

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 $\text{C}_3\text{-N}$ bond cleavage and cyclisation at the terminal vinylic carbon atom.

Studies¹ 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 reagents¹⁻⁴ 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 thermolysis⁶ of the readily available 3,3-dialkyl-2-amino-1-azirines causes rupture of the C₂-C₃ bond of the azirine ring to yield aminocarbenes which rearrange to 1-amino-2-azadienes. These were found⁶ to be useful synthons for the synthesis of pyridine derivatives.

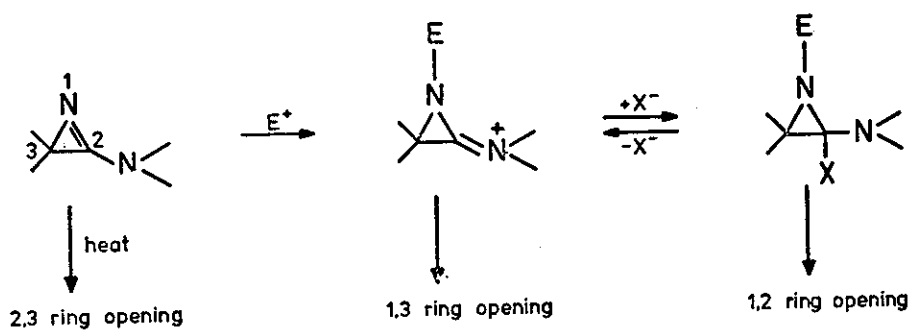
The fate of the intermediate aminoazirinium ions or aminocarbenes is expected to vary with substitution. Thus a double bond at position 3 of the azirine ring should permit cyclisations of these intermediates at the terminal

vinyl carbon-atom.

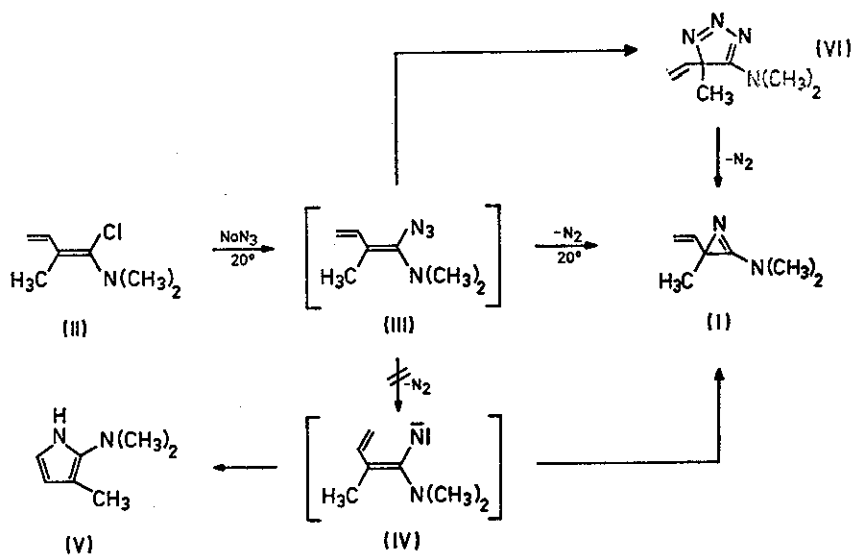
3-Methyl-3-vinyl-2-dimethylamino-1-azirine (I) was prepared by the reaction of 1-chloro-1-dimethylamino-2-methylbuta-1,3-diene⁷ (58 g, 0.4 mole) (II) with a suspension of NaN_3 (35 g, dried in vacuum) in 350 ml of dry ether. The reaction takes place at room temperature and can be monitored by the evolution 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} ($\text{C}=\text{N}$); NMR (CCl_4) : δ 1.36 (s, 3H), δ 2.93 (s, 6H), δ 4.96 (2 x dd, 2H, $J_{\text{gem}}=2\text{ Hz}$), δ 5.55 (dd, 1H, $J_{\text{cis}}=9\text{ Hz}$, $J_{\text{trans}}=18\text{ Hz}$).

Scheme 2

The reaction probably involves the intermediate formation of an α -azidoenamine (III) which, in contrast to other vinyl azides⁸, 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 results⁸ 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);
 1H -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, $\underline{CH_3}$),
 δ 43.82 (q, $N(\underline{CH_3})_2$), 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 singlets.

Therefore it appears that, even in the presence of a stabilising⁹ 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 observed⁶ 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 CH₂Cl₂-ether : m.p. 124,5-125,5°C; m/e (M⁺) 266; IR (CHCl₃) 1730, 1685, 1640, 1525 cm⁻¹; ¹H-NMR (CDCl₃) 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. (CH₃OH) δ_{max} 320 nm (log ε = 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 CH₂Cl₂-ether.

Scheme 4

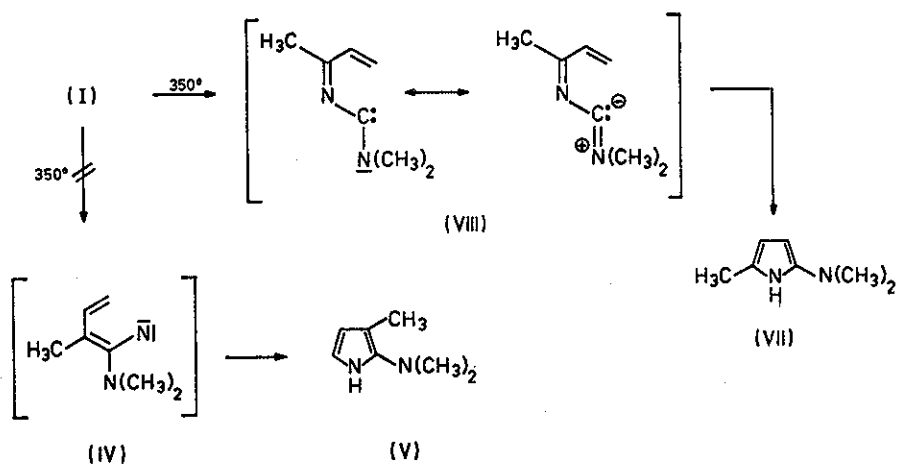
The observed Laue symmetry and extinctions correspond uniquely to the space group P2₁/a with a = 18.351 (7), b = 8.595 (4), c = 8.610 (3) Å; β = 94.51 (2)°. This cell

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 $CuK\alpha$, Ni-filtered radiation.

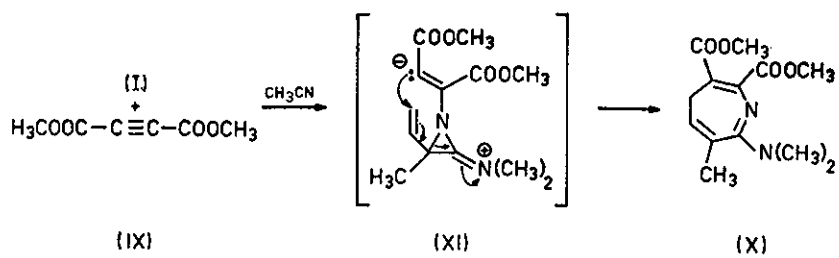
The structure was readily solved by direct methods using the MULTAN-76 system of programs¹⁰. It was refined by anisotropic block-diagonal least squares (X-ray 72)¹¹. The parameters of the hydrogen atoms, located on a differential Fourier-synthesis, were included in the refinement with isotropic temperature factors. Final conventional R value is 0.065 for 1289 observed reflexions ($I \geq 2.5\sigma(I)$). Fig. 1 shows the molecular structure and the bond lengths. These lengths indicate electron delocalisation along $N-C_2=N_1-C_6-C = 0$. 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 : $N_1-C_2 = 16^\circ$, $C_2-C_3 = -50^\circ$, $C_3-C_4 = -5^\circ$, $C_4-C_5 = 73^\circ$, $C_5-C_6 = -64^\circ$, $C_6-C_7 = -5^\circ$, $C_7-N_1 = 36^\circ$.

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

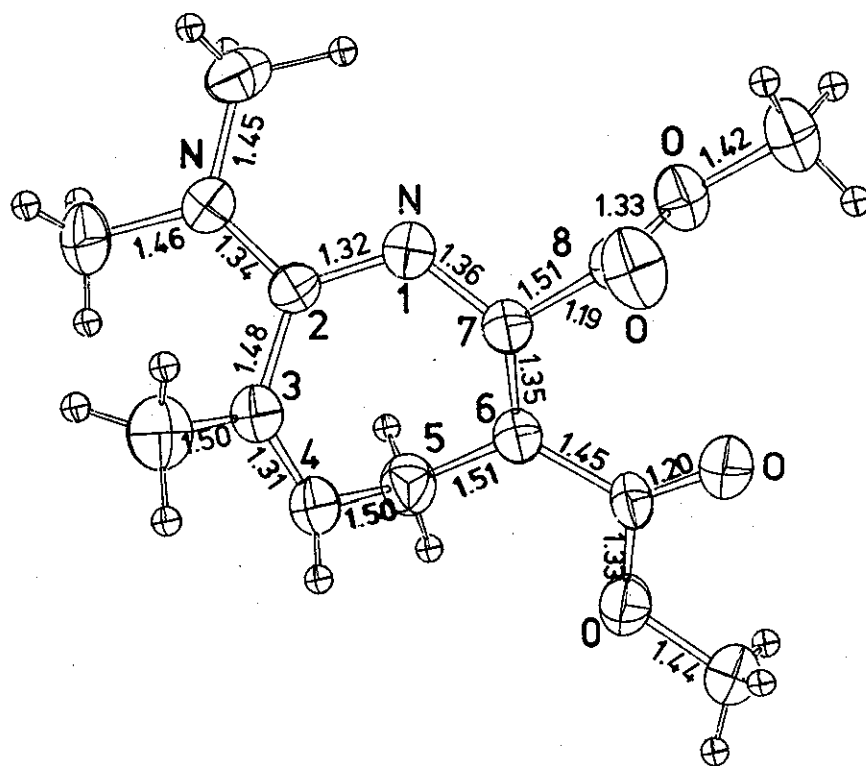


Fig.1. Molecular structure and bond lengths. The thermal ellipsoids are scaled to include 50% probability.

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