Evaporation of the solvent gave a residue, which by crystallization from benzene yielded perchloro-1,2,3-triphenyl-3,4-dihydronaphthalene (8) (0.112 g): mp 185 °C dec; IR (KBr) 1530 (w), 1400 (w), 1380 (w), 1338 (s), 1318 (s), 860 (m), 830 (m), 810 (m), 755 (s), 730 (m), 710 (s) cm^{-1}; UV (C_6H_{12}) 218 nm, 229, 280 (sh), 307 (sh) (ε 73 500, 73 400, 10 500, 3930). Anal.[33] Calcd for $C_{28}Cl_{22}{}^{1}/_{2}C_6H_6$: C, 32.2; H, 0.3; Cl, 67.5. Found: C, 32.2; H, 0.5; Cl, 67.2. Evaporation of the mother liquors gave a residue, which by TLC (silica gel, CCl_4) afforded more dihydronaphthalene 8 (0.035 g; 72% overall yield) and starting naphthalene 5 (0.020 g; 10% recovery).

Thermal Dechlorination of Dihydronaphthalene 8. Compound 8 (0.030 g) was heated (190 °C; 10 min) under argon in a sealed glass tube. The resulting mass was passed through silica gel in CCl_4 to give naphthalene 5 (0.026 g; 93%). This dechlorination can be effected slowly (days) in boiling CCl_4.

Reaction of Tolane 2 with Oleum. (1) A mixture of tolane 2 (0.500 g) and 20% oleum (300 mL) was heated (100 °C; 24 h) with stirring. The resulting mixture was poured into ice and extracted with $CHCl_3$. The organic extract was dried and concentrated to a small volume, giving a white precipitate that was identified as starting material (0.212 g; 42%). Evaporation of the solvent gave a yellowish residue (0.196 g), which by TLC (silica gel; $CHCl_3$) afforded the following. (a) Starting material: 0.021 g; 4%. (b) 4,5-Bis(pentachlorophenyl)-1,3,2-dioxathiole 2,2-dioxide (α,α'-dihydroxydecachlorostilbene cyclic sulfate) (12) (0.123 g; 21%): white crystals, mp 230 °C dec; IR (KBr) 1530 (w), 1430 (s), 1350 (m), 1315 (m), 1275 (m), 1220 (s), 1157 (m), 1078 (m), 1010 (m), 795 (s), 725 (m), 718 (m), 698 (m) cm^{-1}; UV (C_6H_{12}) 224 nm, 243 (sh), 284, 304 (sh) (ε 49 000, 28 800, 10 100, 4390); MS (all ^{35}Cl), m/z 275 ($C_7Cl_5O^+$), 247 ($C_6Cl_5^+$), 212 ($C_6Cl_4^+$), 177 ($C_6Cl_3^+$). Anal. Calcd for $C_{14}Cl_{10}O_4S$: C, 27.2; Cl, 57.3;, S, 5.2. Found: C, 27.1; Cl, 57.5; S, 4.9. In one experiment, a small proportion of bis(pentachlorophenyl)carbinol (13) was isolated, which was identified by its mp [285–90 °C dec (lit.[25] mp 281–89 °C dec)] and IR spectrum.[25]

(2) This reaction was repeated with 65% oleum (50 ml) and tolane 2 (0.100 g) at room temperature (48 h). Cyclic sulfate 12 (0.090 g; 76%) was obtained.

(33) This compound crystallized with $^{1}/_{2}$ mol of benzene that could not be eliminated by drying at high vacuum.

Thermolysis of Cyclic Sulfate 12. Compound 12 was heated (250 °C; 2 h) in a sealed glass tube. The yellow residue was purified through silica gel in CCl_4, yielding perchlorodiphenylethanedione (perchlorobenzil) (14) (0.040 g; 89%): yellow crystals, mp 312–315 °C (lit.[26] mp 310.5–311.0 °C); IR (KBr) 1725 (s), 1530 (w), 1348 (s), 1334 (s), 1309 (w), 1230 (s), 1130 (s), 951 (s), 800 (m), 700 (s), 656 (m) cm^{-1}; UV (C_6H_{12}) 212 nm, 238, 290, 298, 315 (sh) (ε 99 200, 25 900, 2020, 1990, 1420); MS (all ^{35}Cl), m/z 275 ($C_7Cl_5O^+$), 247 ($C_6Cl_5^+$), 212 ($C_6Cl_4^+$), 177 ($C_6Cl_3^+$). Anal. Calcd for $C_{14}Cl_{10}O_2$: C, 30.3; Cl, 63.9. Found: C, 30.3; Cl, 63.8.

Hydrolysis of Cyclic Sulfate 12. (1) A mixture of cyclic sulfate 12 (0.050 g), acetonitrile (10 mL), and aqueous 0.01 N NaOH (7 mL) was refluxed (3 h) with stirring. The resulting mixture was extracted with $CHCl_3$, and the organic layer was washed with water, dried with Na_2SO_4, and evaporated. The resulting solid by fractional crystallization from hexane gave starting material (0.025 g; 50% recovery) and benzil 14[26] (0.018 g; 40%).

(2) A mixture of cyclic sulfate 12 (0.050 g), dioxane (40 mL), and aqueous 0.01 N NaOH (9 mL) was stirred (6 h) at room temperature. The resulting mixture was diluted with water and treated as in the preceeding paragraph to give starting material 12 (0.017 g; 34% recovery) and benzil 14 (0.018 g; 40%).

Reaction of Dihydronaphthalene 8 with Oleum. A mixture of dihydronaphthalene 8 (0.200 g) and 20% oleum (70 ml) was heated (100 °C; 24 h) with stirring. The resulting mass was poured into ice and extracted with $CHCl_3$. The organic extract was washed with water, dried with Na_2SO_4, and evaporated. The residue by TLC (SiO_2, CCl_4) gave starting material 8 (0.053 g; 26.5% recovery) and perchloro-4,5,6-triphenylinden-1-one (18) (0.052 g; 30%): yellow crystals, mp 286 °C dec; IR (KBr) 1732 (s), 1580 (w), 1550 (w), 1532 (w), 1334 (s), 1316 (s), 1188 (m), 981 (m), 860 (m), 831 (m), 800 (m), 787 (s), 710 (m), 692 (m), 678 (m) cm^{-1}; UV-vis ($CHCl_3$) 238 nm, 246 (sh), 268 (sh), 355, 370, 408 (sh) (ε 63 000, 58 400, 38 500, 2220, 2120, 1120); MS (all ^{35}Cl), m/z 970 ($C_{27}Cl_{18}O^+$), 935 ($C_{27}Cl_{17}O^+$), 397.5 ($C_{27}Cl_{13}O^{2+}$), 366 ($C_{26}Cl_{12}^{2+}$), 331 ($C_{26}Cl_{10}^{2+}$). Anal. Calcd for $C_{27}Cl_{18}O$: C, 33.1. Found: C, 33.1.

Registry No. 1a, 76570-98-4; 1b, 52789-10-3; 2, 20094-80-8; 3, 100231-15-0; 4, 100231-16-1; 5, 66341-44-4; 6, 100231-17-2; 7, 72760-93-1; 8, 100231-18-3; 12, 100231-19-4; 13, 33240-66-3; 14, 19349-29-2; 18, 100231-20-7; tetrachloroethylene, 127-18-4.

Proton Affinities of Azoles: Experimental and Theoretical Studies

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The proton affinities (PA's) of a series of azoles as measured by pulsed high-pressure mass spectrometry are (in kcal/mol) isoxazole, 202.3; oxazole, 207.8; 1,2,4-triazole, 212.4; pyrazole, 212.8; thiazole, 213.2; imidazole, 222.1; 4-methylimidazole, 224.8; 1-methylimidazole, 228.0. Ab initio protonation enthalpies calculated at the MP2/6-31G(d,p) level reproduce the above order and give approximate numerical values. Additionally, these calculations show that the protonation sites are N_3 in imidazole and oxazole and N_4 in 1,2,4-triazole, the alternate protonation sites of N_1, O, and N_2, respectively, being less favorable by 53, 57, and 13 kcal/mol. These ab initio studies also indicate a correlation between lone pair n orbital energies and proton affinities.

Azoles are a large and important class of heterocycles that are often found as components of enzymes and coenzymes as well as in numerous pharmaceuticals, dyes, and explosives. Azoles are also starting materials for the synthesis of a variety of complex natural and synthetic species. Much of the interesting chemistry and biochemistry of azoles arises from their properties as bases, since they may undergo protonation or hydrogen bonding in acidic media.

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As a step toward understanding the basicity of these compounds, we have obtained experimental and computed ab initio gas phase proton affinities for a series of azoles. In this paper we will present the experimental and theoretical results and will analyze these data so as to gain insight into this important property of these bases.

Experimental Procedures

The experimental measurements were carried out on the NBS pulsed high-pressure mass spectrometer.[1] Mixtures composed of 0.001–0.1% of the azole and a reference compound dissolved in methanol were prepared and injected into a heated bulb. The mixtures were allowed to flow to the ion source of the mass spectrometer through stainless steel lines heated to about 200 °C. The mixtures were subjected to 1-ms pulses of 500–1000 eV electrons, which generated the ions $CH_3OH_2^+$ and $(CH_3OH)_2H^+$. These reagent ions in turn protonated the azoles A and reference compounds B to yield the ions AH^+ and BH^+. No additional ions appeared to be formed. The commercially obtained compounds were of nominal purity of 98% or higher and showed no significant impurities in their mass spectra; therefore, they were used without any additional purification.

The gas phase basicities were obtained from proton transfer equilibria (1). The reactions were observed 2–4 ms after the

$$BH^+ + A \rightleftharpoons AH^+ + B \quad (1)$$

ionizing electron pulse. During this time the ion intensity ratio $[AH^+]/[BH^+]$ reached a constant value. The equilibrium constant was then calculated from (2), where P(A) and P(B) are the partial

$$K = \{[AH^+]P(B)\}/\{[BH^+]P(A)\} \quad (2)$$

pressures of the azole and of the reference compound in the ion source. In general, P(A) and P(B) are known from the composition of the initial mixture and the total gas pressure in the ion source. However, some of the azoles (imidazole, pyrazole, 1,2,4-triazole, and 4-methylimidazole) had sufficiently low volatility to allow partial condensation in the sample bulb, the flow lines, and/or the ion source. In these cases, a kinetic method was used to measure P(A). This was done by measuring the pseudo-first-order rate constants k_1 of exothermic proton transfer reactions as in (1) or from the reagent ions to A. Equation 3 was used to calculate

$$k_1 = k_2 N(A) \quad (3)$$

the number density, N(A), and subsequently the pressure P(A) of species A. The second-order rate constants k_2 of the exothermic reactions were assumed to be equal to the collision rate, i.e., about 10^{-9} cm^3 s^{-1}. A similar method had previously been used to measure ionization potentials of polycyclic aromatics of low volatility, and good agreement with spectroscopic values had been obtained.[2]

Values of gas phase basicity, i.e., ΔG^{600} are directly obtained from the equilibrium constants for the reactions at 600 K. These experimentally determined values are shown in Table I. Following standard practice[3,4] protonation enthalpies, ΔH^{298}, were obtained from the ΔG^{600} values by direct inclusion of rotational entropy corrections and thermal corrections. We report $\Delta H^{600} = \Delta G^{600} + 600\ \Delta S_{\text{rot sym}}$ values, and assume $\Delta H^{298} \approx \Delta H^{600}$, since ΔC_p for reaction 1 should be negligible. The proton affinities reported in Table I are the average values determined from measurements with several reference compounds[3] and so constitute a self-consistent thermochemical "ladder".[3,4] The main source of experimental error in the present study is the uncertainty in the accuracy of the pressure measurement, P(A). With this uncertainty and from the values obtained by the use of the different reference compounds (see the "ladder"), the error in the proton affinities of the azoles is estimated to be ±1–2 kcal/mol.

Theoretical Methods

Gradient optimization techniques[5,6] have been employed to optimize the geometries of both the neutral and the protonated azoles at the single determinant Hartree–Fock level by using the minimal STO-3G basis set.[7] These optimizations were performed for azoles containing only first long-row elements and hydrogen and were carried out assuming a planar ring geometry with C_s symmetry for the bases and σ-protonated ions and C_1 symmetry for the π-protonated species. To obtain values of the protonation energy, single-point second-order Møller–Plesset correlated energies (MP2)[8,9] were then computed for the bases and ions at their optimized STO-3G geometries by using the 6-31G(d,p) basis set.[10] This basis set is a split-valence basis with d polarization functions on C, N, and O and p polarization functions on H. For the correlation calculations, the inner shell 1s electrons on C, N, and O were not correlated, that is, they were frozen in the Hartree–Fock 1s orbitals. The theoretical method employed to obtain the electronic energies (E_e^0) is designated MP2/6-31G-(d,p)//HF/STO-3G. As demonstrated previously,[11] even at this level of theory with correlation and a moderately large basis set, the computed proton affinities may be overestimated by 5–10 kcal/mol.

Optimized Hartree–Fock geometries for the bases and ions were also computed with the 3-21G basis set.[12] Second derivatives of the electronic energy with respect to the nuclear coordinates were calculated analytically with this basis set for each species. From the force constants, harmonic vibrational frequencies and associated zero-point vibrational energies (E_v^0) were determined. Details of such calculations and some estimates of the accuracy of these Hartree–Fock frequencies have been reported.[13–15] Since the vibrational frequencies are generally overestimated by approximately 10%, the zero-point vibrational energy contribution to the proton affinity will be correspondingly too large.[16]

The experimental protonation enthalpy is generally reported at 298 K as the thermochemical quantity ΔH^{298} for reaction 4. (The proton affinity is the negative of the

$$B + H^+ \rightarrow BH^+ \quad (4)$$

protonation enthalpy.) In order to compare experimental and theoretical results, other terms in addition to the electronic energy change (ΔE_e^0) and the zero-point vibrational energy change (ΔE_v^0) must be evaluated. These terms include the vibrational energy change owing to the thermal population of vibrational modes at 298 K [Δ-

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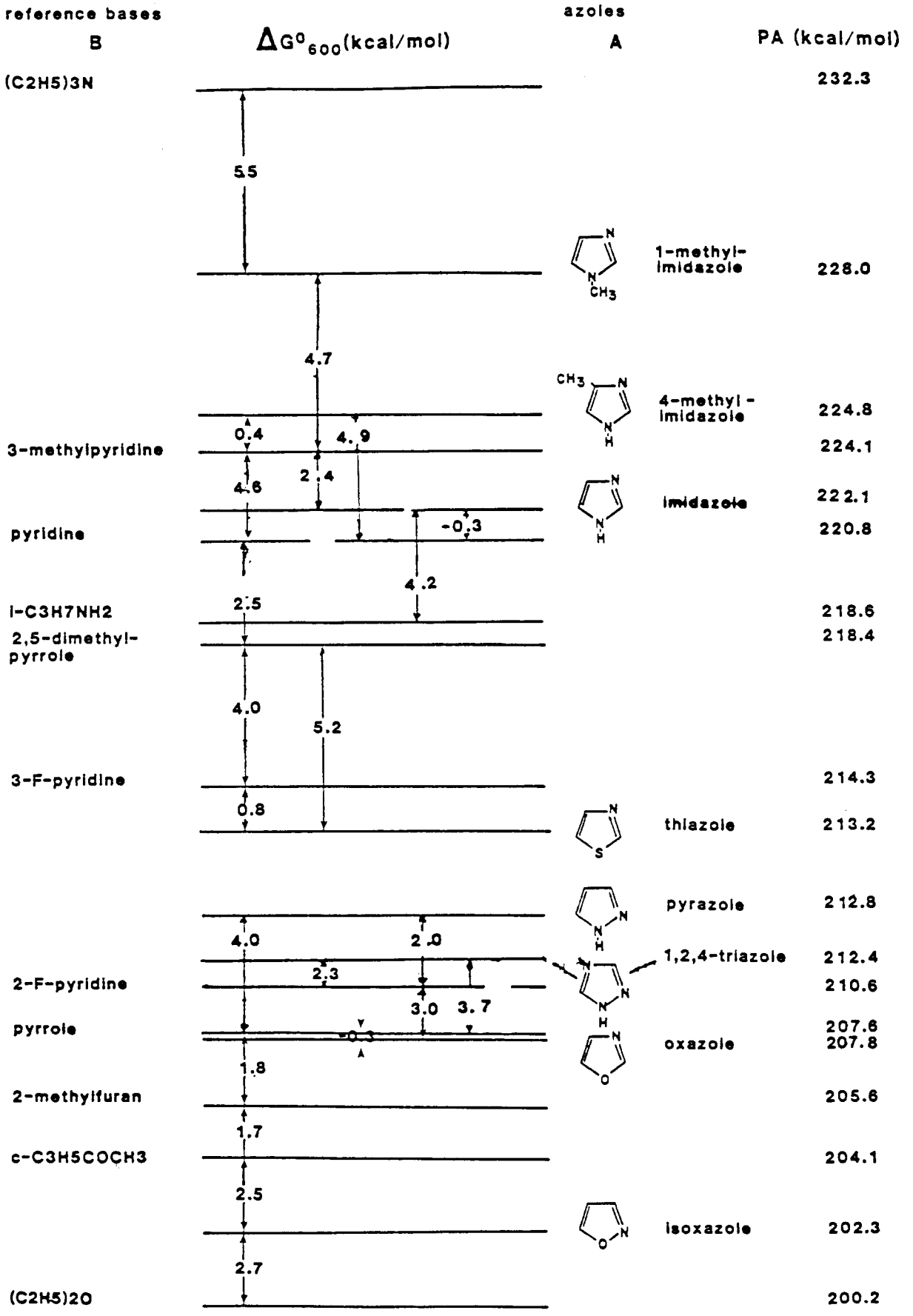
Table I



(ΔE_v)^{298}], the rotational (ΔE_r^{298}) and translational (ΔE_t^{298}) energy changes, and the PV term (ΔnRT). For each neutral and protonated azole, the vibrational energy due to the thermal population of vibrational modes at 298 K was directly evaluated by using the appropriate partition function.[17] It is important to note that since the three

Table II. Protonation Enthalpies (kcal/mol) of the Azoles

base	ΔE_e[a] HF	ΔE_e[a] MP	ΔE_v[b] ΔE_v^0	ΔE_v[b] $\Delta(\Delta E_v)^{298}$	ΔE_r	ΔE_t	ΔnRT	ΔH_{calcd}^{298}	ΔH_{exptl}^{298}[c]
1-methylimidazole	-246.2	-242.7	9.5	0.0	0.0	-0.9	-0.6	-234.7	-228.0
4-methylimidazole	-245.2	-241.9	9.7	0.0	0.0	-0.9	-0.6	-233.7	-224.8
imidazole									
H^+ at N_3	-241.4	-238.1	9.6	0.0	0.0	-0.9	-0.6	-230.0	-222.1
H^+ at N_1	-188.8	-183.3	7.7	0.2	0.0	-0.9	-0.6	-176.9	
pyrazole	-228.9	-223.5	8.9	0.1	0.0	-0.9	-0.6	-216.0	-212.8
1,2,4-triazole									
H^+ at N_4	-225.6	-222.2	9.2	0.0	0.0	-0.9	-0.6	-214.5	-212.4
H^+ at N_2	-214.7	-208.4	8.6	0.1	0.0	-0.9	-0.6	-201.2	
oxazole									
H^+ at N_3	-222.9	-219.6	9.1	0.0	0.0	-0.9	-0.6	-212.0	-207.8
H^+ at O_1	-165.0	-160.4	6.4	0.4	0.0	-0.9	-0.6	-155.1	
isoxazole	-215.2	-209.6	8.8	0.1	0.0	-0.9	-0.6	-202.2	-202.3

[a] Hartree–Fock and MP2 6-31G(d,p) energies at optimized STO-3G geometries. [b] Determined from Hartree–Fock 3-21G frequencies. [c] This work.

new vibrational modes resulting from protonation have relatively high frequencies, the thermal vibrational contribution to the reaction enthalpy is small. Since the number of rotational degrees of freedom does not change when the azoles are protonated ΔE_r^{298} is zero. Finally, the translational energy change together with the ΔnRT term contribute -1.5 kcal/mol to the reaction enthalpy, as there is a loss of 1 mole of gas and correspondingly three translational degrees of freedom as reactants ($A + H^+$) are converted to product (AH^+). All calculations were performed on an AMDAHL 470 V/6 computer by using a modified version of the GAUSSIAN 82 system of computer programs.[18] The structures of the neutral and protonated azoles are available as supplementary materials.

Results and Discussion

Table II presents the computed values for all terms contributing to the protonation enthalpy and a comparison of the theoretical and experimental ΔH^{298} values for protonation of the azoles. Except for isoxazole, the computed protonation enthalpies are greater than the experimental, the largest difference being an 8.9 kcal/mol overestimation of the protonation enthalpy of 4-methylimidazole. The level of theory employed in this study cannot reliably give protonation enthalpies to within 3 kcal/mol. Achieving this accuracy requires use of a larger basis set which includes diffuse functions on non-hydrogen atoms and the evaluation of the correlation contribution at fourth-order Møller–Plesset theory.[11] Nevertheless, the computed protonation enthalpies are reasonable, and the experimental order of increasing protonation enthalpy is reproduced. The data of Table II show that both the correlation energy contribution and the zero-point vibrational energy correction decrease the protonation enthalpy. The latter is the larger effect and reflects the increased zero-point vibrational energy of the protonated base owing to the three new high-frequency vibrational modes. Positive correlation energy contributions for protonation of oxygen and nitrogen bases have been observed previously,[11] indicating that correlation stabilizes the base relative to the ion. This may be due at least in part to the fact that while the base and ion are isoelectronic, the ion, with an additional nuclear center, has more basis functions and a more delocalized electron distribution. Hence, it is better described at the Hartree–Fock level of theory.

Table III. Experimental Ionization Potentials and Computed n Orbital Energies (in eV)

compound	experimental IP[a]	n orbital energy
imidazole	8.78	-11.73
pyrazole	9.15	-12.35
1-methylimidazole	8.66	-11.57
4-methylimidazole		-11.61
oxazole	10.2	-12.58
isoxazole	9.6[b]	-12.98
thiazole	9.5	

[a] All experimental values, except where noted, are from photoelectron spectroscopy measurements and correspond to vertical ionization processes. See ref 20. [b] This quantity was determined by electron impact. Its accuracy has not been assessed.

The enthalpies corresponding to protonation of two different sites in imidazole (N_1 and N_3), in 1,2,4-triazole (N_2 and N_4), and in oxazole (O and N) are also included in Table II. These data show that N_3 σ protonation is preferred over N_1 π protonation in imidazole by 53 kcal/mol, N over O protonation in oxazole is preferred by 57 kcal/mol, and protonation at N_4 in 1,2,4-triazole is 13 kcal/mol more favorable than N_2 protonation. No experimental data to compare the protonation enthalpies for protonation at a nonprimary site are available.

As noted above, protonation of imidazole at N_3 is favored over N_1 protonation by 53 kcal/mol. This reflects the fact that protonation is most favorable at a σ lone pair of electrons which is localized at a specific protonation site. Such is the case for N_3, which is the basic site in the molecular plane of imidazole. In contrast, N_1 does not have a σ lone pair but donates two electrons to the aromatic sextet, which is delocalized over the entire molecule. The nature of the product ion also favors protonation of N_3 over N_1. N_3 protonation of imidazole leaves the aromatic sextet intact as N_3 and N_1 become equivalent; N_1 protonation destroys the aromatic sextet.

In the absence of theoretical and experimental data, more qualitative physical organic arguments have often been used to approximate protonation enthalpies. Thus, the N_1 protonation enthalpy of imidazole may be estimated from available data,[3] beginning with the protonation enthalpy of pyrrolidine. (a) Start with the PA of pyrrolidine, 225 kcal/mol. (b) Decrease it by the inductive effect of the β nitrogen, taken as the difference between the PA's of pyridine and pyrimidine (221 - 211 kcal/mol) or 10 kcal/mol. (c) Decrease it further by the inductive effect of the two double bonds, approximated as twice the difference of the PA's of quinuclidine and its corresponding nonconjugated dehydro derivative or enamine, 1-azabicyclo[2.2.2]octene [2(232 - 229)kcal/mol] or 6 kcal/mol. (d)

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Table IV. Isomerization Enthalpies (kcal/mol)[a]

	ΔE_e[b]		ΔE_v[c]			
	HF	MP2	ΔE_v^0	$\Delta(\Delta E_v)^{298}$	ΔH_{calcd}^{298}	ΔH_{exptl}^{298}[d]
pyrazole → imidazole	−14.1	−10.3	0.1	0.0	−10.2	−9.6[d]
isoxazole → oxazole	−27.7	−22.7	0.4	0.0	−22.3	−22.3[e]
1-methylimidazole → 4-methylimidazole	−7.1	−6.6	0.0	0.0	−6.6	

[a] ΔE_r, ΔE_t, and ΔnRT for these isomerization reactions are equal to zero. [b] Hartree–Fock and MP2 6-31G(d,p) energies at optimized STO-3G geometries. [c] Hartree–Fock 3-21G frequencies. [d] Sabbah, R. *Thermochim. Acta.* **1980**, *41*, 33. [e] McCormick, D. G.; Hamilton, W. S. *J. Chem. Thermodyn.* **1978**, *10*, 275.

Adjust it by the energy lost in converting the aromatic sextet into a conjugated diene. This may be estimated by taking the difference between the hydrogenation enthalpies of pyrrole and cyclopentadiene, in the absence of data for imidazole and 3*H*-pyrrole. These enthalpies, derived from the heats of formation of the appropriate unsaturated and saturated five-membered rings are 27 and 50 kcal/mol,[19] giving an energy loss of about 23 kcal/mol. Combining all of these numbers (225 − 10 − 6 − 23) results in an approximate N_1 proton affinity of imidazole of 186 kcal/mol, which is in agreement (to within 10 kcal/mol) with the value of 177 kcal/mol computed at MP2/6-31G(d,p).

1,2,4-Triazole has two σ protonation sites, N_2 and N_4. Table II indicates that protonation occurs at N_4 rather than N_2. If it is assumed that the presence of the third nitrogen in the ring affects the basicity of N_2 and N_4 equally, then the difference in the N_2 and N_4 protonation enthalpies should be similar to the difference in the protonation enthalpies of imidazole and pyrazole. The protonation enthalpy of imidazole is greater than that of pyrazole by 9.3 kcal/mol (experiment) and 14.0 kcal/mol (theory). The computed difference between N_4 and N_2 protonation of 1,2,4-triazole is 13.3 kcal/mol.

The protonation enthalpy of oxazole should be lower than that of imidazole since oxygen is more electronegative than nitrogen, with the result that oxygen compounds are usually less basic than their nitrogen analogues. This applies not only to the basicity of an oxygen vs. a nitrogen site (amines vs. ethers, for example) but also to the effect of nitrogen substitution by oxygen on the basicity of some other site in the molecule. [An example is the relative proton affinities of the saturated six-membered rings dioxane (193.8 kcal/mol) and morpholine (219.4 kcal/mol).] An experiment to measure the oxygen proton affinity of oxazole would be challenging; however, it has been computed as readily as the nitrogen proton affinity, and it may be estimated in a manner similar to that employed to estimate the N_1 proton affinity of imidazole. (a) Begin with the PA of tetrahydrofuran (199 kcal/mol). (b) Reduce it by the inductive effect of a β nitrogen (10 kcal/mol). (c) Reduce it further by the effect of two double bonds (6 kcal/mol). (d) Adjust it by the energy lost in converting the aromatic sextet into a conjugated diene, estimated by the difference in the hydrogenation enthalpies of furan and cyclopentadiene (15 kcal/mol).[19] This results in an approximate oxygen proton affinity for oxazole of 168 kcal/mol, in fairly good agreement with the computed MP2/6-31G(d,p) value of 155 kcal/mol.

It is of interest to compare the proton affinities of the isomeric pairs oxazole and isoxazole and pyrazole and imidazole. The presence of an heteroatom in the ring and in the case of oxazole and isoxazole interactions involving σ lone pairs are factors which influence the relative proton affinities of these bases. For oxazole and isoxazole the presence of the electron-withdrawing oxygen atom in the ring stabilizes the σ lone pair of electrons at the nitrogen and this tends to reduce the proton affinity of these bases. This inductive effect would be expected to be greater in the 1,2-isomer (isoxazole). On the other hand, lone pair–lone pair repulsion would tend to destabilize the nitrogen lone pair in the 1,2-isomer relative to 1,3. Upon nitrogen protonation the interaction between the N–H group and the adjacent oxygen lone pair would then stabilize the 1,2-isomer. These lone pair effects would tend to increase the proton affinity of isoxazole. The fact that the 1,3-isomer (oxazole) has the greater proton affinity suggests that the electron-withdrawing effect dominates in this case. No lone pair interactions are found in imidazole and pyrazole, and, so once again, the 1,3-isomer (imidazole) has the higher proton affinity. That lone pair effects may be important in determining relative proton affinities is evident from the higher proton affinity of 1,2-diazine (pyridazine, 215.6 kcal/mol) relative to 1,3-diazine (pyrimidine, 210.5 kcal/mol).

It is also interesting to note that the effect of methylation of imidazole is to increase the proton affinity, with methylation at N_1 having a slightly greater effect than C_4 methylation. C_4 methylation in imidazole is comparable to C_2 methylation in pyridine as methylation occurs at a carbon adjacent to the protonation site. In pyridine, C_2 methylation increases the protonation enthalpy by 4.2 kcal/mol; C_4 methylation in imidazole increases the protonation enthalpy by 2.7 kcal/mol (experiment) and 3.7 kcal/mol (theory).

Computed n orbital energies of a series of bases may be of value in predicting relative proton affinities, provided that the n orbitals being compared are similar and associated with the protonation site. Since the negative of the n orbital energy generally approximates the ionization potential of the base (Koopmans' theorem), this suggests a relationship between the experimental ionization potential and the proton affinity. Table III reports the computed n orbital energies (E_n) and the experimental ionization potentials.[20] The following least-squares results have been obtained.

$$\text{theory:} \quad PA = 22.7E_n(\text{eV}) + 497.1 \qquad (5)$$

with a correlation coefficient of 0.999

$$\text{experiment:} \quad PA = -13.6\text{IP(eV)} + 340.7 \qquad (6)$$

with a correlation coefficient of 0.830

Experimental heats of formation are available for pyrazole, imidazole, oxazole, and isoxazole, and from these isomerization enthalpies may be determined. A comparison of the isomerization enthalpies reported in Table IV shows that there is excellent agreement between the computed and experimental values. The computed enthalpies at 298 K are determined exclusively by the differences in the electronic energies of these isomeric pairs. These

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differences are better described with correlation than at the Hartree–Fock level. Table IV also reports the enthalpy for the isomerization reaction involving 1-methylimidazole and 4-methylimidazole for which no experimental data are available. The computed results predict that 4-methylimidazole is the more stable isomer by 6.6 kcal/mol.

Conclusions

In this study, the following experimental gas phase proton affinities (in kcal/mol) for a series of azoles have been determined: isoxazole, 202.3; oxazole, 207.8; 1,2,4-triazole, 212.4; pyrazole, 212.8; thiazole, 213.2; imidazole, 222.1; 4-methylimidazole, 224.8; and 1-methylimidazole, 228.0. Ab initio protonation enthalpies for first-row azoles computed at the MP2/6-31G(d,p) level of theory reproduce the above order but tend to overestimate the experimental values, the largest difference being 8.9 kcal/mol for the proton affinity of 4-methylimidazole. These calculations show that the protonation sites are N_3 in imidazole and oxazole and N_4 in 1,2,4-triazole, the alternate protonation sites of N_1, O, and N_2, respectively, being less favorable by 53, 57, and 13 kcal/mol.

These calculations also indicate a correlation between lone pair n orbital energies and proton affinities for those azoles in which the lone pair is localized at the protonation site. The methyl substituent effect on the proton affinity of imidazole and the differences in the proton affinities of the isomeric pairs oxazole and isoxazole and imidazole and pyrazole are reproduced by these calculations. Computed isomerization energies for pyrazole and imidazole and oxazole and isoxazole are in excellent agreement with the experimental values.

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Registry No. 1-Methylimidazole, 616-47-7; 4-methylimidazole, 822-36-6; imidazole, 288-32-4; thiazole, 288-47-1; pyrazole, 288-13-1; 1,2,4-triazole, 288-88-0; oxazole, 288-42-6; isoxazole, 288-14-2.

Supplementary Material Available: STO-3G and 3-21G structures of neutral and protonated azoles (34 pages). Ordering information is given on any current masthead page.

Methylenecyclopropane Rearrangement as a Probe for Free Radical Substituent Effects. Effect of Sulfur in Various Oxidation States

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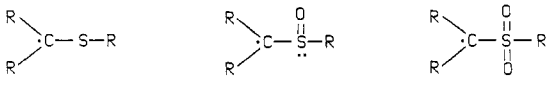
A series of 3-aryl-2,2-dimethylmethylenecyclopropanes **4** with the sulfur-containing substituents SCH_3, $SOCH_3$, SO_2CH_3, and $PS(OEt)_2$ in the para and meta positions have been prepared. These substrates undergo thermal rearrangement at 80 °C in C_6D_6 to give the corresponding 2-arylisopropylidenecyclopropanes **5** at rates which vary as a function of substituent. The para-substituted substrates all rearrange at faster rates than the unsubstituted system. Comparison with the meta isomers suggests that the rate-enhancing effect is conjugative in nature. The singlet trimethylenemethane biradical intermediate is suggested to be stabilized by *p*-SCH_3, *p*-$SOCH_3$, and *p*-SO_2CH_3 substituents, with *p*-SCH_3 providing the greatest stabilization. The *p*-$PS(OEt)_2$ substituent is also quite effective at increasing rate. These rate effects are considered in terms of interaction of the nonbonding electron pair of SCH_3 with the developing benzylic radical center. A further stabilizing interaction involving vacant d orbitals is considered to account for the greater stabilizing effect of SCH_3 relative to OCH_3, as well as the relatively large stabilizing effects of $SOCH_3$, SO_2CH_3, and $PS(OEt)_2$ on the transition state for this methylenecyclopropane rearrangement.

The effect of sulfur-containing groups on free radicals is an area of current interest. Neighboring sulfide substituents are thought to stabilize free radicals. Evidence for this comes from a variety of studies including vinyl sulfide copolymerization data,[1] azocumene pyrolyses,[2] hydrogen atom abstraction data,[3a] and ESR data.[4] The effect of sulfur in oxidized forms (as in sulfoxides and sulfones) is not as clear. While α-sulfinyl[3b] as well as α-sulfonyl radicals[3c] have been generated in the past, the effect of these substituents on radical stability is not as well understood. We wanted a more quantitative comparison of the effect of sulfide, sulfoxide, and sulfone on free radicals such as **1**–**3**.



1 **2** **3**

Large polar effects are often observed in reactions leading to free radicals. Hydrogen atom abstraction reactions are a classic example and rate data for such processes often reflect the polar nature of the transition state which can overwhelm any true radical stabilizing effects.[5] We therefore sought a reaction which was devoid of significant polar character to evaluate true free radical stabilizing effects. A number of years ago we suggested[6] that the methylenecyclopropane rearrangement of **4** to **5** could

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