Ionization Potentials and Hydrogen Affinities. The ionization potentials (IP) determined from Koopmans' theorem[34] for the neutral species are reported in Table XII together with the dipole moments calculated with the larger basis sets. The ionization potential of CH_2NH is somewhat higher than that of CH_3NH_2 [10.48 eV (calculated[27]), 8.9 eV (experimental[35])]. Substitution of an α-methyl group to give **2** lowers the IP by 0.3 eV. The IP for vinylamine, in contrast to the imines, is much lower. For **1a**, the ionization potential decreases in the N-planar form as expected from results on methyl-substituted amines. This decrease in IP is significantly smaller for **1** than for the amines as expected from the small inversion barrier in **1**. Rotation about the CN bond which destroys the conjugation increases the ionization potential by 1.2 eV. In the planar form of **1b**, an increase in IP from that in pyramidal **1b** is actually predicted. This is contrary to the general observation that IP's decrease at planar nitrogens.

(34) T. Koopmans, *Physica* **1**, 104 (1933).
(35) H. M. Rosenstock, K. Draxl, B. W. Steiner, and J. T. Herron, *J. Phys. Chem. Ref. Data, Suppl. 1*, 6 (1977).

The hydrogen affinity (HA) defined by the reaction $MH^+ \rightarrow M^+ + H$ is related to the proton affinity (PA) as follows:

$$HA = PA + IP(B) - IP(H)$$

where IP is the appropriate ionization potential. The hydrogen affinities determined from our theoretical values are given in Table XII for the DZP results. These values are only approximate owing to errors in determining the IP from Koopmans' theorem and to errors in the absolute proton affinities; the qualitative trends, however, should be correct. The values for HA of the imines **2** and **3** are comparable showing a slight increase on methyl substitution. This is opposite to the effect of methyl substitution on HA's in amines. The hydrogen affinity for vinylamine is lower than that of its isomeric imine by ~50 kcal/mol. This is due primarily to the large difference in ionization potentials between the imine and the isomeric enamine.

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Proton Affinities and the Site of Protonation of Enamines in the Gas Phase

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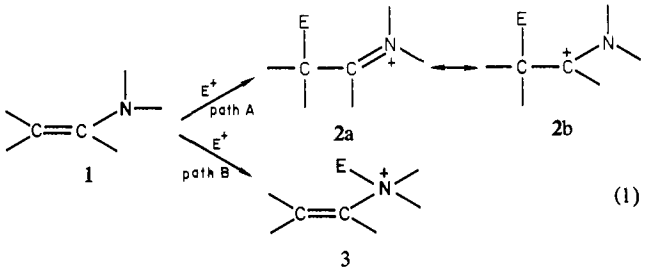
Abstract: The gas-phase proton affinities of a number of methyl-substituted enamines and imines have been measured using ion cyclotron resonance spectroscopy. Comparison of the effect of substituents on the proton affinities of the enamines with those of corresponding amines is used to show that protonation in the gas phase occurs at carbon leading to the formation of an iminium ion. The observation of a large substituent effect for substitution of an α-methyl group also suggests that there is a significant amount of delocalization of positive charge in the iminium ion. A comparison with solution-phase basicities of enamines is also presented.

Introduction

The enamine functional group is commonly employed in synthetic organic chemistry[1] and commonly encountered in biological chemistry.[2] It represents a classic example of an ambident reactant, showing nucleophilic reactivity at both the nitrogen and β-carbon atoms (reaction 1). In solution, the competition between



(1)

C and N attack appears to be a very sensitive function of electrophile structure, enamine structure, and solvent.[3] In the particular case when E^+ is a proton, most mechanistic studies have shown preferential attack at N in some cases followed by rearrangement to the more stable C-protonated form.[4] In order to determine how intrinsic and solvation influences combine to direct reactivity in this interesting class of compounds, we have undertaken concurrent experimental and theoretical studies of the gas-phase ion chemistry of enamines.

We report here proton affinities of a number of differently substituted acyclic enamines as determined by ion cyclotron resonance (ICR) spectroscopy. In an accompanying paper extensive ab initio calculations on the simplest enamine and related imines are reported. A self-consistent picture of the gas-phase proton-transfer reactions of enamines and their isomeric imines is developed predicated on the following implications of the ICR data: (1) gas-phase protonation of enamines occurs exclusively at the β carbon atom to yield iminium ions (path A, Figure 1); (2) deprotonation of iminium ions having hydrogens at nitrogen

‡Alfred P. Sloan Foundation Fellow (1977–1981), Camille and Henry Dreyfus Teacher Scholar (1978–1983), DuPont Young Faculty Grantee (1978).

(1) S. F. Dyke, "The Chemistry of Enamines", Cambridge University, Press, London, (1973), and references therein.
(2) W. I. Taylor, "Indole Alkaloids: An Introduction to the Enamine Chemistry of Natural Products", Pergamon Press, Oxford, 1966; (b) J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, *Adv. Heterocycl. Chem., Suppl. 1*, (1976).
(3) M. Liler, *Adv. Phys. Org. Chem.*, **11**, 267 (1975); see also ref 1.
(4) (a) G. Opitz and A. Greisinger, *Justus Liebigs Ann. Chem.*, **665**, 101 (1963); (b) J. Elguero, R. Jacquier, and G. Tarrago, *Tetrahedron Lett.*, 471 (1965); (c) J. Elguero, R. Jacquier, and G. Tarrago, *ibid.*, 1112 (1966); (d) L. Alais, R. Michelot, and B. Tchovbar, *C. R. Acad. Sci., Ser. C*, 273, 261 (1971), for a case of preferential C-protonation.

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occurs preferentially at N to yield imines; and (3) iminium ions possess substantial electron deficiency at the carbon α to nitrogen. We have previously reported the proton affinity of the simplest enamine, vinylamine, which was obtained via this combined theoretical/experimental approach.[5]

Experimental Section

Materials: General. Reagents used as standards for bracketing studies, precursors to iminium ions, and starting materials in enamine syntheses were obtained from commercial sources and either distilled or used without further purification. All compounds introduced into the ICR were degassed by freeze–pump–thaw cycles. For those materials used directly in ICR experiments, positive ion mass spectra obtained at low pressure in the ICR were consistent with expectations for the pure materials.

Enamines. All of the stable enamines in this work were prepared by condensation of the appropriate secondary amine with the appropriate aldehyde or ketone following standard procedures.[6] A typical procedure, in this case for the preparation of (*E*)-*N*,*N*-dimethyl-2-propenylamine, is given below.

Propionaldehyde (4.78 g, 0.082 mol) is added slowly with stirring to a mixture of 7.50 g (0.166 mol) of anhydrous dimethylamine, 6.50 mL of anhydrous ether, and ~7 g of 3-Å molecular sieves (preactivated by heating to 150 °C on a vacuum line). The addition is carried out under a nitrogen atmosphere at −5 °C. The mixture is stirred at room temperature for 16 h and transferred through a cannula to a clean, dry flask for distillation. Careful distillation (~45 °C (100 mm)) through a column packed with glass helices yields (*E*)-*N*,*N*-dimethyl-2-propenylamine in approximately 60% yield. The ^{1}H NMR is identical with the literature spectrum for the *E* isomer.[7]

Isopropyldimethylamine was prepared from isopropylamine by the Eschweiler–Clarke procedure.[8]

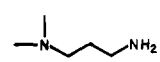
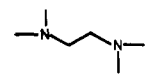
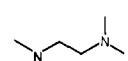
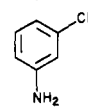
Instrumentation. These studies were performed on a modified Varian V-5900 ICR spectrometer. Experiments were carried out at fixed frequency (usually 153.5 kHz) and variable field 0–13 kG. A standard rectangular cell operated in the drift mode was employed. The instrumentation has been previously described.[9] Operating pressures ranged typically from 1×10^{-5} to 2×10^{-4} Torr as measured by a Varian UHV ionization gauge calibrated against an MKS Baratron Type 90 capacitance manometer. Double-resonance experiments were carried out by sweeping the frequency of a second oscillator at varying voltages. Typical double-resonance rf voltages were 50 mV peak-to-peak applied to the analyzer region of the cell.

Generation of Ions. All proton affinities were obtained by the bracketing technique. Two methods have been applied within this context to generate protonated forms of the enamines.

(1) For the stable neutral enamines, the protonated parent is generated by H^+ transfer to the neutral enamine from ions generated in the electron-impact process. Proton transfer is observed from the conjugate acids of bases of known proton affinity to the enamine under study, or vice versa. Making the conventional assumption that all exothermic proton transfers will be observed while endothermic will not,[10] and systematically varying the strength of the reference base leads to the bracketing of the enamine proton affinity between two known values. All reactions were confirmed by double resonance, and, for every enamine/base pair, a positive double resonance result was obtained in at least one direction.

(2) Some protonated enamines which cannot be prepared in the above fashion can be obtained starting from electron-impact-induced fragmentation of appropriate amines. Isopropylamine, for example,[5] at 18 eV fragments by loss of a methyl radical to form the iminium ion which is the C-protonated conjugate acid of vinylamine (**2** with all substituents = H). Proton-transfer reactions of the form $\mathbf{2} + B \rightarrow A + BH^+$ are observed. The proton affinity of A may then be established by bracketing techniques as described above through systematic variation of the proton affinity of B. However, since there is very little A formed, double resonance can only be observed in the one direction shown above. This general method for obtaining proton affinities has been used by others[11]

Table I. Bracketing Reactions Employed in the Determination of Enamine and Imine Proton Affinities[a]

base[b]	enamine/imine		double resonance result[c]	PA(base)[d]
		5	+	23.2[f]
		5	±	25.1
		5	±	g
		5	−	25.3
		6	+	23.2[f]
		6	±	g
i-Pr_2NH		6	−	24.7
		6	−	25.3
		7	+	32.0[h]
		7	−	33.2
Et_3N		8	+	26.2
		8	±	33.2
		4[e]	0	20.4
		4[e]	−	23.2[f]
		9[e]	0	9.3
		9[e]	−	9.8
		10[e]	0	15.5
		10[e]	−	16.3

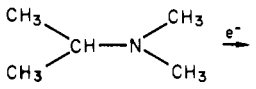
[a] The reaction $BH^+ + E \rightleftarrows EH^+ + B$ was studied where B is the base and E the enamine (imine). [b] Reference bases B. [c] + means that the reaction $BH^+ + E \rightarrow EH^+ + B$ is observed; − indicates that the reaction $EH^+ + B \rightarrow BH^+$ is observed; ± indicates that reactions in both directions are observed; 0 implies that no reaction is observed. This last observation is employed only when EH^+ is formed by a fragmentation mechanism and essentially no E is present. [d] Proton affinity of reference base from ref 12 (unless noted) in kcal/mol relative to $PA(NH_3) = 0.0$. A positive PA implies a $PA(B) > PA(NH_3)$. [e] EH^+ generated by fragmentation mechanism. [f] This value was measured in our laboratory (M. Hendewerk, M. R. Ellenberger, W. E. Farneth, and D. A. Dixon, unpublished results) by bracketing reactions to be between PA(*n*-Pr_2NH) and PA(*i*-Pr_2NH). [g] Value determined in this study. [h] This value is given as 34.8 kcal/mol in ref 12. Our double-resonance studies on enamines indicated a reverse ordering for PA of this compound and the base, $(CH_3)_2N(CH_2)_2N(CH_3)_2$ (a). Indeed, double resonance showed that $(CH_3)_2N(CH_2)_3NH_2$ (b) protonates compoud a. Based on substituent effects reported for other diamines in ref 12, we conclude that the value for PA(a) is probably correct and that the value for PA(b) should be lowered (M. Hendewerk, M. R. Ellenberger, W. E. Farneth, and D. A. Dixon, unpublished results).

(5) M. R. Ellenberger, R. A. Eades, M. W. Thomsen, W. E. Farneth, and D. A. Dixon, *J. Am. Chem. Soc.*, **101**, 7151 (1979).
(6) C. Mannich and H. Davidsen, *Ber.*, B69, 2106 (1936).
(7) J. Sauer and H. Prahl, *Chem. Ber.*, **102**, 1917 (1969).
(8) S. H. Pine and B. L. Sanchez, *J. Org. Chem*, 36, 829 (1971).
(9) J. L. Beauchamp, *Annu. Rev. Phys. Chem.*, **22**, 527 (1971).
(10) (a) D. E. Smith and B. Munson, *J. Am. Chem. Soc.*, **100**, 479 (1978); (b) D. J. DeFrees, R. T. McIver, and W. J. Hehre, *ibid.*, **99**, 3854 (1977); (c) J. I. Brauman and L. K. Blair, *ibid.*, **92**, 5986 (1970).
(11) (a) J. Vogt and J. L. Beauchamp, *J. Am. Chem. Soc.*, **97**, 6682 (1975); (b) S. K. Pollack and W. J. Hehre, *ibid.*, **99**, 4845 (1977).

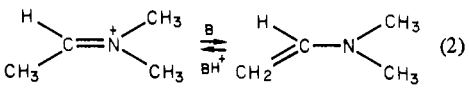
and discussed in detail in a previous report.[5] As discussed below and in ref 5, this may not yield the proton affinity of the desired enamine directly.

Results

Bracketing reactions used in establishing the proton affinities of the enamines and imines examined in this study are shown in Table I. A substantial number of experiments not shown in Table I have also been carried out with stronger or weaker bases than those that most closely bracket the enamine. These results are uniformly consistent with the bracketing results shown. Proton affinities are from the recent tabulation of Aue and Bowers unless otherwise noted.[12] All proton affinities are reported relative to $PA(NH_3)$.[13] The proton affinities of compounds **5–8** were generated via bracketing techniques on the stable neutral enamines. The proton affinity for compound **4** was obtained from bracketing experiments using the protonated ion generated by the fragmentation technique (reaction 2). Fragmentation of iso-



11

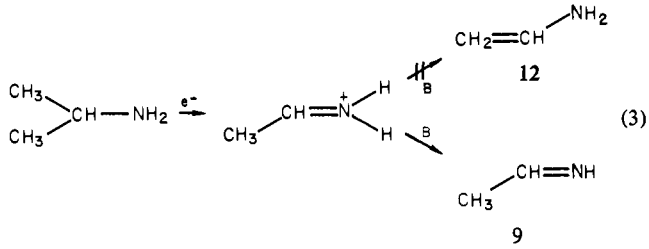


(2)

4

propyl-dimethylamine (**11**) as shown in reaction 2 yielded the iminium ion from C-protonation of *N,N*-dimethylvinylamine (**4**). Deprotonation of this ion can occur only at carbon to yield the enamine **4** since there are no protons at nitrogen, making an imine of mass 71 inaccessible without substantial internal rearrangement.

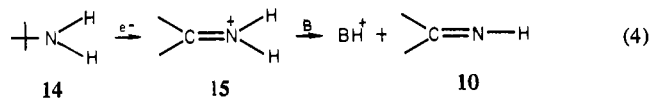
The proton affinities for vinylamine (**12**) and α-methylvinylamine (**13**) cannot be obtained directly from experiments of this kind. Because there are protons at N instead of methyl groups as in **4**, deprotonation of the corresponding iminium ion could occur either at the β carbon, as above, or at N. Deprotonation at N would lead to the isomeric imine rather than the enamine. In a previous study of **12**,[5] it was demonstrated, using deuterium labeling, that deprotonation occurred almost exclusively at N to yield the imine **9** (reaction 3). The isomerization energy for the



(3)

9

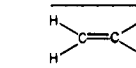
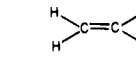
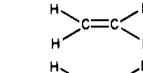
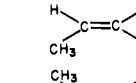
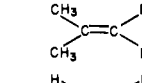
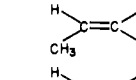
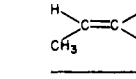
conversion of the imine to its isomeric enamine has been calculated to be 5.2 kcal/mol, using polarized double ζ basis sets.[14a] Thus the proton affinity of **12** is computed to be 5.2 kcal/mol higher than the measured proton affinity of **9**. The proton affinity of **13** can be determined in an analogous fashion (reaction 4).[15]



(4)

14 15 10

Table II. Enamine and Amine Proton Affinities Relative to NH_3 in kcal/mol

enamine struct		PA,[a] kcal/mol	corresponding satd amine	PA,[b] kcal/mol
	(12)	14.8	$CH_3CH_2NH_2$	12
	(13)	21.1	$(CH_3)_2CHNH_2$	14.5
	(4)	21.8	$CH_3CH_2N(CH_3)_2$	21.5
	(5)	24.2	$CH_3CH_2CH_2N(CH_3)_2$	22[c]
	(6)	24.2	$(CH_3)_2CHCH_2N(CH_3)_2$	23[c]
	(7)	32.6	$CH_3CH_2CH(CH_3)N(CH_3)_2$	24[c]
	(8)	~34	$(CH_3CH_2)_2CHN(CH_3)_2$	25[c]

[a] Determined in this work. All values are ±1 kcal/mol. [b] Proton affinities from ref 12 or estimated from values in ref 12. [c] Estimated values.

tert-Butylamine forms the iminium ion **15** on electron-impact-induced fragmentation. Bracketing of the deprotonation reaction of the fragment with known bases B should yield the proton affinity of the imine isomer **10** as was shown to be the case for vinylamine. The measured imine proton affinity is converted into an isomeric enamine proton affinity using the 5.2-kcal/mol isomerization energy calculated for vinylamine.[14a] In the cases of **4**, **9**, and **10**, the bracketing experiments are characterized by a sharp thermochemical threshold separating positive double resonance results from negative. These thresholds are independent of total pressure or gas composition.[5]

The proton affinities of the enamines generated in this study are summarized in Table II where they are compared with the corresponding saturated amines. The imine proton affinities are −9.6 kcal/mol for **9** (the isomer of **12**) and −15.9 kcal/mol for **10** (the isomer of **13**).

Discussion

In the section that follows, two lines of argument will be developed leading to the conclusion that the enamines studied protonate exclusively at carbon in the gas phase. These are (1) a comparison of methyl substituent effects on enamines and amines and (2) a comparison of the relative values for the proton affinities of enamines with estimates for C or N protonation.

(1) Site-specific methyl substituent effects on the proton affinities of enamines and the corresponding saturated amine skeletons are shown in Figure 1. It is clear that methyl substitution at the carbon atom β to nitrogen (paths c and e) leads to small proton affinity changes in both skeletons. The addition of one methyl group on the β carbon has a somewhat larger effect on the enamines than on the amines. Methyl substitution at the α carbon (paths a and f) yields substantially larger changes on enamine proton affinities than amines. Dimethyl substitution at nitrogen (paths b and d), on the other hand, produces slightly smaller effects on the enamine than on the amine skeleton.

These observations are, in general, consistent with the expectations for C-protonation, but inconsistent with N-protonation. Protonation at N would lead to an enammonium ion (**3**) with electron deficiency only at nitrogen. One expects, therefore, a pattern of alkyl-substituent effects similar to that observed for saturated amines; that is, the largest methyl stabilization effects should be found at nitrogen with a fall-off in magnitude at positions

(12) D. H. Aue and M. T. Bowers in "Gas Phase Ion Chemistry", Vol. 2, Academic Press, New York, 1979, p 2.

(13) Because the absolute proton affinity of NH_3 is not well established experimentally, absolute proton affinities are not reported in this work. A thorough discussion of the absolute proton affinity of NH_3 can be found in R. A. Eades, K. Scanlon, M. R. Ellenberger, D. A. Dixon, and D. S. Marynick, *J. Phys. Chem.*, **84**, 2840 (1980).

(14) (a) R. A. Eades, D. A. Weil, M. R. Ellenberger, W. E. Farneth, D. A. Dixon, and C. H. Douglass, Jr., *J. Am. Chem. Soc.*, preceding paper in this issue; (b) P. A. Kollman, *Adv. Org. Chem.*, **9**, 1 (1976).

(15) The assumption implicit in using the isomerization energy of vinylamine is that the α-methyl group affects ΔH_f of the enamine and imine equivalently. See discussion below.

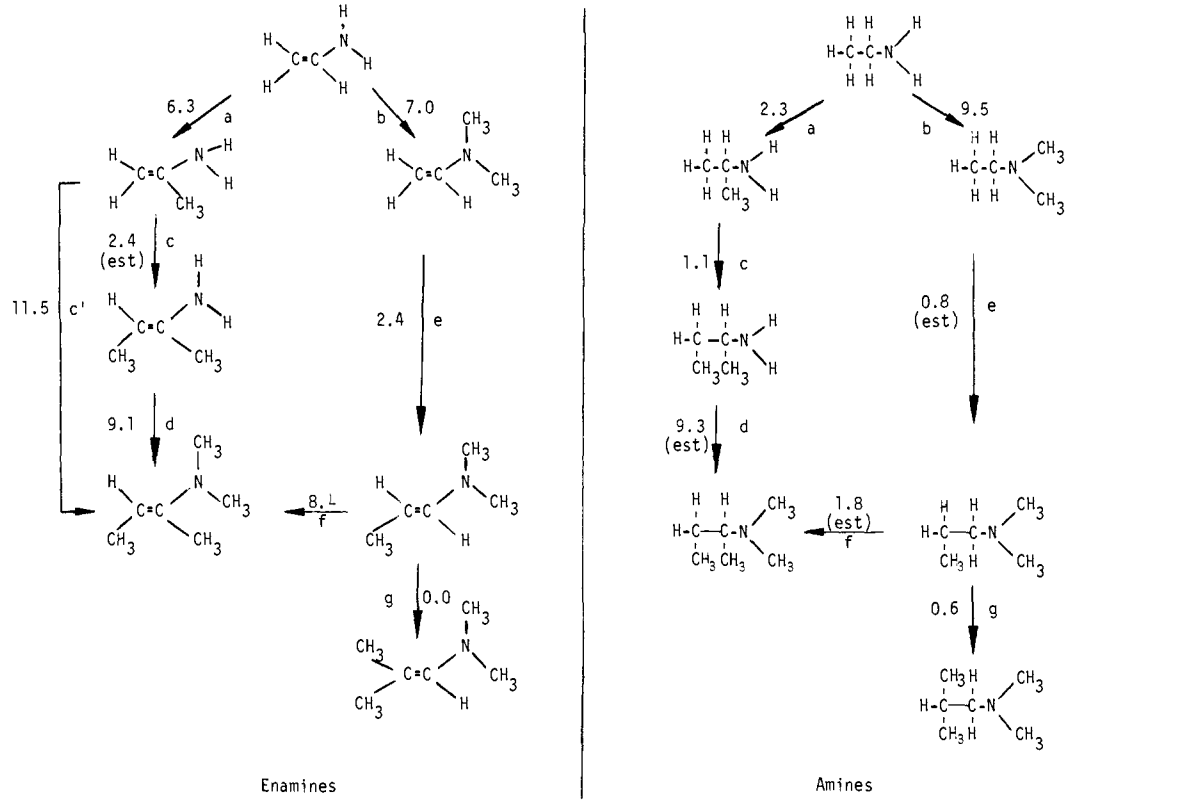


Figure 1. Increases in proton affinity accompanying methyl substitution at various sites in the enamine and amine skeletons. Estimated values are given as est. In the enamine sequence the value for path c was taken from path e. In the amine sequence, the values are taken from ref 12 or based on estimates using values from ref 12. The value for path d was estimated from PA(*i*-PrNH$_2$) − PA(*i*-PrNMe$_2$). The value for path e was estimated from PA(Et$_3$N) − PA(Et$_2$N-n-Pr). The value for path f was taken as 0.5 [PA(*n*-Pr$_2$NH) − PA(*sec*-Bu$_2$NH)]. The value for path g was taken as 0.5 [PA(*n*-Pr$_2$NH) − PA(*t*-Bu$_2$NH)].

more remote from the electron-deficient site. Protonation at C, on the other hand, leads to an iminium ion best represented as a hybrid of Lewis structures **2a** and **2b**. To the extent that **2b** is important, i.e., that charge delocalization is important, α-carbon methyl stabilization effects should be enhanced and *N*-methyl diminished relative to the same positions in the amine skeleton. Some enhancement at the β carbon would also be expected if there is a significant amount of positive charge on the α carbon.[15] The observed effects (Figure 1) are in accord with these expectations. Substitution of an ethyl for a methyl group at the α carbon leads to an increase in proton affinity which is again consistent with this conclusion.

Similar arguments have been used to deduce the site of protonation in aniline and some of its methyl-substituted derivatives.[16] In that case it was concluded that C- and N-protonation are rather closely balanced in energy and that methyl substitution at either N or the ortho, para positions in the ring could shift the balance in favor of one site or the other. For example, while aniline itself prefers C-protonation, *N,N*-dimethylaniline protonates on nitrogen. In the case of vinylamines, our results show that both *N,N*-dihydrogen and *N,N*-dimethyl systems prefer C-protonation. The difference between the behavior of simple enamines and anilines could be related to the presence of the benzene resonance energy in the latter compounds. A simple iminium ion is considerably more stable than the isomeric vinylammonium ion as our experimental and theoretical calcualtions (see accompanying paper) on vinylamine suggest, but in anilines, the loss of benzene stabilization energy that accompanies C-protonation effectively counterbalances this preference.

The magnitude of the α-carbon methyl substituent effect indicates substantial electron deficiency at carbon in the iminium ion. From the proton affinities of **12** and **13** and an estimated difference in neutral heats of formation from group additivity

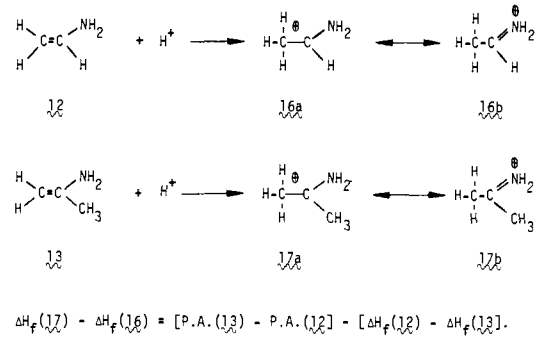


Figure 2. Thermodynamic evaluation of $\Delta\Delta H_{f(295°)}$ for **16** and **17**.

Table III. $\Delta\Delta H_{f(298)}$ for (R = CH_3) − (R = H) in Structure A as a Function of X

	X	$\Delta\Delta H_{f(298°)}$, kcal/mol
	CH_3	−25[a]
	NH_2	−14[b]
	OH	−19[a]

[a] Reference 18. [b] This work.

relationships,[17] the difference in heats of formation of the iminium ions derived from protonation of **12** and **13** may be calculated. The value obtained is $\Delta\Delta H_{f(298°)} \cong -14$ kcal/mol (Figure 2). In Table III, the α-methyl stabilization effects on "onium" ion heats of formation for carbonium, oxonium, and iminium ions are shown. Lossing has argued that the similar methyl stabilization effect

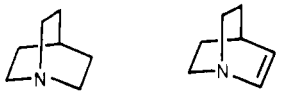
(16) S. K. Pollack, J. L. Devlin, III, K. D. Symmerhays, R. W. Taft, and W. J. Hehre, *J. Am. Chem., Soc.*, **99**, 4583 (1977).

(17) S. W. Benson, "Thermochemical Kinetics", 2nd ed., Wiley-Interscience, New York, 1976. The difference in $\Delta H_f°_{298°}$ between the groups [Cd−(N)(H)] and [Cd−(N)(C)] is assumed to be 2 kcal/mol. Differences between [Cd−(X)(H)] and [Cd−(X)(C)] groups included in the tables range from 1.7 to 2.5 kcal/mol.

in the carbon and oxygen systems implies that the oxonium ion structure is dominated by the carbonium ion type Lewis structure in the gas phase.[18] In the iminium ion, the difference in heats of formation is slightly more than half the carbonium ion value. Without an adequate model for the α-methyl effect on the heats of formation of the other charge-localized Lewis structure $(CH_3)C(R)=^+NH_2$, a less definitive but more certain conclusion in this case would be that both forms contribute significantly to the hybrid structure.[19] The theoretical results[14] reported by us and by Kollman support the conclusion that a significant amount of charge delocalization to the carbon is present.

(2) Absolute values of enamine proton affinities also are consistent with C- rather than N-protonation. An estimate of the N-proton affinity of an enamine can be made from the corresponding saturated tertiary amine corrected for the influence of unsaturation in one substituent. The olefinic substituent will have both conjugative and nonconjugative influences on the proton affinity. The magnitude of the former can be estimated from the barrier to rotation about the C–N bond in vinylamine. The conjugative stabilization results from a preferred conformation in which the lone pair eclipses the π bond of the olefin in vinylamine. We have calculated this barrier to be 6 kcal/mol.[14a] This suggests that the proton affinity for the N-protonated enamine would be 6 kcal/mol lower than the corresponding saturated amine strictly owing to the loss of conjugative stabilization.

Nonconjugative effects of unsaturation can be estimated from data reported by Aue and Bowers.[20] The relative proton affinities of quinuclidine (**18**) and its α,β-unsaturated counterpart **19** are 18 and 15 kcal/mol, respectively. These data in which geometric



18 19

constraints prevent lone pair–π orbital conjugation in the enamine suggest that the nonconjugative influence of the olefin in the enamine skeleton will decrease the N-protonation proton affinity relative to the corresponding saturated amine by ~3 kcal/mol. The fact that our estimated values for the conjugative and nonconjugative effects are large and reinforcing leads to the fairly secure prediction that N-protonation proton affinities of enamines should be lower than those of corresponding saturated amines. The experimental observation (Table II) is that enamine proton affinities are from 1 to 9 kcal/mol greater than those of corresponding saturated amines. The 5-kcal/mol difference between vinylamine and ethylamine combined with the hypothetical ~9 kcal/mol lowering of the N-proton affinity deduced above yields a difference of approximately 14 kcal/mol between the C and N proton affinities of vinylamine. This difference appears to be of the appropriate magnitude for the aniline argument made earlier (i.e., C-protonation in benzene is ~14 kcal/mol less favorable than in simple olefins), and in good agreement with our calculations[14a] and those from several other groups.[14b,21]

Proton affinities of several simple imines have recently been reported.[22] Protonation of imines should occur exclusively at N to yield the same iminium ions that are obtained from C-protonation of the isomeric enamines. Within the combination of existing gas-phase enamine and imine thermochemical data,

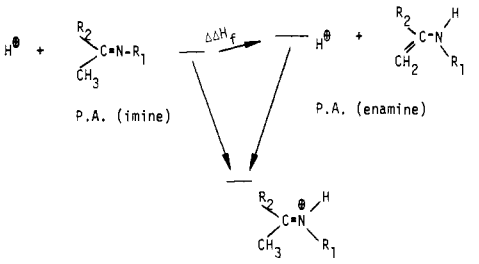
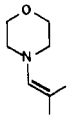
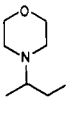
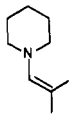
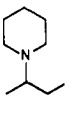
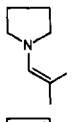
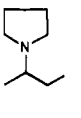
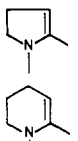
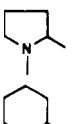
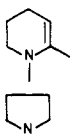
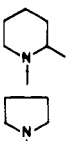
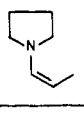
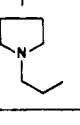


Figure 3. Thermodynamic cycle showing the relationship of imine and enamine proton affinities to the isomerization energy.

Table IV. Enamine and Amine Basicities from Solution Experiments

	enamine struct	N-protonated pK_a	C-protonated pK_a	corresponding satd amine	pK_a	ref
1.		5.45			7.82	29
2.		8.35			10.44	29
3.		8.84			10.38	29
4.			11.94		10.24	30
5.			11.42		10.25	30
6.			10.66		10.23	30

there are numerous ways to demonstrate internal consistency. Aue and Bowers[22] report proton affinities of *N*-ethylisopropylidenimine $(CH_3C(CH_3)=NCH_2CH_3)$ (PA = 24.5) and *N*-ethylethylidenimine $(CH_3C(H)=NCH_2CH_3)$ (PA = 18) yielding an α-methyl substituent effect of 6.5 kcal/mol. In the enamine skeleton a value of 7.0 ± 1 kcal/mol has been obtained from our results. These numbers will be identical if (1) α-CH_3 substitution affects the heats of formation of imines and enamines equivalently,[23] and (2) the magnitude of the α-CH_3 stabilization of iminium ions is essentially insensitive to the substitution at nitrogen.[24] A thermochemical cycle involving the proton affinities of isomeric imines and enamines, and the differences in neutral heats of formation may be constructed (Figure 3). For any given substitution pattern (R_1, R_2), knowledge of two of the three legs of the cycle determines the third. The internal consistency of the imine and enamine data may be further demonstrated using this cycle. For example, the

(18) F. P. Lossing, *J. Am. Chem. Soc.*, **99**, 7526 (1977).

(19) $\Delta H_f°_{298}((CH_3)_2CHNH_3^+) - \Delta H_f°_{298}(CH_3CH_2NH_3^+) = -11$ kcal/mol. To the extent that the saturated amine constitutes an adequate model for the α-methyl substituent effect on the stability of the Lewis structure **13b**, (−11 kcal/mol), the observed substituent effect (−14 kcal/mol) is consistent with a hybrid structure.

(20) Reference 12, p 24.

(21) (a) The experimental proton affinity for the preferred N-protonation of aniline is 5.5 kcal/mol greater than ammonia, that is ~12 kcal/mol less than the preferred C-proton affinity of vinylamine. (b) K. Müller and L. D. Brown, *Helv. Chem. Acta*, **61**, 1407 (1978) (9.7 kcal/mol); (c) J. Teysseyre, J. Arrian, A. Dargelos, and J. Elguero, *J. Chim. Phys.*, **72**, 303 (1975) (32.0 kcal/mol); (d) ref 14a (18.3 kcal/mol).

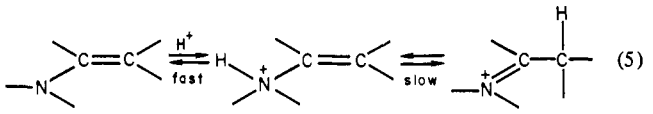
(22) Reference 12, p 25.

(23) In a group additivity approach, this is equivalent to arguing that the difference in group contributions to $\Delta H_f°_{298°}$, [Cd–(H)(X)] – [Cd–(C)(X)], is independent both of X and the atom to which Cd is double bound. Existing data suggest this is a reasonable approximation: e.g., for double bonds to carbon [Cd–$(H)_2$] – [Cd–(H)(C)] = 2.33 kcal/mol, [Cd–(H)(C)] – [Cd–$(C)_2$] = 1.75 kcal/mol, [Cd–(H)(Cd)] – [Cd–(C)(Cd)] = 2.10 kcal/mol; for double bonds to oxygen [Cd–$(H)_2$] – [Cd–(H)(C)] = 3.10 kcal/mol, [Cd–(H)(C)] – [Cd–$(C)_2$] = 2.3 kcal/mol, [Cd–(H)(O)] – [Cd–(C)(O)] = 3.0 kcal/mol; for double bonds to nitrogen [Cd–(C)(H)] – [Cd–$(C)_2$] = 1.75 kcal/mol, [Cd–(O)(H)] – [Cd–(O)(C)] = 2.9 kcal/mol: R. Shaw in "The Chemsitry of Amidines and Imidates", S. Patai, Ed., Wiley New York, 1975, p 547.

(24) This is suggested by the data in Figure 1. The proton affinity changes induced by α methylation in vinylamine and *N,N*-dimethylvinylamine differ by only 1.7 kcal/mol.

proton affinity of $(CH_3)_2C{=}NCH_2CH_3$, (24.5) from ref 22 and $CH_2{=}C(CH_3)N(H)(CH_2CH_3)$ (30 ± 2) which may be estimated from our data[25] yields an isomerization energy of 5.5 ± 2 kcal/mol. This value is in excellent agreement with our calculations[14a] and consistent with the available experimental data.[26]

Various solution-phase studies of enamine basicities are scattered through the literature of the last 40 years. It appears that protonation usually follows the course shown in (reaction 5): rapid



(5)

protonation at nitrogen followed by rearrangement to the more stable iminium ion on a longer timescale.[27]

It has been demonstrated, however, that the rates of both of these steps are quite sensitive to reaction conditions.[28] On the basis of this mechanism, it is possible to measure either the C or N basicity of enamines in solution depending on the nature of the experiment. Representative values of pK_a's of the C- and N-protonated forms of several enamines in aqueous solution are compared with the corresponding saturated amines in Table IV. The general solution-phase picture is thus in good agreement with what we have observed in the gas phase; C-protonation is more favorable than N-protonation. The corresponding amine is intermediate in basicity. Perhaps this is best illustrated by a comparison of entries 3 and 6. The following more specific points are also implied.

(1) Solvent effects attenuate basicity differences between enamines and corresponding saturated amines. For example, the enamine and amine in entry 4 of Table IV differ by 1.7 pK units or approximately 2.4 kcal/mol (298K). These same compounds would be predicted to differ by about 8 kcal/mol in gas-phase basicity from our data.[31] This type of leveling effect of solvent is quite general when relative gas- and solution-phase basicities are compared. It has previously been discussed for both substituted amines[32] and pyridines.[33]

(2) α-Alkyl substituents have a significant effect on enamine basicities in both vapor and aqueous phases [entry 6 compared to entry 5, Table IV and data in Table II]. Most solution basicity measurements have been made on α-alkylated enamines. Hinman has pointed out that the conclusion that enamines are stronger solution-phase bases in C-protonation than the corresponding saturated amines may apply only to a α-substituted derivatives.[34]

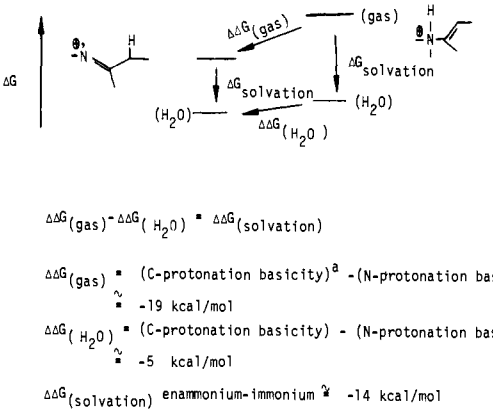


Figure 4. Thermodynamic cycle showing the relationship of gas-phase and solution-phase values of $\Delta\Delta G$ for enamine basicities: (a) measured (vide infra); (b) estimated as follows: The calculated C/N proton affinity difference for vinylamine in conjunction with the measured C-proton affinity yields the N-proton affinity (Assuming substituent effects on the N-proton affinity are identical with those in saturated amines, this value is corrected for the permutation of 2H and Et to $2CH_3$ and *sec*-Bu at N.); (c) this difference estimated as 3 pK units from the data in Table IV.

In the gas phase, as we have demonstrated, the α-stabilizing effect is larger than in the saturated amines, but the N effects are smaller. Therefore, the gas-phase basicities of enamine and saturated amine are nearly the same for compounds like **6** in Table II that are highly branched at N and C-β but unalkylated at C-α. Differential solvation effects could easily invert the ordering in this type of system.

(3) It would be very interesting to attempt to estimate the relative free energies of solvation of isomeric iminium and enammonium ions. Unfortunately, this cannot be done with any precision using presently existing data simply because all four quantities required (C and N basicities both in aqueous solution and the gas phase) are not simultaneously known for a single compound. Nevertheless, using the thermochemical cycle in Figure 4 and some reasonable approximations, an estimate of solvation energies in the conjugate acids of *N,N*-dimethyl-2-but-2-enylamine can be made. This analysis suggests that the enammonium ion is significantly better solvated in water than the isomeric iminium ion. While the analysis is surely quantitatively inaccurate, the suggested differential solvation energy is large and the qualitative conclusion probably sound. In extensive studies of relative aqueous solvation effects in ammonium and oxonium ions, Taft et al.[35] have argued that for ions of equivalent hydrocarbon content and substitution pattern, relative aqueous solvation free energies should be dominated by differences in hydrogen bonding. In accord with this point of view, it seems reasonable to expect much more significant hydrogen bonding to the N-protonated than the C-protonated ion. On would expect the isomeric enammonium and iminium ions to constitute an excellent system for testing these ideas since they are so similar in gross structure. It also seems reasonable to postulate that it is the importance of these differential solvent effects in the proton transfer transition states that allows protonation at nitrogen to compete kinetically with the thermodynamically more favorable carbon protonation in aqueous solution.

Acknowledgment. We thank the Graduate School of the University of Minnesota for partial support of this work, and Monica Hendewerk for carrying out some of the proton affinity determinations. Mark R. Ellenberger thanks Eastman Kodak, Henkel Corporation, and Mobil Corportion for fellowship support.

(25) Estimate based on $H_2C{=}C(CH_3)NH_2$ = 23 kcal/mol + ethyl substituent effect at $N \simeq 7$ kcal/mol from the observed ethyl substituent effect in the corresponding saturated amines weighted (×0.75) as suggested by the data in Table I.

(26) M. J. Cook, A R. Katritzky, P. Linda, and R. D. Tack, *J. Chem. Soc. Perkin Trans. 2* 1295 (1972).

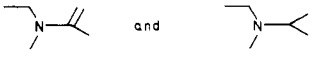
(27) M. J. Cook, A. R. Katritzky, P. Linda, and R. D. Tack, *J. Chem. Soc., Perkin Trans. 2*, 1080 (1973).

(28) J. Taysseyre, J. Arrian, A. Dargelos, J. Elguero, and A. R. Katritzky, *Bull. Soc. Chim. Belg.*, **85**, 39 (1976).

(29) E. J. Stamhuis, W. Maas, and H. Wynberg, *J. Org. Chem.*, **30**, 2160 (1965).

(30) R. Adams and J. E. Mahan, *J. Am. Chem. Soc.*, **64**, 2588 (1942).

(31) ΔPA was estimated as follows: It is assumed that including the N atom in a five-membered ring does not alter the relative proton affinities of the enamine and corresponding saturated amine. Therefore, appropriate acyclic model compounds would be the two shown below. The proton affinity



difference between the model compounds may be estimated from **7** (Table I), by correcting for the small relative effect of changing a CH_3 to CH_2CH_3 at N, and an H to CH_3 at the β carbon.

(32) D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Am. Chem. Soc.*, **98**, 318 (1976).

(33) D. H. Aue, H. M. Webb, M. T. Bowers, C. L. Liotta, C. J. Alexander, and H. P. Hopkins, *J. Am. Chem. Soc.* **98**, 854 (1976).

(34) R. L. Hinman, *Tetrahedron*, **24**, 285 (1968).

(35) R. W. Raft, J. F. Wolf, J. L. Beauchamp, G. Scorrano, and E. M. Arnett, *J. Am. Chem. Soc.*, **100**, 1240 (1978).