PREPARATION AND CHARACTERIZATION OF (OXAZAPENE AND IMIDAZOLODIN-4-ONE) DERIVATEVES WITH THIAZOLE MOIETY

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Abstract

The research includes preparation of new heterocyclic derivatives such (oxazepine and imidazolodine-2-one),starting from 2-amino thiazole. This work is divided in two parts:

Part one: include three steps: The first step includes the synthesis of Schiff base derivatives from the reaction (2-amino thiazole) with 4-amino benzaldehyde ,while the second step include the reaction of Schiff base with isatine to form new Schiff base ,the third step includes reaction of maleic and phthaleic anhydride and tyrosine amino acid with the prepared Schiff base to form various five and seven heterocyclic rings.

Part two include two steps:

The first step includes the synthesis of Schiff base derivatives by the reaction of (2-amino thiazol) with acetyl acetone, then the reaction involves prepared of Schiff base with maleic and phthaleic anhydride to form seven membered ring ; All these compounds were characterized by (FT-IR)and (C.H.N) and some of them by (^{1}H-NMR).

Key word:

Thiazole. 2-aminothiazole, Imidazolodine, isatine, amino acids, Schiff base, oxazepine.

Introduction

Thiazole is heterocyclic compound has containing of both nitrogen and sulfur atoms as apart of the aromatic five-membered ring. Thiazole and concerning compounds are called 1,3-azole .there are isomeric with 1,2-Thiazole derivatives [(1)].Thiazole is aromatic on the basis of delocalization of alone pair of electron from sulfur atom completing the needed 6π electrons to satisfy Hoel's rule[(2)].

Thiazole derivatives have a wide range of biological activities such as cardiotonical[(3)],fungicidal[(4)],sedative[(5)],anesthetic[(6)],bactericidal and anti-inflammatory[(7)].The synthesis of thiazole derivatives is important of their wide range of pharmaceutical and biological properties[(8)]. The most straight forward procedure reported by Hantzch in1887 in volve condensation of halo ketones and thiourea or thioamide [(9)]. This method is long reaction time (24-25hrs) Harsh reaction conditions[(10)]. In modern study [(11)] have been synthesized

oxazepine derivatives from react 2-amino thiazole with terphthaldyhyde to form Schiff base and then enclosed by maleic and phthaleic anhydride to form oxazepine derivatives.

So Mishra et.al.[12] have been synthesized Schiff base from react of 2-amino thiazole with substituted aromatic aldehyde .the Schiff bases show a good activity against to Gram-positive bacteria.

Experimental

Measurements

Melting points(m.p) of synthesized compounds were determined in open capillary tube and are uncorrected by Barnstead Electro Thermal melting point, 900-U.K. The IR spectrum (ύ-cm^{-1}) was optioned with Test on shimatzu (FT:IR8000 series, Japan) using the KBr pellet technique. The Elemental analysis was measured by Euro vector, EA3000A, Italy. Thin Layer Chromatography (TLC) was performed in silica gel for (TLC).All products the TLC showed that the reaction was completed and the spots were visualized by Iodine

Synthesis of N-(4-aminobenzylidene)thiazol-2-amine (A1)

Was dissolved of 2-amino thiazole (0.5gm,0,005 mol) in 30ml of absolute ethanol containing three drops of glacial acetic acid ,then (0.605gm,5mmol) of 4-amino benzaldehyde were added . the reaction mixture was refluxed with stirring for (6-8hrs.). TLC showed that the reaction was completed. The mixture was allowed to cool at room temperature and recrystallized from ethanol. The physical properties of prepared compound(A1) m.p;135 C°, ylide; 83%, Rf; 0,88, and the Color; Nutty.

Synthesis of (3E)-3-((4-((thiazol-2-ylimino)methyl)phenyl)imino)indolin-2-one (A2).

This compound prepared from solvation of (A1) (0.812gm,4mmol) in 30ml of absolute ethanol containing three drops of glacial acetic acid ,then (0.588gm,4mmol) of isatine were added .the reaction mixture was refluxed with stirring for (10hrs) . The physical properties of prepared compound (A2) m.p;(140-141) C°, ylide; 83%, Rf ;0,77, and the Color; Brown.

Synthesis of 3'-(4-(4,7-dioxo-3-(thiazol-2-yl)-2,3,4,7-tetrahydro-1,3-oxazepin-2-yl)phenyl)-3'H-spiro[indoline-3,2'-[1,3]oxazepine]-2,4',7'-trione (A3)

Dissolved of (0.4224gm,1.2mmol) of (A2) in 30ml of dry benzene ,then (0.473gm,3.2mmol) of maleic anhydride were added. The reaction mixture was refluxed with stirring for (8)hrs. The physical properties of prepared compound(A3) m.p;(120-122) C°, ylide: 67%, Rf:0,63, and the Color: Nutty.

Synthesis of 4-(4-(1,5-dioxo-4-(thiazol-2-yl)-1,3,4,5-tetrahydrobenzo[e][1,3]oxazepin-3-yl)phenyl)-1H-spiro[benzo[e][1,3]oxazepine-3,3'-indoline]-1,2',5(4H)-trione (A4).

Dissolved of (0.3168gm,1mmol) in 30m of dry benzene ,then (0.3168gm,2mmol) of phathaleic anhydride were added. The reaction mixture was refluxed with stirring for (5-8hrs). The physical properties of prepared compound(A4) m.p;(110-112) C°, ylide; 84%, Rf ;0,62, and the Color; Dark brown.

Synthesis of 4-(4-hydroxybenzyl)-1-(4-(4-(4-hydroxybenzyl)-5-oxo-1-(thiazol-2-yl)imidazolidin-2-yl)phenyl)spiro[imidazolidine-2,3'-indoline]-2',5-dione (A5).

A mixture of (0.166gm,1mmol) of (A2) and (0.181gm,2mmol) of tyrosine was dissolved in 30ml of THF. The reaction mixture was refluxed with stirring for 24hrs. the mixture was allowed to cool at room temperature and recrystallized from ethanol. The physical properties of prepared compound (A5) m.p;(185-187) C°, ylide; 89%, Rf ;0,45,and the Color; Yellow.

Synthesis of N,N'-(pentane-2,4-diylidene)bis(thiazol-2-amine) (A6).

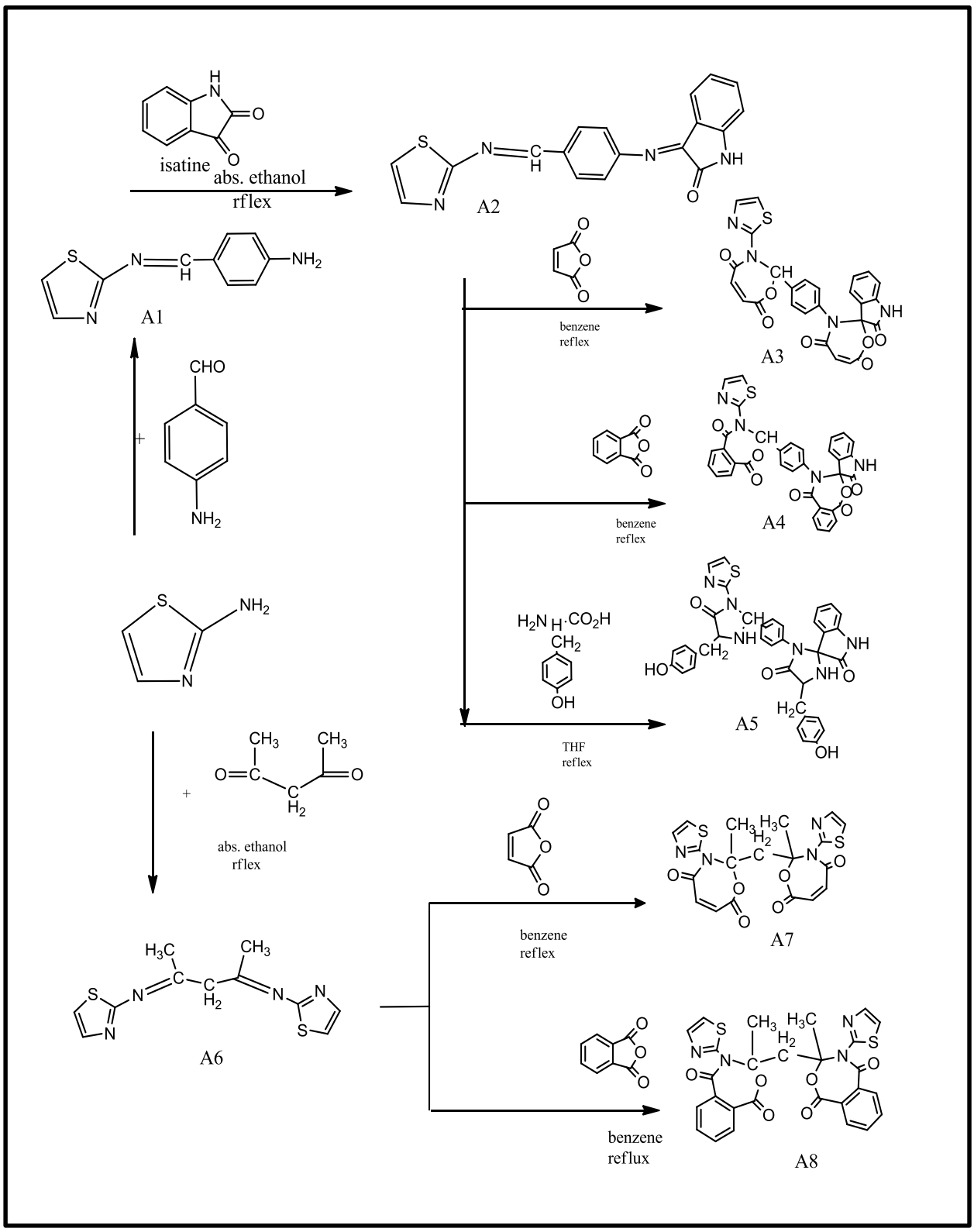
2-amino thiazole (0.6gm,2mole) was dissolved in 30ml of absolute ethanol containing three drops of glacial acetic acid ,then (0.3gm,0.003mole) of acetyl acetone was added . The reaction mixture was refluxed with stirring for (8hrs). The physical properties of prepared compound(A6) m.p;(107-108) C°, ylide ; 67%, Rf ;0,67, and the Color; Nutty.

Synthesis of 2,2'-methylenebis(2-methyl-3-(thiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione) (A7).

From (A6) (0.4224gm, 2mmol) was dissolved in 30ml of dry benzene ,then (0.4736gm,2mmol)of maleic anhydride was added. The reaction mixture was refluxed with stirring for (12hrs). The physical properties of prepared compound(A7) m.p;(130-131) C°,ylide; 78%, Rf;0,48, and the Color; Ashen.

Synthesis of 3,3'-methylenebis(3-methyl-4-(thiazol-2-yl)-3,4-dihydrobenzo[e][1,3]oxazepine -1,5-dione) (A8).

From (A6) (0.3168gm,1.2mmol) was dissolved in 30ml of dry benzene ,then (0.3552gm ,2.4mmol) of phthaleic anhydride were added. the reaction mixture was refluxed with stirring for (10hrs) . The physical properties of prepared compound(A6) m.p;(122-123) C°,ylide;65%, Rf; 0,52, and the Color; Grass yellowish.



Scheme(1)Synthetic pathway for preparation of compound (A_1-A_8)

RESULT AND DISSCUSTION

FTIR Spectrum of compounds (A1-A8)

The FTIR spectrum of compound (A1) showed disappearance of two absorption bands at ($3500cm^{-1}$,$3288cm^{-1}$)due to stretching vibration of (NH_2) group. FTIR also showed the appearance of absorption band at ($1620cm^{1}$)due to stretching vibration of (N=CH)..and appearance of absorption at($1440cm^{-1}$) due to stretching vibration of (C=N) thiazole. Figure (1)
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The FTIR spectrum of compound (A2) showed disappearance of absorption band at ($1720cm^{-1}$) due to stretching vibration of (C=O)ami.de group of isatine compound and also showed the appearance of absorption band at ($1620cm^{-1}$)due to stretching vibration of (N=CH)and also it showed the appearance of absorption band at ($3292cm^{-1}$)due to stretching vibration of (NH)of isatine. Figure (2).

The FTIR spectrum of compound (A3) Fig. (3). showed the absorption band at ($3120cm^{-1}$)due to stretching vibration of (CH)aromatic .and appearance of absorption band at ($2935cm^{-1}$) of (CH) aliphatic.and appearance of two absorption band at ($1716,1735cm^{-1}$) due to stretching vibration of the absorption band at ($3194cm^{-1}$)of (NH) amide group.

The FTIR spectrum of compound(A4). showed disappearance of the absorption band at($3180cm^{-1}$)due to stretching vibration of (NH) amide group of isatine compound and appearance two absorption band at ($1735\text{-}1678cm^{-1}$) due to stretching vibration of (C=O)amide and lactone. Fig.(4).

FTIR spectrum of compound (A5) Fig. (5) showed disappearance of absorption band at ($3415cm^{-1}$)due to stretching vibration of (OH) and appearance of absorption band at ($3300cm^{-1}$) due to stretching vibration of (NH)and appearance of absorption band at ($1635cm^{-1}$)due to stretching vibration of (C=O)ketone and appearance of absorption band at ($3120cm^{-1}$) due to stretching vibration of (C-H) aromatic**.**

The FTIR spectrum of compound (A6) Fig. (6) showed the absorption band at ($1608cm^{-1}$) due to stretching vibration of imine group (C=N) and appearance of absorption band at ($2972cm^{-1}$) due to stretching vibration of (C=H) and appearance of absorption band at ($1442cm^{-1}$) for (C=N) of thiazole.

FTIR spectrum of compound (A7) Fig. (7) showed disappearance of the absorption band at ($1714.77cm^{-1}$)and ($1662.00cm^{-1}$)due to stretching vibration of (C=O)of lactone and

(C=O)amide. and absorption band at (2928.11cm^{-1})due to stretching vibration of (C-H)aliphatic.

Figure (8)of compound (A8) FTIR spectrum showed disappearance of the absorption band at (3120cm^{-1}) due to stretching vibration of (C-H)aromatic and appearance of the absorption band at (2935cm^{-1})for (C-H)aliphatic and appearance two absorption band at (1680cm,1714cm^{-1}) due to absorption band of (C=O)amide and lactone.

^{1}H-NMR-Spectrum

Figure (9) showed the (^{1}H-NMR) spectrum of compound (A4) The following characterization chemical shift ($CHCl_3$ as a solvent)singlet signal at δ(9ppm)that could be attributed to the proton of azomethine group(-CH=N).The singlet single at δ(8.024ppm)that could be attributed to the one proton of(-NH)of isatine .while the multiplet single at (6.9-7.88ppm) that could be attributed to the aromatic proton of phenyl rings and oxazepine. Doublet signle at (7.5 and 7.9 ppm) that could be attributed to the five proton of thiazol and four proton of thazol. the singlet signal at (2.5 ,3.37 ppm) that could be attributed to proton of solvent.

Table(1):Elemental analysis of compounds (A3,A4,A5,A8)

Compound No		%N	%H	%C	%S
A3 ($C_{26}H_{16}N_4O_7S$)	Pragmatic	10.1	3	58.8	5.97
	Theoretic	10.6	3.03	59.09	6.06
A4 ($C_{34}H_{20}N_4O_7S$)	Pragmatic	7.05	3.15	64	5
	Theoretic	8.9	3.18	64.9	5.09
A5 ($C_{29}H_{28}N_6O_4S_2$)	Pragmatic	12.98	4.2	67.6	4.8
	Theoretic	13.2	4.4	67.92	5.03
A8 ($C_{27}H_{20}N_4O_6S_2$)	Pragmatic	9.88	3.44	57	11.08
	Theoretic	10	3.57	57.85	11.42

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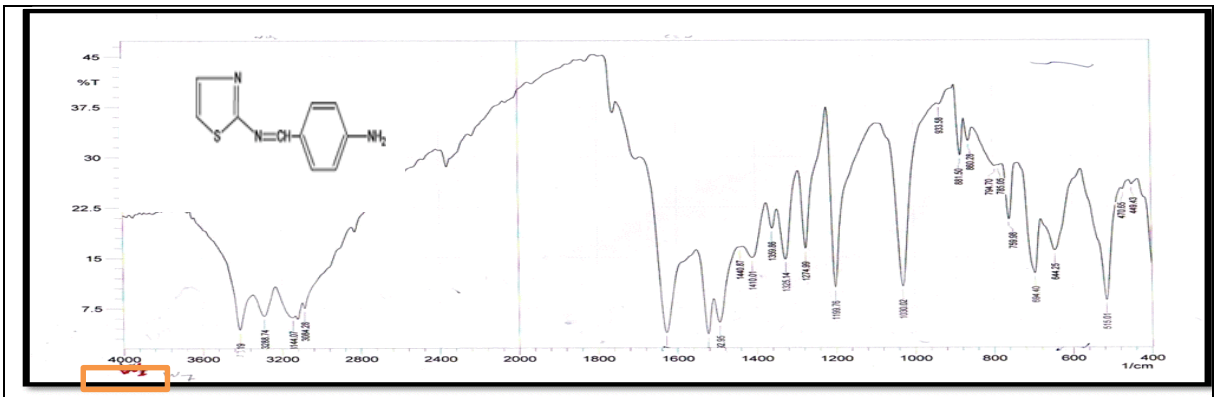

Fig.(1): FTIR of compound (A1)

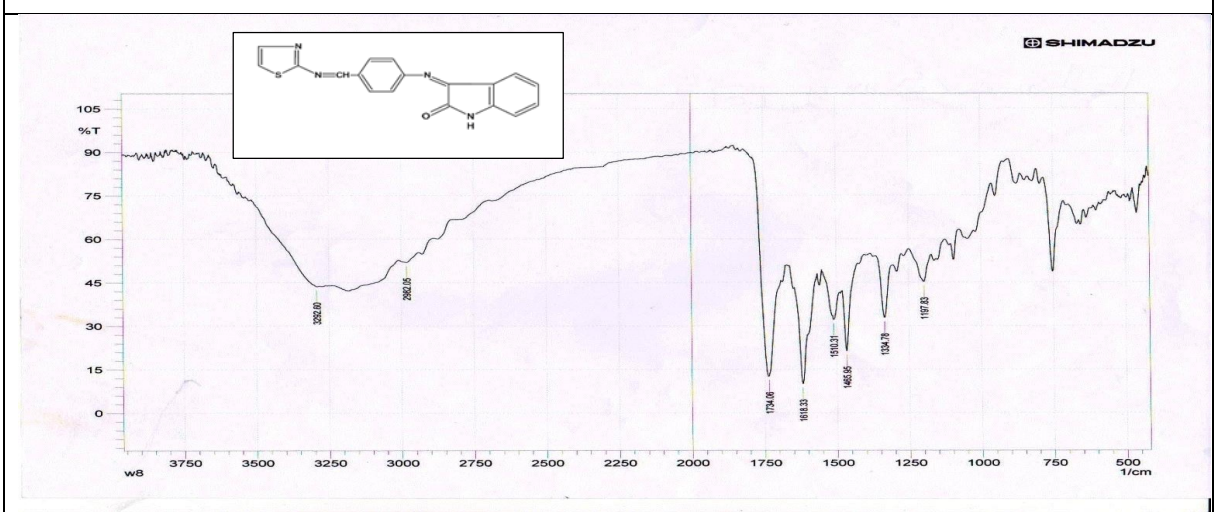

Fig.(2): FTIR of compound (A2)

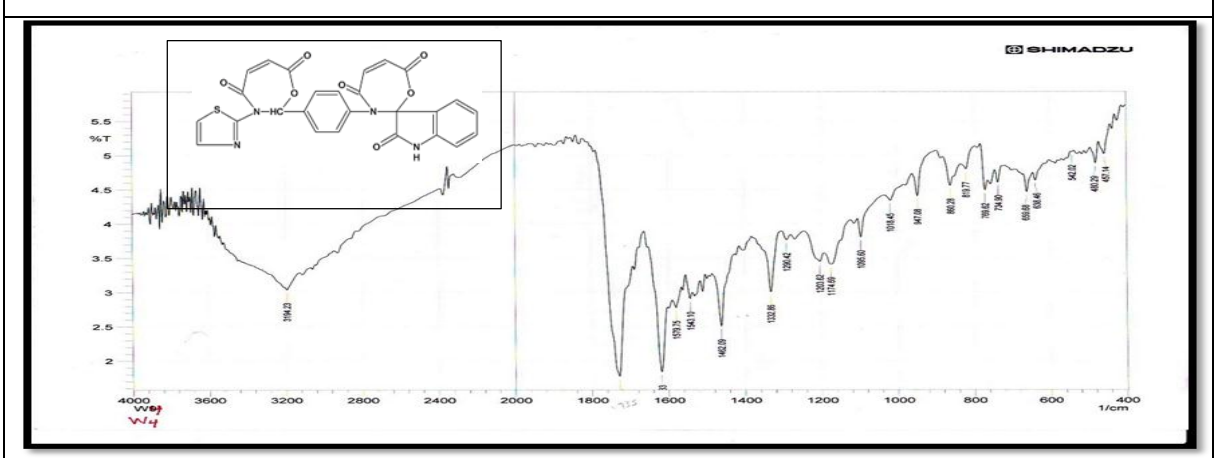

Fig.(3) :FTIR of compound (A3)

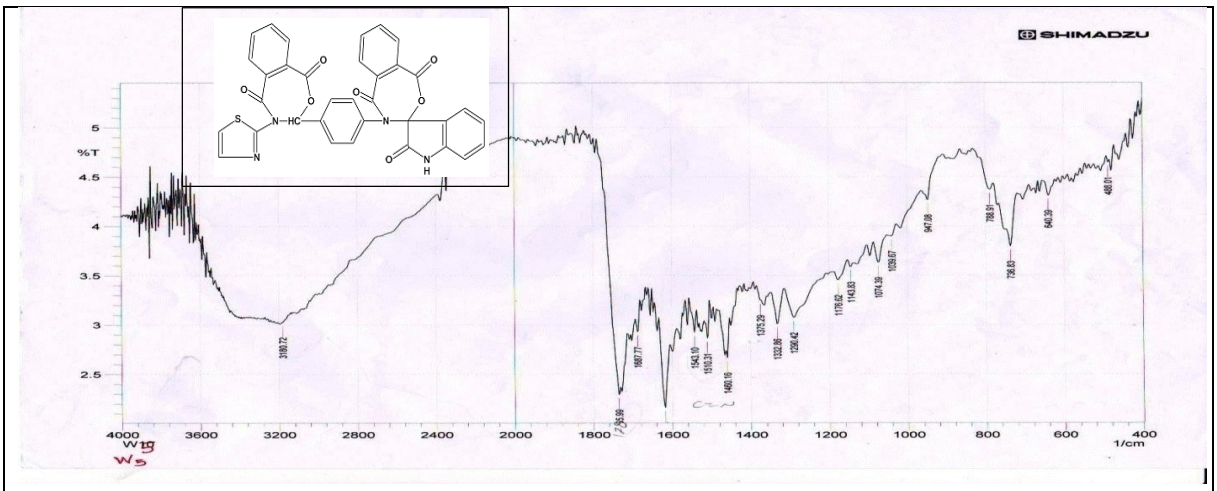

Fig.(4) :FTIR of compound (A4)

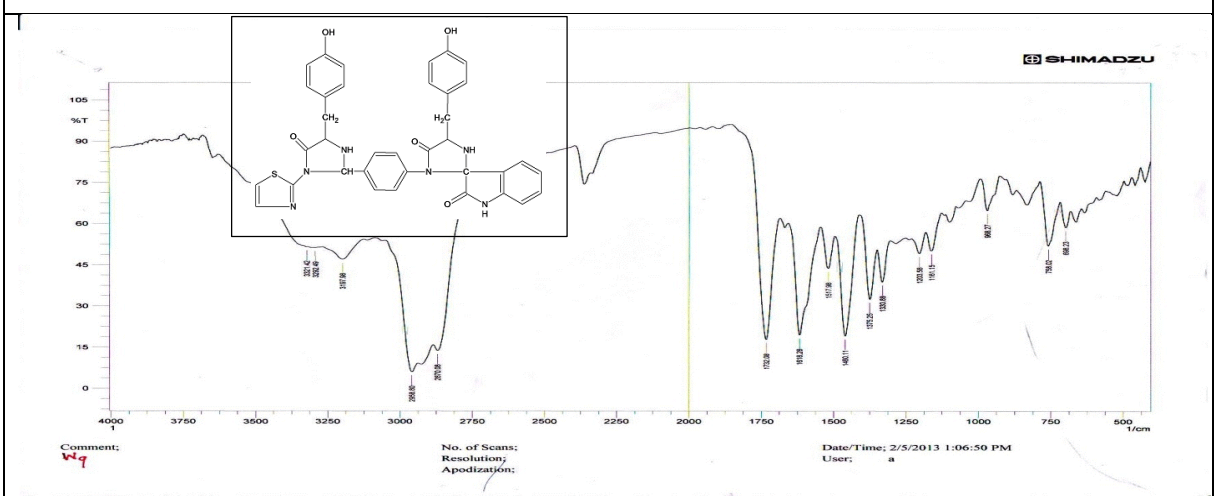

Fig.(5) :FTIR of compound (A5)

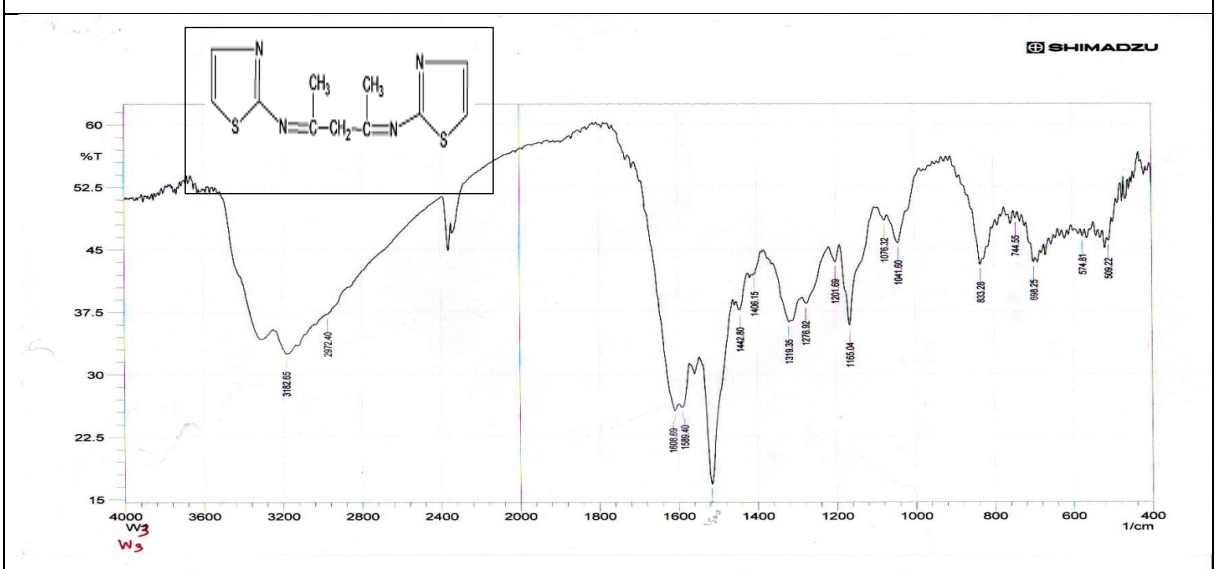

Fig.(6) :FTIR of compound (A6)

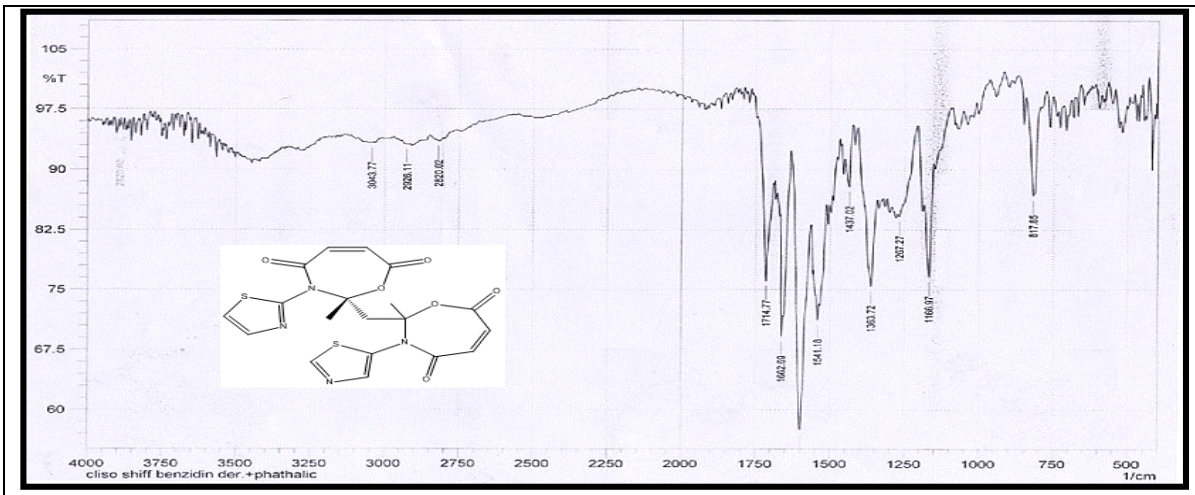

Fig.(7) :FTIR of compound (A7)

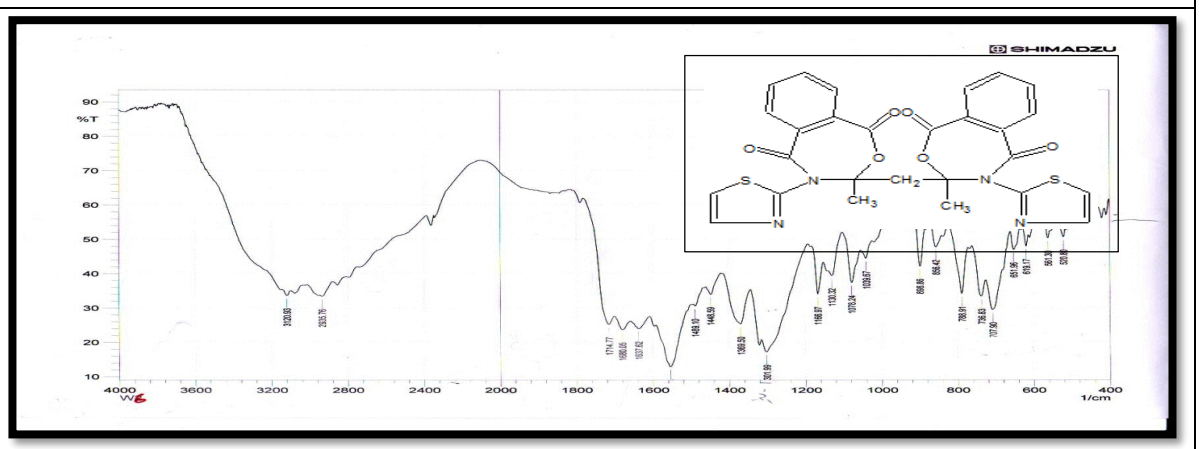

Fig.(8) :FTIR of compound (A8)

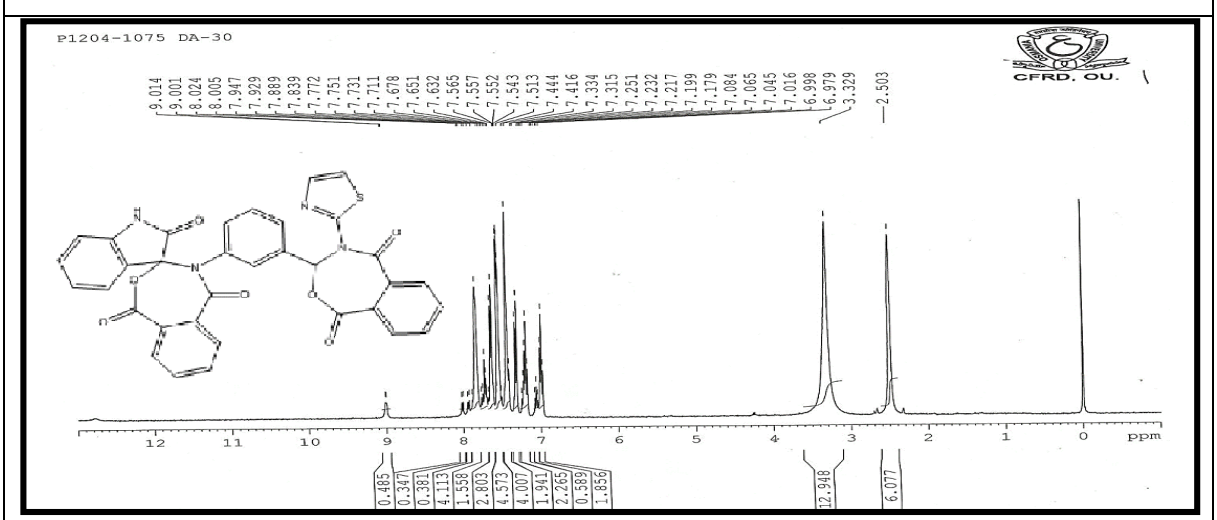

Fig.9:1H-NMR spectrum of compound (A4)