Anal. Calcd. for $C_8H_{11}NO_3$: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.81; H, 6.36; N, 8.35.

Mixture of *cis*- and *trans*-Methyl α-Cyano-β-methoxy-β-isopropylacrylate (VIa, VIb).—To a solution of 5.9 g. of methyl isobutyrylcyanoacetate [b.p. 137–139° (48 mm.), 119–120° (18 mm.), m.p. 36–37°; lit.[23] b.p. 139° (48 mm.), m.p. 36–37°] in 10 ml. of dry ether was added to −10° an ethereal solution of diazomethane (prepared from 15 g. of *p*-tolylsulfonylmethylnitrosamide) and the mixture was allowed to stand in an icebox overnight. Then, the mixture was subjected to fractional distillation under reduced pressure. The fraction boiling at 136–138° (20 mm.) was collected; it gave a wet mass on cooling; yield, 5.1 g. (80%).

Repeated crystallization of the product from methanol afforded a product as colorless plates melting at 71–72°, which has been the stable isomer VIa of the pair. The labile isomer was not isolated.

Anal. Calcd. for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 59.06; H, 7.13; N, 7.52.

Mixture of *cis*- and *trans*-Ethyl α-Cyano-β-methoxy-β-isopropylacrylate (VIIa, VIIb).—This mixture was prepared in 63% yield by reaction of diazomethane with ethyl isobutyrylcyanoacetate [b.p. 123–125° (20 mm.), lit.[24] b.p. 135–137° (20 mm.)]. The fraction boiling at 138–140° (20 mm.) was collected and no attempt to isolate the pure isomers was made.

Anal. Calcd. for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.73; H, 7.38; N, 7.30.

Mixture of *cis*- and *trans*-α-Cyano-β-methoxy-β-*t*-butylacrylate (VIIIa, VIIIb).—A mixture of 8.0 g. of pivaloylchloride, 6.6 g. of methyl cyanoacetate, and 9.2 g. of anhydrous potassium carbonate in 30 ml. of benzene was refluxed for 3 hr. After cooling, the mixture was dissolved in water, acidified with 15% hydrochloric acid, and then extracted twice with benzene. The combined extracts were dried with sodium sulfate and evaporated to remove benzene. The residue was distilled under reduced pressure giving methyl pivaloylcyanoacetate; yield, 3.0 g. (20.4%); b.p. 119–122° (20 mm.); m.p. 28–30°.

Anal. Calcd. for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 59.00; H, 7.12; N, 7.54.

To a solution of 10 g. of methyl pivaloylcyanoacetate in 5 ml. of methanol was slowly added at −5° an ethereal solution of diazomethane prepared from 22 g. of *p*-tolylsulfonylmethylnitrosamide, and the mixture was allowed to stand overnight at room temperature. After the solvent was removed, the residue was distilled under reduced pressure to give 8.0 g. of the product, b.p. 129–134° (10 mm.). The product was further purified by shaking with 40 ml. of a solution saturated with cupric acetate to remove unaltered methyl pivaloylcyanoacetate and extracting with benzene. The benzene layer was dried over sodium sulfate. The benzene was distilled *in vacuo*, and the distillation was continued to give 5.0 g. (46.5%) of methyl α-cyano-β-methoxy-β-*t*-butylacrylate, b.p. 134–135° (10 mm.).

Anal. Calcd. for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.97; H, 7.50; N, 7.15.

Isomerization of Ethyl α-Cyano-β-acetoxy-β-methylacrylate (IV).—Isomerization of the ester was induced by a trace amount of sodium methoxide. The sample was allowed to stand at room temperature through a week, and then was distilled under vacuum.

Acknowledgment.—The authors are much indebted to Mr. Shoichi Hayashi of this Institute for running many of the n.m.r. spectra and to Miss Ritsu Suzuki of St. Paul's University for the dipole moment measurements. Thanks are also due to Dr. Yuzo Kakiuti, Professor of St. Paul's University, for helpful discussions.

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(24) A. F. Campbell and J. F. Thorpe, *J. Chem. Soc.*, **97**, 1311 (1910).

Mechanism of Hydrolysis of Ethyl Benzimidates in Acidic Solutions

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The effects of aryl substituents and temperature on the kinetics of acid hydrolysis of a series of *m*- and *p*-substituted ethyl benzimidates and the deuterium oxide solvent isotope effect on the hydrolysis of one of them were studied. The data obtained and data from the literature suggest that acid hydrolysis of ethyl benzimidates involves rate-determining general base catalyzed dissociation of a tetrahedral hydrated conjugate acid into an ethyl benzoate and ammonium ion.

Hydrolysis of conjugate acids of the simple imidic esters was first studied by Pinner, who found that ammonium ion and a carboxylate ester are the initial reaction products.[1] He observed that hydrolysis of

$$RC(=NH_2)OR'^+ + H_2O \longrightarrow RCO_2R' + NH_4^+$$

low molecular weight aliphatic imidic ester hydrochlorides is rapid, while hydrolysis of benzimidic and higher aliphatic imidic ester hydrochlorides is considerably slower.

The kinetics and mechanisms of imidic ester hydrolyses have received little attention. The only kinetic studies thus far have involved ethyl benzimidates. Stieglitz and co-workers, in the course of their early study of the mechanism of acid catalysis, investigated the hydrolysis of the hydrochlorides of ethyl benzimidate and ethyl *m*-nitrobenzimidate.[2] Stieglitz demonstrated that the catalytic effect of hydrogen ion on benzimidate hydrolysis is due to formation of the conjugate acid of the ester, and that addition of acid to a solution of the ester hydrochloride actually slows the hydrolysis reaction. This was confirmed by Edward and Meacock, who found that the rate of hydrolysis of methyl benzimidate decreases sharply as the hydrochloric acid concentration of the reaction solution increases above 0.1 *N*.[3] More recently, Hand and Jencks found that hydrolysis of ethyl benzimidate is general acid catalyzed in acetate buffers.[4]

In order to gain additional information pertinent to the mechanism of benzimidic ester hydrolysis, we studied the effects of aryl substituents and temperature on the kinetics of acid hydrolysis of a series of *m*- and *p*-substituted ethyl benzimidates, and the deuterium oxide solvent isotope effect on the hydrolysis of one of them.

Experimental

Preparation of Ethyl Benzimidates.—The imidic ester hydrochlorides were prepared from the corresponding nitriles by the

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(1) A. Pinner, "Die Imidoather und Ihre Derivative," Robert Opheim, Berlin, 1892.

(2) J. Stieglitz, *Am. Chem. J.*, **39**, 29, 166 (1908); I. H. Derby, *ibid.*, **39**, 586 (1908); H. I. Schlesinger, *ibid.*, **39**, 719 (1908); J. Stieglitz, *J. Am. Chem. Soc.*, **32**, 221 (1910).

(3) J. T. Edward and S. C. R. Meacock, *J. Chem. Soc.*, 2009 (1957).

(4) E. S. Hand and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 3595 (1962).

method of Pinner.[1] Benzonitrile, *p*-chlorobenzonitrile, *p*-anisonitrile, *p*-nitrobenzonitrile, and *m*-nitrobenzonitrile from Eastman Kodak Co., *m*-chlorobenzonitrile from Aldrich Chemical Co., and *m*- and *p*-tolunitrile from Matheson Coleman and Bell were used. Pinner specified that the stoichiometric amounts of dry hydrogen chloride and ethanol be used, and recommended that the reaction mixture (absolute ethanol, nitrile, and hydrogen chloride) be kept cold until the reaction is complete. We found that satisfactory yields are also obtained if a solution of the nitrile in a 2–3-fold excess of ethanol (plus ether or dioxane if the nitrile is insufficiently soluble in ethanol) is saturated with anhydrous hydrogen chloride and allowed to stand at room temperature until crystallization of the ethyl benzimidate is complete. Observed decomposition temperatures and values from the literature follow: ethyl benzimidate hydrochloride, obsd. 125.5–126.5°, lit. 128–129°,[5] 121–22°[4]; ethyl *m*-chlorobenzimidate hydrochloride, obsd. 123–126° (new compound); ethyl *p*-anisimidate hydrochloride, obsd. 133–134°, lit. 130°[6]; ethyl *m*-toluimidate hydrochloride, obsd. 125–126° (new compound); ethyl *p*-toluimidate hydrochloride, obsd. 126–129°, lit. 130–131°[7]; ethyl *m*-nitrobenzimidate hydrochloride, obsd. 135–136°, lit. 140°[4]; ethyl *p*-nitrobenzimidate hydrochloride, obsd. 206–207°, lit. 192–194°.[8]

The imidic esters were obtained from the hydrochlorides by extracting an ether suspension of the hydrochloride with aqueous alkali. The ether layer was separated, washed with water, dried, and fractionally distilled at reduced pressure. With the exception of ethyl *p*-nitrobenzimidate, all of the esters are liquids at room temperature. Observed properties of the esters, together with elementary analyses of new compounds, are listed below.[9]

Ethyl benzimidate had b.p. 107.5–109 (16.5 mm.); n^{25}_{D} 1.5252; infrared peaks at 3300 (N–H) and 1640 cm.$^{-1}$ (C=N) (0.025 mm., neat); and an ultraviolet spectrum (in 0.06 *N* HCl), $\lambda_{\min}$ 215 mμ and $\lambda_{\max}$ 243 mμ (ϵ 12,900).

Ethyl *m*-chlorobenzimidate had b.p. 109–110.5 (5.5 mm.); n^{25}_{D} 1.5400; d^{25}_{4} 1.161; peaks at 3305 and 1637 cm.$^{-1}$; and (in 0.06 *N* HCl) $\lambda_{\min}$ 224 mμ and $\lambda_{\max}$ 243 mμ (ϵ 13,400).

Anal. Calcd. for $C_9H_{10}ClNO$: C, 58.84; H, 5.44. Found: C, 58.56; H, 5.46.

Ethyl *p*-chlorobenzimidate had b.p. 107.5–108° (4.5 mm.); n^{25}_{D} 1.5444; d^{25}_{4} 1.157; peaks at 3300 and 1635 cm.$^{-1}$; and (in 0.06 *N* HCl) $\lambda_{\min}$ 222 mμ and $\lambda_{\max}$ 254 mμ (ϵ 17,300).

Anal. Calcd. for $C_9H_{10}ClNO$; C, 58.84; H, 5.44. Found: C, 58.80; H, 5.47.

Ethyl *p*-anisimidate had b.p. 108.5–109.5 (0.8 mm.); n^{25}_{D} 1.5410; d^{25}_{4} 1.005; peaks at 3340 and 1625 cm.$^{-1}$; and (in 0.06 *N* HCl) $\lambda_{\min}$ 234 mμ and $\lambda_{\max}$ 281 mμ (ϵ 16,000).

Ethyl *m*-toluimidate had b.p. 97.5–98° (4.5 mm.); n^{25}_{D} 1.5234; d^{25}_{4} 1.007; peaks at 3340 and 1625 cm.$^{-1}$; and (in 0.06 *N* HCl) $\lambda_{\min}$ 221 mμ and $\lambda_{\max}$ 248 mμ (ϵ 12,200).

Anal. Calcd. for $C_{10}H_{13}NO$: C, 73.53; H, 7.97. Found: C, 72.94; H, 8.01.

Ethyl *p*-toluimidate had b.p. 115–117 (11.5 mm.); n^{25}_{D} 1.5253; d^{25}_{4} 1.082; peaks at 3340 and 1632 cm.$^{-1}$; and (in 0.06 *N* HCl) $\lambda_{\min}$ 221 mμ and $\lambda_{\max}$ 255 mμ (ϵ 14,000).

Ethyl *m*-nitrobenzimidate had b.p. 102–105° (0.2 mm.); n^{25}_{D} 1.5562; d^{25}_{4} 1.224; and (in 0.06 *N* HCl) $\lambda_{\max}$ 226 (ϵ 19,000).

Anal. Calcd. for $C_9H_{10}N_2O_3$: C, 55.61; H, 5.15. Found: C, 55.00; H, 5.24.

Ethyl *p*-nitrobenzimidate had m.p. 75–77° (lit.[8] m.p. 76–77°); and (in 0.06 *N* HCl) $\lambda_{\min}$ 226 mμ and $\lambda_{\max}$ 262 mμ (ϵ 13,800).

Kinetic Measurements.—Hydrolysis rates were determined spectrophotometrically at three temperatures using a Cary Model 14 recording spectrophotometer with a thermostatted cell compartment. Milligram amounts of the imidic ester were added to 0.120 *N* hydrochloric acid in a quartz cell at reaction temperature. The cell was shaken vigorously, returned to the cell compartment, and allowed to come to thermal equilibrium with the cell holder. Change in absorption at an appropriate wave length was recorded as a function of time for at least two half-lives.

TABLE I

RATE CONSTANTS FOR HYDROLYSIS OF X-$C_6H_4C(=NH)OC_2H_5$ IN 0.120 *N* HYDROCHLORIC ACID

	$10^4 k_{\Psi}$, sec.$^{-1}$		
X	30.0°	45.0°	60.0°
p-CH_3O	0.230 ± 0.007[a]	0.991 ± 0.02	4.74 ± 0.10
p-CH_3	0.444 ± 0.013	2.12 ± 0.01	7.17 ± 0.25
m-CH_3	0.777 ± 0.039	3.23 ± 0.07	13.2 ± 0.15
H	0.868 ± 0.007	3.94 ± 0.03	15.7 ± 0.2
p-Cl	1.34 ± 0.01	6.32 ± 0.08	23.7 ± 0.5
m-Cl	2.80 ± 0.07	12.5 ± 0.4	43.4 ± 0.8
m-NO_2	6.94 ± 0.05	26.8 ± 0.3	120 ± 3
p-NO_2	8.82 ± 0.30	33.5 ± 0.3	143 ± 1

[a] Errors are expressed as deviations from the mean.

First-order rate constants were determined graphically from linear plots of log (A − A_∞) or log (A_∞ − A) *vs.* time in seconds. Rate constants reported in Table I are averages of two or three determinations with average deviations usually less than 3%. Temperature control was to within ±0.05°. Good Hammett $\rho\sigma$-plots were obtained for the data at each of the three temperatures[10] (Table II).

TABLE II

LEAST-SQUARES CALCULATION OF HAMMETT ρ-VALUES FOR ETHYL BENZIMIDATE HYDROLYSIS[a]

	Temp. of hydrolysis		
	30°	45°	60°
ρ	1.40	1.34	1.35
Standard deviation	0.082	0.091	0.076
Correlation coefficient	0.994	0.987	0.990

[a] H. H. Jaffé, *Chem. Rev.*, **53**, 222 (1953).

Identification of Products.—A solution of ethyl benzimidate (0.32 g., 2.13 mmoles) in 50 ml. of 0.120 *N* HCl was kept at 60° for 1 hr. Turbidity developed within the first few minutes. The infrared spectrum of a chloroform extract of the reaction mixture was identical with that of a solution of ethyl benzoate in chloroform (minor peaks at 1320, 1370, and 1470 cm.$^{-1}$; a major peak at 1717 cm.$^{-1}$; and a weak peak at 2450 cm.$^{-1}$), and has no peaks at 3510 and 3400 cm.$^{-1}$, the NH stretching peaks characteristic of benzamide. Similar evidence for the formation of only ethyl benzoate was obtained in a run at room temperature.

A suspension of 0.212 g. of ethyl *p*-nitrobenzimidate in 50 ml. of 0.120 *N* HCl was shaken for 1 hr. Extraction with ether and evaporation of the solvent yielded 0.125 g. of residue, m.p. 55.5°. A mixture of this with authentic ethyl p-nitrobenzoate (m.p. 55.5–56°) melted at 55.5°.

Enthalpies and Entropies of Activation.—Enthalpies and entropies of activation listed in Table III were calculated as described by Bunnett,[11] using Arrhenius activation energies and pre-exponential factors calculated by the least-squares method from the data of Table I. Each of the rate constants used was the

TABLE III

ARRHENIUS ACTIVATION ENERGIES, AND ENTHALPIES AND ENTROPIES OF ACTIVATION FOR HYDROLYSIS OF X-$C_6H_4C(=NH)OC_2H_5$ IN 0.120 *N* HYDROCHLORIC ACID

X	Relative hydrolysis rate, 30°	E_a, kcal./mole	ΔH^*(30°), kcal./mole	ΔS^*(30°), e.u.
p-CH_3O	0.26	20.3	19.7	−15
p-CH_3	0.51	18.7	18.1	−19
m-CH_3	0.89	19.0	18.4	−17
H	1.00	19.4	18.8	−15
p-Cl	1.54	19.2	18.6	−15
m-Cl	3.2	18.4	17.8	−16
m-NO_2	8.0	19.1	18.5	−12
p-NO_2	10.1	18.6	18.0	−13

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(5) C. A. MacKenzie, G. A. Schmidt, and L. R. Webb, *J. Am. Chem. Soc.*, **73**, 4990 (1951).

(6) J. Tafel and C. Enoch, *Ber.*, **23**, 106 (1890).

(7) G. D. Lander and F. T. Jewson, *J. Chem. Soc.*, **83**, 766 (1903).

(8) M. Yamazaki, Y. Kitagawa, S. Hiraki, and Y. Tsukamoto, *J. Pharm. Soc. Japan*, **73**, 294 (1953).

(9) Ultraviolet absorption spectra were determined with a Cary Model 14 recording spectrophotometer; infrared spectra were measured with a Beckman IR-7 spectrophotometer. Analyses were preformed by Australian Microanalytical Service, Chemistry Department, University of Melbourne, Parkville, N.2, Victoria, Australia.

(10) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 186.

(11) J. F. Bunnett, "Technique of Organic Chemistry: Investigation of Rates and Mechanisms of Reactions," Vol. III, part I, A. Weissberger. Ed., Interscience Publishers, Inc., New York, N. Y., 1961, p. 201.

average of two or three experimental measurements. In 21 out of 24 instances the deviation from the mean was less than 3%. If it is assumed that the maximum possible fractional error is 0.035, it can be shown that the maximum uncertainty in ΔH^* is about ± 0.5 kcal., and the maximum uncertainty in ΔS^* is about ± 1.6 e.u.[12]

Solvent Isotope Effect.—The deuterium oxide solvent isotope effect on acid hydrolysis of ethyl *m*-toluimidate was determined at 65.0° by measuring the rate of hydrolysis of the imidic ester hydrochloride in solutions containing 2.60 ml. of D_2O (or H_2O) and 0.030 ml. of 12 *N* HCl. The deuterium oxide (99.8% D_2O) was obtained from Bio-Rad Laboratories. These solutions were approximately 0.14 *N* in HCl, and the water of the heavy water solution was about 99.0% D_2O. The experimental rate constants were 1.82×10^{-3} sec.$^{-1}$ in H_2O and 8.67×10^{-4} sec.$^{-1}$ in D_2O. Therefore $k_{H_2O}/k_{D_2O} = 2.1$.

Discussion

A number of observations from this and previous studies of ethyl benzimidate hydrolysis in acidic solutions are pertinent to the mechanism of the reaction. Hydrolysis under acidic conditions yields a benzoate ester and ammonium ion as the only identifiable products, and the reaction is general acid catalyzed in acetate buffers.[4] Hydrolysis of ethyl benzimidate hydrochloride is slowed by addition of hydrochloric acid[3] or neutral electrolytes[4] to the reaction solution. The large Bunnett *w*-value for this reaction (+6.3) suggests that this is due to the effect of electrolytes on the activity of water in the reaction solutions.[13]

In the present study, we found that the hydrolysis of substituted ethyl benzimidates in dilute hydrochloric acid solutions correlates well with the Hammett equation,[10] with $\rho = +1.4$ at three temperatures (Table II). The reaction exhibits substantial negative entropies of activation for all of the esters studied. Interestingly, ethyl benzimidate hydrolysis is one of the few known reactions which give good Hammett plots, but in which reactivity is controlled by entropy of activation rather than enthalpy of activation.[14] With the exception of ethyl *p*-anisimidate, the values of ΔH^* are identical within experimental error (Table III). The deuterium oxide solvent isotope effect, $k_{H_2O}/k,_{D_2O}$ for hydrolysis of ethyl *m*-toluimidate in dilute hydrochloric acid solutions is 2.1.

In aqueous mineral acid solutions, the experimental evidence requires a rate-limiting step whose transition state contains the imidic ester, a proton, and several water molecules held by strong hydrogen bonds or partial covalent bonds. The evidence also strongly suggests that one or more protons in this transition state are in the process of being transferred from one basic site to another.

In acidic solutions, in which imidic esters are almost completely protonated, it is reasonable to assume that the reactive form of the substrate is the conjugate acid. The other possibility, general acid catalyzed hydrolysis of the unprotonated ester, is rendered very unlikely by the observation that electronegative aryl substituents facilitate hydrolysis. Since electron-withdrawing substituents should increase the equilibrium concentration of the unprotonated ester, but decrease the rate of proton transfer to it from general acids, a rate-determining acid-catalyzed reaction of the free ester should be relatively insensitive to substituent effects. If the conjugate acid is the species undergoing hydrolysis, two types of mechanisms are compatible with the observed general acid catalysis: nucleophilic attack by water or a general base on the conjugate acid or an intermediate in equilibrium with it; or proton transfer from the conjugate acid or an intermediate in equilibrium with it to water or a general base.

The available evidence is best rationalized by a mechanism involving general base catalyzed hydrolysis of a tetrahedral hydrate in equilibrium with the conjugate acid of the ester. A mechanism involving nucleophile-catalyzed hydrolysis of the conjugate acid can be excluded with considerable confidence on the basis of the Bunnett *w*-value and the solvent isotope effect for ethyl benzimidate hydrolysis. The observed *w*-value, +6.3, is substantially larger than the values (from +1.2 to +3.3) observed for reactions in which water functions as a nucleophile in the rate-limiting step, but is in the range observed for reactions in which water functions as a proton transfer agent. The solvent isotope effect is also larger than would be expected for nucleophilic attack by water on the conjugate acid of the ester.[15] We conclude, therefore, that nucleophilic interaction between a general base and the acyl carbon atom is not the driving force for the rate-limiting step in ethyl benzimidate hydrolysis. A more complex mechanism involving simultaneous proton transfer from a water molecule to nitrogen and nucleophilic attack by water on the acyl carbon atom of the ester is compatible with most of the evidence for reactions in mineral acid solutions. However, a similar mechanism cannot account for the acetic acid catalyzed hydrolysis, since, if acetic acid functioned as both proton transfer agent and nucleophile, reaction would be second order in acetic acid.

A more likely mechanism is one similar to that proposed by Hand and Jencks[4] for acid-catalyzed aminolysis of imidic esters, for which there is compelling evidence for the involvement of a tetrahedral intermediate. According to this mechanism, ethyl benzimidate hydrolysis in acidic solutions involves rate-determining general base catalyzed dissociation of the tetrahedral product of addition of a molecule of water to the conjugate acid of the imidic ester as shown in eq. 1–4 where B: may be either a water molecule or a general base.

$$\mathrm{ArC({=}NH)OC_2H_5 + H^+ \rightleftharpoons ArC({=}NH_2)OC_2H_5^+} \quad (1)$$

$$\mathrm{ArC({=}NH_2)OC_2H_5^+ + H_2O \rightleftharpoons ArC(OH)(NH_3)OC_2H_5^+} \quad (2)$$

$$\mathrm{ArC(OH)(NH_3)OC_2H_5^+ + B{:} \longrightarrow ArCO_2C_2H_5 + NH_3 + BH^+} \quad (3)$$

$$\mathrm{BH^+ + NH_3 \rightleftharpoons B{:} + NH_4^+} \quad (4)$$

This mechanism accounts for the observed general acid catalysis, since the transition state of reaction 3 contains the elements of BH. It also accounts for the large *w*-value, since in reaction 3 the transition state is solvated by three strongly hydrogen-bonded water molecules in addition to the one functioning as a proton transfer agent. This mechanism, involving considerable interaction with water molecules in the rate-limiting step, is also consistent with the observed negative entropies of activation.

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[12] R. C. Petersen, J. H. Markgraf, and S. D. Ross, *J. Am. Chem. Soc.*, **83**, 3819 (1961).

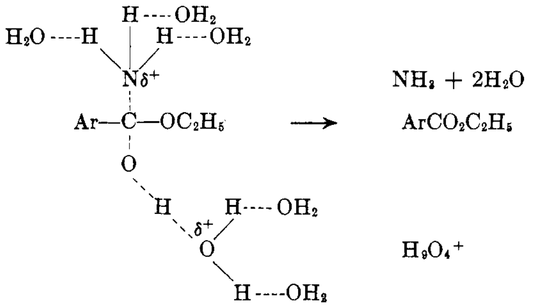
[13] J. F. Bunnett, *ibid.*, **83**, 4956 (1961).

[14] H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

[15] S. L. Johnson, *J. Am. Chem. Soc.*, **84**, 1729 (1962).

It is also possible to rationalize substituent effects on reactivity and activation parameters in terms of this mechanism. Since the equilibrium of eq. 1 is far to the right for all of the esters in dilute acid solutions, reactivity is determined by the effects of substituents on equilibrium 2 and rate-determining step 3. The tetrahedral product of equilibrium 2 forms one more strong hydrogen bond to water than does the ester conjugate acid. ΔS should therefore be negative, and should be more negative the greater the electron-attracting power of the aryl substituent. Electron-attracting substituents should also make ΔH more negative. Substituent effects on ΔH and ΔS of 2 should be compensatory, and the value of the equilibrium constant may be relatively insensitive to substituent effects.

Reaction 3, however, should be facilitated by electron-attracting substituents. In the transition state for this reaction the entropy decrease associated with solvation of the developing hydronium ion should be relatively insensitive to structural changes in the aryl group. On the other hand, the entropy increase accompanying C–N bond cleavage should be greater when the aryl group has an electron-attracting substituent than when it has an electron-repelling substituent, since the hydrogen bonds being broken are stronger in the former case than in the latter. Therefore ΔS^* for reaction 3 should be less negative for aryl groups with electron-attracting substituents. ΔH^* for reaction 3 should be relatively insensitive to substituent effects. If a concerted mechanism is involved, the electronic effects of substituents on O–H bond breaking and C–N bond breaking should be in opposite directions and might nearly cancel. In summary, equilibrium 2 should be relatively insensitive to the nature of the aryl group, and substituents should have a much greater effect on ΔS^* than on ΔH^* for rate-determining reaction 3. The proposed mechanism correctly predicts that ΔS^* should be less negative for esters having electron-attracting substituents than for those having electron-releasing substituents.



This mechanism fulfills the minimum requirement of rationalizing all of the available data. It accounts for the reaction products, the observed general acid catalysis, the solvent isotope effect, the large dependency of reaction rate on water activity, the positive ρ-value, and the fact that ΔS^* and not ΔH^* determines reactivity.

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s-Triazines. II.[1a] Syntheses of Dialkyl-*s*-triazines by Grignard Reaction

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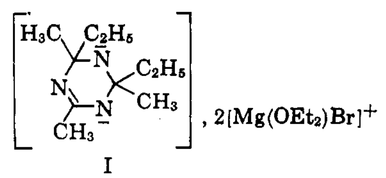
2,4-Dialkyl-6-halo- and 6-alkoxy-1,3,5-triazines were obtained from reactions of alkyl cyanurates, cyanuric chloride, or mixed alkoxyhalo-*s*-triazines with alkylmagnesium halides. Limitations of the individual reactions are discussed in terms of relative reactivities of groups displaced and of competing reactions, such as quaternization and additions leading to *gem*-dialkyldihydrotriazines.

Reactions of alkylmagnesium halides with cyanuric chloride have been reported as giving 2-monoalkyl or 2-monoaralkyl-4,6-dichloro-*s*-triazines.[2] A generalization was made to the effect that "one of the chlorine atoms of cyanuric acid reacts with alkyl Grignard reagents; in the case of some aryl Grignard reagents, two chlorine atoms undergo replacement."[3] No work has been reported in the literature on reactions of other organometallic reagents with cyanuric chloride, or on displacements with Grignard reagents on triazines other than cyanuric chloride.

Recently, however, Ostrogovich and Simonescu[4] studied the behavior of trimethyl-*s*-triazine with ethylmagnesium bromide. They showed that the solid products formed resulted from single or double additions of the Grignard reagent to the double bonds of the triazine. They postulated structures such as I.



I

We have found that, under milder, more controlled conditions than those used in earlier[2,3] work, halo- and alkoxy-*s*-triazines can be converted with alkyl Grignard reagent to the dialkylhalo- or dialkylalkoxy-*s*-triazines. Our results are summarized in Table I.

It seems clear that at low temperature (about −15°) smaller amounts of solid complexes and higher yields of

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[1] (a) Part I: H. Bader and N. M. Smyth, *J. Org. Chem.*, **29**, 952 (1964). (b) To whom correspondence should be addressed at Aldrich Chemical Co., Milwaukee, Wis.

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