4-AMINO-Δ^2-1,2,4-OXADIAZOLINES

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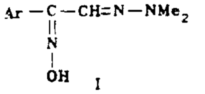
Reaction of 4-nitrobenzonitrile N-oxide with acetone azine and the dimethylhydrazones of acetone, acetaldehyde, and glyoxal affords the hitherto unknown 4-amino-Δ^2-1,2,4-oxadiazolines. The reaction with acetone methylhydrazone also gives a 1,2,4,5-oxatriazine.

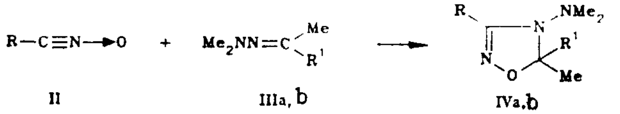
Nitrile oxides usually react with azomethines to give [3 + 2]-cycloaddition products [1], but such reactions are unknown with hydrazones. N-Methylhydrazones add to nitrile oxides as NH-nucleophiles, and the resulting hydrazidooximes cyclize to 1,2,4-triazoles [2] or 1,2,4,5-oxatriazines [3]. Hussein et al. [3] interpret the absence of addition products as being due to the inadequate dipolarophilic reactivity of the C=N bond in hydrazones.



$Ar-C(=N-OH)-CH=N-NMe_2$

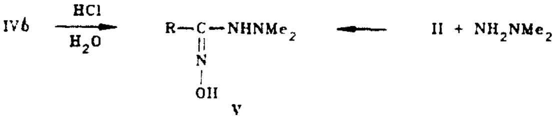
I

In order to avoid side reactions, we have examined the reactions of nitrile N-oxides with hydrazones which do not contain an NH group. Under these conditions, formaldehyde dimethylhydrazone, as previously reported [4], gives the oximinohydrazone (I), while reaction of 4-nitrobenzonitrile N-oxide (II) with acetaldehyde dimethylhydrazone (IIIa) or acetone dimethylhydrazone (IIIb) readily affords the [3 + 2]-cycloadditon products (IVa, b), which are the first representatives of the previously unknown 4-amino-Δ^2-1,2,4-oxadiazolines:

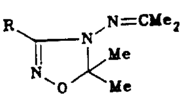


Here & later $R=4\text{-}O_2NC_6H_4$; III, IV a $R^1=H$; b $R^1=Me$

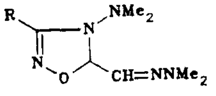
It is noteworthy that the acetaldehyde derivative (IIIa) does not give an oximinohydrazone (I). The structure of the oxadiazoline (IVb) was confirmed by hydrolysis to the hydrazidooxime (V), which has been obtained by direct synthesis.



Reaction of the N-oxide (II) with acetone azine or glyoxal bisdimethylhydrazone gives cycloaddition products at only one C=N bond (VI and VII, respectively).



VI



VII

In neither case was it possible to obtain a bisoxazolidine, even when an excess of the N-oxide (II) was used.

The 1,2,4-oxadiazolines (IV), (VI), and (VII) were obtained with great ease, so that the reported absence of cycloaddition products with N-methylhydrazones [3] was surprising. For this reason, we reacted the N-oxide (II) with

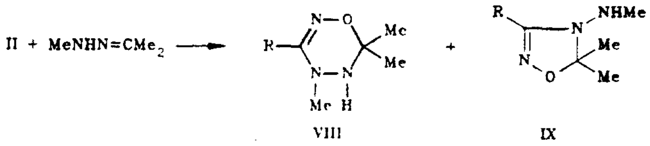


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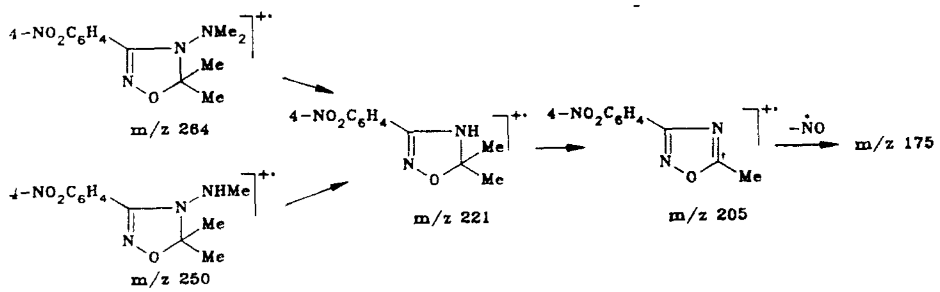
TABLE 1. Properties of (IV)-(IX)

Compound	Empirical formula	Mp, °C	PMR spectrum, δ, ppm (J, Hz)				Yield, %
			$4\text{-}NO_2C_6H_4$	CH_3N	CH_3C	others	
IVa	$C_{11}H_{14}N_4O_3$	88 . . . 90	7,93; 8,23 (9,0)	2,38	1,31	6,07 (CH)	56
IVb	$C_{12}H_{16}N_4O_3$	85 . . . 86	7,93; 8,31 (9,0)	2,51	1,49		79
V	$C_9H_{12}N_4O_3$	124 . . . 125	7,69; 8,13 (9,0)	2,51		6,71 (NH); 10,44 (OH)	33 (A), 64 (B)
VI	$C_{13}H_{16}N_4O_3$	138 . . . 140	7,64; 8,18 (8,5)		1,42	1,93 2,15 $(CH_3)_2C{=}N$	59
VII	$C_{13}H_{18}N_6O_3$	113 . . . 115	7,91; 8,24 (8,5)	2,42		2,80 $((CH_3)_2NN{=}C)$; 6,18 (CH); 6,47 (CH)	68
VIII	$C_{11}H_{14}N_4O_3$	140 . . . 142	7,67; 8,24 (9,5)	2,96	1,42	4,18 (NH)	60
IX	$C_{11}H_{14}N_4O_3$	88 . . . 90	7,87; 8,23 (9,5)	2,69	1,61	3,44 (NH)	20

acetone methylhydrazone, when it was found that a mixture of the 1,2,4,5-oxatriazine (VIII) and the 4-amino-1,2,4-oxadiazoline (IX) was formed in a ratio of 3:1, this mixture being separated on silica gel. The structure of the product (VIII) was established by comparing the PMR and mass spectra of (VIII) with those of related 1,2,4,5-oxatriazines [3].

The structures of all the 4-amino-1,2,4-oxadiazolines were confirmed by their PMR spectra (Table 1). The mass spectra of the N-(dimethylamino) compound (IVb) and the N-(methylamino) compound (IX) showed molecular ion peaks M^+ and common fragment ions with m/z 221, 205, and 175. It will be recalled that breakdown with ejection of ·NO is characteristic of 1,2,4-oxadiazoles [5].



EXPERIMENTAL

PMR spectra were obtained on a Bruker WH-90 in DMSO-D_6 and $CDCl_3$, internal standard TMS, and mass spectra on an AET MS50, ionizing electron energy 70 eV.

The elemental analyses for C, H, and N were in agreement with the calculated values.

4-Dimethylamino-5-methyl-3-(4-nitrophenyl)-Δ^2-1,2,4-oxadiazoline (IVa). To a solution of 0.86 g (10 mmoles) of acetaldehyde dimethylhydrazone in 20 ml of acetonitrile was added dropwise at 10-15°C a solution of 0.82 g (5 mmoles) of the N-oxide (II) in 40 ml of acetonitrile. After 2 days, the solvent was distilled off and the product recrystallized from aqueous acetone (1:1).

4-Dimethylamino-5,5-dimethyl-3-(4-nitrophenyl)-Δ^2-1,2,4-oxadiazoline (IVb). To a solution of 2.0 g (20 mmoles) of acetone dimethylhydrazone in 20 ml of acetone was added dropwise at 10-15°C a solution of 1.64 g (10 mmoles) of the N-oxide (II) in 30 ml of acetone. After 3 h, the acetone was removed, the residue treated with water, and the product filtered off and recrystallized from aqueous acetone (1:1).

N',N'-Dimethyl-4-nitrobenzohydrazide Oxime (V). A. A mixture of 0.8 g (3 mmoles) of the oxadiazoline (IVb) and 15 ml of concentrated HCl was stirred for 2 h at room temperature. The acid was neutralized with saturated sodium carbonate solution, and the precipitated hydrazide oxime (V) was filtered off and recrystallized from benzene.

B. To a solution of 0.6 g (10 mmoles) of 1,1-dimethylhydrazine in 20 ml of alcohol was added dropwise at 10-15°C a solution of 0.82 g (5 mmoles) of the N-oxide (II) in 30 ml of alcohol. After 1 h, the alcohol was distilled off, water added to the residue, and the product filtered off and recrystallized from benzene. The product was identical in its melting point and PMR spectrum to the sample obtained by method A.

4-Isopropylideneamino-5,5-dimethyl-3-(4-nitrophenyl)-Δ^2-1,2,4-oxadiazoline (VI). To a solution of 1.12 g (10 mmoles) of acetone azine in 20 ml of acetone was added dropwise at 10-15°C a solution of 1.64 g (10 mmoles) of the N-oxide (II) in 30 ml of acetone. On the following day, the acetone was distilled off, the residue treated with hexane, and the product filtered off and recrystallized from aqueous acetone (1:1).

4-Dimethylamino-5-(dimethylhydrazonomethyl)-3-(4-nitrophenyl)-Δ^2-1,2,4-oxadiazoline (VII). To a solution of 1.44 g (10 mmoles) of glyoxal bisdimethylhydrazone in 20 ml of acetonitrile was added at 10-15°C 1.64 g (10 mmoles) of the N-oxide (II). On the following day, the solvent was distilled off, the residue treated with 5 ml of alcohol, and the product filtered off and recrystallized from alcohol.

4,6,6-Trimethyl-2-(4-nitrophenyl)-5,6-dihydro-4H-1,2,4,5-oxatriazine (VIII) and 5,5-Dimethyl-4-methylamino-3-(4-nitrophenyl)-Δ^2-1,2,4-oxadiazoline (IX). To a solution of 0.17 g (20 mmoles) of acetone methylhydrazone in 20 ml of tetrahydrofuran was added dropwise at 10-15°C a solution of 3.28 g (20 mmoles) of the N-oxide (II) in 40 ml of tetrahydrofuran. After 4 h, the tetrahydrofuran was distilled off, and the residue chromatographed on silica gel (eluent hexane—ether, 3:1).

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