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Synthesis of Isoxazole Derivatives of 4,5-Dihydro-1*H*-pyrazole

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Abstract—Cyclocondensation of pent-1-en-4-yn-3-one with phenylhydrazine and *p*-tolylhydrazine occurs at the positions *1*, *3*. Proceeding from the 1-aryl-3-ethynyl-4,5-dihydro-1*H*-pyrazoles formed in the reaction in yields up to 95% we prepared potentially biologically active isoxazole derivatives of pyrazoline. The structure of 5-[1-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-3-phenyl-1,2-oxazole was studied by X-ray diffraction analysis.

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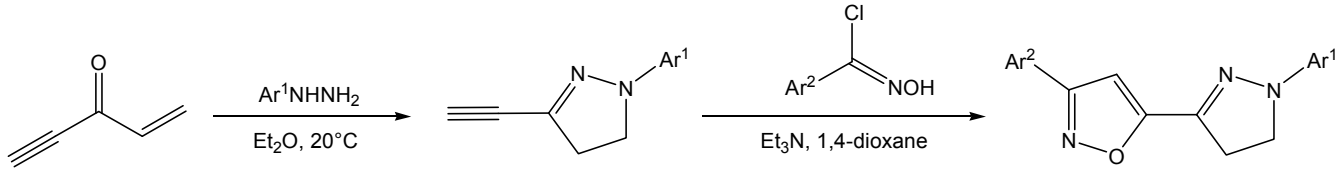
Bisazaheterocycles based on 1,2-oxazole (isoxazole) and pyrazole (pyrazoline) cycles [1, 2], as well as their condensed analogs [3–5] have useful biological activity. For example, some of 3-(1,2-oxazol-5-yl)indazole derivatives have a weak inhibitory effect on the hypoxia-inducible factor [3], and pyrazolinyl-substituted 1,2-benzoxazoles are regarded as inhibitors of nitrogen oxide synthesis enzymes [4]; 3-(pyrazol-4-yl)-1,2-oxazole derivatives are effective analgesic agents comparable in their activity to standard drugs [2].

The development of methods for the synthesis of new specimens of such heterocycles and the study of their properties remain an urgent task. One of the effective methods for the synthesis of bisazole systems is a two-step functionalization of conjugated enyne ketones [6, 7]. We have prepared isoxazole derivatives of 4,5-dihydro-1*H*-pyrazole proceeding from preparative available reagents, and their molecular and crystalline structure has been established. Pent-1-en-4-yn-3-one **1** obtained by oxidation of the corresponding alcohol with active manganese dioxide [8] was used as the initial compound. Taking into account that ketone **1** attaches benzonitrile oxide in a non-regioselective way to form (3-phenyl-4,5-dihydro-1,2-oxazol-5-yl)(3-phenyl-1,2-oxazol-5-yl)methanone [9], in the first stage it was reacted with arylhydrazines. According to the published data, the cyclocondensation of cross-conjugated pentenynones with hydrazines can proceed both at the triple bond with the formation of pyrazoles [10–12] and at the double bond with the formation of the corresponding 4,5-dihydro-1*H*-pyrazole derivatives [13, 14]. A complex mixture of compounds with the predominance of 1-aryl-3-ethynyl-4,5-dihydro-1*H*-pyrazole **2** is formed when ketone **1** reacts with arylhydrazines, and the solvent used in the synthesis has a significant effect on its yield.

Scheme 1.



1 **2a**, **2b** **3a–3e**

2, Ar^1 = Ph (**a**), 4-MeC_6H_4 (**b**); **3**, Ar^2 = Ph, Ar^1 = Ph (**a**), 4-MeC_6H_4 (**b**); Ar^1 = Ph, Ar^2 = 4-$MeOC_6H_4$ (**c**),

Effect of the conditions of reaction between pent-1-en-4-yn-3-one **1** and phenylhydrazine (base) on the yield of pyrazoline **2a**

Solvent	Temperature, °C	Reaction time, h	Ketone **1** conversion, %[a]	Yield of pyrazoline **2a**, %[a]
MeOH	20	2	83	23
MeOH	5	2	68	31
Et_2O	20	1	72	36
Et_2O	0→20	18	63	40
C_6H_6	20	1	70	25
C_6H_6	20	2	76	32
MeCN	20	1	84	18
MeCN	20	2	85	20

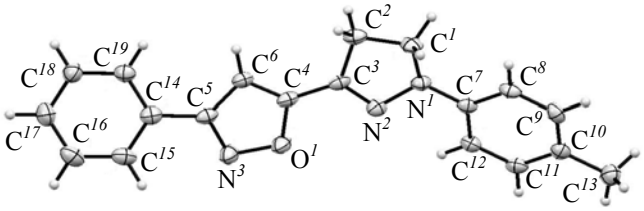
[a] Gas chromatographic analysis data of the reaction mixture.

In the absence of a solvent, the interaction of ketone **1** with phenylhydrazine proceeds explosively to form a complex mixture of oligomers. In the reaction in methanol the nucleophilic addition occurs of alcohol to pyrazoline **2** (GC-MS data). In benzene and acetonitrile the reaction also takes place with the formation of many by-products. Satisfactory results were obtained by slowly heating the reagents in an anhydrous diethyl ether from 0°C to room temperature (see the table). According to GC-MS data, phenylhydrazone of pent-1-en-4-yn-3-one was present in the reaction mixtures during the preparation of pyrazoline **2a**, but its fraction was insignificant (no more than 5%). The pyrazolines **2a** and **2b** separated from the reaction mixture by column chromatography are colorless crystalline substances rapidly darkening during storage. The structure of pyrazolines **2** is reliably confirmed by a combination of spectroscopic data. In the ^{1}H NMR spectra two multiplets at 3.0 and 3.8 ppm correspond to the protons of the pyrazoline ring, and the singlet at ~4.5 ppm, to a proton at a triple bond. Two signals in ^{13}C NMR spectra at 78 and 86 ppm as well as bands of stretching vibrations at 3280 and 2100 cm^{-1} in IR spectra unambiguously confirm the presence of a monosubstituted triple bond (Scheme 1).

The triple bond in compounds **2** is an active dipolarophile, which readily binds the arenecarbonitrile oxides generated *in situ* from *N*-hydroxyarenecarboximidoyl chloride. The latter in turn are obtained by the treatment of aldoximes with N-chlorosuccinimide [15]. Isoxazole derivatives of 4,5-dihydro-1*H*-pyrazole **3**, yellow crystalline substances stable at prolonged storage, were obtained in 75–95% yield.

In the ^{1}H NMR spectra of compounds **3** in the region of 3.33–3.39 and 3.99–4.04 ppm two multiplets are present of the protons of the pyrazoline ring H^4 and H^5, respectively, and at 7.23–7.53 ppm there is the singlet of the isoxazole proton. The assignment of signals in the ^{13}C NMR spectra of compounds 3 was made with the help of two-dimensional heteronuclear experiments HMQC and HMBC (^{1}H–^{13}C). According to these data, the signals of the C^3, C^4, and C^5 atoms of the pyrazoline ring appear in the range of 161–163, 31–32, and 48–49 ppm, and the C^3, C^4, and C^5 atoms of the isoxazole fragment, in the 164–166, 100–101, and 142–145 ppm, respectively. In the mass spectra of electronic ionization of heterocycles **3a–3e** peaks of molecular ions are present whose relative intensity in all cases was 100%. The main direction of the fragmentation of molecular ions is the cleavage of C^3–C^4 and C^3–O bonds of the isoxazole ring with the formation of ions of *m/z* 171 (**3a**, **3c–3e**) and 185 (**3b**).

The investigation of the structure of compound **3b** was carried out using single-crystal X-ray diffraction analysis (see the figure for the numbering of atoms). The bond lengths in the pyrazoline ring alternate, the bond angles are characteristic of sp^3-hybridized (N^1, C^1, C^2) and sp^2-hybridized (N^2, C^3) atoms. However, the lengths of the N^1–C^7 and C^3–C^4 bonds are noticeably shorter than the length of the corresponding ordinary bonds, whereas the distance between the phenyl substituent and the isoxazole ring, according to X-ray diffraction analysis, is close to the standard value [C^6–C^{14} 1.467(3) Å]. The pyrazoline ring is in the *envelope* conformation, where the C^1 atom is off the plane formed by the remaining atoms by 0.379(4) Å [mean deviation of the other atoms



General appearance of the molecule of 5-[1-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-3-phenyl-1,2-oxazole **3b** presented in thermal ellipsoids of 50% probability.

0.007(11) Å]. The average deviation of the atoms from the plane in the isoxazole ring is 0.0025(15) Å. The phenyl substituent at the C^6 atom is turned by 28.4(3)° with respect to the plane of the isoxazole ring, and the *p*-tolyl group in the pyrazoline ring is approximately coplanar to it [the dihedral angle is 19.27(12)°, the angle between the pyrazoline and isoxazole planes is 6.43(11)°].

Thus, the interaction of pent-1-en-4-yn-3-one with phenylhydrazine and *p*-tolyl hydrazine occurs at a double bond and a carbonyl group to form 1-aryl-3-ethynyl-4,5-dihydro-1*H*-pyrazoles. The resulting terminal acetylene derivatives readily enter the 1,3-dipolar cycloaddition reaction, which provides a possibility to easily synthesize the isoxazole derivatives of 4,5-dihydro-1*H*-pyrazole.

EXPERIMENTAL

IR spectra were recorded on a FSM-1201 Fourier spectrometer from pellets with KBr for crystalline samples, and from a thin film between the KBr plates for liquids. The ^{1}H and ^{13}C NMR spectra were taken on spectrometers Bruker AM-300 (300.13 and 75.00 MHz), Bruker Avance III 500 (500.13 and 125.76 MHz), and Bruker Avance III 400 (400.00 and 101.00 MHz), internal reference TMS. 2D experiments COSY, HMBC, and HMQC were performed on a Bruker Avance II 400 instrument. NMR spectra of compounds **3a–3e** were recorded at 80°C, of the remaining substances, at room temperature. High-resolution mass spectra were taken on a Bruker maXis HRMS-ESI-QTOF instrument, mass spectra of electronic ionization were recorded on a Shimadzu GCMS-QP2010 Ultra chromatography-mass spectrometer with a Rtx-5MS capillary column (30 m), ionizing electrons energy 70 eV. The progress of reactions and the homogeneity of the compounds obtained were monitored by TLC on Sorbfil plates in the EtOAc-cyclohexane system, and also by the GLC method on a Kristallyuks 4000M chromatograph with a flame ionization detector and a ZB-1 capillary column (50 m × 0.25 mm). The melting points of substances were measured in open capillaries and were not corrected.

Acrolein (Fluka) was distilled with hydroquinone just before use; phenylhydrazine (Aldrich) was predistilled in vacuo under argon. *p*-Tolylhydrazine was produced from its hydrochloride by treating with a concentrated solution of KOH, followed by extraction with ether. The residue, after distilling off ether, was purified by sublimation in vacuo. *N*-Hydroxyarenecarboximidoyl chlorides were prepared according to [15] and recrystallized from petroleum ether, 40–70.

A single crystal of compound **3b** was obtained by a slow crystallization from aqueous acetone, the linear dimensions of the crystal were 0.5 × 0.3 × 0.2 mm. Colorless prismatic crystals, $C_{19}H_{17}N_3O$ (*M* 303.35) are monoclinic; at 120 K, *a* 17.754(9), *b* 14.004(7), *c* 6.086(3) Å, β 98.501(12)°, *V* 1496.6(13) Å^3, d_{calc} 1.346 mg/mm^3. Space group $P2_1/c$, *Z* 4. A set of 9495 reflections was obtained on a Bruker Apex II CCD area detector, λ (MoK_α) 0.71073 Å radiation, graphite monochromator, $2\theta_{max}$ 51.998°. The extinction was accounted for using the SADABS program [16]. The structure was solved applying the SHELXT program [17], all nonhydrogen atoms were localized in the difference syntheses of electron density and refined with respect to F^2_{hkl} in an anisotropic approximation; all hydrogen atoms were placed in geometrically calculated positions and refined isotropically in the *rider* model, U_{iso}(H) = 1.5 U_{eq}(C) for the methyl group and 1.2 U_{eq}(C) for the other hydrogen atoms. *U*(C) is the equivalent temperature factor of the atom with which the corresponding H atom is bound. The final values of the divergence factors are as follows: R_f 0.054 [for 1710 reflections with $I > 2\sigma(I)$], wR_2 0.1417 (for 2940 independent reflections, R_{int} 0.0858), *GOF* 1.013. All calculations were carried out applying the SHELXL–2014 [17] and OLEX2 [18] program complexes. The compound is registered in the Cambridge Crystallographic Data Center (CCDC 1543866).

Pent-1-en-4-yn-3-ol was obtained from acrolein and lithium acetylide in liquid NH_3 at –70–65°C by procedure [19]. Colorless liquid, mp 58–60°C (40 mmHg). IR spectrum, ν, cm^{-1}: 3367 br [ν(OH)], 3295 [ν(C≡CH)], 3090 [ν(HC=CH$_2$)], 2117 [ν(C≡C)], 1873 (overtone), 1643 [ν(C=C)], 935 [ν(HC=CH$_2$)]. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 2.55 d

(1H, HC≡, *J* 2.2 Hz), 4.09 s (1H, OH), 4.79 d.d.d (1H, H^3, *J* 2.1, 2.4, 7.6 Hz), 5.13 d.t (1H, H^{1A}, *J* 2.0, 11.0 Hz), 5.38 d.t (1H, H^{1B}, *J* 2.0, 17.1 Hz), 5.87 d.d.d (1H, H^2, *J* 5.4, 10.2, 17.2 Hz). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 62.3 (C^3), 74.4 (C^5), 82.5 (C^4), 116.5 (C^1), 136.2 (C^2). Mass spectrum, *m/z* (I_{rel}, %): 81 (100) $[M - 1]^+$, 64 (29), 53 (89.8), 39 (76.2), 30 (4.0).

Pet-2-en-4-yn-3-one (1) was prepared by oxidation of pent-2-en-4-yn-3-ol with active MnO_2 in CH_2Cl_2 at room temperature by procedure [8]. Light yellow liquid, a strong lacrimator. IR spectrum, ν, cm^{-1}: 3260 (C≡CH), 2097 (C≡C), 1654 (C=O), 1614 (C=C), 984 (HC=CH_2). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 3.31 s (1H, HC≡), 6.27 d.d (1H, H^{1A}, *J* 1.5, 10.3 Hz), 6.42 (1H, H^{1B}, *J* 10.3, 17.2 Hz), 6.64 d.d (1H, H^2, *J* 1.5, 17.2 Hz). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 79.9 (C^5), 82.8 (C^4), 134.9 (C^1), 137.5 (C^2), 178.2 (C^3). Mass spectrum, *m/z* (I_{rel}, %): 80 (100) $[M]^+$, 61 (5.2), 53 (100), 37 (4.5).

Compounds 2a and 2b. To a solution of 82 mg (1.03 mmol) of enynone **1** in 1 mL of anhydrous diethyl ether cooled to 0–5°C was added dropwise with stirring a solution of 1.03 mmol of arylhydrazine in 1.5 mL of ether. The reaction mixture was left at room temperature for 14–16 hours, after which the solvent was removed in a vacuum. The reaction products were isolated by chromatography on silica gel (EtOAc–petroleum ether mixture, 1 : 50).

1-Phenyl-3-ethynyl-4,5-dihydro-1*H*-pyrazole (2a). Yield 40%. Colorless lamellar crystals, darkening in air, mp 86–87°C (EtOAc–petroleum ether). IR spectrum, ν, cm^{-1}: 3279 (C≡CH), 2096 (C≡C). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 2.97–3.01 m (2H, H^5), 3.79–3.82 m (2H, H^4), 4.53 s (1H, HC≡), 6.82 t (1H_{arom}, *J* 7.3, 14.6 Hz), 6.97 d (2H_{arom}, *J* 7.8 Hz), 7.24 t (2H_{arom}, *J* 8.1, 15.9 Hz). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ, ppm: 35.2 (C^5), 48.3 (C^4), 78.4 (C≡<u>C</u>H), 86.5 (<u>C</u>≡CH), 113.4 (C_{arom}), 120.0 (C_{arom}), 129.5 (C_{arom}), 133.5 (C_{arom}), 144.8 (C^3). Mass spectrum, *m/z* (I_{rel}, %): 170 (100) $[M]^+$, 142 (4.2), 115 (10.1), 104 (6.4), 91 (29.1), 77 (36.6), 64 (7.7), 51 (10.6). Found, *m/z* 170.0841 $[M + H]^+$. $C_{11}H_{10}N_2$. Calculated, *M* + H 170.0844.

1-(4-Methylphenyl)-3-ethynyl-4,5-dihydro-1*H*-pyrazole (2b). Yield 43%. Colorless lamellar crystals, darkening in air, mp 75–76°C (EtOAc–petroleum ether). IR spectrum, ν, cm^{-1}: 3287 (C≡CH), 2097 (C≡C). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 2.24 s (3H, Me), 2.98–3.02 m (2H, H^5), 3.80–3.83 m (2H, H^4), 4.55 s (1H, HC≡), 6.92 d (2H_{arom}, *J* 8.6 Hz), 7.09 d (2H_{arom}, *J* 8.8 Hz). ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 20.1 (Me), 37.7 (C^5), 48.2 (C^4), 78.0 (C≡<u>C</u>H), 85.8 (<u>C</u>≡CH), 113.0 (C_{arom}), 128.3 (C_{arom}), 129.5 (C_{arom}), 132.4 (C_{arom}), 142.4 (C^3). Mass spectrum, *m/z* (I_{rel}, %): 184 (100) $[M]^+$, 168 (4.6), 154 (1.7), 132 (3.1), 118 (5.8), 105 (21.4), 91 (38.9), 78 (6.6), 65 (12.0), 51 (4.3). Found, *m/z* 185.1071 $[M + H]^+$. $C_{12}H_{12}N_2$. Calculated, *M* + H 185.1073.

Compounds 3a–3e. To a solution of 0.24 mmol of pyrazoline **2** and 0.24 mmol of the corresponding benzhydroxymoyl chloride in 0.65 mL of 1,4-dioxane was added a solution of 35 mg (0.35 mol) of Et_3N. The reaction mixture was left at room temperature for 14-16 hours until the reaction was completed, afterwards 10 mL of water was added, the precipitate was filtered off, washed with water and then with 4 mL of cold 50% EtOH, and air-dried.

3-Phenyl-5-(1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-1,2-oxazole (3a). Yield 91%. Light yellow needles, mp 176.5–177.5°C (Me_2CO-H_2O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.33–3.39 m (2H, H^4), 3.99–4.04 m (2H, H^5), 6.90 t (1H_{arom}, *J* 7.3 Hz), 7.14 d (2H_{arom}, *J* 7.9 Hz), 7.32 t (2H_{arom}, *J* 7.9 Hz), 7.38 s (1H, H_{isox}), 7.52–7.57 m (3H_{arom}), 7.92–7.96 m (2H_{arom}). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm: 31.8 (C^4H_2), 48.6 (C^5H_2), 101.1 (C^4_{isox}); 113.6, 120.4, 127.2, 128.7, 129.6, 129.7, 130.9, 138.7 (C_{arom}); 144.7 (C^5_{isox}), 162.7 ($C^3_{pyrazole}$), 164.8 (C^3_{isox}). Mass spectrum, *m/z* (I_{rel}, %): 289 (100) $[M]^+$, 171 (25.0), 144 (37.3), 130 (4.3), 116 (13.5), 104 (12.3), 91 (6.9), 77 (32.9), 64 (2.6), 51 (7.4). Found, *m/z* 290.1288 $[M + H]^+$. $C_{18}H_{15}N_3O$. Calculated, *M* + H 290.1288.

5-[1-(4-Methylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-3-phenyl-1,2-oxazole (3b). Yield 94%. Light yellow needles, mp 184-185°C (Me_2CO–H_2O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.27 s (3H, Me), 3.31–3.37 m (2H, H^4), 3.96–4.00 m (2H, H^5), 7.06 d (2H_{arom}, *J* 8.5 Hz), 7.14 d (2H_{arom}, *J* 8.5 Hz), 7.27 s (1H, H_{isox}), 7.51–7.56 m (3H_{arom}), 7.91–7.94 m (2H_{arom}). NMR spectrum^{13}C (100 MHz, DMSO-d_6), δ, ppm: 20.6 (Me), 31.9 (C^4H_2), 49.0 (C^5H_2), 100.7 (C^4_{isox}), 113.8, 127.1, 128.9, 129.4, 129.6, 130.1, 130.7, 138.1 (C_{arom}), 142.8 (C^5_{isox}), 162.7 ($C^3_{pyrazole}$), 165.0 (C^3_{isox}). Mass spectrum, *m/z* (I_{rel}, %): 303 (100) $[M]^+$, 185 (22.3), 144 (47.5), 116 (14.6), 91 (22.9), 77 (20.2), 65 (7.5). Found, *m/z* 304.1444 $[M + H]^+$. $C_{19}H_{17}N_3O$. Calculated, *M* + H 304.1444.

3-(4-Methoxyphenyl)-5-(1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-1,2-oxazole (3c). Yield 75%. Light

yellow needles, mp 192.5-193.5°C (Me_2CO–H_2O). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.33–3.37 m (2H, H^4), 3.84 s (3H, MeO), 3.99–4.03 m (2H, H^5), 6.90 t (1H_{arom}, *J* 7.32 Hz), 7.09 d (2H_{arom}, *J* 8.6 Hz), 7.15 d (2H_{arom}, *J* 7.9 Hz), 7.23 s (1H, H_{isox}), 7.29–7.35 m (2H_{arom}), 7.87 (2H_{arom}, *J* 8.5 Hz). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm: 31.9 (C^4H_2), 48.7 (C^5H_2), 55.9 (MeO), 100.9 (C^4_{isox}); 113.7, 115.1, 120.4, 121.3, 128.7, 129.6, 138.8 (C_{arom}); 144.9 (C^5_{isox}), 161.4, 162.4 ($C^3_{pyrazole}$), 164.6 (C^3_{isox}). Mass spectrum, *m/z* (I_{rel}, %): 319 (100) $[M]^+$, 275 (5.1), 187 (4.4), 171 (27.8), 159 (11.0), 146 (50.4), 131 (5.1), 119 (6.5), 104 (17.7), 91 (8.2), 77 (31.8), 64 (6.5), 51 (5.9). Found, *m/z* 320.1394 $[M + H]^+$. $C_{19}H_{17}N_3O_2$. Calculated, *M* + H 320.1394.

5-(1-Phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-3-(4-chlorophenyl)-1,2-oxazole (3d). Yield is 95%. Yellow needles, mp 205°C (Me_2CO–H_2O). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.34–3.38 m (2H, H^4), 4.00–4.05 m (2H, H^5), 6.91 t (1H_{arom}, *J* 7.2 Hz), 7.15 d (2H_{arom}, *J* 7.9 Hz), 7.30–7.36 m (3H_{arom} + H_{isox}), 7.60 d (2H_{arom}, *J* 8.2 Hz), 7.96 d (2H_{arom}, *J* 8.6 Hz). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm: 31.9 (C^4H_2), 48.8 (C^5H_2), 100.9 (C^4_{isox}); 113.8, 120.5, 127.8, 129.0, 129.6, 129.7, 135.6, 138.6 (C_{arom}); 144.8 (C^5_{isox}), 161.9 ($C^3_{pyrazole}$), 165.1 (C^3_{isox}). Mass spectrum, *m/z* (I_{rel}, %): 323 (100) $[M]^+$, 184 (5.7), 171 (36.6), 150 (30.3), 123 (11.1), 104 (26.9), 91 (15.0), 77 (44.1), 64 (6.3), 51 (11.1). Found, *m/z* 324.0898 $[M + H]^+$. $C_{18}H_{14}ClN_3O$. Calculated, *M* + H 324.0898.

3-(3-Nitrophenyl)-5-(1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-1,2-oxazole (3e). Yield 95%, Yellow needles, mp 205-206°C (Me_2CO–H_2O). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.35–3.40 m (2H, H^4), 4.02–4.06 m (2H, H^5), 6.91 t (1H_{arom}, *J* 7.3 Hz), 7.16 d (2H_{arom}, *J* 7.9 Hz), 7.33 t (2H_{arom}, *J* 7.9 Hz), 7.53 s (1H, H_{isox}), 7.85 t (1H_{arom}, *J* 8.1 Hz), 8.34–8.41 m (2H_{arom}) 8.70 s (1H_{arom}). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm: 31.8 (C^4H_2), 48.8 (C^5H_2), 101.1 (C^4_{isox}); 113.8, 120.6, 121.7, 125.3, 129.6, 130.5, 131.4, 133.4, 138.4 (C_{arom}); 144.7 (C^5_{isox}), 149.0, 161.3 ($C^3_{pyrazole}$), 165.6 (C^3_{isox}). Mass spectrum, *m/z* (I_{rel}, %): 334 (100) $[M]^+$, 304 (7.2), 288 (10.0), 189 (17.2), 171 (25.4), 157 (7.0), 143 (22.4), 130 (6.2), 115 (13.5), 104 (35.5), 91 (18.5), 77 (61.5), 64 (9.2), 51 (11.5). Found, *m/z* 335.1139 $[M + H]^+$. $C_{18}H_{14}N_4O_3$. Calculated, *M* + H 335.1139.

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REFERENCES

1. Abass, M., Abdel-Megid, M., and Hassan, M., *Synth. Commun*., 2013, vol. 43, p. 329.
2. Karthikeyan, K., Seelan, T.V., Lalitha, K.G., and Perumal, P.T., *Bioorg. Med. Chem. Lett*., 2009, vol. 19, p. 3370.
3. An, H., Kim, H.-J., Jung, N.-J., Jang, H., Park, J.-W., and Suh, Y.-G., *Bioorg. Med. Chem. Lett*., 2011, vol. 21, p. 6297.
4. Carrión, M.D., Camacho, M.E., León, J., Escames, G., Tapias, V., Acuna-Castroviejo, D., Gallo, M.A., and Espinosa, A., *Tetrahedron*, 2004, vol. 60, p. 4051.
5. Spiteri, C., Keeling, S., and Moses, J.E., *Org. Lett*., 2010, vol. 12, p. 3368.
6. Golovanov, A.A. and Odin, I.S., *Russ. J. Org. Chem*., 2015, vol. 51, p. 447. doi 10.1134/S1070428015030306
7. Golovanov, A.A., Odin, I.S., Bekin, V.V., Vologzhanina, A.V., Bushmarinov, I.S., Zlotskii, S.S., Gerasimov, Yu.L., and Purygin, P.P., *Russ. J. Org. Chem*., 2016, vol. 52, p. 414. doi 10.1134/S1070428016030209
8. Malacria, M. and Roumestant, M.L., *Tetrahedron*, 1977, vol. 33, p. 2813.
9. Bondarev, G.N., Ryzhov, V.A., Chistokletov, V.N., and Petrov, A.A., *Zh. Org. Khim*., 1967, vol. 3, p. 821.
10. Reimlinger, H. and Vandewalle, J.J.M., *Lieb. Ann*., 1968, vol. 720, p. 117. doi 10.1002/jlac.19687200110
11. Nightingale, D. and Wadsworth, F., *J. Am. Chem. Soc*., 1945, vol. 67, p. 416.
12. Miller, R.D. and Reiser, O., *J. Heterocycl. Chem*., 1993, vol. 30, p. 775.
13. Botvinnik, E.V., Blandov, A.N., and Kuznetsov, M.A., *Russ. J. Org. Chem*., 2001, vol. 37, p. 421. doi 10.1023/A:1012448911890
14. Braude, E.A., Linstead, R.P., and Wooldridge, K.R., *J. Chem. Soc*., 1956, p. 3070.
15. Liu, K.-C., Shelton, B.R., and Howe, R.K., *J. Org. Chem*., 1980, vol. 45, p. 3916.
16. Sheldrick, G.M., *SADABS v. 2.01*, *Bruker/Siemens Area Detector Absorption Correction Program*, Madison, Wisconsin, USA: Bruker AXS, 1998.
17. Sheldrick, G.M., *Acta Cryst*., 2015, vol. A71, p. 3.
18. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K., and Puschmann, H., *J. Appl. Cryst*., 2009, vol. 42, p. 339.
19. Brandsma, L., *Preparative Acetylenic Chemistry*, Amsterdam–Oxford–New York–Tokyo: Elsevier, 1988.