

with ice water until the washes were neutral, dried, and reisolated by retention at  $-40^\circ$  during vacuum transfer, thereby removing acidic impurities.

*Anal.* Calcd for  $C_{18}H_{16}F_4N_2O_2$ : C, 29.41; H, 3.92; N, 13.73; F, 37.25. Found: C, 29.51; H, 4.75; N, 14.04; F, 36.92.

The  $^{19}F$  nmr spectrum consisted of a very strong line at  $\delta -13$  flanked at  $\pm 630$  cps by two weak lines. The spectrum was interpreted as an AA'BB'X<sub>3</sub> type with  $J_{AB} = J_{A'B'} = 630$  cps.

Coupling of all fluorine with the methyl group is visible in the proton spectrum with  $J_{AX} \sim 2.5$  cps.

**Registry No.**—Difluoramine, 10405-27-3; 2,2-bis-(difluoramino)propanol, 20122-29-6; bis(difluoramino)-methane, 18338-50-6; ethyl  $\alpha,\alpha$ -bis(difluoroamino)-propionate, 20122-31-0.

## General Base Catalyzed Hydrolysis of N,N'-Dimethyl-N,N'-diphenylamidinium Salts

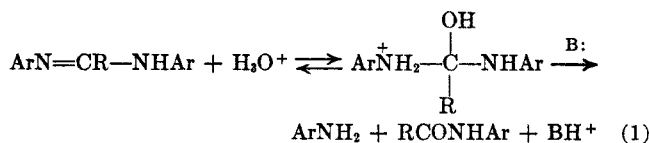
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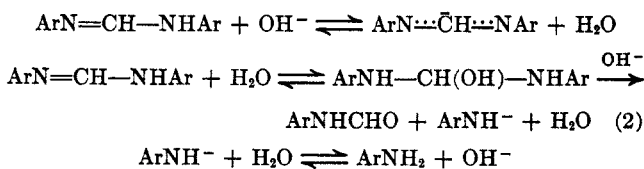
The hydrolyses of N,N'-dimethyl-N,N'-diphenylformamidinium, -acetamidinium, and -benzamidinium salts in aqueous solutions are general base catalyzed, with Brønsted catalysis law  $\beta$  values near 0.4. Hydroxide ion catalyzed hydrolysis of tetrasubstituted amidinium salts is characterized by large negative entropies of activation and by kinetic solvent isotope effects,  $k_{H_2O}/k_{D_2O}$ , less than unity. Base-catalyzed hydrolysis of amidinium cations is slowed by bulky acyl substituents, and hydrolysis of substituted benzamidinium cations is accelerated by electron-attracting aryl substituents ( $\rho = 1.6$ ). Hydroxide ion catalyzed hydrolysis of the formamidinium and benzamidinium salts is approximately first order in hydroxide ion concentration. The rate of hydrolysis of the acetamidinium salt tends to become independent of hydroxide ion concentration at high hydroxide ion concentrations, possibly due to reversible formation of a ketene aminal. All of these observations are satisfactorily accounted for by a mechanism involving rate-limiting general base catalyzed conversion of a tetrahedral hydrate of the amidinium cation into N-methylaniline and an N-methylanilide.

Hydrolysis reactions of N,N'-diarylformamidines and N,N'-diarylacetylamidines in acidic solutions are characterized by large positive Hammett  $\rho$  values, large negative entropies of activation, and rates which are directly proportional to the hydrogen ion concentration and water activity, and inversely proportional to the acidity ( $h_0$ ) of the reaction solutions. The diarylformamidines are about a thousand times more reactive than the diarylacetylamidines in aqueous 20% dioxane hydrochloric acid solutions.<sup>2-4</sup> Hydrolysis of N,N'-diarylformamidinium ions is general base catalyzed, with a Brønsted catalysis law  $\beta$  value of 0.3.<sup>2,3</sup> These observations are consistent with a mechanism involving rate-limiting general base catalyzed conversion of a protonated tetrahedral intermediate into products (eq 1).<sup>3,5</sup>



The kinetics of hydrolysis of N,N'-diarylformamidines under alkaline conditions is complex.<sup>6</sup> The rate of hydrolysis of formamidines having electron-releasing N-aryl substituents is nearly independent of hydroxide ion concentration and the structure of the aryl groups. Amidines having electron-withdrawing aryl substituents undergo hydrolysis by two processes, one which is independent of hydroxide ion concentration, and another whose rate is a nonlinear function of hydroxide ion concentration. Hydroxide ion catalyzed hydrolysis of N,N'-diarylformamidines probably involves rate-

limiting reaction of a tetrahedral hydrate of the amidine with hydroxide ion, complicated by a side equilibrium between the amidine and an unreactive conjugate base (eq 2).



The hydroxide-independent reaction is best rationalized in terms of rate-limiting reaction of the hydrated conjugate acid of the amidine with hydroxide ion (eq 1).

Alkaline hydrolysis of N,N'-disubstituted amidines is complicated by the existence of pH-dependent equilibria between the free amidines, their conjugate acids, and their conjugate bases. The amidinium ions are the more interesting of these three species, since they are implicated as intermediates under both acid and alkaline conditions.

Accordingly, we selected a series of N,N'-dimethyl-N,N'-diphenylamidinium cations,  $\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2\text{C}^+\text{R}$ , as substrates for a study of solvent, salt, and substituent effects on amidinium ion hydrolysis. These tetrasubstituted amidinium ions are isoelectronic with the conjugate acids of N,N'-disubstituted amidines, but possess no acidic proton.

### Experimental Section

**Preparation of Amidinium Salts.**—N,N'-Dimethyl-N,N'-diphenylformamidinium tetrafluoroborate was prepared by adding 10 g of N,N',N''-trimethyl-N,N',N''-triphenyl orthoformamide<sup>7</sup> to 90 ml of 12% fluoroboric acid, heating the mixture on a steam bath until the orthoamide dissolved, adding 200 ml of water, and

(7) D. H. Clemens, E. Y. Shropshire, and W. D. Emmons, *J. Org. Chem.*, **28**, 1108 (1963).

(1) Taken from the M.A. Thesis of M. W. C.

(2) R. H. DeWolfe and R. M. Roberts, *J. Amer. Chem. Soc.*, **75**, 2942 (1953).

(3) R. H. DeWolfe, *ibid.*, **82**, 1581 (1960).

(4) R. H. DeWolfe and J. R. Keefe, *J. Org. Chem.*, **27**, 493 (1962).

(5) J. F. Bunnett, *J. Amer. Chem. Soc.*, **83**, 4971 (1961).

(6) R. H. DeWolfe, *ibid.*, **86**, 864 (1964).

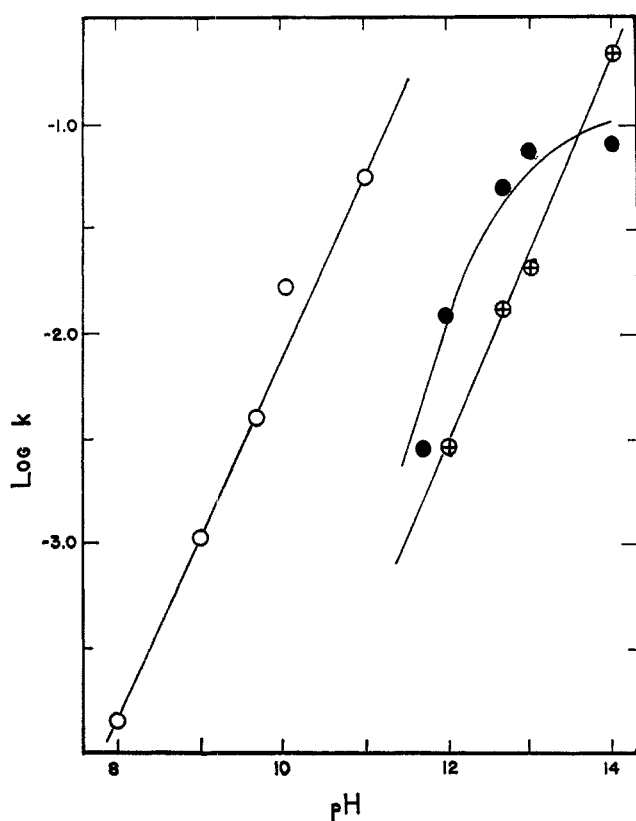


Figure 1.—Log  $k$  vs. pH for hydrolysis of tetrasubstituted amidinium salts in aqueous solutions at 30°: open circles,  $N,N'$ -dimethyl- $N,N'$ -diphenylformamidinium fluoborate; filled circles,  $N,N'$ -dimethyl- $N,N'$ -diphenylacetamidinium perchlorate; crossed circles,  $N,N'$ -dimethyl- $N,N'$ -diphenylbenzamidinium perchlorate.

cooling the resulting solution in an ice bath. The crude product (10.2 g), collected by suction filtration, was recrystallized from dichloromethane-carbon tetrachloride: mp 110–113° (lit.<sup>7</sup> mp 115–117°).

$N,N'$ -Dimethyl- $N,N'$ -diphenylacetamidinium perchlorate was prepared by the procedure of Jutz and Amschler.<sup>8</sup> A similar procedure was used for the preparation of a series of  $N,N'$ -dimethyl- $N,N'$ -diphenylbenzamidinium perchlorates. The appropriate benzoic acid (0.075 mol) and 32.1 g (0.3 mol) of  $N$ -methylaniline were added slowly at 0° to 30.6 g (0.2 mol) of phosphorus oxychloride. The reaction mixture was heated at a temperature between 130 and 160° for 2 hr, and 200 ml of ice-cold 17% sodium perchlorate solution was added to the cooled, syrupy mixture. The solid  $N,N'$ -dimethyl- $N,N'$ -diphenylbenzamidinium perchlorates were recrystallized from 95% ethanol. Yields ranged from 70 to 90%. Meltingpoints and ultraviolet absorption maxima and minima of aqueous solutions of the amidinium perchlorates are summarized in Table I.

TABLE I  
 $N,N'$ -DIMETHYL- $N,N'$ -DIPHENYLAMIDINIUM  
PERCHLORATES,  $R-C[N(CH_3)_2C_6H_5]_2ClO_4^-$

R	Registry No.	$\lambda_{max}$ , $m\mu$	$\lambda_{min}$ , $m\mu$	Mp, °C	
				Obsd	Lit. <sup>8</sup>
CH <sub>3</sub>	20449-29-0	255	230	155–158	167–168
C <sub>6</sub> H <sub>5</sub>	20449-30-3	280	255	208–212	216–217
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	20449-31-4	285	247	218–223	225–226
<i>m</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	20449-32-5	282	245	110–116	...
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	20449-33-6	287	245	160–163	165–166
<i>m</i> -ClC <sub>6</sub> H <sub>4</sub>	20449-26-7	285	255	120–125	...
<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	20449-27-8	293	250	199–200	199–200
<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	20449-28-9	325	250	173–174	...

**Solutions for Kinetic Runs.**—Sodium hydroxide solutions which were 1.0, 0.1, 0.05, 0.01, and 0.005  $N$  in NaOH were prepared

(8) C. Jutz and H. Amschler, *Chem. Ber.*, **97**, 2100 (1963).

by diluting British Drug House Ltd. standardized solutions with boiled distilled water. A series of solutions which were 0.005  $N$  in NaOH and 0.05, 0.025, 0.01, and 0.005  $N$  in NaCl were prepared similarly from standardized NaOH solutions and reagent grade sodium chloride.

Buffer solutions were prepared by the procedure of Perrin,<sup>9</sup> using  $n$ -butylamine [bp 76–78° (760 mm)] from Matheson Coleman and Bell, standardized hydrochloric acid solutions from British Drug House Ltd. reagent grade sodium carbonate monohydrate from Allied Chemical Corp., sodium bicarbonate from Hoyt Brothers, and reagent grade borax and boric acid from Mallinckrodt Chemical Works.  $n$ -Butylamine-butylammonium chloride, sodium carbonate-sodium bicarbonate, and borax-boric acid buffers were used for rate determinations at pH 10.85, 10, and 9 respectively. The ionic strength of all of these solutions was adjusted to 0.01 with sodium chloride.

**Kinetic Measurements.**—Hydrolysis rates were determined spectrophotometrically by measuring the decrease in absorbance as the amidinium salt hydrolyzed. Reactions having first-order rate constants larger than  $3 \times 10^{-5} \text{ sec}^{-1}$  were followed using a Cary Model 14 spectrophotometer or a Gilford recording spectrophotometer, each of which was equipped with a thermostated cell compartment. Cell temperatures were regulated to within  $\pm 0.05^\circ$ . Reactions were started by adding stock solutions of the amidinium salts to 3 ml of the thermostated buffer solution by means of a microsyringe. Runs having first-order rate constants smaller than  $3 \times 10^{-6} \text{ sec}^{-1}$  were carried out by spectrometric analysis of aliquots of reaction solutions which were kept in a thermostated water bath. The wavelength used in following a hydrolysis reaction was chosen so as to give a maximum change in absorbance.

**Identification of Hydrolysis Products.**—The hydrolysis products of  $N,N'$ -dimethyl- $N,N'$ -di-*p*-nitrophenylformamidinium tetrafluoroborate in neutral solution were reported to be  $N$ -methyl-*p*-nitroaniline and  $N$ -methyl-*p*-nitroformanilide.<sup>7</sup>  $N$ -Methylacetanilide, mp 98–100° (lit.<sup>10</sup> mp 101°), was isolated from the products of hydrolysis of  $N,N'$ -dimethyl- $N,N'$ -diphenylacetamidinium perchlorate in 4  $N$  NaOH, and  $N$ -methyl-*p*-toluanilide, mp 68–69° (lit.<sup>11</sup> mp 70°), was isolated from the products of alkaline hydrolysis of  $N,N'$ -dimethyl- $N,N'$ -diphenyl-*p*-toluamidinium perchlorate.

**Calculations.**—The hydrolysis reactions are kinetically first order under the conditions used. First-order rate constants, expressed in reciprocal seconds, were calculated from slopes of  $\log (A_t - A_\infty)$  vs.  $t$  plots, or by the Guggenheim method.<sup>12</sup> Arrhenius activation energies were calculated from slopes of  $\log k$  vs.  $1/T$  plots, and entropies of activation at 30° were calculated from the relation  $\Delta S^\ddagger = 4.576 (\log k - 10.753 - \log T + E_a/4.576)$ , where  $k$  is the rate constant at temperature  $T$ .<sup>13</sup>

## Results

**Variation of Hydrolysis Rate with Hydroxide Ion Concentration.**— $N,N'$ -Dimethyl- $N,N'$ -diphenylformamidinium tetrafluoroborate,  $N,N'$ -dimethyl- $N,N'$ -diphenylacetamidinium perchlorate, and  $N,N'$ -dimethyl- $N,N'$ -diphenylbenzamidinium perchlorate were hydrolyzed in solutions of different hydroxide ion concentrations at 30°. The kinetic data are summarized in Table II and Figure 1.

The  $\log k_{OH}$  vs. pH plots for hydrolysis of the formamidinium and acetamidinium salts are linear, with slopes of 0.85 and 0.96, respectively. The plot for the acetamidinium salt levels off at high hydroxide ion concentration. A possible explanation for this behavior is discussed below.

**Buffer Catalysis.**—Hydrolyses of  $N,N'$ -dimethyl- $N,N'$ -diphenylformamidinium-, -acetamidinium, and -benzamidinium salts are general base catalyzed in

(9) D. D. Perrin, *Australian J. Chem.*, **16**, 572 (1963).

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(11) E. Lellmann and R. Just, *ibid.*, **24**, 2114 (1891).

(12) E. A. Guggenheim, *Phil. Mag.*, (7) **2**, 538 (1926).

(13) J. F. Bunnett in "Technique of Organic Chemistry: Investigation of Rates and Mechanisms of Reactions," Vol. III, 2nd ed, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1956, p 801.

TABLE II  
pH DEPENDENCE OF HYDROLYSIS OF  
N,N'-DIMETHYL-N,N'-DIPHENYLAMIDINIUM SALTS AT 30°

pH	HC[N(CH <sub>3</sub> )C <sub>6</sub> H <sub>5</sub> ] <sub>2</sub> <sup>+</sup>				
	8	9	9.7	10.3	11
10 <sup>4</sup> k, sec <sup>-1</sup> <sup>a</sup>	1.55	10.6	39.9	165	548
pH	CH <sub>3</sub> C[N(CH <sub>3</sub> )C <sub>6</sub> H <sub>5</sub> ] <sub>2</sub> <sup>+</sup>				
	11.7	12	12.7	13	14
10 <sup>4</sup> k, sec <sup>-1</sup> <sup>a</sup>	28.1	123	513	763	796
pH	C <sub>6</sub> H <sub>5</sub> C[N(CH <sub>3</sub> )C <sub>6</sub> H <sub>5</sub> ] <sub>2</sub> <sup>+</sup>				
	12	12.7	13	14	14
10 <sup>4</sup> k, sec <sup>-1</sup> <sup>a</sup>	28.6	133	204	2140	

<sup>a</sup> Hydroxide-catalyzed reaction.

butylamine, carbonate, and borate buffers. The rate equation for these reactions in buffer solutions is  $k_{\text{obsd}} = k_0 + k_{\text{OH}}[\text{OH}^-] + \sum_i k_{\text{B}_i}[\text{B}_i]$ . The rate of the spontaneous reaction is negligible in the buffers used in this study. Buffer base catalytic coefficients,  $k_{\text{B}}$ , obtained from slopes of plots of  $k_{\text{obsd}}$  vs.  $[\text{B}]$ , are summarized in Table III.

TABLE III  
BUFFER BASE CATALYTIC COEFFICIENTS FOR  
HYDROLYSIS OF RC[N(CH<sub>3</sub>)C<sub>6</sub>H<sub>5</sub>]<sub>2</sub><sup>+</sup> IN  
AQUEOUS BUFFERS

R	Buffer base	Temp, °C	10 <sup>3</sup> k <sub>B</sub> , l./mol sec
H	BuNH <sub>2</sub>	30	183
H	CO <sub>3</sub> <sup>2-</sup>	30	127
H	B(OH) <sub>4</sub> <sup>-</sup>	30	1.68
CH <sub>3</sub>	BuNH <sub>2</sub>	30	2.24
CH <sub>3</sub>		40	2.79
CH <sub>3</sub>		60	8.15
CH <sub>3</sub>	CO <sub>3</sub> <sup>2-</sup>	30	1.83
CH <sub>3</sub>	B(OH) <sub>4</sub> <sup>-</sup>	30	8.2 × 10 <sup>-3</sup>
C <sub>6</sub> H <sub>5</sub>	BuNH <sub>2</sub>	30	0.783
C <sub>6</sub> H <sub>5</sub>		40	1.73
C <sub>6</sub> H <sub>5</sub>		50	2.45
C <sub>6</sub> H <sub>5</sub>		60	4.33
C <sub>6</sub> H <sub>5</sub>	CO <sub>3</sub> <sup>2-</sup>	30	0.559
C <sub>6</sub> H <sub>5</sub>	B(OH) <sub>4</sub> <sup>-</sup>	30	1.2 × 10 <sup>-2</sup>

Plots of  $-\text{p}K_{\text{B}}$  vs.  $\log k_{\text{B}}$  for hydroxide ion, butylamine, and carbonate ion catalyzed hydrolyses are linear, with slopes  $\beta = 0.4$  for the formamidinium and acetamidinium salts and 0.35 for the benzamidinium salt. These  $\beta$  values are only approximate, owing to the small number of bases used.

**Energies and Entropies of Activation.**—Arrhenius activation energies and entropies of activation at 30° were calculated for hydroxide ion catalyzed hydrolysis of the formamidinium, acetamidinium, and benzamidinium salts, and for the *n*-butylamine catalyzed hydrolysis of the acetamidinium and benzamidinium salts. The catalytic coefficients, energies of activation, and entropies of activation are given in Table IV.

**Substituent Effects.**—Whether the catalyst is hydroxide ion, butylamine, or carbonate ion, N,N'-dimethyl-N,N'-diphenylformamidinium ion is much more reactive than N,N'-dimethyl-N,N'-diphenylacetamidinium ion, which is somewhat more reactive than N,N'-dimethyl-N,N'-diphenylbenzamidinium ion (see Table V).

Table VI lists hydrolysis rates of a series of *meta*- and *para*-substituted N,N'-dimethyl-N,N'-diphenylbenz-

TABLE IV  
ACTIVATION PARAMETERS FOR HYDROXIDE ION  
AND BUTYLAMINE CATALYZED HYDROLYSIS  
OF RC[N(CH<sub>3</sub>)C<sub>6</sub>H<sub>5</sub>]<sub>2</sub><sup>+</sup>

R	Temp, °C	k <sub>B</sub> , l./mol sec	E <sub>a</sub> , kcal/mol	ΔS <sup>‡</sup> , eu <sup>a</sup>
Hydroxide Ion Catalyzed Hydrolysis				
H	10	11.3	13.4	-8
H	30	54.8		
CH <sub>3</sub>	30	0.562		
CH <sub>3</sub>	40	1.19	11.7	-23
CH <sub>3</sub>	50	1.83		
C <sub>6</sub> H <sub>5</sub>	30	0.122		
C <sub>6</sub> H <sub>5</sub>	40	0.288	15.8	-13
C <sub>6</sub> H <sub>5</sub>	50	0.622		
Butylamine Catalyzed Hydrolysis				
CH <sub>3</sub>	30	0.0224		
CH <sub>3</sub>	40	0.0279	9.0	-38
CH <sub>3</sub>	60	0.0815		
C <sub>6</sub> H <sub>5</sub>	30	0.0078		
C <sub>6</sub> H <sub>5</sub>	40	0.0173		
C <sub>6</sub> H <sub>5</sub>	50	0.0245	11.0	-34
C <sub>6</sub> H <sub>5</sub>	60	0.0533		

<sup>a</sup> Calculated for 30°.

TABLE V  
RELATIVE REACTIVITIES OF RC[N(CH<sub>3</sub>)C<sub>6</sub>H<sub>5</sub>]<sub>2</sub><sup>+</sup> AT 30°

R	k <sub>B</sub>	k <sub>B</sub> (rel)
Hydroxide Ion Catalysis		
H	54.8	450
CH <sub>3</sub>	0.562	4.60
C <sub>6</sub> H <sub>5</sub>	0.122	1.00
Butylamine Catalysis		
H	1.83	234
CH <sub>3</sub>	2.24 × 10 <sup>-2</sup>	2.86
C <sub>6</sub> H <sub>5</sub>	7.83 × 10 <sup>-3</sup>	1.00
Carbonate Ion Catalysis		
H	1.27	227
CH <sub>3</sub>	1.83 × 10 <sup>-2</sup>	3.27
C <sub>6</sub> H <sub>5</sub>	5.6 × 10 <sup>-3</sup>	1.00

amidinium salts in butylamine buffers ( $[\text{BuNH}_2] = 0.0153 \text{ M}$ ,  $[\text{BuNH}_3^+] = 0.0092 \text{ M}$ ) at 30°. The rate constants are composites of hydroxide and butylamine catalyzed terms in which the hydroxide term predominates. They give an excellent Hammett  $\rho\sigma$  plot with  $\rho = 1.57$  (Figure 2).

TABLE VI  
RATE CONSTANTS FOR HYDROLYSIS OF  
Y-C<sub>6</sub>H<sub>4</sub>C(NMeC<sub>6</sub>H<sub>5</sub>)<sub>2</sub>+ClO<sub>4</sub><sup>-</sup> IN BuNH<sub>2</sub>+BuNH<sub>3</sub><sup>+</sup> BUFFER  
SOLUTIONS (pH 10.85) AT 30°

Y	σ <sup>a</sup>	k × 10 <sup>4</sup> , sec <sup>-1</sup>
<i>p</i> -NO <sub>2</sub>	0.778	53.5
<i>m</i> -Cl	0.366	10.4
<i>p</i> -Cl	0.227	7.28
<i>p</i> -H	0.000	2.75
<i>p</i> -CH <sub>3</sub>	-0.170	1.78
<i>m</i> -CH <sub>3</sub>	-0.082	1.55
<i>p</i> -OCH <sub>3</sub>	-0.268	1.21

<sup>a</sup> E. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart, & Winston, Inc., New York, N. Y., 1959, p 221.

**Salt Effects.**—N,N'-Dimethyl-N,N'-diphenylacetamidinium perchlorate and N,N'-dimethyl-N,N'-diphenylbenzamidinium perchlorate were hydrolyzed

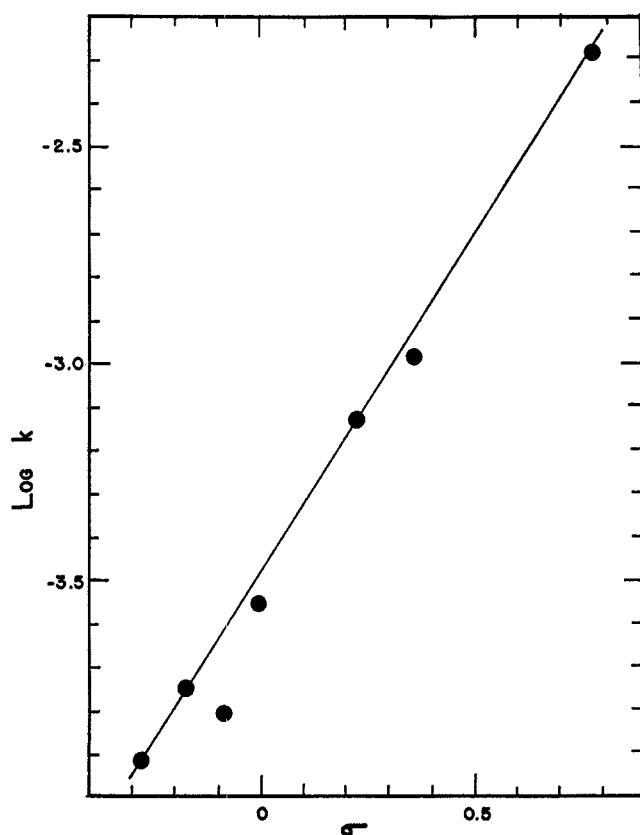


Figure 2.—Hammett  $\rho\sigma$  plot for hydrolysis of  $N,N'$ -dimethyl- $N,N'$ -diphenylbenzamidinium perchlorates in aqueous butylamine buffers at  $30^\circ$ .

at  $30^\circ$  in 0.005  $N$  sodium hydroxide solutions which were 0.0025, 0.005, 0.01, 0.025, and 0.05  $N$  in sodium chloride. For each compound the hydrolysis rates were the same within experimental error, and showed no systematic dependence upon ionic strength. These reactions show a negligible salt effect.

**Solvent Isotope Effect.**—The solvent isotope effect on hydrolysis of  $N,N'$ -dimethyl- $N,N'$ -diphenylacetamidinium and -benzamidinium perchlorates is shown in Table VII.

TABLE VII  
SOLVENT ISOTOPE EFFECT ON HYDROLYSIS OF  
 $RC[N(CH_3)C_6H_5]_2^+$  IN ALKALINE  
SOLUTIONS AT  $30^\circ$

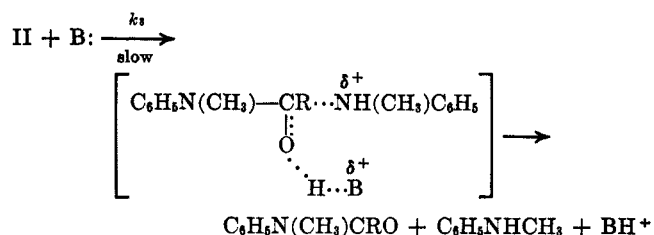
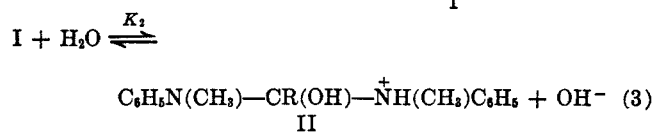
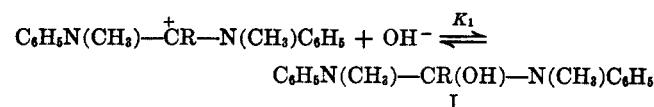
R	$[OH^-]$	$10^4 k_{H_2O}$	$10^4 k_{D_2O}$	$k_{H_2O}/k_{D_2O}$
$CH_3$	0.0152	21.4	26.9	0.79
$C_6H_5$	0.0115	3.42	6.06	0.56

### Discussion

The experimental results described above show that hydrolysis of  $N,N,N',N'$ -tetrasubstituted amidinium cations is general base catalyzed, with Brønsted catalysis law  $\beta$  values near 0.4. The hydrolysis reactions have large negative entropies of activation, are retarded by bulky acyl substituents, and are accelerated by electron-withdrawing groups on the acyl substituent. They exhibit negligible salt effects and are faster in deuterium oxide solutions than in protium oxide solutions.

A mechanism similar to that recently proposed by Jencks and Robinson<sup>14,15</sup> for the general base catalyzed

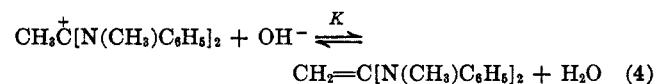
hydrolysis of 1,3-diphenylimidazolium chloride, a heterocyclic formamidinium salt, satisfactorily accounts for these experimental observations. This mechanism is outlined in eq 3.



Robinson<sup>15</sup> obtained experimental evidence for the formation of a tetrahedral intermediate analogous to I in the hydroxide ion catalyzed hydrolysis of 1,3-diphenylimidazolium chloride, and Robinson and Jencks<sup>14</sup> presented convincing arguments that the rate-limiting step of the second-order portion of the reaction involves a general base catalyzed reaction of an intermediate analogous to II. Mechanism 3 requires that the reaction be first order in amidinium salt and catalyzing base, as observed for the formamidinium and benzamidinium salts.

Alkaline hydrolyses of the formamidinium and benzamidinium salts studied in this work differ from hydrolysis of the diphenylimidazolium salt in one significant respect. Hydrolysis of the acyclic amidinium cations is first order in hydroxide ion up to pH 11 for the formamidinium salt and up to pH 14 for the benzamidinium salt (see Table II and Figure 1), whereas hydrolysis of the imidazolium salt above pH 10 is largely due to a reaction which is second order in hydroxide ion.<sup>14</sup> This second-order hydroxide dependence was ascribed to a general acid catalyzed reaction of the conjugate base of the tetrahedral intermediate. The absence of terms second order in hydroxide ion for hydrolysis of the acyclic amidinium salts indicates that the tetrahedral intermediates II ( $R = H, C_6H_5$ ) are substantially less acidic than 2-hydroxy-1,3-diphenylimidazolidine.

As shown in Figure 1, the rate of hydrolysis of  $N,N'$ -dimethyl- $N,N'$ -diphenylacetamidinium ion levels off at high pH. This result may be due to reversible reaction of the acetamidinium ion with hydroxide to form a ketene aminal (eq 4). If reaction 4 is a parasitic side



equilibrium, the observed rate constant would be  $k_{\text{obsd}} = k_2[OH^-]/(1 + K[OH^-])$ , where  $k_2$  is the rate constant for reaction of the acetamidinium ion with

(14) D. R. Robinson and W. P. Jencks, *J. Amer. Chem. Soc.*, **89**, 7088 (1967).

(15) D. R. Robinson, *Tetrahedron Lett.*, 5007 (1968).

hydroxide ion and  $K$  is the equilibrium constant for ketene aminal formation. When  $K[\text{OH}^-] \gg 1$ , the experimental hydrolysis rate is independent of hydroxide ion concentration.

Ketene acetals are known to react rapidly with water under acidic conditions, but more slowly under neutral conditions.<sup>16</sup> It seems likely that ketene aminals may behave similarly. Obvious experimental tests of the validity of this proposal would be to isolate the ketene aminal from a reaction mixture, and to demonstrate that pre-synthesized ketene aminal hydrolyzes at the same rate as the acetamidinium salt.

N,N'-Dimethyl-N,N'-diphenylformamidinium, -acetamidinium and -benzamidinium salt hydrolyses all exhibit buffer catalysis, which we attribute to catalysis by the buffer bases (see Table III). Brønsted catalysis law plots of  $\log K_b$  vs.  $\log k_B$  for the hydroxide, butylamine, and carbonate ion catalyzed reactions are straight lines of slopes  $\beta = 0.4, 0.4,$  and  $0.35$  for hydrolysis of the formamidinium, acetamidinium, and benzamidinium salts, respectively. The points for borate catalysis fall below the lines defined by the other three catalysts. These admittedly imprecise  $\beta$  values are similar to the value of  $0.44$  observed for general base catalyzed hydrolysis of 1,3-diphenylimidazolium chloride.<sup>14</sup>

The large negative entropies of activation observed for the hydroxide and butylamine catalyzed hydrolysis of the tetrasubstituted amidinium salts are consistent with the mechanism outlined in eq 3. The transition state for this mechanism is assembled from the amidinium ion, a water molecule, and the basic catalyst. A substantial decrease in entropy should accompany its formation from its components.

Reactions of nucleophiles with substances at the carboxyl level of oxidation are sensitive to both the steric and electronic properties of substituents on the acyl carbon, and amidinium ions are no exception. N,N'-Dimethyl-N,N'-diphenylformamidinium ion hydrolyzes much more rapidly than N,N'-dimethyl-N,N'-diphenylacetamidinium ion, which hydrolyzes somewhat more rapidly than N,N'-dimethyl-N,N'-diphenylbenzamidinium ion, whether the catalyst is hydroxide ion, *n*-butylamine, or carbonate ion (Table V). This reactivity sequence can be accounted for by considering the effects of acyl substituents on the free energy of activation for amidinium ion hydrolysis. The energy of activation is equal to the energy difference between the rate-limiting transition state and the amidinium ion, water molecule, and basic catalyst from which it is assembled (see eq 3). Structural features which stabilize the amidinium ion or destabilize the transition state will increase the free energy of activation; those which stabilize the transition state or destabilize the initial state reduce the energy of activation.

If the free energy of the formamidinium ion is selected as the reference point, replacing the formyl proton by a methyl group might be expected to stabilize the amidinium ion, which is a diaminocarbonium ion. The acyl methyl group will destabilize the nearly tetrahedral transition state by steric interaction with the two methylphenylamino groups, and slightly stabilize it by a charge-dipole interaction with the protonated nitrogen atom. The net result of stabilizing the initial

state and destabilizing the transition state is to make the acetamidinium ion less reactive than the formamidinium ion. If the acyl phenyl group of the benzamidinium ion can enter into resonance with the bismethylphenylaminocarbonium system, it should be even more effective than a methyl group in stabilizing the amidinium ion. It should destabilize the transition state both by steric interactions with the methylphenylamino groups and by charge-dipole interaction with the protonated nitrogen. All three of these interactions would increase the energy of activation relative to that for hydrolysis of the formamidinium ion. Since carbonium ion stabilization and steric bulk<sup>17</sup> are both predicted to be greater for the acyl phenyl than for the acyl methyl substituent, it is not surprising that the benzamidinium ion is less reactive than the acetamidinium ion. What is surprising is that the reactivity difference is so small. This small reactivity difference, together with the fact that substituents on the acyl phenyl group of substituted benzamidinium ions appear to influence reactivity by an inductive rather than a mesomeric process, suggests that acyl phenyl groups do not significantly stabilize amidinium ions by resonance. Inspection of molecular models indicates that this may be due to severe steric hindrance to formation of the coplanar conformation required for resonance between the acyl phenyl group and the carbonium system of the benzamidinium ion.

The rather imprecise Arrhenius activation energies and entropies of activation listed in Table IV suggest that differences in entropies of activation are more important than differences in enthalpies of activation in determining relative reactivities of amidinium ions toward base-catalyzed hydrolysis. The steric effect of acyl substituents appears to play an important role in determining the hydrolytic reactivity of N,N,N',N'-tetrasubstituted amidinium salts. In contrast, the influence of acyl substituents on hydrolytic reactivity of N,N'-diarylformamidinium ions in acidic solution is due almost entirely to their effect on enthalpies of activation.<sup>4</sup> This is reasonable, since the transition states for hydrolysis of the N,N'-disubstituted amidinium ions should be relatively free of steric hindrance.

Comparison of reactivities of a series of *meta*- and *para*-substituted N,N'-dimethyl-N,N'-diphenylbenzamidinium salts, for which steric acyl substituent effects should be almost constant, permits evaluation of electronic effects of acyl substituents on reactivity (Table VI). The positive  $\rho$  value ( $\rho = 1.57$ ) of a Hammett plot of these data (Figure 2) shows that electron withdrawal from the amidinium acyl carbon increases reactivity, as expected. (Electron-withdrawing substituents should raise the energy of the amidinium ion by their inductive effect more than they raise the energy of the transition state.) It is apparent from these data that resonance effects are relatively unimportant in determining reactivity of benzamidinium ions. If resonance interactions between the *p*-methyl and *p*-methoxy substituents and the acyl carbon of the amidinium ions significantly stabilized the cations, the *p*-toluamidinium and *p*-anisamidinium ions should be less reactive than would be predicted from a Hammett Plot drawn to fit the other substituents. This is

(16) S. M. McElvain, *Chem. Rev.*, **45**, 470 (1949).

(17) R. W. Taft, in M. S. Newman, "Steric Effects in Organic Chemistry", John Wiley & Sons, Inc., New York, N. Y., 1956, p. 601.

clearly not the case. Figure 2 shows also that the two *meta*-substituted benzamidinium salts are somewhat less reactive than predicted from the  $\rho$  value determined for the *para*-substituted compounds. This may be due to an appreciable steric effect of the *meta* substituents on this reaction.

Rates of hydroxide ion catalyzed hydrolysis of N,N'-dimethyl-N,N'-diphenylacetamidinium and -benzamidinium perchlorates were found not to be significantly influenced by the ionic strength of the reaction solutions in the range  $\mu = 0.0075$  to  $\mu = 0.055$ . The two preequilibria of eq 3 should be influenced approximately equally but in opposite directions by changes in ionic strength of the medium, since the first involves ionic association and the second involves dissociation. In the rate-limiting step with hydroxide ion as a catalyst, there is a partial neutralization of charge, a process which should occur somewhat less readily at high than at low ionic strengths. The low Brønsted  $\beta$  value for the reaction indicates that proton transfer from the hydroxyl group of the tetrahedral intermediate to the catalyst is far from complete in the transition state, so that the charge distribution in the transition state is not greatly different from the charge distribution im-

mediately preceding its formation. A large salt effect is therefore not anticipated, and is not observed.

The rate equation for hydroxide ion catalyzed hydrolysis of tetrasubstituted amidinium salts required by eq 3 is  $k_{\text{exp}} = K_1 K_2 k_3 [\text{OH}^-]$ . The solvent deuterium isotope effect on the reaction is therefore a composite of the isotope effects on the two equilibria and the rate-limiting step of the reaction. That is,

$$k_{\text{exp H}}/k_{\text{exp D}} = (K_{1\text{H}}/K_{1\text{D}}) (K_{2\text{H}}/K_{2\text{D}}) (k_{3\text{H}}/k_{3\text{D}}) \text{ (if } [\text{OH}^-] = [\text{OD}^-])$$

The solvent isotope effects on the preequilibria and the rate-limiting step may be estimated by the method of Bunton and Shiner.<sup>18,19</sup> Application of this method yields  $K_{1\text{H}}/K_{1\text{D}} = 0.65$ ,  $K_{2\text{H}}/K_{2\text{D}} = 2.5$ , and  $k_{3\text{H}}/k_{3\text{D}} = 0.5$ . The product of these three values is 0.8. This value, although only a rough approximation, is in reasonable agreement with experimental observation.  $k_{\text{exp H}}/k_{\text{exp D}}$  was found to be 0.79 for N,N'-dimethyl-N,N'-diphenylacetamidinium perchlorate, and 0.56 for the analogous benzamidinium salt (see Table VII).

(18) C. A. Bunton and V. J. Shiner, *J. Amer. Chem. Soc.*, **83**, 42 (1961).

(19) C. A. Bunton and V. J. Shiner, *ibid.*, **83**, 3207 (1961).

## Carbonium Ion Formation in Solvolysis of Phosphate Triesters

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The mechanisms of solvolysis of some triesters of phosphoric acid which might form carbonium ions have been investigated. Such a pathway is shown to be predominant in the solvolysis of tri-*t*-butyl and triisopropyl phosphates, but to be negligible in the case of triallyl phosphate. The solvolytic behavior of some five-membered cyclic tertiary alkyl esters is briefly discussed.

It has been known qualitatively for many years that triesters of phosphoric acid are hydrolyzed in basic solution rather readily to the corresponding diesters, but that subsequent stages of hydrolysis are relatively slow.<sup>2</sup> The behavior of trimethyl phosphate and of triphenyl phosphate, recently examined in detail by Barnard, Bunton, Llewellyn, Vernon, and Welch,<sup>3</sup> may probably be taken as characteristic of the reactions of the triesters of primary alcohols, phenols, and thiols with hydroxide ion.

The hydrolysis of trimethyl phosphate in aqueous base is first order in hydroxide ion and first order in the ester. Isotopic tracer experiments show that the phosphorus-oxygen bond is broken exclusively;<sup>3,4</sup> furthermore, within the limit of experimental error of the isotopic analysis, no isotopic exchange occurs prior to hydrolysis between the phosphoryl oxygen and the oxygen atoms of the solvent.<sup>3</sup> A small depression of rate is observed on changing the solvent from water to 75% dioxane-25% water. The few available data suggested

that changes of neutral salt concentration do not noticeably affect the rate of saponification of the triesters. The hydrolysis of triphenyl phosphate in 75% dioxane-25% water was found also to be first order in both hydroxide ion and the ester.

The kinetic order of these hydrolyses, together with the position of bond fission, establishes that hydroxide ion attacks the phosphorus atom in the rate-controlling step of the sequence.

Corresponding data are very scanty for tertiary alcohol esters of phosphoric acid. The synthesis and qualitative observations concerning the hydrolysis of tri-*t*-butyl phosphate have been briefly reported.<sup>5</sup> The hydrolysis of mono-*t*-butyl phosphate has been studied in detail by Lapidot, Samuel, and Weiss-Brodsky;<sup>6</sup> the undissociated acid undergoes facile carbon-oxygen cleavage, with formation of the *t*-butyl carbonium ion. Evidence has been presented that the phosphate ester of the tertiary alcohol function of mevalonic acid pyrophosphate undergoes concerted decarboxylation and phosphate elimination to form isopentenyl pyrophosphate.<sup>7</sup>

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