

Short Note

# 1-[*N*-Methyl-*N*-(Phenyl)amino]-3-(4-Methylphenyl)-Thiourea

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Received: 20 February 2019; Accepted: 8 March 2019; Published: 11 March 2019

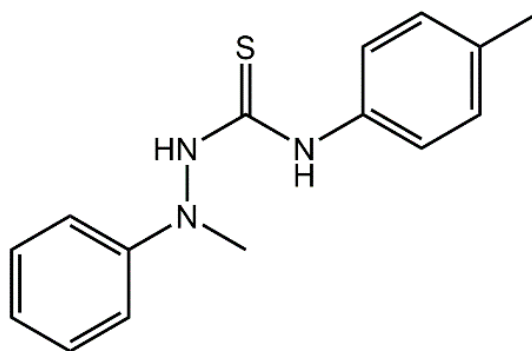


**Abstract:** The title compound, 1-[*N*-methyl-*N*-(phenyl)amino]-3-(4-methylphenyl)thiourea (**1**), was synthesized by the reaction of 1-methyl-1-phenyl hydrazine and 4-tolyl isothiocyanate, and was characterized by spectroscopy ( $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR, IR, and UV), elemental analysis as well as by single crystal X-ray crystallography. In the solid state, the molecule exists as the thioamide tautomer and features an anti-disposition of the thioamide-*N*-H atoms; an intramolecular *N*-H  $\cdots$  *N* hydrogen bond is noted. The molecular conformation resembles that of the letter L. In the molecular packing, thioamide-*N*1-H  $\cdots$  S1(thione) hydrogen bonds lead to centrosymmetric eight-membered  $\{\cdots\text{HNCS}\}_2$  synthons. The dimers are assembled into a supramolecular layer in the *bc*-plane by phenyl- and methyl-C-H  $\cdots$   $\pi$ (phenyl) interactions.

**Keywords:** thiourea; hydrogen bonding; X-ray crystallography

## 1. Introduction

Thiourea,  $\text{H}_2\text{NC}(=\text{S})\text{NH}_2$ , is susceptible for to up to four substitutions to give a wide range of compounds,  $\text{R}^1(\text{R}^2)\text{NC}(=\text{S})\text{N}(\text{R}^3)\text{R}^4$  for  $\text{R}^{1-4} = \text{alkyl/aryl}$  [1]. These molecules can possess interesting properties and are well known for their ability to complex metal ions [1]. Recent interest in thiourea derivatives revolves around their applications in dual hydrogen bonding catalysis for asymmetric synthesis [2,3] and for their potential biological potency [4], including when complexing metals [5]. Indeed, the original interest in the title compound 1-[*N*-methyl-*N*-(phenyl)amino]-3-(4-methylphenyl)thiourea (**1**), Scheme 1, related to the investigation of antiviral activity [6]; since then there have been no other reports of (**1**) in the literature. Herein, the synthesis, spectroscopic characterization, and X-ray crystal structure determination of the title compound, (**1**), are described.

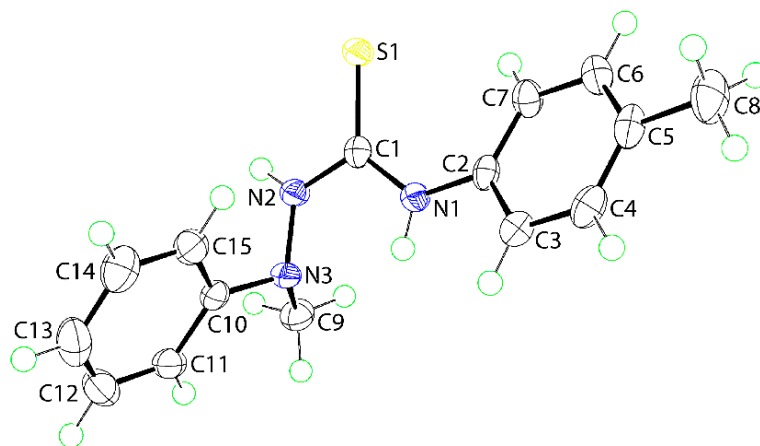


**Scheme 1.** Chemical diagram for 1-[*N*-methyl-*N*-(phenyl)amino]-3-(4-methylphenyl)thiourea (**1**).

## 2. Results and Discussion

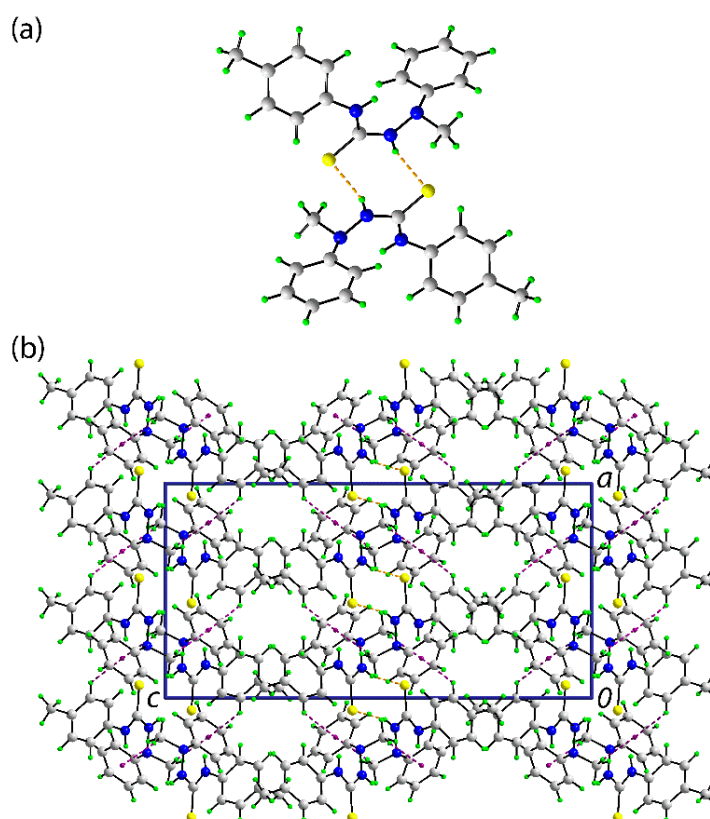
The reaction of 1-methyl-1-phenylhydrazine and 4-tolyl isothiocyanate yielded the title compound (**1**) in good yield (71%). The compound was characterized by spectroscopy; see the Supplementary Materials for original spectra. The  $^1\text{H}$  spectrum showed the expected resonances and integration. The downfield shift for the NH proton proximate to the C=S and N(Me)Ph groups cf. NH(4-tolyl) is ascribed to the proximity to the nitrogen bound lone pair of electrons. The most prominent feature of the  $^{13}\text{C}\{^1\text{H}\}$  spectrum was the downfield resonance at  $\delta$  180.2 ascribed to  $\text{N}_2\text{C}(=\text{S})$ . In the IR spectrum, characteristic bands of  $\nu(\text{N-H})$  [3266 (m)],  $\nu(\text{C-N})$  [1485 (vs)], and  $\nu(\text{C=S})$  [1256 (vs)] were observed. In the UV spectrum, two bands were observed at  $\lambda_{\text{abs}}$  242 nm and 267 nm and are ascribed to  $\pi$ - $\pi^*$  and  $n$ - $\pi^*$  transitions, respectively.

The molecular structure of (**1**) was also determined by X-ray crystallographic methods and is shown in Figure 1. The five atoms of the central chromophore, that is, S1, C1, and N1–N3, are effectively co-planar as evidenced in the root mean square deviation of 0.0223 Å; the maximum deviation from the least-squares plane was 0.0337(8) Å for the N2 atom. The appended C2–tolyl and C10–phenyl rings form dihedral angles of 25.42(6) and 81.18(3)° with the central residue, respectively, indicating skewed and orthogonal relationships. The dihedral angle between the terminal rings is 74.05(4)° which suggests that, to a first approximation, the molecule has the shape of the letter L. The C1–N1, N2 bond lengths are similar [1.3491(16) cf. 1.3458(16) Å] but, the S1–C1–N1 angle [127.50(10)°] is significantly wider than the S1–C1–N2 angle [117.36(9)°], presumably to minimize steric repulsion. The thioamide–NH atoms adopt an anti-disposition. An intramolecular thioamide–N1–H $\cdots$ N3 hydrogen bond is noted [N1–H1n $\cdots$ N3: H1n $\cdots$ N3 = 2.200(14) Å, N1 $\cdots$ N3 = 2.6684(15) Å with angle at H1n = 113.5(11)°] that closes an S(5) loop.



**Figure 1.** The molecular structure of (**1**) showing atom labeling and displacement ellipsoids at the 70% probability level. Selected geometric parameters: C1–S1 = 1.6895(13) Å, N2–N3 = 1.4081(15) Å, C1–N1 = 1.3491(16) Å, and C1–N2 = 1.3458(16) Å; C1–N1–C2 = 129.77(11)°, C1–N2–N3 = 122.11(11)°, S1–C1–N1 = 127.50(10)°, S1–C1–N2 = 117.36(9)°, and N1–C1–N2 = 115.14(11)°.

In the crystal of (**1**), the most prominent feature of the molecular packing is the formation of thioamide–N1–H $\cdots$ S1(thione) hydrogen bonds. These lead to the formation of a supramolecular dimer via a centrosymmetric, eight-membered  $\{\cdots\text{HNCS}\}_2$  synthon, as shown in Figure 2a; geometric details characterizing intermolecular interactions discussed herein are given in the figure caption. The connections between the dimers are of the type phenyl- and methyl–C–H $\cdots$  $\pi$ (phenyl) whereby the C10–C15 phenyl ring effectively functions as a bridge between the dimers. The result is a supramolecular layer in the *bc*-plane. Layers stack along the *a*-axis with no directional interactions between them. A view of the unit cell contents is shown in Figure 2b.



**Figure 2.** The molecular packing in the crystal of (1): (a) a view of the supramolecular dimer sustained by thioamide–N–H···S(thione) hydrogen bonding [ $N2-H2n \cdots S1^i$ :  $H2n \cdots S1^i = 2.474(14)$  Å,  $N2 \cdots S1^i = 3.3155(12)$  Å, angle at  $H1n = 161.2(12)^\circ$  for symmetry operation  $i: 1 - x, 1 - y, 1 - z$ ] shown as orange dashed lines and (b) a view of the unit cell contents shown in projection down the  $b$ -axis. The phenyl- and methyl–C–H··· $\pi$ (phenyl) interactions [ $C6-H6 \cdots Cg(C10-C15)^{ii}$ :  $H6 \cdots Cg(C10-C15)^{ii} = 2.77$  Å,  $C9 \cdots Cg(C10-C15)^{ii} = 3.6338(15)$  Å with angle at  $H6 = 137^\circ$ , and  $C9-H9c \cdots Cg(C10-C15)^{ii}$ :  $H9c \cdots Cg(C10-C15)^{ii} = 2.72$  Å,  $C9 \cdots Cg(C10-C15)^{ii} = 3.5286(15)$  Å, angle at  $H9c = 156^\circ$  for symmetry operations  $ii: \frac{1}{2} - x, \frac{1}{2} + y, z$  and  $iii: -\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$ ] are shown as purple dashed lines.

There is a closely related structure in the literature where the N-bound phenyl group of (1) is substituted by a methyl group and the original 4-tolyl ring is now a phenyl ring, that is,  $Me_2NN(H)C(=S)N(H)Ph$  (2) [7]. Molecule (2) adopts essentially the same conformation as just described for (1) but, some systematic changes in the key bond lengths are evident. Thus, while the  $C1=S1$  [ $1.6813(18)$  Å] bond length in (2) is experimentally equivalent to that in (1), the  $C1-N1$  [ $1.330(2)$  Å] and  $C1-N2$  [ $1.330(3)$  Å] bond lengths in (2) are shorter. The reduction in the specified bond lengths is consistent with there being reduced delocalization of  $\pi$ -electron density over the ring as a result of replacing phenyl in (1) with electron donating methyl in (2), and 4-tolyl with electron-withdrawing phenyl. The molecular packing of (2) features the same eight-membered  $\{\cdots HNCS\}_2$  synthon seen in the crystal of (1).

In conclusion, an X-ray crystallographic analysis on (1) confirms the molecule to exist as the thioamide tautomer, to have an anti-disposition of the thioamide–N–H atoms and an intramolecular  $N1-H \cdots N3$  hydrogen bond. Overall, the conformation of the molecule resembles that of the letter L. The presence of thioamide–N–H···S(thione) hydrogen bonds in the molecular packing leads to the formation of eight-membered  $\{\cdots HNCS\}_2$  synthons.

### 3. Materials and Methods

#### 3.1. General Information

All standard chemicals and solvents were sourced from Merck (Darmstadt, Germany) and used without further purification. The melting point was determined on a Biobase automatic melting point apparatus MP450 (Biobase Group, Jinan, Shandong Province, China). The IR spectrum was measured on a Bruker Vertex 70v FTIR (Billerica, MA, USA) spectrophotometer from 4000 to 80  $\text{cm}^{-1}$ . Elemental analyses were performed on a Leco TruSpec Micro CHN Elemental Analyzer (Saint Joseph, MI, USA).  $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra were recorded in  $\text{CDCl}_3$  solution on a Bruker Ascend 400 MHz NMR (Billerica, MA, USA) spectrometer with chemical shifts relative to tetramethylsilane. The optical absorption spectra were obtained from an acetonitrile solution of  $1 \times 10^{-5}$  M in the range 200–800 nm on a Shimadzu UV-3600 plus UV/VIS/NIR (Shimadzu Corporation, Kyoto, Japan) spectrophotometer.

#### 3.2. Synthesis and Characterization of (1)

1-Methyl-1-phenylhydrazine (0.01 mol, 1.18 mL) was added dropwise to 4-tolyl isothiocyanate (0.01 mol, 1.49 g) in acetone (15 mL). The resulting mixture was stirred for 2 h and then left for slow evaporation under ambient conditions. The solid obtained was recrystallized in the solvent mixture 1:1 *v/v* chloroform/acetonitrile. Colorless crystals were formed after two weeks. Yield: 1.93 g, 71%. M. pt: 159.5–161.7 °C; Lit. 165 °C [6]. Anal. Calc. for  $\text{C}_{15}\text{H}_{17}\text{N}_3\text{S}$ : C, 66.39; H, 6.31; N, 15.48%. Found: C, 66.34; H, 6.26; N, 15.35%. IR ( $\text{cm}^{-1}$ ): 3266 (m)  $\nu(\text{N-H})$ , 3138 (m)  $\nu(\text{C-H})$ , 1485 (vs)  $\nu(\text{C-N})$ , 1256 (vs)  $\nu(\text{C=S})$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  8.78 (s, br, 1H, Ph-NH), 7.69 (s, br, 1H, N-NH), 7.41 (d, 2H,  $\text{C}_6\text{H}_4$ -3,  $^3J_{\text{HH}} = 8.26$  Hz), 7.36–7.32 (m, 2H,  $\text{C}_6\text{H}_5$ -3), 7.15 (d, 2H,  $\text{C}_6\text{H}_4$ -2,  $^3J_{\text{HH}} = 8.13$  Hz), 7.05–7.00 (m, 3H,  $\text{C}_6\text{H}_5$ -2,4), 3.21 (s, 3H, NCH<sub>3</sub>), 2.32 (s, 3H, aryl-CH<sub>3</sub>).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  180.2 (Cq), 148.9 ( $\text{C}_6\text{H}_5$ , C1), 136.1 ( $\text{C}_6\text{H}_4$ , C1), 135.0 ( $\text{C}_6\text{H}_4$ , C4), 129.5 ( $\text{C}_6\text{H}_4$ , C3, C5), 129.3 ( $\text{C}_6\text{H}_4$ , C2, C6), 124.7 ( $\text{C}_6\text{H}_5$ , C3, C5), 122.4 ( $\text{C}_6\text{H}_5$ , C4), 114.8 ( $\text{C}_6\text{H}_5$ , C2, C6), 41.8 (NCH<sub>3</sub>), 21.0 ( $\text{C}_6\text{H}_4$ -CH<sub>3</sub>). UV (acetonitrile; nm,  $\text{L}\cdot\text{cm}^{-1}\cdot\text{mol}^{-1}$ ):  $\lambda_{\text{abs}} = 267$ ,  $\epsilon = 26,700$ ;  $\lambda_{\text{abs}} = 242$ ,  $\epsilon = 22,500$ .

#### 3.3. Crystallography

Intensity data for (1) were measured at  $T = 100(2)$  K on a XtaLAB Synergy Dual AtlasS2 (Rigaku Polska SP. Z O O, Wrocław, Poland) diffractometer fitted with Cu  $K\alpha$  radiation ( $\lambda = 1.54184$  Å) using  $\omega$ -scans in the  $\theta_{\text{max}}$  range 3.8°–67.1°. Data reduction, including absorption correction, was accomplished with CrysAlis Pro [8]. Of the 18,012 reflections measured, 2550 were unique ( $R_{\text{int}} = 0.030$ ), and of these, 2356 data satisfied the  $I \geq 2\sigma(I)$  criterion of observability. The structure was solved by direct methods [9] and refined (anisotropic displacement parameters and C-bound H atoms in the riding model approximation) on  $F^2$  [10]. The thioamide-N-H atoms were located from a difference map and refined with a N-H restraint of  $0.88 \pm 0.01$  Å. A weighting scheme of the form  $w = 1/[\sigma^2(F_o^2) + (0.039P)^2 + 1.297P]$  was introduced, where  $P = (F_o^2 + 2F_c^2)/3$ . Based on the refinement of 180 parameters, the final values of  $R$  and  $wR$  (all data) were 0.028 and 0.077, respectively. The molecular structure diagram was generated with ORTEP for Windows [11] and the packing diagram using DIAMOND [12].

Crystal data for  $\text{C}_{15}\text{H}_{17}\text{N}_3\text{S}$  (1):  $M = 271.38$ , orthorhombic,  $Pbca$ ,  $a = 10.50030(10)$  Å,  $b = 11.70230(10)$  Å,  $c = 23.2486(3)$  Å,  $V = 2856.73(5)$  Å<sup>3</sup>,  $Z = 8$ ,  $D_x = 1.262$  g  $\text{cm}^{-3}$ ,  $F(000) = 1152$  and  $\mu = 1.918$  mm<sup>-1</sup>. CCDC deposition number: 1898244.

**Supplementary Materials:** The following are available online:  $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR, IR, and UV spectra, and crystallographic data for (1) in crystallographic information file (CIF) format. CCDC 1898244 also contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>.

**Author Contributions:** Synthesis and spectroscopic characterization was carried out by C.I.Y. X-ray crystallography was performed by E.R.T.T. The manuscript was written by C.I.Y. and E.R.T.T.

**Funding:** This research received no external funding. The APC was funded by Sunway University.

**Acknowledgments:** Sunway University Sdn Bhd is thanked for financial support of this work. The X-ray crystallography laboratory at Sunway University is thanked for the X-ray intensity data.

**Conflicts of Interest:** The authors declare no conflict of interest.

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**Sample Availability:** Not available.



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