The Mechanism of the Thermal Rearrangement of 1-Substituted 1*H*-Azepines to 6-Aminofulvenes

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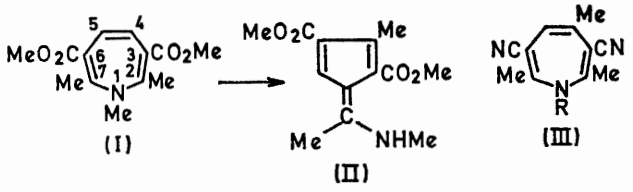
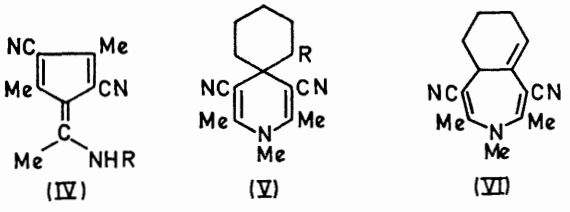
Summary Thermal rearrangement of the fully-substituted azepine (VII) yields a 1,1-disubstituted cyclopentadiene (VIII): such compounds are considered to be intermediates in the thermal rearrangement of 1-substituted 1*H*-azepines to fulvenes where a subsequent [1,5]-sigmatropic rearrangement of the ketone-imine group is also involved.

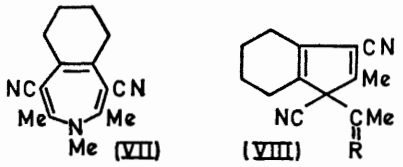
WE have described previously[1] a mild thermal rearrangement of certain 1-substituted 1*H*-azepines [e.g. (I)] to yield derivatives of 6-aminofulvene [*e.g.* (II)].



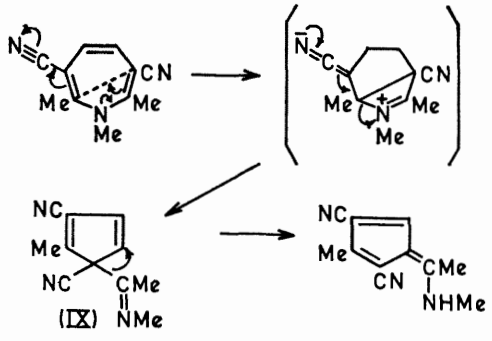
Only a tentative, speculative mechanism was advanced at the time to account for this remarkable rearrangement, but we have now carried out further experiments, the results of which enable us to define the mechanistic pathway. We knew from our previous work[2] that the formation of fulvenes in the above reaction does not necessitate unsubstituted positions at both C-4 and C-5 of the azepine rings, because when the azepines (III; R = Me and Ph) were heated in boiling toluene, the fully-substituted fulvenes (IV; R = Me and Ph) were obtained in approximately 50% yield.



It therefore appeared that the thermal rearrangement of a fully-substituted azepine might give an intermediate product as, in this case, rearrangement to the fulvene could occur only by loss of a substituent. To test this concept, we prepared the appropriate dihydropyridine starting material (V; R = Cl) by condensation of 2-chlorocyclohexanone with 2-methylaminocrotononitrile, following an earlier preparation[3] of (V; R = Me) from 2-methylcyclohexanone. Treatment of the spirodihydropyridine (V; R = Cl) with potassium t-butoxide in 1,2-dimethoxyethane gave the dihydroazepine (VI; 51%), which was rearranged to the azepine (VII; 71%) with trifluoroacetic acid in chloroform. Reaction of (V; R = Cl) with potassium carbonate in aqueous ethanolic dimethyl sulphoxide gave a mixture of (VI) and (VII). When the azepine (VII) was heated under reflux in xylene for 5 days it gave a product, which after purification by chromatography on silica, gave colourless crystals. On the basis of the spectral properties, (i.r., n.m.r., and mass) these were formulated as a mixture of the methylimine and the corresponding ketone (VIII; R = NMe and R = O).



The mixture was separated by t.l.c. (silica), when the pure ketone was obtained (10%) as colourless needles,† m.p. 144—145°, the mass spectrum of which was consistent with the assigned structure. It therefore appears the rearrangement of 1-substituted 1*H*-azepines to 6-aminofulvenes involves 1,1-disubstituted cyclopentadienes [*e.g.* (IX) see Scheme] as intermediates and that the ketone-imine substituent then migrates by a concerted [1,5] thermally-allowed rearrangement to the fulvene.‡ Related rearrangements of cyclopentadiene acetyl substituents have been described recently.[4]



SCHEME

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† Satisfactory analyses and spectral data have been obtained for all the compounds mentioned in this Communication.

‡ The possibility of the operation of this mechanism was suggested to us by Dr. Ian Fleming, University of Cambridge, whom we thank for his interest.

[1] R. F. Childs, R. Grigg, and A. W. Johnson, *J. Chem. Soc.* (*C*), 1967, 201.

[2] G. B. Gill, D. J. Harper, and A. W. Johnson, *J. Chem. Soc.* (*C*), 1968, 1675; D. J. Harper, Ph.D. Thesis, University of Nottingham, 1968.

[3] E. von Meyer, *J. prakt. Chem.*, 1915, (2), **92**, 174.

[4] M. J. Jorgenson and A. F. Thacher, *Chem. Comm.*, 1969, 1030.