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ACYLATION OF AMINES WITH 5-PHENYLTETRAZOL-2-YLACETYL CHLORIDE

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The acylation of primary and secondary amines by 5-phenyltetrazol-2-ylacetyl chloride leads to the corresponding tetrazolylacetamides irrespective of the nature of the substituent in the structure of the amine.

Keywords: 5-phenyltetrazol-2-ylacetamide, 5-phenyltetrazol-2-ylacetyl chloride, acylation.

Tetrazolylacetic acids and their derivatives are regarded as potential biologically active compounds. A special position is occupied by the amides of tetrazolylacetic acids, which are intermediate products for the synthesis of biologically active compounds. For example, antibiotics of the cephalosporin series (kefzol, ceftezol), which contain a tetrazolylacetic acid fragment in their chemical structure, have found widespread use in clinical practise [1]. These drugs form a group of semisynthetic cephalosporin antibiotics that are highly effective and have extended therapeutic activity. The search for analogous compounds having improved characteristics and also investigation of the reactivity of the key reagents in the synthesis of compounds of diverse practical significance present an urgent task in modern medical chemistry [2, 3].

The esters of tetrazolylacetic acids play a special role in the synthesis of antibiotics containing a tetrazole fragment [4]. In previous work we showed for the case of ethyl 5-phenyltetrazol-2-ylacetate that such esters can be regarded as key reagents in the synthesis of certain tetrazolylacetamides [5]. However, the aminolysis of tetrazolylacetic esters does not make it possible to obtain the corresponding amides from amines with branched structures and aromatic or heterocyclic substituents [5].

An alternative to aminolysis of the esters may be acylation of the amines by carboxylic acid chlorides. Unfortunately, there are no published data that would characterize the ability of tetrazolylacetyl chlorides to enter into the acylation of nitrogen compounds. Exceptions are the reactions with 7-aminocephalosporanic acid and its derivatives and also the transacylation of tetrazoles [4, 6, 7].

In the present work we studied the acylation of various amines by 5-phenyltetrazol-2-ylacetyl chloride. In order to produce the respective acetamides we used amines with low basicity (aniline and its derivatives) and with branched aliphatic and bulky substituents containing several reactive amino groups and also some weakly nucleophilic heterocyclic amines.

The acylation was conducted in ether, chloroform, or THF depending on the solubility of the amine [7]. Triethylamine was used as base to combine with the released hydrogen chloride. The amides of 5-phenyltetrazol-2-ylacetamides were synthesized from the respective acid chlorides according to the following scheme:

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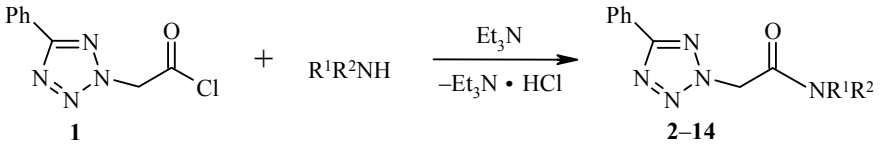
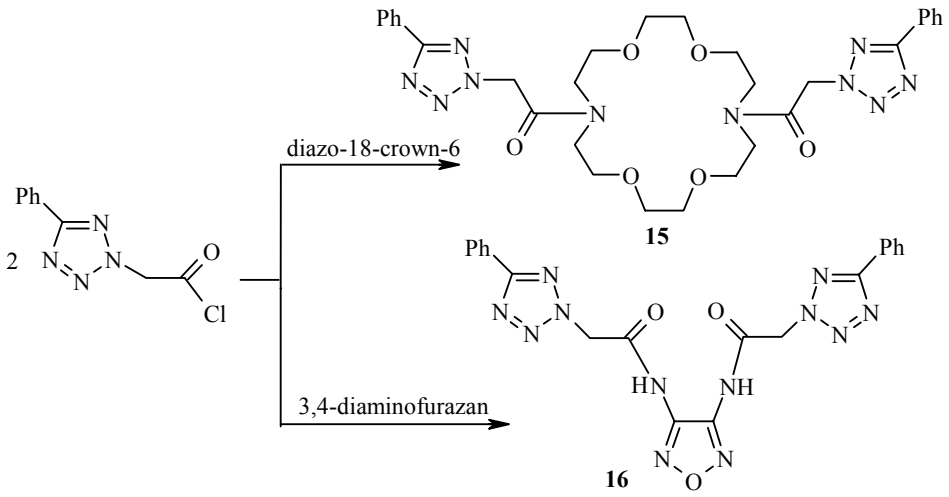


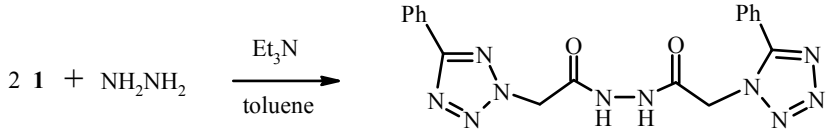
1 **2–14**

2 $R^1 = R^2 =$ Et; **3** $R^1 = R^2 = CH_2CH_2CN$; **4** $R^1R^2 = (CH_2)_5$; **5** $R^1R^2 = (CH_2)_2O(CH_2)_2$;
6 $R^1R^2 = (CH_2)_2N(CO_2Et)(CH_2)_2$; **7-14** $R^1 = H$; $R^2 =$ Ph, **8** $R^2 = 4\text{-}O_2NC_6H_4$, **9** $R^2 = 3\text{-}NO_2C_6H_4$,
10 $R^2 = 2\text{-}O_2NC_6H_4$, **11** $R^2 = 3,5\text{-}(NO_2)_2C_6H_3$, **12** $R^2 =$ MeCHPh,
13 $R^2 =$ (1,2,4-triazol-4-yl), **14** $R^2 =$ (4-methylfurazan-3-yl)

By the effective acylation of sterically blocked and low-basicity amines with 5-phenyltetrazol-2-ylacetyl chloride it was possible the extend this strategy to the synthesis of the amides from bifunctional amines. As model bifunctional amines we used diazo-18-crown-6 (having sterically blocked amino groups) and 3,4-diaminofurazan, which contains amino groups with reduced nucleophilicity [8]. The above-mentioned amines were acylated with a twofold molar excess of the acid chloride **1**. In both cases we obtained the products from exhaustive substitution, i.e., N,N'-bis(5-phenyltetrazol-2-ylacetyl)-1,4,10,13-tetraoxa-7,16-diazacyclo-octadecane (**15**) and N,N'-bis(5-phenyltetrazol-2-ylmethylcarbonyl)-3,4-diaminofurazan (**16**).



While continuing this direction of investigation, we attempted the exhaustive acylation of hydrazine. However, during the reaction in THF we only isolated the monosubstitution product. For this reason it was necessary to use more rigorous conditions and to use boiling toluene, in which the monosubstitution product formed at the first stage of acylation is readily soluble. Under these conditions exhaustive acylation is complete in 10 h (monitored by TLC) with the formation of N,N'-bis(5-phenyltetrazol-2-ylmethylcarbonyl)-1,2-hydrazine (**17**).



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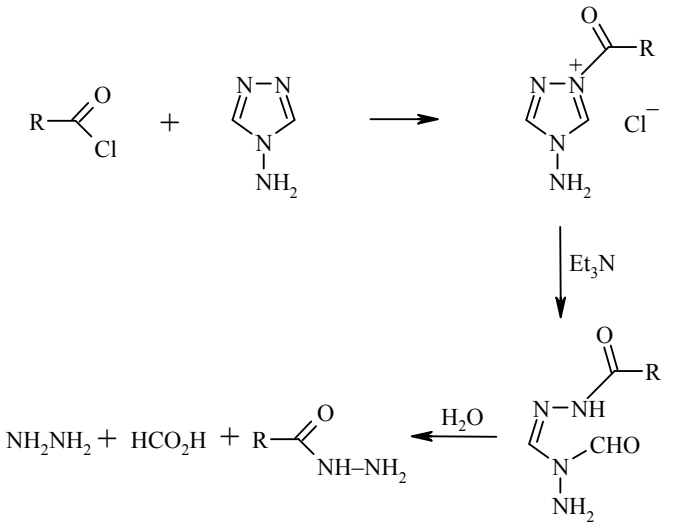
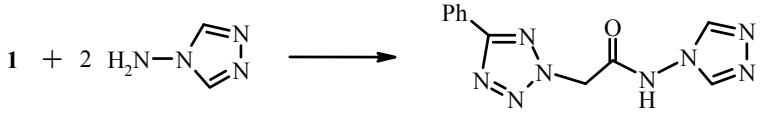
Unfortunately, we were unable to obtain the amide **13** by this method. Analysis of the published data showed that quaternary 1,2,4-triazolium salts are formed during the acylation of 4-amino-1,2,4-triazole with carboxylic acid chlorides used in equimolar amounts. With the addition of a base (such as triethylamine) these salts undergo cleavage of the triazole ring [9].



We used 4-amino-1,2,4-triazole itself as base for the acylation of 4-amino-1,2,4-triazole at the amino group. N-(1,2,4-Triazol-2-yl)-5-phenyltriazol-2-ylacetamide (**13**) was isolated as a result of the reaction.



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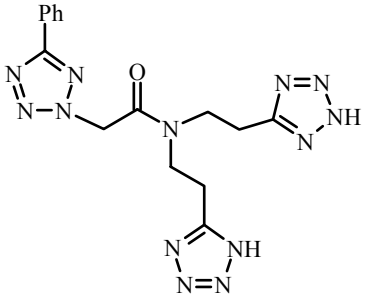
Thus, acylation with 5-phenyltetrazol-2-ylacetyl chloride takes place readily both with highly basic amines containing branched substituents and with low-basicity amines. At the same time it was not possible to acylate N,N-diphenylamine with the acid chloride (**1**). Steric hindrances probably play a significant role in this case [10].

The tetrazolylacetamides, which have become accessible as a result of the present investigation, in turn open up the way to further functionalization with the production of polynuclear tetrazoles. Thus, the corresponding tritetrazole **18** was obtained from the amide **3** containing two cyanoethyl groups.



18

It is interesting that an attempt at the production of the tritetrazole **18** using the cycloaddition [11] of dimethylammonium azide to the dinitrile **3** in DMF did not lead to the desired result. We therefore used the recently proposed conditions [12] (azidization with triethylammonium azide in toluene) for the preparation of the tritetrazole **18**. By optimizing these conditions it was possible to reduce the temperature of the process from 110 to 95°C and to shorten the reaction time from 24 to 6 h (monitored by TLC).

TABLE 1. The ^{1}H NMR Spectra of the Amides **2-18**

Compound	Chemical shifts of signals, δ, ppm (*J*, Hz)		
	$C_{(5)}$–C_6H_5 (m)	$N_{(2)}$–CH_2 (s) [NH (s)]	Other signals
2	8.09-8.07 (2H), 7.60-7.54 (3H)	5.91	3.43 (2H, q, *J* = 7.0, CH_2); 3.31 (2H, q, *J* = 7.0, CH_2); 1.20 (3H, t, *J* = 6.9, CH_3); 1.05 (3H, t, *J* = 6.9, CH_3)
3	8.09-8.07 (2H), 7.60-7.55 (3H)	6.10	3.83 (2H, t, *J* = 6.9, CH_2); 3.63 (2H, t, *J* = 6.9, CH_2); 3.03 (2H, t, *J* = 6.9, CH_2); 2.78 (2H, t, *J* = 6.9, CH_2)
4	8.09-8.06 (2H), 7.60-7.56 (3H)	5.95	3.48-3.43 (4H, m, CH_2); 1.61 (4H, s, CH_2); 1.48 (2H, s, CH_2)
5	8.09-8.06 (2H), 7.61-7.53 (3H)	5.99	3.69 (2H, t, *J* = 4.4, CH_2); 3.61 (2H, t, *J* = 4.4, CH_2); 3.54 (2H, t, *J* = 4.4, CH_2); 3.47 (2H, t, *J* = 4.4, CH_2)
6	8.08-8.06 (2H), 7.60-7.55 (3H)	6.01	4.08 (2H, q, *J* = 7.2, CH_2); 3.54-3.47 (6H, m, CH_2); 3.42-3.40 (2H, m, CH_2); 1.20 (3H, t, *J* =7.0, CH_3)
7	8.10-8.08 (2H), 7.61-7.55 (3H)	5.77 [10.64]	7.61-7.55 (2H, m, CONH-C_6H_5); 7.35 (2H, t, *J* = 7.1 Hz, CONH-C_6H_5); 7.11 (1H, t, *J* = 7.0 Hz, CONH-C_6H_5)
8	8.11-8.07 (2H), 7.60-7.52 (3H)	5.87 [11.25]	8.25 (2H, d, *J* = 9.5, CH); 7.84 (2H, d, *J* = 8.7, CH)
9	8.11-8.07 (2H), 7.60-7.53 (3H)	5.84 [11.11]	8.58 (1H, s, CH); 7.98-7.90 (2H, m, CH); 7.65 (1H, t, *J* = 8.4, CH)
10	8.11-8.09 (2H), 7.60-7.55 (3H)	5.90 [10.92]	8.01 (1H, d, *J* = 7.0, CH); 7.76 (2H, d, *J* = 7.0, CH); 7.45 (1H, *J* = 5, CH)
11	8.11-8.08 (2H), 7.61-7.55 (3H)	5.92 [11.57]	8.82 (2H, d, *J* = 2.2, CH); 8.56 (1H, t, *J* = 2.0, CH)
12	8.10-8.01 (2H), 7.61-7.51 (3H)	5.57 [9.01]	7.40-7.31 (4H, m, CH-C_6H_5); 7.30-7.22 (1H, m, CH-C_6H_5); 4.94 (1H, q, *J* = 7.2, CH); 1.41 (3H, d, *J* = 7.2, CH_3)
13	8.13-8.03 (2H), 7.63-7.52 (3H)	5.86 [12.30]	8.76 (2H, s, in triazole)
14*	8.18-8.11 (2H), 7.59-7.50 (3H)	5.95 [10.40]	2.39 (3H, s, CH_3)
15	8.09-8.04 (4H), 7.58-7.52 (6H)	5.95 (4H)	3.80-3.54 (24H, m, CH_2)
16	8.16-8.03 (4H), 7.65-7.49 (6H)	5.89 (4H) [11.24 (2H)]	—
17	8.12-8.03 (4H), 7.61-7.51 (6H)	5.68 (4H) [10.92 (2H)]	—
18	8.12-8.03 (2H), 7.60 7.53 (3H)	5.99	17.1-12.8 (2H, br. s, CN_4H); 3.87 (2H, t, *J* = 6.9, CH_2); 3.69 (2H, t, *J*=6.9, CH_2); 3.37 (2H, t, *J* = 6.9, CH_2); 3.16 (2H, t, *J* = 6.9, CH_2)

* The ^{1}H NMR spectrum of compound **14** was recorded in acetone-d_6, and the spectra of the other compounds were recorded in DMSO-d_6.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra of the synthesized amides were recorded on a Bruker DPX-300 instrument (300 MHz for ^{1}H and 75 MHz for ^{13}C) with DMSO-d_6 as internal standard. The IR spectra were obtained on a Perkin-Elmer Spectrum 1000 instrument for tablets with potassium bromide. Elemental analysis was performed on a semiautomatic Hewlett-Packard 185 C,H,N analyzer. The melting points were determined on a PTP instrument at 1 deg/min in the melting range. The reaction was monitored by TLC on Merck Kieselgel 60F_{245} plates with development in UV light.

TABLE 2. The ^{13}C NMR Spectra of the Amides **2-18**

Compound	Chemical shifts, δ, ppm				
	CH_2–C=O	CN_4	C_6H_5	$N_{(2)}$–CH_2	Other signals
2	163.9	163.4	130.5, 129.3, 126.9, 126.3	53.9	13.9 (CH_2), 12.7 (CH_3)
3	165.2	164.1	130.6, 129.3, 126.8, 126.3	53.9	118.8 (C≡N), 42.4 (CON–CH_2), 41.5 (CON–CH_2), 16.6 (CH_2–CN), 15.2 (CH_2–CN)
4	163.9	162.6	130.5, 129.3, 126.9, 126.2	54.0	45.3, 42.5, 25.7, 25.1, 23.7 (CH_2)
5	164.0	163.3	130.5, 129.3, 126.9, 126.2	53.9	65.8 (CH_2–O–CH_2), 44.8, 41.9 (CH_2)
6	164.0	163.4	130.6, 129.3, 126.9, 127.3	54.0	154.6 (CO–O), 61.0 (CH_2), 44.1, 43.1, 42.9, 41.3 (CH_2), 14.5 (CH_3)
7	164.2	162.9	130.6, 139.3, 126.8, 126.3	55.3	138.2, 128.9, 124.0, 119.3 (NH–C_6H_5)
8	164.3	164.1	130.7, 129.3, 126.7, 126.4	55.5	144.2 (C–NO_2), 142.8 (CONH–C), 125.1 (CH–C–NO_2), 119.2 (CONH–C–CH)
9	164.3	163.8	130.6, 129.3, 126.7, 126.3	55.3	139.2, 130.2, 125.3, 118.5, 113.5 (C in the substituent)
10	164.3	163.7	130.6, 129.3, 126.7, 126.4	55.0	142.5, 134.1, 130.1, 126.1, 125.7, 125.1 (C in the substituent)
11	164.5	163.7	130.7, 130.2, 126.7, 126.4	55.4	155.8, 151.5, 148.3, 140.1, 118.8, 113.2 (C in the substituent)
12	164.1	163.2	130.6, 129.3, 126.9, 126.3	54.8	143.9, 128.3, 126.0 (CH–C_6H_5), 48.5 (CH), 22.4 (CH_3)
13	164.6	164.4	130.8, 129.4, 126.6, 126.4	53.4	143.4 ($C_{(3)}$ and $C_{(5}$ in tetrazole)
14*	165.9	164.9	131.3, 129.9, 128.3, 127.4	55.6	151.2, 149.2 ($C_{(3)}$ and $C_{(4)}$ in furazan), 8.9 (CH_3)
15	164.9	163.9	130.5, 129.2, 126.9, 126.3	54.1	70.1, 70.0, 69.4, 69.3, 68.4, 68.3, 49.5, 48.1 (C in the substituent)
16	164.3	164.1	130.7, 129.4, 126.7, 126.4	54.8	152.2 ($C_{(3)}$ and $C_{(4)}$ and furazan)
17	165.1	163.9	131.6, 130.2, 127.6, 127.2	54.2	—
18	164.8	164.1	130.6, 129.3, 126.9, 126.3	54.0	153.7 ($C_{(5)}$ in tetrazole), 43.6 (CON–CH_2), 42.4 (CON–CH_2), 22.4 (CH_2–$C_{(5)}$), 21.2 (CH_2–$C_{(5)}$)

*The NMR spectra of compound **14** were recorded in acetone-d_6, and the others in DMSO- d_6.

5-Phenyltetrazol-2-ylacetyl Chloride (1). A mixture of 5-phenyltetrazol-2-ylacetic acid (6 g, 30 mmol) and phosphorus pentachloride (6.75 g, 32 mmol) was heated at 100°C until homogeneous with the formation of a colorless solution. To the hot solution we added 75 ml of boiling hexane. As the solution cooled colorless crystals were formed. The suspension was filtered, and the acid chloride was crystallized from hexane. We obtained 6.43 g (96%) of compound **1**; mp 103-104°C. ^{1}H NMR spectrum, δ, ppm: 8.17-8.14 (2H, m, C_6H_5); 7.53-7.49 (3H, m, C_6H_5); 5.84 (2H, s, $N_{(2)}$–CH_2). ^{13}C NMR spectrum, δ, ppm: 166.5 (C=O), 166.2 (CN_4), 131.0, 129.2, 127.2, 126.6 (C_6H_5), 60.7 ($N_{(2)}$–CH_2). IR spectrum, ν, cm^{-1}: 1777 (C=O), 2985, 2945 (C–H), 1450, 1278, 1148, 1073, 1022, 933 (vibration of the tetrazole ring), 729, 688 (C_6H_5). Found, %: C 48.31; H 3.20; N 25.60. $C_9H_7ClN_4O$. Calculated, %: C 48.55; H 3.17; N 25.17.

Preparation of Tetrazolylacetamides 2-12. (General Procedure). To a solution of the substrate **1** (10 mmol) in ether (chloroform or THF) (50 ml) at 0-2°C with stirring we added the amine (10 mmol) in ether (chloroform or THF) (20 ml) and triethylamine (10 mmol) in the same solvent (10 ml). An exothermic effect was observed during the reaction. After 1-2 h at room temperature the solvent was evaporated under vacuum, and the residue was washed with distilled water (3×20 ml) and crystallized from the respective solvent or solvent system.

Diethylamide of 5-Phenyltetrazol-2-ylacetic Acid (2). By crystallization from 50% ethanol we obtained 1.25 g (48%) of the amide **2**; mp 98-99°C. R_f 0.74 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1658 (C=O), 2982, 2936 (C–H), 1425, 1269, 1205, 1144, 1100, 1073, 1023 (vibration of the tetrazole ring), 730, 690 (C_6H_5). Found, %: C 60.57; H 6.97; N 27.34. $C_{13}H_{17}N_5O$. Calculated, %: C 60.21; H 6.61; N 27.01.

Bis(2-cyanoethyl)amide of 5-Phenyltetrazol-2-ylacetic Acid (3). By crystallization from 2-propanol we obtained 2.25 g (73%) of the amide **3**; mp 162-163°C. R_f 0.54 (95:5 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1672 (C=O), 2999 (C–H), 1435, 1261, 1203, 1177, 1072, 1027 (vibration of the tetrazole ring), 729, 692 (C_6H_5), 2252 (C≡N). Found, %: C 58.28; H 4.59; N 32.03. $C_{15}H_{15}N_7O$. Calculated, %: C 58.24; H 4.89; N 31.70.

Piperidide of 5-Phenyltetrazol-2-ylacetic Acid (4). By crystallization from ethanol we obtained 1.32 g (42%) of the amide **4**; mp 178-179°C. R_f 0.76 (95:5 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1662, 1649 (C=O), 2987, 2939, 2857 (C–H), 1425, 1254, 1230, 1138, 1097, 1030 (vibration of the tetrazole ring), 728, 691 (C_6H_5). Found, %: C 62.25; H 5.67; N 25.47. $C_{14}H_{17}N_5O$. Calculated, %: C 61.98; H 6.32; N 25.81.

Morpholide of 5-Phenyltetrazol-2-ylacetic Acid (5). By crystallization from 25% ethanol we obtained 0.71 g (26%) of the amide **5**; mp 178-179°C. R_f 0.62 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1667, 1651 (C=O), 2986, 2944, 2851 (C–H), 1426, 1241, 1200, 1157, 1120, 1072, 1020 (vibration of the tetrazole ring),729, 691 (C_6H_5), 1273 (C–O–C). Found, %: C 57.27; H 5.23; N 25.93. $C_{13}H_{15}N_5O_2$. Calculated, %: C 57.13; H 5.53; N 25.63.

N'-Ethoxycarbonylpiperazide of 5-Phenyltetrazol-2-ylacetic Acid (6). By crystallization from 50% 2-propanol we obtained 1.24 g (40%) of the amide **6**; mp 132-133°C. R_f 0.72 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1672, 1665 (N–C=O), 1730 (O–C=O), 2993, 2932, 2874 (C–H), 1421, 1254, 1210, 1154, 1090, 1071, 1027 (vibration of the tetrazole ring), 732, 694 (C_6H_5). Found, %: C 56.70; H 5.41; N 25.03. $C_{16}H_{20}N_6O_3$. Calculated, %: C 55.80; H 5.85; N 24.40

Anilide of 5-Phenyltetrazol-2-ylacetic Acid (7). By crystallization from 60% 2-propanol we obtained 2.95 g (70%) of the amide **7**; mp 189-190°C. R_f 0.28 (chloroform). IR spectrum, ν, cm^{-1}: 1672 (C=O), 2998, 2954, 2851 (C–H), 3440, 3275 (NH), 1447, 1255, 1204, 1140, 1072, 1027 (vibration of the tetrazole ring), 730, 692 (C_6H_5). Found, %: C 65.03; H 5.18; N 25.17. $C_{15}H_{13}N_5O$. Calculated, %: C 64.51; H 4.61; N 25.07.

***p*-Nitroanilide of 5-phenyltetrazol-2-ylacetic Acid (8).** By crystallization from 50% ethanol we obtained 2.14 g (66%) of the amide **8**; mp 211-212°C. R_f 0.8 (95:5 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1694 (C=O), 3336 (NH), 2990, 2930, 2845 (C–H), 1555, 1512, 1345 (NO_2), 1448, 1252, 1192, 1150, 1109, 1069, 1023 (vibration of the tetrazole ring), 729, 688 (C_6H_5), 844 (1,4-disubstituted benzene). Found, %: C 55.77; H 3.58; N 26.10. $C_{15}H_{12}N_6O_3$. Calculated, %: C 55.56; H 3.73; N 25.91.

***m*-Nitroanilide of 5-Phenyltetrazol-2-ylacetic Acid (9).** By crystallization from 50% ethanol we obtained 2.53 g (78%) of the amide **9**; mp 217-218°C. R_f 0.70 (95:5 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1686 (C=O), 3330 (NH), 3000, 2943, 2840 (C–H), 1551, 1529, 1355 (NO_2), 1450, 1255, 1207, 1150, 1104, 1072, 1021 (vibration of the tetrazole ring), 729, 689 (C_6H_5), 801 (1,3-disubstituted benzene). Found, %: C 55.32; H 4.00; N 26.28. $C_{15}H_{12}N_6O_3$. Calculated, %: C 55.56; H 3.73; N 25.91.

***o*-Nitroanilide of 5-Phenyltetrazol-2-ylacetic Acid (10).** By crystallization from 50% ethanol we obtained 2.31 g (71%) of the amide **10**; mp 196-197°C. R_f 0.85 (95:5 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1718 (C=O), 3293 (NH), 2995, 2950, 2860 (C–H), 1560, 1520, 1353 (NO_2), 1450, 1269, 1203, 1149, 1098, 1073, 1020 (vibration of the tetrazole ring), 730, 689 (C_6H_5), 743 (1,2-disubstituted benzene). Found, %: C 55.21; H 4.06; N 25.80. $C_{15}H_{12}N_6O_3$. Calculated, %: C 55.56; H 3.73; N 25.91.

3,4-Dinitroanilide of 5-Phenylthiazol-2-ylacetic Acid (11). By crystallization from 50% ethanol we obtained 2.52 g (68%) of the amide **11**; mp 218-219°C. R_f 0.40 (95:5 chloroform–ethanol). IR spectrum, ν, cm^{-1}: 1713 (C=O), 3361 (NH), 2994, 2948, 2843 (C–H), 1550, 1536, 1346 (NO_2), 1452, 1261, 1199, 1147, 1109, 1076, 1025 (vibration of the tetrazole ring), 727, 685 (C_6H_5), 828, 787 (1,3,5-trisubstituted benzene). Found, %: C 48.27; H 2.91; N 26.34. $C_{15}H_{11}N_7O_5$. Calculated, %: C 48.79; H 3.00; N 26.55.

N-(1-Phenylethyl)amide of 5-Phenyltetrazol-2-ylacetic Acid (12). By crystallization from 70% 2-propanol we obtained 2.0 g (65%) of the amide **12**; mp 169-170°C. R_f 0.63 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1657 (C=O), 3270 (NH), 2990, 2947 (C–H), 1448, 1247, 1205, 1100, 1043, 1026 (vibration of the tetrazole ring), 1385 (C–N), 731, 692 (C_6H_5). Found, %: C 66.64; H 5.73; N 22.55. $C_{17}H_{17}N_5O$. Calculated, %: C 66.43; H 5.57; N 22.79.

N-(1,2,4-Triazol-4-yl)amide of 5-Phenyltetrazol-2-ylacetic Acid (13). During the synthesis of this amide 4-amino-1,2,4-triazole, taken in a 2:1 molar ratio in relation to the acid chloride **1**, was used instead of triethylamine. By crystallization from 50% ethanol we obtained 1.83 g (68%) of the amide **13**; mp 216-217°C. IR spectrum, ν, cm^{-1}: 1722 (C=O), 3120 (NH), 2994, 2950 (C–H), 1451, 1260, 1200, 1173, 1071, 1044 (vibration of the tetrazole ring), 1359 (C–N), 734, 694 (C_6H_5). Found, %: C 48.93; H 4.09; N 41.46. $C_{11}H_{10}N_8O$. Calculated, %: C 48.89; H 3.73; N 41.46.

N-(4-Methylfurazan-3-yl)amide of 5-Phenyltetrazol-2-ylacetic Acid (14). By crystallization from 50% 2-propanol we obtained 2.02 g (71%) of the amide **14**; mp 190-191°C. R_f 0.36 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1704 (C=O), 3273 (NH), 2996, 2953 (C–H), 1448, 1252, 1200, 1155, 1100, 1043, 1024 (vibration of the tetrazole ring), 1388 (C–N), 727, 686 (C_6H_5). Found, %: C 50.27; H 3.64; N 34.64. $C_{12}H_{11}N_7O_2$. Calculated, %: C 50.53; H 3.89; N 34.37.

N,N'-Bis(5-phenyltetrazol-2-ylacetyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadodecane (15). During the synthesis of this amide we used compound **1** (20 mmol) in chloroform (100 ml) and triethylamine (20 mmol) in chloroform (20 ml). By crystallization from ethanol we obtained 3.0 g (47%) of the diamide **15**; mp 183-184°C. R_f 0.68 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1665 (C=O), 3004, 2959, 2856 (C–H), 1450, 1249, 1203, 1140, 1110 1090, 1029 (vibration of the tetrazole ring), 1296, 1050 (C–O–C), 1336, 1029 (C–N), 730, 696 (C_6H_5). Found, %: C 57.42; H 6.01; N 22.27. $C_{30}H_{38}N_{10}O_6$. Calculated, %: C 56.77; H 6.03; N 22.07.

N,N'-Bis(5-phenyltetrazol-2-ylmethylcarbonyl)-3,4-diaminofurazan (16). During the synthesis of this amide we used compound **1** (20 mmol) in THF (100 ml) and triethylamine (20 mmol) in THF (20 ml). By crystallization from 50% ethanol we obtained 5.34 g (62%) of the amide **16**; mp 196°C (decomp.). R_f 0.46 (9:1 chloroform–methanol). IR spectrum, ν, cm^{-1}: 1698 (C=O), 3000, 2948 (C–H), 1449, 1246, 1200, 1142, 1104, 1046, 1026 (vibration of the tetrazole ring), 1353 (C–N), 730, 690 (C_6H_5). Found, %: C 50.21; H 3.83; N 36.06. $C_{20}H_{16}N_{12}O_3$. Calculated, %: C 50.85; H 3.41; N 35.58.

N,N'-Bis(5-phenyltetrazol-2-ylmethylcarbonyl)-1,2-hydrazine (17). To a solution of the acid chloride **1** (4.7 g, 21 mmol) in toluene (100 ml) at 0-2°C with stirring we added hydrazine hydrate (0.5 g, 10 mmol) in toluene (10 ml) and triethylamine (2.02 g, 20 mmol) in toluene (10 ml). The reaction mixture was boiled for 10 h on a salt bath, the solvent was evaporated under vacuum, and the residue was washed with

distilled water (3×20 ml) and crystallized from aqueous DMF. We obtained 1.66 g (41%) of the hydrazine **17**; mp 246-248°C. IR spectrum, ν, cm^{-1}: 1629 (C=O), 3217 (NH), 3001, 2994 (C–H), 1449, 1232, 1140, 1060, 1029 (vibration of the tetrazole ring), 1399 (C–N), 729, 689 (C_6H_5). Found, %: C 52.83; H 4.48; N 34.24. $C_{18}H_{16}N_{10}O_2$. Calculated, %: C 53.46; H 3.99; N 34.64.

N,N'-Bis[2-(tetrazol-5-yl)ethyl]amide of 5-Phenyltetrazol-2-ylacetic Acid (18). To a suspension of compound **3** (1 g, 3.2 mmol) in toluene (100 ml) we added triethylamine hydrochloride (2.67 g, 19.2 mmol) and sodium azide (1.26 g, 19.2 mmol). The mixture was stirred at 98-100°C for 5 h, cooled to room temperature, and washed with water (3×70 ml). The aqueous layer was separated and acidified to pH 1-2 with concentrated hydrochloric acid. The precipitate was filtered off and crystallized from ethanol. We obtained 0.9 g (70%) of the tetrazole **18**; mp 124-126°C. IR spectrum, ν, cm^{-1}: 1631 (C=O), 1453, 1238, 1100, 1066 (vibration of the tetrazole ring), 3428 (NH-tetrazole), 1379 (C–N), 731, 693 (C_6H_5). Found, %: C 45.12; H 4.65; N 45.65. $C_{15}H_{17}N_{13}O$. Calculated, %: C 45.57; H 4.33; N 46.05.

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