

Full Length Research Paper

Synthesis, spectral characterization and crystal structural of 1-(2-Morpholinoethyl)-3-(3-phenylacryloyl)thiourea

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Accepted 9 November, 2011

Novel cinnamoyl thiourea derivative of 2-morpholino ethylamine, namely 1-(2-Morpholinoethyl)-3-(3-phenylacryloyl)thiourea have been successfully synthesized. The reaction of cinnamoylisothiocyanate with 2-morpholino ethylamine gave the compounds (I). The new compound was analyzed and characterized by typical spectroscopic techniques, namely IR and ¹H and ¹³C multi-nuclear magnetic resonance (NMR). The structure of I was determined by single crystal X-ray diffraction method and crystallised in the triclinic system with space group P $\bar{1}$, a = 6.1452(14)Å, b = 9.731(2)Å, c = 14.690(3)Å, α = 98.711(4)°, β = 93.971(4)°, γ = 104.444(4)° and Z = 2. The molecule adopts cis-trans configuration with respect to the position of the 2-morpholino ethylamine moiety and cinnamoyl groups against the S atom across the C-N bonds. The infrared spectra of I showed four significant stretching vibrations of $\nu(\text{N-H})$, $\nu(\text{C=O})$, $\nu(\text{C-N})$ and $\nu(\text{C=S})$ at 3167, 1675, 1330 and 845 cm⁻¹, respectively. The ¹³C NMR chemical shift for the thiourea moiety appeared at ca. δ C 179 ppm.

Key words: Thiourea, spectroscopy, x-ray crystallography.

INTRODUCTION

Thiourea derivatives derived as substituted aroylthiourea derivatives are attractive model compounds for the studies in solid-state chemistry due to their tendency for the formation of intra- and intermolecular hydrogen bonds of the N-H proton-donor groups to sulphur and carbonyl oxygen atoms (El-Bahy et al., 2003; Rachid et al., 2009). To date, these derivatives are widely used in numerous applications, such as in pharmaceutical industry for potential therapeutic agents as antibacterial (Farrugia et al., 1997; Ahmad et al., 2010; Win et al., 2010), anti-HIV, anticancer drugs, antidepressants and antihyperlipidemic, anti-allergic, antiparasitic, platelet antiaggregating and antiproliferative activities (Rauf et al., 2006; Yusof et al., 2007a, b; Salih and Satyanarayana, 2009). Previous studies have reported that the compounds containing thiourea moieties. Have been used extensively and

commercially as herbicides, fungicides and insecticides agents in the agrochemical industries (Yamin et al., 2008a, b; Yusof et al., 2006). Several studies have revealed that thiourea derivatives have not only been used in medical and agriculture applications, but also, they play major contribution in the environmental and industrial applications. The chelating resin was reported to be derived from copolymerization of bithiourea/thiourea/glutaraldehyde which was successfully applied to determine Hg(II) from a real matrix (Donia et al., 2008). On the other hand, thiourea and its derivatives can serve as useful host material or inclusion compounds exhibiting wide range applications in the development of electronics and optoelectronics devices (Merchan et al., 2008; Lam et al., 2000; Prakash et al., 2011). Thiourea and its derivatives have been found as an effective corrosion inhibitors agent, because sulphur atom is easily protonated in acidic solution (Shen et al., 2006; Rafiquee et al., 2007). Thiourea ligands are thermally stable and insensitive to air and moisture, thus, the reaction may be

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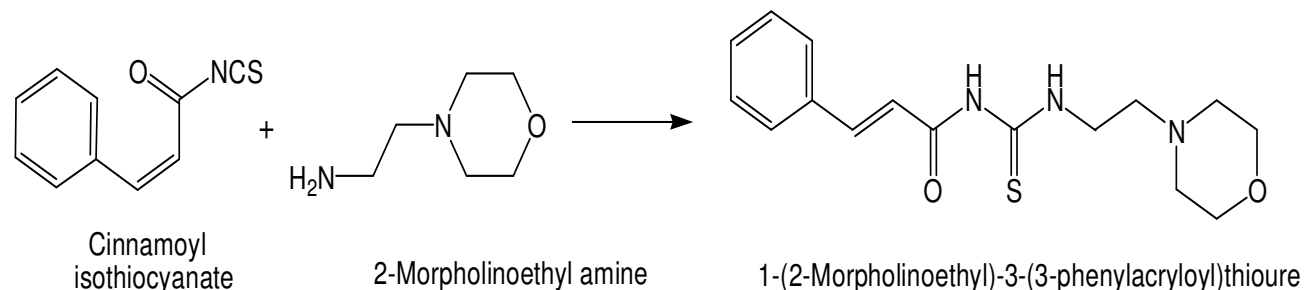


Figure 1. Reaction of cinnamoyl isothiocyanate with 2-morpholinoethyl amine.

conducted at ambient environment (Yang et al., 2004; Dai et al., 2004; Zhang and Allen, 1999). The survey of literature reveals that no work has been reported on the synthesis of 1-(2-morpholinoethyl)-3-(3-phenylacryloyl) thiourea. This novel compound was very interesting, of which we can carry out a lot of synthetic reactions, especially with cinnamoylthiourea derivatives.

EXPERIMENTAL

Physical measurements

All chemicals were purchased from Sigma Aldrich or MERCK and were used as received without further purification. Infrared spectra of the synthesised compounds were recorded from KBr pellets using Fourier transform infrared (FTIR) Perkin Elmer 100 Spectrophotometer in the spectral range of 4000-400 cm^{-1} . ^1H 400.11 MHz and ^{13}C 100.61 MHz nuclear magnetic resonance (NMR) spectra were recorded using Bruker Avance III 400 Spectrometer in DMSO- d_6 as a solvent at room temperature in the range between 0 to 15 ppm and 0 to 200 ppm. Room temperature diffraction data for 2a was collected on a Bruker SMART APEX 4 K CCD diffractometer (Mo K α radiation, $k = 0.71073\text{\AA}$). The structure was solved and refined by using SHELX suit (Sheldrick, 1997). All non-hydrogen atoms were refined anisotropically. The perspective view of the molecule was obtained using ORTEP-32 for Windows (Farrugia, 1997). Data collection: SMART (Bruker, 2000); cell refinement: SAINT (Bruker, 2000); data reduction: structure: SHELXS 97 (Sheldrick, 1997); molecular graphics: SHELXL 97 (Sheldrick, 1997); software used to prepare material for publication: SHELXTL (Sheldrick, 1997) and PLATON: software to calculate the hydrogen bonds (Spek, 2009).

Preparation of 1-(2-Morpholinoethyl)-3-(3-phenylacryloyl)-thiourea

Cinnamoyl isothiocyanate was first prepared by adding an acetone solution containing ammonium thiocyanate into cinnamoyl chloride in acetone. The mixtures were stirred for 10 min before the precipitate was filtered and washed with cold acetone. The reaction between cinnamoyl isothiocyanate and 2-morpholino ethylamine in acetone was stirred for 15 min under 70°C with a mol ratio of 1:1. The mixture was refluxed for 3 h and filtered into a beaker containing some ice. White precipitate of 1-(2-Morpholinoethyl)-3-(3-phenylacryloyl) thiourea, with a melting point of 177.3 to 178°C, was formed immediately (Figure 1).

RESULTS AND DISCUSSION

Spectroscopic studies

Spectroscopic studies infrared spectra of (I) reveal all the expected frequency region of the $\nu(\text{N-H})$, $\nu(\text{C=O})$, $\nu(\text{C-N})$ and $\nu(\text{C=S})$. The band at 3167 cm^{-1} represent stretching vibration of the $\nu(\text{N-H})$ in the secondary thioamide group. This assignment was supported by the literature that $\nu(\text{N(2)-H(2)})$ can be seen at above 3000 cm^{-1} , have been examined due to the existence of intramolecular hydrogen bonding (Bencivenni et al., 1998; Rauf et al., 2006; Yuan et al., 1997; Mido et al., 1995). The trans-cis conformation of the novel compound is related to the N-H stretching frequencies range which depends on the position-NHC(S)NHC(O)-group vibration and stabilized by hydrogen bonding. The carbonyl band $\nu(\text{C=O})$ of the title compound is clearly observed at above 1660 cm^{-1} which might be related to the resonance effect with the phenyl rings and existence of intramolecular hydrogen bonding with N-H (Estévez et al., 2005; Nasir et al., 2011a, b, c, d), whilst the $\nu(\text{C=S})$ stretching vibration can be observed at 845 cm^{-1} that is in close agreement with previous studies of other thiourea derivatives (Rauf et al., 2006; Estévez et al., 2005; Yuan et al., 1997). For instance, this vibrational mode shows a good agreement with the 3-monosubstituted furoylthioureas series in the wide range at ca. 700 cm^{-1} (Yuan et al., 1997; Baul et al., 2001). The FTIR spectra are as shown in Figure 2.

In ^1H NMR spectrum, the unresolved resonance of aromatic protons of (I) can be clearly observed as distinctive multiplet resonances between δH 7.21 to 7.95 ppm. These characteristics are due to the overlapping proton signals in the aromatic rings. Two signals noted as singlet, corresponds to one proton at ca. δH 9 ppm which is assigned to the N(1)H proton which is substituted to the carbonyl and N(2)H proton and to the thione presence at ca. δH 10 ppm. These signals are different in term of chemical shift which is due to the intramolecular hydrogen bonded N-H bonds in the trans and cis conformations, respectively. As seen, both NH signals are very close chemical shifts between δH 9 to 10 ppm due to deshielding aromatic ring. In ^{13}C NMR spectrum,

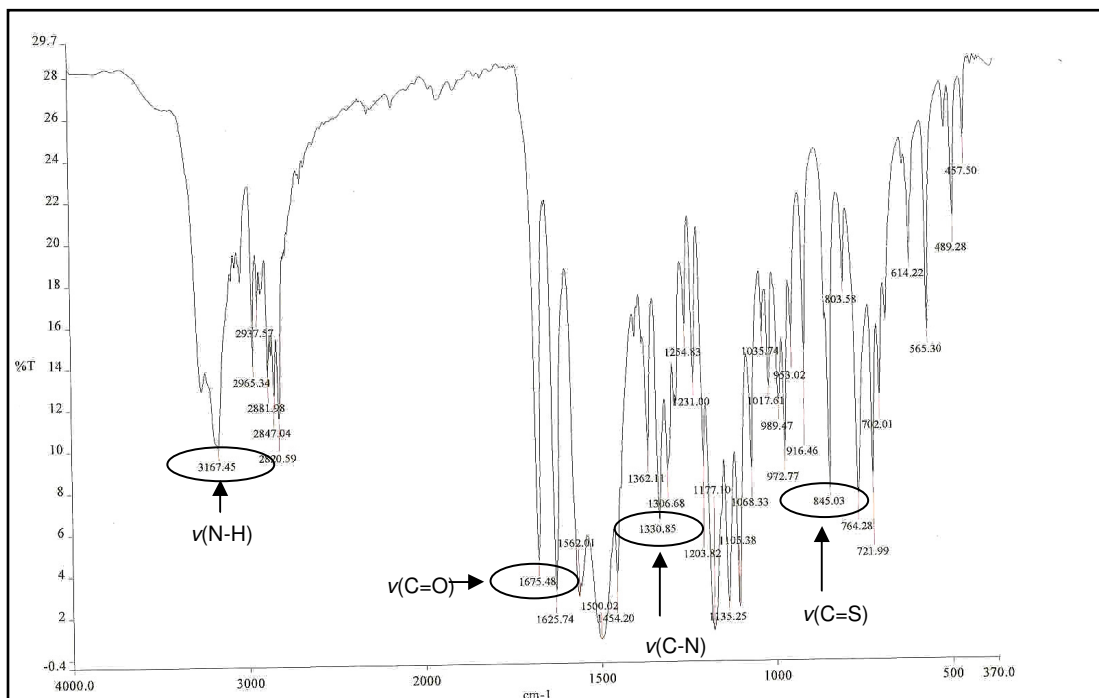


Figure 2. Infrared spectrum of (I).

the aromatic carbon resonances can be found between δ C 128.4 to 130.9 ppm which is corresponding to phenyl rings in the compounds. The carbonyl and thione carbons can be clearly observed at between δ C 179.5 to 165.2 ppm and more slightly deshielded in the spectrum. Formation of intramolecular hydrogen bonding, the increasing electronegative of oxygen and sulphur atoms and different environment and conformations cause a deshielding effect for these signals.

Crystal structure determination of I

Molecule I is discrete, crystallised in triclinic crystal system with $P\bar{1}$ space group, $a = 6.1452(14)\text{\AA}$, $b = 9.731(2)\text{\AA}$, $c = 14.690(3)\text{\AA}$, $\alpha = 98.711(4)^\circ$, $\beta = 93.971(4)^\circ$, $\gamma = 104.444(4)^\circ$ and $Z = 2$. The crystallographic and refinement data of I is shown in Table 1.

The title compound, I, is analogous to the previously reported, cinnamoylthiourea, methyl 2-(3-cinnamoylthioureido)acetate and ethyl 2-(3-cinnamoylthioureido)acetate (Hassan et al., 2010a, b, c) with the difference of 2-morpholinoethyl amine replaced by the hydrogen atom, methyl 2-aminoacetate and ethyl 2-aminoacetate groups (Figure 3). The compound adopts trans-cis configuration with respect to the position of the cinnamoyl and 2-morpholinoethyl amine groups relative to the S1 atom across their C10-N1 and C10-N2 bonds, respectively. The cinnamoyl and 2-morpholinoethyl

groups are trans and cis, respectively, to the S atom across the thiourea C-N bonds (Table 2). The morpholine group adopts a chair conformation. The bond lengths and angles are in normal ranges (Allen et al., 2004) and in agreement with other thiourea derivatives reported previously (Hassan et al., 2009; Hassan et al., 2011). The C7-C8 bond [$1.311(3)\text{\AA}$] has double-bond character, with a trans configuration with respect to the H atoms at both C atoms. The maximum deviation from the plane of the central fragment (S1/O1/N1/N2/C7-C10) is $0.049(2)\text{\AA}$ for atom O1. The dihedral angle between this plane and the phenyl group (C1-C6) is $22.39(9)^\circ$.

Three intramolecular hydrogen bonds, $N2-H2A\cdots O1$, $N2-H2A\cdots N3$ and $C7-H7\cdots O1$, are observed (Figure 4 and Table 3). As a result, two pseudo-five-membered (C7/C8/C9/O1/H and N3/C12/C11/N2/H2A) and one pseudo-six-membered (C9/N1/C10/N2/H2A/O1) rings are formed. In the crystal structure, the molecule is stabilized by intermolecular $N1-H1A\cdots O2i$ [symmetry code: (i) $x, 1 +, z$; (Table 2)] hydrogen bonds, forming one-dimensional chains extending along the b axis (Figure 3).

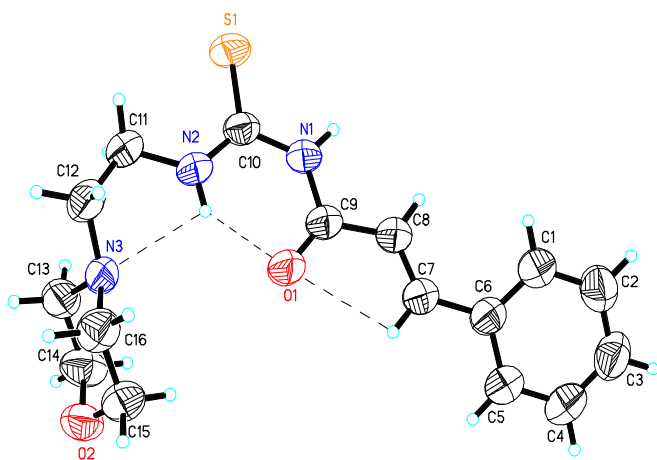
H atoms of both C and N atoms were positioned geometrically and allowed to ride on their parent atoms, with $U_{iso} = 1.2U_{eq}$ (C) for aromatic 0.93\AA , $U_{iso} = 1.2U_{eq}$ (C) for CH2 0.97\AA , $U_{iso} = 1.5U_{eq}$ (C) for CH3 0.96\AA and $U_{iso} = 1.2U_{eq}$ (N) for N-H 0.86\AA .

Conclusion

Novel thiourea derivative of 1-(2-morpholinoethyl)-3-(3-

Table 1. Crystal data and structure refinement for I.

Parameter	Data
Empirical formula	C ₁₆ H ₂₁ N ₃ O ₂ S
Formula weight	319.42
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, <i>P</i> $\bar{1}$
Unit cell dimensions	$a = 6.1452(14)$ Å $\alpha = 98.711(4)^\circ$ $b = 9.731(2)$ Å $\beta = 93.971(4)^\circ$ $c = 14.690(3)$ Å $\gamma = 104.444(4)^\circ$
Volume	835.6(3) Å ³
Z, Calculated density	2, 1.270 Mg/m ³
Absorption coefficient	0.20 mm ⁻¹
F (000)	340
Crystal size	0.41 × 0.34 × 0.20 mm
Theta range for data collection	1.41 to 26.0°
Limiting indices	-7 ≤ h ≤ 7, -12 ≤ k ≤ 12, -18 ≤ l ≤ 18
Reflections collected / unique	8635 / 3267 [R(int) = 0.0190]
Completeness to theta = 26.00	99.5 %
Max. and min. transmission	0.9603 and 0.9210
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3267 / 0 / 199
Goodness-of-fit on F ²	1.174
Final R indices [I > 2σ(I)]	R ₁ = 0.0538, wR ₂ = 0.1243
R indices (all data)	R ₁ = 0.0654, wR ₂ = 0.1298
Largest diff. peak and hole	0.214 and -0.156 e.Å ⁻³

**Figure 3.** Crystal structure of I.

phenylacryloyl)thiourea has been successfully prepared and fully characterised by typical spectroscopic methods. Its conformation is analogous to other aroylthiourea and the presence of inter- and intramolecular hydrogen measurements and single crystal X-ray diffractometer data. The molecular structure of the new compound was determined using single crystal X-ray diffractometer and exhibit triclinic crystal system. This new derivative is

Table 2. Selected bond lengths Å and angles ° for I.

Bond length (Å)			
S1-C10	1.389 (3)	N1-C10	1.6675 (19)
O1-C9	1.219 (2)	N2-C10	1.314 (3)
O2-C15	1.425 (3)	N2-C11	1.449 (3)
O2-C14	1.426 (3)	C11-C12	1.503 (3)
N1-C9	1.377 (2)	C7-C8	1.311 (3)
Bond angle (°)			
C9-N1-C10	28.18 (17)	N1-C9-C8	114.75 (18)
C10-N2-C1	124.72 (17)	N2-C10-S1	124.57 (15)
O1-C9-N1	22.44 (19)	N1-C10-S1	119.00 (15)
O1-C9-C8	22.82 (18)	N2-C11-C12	108.08 (17)
N2-C10-N1	16.43 (17)	-	-

currently bringing great potential and interest in the coordination chemistry as it polydentate ligands to bind with wide range of metal ions for numerous promising applications in the near future bonding is supported by the IR spectra, NMR.

ACKNOWLEDGEMENTS

The authors thank Universiti Kebangsaan Malaysia for

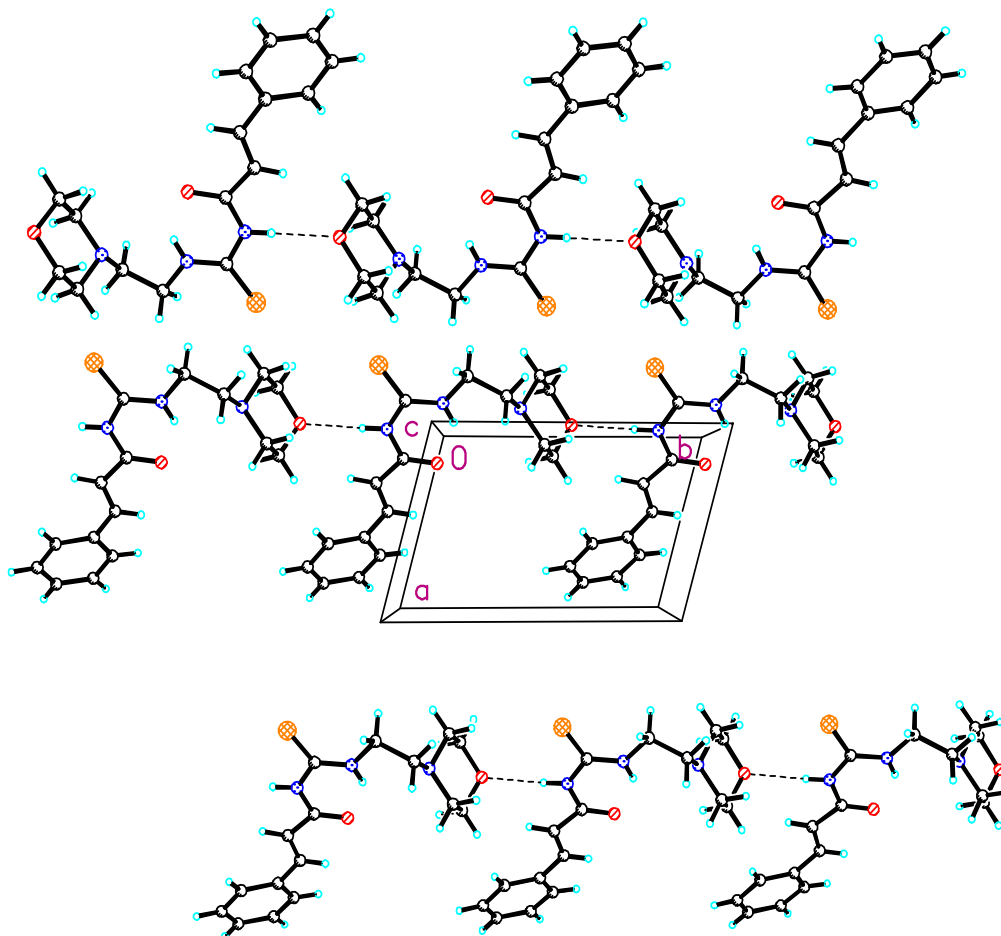


Figure 4. Crystal packing for I.

Table 3. Hydrogen bonding geometry (Å), (°).

D-H...A	D-H	H...A	D...A	D-H
N2-H2A...O1	0.86	1.95	2.642 (3)	136
N2-H2A...N3	0.86	2.39	2.758 (2)	107
C7-H7...O1	0.93	2.48	2.813 (3)	101
N1-H1A...O2 ⁱ	0.86	2.27	3.114 (2)	169

Symmetry code: (i) = x, 1+y, z.

providing the facilities and grants (postdoctoral for I. N. Hassan, UKM-GUP-BTT-07-30-190 and UKM-OUP-TK-16-73/2010&2011) and the Kementerian Pengajian Tinggi, Malaysia for the research fund No. UKM-ST-06-FRGS0111-2009.

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