Reactions of 1,2,4,5-tetrazines with S-nucleophiles*

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The reactions of 3,6-disubstituted and azoloannulated 1,2,4,5-tetrazines containing heterocyclic leaving groups with S-nucleophiles were studied. The methods of introduction of functionalized thiols, including thiol derivatives of 1,7- and 1,2-dicarba-*closo*-dodecaboranes, into the tetrazine ring were developed. It was established for the first time that, instead of replacement of a leaving group in the tetrazine ring, the attack of S-nucleophile at the unsubstituted carbon atom occurs in the case of imidazo[1,2-*b*][1,2,4,5]tetrazines to form previously unknown products of nucleophilic substitution of the hydrogen atom.

Key words: 1,2,4,5-tetrazines, [1,2,4]triazolo[4,3-*b*][1,2,4,5]tetrazines, imidazo[1,2-*b*]-[1,2,4,5]tetrazines, S-nucleophiles, nucleophilic substitution.

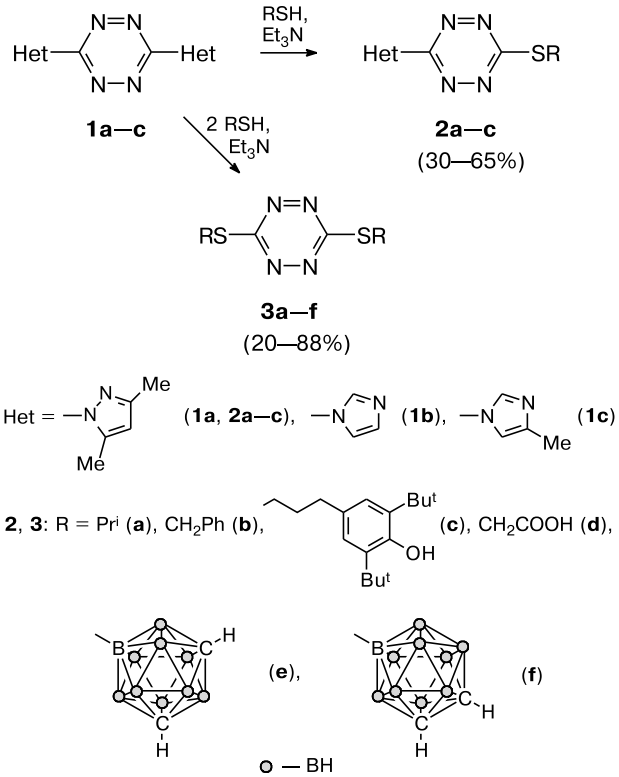
1,2,4,5-Tetrazines substituted by S-nucleophiles are of interest as materials possessing electrochemical activity, luminiscence properties,[1,2] ability to form molecular complexes with organic molecules,[3] which opens prospects for their application in sensory devices and molecular electronics. The ability of 1,2,4,5-tetrazines to react with thiols, in particular, with thio groups of amino acids as part of proteins, can be used for labeling and analysis of biological objects.[4]

At the present time, there are only singular examples of introduction of S-nucleophile residues into the tetrazine ring.[1,2,5] These reactions are usually carried out based on insufficiently stable and hardly accessible halogenated 1,2,4,5-tetrazine derivatives. At the same time, it is known[5—8] that the 1,2,4,5-tetrazines containing heterocyclic leaving groups are convenient substrates for modification of the tetrazine ring in the reactions with N- and O-nucleophiles.

In the present work, we studied in detail the reactions of 3,6-diazolyl-1,2,4,5-tetrazines **1a**—**c** with S-nucleophiles. A series of products of mono- (**2**) and disubstitution (**3**) in tetrazines **1a**—**c** by various functionalized thiols, including thiol derivatives of *o*- and *m*-carboranes, was synthesized (Scheme 1).

Compounds **2** and **3** were synthesized in acetonitrile at room temperature in the presence of catalytic amounts of triethylamine. Replacement of heterocyclic leaving groups in the tetrazine ring is the main reaction pathway of

Scheme 1



* Dedicated to Academician V. N. Charushin on the occasion of his 60th birthday.

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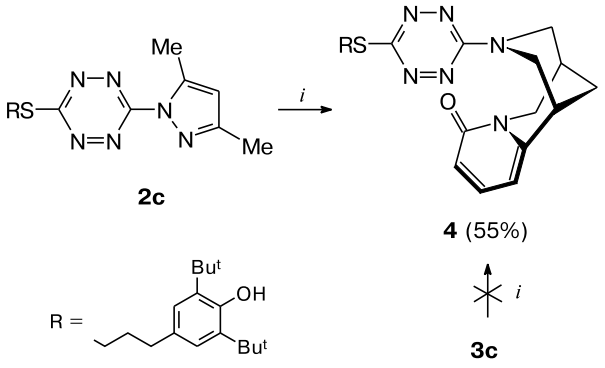
3,6-diazolyl-1,2,4,5-tetrazines with S-nucleophiles. However, according to the data from TLC, the reactions mixtures contained generally also dihydrotetrazines and disulfides, which are products of the side redox reactions proceeding due to a high electrophilicity of the 1,2,4,5-tetrazine ring. Heating of the reaction mixtures resulted in the increase in the amount of these side products and decrease in the yields of target substituted tetrazines.

It was established that the imidazolyl fragments are easier substituted by S-nucleophiles than the 3,5-dimethylpyrazolyl group. For example, the reactions of thiols with compounds **1b,c** afforded only the corresponding disubstituted derivatives **3**, while tetrazine **1a** form mixtures of mono- and disubstitution products with predominance of derivatives **2**. The reaction of compound **1a** with thioglycolic acid is an exception, which proceeds without basic catalysis to afford disubstituted tetrazine **3d** at any reagent ratio. The structures of the synthesized thiol derivatives were confirmed by the X-ray diffraction data for 3,6-dibenzylthio-1,2,4,5-tetrazine (**3b**) (Fig. 1).

By the example of the reaction of tetrazine **2c** with cytisine, it was shown that the 3,5-dimethylpyrazolyl group in the products **2** can be substituted further by N-nucleophiles (Scheme 2). Compound **4** containing the thiol and amine fragments was obtained upon refluxing reagents in acetonitrile in a yield of 55%. We failed to synthesize compound **4** by substitution of the alkylthio group in compound **3c**.

Scheme 2



i. Cytisine.

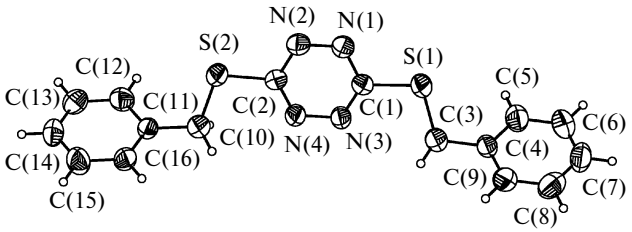
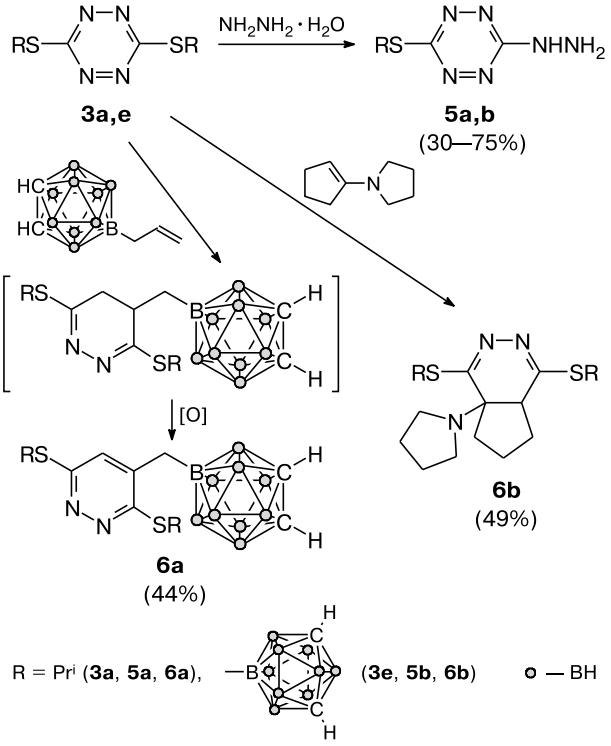


Fig. 1. Molecular geometry of **3b** in the crystal (the thermal ellipsoids are shown with 50% probability).

At the same time, hydrazine, which is a stronger nucleophile, replace readily one of the alkylthio group in tetrazines **3**. In such a manner, we synthesized hydrazinotetrazines **5a,b** (Scheme 3) containing, respectively, the isopropylthio group and *m*-carboranylthio fragment, which is promising unit in the medicaments for boron neutron capture therapy of oncological diseases. Introduction of the hydrazine group open the way for subsequent chemical modification of tetrazines **5a,b**.

Scheme 3



By the example of compounds **3a,e**, it was shown that the tetrazines containing the fragments of S-nucleophiles enter into the [4+2] cycloaddition reactions with inverted electronic requirements similarly to diazolyltetrazines **1**[9], which are accompanied by release of molecular nitrogen. Novel pyridazines **6a,b** (see Scheme 3) having the carborane substituents and lipophilic alkyl fragments in their structures were obtained by these transformations. Dihydropyridazine, which formed as a result of the addition of allylcarborane, was not isolated, since under the reaction conditions it was oxidized by the starting tetrazine **3a** to pyridazine **6a**. The structure of pyridazine **6a** was confirmed by X-ray diffraction (Fig. 2).

It is known[10,11] that the heterocyclic leaving group in the tetrazine ring of [1,2,4]triazolo[4,3-*b*]- and imidazo[1,2-*b*][1,2,4,5]tetrazines is readily substituted by N- and O-nucleophiles as in the unannulated derivatives. It was established that azoloannulation causes change in

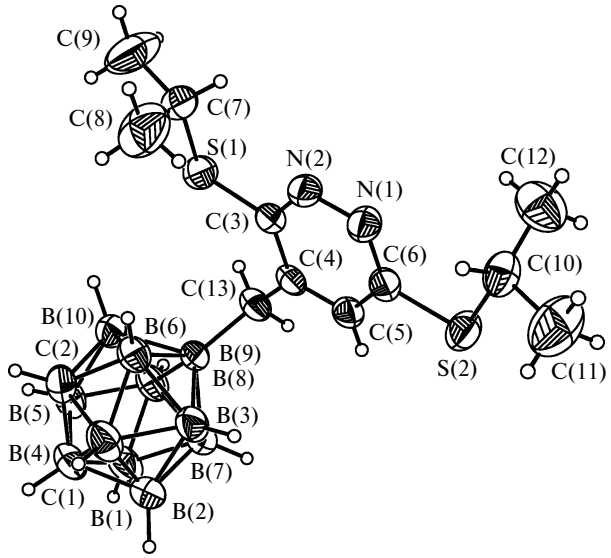
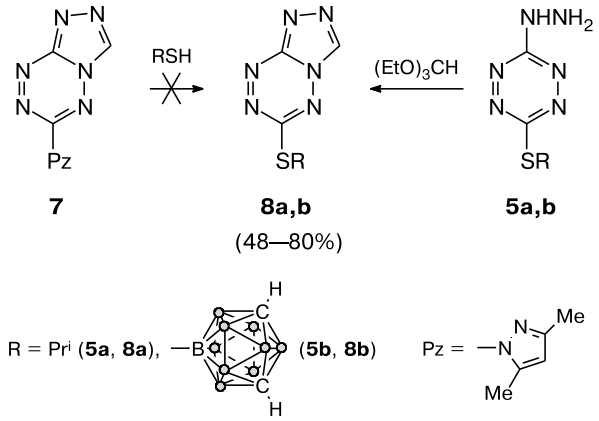


Fig. 2. Molecular geometry of **6a** in the crystal (the thermal ellipsoids are shown with 50% probability).

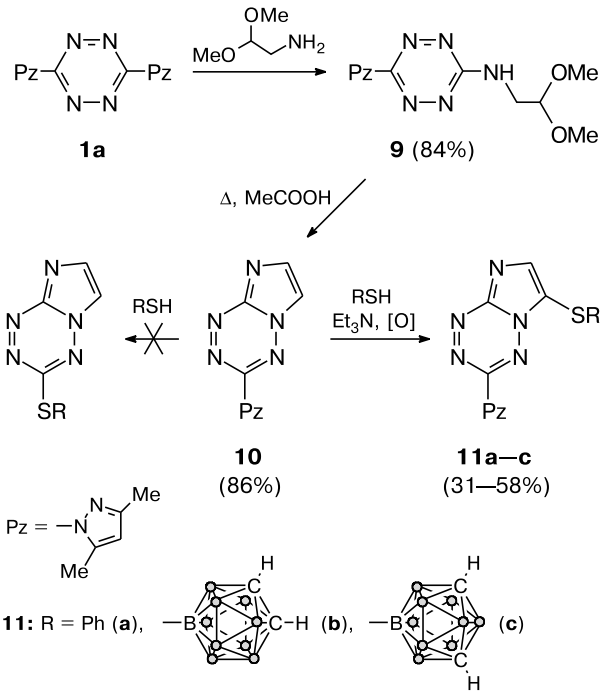
the reactivities of tetrazines in the reactions with S-nucleophiles. For examples, in contrast to the 3,6-disubstituted derivatives **1**, [1,2,4]triazolo[4,3-*b*][1,2,4,5]tetrazine **7** affords no products of replacement of the pyrazolyl group by thiols even upon heating in the presence of triethylamine. To synthesize the targeted triazolotetrazines **8a,b** containing the thiol fragment in the position 6, cyclocondensation of the hydrazine derivatives **5a,b** with triethylorthoformate was carried out (Scheme 4).

Scheme 4



The influence of the annulated imidazole ring on the reactivities of 1,2,4,5-tetrazines in the reactions with S-nucleophiles was studied by the example of 3-(3,5-dimethylpyrazol-1-yl)imidazo[1,2-*b*][1,2,4,5]tetrazine (**10**) (Scheme 5). Compound **10** was obtained in a high yield (86%) by cyclocondensation of tetrazine **9** containing the aminoacetal fragment. The earlier described[12] method of synthesis of compound **10** from 3-amino-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine and chloroacetaldehyde allowed us to obtain the targeted product in a yield of only 13%.

Scheme 5



The reaction of imidazo[1,2-*b*][1,2,4,5]tetrazine **10** with thiols in acetonitrile in the presence of triethylamine affords no substitution products of the heterocyclic leaving group in the tetrazine ring. Previously unknown products of nucleophilic substitution of the hydrogen atom in the imidazole fragment **11a**—**c** were isolated in these reactions. The structures of these compounds were confirmed by the X-ray diffraction data for **11c** (Fig. 3).

Thus, 3,6-disubstituted 1,2,4,5-tetrazines containing heterocyclic leaving groups form readily the mono- and disubstitution products under the action of S-nucleophiles. Azoloannulation results in the change in the reactivities of 1,2,4,5-tetrazines.

Experimental

Compound **1a**—**c**, **7** have been described earlier.[7,13—15] 9-Mercapto-*o*- and 9-mercapto-*m*-carboranes were prepared according to a known procedure.[16]

NMR spectra were recorded on a Avance DRX-400 (Bruker) spectrometer at 400 MHz using Me_4Si as the internal standard. The chemical shifts are given in the δ scale in ppm. Melting points were determined using a Stuart instrument. Elemental analysis was performed on a CHN PE 2400 Ser. II (Perkin—Elmer) analyzer. The course of reactions and purity of com-

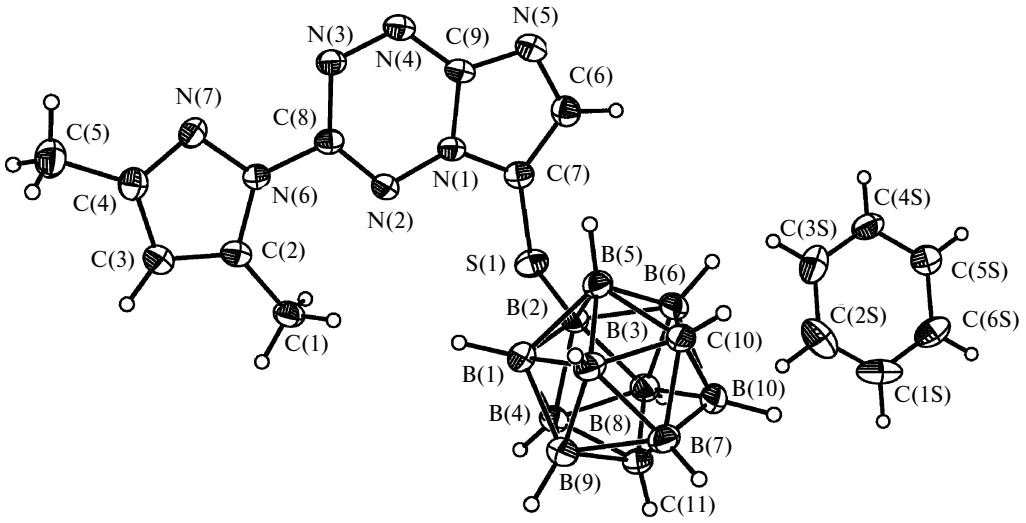


Fig. 3. Molecular geometry of **11c** in the crystal (the thermal ellipsoids are shown with 50% probability).

pounds obtained was monitored by TLC on Sorbfil plates, the eluent was a benzene—acetonitrile (1 : 1) mixture. Silica gel (Lancaster 0.040—0.063 mm, 230—400 mesh) was used for column chromatography, the eluent was a benzene—acetonitrile (1 : 1) mixture.

3-Alkylthio-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazines 2a—c. To a solution of tetrazine **1a** (270 mg, 1 mmol) in acetonitrile (15 mL), alkylthiol (1 mmol) and triethylamine (50 mg, 0.5 mmol) were added with stirring. The reaction mixture was stirred for 1—5 h at room temperature (TLC control). The solvent was evaporated and compounds **2a—c** were isolated by column chromatography (R_f 0.7—0.8).

3-(3,5-Dimethylpyrazol-1-yl)-6-isopropylthio-1,2,4,5-tetrazine (2a). The yield was 162 mg (65%), m.p. 89—90 °C. Found (%): C, 48.33; H, 5.60; N, 33.25. $C_{10}H_{14}N_6S$. Calculated (%): C, 47.98; H, 5.64; N, 33.57.

3-Benzylthio-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (2b). The yield was 89 mg (30%), m.p. 90—93 °C. Found (%): C, 56.54; H, 4.77; N, 27.92. $C_{14}H_{14}N_6S$. Calculated (%): C, 56.36; H, 4.73; N, 28.17.

3-[3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)propylthio]-6-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (2c). The yield was 223 mg (49%), m.p. 98—100 °C. Found (%): C, 63.09; H, 7.58; N, 18.43. $C_{24}H_{34}N_6OS$. Calculated (%): C, 63.40; H, 7.54; N, 18.49.

3,6-Diisopropylthio-1,2,4,5-tetrazine (3a). To a suspension of tetrazine **1b** (214 mg, 1 mmol) in acetonitrile (10 mL), isopropylthiol (152 mg, 2 mmol) and triethylamine (50 mg, 0.5 mmol) were added. The reaction mixture was stirred for 5 min at room temperature. The solvent was evaporated, the product was extracted with pentane, and the crystals obtained after evaporation of pentane were washed with water and recrystallized from pentane. The yield was 170 mg (74%), m.p. 59 °C. Found (%): C, 41.73; H, 6.19; N, 24.22. $C_8H_{14}N_4S_2$. Calculated (%): C, 41.71; H, 6.13; N, 24.32.

3,6-Dibenzylthio-1,2,4,5-tetrazine (3b). To a suspension of tetrazine **1b** (214 mg, 1 mmol) in acetonitrile (10 mL), benzylthiol (248 mg, 2 mmol) and triethylamine (50 mg, 0.5 mmol) were added. The reaction mixture was stirred for 1 h at room temperature. The precipitate that formed was filtered off and recrystallized from acetonitrile. The yield was 203 mg (62%), m.p. 139—140 °C. Found (%): C, 59.09; H, 4.19; N, 17.17. $C_{16}H_{14}N_4S_2$. Calculated (%): C, 58.87; H, 4.32; N, 17.16.

3,6-Di[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylthio]-1,2,4,5-tetrazine (3c). To a suspension of tetrazine **1b** (214 mg, 1 mmol) in acetonitrile (10 mL), 2,6-di-*tert*-butyl-4-(3-thiolpropyl)phenol (561 mg, 2 mmol) and triethylamine (50 mg, 0.5 mmol) were added. The reaction mixture was stirred for 5 min at room temperature. The solvent was evaporated, the product was extracted with pentane, and the crystals obtained of evaporation of pentane were washed with water and recrystallized from pentane. The yield was 249 mg (39%), m.p. 123—125 °C. Found (%): C, 67.94; H, 8.68; N, 8.78. $C_{36}H_{54}N_4O_2S_2$. Calculated (%): C, 67.67; H, 8.52; N, 8.77.

3,6-Dicarboxymethylthio-1,2,4,5-tetrazine (3d). To a solution of tetrazine **1a** (270 mg, 1 mmol) in acetonitrile (10 mL), thioglycolic acid (184 mg, 2 mmol) was added. The reaction mixture was stirred for 15 min at room temperature. The precipitate that formed was filtered off and washed with acetonitrile. The yield was 215 mg (79%), m.p. 204 °C (decomp.). Found (%): C, 26.42; H, 2.52; N, 20.70. $C_6H_6N_4O_4S_2 \cdot 0.5H_2O$. Calculated (%): C, 26.57; H, 2.60; N, 20.65.

3,6-Di(1,7-dicarba-*closo*-dodecaboran-9-yl)thio-1,2,4,5-tetrazine (3e). To a suspension of tetrazine **1c** (242 mg, 1 mmol) in acetonitrile (10 mL), 9-mercapto-*m*-carborane (352 mg, 2 mmol) and triethylamine (50 mg, 0.5 mmol) were added. The reaction mixture was stirred for 3 h at room temperature. The precipitate that formed was filtered off and washed with acetonitrile. The yield was 379 mg (88%), m.p. 241—243 °C. Found (%): C, 17.00; H, 5.18; N, 13.08. $C_6H_{22}B_{20}N_4S_2$. Calculated (%): C, 16.74; H, 5.15; N, 13.01.

3,6-Di(1,2-dicarba-*closo*-dodecaboran-9-yl)thio-1,2,4,5-tetrazine (3f). To a suspension of tetrazine **1c** (242 mg, 1 mmol) in acetonitrile (10 mL), 9-mercapto-*o*-carborane (352 mg, 2 mmol) and triethylamine (50 mg, 0.5 mmol) were added. The reaction mixture was stirred for 3 h at room temperature and then kept for 24 h at −20 °C. The precipitate that formed was filtered off and washed with acetonitrile. The yield was 90 mg

(20%), m.p. 250 °C (decomp.). Found (%): C, 18.39; H, 5.51; N, 13.58. $C_6H_{22}B_{20}N_4S_2 \cdot 0.5CH_3CN$. Calculated (%): C, 18.64; H, 5.25; N, 13.97.

***N*-{6-[3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)propylthio]-1,2,4,5-tetrazine-3-yl}cytisine (4).** A solution of compound **2c** (227 mg, 0.5 mmol) and cytisine (95 mg, 0.5 mmol) was refluxed for 6 h. The solvent was concentrated and product **4** was isolated by column chromatography, R_f 0.35. The yield was 312 mg (55%), m.p. 83—85 °C. Found (%): C, 63.81; H, 7.27; N, 14.67. $C_{30}H_{40}N_6O_2S \cdot H_2O$. Calculated (%): C, 63.58; H, 7.47; N, 14.83.

3-Hydrazino-6-isopropylthio-1,2,4,5-tetrazine (5a). To a solution of compound **3a** (230 mg, 1 mmol) in acetonitrile (5 mL), hydrazine hydrate (50 mg, 1 mmol) was added with stirring. The reaction mixture was stirred for 15 min at room temperature. The solvent was concentrated and product **5a** was isolated by column chromatography, R_f 0.5. The yield was 147 mg (79%), m.p. 91—92 °C. Found (%): C, 32.27; H, 5.52; N, 45.45. $C_5H_{10}N_6S$. Calculated (%): C, 32.25; H, 5.41; N, 45.13.

3-Hydrazino-6-(1,7-dicarba-*closo*-dodecaboran-9-yl)thio-1,2,4,5-tetrazine (5b). To a suspension of compound **3e** (215 mg, 0.5 mmol) in an acetonitrile—DMF (4 : 1) mixture (5 mL), hydrazine-hydrate (30 mg, 0.6 mmol) was added with stirring. The reaction mixture was stirred for 15 min at room temperature. The solvent was removed under reduced pressure and product **5b** was isolated by column chromatography, R_f 0.7. The yield was 108 mg (76%), m.p. 145—146 °C. Found (%): C, 17.01; H, 5.12; N, 29.18. $C_4H_{14}B_{10}N_6S$. Calculated (%): C, 16.78; H, 4.93; N, 29.35.

3,6-Diisopropylthio-4-(1,2-dicarba-*closo*-dodecaboran-9-yl)methylpyridazine (6a). A solution of compound **3a** (230 mg, 1 mmol) and 9-allyl-*o*-carborane (184 mg, 1 mmol) in mesitylene (10 mL) was refluxed for 5 h. The solvent was removed under reduced pressure and the residue was recrystallized from acetonitrile. The yield was 173 mg (45%), m.p. 146—148 °C. Found (%): C, 40.65; H, 7.57; N, 7.38. $C_{13}H_{28}B_{10}N_2S_2$. Calculated (%): C, 40.60; H, 7.34; N, 7.28.

1,4-Di(1,7-dicarba-*closo*-dodecaboran-9-yl)thio-4a-(pyrrolidin-1-yl)-5,6,7,7a-tetrahydro-4a*H*-cyclopenta[*d*]pyridazine (6b). To a suspension of compound **3e** (215 mg, 0.5 mmol) in acetonitrile (8 mL), 1-pyrrolidinecyclopentene (69 mg, 0.5 mmol)

Table 1. ^{1}H NMR spectra of compounds **2a—c**, **3a—f**, **4**, **5a,b**, **6a,b**, **8a,b**, **9**, **10**, and **11a—c** in DMSO-d_6

Compound	δ (*J*/Hz)
2a[a]	1.54 (d, 6 H, 2 Me (Pr^i), *J* = 6.8); 2.38, 2.68 (both s, 3 H each, 2 Me (Pyr)); 4.17 (m, 1 H, CH (Pr^i)); 6.17 (s, 1 H, H(4) (Pyr))
2b[a]	2.38, 2.66 (both s, 3 H each, 2 Me (Pyr)); 4.58 (s, 2 H, CH_2); 6.16 (s, 1 H, H(4) (Pyr)); 7.29—7.36 (m, 3 H, Ph); 7.49 (m, 2 H, Ph)
2c	1.36 (s, 18 H, 2 Bu^t); 2.03 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.26, 2.54 (both s, 3 Heach, 2 Me (Pyr)); 2.66 (t, 2 H, $C\underline{H}_2Ar$, *J* = 7.7); 3.36 (t, 2 H, $SC\underline{H}_2$, *J* = 7.2); 6.32 (s, 1 H, H(4) (Pyr)); 6.72 (s, 1 H, OH); 6.94 (s, 2 H, Ar)
3a[a]	1.50 (d, 12 H, 4 Me (2 Pr^i), *J* = 6.8); 4.09 (m, 2 H, 2 CH (2 Pr^i))
3b[a]	4.51 (s, 4 H, 2 CH_2); 7.28—7.36 (m, 6 H, 2 Ph); 7.45 (m, 4 H, 2 Ph)
3c	1.36 (s, 36 H, 4 Bu^t); 1.99 (m, 4 H, 2 $CH_2C\underline{H}_2CH_2$); 2.63 (t, 4 H, 2 $C\underline{H}_2Ar$, *J* = 7.5), 3.27 (t, 4 H, 2 SCH_2, *J* = 7.3); 6.71 (s, 2 H, 2 OH); 6.92 (s, 4 H, 2 Ar)
3d	4.17 (s, 4 H, 2 CH_2); 13.01 (br.s, 2 H, 2 COOH)
3e[b]	1.60—3.30 (m, 18 H, 18 BH); 4.21 (br.s, 4 H, 4 CH)
3f	1.60—3.10 (m, 18 H, 18 BH); 5.09, 5.11 (both br.s, 2 H each, 4 CH)
4[a]	1.43 (s, 18 H, 2 Bu^t); 2.01—2.16 (m, 4 H, 2 CH_2); 2.31, 2.49 (both m, 1 H each, 2 CH); 2.68—2.73 (m, 2 H, CH_2); 3.21—3.37 (m, 6 H, 3 CH_2); 4.86—4.96 (m, 2 H, CH_2); 5.06 (br.s, 1 H, OH); 6.10 (dd, 1 H, H(3) of the pyridone fragment of cytisine, J^1 = 7.0, J^2 = 1.2); 6.38 (dd, 1 H, H(1) of the pyridone fragment of cytisine, J^1 = 9.2, J^2 = 1.2); 7.00 (s, 2 H, Ar); 7.24 (t.d, 1 H, H(2) of the pyridone fragment of cytisine, J^1 = 9.2, J^2 = 7.0)
5a	1.38 (d, 6 H, 2 Me (Pr^i), *J* = 6.8); 3.90 (m, 1 H, CH (Pr^i)); 4.54 (br.s, 2 H, NH_2); 9.40 (br.s, 1 H, NH)
5b	1.60—3.60 (m, 9 H, 9 BH); 4.15 (br.s, 2 H, 2 CH); 4.61 (br.s, 2 H, NH_2); 9.54 (br.s, 1 H, NH)
6a[a]	0.80—3.00 (m, 9 H, 9 BH); 1.42 (d, 12 H, 4 Me (2 Pr^i), *J* = 6.8); 2.13 (s, 2 H, CH_2); 3.45, 3.51 (both br.s, 1 H each, 2 CH); 4.20, 4.28 (both m, 1 H each, 2 CH (2 Pr^i)); 6.74 (s, 1 H, H(5) pyridazine)
6b[a]	1.44—3.46 (m, 25 H, 18 BH, 3 CH_2, CH); 1.46—1.55 (m, 4 H, 2 CH_2 pyrrolidine); 2.96 (br.s, 4 H, 4 CH); 3.02 (t, 4 H, 2 CH_2 pyrrolidine, *J* = 7.6)
8a	1.48 (d, 6 H, 2 Me (Pr^i), *J* = 6.8); 3.88 (m, 1 H, CH (Pr^i)); 9.84 (s, 1 H, CH)
8b	1.50—3.20 (m, 9 H, 9 BH); 4.28 (br.s, 2 H, 2 CH); 9.82 (s, 1 H, CH)
9[a]	2.36, 2.57 (both s, 3 H each, 2 Me (Pyr)); 3.46 (s, 6 H, 2 MeO); 3.79 (m, 2 H, CH_2); 4.60 (t, 1 H, CH, *J* = 5.1); 6.06 (br.s, 1 H, NH); 6.11 (s, 1 H, H(4) (Pyr))
10[a]	2.39, 2.77 (both s, 3 H each, 2 Me (Pyr)); 6.18 (s, 1 H, H(4) (Pyr)); 8.19, 8.44 (both d, 1 H each, 2 CH, *J* = 0.8)
11a	2.25, 2.36 (both s, 3 H each, 2 Me (Pyr)); 6.26 (s, 1 H, H(4) (Pyr)); 7.26—7.34 (m, 5 H, Ph); 8.79 (s, 1 H, CH)
11b[a]	1.40—3.20 (m, 9 H, 9 BH); 2.38, 2.73 (both s, 3 H each, 2 Me (Pyr)); 3.58, 3.68 (both br.s, 1 H each, 2 CH of carborane); 6.16 (s, 1 H, H(4) (Pyr)); 8.41 (s, 1 H, CH)
11c	1.50—3.10 (m, 9 H, 9 BH); 2.28, 2.61 (both s, 3 H each, 2 Me (Pyr)); 4.17 (br.s, 2 H, 2 CH of carborane); 6.31 (s, 1 H, H(4) (Pyr)); 8.69 (s, 1 H, CH)

[a] The spectrum was recorded in $CDCl_3$.

[b] The spectrum was recorded in DMF-d_7.

was added. The reaction mixture was stirred for 30 min at 60 °C until completion of gas evolution and complete dissolution of the starting substance. The product was swaged with water (3 mL), filtered off, and recrystallized from acetonitrile. The yield was 173 mg (62%), m.p. 102—104 °C. Found (%): C, 32.30; H, 7.05; N, 7.53. $C_{15}H_{37}B_{20}N_3S_2 \cdot H_2O$. Calculated (%): C, 32.70; H, 6.74; N, 7.08.

[1,2,4]Triazolo[4,3-*b*][1,2,4,5]tetrazines 8a,b. Compound **5** (1 mmol) was refluxed for 3—4 h (TLC control) in a $CH_3COOH—CH(OEt)_3$ (1 : 3) mixture (8 mL). The solvent was removed under reduced pressure. The residue was washed with hexane (**8a**) or diethyl ether (**8b**).

6-(Isopropylthio)[1,2,4]triazolo[4,3-*b*][1,2,4,5]tetrazine (8a). The yield was 157 mg (80%), m.p. 86—88 °C. Found (%): C, 37.00; H, 4.24; N, 42.62. $C_6H_8N_6S$. Calculated (%): C, 36.72; H, 4.11; N, 42.83.

6-(1,7-Dicarba-*closo*-dodecaboran-9-yl)thio[1,2,4]triazolo-[4,3-*b*][1,2,4,5]tetrazine (8b). The yield was 142 mg (48%), m.p. 181—183 °C. Found (%): C, 20.44; H, 4.21; N, 28.05. $C_5H_{12}B_{10}N_6S$. Calculated (%): C, 20.26; H, 4.08; N, 28.36.

6-(2,2-Dimethoxyethylamino)-3-(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (9). To a suspension of tetrazine **1a** (1 mmol) in acetonitrile (6 mL), 2,2-dimethoxyethylamine (110 mg, 1.05 mmol) was added. The reaction mixture was stirred for 10 min at room temperature. The solvent was removed under reduced pressure and the residue was washed with hexane. The yield was 235 mg (84%), m.p. 95—96 °C. Found (%): C, 47.33; H, 6.12; N, 35.36. $C_{11}H_{17}N_7O_2$. Calculated (%): C, 47.30; H, 6.14; N, 35.10.

3-(3,5-Dimethylpyrazol-1-yl)imidazo[1,2-*b*][1,2,4,5]tetrazine (10). Compound **9** (0.5 mmol) was refluxed for 4 h in CH_3COOH (5 mL). The solvent was removed under reduced pressure and the residue was washed with ethanol. The yield was 93 mg (86%), m.p. 194—195 °C. Found (%): C, 50.29; H, 4.21; N, 45.36. $C_9H_9N_7$. Calculated (%): C, 50.23; H, 4.22; N, 45.56.

6-Substituted 3-azolylimidazo[1,2-*b*][1,2,4,5]tetrazines 11a—c. To a solution of imidazo[1,2-*b*][1,2,4,5]tetrazine **10** (0.5 mmol) in acetonitrile (5 mL), thiol (0.6 mmol) and triethylamine (50 mg, 0.5 mmol) were added. The reaction mixture was stirred for 5—7 h at room temperature (TLC control). The solvent was concentrated. Compounds **11a—c** were isolated by column chromatography (R_f 0.7—0.8).

3-(3,5-Dimethylpyrazol-1-yl)-6-(phenylthio)imidazo[1,2-*b*]-[1,2,4,5]tetrazine (11a). The yield was 61 mg (38%), m.p. 137—140 °C. Found (%): C, 55.61; H, 3.76; N, 30.31. $C_{15}H_{13}N_7S$. Calculated (%): C, 55.71; H, 4.05; N, 30.32.

6-[(1,2-Dicarba-*closo*-dodecaboran-9-yl)thio]-3-(3,5-dimethylpyrazol-1-yl)imidazo[1,2-*b*][1,2,4,5]tetrazine (11b). The yield was 60 mg (31%), m.p. 187—190 °C. Found (%): C, 34.13; H, 5.24; N, 24.93. $C_{11}H_{19}B_{10}N_7S$. Calculated (%): C, 33.92; H, 4.92; N, 25.17.

6-[(1,7-Dicarba-*closo*-dodecaboran-9-yl)thio]-3-(3,5-dimethylpyrazol-1-yl)imidazo[1,2-*b*][1,2,4,5]tetrazine (11c). The yield was 113 mg (58%), m.p. 170—173 °C. Found (%): C, 33.79; H, 4.87; N, 25.16. $C_{11}H_{19}B_{10}N_7S$. Calculated (%): C, 33.92; H, 4.92; N, 25.17.

Table 2. Principal crystallographic data for compounds **3b**, **6a**, and **11c**

Compound	**3b**	**6a**	**11c**
Molecular formula	$C_{16}H_{14}N_4S_2$	$C_{13}H_{28}B_{10}N_2S_2$	$C_{11}H_{19}B_{10}N_7S \cdot C_6H_6$
Molecular weight	326.43	384.59	467.60
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	$P2(1)/c$	$P2(1)/n$	$P\bar{1}$
a/Å	9.7789(12)	10.9319(3)	8.8455(9)
b/Å	5.5097(6)	12.0400(3)	11.7839(11)
c/Å	29.099(4)	17.3565(5)	13.4495(12)
α/deg	90	90.00	66.345(9)
β/deg	95.760(10)	106.621(2)	88.425(8)
γ/deg	90	90.00	69.879(9)
V/Å^3	1559.9(3)	2189.01(10)	1195.7(2)
Z	4	4	2
d_{calc}/g cm^{-3}	1.390	1.167	1.299
μ/mm^{-1}	0.342	0.244	0.158
Scan range in θ/deg	$26.37 \geq \theta \geq 2.81$	$30.51 \geq \theta \geq 2.98$	$28.28 \geq \theta \geq 2.76$
Number of measured reflections (R_{int})	9421 (0.0326)	19348 (0.0162)	7020 (0.0221)
Number of independent reflections	3146	6498	5787
Number of reflections with $I > 2\sigma(I)$	1719	4056	3776
Number of refined parameters	215	303	364
R_1 (over $I > 2\sigma(I)$)	0.0313	0.0403	0.0385
wR_2 (over $I > 2\sigma(I)$)	0.0453	0.1072	0.0908
R_1 (over all reflections)	0.0786	0.0661	0.0686
wR_2 (over all reflections)	0.0486	0.1123	0.0962

The ^{1}H NMR spectra of compounds **2a—c**, **3a—f**, **4**, **5a**,**b**, **6a**,**b**, **8a**,**b—10a**,**b**, and **11a—c** are given in Table 1.

X-ray diffraction study of compounds 3b, 6a, and 11c. The single crystals of compounds **3b** and **6a** were obtained by recrystallization from MeCN and the single crystal of compound **11c** was obtained by recrystallization from benzene. The experiment was performed on a Xcalibur-3 X-ray diffractometer with a CCD detector (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, ω- and φ-scanning, T = 295 (**3b**, **6a**) and 120 K (**11c**)). The structures were solved by the direct method according to the SHELXS-97 program and refined using the SHELXL-97 program. The positions and temperature parameters of non-hydrogen atoms were refined in the isotropic approximation and then in the anisotropic approximation by the full-matrix least square method. The crystal structure of **11c** contain solvate molecule of the solvent. The hydrogen atoms were localized at the electron density maxima and involved in the refinement in the riding model. The main parameters of the X-ray diffraction experiment are given in Table 2.

The X-ray diffraction data are deposited in Cambridge Crystallographic Data Centre under the Nos 818 588—818 590 (compounds **3b**, **6a**, and **11c**, respectively). These materials are free accessible and can be requested at www.ccdc.cam.ac.uk/data_request/cif.

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