Synthesis and characterization of some heterocyclic compounds (benzoxazpine, oxazpine, tetrazol and imidazoldin-4-one) from condensation of isatin with dapson

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Abstract

The present work includes, synthesis of novel (Schiff's) compounds in high yield. Which reacts with phthalic anhydride, Maleic anhydride, succunic anhydride, sodium azid, leucin amino acid and alanine amino acid via refluxing of reactions to produce various heterocycles (seven and five) members rings like (benzoxazpine, oxzaepine, tetrazol, and imidazoldin), the structure of the new synthesized compounds are monitored by (TLC) and identified by many techniques (FTIR,) and melting points

Keywords (*isatin, Schiff's bases, benzoxazepin, oxazepin, tetrazol, imidazoldine***)**

Intdoduction

Dapson is a term used to refer to white color crystal powder. It is named 4,4-diamino diphenyl sulphon and its formula is ($C_{12}H_{12}N_2So_2$)[1], Dapson has been used for the medication of leprosy, dermatitis. herpetformis, pneumocystis and ocular-side effects have seldom been reported[2]. Dapson analog has been proved to be a strong antimicrobial agent[3]. Isatin is a chemical compound with a hetrocyclic indol ring and a molecular formula $C_8H_5O_2N$. It was prepared by Erdmann and Laurent in 1841[4]. As a product from the oxidation of indigo blue dye by nitric acid and chromic acids. The compound has many benefits it's wide spectrum of biological activities[5]. It has been identified as an endogenous multifunctional compound in plants, fungi, marine organisms, and mammals[6].

Hugo Schiff describes the condensation between an Keton such as (isatin) and an primary amine such as (dapson) leading to produce Schiff bases[7]. Schiff bases constitute one class of important compounds in medical and pharmaceutical fields[8]. Schiff bases connected to antibacterial, and antitubercular activities and have diverse biological activities[9].

Heterocyclic compounds consist of seven and five membered rings. They have given more significance in the recent decades for industrial and medical reasons[10]. Imidazoldine and tetrazol derivatives play a significant role in medical and industrial fields[11].

Imidazoldine is five membered ring hetrocyclic compounds and its forula is ($C_3H_8N_2$)[12].

Experimental

1. **Synthesis of Schiff base (3,3′-(sulfonylbis(4,1-phenyle bis(azaneyl ylidene) bis(indolin-2-one)[13]**

   Isatin (5.88gm, 0.001 mol) was refluxed with (2.48 gm , 0.002 mol) of dapson in absolute ethanol 60 ml and a catalytic amount of GAA (two or three drops) of The reaction mixture was refluxed 9 hrs at 80°C and the Mixture was monitored by TLC. The product was collected by filtration and recrystallized by absolute ethanol.

2. **Synthesis 4,4″-(sulfonylbis(4,1-phenylene) bis (1H-spiro [benzo [e] [1,3]oxazepin-3,3′-indoline]-1,2,5-(4H)-trion[14]**

   Schiff base (0.506 gm, 0.00l mol) was refluxed with (0.296 gm, 0.002 mol) of phathalic anhydride in 20 ml dry benzene, was added at 75°C. the reaction mixture was refluxed 22 hrs the mixture was monitored by TLC. The product was collected by filtration and recrystallized by ethanol.

3. **Synthesis 3′,3″-(sulfonylbis(4,1-phenylene) bis (1H-spiro [indoline-3,2′[1,3]oxazepin-3,3′-]-2,4,7-trion[14]**

   Shiff base (0.506 gm, 0.001 mol) was refluxed with (0.196gm. 0.002 mol) of Maleic anhydride in 20 ml drybenzen. Was added at 75°C. the reaction mixture was refluxed 24 hrs the mixture was monitored by TLC. The product was collected by filtration and recrystallized by ethanol.

4. **Synthesis 3′,3″′-(sulfonylbis(4,1-phenylene) bis (1H-spiro [indoline -3,2′ [1,3]oxazepin-3,3′-]-2,4′,7-trion[14]**

   Schiff base (0.506 gm, 0.001 mol) was refluxed with (0.2 gm, 0.002 mol) of succunic anhydride in 20 ml dry benzene. Was added at 75°C. the reaction mixture

was refluxed 22 hrs the Mixture was monitored by TLC. The product was collected by filtration and recrystallized by ethanol.

5. **Synthesis 1′,1′″-(sulfonylbis(4,1-phenylene) bis (1′,4′-dihyrospiro [indoline -3,5′-tetrazol]-2-one)[15]**

   Schiff base (0.506 gm, 0.001 mol) was refluxed with (0.13 gm, 0.002 mol) of sodium azid in 20 ml DMSo was added at 75°C. the reaction mixture was refluxed 24 hrs the mixture was monitored by TLC. The product was collected by filtration and recrystallized by ethanol.

6. **Synthesis (1,1″-(sulfonyl bis(4,1-phenylene)bis(4-isobutyl spiro [imidazolidine-2,3-indoline]-2,5-dione)[16]**

   Schiff base (0.506 gm, 0.001 mol) was refluxed with (0.262 gm, 0.002 mol) of leucin amino acid in 20 ml dry benzene, was added at 75°C. the reaction mixture was refluxed 22 Hrs the mixture was monitored by TLC. The product was collected by filtration and recrystallized by ethanol.

7. **Synthesis (1.1″-(sulfonyl bis(4,1-phenylene)bis(4-methyl spiro [imidazolidine-2,3′-indoline]-2′,5-dione[16]**

   Schiff base (0.506 gm, 0.001 mol) was refluxed with (0.178 gm, 0.002 mol) of alanine amino acid in 20 ml dry benzene. Was added at 75°C. the reaction mixture was refluxed 22 hrs the mixture was monitored by TLC. The product was collected by filtration and recrystallized by ethanol.

Table 1: physical properties and other characteristics for the synthesized compounds

No.	Molecular Formula	M.wt g/mol	M.PC^0	color	Rf 1Me, 4Ben	Solvent	Reflex Time	Yield %
T_1	$C_{28}H_{18}N_4S_1O_4$	506	250	Yellow	0.75	EtoH	9 Hrs	78.12
T_2	$C_{44}H_{26}N_4S_1O_{10}$	802	150	Pale yellow	0.78	Benz	22 Hrs	70.2
T_3	$C_{36}H_{22}N_4S_1O_{10}$	702	120	Pale yellow	0.73	Benz	24 Hrs	63.5
T_4	$C_{36}H_{26}N_4S_1O_{10}$	706	132	Orange red	0.74	Benz	22 Hrs	65.5
T_5	$C_{28}H_{20}N_{10}S_1O_4$	592	220	Brown	0.77	Dmso	24 Hrs	60
T_6	$C_{40}H_{40}N_6S_1O_6$	732	180	Orange	0.78	Benz	22 Hrs	55.15
T_7	$C_{34}H_{28}N_6S_1O_6$	648	150	orange	0.76	Benz	22 Hrs	62.2

Results and discussion

Schiff base T_1: The infrared spectrum data of compound (T1) showed band at (3271cm^{-1} for (N-H), (3018) cm^{-1} for (C-H, benzene), (1710 cm^{-1} for (C=O, pyrrolidin), (1623) Cm-1 for (C=N, imine), (1423 and 1500) cm^{-1} for (C=C, benzen), (1350) cm^{-1} for (O=S=O). fig (1)

Compound T_2: The infrared spectrum data of compound (T_2) showed band at (3350 and 3437) cm^{-1} for (N-H) pyrrolidin form) (2900, 3020, 3076) cm^{-1} (C-H, benzene), (1695) cm^{-1} for (C=O, lacton, oxazepin), (1620) cm^{-1} for (lactam, oxazepin), (1404 and 1589) cm^{-1} for (C=C, benzene), (1282) cm^{-1} for (O=S=O). fig (2)

Compound T_3: The infrared spectrum data of compound (T_3) showed band at (3309,3442) cm^{-1} for (N-H), (3194 and 3219) cm^{-1} for (-CH=CH-,oxazpim), (3037,3061,3113) cm^{-1} for (C-H, benzene) (1730) cm^{-1} for (lacton, oxazepin), (1620) cm^{-1} for (lactam, oxazepin), (1400 – 1585) cm^{-1} for (C=C, benzene), (1330) cm^{-1} for (O=S=O) fig (3)

Compound T_4

The infrared spectrum data of compound (T_4) showd band at (3429) cm^{-1} for (N-H),

(3066 – 3182) cm^{-1} for (C-H,benzene), (2760,2926) cm^{-1} for (C-H, aliphatic), (1741) cm^{-1} for (C=O, pyrrolidin), (1697, 1722) cm^{-1} for (C=O, lacton, oxazepin), (1614) cm^{-1} for (C=O, lactam, Oxazepin) (1531 , 1587) cm^{-1} for (C=C, benzene), (1417, 1463) cm^{-1} For (C-C), (1332) cm^{-1} for (O=S=O).fig4.

Compound T_5:

The infrared spectrum data of compound (T_5) showed band at (3272) cm^{-1} for (N-H), (1690) (C=O), (1608) cm^{-1} for (N=N), (1444) cm^{-1} for (S=O), (1145) cm^{-1} for (C-N), (1064) cm^{-1} (N-N) fig (5).

Compound T_6:

The infrared spectrum data of compound (T_6) showed band at (3442) cm^{-1} for (N-H, amine), (3265) cm^{-1} for (N-H, amide), (3101 – 3188) cm^{-1} for (C-H, benzene), (2872,2960) cm^{-1} for (C-H, aliphatic), (1741) cm^{-1} for (C=O, pyrrolidin), (1664) cm^{-1} for (C=O, imidazole) (1406 – 1614) cm^{-1} for (C=C, benzene), (1332) cm^{-1} for (O=S=O) fig (6).

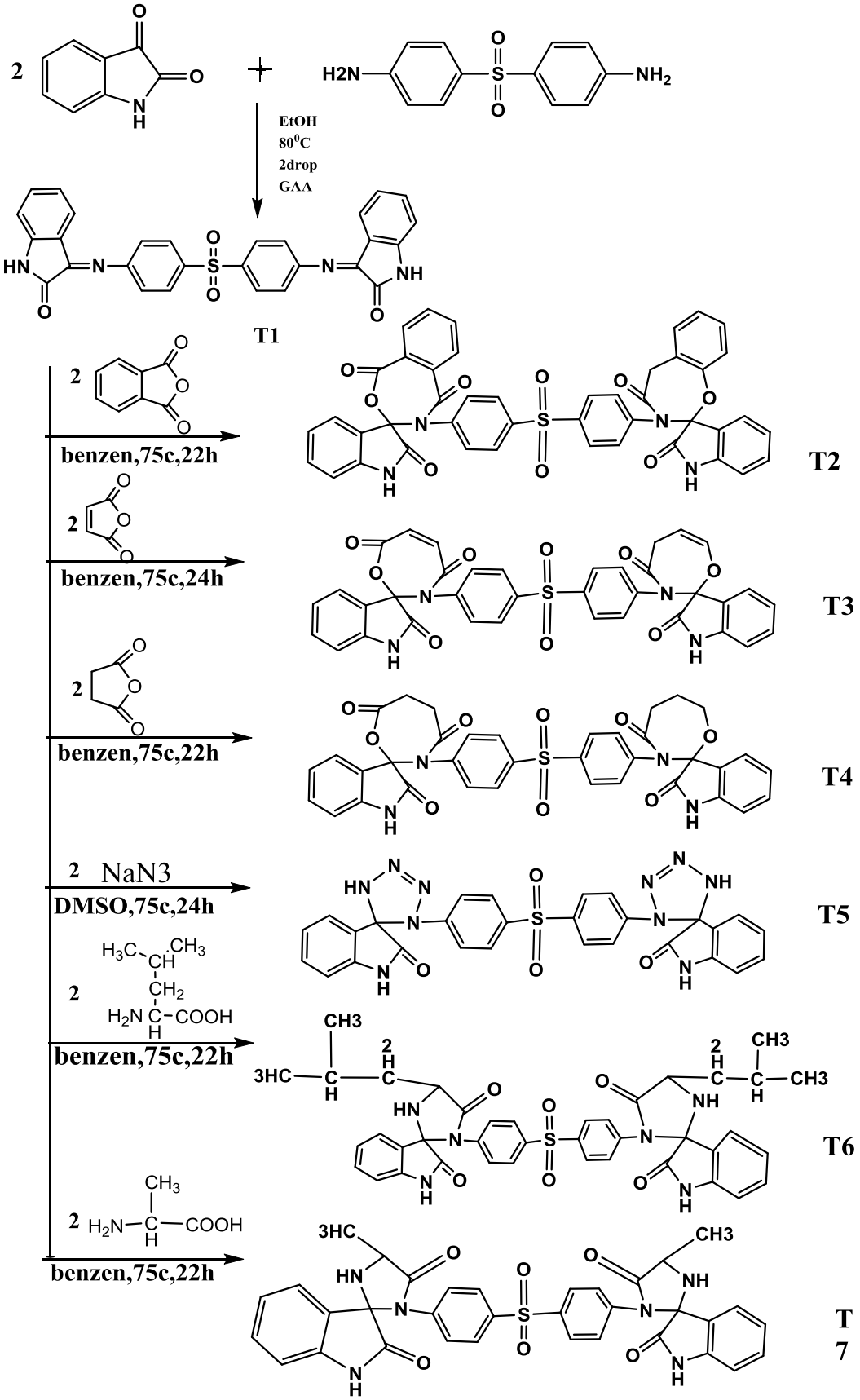
Compound T_7:

The infrared spectrum data of compound (T_7) showed band at (3429) cm^{-1} for (N-H, amine), (3421) cm^{-1} for (N-H, amide), (2920) cm^{-1} for (C-H, benzene), (2850) cm^{-1} for (C-H, aliphatic), (1739) cm^{-1} for (C=O, pyrrolidin), (1620) cm^{-1} for (C=O, imidazole) (1465) cm^{-1} for (C=C, benzene), (1300) cm^{-1} for (O=S=O) fig (7).

Biological activity

In this research. Biological activity is studied to some of compounds (5) by using wells diffusion method. On two types of Gram – positive bacteria (sta-aureus, Entro-coccous) and Gram – Negative (prot – mirabilis, P-aeruginouse). Producted agar and petri dishes were sterilized by autoclaving for 20 min at 200°C. these plates were incubated for 24h at 37C. for both bacteria. DMSO was used as a solvent to prepare solutions of the different compounds were ($1 X 10^{-2}$, $1 X 10^{-4}$, $1 X 10^{-6}$) the inhibition region caused the various compounds.

The results of the preliminary screening tests are listed in table 2,3,4.[17]


2
EtOH
80⁰C
2drop
GAA
T1
benzen,75c,22h
T2
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T3
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T4
NaN3
DMSO,75c,24h
T5
benzen,75c,22h
T6
benzen,75c,22h
T7

Table (2) biological activity for compounds (T_1,T_2,T_4,T_5,T_7) in concentration 1 X 10^{-2}

Compound / Bacteria	G (+ve)		G (-Ve)	
	Sta-aureus	***Entro-coccus***	***Prot-mirabitis***	***p-aeruginous***
T_1	10	10	20	22
T_2	10	11	10	9
T_4	15	12	12	10
T_5	17	15	8	5
T_7	11	10	20	23

Table (3) biological activity for compounds (T_1,T_2,T_4,T_5,T_7) in concentration 1 X 10^{-4}

Compound / Bacteria	G (+ve)		G (-Ve)	
	Sta-aureus	***Entro-coccus***	***Prot-mirabitis***	***p-aeruginous***
T_1	7	9	5	3
T_2	9	8	6	6
T_4	15	10	15	12
T_5	10	12	5	3
T_7	2	3	9	7

Table (4) biological activity for compounds (T_1,T_2,T_4,T_5,T_7) in concentration 1 X 10^{-6}

Compound / Bacteria	G (+ve)		G (-Ve)	
	Sta-aureus	***Entro-coccus***	***Prot-mirabitis***	***p-aeruginous***
T_1	5	3	2	3
T_2	5	8	5	4
T_4	4	6	8	10
T_5	10	8	7	5

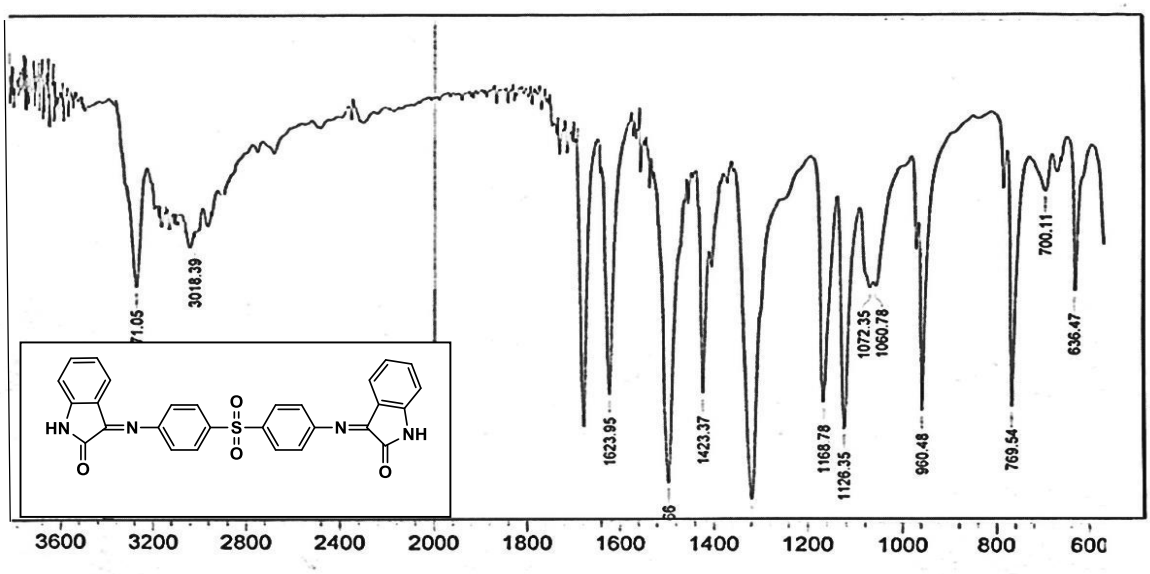
T_7	5	5	7	10

Highly active = Inhibition zone > 12 mm

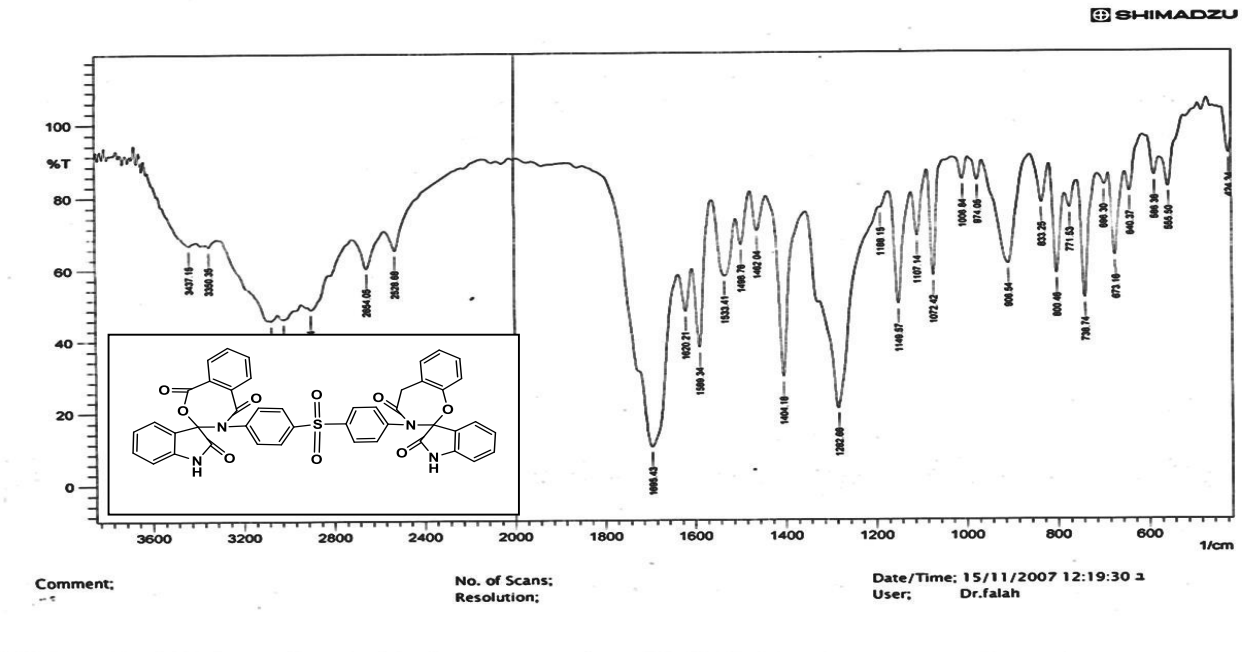
Moderately = inhibition zone = 9 – 12 mm

Silightly = inhibition zone = 6 – 8 mm

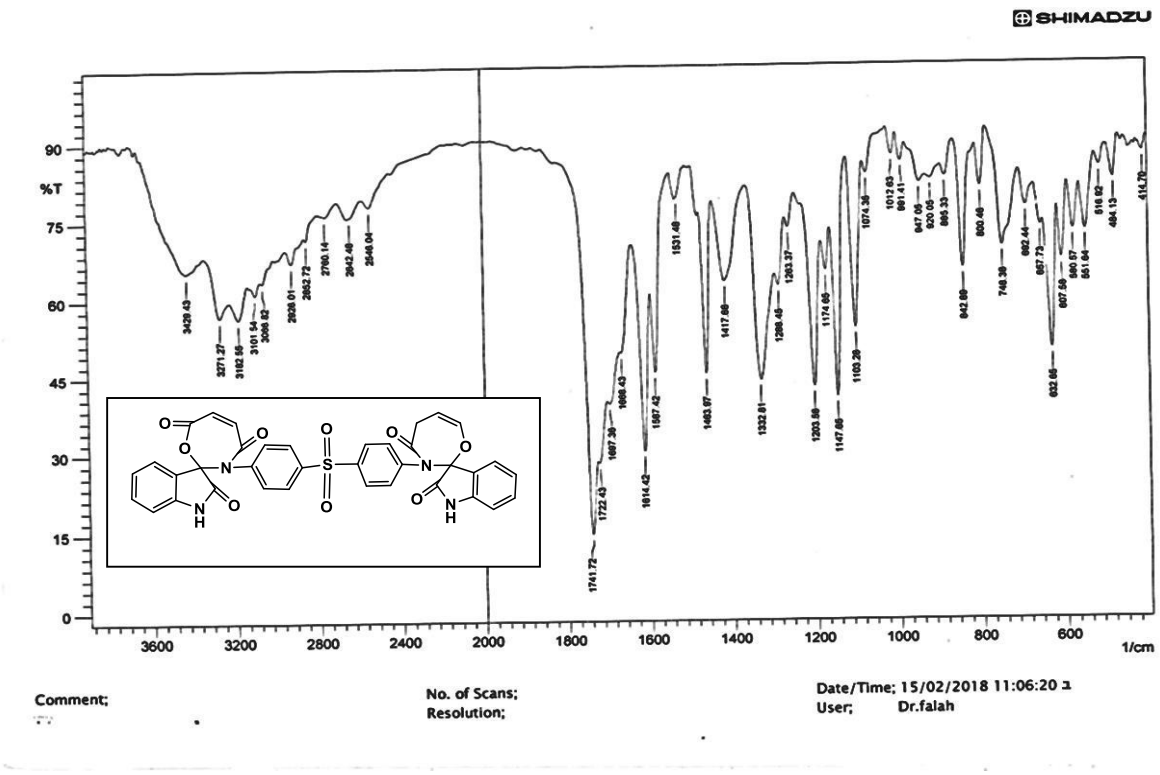
Inactive = inhibition zone < 6



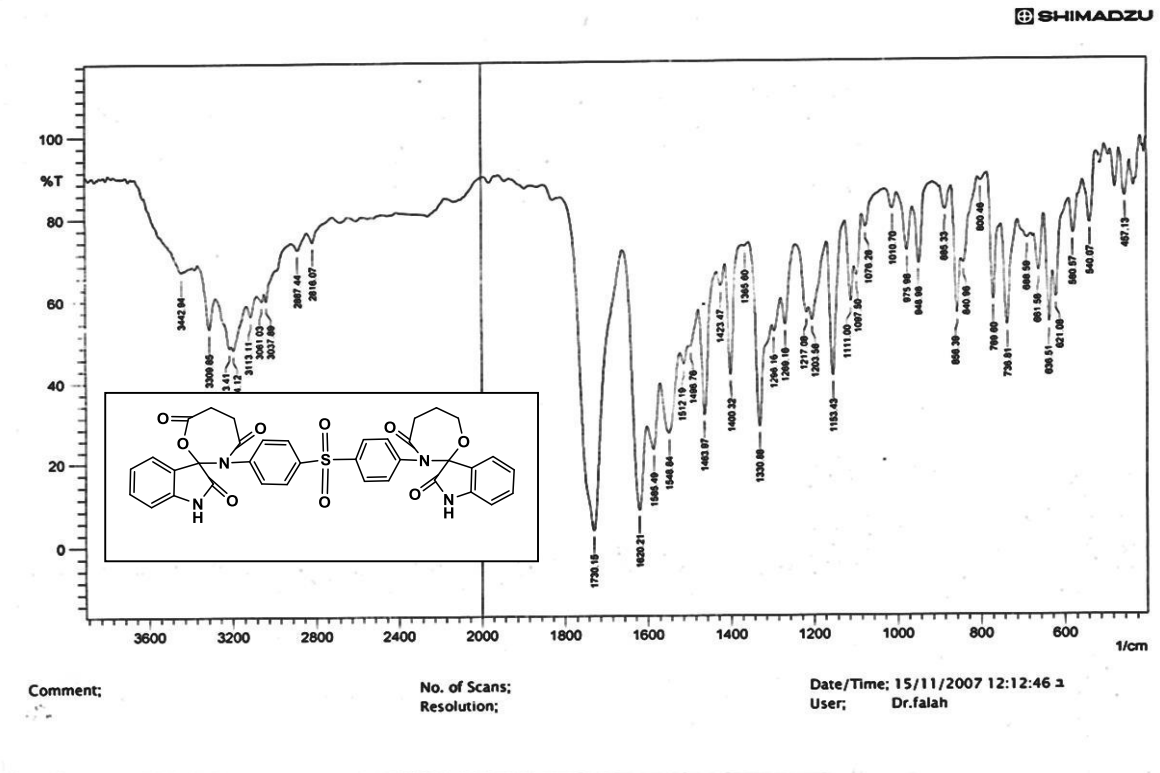
fig(1) FTIR Spectrum of Schiff base Compound T1



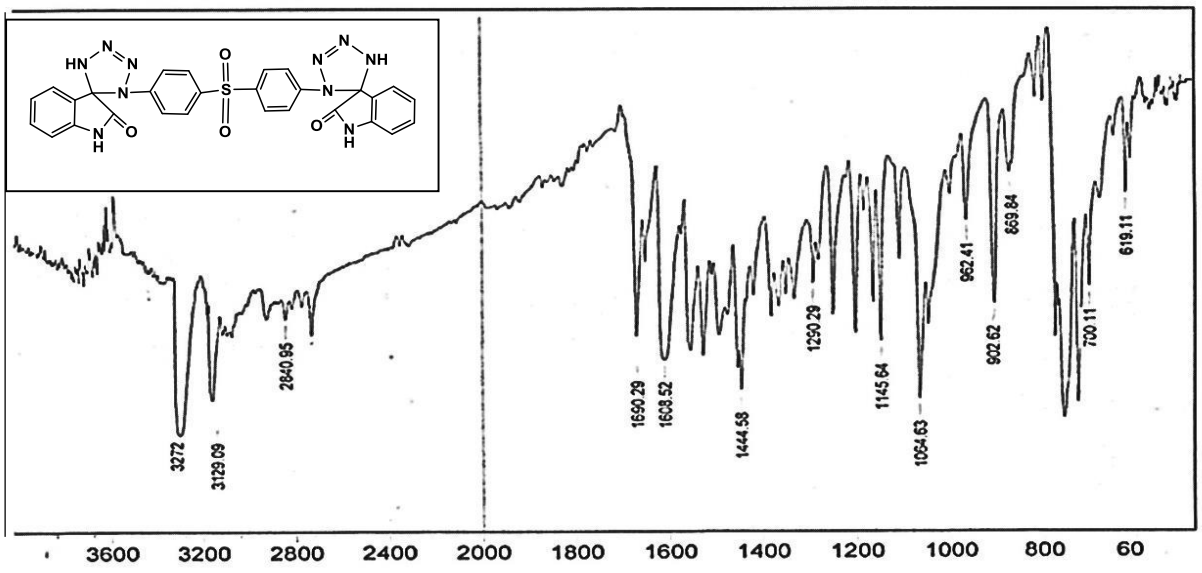
fig(2) FTIR Spectrum of Schiff base Compound T2



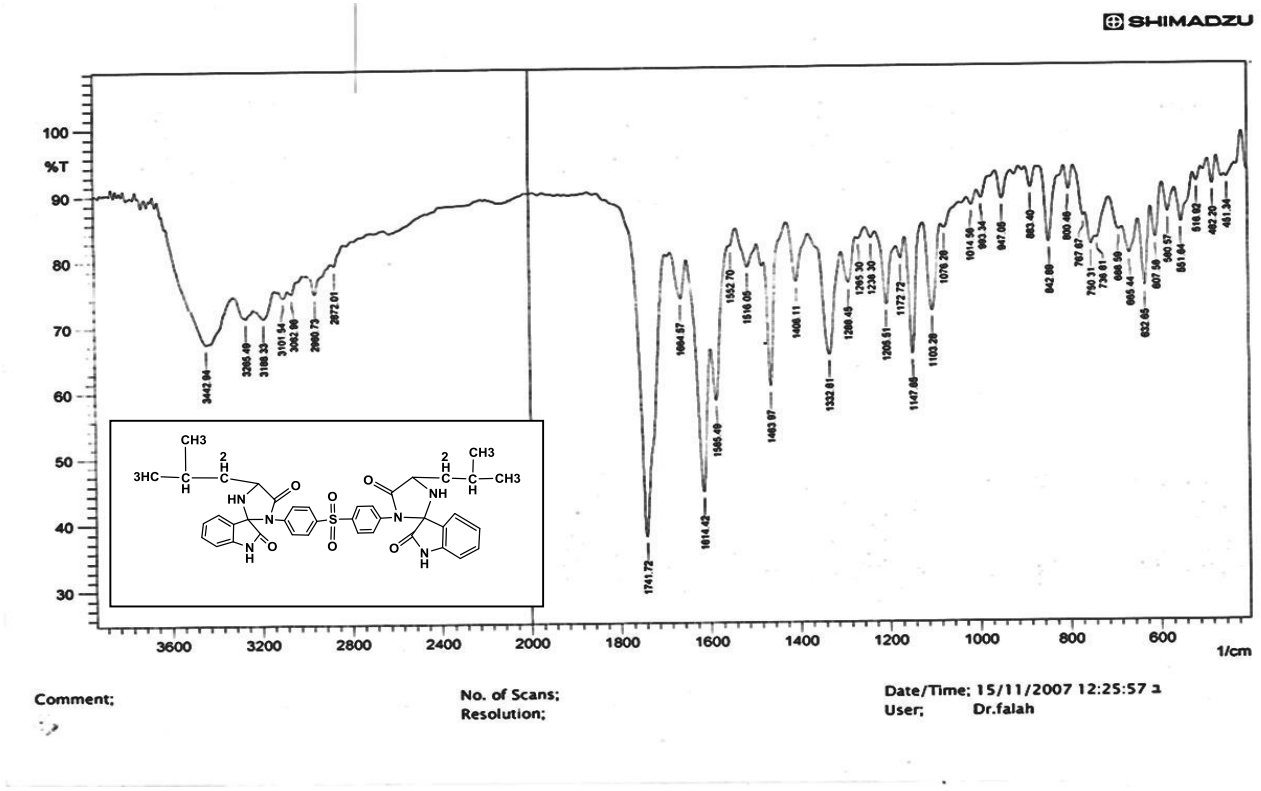
fig(3) FTIR Spectrum of Schiff base Compound T3



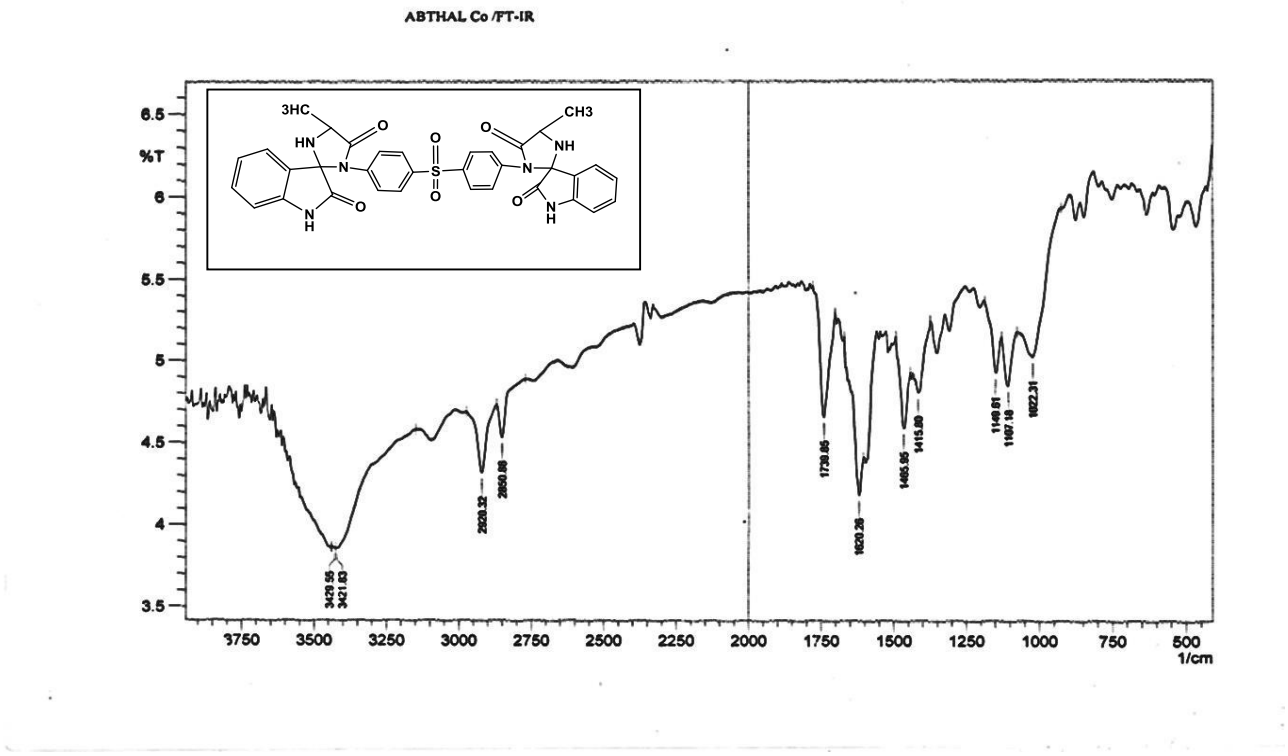
fig(4) FTIR Spectrum of Schiff base Compound T4



fig(5) FTIR Spectrum of Schiff base Compound T5



fig(6) FTIR Spectrum of Schiff base Compound T6



fig(7) FTIR Spectrum of Schiff base Compound T7

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