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# A KINETIC INVESTIGATION OF THE THERMAL REARRANGEMENT OF N-PYRIDINO-2-VINYL-AZIRIDINES.

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Summary : The first-order rate constants of the thermal rearrangement of several N-pyridino-2-vinyl-aziridines into the corresponding pyrido-azepines have been determined. Substituent effects on this isomerization were found to be completely analogous to the related benzenic O-Claisen rearrangement.

N-phenyl-2-vinyl-aziridines are known readily to undergo a thermal ring expansion to benzazepine derivatives[1,2]. We recently reported that several heteroaromatic nuclei could take the place of the benzene ring in this reaction, leading to relatively unexplored or unknown classes of compounds[3]. The ease of isomerization, however, was seen to be strongly dependent on the type of heterocycle involved ; we now wish to report a kinetic study of the influence of substituents in the allylic part of the molecule and of the pyridine nitrogen atom position on the rate of rearrangement of the N-pyridino-2-vinyl-aziridines shown in Figure I.

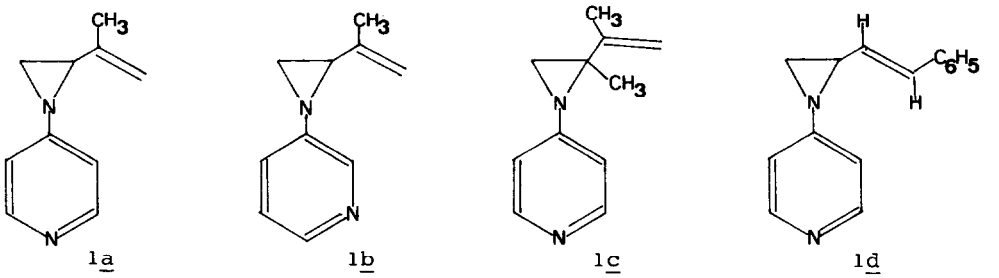


Figure I.

Compounds 1a and b have been described previously[3] ; 1c and 1d were synthesized according to Scheiner's method[4] by 1,3-dipolar cycloaddition reaction of 4-azido-pyridine[5], respectively with 2,3-dimethyl-[6] and with trans-1-phenyl-butadiene[7] at 50°C during two weeks ; the corresponding triazolines (2c : 62%, F.: 79°C (P.E.) ; 2d : 40%, F.: 135°C (acetone)) have subsequently been photolysed in THF at room temperature (Hanovia, medium

pressure, 450 W, pyrex filter), yielding the aziridines 1c and 1d together with a considerable amount of imines 3c and 3d respectively (Figure II) which could not be separated by chromatographic techniques. Similar mixtures of 1a/3a and 1b/3b have already been obtained by the same method[3]. The ratios aziridine-imine, determined by NMR, are mentioned in Table 1.

| | a | b | c | d |
|---|---|---|---|---|
| azir./imine | 50/50 | 75/25 | 55/45 | 60/40 |

Table 1.

These mixtures have been heaten in refluxing toluene ; under these conditions, the aziridines smoothly yield the corresponding azepines 4a-4e (Figure II).

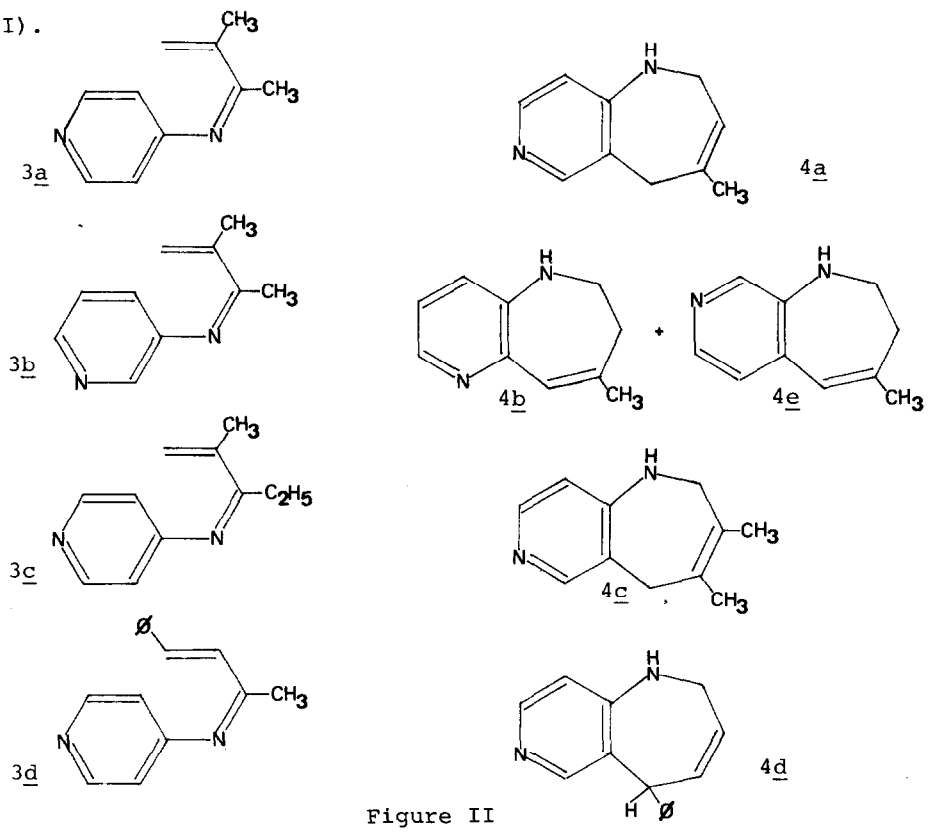


Figure II

The disappearance of the aziridines (peak-height) was followed quantitatively by analytical High Pressure Liquid Chromatography (Alox T column 25 cm long ; eluant EtOAc/iso-octane 20/80 ; UV detection at 254 nm), the thermally stable imines being used as internal standard. In each case, an excellent first-order kinetic plot was obtained. About 15 readings were taken during a kinetic experiment and values of $k_{obs.}$ determined for each of these readings ;

the mean rate constants, together with the different half-life times are given in Table 2.

| Reaction | $10^5.\bar{k}(sec^{-1})$ | $10^5.s^c$ | t $\frac{1}{2}$ (min.) | $r^d$ |
|---|---|---|---|---|
| 1a → 4a | 1.38[a] | 0.07 | 400 | 0.999 |
| 1b → 4b | 9.29[b] | 0.42 | 82 | 0.995 |
| 1b → 4e | 4.64[b] | 0.22 | | |
| 1c → 4c | 8.03[a] | 0.45 | 72 | 0.999 |
| 1d → 4d | 3.74[a] | 0.45 | 162 | 0.998 |

Table 2.

a: For these reactions, $\bar{k}(sec^{-1})=\frac{1}{2}.\bar{k}_{obs}$ in order to take account of the two possible (but equivalent) positions of cyclization.

b: Determined from the observed mean first-order rate constant $\bar{k}_{obs}=13.93.10^{-5}$ $sec^{-1}$ and the final product distribution (4b and 4e).

c: S is the 95% confidence limit of the mean value[17].

d: Correlation coefficient of the regression line $\ln \frac{A}{A_o} = -k.t$

After completion of the reaction, the resulting mixtures of azepines and imines were separated by column chromatography (neutral alumina, eluant: EtOAc/$CHCl_3$ : 20/80). The yields of the new azepines are : 4c : 73%, 149°C (P.E.) ; 4d : 33% (unstable oily product) ; imines 3a, b and c are oily products ; 3d is a white solid (F.: 112°C, from ether at -50°C, followed by sublimation at $10^{-2}$ mm Hg/90°C)[8].

The kinetic data listed in Table 2 definitely rule out on a quantitative basis a mechanism where the heterolytic cleavage of the aziridine $N_1$-$C_2$ bond is the rate-determining step. If this was the case indeed, the negative charge developed on the nitrogen atom α to the pyridine ring in the zwitterionic intermediate would be much more stabilized by a nitrogen atom in the para-position than in the meta-position on the heterocycle, as can be expected from their respective $\sigma^-$-values : 1.17 and 0.59[9]. This would lead to a rate sequence opposite to the one observed. On the other hand, a comparison of the kinetic data for the rearrangements of 1a and 1c show that the introduction of a methyl group at the 2-position of the aziridine produce a more than five-fold enhancement of the reaction rate ; a similar, although less important effect is observed when a trans-phenyl group is introduced at the vinylic carbon atom β to the microcycle (1d).

All these observations are almost identical to those made for the closely related benzenic O-Claisen rearrangement. Indeed, W.N. White[10] and H.L. Goering[11] and co-workers have shown on a series of p-substituted phenyl-allyl-ethers that their relative reactivities can be linearly correlated to the

$\sigma^+$-substituent constants, electron-withdrawing substituents decreasing the reaction rate ; this is consistent with the low reactivity of 1a ($\sigma^+$ = 1.16 for N-para[9]) as compared to 1b ($\sigma^+$ = 0.54 for N-meta[9]). As was pointed out in our previous publication[3], also the preferred cyclisation of 1b to 4b rather than 4e is in agreement with the reported influence of electron-withdrawing meta-substituents in the O-Claisen rearrangement[12]. Furthermore, H.L. Goering showed that an allylic methyl substituent (α to the oxygen atom) had a similar, although somewhat larger, rate-increasing effect[11] on the benzenic O-Claisen rearrangement, while N.C. White found a comparable difference in reaction rate between several p-substituted phenyl allyl-[10] and the corresponding phenyl-cinnamyl-ethers[13,14].

Thus it appears that the thermal isomerization of N-pyridino-2-vinyl-aziridines to pyrido-azepines show substituent effects completely analogous to the related benzenic O-Claisen rearrangement. This is an argument in favor of a similar transition state for both reactions ; the ring expansion of N-aryl-2-vinyl-aziridines should thus be described as a concerted [3,3] sigmatropic rearrangement[15,16].

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References

1. P. Scheiner, J. Org. Chem. 32, 2628 (1967).
2. A. Sauleau, J. Sauleau, H. Bourget and J. Huet, Compt. Rend. 279C, 473 (1974) ; J. Sauleau, A. Sauleau and J. Huet, Bull. Soc. Chim. France (II) 97 (1978).
3. H.P. Figeys and R. Jammar, Tetrahedron Letters 21, 2995 (1980).
4. P. Scheiner, Tetrahedron 24, 349, 2757 (1968).
5. A.V. Eltsov, A. Hantschmann and N.I. Rtishchev, Zh. Org. Khim. 13, 465 (1977).
6. C.F.H. Allen and Alan Bell, Org. Syntheses Coll.Vol. 3, 312 (1954)
7. Duncan G. Foster, Org. Syntheses Coll.Vol. 3, 771 (1954).
8. Variable temperature (30°C to 130°C) NMR-studies show that 3d exists as a mixture of two interconverting Z- and E-isomers of the imino-linkage.
9. P. Tomasik and C.D. Johnson, in "Advances in Heterocyclic Chemistry",Vol.20, A.R. Katritzky and A.J. Boulton Ed., Academic Press, London, 1976, p.1.
10. W.N. White, D. Gwynn, R. Schlitt, C. Girard and W. Fife, J. Amer. Chem. Soc. 80, 3271 (1958).
11. H.L. Goering and R.R. Jacobson, J. Amer. Chem. Soc. 80, 3277 (1958).
12. W.N. White and C.D. Slater, J. Org. Chem. 26, 3631 (1961).
13. W.N. White and W.K. Fife, J. Amer. Chem. Soc. 83, 3846 (1961).
14. It has been shown[11] that substitution of the hydrogen atom β to the heteroatom by a methyl group has essentially no effect on the rate of the benzenic O-Claisen rearrangement.
15. S.J. Rhoads and N.R. Raulins, Org. Reactions 22, 1 (1975).
16. S. Jolidon and H.J. Hansen, Helv. Chim. Acta 60, 978 (1977) have recently proposed the same mechanism for the benzenic amino-Claisen rearrangement.
17. T.D.V. Swinscow, "Statics at Square One", British Medical Association, London, 1977, p. 34.

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