

## SYNTHESIS AND STRUCTURAL STUDIES OF *N*-(HALOGENOCARBOXYL)-*N'*-(ARYL)THIOUREA

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### ABSTRACT

The number of structure of carbonylarylthiourea derivatives is increasing because of their potential in biological properties. The structural informations are important for the structure-activity relationship studies or rational drug design work. However, the thioureas containing halogen in the carbonyl fragment is still very scarce. *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl)thiourea(I) and *N*-(3-chloropropionyl)-*N'*-(4-methylphenyl)thiourea(II) were synthesized and characterized by FTIR and NMR spectroscopic techniques. The compound (I) was obtained as twinned crystal. The X-ray study showed that the asymmetric unit consists two independent molecules. The *trans-cis* configuration of the chloropropionyl and methyl phenyl groups respectively, against the thiono about their C-N bonds is maintained.

*Key word:* thiourea, 3-chloropropionylchloride, Single-Crystal X-ray Study.

### INTRODUCTION

Thiourea derivatives have shown high biological activities as agrochemicals such as herbicides, pesticides and fungicides (Saeed *et al.*, 2009). One interesting application of current interest is the use of thiourea derivatives as ion sensors. They have strong anion binding ability, more than those of the corresponding urea, because of the higher acidity (Liu *et al.* 2006), therefore many thiourea derivatives have been successfully used in the extraction of Cu(II), Ni(II), Co(II), Pd(II), Pt(II), Co(III), Au(III) and Rh(III) from acidic media(Arslan & Florke, 2004). These potential applications of thiourea derivatives have driven the growth for the synthesis of new thiourea derivatives. It is realized that halogeno-thiourea compounds are still very limited. In our continuing work on the synthesis of thiourea derivatives, two isomeric *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl)thiourea(I) and *N*-(3-chloropropionyl)-*N'*-(4-methylphenyl) thiourea(II) were synthesized and characterized including the crystal structure of (II).

### METHODOLOGY

All chemicals were purchased from Aldrich or Merck were reagent grade and used without further purification. The solvents were distilled and kept in dried condition. Infrared spectrophotometer used for recording the spectra of the sample was model Perkin Elmer with wave number range between 4000 and 400  $\text{cm}^{-1}$ . The 400MHz Joel superconductor NMR spectrometer was used for recording the  $^1\text{H}$  and  $^{13}\text{C}$  spectra of the compounds. CHNS analyzer model carlo Elba was used for the microelemental analysis. X-ray crystallographic investigation was carried out by the X-ray Crystallography laboratory of Pusat Pengajian Sains Kimia and Teknologi Makanan using Bruker SMART APEX single crystal diffractometer. **Synthesis of the thiourea derivatives :** An acetone solution (50mL) of ortho or para-toluidine (0.03 mol, 3.21 g) was added dropwise into a two-necked round-bottomed flask containing 3-chloropropionylisothiocyanate(0.03 mol). The mixtures were refluxed for about 4 h and then filtered into a beaker containing ice cubes. The filtrate gave colourless crystals after 7 days of evaporation.

### RESULTS AND DISCUSSIONS

The microelemental analysis CHNS-O data (Table1) are in agreement with the expected formula of the compound *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl)thiourea(I) and *N*-(3-chloropropionyl)-*N'*-(4-methylphenyl)thiourea(II). Infrared spectra of compound(I) (Fig.1a) and compound(II)(Fig.2a) are nearly identical, as both compounds are isomeris. The characteristic stretching frequencies of  $\nu(\text{N-H})$  and  $\nu(\text{C=O})$  are at about 3020.40, 1690.86  $\text{cm}^{-1}$ , respectively. The  $\nu(\text{C-N})$  for the compounds are at 1252.72 and 1240.29  $\text{cm}^{-1}$ , respectively. The stretching absorptions of  $\nu(\text{C=C})_{\text{aromatic}}$  appear at 1551  $\text{cm}^{-1}$  for both compounds. The  $^1\text{H}$  NMR spectra of both compounds I and II (Fig2) are quite similar showing the same values for the chemical shifts

of  $\delta\text{H}(\text{N}_2)$  amide and  $\delta\text{H}(\text{CH}_3)$  as shown in the Table 2 except  $\delta\text{H}(\text{N}_1)$  thioamide for the compound(I) which is slightly at higher field compare to that in compound(II). The  $^{13}\text{C}$  NMR chemical shifts for C(7)=S thione, C(8)=O carbonyl and  $\text{CH}_3$  in both compounds have about the same values (Fig 3, table 3). The X-ray investigation of the compound (I) showed that compound crystallized in triclinic system with space group of  $\text{P}\bar{1}$ . The unit cell dimension are  $a = 8.438 \text{ \AA}$ ,  $b = 10.570 \text{ \AA}$ ,  $c = 14.200 \text{ \AA}$ .  $\alpha = 109.14^\circ$ ,  $\beta = 93.53^\circ$ ,  $\gamma = 91.13^\circ$ ,  $V = 1188.18(14) \text{ \AA}^3$  and  $Z = 4$ . There are two independent molecules in the asymmetric unit (Fig 4).

Table-1: Microelemental analysis data and melting points of the compound (I) and (II)

Compound	m.p (K)	C%	H%	N%	S%	O%
$\text{C}_{11}\text{H}_{13}\text{N}_2\text{OSCl}$ (I)	442.1-443.2	50.97	5.08 (51.46)	10.29 (5.10)	12.25 (10.91)	(12.49)
$\text{C}_{11}\text{H}_{13}\text{N}_2\text{OSCl}$ (II)	483-484	51.01	5.57 (51.46)	10.15 (5.10)	11.53 (10.91)	(12.49)

The calculated values are in the bracket

Figure 1. IR spectra of (a) *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl)thiourea(I) and (b) *N*-(3-chloropropionyl)-*N'*-(4-methylphenyl)thiourea(II).Table 2  $^1\text{H}$  NMR Spectral data for compound (I) and (II) in DMSO ( $\delta$ ,ppm)

Compound	$\delta\text{H}(\text{N}_1)$	$\delta\text{H}(\text{N}_2)$	$\delta\text{H}(\text{CH}_3)$	$\delta\text{H}$ of phenyl rings
I	12.05	11.64	2.20	7.21-7.53
II	12.31	11.58	2.26	7.18-7.49

Table 3  $^{13}\text{C}$  NMR Spectral data for the compound (I) and (II) in DMSO ( $\delta$ ,ppm)

Compound I \ortho		Compound II \Para	
Chemical shift(ppm)		Chemical shift(ppm)	
C(7)=S	179.56	C(7)=S	178.59
C(8)=O	172.14	C(8)=O	172.19
C <sub>1</sub>	136.74	C <sub>3</sub>	135.83
C <sub>6</sub>	133.31	C <sub>6</sub>	135.21
C <sub>2</sub>	130.46	C <sub>2</sub> ,C <sub>4</sub>	129.19
C <sub>5</sub>	127.13	C <sub>1</sub> ,C <sub>5</sub>	124.26
C <sub>4</sub>	126.57	C <sub>10</sub>	39.71
C <sub>3</sub>	126.19	C <sub>9</sub>	39.29
C <sub>10</sub>	39.70	C <sub>11</sub>	20.66
C <sub>9</sub>	39.29	-	-
C <sub>11</sub>	17.63	-	-

Both molecules adopt the common *trans-cis* configuration with respect to the positions of the chlorocarbonyl and aryl groups respectively, against the thiono about their C-N bonds. The central carbonyl thiourea moieties in both molecules [S1A\C7A\N1A\N2A\C8A\O1A] and [S1B\C7B\N1B\N2B\C8B\O1B] are nearly planar with maximum deviations of -0.109(8) Å for N1A atom and 0.115(8) Å for O1B atom respectively. Both central carbonyl thiourea moieties make a dihedral angle of 37.3(4) and 46.3(4) $^\circ$  with phenyl rings of [C1A-C6A] and [C1B-C6B], respectively. The bond lengths and angles of the molecule are in normal ranges (Allen et al.1987) and comparable to those in its analog of *N*-(3-chloropropionyl)-*N'*- phenylthiourea (Othman et al. 2010). There are two intramolecular hydrogen bond for each molecule, N1-H1 $\cdots$ O1 and C5-H5 $\cdots$ S1 (Table 4). The crystal structure is stabilized by N2-H2 $\cdots$ S1 and C11-H11 $\cdots$ C11 intermolecular hydrogen bonds (Fig. 5)

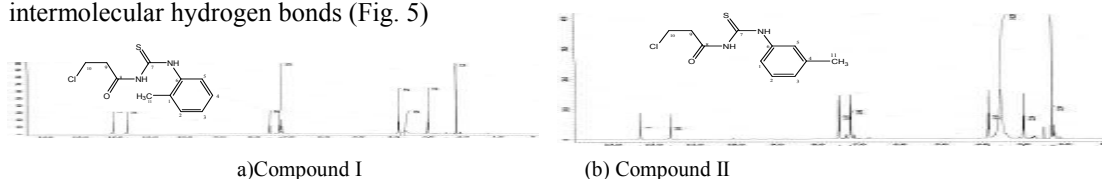
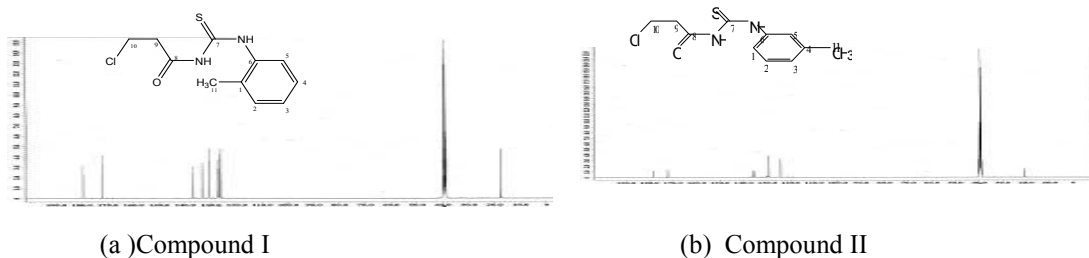
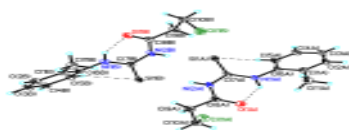


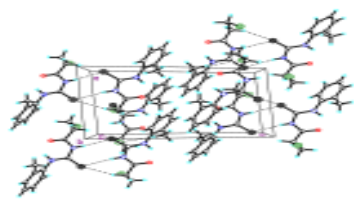
Figure 2.  $^1\text{H}$  NMR Spectral spectra of (a) *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl) thiourea(I) and (b) *N*-(3-chloropropionyl)-*N'*-(4-methylphenyl)thiourea(II) in DMSO- $d_6$ .

(a) Compound I

(b) Compound II

Figure 3.  $^{13}\text{C}$  NMR Spectral spectra of (a) *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl) thiourea(I) and (b) *N*-(3-chloropropionyl)-*N'*-(4-methylphenyl)thiourea(II) in DMSO- $d_6$ .Figure 4. The molecular structure of *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl)thiourea with 50% probability displacement ellipsoids. The dashed line indicates the intramolecular hydrogen bond.Table-4: Hydrogen geometric parameters (A, °) of *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl) thiourea

D—H...A	D—H	H...A	D...A	D—H...A
N1A-H1NA.....O1A	0.88(9)	1.97(9)	2.630(10)	131.(7)
N2B-H2NB.....S1A	0.91(11)	2.51(11)	3.394(7)	165.(7)
N1B-H1NB.....O1B	0.96(12)	1.85(11)	2.629(10)	136.(9)
N2A-H2NA.....S1B	0.90(12)	2.54(12)	3.416(7)	166.(9)
C5A-H5AA.....S1A	0.95	2.70	3.180(8)	112
C5B-H5BA.....S1B	0.95	2.83	3.241(8)	107
C11B-H11D.....C11A	0.98	2.81	3.775(10)	1170
C9B-H9BB.....S1A	0.99	2.81	3.716(10)	152

Figure 5: Molecular packing of *N*-(3-chloropropionyl)-*N'*-(2-methylphenyl)thiourea (I) viewed down the b axis.

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