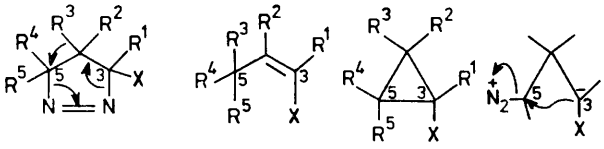
A New Mechanism for the Formation of Cyclopropane Derivatives in the Thermolysis of Pyrazolines

By MICHAEL J. BEGLEY
(*Department of Chemistry, The University of Nottingham, Nottingham* NA7 2RD)
and FRANCIS M. DEAN, LEONARD E. HOUGHTON, ROBERT S. JOHNSON, and B. KEVIN PARK
(*The Robert Robinson Laboratories, The University of Liverpool, Liverpool* L69 3BX)

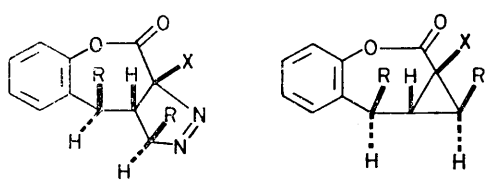
Summary Evidence is presented for a mechanism in which ionisation of a pyrazoline permits a ring expansion and then extrusion of nitrogen in an electrocyclic process consistent with retention of stereochemistry by the resulting cyclopropane.

THE thermolysis of Δ^1-pyrazolines (**1**) with an electronegative substituent X at position 3 presents several puzzling features.[1-3] It is agreed[4-6] that collapse as indicated in (**1**) is determined by conformational factors and is under strict stereochemical control, but the alkenes (**2**) so



(1) (2) (3) (4)

formed are often accompanied by cyclopropane derivatives (**3**) which may even be the main products. It is required to explain how the product (alkene *vs.* cyclopropane) is determined, and why some reactions giving cyclopropanes are highly stereospecific, others only partly so, and yet others not at all. A mechanism is required that will account for the fact that, when cyclopropanes are formed stereospecifically in the thermal reaction, retention at both the 3- and 5-positions is found,[2] just as in (unsensitized) photolyses. Loss of stereospecificity may be incurred by inversion at either position or at both.[2] Earlier it had been suggested that a preliminary ionisation may give a zwitterion (**4**) in which rotation may invert the 3-position while backside attack may invert the 5-position as indicated.[1] However, there is no clear evidence for ionization and the hypothesis is incapable of explaining double retention unless unusually strained transition states are implicated.[6]



(5) (6)

	X	R
a;	Bu^{t}CO	Me
b;	NO_2	Me
c;	MeCO	Bu^t
d;	MeCO	Me
e;	PhCO	Me

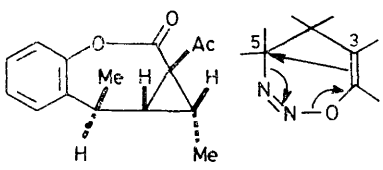
We studied pyrazolines in the series[7a] (**5a**—**e**) with two electronegative substituents at the 3-position in order to magnify ionic effects, if any, in cyclopropane formation. The configuration shown was determined for (**5a**) by *X*-ray crystallography and assigned to the rest on the basis of n.m.r. spectroscopy. Thermolysis of (**5a**) gave alkenes as in process (**1**) and one cyclopropane which was assigned structure and configuration (**6a**) by *X*-ray crystallography. Other cyclopropanes were assigned the same configuration by n.m.r. methods except for (**6c**) in which the two t-butyl groups cause distortions and which was therefore assigned its configuration by the *X*-ray method. Each pyrazoline (**5**) gave the corresponding single cyclopropane (**6**) with retention at both 3- and 5-positions. In general, pyrazolines with other configurations were not available, but the residues from the preparation of (**6d**) clearly contained an epimer and gave as the major cyclopropane that with configuration (**7**). Hence double retention was observed here also, though it may not have been complete.

Our pyrazolines are fairly stable in cold hydrocarbons but are rapidly decomposed by polar solvents, especially alcohols. Moreover, polar solvents strongly favour cyclopropane formation over alkene (Table). Again, it is the more electronegative substituents that favour cyclopropanes; for example, 3-acetylcoumarin with diazomethane yields a pyrazoline that instantly collapses to 3-acetyl-4-methylcoumarin[7b] whereas 3-nitrocoumarin yields only the cyclopropane (a claim that the product is a 4-methylcoumarin has been withdrawn[8]).

TABLE. Effect of solvent polarity upon the product ratio in the thermolysis of the pyrazoline (**5d**).

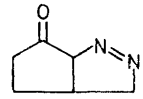
Solvent	Dielectric constant	Products (%) Cyclopropane (**6d**)	Alkenes
C_6H_6	2·3	19	81
EtOH	22	47	53
$HCONMe_2$	28	56	34
MeCN	32	48	52

Thus ionisation is important for the formation of cyclopropanes but is under strict stereochemical control leading to double retention. We suggest that ionisation does not lead immediately to the zwitterion (**4**) by dissociation, but only to a tight ion pair or a charge transfer complex in which migration can occur until a new covalent bond can be formed giving the ring system (**8**). Electrocyclic elimination of nitrogen as indicated in (**8**) now affords a cyclopropane with retention at positions 3 and 5 as required. Theoretically the elimination could occur earlier, in the ion pair, but the argument is presented in terms of (**8**) since models can be made of it.

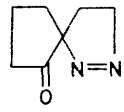


(7)

(8)



(9)



(10)

Independent support for this mechanism, even if applied to pyrazolines (**1**) with only one activating group, comes from its ability to link cyclopropane formation not only with the nature of the activation but also the configuration and conformation of the pyrazoline. The migration giving (**8**) will be easy only when the acetyl group (or equivalent) can readily occupy a pseudoaxial site with the oxygen atom pointing inwards. Being linear, the cyano group cannot fulfil the conditions; accordingly, it does not favour cyclopropane formation by itself[9] or in conjunction with a carbonyl group that cannot take up the correct disposition.[10] In the structural unit (**9**) the carbonyl group is badly placed and the extent of cyclopropane formation is small at best;[11] in contrast, the carbonyl group is well placed in structural unit (**10**) which usually affords cyclopropanes in high yield and very rapidly.[12]

The mechanism also explains most of the detailed stereochemical results obtained by McGreer and McKinley,[2] which will be more fully discussed at a later date. These workers noted inversions at the 5-position (up to 26%) when stereochemical control was poor. Our views do not account for this directly. However, it would be expected that, when the partial ionisation we invoke leads to no very favourable conformation, ion separation may occur in which case the zwitterion (**4**) would be produced and inversion at position 5 would result as envisaged previously.

(*Received*, 14*th February* 1978; *Com.* 155.)

[1] T. V. Van Auken and K. L. Rinehart, *J. Amer. Chem. Soc.*, 1962, **84**, 3736; D. E. McGreer, N. W. Chiu, M. G. Vinje, and K. C. K. Wong, *Canad. J. Chem.*, 1965, **43**, 1407; D. E. McGreer, N. W. K. Chiu, and M. C. Vinje, *ibid.*, 1964, **43**, 1398.
[2] D. E. McGreer and J. W. McKinley, *Canad. J. Chem.*, 1971, **49**, 105.
[3] J. P. Deleux, G. Leroy, and J. Weiler, *Tetrahedron*, 1973, **29**, 1135.
[4] I. Tabushi, K. Takagi, M. Okano, and R. Oda, *Tetrahedron*, 1967, **23**, 2621.
[5] J. Hamelin and R. Carrié, *Bull. Soc. chim. France*, 1968, 2521.
[6] D. E. McGreer, I. M. E. Masters, and M. T. H. Liu, *J.C.S. Perkin II*, 1975, 1791.
[7] (a) R. Clinging, F. M. Dean, and L. E. Houghton, *J.C.S. Perkin I*, 1974, 66, and current work; (b) *J. Chem. Soc.* (*C*), 1970, 897.
[8] H. Junek and W. Wilfinger, *Monatsh*, 1970, **101**, 1123, and personal communication.
[9] J. B. Bastus, *Tetrahedron Letters*, 1963, 955.
[10] R. Clinging, F. M. Dean, L. E. Houghton, and B. K. Park, *Tetrahedron Letters*, 1976, 1227.
[11] W. I. Awad, S. M. Abdel, R. Omran, and M. Sobhy, *J. Org. Chem.*, 1961, **26**, 4126; M. Franck-Neumann, *Angew. Chem. Internat. Edn.*, 1968, **7**, 65.
[12] A. Mustafa, W. Asker, A. H. Harhash, and A. M. Fleifel, *Tetrahedron*, 1965, **21**, 2215; P. Schuster, F. Wessely, and A. Stephen, *Monatsh.*, 1967, **98**, 1772; G. Billek, O. Saiko, A. Stephen, and F. Wessely, *ibid.*, 1966, **97**, 663.