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ON THE THERMAL TRANSFORMATION OF ALLYL SUBSTITUTED 2H-AZIRINES TO PYRIDINES

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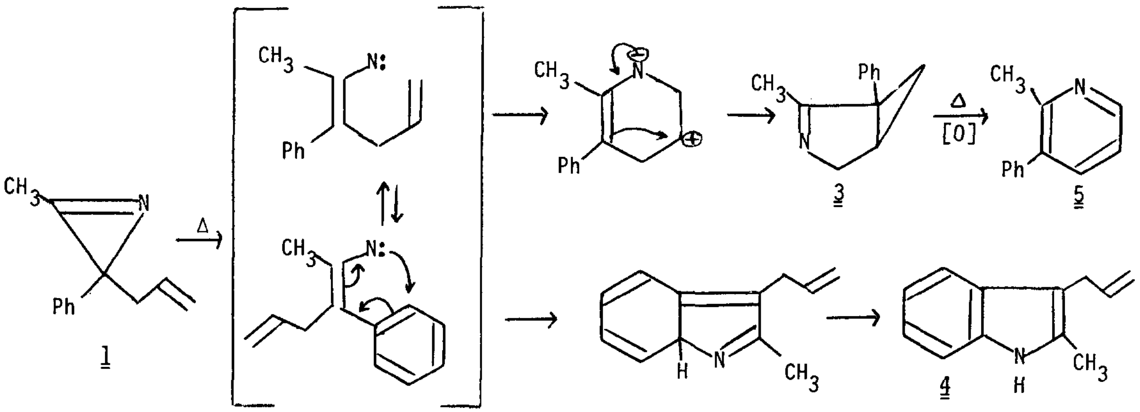
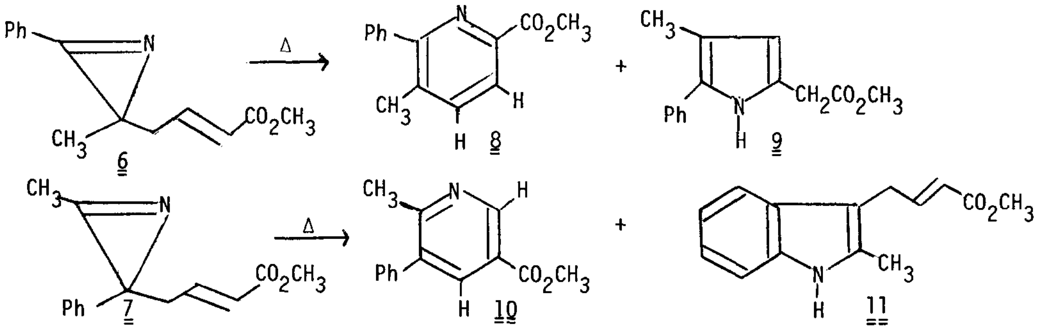
Photochemical and thermal cleavage preferences in 2H-azirines appear to be quite distinct.[1,2] Products formed during photochemical excitation appear to involve nitrile ylides as intermediates[3,4] while thermal isomerization products seem to arise from transient vinyl nitrenes.[5-7] Since examples of the direct addition of nitrenes to olefins to give aziridines have appeared infrequently in the literature,[8] we decided to investigate the thermolysis of a number of allyl substituted 2H-azirines in order to determine whether the initially generated vinyl nitrene would undergo addition to the neighboring double bond.[9] In this communication we describe a previously unobserved thermal reaction in the 2H-azirine system and call attention to a novel substituent effect which operates in this system.

Thermolysis of 3-methyl-2-allyl-2-phenyl-2H-azirine (1) in toluene at 180° for 28 hr gave rise to a mixture of 1-phenyl-2-methyl-3-azabicyclo[3.1.0]hex-2-ene (3, 31%) and 3-allyl-2-methylindole (4, 58%). The identity of 3 was determined by its straightforward spectral characteristics as well as its facile conversion into 2-methyl-3-phenylpyridine (5) on further heating. The structure of indole 4 was verified by comparison with an authentic sample prepared from the reaction of 2-methylindole with allyl bromide.

The formation of 3 can best be rationalized in terms of an equilibration of the 2H-azirine with a transient vinyl nitrene which undergoes subsequent addition onto the adjacent π-bond to give a six-membered ring zwitterion. Collapse of this species will result in the formation of the observed azabicyclohexene system. Indole formation can be attributed to a competitive electrocyclic ring closure of the vinyl nitrene on the neighboring phenyl ring. Several examples are available in the literature which provide good analogy for cyclization of a butadienyl nitrene to a five-membered ring.[10,11] The distribution of products will be controlled by the rates of nitrene attack on the double bond vs electrocyclization on the adjacent phenyl ring.

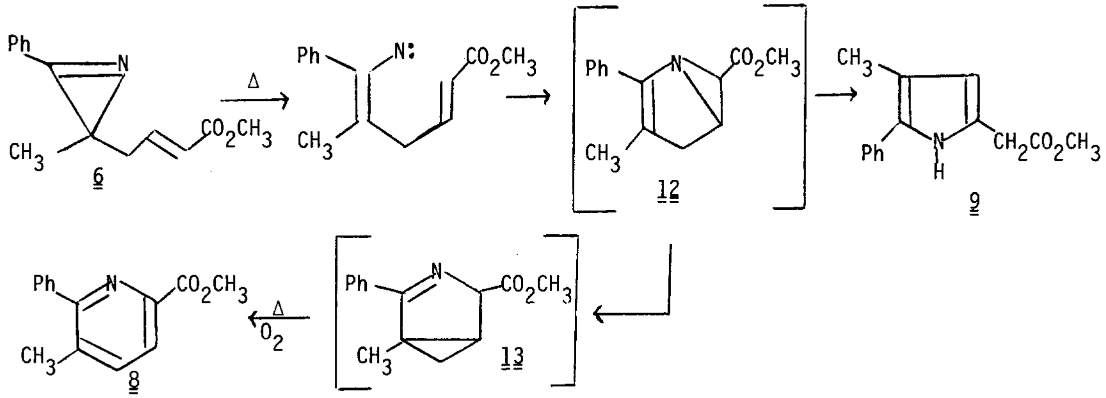


We have also examined the thermolysis of the closely related carbomethoxy substituted 2*H*-azirines 6 and 7 and find that these compounds exhibit substantially different chemical behavior. Heating a sample of azirine 6 in toluene at 180° gave rise to pyridine 8 (47%) and pyrrole 9 (37%). The structure of 8 was confirmed by its straightforward conversion (LAH, M_sCl, LAH) to 2,5-dimethyl-6-phenylpyridine[12] while the identity of 9 was established by comparison with an independently synthesized sample prepared from the reaction of 2-phenyl-3-pyrrole with methyl-

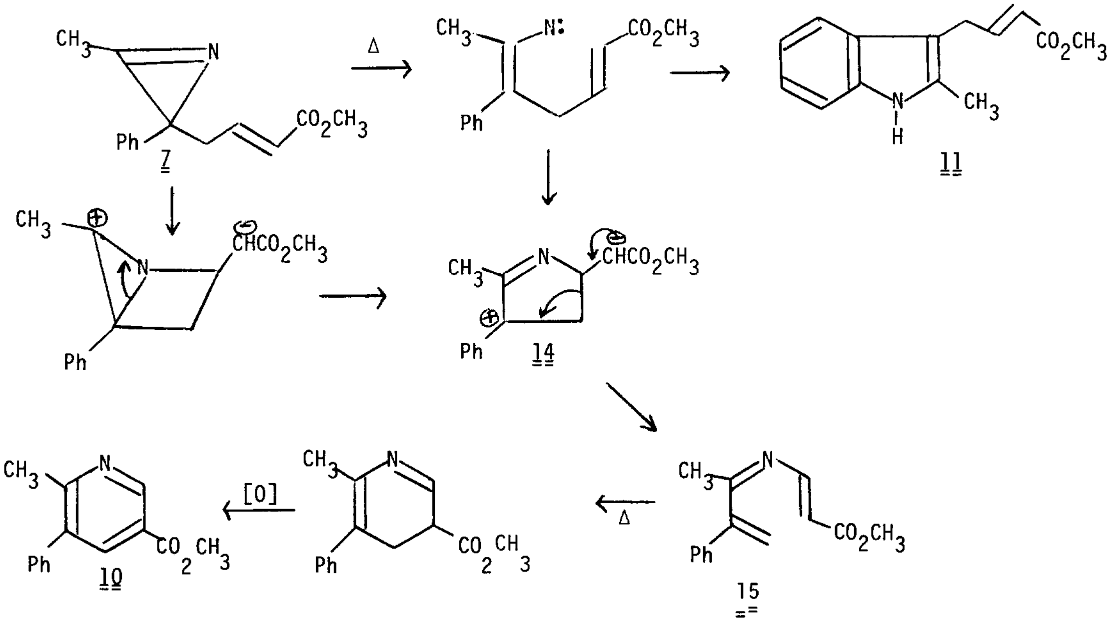


α-bromoacetate. In contrast, thermolysis of 7 gave 2-methyl-3-phenyl-5-carbomethoxypyridine (10, 70%) and indole 11 (30%) as the only characterizable material. The structures of these products were verified by comparison with authentic samples.[13]

Although information on the mechanistic details of these reactions are minimal, tentative yet reasonable rationale can be advanced. Thus, attack of the vinyl nitrene derived from 6 onto the neighboring double bond could lead to the production of a short lived bicycloaziridine 12. Heterolytic cleavage of the C-N bond followed by proton reorganization would furnish pyrrole 9. The initially produced six-ring zwitterion (or structure 12) would also be expected to afford the azabicyclohexene ring system 13 which could, in turn, give rise to pyridine 8 on further heating.



The conversion of 7 to pyridine 10, on the other hand, proceeds by an entirely different pathway. This pyridine may arise by conjugate addition of the vinylnitrene onto the electron deficient double bond. The initially produced five-ring zwitterion 14 can then undergo a subsequent fragmentation to give azatriene 15. This species would be expected to undergo a ready electrocyclic closure followed by oxidation to ultimately afford pyridine 10. An alternate path involving nucleophilic attack by the available lone pair of electrons in starting material onto the conjugated double bond also seems possible. The difference in behavior of the two systems (i.e. 6 vs 7) can be attributed to the difference in nucleophilicity of the nitrogen atom present in starting material or in the vinyl nitrene intermediate.



Studies to probe more deeply the mechanistic details of these reactions are continuing.

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13. The structure of pyridine **10** was established by comparison with an authentic sample; M. Julia, H. Pinhas and J. Igolen, Bull. Soc. Chim. Fr., 2387 (1966). We thank Professor Julia for supplying us with a sample of this compound.