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RESEARCH ARTICLE

Synthesis and Characterization of 5- Amino-1, 3, 4-Thiadiazole-2-thiol and its Amine Group Derivatives

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Abstract

This work includes preparation of 5-Amino-1,3,4-thiadiazole-2-thiol from thiosemicarbazide with Carbon disulfide (CS_2) and KOH as catalyst. Also reaction of 5-Amino-1,3,4-thiadiazole-2-thiol 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. All synthetic compounds were definited 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, Thiosemicarbazide, Schiff bases, heterocyclic compounds, thiadiazole.*

Introduction

Heterocyclic compounds are a good scientific importance since they are used as key starting materials for active pharmaceutical component. Some of them, derivatives of 1,3,4-oxadiazole/thiadiazole have been found to display different biological activities such as analgesic anti-inflammatory, antimicrobial, antifungicidal, antioxidant and other biological properties [1]. Also, Thiosemicarbazide serves as structural form for the synthesis of a wide set of N and S containing heterocyclic compounds. Moreover, the presence of NH and C=S moieties plays major role for the synthesis of various metal complexes.

Thiosemicarbazides have been evaluated over the last 50 years as antiviral, antibacterial, and anticancer therapeutics and their biological activities are a function of parent aldehyde or ketone moiety [2].Thiadiazole contains the five membered ring structure composed of two nitrogen atoms and one sulfur atom. There are four isomeric types: 1,2,3-thiadiazole, 1,3,4-thiadiazole, 1,2,4-thiadiazole and 1,2,5-thiadiazole [3], several 1,3,4-thiadiazole derivatives are important for pharmaceuticals use as well as useful compounds in the organic synthesis.

Thiadiazole and its derivatives show private activity as drugs for the treatment of thrombosis, as soothing and more recently as plant activators or initiator of systemic acquired resistance (SAR) in plants [4]. Schiff bases are nitrogen analogs of the aldehydes or ketones and their complexes are reported to have more biological possibility than simple organic compounds [2].

Schiff bases can be readily synthesized by reaction primary amines with aldehyde or ketones in acidic medium. Schiff base has good fungicidal, antimicrobial [5] and pharmacological applications [6] in this research paper, a series of 1,3,4 thiadiazole derivatives containing imine group were prepared and all these compound were confirmed by FT-IR.

Chemicals and Instruments

Chemicals

All chemicals were purchased from Fluke and BDH.

Instruments

- Melting point measurements were recorded using Gallenkamp capillary melting point apparatus.

- FT-IR spectra were recorded using KBr disc on shimadzu FT-IR8400 Fourier Transform Infrared spectrophotometer.
- Some of the prepared compounds were characterized by ^{1}H-NMR spectra that recorded on nuclear magnetic resonance in 400 MHz (Laboratory of Isfahan University) and DMSO as solvent.

Experimental

Preparation of 5 - Amino -1, 3, 4-thiadiazole - 2- Thiol (A). [7]

Thiosemicarbazide (4g, 0.043 mole) was dissolved in absolute ethanol (30ml) in round bottom flask (250ml), potassium hydroxide (2.23g, 0.021mole) and CS_2 (9.5g, 0.125mole) were then added respectively with continues stirring. The reactant mixture was refluxed for 7-9hours, then evaporate the excess solvent, the residue was acidified with concentrated hydrochloric acid in ice path to neutralize the mixture, Then the precipitate was filtered and washed with distilled water.

Synthesis of New Schiff bases from 5-amino-1, 3, 4-thiadiazole-2- Thiol (1-8). [8]

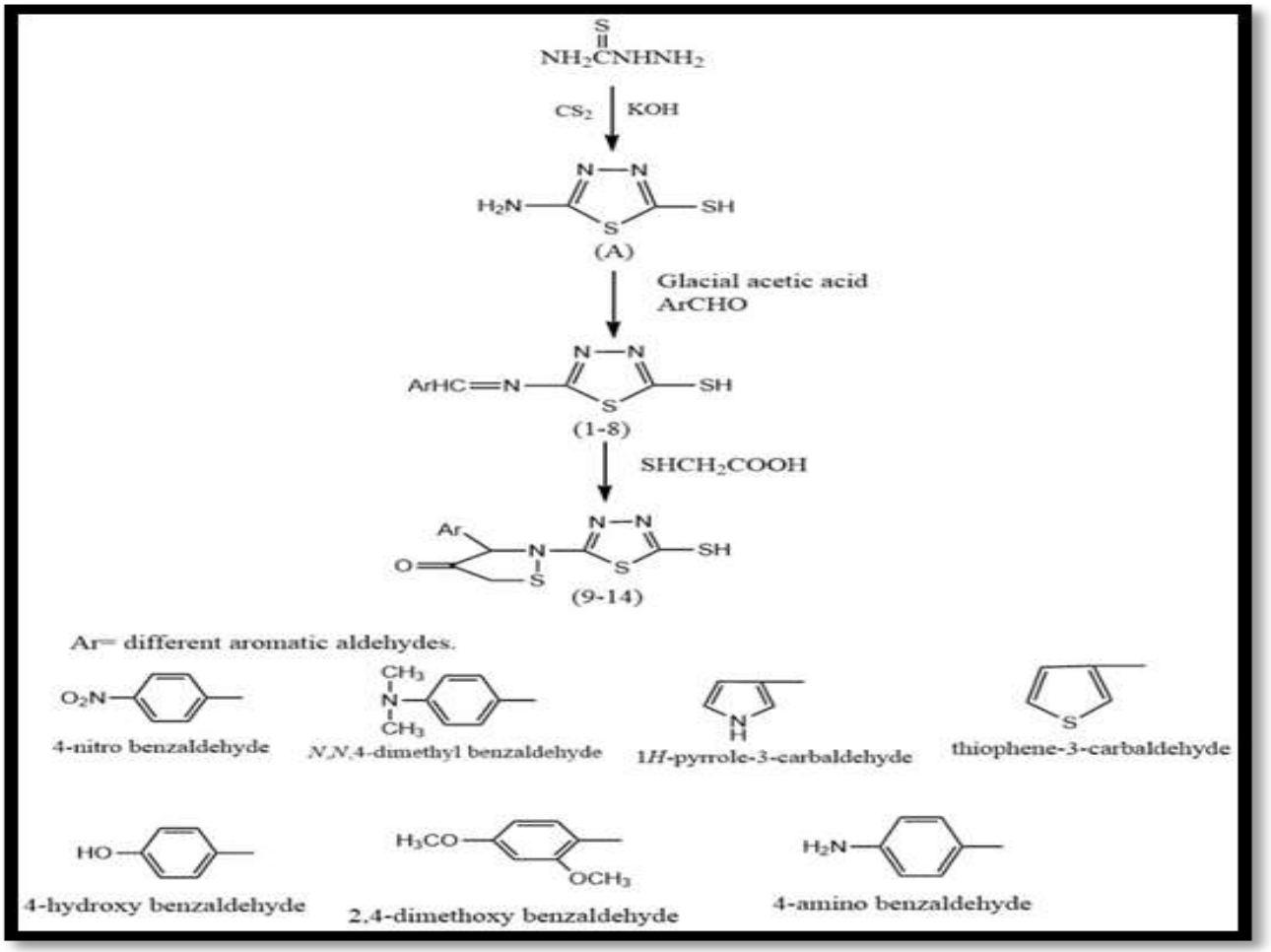
A mixture of compound (A) (0.0015 mol) and different aromatic aldehydes (0.0015 mol) in absolute ethanol (10 ml) and few drops of glacial acetic acid was refluxed for 6 hr. the mixture was evaporated and the formed product was recrystallized from ethanol. Physical properties of compounds (1-8) are listed in table (3.1).

Synthesis of Isothiazolidinone Derivatives (9-14). [9]

A mixture of Schiff bases (1-8) (0.00037 mol) and excess of thioglycolic acid (0.00074 mol) in tetrahydrofuran. The reaction was refluxed for (18-20 hr.). The excess solvent was evaporated and residue was neutralized with 5% sodium bicarbonate solution to remove excess acid, the formed precipitate was filtered, washed with distilled water and recrystallized from ethanol. Physical properties of compounds (9-14) are listed in Table (3.1).

Results and Discussion

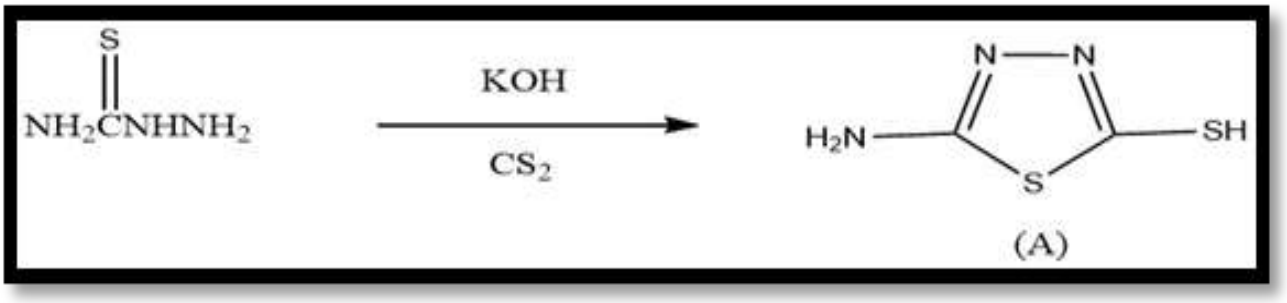
The Present work includes reaction and synthesis new derivatives of 1,3,4 thiadiazole as shown in Scheme (3-1).



Scheme 3-1:

Preparation of 5-Amino-1,3,4-thiadiazole-2-thiol (A)

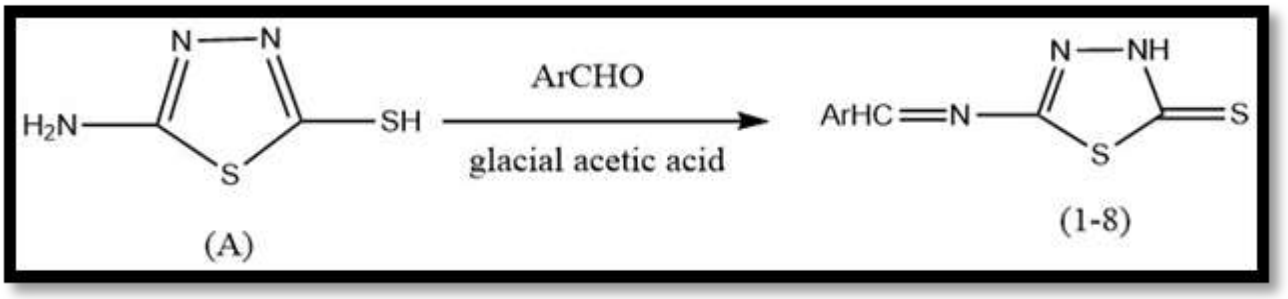
Thiosemicarbazide react with Carbon disulfide and Potassium hydroxide as catalyst to prepare compound (A) as shown in equation (3.1). Off white, M.P. (234-236) C^0 yield (70%). FT-IR Spectra data of compound (A) show the appearance of characteristic absorption band at (3338,3253) cm^{-1} belong to ν (NH_2) asym. Sym., characteristic absorption band at (2646) cm^{-1} belong to ν (SH) and characteristic absorption band at (1610) cm^{-1} due to (C=N). ^{1}H-NMR Spectrum of compound (A) showed signals at (7.1) ppm belong to (NH_2) protons and (13.1) ppm belongs to (SH) protons.



Equation 3.1:

Synthesis of new Schiff bases from 5-amino-1,3,4-thiadiazole-2-thiol (1-8)

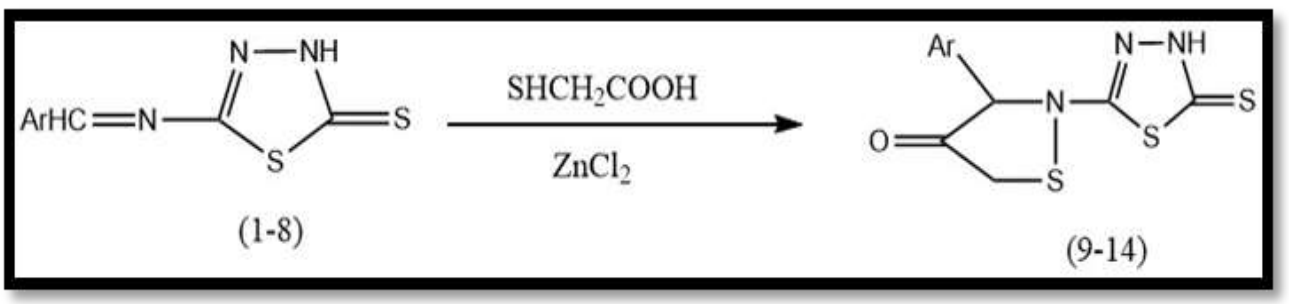
The compounds were synthesized from the reaction between compound (A) and different aromatic aldehydes in absolute ethanol and glacial acetic acid as shown in equation (3.2). FT-IR spectrum data of compounds (1-7) show appearance of characteristic bands at (1670-1650) cm^{-1} belong to ν (C=N), characteristic bands at (3350-3100) cm^{-1} belong to ν (NH) and disappearance of absorption bands (3338,3253) cm^{-1} belong to ν (NH_2). All details of FT-IR spectral data of compounds (1-8) are listed in table (3.2). ^{1}HNMR see in Table (3.3).



Equation 3.2:

Synthesis of Isothiazolidinone Derivatives (9-14)

The compounds were synthesized by refluxing equimolar amounts from the compounds (1-8) with mercapto-acetic acid in ethanol as shown in equation (3.3). FT-IR spectrum data of compounds (9-14) showed appearance of stretching band of carbonyl group at (1750-1700) cm^{-1} and disappearance of the absorption band (1670-1650) cm-1 belong to ν(C=N). All details of FT-IR spectral data of compounds (9-14) are listed in Table (3.2). ^{1}HNMR see in Table (3.3).



Equation 3.3:

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.

Physical properties of 5-Amino-1,3,4-thidiazole-2-thiol Compound

Formula	M.Wt gm/mol.	M.P C^0	Color	yield
$C_2H_3N_3S_2$	133.2	234-236	Off white	70%

FT-IR Spectral data (cm^{-1}) of 5-Amino-1,3,4-thidiazole-2-thiol Compound

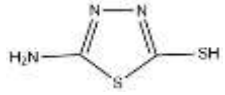
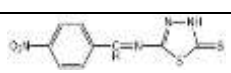
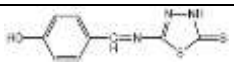
Compound structure	FT-IR spectral data, cm^{-1}
	v (NH_2)=3338,3253, v (C=N) = 1610, v (SH)= 2646

Table 3-1: physical properties of compounds [1-14]

NO.	Formula	M.Wt g/mol	M.P C^0	Color	Yield (%)
1	$C_9H_6N_4S_2O_2$	266	198-200	orange	90
2	$C_9H_7N_3S_2O$	237	70-72	orange	80
3	$C_{11}H_{11}N_3S_2O_2$	281	200-202	yellow	86
4	$C_9H_5N_3S_3$	236	192-194	red	60
5	$C_7H_8N_4S_2$	210	138-140	yellow	72
6	$C_7H_6N_4S_2$	227	d 250	brown	55
7	$C_9H_6N_4S_2O$	266	150-152	yellow	90
8	$C_{11}H_{12}N_4S_2$	264	240-242	orange	78
9	$C_{11}H_7N_4S_3O_3$	339	d 278	orange	75
10	$C_{11}H_9S_3N_3O_2$	311	d 310	orange	95
11	$C_{13}H_{13}N_3S_3O_3$	355	318-320	yellow	83
12	$C_{11}H_{10}N_4S_3O$	310	d 275	orange	90
13	$C_9H_7N_3S_4O$	301	d 310	Light orange	50
14	$C_9H_8N_4S_3O$	284	d 285	black	80

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

NO.	Compounds structure	FT-IR spectral data, cm^{-1}
1		v(N-H)= 3272, v (C-H)= 2931, v (C=N)imine= 1658, v (C=N)= 1608, v (NO_2)= Asym.(1523) and Sym.(1348)
2		v (N-H)= 3253, v (C-H)= 2925, v (C=N)imine=1668, v (C=N)= 1600, v (O-H)= 3417

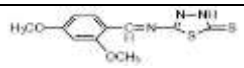
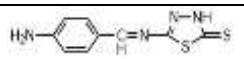
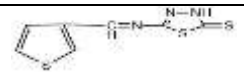
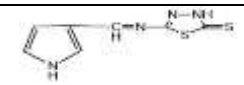
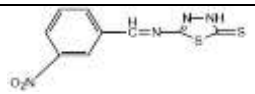
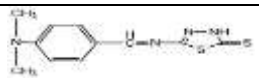
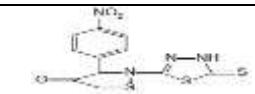
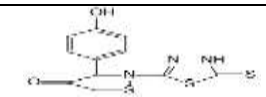
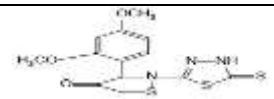
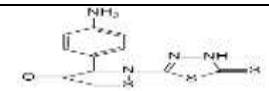
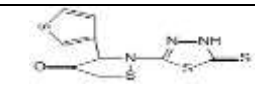
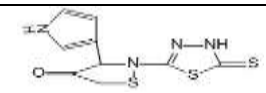
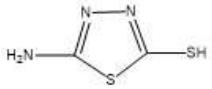
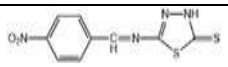
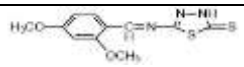
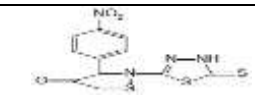
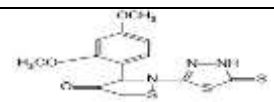
3		ν (N-H)= 3257, ν (C-H)= 2923, ν (C=N)imine=1662, ν (C=N)= 1596, ν (O-CH_3)= 1269
4		ν (N-H)= 3128, ν (C-H)= 2927, ν (C=N)imine=1677, ν (C=N)= 1606, ν (NH_2)= 3334,3253
5		ν (N-H)= 3249, ν (C-H)= 2923, ν (C=N)imine=1652, ν (C=N)= 1608
6		ν (N-H)= 3188, ν (C-H)= 2912, ν (C=N)imine=1649, ν (C=N)= 1616
7		ν(N-H)= 3224, ν (C-H)= 2923, ν (C=N)imine= 1656, ν (C=N)= 1616, ν (NO_2)= Asym.(1531) and Sym.(1348)
8		ν(N-H)= 3095, ν (C-H)= 2962, ν (C=N)imine= 1652, ν (C=N)= 1593
9		ν(N-H)= 3172, ν (C-H)= 2927, ν (C=N)= 1595, ν (C=O)= 1701, ν (NO_2)= Asym.(1521) and Sym.(1346)
10		ν(N-H)= 3209, ν (C-H)= 2833, ν (C=N)= 1593, ν (C=O)= 1677, ν (OH)= 3414
11		ν(N-H)= 3309, ν (C-H)= 2972, ν (C=N)= 1600, ν (C=O)= 1741, ν (O-CH_3)= 1294
12		ν(N-H)= 3232, ν (C-H)= 2914, ν (C=N)= 1581, ν (C=O)= 1731, ν (NH_2)= 3390,3307
13		ν(N-H)= 3294, ν (C-H)= 2958, ν (C=N)= 1608, ν (C=O)= 1710
14		ν(N-H)= 3323, ν (C-H)= 2929, ν (C=N)= 1612, ν (C=O)= 1751

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

NO.	Compounds structure	^{1}H-NMR spectral data (δ ppm)
1		7.1 (s,2H,N<u>H</u>$_2$), 13.1(s,1H,S<u>H</u>)
2		8.2(s,1H,N=C<u>H</u>), 13.5(s,1H,S<u>H</u>), 12.2(s,1H,NH), 7.1-8.0(m,4H,Ar-<u>H</u>)
3		8.7(s,1H,N=C<u>H</u>), 14.3(s,1H,S<u>H</u>), 13.1(s,1H,NH), 6.5-7.9(m,3H,Ar-<u>H</u>), 3.8(s,3H,O-C<u>H</u>3)
4		10.2(s,1H,N<u>H</u>), 7.1-8.5(m,4H,Ar-<u>H</u>), 3.3,3.5(s,2H,C<u>H</u>$_2$-S) 5.5(s,2H,C<u>H</u>$_2$-C=O)
5		10.1(s,1H,N<u>H</u>), 6.5-8.0(m,3H,Ar-<u>H</u>), 3.9(s,2H,C<u>H</u>$_2$-S) 4.0(s,2H,C<u>H</u>$_2$-C=O), 3.6(s,3H,O-C<u>H</u>3)

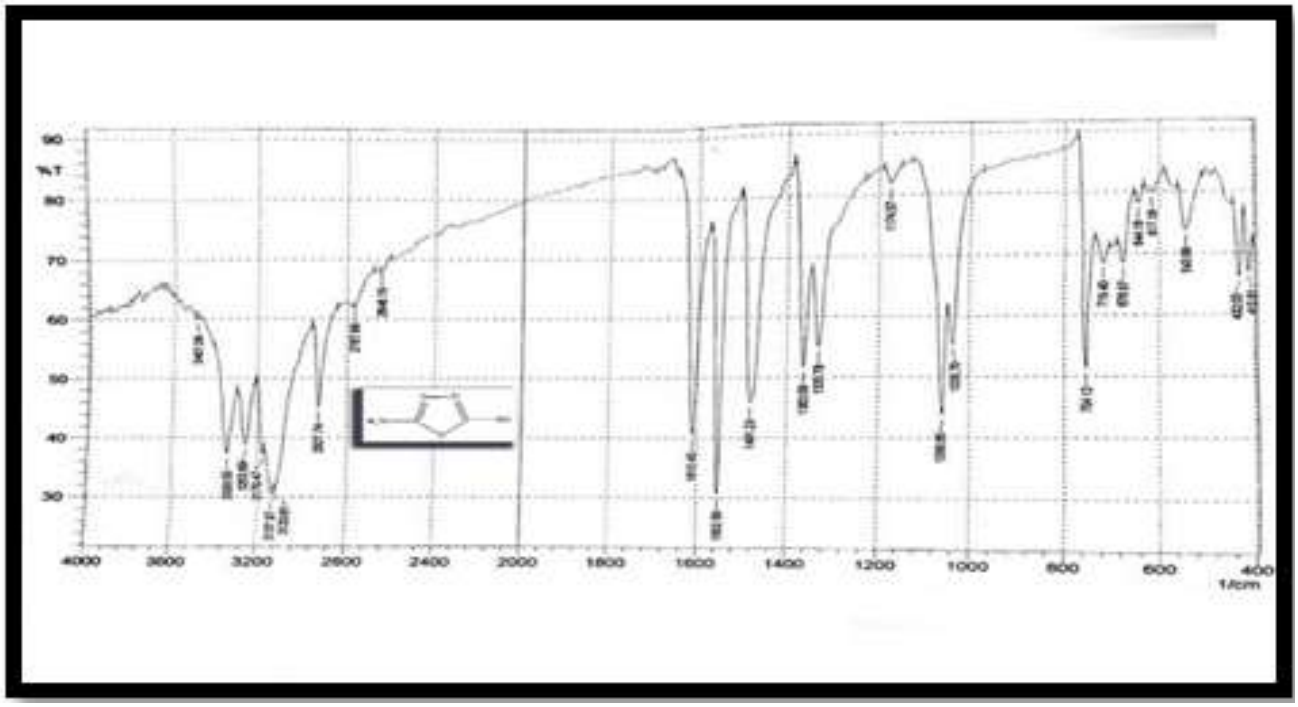


Figure 1: FT-IR spectral of compound(A)

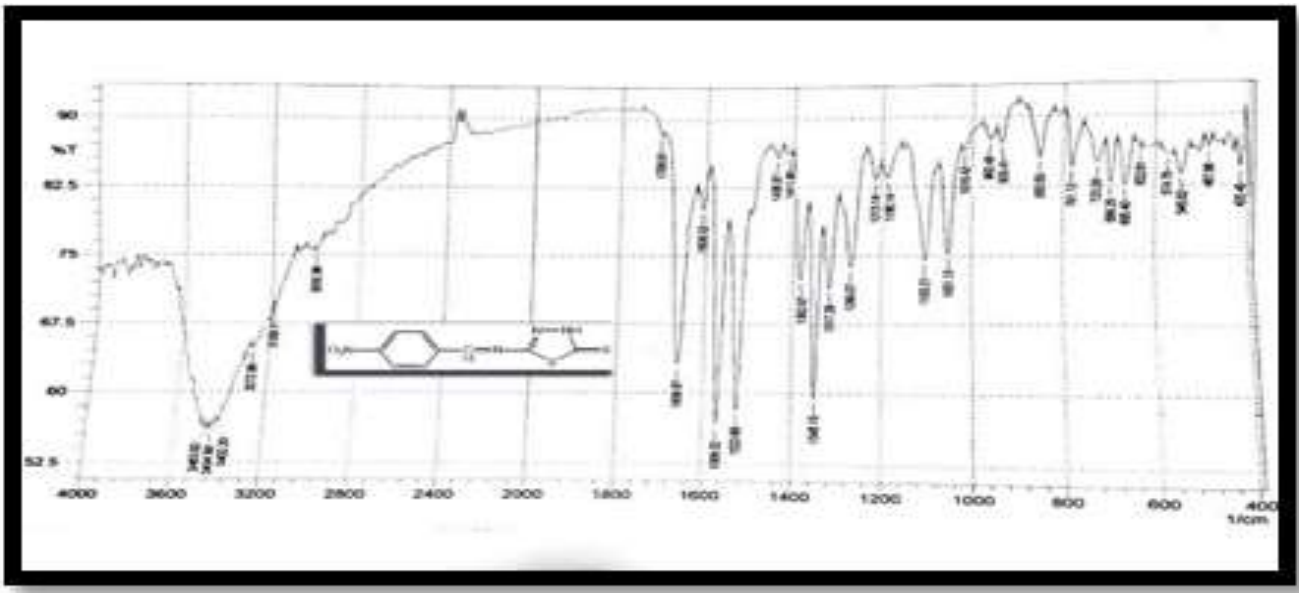


Figure 2: FT-IR spectral of compound(1)

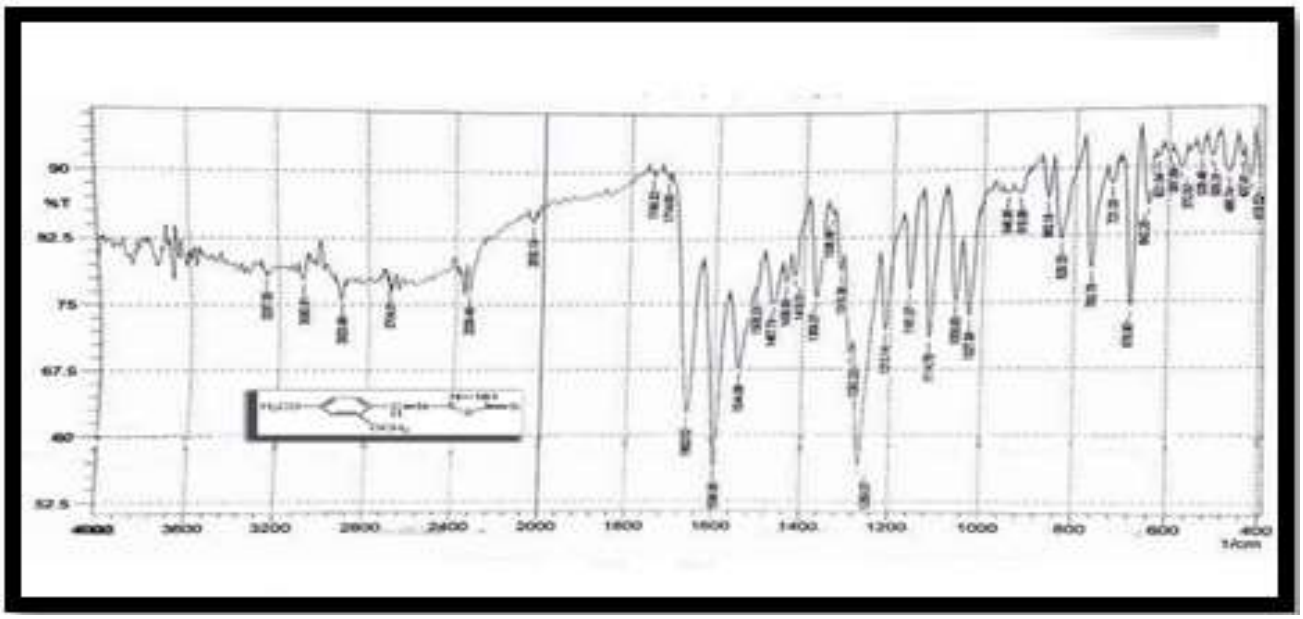


Figure 3: FT-IR spectral of compound(3)

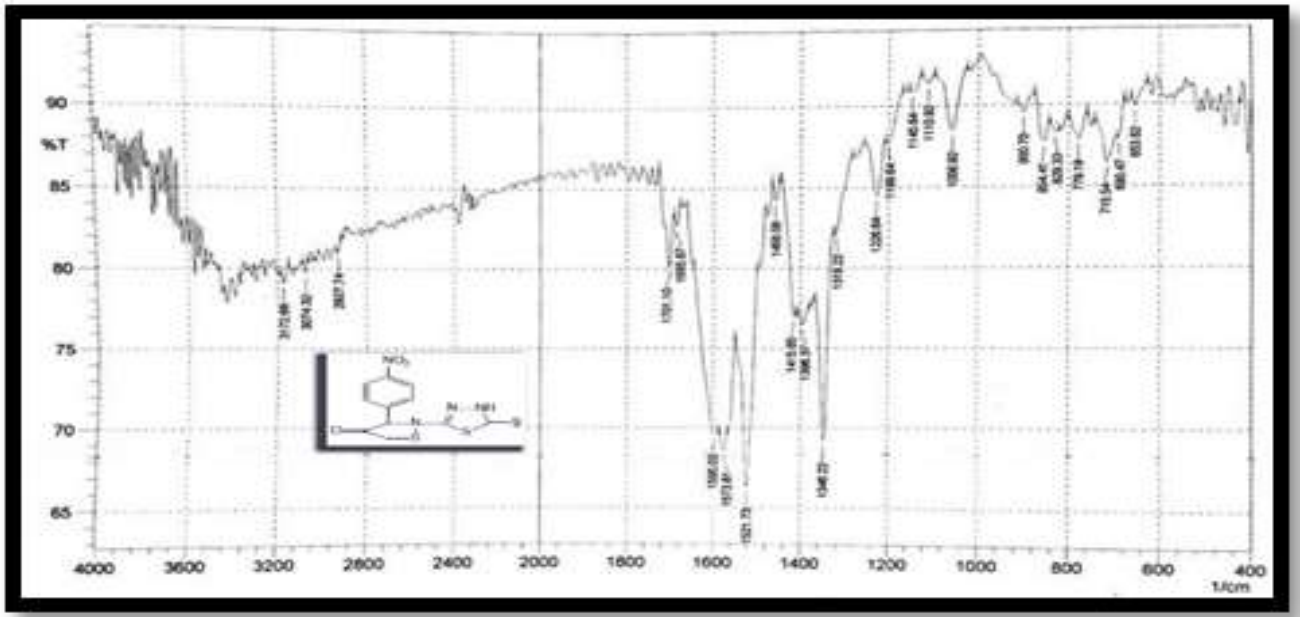


Figure 4: FT-IR spectral of compound(9)

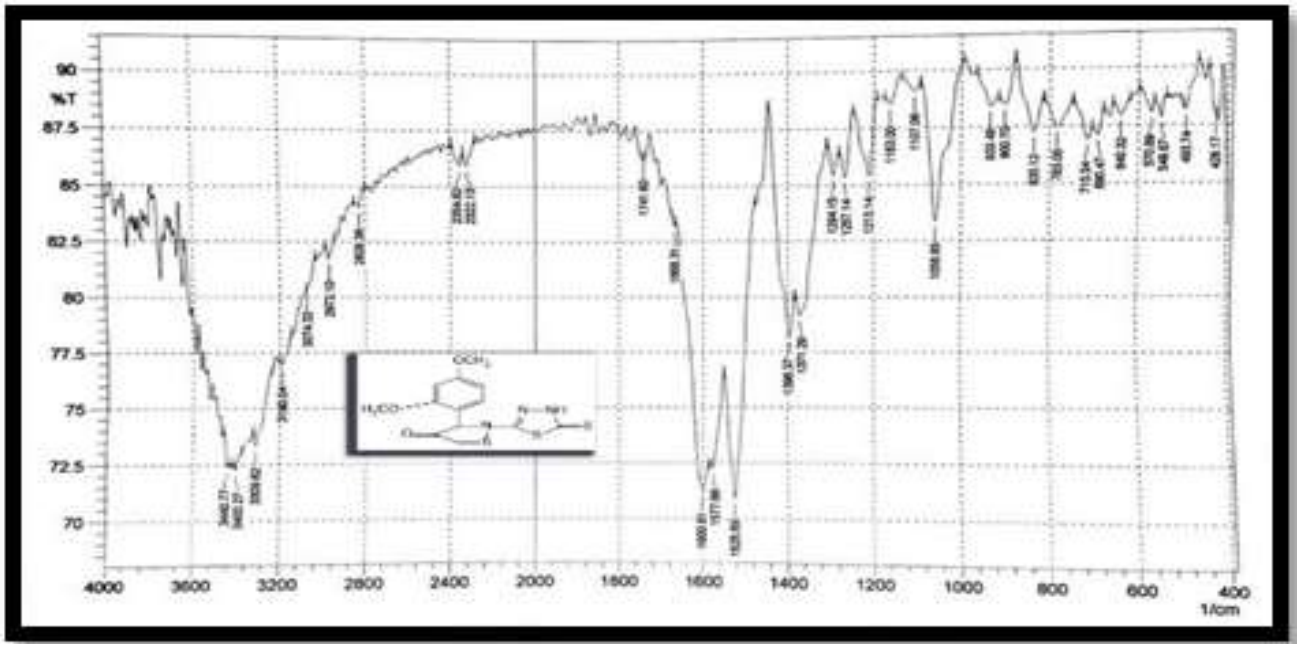


Figure 5: FT-IR spectral of compound(11)

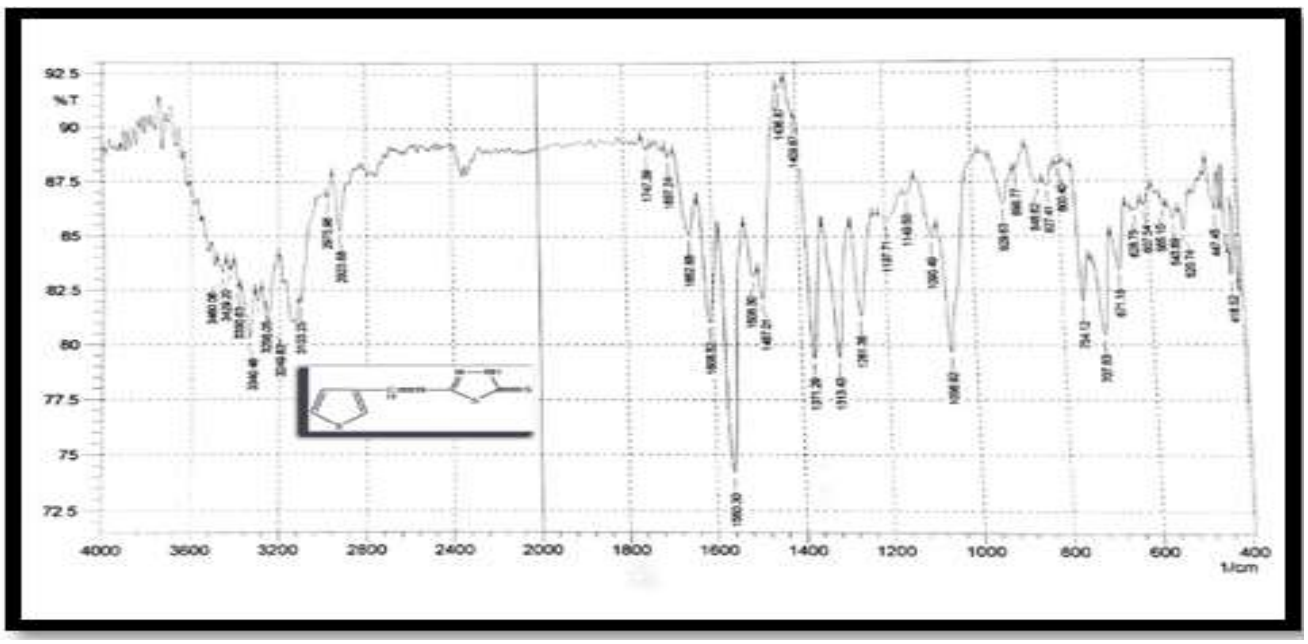


Figure 6: FT-IR spectral of compound(5)

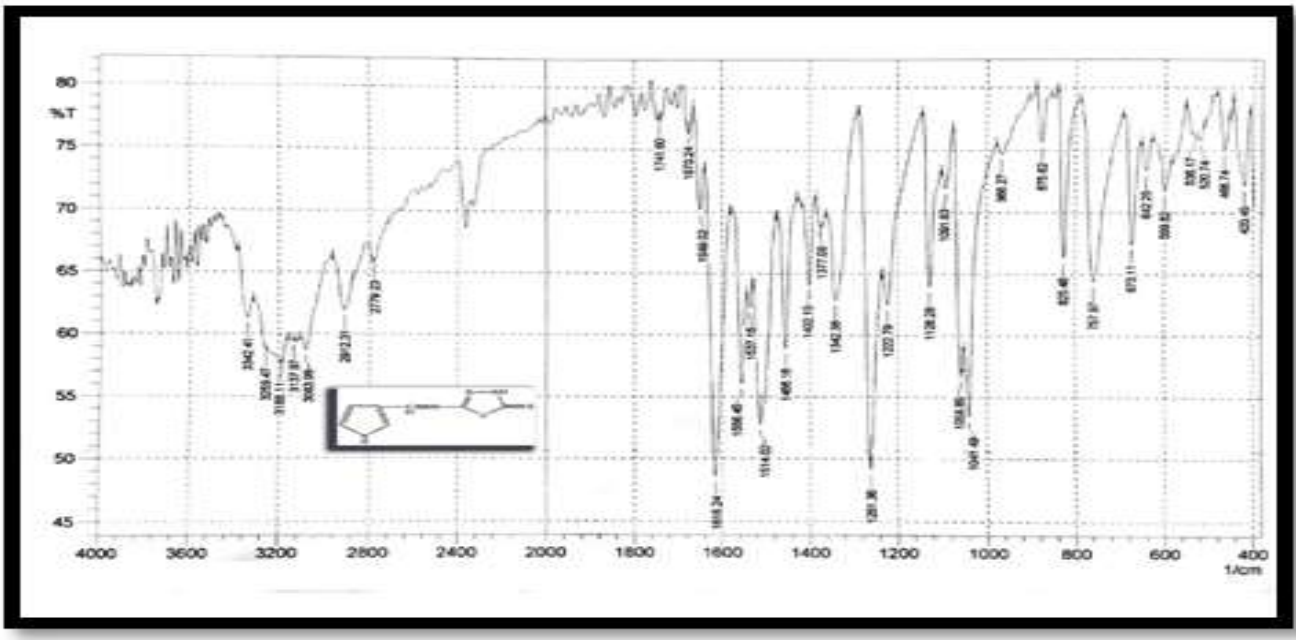


Figure 7: FT-IR spectral of compound(6)

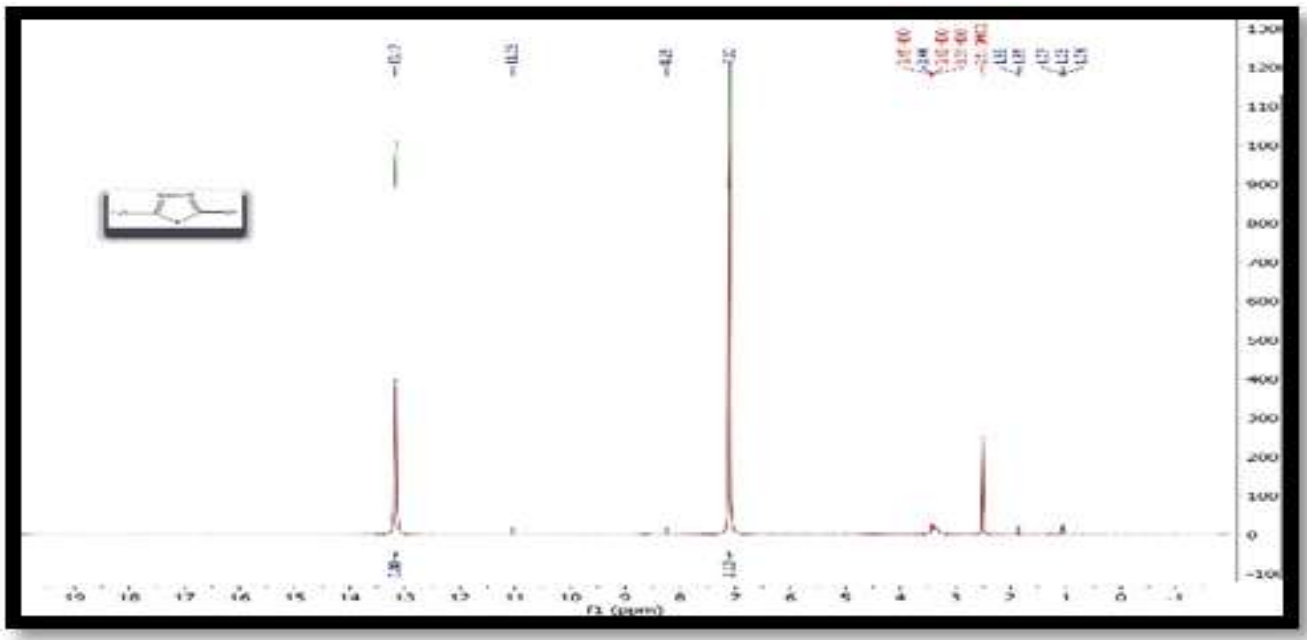


Figure 8: ^{1}H-NMR spectrum of compound (A)

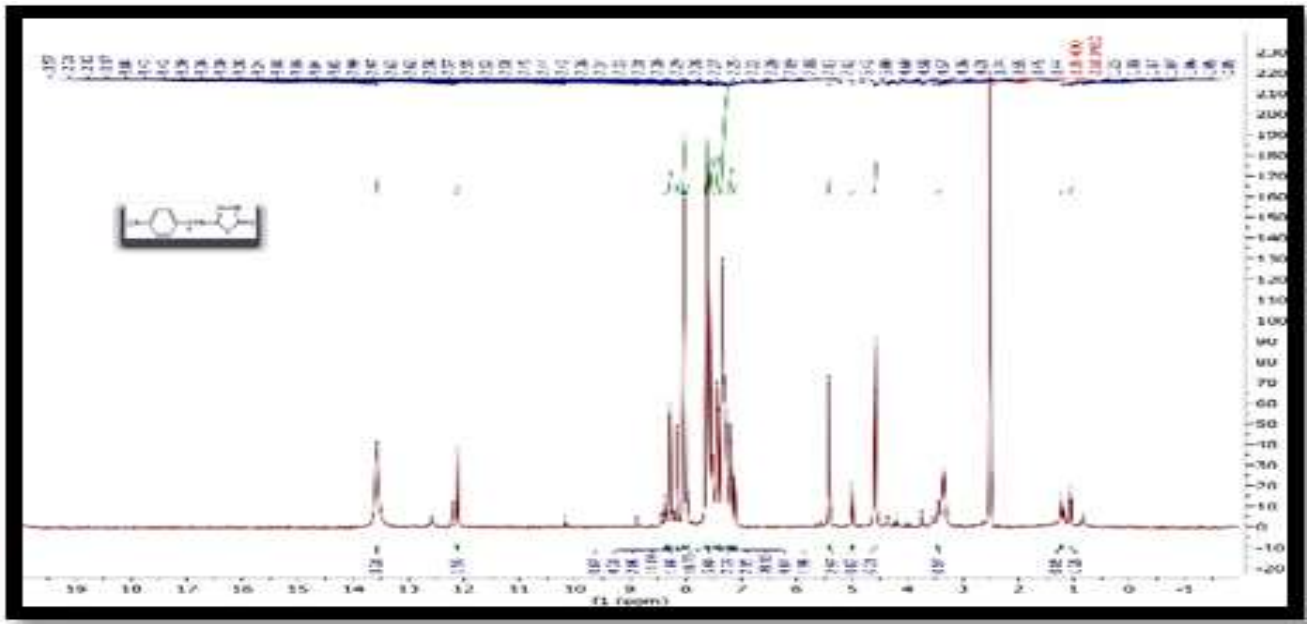


Figure 9: ^{1}H-NMR spectrum of compound (1)

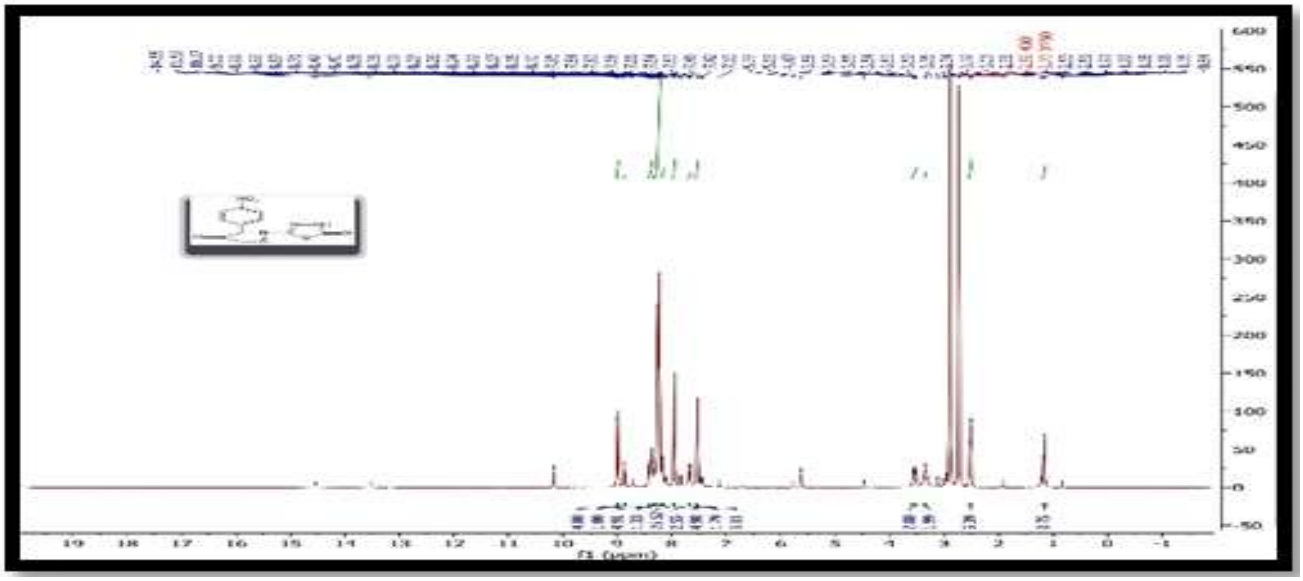


Figure 10: ^{1}H-NMR spectrum of compound (9)

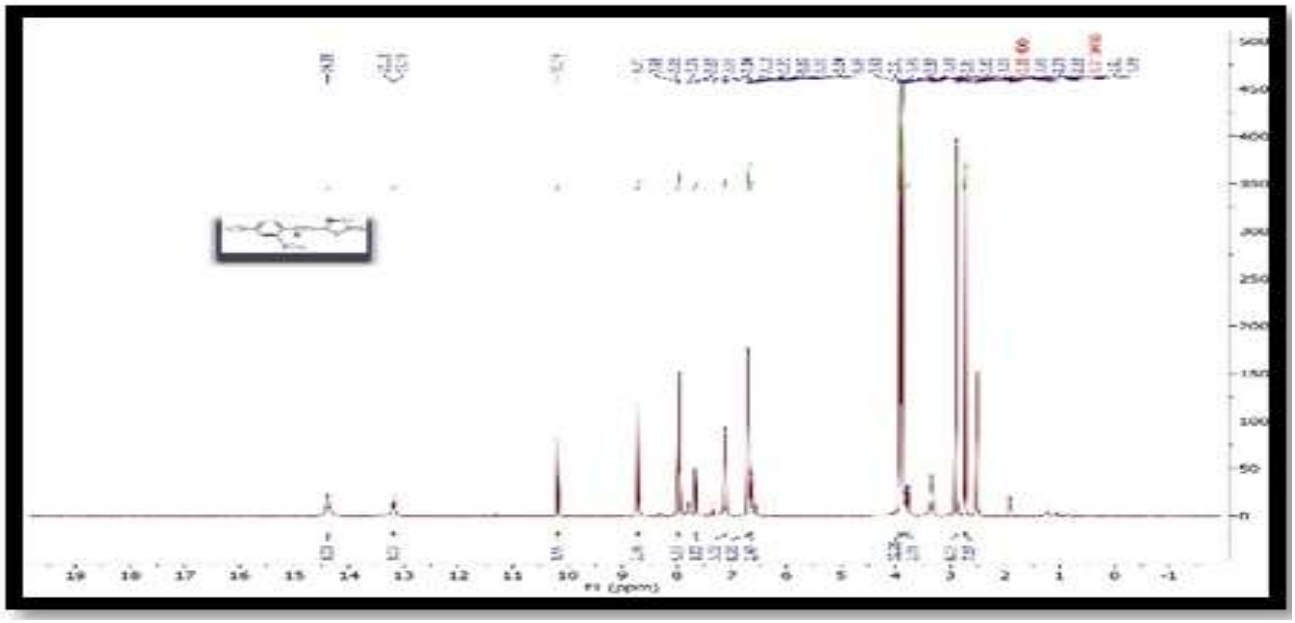


Figure 11: ^{1}H-NMR spectrum of compound (3)

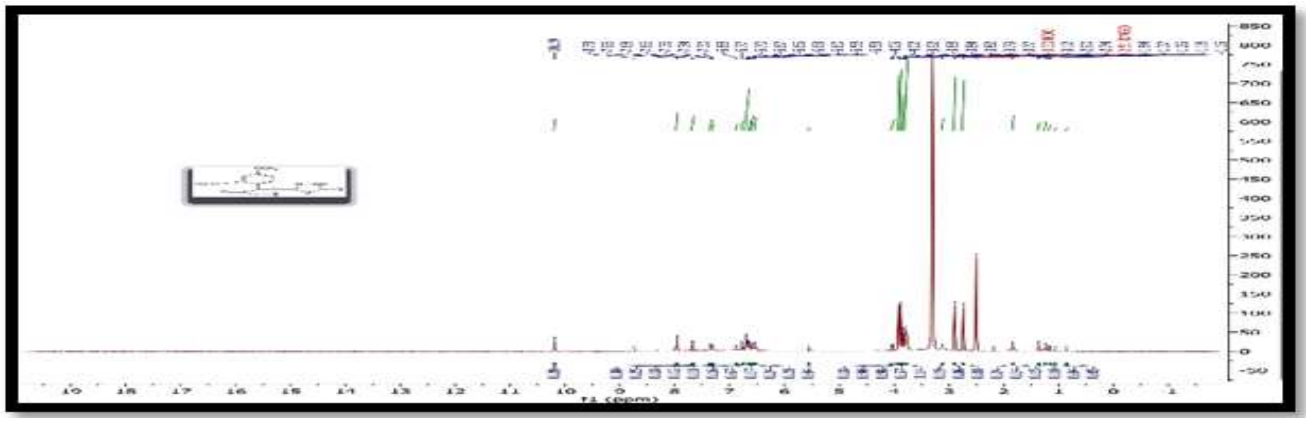


Figure 12: ^{1}H-NMR spectrum of compound (11)

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