SYNTHESIS AND RING EXPANSION OF 3-METHYL-3-VINYL-2-DIMETHYLAMINO-1-AZIRINE

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The reaction of 1-chloro-1-dimethylamino-2-methylbuta-1,3-diene with NaN_3 gave directly the title 2-amino-1-azirine (I) and molecular nitrogen. (I) thermally rearranged in the vapour phase to give an aminocarbene resulting from C-C bond cleavage. This carbene cyclised to form an aminopyrrole. With dimethylacetylenedicarboxylate, (I) gave a seven-membered heterocycle resulting from C_3-N bond cleavage and cyclisation at the terminal vinylic carbon atom.

Studies[1] in these laboratories have led to the development of a general route to 2-amino-1-azirines, a novel class of cyclic amidines. These are readily attacked by electrophilic reagents[1-4] to give 2-amino-1-azirinium ions which can be regarded as iminium derivatives of α-lactams. These highly energetic amidinium salts are unstable and readily undergo (a) a 1-3 ring opening analogous to a cyclopropyl-allyl cationic rearrangement, (b) a recombination with a nucleophilic species followed by a 1-2 ring opening.

Scheme 1

Treatment of 3,3-dimethyl-2-amino-1-azirines with various electrophilic cumulenes[1,5] probably leads to similar intermediates which cyclise to five-membered heterocycles. Furthermore thermolysis[6] of the readily available 3,3-dialkyl-2-amino-1-azirines causes rupture of the C_2-C_3 bond of the azirine ring to yield aminocarbenes which rearrange to 1-amino-2-azadienes. These were found[6] to be useful synthons for the synthesis of pyridine derivatives.

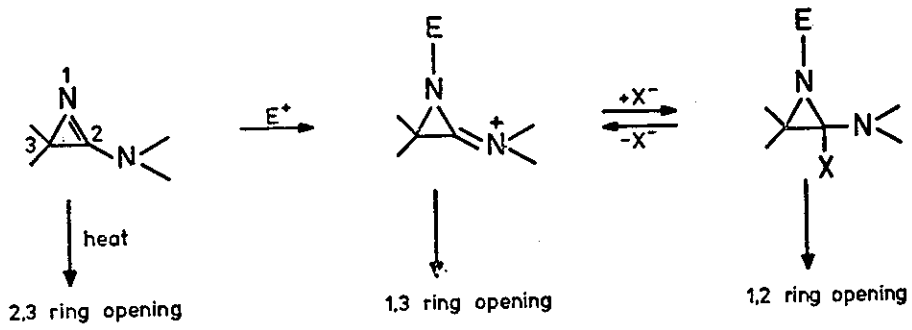
The fate of the intermediate aminoazirinium ions or aminocarbenes is expected to vary with substitution. Thus a double bond at position 3 of the azirine ring should permit cyclisations of these intermediates at the terminal

vinylic carbon-atom.

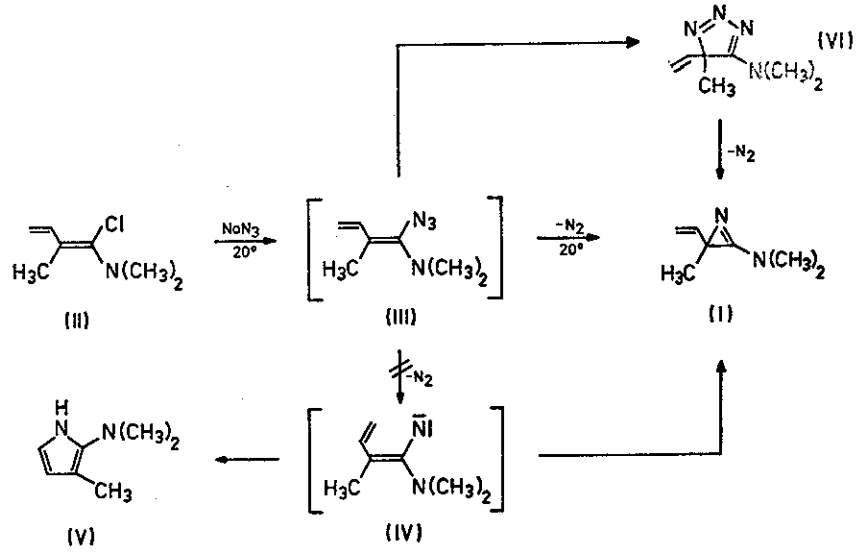
3-Methyl-3-vinyl-2-dimethylamino-1-azirine (I) was prepared by the reaction of 1-chloro-1-dimethylamino-2-methylbuta-1,3-diene[7] (58 g, 0.4 mole) (II) with a suspension of NaN_3 (35 g, dried in vacuum) in 350 ml of dry ether. The reaction takes place at room temperature and can be monitored by the evolution of nitrogen. Distillation (25-30°/0.1 Torr) yielded 45 g (90 %) of pure (I) : m/e (M^+) 124 (100 %); IR (film) 1775 cm^{-1} (C=N); NMR (CCl_4) : δ 1.36 (s,3H), δ 2.93 (s,6H), δ 4.96 (2 x dd, 2H, J_{gem}=2 Hz), δ 5.55 (dd,1H,J_{cis}= 9 Hz, J_{trans}= 18 Hz).

Scheme 2

The reaction probably involves the intermediate formation of an α-azidoenamine (III) which, in contrast to other vinyl azides[8], spontaneously loses a nitrogen molecule at 20°. This suggests anchimeric assistance from the electron-donating amine substituent. On this basis and in accord with kinetic results[8] on the decomposition of simple vinyl azides, an intermediate nitrene (IV) can be excluded. This is further supported by the absence of pyrrole (V) in the crude reaction mixture. A concerted process involving ring closure and departure of nitrogen assisted by the amine group is consistent with the data.



Scheme 1



Scheme 2

However the formation of an unstable triazole (VI) which would rapidly lose nitrogen is not ruled out by our findings.

(I) (0.81 g, 6.5 mmole) was thermolysed by passage of the vapour through a pyrex tube (80 x 1.5 cm) filled with glass beads at 350° and 0.1 Torr. The colourless product was collected in a vessel cooled in liquid nitrogen. The product which rapidly turned red at 20° was found to be 2-dimethylamino-5-methylpyrrole (VII) (yield > 93 % by NMR integration with benzene as standard) :

Scheme 3

m/e : (M^+) 124 (100 %); IR (CCl_4) : 3490 cm^{-1} (N-H); ^{1}H-NMR (CCl_4) : δ 2.1 (s,3H), δ 2.6 (s,6H), δ 5.05 (m,1H), δ 5.36 (m,1H), δ 8.34 (broad,1H). The ^{13}C-NMR spectra (CCl_4, TMS) consist of six signals at δ 13.03 (q,$\underline{C}H_3$), δ 43.82 (q, $N(\underline{C}H_3)_2$), δ 90.57 (d,C_3-H), δ 104.55 (d,C_4-H); δ 120.44 (s,C_5), δ 142.5 (s, C_2-N).

The isomeric structure (V) which would result from another mode of opening of the azirine ring was ruled out on the following basis : the signals at lower fields corresponding to the C-2 and C-5 atoms deshielded by the neighbouring nitrogen substituents appear as <u>singlets</u>.

Therefore it appears that, even in the presence of a stabilising[9] group (vinyl) at C-3, thermolysis of a

2-amino-1-azirine does not give rise to C-N bond cleavage but rather yields a stabilised carbene (VIII) resulting from C-C bond cleavage. However this intermediate carbene (VIII) undergoes an electrocyclisation rather than the 1,4 hydrogen shift which was observed[6] for other aminoazirines.

The role of the vinyl substituent on the fate of an aminoazirinium ion is illustrated by the reaction of (I) with dimethylacetylenedicarboxylate (IX) : 2 g (16 mmoles) of (I) were added to a solution of 2,3 g (16 mmoles) of (IX) in 20 ml acetonitrile at -30°. After 6 hours at 20°, the mixture was evaporated and chromatographed on silicagel to give 4,1 g (94 %) (X) after recrystallisation from CH_2Cl_2-ether : m.p. 124.5-125.5°C; m/e (M^+) 266; IR ($CHCl_3$) 1730, 1685, 1640, 1525 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.81 (s,3H), δ 2.95 (s,6H), δ 3.63 (s,3H), δ 3.76 (s,3H); δ 5.75 (t,1H,J=7 Hz), U.V. (CH_3OH) δ_{max} 320 nm ($\log\varepsilon$ = 4.88). These spectroscopic data suggested structure (X) but were not unambiguous. Therefore an X-ray crystallographic analysis was undertaken on single crystals of sufficient size obtained from CH_2Cl_2-ether.

Scheme 4

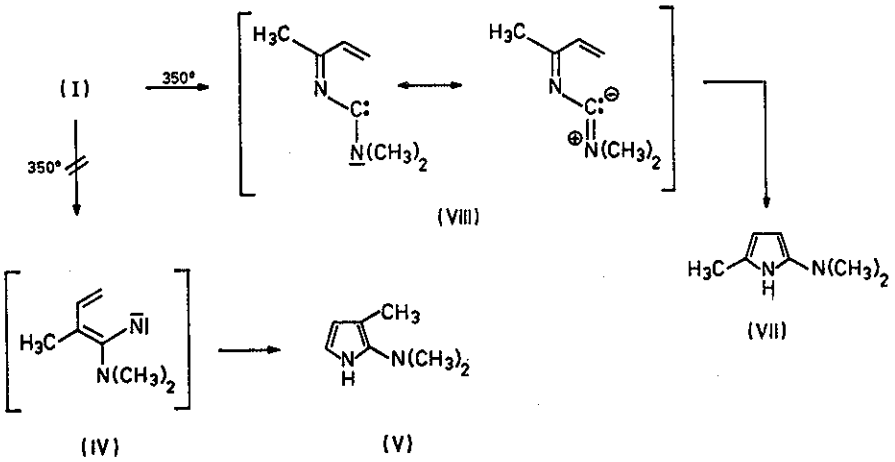
The observed Laue symmetry and extinctions correspond uniquely to the space group $P2_1/a$ with a = 18.351 (7), b = 8.595 (4), c = 8.610 (3) Å; β = 94.51 (2)°. This cell

contains four molecules $C_{13}H_{18}N_2O_4$. The intensities of 1769 independent reflexions were measured on a Picker semi-automated diffractometer, using CuKα, Ni-filtered radiation.

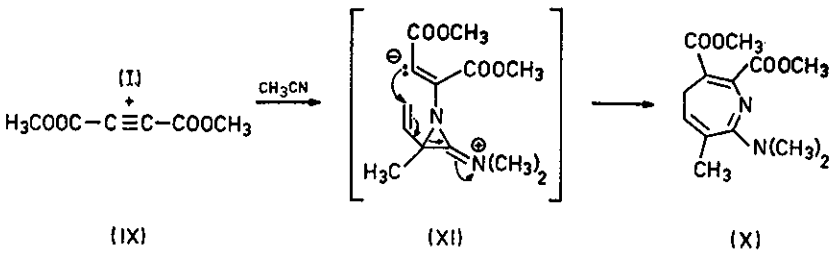
The structure was readily solved by direct methods using the MULTAN-76 system of programs[10]. It was refined by anisotropic block-diagonal least squares (X-ray 72)[11]. The parameters of the hydrogen atoms, located on a differential Fourier-synthesis, were included in the refinement with isotropic temperature factors. Final conventional R value is 0.065 for 1289 observed reflexions ($1 \geq 2.5\sigma$ (I)). Fig. 1 shows the molecular structure and the bond lengths. These lengths indicate electron delocalisation along $N\text{-}C_2\text{=}N_1\text{-}C_6\text{-}C = O$. The endocyclic bond angles are (from N_1 to C_7) : 124, 123, 119, 121, 105, 117 and 128°. The endocyclic torsion angles are, according to Prelog's convention : $N_1\text{-}C_2 = 16°$, $C_2\text{-}C_3 = -50°$, $C_3\text{-}C_4 = -5°$, $C_4\text{-}C_5 = 73°$, $C_5\text{-}C_6 = -64°$, $C_6\text{-}C_7 = -5°$, $C_7\text{-}N_1 = 36°$.

Fig 1

Thus the structure of the adduct of (I) with (IX) is unequivocally the 7-membered ring (X). Its formation probably results from the cyclisation and rearrangement of the dipolar ion (XI). This result suggests 3-vinylsubstituted aminoazirine as a potential precursor of 7-membered rings.



Scheme 3



Scheme 4

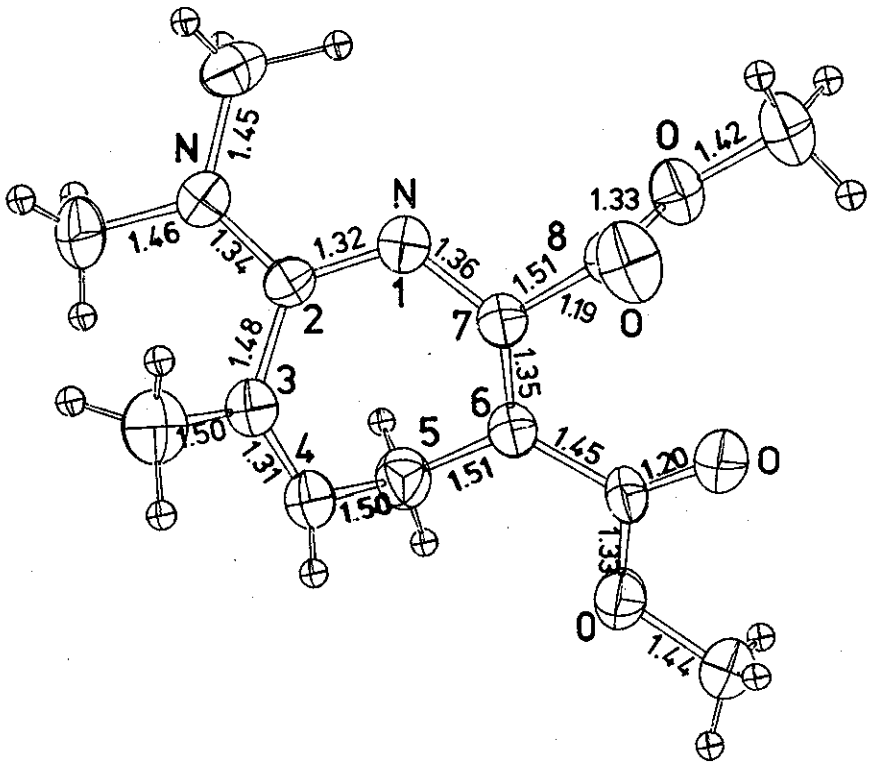


Fig.1. Molecular structure and bond lengths. The thermal ellipsoids are scaled to include 50% probability.

ACKNOWLEDGEMENTS We gratefully acknowledge support of this work by the "Fonds National de la Recherche Scientifique" (fellowships to Etienne Sonveaux and Jean-Paul Declercq), the "Institut pour l'Encouragement de la Recherche dans l'Industrie et l'Agriculture" (graduate fellowships to André Demoulin and Michel Henriet). The CFT-20 NMR spectrometer was purchased with the aid of the "Fonds de la Recherche Fondamentale Collective".

REFERENCES

1 M. Rens and L. Ghosez, Tetrahedron Lett., 1970, 3765; M. Rens, Dissertation, University of Louvain, 1973.

2 P. Vittorelli, H. Heimgartner, H. Schmid, P. Hoet and L. Ghosez, Tetrahedron, 1974, 30, 3737; P. Hoet, Dissertation, University of Louvain, 1975.

3 B.P. Chandrasekhar, U. Schmid, R. Schmid, H. Heimgartner and H. Schmid, Helv. Chim. Acta., 1975, 58, 1191; S. Chaloupka, B.P. Chandrasekhar, U. Schmid, R. Schmid, H. Heimgartner and H. Schmid, Chimia, 1977, 31, 66.

4 E. Schaumann, E. Kausch and W. Walter, Ber., 1975, 108, 2500.

5 E. Schaumann, E. Kausch and W. Walter, Chem. Ber., 1974, 107, 3574; U. Schmid, H. Heimgartner, H. Schmid, P. Schönholzer, H. Link and K. Bernauer, Helv. Chim. Acta., 1975, 58, 2222; S. Chaloupka, H. Heimgartner, H. Schmid,

H. Link, P. Schönholzer and K. Bernauer, Helv. Chim. Acta., 1976, 59, 2566; U. Schmid, H. Heimgartner, H. Schmid and W.E. Oberhänsli, Helv. Chim. Acta., 1976, 59, 2768.

6 A. Demoulin, H. Gorissen, A.M. Hesbain-Frisque and L. Ghosez, J. Amer. Chem. Soc., 1975, 97, 4409.

7 This α-chloroenamine is readily available from N-dimethyl-tiglic amide, phosgene and triethylamine; L. Ghosez and J. Marchand-Brynaert, "Iminium Salts in Organic Chemistry", H. Böhme and H.G. Viehe eds., 9, Part 1 in the series "Advances in Organic Chemistry", E.C. Taylor, ed., Wiley-Interscience, New-York, N.Y., 1976, 421.

8 Review : G. L'Abbé, Angew. Chem. Internat. Ed. Engl., 1975, 14, 775 and references cited therein.

9 L.A. Wendling and R.G. Bergman, J. Amer. Chem. Soc., 1974, 96, 308; L.A. Wendling and R.G. Bergman, J. Org. Chem., 1976, 41, 831.

10 P. Main, M.M. Woolfson, L. Lessinger, G. Germain and J.P. Declercq, MULTAN-76, a system of Computer Programmes for the automatic solution of crystal structures from X-Ray diffraction data, Univ. of York, U.K. and Univ. of Louvain, Belgium, 1976.

11 J.M. Stewart, G.J. Kruger, H.L. Ammon, C. Dickirson and S.R. Hall, X-Ray System, Technical Report TR-192, 192, 1972, Computer Science Center, Univ. of Maryland, U.S.A.

Received, 31st August, 1977