



Synthesis, Characterization, Spectroscopic and X-Ray Diffraction Studies of Novel Pair of Thiourea Derivatives of 2-Morpholin-4-yl-ethylamine

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A novel pair of thiourea derivatives of cinnamoyl and benzoyl with 2-morpholin-4-yl-ethylamine namely 1-(2-morpholinoethyl)-3-cinnamoylthiourea (**I**) and 1-(2-morpholinoethyl)-3-benzoylthiourea (**II**) have been successfully synthesized and characterized *via* IR, NMR, CHNS-O, UV techniques and X-ray diffraction for single crystal. The important stretching bands for $\nu(\text{C}=\text{O})$, $\nu(\text{N}-\text{H})$, $\nu(\text{C}=\text{S})$ and $\nu(\text{C}-\text{N})$ were around 1600, 3300, 700 and 1300 cm^{-1} , respectively, were shown by IR spectra. There is an important chromophore, $\text{C}=\text{O}$, observed in the UV spectra with a maximum absorption at around 240 nm. The crystal structures of (**I**) and (**II**) have been determined by X-ray diffraction analysis for single crystal. Both the molecules adopt *trans-cis* configuration relative to the position of phenyl ring and 2-morpholin-4-yl-ethyl groups with respect to the thiono S atom, across C-N bonds. In both compounds, there were two intramolecular hydrogen bonds, $\text{N}-\text{H}\cdots\text{O}$ and $\text{N}-\text{H}\cdots\text{N}$, that form of pseudo-six-membered and pseudo-five-membered rings, respectively, in addition to a pseudo-five-membered ring, $\text{C7}-\text{H6}\cdots\text{O1}$, in (**I**) which stabilizes the molecule. In the crystal frame, the molecules were linked by intermolecular hydrogen bonds $\text{N}-\text{H}\cdots\text{O}$ and $\text{C}-\text{H}\cdots\text{O}$ forming polymeric (**I**) and chain network (**II**). ^1H NMR spectra show chemical shift at δ_{H} 10.86-10.97 ppm and δ_{H} 9.07-9.12 ppm were assigned for NH protons. While the chemical shift for ^{13}C NMR analysis of $\text{C}=\text{S}$ and $\text{C}=\text{O}$ presence at δ_{C} 169-179 ppm.

Keywords: Thiourea, Benzoyl, 2-Morpholin-4-yl-ethylamine, X-ray crystallography.

INTRODUCTION

Thiourea derivatives derived as substituted aroylthiourea derivatives are attractive compounds in solid-state chemistry because of their tendency for the formation of intramolecular and intermolecular hydrogen bonds of the N-H proton-donor groups to carbonyl oxygen and sulphur atoms¹⁻³. These derivatives are commonly used in many applications such as anti-cancer drugs, antibacterial, platelet antiaggregating, antidepressants, anti-HIV, antihyperlipidemic, antiparasitic, antiallergic and antiproliferative activities⁴⁻⁶. Previous studies reported that thiourea compounds moieties have been used widely as herbicides, insecticides and fungicides agents⁷⁻¹⁰. In addition to medical and agriculture applications, thiourea derivatives also play major influence in the industrial and environmental applications. Alternatively, thiourea derivatives are useful inclusion compounds or host material showing varied applications in developing the electronics and optoelectronics devices^{11,12}. Due

to the sulphur atom is easily protonated in acidic solution, thiourea derivatives are an effective corrosion inhibitors agents^{13,14}. Thiourea ligands are insensitive to air and moisture and thermally stable may be carried on at an ambient environment¹⁵⁻¹⁷. The survey of literature reveals that no work has been reported on the synthesis of cinnamoyl and benzoyl thiourea with 2-morpholin-4-yl-ethylamine. These novel compounds were very interesting that we can carry out a lot of synthetic reactions, especially with cinnamoyl thiourea derivatives. Therefore, the spectral and structural properties of 1-(2-morpholinoethyl)-3-cinnamoyl-thiourea (**I**) and 1-(2-morpholinoethyl)-3-benzoylthiourea (**II**) (Fig. 1) are discussed in this paper.

EXPERIMENTAL

All chemicals used were purchased from Sigma Aldrich or MERCK. Infrared spectra (IR) of the novel compounds were recorded from KBr pellets using Perkin Elmer FTIR 100

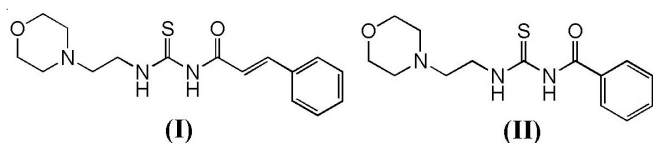


Fig. 1. Molecular structural representations of 1-(2-morpholinoethyl)-3-cinnamoylthiourea (**I**) and 1-(2-morpholinoethyl)-3-benzoylthiourea (**II**)

spectrophotometer in the range of 4000–400 cm^{-1} . NMR spectra for ^1H 400.11 MHz and ^{13}C 100.61 MHz were recorded using NMR Bruker Avance III 400 Spectrometer in $\text{DMSO-}d_6$ as a solvent at room temperature in the range of 0–15 ppm and 0–200 ppm. The structure of the new compounds was solved and refined using SHELX¹⁸. The view of the molecule was obtained by using ORTEP-32 for Windows¹⁹. Data collection: SMART²⁰; molecular graphics: SHELXL 97²¹; cell refinement: SAINT and data reduction: structure: SHELXS 97²² software used to prepare material for publication: SHELXTL²³ and PLATON software to calculate the hydrogen bonds²⁴.

Synthesis of compounds I and II: Cinnamoyl/benzoyl isothiocyanate was first prepared by adding an acetone solution containing ammonium thiocyanate into cinnamoyl/benzoyl chloride in acetone. The mixtures were stirred for 10 min before the precipitate was then filtered and washed in cold acetone. The reaction between of cinnamoyl/benzoyl isothiocyanate and 2-morpholino ethylamine in acetone was stirred for 15 min under 70 °C with a mol ratio of 1:1. The combination was refluxed for 3 h and filtered and poured onto ice. White precipitate was formed immediately, with a melting point of 176.3–179.1 °C, filtered off and underwent product isolation (Fig. 2).

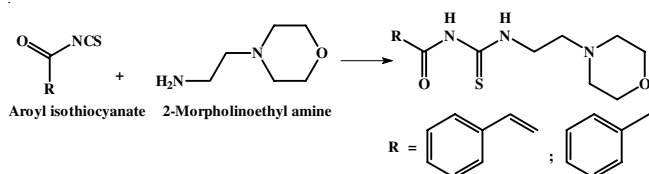


Fig. 2. Synthetic routes of cinnamoyl/benzoyl isothiocyanate with 2-morpholinoethyl amine

RESULTS AND DISCUSSION

Infrared spectra: The IR spectra revealed the expected frequencies of the $\nu(\text{N-H})$, $\nu(\text{C=O})$, $\nu(\text{C-N})$ and $\nu(\text{C=S})$ in both compounds. An average intensity bands at 3167.45 cm^{-1} (**I**) and 3315.15 cm^{-1} (**II**) relates to stretching $\nu(\text{N-H})$ (Fig. 3). The stretching band of $\nu(\text{N-H})$ (**I**) has lower frequency comparing with compound (**II**) because of the position of electron withdrawing group around NH moiety. The absorption bands nearby 1675.48 cm^{-1} represent the stretching of $\nu(\text{C=O})$ and it differs in frequencies comparing with typical carbonyl (1700 cm^{-1})²⁵. This due to conjugated resonance of phenyl group and the formation of intramolecular hydrogen bonding with N-H²⁶. The stretching vibrations of $\nu(\text{C-N})$ band are at 1330.85 cm^{-1} (**I**) and 1313.30 cm^{-1} (**II**). The bands around 870 cm^{-1} show the stretching of $\nu(\text{C=S})$. From IR spectra, (Table-1) shows that thiourea group of compounds (**I**) and (**II**) in agreement with previous studies^{27,28}.

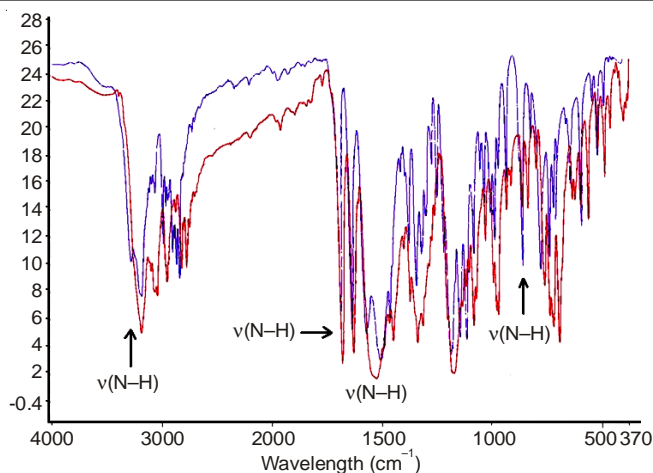


Fig. 3. FTIR spectra of compounds (**I**) and (**II**)

TABLE-1
IR ABSORPTION DATA FOR COMPOUNDS (**I**) AND (**II**)

Compound	Wavenumber (cm^{-1})			
	$\nu(\text{N-H})$	$\nu(\text{C=O})$	$\nu(\text{C-N})$	$\nu(\text{C=S})$
(I)	3167.45	1675.48	1330.85	845.03
(II)	3315.15	1672.68	1313.30	870.41

Ultraviolet spectra: UV absorption for compounds (**I**) and (**II**) exhibit $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition (HOMO \rightarrow LUMO). The ultraviolet spectra showed an important bands for chromophore carbonyl (C=O) group. Both compounds show maximum absorption bands for chromophore C=O in compounds (**I**) and (**II**) at 243.90 nm and 241.00 nm, respectively (Fig. 4). Table-2 shows the maximum absorption (**I**) and (**II**).

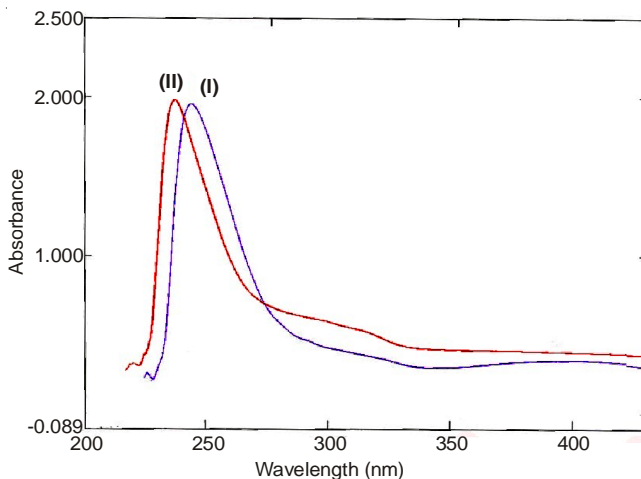


Fig. 4. UV spectra of compounds (**I**) and (**II**)

TABLE-2
UV ABSORPTION OF COMPOUNDS (**I**) AND (**II**)

Compound	$\nu(\text{C=O}) \lambda_{\text{max}}$ (nm)	$\nu(\text{C=O})$ transition
(I)	243.90	$n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$
(II)	241.00	$n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$

X-ray crystallographic studies: Both compounds (**I**) and (**II**) were obtained as single crystals suitable for X-ray diffractometer analysis (Table-3). Both compounds adopt *cis-trans* configuration with respect to position of 2-morpholino-4-yl-ethyl and the phenyl groups relative to the S atom, across

TABLE-3
CRYSTAL DATA FOR COMPOUNDS (I) AND (II)

Subject	(I)	(II)
Empirical formula	C ₁₆ H ₂₁ N ₃ O ₂ S	C ₁₄ H ₁₉ N ₃ O ₂ S
Formula weight	148.15	1173.53
Crystal system	Triclinic	Monoclinic
Space group	P $\bar{1}$	C 2/c
a (Å)	6.1452(14)	31.033(3)
b (Å)	9.731(2)	5.9352(6)
c (Å)	14.690(3)	20.0798(14)
α (°)	98.711(4)	90
β (°)	93.971(4)	123.099(5)
γ (°)	104.444(4)	90
Volume (Å ³)	835.6(3)	3098.3(5)
Z, Calculated density (mg/m ³)	2, 1.270	1, 0.629
Absorption coefficient (mm ⁻¹)	0.20	0.107
F(000)	340	624
Crystal size (mm)	0.41 × 0.34 × 0.20	0.41 × 0.29 × 0.23
Crystal description	Slap	Slap
Crystal colour	Colourless	Colourless
θ Range°	1.41-26.0	1.57-28.33
Index ranges	-7 ≤ h ≤ 7 -12 ≤ k ≤ 12 -18 ≤ l ≤ 18	-40 ≤ h ≤ 39 -7 ≤ k ≤ 7 -26 ≤ l ≤ 26
Independent reflections	8635/3267 [R(int) = 0.0190]	16865/3695 [R(int) = 0.0359]
Max. and min. transmission	0.9603 and 0.9210	0.9758 and 0.9575
Procession method	Full-matrix least-squares on F ²	Full-matrix least-squares on F ²
Data/restraints/parameters	3267/0/199	3695/0/200
Goodness-of-fit on F ²	1.174	1.212
Largest diff. peak (e.Å ⁻³)	0.214	0.305
Largest diff. hole (e.Å ⁻³)	-0.156	-0.145
R, wR	0.0538, 0.1243	0.0589, 0.1491
RwR (all reflection)	0.0654, 0.1298	0.0923, 0.1652

C-N bonds (Figs. 5 and 6). The central moiety, C7/O1/N1/S1/N2/C8/C9/C10, in compound (I) [maximum deviation 0.049(2) Å at atom O1] and the phenyl group (C1-C6) are planar and dihedral angle between the least planes is 22.39(9)°. The morpholine group adopts a chair conformation. The C7-C8 of the bond length [1.311(3) Å] is a double bond character and has H atoms at C7 and C8 atoms *trans* to each other.

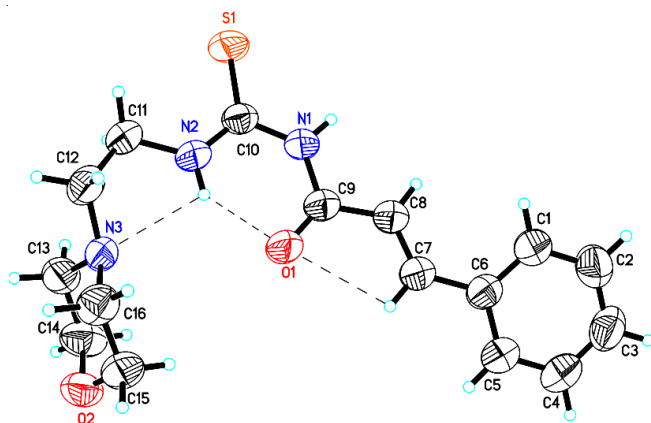


Fig. 5. Molecular structure of 1-(2-morpholinoethyl)-3-cinnamylthiourea (I) (with 50 % probability displacement ellipsoids) with intramolecular hydrogen bonds

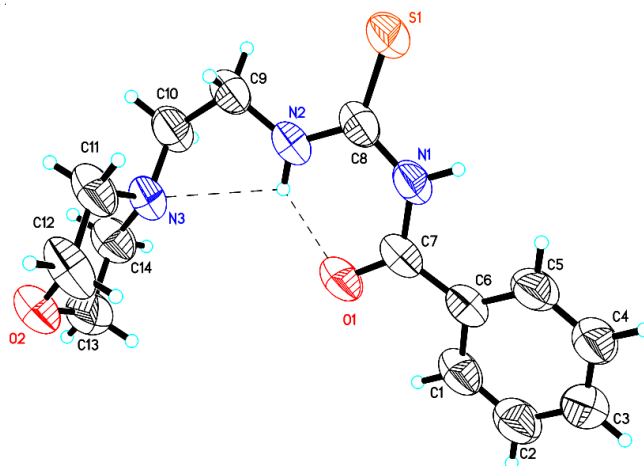


Fig. 6. Molecular structure of 1-(2-morpholinoethyl)-3-benzoylthiourea (II) (with 50 % probability displacement ellipsoids) with intramolecular hydrogen bond

Table-4 showed that the bond lengths and angles were in normal ranges²⁹ and analogous to other thiourea derivatives^{30,31}. Nevertheless, N1-C10 in (I) is longer than N2-C10 by 0.075 Å, while in (II) N1-C8 is longer than N2-C8 by 0.091 Å. The differences are probably because of the interaction of the intramolecular hydrogen bonding³². C=O and C=S bond distances for (I) and (II) show the expected double bond character.

TABLE-4
SELECTED BOND LENGTHS (Å) AND ANGLES (°) FOR COMPOUNDS (I) AND (II)

Bond	Bond distances (Å)	Distances	Angles distances (°)
Compound (I)			
S1-C1	1.6675(19)	C9-N1-C10	128.18(17)
O1-C9	1.219(2)	C10-N2-C11	124.72(17)
O2-C15	1.425(3)	O1-C9-N1	122.44(19)
O2-C14	1.426(3)	O1-C9-C8	122.82(18)
N1-C9	1.377(2)	N2-C10-N1	116.43(17)
N1-C10	1.389(3)	N2-C10-S1	124.57(15)
N2-C10	1.314(3)	N1-C10-S1	119.00(15)
Compound (II)			
S(1)-C(8)	1.661(2)	C(7)-N(1)-C(8)	128.46(15)
O(1)-C(7)	1.220(2)	C(8)-N(2)-C(9)	124.49(17)
N(1)-C(7)	1.372(2)	O(1)-C(7)-N(1)	121.85(19)
N(1)-C(8)	1.400(3)	N(1)-C(8)-S(1)	118.49(13)
N(2)-C(8)	1.309(2)	N(2)-C(8)-N(1)	116.50(17)
N(2)-C(9)	1.445(3)	N(2)-C(8)-S(1)	125.01(17)

There are two intramolecular hydrogen bonds in both molecules, N-H...N and N-H...O, which form pseudo-six-membered and pseudo-five-membered rings, respectively, in addition to a pseudo-five-membered ring, C7-H6...O1, in (I) which further stabilizes the molecule (Table-5). Molecule (I) has bit shorter distance of N2-H2...O1, 2.642(3) Å comparing with (II), the distance of N2-H2...O1 was 2.645(3) Å. This difference indicates steric and electronic effect of the molecules.

In the crystal packing of (I), intermolecular hydrogen bonds N1-H1A...O2 linked the molecules to form polymeric network. Whereas in (II), the intermolecular hydrogen bonds

TABLE-5
INTRA-MOLECULAR AND INTER-MOLECULAR
HYDROGEN BOND DISTANCES (Å) AND
ANGLES (°) FOR COMPOUNDS (I) AND (II)

Compd.	D	A	D-H	H...A	D-H...A	D-H...A
Intra-molecular						
(I)	N2	O1	0.86	1.95	2.642(3)	136
	N2	N3	0.86	2.39	2.758(2)	107
	C7	O1	0.93	2.48	2.813(3)	101
(II)	N2	O1	0.86	1.96	2.645(3)	136
	N2	N3	0.86	2.49	2.827(2)	104
Inter-molecular						
(I)	N1	O2	0.86	2.27	3.114(2)	169
(II)	N1	O2	0.86	2.39	3.138(2)	146
	C2	O1	0.93	2.54	3.309(3)	140

N1-H1A...O2 and C2-H2...O1 are forming chain network (Figs. 7 and 8).

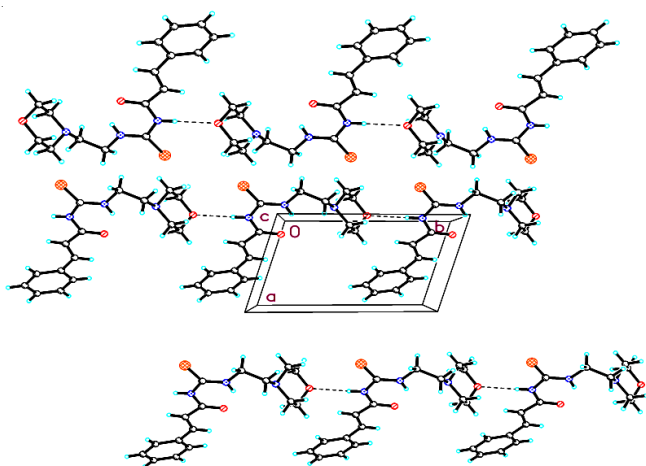


Fig. 7. Molecular packing of 1-(2-morpholinoethyl)-3-cinnamoylthiourea (I) thiourea viewed down the c-axis

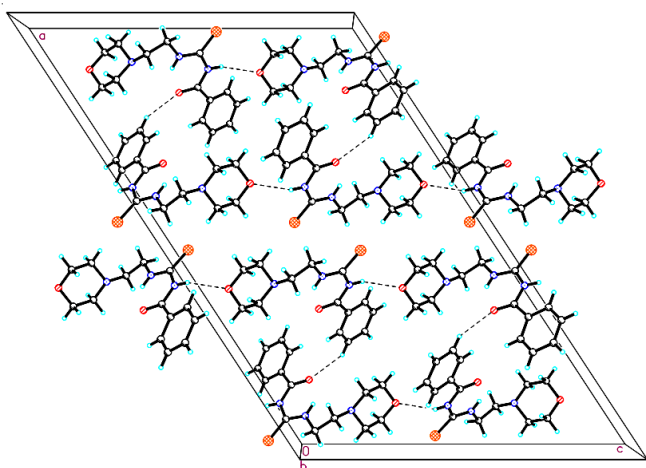


Fig. 8. Molecular packing of 1-(2-morpholinoethyl)-3-benzoylthiourea (II) viewed down the ac face.

Nuclear magnetic resonance: ^1H NMR and ^{13}C NMR spectra are comparable and reliable with the structures resulted from the X-ray analysis. There are multiplet signals at δ_{H} 7.21–7.95 ppm which represent the aromatic protons of phenyl ring in (I) and (II). The two most deshielded signals were repre-

sented NH proton at δ_{H} 9.12, δ_{H} 10.96 ppm (I) and δ_{H} 9.00, δ_{H} 10.97 ppm (II). These signals are similar to those found in the analogous molecules. The ^{13}C NMR spectra show a signal for C=S and C=O which was observed at δ_{C} 179.527 and 165.259 ppm (I) and 179.425 and 166.480 ppm (II), respectively. While the aromatic carbons of the phenyl ring were around δ_{C} 128–129 ppm for both compounds. Generally, the chemical shifts of (I) and (II) show no major difference in ^{13}C and ^1H NMR analysis.

Conclusion

In this paper, the synthesis of two novel thiourea derivatives (I) and (II) have been synthesized and characterized by using infrared, nuclear magnetic resonance analysis and ultraviolet (UV-vis). The infrared spectra show the important stretching bands for $\nu(\text{C}=\text{O})$, $\nu(\text{N}-\text{H})$, $\nu(\text{C}=\text{S})$ and $\nu(\text{C}-\text{N})$ for (I) and (II). An important vital chromophores C=O which is responsible to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition are observed in the UV spectra for both (I) and (II). The structures of the new molecules were determined by using single crystal X-ray diffraction analysis and exhibit triclinic and monoclinic crystal system in (I) and (II), respectively.

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