sonable to suppose that either the distonic ion is not formed from the molecular ion (at least in this sort of time frame) or the distonic ion once formed decomposes rapidly.

Turning to the isotope effects in the diether, the $^{16}O/^{18}O$ effects are normal (i.e. >1) and their magnitudes can be explained more or less satisfactorily using either the concerted or the stepwise mechanism. As modeled, both the concerted and the stepwise mechanisms predict that the $^{16}O/^{18}O$ isotope effect in the H_{10} molecule (IV) should be a little greater than that in the D_{10} molecular (V), thereby matching the experimental results. When we use the stepwise mechanism and stay within the limits mentioned for the energetics, the calculated $^{16}O/^{18}O$ isotope effects can be raised, but the fit to the H/D isotope effects is worsened as a result of the back-reaction from distonic ion to molecular ion becoming more important. In modeling a stepwise mechanism, the energy barrier to the second step can be kept low so that the second step is sufficiently fast to exclude back-reaction. Under these conditions, the predicted $^{16}O/^{18}O$ isotope effect tends to become inverse[26] due to what is sometimes called the "statistical weight effect".[31] Lowering the energy barrier to the second step means that the excess energy is high for this step, and, as a result, the calculated isotope effect depends more strongly on densities of states than on small differences in critical energies.

In the stepwise mechanism, the back-reaction grows in importance as the relative rate of the second step is cut back. In a deuterium-labeled species such as II or III, there will be an isotope effect on this back-reaction, with H transfer being more rapid than D transfer. The overall consequence of this isotope effect on the back-reaction is, in the case of II for example, to reduce somewhat the extent to which loss of C_2H_4O exceeds loss of C_2H_3DO. The isotope effect on the back-reaction is greater in the case of III, where C_2D_4O and C_2H_4O loss compete, than in the case of II, *given the model described here* in which replacing the methyl hydrogen atoms by D atoms tends to reduce marginally rate constants for the hydrogen transfer step. Consequently, the ratio $[C_2H_4O\ \text{loss}]/[C_2H_3DO\ \text{loss}]$ with II is predicted to exceed the ratio $[C_2H_4O\ \text{loss}]/[C_2D_4O\ \text{loss}]$ with III in the case of the stepwise mechanism. The opposite is predicted in the case of the concerted mechanism, because here there is no back-reaction and the reduction of the rate of hydrogen transfer due to replacement of the methyl H atoms by D atoms causes $[M - C_2H_4O]^{\bullet+}/[M - C_2D_4O]^{\bullet+}$ from III to exceed $[M - C_2H_4O]^{\bullet+}/[M - C_2H_3DO]^{\bullet+}$ from II.

Conclusion

The loss of acetaldehyde from benzyl ethyl ether molecular ions is distinguished from the, in some ways, analogous reaction in for example ketone molecular ions by the absence of hydrogen scrambling in the microsecond time frame. The suggestion[4] has been made that hydrogen scrambling does occur in these ether molecular ions but that it is unusually slow, being manifested only at times approaching 100 μs. It has been suggested that this hydrogen scrambling involves the distonic ion intermediate located in a deep well. We have not been able to observe scrambling at the long times. We conclude that the benzyl ethyl ether ion, and the diether ion, remain distinguished from ketone and other molecular ions with regard to hydrogen scrambling.

The stepwise mechanism with twin energy barriers of comparable heights and a deep intermediate well leads to the prediction that hydrogen scrambling should occur not only in the microsecond time frame but also at times as short as nanoseconds. The stepwise mechanism, as modeled here, leads to the prediction that the H/D isotope effect should be lower in the D_5 compound (III) than in the D_2 compound (II). The concerted mechanism, as modeled here, leads to the prediction that the H/D isotope effect should be greater in the D_5 compound, which is what has been found experimentally. The concerted mechanism leads to predicted $^{16}O/^{18}O$ isotope effects, which are in satisfactory agreement with the experimental results. Our conclusion is that loss of acetaldehyde from the α,α′-diethoxy-*p*-xylene molecular ion is a concerted, synchronous reaction. The concertedness of this reaction may be a consequence of aromaticity of the reactant and facilitation of hydrogen addition by simultaneous development of the exo double bond.

Acknowledgment. We acknowledge stimulating and valuable discussion with Prof. F. W. McLafferty. Appearance energies were measured by Dr. J. C. Traeger. Financial support (to J.H.B. and P.J.D.) under the Australian Research Grants Scheme is gratefully acknowledged.

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Carbon Acidities of Aromatic Compounds

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Contribution from the Chemical Kinetics Division, Center for Chemical Physics, National Bureau of Standards, Gaithersburg, Maryland 20899. *Received January 25, 1988*

Abstract: We report experimental intrinsic carbon acidities and theoretical AM1 results on benzene derivatives and nitrogen heterocyclics. When benzene and pyridine are compared, in-ring aza substitution increases the acidity, i.e. decreases the acid dissociation energy ($\Delta H^\circ_{\text{acid}}$) by 9.7 kcal/mol. Further aza substitution in 1,2- and 1,3-diazine increases the acidity by an additional 8.6 and 5.8 kcal/mol, respectively. However, in 1,4-diazine, where the deprotonated carbon must be adjacent to nitrogen, lone-pair repulsion decreases the acidity below pyridine. The in-ring aza-substitution effects are qualitatively similar to those observed in azoles by Taft et al., but their parameters for lone-pair repulsion and electronegative substituents do not reproduce the effects quantitatively. The electron-withdrawing substituents F, CF_3, CN, and NO_2 also increase the acidity of benzene by 13.5, 13.6, 17.5, and 46.5 kcal/mol, and $CHCH_2$ increases it by 9.7 kcal/mol. The effects of F and $CHCH_2$ demonstrate that the ring acidity is affected by the σ rather than π donating or withdrawing ability of substituents. Ab initio calculations at the MP2=FC/6-31G*//RHF/6-31G level were performed on pyridine and diazines. The computed ab initio DPEs were consistently higher than the experimental values by about 22 kcal/mol. Semiempirical computations using Dewar's AM1 method for 1,4-diazine suggest that a correction of 11 kcal/mol is needed for adjacent lone-pair repulsion. With this correction, AM1 predicts qualitatively sensible deprotonation sites for diazines and F-, CN-, CF_3-, and $CHCH_2$-substituted benzenes and reproduces the deprotonation energies within 6 kcal/mol.

The intrinsic gas-phase acidities of organic compounds reflect structural effects on the stabilities of the conjugate anions in the absence of complicating solvent effects. Also, many organic anions can be generated readily in the gas phase but in solution only under extreme conditions. These facts allowed the measurement of the gas-phase acid dissociation energies $\Delta H^\circ_{\text{acid}} = \Delta H^\circ_D(A^- - H^+)$ of many carbon acids such as acetylene, aldehydes and ketones, cyclopentadiene derivatives, and substituted toluenes.[1,2] Some of the intrinsic acidities were found to be surprisingly strong; for example, $(CH_3CO)_2CH_2$ is a stronger gas-phase acid than acetic acid, and 2,4,6-trinitrotoluene is a stronger acid than HCl. Such observations show that the relatively weak acidities of many carbon acids in solution are due to the weak solvation of the conjugate anions.

To extend the data on carbon acidities, we investigate in this work the acidity of benzene and the effects of electron withdrawal in ring aza substitution and external substituents. The effects of in-ring aza substitution are of interest since Taft et al.[3] have recently analyzed such effects in azoles in terms of lone-pair repulsion and electronegative aza-substituent contributions. We shall investigate whether similar relationships can be established also in the diazines. However, our experimental results are not informative about the nature of the site, in the parent molecule, that is most likely to lose the protonic hydrogen. This led us to carry out theoretical computations using the ab initio GAUSSIAN 86 method[4a] on a selected number of molecules and their anions. Furthermore, semiempirical calculations using the AM1 program[4b] on the various neutral molecules and their corresponding anions were performed. Simple qualitative arguments based on the net charge distribution in the parent compounds and nonbonding interactions are presented for understanding the effect of chemical substitution on the acidity of benzene and for predicting the most acidic sites in aromatic compounds.

Experimental Method

The measurements were performed with the NBS pulsed high-pressure mass spectrometer and standard techniques.[5] The reactant mixture usually contained 5–20% N_2O in CH_4 as a carrier gas and the compounds of interest, AH and reference compounds BH, in concentrations of 0.01–1%. In these mixtures, electron capture by N_2O generates O^-, which reacts to give OH^-. This in turn reacts with the reactants to generate A^- and B^-. In some experiments, a trace amount of CH_3ONO was used as electron-capture reagent, yielding CH_3O^- as the chemical ionizing reagent.

Reaction mixtures were made in a glass bulb heated to 150–200 °C, and were introduced to the ion source through stainless-steel and glass lines heated to similar temperatures. Some of the reactants were fairly involatile, and it was necessary to let the mixture flow for about 30–60 min until the measured equilibrium constants reached a constant value. With such involatile samples, kinetic measurements were used to confirm that the measured rate constants of fast proton-transfer reactions were near the expected capture collision rate. This confirmed that the actual concentrations in the ion source were indeed the nominal concentrations as calculated from the composition of the gas mixture.

The samples were obtained from commercial sources. Their purities were greater than 98% and were used as purchased.

Computational Method

All semiempirical calculations reported here were done by the AM1 method of Dewar et al.[4b] The restricted Hartree–Fock (RHF) option was used in all calculations. For all of the computations, all geometries were fully optimized. Planarity was the only assumption made during the optimizations. Dihedral angles were optimized in the cases where tetrahedral centers were present in the molecule or anion.

In a related study, Dewar and Dieter[4c] tested AM1 for computing deprotonation enthalpies (DPE) of a variety of compounds. The results of these calculations showed that the average error in calculated DPEs was about 6 kcal/mol. The main problems encountered with AM1 involved small anions (three atoms or less) where the charge is highly localized on one atom and in anions formed by deprotonating oximes.[4c] These types of anions were not studied in this work.

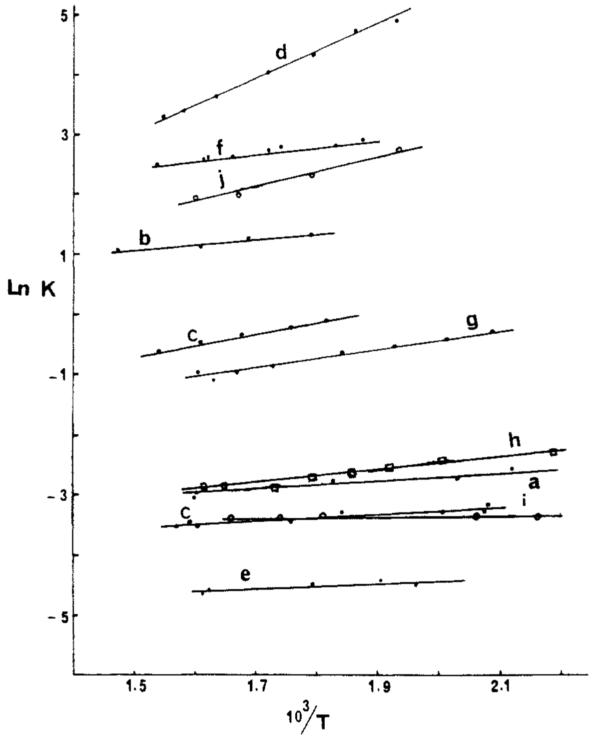

Figure 1. van't Hoff plots for proton-transfer equilibria $A^- + BH = B^- + AH$. Parts for A^- and BH are as follows: (a) $C_6H_4CN^- + CH_3OH$, (b) $C_6H_4F^- + C_6H_5CF_3$, (c) (pyridine-H)$^-$ + H_2O, (d) (pyridine-H)$^-$ + CH_3OH, (e) (1,2-diazine-H)$^-$ + CH_3OH, (f) (1,3-diazine-H)$^-$ + C_6H_5CN, (g) (1,3-diazine-H)$^-$ + CH_3OH, (h) (1,4-diazine-H)$^-$ + H_2O, (i) $C_6H_5C{=}CH_2^- + H_2O$, (j) $C_6H_5CC^- + C_6H_5NH_2$.

Reliable DPEs could be obtained from ab initio methods provided that the basis set contains polarization functions and allowance for electron correlation by second or higher order Moller–Plesset perturbation theory is taken into account during the calculations.[6] The presence of polarization functions in the basis set, e.g. the 6-31G*, are necessary to account for the weakly bound electron in the anion and the diffuse charge distribution. However, carrying out such calculations for the systems of interest is quite expensive due to the large number of basis functions involved in the computations. This led us to use the split-valence 6-31G basis set, which does not have the diffuse functions present in the 6-31G* basis set, for the geometry optimizations.

The ab initio calculations performed for this study were done by the GAUSSIAN 86 program[4a] on pyridine, the various diazines, and their corresponding most stable anions. The choice of the most stable anions for the ab initio computations was based on the qualitative model and the AM1 results, as will be discussed later.

The RHF method, using the standard 6-31G basis set, was used for calculating the total energies of the parent molecules and anions. Full-geometry optimizations were performed on the species of interest. Throughout these computations, the C–H bond lengths were assumed to be equal.[7b] Minima in the potential surfaces of the various species were located with analytical gradients.

Electron correlation was partially accounted for by performing frozen-core (FC) single-point calculations on the optimum RHF/6-31G geometries using Moller-Plesset (MP) perturbation theory to second order. These calculations will be denoted by MP2=FC/6-31G//RHF/6-31G.[6] Moreover, MP2=FC/6-31G*//RHF/6-31G calculations were also performed on the species of interest. Higher order MP opti-

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(1) Lias, S. G.; Bartmess, J. E.; Liebman, J. E.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data*, in press.

(2) (a) Cummings, J. B.; Kebarle, P. *Can. J. Chem.* **1978**, *56*, 1–9. (b) Kebarle, P.; Chowdhury, S. *Chem. Rev.* **1987**, *87*, 513, and references cited therein.

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(4) (a) Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fleuder, E. M.; Pople, J. A. *Gaussian 86*; Carnegie-Mellon Quantum Chemistry Publishing Unit: Pittsburgh, PA, 1984. (b) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. (c) Dewar, M. J. S.; Dieter, K. M. *J. Am. Chem. Soc.* **1986**, *108*, 8075. (d) Fernandez, J.; Anguiano, J.; Villarrassa, J. *J. Comput. Chem.*, in press.

(5) Sieck, L. W.; Meot-Ner (Mautner), M. *J. Phys. Chem.* **1985**, *89*, 5552.

(6) (a) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab. Initio Molecular Orbital Theory*; Wiley: New York, 1986. (b) Jordan, K. D.; Burrow, P. D. *Chem. Rev.* **1987**, *87*, 557.

(7) (a) Kafafi, S. A.; Krauss, M.; Meot-Ner (Mautner), M., to be submitted for publication. (b) To confirm this assumption, we have performed full-geometry optimizations on pyridine and the *p*-pyridinyl anion at the HF/6-31G level of theory. All C–H bond lengths were allowed to vary during the optimizations. For pyridine, the C–H bonds that are closest to the nitrogen were 0.001 Å shorter than the other C–H bonds. For the *p*-pyridinyl anion, this difference was 0.002 Å. The total HF/6-31G energies of pyridine and the *p*-pyridinyl anion differed from those given in Table II for these species by less than 0.2 kcal/mol.

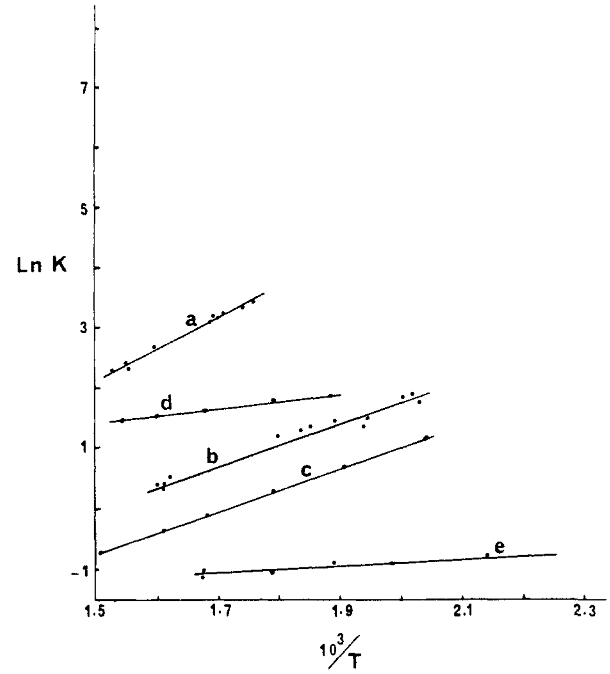

Figure 2. van't Hoff plots for proton-transfer equilibria $A^- + BH = B^- + AH$. Parts A^- and BH are as follows: (a) $C_6H_5^- + H_2O$, (b) $C_6H_4F^- + CH_3OH$, (c) $C_6H_4CF_3^- + CH_3OH$, (d) (acenaphthene-H)$^-$ + $C_6H_5NH_2$, (e) (acenaphthene-H)$^-$ + C_6H_5CCH.

mizations on the present species are in progress.[7a]

All ab initio calculations were done on a VAX 11/785 at the National Bureau of Standards. Each 6-31G optimization took 1.5 days of cpu time, and each MP2=FC/6-31G* single-point calculation took 23 h of cpu.

Experimental Results

The measurements yielded equilibrium constants for proton-transfer reactions 1, where AH is the compound of interest and BH is a reference compound with known acidity.

$$B^- + AH = A^- + BH \qquad (1)$$

The acid dissociation energies of interest $\Delta H^\circ_{acid}(AH)$ may be obtained from $\Delta H^\circ_{acid}(B)$ and ΔH°_1. To obtain the latter directly, we performed temperature studies on several of the equilibria. The van't Hoff plots are shown in Figures 1 and 2. For other reactions, ΔH° was calculated from ΔG°, assuming $\Delta S^\circ = \Delta S^\circ_{rot\,sym}$. When the symmetry was ambiguous because of several possible deprotonation sites on the ring, the lowest symmetry product was assumed.

For temperature studies, the error in ΔH° and ΔS° was estimated from the standard deviations of the slopes and intercepts of the van't Hoff plots and from reproducibility as ±1 kcal/mol and ±2 cal/mol·K, respectively. For ΔG°, the error is usually ±0.5 kcal/mol. The uncertainty in the estimates of ΔS° is probably ±2 cal/mol·K, which at 600 K introduces a further uncertainty of ±1.2 kcal/mol into the calculated ΔH°, for a total of about ±2 kcal/mol for ΔH° values derived in this manner.

The ΔH°_{acid} for the reference compounds are obtained from recent tabulations[1] and from measurements in this laboratory,[5,8] based on a ladder of ΔH° values from temperature measurements. ΔH°_{acid} values for the present compounds can be obtained from the reference compounds by several paths in the ladders in Figure 3. To maximize the number of alternative paths, the ladders also include annelated compounds, which will be presented in the following paper.[9] The weighted average from multiple paths was used as the assigned ΔH°_{acid}. However, for the difference between H_2O and CH_3OH, we used the values from the detailed direct measurement that we reported recently.[10]

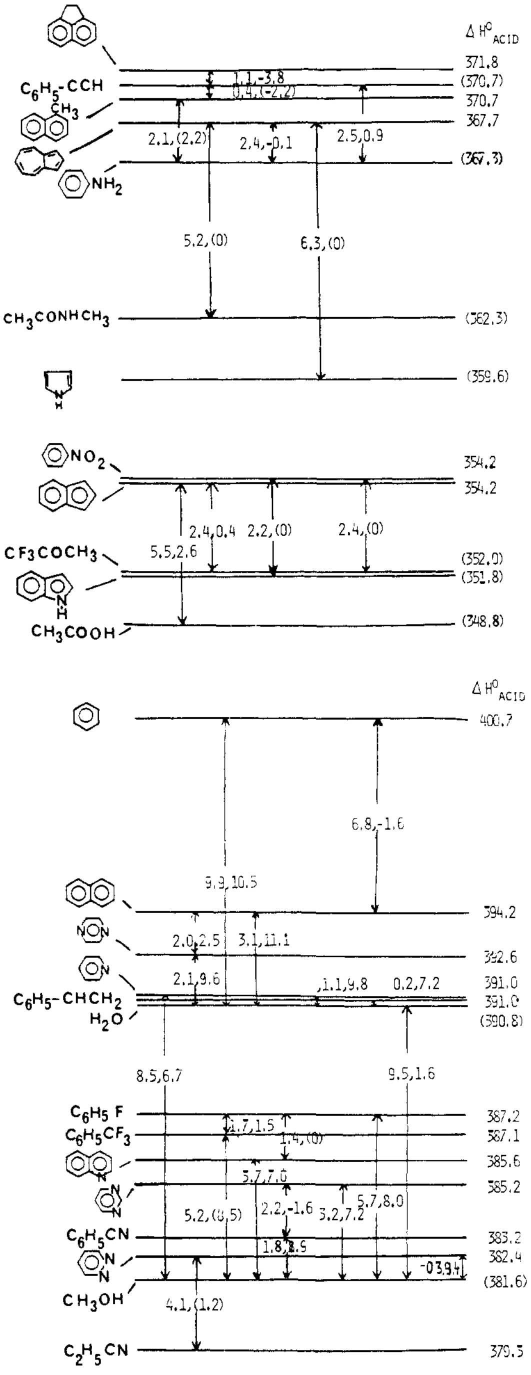

Figure 3. Acidity ladder for aromatic compounds and reference gas-phase acids. Numbers in arrows are ΔH° (kcal/mol) and ΔS°(cal/K·mol). For $A^- + BH = B^- + AH$, AH and BH are the bottom and top compounds connected by the arrow. For the reactions ΔH° values are derived from measured ΔG°_{600} values, with $\Delta H^\circ = \Delta G^\circ_{600} + 600\Delta S^\circ_{rot\,sym}$. ΔH°_{acid} values for each compound are the best values from several paths.

Several of the present reactions showed large entropy changes, associated with the loss of molecular or internal rotation upon the deprotonation of H_2O and CH_3OH, respectively. For the $H_2O \rightarrow OH^-$ transition, the average from five reactions, after accounting for $\Delta S^\circ_{rot\,sym}$ of the reaction partner, is 8.0 ± 2 cal/mol·K, and without symmetry corrections, 9.4 ± 2 kcal/mol. For $CH_3OH \rightarrow CH_3O^-$, the results are 6.2 ± 2 kcal/mol with symmetry corrections and 7.6 ± 2 cal/mol·K without such corrections. The assigned uncertainty is due in part to the unknown symmetries

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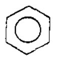
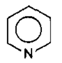
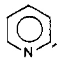
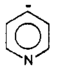
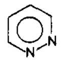
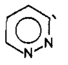
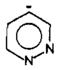
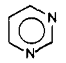
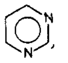
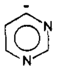
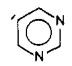
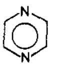
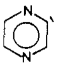
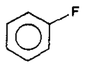
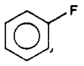
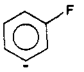
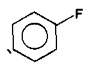
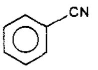
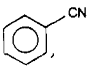
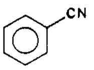
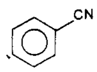
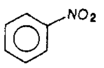
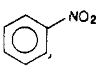
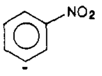
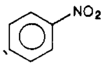
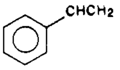
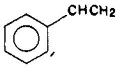
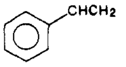
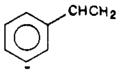
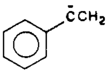
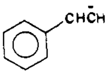
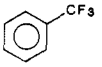
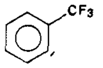
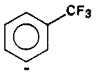
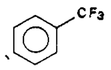
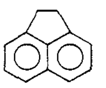
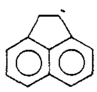
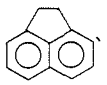
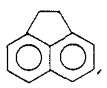
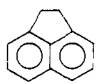
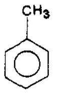
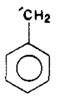
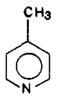
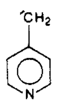
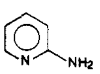
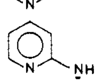
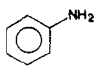
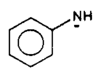
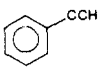
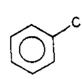
(8) Meot-Ner (Mautner), M.; Sieck, L. W., unpublished results.

(9) Meot-Ner (Mautner), M.; Liebman, J. F.; Kafafi, S. A. *J. Am. Chem. Soc.*, following paper in this issue.

(10) Meot-Ner (Mautner), M.; Sieck, L. W. *J. Phys. Chem.* **1986**, *90*, 6687.

Table I. Comparison between Experimental and Theoretical, AM1, Deprotonation Enthalpies (DPE)[a]

	molecule	anion	deprotonation enthalpy		error	corrected AM1-DPE[b]
			exptl	AM1		
1			400.7	402.6	1.9	
2				389.9		400.6
3				395.7		
4			391.0	394.8	3.8	
5				382.8		393.5
6			382.4	386.2	3.8	
7				376.3		397.7
8				381.6		392.3
9			385.2	388.8	3.8	
10			392.6	381.9	-10.7	392.6
11				393.9		
12			387.2	393.7	6.5	
13				395.2		
14			383.2	387.6	4.4	
15				389.7		
16				388.5		
17				379.1		
18				380.8		
19			354.2	378.9	24.7	
20			391.0	397.7	6.7	
21				399.3		
22				401.2		
23				403.4		
24				384.0		391.0
25				386.7		
26			387.1	386.0	-1.1	
27			372.5	363.5	-9.0	368.5
28				395.9		
29				395.9		
30				395.8		
31			397.4[c]	373.5	-5.9	378.5
32			370.0	365.2	-4.8	370.2
33			363.1	355.9	-7.1	362.9
34			368.6	365.9	-2.7	
35			371.2	370.4	-0.8	

[a] All values are in kcal/mol. $\Delta H_f(\mathrm{H}^+)$ = 367.2 kcal/mol. [b] See text. [c] Reference 1.

of the product ions of the reaction partners. The results are in good agreement with the values calculated from statistical mechanics.

Theoretical Results

In Table I we compare the experimentally determined DPEs with those obtained from AM1 for the various species of interest.

As shown in Table I, the position of the negative charge in the anion denotes the deprotonated site.

For many neutral molecules several deprotonation sites are available. In most cases, we have calculated DPEs of these various positions. The site having the lowest DPE is the most acidic one. The errors in computed DPEs by AM1 are also given in Table I for the most acidic site in the parent compounds only. Moreover, in the cases where AM1 made serious errors in DPEs, we corrected these values in the last column of Table I, as will be discussed below.

In Table II, we list the RHF/6-31G and MP2=FC/6-31G//RHF/6-31G total energies of pyridine, diazines, and their most stable anions obtained from ab initio calculations. The corresponding energies, for the species of interest, obtained from RHF/6-31G*//RHF/6-31G and MP2=FC/6-31G*//RHF/6-

Table II. Ab Initio RHF/6-31G and MP=FC/6-31G//RHF/6-31G Total Energies (au) of Pyridine, Diazines, and Their Most Stable Anions and DPEs (kcal/mol)

	total energy		
species	RHF/6-31G	MP2=FC/ 6-31G//RHF-6-31G	DPE[a]
pyridine	−246.593 90	−247.127 35	
			416.7 (418.0)
4-pyridinyl	−245.927 78	−246.463 25	
1,2-diazine	−262.524 62	−263.085 45	
			403.9 (405.7)
1,2-diazin-4-yl	−261.878 09	−262.4451 78	
1,3-diazine	−262.564 48	−263.119 08	
			406.1 (410.6)
1,3-diazin-5-yl	−261.910 15	−262.471 89	
1,4-diazine	−262.557 16	−263.113 63	
			414.2 (416.7)
1,4-diazin-2-yl	−261.893 06	−262.453 61	

[a] The DPEs are calculated from the difference between the MP2 total energy of the neutral molecule and its anion. The DPEs computed from the RHF/6-31G total energies are given in parentheses. (1 au = 627.5 kcal/mol.)

Table III. Ab Initio RHF/6-31G*//RHF/6-31G and MP2=FC/6-31G*//RHF/6-31G Total Energies (au) of Pyridine, Diazines, and Their Most Stable Anions and DPEs (kcal/mol)

	total energy		
species	RHF/6-31G*	MP2=FC/6-31G*	DPE[a]
pyridine	−246.695 17	−247.480 74	
			413.8 (416.6)
4-pyridinyl	−246.031 21	−246.820 97	
1,2-diazine	−262.649 10	−263.471 88	
			402.5 (406.1)
1,2-diazin-4-yl	−262.001 94	−262.830 42	
1,3-diazine	−262.691 92	−263.507 22	
			404.6 (411.7)
1,3-diazin-5-yl	−262.035 72	−262.862 35	
1,4-diazine	−262.681 65	−263.501 03	
			414.2 (418.8)
1,4-diazin-2-yl	−262.014 18	−262.840 95	

[a] The DPEs are calculated from the difference between the MP2 total energy of the neutral molecule and its anion. The DPEs computed from the RHF/6-31G* total energies are given in parentheses. (1 au = 627.5 kcal/mol.)

31G single-point calculations are given in Table III. Assuming that the zero-point energies and thermal corrections (from 0 to 298 K) of the parent compounds are the same as their corresponding anions, DPEs can be equated to the difference between the total energies of the anions and their neutral molecules. These DPEs are given in the last columns of Tables II and III.

Discussion

Experimental Methods. The results display the effects of aza substitution and several electron-withdrawing substituents on the acidity of aromatic sp^2 carbons and also some effects on sp^3 carbon acidities.

For aza-substitution effects, we may compare benzene with pyridine and the isomeric diazines, and naphthalene, with quinoline. In relation to aza-substitution effects in azoles, Taft et al.[3] found that the major effects on the stability of the ions were as follows: adjacent lone-pair repulsion contributes 6.5 kcal/mol; the electronegative 2-aza-substituent effect is −12.5 kcal/mol, and the 3-aza substituent effect is −8.5 kcal/mol.

To analyze aza-substituent effects here, we note that from benzene to pyridine $\Delta H°_{\text{acid}}$ decreases, i.e. the acidity increases, by about 10 kcal/mol and the 1,2- and 1,3-diazine by another 6–8 kcal/mol. However, the $\Delta H°_{\text{acid}}$ of 1,4-diazine is larger, i.e. the acidity is lower, than those of the other diazines by 8–10 kcal/mol. We observe that, of all these compounds, only in 1,4-diazine must the deprotonation site be adjacent to a nitrogen. Therefore, the lone-pair repulsion would explain the substantially lower acidity of this compound compared to the other diazines. Qualitatively, this agrees with the conclusions of Taft et al.[3]

Quantitatively, however, the parameters of Taft et al.[3] can reproduce the results only if some unlikely assumptions are made. The results can be reproduced within 2 kcal/mol by assuming that, in relation to the deprotonation site, 2-aza substitution has no effect, due to a cancellation of lone-pair repulsion and electronegativity stabilization, and 3- and 4-aza substituents are stabilizing by 8 kcal/mol. This would reproduce all the results, if deprotonation in pyridine, 1,2-diazine, and 1,3-diazine are assumed to occur at sites not adjacent to the nitrogen atom. However, these parameters would require that lone-pair repulsion is destabilizing by 8 kcal/mol *and* the 2-aza substitution is stabilizing by the same amount as 3- and 4-substitution, i.e., by 8 kcal/mol. The latter relation is unreasonable, but if the electronegative stabilizing effect of 2-aza substitution is assumed greater than 3- or 4-substitution, i.e., greater than 8 kcal/mol, then lone-pair repulsion must be assumed also proportionally more destabilizing, and therefore unreasonably large. More realistically, it can be assumed that the effects of multiple aza substitution are not additive.

Annelation does not seem to decrease the aza-substituent effect. The difference between naphthalene and quinoline, 8.6 kcal/mol, is similar to that between pyridine and benzene, 9.7 kcal/mol. Annelation effects are discussed in more detail in the next paper.[9]

Similar to in-ring aza substitutions, out-of-ring electron-withdrawing substituents also increase the acidity significantly. The substituents F, CF_3, CN, and NO_2 are all electron withdrawing, and they increase the acidity of the ring carbons by 14, 15, 18, and 47 kcal/mol, respectively. These may be compared with the effects of the same groups on para-substituted toluenes, phenols, and anilines. On toluene, the results are 2, 12, 16, and 26 kcal/mol; in phenols, we find 2, 11, 17, and 22 kcal/mol; in anilines, we get 2, 11, 17, and 21 kcal/mol.[1] These three classes of compounds involve effects on acidic sites external to the ring, and they are markedly similar to each other. The results on the substituted benzenes show that the same order of substituents is preserved when the acidic site is a ring carbon. Quantitatively, the magnitudes of the substituent effects are different. In particular, while the effects of CF_3 and CN on ring and external acidic sites are comparable, NO_2 and F have much larger effects on the ring acidity.

The much larger effect of F on ring carbon acidity may be explained on the basis that it withdraws electrons mostly from the σ-bond system of benzene and has but a small effect on the π-bond system.[11] This will affect the stabilities of the sp^2 lone pair in deprotonated benzene and its derivative but much less the lone pairs on the CH_2^-, O^-, and NH^- in deprotonated toluene, phenol, and aniline where the lone pairs are conjugated with the ring π system. On the other hand, the CF_3, CN, and NO_2 substituents are both σ and π withdrawing and, therefore, affect both the ring and out-of-ring acidities.[11b]

We note here that nitrobenzene is substantially more acidic than the other benzene derivatives. This is in accordance with the large effects of nitro substitution on alkanes, which is also much larger than CN, F, or CF_3 substitution.

Concerning substitution effects on toluene and aniline, it is interesting that in-ring aza substitution, from toluene to 4-methylpyridine and from aniline to 2-aminopyridine, has significant effect, 9.4 and 5.5 kcal/mol, respectively, on the extra-ring acidic sites.

Interestingly, according to the AM1 results shown in Table I, styrene is deprotonated on the ring. The vinyl substituent increases the acidity of benzene by a substantial 9.7 kcal/mol. This may be due mostly to increased polarizability that stabilizes the ion. However, the vinyl group is σ withdrawing and π donating, and it is clear that the ring acidity is affected by the substituent's effect on the σ rather than the π system.[11]

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(11) To test these qualitative findings, we have performed single-point ab initio calculations, at the RHF/6-31G* level, using the AM1 optimum geometries of ortho, meta, and para anions of pyridine. The *p*-pyridinyl anion was found to be the most stable, *E*(total) = −246.025 59 au, and the ortho isomer, the least stable, *E*(total) = −246.006 34 au. The meta isomer was slightly less stable than *p*-pyridinyl, *E*(total) = −246.020 24 au.

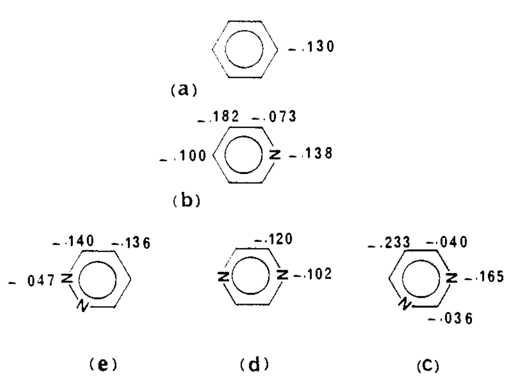

Figure 4. AM1 charge densities in (a) benzene, (b) pyridine, (c) 1,3-diazine, (d) 1,4-diazine, and (e) 1,2-diazine.

Theoretical Methods. This section is divided into three parts. In the first part, we use the AM1 charge density pattern and through-space nonbonding interaction arguments to qualitatively predict the most acidic sites in benzene, pyridine, and the various diazines. In the second section we compare the DPEs calculated by AM1 with those determined experimentally. Some of the errors reflected in the computed DPEs by AM1 are identified and corrected. The ab initio calculations on pyridine and the diazines are then presented and compared to AM1 results.

(i) Qualitative Model. From Figure 4, it is clear that in benzene all protons are equivalent. In pyridine, the carbon atoms that are one bond length away from nitrogen carry the smallest charge densities, −0.073. Therefore, one would expect that they are the most acidic sites in pyridine. However, removing a proton from one of these carbons will yield the corresponding anion whose negative charge is localized at the deprotonation site and is near the nitrogen lone pair of electrons. The nonbonded electrons' repulsion is expected to destabilize the *o*-pyridinyl anion. Avoiding this repulsion in the anion should stabilize it. As is clear from Figure 4, the carbon atom in pyridine that is para to the nitrogen has a net charge density slightly higher than the ortho carbon. Moreover, the localized negative charge in *p*-pyridinyl anion is farthest from the nitrogen lone pair of electrons. Therefore, we should expect *p*-pyridinyl anion to be more stable than the *o*-pyridinyl one. The *m*-pyridinyl anion, on the other hand, is expected to be slightly less stable than *p*-pyridinyl.[11]

Extending the above arguments to the anions of the various diazines and referring to Figure 4, we can see which protons in these species are most acidic. In 1,2- and 1,3-diazines, these are the protons that are farthest from the nitrogens. As to 1,4-diazine, the deprotonation site has to be near one of the nitrogen atoms.

The effects of electron-withdrawing groups on the charge density of the ring carbon atoms in benzene were discussed in detail by others.[12] The patterns of charge densities obtained from AM1 for substituted benzene are in agreement with the ab initio ones reported by Pross and Radom.[12]

(ii) Comparison of Experimental and Theoretical DPEs. In this section we compare the experimentally determined DPEs with those obtained from AM1. The qualitative arguments presented in the previous section are used to identify some of the errors in calculated AM1-DPEs and to suggest the necessary corrections.

In Table I we compare the DPEs for the various species of interest, obtained from experiment and from AM1. The computed AM1-DPE of benzene, **1**, is in good agreement with experiment.

Now consider pyridine, **2**, and the various diazines, **5–10**. It is clear from Table I that the trend in DPEs of these species calculated by AM1 contradicts our qualitative expectations presented in the previous section. That is, AM1 predicts that the most acidic sites in pyridine and diazines are those that are nearest to the nitrogen atom(s). It is known that AM1 underestimates the repulsion between neighboring lone pairs,[4d] in the present case between the nitrogen nonbonding electrons and the neighboring localized negative charge in the anion. This would lead to a wrong order of acidities of the various sites in pyridine and diazines. The AM1-DPE of 1,4-diazine, **10**, where the deprotonation site must necessarily be ortho to nitrogen, is 10.7 kcal/mol lower than the experimental value. Because the geometrical relation between the carbon lone pair and the nitrogen lone pair in this ion is known, we equate this value to the error in computed lone-pair repulsions by AM1. Adjusting the DPEs of the ortho anions in pyridine and the diazines (last column in Table I) renders these the least acidic sites. The acidities of the most acidic sites in these species give then a consistent difference, 3.8 kcal/mol, with the experimental ones. Our correction for lone-pair repulsion is similar to the value found by Fernandez et al.[4d] who reported ab initio, MNDO, and AM1 calculations on several six-membered nitrogenated heterocyclic compounds and their protonated forms. Their calculated proton affinities by AM1 agreed well with the experimental values if they are corrected by 10 kcal/mol for the species where neighboring lone-pair repulsion occurred.

From our results on 2-aminopyridine, **33**, and those of Dewar and Dieter,[4c] it appears that lone-pair repulsion corrections are also necessary where a ring lone pair interacts with a substituent lone pair external to the ring. AM1 also underestimates this interaction. A correction of 7 kcal/mol would yield the correct values of DPEs.

AM1 behaved better for benzene derivatives with an electron-withdrawing group such as F, CN, NO_2, or CF_3, **11–19** and **24–26**, or a π electron-donating one such as $CH{=}CH_2$, **20–23**. The errors in computed DPEs were within the average error reported by Dewar and Dieter,[4c] 6 kcal/mol. The exception was nitrobenzene, **19**, where AM1 overestimated its acidity by 24.7 kcal/mol. The relative acidities of benzene derivatives are fairly well reproduced by AM1.

DPEs of fused-ring compounds were reasonably reproduced by AM1, within its average error. Annelation effects are discussed in more detail in the next paper.[9]

Moreover, AM1 tends to overestimate the stability of the anions produced by deprotonating acenaphthene, **27**, toluene, **31**, and *p*-methylpyridine, **32**, by 5 kcal/mol. Dewar and Dieter's[4c] results also show similar errors in methyl-substituted anions. The corrected DPEs of these species are given in Table I.

To conclude, we see from the above results that AM1 appears to be suitable for *estimating* DPEs of *hydrocarbons* with an average error of about 6 kcal/mol. AM1 underestimate the repulsion between neighboring nonbonded electrons by about 11 kcal/mol, and 7 kcal/mol if the repulsion is between a substituent and the ring lone pairs. This was apparent for all compounds containing nitrogen in a five- or six-membered rings. It also underestimates the acidity of methyl-substituted compounds by 5 kcal/mol. If AM1 is used for compounds where lone-pair repulsion or methyl substitution occurs, these corrections must be considered.

(iii) Ab Initio Results. In Table II we list the total energies of pyridine and diazines obtained from the RHF/6-31G optimizations and MP2=FC/6-31G single-point calculations. The DPEs, given in the last column of Table II, are computed from the difference between the MP2 total energies of the anion and its parent molecule. The corresponding RHF/6-31G DPEs are given in parentheses. The corresponding ab initio results obtained from the single-point calculations with the 6-31G* basis set are given in Table III.

As shown in Tables II and III, the relative acidities of pyridine and diazines are well reproduced at the levels of theory used.

The DPEs obtained from the RHF/6-31G ab initio calculations are consistently higher than the experimental ones by 22–27 kcal/mol. The single-point MP2/6-31G calculations lowered the ab initio acidities by 2–3 kcal/mol (see Table II). The results of the calculations at the MP2=FC/6-31G*//RHF/6-31G level of theory listed in Table III show that the errors in DPEs are further reduced by an additional 2–3 kcal/mol. The exception is the DPE of 1,4-diazine. In order to reduce these errors further, the geometries of the parent molecule and its corresponding anion

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must be optimized, at least, at the MP2/6-31G level of theory and the zero-point and thermal energy corrections for the neutrals and their corresponding anions must be calculated.[7,13]

At the present level of theory, ab initio is preferable for relative deprotonation energies, and AM1, especially with the corrections suggested, for absolute deprotonation energies.

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Registry No. 1, 71-43-2; **1** (anion), 30922-78-2; **2**, 110-86-1; **2** (*o*-anion), 100646-80-8; **3**, 100646-84-2; **4**, 100646-85-3; **5**, 289-80-5; **5** (3-anion), 115590-45-9; **6**, 115561-55-2; **7**, 289-95-2; **7** (2-anion), 115561-56-3; **8**, 115561-57-4; **9**, 115561-58-5; **10**, 290-37-9; **10** (anion), 115561-59-6; **11**, 462-06-6; **11** (*o*-anion), 72863-52-6; **12**, 77748-35-7; **13**, 77748-43-7; **14**, 100-47-0; **14** (*o*-anion), 77748-26-6; **15**, 77748-32-4; **16**, 77748-40-4; **17**, 98-95-3; **17** (*o*-anion), 77748-25-5; **18**, 77748-31-3; **19**, 77748-39-1; **20** (*o*-anion), 115561-60-9; **21**, 100-42-5; **21** (*m*-anion), 115561-61-0; **22**, 78427-92-6; **23**, 115561-62-1; **24**, 98-08-8; **24** (*o*-anion), 77748-27-7; **25**, 77748-33-5; **26**, 77748-41-5; **27**, 83-32-9; **27** (1-anion), 115561-63-2; **28**, 115561-64-3; **29**, 115561-65-4; **30**, 115561-66-5; **31**, 108-88-3; **31** (anion), 18860-15-6; **32**, 108-89-4; **32** (anion), 18860-18-9; **33**, 504-29-0; **33** (anion), 41458-22-4; **34**, 62-53-3; **34** (anion), 27547-14-4; **35**, 536-74-3; **35** (anion), 20404-08-4; $CH_3CONHCH_3$, 79-16-3; CF_3COCH_3, 421-50-1; CH_3COOH, 64-19-7; H_2O, 7732-18-5; CH_3OH, 67-56-1; C_2H_5CN, 107-12-0; 1-methylnaphthalene, 90-12-0; azulene, 275-51-4; pyrrole, 109-97-7; indene, 95-13-6; indole, 120-72-9; naphthalene, 91-20-3; quinoline, 91-22-5.

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Proton Affinities and pK_a Values of Tetraalkylhydrazines

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Abstract: Proton affinities for 16 saturated tetraalkylhydrazines were determined by equilibration with triethylamine, 2,6-dimethylpyridine, and 2,6-diethylpyridine using high-pressure mass spectrometry, and pK_a measurements in water were made for the 14 compounds which proved sufficiently soluble. Proton-transfer equilibria for these compounds are compared with electron-transfer equilibria previously measured.

Studies of the effect of changing alkyl groups in tetraalkylhydrazines on equilibrium[1] and rate constants[2] for electron transfer in the gas phase were recently reported, allowing comparison with previous studies in solution. A particularly unexpected result from the comparison of gas- and acetonitrile solution-phase electron-transfer equilibria was that the effect of changing alkyl group size on solvation energy is linear[1b] with the gas-phase "alkyl inductive effect" parameter *n*(eff).[3] *n*(eff) is measured from the ionization potential (IP) lowering effect of larger alkyl groups compared with methyl groups on lone-pair ionizations. It was shown that *n*(eff) can be simply estimated for cyclic and bicyclic alkyl groups and does effectively describe the IP lowering observed when lone-pair rehybridization does not occur. In this work we report equilibrium constant data for gas- and solution-phase proton transfer for a series of tetraalkylhydrazines, allowing comparison of electron loss and proton addition equilibria, both of which generate cations from the neutral compounds.

Results

Gas-phase proton-transfer equilibria for 16 saturated tetraalkylhydrazines were measured at 550 K by high-pressure mass spectrometry by determining their proton-transfer equilibrium constants with monoamines. Triethylamine was used as the primary standard (we took its proton affinity value as PA = 232.3 kcal/mol[4]), and 2,6-dimethylpyridine (A, PA = 228.0) and 2,6-diethylpyridine (B, PA = 230.0) were used as secondary standards, the PA values listed being determined by their equilibration with triethylamine in this work. The $\Delta G°$ (550 K) values measured appear in Table I.

Table I. Proton Affinity Data at 550 K. $\Delta G°$ Values (kcal/mol) for Proton Transfer Relative to Standard Amines

no.	compound	rel to A	rel to B	rel to Et_3N
1	Me$_2$N]$_2$	+2.8		
2	EtMeN]$_2$	−0.5	+1.4	
3	nPrMeN]$_2$	−2.6		+2.3
4	nBuMeN]$_2$	−3.3		+1.1
5	nPeMeN]$_2$	−3.7		+0.9
6	iBuMeN]$_2$		−2.0	+0.2
7	neoPeMeN]$_2$		−1.4	+0.5
8	r5N]$_2$		−1.8	0.0
9	r6N]$_2$	(−5.1)	−2.2	−0.3
10	{5}Me$_2$	+0.2	+2.8	
11	{6}Me$_2$	−1.7	+0.4	
12	{7}Me$_2$	−1.3	+0.7	
13	{5,5}	−3.9		+0.7
14	{6,6}		−1.7	+0.4
15	{221}Me$_2$	−3.0		+1.3
16	{222}Me$_2$	−4.5		0.0
17	u{6}Me$_2$	−1.6		

Symmetrical hydrazines having two formally equivalent nitrogens were studied, including acyclic compounds **1**–**7** (see the

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