Preparation and evaluation of the anti-bacterial Activity for some Formazans

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Abstract: In the present research, a series of Formazans derivatives 7a-j have been prepared by the condensation of Schiff bases (4,5) and diazonium salt of substituted aromatic amines Heterocycl, 6a-e. The intermediate Schiff bases (4,5), was itself synthesized by condensation of2-amino benzothiazole (1), with 4-nitro and dimethylamino benzaldehyde, (2,3). All the reaction were routinely monitored and purity was determind on thin layer chromatography using coated aluminum plates and spots were visualized by exposing the dry plates in iodine vapours.The structures of the compounds have been confirmed by , Mass spectroscopy ^{1}H NMR, U.V, IR spectral data and melting points. The antibacterial activity of the compounds has also been screened.

Key words: formazans, diazonium salt , Schiff bases ,Antimicrobial activity.

تحضير وتقييم الفعالية المضادة للبكتريا لبعض مركبات الفورمازان

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الملخص

في هذا البحث تم تحضير سلسله جديده من مشتقات الفورمازان (7a-j) بواسطة تكاثف قواعد شف (مركب وسطي) (5,4) وملح الدايازونيوم لامينات اروماتية حلقية غير متجانسة (6a-e) , وقواعد شف الوسطية تم تحضيرها من تكاثف 2-امينو بنزوثايازول مع 4-نايتر و ثنائي مثيل امينو بنزلديهايد . وتمت متابعة التفاعلات باستخدام تقنية كروموتوغرافيا الطبقة الرقيقة وشخصت المركبات المحضرة بواسطة اطياف الرنين النووي المغناطيسي للبروتون والأشعة تحت الحمراء والأطياف المرئية وفوق البنفسجية وطيف الكتلة وقيست درجة الانصهار لجميع المركبات المحضرة . كما تم فحص الفعالية المضادة للبكتريا لبعض المركبات .

الكلمات المفتاحية : الفورمازان , ملح الدايازونيوم , قواعد شف , الفعالية المضادة للبكتريا .

1- INTRODUCTION:

Formazans have been found to possess important medical applications[1]. Formazans are known for their spectrum of biological activities such as antibacterial, anti-fertility[2] and antifungal[3]. Several formazans show promising anticonvulsant and therapeutic activity further ,some formazans were studied as corrosion inhibitor .The result showed that the corrosion inhibition efficiency of these compounds was found to vary with the temperature and acid concentration [4]. Schiff bases are utilized as starting material in the synthesis of pharmaceutically important compounds such as formazans derivatives which have already attracted considerable attention in the analytical chemistry because of their high sensitivity toward many metals and organo metals[5]. Our idea was to combine azomethine group and azo group in one single molecule to get formazan derivatives.

2. EXPERIMENTAL:

All chemicals were obtained from commercial sources and purified by distillation or recrystallization before use All melting points were determined in open Capillary tubes using Electrothermal (Gallen Kamp) apparatus and were un corrected. All the reaction were routinely monitored and purity was determind on thin layer chromatography using coated aluminum plates and spots were visualized by exposing the dry plates in iodine vapours.Elemental analysis were performed with a Themo Finniganl Eger 300F in Iran ^{1}H-NMR spectra were recorded on a Bruker's 500 FT MHz NMR instrument using DMSO as solvent and TMS as internal reference (chemical shifts in $^{\delta}$ ppm) in Iran.IR spectra were recorded on Shimadzu FTIR-8400S spectrophotometer in Iraq.Elecronic spectra were measured in the region(200-600 nm) for solution in DMSO at room temperature using (Spectro Scan 80D) Uv.Vis Spectrophotometer-U.K in Iraq. Mass spectra were recorded on MSD Direct probe using Acq method test dp.M in Iraq

2-1-Preparation of Schiff bases (4,5)[6]:

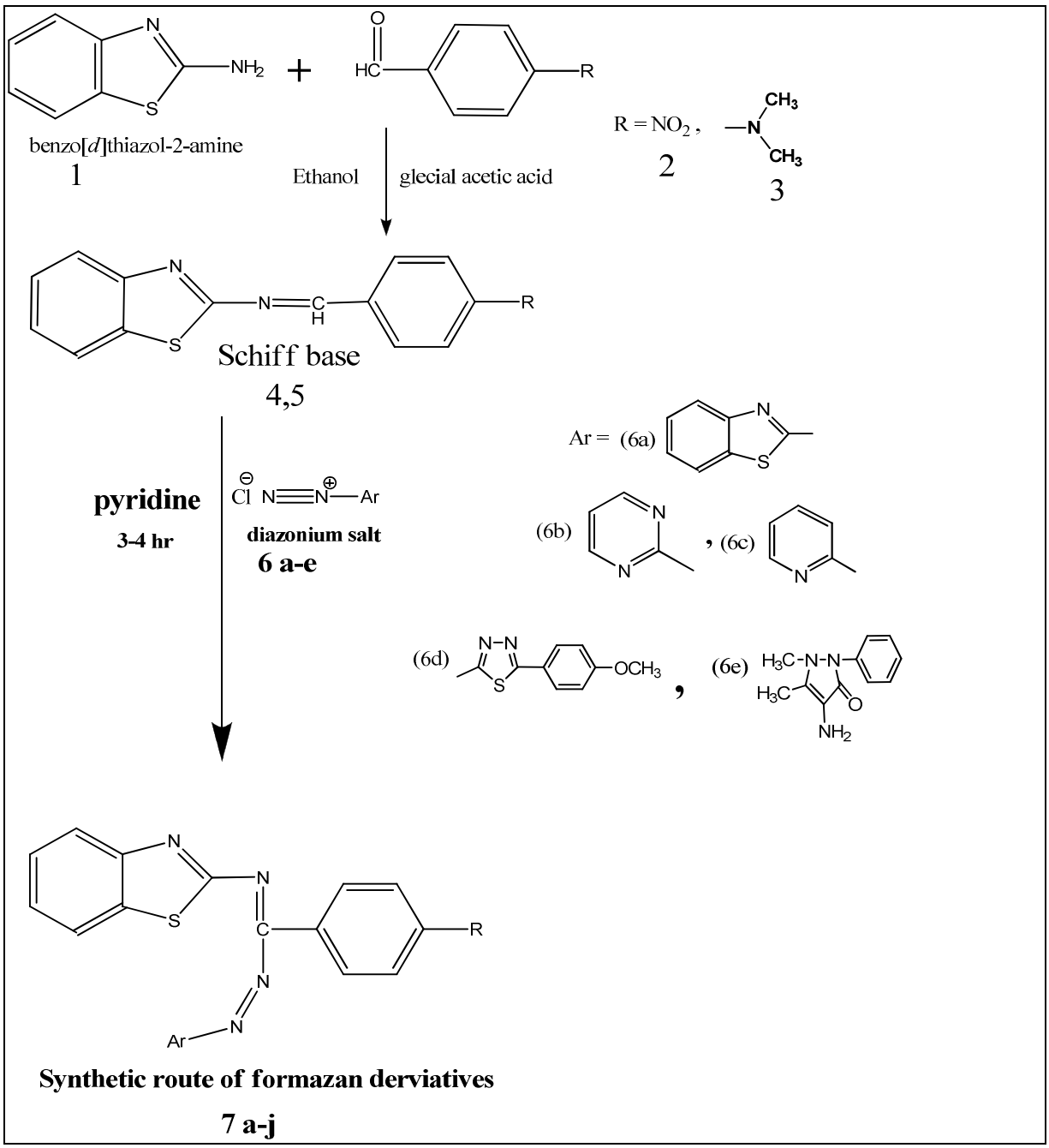
A mixture of equimolar amount (0.006 mol) of 2-amino benzothiazol(1),4-nitro benzaldehyde and 4-dimethyl amino benzaldehyde (2,3)in ethanol (20ml) and glacial acetic acid (3-4 drope)was refluxed for 3hrs.The reaction mixture was concentrated ,cooled,the solid obtained was filtered and recrystallized from ethanol to give Schiff bases(3)of N-(4-nitrobenzylidene)benzo[d]thiazol-2-amine and N-(4-dimethylamino)benzylidene) benzo[d]thiazol-2-amine [4,5] .The obtained yields were [88,90] % .

2-2- Diazotization of amine (6a-e)[7] :

aromatic amine 0.001 mol of dissolved in 7ml acidic solution of HCl 37% (5ml distilled water + 2 ml HCL) at a temperature (0 - 5 c) with stirring and after completing add aqueous solution of $NaNO_2$ was added (0.06 gm, 0.001 mol of $NaNO_2$ in less amount of distilled water at a temperature (0 - 5 C^0) was added dropwise we note added color change when the evidence be diazonium salt and keep it at temperature (0 - 5 C^0).

2-3- Preparation derivatives Formazan(7a-j):

The Solution of Schiff bases (4) (0.001 mole) in pyridine (10ml) was reacted with cold diazonium salt(6a) (0.001mole) and the stirring in ice bath at 0-5 ^{0}C for 3 hour coloured product obtained was filtered and washed with water till it was free from excess pyridine and crystallized from ethanol[8] , Other compounds (7 a-j) were prepared in similar manner and the characterization data for different substituted formazans are given. in table (1)



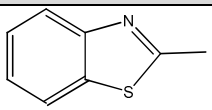
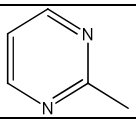
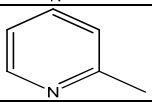
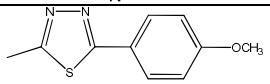
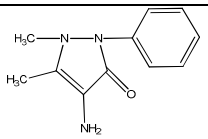
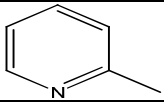
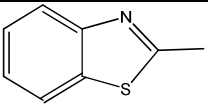
3- RESULTS AND DISCUSSION:

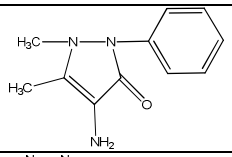
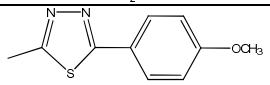
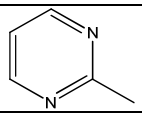
The physical properties of Schiff base and novel formazans derivatives are Presented in Table1.The compounds are quite stable in dry air and they are soluble in most organic solvent.

Synthetic routes leading to target compounds are summarized in Scheme1.The structure of these compounds were proven on the basis of melting points and spectral data.

Table 1: physical properties and of Compounds Synthesized

Comp . No.	R	Molecular Formula M.Wt g/mol	Colour	M.P C^0	Yield %	Rf
4-	NO_2	$C_{14}H_9N_3O_2S$ 283	Yellow	237 – 239	90	0.90
5-	$N(CH_3)_2$	$C_{16}H_{15}N_3S$ 281	Dark Red	182 – 184	88	0.82

Comp . No.	R	Ar	Molecular Formula M.Wt g/mol	Colour	M.P C^0	Yield %	Rf
7a -	NO_2		$C_{21}H_{12}N_6O_2S_2$ 444	Yellow	228 – 230	58	0.83
7b-	NO_2		$C_{18}H_{11}N_7O_2S$ 389	Yellow	240 – 242	58	0.64
7c-	NO_2		$C_{19}H_{12}N_6O_2S$ 388	Yellow	238 – 240	53	0.57
7d-	NO_2		$C_{23}H_{15}N_7O_3S_2$ 501	Dark red	81 – 83	66	0.69
7e-	NO_2		$C_{25}H_{19}N_7O_3S$ 497	Brown	162-164	53	0.65
7f-	$N(CH_3)_2$		$C_{21}H_{18}N_6S$ 386	Black	204 – 206	52	0.70
7g-	$N(CH_3)_2$		$C_{23}H_{18}N_6S_2$ 442	Black	224 – 226	57	0.90

7h-	**$N(CH_3)_2$**		**$C_{27}H_{25}N_7OS$ 495**	**Black**	**197 – 199**	**50**	**0.89**
7i-	**$N(CH_3)_2$**		**$C_{25}H_{21}N_7S_2O$ 499**	**Black**	**178 – 180**	**89**	**0.71**
7j-	**$N(CH_3)_2$**		**$C_{20}H_{17}N_7S$ 387**	**Black**	**300 Dec.**	**47**	**0.85**

3-1- IR spectra:

The IR spectra of all compounds in this study are recorded in the solid state using KBr disk technique. Selected bands of diagnostic importance are listed in Table 2. The formation of Schiff base (4,5) was indicated by their IR spectra from the appearance of azomethine (CH=N) stretching band at 1674,1612 cm^{-1} combined with the disappearance of IR absorption band in region 3378 cm^{-1} and 1710 cm^{-1} corresponding to NH_2 group and C=O group of 2-amino benzothiazole (1) and 4-nitro and dimethylamin benzaldehyde (2,3) respectively. While formazans derivatives (7a-j) confirmed by the appearance of IR absorption band in the region1437-1455 cm^{-1} due to -N=N- group[9] .

3-2-^{1}H-NMR spectra:

^{1}H-NMR spectra of formazans derivatives (7d-h)shows the disappearance of signal at 8.75 ppm due to (CH=N), besides the appearance of the ring protons (7.00 – 8.50 ppm)[10].

3-3-UV-Visible spectra:

(Vis-UV) spectra show short wave lengths (maxλ) at (224-254) nm due to the transitions (π-π^*) and wave lengths long (maxλ) at term (387-400) nm due to electronic transitions of type(n-π^*)[10] .

3-4-Mass spectra[10] :

The mass spectrum of Schiff base (4) exhibits parent peak m/z 283.

3-5-Antibacterial activity[11]:

The effect of some of the prepared compounds in this research on the growth of bacteria, namely:

1- *Eschershia coli*

2- *Psudomonas aeruginosa*

3- *Staphylococcus aureus*

Antibacterial activity of the prepared compounds are studied and the results showed that some of the prepared compounds possess good antibacterial activity. The results are shown in table(3).

Table 2 : Major IR absorption bands (cm^{-1}) of Synthesized Compounds

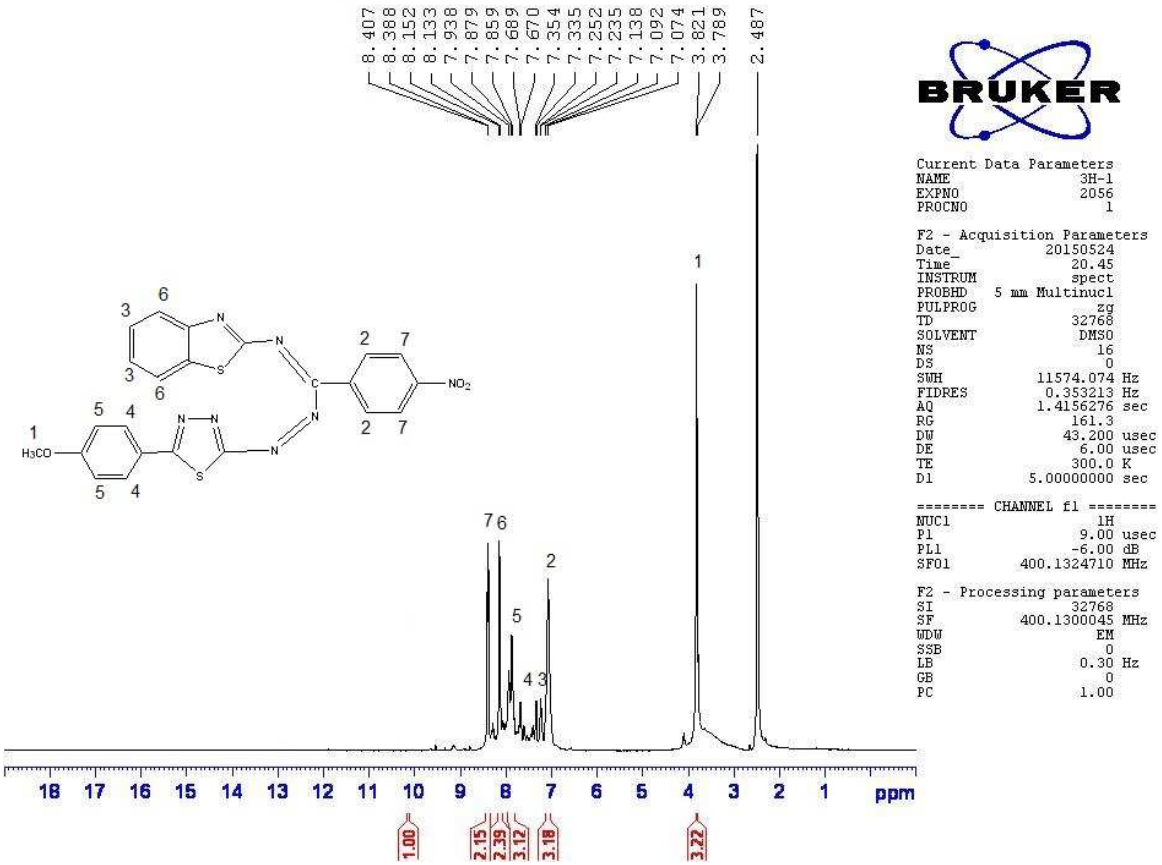
Comp. NO.	IR(KBr),cm^{-1}							
	ν=C-H Aromatic	ν-C-H Aliphatic	νC =N	ν C=C Ar.	N=N ν	ν C-N	ν C-H Out of plane	Others
4	3016	-	1674	1593	-	1282	767 833	NO_2 νasy(1500) νsy(1330)
5	3047	2980	1685	1525 1575	-	1311	754 815	----------
7a	3072	-	1658	1591 1489	1448	1242	763 842	**NO_2** νasy(1517) νsy(1340)
7b	3066	-	1678	1589 1485	1450	1251	769 844	**NO_2** νasy(1517) νsy(1340)
7c	3097	-	1651	1593 1494	1456	1244	767 844	**NO_2** νasy(1517) νsy(1340)
7d	3085	2945	1695	1600 1455	1438	1253	762 838	**NO_2** νasy(1517) νsy(1340)
7e	3066	2931	1678	1595 1485	1437	1232	754 837	**NO_2** **νasy(1523)** **νsy(1338)**
7f	3053	2920	1681	1599 1492	1452	1232	758 825	----------

7g	3052	2978	1683	1602 1492	1454	1251	756 829	----------
7h	3055	2951	1681	1599 1494	1456	1234	758 815	----------
7i	3048	2960	1672	1600 1498	1435	1257	758 827	**γC-O** 1139
7j	3014	2933	1680	1602 1491	1440	1255	759 823	----------

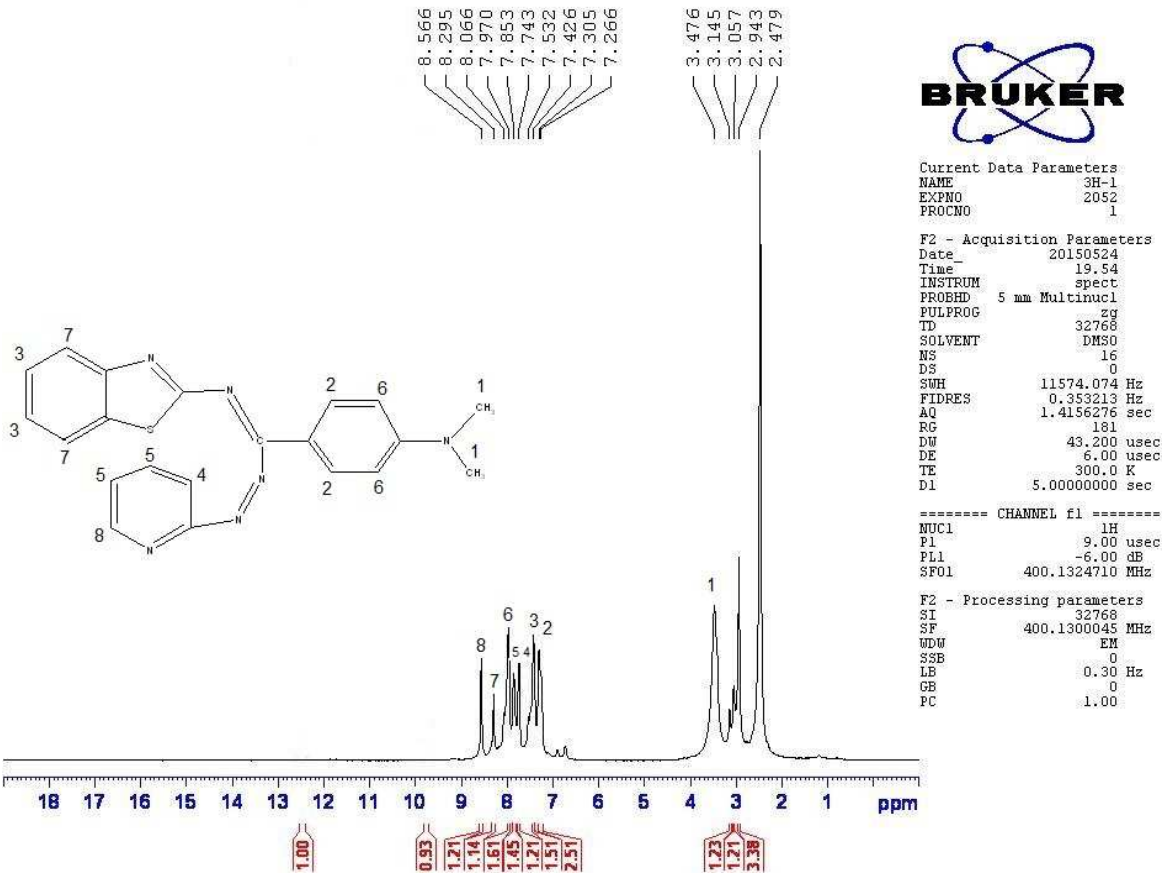
Table –3. In vitro antibacterial activity substituted formazans , 7a,b,f and Schiff . bases 4,5 .

Comp. No.	*Staphylococci Aurues*	*Eschershia Coli*	*Psudomonas Aeruginosa*
4	+++	++	-
5	+	++	+++
7a	+++	++	++
7b	++	++	++
7f	++	++	++

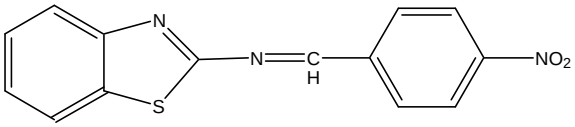
Key to symbols:
Highly active = +++ (inhibition zone > 20 mm).
Moderately active = ++ (inhibition zone 11-20 mm).
Slightly active = + (inhibition zone 5-10 mm).
Inactive = - (inhibition zone <5 mm).



Fig(1) ^{1}HNMR of Compound 7d

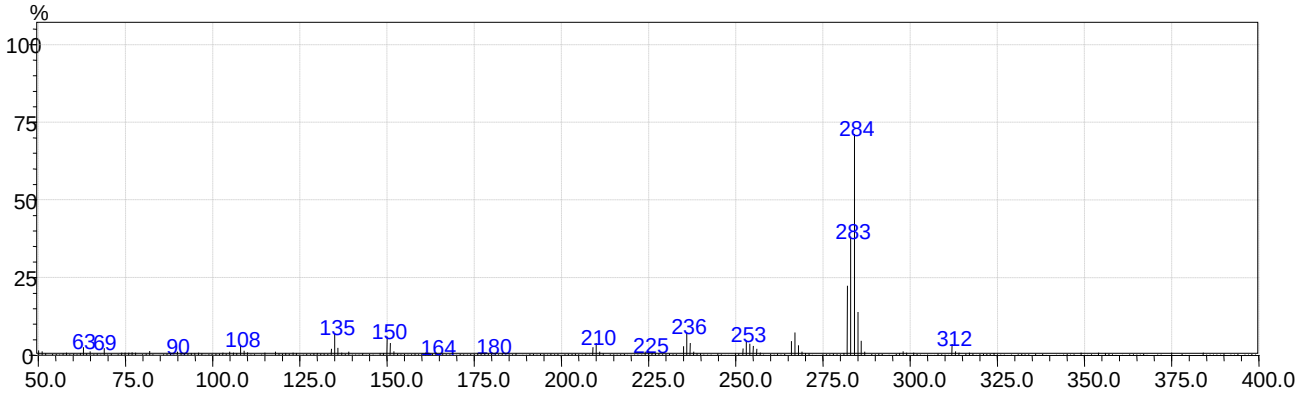


Fig(2) ^{1}HNMR of Compound 7f

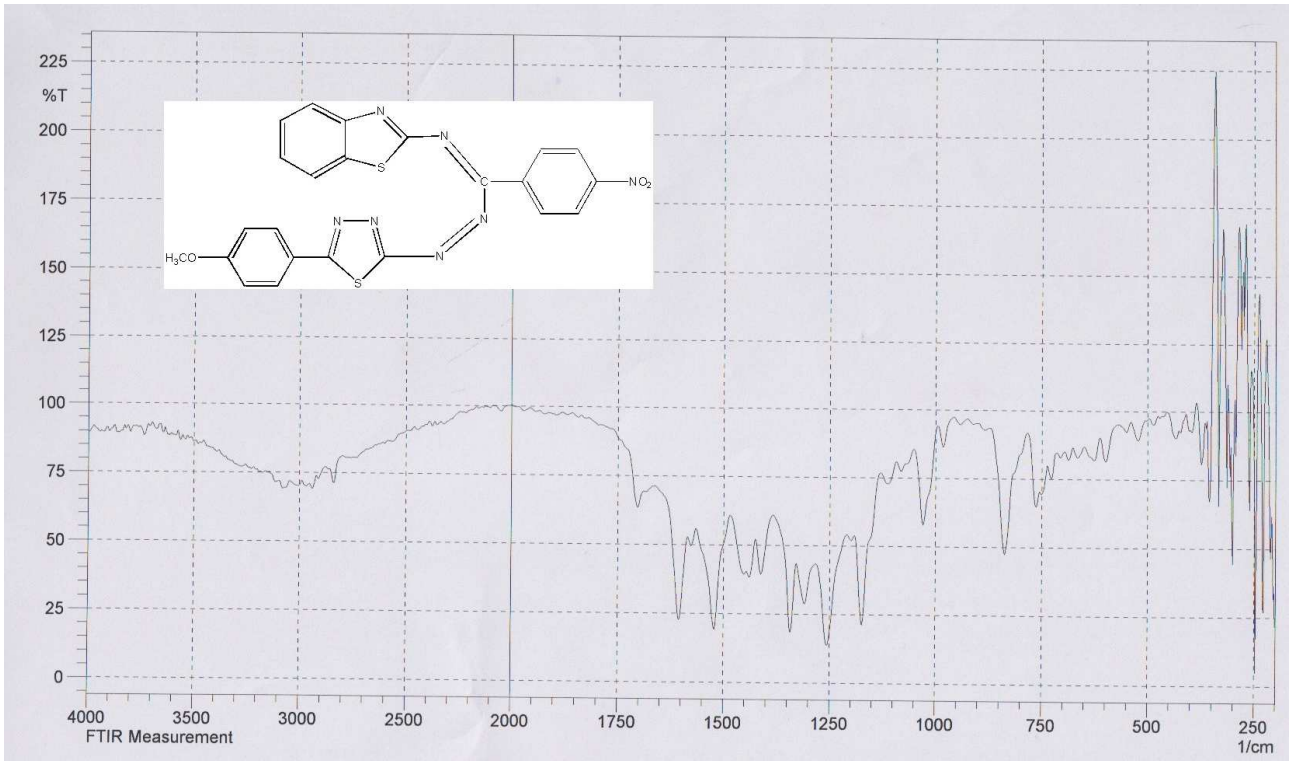


N-(4-nitrobenzylidene)benzo[*d*]thiazol-2-amine

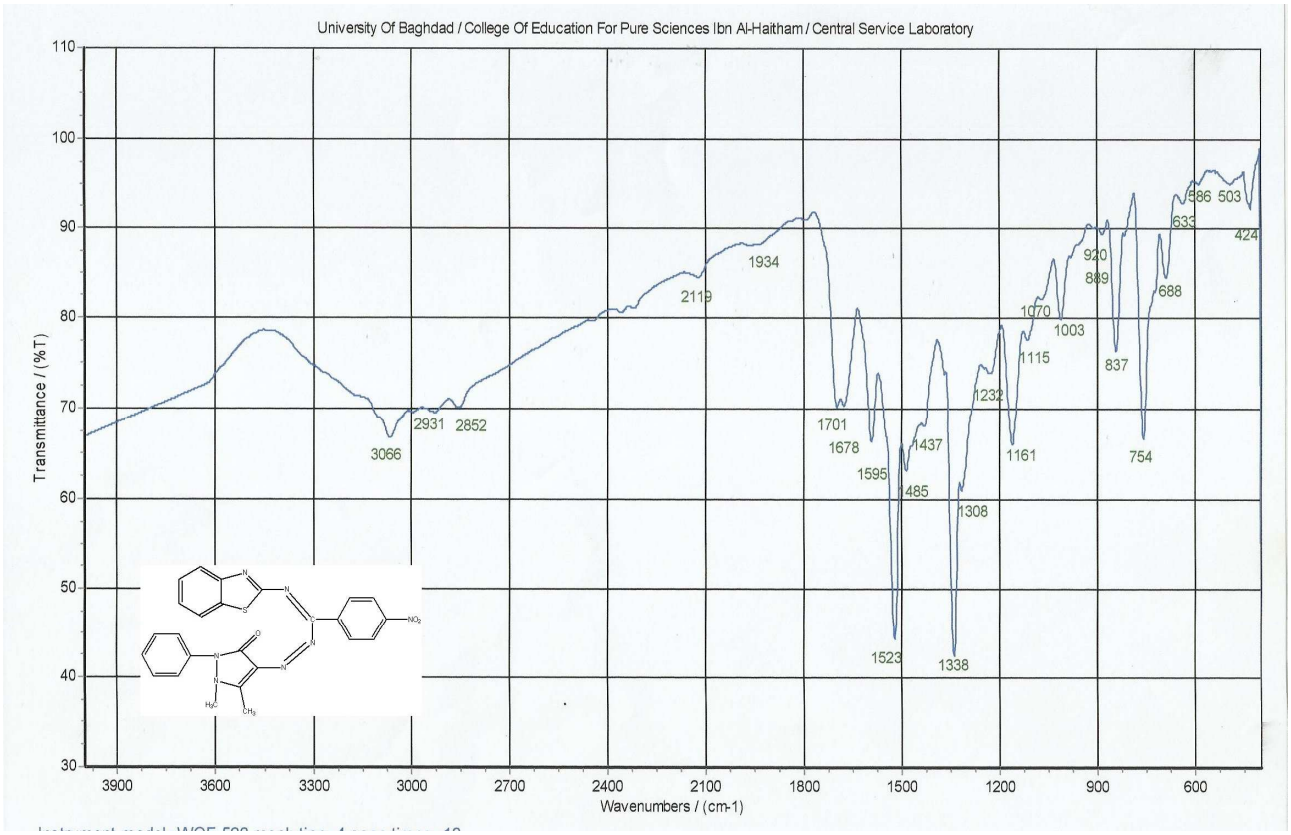
Compound 4



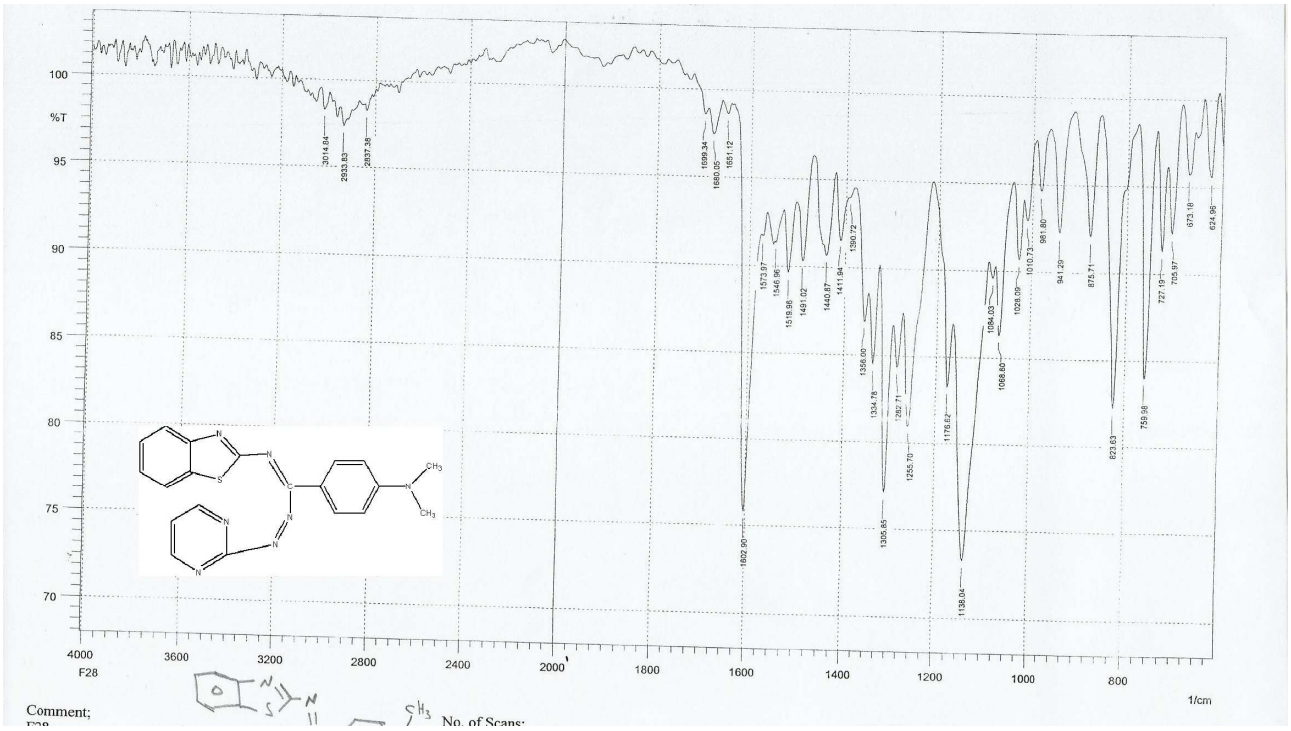
Fig(3) Mass Spectra of Compound 4



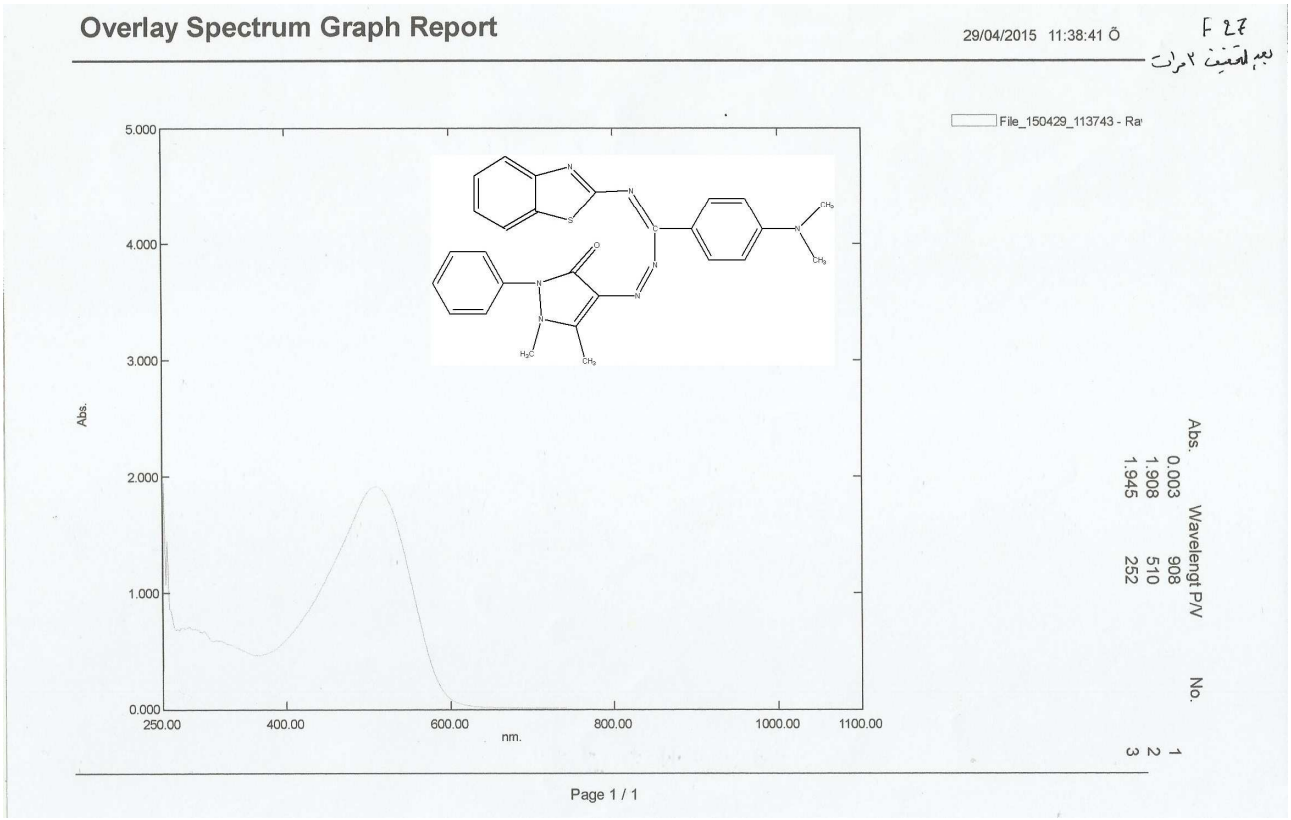
Fig(4) FT- IR of Compound 7d



Fig(5) FT- IR of Compound 7e



Fig(6) FT- IR of Compound 7j



Fig(7) UV-Visible spectra of Compound 7h

Figure(8): Inhibition zones of the compounds (7a,4), (7f,5)

Figure(8): Inhibition zones of the compounds (7a,4) ,(7f,5)

Figure(8): Inhibition zones of the compounds (7a,4) , (7f,5)

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