function. The different photochemistry of the 1-acyl-7-nitroindolines **1** cannot, however, be attributed to the additional substituent X (X = Br or NO_2). This is corroborated by our finding that 1-benzoyl-6-bromo-8-nitrotetrahydroquinoline and 1-benzoyl-6,8-dinitrotetrahydroquinoline did not undergo photosolvolysis upon irradiation in methanol or ethanol, but afforded free benzoic acid in 85% yields (unpublished results), thus behaving as 1-acyl-8-nitrotetrahydroquinolines[3] which bear no substituents.

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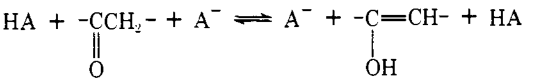
The Lack of Concertedness in the General Acid-Base Catalysis of the Enolization of Oxalacetic Acid. A Case for Stepwise Nucleophilic-General Base Catalysis

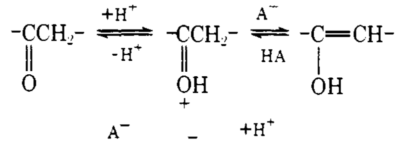
Sir:

Since the early studies of Dawson and Spivey[1] on the enolization of acetone, chemists have been concerned with the question of concerted general acid-general base (eq 1)

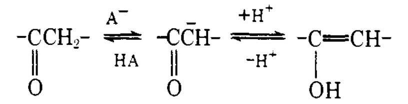


$$\mathrm{HA} + \underset{\displaystyle\mathrm{O}}{\underset{\|}{\mathrm{-C}}}\mathrm{CH_2-} + \mathrm{A^-} \rightleftharpoons \mathrm{A^-} + \underset{\displaystyle\mathrm{OH}}{\underset{|}{\mathrm{-C}}}\mathrm{{=}CH-} + \mathrm{HA} \qquad (1)$$

as compared to stepwise general acid and general base catalysis (eq 2 and 3) in enolization reactions.[2] These con-



$$\underset{\displaystyle\mathrm{O}}{\underset{\|}{\mathrm{-C}}}\mathrm{CH_2-} \underset{\mathrm{-H^+}}{\overset{\mathrm{+H^+}}{\rightleftharpoons}} \underset{\displaystyle\overset{+}{\mathrm{OH}}}{\underset{\|}{\mathrm{-C}}}\mathrm{CH_2-} \underset{\mathrm{HA}}{\overset{\mathrm{A^-}}{\rightleftharpoons}} \underset{\displaystyle\mathrm{OH}}{\underset{|}{\mathrm{-C}}}\mathrm{{=}CH-} \qquad (2)$$



$$\underset{\displaystyle\mathrm{O}}{\underset{\|}{\mathrm{-C}}}\mathrm{CH_2-} \underset{\mathrm{HA}}{\overset{\mathrm{A^-}}{\rightleftharpoons}} \underset{\displaystyle\mathrm{O}}{\underset{\|}{\mathrm{-C}}}\overset{-}{\mathrm{C}}\mathrm{H-} \underset{\mathrm{-H^+}}{\overset{\mathrm{+H^+}}{\rightleftharpoons}} \underset{\displaystyle\mathrm{OH}}{\underset{|}{\mathrm{-C}}}\mathrm{{=}CH-} \qquad (3)$$

cerns have revolved around the feasibility of concerted motion of heavy and light atoms in a single transition state[3,4] and the actual experimental detection of kinetic terms containing the concentration of ketone, general acid, and general base (i.e., $k_{ab}[\mathrm{K}][\mathrm{AH}][\mathrm{A^-}]$). The most convincing experimental evidence for a $k_{ab}[\mathrm{K}][\mathrm{AH}][\mathrm{A^-}]$ term has appeared to be that of Banks[5,6] for the enolization of oxalacetic acid (OA).[7] The present communication describes the most pertinent aspects of our reinvestigation of the enolization of OA. We find no evidence for concertedness in the reaction in the presence of buffers such as phosphate and imidazole as claimed by Banks.[6] In the presence of tertiary amines, the enolization of OA occurs via a mechanism ascribable to stepwise carbinolamine formation followed by general base catalyzed elimination of amine. To the knowledge of the investigators, nucleophilic catalysis has not been previously reported as a mechanism for enolization.

The rates of enolization of OA in water at 30 °C and μ = 0.5 (KCl) were determined using a stopped-flow spectrophotometer. Increase in absorption at 270 nm due to formation of the enol was monitored with 11 different buffer systems, with each buffer being investigated at two-four different pH values. The buffer dilution plots obtained with imidazole are given in Figure 1. If a concerted reaction were involved a plot of k_{obs} vs. [Imidazole] would exhibit upward curvature. There is no evidence of any upward curvature in this or in any of the other buffer dilutions obtained for this study. In the insert to Figure 1 is plotted Banks' data at pH 7.12 for imidazole (T = 1.5 °C, μ = 0.1). The positive deviation of the rate at 0.20 M total buffer and less marked positive deviations in other buffer dilution plots were responsible for the report of the operation of a concerted mechanism.[6] The evidence for the concerted mechanism, therefore, is less than convincing.[7] Since the experiments of Banks were carried out at low temperature, we investigated the reaction of imidazole at 3.8 °C (pH 7.12, μ = 0.5) at concentrations up to 1.0 M. The plots of k_{obsd} vs. [imidazole] obtained evidence linearity up to 0.2 M (slope = 0.16) followed by downward curvature leading to a slope of 0.04. This break in the buffer dilution plot is suggestive of intermediate carbinolamine formation as is seen with OA and tertiary amines at 30 °C (see below). As with imidazole at 30 °C, k_{obsd} is a linear function of [buffer] when phosphate and carbonate buffers are employed [0.02-0.20 M] at this temperature. The second-order rate constants for the general base catalysis of the mechanism of

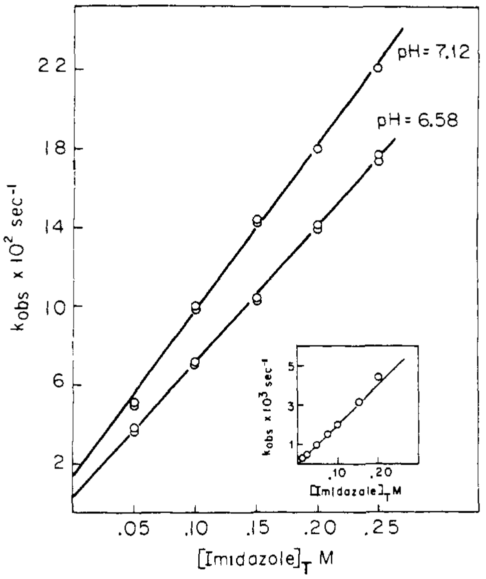


Figure 1. Plots of the observed first-order rate constants for the reaction of oxalacetic acid with imidazole (H_2O, μ = 0.5, 30 °C) vs. the total concentration of imidazole at two hydrogen ion concentrations. Insert to figure: data reported by Banks for the reaction of oxalacetic acid with imidazole (H_2O, μ = 0.1, 1.5 °C, pH 7.12).[6]

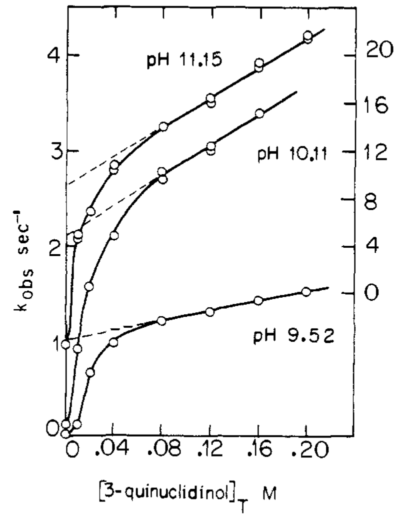
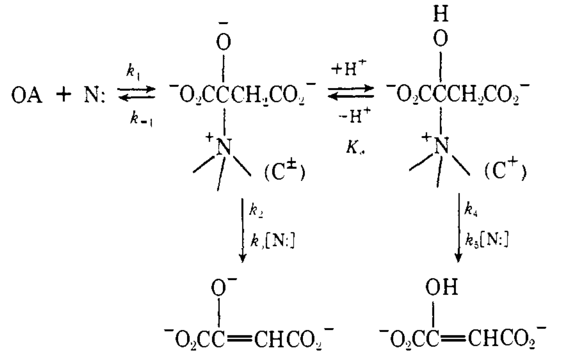


Figure 2. Plots of the observed first-order rate constants for the reaction of oxalacetic acid with 3-quinuclidinol (H_2O, μ = 0.5, 30 °C) vs. the total concentration of 3-quinuclidinol at three pH values. The pK_a of 3-quinuclidinol is 10.11. Left-hand axis pertains to experiments at 9.52 and 10.11 while the right-hand axis pertains to experiments at pH 11.15. Intercepts of dashed lines at [amine] = 0 provides k_{obsd} values for lyate species catalysis of the enolization of carbinolamine species. These values are seen to greatly exceed the k_{obsd} values for lyate species catalysis of enolization of OA.

eq 3 are 0.26, 0.49, 1.9, 13, and 460 $M^{-1}\ s^{-1}$ for HPO_4^{2-}, Im, CO_3^{2-}, PO_4^{3-}, and HO^- giving a Bronsted β of 0.35. A $-\alpha$ value of 0.43 is obtained for the general acid catalyzed mechanism of eq 2; the second-order rate constants are 1.4, 2.3, 11, and 9000 $M^{-1}\ s^{-1}$ for ImH^+, $H_2PO_4^-$, pyridine-H^+, and H_3O^+, respectively.

More than general acid-base catalysis is involved in the catalysis of the enolization of OA by tertiary amines in water (30 °C, $\mu = 0.5$).[8] Plots of k_{obsd} vs total amine concentration ($[N]_T = [N:] + [NH^+]$) exhibit a break with k_{obsd} becoming first order in $[N]_T$ at its higher values (Figure 2). Extrapolation of the upper portion of the curves, where k_{obsd} is a linear function of $[N]_T$, to $[N]_T = 0$ provides intercepts which are from 25- to 500-fold greater (depending upon the pH) than the value of k_{obsd} for enolization at the same pH but in the absence of amine and other buffer species.[9] This finding establishes that OA and tertiary amine form an intermediate species which yields enol on reaction with additional amine (the addition intermediate is required to be along the reaction path). The addition elimination mechanism of eq 4 is proposed.[10] At any constant pH the mechanism of eq 4 prescribes (by assuming either steady-state or preequilibrium formation of $C^{\pm}$ and C^+) a rate equation of the mathematical form of eq 5. At



(4)

$$k_{obsd} = \frac{K_I[N]^2 + K_{II}[N]}{1 + K_{III}[N]} \tag{5}$$

values of [N] where the reaction becomes first order in this species (i.e., $K_{III}[N] > 1$), eq 6 pertains. In eq 6, K_I/K_{III} =

$$k_{obsd} = \frac{K_I[N]}{K_{III}} + \frac{K_{II}}{K_{III}} \tag{6}$$

k_1 [steady state] or $(k_3K_a + k_5a_H)/(K_a + a_H)$ [preequilibrium formation of carbinolamines] while K_{II}/K_{III} = $(k_1k_2K_a + k_4a_H)/(k_3K_a + k_5a_H)$ [steady state] or $(k_2K_a + k_4a_H)/(K_a + a_H)$ [preequilibrium]. Assuming preequilibrium formation of carbinolamine at high [N] and employing a pK_a for C^+ of 11.3, determined by the ρ_I method as used by Fox and Jencks,[11] the values of k_3 and k_5 may be calculated from the data of Figure 2 to be 151 ± 3 $M^{-1}\ s^{-1}$ and 7.4 ± 3 $M^{-1}\ s^{-1}$, respectively. Extrapolation of the linear portion of the plots of Figure 2 at high [N] to [N] = 0 (dashed lines in Figure 2) provides the term K_{II}/K_{III} of eq 6. By employing $pK_a = 11.3$ and the known pH, the values of k_2 and k_4 may be approximated as 22 ± 2 s^{-1} and 0.70 ± 0.10 s^{-1}, respectively. These results establish that at high [N] the carbinolamines and ketone are in equilibrium and that the rate determining steps are amine (k_3 and k_5) and water catalyzed (k_2 and k_4) proton abstraction from carbinolamine. That $k_3 > k_5$ and $k_2 > k_4$ require that the negative charge on the carbinolamine oxygen provides considerable driving force for the elimination of amine. The details of the mechanism for the enolization of oxalacetate and its diethyl ester in the presence of oxyanion bases and tertiary amines will be given in a full paper.

Acknowledgment. This research was supported by a grant from the National Institutes of Health.

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(2) For a historical review see T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms", Vol. I, W.A. Benjamin, New York, N.Y., 1966, p 334.
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(6) B. E. C. Banks, *J. Chem. Soc.*, 63 (1962).
(7) E. S. Hand and W. P. Jencks report that the enolization of cyclohexanone exhibits a $k_m[CH_3COOH][CH_3COO^-]$[ketone] term at pH = pK_a of CH_3COOH and when $[CH_3COOH + CH_3COO^-]$ values up to 2 M are employed (unpublished data).
(8) Tertiary amines employed were quinuclidine, 3-quinuclidinol, 3-chloroquinuclidine, 3-quinuclidinone, trimethylamine, triethylamine, and pyridine. Of these only pyridine failed to act as a nucleophilic catalyst.
(9) Determined by employing a pH-stated spectrophotometric cell.
(10) In the reaction scheme of eq 4 amine catalyzed enolization of ketone has been ignored. Inclusion of this pathway provides a kinetic equation identical in form with that of eq 5. Most importantly, however, if amine catalysis through carbinolamine species is ignored and enolization of ketone by amine and/or lyate species is considered then a rate equation is obtained which does not accommodate the experimental results.
(11) J. P. Fox and W. P. Jencks, *J. Am. Chem. Soc.*, **96**, 1436 (1974).

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A ^{205}Tl Nuclear Magnetic Resonance Method of Determining Solvation Effects on Alkali Ion Selectivity

Sir:

The thallous ion has been proposed as a probe of the role of the alkali ions in biological systems[1-4] because its chemistry is like that of the alkali ions[5] and because of the comparative spectroscopic ease with which the thallous ion can be monitored. Two types of applications have been successful. One is the use of Tl^+ as a structural probe where the effect of a paramagnetic ion on the Tl^+ relaxation time is used to deduce the distance between the Tl^+ and the paramagnetic ion binding sites.[6,7] The other utilizes the quenching of Tl^+ luminescence upon complexation to determine the relative binding constants of the alkali ions through competition with the Tl^+.[8] Neither method yields information about the nature of the ligands comprising the binding site. The latter method is limited to methanol and water solutions because of the quenching of Tl^+ luminescence by most other solvents.[8]

We report here the use of the Tl^+ NMR chemical shift as a method which not only provides the relative binding constants of alkali ions but may also be useful in determining the type of donor atoms which comprise the binding site. The binding constants can be determined in a variety of solvents allowing the effect of ionic solvation on the ion selectivity to be measured. The chemical shift of the bound thallous ion is often diagnostic of the type of donor ligands involved in binding.[9,10]

The relative stability constants are calculated from eq 1.

$$K^M/K^{Tl} = \frac{P\{[I]_{tot} - (1 - P)[Tl^+]_{tot}\}}{(1 - P)\{[M^+]_{tot} - [I]_{tot} + (1 - P)[Tl^+]_{tot}\}} \tag{1}$$

$[I]_{tot}$ and $[M^+]_{tot}$ are the total concentrations of ionophore and of added alkali ion, respectively. The population of uncomplexed Tl^+, P, is calculated from the chemical shift information as shown in eq 2.