Synthesis and some transformations of 2-[(4-aminofurazan-3-yl)-1*H*-1,2,4-triazol-5-yl]acetic acid derivatives*

N. S. Aleksandrova,[a] S. S. Semyakin,[a] A. A. Anisimov,[b] M. I. Struchkova,[a] and A. B. Sheremetev[a]★

[a]*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. E-mail: sab@ioc.ac.ru*

[b]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation*

Two methods for the synthesis of 1,2,4-triazolylacetic ester bearing an aminofurazanyl substituent at the position 5 were developed. The triazole cycle was formed *via* the cyclocondensation of 3-aminofurazanecarboxylic acid hydrazide or amidrazone with ethoxycarbonylethyl acetimidate hydrochloride.

Key words: 1,2,4-triazole, furazan, cyclocondensation, single crystal X-ray diffraction.

The 1,2,4-triazole ring is widely applied as a structural unit in the development of pharmaceuticals, herbicides, and materials.[1—4] A design of the new derivatives is usually based on the functionalized molecules, the so-called building blocks, which possess several reaction centers. An opportunity to involve these blocks in various reactions is employed in the directed synthesis. The derivatives of 2-(3-R-1,2,4-triazol-5-yl)acetic acid are fairly efficient building blocks.[5—12] However, there was only the one such compound reported, wherein the substituent R is an azolyl, 3,3′-bi(1,2,4-triazol-5-yl)-5,5′-diacetic acid.[5]

To continue our ongoing research on the synthesis of 1,2,4-triazoles linked with 1,2,5-oxadiazole (furazan) ring,[13] herein we report on the possible methods for preparation of 2-[(3-furazan-3-yl)-1*H*-1,2,4-triazol-5-yl]-acetic acids and some of their transformations, as well as single crystal X-ray diffraction studies of the intermediate and target products.

In 1959, it was shown that a convenient pathway to 1,2,4-triazole ring formation is the cyclocondensation reaction of imino esters with acid hydrazides.[14] However, it was reported that this reaction in some cases resulted in either 1,3,4-oxadiazoles instead of triazoles,[15] or stopped at the step of formation of linear products of the condensation, or was accompanied by an resinification.[5] Amidrazones can be used as the alternative of acid hydrazides in the cyclization reaction with iminoesters, giving the expected 1,2,4-triazoles.[5] The both approaches were utilized in this work.

The starting 3-aminofurazancarboxylic acid hydrazide (**1**) can be readily obtained from methyl ester of this acid.[16] The reaction of hydrazide **1** with available ethoxycarbonylacetimidate ethyl ester hydrochloride **2** in a boiling alcohol, *i.e.* under the conditions used for condensations of **2** earlier,[5] led to a mixture of products (according to TLC control, there were seven spots of similar intensity). Fusion[14] of hydrazide **1** with iminoester **2** resulted in an inseparable resinified mixture. Our studies revealed that the cyclocondensation between compounds **1** and **2** proceeds smoothly in the presence of triethylamine and acetic acid in boiling acetonitrile. At the optimal ratio between the reactants, triazolylacetic ester **3** was prepared in the yield of 85% (Scheme 1). It should be noted that the formation of side product **4** containing an 1,3,4-oxadiazole cycle was not observed under the found conditions.

The structure of triazole **3** was confirmed by spectral methods and also unambiguously proved by the single crystal X-ray diffraction. Compound **3** crystallized in the form of four symmetrically independent molecules (A, A′, A″, and AA). Figure 1 shows a general view for one of the independent molecules (A). In all the molecules, both heterocycles are located at the same plane, and a relatively weak intramolecular bond N(3)—H(3)...N(4) is formed (Table 1). The carboxyl moiety is rotated with respect to

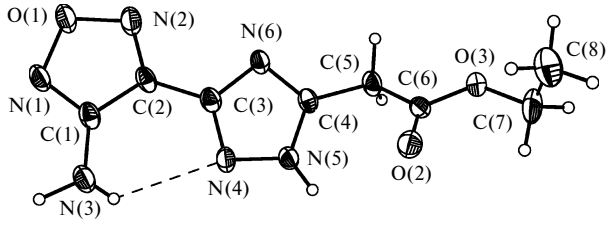

Fig. 1. Molecular structure of compound **3** with thermal ellipsoids drawn at 50% probability level.

* Dedicated to Academician of the Russian Academy of Sciences B. A. Trofimov on the occasion of his 80th birthday.

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Scheme 1

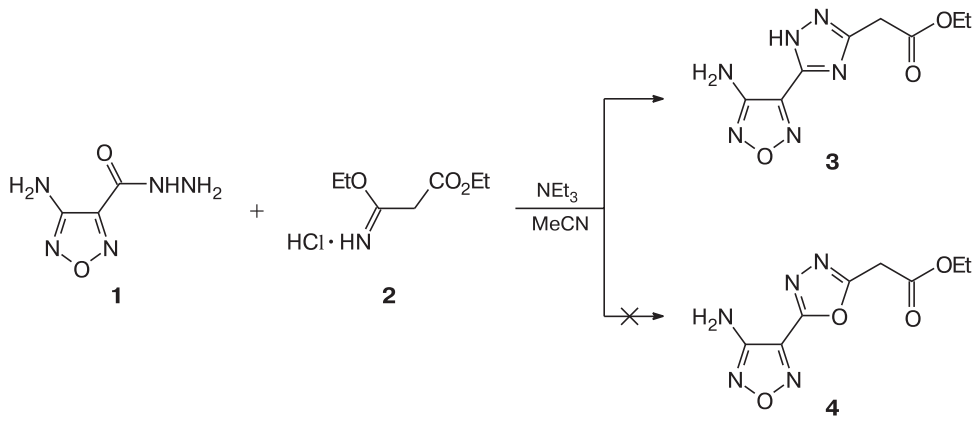


Table 1. Parameters of intra- (IntraM) and intermolecular (InterM) hydrogen bonds (HB) in the structure of compound **3**

Moiety	*d*/Å			ω/deg	Symmetry operation	HB
	N—H	H...N(O)	N...N(O)	N—H—N(O)		
N(5)—H(5)...N(6″)	0.85(4)	2.04(4)	2.870(5)	165(3)	$1-x,1-y,-z$	InterM (A, A″)
N(3)—H(3A)...N(4)	0.75(4)	2.51(4)	3.016(5)	127(3)	x, y, z	IntraM
N(3)—H(3B)...N(1)	1.02(4)	2.15(4)	3.137(6)	164(3)	$1-x, 2-y,1-z$	InterM (A, A)
N(5′)—H(5′)...N(6A)	0.92(4)	1.90(4)	2.812(5)	171(3)	x, y, z	InterM (A′, AA)
N(3′)—H(3′A)...N(4′)	0.77(4)	2.52(4)	3.048(5)	127(3)	x, y, z	IntraM
N(3′)—H(3′B)...N(1″)	0.81(4)	2.32(4)	3.098(6)	161(3)	$1-x,1-y,1-z$	InterM (A′, A″)
N(5″)—H(5″)...N(6)	0.98(4)	1.88(4)	2.854(5)	171(3)	$2-x, 1-y, -z$	InterM (A″, A)
N(3″)—H(3″A)...N(4″)	0.80(4)	2.51(4)	3.024(6)	124(3)	x, y, z	IntraM
N(3″)—H(3″)B...N(1′)	0.87(4)	2.35(4)	3.170(6)	157(3)	$1-x,1-y,1-z$	InterM (A″, A′)
N(5A)—H(5A)...N(6′)	0.99(4)	1.86(4)	2.831(5)	164(3)	$x+1, y, z$	InterM (AA, A′)
N(3A)—H(3AA)...N(4A)	0.81(4)	2.54(4)	3.072(5)	124(3)	x, y, z	IntraM
N(3A)—H(3AB)...O(2′)	0.87(4)	2.11(4)	2.977(5)	175(3)	$2-x,1-y,-z$	InterM (AA, A′)

the plane of heterocycles so that the expected intramolecular hydrogen bond N(5)—H(5)...O(2) is not formed.

Differences in O—N bond lengths of the furazan ring obey the tendency discovered previously:[17–19] the N—O bond at a donor substituent is longer (Table 2).

Differences in the molecular structure of independent molecules are due mainly to the orientation of carboxyl moiety relative to the plane containing the heterocycles (see Table 2).

In the each of four molecules, the hydrogen atom is located at the N(5) atom of the triazole ring. Calculations for three possible tautomers (the hydrogen atom at N(5), N(4), or N(6) atoms)* demonstrated that the N(5)—H tautomer is more favorable by 0.7 and 2.6 kcal mol^{-1} than the N(4)—H and N(6)—H tautomers, respectively, which

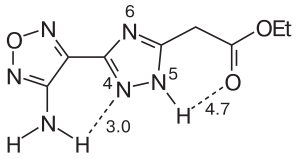
* The numbering of nitrogen atoms corresponds to that shown in Fig. 1.

Table 2. Selected bond lengths (*d*) and torsion angles (φ) of symmetrically independent molecules in the crystal structure of compound **3**

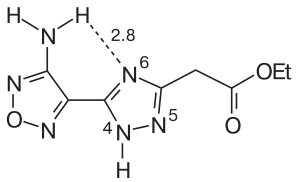
Molecule	*d*/Å		φ/deg	
	N(1)—O(1)	N(2)—O(1)	N(5)—C(4)—C(5)—C(6)	C(4)—C(5)—C(6)—O(2)
A	1.400(4)	1.383(4)	−50.8(5)	7.2(5)
A′	1.400(4)	1.379(4)	67.6(5)	163.8(4)
A″	1.409(4)	1.374(4)	79.4(4)	−19.2(5)
AA*	1.404(4)	1.374(4)	−90.7(15)	8(3)

* The angle values are given only for the major component of disordered moiety (see Experimental).

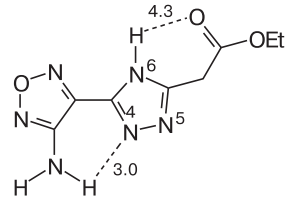
could be due to the formation of the intramolecular N(5)—H(5)...O(2) bond in the isolated molecule. However, there was no such bond in the real crystal. Probably, the formation of N(5)—H tautomer in the crystal is related to its stabilization by a system of intermolecular hydrogen bonds (see Table 1). It is important that the strongest intermolecular H-bonds are formed between the symmetrically independent molecules, which can apparently explain their formation. A similar situation is usually observed in cocrystals, crystalline solvates, and crystals with $Z' > 1$ (see Refs 20—26).



N(5)—H



N(4)—H



N(6)—H

The condensation of amidrazone **5** with iminoester **2** in DMF or DMSO at ~100 °C is stopped at the formation of linear product (Scheme 2),[27,28] whose yield depends marginally on the heating time (1—4 h) and the concentration of reactants in the solvent, being of 31—37%. According to data reported in the literature, the reaction of iminoesters with hydrazides can produce two types of linear products as a result of substitution of (i) the imino group in the iminoether,[5] the product of type **6**, or (ii) ethoxy groups,[12,14,29] the product of type **6′**.

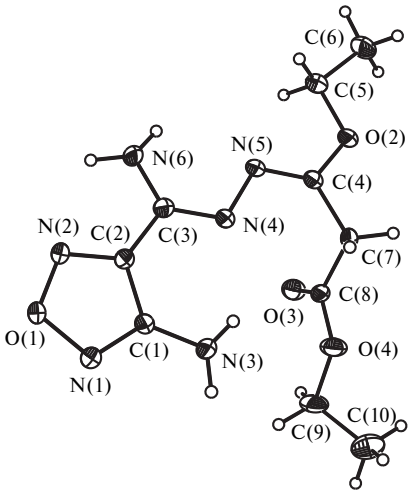
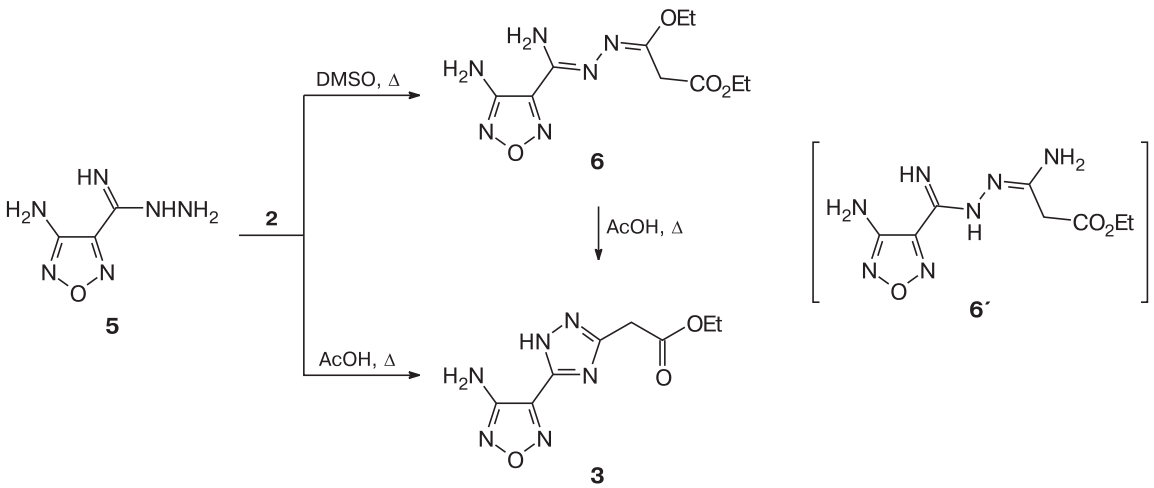


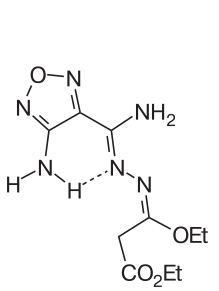
Fig. 2. Molecular structure of compound **6** with thermal ellipsoids drawn at 50% probability level.

According to ^{1}H and ^{13}C NMR spectra, the product contained two ethoxy groups, *i.e.* it was compound **6**, whose structure was also confirmed by the single crystal X-ray diffraction. Compound **6** crystallized in the form of two symmetrically independent molecules (A and A′) possessing the similar structure (Fig. 2).

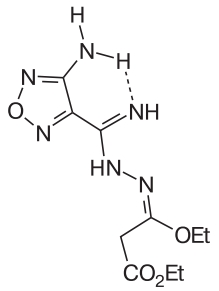
As in the case of compound **3**, molecule **6** can hypothetically be existed in the form of three tautomers. The two most probable forms are shown below.

Scheme 2





(NH_2)-**6**



(NH—N)-**6**

According to the quantum chemical calculations, there are two intramolecular H-bonds in the both forms (in the crystal, only the N(3)—H(3A)...N(4) bond is observed) (Table 3). While in the isolated state, the tautomer bearing the amino group at the C=NN bond, the NH_2-tautomer (observed experimentally), is more energetically favorable by 10.1 kcal mol^{-1} than the tautomer in which the proton is located at the hydrazine nitrogen atom, the NH—N-tautomer. As in compound **3**, the N(1)—O(1) bond at the NH_2 group in the both independent molecules of compound **6** is significantly longer (N(1)—O(1): 1.404(3), N(2)—O(1): 1.372(3) Å in molecule A; N(1′)—O(1′): 1.409(3), N(2′)—O(1′): 1.377(3) Å in molecule A′). The most strongly bound dimer in the crystal (due to the two N(3)—H(1)...N(1′) and N(3′)—H(1′)...N(1) H-bonds) is precisely formed between the symmetrically independent molecules (see Table 3). At the same time, fairly strong H-bonds were also observed for symmetrically dependent molecules.

A reflux of the solution of compound **6** in acetic acid for 8—10 h was accompanied by the cyclocondensation leading to the formation of same triazole **3** in the yield of 28—30%. It should be noted that triazole **3** can be directly prepared *via* the interaction of compound **5** with **2** in refluxed acetic acid (see Scheme 2). The yield of triazole **3** did not exceed 20%, but it is greater than that of overall reaction **5**→**6**→**3** (9—11%).

The saponification of ester **3** under both alkaline and acidic conditions led smoothly to the formation of acid **7** in a practically quantitative yield (Scheme 3). The treatment of ester **3** with aqueous ammonia was of the same efficiency giving amide **8**. *N*-Methylation of compound **3** with dimethyl sulfate in the presence of KOH occurred at the N(1) and N(2) atoms of triazole ring (see Scheme 2) providing a mixture of two isomeric products **9** and **10** (~1 : 1) in the yield of 82%, which were separated chromatographically. While this reaction was carried out in the presence of NaOH, the yield of methylation products was almost two times decreased, but their ratio did not change. The structure of isomers **9** and **10** was unambiguously confirmed by 2D correlation spectroscopy of $^{1}H—^{13}C$ HMBC NMR. The spectrum of compound **9** contains a cross-peak of the hydrogen atoms of Me group with the carbon atom of triazole ring at the furazanyl substituent, while there was that with the carbon atom $\underline{C}—CH_2CO_2Et$ in the case of compound **10**.

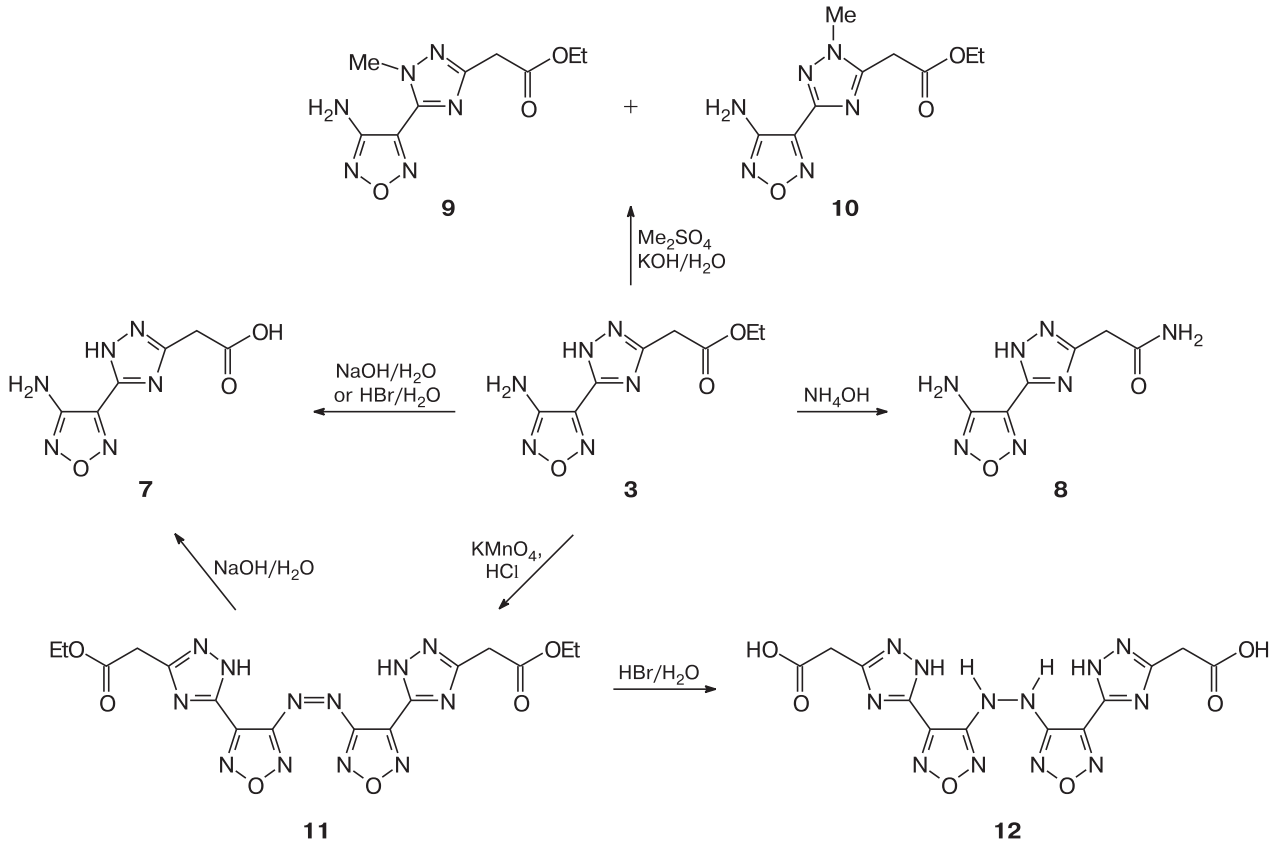
The oxidation of amino group in compound **3** by the $KMnO_4$—HCl system used traditionally for the synthesis of azofurazans[30] led to the formation of azo compound **11** in the yield of 87%. It should be noted that during the saponification of azo compound **11**, there was observed not only the expected reaction, but also a reduction of the azo group. Thus, the azo group was reduced to an amino group upon the treatment with an aqueous alkali, which led to the formation of acid **7**. In the case of hydrolysis by aqueous HBr, the azo group was reduced to a hydrazo group giving diacid **12** in the yield of 73% (see Scheme 3).

In conclusion, the condensation of aminofurazanecarboxylic acid hydrazide with ethoxycarbonylethyl acetimidate hydrochloride was demonstrated as the efficient preparative method for 1,2,4-triazole-3-ethyl ester bearing the aminofurazanyl substituent at the position 5. This compound containing several reaction sites is the convenient precursor for a target-oriented synthesis. More opportunities of its applications will be published in our upcoming reports. It should be noted that in the last decade there has been an intense growth of interest in compounds, the framework of which is constructed from an ensemble of azoles, including the furazan ring, which has in 2016 become the subject of comprehensive review.[31] Since the publication of this review, a number of furazan derivatives combined with pyrazole,[32] various oxadiazoles,[33—37] triazole,[38] and tetrazole[39—43] rings has been obtained. Compounds incorporating these structural combinations

Table 3. Parameters of intra- (IntraM) and intermolecular (InterM) hydrogen bonds (HB) in the structure of compound **6**

Moiety	*d*/Å			ω/deg N—H—N(O)	Symmetry operation	HB
	N—H	H...N(O)	N...N(O)			
N(3)—H(1)...N(1′)	0.85(4)	2.31(4)	3.150(5)	170(3)	$x, y-1, z$	InterM (A, A′)
N(3′)—H(1′)...N(1)	0.95(4)	2.23(4)	3.114(5)	154(3)	$x, y+1, z$	InterM (A′, A)
N(6)—H(3)...O(3)	0.87(4)	2.12(3)	2.951(4)	160(3)	$2-x,-y,1-z$	InterM (A, A)
N(6′)—H(3′)...O(3′)	0.87(4)	2.26(3)	3.048(4)	151(3)	$2-x, 1-y, 2-z$	InterM (A′, A′)
N(3)—H(2)...N(4)	0.83(4)	2.23(4)	2.877(5)	136(3)	x, y, z	IntraM
N(3′)—H(2′)...N(4′)	0.85(4)	2.32(4)	2.894(5)	125(3)	x, y, z	IntraM

Scheme 3



are considered promising materials. The design of more advanced materials requires the development of new methods and building blocks appropriate for their synthesis. The compounds reported in this work will expand the opportunities in the design of future materials.

Experimental

IR spectra were recorded on a Bruker ALPHA spectrometer in KBr pellets. ^1H, ^{13}C, and ^{15}N NMR spectra were recorded on a Bruker AM-300 spectrometer (300, 75, and 51 MHz, respectively) in DMSO-d_6 or $CDCl_3$. Chemical shifts in the NMR spectra were determined with respect to solvent residual signals (2.50 ppm for ^1H and 39.5 ppm for ^{13}C) or to the external standard, $MeNO_2$, for ^{15}N. Mass spectra were recorded on a Finnigan MATINCOS 50 spectrometer (direct input, EI ionization, 70 eV). High-resolution mass spectra (HRMS) were obtained using on a Bruker MicroOTOFII instrument with electrospray ionization. Elemental analysis was performed on a PerkinElmer Series II 2400 instrument. Melting points were determined in a Gallenkamp melting block without any corrections. The reaction progress and purity of obtained compounds were monitored by TLC on Sorbfil 60 F254 plates. The starting methyl ester and amidrazone of 4-aminofurazan-3-carboxylic acid (**5**) were prepared according to the known procedures.[16,27,28]

Hydrazide of 4-aminofurazan-3-carboxylic acid (1). Hydrazine hydrate (2.2 g, 0.044 mol) was added dropwise at room temperature to a solution of methyl 3-amino-furazancarboxylate (6.3 g, 0.044 mol) in methanol (150 mL). The reaction mixture was stirred for 1 h and stored for 16 h, then evaporated to dryness. The residue was recrystallized from water. Colorless crystalline product **1** was isolated in the yield of 5.37 g (85%), m.p. 170—171 °C. IR, ν/cm^{-1}: 3426, 3355, 3333, 3158, 2962, 2887, 1699, 1683, 1630, 1559, 1536, 1491, 1427, 1361, 1328, 1217, 1124, 1004, 984, 952. ^1H NMR ($CDCl_3$), δ: 4.7 (br.s, 2 H, NN$\underline{H}_2$); 6.32 (s, 2 H, CN$\underline{H}_2$); 10.31 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 140.0, 156.1, 157.1. MS (EI, 70 eV), *m*/*z* (I_{rel} (%)): 143 $[M]^+$ (113). Found (%): C, 25.26; H, 3.57; N, 48.88. $C_3H_5N_5O_2$ (143.11). Calculated (%): C, 25.18; H, 3.52; N, 48.94.

Ethyl 3-(4-aminoufurazan-3-yl)-1,2,4-triazol-5-acetate (3). ***A***. NEt_3 (6.4 mL, 44.8 mmol) was added to a suspension of iminoester hydrochloride **2** (9 g, 46 mmol) in acetonitrile (52 mL) at 25 °C under stirring, and 30 min later, hydrazide **1** (5.44 g, 38 mmol) and acetic acid (1.15 mL, 20 mmol) were added to the mixture. The resulting mixture was refluxed for 5 h, cooled, and evaporated on a rotary evaporator. The dry residue was crystallized from water to give colorless crystals of product **3** (7.7 g, 85%), R_f 0.3 (CCl_4—MeCN, 3 : 1), m.p. 188—189 °C. IR, ν/cm^{-1}: 3508, 3466, 3406, 2989, 2943, 2818, 2755, 2704, 1733, 1626, 1597, 1465, 1395, 1369, 1324, 1220, 1183, 1063, 1026, 984, 874. ^1H NMR (DMSO-d_6), δ: 1.19 (t, 3 H, Me, J = 6.7 Hz); 4.04 (s, 2 H, CH_2CO); 4.13 (m, 2 H, CH_2Me); 6.43 (s, 2 H, NH_2); 14.66 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 13.8, 32.1, 61.0, 139.2, 151.2, 151.5, 155.1, 167.8. MS (EI, 70 eV), *m*/*z*: 238 $[M]^+$ 193, 181, 165, 153, 135, 107, 83. Found (%): C, 40.42; H, 4.27;

N, 35.22. $C_8H_{10}N_6O_3$ (238.08). Calculated (%): C, 40.34; H, 4.23; N, 35.28.

B. A solution of compound **6** (0.16 g, 0.56 mmol) in acetic acid (3 mL) was refluxed for 8 h. The solvent was evaporated, the residue was washed with water (0.5 mL) and crystallized from water. Product **3** was isolated in the yield of 0.04 g (30%), m.p. 188—189 °C.

C. Similarly to method ***A***, product **3** (0.11 g, 19%) identical to the known sample was prepared from amidrazone **5** (0.36 g, 2.53 mmol) and iminoester **2** (0.5 g, 2.55 mol) in acetic acid (5 mL).

Ethyl 3-[3-(4-aminofurazan-3-yl)-3-aminomethylidenehydrazono]-3-ethoxypropanoate (6). A mixture of iminoester **2** (0.59 g, 3 mmol) and amidrazone **5** (0.43 g, 3 mol) in DMSO (5 mL) was heated at 100—105 °C for 2 h. The reaction mixture was cooled and diluted with water (10 mL). The precipitate was filtered, washed with water, dried in air, and recrystallized from ethanol. Light cream product **6** was obtained in the yield of 0.27 g (31%), R_f = 0.7 (CCl_4—MeCN, 3 : 1), m.p. 102—103 °C. IR, ν/cm^{-1}: 3492, 3376, 2955, 1708, 1637, 1572, 1533, 1372, 1331, 1288, 1275, 1179, 1052, 1034, 1002. ^{1}H NMR (DMSO-d_6), δ: 1.14 (t, 3 H, Me, J = 6.7 Hz); 1.26 (t, 3 H, Me, J = 6.8 Hz); 3.55 (s, 2 H, CH_2CO); 4.05 (d, 2 H, CH_2Me, J = 6.9 Hz); 4.28 (d, 2 H, CH_2Me, J = 6.9 Hz); 6.41 (s, 2 H, NH_2); 6.76 (s, 2 H, NH_2). ^{13}C NMR (DMSO-d_6), δ: 13.7, 13.9, 36.2, 60.5, 62.4, 140.5, 147.5, 154.9, 161.0, 167.6. ^{15}N NMR (DMSO-d_6), δ: 33.6, −11.2, −99.5, −114.7, −297.9, −328.2. Found (%): C, 42.31; H, 5.69; N, 35.22. $C_8H_{10}N_6O_3$ (284.28). Calculated (%): C, 42.25; H, 5.67; N, 35.16.

3-(3-Aminofurazan-4-yl)-1,2,4-triazole-5-acetic acid (7). ***A.*** A suspension of ester **3** (2 g, 8.4 mmol) in aqueous (18 mL) solution of NaOH (0.7 g, 17.5 mmol) was stirred at 70 °C for 1 h. The reaction mixture was cooled to 10 °C and acidified to pH 3 with H_2SO_4 (20%). The formed precipitate was filtered off, washed with water (2×5 mL), and dried in air. Product **7** was isolated as a colorless amorphous solid in the yield of 1.69 g (96%), m.p. 258—264 °C. After recrystallization from water, m.p. was 264—265 °C. IR, ν/cm^{-1}: 3478, 3461, 3342, 2938, 2706, 1742, 1706, 1632, 1596, 1468, 1421, 1396, 1332, 1278, 1237, 1189, 1128, 1064, 1016, 986, 935, 900, 872. ^{1}H NMR ($CDCl_3$), δ: 3.95 (s, 2 H, CH_2); 6.41 (s, 2 H, NH_2); 14.5 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 32.4, 139.2, 150.5, 152.4, 155.2, 169.4. MS (EI, 70 eV), m/z (I_{rel} (%)): 210 $[M]^+$ (5), 166 (8), 153 (30), 135 (19), 109 (75), 44 (100). Found (%): C, 34.34; H, 2.90; N, 39.91. $C_6H_6N_6O_3$ (210.15). Calculated (%): C, 34.29; H, 2.88; N, 39.99.

B. Ester **3** (0.5 g, 2.1 mmol) was suspended in aqueous HBr (48%, 5 mL) and stirred with stirbar at room temperature. After 1 h, a homogeneous solution was formed, which was additionally stirred for 24 h; this resulted in a suspension. Then the pH of reaction mixture was adjusted to 3 with NaOH (10%) at 5 °C. The formed precipitate was filtered off, washed with water (3×5 mL), and dried in air. Product **7** was isolated in the yield of 0.42 g (96%), m.p. 259—260 °C. After recrystallization from water, m.p. was 264—265 °C. The compound was identical to the product obtained according to method ***A***.

C. A suspension of azo compound **11** (0.348 g, 0.7 mmol) in aqueous (3.1 mL) solution of NaOH (0.12 g, 3 mmol) was heated to 70 °C and stirred at this temperature for 2 h. The reaction mixture was cooled to 10 °C and acidified to pH 3 with H_2SO_4 (20%). The formed precipitate was filtered off, washed with water, and dried in air. A colorless amorphous solid was isolated in the yield of 0.16 g (52%), and then crystallized from water, m.p. 264—265 °C. The product was identical to compound **7** obtained according to method ***A***.

3-(3-Aminofurazan-4-yl)-1,2,4-triazole-5-acetamide (8). Ester **3** (0.238 g, 1 mmol) was added to an aqueous solution of ammonia (24%, 5 mL). The resulting suspension was stirred at 50 °C until the solution was formed (~1 h). The reaction mixture was evaporated on a rotary evaporator, and the dry residue was recrystallized from water. Colorless amorphous product **8** was obtained in the yield of 0.195 g (93%), m.p. 294—295 °C (decomp.). IR, ν/cm^{-1}: 3459, 3346, 3305, 3202, 3051, 2975, 2934, 2812, 2755, 2909, 1677, 1636, 1594, 1560, 1471, 1428, 1393, 1332, 1270, 1176, 1131, 1064, 1014, 983, 866. ^{1}H NMR ($CDCl_3$), δ: 3.79 (s, 2 H, CH_2); 6.41 (s, 2 H, NH_2); 7.23 (s, 1 H, CONH); 7.72 (s, 1 H, CONH); 14.55 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 33.3, 139.4, 150.5, 152.9, 155.2, 168.6. Found (%): C, 34.52; H, 3.39; N, 46.82. $C_6H_7N_7O_2$ (209.17). Calculated (%): C, 34.45; H, 3.37; N, 46.88.

Methylation of compound 3. A solution of KOH (0.56 g, 10 mmol) in abs. ethanol (17 mL) was added to a suspension of triazole **3** (2 g, 8.4 mmol) in abs. ethanol (17 mL) under stirring. Dimethyl sulfate (1.59 g, 12.6 mmol) was added to the resulting solution. The reaction mixture was stirred under reflux for 3.5 h, cooled, and poured into methylene chloride (400 mL). The resulting solution was washed with brine (3×100 mL), dried over $MgSO_4$, and evaporated. The mixture of isomers **9** and **10** was obtained in the yield of 1.74 g (82%). The isomers were separated by column chromatography (SiO_2 40/100, eluent was $CHCl_3$—CCl_4, 1 : 1). Isomer **9** was eluted first from the column, then **10**.

Ethyl {2-[5-(4-aminofurazan-3-yl)-1-methyl-1*H*-1,2,4-triazol-3-yl]}acetate (9) was recrystallized from $CHCl_3/CCl_4$ to give colorless amorphous solid (0.8 g, 37.8%), m.p.122—123 °C. IR, ν/cm^{-1}: 3402, 3292, 3247, 3214, 3187, 2957, 1737, 1636, 1572, 1500, 1446, 1409, 1402, 1371, 1336, 1286, 1211, 1185, 1095, 1079, 1055, 1040, 1022, 993, 907, 881, 861. ^{1}H NMR (DMSO-d_6), δ: 1.19 (t, 3 H, Me, J = 7.0 Hz); 3.83 (s, 2 H, CH_2CO); 4.11 (q, 2 H, $OC\underline{H}_2Me$, J = 7.0 Hz); 4.13 (s, 3 H, $NC\underline{H}_3$); 6.58 (s, 2 H, NH_2). ^{13}C NMR (DMSO-d_6), δ: 14.0, 33.9, 37.8, 60.8, 136.5, 142.9, 155.4, 156.9, 168.9. ^{15}N NMR (DMSO-d_6), δ: 32.5, −12.4, −71.4, −122.6, −166.2, −329.0. MS (EI, 70 eV), m/z (I_{rel} (%)): 252 $[M]^+$ (3), 195 (12), 179 (5), 167 (3), 149 (19), 121 (100). Found (%): C, 42.91; H, 4.82; N, 33.24. $C_9H_{12}N_6O_3$ (252.23). Calculated (%): C, 42.86; H, 4.80; N, 33.32.

Ethyl {2-[3-(4-aminofurazan-3-yl)-5-methyl-5*H*-1,2,4-triazol-5-yl]}acetate (10) was crystallized from $CHCl_3/CCl_4$ to give colorless amorphous solid (0.82 g, 38.7%), m.p. 120—121 °C. IR, ν/cm^{-1}: 3476, 3311, 2989, 1706, 1627, 1598, 1525, 1483, 1457, 1399, 1375, 1335, 1214, 1157, 1094, 1021, 980, 901, 876, 869. ^{1}H NMR (DMSO-d_6), δ: 1.20 (t, 3 H, Me, J = 12.0 Hz); 3.94 (s, 3 H, $NC\underline{H}_3$); 4.14 (q, 2 H, $OC\underline{H}_2Me$, J = 12.0 Hz); 4.18 (s, 2 H, CH_2CO); 6.40 (s, 2 H, NH_2). ^{13}C NMR (DMSO-d_6), δ: 13.8, 31.7, 35.9, 61.2, 139.0, 149.7, 151.2, 155.2, 167.5. ^{15}N NMR (DMSO-d_6), δ: 32.7, −11.6, −74.5, −121.7, −163.0, −329.9. Found (%): C, 42.89; H, 4.84; N, 33.27. $C_9H_{12}N_6O_3$ (252.23). Calculated (%): C, 42.86; H, 4.80; N, 33.32.

4,4′-Bis(3-ethoxycarbonylmethyl-1,2,4-triazol-5-yl)azofurazan (11). A solution of $KMnO_4$ (1.26 g, 8 mmol) in water (50 mL) was added dropwise at room temperature and under vigorous stirring to a suspension of compound **3** (2.4 g, 10 mmol) in a mixture of conc. HCl (10 mL) and water (20 mL). The reaction

Table 4. Crystallographic data and X-ray diffraction experiment parameters for compounds **3** and **6**

Parameter	Compound **3**	Compound **6**
Formula	$C_8H_{10}N_6O_3$	$C_{10}H_{16}N_6O_4$
Molecular weight	238.22	284.29
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
a/Å	9.692(4)	7.9614(14)
b/Å	14.133(6)	9.5073(17)
c/Å	16.144(6)	19.959(4)
α/deg	85.798(9)	82.080(3)
β/deg	75.141(9)	78.880(3)
γ/deg	88.914(9)	65.541(3)
V/Å^3	2131.8(15)	1346.5(4)
Z	8	4
d_{calc}/g cm^{-3}	1.484	1.402
Absorption coefficient μ/mm^{-1}	0.118	0.111
F(000)	992	600
θ range for the data collection/deg	1.88—27.00	1.04—26.19
The number of reflections		
measured	20807	4898
independent (R_{int})	9299 (0.1026)	4898 (0.1028)
with $I \geq 2\sigma(I)$	4089	2965
The number of refined parameters	736	394
Completeness of a dataset (%)	99.9	96.1
GOOF	0.949	1.085
Convergent reliability index ($R_1(F)$)[a] [$I \geq 2\sigma(I)$]	0.0691	0.0889
Convergent reliability index ($wR_2(F^2)$[b] [all data]	0.1720	0.1862
Residual electron density (ρ_{max}/ρ_{min})/e Å^3	0.489/−0.332	0.309/−0.345

[a] $R_1 = \sum |F_o - |F_c|| / \sum(F_o)$; [b] $wR_2 = (\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]^{1/2}$.

mixture after 2 h was discolored with oxalic acid and extracted with ethyl acetate (5×50 mL). The combined extracts were washed with brine (2×25 mL), dried over $MgSO_4$, and evaporated. The residue was recrystallized from MeCN to give yellow product **11** (2 g, 86%), m.p. 203—204 °C. R_f 0.3 (CCl_4 : MeCN, 3 : 1). IR, ν/cm^{-1}: 3128, 2991, 1738, 1726, 1439, 1372, 1335, 1299, 1216, 1138, 1032, 990, 982, 933, 844. ^{1}H NMR ($CDCl_3$), δ: 1.18 (br.s, 3 H, Me); 4.05 (br.s, 2 H, CH_2); 4.13 (br.m, 2 H, CH_2); 14.76 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 13.8, 32.3, 61.2, 143.9, 148.4, 152.9, 161.9, 168.0. HRMS: found, m/z 473.1381 $[M + H]^+$; $C_{16}H_{16}N_{12}O_6$; calculated, m/z 473.1394. Found (%): C, 40.75; H, 3.44, N, 35.49. $C_{16}H_{16}N_{12}O_6$ (472.38). Calculated (%): C, 40.68; H, 3.41; N, 35.58.

1,2-Bis(3-(1*H*-3-carboxymethyl-1,2,4-triazol-5-yl)furazan-4-yl)hydrazine (12). Azo compound **11** (0.4 g, 0.84 mol) was stirred in aqueous HBr (48%, 5 mL) at 30—40 °C. The solution was being gradually formed. The reaction mixture was stirred for 3 days and cooled to 5 °C; the precipitate was filtered off, washed with water, and dried in air. Product **12** was obtained in the yield of 0.26 g (73%), m.p. 154—155 °C. IR, ν/cm^{-1}: 3449, 3281, 3229, 3088, 1717, 1582, 1551, 1290, 1221, 1190, 1056, 1030, 948, 915. ^{1}H NMR ($CDCl_3$), δ: 3.97 (s, 3 H, CH_2); 6.2 (br.s, NH + H_2O); 8.74 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 32.4, 138.7, 149.9, 152.6, 156.3, 169.3. HRMS: found, m/z: 419.0919 $[M + H]^+$; $C_{12}H_{11}N_{12}O_6$; calculated, m/z 419.0924. Found (%): C, 34.52; H, 2.47; N, 40.11. $C_{12}H_{10}N_{12}O_6$ (418.29). Calculated (%): C, 34.46; H, 2.41; N, 40.18.

X-ray diffraction analysis of compounds **3** and **6** was performed on an APEX II CCD diffractometer (λ(Mo-$K\alpha$) = 0.71073 Å, graphite monochromator, ω-scan) at 120 K. The structures were solved by the direct method and refined using the full-matrix least-squares on F^2_{hkl} in the anisotropic approximation for non-hydrogen atoms. Hydrogens at the N atoms were located in a difference electron density maps and refined in the isotropic approximation. The other hydrogen atoms were added geometrically. The major parameters of crystal structure are given in Table 4. The ester moiety of compound **3** in all the four symmetrically independent molecules is partially or completely disordered. The detailed information is provided in the CIF file. The both structures are deposited with the Cambridge Crystallographic Data Centre CCDC 1861870 and 1861871 for compounds **3** and **6**, respectively, and available at www.ccdc.cam.ac.uk.

Calculation procedure. The molecules of compounds **3** and **6** were optimized using GAUSSIAN03 software package[44] at the M052X/6-311G(df,pd) approximation. The adequacy of this approximation for the calculation of structure and energy of various nitrogenous heterocycles was reported in a number of works.[45—48] The calculated electron density distribution was analyzed within the framework of theory of R. Bader "Atoms in molecules"[49] using the AIMALL program.[50] To estimate the energy of contacts, its correlation with the potential energy density $V(r)$ at the critical point of bond ($E_{int} = ½V(r)$)[51,52] was used, which is useful for the analysis of various types of interactions.[53—56]

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