Synthesis and Characterization of Some New Derivatives From 2-Mercaptobenzoxazole

Mohammad R. Ahmad, Ali A. Mohsen *
Department of Chemistry, College of science, Baghdad University, Baghdad, Iraq.

Abstract:
In this work 2-mercaptobenzoxazole (2-MBO) (1), was prepared by using homemade Auto clave .The synthesis involve treatment of 2-MBO with 2-chloro acetyl chloride to give 2-chloroacetyl thio benzoxazole (2), the product was treated with phenyl hydrazine to give 2-phenyl hydrazide acetyl thio benzoxazole (3). The new derivatives (4-13) were synthesized by reaction of 2-phenyl hydrazide acetyl thio benzoxazole (3) with different aromatic aldehydes in the presence of acetic acid. The compound (2) was treated with hydrazine hydrate to give product (14) then treated with different aromatic aldehydes in the presence of glacial acetic acid to give Schiff bases derivatives (15-24). Structure of all the prepared compounds confirmation were proved using (FT-IR), (^{1}H-NMR), (^{13}C-NMR) spectra and elemental analysis (C .H .N.S) in addition to melting points.

Keywords: Benzoxazole, Phenyl hydrazine, Schiff's base**.**

تحضير وتشخيص بعض المشتقات الجديدة من 2- مركبتو بنزواوكسازول

محمد رفعت احمد ، علي أياد محسن*
قسم الكيمياء ، كلية العلوم ، جامعة بغداد ، بغداد ، العراق .

الخلاصة
حضر2- مركبتو بنزواوكسازول (1) ،حيث تم تحضير المركب (1) بواسطة جهاز (Auto clave) المصنع محليا. التحضير بتضمن معاملة 2- مركبتوبنزواوكسازول مع 2- كلورواستيل كلورايد ليعطي 2- كلورواسيتل ثايو بنزواوكسازول (2)،ثم معاملة الناتج مع فنيل هيدرازين ليعطي 2- فنيل هيدرازايد استيل ثايو بنزواوكسازول (3). ثم فوعل مركب (3) مع الالديهايدات الاروماتية المختلفة بوجود حامض الخليك للحصول على المشتقات الجديدة (4-13)، اما المركب (2) فعومل مع الهيدرازين المائي ليعطي مركب (14)، حيث يتم معامله هذا المركب مع الالديهايات الاروماتية المختلفة بوجود حامض الخليك الثلجي للحصول على مشتقات من قواعد الشيف (15-24) .وتم تشخيص تراكيب جميع المركبات المحضرة بمطياف (FT-IR)، (^{1}H-NMR)،(^{13}C-NMR) والتحليل الدقيق للعناصر (C.H.N.S) اضافة الى درجة الانصهار.

Introduction

Chemistry of heterocyclic compounds is one of the leading lines of investigations in the organic chemistry. Heterocyclic compounds are widely distributed in nature and are essential for life [1]. Biologically active benzoxazole derivatives have been known for long time, since they are the

---

*Email:Aliayad120@yahoo.com

isosteres of naturally occurring cyclic nucleotides and they may easily interact with the biopolymers of the organisms [2]. Benzoxazole (I) and Benzoxazole-2-thiol (II) Figure (1) have been reported to show a broad spectrum of biological activities [3]. such as antimicrobial[4] , anti-tubercular,[5] and cytotoxicactivity[6-8] ,antileukemic ,[9] anti- helminthic, anticonvulsant [10],anticancer and antimicrobial ,[11] antitumor[12,13], antitubarecular [14], , antifungal [15,16], antiulcer [17], activities. Similarly 4-oxothiazolodines are also known to possess various biological activities[18-21].
2-Mercaptobenzoxazole, is insoluble in water, but is soluble in aqueous alkali and common organic solvents; $pka_1 = 6.58$ and $pka_2 = 11.46$. This reagent has been recommended as an extraction photometric reagent for some metal ions such as Os(III) and Ru(III). 2-mercaptobenzoxazole use a good ionophore in construction of a copper (II)-PVC membrane electrode [22].

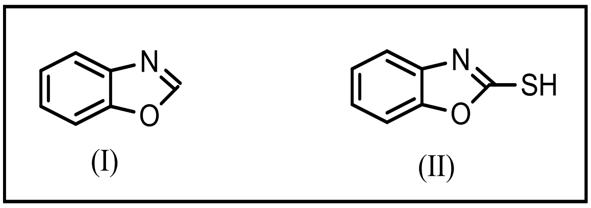


Figure 1- Chemical structure of Benzoxazole (I) and Benzoxazole-2-thiol (II).

Experimental

Materials and Instruments

Chemicals: All chemicals used were of high purity as the manufactures supplied starting chemical compounds were obtained from BDH, Sigma Aldrich, Fluka and used as received.

Instruments

Instruments were used: ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Burker 300 MHz instrument using DMSO-d_6 as solvent and TMS as internal reference, The FT-IR spectra in the range (4000-200) cm^{-1} were recorded as KBr disc on a Shimadzu FT-IR 8300 spectrophoto- meter, elemental analysis (C.H.N.S) was carried out at the Ministry of Oil. The 2- MBO was prepared by using the manufacturer domestic autoclave made from stainless steel with a capacity of 300 ml and of 12.5 cm diameter as shown below in figure -2.

Figure 2- The manufacturer domestic Autoclave.

Preparation methods

1-Synthesis of 2-mercaptobenzoxazole (2-MBO) (1) [23].

2-Amino phenol (10.91gm, 0.1mole) was mixed with (100 ml) absolute ethanol and (0.1mole, 6.19ml) of carbon disulfide. The mixture was transferred in to Autoclave and was closed it very well to insure getting a high temperature and pressure. This set- up was heated in a sand bath at 180 ^{o}C for (6-8) hrs. The resulted mixture was placed in a beaker and added (7ml) of 10% Sodium hydroxide to remove unreacted amine. Few drops of concentrated hydrochloric acid were added until the mixture became acidic to precipitate thiol. The precipitate was filtered off and followed by addition of (7 ml) 25 % sodium carbonate .The filtered mixture was dried and recrystallized from ethanol. The physical properties of compound (1) are listed in table -1.

2- Synthesis of 2-chloro acetyl thio benzoxazole (2) [24].

Equimolar of 2-mercaptobenzoxazole (1) (15.11g , 0.1 mol.) with chloroacetyl chloride (7.96 ml, 0.1 mol.) in chloroform (50 ml) and in the presence of trace quantities anhydrous potassium carbonate was refluxed on a water bath for about 14 hrs. The solvent was removed by vacuum. The residue was recrystallized from methanol. The physical properties of compound (2) are listed in table -1.

3- Synthesis of 2-phenyl hydrazide acetyl thio benzoxazole (3) [25].

A mixture of 2-chloroacetyl thio benzoxazol (2) (22.76g, 0.1 mol.) and phenyl hydrazine (9.9 ml, 0.1 mol.) in 80 ml ethanol was stirred at room temperature for 2 days. The product was obtained by leaving the reaction mixture dries in the air in a petri dish. The product was filtered off and recrystallized from ethanol. The physical properties of compound (3) are listed in table -1.

4- Synthesis of 2-[5-substituted-5-hydroxy-4-phenyl aceto hydrazide] thio benzoxazole(4-13) [25].

Equimolar of quantities of 2-phenyl hydrazide acetyl thio benzoxazole (3) (0.1mol.) and aromatic aldehydes (0.1mol.) in (25 ml) of ethanol containing few drops of acetic acid was refluxed on water bath for about 4-5 hrs. The product was obtained by leaving the reaction mixture dries in the air in a petri dish. The product was filtered off and recrystallized from ethanol. The physical properties of compounds (4-13) are listed in table -1.

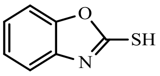
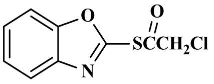
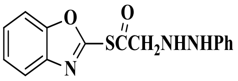
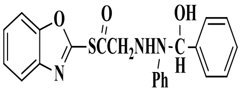
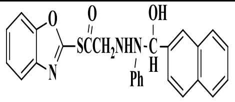
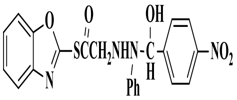
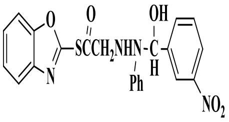
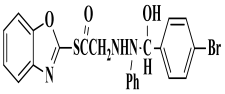
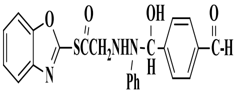
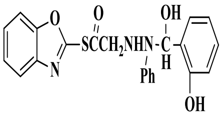
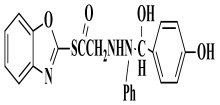
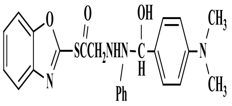
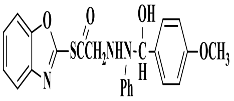
5- Synthesis of 2- hydrazide acetyl thio benzoxazole (14) [24].

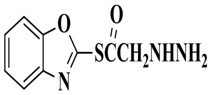
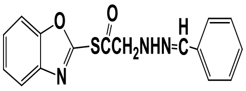
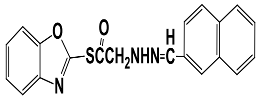
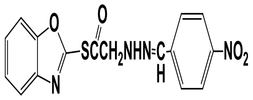
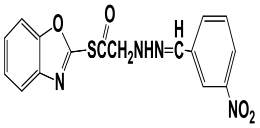
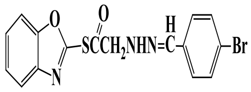
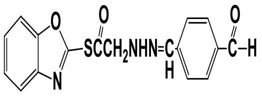
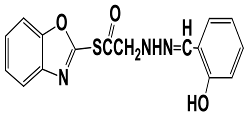
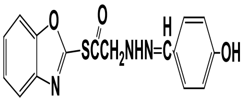
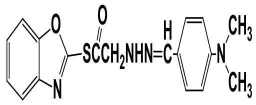
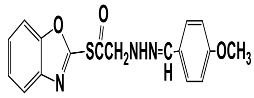
A mixture of 2-chloroacetyl thio benzoxazole (2) (22.76g ,0.1mol) and hydrazine hydrate (4.9 ml , 0.1mol) in (50mL) ethanol were stirred at room temperature for about 5 hrs. After cooling the solvent was removed under reduced pressure and the residue to offer the product .The solid precipitate was filtered off and recrystallized from benzene. The physical properties of compound (14) are listed in table -1.

6-Synthesis of 2- [α – (Arylidine hydrazino) acetyl] thio benzoxazole (15-24) [26,27].

Equimolar quantities of 2- hydrazide acetyl thio benzoxazole (14) (0.1mol) and aromatic aldehydes (0.1mol.) in (30 ml) of absolute ethanol and 3-4 drops of glacial acetic acid was refluxed on a water bath for about 4-5 hrs. at (50 ^{o}C) . The solvent was removed under reduced pressure to offer the product. The solid product thus obtained was recrystallized from ethanol. The physical properties of compounds (15-24) are listed in table -1.

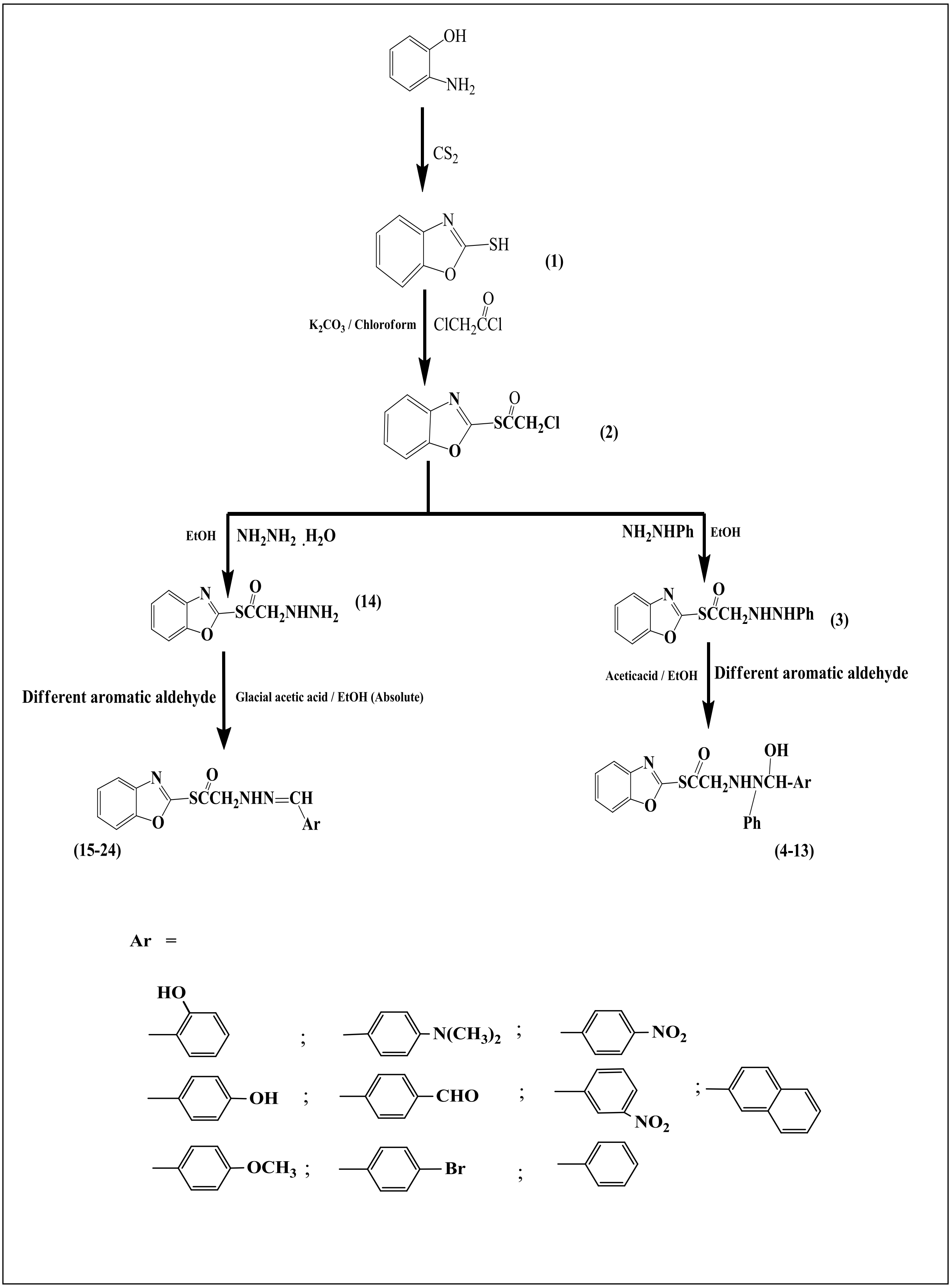
Table 1- Physical Properties and Spectral Data of the Prepared Compounds (1-24).

Com. No.	**Structures**	**Physical Properties**			**FT-IR spectral data of compounds cm^{-1}**				
		M. P. ^{0}C	**Color**	**Yield%**	**ν (N-H)**	**ν (C=O)**	**ν (O-H) (broad)**	**ν (C=N)**	**Other Bands**
1-		191	Light-Browne	73	3319 Tauto.	-	-	1618	ν (C=S) 1280 ν (S-H) 2610
2-		112	Red	93	-	1731	-	1618	ν (C-Cl) 786
3-		Oily	Orange	84	3313 3207	1670	-	1602	-
4-		Oily	Browne	68	3232	1687	3310	1618	-
5-		Oily	Black	50	3200	1691	3300	1623	-
6-		63	Dark-Red	56	3225	1704	3301	1598	ν (N=O) Sym 1521 Asym 1336
7-		Oily	Brown	62	3280	1703	3320	1618	ν (N=O) Sym 1531 Asym 1352
8-		91	Browne	53	3240	1703	3313	1596	ν (C-Br) 646
9-		74	Black	74	3220	1695 1710 (alde.)	3385	1602	$\nu(\overset{O}{\overset{/\!/}{C}}-\underline{H})$ 2785
10-		Oily	Red-Black	67	3260	1645	3360 3320	1600	-
11-		Oily	Dark-Yellow	66	3174	1666	3213 3225	1598	-
12-		Oily	Red	73	3238	1650	3463	1595	-
13-		Oily	Yellow	66	3230	1639	3320	1600	-

Com No.	**Structures**	**Physical Properties**			**FT-IR spectral data of compounds cm^{-1}**				
		M. P. ^{0}C	**Color**	**Yield%**	**ν (N-H)**	**ν (C=O)**	**ν (C=N) oxazole**	**ν(C=N) Schiff**	**Other Bands**
14-		143	Light -Gray	83	3194	1635	1598	-	ν(NH_2) Sym 3414 Asym 3317
15-		198	Yellow	61	3220	1622	1573	1600	-
16-		240	Yellow	56	3317	1618	1552	1652	-
17-		183	Bale-Yellow	53	3440	1600	1558	1625	ν (N=O) Sym 1523 Asym 1355
18-		340	Yellow	55	3282	1623	1558	1645	ν (N=O) Sym 1519 Asym 1346
19-		175	Yellow -Light	57	3328	1625	1583	1650	ν(C-Br) 493
20-		198	Green	71	3410	1622 1699 (alde.)	1577	1606	ν($\overset{O}{\overset{\|}{C}}-\underline{H}$) 2752
21-		230	Yellow	67	3421	1623	1571	1660	ν (O-H) 3479
22-		223	Orange – Yellow	59	3319	1608	1560	1593	ν (O-H) 3338
23-		175	Red	65	3313	1612	1600	1651	-
24-		163	Yellow	69	3163	1624	1600	1671	-

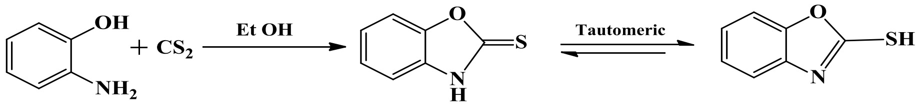
Results and discussion:

The reaction sequence for titled compounds is out lined in scheme -1.



Scheme 1- Preparation new series of 2-mercaptobenzoxazole.

2-MBO was obtained from the reaction of 2-aminophenole with carbon disulfide in absolute ethanol by using closed system. This method was selected because it gave 2-MBO in a good yield and high purity [28]. According to the equation below:



The structure of the compounds was confirmed from its melting point and FT-IR spectrum table -1, the ^{1}H-NMR analysis table -2, ^{13}C-NMR analysis table-3 and the C.H.N.S analysis table -4.

The FT-IR spectrum of compound (1) showed clear absorption bands at (3319) cm^{-1} due to ν(N-H); ν(C-H) aromatic at (3068-3039) cm^{-1}; (1618) cm^{-1} due to ν(C=N) oxazole ring ; (1506,1446) cm^{-1} due to ν(C=C) aromatic ; (1280) cm^{-1} due to ν(C=S) ; (2610) cm^{-1} due to ν(S-H) and disappearance of the two absorption bands at (3376,3305) cm^{-1} which could be attributed to asymmetric and symmetric stretching vibration (NH_2) group of 2-aminophenole[29]. All details of FT-IR spectral data of compound (1) are listed in table-1.

The reaction 2-mercaptobenzoxazole with 2-chloroacetyl chloride in alkali media (K_2CO_3) was used to prepare the compound (2). The halo group in 2-chloroacetyl chloride is good leaving group and sulfur compounds are a good nucleophile Thus, the reaction is a typical of the nucleophilic substitution reaction of the thiol group [30].

The FT-IR spectrum of compound (2) showed the appearance of absorption bands at (2925, 2854) cm^{-1} due to ν(C-H) aliphatic , absorption band at (1731) cm^{-1}due to ν(C=O) while absorption band due to ν(C-Cl) at (786) cm^{-1} ,these bands and others are shown in table -1.Then reaction compound (2) was stirred with phenyl hydrazine to gave 2-phenyl hydrazide acetyl thio benzoxazole (3).

The purity and structure of compound (3) was confirmed by FT-IR spectroscopy indicated the appearance of the characteristic absorption bands at (3313,3209) cm^{-1} due to ν(N-H) ,(1670) cm^{-1} characteristics of strong band due to ν(C=O) and there is also a band disappear ν(C-Cl). These bands and others are shown in table-1.^{1}H-NMR spectrum data of compound (3) showed singlet signal at δ= (4.22) ppm due to ((C=O)-C$\underline{H_2}$) protons, singlet signal at δ= (3.37) ppm due to (CH_2-N$\underline{H}$-NH) proton, singlet signal at δ= (6.53) ppm due to (NH-N$\underline{H}$-ph) proton and multi signals at δ= (6.68-7.78) ppm due to aromatic protons.[31] ^{1}H-NMR Spectral data of compound (3) are listed in table -2 and showed in Figure (3). ^{13}C-NMR spectrum data of compounds (3) showed signals at δ = (34.60) ppm due to ((C=O)-$\underline{C}$H2), δ = (148.12) ppm due to ($\underline{C}$=N) oxazole ring, δ = (180.11) ppm due to ($\underline{C}$=O) and signals δ= (109.93-131.18) ppm due to (C=C) aromatic [31]. ^{13}C-NMR Spectral data of compound (3) are listed in table -3 and showed in figure -4.

The derivatives (4-13) were obtained through the reaction of 2-phenyl hydrazide acetyl thio benzoxazole (3) with different aromatic aldehydes, Synthesis of compound (4-13) involved nucleophilic attack [32] of amino group in compound (3) on carbonyl group in different aromatic aldehyde. The FT-IR spectrum showed strong stretching bands at (3500-3200 cm^{-1}) broad belong to ν(O-H); (3150-3250) cm^{-1} belong to ν(N-H) and (1710-1639) cm^{-1} belong to ν(C=O). All details of FT-IR spectral data of compounds (4-13) are listed in table -1.

After that reaction 2-chloro acetyl thio benzoxazole (2) was stirred with hydrazine hydrate to gave 2-hydrazide acetyl thio benzoxazole (14).The FT-IR spectrum of compound (14) show a stretching bands at (3414, 3317) cm^{-1} belong to ν (NH_2) sym. and asym. bands, and disappearance of the absorption band (786) cm^{-1} due to ν(C-Cl), as shown in table -1. ^{1}H-NMR spectrum data of compound (14) showed singlet signal at δ= (3.97) ppm due to ((C=O)-C$\underline{H_2}$) protons, singlet signal at δ= (4.12) ppm due to (CH_2-N$\underline{H}$-NH_2) proton, singlet signal at δ= (2.40) ppm due to (NH_2) protons and multi signals at δ= (7.16-8.06) ppm due to aromatic protons. ^{1}H-NMR Spectral data of compound (14) are listed in table-2 and showed in figure -5.^{13}C-NMR spectrum data of compounds (14) showed signals at δ = (34.61) ppm due to ((C=O)-$\underline{C}H_2$), δ = (141.84) ppm due to ($\underline{C}$=N), δ = (168.72) ppm due to ($\underline{C}$=O) and signals δ= (104.78-127.29) (C=C) aromatic.^{13}C-NMR Spectral data of compound (14) are listed in table -3 and showed in figure -6.

The condensation reaction between 2- hydrazide acetyl thio benzoxazole (14) and different aromatic aldehydes involved nucleophilic addition [33] of hydrazine compound to carbonyl group producing which eliminate water molecule to afford the desirable Schiff's' bases (15-24).

The FT-IR spectra of compounds (15-24) showed bands at (3163-3440) cm^{-1} due to ν(N-H); (1600-1699) cm^{-1} due to ν (C=O); (1600-1552) cm^{-1} due to ν (C=N) oxazole ring ; (1671-1600) cm^{-1} due to ν (C=N) Schiffs' bases and disappearance absorption bands at (3414,3317) cm^{-1} due to ν(NH_2) sym. and asym. bands. All details of FT-IR spectral data of compound (15-24) are listed in table -1.

^{1}H-NMR spectrum data of compound (22) showed singlet signal at δ= (3.97) ppm due to ((C=O)-C$\underline{H}_2$) protons, singlet signal at δ= (7.02) ppm due to (CH_2-N$\underline{H}$-N) proton, singlet signal at δ= (7.24) ppm due to (Ar-O$\underline{H}$) proton, singlet signal at δ= (8.31) ppm due to (N=C-$\underline{H}$) proton and multi signals at δ= (6.62-7.47) ppm due to aromatic protons. ^{1}H-NMR Spectral data of compound (22) are listed in table-2 and showed in Figure (7).^{13}C-NMR spectrum data of compounds (22) showed signals at δ = (40.37) ppm due to ((C=O)-$\underline{C}$H2), δ = (160.24) ppm due to (H$\underline{C}$=N-NH) , δ = (180.21) ppm due to ($\underline{C}$=O) and signals δ= (105.90-131.80) (C=C) aromatic.^{13}C-NMR Spectral data of compound (22) are listed in table -3 and showed in figure -8.

Table 2-^{1}H-NMR spectral data (δ ppm) for compounds.

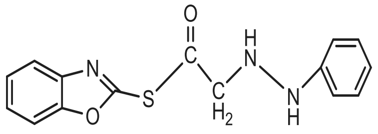
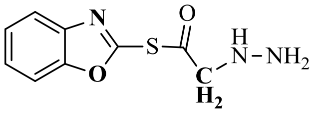
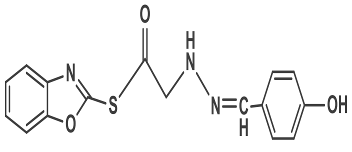
Comp. No.	**Compound structure**	**^{1}H-NMR spectral data (δ ppm)**
3-		4.22(2H, S, (C=O)-C$\underline{H}_2$)), 3.37 (1H,S, (CH2-N$\underline{H}$-NH)) , 6.53 (1H, S, (NH-N$\underline{H}$-ph) , 6.68 -7.78 (9H, m, aromatic (Ar-$\underline{H}$)).
14-		2.40(2H,S,(NH_2) protons), 3.97 (2H,S,(C=O)-C$\underline{H}_2$)), 4.12(1H,S,(CH_2-N$\underline{H}$-NH_2)),7.16-8.06 (4H ,m , Ar-$\underline{H}$)
22-		3.97 (2H,S, (C=O)-C$\underline{H}_2$)), 7.02 (1H, S, (N$\underline{H}$-N=CH)),7.24 (1H,S,(Ar-O$\underline{H}$) , 8.31 (NH-N=C-$\underline{H}$) , 6.62-7.47 (8H,m, aromatic (Ar-$\underline{H}$)).

Table 3- ^{13}C-NMR spectral data (δ ppm) for compounds.

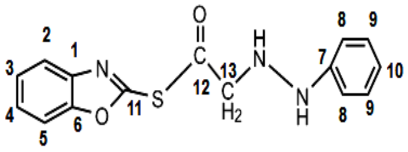
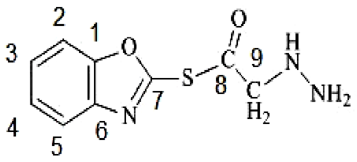
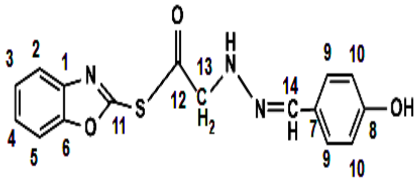
Comp. No.	Compound structure	^{13}C-NMR spectral data (δ ppm)
3-		34.60(C13), 109.93-125.09 (C2,C3,C4,C5,C8.C9,C10), 128.90-131.18 (C1,C6,C7), 148.12(C11), 180.11(C12).
14-		34.61(C9), 104.78-118.19(C2,C3,C4,C5), 122.97-127.29(C1,C6), 141.84(C7), 168.72(C8).
22-		40.37(C13), 124.96-131.80(C2,C3,C4,C5,C9,C10) 105.90-123.54(C1,C6,C7) 130.01(C8), 148.24(C11), 160.24(C14), 180.21(C12).

Table 4- The C.H.N.S. analysis of some prepared compounds.

Comp. No.	Molecular Formula	Calculate%				Found%			
		C	H	N	S	C	H	N	S
1-	C_7H_5NOS	55.61	3.33	9.26	21.21	55.33	3.12	8.99	21.18
2-	$C_9H_6ClNO_2S$	47.48	2.66	6.15	14.08	46.98	2.56	6.15	14.01
3-	$C_{15}H_{13}N_3O_2S$	60.18	4.38	14.04	10.71	60.10	4.36	14.00	10.70
7-	$C_{22}H_{18}N_4O_5S$	58.66	4.03	12.44	7.12	58.32	3.99	12.21	7.09
11-	$C_{22}H_{19}N_3O_4S$	62.69	4.54	9.97	7.61	62.49	4.44	9.86	7.42
12-	$C_{24}H_{24}N_4O_3S$	64.27	5.39	12.49	7.15	64.11	5.63	12.48	7.09
14-	$C_9H_9N_3O_2S$	48.42	4.06	18.82	14.36	48.31	4.01	18.66	14.21
24-	$C_{17}H_{15}N_3O_3S$	59.81	4.43	12.31	9.39	59.61	4.22	12.21	9.22

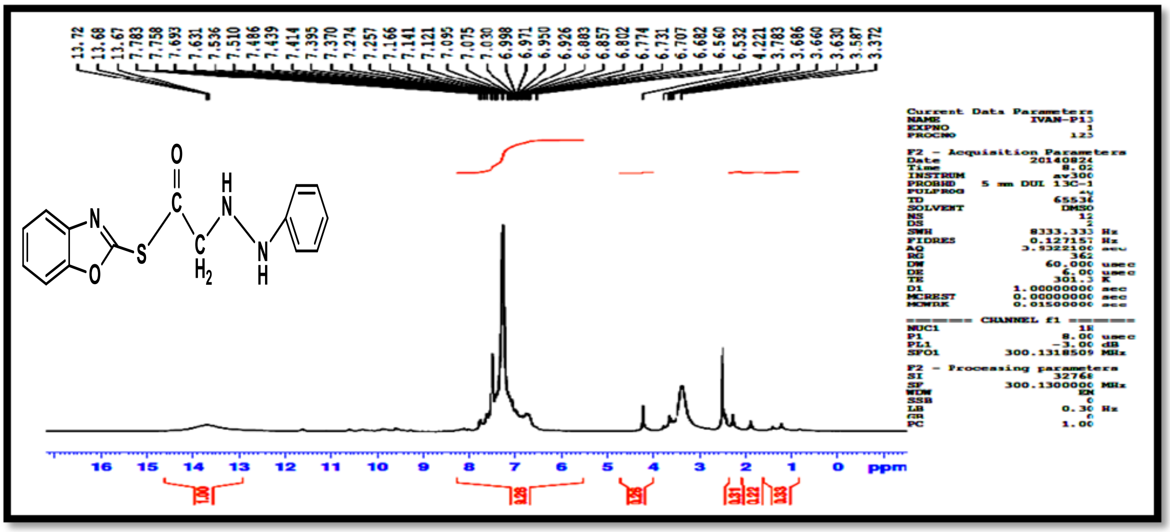


Figure 3- ^{1}H-NMR spectrum of compound (3).

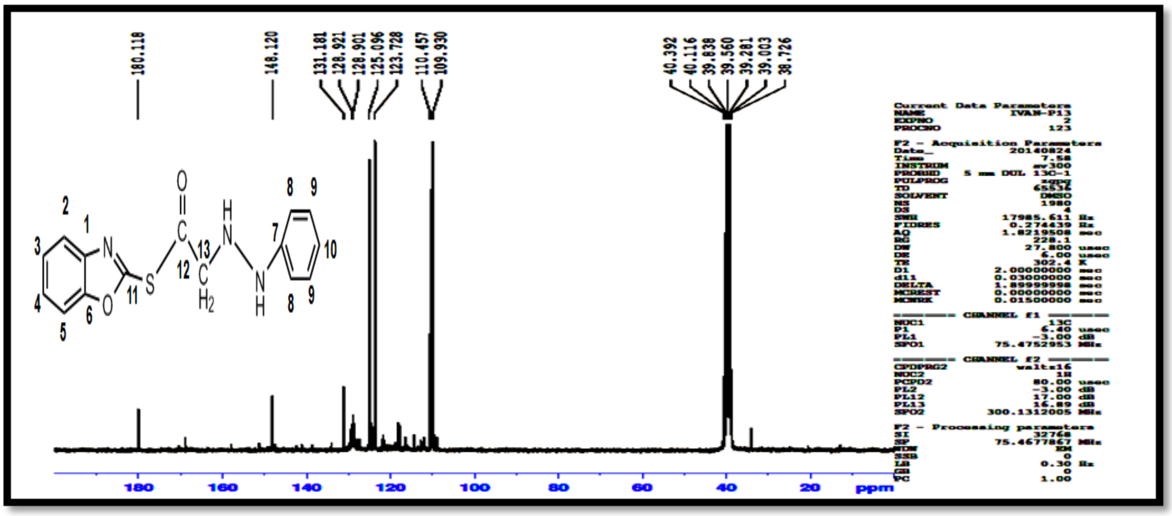


Figure 4- ^{13}C-NMR spectrum of compound (3).

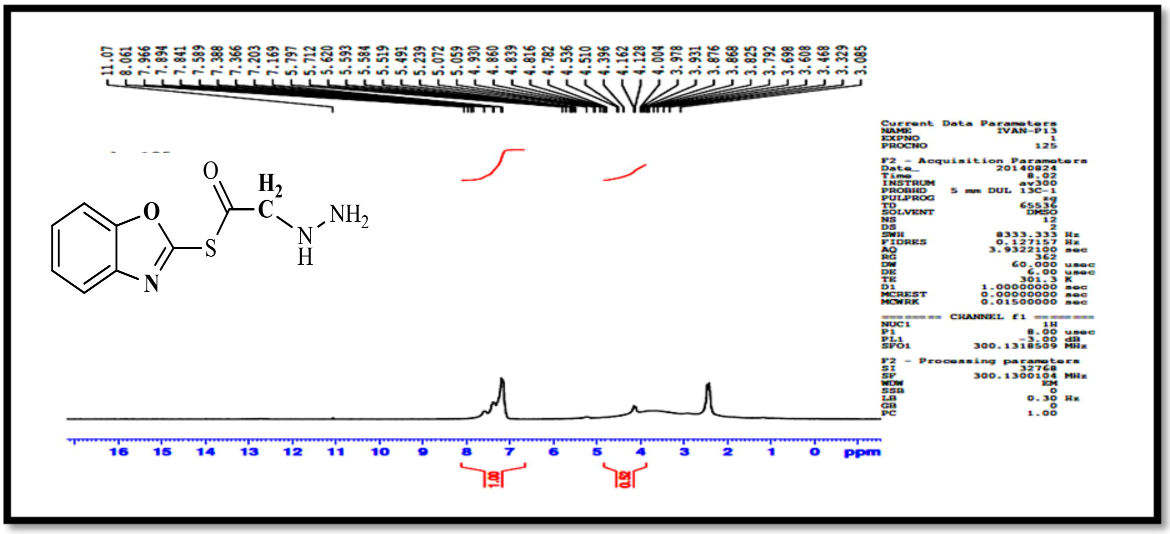


Figure 5- ^{1}H-NMR spectrum of compound (14).

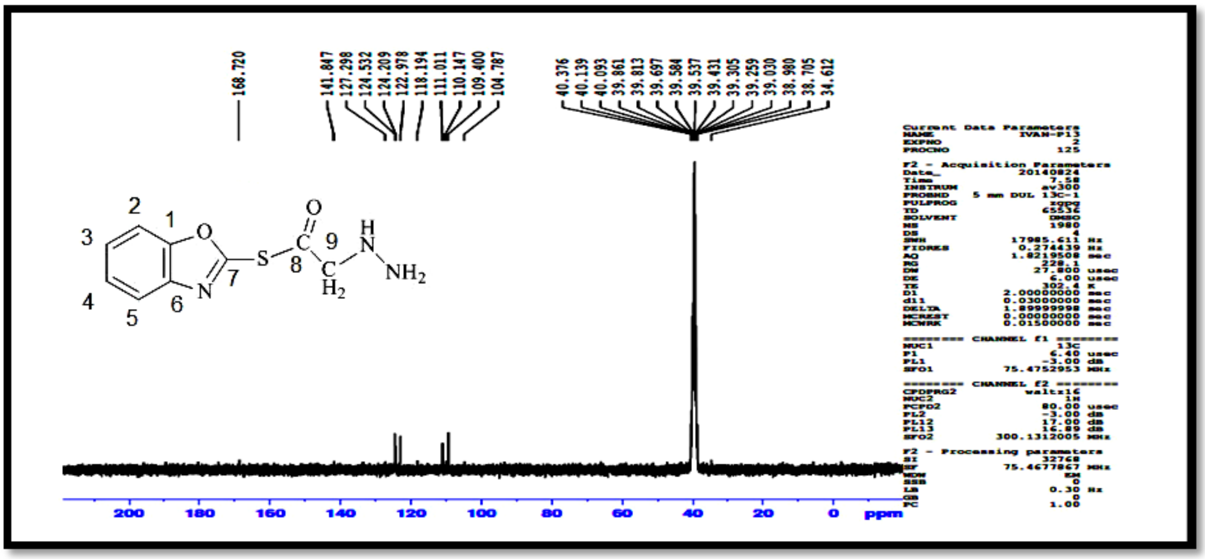


Figure 6- ^{13}C-NMR spectrum of compound (14).

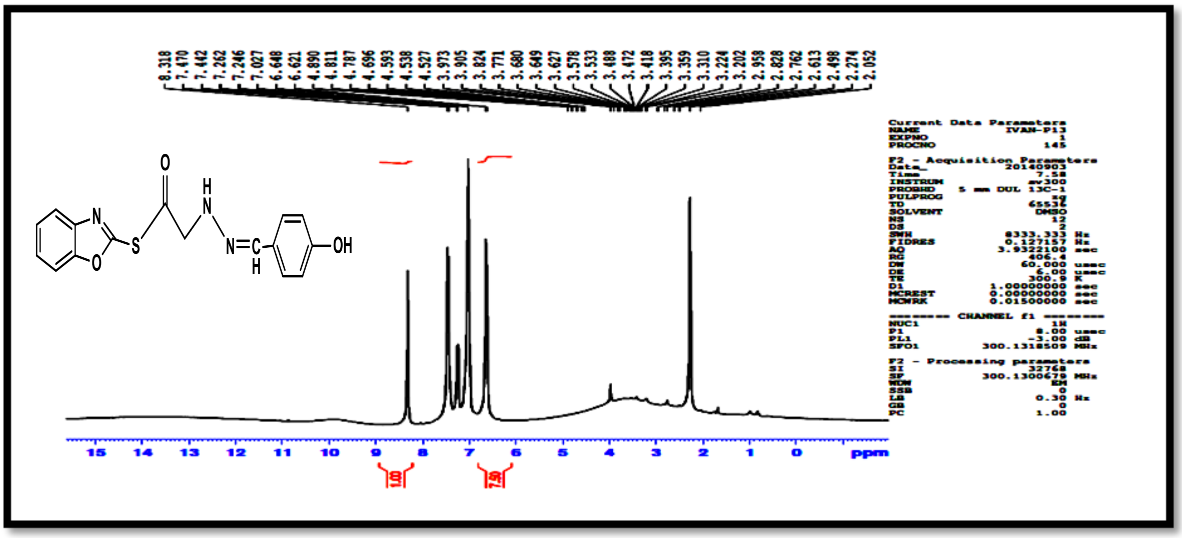


Figure 7- ^{1}H-NMR spectrum of compound (22).

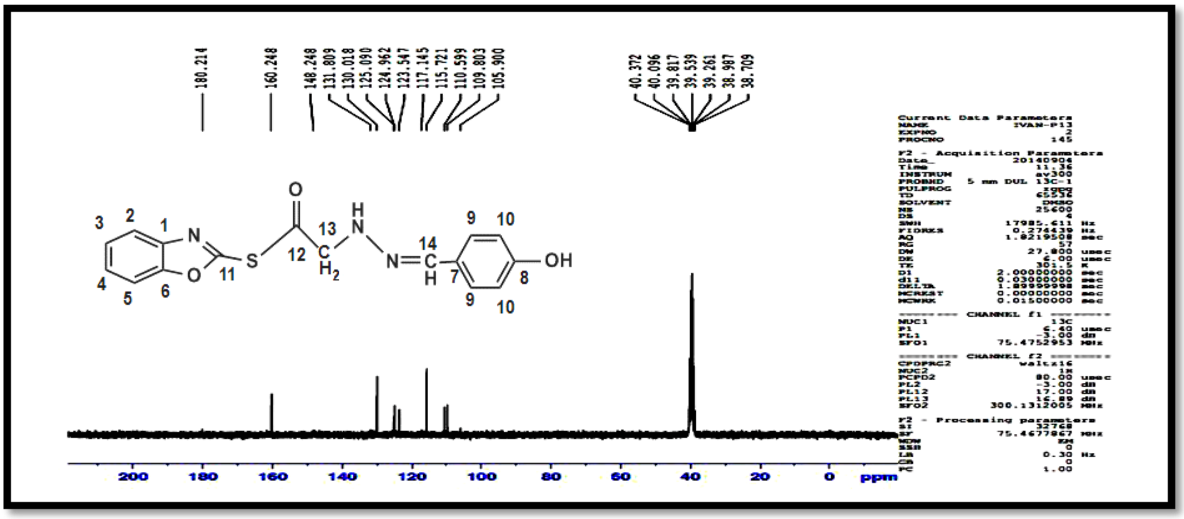


Figure 8- ^{13}C-NMR spectrum of compound (22).

Reference:

1. Rekha,S. Prateek ,S. Chandrashekhara, S. Shantharam, U. Vineeth, C. and Prof. Satyanand, T. **2013**. Synthesis, Characterization and Evaluation of Microbial Activity of some heterocyclic compounds Containing benzothiazole moieties, *J. Drug Discovery and Therapeutics*, 1 (5) , pp: 29-36.
2. Turker, L. Sener, E. Yalcin, I. Akbulut ,U. and Kayalidere ,I. **1990** . SAR of some antigungal – active benzoxazole using the quantum chemical parameters. *Scientia Pharmaceutica*, 58, pp: 107-113.
3. Singh, L. P. Chawla,V. Chawla, P. and Saraf, S. K.**2010**. Synthesis and antimicrobial activity of some 2-phenyl-benzoxazole derivatives. *Der Pharma Chemica* , 2(4), pp:206-212.
4. Ramalingan,C. Balasubramanian,S. Kabilan,S. and Vasudevan, M. **2004**.Synthesis and Study of antibacterial and antifungal activities of novel1-[2-(benzoxazol-2-yl)ethoxy]- 2,6-diarylpiperidin-4-ones. *Euro J. Med. Chem*, 39,pp: 527–533.
5. Saleh, M. Makki, I.T. Abdel-Rahman, R.M. Faidallah, H.M. and Khan, K.A. **2013**. Synthesis of new fluorine substituted heterocyclic nitrogen systems derived from *p*-aminosalicylic acid as antimyco bacterial agents. *J. Chem*, pp: 1–8.
6. Balaswamy, G. Srinivas, K. Pradeep, P. and Sarangapani, M. **2012**. Synthesis, characterization and anti-microbial activity of novel substituted benzoxazole derivatives. *Int. J. Chem Sci*, 10(2), pp: 619-626.
7. Eshbha, N. N. and Dalama , H. M .**1985**. 5-(2-Oxo-3-indolinylidene) thiazolidine-2, 4-dione-1,3-di-Mannich base derivatives: Synthesis and evaluation for antileukemic activity. *Pharmazie*, pp: 40 :320.
8. Balaswamy, G. Pradeep, P. Srinivas, K. and Rajakomuraiah, T. **2012**.Synthesis, characterization and anti-microbial activity of new series of benzoxazole derivatives. *Int. J. Chem. Sci*, 10(2), pp: 619-626.
9. Rajopadhye, M. and Popp, F.D. **1987** .Synthesis and antileukemic activity of Spiro [indoline-3,2′-thiazolidine]-2,4′-diones. *J. Hetero Chem*, 24, pp: 1637–42.
10. Biradar, S.J. and Manjunath, S.Y. **2004** .Synthesis and biological activities of novel 2-(5'-substituted-3'-phenylindole-2'- yl)-1,3,4-oxadiazino[5,6-b]indole and 3-(5'-substituted-3'-phenylindole-2'-amido) spiro-(indol-3'',2- thiazolidine)-2'',4-diones. *Ind. J. Chem.*, 43B, pp: 389–92.
11. Samia, M. A, Fawzia. Soad, A. Mona, M. Mona, H. and Manal, A. **2005**. Synthesis of Some Novel Benzoxazole Derivatives as Anticancer Anti-H1V1 and Antimicrobial Agents. *European J. Medical Chemistry*, 40 (9), PP: 949-959.
12. Yi-Ping, T. and Yan-Wen, L.**2009**. Synthesis, structure, photoluminescence and theoretical studies of an In (III) complex with 2-(2'-hydroxylphenyl) benzoxazole. *Inorganica Chimica Acta*, 362, pp: 2033–2038.
13. Stefania, A. Geoffrey, W. Erica, L.S. Hachemi, K. and Rana, B. **2008**. Synthesis and Biological Properties of Benzothiazole, Benzoxazole, and Chromen-4-one Analogues of the Potent Antitumor Agent 2-(3,4-Dimethoxyphenyl)-5-fluorobenzothiazole. *J. Med Chem*, 51, pp: 5135–5139.
14. Vera, K. Jan, K. Korel, W. and Jarmila, K . **2009** . Preaparation and invitro evaluation of benzylsulfonyl benzoxazole derivative as potential antituberculosis agents. *Eur J. med chem*, 44, pp: 2286-2293.
15. Zafer, A. Kaplancikli, Gülhan,T.Z., Gilbert, R. and Kiymet, G. **2004** .Synthesis and Study of Antibacterial and Antifungal Activities of Novel 2-[[(Benzoxazole/benzimidazole-2-yl)sulfanyl] acetylamino]thiazoles. *Arch Pharm Res.* , 27(11), pp: 1081-1085.
16. Ismail,Y. likay,O. Ozlem,T.and Esin ,A.S. **2000** . QSARs of some novel isosteric heterocyclics with antifungal activity. *Acta biochemical Polonica.* , 47(2), pp: 481–486.
17. Megumi ,Y. Yasuo, S. and Kazako, K . **1998** . A new 5-HT3 Receptor ligand II. Structure-Activity Analysis of -HT3 Receptor Agonist Action in the Guts. *Chem pharm Bull.* , 46(3), pp: 445-451.
18. Rao,G.K. Sen,S. and Rajendra, B.**2004**. Synthesis of 3-(4-Chlorophenoxymethyl)-6-substitued phenyl-5, 6-dihydrotriazalo (3, 4-b) (1,3,4)-thiadiazols as antimicrobial agents . *Indian Drugs*, 41(9), pp: 524.

19. Desai, K.G. and Desai, K.R. **2005**. Synthesis of some novel pharmacologically active Schiff bases using microwave method and their derivatives formazans by conventional method. *Indian J. Chem.*, 44B, pp : 2097-2101.

20. Shaaer, H.M. Abdel, A. Allimony, H.A. and Abdel, R .**1997** . Synthesis and antimicrobial activities of some new 2-substituted benzoxazole/benzothiazole derivatives . *Pharmazie*, 52(8), pp : 585-589.

21. Ramón, G. Domenech, B. Ana, C. Gregori, C. and Calabuig, C. **2002** .Predicting Antifungal Activity: A Computational Screening Using Topological Descriptors. *Internet Electron. J. Mol. Des., Bio Chem Press*,1(7) , pp: 339-350.

22. Morteza,A. Mehrorang ,G. and Javad ,T. **2005** . Development of a New Copper(II) Ion-selective Poly(vinyl chloride) Membrane Electrode Based on 2-Mercaptobenzoxazole. *Bull. Korean Chem. Soc.*, 26, pp: 882 -886.

23. Ahlam,J. H . **2006**. Synthesis of 2-Mercaptobenzothiazole and Some of its derivatives and study it effect on some strains of Bacteria .M.Sc.Thesis ,Department of Chemistry ,College of Science ,University of Baghdad, Baghdad , Iraq. P: 24.

24. Rambir,S. Nagori, B.P. and Navneet,A.**2013**. Synthesis and Antimicrobial activity of some new schiff's bases and 4-oxothiazolidine derivatives of 2-mercaptobenzoxazole. *Pharmacophore*, 4 (1), pp :10-14.

25. Luma, S.A.**2005**.Synthesis And Biological Activity study of new C-and N-substituted Phenothiazine Derivatives .M.Sc. Thesis, Department of Chemistry, College of Science, University of Baghdad .Baghdad, Iraq. P:20.

26. Shriner,R.L. and Robert,W.U.**1941**. Synthesis of bis-benzimidazoles from dibasic acids. *J.Organic Chemistry*, 63(8), pp: 2277.

27. Ramesh, D. **2013** .Synthesis and Characterization of 2-[1H- benzimi -dazole-2yl-sulfanyl]-N-[(E)-(3-methylphenyl) methylidene] acetohydrazide**.** *J. Chem. Bio. Phy. Sci. Sec.*,3 (1) ,pp:9-15.

28. Hamood A. J**. 2006**. Synthesis of 2-Mercaptobenzothiazole and Some of its derivatives and study it effect on some strains of Bacteria. M.Sc. Thesis, Department of Chemistry ,College of Science ,University of Baghdad, Baghdad, Iraq, pp:39.

29. Sliverstien, R.M. and Websters X. **1998**. *Spectrometric Identification of organic compounds*. 6 th Edition, John Wiely and Sons , New York.

30. Suaad, M.H. Al-Majidi and Khitam, T.A., Al- Sultani. **2010**. Synthesis and antimicrobial activity of some new acetylenic amine of isatin derivatives. *J. Al-Mustansirya Sci.*, 21 (4), pp: 61-72.

31. Ernö, P. Philippe, B.and Martin, B. **2009**.*Structure Determination of Organic Compounds*. 4 th Ed, Revised and Enlarged Edition ,Springer , Verlag, Berlin ,Heidelberg.

32. Vogel,A**. 1989**. *Vogel 's A Textbook of Practical Organic Chemistry*. 5th Edition, revised by B. Furniss, A. Hannaford, P. Smith, and A. Tatchell, Longman group limited, London, UK,.

33. John, M. **2008** .*Organic Chemistry*. 7th Edition, Mcgraw hill, Now york.