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Some Aspects of the Azide–Alkyne 1,3-Dipolar Cycloaddition Reaction

N. T. Pokhodylo[a], M. A. Tupychak[a], O. Ya. Shyyka[a], and M. D. Obushak[a]*

[a] *Ivan Franko National University of Lviv, Lviv, Ukraine*
**e-mail: mykola.obushak@lnu.edu.ua*

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Abstract—Some peculiar features of two most commonly used catalytic systems (CuI and $CuSO_4$/sodium ascorbate) controlling the regioselectivity of 1,3-dipolar cycloaddition of azides to terminal alkynes have been studied. Their potentialities, main disadvantages, and limitations have been demonstrated by a number of examples, including reactions of low-molecular-weight azides and alkynes containing heterocyclic substituents. The possibility of using novel reagents in click reactions is discussed.

Keywords: azides, alkynes, 1,3-dipolar cycloaddition, click reactions, catalysis, 1,2,3-triazole derivatives.

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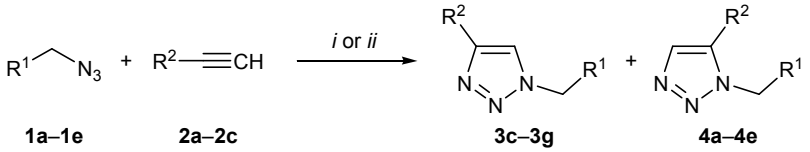
In recent years, azide–alkyne 1,3-dipolar cycloaddition reactions (AAC) have been widely used for the preparation of functional materials for different purposes, as well as of polymers [1]; they provide an efficient tool for the design of new biologically active compounds in pharmaceutical and medicinal chemistry [2–4]. In our recent review [5], we have discussed regioselectivity of these reactions, their mechanisms, and application in multicomponent syntheses. Despite numerous examples of such reactions occurring with high yield and selectivity [6, 7], analogous reactions with a number of accessible reagents have been poorly studied. In the present work we studied click reactions with such reagents.

Due to the risk of explosion, low-molecular-weight azides have rarely been involved in copper-catalyzed AAC reactions. We examined the reactivity of some "small" azides **1a**–**1e** and selectivity of their reactions with most commonly used alkynes (Boc-protected propargylamine **2a**, propargyl alcohol **2b**, and methyl propiolate **2c**) without a catalyst and in the presence of copper catalyst (Scheme 1).

In the absence of a catalyst, azides **1b**–**1e** reacted with alkynes **2a**–**2c** only on heating in toluene at 80–90°C, and the products were mixtures of regioisomeric 1,2,3-triazoles **3** and **4**, the former slightly prevailing in the reactions with amine **2a**. In the reaction of methyl azide (**1a**) with methyl propynoate (**2c**) in benzene at room temperature, the 1,4-disubstituted regioisomer was the major product (isomer ratio 9:1). Here, methyl azide behaved similarly to trimethylsilyl azide [8]. Taking into account that the regioselectivity in the non-catalytic click reaction of methyl azide is determined mainly by the thermodynamic factor, this reaction can be used as a model in quantum chemical simulation of AAC reactions.

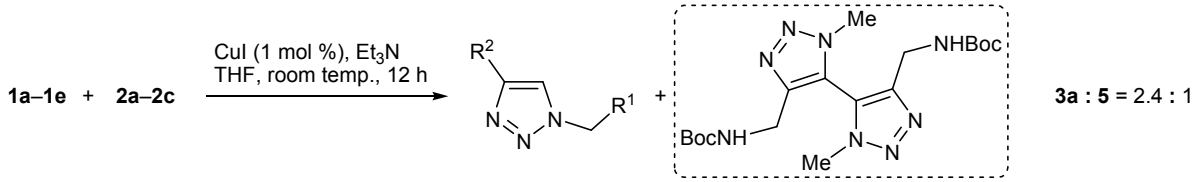
The reactions of azides **1a**–**1e** with alkynes **2a** and **2b** in the presence of copper(I) iodide were regioselective, and triazoles **3a**–**3g** were generally formed as the major products. An exception was the reaction of **1a** with **2a**, which resulted in a mixture of triazole **3a** and 5,5′-bitriazole **5** at a ratio of 2.4:1. Compounds **3a** and **5** can readily be separated by chromatography. In the other cases, no 5,5′-bitriazoles like **5** were detected. Presumably, 5,5′-bitriazole **5** is formed as a result of oxidative dimerization of intermediate **A** (Scheme 2) [9, 10]. Such 5,5′-bitriazoles are considered to be undesirable by-products, and their formation depends on both substrate structure and catalyst, base, and reaction conditions. For example, bitriazole was selectively obtained in the presence of 0.1 equiv of CuBr as a catalyst and sodium ethoxide as a base at 0°C, whereas only 1,4-disubstituted triazole was formed at 60°C in the presence of KOH as a base [11]. These data indicate that increase of the lifetime of copper-containing intermediate **A** increases the probability of formation of structure **5**. Intermediate **A** is stabilized by copper coordination to the amide nitrogen

Scheme 1.



1a–1e **2a–2c** **3c–3g** **4a–4e**

i: R^1 = H, R^2 = COOMe, PhH, –20°C to room temperature, 12 h; *ii*: $R^1 \neq$ H, PhMe, 80–90°C, 24 h;
3c : **4a** = 9 : 1, **3d** : **4b** = 1.4 : 1, **3e** : **4c** = 1.1 : 1, **3f** : **4d** = 1 : 1, **3g** : **4e** = 1.4 : 1.



3a–3g **5**

1, R^1 = H (**a**), CH_2OH (**b**), CN (**c**), COOEt (**d**), $CONH_2$ (**e**); **2**, R^2 = CH_2NHBoc (**a**), CH_2OH (**b**), COOMe (**c**); **3**, R^1 = H, R^2 = CH_2NHBoc (**a**), CH_2OH (**b**), COOMe (**c**); R^1 = CH_2OH, R^2 = CH_2NHBoc (**d**); R^1 = CN, R^2 = CH_2NHBoc (**e**); R^1 = COOEt, R^2 = CH_2OH (**f**); R^1 = $CONH_2$, R^2 = CH_2NHBoc (**g**); **4**, R^1 = H, R^2 = COOMe (**a**), R^1 = CH_2OH, R^2 = CH_2NHBoc (**b**); R^1 = CN, R^2 = CH_2NHBoc (**c**); R^1 = COOEt, R^2 = CH_2OH (**d**); R^1 = $CONH_2$, R^2 = CH_2NHBoc (**e**).

atom, and the small size of the substituent (methyl group) on the N^1 nitrogen atom of the triazole ring favors dimerization. Bulkier substituents should hamper such transformation. It should be noted that (1-methyl-1*H*-1,2,3-triazol-4-yl)methanamine (**3a**) is a promising building block for combinatorial chemistry; however, it remains poorly explored. An alternative synthesis of **3a** by reduction of 1-methyl-1*H*-1,2,3-triazole-4-carboxamide with lithium tetrahydridoborate in diethylene glycol at 155°C was described in patent [12] related to the synthesis of anti-inflammatory drugs.

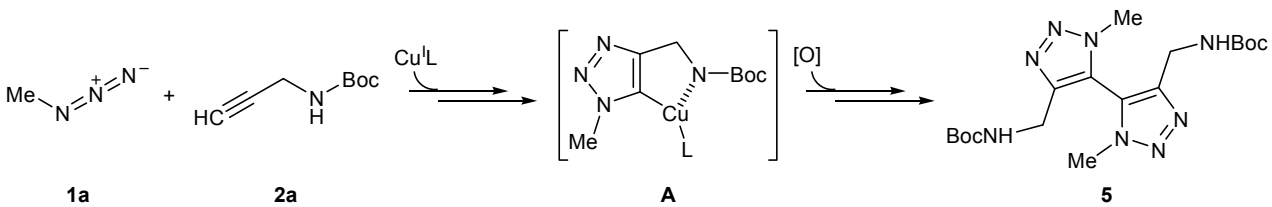
Under similar conditions, azide with a longer aliphatic chain, 3-(azidomethyl)heptane (**1f**), reacted with phenylacetylene (**2d**) at a low rate, and the yield of triazole **3h** was low. We succeeded in obtaining target product **3h** in a high yield (90%) by using copper(I) iodide as a catalyst in combination with a catalytic amount of benzoic acid (Scheme 3). The catalytic system Cu(I)/BzOH was proposed for the first time in [13] and was efficient in reactions with azides containing lipophilic fragments.

We also studied CuAAC reactions of diazides capable of coordinating copper ion during the process. The reaction of 1,3-diazidopropane (**6a**) with both 1 and 2 equiv of alkyne **2c** in the presence of CuI gave bis-triazole **7** in a good yield, and no by-products were detected (Scheme 4). The reaction of diazide **6b** with excess phenylacetylene **2d** in the presence of $CuSO_4$/sodium ascorbate also afforded bis-triazole **9**; the reaction was fast and was accompanied by appreciable evolution of heat.

The acceleration effect observed in the reactions of diazides **6a** and **6b** with phenylacetylene can be rationalized by specific coordination of copper ion to the triazole ring, which maintains a high concentration of catalytically active copper species and thus favors CuAAC reaction. The nature of such bonding and its effect on the catalytic process are insufficiently clear. It is believed that ligands affect the reaction rate by shifting the equilibrium between copper clusters in solution [14]. Presumably, if an azide contains a group or a fragment capable of disrupting equilibrium processes, the reaction will be accelerated or slowed down.

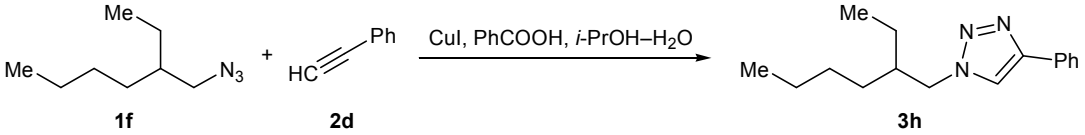
Taking into account the structure of some known co-catalysts of CuAAC reactions [15], containing a triazole ring, we have synthesized new triazole derivatives for this purpose. Starting from phenyl azide

Scheme 2.



1a **2a** **A** **5**

Scheme 3.



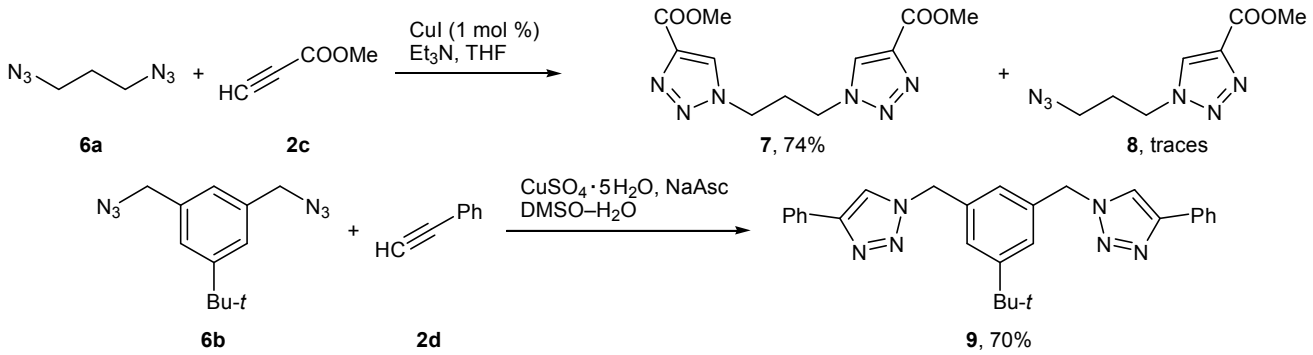
1f **2d** **3h**

(**10a**), we obtained intermediate (1-phenyl-1*H*-1,2,3-triazol-4-yl)methanol (**11**) which was converted to aldehyde **12** and acid **13**. The latter is a potential co-catalyst. Alcohol **11** was treated with phosphorus(III) bromide in benzene, and bromomethyl derivative **14** thus formed was treated with sodium azide. The resulting 4-(azidomethyl)-1-phenyl-1*H*-1,2,3-triazole (**15**) proved to be quite active in the reaction with phenylacetylene (**2d**) catalyzed by CuI (Scheme 5). The reaction required a minimum amount of the catalyst, and product **16** was formed in a high yield. These findings indicate that triazole ring is one of the best ligands for solving the problem of stabilization of active copper species in the catalysis of AAC reactions.

A similar pattern was observed in the reaction with azide containing a benzotriazole fragment. The synthesis of a compound with the azido group and triazole ring linked to the same carbon atom was difficult; therefore, we synthesized a 1-(2-azidoethyl)benzotriazole derivative. Furthermore, donor methyl groups were introduced into the benzene ring of the 1,2,3-benzotriazole fragment to achieve better complexation. Starting from 4,5-dimethyl-2-nitroaniline, we obtained azide **17** as shown in Scheme 6. Azide **17** was reacted with alkynes **2c** and **2e**. The reaction with diethyl acetylenedicarboxylate (**2e**) in toluene afforded triazole **18** in nearly quantitative yield. The reaction of **17** with methyl propynoate (**2c**) in the presence of a minimum amount of CuI without a base gave 94% of triazole **19**, regardless of the solvent used (*t*-BuOH or THF), which indicated positive effect of the benzotriazole fragment of **17** on the concentration of catalytically active copper species.

It should be noted that the reactivity of azide **20** containing an imidazo[1,2-*a*]pyridine fragment was

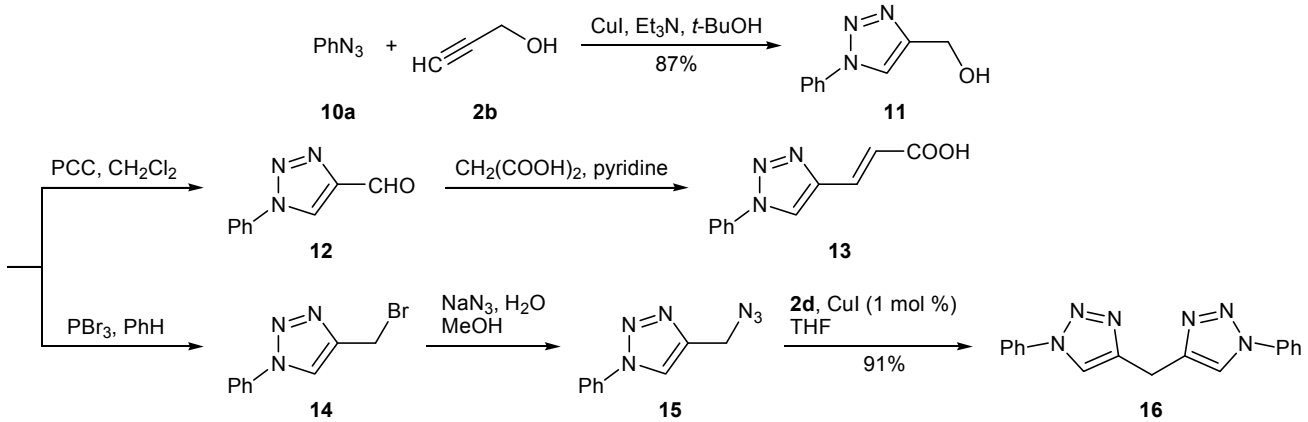
Scheme 4.



6a **2c** **7**, 74% **8**, traces

6b **2d** **9**, 70%

Scheme 5.

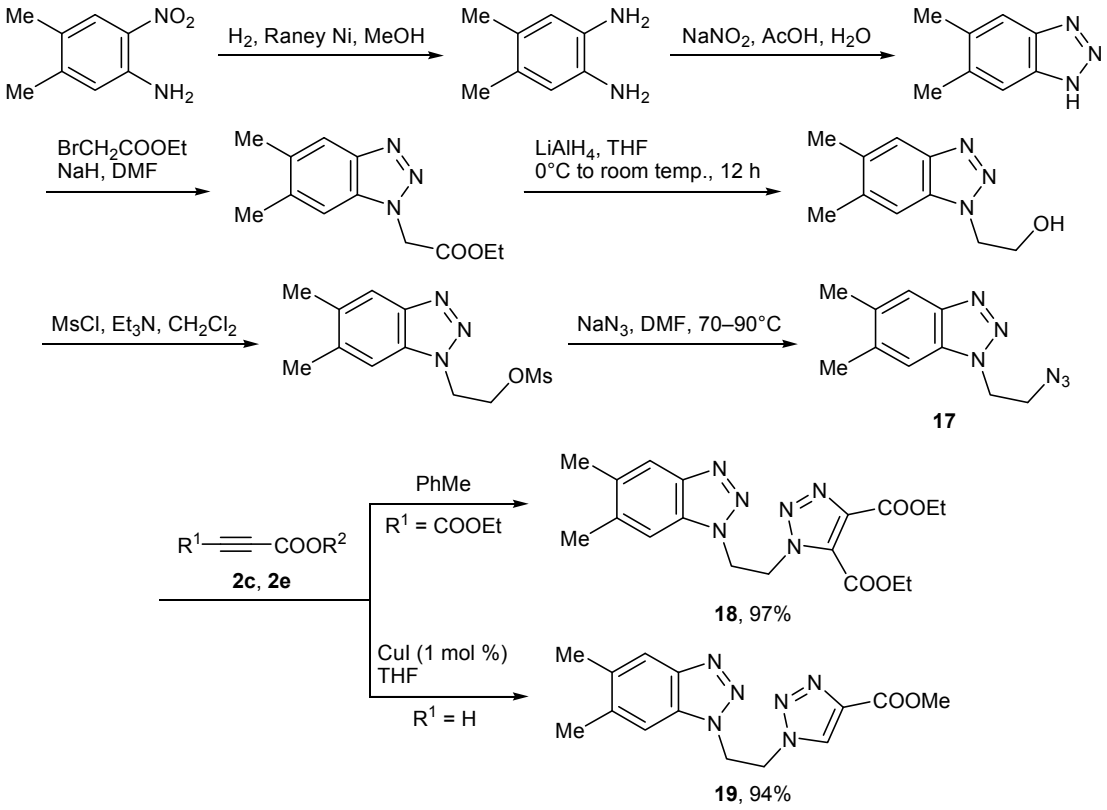


10a **2b** **11**

12 **13**

14 **15** **16**

Scheme 6.

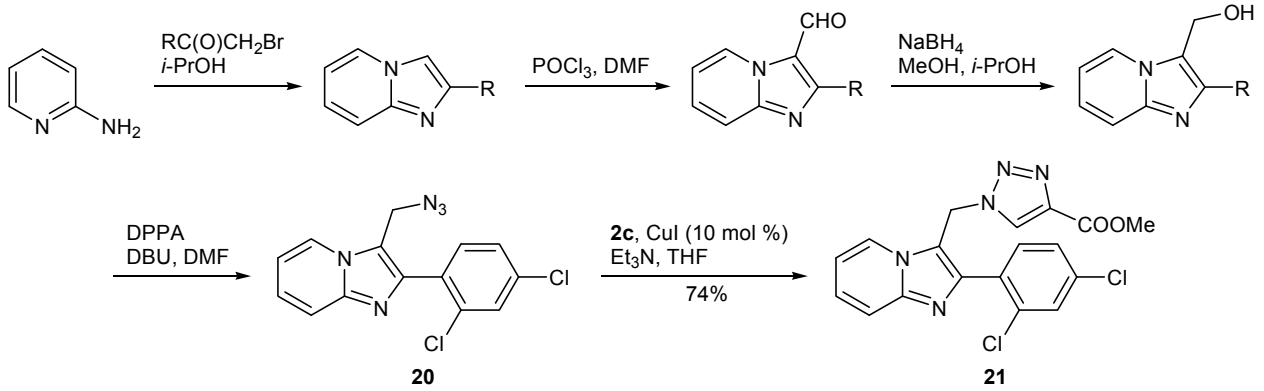


2c, R^1 = H, R^2 = Me; **2e**, R^1 = COOEt, R^2 = Et.

appreciably lower. Azide **20** was synthesized from pyridin-2-amine via a series of transformations shown in Scheme 7, and it slowly reacted even with such a reactive dipolarophile as acetylenecarboxylate **2c** in *tert*-butyl alcohol only in the presence of a basic co-catalyst. Under the optimal conditions, the yield of triazole **21** was 74%. Our results are very consistent with the data of [16], according to which structurally related azides were converted to the corresponding triazoles in about 50% yield in the system CuI/PEG-400/H_2O.

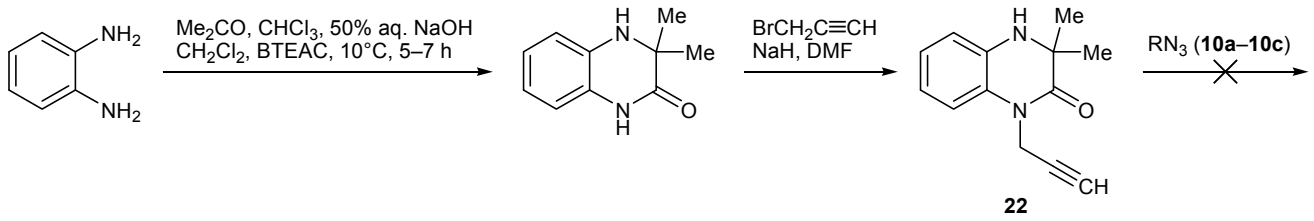
Su et al. [17] recently reported the synthesis of biologically active 1,4-disubstituted 1,2,3-triazoles containing a 2*H*-1,4-benzoxazin-3(4*H*)-one fragment by 1,3-dipolar cycloaddition of *N*-propargyl-2*H*-1,4-benzoxazin-3(4*H*)-one with benzyl azide in the presence of CuI [17]. This reaction was difficult to accomplish, and much effort was made to optimize the

Scheme 7.



R = 2,4-$Cl_2C_6H_3$.

Scheme 8.



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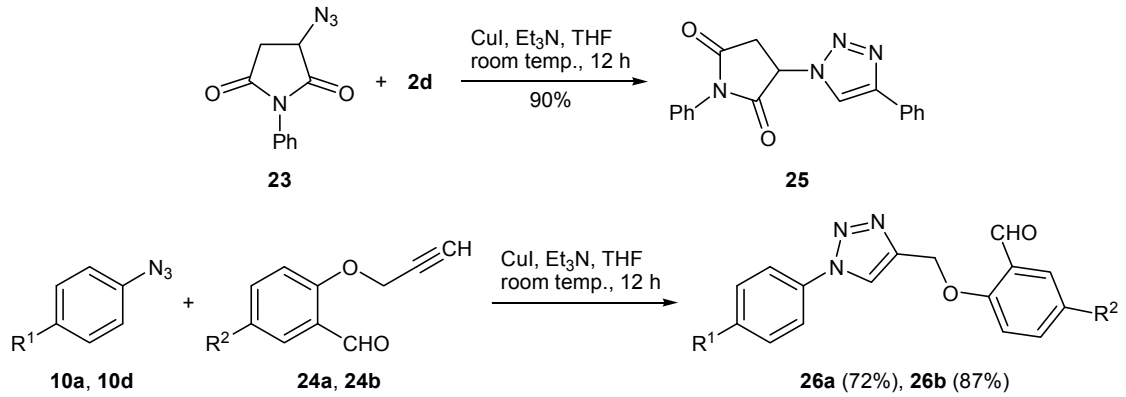
Scheme 9.



23 **25**

10a, **10d** **24a**, **24b** **26a** (72%), **26b** (87%)

10, R^1 = H (**a**), NO_2 (**d**); **24**, R^2 = H (**a**), Br (**b**); **26**, R^1 = H, R^2 = H (**a**), R^1 = NO_2, R^2 = Br (**b**).

conditions. Acceptable yields were achieved by heating the reactants (1.2 equiv of benzyl azide was taken) in dioxane at 80°C using 30 mol % of CuI [17]. We have synthesized a structural analog of the reported products, 3,3-dimethyl-1-(prop-2-yn-1-yl)-3,4-dihydroquinoxalin-2(1*H*)-one (**22**), which is promising for the design of biologically active compounds. 3,4-Dihydroquinoxalin-2(1*H*)-one was synthesized in one step from *o*-phenylenediamine, and its alkylation with propargyl bromide gave compound **22** (Scheme 8) which failed to react with phenyl and 4-fluorophenyl azides **10a** and **10b**, as well as with methyl 3-azidothiophene-2-carboxylate (**10c**), in the presence of different catalytic systems on prolonged heating.

The reactions of 3-azido-1-phenylpyrrolidine-2,5-dione (**23**, obtained from *N*-phenylmaleimide) with phenylacetylene (**2d**) and of aryl azides **10a** and **10d** with propargyl ethers **24a** and **24b** under similar conditions (CuI/Et_3N) afforded triazoles **25** and **26a**, **26b**, respectively, in high yields (Scheme 9).

Our results led us to draw the following conclusions. In the copper-catalyzed azide–alkyne cycloaddition reactions with "small" azides, the substituent does not shield the copper ion in the triazolyl–cuprate intermediate, so that there is the possibility of copper coordination to one more triazole ring, which favors oxidative coupling (dimerization) with the formation of 5,5′-bitriazoles. Aminomethyl substituent in the acetylenic component favors additional copper coordination in the triazolyl–cuprate intermediate, which accelerates the reaction and makes it possible to introduce an electrophile into the 5-position of the triazole ring. In CuAAC reactions with azides containing a bulky lipophilic substituent, organic acids (e.g., benzoic acid) act as efficient co-catalysts by mediating copper(I) ion transfer between copper clusters to protonate the triazolyl–cuprate intermediate. The copper catalyst in CuAAC reactions is very sensitive to coordination to a heterocyclic core, and this coordination could both accelerate and inhibit the process.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Varian Unity Plus 400 and Bruker Avance 500 spectrometers at 400 and 500 MHz, respectively, using tetramethylsilane as internal standard. The mass spectra (atmospheric pressure chemical ionization) were obtained on an Agilent 1100 LC/MSD instrument. The elemental analyses were performed with a Carlo Erba 1106 analyzer. The melting points were measured on a Boetius hot stage. The products were isolated by column chromatography on silica gel using hexane–ethyl acetate (9 : 1) as eluent.

Methyl azide (1a) [18]**.** A solution of 2.5 g (0.0625 mol) of sodium hydroxide and 8.2 g (0.126 mol) of sodium azide in 70 mL of water was heated to 70°C, and 11.8 mL (0.125 mol) of dimethyl sulfate was added with vigorous stirring. Water–methylazide azeotrope (bp 26°C) was distilled off into a receiver cooled with liquid nitrogen, and the product was used without further purification. **CAUTION!** Methyl azide is toxic and explosive.

Alkyl azides 1b–1e, 6a, 6b, 15, and 23 (*general procedure***).** The corresponding halogen derivative, 0.1 mol (or 0.05 mol of dihalo derivative), was dissolved in 120 mL of methanol, and 20 mL of water and 7.8 g (0.12 mol) of sodium azide were added. The mixture was stirred for 2 h at 50–60°C, methanol was distilled off under reduced pressure, and 30 mL of water was added to the residue. The product was extracted into methylene chloride (2×15 mL), the extract was dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was used without further purification. 2-Azidoethanol (**1b**) [19], yield 73%; 2-azidoacetonitrile (**1c**) [20], yield 83%; ethyl 2-azidoacetate (**1d**) [21], yield 94%.

2-Azidoacetamide (1e) [22]**.** Yield 9.50 g (95%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.69 s (2H, CH_2), 7.13 s and 7.39 s (1H each, NH).

1,3-Diazidopropane (6a) [23]**.** Yield 5.54 g (88%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.70–1.85 m (2H, CH_2), 3.40 t (4H, CH_2, J = 6.5 Hz).

1,3-Bis(azidomethyl)-5-*tert*-butylbenzene (6b). Yield 10.08 g (90%), viscous oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 1.31 s (9H, *t*-Bu), 4.31 s (4H, CH_2), 7.05–7.07 m (1H, H_{arom}), 7.27 d (2H, H_{arom}, J = 1.5 Hz). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ_C, ppm: 31.3, 54.9, 125.0, 125.1, 135.8, 152.7. Found, %: C 59.31; H 6.42; N 34.62. $C_{12}H_{16}N_6$. Calculated, %: C 59.00; H 6.60; N 34.40.

4-(Azidomethyl)-1-phenyl-1*H*-1,2,3-triazole (15). Yield 19.40 g (97%), mp 55–56°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.62 s (2H, CH_2), 7.36–7.72 m (3H, *m*-H, *p*-H), 7.91 d (2H, *o*-H, J = 7.9 Hz), 8.90 s (1H, 5-H). Found, %: C 53.89; H 4.17; N 41.83. $C_9H_8N_6$. Calculated, %: C 53.99; H 4.03; N 41.98.

3-Azido-1-phenylpyrrolidine-2,5-dione (23). Yield 19.22 g (89%), mp 106–107°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.71 d.d (1H, CH_2, J = 17.7, 4.6 Hz), 3.15 d.d (1H, CH_2, J = 17.6, 8.9 Hz), 5.03 d.d (1H, CH, J = 8.1, 5.2 Hz), 7.31 d (2H, *o*-H, J = 7.3 Hz), 7.40–7.55 m (3H, *m*-H, *p*-H). Found, %: C 55.68; H 3.83; N 25.76. $C_{10}H_{17}N_5O_3$. Calculated, %: C 55.55; H 3.73; N 25.91.

Cycloaddition of methyl azide (1a) to alkynes 2a–2c. Alkyne **2a**–**2c** (25 mmol), copper(I) iodide (0.05 g), and triethylamine (2.1 mL), were quickly added to a solution of methyl azide (**1a**, ~50 mmol) in 25 mL of THF cooled to –20°C. The reactor was hermetically closed, and the mixture was vigorously stirred for 12 h. The solvent, triethylamine, and excess methyl azide were evaporated, the residue was dissolved in methylene chloride, and the solution was filtered from inorganic materials. The filtrate was evaporated to obtain triazoles **3a**–**3c**. In the reaction of azide **1a** with alkyne **2a**, a mixture of **3a** and bitriazole **5** was formed at a ratio of 2.4:1. Pure compounds **3a** and **5** were isolated by column chromatography.

***tert*-Butyl (1-methyl-1*H*-1,2,3-triazol-4-yl)-methylcarbamate (3a)** [24]**.** Yield 2.62 g (49%), mp 104–105°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.41 s (9H, *t*-Bu), 4.03 s (3H, CH_3), 4.16 d (2H, CH_2, J = 5.8 Hz), 7.00 t (1H, NH, J = 5.8 Hz), 7.72 s (1H, 5-H). Mass spectrum: m/z 213 $[M + H]^+$. Found, %: C 50.98; H 7.71; N 26.34. $C_9H_{16}N_4O_2$. Calculated, %: C 50.93; H 7.60; N 26.40.

(1-Methyl-1*H*-1,2,3-triazol-4-yl)methanol (3b) [25]**.** Yield 2.66 g (94%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.03 s (3H, CH_3), 4.50 s (2H, CH_2), 4.97 s (1H, OH), 7.79 s (1H, 5-H).

Methyl 1-methyl-1*H*-1,2,3-triazole-4-carboxylate (3c) [25]**.** Yield 3.08 g (97%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.85 s (3H, CH_3O), 4.12 s (3H, CH_3), 8.60 s (1H, 5-H).

Di-*tert*-butyl [3,3′-dimethyl-3*H*,3′*H*-4,4′-bi-1,2,3-triazole-5,5′-diylbis(methylene)]dicarbamate (5). Yield 1.09 g (21%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.31 s (18H, *t*-Bu), 3.76 s (6H, CH_3), 4.16 d (4H, CH_2, J = 5.8 Hz), 6.93 t (2H, NH, J = 5.8 Hz). Mass spectrum: m/z 423 (I_{rel} 100%) $[M + H]^+$. Found, %: C 51.11; H 7.21; N 26.55. $C_{18}H_{30}N_8O_4$. Calculated, %: C 51.17; H 7.16; N 26.52.

Cycloaddition of methyl azide (1a) to methyl propynoate (2c). Azide **1a**, 5.7 g (0.2 mol), was cooled to –20°C, and 8.2 mL (0.1 mol) of ester **2c** in 80 mL of benzene was quickly added. The reactor was hermetically closed, and the mixture was vigorously stirred for 48 h. The solvent was evaporated to leave a mixture of triazoles **3c** and **4a** at a ratio of 9:1. The pure products were isolated by column chromatography.

Methyl 1-methyl-1*H*-1,2,3-triazole-5-carboxylate (4a) [26]**.** Yield 1.41 g (9.5%), mp 50–51°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.90 s (1H, CH_3O), 4.27 s (3H, CH_3), 8.10 s (1H, 4-H).

Noncatalytic cycloaddition of azides to alkynes (*general procedure*). A solution of equimolar amounts (2.5 mmol) of the corresponding azide and alkyne in toluene was heated at 80–90°C for 2–8 h until the reaction was complete (TLC). The solvent was removed under reduced pressure. If a mixture of isomeric triazoles was formed, the products were isolated by chromatography.

***tert*-Butyl {[1-(2-hydroxyethyl)-1*H*-1,2,3-triazol-4-yl]methyl}carbamate (3d).** Yield 0.31 g (52%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.41 s (9H, *t*-Bu), 3.78 t (2H, CH_2, J = 5.0 Hz), 4.19 d (2H, CH_2N, J = 5.6 Hz), 4.33–4.46 m (2H, CH_2O), 4.93 s (1H, OH), 6.99 d (1H, NH, J = 4.9 Hz), 7.75 s (1H, 5-H). Mass spectrum: m/z 243 (I_{rel} 100%) $[M + H]^+$. Found, %: C 49.51; H 7.41; N 23.19. $C_{10}H_{18}N_4O_3$. Calculated, %: C 49.58; H 7.49; N 23.13.

***tert*-Butyl {[1-(2-hydroxyethyl)-1*H*-1,2,3-triazol-5-yl]methyl}carbamate (4b).** Yield 0.22 g (37%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.41 s (9H, *t*-Bu), 3.78 t (2H, CH_2, J = 5.0 Hz), 4.28 d (2H, CH_2N, J = 5.6 Hz), 4.33–4.46 m (2H, CH_2O), 4.93 s (1H, OH), 7.17 d (1H, NH, J = 4.9 Hz), 7.42 s (1H, 4-H). Mass spectrum: m/z 243 (I_{rel} 100%) $[M + H]^+$. Found, %: C 49.64; H 7.54; N 23.21. $C_{10}H_{18}N_4O_3$. Calculated, %: C 49.58; H 7.49; N 23.13.

***tert*-Butyl {[1-(cyanomethyl)-1*H*-1,2,3-triazol-4-yl]methyl}carbamate (3e).** Yield 0.24 g (40%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.41 s (9H, *t*-Bu), 4.20 d (2H, CH_2N, J = 5.6 Hz), 5.68 s (2H, CH_2), 7.11 s (1H, NH, J = 5.6 Hz), 7.97 s (1H, 5-H). Mass spectrum: m/z 238 (I_{rel} 100%) $[M + H]^+$. Found, %: C 50.71; H 6.31; N 29.54. $C_{10}H_{15}N_5O_2$. Calculated, %: C 50.62; H 6.37; N 29.52.

***tert*-Butyl {[1-(cyanomethyl)-1*H*-1,2,3-triazol-5-yl]methyl}carbamate (4c).** Yield 0.21 g (36%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.41 s (9H, *t*-Bu), 4.30 d (2H, CH_2N, J = 5.8 Hz), 5.56 s (2H, CH_2), 7.28 d (1H, NH, J = 5.6 Hz), 7.54 s (1H, 4-H). Mass spectrum: m/z 238 (I_{rel} 100%) $[M + H]^+$. Found, %: C 50.73; H 6.39; N 29.60. $C_{10}H_{15}N_5O_2$. Calculated, %: C 50.62; H 6.37; N 29.52.

Ethyl 2-[4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]acetate (3f) [27]**.** Yield 0.22 g (47%), mp 72–73°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.27 t (3H, CH_3, J = 7.0 Hz), 4.20 q (2H, OCH_2, J = 7.0 Hz), 4.55 s (2H, CH_2), 5.25 s (2H, C**H**$_2$OH), 5.36 s (1H, OH), 7.86 s (1H, 5-H). Mass spectrum: m/z 186 (I_{rel} 100%) $[M + H]^+$. Found, %: C 45.53; H 5.91; N 22.84. $C_7H_{11}N_3O_3$. Calculated, %: C 45.40; H 5.99; N 22.69.

Ethyl 2-[5-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]acetate (4d) [28]**.** Yield 0.22 g (47 %), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.28 t (3H, CH_3, J = 7.0 Hz), 4.20 q (2H, OCH_2, J = 7.0 Hz), 4.55 s (2H, CH_2), 5.06 s (1H, OH), 5.27 s (2H, C**H**$_2$OH), 7.51 s (1H, 4-H). Mass spectrum: m/z 186 (I_{rel} 100%) $[M + H]^+$. Found, %: C 45.25; H 5.85; N 22.64. $C_7H_{11}N_3O_3$. Calculated, %: C 45.40; H 5.99; N 22.69.

***tert*-Butyl {[1-(2-amino-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl]methyl}carbamate (3g).** Yield 0.35 g (55%), mp 138–139°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.40 s (9H, *t*-Bu), 4.19 d (2H, CH_2N, J = 5.4 Hz), 4.96 s (2H, CH_2), 7.01 t (1H, NH, J = 5.4 Hz), 7.22 s and 7.52 s (1H each, $CONH_2$), 7.74 s (1H, 5-H). Mass spectrum: m/z 256 (I_{rel} 100%) $[M + H]^+$. Found, %: C 47.14; H 6.63; N 27.49. $C_{10}H_{17}N_5O_3$. Calculated, %: C 47.05; H 6.71; N 27.43.

***tert*-Butyl {[1-(2-amino-2-oxoethyl)-1*H*-1,2,3-triazol-5-yl]methyl}carbamate (4e).** Yield 0.26 g (40%), mp 150–151°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.40 s (9H, *t*-Bu), 4.19 d (2H, CH_2N, J = 5.4 Hz), 5.05 s (2H, CH_2), 7.13 t (1H, NH, J = 5.4 Hz), 7.27 s (1H, $CONH_2$), 7.43 s (1H, 4-H), 7.64 s (1H, $CONH_2$). Mass spectrum: m/z 256 (I_{rel} 100%) $[M + H]^+$. Found, %: C 47.00; H 6.79; N 27.54. $C_{10}H_{17}N_5O_3$. Calculated, %: C 47.05; H 6.71; N 27.43.

Diethyl 1-[2-(5,6-dimethyl-1*H*-1,2,3-benzotriazol-1-yl)ethyl]-1*H*-1,2,3-triazole-4,5-dicarboxylate (18). Yield 0.94 g (97%), mp 123–124°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.19 t (3H, CH_3, J = 7.0 Hz), 1.26 t (3H, CH_3, J = 7.0 Hz), 2.35 s (6H, CH_3), 4.13 q (2H, CH_2O, J = 7.0 Hz), 4.29 q (2H, CH_2O, J = 7.0 Hz), 5.13 t (2H, CH_2, J = 5.7 Hz), 5.18 t (2H, CH_2, J = 5.5 Hz), 7.37 s (1H, H_{arom}), 7.74 s (1H, H_{arom}). Mass spectrum: m/z 387 (I_{rel} 100%) $[M + H]^+$. Found, %: C 55.87; H 5.79; N 21.81. $C_{18}H_{22}N_6O_4$. Calculated, %: C 55.95; H 5.74; N 21.75.

Cycloaddition of azides to alkynes in the presence of copper(I) iodide. The corresponding azide (1 mmol) and terminal alkyne (1 mmol or 2 mmol in the reactions with diazides) were dissolved in 5 mL of THF or *tert*-butyl alcohol. Water was added to the

solution until an emulsion began to form, and a catalytic amount of copper(I) iodide (1–10 mol %, depending on the azide reactivity) was added. In the reactions with weakly reactive azides, 0.4 mL (2.8 mmol) of triethylamine as a co-catalyst was added. The mixture was stirred at room temperature until the initial azide disappeared (according to the TLC or IR data). The mixture was treated with 15 mL of water and 15 mL of concentrated aqueous ammonia and extracted with methylene chloride (3×10 mL). The extract was dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. If necessary, the product was purified by recrystallization or column chromatography. Compounds **3d**–**3g** were obtained as the only products: **3d**, yield 95%; **3e**, yield 89%; **3f**, yield 91%; **3g**, yield 67%.

Dimethyl 1,1′-(propane-1,3-diyl)bis(1*H*-1,2,3-triazole-4-carboxylate) (7). Yield 0.22 g (74%), mp 196–197°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.23–1.75 m (2H, CH_2). 3.73–3.80 m (4H, CH_2), 3.86 s (6H, OCH_3), 8.71 s (2H, 5-H). Mass spectrum: *m*/*z* 295 (I_{rel} 100%) [M + H]$^+$. Found, %: C 44.99; H 4.73; N 28.41. $C_{11}H_{14}N_6O_4$. Calculated, %: C 44.90; H 4.80; N 28.56.

(1-Phenyl-1*H*-1,2,3-triazol-4-yl)methanol (11) [29]**.** Yield 0.15 g (87%).

1-Phenyl-4-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)-methyl]-1*H*-1,2,3-triazole (16). Yield 0.27 g (91%), mp 189–190°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.85 s (2H, CH_2), 7.33 t (1H, *p*-H, J = 6.9 Hz), 7.44 t (2H, *m*-H, J = 7.2 Hz), 7.50 t (1H, *p*-H, J = 7.1 Hz), 7.60 t (2H, *m*-H, J = 7.2 Hz), 7.86 d (2H, *o*-H, J = 7.6 Hz), 7.91 d (2H, *o*-H, J = 7.8 Hz), 8.66 s (1H, 5-H), 8.95 s (1H, 5-H). Mass spectrum: *m*/*z* 303 [M + H]$^+$. Found, %: C 67.51; H 4.77; N 27.95. $C_{17}H_{14}N_6$. Calculated, %: C 67.54; H 4.67; N 27.80.

Methyl 1-{2-(5,6-dimethyl-1*H*-1,2,3-benzotriazol-1-yl)ethyl}-1*H*-1,2,3-triazole-4-carboxylate (19). Yield 0.28 g (94%), mp 129–130°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 2.42 s (3H, CH_3), 3.83 s (3H, OCH_3), 5.13 q (2H, CH_2, J = 5.7 Hz), 5.04 q (2H, CH_2, J = 5.5 Hz), 7.37 s (1H, H_{arom}), 7.77 s (1H, H_{arom}), 8.70 s (1H, 5-H). Mass spectrum: *m*/*z* 301 [M + H]$^+$. Found, %: C 55.93; H 5.59; N 27.90. $C_{14}H_{16}N_6O_2$. Calculated, %: C 55.99; H 5.37; N 27.98.

Methyl 1-{[2-(2,4-dichlorophenyl)imidazo-[1,2-*a*]pyridin-3-yl]methyl}-1*H*-1,2,3-triazole-4-carboxylate (21). Yield 0.30 g (74%), mp 229–230°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.19 s (2H, CH_2), 7.02 t (1H, 6-H_{Py}, J = 6.6 Hz), 7.41 t (1H, 7-H_{Py}, J = 7.6 Hz), 7.47 d.d (1H, 5″-H, J = 8.3, 1.7 Hz), 7.52 d (1H, 6″-H, J = 8.2 Hz), 7.56–7.64 m (2H, H_{arom}), 8.47 d (1H, 5-H_{Py}, J = 6.8 Hz), 8.70 s (1H, 5-H). Mass spectrum: *m*/*z* 402/404/406 [M + 1]$^+$. Found, %: C 53.70; H 3.32; N 17.53. $C_{18}H_{13}Cl_2N_5O_2$. Calculated, %: C 53.75; H 3.26; N 17.41.

1-Phenyl-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyrrolidine-2,5-dione (25). Yield 0.29 g (90%), mp 189–190°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.45 d.d (1H, CH_2, J = 17.8, 5.7 Hz), 3.60 d.d (1H, CH_2, J = 17.8, 9.2 Hz), 6.15 d.d (1H, CH, J = 9.2, 5.7 Hz), 7.30–7.41 m (3H, H_{arom}), 7.44–7.51 m (3H, H_{arom}), 7.55 t (2H, *m*-H, J = 7.3 Hz), 7.86 d (2H, *o*-H, J = 7.1 Hz), 8.95 s (1H, 5-H). Mass spectrum: *m*/*z* 319 (I_{rel} 100%) [M + H]$^+$. Found, %: C 67.75; H 4.39; N 17.71. $C_{18}H_{14}N_4O_2$. Calculated, %: C 67.92; H 4.43; N 17.60.

2-[(1-Phenyl-1*H*-1,2,3-triazol-4-yl)methoxy]-benzaldehyde (26a). Yield 0.20 g (72%), mp 155–156°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6–CCl_4), δ, ppm: 5.47 s (2H, CH_2). 7.14 t (1H, *p*-H, J = 7.1 Hz), 7.51 d.d (2H, 4′-H, 5′-H, J = 7.8, 14.8 Hz), 7.62 t (2H, *m*-H, J = 7.4 Hz), 7.71 d.d (2H, 3′-H, 6′-H, J = 7.8, 14.9 Hz), 7.84 d (2H, *o*-H, J = 7.4 Hz), 8.96 s (1H, 5-H), 10.44 s (1H, CHO). Mass spectrum: *m*/*z* 280 [M + H]$^+$. Found, %: C 68.60; H 4.85; N 15.29. $C_{16}H_{13}N_3O_2$. Calculated, %: C 68.81; N 4.69; N 15.05.

5-Bromo-2-{[1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]methoxy}benzaldehyde (26b). Yield 0.35 g (87%), mp 235–236°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.46 s (2H, CH_2), 7.31 d (2H, *o*-H, J = 9.0 Hz), 7.77 s (1H, 3′-H), 8.24 d (2H, *m*-H, J = 9.0 Hz), 8.28 d (1H, 5′-H, J = 9.1 Hz), 8.44 d (1H, 6′-H, J = 9.1 Hz), 9.19 s (1H, 5-H), 10.40 s (1H, CHO). Mass spectrum: *m*/*z* 403/405 (I_{rel} 100%) [M + H]$^+$. Found, %: C 47.74; H 2.81; N 13.97. $C_{16}H_{11}BrN_4O_4$. Calculated, %: C 47.66; H 2.75; N 13.90.

2-Ethylhexyl azide (1f). 2-Ethylhexyl bromide, 3 g (19.3 mmol), was dissolved in 15 mL of DMSO, and 1.51 g (23.2 mmol) of sodium azide, 2 mL of water, and a catalytic amount of potassium iodide were added. The mixture was stirred for 24 h at 70°C, cooled to room temperature, diluted with 200 mL of water, and extracted with methylene chloride. The extract was washed with brine and dried over $MgSO_4$, and the solvent was evaporated under reduced pres-

sure. Azide **1f** was obtained as a light yellow liquid. Yield 2.69 g (90%). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 0.89–0.97 m (3H, CH_3), 0.98 t (3H, CH_3, J = 7.4 Hz), 1.23–1.50 m (8H, CH_2), 2.04 d.t (1H, CH, J = 12.1, 5.4 Hz), 4.40 d (2H, CH_2N_3, J = 6.7 Hz). Found, %: C 61.57; H 11.12; N 27.19. $C_8H_{17}N_3$. Calculated, %: C 61.89; H 11.04; N 27.07.

1-(2-Ethylhexyl)-4-phenyl-1*H*-1,2,3-triazole (3h). 2-Ethylhexyl azide (0.40 g, 2.6 mmol), phenylacetylene (0.28 mL, 2.8 mmol), copper(I) iodide (49.5 mg, 0.26 mmol), and benzoic acid (31.7 mg, 0.26 mmol) were added to 5 mL of a 1:2 propan-2-ol–water mixture. The mixture was stirred for 24 h at room temperature, diluted with 100 mL of water, and extracted with diethyl ether (2×50 mL). The extract was washed with brine and dried over $MgSO_4$, and the solvent was evaporated under reduced pressure to obtain triazole **3h** which did not require further purification. Yield 0.60 g (90%), yellow viscous liquid. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 0.80–1.00 m (6H) and 1.18–1.44 m (8H) (CH_3, CH_2), 1.94 sept (1H, CH, J = 5.8 Hz), 4.32 d (2H, NCH_2, J = 6.7 Hz), 7.34 t (1H, H_{arom}, J = 7.2 Hz), 7.43 t (2H, H_{arom}, J = 6.4 Hz), 7.76–7.99 m (3H, H_{arom}, 5-H), Mass spectrum: m/z 258 $[M + H]^+$. Found, %: C 74.54; H 9.12; N 16.45. $C_{16}H_{23}N_3$. Calculated, %: C 74.67; H 9.01; N 16.33.

1,1′-[5-*tert*-Butyl-1,3-phenylene)bis(methylene)]-bis(4-phenyl-1*H*-1,2,3-triazole) (9). Diazide **6b** (0.12 g, 0.5 mmol) and phenylacetylene (0.12 mL, 1.1 mmol) were dissolved in 5 mL of DMSO, and 1 mL of water, 40 mg (0.2 mmol) of sodium ascorbate, and 25 mg (0.1 mmol) of $CuSO_4 \cdot 5H_2O$ were added. The mixture was vigorously stirred for 12 h at room temperature, diluted with 30 mL of water, and extracted with methylene chloride (3×10 mL). The combined extracts were dried over $MgSO_4$, the solvent was evaporated under reduced pressure, and the residue was washed with pentane and dried under reduced pressure. Yield 0.16 g (70%), mp 109°C (decomp.). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 1.27 s (9H, *t*-Bu), 5.54 s (4H, NCH_2), 7.04 s (1H, H_{arom}), 7.28–7.35 m (4H, H_{arom}), 7.39 t (5H, H_{arom}, J = 6.9 Hz), 7.71–7.89 m (5H, H_{arom}, 5-H). Mass spectrum: m/z 449 (I_{rel} 100%) $[M + H]^+$. Found, %: C 75.19; H 6.41; N 18.59. $C_{28}H_{28}N_6$. Calculated, %: C 74.97; H 6.29; N 18.74.

1-Phenyl-1*H*-1,2,3-triazole-4-carbaldehyde (12) [29]**.** A solution of 8.75 g (0.05 mol) of (1-phenyl-1*H*-1,2,3-triazol-4-yl)methanol (**11**) in 100 mL of methylene chloride was added in one portion with thorough stirring to a suspension of 16.15 g (0.075 mol) of freshly prepared pyridinium chlorochromate (PCC) in 200 mL of anhydrous methylene chloride. The mixture was stirred for 90 min at room temperature, 200 mL of anhydrous diethyl ether was added, the solution was separated from the black precipitate by decanting, and the precipitate was washed with diethyl ether (2×50 mL). The combined extracts were filtered through 20 g of silica gel, the solvent was distilled off under reduced pressure, and the residue was recrystallized from carbon tetrachloride. Yield 6.75 g (78%). mp 96–97°C. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 7.57 t (1H, *p*-H, J = 7.2 Hz), 7.65 t (2H, *m*-H, J = 7.2 Hz), 8.03 d (2H, *o*-H, J = 7.2 Hz), 9.59 s (1H, 5-H), 10.24 s (1H, CHO). Mass spectrum: m/z 174 $[M + H]^+$. Found, %: C 62.45; H 4.14; N 24.21. $C_9H_7N_3O$. Calculated, %: C 62.42; H 4.07; N 24.27.

***(E)*-3-(1-Phenyl-1*H*-1,2,3-triazol-4-yl)prop-2-enoic acid (13).** A mixture of 5.3 g (0.03 mol) of aldehyde **12** and 4.2 g (0.04 mol) of malonic acid in 20 mL of pyridine was refluxed for 3 h. Pyridine was distilled off under reduced pressure, the residue was treated with 35 mL of water and acidified with concentrated aqueous HCl, and the precipitate was filtered off. Yield 5.61 g (87%), mp 240–242°C (decomp.). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 6.64 d (1H, CH=, J = 15.7 Hz), 7.55 d (1H, *p*-H, J = 6.7 Hz), 7.60 d (1H, CH=, J = 15.7 Hz), 7.65 t (2H, *m*-H, J = 6.8 Hz), 7.91 d (2H, *o*-H, J = 6.8 Hz), 9.23 s (1H, 5-H). Mass spectrum: m/z 216 $[M + H]^+$. Found, %: C 61.44; H 4.28; N 19.41; $C_{11}H_9N_3O_2$. Calculated, %: C 61.39; H 4.22; N 19.53.

4-(Bromomethyl)-1-phenyl-1*H*-1,2,3-triazole (14). Phosphorus(III) bromide, 9.7 mL (0.05 mol), was added with vigorous stirring to a solution of 8.75 g (0.05 mol) of (1-phenyl-1*H*-1,2,3-triazol-4-yl)methanol (**11**) in 200 mL of anhydrous benzene. The mixture was heated for 2 h and cooled, 50 g of crushed ice was added, and the mixture was neutralized with a saturated solution of sodium carbonate. The organic layer was separated and washed with a saturated solution of sodium carbonate, and the solvent was evaporated under reduced pressure. Yield 10.0 g (84%), mp 124–126°C. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 4.84 s (2H, CH_2), 7.52 t (1H, *p*-H, J = 7.2 Hz), 7.62 t (2H, *m*-H, J = 7.2 Hz), 8.92 s (1H, 5-H), 7.91 d (2H *o*-H, J = 7.2 Hz). Mass spectrum, m/z (I_{rel}, %): 238 (100), 240 (97) $[M + H]^+$. Found, %: C 45.23; H 3.30; N 17.62. $C_9H_8BrN_3$. Calculated, %: C 45.40; H 3.39; N 17.65.

1-(2-Azidoethyl)-5,6-dimethyl-1*H*-1,2,3-benzotriazole (17). Raney nickel, 5 g, was added to a solution of 5 g (0.03 mol) of 4,5-dimethyl-2-nitroaniline in 150 mL of methanol, and the mixture was stirred overnight in a hydrogen atmosphere. The mixture was filtered through a layer of silica gel, and the solvent was evaporated to give 4,5-dimethylbenzene-1,2-diamine in quantitative yield; the product was used in the next stage without further purification. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.50 s (6H, CH_3), 3.89 s (4H, NH_2), 6.30 s (2H, H_{arom}). A 3.5-g (0.026-mol) portion of 4,5-dimethylbenzene-1,2-diamine was dissolved in a mixture of 3 mL of acetic acid and 7.5 mL of water. The solution was cooled to 4°C, and a solution of 1.9 g (0.027 mol) of sodium nitrite in 3 mL of water was added. The mixture was heated to 70°C, kept for 12 h at room temperature, and cooled to 0°C over a period of 1 h. The precipitate was filtered off, washed on a filter with 12 mL of water and with dilute aqueous alcohol, and dried. Yield of 5,6-dimethyl-1*H*-benzotriazole 3 g (78%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6) δ, ppm: 2.39 s (6H, CH_3), 7.44 s (1H, H_{arom}), 7.69 s (1H, H_{arom}), 15.16 s (1H, NH). The product, 2.57 g (0.0175 mol), was dissolved in 7 mL of DMF, 0.48 g (0.02 mol) of sodium hydride was added with stirring, the mixture was cooled to –5°C, and 2.1 mL (0.02 mol) of ethyl 2-bromoacetate was added dropwise. The mixture was left to stand for 7 h and diluted with water, and the precipitate was filtered off and washed with water and methylene chloride–hexane (1:5). Yield of ethyl 2-(5,6-dimethyl-1*H*-1,2,3-benzotriazol-1-yl)acetate 2.45 g (60%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.29 t (3H, CH_3, J = 6.9 Hz), 2.41 s (3H, CH_3), 2.42 s (3H, CH_3), 4.22 q (2H, CH_2O, J = 7.0 Hz), 5.53 s (2H, CH_2), 7.47 s (1H, H_{arom}), 7.72 s (1H, H_{arom}). The product, 2.32 g (10 mmol), was dissolved in 40 mL of THF, the solution was cooled to 0°C, 0.4 g (10.4 mmol) of lithium tetrahydridoaluminate was added in portions with stirring, and the mixture was left to stand for 7 h. The mixture was cooled, 0.4 mL of water, 0.8 mL of 10% aqueous sodium hydroxide, and an additional 0.8 mL of water were added, and the mixture was stirred for 15 min at room temperature and filtered through a layer of silica gel. The solvent was evaporated under reduced pressure to isolate 1.88 g (98%) of 2-(5,6-dimethyl-1*H*-1,2,3-benzotriazol-1-yl)ethanol. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 2.41 s (3H, CH_3), 3.89 q (2H, OCH_2, J = 5.0 Hz), 4.64 t (2H, CH_2, J = 5.2 Hz), 4.89 t (1H, OH, J = 4.6 Hz), 7.53 s (1H, H_{arom}), 7.68 s (1H, H_{arom}). A solution of 1.6 g (8.2 mmol) of 2-(5,6-dimethyl-1*H*-1,2,3-benzotriazol-1-yl)ethanol and 1.67 mL (11.9 mmol) of triethylamine in 20 mL of methylene chloride was cooled to 0°C, 0.77 mL (9.93 mmol) of methanesulfonyl chloride was added with vigorous stirring, and the mixture was stirred for 3 h at room temperature. The mixture was washed with water and with a saturated solution of sodium carbonate, and the solvent was evaporated to obtain 2-(5,6-dimethyl-1*H*-1,2,3-benzotriazol-1-yl)ethyl methanesulfonate in quantitative yield. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 2.42 s (3H, CH_3), 2.92 s (3H, CH_3), 4.66 t (2H, CH_2, J = 5.0 Hz), 4.95 t (2H, CH_2, J = 5.0 Hz), 7.56 s (1H, H_{arom}), 7.69 s (1H, H_{arom}). The product, 2 g (7.5 mmol), was dissolved in 25 mL of DMF, 1 g (15 mmol) of sodium azide was added with stirring, and the mixture was heated to 70–90°C. The mixture was cooled and diluted with water, and the precipitate was filtered off and washed with water and hexane. Yield of azide **17** 1.1 g (68%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 2.42 s (3H, CH_3), 3.87 t (2H, CH_2, J = 5.2 Hz), 4.78 t (2H, CH_2, J = 5.3 Hz), 7.53 s (1H, H_{arom}), 7.69 s (1H, H_{arom}). Found, %: C 55.43; H 5.54; N 38.98. $C_{10}H_{12}N_6$. Calculated, %: C 55.54; H 5.59; N 38.86.

3-(Azidomethyl)-2-(2,4-dichlorophenyl)imidazo[1,2-*a*]pyridine (20). 2-Bromo-1-(2,4-dichlorophenyl)ethanone, 27 g (0.1 mol), was added to a solution of 9.4 g (0.1 mol) of pyridin-2-amine in 50 mL of ethanol, and the mixture was left overnight. It was then refluxed for 7 h, 0.1 mL of concentrated aqueous HCl was added, and the mixture was refluxed for 2 h more. The mixture was cooled, the precipitate was filtered off and dispersed in water, and the mixture was neutralized with a solution of sodium carbonate. The precipitate of 2-(2,4-dichlorophenyl)imidazo[1,2-*a*]-pyridine was filtered off. Yield 23.14 g (88%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 6.88 t (1H, 6-H, J = 6.7 Hz), 7.27 t (1H, 7-H, J = 7.7 Hz), 7.45 d (1H, 5′-H, J = 8.5 Hz), 7.51–7.58 m (2H, H_{arom}), 8.33 d (1H, 6′-H, J = 8.5 Hz), 8.52–8.60 m (2H, H_{arom}). Dimethylformamide, 100 mL, was cooled to 0°C, 10 mL (0.1 mol) of $POCl_3$ and 12 g (0.046 mol) of 2-(2,4-dichlorophenyl)imidazo[1,2-*a*]-pyridine were added, and the mixture was kept for 1 h in an ice bath. The mixture was slowly (over a period of 3 h) heated to 75°C and kept for 7 h at that temperature. It was then cooled, poured into water, and neutralized with a solution of sodium hydroxide, and the precipitate of 2-(2,4-dichlorophenyl)imidazo-[1,2-*a*]pyridine-3-carbaldehyde was filtered off. Yield

11.51 g (86%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 7.40 t (1H, 6-H, J = 6.8 Hz), 7.62 d (1H, 5′-H, J = 8.2 Hz), 7.73 d (1H, 8-H, J = 8.3 Hz), 7.78 t (1H, 7-H, J = 7.9 Hz), 7.85 s (1H, 3′-H), 7.94 d (1H, 6′-H, J = 8.9 Hz), 9.52 d (1H, 5-H, J = 6.7 Hz), 9.71 s (1H, CHO). The product, 1.94 g (6.7 mmol) was dissolved in 20 mL of methanol, 0.5 g (13.5 mmol) of sodium tetrahydridoborate was added, and the mixture was refluxed for 1.5 h. Propan-2-ol, 20 mL, was added, and the mixture was heated for 1.5 h more. The mixture was cooled and concentrated under reduced pressure, and the residue was treated with 10 mL of water and extracted with methylene chloride (30 mL). Evaporation of the extract under reduced pressure gave 1.86 g (95%) of pure {2-(2,4-dichlorophenyl)imidazo[1,2-*a*]pyridin-3-yl}methanol. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.71 d (2H, CH_2, J = 5.2 Hz), 5.12 t (1H, OH, J = 5.1 Hz), 6.96 t (1H, 6-H, J = 6.8 Hz), 7.31 t (1H, 7-H, J = 7.9 Hz), 7.44 d.d (1H, 5′-H, J = 8.2, 1.3 Hz), 7.53–7.63 m (3H, H_{arom}), 8.46 d (1H, 5-H, J = 6.8 Hz). The product, 0.31 g (1.1 mmol), was dissolved in 2 mL of DMF, 0.5 mL (1.1 mmol) of diphenylphosphoryl azide (DPPA) and 0.4 mL of l,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were added, and the mixture was stirred for 7 h at room temperature. The mixture was diluted with water (5 mL), and the precipitate of azide **20** was filtered off. Yield 0.27 g (77%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.82 s (2H, CH_2), 7.03 t (1H, 6-H, J = 6.6 Hz), 7.39 t (1H, 7-H, J = 7.6 Hz), 7.47 d.d (1H, 5′-H, J = 8.3, 1.7 Hz), 7.50 d (1H, 6′-H, J = 8.2 Hz), 7.58–7.66 m (2H, H_{arom}), 8.48 d (1H, 5-H, J = 6.8 Hz). Found, %: C 52.94; H 2.71; N 22.14. $C_{14}H_9Cl_2N_5$. Calculated, %: C 52.85; H 2.85; N 22.01.

3,3-Dimethyl-1-(prop-2-yn-1-yl)-3,4-dihydroquinoxalin-2(1*H*)–one (22). A solution of 1.14 g of benzyl(triethyl)ammonium chloride in 50 mL of methylene chloride was added to a mixture of 10.8 g (0.1 mol) of *o*-phenylenediamine, 16.2 mL of chloroform, and 18.4 mL of acetone. The mixture was cooled, and 40 g of 50% aqueous sodium hydroxide was slowly added with vigorous stirring at such a rate that the temperature did not exceed 10°C. The mixture was kept for 5–7 h at 10°C and diluted with water, and the precipitate was filtered off and washed with water and methylene chloride–hexane (1:3). If necessary, the precipitate was recrystallized from methylene chloride–hexane (1:3). Yield of 3,3-dimethyl-3,4-dihydroquinoxalin-2(1*H*)-one [30] 3.4 g (76%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.24 s (6H, CH_3), 5.67 s (1H, NH), 6.54 t (1H, H_{arom}, J = 7.0 Hz), 6.62 d (1H, H_{arom}, J = 7.5 Hz), 6.64–6.77 m (2H, H_{arom}), 9.99 s (1H, CONH). The product, 1.76 g (0.01 mol), was dissolved in 5 mL of DMF, 0.4 g (0.01 mol) of sodium hydride and 0.9 mL (0.01 mol) of propargyl bromide were added with stirring, and the mixture was left overnight. The mixture was then diluted with water, and the precipitate was filtered off and washed with water, methylene chloride, and hexane. Yield of **22** 1.3 g (61%), mp 130–131°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.26 s (6H, CH_3), 2.84 s (1H, ≡CH), 4.63 s (2H, CH_2), 5.90 s (1H, NH), 6.61–6.71 m (2H, H_{arom}), 6.84 t (1H, H_{arom}, J = 7.3 Hz), 7.01 d (1H, H_{arom}, J = 7.6 Hz). Mass spectrum: m/z 215 $[M + H]^+$. Found, %: C 72.93; H 6.55; N 13.01. $C_{13}H_{14}N_2O$. Calculated, %: C 72.87; H 6.59; N 13.07.

CONFLICT OF INTERESTS

No conflict of interests is declared by the authors.

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