

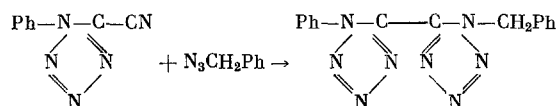
# SYNTHESIS OF TETRAZOLES BY THE REACTION OF FURAN AND THIOPHENE NITRILES WITH ORGANIC AZIDES UNDER HIGH PRESSURE

M. M. Krayushkin, A. M. Beskopyl'nyi,  
E. B. Zhuravleva, and V. M. Zhulin

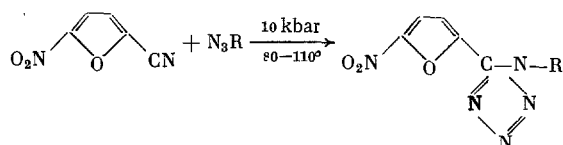
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The search for new synthetic approaches for the preparation of compounds containing directly bound heterocyclic and tetrazole fragments has resulted due to the physiological activity of these compounds [1].

One of the general methods for the synthesis of such products is the reaction of heterocyclic nitriles with organic azides under high pressure [2, 3]. Thus, we have previously shown that 1-phenyl-5-cyanotetrazole with benzyl azide gives a good yield of a ditetrazole derivative [3]



In the present work, we studied the reactions of furan and thiophene nitriles with methyl, amyl, and benzyl azides as well as with ethyl azodiacetate

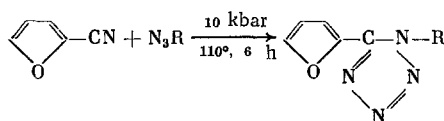


R = Me (I), PhCH<sub>2</sub> (II), EtO<sub>2</sub>CCH<sub>2</sub> (III), C<sub>5</sub>H<sub>11</sub> (IV).

The physicochemical indices for (I)-(III) coincide with those given by Snyder [1]. The structure of (IV) was supported by its elemental analysis and spectral methods.

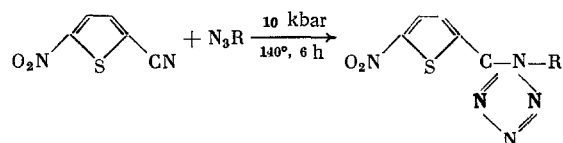
Phenyl azide does not react under these conditions. Similar behavior was observed in an attempt to obtain a ditetrazole derivative by the reaction of phenyl azide with 1-phenyl-5-cyanotetrazole [3]. In both cases, the lack of reaction is presumably a result of steric factors.

The absence of an electron-withdrawing nitro group on the furan ring sharply reduces the efficiency of this reaction. Thus, the reaction of 2-furonitrile with benzyl azide and ethyl azodiacetate leads to the formation of tetrazoles only in 7 and 11% yields, respectively



R = PhCH<sub>2</sub> (V), EtO<sub>2</sub>CCH<sub>2</sub> (VI).

The preparation of tetrazoles with comparable yields by the reactions of organic azides with 5-nitro-2-cyanothiophene requires more vigorous conditions than those for nitrofuronitrile

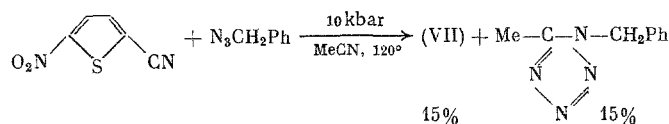


R = PhCH<sub>2</sub> (VII), EtO<sub>2</sub>CCH<sub>2</sub> (VIII).

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya*, No. 2, pp. 461-463, February, 1985. Original article submitted April 25, 1964.

As in the case of the unsubstituted furonitrile, this apparently is a consequence of the weaker electron-withdrawing capacity of the nitrothiophene fragment in comparison with the nitrofuran fragment.

Methylene chloride was used as the solvent for the reaction of nitrothiophenonitrile. This reaction at 10 kbar and 120°C gives (VII) and the adduct of (VII) with benzyl azide



An increase in the pressure to 14 kbar leads to an increase in the yield of (VII) up to 30%, although the yield of (IX) in this case is 26%. This is the first example of the formation of a tetrazole from an unactivated nitrile and an organic azide. The formation of 5-methyltetrazole derivatives apparently requires that the reactions of organic azides with nitriles in acetonitrile be carried out at  $\geq 110^\circ\text{C}$ .

Thus, the use of high-pressure techniques is useful for the preparation of tetrazoles by the reactions of furan and thiophene nitriles with organic azides.

#### LITERATURE CITED

The high-pressure syntheses were carried out in a system described in our previous work [4]. The IR spectra were taken in KBr pellets on a UR-20 spectrophotometer. The PMR spectra were taken in KBr pellets on a UR-20 spectrophotometer. The PMR spectra were taken on a Perkin-Elmer R-12 spectrometer at 60 MHz in  $\text{CD}_3\text{COCD}_3$  with HMDS as the internal standard.

**1-Methyl-5-(5-nitro-2-furyl)tetrazole (I).** A solution of 0.15 g (1.1 mmoles) 5-nitro-2-furonitrile [5] and 0.13 g (2.2 mmoles) methyl azide in 0.5 ml acetonitrile was maintained for 6 h at 10 kbar and  $90^\circ\text{C}$ . The solvent was distilled off and the residue was crystallized from 2-butanol to give 0.12 g (56.8%) (I), mp  $153-154^\circ\text{C}$  [1]. PMR spectrum ( $\delta$ , ppm): 4.41 s (3H, Me), 7.68 d (2H, CH,  $J = 6.65$  Hz). IR spectrum ( $\nu$ ,  $\text{cm}^{-1}$ ): 1360, 1520 ( $\text{NO}_2$ ), 3150 (CH).

**1-Benzyl-5-(5-nitro-2-furyl)tetrazole (II).** A solution of 0.2 g (1.5 mmoles) 5-nitro-2-furonitrile and 0.39 g (2.9 mmoles) benzyl azide in 0.5 ml acetonitrile was maintained for 6 h at 10 kbar and  $100^\circ\text{C}$ . The solvent was distilled off and the residue was crystallized from 4:1  $\text{CHCl}_3$ -hexane to give 0.28 g (78%) (II), mp  $134-135^\circ$  [1]. PMR spectrum ( $\delta$ , ppm): 5.71 s (2H,  $\text{CH}_2$ ), 7.21 s (5H, Ph), 7.43 d (2H, VH,  $J = 6.65$  Hz). IR spectrum ( $\nu$ ,  $\text{cm}^{-1}$ ): 3040, 3150 (CH), 1360, 1520 ( $\text{NO}_2$ ).

**Ethyl Ester of [5-(5-nitro-2-furyl)tetrazolyl-1]acetic Acid (III).** A solution of 0.15 g (1.1 mmoles) 5-nitro-2-furonitrile and 0.28 g (2.2 mmoles) ethylazodiazacetate in 0.5 ml acetonitrile was maintained for 6 h at 10 kbar and  $100^\circ\text{C}$ . The solvent was distilled off and the residue was crystallized from 2-butanol to give 0.25 g (85%) (III), mp  $118-119^\circ\text{C}$  [1]. PMR spectrum ( $\delta$ , ppm): 1.21 t (3H,  $\text{CH}_3$ ,  $J = 6.65$  Hz), 4.20 q (2H,  $\text{CH}_2$ ,  $J = 7.30$  Hz), 5.58 s (2H,  $\text{CH}_2$ ), 7.50 d (2H, CH,  $J = 3.99$  Hz). IR spectrum ( $\nu$ ,  $\text{cm}^{-1}$ ): 1520, 1350 ( $\text{NO}_2$ ), 1755 ( $\text{C}=\text{O}$ ), 3140 (CH).

**1-Amyl-5-(5-nitro-2-furyl)tetrazole (IV).** A solution of 0.15 g (1.1 mmoles) 5-nitro-2-furonitrile and 0.25 g (2.2 mmoles) amyl azide in 0.5 ml acetonitrile was maintained for 6 h at 10 kbar and  $100^\circ\text{C}$ . The solvent was distilled off and the residue was crystallized from 2-butanol to give 0.12 g (42.4%) (IV), mp  $108-109^\circ\text{C}$ . PMR spectrum ( $\delta$ , ppm): 4.42 t (2H,  $\text{CH}_2$ ,  $J = 7.0$  Hz), 7.64 d (2H, CH,  $J = 6.65$  Hz). IR spectrum ( $\nu$ ,  $\text{cm}^{-1}$ ): 1370, 1520 ( $\text{NO}_2$ ), 2885, 2950, 3150 (CH). Found: C 47.73; H 5.08; N 27.70%. Calculated for  $\text{C}_{10}\text{H}_{13}\text{O}_3\text{N}_5$ : C 47.81; H 5.18; N 27.89%.

**1-Benzyl-5-(5-nitro-2-thienyl)tetrazole (VII).** A solution of 0.15 g (0.974 mmole) 5-nitro-2-thiophenonitrile [6] and 0.26 (1.954 mmoles) benzyl azide in 0.5 ml  $\text{CH}_2\text{Cl}_2$  was maintained for 6 h at 10 kbar and  $140^\circ\text{C}$ . The solvent was distilled off and the residue was crystallized from 3:1  $\text{CHCl}_3$ -hexane to give 0.16 g (58%) (VII), mp  $121-122^\circ\text{C}$ . PMR spectrum ( $\delta$ , ppm): 5.93 s (2H,  $\text{CH}_2$ ), 6.83 s (5H, Ph), 7.25 d (2H, CH,  $J = 4.65$  Hz). IR spectrum ( $\nu$ ,  $\text{cm}^{-1}$ ): 1350, 1520 ( $\text{NO}_2$ ), 3095, 3120 (CH). Found: C 49.82; H 3.12; N 23.68; S 10.87%. Calculated for  $\text{C}_{12}\text{H}_9\text{O}_2\text{N}_5\text{S}$ : C 50.16; H 3.15; N 24.37; S 11.15%.

**Ethyl Ester of [5-(5-Nitro-2-thienyl)tetrazolyl-1]acetic Acid (VIII).** A solution of 0.15 g (0.974 mmole) 5-nitro-2-thiophenonitrile and 0.25 g (1.948 mmoles) ethyl diazoacetate in 0.5  $\text{CH}_2\text{Cl}_2$  was maintained for 6 h at 10 kbar and  $140^\circ\text{C}$ . The solvent was distilled off and the residue was crystallized from 2-butanol to give 0.18 g (64%) (VIII), mp  $63-64^\circ\text{C}$ . PMR spectrum ( $\delta$ , ppm): 1.25 t (3H,  $\text{CH}_3$ ,  $J = 7.0$  Hz), 4.05 q (2H,  $\text{CH}_2$ ,  $J = 7.00$  Hz), 5.33 s (2H,  $\text{CH}_2$ ), 7.67 d (2H, CH,  $J = 4.20$  Hz). IR spectrum ( $\nu$ ,  $\text{cm}^{-1}$ ): 1350, 1525 ( $\text{NO}_2$ ), 1755 ( $\text{C}=\text{O}$ ), 3120 (CH). Found: C 37.84; H 3.12; N 24.35; S 11.14%. Calculated for  $\text{C}_9\text{H}_9\text{O}_4\text{N}_5\text{S}$ : C 38.16; H 3.20; N 24.72; S 11.31%.

## CONCLUSIONS

The reactions of furan and thiophene nitriles with organic azides under high pressure yielded compounds containing tetrazolefuran and tetrazolythiophene fragments.

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## STRUCTURE OF TRIMETHYLSILYL DERIVATIVES OF ACETIC ACID HYDRAZIDES

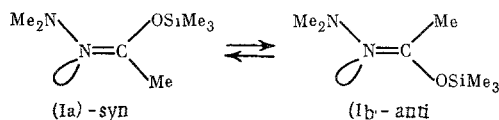
I. D. Kalikhman, O. B. Bannikova,  
A. V. Kalinin, B. N. Khasapov,  
S. L. Ioffe, V. A. Tartakovskii,  
and M. G. Voronkov

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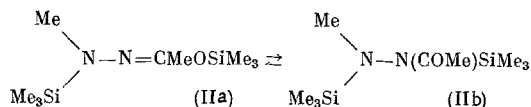
There have been virtually no structural studies of trimethylsilyl derivatives of carboxylic acid hydrazides [1, 2]. In the general case, these compounds may exist as several isomers due to equilibrium of hydrazone and hydrazide forms and hindered rotation about the C=N and C(O)-N bonds. According to our previous work [3], silylated hydrazides of trifluoroacetic acid exist predominantly in the hydrazone form.

In the present work, NMR spectroscopy was used to study mono- and bistrimethylsilyl derivatives of N'-methyl- and N',N'-dimethylhydrazides of acetic acid  $RNMeN(COMe)SiMe_3$ , where  $R = Me$  (I) or  $Me_3Si$  (II). Two isomers in mobile equilibrium are found for both compounds in the temperature range from  $-80$  to  $+100^\circ C$ .

According to our criteria for the structural assignment of isomers [3, 4], (I) may be considered to exist as an equilibrium mixture of two O isomers



and (II) may be considered to exist as an equilibrium mixture of O and N forms



Indeed, the  $^{17}\text{O}$  NMR spectrum of (I) has two overlapping signals (116.3 and 100.3 ppm) which are characteristic for the oxygen atom of the  $Me_3SiO$  group [5] and lacks signals in the reaction characteristic for carbonyl oxygen atoms. The  $^{15}\text{N}$  NMR spectrum of (I\*) shows two singlets (81.5 and 93.7 ppm) corresponding to  $sp^2$ -hybridized

Institute of Organic Synthesis, Siberian Branch, Academy of Sciences of the USSR, Irkutsk. N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya*, No. 2, pp. 464-466, February, 1985. Original article submitted May 28, 1984.