

A Novel Ring-opening of a 2-Alkyl-5-imino-4-nitro-2,5-dihydroisothiazole by Cyanide Ion

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Reaction of 2-methyl-3-methylamino-4-nitro-5-phenylimino-2,5-dihydroisothiazole (1b) with cyanide ion proceeds with two successive sequences of ring-opening and ring-closure with the ultimate generation of 2,5-bis(methylamino)-4-nitro-3-phenylimino-3H-pyrrole (2b) or its tautomer (2a).

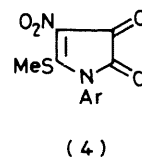
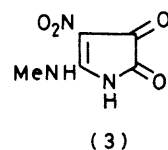
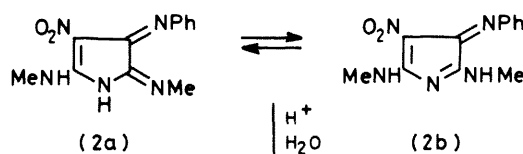
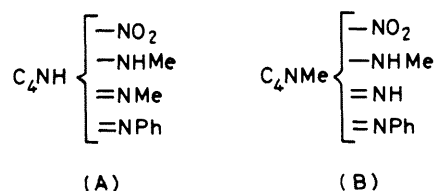
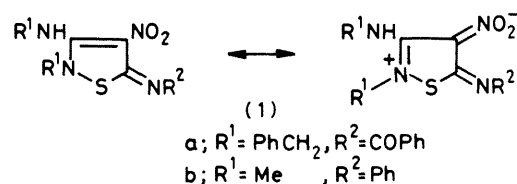
It has been conjectured¹ that the 2-alkyl-3-alkylamino-5-imino-4-nitro-2,5-dihydroisothiazole system (1), being a masked nitroenamine, would retain considerable amidinium nitronate character. The resultant positive charge on the nuclear nitrogen would facilitate cleavage of the N-S bond. In the example cited,¹ 5-benzoylimino 2-benzyl-3-benzylamino-4-nitro-2,5-dihydroisothiazole (1a) underwent base-catalysed fragmentation with sulphur-extrusion to provide 3,3-bis(benzylamino)-2-nitroacrylonitrile. We report here another intriguing sulphur-extrusion reaction of the 4-nitro-2,5-dihydroisothiazole system (1) on treatment with cyanide ion.

Treatment of 2-methyl-3-methylamino-4-nitro-5-phenylimino-2,5-dihydroisothiazole² (1b) with sodium cyanide for a short time gave orange crystals of compound (2) having the molecular formula C₁₂H₁₃N₃O₂. The product did not have a nitrile group (i.r.). The mass spectrum showed the molecular ion to be at 259, and a peak at *m/z* 213 corresponding to loss of NO₂. In the ¹H n.m.r. spectrum (CDCl₃-CD₃SOCD₃), the compound exhibited the following bands: δ 3.15 (s, NMe), 3.30 (d, NHMe, *J* 5 Hz), 6.7-7.3 (m, 5 ArH), 9.23 (br, NH), and 9.62 (q, NH); on adding D₂O, the NH signals disappeared and the doublet at 3.30 collapsed to a singlet. These data point to the presence in compound (2) of -NHMe, >NMe, >NPh and NO₂. Most noteworthy is the extrusion of sulphur in this reaction. Two partial structures (A) and (B) can be considered for compound (2) at this stage.

Acid hydrolysis of (2) gave colourless crystals of compound (3), having the formula C₅H₅N₃O₄ (*M* 171 from the mass spectrum). In the i.r. spectrum (KBr), bands occurred at 1790 and 1670 cm⁻¹, while the ¹H n.m.r. spectrum (CDCl₃-CD₃SOCD₃), had peaks at δ 3.22 (d, NHMe, *J* 5 Hz), 10.23 (q, NH), and 12.27 (br, NH); on addition of D₂O, the NH signals disappeared and the doublet at 3.22 collapsed to a singlet. The loss of aniline and methylamine moieties in this hydrolysis strongly suggests that partial structure (A) is the correct one for compound (2); this then can be extrapolated to structure (2a) for this molecule, which on acid hydrolysis leads to the pyrroledione (3). In support of this assignment, the related dione (4) has been shown³ to have i.r. bands at 1795 and 1720 cm⁻¹.

Conclusive proof of the above deductions was obtained when the solid state structure of the orange product (2) was unambiguously determined by X-ray crystallography to be (2b), a tautomer of (2a) with the hydrogen atom on the exocyclic nitrogen of the amidine system (Figure).

The conversion of (1b) into (2) by cyanide ion under mild conditions is an extraordinary transformation, which must involve two successive sequences of ring-opening and -closure. Of the several possible pathways, we prefer the route shown in Scheme 1.



The behaviour of the nitrodihydroisothiazole system in this reaction is in marked contrast to that of the 2-methylisothiazolium ion. The latter has been shown⁴ to undergo attack at sulphur with N-S bond cleavage; the resulting species undergoes recyclization with ring-enlargement (Scheme 2).

Experimental

¹H N.m.r. spectra were recorded on a Bruker WH 90 spectrometer. Chemical shifts are quoted as δ values downfield from

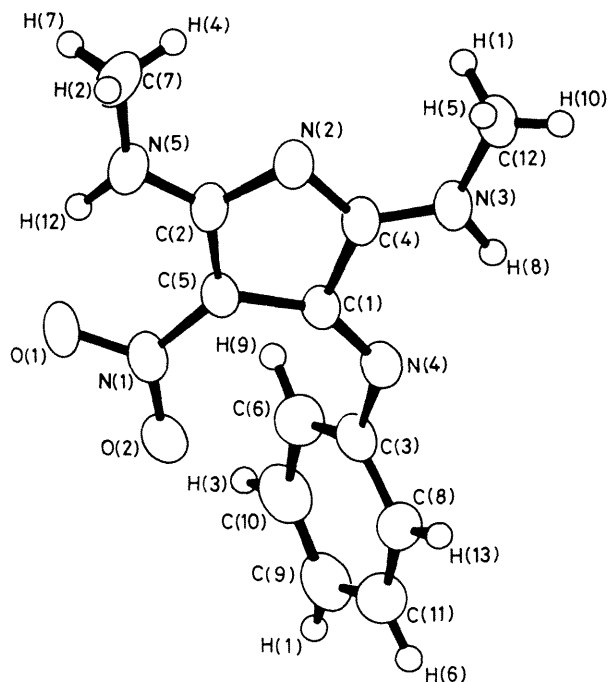
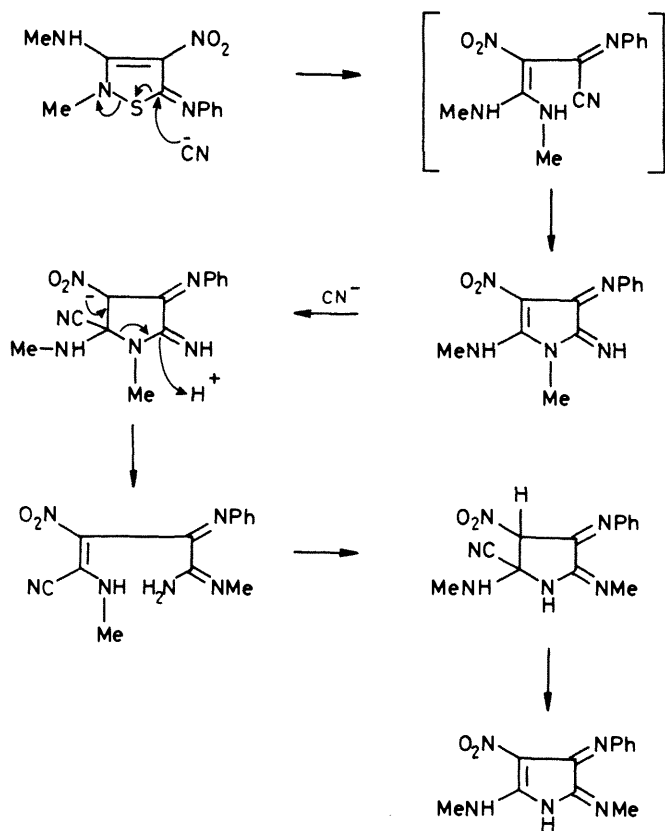
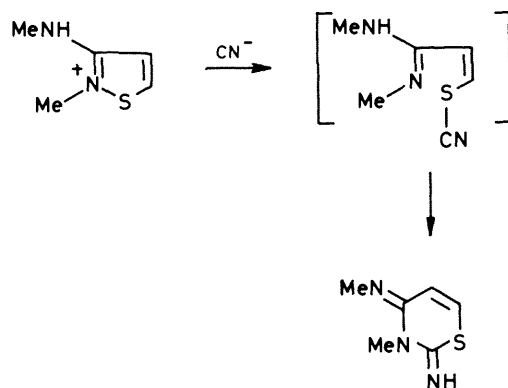


Figure. Molecular structure of compound (2) showing the crystallographic numbering scheme



Scheme 1.

SiMe₄. Mass spectra were determined on a Varian Mat CH-7 instrument at 70 eV by direct insertion. Ether refers to diethyl ether.



Scheme 2.

Table 1. Positional ($\times 10^4$)^a and thermal parameters for compound (2) with e.s.d.s in parentheses

Atom	x/a	y/b	z/c	B_{eq} (\AA^2) ^b
O(1)	2 613(1)	9 080(1)	4 686(1)	3.97
N(1)	3 056(1)	8 270(1)	5 025(1)	3.45
N(2)	-234(1)	6 926(1)	2 762(1)	3.23
O(2)	4 427(1)	8 106(1)	5 847(1)	3.91
N(3)	429(1)	5 428(1)	3 412(1)	3.30
N(4)	3 143(1)	6 079(1)	5 500(1)	3.34
N(5)	-116(2)	8 493(1)	2 771(1)	3.71
C(1)	2 183(2)	6 647(1)	4 684(1)	2.87
C(2)	513(2)	7 718(1)	3 301(1)	3.09
C(3)	4 375(1)	6 299(1)	6 757(2)	3.14
C(4)	716(2)	6 291(1)	3 551(1)	2.91
C(5)	1 988(2)	7 598(1)	4 447(1)	3.02
C(6)	4 103(2)	6 832(1)	7 759(2)	4.13
C(7)	-1 613(2)	8 595(1)	1 608(2)	4.31
C(8)	5 863(2)	5 888(1)	7 042(2)	3.86
C(9)	6 809(2)	6 576(1)	9 307(2)	4.64
C(10)	5 320(2)	6 965(1)	9 030(2)	4.69
C(11)	7 069(2)	6 048(1)	8 306(2)	4.57
C(12)	-1 001(2)	5 035(1)	2 400(2)	3.85
H(1)	759(2)	668(1)	1 018(2)	5.31
H(2)	-144(3)	870(2)	72(3)	14.34
H(3)	511(2)	735(1)	975(2)	6.55
H(4)	-225(3)	809(2)	148(3)	10.65
H(5)	-110(2)	516(1)	142(2)	8.34
H(6)	808(2)	578(1)	847(2)	6.38
H(7)	-219(2)	905(1)	175(2)	8.89
H(8)	121(2)	505(1)	412(2)	5.14
H(9)	303(2)	709(1)	758(2)	5.67
H(10)	-097(2)	443(2)	245(2)	9.17
H(11)	-198(3)	535(2)	230(2)	10.13
H(12)	54(2)	895(1)	326(2)	6.19
H(13)	600(2)	552(1)	632(2)	5.58

^a The hydrogen positional parameters are multiplied by 10³.

^b $B_{eq} = [8\pi^2(U_{11} + U_{22} + U_{33})]/3.0$.

Reaction of 2-Methyl-3-methylamino-4-nitro-5-phenylimino-2,5-dihydroisothiazole (1b) with Cyanide Ion.—Compound (1b)² (1.3 g) in ethanol (50 ml) was cooled to 5 °C and treated dropwise with stirring with a solution of NaCN (0.3 g) in water (2.3 ml). The mixture was stirred for 10 min at 5 °C and then filtered to remove a small amount of insoluble material. The filtrate was concentrated under reduced pressure at 35 °C and treated with ice-water. The solid was extracted with methylene dichloride, dried and evaporated. Digestion of the residue with ether gave compound (2) (0.3 g), m.p. 225–227 °C (decomp). A sample was recrystal-

Table 2. Bond lengths (Å) (not involving hydrogen atoms) with e.s.d.s in parentheses

C(7)-N(5)	1.448(1)	C(4)-N(3)	1.309(1)
N(5)-C(2)	1.313(1)	N(3)-C(12)	1.452(1)
C(2)-N(2)	1.372(1)	C(1)-N(4)	1.281(1)
N(2)-C(4)	1.335(1)	N(4)-C(3)	1.404(1)
C(4)-C(1)	1.504(1)	C(3)-C(8)	1.395(1)
C(1)-C(5)	1.438(1)	C(8)-C(11)	1.380(1)
C(5)-C(2)	1.431(1)	C(11)-C(9)	1.376(2)
C(5)-N(1)	1.363(1)	C(9)-C(10)	1.383(2)
N(1)-O(1)	1.279(1)	C(10)-C(6)	1.383(1)
N(1)-O(2)	1.239(1)	C(6)-C(3)	1.386(1)
N(2)-C(2)	1.372(1)	N(1)-C(5)	1.363(1)

Table 3. Bond angles (°) (not involving hydrogen atoms) with e.s.d.s in parentheses

C(7)-N(5)-C(2)	124.5(1)	C(4)-C(1)-N(4)	117.9(1)
N(5)-C(2)-N(2)	120.9(1)	C(5)-C(1)-N(4)	140.7(1)
N(5)-C(2)-C(5)	125.7(1)	C(1)-C(5)-C(2)	106.4(1)
N(2)-C(2)-C(5)	113.4(1)	C(2)-C(5)-N(1)	124.2(1)
C(2)-N(2)-C(4)	104.6(1)	C(1)-C(5)-N(2)	128.8(1)
N(2)-C(4)-C(1)	114.2(1)	C(1)-N(4)-C(3)	124.8(1)
N(2)-C(4)-N(3)	124.9(1)	N(4)-C(3)-C(6)	121.9(1)
N(3)-C(4)-C(1)	120.9(1)	C(6)-C(3)-C(8)	119.9(1)
C(4)-N(3)-C(12)	124.2(1)	C(3)-C(8)-C(11)	119.2(1)
O(1)-N(1)-O(2)	120.4(1)	C(8)-C(11)-C(9)	121.2(1)
C(5)-N(1)-O(2)	121.3(1)	C(11)-C(9)-C(10)	119.3(1)
C(5)-N(1)-O(1)	118.3(1)	C(9)-C(10)-C(6)	120.6(1)
N(4)-C(3)-C(8)	117.9(1)	C(10)-C(6)-C(3)	119.7(1)
C(4)-C(1)-C(5)	101.4(1)		

lised rapidly from methanol; the compound tended to decompose on prolonged heating in methanol; m.p. 247—248 °C (decomp.) (Found: C, 55.5; H, 5.4; N, 26.6. Calc. for $C_{12}H_{13}N_5O_2$: C, 55.6; H, 5.05; N, 27.0%).

* For details of the Supplementary Publications Scheme see Instructions for Authors (1983), *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

Hydrolysis of Compound (2).—The above compound (2) (0.2 g) in 1M-aqueous HCl (10 ml) was heated at 80—100 °C for 10 min and cooled. The colourless solid was filtered off, washed with water and dried to give 5-methylamino-4-nitropyrrole-2,3-dione (3) (0.1 g), m.p. 287—290 °C (decomp.) (Found: C, 35.0; H, 3.1; N, 24.5. Calc. for $C_5H_5N_3O_4$: C, 35.1; H, 2.95; N, 24.6%).

Crystal Data.— $C_{12}H_{13}N_5O_2$, $M = 259$, orange crystals, monoclinic, $a = 8.918(2)$, $b = 14.896(2)$, $c = 10.248(1)$ Å, $\beta = 110.75(5)^\circ$, $U = 1273$ Å³, $Z = 4$, $D_c = 1.35$ g cm⁻³, $\mu = 8.2$. Space group $P2_1/A$, Cu- K_α radiation; single crystal ENRAF NONIUS CAD4 diffraction data to Bragg angle 77°.

The structure was solved by direct methods and refined by full matrix least squares to a final R factor of 0.044 for 2378 observed reflections. The molecule and the atom numbering are shown in the Figure and the fractional atomic co-ordinates and their thermal parameters are given in Table 1 (with estimated standard deviations in brackets for the last significant figure). Table 2 gives the bond lengths and Table 3 the bond angles with their estimated standard deviations involving non-hydrogen atoms. Structure factors are available as a Supplementary Publication (SUP No. 23671, 14 pages).*

Acknowledgements

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