JOURNAL

OF THE AMERICAN CHEMICAL SOCIETY

VOLUME 110, NUMBER 9 APRIL 27, 1988

Study of the Gas-Phase Basicity of 1-Methylazaindole, 7-Methyl-7*H*-pyrrolo[2,3-*b*]pyridine, and Related Compounds

J. Catalán,[†] J. L. G. de Paz,[†] M. Yáñez,[†] F. Amat-Guerri,[‡] R. Houriet,[§] E. Rolli,[§] R. Zehringer,[‖] P. Oelhafen,[‖] R. W. Taft,*[⊥] F. Anvia,[⊥] and J. H. Qian[⊥]

Contribution from the Departamento de Química Física y Química Cuántica, Facultad de Ciencias, C-XIV, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain, Instituto de Química Orgánica General, CSIC, Juan de la Cierva, 3, 28006 Madrid, Spain, Institute of Physical Chemistry, Swiss Federal Institute of Technology, EPFLP, CH-1015 Lausanne, Switzerland, Institute for Physics, University of Basel, Klingelbergstrasse 82, CH-4056 Basel, Switzerland, and Department of Chemistry, University of California, Irvine, California 92717. *Received April 20, 1987*

Abstract: The gas-phase basicities of 1-methylazaindole (NMAI), 7-methyl-7*H*-pyrrolo[2,3-*b*]pyridine (7MPP), pyrazolo-[1,5-*a*]pyridine (A), imidazo[1,5-*a*]pyridine (B), imidazo[1,2-*a*]pyridine (C), benzoxazole (D), and 2-methylbenzoxazole (E) were obtained by ion cyclotron resonance techniques and their N 1s binding energies measured by X-ray photoelectron spectroscopy. Simultaneously, ab initio calculations at the STO-3G and 4-31G levels were carried out for the same compounds and their protonated forms. The results obtained show that 7MPP is a very basic compound in the gas phase and confirm previous theoretical estimations, which indicate that this derivative should be much more basic than its tautomer NMAI. The linear relationships between gas-phase PA's and N 1s binding energies are very sensitive to details of local bonding at the basic center. Compounds A–C present an enhanced basicity with regard to imidazole and pyrazole, but the gap between the PA's of compounds A and C is identical with that reported for the couple imidazole–pyrazole. Compound B constitutes an exception and presents a gas-phase basicity somewhat dampened, because mesomeric forms do not accumulate charge at the basic center in this particular case. The calculated relative PA's as well as the relative N 1s orbital energies are basis set dependent, at least for these kinds of compounds.

1. Introduction

The constant expansion of the gas-phase ion chemistry in the last 10 years led to a rapid accumulation of data on the intrinsic basicity of a considerable number of organic and inorganic compounds. As a consequence, rapidly increasing information is being gathered regarding solution and substituent effects on gas-phase proton affinities.[1] Besides, more and more frequently, combined theoretical and experimental studies[2] on these topics appeared in the literature, among other things, because ab initio SCF calculations provide, quite often, useful information on the role played by substituents on the structure and reactivity of a given system. In this respect, a considerable number of useful linear relationships between experimental gas-phase PA's and some theoretically calculated indexes have been proposed.

Linear correlations between the gas-phase PA's and the 1s binding energies (or, alternatively, the corresponding SCF 1s orbital energy) of the basic center have been heavily used.[3] In some particular cases, these correlations were employed to theoretically predict the intrinsic basicity of compounds whose experimental gas-phase basicity was unknown.[4] In this respect it has been postulated,[5] for instance, that tautomeric changes in nitrogen containing heterocycles lead to geometrical changes as well as noticeable differences between the intrinsic basicities of the tautomers. 7-Methyl-7*H*-pyrrolo[2,3-*b*]pyridine (7MPP) and its isomer 1-methyl-7-azaindole (NMAI) constitute a suitable example. These two compounds exhibit noticeable differences in their electronic structures—for both the ground and first excited states—as revealed by different theoretical[6] and experimental studies.[7] Moreover, we have predicted[4] recently also a very different gas-phase basicity for both systems, 7MPP being much more basic in the gas phase than its isomer, NMAI.

This considerable increase in the gas-phase basicity on going from NMAI to 7MPP was postulated as a direct consequence of

---

[†] Universidad Autônoma de Madrid.

[‡] Instituto de Química Orgânica General.

[§] Swiss Federal Institute of Technology.

[‖] University of Basel.

[⊥] University of California.

(1) See, for instance: Taft, R. W. *Prog. Phys. Org. Chem.* **1983**, *14*, 247. Moyland, C. R.; Brauman, J. I. *Annu. Rev. Phys. Chem.* **1983**, *34*, 187, and references therein.

(2) See, for instance: (a) Hehre, W. J.; Taagepera, M.; Taft, R. W.; Topson, R. W. *J. Am. Chem. Soc.* **1981**, *103*, 1344. (b) Bollinger, J. C.; Houriet, R.; Kern, C. W.; Perret, D.; Weber, J.; Yvernault, T. *J. Am. Chem. Soc.* **1985**, *107*, 5352.

(3) (a) Martin, R. L.; Shirley, D. A. *J. Am. Chem. Soc.* **1984**, *96*, 5299. (b) Catalán, J.; Yáñez, M. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1627. (c) Catalán, J.; Mó, O.; Pérez, P.; Yáñez, M. *J. Am. Chem. Soc.* **1979**, *101*, 6520.

(4) Catalán, J.; Mó, O.; Pérez, P.; Yáñez, M.; Amat-Guerri, F. *Nouv. J. Chim.* **1984**, *8*, 87.

(5) Catalán, J.; Mó, O.; Pérez, P.; Yáñez, M. *J. Mol. Struct.* **1983**, *74*, 143.

(6) Catalán, J.; Pérez, P. *J. Theor. Biol.* **1979**, *74*, 143.

(7) Cox, R. H.; Sankar, S. *Org. Magn. Reson.* **1980**, *14*, 150.

0002-7863/88/1510-2699$01.50/0

Table I. Gas-Phase Basicities and Proton Affinities from ICR Proton-Transfer Equilibria Determinations with Standard Bases (kcal/mol)

base	std used	$\delta\Delta G^\circ_{NH_4^+(S)}$[a]	ΔG_i°[b]	$\delta\Delta G^\circ_{NH_4^+(B)}$[c]	$\delta\Delta H^\circ_{NH_4^+(B)}$[d]	PA (best value)[e]
1H7A	*tert*-amyl-NH_2	+19.2	0.1[f]	+19.3	18.5	
	2-OMepy	18.2	1.4[g]	19.6	18.8	
	3-Mepy	20.3	−1.0[g]	19.3	18.5	222.6 ± 0.1
NMAI	pyrr	21.3	−0.4[f]	20.9	20.1	
	4-Mepy	21.1	0.1[f]	21.2	20.4	224.2 ± 0.2 (223.9)[h]
7MPP	$(n\text{-Bu})_3N$	32.7	0.4[f]	33.1	32.3	
	4-NMe_2py	33.2	−0.6[g]	32.6	31.8	
	$(n\text{-Pr})_3N$	31.3	+1.0[g]	32.3	31.5	235.9 ± 0.3 (251.5)[h]
A	Me_2NH	17.1	−1.2[f]	15.9	15.1	
	i-$BuNH_2$	15.5	−0.1[f]	15.4	14.6	
	i-$PrNH_2$	15.4	−0.1[f]	15.3	14.5	
	n-$BuNH_2$	14.6	+0.3[g]	14.9	14.1	
	4-CF_3pip	16.0	−0.8[g]	15.2	14.4	218.5 ± 0.3
B	1-MeIm	23.8	−1.1,[f] −0.4[g]	22.7, 23.4	22.3	
	pip	22.3	0.5,[f] 1.0[g]	22.8, 23.3	22.3	
	$(n\text{-Pr})_2NH$	24.1	−1.2[f]	22.9	22.1	
	$(CH_2)_6NH$	23.1	−0.2,[f] 0.4[g]	22.9, 23.5	22.4	226.3 ± 0.3
C	1-Mepip	26.6	0.3[f]	26.9	26.1	
	$(i\text{-Pr})_2NH$	26.4	0.4,[f] 0.4[g]	26.8	26.0	
	3-NMe_2py	26.9	−0.4[f]	26.5	25.7	229.9 ± 0.2
D	2-Fpy	7.4	1.0[f]	8.4	7.6	211.6
E	$EtNH_2$	12.6	0.1[f]	12.7	11.9	215.9

[a] ΔG° (kcal/mol) for the gas-phase reaction: $NH_4^+ + B \rightleftharpoons BH^+ + NH_3$, as given in ref 1 or as submitted to S. G. Lias for inclusion with revised scales in: *J. Phys. Chem. Ref. Data* **1984**, *13*, 695. [b] Observed ΔG° for $BH^+ + S \rightleftharpoons SH^+ + B$. [c] $\delta\Delta G^\circ_{NH_4^+(B)} = \delta\Delta G^\circ_{NH_4^+(S)} + \Delta H_i^\circ$. [d] $\eta\Delta H^\circ_{NH_4^+(B)} = \delta\Delta H^\circ_{NH_4^+(B)} - 0.8$ for all bases of this table; cf. reference in footnote *a* above. [e] $PA_B = 204.0 +$ average value of $\eta\Delta H^\circ_{NH_4^+(B)}$. [f] Results obtained at Swiss Federal Institute of Technology. [g] Results obtained at the University of California, Irvine. [h] Theoretical estimations taken from ref 4.

the strong migration of charge, from the six- to the five-membered ring, which takes place upon tautomerization. This charge migration gives rise not only to an important increase of the intrinsic basicity of the system but also to a considerable increase in its polarity, reflected by the corresponding dipole moment. Almost simultaneously to the presentation of our theoretical results, an experimental paper[8] on 7MPP confirmed that the dipole moment of this molecule is more than twice that of its isomer NMAI.

The great gas-phase basicity predicted for 7MPP was a challenging problem, since it would imply this molecule to be one of the most basic known compounds in the gas phase.

Therefore, one of the aims of this paper is to investigate, from an experimental point of view, by means of ICR techniques the gas-phase basicity of these two systems.

However, a detailed analysis of these two bases requires an extension of this study to other related systems. Actually, the gas-phase basicity of NMAI and 7MPP was predicted by using linear relationships between gas-phase PA's and ab initio N 1s (or C 1s) orbital energies, previously established for 3- and 4-substituted pyridines[3c] (or aromatic carbon bases[3b]).

It seems clear that 3- and 4-substituted pyridines are not adequate model compounds to estimate the basicity of 7MPP, where the basic center is located in an azolic ring. In fact, we had previously shown that linear relationships between PA's and N 1s orbital energies are sensitive to details of local bonding at the nitrogen site. Hence, the theoretical value reported in ref 4 could be affected by nonnegligible error. Unfortunately, the lack of experimental information of both the gas-phase basicity and the N 1s binding energies of compounds analogous to 7MPP prevented a more realistic prediction. Accordingly, we have considered it interesting to establish analogous relationships to those proposed for 3- and 4-substituted pyridines but involving compounds of characteristics similar to those of 7MPP, from both the experimental and the theoretical points of view. Consequently, we have included also an investigation of the gas-phase basicity of pyrazolo[1,5-*a*]pyridine (A), imidazo[1,5-*a*]pyridine (B), imidazo[1,2-*a*]pyridine (C), benzoxazole (D), and 2-methylbenzoxazole (E) (see Figure 1).

These compounds were not capriciously chosen. All of them are heterocycles containing fused 5,6-rings, their basic center is a nitrogen atom located at the azolic ring, and their relatively high volatilities make them amenable for ICR experiments. Moreover, as we shall show in section 3, they present molecular electrostatic potentials quite similar to those reported for 7MPP,[4] and therefore one may assume a priori that they form an homologous set of compounds from the gas-phase basicity point of view.

2. Experimental Section

7-Methyl-7*H*-pyrrolo[2,3-*b*]pyridine was obtained by potassium carbonate treatment of the pyridinium salt formed from 7-azaindole and methyl *p*-toluenesulfonate.[4,9] 7-Azaindole (1H7A) (Aldrich) was purified as described elsewhere.[4]

Imidazo[1,2-*a*]pyridine was obtained from the reaction between 2-aminopyridine and excess bromoacetaldehyde, essentially as described.[10] The product so obtained was dried over solid KOH at 60 °C and vacuum distilled; bp 138–140 °C [15 Torr].

Imidazo[1,5-*a*]pyridine was the main result of cyclization of 2-(formamidomethyl)pyridine with phosphoryl chloride.[11] Traces of byproducts were separated by column chromatography (silica gel, ethyl acetate). The purified compound obtained was crystallized from the mixture $CHCl_3$–hexane and dried over P_2O_5 under vacuum; mp 52–54 °C [1 Torr].

Pyrazolo[1,5-*a*]pyridine was obtained from 2-(2-aminoethyl)pyridine by potassium ferricyanide oxidation.[12] It was purified by column chromatography (silica gel, benzene–methanol, 98:2) and vacuum distillation over solid KOH; bp 95–96 °C [15 Torr].

Benzoxazole (Aldrich) and 2-methylbenzoxazole (Merck) were also purified by vacuum distillation.

All purified compounds gave only one spot on TLC plates with several eluents. Their combustion data and ^1H NMR and mass spectra were in agreement with their structures. Their water contents were always less than 0.1% by weight (^1H NMR).

Gas-phase basicities were determined from equilibrium proton-transfer reactions conducted in an ICR spectrometer under conditions similar to those already described.[2b] Briefly, the equilibrium constant K_{eq} for the reaction $BH^+ + S \rightleftarrows B + SH^+$ was determined for reaction times up to 1 s and for pressures in the range of 10^{-6} Torr (B stands for one of the nitrogen bases under investigation and S for a reference compound of known basicity[13]). The concentrations of the neutrals were obtained from pressure measurements corrected for the ionization cross sections as described in ref 2b. The change in free energy is given by the relationship $\Delta G_i = -RT \ln K_{eq}$, with $T = 313$ K. The proton affinity of B is then obtained as given in footnotes *a*, *c–e* of Table I.

Ultraviolet photoelectron spectroscopy measurements (UPS) have been performed with He I and He II excitation ($h\nu = 21.2$ and 40.8 eV,

---

(8) Waluk, J.; Pakula, B.; Balakier, G. *Chem. Phys. Lett.* **1983**, *94*, 58.

(9) Robison, M. M.; Robison, B. L. *J. Am. Chem. Soc.* **1955**, *77*, 6554.

(10) Roe, A. M. *J. Chem. Soc.* **1963**, 2195.

(11) Bower, J. D.; Ramage, G. R. *J. Chem. Soc.* **1955**, 2834.

(12) Bower, J. D.; Ramage, G. R. *J. Chem. Soc.* **1957**, 4506.

(13) Taft, R. W. *Prog. Phys. Org. Chem.* **1983**, *14*, 247.

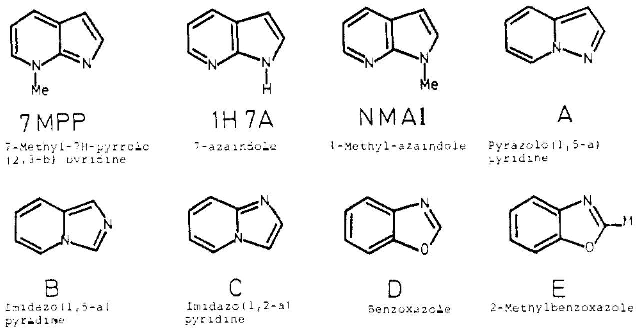


Figure 1. Compounds included in this study.

respectively) and X-ray photoelectron spectroscopy with Mg Kα radiation ($h\nu = 1253.6$ eV) by the electron energy analyzer (Leybold-Heraeus, EA 10/100) in the constant-pass energy mode (5, 10, 20, or 50 eV). The compounds have been deposited at −195 °C on a gold substrate cleaned by Ar ion sputtering. Particular attention has been paid to the deposition of the samples in order to avoid charging of the sample and disturbances caused by impurities. The most important requirement for the sample preparation was therefore the purification under UHV conditions and the possibility of introducing the substances into the spectrometer without breaking the vacuum. This has been realized by a separate heatable UHV-inlet system describe elsewhere.[14]

The thickness of the films has been optimized with the help of the UPS spectra. During the deposition process, the decrease of the intensity of the substrate Fermi edge has been monitored and taken as a measure of relative thickness of the overlayer. According to our experience, sample charging can be avoided by stopping the deposition process while the Fermi edge is still visible and no peak shifts appear. Under these conditions we assume that XPS measurements will also be free of charging effects since the UV light is focused on a smaller area on the sample and, as a consequence, tend even more to charge the sample surface.

In addition UPS spectra have been used to check the quality of the samples during and after XPS measurements. In some cases it was necessary to reduce the measuring time in order to minimize sample degradation effects, which could be detected by XPS measurements. The presence of water can be detected with either mass spectrometry or its typical features in the UPS spectra.

Apart from the N 1s binding energies, XPS measurements were taken in order to check the sample purity. The carbon to nitrogen intensity ratio yielded the expected stoichiometry within a few atomic percent.

3. Computational Details

We have previously shown[5] that tautomeric changes, like those that connect NMAI and 7MPP, are usually accompanied by noticeable geometrical changes[4] due to valence-shell electron pair repulsions and variations of the π (bonding or antibonding) densities in the HOMO. Therefore, it seems necessary to employ fully optimized structures when relative gas-phase basicities are studied. In order to be consistent with our previous theoretical study on NMAI and 7MPP, we have adopted the same geometrical model[15] based on fully optimized INDO geometries. To account for the fact that this method overestimates all C–H and N–H bond lengths, we have scaled all C–H bond lengths by a factor 0.974, which is the ratio of the experimental C–H bond length in naphthalene (1.0926 Å) to the INDO-optimized value (1.122 Å). The scaling factor for N–H bond lengths (0.935) is the ratio of the experimental N–H bond length in pyrrole (0.996 Å) to the corresponding INDO-optimized value (1.065 Å). Although displacements of the atoms out of the molecular plane were allowed, the planar conformation was always the most stable one. The optimized geometries obtained for NMAI and 7MPP have been reported elsewhere.[4] Those corresponding to compounds A–E are summarized in Table II and will not be discussed here. It should be emphasized, however, that the internal ring angle centered on the basic nitrogen is practically constant (about 104°) for all these compounds. This geometrical parameter is quite relevant since its almost constant value can be taken as an indication that the hybridization at the basic center is practically equivalent for all molecules considered here.

The corresponding ab initio calculations were carried out at two different levels: minimal and split-valence basis (to be referred hereafter as STO-3G//INDO and 4-31G//INDO, respectively). Protonation energies were obtained as the energy difference between the corresponding protonated and unprotonated forms. Ab initio electrostatic molecular potentials were evaluated with the equations of Srebrenick et al.,[16] which we have implemented in the framework of GAUSSIAN-70 series of programs.

For some particular cases, in order to complete our discussion, we have also carried out a localization of the canonical molecular orbitals using the procedure of Foster and Boys.[17]

4. Results and Discussion

The first step of our study was a prospective theoretical work, since it was necessary to assess (prior to the synthesis and experimental measurements) that the compounds proposed and that fulfilled a certain number of a prioristic conditions already mentioned in the introduction constituted indeed an homologous series of compounds.

Since, as we have pointed out above, the linear relationships between gas-phase PA's and 1s orbital energies, and the proton affinities themselves, are particularly sensitive to details of hybridization at the basic center, this was the first point analyzed. We have indicated, in the previous section, that the constancy of the endocyclic angle centered at the basic nitrogen revealed that hybridization at that center must be somewhat similar for all compounds under consideration. (Obviously, NMAI is an exception since its basic center is located at the six-membered ring.) This assumption is confirmed when the corresponding localized molecular orbitals (at the STO-3G level) and particularly that corresponding to the nitrogen lone-pair orbital directly involved in the protonation process are obtained. Their wave functions are remarkably similar, with almost identical contributions from the s and p atomic orbitals centered on the basic nitrogen.

Another characteristic of these systems could be related to their molecular electrostatic potential maps. Actually, the one reported[4] for 7MPP is quite peculiar, in the sense that the region above the six-membered ring is clearly repulsive. Here, we present in Figure 2 the molecular electrostatic potential maps for compounds A–C, as an illustration. For the sake of consistency with previous calculations,[4] they were evaluated in a plane parallel to and 1.6 Å above the molecular plane by the minimal basis set. All of these maps present the same basic characteristics as the one already discussed for 7MPP: the only attractive areas appear located above the five-membered ring, whereas the region above the six-membered ring is always repulsive.

Proton Affinities. The GB (or PA) values determined in the ICR experiments are reported in Table I. The two azaindole compounds show values of PA(1H7A) = 222.6 kcal/mol and PA(NMAI) = 224.2 kcal/mol, indicating that their protonated forms probably have the structure of substituted pyridinium ions (compare with PA(pyridine) = 220.8 kcal/mol[13]) in agreement with previous theoretical predictions.[4] As anticipated,[4] 7MPP is found more basic than its isomer NMAI but to a lesser extent than predicted,[4] from the corresponding (STO-3G) N 1s orbital energies.

This disagreement corroborates, once more, that the linear relationships between gas-phase PA's and 1s binding energies are quite sensitive to details of local bonding (i.e., to details of hybridization) at the basic center. In NMAI the active center toward protonation is a pyridine-type nitrogen, which presents a hybridization very similar to that exhibited by the ring nitrogen of 3- and 4-substituted pyridines. It is not surprising, then, that the gas-phase PA predicted for this compound by the linear correlation of PA's vs N 1s orbital energies, which holds for 3- and 4-substituted pyridines, agrees with the experimental value. This is not the case for 7MPP, where the basic center is an azolic–nitrogen, which presents a hybridization quite different from that

---

(14) Zehringer, R.; Oelhafen, P., to be submitted for publication.

(15) Catalán, J.; Pérez, P.; Yáñez, M. *Tetrahedron* **1982**, *38*, 3693.

(16) Srebrenick, S.; Weinstein, H.; Pauncz, R. *Chem. Phys. Lett.* **1973**, *20*, 410.

(17) Boys, S. H. In *Quantum Theory of Atoms, Molecules and Solid State*; Löwdin, P. O., Ed.; Academic: New York, 1966; p 252.

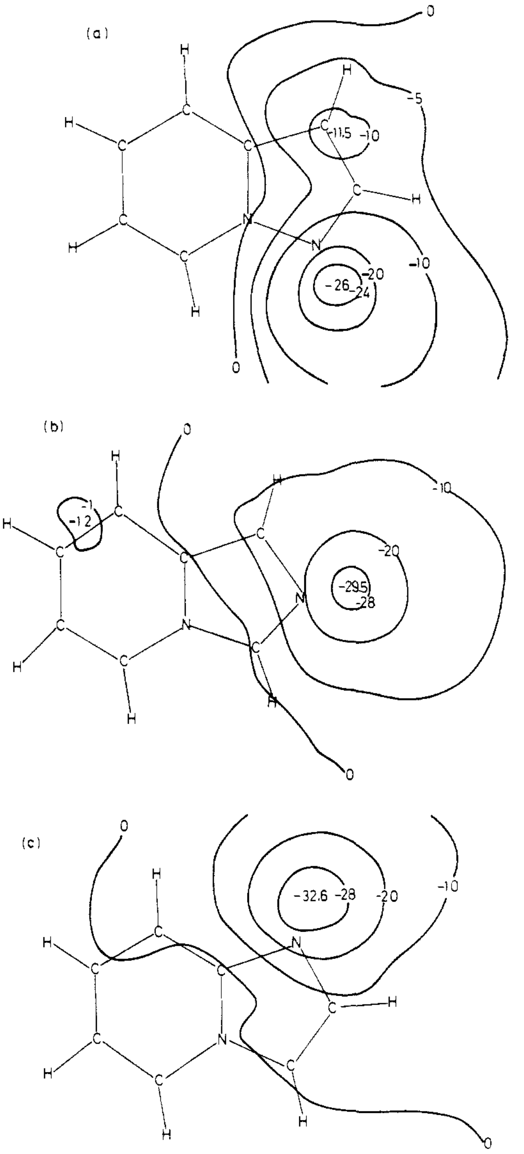


Figure 2. Molecular electrostatic potential maps, evaluated in a plane parallel to and 1.6 Å above the molecular plane (STO-3G level), for (a) pyrazolo[1,2-*a*]pyridine (A), (b) imidazo[1,5-*a*]pyridine (B), (c) imidazo[1,2-*a*]pyridine (C).

observed in its tautomer NMAI or in 3- and 4-substituted pyridines. Actually, as we shall illustrate later, the linear relationship between gas-phase PA's and N 1s orbital energies that holds for 7MPP and related compounds is noticeably different from that reported for 3- and 4-substituted pyridines.[3c]

The three isomers A–C show quite distinct features: the PA's increase in the order A < B < C with an 11 kcal/mol difference between A and C. In the first approximation, we interpret the greater basicity of compounds B and C as a measure of the stabilization energy of the ions BH$^+$ and CH$^+$, which is brought about by the resonance

Moreover, it is interesting to note that the gap between the PA's of compounds C and A (ΔPA(C–A) = 11.4 kcal/mol) is almost identical with the one measured[18] for the couple imidazole–pyrazole (10.9). This indicates that in compounds A and C the

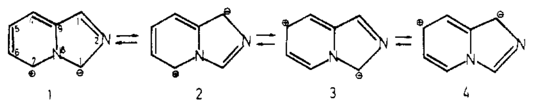


Figure 3. Mesomeric forms that contribute to the structure of imidazo[1,5-*a*]pyridine.

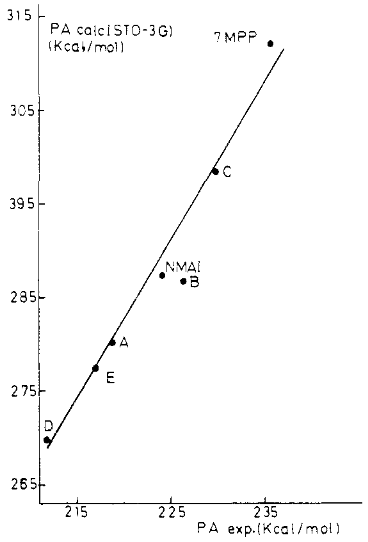


Figure 4. Linear correlation between calculated (STO-3G level) and experimental gas-phase proton affinities.

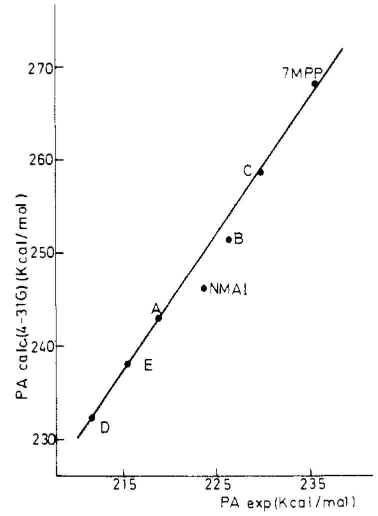


Figure 5. Linear correlation between calculated (4-31G level) and experimental gas-phase proton affinities.

existence of a six-membered ring fused to the azolic system does not alter the relative basicity of the azolic fragment. The basicity of B is, however, a little smaller than that of C (although it can be also considered as an imidazole fused to a benzene ring) because mesomeric forms for these systems (see Figure 3) accumulate π-electronic charge on positions 1 and 3, not 2. Accordingly, compound B behaves as an imidazopyridine with a slightly dampened basicity.

These results are in agreement with our 4-31G ab initio calculations, which predict a difference in the gas-phase basicity of compounds A and C of about 15.5 kcal/mol, similar to the one calculated (14.4 kcal/mol)[14] for the couple imidazole–pyrazole, at the same level of accuracy.

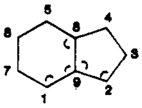
Incorporation of an electronegative center such as the oxygen atom in benzoxazole further reduces basicity, PA(D) = 211.6 kcal/mol, the effect being somewhat counterbalanced by the introduction of a polarizable substituent such as the methyl group in 2-methylbenzoxazole, PA(E) = 217.0 kcal/mol.

It should also be noticed that there is a good linear correlation between measured proton affinities and those calculated at the

---

[18] (a) Taft, R. W.; Anvia, F.; Taagepera, M.; Catalán, J.; Elguero, J. *J. Am. Chem. Soc.* **1986**, *108*, 3237. (b) A value 9.3 ± 1.0 kcal mol^{-1} was given by: Mautner, M.; Liebman, J. F.; Del Bene, J. *J. Org. Chem.* **1986**, *51*, 1105.

Table II. INDO-Optimized Geometries and ab Initio Energies and Dipole Moments



	7MPP	7MPPH$^+$	NMAI	NMAIH$^+$	A	AH$^+$	B	BH$^+$
				Bond Lengths, Å				
1–9	1.3896	1.3744	1.3545	1.3704	1.3801	1.3769	1.3861	1.3960
9–2	1.3488	1.3785	1.4025	1.3812	1.3253	1.3367	1.3797	1.3604
203	1.3845	1.3965	1.3956	1.4022	1.3521	1.3789	1.3333	1.3544
3–4	1.3684	1.3575	1.3588	1.3572	1.3915	1.3653	1.3738	1.3823
4–8	1.4345	1.4413	1.4401	1.4411	1.4015	1.4235	1.3849	1.3811
8–5	1.3746	1.3901	1.3963	1.3893	1.4170	1.4066	1.4245	1.4272
5–6	1.4055	1.3936	1.3823	1.3950	1.3627	1.3709	1.3564	1.3547
6–7	1.3680	1.3760	1.3912	1.3750	1.4140	1.4065	1.4231	1.4240
7–1	1.3718	1.3695	1.3420	1.3651	1.3596	1.3641	1.3529	1.3501
8–9	1.4532	1.4255	1.4214	1.4261	1.4049	1.3939	1.4152	1.4146
X-CH3	1.4116	1.4181	1.4044	1.4107				
				Bond Angles, deg				
7-1-9	119.3	116.7	113.0	119.6	120.5	118.5	120.8	119.8
1-9-8	120.4	124.2	127.3	122.0	121.7	124.3	121.2	121.4
9–8–5	117.4	115.9	115.0	116.4	116.8	116.0	116.9	117.3
8-9-2	116.4	109.8	109.7	112.0	113.1	108.4	105.6	108.2
9-2-3	99.3	106.5	105.4	104.0	104.1	103.6	113.8	108.8
∠N or ∠N-H$^+$	99.3	106.5	113.0	119.6	104.1	103.6	103.2	108.7
				Ab Initio Energies, au (Dipole Moments, D)				
STO-3G// INDO	−411.31780 (4.19)	−411.81532	−411.36056 (1.43)	−411.81414	−372.75496 (2.29)	−373.20116	−372.76413 (3.58)	−373.22107
4-31G// INDO	−415.84258 (4.47)	−416.26984	−415.87527 (1.65)	−415.26748	−376.86426 (2.69)	−377.25137	−376.87351 (4.20)	−377.27404

	C	CH$^+$	D	DH$^+$	E	EH$^+$	1H7A	1H7AH$^+$
				Bond, Lengths, Å				
1-9	1.3780	1.3767	1.3864	1.3859	1.3864	1.3875	1.3544	1.3692
9-2	1.3930	1.4050	1.3821	1.3910	1.3799	1.3855	1.3954	1.3761
2-3	1.3671	1.3533	1.3614	1.3319	1.3727	1.3890	1.3897	1.3975
3-4	1.3720	1.3899	1.3090	1.3342	1.3211	1.3447	1.3592	1.3573
4-8	1.3527	1.3799	1.4091	1.4167	1.4050	1.3495	1.4403	1.4419
8-5	1.4177	1.4014	1.3923	1.3893	1.3927	1.4145	1.3969	1.3894
5-6	1.3620	1.3727	1.3867	1.3862	1.3867	1.3887	1.3821	1.3951
6-7	1.4151	1.4060	1.3913	1.3931	1.3918	1.3868	1.3916	1.3747
7-1	1.3590	1.3645	1.3875	1.3870	1.3877	1.3926	1.3471	1.3658
8-9	1.4066	1.3872	1.4135	1.4083	1.4122	1.3875	1.4217	1.4262
X-CH3					1.4519	1.4441		
				Bond Angles, deg				
7-1-9	120.6	120.0	115.2	114.0	115.2	114.0	112.8	119.3
1-9-8	121.8	120.5	124.2	123.7	124.3	123.6	127.7	122.4
9-8-5	117.0	120.5	118.6	121.3	119.4	121.3	115.1	116.2
8-9-2	105.8	108.1	107.9	109.2	107.5	108.7	108.1	110.3
9-2-3	105.7	108.1	101.8	105.5	104.1	107.9	107.6	106.2
∠N or ∠N-H$^+$	104.0	109.2	100.9	107.0	103.7	109.3	112.8	119.3
				Ab Initio Energies, au (Dipole Moments, D)				
STO-3G// INDO	−372.76853^a (3.46)	−373.24402	−392.31594 (1.43)	−392.74584	−430.90495 (1.24)	−431.34672	−372.77577 (1.43)	−373.23302
4-31G// INDO	−376.88332 (4.14)	−377.29517	−396.68666 (1.66)	−397.05660	−435.68184 (1.16)	−436.06087		

[a] $E = -376.37263$ and $\mu = 3.5$ D were given by: Palmer, M. H.; et al. *J. Mol. Struct.* **1977**, *42*, 85.

STO-3G//INDO level, with the only exception of imidazo[1,5-*a*]pyridine (B) (see Figure 4), which is predicted to be much less basic than imidazo[1,2-*a*]pyridine (C), in contrast with the experimental evidence. This discrepancy is clearly corrected at the 4-31G//INDO level (see Figure 5). Whereas at the STO-3G//INDO level compound B is predicted to be slightly less basic than NMAI (and much less basic than compound C), at the 4-31G//INDO level, compound B presents a gas-phase basicity more than 5 kcal/mol greater than that of NMAI and close to that of compound C. Moreover, the linear correlation of Figure 5 presents a slope smaller (and closer to unity) than that of Figure 4. This shows that minimal basis sets significantly overestimate not only the absolute but also the relative values of the proton affinities.[19-23] Moreover, relative gas-phase PA's seem to be, at least for the present case, basis set dependent. We have already indicated the most conspicuous case (compound B), but this is not unique and the problem, although attenuated, is also present for other compounds.

To facilitate the discussion, we present in Table III the protonation energies, at both levels of accuracy, relative to the least basic compound (D). It is clear that, by enlarging the basis set,

---

(19) Del Bene, J.; Frisch, M. J.; Rahavacham, K.; Pople, J. A. *J. Phys. Chem.* **1982**, *86*, 1529.

(20) Del Bene, J.; Mette, H. D.; Frisch, M. J.; Luke, B. T.; Pople, J. A. *J. Phys. Chem.* **1983**, *87*, 3279.

(21) Del Bene, J. *J. Comput. Chem.* **1985**, *6*, 290.

(22) Del Bene, J. *Chem. Phys. Lett.* **1983**, *94*, 21.

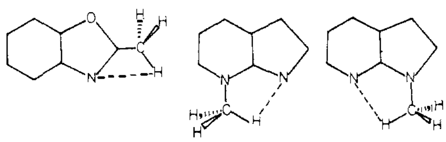
(23) Mó, O.; de Paz, J. L. G.; Yáñez, M. *J. Phys. Chem.* **1986**, *90*, 5597.

Table III. Calculated Proton Affinities Relative to the Least Basic Compound, D (kcal/mol)

compd	STO-3G//INDO	4-31G//INDO	exptl
D	0.0 (269.8)[a]	0.0 (232.2)[a]	0.0 (211.6)[a]
E	7.5	5.7	4.3
A	10.3	10.8	6.9
B	17.0	19.2	14.7
C	28.6	26.3	18.3
NMAI	17.2	14.0	12.6
7MPP	42.5	36.0	24.3

[a] Absolute proton affinities.

Chart I



the relative basicity of 2-methylbenzoxazole decreases about 2 kcal/mol. The same effect is quantitatively more important for NMAI and 7MPP, whose relative gas-phase PA's decrease about 3 and 6 kcal/mol, respectively.

Similar findings have been observed[18] when the gas-phase basicities of methylpyrazoles and methylimidazoles were investigated. For these compounds the substituent interaction energies[24] for the unprotonated forms of α-substituted derivatives increase by about 1.2 kcal/mol when the basis set from STO-3G to 4-31G[25] is enlarged.

Two different effects are involved in this extrastabilization of α-substituted compounds when the basis set is enlarged. On one hand, the hyperconjugative interaction between the substituent (methyl) and the π-aromatic system is better described at the split-valence level, because these types of basis sets allow for a better dispersal of the positive charge on the methyl hydrogen atoms. On the other hand, the stabilizing nonbonding interactions between the basic center and the hydrogens of the substituent (see Chart I) are also better described at the 4-31G level than at the STO-3G one. Both effects contribute to stabilize more the unprotonated species when the larger basis is used and, accordingly, the corresponding PA decreases.

Since the interactions mentioned above should be greater, the greater is the polarity between the basic nitrogen and the hydrogen of the substituent and the smaller is their mutual separation, it is reasonable to expect these effects to be quantitatively more important for NMAI and 7MPP than for 2-methylbenzoxazole.

The better agreement between the 4-31G-calculated PA's for compounds A–C and the corresponding experimental values is a consequence of two concomitant facts: on one hand, when the basis set is enlarged, the relative PA of compound B increases by about 2.0 kcal/mol while that of compound C decreases by about the same amount. As before, these variations arise from a better description of either the unprotonated or the protonated forms when the basis set is enlarged. We present in Table IV the relative stability of the three isomers A–C and their protonated forms, with respect to the least stable one (compound A). Compound C is predicted to be much more stable at the 4-31G level, while the stabilization of its protonated form is much smaller. Hence, its relative PA decreases. For compound B things are different; the neutral form is almost equally stable at both levels of accuracy, while the protonated species becomes more stable at the 4-31G level and, accordingly, its relative PA higher.

These results indicate again that when the position α to the basic center becomes substituted (and we can consider that this is the case for compound C), the neutral molecule is much better described if the basis set has a split-valence quality. This finding is likely due to a better description of the polarization undergone by the six-membered ring carbons and caused by the heteroatom.

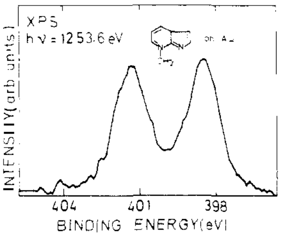


Figure 6. X-ray photoelectron spectrum for 7MPP showing two lines corresponding to the nonequivalent nitrogen atoms.

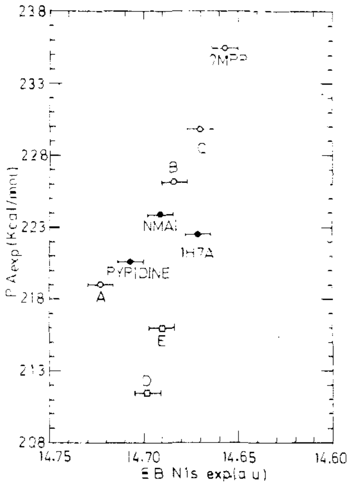


Figure 7. Correlation between experimental gas-phase PA's and experimental N 1s binding energies for 7MPP and related compounds: (●) compounds that protonate on pyridine-type nitrogens; (○) compounds that protonate on azolic-type nitrogens; (□) compounds that protonate on azolic-type nitrogens but do not follow the general trend (see text).

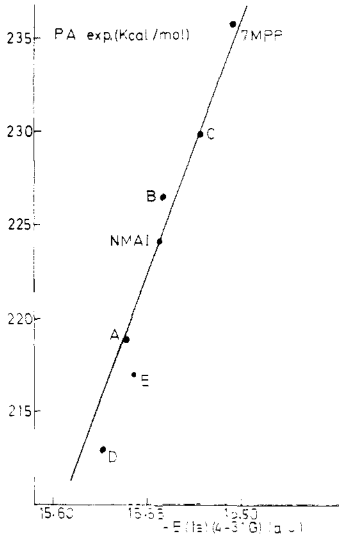


Figure 8. Linear relationship between experimental gas-phase proton affinities and N 1s orbital energies evaluated at the 4-31G level.

In fact, when a split-valence basis set is used, the separation of the atomic charge into inner and outer components leads to a more realistic description of the σ-inductive effects. This is reflected by the corresponding net charges (see Table V), which are much greater at the 4-31G than at the STO-3G level. These differences arise almost exclusively from differences between σ-charge densities, since both basis sets yield almost identical π ones.

Correlation between PA's and N 1s Binding Energies. N 1s core-electron binding energies determined with XPS are reported in Table VI along with the corresponding STO-3G//INDO- and 4-31G//INDO-calculated values. Since our measurements were taken in the condensed phase, the spectra give binding energies relative to the Fermi level of the substrate, while the usual

---

(24) Taagepera, M.; Summerhays, K. D.; Hehre, W. J.; Topson, R. D.; Pross, A.; Radom, L.; Taft, R. W. *J. Org. Chem.* **1981**, *46*, 891.

(25) Catalán, J.; Mó, O.; de Paz, J. L. G.; Pérez, P.; Yáñez, M.; Elguero, J. *J. Org. Chem.* **1984**, *49*, 4379.

Table IV. Relative Stability (ΔE) of Compounds A–C and Their Respective Protonated Forms (ΔE^+) and Variations of the Gas-Phase PA's (ΔPA) and the Corresponding N 1s Orbital Energies (ΔE(1s)) (kcal/mol)

	ΔE		ΔE^+		ΔPA		ΔE(1s)	
compd	STO-3G	4-31G	STO-3G	4-31G	STO-3G	4-31G	STO-3G	4-31G
A	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
B	−5.7	−5.8	−12.5	−14.2	6.7	8.4	10.4	11.2
C	−8.5	−11.9	−26.9	−27.5	18.3	15.5	31.6	24.0

Table V. Mulliken Net Charges[a]

	NMAI		7MPP		A		B		C		D		E	
1	−0.26	−0.95	−0.33	−0.61	−0.18	−0.27	+0.10	+0.36	−0.01	+0.10	−0.21	−0.71	−0.22	−0.75
2	+0.05	+0.17	+0.02	+0.04	+0.01	+0.05	−0.25	−0.52	+0.00	−0.02	+0.17	+0.40	+0.24	+0.59
3	−0.11	−0.21	−0.13	−0.21	−0.12	−0.30	−0.03	−0.04	−0.29	−0.58	−0.26	−0.50	−0.28	−0.55
4	−0.05	−0.10	−0.03	−0.09	−0.06	−0.18	−0.06	−0.14	−0.06	−0.18	−0.05	−0.13	−0.06	−0.13
5	−0.09	−0.25	−0.10	−0.29	−0.05	−0.17	−0.06	−0.19	−0.06	−0.18	−0.06	−0.20	−0.07	−0.20
6	+0.04	+0.07	+0.08	+0.24	−0.07	−0.27	−0.07	−0.025	−0.07	−0.26	−0.05	−0.20	−0.05	−0.20
7	−0.27	−0.59	−0.23	−0.98	+0.06	+0.26	+0.05	+0.23	+0.06	+0.24	−0.07	−0.14	−0.08	−0.14
8	+0.19	+0.60	+0.20	+0.60	−0.13	−0.83	−0.23	−1.04	−0.22	−1.02	+0.10	+0.31	+0.11	+0.32
9	−0.03	−0.13	−0.03	−0.12	+0.09	+0.38	+0.08	+0.29	+0.18	+0.60	+0.04	+0.08	+0.05	+0.09

[a] The first column of each entry corresponds to STO-36 values and the second one to 4-31G results.

Table VI. N 1s Electron Binding Energies of Related Compounds Measured by X-ray Photoelectron Spectroscopy and Calculated at the STO-3G and 4-31G Levels (eV)

	1 peak			2 peak		
		calcd			calcd	
compd	exptl	STO-3G	4-31G	exptl	STO-3G	4-31G
NMAI	399.76	417.03	422.93	401.16	419.15	423.91
7MPP	398.84	415.01	421.87	401.65	420.74	425.15
1H7A	399.21	425.06		400.21	427.06	
pyridine	400.20					
A	400.63	417.43	423.41	402.15	421.48	425.75
B	399.57	416.98	422.93	401.83	420.64	425.23
C	399.18	416.07	422.37	401.81	419.91	425.34
D	399.94	417.63	423.77			
E	399.72	417.05	423.31			

measurements on samples in the gas phase give ionization energies that are defined with respect to the vacuum level. It is known that binding energies and ionization energies differ not only by the work function of the compound, but additional corrections have to be taken into account; they are due to interactions between the molecules causing a change of nuclear charge screening. We assume, however, that these effects follow the same trends in our sample set, and therefore the relative energies should be the same as in the gas-phase measurements.[26] Figure 6 shows a typical N 1s region with two lines corresponding to the nonequivalent nitrogen atoms in the 7MPP compound. N 1s binding energies have been calculated by fitting the core line with a Gaussian. The binding energy scale has been calibrated by assuming a binding energy of 84.0 eV for the Au $4f_{7/2}$ core level of the clean Au substrate.

The correlation PA vs N 1s binding energies (see Figure 7) is fairly good as far as compounds A–C, pyridine, NMAI, and 7MPP are concerned. 1H7A is unexpectedly somewhat off the correlation whereas benzoxazole (D) and 2-methylbenzoxazole (E) clearly deviate.

Similar characteristics are exhibited by the corresponding relationship between experimental gas-phase PA's and calculated N 1s orbital energies. We show in Figure 8, as an illustration, the correlation obtained when N 1s orbital energies evaluated at the 4-31G//INDO level are used. Again, benzoxazole and 2-methylbenzoxazole deviate significantly from the correlation followed by the remaining compounds of the series. This shows that these kinds of relationships are very sensitive to details of local bonding at the basic center.

It should be indicated that, as anticipated in the previous section, the linear correlation between experimental PA's and N 1s orbital energies obtained here for 7MPP and related compounds is clearly different from the one that holds for 3- and 4-substituted pyridines,[3c] explaining why the previously estimated PA for 7MPP,[4] obtained by using the latter, was in considerable error.

The last column of Table IV shows that the relative values of N 1s orbital energies vary, when the basis set is enlarged, in a manner parallel to that already discussed for the calculated PA's. As a consequence, the linear relationship between both magnitudes presents a much smaller scatter at the 4-31G level than at the STO-3G one.

5. Conclusions

From the results discussed in this paper we can conclude that the experimental PA of NMAI is in very good agreement with the value predicted from the linear relationship between gas-phase PA's and N 1s orbital energies, which holds for 3- and 4-substituted pyridines, indicating that its protonated form must have the structure of a substituted pyridinium ion. Our measurements also confirm that its isomer 7MPP is a much more basic compound in the gas phase, although its experimental basicity is much smaller than that predicted with the same linear correlation mentioned above. This corroborates that these kinds of linear relationships are very sensitive to details of bonding at the basic center.

The STO-3G minimal basis set tends to overestimate the relative PA's.[19–23] Moreover, these relative PA's are basis-set dependent, namely for those cases where the compound presents some kind of substitution α to the basic atom. In these cases, at least a basis set of split-valence quality must be used. Since, at this level of accuracy, similar effects have been found to occur regarding the corresponding N 1s orbital energies, the linear correlation between experimental gas-phase PA's vs N 1s orbital energies improves noticeably on going from the STO-3G to the 4-31G level.

Compound C behaves also as a very strong base in the gas phase; but the most important fact is that the gap between the PA's of imidazo[1,2-*a*]pyridine (C) and pyrazolo[1,5-*a*]pyridine (A) from both the theoretical and the experimental point of view is very nearly equal to that observed between imidazole and pyrazole. This seems to indicate that although the absolute gas-phase basicity of these systems has been enhanced by the presence of the six-membered aromatic fragment, the relative basicity of the azolic fragment does not change. Imidazo[1,5-*a*]pyridine (B) constitutes an exception to this rule, because any of the possible mesomeric forms contributing to the stability of this kind of molecules accumulate charge at position 2 (the one occupied, in this case, by the basic center). Consequently, imidazo[1,5-*a*]pyridine (B) presents a slightly dampened basicity compared to imidazo[1,2-*a*]pyridine (C). This effect is somewhat overestimated by the theoretical calculations at the STO-3G level, but it seems to be reasonably well reproduced at the 4-31G level.

Acknowledgment. All calculations were performed at the UAM/IBM and CC/UAM centers, Madrid.

---

(26) Clark, D. T. In *Handbook of X-Ray and Ultraviolet Photoelectron Spectroscopy*; Briggs, D., Ed.; Heyden: London, 1977.