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Synthesis of 1,2,3-Triazole Derivatives by Cyclocondensation of Alkyl Azides with Active Methylene Ketones in the System K_2CO_3/DMSO

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Abstract—The reaction of β-keto esters or acetylacetone with alkyl azides in the system K_2CO_3/DMSO proved to be a convenient method of synthesis of tri- and disubstituted 1-alkyl-1*H*-1,2,3-triazoles.

Keywords: azides, 1,2,3-triazoles, Dimroth reaction, 1,3-dicarbonyl compounds, cyclocondensation

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INTRODUCTION

Interest in 1*H*-1,2,3-triazole derivatives is largely determined by biological activity of compounds containing an 1*H*-1,2,3-triazole fragment [1, 2]. In particular, some 1,2,3-triazole derivatives have been found to exhibit antitumor activity, and structure–activity relations have been derived, which make it possible to optimize the search for more active compounds [3–5].

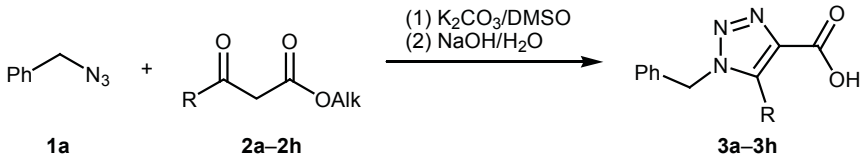
In recent years, the reaction of azides with active methylene compounds such as β-keto esters and β-diketones (Dimroth reaction) [6–17] has become popular as one of the most convenient methods of synthesis of 1,2,3-triazoles, since some versions of this reaction conform to the "click chemistry" concept as they require no heavy metal catalyst. Furthermore, these transformations can be accomplished in a one-pot fashion, as shown with the synthesis of 1,2,3-triazoles via conversion of alcohols to azides by treatment with sodium azide in the presence of *N*-(*p*-toluenesulfonyl)-imidazole, tetrabutylammonium iodide, and triethylamine, followed by cyclization of azides with active methylene ketones [18]. These transformations were called "organo-click reactions"; they are commonly assumed to proceed through 1,3-dipolar [3+2]-cycloaddition mechanism [19–21].

It was believed that reactions of azides with β-keto esters are chemoselective. However, we recently found that the ester group of β-keto esters can compete with the keto group in the reaction with azides [12, 15]. In particular, study of the Dimroth reaction of aryl azides with alkyl 3-R-3-oxopropanoates in methanol in the presence of sodium methoxide showed that in some cases the products were stable *N*-aryl-3-R-2-diazo-3-oxopropanamides resulting from attack of the azido group on the ester fragment. The highest yields of such diazo compounds were obtained when R = isopropyl, cyclopropyl, or diethoxymethyl group and aryl azide contained an electron-withdrawing substituent, and the main factor determining the yield of diazo compounds was the system base–solvent [15].

RESULTS AND DISCUSSION

In this work we studied the reaction of β-keto esters with alkyl azides. Unlike aromatic azides, alkyl azides are less reactive, and their cyclizations with active methylene compounds have been explored to a much lesser extent. Reactions of alkyl azides with ethyl acetoacetate were commonly studied. For example, 3-aryl-2-azidopropanoic acid esters [22] and 2-azidonorbornene [23] were reported. Compounds exhibiting a broad spectrum of biological activity were obtained on the basis of 1-alkyl-1*H*-1,2,3-triazole-4-carboxylic acids; in particular, they were found to activate large-conductance potassium channels [24], inhibit succinate dehydrogenase [25], and possess fungicidal and insecticidal properties [26].

Scheme 1.



1a **2a–2h** **3a–3h**

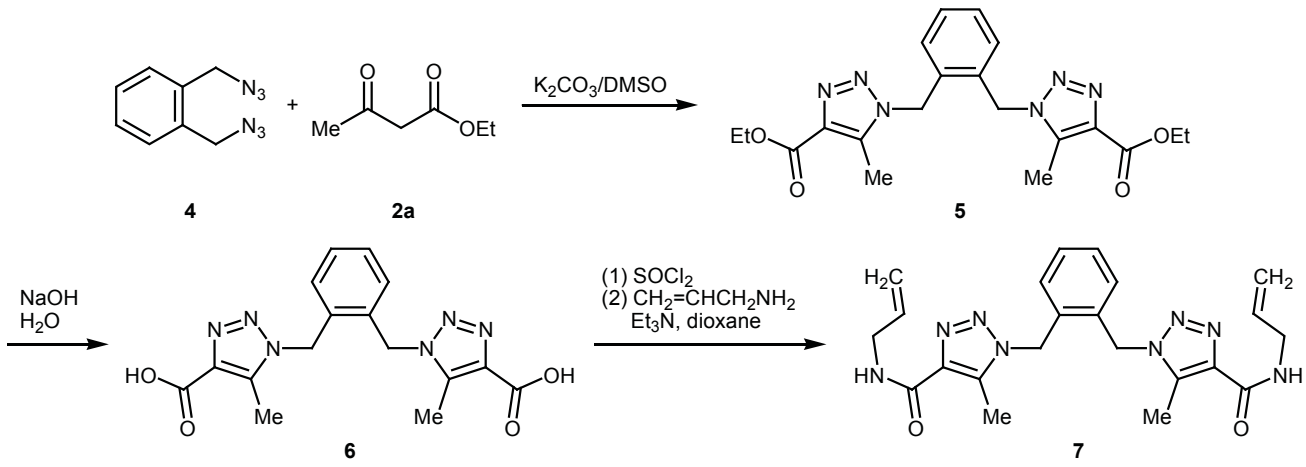
R = Me (**a**), Et (**b**), Pr (**c**), *i*-Pr (**d**), *cyclo*-C_3H_5 (**e**), $EtSCH_2$ (**f**), Ph (**g**), furan-2-yl (**h**).

As shown previously [27], benzyl azides are convenient precursors to 1,4,5-trisubstituted 1,2,3-triazoles in the system K_2CO_3/DMSO. Herein, we report the results of our study of the reaction of benzyl azide (**1a**) with a series of β-keto esters containing alkyl, aryl, and hetaryl substituents. We found that azide **1a** reacts with 3-alkyl-3-oxopropanoates **2a**–**2f**, 3-oxo-3-phenylpropanoate **2g**, and 3-(furan-2-yl)-3-oxopropanoate **2h** with high chemoselectivity and that the products were the corresponding 1-benzyl-5-R-1,2,3-triazole-4-carboxylic acids **3a**–**3h** (Scheme 1) which were formed in good yields, whereas no diazo compounds were detected.

1,2-Bis(azidomethyl)benzene (**4**) was used to synthesize compounds containing two triazole rings. The condensation of diazide **4** with ethyl acetoacetate (**2a**) gave 87% of compound **5** (Scheme 2), which was then converted to dicarboxylic acid **6** and *N*,*N*′-diallyl diamide **7**. Diamide **7** is a promising chelating ligand capable of forming π complexes with transition metals. As shown in [28], *N*-allyl-1,2,3-triazole-4-carboxamides and copper(I) form π complexes in which the coordination sphere of Cu(I) includes the allyl fragment, carbonyl oxygen atom, and N^3 atom of the triazole ring.

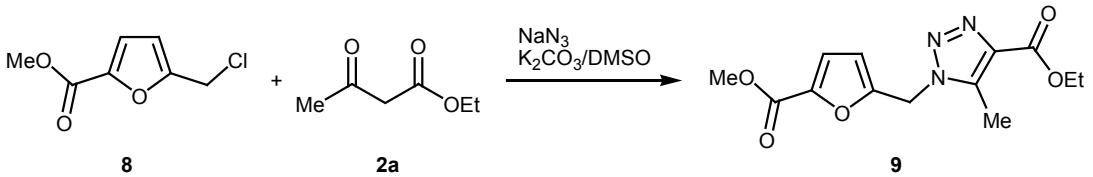
As we already noted, one-pot syntheses involving in situ generation of azides and their subsequent reactions with active methylene carbonyl compounds have been widely used in recent time. We utilized this approach with methyl 5-(chloromethyl)furan-2-carboxylate (**8**) as precursor to the corresponding azide. Nucleophilic substitution of the chlorine atom in **8** by azido group and cyclization of ethyl acetoacetate with the resulting azide without isolation of the latter gave compound **9** in 57% yield (Scheme 3). Likewise, 4,4′-bis(bromomethyl)biphenyl (**10**) was converted to diester **11** whose alkaline hydrolysis smoothly afforded the corresponding dicarboxylic acid **12** (Scheme 4). The hydrol-

Scheme 2.



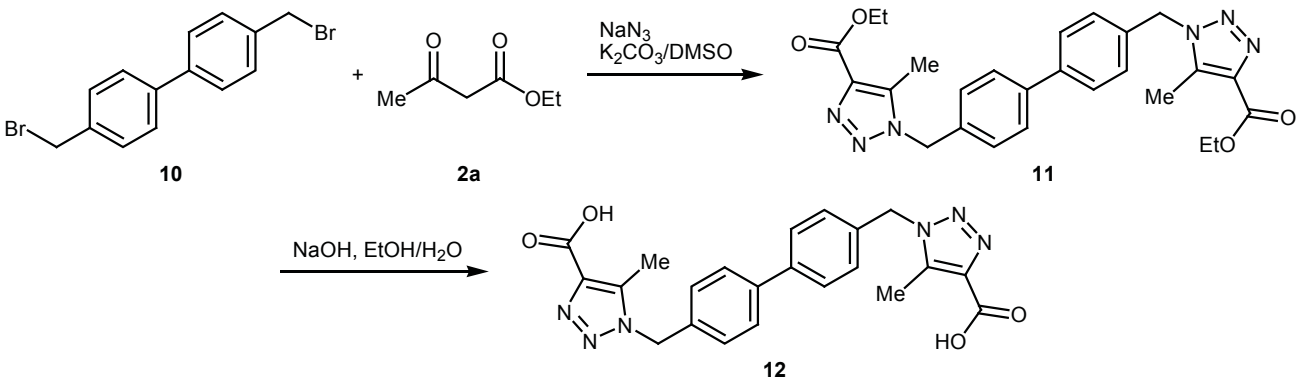
4 **2a** **5** **6** **7**

Scheme 3.

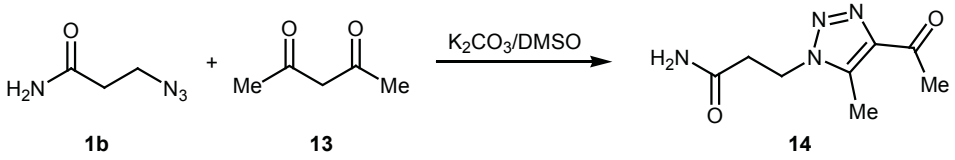


8 **2a** **9**

Scheme 4.



Scheme 5.



ysis process was monitored by IR spectroscopy, following variation of the intensities of the carbonyl stretching bands of **11** (1708 cm^{-1}) and **12** (1682 cm^{-1}).

3-Azidopropanamide (**1b**) reacted with acetylacetone (**13**) in the system K_2CO_3/DMSO to produce triazole **14** in a good yield (83%; Scheme 5). 4-Acetyltriazoles like **14** are convenient intermediate products for further transformations involving the acetyl group [29, 30]. The amide fragment of **14** can also be subjected to further modifications.

The developed procedure was used to synthesize compounds containing a 5-(1,3-benzodioxol-5-yl)-1*H*-1,2,3-triazole fragment. This fragment was selected taking into account that {5-(1,3-benzodioxol-5-yl)-1*H*-tetrazol-1-yl}acetic acid derivatives demonstrated a significant antitumor activity against breast cancer cell lines [31]. For this purpose, azides **1b** and **1c** were reacted with ester **2i** to obtain triazoles **15a** and **15b** in moderate yields (Scheme 6). Ester **15a** was reduced with lithium tetrahydridoaluminate to alcohol **16**. Compound **15b** was hydrolyzed to acid **17** whose decarboxylation gave 1,5-disubstituted triazole derivative **18**, and the amide moiety of the latter was reduced to amine **19**.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Varian Unity+ 400 (USA) and Bruker Avance 500 (USA) spectrometer at 400 and 500 MHz, respectively, using tetramethylsilane as internal standard. The mass spectra (atmospheric pressure chemical ionization) were run on an Agilent 1100 LC/MSD instrument (USA). The IR spectra were recorded on a Perkin Elmer Spectrum 2000 FTIR spectrometer. Elemental analyses were obtained with a Carlo Erba 1106 analyzer (Italy). The melting points were measured on a Boetius melting point apparatus (Wägetechnik Rapido, Germany). The progress of reactions was monitored by TLC on Silufol UV-254 plates.

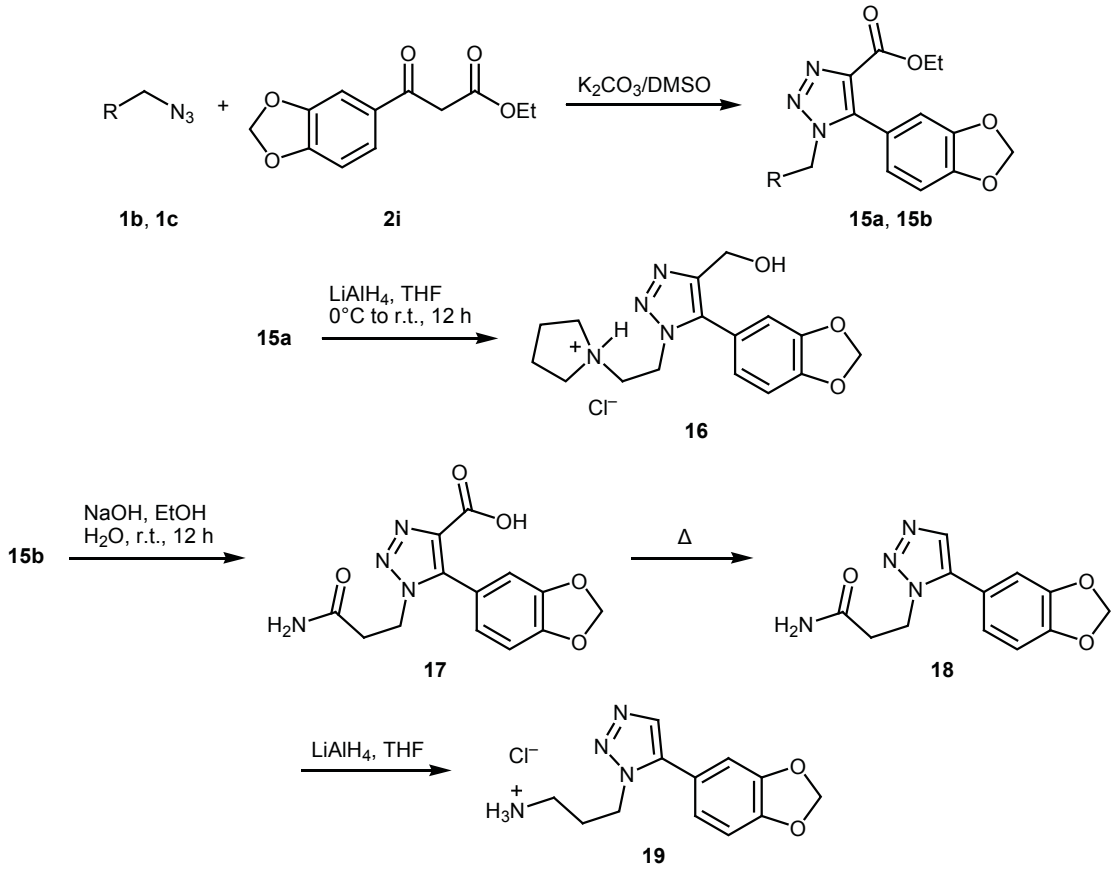
Keto esters **2** were synthesized according to the procedure described by us previously [32].

Azides 1a–1c (*general procedure***).** A solution of 6.5 g of sodium azide in 15 mL of water was added to a solution of the corresponding halogen derivative (0.1 mol) in 50 mL of methanol, and the mixture was refluxed for 2–3 h. The mixture was evaporated under reduced pressure, and the residue was extracted with methylene chloride. Evaporation of the extract under reduced pressure gave pure azide **1a**–**1c**.

Benzyl azide (1a). Yield 12.65 g (95%), colorless liquid [27]. Mass spectrum: *m*/*z* 134 $[M + H]^+$. Found, %: C 63.07; H 5.43; N 31.51. $C_7H_7N_3$. Calculated, %: C 63.14; H 5.30; N 31.56.

3-Azidopropanamide (1b). Yield 10.61 g (93%), mp 55–57°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.34 t (2H, CH_2, J = 6.5 Hz), 3.46 t (2H, CH_2, J = 6.5 Hz), 6.85 s (1H, NH), 7.36 s (1H, NH). Mass spectrum: *m*/*z* 115 $[M + H]^+$. Found, %: C 31.51; H 5.34; N 49.07. $C_3H_6N_4O$. Calculated, %: C 31.58; H 5.30; N 49.10.

Scheme 6.



1, R = $H_2NC(O)CH_2$ (**b**), pyrrolidin-1-ylmethyl (**c**).

1-(2-Azidoethyl)pyrrolidine (1c). Yield 13.31 g (95%), colorless liquid. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.72–1.85 m (4H, CH_2), 2.54–2.62 m (4H, CH_2), 2.70 t (2H, CH_2, J = 6.1 Hz), 3.35 t (2H, CH_2, J = 6.1 Hz). Mass spectrum: m/z 141 [M + H]$^+$. Found, %: C 51.52; H 8.71; N 39.83. $C_6H_{12}N_4$. Calculated, %: C 51.41; H 8.63; N 39.97.

1,2-Bis(azidomethyl)benzene (4) was synthesized in a similar way using 2 equiv of sodium azide. Yield 18.05 g (96%), colorless liquid [33]. Mass spectrum: m/z 189 [M + H]$^+$. Found, %: C 51.14; H 4.22; N 44.71. $C_8H_8N_6$. Calculated, %: C 51.06; H 4.28; N 44.66.

1,2,3-Triazole-4-carboxylic acids 3a–3h, 5, 14, 15a, and 15b (*general procedure***).** The corresponding azide (0.01 mol), was dissolved in 4 mL of DMSO, 9.6 g (0.07 mol) of potassium carbonate and 0.01 mol of β-keto ester **2** or acetylacetone (**13**) were added (in the synthesis of **5**, double amounts of DMSO, K_2CO_3, and ethyl acetoacetate were used). The resulting suspension was stirred at 40–50°C for 10 h, cooled to 5°C, and treated with 30 mL of water. The precipitate (ester) was filtered off and dissolved in 10 mL of ethanol, and 4 mL of 30% aqueous sodium hydroxide was added (4 mL of 60% aq. NaOH in the synthesis of **6**). The mixture was refluxed for 1 h, cooled to room temperature, and acidified to pH 1.0 with aqueous HCl. The precipitate was filtered off and (if necessary) recrystallized from ethanol or aqueous ethanol.

1-Benzyl-5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid (3a) [27]**.** Yield 1.58 g (73%), mp 160–161°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.44 s (3H, CH_3), 5.59 s (2H, CH_2), 7.19 d (2H, *o*-H, J = 7.2 Hz), 7.25–7.38 m (3H, *m*-H, *p*-H), 12.75 br.s (1H, COOH). Mass spectrum: m/z 218 [M + H]$^+$. Found, %: C 60.65; H 5.19; N 19.38. $C_{11}H_{11}N_3O_2$. Calculated, %: C 60.82; H 5.10; N 19.34.

1-Benzyl-5-ethyl-1*H*-1,2,3-triazole-4-carboxylic acid (3b). Yield 1.78 g (77%), mp 108–109°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.90 t (3H, CH_3, J = 7.4 Hz), 2.91 q (2H, CH_2, J = 7.4 Hz), 5.64 s (2H, PhC**H**$_2$), 7.21 d (2H, *o*-H, J =

7.2 Hz), 7.27–7.46 m (3H, *m*-H, *p*-H), 12.92 br.s (1H, COOH). Mass spectrum: *m*/*z* 232 $[M + H]^+$. Found, %: C 62.43; H 5.78; N 18.22. $C_{12}H_{13}N_3O_2$. Calculated, %: C 62.33; H 5.67; N 18.17.

1-Benzyl-5-propyl-1*H*-1,2,3-triazole-4-carboxylic acid (3c). Yield 1.84 g (75%), mp 72–73°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.78 t (3H, CH_3, J = 7.2 Hz), 1.23–1.41 m (2H, CH_2), 2.87 t (2H, CH_2, J = 7.6 Hz), 5.64 s (2H, CH_2N), 7.21 d (2H, *o*-H, J = 7.4 Hz), 7.26–7.47 m (3H, *m*-H, *p*-H), 12.93 br.s (1H, COOH). Mass spectrum: *m*/*z* 246 $[M + H]^+$. Found, %: C 63.81; H 6.02; N 17.02. $C_{13}H_{15}N_3O_2$. Calculated, %: C 63.66; H 6.16; N 17.13.

1-Benzyl-5-(propan-2-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (3d). Yield 1.74 g (71%), mp 80–81°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.14 d (6H, CH_3, J = 6.9 Hz), 3.42 sept (2H, CH, J = 6.9 Hz), 5.71 s (2H, CH_2), 7.14 d (2H, *o*-H, J = 7.2 Hz), 7.24–7.41 m (3H, *m*-H, *p*-H), 12.95 br.s (1H, COOH). Mass spectrum: *m*/*z* 246 $[M + H]^+$. Found, %: C 63.74; H 6.11; N 17.01. $C_{13}H_{15}N_3O_2$. Calculated, %: C 63.66; H 6.16; N 17.13.

1-Benzyl-5-cyclopropyl-1*H*-1,2,3-triazole-4-carboxylic acid (3e). Yield 1.58 g (65%), mp 64–65°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.94–0.98 m (4H, C_3H_5), 1.71–1.75 m (1H, C_3H_5), 5.65 s (2H, CH_2N), 7.19 d (2H, *o*-H, J = 6.8 Hz), 7.28 t (1H, *p*-H, J = 6.8 Hz), 7.33 t (2H, *m*-H, J = 6.8 Hz). Mass spectrum: *m*/*z* 244 $[M + H]^+$. Found, %: C 63.99; H 5.58; N 17.13. $C_{13}H_{13}N_3O_2$. Calculated, %: C 64.19; H 5.39; N 17.27.

1-Benzyl-5-[(ethylsulfanyl)methyl]-1*H*-1,2,3-triazole-4-carboxylic acid (3f). Yield 1.77 g (64%), mp 53–54°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.11 t (3H, CH_3, J = 7.3 Hz), 2.43 q (2H, C**H**$_2$CH$_3$, J = 7.3 Hz), 4.15 s (2H, CH_2S), 5.67 s (2H, CH_2N), 7.27 d (2H, *o*-H, J = 7.8 Hz), 7.30–7.42 m (3H, *m*-H, *p*-H). Mass spectrum: *m*/*z* 278 $[M + H]^+$. Found, %: C 56.50; H 5.64; N 15.26. $C_{13}H_{15}N_3O_2S$. Calculated, %: C 56.30; H 5.45; N 15.15.

1-Benzyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylic acid (3g). Yield 1.87 g (67%), mp 188–189°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.45 s (2H, CH_2N), 6.93–7.00 m (2H, H_{arom}), 7.22–7.28 m (3H, H_{arom}), 7.31 d (2H, H_{arom}, J = 7.8 Hz), 7.42–7.49 m (3H, H_{arom}). Mass spectrum: *m*/*z* 280 $[M + H]^+$. Found, %: C 68.91; H 4.74; N 15.17. $C_{16}H_{13}N_3O_2$. Calculated, %: C 68.81; H 4.69; N 15.05.

1-Benzyl-5-(furan-2-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (3h). Yield 1.70 g (63%), mp 156–157°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.82 s (2H, CH_2), 6.62 d.d (1H, 4-H_{Fu}, J = 1.6, 3.2 Hz), 7.12 d (2H, *o*-H, J = 7.6 Hz); 7.25–7.28 m (4H, *m*-H, *p*-H, 3-H_{Fu}), 7.84 br.s (1H, 5-H_{Fu}), 13.00 br.s (1H, COOH). Mass spectrum: *m*/*z* 270 $[M + H]^+$. Found, %: C 62.67; H 3.96; N 15.73. $C_{14}H_{11}N_3O_3$. Calculated, %: C 62.45; H 4.12; N 15.61.

Diethyl 1,1′-[1,2-phenylenebis(methylene)]bis-(5-methyl-1*H*-1,2,3-triazole-4-carboxylate) (5). Yield 2.84 g (69%), mp 98–99°C. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 1.33 t (6H, CH_2C**H**$_3$, J = 7.3 Hz), 2.50 s (6H, 5-CH_3), 4.33 q (4H, C**H**$_2$CH$_3$, J = 7.3 Hz), 5.85 s (4H, CH_2N), 6.74–6.78 m (2H, H_{arom}), 7.30–7.34 m (2H, H_{arom}). Mass spectrum: *m*/*z* 413 $[M + H]^+$. Found, %: C 58.41; H 5.66; N 20.23. $C_{20}H_{24}N_6O_4$. Calculated, %: C 58.24; H 5.87; N 20.38.

3-(4-Acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)propanamide (14). Yield 1.63 g (83%), mp 63–64°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.47 s (3H, CH_3), 2.51 s (3H, CH_3), 2.68 t (2H, CH_2, J = 5.2 Hz), 4.42 t (1H, CH_2N, J = 5.2 Hz), 6.89 s (1H, NH), 7.40 s (1H, NH). Mass spectrum: *m*/*z* 197 $[M + H]^+$. Found, %: C 48.90; H 6.27; N 28.48. $C_8H_{12}N_4O_2$. Calculated, %: C 48.97; H 6.16; N 28.56.

Ethyl 5-(1,3-benzodioxol-5-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1*H*-1,2,3-triazole-4-carboxylate (15a). Yield 1.83 g (51%), mp 42–43°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.24 t (3H, CH_3, J = 7.1 Hz). 1.59–1.71 m (4H, CH_2), 2.26–2.37 m (4H, CH_2N), 2.80 t (2H, CH_2N, J = 6.0 Hz), 4.20 q (2H, CH_2O, J = 7.1 Hz), 4.31 t (2H, CH_2N, J = 6.0 Hz), 6.10 s (2H, OCH_2O), 6.91 d (1H, 7-H, J = 8.0 Hz), 6.94–7.03 m (2H, 4-H, 6-H). Mass spectrum: *m*/*z* 359 $[M + H]^+$. Found, %: C 60.41; H 6.28; N 15.52. $C_{18}H_{22}N_4O_4$. Calculated, %: C 60.32; H 6.19; N 15.63.

Ethyl 1-(3-amino-3-oxopropyl)-5-(1,3-benzodioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate (15b). Yield 2.49 g (75%), mp 58–59°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.08 t (3H, CH_3, J = 7.2 Hz), 2.74 t (2H, CH_2, J = 6.8 Hz), 4.20 q (2H, CH_2O, J = 7.2 Hz), 4.34 t (1H, CH_2N, J = 6.8 Hz), 6.10 s (2H, OCH_2O), 6.76 s (1H, NH), 6.93–7.01 m (2H, 6-H, 7-H), 7.03 s (1H, 4-H), 7.38 s (1H, NH). Mass spectrum: *m*/*z* 333 $[M + H]^+$. Found, %: C 54.34; H 4.97; N 16.81. $C_{15}H_{16}N_4O_5$. Calculated, %: C 54.21; H 4.85; N 16.86.

One-pot synthesis of 1,2,3-triazole-4-carboxylates 9 and 11 (*general procedure*). Sodium azide, 1.25 g (0.019 mol), was added to a solution of 2.86 g (0.016 mol) of methyl 5-(chloromethyl)furan-2-car-

boxylate (**8**) or 2.72 g (0.008 mol) of 4,4′-bis(bromomethyl)biphenyl (**10**) in 10 mL of DMSO. The suspension was stirred at room temperature for 5 h, 10 g (0.072 mol) of potassium carbonate and 2.05 mL (0.016 mol) of ethyl acetoacetate were added, and the mixture was stirred at 40–50°C for 12 h. It was then cooled to 5°C, 100 mL of water was added, and the mixture was extracted with 50 mL of methylene chloride. The extract was dried over sodium sulfate, and the solvent was evaporated.

Ethyl 1-{[5-(methoxycarbonyl)furan-2-yl]-methyl}-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (9). Yield 2.67 g (57%), yellow liquid. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.26 t (3H, CH_3, J = 6.8 Hz), 2.46 s (3H, CH_3), 3.74 s (3H, CH_3O), 4.26 q (2H, CH_2O, J = 6.8 Hz), 5.76 s (2H, CH_2N), 6.70 d (1H, H_{Fu}, J = 3.2 Hz),7.24 d (1H, H_{Fu}, J = 3.2 Hz). Mass spectrum: m/z 294 $[M + H]^+$. Found, %: C 53.30; H 5.24; N 14.21. $C_{13}H_{15}N_3O_5$. Calculated, %: C 53.24; H 5.16; N 14.33.

Diethyl 1,1′-[biphenyl-4,4′-diylbis(methylene)]-bis(5-methyl-1*H*-1,2,3-triazole-4-carboxylate) (11). Yield 2.81 (72%), mp 166–167°C. IR spectrum, ν, cm^{-1}: 2988, 2934, 2906, 1708 (C=O), 1567, 1480, 1450, 1425, 1398, 1370, 1341, 1305, 1242, 1200, 1185, 1099, 1081, 1021, 981, 848, 796, 786. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.40 t (6H, C**H**$_3$CH$_2$, J = 7.1 Hz), 2.48 s (6H, 5-CH_3), 4.41 q (4H, CH_3C**H**$_2$, J = 7.1 Hz), 5.56 s (4H, NCH_2), 7.23 d (4H, H_{arom}, J = 8.2 Hz), 7.51 d (4H, H_{arom}, J = 8.2 Hz). Mass spectrum: m/z 489 $[M + H]^+$. Found, %: C 63.79; H 5.67; N 17.40. $C_{26}H_{28}N_6O_4$. Calculated, %: C 63.92; H 5.78; N 17.20.

Hydrolysis of esters 5 and 11 (*general procedure*). Ester **5** or **11** (0.01 mol) was dissolved in 20 mL of ethanol, 4 mL of 60% aqueous sodium hydroxide was added, and the mixture was refluxed for 1 h. The mixture was cooled to room temperature and acidified to pH 1.0 with aqueous HCl. The precipitate was filtered off and (if necessary) recrystallized from ethanol or aqueous ethanol.

1,1′-[1,2-Phenylenebis(methylene)]bis(5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid) (6). Yield 3.38 g (95%), mp 218–219°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.49 s (6H, 5-CH_3), 5.84 s (4H, CH_2), 6.74–6.80 m (2H, H_{arom}), 7.30–7.37 m (2H, H_{arom}). Mass spectrum: m/z 357 $[M + H]^+$. Found, %: C 53.75; H 4.67; N 23.40. $C_{16}H_{16}N_6O_4$. Calculated, %: C 53.93; H 4.53; N 23.58.

1,1′-[Biphenyl-4,4′-diylbis(methylene)]bis(5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid) (12). Yield 3.59 g (83%), mp 256–257°C. IR spectrum, ν, cm^{-1}: 3040, 2885, 2657, 2586, 1682 (C=O), 1574, 1479, 1451, 1337, 1301, 1266, 1234, 1195, 1097, 932, 781, 757. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.50 s (6H, CH_3), 5.69 s (4H, CH_2), 7.31 d (4H, H_{arom}, J = 8.0 Hz), 7.68 d (4H, H_{arom}, J = 8.0 Hz), 13.04 br.s (2H, COOH). Mass spectrum: m/z 433 $[M + H]^+$. Found, %: C 61.01; H 4.74; N 19.57. $C_{22}H_{20}N_6O_4$. Calculated, %: C 61.10; H 4.66; N 19.43.

1,1′-[1,2-Phenylenebis(methylene)]bis[*N*-(prop-2-en-1-yl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide] (7). A mixture of 5 g (0.014 mol) of acid **6** and 10 mL of thionyl chloride was refluxed for 3 h. Excess thionyl chloride was removed under reduced pressure to obtain the corresponding acid chloride in quantitative yield. The product (3.93 g, 0.01 mol) was added in portions to a solution of 1.14 g (0.02 mol) of allylamine and 2.8 mL (0.02 mol) of triethylamine in 10 mL of dioxane, cooled in an ice bath, and the mixture was left overnight at room temperature. It was then treated with 30 mL of water, and the precipitate was filtered off and recrystallized from ethanol. Yield 3.65 g (84%), mp 117–118°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.54 s (6H, CH_3), 3.86–3.90 m (4H, C**H**$_2$NHCO), 5.07 d.d (2H, =CH_2, *cis*, J = 1.4, 10.2 Hz), 5.15 d.d (2H, CH_2, *trans*, J = 1.4, 17.1 Hz), 5.85 s (4H, CH_2), 5.93–5.97 m (2H, CH=), 6.67–6.72 m (2H, H_{arom}), 7.29–7.33 m (2H, H_{arom}), 8.65 br.s (2H, NH). Mass spectrum: m/z 435 $[M + H]^+$. Found, %: C 60.71; H 5.81; N 25.90. $C_{22}H_{26}N_8O_2$. Calculated, %: C 60.81; H 6.03; N 25.79.

{5-(1,3-Benzodioxol-5-yl)-1-[2-(pyrrolidin-1-yl)-ethyl]-1*H*-1,2,3-triazol-4-yl}methanol hydrochlride (16). A solution of 1.18 g (0.0033 mol) of compound **15a** in 50 mL of THF was cooled to 0°C, 0.14 g (0.0033 mol) of $LiAlH_4$ was added in portions with stirring, and the mixture was left overnight. The mixture was cooled, 0.14 mL of water, 0.28 mL of 10% aqueous sodium hydroxide, and an additional 0.28 mL of water were added in succession, the mixture was stirred at room temperature for 15 min and filtered through a thin layer of silica gel, and the filtrate was evaporated under reduced pressure. The residue was treated with 4 mL of diethyl ether saturated with hydrogen chloride (~2.0 M), and the precipitate was filtered off. Yield 0.98 g (95%), mp 176°C (decomp.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.73–1.85 m (2H, CH_2), 1.88–2.03 m (2H, CH_2), 2.87–3.00 m (2H, CH_2), 3.38–3.49 m (2H, CH_2), 3.61–3.69 m (2H, CH_2), 4.36–4.41 m (3H, CH_2, OH), 4.68 t (2H, CH_2, J = 6.5 Hz), 6.12 s (2H, OCH_2O), 7.05 d

(1H, 7-H, J = 7.9 Hz), 7.09 d (1H, 6-H, J = 7.9 Hz), 7.17 s (1H, 4-H), 10.97 s (1H, NH). Mass spectrum: m/z 317 $[M + H]^+$. Found, %: C 54.33; H 6.14; N 15.96. $C_{16}H_{20}N_4O_3 \cdot HCl$. Calculated, %: C 54.47; H 6.00; N 15.88.

1-(3-Amino-3-oxopropyl)-5-(1,3-benzodioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (17). Ester **15b** (0.64 g, 2 mmol) was dissolved in 30 mL of ethanol, a solution of 0.08 g (2 mmol) of sodium hydroxide in 1 mL of water was added, and the mixture was left overnight. The solvent was evaporated, the residue was dissolved in water, the solution was extracted with methylene chloride. The aqueous layer was acidified with aqueous HCl, and the precipitate was filtered off. Yield 0.56 g (92%), mp 156–157°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.73 t (2H, CH_2, J = 7.1 Hz), 4.33 t (2H, CH_2, J = 6.8 Hz), 6.11 s (2H, OCH_2O), 6.75 s (1H, NH), 6.93–7.00 m (2H, 6-H, 7-H), 7.02 s (1H, 4-H), 7.35 s (1H, NH), 12.56 br.s (1H, COOH). Mass spectrum: m/z 305 $[M + H]^+$. Found, %: C 51.45; H 3.92; N 18.37. $C_{13}H_{12}N_4O_5$. Calculated, %: C 51.32; H 3.98; N 18.41.

3-[5-(1,3-Benzodioxol-5-yl)-1*H*-1,2,3-triazol-1-yl]propanamide (18). Acid **17** was heated at the melting point until carbon dioxide no longer evolved. The melt was cooled. Yield quantitative, mp 128–129°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.71 t (2H, CH_2, J = 7.1 Hz), 4.35 t (2H, CH_2, J = 6.8 Hz), 6.12 s (2H, OCH_2O), 6.75 s (1H, NH), 6.94–7.02 m (2H, 6-H, 7-H), 7.02 s (1H, 4-H), 7.61 s (1H, 4′-H), 7.33 s (1H, NH). Mass spectrum: m/z: 261 $[M + H]^+$. Found, %: C 55.25; H 4.53; N 21.40. $C_{12}H_{12}N_4O_3$. Calculated, %: C 55.38; H 4.65; N 21.53.

3-[5-(1,3-Benzodioxol-5-yl)-1*H*-1,2,3-triazol-1-yl]propan-1-amine hydrochloride (19). A solution of 0.26 g (1 mmol) of amide **18** in 5 mL of THF was cooled to 0°C, 0.1 g (2.1 mmol) of $LiAlH_4$ was added in portions with stirring, and the mixture was left overnight. The mixture was then refluxed for 2 h and cooled, and 0.1 mL of water, 0.2 mL of 10% aqueous sodium hydroxide, and an additional 0.1 mL of water were added in succession, and the mixture was stirred at room temperature for 15 min. The mixture was filtered through a thin layer of silica gel, the filtrate was evaporated under reduced pressure, and the residue was treated with 1 mL of diethyl ether saturated with hydrogen chloride (~2.0 M). The viscous oily material was separated. Yield 0.21 g (75%). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.09 t (2H, CH_2, J = 7.2 Hz). 3.26–3.47 m (2H, CH_2), 4.46 t (2H, CH_2, J = 7.1 Hz), 6.12 s (2H, OCH_2O), 7.02 d (1H, 7-H, J = 7.5 Hz), 7.09 d (1H, 6-H, J = 7.6 Hz), 7.15 s (1H, 4-H), 7.83 s (1H, 4′-H), 7.89 br.s (3H, NH_3^+). Mass spectrum: m/z 247 $[M + H]^+$. Found, %: C 50.84; H 5.22; N 19.98. $C_{12}H_{15}ClN_4O_2$. Calculated, %: C 50.98; H 5.35; N 19.82.

CONCLUSIONS

Base-catalyzed cyclocondensation of alkyl azides with β-keto esters or 1,3-diketones is a convenient method for the synthesis of 1-alkyl-1*H*-1,2,3-triazole derivatives that attract interest as potential antitumor agents.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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