

Synthesis and Characterization *O*-, *M*- and *Para*-Toluyyl Thiourea Substituted *Para*-Pyridine and *Ethyl* Pyridine as a Chromoionophore

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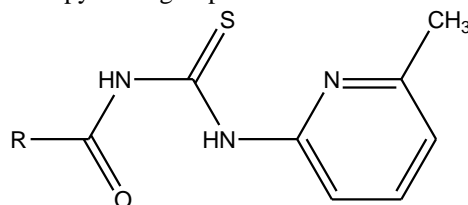
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Abstract: Six new derivatives of carbonyl thiourea comprises of *o*-, *m*- and *p*-toluyyl at one end of Nitrogen atom and *p*-methylpyridine or ethyl pyridine at another one end of Nitrogen atom has been synthesized. The compounds are, 2-methyl-*N*-[(4-methylpyridine-2-yl) carbamothiol] benzamide (I), 3-methyl-*N*-[(4-methylpyridine-2-yl) carbamothiol] benzamide (II) and 4-*N*-[(4-methylpyridine-2-yl) carbamothiol] benzamide (III) for Toluyyl-MP while 2-methyl-*N*-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (IV), 3- methyl-*N*-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (V) and 4- methyl-*N*-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (VI) for isomer Toluidal-AEP have been successfully synthesized and characterized by elemental analysis, Infrared Spectroscopy analysis (FT-IR), Nuclear Magnetic Resonance Spectroscopy (NMR) and Ultraviolet-visible (UV-vis). All products shown stretching modes of $\nu(N-H)$, $\nu(C=O)$, $\nu(C-N)$, and $\nu(C=S)$ around 3276 cm^{-1} , 1671 cm^{-1} , 1315 cm^{-1} and 1148 cm^{-1} respectively. All products shown two maximum absorption around 262 nm and 290 nm respectively for carbonyl C=O and thione C=S chromophore. Those both values contributed by $n \rightarrow n^*$ transition. ^1H nuclear magnetic resonance spectrum showed presence of aromatic, methyl, methine and amide protons except for product III. All products showed presence of carbon thione in ^{13}C nuclear magnetic resonance except for product III. Ionophor interpretation with acetate anion shows color changes by naked eye for compound (I) and (III).

Keywords: Carbonylthiourea, Spectroscopy, chromoionophore.

I. Introduction

Thiourea with a formula, $\text{SC}(\text{NH}_2)_2$ is a versatile reagent in organic synthesis. One type of thiourea that has been studied recently is the carbonyl thiourea. In 2000, synthesis thiourea derivatives research has grown and get much attention among researchers all over the world. Carbonyl which attached to thiourea carbonyl has high polarisation and easy to make a hydrogen bonding[51]. There are four hydrogen bonding in the thiourea molecule which can be substituted with another good leaving group. In this research, carbonyl thiourea derivatives has been conducted by exchanging one hydrogen bonding at Nitrogen atom with another carbonyl group and another one site is with pyridine group.



Rajah 1.4 One of the carbonyl thiourea structure where R is the substituent

Carbonyl and thiocarbonyl existence in thiourea derivatives moieties has grab attention and excitement of the chemist researchers in ligand coordination. This has make thiourea and its derivatives as a very useful ligand in synthesizing new compound and can also be as an intermediate to be use in huge application such as industrial, pharmaceutical and medication. There is a research which has been done as a catalyst in organic reaction. The catalyst could activated carbonyl, iminyl and nitro group via existence of hydrogen bonding [66].

In the present study, we report herein the synthesis and characterization of *o*-, *m*- and *p*-toluyyl at one end of Nitrogen atom and *p*-methyl pyridine or ethyl pyridine at another one end of Nitrogen atom has been synthesized as report in Figure 1.

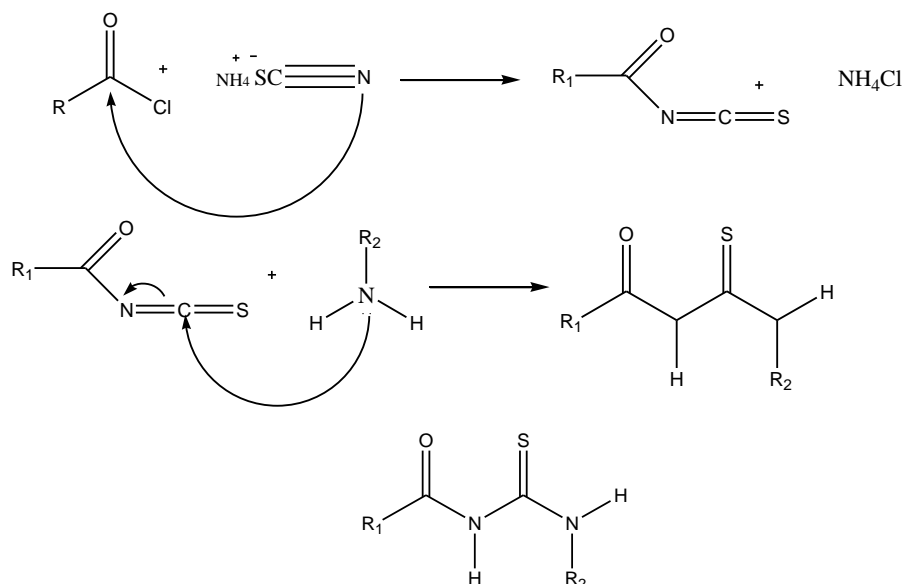


Figure 1 Carbonyl thiourea structure R1= *o*, *m*, and *p* toluyylchloride R2= pyridine substituent

II. Experimental

2.1. Physical measurements

All reactions were performed under an ambient atmosphere and no special precautions were taken to exclude air or moisture. Chemicals were purchased from MERCK or Sigma Aldrich was used as received without further purification. The solvent were left overnight with freshly molecular sieve before used. Melting points were measured using BÜCHI Melting Point B-545 and the elemental analyses were conducted using CHNS Analyzer Flash EA 1112 series. Infrared spectra were obtained using FTIR Perkin Elmer 100 Spectrophotometer in the spectral range of 4000-350 cm⁻¹. ¹H NMR spectra were recorded using Bruker Avance III 300 Spectrometer at room temperature. The elemental analyses were conducted using CHNS Analyzer Flash EA 1112 series.

2.2. Synthesis of the ligands

Freshly prepared substituted *Orto*-, *Meta*- and *Para*- benzoyl chloride (13 mmol) was added drop wise to a stirring acetone solution (30 ml) of ammonium thiocyanate (13 mmol). The solution mixture was stirred about 10 minutes. A solution of C₈H₈N₂ 2 Amina-4-Methylpyridine (6.5 mmol) and C₇H₁₆O₂ 2-(2-Aminaethhhyl pyridine), in acetone was added and the reaction solution was heated under reflux for 3 hours. The solution was poured into a beaker containing some ice cubes. The resulting precipitate was collected by filtration, washed several times with cold ethanol/water and purified by recrystallization from ethanol[28].

2-methyl-N-[(4-methylpyridine-2-yl) carbamothiol] benzamide (I): Yield 67 %; colourless, m. 126.3 °C. IR (KBr pellet, cm⁻¹): ν(C=O) 1683.24(s), ν(N-H) 3237.13(s), ν(C-N) 1329.67(s), ν(C=S) 1157.59(s). ν(C=C) 1546.97(s)¹H NMR (dmsO-d₆, 500 MHz): δ 2.06 (δH N1); 10.49 (δH N1); 13.21, (δH C7); 2.35, (δHC15); 2.37, (δH Aromatic); 7.10(d), 7.35(d), 7.47(td), 7.64(d), 8.30(t), 8.82(s). Anal Calc. For C₁₅ H₁₅ N₃ O S: C, 64.5838; H, 15.0506; N, 5.1240; S, 11.9046. Found: C, 66.8815; H, 15.0506; N, 5.6133; S, 8.3210

3-methyl-N-[(4-methylpyridine-2-yl) carbamothiol] benzamide (II) Yield 58 %; Light yellow, m. 153.0 °C. IR (KBr pellet, cm⁻¹): ν(C=O) 1666.42 (s), ν(N-H) 3282.57 (s), ν(C-N) 1334.57(s), ν(C=S) 1161.70(s). ν(C=C) 1546.41 (s)¹H NMR (dmsO-d₆, 500 MHz): δ 2.06 (δH N1); 10.29 (δH N1); 13.29, (δH C7); 2.40, (δHC15); 2.40, (δH Aromatic); 7.09(d), 7.49(dd), 7.89(t), 8.28(d), 8.78(s), 8.28(d). Anal Calc. For C₁₅ H₁₅ N₃ O S: C, 64.5882; H, 5.4565; N, 15.3297; S, 9.3370. Found: C, 63.1337; H, 5.2984; N, 14.7258; S, 11.2372

4-N-[(4-methylpyridine-2-yl) carbamothiol] benzamide (III) Yield 75 %; Yelowish, m. 126.9 °C. IR (KBr pellet, cm⁻¹): ν(C=O) 1681.70 (s), ν(N-H) 3236.0(s), ν(C-N) 1304.06 (s), ν(C=S) 1157.81 (s). ν(C=C) 1547.49 (s)¹H NMR (dmsO-d₆, 500 MHz): δ 2.06 (δH N1); 10.49 (δH N1); 13.21, (δH C7); 2.05, (δHC15); 2.42, (δH Aromatic); 7.09(d), 7.36-7.42(dd), 7.93-7.95(d), 7.98(dd) Anal Calc. For C₁₅ H₁₅ N₃ O S: C, 64.5838; H, 5.1341; N, 14.9805; S, 7.8268. Found: C, 63.1336; H, 15.0506; N, 14.7263; S, 11.2735

2-methyl-N-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (IV) Yield 73 %;

White transparent, m. 127.8 °C. IR (KBr pellet, cm⁻¹): $\nu(\text{C=O})$ 1662.82(s), $\nu(\text{N-H})$ 3237.13(s), $\nu(\text{C-N})$ 1329.67(s), $\nu(\text{C=S})$ 1157.59(s). $\nu(\text{C=C})$ 1546.97(s)¹H NMR (dmsO-d6, 500 MHz): δ 2.06 ($\delta\text{H N1}$); 10.11 ($\delta\text{H N2}$); 11.05, ($\delta\text{H C6}$); 2.42, (δHC10);4.13, (δHC11);3.21 ($\delta\text{H Aromatic}$); 7.24(m),7.27(dd),7.34(d), 7.40(td),7.51(d).Anal Calc. For C₁₅ H₁₅ N₃ O S: C,64.7483; H, 5.3804; N, 15.3349; S, 11.9046. Found: C, 66.8890; H, 5.6140; N, 15.6023;S, 11.9059

3- methyl-N-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (V) Yield 50 %;

Light yellow, m. 135.6°C. IR (KBr pellet, cm⁻¹): $\nu(\text{C=O})$ 1683.24(s), $\nu(\text{N-H})$ 3225.71(s), $\nu(\text{C-N})$ 1297.27 (s), $\nu(\text{C=S})$ 1152.04 (s). $\nu(\text{C=C})$ 1548.67 (s)¹H NMR (dmsO-d6, 500 MHz): δ 2.06 ($\delta\text{H N1}$); 9.98 ($\delta\text{H N2}$); 11.14, ($\delta\text{H C6}$); 2.39, (δHC10);4.13, (δHC11);3.23 ($\delta\text{H Aromatic}$);7.28(dd),7.31(d),7.35(d),7. 40(m),7.44(dd),7.76(m),7. 80(s),8.55-8.56(d); Anal Calc. For C₁₅ H₁₅ N₃ O S: C, 64.0862; H, 5.5528; N, 15.4739; S, 7.4759, Found: C, 64.1868; H, 5.7230; N, 14.0361;S, 10.7109

4- methyl-N-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (VI) Yield 65 %;

White transparent, m. 126.3 °C. IR (KBr pellet, cm⁻¹): $\nu(\text{C=O})$ 1566.13(s), $\nu(\text{N-H})$ 3185.01 (s), $\nu(\text{C-N})$ 1330.85(s), $\nu(\text{C=S})$ 1161.00(s). $\nu(\text{C=C})$ 1546.97(s)¹H NMR (dmsO-d6, 500 MHz): δ 2.06 ($\delta\text{H N1}$); 9.98 ($\delta\text{H N2}$); 11.01, ($\delta\text{H C6}$); 2.41, (δHC10);4.12, (δHC11);3.20 ($\delta\text{H Aromatic}$); 7.22(dd),7.34(t),7.73(td), 7.84(d), 8.55(d).. Anal Calc. For C₁₅ H₁₅ N₃ O S: C, 64.9060; H, 5.6358; N, 15.9032; S, 8.1728. Found: C, 64.1858; H, 5.7238; N, 14.3733;S, 10.7107.

2.3 Acetate ion naked eye test.

0.05 gram of synthesized compound were dissolved in 10 ml of acetone. A few drops of acetic acids slowly added in to the solution. This simple method is repeat by using different five more thiourea derivatives. The acetic acid is added drop by drop until there is a change in color. Observation was made to be recorded[36]

III. Results And Discussion

3.1. Chemical analysis

The micro elemental analysis data (Table 1) of the product is in agreement with the formula as referred. The melting point of the ligands was found between 193°C to 206°C.

Table 1. Micro elemental analysis data of the compound (1), (2), (3), (4) (5) and (6).

Compound	Physical colour	Yield (%)	Melting Point(%)
1	Colourless	67	121.4-126.3
2	Light yellow	58	146.1-153.0
3	Yellowish	75	128.4-126.9
4	White transparent	73	146.1-149.2
5	Light Yellow	50	124.2-127.8
6	White transparent	65	133.4-135.6

3.2. Spectroscopic studies

The characteristic IR bands of all thiourea ligands showed the expected frequencies of $\nu(\text{C=O})$, $\nu(\text{N-H})$, $\nu(\text{C-N})$, $\nu(\text{C=S})$ and $\nu(\text{C=C})$. The presence of strong absorption bands at 3342.40 cm⁻¹(T3) corresponds to $\nu(\text{N-H})$ stretching. The medium intensity bands around 1663 cm⁻¹ attributes to the stretching of $\nu(\text{C=O})$. The $\nu(\text{C-N})$ bands appeared at 1253.89 cm⁻¹. The medium bands at 890.79 cm⁻¹ assigned for $\nu(\text{C=S})$ stretching. These assignments of thiourea derivatives were also confirmed by [1] [37]. The ¹H NMR spectra of the ligands were recorded in deuterated DMSO. Very similar spectra were obtained for the ligand.¹H NMR data demonstrate the existence of methoxy proton substituent attached to the benzyl ring between 3.79 to 4.01 ppm and aromatic proton in the range 7.28 to 8.56.The ¹H NMR data showed the unresolved resonance aromatic protons signal appearing at 7.22 to 8.55 ppm which can be attributed to the overlapping proton signals in the aromatic rings. The carbon chemical shifts of the CONH group appear upfield 10.41 ppm. There is a signal appear for thioamide group (CSNH) proton at 13.21ppm

3.3. Acetate chromoionophor test

Solution of the compound which were (I), (II) and (III) dissolves in acetone and show colorless, light yellow and yellowish color respectively as shown in the figure below. While compound (IV), (V) and (VI) shows colorless, light yellow and brownish color respectively. Drop by drop of acetic acid and sodium nitrate is proof by naked eyes show color changes for compound (I) and (III). This was colorless turn to yellowish. And light yellow turn to colorless. This can make a conclusion the interaction of all the compound synthesized were

not give changes of color except for compound (I) and (III) to the solutions as the figure 3.8. This type of test is the first research before analysis by any other electronic instrument such as UV-visible was future research.

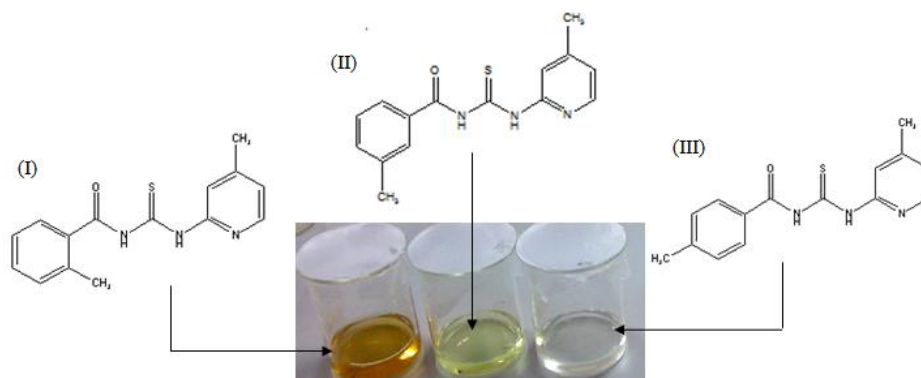


Figure Colour of the compound (I), (II) dan (III)

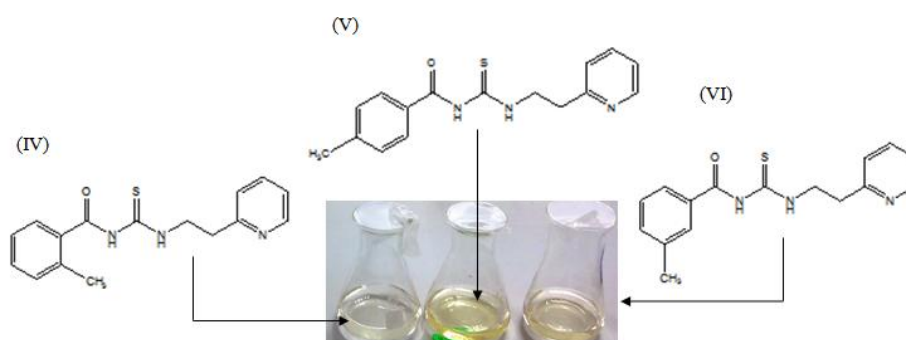


Figure Colour of the compound (IV), (V) dan (VI)

3.4 X-Ray Chrystallography –product 1

Product 1 crystalized in triclinic system with $C2/c$, space group. $a=8.549(5)\text{\AA}$, $b=8.755(5)\text{\AA}$, $c=11.083(6)\text{\AA}$, $\beta=83.430(11)^\circ$, $V=791.2(7)\text{ \AA}^3$ dan $Z=2$. Crystal data and structure refinement was shown in Table below. Atomic coordnation, parameter isotropic and anisotropic shifts, and atomic hydrogen atom are attached in attachment E.

Table 1. Crystal data and structure refinement for 1-(2-Metil-benzoil)-3-(2- piridina-3-il-etil)-tiourea

Identification	Data
Empirical formula	$C_{16}H_{17}N_3O S$
Wavelength	0.71073 \AA
Crystal system	Triclinic-P1
space group	$C2/c$
Unit cell dimensions	$a = 8.549(5)\text{ \AA}$ $\alpha = 86.232(11)^\circ$ $b = 8.755(5)\text{ \AA}$ $\beta = 83.430(11)^\circ$ $c = 11.083(6)\text{ \AA}$ $\gamma = 73.887(10)^\circ$
Volume	$791.2(7)\text{ \AA}^3$
Z, Calculated density	2, 1.257 Mg/m
Absorption coefficient	0.207 mm^{-1}
F(000)	316
Crystal size	0.50 x 0.29 x 0.17 mm
Theta range for data collection	1.8 to 25.5 deg.
Limiting indices	$-10 \leq h \leq 10$, $-10 \leq k \leq 10$, $-13 \leq l \leq 13$
Reflections collected / unique	8447 / 2936 [R(int) = 0.0231]
Completeness to theta = 25.5	99 %
Max. and min. transmission	0.9657 and 0.9037
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2936 / 0 / 191
Goodness-of-fit on F^2	1.04
Final R indices	R1 = 0.0382, wR2 = 0.1091
R indices (all data)	R1 = 0.0462, wR2 = 0.1159
Largest diff. peak and hole	0.20 and -0.17 $e.\text{\AA}^{-3}$

Figure below show molecular structure of 1-(2-Metil-benzoil)-3-(2-piridina-3-il-etil) with numbering scheme.

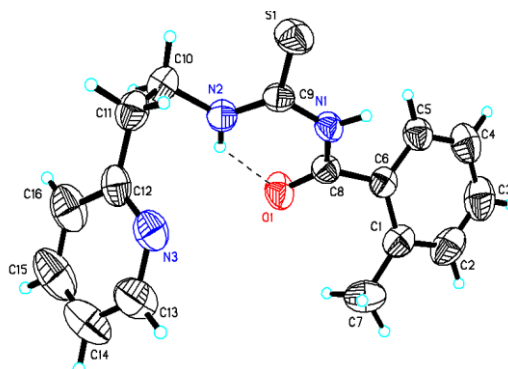


Figure 3.12 ORTEP diagram of 1-(2-Methyl-benzoyl)-3-(2-pyridine-3-yl-ethyl) thiourea with 50% ellipsoidal. The line shows hydrogen intramolecular formed.

Methyl benzoyl was in *trans* towards thione configuration at the axis of C9-N1. Ethyl pyridine group was in *cis* at the axis of C9-N2. This *trans-cis* configuration is normal in carbonyl thiourea configuration.

This molecule consist of a benzene ring. Intramolecular hydrogen bonding were found, N2-H2...O1 which produce pseudo six member ring (N2/H2/O1/C8/N1/C9). Angle and bond length were in normal condition of thiourea.(Table 3.11)

Table 3.11 Atomic coordinates and equivalent isotropic displacement parameters for 1-(2-Metil-benzoil) 3-(2-piridina-3-il-etil)-tiourea. Bond lengths and angles for 1-(2-Metil-benzoil) 3-(2-piridina-3-il-etil)-tiourea

Ikatan	Panjang ikatan (Å)
S(1) C(9)	1.6699(16)
O(1) C(8)	1.2255(19)
N(1) C(8)	1.368(2)
N(1) C(9)	1.392(2)
N(2) C(9)	1.325(2)
N(2) C(10)	1.455(2)
N(3) C(12)	1.331(2)

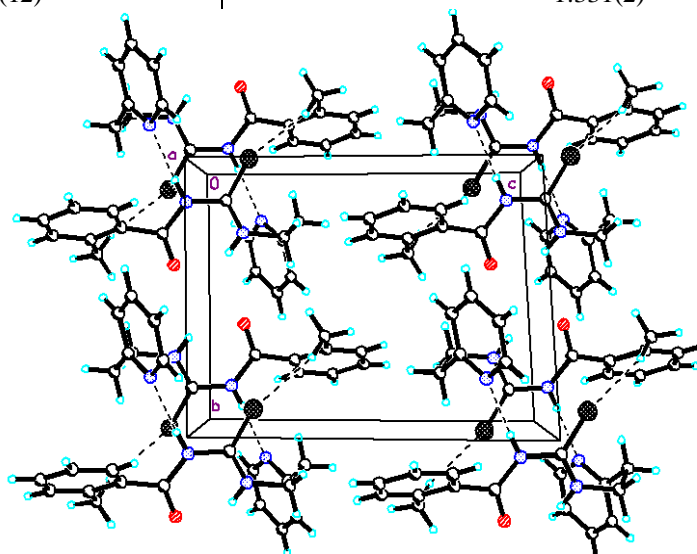


Figure 3.13 Figure show packing molecular structure of -(2-Methyl-benzoyl)-3-(2-pyridine-3-yl-ethyl)thiourea. The line shows hydrogen intramolecular formed.

This crystal structure was stabilized with hydrogen bonding which occurred between the molecule (intermolecule) to form a dimer. Figure show packing molecular structure of -(2-Methyl-benzoyl)-3-(2-pyridine-3-yl-ethyl)thiourea.

3.5 X-Ray Crystallography –product 2

Product 2 crystallized in triclinic system with $C2/c$, $a=11.567(3)$ Å, $b=6.1521(15)$ Å, $c=20.657(5)$ Å, $\beta=101.423(5)$ (11°), $V=1440.9(6)$ Å³ and $Z=4$. Crystal data and structure refinement was shown in Table below. Atomic coordination, parameter isotropic and anisotropic shifts, and atomic hydrogen atom are attached in attachment E.

Table 3.12 Data and structure refinement for 1-(4-Methyl-benzoyl 3-(4-methyl-pyridine-2-yl)-thiourea

Identification	Characteristic
Empirical formula	C ₁₅ H ₁₅ N ₃ O S
Molecular formula	285.36
Wavelength	298(2) K
Crystal System	0.71073 Å triklinik
Space group	$C2/c$
Unit cell dimensional	$a=11.567(3)$ Å $\alpha=90^\circ$ $b=6.1521(15)$ Å $\beta=101.423(5)^\circ$ $c=20.657(5)$ Å $\gamma=90^\circ$
Volume	1440.9(6) Å ³
Z, Calculated density	Z, 4, 1.315 Mg/m ³
Absorption coefficient	0.224 mm ⁻¹
F(000)	600
Crystal size	0.50 x 0.46 x 0.16 mm
Theta range for data collection	1.80 to 25.50 deg.
Limiting indices	$-12 \leq h \leq 14$, $-7 \leq k \leq 6$, $-25 \leq l \leq 23$
Reflections collected / unique	8166 / 2674 [R(int)=0.0236]
Completeness to theta = 25.0	25.50 99.8 %
Max. and min. transmission	0.9651 and 0.8964
Refinement method	Full-matrix least- squares on F ²
Data / restraints / parameters	2674 / 0 / 183
Goodness-of-fit on F ²	1.047
Final R indices	R1 = 0.0457, wR2 = 0.1209
R indices (all data)	R1 = 0.0565, wR2 = 0.1292
Largest diff. peak and hole	0.226 and -0.155 e.Å ⁻³

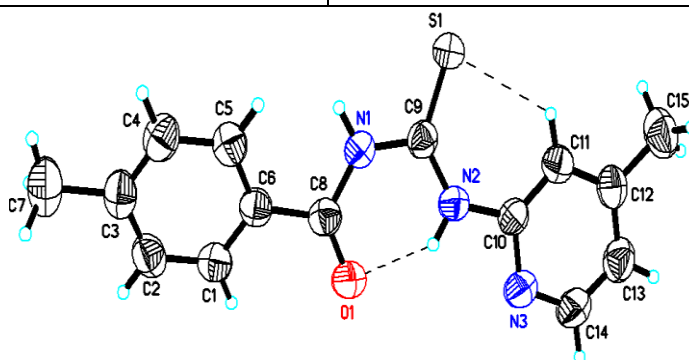


Figure 3. ORTEP diagram of 1-(4-Methyl-benzoyl)-3-(4-methyl-pyridine-2-yl) thiourea with 50% ellipsoidal. The line shows hydrogen intermolecular formed.

Methyl benzoyl was in *trans* towards thione configuration at the axis of C9-N1. methyl pyridine group was in *cis* at the axis of C9-N2. This *trans-cis* configuration is normal in carbonyl thiourea configuration.

This molecule consist of two benzene ring. Two intramolecular hydrogen bonding were found, N2-H2A...O1 which produce pseudo six member ring (N2/H2A/O1/C8/N1/C9). The other intrahydrogen bond is C11-H11...S1 which produce a new pseudo six membered ring benzene ring (C11/H11/S1/C9/N2/C10). Angle and bond length were in normal condition of thiourea.(Table 3.13).

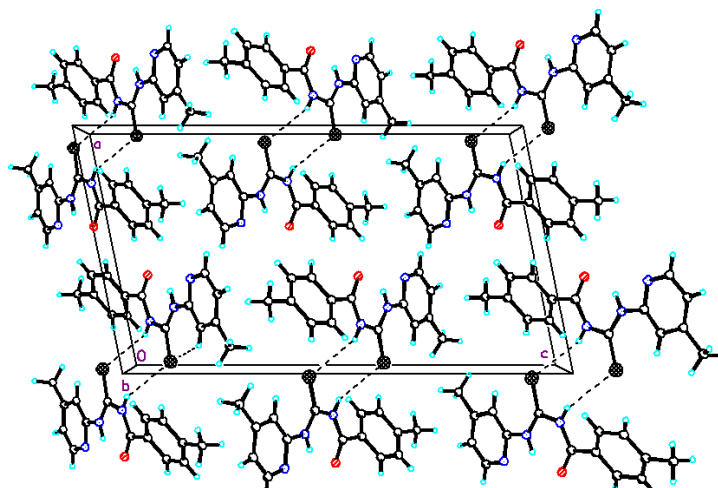


Figure show packing molecular structure of-(4-Methyl-benzoyl)-3-(4-methyl pyridine 2-yl) thiourea. The line shows hydrogen intramolecular formed.

This crystal structure was stabilized with hydrogen bonding which occurred between the molecule (intermolecule) to form a dimer. Figure show packing molecular structure of thiourea 1-(4-Methyl-benzoyl)-3-(4-methyl-pyridine-2-il) tiourea.

Table 3.11 Atomic coordinates and equivalent isotropic displacement parameters for 1-(2-Methyl-benzoyl) 3-(2-pyridine-3-il-etil)-tiourea. Bond lengths and angles for 1-(4-Methyl-benzoyl)-3-(4-methyl pyridine-2-il) tiourea

Ikatan	Panjang ikatan (Å)
S(1)-C(9)	1.662(2)
O(1)-C(8)	1.223(2)
N(1)-C(9)	1.385(2)
N(1)-C(8)	1.387(2)
N(2)-C(9)	1.334(2)
N(2)-C(10)	1.408(2)
N(3)-C(14)	1.328(3)
N(3)-C(10)	1.334(2)
C(1)-C(2)	1.376(3)
C(1)-C(6)	1.393(3)
C(2)-C(3)	1.383(3)
C(3)-C(4)	1.385(3)
C(3)-C(7)	1.509(3)
C(4)-C(5)	1.383(3)
C(5)-C(6)	1.383(3)
C(6)-C(8)	1.482(3)
C(10)-C(11)	1.379(3)
C(11)-C(12)	1.387(3)
C(12)-C(13)	1.374(3)
C(12)-C(15)	1.501(3)
C(13)-C(14)	1.370(3)
C(9)-N(1)-C(8)	129.35(16)
C(9)-N(2)-C(10)	132.35(17)
C(14)-N(3)-C(10)	116.37(19)
C(2)-C(1)-C(6)	120.0(2)
C(1)-C(2)-C(3)	121.4(2)
C(2)-C(3)-C(4)	118.21(19)

IV. Conclusion

To conclude, a series of carbonyl thiourea ligands, namely 2-methyl-*N*-[(4-methylpyridine-2-yl) carbamothiol] benzamide (**I**), 3-methyl-*N*-[(4-methylpyridine-2-yl) carbamothiol] benzamide (**II**) and 4-*N*-[(4-methylpyridine-2-yl) carbamothiol] benzamide (**III**) for Toluyyl-MP while 2-methyl-*N*-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (**IV**), 3- methyl-*N*-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (**V**) dan 4-

methyl-*N*-[(2-pyridine-2-yl-ethyl) carbamothiol] benzamide (**VI**) have been successfully synthesised and fully characterized by spectroscopic methods. Both of the crystal compound show methyl benzoyl were in *trans* towards thione configuration at the axis of C9-N1. While ethyl and methyl pyridine group were in *cis* at the axis of C9-N2. Both *trans-cis* configuration is a normal in carbonyl thiourea found in the configuration. Both of the crystal structure show intramolecular hydrogen bonding. First crystal structure shows only one hydrogen bonding while second crystal structure shows two intramolecular hydrogen bonding. Each structure shows a pseudo benzene ring formed by the hydrogen bonding. Ionophore interpretation with acetate anion shows color changes by naked eye for compound (I) and (III).

Acknowledgements

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