(.00)	+ .62	+0.59	.00	+ .59
				Av.	±0.54		Av.	±0.46

[a] Estimated as 5% greater than σ^* for CCl_3. The σ^* value for CH_2F and CHF_2 is in each case 5% larger than that for CH_2Cl and $CHCl_2$, respectively (reference 8). [b] Estimated from σ^* values for $CNCH_2$ and C_2H_5 on the basis of the additivity principle (reference 8). [c] Estimated as E_s for the $(CH_3)_3C$ group. The E_s value for the $(C_2H_5)_3N^+CH_2$ group (obtained from the data of R. P. Bell and E. J. Lindars, *J. Chem. Soc.*, 4601 (1954)) is closely similar to that for the $(C_2H_5)_3C-$ group. [d] Obtained in present paper.

rearranging and integrating, we have

$$\ln\left(\frac{a}{a-x}\right) = \left(\frac{k_2(OH^-)}{1+(OH^-)(K_{-1})}\right) t = k_1 t$$

Hence the pseudo first-order constant, k_1, is given by

$$k_1 = \frac{k_2(OH^-)}{1+(K_{-1})(OH^-)}$$

or

$$1/k_1 = \frac{1}{k_2(OH^-)} + K_{-1}/k_2$$

This equation is of the form of the observed rate equation 2, $1/k_1 = a + b/(OH^-)$, for which $a = K_{-1}/k_2$ and $b = 1/k_2$. From the values of a and b given in Table I, the following values of k_2 and K_{-1} are obtained

	K_{-1}	k_2, l.-mole^{-1}-min.$^{-1}$
For water, 25.5° μ = 0.006 to 0.577 *M*	122	5.56
For 50% (vol.) dioxane-water 25°, μ = 0.500 *M*	37.2	0.62

From the value of K_{-1} in water one obtains for the pK_a of trifluoroacetanilide at 25° the value 11.9.

For N-methylacetanilide hydrolysis

$$dx/dt = k_2(OH^-)(a-x) + k_3(OH^-)^2(a-x)$$

rearranging and integrating, we have

$$\ln\left(\frac{a}{a-x}\right) = [k_2(OH^-) + k_3(OH^-)^2] \quad t = k_1 t$$

Hence the pseudo first-order constant, k_1, is given by $k_1 = k_2(OH^-) + k_3(OH^-)^2$, which is the rate equation 3.

The observed kinetic rate equation is consistent with, but does not distinguish between, either the formation of the intermediate III or its decomposition as the rate-determining step of the third-order process. The effect of structure on hydrolysis rates provides evidence bearing on this point and further consideration is given in the discussion of the following section.

The Effect of Structure on Reactivity

Pavelich and Taft have correlated with relatively good precision the effects of unconjugated (α,β-saturated) substituents R on the methoxide ion-catalyzed methanolysis of *l*-menthyl esters, $RCO_2C_{10}H_{19}$ in methanol at 30° by the equation[24]

$$\log (k/k_0) = \sigma^*\rho^* + \delta E_s \qquad (5)$$

The symbols σ^* and E_s refer to polar and steric substituents constants, respectively, obtained by Taft from ester hydrolysis rates[8]; $\rho^* = 2.702 \pm 0.067$ and $\delta = 1.301 \pm 0.055$ are reaction constants which measure the susceptibility of the reaction series to polar and steric requirements of the substituent. The relative rate, k/k_0, is that for any ester $RCO_2C_{10}H_{19}$ compared to the acetate ester $CH_3CO_2C_{10}H_{19}$. The correlation covers a range of six powers of ten in the rate with the probable error of a single point of 0.10 log unit.

Equation 5 attributes the effect of structure on the free energy of activation to the sum of independent polar and steric effects, which in turn follow linear polar and steric energy relationships. Although the general applicability of the linear polar energy relationship appears to be well established, the scope of the linear steric energy relationship remains in question.[8]

The effects of structure on the rates of alkaline hydrolysis of N-methylacetanilides, $RCO_2N(CH_3)$-C_6H_5, have been determined in the interest of testing the applicability of the linear steric energy relationship (in the form of equation 5). To make the test rigorous, we have used a series of substituents for which the polar and steric requirements are quite different functions of structure.

The best fit of log (k/k_0) values to equation 5 has been determined by least squares methods[24] for both the second- and third-order hydrolysis rates. Since the rate of hydrolysis of N-methylacetanilide proved to be too slow to measure at 25°, this substance cannot be used according to the usual convention as the standard of comparison (as defined by Taft, $\sigma^* = 0.000$ and $E_s = 0.000$ for $R = R_0 = CH_3$). Accordingly, the N-methylformanilide has been used as the standard of comparison, and the substituent constants, σ^* and E_s, have been adjusted to a scale with H as the standard of comparison.

Table IV lists values of the adjusted σ^* and E_s values, and log (k/k_0) values calculated from these parameters by equation 5 using the indicated values

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[24] W. A. Pavelich and R. W. Taft, Jr., THIS JOURNAL, **79**, 4935 (1957).

of ρ^* and δ which give best fit to the experimental data. *It is apparent that the correlation* of the observed effects of structure on both the second- and third-order hydrolysis rates *is far from satisfactory.* In view of the generality of the linear polar energy relationship (*i.e.*, the generality of the correlation of polar effects by corresponding σ^* values),[8] the failure of the steric effects in the anilide hydrolysis to parallel those of ester hydrolysis (*i.e.*, failure of the linear steric energy relationship) is implied.

The correlation of the structural effects on the anilide hydrolysis rates by linear free energy relationships is equally unsuccessful. The logarithms of either the second- or third-order rate constants plotted *vs.* the logarithm of (1) the ionization constants of corresponding carboxylic acids or (2) the rate constants for alkaline saponification of corresponding esters in each instance give plots with widely scattered points. A similar plot for the third-order *vs.* the second-order N-methylanilide hydrolysis rate constants, although showing a trend toward correlation, is not of satisfactory precision to be regarded as a useful linear free energy relationship.

Since the second- and third-order hydrolysis rate constants are based on a common ground state and the transition state for the latter has an additional negative charge compared to that of the former, correlation of the logarithm of the ratio of rate constants, k_3/k_2, with the polar substituent constant, σ^*, is suggested. Although there is a distinct trend toward increasing values of the ratio k_3/k_2 as the σ^* value of the substituent increases (becomes more electron-withdrawing), the correlation is likewise not of good precision.

The values of log (k_3/k_2) are correlated with reasonable precision by equation 5 in the form

$$\log (k_3/k_2) = (+1.575)\sigma^* + (+0.713)(E_s) + 0.43 \quad (6)$$

The correlation covers a range of 2.6 powers of ten in the ratio k_3/k_2, with the probable error of a single point of 0.09 log unit. The fit of the data to equation 6 is illustrated in Table V.

TABLE V

CORRELATION OF THE RATIO k_3/k_2, THIRD-ORDER TO SECOND-ORDER CONSTANT BY EQUATION 6

R	log $(k_3/k)_{3/2}$calcd.	log (k_3/k_2)exptl.
CF_3	+2.36	+2.28
CHF_2	+1.54	+1.53
CH_2Cl	+0.25	+0.30
H	+ .43	+ .53
$CH_2OC_6H_5$	− .12	− .15
$C(CH_3)_2CN$	− .04	− .30
$CH_2N(CH_3)_3^+$	+ .67	+ .75

$\rho = +1.575$; $\delta = +0.713$

This correlation appears to be quantitatively significant (it is certainly so qualitatively), but there is a small probability of a coincidental fit of the data to equation 6. Although there is definitely not a direct quantitative relationship between the σ^* and E_s values, the σ^* values for all the substituents studied are positive and all of the E_s values are negative (*cf.* Table IV). Coincidental fits to equation 5 or 6 can be eliminated with certainty only when the correlation covers a relatively large number of substituents within which the σ^* and E_s values run in both the same and in opposite directions. We have been unable to find a series of substituents which completely fulfills this requirement and for which the second- and third-order N-methylanilide hydrolysis rates can be measured at 25°.

Since both of the reaction constants of equation 6 are positive, it follows that $\rho^*_3 > \rho^*_2$ and $\delta_3 > \delta_2$, that is, the third-order rate constant is more susceptible to the polar and to the steric requirements of the substituents than is the second-order constant. The k_3/k_2 ratio increases with increasing electron-withdrawing power and with decreasing steric requirements of the substituent. For the substituents studied, the polar effect is generally the predominant one.

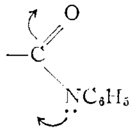
The greater susceptibility of the third-order constant than the second-order constant to electron withdrawal is correlated with the additional negative charge in the transition state. A greater decrease in the electron demand at the reaction center between the reactant and the transition states is accordingly expected for the k_3 than the k_2 process.

The greater susceptibility to steric requirements bears on the question of the rate-determining step of the third-order hydrolysis. If the decomposition of the dianion III is rate-determining, then the transition states of the third- and second-order processes differ only by the presence in the latter of an added proton. This proton is not expected to produce measurable steric effects. Steric effects could conceivably arise from the greater solvation of the divalent anion transition state which would result in a greater crowding at the reaction center.

If the rate-determining step is a proton transfer from intermediate II to hydroxide ion, the transition state would contain a highly solvated hydroxide group which would be expected to make the steric crowding in the transition state greater than that for the second-order hydrolysis. This second interpretation seems to us to be the more reasonable and is in accord with the mechanism of acetylacetone cleavage.[22]

The fact that the rate constants k_2 or k_3 are not, but the ratio k_3/k_2 is correlated by equation 5 indicates that there is a factor (probably a steric effect) present in the rate constants which cancels in the ratio of these constants. The steric effects which remain in the ratio k_3/k_2 are quantitatively related to those of ester hydrolysis, *i.e.*, are given by δE_s. However, the additional steric effects present in either k_3 or k_2 are not directly related to the steric substituent constants, E_s.

We tentatively suggest that the "additional" steric effect in N-methylanilide hydrolysis results from steric inhibition to resonance within the anilide function



an inhibition which is increased by steric interaction between the substituent of the acyl component and the N-methyl group. The rate of hydrolysis is expected to increase with increasing steric inhibition of resonance in the reactant state. Since the reactant state is common to both k_2 and k_3 and the resonance interaction with the carbonyl group may be expected to be lost in both "saturated" transition states, this steric effect should cancel in the k_3/k_2 ratio.

The proposed steric inhibition of resonance in the anilide is consistent with the fact that the second-order hydrolysis constant for trifluoro-N-methylacetanilide is twenty-five times greater than that for trifluoroacetanilide. The greater rate constant for the N-methylanilide cannot be attributed to the greater electron-releasing power of the methyl group or to "ordinary" steric hindrance to addition to the carbonyl reaction center. These factors are both expected to decrease instead of increase the rate.

It is of interest to consider the predictions of equation 6 with respect to the N-methylanilides of alkanecarboxylic acids. Considering as an example N-methylacetanilide, the adjusted σ^* and E_s values for the methyl group (-0.490 and -1.24, respectively) substituted in equation 6 give $k_3/k_2 = 0.06$. Thus at 1 M hydroxide concentration, while about 77% of the hydrolysis of N-methylformanilide occurs by the third-order process, it is predicted that only 5% of the N-methylacetanilide hydrolysis would be third-order. In 0.1 M NaOH, the figure expected for third-order hydrolysis of N-methylacetanilide is less than 1%. Since much of the previous work on the alkaline hydrolysis of anilides and amides has involved the derivatives of alkanecarboxylic acids, equation 6 suggests an explanation for the apparent inconsistency between the rate equations established in the present work and the "classical" second-order kinetics reported in the previous studies.

UNIVERSITY PARK, PENNA.

[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

The Evaluation of Inductive and Steric Effects on Reactivity. The Methoxide Ion-catalyzed Rates of Methanolysis of *l*-Menthyl Esters in Methanol[1]

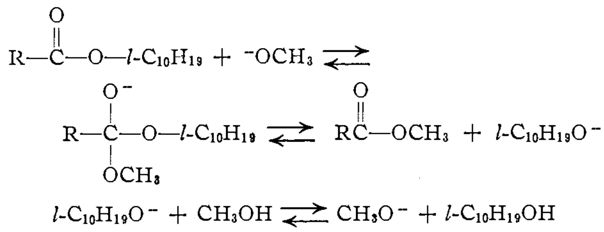
BY WILLIAM A. PAVELICH AND ROBERT W. TAFT, JR.

RECEIVED APRIL 8, 1957

The sodium methoxide-catalyzed rates of methanolysis of a series of *l*-menthyl esters of the general formula $RCO_2C_{10}H_{19}$ have been determined polarimetrically in methanol at 30°. The results indicate that the reaction takes place by the normal $B_{Ac}2$ mechanism. The substituents R have been varied over a wide range of polar and steric requirements leading to a spread of reactivities of six powers of ten. The effects of unconjugated (α,β-saturated) substituents on the rate are correlated with acceptable precision by equation 1: $\log(k/k_0) = \sigma^*\rho^* + \delta E_s$. Evidence is thus provided that the effects of structure on the free energy of activation may be separated to the sum of independent polar and steric effects. The enthalpies and entropies of activation obtained for the formate, acetate, dichloroacetate and benzoate esters are discussed.

The present investigation has been carried out to provide further information on the mechanism and the effect of structure on the rates of base-catalyzed ester interchange. Despite the similarity in reactions, the kinetic evidence pertinent to ester interchange is far less extensive than that for the saponification of esters.

The sodium methoxide-catalyzed methanolysis of *o*-, *m*- and *p*-substituted *l*-menthyl benzoates in methanol has been shown to proceed by a mechanism analogous to that for normal ($B_{Ac}2$)[2] alkaline saponification[3]



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-O-l\text{-}C_{10}H_{19} + {}^{-}OCH_3 \rightleftarrows$$

$$R-\underset{\underset{\displaystyle OCH_3}{|}}{\overset{\overset{\displaystyle O^-}{|}}{C}}-O-l\text{-}C_{10}H_{19} \rightleftarrows R\overset{\overset{\displaystyle O}{\|}}{C}-OCH_3 + l\text{-}C_{10}H_{19}O^-$$

$$l\text{-}C_{10}H_{19}O^- + CH_3OH \rightleftarrows CH_3O^- + l\text{-}C_{10}H_{19}OH$$

The reaction rates for *m*- and *p*-substituted benzoates follow the Hammett linear free energy relationship, $\log(k/k_0) = \sigma\rho$, with a reaction constant, ρ, essentially equal to that for the saponification of corresponding ethyl benzoates. The reaction rates for *o*-substituted benzoates show classical steric hindrance effects.

The rates of acid-catalyzed methanolysis, *n*-propanolysis and isopropanolysis of six β-naphthyl esters of alkane carboxylic acids parallel corresponding ester hydrolysis and carboxylic acid esterification rates.[4] The retarding effect of α,β-unsaturated substituents in the acyl component on the rates of acid-catalyzed methanolysis of *l*-menthyl esters has been investigated.[5]

A study of the effect of structure on the position of equilibrium in the ester interchange reaction has shown only relatively minor effects, in contrast to the large effects found (in the present study, for example) in the reaction rates.[6]

In the present investigation the kinetics of the sodium methoxide ion-catalyzed methanolysis of twelve *l*-menthyl esters of the general formula, $RCO_2C_{10}H_{19}$ have been determined polarimetrically at 30.0°. The effect of structure of the group R on the reaction rates, which was of special interest,

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[2] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 754.

[3] R. W. Taft, Jr., M. S. Newman and F. H. Verhoek, THIS JOURNAL, **72**, 4511 (1950).

[4] M. Harfenist and R. Baltzly, *ibid.*, **69**, 362 (1947).

[5] B. Dasannacharya, *ibid.*, **46**, 1627 (1924).

[6] P. R. Fehlandt and H. Adkins, *ibid.*, **57**, 193 (1935).