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Preparation, investigation and studying the (physical, spectral and biological activity) of new monomers and heterocyclic compounds containing nitrogen and oxygen

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ABSTRACT

This study involves the preparation of seven new compounds, some of them contain two functional groups that are considered condensation monomers. On the other hand, other compounds contain double bonds that are considered addition monomers. They started from 2- amino Thiazole with 2-hydroxy benzaldehyde (salicylaldehyde) in ethanol and hydrochloric acid to prepare azo compound (A), which reacted with acetophenone derivatives (p-bromo, p-chloro and p-hydroxy acetophenone) to prepare chalcone monomers derivatives (H1-H3). Also, the work includes preparing seven-membered heterocyclic rings through two consecutive steps; the first step includes the preparation of Schiff base compound (S). The second step includes the preparation of the oxazepine derivatives (Z1, Z2) through the cyclic closure of compound (S) with the (maleic, phthalic) anhydrides, respectively. All compounds were investigated with FT-IR, H1NMR, and 13CNMR techniques. The physical properties and the antibacterial activity were also studied for all the prepared compounds and showed good results.

Keywords: ***Synthesis, condensation, addition, monomers, polymers, 2-amino thiaole, chalcone* compound, *Azo* compound, *Schiff base, oxazepine, biological activity***

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1. Introduction

There are two main types of polymerization depending on the structure of the monomer: addition and condensation polymerization, also called chain-growth polymerization [1, 2]. Condensation monomers are widely used to prepare many synthetic polymers, such as polyester and polyamide [3]. They should have two functional groups, similar or different groups [4], used to link up the monomer molecule with other monomers and form the polymer [5]. While the addition monomers should have double bonds in their structure, they can open easily in the presence of an initiator and link with a similar or another double to form homo or hetero polymers, respectively [6]. Some of the prepared heterocyclic compounds contain two heterocyclic atoms in their composition, a sulfur atom and a nitrogen atom, in addition to carbon atoms [7]; the thiazole ring is planar, aromatic, possesses a non-asymmetric electron pair and possesses a degree of delocalization [8]. Thiazoles are present in many natural compounds, with biological activity, including vitamin B1 and penicillin [9]. There are plenty of prepared heterocyclic compounds containing thiazole rings which have shown various biological activities [10], such as anti (bacterial, viral [11], inflammatory, tumour, cancer [12-14] and antioxidant [15]. Its derivatives are used as a basic material for generating new bioactive molecules and drugs [16]. It is a type of heterocyclic compound that contains two (N, S) atoms to form a thiazide ring or two (N, O) atoms to form an oxazine ring [17]. The heterocyclic compounds containing the thiazines ring show different biological and pharmacological activity, including antioxidant [18], anti-inflammatory [19], antiviral, and antibacterial based on analgesic sedative, antipyretic, anticonvulsant [20-22], antifungal [23], antitumor [24] and anti-cancer [25]. Many researchers have been interested in preparing oxazine, chalcone, Schiff base and other heterocyclic

derivatives because of their importance, especially in the production of new heterocyclic monomers in industrial chemistry with good thermal and biological activity properties [26,27] as well as liquid crystal properties [28].

2. Methods

With high purity, international companies such as Sigma and GCC supplied all the materials used in this research. The electro-thermal 9300 melting point engineering (LTD) was used (8400) used to record FT-IR spectra in (cm^{-1}) for all compounds, H^1NMR spectra and C^1NMR spectra in DMSO solvent in (ppm) units detected by Bruker –AVANCE AQS-300MH_Z, at Iran, (TLC) Thin layer chromatography with silica gel using a solvent consisting of (Benzene: methanol).

2.1. Synthesis of azo compound (A)

Preparing Compound (A) was through dissolving (0.0149 mol, 1.5 g) of 2-aminothiazole in a solution formed of (5 ml concentrated Hydrochloric acid with 20 ml distilled water), then cooling the solution by ice-bath at (0-5)°C. (10 ml) of sodium nitrite solution was added drop by drop to the solution (0.0149 mol, 1.028 g) while stirring and maintaining the temperature-rang within the (0-5) °C and the mixture was left for 20 minutes. The formed diazonium salt solution was added dropwise with continuous stirring to a solution of (0.0149 mol, 1.8178 g) of (salicylaldehyde) dissolved in (20 ml) of ethanol and (10 ml) of sodium hydroxide (10%) solution. Orange colouration of the mixture was observed when (pH = 6) the mixture was left for 2 h, filtered and washed several times with distilled water; then, the compound was dried and recrystallized by using ethanol absolute, as shown below [29].

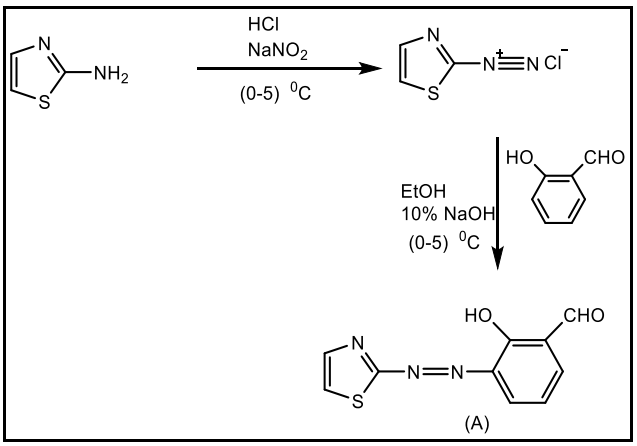


Figure 1. Preparing Compound (A)

2.2. Synthesis of chalcone monomers (H1-H3)

A magnetic transducer and apparatus heated to a magnetic stirrer (0.00183 mol) from acetophenone derivatives (p-bromo,p-chloro and p-hydroxy acetophenone), (10 mL) of a solution of NaOH (10%), then (0.5 g; 0.0018 mol) from the prepared azo (A)compound was added, The reaction was monitored by thin film chromatography with a mobile phase of (benzene - methanol) by volume ratio (V: V) (3.5 ml benzene: 1.5 ml methanol), followed by the reaction of the equation with acid Diluted HCl (5%), filtered and washed with cold distilled water, then dried and recycled by using ethanol absolute, as shown below [30].

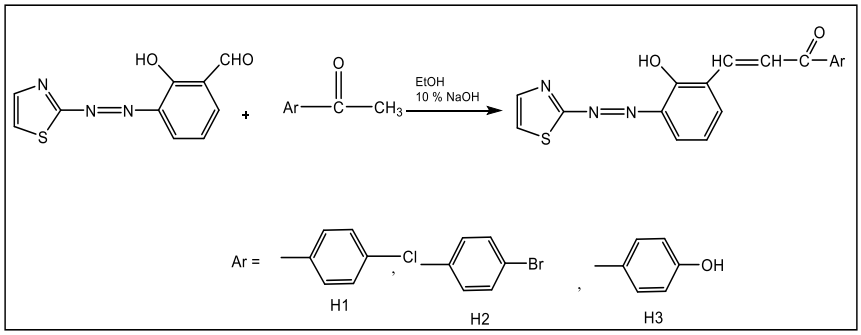
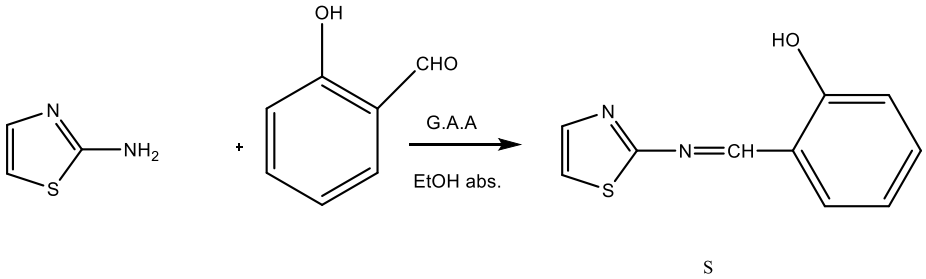


Figure 2. Synthesis of chalcone compounds (H1-H3)

2.3. Schiff base compound synthesis (S)

The reaction of (0.3 gm,0.002 mol) from 2-hydroxy benzaldehyde with (0.750 gm, 0.002 mol) from 2-aminothaizol as a catalyst with (2-3) drops of glacial acetic acid was used to prepare the Schiff base derivative, Then refluxing the mixture for 14 hours at about $78C^0$ to give compound (S) which dried and recrystallized with absolute ethanol as shown in below [31].



S

Figure 3. Schiff base compound synthesis (S)

2.4. Synthesis of the oxazepine derivatives (Z1-Z2)

The derivatives Z1 and Z2 were synthesized by the reaction of (0.01 mol) from Schiff base derivative (S) and (0.01 mol) of phthalic anhydride and malice anhydride using a solvent of dry benzene; and refluxing the mixture for 25 hours at about $60C^0$, as shown in below [32].

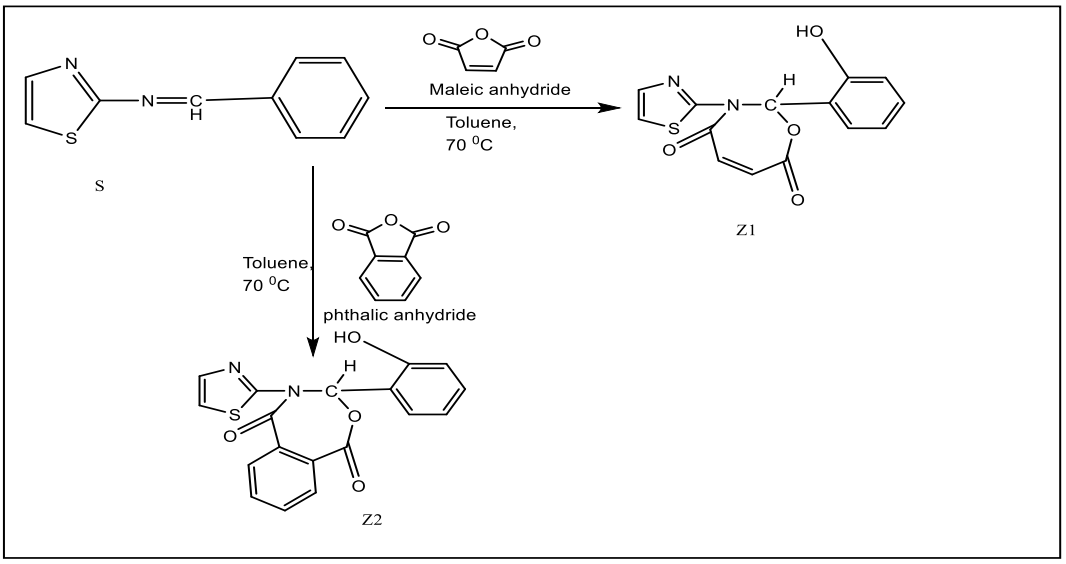


Figure 4. Synthesis of the oxazepine derivatives (Z1-Z2)

2.5. The biological activity study of prepared compounds using (paper disks technique)

White man NO.1 filtering paper was used to study the Antibacterial activity by preparing 120 pills after purification, and putting these pills in a test tube, about five pills per tube, then adding one ml of the compounds solutions; about (5mg,10 mg,20mg) from the prepared compound. The antibacterial activity of the synthesized compounds is found in Table 2.

3. Results and discussion

All the prepared compounds contain a hydroxyl group, which is important in many reactions, and another functional group; compound H1 has another hydroxyl group, so it is called a similar bi-functional condensation monomer, while compounds H2 and H3 have a halogen group in their structures, which is considered a good leaving group and when it attached to aromatic ring it can transfer to another hydroxyl group by hydrolysis reaction. All these compounds contain double bonds and are considered additional monomers .2-aminothiazole is reacted with 2-hydroxy benzaldehyde (salicylaldehyde) in ethanol and hydrochloric acid to produce an azo compound (A) has an aldehyde group beside the hydroxyl, which then reacted with acetophenone derivatives

(p-bromo, p-chloro, and p-hydroxy acetophenone) to produce new compounds with heterocyclic rings. Also, the work included two steps to create seven-membered heterocyclic rings. Step one involves forming a Schiff base molecule (S). Second, by combining the (maleic) and (phthalic) anhydrides with the (Schiff) base compound (S), the oxazepine derivatives (Z1, Z2) can be made. FT-IR, H1NMR, and 13CNMR spectroscopies were used to study all the substances [33-36]. All the produced compounds were further investigated for their physical characteristics and antibacterial activity, with promising results. Here, we will present all analytical chemical results for all compounds with features in detail as follows:

Compound A: 2-hydroxy-3-(thiazol-2-yldiazenyl)benzaldehyde.

FT-IR (KBr) (cm^{-1}): 3450(O-H related to hydroxyl), 3040 of aromatic (C-H), 1670(CHO)carbonyl ,1470(N=N) azo group.

1H-NMR (DMSO): δ 12.3 (s., OH, 1H) belong to hydroxy, δ 7.0-7.9 (m., phenyl cycle).

13CNMR(DMSO): 177.986 (C of C=O)carbonyl group, 153.514 (C-OH) of hydroxy, (111.646-133.423) (C; phenyl).

Compound H1: (2E)-1-(4-chlorophenyl)-3-(2-hydroxy-3-(thiazol-2-yldiazenyl)phenyl)prop-2-en-1-one.

FT-IR (KBr)(cm^{-1}): 3240 (O-H hydroxyl), 3045 belong to aromatic(C-H), 1660(C=O)carbonyl ,1475(N=N) azo,

H1-NMR (DMSO): δ 11.7 (s- OH-1H) belong to hydroxyl, δ7.3-7.9(m, phenyl group, 13CNMR(DMSO): 175.986 (C ; C=O)carbonyl,155.515(C ; C-OH) related to hydroxyl, 162.514 (C ; C=C) ethylene, 111.646 - 133.424(C ; phenyl ring).

Compound H2: (2E)-1-(4-bromophenyl)-3-(2-hydroxy-3-(thiazol-2-yldiazenyl)phenyl)

prop-2-en-1-one

FT-IR (KBr) (cm^{-1}): 3250 (O-H) hydroxyl,3070(CH)aromatic,1680(C=O)carbonyl ,1478(N=N) azo,

H1-NMR (DMSO): δ 11.3 (s- OH- 1H) related of hydroxyl, δ7.1-7.9 (m, phenyl group), 13CNMR (DMSO): 170.986 (C; C=O) of carbonyl, 154.514 (C; C-OH) of hydroxy, 161.515 (C; C=C) ethylene, 118.647-133.425 (C of phenyl group).

Compound H3: (2E)-3-(2-hydroxy-3-(thiazol-2-yldiazenyl)phenyl)-1- (4-hydroxyphenyl)prop-2-en-1-one

FT-IR (KBr) (cm^{-1}): 3240(O-H) of hydroxyl,3045(C-H)of aromatic,1660(C=O)carbonyl ,1475(N=N) azo,

1H-NMR (DMSO): δ 11.7 (s, OH,1H) of hydroxyl group, δ7.3-7.9(m, phenyl group), 13CNMR (DMSO): 170.986 (C of C=O) carbonyl, 153.515(C, C-OH) of hydroxyl group, 163.515(C, C=C) of ethylene, 119.647-137.425(C - phenyl).

Compound S: 2-((thiazol-2-amino) methyl) phenol.

FT-IR (KBr) (cm^{-1}): 3240 to (OH) hydroxyl, 3045 of aromatic(C-H),1660 to (C=O)carbonyl,1475(N=N) azo,

1H-NMR (DMSO): δ 11.8 (s, OH,1H)hydroxyl group, δ8.5 (s, C=N,1H)hydroxyl group δ7.3-7.9(m, phenyl group,13CNMR (DMSO): 170.986 (C of C=O)carbonyl group, 153.515(C, C-OH) of hydroxyl, 163.515(C, C=C) of ethylene,

119.647-137.425 (C -phenyl).

Compound Z1: 2-(2-hydroxyphenyl)-3-(thiazol-2-yl)-2,3-dihydro-1, 3-oxazepine-4,7-dione.

FT-IR(KBr) (cm^{-1}): ν3412 (OH), ν3070-3005 aromatic(C-H), ν2877 (C-H)aliphatic, ν1739 (O-C=O)lactone, ν1699 of lactam(N-C=O); ν1680 of (N-C=O) ,ν1620-1583 of (C=C) .

H1-NMR(DMSO) : δ 11.4 (S- OH-1H) of hydroxyl group , δ 8.9(S ;N-C-H) of oxazepine; δ 6.1 -7.8 (m; of phenyl) , δ1.8 (d; 2H; CH_2).

13C-NMR (DMSO): δ 174.989 (C; C=O) of lactone; δ 172432(C; C=O) of lactam;

δ170.989(C; C=O) belong to amide, 159.732 (C; N-CH) of oxazepine, δ 157.679(C; C-OH) of hydroxy, (106.176-142.468) (C-phenyl); δ27(C- CH_2).

Compound Z2: 3-(2-hydroxyphenyl)-4-(thiazol-2-yl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione.

FT-IR(KBr) (cm^{-1}): 3421(OH), ν3043(C-H) aromatic, ν1720(O-C=O) Lactone; ν1674(N-C=O) Lactam, ν1620-1577 of (C=C).

H1- NMR (DMSO): δ 11.3 (s, OH; 1H) of hydroxy, δ 8.3(s; N-C-H) of oxazepane, δ (6.9 -7.6) (m; phenyl), δ (6.58-6.51) (d; 2H; CH=CH), δ 1.8 (d; 2H, CH_2).

13C- NMR (CNMR): δ 177.111 of lacton (C; C=O), δ 173.644 of lactam (C; C=O), δ 171 (C; of amide C=O), δ 161.977 (C of alkene C=C), 159.676 (C of oxazepine N-CH), δ 154.150 (C; C-OH), δ (112.266-143.594) (C; phenyl),115.898 (C; C-Br).

The investigated compounds' findings agreed with the outcomes in reported studies [37-47].

Table 1. IR findings for the investigated compounds

compounds	Aromatic ν –CH	Aromatic ν C=C	ν C=O	ν OH	Schiff ν C=N	Azo ν N=N	ν Cl	ν Br
A	3040	1580	1670	3450	–	1470	–	–
H1	3045	1600	1660	3240	–	–	–	650
H2	3070	1588	1680	3255	–	–	720	–
H3	3045	1610	1660	3240	–	–	–	–
S	3055	1630	1680	3242	1555	–	–	–
Z1	3043	1583	1699	3412	–	–	–	–
Z2	3070	1620	1720	3421	–	–	–	–

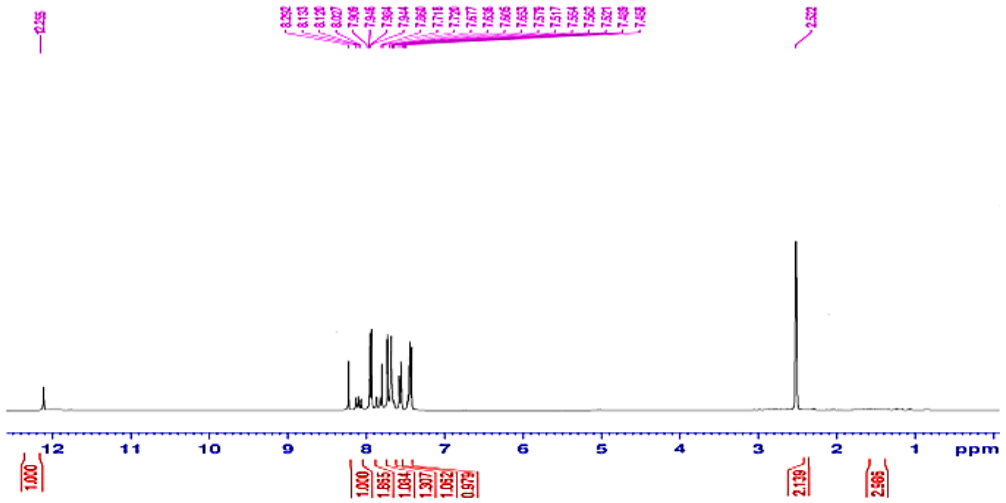


Figure 5.[1] HNMR of the comp.(A)

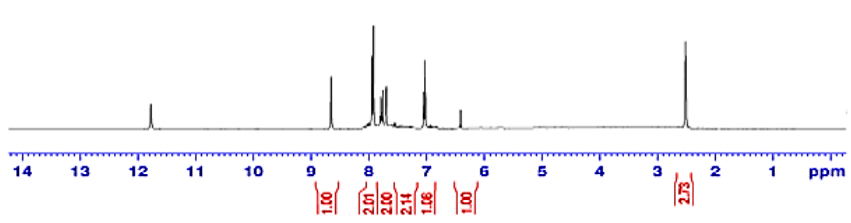


Figure 6.[1] HNMR of the comp.(H1)

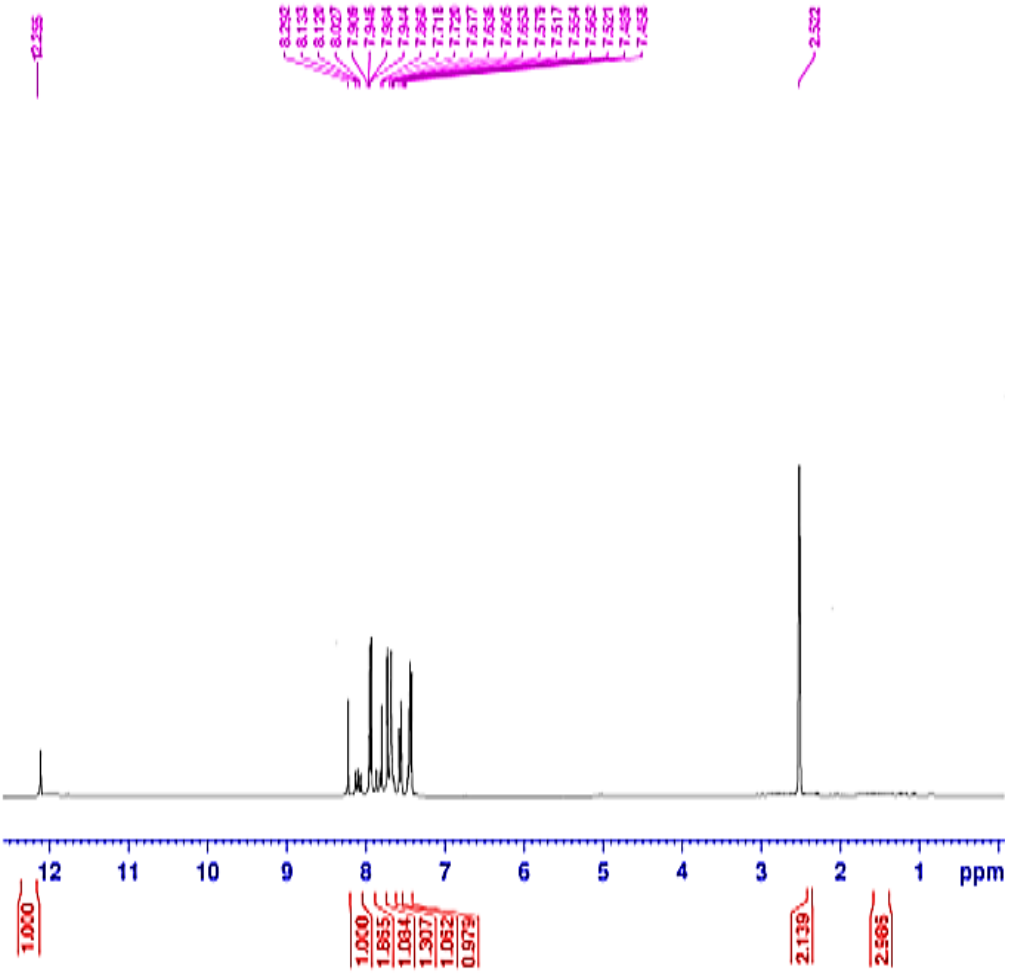


Figure 7.[1] HNMR of the comp.(H2)

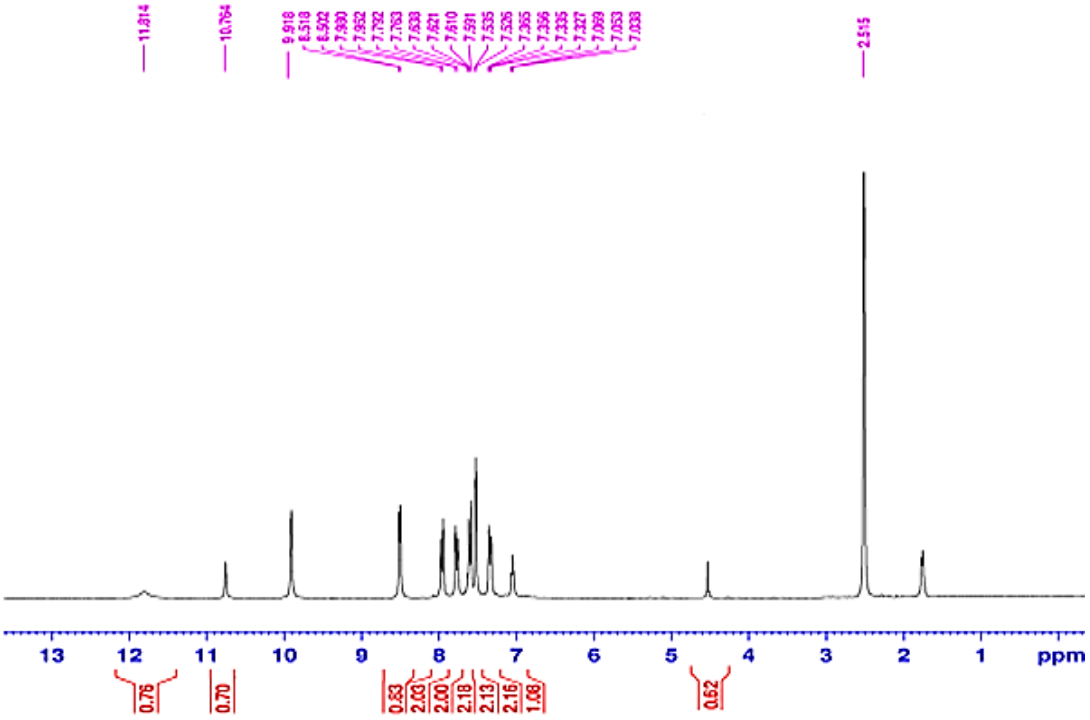


Figure 8.[1] HNMR of the comp.(H3)

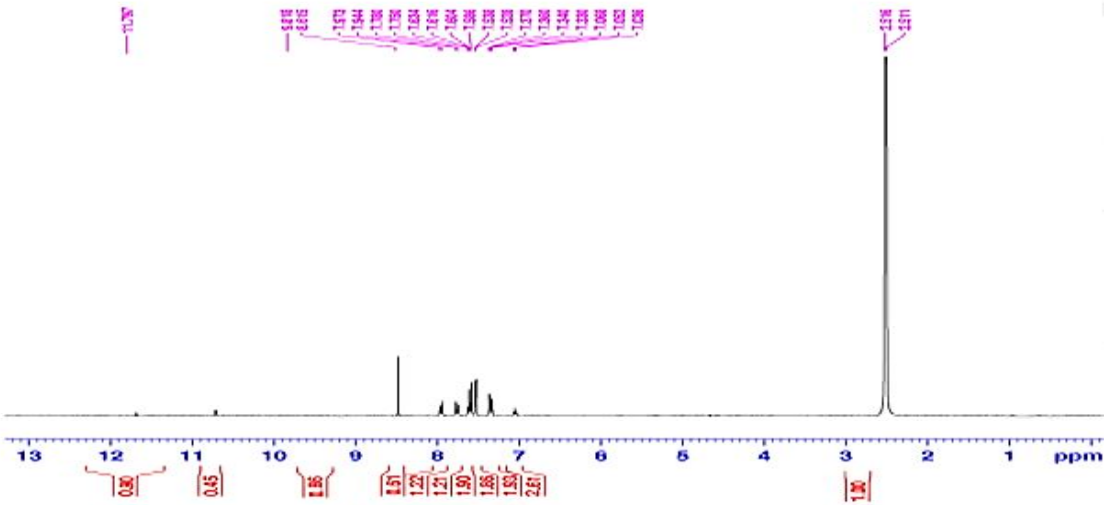


Figure 9. [1] HNMR of the comp.(S)

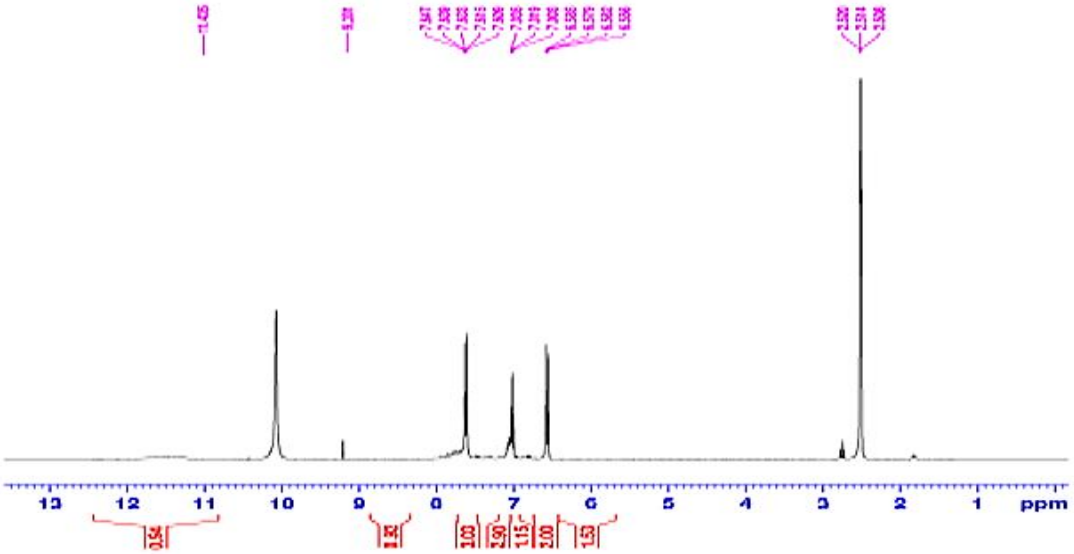


Figure 10.[1] HNMR of the comp.(Z1)

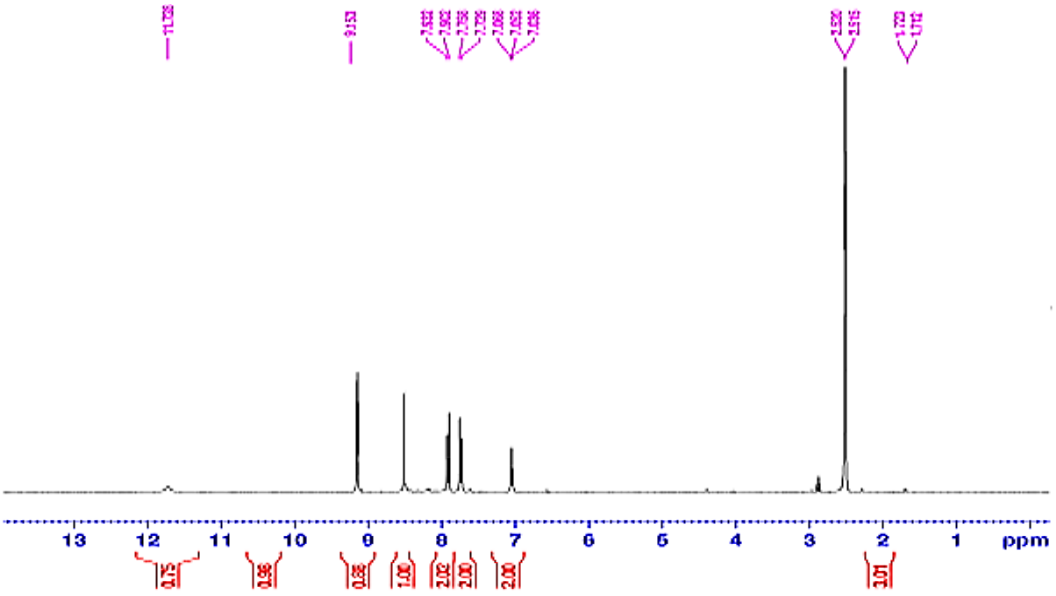


Figure 11. [1] HNMR of the comp.(Z2)

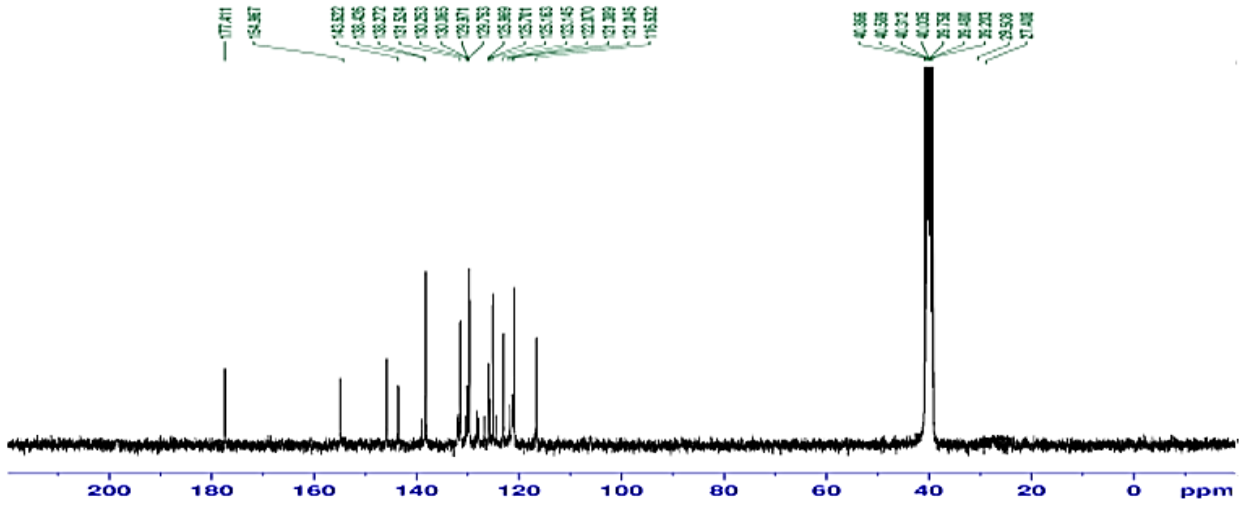


Figure 12. [13] C-NMR of the comp. (A)

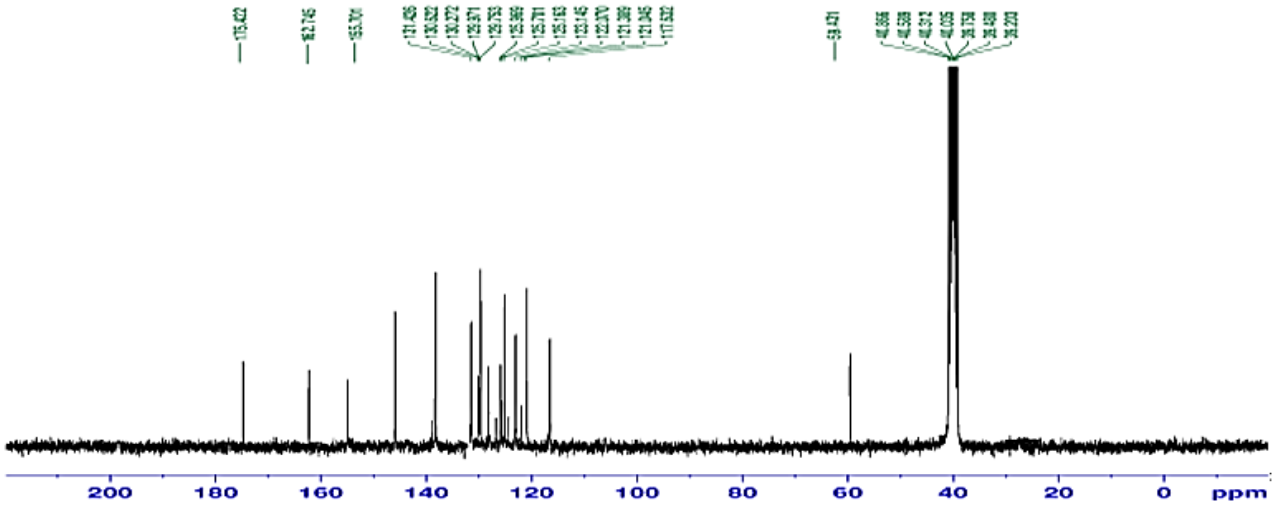


Figure 13. [13] CNMR of the comp.(H1)

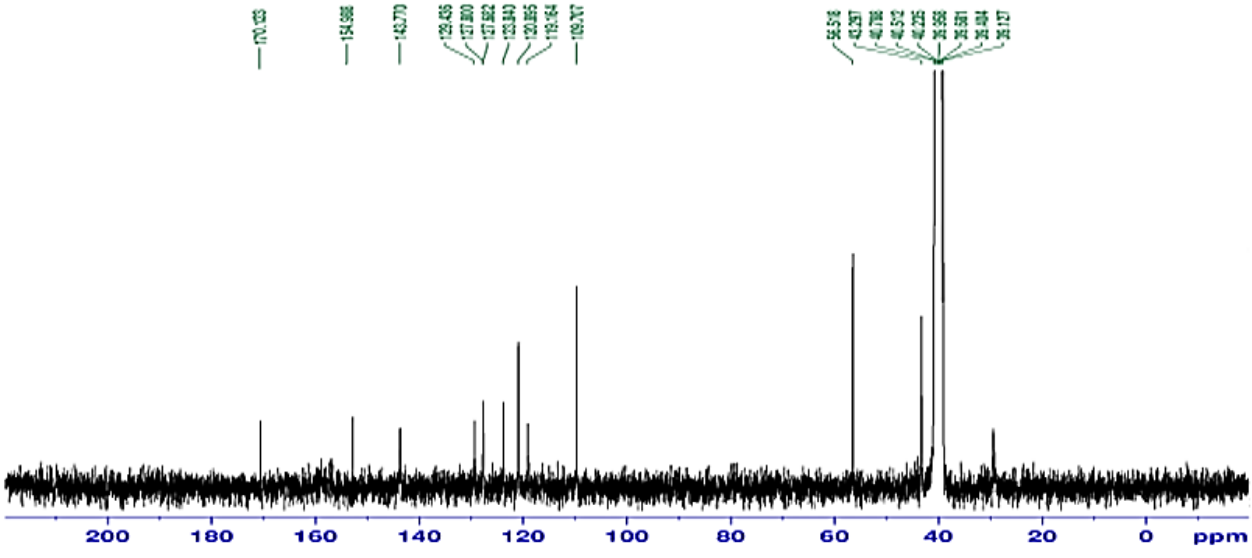


Figure 14.[13] CNMR of the comp.(H2)

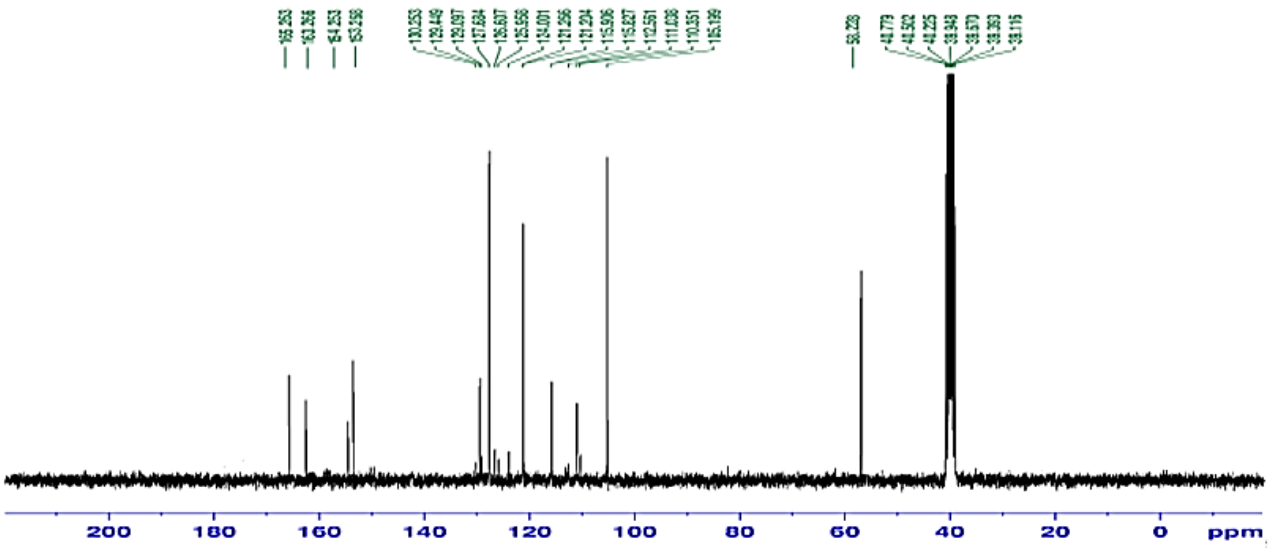


Figure 15. [13]CNMR of the comp.(H3)

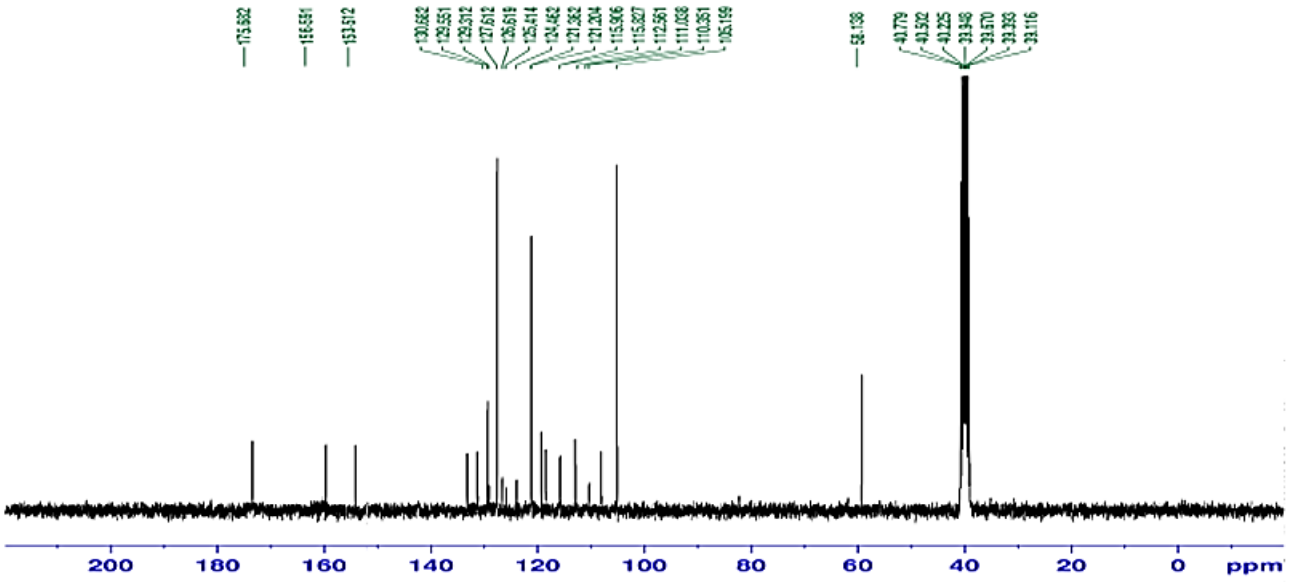


Figure 16. [13] CNMR of the comp.(S)

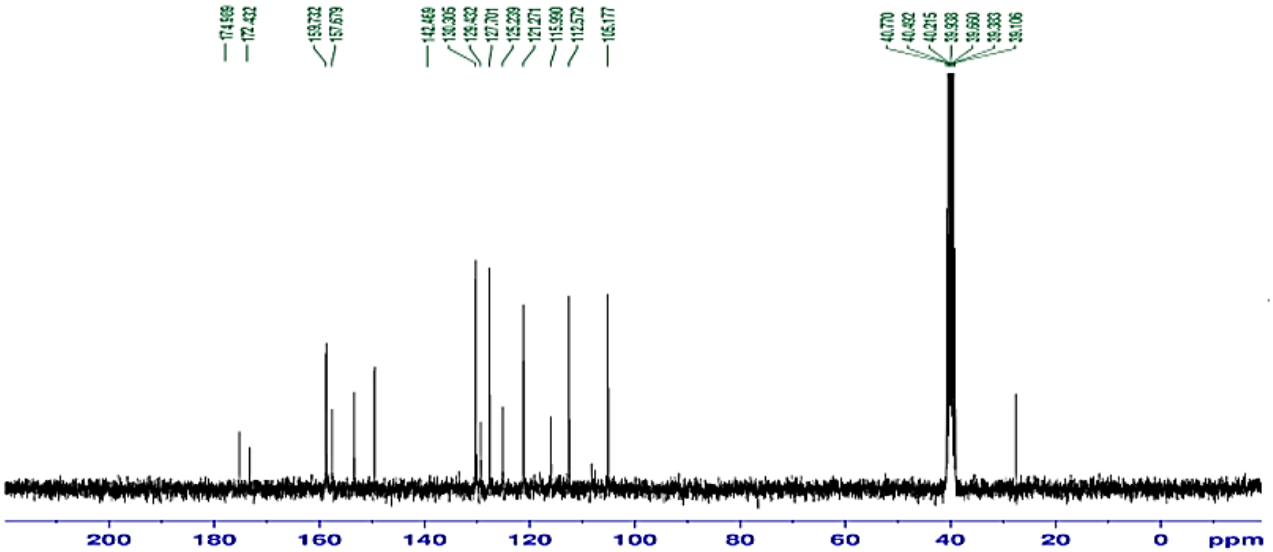


Figure 17. [13] CNMR of the comp.(Z1)

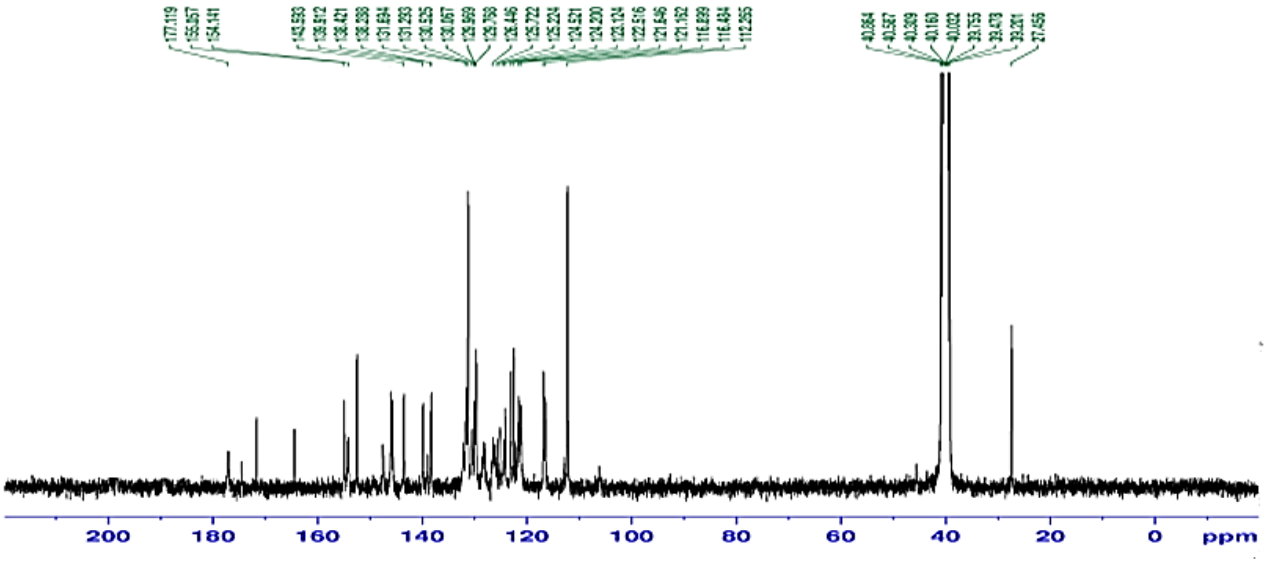


Figure 18.[13] CNMR of the comp.(Z2)

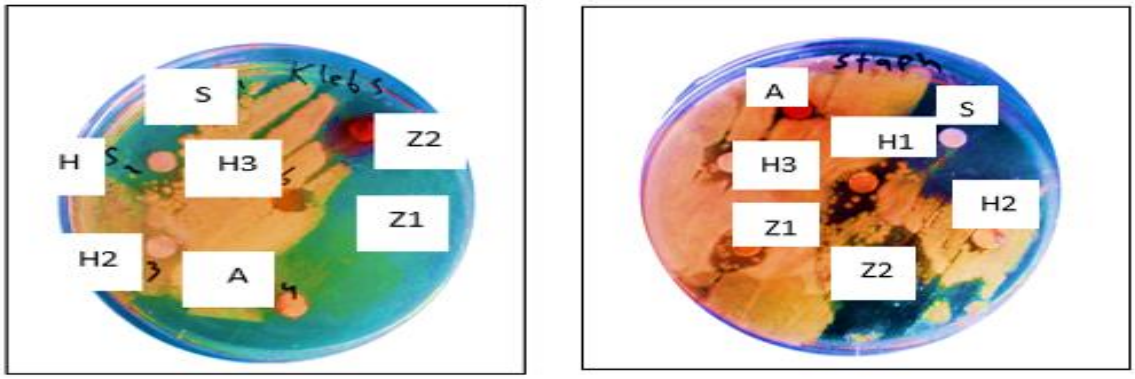


Figure 19. The biological activity study of the prepared compounds

Table 2. Antibacterial activity of synthesized compounds

Bacteria / Comp.	inhibition zone (mm) 5mg 10mg 20mg (mg\mol)			
	klebsiella pneumonia	*Staphylococcus*	*Enterococcus faecalis*	*pseudomonas aeruginosa*
A	**-,5,8**	**-, -,10**	**-,-,5**	**-,-,6**
H1	**-,-,5**	**-, -, 8**	**-,-,5**	**-,-,8**
H2	**-**	**-, - ,5**	**-,-,8**	**-,-,8**
H3	**-, -, 8**	**-, 5, 8**	**-,-,-**	**-,-,6**
S	**-,-, 6**	**-,-, 10**	**8, 10, 20**	**-, -, 10**
Z1	**-**	**-,-, 10**	**-,8, 10**	**-,-,7**
Z2	**-**	**-**	**-, 8, 10**	**12, 18, 20**

Table 3. The physical characteristics of prepared compounds

Comp.	MF	M.WT gm.\mol	MP	R_F	Colour	%yield	The Solvent
A	C10H7N3O2S	233.25	90-93	0.8	yellow	87	Ethanol
H_1	C19H16ClN3O2S	369.82	95-97	0.6	yellow	77	Ethanol
H_2	C18H13N3O3S	414.28	186-189	0.75	Red	85	Ethanol
H_3	C19H16ClN3O2S	351.38	221-223	0.93	yellow	76	Ethanol
S_4	C10H8N2OS	204.25	251-252	0.91	orange	76	Ethanol

Comp.	MF	M.WT gm.\mol	MP	R_F	Colour	%yield	The Solvent
Z_1	C18H12N3O4S	302.31	317-319	0.82	Yellow	81	Toluene
Z_2	C14H10N3O4S	352.36	304-306	0.75	yellow	83	Toluene

4. Conclusion

The consequences for spectrum studies indicated the compositions of the compounds prepared in this research by observing the disappearance of several bands and the appearance of new other bands represented by cyclic compounds having oxygen and nitrogen. The biological study of antibacterial also gave good data on the effectiveness of the synthesized compounds against the used bacteria strains.

Declaration of competing interest

The authors state that they have no conflicts of interest related to the contents of this work, either financial or otherwise.

Funding information

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