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SYNTHESIS OF 2-SUBSTITUTED TETRAZOLE-5-THIOLS AND 5,5'-DISULFANDIYLBIS(2-ALKYL-2*H*-TETRAZOLES)

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A method has been proposed for the synthesis of 2-alkyltetrazole-5-thiols. It was shown that these compounds are readily oxidized to the corresponding disulfides and their further functionalization has been studied.

Keywords: 2-alkyltetrazole-5-thiols, 5,5'-disulfandiylbis(2-alkyl-2*H*-tetrazoles), alkylation, protecting group.

Amongst currently known tetrazoles with different structures a special place is occupied by 1-substituted thiotetrazoles. Amongst these there are found compounds having high antiviral, antiulcer, antitubercular, and antimycobacterial activity and also with antihypoxic properties [1].

In addition, these compounds have proved to be convenient synthons for the preparation of variously substituted tetrazoles [2, 3]. However, 2-substituted tetrazole-5-thiols remained virtually unstudied until recent times due to the absence of general synthetic methods for such compounds. The methods proposed in the literature for the preparation of 2-alkyltetrazole-5-thiols have needed prolonged, multistage syntheses, forcing conditions, and the use of hazardous reagents which lead to low yields of the target products [4, 5]. Hence this extension of tetrazole chemistry needs the development of a general and safe method for preparing 2-substituted tetrazole-5-thiols.

The method we have proposed for the synthesis of 2-substituted tetrazole-5-thiols involves the use of a phenacyl protecting group on the sulfur atom. The readily available 2-oxo-2-phenylethyl thiocyanate **1** [6] was selected as the starting material, and the described method [7] was used for the preparation of the tetrazole **2**.

Alkylation of compound **2** with iodomethane, (bromomethyl)benzene, and 1-bromo-4-(bromomethyl)-benzene gave a mixture of the 1- and 2-alkyltetrazoles **3a-c** and **4a-c**, respectively, in a **3**/**4** ratio of about 1:2. The ratio of isomers formed upon alkylation was determined from the ^{1}H NMR spectrum of their mixture [8]. Separation of the isomers was performed using column chromatography. Identification of these compounds was carried out using ^{1}H NMR spectroscopy. The signal for the protons of the alkyl group in the 1-isomer occurred at higher field relative to the signal of the protons of the alkyl group in the 2-isomer.

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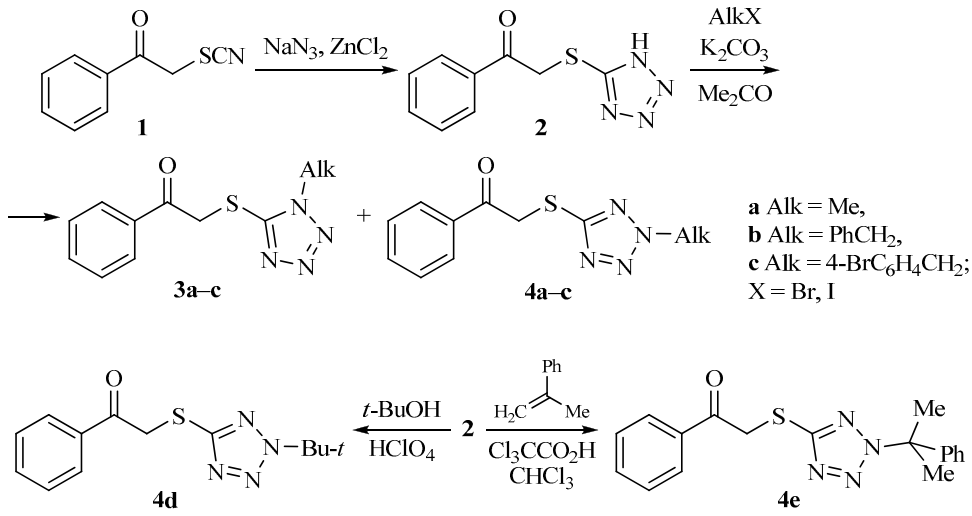
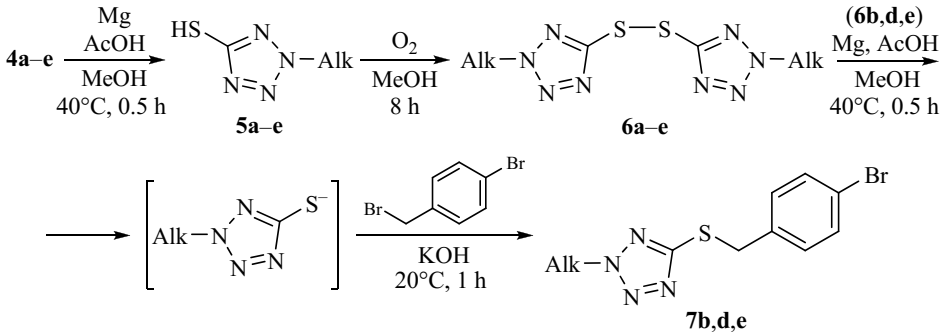


Greater selectivity in alkylation was achieved using *tert*-butanol in perchloric acid [9] and α-methylstyrene in the presence of trichloroacetic acid [10] as alkylation agents. Under these conditions, the 2-substituted tetrazoles **4d**,**e** were obtained in good yields without the use of chromatographic purification methods.

Removal of the protecting group was performed by reduction with magnesium in methanol in the presence of acetic acid [11]. All of the obtained 2-alkyltetrazole-5-thiols **5a**-**e** oxidized to the corresponding disulfides upon storage in air. This oxidation occurred particularly rapidly in the case of compounds **5d**,**e**. Formation of disulfides **6a**-**e** can be accelerated by the passage of air through solutions of the thiols **5a**-**e** in methanol. It should be noted that the thiols and disulfides cannot be reliably characterized using ^{1}H NMR and ^{13}C NMR spectroscopy. The formation of disulfides from the corresponding 2-alkyltetrazole-5-thiols **5a**-**e** was confirmed from mass spectrometric and IR spectroscopic analysis. In the IR spectra of the thiols **5a**-**e** a clear signal for an SH group is observed in the region 2560-2547 cm^{-1}. Storage of compounds **5a**-**e** caused the intensity of the band indicated to decrease until its disappearance along with the appearance in the region 474-456 cm^{-1} of a band corresponding to the S–S bond.



5, **6 a** Alk = Me, **b** Alk = $PhCH_2$, **c** Alk = 4-$BrC_6H_4CH_2$, **d** Alk = *t*-Bu, **e** Alk = $PhMe_2C$;
7 b Alk = $PhCH_2$, **d** Alk = *t*-Bu, **e** Alk = $PhMe_2C$

The ease of formation of disulfides **6a**-**e** from the corresponding 2-alkyltetrazole-5-thiols **5a**-**e** can hinder functionalization of the latter. In the case of compounds **6b**,**d**,**e** we were able to show the possibility of preparing the 2-substituted 5-alkylsulfanyltetrazoles by carrying out the alkylation in the presence of a reducing agent. Synthesis of the 2-alkyl-5-alkylsulfanyltetrazoles **7b**,**d**,**e** from the disulfides **6b**,**d**,**e** was performed in the presence of magnesium and potassium hydroxide at 20ºC in methanol. Under these conditions, compounds **7b**,**d**,**e** were obtained in high yields (82-89%).

Hence, we have developed a general method for the synthesis of 2-substituted tetrazole-5-thiols using a phenacyl protecting group. It was found that the 2-substituted tetrazole-5-thiols readily undergo oxidation by atmospheric oxygen to the corresponding disulfides. It was shown that further reaction at the sulfur atom was possible when the reaction was carried out in a reducing medium.

EXPERIMENTAL

IR spectra were registered on a Shimadzu FTIR-8400S spectrometer for KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECX 400A spectrometer (400 and 100 MHz, respectively) using DMSO-d_6 with the residual solvent signals as internal standard (2.50 ppm for the ^{1}H nucleus and 40.45 ppm for the ^{13}C nucleus). Mass spectra were recorded on a Bruker MaXis 4G spectrometer using ESI+ electrospray ionization with direct introduction of the sample in acetonitrile into the detector. Elemental analysis was performed on a LECO CHNS-932 analyzer. Refractive indices were determined on an IRF-454 B2M refractometer. Melting points were determined on a Kofler hot bench. Monitoring of the purity of the products was carried out by TLC on Silufol UV-254 plates. Compound **1** was prepared using method [5] and compound **2** using method [6]; the remaining compounds were commercial.

2-[(1-Methyl-1*H*-tetrazol-5-yl)sulfanyl]-1-phenylethanone (3a) and 2-[(2-Methyl-2*H*-tetrazol-5-yl)-sulfanyl]-1-phenylethanone (4a). K_2CO_3 (1.25 g, 9.0 mmol) was added to a solution of the 2-(1*H*-tetrazol-5-ylsulfanyl)-1-phenylethanone (**2**) (1.00 g, 4.5 mmol) and iodomethane (0.64 g, 4.5 mmol) in acetone (25 ml). The reaction mixture was stirred for 1 h at 20°C, and the solvent was distilled off *in vacuo*. The residue was treated with water (20 ml), and the reaction product was extracted with EtOAc (3×10 ml). The organic layer was dried over Na_2SO_4, and the solvent was removed *in vacuo*. The residue contained compounds **3a** and **4a** in the ratio 36:64 and was separated by column chromatography using CCl_4–EtOAc (8:2) as eluent.

Compound 3a. Yield 0.31 g (29%), colorless crystals, mp 131-132°C (EtOH). IR spectrum, ν, cm^{-1}: 2955 (CH_3), 2917 (CH_2), 1684 (C=O), 1596 (C=N), 1580 (Ar), 1446 (Ar), 1197 (C–N), 703 (C–S). ^{1}H NMR spectrum, δ, ppm: 3.98 (3H, s, CH_3); 5.08 (2H, s, CH_2); 7.52-7.57 (2H, m, H Ph); 7.65-7.70 (1H, m, H Ph); 8.00-8.02 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 193.2 (C=O); 153.8 (C–S); 135.6 (C Ph); 134.5 (C Ph); 129.4 (C Ph); 129.0 (C Ph); 41.9 (CH_2); 34.2 (CH_3). Found, %: C 51.42; H 4.16; N 23.83; S 13.82. $C_{10}H_{10}N_4OS$. Calculated, %: C 51.27; H 4.30; N 23.91; S 13.69.

Compound 4a. Yield 0.56 g (53%), colorless crystals, mp 79-80°C (EtOH). IR spectrum, ν, cm^{-1}: 2960 (CH_3), 2916 (CH_2), 1680 (C=O), 1595 (C=N), 1580 (Ar), 1447 (Ar), 1198 (C–N), 692 (C–S). ^{1}H NMR spectrum, δ, ppm: 4.27 (3H, s, CH_3); 4.96 (2H, s, CH_2); 7.52-7.56 (2H, m, H Ph); 7.64-7.68 (1H, m, H Ph); 7.99-8.01 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 193.5 (C=O); 162.9 (C–S); 135.8 (C Ph); 134.3 (C Ph); 129.4 (C Ph); 128.9 (C Ph); 40.1 (CH_2); 38.4 (CH_3). Found, %: C 51.20; H 4.36; N 23.98; S 13.89. $C_{10}H_{10}N_4OS$. Calculated, %: C 51.27; H 4.30; N 23.91; S 13.69.

Compounds **3b**,**c** and **4b**,**c** were synthesized similarly with reaction times and column chromatography eluents given below.

2-[(1-Benzyl-1*H*-tetrazol-5-yl)sulfanyl]-1-phenylethanone (3b) and 2-[(2-Benzyl-2*H*-tetrazol-5-yl)-sulfanyl]-1-phenylethanone (4b). The reaction mixture was stirred for 8 h at 20°C. After isolation of the product, the residue contained compounds **3b** and **4b** in the ratio 34:66 and was separated by column chromatography using hexane–EtOAc (9:1) as eluent.

Compound 3b. Yield 0.48 g (29%), colorless crystals, mp 108-109°C (hexane–EtOAc, 1:1). IR spectrum, ν, cm^{-1}: 2921 (CH_2), 1686 (C=O), 1594 (C=N), 1579 (Ar), 1459 (Ar), 1205 (C–N), 687 (C–S). ^{1}H NMR spectrum, δ, ppm: 5.11 (2H, s, CH_2); 5.62 (2H, s, CH_2); 7.27-7.40 (5H, m, H Ph); 7.52-7.56 (2H, m, H Ph); 7.65-7.69 (1H, m, H Ph); 7.99-8.01 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 193.0 (C=O); 162.7 (C–S); 135.6 (C Ph); 134.5 (C Ph); 134.4 (C Ph); 129.5 (C Ph); 129.4 (C Ph); 129.1 (C Ph); 128.9 (C Ph); 128.5 (C Ph);

50.8 (NCH_2); 41.9 (SCH_2). Found, %: C 61.80; H 4.69; N 17.97; S 10.21. $C_{16}H_{14}N_4OS$. Calculated, %: C 61.92; H 4.55; N 18.05; S 10.33.

Compound 4b. Yield 0.91 g (55%), colorless crystals, mp 95-96°C (EtOH). IR spectrum, ν, cm^{-1}: 2923 (CH_2), 1682 (C=O), 1595 (C=N), 1579 (Ar), 1455 (Ar), 1198 (C–N), 695 (C–S). ^{1}H NMR spectrum, δ, ppm: 4.96 (2H, s, SCH_2); 5.84 (2H, s, NCH_2); 7.28-7.35 (5H, m, H Ph); 7.53-7.55 (2H, m, H Ph); 7.63-7.68 (1H, m, H Ph); 7.97-7.99 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 193.6 (C=O); 163.3 (C–S); 135.8 (C Ph); 134.4 (C Ph); 134.3 (C Ph); 129.4 (C Ph); 129.2 (C Ph); 129.0 (C Ph); 128.9 (C Ph); 56.7 (NCH_2); 38.4 (SCH_2). Found, %: C 61.99; H 4.44; N 18.19; S 10.41. $C_{16}H_{14}N_4OS$. Calculated, %: C 61.92; H 4.55; N 18.05; S 10.33.

2-{[1-(4-Bromobenzyl)-1*H*-tetrazol-5-yl]sulfanyl}-1-phenylethanone (3c) and 2-{[2-(4-bromobenzyl)-2*H*-tetrazol-5-yl]sulfanyl}-1-phenylethanone (4c). The reaction mixture was stirred for 3 h at 20ºC. After isolation of the reaction product, the residue containing **3c** and **4c** (in the ratio 34:66) was separated by column chromatography using hexane–EtOAc–$CHCl_3$ (7:2:1) as eluent.

Compound 3c. Yield 0.53 g (30%), colorless crystals, mp 114-115°C (EtOH). IR spectrum, ν, cm^{-1}: 2919 (CH_2), 1679 (C=O), 1594 (C=N), 1448 (Ar), 1199 (C–N), 691 (C–S), 641 (C–Br). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.11 (2H, s, CH_2); 5.62 (2H, s, CH_2); 7.24 (2H, d, *J* = 8.0, H Ar); 7.52-7.60 (4H, m, H Ar); 7.65-7.69 (1H, m, H Ar); 7.99 (2H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 192.9 (C=O); 154.1 (C–S); 135.6 (C Ar); 134.5 (C Ar); 133.8 (C Ar); 132.4 (C Ar); 130.8 (C Ar); 129.4 (C Ar); 128.9 (C Ar); 122.4 (C Ar); 50.2 (NCH_2); 41.9 (SCH_2). Found, %: C 49.51; H 3.49; N 14.45; S 8.37. $C_{16}H_{13}BrN_4OS$. Calculated, %: C 49.37; H 3.37; N 14.39; S 8.24.

Compound 4c. Yield 0.94 g (53%), colorless crystals, mp 120-121°C (CCl_4). IR spectrum, ν, cm^{-1}: 2916 (CH_2), 1692 (C=O), 1595 (C=N), 1448 (Ar), 1201 (C–N), 683 (C–S), 648 (C–Br). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.97 (2H, s, SCH_2); 5.85 (2H, s, NCH_2); 7.26 (2H, d, *J* = 8.0, H Ar); 7.51-7.66 (5H, m, H Ar); 7.98 (2H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 193.5 (C=O); 163.5 (C–S); 135.8 (C Ar); 134.4 (C Ar); 133.7(C Ar); 132.3 (C Ar); 131.2 (C Ar); 129.4 (C Ar); 128.9 (C Ar); 122.6 (C Ar); 55.9 (NCH_2); 38.8 (SCH_2). Found, %: 49.52; H 3.25; N 14.23; S 8.11. $C_{16}H_{13}BrN_4OS$. Calculated, %: C 49.37; H 3.37; N 14.39; S 8.24.

2-[(2-*tert*-Butyl-2*H*-tetrazol-5-yl)sulfanyl]-1-phenylethanone (4d). *tert*-Butanol (0.71 g, 9.5 mmol) was added to a solution of the 2-(1*H*-tetrazol-5-ylsulfanyl)-1-phenylethanone (**2**) (1.00 g, 4.5 mmol) in 72% $HClO_4$ (10 ml). The reaction mixture was stirred for 1.5 h at 20°C, poured into cold water (50 ml), and the precipitate formed was filtered off. Yield 0.95 g (76%), colorless crystals, mp 56-57°C (2-PrOH). IR spectrum, ν, cm^{-1}: 2917 (CH_2), 1676 (C=O), 1595 (C=N), 1450 (Ar), 1200 ($C(CH_3)_3$), 1095 (C–N), 686 (C–S). ^{1}H NMR spectrum, δ, ppm: 1.58 (9H, s, $C(CH_3)_3$); 4.92 (2H, s, CH_2); 7.51-7.55 (2H, m, H Ph); 7.64-7.68 (5H, m, H Ph); 7.99-8.01 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 193.9 (C=O); 162.4 (C–S); 136.0 (C Ph); 134.3 (C Ph); 129.4 (C Ph); 128.9 (C Ph); 64.9 ($\underline{C}(CH_3)_3$); 39.6 (CH_2); 29.1 (CH_3). Found, %: C 56.59; H 5.80; N 20.18; S 11.80. $C_{13}H_{16}N_4OS$. Calculated, %: C 56.50; H 5.84; N 20.27; S 11.60.

1-Phenyl-2-{[2-(2-phenylpropan-2-yl)-2*H*-tetrazol-5-yl]sulfanyl}ethanone (4e). A solution of 2-(1*H*-tetrazol-5-ylsulfanyl)-1-phenylethanone (**2**) (1.00 g, 4.5 mmol) and Cl_3CCO_2H (2.23 g, 13.5 mmol) in $CHCl_3$ (20 ml) was stirred for 5 min at 20ºC. A solution of α-methylstyrene (0.54 g, 4.5 mmol) in $CHCl_3$ (10 ml) was added dropwise over 10 min. The reaction mixture was stirred for 0.5 h at 20°C, cooled to 10°C; and a 10% aqueous NaOH solution (10 ml) was added dropwise to a basic reaction. The organic layer was separated, washed with water (1×10 ml), saturated NaCl solution (1×10 ml), and again water (1×10 ml), and dried over Na_2SO_4. The solvent was distilled off *in vacuo*. Yield 1.15 g (75%), colorless crystals, mp 68-69°C (CCl_4–hexane, 2:1). IR spectrum, ν, cm^{-1}: 2981 (CH_3), 2917 (CH_2), 1677 (C=O), 1595 (C=N), 1497 (Ar), 1452 (Ar), 1196 (C–N), 703 (C–S). ^{1}H NMR spectrum, δ, ppm: 2.00 (6H, s, $2CH_3$); 4.93 (2H, s, CH_2); 7.02-7.04 (2H, m, H Ph); 7.26-7.30 (3H, m, H Ph); 7.50-7.54 (2H, m, H Ph); 7.63-7.67 (1H, m, H Ph); 7.96-7.99 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 193.8 (C=O); 162.7 (C–S); 144.2 (C Ph); 135.9 (C Ph); 134.3 (C Ph); 129.2 (C Ph); 128.9 (C Ph); 128. 4 (C Ph); 125.1 (C Ph); 69.3 ($PhC(CH_3)_2$); 39.9 (CH_2); 28.9 ($PhC(\underline{C}H_3)_2$). Found, %: C 63.99; H 5.43; N 16.62; S 9.33. $C_{18}H_{18}N_4OS$. Calculated, %: C 63.88; H 5.36; N 16.56; S 9.47.

2-Methyl-2*H*-tetrazole-5-thiol (5a). Magnesium (0.62 g, 25.6 mmol) was added to a solution of 2-[(2-methyl-2*H*-tetrazol-5-ylsulfanyl)-1-phenylethanone (**4a**) (1.00 g, 4.3 mmol) and AcOH (0.25 g, 4.3 mmol) in MeOH (20 ml). The reaction mixture was stirred for 1 h at 40°C, and the solvent was removed *in vacuo*. The residue was treated with water (20 ml), and the precipitate formed was filtered off. The filtrate was extracted with $CHCl_3$ (3×10 ml). The aqueous layer was acidified with conc. HCl to pH 1 and extracted with EtOAc (3×10 ml). The organic layer was dried over Na_2SO_4, and the solvent distilled *in vacuo*. Yield 0.41 g (82%), yellow oil, with n_D^{20} 1.4922. IR spectrum, ν, cm^{-1}: 2957 (CH_3), 2548 (SH), 1630 (C=N), 1057 (C–N), 719 (C–S). ^1H NMR spectrum, δ, ppm: 4.37 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 161.6 (C–S); 40.8 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 117 $[M+H]^+$. Found, %: C 20.87; H 3.59; N 48.10; S 27.43. $C_2H_4N_4S$. Calculated, %: C 20.68; H 3.47; N 48.24; S 27.61.

Compounds 5b-e were prepared similarly.

2-Benzyl-2*H*-tetrazole-5-thiol (5b). Yield 0.52 g (84%), colorless oil, n_D^{20} 1.4740. IR spectrum, ν, cm^{-1}: 2925 (CH_2), 2559 (SH), 1604 (C=N), 1457 (Ar), 1180 (C–N), 722 (C–S). ^1H NMR spectrum, δ, ppm: 5.90 (2H, s, CH_2); 7.29-7.35 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 162.1 (C–S); 134.0 (C Ph); 129.4 (C Ph); 129.3 (C Ph); 128.9 (C Ph); 57.2 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 193 $[M+H]^+$. Found, %: C 50.16; H 4.35; N 29.30; S 16.49. $C_8H_8N_4S$. Calculated, %: C 49.98; H 4.19; N 29.14; S 16.68.

2-(4-Bromobenzyl)-2*H*-tetrazole-5-thiol (5c). Yield 0.54 g (77%), colorless crystals, mp 57-58°C (2-PrOH). IR spectrum, ν, cm^{-1}: 2918 (CH_2), 2557 (SH), 1595 (C=N), 1489 (Ar), 1175 (C–N), 696 (C–S), 627 (C–Br). ^1H NMR spectrum, δ, ppm (*J*, Hz): 5.94 (2H, s, CH_2); 7.29 (2H, d, *J* = 8.0, H Ar); 7.56 (2H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum , δ, ppm: 162.2 (C–S); 133.4 (C Ar); 132.4 (C Ar); 131.3 (C Ar); 122.7 (C Ar); 56.4 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 270 $[M+H]^+$ Found, %: C 35.59; H 2.70; N 20.60; S 11.97. $C_8H_7BrN_4S$. Calculated, %: C 35.44; H 2.60; N 20.66; S 11.83.

2-*tert*-Butyl-2*H*-tetrazole-5-thiol (5d). Yield 0.46 g (81%), yellow oil, n_D^{20} 1.5013. IR spectrum, ν, cm^{-1}: 2548 (SH), 1630 (C=N), 1236 ($C(CH_3)_3$), 1052 (C–N), 609 (C–S). ^1H NMR spectrum, δ, ppm: 1.64 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum, δ, ppm: 161.2 (C–S); 65.7 ($\underline{C}(CH_3)_3$); 29.1 ($C(\underline{C}H_3)_3$). Mass spectrum, *m*/*z* (I_{rel}, %): 159 $[M+H]^+$. Found, %: C 38.11; H 6.50; N 35.27; S 20.38. $C_5H_{10}N_4S$. Calculated, %: C 37.95; H 6.37; N 35.41; S 20.27.

2-(2-Phenylpropan-2-yl)-2*H*-tetrazole-5-thiol (5e). Yield 0.51 g (78%), colorless crystals, mp 59-60°C (EtOH–H_2O, 1:2). IR spectrum, ν, cm^{-1}: 2947 (CH_3), 2560 (SH), 1599 (C=N), 1497 (Ar), 1158 (C–N), 697 (C–S). ^1H NMR spectrum, δ, ppm: 2.04 (6H, s, $2CH_3$); 7.02-7.04 (2H, m, H Ph); 7.25-7.30 (3H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 161.6 (C–S); 143.9 (C Ph); 129.2 (C Ph); 128.5 (C Ph); 125.1 (C Ph); 70.1 ($Ph\underline{C}(CH_3)_2$); 28.9 ($PhC(\underline{C}H_3)_2$). Mass spectrum, *m*/*z* (I_{rel}, %): 221 $[M+H]^+$. Found, %: C 54.69; H 5.60; N 25.27; S 14.48. $C_{10}H_{12}N_4S$. Calculated, %: C 54.52; H 5.49; N 25.43; S 14.56.

5,5'-Disulfandiylbis(2-methyl-2*H*-tetrazole) (6a). Air was bubbled through a solution of the 2-methyl-2*H*-tetrazole-5-thiol (**5a)** (1.00 g, 8.6 mmol) in methanol (20 ml) for 8 h, and the solvent was then evaporated. Yield 0.97 g (98%), colorless crystals, mp 77-78°C (2-PrOH–H_2O, 1:1). IR spectrum, ν, cm^{-1}: 2957 (CH_3), 1613 (C=N), 1058 (C–N), 715 (C–S), 474 (S–S). ^1H NMR spectrum, δ, ppm: 4.37 (6H, s, $2CH_3$). ^{13}C NMR spectrum, δ, ppm: 161.6 (C–S); 40.8 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 231 $[M+H]^+$. Found, %: C 20.97; H 2.76; N 48.60; S 27.77. $C_4H_6N_8S_2$. Calculated, %: C 20.86; H 2.63; N 48.66; S 27.85.

Compounds 6b-e were prepared similarly.

5,5'-Disulfandiylbis(2-benzyl-2*H*-tetrazole) (6b). Yield 0.96 g (97%), colorless crystals, mp 63-64°C (EtOH–H_2O, 1:1). IR spectrum, ν, cm^{-1}: 2935 (CH_2), 1567 (C=N), 1458 (Ar), 1180 (C–N), 723 (C–S), 457 (S–S). ^1H NMR spectrum, δ, ppm: 5.90 (4H, s, $2CH_2$); 7.29-7.35 (10H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 162.1 (C–S); 134.0 (C Ph); 129.4 (C Ph); 129.3 (C Ph); 128.9 (C Ph); 57.2 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 383 $[M+H]^+$. Found, %: C 50.36; H 3.79; N 29.41; S 16.63. $C_{16}H_{14}N_8S_2$. Calculated, %: C 50.25; H 3.69; N 29.30; S 16.77.

5,5'-Disulfandiylbis[2-(4-bromobenzyl)-2*H*-tetrazole] (6c). Yield 0.98 g (99%), colorless crystals, mp 78-79°C (2-PrOH). IR spectrum, ν, cm^{-1}: 2915 (CH_2), 1596 (C=N), 1489 (Ar), 1184 (C–N), 693 (C–S), 628 (C–Br), 474 (S–S). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.94 (4H, s, $2CH_2$); 7.29 (4H, d, *J* = 8.0, H Ar); 7.56 (4H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 162.2 (C–S); 133.4 (C Ar); 132.4 (C Ar); 131.3 (C Ar); 122.7 (C Ar); 56.4 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 540 $[M+H]^+$. Found, %: C 35.66; H 2.35; N 20.70; S 11.69. $C_{16}H_{12}Br_2N_8S_2$. Calculated, %: C 35.57; H 2.24; N 20.74; S 11.87.

5,5'-Disulfandiylbis(2-*tert*-butyl-2*H*-tetrazole) (6d). Yield 0.97 g (98%), yellow oil, n_D^{20} 1.5326. IR spectrum, ν, cm^{-1}: 1636 (C=N), 1234 ($C(CH_3)_3$), 1051 (C–N), 713 (C–S), 474 (S–S). ^{1}H NMR spectrum, δ, ppm: 1.64 (18H, s, $2C(CH_3)_3$). ^{13}C NMR spectrum, δ, ppm: 161.2 (C–S); 65.7 ($\underline{C}(CH_3)_3$); 29.1 ($C(\underline{C}H_3)_3$). Mass spectrum, *m*/*z* (I_{rel}, %): 315 $[M+H]^+$. Found, %: C 38.11; H 5.70; N 35.73; S 20.23. $C_{10}H_{18}N_8S_2$. Calculated, %: C 38.20; H 5.77; N 35.64; S 20.40.

5,5'-Disulfandiylbis(2-phenylpropan-2-yl)-2*H*-tetrazole (6e). Yield 0.96 g (97%), colorless crystals, mp 61-62°C (EtOH–H_2O, 2:1). IR spectrum, ν, cm^{-1}: 2942 (CH_3), 1601 (C=N), 1497 (Ar), 1162 (C–N), 696 (C–S), 456 (S–S). ^{1}H NMR spectrum, δ, ppm: 2.04 (12H, s, $2C(C\underline{H}_3)_2$); 7.02-7.04 (4H, m, H Ph); 7.25-7.30 (6H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 161.6 (C–S); 143.9 (C Ph); 129.2 (C Ph); 128.5 (C Ph); 125.1 (C Ph); 70.1 ($\underline{C}(CH_3)_2$); 28.9 ($C(\underline{C}H_3)_2$). Mass spectrum, *m*/*z* (I_{rel}, %): 439 $[M+H]^+$ (100). Found, %: C 54.87; H 4.99; N 25.67; S 14.50. $C_{20}H_{22}N_8S_2$. Calculated, %: C 54.77; H 5.06; N 25.55; S 14.62.

2-Benzyl-5-[(4-bromobenzyl)sulfanyl]-2*H*-tetrazole (7b). Magnesium (0.38 g, 15.6 mmol) was added to a solution of the 5,5'-disulfandiylbis(2-benzyl-2*H*-tetrazole) (**6b)** (1.00 g, 2.6 mmol) and AcOH (0.15 g, 2.6 mmol) in MeOH (20 ml). The reaction mixture was stirred for 0.5 h at 40°C and cooled to 20°C. 1-Bromo-4-(bromomethyl)benzene (1.30 g, 5.2 mmol) and KOH to pH 10 were added, the product was stirred for 1 h, and the solvent was evaporated *in vacuo*. The residue was treated with water (20 ml), and the reaction product was extracted with EtOAc (3×10 ml). The organic layer was dried over Na_2SO_4, and the solvent was removed *in vacuo*. Yield 0.82 g (87%), colorless crystals, mp 64-65°C (hexane). IR spectrum, ν, cm^{-1}: 2966 (CH_2), 1587 (C=N), 1485 (Ar), 1442 (Ar), 1169 (C–N), 715 (C–S), 676 (C–Br). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.32 (2H, s, SCH_2); 5.82 (2H, s, NCH_2); 7.23 (2H, d, *J* = 8.0, H Ar); 7.34-7.38 (5H, m, H Ar); 7.46 (2H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 161.3 (C–S); 137.2 (C Ar); 134.3 (C Ar); 131.6 (C Ar), 129.4 (C Ar); 128.3 (C Ar); 126.9 (C Ar); 125.9 (C Ar); 121.1 (C Ar); 56.8 (NCH_2); 35.3 (SCH_2). Found, %: C 49.78; H 3.51; N 15.60; S 8.69. $C_{15}H_{13}BrN_4S$. Calculated, %: C 49.86; H 3.64; N 15.52; S 8.87.

Compounds 7d-e were prepared similarly.

5-[(4-Bromobenzyl)sulfanyl]-2-*tert*-butyl-2*H*-tetrazole (7d). Yield 1.71 g (82%), yellow oil, n_D^{20} 1.6325. IR spectrum, ν, cm^{-1}: 2984 (CH_2), 1592 (C=N), 1484 (Ar), 1235 ($C(CH_3)_3$), 1173 (C–N), 712 (C–S), 610 (C–Br). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.58 (9H, s, $C(CH_3)_3$); 4.33 (2H, s, CH_2); 7.28 (2H, d, *J* = 8.0, H Ar); 7.42 (2H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 162.1 (C–S); 137.4 (C Ar); 131.7 (C Ar), 129.1 (C Ar); 121.1 (C Ar); 64.9 ($\underline{C}(CH_3)_3$); 35.3 (CH_2); 29.1 ($C(\underline{C}H_3)_3$). Found, %: C 44.14; H 4.55; N 17.27; S 9.60. $C_{12}H_{15}BrN_4S$. Calculated, %: C 44.03; H 4.63; N 17.11; S 9.81.

5-[(4-Bromobenzyl)sulfanyl]-2-(2-phenylpropan-2-yl)-2*H*-tetrazole (7e). Yield 1.61 g (89%), colorless crystals, mp 45-46°C (EtOAc). IR spectrum, ν, cm^{-1}: 2946 (CH_3), 2976 (CH_2), 1591 (C=N), 1487 (Ar), 1449 (Ar), 1159 (C–N), 696 (C–S), 647 (C–Br). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.00 (6H, s, $C(C\underline{H}_3)_2$); 4.31 (2H, s, CH_2); 6.96 (2H, d, *J* = 8.0, H Ar); 7.20-7.25 (5H, m, H Ar); 7.37 (2H, d, *J* = 8.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 162.4 (C–S); 144.1 (C Ar); 137.3 (C Ar); 131.7 (C Ar), 129.1 (C Ar); 128.4 (C Ar); 125.1 (C Ar); 121.0 (C Ar); 69.3 ($\underline{C}(CH_3)_2$); 28.9 ($C(\underline{C}H_3)_2$). Found, %: C 52.54; H 4.49; N 14.28; S 8.31. $C_{17}H_{17}BrN_4S$. Calculated, %: C 52.45; H 4.40; N 14.39; S 8.24.

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