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THE EFFECT OF THE PHENYL SUBSTITUENT ON THE NITROGEN INVERSION BARRIER IN A 2-PHENYLOXAZIRIDINE

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Comparisons of the pyramidal inversion barrier[2] with changes in substituent have recently been made for amines and arsines relative to phosphines[3] as shown in Figure 1. The slope of the correlation line was used as a measure of the sensitivity of the inverting center to substituent effects.[3] From data in the literature for aziridines,[4] in which the nitrogen atom is subjected to the barrier raising constraints of the three membered ring, a similar correlation line shows a much greater sensitivity to substituent than for the amines (Figure 1) and approximately the same sensitivity to substituent as for the phosphines. However, the aziridine inversion barriers are ∿17 kcal/mol less than for the phosphines.

The nitrogen inversion barriers of 2-methyl-3,3-disubstituted oxaziridines[5] are ∿14 kcal/mol greater than those of 1-methyl-2,2-dimethylaziridines[4d] due to the barrier raising effect of the electronegative oxygen atom in the ring. No inversion data have been available for other kinds of substituents on the nitrogen atom in oxaziridines primarily because many of these oxaziridines undergo other thermal reactions. Until this time the known 2-aryloxaziridines were thermally too unstable to observe for nitrogen inversion.[6] We have now prepared 2,3-diphenyl-3-methyloxaziridine in predominantly the cis form and have observed its equilibration to 70% trans:30% cis-oxaziridine before rearrangement reactions occurred.[7]

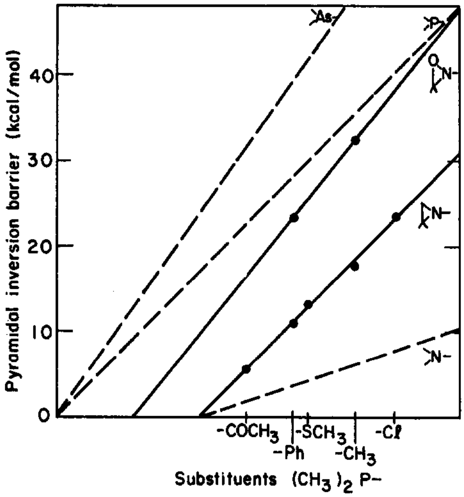
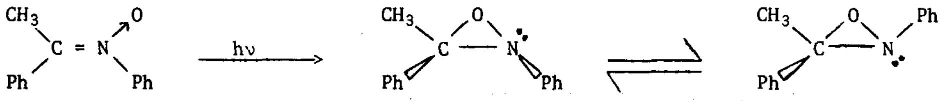


Fig. 1. Correlation lines: -----, as determined in Ref. 3; ———, determined from data in Ref. 4 and this work (see text).



cis-I cis-II trans-II

The nmr spectrum of nitrone I[8] in carbon tetrachloride showed a single methyl resonance at τ 7.47 (3H,s) and aromatic proton resonances at τ 2.95 (10H,m), indicative of a single isomer, the cis-nitrone I.[10] A solution of 50 mg of I in 100 ml methylene chloride was irradiated for 4 minutes in a Pyrex immersion apparatus equipped with a 450 watt Hanovia medium pressure mercury lamp. Removal of the solvent in vacuo afforded an oil, II: $uv_{max}^{CH_3CN}$, end absorption at 230 nm (ε 9400). Its ir showed no carbonyl or imine bands and iodometric titration gave a 90% active oxygen content. Reflux of II in acetonitrile for 24 hours resulted in a 2:1 mixture of N-methylbenzanilide and acetyldiphenylamine. These properties were consistent with the structure of 2,3-diphenyl-3-methyloxaziridine for II.

An nmr spectrum of II in carbon tetrachloride taken as soon as possible after preparation showed two methyl resonances at τ 8.08 and τ 8.46 in a ratio of about 80%:20%.[13] Peak integration also showed the expected 10:3 ratio between aromatic and methyl hydrogens.

On standing at room temperature, the τ 8.08 resonance slowly decreased while the τ 8.46 resonance increased until an equilibrium ratio of 30%:70% was obtained. The ir, uv, and active oxygen measurements remained unchanged during the isomerization. Oxaziridines prepared by the irradiation of the corresponding nitrones have been shown to have the same stereochemistry as the nitrone.[11] Therefore, the τ 8.08 resonance in the oxaziridine was assigned to cis-oxaziridine II and the τ 8.46 resonance to trans-oxaziridine II. This assignment is consistent with the more stable oxaziridine being the trans-oxaziridine.[14]

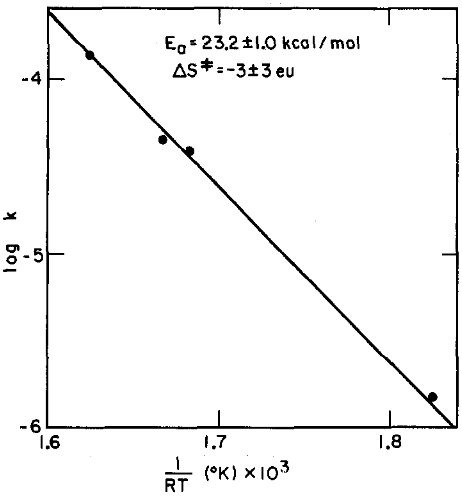


Fig. 2. Arrhenius plot for the inversion of cis-II to trans-II in CCl_4.

The first order rate constants for the isomerization (inversion) of cis-II to trans-II were determined at several temperatures.[15] In Figure 2 is shown an Arrhenius plot from which

E_a = 23.2 ± 1 kcal/mol and $\Delta S^\ddagger$ = -3 ± 3 eu were calculated. The $\Delta S^\ddagger$ values for other pyramidal inversions have been found to be relatively small[2,4] and valid comparisons have been shown with $\Delta H^\ddagger$ values when the same value of $\Delta S^\ddagger$ was used for a series of the same type of compounds.[16] When $\Delta S^\ddagger = 0$, which is a reasonable assumption for pyramidal inversions, $\Delta H^\ddagger = \Delta G^\ddagger$.

The $\Delta G^\ddagger$ of 23.4 kcal/mol for the inversion of oxaziridine II was calculated from the rate constants using the Eyring equation. From this value of $\Delta G^\ddagger$ and the $\Delta G^\ddagger$ values for 2-methyl-3,3-disubstituted-oxaziridines reported previously,[5] an approximate correlation line was drawn for the oxaziridines as shown in Figure 1. A comparison of the slopes shows that the oxaziridines have a greater sensitivity to substituent than the aziridines, which in turn have a greater sensitivity than the amines.

REFERENCES AND FOOTNOTES

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3. R.D. Baechler, J.D.Andose, J. Stackhouse and K. Mislow, J.Amer.Chem.Soc., 94, 8060 (1972).
4. Representative substituents were placed on the abscissa according to the magnitude of their calculated $(CH_3)_2P$- inversion barriers (slope = 1)[3]. The correlation line for the corresponding 1-substituted aziridines was drawn utilizing the following values for $\Delta G^\ddagger$ (kcal/mol) adjusted to 25°C assuming $\Delta S^\ddagger = 0$. The aziridines were chosen, where possible, for structural similarities to 3,3-disubstituted oxaziridines. The solvents are given in parentheses. (a) 1-acetyl-, <5.6 (vinyl chloride); F.A. Anet and J.M. Osyany, J.Amer.Chem.Soc., 89, 352 (1967). (b) 1-phenyl-2,2-dimethyl-, 11.1 (CF_2Cl_2); J.D. Andose, J.M. Lehn, K. Mislow and J. Wagner, J.Amer.Chem.Soc., 92, 4050 (1970). (c) 1-methylsulfenyl-2,2-dimethyl-, 13.2 ($CDCl_3$); J.M. Lehn and J. Wagner, Chem.Commun., 1298 (1968). (d) 1-methyl-2,2-dimethyl-, 17.6 (toluene); T. Drakenberg and J.M. Lehn, J.Chem.Soc., Perkin II, 532 (1972). (e) 7-chloro-7-azabicyclo[4.1.0]heptane, 23.6 (C_6H_6); D. Felix and A. Eschenmoser, Angew.Chem., Int.Ed. Engl., 7, 224 (1968).
5. (a) $\Delta G^\ddagger_{25°}$ = 32.2 kcal/mol, calculated from rates given in F. Montanari, I. Moretti and G. Torre, Chem.Commun. 1086 (1969). (b) $\Delta G^\ddagger_{25°}$ = 32.2 kcal/mol; A. Mannschreck, J. Linss and W. Seitz, Ann., 727, 224 (1969).
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7. Similar results were found with 3-(4-methoxyphenyl)-2,3-diphenyloxaziridine.
8. I was prepared by reacting acetophenone hydrazone (9a) first with silver oxide and then with nitrosobenzene in petroleum ether (9b) and collecting the resulting precipitate; mp 93-96°;

uv$_{max}^{CH_3CN}$ 291 nm (ε 8,800); ms (70 ev) m/e (rel. int.) 211 (M^+, 27), 210(8) 195 (10), 180 (18), 91 (100), 77 (40). It was thermally unstable, hydrolyzing to acetophenone after several days at room temperature.

9. (a) G. Lock and K. Stach, Chem.Ber., **77B**, 293 (1944); (b) H.G. Aurich, ibid., **98**, 3917 (1965).

10. The nmr spectra of *trans*-α-arylnitrones exhibit downfield shifts of the ortho protons. This characteristic is absent in the *cis* isomers[11] or when the ortho protons are substituted with methyl groups.[12]

11. J.S. Splitter, T. Su, H. Ono and M. Calvin, J.Amer.Chem.Soc., **93**, 4075 (1971).

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13. Since considerable time was involved in the preparation of the nmr sample, the original ratio of the two isomers after irradiation is probably even greater than 4:1. In a series of isolable 2,3-diaryloxaziridines, nmr measurements in CCl_4 at room temperature showed only a single α-hydrogen resonance which remained unchanged with time: 2-(4-cyanophenyl)-3-phenyl oxaziridine, τ 5.55(s); 2-(4-nitrophenyl)-3-phenyloxaziridine, τ 5.37(s); 3-styryl-2-phenyloxaziridine, τ 5.70(d). This indicated either rapid nitrogen inversion or, more probably, the existence of a single isomeric species.

14. The downfield shift of the *cis*-3-methyl group is analogous to the downfield shifts of the *cis*-3-H relative to the *trans*-3-H-oxaziridines; D.M. Jerina, D.R. Boyd, L. Paolillo, and E.D. Becker, Tetrahedron Lett., 1483 (1970).

15. Kinetics were measured in a Varian A-60 nmr spectrometer equipped with a constant temperature probe. The 1° kinetics were done in an ice bath, the sample being transferred to the nmr spectrometer at various intervals. The rate constants (sec^{-1}) found were: at 35°, 13.6 x 10^{-5}; at 27°, 4.37 x 10^{-5}; at 24°, 3.80 x 10^{-5}; at 1°, 0.15 x 10^{-5}.

16. J. Lehn and J. Wagner, Tetrahedron, **26**, 4227 (1970).