The purified mixed sulfides were transformed ($H_2O_2$–HOAc) into the mixed sulfones. Pure sulfone isomers (mp 88–89 and 139–140°; *cf.* ref 3a) were isolated by fractional crystallization (1:3 $Et_2O$–pentane). The $SO_2$ bands were identical (in $CS_2$: 1312, 1135 $cm^{-1}$), as were their other ir bands, but their nmr chemical shifts were sufficiently different to allow isomer distinguishability but not configurational assignment.[3a]

From another portion of distillate each sulfide was isolated by vpc[5] but their respective configurations were not obvious even though their chemical shifts also were quite different.[3b] Each sulfide was cautiously oxidized to its sulfoxide (1 equiv of $H_2O_2$ in HOAc, 0–5°)[7] as well as sulfone. The sulfide of lower retention time provided the sulfoxide (S–O, neat, 1040 $cm^{-1}$) that clearly exhibited proton nonequivalence[8] and the sulfone that was identical with that melting at 89°. This series was assigned the *dl* configuration. The other sulfide yielded the sulfoxide (S–O, neat, 1033 $cm^{-1}$) exhibiting equivalent signals for both methyl groups as well as methine protons, respectively, and the sulfone identical with that melting at 140°. This series was assigned the *meso* configuration.[9]

We have observed striking differences in the reactivity of the two sulfones which now can be directly related to their respective configurations.[13] This is especially important in light of the opposite tentative assignments recently reported.[3a] Assignments to other diastereomers by this method are now being investigated.

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(7) The absence of sulfide was verified by vpc and nmr, and of sulfone by ir and nmr.

(8) As would be expected from nonequivalent dimethyl substituents their shifts were different but their areas were equal. It is highly unlikely that the nonequivalence represented the two *meso* sulfoxides formed in exactly equal amounts.[9] If this were so, moreover, the sulfoxide exhibiting proton equivalence would be the *dl* isomer, also highly unlikely.

(9) It is strongly suspected that the less hindered of the two possible *meso* sulfoxides was formed preferentially: (1) *cf.* the exclusive formation of one *meso*-2-butene episulfoxide (depicted as *anti*)[10] and the 24:1 selectivity in *meso* sulfite esters.[4c] (2) The *meso* sulfoxide was unchanged when treated with polyphosphoric acid, a rapid sulfoxide epimerization agent.[11] (3) No sulfoxide resulted when the *meso* sulfide was treated with *t*-BuOCl in *t*-BuOH, a sulfide oxidation agent whose two-step mechanism for S–O bond formation apparently requires a minimum approach barrier from *both* sides of the sulfur atom.[12]

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## The Acetylpyridinium Ion Intermediate in Pyridine-Catalyzed Acyl Transfer[1]

*Sir:*

We wish to report the direct observation of the formation and disappearance of an acetylpyridinium ion intermediate in the course of the pyridine-catalyzed hydrolysis of acetic anhydride in aqueous solution (eq 1). It has been generally believed that this intermediate is too unstable to permit its accumulation in easily detectable concentrations,[2,3] although the inhibition of the over-all reaction by acetate ion, the rapid reaction rate, and the even faster pyridine-catalyzed exchange of labeled acetate into acetic anhydride provide strong kinetic evidence for such an intermediate.[4] Similarly, inhibition of the pyridine-catalyzed hydrolysis of substituted phenyl acetates by low concentrations of the leaving phenolate ion provides evidence for the same intermediate in these reactions.[5] Estimates of the expected kinetic and thermodynamic stability of the acetylpyridinium ion, based on equilibrium and rate constants for reactions of acetylimidazolium and phosphorylpyridinium ions,[6] led us to search for direct evidence for its formation.

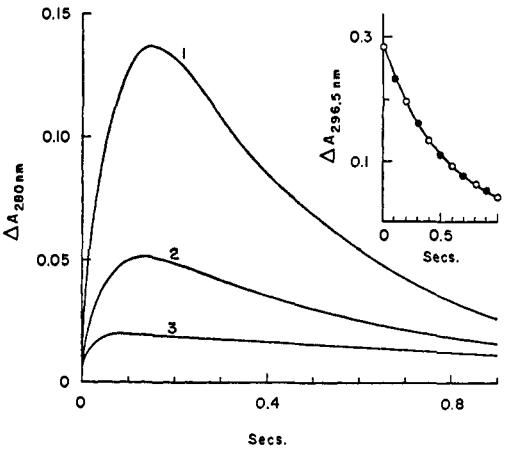


Figure 1. The formation and hydrolysis of acetylpyridinium ion, followed at 280 nm, during the hydrolysis of $2 \times 10^{-4}$ *M* acetic anhydride catalyzed by pyridine buffer (0.06 *M* free base, pH 5.5) at 25°, ionic strength 1.0, maintained with potassium chloride. Added sodium acetate: curve 1, $4 \times 10^{-3}$ *M*; curve 2, $10^{-2}$ *M*; curve 3, $5 \times 10^{-2}$ *M*. Inset: the disappearance of $10^{-3}$ *M* (open circles) and $5 \times 10^{-4}$ *M* (closed circles) *p*-anisidine in the presence of $10^{-4}$ *M* acetic anhydride and pyridine buffer (0.02 *M* free base, pH 6.5), followed at 296.5 nm, ionic strength 1.0, 25°.

$$\mathrm{Pyr} + \mathrm{Ac_2O} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{AcPyr^+} + \mathrm{AcO^-} \xrightarrow{k_2} \mathrm{Pyr} + \mathrm{AcOH} \qquad (1)$$

The formation and subsequent disappearance of this intermediate may be followed spectrophotometrically at 280–290 mμ after mixing aqueous solutions of pyridine and acetic anhydride in a stopped-flow apparatus (Figure 1). Increasing concentrations of acetate ion decrease the amount of acetylpyridinium ion formation by increasing the rate of the back reaction ($k_{-1}$, eq 1). Increasing pyridine concentration was found to increase

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the rate and amount of intermediate formation. Kinetic analysis of these data[7] gave the following approximate values for the rate constants of eq 1 at ionic strength 1.0: $k_1$, 80 $M^{-1}$ sec$^{-1}$; $k_{-1}$, 900 $M^{-1}$ sec$^{-1}$; $k_2$, 7.5 sec$^{-1}$. The value of $k_2$ is extrapolated to zero pyridine and acetate concentrations to correct for buffer catalysis of the hydrolysis of the intermediate.

The pyridine-catalyzed acetylation of $5 \times 10^{-4}$ and $10^{-3}$ $M$ anisidine by acetic anhydride follows a pseudo-first-order course with a rate constant which is independent of anisidine concentration (Figure 1, inset). This shows that this acyl transfer reaction occurs through a rate-determining formation of the acetylpyridinium ion intermediate. The second-order rate constants of 83 and 78 $M^{-1}$ sec$^{-1}$ obtained by the use of anisidine and toluidine, respectively, as trapping reagents agree with the value of $k_1$ obtained from the hydrolysis experiments.

The rate of acetylpyridinium ion hydrolysis is decreased 700-fold to 0.01 sec$^{-1}$ in 9 $M$ sodium perchlorate. This large salt effect is similar to that observed with acetylimidazolium ion.[8] The rate constants for the hydrolysis of acetylpyridinium chloride, synthesized at $-60°$,[9] may be determined directly in sodium perchlorate solutions and fall on the same straight line in a plot of log $k$ against salt concentration as those for the hydrolysis of the intermediate formed during the pyridine-catalyzed hydrolysis of acetic anhydride.

The molar extinction coefficient of acetylpyridinium ion at 280 nm in 1 $M$ potassium chloride and 4 and 6 $M$ sodium perchlorate solutions was estimated to be $3.2 \times 10^3$ from the results of kinetic experiments. Difference spectra, corrected for changes in pyridine concentration, gave absorption maxima at 272 nm ($\epsilon$ *ca.* $4.3 \times 10^3$) and 225 nm ($\epsilon$ *ca.* $7 \times 10^3$); compare 3-acetylpyridinium chloride, $\lambda_{max}$ 269 nm ($\epsilon$ $3.9 \times 10^3$) and 224 nm ($\epsilon$ $5.8 \times 10^3$) in ethanol.[10]

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## Gas-Phase Acidities of Amines

*Sir:*

We wish to report the relative gas-phase acidities of some simple aliphatic amines and ammonia.[1] The results parallel those found in our previous studies of alcohols[1b] in that the acidities of primary amines increase with increasing alkyl substitution. Thus, the phenomenon of increasing electron affinity of radicals with increasing substitution appears to be general for simple saturated systems. By virtue of the N–H bond strength differences between primary and secondary amines we can, for the first time, derive an estimate of the magnitude of the stabilizing effect of alkyl groups on negative charges. In addition, we have made the first direct measurement of the relative acidities of water and ammonia.

As in the previous work, we have utilized ion cyclotron resonance (ICR) and pulsed double-resonance spectroscopy. In our experiments we are able to analyze the behavior of various negative ions (amide ions) in the presence of a mixture of their conjugate acids (amines). By pulsed double-resonance spectroscopy, we can perturb the velocity of ions of one mass and examine the effect on abundances of ions of another mass. In studying reactions[2] of type 1, we find that the reactions often proceed essentially only

$$RNH_2 + R'NH^- \rightleftharpoons RNH^- + R'NH_2 \qquad (1)$$

in one direction, thereby giving the sign of $\Delta H°$. Assuming $\Delta S° \cong 0$, we thus obtain an order of relative acidities. For reactions proceeding in both directions we have taken the relative acidities to be approximately equal.

The ordering of acidities is: diethylamine > neopentylamine $\geqslant$ *t*-butylamine $\geqslant$ dimethylamine $\geqslant$ isopropylamine > *n*-propylamine > ethylamine > methylamine > ammonia. In addition, we have found the acidity order diethylamine > water > ammonia.

In analyzing these results, we again[1b,4] find it convenient to treat the energetics of acid ionization as the sum of three thermodynamic processes: (i) bond dissociation (to a radical and a hydrogen atom), (ii) ionization of the hydrogen atom (to a proton), and (iii) electron affinity of the radical (to an anion). Clearly, substitution of groups can affect acidity by changing i and iii. The acidity order for the series of primary amines, neopentylamine through methylamine, parallels that for the series of alcohols studied previously in that large alkyl groups increase acidity. If we assume, by analogy with hydrocarbons[5a,b] and alcohols,[5c] that for primary amines the RNH–H bond strength (i) remains constant independent of R, then the large alkyl groups increase acidity by increasing the electron affinity of the corresponding radical (iii), as is true for alcohols.

Since there is a decrease in N–H bond strength (i) between primary and secondary amines, it is, in general, impossible to ascertain the extent to which the increased acidity of secondary amines arises from alkyl group effects on i and iii. However, the observation that *t*-butylamine and dimethylamine have approximately

(1) For previous work see: (a) J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **90**, 5636 (1968); (b) J. I. Brauman and L. K. Blair, *ibid.*, **90**, 6561 (1968).

(2) Amines were of reagent grade and used without further purification. Degassed mixtures of amines and ammonia were prepared on a vacuum line and introduced into the unheated inlet of a Varian V-5900 ICR spectrometer modified for double-resonance experiments. In these mixtures the maximum in the ionization efficiency curves for all amide ions (and $OH^-$ in the case of the ammonia–water mixture) was identical with that for $NH_2^-$, at 5.1 eV (uncorrected). It thus appears that alkylamide ions are generated in secondary reactions.
Reactions were studied at pressures of *ca.* $10^{-5}$ torr using techniques described previously.[3] Transfer of only N–H protons was demonstrated in experiments with $C_2D_5NH_2$.
(3) See ref 1a for pertinent literature citations and a description of the experiment. Some negative ion–molecule reactions of $NH_2^-$ have been studied: C. E. Melton, *J. Chem. Phys.*, **45**, 4414 (1966); J. G. Dillard and J. L. Franklin, *ibid.*, **48**, 2353 (1968).
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