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POLYNUCLEAR BRANCHED TETRAZOLE SYSTEMS. 2*. NEW 2-(5-TETRAZOLYL)ETHYL PODANDS AND THEIR NH-ACIDITY

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Nine new polynuclear 2-(5-tetrazolyl)ethyl podands have been obtained by the azidation of the corresponding nitriles. Using Bjerrum distribution functions, the values of pK_a^1, pK_a^2, pK_a^3, and pK_a^4 have been determined by a potentiometric method for 14 polynuclear tetrazoles in aqueous and aqueous methanolic solution. The found values lie in the range from 3.5 to 7.5 pH units. The overall rules and the sequence of the ionization of the spatially separated tetrazole fragments in these podand systems are discussed.

Keywords: polynuclear NH-tetrazoles, acidity, multistep ionization, Bjerrum function.

Previously we reported the synthesis of a series of podand (polydentate ligand) systems containing from two to four 2-(5-tetrazolyl)ethyl fragments in one molecule [1]. The molecular structure and physicochemical properties of these tetrazole podands enabled their high complex-forming activity in relation to metal ions to be predicted [1,2]. Efficient filtering materials based on these complexones have been developed recently for the thorough purification of biological fluids from heavy metals and radionuclides [3]. In connection with the above the urgent problem is the extension of the series of 2-(5-tetrazolyl)ethyl podands and also a more detailed investigation of those physicochemical properties of these compounds which will determine their complex-forming activity.

In the present work we have synthesized nine new polynuclear NH-tetrazoles, differing both in the number of tetrazole groups and in the chain length separating these terminal fragments. Values of pK_a^1, pK_a^2, pK_a^3, and pK_a^4 were determined by a potentiometric method in aqueous and aqueous methanolic solution for the polynuclear tetrazoles described previously in [1] and for those obtained for the first time in the present work.

Tetrazoles **1-8** were synthesized by the general procedure of [1] by 1,3-dipolar cycloaddition of dimethylammonium azide to the appropriate nitrile*[2]. Hydrolysis of the ester groups of the previously reported ditetrazole **11** leads to the corresponding tetrabasic derivative of malonic acid **9**. The initial nitriles were obtained by the Michael addition [4-7] of the appropriate CH, OH, and NH acids to acrylonitrile (see Experimental). The structure of the nitriles and of the corresponding tetrazoles was demonstrated by a set of physicochemical methods.

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* For Part 1 see [1].

*[2] Tritetrazole **2** was synthesized by the azidation of 3-cyano-3-ethoxycarbonylpimelonitrile with simultaneous decarboxylation of the ester group.

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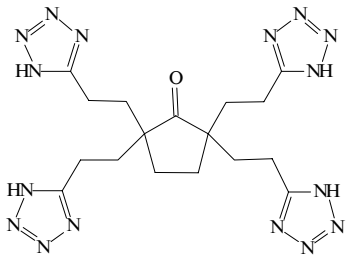

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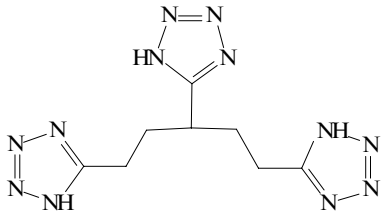

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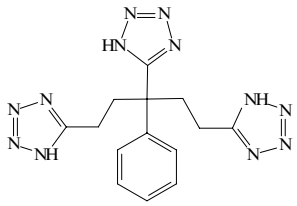

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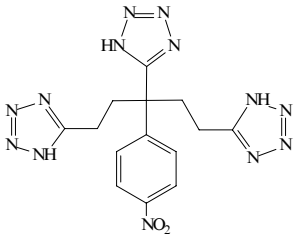

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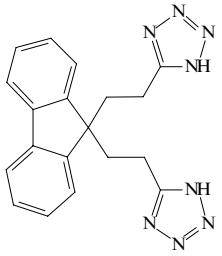

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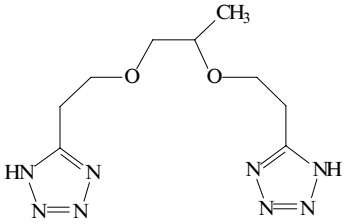

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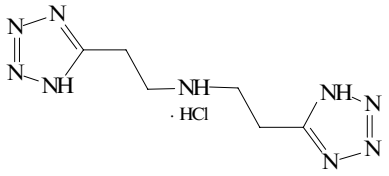

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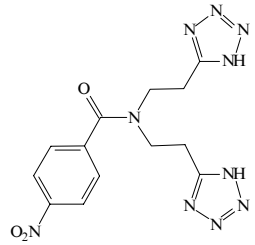

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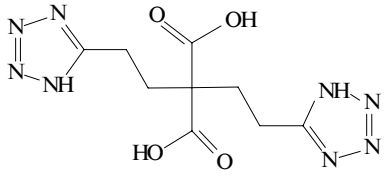

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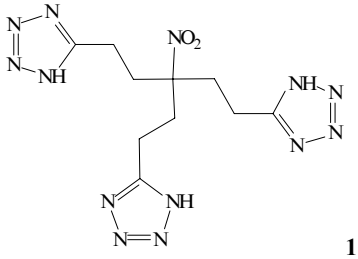

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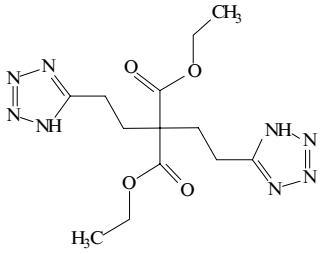

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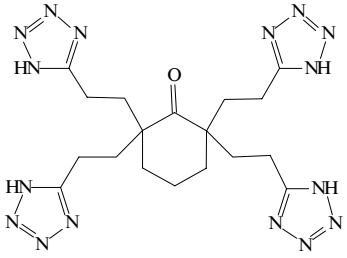

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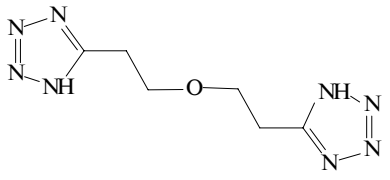

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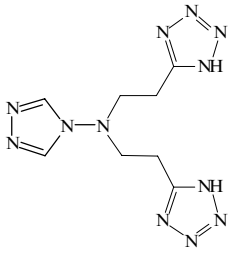

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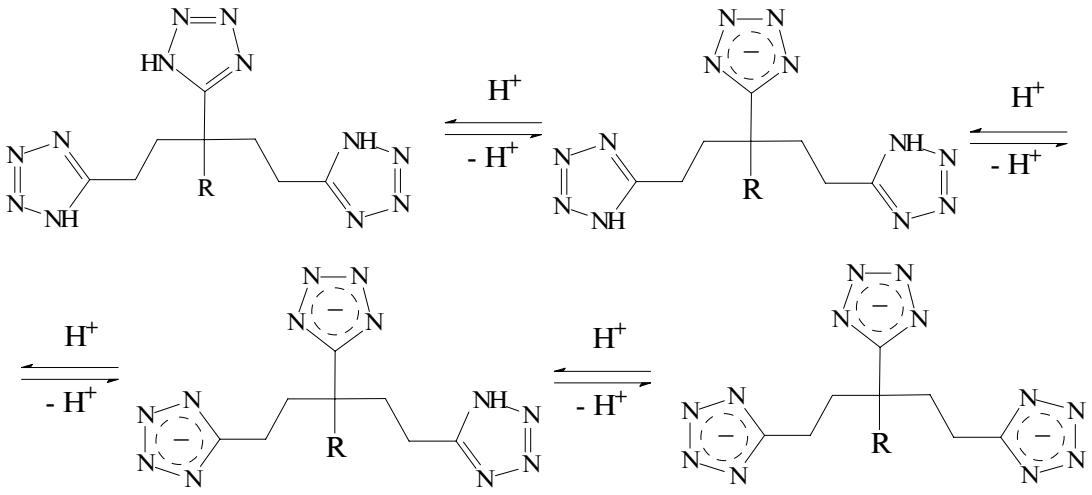
One of the properties allowing assessment of the ability of these compounds to form complexes is acidity. Potentiometric titration of compounds **1-14** was carried out in aqueous and aqueous methanolic (when the water solubility was limiting) solution under conditions of constant ionic strength (0.1 N sodium nitrate solution). Processing of the titration curves for dihydric acids was carried out by an algebraic method [8], and in the case of tri- and tetrahydric acids the characteristics of the acid dissociation constants were calculated using a distribution function (Bjerrum's method) [9,10]. The values calculated in this way for the acid dissociation constants of tetrazoles **1-14** are given in Table 1. The values of pK_a of both the first and second dissociation stages of tetrazoles **7** and **13**, determined in the present work, agreed within the limits of permissible error with those obtained previously by Latosh and coworkers [11].

Since the pK_a values of tetrazoles **1-14** given in Table 1 characterize equilibria in different media it is difficult to compare them quantitatively [12]. Nonetheless certain generalized qualitative tendencies of the changes in acid dissociation constants may become apparent depending on the various gradations of structure of the podand system as a whole. Extremely significant in the present case is the comparison not so much of absolute values of pK_a, as more of a comparison of the differences (Δ^n) between the size of pK_a^{n+1} and pK_a^n (see Table 1). For all the studied compounds the values Δ^1, Δ^2, and Δ^3 are significantly greater than statistical (the difference in the values of pK_a^{n+1} and pK_a^n in the absence of a mutual electronic influence of the acid dissociation centers) [13,14]. This indicates that the terminal tetrazole fragments appreciably influence one another, even at significant mutual separation (five and more sp^3-hybridized carbon atoms). Usually the values of Δ^n lie in the range from 0.6 to 1.6 log. units. The exceptions are the ditetrazolylamine **7** and the ditetrazolylmalonic acid **9**, the values for which were appreciably greater and reached 4.6 log. units. This is explained by the different nature of the ionized fragments (tetrazolyl, ammonium, and carboxyl). It may also be mentioned that for compounds **2-4** the values of Δ^1 were significantly greater than those of all the remaining polytetrazoles investigated. This observation indicates that the tetrazole ring located at the tertiary carbon atom dissociates first.



2 R = H, **3** R = Ph, **4** R = 4-$O_2NC_6H_4$

TABLE 1. Acid Dissociation Constants of Tetrazoles **1-14*** and Values of the Differences Between Them Δ^{n}*[2]

Acids*[3]	pK_a^1	pK_a^2	pK_a^3	pK_a^4	Δ^1	Δ^2	Δ^3	s*[4]
Dihydric NH-acids								
9,9-Bis[2-(5-tetrazolyl)ethyl]fluorene (**5**)	5.82±0.03	6.73±0.03			0.91			
1,2-Bis[2-(5-tetrazolyl)ethoxy]propane (**6**)	5.05±0.03	5.80±0.03			0.75			
Bis[2-(5-tetrazolyl)ethyl]amide of 4-nitrobenzoic acid (**8**)	4.54±0.04	5.57±0.05			1.03			
3,3-Bis(ethoxycarbonyl)-1,5-bis(5-tetrazolyl)pentane (**11**)	4.82±0.02	5.76±0.02			0.94			
1,5-Bis(5-tetrazolyl)-3-oxapentane (**13**)	4.63±0.02	5.67±0.03			1.04			
4-Bis[2-(5-tetrazolyl)ethyl]amino-1,2,4-triazole (**14**)	4.48±0.03	5.46±0.04			0.98			
Trihydric NH-acids								
1,3,5-Tris(5-tetrazolyl)pentane (**2**)	4.42	5.56	6.48		1.14	0.92		0.01
3-Phenyl-1,3,5-tris(5-tetrazolyl)pentane (**3**)	4.47	5.87	6.88		1.40	1.01		0.06
3-(4-Nitrophenyl)-1,3,5-tris(5-tetrazolyl)pentane (**4**)	3.85	5.43	6.32		1.58	0.89		0.02
Bis[2-(5-tetrazolyl)ethyl]amine hydrochloride (**7**)	3.58	4.30	8.91		1.72	4.61		0.04
Tris[2-(5-tetrazolyl)ethyl]nitromethane (**10**)	4.03	4.84	5.72		0.81	0.88		0.03
Tetrahydric NH-acids								
2,2,5,5-Tetrakis[2-(5-tetrazolyl)ethyl]cyclopentanone (**1**)	4.32	5.19	5.85	6.79	0.87	0.66	0.94	0.05
Bis[2-(5-tetrazolyl)ethyl]malonic acid (**9**)	3.08	5.22	6.23	8.40	2.14	1.01	2.17	0.05
2,2,6,6-Tetrakis[2-(5-tetrazolyl)ethyl]cyclohexanone (**12**)	4.82	5.75	6.35	7.32	0.93	0.60	0.97	0.03

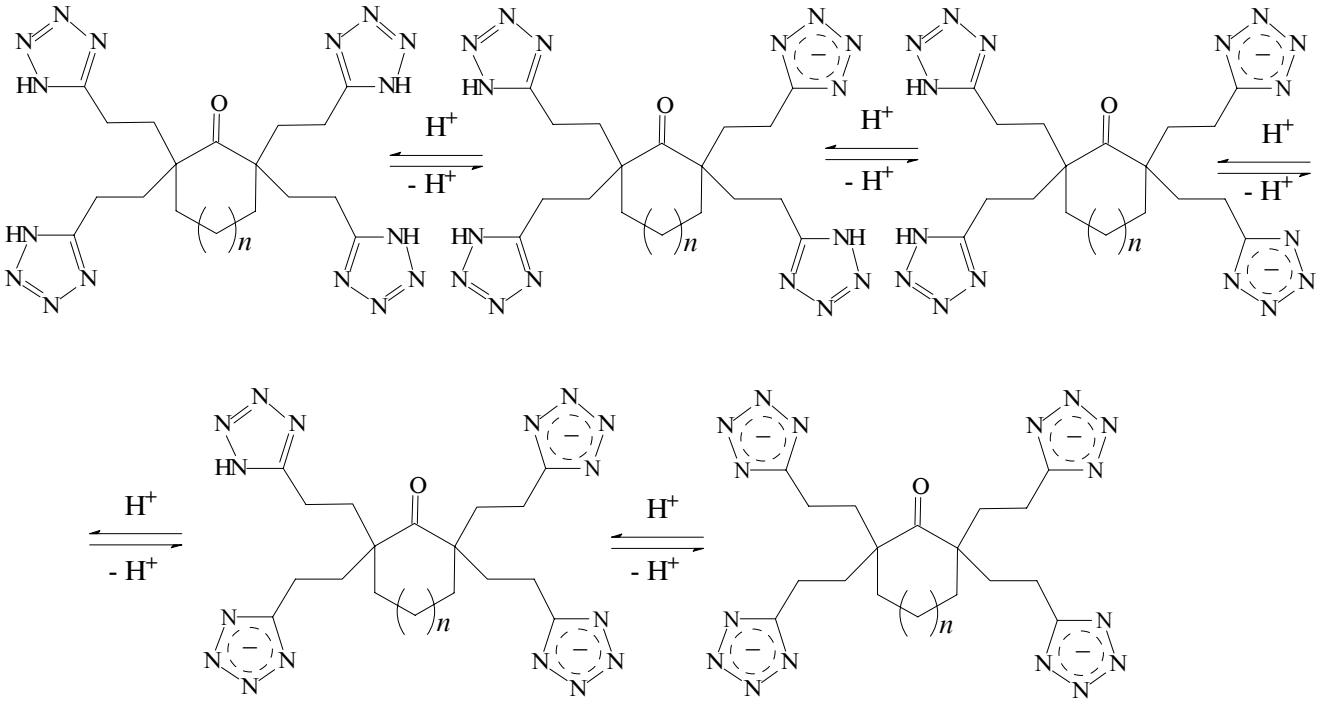
* NH-acids **2-4**, **7-11**, and **13** were titrated in 0.1 N solutions of $NaNO_3$ at 25°C, NH-acid **5** in pure methanol, solutions of NH-acids **1**, **6**, **12**, and **14** in methanol–0.1 N aqueous $NaNO_3$ solution, 50:50.

*[2] $\Delta^n = pK_a^{n+1} - pK_a^n$.

*[3] According to [11], pK_a^1 and pK_a^2 for ditetrazole **13** are 4.69 and 5.68 respectively, pK_a^1, pK_a^2, and pK_a^3 for ditetrazole **7** are 3.61, 4.32, and 8.89 respectively.

*[4] Statistical error of calculation using the distribution function.

For the tetrahydric NH-acids **1** and **12** the values of Δ^1 and Δ^3 are close to one another and significantly exceed Δ^2. Probably those NH-tetrazole rings which are spatially close to one another dissociate first and second. The dissociation of compounds **1** and **12** may be described by the following scheme.



The terminal tetrazole rings show significant mutual effects even at a distance. This may be caused by electronic, spatial, or other factors, such as hydrogen bonds [15].

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer (200 and 50 MHz respectively) in DMSO, internal standard was the signal of the solvent. The IR spectra were obtained on a Specord M-80 instrument in KBr disks. Elemental analysis was carried out on a Hewlett-Packard 185B C,H,N-analyzer. Melting points were determined on a type PTP instrument with a heating rate of 1°C/min in the melting range. Potentiometric titration was carried out on a pH 121 potentiometer (electrodes: glass EVL-1M3, silver chloride ESL-63-07T4.1). All potentiometric measurements were carried out at 25°C in solutions of constant ionic strength (0.1 N sodium nitrate solution).

The synthesis and physicochemical characteristics of tetrazoles **10-14** and of their nitrile precursors are given in [1].

2,2,5,5-Tetrakis(2-cyanoethyl)cyclopentanone. Acrylonitrile (13.25 g, 250 mmol) was added dropwise with cooling to a mixture of cyclopentanone (4.2 g, 50 mmol), benzyltriethylammonium chloride (0.1 g, 0.5 mmol), and NaOH (0.02 g, 0.5 mmol) in 1,4-dioxane (30 ml) and water (2 ml) at such a rate that the temperature of the reaction mixture did not exceed 40-45°C. The reaction mass was kept at room temperature for 2 h, neutralized with dilute hydrochloric acid, the precipitated crystals were filtered off, washed with water, and dried. The corresponding tetranitrile (13.6 g, 92%) was obtained as colorless crystals; mp 174-175°C (acetone). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.80 (12H, s, 2β-CH_2 in cyclopentanone and 4C$\underline{H}_2$CH_2CN);

2.32 (8H, t, J = 14.6, $CH_2C{\equiv}N$). ^{13}C NMR spectrum, δ, ppm: 213.5 (C=O); 120.7 (C≡N); 49.7 (C_{quat}); 29.1 (β-CH_2 in cyclopentanone); 28.1 ($\underline{C}H_2CH_2C{\equiv}N$); 11.6 ($\underline{C}H_2C{\equiv}N$). IR spectrum, ν, cm^{-1}: 2445 (C≡N), 1680 (C=O), 1550, 1460. Found, %: C 68.68; H 7.12; N 18.74. $C_{17}H_{20}N_4O$. Calculated, %: C 68.89; H 6.80; N 18.90.

Attention. In view of the highly exothermal nature of the cyanoethylation reaction rapid addition of acrylonitrile may lead to strong initial heating and ejection of the reaction mass.

3-Cyano-3-ethoxycarbonylpimelonitrile. Acrylonitrile (13.25 g, 250 mmol) was added dropwise with cooling to a mixture of ethyl cyanoacetate (13.4 g, 100 mmol), benzyltriethylammonium chloride (0.1 g, 0.5 mmol), and NaOH (0.02 g, 0.5 mmol) in 1,4-dioxane (50 ml) and water (2 ml), at such a rate that the temperature of the reaction mass did not exceed 40-45°C. The reaction mass was kept at room temperature for 1 h, neutralized with dilute hydrochloric acid, and poured into water (200 ml) cooled to 5°C. The oily liquid insoluble in water was separated and dried in vacuum. The corresponding trinitrile (20.62 g, 86%) was obtained as colorless crystals; mp 36-37°C (ethanol). ^1H NMR spectrum, δ, ppm (J, Hz): 1.25 (3H, t, J = 7.3, CH_3 in OEt); 2.25 (4H, t, J = 7.3, $CH_2C{\equiv}N$); 2.65 (4H, t, J = 7.3, $C\underline{H}_2CH_2C{\equiv}N$); 4.22 (2H, q, J = 7.3, CH_2 in OEt). ^{13}C NMR spectrum, δ, ppm: 166.6 (C=O); 119.0 and 119.5 (C≡N); 63.4 (CH_2 in OEt); 47.6 (C_{quat}); 30.9 ($\underline{C}H_2CH_2C{\equiv}N$); 13.1 ($CH_2C{\equiv}N$); 13.6 ($CH_3$ in OEt). IR spectrum, ν, cm^{-1}: 2250 (C≡N), 1740, 1695 (COO), 1470, 1440, 1355. Found, %: C 60.12; H 6.08; N 18.88. $C_{11}H_{13}N_3O_2$. Calculated, %: C 60.26; H 5.98; N 19.17.

3-Cyano-3-phenylpimelonitrile. Acrylonitrile (23.85 g, 450 mmol) was added dropwise with cooling to a mixture of benzyl cyanide (11.7 g, 100 mmol), benzyltriethylammonium chloride (0.1 g, 0.5 mmol), and NaOH (0.02 g, 0.5 mmol) in 1,4-dioxane (50 ml) and water (2 ml) at such a rate that the temperature of the reaction mass did not exceed 40-45°C. The reaction mass was maintained at room temperature for 2 h, neutralized with dilute hydrochloric acid, after which the precipitated crystals were filtered off, washed with water, and dried. The corresponding trinitrile (10.5 g, 90%) was obtained as colorless needle-like crystals; mp 69-70°C (ethanol). ^1H NMR spectrum, δ, ppm (J, Hz): 2.30 (4H, t, J = 7.3, $CH_2C{\equiv}N$); 2.60 (4H, t, J = 7.3, $C\underline{H}_2CH_2C{\equiv}N$); 7.80-8.50 (5H, arom.). ^{13}C NMR spectrum, δ, ppm: 147.8, 142.5, 128.3, 124.6 (Ph); 119.3 and 119.0 (C≡N); 34.0 ($\underline{C}H_2CH_2C{\equiv}N$); 13.1 ($\underline{C}H_2C{\equiv}N$). IR spectrum, ν, cm^{-1}: 2240 (C≡N), 1630, 1475, 1450, 745. Found, %: C 75.12; H 6.03; N 18.64. $C_{14}H_{13}N_3$. Calculated, %: C 75.31; H 5.87; N 18.82.

3-Cyano-3-(4-nitrophenyl)pimelonitrile was obtained analogously to 3-cyano-3-phenylpimelonitrile from 4-nitrobenzyl cyanide (7.6 g, 47 mmol) in a yield of 7.15 g (94%) as colorless needle-like crystals; mp 147-148°C (ethanol). ^1H NMR spectrum, δ, ppm (J, Hz): 2.30 (4H, t, J = 7.3, $CH_2C{\equiv}N$); 2.60 (4H, t, J = 7.3, $C\underline{H}_2CH_2C{\equiv}N$); 7.80-8.30 (4H, arom.). ^{13}C NMR spectrum, δ, ppm: 147.8, 142.5, 128.2, 124.5 (4-$NO_2C_6H_4$); 119.5 and 119.0 (C≡N); 34.0 ($\underline{C}H_2CH_2C{\equiv}N$); 13.0 ($\underline{C}H_2C{\equiv}N$). IR spectrum, ν, cm^{-1}: 2240 (C≡N), 1630, 1525 (NO_2), 1480, 1445, 760. Found, %: C 62.43; H 4.85; N 20.72. $C_{14}H_{12}N_4O_2$. Calculated, %: C 62.68; H 4.51; N 20.88.

9,9-Bis(2-cyanoethyl)fluorene. Acrylonitrile (11.14 g, 210 mmol) was added dropwise with cooling to a mixture of fluorene (16.62 g, 100 mmol), benzyltriethylammonium chloride (0.1 g, 0.5 mmol), and NaOH (0.02 g, 0.5 mmol) in 1,4-dioxane (50 ml) and water (2 ml) at such a rate that the temperature of the reaction mass did not rise above 40-45°C. The reaction mass was maintained for 2 h at ~20°C, neutralized with dilute hydrochloric acid, the precipitated crystals were then filtered off, washed with water, and dried. The dinitrile (12.0 g, 72%) was obtained as fine long colorless needle-like crystals; mp 118-119°C (ethanol). ^1H NMR spectrum δ, ppm (J, Hz): 1.57 (4H, t, J = 7.3, CH_2CN); 2.43 (4H, t, J = 7.3, $C\underline{H}_2CH_2C{\equiv}N$); 7.30-7.90 (8H, arom.). ^{13}C NMR spectrum, δ, ppm: 145.7, 140.7, 128.4, 128.0, 123.7, 120.5 (fluorene); 119.8 (C≡N); 53.4 (C_{quat}); 33.8 ($\underline{C}H_2CH_2C{\equiv}N$); 11.7 ($\underline{C}H_2C{\equiv}N$). IR spectrum, ν, cm^{-1}: 2235 (C≡N), 1650, 1635, 1480, 1450, 780, 745. Found, %: C 83.55; H 6.18; N 10.15. $C_{19}H_{16}N_2$. Calculated, %: C 83.79; H 5.92; N 10.29.

1,2-Bis(cyanoethoxy)propane. A mixture of acrylonitrile (26.5 g, 500 mmol), 1,4-dioxane (25 ml), and 1,2-propanediol (19.02 g, 250 mmol) was stirred for 5 h at 45°C. The reaction mass was neutralized with dilute hydrochloric acid, the dioxane was distilled off in vacuum, and the residue was distilled at 178-180°C (5 mm Hg). The appropriate dinitrile (18.7 g, 41%) was obtained. ^1H NMR spectrum, δ, ppm (J, Hz): 1.09 (3H,

d, J = 5.0, CHC<u>H</u>$_3$); 2.72 (4H, t, J = 5.8, $CH_2C{\equiv}N$); 3.42 (2H, d, J = 5.0, C<u>H</u>$_2$CHCH$_3$); 3.64 (4H, t, J = 5.8, C<u>H</u>$_2$CH$_2$C≡N). ^{13}C NMR spectrum, δ, ppm: 119.4 and 119.3 (C≡N); 74.3 and 74.0 (CH_2–CH); 65.6 and 63.6 (<u>C</u>H$_2$CH$_2$C≡N); 18.7 and 18.2 (<u>C</u>H$_2$C≡N); 16.9 (CH_3). IR spectrum, ν, cm^{-1}: 2888 (CH_2), 2240 (C≡N), 1470, 1410, 1200, 1135. Found, %: C 58.96; H 7.95; N 15.12. $C_9H_{14}N_2O_2$. Calculated, %: C 59.32; H 7.74; N 15.37.

Bis(2-cyanoethyl)amine. Acrylonitrile (95 g, 1.8 mol) was added dropwise with stirring and cooling during 2 h to an aqueous solution of ammonia (950 ml, ~18 mol) saturated in the cold. The rate of addition was regulated such that a second layer was not formed and the reaction temperature did not exceed 35°C. The reaction mixture was maintained at ~20°C for a further 30 min, and the water distilled off in vacuum. The residue was fractionally distilled. 2-Aminopropionitrile (375 g, 30%) and bis(2-cyanoethyl)amine (52 g, 47%) were obtained, the latter as a viscous colorless liquid; bp 205°C (25 mm Hg). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.65 (4H, t, J = 5.0, $CH_2C{\equiv}N$); 3.60 (4H, t, J = 5.0, C<u>H</u>$_2$CH$_2$C≡N); 9.20 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 119.1 (C≡N); 64.7 (<u>C</u>H$_2$CH$_2$C≡N); 18.5 (<u>C</u>H$_2$C≡N). IR spectrum, ν, cm^{-1}: 2300-2800 (NH), 2260 (C≡N), 1470, 1450, 1300. Found, %: C 58.59; H 7.64; N 33.87. $C_6H_9N_3$. Calculated, %: C 58.51; H 7.37; N 34.12.

Bis(2-cyanoethyl)amide of 4-Nitrobenzoic Acid. A mixture of 4-nitrobenzamide (16.6 g, 100 mmol), benzyltriethylammonium chloride (0.1 g, 0.5 mmol), and NaOH (0.02 g, 0.5 mmol) in acrylonitrile (50 ml) was cautiously heated to homogenization. An exothermal reaction was observed. The crystals precipitated after cooling the reaction mass were filtered off, washed with water, and dried. The appropriate dinitrile (19.0 g, 70%) was obtained as colorless needle-like crystals; mp 148-150°C (ethanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.67 and 2.75 (4H, t, J = 7.3, $CH_2C{\equiv}N$); 3.45 and 3.60 (4H, t, J = 7.3, C<u>H</u>$_2$CH$_2$C≡N); 7.85-8.20 (4H, arom.). ^{13}C NMR spectrum, δ, ppm: 169.1 (CON); 147.4, 142.5, 128.0, 122.6 (4-$NO_2C_6H_4$); 118.9 (C≡N); 44.8 and 40.1 (<u>C</u>H$_2$CH$_2$C≡N); 16.2 and 15.6 (<u>C</u>H$_2$C≡N). IR spectrum, ν, cm^{-1}: 2240 (C≡N), 1770 (COO), 1610, 1530 (NO_2), 1450, 1415, 760. Found, %: C 57.06; H 4.77; N 20.44. $C_{13}H_{12}N_4O_3$. Calculated, %: C 57.35; H 4.44; N 20.58.

General Procedure for Obtaining Tetrazoles 1-8. A mixture of the 2-cyanoethyl derivative (25 mmol) and a 10% molar excess of sodium azide and dimethylamine hydrochloride, calculated for each nitrile group in the substrate, in DMF (50 ml) was heated to 110-115°C and left for 15-20 h. The precipitated solid sodium chloride was filtered off, the filtrate evaporated, the residue was dissolved in water (100 ml), and the solution acidified to pH <2 with dilute hydrochloric acid. The precipitated solid was filtered off, washed with water, dried, and crystallized from ethanol or an ethanol–DMF mixture.

2,2,5,5-Tetrakis[2-(5-tetrazolyl)ethyl]cyclopentanone (1). Yield 8.65 g (74%); mp 215°C (decomp., EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 1.95 (12H, s, 2CH_2 in cyclopentanone and 4C<u>H</u>$_2$CH$_2$CN$_4$H); 2.85 (8H, br. s, C<u>H</u>$_2$CN$_4$H); 14.8 (4H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 214.1 (C=O); 155.9 ($C_{(5)}$ in tetrazole); 51.3 (C_{quat}); 31.3 (<u>C</u>H$_2$CH$_2$CN$_4$H); 30.0 (CH_2 in cyclopentanone); 18.1 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 3000-3200 (NH), 1670 (C=O), 1560, 1420, 1250, 1105 (tetrazole). Found, %: C 43.28; H 5.45; N 47.62. $C_{17}H_{24}N_{16}O$. Calculated, %: C 43.58; H 5.16; N 47.84.

1,3,5-Tris(5-tetrazolyl)pentane (2). Yield 4.4 g (64%); mp 218°C (decomp., ethanol). ^{1}H NMR spectrum, δ, ppm: 2.20 (4H, br. s, C<u>H</u>$_2$CH$_2$CN$_4$H); 2.80 (4H, br. s, C<u>H</u>$_2$CN$_4$H); 3.30 (1H, m, CH); 15.70 (3H, br. s, CN$_4$<u>H</u>). ^{13}C NMR spectrum, δ, ppm: 158.0 and 155.4 ($C_{(5)}$ in tetrazoles); 38.2 (CH); 30.8 (<u>C</u>H$_2$CH$_2$CN$_4$H); 18.2 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 2800-3100 (NH), 1550, 1470, 1255, 1145, 1040 (tetrazole). Found, %: C 34.52; H 4.64; N 60.41. $C_8H_{12}N_{12}$. Calculated, %: C 34.78; H 4.38; N 60.84.

3-Phenyl-1,3,5-tris(5-tetrazolyl)pentane (3). Yield 7.05 g (80%); mp 224-225°C (decomp., ethanol). ^{1}H NMR spectrum, δ, ppm: 2.50-3.00 (8H, m, C<u>H</u>$_2$CN$_4$H and C<u>H</u>$_2$CH$_2$CN$_4$H); 7.15-7.50 (5H, m, Ph); 16.00 (3H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 161.3 and 155.6 ($C_{(5)}$ in tetrazoles); 141.9, 129.0, 127.6, 126.9 (Ph); 45.0 (Ph–<u>C</u>–CN$_4$H); 34.4 (<u>C</u>H$_2$CH$_2$CN$_4$H); 18.5 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 2900-3200 (NH), 1630, 1550, 1475, 1450, 1255, 1135, 810 (tetrazole). Found, %: C 47.48; H 4.88; N 47.52. $C_{14}H_{16}N_{12}$. Calculated, %: C 47.72; H 4.58; N 47.70.

3-(4-Nitrophenyl)-1,3,5-tris(5-tetrazolyl)pentane (4). Yield 8.12 g (82%); mp 210.5-211.5°C (decomp., ethanol). ^{1}H NMR spectrum, δ, ppm: 2.50-2.80 (8H, m, C<u>H</u>$_2$CN$_4$H and C<u>H</u>$_2$CH$_2$CN$_4$H); 7.22-7.41 (4H, m, 4-NO$_2$C$_6$H$_4$); 15.98 (3H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 161.2 and 155.5 (C$_{(5)}$ in tetrazoles); 141.8, 128.9, 127.5, 126.8 (4-NO$_2$C$_6$H$_4$); 67.2, 45.0 (C$_{quat}$); 34.3 (<u>C</u>H$_2$CH$_2$CN$_4$H); 18.4 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 2900-3200 (NH), 1640, 1555, 1530, 1250, 1080, 790 (tetrazole). Found, %: C 41.93; H 4.10; N 45.57. C$_{14}$H$_{15}$N$_{13}$O$_2$. Calculated, %: C 42.32; H 3.80; N 45.82.

9,9-Bis[2-(5-tetrazolyl)ethyl]fluorene (5). Yield 7.70 g (86%); mp 280°C (decomp., ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz); 2.05 (4H, t, *J* = 9.4, C<u>H</u>$_2$CN$_4$H); 2.52 (4H, t, *J* = 9.4, C<u>H</u>$_2$CH$_2$CN$_4$H); 7.30-8.00 (8H, arom.); 15.60 (2H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 155.6 (C$_{(5)}$ in tetrazole); 147.4, 140.8, 127.9, 123.3, 120.4, 54.1 (fluorene); 36.5 (<u>C</u>H$_2$CH$_2$CN$_4$H); 18.2 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 2900-3100 (NH), 1640, 1550, 1465, 1250, 1100, 770 (tetrazole). Found, %: C 63.31; H 5.38; N 30.96. C$_{19}$H$_{18}$N$_8$. Calculated, %: C 63.67; H 5.06; N 31.27.

1,2-Bis[2-(5-tetrazolyl)ethoxy]propane (6). Yield 2.95 g (44%); mp 97-100°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08 (3H, d, *J* = 6.5, CHC<u>H</u>$_3$); 3.05 (4H, t, *J* = 7.5, C<u>H</u>$_2$CN$_4$H); 3.28 (2H, d, *J* = 6.5, C<u>H</u>$_2$CHCH$_3$); 3.50 (1H, m, *J* = 6.5, CH$_2$C<u>H</u>CH$_3$); 3.70 (4H, t, *J* = 7.5, C<u>H</u>$_2$CH$_2$CN$_4$H); 15.80 (2H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 154.1 (C$_{(5)}$ in tetrazole); 73.8 and 74.0 (CH$_2$–CH); 67.6 and 65.5 (<u>C</u>H$_2$CH$_2$CN$_4$H); 24.5 and 24.1 (<u>C</u>H$_2$CN$_4$H); 16.9 (CH$_3$). IR spectrum, ν, cm^{-1}: 3000-3200 (NH), 1605, 1570, 1550, 1450, 1340, 1250, 1120, 1050 (tetrazole). Found, %: C 39.98; H 6.27; N 41.56. C$_9$H$_{16}$N$_8$O$_2$. Calculated, %: C 40.29; H 6.01; N 41.77.

Bis[2-(5-tetrazolyl)ethyl]amine Hydrochloride (7). Yield 4.17 g (68%); mp 152-154°C (decomp., ethanol). ^{1}H NMR spectrum, δ, ppm: 3.05 (4H, br. s, C<u>H</u>$_2$CN$_4$H); 3.70 (4H, br. s, C<u>H</u>$_2$CH$_2$CN$_4$H); 9.00 (1H, s, NH); 16.00 (2H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 154.3 (C$_{(5)}$ in tetrazole); 66.7 (<u>C</u>H$_2$CH$_2$CN$_4$H); 23.5 (<u>C</u>H$_2$CN$_4$H). IR spectrum, cm^{-1}: 3000-3200, 2200-2800 (NH), 1560, 1450, 1380, 1255, 1100, 950 (tetrazole). Found, %: C 29.20; H 5.16; N 51.08. C$_6$H$_{11}$N$_9$·HCl. Calculated, %: C 29.33; H 4.92; 51.31.

Bis[2-(5-tetrazolyl)ethyl]amide of 4-Nitrobenzoic Acid (8). Yield 5.07 g (85%); mp 73-74°C (decomp., methanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.00 and 3.12 (4H, t, *J* = 7.5, C<u>H</u>$_2$CN$_4$H); 3.60 and 3.82 (4H, t, *J* = 7.5, C<u>H</u>$_2$CH$_2$CN$_4$H); 7.40 (2H, d, *J* = 4.0, 4-NO$_2$C$_6$H$_4$); 8.22 (2H, d, *J* = 4.0, 4-NO$_2$C$_6$H$_4$); 16.00 (2H, br. s, CN$_4$H). ^{13}C NMR spectrum, δ, ppm: 169.1 (CON); 154.0 (C$_{(5)}$ in tetrazole); 147.8, 142.4, 127.7, 123.9 (4-NO$_2$C$_6$H$_4$); 46.5 and 42.3 (<u>C</u>H$_2$CH$_2$CN$_4$H); 22.3 and 21.2 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 2900-3200 (NH), 1760 (COO), 1645, 1550, 1535, 1250, 1100, 780. Found, %: C 43.14; H 4.15; N 38.73. C$_{13}$H$_{14}$N$_{10}$O$_3$. Calculated, %: C 43.58; H 3.94; N 39.09.

Bis[2-(5-tetrazolyl)ethyl]malonic Acid (9). A solution of ditetrazole **11** (3.52 g, 10 mmol) and NaOH (4.0 g, 100 mmol) in water (50 ml) was boiled for 10 h, cooled, and acidified to pH 1 with dilute hydrochloric acid. The precipitated solid was filtered off, washed with distilled water, dried, and crystallized from ethyl acetate. Compound **9** was obtained (2.52 g, 85%); mp 172-173°C (decomp., ethyl acetate). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.25 (4H, t, *J* = 7.0, C<u>H</u>$_2$CN$_4$H); 2.85 (4H, t, *J* = 7.0, C<u>H</u>$_2$CH$_2$CN$_4$H); 8.00-18.00 (4H, br. s, CN$_4$H and COOH). ^{13}C NMR spectrum, δ, ppm: 172.1 (COOH), 155.5 (C$_{(5)}$ in tetrazole); 56.0 (C$_{quat}$); 29.8 (<u>C</u>H$_2$CH$_2$CN$_4$H); 18.6 (<u>C</u>H$_2$CN$_4$H). IR spectrum, ν, cm^{-1}: 2900-3200 (NH and OH), 1760 (COO), 1645, 1550, 1535, 1250, 1100, 780. Found, %: C 36.05; H 4.22; N 37.54. C$_9$H$_{12}$N$_8$O$_4$. Calculated, %: C 36.49; H 4.08; N 37.82.

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REFERENCES

1. V. Yu. Zubarev, G. V. Gurskaya, V. E. Zavodnik, and V. A. Ostrovskii, *Khim. Geterotsikl. Soedin.*, 1494 (1997).
2. V. Yu. Zubarev and V. A. Ostrovskii, *Khim. Geterotsikl. Soedin.*, 867 (2000).
3. A. V. Makarevich, P. S. Pinchuk, V. A. Ostrovskii, V. Yu. Zubarev, and P. S. Plevachuk, Belarus Patent BY 2406 C1 (B 01 D 39/16), 18.04.1998.
4. H. A. Bruson, *Org. React.*, 79 (1949).
5. O. Bayer, *Angew. Chem.*, **61**, 229 (1949).
6. A. P. Terent'ev and A. N. Kost, in *Reactions and Methods of Investigating Organic Compounds*, Vol. 2 [in Russian], Goskhimizdat, Moscow–Leningrad (1952), p. 47.
7. E. D. Bergmann, D. Ginsburg, and R. Pappo, in *Organic Reactions*, Vol. 10, John Wiley, New York (1959), p. 179.
8. A. Albert and E. P. Serjeant, *Ionization Constants of Acids and Bases,* John Wiley, New York (1962), 179 pp.
9. F. Rossotti and H. Rossotti, *Determination of Stability Constants and Other Equilibrium Constants in Solutions*, McGraw-Hill, New York (1961), 425 pp.
10. M. Beck and I. Nagypal, *Investigation of Complex Formation by the Newest Methods* [Russian translation], Mir, Moscow (1989), 411 pp.
11. M. I. Ermakova, I. A. Shikhova, T. A. Sinitsyna, and N. I. Latosh, *Zh. Obshch. Khim.*, **49**, 1387 (1979).
12. A. P. Kreshkov, L. N. Bykova, and N. A. Kazaryan, *Acid-Base Titration in Nonaqueous Media* [in Russian], Khimiya, Moscow (1967).
13. J. Catalan, J. L.-M. Abboud, and J. Elguero, *Adv. Heterocycl. Chem.*, **41**, 187 (1987).
14. N. Bjerrum, *Z. Phys. Chem.*, **106**, 219 (1923).
15. J.-M. Lehn, *Supramolecular Chemistry* [Russian translation], Nauka, Novosibirsk (1998).