ISSN 1070-4280, Russian Journal of Organic Chemistry, 2020, Vol. 56, No. 8, pp. 1421–1431. © Pleiades Publishing, Ltd., 2020.
Russian Text © The Author(s), 2020, published in Zhurnal Organicheskoi Khimii, 2020, Vol. 56, No. 8, pp. 1268–1279.

Synthesis of (1*H*-1,2,3-Triazol-1-yl)acetic Acid Derivatives

N. T. Pokhodylo[a], R. D. Savka[a], and M. D. Obushak[a,*]

[a] *Ivan Franko National University of Lviv, Lviv, 79005 Ukraine*
**e-mail: mykola.obushak@lnu.edu.ua*

Received April 5, 2020; revised April 13, 2020; accepted April 18, 2020

Abstract—A convenient synthetic approach to (1*H*-1,2,3-triazol-1-yl)acetic acid derivatives via the reaction of azidoacetamides with β-ketoesters and acetylacetone is proposed. Based on this strategy, 1,5-disubstituted 1,2,3-triazoles were prepared from available reagents under metal-free conditions. A one-pot protocol for the synthesis of (5-methyl-1*H*-1,2,3-triazol-1-yl)acetamides derived from *N*-substituted chloroacetamides is developed.

Keywords: azides, 1,2,3-triazoles, Dimroth reaction, (1*H*-1,2,3-triazol-1-yl)acetic acids, 1,3-dicarbonyl compounds

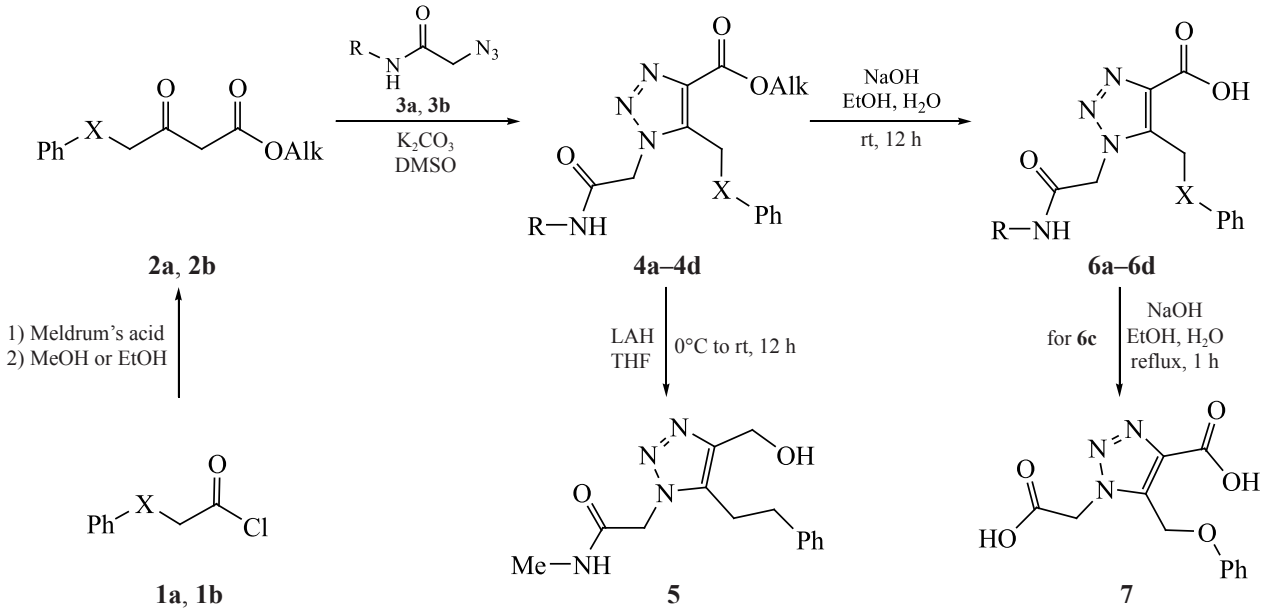
DOI: 10.1134/S1070428020080138

The 1,2,3-triazole ring is a structural fragment, whose presence in compounds make them attractive for screening for biological activity, because it is an isostere of the amide bond, resistant to metabolic degradation, and can form hydrogen bonds, which is important for binding with biological targets [1]. The introduction of a carboxyl function in the 1,2,3-triazole ring favors creation of convenient structural blocks for the synthesis of combinatorial libraries. In particular, 1*H*-1,2,3-triazole-4-carboxylic acid derivatives were used for the synthesis of compounds that exhibited antifungal activity [2–4], antimicrobial activity against the mycobacterium tuberculosis strain H37Rv [5], antiviral activity against replication of influenza A and herpes simplex virus type 1 (HSV-1) [6], as well as anticancer activity against various cancer cell lines [7–10]. (1*H*-1,2,3-Triazol-1-yl)-acetic acids were used to synthesize compounds active against methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci [11], antagonists of monoacylglycerol lipase [12], agonists and antagonists of sphingosine-1-phosphate receptors [13], inhibitors of stearoyl-coenzyme delta-9 [14], as well as anticancer and antiviral agents [16]. The synthesis and biological testing of a number of (1*H*-1,2,3-triazol-1-yl)acetic acid derivatives made possible their application as inhibitors of the HIV-1 capsid (HIV-1 CA) for the design of antiviral drugs on their basis [17].

(1*H*-1,2,3-Triazol-1-yl)acetic acids were most commonly prepared by the 1,3-dipolar cycloaddition reactions of azides to terminal acetylenes. In the present work studied the use of Dimroth cyclocondesation of azidoacetic acid derivatives with dicarbonyl compounds for preparing compounds of this type. In case of success, such approach would allow introduction of a much wider range of substituents in the triazole ring of triazolylacetic acids.

The reaction of 2-azidoacetamides **3a** and **3b** with 4-benzyl- and 4-phenoxyacetoacetic acids **2a**, and **2b**, prepared from the corresponding chlorides **1a** and **1b** by acylation of the Meldrum's acid was studied. It was found that the reaction in the presence of K_2CO_3 in DMSO in mild conditions gave triazoles **4a–4d** in good yields (Scheme 1). The K_2CO_3–DMSO catalytic system was chosen, because it showed high performance in reactions of alkyl azides (norbornan-2-yl azide, alkyl 2-azido-3-arylpropanoates) with acetoacetic ester [18, 19] and of azides with 2-oxophosphonates [20]. Selective cyclocondensations under the same conditions were reported for β-keto esters [21], sterically hindered azides [22, 23], and electron-deficient aromatic azides, 2-azidothiazoles, and 2-azidothiadiazoles [24]. The triazole core enhances the reactivity of the carbonyl group, which allows selective transformations of the ester group. The selective reduction of the ester group in compound **4b** gave alcohol **5** (Scheme 1). Hydrolysis of compounds **4a–4d** occurred at room temperature and formed acids **6a–6d** in quantitative yields. Alkaline hydrolysis of acid **6c** under heating afforded dicarboxylic acid **7**.

Scheme 1.

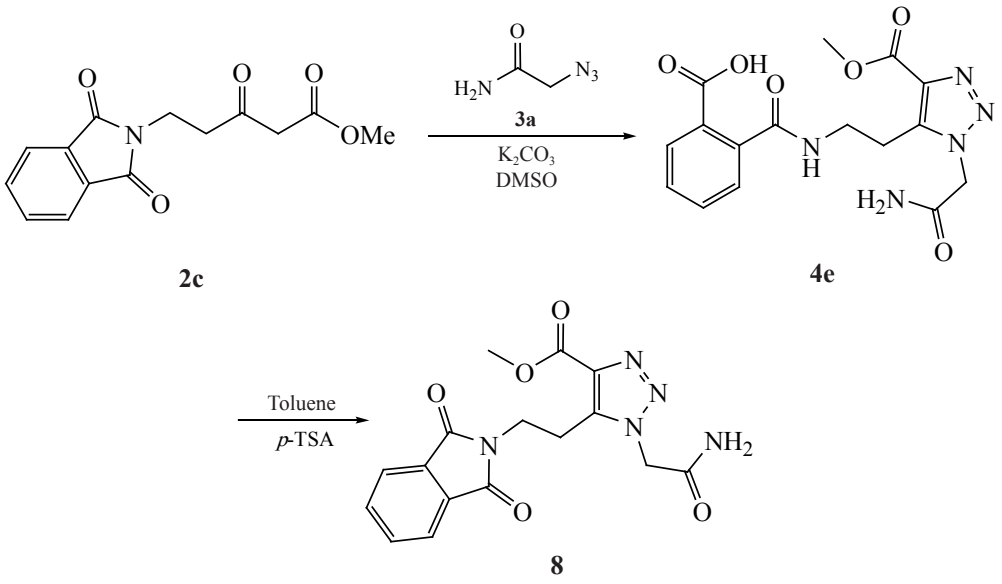


1, **2**, X = CH_2 (**a**), O (**b**); **3**, R = H (**a**), Me (**b**); Alk = Me, Et; **4**, **6**, R = H, X = CH_2 (**a**), R = Me, X = CH_2 (**b**), R = H, X = O (**c**), R = Me, X = O (**d**).

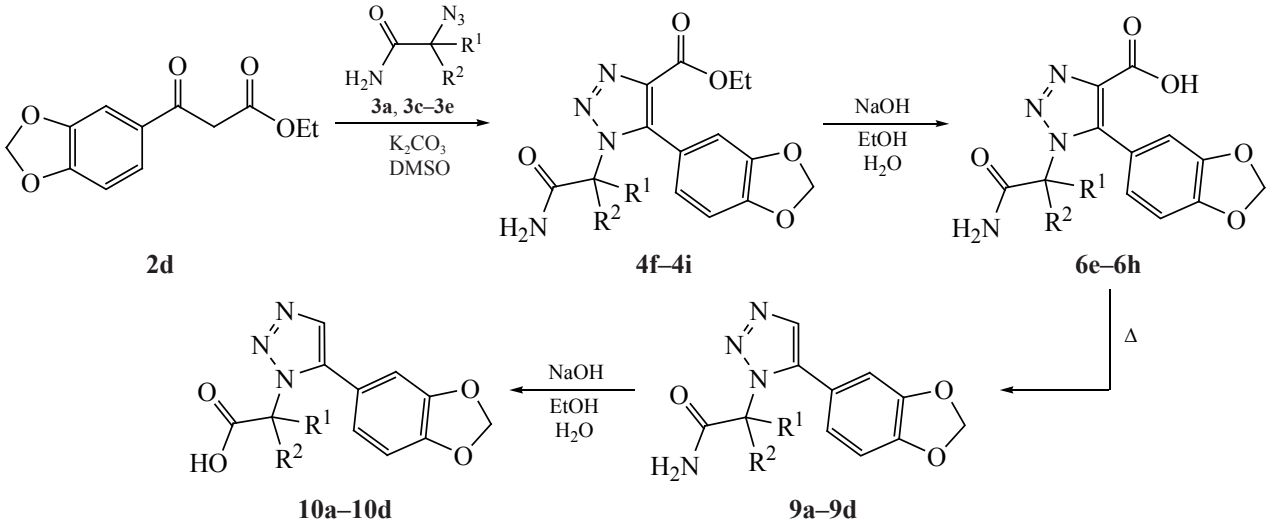
Aimed at introducing the amino group to the side chain of triazoles, we allowed azidoacetamide **3a** to react with β-ketoester **2c** containing a phthalimide fragment. It was found that the reaction, along with the formation of the triazole ring, involves cleavage of the phthalimide fragment to form compound **4e** (Scheme 2). The latter was converted into triazole **8** by refluxing in toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid.

Searching for (1*H*-1,2,3-triazol-1-yl)acetic acid derivatives that might be useful for developing anticancer agents, we focused on {5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-tetrazol-1-yl}acetic acid as a core structure for the synthesis a series of tetrazolohydrazones that showed activity against MCF-7, MDA-MB-231, and ZR-75 breast cancer cells [25]. Taking into account that 1,5-disubstituted 1,2,3-triazoles and tetrazoles, being the closest

Scheme 2.



Scheme 3.



2d **4f–4i** **6e–6h**

10a–10d **9a–9d**

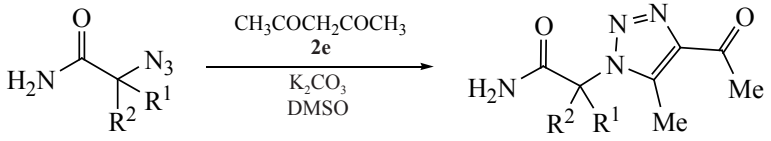
R^1 = H, R^2 = H (**3a**, **4f**, **6e**, **9a**, **10a**); R^1 = H, R^2 = Me (**3c**, **4g**, **6f**, **9b**, **10b**); R^1 = Me, R^2 = Me (**3a**, **4h**, **6g**, **9c**, **10c**); R^1 = H, R^2 = Et (**3a**, **4i**, **6h**, **9d**, **10d**).

isosteres of the *cis*-peptide bond [26, 27], have similar biophysical properties, we have developed a convenient synthetic approach to {5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-triazol-1-yl}acetic acids. The earlier reported synthesis of 5-substituted triazol-1-ylacetic acids made use of ruthenium complexes [28, 29]. In view of the high cost of such catalysts, we developed a different approach, which excludes the use of transitions metal catalysts. From the readily available ethyl 3-(benzo[*d*][1,3]dioxol-5-yl)-3-oxopropanoate (**2d**) we prepared 5-(benzo[*d*]-[1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylates **4f–4i** and further converted them to acids **6e–6h** (Scheme 3). When heated to the melting points, acids **6** underwent decarboxylation to form 1,5-disubstituted 1,2,3-triazoles **9a–9d**. The latter were hydrolyzed to obtain the target (1*H*-1,2,3-triazol-1-yl)acetic acids **10a–10d** with a total yield of more than 70 % (per the starting β-keto ester **2d**). The high yields make the developed approach competitive to the ruthenium-catalyzed azide–alkyne cycloaddition, especially in view of the high cost of the catalyst and hard accessibility of terminal alkynes.

It was also found that, under the found conditions, azidoamides **3c** and **3d** react with acetylacetone **2e**, forming 4-acetyltriazoles **11a** and **11b** in high yields (Scheme 4). We earlier showed that such 4-acetyltriazoles are convenient precursors for the Willgerodt–Kindler synthesis of (1*H*-1,2,3-triazole-4-yl)acetic acids [30].

The example of chloroacetamides **12** was used to demonstrate the feasibility of one-pot synthesis of (1*H*-1,2,3-triazol-1-yl)acetamides. Thus, chloroacetamides **12a–12c** were reacted with sodium azide and acetoacetic ester **2f** and obtained novel triazoles **13a–13c** in high yields (Scheme 5). Compounds **13a** and **13c** undergo selective hydrolysis in the presence of a small excess of alkali to afford 1,2,3-triazole-4-carboxylic acids **14a** and **14b**. Decarboxylation of acid **14a** followed by hydrolysis of the amide fragment allowed synthesis of a hardly accessible 2-(5-methyl-1*H*-1,2,3-triazol-1-yl)-acetic acid (**16**). The latter is a convenient low-molecular-weight structural block for constructing libraries of 2-(5-methyl-1*H*-1,2,3-triazol-1-yl)acetic acid derivatives.

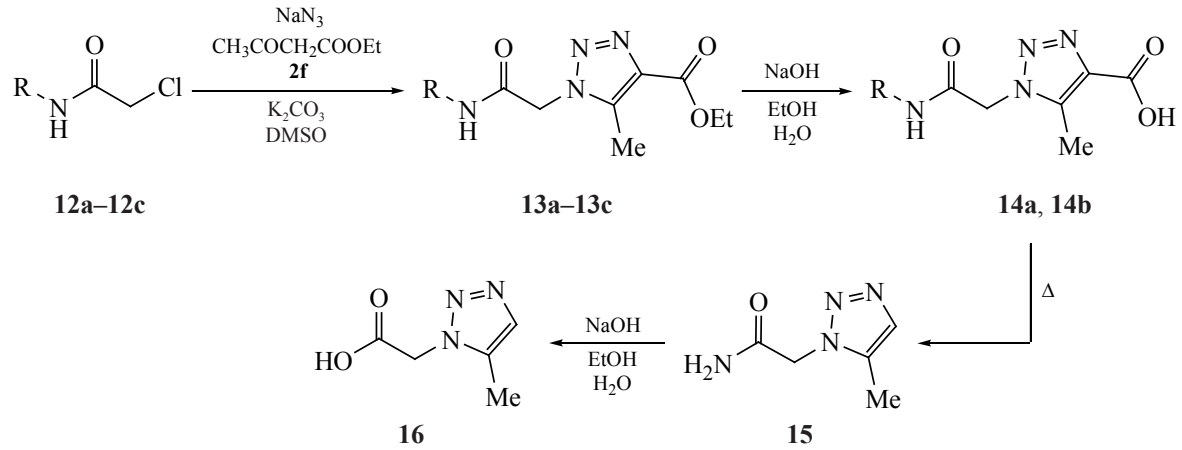
Scheme 4.



3c, **3d** **11a**, **11b**

R^1 = H, R^2 = Me (**3c**, **11a**); R^1 = Me, R^2 = Me (**3d**, **11b**).

Scheme 5.



12, **13**, R = H (**a**), Ph (**b**), Mes (**c**); **14**, R = H (**a**), Ph (**b**).

Hydrolysis of the ester group in compound **13c** was monitored by IR spectroscopy, following the changes in the frequencies of the strong carbonyl absorption bands: from $\nu_{(COOEt)}$ = 1706 cm^{-1} and $\nu_{(NHCO)}$ = 1655 cm^{-1} for ester **13c** to $\nu_{(COOH)}$ = 1685 cm^{-1} and $\nu_{(NHCO)}$ = 1669 cm^{-1} for acid **14b**. The spectra of compounds **13c** and **14b** also displayed medium bands due to stretching vibrations of the N–H bond (ν = 3270 cm^{-1} for **13c** and ν = 3262 cm^{-1} for **14b**).

Thus we showed that the base-catalyzed cyclocondensation of 2-azidoacetamides with β-keto esters or 1,3-diketones provides a convenient synthetic approach to (1*H*-1,2,3-triazol-1-yl)acetic acid derivatives. A method of synthesis of 1,5-disubstituted 1*H*-1,2,3-triazoles from available reagents and in the absence of metal catalysts, as well as a one-pot synthesis of (1*H*-1,2,3-triazol-1-yl)-acetic acid from chloroacetamides. Note that the synthesized compounds all comply with the Lipinski rule of five and they can be tested for biological activity, while low-molecular-weight (1*H*-1,2,3-triazol-1-yl)acetic acids can be used as building blocks in synthesis, as well as for creation of combinatorial libraries.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a VarianUnity +400 spectrometer at 400 MHz, internal reference TMS. The mass spectra were obtained on an Agilent 1100 LC/MSD instrument with an APCI ionization source. The IR spectra were measured on a Perkin Elmer Spectrum 2000 FTIR spectrometer. The elemental analyses were obtained on a Carlo Erba 1106 analyzer. The melting points were measured on a Boëtius hot stage.

Synthesis of β-keto esters 2a–2c (*general procedure*). Acid chloride **1a** or **1b** (40.8 mmol) was added in portions to a stirred to a solution of 6.05 g (40.8 mmol) of the Meldrum's acid in 6.8 mL (81.6 mmol) of pyridine at 0°C. The reaction mixture was stirred at 0°C for 1 h, let to warm up to room temperature, and allowed to stand at 1 h. A concentrated solution of NaCl (30 mL) was then added, and the product was extracted with dichloromethane (3 × 100 mL). The solvent was evaporated in a vacuum, the residue was dissolved in 30 mL of methanol or ethanol, and the solution was refluxed for 5 h. The alcohol was evaporated, and the residue was dissolved in 200 mL of dichloromethane, and the solution was washed with 30 mL of 5% HCl. The solvent was evaporated, and the residue was distilled in a vacuum. Compound **2c** was recrystallized from aqueous alcohol.

Methyl 3-oxo-5-phenylpentanoate (2a). Yield 6.3 g (75%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.81 t (2H, CH_2, *J* 7.2 Hz), 2.86 t (2H, CH_2, *J* 7.2 Hz), 3.58 s (2H, CH_2), 3.64 s (3H CH_3O), 7.16–7.23 m (3H$_{arom}$), 7.24–7.33 m (2H$_{arom}$). Mass spectrum (CI), *m/z*: 207 $[M + H]^+$. Found, %: C 69.81; H 6.79. $C_{12}H_{14}O_3$. Calculated, %: C 69.89; H 6.84. The characterisics of the synthesized compound are consistent with published data [31].

Ethyl 3-oxo-4-phenoxybutanoate (2b). Yield 7.2 g (79%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.26 t (3H, CH_3, *J* 7.1 Hz), 3.64 s (2H, CH_2), 4.14 q (2H, CH_2O, *J* 7.1 Hz), 4.82 s (2H, OCH_2), 6.74 d (2H$_{arom}$, *J* 8.1 Hz), 6.89 t (1H$_{arom}$, *J* 8.6 Hz), 7.12 t (2H$_{arom}$, *J* 8.1 Hz). Mass spectrum (CI), *m/z*: 223 $[M + H]^+$. Found, %: C 64.78; H 6.31. $C_{12}H_{14}O_4$. Cal-

culated, %: C 64.85; H 6.35. The characterisics of the synthesized compound are consistent with published data [32].

Mehtyl 5-(1,3-dioxoisoindolin-2-yl)-3-oxopentanoate (2c). Yield 8.90 g (79%), mp 105–106°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.96 t (2H, CH_2, *J* 7.1 Hz), 3.57 s (2H, CH_2), 3.65 s (3H, CH_3O), 3.81 t (2H, CH_2, *J* 7.1 Hz), 7.75–7.90 m ($4H_{arom}$). Mass spectrum (CI), *m/z*: 276 $[M + H]^+$. Found, %: C 61.24; H 4.58; N 5.23. $C_{14}H_{13}NO_5$. Calculated, %: C 61.09; H 4.76; N 5.09.

Ethyl 3-(benzo[*d*][1,3]dioxol-5-yl)-3-oxopropanoate (2d) was prepared by the condensation of 1-(benzo-[*d*][1,3]dioxol-5-yl)ethanone with diethyl carbonate by the general procedure of the synthesis of ethyl 3-aryl-3-oxopropanoates [33].

Synthesis of azides 3a–3e (*general procedure*). A solution of 6.5 g of NaN_3 in 15 mL of water was added to a solution of 0.1 mol of the corresponding chloroacetamide in 50 mL of methanol, and the mixture was refluxed for 3–4 h. The solvent was evaporated in a vacuum, and the resulting alkylazide was extracted with dichloromethane. The solvent was evaporated with caution to obtain the target product.

2-Azidoacetamide (3a). Yield 9.6 g (96%), mp 52–53°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.69 s (2H, CH_2), 7.13 s (1H, NH_2), 7.39 s (1H, NH_2). Mass spectrum (CI), *m/z*: 101 $[M + H]^+$. Found, %: C 23.92; H 4.11; N 55.99. $C_2H_4N_4O$. Calculated, %: C 24.00; H 4.03; N 55.98. The characterisics of the synthesized compound are consistent with published data [34].

2-Azido-*N*-methylacetamide (3b). Yield 10.7 g (94%), mp 43–44°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.66 d (3H, CH_3, *J* 4.6 Hz), 3.70 s (2H, CH_2), 7.91 br.s (1H, NH). Mass spectrum (CI), *m/z*: 115 $[M + H]^+$. Found, %: C 31.53; H 5.37; N 49.21. $C_3H_6N_4O$. Calculated, %: C 31.58; H 5.30; N 49.10. The characterisics of the synthesized compound are consistent with published data [35].

2-Azidopropanamide (3c). Yield 9.5 g (83%), mp 75–77°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.36 d (3H, CH_3, *J* 6.8 Hz), 3.73 q (1H, C*H*, *J* 6.8 Hz), 7.13 s (1H, NH_2), 7.41 s (1H, NH_2). Mass spectrum (CI), *m/z*: 115 $[M + H]^+$. Found, %: C 31.70; H 5.37; N 49.21. $C_3H_6N_4O$. Calculated, %: C 31.58; H 5.30; N 49.10. The characterisics of the synthesized compound are consistent with published data [36].

2-Azido-2-methylpropanamide (3d). Yield 10.0 g (78%), mp 93–94°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.40 s (6H, CH_3), 7.14 s (1H, NH_2), 7.20 s (1H, NH_2). Mass spectrum (CI), *m/z*: 129 $[M + H]^+$. Found, %: C 37.43; H 6.34; N 43.78. $C_4H_8N_4O$. Calculated, %: C 37.49; H 6.29; N 43.73. The characterisics of the synthesized compound are consistent with published data [37].

2-Azidobutanamide (3e). Yield 10.4 g (81 %), mp 38–39°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.95 t (3H, CH_3, *J* 7.4 Hz), 1.61–1.85 m (2H, CH_2), 3.56 t (1H, CH, *J* 6.8 Hz), 7.12 s (1H, NH_2), 7.42 s (1H, NH_2). Mass spectrum (CI), *m/z*: 129 $[M + H]^+$. Found, %: C 37.45; H 6.21; N 43.77. $C_4H_8N_4O$. Calculated, %: C 37.49; H 6.29; N 43.73. The characterisics of the synthesized compound are consistent with published data [37].

Synthesis of 1*H*-1,2,3-triazole-4-carboxylates 4a–4i, 11a, and 11b (*general procedure*). Keto ester **2** or acetylacetone (10 mmol) was dissolved in 9 mL of DMSO, after which 9 g of K_2CO_3 and 10 mmol of azide **3** were added. The mixture was allowed to stand for 12 h at room temperature and then heated for 7 h at 50°C. After cooling, 50 mL of water (in the case of compound **4e**, the reaction mixture was acidified with HCl to pH 2.0) was added, and the precipitate that formed was filtered off and recrystallized, when necessary.

Methyl 1-(2-amino-2-oxoethyl)-5-(2-phenylethyl)-1*H*-1,2,3-triazole-4-carboxylate (4a). Yield 2.25 g (78%), mp 148–149°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.86 t (2H, CH_2, *J* 8.3 Hz), 3.12 t (2H, CH_2, *J* 8.3 Hz), 3.88 s (3H, CH_3O), 4.94 s (2H, CH_2), 7.15–7.33 m ($5H_{arom}$), 7.38 s (1H, NH_2), 7.77 s (1H, NH_2). Mass spectrum (CI), *m/z*: 289 $[M + H]^+$. Found, %: C 58.42; H 5.51; N 19.37. $C_{14}H_{16}N_4O_3$. Calculated, %: C 58.32; H 5.59; N 19.43.

Methyl 1-[2-(methylamino)-2-oxoethyl]-5-(2-phenylethyl)-1*H*-1,2,3-triazole-4-carboxylate (4b). Yield 2.23 g (74%), mp 166–167°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.70 d (3H, CH_3NH, *J* 3.3 Hz), 2.85 t (2H, CH_2, *J* 7.3 Hz), 3.15 t (2H, CH_2, *J* 7.3 Hz), 3.86 s (3H, CH_3O), 4.91 s (2H, CH_2), 7.14–7.32 m ($5H_{arom}$), 8.24 br.s (1H, N*H*). Mass spectrum (CI), *m/z*: 303 $[M + H]^+$. Found, %: C 59.56; H 5.89; N 18.61. $C_{15}H_{18}N_4O_3$. Calculated, %: C 59.59; H 6.00; N 18.53.

Methyl 1-(2-amino-2-oxoethyl)-5-(phenoxymethyl)-1*H*-1,2,3-triazole-4-carboxylate (4c). Yield 2.20 g (76%), mp 161–162°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.91 s (3H, CH_3O), 5.20 s (2H, CH_2), 5.47 s (2H, CH_2), 6.95–7.06 m (3H$_{arom}$), 7.29 t (2H, $H^{3,5}_{arom}$, *J* 7.8 Hz), 7.36 s (1H, NH_2), 7.73 s (1H, NH_2). Mass spectrum (CI), *m/z*: 291 $[M+H]^+$. Found, %: C 53.65; H 4.93; N 19.37. $C_{13}H_{14}N_4O_4$. Calculated, %: C 53.79; H 4.86; N 19.30.

Methyl 1-(2-(methylamino)-2-oxoethyl)-5-(phenoxymethyl)-1*H*-1,2,3-triazole-4-carboxylate (4d). Yield 2.25 g (74%), mp 139–141°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.64 d (3H, CH_3N, *J* 3.3 Hz), 3.90 s (3H, CH_3O), 5.18 s (2H, CH_2), 5.47 s (2H, CH_2), 6.92–7.02 m (3H$_{arom}$), 7.28 t (2H, $H^{3,5}_{arom}$, *J* 7.7 Hz), 8.18 br.s (1H, NH). Mass spectrum (CI), *m/z*: 305 $[M+H]^+$. Found, %: C 55.38; H 5.37; N 18.44. $C_{14}H_{16}N_4O_4$. Calculated, %: C 55.26; H 5.30; N 18.41.

2-{2-[1-(2-Amino-2-oxoethyl)-4-(methoxycarbonyl)-1*H*-1,2,3-triazol-5-yl]ethylcarbamoyl}benzoic acid (4e). Yield 2.66 g (71%), mp 208–209°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.27 t (2H, CH_2, *J* 6.7 Hz), 3.67 s (3H, CH_3O), 3.83–3.95 m (2H, CH_2N), 5.13 s (2H, CH_2), 7.37 s (1H, NH), 7.74–7.91 m (6H, H_{arom} + NH_2). Mass spectrum (CI), *m/z*: 376 $[M+H]^+$. Found, %: C 51.27; H 4.51; N 18.72. $C_{16}H_{17}N_5O_6$. Calculated, %: C 51.20; H 4.57; N 18.66.

Ethyl 1-(2-amino-2-oxoethyl)-5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate (4f). Yield 2.57 g (81%), mp 198–199°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.25 t (3H, CH_3, *J* 7.0 Hz), 4.21 q (2H, CH_2O, *J* 7.0 Hz), 4.85 s (2H, CH_2), 6.09 s (2H, OCH_2O), 6.90–7.01 m (3H$_{arom}$), 7.31 s (1H, NH_2), 7.64 s (1H, NH_2). Mass spectrum (CI), *m/z*: 319 $[M+H]^+$. Found, %: C 52.70; H 4.41; N 17.71. $C_{14}H_{14}N_4O_5$. Calculated, %: C 52.83; H 4.43; N 17.60.

Ethyl 1-(1-amino-1-oxopropan-2-yl)-5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate (4g). Yield 2.54 g (77%), mp 124–125°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.22 t (3H, CH_3, *J* 6.8 Hz), 1.77 d (2H, CH_3, *J* 7.0 Hz), 4.19 q (2H, CH_2O, *J* 6.8 Hz), 4.86 q (1H, CH, *J* 7.0 Hz), 6.09 s (2H, OCH_2O), 6.84 d (1H, H^6_{arom}, *J* 7.6 Hz), 6.89 s (1H, H^2_{arom}), 6.95 d (1H, H^5_{arom}, *J* 7.6 Hz), 7.24 s (1H, NH_2), 7.34 s (1H, NH_2). Mass spectrum (CI), *m/z*: 333 $[M+H]^+$. Found, %: C 54.25; H 4.89; N 16.74. $C_{15}H_{16}N_4O_5$. Calculated, %: C 54.21; H 4.85; N 16.86.

Ethyl 1-(1-amino-2-methyl-1-oxopropan-2-yl)-5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (4h). Yield 2.42 g (70%), mp 202–203°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.15 t (3H, CH_3, *J* 7.1 Hz), 1.67 s (6H, CH_3), 4.12 q (2H, CH_2O, *J* 7.1 Hz), 6.07 s (2H, OCH_2O), 6.77 d (1H, H^6_{arom}, *J* 8.0 Hz), 6.80 s (1H, H^2_{arom}), 6.87 d (1H, H^5_{arom}, *J* 8.0 Hz), 7.21 s (1H, NH_2), 7.26 s (1H, NH_2). Mass spectrum (CI), *m/z*: 347 $[M+H]^+$. Found, %: C 55.31; H 5.28; N 16.05. $C_{16}H_{18}N_4O_5$. Calculated, %: C 55.49; H 5.24; N 16.18.

Ethyl 1-(1-amino-1-oxobutan-2-yl)-5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate (4i). Yield 2.60 g (75%), mp 109–111°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.78 t (3H, CH_3, *J* 7.2 Hz). 1.24 t (3H, CH_3, *J* 7.1 Hz), 2.17–2.38 m (2H, CH_2), 4.20 d (2H, CH_2O, *J* 7.1 Hz), 4.61 d.d (1H, CH, *J* 10.3, 4.7 Hz), 6.10 s (1H, OCH_2O), 6.11 s (1H, OCH_2O), 6.82 d (1H, H^6_{arom}, *J* 8.0 Hz), 6.86 s (1H, H^2_{arom}), 6.97 d (1H, H^5_{arom}, *J* 7.9 Hz), 7.30 s (1H, NH_2), 7.33 s (1H, NH_2). Mass spectrum (CI), *m/z*: 347 $[M+H]^+$. Found, %: C 55.54; H 5.18; N 16.24. $C_{16}H_{18}N_4O_5$. Calculated, %: C 55.49; H 5.24; N 16.18.

2-(4-Acetyl-5-methyl 1*H*-1,2,3-triazol-1-yl)propanamide (11a). Yield 1.60 g (81%), mp 174–175°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.78 d (3H, CH_3CH, *J* 6.8 Hz), 2.44 s (3H, CH_3), 2.56 s (3H, CH_3), 5.21 q (1H, CH, *J* 6.8 Hz), 7.45 s (1H, NH_2), 7.68 s (1H, NH_2). Mass spectrum (CI), *m/z*: 197 $[M+H]^+$. Found, %: C 48.90; H 6.23; N 28.51. $C_8H_{12}N_4O_2$. Calculated, %: C 48.97; H 6.16; N 28.56.

2-(4-Acetyl-5-methyl 1*H*-1,2,3-triazol-1-yl)-2-methylpropanamide (11b). Yield 1.77 g (84%), mp 168–169°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.80 s (6H, CH_3), 2.44 s (3H, CH_3), 2.57 s (3H, CH_3), 7.53 s (1H, NH_2), 7.56 s (1H, NH_2). Mass spectrum (CI), *m/z*: 211 $[M+H]^+$. Found, %: C 51.35; H 6.77; N 26.73. $C_9H_{14}N_4O_2$. Calculated, %: C 51.42; H 6.71; N 26.65.

2-[4-(Hydroxymethyl)-5-(2-phenylethyl)-1*H*-1,2,3-triazol-1-yl]-*N*-methylacetamide (5). Lithim aluminum hydride (0.14 g, 3.3 mmol) was added in portions to a solution of 1.0 g (3.3 mmol) of ester **4b** in 50 mL of THF at 0°C, and the mixture was left to stand overnight, after which 0.14 mL of water, 0.28 mL of 10% NaOH, and 0.28 mL of water were added in succession with cooling. The mixture was stirred at room temperature for 15 min, filtered through a thin bed of silica gel, and THF was

evaporated in a vacuum to obtain a pure alcohol **5**. Yield 0.88 g (97%), mp 105–107°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.69 d (3H, CH_3, *J* 4.1 Hz), 2.81–2.90 m (2H, CH_2), 2.90–3.00 m (2H, CH_2), 4.36 d (2H, CH_2O, *J* 5.1 Hz), 4.78 s (2H, CH_2), 4.85 t (1H, OH, *J* 5.1 Hz), 7.13–7.20 m (3H_{arom}), 7.23 t (2H, $H^{3,5}_{arom}$, *J* 6.9 Hz), 8.13 s (1H, NH). Mass spectrum (CI), *m/z*: 275 [*M* + H]$^+$. Found, %: C 61.39; H 6.72; N 20.47. $C_{14}H_{18}N_4O_2$. Calculated, %: C 61.30; H 6.61; N 20.42.

Synthesis of 1*H*-1,2,3-triazole-4-carboxylic acids 6a–6h, 14a, and 14b (*general procedure*). A solution of 80 mg (2 mmol) of NaOH in 1 mL of water was added to a solution of 2 mmol of 1,2,3-triazole-4-carboxylic acid ester **4** or **13** in 15 mL of methanol, and the mixture was left to stand for 12 h. methanol was then evaporated in a vacuum, the residue was dissolved in 2 mL of water, treated with dichloromethane, the aqueous layer was acidified with HCl, and the precipitate that formed was filtered off.

1-(2-Amino-2-oxoethyl)-5-(2-phenylethyl)-1*H*-1,2,3-triazole-4-carboxylic acid (6a). Yield 0.53 g (96%), mp 192–193°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.89 t (2H, CH_2, *J* 8.4 Hz), 3.13 t (2H, CH_2, *J* 8.4 Hz), 4.88 s (2H, CH_2), 7.17–7.23 m (3H_{arom}), 7.27 t (2H, $H^{3,5}_{arom}$, *J* 7.3 Hz), 7.36 s (1H, NH_2), 7.72 s (1H, NH_2). Mass spectrum (CI), *m/z*: 275 [*M* + H]$^+$. Found, %: C 56.78; H 5.24; N 20.46. $C_{13}H_{14}N_4O_3$. Calculated, %: C 56.93; H 5.14; N 20.43.

1-[2-(Methylamino)-2-oxoethyl]-5-(2-phenylethyl)-1*H*-1,2,3-triazole-4-carboxylic acid (6b). Yield 0.54 g (95%), mp 199–200°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.69 d (3H, CH_3, *J* 4.5 Hz), 2.85 t (2H, CH_2, *J* 6.8 Hz), 3.13 t (2H, CH_2, *J* 6.8 Hz), 4.84 s (2H, CH_2), 7.14–7.22 m (3H_{arom}), 7.25 t (2H, $H^{3,5}_{arom}$, *J* 7.3 Hz), 8.20 s (1H, NH). Mass spectrum (CI), *m/z*: 289 [*M* + H]$^+$. Found, %: C 58.41; H 5.52; N 19.48. $C_{14}H_{16}N_4O_3$. Calculated, %: C 58.32; H 5.59; N 19.43.

1-(2-Amino-2-oxoethyl)-5-(phenoxymethyl)-1*H*-1,2,3-triazole-4-carboxylic acid (6c). Yield 0.52 g (95%), mp 196–197°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.17 s (2H, CH_2). 5.49 s (2H, CH_2), 6.96 t (1H, H^4_{arom}, *J* 7.4 Hz), 7.01 d (2H, $H^{2,6}_{arom}$, *J* 8.0 Hz), 7.28 t (2H, $H^{3,5}_{arom}$, *J* 7.9 Hz), 7.32 s (1H, NH_2), 7.68 s (1H, NH_2). Mass spectrum (CI), *m/z*: 277 [*M* + H]$^+$. Found, %: C 52.11; H 4.45; N 20.12. $C_{12}H_{12}N_4O_4$. Calculated, %: C 52.17; H 4.38; N 20.28.

1-[2-(Methylamino)-2-oxoethyl]-5-(phenoxymethyl)-1*H*-1,2,3-triazole-4-carboxylic acid (6d). Yield 0.54 g (93%), mp 195–196°C (decomp.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.63 d (3H, CH_3, *J* 4.3 Hz), 5.15 s (2H, CH_2), 5.48 s (2H, CH_2), 6.90–7.09 m (3H_{arom}), 7.26 t (2H, $H^{3,5}_{arom}$, *J* 7.7 Hz), 8.16 br.s (1H, NH). Mass spectrum (CI), *m/z*: 291 [*M* + H]$^+$. Found, %: C 53.85; H 4.94; N 19.23. $C_{13}H_{14}N_4O_4$. Calculated, %: C 53.79; H 4.86; N 19.30.

1-(2-Amino-2-oxoethyl)-5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (6e). Yield 0.56 g (97%), mp 215–217°C (decomp.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.82 s (2H, CH_2), 6.08 s (2H, OCH_2O), 6.89–7.00 m (3H_{arom}), 7.28 s (1H, NH_2), 7.60 s (1H, NH_2), 12.59 br.s (1H, COOH). Mass spectrum (CI), *m/z*: 291 [*M* + H]$^+$. Found, %: C 49.73; H 3.53; N 19.43. $C_{12}H_{10}N_4O_5$. Calculated, %: C 49.66; H 3.47; N 19.30.

1-(1-Amino-1-oxopropan-2-yl)-5-(benzo[*d*][1,3]-dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (6f). Yield 0.58 g (96%), mp 214–215°C (decomp.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.76 d (3H, CH_3, *J* 7.1 Hz), 4.82 q (1H, CH, *J* 7.3 Hz), 6.09 s (1H, OCH_2O), 6.10 s (1H, OCH_2O), 6.84 d (1H, H^6_{arom}, *J* 8.0 Hz), 6.89 s (1H, H^2_{arom}), 6.95 d (1H, H^5_{arom}, *J* 7.9 Hz), 7.23 s (1H, NH_2), 7.31 s (1H, NH_2), 12.65 br.s (1H, COO*H*). Mass spectrum (CI), *m/z*: 305 [*M* + H]$^+$. Found, %: C 51.42; H 3.91; N 18.28. $C_{13}H_{12}N_4O_5$. Calculated, %: C 51.32; H 3.98; N 18.41.

1-(1-Amino-2-methyl-1-oxopropan-2-yl)-5-(benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (6g). Yield 0.60 g (95%), mp 203–204°C (decomp.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.66 s (6H, CH_3), 6.08 s (2H, OCH_2O), 6.78 d (1H, H^6_{arom}, *J* 8.0 Hz), 6.80 s (1H, H^2_{arom}), 6.87 d (1H, H^5_{arom}, *J* 7.9 Hz), 7.18 s (1H, NH_2), 7.24 s (1H, NH_2), 12.45 br.s (1H, COOH). Mass spectrum (CI), *m/z*: 319 [*M* + H]$^+$. Found, %: C 52.71; H 4.49; N 17.71. $C_{14}H_{14}N_4O_5$. Calculated, %: C 52.83; H 4.43; N 17.60.

1-(1-Amino-1-oxobutan-2-yl)-5-(benzo[*d*][1,3]-dioxol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (6h). Yield 0.62 g (96%), mp 131–132°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.76 d (3H, CH_3, *J* 8.0 Hz), 2.17–2.35 m (1H, CH_2), 4.52–4.63 m (1H, CH), 6.11 s (2H, OCH_2O), 6.80 d (1H, H^6_{arom}, *J* 7.2 Hz), 6.85 s (1H, H^2_{arom}), 6.96 d (1H, H^5_{arom}, *J* 7.8 Hz), 7.29 s (2H, NH_2), 12.68 br.s (1H, COOH). Mass spectrum (CI),

m/z: 319 $[M + H]^+$. Found, %: C 52.76; H 4.35; N 17.55. $C_{14}H_{14}N_4O_5$. Calculated, %: C 52.83; H 4.43; N 17.60.

1-(2-Amino-2-oxoethyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid (14a). Yield 0.33 g (91%), mp 210°C (decomp.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.43 s (3H, CH_3). 4.99 s (2H, CH_2), 7.30 s (1H, NH_2), 7.68 s (1H, NH_2). Mass spectrum (CI), *m/z*: 185 $[M + H]^+$. Found, %: C 39.21; H 4.33; N 30.51. $C_6H_8N_4O_3$. Calculated, %: C 39.13; H 4.38; N 30.42.

1-[2-(2,4,6-Trimethylphenylamino)-2-oxoethyl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid (14b). Yield 0.58 g (97%), mp 236–237°C. IR spectrum, ν, cm^{-1}: 3262 (NH), 2919, 2676, 2593, 1685 (COOH), 1669 (NHCO), 1580, 1537, 1485, 1455, 1307, 1265, 1243, 1207, 1105, 968, 939, 846, 789, 779, 709. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.12 s (6H, 2,6-Me_2), 2.22 s (3H, 4-Me), 2.67 s (3H, $Me_{triazol}$), 5.38 s (2H, CH_2), 6.89 s (2H_{arom}), 9.74 s (1H, NH). Mass spectrum (CI): *m/z* 303 $[M + H]^+$. Found, %: C 59.43; H 5.89; N 18.62. $C_{15}H_{18}N_4O_3$. Calculated, %: C 59.59; H 6.00; N 18.53.

Decarboxylation of triazolylcarboxylic acids 6e–6h and 14a (*general procedure*). Acid **6** or **14** (2 mmol) was heated at the melting point until gas no longer evolved. After cooling, the target triazole was obtained in quantitative yield.

2-{5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl}acetamide (9a). Yield 0.50 g (100%), mp 205–206°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.92 s (2H, CH_2), 6.05 s (2H, OCH_2O), 6.92 d (1H, H^5_{arom}, *J* 7.9 Hz), 6.97 d (1H, H^6_{arom}, *J* 8.2 Hz), 7.03 s (1H, H^2_{arom}), 7.28 s (1H, NH_2), 7.61 s (1$H_{triazol}$), 7.64 s (1H, NH_2). Mass spectrum (CI), *m/z*: 247 $[M + H]^+$. Found, %: C 53.49; H 4.14; N 22.78. $C_{11}H_{10}N_4O_3$. Calculated, %: C 53.66; H 4.09; N 22.75.

2-{5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl}propanamide (9b). Yield 0.52 g (100%), mp 201–202°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.79 d (3H, CH_3, *J* 7.2 Hz), 5.14 q (1H, CH, *J* 7.2 Hz), 6.08 s (2H, OCH_2O), 6.89 d (1H, H^6_{arom}, *J* 8.0 Hz), 6.93 s (1H, H^2_{arom}), 6.97 d (1H, H^5_{arom} *J* 8.0 Hz), 7.23 s (1H, NH_2), 7.33 s (1H, NH_2), 7.61 s (1$H_{triazol}$). Mass spectrum (CI), *m/z*: 261 $[M + H]^+$. Found, %: C 55.44; H 4.54; N 21.59. $C_{12}H_{12}N_4O_3$. Calculated, %: C 55.38; H 4.65; N 21.53.

2-{5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl}-2-methylpropanamide (9c). Yield 0.54 g (100%), mp 198–199°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.68 s (6H, CH_3), 6.06 s (2H, OCH_2O), 6.81 d (1H, H^6_{arom}, *J* 7.9 Hz), 6.85 s (1H, H^2_{arom}), 6.88 d (1H, H^5_{arom}, *J* 8.0 Hz), 7.10 s (1H, NH_2), 7.26 s (1H, NH_2), 7.48 s (1$H_{triazol}$). Mass spectrum (CI), *m/z*: 275 $[M + H]^+$. Found, %: C 56.99; H 5.05; N 20.51. $C_{13}H_{14}N_4O_3$. Calculated, %: C 56.93; H 5.14; N 20.43.

2-{5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl}butanamide (9d). Yield 0.54 g (100%), mp 114–115°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.74 t (3H, CH_3, *J* 7.2 Hz), 2.19–2.33 m (2H, CH_2), 4.85 d.d (1H, CH, *J* 9.1, 6.2 Hz), 6.11 s (2H, OCH_2O), 6.87 d (1H, H^6_{arom}, *J* 7.7 Hz), 6.89 s (1H, H^2_{arom}), 6.97 d (1H, H^5_{arom}, *J* 7.8 Hz), 7.29 s (1H, NH_2), 7.32 s (1H, NH_2), 7.61 s (1$H_{triazol}$). Mass spectrum (CI), *m/z*: 275 $[M + H]^+$. Found, %: C 56.75; H 5.11; N 20.32. $C_{13}H_{14}N_4O_3$. Calculated, %: C 56.93; H 5.14; N 20.43.

2-(5-Methyl-1*H*-1,2,3-triazol-1-yl)acetamide (15). Yield 0.28 g (100%), mp 132–133°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.25 s (3H, CH_3). 4.93 s (2H, CH_2), 7.21 s (1H, NH_2), 7.36 s (1$H_{triazol}$), 7.58 s (1H, NH_2). Mass spectrum (CI), *m/z*: 141 $[M + H]^+$. Found, %: C 42.73; H 5.79; N 39.91. $C_5H_8N_4O$. Calculated, %: C 42.85; H 5.75; N 39.98.

Synthesis of carboxylic acids 7, 10a–10d, and 16 (*general procedure*). The corresponding ester (1 mmol) was added to a solution of 80 mg (2 mmol) of NaOH in 1 mL of water, the mixture was refluxed for 2 h, acidified with HCl, and the precipitate of the target acid that formed was filtered off.

1-(Carboxymethyl)-5-(phenoxymethyl)-1*H*-1,2,3-triazole-4-carboxylic acid (7). Yield 0.26 g (94%), mp 198–199°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.30 s (2H, CH_2), 5.51 s (2H, CH_2), 6.91–7.01 m (3H_{arom}), 7.27 t (2H, $H^{3,5}_{arom}$, *J* 8.0 Hz). Mass spectrum (CI), *m/z*: 278 $[M + H]^+$. Found, %: C 51.91; H 4.07; N 15.01. $C_{12}H_{11}N_3O_5$. Calculated, %: C 51.99; H 4.00; N 15.16.

2-{5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl}acetic acid (10a). Yield 0.24 g (96%), mp 191–192°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.10 s (2H, CH_2). 6.06 s (2H, OCH_2O), 6.87–7.00 m (3H_{arom}), 7.63 s (1$H_{triazol}$), 13.28 br.s (1H, COOH). Mass spectrum (CI), *m/z*: 248 $[M + H]^+$. Found, %: C 53.51; H 3.78; N 17.04. $C_{11}H_9N_3O_4$. Calculated, %: C 53.44; H 3.67; N 17.00.

2-(5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl)propanoic acid (10b). Yield 0.25 g (97%), mp

208–209°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.79 d (3H, CH_3, *J* 7.2 Hz), 5.14 q (1H, CH, *J* 7.2 Hz), 6.08 s (2H, OCH_2O), 6.89 d (1H, H^6_{arom}, *J* 8.0 Hz), 6.93 s (1H, H^2_{arom}), 6.97 d (1H, H^5_{arom}, *J* 7.9 Hz), 7.61 s ($1H_{triazol}$), 13.23 br.s (1H, COOH). Mass spectrum (CI), *m/z*: 262 $[M + H]^+$. Found, %: C 55.25; H 4.31; N 16.15. $C_{12}H_{11}N_3O_4$. Calculated, %: C 55.17; H 4.24; N 16.09.

2-(5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl)-2-methylpropanoic acid (10c). Yield 0.26 g (96%), mp 221–222°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.73 s (6H, CH_3), 6.08 s (2H, OCH_2O), 6.73–6.80 m ($2H_{arom}$), 6.90 d (1H, H^5_{arom}, *J* 8.4 Hz), 7.49 s ($1H_{triazol}$), 13.33 br.s (1H, COOH). Mass spectrum (CI), *m/z*: 276 $[M + H]^+$. Found, %: C 56.75; H 4.84; N 15.36. $C_{13}H_{13}N_3O_4$. Calculated, %: C 56.72; H 4.76; N 15.27.

2-{5-(Benzo[*d*][1,3]dioxol-5-yl)-1*H*-1,2,3-triazol-1-yl}butanoic acid (10d). Yield 0.26 g (95%), mp 190–191°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.75 t (3H, CH_3, *J* 7.2 Hz), 2.21–2.35 m (2H, CH_2), 4.87 d.d (1H, CH, *J* 9.1, 6.2 Hz), 6.09 s (2H, OCH_2O), 6.87 d (1H, H^6_{arom}, *J* 7.7 Hz), 6.89 s (1H, H^2_{arom}), 6.97 d (1H, H^5_{arom}, *J* 7.8 Hz), 7.62 s ($1H_{triazol}$). Mass spectrum (CI), *m/z*: 276 $[M + H]^+$. Found, %: C 56.59; H 4.72; N 15.19. $C_{13}H_{13}N_3O_4$. Calculated, %: C 56.72; H 4.76; N 15.27.

2-(5-Methyl-1*H*-1,2,3-triazol-1-yl)acetic acid (16). Yield 0.13 g (91%), mp 177–178°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.26 s (3H, CH_3), 5.10 s (2H, CH_2), 7.37 s ($1H_{triazol}$). Mass spectrum (CI), *m/z*: 142 $[M + H]^+$. Found, %: C 42.51; H 5.12; N 29.71. $C_5H_7N_3O_2$. Calculated, %: C 42.55; H 5.00; N 29.77.

Methyl 1-(2-amino-2-oxoethyl)-5-[2-(1,3-dioxoisoindolin-2-yl)ethyl]-1*H*-1,2,3-triazole-4-carboxylate (8). Compound **4e** (1 mmol) was heated in toluene with a catalytic amount of toluenesulfonic acid for 1 h. After cooling, the reaction mixture was washed with saturated $NaHCO_3$ and toluene was evaporated in a vacuum to obtain a pure compound **8**. Yield 0.33 g (92%), mp 188–189°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.27 t (2H, CH_2, *J* 6.3 Hz), 3.67 s (3H, CH_3O), 3.89 t (2H, CH_2, *J* 6.0 Hz), 5.13 s (2H, CH_2), 7.38 s (1H, NH_2), 7.73–7.88 m (5H, H_{arom} + NH). Mass spectrum (CI), *m/z*: 358 $[M + H]^+$. Found, %: C 53.63; H 4.29; N 19.71. $C_{16}H_{15}N_5O_5$. Calculated, %: C 53.78; H 4.23; N 19.60.

Multicomponent synthesis of 1,2,3-triazole-4-carboxylic acid esters 13a–13c (*general procedure*). Sodium azide (1.25 g, 19 mmol) was added to a solution of 16 mmol of the corresponding halo derivative **12** in 10 mL of DMSO. The suspension was stirred at room temperature for 5 h, after which 10 g (70 mmol) K_2CO_3 and 2.05 mL (16 mmol) of acetoacetic ester **2f** were added. The resulting suspension was stirred at 40–50°C for 12 h, cooled to 5°C, and diluted with 50 mL of water. The precipitate that formed was filtered off, washed with water, ad recrystallized from alcohol or aqueous alcohol.

Ethyl 1-(2-amino-2-oxoethyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (13a). Yield 2.51 g (74%), mp 170–171°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.39 t (3H, CH_3CH_2, *J* 7.1 Hz), 2.48 s (3H, CH_3), 4.33 q (2H, CH_2O, *J* 7.0 Hz), 5.05 s (2H, CH_2), 7.34 s (1H, NH_2), 7.73 s (1H, NH_2). Mass spectrum (CI): *m/z* 213 $[M + H]^+$. Found, %: C 45.16; H 5.79; N 26.31. $C_8H_{12}N_4O_3$. Calculated, %: C 45.28; H 5.70; N 26.40.

Ethyl 5-methyl-1-[2-oxo-2-(phenylamino)-ethyl-1*H*-1,2,3-triazole-4-carboxylate (13b). Yield 3.96 g (86 %), mp 150–151°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.33 t (3H, CH_3CH_2, *J* 6.7 Hz), 3.36 s (3H, CH_3), 4.33 q (2H, CH_2, *J* 6.7 Hz), 5.39 s (2H, CH_2), 7.10 t (1H, H^4_{arom}, *J* 6.9 Hz), 7.34 t (2H, $H^{3,5}_{arom}$, *J* 7.2 Hz), 7.58 d (2H, $H^{2,6}_{arom}$, *J* 7.6 Hz), 10.59 s (1H, NH). Mass spectrum (CI): *m/z* 289 $[M + H]^+$. Found, %: C 58.21; H 5.48; N 19.64. $C_{14}H_{16}N_3O_4$. Calculated, %: C 58.32; H 5.59; N 19.43.

Ethyl 1-[2-(2,4,6-trimethylphenylamino)-2-oxoethyl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (13c). Yield 4.33 g (82%), mp 201–202°C. IR spectrum, ν, cm^{-1}: 3270 (NH), 2992, 1706 (COOEt), 1655 (NHCO), 1576, 1537, 1477, 1438, 1373, 1347, 1296, 1246, 1196, 1104, 1088, 967, 851, 787, 726, 694, 654. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.41 t (3H, CH_3, *J* 7.0 Hz), 2.07 s (6H, 2,6-Me_2), 2.22 s (3H, 4-Me), 2.65 s (3H, CH_3), 4.41 q (2H, CH_2, *J* 7.0 Hz), 5.18 s (2H, CH_2), 6.83 s ($2H_{arom}$), 7.45 br.s (1H, NH). Mass spectrum (CI): *m/z* 331 $[M + H]^+$. Found, %: C 61.85; H 6.72; N 17.10. $C_{17}H_{22}N_4O_3$. Calculated, %: C 61.80; H 6.71; N 16.96.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Horne, W.S., Yadav, M.K., Stout, C.D., and Ghadiri, M.R., *J. Am. Chem. Soc*., 2004, vol. 126, p. 15366.

https://doi.org/10.1021/ja0450408

2. Sangshetti, J.N., Nagawade, R.R., and Shinde, D.B., *Bioorg. Med. Chem. Lett*., 2009, vol. 19, p. 3564. https://doi.org/10.1016/j.bmcl.2009.04.134
3. Sangshetti, J.N. and Shinde, D.B., *Bioorg. Med. Chem. Lett*., 2010, vol. 20, p. 742. https://doi.org/10.1016/j.bmcl.2009.11.048
4. Sangshetti, J.N., Chabukswar, A.R., and Shinde, D.B., *Bioorg. Med. Chem. Lett*., 2011, vol. 21, p. 444. https://doi.org/10.1016/j.bmcl.2010.10.120
5. Boechat, N., Ferreira, V.F., Ferreira, S.B., Ferreira, M.D.L.G., da Silva, F.C., Bastos, M.M., Costa, M.S., Lourenço, M.C.S., Pinto, A.C., Krettli, A.U., Aguiar, A.C., Teixeira, B.M., da Silva, N.V., Martins, P.R.C., Bezerra, F.A.F.M., Camilo, A.L.S., da Silva, G.P., and Costa, C.C.P., *J. Med. Chem*., 2011, vol. 54, p. 5988. https://doi.org/10.1021/jm2003624
6. de Lourdes, M., Ferreira, G., Pinheiro, L.C.S., Santos-Filho, O.A., Pecanha, M.D.S., Sacramento, C.Q., Machado, V., Ferreira, V.F., Souza, T.M.L., and Boechat, N., *Med. Chem. Res*., 2014, vol. 23, p. 1501. https://doi.org/10.1007/s00044-013-0762-6
7. Pokhodylo, N.T., Shyyka, O.Ya, Skrobala, V.E., and Matiychuk, V.S., *Clin. Pharmacy, Pharmacother. Med. Standardization*, 2012, vol. 16–17, p. 92 (in ukrainian).
8. Pokhodylo, N., Shyyka, O., and Matiychuk, V., *Sci. Pharm*., 2013, vol. 81, p. 663. https://doi.org/10.3797/scipharm.1302-04
9. Pokhodylo, N.T., Shyyka, O.Ya., and Matiychuk, V.S., *Med. Chem. Res*., 2014, vol. 23, p. 2426. https://doi.org/10.1007/s00044-013-0841-8
10. Pokhodylo, N.T., Shyyka, O.Ya., and Finiuk, N.S., *Biopolym. Cell*., 2019, vol. 35, p. 321. https://doi.org/10.7124/bc.000A0F
11. Sugawara, A., Sunazuka, T., Hirose, T., Nagai, K., Yamaguchi, Y., Hanaki, H., Sharpless, K.B., and Omura, S., *Bioorg. Med. Chem. Lett*., 2007, vol. 17, p. 6340. https://doi.org/10.1016/j.bmcl.2007.08.068
12. Gao, G., Smiesko, M., Schwardt, O., Gaethje, H., Kelm, S., Vedani, A., and Ernst, B., *Bioorg. Med. Chem*. 2007, vol. 15, p. 7459. https://doi.org/10.1016/j.bmc.2007.07.033
13. Wallace, G.A., Breinlinger, E.C., Cusack, K.P., Fix-Stenzel, S.R., Gordon, T.D., Hobson, A.D., Hayes, M.E., Ansell, G.K., and Grongsaard, P., WO Patent Appl. no. WO 2008079382; *Chem. Abstr*., 2008, vol. 149, no. 128619.
14. Fortin, R., Lachance, N., Li Chun, S., and Tranmer, G., WO Patent Appl. no. WO 2011047481; *Chem. Abstr*., 2011, vol. 154, no. 513424.
15. Lolk, L., Jepsen, A.S., Nielsen, H., Steffansen, S.I., Sparving, L., Nielsen, A.B., Nielsen, P., Pohlsgaard, J., Hansen, L.H., and Vester, B., *J. Med. Chem*., 2008, vol. 51, p. 4957. https://doi.org/10.1021/jm800261u
16. Corrales, R.C.N.R., de Souza, N.B., Pinheiro, L.S., Abramo, C., Coimbra, E.S., and da Silva, A.D., *Biomed. Pharmacother*., 2011, vol. 65, p. 198. https://doi.org/10.1016/j.biopha.2010.10.013
17. Sun, L., Huang, T., Dick, A., Meuser, M.E., Zalloum, W.A., Chen, C.H., Ding, X., Gao, P., Cocklin, S., Lee, K.-H., Zhan, P., and Liu, X., *Eur. J. Med. Chem*., 2020, vol. 190, p. 112085. https://doi.org/10.1016/j.ejmech.2020.112085
18. Pokhodylo, N.T., Matiichuk, V.S., and Obushak, M.D., *Russ. J. Org. Chem*., 2017, vol. 53, p. 481. https://doi.org/10.1134/S1070428017030332
19. Pokhodylo, N.T., Savka, R.D., and Obushak, M.D., *Russ. J. Org. Chem*., 2017, vol. 53, p. 734. https://doi.org/10.1134/S1070428017050141
20. Pokhodylo, N.T., Shyyka, O.Ya., Goreshnik, E.A., and Obushak, M.D., *ChemistrySelect*, 2020, vol. 5, p. 260. https://doi.org/10.1002/slct.201904688
21. Pokhodylo, N.T., Shyyka, O.Ya., Matiychuk, V.S., Obushak, M.D., and Pavlyuk, V.V., *ChemistrySelect*, 2017, vol. 2, p. 5871. https://doi.org/10.1002/slct.201700577
22. Pokhodylo, N.T., Shyyka, O.Ya., and Obushak, M.D., *Chem. Heterocycl. Compd*., 2018, vol. 54, p. 773. https://doi.org/10.1007/s10593-018-2348-1
23. Pokhodylo, N.T. and Obushak, M.D., *Russ. J. Org. Chem*., 2019, vol. 55, p. 1241. https://doi.org/10.1134/S107042801908027X
24. Pokhodylo, N.T., Shyyka, O.Y., Savka, R.D., and Obushak, M.D., *Russ. J. Org. Chem*., 2018, vol. 54, p. 1090. https://doi.org/10.1134/S1070428018070205
25. Arshad, M., Bhat, A.R., Pokharel, S., Kim, J.-E., Lee, E.J., Athar, F., and Choi, I., *Eur. J. Med. Chem*., 2014, vol. 71, p. 229. https://doi.org/10.1016/j.ejmech.2013.11.008
26. Tam, A., Arnold, U., Soellner, M.B., and Raines, R.T., *J. Am. Chem. Soc*., 2007, vol. 129, p. 12670. https://doi.org/10.1021/ja075865s
27. Boteju, L.W., Zalewska, T., Yamamura, H.I., and Hruby, V.J., *Bioorg. Med. Chem. Lett*., 1993, vol. 3,

p. 2011.
https://doi.org/10.1016/S0960-894X(01)81005-2

28. Stanley, N.J., Abell, A.D., Pedersen, D.S., Nielsen, B., Kvist, T., Mathiesen, J.M., Braeuner-Osborne, H., and Taylor, D.K., *Bioorg. Med. Chem. Lett*., 2010, vol. 20, p. 7512.
https://doi.org/10.1016/j.bmcl.2010.09.139
29. Johansson, J.R., Lincoln, P., Norden, B., and Kann, N., *J. Org. Chem*., 2011, vol. 76, p. 2355.
https://doi.org/10.1021/jo200134a
30. Pokhodylo, N.T. Savka, R.D., Matiichuk, V.S., and Obushak, N.D., *Russ J. Gen. Chem*., 2009, vol. 79, p. 309.
https://doi.org/10.1134/S1070363209020248
31. Huckin, S.N. and Weiler, L., *J. Am. Chem. Soc*., 1974, vol. 96, p. 1082.
https://doi.org/10.1021/ja00811a023
32. Deshayes, C., Chabannet, M., and Gelin, S., *J. Heterocycl. Chem*., 1986, vol. 23, p. 1595.
https://doi.org/10.1002/jhet.5570230567
33. Kumar, S., Namkung, W., Verkman, A.S., and Sharma, P.K., *Bioorg. Med. Chem*., 2012, vol. 20, p. 4237.
https://doi.org/10.1016/j.bmc.2012.05.074
34. Fabre, B., Pícha, J., Vaněk, V., Selicharová, I., Chrudinová, M., Collinsová, M., Žáková, L., Buděšínský, M., and Jiráček, J., *ACS Comb. Sci*., 2016, vol. 18, p. 710.
https://doi.org/10.1021/acscombsci.6b00132
35. Froyen, P., *Phosphorus Sulfur Silicon Relat. Elem*., 1991, vol. 63, p. 283.
https://doi.org/10.1080/10426509108036831
36. Forster, M.O. and Fierz, H.E., *J. Chem. Soc., Trans*., 1908, vol. 93, p. 1859.
https://doi.org/10.1039/CT9089301859
37. Forster, M.O. and Müller, R., *J. Chem. Soc., Trans*., 1909, vol. 95, p. 191.
https://doi.org/10.1039/CT9099500191