REARRANGEMENT OF 1-OXA-2-AZOLES. 5*. SYNTHESIS AND REARRANGEMENT OF α-OXIMODIMETHYL-HYDRAZONES OF 1,2,4-OXADIAZOLYL-3-GLYOXAL

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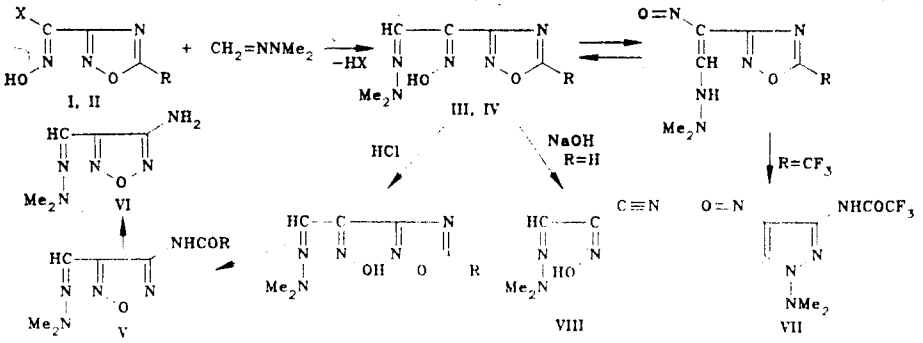
The acid halides of 1,2,4-oxadiazol-3-carbohydroxamic acids react with formaldehyde dimethylhydrazone to give the corresponding α-oximohydrazones, which with hydrochloric acid rearrange to yield the dimethylhydrazone of 3-amino-4-formylfurazane. In the absence of an acid catalyst, the 5-trifluoromethyl derivative undergoes a rearrangement to give 1-dimethylamino-4-nitroso-3-trifluoroacetamidopyrazole.

The rearrangement of oximes of 1,2,4-oxadiazoles is an easy method for the synthesis of aminofurazanes, and for this purpose it is convenient to use the acid halides of 1,2,4-oxadizole-3-carboxylic acids as a starting material. The halogen is readily replaced to give a substituted oxime, which undergoes rearrangement to yield an aminofurazane with retention of the initial functional groups. Earlier [2], we showed that N-substituted diaminofurazanes can be obtained in this way. In a continuation of this work we have studied the rearrangement of the products formed by the reaction of the halogenoximes I and II with formaldehyde dimethylhydrazone:



I, III R=H, X=Cl; II, IV R=CF_3, X=Br

Formaldehyde dimethylhydrazone, in contrast to the hydrazones of other carbonyl compounds, forms oximohydrazones with nitrile oxides, rather than cycloaddition products [3]. Addition to nitrile oxides proceeds regiospecifically and always leads to the formation of oximes having the Z-configuration [4] (i.e., those in which the hydroxyl group and the addition group are in the syn-position). The rearrangement only takes place if the oxime group has the E-configuration. The isomerization of oximes is acid catalyzed, and the oxadiazoles III and IV were readily converted by hydrochloric acid to the aminofurazane VI. The intermediate amide V, under these conditions, was hydrolyzed to the dimethylhydrazone of 3-amino-4-formylfurazane (VI).

It was found that the oxadiazole III, which has no substituent at position 5, was unstable in the absence of acid, but the trifluoromethyl analog IV, readily isomerized at room temperature to give a yellow-green product, which dissolved in organic solvents to give deep blue or green solutions. IR and PMR spectral data confirmed the presence of trifluoroacetamide and dimethylamino groups in the molecule. However, the PMR spectrum showed a downfield shift for the CH proton compared with the dimethylhydrazones III, IV, and VI. The characteristic color of the product suggests that there is a nitroso group in the molecule, indicating a different reaction path in which the hydrazone, and not the oxime group participates in the rearrangement. As a result the reaction product is the nitrosopyrazole VII.

*For Communication 4, see [1].

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It is possible that the recyclization step precedes the tautomeric change from oximohydrazone to nitrosohydrazine, but in principle the intermediate hydrazone IV or its anion could also take part in the reaction. The latter is confirmed by the fact that in the presence of sodium bicarbonate, the rearrangement of the oxadiazole IV goes much faster.

It might be expected that in the presence of base, the oxadiazole III would also rearrange, but in fact a different reaction occurred, involving ring opening and formation of the cyanoderivative VIII. This product was also obtained by the reaction of the oxadiazole III with aqueous ammonia, but this reaction took place much more slowly.

EXPERIMENTAL

PMR spectra were taken on a Bruker WH-90 using DMSO-D_6 as solvent, internal standard TMS; IR spectra were recorded on a Perkin—Elmer 580B, compounds were prepared as Nujol mulls.

Elemental analysis data for C, H, and N were in good agreement with calculated values.

3-(β-Dimethylhydrazono-α-oximinoethyl)-1,2,4-oxadiazole (III, $C_6H_9N_5O_2$). To dimethylhydrazine (0.8 g, 13 mmoles) was added an ice-cold solution of formalin (1.3 ml, 40%), followed by a saturated solution of sodium bicarbonate (10 ml) and ethyl acetate (20 ml). This mixture was cooled to 10-15°C and 1,2,4-oxadiazole-3-carbohydroxamoyl chloride (1.2 g, 8 mmoles) added portionwise over a period of 5 min. After 30 min, the organic layer was separated and the ethyl acetate distilled off at reduced pressure. Water was added to the residue and the precipitated material filtered off to give 0.85 g (57%) of III with mp 110-112°C (from benzene). PMR spectrum: 2.93 (6H, s, Me_2N); 7.31 (1H, s, hydrazone CH); 9.56 (1H, s, ring CH); 11.78 ppm (1H, s, OH). IR spectrum: 3225 (OH); 3120 (ring CH); 1584 (C=N); 1572 cm^{-1} (C=N).

3-(β-Dimethylhydrazono-α-oximinoethyl)-5-trifluoromethyl-1,2,4-oxadiazole (IV, $C_7H_8F_3N_5O_2$) was obtained in the same way as compound III from 5-trifluoromethyl-1,2,4-oxadiazole-3-carbohydroxamoyl bromide (II). Yield 49%, mp 70-72°C. PMR spectrum: 2.96 (6H, s, Me_2N); 7.32 (1H, s, CH); 12.13 ppm (1H, s, OH). IR spectrum: 3300 (OH); 1595 (C=N); 1150-1250 cm^{-1} (CF_3).

Dimethylhydrazone of 3-Amino-4-formylfurazane (VI, $C_5H_9N_5O$). Compound III (0.1 g, 0.6 mmoles) was dissolved in concentrated HCl (0.5 ml). After 6 h, the reaction mixture was neutralized with saturated $NaHCO_3$ solution and the precipitated material filtered off to give 0.06 g (85%) of VI, mp 122-124°C (benzene). PMR spectrum: 3.02 (6H, s, Me_2N); 6.22 (2H, broad s, NH_2), 7.33 ppm (1H, s, CH). IR spectrum: 3435 and 3320 (NH_2), 1631 cm^{-1} (C=N).

The rearrangement of the oxadiazole IV was carried out in the same way.

1-Dimethylamino-4-nitroso-3-trifluoroacetamidopyrazole (VII, $C_7H_8F_3N_5O_2$). The oxadiazole IV was converted to the pyrazole VII either by allowing to stand for 3 days at room temperature or by boiling for 20 min in hexane solution. Yield 88%, mp 77-79°C (from hexane). PMR spectrum: 2.87 (6H, s, Me_2N); 9.07 (1H, s, CH); 12.09 ppm (1H, broad s, NH). IR spectrum: 3285 (NH); 3196 (ring CH); 1754 (C=O); 1560 (N=O); 1130-1260 cm^{-1} (CF_3).

β-Dimethylhydrazono-α-oximinopropionitrile (VIII, $C_5H_8N_4O$). The oxadiazole III (0.2 g, 1.1 mmoles) was dissolved in NaOH (1 ml, 20%). After 10 min, the solution was neutralized with HCl and the precipitated material filtered off. Yield 0.11 g (72%), mp 142-144°C (from water). PMR spectrum: 3.07 (6H, s, Me_2N); 7.07 (1H, s, CH); 12.62 ppm (1H, s, OH). IR spectrum: 3130 (OH), 2250 (C=N), 1594 cm^{-1} (C=N).

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