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Synthesis of 1,2,4,5-Tetrazines, Symmetrically and Unsymmetrically 3,6-Disubstituted by *N*-Nucleophiles

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Abstract—6-R-3-(3,5-Dimethylpyrazol-1-yl)-1,2,4,5-tetrazines with aliphatic, cycloaliphatic, and aromatic amines, and also with NH-heterocycles undergo a nucleophilic substitution of the dimethylpyrazole moiety yielding symmetrically and unsymmetrically substituted 1,2,4,5-tetrazines. In the 3,6-diimidazolyl- and 3,6-dibenzotriazolyl derivatives reactions of nucleophilic substitution of the heterocyclic moiety also occur. In some cases an ipso-substitution of amino, hydrazino, and azido groups is observed.

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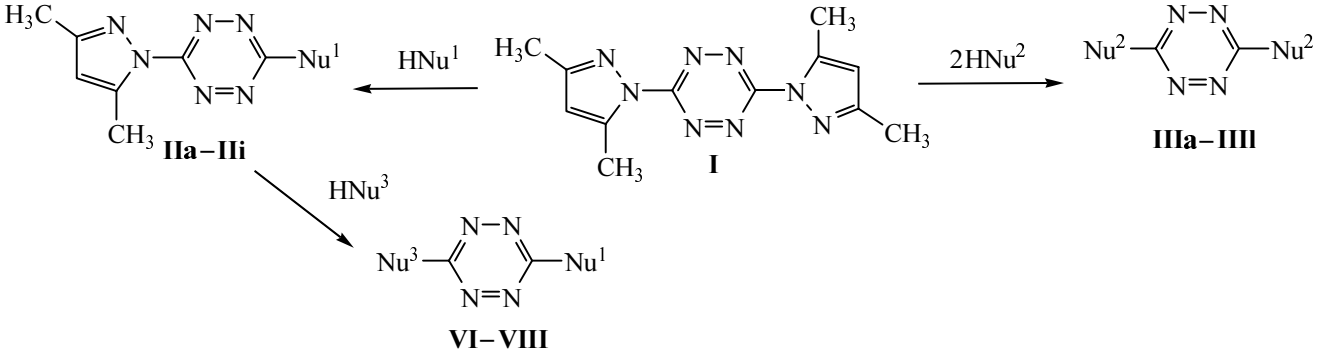
3,6-Bis(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (**I**) in reaction with aliphatic, cycloaliphatic, and aromatic amines at room temperature is known [1–4] to undergo a substitution of dimethylpyrazolyl moiety to furnish in a high yield unsymmetrically substituted tetrazines **II**. In these reactions as nucleophiles served aliphatic, cycloaliphatic, and aromatic amines. At the same time in certain reactions of tetrazine **I** with the primary aliphatic amines products of two pyrazolyl groups substitution **III** were isolated. Therefore compound **I** is a promising synthon for preparation of a large series of symmetrically and unsymmetrically 3,6-disubstituted 1,2,4,5-tetrazines often unavailable by other synthetic methods. However the application in this respect of 3-amino-substituted 6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazines reactions with nucleophiles is poorly investigated. In a recent article [5] reactions of these tetrazines with hydrazine and KOH were considered.

In the present study we more thoroughly investigated the prospects of synthetic applications of the nucleophilic substitution of the dimethylpyrazolyl moiety in 6-R-3-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazines **IIa–IIi** with various amines.

Scheme 1.



II, Nu^1 = 1-indolyl (**a**), 5-bromoindol-3-yl (**b**), BnNH (**c**), $HOCH_2CH_2NH$ (**d**), NH_2 (**e**), N_2H_3 (f), N_3 (**g**), 4-FC_6H_4NH (**h**), 1-adamantylamino (**i**); **III**, Nu^2 = BnNH (**a**), $HOCH_2CH_2NH$ (**b**), CH_2=$CHCH_2NH$ (**c**), PhCONH (**d**), pyrrolidino (**e**), morpholino (**f**), cyclohexylamino (**g**), cycloheptylamino (**h**), 5-bromoindol-3-yl (**i**), 1-imidazolyl (**j**), 1-benzotriazolyl (**k**), PhNH (**l**); **VI–VIII**, Nu^1 = PhNH (**a**), 4-MeC_6H_4NH (**b**), 3-MeC_6H_4NH (**c**), 3,4-$Me_2C_6H_3NH$ (**d**), 4-$MeOC_6H_4NH$ (**e**), 4-FC_6H_4NH (**f**), 4-ClC_6H_4NH (**g**), 4-BrC_6H_4NH (**h**), thiomorpholino (**i**), 1-adamantylamino (**j**); Nu^3 = BnNH (**VI**), $HOCH_2CH_2NH$ (**VII**), CH_2=$CHCH_2NH$ (**VIII**).

We found that at boiling compound **I** in acetonitrile the primary aliphatic amines (benzylamine, ethanolamine, and allylamine) easily replaced both dimethyl-pyrazolyl groups. As a result compounds **IIIa–IIIc** formed in high yields (Scheme 1).

Weak nucleophiles, like acid amides, are involved into the substitution reaction with 1,2,4,5-tetrazines only in the presence of strong bases. For instance, it was shown recently that this substitution occurred with methylsulfanyltetrazines when introducing butyllithium into the reaction mixture [6]. We carried out reaction of tetrazine **I** with benzamide in the presence of potassium *tert*-butylate and isolated in a 48% yield the corresponding product of disubstitution, 3,6-dibenzamido-1,2,4,5-tetrazine (**IIId**) that had been previously obtained by acylation of 3,6-diamino-1,2,4,5-tetrazine (yield 30%) [7]. The substitution of pyrazolyl groups is favored by high pressure. Thus the symmetrically 3,6-disubstituted tetrazines **IIIe–IIIh** containing pyrrolidine, morpholine, cyclohexylamine, and cycloheptylamine rests were successfully prepared in good yields heating for 3–4 h at 80°C and a pressure of 500 MPa (at higher temperature the decomposition of the tetrazine ring was observed). Product **IIIf** formed in a low yield also at the ordinary pressure when tetrazine **IIIj** was boiled in neat morpholine.

We established that NH-heterocyclic compounds also could be involved into the nucleophilic substitution of the pyrazole moieties. In particular, we studied the reactions of tetrazine **I** with indole, 5-bromoindole, imidazole, and benzotriazole. Tetrazine **I** readily reacted with indole in acetonitrile at 20°C in the presence of triethylamine furnishing a product of substitution of a single pyrazolyl group **IIa** in a 73% yield. We failed to obtain a product of the second pyrazolyl group substitution at prolonged boiling of tetrazine **I** in acetonitrile with excess indole; the process was accompanied by formation of an intractable mixture of substances. 5-Bromoindole with tetrazine **I** in acetonitrile in the presence of triethylamine furnished products of mono- and disubstitution **IIb** and **IIIi** in 70 and 86% yields respectively. The reaction of tetrazine **I** with imidazole occurred even in the absence of a base at 40°C giving 3,6-bis(imidazol-1-yl)-1,2,4,5-tetrazine (**IIIj**). Therewith the yield of tetrazine **IIIj** at the use of anhydrous acetonitrile attained 93–95%.

The reaction of tetrazine **I** with benzotriazole occurred in a different fashion. Just after the dissolution in acetonitrile fine orange crystals of derivative **IV** precipitated which were identified as a complex of compound **I** with the benzotriazole in 1:2 ratio. At heating the complex obtained over its melting point the pyrazolyl groups underwent substitution furnishing 3,6-bis(benzotriazol-1-yl)-1,2,4,5-tetrazine (**IIIk**) (yield 53%). This compound can also be obtained in a simpler way by boiling initial tetrazine **I** with benzotriazole in benzene. As a side product another complex **V** of tetrazine **IIIk** with 3,5-dimethylpyrazole in a 1:1 ratio was isolated in an 11% yield.

The formation of tetrazine **IIIk** was unambiguously confirmed by the data of ^{1}H NMR spectroscopy: Four groups of nonequivalent protons were observed. If the reaction occurred at the position N^2 of the benzotriazole in the ^{1}H NMR spectrum should appear only two groups of signals due to the presence of protons equivalent in pairs.

Compounds **II** whose synthesis was described in [3] by reactions with N-nucleophiles gave rise to unsymmetrically substituted tetrazines **VI–VIII**.

It was established that the substitution of the dimethylpyrazolyl group in compounds **IIa–IIi** by primary aliphatic amines occurred at boiling for 3–12 h with a small excess of the amine in acetonitrile. Under these conditions the secondary aliphatic amines were not involved into the substitution reaction.

The primary amines can substitute in compounds **IIa–IIi** the pyrazolyl group as well as the earlier introduced nucleophile. For instance, the storage of tetrazine **IIc** with ethanolamine at 20°C for 12 days resulted in solution containing according to TLC tetrazine **IIc**, **IId, IIIa**, and **IIIb**.

Therefore the preparation from compound **I** of unsymmetrical diamino-substituted tetrazines **VI–VIII** requires first bringing into the reaction the aromatic or secondary aliphatic amine and then the primary aliphatic amine.

We found that the amino group in tetrazine **IIe** was the first to be replaced in reactions with primary and secondary aliphatic amines, and then the pyrazolyl group was also substituted similarly to reactions described in [5] of 1,2,4,5-tetrazines with hydrazine hydrate or KOH. In particular, after 3 h of boiling the said tetrazine in acetonitrile with two equiv of benzylamine a mixture of products formed containing according to NMR data 6-benzylamino-3-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (**IIc**) as the main component and in a lesser amount 3,6-bis(benzylamino)-1,2,4,5-tetrazine (**IIIa**) (in a ratio ~6:1). On bringing into the reaction additional quantity of benzylamine we obtained as the main product tetrazine **IIIa**. At heating hydrazinotetrazine **IIf** with benzylamine also the substitution of the hydrazine moiety was observed. Azidotetrazine **IIg** obtained in its turn by nitrosation of

tetrazine **IIf** reacted with benzylamine already at room temperature giving in a high yield the product of azide group substitution **IIc**.

Thus the nucleophilic substitution of the dimethylpyrazolyl group in the amino, hydrazino, and azido derivatives of tetrazine by the method described is complicated by the possibility of replacement of NH_2, N_2H_3, and N_3 groups. With hydrazine derivatives this problem can be solved by their transformation into hydrazones. For instance, in hydrazones **IXa–IXc** obtained like in [3] the pyrazolyl group was substituted in the acetonitrile solution by dodecylamine and benzylamine (Scheme 2).

The imidazolyl and benzotriazolyl moieties in 1,2,4,5-tetrazines **IIIj** and **IIIk**, like the pyrazolyl groups in compound **I**, can be replaced by amines, but in compounds **IIIj** and **IIIk** the heterocyclic substituents are more labile. For instance, after boiling for 12 h of tetrazines **I** or **IIIk** in neat aniline 3,6-bis(phenylamino)-1,2,4,5-tetrazine **IIIl** was isolated in 42 and 54% yields respectively. The departing ability of imidazole moiety in reaction of tetrazine **IIIj** with aniline proved to be even greater: Product **IIIl** was isolated in a 64% yield already after 5 h of boiling. Under less stringent conditions only one heterocyclic moiety was replaced. 3-(Benzotriazol-1-yl)-6-phenylamino-1,2,4,5-tetrazine (**XIIa**) was obtained in the reaction of tetrazine **IIIk** with exess aniline (5 equiv) in acetonitrile.

The use of the procedure of the nucleophilic substitution of dimethylpyrazolyl, and also benzotriazolyl and imidazolyl groups in the derivatives of 1,2,4,5-tetrazine considerably extends the bank of various symmetrically and unsymmetrically substituted 1,2,4,5-tetrazines.

EXPERIMENTAL

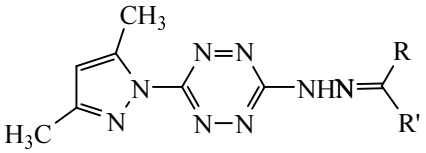
All compounds obtained were as a rule crystalline substances of bright color from orange to violet.

The reactions progress was monitored and the purity of compounds obtained was checked by TLC on Silufol plates with fixed layer, eluents chloroform–ethanol, 9:1, or benzene–acetonitrile, 1:1.

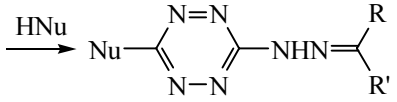
Elemental analysis was carried out on automatic CHN-analyzers EA1108 (Carlo Erba Instruments) and PE 2400 series (II) (Perkin Elmer). Melting points were measured on the Boetius heating block and were reported uncorrected. Initial reagents and solvents were purified by standard procedures.

^{1}H NMR spectra were registered on spectrometers Tesla BS567A (80 MHz; for compounds **IIIg**, **IXa**, **IXb,** **Xa–Xc**) and Bruker Avance DRX-400 (400 MHz; for all other compounds). Chemical shifts were measured relative HMDS or TMS. Spectra of compounds **IIa, IIb, IIg, IIk, IXa, IXb**, and **Xa–Xc** were registered in $CDCl_3$, all other, in DMSO-d_6.

Scheme 2.



IXa – IXc



Xa – Xc, XIa – XIc

R = H, R' = Ph (**a**); R= Me, R' = Ph (**b**); R = Me, R' = 4-ClC_6H_4(**c**); Nu = NHBn (**X**), $NH(CH_2)_{11}CH_3$ (**XI**).

6-(3,5-Dimethylpyrazol-1-yl)-3-(indol-1-yl)-1,2,4,5-tetrazine (IIa). To a dispersion of 0.27 g (1.0 mmol) of tetrazine **I** and 0.14 g (1.2 mmol) of indole in 10 ml of acetonitrile was added 0.1 ml of triethylamine, the mixture was heated till it homogenized, then it was maintained for 2 h at 18–20°C, the solution was evaporated, and the residue was recrystallized from ethanol. Yield 73%, mp 161–163°C (from C_2H_5OH). ^{1}H NMR spectrum, d, ppm: 2.41 s (3H, CH_3), 2.74 s (3H, CH_3), 6.20 s (1H, H^4_{Pz}), 6.89–6.90 m (1H, H^3_{Ind}), 7.32–7.36 m, 7.4–7.45 m, 7.67–7.71 m, 8.68–8.72 m (4H, $H^{4,5,6,7}_{Ind}$), 8.33 m (1H, H^2_{Ind}). Found, %: C 61.87; H 4.49; N 33.88. $C_{15}H_{13}N_7$. Calculated, %: C 61.84; H 4.50; N 33.66.

3-(5-Bromoindol-1-yl)-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (IIb). From the filtrate of the reaction mixture obtained on isolation of tetrazine **IIIi** (its preparation is described below) after 0.5 h a red precipitate separated which was tetrazine **IIb**; it was filtered off and recrystallized from acetonitrile. Yield 70%, mp 199–200°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 2.41 s (3H, CH_3), 2.73 s (3H, CH_3), 6.21 s (1H, H^4_{Pz}), 6.83 d, 7.81 d (2H, at $H^{2,3}_{Ind}$), 8.33 d, 8.55 d (2H, $H^{6,7}_{Ind}$), 7.51 d.d (1H, H^4_{Ind}). Found, %: C 48.65; H 3.13; N 26.46. $C_{15}H_{12}BrN_7$. Calculated, %: C 48.67; H 3.27; N 26.48.

Substitution of amino group in 3-amino-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (IIe). A dispersion of 0.30 g (1.57 mmol) of tetrazine **IIe** [3] and 0.35 ml (2 equiv) of benzylamine in 5 ml of CH_3CN was boiler for 3 h (TLC monitoring), then the reaction mixture

was evaporated, the residue was washed with water and recrystallized from methanol. Yield of tetrazine **IIc** 0.26 g (59%).

Likewise the heating for 12 h of 0.300 g (1.57 mmol) of tetrazine **IIe** and 0.52 ml (3 equiv) of benzylamine in 5 ml of CH_3CN resulted in formation of tetrazine **IIIa**. The reaction mixture was evaporated, the residue was washed with hexane and recrystallized from methanol. Yield 0.24 g (52%). According to NMR data the product contained about 5% of tetrazine **IIc**. The analytically pure sample identical to that synthesized from tetrazine **I** was obtained after repeated recrystallization from methanol.

3-Azido-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (IIg). To a dispersion of 0.87 g (4.20 mmol) of tetrazine **IIc** [3], 7 ml CH_3CN, and 3 ml of acetic acid was added at stirring 0.36 g (5.14 mmol) of sodium nitrite. After 3 min the slightly self-heated solution was evaporated. The azidotetrazine obtained was extracted from the oily residue with acetonitrile (10 ml), and the extract was evaporated. The oily residue was washed with a little water, then dissolved in petroleum ether at heating. From the cooled solution on the next day precipitated pure azidotetrazine **IIg** like crystals or oil drops; the latter were ground in petroleum ether till crystallization. Yield 0.71 g (78%), mp 51–52°C (from petroleum ether). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, 3^{Pr}-CH_3); 2.68 d (3H, 5^{Pz}-CH_3, *J* 0.8 Hz); 6.19 s (1H, 4^{Pz}-CH). Found, %: C 38.73; H 3.17; N 57.92. $C_7H_7N_9$. Calculated, %: C 38.71; H 3.25; N 58.04.

Substitution of azido group in 3-azido-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (IIg). To a solution of 0.06 g (0.26 mmol) of azidotetrazine **IIg** in 1.5 ml of CH_3CN was added at stirring 0.04 ml (0.36 mmol) of benzylamine. Within several minutes crystalline tetrazine **IIc** precipitated from the solution. After 15 min the solvent was removed in air, the residue was washed with water and recrystallized. Yield 0.05 g (63%).

3-(3,5-Dimethylpyrazol-1-yl)-6-(*p*-fluorophenyl)-amino-1,2,4,5-tetrazine (IIh). To 0.50 g (1.85 mmol) tetrazine **I** in 7 ml of acetonitrile was added 0.30 ml (2.70 mmol) of *p*-fluoroaniline, and the mixture was stirred for 2 h at 40–50°C. On cooling the solution to 0°C the precipitated dark-red needle crystals were filtered off and recrystallized from methanol. Yield 0.47 g (88%), mp 191–192°C (from CH_3OH). ^{1}H NMR spectrum, δ, ppm: 2.46 s (3H, CH_3), 2.50 s (3H, CH_3), 6.23 s (1H, CH), 7.26 m (2H, CH_{arom}), 7.71 m (2H, CH_{arom}), 10.99 s (1H, NH). Found, %: C 54.70; H 4.19; N 34.40. $C_{13}H_{12}FN_7$. Calculated, %: C 57.73; H 4.24; N 34.37

6-(1-Adamantylamino)-3-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (IIi). In 7 ml of acetonitrile was charged 0.31 g (1.2 mmol) of tetrazine **I** and 0.24 g (1.5 mmol) of 1-aminoadamantane. The mixture was heated for 3 h at 50–60°C, then cooled to 0°C. The separated bright-red precipitate was filtered off, washed with cold acetonitrile and recrystallized from ethanol. Yield 0.31 g (83%), mp 162–164°C (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 1.69 m (6H, H_{Ad}), 2.13 m (9H, H_{Ad}), 2.21 s (3H, 3^{Pz}-CH_3), 2.40 s (3H, 5^{Pz}-CH_3), 6.18 s (1H, 4^{Pz}-CH), 8.43 (1H, NH). Found, %: C 62.73; H 7.12; N 30.08. $C_{17}H_{23}N_7$. Calculated, %: C 62.75; H 7.12; N 30.13.

Symmetric disubstituted tetrazines IIIa–IIIc and 3,6-unsymmetric disubstituted 1,2,4,5-tetrazines VI–VIII. A mixture of 1.2–1.5 mmol of 3-amino-substituted 6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine **II** (the synthesis and properties of compounds **II** are published in [3] save those of **IIa**, **IIb**, **IIg–IIi**) and 1.5–2.0 mmol (in the synthesis of compounds **VI–VIII**) or 3–4 mmol (in preparation of compounds **IIIa–IIIc**) of an appropriate amine was boiled in CH_3CN for 3–12 h (TLC monitoring). On cooling the reaction mixture the precipitate was filtered off and recrystallized.

***N,N'*-Dibenzyl-1,2,4,5-tetrazine-3,6-diamine (IIIa).** Yield 87%, mp 154–155°C (from CH_3OH). ^{1}H NMR spectrum, δ, ppm: 4.50 d (4H, $2CH_2$, *J* 6.3), 7.18–7.38 m (10H, H_{arom}), 8.00 t (2H, NH_{aliph}, *J* 6.3 Hz). Found, %: C 65.68; H 5.44; N 28.85. $C_{16}H_{16}N_6$. Calculated, %: C 65.74; H 5.52; N 28.74.

3,6-Bis(hydroxyethylamino)-1,2,4,5-tetrazine (IIIb). Yield 72%, mp 125–126°C (from C_2H_5OH). ^{1}H NMR spectrum, δ: ppm: 3.33–3.41 m (2H, CH_2), 3.53–3.58 m (2H, CH_2), 4.2 br.s (1H, OH), 7.16 t (1H, NH, *J* 5.8 Hz). Found, %: C 36.12; H 5.88; N 42.01. $C_6H_{12}N_6O_2$. Calculated, %: C 36.00; H 6.04; N 41.98.

***N,N'*-Diallyl-1,2,4,5-tetrazine-3,6-diamine (IIIc).** Yield 74%, mp 116–117°C (from CH_3OH–H_2O) [8]. ^{1}H NMR spectrum, δ, ppm: 3.92–3.95 m (2H, CH_2), 5.05–5.23 m (2H, $=CH_2$), 5.86–5.96 m (1H, =CH), 7.39 t (1H, NH_{aliph}, *J* 6.0 Hz). Found, %: C 50.17; H 6.37; N 43.88. $C_8H_{12}N_6$. Calculated, %: C 49.99; H 6.29; N 43.72.

***N*-Benzyl-*N'*-phenyl-1,2,4,5-tetrazine-3,6-diamine (VIa).** Yield 58%, mp 184°C (from CH_3OH). ^{1}H NMR spectrum, δ, ppm: 4.58 d (2H, CH_2, *J* 6.5 Hz), 6.72–7.35 m (10H, H_{arom}), 8.34 t (1H, NH_{aliph}, *J* 6.5 Hz), 9.91 s (1H, NH_{arom}). Found, %: C 65.44; H 5.26; N 29.80. $C_{15}H_{14}N_6$. Calculated, %: C 64.73; H 5.07; N 30.20.

***N*-Benzyl-*N*'-*p*-tolyl-1,2,4,5-tetrazine-3,6-diamine (VIb).** Yield 48%, mp 231°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 2.24 s (3H, CH_3), 4.57 d (2H, CH_2, *J* 6.3 Hz), 7.05–7.56 m (9H, H_{arom}), 8.31 t (1H, NH_{aliph}, *J* 6.3 Hz), 9.88 C (1H, NH_{arom}). Found, %: C 65.78; H 5.59; N 28.70. $C_{16}H_{16}N_6$. Calculated, %: C 65.74; H 5.51; N 28.75.

***N*-Benzyl-*N*'-*m*-tolyl-1,2,4,5-tetrazine-3,6-diamine (VIc).** Yield 55%, mp 237°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 2.27 s (3H, CH_3), 4.58 d (2H, CH_2, *J* 6.3 Hz), 6.95–7.59 m (9H, H_{arom}), 8.36 t (1H, NH_{aliph}, *J* 6.3 Hz), 9.98 C (1H, NH_{arom}). Found, %: C 65.38; H 5.28; N 28.98. $C_{16}H_{16}N_6$. Calculated, %: C 65.74; H 5.51; N 28.75.

***N*-Benzyl-*N*'-(3,4-dimethylphenyl)-1,2,4,5-tetrazine-3,6-diamine (VId).** Yield 43%, mp 199°C (from CH_3CN). ^1H NMR spectrum, δ, ppm: 2.16 s (3H, CH_3), 2.19 s (3H, CH_3), 4.57 d (2H, CH_2, *J* 6.5 Hz), 6.99–7.50 m (9H, H_{arom}), 8.28 t (1H, NH_{aliph}, *J* 6.5 Hz), 9.78 s (1H, NH_{arom}). Found, %: C 66.68; H 5.86; N 27.53. $C_{17}H_{18}N_6$. Calculated, %: C 66.65; H 5.92; N 27.43.

***N*-Benzyl-*N*'-(4-methoxyphenyl)-1,2,4,5-tetrazine-3,6-diamine (VIe).** Yield: 49%, mp 226°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 3.70 s (3H, OCH_3), 4.55 d (2H, CH_2, *J* 6.6 Hz), 6.83–7.38 m (9H, H_{arom}), 8.23 t (1H, NH_{aliph}, *J* 6.6 Hz), 9.73 C (1H, NH_{arom}). Found, %: C 62.36; H 5.10; N 27.15. $C_{16}H_{15}N_6O$. Calculated, %: C 62.53; H 4.92; N 27.34.

***N*-Benzyl-*N*'-(4-fluorophenyl)-1,2,4,5-tetrazine-3,6-diamine (VIf).** Yield: 46%, mp 216–217°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 4.58 d (2H, CH_2, *J* 6.10 Hz), 7.09–7.40 m (7H, H_{arom}), 7.60–7.66 m (2H, H_{arom}), 8.31 t (1H, NH_{aliph}, *J* 6.1 Hz), 10.31 s (1H, NH_{arom}). Found, %: C 60.52; H 4.27; N 28.10. $C_{15}H_{13}FN_6$. Calculated, %: C 60.80; H 4.42; N 28.36.

***N*-Benzyl-*N*'-(4-chlorophenyl)-1,2,4,5-tetrazine-3,6-diamine (VIg).** Yield 56%, mp 229–230°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 4.59 d (2H, CH_2, *J* 6.1 Hz), 7.16–7.94 m (9H, H_{arom}), 8.42 t (1H, NH_{aliph}, *J* 6.1 Hz), 10.16 s (1H, NH_{arom}). Found, %: C 57.91; H 4.16; N 26.92. $C_{15}H_{13}ClN_6$. Calculated, %: C 57.61; H 4.19; N 26.87.

***N*-Benzyl-*N*'-(4-bromophenyl)-1,2,4,5-tetrazine-3,6-diamine (VIh).** Yield: 65%, mp 238°C (from CH_3OH). ^1H NMR spectrum, δ, ppm: 4.59 d (2H, CH_2, *J* 6.3 Hz), 7.26-7.67 m (9H, H_{arom}), 8.42 t (1H, NH_{aliph}, *J* 6.3 Hz), 10.16 s (1H, NH_{arom}). Found, %: C 50.51; H 3.59; N 23.76. $C_{15}H_{13}BrN_6$. Calculated, %: C 50.44; H 3.67; N 23.53.

Benzyl(6-thiomorpholino-1,2,4,5-tetrazin-3-yl)amine (VIi). Yield 43%, mp 103°C (from CH_3OH–H_2O). ^1H NMR spectrum, δ, ppm: 2.63–2.67 m (4H, $S(CH_2)_2$), 3.97–4.01 m (4H, $N(CH_2)_2$), 4.54 d (2H, CH_2, *J* 6.3 Hz), 7.22–7.38 m (5H, H_{arom}); 8.16 t (1H, NH_{aliph}, *J* 6.3 Hz). Found, %: C 54.05; H 5.66; N 28.98. $C_{13}H_{16}N_6S$. Calculated, %: C 54.15; H 5.59; N 29.14.

[6-(1-Adamantylamino)-1,2,4,5-tetrazin-3-yl]benzylamine (VIj). Yield 55%, mp 133–134°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 1.68 m (6H, $H_{adamantyl}$), 2.08 m (9H, $H_{adamantyl}$), 4.51 d (2H, CH_2, *J* 6.4 Hz), 6.62 C (1H, NH_{arom}), 7.29 m (5H, H_{arom}), 7.69 t (1H, NH_{aliph}, *J* 6.4 Hz). Found, %: C 67.90; H 7.18; N 25.22. $C_{19}H_{24}N_6$. Calculated, %: C 67.83; H 7.19; N 24.98.

2-(6-Phenylamino-1,2,4,5-tetrazin-3-ylamino)-ethanol (VIIa). Yield: 55%, mp 213–214°C (from CH_3OH). ^1H NMR spectrum, δ, ppm: 3.41–3.48 m (2H,CH_2), 3.56–3.61 m (2H,CH_2), 4.69 t (1H, OH, *J* 5 Hz), 6.92–6.98 m (1H, H_{arom}), 7.27–7.30 m (2H, H_{arom}), 7.61–7.65 m and 7.62 t (3H, 3H, $2H_{arom}$ and NH_{aliph}), 9.90 s (1H, NH_{arom}). Found, %: C 51.55; H 4.97; N 36.21. $C_{10}H_{12}N_6O$. Calculated, %: C 51.72; H 5.21; N 36.19.

2-(6-*p*-Tolylamino-1,2,4,5-tetrazin-3-ylamino)-ethanol (VIIb). Yield: 39%, mp 244–245°C (from CH_3OH). ^1H NMR spectrum, δ, ppm: 2.25 s (3H, CH_3), 3.40–3.47 m (2H,CH_2), 3.56–3.63 m (2H,CH_2), 4.69 t (1H, OH, 5.5 Hz), 7.09–7.12 m (2H, H_{arom}, *J* 8 Hz); 7.50–7.54 m and 7.55 t (3H, $2H_{arom}$ and NH_{aliph}, *J* 8 Hz), 9.78 s (1H, NH_{arom}). Found, %: C 53.57; H 5.68; N 33.98. $C_{11}H_{14}N_6O$. Calculated, %: C 53.65; H 5.73; N 34.13.

2-(6-*m*-Tolylamino-1,2,4,5-tetrazine-3-ylamino)-ethanol (VIIc). Yield 46%, mp 141–142°C (from CH_3OH–H_2O). ^1H NMR spectrum, δ, ppm: 2.29 s (3H, CH_3); 3.41–3.48 m (2H,CH_2), 3.57–3.69 m (2H, CH_2), 4. 69 t (1H, OH, *J* 5.5 Hz), 6.73 d (1H, H_{arom}); 7.14–7.20 m (1H, H_{arom}), 7.40–7.47 m (2H, H_{arom}); 7.60 t (1H, NH, *J* 5.5 Hz), 9.82 s (1H, NH_{arom}). Found, %: C 53.39; H 5.78; N 34.03. $C_{11}H_{14}N_6O$. Calculated, %: C 53.65; H 5.73; N 34.13.

2-[6-(4-Methoxyphenylamino)-1,2,4,5-tetrazin-3-ylamino]ethanol (VIIe). Yield 51%, mp 227–228°C (from C_2H_5OH). ^1H NMR spectrum, δ, ppm: 3.38–3.46 m (2H, CH_2), 3.55–3.73 m (2H, CH_2), 3.73 s (3H, CH_3), 4.68 t (1H, OH, *J* 5.5 Hz), 6.86–6.92 m (2H, H_{arom}), 7.50–7.55 m and 7.51 t (3H, $2H_{arom}$ and NH_{aliph}, *J* 3.4 Hz), 9.68 s (1H, NH_{arom}). Found, %: C 50.38;

H 5.34; N 31.91. $C_{11}H_{14}N_6O_2$. Calculated, %: C 50.38; H 5.38; N 32.04.

2-[6-(4-Fluorophenylamino)-1,2,4,5-tetrazin-3-ylamino]ethanol (VIIf). Yield 53%, mp 221–222°C (from CH_3COCH_3). ^{1}H, δ, ppm: 3.40–3.47 t (2H, CH_2, *J* 5.5 Hz), 3.56–3.62 m (2H, CH_2), 4.69 t (1H, OH, *J* 5.5 Hz), 7.10–7.17 m (2H, H_{arom}), 7.59–7.66 m and 7.61 t (3H, $2H_{arom}$ and NH_{aliph}), 9.92 s (1H, NH_{arom}). Found, %: C 48.04; H 4.40; N 33.57. $C_{10}H_{11}FN_6O$. Calculated, %: C 48.00; H 4.43; N 33.58.

2-[6-(4-Chlorophenylamino)-1,2,4,5-tetrazin-3-ylamino]ethanol (VIIg). Yield 73%, mp 247–248°C (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 3.41–3.48 m (2H, CH_2), 3.56–3.63 m (2H, CH_2), 4.69 t (1H, OH, *J* 5 Hz), 7.31–7.37 m (2H, H_{arom}), 7.63–7.70 m and 7.67 t (3H, $2H_{arom}$ and NH_{aliph}, *J* 5 Hz), 10.07 s (1H, NH_{arom}). Found, %: C 45.16; H 4.04; N 31.43. $C_{10}H_{11}ClN_6O$. Calculated, %: C 45.04; H 4.16; N 31.51.

2-[6-(4-Bromophenylamino)-1,2,4,5-tetrazine-3-ylamino]ethanol (VIIh). Yield 64%, mp 249–250°C (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 3.41–3.47 m (2H,CH_2), 3.55–3.61 m (2H, CH_2), 4.69 t (1H, OH, *J* 5.5 Hz), 7.41–7.47 m (2H, H_{arom}), 7.58–7.63 m (2H, H_{arom}), 7.68 t (1H, NH, *J* 5 Hz), 10.08 s (1H, NH_{arom}). Found, %: C 38.41; H 3.54; N 27.09. $C_{10}H_{11}BrN_6O$. Calculated, %: C 38.60; H 3.56; N 27.01.

2-[6-Morpholino-1,2,4,5-tetrazine-3-ylamino]-ethanol (VIIi). Yield 65%, mp 80°C (from CH_3OH). ^{1}H NMR spectrum, δ, ppm: 2.65–2.69 m [4H, $N(CH_2)_2$], 3.36–3.43 m (2H,CH_2), 3.53–3.57 m (2H, CH_2), 3.98–4.02 m [2H, $S(CH_2)_2$], 4.65 t (1H, OH, *J* 5.5 Hz), 7.42 t (1H, NH, *J* 5.5 Hz). Found, %: C 39.55; H 5.89; N 34.51. $C_8H_{14}N_6OS$. Calculated, %: C 39.66; H 5.82; N 34.68.

[6-(1-Adamantylamino)-1,2,4,5-tetrazine-3-ylamino]ethanol (VIIj). Yield 66%, mp 158–159°C (from CH_3OH–H_2O). ^{1}H NMR spectrum, δ, ppm: 1.61–1.68 m (6H, H_{Ad}); 2.05–2.08m (9H, H_{Ad}), 3.34–3.38 m (2H,CH_2), 3.54–3.57 m (2H,CH_2), 4.47 br.s (1H, OH), 6.81 C (1H, NH_{arom}), 6.89 t (1H, NH, *J* 6.0 Hz). Found, %: C 57.88; H 7.50; N 28.91. $C_{14}H_{22}N_6O$. Calculated, %: C 57.91; H 7.64; N 28.94.

***N*-Allyl-*N′*-phenyl-1,2,4,5-tetrazine-3,6-diamine (VIIIa).** Yield: 79%, mp 216–217°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 3.94–4.06 m (2H, $=CH_2$), 5.05–5.32 m (2H, $NHCH_2$), 5.77–6.12 m (1H, =CH), 6.87–7.67 m (5H, H_{arom}), 7.96 t (1H, NH_{aliph}, *J* 5.5 Hz), 9.74 s (1H, NH_{arom}). $C_{11}H_{12}N_6$. Found, %: C 57.68; H 5.35; N 36.81. Calculated, %: C 57.88; H 5.30; N 36.82.

***N*-Allyl-*N′*-*p*-tolyl-1,2,4,5-tetrazine-3,6-diamine (VIIIb).** Yield: 66%, mp 214–215°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 2.25 s (3H, CH_3); 3.94–4.06 m (2H, $=CH_2$), 5.04–5.32 m (2H, $NHCH_2$), 5.77–6.15 m (1H, =CH), 7.05–7.14 m (2H, H_{arom}, *J* 8 Hz), 7.48–7.57 m (2H, H_{arom}, *J* 8 Hz), 7.90 t (1H, NH_{aliph}, *J* 5.3 Hz), 9.86 s (1H, NH_{arom}). Found, %: C 59.52; H 6.02; N 34.93. $C_{12}H_{14}N_6$. Calculated, %: C 59.49; H 5.82; N 34.69.

***N*-Allyl-*N′*-*m*-tolyl-1,2,4,5-tetrazine-3,6-diamine (VIIIc).** Yield 39%, mp 179–180°C (from C_2H_5OH–H_2O). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 4.11–4.26 m (2H, $=CH_2$), 5.15–5.44 m (2H, $NHCH_2$), 5.83–6.21 m (1H, =CH), 6.84–7.74 m (4H, H_{arom}), 7.52 t (1H, NH_{aliph}), 8.31 s (1H, NH_{arom}). C_2H_5OH–H_2O). Found, %: C 59.47; H 5.86; N 34.68. $C_{12}H_{14}N_6$. Calculated, %: C 59.49; H 5.82; N 34.69.

***N*-Allyl-*N′*-(3,4-dimethylphenyl)-1,2,4,5-tetrazine-3,6-diamine (VIIId).** Yield 37%, mp 193–194°C (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 2.16 s (3H, CH_3), 2.19 s (3H, CH_3), 3.94–4.05 m (2H, $=CH_2$), 5.04–5.32 m (2H, $NHCH_2$), 5.77–6.15 m (1H, =CH), 6.99–7.42 m (4H, H_{arom}), 7.87 t (1H, NH_{aliph}, *J* 5.7 Hz), 9.76 s (1H, NH_{arom}). Found, %: C 61.04; H 6.53; N 33.14.$C_{13}H_{16}N_6$. Calculated, %: C 60.92; H 6.29; N 32.79.

***N*-Allyl-*N′*-(4-methoxyphenyl)-1,2,4,5-tetrazine-3,6-diamine (VIIIe).** Yield 35%, mp 207–208°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 3.72 s (3H, CH_3), 3.90–4.04 m (2H, $=CH_2$), 5.04–5.32 m (2H, $NHCH_2$), 5.62–6.14 m (1H, =CH), 6.84–6.95 m (2H, H_{arom}, *J* 9 Hz), 7.49–7.58 m (2H, H_{arom}, *J* 9 Hz), 7.85 t (1H, NH_{aliph}, *J* 6.4 Hz), 9.79 s (1H, NH_{arom}). Found, %: C 55.83; H 5.42; N 32.66. $C_{12}H_{14}N_6O$. Calculated, %: C 55.80; H 5.46; N 32.54.

***N*-Allyl-*N′*-(4-chlorophenyl)-1,2,4,5-tetrazine-3,6-diamine (VIIIg).** Yield 73%, mp 242–243°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 3.94–4.05 m (2H, $=CH_2$), 5.04–5.32 m (2H, $NHCH_2$), 5.77–6.10 m (1H, =CH), 7.40–7.67 m (4H, H_{arom}), 8.03 t (1H, NH_{aliph}, *J* 6.2 Hz), 10.15 s (1H, NH_{arom}). Found, %: C 50.40; H 4.05; N 32.17. $C_{11}H_{11}ClN_6$. Calculated, %: C 50.29; H 4.22; N 31.99.

***N*-Allyl-*N′*-(4-bromophenyl)-1,2,4,5-tetrazine-3,6-diamine (VIIIh).** Yield 77%, mp 239–240°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 3.95–4.05 m (2H, $=CH_2$), 5.05–5.32 m (2H, $NHCH_2$), 5.77–6.15 m (1H, =CH), 7.27–7.42 m (2H, H_{arom}, *J* 8 Hz), 7.60–7.73 m

(2H, H_{arom}, *J* 8 Hz), 8.02 t (1H, NH_{aliph}, 6 Hz), 10.14 s (1H, NH_{arom}). Found, %: C 43.27; H 3.70; N 27.39. $C_{11}H_{11}BrN_6$. Calculated, %: C 43.02; H 3.61; N 27.36.

Allyl(6-morpholino-1,2,4,5-tetrazin-3-yl)-amine (VIIIi). Yield 66%, mp 87–88°C (from C_2H_5OH–H_2O). ^{1}H NMR spectrum, δ, ppm: 2.65–2.69 m [4H, $N(CH_2)_2$], 3.93–4.02 m [6H, $S(CH_2)_2$ and $=CH_2$], 5.05–5.22 m (2H, $NHCH_2$), 5.85–6.00 m (1H, =CH), 7.74 t (1H, NH_{aliph}, *J* 9 Hz). Found, %: C 45.49; H 5.60; N 35.18. $C_9H_{14}N_6S$. Calculated, %: C 45.36; H 5.92; N 35.26.

3,6-Dibenzamido-1,2,4,5-tetrazine (IIId). To a dispersion of 0.5 g (1.85 mmol) of tetrazine **I** and 0.45 g (3.70 mmol) of benzamide in 8 ml of anhydrous THF was added at stirring 0.62 g (5.52 mmol) of sodium *tert*-butylate. The reaction mixture was boiled for 5 min, cooled, 0.5 ml of trifluoroacetic acid and then 100 ml of water was added, after 15 min the separated precipitate was filtered off and washed with methanol. Yield 0.30 g (48%), mp 280–282°C [7] (from DMF–CH_3OH). ^{1}H NMR spectrum, δ, ppm: 7.57–7.61 m (4H, CH^m), 7.61–7.70 m (2H, CH^p), 8.08–8.10 m (4H, CH^o), 12.08 s (2H, 2NH). Found, %: C 60.17; H 3.56; N 26.55. $C_{16}H_{12}N_6O_2$. Calculated, %: C 60.00; H 3.77; N 26.23.

3,6-Symmetric disubstituted 1,2,4,5-tetrazines IIIe–IIIh. Into a teflon ampule of 1 ml capacity was placed 0.04 mmol of tetrazine **I** and 0.15 mmol of an appropriate amine. The ampule was filled with acetonitrile and placed into a hydraulic press. The ampule was maintained for 3 h at 500 MPa and 80°C, then it was cooled under pressure. On opening the ampule the crystalline precipitate was filtered off and recrystallized.

3,6-Di(pyrrolidin-1-yl)-1,2,4,5-tetrazine (IIIe). Yield 61%, mp 183–184°C (from H_2O–CH_3CN) (publ.: mp 178–179°C [9]). ^{1}H NMR spectrum, δ, ppm: 1.95–2.00 m (8H, β-CH_2), 3.49–3.54 m (8H, α-CH_2). Found, %: C 54.48; H 7.42; N 37.92. $C_{10}H_{16}N_6$. Calculated, %: C 54.52; H 7.32; N 38.15.

3,6-Bis(cyclohexylamino)-1,2,4,5-tetrazine (IIIg). Yield 78%, mp 248–249°C (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 1.10–1.20 m, 1.72–1.93 m (8H and 12H, $10CH_2$), 3.59–3.62 m (2H, 2CH), 7.12 d (2H, 2NH, *J* 7.6 Hz). Found, %: C 60.78; H 8.79; N 30.26. $C_{14}H_{24}N_6$. Calculated, %: C 60.84; H 8.75; N 30.41.

3,6-Bis(cycloheptylamino)-1,2,4,5-tetrazine (IIIh). Yield 84%, mp 214–216°C (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 1.36–1.71 m, 1.86–1.95 m (24H, $12CH_2$), 3.80 m (2H, 2CH), 7.15 d (2H, 2NH, *J* 7.9 Hz). Found, %: C 63.01; H 9.35; N 27.81. $C_{16}H_{28}N_6$. Calculated, %: C 63.12; H 9.27; N 27.61.

3,6-Dimorpholino-1,2,4,5-tetrazine (IIIf). *b*. To 1 mmol (0.214 g) of tetrazine **IIIj** in 5 ml of anhydrous acetonitrile was added 11.5 mmol (1.0 ml) of morpholine and 5 mg of potassium *tert*-butylate. The mixture was boiled for 30 h (TLC monitoring, eluent benzene–acetonitrile, 1:1). On cooling the separated precipitate was filtered off and recrystallized from acetonitrile. Yield 0.35 g (14%) (80% by the general procedure), mp 259–260°C (subl.) (from C_2H_5OH). ^{1}H NMR spectrum, δ, ppm: 3.64–3.66 m (8H, $4CH_2$); 3.73–3.76 m (8H, $4CH_2$). Found, %: C 47.85; H 6.52; N 33.39. $C_{10}H_{16}N_6O_2$. Calculated, %: C 47.61; H 6.39; N 33.31.

3,6-Bis(5-bromoindol-1-yl)-1,2,4,5-tetrazine (IIIi). In 20 ml of acetonitrile was dispersed 4 g (2.0 mmol) of tetrazine **I** and 0.59 g (3.0 mmol) of 5-bromoindole, 0.2 ml of triethylamine was added, and the mixture was heated for 2–3 min to attain homogenizing. On cooling within 5 min a brigh scarlet precipitate separated, it was filtered off, twice recrystallized from DMF, and dried in a vacuum. Yield 0.28 g (86%), mp 293–294°C (from DMF). ^{1}H NMR spectrum, δ, ppm: 8.51 s, 8.53 s (2H, $4^{indolyl}$-CH); 8.00 d, 8.46 d (4H, $H^{6,7}$ indolyl), 7.00 d (2H, $2^{indolyl}$-CH); 7.61 d.d (2H, $4^{indolyl}$-CH). Found, %: C 45.93; H 2.33; N 18.24. $C_{18}H_{10}Br_2N_6$. Calculated, %: C 45.98; H 2.14; N 17.88.

3,6-Bis(1-imidazolyl)-1,2,4,5-tetrazine (IIIj). To 20 ml of acetonitrile was added 1.08 g (4 mmol) of tetrazine **I**, 0.81 g (12 mmol) of imidazole, the mixture was slightly heated for 1 min to attain homogenizing. Immediately after dissolution of the initial reagents a crystalline orange precipitate started to form in the solution. The precipitate was filtered off, washed with 5 ml of acetonitrile, and dried. Yield 0.68 g (79%), mp >360°C. ^{1}H NMR spectrum, δ, ppm: 7.37 m ($2H_{arom}$), 8.04 d.d ($2H_{arom}$, *J* 1.5 Hz), 8.78 d.d ($1H_{arom}$). Found, %: C 44.69; H 2.66; N 52.25. $C_8H_6N_8$. Calculated, %: C 44.86; H 2.82; N 52.32.

3,6-Bis(benzotriazol-1-yl)-1,2,4,5-tetrazine (IIIk). In a round-bottom flask 0.25 g (0.5 mmol) of complex **IV** was heated for 0.5 h at 170–180°C (silicon bath). At heating the complex melted, some benzotriazole appeared on the walls of the flask, and then the content of the flask solidified. From the crystalline mass the benzotriazole was washed with benzene, then it was washed with hot acetonitrile to remove tetrazine **I** impurity, and the remaining tetrazine **IIIk** was dried. Yield 0.08 g (53%), mp 280°C. ^{1}H NMR spectrum, δ, ppm: 8.61 d, 8.32 d (4H, *J* 8.4 Hz), 7.84 m, 7.66 m ($4H_{aryl}$). Found, %: C 53.34; H 2.41; N 44.50. $C_{14}H_8N_{10}$. Calculated, %: C 53.16; H 2.54; N 44.29.

3,6-Diphenylamino-1,2,4,5-tetrazine (IIIl) *a*. A solution of 0.21 g (1.0 mmol) of tetrazine **IIIj** in 3 ml of aniline was boiled for 5 h, and then left standing for 12 h at room temperature. The precipitated crystals were filtered off and washed with methanol. Yield 0.17 g (64%), mp 323°C. ^{1}H NMR spectrum, δ, ppm: 6.98–7.02 m (2H, H^p), 7.32–7.36 m (4H, H^m), 7.69–7.71 m (4H, H^o), 10.26 s (2H, 2NH). Found, %: C 63.76; H 4.30; N 32.06. $C_{14}H_{12}N_6$. Calculated, %: C 63.62; H 4.58; N 31.80.

b. In a similar way 0.27 g (1.0 mmol) of tetrazine **I** boiled for 12.5 h in 3 ml of aniline afforded tetrazine **IIIl** in a 42% yield.

c. In a similar way 0.27 g (1.0 mmol) of tetrazine **IIIk** boiled for 12 h in 3 ml of aniline afforded tetrazine **IIIl** in a 54% yield.

Complex of 3,6-bis(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine with benzotriazole, 1:2 (IV). A mixture of 0.27 g (1 mmol) of tetrazine **I** and 0.24 g (2 mmol) of benzotriazole was heated in 20 ml of acetonitrile till dissolution (3–5 min). After several minutes fine orange crystals precipitated, the precipitate was filtered off, and dried. Yield 0.48 g (94%), mp 162°C. In the NMR spectrum (DMSO-d_6) were registered signals of tetrazine **I** and benzotriazole (the complex decomposed). Found, %: C 56.83; H 4.46; N 38.71. $C_{24}H_{24}N_{14}$. Calculated, %: C 56.68; H 4.76; N 38.56.

Complex of 3,6-bis(benzotriazol-1-yl)-1,2,4,5-tetrazine with 3,5-dimethylpyrazole, 1:2 (V). The benzene extract from the above described synthesis of compound **IIIk** consisting of a mixture of tetrazine **I**, benzotriazole, and the second reaction product (R_f 0.8, acetonitrile–benzene, 1:1) was evaporated. The residue was treated with methanol, the insoluble orange compound was filtered off, washed with methanol on the filter, and dried. Yield 0.03 g (11%), mp 153–154°C. Found, %: C 56.68; H 4.82; N 38.56. $C_{24}H_{24}N_{14}$. Calculated, %: C 56.68; H 4.76; N 38.56.

3-Hydrazono-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazines IXa–IXc. To a dispersion of 2.0 g (9.7 mmol) of tetrazine **I** in 20 ml of methanol was added dropwise 9.7 mmol of aldehyde or ketone, several drops of acetic acid was added, and the mixture was stirred for 3 h. The separated precipitate was filtered off. Yield 79–91 %.

***N*-Benzylidene-*N*'-[6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazin-3-yl]hydrazine (IXa)** was described in [3].

***N*-[6-(3,5-Dimethylpyrazol-1-yl)-1,2,4,5-tetrazin-3-yl]-*N*'-(1-phenylethylidene)hydrazine (IXb).** Yield 78%, mp 175–177°C. ^{1}H NMR spectrum, δ, ppm: 2.37 s, 2.46 s, 2.62 s (3H each, 3CH$_3$); 6.13 s (1H, H^4 Pz), 7.36–7.93 m (5H, Ph), 8.97 br.s (1H, NH–N=). Found, %: C 58.61; H 5.34; N 36.42. $C_{15}H_{16}N_8$. Calculated, %: C 58.42; H 5.23; N 36.35.

***N*-[6-(3,5-Dimethylpyrazol-1-yl)-1,2,4,5-tetrazin-3-yl]-N'-[1-(4-chlorophenyl)ethylidene]hydrazine (IXc).** Yield 70%, mp 182–184°C. ^{1}H NMR spectrum, δ, ppm: 2.40 s (6H, 2CH$_3$), 2.63 s (3H, CH$_3$), 7.34–7.87 m (4H, H$_{arom}$), 6.14 s (H^4 Pz); 8.96 br.s (1H, NHN=). Found, %: C 52.29; H 4.33; N 32.55. $C_{15}H_{15}ClN_8$. Calculated, %: C 52.56; H 4.41; N 32.69.

3-Hydrazono-6-amino-substituted 1,2,4,5-tetrazines X and XI. To 1 mmol of an appropriate hydrazone **IXa–IXc** in 10–25 ml of acetonitrile was added at stirring 1.1–3.65 mmol of dodecylamine or benzylamine. The reaction mixture was heated for 3 h at 50°C (for preparation of compounds **Xa–Xc** and **XIa**) or it was stirred at room temperature (for preparation of compounds **XIb** and **XIc**). The separated precipitate was filtered off (after 12 h for compounds **X**) and recrystallized from acetonitrile. Yield 22–65%.

Benzyl-[6-(*N*'-benzylidenehydrazino)-1,2,4,5-tetrazin-3-yl]amine (Xa). Yield 22%, mp 220–223°C (from CH$_3$CN). ^{1}H NMR spectrum, δ, ppm: 3.48 s (1H, N=CH), 4.60 d (2H, Ph–CH$_2$NH), 7.33–8.39 m (11H, 2Ph, CH$_2$NH), 11.57 br.s (1H, NHN=). Found, %: C 62.96; H 4.78; N 32.34. $C_{16}H_{15}N_7$. Calculated, %: C 62.94; H 4.95; N 32.11.

Benzyl-{6-[*N*'-(1-phenylethylidene)hydrazino]-1,2,4,5-tetrazin-3-yl}amine (Xb). Yield 65%, mp 174–175.5°C (from CH$_3$CN). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH$_3$), 4.74 d (2H, PhCH$_2$NH), 5.7 t (1H, NHCH$_2$Ph), 7.33–7.91 m (10H, 2 CH$_2$NH), 5.7 t (1H, NHCH$_2$Ph), 7.33–7.91 m (10H, 2Ph), 8.30 br.s (1H, NHN=). Found, %: C 63.97; H 5.31; N 30.90. $C_{17}H_{17}N_7$. Calculated, %: C 63.93; H 5.37; N 30.70.

Benzyl(6-{*N*'-[1-(4-chlorophenyl)ethylidene]-hydrazino}-1,2,4,5-tetrazin-3-yl)amine (Xc). Yield 24%, mp 182–183°C (from CH$_3$CN). ^{1}H NMR spectrum, δ, ppm: 2.34 s (3H, CH$_3$); 4.74 (d, 2H, PhCH$_2$NH), 5.76 t (1H, NHCH$_2$Ph), 7.28–7.88 m (9H$_{arom}$), 8.33 br.s (1H, NHN=). Found, %: C 57.72; H 4.39; N 27.59. $C_{17}H_{16}ClN_7$. Calculated, %: C 57.71; H 4.56; N 27.71.

[6-(*N*'-Benzylidenehydrazino)-1,2,4,5-tetrazin-3-yl]dodecylamine (XIa). Yield 24%, mp 204–205°C (from CH$_3$CN). ^{1}H NMR spectrum, δ, ppm: 0.85 t (3H, CH$_2$CH$_3$, *J* 7.0 Hz), 1.15–1.24 m (20H, 10CH$_2$), 1.58 q

(2H, NH–C$\underline{H}_2$, *J* 7.0 Hz), 2.36 s (3H, CH_3), 7.34–7.43 m (3H, H_{arom}), 7.80–7.84 m (3H, $\underline{NH}CH_2$, H_{arom}), 10.45 br.s (1H, $\underline{NH}$–N). Found, %: C 65.51; H 8.85; N 25.54. $C_{21}H_{33}N_7$. Calculated, %: C 65.76; H 8.67; N 25.57.

Dodecyl-{6-[*N*'-(1-phenylethylidene)hydrazino]-1,2,4,5-tetrazin-3-yl}amine (XIb). Yield 60%, mp 156°C (from CH_3CN) ^{1}H, δ, ppm: 0.85 t (3H, $CH_2\underline{CH}_3$, *J* 7.0 Hz), 1.15–1.24 m [18H, $(CH_2)_9$], 1.56–1.60 m (2H, $\underline{CH}_2CH_3$), 2.36 s (3H, CH_3), 3.35 m (2H, $NH\underline{CH}_2$), 7.34–7.43 m, 7.80–7.84 m (6H, $5H_{arom}$, NH), 10.4 br.s (1H, NH=N). Found, %: C 66.44; H 8.80; N 24.68. $C_{22}H_{35}N_7$. Calculated, %: C 66.46; H 8.87; N 24.66.

Dodecyl(6-{*N*'-[1-(4-chlorophenyl)ethylidene]-hydrazino}-1,2,4,5-tetrazin-3-yl)amine (XIc). Yield 74%, mp 165°C (from CH_3CN). ^{1}H NMR spectrum, δ, ppm: 0.85 t (3H, $CH_2\underline{CH}_3$, *J* 7.0 Hz), 1.15–1.24 m (20H, $10CH_2$), 1.57–1.59 m (2H, $NHC\underline{H}_2$); 2.34 s (3H, CH_3), 7.46 d ($2H_{arom}$, *J* 7.0 Hz), 7.82–7.87 m (3H, $\underline{NH}CH_2$, H_{arom}), 10.53 br.s (1H, $\underline{NH}$–N). Found, %: C 61.38; H 7.95; N 22.71. $C_{22}H_{34}ClN_7$. Calculated, %: C 61.16; H 7.93; N 22.69.

3-(Benzotriazol-1-yl)-6-phenylamino-1,2,4,5-tetrazine (XIIa). A mixture of 0.32 g (1 mmol) of tetrazine **IIIk** and 0.46 ml (5 mmol) of aniline in 5 ml of acetonitrile was heated for 5 min till homogenizing, then the mixture was stirred for 2 h at room temperature,evaporated, the residue was thoroughly washed with ethyl ether and chloroform. Yield 80%, mp 228–229°C. ^{1}H NMR spectrum, δ, ppm: 7.12 t (1H, H^p, *J* 7.2 Hz), 7.55–7.59 m, 7.82–7.84 m (2H, $4CH_{Ph}$), 7.55–7.59 m, 7.72–7.75 m (1H each, H_{Bt}), 8.20 d, 8.31 s (1H each, H_{Bt}, *J* 8.4 Hz), 11.24 br.s (1H, NH). Found, %: C 57.95; H 3.50; N 38.34. $C_{14}H_{10}N_8$. Calculated, %: C 57.93; H 3.47; N 38.60.

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