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A Convenient One-Pot Synthesis of 1,5-Disubstituted Tetrazoles Containing an Amino or a Carboxy Group

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Abstract—A convenient method is proposed for constructing the tetrazole ring by a one-pot reaction of amides with phosphorus oxychloride and sodium azide. A series of 1,5-disubstituted tetrazoles containing an amino or a carboxy group, which present interest as buildings blocks for the synthesis of biologically active substances, were obtained.

Keywords: tetrazole, imidoyl chlorides, amides, phthalimides, sodium azide, one-pot synthesis

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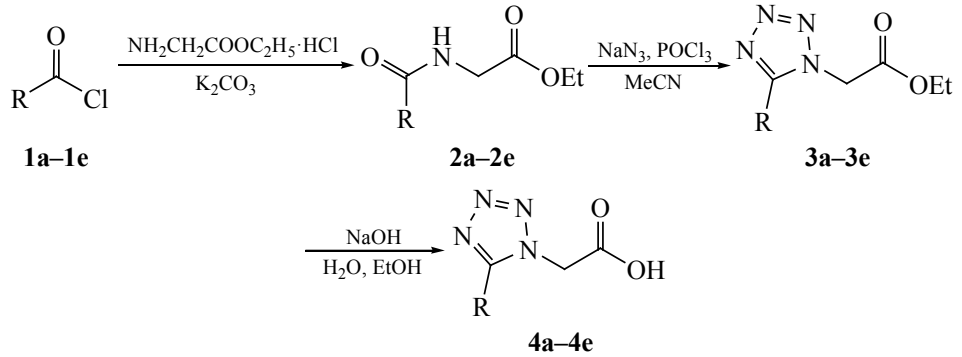
The bioisosterism of the tetrazole ring and the carboxy or amido groups makes tetrazole derivatives attractive for medicinal chemistry applications. The replacement of the *cis*-amide bond by a 1,5-disubstituted tetrazole increases the metabolic stability of the molecule but does not reduce its pharmacological activity. At present, compounds containing a 1,5-disubstituted tetrazole fragment are used as drugs [1]. For example, 5-[β-(10-phenothiazinyl)ethyl]-1-acyltetrazoles showed high analgetic and anti-inflammatory activities [1]. The synthetic analogs of *N*-acyl homoserine lactone (AHL), where the amide bond is substituted by a tetrazole ring, were tested as LuxR-dependent QS (Quorum Sensing) modulators [2]. Some tetrazole derivatives act as antimycotic agents [1]. A series of tetrazolebiarylpyrazoles were tested as inhibitors of binding of the CB1 and CB2 cannabinoid receptors, which provides evidence for the hypothesis that the amide group in the antiobesity drug rimonabant [3] can be replaced by its bioisosteric tetrazole moiety. Tetrazole derivatives were tested as inhibitors of cellular anandamide (endocannabinoid) uptake [1], cyclooxygenase (COX) inhibitors [4], and hard combretastatin analogs with significant antiproliferative and antitumor effects [5, 6].

Of special mentioning are extensive studies on the biological activity of isomeric 1*H*-tetrazolylacetic acids. Such compounds act as thymidylate synthase inhibitors and potential antitumor compounds, HIV protease inhibitors, selective stearoyl coenzyme A delta-9 desaturase (SCD1) inhibitors for the prevention and treatment of diseases associated with disorders in fat synthesis and metabolism, including atherosclerosis [1]. Derivatives of such acids as acetylhydrazones derived from tetrazole act on ER +/– breast cancer cell lines [7].

Along with 1*H*-tetrazolylacetic acids, considerable researcher's interest has been focused on compounds containing a (1*H*-tetrazol-5-yl)methylamine moiety. One of the first studies this class of compounds assessed structure–activity correlations for tetrazole-containing retroamides. Later such compounds were studied as CCR3 β-chemokine receptor antagonists for treatment of inflammatory disorders and Alzheimer's disease and for prevention and treatment of type II diabetes mellitus [1], as well as inhibitors of type 4 and 5 phosphodiesterase and MDM2-p53 interactions [8]. These compounds were also tested for antibacterial [9–11] and antiprotozoal activity [12].

Compounds with a (1-methyl-1*H*-tetrazol-5-yl)methanamine moiety, too, exhibit biological activity. They are used as tachykinin antagonists, cholesterol ester transporter protein inhibitors (CETP), and progesterone receptor (PR) ligands for the treatment and prevention of inflammatory, demyelinating diseases and tumor metastases, HIV infection, cerebral insufficiency, including increased receptor function in synapses in brain networks, orexin 2 receptor dysfunction, as well as diseases associated with

Scheme 1.



R = $PhCH_2CH_2$ (**a**), *trans*-PhCH=CH (**b**), $PhOCH_2$ (**c**), 2-$ClC_6H_4OCH_2$ (**d**), 4-$ClC_6H_4OCH_2$ (**e**).

lipoprotein metabolism, monoamine neurotransmitter reuptake, and purinergic receptor P2X7 inhibitors [1].

Tetrazole derivatives are also of interest as chelating agents for metals [13–15] and candidates for the design of functional materials, in particular, those with nonlinear optical properties [16, 17].

Thus, the development of convenient methods of synthesis of tetrazole derivatives is a relevant task. There are a few main synthetic approaches to 1,5-disubstituted tetrazoles: 1,3-dipolar cycloaddition of azides to nitriles; synthesis of imidoyl chlorides and imidoyl azides from amides and thioamides followed by the reaction of the products with azide anion; reactions of trimethylsilyl azide with ketones in the presence of a Lewis acid, involving the Schmidt rearrangement; reactions of 1-substituted tetrazoles; and synthesis from heterocumulenes (isocyanates, isothiocyanates, carbodiimides). These approaches have been described in detail in the literature, in particular, in a recent review [18].

It should be noted that the conversion of readily available amides to the corresponding imidoyl chlorides and subsequent reaction of the latter with sodium azide remains one of the most convenient approaches to constructing the tetrazole ring, which involves no by-product formation, unlike some of the other methods mentioned above. Thus, the alkylation of 5-substituted tetrazoles forms a mixture of products [19, 20], and only a few examples of the introduction of substituents to position 5 of the tetrazole ring, on account of the instability of the latter in basic media [21–23].

Amides or thioamides are converted to imidoyl chlorides by means of PCl_5, PCl_3, $POCl_3$, $SOCl_2$, and oxalyl chloride. With amides, a two-stage scheme is often used: treatment of amides with PCl_5 or PCl_3 followed by heating of imidoyl chloride with HN_3 [24, 25]. Phosgene and tetramethylguanidinium azide [26] ammonium cerium(IV) nitrate, trimethylsilyl azide, triphenylphosphine, and diethyl azodicarboxylate are also used [27]. The most common reagents for transforming the thioamide bond into a tetrazole ring include trimethylsilyl azide, diisopropyl azodicarboxylate, and triphenylphosphine in THF [28], as well as hydrogen azide [29].

In the present work we developed a facile and convenient one-pot synthesis of 1,5-disubstituted tetrazoles containing an amino or a carboxy group, based on the conversion of the amide under the action of $POCl_3$ into imidoyl chloride and its in situ reaction with sodium azide.

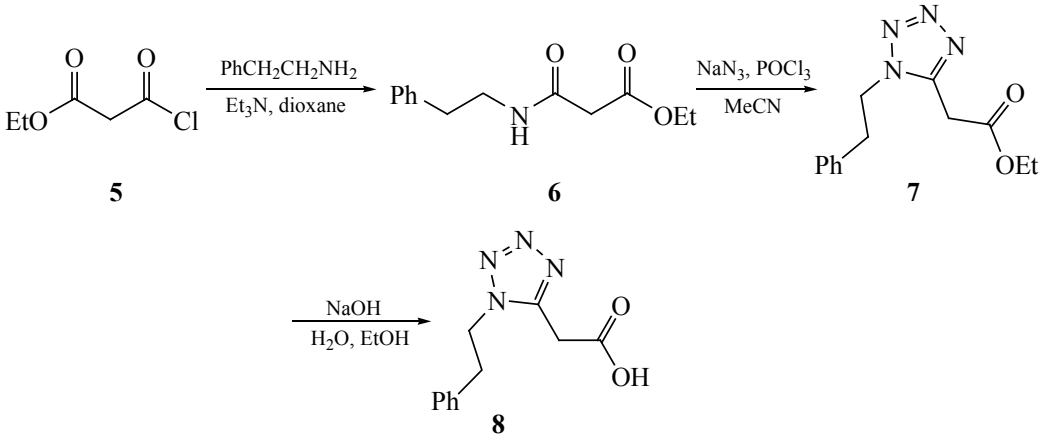
Starting from commercially available acids, we prepared chlorides **1** and used them to acylate ethyl glycinate hydrochloride to prepare amides **2**. The latter were almost quantitatively converted into tetrazoles **3** in the $POCl_3/NaN_3$ system (Scheme 1). Hydrolysis of esters **3** gave acids **4**.

Tetrazole derivatives **7** and **8** were prepared in a similar way starting from chloride **5** via amide **6** (Scheme 2).

Note that, alternatively 1*H*-tetrazol-5-ylacetic acids can be prepared by the lithiation of 5-methyltetrazoles followed by carbonylation [30].

To prepare 5-tetrazolylmethylamines, we used accessible acids containing a phthalimide fragment. By treatment with $SOCl_2$ the acids were converted into chlorides **9a** and **9b**, which were reacted with amines **10a–10c** to obtain amides **11a–11e** (Scheme 3). Amides **11** were reacted with $POCl_3$ and sodium azide in acetonitrile to find that they, like compounds **2**, form a tetrazole

Scheme 2.



ring in these conditions; therewith, compounds **12** were obtained in nearly quantitative yields. The cleavage of the phthalimide fragment with hydrazine hydrate gave amines **13a–13e** in high yields.

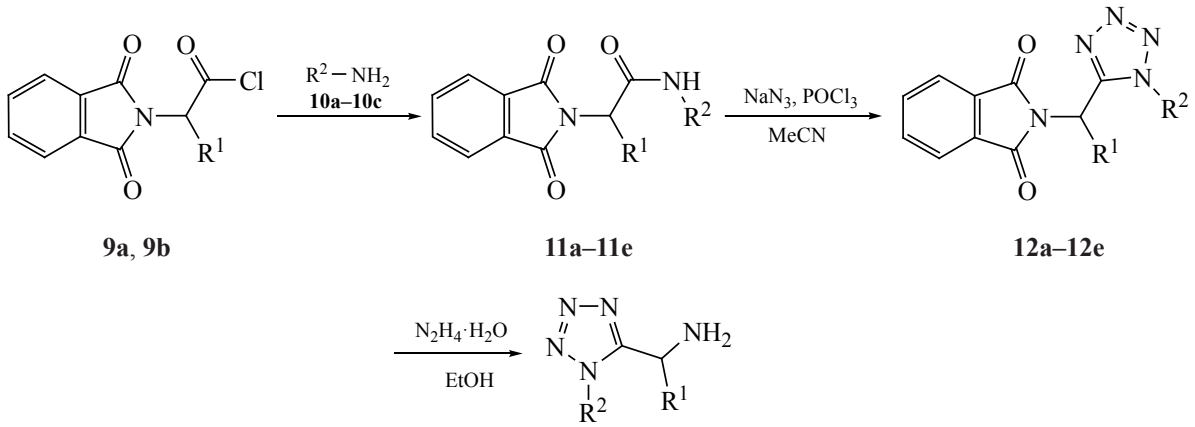
5-Tetrazolylethylamines can be prepared in the same way, which was demonstrated by the synthesis of compound **17**. Starting from substituted alanine chloride **14** we prepared amide **15** and further tetrazoles **16** and **17** (Scheme 4).

Anilines with a tetrazole fragment can be synthesized starting from nitrobenzoic acids. It was shown that nitrobenzoic acid chlorides **18a** and **18b** can be converted by the developed scheme to tetrazoles **20a** and **20b** and further to amines **21a** and **21b** (Scheme 5). The same scheme was applied to obtain 4-(5-methyl-1*H*-tetrazol-1-yl)benzoic acid (**24**) (Scheme 6).

Some problems with realization of the proposed procedure arise in the case of amides containing active halogen which can react with azide ion. For example, amides **25a** and **25b** were converted into the corresponding tetrazoles with medium yields (Scheme 7), while this reaction with amide **27** formed a mixture of products, comprising the target bromide **28a**, chloride **28b**, and vinyltetrazole **28c** (Scheme 8).

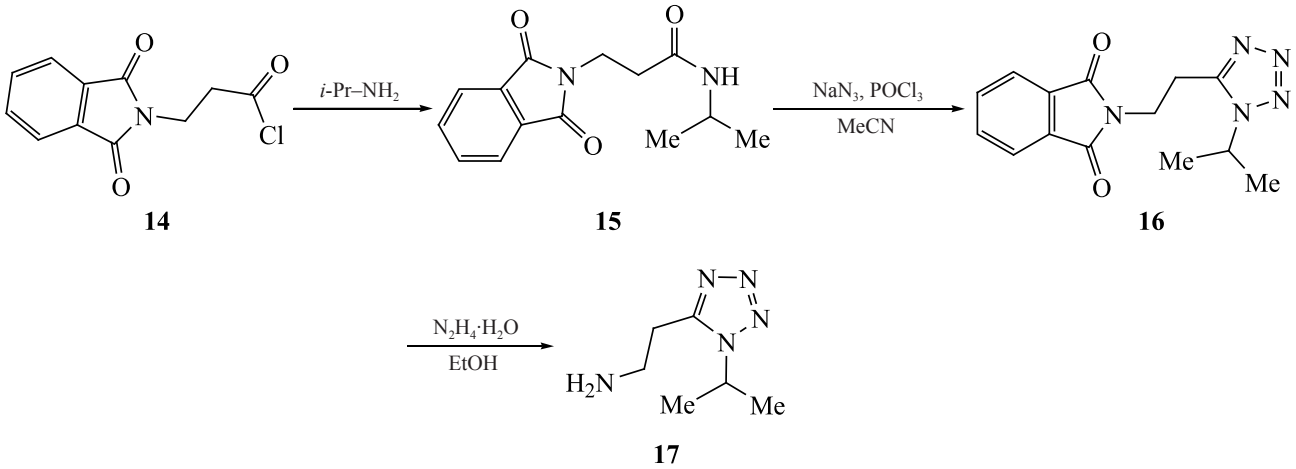
Thus, the one-pot synthesis of 1,5-disubstituted tetrazoles by the reaction of amides with $POCl_3$ and sodium azide is a convenient method for constructing structural blocks with a tetrazole ring.

Scheme 3.



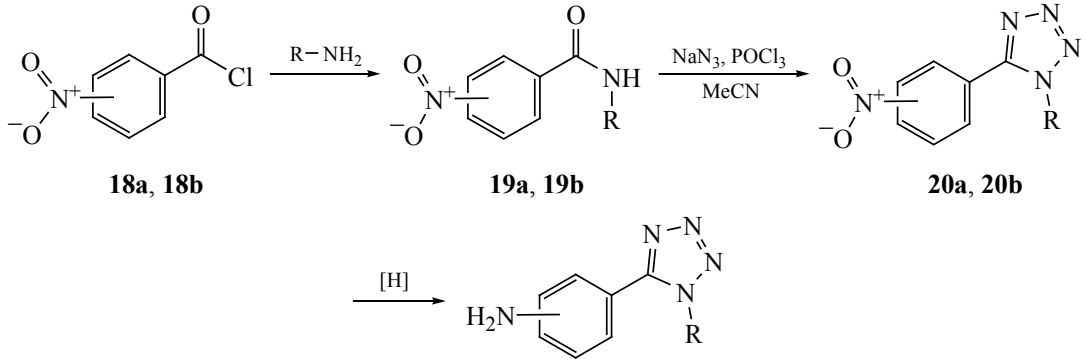
9, R^1 = H (**a**), Me (**b**); **10**, R^2 = Me (**a**), 3-BrC_6H_4 (**b**), 4-BrC_6H_4 (**c**); **11**, **12**, **13**, R^1 = H, R^2 = Me (**a**); R^1 = H, R^2 = 3-BrC_6H_4 (**b**); R^1 = H, R^2 = 4-BrC_6H_4 (**c**), R^1 = Me, R^2 = 3-BrC_6H_4 (**d**), R^1 = Me, R^2 = 4-BrC_6H_4 (**e**).

Scheme 4.



14 **15** **16** **17**

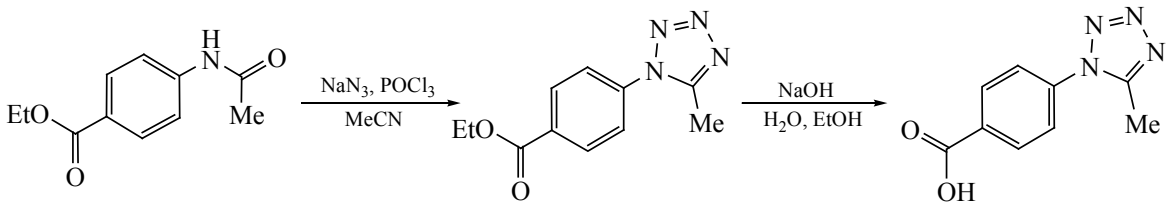
Scheme 5.



18a, **18b** **19a**, **19b** **20a**, **20b** **21a**, **21b**

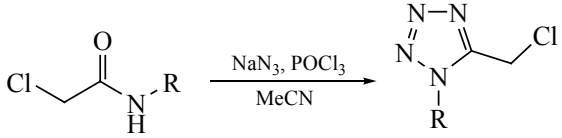
18, 3-NO_2 (**a**), 4-NO_2 (**b**); **19**, **20**, **21**, 3-NO_2, R = *i*-Bu (**a**); 4-NO_2, R = Me (**b**). [H] = $SnCl_2$, HCl or H_2, Pd/C, 5%.

Scheme 6.



22 **23** **24**

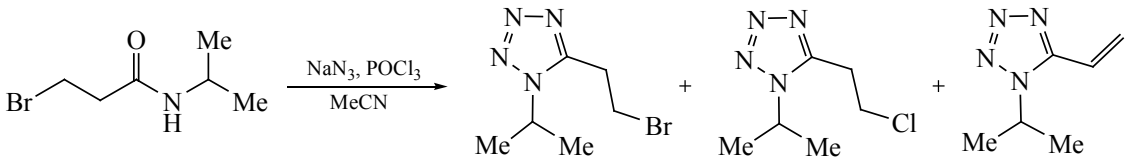
Scheme 7.



25a, **25b** **26a**, **26b**

R = Me (**a**), Ph (**b**).

Scheme 8.



27 **28a** **28b** **28c**

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Varian Unity +400 and Bruker Avance 500 spectrometers at 400 and 100 MHz, respectively; internal reference TMS. The APCI mass spectra were obtained on an Agilent 1100 LC/MSD instrument. Elemental analysis was performed on a Carlo Erba 1106 analyzer. The melting points were measured on a Boëtius hot stage.

Acid chlorides 1a–1e, 5, 9a, 9b, 14, 18a, and 18b were prepared by refluxing commercially available acids with an excess (1.6 equiv) of thionyl chloride for 2 h and subsequent vacuum distillation of unreacted thionyl chloride.

Amides 2a–2e (*general procedure*). Chloride **1** (20 mmol) was added under vigorous stirring to a suspension of 3 g of potash and 3.1 g (22 mmol) of ethyl glycinate hydrochloride in 50 mL of methylene chloride, and the mixture was stirred for 12 h, washed with water, and methylene chloride was evaporated in a vacuum to leave a pure amide.

Ethyl 2-(3-phenylpropanamido)acetate (2a). Yield 4.6 g (97%), mp 49–50°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.23 t (3H, CH_3, *J* 7.1 Hz), 2.51 t (2H, CH_2, *J* 7.7 Hz), 2.84 t (2H, CH_2, *J* 7.7 Hz), 3.80 d (2H, CH_2N, *J* 5.2 Hz), 4.11 q (2H, CH_2O, *J* 7.1 Hz), 7.17–7.33 m (5H, Ph), 8.23 t (1H, NH, *J* 5.2 Hz). Mass spectrum (CI), *m/z*: 236 $[M + H]^+$. Found, %: C 66.21; H 7.30; N 5.90. $C_{13}H_{17}NO_3$. Calculated, %: C 66.36; H 7.28; N 5.95. The characteristics of the product are consisten with published data [31].

Ethyl {[(2*E*)-3-phenylprop-2-enoyl]amino}acetate (2b). Yield 4.4 g (94%), mp 88–89°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.24 t (3H, *J* 7.1 Hz, CH_3), 3.94 d (2H, CH_2N, *J* 6.0 Hz), 4.13 q (2H, CH_2O, *J* 7.1 Hz), 6.69 d (1H, CH=, *J* 15.8 Hz), 7.32–7.50 m (4H, H_{arom} + CH=), 7.56 d (2H, $H^{2,6}_{arom}$, *J* 6.9 Hz), 8.46 t (1H, NH, *J* 5.8 Hz). Mass spectrum (CI), *m/z*: 234 $[M + H]^+$. Found, %: C 66.99; H 6.43; N 5.94. $C_{13}H_{15}NO_3$. Calculated, %: C 66.94; H 6.48; N 6.00.

Ethyl 2-(2-phenoxyacetamido)acetate (2c). Yield 4.6 g (96%), mp 54–56°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.27 t (3H, CH_3, *J* 6.8 Hz), 3.89 d (2H, CH_2N, *J* 5.3 Hz), 4.14 q (2H, CH_2O, *J* 6.9 Hz), 4.49 s (2H, OCH_2), 6.83–7.02 m ($3H_{arom}$), 7.29 t (2H, $H^{3,5}_{arom}$, *J* 7.5 Hz), 8.34 t (1H, NH, *J* 5.8 Hz). Mass spectrum (CI), *m/z*: 238 $[M + H]^+$. Found, %: C 60.70; H 6.43; N 5.97. $C_{12}H_{15}NO_4$. Calculated, %: C 60.75; H 6.37; N 5.90. The characteristics of the product are consistent with published data [32].

Ethyl 2-[2-(2-chlorophenoxy)acetamido]acetate (2d). Yield 5.0 g (92%), mp 44–45°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.27 t (3H, CH_3, *J* 7.1 Hz), 3.92 d (2H, CH_2N, *J* 5.8 Hz), 4.15 q (2H, CH_2O, *J* 7.1 Hz), 4.60 s (2H, OCH_2), 6.96 t (1H, H^4_{arom}, *J* 7.9 Hz), 7.05 d (1H, H^6_{arom}, *J* 8.2 Hz), 7.25 t (1H, H^5_{arom}, *J* 7.7 Hz), 7.37 d (1H, H^3_{arom}, *J* 7.5 Hz), 8.14 t (1H, NH, *J* 5.8 Hz). Mass spectrum (CI), *m/z*: 272 $[M + H]^+$. Found, %: C 53.11; H 5.23; N 5.03. $C_{12}H_{14}ClNO_4$. Calculated, %: C 53.05; H 5.19; N 5.16.

Ethyl 2-[2-(4-chlorophenoxy)acetamido]acetate (2e). Yield 5.2 g (95%), mp 88–90°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.26 t (3H, CH_3, *J* 7.1 Hz), 3.87 d (2H, CH_2N, *J* 5.9 Hz), 4.15 q (2H, CH_2O, *J* 7.1 Hz), 4.49 s (2H, OCH_2), 6.97 d (2H, $H^{2,6}_{arom}$, *J* 8.9 Hz), 7.26 d (2H, $H^{3,5}_{arom}$, *J* 8.9 Hz), 8.35 t (1H, NH, *J* 5.9 Hz). Mass spectrum (CI), *m/z*: 272 $[M + H]^+$. Found, %: C 53.19; H 5.11; N 5.21. $C_{12}H_{14}ClNO_4$. Calculated, %: C 53.05; H 5.19; N 5.16.

Amides 11a and 18b (*general procedure*). Acid chloride (30 mmol) was added to a cold (0°C) and vigorously stirred mixture of 3.4 mL of 25% aqueous methylamine and 25 mL of dioxane, and the resulting mixture was allowed to stand at room temperature for 30 min and then diluted with water, the precipitate that formed was filtered off and recrystallized from ethanol.

2-(1,3-Dioxoisoindolin-2-yl)-*N*-methylacetamide (11a). Yield 5.6 g (85%), mp 250–252°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.64 d (3H, CH_3, *J* 4.5 Hz), 4.15 s (2H, CH_2), 7.79–7.91 m ($4H_{arom}$), 8.02 q (1H, NH, *J* 4.5 Hz). Mass spectrum (CI), *m/z*: 219 [*M* + H]$^+$. Found, %: C 60.67; H 4.70; N 12.81. $C_{11}H_{10}N_2O_3$. Calculated, %: C 60.55; H 4.62; N 12.84. The characteristics of the product are consistent with published data [33].

***N*-Methyl-4-nitrobenzamide (18b).** Yield 4.9 g (90%), mp 214–215°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.87 d (3H, CH_3, *J* 4.1 Hz), 8.10 d (2H, $H^{2,6}_{arom}$, *J* 8.6 Hz), 8.30 d (2H, $H^{3,5}_{arom}$, *J* 8.6 Hz), 8.66 br.s (1H, NH). Mass spectrum (CI), *m/z*: 181 [*M* + H]$^+$. Found, %: C 53.37; H 4.59; N 15.39. $C_8H_8N_2O_3$. Calculated, %: C 53.33; H 4.48; N 15.55. The characteristics of the product are consistent with published data [34].

Amides 6, 11b–11d, 15, 19a, and 27 (*general procedure*). Acid chloride (50 mmol) was added to a cold (0°C) and vigorously stirred solution of amine (50 mmol) in 50 mL of dioxane and 9 mL of triethylamine (in the synthesis of compounds **15** and **27**, a double excess of isopropylamine was used instead of triethylamine). The mixture was allowed to stand for 1 h at room temperature and then heated to boiling, cooled, and diluted with water. The resulting amide was filtered off and washed with saturated soda solution and ice water. When necessary, recrystallization from ethanol was applied.

Ethyl 3-oxo-3-(phenethylamino)propanoate (6). Yield 10.8 g (92%), mp 62–63°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.25 t (3H, CH_3, *J* 7.1 Hz), 2.74 t (2H, CH_2, *J* 7.3 Hz), 3.13 s (2H, CH_2), 3.30 q (2H, CH_2N, *J* 6.7 Hz), 4.10 q (2H, CH_2O, *J* 7.1 Hz), 7.12–7.34 m ($5H_{arom}$), 8.01 t (1H, NH, *J* 6.7 Hz). Mass spectrum (CI), *m/z*: 236 [*M* + H]$^+$. Found, %: C 66.47; H 7.34; N 5.91. $C_{13}H_{17}NO_3$. Calculated, %: C 66.36; H 7.28; N 5.95. The characteristics of the product are consistent with published data [35].

***N*-(3-Bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)-acetamide (11b).** Yield 16.9 g (94%), mp 152–154°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.42 s (2H, CH_2). 7.04–7.31 m ($2H_{arom}$), 7.47 d ($1H_{arom}$, *J* 7.7 Hz), 7.78–8.15 m ($5H_{arom}$), 10.35 s (1H, NH). Mass spectrum (CI), *m/z*: 359, 361 [*M* + H]$^+$. Found, %: C 53.54; H 3.14; N 7.87. $C_{16}H_{11}BrN_2O_3$. Calculated, %: C 53.50; H 3.09; N 7.80.

***N*-(4-Bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)-acetamide (11c).** Yield 17.0 g (95%), mp 209–210°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.41 s (2H, CH_2), 7.38 d (2H, $H^{2,6}_{arom}$, *J* 8.7 Hz), 7.53 d (2H, $H^{3,5}_{arom}$, *J* 8.7 Hz), 7.72–8.09 m ($4H_{arom}$), 10.31 s (1H, NH). Mass spectrum (CI), *m/z*: 359, 361 [*M* + H]$^+$. Found, %: C 53.66; H 3.02; N 7.88. $C_{16}H_{11}BrN_2O_3$. Calculated, %: C 53.50; H 3.09; N 7.80. The characteristics of the product are consistent with published data [36].

***N*-(3-Bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)-propanamide (11d).** Yield 17.7 g (95%), mp 201–202°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.63 d (3H, CH_3, *J* 7.1 Hz), 4.89 q (1H, CH, *J* 6.8 Hz), 6.98–7.38 m ($2H_{arom}$), 7.54 d (1H, H^4_{arom}, *J* 7.4 Hz), 7.75–8.17 m ($5H_{arom}$), 9.90 s (1H, NH). Mass spectrum (CI), *m/z*: 373, 375 [*M* + H]$^+$. Found, %: C 54.60; H 3.46; N 7.43. $C_{17}H_{13}BrN_2O_3$. Calculated, %: C 54.71; H 3.51; N 7.51.

***N*-(4-Bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)-propanamide (11e).** Yield 17.9 g (96%), mp 145–147°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.64 d (3H, CH_3, *J* 7.1 Hz), 4.89 q (1H, CH, *J* 7.1 Hz), 7.37 d (2H, $H^{2,6}_{arom}$, *J* 8.6 Hz), 7.52 d (2H, $H^{3,5}_{arom}$, *J* 8.7 Hz), 7.72–8.02 m ($4H_{arom}$), 9.89 s (1H, NH). Mass spectrum (CI), *m/z*: 373, 375 [*M* + H]$^+$. Found, %: C 54.66; H 3.32; N 7.47. $C_{17}H_{13}BrN_2O_3$. Calculated, %: C 54.71; H 3.51; N 7.51.

3-(1,3-Dioxoisoindolin-2-yl)-*N*-isopropylpropanamide (15). Yield 12.35 g (95%), mp 219–221°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.02 d (6H, CH_3, *J* 6.6 Hz), 2.36 t (2H, CH_2, *J* 7.4 Hz), 3.73–3.86 m (3H, CH_2 + CH), 7.66 d (1H, H^2_{arom}, *J* 7.1 Hz), 7.77–7.87 m ($3H_{arom}$). Mass spectrum (CI), *m/z*: 261 [*M* + H]$^+$. Found, %: C 64.47; H 6.11; N 10.65. $C_{14}H_{16}N_2O_3$. Calculated, %: C 64.60; H 6.20; N 10.76. The characteristics of the product are consistent with published data [37].

***N*-Isobutyl-3-nitrobenzamide (19a).** Yield 10.3 g (92%), mp 126–127°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.89 d (6H, CH_3, *J* 6.5 Hz), 1.77–1.97 m (1H, CH), 3.11 t (2H, CH_2, *J* 6.2 Hz), 7.76 t (1H, H^5_{arom}, *J* 7.9 Hz), 8.28 d (1H, H^6_{arom}, *J* 7.4 Hz), 8.37 d (1H, H^4_{arom}, *J* 8.0 Hz), 8.67 s (1H, H^2_{arom}), 8.84 t (1H, NH, *J* 5.2 Hz). Mass spectrum (CI), *m/z*: 223 [*M* + H]$^+$. Found, %: C 59.34; H 6.31; N 12.70. $C_{11}H_{14}N_2O_3$. Calculated, %: C 59.45; H 6.35; N 12.61.

3-Bromo-*N*-isopropylpropanamide (27). Yield 7.8 g (81%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.08 d (6H, CH_3, *J* 6.6 Hz), 2.61 t (2H, CH_2, *J* 6.7 Hz), 3.57 t (2H, CH_2Br, *J* 6.7 Hz),

3.78–3.96 m (1H, CHN), 7.68 d (1H, NH, *J* 5.8 Hz). Mass spectrum (CI), *m/z*: 194, 196 $[M + H]^+$. Found, %: C 37.02; H 6.17; N 7.07. $C_6H_{12}BrNO$. Calculated, %: C 37.13; H 6.23; N 7.22.

1,5-Disubstituted 1*H*-tetrazoles 3a–3e, 7, 12a–12e, 16, 20a, 20b, 23, 26a, 26b, and 28a–28c (*general procedure*). Phosphorus oxychloride, 4.8 mL (7.7 g, 50 mmol) and 1.3 g (20 mmol) of NaN_3 were added to a vigorously stirred solution of amide **2a–2e**, **6**, **11a–11e**, **15**, **19a**, **19b**, **22**, **25a**, **25b**, or **27** (10 mmol) in 20 mL of acetonitrile. The mixture was refluxed for 5–7 h, acetonitrile was evaporated, the residue was dissolved in water with ice, and the solution was neutralized with saturated soda solution. The precipitate that formed was filtered off. Liquid tetrazoles were extracted with methylene chloride, and the solvent was evaporated in a vacuum.

Ethyl 2-[5-(2-phenylethyl)-1*H*-tetrazol-1-yl]acetate (3a). Yield 2.4 g (91%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.28 t (3H, CH_3, *J* 7.1 Hz), 3.03–3.18 m (4H, CH_2), 4.21 q (2H, CH_2O, *J* 7.0 Hz), 5.34 s (2H, CH_2N), 7.12–7.40 m (5H, Ph). Mass spectrum (CI), *m/z*: 261 $[M + H]^+$. Found, %: C 59.91; H 6.09; N 21.58. $C_{13}H_{16}N_4O_2$. Calculated, %: C 59.99; H 6.20; N 21.52.

(*E*)-Ethyl 2-(5-styryl-1*H*-tetrazol-1-yl)acetate (3b). Yield 2.2 g (83%), mp 94–96°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.28 t (3H, CH_3, *J* 7.1 Hz), 4.23 q (2H, CH_2O, *J* 7.0 Hz), 5.58 s (2H, CH_2N), 7.32–7.47 m (4H, $H_{arom}^{3,4,5}$ + CH=), 7.73 d (2H, $H_{arom}^{2,6}$, *J* 7.3 Hz), 7.80 d (1H, CH=, *J* 16.0 Hz). Mass spectrum (CI), *m/z*: 259 $[M + H]^+$. Found, %: C 60.29; H 5.34; N 21.74. $C_{13}H_{14}N_4O_2$. Calculated, %: C 60.45; H 5.46; N 21.69.

Ethyl 2-[5-(phenoxymethyl)-1*H*-tetrazol-1-yl]-acetate (3c). Yield 2.4 g (93%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.21 t (3H, CH_3, *J* 7.0 Hz), 4.15 q (2H, CH_2O, *J* 7.0 Hz), 5.48 s (2H, OCH_2), 5.50 s (2H, CH_2N), 6.92–7.05 m (3H, $H_{arom}^{2,4,6}$), 7.30 t (2H, $H_{arom}^{3,5}$, *J* 7.4 Hz). Mass spectrum (CI), *m/z*: 263 $[M + H]^+$. Found, %: C 55.09; H 5.33; N 21.23. $C_{12}H_{14}N_4O_3$. Calculated, %: C 54.96; H 5.38; N 21.36.

Ethyl 2-{5-[(2-chlorophenoxy)methyl]-1*H*-tetrazol-1-yl}acetate (3d). Yield 2.63 g (89%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.20 t (3H, CH_3, *J* 7.1 Hz), 4.15 q (2H, CH_2O, *J* 7.1 Hz), 5.56 s (2H, OCH_2), 5.59 s (2H, CH_2N), 7.00 t (1H, H_{arom}^5, *J* 7.1 Hz), 7.33–7.21 m (2H, $H_{arom}^{4,6}$), 7.37 d (1H, H_{arom}^3, *J* 7.7 Hz). Mass spectrum (CI), *m/z*: 297 $[M + H]^+$. Found, %: C 48.52; H 4.28; N 18.81. $C_{12}H_{13}ClN_4O_3$. Calculated, %: C 48.58; H 4.42; N 18.88.

Ethyl 2-{5-[(4-chlorophenoxy)methyl]-1*H*-tetrazol-1-yl}acetate (3e). Yield 2.8 g (94%), mp 92–93°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.22 t (3H, CH_3, *J* 7.1 Hz), 4.17 q (2H, CH_2O, *J* 7.1 Hz), 5.48 s (2H, CH_2), 5.50 s (2H, OCH_2), 7.01 d (2H, $H_{arom}^{2,6}$, *J* 8.9 Hz), 7.28 d (2H, $H_{arom}^{3,5}$, *J* 8.9 Hz). Mass spectrum (CI), *m/z*: 297 $[M + H]^+$. Found, %: C 48.64; H 4.45; N 19.03. $C_{12}H_{13}ClN_4O_3$. Calculated, %: C 48.58; H 4.42; N 18.88.

Ethyl 2-[1-(2-phenylethyl)-1*H*-tetrazol-5-yl]acetate (7). Yield 2.4 g (91%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.26 t (3H, CH_3, *J* 7.1 Hz), 3.19 t (2H, CH_2Ph, *J* 7.5 Hz), 3.92 s (2H, CH_2), 4.16 q (2H, CH_2O, *J* 7.1 Hz), 4.58 t (2H, CH_2N, *J* 7.5 Hz), 6.83–7.51 m ($5H_{arom}$). Mass spectrum (CI), *m/z*: 261 $[M + H]^+$. Found, %: C 59.91; H 6.32; N 21.59. $C_{13}H_{16}N_4O_2$. Calculated, %: C 59.99; H 6.20; N 21.52.

2-[(1-Methyl-1*H*-tetrazol-5-yl)methyl]isoindoline-1,3-dione (12a). Yield 2.2 g (89%), mp 270–271°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.18 s (3H, CH_3), 5.16 s (2H, CH_2), 7.82–7.99 m ($4H_{arom}$). Mass spectrum (CI), *m/z*: 244 $[M + H]^+$. Found, %: C 54.28; H 3.53; N 28.65. $C_{11}H_9N_5O_2$. Calculated, %: C 54.32; H 3.73; N 28.79. The characteristics of the product are consistent with published data [38].

2-{[1-(3-Bromophenyl)-1*H*-tetrazol-5-yl]methyl}-isoindoline-1,3-dione (12b). Yield 3.5 g (92%), mp 160–161°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.18 s (2H, CH_2), 7.56 t (1H, H_{arom}^5, *J* 8.1 Hz), 7.75 d (2H, $H_{arom}^{4,6}$, *J* 7.9 Hz), 7.91–7.81 m ($4H_{arom}$), 7.98 s (1H, H_{arom}^2). Mass spectrum (CI), *m/z*: 384, 386 $[M + H]^+$. Found, %: C 50.12; H 2.67; N 18.11. $C_{16}H_{10}BrN_5O_2$. Calculated, %: C 50.02; H 2.62; N 18.23.

2-{[1-(4-Bromophenyl)-1*H*-tetrazol-5-yl]methyl}-isoindoline-1,3-dione (12c). Yield 3.6 g (95%), mp 217–218°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.16 s (2H, CH_2), 7.71 d (2H, $H_{arom}^{2,6}$, *J* 8.5 Hz), 7.77 d (2H, $H_{arom}^{3,5}$, *J* 8.5 Hz), 7.82–7.96 m ($4H_{arom}$). Mass spectrum (CI): *m/z* 384, 386 $[M + H]^+$. Found, %: C 50.11; H 2.49; N 18.19. $C_{16}H_{10}BrN_5O_2$. Calculated, %: C 50.02; H 2.62; N 18.23.

2-{1-[1-(3-Bromophenyl)-1*H*-tetrazol-5-yl]ethyl}-isoindoline-1,3-dione (12d). Yield 3.6 g (91%), mp 215–216°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.86 d (3H, CH_3, *J* 6.6 Hz), 5.92 q (1H, CH, *J*

6.5 Hz), 7.35 t (1H, H^5_{arom}, *J* 8.1 Hz), 7.74 d (2H, $H^{4,6}_{arom}$, *J* 7.9 Hz), 7.76–7.98 m ($5H_{arom}$). Mass spectrum (CI), *m/z*: 398, 400 $[M + H]^+$. Found, %: C 51.21; H 3.13; N 17.50. $C_{17}H_{12}BrN_5O_2$. Calculated, %: C 51.27; H 3.04; N 17.59.

2-{1-[1-(4-Bromophenyl)-1*H*-tetrazol-5-yl]ethyl}-isoindoline-1,3-dione (12e). Yield 3.7 g (93%), mp 155–156°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.88 d (3H, CH_3, *J* 6.9 Hz), 5.92 q (1H, CH, *J* 6.9 Hz), 7.34 d (2H, $H^{2,6}_{arom}$, *J* 8.7 Hz), 7.40 d (2H, $H^{3,5}_{arom}$, *J* 8.7 Hz), 7.60–7.69 m ($2H_{arom}$), 7.74–7.90 m ($2H_{arom}$). Mass spectrum (CI), *m/z*: 398, 400 $[M + H]^+$. Found, %: C 51.44; H 3.11; N 17.71. $C_{17}H_{12}BrN_5O_2$. Calculated, %: C 51.27; H 3.04; N 17.59.

2-[2-(1-Isopropyl-1*H*-tetrazol-5-yl)ethyl]isoindoline-1,3-dione (16). Yield 2.2 g (90%), mp 118–119°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.57 d (6H, CH_3, *J* 6.8 Hz), 3.29 t (2H, CH_2, *J* 6.9 Hz), 3.99 t (2H, CH_2, *J* 6.9 Hz), 4.83 septet (1H, CH, *J* 7.1 Hz), 7.78–7.93 m ($4H_{arom}$). Mass spectrum (CI), *m/z*: 286 $[M + H]^+$. Found, %: C 58.82; H 5.37; N 24.65. $C_{14}H_{15}N_5O_2$. Calculated, %: C 58.94; H 5.30; N 24.55.

1-Isobutyl-5-(3-nitrophenyl)-1*H*-tetrazole (20a). Yield 2.2 g (90%), mp 82–83°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 0.79 d (6H, CH_3, *J* 6.6 Hz), 1.98–2.22 m (1H, CH), 4.36 d (2H, CH_2, *J* 7.2 Hz), 7.92 t (1H, H^5_{arom}, *J* 8.0 Hz), 8.23 d (1H, H^6_{arom}, *J* 7.7 Hz), 8.48 d (1H, H^4_{arom}, *J* 8.3 Hz), 8.60 s (1H, H^2_{arom}). Mass spectrum (CI), *m/z*: 248 $[M + H]^+$. Found, %: C 53.39; H 5.38; N 28.45. $C_{11}H_{13}N_5O_2$. Calculated, %: C 53.43; H 5.30; N 28.32.

1-Methyl-5-(4-nitrophenyl)-1*H*-tetrazole (20b). Yield 1.8 g (88%), mp 112–113°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.23 s (3H, CH_3), 8.17 d (2H, $H^{2,6}_{arom}$, *J* 8.7 Hz), 8.42 d (2H, $H^{3,5}_{arom}$, *J* 8.7 Hz). Mass spectrum (CI), *m/z*: 206 $[M + H]^+$. Found, %: C 46.91; H 3.52; N 34.06. $C_8H_7N_5O_2$. Calculated, %: C 46.83; H 3.44; N 34.13.

Ethyl 4-(5-methyl-1*H*-tetrazol-1-yl)benzoate (23). Yield 2.0 g (86%), mp 72–73°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.40 t (3H, CH_3, *J* 7.2 Hz), 2.50 s (3H, CH_3), 4.38 q (2H, CH_2O, *J* 7.2 Hz), 7.81 d (2H, $H^{3,5}_{arom}$, *J* 7.2 Hz), 8.20 d (2H, $H^{2,6}_{arom}$, *J* 7.2 Hz). Mass spectrum (CI), *m/z*: 232 $[M + H]^+$. Found, %: C 57.00; H 5.06; N 24.05. $C_{11}H_{12}N_4O_2$. Calculated, %: C 56.89; H 5.21; N 24.12.

5-Chloromethyl-1-methyl-1*H*-tetrazole (26a) [24]. Yield 0.7 g (51%), mp 61–62°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.13 s (3H, CH_3), 5.09 s (2H, CH_2). Mass spectrum (CI), *m/z*: 133 $[M + H]^+$. Found, %: C 27.09; H 3.76; N 42.36. $C_3H_5ClN_4$. Calculated, %: C 27.18; H 3.80; N 42.27.

5-Chloromethyl-1-phenyl-1*H*-tetrazole (26b) [39]. Yield 1.2 g (62%), mp 72–73°C. Mass spectrum (CI), *m/z*: 195 $[M + H]^+$. Found, %: C 49.31; H 3.58; N 28.86. $C_8H_7ClN_4$. Calculated, %: C 49.37; H 3.63; N 28.79.

5-(2-Bromoethyl)-1-isopropyl-1*H*-tetrazole (28a). Yield 0.76 g (35%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.53 d (6H, CH_3, *J* 6.6 Hz), 3.42 t (2H, CH_2, *J* 6.6 Hz), 3.99 t (2H, CH_2Br, *J* 6.6 Hz), 4.85 septet (1H, CH, *J* 6.6 Hz). Mass spectrum (CI), *m/z*: 219, 221 $[M + H]^+$. Found, %: C 32.98; H 5.00; N 25.49. $C_6H_{11}BrN_4$. Calculated, %: C 32.89; H 5.06; N 25.57.

5-(2-Chloroethyl)-1-isopropyl-1*H*-tetrazole (28b). Yield 0.46 g (26.5%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.53 d (6H, CH_3, *J* 6.6 Hz), 3.53 t (2H, CH_2, *J* 6.7 Hz), 3.83 t (2H, CH_2Cl, *J* 6.7 Hz), 4.85 septet (1H, CH, *J* 6.4 Hz). Mass spectrum (CI), *m/z* (I_{rel}, %): 175 (100), 177 (30) $[M + H]^+$. Found, %: C 41.21; H 6.47; N 32.01. $C_6H_{11}ClN_4$. Calculated, %: C 41.27; H 6.35; N 32.08.

1-Isopropyl-5-vinyl-1*H*-tetrazole (28c). Yield 0.15 g (10.6%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.53 d (6H, CH_3, *J* 6.6 Hz), 4.96 septet (1H, CH, *J* 6.6 Hz), 5.85 d.d (1H, $=CH_2$, *J* 11.2, 1.1 Hz), 6.40 d.d (1H, $=CH_2$, *J* 17.2, 1.1 Hz), 6.93 d.d (1H, CH=, *J* 17.2, 11.2 Hz). Mass spectrum (CI), *m/z*: 139 $[M + H]^+$. Found, %: C 52.22; H 7.35; N 40.52. $C_6H_{10}N_4$. Calculated, %: C 52.16; H 7.30; N 40.55.

Tetrazolylacetic acids 4a–4e, 8, and 24 (*general procedure*). A solution of 1 g (25 mmol) of NaOH in 10 mL of water was added to a solution of the corresponding ester (10 mmol) in 50 mL of ethanol. The reaction mixture was heated for 3 h at 50°C, ethanol was evaporated, the residue was dissolved in water, and the aqueous solution was treated with methylene chloride. The aqueous layer was made acidic with conc. HCl, and the white precipitate that formed was filtered off and dried in a vacuum.

2-[5-(2-Phenylethyl)-1*H*-tetrazol-1-yl]acetic acid (4a). Yield 2.2 g (94%), mp 108–109°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.03–3.18 m

(4H, CH_2), 5.18 s (2H, CH_2N), 7.15–7.21 m (1H_{arom}), 7.22–7.36 m (4H_{arom}). Mass spectrum (CI), *m/z*: 233 [*M* – H]$^+$. Found, %: C 56.71; H 5.25; N 24.19. $C_{11}H_{12}N_4O_2$. Calculated, %: C 56.89; H 5.21; N 24.12.

(*E*)-2-(5-Styryl-1*H*-tetrazol-1-yl)acetic acid (4b). Yield 2.2 g (95%), mp 128–129°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.45 s (2H, CH_2N), 7.31–7.50 m (4H, $H_{arom}^{3,4,5}$ + CH=), 7.75 d (2H, $H_{arom}^{2,6}$, *J* 6.9 Hz), 7.80 d (1H, CH=, *J* 16.1 Hz). Mass spectrum (CI), *m/z*: 231 [*M* + H]$^+$. Found, %: C 57.33; H 4.43; N 24.21. $C_{11}H_{10}N_4O_2$. Calculated, %: C 57.39; H 4.38; N 24.34.

2-[5-(Phenoxymethyl)-1*H*-tetrazol-1-yl]acetic acid (4c). Yield 2.3 g (97%), mp 112–113°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.37 s (2H, OCH_2), 5.46 s (2H, CH_2N), 6.95–7.04 m (3H_{arom}), 7.29 t (2H, $H_{arom}^{3,5}$, *J* 7.7 Hz). Mass spectrum (CI), *m/z*: 235 [*M* + H]$^+$. Found, %: C 51.18; H 4.35; N 23.97. $C_{10}H_{10}N_4O_3$. Calculated, %: C 51.28; H 4.30; N 23.92.

2-{5-[(2-Chlorophenoxy)methyl]-1*H*-tetrazol-1-yl}acetic acid (4d). Yield 2.6 g (96%), mp 127–128°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.45 s (2H, CH_2N), 5.58 s (2H, OCH_2), 6.99 t (1H, H_{arom}^5, *J* 7.2 Hz), 7.35–7.23 m (2H, $H_{arom}^{4,6}$), 7.38 d (1H, H_{arom}^3, *J* 7.8 Hz). Mass spectrum (CI), *m/z*: 269 [*M* + H]$^+$. Found, %: C 44.77; H 3.44; N 20.71. $C_{10}H_9ClN_4O_3$. Calculated, %: C 44.71; H 3.38; N 20.85.

2-{5-[(4-Chlorophenoxy)methyl]-1*H*-tetrazol-1-yl}acetic acid (4e). Yield 2.6 g (97%), mp 142–143°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.29 s (2H, OCH_2), 5.45 s (2H, CH_2N), 7.03 d (2H, $H_{arom}^{2,6}$, *J* 8.8 Hz), 7.27 d (2H, $H_{arom}^{3,5}$, *J* 8.8 Hz). Mass spectrum (CI), *m/z*: 269 [*M* + H]$^+$. Found, %: C 44.59; H 3.40; N 20.75. $C_{10}H_9ClN_4O_3$. Calculated, %: C 44.71; H 3.38; N 20.85.

2-[1-(2-Phenylethyl)-1*H*-tetrazol-5-yl]acetic acid (8). Yield 2.2 g (95%), mp 98–99°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 3.18 t (2H, CH_2Ph, *J* 7.4 Hz), 3.82 s (2H, CH_2), 4.56 t (2H, CH_2N, *J* 7.4 Hz), 7.07–7.39 m (5H_{arom}). Mass spectrum (CI), *m/z*: 233 [*M* + H]$^+$. Found, %: C 56.93; H 5.28; N 24.19. $C_{11}H_{12}N_4O_2$. Calculated, %: C 56.89; H 5.21; N 24.12.

4-(5-Methyl-1*H*-tetrazol-1-yl)benzoic acid (24). Yield 2.0 g (97%), mp 262–263°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.50 s (3H, CH_3), 7.81 d (2H, $H_{arom}^{3,5}$, *J* 7.2 Hz), 8.20 d (2H, $H_{arom}^{2,6}$, *J* 7.2 Hz). Mass spectrum (CI), *m/z*: 205 [*M* – H]$^+$. Found, %: C 52.83; H 3.90; N 27.26. $C_9H_8N_4O_2$. Calculated, %: C 52.94; H 3.95; N 27.44.

Amines 13a–13e and 17 (*general procedure*). Hydrazine hydrate, 2.5 mL, was added to a solution of 10 mmol of phthalimide derivative in 100 mL of ethanol, and the reaction mixture was heated under reflux for 1 h. After cooling to –10°C, and phthalazine dione was filtered off. Ethanol was evaporated, and the residue was dissolved in methylene chloride. A little of phthalazine dione was filtered off, and the solvent was evaporated to obtain a pure amine.

(1-Methyl-1*H*-tetrazol-5-yl)methanamine (13a). Yield 1.0 g (91%), viscous oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 1.52 br.s (2H, NH_2), 4.09 s (3H, CH_3), 4.11 s (2H, CH_2). Mass spectrum (CI), *m/z*: 114 [*M* + H]$^+$. Found, %: C 31.78; H 6.19; N 62.02. $C_3H_7N_5$. Calculated, %: C 31.85; H 6.24; N 61.91. The characteristics of the product are consistent with published data [37].

[1-(3-Bromophenyl)-1*H*-tetrazol-5-yl]methanamine (13b). Yield 2.3 g (92%), mp 73–74°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.35 br.s (2H, NH_2), 4.06 s (2H, CH_2), 7.58 t (1H, H_{arom}^5, *J* 8.0 Hz), 7.67–7.84 m (2H, $H_{arom}^{4,6}$), 7.99 s (1H, H_{arom}^2). Mass spectrum (CI), *m/z*: 254, 256 [*M* + H]$^+$. Found, %: C 37.97; H 3.21; N 27.51. $C_8H_8BrN_5$. Calculated, %: C 37.82; H 3.17; N 27.56.

[1-(4-Bromophenyl)-1*H*-tetrazol-5-yl]methanamine (13c). Yield 2.4 g (94%), mp 77–78°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.60 br.s (2H, NH_2), 4.04 s (2H, CH_2), 7.72 d (2H, $H_{arom}^{2,6}$, *J* 8.6 Hz), 7.78 d (2H, $H_{arom}^{3,5}$, *J* 8.6 Hz). Mass spectrum (CI), *m/z*: 254, 256 [*M* + H]$^+$. Found, %: C 37.88; H 3.09; N 27.68. $C_8H_8BrN_5$. Calculated, %: C 37.82; H 3.17; N 27.56.

1-[1-(3-Bromophenyl)-1*H*-tetrazol-5-yl]ethanamine (13d). Yield 2.4 g (90%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.46 d (3H, CH_3, *J* 6.6 Hz), 2.21 br.s (2H, NH_2), 4.21 q (1H, CH, *J* 6.4 Hz), 7.57 t (1H, H_{arom}^5, *J* 8.0 Hz), 7.75 t (2H, $H_{arom}^{4,6}$, *J* 7.8 Hz), 7.98 s (1H, H_{arom}^2). Mass spectrum (CI), *m/z*: 268, 270 [*M* + H]$^+$. Found, %: C 40.42; H 3.71; N 26.03. $C_9H_{10}BrN_5$. Calculated, %: C 40.32; H 3.76; N 26.12.

1-[1-(4-Bromophenyl)-1*H*-tetrazol-5-yl]ethanamine (13e). Yield 2.5 g (95%), viscous oil. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.46 d (3H, CH_3, *J* 6.7 Hz), 2.17 br.s (2H, NH_2), 4.21 q (1H, CH, *J* 6.6 Hz),

7.70 d (2H, $H^{2,6}_{arom}$, *J* 8.7 Hz), 7.78 d (2H, $H^{3,5}_{arom}$, *J* 8.7 Hz). Mass spectrum (CI), *m/z*: 268, 270 $[M + H]^+$. Found, %: C 40.45; H 3.72; N 26.23. $C_9H_{10}BrN_5$. Calculated, %: C 40.32; H 3.76; N 26.12.

2-(1-Isopropyl-1*H*-tetrazol-5-yl)ethanamine (17). Yield 1.4 g (92%), viscous oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 1.56 br.s (2H, NH_2), 1.59 d (6H, CH_3, *J* 6.7 Hz), 2.92 t (2H, CH_2, *J* 6.3 Hz), 3.17 t (2H, CH_2, *J* 6.2 Hz), 4.68 septet (1H, CH, *J* 6.4 Hz). Mass spectrum (CI), *m/z*: 156 $[M + H]^+$. Found, %: C 46.49; H 8.41; N 45.07. $C_6H_{13}N_5$. Calculated, %: C 46.43; H 8.44; N 45.12.

3-(1-Isobutyl-1*H*-tetrazol-5-yl)aniline (21a). Palladium on carbon (0.22 g) was added to a solution of 2.2 g (10 mmol) of nitro compound **20a** in 50 mL of methanol. The reaction mixture was stirred in an argon atmosphere for 12 h, filtered through a thin bed of silica gel, and methanol was evaporated to leave a pure amine. Yield 2.1 g (98%), mp 85–86°C. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 0.78 d (6H, CH_3, *J* 6.7 Hz), 2.03–2.16 m (1H, CH), 4.29 d (2H, CH_2, *J* 7.3 Hz), 5.48 s (2H, NH_2), 6.78 d (1H_{arom}, *J* 8.0 Hz), 6.82 d (1H_{arom}, *J* 7.4 Hz), 6.89 s (1H, H^2_{arom}), 7.23 t (1H H^5_{arom}, *J* 7.8 Hz). Mass spectrum (CI), *m/z*: 218 $[M + H]^+$. Found, %: C 60.91; H 6.83; N 32.38. $C_{11}H_{15}N_5$. Calculated, %: C 60.81; H 6.96; N 32.23.

4-(1-Methyl-1*H*-tetrazol-5-yl)aniline (21b). Nitro compound **20b** (6 g, 0.03 mol) was added at 50°C to a solution of 21 g of $SnCl_2 \cdot 2H_2O$ in 70 mL of HCl, and the mixture was heated at 70°C for 3 h. After cooling, HCl was evaporated, and the amine hydrochloride was stirred with 20% aqueous NaOH until a strongly alkaline reaction. The precipitate that formed was filtered off and recrystallized from dilute ethanol. Yield 4.3 g (82%), mp 163–164°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 4.13 s (3H, CH_3) 5.59 s (2H, NH_2), 6.71 d (2H, $H^{2,6}_{arom}$, *J* 8.2 Hz), 7.49 d (2H, $H^{3,5}_{arom}$, *J* 8.1 Hz). Mass spectrum (CI), *m/z*: 176 $[M + H]^+$. Found, %: C 54.91; H 5.09; N 39.91. $C_8H_9N_5$. Calculated, %: C 54.85; H 5.18; N 39.98.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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