

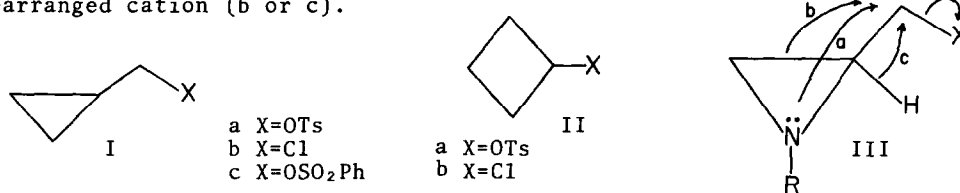
AZIRIDINE AS A NEIGHBORING GROUP

James A. Deyrup and Calvin L. Moyer (1)

Department of Chemistry, University of Florida, Gainesville, Florida 32601

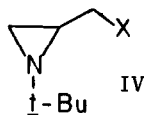
(Received in USA 17 October 1968; received in UK for publication 13 November 1968)

The enhanced rates with which cyclopropylcarbinyl (I) and cyclobutyl derivatives (II) undergo solvolytic ionization and rearrangement has attracted considerable attention. (2) As a result of extensive and ingenious experiments, it seems clear that this reactivity is attributable to charge delocalization by these small rings. (3) Our interest in small ring heterocyclic compounds led us to wonder whether nitrogen analogs of I and II would exhibit similar reactivity. We were particularly intrigued by the multiple avenues for assisted ionization potentially available to III. For example, charge stabilization might be achieved by ring participation analogous to that proposed for I (but perturbed to some extent by nitrogen). Alternatively, advantage might be taken of the unshared electron pair either directly, as a neighboring group (a), or via resonance stabilization of a rearranged cation (b or c).

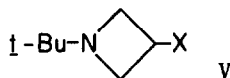


We have prepared IVa and Va from IVb (4) and Vb (5) respectively. (6) We would like to report some preliminary studies of their chemistry which reveal major differences between them and their homocyclic analogs. Thus, reaction of IVa with NaOC₂H₅ in ethanol at 25° for 48 hrs produced IVc as the sole product. Other displacement products including bromides IVd and Vd (from Bu₄NBr in benzene) as well as ether Vc (NaOC₂H₅ in ethanol), could easily be prepared. In each case, the conversion was quantitative and without detectable isomeric contamination.

The formation of IVc was apparently the result of bimolecular displacement since IVa could be reisolated from absolute ethanol (over Na_2CO_3) at 60° after 48 hrs.



- a X=OTs
- b X=OH
- c X=OC₂H₅
- d X=Br
- e X=ONs
- f X=Cl



- a X=OTs
- b X=OH
- c X=OC₂H₅
- d X=Br
- e X=Cl

This lack of reactivity (in the absence of nucleophiles) of IVa is in contrast to the reported complete reaction of Ic within 24 hrs at 20° in absolute ethanol. (7) We conclude, therefore, that the heterocyclic system is qualitatively less reactive towards ionization. In order to seek further support for this conclusion, we extended our investigation of IVa and Va to better ionizing media.

It is well known that the protonated aziridine ring is subject to ring opening. For this reason, we chose to avoid acidic solvents and the build up of acid. (8)

The latter was accomplished by the addition of equivalent amounts of triethylamine to all of the subsequently discussed solvolyses. (10) In 5% aqueous ethanol (25° , 6 days) IVa yielded rearrangement products Vb (38%) and Vc (4%) in addition to IVb (5%). Under the same conditions, Va was converted to Vb (16%) and Vc (20%). (11)

Solvolytic rate constants were obtained which confirmed our qualitative conclusion concerning the low reactivity of IVa and which also revealed a large difference between the three- and four-membered rings. These results are summarized in Table I (along with data from other sources on the homocyclic analogs). Rate constants were determined by quantitative nmr spectral analysis of CCl_4 soluble extracts of aliquots from which ethanol has been removed by evaporation. First order kinetics at several concentrations (0.002-0.01 molar) were obtained. (12)

Table I reveals a difference in the four-/three-membered ring reactivity ratios. The magnitude of this difference (homocyclic $\approx 10^{-1}$ vs heterocyclic $\approx 10^{-4}$) suggests a difference in mechanism in the two series. In particular, it suggests that although both four-membered rings undergo assisted ionization, they must receive their stabilization from different sources. In view of the observed products, transannular nitrogen participation to form VI would seem a reasonable explanation for the reactivity of Va. This explanation is consistent with the diminished reactivity of IVa in terms of the expected poorer electron donation by

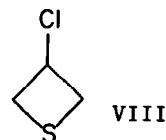
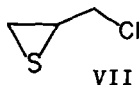
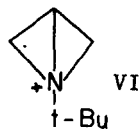
orbitals external to a strained ring. (13) It is interesting to note that a

Table I. Solvolytic Reactivity of Small Ring Sulfonates

Compound	Rate (sec ⁻¹)	Temp, °C	Relative Reactivity
IVa a,c	1.3 ± 0.6 x 10 ⁻⁶	25 ± 2	3.5 x 10 ⁻⁵ d
IVe a,c	8.3 ± 1.7 x 10 ⁻⁶	20.0 ± 0.1	4.5 x 10 ⁻⁴ e
Va b,c	1.6 ± 0.3 x 10 ⁻⁶	20.0 ± 0.1	0.5 f
Ia a	1.8 x 10 ⁻² f	20	1
Ia a	3.5 x 10 ⁻² f	25	
Ia b	3.2 x 10 ⁻⁵ g	20	
IIa			4 x 10 ⁻² h

(a) Rate constant in 50% aqueous ethanol. (b) Rate constant in 100% ethanol. (c) An equivalent amount of triethylamine was added to suppress protonation of the aziridine. (d) Relative to Ia at 25° in 50% ethanol. (e) Relative to Ia at 20°. A factor of 14 is expected for a change in leaving group from tosylate to nosylate - A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N.Y., 1962, p 82. (f) Extrapolated from published temperature and solvent dependency data. g' (g) D. D. Roberts, *J. Org. Chem.*, **29**, 295 (1964). (h) Estimated from relative rates of Ib and Iib in 50% ethanol. 2a

similar ratio of four-/three-membered ring reactivities ($\approx 10^3$) has also been noted for the sulfur analogs VII and VIII by Martin and Anderson. (14) These authors decided that both compounds reacted with sulfur participation via a common thia-bicyclobutonium ion.



The most interesting conclusion which is allowed by our results is that replacement of a methylene group by a t-butylamino group severely dampens the ability of the three-membered ring to delocalize charge. The most obvious cause of this effect is the electronegativity of the nitrogen atom. In principle, this electronegativity could manifest itself via depletion of the ring's ability to donate electrons in the non classical sense and/or via inductive "tightening" of the C-O bond. The different geometry and electron distribution anticipated for transition states which resemble the cyclopropylcarbanyl cation and VI suggests that suitable steric and electronic alteration of IV and V should help clarify the (as yet un-

clear) mechanism by which IV reacts. Such alterations may even make possible observations of several limiting types of participation. Work along these lines are now in progress.

REFERENCES

1. Presented at the 156th National Meeting of the American Chemical Society, Atlantic City, New Jersey, September 1968, Abstract: ORGN 2. Support of this research by National Science Foundation Grants GP-5531 and GP-8044 as well as a Research Corporation Grant is gratefully acknowledged.
2. (a) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1961); (b) K. B. Wiberg and J. E. Hiatt, *Tetrahedron Letters*, 3009 (1968).
3. P. von R. Schleyer and G. W. Van Dine, *J. Am. Chem. Soc.*, **88**, 2321 (1966); K. B. Wiberg and A. J. Ashe, *ibid.*, **90**, 60 (1968).
4. C. L. Moyer, Ph.D. Thesis, Harvard University, Cambridge, Mass., 1968.
5. V. R. Gaertner, *J. Org. Chem.*, **32**, 2972 (1967).
6. Satisfactory nmr and mass spectral data as well as elemental analyses were obtained for all compounds except Vc which was characterized spectrally. The nmr spectra allowed unequivocal structure assignment and permitted detection of isomeric ring structures.
7. C. G. Bergstrom and S. Siegel, *J. Am. Chem. Soc.*, **74**, 145 (1952).
8. After this work was completed we learned of the study of IVf and Ve in buffered acetic acid. Under these conditions, both compounds suffered extensive ring opening and reclosure.
9. V. R. Gaertner, 156th National Meeting of the American Chemical Society, Atlantic City, New Jersey, September 1968, Abstract: ORGN 1. We would like to thank Dr. Gaertner for communications concerning his results.
10. This amine showed no detectable reaction with IVa after 3 days at 60°.
11. Although alcohols IVb and Vb were stable to the reaction conditions (in the presence of equimolar amounts of triethylamine and toluene sulfonic acid, we failed to recover all the material from these reactions. The remainder of the material was viscous and apparently polymeric in nature.
12. While this method of kinetic analysis is not capable of great precision, the data are adequate for the conclusions which we wish to draw. The use of acidic conditions commonly used to determine sulfonate ester solvolysis rate constants leads to ring opening and results⁹ which are in conflict with both our qualitative and quantitative observations of k_{IVa}/k_{Ia} . We are currently attempting to devise a technique which is both accurate and compatible with the acid sensitive nature of these compounds.
13. E.g. S. Searles, M. Tamres, F. Block and L. A. Quarterman, *J. Am. Chem. Soc.*, **78**, 4917 (1956) reported pK_a 's of 7.86 for N-methylaziridine and 10.4 for N-methylazetidene.
14. J. C. Martin and D. J. Anderson, presented at the 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961, Abstract: 31-0.