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Synthesis and Structure of New Ditopic Ligands Containing Tetrazole and 3-Nitro-1,2,4-triazole Fragments

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Abstract—Alkylation of 3-nitro-1,2,4-triazole with haloalkyltetrazoles has afforded in high yields previously unknown 1-[2-(3-nitro-1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-tetrazole and 2-*tert*-butyl-5-(3-nitro-1*H*-1,2,4-triazol-1-ylmethyl)-2*H*-tetrazole. The molecular and crystal structure of these compounds has been established by X-ray diffraction analysis (XRD).

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Derivatives of 1,2,4-triazole and tetrazole are used in various fields of human activity: in special technology, in industry, in agriculture as fungicides and herbicides, in biochemistry and pharmacology [1, 2]. In this connection compounds possessing in their structure both azole fragments are very interesting from the theoretical as well as practical viewpoint. They may have a complex of useful properties and the study of their behavior in various chemical processes is of interest for the development of the theory of heterocycles reactivity. Moreover since these compounds are specimens of ditopic ligands they are promising for designing hybrid organic-inorganic homo- and heterometallic systems possessing unique catalytic, adsorption, magnetic, and other physicochemical characteristics [3–6].

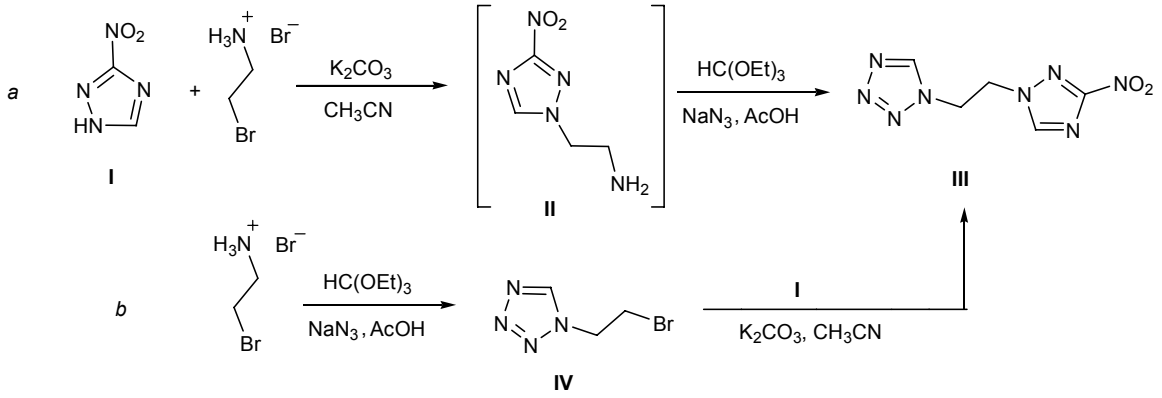
In extension of our research on functionalization of 3-nitro-1,2,4-triazole (**I**) [7–9] we showed in this study the possibility to use the classic procedures of nitrogen heterocycles functionalization for the synthesis of compounds combining in their molecules 3-nitro-1,2,4-triazol-1-yl with tetrazol-1-yl or tetrazol-5-yl fragments.

One of convenient methods of the preparation of 1-substituted tetrazoles consists in the heterocyclization of primary amines with triethyl orthoformate and sodium azide [10, 11]. Therefore in order to introduce into the molecule of azole **I** of an aminoethyl fragment whose amino group might be transformed into a tetrazole ring we have studied the alkylation of substrate **I** with 2-bromoethylamine. It was established by NMR spectroscopy that the alkylation occurred prevailingly with the formation of 1-(2-aminoethyl)-3-nitro-1,2,4-triazole (**II**). The oily substance was contaminated with 2-(2-aminoethyl)-3-nitro-1,2,4-triazole and also with initial azole **I** and 2-bromoethylamine. Considering the intermediate character of obtained amine **II** and the difficulties in its purification from the above mentioned impurities we used in the heterocyclization with triethyl orthoformate and sodium azide unpurified azole **II** separated from the reaction mixture after alkylation by filtration and evaporation of the filtrate in a vacuum. As a result we obtained in an overall yield of 20% 1-[2-(3-nitro-1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-tetrazole (**III**) whose molecule contained 3-nitro-1,2,4-triazol-1-yl and tetrazol-1-yl moieties connected by ethyl bridge (Scheme 1, method *a*).

Taking into account the relatively small yield of compound **III** we developed an alternative method of its preparation (Scheme 1, method *b*) including the stages of the synthesis of 1-(2-bromoethyl)tetrazole (**IV**) by heterocyclization of 2-bromoethylamine hydrobromide with triethyl orthoformate and sodium azide followed by the alkylation with compound **IV** of azole **I**. As a result compound **III** was obtained in over 90% yield.

Aiming at the preparation of a biheterocyclic compound containing in the structure 3-nitro-1,2,4-triazol-1-yl and tetrazol-5-yl fragments we studied the alkylation of azole **I** with 2-*tert*-butyl-5-chloromethyltetrazole that in boiling acetonitrile in the

Scheme 1.



presence of potassium carbonate led to practically selective formation of 2-*tert*-butyl-5-(3-nitro-1*H*-1,2,4-triazol-1-ylmethyl)-2*H*-tetrazole (**V**) in 95% yield (Scheme 2).

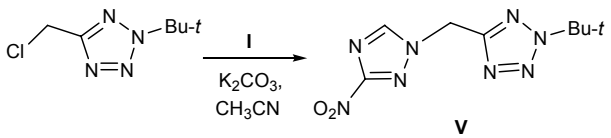
The virtually selective formation of compounds **III** and **V** in the studied conditions is well consistent with published data indicating that the alkylation of azole **I** with haloalkanes in the presence of bases affords in high yields either exclusively the corresponding 1-isomers [9, 12–15], or mixtures of 1- and 2-isomers with the prevalence of 1-isomer [16].

The composition and structure of compounds **III** and **V** were confirmed by the data of elemental analysis, by NMR and IR spectra, and by XRD analysis.

According to XRD data compound **III** crystallized in the monoclinic space group $P2_1/c$ with the following parameters of the unit cell: *a* 12.9269(5), *b* 5.4500(2), *c* 14.4116(7) Å, β 120.231(2)º, *Z* 4. All atoms are located in general positions (Fig. 1). In the tetrazole ring the formally double bonds are the shortest: N^2–N^3 1.2883(19) Å and N^4–C^5 1.302(2) Å. The lengths of the other bonds are in the range 1.3201(19)–1.346(2) Å. In the triazole ring also the formally double bonds are the shortest: N^9–C^{10} 1.3081(18) and N^{11}–C^{12} 1.319(2) Å. The lengths of the other bonds are in the range 1.331(2)–1.3485(16) Å. The tetrazole and triazole rings are nearly planar, with an average deviation of the atoms of rings from the least-squares plane of 0.0019(11) Å and 0.002(2) Å respectively.

The crystal structure of compound **III** contains intermolecular non classical hydrogen bonds C–H···O involving the C^6 of the methylene group and C–H···N

Scheme 2.



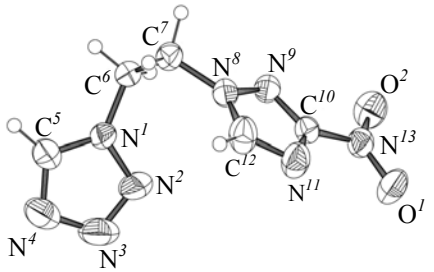


Fig. 1. Structure of the molecule of 1-[2-(3-nitro-1*H*-1,2,4-triazol-1-yl)-ethyl]-1*H*-tetrazole (**III**). Displacement ellipsoids are shown at the 50% probability level.

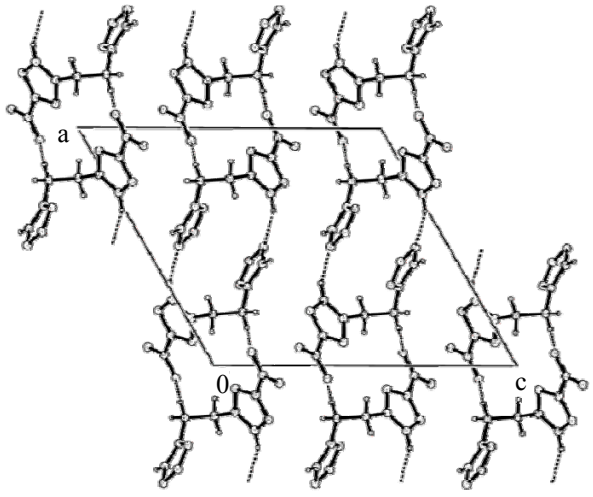


Fig. 2. Crystal packing of molecules of 1-[2-(3-nitro-1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-tetrazole (**III**). Hydrogen bonds are shown by dashed lines.

Table 1. Geometry of hydrogen bonds in the crystal structure of compounds **III** and **V**

Compound no.	D–H···A	D–H	H···A	D···A	Angle D–H···A, deg
III	C^{6}–H^{6A}···O^{2a}	0.963(15)	2.518(16)	3.405(2)	153.0(12)
	C^{12}–H^{12}···N^{4b}	0.933(18)	2.480(19)	3.338(2)	152.9(14)
V	C^{10}–H^{10B}···N^{4c}	0.962(14)	2.564(14)	3.5009(14)	164.5(11)
	C^{15}–H^{15}···N^{3c}	0.929(16)	2.426(16)	3.3174(15)	160.9(12)

Symmetry transformations: [a] $-x, -y + 1, -z$; [b] $-x + 1, y + 1/2, -z + 1/2$; [c] $-x + 1/2, y + 1/2, -z + 1/2$.

with the participation of the C–H group of the triazole ring (see the table). The first type of hydrogen bonds forms dimers which form layers normal to *c* axis owing to the second type of hydrogen bonds (Fig. 2).

According to XRD data compound **V** crystallized in the monoclinic space group $P2_1/n$ [*a* 11.6380(2), *b* 7.17920(10), *c* 13.9321(3) Å, β 91.2580(10)°, *V* 1163.77(4) Å^3, *Z* 4. All atoms are located in common positions (Fig. 3). In the tetrazole ring the longest bond is N^4–C^5 1.3437(14) Å, the other bond distances are in the range 1.3183(12)–1.3298(12) Å. In the triazole ring the longest bond is N^{11}–N^{12} 1.3533(12) Å, the other bond distances are in the range 1.3134(13)–1.3380(14) Å. The tetrazole and triazole rings are planar, with an average deviation of the atoms of rings from the least-squares plane of 0.0012(6) Å and 0.0011(7) Å respectively.

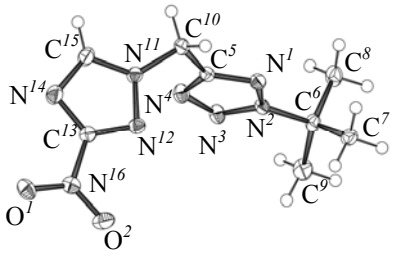


Fig. 3. Structure of the molecule of 2-*tert*-butyl-5-(3-nitro-1*H*-1,2,4-triazol-1-ylmethyl)-2*H*-tetrazole (**V**). Displacement ellipsoids are shown at the 50% probability level.

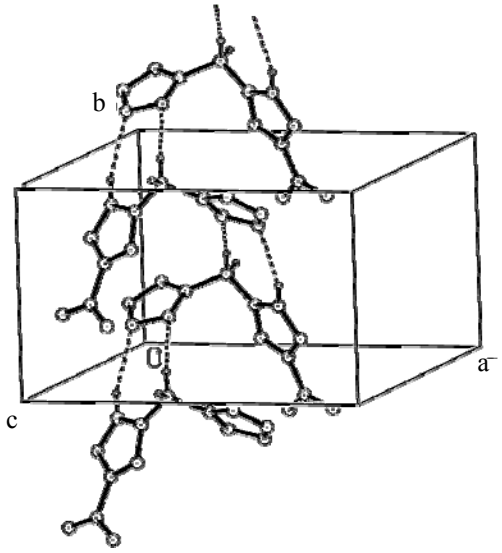


Fig. 4. Polymer chain bound by hydrogen bonds in the crystal structure of 2-*tert*-butyl-5-(3-nitro-1*H*-1,2,4-triazol-1-ylmethyl)-2*H*-tetrazole (**V**). *tert*-Butyl groups are not shown.

In the crystal structure of compound **V** only non-classical hydrogen bonds C–H···N are present between the hydrogen atoms of the methylene groups and the C–H groups of the triazole rings (see the table). These hydrogen bonds form polymer chains along the *b* axis (Fig. 4).

Considering the presence in the structure of compounds synthesized of two energetic heterocycles it was interesting to investigate their thermal behavior. The data of the complex thermal analysis* show that compound **III** after melting at 136°C (endo effect without mass loss) starts to decompose at the temperature around 180°C. The decomposition proceeds in three stages, two of which are accompanied with exo effects and correspond to the degradation of azole heterocycles. It is therewith presumable basing on the thermogravimetric data that in the first stage (exo effect maximum at 229°C) the decomposition of the tetrazole ring occurs with the ejection of the nitrogen molecule, and in the second stage (exo effect maximum at 315°C) the nitrotriazole ring is cleaved with ejection of CNO_2 fragment. Further the thermolysis products burning takes place.

Compound **V** melts at 73°C (endo effect without mass loss) and starts to decompose at the temperature around 180°C. The decomposition proceeds in two stages, one of which is accompanied with a pronounced exo effect with the maximum at 282°C. The

* The DSC and TGM curves are available from the authors by email.

weight loss at this thermolysis stage reached over 75%, indicating the materially simultaneous decomposition of both heterocycles present in the molecule.

EXPERIMENTAL

NMR spectra were registered on a spectrometer Bruker Avance-500 in DMSO-d_6 at operating frequencies 500.13 (^{1}H) and 125.76 MHz (^{13}C).

XRD data were obtained on a diffractometer Smart Apex II [17] [MoK_α radiation, graphite monochromator, λ 0.71073 Å, temperature 296 K for compound **III**, 100 K for compound **V**]. Crystal structures were solved by direct methods using program SIR2004 [18] and refined in the full-matrix least-squares method with respect to F^2 using SHELXL-97 software [19]. The molecular graphics was performed with the use of program packages ORTEP-3 for Windows [20] and PLATON [21]. The crystallo-graphic data on compounds **III** and **V** are deposited in Cambridge Crystallographic Data Center and are available by the numbers CCDC 940230 and 940231 respectively [22].

Differential thermal analysis was carried out on a thermal analyzer STA 449 (Netzsch) in a nitrogen atmosphere.

3-Nitro-1,2,4-triazole (**I**) was obtained from 3-amino-1,2,4-triazole and sodium nitrite in acid environment by the method [23]. 2-*tert*-Butyl-5-chloromethyltetrazole was obtained by the alkylation of 5-(chloromethyl)tetrazole with *t*-BuOH in sulfuric acid [24], 1-[2-(bromoethyl)]tetrazole (**II**) was prepared by heterocyclization of 2-bromoethylamine with triethyl orthoformate and sodium azide [25].

1-[2-(3-Nitro-1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-tetrazole (III). *a*. A mixture of 1.14 g (10 mmol) of azole **I**, 2.35 g (12 mmol) of bromoethylamine hydrobromide, and 3.45 g (25 mmol) of K_2CO_3 in 50 mL of acetonitrile was stirred at reflux for 20 h. Then the reaction mixture was cooled to room temperature, filtered, the precipitate on the filter was washed with 10 mL of acetonitrile, and the filtrate was evaporated in a vacuum. To the residue was added 0.715 g (11 mmol) of NaN_3, 4.38 g (30 mmol) of triethyl orthoformate, and at stirring was added 6.0 g (100 mmol) of glacial acetic acid. The mixture was stirred for 3 h at 100ºC, cooled, 2 mL of conc. HCl was added, the reaction mixture was filtered, and the filtrate was evaporated in a vacuum. The residue was recrystallized from a mixture ethanol–2-propanol, 1 : 10, yield 0.42 g (20%), yellowish needle crystals, mp 135–136°C. ^{1}H NMR spectrum, δ, ppm: 4.88 t (2H, CH_2), 5.02 t (2H, CH_2), 8.74 s (1H, $CH_{triazole}$), 9.31 s (1H, $CH_{tetrazole}$). ^{13}C NMR spectrum, δ, ppm: 46.6 (CH_2), 49.7 (CH_2), 144.4 ($CH_{tetrazole}$), 147.4 ($CH_{triazole}$), 162.2 (CNO_2). Found, %: C 28.69; H 2.71; N 53.49. $C_5H_6N_8O_2$. Calculated, %: C 28.57; H 2.86; N 53.33.

b. To a heated to boiling stirred slurry of 0.775 g (6.8 mmol) of azole **I** and 0.94 g (6.8 mmol) of K_2CO_3 in 30 mL of acetonitrile was slowly added a solution of 1.2 g (6.8 mmol) of 1-[(2-bromoethyl)]tetrazole (**II**) in 20 mL of acetonitrile. The reaction mixture was stirred at reflux for 20 h, cooled to room temperature, filtered, the precipitate on the filter was washed with 10 mL of acetonitrile, and the filtrate was evaporated in a vacuum. The residue was dissolved in acetone, the solution was filtered, and the filtrate was evaporated in a vacuum. Thus a spectrally pure compound **III** was obtained as oily substance that crystallized within 24 h. Yield 1.35 g (95%). After recrystallization from water or from a mixture ethanol–2-propanol, 1 : 10, mp 135–136°C.

2-*tert*-Butyl-5-(3-nitro-1*H*-1,2,4-triazol-1-ylmethyl)-2*H*-tetrazole (V). To a heated to boiling stirred slurry of 0.69 g (6 mmol) of azole **I** and 0.9 g (6.5 mmol) of K_2CO_3 in 30 mL of acetonitrile was slowly added a solution of 1.1 g (6.2 mmol) of 2-*tert*-butyl-5-chloromethyltetrazole in 20 mL of acetonitrile. The reaction mixture was stirred at reflux for 20 h, cooled to room temperature, filtered, the precipitate on the filter was washed with 10 mL of acetonitrile, and the filtrate was evaporated in a vacuum. The residue was dissolved in ethyl acetate, the solution was filtered, and the filtrate was evaporated in a vacuum. Yellow oily substance slowly crystallized on storage. Yield 1.44 g (95%). After recrystallization from water mp 71–73°C. ^{1}H NMR spectrum, δ, ppm: 1.68 s [9H, $C(CH_3)_3$], 5.99 s (2H, CH_2), 9.08 s (1H, $CH_{triazole}$). ^{13}C NMR spectrum, δ, ppm: 28.7 (CH_3), 45.2 (CH_2), 64.4 [$C(CH_3)_3$], 147.5 ($CH_{triazole}$), 159.7 ($C_{tetrazole}$), 162.2 (CNO_2). Found, %: C 40.81; H 5.13; N 41.29. $C_8H_{12}N_7O_2$. Calculated, %: C 40.34; H 5.04; N 41.18.

REFERENCES

1. Curtis, A.D.M. and Jenings, N., *Compr. Heterocycl. Chem. 3*, 2008, vol. 5, p. 160.
2. Ostrovskii, V.A., Koldobskii, G.I., and Trifonov, R.E., *Compr. Heterocycl. Chem. 3*, 2008, vol. 6, p. 257.

3. Gaponik, P.N., Voitekhovich, S.V., and Ivashkevich, O.A., *Russ. Chem. Rev.*, 2006, vol. 75, p. 507.
4. Boland, Y., Hertsens, P., Marchand-Brynaert, J., and Garcia, Y., *Synthesis*, 2006, p. 1504.
5. Aromi, G., Barrios, L.A., Roubeau, O., and Gamez, P., *Coord. Chem. Rev.*, 2011, vol. 255, p. 485.
6. Kharisov, B.I., Martinez, P.E., Jimenez-Perez, V.M., Kharissova, O.V., Martinez, B.N., and Perez, N., *J. Coord. Chem.*, 2010, vol. 63, p. 1.
7. Grigoriev, Yu.V., Voitekhovich, S.V., and Ivashkevich, O.A., *Russ. J. Org. Chem.*, 2012, vol. 48, p. 610.
8. Matulis, V.E., Halauko, Y.S., Ivashkevich, O.A., Grigoriev, Y.V., and Gaponik, P.N., *Tetrahedron*, 2010, vol. 66, p. 3415.
9. Degtyarik, M.M., Lyakhov, A.S., Ivashkevich, L.S., Voitekhovich, S.V., Sukhanov, G.T., and Grigoriev, Y.V., *Z. anorg. allg. Chem.*, 2012, vol. 638, p. 950.
10. Gaponik, P.N., Karavai, V.P., and Grigor'ev, Yu.V., *Chem. Heterocycl. Comp.*, 1985, vol. 21, p. 1255.
11. Grigor'ev, Yu.V., Maruda, I.I., and Gaponik, P.N., *Proceed. Nat. Acad. Sci. Bel., Ser. Chem. Sci.*, 1997, no. 4, p. 80.
12. Mugunthan, G., Ramakrishna, K., Ravindranathan, K.K.P., Sriram, D., and Yogeeswari, P., *Eur. J. Med. Chem.*, 2011, vol. 46, p. 4725.
13. Papadopoulou, M.V., Bloomer, W.D., Rosenzweig, H.S., Chatelain, E., Ioset, J.-R., Kaizer, M., Wilkinson, S.R., and McKenzie, C., *J. Med. Chem.*, 2012, vol. 55, p. 5554.
14. Ulhag, S., Chinje, E.C., Naylor, M.A., Jaffar, M.S., Ian, J., and Thread-gill, M.D., *Bioorg. Med. Chem.*, 1998, vol. 6, p. 2139.
15. Roman, G., Szarek, W.A., Rahman, M.N., Jia, Z., Vukomanovich, D., and Nakatsu, K., *Chemical Biol. Drug Des.*, 2010, vol. 75, p. 68.
16. Sukhanov, G.T. and Lukin, A.Yu., *Chem. Heterocycl. Comp.*, 2005, vol. 41, p. 861.
17. Bruker (2010). APEX2 and SAINT. Bruker AXS Inc., Madison, Wisconsin, USA.
18. Burla, M.C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G.L., De Caro, L., Giacovazzo, C., Polidori, G., and Spagna, R., *J. Appl. Crystallogr.*, 2005, vol. 38, p. 381.
19. Sheldrick, G.M., *Acta Crystallogr.*, 2008, A64, p. 112.
20. Farrugia, L.J., *J. Appl. Crystallogr.*, 1997, vol. 30, p. 565.
21. Spek, A.L., *Acta Cryst.*, 2009, D65, p. 148.
22. *https://www.ccdc.cam.ac.uk/services/structure_deposit/.*
23. Closset, J.-L., Copin, A., Dreze, Ph., Alderweireldt, F., Durant, F., Evrard, G., and Michel, A., *Bull. Soc. Chim. Belg.*, 1975, vol. 84, p. 1023.
24. Koren', A.O. and Gaponik, P.N., *Chem. Heterocycl. Comp.*, 1990, vol. 26, p. 1366.
25. Grunert, C.M., Weinberger , P., Schweifer, J., Hampel, C., Stassen, A.F., Mereiter, K., and Linert, W., *J. Mol. Struct.*, 2005, vol. 733, p. 41.