The Malaysian Journal of
ANALYTICAL
SCIENCES
ISSN 1394-2506

STRUCTURAL AND SPECTROSCOPIC STUDIES OF NOVEL METHYLBENZOYLTHIOUREA DERIVATIVES

(Struktur Dan Kajian Spektroskopi Terbitan Metilbenzoilthiourea)

Rabia'tun Hidayah Jusoh[1], Wan M. Khairul [1], M. Sukeri M. Yusof[1*], Maisara Abdul Kadir[1], Bohari M.Yamin[2]

[1]*Department of Chemical Sciences,*
Faculty of Science and Technology,
Universiti Malaysia Terengganu, 21030 Kuala Terengganu, Malaysia.
[2]*School of Chemical Sciences and Food Technology,*
Faculty of Science and Technology,
Universiti Kebangsaan Malaysia, 43650 Bangi, Selangor, Malaysia.

**Corresponding author: mohdsukeri@umt.edu.my*

Abstract

Three new compounds, *N*-(2-methybenzoyl)-*N'*-(3-methyl-2-pyridyl)thiourea **(I)**, *N*-(3-methylbenzoyl)-*N'*-(6-methyl-2-pyridyl)thiourea **(II)** are isomers and *N*-(2-methylbenzoyl)-*N'*-(6-methylpyridine-2-yl)thione **(III)** have been successfully synthesised and characterised by typical spectroscopic techniques, IR, UV-Visible, ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) and CHNS analysis. The molecular structures were confirmed by single crystal X-ray diffractometer analysis. The Infrared spectra of these compounds showed four significant stretching vibrations, ν(N-H), ν(C=O), ν(C-N) and ν(C=S) at 3187-3375 cm^{-1}, 1683-1713 cm^{-1}, 1326-1384 cm^{-1} and 666-785 cm^{-1}, respectively. The UV-Visible spectra of all compounds show three bands obtained in the range of 205-287 nm, which may be due to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. In ^{13}C NMR spectra, the signal of carbon carbonyl for **(I)** and **(II)** can be observed at *ca.* δc 170 ppm. Whilst, chemical shift of the carbon thione groups for **(I)** and **(II)** appeared at *ca.* 180 ppm. Molecule **(I)**, **(II)** and **(III)** crystallise in the monoclinic crystal system with space group $P2_1/n$. Molecule **(I)** adopts *trans-cis* configuration in comparison with **II** which adopts *cis-trans* configuration of the pyridine and methylbenzoyl groups with respect to the thione S atom across the thiourea C-N bonds. However, (**III**) is planar due to cyclisation forming two five-membered rings. All molecules are stabilised by intra-molecular hydrogen bonds, N-H$\cdots$O, C-H$\cdots$N, N-H$\cdots$N and C-H$\cdots$O lead to the formation of pseudo seven-membered rings **(I)** and pseudo six-membered **(II & III)** rings. In the crystal lattice, molecule **(I)** are linked by the N-H$\cdots$O, C-H$\cdots$S and N-H$\cdots$S **(II)** inter-molecular hydrogen bonds, whilst for **(III)**, there are no inter-molecular hydrogen bond was observed.

Keywords: Methylbenzoylthiourea, carbonylthiourea, thiourea, spectroscopic studies

Abstrak

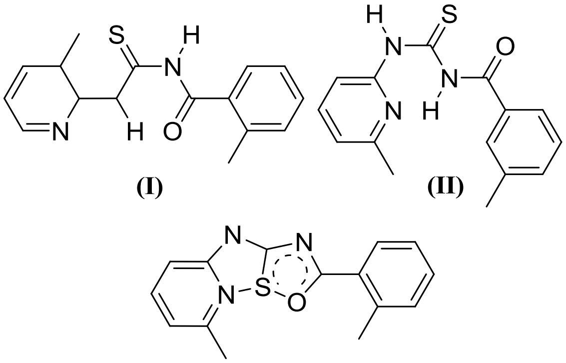
Sebanyak tiga sebatian baru, *N*-(2-metilbenzoil)-*N'*-(3-metil-2-piridil)tiourea **(I)**, *N*-(3-metilbenzoil)-*N'*-(6-metil-2-piridil)tiourea **(II)** dan *N*-(2-metilbenzoil)-*N'*-(6-metilpiridin-2-il)tiourea **(II)** telah berjaya disintesis dan dicirikan dengan teknik spektroskopi iaitu spektroskopi infra merah (IR), ultralembayung (UV-Vis), ^{1}H dan ^{13}C resonans magnet nukleus (NMR) dan analisis unsur CHNS. Struktur hablur yang diperolehi dikaji dengan kristalografi sinar-X hablur tunggal. Analisis IR menunjukkan kehadiran empat puncak utama serapan, iaitu ν(N-H), ν(C=O), ν(C-N) and ν(C=S) masing-masing berada pada julat 3187-3375 cm^{-1}, 1683-1713 cm^{-1}, 1326-1384 cm^{-1} dan 666-785 cm^{-1}. Analisis spektroskopi ultralembayung bagi kesemua sebatian mempunyai tiga puncak maksimum pada panjang gelombang 205-287 nm disebabkan pencampuran peralihan elektronik $n \rightarrow \pi^*$ dan $\pi \rightarrow \pi^*$. Dalam spektra ^{13}C NMR, kehadiran isyarat bagi karbon karbonil **(I)** dan **(II)** dapat diperhatikan pada sekitar δ_H 170 ppm. Manakala, anjakan kimia pada sekitar 180 ppm adalah menunjukkan kehadiran karbon tion. Molekul **(I)**, **(II)** dan **(III)** mempunyai sistem hablur monoklinik dan kumpulan ruang $P2_1/n$. Molekul **(I)** mempunyai konfigurasi *trans-cis* berbanding molekul **(II)** yang mempunyai *cis-trans* merujuk kepada kedudukan kumpulan piridina dan metilbenzoil terhadap kumpulan tion, S pada paksi C-N masing-masing. Namun begitu, molekul **(III)** adalah planar disebabkan pensiklikan dua gelang lima ahli. Kesemua molekul ini distabilkan oleh ikatan hidrogen intermolekul N-H$\cdots$O, C-H$\cdots$N, N-H$\cdots$N dan C-H$\cdots$O yang membentuk satu gelang pseudo tujuh ahli **(I)** dan pseudo enam ahli **(II & III)**. Dalam kekisi hablur, molekul **(I)** distabilkan oleh ikatan hidrogen inter-molekul N-H$\cdots$O, C-H$\cdots$S dan N-H$\cdots$S **(II)**, manakala, molekul **(III)** tidak mempunyai ikatan hidrogen inter-molekul.

Kata kunci: Metilbenzoiltiourea, karboniltiourea , tiourea , kajian spektroskopi

Introduction

Since it was synthesised and found by Nencki in 1873 [1], there has been a great interest on thiourea derivatives as a versatile ligand and have been used in numerous applications such as in agriculture, pharmaceutical, materials and catalysis [2-10]. In addition, there a lot of current studies discussing on the ability of these derivatives which are able to possess antitumor [11] antimalarial and anticancer [12], anti-Hiv [13] as well as antituberculosis properties [14]. Many researchers also propose that thiourea derivatives show promising potential in laser technology, optical communication and optical data storage owing to their non-linear properties and ease of coordination with metals [5, 15-16]. In the environmental aspect, thiourea also can act as an organic reagent to identify Cu^{2+} in aqueous solution to control pollution especially in industrial waste [17]. Domínguez *et al.*, (2002) have recently synthesised *N*-benzoyl-*N',N'*-diethylthiourea which have great potential interest to be used as a highly selective reagent for the liquid-liquid extraction of metal cations namely palladium(II) and gold(III) [18].

In this contribution, three new types of N^1N^2-diarylthioureas have been prepared with *o*,*m*-methyl substitution to the aromatic rings at N^1 and 3-methyl and 6-methyl pyridine substituents at N^2 as shown in Figure 1. Their solid state properties were fully investigated by typical spectroscopic methods to give wide electronic variations and the structures were confirmed with X-ray diffraction. The isomers molecular conformations of **(I)** and **(II)** can be found in *trans-cis* and *cis-trans* which depend on their position –NHCSNH- grouping. As shown in Figure 1, **(III)** underwent cyclisation that have some partial double bond characters of the C-N due to delocalisation of the nitrogen lone pair electron to the C=S and C=O groups.



(I) **(II)**

(III)

Figure 1: The molecular structures of *N*-(2-methybenzoyl)-*N'*-(3-methyl-2-pyridyl)thiourea **(I)**, *N*-(3-methylbenzoyl)-*N'*-(6-methyl-2-pyridyl)thiourea **(II)** and *N*-(2-methylbenzoyl)-*N'*-(6-methyl pyridine-2-yl)thione **(III)**.

Experimental

All reactions were carried out under an ambient atmosphere and no special precautions were taken to exclude air or moisture during work-up. All chemicals were purchased from Sigma Aldrich, E. Merck and Fluka and used as received. Infrared spectra of the synthesised compounds were recorded from KBr pellets using FTIR Perkin Elmer 100 Spectrophotometer in the spectral range of 4000 cm^{-1} to 400 cm^{-1}. The absorption spectra were recorded in cells of quartz 1 cm using a Shimadzu UV-Vis spectrophotometer 1601 series. All compounds were dissolved in pure methanol with concentration in the range of 10^{-5} M. The spectra of methylbenzoylthiourea derivatives were recorded at wavelength of 200 nm to 400 nm where there were two distinctive chromophores can be identified.

While the ^{1}H 400.11 MHz and ^{13}C 100.61 MHz NMR spectra were recorded using Bruker Avance III 400 Spectrometer in DMSO-d$_6$ as solvent at room temperature in the range between δ_H 0-15 ppm and δ_C 0-200 ppm. In the experiment, trimethylsilyl (TMS) was used as an internal standard. Whilst for crystallographic structure determination, diffraction data were collected on a Bruker SMART APEX 4K CCD with Mo Kα (λ = 0.71073 Å) radiation.

Preparation of $(C_5H_3N)NHC(S)NHC(O)C_6H_4(Me)_2$ (I)

A solution of 2-methylbenzoyl chloride (1.5 g, 10 mmol) in acetone (25 ml) was added dropwise to ammonium thiocyanate (0.74 g, 10 mmol) in acetone (25 ml) followed by stirring at room temperature for *ca*. 10 minutes. A solution of 2-amino-3-methylpyridin (1.05 g, 10 mmol) in acetone (20 ml) was added dropwise to the stirring mixture. The reaction mixture was heated under reflux for 2 hours and the solution was filtered and cooled to room temperature. The solid product was then recrystallised by methanol to give colourless crystals of the title compound (1.77 g, 62%). IR (KBr pellets): ν(N-H) 3375 cm^{-1} s, ν(C=O) 1683 cm^{-1} s, ν(C-N) 1326 cm^{-1} m, ν(C=S) 666 cm^{-1} s. ^{1}H NMR (DMSO-d$_6$, 400.11 MHz): δ 2.32, 2.44 (2 x s, 6H, Me); 7.30-7.34 (m, 3H, C_6H_4); 7.45 (t, J_{HH} = 7 Hz, 1H, C_5H_3); 7.53 (d, J_{HH} = 8 Hz, 1H, C_6H_4); 7.76 (d, J_{HH} = 7 Hz, 1H, C_5H_3); 8.34 (d, J_{HH} = 4 Hz, 1H, C_5H_3); 11.85, 12.17 (2 x s, 1H, NH). ^{13}C NMR (DMSO-d$_6$, 100.61 MHz): δ 17.7, 19.9 (2 x s, Me); 123.5, 123.8, 126.1, 128.5, 131.1, 131.4, 134.6, 136.5, 139.9, 146.7, 150.7 (11 x s, Ar); 170.8 (s, C=O); 180.6 (s, C=S). UV-Vis (MeOH): λ_{max}, nm; (ε, L mol^{-1} cm^{-1}) 206 (92240), 237 (54140), 276 (61600).

Preparation of $(C_5H_3N)NHC(S)NHC(O)C_6H_4(Me)_2$ (II)

In a manner similar to that described above, **(II)** was obtained as yellowish crystals by recrystallisation from methanol (2.73 g, 67 %). IR (KBr pellets): ν(N-H) 3187 cm^{-1} s, ν(C=O) 1713 cm^{-1} s, ν(C-N) 1329 cm^{-1} m, ν(C=S) 785 cm^{-1} s. ^{1}H NMR (DMSO-d$_6$, 400.11 MHz): δ 2.33, 2.41 (2 x s, 6H, Me); 7.43-7.59 (m, 3H, C_6H_4); 7.79-7.81 (m, 1H, C_5H_3); 7.86 (s, 1H, C_6H_4); 7.96 (d, J_{HH} = 8 Hz, 1H, C_5H_3); 8.11 (d, J_{HH} = 8 Hz, 1H, C_5H_3); 11.79, 12.85 (2 x s, 1H, NH). ^{13}C NMR (DMSO-d$_6$, 100.61 MHz): δ 21.3, 23.9 (2 x s, Me); 125.4, 126.4, 128.4, 128.9, 129.7, 130.5, 132.3, 132.6, 134.3, 134.4, 138.4 (11 x s, Ar); 168.8 (s, C=O); 181.4 (s, C=S). UV-Vis (MeOH): λ_{max}, nm; (ε, L mol^{-1} cm^{-1}) 205 (83200), 234 (55530), 287 (43420).

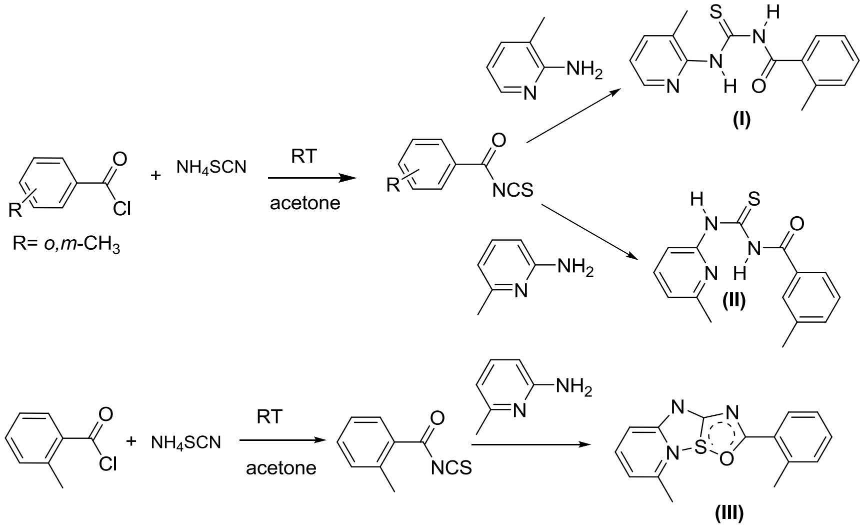
Preparation of $(C_5H_3N)NCSNCOC_6H_4(Me)_2$ (III)

In a manner similar to that described above, **(III)** was obtained as colourless crystals by recrystallisation from methanol (1.5 g mg, 48 %). IR (KBr pellets): ν(C⎓O) 1683 cm^{-1} w, ν(C⎓N) 1384 cm^{-1} s, ν(C⎓S) 735 cm^{-1} s. ^{1}H NMR (DMSO-d$_6$, 400.11 MHz): δ 2.67, 2.85 (2 x s, 6H, Me); 7.33-7.39 (m, 3H, C_5H_3); 7.49 (d, J_{HH} = 8 Hz, 1H, C_6H_4); 7.78 (d, J_{HH} = 9 Hz, 1H, C_6H_4); 8.07 (t, J_{HH}= 8 Hz, 1H, C_6H_4); 8.19 (d, J_{HH} = 8 Hz, 1H, C_6H_4). ^{13}C NMR (DMSO-d$_6$, 100.61 MHz): δ 20.6, 22.1 (2 x s, Me); 31.2 (s, C⎓O); 116.6, 117.7, 126.4, 130.9, 132.1, 132.2, 133.0, 139.3, 139.6, 146.3, 155.9 (11 x s, Ar); 179.0 (s, C⎓S). UV-Vis (MeOH): λ_{max}, nm; (ε, L mol^{-1} cm^{-1}) 205 (84530), 229 (48470), 281(43440).

Results and Discussion

Syntheses

The title compounds were prepared by methods as shown in Scheme 1, **(I)** and **(II)** were produced from the synthesis of *o,m*-methylbenzoyl chloride with 2-amino-3-methylpyridine and 2-amino-6-methylpyridine. Here, the cyclisation of **(III)** was obtained from the reaction of *o*-methylbenzoyl chloride with 2-amino-6-methylpyridine in the refluxing acetone with constant stirring (Scheme 1).



Scheme 1: The preparation of **(I)**, **(II)** and (**III).**

Infrared spectroscopy

The FTIR spectra and absorption bands data of all the synthesised compounds are shown in Figure 2 and Table 1. Infrared spectra of these compounds have been analysed in the expected frequency region of the ν(N-H), ν(C=O), ν(C-N) and ν(C=S). The IR spectra of **(I)** and **(II)** show strong absorption bands at 3375 cm^{-1} and 3187 cm^{-1} which is due to the ν(N-H) and indicate the existence of intra-molecular hydrogen bond. However, the band of ν(N-H) of **(III)** is not observed in the IR spectrum, this is probably due to the electron delocalisation has taken place between C-S and C-N fragment caused by deprotonated of hydrogen at the N atom. The strong absorption of **(I)** and **(II)** are observed at the 1683 cm^{-1} and 1713 cm^{-1}, respectively, which can be attributed to the ν(C=O). Whilst in **(III)**, it shows the ν(C=O) as a weak carbonyl-like band with the double bond character is presence at 1683 cm^{-1}. Molecule **(I)**, **(II)** and **(III)** exhibit vibration of ν(C-N) at 1326 cm^{-1}, 1329 cm^{-1} and 1384 cm^{-1}, respectively. The strong bands of **(I)** and **(II)** at 666 cm^{-1}, 785 cm^{-1} can be assigned to the stretching vibration of ν(C=S) assignable to literature [10, 19-20]. While the stretching vibration of ν(C=S) indicates some double bond character for **(III)** which clearly can be observed at 735 cm^{-1}.

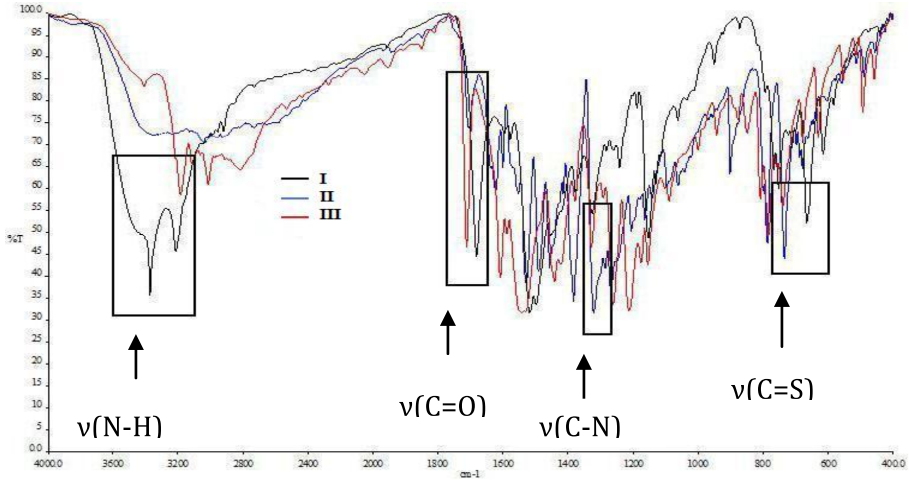


Figure 2: IR spectra of all the synthesised compounds.

Table 1: Infrared absorption bands for molecule **(I)**, **(II)** and **(III)**.

Molecule/ cm^{-1}	ν (N-H)	ν (C=O) ν (C$\underset{---}{-}$O)*	ν (C-N) ν (C$\underset{---}{-}$N)*	ν C=S ν (C$\underset{---}{-}$S)*
I	3375 s	1683 s	1326 m	666 s
II	3187 s	1713 s	1329 m	785 s
III	-	1683 w*	1384 s*	735 s*

s strong, m medium, w weak
*indicates the partial double bond

UV-Vis spectroscopy
All the absorption bands of these compounds are shown in Figure 3 and Table 2. The electronic absorption spectra of the ligands **(I)**, **(II)** and **(III)** showed three absorption peaks and were recorded in methanol (10^{-5} M). These spectra have three distinctive bands that is due to a mixture of n→π* and π→π* transitions. The absorption bands at 205-237 nm (ε = 48470 to 92240 M^{-1} cm^{-1}) can be assigned to π→π* transition of the aromatic systems. However, the band observed in the range of 205 to 237 nm is due to perturbation of solvent and overlapping of carbonyl's compounds chromophores in these compounds. These compounds exhibit broad band in the range 229-237 nm (ε = 48470 to 54140 M^{-1} cm^{-1}) and 276-287 nm (ε = 43420 to 61600 M^{-1} cm^{-1}) which can be assigned to n→π* and π→π* transitions which arise from the lone pair of electrons on the oxygen and sulphur of C=O and C=S. The introduction of auxochromes methyl substituent groups at the *o* and *m*- position and the electron conjugated π bond in phenyl ring and NH groups produces bathochromic shift in the spectra.

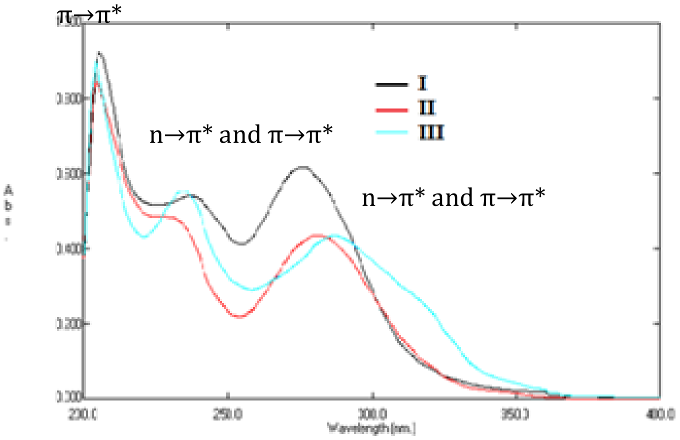


Figure 3: The UV spectra of the **(I)**, **(II)** and **(III)**.

Table 2. The principal UV absorption bands observed for **(I)**, **(II)** and **(III)**.

Compounds No.	Absorption λ / nm (Extinction Coefficient ε / M^{-1} cm^{-1})				
	Peak 1	Assignment	Peak 2	Peak 3	Assignments
(1)	206 (92240)	π→π*	237 (54140)	276 (61600)	Mixed n→π*, π→π*
(II)	205 (83200)	π→π*	234 (55530)	287 (43420)	Mixed n→π*, π→π*
(III)	205 (84530)	π→π*	229* (48470)	281* (43440)	Mixed n→π*, π→π*

*indicates the partial double bond

NMR spectroscopy

The NMR spectroscopic data of all the synthesised compounds are shown in Table 3. The ^{1}H NMR spectra of compounds **(I)**, **(II)** and **(III)** showed the expected methyl resonance between δ_H 2.32-2.85 ppm. In addition, the overlapping unresolved signal of the aromatic protons of **(I)**, **(II)** and **(III)** can be observed as distinctive multiple resonances between δ_H 7.30-8.34 ppm. These characteristic resonances are strongly influenced by the *o* and *m*-substituents positions of methyl groups at the phenyl and pyridine rings. Compounds **(I)** and **(II)** showed the presence of the *N*(2)H at δ_H 11.85 ppm and 11.79 ppm. For *N*(1)H attached to the methylbenzoyl substituents, the resonance can be seen at δ_H 12.17 ppm and δ_H 12.85 ppm. Surprisingly, there is no expected N-H signal observed for **(III)** which are due to the electrons are localised over the C-N moiety. In ^{13}C NMR spectra, the methyl resonance can be observed between δ_C 17.7-23.9 ppm. Meanwhile the aromatic carbon resonances can be found between δ_C 116.5-155.9 ppm which are corresponding to phenyl rings in the compounds. In addition, one resonance is observed at between δ_C 168.8-170.8 ppm and in between δ_C 180.6-181.4 ppm which is due to the carbon of C=O and C=S for **(I)** and **(II)**. Whilst, in the case of **(III)** which showed the partial double bond character C=O and C=S, the resonances can be found at *ca.* δ_C 31 ppm and δ_C 179.0 ppm which due to its high delocalisation on the cyclisation formed in the molecule.

Table 3: Selected NMR spectroscopic data for the compounds.

Compounds No.	^{1}H NMR/ δ_H (ppm)	^{13}C NMR/ δ_C (ppm)
(I)	2.32, 2.44 (2 x s, 6H, Me), 7.30-7.34 (m, 3H, C_6H_4), 7.45 (t, J_{HH} = 7 Hz, 1H, C_5H_3), 7.53 (d, J_{HH} = 8 Hz, 1H,C_6H_4), 7.76 (d, J_{HH} = 7 Hz,1H,C_5H_3), 8.34 (d, J_{HH} = 4 Hz,1H,C_5H_3),11.85, 12.17 (2 x s, 1H, NH)	17.7, 19.9 (2 x s, Me), 123.5, 123.8, 126.1, 128.5, 131.1, 131.4, 134.6, 136.5, 139.9, 146.7, 150.7 (11 x s, Ar), 170.8 (s, C=O), 180.6 (s, C=S)
(II)	2.33, 2.41 (2 x s, 6H, Me), 7.43-7.59(m, 3H, C_6H_4), 7.79-7.81 (m, 1H, C_5H_3), 7.86 (s, 1H, C_6H_4), 7.96 (d, J_{HH} = 8 Hz, 1H,C_5H_3), 8.11 (d, J_{HH} =8 Hz, 1 H,C_5H_3), 11.79, 12.85 (2 x s, 1H, NH)	21.3, 23.9 (2 x s, Me), 125.4, 126.4, 128.4, 128.9, 129.7, 130.5, 132.3, 132.6, 134.3, 134.4, 138.4 (11 x s, Ar), 168.8 (s, C=O), 181.4 (s, C=S)
(III)	2.67, 2.85 (2 x s, 6H, Me), 7.33-7.39 (m, 3H, C_5H_3), 7.49 (d, J_{HH} = 7 Hz, 1H,C_6H_4), 7.78 (d, J_{HH} = 9 Hz, 1H,C_6H_4), 8.07 (t, J_{HH}= 8 Hz, 1H, C_6H_4), 8.19 (d, J_{HH} = 8 Hz, 1H, C_6H_4)	20.6, 22.1 (2 x s, Me), 31.2 (s, C⎓O), 116.6, 117.7, 126.4, 130.9, 132.1, 132.2, 133.0, 139.3, 139.6, 146.3, 155.9 (11 x s, Ar), 179.0 (s, C⎓S)

Molecular Structural Analysis

All these compounds have been analysed by single crystal X-ray diffraction and exhibit monoclinic crystal system, $P2_1/n$ space group. The crystallographic data and refinement of methylbenzoylthiourea derivatives are shown in Table 4. The thiourea moieties in the compounds are essentially planar. Molecule **(III)** is planar compared to **(I)** and **(II)** due to the formation of bonding between N3-S1 and S1-O1. The planarity conformation of thiourea moieties in **(I)** and **(II)** also influenced by intra-molecular N2-H2A···O1 and N1-H1A···N3 hydrogen bonds. Molecule **(I)** adopts a *trans-cis* configuration with respect to the positions of the 2-methylbenzoyl and 3-methyl-2-pyridiyl groups, whilst **II** adopts a *cis-trans* configuration with respect to the positions of the 3-methylbenzoyl and 6-methyl-2-pyridyl groups which is relative to the thione S atom across the thiourea C-N bonds (Figure 4).

Table 4: Crystallographic data and refinement of the structures of **(I)**, **(II)** and **(III)**.

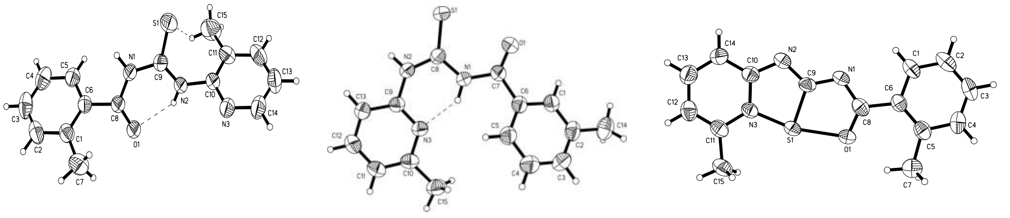
Parameter	**(I)**	**(II)**	**(III)**
Empirical formula	C_{15} H_{15} N_3 OS	$C_{15}H_{15}N_3OS$	$C_{15}H_{13}N_3OS$
Formula weight	285.36	285.36	283.34
Crystal system	monoclinic	monoclinic	monoclinic
Space group	P2(1)/n	P2(1)/n	P2(1)/n
Unit cell dimension	a = 7.955 (3) Å, b = 7.811 (3)Å, c = 23.414 (8) Å, β = 90.827 (6) º	a = 7.1981(19) Å, b = 10.092(3) Å, c = 19.372(5) Å, β =95.826(5) º	a = 8.117(3) Å, b = 14.545(5) Å, c = 11.125(4) Å, β = 98.782(8) º
Volume	1454.6 (9) Å^3	1399.9(6) Å^3	1298.1(8) Å^3
z, Calculated density	4, 1.303 Mg/m^3	4, 1.354 Mg/m^3	4, 1.450 Mg/m^3
F (000)	600	600	592
Crystal size	0.49 x 0.46 x 0.17 mm	0.50 x 0.32 x 0.28 mm	0.43 x 0.14 x 0.12 mm
Theta range for data collection	1.74 to 24.99º	2.11 to 25.00º	2.32 to 24.99º
Limiting indices	-9<=h<=9, 9<=k<=9, -16<=1<=27	-8<=h<=8, -8<=k<=12, -20<=l<=23	-9<=h<=9, 17<=k<=17, -10<=l<=13
Reflections collected/ unique	7218/2560 [R(int)= 0.0182]	6913/2459 [R(int) = 0.0201]	6574/2266 [R(int)= 0.0575]
Completeness of theta	99.7%	99.9 %	99.2 %
Max and min transmission	0.9633 and 0.8993	0.9384 and 0.8936	0.9709 and 0.9010
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/ restraints/ parameters	2560 / 0/ 183	2459 / 0 / 183	2266 / 0 / 181
Goodness-of-fit on F^2	1.029	1.045	0.980
Final R indices [I>2sigma(1)]	R1 = 0.0410, wR2 = 0.1072	R1 = 0.0453, wR2 = 0.1245	R1 = 0.0726, wR2 = 0.1905
R indices (all data)	R1 = 0.0542, wR2 = 0.1148	R1 = 0.0574, wR2 = 0.1328	R1 = 0.1200, wR2 = 0.2259
Largest different peak and hole	0.229 and -0.150 e.A^{-3}	0.263 and -0.143 e.A^{-3}	0.465 and -0.297 e.A^{-3}

The bond lengths and angles of all compounds are in agreement with the anologues of 1-Benzoyl-3-(6-methylpyridin-2-yl)thiourea [21] and 4-Chloro-*N*-[*N*-(6-methyl-2-pyridyl)-carbamothioyl]benzamide [1]. The selected bond lengths (Å) and angles (°) are listed in Table 5.

Table 5: Selected the bond lengths (Å) and angles (°) for **(I)**, **(II)** and **(III)**.

Bond lengths		Bond angles	
(I)			
S1-C9	1.655(2)	O1-C8-C6	122.96(16)
O1-C8	1.214(2)	N1-C8-C6	114.88(15)
N1-C8	1.373(2)	N2-C9-N1	116.11(16)
N1-C9	1.394(2)	N2-C9-S1	126.01(14)
N2-C9	1.327(2)	N1-C9-S1	117.88(14)
(II)			
S1-C8	1.665 (2)	C8-N1-C7	129.14 (17)
O1-C7	1.211 (2)	N2-C8-N1	115.07 (17)
N1-C8	1.363 (2)	N2-C8-S1	119.47 (14)
N1-C7	1.388(2)	C8-N2-C9	131.45(16)
N2-C8	1.359(3)	N1-C8-S1	125.46 (15)
(III)			
S1-C9	1.766(4)	C9-S1-N3	85.80(18)
S1-N3	1.783(4)	C9-S1-O1	79.87(17)
S1-O1	2.123(3)	N3-S1-O1	165.66(14)
O1-C8	1.248(5)	C8-O1-S1	105.7(3)
N2-C9	1.329(5)	C9-N2-C10	112.6(4)
N2-C10	1.331(5)	C9-N1-C8	113.0(4)
N1-C9	1.321(5)	N1-C9-N2	124.9(4)
N1-C8	1.337(6)	N1-C9-S1	119.8(3)

The molecular structure of **(I)**, **(II)** and **(III)** and their packing diagrams are illustrated in Figure 4 and 5, respectively. The central thiourea moiety, S1/N1/N2/C9, 3-methylpyridine N3/(C10-C15), and 2-methylphenyl, (C1-C6) rings in **(I)** are essentially planar with maximum deviation of 0.032 (2)Å for N2 atom from the least square plane. The central thiourea moiety makes dihedral angle with the pyridine and 2-methylphenyl rings of 65.53(7)° and 61.82(8)°, respectively. The inclination angle between the pyridine and benzene rings is 12.63(8)° are smaller if compared to **(II)** 26.06°. The molecular structure of **(II)** is closely related to **(I)** with relatively identical in bond lengths and angles. The (6-methyl-2-pyridyl)thiourea fragment (C7/C8/S1/N1/N2/N3/C9-C13/C15) in **(II)** is essentially planar with maximum deviation of 0.066(1)Å for atom N1 from the least square plane. This fragment makes dihedral angles of 30.29(8)° with respect to the benzene ring (C1-C6) plane. The inclination angle between the two aromatic rings is 26.06°.

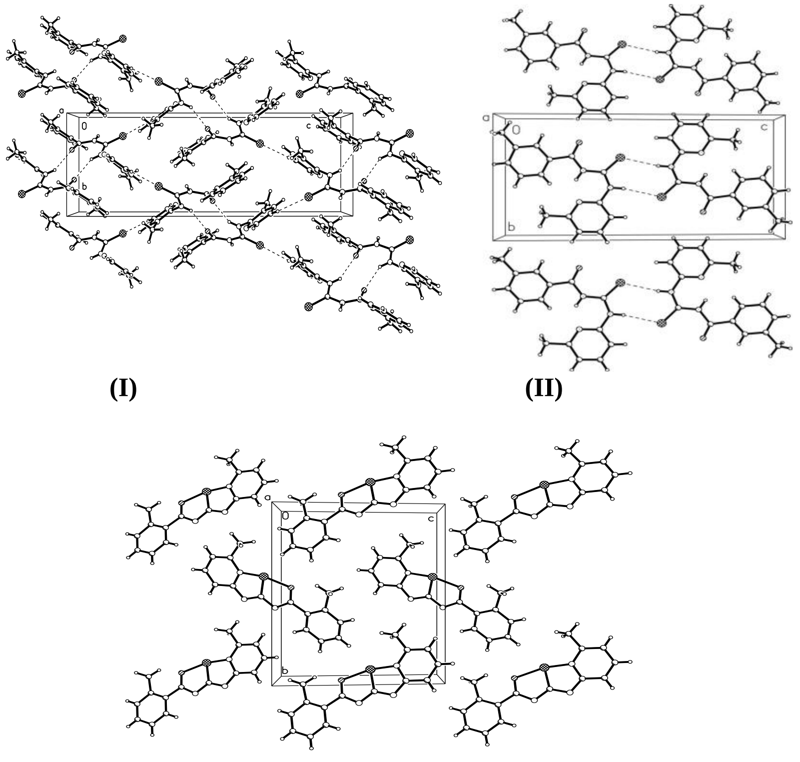


(I) **(II)** **(III)**

Figure 4: The molecular structures of **(I)**, **(II)** and **(III)** with displacement ellipsoids drawn at 50% probability level. The dashed lines indicate the existence of intramolecular hydrogen bonds.

The molecular structural analysis of these compounds show the cyclisation of **(III)** (Figure 4) through the nitrogen at pyridine, N3 and carbonyl oxygen atom, O1 bonded to the sulphur atom forming two planar five-membered ring structures. This cyclisation is believed as a result of transfer of electron density between nitrogen atom in pyridine and carbonyl oxygen to sulphur form two chelate rings. The bond length of the C-S, C-O and C-N indicate of some partial double bond character whereas it shows that the C=S bond is longer 1.766 Å than in **(I)** and (**II)**, and comparable by previous reported that the C-S lies at 1.74 Å [22]. These result occur due to the conjugation of lone electron pairs of nitrogen atoms with π-electron of the C=S.

Molecule **(I)** maintains the *trans-cis* configuration of the thiourea moiety is stabilised by the intra-hydrogen bond between the carbonyl oxygen atom O1 and the thioamide hydrogen atom, H15A (Figure 4). In the crystal lattice, the molecules are linked by the N2-H2···O1 and C13-H13···S1 inter-molecular hydrogen bonds forming two-dimensional (Figure 5). Similar case in **(II)**, there is an intra-molecular hydrogen bond, N1-H1···N3 (Figure 4) and resulting a pseudo-six-membered ring, N3···H1–N1–C8–N2–C9, is formed. In the crystal lattice, the molecules are linked to form centrosymmetric dimers through N2-H2···S1 inter-molecular interactions (Figure 5). Whilst, in (**III)** it is stabilised by the intra-hydrogen C7-H7···O1 resulting a pseudo-six-membered ring. However, in crystal lattice the case of **(III)** there is no intermolecular hydrogen interaction bonding involves (Figure 5). Hydrogen-bond geometry of all the synthesised compounds is listed in Table 6.



(I) **(II)**

(III)

Figure 5: Representative molecular packing diagram for **(I)**, **(II)** and **(III)**.

Table 6: Hydrogen-bond geometry (Å).

D-H···A	D-H	H···A	D···A	D-H···A
(I)				
N2-H2A···O1	0.86	2.06	2.698(2)	130
C15-H15A···N2	0.96	2.56	2.962(3)	105
N2-H2A···O1^{i}	0.86	2.27	3.021(2)	146
C13-H13···S1^{ii}	0.93	2.84	3.701(3)	154
Symmetry codes: *(i)*1- x, 1 - y, -z *(ii)* 3/2 -x, 1/2 + y, 1/2- z				
(II)				
N1-H1A···N3	0.86	1.94	2.657 (2)	140
N2-H2A···S1^{i}	0.86	2.60	3.4478 (19)	169
Symmetry code: *(i)* -x + 1, -y, -z.				
(III)				
C7-H7A···O1	0.96	1.99	2.764(6)	136

Conclusion

To conclude, two isomers of methylbenzoylthiourea derivatives and the unexpected secondary amide have been successfully prepared and fully characterised via IR, UV-Visible, ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) as well as single crystal X-ray diffractometer. Infrared spectra showed four significant absorptions within the range. The UV-Visible spectra of the compounds were assigned as a mixture of $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ transitions which could be contributed by phenyl rings, C=O and C=S chromophores. In the NMR spectroscopy, the NH group acts as hydrogen-bond donor for compounds **(I)** and **(II)** and the presence of C=S plays an important role in the identification of the proposed structures. The crystal structure of the title compounds showed intra- and inter-molecular interaction which may increase the hydrogen-bond donors and hydrogen-bond acceptors. Indeed, the presence of S, N and O electron donors in these derivatives have attracted great opportunity in the near future as polydentate ligands to bind with wide range of metal ions in the interest of coordination chemistry.

Acknowledgement

The authors gratefully acknowledge Ministry of Higher Education Malaysia for FRGS research grant No:59001, Ministry of Science Technology and Innovation (MOSTI), HRD (S&T) National Science Fellowship (NSF) for the postgraduate scholarship, Universiti Malaysia Terengganu and Universiti Kebangsaan Malaysia for providing research facilities.

References

1. Binzet, G., Emen, F. M., Flörke, U., Ilkaynak,T., Külcü, N. and Arslan,H. 2009. 4-Chloro-*N*-[*N*-(6-methyl-2-pyridyl)-carbamothioyl]benzamide. Acta Cryst. E65. 081-082.
2. Xue, S. J., Zou, J. S. and Yang, H. J. 2000. Synthesis and Herbicidal Activities of *N'*-(substituted pyrimidin-2-yl)-*N*-Substituted Phenoxyacetyl Thiourea Derivatives. Chinese Chemical Letters 11(1): 19-20.
3. Ranise, A., Spallarossa, A., Bruno, O., Schenone, S., Fossa, P., Menozzi, G., Bondavalli, F., Mosti, L., Capuano, A., Mazzeo, F., Falcone, G. and Filippelli, W. 2003. Synthesis of *N*-substituted-*N*-acylthioureas of 4-substituted piperazines endowed with local anaesthetic, antihyperlipidemic, antiproliferative activities and antiarrythmic, analgesic, antiaggregating actions. IL Farmaco 58: 765-780.
4. Xu, X., Qian, X., Li, Z., Huang, Q. and Chen, G. 2003. Synthesis and insecticidal activity of new substituted *N*-aryl-*N'*-benzoylthiourea compounds. Journal of Fluorine Chemistry 121: 51-54.
5. Weiqun, Z., Kuisheng, L., Yong, Z. and Lu, L. 2003. Structural and spectral studies of *N*-(4-chloro)benzoyl-*N'*-2-Tolylthiourea. Journal of Molecular Structure 657: 215-223.
6. Weiqun, Z., Baolong, L., Liming, Z., Jiangang, D., Yong, Z., Lude, L. and Xujie, Y. 2004. Structural and spectral studies on *N*-(4-chloro)benzoyl-*N'*-(4-tolyl)thiourea. Journal of Molecular Structure 690: 145-150.

7. Ke, S.-Y. and Xue, S.-J. 2006. Synthesis and herbicidal activity of *N*-(*o*-fluorophenoxyacetyl)thioureas derivatives and related fused heterocyclic compounds. ARKIVOC (x): 63-68.
8. Liu, B. and Tian, L. 2006. 1-Cyclopropylcarbonyl-3-(2-pyridyl)thiourea. Acta Cryst. E62, 04280-04281.
9. Selvaraju, K., Valluvan, R. and Kumararaman, S. 2007. A new metal-organic crystal: Potassium thiourea chloride. Material Letters 61:751-753.
10. Yang, W., Weiqun, Z. and Zhang, Z. 2007. Structural and spectroscopic study on *N*-2-fluorobenzoyl-*N*'-4-methoxyphenylthiourea. Journal of Molecular Structure 828: 46-53.
11. Li, J., Tan, J.-Z., Chen, L.-L., Zhang, J., Shen, X., Mei, C.-L., Fu, L.-L., Lin, L.-P., Ding, J., Xiong, X.-S., Liu, H., Luo, X.-M. and Jiang, H.-L. 2006. Design, synthesis and antitumor evaluation of a new series of *N*-substituted-thiourea derivatives *N*-(2-oxo-1,2-dihydroquinolin-3-yl-methyl)-thiourea. Acta Pharmacologica Sinica 27 (9): 1259.
12. Mahajan, A., Yeh, S., Nell, M., Van Rensburg, C. E. J. and Chibalea, K. 2007. Synthesis of new 7-chloroquinolinyl thioureas and their biological investigation as potential antimalarial and anticancer agents. Bioorganic & Medicinal Chemistry Letters 17: 5683-5685.
13. Dong, Y., Venkatachalam, T. K., Narla, R. K., Trieu, V. N., Sudbeck, E. A. and Uckun, F. M. 2000. Antioxidant Function of Phenethyl-5-bromo-pyridyl Thiourea Compounds with Potent Anti-HIV Activity. Bioorganic & Medicinal Chemistry Letters 10: 87-90.
14. Karakus¸ S. and Rollas, S. 2002. Synthesis and antituberculosis activity of new *N*-phenyl-*N*-[4-(5-alkyl/arylamino-1,3,4 thiadiazole-2-yl)phenyl]thioureas. IL Farmaco 57: 577-581.
15. Raj, S. S. S., Puviarasan, K., Velmurugan, D., Jayanthi, G. and Fun, H.-K. 1999. N-H···S hydrogen bonding in *N*-benzoyl-*N'*-methyl-*N'*-phenylthiourea and *N*-benzoyl-N''-(3,4 dimethylphenyl)thiourea. Acta Cryst. C55: 1318-1320.
16. Caroline, M. L. and Vasudevan, S. 2009. Growth and characterization of pure and doped bis thiourea zinc acetate: Semiorganic nonlinear optical single crystals. Current Applied Physics 9: 1054-1061.
17. Ma, D. L., Xia, D. S., Cui, F. L., Li, J. P. and Wang, Y. 1999. A new sensitive reagent for identifying and determining Cu^{2+}. Talanta 48: 9-13.
18. Domínguez, M., Anticó, E., Beyer, L., Aguirre, A., Garcıà-Granda, S. and Salvadó, V. 2002. Liquid/liquid extraction of palladium(II) and gold(III) with *N*-benzoyl-*N',N'*-diethylthiourea and the synthesis of a palladium benzoylthiourea complex. Polyhedron 21: 1429-1437.
19. Bencivenni, L., Cesaro, S. N. and Pieretti, A. 1998. Matrix and ab initio infrared spectra of thiourea and thiourea-d_4 Vibrational Spectroscopy 18: 91–102.
20. Dillen, J.,Woldu, M. G. and Koch, K. R. 2006. *N,N*-(Heptane-2,6-diyl)-*N'*-(3,4,5-methoxybenzoyl)thiourea. Acta Cryst. E62: 05225-05227.
21. Yusof, M. S. M., Soh, S. K. C., Ngah, N. and Yamin, B. M. 2006. 1-Benzoyl-3-(6-methylpyridin-2-yl)thiourea. Acta Cryst. E62: 01446-0144.
22. Allen, F. H., Bird, C. M., Rowland, R. S. and Raithby, P. R. 1997. Resonance-Induced Hydrogen Bonding at Sulfur Acceptors in $R_IR_2C{=}S$ and R_ICS_2 Systems. Acta Cryst. B53: 680-695.