Ring-size Effects on the Ionization Potentials of *N*-Substituted Azacycloalkanes

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The ionization potential of the lone-pair electrons of nitrogen has been determined for *N*-methyl- and *N*-tosyl-azacycloalkanes by means of gas-phase u.v. photoelectron spectroscopy. The cyclic compounds examined contain small, common, medium, and large-membered rings. The ionization potentials are affected by conformational features and, in particular, by the strain present in the ring. More precisely, the IPs reflect changes of hybridization of the nitrogen lone pair upon varying the ring size, whereby a lower or higher energy is required for the ionization process of the cyclic compounds relative to a series of open-chain alkyl amines taken as reference. Steric inhibition of resonance by the *N*-tosyl substituent takes place in the case of the strained small rings.

The influence of ring size on the properties of cyclic molecules is well known.[1] We are currently interested in finding correlations between physicochemical properties and conformational features of cyclic compounds. Following an n.m.r. study upon the structure of series of cyclic amines,[2] and with particular emphasis on the effect of ring strain, we now report the determination of the vertical ionization potential (IP_v) of the lone-pair electrons of the nitrogen atom in two series of azacycloalkanes.

Alkyl substituents, due to their electron-releasing ability, are known to lower the IPs of atoms or groups to which they are attached.[3] In open-chain heteroatomic compounds it is found that the lowering is proportional to the number of carbon atoms in the alkyl chain, the ionization potential decreasing regularly on increasing the chain length. Danby and his co-workers[4] have shown that the relationship between the IP_v of the lone pair of the heteroatom and the number of alkyl groups can be expressed by the empirical equation (1) where μ_R is the

$$IP_v(RX) = IP_v(CH_3X) + \chi\mu_R \qquad (1)$$

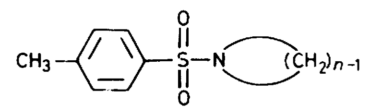
substituent parameter, and χ is a homologous series parameter.

We have here attempted a comparison between the ionization behaviour of the nitrogen lone pair in a series of homologous *N*-substituted azacycloalkanes and in their open-chain counterparts, in order to assess whether and to what extent the effect of ring size and of ring strain is reflected in the IP_v values along the series.

The determination of the IP_vs was performed by means of gas-phase u.v. photoelectron spectroscopy (u.p.s.). Previous u.p.s. studies on this subject[3,5–7] are confined to a short range of cyclic compounds, namely, to the small- (3- and 4-) and common- (5-, 6-, and 7-) membered azacycloalkanes. We have extended the study to a wider range of ring dimensions including medium- (8—12) and large-membered homologues. Moreover, we have investigated effect(s) due to the presence of *N*-substituents of different kinds.

We measured the u.p. spectra of two series of cyclic amines, (**1**) (n = 3—11, 13, and 16) and (**2**) (n = 3—10, 12, 13, and 17).

(**1**)



(**2**)

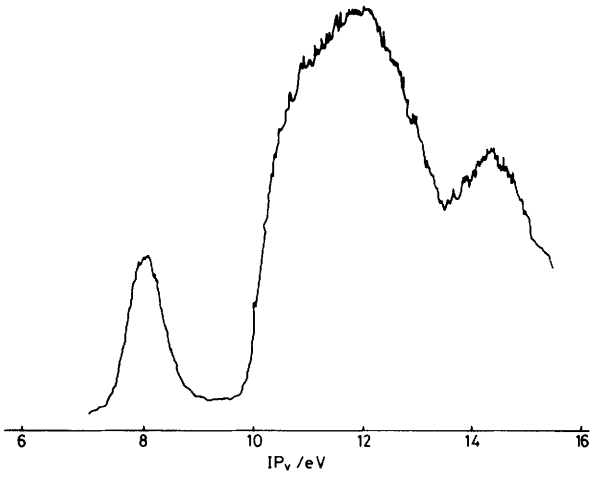


Figure 1. Gas-phase He^I photoelectron spectrum of *N*-methylazacyclooctane (**1**; n = 8)

Results and Discussion

Both He^I (21.22 eV) and He^{II} (40.81 eV) spectra were run, but no significant difference in bands shape and intensity ratios was observed upon changing the energy of the ionizing radiation. Representative He^I u.p. spectra of compounds (**1**) and (**2**) are shown in Figures 1 and 2; the measured IP_vs are in Table 1. The IP_v values result from the average of several measurements and are approximated to the first decimal place whenever the broad shape of the u.p.s. bands recommends it.

In both series the band at lower IP_v accounts for ionization of the nitrogen lone pair. The broad band envelope beyond 10 eV in the spectra of the compounds (**1**) arises from ionization of the σ_{C-C} and σ_{C-H} orbitals. The spectra of series (**2**) are more complex, also displaying bands associated with the tosyl group (see Table 1). More precisely, the second band at *ca.* 9.5 eV is related to the highest π orbital of the phenyl ring (e_{1g} in benzene),[8] unsplit despite substitution and shifted to higher IP_v with respect to benzene due to the electron-withdrawing ability of the sulphonyl group. The u.p. spectrum of methyl phenyl sulphone[9] also shows a unique band, at 9.74 eV, corresponding to the two almost degenerate π orbitals of the phenyl ring. The

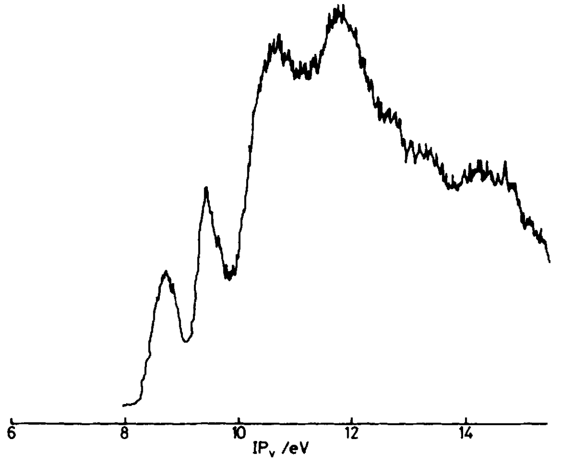


Figure 2. Gas-phase He^I photoelectron spectrum of *N*-tosylazacyclodecane (**2**; $n = 10$)

Table 1. Experimental vertical ionization potentials (IP$_v$/eV) of some *N*-substituted azacycloalkanes (**1**) and (**2**)

Ring size	Series (**1**)	Series (**2**)		
	n_N	n_N	πPh^a	$\pi SO_2{}^a$
3	9.20	9.32	9.8	10.7
4	8.93	8.98	9.6	10.6
5	8.40	8.78	9.5	10.6
6	8.30	8.76	9.5	10.6
7	8.05	8.60	9.4	10.6
8	8.08	8.58	9.4	10.6
9	7.93	8.59	9.4	10.5
10	8.10	8.67	9.4	10.6
11	8.00			
12		8.66	9.4	10.6
13	8.11	8.67		
16	8.16			
17		8.66		

[a] Data are approximated to the first decimal figure due to the broad shape of the bands.

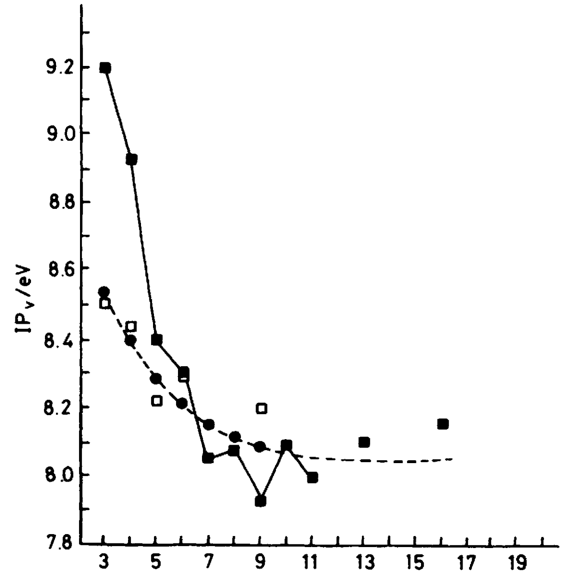


Figure 3. Plot of the experimental IP$_v$s for series (**1**) (■) *versus* ring size. Calculated (●) and experimental (□) IP$_v$ values for open-chain methyldialkylamines having the same number of carbon atoms are also shown

next band in the spectra of the tosyl derivatives, at *ca.* 10.5 eV, may be assigned as arising from ionization of a π orbital of the sulphonyl group (see, for instance, the band at 10.45 eV in methyl phenyl sulphone[9] arising from ionization of an orbital substantially localized on sulphur and oxygen). The remaining part of the spectrum shows a series of overlapping bands associated with ionization of σ orbitals.

The trend of the IP$_v$s *versus* the ring size is given in Figure 3 for series (**1**). For comparison purposes, the trend of the calculated IP$_v$ values of the corresponding open-chain methyldialkylamines [according to a slightly improved version of equation (1), as suggested in ref. 3], possessing an equal number of carbon atoms, is also represented. The latter trend shows the expected[4] regular drop of IP$_v$ on increasing the carbons number. Figure 3 also shows the experimental IP$_v$ values for some of the methyldialkylamines, either obtained by us or available in the literature.[3] All the data are reported in Table 2. The agreement between experimental and calculated IP$_v$ values for the open-chain compounds can be considered to be satisfactory, in view of the conformational flexibility of the alkyl chains. Therefore there are good reasons to trust the trend of the calculated IP$_v$ values even when it is extrapolated to the region of many carbon atoms. This theoretical curve then provides a 'base line' for analysing, with respect to the experimental IP$_v$s of series (**1**), effects specifically related to the ring structure. The experimental IP$_v$ profile of series (**1**), although showing the expected decrease of IP$_v$ on increasing the number of carbons, is rather structured. Nevertheless we can recognize two main features. The first is a crossing, for $n = 6$, with the calculated curve of the open-chain compounds. The second is that, in the limit of the large-ring region and within experimental error, the IP$_v$ profile of series (**1**) is likely to converge toward a constant value, reasonably close to the extrapolated limit of the calculated curve of the open-chain compounds. Inasmuch as the six-membered and large-membered rings can be considered strainless,[1b] this implies that an analogous behaviour does exist in the ionization process between cyclic and the open-chain aza compounds, provided that the numbers of carbons are equal. The highly strained[1b] small rings have instead IP$_v$ values much larger than those of the corresponding open-chain compounds. On the other hand, in the strained[1b] medium-ring region the IP$_v$ curve of series (**1**) lies a little below the calculated reference curve, after crossing at $n = 6$: such an effect is more apparent when comparing the experimental IP$_v$ value of the open-chain methyldibutylamine (8.20 eV) with that of *N*-methylazacyclononane (7.93 eV). The column 'Dev' in Table 2 lists the deviations of the cyclic compounds from the calculated trend, reckoned as Dev = $IP_v^{exp} - IP_v^{calc}$. The apparently conflicting behaviour of the two families of strained terms arises, in our opinion, from factors related to the difference in hybridization of the nitrogen lone pairs being ionized.[2,10] Alicyclic medium rings, as a consequence of their geometric constraint, are suggested to have intra-ring $C\hat{C}C$ angles slightly wider than the normal 109.5° value.[11] This would imply that a carbon atom will have a higher *s* character in the hybrids of the intra-ring C–C bonds and, as a consequence, higher *p* character in the hybrids of the exocyclic C–H bonds.[1a,10,12] The distortion would be shared as an average by all the carbon atoms of the ring: it would also effect the heteroatom in a heterocyclic compound. Hence, in the

Table 2. Vertical ionization potentials of the compounds (**1**) and (**2**)[a]

Experimental $MeN(CH_2)_{n-1}$		Calculated[b] open chain		Dev[c] (eV)	α_{est}[b]	Experimental open chain		Experimental $TsN(CH_2)_{n-1}$		Experimental open chain		Strain energy in cycloalkanes (kcal mol^{-1})[d]	
n[e]	IP_v		IP_v				IP_v	n[e]	IP_v		IP_v	n[e]	IP_v
3	9.20	$MeNMe_2$,	8.53	+0.67	h	Me_3N,	8.50[i]	3	9.32	$TsNMe_2$	8.90	3	27.0
4	8.93[f]	MeNMeEt,	8.40	+0.53	h	MeNMeEt,	8.44[i]	4	8.98			4	26.2
5	8.40	$MeNEt_2$,	8.28	+0.12	h	$MeNEt_2$,	8.22[i]	5	8.78			5	6.2
6	8.30	MeNEtPr,	8.21	+0.09	110.0	MeNEtPr,	8.30	6	8.76			6	0.0
7	8.05	$MeNPr_2$,	8.15	−0.10	111.8			7	8.60			7	6.1
8	8.08	MeNPrBu,	8.12	−0.04	111.2			8	8.58			8	9.5
9	7.93	$MeNBu_2$,	8.09	−0.16	112.5	$MeNBu_2$,	8.20	9	8.59	$TsNBu_2$	8.60	9	12.5
10	8.10			+0.02[g]	110.6			10	8.67			10	13.0
11	8.00			−0.07[g]	111.5							11	11.9
								12	8.66			12	7.6
13	8.11			+0.04[g]	110.4			13	8.67			13	6.2
16	8.16			+0.09[g]	109.9							16	2.0
								17	8.66				

[a] All IP_v values are in eV. [b] According to ref. 3; see text. [c] Dev = $IP_v^{exp} - IP_v^{calc}$. [d] Cyclohexane is taken as reference. Data from ref. 1*b*. [e] Ring size. [f] Taken from P. D. Mollere and K. N. Houk, *J. Am. Chem. Soc.*, 1977, **99**, 3226. [g] Extrapolated from the plot in Figure 3. [h] Not evaluated due to the inadequacy of the equation. [i] Ref. 5.

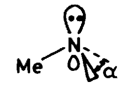


Figure 4. Conformation at nitrogen

case of a medium-membered ring of series (**1**), the nitrogen lone-pair hybrid (see Figure 4), on widening the intra-ring angle α, would shift from a *quasi-sp*^{3} hybrid to a hybrid possessing more pronounced *p* character. Consequently it will ionize more easily (*i.e.* at lower IP_v) than the corresponding open-chain counterpart, as we indeed find in the experimental u.p. spectra. We can calculate (see Table 2) the angle α for medium and large rings of series (**1**) making use of equation (5) of ref. 3 and of the Dev values given in Table 2. If we recall[3] that the angle α in a strainless tertiary amine is *ca.* 110.8°, then the angular distortion involved is rather small. This supports both our previous n.m.r. evidence[2] and the current opinion[13] that the major source of strain in the medium rings is due to transannular diaxial interactions or to eclipsing interactions,[1c] rather than to bond-angle deformations.[11]

Conformational factors appear to play a much more profound role, instead, on the IP_v values of small rings. Ionization of the nitrogen lone-pair electrons occurs at increasingly higher energy, with respect to the open-chain model compounds, on going from the five- to the three-membered ring of series (**1**). This happens because small rings present severe bond-angle distortions, ranging from 110 to 60°. A smaller angle α (Figure 4) leads to higher *p* character in the intra-ring bond hybrid, and to more pronounced *s* character of the exocyclic hybrid of the nitrogen lone pair.[3,7,10] The energy required for the ionization process becomes higher[5] and, in particular, much higher than that of the open-chain reference series.

The situation here bears a close analogy with the relative reactivity showed in homologous series of ring compounds undergoing a change in hybridization during a reaction, as is the case in the addition of CN^- to cyclic ketones.[1c,14] Medium rings present lower reactivity, due to an increase in transannular interactions and consequently of the overall *I*-strain while the *sp*^{2} carbonyl carbon gradually becomes *sp*^{3} in the transition state leading to the cyclic cyanohydrin. A relief of strain is instead experienced by the common rings and it is manifested in higher reactivity with respect to a strainless situation. Hence, the rationalization we offer for the experimental IP_vs of series (**1**) is well in keeping with current opinions which relate reactivity of cyclic compounds with conformational factors.[1a]

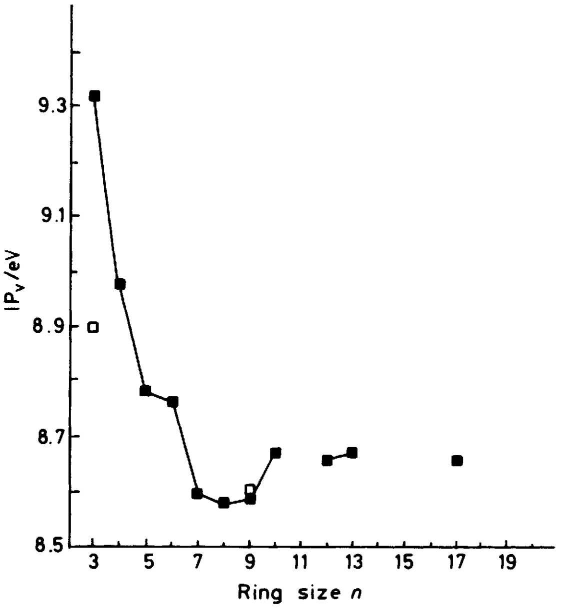
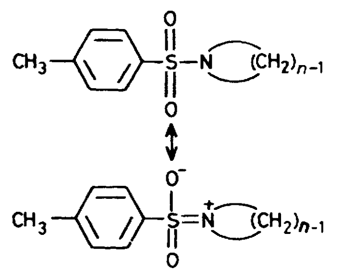


Figure 5. Plot of the experimental IP_vs for series (**2**) (■) *versus* ring size. Experimental (□) IP_v values for open-chain tosyldialkylamines having the same number of carbon atoms are also shown

The IP_v trend of series (**2**) (Figure 5), where a tosyl substituent is present, is at first glance rather close to that found for the *N*-methyl analogues (Figure 3), thus reinforcing previous considerations. Here indeed, the levelling off of the IP_v value for the strainless large rings is more clearly visible. The slight hint of a minimum in the medium-ring region appears again, although a precise evaluation of it is prevented because we are not able to calculate the theoretical reference profile of the IP_vs for the open-chain tosyldialkylamines, and because we have only two open-chain model compounds for direct experimental IP_v determination. Nevertheless it appears that in general ring strain plays an analogous role in affecting the ionization



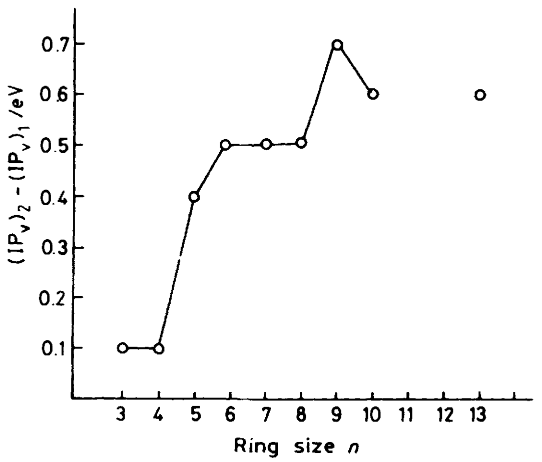


Figure 6. Difference in IP$_v$s between series (**2**) and (**1**) *versus* ring size

processes for series (**1**) and (**2**). However, the limiting IP$_v$ value in the large-ring region is some 0.5 eV higher in series (**2**) than in (**1**), and this upward drift of the IP$_v$ values is rather uniformly found in the medium and common rings, but gradually disappears in the small rings (Table 2). The latter compounds show comparable IP$_v$ values in the two series and for this reason the IP$_v$ profile of series (**2**) appears to be less spread, spanning a more limited interval. While the IP$_v$ value of *N*-tosylaziridine (**2**; $n = 3$) is only 0.42 eV higher than that of its corresponding open-chain tosyl dimethylamine, in series (**1**) the difference between *N*-methylaziridine and trimethylamine is 0.67 eV, *i.e. ca.* 50% larger.

A rationalization can be offered on the ground that compounds (**2**) are sulphonamides and, owing to the electron-withdrawing character of the *N*-sulphonyl group, they are intrinsically less basic than amines. Stabilization by resonance reduces the availability of the lone pair with respect to series (**1**) and increases (*ca.* 0.5 eV) the energy required for photoelectron ionization in series (**2**). We think, however, that a resonance structure with an exocyclic double bond will hardly give a contribution in the case of the smaller rings, due to obvious steric reasons.[1c] As an effect, *N*-tosylaziridine and *N*-tosylazetidine, and to a smaller extent also *N*-tosylpyrrolidine, would have higher availability of the lone pair with respect to their larger cyclic homologues. Presumably, they will have a basicity comparable with that of the corresponding compounds of series (**1**). The situation has been represented in Figure 6, where the ΔIP$_v$ between series (**2**) and (**1**) is plotted against ring size. The discrepancy in the small-ring region is striking. Hence the experimental IP$_v$ values for the small rings of series (**2**) result from a balance of two opposite factors: (i) a specific higher basicity, causing a reduction of the IP$_v$, and (ii) more pronounced *s* character of the nitrogen lone-pair hybrid according to the general explanation given for series (**1**), causing an increase of the IP$_v$. We think that it is possible to rationalize in this way the origin of a more compressed IP$_v$ profile for series (**2**). Clearly we were able to detect such an effect only on the basis of our previous determination of the trend for the 'well behaved' series (**1**).

Experimental

N-Methylpyrrolidine (Schuchardt) and *N*-methylpiperidine (Fluka) were reagent grade commercial samples and were used as received.

Preparations of *N*-methylazacycloalkanes[15] and of *N*-tosylazacycloalkanes[16,17] were reported previously. *NN*-Dimethyltoluene-*p*-sulphonamide was prepared by double alkylation of toluene-*p*-sulphonamide with MeI and KOH (2 equiv.) in Me$_2$SO, according to the conditions of ref. 17, m.p. 80—81 °C (lit.,[18] 80—81 °C).

Gas-phase u.p. 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 80—120 °C for the solid ones. In the case of *N*-tosylaziridine (**2**; $n = 3$) the temperature did not exceed 80 °C, in view of the instability of the compound. Calibration was with N_2 and self-ionizing He.

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