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SYNTHESIS AND THERMAL REARRANGEMENT
OF 2-ALLYL SUBSTITUTED 2H-PYRROLE DERIVATIVES

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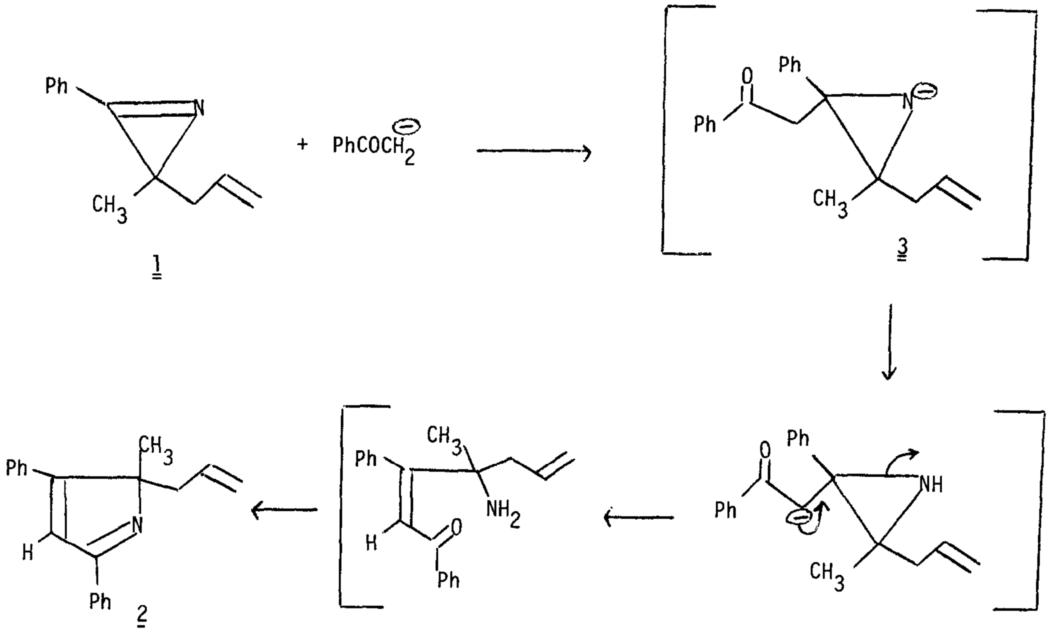
Interest in the chemistry of 2H-azirines has increased considerably over the past several years.[1-4] As a synthetic reagent the 2H-azirine ring occupies a position of particular utility. An unusual feature of this three-membered heterocyclic ring is that it is susceptible to attack by both electrophilic and nucleophilic reagents.[1] In addition, the 2π-electrons present in the ring can participate in thermally allowed $[\pi_4S+\pi_2S]$-cycloadditions as dienophiles[5,6] or as dipolarophiles.[7] Cycloaddition reactions utilizing 2H-azirines include thermal reactions with ketenes,[8,9] ketenimines,[9] nitrile oxides,[7] cyclopentadienones,[10,11] cyclopentadiene,[12] diphenylisobenzofuran[13,14] and diazomethane[7] to yield a variety of unusual heterocyclic ring systems. As part of a research program designed to uncover new reactions of 2H-azirines, we initiated a study dealing with the base induced addition of ketones to 3-phenyl-2-methyl-2-allyl substituted 2H-azirines. We have found that the reaction proceeds smoothly to afford 2H-pyrroles in good yield. These compounds undergo smooth thermal reorganization to 3-allyl substituted pyrroles. This communication summarizes some of our observations in this area with particular reference to the mechanism of the thermal rearrangement.

2-Allyl substituted 2H-azirines were prepared by a modified Neber reaction in which variously substituted 2-methyl-1-phenyl-4-penten-1-ones were allowed to react with dimethylhydrazine according to the general procedure of Leonard and Zwanenburg.[15] Treatment of the appropriate dimethylhydrazine with methyl iodide followed by reaction with base gave the desired azirine ring in good yield. Treatment of a dimethyl sulfoxide solution of acetophenone and azirine **1** with sodium hydride at 25° for 16 hr gave 2-allyl-2-methyl-3,5-diphenyl-2H-pyrrole (**2**) as a pale yellow oil: NMR ($CDCl_3$, 100 MHz) τ 8.48 (s, 3H), 7.44 (dd, 1H, J = 16.0 and 7.0

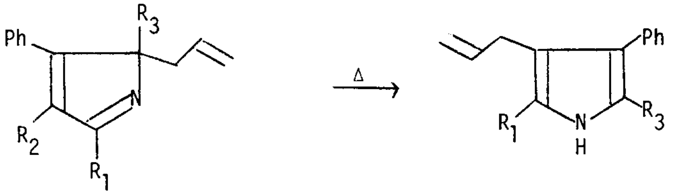
Hz), 7.04 (dd, 1H, J = 16.0 and 7.0 Hz), 5.20 (d, 1H, J = 9.0 Hz), 5.16 (d, 1H, J = 16.0 Hz), 4.36-4.78 (m, 1H), 3.01 (s, 1H) and 2.04-2.80 (m, 10H). The formation of 2 involves initial attack of the enolate anion of acetophenone on the carbon nitrogen double bond to give 3 which



undergoes subsequent proton transfer, ring opening and cyclization. Related additions of enolate anions to 3-phenyl-2H-azirine have been reported in the literature and provide good chemical analogy for the above set of reactions.[16,17]

Thermolysis of 2 in a benzene-pyridine solution at 175° for 70 min resulted in a quantitative rearrangement to 3-allyl-2,4-diphenyl-5-methylpyrrole (3). The identity of 3 was determinated by its straightforward spectral characteristics: NMR (CCl_4, 100 MHz) τ 7.80 (s, 3H), 6.80 (broad s, 2H), 5.0-5.2 (m, 2H), 3.96-4.28 (m, 1H), 2.60-3.0 (m, 10H) and 2.30 (s, NH). Further examples which would support the generality of this rearrangement were sought. With this in mind, we investigated the thermal behavior of the isomeric 2H-pyrrole derivative 4. Thermolysis of a sample of 4 was also found to give a rearranged pyrrole (i.e. 5) in high yield. When the 4-position of the 2H-pyrrole ring was substituted with a methyl group (i.e. 6), the rearrangement failed to take place. In this case only starting material could be recovered.

The mechanism by which these 2-allyl substituted 2H-pyrroles undergo rearrangement is

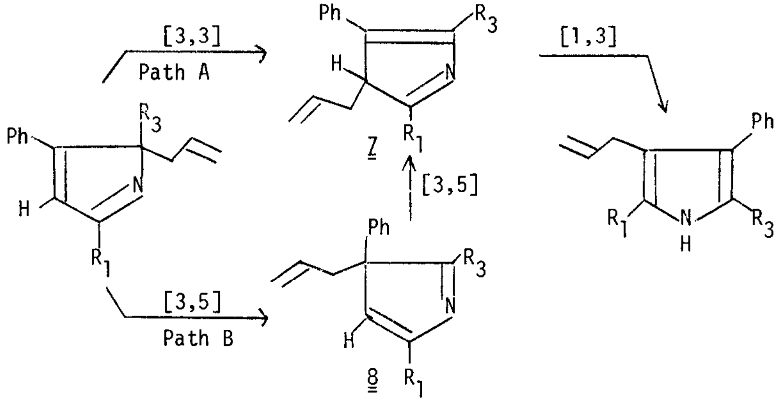


2; R_1=Ph; R_2=H; R_3=CH_3
4; R_1=CH_3; R_2=H; R_3=Ph
6; R_1=Ph; R_2=R_3=CH_3

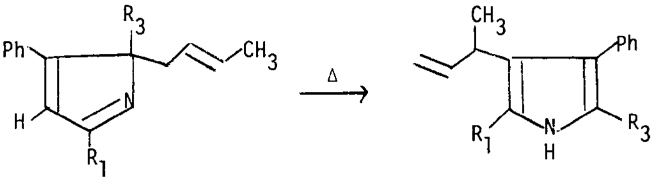
3; R_1=Ph; R_3=CH_3
5; R_1=CH_3; R_3=Ph

of considerable interest. Two fundamentally different mechanisms seem possible and are presented in Scheme I. Path A involves a 3,3-sigmatropic rearrangement to give 7 which undergoes a subsequent 1,3-H shift to the observed product.

Scheme I



The alternate path involves two consecutive [3,5]-sigmatropic shifts of the allyl group.[18] Support for Path A was obtained from the thermolysis of 2-butenyl substituted pyrroles 9 and 10. Heating these compounds at 175° produced pyrroles 11 and 12 in quantitative yield. The location of the methyl substituent in the allyl side chain was easily determined by examination of



9; R_1=Ph; R_3=CH_3
10; R_1=CH_3; R_2=Ph

11; R_1=Ph; R_3=CH_3
12; R_1=CH_3; R_3=Ph

the NMR spectra of the rearranged pyrroles. The formation of the 3-(1-methylallyl)-substituted pyrrole system is only compatible with the 3,3-sigmatropic rearrangement route (i.e. Path A).

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17. Similar results have been observed by Professor A. Laurent and P. Misson and we wish to thank them for sharing this information with us.
18. Two consecutive 1,5-shifts represents still another pathway for the rearrangement. The experiments with **9** and **10**, however, also rule out this mode.

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