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# Azolyl-Substituted 1,2,3-Triazoles

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**Abstract**—Huisgen reaction of (*E*)-1,5-diarylpent-2-en-4-yn-1-ones and (*E*)-1,5-diarylpent-1-en-4-yn-3-ones afforded 1-aryl-3-(5-aryl-1*H*-1,2,3-triazol-4-yl)prop-2-en-1-ones and 3-aryl-1-(5-aryl-1*H*-1,2,3-triazol-4-yl)-prop-2-en-1-ones, respectively. (*E*)-1-Aryl-3-(5-phenyl-1*H*-1,2,3-triazol-4-yl)prop-2-en-1-ones reacted with hydrazine hydrate and phenylhydrazine to give 72–93% of 4-(3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)-5-phenyl-1*H*-1,2,3-triazoles which underwent dehydrogenation on heating in boiling acetic acid with formation of the corresponding pyrazole derivatives. The molecular structures of (*E*)-3-phenyl-1-(5-phenyl-1*H*-1,2,3-triazol-4-yl)prop-2-en-1-one and 4-[3-(4-methylphenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl]-5-phenyl-1*H*-1,2,3-triazole were studied by X-ray analysis. 4-(3-Aryl-4,5-dihydro-1*H*-pyrazol-5-yl)-5-phenyl-1*H*-1,2,3-triazoles showed toxicity against *Daphnia magna*.

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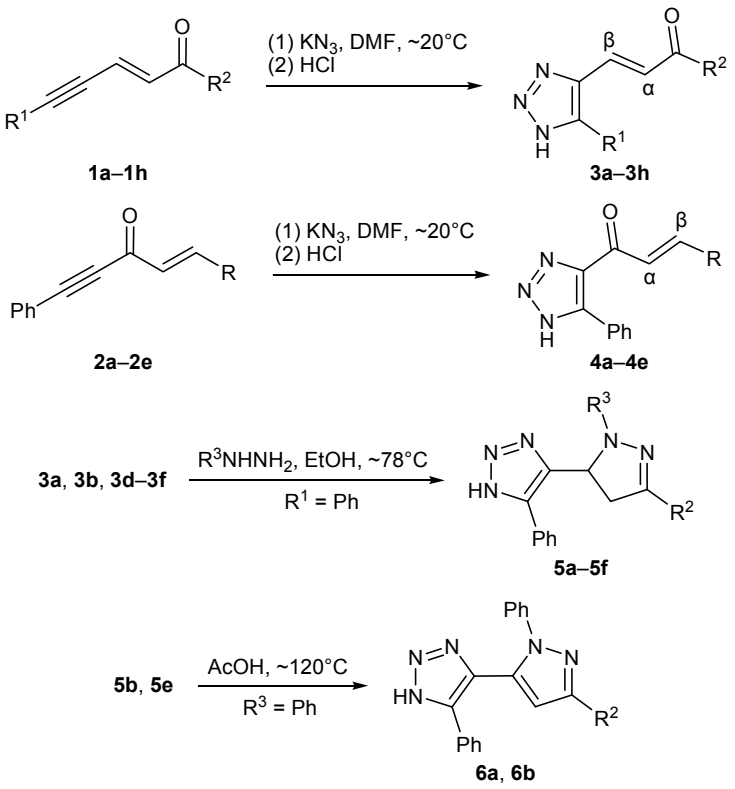
1,2,3-Triazole derivatives exhibit a broad spectrum of biological activity [1–3]; for example, cinnamoyl-substituted 1,2,3-triazoles and 1,2,3-benzotriazoles (azachalcones) efficiently inhibit transglutaminase [4, 5]. These compounds can be used to obtain triazolyl-substituted heterocyclic systems [6–9] which were reported to possess pronounced antimicrobial activity [10, 11]. Therefore, synthesis of new 1,2,3-triazole derivatives and study of their properties are topical problems.

Cinnamoyl-substituted 1,2,3-triazoles can be synthesized by cycloaddition of azides to unsaturated ketones [4, 12]. In the preliminary communication [13] we showed the possibility for preparing azolyl-substituted 1,2,3-triazoles from 1,5-disubstituted (*E*)-pent-2-en-4-yn-1-ones **1**. Herein we report the synthesis of a series of 5-aryl-4-(azol-5-yl)-1,2,3-triazoles from ketones **1** and the results of studying their structure and toxicity.

Aryl acetylenylvinyl ketones **1a**–**1h**, as well as vinylacetylenyl ketones **2a**–**2g**, are reactive dipolarophiles which reacted with $KN_3$ in DMF at room temperature. The reactions were complete in less than 1 h; after removal of the solvent and acidification, we isolated 89–98% of isomeric chalcones **3a**–**3h** and **4a**–**4e** (Scheme 1). Compounds **3** and **4** are colorless or light yellow crystalline finely crystalline substances with sharp melting points, which are stable on storage. The cycloaddition was regioselective; according to the TLC and $^1$H NMR data, compounds **3** and **4** were formed as a single isomer. Analogous regioselectivity was observed previously in the reactions of some activated acetylenes with azides [14, 15].

The structure of compounds **3a**–**3h** and **4a**–**4e** was confirmed by elemental analyses and IR, NMR, and mass spectra. The IR spectra of **3** and **4** contained absorption bands typical of stretching vibrations of carbonyl (1665–1652 and 1675–1637 cm$^{-1}$, respectively) and endocyclic NH group (3232–3174 and 3200–3090 cm$^{-1}$, respectively). In the $^1$H NMR spectra of **3** and **4**, protons on the *trans*-configured double bond resonated as doublets at δ 7.60–7.93 ppm ($J$ = 15–16 Hz), and the NH signal appeared as a broadened singlet at δ 7.5–12.4 (**3**) or 10.9–16.0 ppm (**4**). The carbonyl carbon signal was observed in the $^{13}$C NMR spectra at $\delta_C$ 181–190 ppm.

**Scheme 1.**




**1**, **3**, $R^1 = R^2$ = Ph (**a**); $R^1$ = Ph, $R^2$ = 4-$MeC_6H_4$ (**b**), 4-$MeOC_6H_4$ (**c**), 4-$ClC_6H_4$ (**d**), 4-$BrC_6H_4$ (**e**), thiophen-2-yl (**f**); $R^1$ = 4-$MeC_6H_4$, $R^2$ = Ph (**g**); $R^1 = R^2$ = 4-$BrC_6H_4$ (**h**); **2**, **4**, R = Ph (**a**), 4-$ClC_6H_4$ (**b**), 3-$BrC_6H_4$ (**c**), 4-$Me_2NC_6H_4$ (**d**), thiophen-2-yl (**e**); **5**, $R^2 = R^3$ = Ph (**a**); $R^3$ = Ph, $R^2$ = 4-$MeC_6H_4$ (**b**), 4-$ClC_6H_4$ (**c**), 4-$BrC_6H_4$ (**d**), thiophen-2-yl (**e**); $R^2$ = Ph, $R^3$ = H (**f**); **6**, $R^2$ = 4-$MeC_6H_4$ (**a**), 4-$BrC_6H_4$ (**b**).

Compounds **3** fairly readily reacted with hydrazine hydrate and phenylhydrazine hydrochloride on heating in boiling ethanol to afford 72–93% of 4-(4,5-dihydro-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazoles **5a**–**5f**. Compounds **5** displayed in the $^1$H NMR spectra signals from two diastereotopic protons on $C^4$ of the pyrazole ring (δ 3.18–3.51 ppm) and 5-H (δ 5.71–7.69 ppm), as well as a broadened singlet from the triazole NH proton (δ ~15.3 ppm). The $^1$H NMR spectrum of **5a** showed two NH signals at δ 14.95 and 15.51 ppm, presumably due to the presence of two tautomers.

The described procedure for the synthesis of azolyl-substituted 1,2,3-triazoles is characterized by high yields and selectivity and easy workup (no chromatographic separation is necessary), and it can be regarded as an alternative to the previously proposed method of synthesis of analogous nonfused biheterocycles [16].

Heating of compounds **5b** and **5e** in boiling acetic acid on exposure to air resulted in their dehydrogenation with formation of pyrazolyl-substituted 1,2,3-triazoles **6a** and **6b** (yield 82–89%). Their structures were confirmed by high-resolution mass spectra. The $^{13}$C and $^1$H NMR spectra of **6a** and **6b** indicated the absence in their molecules of $CH_2$ and $C_{sp^3}H$ groups. According to [17], triazoles **6** can exist as several tautomers.

The structure of **4a** was studied by X-ray powder diffraction (Fig. 1). The results confirmed *E* configuration of the exocyclic double bond and *s*-*cis* conformation of the enone fragment. Molecules **4a** in crystal are linked through strong hydrogen bonds $N^8$–H···$O^4$ ($r_{N\cdots O}$ 2.83 Å) to form infinite chains.

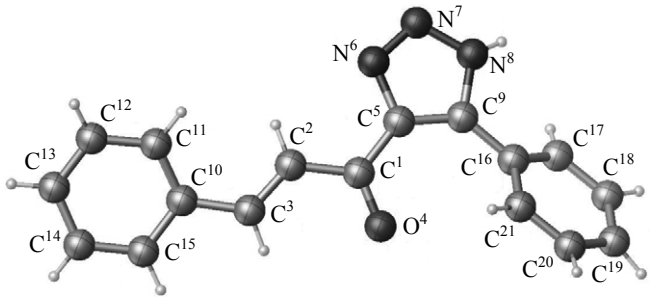



**Fig. 1.** Structure of the molecule of (*E*)-3-phenyl-1-(5-phenyl-1*H*-1,2,3-triazol-4-yl)prop-2-en-1-one (**4a**) in crystal.

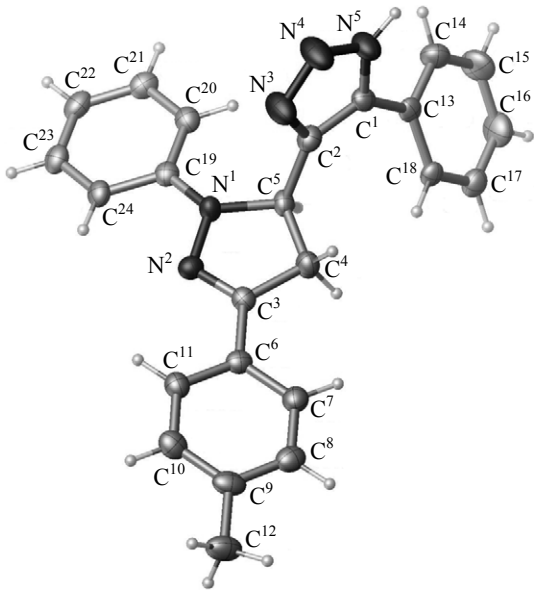



**Fig. 2.** Structure of the molecule of 4-[3-(4-methylphenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl]-5-phenyl-1*H*-1,2,3-triazole (**5b**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

The molecular structure of 4-[3-(4-methylphenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl]-5-phenyl-1*H*-1,2,3-triazole (**5b**) is shown in Fig. 2. Molecule **5b** possesses an asymmetric carbon atom, and this compound crystallized in non-centrosymmetric space group (*Fdd*2), indicating the presence of both enantiomers (racemic compound). The dihydropyrazole ring is characterized by bond alternation, and the bond angles are typical of $sp^3$- ($N^1$, $C^4$, $C^5$) and $sp^2$-hybridized atoms ($N^2$, $C^3$). The bond lengths in the triazole ring and bond angles therein indicate delocalization of electron density. The $C^2$–$C^5$ bond between the heterocycles [1.493(6) Å] is close to standard carbon–carbon bond, whereas the bonds between the aryl substituents and the heterocycles are somewhat shortened. The other bond lengths and bond angles in molecule **5b** are similar to the corresponding reference values. The 1,2,3-triazole ring is planar within 0.003(3) Å. The dihydropyrazole ring adopts an *envelope* conformation where the $N^1$ atom deviates by 0.087(6) Å from the plane formed by the other atoms [the mean deviation of atoms is 0.005(3) Å]. The dihydropyrazole and triazole ring planes form a dihedral angle of 75.3(2)°. The aryl substituents on the dihydropyrazole ring are almost coplanar [the dihedral angles are 7.9(2)° for the 4-methylphenyl ring and 15.1(2)° for the phenyl ring]. The phenyl ring on $C^1$ is turned through an angle of 34.1(2)° with respect to the 1,2,3-triazole ring plane.

The toxicity of compounds **3b** and **5b**–**5d** was studied against *Daphnia magna* (laboratory culture) which is commonly used for quantitative assays of toxic effect of many organic compounds [18]. Lethal concentrations ($LC_{50}$), lowest lethal concentrations ($LC_{Lo}$), and minimal concentrations inhibiting and completely suppressing reproduction of *Daphnia magna* were determined (Table 1). Compounds **3b** and **5b**–**5d** were characterized by close $LC_{50}$ values. Their lethal effect was observed starting from a concentration of 0.01 mg/L, and the total death, from a concentration of 0.5–1.0 mg/L. All compounds showed negative effect on the reproduction of *Daphnia magna* and increased the fetal period.

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were recorded on Bruker AM-300 (300 and 75.47 MHz, respectively) and Jeol ECX-400A spectrometers (400 and 100 MHz, respectively) using tetramethylsilane as internal standard. The IR spectra were measured in KBr on an FSM-1201 spectrometer with Fourier transform. The elemental analyses were obtained on a Perkin Elmer Model 2400 CHN analyzer. The electron impact mass spectra (70 eV) were recorded on a Shimadzu GCMS-QP2010Ultra instrument equipped with a 30-m Rtx-5MS capillary column. The high-resolution mass spectra (HESI) were obtained on a Q Exactive mass spectrometer. The progress of reactions was monitored, and the purity of the isolated compounds was checked,

**Table 1.** Toxicity parameters of compounds **3b** and **5b**–**5d** against *Daphnia magna* (mg/L)

| Compound no. | $LC_{50}$ | Minimal lethal concentration | Minimal concentration inhibiting reproduction | Minimal concentration suppressing reproduction |
|---|---|---|---|---|
| **3b** | 1.66±0.85 | 0.5 | 0.005 | 2.0 |
| **5b** | 1.75±0.25 | 1.0 | 0.005 | 2.0 |
| **5c** | 1.77±0.75 | 0.5 | 0.01 | 1.6 |
| **5d** | 1.15±0.13 | 0.1 | 0.005 | 2.0 |

by TLC on Sorbfil plates (ethyl acetate–cyclohexane, 2 : 1). The melting points were determined in open capillaries.

The X-ray powder diffraction pattern of compound **4a** was obtained on a Bruker D8 AdvanceVario diffractometer equipped with a Ge(111) monochromator and a LynxEye position-sensitive detector (Cu$K_{\alpha 1}$ radiation, λ = 1.540596 Å; scan range 2θ 3.8–80°, scan step 0.01048°). All calculations were performed using Bruker TOPAS software [19]. The X-ray powder pattern was indexed by the SVD technique [20] implemented in TOPAS. Orthorhombic crystal system; unit cell parameters: $a$ = 26.44840(30), $b$ = 13.01737(10), $c$ = 8.249606(51) Å; $V$ = 2840.25(4) Å$^3$. The *Pbca* space group was determined from systematic extinction. The volume of the independent part of the unit cell corresponded to one formula unit. The structure was solved in the direct space by the parallel tempering algorithm implemented in FOX [21]. The structure proposed on the basis of the NMR data and calculated for the gas phase by the PM3 method (Hyperchem) was used as model. The Rietveld refinement was performed with restraints on bond lengths and bond angles. The positions of hydrogen atoms were refined according to the riding model, using the same isotropic thermal parameter for each type of atoms in each molecule. A symmetric modification of the previously reported soft restraints on bond lengths [22] was applied; the lack of overshots (with account taken of mean-square deviations) in bond length distribution over a wide range of restraint strengths (parameter $K_1$) indicated the validity of the refined structural model. Corrections for preferred sample orientations (Järvinen fourth-order spherical harmonics, texture index 1.06) and anisotropic line broadening were applied. The line asymmetry was refined according to the axial divergence model [23]. The simulated diffractogram ($K_1$ = 8.00, mean-square deviation for bond lengths 0.014 Å) conformed well to the experimental pattern, and the divergence factors were comparable with those for the Pawley refinement of line intensities (Table 2).

A 0.5×0.06×0.06-mm light yellow single crystal (needle) of **5b** was obtained by slow crystallization from ethanol; $C_{25}H_{24}N_5O_{0.5}$ ($M$ 379.47); orthorhombic crystal system (120 K) with the following unit cell parameters: $a$ = 18.2477(5), $b$ = 86.222(2), $c$ = 5.7239(2) Å; $V$ = 9005.7(2); $d_{calc}$ = 1.1194 mg/mm$^3$; space group *Fdd*2; $Z$ = 16. A set of 15965 reflections was collected at 120 K on a Bruker Apex II diffractometer (CCD area detector, λCu$K_\alpha$ radiation, multilayer optics microfocus tube, $2\theta_{max}$ = 130°). A correction for absorption was applied using SADABS [24]. The structure was solved by the charge flipping algorithm; all non-hydrogen atoms were localized by difference syntheses of electron density and were refined against $F^2_{hkl}$ in anisotropic approximation; all hydrogen atoms were placed into geometrically calculated positions which were refined in isotropic approximation according to the riding model [$U_{iso}$(H) = 1.5 $U_{eq}$(C) for methyl group or 1.2 $U_{eq}$(X) for the other atoms, where $U$(X) is the equivalent temperate factor of the atom to which the given hydrogen atom is attached]. The unit cell also contained disordered ethanol molecules whose contribution to the total intensity was taken into account without refinement of atom positions using SQUEEZE/PLATON [25]. The molecular formula, molecular weight, and density were calculated with the solvent molecules included. Final divergence factors: $R_F$ = 0.063 [for 3399 reflections with $I > 2\sigma(I)$], $wR_2$ = 0.143 (for 3723 independent reflections, $R_{int}$ = 0.073); goodness of fit 1.07, Flack parameter 0.2(5). All calculations were performed using SHELXTL [26] and OLEX2 [27].

**Table 2.** Divergence factors for structure refinement of compound **4a**

| Factor | Pawley refinement | Rietveld refinement |
|---|---|---|
| $K_1$ | – | 8.00 |
| $R_{wp}$, % | 1.81 | 1.79 |
| $R'_{wp}$,[a] % | 7.67 | 6.01 |
| $R_p$, % | 1.36 | 1.16 |
| $R'_p$,[a] % | 11.27 | 5.84 |
| $R_{Bragg}$, % | 0.04 | 0.65 |
| GOF | 2.40 | 2.20 |

[a] Background-corrected values.

The crystallographic data for compounds **4a** and **5b** were deposited to the Cambridge Crystallographic Data Center, CCDC entry nos. 1015704 (**4a**) and 1009919 (**5b**), and are available at www.ccdc.cam.ac.uk/data_request/cif.

Ketones **1** [28] and **2** [29] and compounds **3**–**5** [13] were synthesized by known methods. Compounds **3a**, **3b**, **3d**, and **5a**–**5c** were described in [13].

**(*E*)-1-(4-Methoxyphenyl)-3-(5-phenyl-1*H*-1,2,3-triazol-4-yl)prop-2-en-1-one (3c).** Yield 90%, light yellow crystals, mp 133–134°C (from benzene–petroleum ether). IR spectrum, ν, cm$^{-1}$: 3193 (NH), 1656

(C=O). $^1$H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 3.79 s (3H, $CH_3O$), 6.86–7.63 m (7H, $H_{arom}$), 7.88 d (1H, β-H, $^3J$ = 15.4 Hz), 8.03–8.11 m (3H, α-H, $H_{arom}$), 10.07 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, $CDCl_3$), $\delta_C$, ppm: 55.5 ($OCH_3$), 114.0–163.9, 188.4 (C=O). Mass spectrum: *m*/*z* 306.1243 $[M + H]^+$. Found, %: C 70.50; H 5.12. $C_{18}H_{15}N_3O_2$. Calculated, %: C 70.80; H 4.96. *M* + H 306.1243.

**(*E*)-1-(4-Bromophenyl)-3-(5-phenyl-1*H*-1,2,3-triazol-4-yl)prop-2-en-1-one (3e).** Yield 98%, light yellow crystals, mp 133–134°C (from benzene–petroleum ether). IR spectrum, ν, $cm^{-1}$: 3207 (NH), 1661 (C=O). $^1$H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 7.43–7.91 m (10H, β-H, $H_{arom}$), 8.00 d (1H, α-H, $^3J$ = 15.4 Hz), 8.70 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, $CDCl_3$), $\delta_C$, ppm: 124.1–136.3, 188.9 (C=O). Mass spectrum: *m*/*z* 354.0240 $[M + H]^+$. Found, %: C 57.26; H 3.40; Br 22.45. $C_{17}H_{12}BrN_3O$. Calculated, %: C 57.64; H 3.42; Br 22.56. *M* + H 354.0243.

**(*E*)-3-(5-Phenyl-1*H*-1,2,3-triazol-4-yl)-1-(thiophen-2-yl)prop-2-en-1-one (3f).** Yield 91%, light yellow crystals, mp 172.5–173.5°C (from aq. EtOH). IR spectrum, ν, $cm^{-1}$: 3187 (NH), 1656 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.26–7.72 m (7H, β-H, $H_{arom}$), 7.87 d (1H, α-H, $^3J$ = 15.4 Hz), 7.93–8.02 m (2H, $H_{arom}$), 15.73 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 123.5–144.8, 181.0 (C=O). Mass spectrum: *m*/*z* 282.0699 $[M + H]^+$. Found, %: C 63.93; H 3.95; N 14.84. $C_{15}H_{11}N_3OS$. Calculated, %: C 70.80; H 4.96; N 14.94. *M* + H 282.0702.

**(*E*)-3-[5-(4-Methylphenyl)-1,2,3-triazol-4-yl]-1-phenylprop-2-en-1-one (3g).** Yield 87%, light yellow crystals, mp 125–126°C (from aq. EtOH). IR spectrum, ν, $cm^{-1}$: 3187 (NH), 1656 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 2.41 s (3H, $CH_3$), 7.25–7.61 m (8H, NH, $H_{arom}$), 7.89 d (1H, β-H, $^3J$ = 15.4 Hz), 7.92–7.97 m (3H, α-H, $H_{arom}$). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 21.4 ($CH_3$), 124.8–139.8, 190.0 (C=O). Mass spectrum: *m*/*z* 290.1291 $[M + H]^+$. Found, %: C 74.52; H 5.41; N 14.23. $C_{18}H_{15}N_3O$. Calculated, %: C 74.72; H 5.23; N 14.52. *M* + H 290.1289.

**(*E*)-1-(4-Bromophenyl)-3-[5-(4-bromophenyl)-1*H*-1,2,3-triazol-4-yl]prop-2-en-1-one (3h).** Yield 91%, colorless crystals, mp 166–167°C (from benzene–petroleum ether). IR spectrum, ν, $cm^{-1}$: 3174 (NH), 1652 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.27–7.67 m (8H, β-H, $H_{arom}$, NH), 7.93 d (1H, α-H, $^3J$ = 15.4 Hz), 7.98–8.01 m (2H, $H_{arom}$). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 122.6–136.1, 187.9 (C=O). Mass spectrum: *m*/*z* 431.9348 $[M + H]^+$. Found, %: C 47.50; H 2.83; N 9.25. $C_{17}H_{11}Br_2N_3O$. Calculated, %: C 47.14; H 2.56; N 9.70. *M* + H 431.9343.

**(*E*)-3-Phenyl-1-(5-phenyl-1,2,3-triazol-4-yl)prop-2-en-1-one (4a).** Yield 89%, colorless crystals, mp 140–141°C (from aq. MeOH). IR spectrum, ν, $cm^{-1}$: 3178 (NH), 1652 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.27–7.87 m (11H, β-H, $H_{arom}$), 7.91 d (1H, α-H, $^3J$ = 15.8 Hz), 10.98 br.s. (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 123.3–145.1, 183.9 (C=O). Mass spectrum, *m*/*z* ($I_{rel}$, %): 275 (35) $[M]^+$, 246 (26), 131 (51), 115 (23), 103 (80), 89 (47), 77 (100), 63 (28), 51 (39). Found: *m*/*z* 276.1124 $[M + H]^+$. $C_{17}H_{13}N_3O$. Calculated: *M* + H 276.1133.

**(*E*)-3-(4-Chlorophenyl)-1-(5-phenyl-1,2,3-triazol-4-yl)prop-2-en-1-one (4b).** Yield 94%, light yellow crystals, mp 171–172°C (from benzene–petroleum ether). IR spectrum, ν, $cm^{-1}$: 3137 (NH), 1637 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.45–7.54 m (5H, $H_{arom}$), 7.75 d (1H, β-H, $^3J$ = 16.1 Hz), 7.79–7.94 m (5H, α-H, $H_{arom}$), 15.94 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 124.5–141.8, 183.2 (C=O). Mass spectrum, *m*/*z* ($I_{rel}$, %): 310.0745 $[M + H]^+$, 309 (17) $[M]^+$, 280 (28), 165 (38), 137 (36), 101 (100), 89 (87), 75 (64), 63 (49), 51 (50). Found, %: C 65.93; H 3.95; N 13.60. $C_{17}H_{12}ClN_3O$. Calculated, %: C 65.92; H 3.90; N 13.57. *M* + H 310.0743.

**(*E*)-3-(3-Bromophenyl)-1-(5-phenyl-1,2,3-triazol-4-yl)prop-2-en-1-one (4c).** Yield 95%, colorless crystals, mp 169–170°C (from benzene–petroleum ether). IR spectrum, ν, $cm^{-1}$: 3132 (NH), 1675 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.35–7.65 m (5H, $H_{arom}$), 7.73 d (1H, β-H, $^3J$ = 16.1 Hz), 7.79–7.95 m (5H, α-H, $H_{arom}$), 15.96 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 124.3–141.4, 182.9 (C=O). Mass spectrum: *m*/*z* 354.0237 $[M + H]^+$. Found, %: C 57.51; H 3.34; N 11.81. $C_{17}H_{12}BrN_3O$. Calculated, %: C 57.65; H 3.41; N 11.86. *M* + H 354.0238.

**(*E*)-3-[4-(Dimethylamino)phenyl]-1-(5-phenyl-1,2,3-triazol-4-yl)prop-2-en-1-one (4d).** Yield 82%, bright red crystals, mp 143–144°C (from benzene–petroleum ether). IR spectrum, ν, $cm^{-1}$: 3090 (NH), 1637 (C=O). $^1$H NMR spectrum (400 MHz, DMSO-$d_6$), δ, ppm: 2.96 s [6H, $(CH_3)_2N$], 6.69–7.83 m (12H, β-H, $H_{arom}$, NH). $^{13}$C NMR spectrum (100 MHz, DMSO-$d_6$),

$\delta_C$, ppm: 40.2 [$(CH_3)_2N$], 112.4–152.6, 183.7 (C=O). Mass spectrum: *m*/*z* 319.1549 [*M* + H]$^+$. Found, %: C 71.49; H 5.76; N 17.35. $C_{19}H_{18}N_4O$. Calculated, %: C 71.68; H 5.70; N 17.60. *M* + H 319.1555.

**(*E*)-1-(5-Phenyl-1,2,3-triazol-4-yl)-3-(thiophen-2-yl)prop-2-en-1-one (4e).** Yield 86%, light yellow crystals, mp 151–152°C (from benzene–petroleum ether). IR spectrum, ν, cm$^{-1}$: 3200 (NH), 1660 (C=O). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.03–7.44 m (6H, $H_{arom}$), 7.60 d (1H, β-H, $^3J$ = 15.8 Hz), 8.00 d (1H, α-H, $^3J$ = 15.8 Hz), 8.02–8.81 m (2H, $H_{arom}$), 12.18 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 122.2–145.0, 183.2 (C=O). Mass spectrum, *m*/*z* ($I_{rel}$, %): 282.0704 [*M* + H]$^+$; 281 (15) [*M*]$^+$, 252 (41), 137 (68), 109 (100), 89 (89), 77 (49), 65 (91), 51 (46). Found, %: C 63.92; H 3.98; N 14.59. $C_{15}H_{11}N_3OS$. Calculated, %: C 64.04; H 3.94; N 14.94. *M* + H 282.0697.

**4-[3-(4-Bromophenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl]-5-phenyl-1*H*-1,2,3-triazole (5d).** Yield 84%, colorless crystals, mp 112–113°C (from aq. MeOH). IR spectrum, ν, cm$^{-1}$: 3258 (NH), 1596 (C=N). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 3.21 d.d (1H, 4-H, $^2J$ = 17.0, $^3J$ = 7.7 Hz), 3.23–3.38 m (1H, 4-H), 5.77 d.d (1H, 5-H, $^2J$ = 12.1, $^3J$ = 7.7 Hz), 6.69–7.68 m (14H, $H_{arom}$), 15.26 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 40.4 ($C^4$), 55.7 ($C^5$), 113.0–146.5. Found: *m*/*z* 444.0818 [*M* + H]$^+$. $C_{23}H_{18}BrN_5$. Calculated: *M* + H 444.0820.

**5-Phenyl-4-[1-phenyl-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl]-1*H*-1,2,3-triazole (5e).** Yield 72%, colorless crystals, mp 95–96°C (from aq. MeOH). IR spectrum, ν, cm$^{-1}$: 3335 (NH), 1595 (C=N). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 3.26 m (1H, 4-H), 3.44 d.d (1H, 4-H, $^2J$ = 17.2, $^3J$ = 12.8 Hz), 5.70–5.77 m (1H, 5-H), 6.62–7.77 m (13H, $H_{arom}$), 15.27 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 40.4 ($C^4$), 55.6 ($C^5$), 112.9–144.1. Found: *m*/*z* 372.1284 [*M* + H]$^+$. $C_{21}H_{17}N_5S$. Calculated: *M* + H 372.1279.

**5-Phenyl-4-[3-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl]-1*H*-1,2,3-triazole (5f).** Yield 85%, colorless crystals, mp 129–130°C (from aq. MeOH). IR spectrum, ν, cm$^{-1}$: 3428 (NH), 3268 (NH), 1588 (C=N). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 3.15–3.24 m (1H, 4-H), 3.38–3.47 m (1H, 4-H), 5.13–5.21 m (1H, 5-H), 7.36–7.73 m (11H, $H_{arom}$, NH), 15.10 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 38.1 ($C^4$), 54.9 ($C^5$), 127.1–141.5, 148.3 (C=N). Found, %: C 70.20; H 5.63. $C_{17}H_{15}N_5$. Calculated, %: C 70.57; H 5.24.

**Compounds 6a and 6b (*general procedure*).** A solution of 0.5 mmol of compound **5b** or **5e** in 5–7 mL of glacial acetic acid was heated for 6–8 h under reflux. The mixture was cooled and poured onto ice under stirring. The precipitate was filtered off, washed with 50% ethanol, and dried first in air and then under reduced pressure (30 mm) at 75–80°C.

**4-[3-(4-Methylphenyl)-1-phenyl-1*H*-pyrazol-5-yl]-5-phenyl-1*H*-1,2,3-triazole (6a).** Yield 82%, colorless crystals, mp 95–97°C (crude). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 2.35 s (3H, $CH_3$), 7.15–7.85 m (15H, $H_{arom}$), 15.62 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), $\delta_C$, ppm: 20.9 ($CH_3$), 107.3, 123.6, 125.3 (2C), 126.5 (2C), 127.3 (2C), 128.7, 128.8 (2C), 129.3, 129.5, 137.6 (2C), 139.2, 151.3. Found: *m*/*z* 378.1707 [*M* + H]$^+$. $C_{24}H_{19}N_5$. Calculated: *M* + H 378.1714.

**4-[3-(4-Bromophenyl)-1-phenyl-1*H*-pyrazol-5-yl]-5-phenyl-1*H*-1,2,3-triazole (6b).** Yield 89%, colorless crystals, mp 122–123°C (crude). $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm: 7.17–7.92 m (15H, $H_{arom}$), 15.39 br.s (1H, NH). $^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$), δ, ppm: 107.7, 119.1, 121.3, 123.7, 126.5, 126.7, 127.4, 127.5 (2C), 127.8, 128.5, 128.8, 131.4, 131.5; 131.7, 139.1, 150.2. Found: *m*/*z* 442.0662 [*M* + H]$^+$. $C_{23}H_{16}BrN_5$. Calculated: *M* + H 442.0663.

The toxicity of compounds **3b** and **5b**–**5d** against *Daphnia magna* laboratory culture was studied according to standard procedure [30] at 21–22°C on exposure to daylight. The test medium was prepared from water with addition of 1% of beaker's east as nutrient and a solution of **3b** or **5b**–**5d** in DMSO. Water was used as control. The number of dead and survived species, the length of the oviposition period, and the time of appearance of young species from brood chambers and their number were determined. All experiments were carried out in triplicate. The $LC_{50}$ values (72 h) were calculated by the Shtabskii criterion, and the validity of reproduction differences was estimated by the Wilcoxon–Mann–Whitney test [31].

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