

REARRANGEMENTS OF N-HETEROAROMATIC-2-VINYL-AZIRIDINES.  
SYNTHESIS OF ISOTHIAZOLO-, PYRIDO- AND THIENO-AZEPINES.

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**Summary:** N-heteroaromatic-2-vinyl-aziridines have been synthesized and thermally isomerized to the corresponding isothiazolo-, pyrido- and thieno-azepine derivatives. The ease of rearrangement is strongly dependent on the nature ( $\pi$ -deficient or -rich) of the aromatic heterocycle.

2-Vinyl-aziridines possessing unsaturated substituents on the nitrogen atom are known readily to undergo ring expansion to pyrroline<sup>(1-3, 7)</sup>- and azepine-derivatives<sup>(2-7)</sup>. Carbon-carbon double bonds<sup>(4)</sup>, carbonyl<sup>(6)</sup> and thiocarbonyl<sup>(7)</sup> groups as well as benzene rings<sup>(2,3,5)</sup> have been involved in this seven-membered ring formation. We have now found that the thermal isomerization of the 2-vinyl-N-heteroaromatic-aziridines shown in Figure 1 exclusively yields the corresponding isothiazolo-, pyrido- and thieno-azepines shown in Figure 3 and which constitute relatively unexplored or unknown classes of compounds.

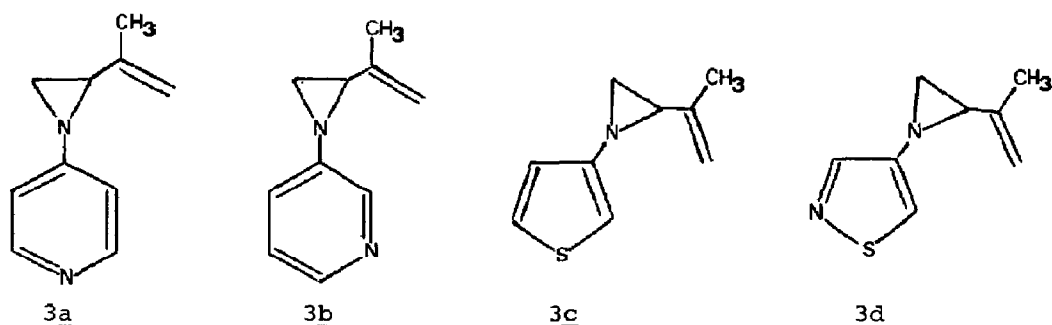


Figure 1

Compounds 3a, b, c and d have been synthesized according to Scheiner's method<sup>(8)</sup> by 1,3-dipolar reaction of the corresponding heteroaromatic azides 1 (9,10,11) with refluxing isoprene and subsequent photolysis of the triazolines 2 so obtained (fig. 2). The reaction times and yields for the triazoline formations are : 2a, 7 days, 45%, F.74°C(P.E.); 2b, 10 days, 48%, F.37°C(P.E.); 2c, 21 days, 16% (oily product purified by column chromatography on alumina, eluant: benzene) ; 2d, 14 days, 62%, F.76°C(P.E.-ethyl acetate). Photolysis of 2a and 2b in THF at room temperature for 15 hours with a medium pressure HANOVIA 450W lamp through a pyrex filter gives a mixture of the aziridines 3



Our results emphasize the dramatic influence of the aromatic substituent on the nitrogen atom. Indeed, while 3a and 3b are quite stable products and rearrange only on heating, 3c and 3d could not be isolated at room temperature. This excludes as a possible mechanism the heterolytic cleavage of the C<sub>2</sub>-N<sub>1</sub> bond of the microcycle as being the rate determining step, leading to an intermediate zwitterion of the type 8 shown at Fig. 4, which could then cyclize to the seven-membered ring in a second and fast step.

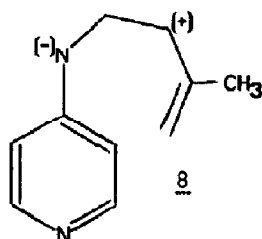


Figure 4

According to Hammond's postulate, the transition state of the reaction should indeed then closely resemble this intermediate; stabilization of the nitrogen negative charge will be more efficient in 8 for instance than e.g. for the corresponding 3-thienyl-compound, leading to a reaction sequence exactly opposite to the one observed. Such a reaction mechanism has been proposed by Fanta<sup>(12)</sup> for the isomerization of N-unsaturated aziridines to 1-azacyclopentene derivatives. On the contrary, our observations parallel closely those made in the case of benzenic O-Claisen rearrangements, where the rate is known to be enhanced by electron-donating substituents<sup>(13)</sup> and high bond-orders<sup>(14)</sup> in the aromatic nucleus. Also the preferred cyclization of 3b to 6b rather than 7b is similar to the previously observed orientational effect of electron-withdrawing meta-substituents<sup>(15)</sup>.

Furthermore, 2-formyl-3-(2-vinylaziridino)thiophene 11 (Figure 5), contrary to 3c, can be isolated and purified at room temperature and isomerizes to 12 only in refluxing toluene; this again cannot be explained by a rate-determining ring-opening step only. By analogy with the benzenic O-Claisen rearrangement, this difference of reactivity may be attributed to a joint effect of steric hindrance for ring-closure and electronic desactivation of the thiophene nucleus by the electron-withdrawing formyl group. Nevertheless, cyclization takes place at the C<sub>2</sub> and not at the C<sub>4</sub>-position<sup>(16)</sup>.

Further experimental investigation of the synthetic possibilities of this kind of reactions in heterocyclic chemistry and of their mechanism is currently under way.

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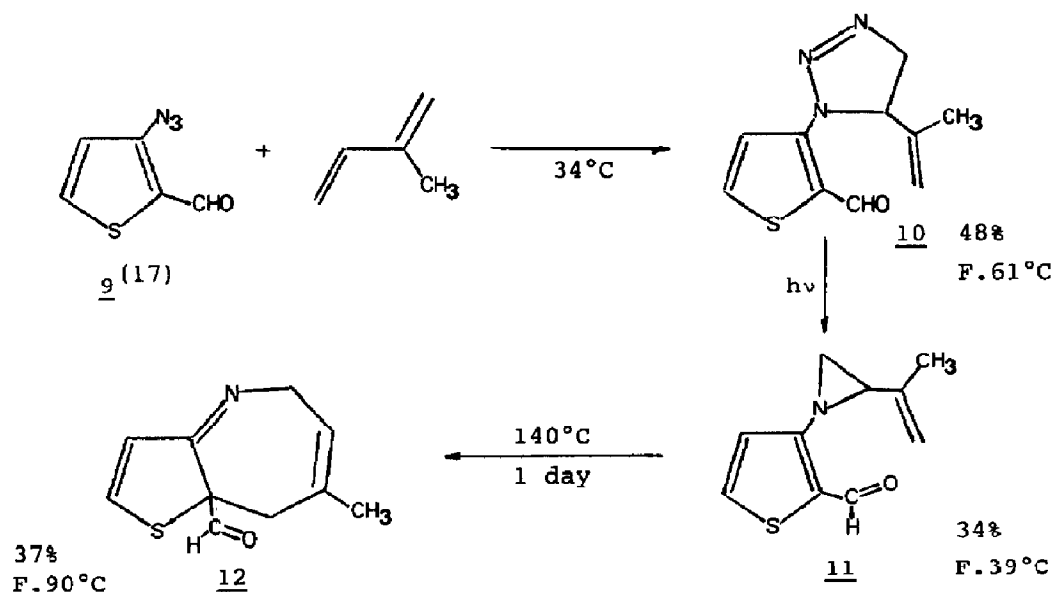


Figure 5

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