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Synthesis and Spectral, Electrochemical, and Antioxidant Properties of 2-(5-Aryl-6-R-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles

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Abstract—New 2-(5-aryl-6-R-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles were synthesized from the corresponding formazans by alkylation and subsequent cyclization of *N*-alkyl derivatives. The products were characterized by ^{1}H and ^{13}C NMR, IR, and mass spectra and X-ray diffraction data. Electrochemical properties and antioxidant activity of the synthesized benzothiazole derivatives were studied.

Keywords: 2-(5-aryl-6-R-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles, dihydrotetrazines, cyclic voltammetry, electrochemical properties, antioxidant activity.

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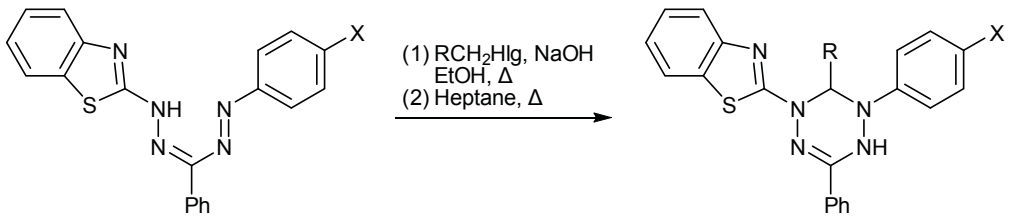
Free radical-induced oxidative degradation of biological components in an organism often causes oxidative stress which is responsible for many degenerative diseases [1, 2]. Antioxidants, i.e., compounds capable of quenching free radicals, are used to avoid or reduce the effect of oxidative stress on living cells [3]. Well known antioxidants are derivatives of phenols and amines, both biogenic and synthetic, as well as of nitrogen heterocycles (indole, carbazole, dihydropyridine, dihydroacridine, etc.) [4–8]. Kozlova et al. [9] previously reported antioxidant activity of tetrazolyl derivatives of 5,6-dihydro-4*H*-1,2,4,5-tetrazine that are precursors to verdazyls. The majority of antioxidants are electrochemically active compounds capable of forming stable radicals.

The goal of the present work was to study electrochemical and antioxidant properties of newly synthesized 2-(5-aryl-6-R-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles **2**–**5** and the relevant structure–property relationships.

Compounds **2**–**5** were synthesized by alkylation of 1-aryl-5-(1,3-benzothiazol-2-yl)-3-phenylformazans **1** with haloalkanes in alcoholic alkali, followed by cyclization of *N*-alkyl derivatives, according to the procedure described previously [10] (Scheme 1). All compounds were characterized by elemental analyses, ^{1}H and ^{13}C NMR, IR, and mass spectra, and X-ray analysis of compound **4b** (Fig. 1). Compounds **2a**, **3a**, and **4a** were reported by us previously [11] and were used for comparison.

The ^{1}H NMR spectra of **2**–**5** showed a singlet at δ 9.52–9.62 ppm from the NH proton. Methylene protons of **2a**–**2f** resonated at δ 5.38–5.49 ppm. The 6-H signal of **3a**–**3e** is shifted downfield relative to the corresponding signal of **2a**–**2e** and is observed in the region δ 6.32–6.40 ppm (δ 6.08–6.18 ppm for **4a**–**4e**). In going from compounds **3** to **4** and then to **5**, the 6-H signal shifts upfield, and the 6-H proton of **5a**–**5e** resonates as a multiplet at δ 6.02–6.05 ppm. In the series of compounds **3a**–**3e** and **4a**–**4e**, the strongest effect of the halogen atom in the aromatic ring on the position of the 6-H signal is observed for fluorine derivatives **3b** and **4b**, whereas there is no such effect for **5a**–**5e**. The position of the C^6 signal in the ^{13}C NMR spectra of **2**–**5** depends on the 6-substituent (R). For compounds **2a**–**2f**, introduction of a fluorine atom into the benzene ring on C^5 shifts the C^6 signal from δ_C 61.99 to 62.89 ppm, and an upfield shift of that signal to δ_C 61.73 ppm is observed for 5-(4-iodophenyl) derivative **2e**. A similar relation is characteristic of compounds **3a**–**3e** [δ_C 66.71 (**3a**), 67.19 (**3b**), 66.64–66.39 ppm (**3c**–**3e**)] and **4a**–**4e** [71.73 (**4a**), 72.24 (**4b**),

Scheme 1.



1, X = H (**a**), F (**b**), Cl (**c**), Br (**d**), I (**e**); **2**, R = H, X= H (**a**), F (**b**), Cl (**c**), Br (**d**), I (**e**), MeO (**f**); **3**, R = Me, X= H (**a**), F (**b**), Cl (**c**), Br (**d**), I (**e**); **4**, R = Et, X = H (**a**), F (**b**), Cl (**c**), Br (**d**), I (**e**); **5**, R = CH_2=CH, X = H (**a**), F (**b**), Cl (**c**), Br (**d**), I (**e**).

71.64–71.39 ppm (**4c**–**4e**)]. It should be noted that the chemical shifts of C^6 in 6-vinyl derivatives **5a**–**5e** (R = CH_2=CH) are similar to those of **4a**–**4e**: 71.19 (**5a**), 71.70 (**5b**), 71.06 (**5d**), and 70.93 ppm (**5e**).

The IR spectra of **2**–**5** displayed an absorption band in the region 3150–3260 cm^{-1} due to NH stretching vibrations, and $[M + H]^+$ ion peaks were present in their mass spectra.

The structure of **4b** was proved by X-ray analysis (Fig. 1a). It crystallized in the centrosymmetric space group belonging to the monoclinic crystal system. The tetrahydrotetrazine ring is not planar, and the C^6 atom deviates by 0.619 Å from the mean-square plane formed by the other five ring atoms whose deviations from that plane do not exceed 0.04 Å. The phenyl substituent on C^3 is oriented approximately in the heterocycle plane (torsion angle $C^7C^3N^2N^1$ 175.9°), and the benzothiazole fragment is slightly turned with respect to the tetrazine ring plane (torsion angle $N^2N^1C^2N^3$ 169.9°). The N^1 atom connecting the two π-electron systems has a flattened configuration, but it deviates from the $N^2C^2C^6$ plane by 0.196 Å. The single and double bonds are readily distinguishable (the difference in their lengths reaches 0.1 Å). Interestingly, even larger difference in the C–N bond lengths of the benzothiazole fragment [C^2–N^3 1.301(3) Å, N^3–C^{13} 1.397(3) Å] does not induce C–S bond asymmetry [S^1–C^2 1.741(2) Å, S^1–C^{18} 1.743(3) Å]. The ethyl group and 4-fluorophenyl substituent occupy (pseudo)-axial positions and are oriented *trans* with respect to each other. The N^4 and N^5 atoms have a trigonal–pyramidal configuration. Molecules **4b** in crystal are linked together through intermolecular hydrogen bonds N^4–H···N^3 [$-x + 1/2$, $y - 1/2$, $-z + 1/2$; N···N 2.996 Å, ∠$N^4H^4N^3$ 160°] (Fig. 1b) to form polymeric bands extending along the 0*b* axis.

As shown previously [10, 12], the presence of an electron-withdrawing substituent X in the aromatic ring on N^1 in initial formazans **1** favors further alkylation of **2** that can be regarded as dihydrotetrazine derivatives. In the reaction with **1e** (X = I), by column chromatography we isolated compound **5e** and one

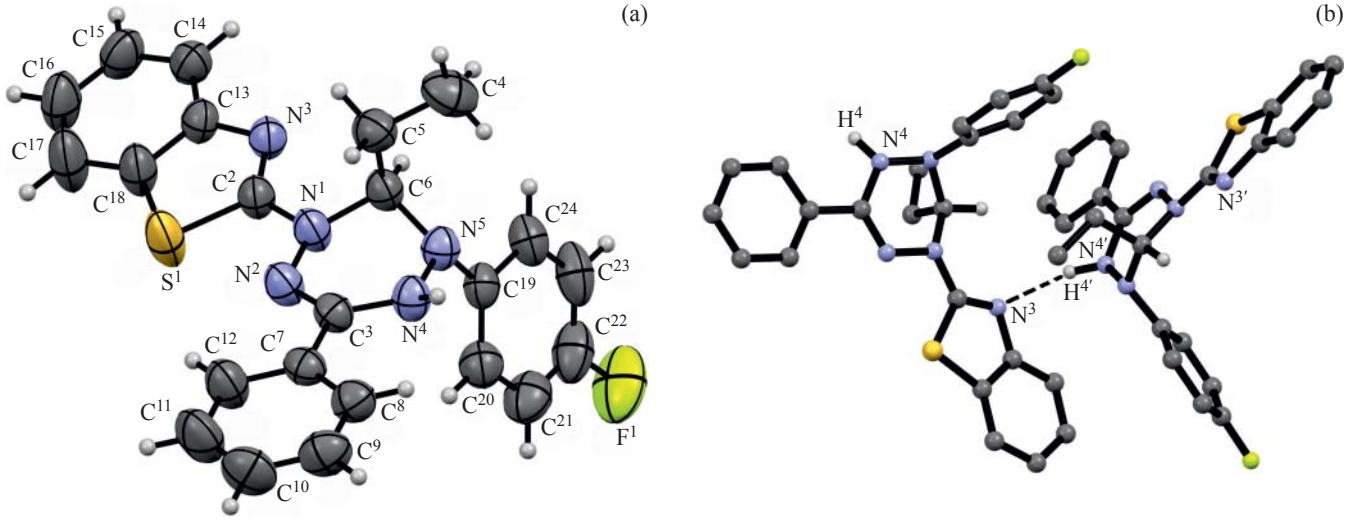
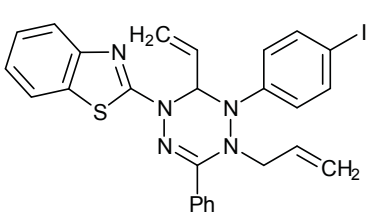


Fig. 1. (a) Structure of the molecule of 2-[6-ethyl-5-(4-fluorophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (**4b**) and (b) intermolecular hydrogen bonds in the crystal structure of **4b** according to the X-ray diffraction data.

Scheme 2.



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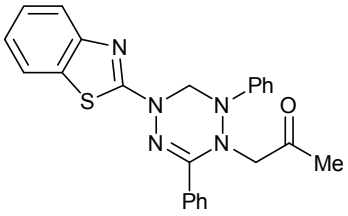

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more product which was assigned the structure of 2-[6-ethenyl-5-(4-iodophenyl)-3-phenyl-4-(prop-2-en-1-yl)-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (**6**) on the basis of its mass spectrum and ^{1}H NMR data (no NH signal was observed, but signals typical of an allyl group were present). It should be noted that alkylation at the N^4 atom can also occur under different conditions. For example, in an attempt to obtain a copper complex of **2a** in acetone, we isolated by column chromatography *N*-acetonyl derivative **7** (Scheme 2) whose structure was determined by X-ray analysis (Fig. 2).

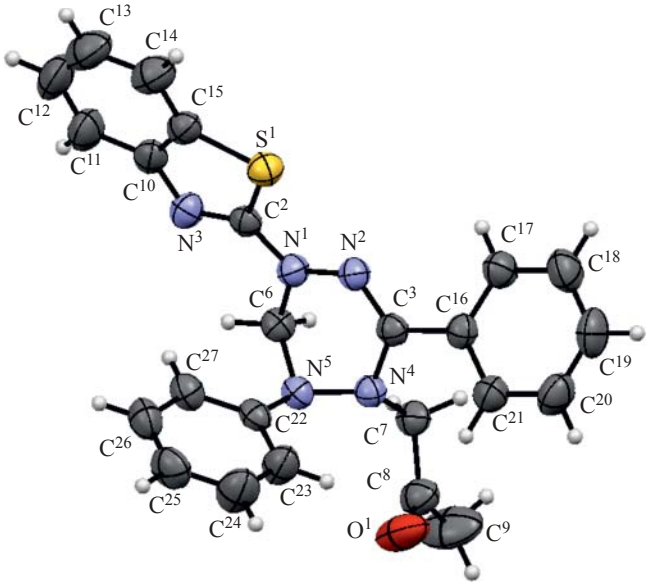

Fig. 2. Structure of the molecule of 1-[4-(1,3-benzothiazol-2-yl)-2,6-diphenyl-3,4-dihydro-1,2,4,5-tetrazin-1(2*H*)-yl]-propan-2-one (**7**) according to the X-ray diffraction data.

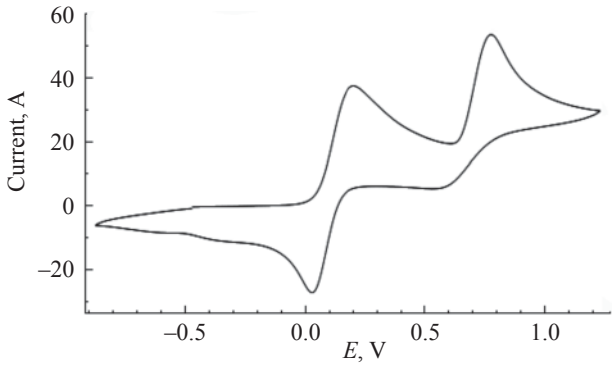

Fig. 3. Cyclic voltammogram of compound **4a**.

According to the X-ray diffraction data, the N^4 atom in molecule **7** is linked to 2-oxopropyl group. Compound **7** crystallized in the centrosymmetric space group of the triclinic crystal system. The tetrahydrotetrazine ring is not planar, and its conformation significantly differs from that in molecule **4b**. The N^1, N^2, C^3, and C^6 atoms lie virtually in one plane (within 0.025 Å), and the N^4 and N^5 atoms deviate from that plane by 0.330 and 0.847 Å, respectively. These nitrogen atoms have a trigonal pyramidal configuration, and the substituents attached thereto appear in (pseudo)-axial positions with *trans* orientation with respect to each other. The phenyl ring on C^3 is turned relative to the tetrazine plane, so that the torsion angle $N^2C^3C^{16}C^{17}$ is 32.9°. The bond length distribution over the conjugation system including the hydrazone fragment of the tetrahydrotetrazine ring is similar to that found for compound **4b**. The crystal packing of **7** is characterized by the presence of short S···S contacts [$1 - x$, $1 - y$, $-z$] with an interatomic distance of 3.40 Å, which is shorter by 0.20 Å than the sum of van der Waals radii. In the ^{1}H NMR spectrum of **7**, the C^6H_2 signal is shifted upfield to δ 4.33 ppm, and methylene protons of the acetonyl group resonated as two broadened singlets at δ 4.93 and 6.36 ppm.

The redox properties of dihydrotetrazine derivatives **2**–**5** were studied in acetonitrile by cyclic voltammetry (CV); the results are collected in Table 1. All compounds **2**–**5** showed two oxidation peaks, the first peak at 0.10–0.18 V (except for **2f**), and the second at 0.60–0.81 V and only one reduction peak. Figure 3 shows the cyclic voltammogram of compound **4a** as an example. The first oxidation step of **4a** was studied by recording the CV curve with the anodic potential not exceeding the second oxidation step potential. The oxidation peak area was 1.6 times larger than the reduction peak area, and the reduction and oxidation

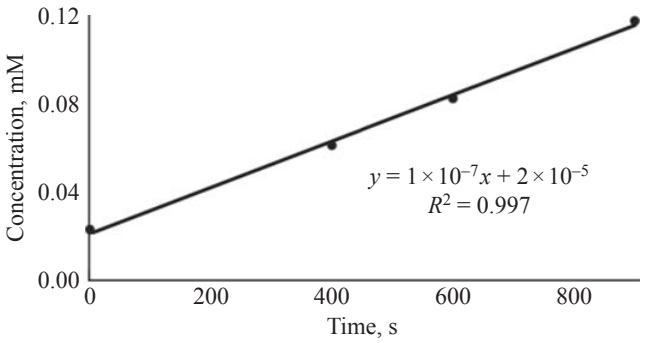

Fig. 4. Plot of the concentration of paramagnetic species generated by electrochemical oxidation of **4a** versus time.

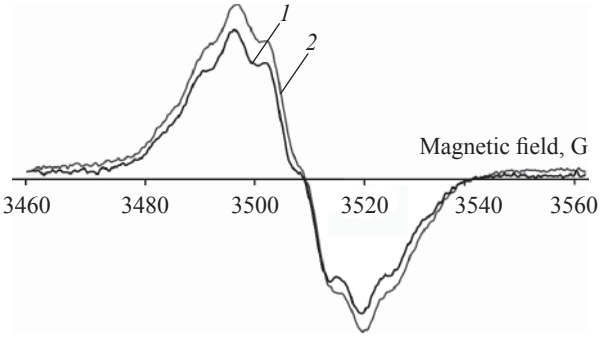

Fig. 5. ESR spectra of (*1*) electrochemically oxidized form of **4a** and (*2*) verdazyl **9**.

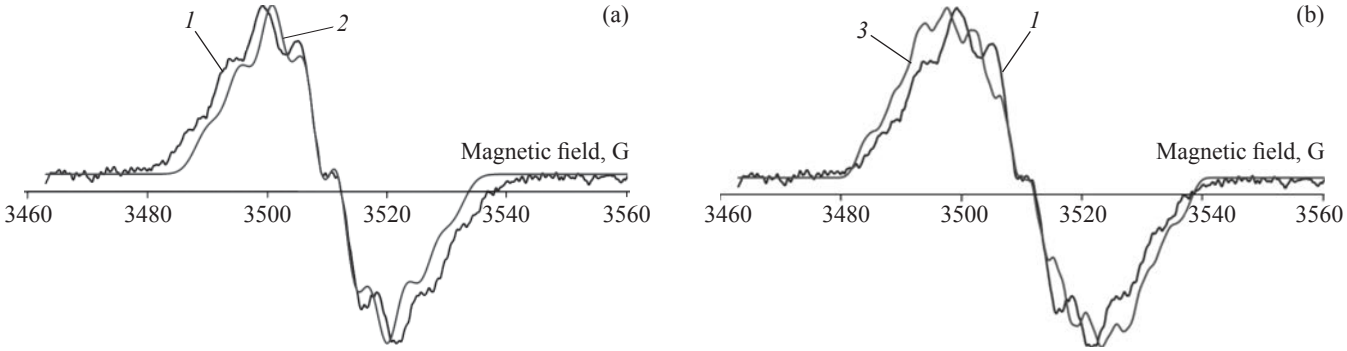

Fig. 6. (*1*) Experimental ESR spectrum of electrochemically oxidized form of **4a** and calculated ESR spectra of (*2*) verdazyl **9** and (*3*) radical cation **8**.

peak potentials differed by 160 mV. Therefore, we cannot define the process even as quasi-reversible. Presumably, the oxidation of **4a** at a potential close to the first step involves transfer of a larger number of electrons than in the reduction step.

In order to identify oxidation products, they were electrochemically generated over periods of 400, 600, and 900 s and examined by ESR, and the concentration of paramagnetic species was measured. Figure 4 shows the dependence of their concentration on the duration of electrolysis. Comparison of the ESR spectrum of the electrochemically generated paramagnetic species with the spectrum of verdazyl **9** obtained by chemical oxidation of **4a** [11] showed their almost complete identity (Fig. 5). Taking into account that CV experiments were carried out under argon, we presumed that the first oxidation step produces radical cation **8** as one of the products (Scheme 3). The spin densities on the nitrogens of **8** and **9** are likely to be similar, and possible effect of the hydrogen atom on N^4 in the electrochemically oxidized form of **4a** is not reflected in the ESR spectrum because of its poor resolution at room temperature.

In order to refine the structure of the paramagnetic electrochemical oxidation product, we performed DFT quantum chemical calculations of radical cation **8** and verdazyl **9** with geometry optimization using the UB3LYP functional and 6-31+G(*d*) basis state. The hyperfine coupling constants (HCC) were calculated at the UB3LYP/IGLO-III level [13]. The calculations

Scheme 3.

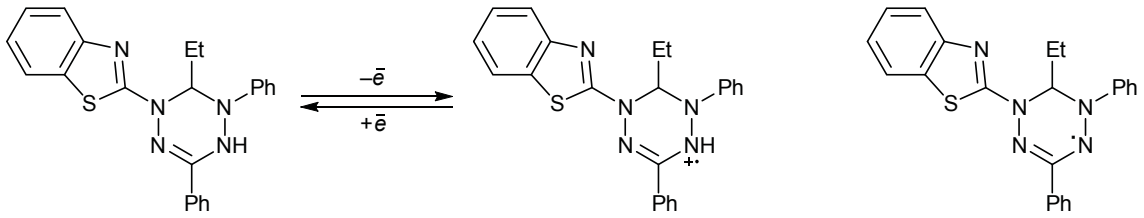

Table 1. Electrochemical parameters of compounds **2–5**

Compound no.	E_{ox1}, V	E_{ox2}, V	Compound no.	E_{ox1}, V	E_{ox2}, V
2a	0.10	0.66	**4a**	0.11	0.70
2b	0.13	0.73	**4b**	0.11	0.74
2c	0.14	0.70	**4c**	0.11	0.62
2d	0.14	0.70	**4d**	0.12	0.75
2e	0.15	0.70	**4e**	0.14	0.72
2f	0.03	0.60	**5a**	0.16	0.73
3a	0.12	0.73	**5b**	0.16	0.76
3b	0.12	0.75	**5c**	0.17	
3c	0.13	0.75	**5d**	0.17	0.81
3d	0.13	0.74	**5e**	0.18	0.72
3e	0.15	0.74			

were carried out using ORCA [14], and the ESR spectra were simulated by EasySpin [15]. The experimental ESR spectrum of the oxidized form of **4a** almost coincided with the calculated spectrum of verdazyl **9** (Fig. 6). These findings led us to conclude that electrochemical oxidation of **4a** at a potential corresponding to the first oxidation peak gives verdazyl **9** rather than radical cation **8**. Presumably, the latter is stabilized as verdazyl **9** via deprotonation in polar medium (acetonitrile).

The second step of electrochemical oxidation of **4a** is irreversible. Most probably, this process involves transformation of the tetrahydrotetrazine ring to triazole. Examples of formation of triazole derivatives from formazans [16] and verdazyls (as autotransformation products) [17] or as by-products in the synthesis of verdazyls [18] have been reported; in the latter case, the structure of substituted triazole was confirmed by X-ray analysis.

The natures of the substituent R and halogen atom only slightly affect the oxidation potentials (Table 1).

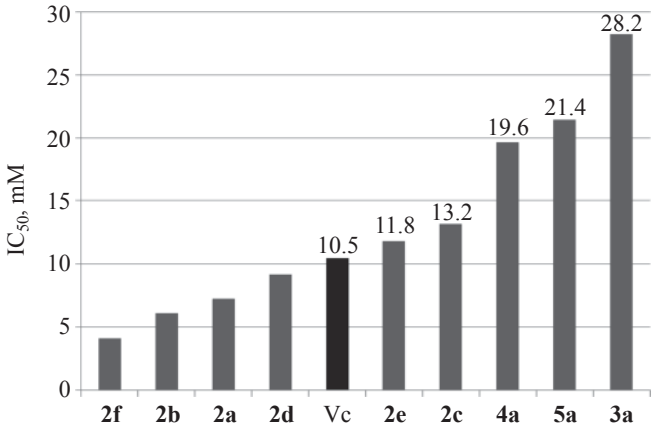

Fig. 7. Diagram of IC_{50} values of dihydrotetrazines **2a–2f** and **3a–5a**.

Vinyl derivatives **5a–5e** (R = CH_2=CH) showed a small shift of the first oxidation potential to more positive values in comparison to compounds **2a–2e** (R = H). In the series **2a–2f**, compound **2f** containing the strongest electron-donating group (X = OMe) was characterized by the least positive first oxidation potential.

The antioxidant activity of dihydrotetrazines was studied in the series **2a–2f** (to trace the effect of the X substituent) and **2a–5a** (to trace the effect of R). The antioxidant activity was evaluated by spectrophotometric monitoring of the hydrogen transfer reaction with a stable chromogen radical, 2,2-diphenyl-1-picrylhydrazyl (DPPH) [19] using vitamin C (Vc) as reference. A solution of DPPH in methanol with a concentration of 200 μM was added to a solution of **2–5** in the same solvent (concentration 5 to 50 μM). The reaction vessel (test tube) was wrapped in foil and kept for 30 min at 30°C, and the optical density was measured at λ 517 nm (DPPH absorption maximum). The antioxidant activity (AO) was calculated by the formula

$$AO = (1 - A_{test}/A_{contr}) \times 100\%,$$

where A_{test} is the optical density of a solution containing a compound to be tested and DPPH, and A_{contr} is the optical density of a solution containing DPPH alone. The half inhibitory concentration (IC_{50}) corresponding to the reduction of the initial DPPH concentration by 50% was determined from the DPPH inhibition percentage plotted against concentration of **2–5** using OriginPro 8.5 program (Model DoseResp). The results are presented in Figs. 7 and 8.

It was found that unsubstituted dihydrotetrazine **2a** (IC_{50} = 7.2 μM) reacted with DPPH most effectively; compounds **4a** (R = Et) and **5a** (R = CH_2=CH) showed

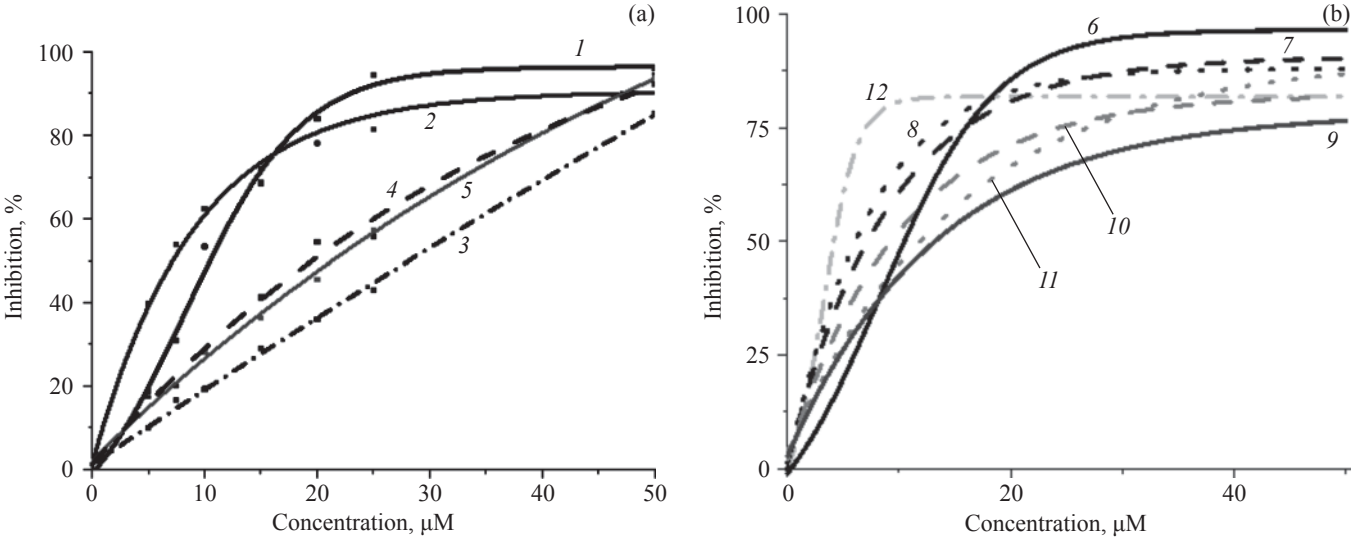

Fig. 8. Concentration dependences of DPPH inhibition by dihydrotetrazines and vitamin C (Vc): (*1*, *6*) Vc, (*2*, *7*) **2a**, (*3*) **3a**, (*4*) **4a**, (*5*) **5a**, (*8*) **2b**, (*9*) **2c**, (*10*) **2d**, (*11*) **2e**, and (*12*) **2f**.

fairly similar IC_{50} values (19.6 and 21.4 μM, respectively), but were significantly inferior to vitamin C (IC_{50} = 10.5 μM; Fig. 8a). Unexpectedly, methyl-substituted dihydrotetrazine **3a** proved to be least active in this series (IC_{50} = 28.2 μM). The effect of the X substituent in the aromatic fragment is determined by its donor–acceptor properties. The stronger the electron-donor power, the higher the antioxidant activity. With respect to their antioxidant activity compounds **2a**–**2f** ranked as follows MeO > F > H > Br > Vc > I > Cl (Fig. 8b). Despite a strong negative inductive effect of fluorine, its positive mesomeric effect appeared to be so significant that the antioxidant activity of fluorophenyl-substituted dihydrotetrazine **2b** (IC_{50} = 6.1 μM) was only slightly lower than the activity of methoxy analog **2f** (IC_{50} = 4.1) and much higher than the activity of vitamin C. As might be expected, more electrochemically active dihydrotetrazines **2f**, **2a**, **2b**, and **2d** exhibited higher antioxidant activity.

Thus, the newly synthesized 2-(5-aryl-6-R-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles are readily oxidizable compounds which show antiradical activity.

EXPERIMENTAL

All solvents were dried and distilled prior to use according to standard procedures. Commercially available reagents were purchased from Sigma–Aldrich and were used without further purification. The melting points were measured with a Stuart SMP3 melting point apparatus. The progress of reactions and the purity of the isolated compounds were monitored by TLC on Sorbfil PTSKh-AF-A-UF plates. Column chromatography was performed using Kieselgel 60 silica gel (grain size 0.040–0.063 mm or 230–400 mesh). The NMR spectra were recorded on a Bruker Avance III-500 spectrometer operating at 500 MHz for ^{1}H. The IR spectra were recorded on a Perkin Elmer Spectrum One spectrometer equipped with a diffuse reflectance accessory. The UV spectra were measured from solutions in methanol on a Shimadzu UV2600 spectrophotometer (Japan). The mass spectra (electrospray ionization) were obtained with a Bruker Daltonics maXis impact HD instrument. Elemental analysis was performed on a Perkin Elmer 2400 Series II automated CHNS analyzer. The ESR spectra were recorded on a Bruker Elexsys E 500 X-band spectrometer equipped with an ER4131VT system; solutions of samples in acetonitrile were diluted to a concentration of about 10^{-4} M.

The X-ray diffraction data for compounds **4b** and **7** were obtained at the Spectroscopy and Analysis of Organic Compounds joint center (Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences) on an Xcalibur 3 automated four-circle diffractometer with a CCD detector according to standard procedure [Mo K_α radiation, graphite monochromator, ω-scanning with a step of 1°, temperature 295(2) K]. A correction for absorption was applied empirically. The structures of **4b** and **7** were solved by the direct statistical method and were refined against F^2 by the full-matrix least-squares method in anisotropic approximation for all

non-hydrogen atoms. Hydrogen atoms linked to carbons were placed in geometrically calculated positions, and the positions of NH hydrogens were refined independently in isotropic approximation. All calculations were performed using SHELXTL package [20].

Cyclic voltammetry experiments were carried out using a Metrohm Autolab PGSTAT128N potentiostat with a standard three-electrode cell comprising a glassy carbon disc (d = 2 mm) as a working electrode, a 0.01 M $Ag/AgNO_3$ reference electrode, and a glassy carbon rod as a counter electrode. The measurements were performed under argon in anhydrous acetonitrile containing 0.1 mol/L of tetrabutylammonium tetrafluoroborate as a supporting electrolyte; potential scan rate 100 mV/s. The $Ag/AgNO_3$ electrode was calibrated against ferrocene/ferrocenium (Fc/Fc^+) redox couple.

Initial formazans **1a**–**1e** were synthesized according to the procedures described in [10, 21, 22].

2-(5-Aryl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles 2–5 (*general procedure***).** Formazan **1a**–**1e** (0.8 mmol) was dispersed in 20 mL of ethanol, a 30% aqueous solution of sodium hydroxide (0.9 mmol) was added, the corresponding alkyl halide (8.0 mmol) was added to the dark violet solution, and the mixture was refluxed for 15 min. The solvent was distilled off under reduced pressure, 30 mL of heptane was added to the residue, and the mixture was refluxed for 1 h. The solvent was distilled off under reduced pressure, and the product was isolated from the residue by column chromatography on silica gel using hexane–chloroform (2:1) as eluent.

2-(3,5-Diphenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl)-1,3-benzothiazoles **2a**, **3a**, and **4a** were reported previously [11].

2-[5-(4-Fluorophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (2b). Yield 137 mg (44%), mp 171–173°C (from MeOH). IR spectrum, ν, cm^{-1}: 3144, 1598, 1530, 1503, 1447, 1280, 1171, 1059, 762, 685. ^1H NMR spectrum, δ, ppm: 5.45 br.s (2H, CH_2), 7.08–7.17 m (3H, H_{arom}), 7.56–7.50 m (4H, H_{arom}), 7.76 d (1H, H_{arom}, J = 7.1 Hz), 7.89–7.91 m (2H, H_{arom}), 9.56 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 55.15, 62.89, 115.67, 115.86, 118.99, 119.37, 119.43, 121.34, 125.79, 126.04, 128.61, 130.63, 130.85, 131.32, 145.17, 145.96, 152.11, 156.98, 158.88, 166.75. Mass spectrum: m/z 390.1183 $[M + H]^+$. Found, %: C 64.74; H 4.11; N 17.95. $C_{21}H_{16}FN_5S$. Calculated, %: C 64.76; H 4.14; N 17.98.

2-[5-(4-Chlorophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (2c). Yield 201 mg (62%), mp 191–193°C (from MeOH). IR spectrum, ν, cm^{-1}: 3136, 1595, 1533, 1503, 1446, 1279, 1166, 1058, 744, 687. ^1H NMR spectrum, δ, ppm: 5.49 br.s (2H, CH_2), 7.07 t (1H, H_{arom}, J = 7.7 Hz), 7.24–7.39 m (5H, H_{arom}), 7.47–7.59 m (4H, H_{arom}), 7.77 d (1H, H_{arom}, J = 7.6 Hz), 7.85–7.95 m (2H, H_{arom}), 9.58 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 62.89, 119.03, 119.20, 121.34, 121.46, 125.80, 126.06, 126.35, 128.61, 129.06, 130.66, 130.85, 131.26, 145.04, 148.47, 152.08, 166.69. Mass spectrum: m/z 406.0880 $[M + H]^+$. Found, %: C 62.12; H 3.96; N 17.23. $C_{21}H_{16}ClN_5S$. Calculated, %: C 62.14; H 3.97; N 17.25.

2-[5-(4-Bromophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (2d). Yield 187 mg (52%), mp 182–184°C (from MeOH). IR spectrum, ν, cm^{-1}: 3143, 1597, 1532, 1502, 1445, 1279, 1165, 1058, 745, 689. ^1H NMR spectrum, δ, ppm: 5.49 br.s (2H, CH_2), 7.09 t (1H, H_{arom}, J = 7.3 Hz), 7.24–7.31 m (3H, H_{arom}), 7.47–7.58 m (6H, H_{arom}), 7.77 d (1H, H_{arom}, J = 7.7 Hz), 7.87–7.91 m (2H, H_{arom}), 9.57 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 61.86, 114.29, 119.04, 119.62, 121.34, 121.46, 125.81, 126.06, 128.62, 130.67, 130.86, 131.26, 145.02, 148.91, 152.08, 166.69. Mass spectrum: m/z 450.0256 $[M + H]^+$. Found, %: C 55.98; H 3.55; N 15.53. $C_{21}H_{16}BrN_5S$. Calculated, %: C 56.01; H 3.58; N 15.55.

2-[5-(4-Iodophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (2e). Yield 215 mg (54%), mp 175–177°C (from MeOH). IR spectrum, ν, cm^{-1}: 3161, 1594, 1525, 1500, 1446, 1278, 1170, 1058, 751, 691. ^1H NMR spectrum, δ, ppm: 5.48 br.s (2H, CH_2), 7.08–7.14 m (3H, H_{arom}), 7.29 t (1H, H_{arom}, J = 7.5), 7.50–7.64 m (4H, H_{arom}), 7.62 d (2H, H_{arom}, J = 8.8 Hz), 7.77 d (1H, H_{arom}, J = 7.7 Hz), 7.87–7.91 m (2H, H_{arom}), 9.56 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 61.73, 85.97, 119.04, 119.92, 121.37, 121.47, 125.82, 126.06, 128.63, 130.67, 130.86, 131.27, 137.77, 144.99, 149.46, 152.09, 166.67. Mass spectrum: m/z 498.0240 $[M + H]^+$. Found, %: C 50.70; H 3.22; N 14.07. $C_{21}H_{16}IN_5S$. Calculated, %: C 50.71; H 3.24; N 14.08.

2-[5-(4-Methoxyphenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (2f). Yield 135 mg (42%), mp 191–193°C (from MeOH). IR spectrum, ν, cm^{-1}: 3331, 1595, 1530, 1508, 1444, 1278, 1177, 1064, 755, 686. ^1H NMR spectrum, δ, ppm: 3.66 s (3H, OCH_3), 5.38 br.s (2H, CH_2), 6.87 d (2H, H_{arom}, J = 9.1 Hz), 7.07 t (1H, H_{arom}, J = 7.3 Hz), 7.17 d (2H, H_{arom}, J = 9.1 Hz), 7.27 t (1H, H_{arom}, J =

7.3 Hz), 7.49 d (1H, H_{arom}, J = 7.8 Hz), 7.52–7.55 m (3H, H_{arom}), 7.75 (1H, H_{arom}, J = 7.3 Hz) 7.86–7.90 m (2H, H_{arom}), 9.52 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 55.15, 62.89, 114.39, 118.91, 119.21, 121.29, 125.75, 126.01, 128.56, 130.54, 130.83, 131.43, 142.98, 145, 145.27, 152.17, 155.09, 166.59. Mass spectrum: m/z 400.1230 $[M - H]^+$. Found, %: C 65.78; H 4.73; N 17.42. $C_{22}H_{19}N_5OS$. Calculated, %: C 65.81; H 4.77; N 17.44.

2-[5-(4-Fluorophenyl)-6-methyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (3b). Yield 164 mg (51%), mp 197–199°C (from MeOH). IR spectrum, ν, cm^{-1}: 3154, 1594, 1526, 1503, 1446, 1276, 1179, 1011, 754, 693. ^{1}H NMR spectrum, δ, ppm: 1.50 d (3H, CH_3, J = 6.2 Hz), 6.32 q (1H, 6-H, J = 6.2 Hz), 7.07 t (1H, H_{arom}, J = 7.6 Hz), 7.14 t (2H, H_{arom}, J = 9.0 Hz), 7.23–7.36 m (3H, H_{arom}), 7.47–7.61 m (4H, H_{arom}), 7.75 d (1H, H_{arom}, J = 7.6 Hz), 7.88–7.97 m (2H, H_{arom}), 9.60 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 16.00, 67.19, 115.62, 115.80, 118.91, 119.64, 119.71, 121.24, 121.29, 125.68, 125.87, 128.59, 130.53, 130.67, 131.05, 144.12, 146.60, 152.21, 156.99, 158.89, 166.03. Mass spectrum: m/z 404.1336 $[M + H]^+$. Found, %: C 65.47; H 4.48; N 17.34. $C_{22}H_{18}FN_5S$. Calculated, %: C 65.49; H 4.50; N 17.36.

2-[5-(4-Chlorophenyl)-6-methyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (3c). Yield 141 mg (42%), mp 203–205°C (from MeOH). IR spectrum, ν, cm^{-1}: 3178, 1595, 1529, 1507, 1447, 1277, 1186, 1011, 750, 696. ^{1}H NMR spectrum, δ, ppm: 1.51 d (3H, CH_3, J = 6.2 Hz), 6.40 q (1H, 6-H, J = 6.2 Hz), 7.09 t (1H, H_{arom}, J = 7.6 Hz), 7.22–7.41 m (5H, H_{arom}), 7.45–7.64 m (4H, H_{arom}), 7.76 d (1H, H_{arom}, J = 7.6 Hz), 7.88–7.99 m (2H, H_{arom}), 9.62 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.88, 66.64, 118.95, 119.46, 121.26, 121.34, 125.70, 125.89, 126.46, 128.61, 129.03, 130.58, 130.68, 130.99, 143.97, 149.03, 152.18, 165.98. Mass spectrum: m/z 420.1008 $[M + H]^+$. Found, %: C 62.92; H 4.32; N 16.68. $C_{22}H_{18}ClN_5S$. Calculated, %: C 62.92; H 4.32; N 16.68.

2-[5-(4-Bromophenyl)-6-methyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (3d). Yield 144 mg (39%), mp 205–207°C (from MeOH). IR spectrum, ν, cm^{-1}: 3173, 1596, 1527, 1506, 1447, 1275, 1189, 1011, 750, 695. ^{1}H NMR spectrum, δ, ppm: 1.50 d (3H, CH_3, J = 6.2 Hz), 6.40 q (1H, 6-H, J = 6.2 Hz), 7.08 t (1H, H_{arom}, J = 7.5 Hz), 7.24 and 7.47 *AA′BB′* (4H, H_{arom}, J = 8.9 Hz), 7.28 t (1H, H_{arom}, J = 7.5 Hz), 7.50–7.62 m (4H, H_{arom}), 7.76 d (1H, H_{arom}, J = 7.6 Hz), 7.84–7.98 m (2H, H_{arom}), 9.62 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.90, 66.59, 114.46, 118.99, 119.20, 121.33, 121.40, 125.77, 125.94, 128.67, 130.65, 130.71, 131.00, 131.97, 143.97, 149.50, 152.22, 166.00. Mass spectrum: m/z 464.0364 $[M + H]^+$. Found, %: C 56.88; H 3.90; N 15.06. $C_{22}H_{18}BrN_5S$. Calculated, %: C 56.90; H 3.91; N 15.08.

2-[5-(4-Iodophenyl)-6-methyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (3e). Yield 143 mg (35%), mp 196–198°C (from MeOH). IR spectrum, ν, cm^{-1}: 3165, 1595, 1525, 1505, 1447, 1274, 1191, 1011, 751, 694. ^{1}H NMR spectrum, δ, ppm: 1.50 d (3H, CH_3, J = 6.2 Hz), 6.40 q (1H, 6-H, J = 6.2 Hz), 7.29 t (1H, H_{arom}, J = 7.9 Hz), 7.07 and 7.77 *AB* (2H, H_{arom}, J = 7.3 Hz), 7.11 and 7.62 *AA′BB′* (4H, H_{arom}, J = 8.5 Hz), 7.48–7.58 m (4H, H_{arom}), 7.91 d (1H, H_{arom}, J = 8.5 Hz), 7.88–7.96 m (2H, H_{arom}), 9.61 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.84, 66.39, 118.95, 120.15, 121.25, 121.33, 125.69, 125.87, 128.59, 130.55, 130.67, 130.98, 137.73, 143.92, 150.00, 152.18, 165.94. Mass spectrum: m/z 512.0395 $[M + H]^+$. Found, %: C 51.65; H 3.54; N 13.66. $C_{22}H_{18}IN_5S$. Calculated, %: C 51.67; H 3.55; N 13.69.

2-[6-Ethyl-5-(4-fluorophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (4b). Yield 127 mg (38%), mp 211–213°C (from MeOH). IR spectrum, ν, cm^{-1}: 3160, 1603, 1535, 1501, 1447, 1278, 1182, 988, 749, 693. ^{1}H NMR spectrum, δ, ppm: 1.11 t (3H, CH_3, J = 7.3 Hz), 1.73–1.88 m (2H, CH_2), 6.05–6.11 m (1H, 6-H), 7.06 t (1H, H_{arom}, J = 7.4 Hz), 7.13 t (2H, H_{arom}, J = 8.6 Hz), 7.19–7.31 m (3H, H_{arom}), 7.45–7.62 m (4H, H_{arom}), 7.73 d (1H, H_{arom}, J = 7.8 Hz), 7.85–7.94 m (2H, H_{arom}), 9.55 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 9.61, 22.81, 72.24, 115.71, 115.88, 118.87, 119.70, 119.70, 121.23, 121.26, 125.72, 125.95, 128.66, 130.64, 130.69, 131.06, 144.55, 146.72, 152.28, 156.99, 158.89, 166.21. Mass spectrum: m/z 418.1496 $[M + H]^+$. Found, %: C 66.15; H 4.81; N 16.78. $C_{23}H_{20}FN_5S$. Calculated, %: C 66.17; H 4.83; N 16.77.

Crystallographic data: $C_{23}H_{20}FN_5S$; monoclinic crystal system, space group $P2_1/n$; unit cell parameters: a = 10.4546(9), b = 11.2072(9), c = 17.7583(16) Å; β = 91.670(8)°; V = 2079.8(3) Å^3; Z = 4; μ = 0.184 mm^{-1}. Total of 13448 reflection intensities were measured in the range 3.48 < θ < 30.82°, including 5534 independent reflections (R_{int} = 0.0439). Final divergence factors: R_1 = 0.1391, wR_2 = 0.1634 (all independent reflections); R_1 = 0.0566, wR_2 = 0.1170 [reflections

with $I > 2\sigma(I)$]; goodness of fit S = 1.004; residual electron density peaks 0.175/–0.344 $\bar{e}$ Å^{-3}. The complete set of X-ray diffraction data for compound **4b** was deposited to the Cambridge Crystallographic Data Centre (CCDC entry no. 1965415).

2-[5-(4-Chlorophenyl)-6-ethyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (4c). Yield 111 mg (32%), mp 243–245°C (from MeOH). IR spectrum, ν, cm^{-1}: 3155, 1595, 1534, 1503, 1447, 1277, 1190, 987, 750, 693. ^{1}H NMR spectrum, δ, ppm: 1.11 t (3H, CH_3, J = 7.4 Hz), 1.69–1.98 m (2H, CH_2), 6.13–6.22 m (1H, 6-H), 6.96 t (1H, H_{arom}, J = 7.8 Hz), 7.13 t (2H, H_{arom}, J = 8.6 Hz), 7.24–7.32 m (3H, H_{arom}), 7.32–7.41 m (2H, H_{arom}), 7.50 d (1H, H_{arom}, J = 8.3 Hz), 7.45–7.60 m (3H, H_{arom}), 7.74 d (1H, H_{arom}, J = 7.8 Hz), 7.85–7.99 m (2H, H_{arom}), 9.57 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 9.54, 22.69, 71.64, 118.91, 119.51, 121.28, 125.74, 125.97, 126.39, 128.67, 129.09, 130.69, 130.99, 144.38, 149.21, 152.24, 166.15. Mass spectrum: *m*/*z* 434.1201 [M + H]$^+$. Found, %: C 63.64; H 4.64; N 16.13. $C_{23}H_{20}ClN_5S$. Calculated, %: C 63.66; H 4.65; N 16.14.

2-[5-(4-Bromophenyl)-6-ethyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (4d). Yield 141 mg (37%). mp 234–236°C (from MeOH). IR spectrum, ν, cm^{-1}: 3150, 1596, 1531, 1502, 1446, 1276, 1192, 987, 750, 692. ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, CH_3, J = 7.3 Hz), 1.72–1.96 m (2H, CH_2), 6.13–6.23 m (1H, CH), 7.08 t (1H, H_{arom}, J = 7.9 Hz), 7.23 and 7.47 *AA′BB′* (4H, H_{arom}, J = 9.3 Hz), 7.27 t (1H, H_{arom}, J = 7.9 Hz), 7.47–7.59 m (4H, H_{arom}), 7.74 d (1H, H_{arom}, J = 7.9 Hz), 7.88–7.95 m (2H, H_{arom}), 9.57 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 9.54, 22.67, 71.52, 114.34, 118.92, 119.92, 121.28, 125.74, 125.97, 128.67, 130.68, 130.69, 130.98, 144.35, 149.64, 152.24, 166.14. Mass spectrum: *m*/*z* 478.0696 [M + H]$^+$. Found, %: C 57.73; H 4.18; N 14.62. $C_{23}H_{20}BrN_5S$. Calculated, %: C 57.74; H 4.21; N 14.64.

2-[6-Ethyl-5-(4-iodophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (4e). Yield 130 mg (31%). mp 233–235°C (from MeOH). IR spectrum, ν, cm^{-1}: 3126, 1595, 1529, 1500, 1447, 1276, 1194, 988, 750, 693. ^{1}H NMR spectrum, δ, ppm: 1.09 t (3H, CH_3, J = 7.3 Hz), 1.69–1.94 m (2H, CH_2), 6.12–6.21 m (1H, 6-H), 7.07 t (1H, H_{arom}, J = 7.8 Hz), 7.09 and 7.61 *AA′BB′* (4H, H_{arom}, J = 9.0 Hz), 7.27 t (1H, H_{arom}, J = 7.9 Hz), 7.47–7.59 m (4H, H_{arom}), 7.74 d (1H, H_{arom}, J = 7.4 Hz), 7.87–7.93 m (2H, H_{arom}), 9.56 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 9.54, 22.65, 71.39, 118.91, 120.20, 121.28, 125.74, 125.96, 128.66, 130.66, 130.68, 130.98, 137.78, 144.33, 150.19, 152.24, 166.12. Mass spectrum: *m*/*z* 526.0548 [M + H]$^+$. Found, %: C 52.57; H 3.81; N 13.32. $C_{23}H_{20}IN_5S$. Calculated, %: C 52.58; H 3.84; N 13.33.

2-[6-Ethenyl-3,5-diphenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (5a). Yield 165 mg (52%), mp 177–178°C (from MeOH). IR spectrum, ν, cm^{-1}: 3203, 1594, 1526, 1506, 1447, 1277, 1180, 1011, 750, 693. ^{1}H NMR spectrum, δ, ppm: 5.33–5.37 m (2H, =CH_2), 6.01–6.07 m (1H, CH), 6.84–6.89 m (1H, CH), 6.95–7.00 m (1H, H_{arom}), 7.07 t (1H, H_{arom}, J = 7.3 Hz), 7.24–2.26 m (5H, H_{arom}), 7.47–7.58 m (4H, H_{arom}), 7.75 d (1H, H_{arom}, J = 7.6 Hz), 7.85–7.92 m (2H, H_{arom}), 9.59 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 71.19, 79.17, 117.74, 118.54, 118.96, 121.34, 122.74, 125.77, 125.99, 128.63, 129.29, 130.62, 130.76, 131.09, 131.52, 144.81, 149.65, 152.21, 166.36. Mass spectrum: *m*/*z* 398.1434 [M + H]$^+$. Found, %: C 69.48; H 4.83; N 17.60. $C_{23}H_{19}N_5S$. Calculated, %: C 69.50; H 4.82; N 17.62.

2-[6-Ethenyl-5-(4-fluorophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (5b). Yield 142 mg (43%), mp 198–200°C (from MeOH). IR spectrum, ν, cm^{-1}: 3203, 1599, 1526, 1502, 1447, 1278, 1183, 1012, 749, 695. ^{1}H NMR spectrum, δ, ppm: 5.26–5.48 m (2H, =CH_2), 5.96–6.10 m (1H, CH), 6.75–6.84 m (1H, CH), 6.95–7.00 m (1H, H_{arom}), 7.08 t (1H, H_{arom}, J = 7.5 Hz), 7.15 t (2H, H_{arom}, J = 8.8 Hz), 7.24–2.36 m (3H, H_{arom}), 7.45–7.58 m (4H, H_{arom}), 7.76 d (1H, H_{arom}, J = 7.5 Hz), 7.84–7.90 m (2H, H_{arom}), 9.61 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 71.70, 115.74, 115.93, 118.59, 118.98, 119.74, 119.79,121.34, 121.39, 125.78, 125.99, 128.62, 130.66, 130.77, 131.03, 131.43, 144.85, 146.09, 152.18, 157.08, 158.99, 166.45. Mass spectrum: *m*/*z* 416.1340 [M + H]$^+$. Found, %: C 66.48; H 4.35; N 16.84. $C_{23}H_{18}FN_5S$. Calculated, %: C 66.49; H 4.37; N 16.86.

2-[5-(4-Chlorophenyl)-6-ethenyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (5c). Yield 152 mg (44%), mp 200–203°C (from MeOH). IR spectrum, ν, cm^{-1}: 3195, 1593, 1525, 1504, 1446, 1275, 1189, 1012, 749, 694. ^{1}H NMR spectrum, δ, ppm: 5.29–5.40 m (2H, =CH_2), 5.97–6.09 m (1H, CH), 6.85–6.93 m (1H, CH), 7.08 t (1H, H_{arom}, J = 7.5 Hz), 7.28 t (1H, H_{arom}, J = 7.5 Hz), 7.36 and 7.33 *AA′BB′* (4H, H_{arom}, J = 9.4 Hz), 7.50 d (1H_{arom}, J = 7.8 Hz) 7.51–7.57 m (2H, H_{arom}), 7.83–7.91 m (2H, H_{arom}), 9.62 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 71.09, 115.15, 115.72, 118.63, 119.08, 119.84,

121.36, 121.40, 125.83, 126.02 128.74, 130.75, 130.82, 131.13, 131.99, 144.78, 148.10, 152.19, 166.43. Mass spectrum: *m*/*z* 432.1024 $[M + H]^+$. Found, %: C 63.93; H 4.17; N 16.20. $C_{23}H_{18}ClN_5S$. Calculated, %: C 63.95; H 4.20; N 16.21.

2-[5-(4-Bromophenyl)-6-ethenyl-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (5d). Yield 156 mg (41%), mp 200–202°C (from MeOH). IR spectrum, ν, cm^{-1}: 3195, 1593, 1525, 1504, 1446, 1275, 1189, 1012, 749, 694. ^1H NMR spectrum, δ, ppm: 5.28–5.44 m (2H, $=CH_2$), 5.97–6.08 m (1H, CH), 6.84–6.93 m (1H, CH), 7.09 t (1H, H_{arom}, J = 7.3 Hz), 7.25–7.33 m (3H, H_{arom}), 7.46–7.52 m (6H, H_{arom}), 7.77 d (1H, H_{arom}, J = 7.8 Hz), 7.84–7.91 m (2H, H_{arom}), 9.62 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 71.06, 114.61, 118.72, 119.02, 119.95, 121.39, 121.46, 125.81, 126.02, 128.64, 130.71, 130.78, 130.96, 131.21, 132.04, 144.68, 149.02, 152.16, 166.38. Mass spectrum: *m*/*z* 476.0539 $[M + H]^+$. Found, %: C 57.98; H 3.78; N 14.69. $C_{23}H_{18}BrN_5S$. Calculated, %: C 57.99; H 3.81; N 14.70.

2-[6-Ethenyl-5-(4-iodophenyl)-3-phenyl-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzothiazole (5e). Yield 163 mg (39%), mp 194–196°C (from MeOH). IR spectrum, ν, cm^{-1}: 3164, 1595, 1530, 1502, 1447, 1275, 1194, 1010, 751, 692. ^1H NMR spectrum, δ, ppm: 5.26–5.49 m (2H, $=CH_2$), 5.94–6.12 m (1H, CH), 6.83–6.93 m (1H, CH), 7.09 t (1H, H_{arom}, J = 7.2 Hz), 7.15 and 7.63 *AA′BB′* (4H, H_{arom}, J = 8.7 Hz), 7.29 t (1H, H_{arom}, J = 7.2 Hz), 7.48–7.59 m (4H, H_{arom}), 7.77 d (1H_{arom}, J = 8.1 Hz), 7.82–7.92 m (2H, H_{arom}), 9.61 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 70.93, 118.72, 119.02, 120.23, 121.38, 121.45, 125.81, 126.01, 128.64, 130.69, 130.78, 130.97, 131.19, 137.85, 144.66, 149.57, 152.16, 166.36. Mass spectrum: *m*/*z* 524.0392 $[M + H]^+$. Found, %: C 52.77; H 3.45; N 13.39. $C_{23}H_{18}IN_5S$. Calculated, %: C 52.78; H 3.47; N 13.38.

2-[6-Ethenyl-5-(4-iodophenyl)-3-phenyl-4-(prop-2-en-1-yl)-5,6-dihydro-4*H*-1,2,4,5-tetrazin-1-yl]-1,3-benzotihazole (6) was isolated as a by-product in the synthesis of **5e**. Yield 16 mg (3.4%), mp 88–90°C (from MeOH). IR spectrum, ν, cm^{-1}: 3161, 1592, 1528, 1506, 1446, 1275, 1194, 1009, 748, 693. ^1H NMR spectrum, δ, ppm: 3.89–4.01 m (2H, CH_2), 5.12 d and 5.43 d (2H, $=CH_2$, J = 10.2 Hz), 5.15 d and 5.29 d (2H, $=CH_2$, J = 17.1 Hz), 5.85–6.00 m (1H, CH), 6.20–6.33 m (1H, CH), 6.97–7.00 m (1H, H_{arom}), 7.09 t and 7.28 t (2H, H_{arom}, J = 7.6 Hz), 7.27 d (1H, H_{arom}, J = 8.8 Hz), 7.46–7.54 m (2H, H_{arom}), 7.54–7.60 m (2H, H_{arom}), 7.54–7.99 m (2H, H_{arom}), 7.63 d (2H_{arom}, J = 8.8 Hz), 7.72–7.78 m (2H, H_{arom}). Mass spectrum: *m*/*z* 564.0715 $[M + H]^+$. Found, %: C 55.41; H 3.92; N 12.41. $C_{26}H_{22}IN_5S$. Calculated, %: C 55.42; H 3.94; N 12.43.

1-[4-(1,3-Benzothiazol-2-yl)-2,6-diphenyl-3,4-dihydro-1,2,4,5-tetrazin-1(2*H*)-yl]propan-2-one (7). A hot solution of 67 mg (0.28 mmol) of copper(II) chloride in 4 mL of acetone was added with stirring to a hot solution of 100 mg (0.26 mmol) of tetrazine **2a** in 5 mL of acetone, and the mixture was stirred at room temperature for 24 h. The solvent was distilled off under reduced pressure, the residue was passed through 50 mL of silica gel using chloroform–acetone (10 : 1) as eluent, the eluate was evaporated under reduced pressure, and the residue was purified by column chromatography with chloroform as eluent. Yield 55 mg (32%), mp 204–206°C (from MeOH). ^1H NMR spectrum, δ, ppm: 2.05 s (3H, CH_3), 4.17–4.46 m (2H, CH_2), 4.79–5.08 m (1H, CH), 6.23–6.52 m (2H, CH_2), 6.94 t and 7.11 t (2H, H_{arom}, J = 7.3 Hz), 7.23–7.35 m (3H, H_{arom}), 7.37–7.44 m (2H, H_{arom}), 7.50–7.62 m (4H, H_{arom}), 7.72–7.82 m (3H, H_{arom}). Mass spectrum: *m*/*z* 428.1543 $[M + H]^+$. Found, %: C 67.41; H 4.94; N 16.39. $C_{24}H_{21}N_5OS$. Calculated, %: C 67.43; H 4.95; N 16.38.

Crystallographic data: $C_{24}H_{21}N_5OS$; triclinic crystal system, space group *P*-1; unit cell parameters: a = 8.8591(9), b = 9.6878(10), c = 13.9252(19) Å; α = 107.923(13), β = 107.267(10), γ = 94.244(8)°; V = 1067.8(2) $Å^3$; Z = 2; μ = 0.178 mm^{-1}. Total of 16033 reflection intensities were measured in the range $3.20 < \theta < 33.70°$, including 7294 independent reflections (R_{int} = 0.0343). Final divergence factors: R_1 = 0.1316, wR_2 = 0.0867 (all independent reflections); R_1 = 0.0443, wR_2 = 0.0814 [reflections with $I > 2\sigma(I)$]; goodness of fit S = 1.002; residual electron density peaks 0.324/–0.261 $\bar{e}Å^{-3}$. The complete set of X-ray diffraction data for compound **7** was deposited to the Cambridge Crystallographic Data Centre (CCDC entry no. 1965416).

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CONFLICT OF INTEREST

The authors declare the absence of conflict of interest.

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