the quantitative work on the labeled and unlabeled *o*-tolyl azides, a slit width of 5 mils was used and the magnetic scan rate was such that the entire spectrum (from *m/e* 160 to *m/e* 28 in most cases) was determined in about 30 sec. For the quantitative work on *o*-tolyl azide, the slit width was set at 20 mils and the scan rate was such that a scan from *ca.* *m/e* 104 to 65 required about 30 sec, and flat-topped peaks were obtained. The high-resolution mass spectra were determined on a CEC-21-110B. All of the azides were known compounds, and their physical properties were in agreement with those reported in the literature. One representative synthesis (4-methyl-2-nitroazidobenzene) is reported here, as is the synthesis of *o*-tolyl azide-α-^{13}C in which the conditions were developed with unlabeled materials, such as to optimize the yields of the precious labeled product.

4-Methyl-2-nitroazidobenzene.—Sodium nitrite (2.8 g, 41 mmol) in water (25 ml) at 0–5° was added dropwise to a mixture of 4-methyl-2-nitroaniline (5.0 g, 33 mmol), concentrated sulfuric acid (6 ml), and water at 0–5°. Urea was added to remove the excess nitrous acid (starch–iodide paper) and the resulting solution was treated with activated charcoal for 30 min at 0°. Sodium azide (3.6 g, 55 mmol) in water (20 ml) at 5° was added slowly. The yellow precipitate which formed was filtered and dried. The solid was recrystallized from pentane to give 4-methyl-2-nitroazidobenzene (3.5 g, 60%), mp 36–38° (lit.[16] mp 35–36°).

Benzyl Alcohol-α-^{13}C.—Benzoic acid $^{13}CO_2H$ (*ca.* 62%) (3 g, 24.6 mmol) in dry ether (60 ml) was added to a 2 *M* solution of lithium aluminum hydride in ether (20 ml, 160 mmol) and the mixture was stirred and boiled under reflux for 24 hr. The cooled (0°) mixture was decomposed with 10% aqueous sodium hydroxide, filtered, dried, diluted with ether to 200 ml, and analyzed by gas chromatography using a 6 ft × $^3/_{16}$ in. column packed with SE-30 (20%) on Gas-Chrom Q (60–100 mesh) at 120° and a helium flow rate of 60 ml/min. *n*-Nonane was used as the internal standard. Yield of benzyl alcohol-α-^{13}C was 89%.

Toluene-α-^{13}C.—The above solution of benzyl alcohol (21.8 mmol) was boiled under reflux for 24 hr with sodium hydride (0.65 g, 27 mmol), cooled to −20°, and treated with *p*-toluenesulfonyl chloride (4.3 g, 22.6 mmol) in dry ether (70 ml, dried over molecular sieves) dropwise, with stirring at −20° for 2 hr and then at room temperature for 2 hr. A solution of 2 *M* lithium aluminum hydride (14 ml) in ether was added, and the mixture was stirred at room temperature for 3 hr and then boiled under reflux for 12 hr. Water (20 ml) and then 3 *N* HCl (100 ml) were added, and the ether layer was washed with water, dried, and evaporated to give toluene-α-^{13}C (67% yield).

***o*-Tolyl Azide-α-^{13}C.**—Toluene-α-^{13}C (1.0 g, 107 mmol) was added in one portion to 100% nitric acid (1 ml) in trifluoroacetic acid (25 ml) at 0°. The dark red-brown solution was allowed to stand for 1.5 hr by which time the color had almost totally disappeared. It was poured into water (250 ml) and the solution neutralized (Na_2CO_3 solid). The mixture was extracted with ether (two 150-ml portions), and the ethereal layer was washed (4% aqueous Na_2CO_3), dried, and evaporated to give a yellow oil (1.2 g) which was chromatographed on basic alumina (120 g). Elution with petroleum ether–benzene (97:3 v/v) gave pure (by glc) *o*-nitrotoluene-α-^{13}C (300 mg, 22% yield). Further elution gave a mixture of the ortho, meta, and para isomers (200 mg) and then the pure para isomer.

o-Nitrotoluene-α-^{13}C (300 mg, 2.2 mmol) was reduced with iron (3 g) in water (1.4 ml) and acetic acid (0.2 ml) to give the pure toluidine (glc) (180 mg, 76%). This was diazotized at 0°, the excess nitrous acid was destroyed with urea, and the solution was treated with ether (2 ml) and then NaN_3 (184 mg) in water (0.8 ml). Extraction with ether, washing the ethereal extract with 10% NaOH (2 × 5 ml), drying, and concentration gave the desired azide as a yellow liquid (67 mg, 30%), bp 28–30° (20 μ).

Registry No.—*o*-Nitrophenyl azide, 1516-58-1; benzofuroxan, 480-96-6; *m*-methoxyphenyl azide, 3866-16-8; *o*-methoxyphenyl azide, 20442-97-1; *p*-methoxyphenyl azide, 2101-87-3; 2-azidobiphenyl, 7599-23-7; 3-azidobiphenyl, 14213-01-5; 4-azidophenyl, 31656-91-4; *o*-tolyl azide, 31656-92-5; *m*-tolyl azide, 4113-72-8; *p*-tolyl azide, 2101-86-2.

Acknowledgments.—This work was supported by an NSF Grant, GP 18557. We thank Merck & Co. for a gift of 2 g of benzoic acid $^{13}CO_2H$.

Notes

The Mechanism of Acid Hydrolysis of Imidazolines

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Recently Haake and Watson[1] have proposed that amidines (and related strong bases) hydrolyze by nucleophilic attack by water on the diprotonated amidines. Their proposal was based on (1) the rate of hydrolysis of the strong base lysidine, 2-methylimidazoline (pK_a = 11),[2] being linearly dependent on acid concentration with a rate maximum at 10–12 *M* sulfuric acid which suggests a transition state consisting of a lysidinium ion, a proton, and water and (2) the large downfield shift in the nmr signals of lysidinium ion in sulfuric acid more concentrated than 102%, which suggests protonation of lysidinium ion to a dication. Because of its novelty, we undertook additional experiments to test the validity of the proposed mechanism. The results, which are reported in this paper, were all consistent with the proposed mechanism.

(1) P. Haake and J. W. Watson, *J. Org. Chem.*, **35**, 4063 (1970).
(2) R. B. Martin and A. Parcell, *J. Amer. Chem. Soc.*, **83**, 4830 (1961).

Experimental Section

Ultraviolet spectra were determined on a Cary Model 15 recording spectrometer. Nmr spectra were determined on a Varian T-60 spectrometer. Acid solutions were standardized as previously described.[1]

2-(*m*-Nitrophenyl)imidazoline.—To 7 ml of concentrated sulfuric acid cooled by an ice bath, 1.72 g of 2-phenylimidazoline was added; 7 ml of concentrated nitric acid was added dropwise to the cooled, stirred solution. The ice bath was removed and the solution was slowly heated to 60° and its temperature maintained at 60° for 10 min. The reaction mixture was then cooled by means of an ice bath and made alkaline with 50% potassium hydroxide. The precipitate was collected and purified by recrystallization from benzene. A yield of 1.2 g, mp 155–156°, was obtained: nmr (CCl_4) τ 1.4–2.8 (4.0 H, multiplet), 5.4 (1.2 H, singlet), τ 6.2 (4.0 H, singlet). Hydrolysis of this compound

gave *m*-nitrobenzoic acid (identified by melting point and nmr spectrum).

The procedure of Sawa, *et al.*,[3] was employed to prepare lysidine and the other 2-arylimidazolines in yields of 40–60%. Melting points and nmr spectra were consistent with the proposed structures: **lysidine**, recrystallized from benzene and vacuum sublimed, mp 101–102° (lit.[1] mp 103°); **2-(*p*-methylphenyl)-imidazoline**, recrystallized from benzene and vacuum sublimed, mp 182–183° (lit.[4] mp 183°); **2-(*p*-methoxyphenyl)imidazoline**, recrystallized from benzene, mp 138–139° (lit.[5] mp 140°); **2-(phenyl)imidazoline**, recrystallized from benzene and vacuum sublimed, mp 102–103° (lit.[5] mp 103°); **2-(*p*-chlorophenyl)-imidazoline**, recrystallized from benzene, mp 185–186° (lit.[5] mp 187°).

Kinetic Method.—The determination of the rates of lysidine hydrolysis by ultraviolet spectroscopy was as previously described.[1]

During the course of the hydrolysis of the 2-arylimidazoline in 9 *M* H_2SO_4 the methylene singlet at ~4.3 ppm upfield from the solvent peak progressively decreased in strength as a new signal arose at 0.5 ppm further upfield. The second signal was confirmed by nmr spectroscopy to be due to ethylene diammonium ion. The extent of hydrolysis was taken equal to $A_{4.3}/(A_{4.3} + A_{4.8})$, where $A_{4.3}$ and $A_{4.8}$ are the areas of the signals at 4.3 and 4.8 ppm from the solvent signal. Plots of ln $A_{4.3}/(A_{4.3} + A_{4.8})$ *vs.* time were linear for four to five points covering approximately two half-lives; the slopes were taken equal to the first-order rate constant. During the course of the hydrolysis of the 2-arylimidazolines, the arylcarboxylic acids (confirmed by melting points and nmr spectra) precipitated from solution and were removed by filtration before the extent of hydrolysis was determined by nmr. The initial concentration of the 2-arylimidazolines was approximately 0.2 *M*.

For the nmr determination of the rate of hydrolysis of lysidine in 4 *M* H_2SO_4, the method was the same as that for the arylimidazolines above. However, in 14 *M* H_2SO_4, because the signal due to ethylenediammonium ion is too broad to permit the accurate determination of its area and that of the methylene protons of lysidine separately, the areas of the methyl signlets of lysidine and the hydrolysis product acetic acid were employed to determine the extent of reaction. The initial concentration of lysidine was approximately 0.35 *M*.

Results and Discussion

The first-order rate constants listed in Tables I–III are the average of at least two determinations which agreed with one another to within 10%. The close similarities of the rates determined by the ultraviolet and nmr methods provides additional support for the view that the reaction which was followed is the hydrolysis of lysidine to acetic acid and ethylenediammonium ion.

TABLE I

OBSERVED FIRST-ORDER RATE CONSTANTS FOR HYDROLYSIS OF LYSIDINE IN SULFURIC ACID

Acid	Molarity	Temp, °C	10^5k_1, sec^{-1}
H_2SO_4	4	90.0	0.190[a]
H_2SO_4	4	90.0	0.210[b]
D_2SO_4	4	90.0	0.282[a]
D_2SO_4	4	90.0	0.284[b]
H_2SO_4	4	99.9	0.503[c]
H_2SO_4	4	108.0	0.899[b]
H_2SO_4	14	90.0	0.219[a]
H_2SO_4	14	90.0	0.227[b]
D_2SO_4	14	90.0	0.284[b]
H_2SO_4	14	99.9	0.55[c]
H_2SO_4	14	108.0	0.885[b]

[a] Rates determined by uv method. [b] Rates determined by nmr method. [c] Data from ref 1.

TABLE II

OBSERVED FIRST-ORDER RATE OF HYDROLYSIS OF LYSIDINE IN DIFFERENT ACIDS AT 90.0° [a]

Acid	H_0[b]	Log a_{H_2O}[c]	10^5k_1, sec^{-1}
3.5 *M* $HClO_4$	−1.47	−0.106	0.0663
3.5 *M* H_2SO_4	−1.62	−0.111	0.181
4 *M* HCl	−1.40	−0.107	0.207

[a] Rates determined by uv method. [b] M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957). [c] J. F. Bunnett, *J. Amer. Chem. Soc.*, **83**, 4956 (1961).

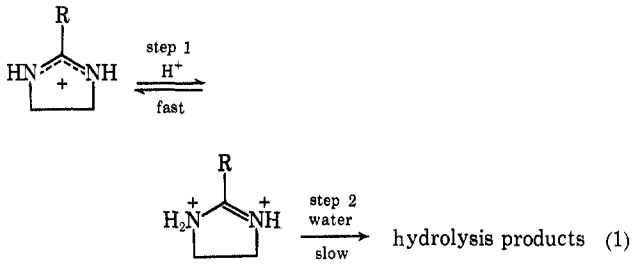
TABLE III

OBSERVED FIRST-ORDER RATE CONSTANTS FOR HYDROLYSIS OF 2-ARYLIMIDAZOLINES IN 9 *M* H_2SO_4 AT 138.5°

2-Aryl group	Registry no.	σ^+ value[a]	10^5k_1, sec^{-1}
p-Methoxyphenyl	6302-84-7	−0.764	1.26
p-Methylphenyl	13623-58-0	−0.306	1.40
Phenyl	936-49-2	0.00	1.45
p-Chlorophenyl	13623-52-4	0.112	1.40
m-Nitrophenyl	31659-42-4	0.662	1.37

[a] Of aryl substituent: K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1964, p 140.

The mechanism proposed in eq 1 for the acid hydrolysis of lysidine consists of the protonation of lysidinium ion[2] (pK_a = 11) in a preequilibrium step to a strongly acidic dication [half conversion of lysidinium ion to the dication occurs in >102% H_2SO_4 (H_0 < −13)] which undergoes rate-determining nucleophilic attack by water.



Because this proposed mechanism is in essence an A2 mechanism[6]—fast equilibrium protonation of the substrate followed by rate-determining nucleophilic attack by water—and consequently requires that the hydrolysis rates respond to reaction conditions and substituent effects in a manner similar to that of other A2 reactions, we have tested the proposed mechanism by determining catalyzing acid, temperature, solvent isotope, and substituent effects on the rate of hydrolysis.

Substituent Effect.—The mechanism of eq 1 predicts that the electronic effects of the substituent R on the rate of hydrolysis should be small if step 2 involves nucleophilic addition of water to the dication at the 2 position. The very similar rates of hydrolysis of the 2-arylimidazolines (Table III) yield a ρ value of essentially zero, which is consistent with the ρ values for related A2 mechanisms. For example, ρ values of 0.144 and −0.222 are observed for the acid hydrolysis of ethyl benzoates and benzamides, respectively, in

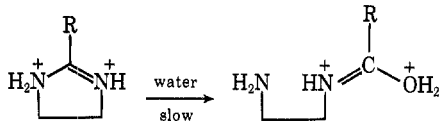
(3) N. Sawa, S. Kishizoe, K. Naga, M. Kuriyama, Y. Tsujino, and T. Shimamura, *Chem. Abstr.*, **63**, 11820c (1965).

(4) A. J. Hill and S. R. Aspinal, *J. Amer. Chem. Soc.*, **61**, 822 (1939).

(5) P. Oxley and W. F. Short, *J. Chem. Soc.*, 497 (1947).

(6) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter XIV.

60% aqueous ethanol at 100°.[7] It would seem quite unlikely that negligible electronic effects on the rate of hydrolysis would be obtained if step 2 consisted of a direct displacement reaction by water.



Because the protonation step should exhibit a negative ρ value (protonation of substituted acetophenones has a ρ^+ value of between -2.0 and -3.0[8]) and the direct displacement step should have a negligible ρ value,[9] the overall ρ value for the reaction should be significant and negative. For example, the acid-catalyzed hydrolysis of 2-aryl-1,3-oxathiolanes, which is considered to proceed by an A2 mechanism involving a rate-determining direct displacement by water step, has a ρ value of -1.66.[10]

Acid Effect.—It has been observed that for solutions of similar water activities (and acidity) that the rates of A2 reactions are faster in hydrochloric and sulfuric acids than in perchloric acid, while the reverse is observed for A1 reactions.[11] The data of Table II indicate that the relative rates of hydrolysis of lysidine in the indicated concentrations of perchloric, sulfuric, and hydrochloric acids are 1:2.7:3.1. This order is consistent with that observed for other A2 reactions—for both amides[11b] and esters[11c] the rates of hydrolysis are twice as fast in 4 M sulfuric acid as in 4 M perchloric acid.

Solvent Isotope Effect.—The solvent deuterium isotope effects, $k_{H_2SO_4}/k_{D_2SO_4}$, of 0.71 and 0.78 on the rates of hydrolysis of lysidine in 4 and 14 M sulfuric acid (Table I) are consistent with an A2 reaction in which the preequilibrium protonation of the substrate is fast and incomplete.[10,12] These isotope effects therefore confirm the previous proposal (based on nmr data which indicated that lysidinium ion is significantly protonated only in solutions more acidic that 102% sulfuric acid) that the inverse dependence of lysidine hydrolysis rate on acid concentration above 12 M sulfuric acid is not due to substantial conversion of the substrate to the reactive dication but to the retarding effect of decreasing water activity outweighing the accelerating effect of increasing medium acidity.[1]

In contrast to lysidine, the hydrolysis of acetamide exhibits a solvent isotope effect $[k(H)/k(D)]$ of 0.7 in 0.1 N acid where acetamide is incompletely protonated and an isotope effect of 1.1 in 4 N acid where it is essentially completely protonated.[12]

Entropies of Activation.—Because of their large orientation and steric requirements, A2 reactions have entropies of activation of approximately -15 to -30 eu.[13] For example, the A2 hydrolyses of acetamide, ethyl acetate, and 2-phenyl-1,3-oxathiolane have entropies of activation of -37, -23, and -18 eu, respectively.[10,13]

From the second-order rate constants $k_1/[H_2SO_4]$ calculable from the data of Table I, entropies of activation of -26 and -31 (± 4) eu may be calculated for the hydrolysis of lysidine in 4 and 14 M sulfuric acid (the corresponding enthalpies of activation are 22 and 21 kcal/mol, respectively). These entropy values, being similar to those for known A2 reactions, are consequently consistent with the mechanism of eq 1.

Thus the four mechanistic criteria which we have applied to the acid hydrolysis of the imidazolines have given results which, being consistent with the results expected for an A2 hydrolysis mechanism, provide evidence for the hydrolysis proceeding as outlined in eq 1. The negligible electronic effects on the rates of hydrolysis of the two arylimidazolines provide good evidence for the proposition that step 2 of eq 1 represents rate-determining nucleophilic addition of water to the dication at position 2 to form a tetrahedral addition intermediate which decomposes to the hydrolysis products (or reverts to reactants by loss of water from the dication).

Additional work in this laboratory has provided similar evidence in support of Haake and Watson's[1] proposal that guanidines also hydrolyze by an A2 mechanism analogous to that of eq 1.[14]

Registry No.—Lysidine, 534-26-9.

Acknowledgments.—We are grateful to the National Institutes of Health for support of this research.

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The Mechanism of Acid Hydrolysis of Guanidines

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Received April 13, 1971

On the basis of the nmr spectra of lysidine, 2-methylimidazoline, in concentrated sulfuric acid solutions and the curvilinear dependence of the rate of hydrolysis of lysidine on sulfuric acid concentration, Haake and Watson proposed that imidazolines and similar strong bases, such as guanidines, hydrolyze in acid solutions by rate-determining nucleophilic attack by water on the diprotonated substrate.[1] In a recent paper we have reported additional data which support their proposed mechanism for the acid hydrolysis of amidines.[2] We report in this communication experimental results which indicate that guanidines hydrolyze by an analogous mechanism as proposed by Haake and Watson[1] (eq 1).

The rates of hydrolysis of 1,1,3,3-tetramethylguanidine, TMG, and its expected hydrolysis products, 1,1-dimethyl- and tetramethylureas, were determined by nmr spectroscopy by following the disappearance of the substrate methyl singlet and the formation of the

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