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RESEARCH ARTICLE

Synthesis and Characterization of New Schiff bases Derivatives of Acetohydrazide and its Cyclization Reaction

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Abstract

This work includes synthesis of hydrazide from 5-Amino-1, 3, 4-thiadiazole-2-thiol. Also reaction of hydrazide with different aromatic aldehydes by using glacial acetic acid as catalyst to synthesis of some new Schiff bases derivatives that coupled with thioglycolic acid to synthesis five- member ring heterocyclic compounds derivatives containing thiazolidinone ring. All synthetic compounds were definite by their melting point, FT-IR spectra and ^{1}H-NMR spectra for some of them.

Keywords: *5-Amino-1, 3, 4-thiadiazole-2-thiol, thiazolidinone, Schiff bases, Heterocyclic compounds, Thiadiazole.*

Introduction

Various 1, 3, 4-thiadiazole derivatives are of interest for pharmaceuticals use as well as useful intermediates in the area of organic synthesis. Thiadiazole and its derivatives show particular activity as drugs for the treatment of thrombosis, as sedative and more recently as plant activators or inducers of systemic acquired resistance (SAR) in plants [1].5-amino-1,3,4-thiadiazole-2-thiol has anti-corrosion properties and adsorbed on the metal surface and formed film that prevent corrosion of the metal [2].

Thiols (also known as mercaptans) can be define as a group of organic compounds rich in (SH) moieties. This moiety is highly reactive and is often found conjugated to other both organic and inorganic molecule [3]. Thiols, or mercaptans, are described by the general formula (R-SH), where R can be either an aromatic or an alkylic group.

They are commonly present in both liquid fuels and natural gas such as kerosene, gasoline, diesel, jet fuels and heating oils. Mercaptans are present as low molecular (C_1-C_4) and mostly straight chain compounds in gas, while in gasoline and middle distillates there are branched and heavier mercaptans [4]. 4-Thiazolidinones are known to possess antifungal, antibacterial, antituberculosis and antiviral properties [5]. Thiazolidine 2, 4-dione is widely used for designing new anti-diabetic drugs. This derivative exhibits a number of activities such as anti-cancer, anti-diabetic, anti-inflammatory, anti-arthritic, antimelanoma and anti-microbial [6]. Schiff bases are condensation products of primary amines with carbonyl group of aldehydes or ketones [7].

They are containing azomethine group (-CH=N-) and were first reported by Hugo Schiff and it mentions to the reaction between a class of compounds containing ketones or aldehydes and amino group, resulting in imine (azomethine) group [8, 9].In this research paper, a series of 1, 3, 4 thiadiazole derivatives containing Schiff bases and thiazolidinone ring were prepared and all these compound were confirmed by FT-IR.

Experimental

Synthesis of 5-((3-nitrobenzylidene) amino)-1, 3, 4-thiadiazole-2-thiol (a) [10]

A mixture of 5-amino-1,3,4-thiadiazole-2-thiol (0.0015 mole) with m-nitro benzaldehyde (0.0015 mole) in ethanol and few drops of glacial acetic acid reflux for 7 hr.

the mixture was evaporated and the formed product was recrystallized from ethanol.

Synthesis of Ethyl 2-((5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazol-2-yl) Thio) Acetate (b) [11]

Compound (a) (1g, 0.002 mole) in dimethylformamide (DMF) (10 ml) and triethyl amine (4ml, 0.028 mole) stirring at room temperature for (10-15 min.). Ethyl chloroacetate (3ml, 0.028mole) was added gradually and the mixture was stirred for ½ hr. then, it was heated for 8hr. at (70-80 C°). The mixture was poured in ice water. The oil product was separated by separating funnel with chloroform and then washed with 5% sodium bicarbonate then with distilled water. The obtained product was recrystallized with ethanol.

Synthesis of 2-((5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazol-2-yl) Thio) Acetohydrazide (c) [12]

A mixture of compound (b) (0.002 mole) was dissolved in absolute ethanol (15 ml) and hydrazine hydrate (99%, 4ml, 0.126 mole) was added to mixture with stirring. Then, the mixture was stirring for (8hr) at room temperature. The product was decantation and poured in petri dish, the product was recrystallized from ethanol.

Synthesis of New Schiff Bases 2-((5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazol-2-yl) thio) Acetohydrazide (1-8) [10]

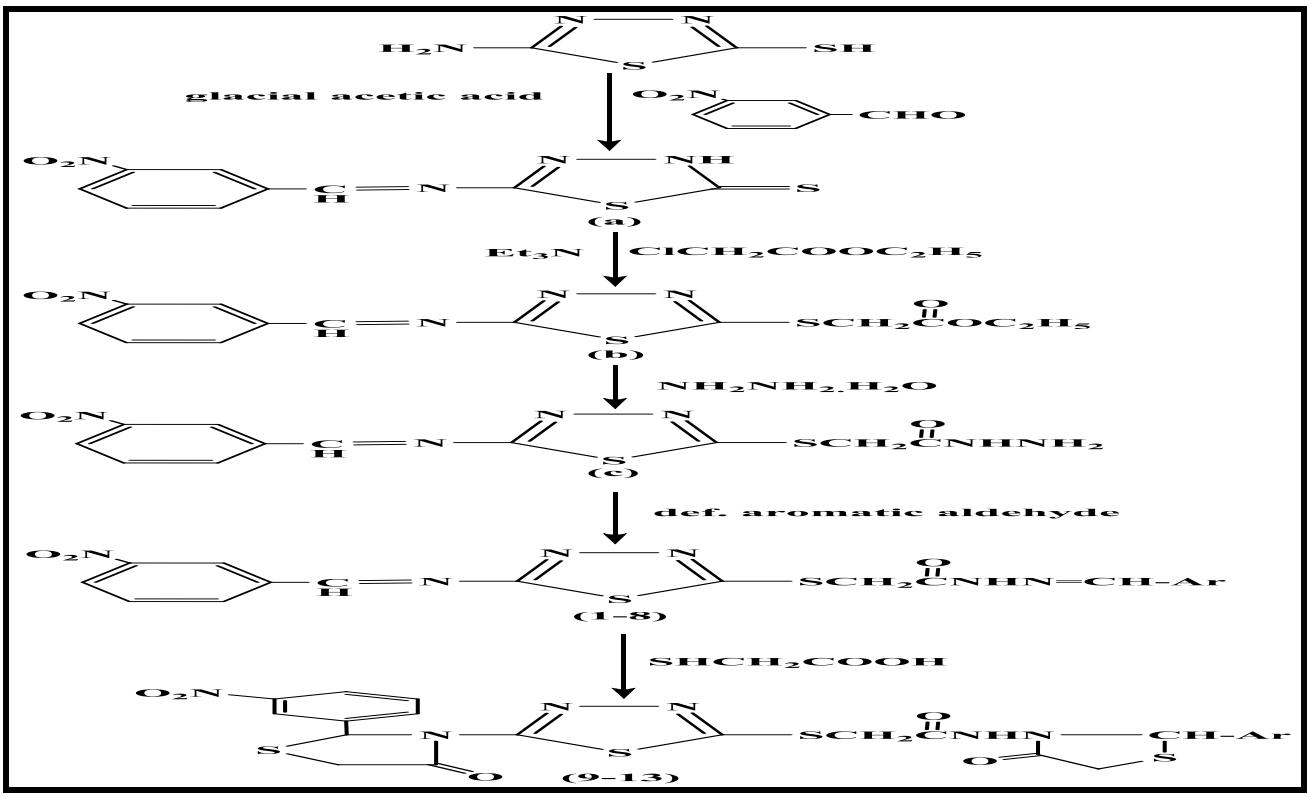
Compound (c) (0.0005mole) and different aromatic aldehyde (0.0005 mole) in absolute ethanol (15 ml) and few drops of glacial acetic acid and reflux for (9 hr) the mixture was evaporated in petri dish and the formed product was recrystallized from ethanol. Physical properties of compounds (1-8) are listed in Table (3-1).

Synthesis of 2-Thiazolidinone Derivatives (9-13) [13]

A mixture of Schiff bases (1-8) (0.001 mole) and excess of thioglycolic acid (0.002 mole) in ethanol. The reaction was refluxed for (20 hr). The excess solvent was evaporated and residue was neutralized with sodium bicarbonate 5% solution to remove excess of thioglycolic acid. The formed precipitate was filtered, washed several times with distilled water and recrystallized from acetone. Physical properties of compounds (9-13) are listed in Table (3-1).

Result and Discussion

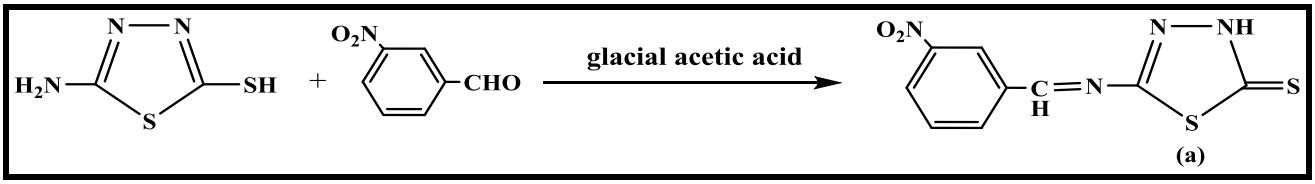
This present work includes synthesis of new heterocyclic ring derivatives as shown in Scheme (3-1).



Synthesis of 5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazole-2-Thiol (a)

5-amino-1, 3, 4-thiadiazole-2-thiol reacted with m-nitro benzaldehyde in acidic medium to prepare compound (a) as shown in equation (3.1). Yellow ppt., M.P. (150-152 C°), yield (90%).

FT-IR spectral data of compound (a) showed the appearance of characteristic absorption bands at (1656) cm^{-1} belong to ν (C=N) of imine group, characteristic absorption bands at (1531, 1348) cm^{-1} belong to ν (NO_2) of a sym. And sym., characteristic absorption bands at (3224) cm^{-1} belong to ν (NH).

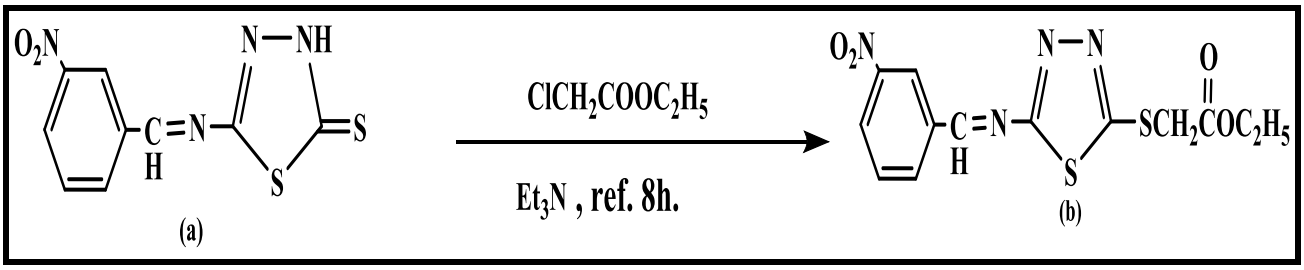


Equation 3.1:

Synthesis of Ethyl 2-((5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazol-2-yl) Thio) Acetate (b)

Compound (a) was reacted with ethyl chloro acetate in alkaline medium to prepare compound (b) as shown in equation (3.2).

Oil product, yield (85%).FT-IR spectral data of compound (b) showed the appearance of characteristic absorption bands at (1731) cm^{-1} belong to ν (C=O), and disappearance of absorption band (3224) cm^{-1} belong to ν (NH). ^{1}H-NMR see in Table (3-3).

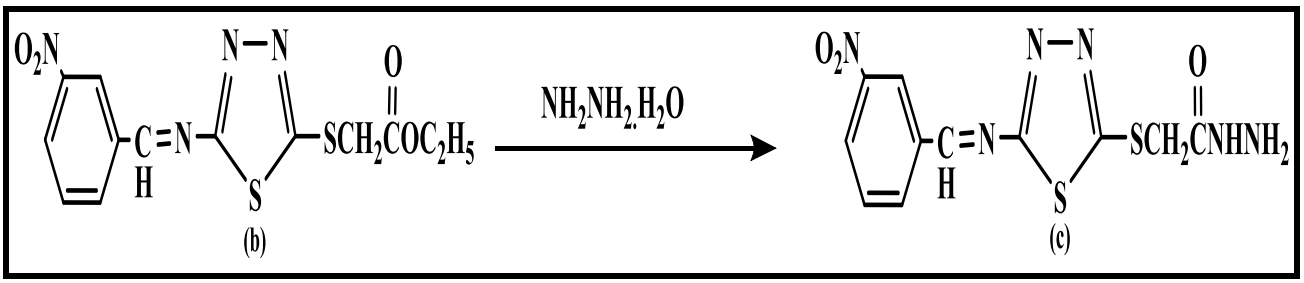


Equation 3.2:

Synthesis of 2-((5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazol-2-yl) Thio) Acetohydrazide (c)

Compound (b) was treated with hydrazine hydrate in absolute ethanol with stirring as shown in equation (3.3) to give compound (c). Yellow ppt., M.P. (80-82 C°), yield (60%).

FT-IR spectral data of compound (c) showed the appearance of characteristic absorption bands at (3452, 3402) cm^{-1} belong to ν (NH_2) asym., sym., characteristic absorption bands at (1631) cm^{-1} ν (C=O) of due to amid carbonyl group, characteristic absorption bands at (3184) cm^{-1} belong to ν (NH). ^{1}H-NMR see in Table (3-3).



Equation 3.3:

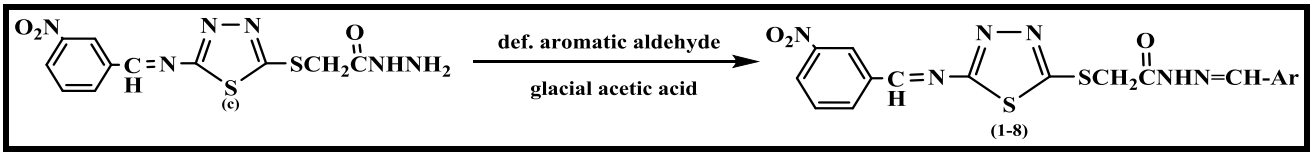
Synthesis of New Schiff Bases 2-((5-((3-Nitrobenzylidene) Amino)-1, 3, 4-Thiadiazol-2-yl) Thio) Acetohydrazide (1-8)

Compound (b) reacted with different aromatic aldehydes in absolute ethanol and glacial acetic acid as shown in equation (3.4).

Physical properties of compounds (1-8) are listed in Table (3-1). %).

FT-IR spectrum data of compounds (1-8) showed appearance of characteristic absorption bands at (1625-1660) cm^{-1} ν (C=O) due to carbonyl amid group, characteristic absorption bands at (1596-1608) cm^{-1} ν

(C=N), and disappearance of absorption band (3452, 3402) cm^{-1} belong to v (NH_2) asym., sym. All details of FTIR spectral data of compounds (1-8) are listed in Table (3-2). ^{1}H-NMR see in Table (3-3).



Equation 3.4:

Synthesis of 2, 5-Dithiazolidinone Derivatives (9-13)

The 2, 5-dithiazolidinone derivatives (9-13) were synthesized by refluxing of some compounds (1-8) with excess of thioglycolic acid in ethanol as shown in equation (3.5). Physical properties of compounds (9-13) are listed in table (3-1). FT-IR spectrum data of compounds (9-13) showed appearance of characteristic absorption bands at (1625-1660) cm^{-1} v (C=O) due to carbonyl amid group, characteristic absorption bands at (1724-1735) cm^{-1} v (C=O) due to carbonyl of thiazolidinone group. All details of FTIR spectral data of compounds (9-13) are listed in Table (3-2). ^{1}H-NMR see in Table (3-3).

Equation 3.5:

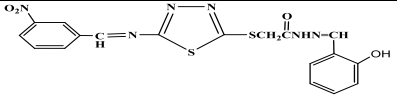
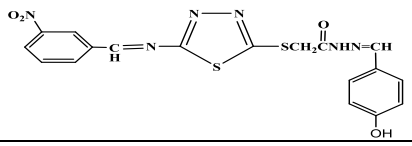
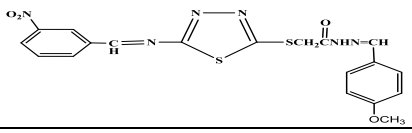
Conclusion

In this work we report the synthesis of new thiadiazole derivatives. The FT-IR and ^{1}H-NMR data for some of them gave good evidence for the formation of the prepared derivatives.

Table 3-1: Physical properties of compounds [1-13]

NO.	Formula	M.Wt g/mol	M.P C⁰	Color	Yield (%)
1	$C_{18}H_{14}N_6S_2O_4$	442.5	130-132	yellow	90
2	$C_{18}H_{14}N_6S_2O_4$	442.5	164-166	yellow	92
3	$C_{19}H_{16}N_6S_2O_4$	456.5	128-130	yellow	90
4	$C_{20}H_{18}N_6S_2O_5$	486.5	142-144	Pale yellow	86
5	$C_{20}H_{19}N_7S_2O_3$	469.5	136-138	orange	90
6	$C_{18}H_{13}N_7S_2O_5$	471.5	188-190	yellow	90
7	$C_{16}H_{12}N_6S_3O_3$	432.5	131-133	yellow	90
8	$C_{18}H_{15}N_7S_2O_3$	441.5	160-162	brown	92
9	$C_{22}H_{18}N_6S_4O_6$	590.7	d 330	yellow	85
10	$C_{22}H_{18}S_4N_6O_6$	590.7	233-235	yellow	85
11	$C_{23}H_{20}N_6S_4O_6$	604.7	320-322	Off white	87
12	$C_{24}H_{22}N_6S_4O_7$	634.7	d 296	Light yellow	86
13	$C_9H_7N_3S_4O$	617.7	d 285	orange	90

Table 3-2: FT-IR spectral data (cm^{-1}) of compounds [1-14]

NO.	Compounds structure	FT-IR spectral data, cm^{-1}
1		v (C=O)= 1623, v (C=N)= 1601, v (O-H)= 3425, v (C=C)aromatic= 1573, v (NH)= 3174
2		v (C=O)= 1627, v (C=N)= 1608, v (O-H)= 3147, v (C=C)aromatic= 1556, v (NH)= 3083
3		v (C=O)= 1625, v (C=N)= 1602, v (C=C)aromatic= 1573, v (NH)= 3083

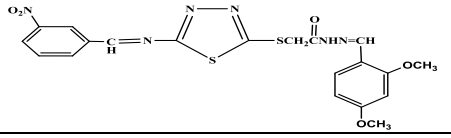
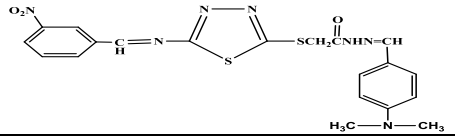
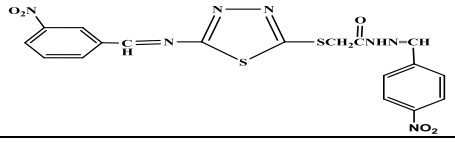
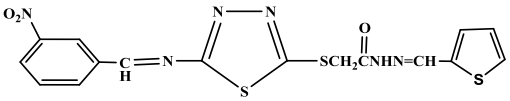
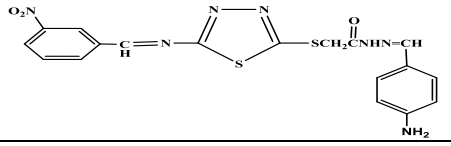
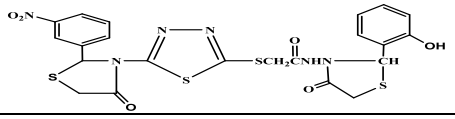
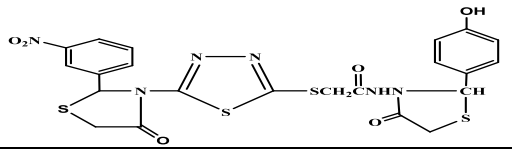
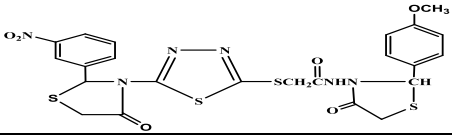
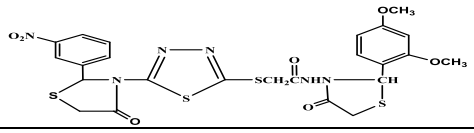
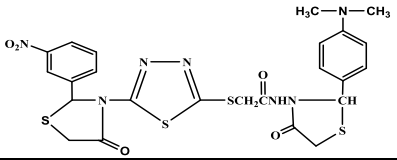
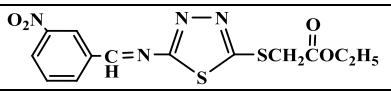
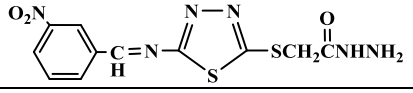
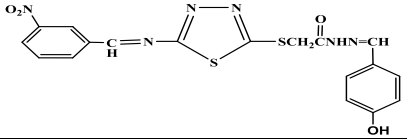
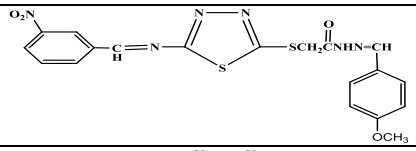
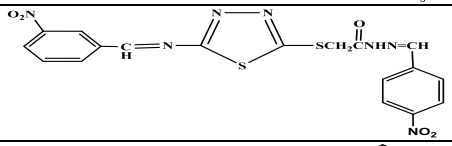
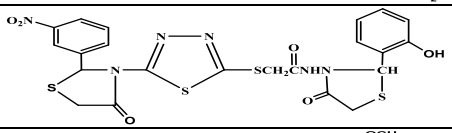
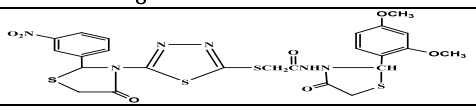
4		ν (C=O)= 1660, ν (C=N)= 1606, ν (C=C)aromatic= 1587, ν (NH)= 3444
5		ν (C=O)= 1627, ν (C=N)= 1604, ν (C=C)aromatic= 1564, ν (NH)= 3085
6		ν (C=O)= 1627, ν (C=N)= 1596, ν (C=C)aromatic= 1573, ν (NH)= 3083
7		ν (C=O)= 1625, ν (C=N)= 1610, ν (C=C)aromatic= 1579, ν (NH)= 3137
8		ν (C=O)= 1625, ν (C=N)= 1608, ν (C=C)aromatic= 1573, ν (NH_2)= 3492asym., 3398sym.
9		ν (C=O)amide= 1625, ν (C=O)2-thiazolidinone= 1683, ν (C=O)5-thiazolidinone= 1730, ν (C=N)= 1610, ν (C=C)aromatic= 1573, ν (O-H)= 3433
10		ν (C=O)amide= 1623, ν (C=O) 2-thiazolidinone = 1681, ν (C=O) 5-thiazolidinone = 1728, ν (C=N)= 1606, ν (C=C)aromatic= 1575, ν (O-H)= 3427
11		ν (C=O)amide= 1625, ν (C=O)) 2-thiazolidinone = 1677, ν (C=O) 5-thiazolidinone = 1728, ν (C=N)= 1604, ν (C=C)aromatic= 1573
12		ν (C=O)amide= 1622, ν (C=O)) 2-thiazolidinone = 1685, ν (C=O) 5-thiazolidinone = 1733, ν (C=N)= 1608, ν (C=C)aromatic= 1571
13		ν (C=O)amide= 1628, ν (C=O)) 2-thiazolidinone = 1680, ν (C=O) 5-thiazolidinone = 1724, ν (C=N)= 1604, ν (C=C)aromatic= 1577

Table 3-3: ^{1}H-NMR spectral data (δ ppm) for some compounds

NO.	Compounds structure	^{1}H-NMR spectral data (δ ppm)
1		1.26 (t,3H,C<u>H</u>$_3$), 4.17(q,2H,OC<u>H</u>$_2$), 4.30(s,2H,SC<u>H</u>$_2$), 10.1(s,1H,N=C<u>H</u>), 7.1-9.0(m,4H,Ar-<u>H</u>)
2		8.05(s,1H,N=C<u>H</u>), 2.5(s,2H,SC<u>H</u>$_2$), 3.3(s,2H,N<u>H</u>$_2$), 7.1-8.0(m,4H,Ar-<u>H</u>), 8.2(s,1H,N<u>H</u>)
3		2.5(s,2H,SC<u>H</u>$_2$), 8.9(s,1H,N<u>H</u>), 8.2(s,1H,N=C<u>H</u>), 7.0-8.1(m,8H,Ar-<u>H</u>), 8.7(s,1H,ONHN=C<u>H</u>), 10.1(s,1H,O<u>H</u>)

4		3.3(s,3H,OC<u>H3</u>), 3.9(s,2H,SC<u>H2</u>), 8.7(s,1H,NHN=C<u>H</u>), 8.85(s,1H,N=C<u>H</u>),8.92(s,1H,N<u>H</u>), 7.5-8.5(m,8H,Ar-<u>H</u>)
5		3.31(s,2H,SC<u>H2</u>), 8.71(s,1H,NHN=C<u>H</u>), 8.87(s,1H,N=C<u>H</u>),8.91(s,1H,N<u>H</u>), 7.0-8.5(m,8H,Ar-<u>H</u>)
6		3.27(s,2H,SC<u>H2</u>), 6.57(s,1H,SC<u>H</u>-Ar), 3.9(s,2H,NC<u>H₂</u>-Ar),11.12(s,1H,N<u>H</u>),10.67(s,1H,O<u>H</u>),6.98(s,4H,SC<u>H₂</u>-CO), 7.0-9.0(m,8H,Ar-<u>H</u>)
7		3.34(s,2H,SC<u>H2</u>), 6.02(s,1H,SC<u>H</u>-Ar), 3.9(s,2H,NC<u>H₂</u>-Ar),8.92(s,1H,N<u>H</u>),2.51(s,6H,OC<u>H₃</u>),5.57(s,4H,SC<u>H₂</u>-CO), 6.5-8.5(m,8H,Ar-<u>H</u>)

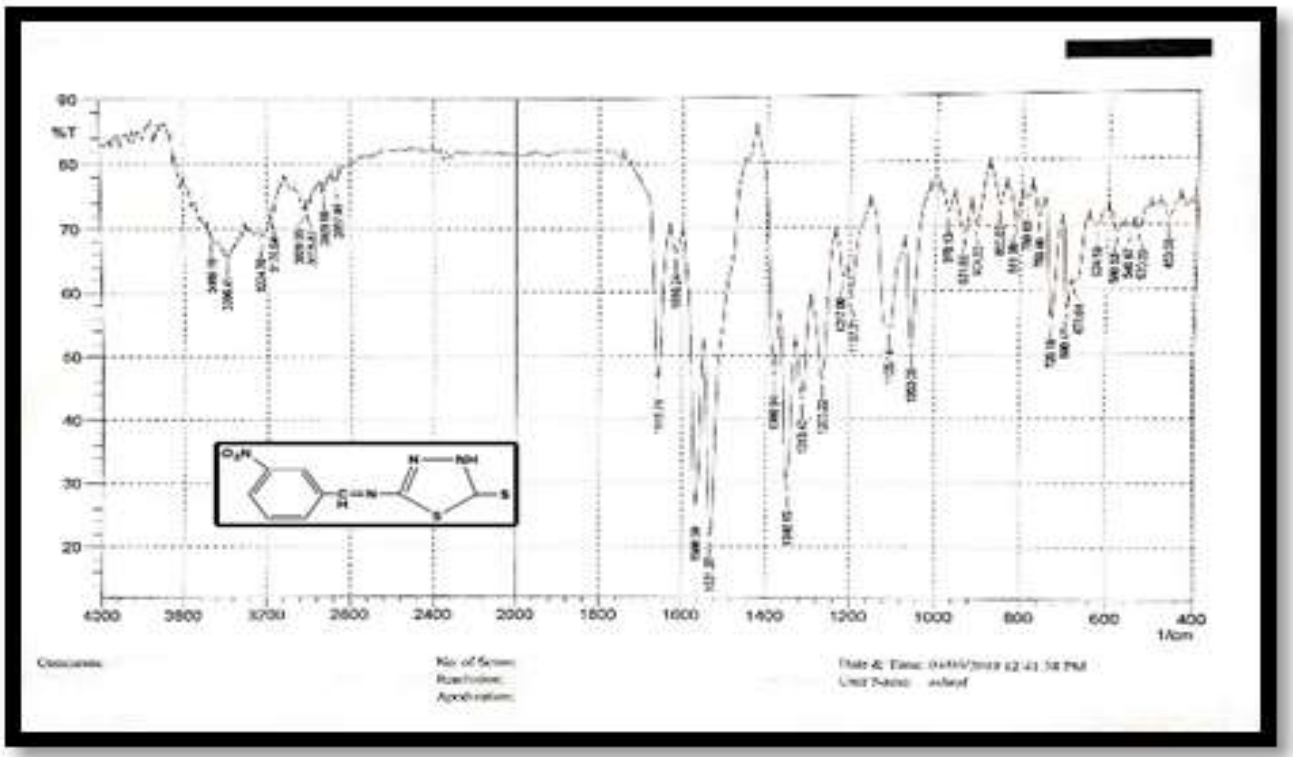


Figure 1: FT-IR spectral of compound (a)

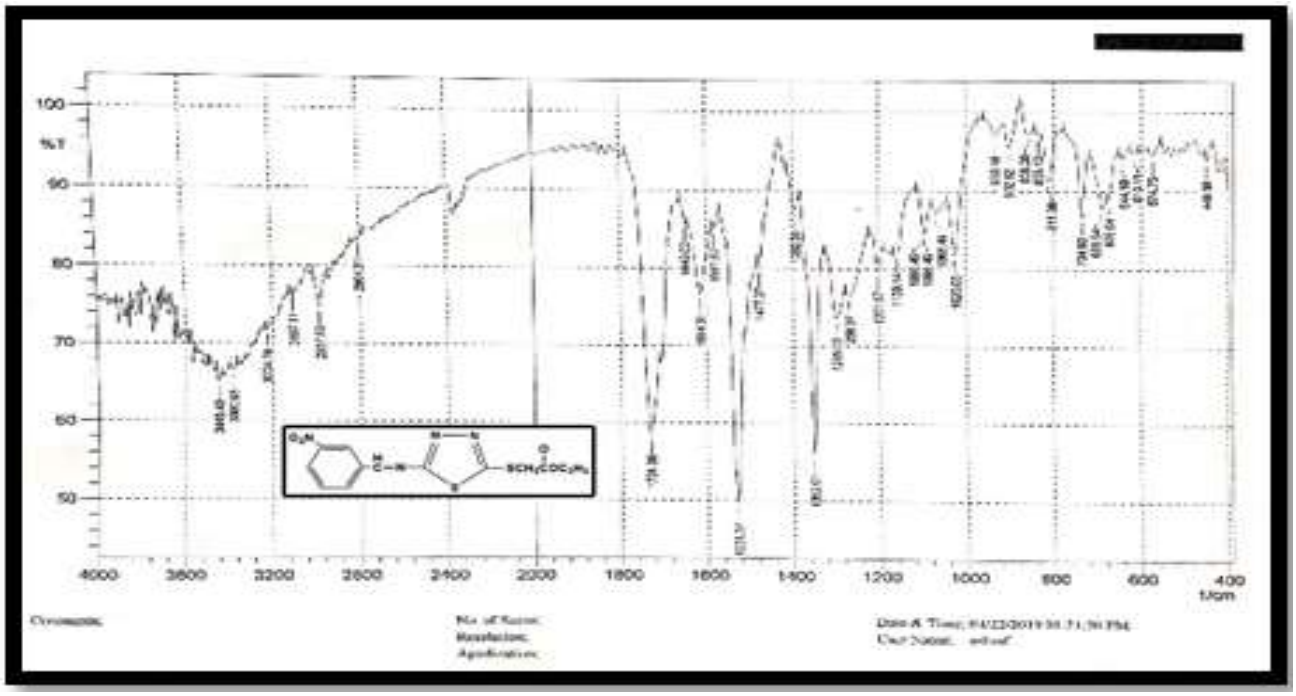


Figure 2: FT-IR spectral of compound (b)

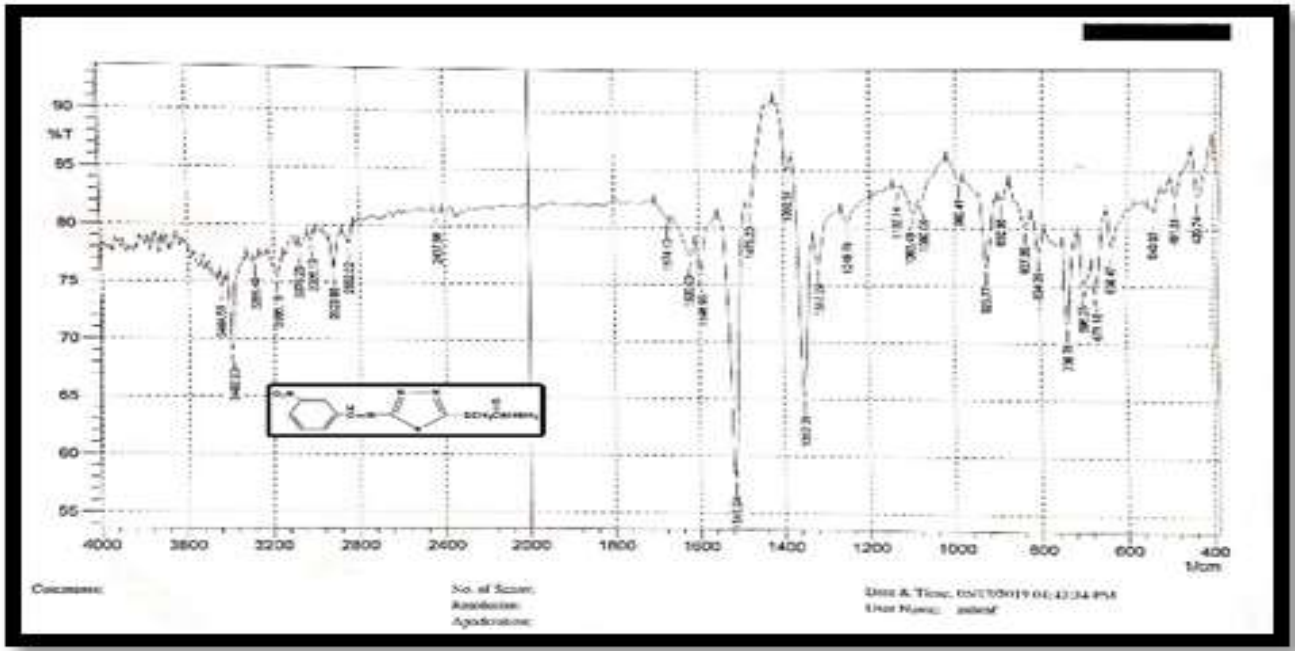


Figure 3: FT-IR spectral of compound(c)

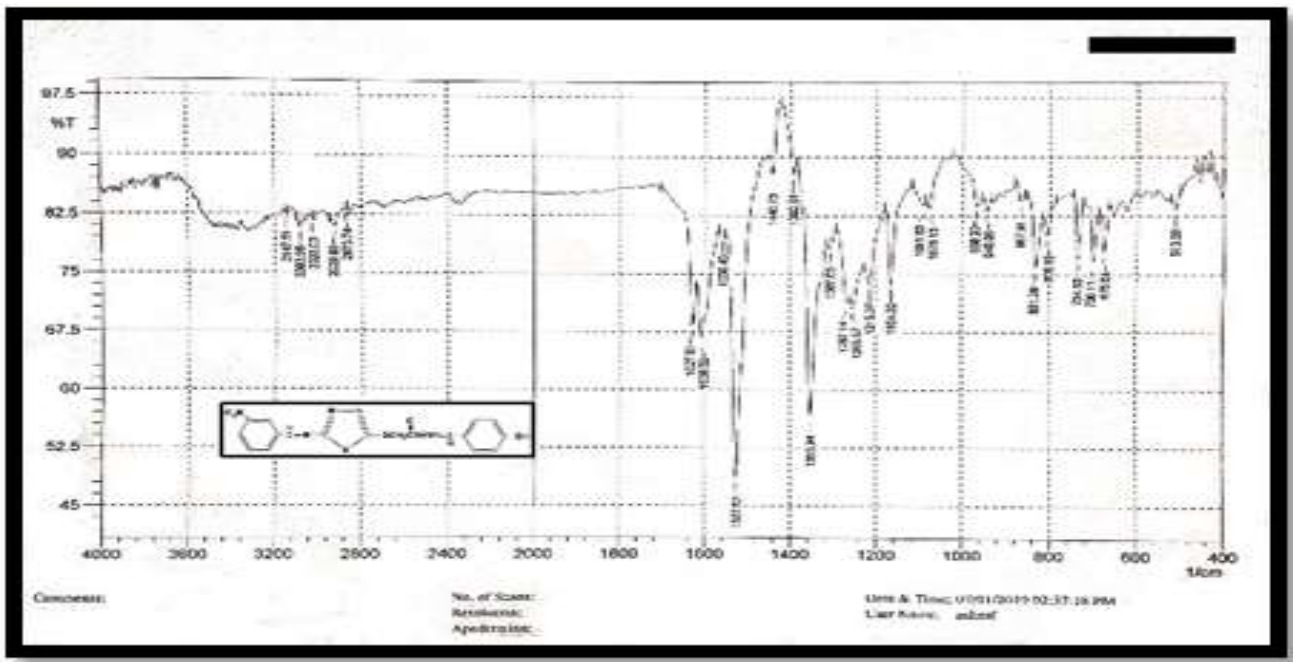


Figure 4: FT-IR spectral of compound (2)

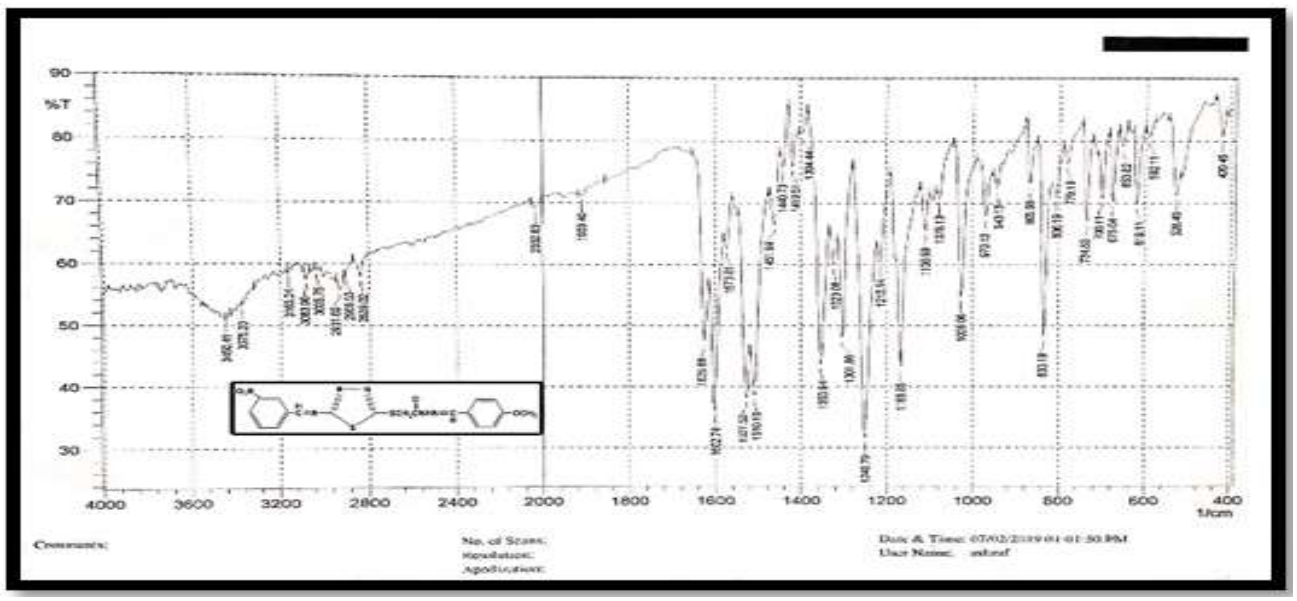


Figure 5: FT-IR spectral of compound (3)

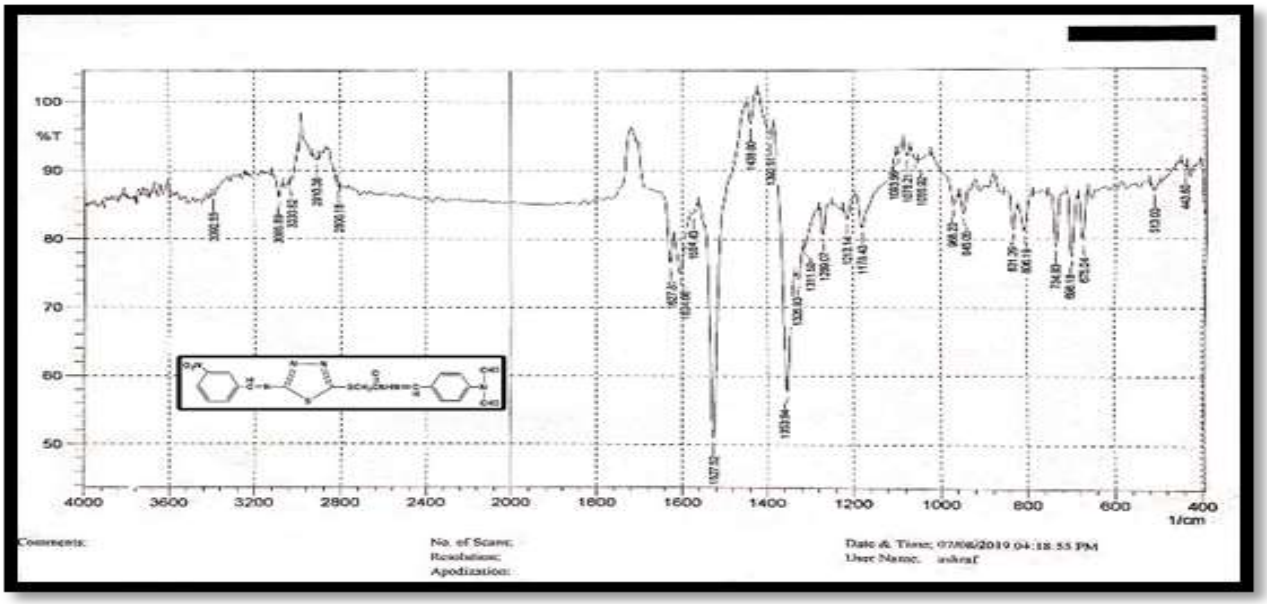


Figure 6: FT-IR spectral of compound (5)

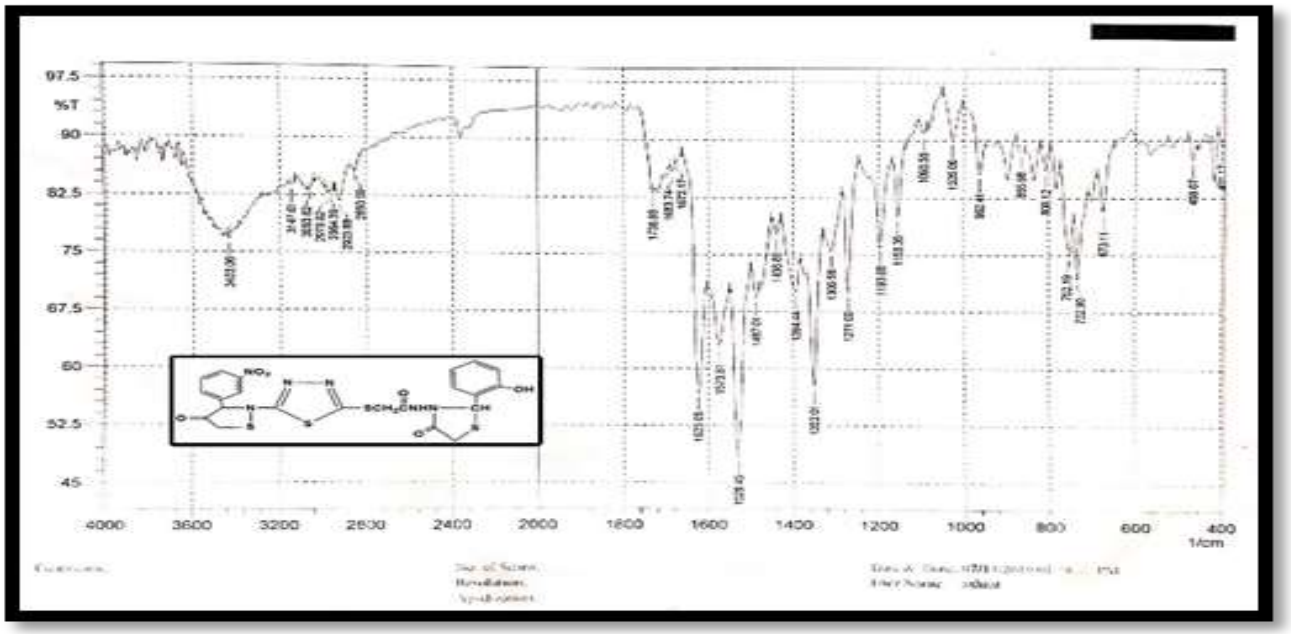


Figure 7: FT-IR spectral of compound (9)

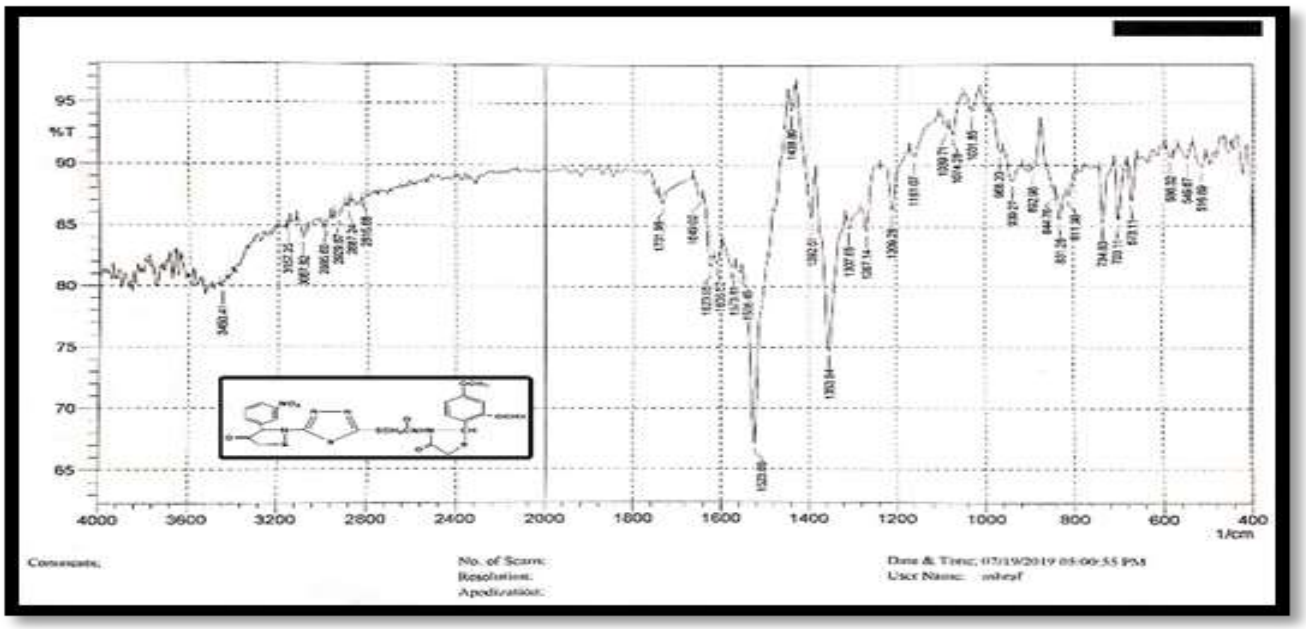


Figure 8: FT-IR spectral of compound (12)

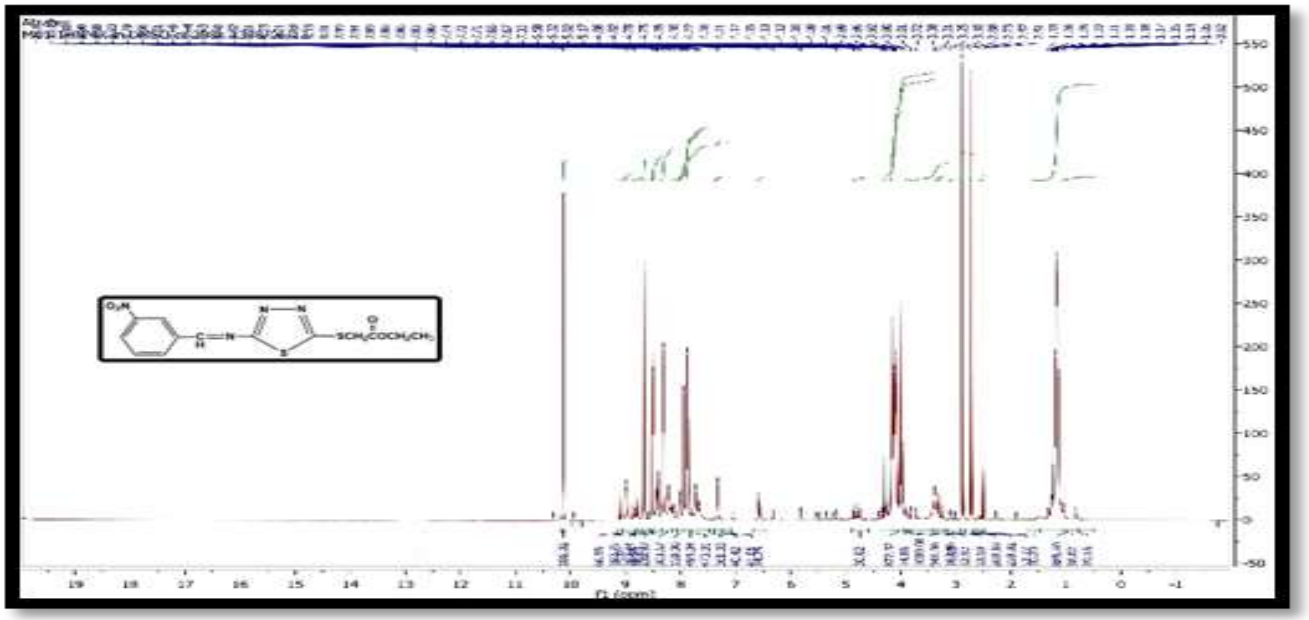


Figure 9: ^{1}H-NMR spectrum of compound (b)

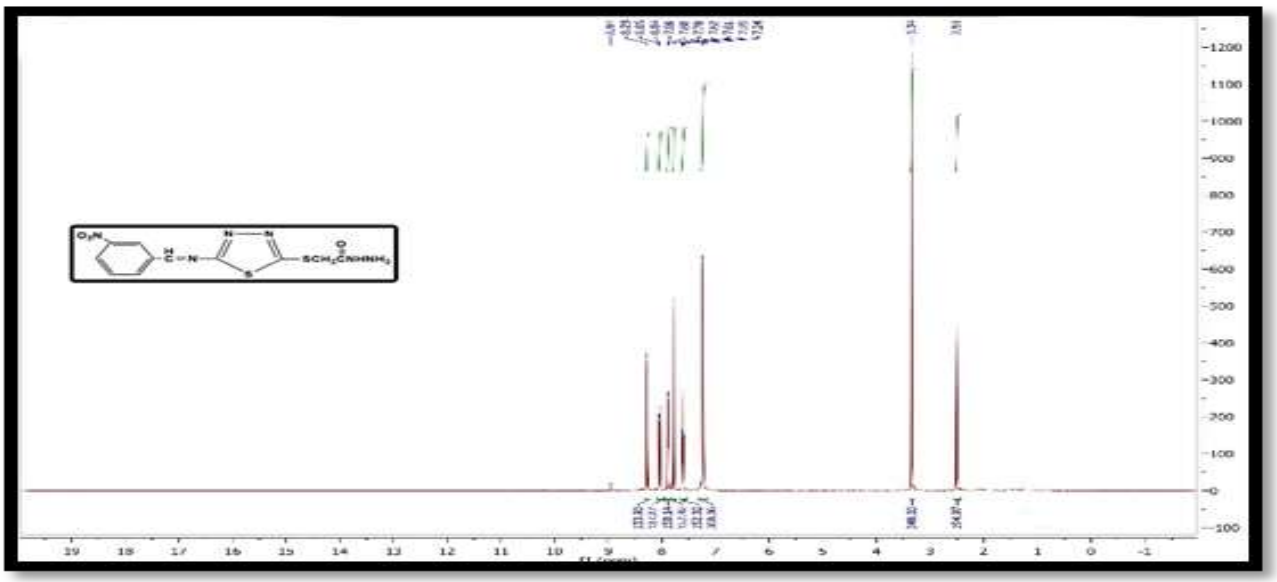


Figure 10: ^{1}H-NMR spectrum of compound (c)

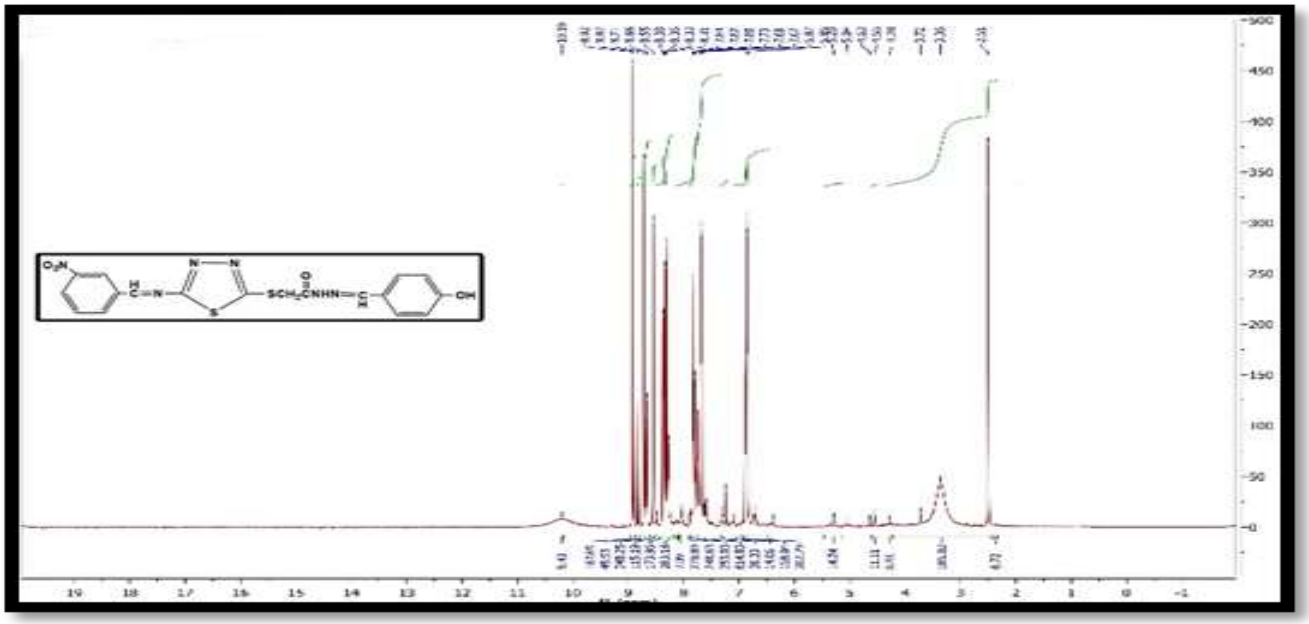


Figure 11: ^{1}H-NMR spectrum of compound (2)

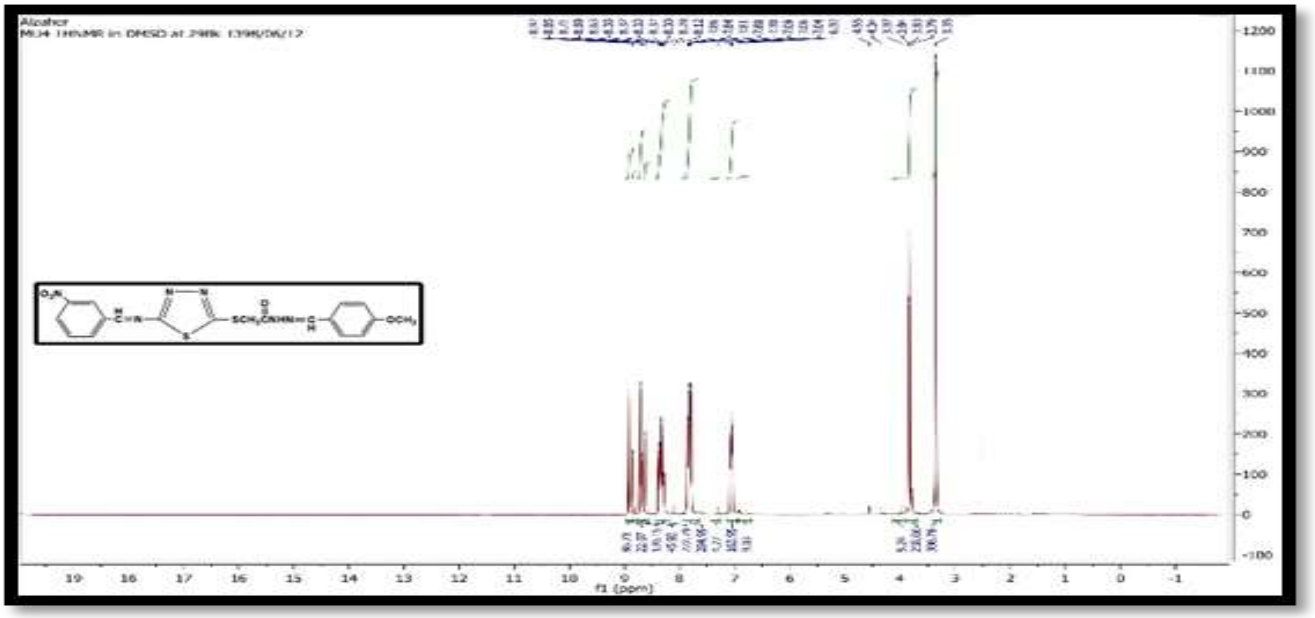


Figure 12: ^{1}H-NMR spectrum of compound (3)

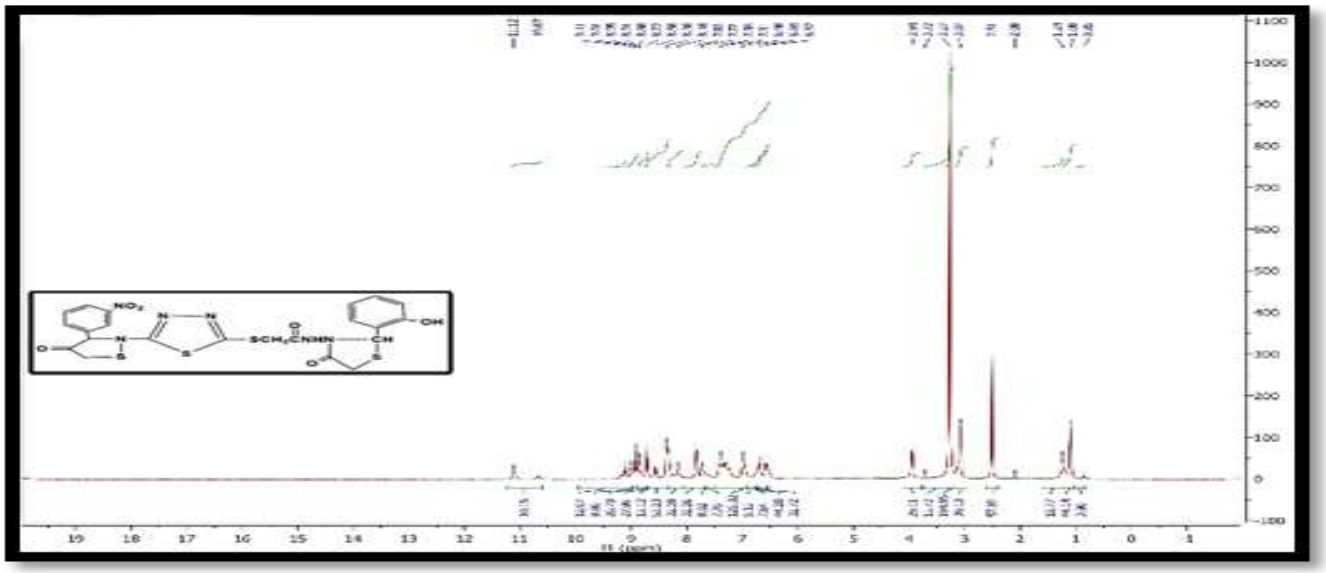


Figure 13: ^{1}H-NMR spectrum of compound (9)

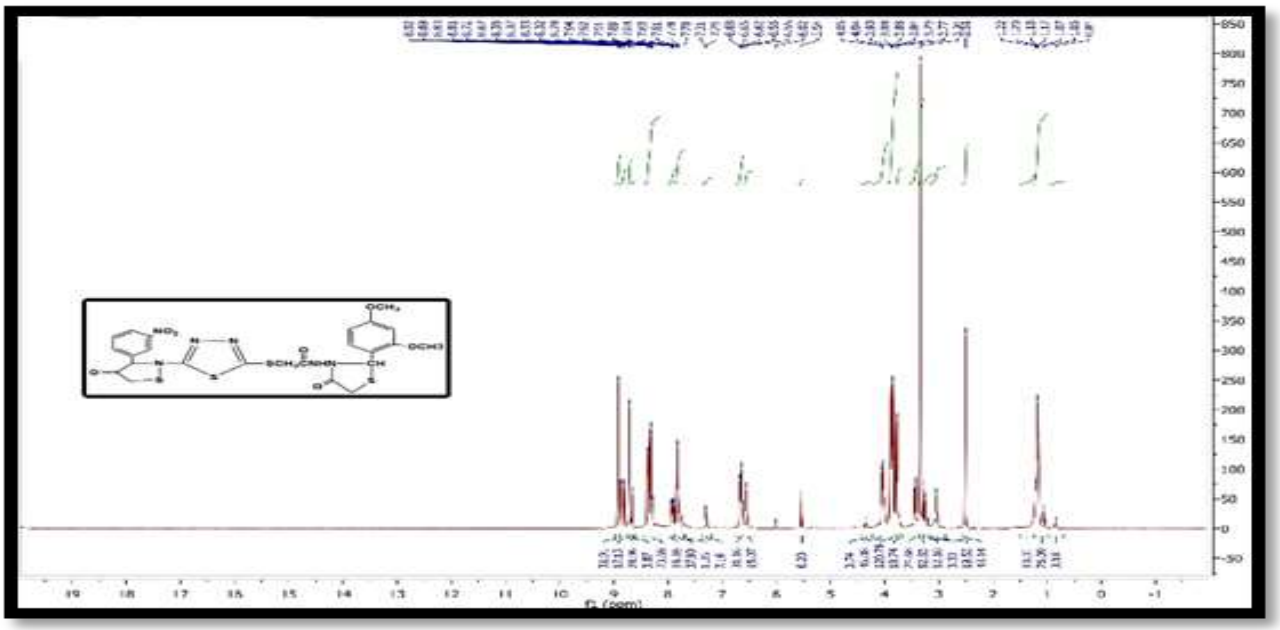


Figure 14: ^{1}H-NMR spectrum of compound (12)

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