ISSN 1070-4280, Russian Journal of Organic Chemistry, 2017, Vol. 53, No. 6, pp. 941–945. © Pleiades Publishing, Ltd., 2017.
Original Russian Text © E.G. Paronikyan, Sh.Sh. Dashyan, N.S. Minasyan, G.M. Stepanyan, 2017, published in Zhurnal Organicheskoi Khimii, 2017, Vol. 53, No. 6, pp. 925–929.

Azido–Tetrazole Tautomerism of Pyrano[3,4-*c*]pyridine Derivatives

E. G. Paronikyan[a], Sh. Sh. Dashyan[a],* N. S. Minasyan[b], and G. M. Stepanyan[a]

[a] *Mndzhoyan Institute of Fine Organic Chemistry, Scientific Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, pr. Azatutyan 26, Yerevan, 0014 Armenia*
**e-mail: Shdashyan@gmail.com*

[b] *Molecular Structure Research Center, Scientific Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, pr. Azatutyan 26, Yerevan, 0014 Armenia*

Received February 14, 2017

Abstract—Treatment of *N*-aryl-8-hydrazinylpyrano[3,4-*c*]pyridine-5-carbonitriles with sodium nitrite in acetic acid afforded the corresponding 8-azido derivatives existing in solution as equilibrium mixtures with cyclic tetrazole tautomer whose fraction attains 48%. Lower solvent polarity and elevated temperature favor increased fraction of the azido tautomer.

DOI: 10.1134/S1070428017060215

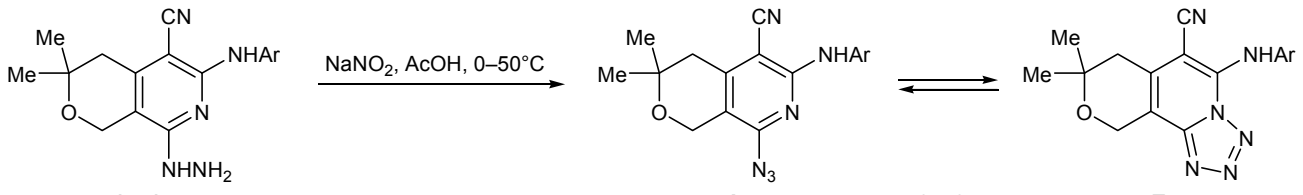
Pyranopyridines constitute an important class of heterocyclic compounds which exhibit interesting biological properties [1–4]. Among these, of particular interest is pyrano[3,4-*c*]pyridine derivative MBX2319 which is a potent antimicrobial agent [5, 6]. In recent years, various methods have been developed for the synthesis of pyrano[3,4-*c*]pyridines [7, 8] and tetrazolo[1,5-*a*]pyridines [9–11]. However, there are no published data on biological properties of azidopyridines and tetrazolo[1,5-*a*]pyridines.

In continuation of our studies on the synthesis and biological activity of amino-substituted pyrano[3,4-*c*]pyridines [12, 13] and their fused analogs [14–16], herein we report the synthesis of pyrano[3,4-*c*]tetrazolo[1,5-*a*]pyridine derivatives.

For this purpose, hydrazinyl-substituted pyranopyridines **1a**–**1g** [17] were treated with sodium nitrite in acetic acid at 0–5°C. The isolated compounds **2a**–**2g** (yield 82–97%) in the solid state were identified as azido derivatives. Their IR spectra (mineral oil) contained a doublet band at 2130–2155 cm^{-1} typical of azido group. These bands indicated the presence of an electron-withdrawing group in the pyridine ring [18]. The stability of azide tautomer in the solid state may be rationalized by electron-withdrawing effect of the cyano group, as well as by steric effect of the anilino group in the 3-position, which hampers tetrazole ring closure through the pyridine nitrogen atom.

It is known that unsubstituted tetrazolo[1,5-*a*]pyridine in crystal has cyclic structure and that it is not converted to azido tautomer in polar or nonpolar solvents. Introduction of electron-withdrawing substituents into the cyclic system favors formation of the azide structure, thus giving rise to equilibrium in solution between cyclic and open-chain tautomers [9–11, 19–21].

Scheme 1.



Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 3-MeC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**), 3-$MeOC_6H_4$ (**e**), 2-$MeOC_6H_4$ (**f**), 4-ClC_6H_4 (**g**).

Table 1. Fractions (%) of the azido (**A**) and tetrazole (**T**) tautomers of 6-anilino-8-azido-3,3-dimethyl-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitriles **2a**–**2g** in different solvents at 30°C

Comp. no.	$CDCl_3$		DMSO-d_6–CCl_4, 1:3		DMSO-d_6	
	A	**T**	**A**	**T**	**A**	**T**
2a	93	7	94	6	69	31
2b	85	15	90	10	73	27
2c	90	10	91	9	70	30
2d	95	5	87	13	52	48
2e	91	9	95	5	73	27
2f	97	3	90	10	53	47
2g	95	5	97	3	78	22

Table 2. Chemical shifts (δ, ppm) of the NH proton of the azido and tetrazole tautomers of compounds **2a**–**2g** in different solvents

Comp. no.	Azido tautomer **A**/tetrazole tautomer **T**		
	$CDCl_3$	DMSO-d_6–CCl_4, 1:3	DMSO-d_6
2a	6.97/6.97	8.84/10.74	9.16/10.70
2b	6.91/6.97	8.71/10.64	9.04/10.62
2c	7.39/7.58	8.72/10.64	9.08/10.64
2d	6.84/6.84	8.68/10.57	9.01/10.56
2e	6.99/6.99	8.79/10.70	9.15/10.68
2f	7.81/7.84	7.91/10.44	8.20/10.52
2g	6.95/7.25	9.07/10.79	9.32/10.76

The azido–tetrazole tautomerism of compounds **2a**–**2g** in solution was studied by ^{1}H NMR. Tetrazole ring is more electronegative than the azido group; therefore, protons of the tetrazole tautomer resonate in a weaker field than those belonging to the azido tautomers. The fractions of the azido and tetrazole tautomers of **2a**–**2g** were estimated by the intensities of the NH, CH_2, and CMe_2 proton signals.

Table 3. Temperature effect on the **A** ⇌ **T** equilibrium of compound **2a** in DMSO-d_6

Temperature, K	Ratio **A**/**T**	K[a]	ΔG, kcal/mol
303	69:31	2.23	–0.48
313	72:28	2.57	–0.58
323	75:25	3.00	–0.70
333	78:22	3.55	–0.84
343	80.5:19.5	4.13	–0.97
353	83:17	4.88	–1.12

[a] $K = [\mathbf{A}]/[\mathbf{T}]$.

Solutions of **2a**–**2g** in $CDCl_3$, DMSO-d_6, and DMSO-d_6–CCl_4 (1:3) contained both azido (**A**) and tetrazole (**T**) tautomers whose ratio depended on the solvent polarity, temperature, and substituent on C^3 (Table 1). The fraction of tautomer **T** in weakly polar $CDCl_3$ ranged from 3 to 15%, depending on the substituent in the benzene ring. The isomer ratio did not change in going to DMSO-d_6–CCl_4 (1:3), whereas in DMSO-d_6 the fraction of tetrazole tautomer increased to 22–48%. It is seen that electron-donating groups (R = Me, OMe) in the benzene ring do not affect the state of the azido–tetrazole equilibrium to an appreciable extent, as compared to unsubstituted compound (R = H). However, introduction of an electron-withdrawing chlorine atom increases the fraction of tetrazole tautomer **T**.

The position of the NH proton signal of both isomers only slightly depends on the substituent in the benzene ring (Table 2), but it strongly changes upon variation of the solvent.

The temperature effect on the **A** ⇌ **T** equilibrium was studied using compound **2a** as an example. The tautomer ratio was determined from the intensities of the NH proton signals in the ^{1}H NMR spectrum. Raising the temperature from 30 to 80°C increased the fraction of tautomer **A**, indicating that the transformation **T** → **A** is endothermic (Table 3).

The temperature dependence of the equilibrium constant is described by a straight line in the $\ln K$—$1/T$ coordinates: $\ln K = -(1680 \pm 55)T^{-1} + (6.32 \pm 0.17)$; $r = 0.998$, $s = 0.02$. The thermodynamic parameters for the azido–tetrazole equilibrium of **2a** were calculated from the slope and free term of the above temperature dependence according to standard methods [22–24]: $\Delta H° = 3.3$ kcal/mol, $\Delta S° = 13.5$ cal mol^{-1} K^{-1}.

Thus, study of the azido–tetrazole tautomerism of 8-azidopyrano[3,4-*c*]pyridines **2a**–**2g** in solution has shown that polar solvents favor formation of the tetrazole tautomer and that rise in temperature increases the fraction of the azido tautomer. The tautomer ratio of compounds **2a**–**2g** also depends on the substituent in the anilino group on C^3.

Compounds **2a**–**2g** were screened for antimicrobial activity against gram-positive *S. aureus* 209p, 1 and gram-negative *Sh. Flexneri* 6858 and *E. coli* 0–55 by the agar diffusion method [25]. Compounds **2b** and **2e** showed a moderate antimicrobial activity against all test cultures (inhibition zone diameter d = 14–18 mm against 24–25 mm for furazolidone taken as reference drug) [26].

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Avatar 330 FT-IR spectrometer from samples dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were measured on a Varian Mercury 300 Vx spectrometer at 300 and 75.462 MHz, respectively, using tetramethylsilane as internal standard. The melting points were determined on a Boetius micro hot stage. The elemental analyses were obtained on a Euro EA 3000 elemental analyzer.

Compounds 2a–2g (*general procedure*). A solution of 1.4 g (20 mmol) of sodium nitrite in 10 mL of water was added dropwise with stirring to a mixture of 10 mmol of compound **1a**–**1g** and 50 mL of glacial acetic acid cooled to 0°C. The mixture was stirred for 12 h at room temperature, and the precipitate was filtered off, washed with water, and recrystallized from EtOH–CH_2Cl_2 (1:3).

6-Anilino-8-azido-3,3-dimethyl-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2a). Yield 2.7 g (85%), mp 203–205°C. IR spectrum, ν, cm^{-1}: 3319 (NH), 2218 (CN), 2154, 2132 (N_3). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 1.31 s (5.58H) and 1.54 s (0.42H) (CMe_2), 2.59 s (1.86H) and 2.75 s (0.14H) (4-H), 4.50 s (2H, 1-H), 7.09–7.15 m (1H, H_{arom}), 7.32–7.39 m (2H, H_{arom}), 7.58–7.63 m (2H, H_{arom}); in DMSO-d_6–CCl_4 (1:3): 1.27 s (5.64H) and 1.34 s (0.36H) (CMe_2), 2.69 s (2H, 4-H), 4.38 s (1.88H) and 4.91 s (0.12H) (1-H), 6.95–7.01 m (1H, H_{arom}), 7.19–7.26 m (2H, H_{arom}), 7.56–7.61 m (2H, H_{arom}); in DMSO-d_6: 1.23 s (4.2H) and 1.30 s (1.8H) (CMe_2), 2.71 s (2H, 4-H), 4.40 s (2H, 1-H), 7.00–7.06 m (1H, H_{arom}), 7.24–7.44 m (3H, H_{arom}), 7.57–7.61 m (1H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 25.8, 37.5, 57.4, 69.2, 88.7, 109.6, 114.5, 121.1, 122.4, 127.4, 138.8, 150.0, 150.9, 154.4. Found, %: C 63.58; H 5.13; N 26.08. $C_{17}H_{16}N_6O$. Calculated, %: C 63.74; H 5.03; N 26.23.

8-Azido-3,3-dimethyl-6-(4-methylanilino)-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2b). Yield 2.7 g (82%), mp 188–190°C. IR spectrum, ν, cm^{-1}: 3328 (NH), 2212 (CN), 2151, 2132 (N_3). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 1.31 s (5.1H) and 1.32 s (0.9H) (CMe_2), 2.35 s (2.55H) and 2.42 s (0.45H) (**Me**C_6H_4), 2.73 s (1.7H) and 2.80 s (0.3H) (4-H), 4.49 s (1.7H) and 4.53 s (0.3H) (1-H), 7.13–7.18 m (2H, H_{arom}), 7.45–7.50 m (2H, H_{arom}); in DMSO-d_6–CCl_4 (1:3): 1.27 s (5.4H) and 1.34 s (0.6H) (CMe_2), 2.32 s (3H, **Me**C_6H_4), 2.42 s (1.8H) and 2.67 s (0.2H) (4-H), 4.37 s (1.8H) and 4.90 s (0.2H) (1-H), 7.01–7.05 m (2H, H_{arom}), 7.44–7.48 m (2H, H_{arom}); in DMSO-d_6: 1.23 s (4.38H) and 1.29 s (1.62H) (CMe_2), 2.26 s (2.19H) and 2.34 s (0.81H) (**Me**C_6H_4), 2.65 s (1.46H) and 2.69 s (0.54H) (4-H), 4.39 s (1.46H) and 4.88 s (0.54H), (1-H), 7.09 d (1H, H_{arom}, J = 8.4 Hz), 7.20–7.27 m (2H, H_{arom}), 7.47 d (1H, H_{arom}, J = 8.4 Hz). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 20.3, 25.8, 37.5, 57.4, 69.3, 88.3, 109.3, 114.6, 121.2, 128.0, 131.4, 136.2, 150.0, 150.9, 154.5. Found, %: C 64.83; H 5.36; N 25.27. $C_{18}H_{18}N_6O$. Calculated, %: C 64.66; H 5.43; N 25.13.

8-Azido-3,3-dimethyl-6-(3-methylanilino)-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2c). Yield 3.1 g (94%), mp 173–175°C. IR spectrum, ν, cm^{-1}: 3335 (NH), 2213 (CN), 2152, 2137 (N_3). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 1.31 s (5.4H) and 1.32 s (0.6H) (CMe_2), 2.38 s (2.7H) and 2.45 s (0.3H) (**Me**C_6H_4), 2.68 s (1.8H) and 2.74 s (0.2H) (4-H), 4.50 s (1.8H) and 4.53 s (0.2H) (1-H), 6.91–6.96 m (2H, H_{arom}), 7.20–7.26 m (1H, H_{arom}), 7.29–7.34 m (1H, H_{arom}); in DMSO-d_6–CCl_4 (1:3): 1.27 s (5.46H) and 1.35 s (0.54H) (CMe_2), 2.32 s (2.73H) and 2.41 s (0.27H) (**Me**C_6H_4), 2.60 s (1.82H) and 2.68 s (0.18H) (4-H), 4.38 s (1.82H) and 4.42 s (0.18H) (1-H), 6.79 br.d (1H, H_{arom}, J = 7.5 Hz), 7.10 t (1H, 5′-H, J = 7.8 Hz), 7.33 br.d (1H, H_{arom}, J = 8.0 Hz), 7.54 br.t (1H, 2′-H, J = 2.0 Hz); in DMSO-d_6: 1.23 s (4.2H) and 1.29 s (1.8H) (CMe_2), 2.27 s (2.1H) and 2.32 s (0.9H) (**Me**C_6H_4), 2.68 s (1.4H) and 2.70 s (0.6H) (4-H), 4.39 s (1.4H) and 4.89 s (0.6H) (1-H), 6.85 br.d (0.7H, H_{arom}, J = 7.5 Hz), 7.08 br.d (0.3H, H_{arom}, J = 7.5 Hz), 7.11–7.37 m (2H, H_{arom}), 7.55 br.s (1H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 20.9, 25.7, 37.5, 57.3, 69.2, 88.6, 109.5, 114.5, 118.0, 121.5, 123.1, 127.3, 136.7, 138.7, 150.0, 150.8, 154.3. Found, %: C 64.78; H 5.36; N 25.25. $C_{18}H_{18}N_6O$. Calculated, %: C 64.66; H 5.43; N 25.13.

8-Azido-6-(4-methoxyanilino)-3,3-dimethyl-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2d). Yield 3.4 g (97%), mp 178–180°C. IR spectrum, ν, cm^{-1}: 3331 (NH), 2224 (CN), 2153, 2138 (N_3). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 1.31 s (5.7H) and 1.32 s (0.3H) (CMe_2), 2.73 s (2H, 4-H), 3.83 s (3H, OCH_3), 4.49 s (2H, 1-H), 6.87–6.92 m (2H, H_{arom}), 7.43–7.50 m (2H, H_{arom}); in DMSO-d_6–CCl_4 (1:3): 1.27 s (5.22H) and 1.34 s (0.78H) (CMe_2), 2.64 s (1.74H) and 2.66 s (0.26H) (4-H), 3.77 s (2.61H) and 3.85 s (0.39H) (OCH_3), 4.37 s (1.74H) and 4.89 s (0.26H), (1-H), 6.75–6.80 m (1.74H, H_{arom}), 6.90–

6.95 m (0.26H, H_{arom}), 7.23–7.27 m (1.74H, H_{arom}), 7.43–7.49 m (0.26H, H_{arom}); in DMSO-d_6: 1.22 s (3.12H) and 1.28 s (2.88H) (CMe_2), 2.62 s (1.04H) and 2.68 s (0.96H) (4-H), 3.73 s (1.56H) and 3.79 s (1.44H) (OCH_3), 4.37 s (1.04H) and 4.87 s (0.96H) (1-H), 6.83–6.89 m (1.04H, H_{arom}), 6.95–7.01 m (0.96H, H_{arom}), 7.29–7.35 m (1.04H, H_{arom}), 7.43–7.49 m (0.96H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 25.8, 37.4, 54.7, 57.5, 69.2, 88.9, 109.8, 114.4, 122.1, 127.8, 130.8, 137.5, 150.1, 150.9, 154.2. Found, %: C 61.82; H 5.24; N 23.85. $C_{18}H_{18}N_6O_2$. Calculated, %: C 61.70; H 5.18; N 23.99.

8-Azido-6-(3-methoxyanilino)-3,3-dimethyl-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2e). Yield 3.1 g (88%), mp 180–181°C. IR spectrum, ν, cm^{-1}: 3307 (NH), 2217 (CN), 2155, 2141 (N_3). ^1H NMR spectrum, δ, ppm: in $CDCl_3$: 1.31 s (5.46H) and 1.34 s (0.54H) (CMe_2), 2.63 s (1.82H) and 2.74 s (0.18H) (4-H), 3.83 s (2.73H) and 3.86 s (0.27H) (OCH_3), 4.50 s (1.82H) and 4.61 s (0.18H) (1-H), 6.66 d.d.d (1H, H_{arom}, J = 8.2, 2.4, 0.9 Hz), 7.05 d.d.d (1H, H_{arom}, J = 8.1, 2.8, 0.9 Hz), 7.22 d (1H, H_{arom}, J = 8.2 Hz), 7.35 d.d (1H, H_{arom}, J = 2.8, 2.4 Hz); in DMSO-d_6–CCl_4 (1:3): 1.27 s (5.7H) and 1.35 s (0.3H) (CMe_2), 2.69 s (2H, 4-H), 3.77 s (2.85H) and 3.82 s (0.15H) (OCH_3), 4.39 s (1.9H) and 4.91 s (0.1H) (1-H), 6.53 d.d.d (0.95H, H_{arom}, J = 8.1, 2.5, 1.0 Hz), 6.79 d.d.d (0.05H, H_{arom}, J = 8.1, 2.5, 1.0 Hz), 7.10 t (1H, 5′-H, J = 8.1 Hz), 7.16–7.25 m (2H, H_{arom}); in DMSO-d_6: 1.23 s (4.38H) and 1.29 s (1.62H) (CMe_2), 2.69 s (1.46H) and 2.70 s (0.54H) (4-H), 3.73 s (2.19H) and 3.75 s (0.81H) (OCH_3), 4.40 s (1.46H) and 4.89 s (0.54H) (1-H), 6.57–6.63 m (1H, H_{arom}), 6.76–6.93 m (1H, H_{arom}), 7.13–7.20 m (1H, H_{arom}), 7.26–7.33 m (1H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 25.7, 37.5, 54.4, 57.4, 69.2, 88.9, 106.2, 108.5, 109.7, 113.1, 114.4, 128.1, 140.0, 150.1, 150.9, 154.2, 159.1. Found, %: C 61.89; H 5.07; N 23.88. $C_{18}H_{18}N_6O_2$. Calculated, %: C 61.70; H 5.18; N 23.99.

8-Azido-6-(2-methoxyanilino)-3,3-dimethyl-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2f). Yield 3.2 g (90%), mp 177–179°C. IR spectrum, ν, cm^{-1}: 3380 (NH), 2208 (CN), 2153, 2132 (N_3). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.31 s (5.82H) and 1.32 s (0.18H) (CMe_2), 2.75 s (1.94H) and 2.79 s (0.06H) (4-H), 3.96 s (2.91H) and 4.10 s (0.09H) (OCH_3), 4.51 s (1.94H) and 4.53 s (0.06H) (1-H), 6.90–7.07 m (3H, H_{arom}), 7.81 br.s (0.97H) and 7.84 br.s (0.03H (NH), 8.45 d.d (1H, H_{arom}, J = 7.7, 1.8 Hz); in DMSO-d_6–CCl_4, 1:3): 1.27 s (5.4H) and 1.33 s (0.6H) (CMe_2), 2.65 s (1.8H) and 2.70 s (0.2H) (4-H), 3.80 s (2.7H) and 3.96 s (0.3H) (OCH_3), 4.40 s (1.9H) and 4.44 s (1-H), 6.86–6.92 m (1H, H_{arom}), 6.95–7.00 m (2H, H_{arom}), 8.25 d.d (1H, H_{arom}, J = 8.0, 1.5 Hz); in DMSO-d_6: 1.23 s (3.18H) and 1.28 s (2.82H) (CMe_2), 2.64 s (1.06H) and 2.71 s (0.94H) (4-H), 3.75 s (1.59H) and 3.85 s (1.41H) (OCH_3), 4.40 s (1.06H) and 4.88 s (0.94H) (1-H), 6.89–7.15 m (3H, H_{arom}), 7.35 br.d (0.53H, H_{arom}, J = 7.6 Hz), 7.97 br.d (0.47H, H_{arom}, J = 7.6 Hz). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 25.7, 37.5, 55.4, 57.3, 69.2, 88.9, 109.7, 109.8, 114.2, 119.2, 119.9, 122.5, 127.6, 148.1, 149.7, 151.2, 153.8. Found, %: C 61.52; H 5.27; N 24.17. $C_{18}H_{18}N_6O_2$. Calculated, %: C 61.70; H 5.18; N 23.99.

8-Azido-6-(4-chloroanilino)-3,3-dimethyl-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridine-5-carbonitrile (2g). Yield 3.2 g (91%), mp 200–201°C. IR spectrum, ν, cm^{-1}: 3329 (NH), 2216 (CN), 2152, 2130 (N_3). ^1H NMR spectrum, δ, ppm: in $CDCl_3$: 1.31 s (4.5H) and 1.35 s (1.5H) (CMe_2), 2.64 t (1.5H, 4-H, J = 1.4 Hz), 2.75 t (0.5H, 4-H, J = 1.1 Hz), 4.50 t (1.5H, 1-H, J = 1.1 Hz), 4.59 t (0.5H, 1-H, J = 1.4 Hz), 7.18–7.21 m (1.5H, H_{arom}), 7.30–7.34 m (0.5H, H_{arom}), 7.53–7.58 m (1.5H, H_{arom}), 7.61–7.65 m (0.5H, H_{arom}); DMSO-d_6–CCl_4 (1:3): 1.27 s (5.82H) and 1.35 s (0.18H) (CMe_2), 2.68 s (2H, 4-H), 4.38 s (1.94H) and 4.92 s (0.06H, 1-H), 7.16–7.25 m (1.94H, H_{arom}), 7.29–7.37 m (0.06H, H_{arom}), 7.57–7.67 m (2H, H_{arom}); in DMSO-d_6: 1.23 s (4.68H) and 1.29 s (1.32H) (CMe_2), 2.69 s (1.56H) and 2.71 s (0.44H) (4-H), 4.39 s (1.56H) and 4.90 s (0.44H) (1-H), 7.23–7.29 m (1.56H, H_{arom}), 7.33–7.39 m (0.44H, H_{arom}), 7.44–7.49 m (1.56H, H_{arom}), 7.58–7.65 m (0.44H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ_C, ppm: 25.7, 37.5, 57.4, 69.2, 88.9, 110.0, 114.3, 122.4, 127.3, 130.2, 137.7, 150.2, 150.8, 154.0. Found, %: C 57.78; H 4.19; N 23.78. $C_{17}H_{15}ClN_6O$. Calculated, %: C 57.55; H 4.26; N 23.69.

This study was performed under financial support by the State Committee of the Ministry of Education and Science of Armenia and by the Russian Foundation for Basic Research (scientific program no. 15RF-027).

REFERENCES

1. Kumar, R.R., Perumol, S., Menandes, J.C., Yugeeswari, P., and Sriram, D., *Bioorg. Med. Chem.*, 2011, vol. 19, p. 3444.

2. Abdel-Wadood, F.K., Abdel-Monem, M.I., Fahamy, A.M., and Geies, A.A., *Z. Naturforsch., Teil B*, 2008, vol. 63, p. 303.
3. Lee, S., Chae, S.M., Yi, K.Y., Kim, N., and Oh, Ch.H., *Bull. Korean Chem. Soc*., 2005, vol. 26, p. 619.
4. Kwak, W.J., Kim, J.H., Cho, Y.B., Jeon, S.D., and Moon, C.K., *Biol. Pharm. Bull*., 2005, vol. 28, p. 750.
5. Opperman, T.J., Kwasny, S.M., Kim, H.S., Nguyen, S.T., Houseweart, C., D'Souza, S., Walker, G.C., Peet, N.P., Nikaido, H., and Bowlin, T.L., *Antimicrob. Agents Chemother*., 2014, vol. 58, p. 722.
6. Nguyen, S.T., Kwasny, S.M., Ding, X., Cardinale, S.C., McCarthy, C.T., Kim, H.S., Nikaido, H., Peet, N.P., Williams, J.D., Bowlin, T.L., and Opperman, T.J., *Bioorg. Med. Chem*., 2015, vol. 23, p. 2024.
7. Panda, B. and Sarkar, T.K., *Tetrahedron Lett*., 2008, vol. 49, p. 6701.
8. Subba Reddy, B.V., Reddy, S.G., Reddy, M.R., Spidhar, B., and Bhadra, M.P., *Tetrahedron Lett*., 2014, vol. 55, p. 4817.
9. Lowe-Ma, Ch.K., Nissan, R.A., and Wilson, W.S., *J. Org. Chem*., 1990, vol. 55, p. 3755.
10. Keith, J.M., *J. Org. Chem*., 2006, vol. 71, p. 9540.
11. Liu, Sh., Lentz, D., and Tzschucke, C.Ch., *J. Org. Chem*., 2014, vol. 79, p. 3249.
12. Paronikyan, E.G., Dashyan, Sh.Sh., Noravyan, A.S., Tamazyan, R.A., Ayvazyan, A.G., and Panosyan, H.A., *Tetrahedron*, 2015, vol. 71, p. 2686.
13. Paronikyan, E.G., Dashyan, Sh.Sh., Dzhagatspanyan, I.A., Paronikyan, R.G., Nazaryan, I.M., Akopyan, A.G., Minasyan, N.S., Ayvazyan, A.G., Tamazyan, R.A., and Babaev, E.V., *Russ. J. Bioorg. Chem*., 2016, vol. 42, no. 2, p. 215.
14. Paronikyan, E.G., Sirakanyan, S.N., Noravyan, A.S., Paronikyan, R.G., and Dzhagatspanyan, I.A., *Pharm. Chem. J*., 2001, vol. 35, no. 1, p. 8.
15. Paronikyan, E.G., Noravyan, A.S., Dzhagatspanyan, I.A., Nazaryan, I.M., and Paronikyan, R.G., *Pharm. Chem. J*., 2002, vol. 36, no. 9, p. 465.
16. Dashyan, Sh.Sh., Paronikyan, E.G., Noravyan, A.S., and Paronikyan, R.G., *Pharm. Chem. J*., 2016, vol. 50, no. 4, p. 221.
17. Paronikyan, E.G., Dashyan, Sh.Sh., Minasyan, N.S., Stepanyan, G.M., Ayvazyan, A.G., and Tamazyan, R.A., *Chem. Heterocycl. Compd*., 2016, vol. 52, no. 12, p. 1078.
18. Bellamy, L.J., *Advances in Infrared Group Frequencies*, London: Methuen, 1968, p. 70.
19. Pochinok, V.Y., Avramenko, L.F., Grigorenko, P.S., and Skopenko, V.N., *Russ. Chem. Rev*., 1975, vol. 44, no. 6, p. 481.
20. Chattopadhyay, B., Vera, C.I.R., Chuprakov, S., and Gevorgyan, V., *Org. Lett*., 2010, vol. 12, p. 2166.
21. Chan, J. and Faul, M., *Tetrahedron Lett*., 2006, vol. 47, p. 3361.
22. Temple, C. and Montgomery, J.A., *J. Am. Chem. Soc*., 1964, vol. 86, p. 2946.
23. Temple, C. and Montgomery, J.A., *J. Org. Chem*., 1965, vol. 30, p. 826.
24. Lioux, Th., Gosselin, G., and Mathe, Ch., *Eur. J. Org. Chem*., 2003, p. 3997.
25. Mironov, A.N., *Rukovodstvo po provedeniyu doklinicheskikh issledovanii lekarstvennykh sredstv* (A Guide to Preclinical Trials of Medicines), Moscow: Meditsina, 2012.
26. Mashkovskii, M.D., *Lekarstvennye sredstva* (Medicines), Moscow: Novaya Volna, 2010, 16th ed.