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 5×10^{-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 3.2×10^3 from the results of kinetic experiments. Difference spectra, corrected for changes in pyridine concentration, gave absorption maxima at 272 nm (ϵ *ca.* 4.3×10^3) and 225 nm (ϵ *ca.* 7×10^3); compare 3-acetylpyridinium chloride, $\lambda_{\max}$ 269 nm (ϵ 3.9×10^3) and 224 nm (ϵ 5.8×10^3) in ethanol.[10]

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[9] A. K. Sheinkman, S. L. Portnova, Yu. N. Sheinker, and A. N. Kost, *Dokl. Akad. Nauk SSSR*, **157**, 1416 (1964).

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A. R. Fersht, W. P. Jencks
Graduate Department of Biochemistry
Brandeis University, Waltham, Massachusetts 02154
Received February 14, 1969

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

$$\mathrm{RNH_2 + R'NH^- \rightleftarrows RNH^- + R'NH_2} \qquad (1)$$

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 ⩾ *t*-butylamine ⩾ dimethylamine ⩾ 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

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[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).

[4] A. Streitwieser, Jr., and J. H. Hammons, *Progr. Phys. Org. Chem.* **3**, 41 (1965).

[5] (a) J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966); (b) S. W. Benson, *J. Chem. Educ.*, **42**, 502 (1965); (c) S. W. Benson and R. Shaw in "Oxidation of Organic Compounds—I," Advances in Chemistry Series, No. 75, American Chemical Society, Washington, D. C., 1968.

equal acidities enables us to obtain some measure of the relative effects of alkyl groups on electron affinities of amino radicals. The N-H bond strength in methylamine[5a] is reported to be 92 kcal/mol; that for dimethylamine[5a] is reported to be 86 kcal/mol. If, again by analogy, this 6-kcal/mol difference holds for all primary and secondary amines, it follows that the electron affinity of the *t*-butylamino radical is about 6 kcal/mol greater than that of the dimethylamino radical. The size of this effect is consistent with our previous suggestion[1b] that polarizable groups are effective in stabilizing charge by an ion-induced dipole interaction. A simple calculation[6] making use of bond polarizabilities which estimates the energy gained by placing a negative charge adjacent to various alkyl groups gives stabilization differences of this order of magnitude. Because we ignore polarization through bonds[7] and cannot evaluate the effective permittivity, this is a drastic oversimplification. Nevertheless, it does suggest that the explanation has some validity.

It is relatively difficult to compare acidities of amines in the gas phase with those in solution. Solution acidities are virtually unknown, and measurements may be expected to be complicated in any case by factors such as ion pairing. For example, in cyclohexylamine solvent, cesium cyclohexylamide is significantly more basic than lithium cyclohexylamide toward triphenylmethane.[8] It is reasonable, however, to expect that solution acidities of primary amines will parallel those of alcohols. That is, bulky primary amide ions will be more basic than small ones, owing to the effects of solvation. It should be noted that amide ions in solution appear to be significantly more basic than hydroxide or alkoxide ions.[9] This may be a consequence of poorer hydrogen bonding to amide ions, among other things.

Our results provide the first direct gas-phase measurement of the relative acidities of water and ammonia, water being more acidic. A simple analysis based on reported values of bond strengths[5] and electron affinities[10] indicates that water is slightly more acidic, but a more refined analysis, including zero-point energy corrections, suggests the opposite.[11] However, it appears that the acidities are close, and small experimental errors in bond strengths and electron affinities would account for a wrong order. The fact that the acidity of water lies between that of diethylamine and ammonia indicates that there may be sufficient overlap in the acidities of water, alcohols, and amines for us to have a reasonable expectation of evaluating fairly small effects on electron affinities in alcohols and amines in the future.

Acknowledgment. We thank Professor J. D. Baldeschwieler for helpful discussions and J. V. Garcia for technical assistance. We gratefully acknowledge support from the National Science Foundation (GP-4924-X; GP-6736), the National Institutes of Health (GM-145752-02), the donors of the Petroleum Research Fund administered by the American Chemical Society (2917-A4), the National Aeronautics and Space Administration (NGR-05-020-250), and the Center for Materials Research, Stanford University.

John I. Brauman,[12] Larry K. Blair[13]
Department of Chemistry, Stanford University
Stanford, California 94305

Received January 13, 1969

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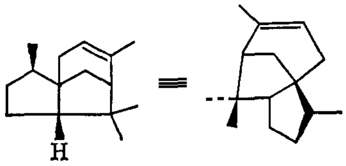
(12) Alfred P. Sloan Fellow, 1968–1970.

(13) National Science Foundation Predoctoral Fellow, 1966–present.

A Biogenetic-Type Synthesis of Cedrene[1]

Sir:

Cedrene, a tricyclic sesquiterpene found in *Juniperus* oil, has been shown to have structure **1** by chemical degradation[2] and synthesis.[3] We wish to describe an alternate synthesis of this natural product by a process utilizing a unique stereoselective dehydrohalogenation and culminating in a step which duplicates the presumed biogenesis.[4,5]



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Ethyl benzyloxyphenylacetate (**2**), on treatment with sodium hydride in diethyl carbonate,[6] was carbethoxylated to yield malonic ester **3** (mp 67–68, 72%)[7] which, in the presence of potassium *t*-butoxide, underwent Michael addition to methyl vinyl ketone. The resulting keto diester **4** (mp 57–57.5, 63%), after sodium borohydride reduction to alcohol **5**, was saponified with alcoholic potassium hydroxide to the lactone acid **6** (formed on acidification of the reaction mixture). On distillation (280° (0.1 mm)) **6** was decarboxylated to afford lactone **7**[7] [mp 140–141°; 66% over-all from **4**; $\nu_{\max}^{CHCl_3}$ 1725 cm^{-1}; δ_{CDCl_3} 1.40 (d, CH_3), 3.68 (m, benzylic methine H), 5.02 ppm (s, CH_2Ph)]. The benzyl protecting group of **7** was removed *via* hydrogenolysis with palladium on carbon (ethanol) yielding the phenol lactone **8**[7] which on standing for 3 days in anhydrous ethanol–hydrogen bromide[8] was converted to diastereomeric bromo esters **9** [oil, 71% from **7**; $\nu_{\max}^{CHCl_3}$ 3615, 3390, 1720 cm^{-1}; δ_{CDCl_3} 1.20 (t) and 4.10 (q) (OCH_2CH_3), 1.63 ppm (d, CH_3)]. Cyclization *via*

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(1) This research was supported in part by funds from Eli Lilly and Co. and Monsanto Chemical Co.

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