

## **S-Methyl(-N-aryl and -N-alkyl)isothioureas derived from 2-aminobenzothiazole**

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**This manuscript is dedicated in honor of Dr. Rosalinda Contreras Theurel on the occasion  
of her 60<sup>th</sup> anniversary**

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### **Abstract**

S-Methylisothioureas, 2-N—H, -N—alkyl and -N—aryl are synthesized from the reaction of ammonia or the corresponding aromatic amines with benzothiazole dithiomethylcarboimidate. The reaction with pyrrolidine and piperazine are reported. Compounds were characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy and the X-ray molecular structure of S-methyl-N-benzothiazolelisothiourea derivative is reported.

**Keywords:** 2-Aminobenzothiazole, carbon disulfide, S-methyl group, isothioureas, guanidines, pyrrolidine, piperazine

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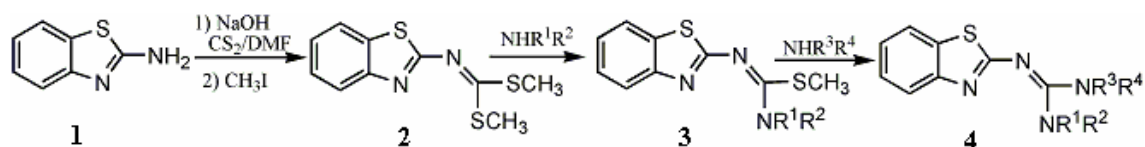
### **Introduction**

Recently, the guanidine group has attracted considerable attention, since it has been found in a wide array of natural and synthetic biologically active compounds.<sup>1</sup> These molecules are basic enough (pKa of their conjugate acids is around 12.5) to get the capacity to form intermolecular contacts mediated by H-bonding interactions.<sup>2</sup> Its positive charge, resulting from protonation in a wide range of pH values, creates a base for specific intermolecular interactions comprising key-steps of many biological reactions, including enzyme-mediated processes and interaction of hormones with their receptors.<sup>3</sup> Guanidinium moiety interacts with functional groups present in enzymes or receptors on the basis of hydrogen bonds and electrostatic interactions. Thus, they are useful pharmacophores in medicinal chemistry.<sup>4</sup> They are also studied because of their ability to form intermolecular associations. On the other hand, molecules containing this group are

interesting because of their nitrogen atoms bearing lone pairs and labile NH hydrogen atoms reactivity are feasible to obtain coordinating compounds.

It has been demonstrated that the introduction of the guanidine group instead of an existing amino group significantly increases the potency and/or selectivity of biologically active compounds.<sup>5</sup> By this, in our currently investigations about biologically active 2-aminobenzothiazoles,<sup>6</sup> we are interested in the functionalization of these aromatic heterocycles to get guanidine derivatives, where the nitrogen atoms can be bonded to hydrogen, alkyl or aryl groups and one or two nitrogen atoms are part of five or six membered heterocycles.

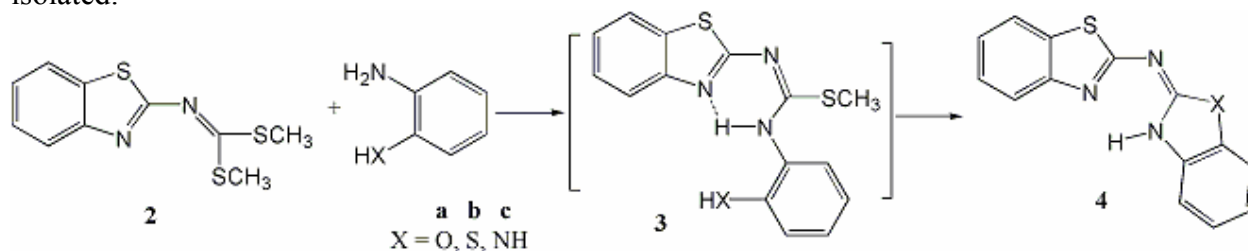
Herein we report the preparation and <sup>1</sup>H and <sup>13</sup>C NMR structural study of a series of *S*-methylisothiourreas **3**, scheme 1, obtained from 2-aminobenzothiazole **1** through dithiomethyl carboimide **2** as intermediate compound<sup>7</sup>. *S*-methylisothiourreas are interesting intermediates because they have a very reactive *S*-methyl functional group that can be used for the synthesis of combined guanidines **4**. X-ray diffraction structure of *N*-benzothiazolyl-*S*-methylisothiurea **3** (R<sub>1</sub> = R<sub>2</sub> = H) is also analysed.



**Scheme 1.** Isothiourreas and guanidines from 2-aminobenzothiazole.

## Results and Discussion

The intermediate dithiomethylcarboimide benzothiazole **2** was obtained from 2-aminobenzothiazole by reaction with carbon disulfide in basic media (20 M NaOH) using DMF as solvent (Merchant, *et al.*)<sup>7</sup>. A detailed study and characterization of the intermediates involved in this reaction have been reported<sup>6</sup>. It has been demonstrated that the reactivity of compound **2** is due to the facility to displace two molecules of HSM<sub>e</sub>, as leaving group, when it reacts with *o*-XH substituted anilines in refluxing DMF to get NH-bisbenzazoles **4**<sup>8</sup>, scheme 2. The reaction should proceed through the intermediacy of isothiurea derivatives **3a-c**, which have not been isolated.

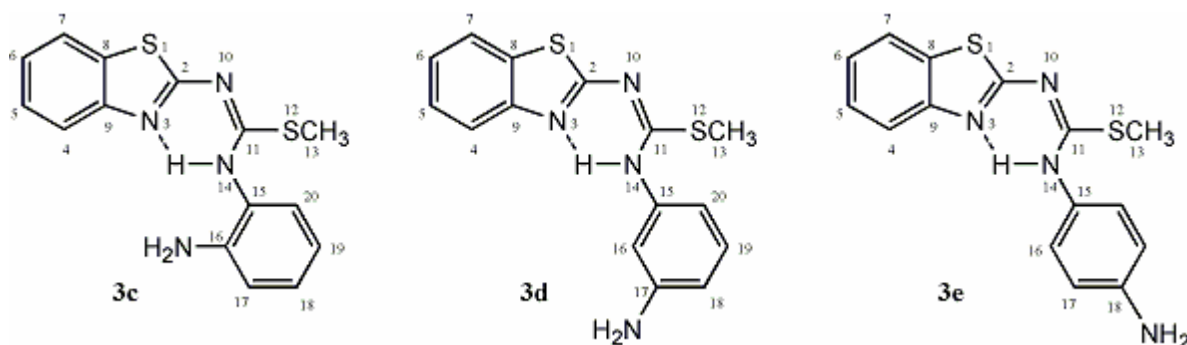


**Scheme 2.** NH-bisbenzazoles from dithiomethylcarboimide benzothiazole **2** with *o*-substituted anilines

In a previous work,<sup>6</sup> we tested the reactivity of compound **2** by using methyl- and *i*-propylamines as nucleophiles to prepare *S*-methyl, *N*-methyl and *S*-methyl, *N*-isopropylisothiouras, and *N,N'*-dimethylguanidine derivatives, when the reaction is carried out in refluxing ethanol. However, this reaction was not generalized to isolate the methylisothiouras intermediates when *o*-, *m*-, and *p*-XH-substituted anilines, ammonia, aniline, or cyclic amines are used.

In order to isolate the methylisothiouras derivatives using *o*-substituted anilines, the reaction was carried out just stirring or refluxing the reaction mixture with solvents of low boiling points like ethanol or chloroform. The reaction with *o*-aminophenol or *o*-aminothiophenol afforded, the corresponding bicyclic derivatives **4a** or **4b**, respectively, whereas *o*-phenylenediamine led to the corresponding *S*-methylisothiouras derivative **3c**, Figure 1. <sup>1</sup>H NMR spectrum of compound **3c** shows a NH signal at 11.9 ppm in CDCl<sub>3</sub>. The high frequency shift of this signal is indicative of an intramolecular hydrogen bonding between the NH proton and the thiazole nitrogen atom, as indicated in figure 1. The SCH<sub>3</sub> signal is present as a singlet at 2.46 ppm, whose integration is 3:8 in relation to the aromatic hydrogen atoms. In <sup>13</sup>C NMR spectrum, 15 signals are present, in agreement with the proposed structure.

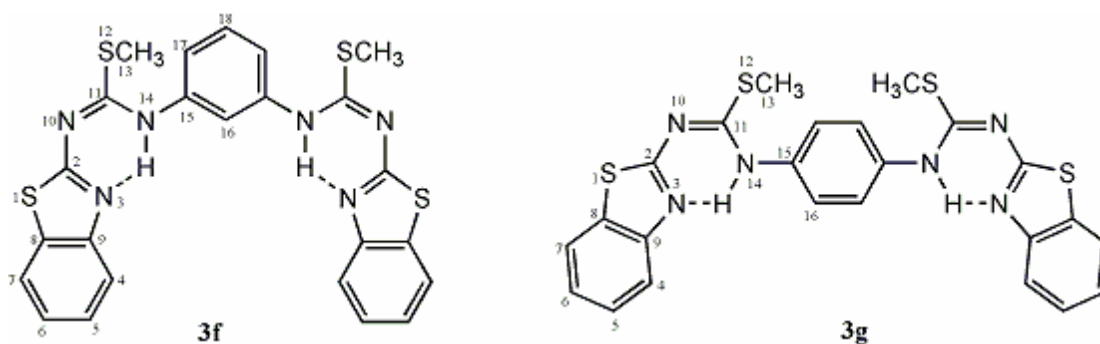
These results can be explained in terms of the acidity of both OH and SH groups, which are more acidic in comparison with the NH<sub>2</sub> group. This make phenoxide and thiolate groups more reactive than the *o*-aniline nitrogen atom, which can be responsible of the stability of intermediate **3c** in comparison with the analogous intermediates derived from *o*-OH or *o*-SH substituted anilines. On the basis of the last results, *m*- and *p*-phenylenediamine isomers were reacted with compound **2** at refluxing ethanol during 16 hours and the corresponding methylisothiouras **3d,e** derivatives were obtained, figure 1.



**Figure 1.** Isothiouras derived from benzothiazole dithiomethylcarboimidate **2** with *o*-, *m*-, and *p*-phenylenediamines.

In all cases, the <sup>1</sup>H NMR data, showed the expected 8:3 aromatic-aliphatic integral ratio and a broad signal appeared in 11.9 ppm (*ortho*), 11.8 (*meta*) and 11.7 (*para*), which integrated for

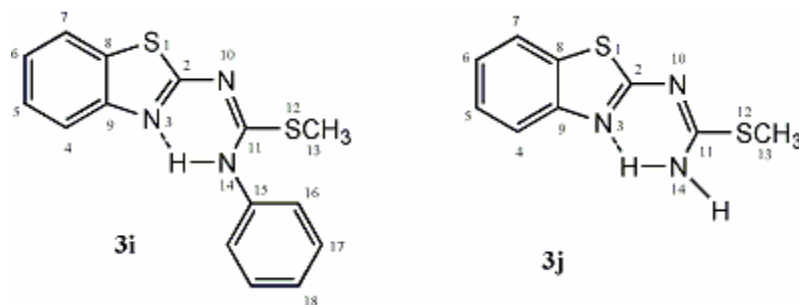
one bridged N-H proton. The aniline NH<sub>2</sub> protons appear in 4.0 ppm (*o*-amino group), 4.7 ppm (*m*-amino group) and 6.34 ppm (*p*-amino group). The presence of fifteen (*o*- and *m*-) and thirteen (*p*-) signals in <sup>13</sup>C NMR spectra confirm the formation of this intermediates. The intermediate compounds **3c-e** possesses an additional –NH<sub>2</sub> group, which can react with a second molecule of compound **2**. The reactions were carried out by using 2 molar equivalents of compound **2** and one molar equivalent of the corresponding phenylenediamine. The reaction with the *ortho* isomer, only produced compound **3c** and one equivalent of compound **2** remained without reaction. The reaction with *m*- and *p*- isomers afforded the corresponding diisothioureidic derivatives **3f** and **3g**, figure 2. Thirteen and eleven carbon signals were observed in <sup>13</sup>C NMR spectra for **3f** and **3g**, respectively.



**Figure 2.** Diisothiureas derived from dithiomethylcarboimidate benzothiazole **2** with *m*-, and *p*-phenylenediamines.

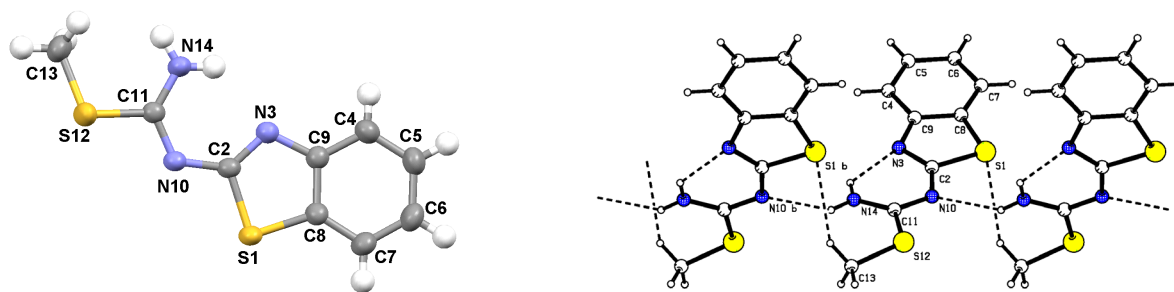
In a previous work,<sup>6</sup> it was reported that the reaction of compound **2** with one and two molar equivalents of methylamine afforded the isothioureidic compound **3h** (R<sub>1</sub> = H, R<sub>2</sub> = CH<sub>3</sub>) and the corresponding guanidine derivative **4h** (R<sub>1</sub> = R<sub>3</sub> = H, R<sub>2</sub> = R<sub>4</sub> = CH<sub>3</sub>) respectively, scheme 1. Characteristic NMR data from which it can be pointed out the chemical shift of C11 in 175.0 ppm in thiocarboimidate compound **2**, 172.5 ppm in the respective isothioureidic compound **3h** and 174.7 ppm in the corresponding guanidine compound **4h**. From these results, we completed the study with aniline, ammonia and cyclic amines as pyrrolidine and piperazine to isolate the isothiurea derivatives.

In the case of the reaction with one molar equivalent of aniline, one S-methyl group of compound **2** is substituted. The <sup>1</sup>H NMR data, showed a 9:3 aromatic-aliphatic integral ratio and a broad signal at 12.4 ppm, assigned to the N-H proton. Thirteen signals in <sup>13</sup>C NMR spectrum are indicative of the presence of the *S*-methyl-benzothiazolyl-phenylisothiurea compound **3i**, figure 3.



**Figure 3.** Isothiureas derived from benzothiazole dithiomethylcarboimidate **2** with aniline and ammonia.

When one molar equivalent of compound **2** were reacted with 3 molar equivalents of aqueous ammonia in stirring ethanol at room temperature during 48 hours, one molar equivalent of thiomethanol were evolved to get the corresponding isothiurea derivative **3j**. The  $^1\text{H}$  NMR data, showed a 4:3 aromatic-aliphatic integral ratio and a broad signal, for two NH protons, appeared at 9.27 ppm. This chemical shift compared with the same NH signal of the aniline analogous **3i** (12.4 ppm) suggests that this hydrogen atoms are more weakly bridged with the thiazole nitrogen. It is explained because in the case of compound **3i**, the electron pairs of the aniline nitrogen atom are conjugated with the aromatic ring and make hydrogen more acid, reinforcing the hydrogen bridge. From a saturated ethanolic solution, *S*-Methyl-*N*-benzothiazolylisothiurea **3j** was crystallized and its structure analyzed by X-ray diffraction, figure 4.

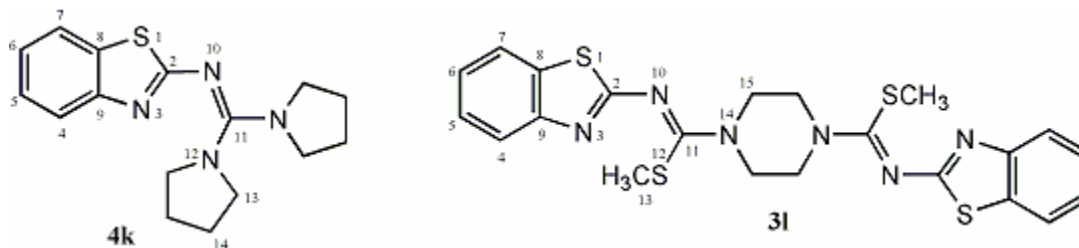


**Figure 4.** Molecular structure of compound **3j** (left) and supramolecular arrangement (right) in b axis direction.

An intramolecular hydrogen bonding interaction between one hydrogen atom of the amine group and the thiazole nitrogen atom to form a six membered ring was observed. The N14H14...N3 distance of 2.11 Å and the angle of 128° (2) are in the range for a strong interaction<sup>9</sup>. The formed hydrogen bond is strong enough that forces the nitrogen atom of NH<sub>2</sub> group to be in a planar delocalized  $\pi$  system between N14-C11-N10-C2-N3 atoms which adopt a U conformation. Torsion dihedral angles C11-N10-C2-N3 (0.3°) and C2-N10-C11-N14 (4.7°) are

in agreement of a full planar system. Examination of bond distances confirm a delocalized  $\pi$ -system: C2—N3 (1.305 Å), C2—N10 (1.358 Å), N10—C11 (1.316 Å) and C11—N14 (1.320 Å) which have intermediate values between a simple and a double bond [ $C(sp^2)=N(sp^2) = 1.28$  Å,  $C(sp^2)—N(sp^2) = 1.35$  Å]<sup>9</sup>. On the other hand, the supramolecular structure, figure 4 (right), is given by intermolecular hydrogen bonds between the second hydrogen atom of the amino group and the N10b of a second molecule with N12—H14...N10b distance of 2.36 Å and angle of 148°, forming a polymer. It is interesting to observe that methyl and amino groups are in a *syn* conformation, N14-C11-S12-C13 torsion angle is 13.03°(19). It is possible this conformation is adopted due to an intermolecular interaction between one hydrogen atom of methyl group and the thiazolic sulfur atom C13—H...S1b bond distance of 2.86 Å and angle of 147°.

The reaction with pyrrolidine, was carried out with one and two molar equivalents, with the aim to obtain monosubstituted and disubstituted compounds, respectively, however in both cases only guanidine compound **4k** was formed, figure 5. It seems that isothioureia intermediate **3k** is not stable enough because of the high basicity of the amine and the lack of N-H intramolecular interaction. A very similar result was obtained when piperazine was used, the reaction give in both molar relations, the diisothioureia derivative **3l**, figure 5. Both <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound **3l**, showed two signals in 3.94, 2.26 and 47.65 16.68 ppm, respectively, on the aliphatic zone, which is in agreement with the symmetry of compound **3l**.



**Figure 5.** Guanidine **4k** and diisothioureia **3l** pobtained from the reaction of dithiomethylcarboimidate benzothiazole **2** with pirrolidine and piperazine, respectively.

## Conclusions

Primary amines in contrast of the more reactive cycloalkylamines afforded isothioureia derivatives. The acidity of hydrogen atom of *o*-XH substituted anilines is determinant in the stability of the isothioureia intermediates. The formation of an intramolecular hydrogen bonding between one hydrogen atom of the amine group and the thiazole nitrogen reinforce the stability of isothioureia derivatives. Compounds **3i** and **3j** were base to assign compounds **3c-g**.

## Experimental Section

**General Procedures.** Melting points were measured on an Electrothermal IA apparatus and are uncorrected. IR spectra were recorded in a film on ZnSe using a Perkin-Elmer 16F PC IR spectrophotometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian Mercury 300 MHz ( $^1\text{H}$ , 300.08;  $^{13}\text{C}$ , 75.46 MHz). The spectra were measured with tetramethylsilane as internal reference following standard techniques. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC **3j**, (650099). For this compound, H atoms were treated as riding atoms, with C-H distances in the range of  $0.93\pm 0.06$  Å and N-H distances of 0.82 Å. X-ray diffraction cell refinement and data collection: BRUKER SMART APEX Diffractometer and SAINT<sup>10</sup>, programs used to solve structures: SHELXS-97<sup>11</sup>; software used to prepare material for publication: PLATON<sup>12</sup> and *WinGX*.<sup>13</sup>

2-Aminobenzothiazole **1** was a commercial product. Benzothiazole dithiomethylcarboimide **2** was prepared according to a literature procedure<sup>7</sup>.

### General procedure

In a 100 mL flask 1.0 g (3.94 mmol) of benzothiazole dithiomethylcarboimide **2** were dissolved with 20 mL of anhydrous ethanol, three molar equivalents of ammonia, or one molar equivalent of the respective aliphatic or aromatic amine were added and the mixture was refluxed for 16 hours in the case of **3c-e**, for 24 hours for compounds **3f,g**, and stirring at room temperature for 24 hours in the case of **3i**. The solvent was reduced to 10 ml by evaporation and cooled to room temperature, after precipitation the resulting solid was filtered and washed with a mixture 1:1 water-ethanol to give, after drying a white solid.

**S-Methyl-N-benzothiazolyl-N'-phenyl-isothiourea (3i).** White solid, 0.9 g (76.5% yield), mp = 90-91°C.  $^1\text{H}$  NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 12.4 (b, 1H, NH), 7.76 (d, 1H, H4), 7.75 (d, 1H, H7), 7.41 (t, 1H, H5), 7.38 (t, 1H, H6), 7.3-7.4 (m, 5H, N-Ph), 2.50 (s, 3H, SCH<sub>3</sub>).  $^{13}\text{C}$  NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 172.3 (s, C11), 165.0 (s, C2), 151.2 (s, C9), 137.38 (s, C15), 132.4 (s, C8), 127.7 (d, C4), 123.7 (d, C7), 121.4 (d, C5), 120.81 (d, C6), 129.5 (d, C16), 126.91 (d, C17), 127.68 (d, C18), 14.6 (q, SCH<sub>3</sub>).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 3053 (w, NH<sub>2</sub>), 1564 (s, C11=N). Elemental analysis: Calculated: %C (60.16), %H (4.38), %N (14.03); Found: %C (59.93), %H (4.39), %N (13.98).  $z/e = 299.2$  (12%)

**S-Methyl-N-benzothiazolyl-isothiourea (3j).** White solid, 0.63 g (71.7% yield), mp = 160 °C.  $^1\text{H}$  NMR [ $\delta$ , ppm, DMSO- $d_6$ ]: 9.27 (b, 2H, NH<sub>2</sub>), 7.83 (d, 1H, H4), 7.66 (d, 1H, H7), 7.36 (t, 1H, H5), 7.22 (t, 1H, H6), 2.43 (s, 3H, SCH<sub>3</sub>).  $^{13}\text{C}$  NMR [ $\delta$ , ppm, DMSO- $d_6$ ]: 172.0 (s, C11), 166.0 (s, C2), 152.0 (s, C9), 132.0 (s, C8), 127.0 (d, C4), 124.0 (d, C7), 122.0 (d, C5), 121.0 (d, C6), 13.8 (q, SCH<sub>3</sub>).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 3200 (w, NH<sub>2</sub>), 1549 (vs, C11=N). Elemental analysis: Calculated: %C (48.40), %H (4.07), %N (18.81); Found: %C (48.57), %H (4.08), %N (18.89).  $z/e = 238.15$  (31%). Crystal data and data collections parameters of **3j**: chem. formula C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>S<sub>2</sub>; formula weight 223.3; crystal system orthorhombic; space group Pbc<sub>a</sub>; cell axes (Å)

11.9075(10), 10.2294(9), 16.2927(14); cell angles (deg) 90.000(0), 90.000(0), 90.000(0); cell volume ( $\text{\AA}^3$ ) 1984.56(3); no. form. units (*Z*) 8; density ( $\text{g/cm}^3$ ) 1.49; abs. coeff. ( $\text{mm}^{-1}$ ) 0.497; *F*(000) 927.8; index range  $-14 < h > 14$ ,  $-12 < k > 12$ ,  $-19 < l > 19$ ; refl. collected 17592; refl. unique 1744; refl. observed 1591; *R* merge 0.030; *R*<sub>all</sub> 0.038; *R*<sub>obs</sub> 0.035; *GOOF* 1.089; *wR2*<sub>all</sub> 0.093; *wR2*<sub>obs</sub> 0.091;  $\Delta\rho$  ( $\text{e \AA}^{-3}$ ) max., 0.319, min. -0.196.

**S-Methyl-*N*-benzothiazolyl-*N'*-*o*-aminophenyl-isothiourea (3c).** White solid, 0.82 g (66.2% yield), mp = 290°C (dec.). <sup>1</sup>H NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 11.9 (b, 1H, NH), 7.70 (d, 1H, H4), 7.65 (d, 1H, H7), 7.35 (t, 1H, H5), 7.22 (t, 1H, H6), 4.0 (b, 2H, NH<sub>2</sub>), 2.46 (s, 3H, SCH<sub>3</sub>), 7.16-7.22 (m, 4H, Ph). <sup>13</sup>C NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 172.35 (C11), 166.9 (s, C2), 151.16 (s, C9), 143.61 (s, C15), 132.4 (s, C8), 129.9 (d, C4), 129.7 (d, C20), 126.0 (s, C16), 123.7 (d, C7), 122.58 (d, C17), 121.37 (d, C5), 120.84 (d, C6), 118.77, (d, C19), 116.3 (d, C18), 14.5 (q, SCH<sub>3</sub>).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 3386 (w, NH), 3300 (b, NH<sub>2</sub>), 1565 (vs, C11=N). Elemental analysis: Calculated: %C (57.29), %H (4.50), %N (17.82); Found: %C (57.07), %H (4.52), %N (17.75). *z/e* = 314.2 (4%)

**S-Methyl-*N*-benzothiazolyl-*N'*-*m*-aminophenyl-isothiourea (3d).** White solid, 0.82 g (66.2% yield), mp = 157-158 °C. <sup>1</sup>H NMR [ $\delta$ , ppm,  $\text{DMSO-d}_6$ ]: 11.8 (b, 1H, NH), 7.82 (d, 1H, H4), 7.71 (d, 1H, H7), 7.36 (t, 1H, H5), 7.25 (t, 1H, H6), 7.22-6.6 (m, 4H, Ph) 4.7 (b, 2H, NH<sub>2</sub>), 2.43 (s, 3H, SCH<sub>3</sub>). <sup>13</sup>C NMR [ $\delta$ , ppm,  $\text{DMSO-d}_6$ ]: 171.8 (s, C11), 166.72 (s, C2), 151.25 (s, C9), 147.52 (s, C15), 132.21 (s, C8), 129.7 (d, C20), 128.5 (d, C4), 123.95 (d, C7), 121.82 (d, C5), 120.93 (d, C6), 127 (s, C17), 122.6 (d, C16), 118.77 (d, C19), 116.3 (d, C18), 14.53 (q, SCH<sub>3</sub>).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 3412 (w, NH), 3320 (b, NH<sub>2</sub>), 1566 (vs, C11=N). Elemental analysis: Calculated: %C (57.29), %H (4.50), %N (17.82); Found: %C (57.47), %H (4.49), %N (17.78). *z/e* = 314.2 (17%)

**S-Methyl-*N*-benzothiazolyl-*N'*-*p*-aminophenyl-isothiourea (3e).** White solid, 0.82 g (66.2% yield), mp = 146-147°C. <sup>1</sup>H NMR [ $\delta$ , ppm,  $\text{DMSO-d}_6$ ]: 11.67 (b, 1H, NH), 7.87 (d, 1H, H4), 7.73 (d, 1H, H7), 7.38 (t, 1H, H5), 7.26 (t, 1H, H6), (7.1, d, 2H and 6.6, d, 2H, Ph), 5.3 (b, 2H, NH<sub>2</sub>) 2.40 (s, 3H, SCH<sub>3</sub>). <sup>13</sup>C NMR [ $\delta$ , ppm,  $\text{DMSO-d}_6$ ]: 171.80 (s, C11), 166.51 (s, C2), 151.35 (s, C9), 149.32 (s, C15), 132.02 (s, C8), 128.63 (d, C16), 126.64 (d, C4), 124.98 (s, C18), 124.20 (d, C5), 122.10 (d, C6), 121.07 (d, C7), 114.46 (d, C17), 14.59 (q, SCH<sub>3</sub>).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 3423 (w, NH), 3332 (b, NH<sub>2</sub>), 1566 (vs, C11=N). Elemental analysis: Calculated: %C (57.29), %H (4.50), %N (17.82); Found: %C (57.12), %H (4.51), %N (17.89). *z/e* = 314.2 (18%)

**S-Methyl-*N*-benzothiazolyl-*N'*-*m*-aminophenyl-bis-isothiourea (3f).** White solid, 0.82 g (66.2% yield), mp = 218-219 °C. <sup>1</sup>H NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 12.41 (b, 1H, NH), 7.64 (d, 1H, H4), 7.60 (d, 1H, H7), 7.34 (t, 1H, H5), 7.21 (t, 1H, H6), 7.14-7.29 (m, 4H, Ph), 2.54 (s, 3H, SCH<sub>3</sub>). <sup>13</sup>C NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 172.10 (s, C11), 164.43 (s, C2), 151.01 (s, C9), 138.27 (s, C15), 132.35 (s, C8), 130.10 (d, C16), 126.023 (d, C17), 125.18 (d, C4), 124.30 (d, C18), 123.78 (d, C7), 121.37 (d, C5), 120.86 (d, C6), 14.60 (q, SCH<sub>3</sub>).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 1571 (vs, C11=N). Elemental analysis: Calculated: %C (55.35), %H (3.88), %N (16.14); Found: %C (55.49), %H (3.89), %N (16.20). *z/e* = 520.1 (13%)

**S-Methyl-*N*-benzothiazolyl-*N'*-*p*-aminophenyl-bis-isothiourea (3g).** White solid, 0.82 g (66.2% yield), mp = 232-233 °C. <sup>1</sup>H NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 12.51 (b, 1H, NH), 7.74 (d, 1H, H4), 7.71 (d, 1H, H7), 7.38 (t, 1H, H5), 7.26 (t, 1H, H6), 2.53 (s, 3H, SCH<sub>3</sub>), 7.44 (s, 4H, Ph).



$^{13}\text{C}$  NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 172.10 (s, C11), 164.56 (s, C2), 151.03 (s, C9), 136.29 (s, C15), 132.35 (s, C8), 127.46 (d, C16), 126.05 (d, C4), 123.80 (d, C5), 121.39 (d, C6), 120.82 (d, C7), 14.55 (q,  $\text{SCH}_3$ ).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 1571 (vs, C11=N). Elemental analysis: Calculated: %C (55.35), %H (3.88), %N (16.14); Found: %C (55.43), %H (3.87), %N (16.08).  $z/e = 520.1$  (7%)

**S-Methyl-N-benzothiazolyl-N'-1,4-piperazine-bis-isothiourea (3I)**. White solid 0.82 g (66.2% yield), mp = 211-212°C.  $^1\text{H}$  NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 7.76 (d, 1H, H4), 7.68 (d, 1H, H7), 7.35 (t, 1H, H5), 7.20 (t, 1H, H6), 3.94 (s, 4H, C-N), 2.26 (s, 3H,  $\text{SCH}_3$ ).  $^{13}\text{C}$  NMR [ $\delta$ , ppm,  $\text{CDCl}_3$ ]: 168.43 (s, C11), 162.57 (s, C2), 151.97 (s, C9), 134.33 (s, C8), 126.05 (d, C4), 125.92 (d, C7), 123.33 (d, C5), 121.32 (d, C6), 47.65 (s, C15), 16.68 (q,  $\text{SCH}_3$ ).  $\nu_{\text{IR}}$  ( $\text{cm}^{-1}$ , film): 1525 (s, C11=N). Elemental analysis: Calculated: %C (53.41), %H (3.67), %N (16.99); Found: %C (53.22), %H (3.68), %N (16.93).  $z/e = 494.7$  (13%).

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