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# Replacement of Dimethylpyrazolyl Group in 1,2,4,5-Tetrazines by Aliphatic Alcohols and Water

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**Abstract**—Reactions of 3,6-bis(4-R-3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazines and 3-amino-6-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazines with aliphatic alcohols and water in the presence of a base involved replacement of the dimethylpyrazolyl group and resulted in the formation of mono- and dialkoxy-1,2,4,5-tetrazines and 6-substituted 3-hydroxy-1,2,4,5-tetrazines. Dissociation constants of the latter were determined by potentiometric titration.

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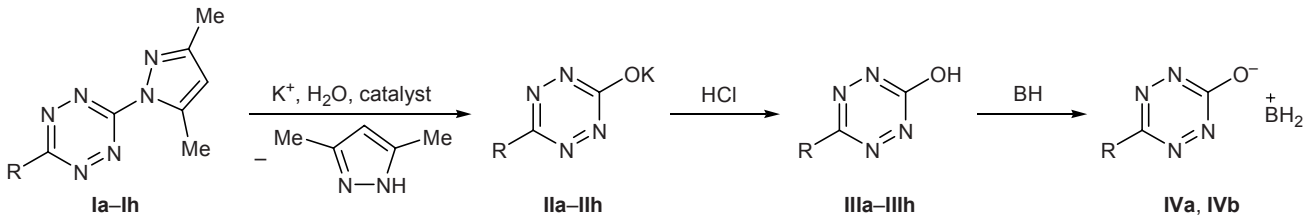
Replacement of the dimethylpyrazolyl group in 3,6-bis(3,5-dimethyl-4-R-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazines **Ia**–**Ic** and their derivatives by nitrogen-centered nucleophiles has been well documented [1–4], while reactions of the same tetrazines with oxygen-centered nucleophiles have been studied poorly. However, 3-hydroxy-6-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazine attracts interest as promising ligand in the synthesis of organometallic clusters with important magnetic properties [5–7].

Hydrolysis of 3,6-bis(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazine (**Ia**) in dilute hydrochloric acid was reported to produce 6-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazin-3-ol (**IIIa**) in 15% yield [8]. We have found that the yield of tetrazine **IIIa** may be increased up to almost quantitative (97%) by carrying out the reaction in aqueous acetic acid. Hydroxytetrazines **IIIa**–**IIIh** can also be obtained in high yields from the corresponding potassium salts **IIa**–**IIh** that are formed form compounds **Ia**–**Ih** in the presence of a base (potassium hydroxide or *tert*-butoxide; see table, Scheme 1).

Hydroxytetrazines **IIIa**–**IIIh** are strong organic OH acids. They form brightly colored salts with both potassium and sodium ions and aliphatic and cycloaliphatic amines, e,g,, with benzylamine and morpholine (salts **IVa** and **IVb**). The acid dissociation constants of hydroxytetrazines **IIIa**–**IIIh** were determined by potentiometric titration of their aqueous solutions at a ionic strength μ of 0.1 (KCl) using glass and calomel electrodes. The following p$K_a$ values were obtained: **IIIa**, 3.00±0.01; **IIIb**, 3.01±0.02; **IIIc**, 3.09±0.02; **IIId**, 4.38±0.01; **IIIe**, 5.54±0.05; **IIIf**, 4.48±0.03; **IIIg**, 3.19±0.04; **IIIh**, 3.31±0.05.

**Scheme 1.**




**I**–**III**, R = 3,5-dimethyl-1*H*-pyrazol-1-yl (**a**), 4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl (**b**), 4-chloro-3,5-dimethyl-1*H*-pyrazol-1-yl (**c**), morpholino (**d**), thiomorpholino (**e**), piperidino (**f**), pyrrolidin-1-yl (**g**), 4-methylpiperazin-1-yl (**h**); **IV**, R = 3,5-dimethyl-1*H*-pyrazol-1-yl, BH = $PhCH_2NH_2$ (**a**), morpholine (**b**).

Alkoxytetrazines can be synthesized via replacement of the pyrazolyl group in compounds **I** by alcohol residues in the presence of a base. For example, 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-6-methoxy-1,2,4,5-tetrazine (**Va**) was obtained in 76% yield by heating tetrazine **Ia** in boiling methanol in the presence of pyridine [3]. The use of triethylamine as a base ensured smooth formation of tetrazine **Va** in a high yield at room temperature, whereas the reaction performed on heating under reflux gave 3,6-dimethoxy-1,2,4,5-tetrazine (**VI**), in contrast to the procedures described previously [9, 10]. In the presence of potassium *tert*-butoxide, compound **VI** was synthesized in 72% yield at room temperature.

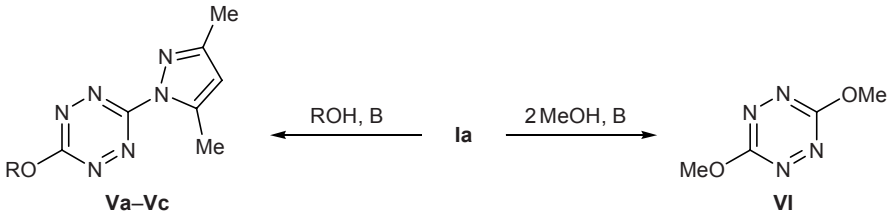
Replacement of the pyrazolyl substituent in tetrazine **Ia** by ethoxy group gave 81% of 6-(3,5-dimethyl-1*H*-pyrazol-1-yl)-3-ethoxy-1,2,4,5-tetrazine (**Vb**) when the reaction was carried out in anhydrous ethanol in the presence of triethylamine. Tetrazine **Ia** also reacted with higher alcohols. For example, by heating compound **Ia** with nonan-1-ol in anhydrous dioxane in the presence of triethylamine we obtained 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-6-nonyloxy-1,2,4,5-tetrazine (**Vc**) in 56% yield (Scheme 2). Likewise, unsymmetrically substituted 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-6-R-1,2,4,5-tetrazines **Id** and **Ii**–**Ir** [3, 4] reacted with oxygen-centered nucleophiles in the presence of potassium *tert*-butoxide to give products of replacement of the pyrazolyl group (Scheme 3). The reactions with methanol were carried out by heating under reflux over a period of 0.5–1.5 h, and the products were methoxytetrazines **VIId** and **VIIi**–**VIIr**. The reactions with propan-1-ol to give compounds **VIIIi**–**VIIIn** and with propan-2-ol to give compounds **IXd**, **IXk**, and **IXl** required a longer time, 2–6 and 10–12 h, respectively, whereas *tert*-butyl alcohol failed to react at all.

Yields and melting points of 6-substituted 3-hydroxy-1,2,4,5-tetrazine potassium salts **IIa**–**IIh**

| Compound no. | Yield, % | mp, °C (decomp.) |
|---|---|---|
| **IIa** | 81 | 300 |
| **IIb** | 88 | 316–320 |
| **IIc** | 91 | 320–322 |
| **IId** | 79 | 292 |
| **IIe** | 92 | 268 |
| **IIf** | 82 | 254–257 |
| **IIg** | 68 | 298 |
| **IIh** | 72 | 278–280 |

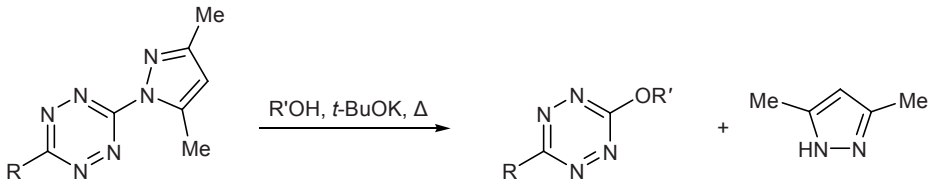
Symmetric 3,6-disubstituted 1,2,4,5-tetrazines reacted with unsaturated alcohols according to the scheme described in [11, 12], but triethylamine was used as base instead of sodium hydride. In the reaction of tetrazine **Ia** with but-3-yn-1-ol, a mixture of furopyridazine **XII** and pyridazine **XIII** was formed at a ratio of 5:1 ($^1$H NMR data). Under analogous conditions, 3,6-bis(1*H*-imidazol-1-yl)-1,2,4,5-tetrazine (**X**)

**Scheme 2.**



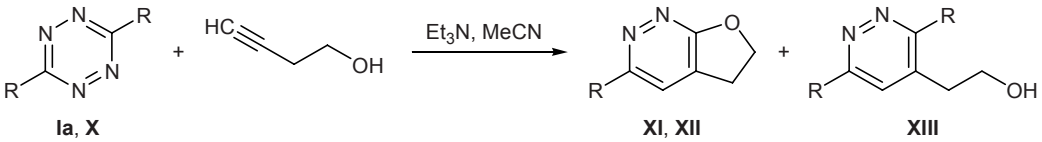

**V**, R = Me (**a**), Et (**b**), $C_9H_{19}$ (**c**).

**Scheme 3.**




R = morpholino (**d**), PhNH (**i**), 4-$MeOC_6H_4NH$ (**j**), 4-$MeC_6H_4NH$ (**k**), 4-$FC_6H_4NH$ (**l**), 4-$ClC_6H_4NH$ (**m**), 4-$BrC_6H_4NH$ (**n**), 3-$MeC_6H_4NH$ (**o**), 3,4-$Me_2C_6H_3NH$ (**p**), 1-adamantylamino (**q**), MeC(Ph)=NNH (**r**); **VII**, R′ = Me; **VIII**, R′ = Pr; **IX**, R′ = *i*-Pr.

**Scheme 4.**




**Ia**, **X** **XI**, **XII** **XIII**

**Ia**, **XII**, **XIII**, R = 3,5-dimethyl-1*H*-pyrazol-1-yl; **X**, **XI**, R = 1*H*-imidazol-1-yl.

was converted in a good yield (75%) into furopyridazine **XI**, presumably via replacement of the imidazolyl group and subsequent intramolecular [4+2]-cycloaddition.

## EXPERIMENTAL

The $^1$H NMR spectra were recorded on a Bruker Avance DRX-400 instrument at 400 MHz using $CDCl_3$ as solvent and tetramethylsilane as internal reference. The melting points were determined on a Boetius melting point apparatus. The progress of reactions and the purity of products were monitored by TLC on Silufol plates using chloroform–ethanol (9 : 1) as eluent. Flash chromatography was performed on silica gel (5–40 μm); eluent benzene–acetonitrile. The acid dissociation constants were determined with the aid of a Radelkis OP-208/1 digital pH-meter.

3,6-Bis(1*H*-imidazol-1-yl)-1,2,4,5-tetrazine (**X**) was synthesized as described in [4].

**6-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazin-3-ol (IIIa).** *a*. A suspension of 5.65 g (20.9 mmol) of tetrazine **Ia** in 35 ml of glacial acetic acid was heated to the boiling point until compound **Ia** dissolved. The solution was filtered, the filtrate was cooled, and the orange crystals were filtered off and washed with acetic acid. Yield 3.90 g (97%), mp 204–206°C. $^1$H NMR spectrum, δ, ppm: 2.22 s (3H, $CH_3$), 2.39 s (3H, $CH_3$), 6.21 s (1H, 4′-H). Found, %: C 43.61; H 4.19; N 43.82. $C_7H_8N_6O$. Calculated, %: C 43.75; H 4.17; N 43.75.

*b*. Potassium *tert*-butoxide, 0.21 g (1.87 mmol), was added in portions under stirring at room temperature to a mixture of 0.46 g (1.7 mmol) of tetrazine **Ia** in 6 ml of propan-2-ol. The originally red crystals gradually turned lilac. After 0.75 h, the crystals were filtered off, washed with propan-2-ol, and dried in air. Yield of potassium salt **IIa** 0.32 g (81%), mp 300°C. The product was dissolved in 7 ml of distilled water, and 18% hydrochloric acid was added dropwise under stirring until pH ~2.5. The crystals (orange needles) were filtered off, washed with water, and dried. Yield 0.21 g (78%), mp 204–206°C.

*c*. Tetrazine **Ia**, 1.00 g (3.6 mmol), was added to a mixture of 15 ml of propan-2-ol and 0.3 g (5.4 mmol) of potassium hydroxide, the mixture was stirred for 1 h, and the product was isolated as described above in *b*. Yield 0.68 g (78%).

6-Substituted 3-hydroxy-1,2,4,5-tetrazines **IIIb**–**IIIh** were synthesized in a similar way.

**6-(4-Bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazin-3-ol (IIIb).** Yield 92%, mp 189°C (decomp.). $^1$H NMR spectrum, δ, ppm: 2.33 s (3H, $CH_3$), 2.63 s (3H, $CH_3$). Found, %: C 31.08; H 2.48; N 30.95. $C_7H_7BrN_6O$. Calculated, %: C 31.00; H 2.58; N 31.00.

**6-(4-Chloro-3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazin-3-ol (IIIc).** Yield 88%, mp 178–180°C (decomp.). $^1$H NMR spectrum, δ, ppm: 2.35 s (3H, $CH_3$), 2.68 s (3H, $CH_3$). Found, %: C 37.01; H 3.12; N 36.98. $C_7H_7ClN_6O$. Calculated, %: C 37.09; H 3.09; N 37.09.

**6-Morpholino-1,2,4,5-tetrazin-3-ol (IIId).** Yield 81%, mp 152–154°C. $^1$H NMR spectrum, δ, ppm: 3.57 t (4H, $CH_2OCH_2$, $J$ = 9.2 Hz), 3.74 t (4H, $CH_2NCH_2$, $J$ = 9.2 Hz). Found, %: C 39.27; H 4.85; N 38.21. $C_6H_9N_5O_2$. Calculated, %: C 39.34; H 4.92; N 38.25.

**6-Thiomorpholino-1,2,4,5-tetrazin-3-ol (IIIe).** Yield 90%, mp 130–132°C. $^1$H NMR spectrum, δ, ppm: 2.69 t (4H, $CH_2SCH_2$, $J$ = 9.6 Hz), 3.96 t (4H, $CH_2NCH_2$, $J$ = 9.6 Hz). Found, %: C 36.09; H 4.45; N 35.09. $C_7H_9N_5OS$. Calculated, %: C 36.18; H 4.52; N 35.18.

**6-Piperidino-1,2,4,5-tetrazin-3-ol (IIIf).** Yield 69%, mp 126°C (decomp.). $^1$H NMR spectrum, δ, ppm: 1.62 m (6H, $CH_2$), 3.62 t (4H, $CH_2NCH_2$, $J$ = 5.2 Hz). Found, %: C 46.32; H 6.16; N 38.58. $C_7H_{11}N_5O$. Calculated, %: C 46.41; H 6.08; N 38.67.

**6-(Pyrrolidin-1-yl)-1,2,4,5-tetrazin-3-ol (IIIg).** Yield 72%, mp 199–200°C (decomp.). $^1$H NMR spectrum, δ, ppm: 2.11 m (4H, $CH_2CH_2$), 3.77 m (4H, $CH_2NCH_2$). Found, %: C 43.22; H 5.33; N 41.85. $C_6H_9N_5O$. Calculated, %: C 43.11; H 5.39; N 41.92.

**6-(4-Methylpiperazin-1-yl)-1,2,4,5-tetrazin-3-ol (IIIh).** Yield 66%, mp 240°C (decomp.). $^1$H NMR

spectrum, δ, ppm: 2.24 s (3H, $NCH_3$), 2.54 t (4H, $NCH_2$, $J$ = 5.0 Hz), 4.02 t (4H, $NCH_2$, $J$ = 5.0 Hz). Found, %: C 42.27; H 6.01; N 42.95. $C_7H_{12}N_6O$. Calculated, %: C 42.86; H 6.12; N 42.86.

**Benzylammonium 6-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazin-3-olate (IVa).** Yield 78%, mp 144–146°C. $^1$H NMR spectrum, δ, ppm: 2.17 s and 2.22 s (3H each, $CH_3$), 4.06 s (2H, C**H**$_2$Ph), 6.04 s (1H, 4′-H), 7.48–7.38 m (5H, Ph), 8.23 br.s (3H, $H_3N^+$). Found, %: C 56.27; H 5.88; N 32.52. $C_{14}H_{17}N_7O$. Calculated, %: C 56.19; H 5.69; N 32.78.

**Morpholinium 6-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazin-3-olate (IVb).** Yield 70%, mp 147–150°C. $^1$H NMR spectrum, δ, ppm: 2.22 s and 2.16 s (3H each, $CH_3$), 3.14–3.12 m (4H, $CH_2NCH_2$), 3.78–3.76 m (4H, $CH_2OCH_2$), 6.05 s (1H, 4′-H), 8.75 br.s (2H, $H_2N^+$). Found, %: C 47.10; H 6.13; N 34.93. $C_{11}H_{16}N_7O_2$. Calculated, %: C 47.48; H 5.79; N 35.23.

**3-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-6-methoxy-1,2,4,5-tetrazine (Va).** Triethylamine, ~0.1 ml, was added to a mixture of 1.0 g (37 mmol) of tetrazine **Ia** and 30 ml of methanol, and the mixture was stirred for 3 h at room temperature (the progress of the reaction was monitored by TLC). The solvent was distilled off, and the residue was recrystallized from methanol–water (3 : 7). Yield 0.61 g (81%), dark red crystals, mp 156–157°C. $^1$H NMR spectrum, δ, ppm: 2.35 s and 2.63 s (3H each, $CH_3$), 4.33 s (3H, $OCH_3$), 6.14 s (1H, 4′-H). Found, %: C 46.72; H 5.12; N 40.53. $C_8H_{10}N_6O$. Calculated, %: C 46.60; H 4.85; N 40.78.

**3-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-6-ethoxy-1,2,4,5-tetrazine (Vb).** A mixture of 0.27 g (1.0 mmol) of tetrazine **Ia**, 0.14 ml (1.0 mol) of triethylamine, and 10 ml of anhydrous ethanol was stirred for 45 min at 50°C. The solvent was evaporated, and the residue was washed with a small amount of anhydrous hexane and recrystallized from hexane. Yield 0.18 g (81%), mp 114–116°C. $^1$H NMR spectrum, δ, ppm: 1.59 t (3H, $CH_3$, $J$ = 7.0 Hz), 2.39 s and 2.65 s (3H each, $CH_3$), 4.76 q (2H, $CH_2$, $J$ = 7.0 Hz), 6.17 s (1H, 4′-H). Found, %: C 49.28; H 5.48; N 38.34. $C_9H_{12}N_6O$. Calculated, %: C 49.08; H 5.49; N 38.16.

**3-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-6-nonyloxy-1,2,4,5-tetrazine (Vc)** was synthesized in a similar way. Yield 60%, bright red syrupy material. $^1$H NMR spectrum, δ, ppm: 0.87 t (3H, $CH_3$, $J$ = 7.0 Hz), 1.2–1.4 m (10H, $CH_2$), 1.53 m (2H, $CH_2$), 1.95 m (2H, $OCH_2$C**H**$_2$), 2.37 s and 2.64 s (3H each, $CH_3$), 4.67 t (2H, $OCH_2$, $J$ = 7.0 Hz), 6.15 s (1H, 4′-H). Found, %: C 60.32; H 8.31; N 26.29. $C_{16}H_{26}N_6O$. Calculated, %: C 60.35; H 8.23; N 26.40.

**3,6-Dimethoxy-1,2,4,5-tetrazine (VI).** *a*. Triethylamine, 0.1 ml, was added to a mixture of 0.5 g (1.85 mol) of tetrazine **Ia** and 20 ml of anhydrous methanol, and the mixture was heated for 30 min under reflux (TLC). The solvent was distilled off, the bright red residue was dissolved in 2 ml of benzene, and the solution was passed through a column charged with silica gel using benzene as eluent to isolate 0.260 g (80%) of compound **VI**.

*b*. Potassium *tert*-butoxide, ~25 mg, was added to a mixture of 0.5 g (1.85 mol) of tetrazine **Ia** and 20 ml of anhydrous methanol, and the solution was stirred for 30 min at room temperature. The product was isolated as described above in *a*. Yield 0.233 g (72%), mp 62°C. $^1$H NMR spectrum: δ 4.18 ppm, s (6H, $OCH_3$). Found, %: C 33.86; H 3.93; N 39.29. $C_4H_6N_4O_2$. Calculated, %: C 33.80; H 4.25; N 39.42.

**6-Substituted 3-alkoxy-1,2,4,5-tetrazines VIId, VIIi–VIIr, VIIIi–VIIIn, IXd, IXk, and IXl (*general procedure*).** A mixture of 0.01 mol of tetrazine **Id** or **Ii–Ir**, a small amount of potassium *tert*-butoxide, and 30 ml of the corresponding alcohol was heated for 2–12 h under reflux, the progress of the reaction being monitored by TLC. The mixture was cooled, and the precipitate was filtered off and purified by recrystallization.

**3-Methoxy-6-morpholino-1,2,4,5-tetrazine (VIId).** Yield 81%, mp 115–116°C. $^1$H NMR spectrum, δ, ppm: 3.86 m (8H, morpholine), 4.17 s (3H, $OCH_3$). Found, %: C 42.51; H 5.71; N 35.64. $C_7H_{11}N_5O_2$. Calculated, %: C 42.69; H 5.71; N 35.53.

**6-Methoxy-*N*-phenyl-1,2,4,5-tetrazin-3-amine (VIIi).** Yield 93%, mp 199–200°C. $^1$H NMR spectrum, δ, ppm: 4.10 s (3H, $OCH_3$); 7.02 m, 7.34 m, and 7.70 m (5H, $H_{arom}$); 10.48 br.s (1H, NH). Found, %: C 53.30; H 4.45; N 34.80. $C_9H_9N_5O$. Calculated, %: C 53.20; H 4.43; N 34.48.

**6-Methoxy-*N*-(4-methoxyphenyl)-1,2,4,5-tetrazin-3-amine (VIIj).** Yield 85%, mp 138–139°C. $^1$H NMR spectrum, δ, ppm: 3.74 s and 4.09 s (3H each, $OCH_3$), 6.92 d and 7.58 d (2H each, $H_{arom}$, $J$ = 9.0 Hz), 10.27 br.s (1H, NH). Found, %: C 51.48; H 4.62; N 30.06. $C_{10}H_{11}N_5O_2$. Calculated, %: C 51.50; H 4.72; N 30.06.

**6-Methoxy-*N*-(4-methylphenyl)-1,2,4,5-tetrazin-3-amine (VIIk).** Yield 85%, mp 166°C. $^1$H NMR spectrum, δ, ppm: 2.27 s (3H, $CH_3$), 4.10 s (3H, $OCH_3$),

7.09 d and 7.57 d (2H each, $H_{arom}$, $J$ = 8.5 Hz), 10.39 br.s (1H, NH). Found, %: C 55.38; H 5.15; N 32.06. $C_{10}H_{11}N_5O$. Calculated, %: C 55.30; H 5.07; N 32.26.

***N*-(4-Fluorophenyl)-6-methoxy-1,2,4,5-tetrazin-3-amine (VIIl).** Yield 91%, mp 232°C (sublimes). $^1$H NMR spectrum, δ, ppm: 4.13 s (3H, $OCH_3$), 7.07 m and 7.70 m (4H, $H_{arom}$), 10.47 br.s (1H, NH). Found, %: C 48.71; H 3.57; N 31.78. $C_9H_8FN_5O$. Calculated, %: C 48.88; H 3.62; N 31.67.

***N*-(4-Chlorophenyl)-6-methoxy-1,2,4,5-tetrazin-3-amine (VIIm).** Yield 88%, mp 218–220°C. $^1$H NMR spectrum, δ, ppm: 4.10 s (3H, $OCH_3$), 7.33–7.43 m and 7.63–7.76 m (4H, $H_{arom}$), 10.64 br.s (1H, NH). Found, %: C 45.45; H 3.21; N 29.66. $C_9H_8ClN_5O$. Calculated, %: C 45.47; H 3.37; N 29.73.

***N*-(4-Bromophenyl)-6-methoxy-1,2,4,5-tetrazin-3-amine (VIIn).** Yield 88%, mp 221°C. $^1$H NMR spectrum, δ, ppm: 4.11 s (3H, $OCH_3$), 7.73–7.47 m (4H, $H_{arom}$), 10.67 br.s (1H, NH). Found, %: C 38.54; H 2.71; N 24.90. $C_9H_8BrN_5O$. Calculated, %: C 38.30; H 2.84; N 24.82.

**6-Methoxy-*N*-(3-methylphenyl)-1,2,4,5-tetrazin-3-amine (VIIo).** Yield 58%, mp 154–155°C. $^1$H NMR spectrum, δ, ppm: 2.31 s (3H, $CH_3$), 4.10 s (3H, $OCH_3$), 7.38 m (3H, $H_{arom}$), 7.53 m (1H, $H_{arom}$), 10.42 br.s (1H, NH). Found, %: C 55.32; H 4.99; N 32.31. $C_{10}H_{11}N_5O$. Calculated, %: C 55.30; H 5.07; N 32.26.

***N*-(3,4-Dimethylphenyl)-6-methoxy-1,2,4,5-tetrazin-3-amine (VIIp).** Yield 59%, mp 189°C. $^1$H NMR spectrum, δ, ppm: 2.19 s and 2.22 s (3H each, $CH_3$), 4.09 s (3H, $OCH_3$), 7.06–7.46 m (3H, $H_{arom}$), 10.35 br.s (1H, NH). Found, %: C 56.93; H 5.55; N 30.42. $C_{11}H_{13}N_5O$. Calculated, %: C 57.14; H 5.63; N 30.30.

***N*-(1-Adamantyl)-6-methoxy-1,2,4,5-tetrazin-3-amine (VIIq).** Yield 63%, mp 174–176°C. $^1$H NMR spectrum, δ, ppm: 1.66 m and 2.07 m (15H, Ad), 4.02 s (3H, $OCH_3$), 7.72 br.s (1H, NH). Found, %: C 59.59; H 7.36; N 26.61. $C_{13}H_{19}N_5O$. Calculated, %: C 59.77; H 7.28; N 26.82.

**1-(6-Methoxy-1,2,4,5-tetrazin-3-yl)-2-(1-phenylethylidene)hydrazine (VIIr).** Yield 76%, mp 177–178°C. $^1$H NMR spectrum, δ, ppm: 2.42 s (3H, $CH_3$), 4.24 s (3H, $OCH_3$), 7.43–7.35 m (3H, $H_{arom}$), 7.88–7.85 m (2H, $H_{arom}$), 8.66 br.s (1H, NH). Found, %: C 53.89; H 4.86; N 34.61. $C_{11}H_{12}N_6O$. Calculated, %: C 54.08; H 4.95; N 34.41.

***N*-Phenyl-6-propoxy-1,2,4,5-tetrazin-3-amine (VIIIi).** Yield 54%, mp 136°C. $^1$H NMR spectrum, δ, ppm: 1.08 t (3H, $CH_3$, $J$ = 7.5 Hz); 1.88 m (2H, C**H**$_2$CH$_3$); 4.42 t (2H, $OCH_2$, $J$ = 6.5 Hz); 6.97–7.01 m, 7.28–7.32 m, and 7.68–7.71 m (5H, $H_{arom}$); 10.42 s (1H, NH). Found, %: C 57.02; H 5.72; N 30.05. $C_{11}H_{13}N_5O$. Calculated, %: C 57.14; H 5.63; N 30.30.

***N*-(4-Methoxyphenyl)-6-propoxy-1,2,4,5-tetrazin-3-amine (VIIIj).** Yield 49%, mp 138–139°C. $^1$H NMR spectrum, δ, ppm: 1.07 t (3H, $CH_3$, $J$ = 7.5 Hz), 1.87 m (2H, C**H**$_2$CH$_3$), 4.39 t (2H, $OCH_2$, $J$ = 6.5 Hz), 6.86 m and 7.57 m (4H, $H_{arom}$), 3.73 s (3H, $OCH_3$), 10.23 br.s (1H, NH). Found, %: C 55.34; H 5.50; N 26.69. $C_{12}H_{15}N_5O_2$. Calculated, %: C 55.17; H 5.75; N 26.82.

***N*-(4-Methylphenyl)-6-propoxy-1,2,4,5-tetrazin-3-amine (VIIIk).** Yield 59%, mp 147–148°C. $^1$H NMR spectrum, δ, ppm: 1.07 t (3H, $CH_3$, $J$ = 7.5 Hz), 1.87 m (2H, C**H**$_2$CH$_3$), 2.30 s (3H, $CH_3$), 4.40 t (2H, $OCH_2$, $J$ = 6.5 Hz), 7.09 d and 7.56 d (2H each, $H_{arom}$, $J$ = 8.5 Hz), 10.33 br.s (1H, NH). Found, %: C 58.92; H 6.01; N 28.32. $C_{12}H_{15}N_5O$. Calculated, %: C 58.78; H 6.12; N 28.57.

***N*-(4-Fluorophenyl)-6-propoxy-1,2,4,5-tetrazin-3-amine (VIIIl).** Yield 68%, mp 172–173°C. $^1$H NMR spectrum, δ, ppm: 1.07 t (3H, $CH_3$, $J$ = 7.5 Hz), 1.88 m (2H, C**H**$_2$CH$_3$), 4.41 t (2H, $OCH_2$, $J$ = 6.5 Hz), 7.07 m and 7.70 m (4H, $H_{arom}$), 10.45 br.s (1H, NH). Found, %: C 50.95; H 4.77; N 29.98. $C_{11}H_{12}FN_5O$. Calculated, %: C 51.01; H 4.82; N 28.11.

***N*-(4-Chlorophenyl)-6-propoxy-1,2,4,5-tetrazin-3-amine (VIIIm).** Yield 72%, mp 201–202°C. $^1$H NMR spectrum, δ, ppm: 1.07 t (3H, $CH_3$, $J$ = 7.5 Hz), 1.88 m (2H, C**H**$_2$CH$_3$), 4.42 t (2H, $OCH_2$, $J$ = 6.5 Hz), 7.29 m and 7.72 m (4H, $H_{arom}$), 10.61 br.s (1H, NH). Found, %: C 49.91; H 4.46; N 26.28. $C_{11}H_{12}ClN_5O$. Calculated, %: C 49.72; H 4.52; N 26.37.

***N*-(4-Bromophenyl)-6-propoxy-1,2,4,5-tetrazin-3-amine (VIIIn).** Yield 54%, mp 136°C. $^1$H NMR spectrum, δ, ppm: 1.07 t (3H, $CH_3$, $J$ = 7.5 Hz), 1.88 m (2H, C**H**$_2$CH$_3$), 4.42 t (2H, $OCH_2$, $J$ = 6.5 Hz), 7.43 m and 7.67 m (4H, $H_{arom}$), 10.61 br.s (1H, NH). Found, %: C 42.50; H 3.82; N 22.64 $C_{11}H_{12}BrN_5O$. Calculated, %: C 42.58; H 3.87; N 22.58.

**3-Isopropoxy-6-morpholino-1,2,4,5-tetrazine (IXd).** Yield 46%, mp 94–95°C. $^1$H NMR spectrum, δ, ppm: 1.39 d (6H, $CH_3$, $J$ = 6.0 Hz), 3.74 m (8H, morpholine), 5.22 m (1H, OCH). Found, %: C 48.09; H 6.58; N 31.00. $C_9H_{15}N_5O_2$. Calculated, %: C 48.00; H 6.67; N 31.11.

**6-Isopropoxy-*N*-(4-methylphenyl)-1,2,4,5-tetrazin-3-amine (IXg).** Yield 59%, mp 162–164°C. $^1$H NMR spectrum, δ, ppm: 1.44 d (6H, $CH_3$, $J$ = 6 Hz), 2.30 s (3H, C**H**$_3$C$_6$H$_4$), 5.26 m (1H, OCH), 7.09 d and 7.56 d (2H each, $H_{arom}$, $J$ = 8.5 Hz), 10.30 br.s (1H, NH). Found, %: C 58.86; H 6.05; N 28.63. $C_{12}H_{15}N_5O$. Calculated, %: C 58.78; H 6.12; N 28.57.

***N*-(4-Fluorophenyl)-6-isopropoxy-1,2,4,5-tetrazin-3-amine (IXh).** Yield 51%, mp 162–163°C. $^1$H NMR spectrum, δ, ppm: 1.48 t (6H, $CH_3$, $J$ = 6 Hz), 5.28 m (1H, OCH), 7.09 m and 7.70 m (4H, $H_{arom}$), 10.30 br.s (1H, NH). Found, %: C 50.79; H 4.92; N 28.22. $C_{11}H_{12}FN_5O$. Calculated, %: C 51.01; H 4.82; N 28.11.

**3-(1*H*-Imidazol-1-yl)-5,6-dihydrofuro[2,3-*c*]pyridazine (XI).** A mixture of 107 mg (0.5 mmol) of tetrazine **X**, 0.1 ml (1.35 mmol) of but-3-yn-1-ol, and 3 drops of triethylamine in 5 ml of anhydrous acetonitrile was heated for 1.5 h under reflux. The precipitate was filtered off, the filtrate was evaporated, and the residue was combined with the first precipitate and recrystallized from anhydrous acetonitrile. Yield 69 mg (73%), mp 243–245°C. $^1$H NMR spectrum, δ, ppm: 3.42 t and 4.73 t (4H, $CH_2$, $J$ = 8.8 Hz); 7.06, 7.85, and 8.39 (3H, 2′-H, 4′-H, 5′-H), 8.04 s (1H, 4-H). Found, %: C 57.80; H 4.24; N 30.05. $C_9H_8N_4O$. Calculated, %: C 57.44; H 4.29; N 29.77.

**Reaction of 3,6-bis(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,2,4,5-tetrazine (Ia) with but-3-yn-1-ol.** A mixture of 135 mg (0.5 mmol) of tetrazine **Ia**, 0.1 ml (1.35 mmol) of but-3-yn-1-ol, and 3 drops of triethylamine in 5 ml of anhydrous acetonitrile was heated for 3 h under reflux (until the initial tetrazine disappeared according to the TLC data). The mixture was cooled, the solvent was distilled off, and the residue was recrystallized from anhydrous acetonitrile. The product was a mixture of compounds **XII** and **XIII** at a ratio of 5:1 (according to the $^1$H NMR data), mp 107–112°C.

**3-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-5,6-dihydrofuro[2,3-*c*]pyridazine (XII).** $^1$H NMR spectrum, δ, ppm: 2.28 s and 2.65 s (3H each, $CH_3$), 3.35 t and 4.74 t (4H, $CH_2$, $J$ = 8.5 Hz), 6.01 s (1H, 4′-H), 7.96 s (1H, 4-H).

**2-[3,6-Bis(3,5-dimethyl-1*H*-pyrazol-1-yl)pyridazin-4-yl]ethanol (XIII).** $^1$H NMR spectrum, δ, ppm: 2.30 s, 2.32 s, 2.42 s, and 2.75 s (3H each, $CH_3$); 2.95 t and 4.03 t (4H, $CH_2CH_2$, $J$ = 5.8 Hz), 6.08 s (2H, 4′-H, 4″-H), 8.24 s (1H, 4-H).

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