Kinetic Study on the Acid Hydrolysis of 1-Aryl-2-phenyl-2-imidazolines.
Basicity-Rate of Hydrolysis and Structure Relationships

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Rate constants (k_{obs}) of hydrolysis in sulfuric acid-water mixtures at 100° for five 1-aryl-2-phenyl-2-imidazolines were determined. The influence of substituents in the phenyl group at N-1 upon the rate of hydrolysis was studied. When the imidazoline ring is considered to be a substituent of the benzene ring at N-1, a good correlation with the Hammett equation is found.

In opposition to the behavior in alkaline media it was observed that reaction rates were enhanced by electron-withdrawing phenyl substituents and reduced by electron-releasing groups providing, similarly, a change in the mechanism of the reaction in the second case that was not observed in the first. Agreement with the Hammett equation allowed comparison between experimental and "calculated" rate constants which are fairly close. An equation relating the rate constants with the pK_a values of the imidazolinium ions is given.

Discussion.

This is an extension of our work on the properties of 1-aryl-2-phenyl-2-imidazolines [1,2]. These compounds show in strong acid media a similar behavior as that in alkaline media undergoing breakdown through the N-1-C-2 bond to give only *N*-aryl-*N'*-benzoylethylenediamines **B** (Scheme I). However, the decreased stability of the latter in acid medium causes the subsequent hydrolysis to *N*-arylethylenediamine and benzoic acid. This decomposition is generally partial and depends on the nature of the imidazoline, the *p*H and the temperature.
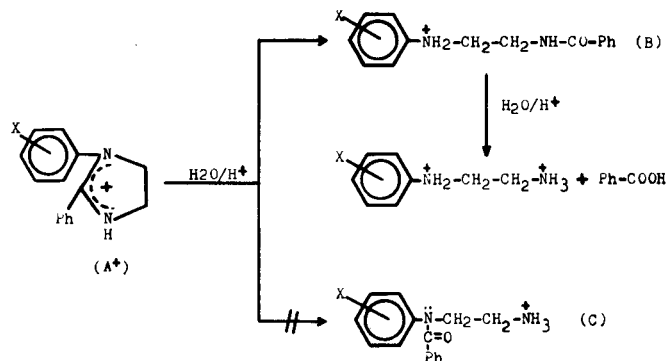

Scheme I

Table I

Rates of Acid Hydrolysis of 1-Aryl-2-phenyl-2-imidazolines in Sulfuric Acid-Water Mixtures at 100°

Compound No.	R	λ selected (nm)	(M)	$10^5 k_{obs}$ [a] $(M^{-1}min^{-1})$	$10^5 k(m^{-1}min^{-1})$ $k = k_{obs}/[H^+]$	$10^5 \bar{k}$ $(M^{-1}min^{-1})$	$t^{1/2}(h)$
1	4-Me	290	0.50	2.30	4.60		
			0.75	3.40	4.53	4.53	255
			1.00	4.47	4.47		
2	3,4-(MeO)₂	300	0.50	2.80	5.60		
			0.75	4.10	5.46	5.52	209
			1.00	5.50	5.50		
3	H	290	0.50	4.80	9.60		
			0.75	7.70	10.20	9.78	118
			1.00	9.54	9.54		
						$\bar{k}(min^{-1})$	
4	4-Cl	290	0.50	25.2			
			0.75	25.4		2.54×10^{-4}	45
			1.00	25.6			
5	4-NO₂	290	0.50	220			
			0.75	223		2.23×10^{-3}	5.1
			1.00	226			

[a] The degree of certainty of the rate constants obtained from duplicate experiments was ± 0.1.

Kinetic studies were performed with five imidazolines in sulfuric acid-water mixtures at 100°. Reactions were followed by uv spectrophotometry, selecting a wavelength where the absorptivity of the degradation products did not interfere. At constant pH the rates of disappearance of the imidazolines were found to be first order and reactions for compounds **1, 2** and **3** (Table I) also showed first order dependence on [H$^+$] below $1M$ sulfuric acid concentrations. Plots of log (absorbance) against time were linear for at least 90% of the reaction for all the samples and rate constants are given in Table I.

Plots of observed rate constants (k_{obs}) versus sulfuric acid molarity showed a different behavior according to the nature of the aryl substituent at N-1 (Figure 1). This was assumed to be produced by a change in the mechanism of the reaction in the case of compounds **1, 2** and **3** which apparently does not occur in compounds **4** and **5**. Thus, we tried to gain further insight into the nature of both mechanisms.
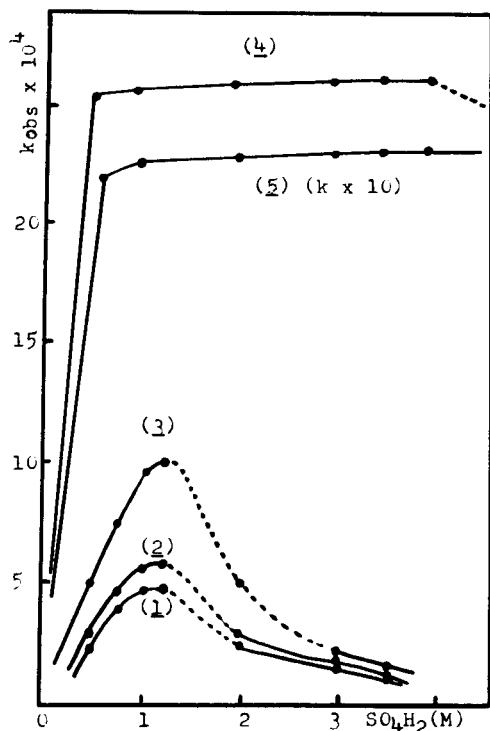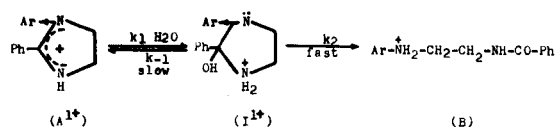

Figure 1

Electron-Withdrawing Groups at N-1.

At low concentrations of acid, sufficient to provide the imidazoline protonation at N-3 [1], it can be observed by hptlc the appearance of a reaction intermediate which coexists with the substrate and slowly undergoes decomposition to the degradation products. Prior observations [3] indicate that this intermediate is formed by nucleophilic addition of water to the cat ion at position 2 to form a tetrahedral addition intermediate which decomposes to the

hydrolysis products. The small variation of observed rate constants on increasing the acid concentration (derivatives **4** and **5**, Figure 1) over a wide range of molarities indicates the absence of acid catalysis in the formation or decomposition of the intermediate. Scheme II illustrates the case.

Scheme II

Chromatographic experiments point out that the imidazoline is not completely converted into the intermediate during the first step of the reaction (*i.e.*, $k_{-1} \neq 0$). However, linearity from the begining in curves (**4**) and (**5**) of Figure 2 indicates that the equilibrium $(A^{1+}) \rightleftharpoons (I^{1+})$ is immediately attained, which implies that $K_{-1} \gg k_1$, so that $k_1/k_{-1} + k_2 \ll 1$. With $k_{obs} = k_1.k_2/(k_{-1} + k_2)$ and taking into account
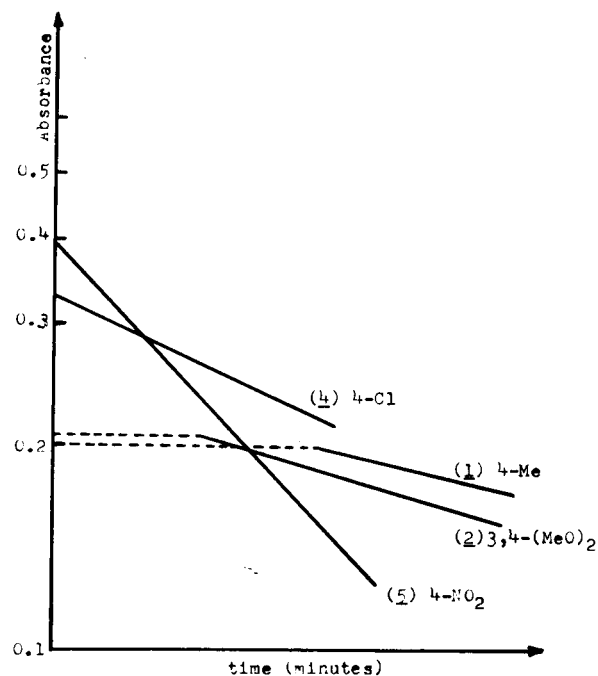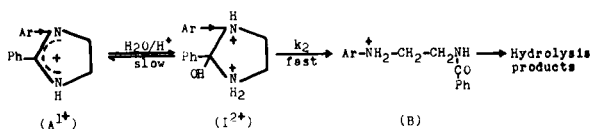

Figure 2

the absence of acid catalysis it is concluded that, when -I and -M electron-attracting groups are present at N-1, reactions exclusively involve the rate determining nucleophilic attack of water to the protonated imidazoline to give the tetrahedral addition intermediate I^{1+} (Scheme II); $v = k$ $[(A^{1+})]a_{H_2O}$.

Though hydrolysis of the 4-NO$_2$ derivative does without catalysis the enthalpy of activation for this reaction ($\triangle H^{\ddagger}$ = 16.1 Kcal/mol) is rather lower than that for the acid catalyzed reaction of the 4-MeO derivative ($\triangle H^{\ddagger}$ = 20.2 Kcal/mol), in spite of their similar steric requirements

($\triangle S^{\ddagger} = $ -27.5 and -26.6 $u.e.$, respectively). This fact points out the major facility of **5** to achieve the transition state due to the contribution of C-2 positivized forms which are favored when electron-attracting groups are present at N-1 and may account for a transition state like **D**. Finally, eventual fall of the curves above (SO_4H_2) 4-5M may be due to extensive protonation of a substrate or to the retarding effect of decreasing water activity.

Electron-Releasing Groups at N-1.

In this case a different variation of the rate constants on increasing the acid concentration is observed (Figure 1). The attainment of bell-shaped curves indicates a change in the mechanism of the reaction on going to higher [H⁺]. Lower ranges of acid reactions (0.25-1.0M) present a first order dependence on hydrogen ion and a similar behavior to that revealed in Figure 2 (lines **4** and **5**). This implies a rapid equilibrium (Imidazoline)$\rightleftharpoons$(Intermediate) and a value much lower than unit for the first step. This fact and the dependence of the reaction on acid concentration allow to suggest, for the ascending side of the curves, a reaction scheme like III in which the mechanism would involve the acid catalyzed formation of the intermediate I^{2+} as the rate determining step of the reaction; $v = k [(A^{1+})][H^+]$.

Scheme III

On increasing [H⁺] it is observed that the appearance of **B** is initially delayed (Figure 2, dashed lines) and rate constants become lower. This fact indicates that the steady state equilibrium $A \rightleftharpoons I$ is not immediately achieved ($k_{-1} \sim k_1$) and reactions do not become first-order until that equilibrium is reached. These results demand that a new barrier appear between I^{2+} and **B** as the acid concentration is increased, $i.e.$, that a new step becomes rate determining at this point. This step must be a simple proton transfer [4] by acid to the intermediate I^{2+} (Scheme IV). As the acid concentration is increased the protonation of I^{2+}
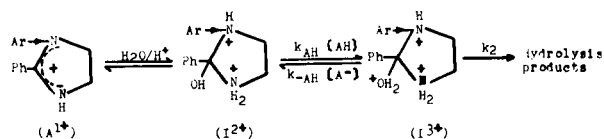
Scheme IV

will be more rapid than its opening and the decomposition of the intermediate becomes rate determining. This agrees with our results. Observed rate constants decrease and become pH independent at the right hand of the curves (Figure 1, compounds **1, 2** and **3**) where the reactions involve rate-determining decomposition of the tetrahedral addition intermediate.

Structure-Rate of Hydrolysis and Basicity Relationships.

A quantitative evaluation of the influence of substituents upon the reaction rates of hydrolysis was made through the Hammett approach [5].

If compound **3** is taken as a reference the plot of $\triangle pk_{obs}$ (Table II) for compounds **1-5** against Hammett σ-constants gave a straight line with $\delta = 1.78$, (r = 0.999, s = 0.06). The value of the slope relatively high points out a good transmission of substituent effects to the site of nucleophilic attack (C-2). Furthermore, the good correlation with Hammett σ-constants suggests the participation of inductive and mesomeric effects in the activation of the reaction site, a fact which supports the existence of regular coplanarity between the benzene ring at N-1 and the heterocyclic ring [6].

Relative rates in Table II indicate that electron-releasing substituents in the benzene ring at N-1 retard hydrolysis while electron-withdrawing groups accelerate it, and this is just opposed to our observations on the basic degradation [2]. This opposite behavior is explained in the actual case considering the contribution of mesomeric structures **E** which favor the attack by water on C-2 and lead to
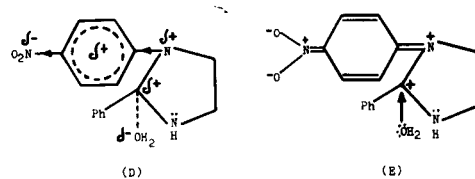

(D)   (E)

Table II

Observed and Calculated Rate Constants of Acid Hydrolysis of 1-Aryl-2-phenyl-2-imidazolines at 100°

Compound No.	σ [a]	σ_{im}	Relative Rate	$10^4 k_{obs}$/min⁻¹	$10^4 k'_{calcd}$/min⁻¹	$10^4 k''_{calcd}$/min⁻¹	pk''_{calcd}	pK_a [b]
1	-0.170	0.112	0.47	0.447	0.476	0.535	4.272	9.48
2	-0.153 [c]	-0.148	0.58	0.550	0.510	0.445	4.352	9.55
3	0.00	0.00	1.00	0.954	0.954	0.954	4.020	9.26
4	0.227	0.143	2.6	2.51	2.41	1.99	3.700	8.98
5	0.778	0.820	23.7	22.6	23.0	66.0	2.180	7.65

[a] Hammett substituent constants [5].   [b] Experimental values obtained in an earlier paper [1].   [c] $\Sigma\sigma$ which gives a better fit to the regression than σ_{found} value -0.117 [9].

five or tenfold higher rates of decomposition in compounds **4** and **5** (Table II).

Following the same theoretical development exposed in our study on the alkaline hydrolysis [2] we have obtained "calculated" rate constants k' (Table II), from the Hammett equation. But better agreement with real values is obtained (k''$_{calcd}$) when new effective substituent constants σ_{im} are used in such equation [7] which makes evident the close linear relationship between rate of hydrolysis and basicity, given by the expression

$$\log k_h = -1.14 \; pK_a -6.56$$

This equation allows to estimate "a priori" the stability of related compounds, under the same experimental conditions, having simply determined their ionization constants.

EXPERIMENTAL

1-Aryl-2-phenyl-2-imidazolines and *N*-Aryl-*N*'-benzoylethylenediamines.

These compounds were synthesized in our laboratory of Organic Chemistry [8] and conveniently purified to perform the kinetic studies.

Kinetic Measurements.

Kinetic runs were performed in sulfuric acid-water mixtures over the range 0.25-3.75 *M* at 100°. Disappearance of the imidazolines was followed by uv spectrophotometry in a Beckman DB-G Grating spectrophotometer, selecting the wavelength where degradation products did not absorb. Additional experiments confirmed the fulfillment of Beer's law at the selected wavelength. Reactions performed with initial concentrations of 2×10^{-3}-1×10^{-2} *M* showed a first-order dependence on the substrate at every acid concentration. All rate constants were obtained from 1×10^{-3} *M* initial concentrations of the imidazolines and reactions showed to be irreversible. First-order rate constants were calculated from plots of log(A-A∞) against time on semilogarithmic graph paper and the relationship $k_{obs} = 0.693/t\frac{1}{2}$.

General Kinetic Procedure.

Stock solutions of H$_2$SO$_4$-H$_2$O were prepared and substrates were dissolved to a concentration 1×10^{-3} *M*. These solutions were distributed into glass ampuls, hermetically sealed and placed in a water-refluxing bath. At known intervals (initially 5, 15, 30 and 60 minutes) ampuls were retired and suddenly cooled to 20°. Aliquots (1.25 ml) were transferred to a volumetric flask (25 ml) and made up to volume with distilled water to give final solutions 5×10^{-5} *M*. The *p*H of these solutions, always above

2.5, prevented any subsequent hydrolysis. The same procedure was followed with the hydrolytic solvent without imidazoline to prepare the blank solution. Absorbances at t∞ were spectrophotometrically obtained after several half-life times and absorbance at time zero was estimated by extrapolation.

Chromatographic Experiments.

Simultaneously with the uv kinetic procedures performed at *p*H values around zero reactions were followed on chromatoplates Hptlc Silica gel 60 F$_{254}$ (10 × 10 cm). Trichloroacetic acid-water solutions (1*M*) providing the same *p*H values as those for the kinetic runs were used as developing solvents. Reactions at H$_o$ = -0.18 (descending side of the bell-shaped curves in Figure 1) showed a partial transformation of substrate (compounds **1**, **2** and **3**) into the intermediate. After several hours the open product *N*-aryl-*N*'-benzoylethylenediamine appeared clearly. The intervals during which the open product was not detected were verified as the same as those occurring in curves of Figure 2 (dashed lines). Reactions were followed until 70-80% appearance of ethylenediamine derivative; however, the spots corresponding to imidazoline and the intermediate could still be observed (*i.e.*, k$_{-1}$ ‡ 0). At infinite time only degradation products were detected, (*i.e.*, k$_2$ = 0).

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[7] These σ_{im} were calculated from ionization of the imidazolines hydrochlorides (1) using the expression $\sigma_{im} = (pK_a^o - pK_a)/1.28$. Accordingly, a plot of the log (k_{obs}·k_{obs}^o) versus σ_{im} for compounds **1-5** gave $\delta = 0.32$; r = 0.9978; s = 0.01.

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