

UNUSUAL SPECTROSCOPIC AND CONFORMATIONAL PROPERTIES OF SOME SPIROCYCLIC OXAZIRIDINES

Jeffrey Aubé and Yuguang Wang*

*Department of Medicinal Chemistry, University of Kansas
Lawrence, Kansas 66045-2506*

Summary: The proton that bears a 1,3-diaxial relationship to the substituted nitrogen atom of some chiral oxaziridines appears in the NMR spectrum at unusually high field. This observation indicates that an unusual rotamer is substantially populated in these systems.

We and others have been interested in the conformational properties of chiral oxaziridines, especially those aspects which bear on the asymmetric synthesis and rearrangement chemistry of this functional group.¹ We wish to report an unusual trend in the nuclear magnetic resonance (¹H NMR) spectra of some of these compounds, and a conformation which accounts for this phenomenon.

We synthesized oxaziridines **1a-d**, **2a-d** and **3a-b** in the usual way^{1a} from the corresponding 4-substituted cyclohexanones. The structure of the major isomer of **3b** was previously determined by X-ray crystallography.^{1c} Although the *N*-benzyl substituted compounds **1a**, **2a** and **3a** showed no unusual features in the ¹H NMR spectra, the arylethyl derivatives (**1b-d**, **2b-d**, and **3b**) each showed a signal for a single proton well upfield of the others, *in one example appearing as high as δ -0.32 ppm*. Through decoupling experiments and coupling constant analysis, it was determined that this upfield proton bears a 1,3-diaxial relationship syn to the nitrogen substituent of the oxaziridine unit (marked H_x in the drawing).²

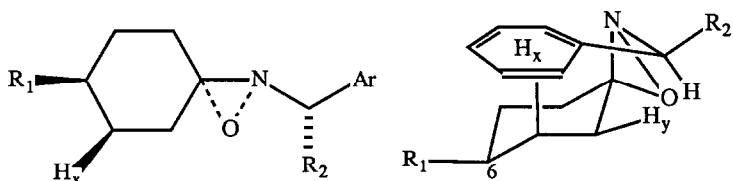
We ascribe the unusually high field of the signal to shielding by the arene ring of the nitrogen substituent; this is supported by the dependence of the chemical shift on the identity of the particular aryl substituent employed. Significantly, this requires the conformation about the N_{oxaziridine}-C_{benzyl} single bond to be largely that shown in the drawing, wherein the arene group is positioned directly over the cyclohexyl group. Such a conformation was found in the X-ray structure of **3b**, but these NMR results are the first evidence that this conformation is also substantially populated in solution and is not solely a consequence of crystal packing forces.^{2a,3} We rationalize that the increased upfield effect of the 1-naphthyl substituent is due to a closer approach of the distal six-membered aromatic ring. When the fused ring cannot obtain such an approach (as in the 2-naphthyl derivative) the chemical shifts revert to values more comparable to those obtained in the phenyl examples.

One possible explanation for these data is that the rotamer depicted is highly populated for cases in which R₂ = methyl, probably due to adverse steric effects encountered in other rotamers, most likely emanating from the equatorial hydrogen atom (H_y) adjacent to the oxaziridine. The absence of a comparable upfield shift for the *N*-

benzyl examples **1a**, **2a** and **3a** suggests that the benzylic methyl group substituent plays a critical role in determining the preferred conformation about the nitrogen-carbon bond. It is also interesting that the isomer which is epimeric at the benzylic position shows no propensity for this conformational preference, as judged by the failure of these materials to show an NMR effect analogous to that described here.

The observations described herein represent one method for the determination of a populated conformer about a flexible carbon-nitrogen bond. Besides the utility of such information in the rationalization of the chemistry of the oxaziridines at hand, similar methods may well prove of use in the understanding of torsional effects in other environments.⁴

Table. NMR Data for Bicyclic Oxaziridines



Compound ^a	R ₁	R ₂	Ar	H _x Chemical Shift (ppm) ^b
1a	-CH ₃	-H	-Ph	>0.90 ^c
b		-CH ₃	-Ph	0.12
c		-CH ₃	-1-naphthyl	-0.32
d		-CH ₃	-2-naphthyl	0.24
2a	-C ₆ H ₅	-H	-Ph	>0.90 ^c
b		-CH ₃	-Ph	0.71
c		-CH ₃	-1-naphthyl	0.12
d		-CH ₃	-2-naphthyl	0.54
3a	-C(CH ₃) ₃	-H	-Ph	>0.90 ^c
b		-CH ₃	-Ph	0.22

^aAll compounds prepared are racemic. Only one enantiomer of the major isomer produced in each reaction is depicted for clarity. ^bNMR spectra measured at 300 MHz in CDCl₃ at 20°C (Varian XL-300). ^cObscured by other methylene signals.

References and Notes:

- (a) Aubé, J.; Burgett, P.M.; Wang, Y. *Tetrahedron Lett.* **1988**, *29*, 151. (b) Aubé, J. *Ibid.*, in press. (c) Lattes, A.; Oliveros, E.; Rivière, M.; Belzecki, C.; Mostowitz, D.; Abramskj, W.; Piccinni-Leopardi, C.; Germain, G.; Van Meersche, M. *J. Am. Chem. Soc.* **1982**, *104*, 3929.
- The proton in question appeared as an apparent doublet of quartets resulting from one small (axial-equatorial) and three large (two axial-axial plus one geminal) couplings. This deceptively simple pattern could be further assigned by decoupling experiments. E.g., for **2b**: irradiation of the signal at δ 0.71 ppm caused partial collapse of the signal at δ 2.47 (t of t, $J = 12, 7$ Hz, C-6 H). The assignment of the signal as syn to the nitrogen substituent is made on the basis of the chemical shift dependence on arene type.
- The chemical shift of H_x for **3b** was not reported in reference 1c.
- We acknowledge partial financial support of this research from the University of Kansas (General Research Fund 3547-XX-0038), the donors of the Petroleum Research Fund (administered by the American Chemical Society), and the National Institutes of Health (GM-39402).

(Received in USA 31 August 1988)