Evidence for Vinyl Nitrene Intermediates in the Thermal Rearrangement of 2*H*-Azirines into Indoles

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Summary Thermal racemization of optically active 3-methyl-2-phenyl-2*H*-azirine was found to be 2039 times faster than its rearrangement into 2-methylindole, which furnished firm evidence for the presence of vinyl nitrenes as intermediates

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Since our discovery of indole formation by the thermal rearrangement of 2-phenyl-2*H*-azirines,[1] thermal 5-membered ring formation from many 2*H*-azirines has been studied [2] Our recent investigations revealed that 6- and 7-membered nitrogen-containing heterocycles were also obtained by thermal rearrangement of 2*H*-azirines,[3,4] showing the versatility of this reaction Because all the products in these thermal reactions of 2*H*-azirines were produced formally by C–N bond fission, vinyl nitrenes have been considered as possible intermediates [4] However, convincing evidence has not yet been reported

Here, we report evidence for vinyl nitrene intermediates, which is provided by kinetic studies on the racemization of, and indole formation from, optically active 3-methyl-2-phenyl-2*H*-azirine (**1**)

Optically active 3-methyl-2-phenyl-2*H*-azirine (**1**) was prepared by asymmetric decomposition, as exemplified below Heating racemic (**1**) and 1/3 mol equiv of *N*-benzyloxycarbonyl-L-leucine in benzene under reflux for 3 h, followed by distilling the hexane-soluble portion of the

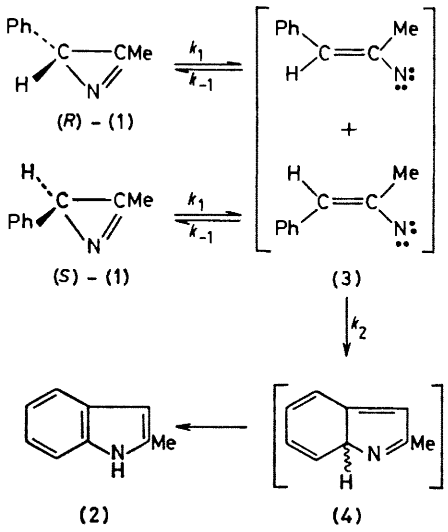
TABLE. Rate constants for thermal racemization and rearrangement of 3-methyl-2-phenyl-2*H*-azirine (**1**) in decalin (0·33M) [a]

	Rate constants $\times 10^{-5}/\mathrm{s}^{-1}$			Rate ratios	
Temp./°C	k_{rac}	k_{rear}	k_{DL}	$k_{\mathrm{rac}}/k_{\mathrm{rear}}$	k_{-1}/k_2
105·0	6·17	0·00255[b]	3·08	2420	1208
110·0	9·93	0·00487[b]	4·96	2039	1018
115·0	16·5	0·00882[b]	8·25	1871	935
120·0	25·7	0·0160[b]	12·8	1606	800
185·0		11·3			
190·0		17·5			
195·0		27·0			
200·0		39·6			

[a] Errors in the rate constants are less than ±3%. [b] Extrapolated rate constants

resulting mixture at 50—60 °C and 1 mmHg, gave optically active (**1**), $[\alpha]_{\mathrm{D}}^{25}$ 14·9°, enantiomeric excess = 7·2%, in 42% yield.

While racemization of (**1**) (k_{rac}) proceeded smoothly below 120 °C in decalin, its rearrangement into 2-methylindole (**2**) (k_{rear}), at a measurable reaction rate, required heating above 185 °C. The rate constants for racemization and rearrangement into (**2**) are listed in the Table. The fact that racemization is much faster than indole formation, as shown in the Table ($k_{\mathrm{rac}}/k_{\mathrm{rear}}$), is best rationalized in terms of a 2-step reaction shown in the Scheme involving the vinyl nitrene intermediate (**3**). Analysis of the kinetic data according to this Scheme shows the ratio k_{-1} to k_2 is equal to that of k_{DL} to k_{rear}, in which k_{DL} is the rate constant for interconversion of enantiomers, obtained by the relationship $2k_{\mathrm{DL}} = k_{\mathrm{rac}} - k_{\mathrm{rear}}$.[5] The value of $k_{-1}/k_2 = 1018$ at 110 °C means that in any given time, 1018 molecules of (**3**) recyclise to (*R*)-(**1**) and to (*S*)-(**1**) for every molecule of (**3**) which cyclises to (**2**). The preference for reclosure, even at the cost of high strain in the 2*H*-azirine ring system, compared to indole formation can be ascribed to the disadvantageous loss of aromatic stability of the phenyl group on formation of the 2-methyl-7a*H*-indole intermediate (**4**), which is analogous to 2*H*-pyrrole formation in the thermal rearrangement of 2-alkenyl-2*H*-azirines.[6]



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[1] K. Isomura, S. Kobayashi, and H. Taniguchi, *Tetrahedron Lett.*, 1968, 3499.
[2] K. Isomura, T. Tanaka, and H. Taniguchi, *Chem. Lett.*, 1977, 397 and references therein.
[3] K. Isomura, H. Taguchi, T. Tanaka, and H. Taniguchi, *Chem. Lett.*, 1977, 401.
[4] K. Isomura, S. Noguchi, M. Saruwatari, S. Hatano, and H. Taniguchi, *Tetrahedron Lett.*, 1980, **21**, 3879, and references cited therein.
[5] E. J. York, W. Dittmer, J. R. Stevenson, and R. G. Bergman, *J. Am. Chem. Soc.*, 1973, **93**, 5680.
[6] K. Isomura, M. Okada, and H. Taniguchi, *Chem. Lett.*, 1972, 629.