

SHORT
COMMUNICATIONS

Nitroguanidine-containing Oxamide Derivatives

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Received February 27, 2004

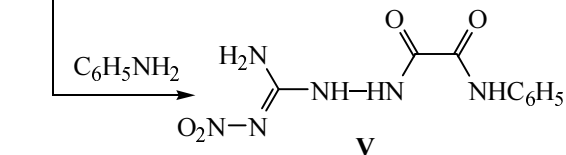
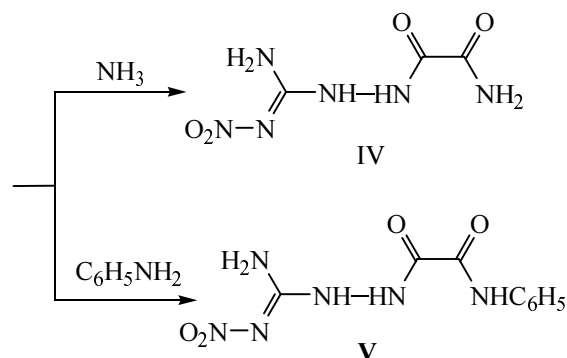
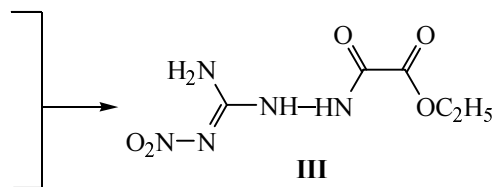
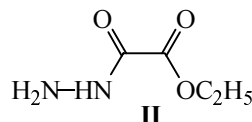
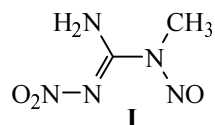
Derivatives of oxamide and oxamic acid are extensively studied for in this series compounds has been found possessing tuberculocidal and antispasmodic properties [1, 2]; in particular 4-ethoxyoxanilic acid hydrazide showed high tuberculocidal activity [3]. At the same time among guanidine derivatives a large number of biologically active compounds is known exhibiting analgesic [4], fungicidal, and herbicidal properties.

We developed a convenient preparative procedure for synthesis of special substituted oxamides containing a nitroguanidine moiety in their structure.

The procedure is underlied by a reaction of ethyl {2-[amino-(nitroimino)methyl]hydrazino}(oxo)acetate (**III**) with ammonia and aniline. Initial compound **III** was obtained by condensation of 1-methyl-2-nitro-1-nitrosoguanidine (**I**) with ethyl (hydrazino)(oxo)acetate (**II**) by a procedure we had developed before [5].

Amination of compound **III** was carried out by treating it in alcoholic solution with aqueous ammonia or by passing through its solution a flow of ammonia gas for 1.5 h at room temperature. The isolated substituted acetamide is a colorless crystalline compound whose structure was derived from spectral characteristics. A two-proton broadened singlet at 8.74 ppm is assigned to the protons of amino group in the nitroamidine fragment (this location of such protons is characteristic of the majority of the known nitroguanidine derivatives [6–9]), the protons from amino group of the amide moiety appear at 8.19 ppm (2H), and singlets belonging to protons of secondary amino groups are observed downfield at 9.98 (1H) and 11.04 ppm (1H).

Reaction of compound **III** with aniline was carried out in methanol at 50°C. Basing on ¹H, IR, and UV spectra the structure of compound **V** was shown to be



similar to that of **IV**; its ¹H NMR spectrum contains signals from all the protons of the structural fragments of the molecule.

1-Methyl-2-nitro-1-nitrosoguanidine (I), **ethyl (hydrazino)(oxo)acetate (II)**, **{2-[amino(nitroimino)methyl]hydrazino}(oxo)acetate (III)** were prepared by methods [10], [11, 12], and [5] respectively.

Amino(nitroimino)methylhydrazino}(oxo)acetamide (IV). (a) To a solution of 2.19 g (0.01 mol) of compound **III** in 30 ml of methanol was added a four-fold excess of 25% aqueous ammonia. The reaction mixture was kept for 3 h at 18–20°C. The formed precipitate was filtered off, and then its dispersion in water was acidified with concn. HCl. We obtained 1.7 g (93%) of compound **IV**, mp 216–217°C (from water). IR spectrum, cm^{-1} : 1690, 1710 (C=O). UV spectrum: λ_{max} , nm (log ϵ): 267 (4.18). Found, %: C 19.10, 19.13; H 3.28, 3.25; N 44.27, 44.24. $\text{C}_3\text{H}_6\text{N}_6\text{O}_4$. Calculated, %: C 18.95; H 3.16; N 44.21.

(b) Through a solution of 2.19 g (0.01 mol) of compound **III** in 30 ml of methanol ammonia was passed for 1.5 h. The reaction mixture was left standing for 2 h, then the separated precipitate was filtered off, and its dispersion in water was acidified with concn. HCl. We obtained 1.8 g (94%) of compound **IV**, mp 216–217°C (from water). No depression of melting point was observed in a mixed sample of compound **IV** obtained by procedures a and b.

[Amino(nitroimino)methylhydrazino}(oxo)acetanilide (V). To a solution of 2.19 g (0.01 mol) of compound **III** in 30 ml of methanol was added 0.90 g (0.01 mol) of aniline. The mixture was heated to 50°C for 3 h and then left standing for 12 h at room temperature. The separated precipitate was filtered off. Yield 2.5 g (94%), mp 199–200°C (from water). IR spectrum, cm^{-1} : 1690 (C=O). UV spectrum: λ_{max} , nm (log ϵ): 267 (4.17). ^1H NMR spectrum, δ , ppm.: 7.79 (C_6H_5), 8.74 (NH_2), 9.85 (C–NH), 10.90 (NH– C_6H_5), 11.13 (NH–C=O). Found, %: C 40.58, 40.61; H 4.14, 4.17; N 31.61, 31.60. $\text{C}_9\text{H}_{10}\text{N}_6\text{O}_4$. Calculated, %: C 40.60; H 3.67; N 31.58.

IR spectra were recorded on InfraLum-FT-02 instrument from mulls in mineral oil. ^1H NMR spectra were registered on spectrometer Bruker AC-200 (200 MHz) in $\text{DMSO}-d_6$ with respect to TMS. UV spectra of water solutions of compounds were measured on spectrophotometer CF-16.

The study was carried out under financial support of ISTC (grant no. 2468p).

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