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LETTERS TO THE EDITOR

Synthesis of 2-Anabasinylmethyl-1,3,4-oxadiazole under Convection Heating and Microwave Irradiation

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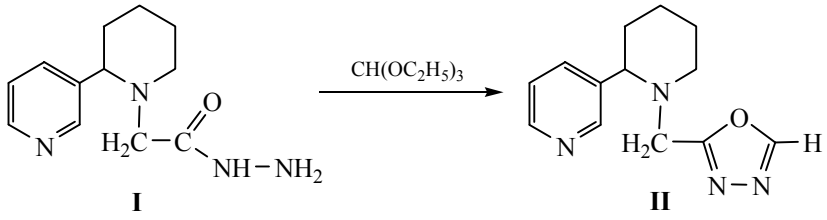
Developing ways of chemical modification of 1,3,4-oxadiazoles is of considerable practical interest primarily due to the search for promising approaches to obtaining synthetic analogues of the known physiologically active substances [1, 2]. The modification of acyl hydrazides with suitable reagents is one of the ways to the synthesis of diazoheterocycles [3]. Given that the substituted 1,3,4-oxadiazoles possess a wide range of pharmacological activity [4, 5], the development of new modified systems on their basis is an important task.

Aiming to obtain new polyfunctional 1,3,4-oxadiazoles containing bioactive groups, we studied the reaction of *N*-anabasinylacetic acid hydrazide **I** with ethyl orthoformate. The starting *N*-anabasinylacetic acid hydrazide **I** was obtained by the method [6].



I **II**

The disadvantages of this reaction are long duration (over 25 h) and low yield (34%) of the reaction product **II**.

To increase the yield of 2-anabasinylmethyl-1,3,4-oxadiazole **II** and to reduce the reaction time, we performed this reaction in an alcoholic medium under microwave irradiation as one pot process [7]. Under microwave activation, uniform heating of the reaction mixture and no inertia at heating should promote the reaction [8]. It favors carrying out various syntheses, may change the selectivity and the reaction direction [9, 10], which cannot be achieved under standard classical conditions.

The reaction conditions were adjusted by varying the time (from 1 to 10 min) and the power of the irradiation (from 70 to 750 W). The most favorable conditions for the reaction of *N*-anabasinylacetic acid hydrazide **I** with ethyl orthoformate in 2-propanol medium are the power of microwave irradiation of 750 W and time of 7 min. In the studied conditions, the yield of the product **II** was 54%.

2-Anabasinylmethyl-1,3,4-oxadiazole **II** is a white powder substance, soluble in various solvents. Use of microwave activation reduces the reaction time from 25 h to 7 min at the irradiation power of 750 W.

The composition and structure of 2-anabasinylmethyl-1,3,4-oxadiazole **II** were confirmed by elemental analysis, IR and ^{1}H NMR spectra.

2-Anabasinylmethyl-1,3,4-oxadiazole (II). *a*. To a solution of 2.34 g (0.01 mol) of *N*-anabasinylacetic acid hydrazide **I** in 10 ml of 2-propanol was added 29.6 g (0.2 mol) of ethyl orthoformate. The mixture

was refluxed at 60–70°C for 25 h. The reaction progress was monitored by TLC. The excess of 2-propanol was distilled off. The thick oil was triturated with petroleum ether and recrystallized from 2-propanol. Yield 0.83 g (34%), mp 180–181°C.

b. To a solution of 2.34 g (0.01 mol) of *N*-anabasinylacetic acid hydrazide **I** in 30 ml of 2-propanol was added 29.6 g (0.2 mol) of ethyl orthoformate. The reaction mixture was subjected to microwave irradiation at 750 W for 7 min with breaks for 20–30 s. Treating was performed as above. Yield 1.31 g (54%), white powder, mp 181–183°C (2-propanol). ^{1}H NMR spectrum (500 MHz), δ, ppm (*J*, Hz): 1.25–1.70 m (6H, H^6, H^7, H^8), 2.96 t (1H, H^5, *J* 14.04), 8.36 d. d (1H, H^2, *J* 4.78), 8.60 s (1H, H^4), 7.22 d (1H, H^3, *J* 7.28), 8.51 d (1H, H^1, *J* 4.73), 7.33 s (2H, CH_2).

The IR spectra were recorded on a Nicolet AVATAR-320 Fourier-spectrometer from KBr pellets. The ^{1}H NMR spectra were taken on a Bruker DRX500 spectrometer at 500 MHz in DMSO-d_6 solution, internal reference TMS. Melting points were determined on a Boetius heating block. TLC analysis was carried out on Sorbfil plates, eluting with an isopropanol–benzene–ammonia mixture (10:5:2) and detecting with iodine vapor.

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