REARRANGEMENTS OF 1-OXA-2-AZOLES.
7.* SYNTHESIS AND HETEROCYCLIZATION OF 3-ACYL-1,2,4-OXADIAZOLE OXIME

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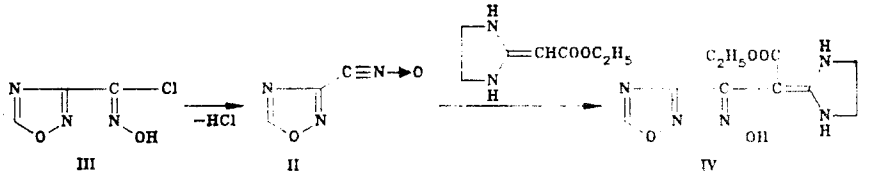
The reaction of 1,2,4-oxadiazole-3-carbonitrile oxide with 2-(ethoxycarbonylmethylene)imidazolidine gives an acyclic addition product, which cyclizes in basic medium into an isoxazole derivative, while in an acid medium it rearranges into an aminofurazan derivative.

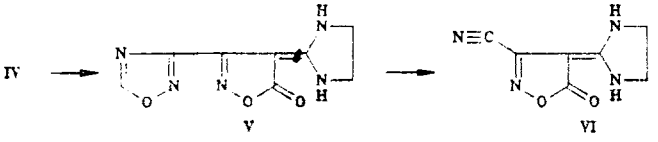
Addition of amines to nitrile oxide, generated from 1,2,4-oxadiazole-3-carbohydroxamoyl chloride [2] leads to Z-amidoximes, which can be rearranged into diaminofurazan derivatives. The use at the first stage of other nucleophiles makes it possible to obtain aminofurazans with various substituents in the ring.

It is known that the reaction of nitrile oxides with compounds containing ethylene bonds usually leads to cycloaddition products — isoxazolines [3]. Contrary to this, 2-(ethoxycarbonylmethylene)imidazolidine (I) in the reaction with 4-nitrobenzonitrile N-oxide gives an acyclic product [4].

We found that the addition of amidazolidine I to 1,2,4-oxadiazole-3-carbonitrile oxide (II) also gives the corresponding oxime IV:



Nitrile oxide II was generated in situ by dehydrochlorination of chlorooxime III with triethylamine. The presence of the oxime group in compound IV was confirmed by the PMR spectrum data in which the proton signal of the hydroxyl group appears at 11.79 ppm. It is known that the addition of nitrile oxides proceeds with the formation of oximes in which the hydroxyl and the substituting group are present in the cis-position. Such a configuration of oxime IV obtained by us is confirmed by the ease of its cyclization into the isoxazole derivative V. The reaction is catalyzed by bases and can proceed in the course of the preparation of oxime IV by the action on it of an excess of triethylamine. By the action of a stronger alkaline agent an opening of the oxadiazole ring in V takes place with the formation of cyanoisoxazole:



As known, acids catalyze the isomerization of the oxime group. Therefore, in an acid medium, oxime IV gives another product (see scheme below).

Isomerization of the oxime group leads to an unstable derivative VII, which rearranges into furazan (VIII). The formyl group splits off under these conditions, and aminofurazan IX is the end product.

*For Communication 6, see [1].

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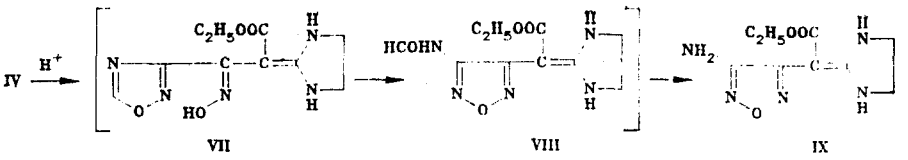

EXPERIMENTAL

The PMR spectra were run on a Bruker WH-90 spectrometer in DMSO-D_6, using TMS as internal standard. The IR spectra were recorded on a Perkin—Elmer 580B spectrophotometer in Nujol. The course of the reaction and the purity of the compounds obtained was monitored by TLC on Silufol UV-254 plates, in an ethyl acetate—hexane (2:1) system, or in ethyl acetate; development in UV light.

The elemental analysis data for C, H, N correspond to the calculated values.

2-[(1,2,4-Oxadiazol-3-yl)(ethoxycarbonyl)methylene]imidazoline Oxime (IV), $C_{10}H_{13}N_5O_4$). Chloroxime III (0.14 g, 0.96 mmole) was added at room temperature in portions to a mixture of 0.15 g (0.96 mmole) of compound I and 0.12 g (1.15 mmoles) of triethylamine in 8 ml of acetone. After 15-20 min, the triethylamine salt was filtered off, and the filtrate was evaporated. Ether was added to the residue, and the mixture was filtered. Yield 0.14 g (55%) of product mp 151-152°C. PMR spectrum: 0.81 (3H, t, CH_3), 3.48 (4H, s, CH_2), 3.47 (2H, m, CH_2), 6.12 (1H, br.s, NH), 7.86 (1H, br.s, NH), 9.45 (1H, s, CH), and 11.79 ppm (1H, s, OH). IR spectrum: 3402 (NH), 3284 (NH), 3110 (CH), and 1635 cm^{-1} (C=N).

4-(Imidazolidin-2-ylidene)-3-(1,2,4-oxadiazol-3-yl)isoxazol-5-one (V, $C_7H_7N_5O_3$). A. Chloroxime III (0.37 g) was added in portions at room temperature to a mixture of 0.39 g (2.5 mmoles) of compound I and 0.30 g (3.0 mmoles) of triethylamine in 15 ml of acetone. After 3 h the precipitate formed was filtered off and washed thoroughly with water. An additional amount of the product was obtained by evaporation of the acetone filtrate and washing of the solid residue with water. Mp >330°C. PMR spectrum: 3.69 (4H, s, CH_2), 8.46 (2H, br.s, NH), 9.88 ppm (1H, s, CH). IR spectrum: 3320 (NH), 3112 (CH), 1700 cm^{-1} (C=O). Overall yield of the product 0.24 g (49%).

B. A suspension of 0.14 g (0.52 mmole) of oxime IV in 2.5 ml of a saturated sodium bicarbonate solution was stirred for several days. The product was filtered off and washed with water. Yield 0.06 g (54%).

4-(Imidazolidin-2-ylidene)-3-cyanoisoxazol-5-one (VI, $C_7H_6N_4O_2$). A mixture of 0.02 g (0.49 mmole) of sodium hydroxide, 5 ml of an 80% ethanol, and 0.1 g (0.45 mmole) of isoxazolone V was held for 1 h, and then neutralized with HCl. The precipitate formed was filtered off and washed with ether, mp 328-329°C. PMR spectrum: 3.66 (4H, s, CH_2) and 8.45 ppm (2H, br.s, NH). IR spectrum: 3325 (NH), 2260 (C≡N), 1692 cm^{-1} (C=O). The yield of the product was 0.025 g (31%).

2-[(3-Aminofurazanyl)(ethoxycarbonyl)methylene]imidazolidine (IX, $C_9H_{13}N_5O_3$). A 2.5 ml portion of a 10% HCl solution was added to 0.10 g (0.37 mmole) of imidazolidine oxime IV. After 24 h, the reaction mixture was neutralized with a saturated sodium bicarbonate solution and extracted with ether. The extract was dried over anhydrous sodium sulfate and evaporated. Mp 106-108°C. PMR spectrum: 1.11 (3H, t, CH_3), 3.46 (4H, s, CH_2), 4.0 (2H, g, CH_2), 5.48 (2H, s, NH_2), 7.43 ppm (2H, br.s, NH). Yield of furazan IX 0.04 g (50%).

LITERATURE CITED

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