Synthesis and characterization of(Oxazepine,Diazepine,Terazole) for Derivatives of 2 . aminobenzolthiazd Derivatives

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Abstract

The present work involved synthesis of serval new substituted (oxazepine, Diazepine and tetrazole via Schiff bases for 2-aminobenzothiazole derivatives by five steps. The first step involved preparation 2-aminobethiazole (1-4) by thiocyanogen method in the presence of a suitable solvent, the second step involved preparation Schiff Bases (1-4) by condensation of 2-aminobenzothiazole derivatives with many substituted aldehydes , then, the third step include, preparation new four oxapezine compounds (5-12) by reaction of phthalic anhydride and malic anhydride with the prepared Schiff Bases in two step. the fourth including reaction compounds (5-12) which prepared in the third step with primary oramatic amines to give new eight Diazepine compounds (13-20). Finally the fifth step, preparation new tetrazole derivatives (21-24) by reaction of the prepared Schiff Bases (in the second step) with sodium azide in THf. The prepared compounds were characterized by physical properties, FT-IR, UV. And some of them by ^{1}H-NMR, ^{13}C-NMR spectroscopy were recorded.

Key words: Schiff Bases, 2-amino benzothiazol oxazepine, Diazepine, Tetrazole.

Introduction

2-Amino benzothiazole derivatives have been studied extensively and found to have diverse chemical reactivity and broad spectrum of biological activity such as antitumor agents[1-2], antimicrobial, analgesics, anti-informatory [3] it was reacted with selected aldehyde ketone and testing give Schiff bases and it is complexest important biological activity[4]. Schiff bases are characterized by the N=CH- (imine) group which is important in elucidating the mechanism of transformation in

biological systems[5]. Due to great flexibility and diverse structural aspects, wide range of Schiff bases have been synthesized and their complexation behaveior was studied. Schiff bases reaet with phthalic anhydride, maleic anhydride to give 1,3-oxazepine-4,7-dione and test it is biological activity[6], oxazepine (benzodiazepine) derivative introduced in1965 for use in relief of the psychoneuros of characterized by anxiety and tension, oxazepam is nonhomologous seven membered ring that contains, two heteroatoms (oxygen and ,nitrogen),[7]. the reaction of oxazepine with primary aromatic amine gives. The corresponding 1,3-diazepine-4,7-dione. Many of the benzodiazepines and their oxides show interesting sedatives, muscie relaxant and anticonvulsant properties in animals[8]. Then Schiff bases react with sodium azide to give tetrazoles. They are aromatic five membered ring four nitrogen atoms, the first tetrozole was reported over a century ago [9]. Tetrazoles have been found to exhibit antibacterial, antifungal, and antihistamine, and ant: inflammator properties[10].

Material and methods

General

Chemicals employed were of analytical grade and used without further purification melting points were determined in Gellen kamp melting point apparatus and were uncorrected. UV-visible spectra were recorded on shimadzu T6ou spectrophotometer using ethanol as a solved, FT-IR spectra were recorded on shimadzu FT-IR-8400 fourier transform infrared spectrophotometer as kBr disc. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker specrospin vitra tetramethyl silane (TMS) as an internal standared and Dmso . as a solvent in Al-Albat university in Jorden.

Preparation of 2-amino benzothiazle derivative[11] (1-4)

In 250 ml round bottomed flask equipped with amagnetic bar stirrer and dropping funnel, a solution of bromine (1.2ml) in glacial acetic acid (75ml) was allowed to run through the dropping funnel dropwise during 30 min. to a mixture of para substituted aromatic amine (0.03mole) and ammonium thiocyanate (0.1mole) in 150 ml glacial acetic and with stirring. The mixture was stirred for 1 hr, then diluted with water and neutrolized with solid sodium hydroxide. the precipitated substance was collected, triturated and recystallized from a suitable solvent to obtain 2-amino benzothiazole derivatives (1-4).

preparation of Schiff bases(12). (1-4)

Aseries of Schiff bases (1-4) were prepared from the reaction of 2-amino benzothiazol derivative (0.01mole) with different aldehydes (0.01mole) in 25 ml ethanol absolute and few drops of glacial acetic acid. This mixture was refluxed for 5hrs. the precipitate was filter and recystallized from ethanol) melting points, yield % data are listed in table(1).

Preparation of oxazepine derivatives[13] (5-12)

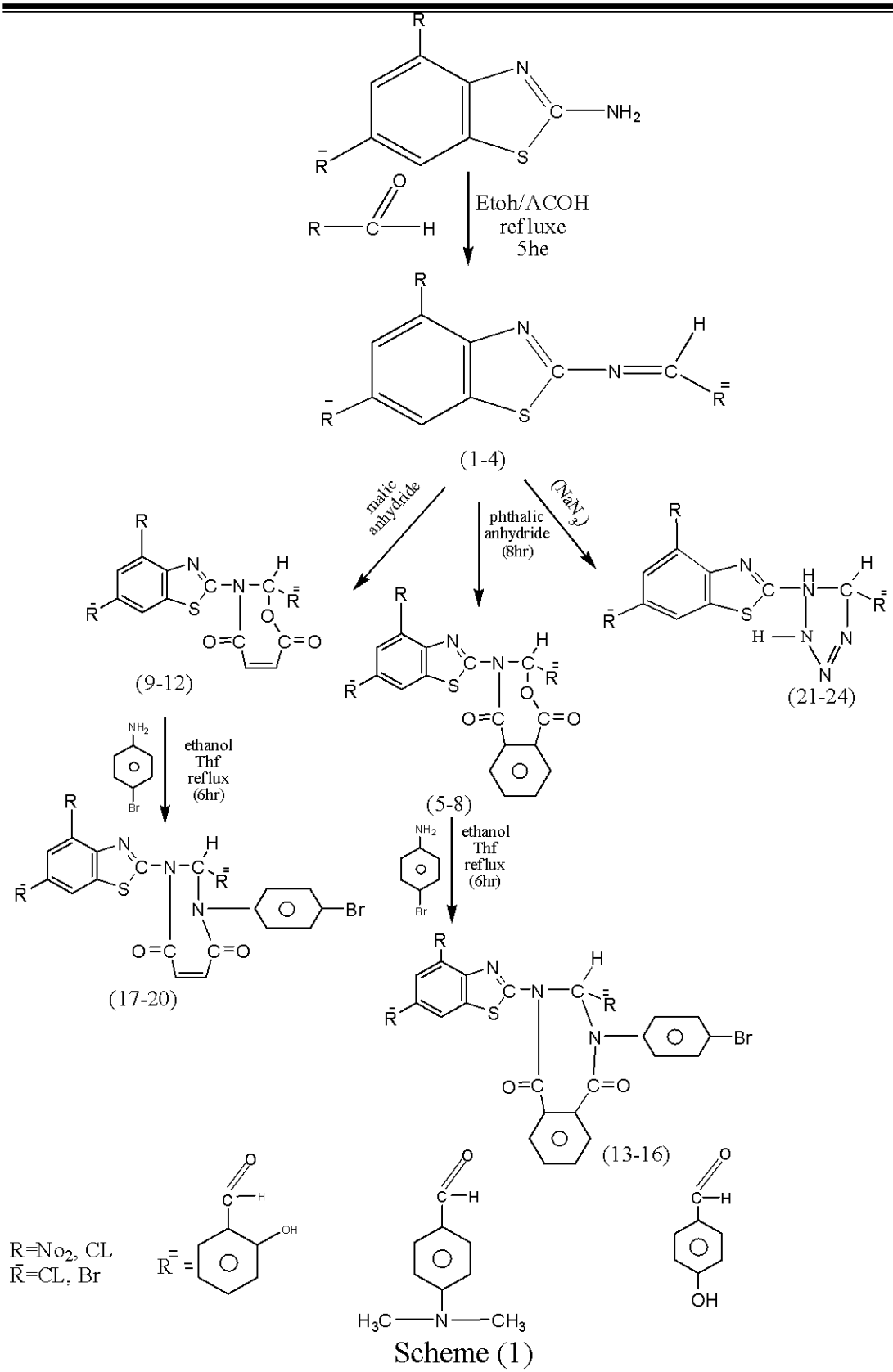
Amixture (0.001mole) of (1-4) compounds and (0.001mole) of phthalic anhydride (or 0.001 mole of malic anhydride) in 25 ml of dry benzene was placed. The mixture was heated for 8hrs. in water bath at (3o), the precipitate was fittered and recystallized from 1,4-dioxane. Melting points, yield data are listed in table (1).

Preparation of diazepine derivatives[14] (13-20)

Amixture (0.001mole) of (5-12) oxazepine compounds, and (0.001mole) of primary oramatic amine (p-bromo aniline) was dissolved in 30ml of tetrahydrofuran. The reaction mixture was refluxed in water bath at 85 for (8hrs.). then allowed to cool (to room) tempreture and siparated crystalline was filterd and recrystallized from ethanol melting point, yield % data are listed in table (1).

Preparation of Tetrazole[15](21-24)

Compounds of (1-4) (0.002mole) was dissolved in 20ml tetra hydrofuran and mixed with (0.002mole) sodium azide. These mixtures were heated in water both at 75C^{0}for 5 hrs. the precipitate was filtered and recrstallized from ethoanol. The end of reaction was cheched by TLC in methanol. Melting points yield % data are listed in table (1).



Scheme (1)

Results and Discussion:

The present work involved five steps.

First step: include preparation of the derivatives of 2-animo benzothiazole[1-4] using thiocyanogen method using different amines such as (2-chloro-4-nitro aniline, 2,4- dichloro aniline, 4-Bromo aniline, 2-nitro-4-chloro aniline) as shown in scheme (1)

Second step: include preparation of new five schiff Bases (1-4) were prepared by reaction of derivative of 2-amino benzothiazole (1-4) in (first step) with different substituted aldehydes. The synthesis of this compounds was carried out lined in scheme (1), and the physical properties for Schiff Bases including melting point range of (124-242) and yield were range of (69-88) and these compounds were identified by FT-IR, spectroscopy, FT-IR spectrum of compound (3) showed characteristic absorftion bands (1666) cm^{-1}, (3039) cm^{-1}, (2819-2962) cm^{-1}, and (3370) cm^{-1} due to (C=N), υ (C-H) aromatic υ (C-H) aliphatic and υ (O-H) respectively as shown in table (2), Fig (1).

UV. Spectrum of compound (3) showed and absorption λmax at (300) nm. Which attributed to (π–π^*)as shown in Fig(7).

Third step: the third step include preparation of new eight oxazepine (5-12) were prepared by reaction of Schiff Bases (1-4) in second step with phthalic anhydride and malic anhydride in dry benzene the synthesis of thiscompounds was carried out lined in scheme (1), and the physical properties for oxazepine (5-12) including melting point range of (125-310) and yield were range (49-77) and these compounds were identifited by FT-IR and UV., ^{1}H-NMR and ^{13}C-NMR spectroscopy. FT-IR spectrum of compound (7) showed clear absorption band at (1681) cm^{-1} tributed to (C=O) imide stretching frequency is good evidence for the success of this step of reaction. Also FT-IR spectra of oxazepin (5-12) showed clear absorption bands at (1168-1280) cm^{-1} due to υ (C-O-C) [17] while disappearance of υ (C=N), as shown in table (2), Fig (2) while compound (11) Fig (3). UV. Spectrum of compound (7) showed an

absorption λmax at (304) nm which at tributed to (π-π*)The absorbtion is

listed in table (2), Fig (8). While compound (11), Fig (9).

In the ^{1}H-NMR specterum of compound (5) showed the signal at (2.498) ppm was attributed to (CH_3) proton, and multiplet shgnals at (7.620) ppm due aromatic protons and signtet signal at (8.173) ppm due to (N-H) proto n for sulfamzthoxazol drug, while the signal at (8.296) ppm for oxazole ring, as shown in Fig (14). In the ^{13}C –NMR spectrum of compound (5) showed the signal at (170.37) ppm for carbonyl group (C=O), while the signal at (128.65-133.26) ppm for aromatic carbons, while the signal at (39, 91) ppm for carbon of methyl group (CH_3), as shown in Fig (13).

Fourth step: in the third step including reaction derivatives of oxazepine (5-12) with p- Bromo aniline (primary aromatic amine) to give new eight Diazepine compounds (13-20). The physical properties for Diazepine (13-20) including by FT-IR and UV. Spectroscopy FT-IR spectrum of compound (15) showed characteristic absorption at (1708)

cm^{-1}, (3332) cm^{-1}, (3078-3178) cm^{-1} and (2970) cm^{-1} due to υ (C=O), υ

(O-H), υ (C-) aromatic and υ (c-H) alphatic respectively as shown in table

(2), Fig (4) while compound (19) Fig (5). The structure of oxazepine substituted is combination of both lacton and lactam 7-membered hetrocyclic ring. This is indicated by the appearance of the characteristic

(C-N) lacton/ C-N lactom)[18].

Absorption band at (1172-1182) cm^{-1} in their FT-IR spectra. The lacton group (cyclic ester) can be converted in to lactam group (cycle

amide) by reaction with aromatic primary amines. (UV) spectrum of compound (15) showed an absorption λmax at (316) nm which attributed to (π-π*)as shown in Fig (6)while compound (19) Fig (5).

Fifth step: tetrazole compounds (21-24) were synthesized from reaction of Schiff Bases (1-4) with sodium azide in THF. All physical properties are listed in table (1) the infrared absorption bands, Fig (6), were utilized to characterize the specific structure of the synthesized compounds, the disappearance of band at (1614-1600) cm^{-1} attributed to (C=N) imine group, stretching frequency is good evidence for the success of this step of reaction. carbon of methyl group (CH_3), as shown in Fig(6).

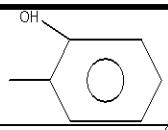
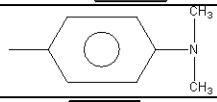
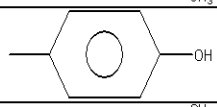
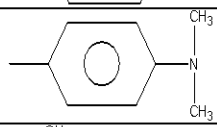
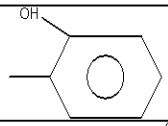
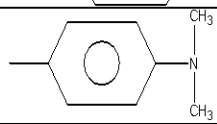
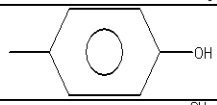
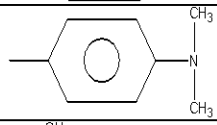
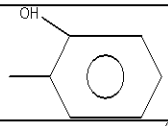
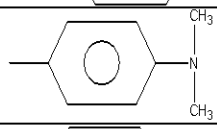
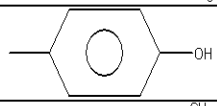
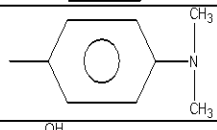
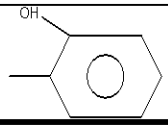
Also FT-IR spectra of trtazoles (21-24) showed elear absorption bands at (1566-1642) cm^{-1} due to υ (N=N). Beside this, the FT-IR spectra of these. compounds were devoid of strong band at (2160 - 2120) cm^{-1} attributed stretching frequency of azide group. the characteristic data are reported in table (2). In the ^{1}H-NMR, the spectrum of compound (21) showed the (N-H) from the triazole ring was observed as asinglet at (8.361) ppm and signal at (3.479) ppm was attributed to (CH_3) protons, and multipl signal at (7.05-7.914) ppm due to aromatic protons and signlet signal at (8.173) ppm due to (NH) for selfsame thoxazole drug (exotetrazole). as shown in Fig (15). In the ^{13}C-NMR spectrum of compound (21) the signal at (12.16) ppm for solvent DMSO, whiles the signal at (124.49-136.13) ppm for aromatic carbons, and the carbon of methyl group (CH_3) at (39.36-4069)ppm as shown in Fig (16). UV. Spectrum of compound (23) showed an absorption λmax at (301) nm, (364) nm which attributed to (π-π*) and (n-π*)as shownin Fig(12).

Conclussion:

In second step which in cluding prepration of new schiff bases these compounds were yields were range of (69-88) but other steps afew.in same step,schiff base were identified by FT-IR Spectroscopy,astrong band in the region of(1589-1654)cm^{-1} assignable to the (C=N) imins group and the reaction was followed by dis appearance

of NH2 abrorption band at(3346-3200)cm^{-1},while in third step , FT-IR Spectrum of compounds (5-12) Showed clear absorption bands of (1681-1770)cm^{-1} of tribute to (C=O) imine., and showed clear absorption bands of (1168-1280)cm^{-1} due to ν (C-O-C) and dis appearance of ν (C=N) stretching frequency is good evidence for the success of this step of reaction.

Table (1) physical properites for all product compounds

Comp. No.	R	R`	R``	Formal	Colour	%yeild	m.p	Solvent
1.	NO_2	Cl		$C_{14}H_8N_3O_3SCl$	dirk yellow	88	124	ethanol
2.	Cl	Cl		$C_{16}H_{13}N_3SCl_2$	yellow	78	144	ethanol
3.	.	Br		$C_{14}H_9N_2OSBr$	yellow	69	242	ethanol
4.	NO_2	Cl		$C_{16}H_{13}N_4O_2SCl$	read	80	200	ethanol
5.	NO_2	Cl		$C_{22}H_{12}N_3O_{62}SCl$	dirk orange	65	125-130	1,4 dioxan
6.	Cl	Cl		$C_{24}H_{17}N_3O_3SCl_2$	dirk yellow	59	197	1,4 dioxan
7.	.	Br		$C_{22}H_{13}N_2O_4SBr$	Light yellow	64	oil	1,4 dioxan
8.	NO_2	Cl		$C_{24}H_{17}N_4O_5SCl$	dark yellow	50	224	1,4 dioxan
9.	NO_2	Cl		$C_{18}H_{10}N_3O_6SCl$	dark yellow	66	310	THF ÷ ethanol
10.	Cl	Cl		$C_{18}H_{15}N_3O_3SCl_2$	Light yellow	58	148	THF ÷ ethanol
11.	.	Br		$C_{18}H_{11}N_2O_4SBr$	orange	77	oil	THF ÷ ethanol
12.	NO_2	Cl		$C_{18}H_{15}N_4O_5SCl$	yellow	49	310	THF ÷ ethanol
13.	NO_2	Cl		$C_{28}H_{16}N_4O_5SClBr$	green	52	170	DMF

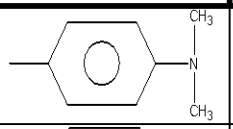
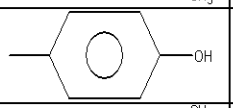
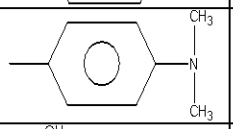
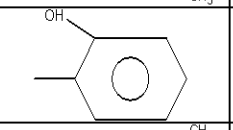
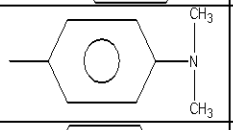
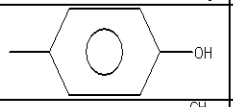
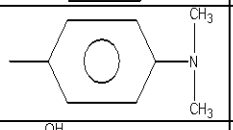
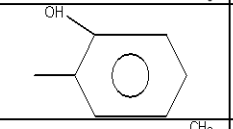
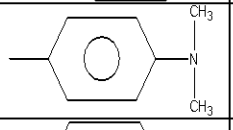
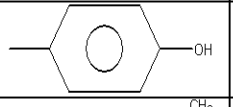
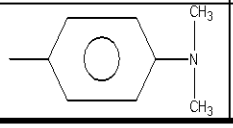
Comp. No.	R	R`	R``	Formal	Colour	Yield	m.p	Solvent
14.	Cl	Cl		$C_{30}H_{21}N_4O_2SCl_2Br$	dark brown	43	210	DMF
15.	.	Br		$C_{28}H_{17}N_3O_3SBr$	yellow	39	Oil	DMF
16.	NO_2	Cl		$C_{30}H_{21}N_5O_4SClBr$	brown	44	320 Dec.	DMF
17.	NO_2	Cl		$C_{24}H_{14}N_4O_5SClBr$	Yellowish brown	60	270-272	DMF
18.	Cl	Cl		$C_{26}H_{19}N_4O_2SCl_2Br$	dark brown	55	199-202	DMF
19.	.	Br		$C_{24}H_{15}N_3O_3SBr_2$	brown	39	oil	DMF
20.	NO_2	Cl		$C_{26}H_{19}N_5O_4SClBr$	brown	33	320 Dec.	DMF
21.	NO_2	Cl		$C_{14}H_9N_6OSCl$	dark read	58	115-120	dry benzene
22.	Cl	Cl		$C_{16}H_{14}N_6SCl_2$	Yellowish green	54	178	dry benzene
23.	.	Br		$C_{14}H_{10}N_5OSBr$	dark yellow	42	235	dry Benzene
24.	NO_2	Cl		$C_{16}H_{14}N_7O_2SCl$	orange	50	290-292	dry benzene

Table (2): FT-IR spectral data for all product compounds

Comp. No.	υ(C-H) aromatic	υ(C-H) alphatic	υ(C=O)	υ(C=N) Inuring	υ(C-N)	υ(C=C)	Others
1.	3086	2877	~~	1697	1485	1624	υ(O-H)3452 υ(C-CL)810, 1149 υ(NO_2)1338, 1531
2.	3066	2931	~~	1635	1477	1581	υ(C-CL) 852, 1107
3.	3039	2819-2962	~~	1666	1485	1600	υ(O-H) 3370 ὐ(C-Br)883
4.	3170	2993	~~	1624	1492	1580	υ(NO_2) 1388,1535 υ(C-CL) 1089
5.	3078	2897-2985	1701	1581	1450	1535	υ(O-H) 3410 υ(C-CL) 829,1072. υ(NO_2) 1338,1489
6.	3070	2939	1697	1635	1481	1581	υ(C-CL),1072
7.	2323	2835-2989	1681	1600	1450	1539	υ(O-H) 3414 υ(C-Br)837
8.	3059	2873	1708	1616	1454	1485	υ(NO_2)1597,1369 υ(C-CL)1157
9.	3090	2900	1740	1647	1460	1604	υ(O-H) 3483 υ(C-CL) 840 ,1180 υ(NO_2)1319, 1535
10.	3074	2897	1701	1535	1435	1577	υ(C-CL) 1072
11.	3062	2989	1724	1635	1516	1600	υ(O-H)3414 υ(c-Br)860
12.	3170	2870	1712	1647	1450	1697	υ(NO_2)1303,1590 υ(C-CL)1168
13.	3020	2954	1770	1647	1430	1610	υ(C-OH) 3425 υ(C-CL) 1050 υ(C-Br) υ(NO_2)1330-1581
14.	3078	2943	1740	1630	1492	1600	υ(C-CL)1080 υ(C-Br)850
15.	3078-3178	2970	1708	1627	1489	1600	υ(O-H)3332 υ(C-Br)883
16.	3066	2839	1740	1660	1454	1620	υ(NO_2) 1489, 1338 υ(C-CL) 1153
17.	3076	2871	1720	1620	1460	1630	υ(NO_2)1530.1320 υ(O-H)810-1120
18.	3130	2870	1716	1630	1435	1651	υ(C-CL) 1050 υ(C-Br) 860

Comp. No.	υ(C-H) aromatic	υ(C-H) alphatic	υ(C=O)	υ(C=N) Inuring	υ(C-N)	υ(C=C)	Others
19.	3059	2993	1708	1658	1489	1600	υ(O-H) 3471 υ(C-Br) 864
20.	3086	2846-2931	1714	1616	1485	1539	υ(NO_2)1338,1570 υ(C-Cl) 1160
21.	3101	2854-2954	----	1504	1485	1600	υ(O-H)3448 υ(C-Cl)856,1545 υ1458, 1321 υ(N=N)1624
22.	3070	2831-2943	----	1635	1431	1531	υ(N=N) 1585 υ(O-H) 4452 υ(NO_2) 1388-1481 υ(C-Cl) 1072
23.	3228	2823	----	1678	1489	1600	υ(O-H) 3475 υ(C-Br)837 υ(N=N) 1566
24.	3010	2920	----	1639	1415	1550	υ(NO_2) 1485-1373 υ(C-Cl) 813,1165 υ(N=N) 1593

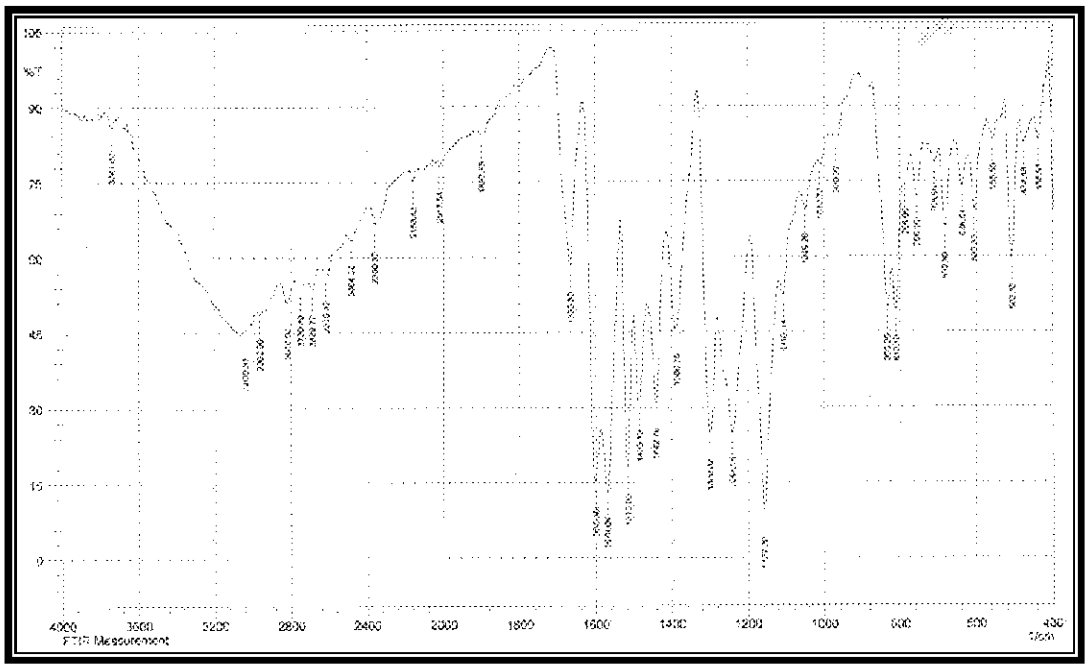


Figure (1): FT-IR spectrum of compound [3]

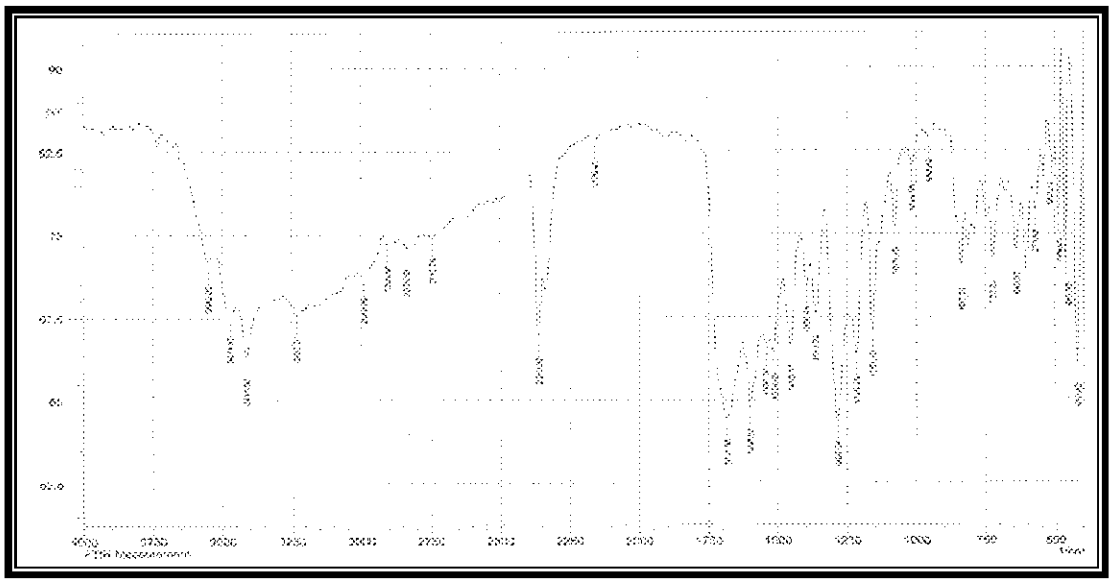
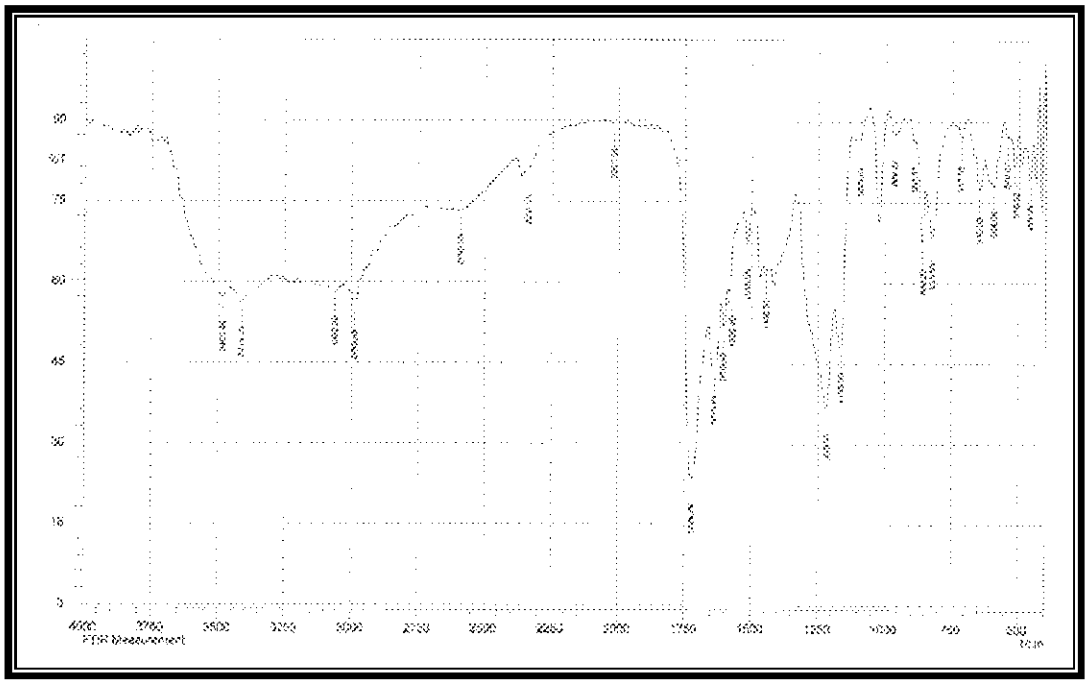
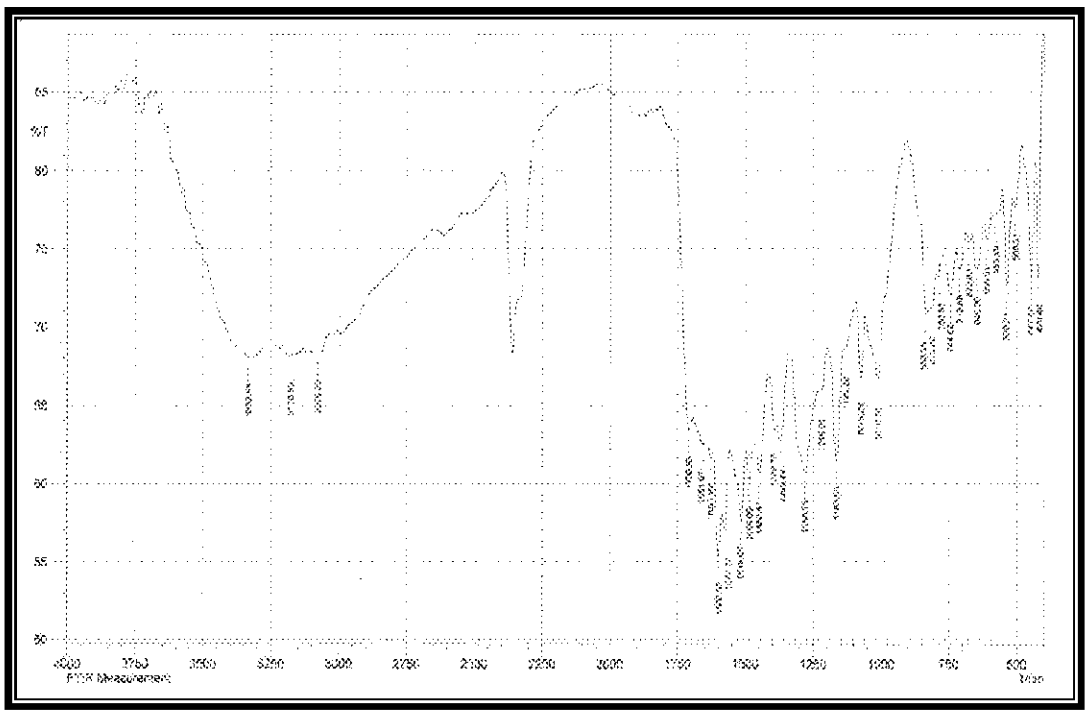


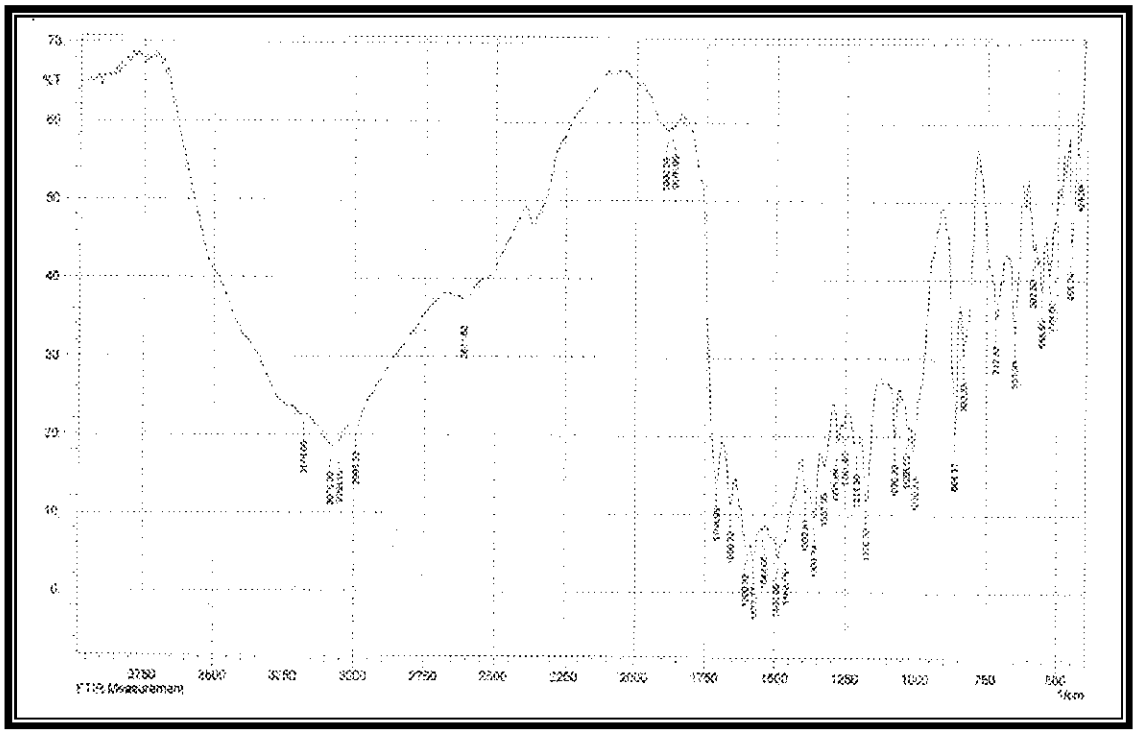
Figure (2): FT-IR spectrum of compound [7]



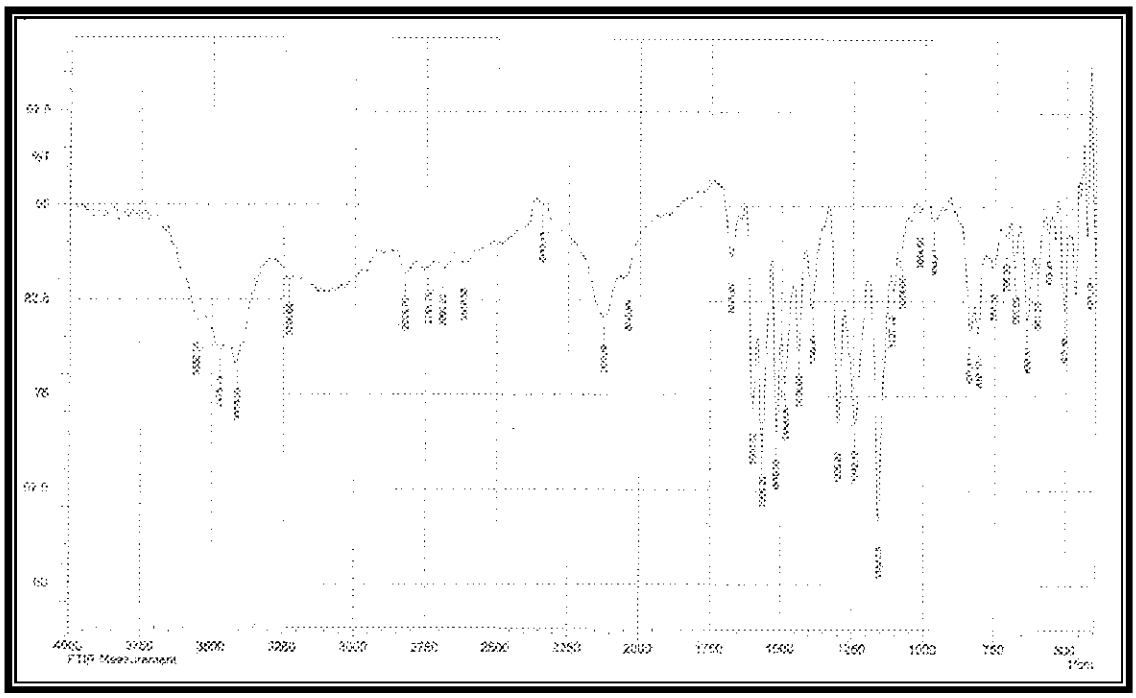
Figure(3):FT-IR spectrum of compound[11]



Figure(4):FT-IR spectrum of compound[15]



Figure(5):FT-IR spectrum of compound [19]



Figure(6):FT-IR spectrum of compound [23]

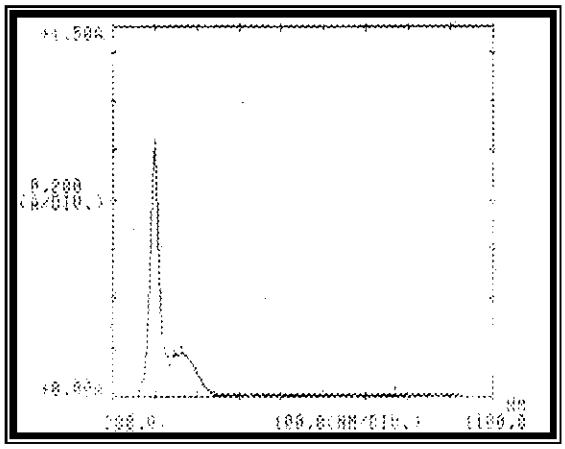


Figure (7): UV. Spectrum of compound [3]

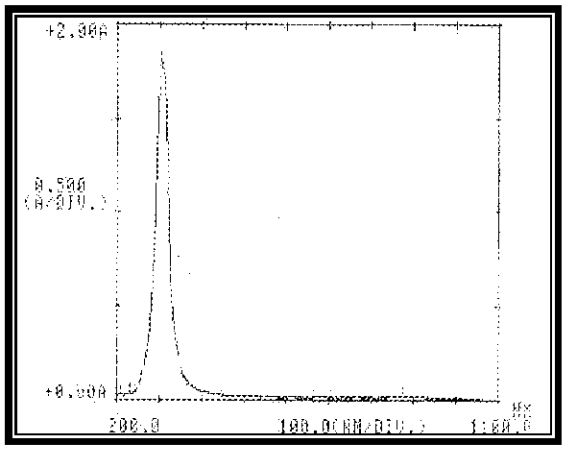


Figure (8): UV. Spectrum of compound [7]

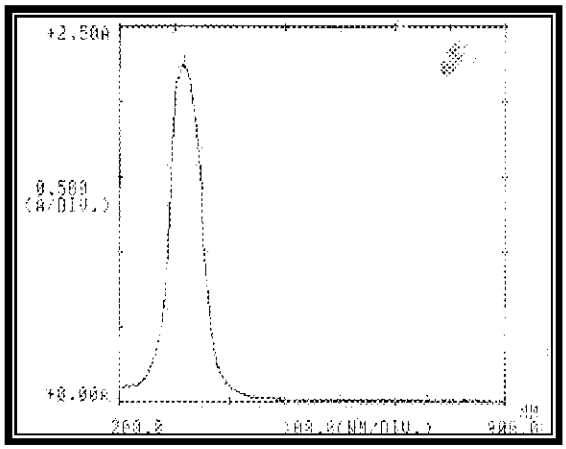


Figure (9): UV. Spectrum of compound [11]

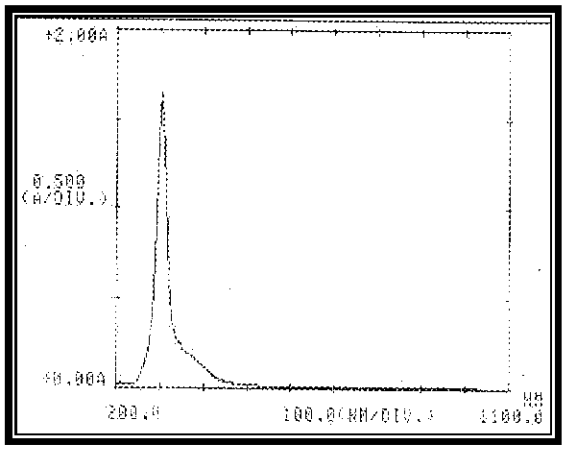


Figure (10): UV. Spectrum of compound [15]

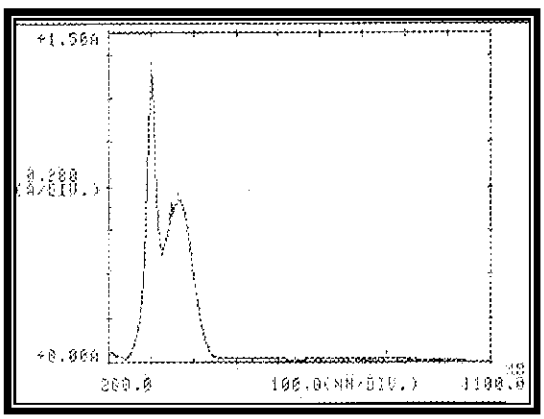


Figure (11): UV. Spectrum of compound [19]

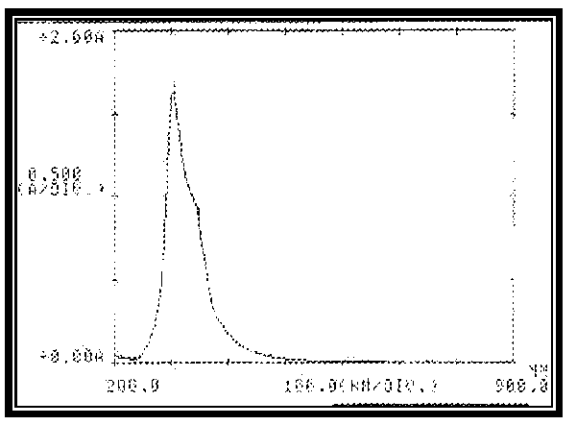
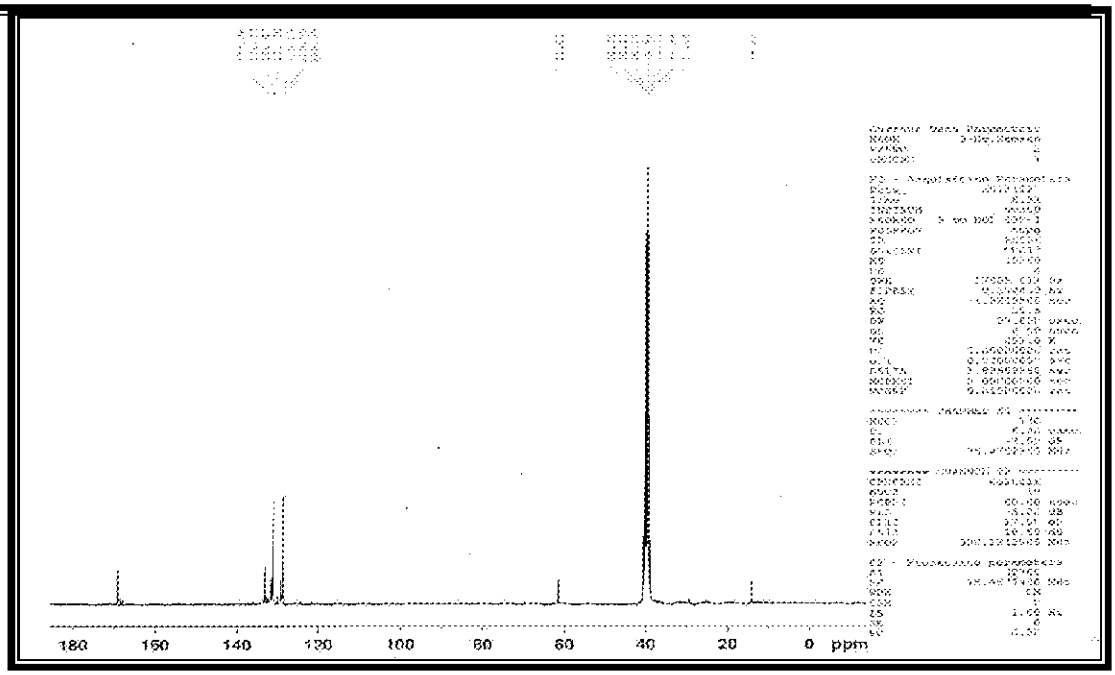
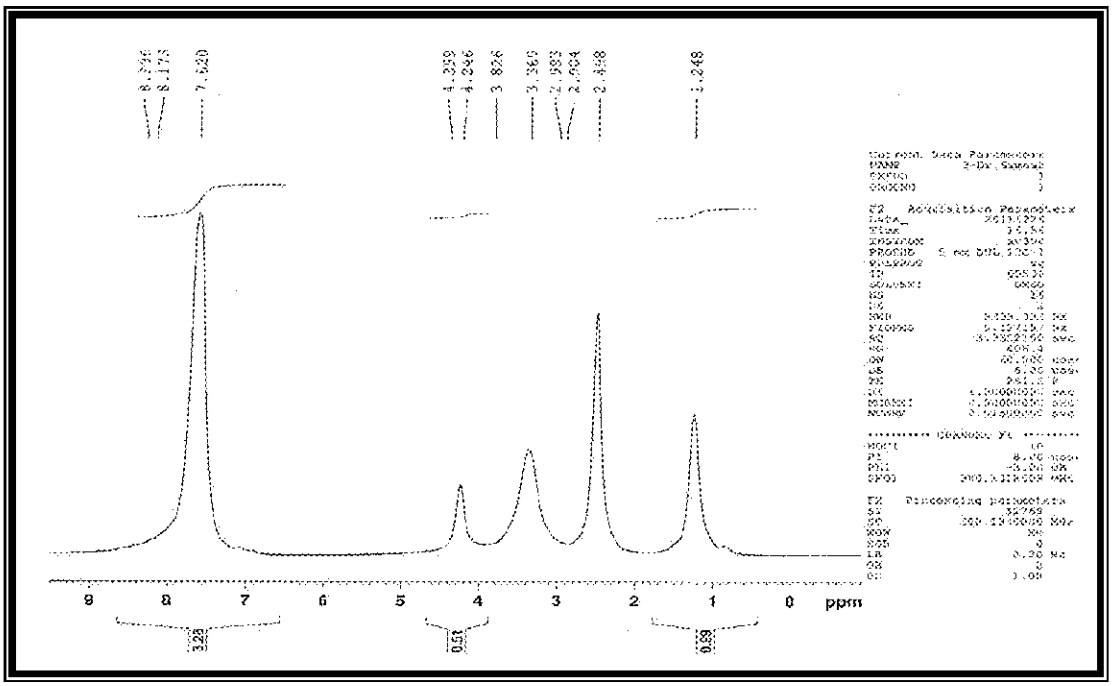


Figure (12): UV. Spectrum of compound [23]



Figure(13): ^{13}C-NMR Spectrum of compound [5]



Figure(14): ^{13}C-NMR Spectrum of compound [5]

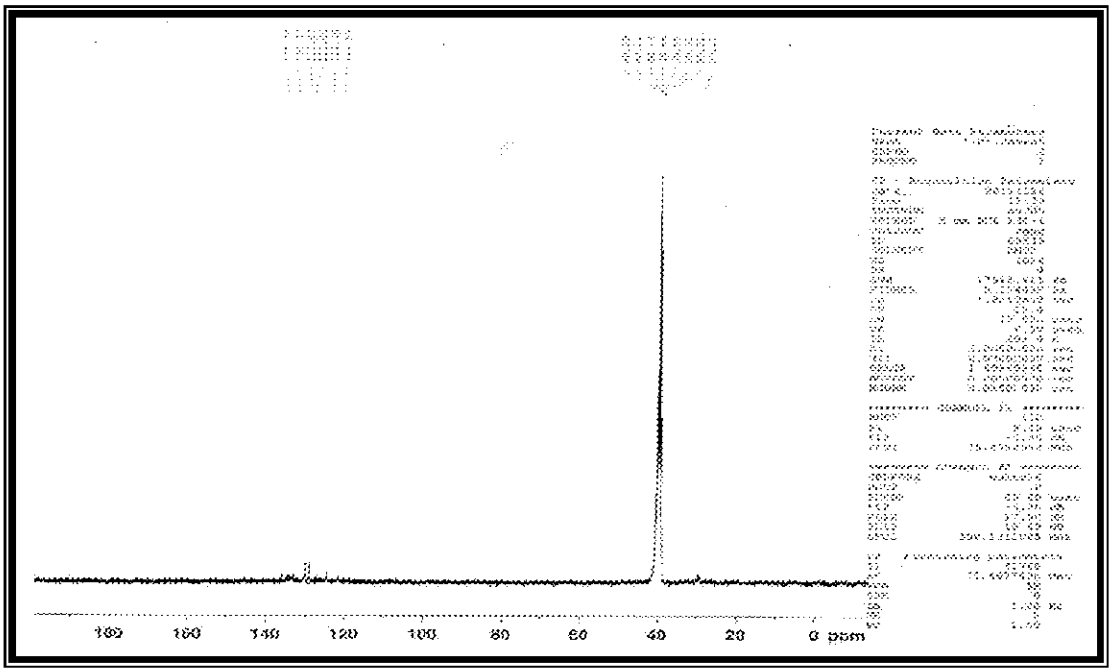


Figure (15): ^{13}C-NMR Spectrum of compound [21]

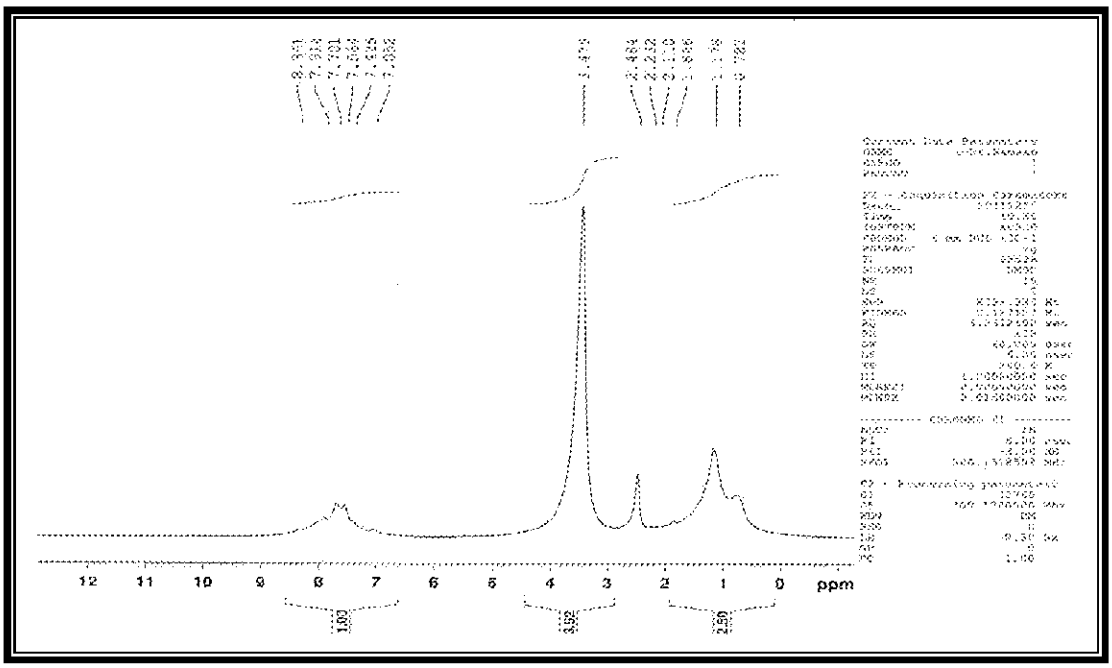


Figure (16): ^{13}C-NMR Spectrum of compound [21]

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تحضير وتشخيص الاوكسازيبين، دايزيبين وتترازول المشتقة من 2- أمينوبنزول ثايازول

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الخلاصة

تم في هذا البحث تحضير بعض المعوضات الجديدة للاوكسازابين, دايزبين وتترازول عن طريق قواعد شف لمشتقات 2- امينو بنزوثايازول وذلك من خلال اجراء خمسة خطوات حيث تضمنت الخطوة الاولى تحضير قواعد شف (1-4) بطريقة الثايوسيانوجين بوجود مذيب مناسب.

اما الخطوة الثانية تضمنت تحضير قواعد شف (1-4) وذلك بتكاثف مشتقات 2-امينو بنزوثايازول مع الديهايدات وكيتونات مختلفة.

اما في الخطوة الثالثة فقد تم تفاعل قواعد شف المحضرة مع فثاليك انهيدريد مرة ومرة اخرى مع ماليك انهيدريد فاعطت مشتقات الاوكسازوبين (5-12) ثم معاملتها لاحقا في الخطوة الرابعة مع امين اروماتي اولي فاعطت ثمانية مشتقات جديدة من الدايزيبين (13-20).

واخيرا تضمنت الخطوة الخامسة تحضير اربعة مشتقات جديدة للتترازول (21-24) من خلال تفاعل قواعد شف المجهزة في الخطوة الثانية مع ازايد الصوديوم بوجود THF كمذيب

ثم تشخيص المركبات المحضرة باستخدام بعض الطرق الطيفية FT-IR وUV و ^{1}H-NMR وكذلك ^{13}C-NMR بالاضافة الى دراسة الخواص الفيزيائية للمركبات المحضرة.