Gas-Phase Basicity and Ionization Energies in Some N-Arylazacycloalkanes

C. Cauletti, G. Cerichelli,[†] F. Grandinetti, L. Luchetti,

Dipartimento di Chimica, Università "La Sapienza" di Roma, Rome, Italy

and M. Speranza*

Dipartimento di Chimica, Università di Camerino, MC, Italy (Received: July 27, 1987; In Final Form: October 7, 1987)

Proton-transfer equilibrium constant and ionization energy measurements were performed in the gas phase for a series of N-arylazacycloalkanes. The techniques used were Fourier transform ion cyclotron resonance (FT-ICR) and UV photoelectron spectroscopy (UPS). The aim was clarifying peculiar aspects of the reactivity in solution of these cyclic molecules, for instance, the significant difference in the velocity of the ring-opening reaction between three- and four-membered rings. The results obtained indicated that this difference is mainly related to intrinsic structural and electronic parameters, whereas environmental factors (i.e., solvation, ion pairing, etc.) play only a minor role.

Introduction

The equilibrium constants of the ring-opening reaction in solution of 1-phenylaziridinium cation and 1-phenylazetidinium cation are largely different, that of the former one being 10⁹ times that of the latter one (free energy difference at least 9 kcal/mol).¹ However, the difference in conventional ring strain energy between aziridine and azetidine, which is estimated as 1.5 kcal/mol,² cannot account for such a large discrepancy. This could be due to the following reasons:

(i) The presence of the phenyl group on nitrogen. In fact, the ring opening reaction of N, N-dimethylaziridinium cation is 10^3 times faster than that of N,N-dimethylazetidinium cation,³ and the ring-closure reaction for the formation of the three-membered ring is only several orders of magnitude faster than that of four-membered ones.⁴ We can therefore guess that the difference in stability between the unsubstituted or alkyl-substituted threeand four-membered rings is consistent with the difference in conventional ring strain energy. The presence of the phenyl group can affect the ring strain energy of the neutral molecules and/or the pK_a of the amines in solution, so that the very fast ring opening of N-phenylaziridinium cation¹ prevents a direct pK_a measurement.

(ii) The specific ion-counterion and ion-solvent interactions, which may alter in solution the intrinsic kinetic and basicity parameters of the substrates in question.

To gain a better insight into the chemical behavior of these cyclic molecules, we decided to undertake a gas-phase investigation, including basicity measurements by Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry and ionization energy determinations by UV photoelectron spectroscopy (UPS) on a series of azacycloalkanes. By operating in the gas phase one can obtain an indication of the relevance of the solvation and counterion effects on the observed phenomena. Combined application of these two methodologies allows comparison of the availability of the nitrogen lone pair to protonation among the various members of the series (FT-ICR) to the nature and composition of the valence molecular orbitals, in particular of the highest occupied MO (HOMO) and of its aptitude to be ionized (UPS). The study has been carried out on the model compounds (I-VIII), and the ensuing basicity and ionization energy results were compared with related gas-phase data concerning representative N-substituted cyclic amines.5-



[†]Centro CNR di Studio sui Meccanismi di Reazione.

TABLE I: Experimental Gas-Phase Basicities (GB/kcal mol⁻¹) and Ionization Energies (IE/eV) of Some N-Substituted Azacycloalkanes

(CH ₂) _{<i>n</i>-1} N—R					
	n	R	GB	IE ^d	
	3	Н	207.5ª	9.80 ^b	
	4	Н	215.74	9.04 ^b	
	5	Н	217.3ª	8.77 ^b	
	6	Н	218.2 ^a	8.66 ^b	
	7	Н	217.8ª		
	8	Н	220.1ª	$9.20^{c} (9.26)^{b}$	
	3	Me	213.8 ^a	8.93°	
	4	Me	219.5ª	$8.40^c (8.41)^b$	
	5	Me	220.9 ^a	8.30^{c} $(8.41)^{b}$	
	6	Me	221.9ª		
	3	Ph	212.4	8.19 ^b	
	4	Ph	214.0	7.61 ^b	
	5	Ph	216.5 (216.9) ^a	7.23 ^b	
	6	Ph	219.8	7.72 ^b	
	7	Ph	219.6		
	5	p-ClPh	215.0	7.29	
	5	p-MePh	218.5	7.02	
	5	p-MeOPh	220.7	6.94	
	5	p-MeCOPh		7.36	

^aReference 12. ^bReference 7. ^cReference 8. ^dOnly first ionization energies are listed.

Results and Discussion

The gas-phase basicities (GBs) and the ionization energies (IEs) of the title compounds are reported in Table I. Figure 1 shows the GBs of selected molecules along with those of the N-H and N-Me analogues. Figure 2 shows an analogous representation of the HOMO ionization energies, taken from literature data.⁵⁻⁸

The comparison between gas-phase basicities of the three families of cyclic amines and their ionization energies permits us to draw some interesting considerations. (i) In the N-H and N-Me series a general parallelism of the GB and IE values does exist. In fact, the GB difference between the two sets ranges from ca. 3.6 kcal/mol for the molecules with n = 5 and 6 to 6.2 kcal/mol

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Figure 1. Gas-phase basicities $(GB/kcal mol^{-1})$ of some N-substituted azacycloalkanes, $R-N(CH_2)_{n-1}$.



Figure 2. Experimental first ionization energies (IE/eV) of some N-substituted azacycloalkanes, $R-N(CH_2)_{n-1}$.

for n = 3. Accordingly, the relevant ΔIE passes from ca. 0.36 eV for n = 5 and 6 to 0.54 eV for n = 3. As a consequence, a good inverse relationship between PAs and IEs is obtained for both classes, as shown in Figure 3, curve a. (ii) As evident from Figure 1, the GBs of N-phenyl derivatives follow a totally different trend, being constantly lower than those of N-Me compounds, while assuming higher or lower values than the N-H molecules, depending on n. On the other hand, a similar discrepancy is observed in the IE trends (see Figure 2). In fact, the IE values of the N-Ph compounds are invariably lower than those of the N-Me derivatives, which in turn are lower than those of the unsubstituted amines. In addition, the N-Ph set displays an inversion of trend in correspondence of n = 5. Inductive effect of the N substituent is responsible for the decrease in IE on passing from the N-H to the N-Me series. This effect, also present in the N-Ph derivatives, is overwhelmed in these compounds by the mesomeric effect, which further destabilizes the HOMO. The inversion in the trend on passing to the member with n = 6 was attributed⁷ to a lower extent of conjugation in the latter compound due to a 48° deviation from coplanarity of the two rings. The peculiar trend of the PAs of the N-Ph molecules cannot be related in a simple way to the corresponding IEs trend, as evident from Figure 3, curve c. This suggests that the factors determining the relative stability of the molecular ions are quite different from those affecting that of the corresponding N-protonated ions. A major indication of this fact is offered by the comparison between the linear correlations shown in Figure 4, concerning the GBs and IEs of N-(p-X-phenyl)pyrrolidine versus the σ_p values of the X



Figure 3. Plots of gas-phase proton affinities (PAs) versus ionization energies (IEs) for N-substituted azacycloalkanes. Curve a: R-N- $(CH_2)_{n-1}$, R = H(+) and Me (\blacksquare). Curve b: R₂NH, R specified in the figure. Curve c: experimental PAs (\triangle , dotted line) for Ph-N(CH₂)_{n-1} and corresponding values, calculated from eq 2, ref 7 (\bigcirc , not connected). Curve d: R₂NPh, R specified in the figure.



Figure 4. (a) Gas-phase basicities (kcal mol⁻¹) versus σ_p values for some N-(p-X-phenyl)pyrrolidines, X specified in the figure. (b) Ionization energies (kcal mol⁻¹) versus σ_p values for some N-(p-X-phenyl)-pyrrolidines, X specified in the figure.

substituents (X = OMe, Me, H, Cl). In these substrates the differential effects of conjugation are expected to be maximized owing to the complete coplanarity of the two rings and the lack of the alicyclic ring strain, which allows the maximum overlap between nitrogen lone pair and π orbitals of the phenyl ring. In this view, the difference in the absolute ρ values of the two correlations of Figure 4 ($\rho_{\rm IE} = 13.3$, $\rho_{\rm GB} = -10.9$) is attributable to the removal of the extended π conjugation from the substituent to the nitrogen by protonation. This implies a lower sensitivity of the GB to the parasubstitution at the phenyl ring.

Rozeboom et al. found⁷ a linear relationship between proton affinities (PAs) and ionization energies (IEs) of alicyclic amines:

$$PA (kcal/mol) = 296.1 - (8.131)IE (eV)$$
 (1)

This correlation is represented by curve a in Figure 3. The same



authors adopted a similar equation to predict the PAs of N-arylazacycloalkanes:

PA (kcal/mol) = 296.1 - (8.131)IE (eV) - 11.7 cos ϑ (2)

where the term 11.7 cos ϑ accounts for the conjugation in the molecular ion between the nitrogen lone pair and the π orbitals of the phenyl ring (ϑ is the rotational angle between the two interacting systems; see Figure 5a). The PAs calculated by eq 2 are reported in Figure 3 (filled circles) along with the experimental values (curve c). Despite the overall qualitative reproduction of the PAs trend, the application of eq 2 to these systems is hardly correct for the following reasons:

(i) The angular coefficient of the correlation PA/IE is not the same for different classes of amines. In fact it varies on passing from alicyclic amines (see Figure 3, curve a) to open-chain aliphatic amines (curve b) and to anilines (curve d). Therefore, for no reason should the curve PA/IE for N-arylazacycloalkanes be coincident with curve a, or parallel to it, if drawn disregarding the term 11.7 cos ϑ .

(ii) For the above considerations, the 11.7 parameter is devoid of any physical meaning and therefore does not reflect adequately the contribution of the π conjugation to the construction of the PA/IE ratio.

In this view, and taking into account the trend of the experimental PA/IE curve (curve c), it should be pointed out that cos ϑ term of eq 2 can hardly account per se for the conjugation hindrance in the whole N-arylazacycloalkanes series. An important role can be played inter alia by the carbocyclic ring strain, affecting the s contribution to the nitrogen lone pair and therefore the ψ angle between this orbital and the axis of the phenyl π system (see Figure 5b). In fact, in curve c of Figure 3, the point corresponding to the N-arylazacycloalkane with n = 5 (where no ring strain is present and $\vartheta = 0^{\circ}$) approaches the aniline linear correlation (curve d). All other points (n = 3, 4, 6) significantly deviate from this correlation. For n = 6, this can be satisfactorily explained with a ϑ largely different from 0° (quoted as 48° in ref 7), without implying any significant ring strain effect. The situation is totally different for n = 4 and n = 3 terms, where ϑ = 0° ,⁷ but a significant increase of the ψ angle due to ring strain, and therefore a decrease of π conjugation, is expected.

Conclusions

Proton-transfer equilibrium constant measurements were performed in gas phase for a series of N-arylazacycloalkanes. The comparison of these data with ionization energies and their dependence on the parasubstituents on the phenyl ring demonstrate that conjugation effects are more important in the molecular ions than in the protonated species. Simple correlations, such as those proposed in previous papers, between PAs and IEs do not seem operative, since they underestimate carbocyclic ring strain effects on the π conjugation in the molecular ions. These contributions appear to be strongly different along the series and can account for the largely different reactivity observed in solution between N-phenyl-substituted aziridine and azetidine with respect to that of the N-H and N-Me ones.

This conclusion points to a minor role of the environmental factors (i.e., solvation, pairing, etc.) in determining the reactivity

of these compounds in solution, which rather appears to be mainly related to their intrinsic structural and electronic parameters.

Experimental Section

All *N*-phenylazacycloalkanes were prepared by standard procedures.^{4a,9} *N*-(*p*-Chlorophenyl)pyrrolidine (compound VIII) was prepared by the following procedure: 4-chloroaniline (7 g, 54.9 mmol) and 1,4-dibromobutane (11.9 g, 54.9 mmol) were added to a suspension of NaHCO₃ (27 g, 0.32 mol) in EtOH (100 mL). The mixture was heated at reflux for 12 h; after addition of 1 N KOH, it was extracted with C₆H₆ and dried (Na₂SO₄). The residue, after evaporation, was crystallized (2-propanol), yielding *N*-(*p*-chlorophenyl)pyrrolidine (3.7 g, 20.5 mmol), mp 86–87 °C (lit. value¹⁰ 85–86 °C). Compounds VI and VII were synthesized by a similar procedure.

The FT-ICR experiments were performed on a commercial Nicolet FT-MS 1000 spectrometer equipped with a superconducting magnet operated at 2.0 T and with a 2.54-cm cubic cell. Sample pressures were measured with a Granville-Phillips 280 Bayard Alpert ion gauge, calibrated against the relative abundance of the ions in pure CH_4 as a function of pressure.¹¹ Resolution was typically 1000 fwhm (full width half-height) at mass 100. Ions were produced by 2-ms electron beam pulses from a filament at an emission current of 500 nA. Ions were trapped in the cell by a different trapping voltage of 1.0 V. The gas-phase basicities were determined by using the bracketing techniques and, where possible, equilibrium measurements. The compounds were introduced via two independent leak valves, and their pressures (not corrected) ranged around 10⁻⁶-10⁻⁷ Torr, with a neutral ratio of about 1. Reference bases used (and their GB values in kcal/mol taken from ref 12) are sec-butylamine (212.1), tert-butylamine (213.4), piperazine (216.4), diethylamine (217.7), piperidine (218.2), di-n-propylamine (219.7), and di-n-butylamine (220.3). The protonated reference bases were isolated after a convenient delay by sweeping out all the undesired ions with two consecutive double-resonance events. The reactions between the protonated bases and the sample were followed at different trapping times, and where possible, the equilibrium constants were determined at room temperature. The estimated average uncertainty in these determinations is ± 0.2 kcal/mol.

Gas-phase UP spectra were recorded on a Perkin-Elmer PS 18 spectrometer, equipped with a He I/He II lamp (Helectros Development), at room temperature for liquid samples and in the range of 50–140 °C for the solid ones. Calibration was performed with N_2 and self-ionizing He.

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