ISSN 1070-4280, Russian Journal of Organic Chemistry, 2018, Vol. 54, No. 8, pp. 1241–1249. © Pleiades Publishing, Ltd., 2018.
Original Russian Text © N.I. Zemlyanaya, T.M. Karnozhitskaya, V.I. Musatov, I.S. Konovalova, S.V. Shishkina, V.V. Lipson, 2018, published in Zhurnal Organicheskoi Khimii, 2018, Vol. 54, No. 8, pp. 1227–1235.

Synthesis and Chemical Transformations of 5-Alkyl(phenyl)-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-oles

N. I. Zemlyanaya[a,b], T. M. Karnozhitskaya[a], V. I. Musatov[b], I. S. Konovalova[b], S. V. Shishkina[b,c], and V. V. Lipson[a–c]*

[a] *Danilevsky Institute of Problems of Endocrine Pathology, National Academy of Sciences of Ukraine, ul. Alchevskikh 10, Kharkiv, 61002 Ukraine*
**e-mail: lipson@ukr.net*

[b] *Institute of Single Crystals, National Academy of Sciences of Ukraine, Kharkiv, 61001 Ukraine*

[c] *Karazin Kharkiv National University, Kharkiv, 61022 Ukraine*

Received August 30, 2017

Abstract—5,5,7-Trimethyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol was synthesized by cyclocondensation of 3-amino-1,2,4-triazole with 4-methylpent-3-en-2-one; its chemical transformations, and also the transformations of 5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol were investigated in reactions with reagents of diverse electronic nature.

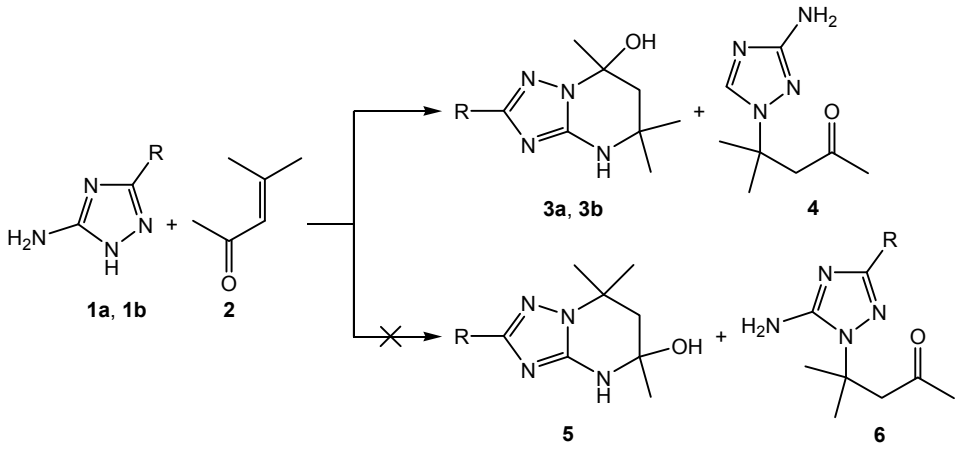
DOI: 10.1134/S1070428018080201

In the investigation of azolopyrimidines with partially or fully hydrogenated azine cycle the interests of organic, medicinal chemistry and pharmacology are combined. These heterocyclic systems are usually referred to as *drug like* molecules, and methods of their synthesis, based on reactions of α-aminoazoles with carbonyl 1,3-bielectrophiles or cascade transformations with synthetic precursors of the latter are widely used to obtain large libraries of compounds, designed to perform pharmacological tests by methods of *high-throughput screening* [1–3]. However the structural diversity of azolopyrimidines may be provided not only by the application of new components in the synthesis, but also due to a chemical modification of compounds containing several functional groups, for example, hydroxy group and secondary amino group, in the pyrimidine ring. Previously we described a method of preparation of such detivatives, 5-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-oles underlain by cyclocondensation of 3-amino-1,2,4-triazoles with cinnamic aldehyde [4]. The purpose of this study is to extend the series of partially hydrogenated azolopyrimidines by reaction products of 3(5)-amino-1,2,4-triazoles **1a** and **1b** with 4-methylpent-3-en-2-one **2** by establishing the direction of this interaction and investigating chemical properties of alkyl-(aryl)tetrahydrotriazolo[1,5-*a*]pyrimidines.

At refluxing amine **1a** with 1,5-fold excess of 4-methylpent-3-en-2-one **2** in acetone in the presence of catalytic amounts of piperidine for 24 h we obtained a mixture of compounds **3a** and **4** in low yields (Scheme 1). The reaction involving amine **1b** in the same conditions was accompanied with tarring. It was possible to raise the yield of triazolopyrimidine **3a** and β-adduct **4** by a prolonged (30 days) keeping at room temperature amine **1a** and enone **2** in a ratio 1 : 3.5 in acetone in the presence of catalytic amounts of piperidine. In similar conditions from aminotriazole **1b** within 10 days only triazolopyrimidine **3b** was obtained. Compounds of isomeric structure **5** and **6** were not detected in any of the experiments.

The structure of compounds **3a**, **3b**, and **4** was proved by spectral methods, the composition was established by elemental analysis. In the IR spectra of triazolopyrimidines **3a** and **3b** the most characteristic wide absorption band is observed in the range 3256–2932 cm^{-1} being a superposition of vibrations of hydroxy, imino, methyl, and methylene groups. The spectrum of β-adduct **4** is distinguished from that described above by the presence of absorption bands of NH_2 group in the region 3432–3152 and of carbonyl group at 1712 cm^{-1}.

Scheme 1.



In the ^{1}H NMR spectra of triazolopyrimidines **3a** and **3b** signals of all methyl groups appear in high-field, methylene protons forming *AD* system are observed as doublet of doublets at 1.91–1.93 ppm, in low-field signals of groups OH and NH are present as broadened singlets, δ 6.27 and 7.07–7.19 ppm respectively, and also singlet of methine proton of the triazole cycle in compound **3a** appears at 7.35 ppm. It is impossible to make definite choice between structures **3** and **5** according to obtained spectral data.

^{1}H NMR spectrum of β-adduct **4** is distinguished from the spectrum of condensed compound **3a** by the region of aliphatic protons resonance (signals of methylene group appear in it as a singlet, δ 2.87 ppm), the lack of the signal of OH group, and the presence of a broadened singlet of the amino group at 5.18 ppm. Also a downfield shift of 0.6 ppm is observed for the signal of the methine proton of the triazole ring as compared with the similar signal in the spectrum of triazolopyrimidine **3a**. This suggests that in compound **4** the substituent is present at the atom N^1, not at the atom N^2 of the triazole ring as in alternative structure **6** [5].

The structure of synthesized compounds was finally proved by X-ray diffraction (XRD) analysis of single crystals of compounds **3a** and **4** (Figs. 1, 2).

In compound **3a** the tetrahydropyrimidine cycle is present in the *semi-chair* conformation in both molecules (A and D) found in the independent part of the unit cell [puckering parameters [6]: *S* 0.70, Θ 35.7°, Ψ 25.7° (A), *S* 0.67, Θ 39.0°, Ψ 15.4° (D)]. Deviations of atoms C^4 and C^5 from the average plane of the other atoms of the ring are –0.38 and 0.29 Å

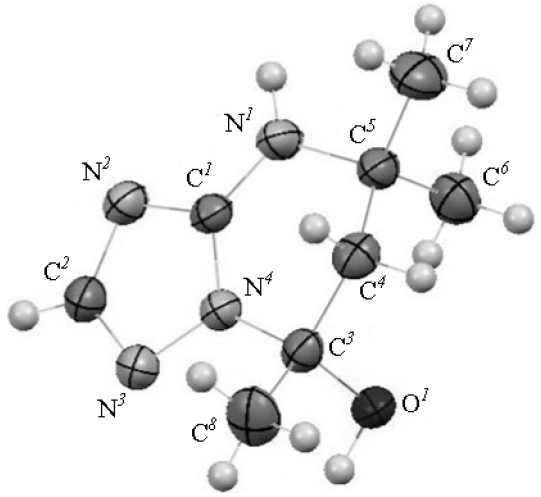


Fig. 1. Structure of the molecule of 5,5,7-trimethyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol **3a** according to XRD data. Thermal ellipsoids are shown at 50% probability level.

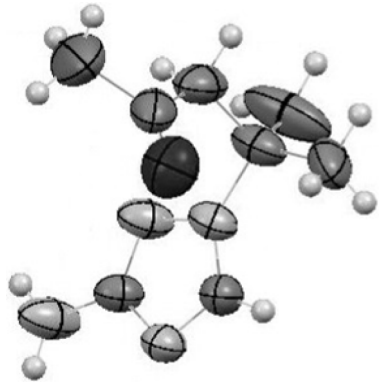
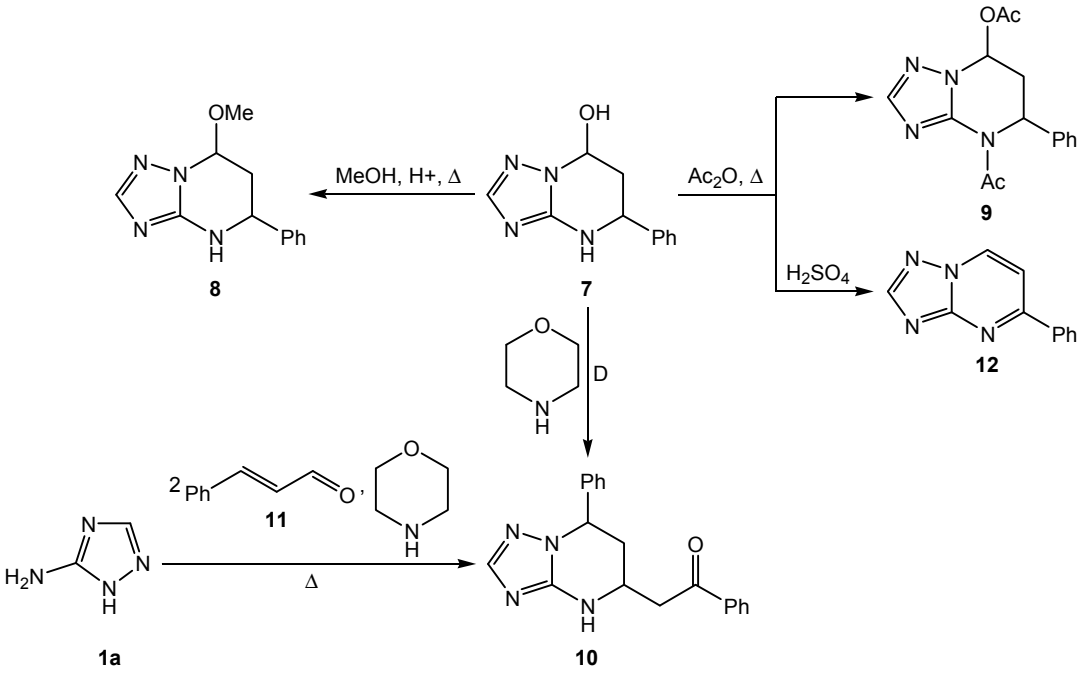


Fig. 2. Structure of the molecule of 4-(3-amino-1*H*-1,2,4-triazol-1-yl)-4-methylpenthan-2-one **4** according to XRD data. Thermal ellipsoids are shown at 50% probability level.

Scheme 2.



(A), 0.47 and –0.17 Å (D). In both molecules the methyl substituent at the atom C^3 occupies the equatorial position, and the hydroxy group, the axial position [torsion angles $C^1N^4C^3C^8$ 135.1(2) (A), 136.9 (2) (D), $C^1N^4C^3O^1$ 102.7(2) (A), –100.1(2)° (D)].

In crystals of compound **4** the substituent at the atom N^2 in both molecules present in the independent part of the unit cell is turned in such a way that the atom C^4 is in a *–ac*-position with respect to the C^2–N^4 bond [torsion angle $C^2N^4C^3C^4$ –118.7(4) (A), –137.1(4)° (D)]. The methylcarbonyl fragment is in a *+sc*-conformation with respect to the N^2–C^3 bond and is slightly non-coplanar to the C^3–C^4 bond [torsion angles $N^2C^3C^4C^5$ 52.8(4) (A), 55.2(5) (B), $C^3C^4C^5O^1$ 16.5(6) (A), 12.4(7)° (D)].

According to the structure of compounds **3a** and **4** it may be assumed that the first act of the reaction between 3-amino-1,2,4-triazole **1a** and enone **2** is the alkylation by the β-carbon atom of unsaturated ketone of the endo- and exocyclic nucleophilic centers in the aminoazole. The product of alkylation at the endocyclic center N^1 (β-adduct **4**) is incapable of further intramolecular cyclocondensation. In the case of 5-amino-3-(methylsulfanyl)-1,2,4-triazole **1b** the electrophile attack on the atom N^2 is apparently prevented by the presence of a substituent at the neighboring carbon atom. Probably that is why the reaction with amine **1b** occurs regioselectively with the formation of triazolopyrimidine **3b**.

The chemical transformations of tetrahydro[1,2,4]-triazolo[1,5-*a*]pyrimidin-7-ols were investigated by the example of 5,5,7-trimethyl derivative **3a** and of previously synthesized 5-phenyl-4,5,6,7-tetrahydro-

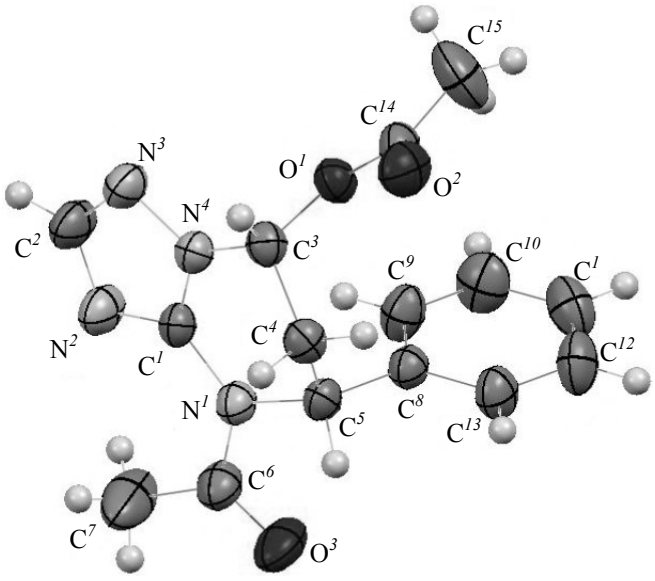


Fig. 3. Structure of the molecule of 4-acetyl-5-phenyl-4,5-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-yl acetate **9** according to XRD data. Thermal ellipsoids are shown at 50% probability level.

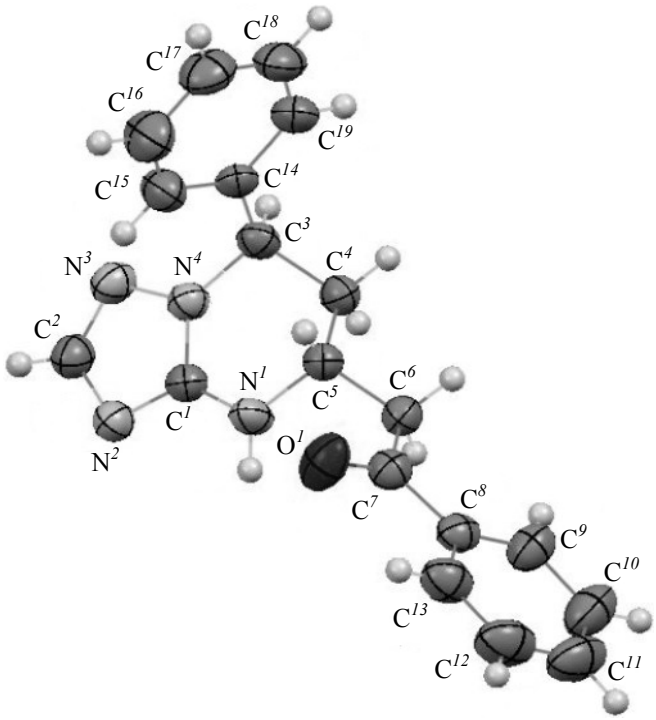


Fig. 4. Structure of the molecule of 1-phenyl-2-(7-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5-yl)-ethan-1-one **10** according to XRD data. Thermal ellipsoids are shown at 50% probability level.

[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol **7** [4]. The presence in the structure of compounds **3a** and **7** of secondary amino and hydroxy groups allows performing their chemical modification by a fairly wide set of reagents (Scheme 2).

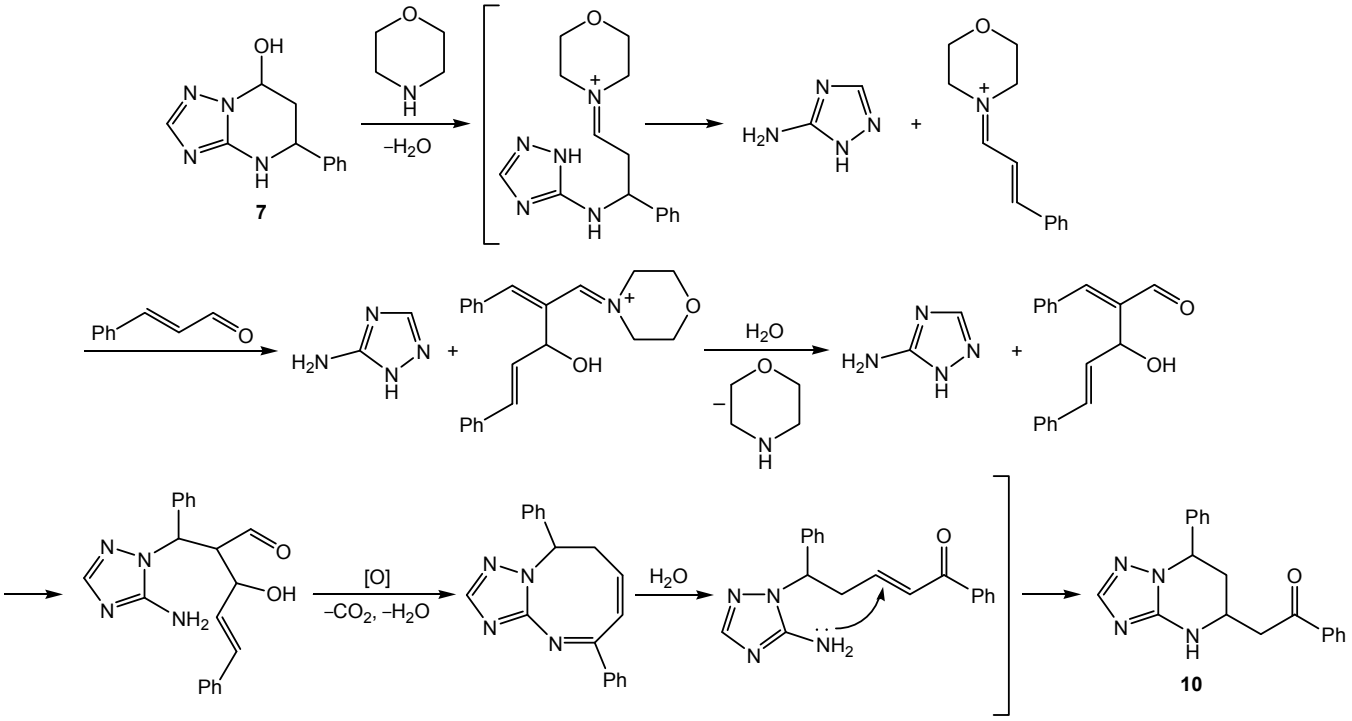
At a prolonged refluxing (40 h) in methanol at acid catalysis alcohol **7** converts into ether **8** in a low yield. The acylation of compound **7** occurs at both nucleophilic centers with the formation of diacetyl derivative **9**, whose structure along with spectral methods was proved by XRD analysis (Fig. 3).

The tetrahydropyrimidine cycle in both molecules of compound **9** found in the independent part of the unit cell is in an asymmetrical *semi-chair* conformation [pucking parameters: *S* 0.70, Θ 35.6°, Ψ 14.2° (A), *S* 0.67, Θ 39.1°, Ψ 18.1° (D)]. Deviations of atoms C^4 and C^5 from the least-squares plane of the other atoms of the ring are 0.50 and –0.16 Å (A), 0.46 and –0.20 Å (D). Phenyl and ester substituents are situated in the axial positions [torsion angles $C^1N^4C^3O^1$ –100.2(2) (A), 105.2(2) (D), $C^1N^1C^5C^8$ 93.7(2) (A), –94.3(2)° (B)] and are in the *cis*-conformation with respect to the ring [pseudo-torsion angle $O^1C^3\cdots C^5C^8$ –3.6(1) (A), 1.1(1)° (D)]. Wherein the planes of the ester and phenyl substituents are slightly turned with respect to the corresponding endocyclic bonds N^4–C^3 and N^1–C^5 [torsion angles $N^4C^3O^1C^{14}$ –165.1(2) (A), 165.7(1) (B), $N^1C^5C^8C^{13}$ –14.5(2) (A), 24.3(2)° (B)].

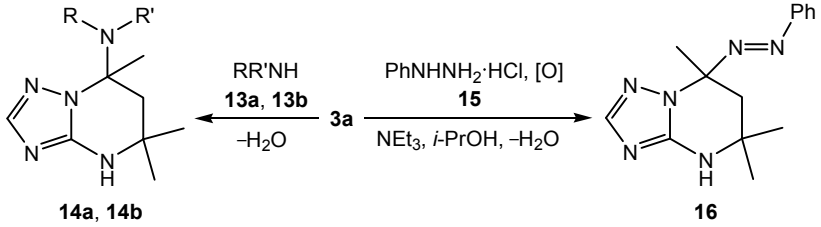
Tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol **7** turned out to be stable enough against dehydration. The attempt at this transformation by refluxing in morpholine resulted not in a dihydro derivative, but in compound **10** in a low yield. According to IR spectroscopy data, in the structure of this compound a carbonyl group is present ($\nu_{C=O}$ 1688 cm^{-1}). In the ^1H NMR spectrum signals appear of two CH_2 groups as multiplets in the region 2.21 and 2.35 ppm, one of which is partially overlapped by the signals of DMSO-d_6, of two protons of CH as a multiplet at 3.79 ppm and a triplet at 5.51 ppm. The signal of the methine proton of the triazole ring is overlapped by the signals of aromatic protons. The broadened singlet of NH group is present at 7.10 ppm, its position is established basing on deutero-exchange with D_2O. The presence of these spectral data and the correlation of results of elemental analysis with the mass spectrum confirmed our understanding that compound **10** forms as a result of decomposition of triazolopyrimidine **7** into aminoazol **1a** and cinnamic aldehyde followed by cascade transformations involving two aldehyde molecules. At the reaction between amine **1a** and cinnamic aldehyde **11** in a molar ratio 1 : 2 in refluxing morpholine compound **10** was obtained in a satisfactory yield. XRD analysis of a single crystal of this compound allowed establishing its structure definitely: 1-phenyl-2-(7-phenyl-4,5,6,7-tetrahydro-[1,2,4]-triazolo[1,5-*a*]pyrimidin-5-yl)ethan-1-one (Fig. 4).

The tetrahydropyrimidine ring of compound **10** is in an asymmetrical *semi-chair* conformation with folding parameters *S* 0.75, Θ 37.9°, Ψ 10.8°. Deviations of atoms C^4 and C^5 from the least-squares plane of other atoms of the cycle are –0.60 and 0.12 Å respectively. Phenyl substituent is in the axial position, and its plane is coplanar with the endocyclic bond N^4–C^3 [torsion angles $C^1N^4C^3C^{14}$ –100.2(1), $N^4C^3C^{14}C^{15}$ 6.3(2)°]. The substituent at the atom C^5 is in the equatorial position [torsion angle $C^1N^1C^5C^6$ –158.9 (1)°]. Benzoyl fragment is in a –*sc*-conformation with respect to N^1–C^5 bond and is practically coplanar to C^5–C^6 bond [torsion angles $N^1C^5C^6C^7$ –69.6(1), $C^5C^6C^7O^1$ –5.1(2)°].

Scheme 3.



Scheme 4.



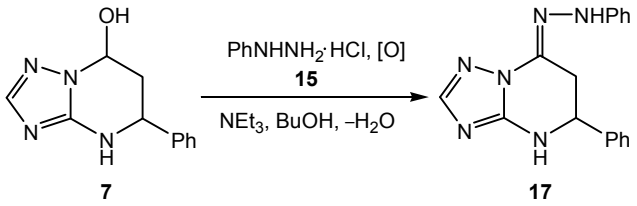
R = H, R' = Bn (**a**); R,R' = $(CH_2)_4$ (**b**).

In keeping with the structure of ketone **10** a mechanism of its generation from triazolo[1,5-*a*]-pyrimidin-7-ol **7** may be assumed (Scheme 3). The reaction is accompanied by a retro-decomposition of triazolopyrimidine **7**, by the catalyzed by morpholine reaction of two molecules of cinnamic aldehyde with the formation of (*E*)-2-[(*E*)-benzylidene]-3-hydroxy-5-phenylpent-4-enal and the addition to it by Michael reaction of aminotriazole with the following oxidation, decarboxylation, and condensation of β-adduct to (4*E*,6*Z*)-5,9-diphenyl-8,9-dihydro[1,2,4]triazolo[1,5-*a*][1,3]diazocine with recyclization of the latter into **10**.

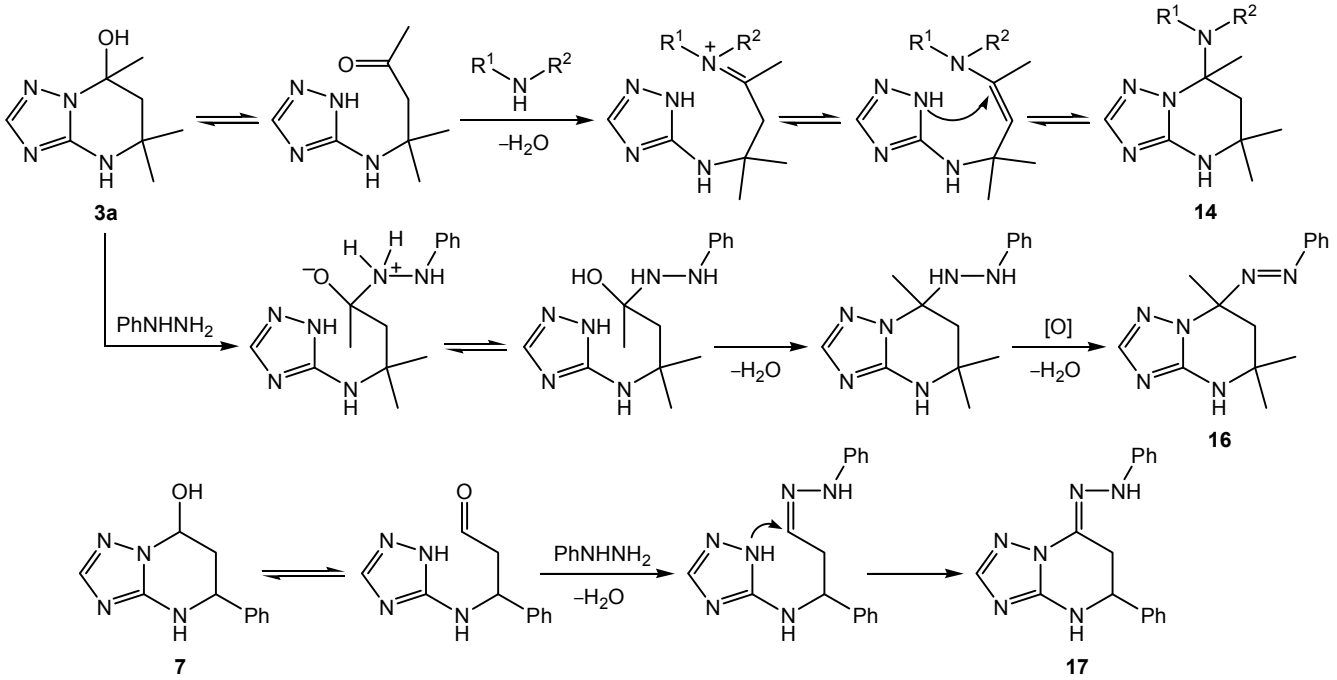
The dehydration of compound **7** that transformed it into heteroaromatic 5-phenyltriazolo[1,5-*a*]pyrimidine **12** succeeded at refluxing in acetic anhydride in the presence of sulfuric acid (Scheme 2). Meanwhile along with water elimination the oxidation was also observed. Compound **12** by physicochemical and spectral characteristics coincides with the product of heteroaromatization of 5-phenyl-4,7-dihydro[1,2,4]-triazolo[1,5-*a*]pyrimidine produced by bromine in acetic acid [7].

In reactions with primary and secondary amines 5,5,7-trimethyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*] pyrimidin-7-ol **3a** demonstrates properties of a cyclic aminal. At a prolonged (10 h) heating compound **3a** with equimolar amount of benzylamine **13a** or pyrrolidine **13b** at 98–100°C 7-aminoderivatives **14a** and **14b** were obtained (Scheme 4). At refluxing triazolopyrimidine **3a** in 2-propanol with two-fold excess of phenylhydrazine hydrochloride **15** in the presence of triethylamine for 22 h compound **16** was obtained.

Scheme 5.



Scheme 6.



5-Phenyltriazolo[1,5-*a*]pyrimidin-7-ol **7** at refluxing in 1-butanol with excess of phenylhydrazine hydrochloride **15** in the presence of the same catalyst for 8 h converts into hydrazone **17** (Scheme 5).

The preservation in the structure of newly synthesized compounds **14a**, **14b**, **16**, and **17** of tetrahydropyrimidine ring and the presence of a residue of the corresponding amine or hydrazine is confirmed by ^{1}H NMR data, mass spectra, and elemental analysis. In the mass spectrum of compound **16** the peak of molecular ion is lacking, however there is a peak, corresponding to the mass of a fragment, formed as a result of elimination from the initial molecule of the residue of phenylhydrazine. The structure of azoloazine **16** was finally confirmed by XRD analysis (Fig. 5).

In compound **16** the tetrahydropyrimidine ring is in an asymmetrical *semi-chair* conformation with folding parameters *S* 0.72, Θ 36.6°, Ψ 21.0°. Deviations of atoms C^4 and C^5 from the least-squares plane of the other atoms of the ring is 0.25 and –0.44 Å respectively. The phenyldiazenyl substituent is oriented axially [torsion angle $C^1N^4C^3N^5$ –110.8(3)°], and the double bond N^5=N^6 is antiperiplanar to the endocyclic bond N^4–C^3 [torsion angle $N^4C^3N^5N^6$ –172.2(3)°]. The aromatic ring is in an *ap*-conformation with respect to the C^3–N^5 bond and is disordered by two positions (A and D) in the ratio 70 : 30 due to the rotation around the N^6–C^9 bond [torsion angles $C^3N^5N^6C^9$ –179.7(3), $N^5N^6C^9C^{14}$ 19.4(6) (A), –13.7(8)° (D)].

Taking into account the structure of compounds **14a**, **14b**, **16**, and **17** the mechanism of their formation from the corresponding hydroxyderivatives may be suggested (Scheme 6). In all cases the reactions involve the opening of the pyrimidine ring with subsequent nucleophilic attack of amine or hydrazine on the carbon atom of the liberated carbonyl group, followed by dehydration and cyclization. In reactions with participation of phenylhydrazine the oxidation

Crystallographic data and XRD parameters of compounds **3a**, **4**, **9**, **10**, and **16**

Parameter	**3a**	**4**	**9**	**10**	**16**
Unit cell *a*, Å	5.6679(6)	26.000(2)	8.718(1)	12.2767(7)	6.390(1)
b, Å	30.761(3)	26.000(2)	11.264(1)	12.4727(5)	29.293(5)
c, Å	10.950(1)	11.924(1)	15.685(2)	11.9634(6)	8.254(1)
α, deg	90.0	90.0	94.367(8)	90.0	90.0
β, deg	90.017(9)	90.0	96.634(9)	117.359(7)	102.55(2)
γ, deg	90.0	90.0	98.894(9)	90.0	90.0
V, Å^3	1909.1(4)	8060.6(3)	1504.6(3)	1627.0(2)	1508.2(4)
F(000)	784	3136	632	672	576
Crystal system	Monoclinic	Tetragonal	Triclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$I4_1/a$	$P1^-$	$P2_1/c$	$P2_1/n$
Z	8	32	4	4	4
T, K	293	293	293	293	293
μ, mm^{-1}	0.089	0.084	0.095	0.084	0.077
D_{calc}, g/cm^3	1.268	1.201	1.326	1.300	1.191
$2\Theta_{max}$, deg	60	50	60	60	50
Measured reflections	17826	27673	17127	16155	10076
Independent reflections	5344	3497	8612	4662	2612
R_{int}	0.067	0.041	0.028	0.038	0.053
Reflections with $F>4\sigma(F)$	3487	1968	5862	2732	1388
Parameters	257	241	401	221	225
R_1	0.069	0.082	0.078	0.050	0.068
wR_2	0.153	0.233	0.244	0.100	0.165
S	1.042	0.936	0.995	0.964	0.924
CCDC	1566886	1566887	1566888	1566890	1566889

occurs of intermediate product with atmospheric oxygen.

Hence in transformations involving amines and hydrazines compounds **3a** and **7** demonstrate the properties of aminoketone and aminal respectively.

EXPERIMENTAL

IR spectra were registered on a spectrometer Perkin Elmer Spectrum One FTIR in tablets of KBr. The ^{1}H NMR spectra were recorded on a spectrometer Varian MR-400 (400 MHz) in DMSO-d_6 with TMS as internal standard. Mass spectra were obtained on an instrument Varian 1200L GC-MS (EI, 70 eV). Elemental analysis was carried out on an elemental analyzer EA-3000 Eurovektor (CHNS-analysis). Melting points were determined on Koeffler heating block.

X-ray diffraction analysis of compounds 3a, 4, 9, 10, and 16 was carried out on a diffractometer Xcalibur-3 (MoK_α-radiation, CCD-detector, graphite monochromator, ω-scanning). The structures were solved by the direct method using software complex SHELXTL [8]. Positions of hydrogen atoms were found from the differential synthesis of electron density and refined in the *rider* model with $U_{iso} = nU_{eq}$ of nonhydrogen atom bound with the corresponding hydrogen (n = 1.5 for methyl groups, n = 1.2 for other hydrogen atoms). In the structures **3a**, **10**, and **16** hydrogen atoms involved in intramolecular hydrogen bonds (of hydroxy and amino groups) were refined in an isotropic approximation. Crystallographic data and

parameters of experiment are compiled in the table. Coordinates of atoms, as well as full tables of bonds lengths and bond angles are deposited in Cambridge Crystallographic Data Centre (e-mail: deposit@ccdc.cam.ac.uk), corresponding numbers of CCDC are given in the table.

5,5,7-Trimethyl-4,5,6,7-tetrahydro[1,2,4]triazolo-[1,5-*a*]pyrimidin-7-ol (3a). *a*. A mixture of 10 mmol of amine **1a**, 15 mmol of ketone **2**, 10 mol % of piperidine in 5 mL of acetone was stirred at refluxing for 24 h, cooled, the precipitate was filtered off. Yield 0.36 g (20%), mp 210–215°C. IR spectrum, ν, cm^{-1}: 3256–2932 (NH, OH, CH_2, CH_3). ^1H NMR spectrum, δ, ppm:1.17 s (3H, CH_3), 1.28 s (3H, CH_3), 1.61 s (3H, CH_3), 1.93 d.d (2H, C^6H_2, J_{AD} 14 Hz), 6.27 br.s (1H, OH), 7.07 br.s (1H, NH), 7.35 s (1H, H^2). Mass spectrum, *m/z* (I_{rel}, %): 182 (45) $[M]^+$, 167 (55), 149 (30), 125 (100), 84 (96). Found, %: C 52.81; H 7.63; N 30.69. $C_8H_{14}N_4O$. Calculated, %: C 52.75; H 7.69; N 30.77. *M* 182.23.

b. A mixture of 10 mmol of amine **1a**, 35 mmol of ketone **2**, 10 mol % of piperidine in 7 mL of acetone was kept at room temperature for 30 days till crystals appeared that were filtered off. Yield 0.67 g (37%). From filtrate compound **4** was isolated.

4-(3-amino-1*H*-1,2,4-triazol-1-yl)-4-methylpen-than-2-on (4). The filtrate after isolating compound **3a** was evaporated. Yield 0.1 g (5%) (*a*), 0.36 g (20%) (*b*), mp 120–122°C. IR spectrum, ν, cm^{-1}: 3432–3152 (NH_2), 2980–2932 (CH_2, CH_3), 1712 (CO). ^1H NMR spectrum, δ, ppm: 1.48 s (6H, $2CH_3$), 1.92 s (3H, CH_3), 2.87 s (2H, CH_2), 5.18 br.s (2H, NH_2), 7.93 s (1H, H^3). Mass spectrum, *m/z* (I_{rel}, %): 181 (25) $[M - 1]^+$, 83 (100), 43 (55). Found, %: C 52.71; H 7.64; N 30.73. $C_8H_{14}N_4O$. Calculated, %: C 52.75; H 7.69; N 30.77. *M* 182.23.

5,5,7-Trimethyl-2-(methylsulfanyl)-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol (3b) was synthesized from amine **1b** by method *b* during 10 days. Yield 1.07 g (47%), mp 209–211°C. IR spectrum, ν, cm^{-1}: 3264–2948 (NH, OH, CH_2, CH_3). ^1H NMR spectrum, δ, ppm: 1.17 s (3H, CH_3), 1.28 s (3H, CH_3), 1.59 s (3H, CH_3), 1.91 d.d (2H, C^6H_2, J_{AD} 14 Hz), 2.40 s (3H, SCH_3), 6.28 br.s (1H, OH), 7.19 br.s (1H, NH). Found, %: C 47.32; H 6.94; N 24.51; S 14.00. $C_9H_{16}N_4OS$. Calculated, %: C 47.37; H 7.02; N 24.56; S 14.04.

7-Methoxy-5-phenyl-4,5,6,7-tetrahydro[1,2,4]-triazolo[1,5-*a*]pyrimidine (8). A solution of 2 mmol of compound **7** in 5 mL of methanol in the presence of catalytic amounts of H_2SO_4 was refluxed for 40 h, the precipitate formed while cooling was filtered off. Yield 0.1 g (20%), mp 204–206°C. IR spectrum, ν, cm^{-1}: 3220–2940 (NH, CH, CH_2). ^1H NMR spectrum, δ, ppm: 1.99–2.14 m (2H, CH_2), 3.47 s (3H, OCH_3) 4.55 d.d (1H, H^5, J_{AD} 3.6 Hz), 5.27 br.s (1H, H^7), 7.33–7.40 m (5H, C_6H_5), 7.47 s (1H, H^2), 7.70 br.s (1H, NH). Found, %: C 62.53; H 6.10; N 24.29. $C_{12}H_{14}N_4O$. Calculated, %: C 62.59; H 6.13; N 24.33.

4-Acetyl-5-phenyl-4,5-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-7-yl acetate (9). A solution of 2 mmol of compound **7** in 1 mL of acetic anhydride was refluxed for 10 h, at cooling from the mixture colorless crystals were filtered off. Yield 0.18 g (60%), mp 136–138°C. IR spectrum, ν, cm^{-1}: 1764 (CO), 1684 (CO), 1200 (C–O–C). ^1H NMR spectrum, δ, ppm: 2.09 s (3H, CH_3), 2.63 s (3H, CH_3), 2.97 m (2H, CH_2), 5.99 m (1H, H^5), 6.20 d.d (1H, H^7, J_{AD} 4 Hz), 7.09–7.34 m (5H, C_6H_5), 7.93 s (1H, H^2). Found, %: C 60.14; H 5.37; N 18.70. $C_{15}H_{16}N_4O^3$. Calculated, %: C 60.00; H 5.33; N 18.67.

1-Phenyl-2-(7-phenyl-4,5,6,7-tetrahydro[1,2,4]-triazolo[1,5-*a*]pyrimidine-5-yl)ethan-1-one (10). *a*. A solution of 1 mmol of compound **7** in 1 mL of morpholine was refluxed for 2 h, 2 mL of 2-propanol was added and the mixture was left in a refrigerator until crystalline precipitate formed, which was filtered off and washed on the filter with 2-propanol.

b. A mixture of 1 mmol of aminoazol **1a** and 2 mmol of 3-phenyl-prop-2-en-1-al in 1.5 mL of morpholine was refluxed for 2.5 h and then processed as in method *a*. Yield 0.07 g (23%) (*a*), 0.13 g (42%) (*b*), mp 255–257°C. IR spectrum, ν, cm^{-1}: 3264–2948 (NH, OH, CH_2, CH_3), 1688 (CO). ^1H NMR spectrum, δ, ppm: 2.21 m (2H, CH_2), 2.35 m (2H, CH_2), 3.79 m (1H, H^5), 5.51 t (1H, H^7, *J* 4.6 Hz), 7.10 br.s (1H, NH), 7.00–7.94 m (11H, H^2, $2C_6H_5$). Mass spectrum, *m/z* (I_{rel}, %): 318 (17) $[M]^+$, 290 (10) $[M - CO]^+$, 213 (28) $[M - PhCO]^+$, 199 (39) $[M - PhCOCH_2]^+$, 186 (21) $[M - PhCOCH_2CH]^+$, 172 (10) $[M - PhCOCH_2CHCH_2]^+$, 105 (69) [PhCO], 77 (100) [Ph]. Found, %: C 71.73; H 5.69; N 17.63. $C_{19}H_{18}N_4O$. Calculated, %: C 71.70; H 5.66; N 17.61. *M* 318.38.

5-Phenyltriazolo[1,5-*a*]pyrimidine (12). A solution of 2 mmol of triazolopyrimidine **7** in 2 mL of acetic anhydride in the presence of catalytic amount of H_2SO_4 was refluxed for 1 h, poured on ice, oily substance formed that was extracted with $CHCl_3$. The extract was washed with a saturated solution of

$NaHCO_3$ until pH 7, dried with Na_2SO_4, the solvent was removed at a reduced pressure, to oily residue a mixture was added of hexane, methanol and CCl_4, 3 : 1 : 1, and the reaction mixture was left in a refrigerator for 2 days, colorless crystals were filtered off. Yield 0.25 g (63%), mp 186–188°C (187–188°C [7]). ^{1}H NMR spectrum, δ, ppm: 7.61 m (3H, *m*,*p*-C_6H_5), 7.99 d (1H, H^6, *J* 7 Hz), 8.30 m (2H, *o*-C_6H_5), 8.69 s (1H, H^2), 9.46 d (1H, H^7, *J* 7 Hz).

***N*-Benzyl-5,5,7-trimethyl-4,5,6,7-tetrahydro-[1,2,4]triazolo[1,5-*a*]pyrimidin-7-amine (14a).** A mixture of 0.5 mmol of compound **3a** and 2 mmol of benzylamine **13a** was heated on a water bath for 10 h, 3 mL of hexane was added and the amorphous precipitate was filtered off and recrystallized from a mixture acetone-hexane, 3 : 1. Yield 0.06 g (45%), mp 138–140°C. IR spectrum, cm^{-1}: 3378–2862 (NH, CH_2, CH_3). ^{1}H NMR spectrum, δ, ppm: 1.20 s (3H, CH_3), 1.27 s (3H, CH_3), 1.64 s (3H, CH_3), 1.96 d.d (2H, C^6H_2, J_{AD} 14 Hz), 2.74 d.d (1H, NH, *J* 6 Hz), 3.21–3.53 m (2H, CH_2), 6.96 br.s (1H, N^4H), 7.16–7.30 m (5H, C_6H_5), 7.43 s (1H, H^2). Mass spectrum, *m/z* (I_{rel}, %): 271 (14) $[M]^+$, 165 (10) $[M - HNCH_2Ph]^+$, 147 (100), 91 (79). Found, %: C 66.45; H 7.78; N 25.76. $C_{15}H_{21}N_5$. Calculated, %: C 66.42; H 7.75; N 25.83. *M* 271.37.

5,5,7-Trimethyl-7-(pyrrolidin-1-yl)-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidine (14b) was synthesized similarly. Yield 0.16 g (33%), mp 148–150°C. IR spectrum, ν, cm^{-1}: 3244–2964 (NH, CH_2, CH_3). ^{1}H NMR spectrum, δ, ppm: 1.15 s (3H, CH_3), 1.27 s (3H, CH_3), 1.56 m (4H, CH_2), 1.60 s (3H, CH_3), 1.73–2.24 d.d (2H, C^6H_2, J_{AD} 14 Hz), 2.35 m (2H, CH_2), 2.80 m (2H, CH_2), 6.92 br.s (1H, N^4H), 7.33 s (1H, H^2). Mass spectrum, *m/z* (I_{rel}, %): 235 (10) $[M]^+$, 165 (70) $[M - N(CH_2)_4]^+$, 150 (10), 125 (50), 110 (100), 83 (62), 68 (40). Found, %: C 61.24; H 8.87; N 29.73. $C_{12}H_{21}N_5$. Calculated, %: C 61.28; H 8.94; N 29.79.

(*E*)-5,5,7-Trimethyl-7-(phenyldiazenyl)-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidine (16). A mixture of 1 mmol of compound **3a** and 2 mmol of phenylhydrazine hydrochloride **15** in 10 mL of 2-propanol in the presence of triethylamine was refluxed for 22 h, cooled, the precipitate was filtered off. Yield 0.11 g (42%), mp 185–186°C. IR spectrum, ν, cm^{-1}: 3392–2850 (NH, CH_2, CH_3). ^{1}H NMR spectrum, δ, ppm: 0.85 s (3H, CH_3), 1.22 s (3H, CH_3), 1.63 s (3H, CH_3), 2.11–2.36 d.d (2H, C^6H_2, J_{AD} 14 Hz), 7.36 br.s (1H, N^4H), 7.50–7.65 m (6H, C_6H_5, H^2). Mass spectrum, *m/z* (I_{rel}, %): 165 (100) $[M - C_6H_5 - N_2]^+$, 135 (12) $[M - C_6H_5 - N_2 - 2(CH_3)]^+$, 77 (55) [Ph]. Found, %: C 62.63; H 6.02; N 31.30. $C_{14}H_{16}N_6$. Calculated, %: C 62.67; H 5.97; N 31.34.

(7*E*)-5-Phenyl-7-(2-phenylhydrazinylidene)-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidine (17) was obtained similarly at refluxing in 1-butanol during 8 h. Yield 0.25 g (82%), mp 212–214°C. IR spectrum, ν, cm^{-1}: 3500–2800 (NH, CH_2), 1684 (C^7=N). ^{1}H NMR spectrum, δ, ppm: 2.96 m (2H, C^6H_2), 4.85 t (1H, H^5, *J* 4 Hz), 6.69–7.22 m (5H, C_6H_5), 7.35 m (5H, C_6H_5), 7.89 s (1H, H^2), 8.60 br.s (1H, N^4H), 10.73, 7.65 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 304 (70) $[M]^+$, 248 (20), 173 (100), 129 (12), 93 (45). Found, %: C 67.15; H 5.19; N 27.56. $C_{17}H_{16}N_6$. Calculated, %: C 67.11; H 5.26; N 27.63. *M* 304.35.

REFERENCES

1. Chebanov, V.A. and Desenko, S.M., *Curr. Org. Chem*., 2006, vol. 10, p. 297.
2. Lipson, V.V. and Gorobets, N.Yu., *Mol. Div*., 2009, vol. 13, p. 399.
3. Bariwal, J., Trivedi, J.C., and Van der Eycken, E.V., *Top. Heterocycl. Chem*., 2010, vol. 25, p. 169.
4. Lipson, V.V., Karnozhitskaya, T.M., Shishkina, S.V., Shishkin, O.V., and Turov, A.V., *Russ. Chem. Bull*., 2009, vol. 58, p. 1441. doi 10.1007/s11172-009-0193-1
5. Lipson, V.V., Karnozhitskaya, T.M., Shishkina, S.V., Shishkin, O.V., and Turov, A.V., *Russ. J. Org. Chem*., 2008, vol. 44, p. 1695. doi 10.1134/S1070428008110225
6. Zefirov, N.S., Palyulin, V.A., and Dashevskaya, E.E., *J. Phys. Org. Chem*., 1990, vol. 3, p. 147.
7. Desenko, S.M., Orlov, V.D., Lipson, V.V., Shishkin, O.V., Lindeman, S.V., and Struchkov, Yu.T., *Chem. Heterocycl. Compd*., 1991, vol. 27, p. 1242. doi 10.1007/BF00471754
8. Sheldrick, G.M., *Acta Cryst., Sect. A*, 2008, vol. 64, p. 112.