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LETTERS TO THE EDITOR

Synthesis of 5-(Morpholinomethyl)-1,3,4-thiadiazole-2-thione under Microwave Irradiation

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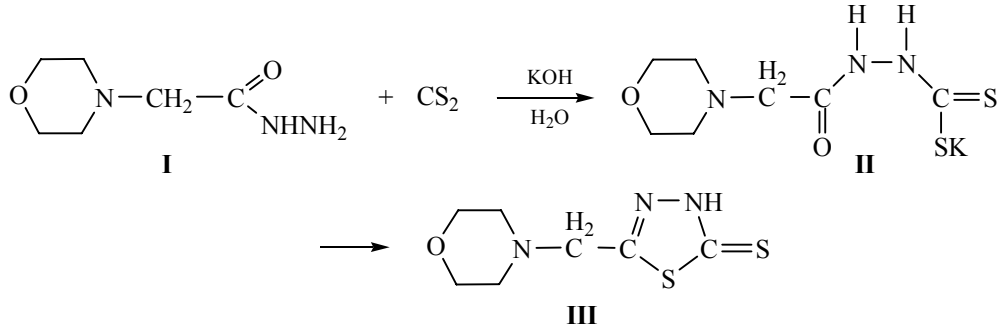
Among of the numerous *N*,*S*-containing heterocycles, 1,3,4-thiadiazole derivatives are of interest as cyclic analogs of bioactive thiosemicarbazones [1–3].

In the previous paper [4], we reported on the two-step synthesis of 5-(morpholinomethyl)-1,3,4-thiadiazol-2-thione **III** via isolation of the intermediate potassium hydrazinocarbodithiomorpholinylacetate followed by the acidic hydrolysis of the latter with concentrated sulfuric acid.

In order to optimize that process, we investigated the one-pot reaction of *N*-morpholinylacetic acid **I** with carbon disulfide in aqueous alkaline medium under microwave irradiation.

By using microwave activation in the synthesis of **III**, we could reduce the reaction duration, identify the alternative reaction pathways, and avoid treatment with sulfuric acid.

We found that at the first stage of the reaction under microwave irradiation, potassium hydrazinodithiomorpholinylacetate **II** underwent cyclization into 5-(morpholinomethyl)-1,3,4-thiadiazol-2(3*H*)-thione **III**.



The reaction conditions were optimized by varying the irradiation duration (1 to 20 min) and irradiation power (70 to 750 W). The optimal conditions were: irradiation power of 350 W (2450 MHz) and reaction duration of 20 min. Under those conditions, the yield of **III** was of 32%.

Compound **III** was white crystalline substance, soluble in a number of solvents.

Thus, microwave activation allowed reducing the reaction duration from 4–5 h to 20 min. No other possible reaction pathways were detected.

Synthesis of 5-(morpholinomethyl)-1,3,4-thiadiazole-2-thione (III). Dropwise, 1.52 g (0.02 mol) of carbon disulfide was added under cooling to a mixture of 1.59 g (0.01 mol) of morpholinylacetic acid hydrazide **I** and 0.84 g (0.015 mol) of potassium

hydroxide dissolved in 20 ml of water. The reaction mixture was microwave-irradiated for 20 min (350 W). Then, the mixture was neutralized with hydrochloric acid solution; the product was extracted with ethyl acetate, dried over potassium carbonate, and the solvent was evaporated. The oily product was rubbed up with 2-propanol. The obtained solid product was filtered off, dried, and recrystallized from ethanol. Yield 0.69 g (32%), mp 134–135°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.46 t [4H, $N(CH_2)_2$, *J* 4.44], 3.32 s (2H, NCH_2), 3.57 t [4H, $O(CH_2)_2$, *J* 4.58], 14.37 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 217 $[M]^+$ (50.3), 132 (20.1), 100 (100), 86 (65.5), 56 (28.8), 55 (24.6), 42 (22.3), 41 (15.7).

REFERENCES

1. Hovsepian, T.R., Dilanian, E.R., Engoyan, A.P., and Melik-Ohanjanian, R.G., *Chem*. *Heterocycl. Comp*., 2004, no. 9, p. 1194.
2. Mamolo, M.G., Vio, L., and Banfi E., *Farmaco*, 1996, vol. 51, no. 1, p. 71.
3. Satpaeva, Zh.B., Nurkenov, O.A., Fazylov, S.D., Baikenov, M.I., and Smakova L.A., Abstract of Papers, *II mezdunarodnaya Kazakhstansko-Rossiiskaya konferentsiya po khimii i khimicheskoi tekhnologii* (II Int. Kazakhstan-Russian Conf. on Chemistry and Chemical Technology), Karaganda, 2012, vol. 1, p. 448.
4. Orlinskii, M.M., *Zh. Org. Khim*., 1996, vol. 32, no. 1, p. 144.