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Synthesis of Some new Formazan Derivatives Derived from the Coumarin and Study There Biological Activity

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Abstract: ***This study includes preparing a number of compounds from coumarin, which is like a nucleus for preparing many heterocyclic compounds such as Formazan. As in the following steps. preparing of 7-hydroxy-4-methyl coumarin (G1) of the resorcinol reaction with ethyl aceto ascetate with drops of sulfonic acid, preparing of ethyl 2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy) acetate (G2) of a compound reaction (G1) with ethyl chloro acetate with potassium carbonate, preparing of 2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy) aceto hydrazide (G3) a compound reaction (G2) with aqueous hydrazine, preparing of (E)-N-(sub.benzylidene)-2-(4-methyl-2-oxo-2H-chromen-7-yl)oxy) acetohydrazide (G4-G10) of a compound reaction (G3) with aldehyde substitutes, preparing of (E,Z)-#-(4-sub.phenyl)-1-(sub.phenyl)-5-(2-((4-methyl-2-oxo-2H-chromen-7yl)0xy) acetyl) farmazan (G11-G24) of a compound reaction (G4-G10) (some Schiff base prepared) with sodium nitrite and -3-amino aceto phenol or -4-amino aceto phenol, The effect of some prepared compounds have been studied on the growth of two types bacterial isolates which are known of their resistance to anti-biotic (Gr-ve) which is Psedudomonos aeruginosa) and (GR+ve) which are the Staphylococcus aureus. The anti-biotic Amoxilicine and Ampicillin have been used as samples to control some prepared compounds, and some of the compounds showed good inhabitation activity against the used bacteria.***

Keywords: coumarin, Formazan, Schiff bases, Amoxilicine, Ampicillin

1. Introduction

The coumarines are among the heterogeneous hexagonal ring compounds that contain oxygen as an atom in the ring. This is a molecule consisting of a ring of benzene with a ring of Byron to be a benzobiron class, which can be distinguished by two types of carbonate [(1)], and previous studies have shown that the quaymarin in the medical field - the control of bacteria, and antagonism in the compound (4), as shown [(2)], and also proved the world (Yasameen Al-Majedy) and his group [(3)] the effectiveness against the virus and immunodeficiency Shura, and in Formazan of colored compounds and contains in the composition of the group is quick (-N - CN - NH -), which caused the word (5) Analytical chemistry [(5)], as well as its industrial importance - the bright color of the eye [(6)] , Formazan has been prepared in a number of ways, including hydroazone and dezionium salts. The process of zooming, coupling, and suitable conditions (0 - 0) 5) and pH (6-8) and using an appropriate solvent such as methane [(16)], the researcher (Gurusamy) and the group [(7)] prepared the fermazan from the interaction of diazium salt with aneline in the presence of hydrochloric acid, writer Haider A. Mahdi and his group [(8)], with the reduction of the Faramazan from a contemporary interaction in the Arabic language, I answered the doctorate in The field of medicine and pharmacology where the researcher Dominic and his group [(9)] (1988) pointed to the inhibitory effect of the Formazan plant on cancer cells, and many previous studies have confirmed the importance of ghee to Formazan as antimicrobial, fungal and inflammatory drugs[(10)].

2. Experimental

2.1 Preparation of 7-hydroxy 4- methyl coumarin (G1)[(11)].

A mixture of (0.2 mol,22g) from recosenol with (0.2 mol, 26g) from ethyl aceto acetate then, it was heated at (50) C^0 with stirring until became red complex and then added to (90 ml. H_2SO_4 cone.) In ice bath for 1h., Late for (24 h.) At room temperature, wish with cold water, the obtained product was crystallized from ethanol give compound **G1**, Color White, M.P (189-190) C^oyield 92%.

2.2 Preparation of ethyle 2-((4-methyl -2-oxo- 2H-chromen -7-yl)oxy) acetat (G2)[(11)]

Dissolve (0.01 mol., 1.76g) from **G1** 30 ml acetone and then added to (0,01mol., 1.38 g) K_2CO3 , ethyl chloroacetate, reflixe (8h.) . filtration hot mixture dry filtrate thin recrystallized from ethanol give compound G2, color yellow, m.p (91-95), yilde 88% .

2.3 Preparation of 2- ((4-methyl-2-oxo- 2H-chromen -7-yl) oxy) acetohydrazide [(12)](G3)

Compound (G2) (0.01 mol., 2.62g) was dissolved in absolute ethanol (25ml) and hydrazine hydrate (0.02mol., 1g) was added to the mixture with stirring. Then reaction mixture was reflex for (6 h.) .The resulting product (G3) was recrystallized from ethanol . color yellow , m.p (191-194), yilde 83%.

2.4 Preparation of Schiff bases derivetaves from2- ((4-methyl-2-oxo- 2H-chromen -7-yl) oxy) acetohydrazide[(11)](G4-G10)

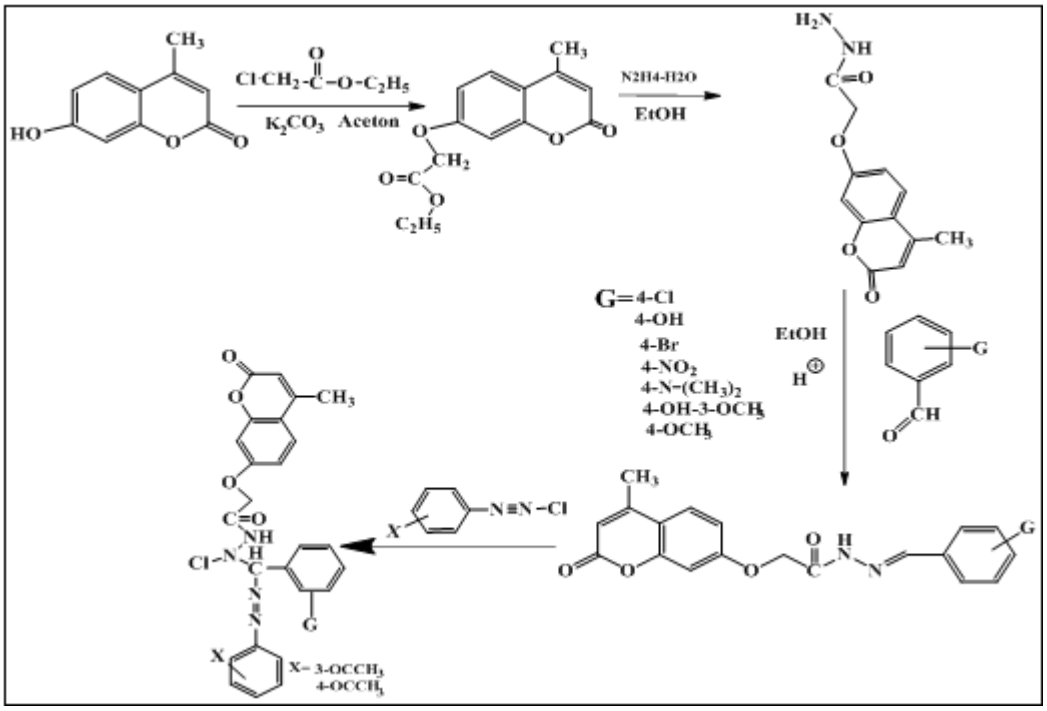
A mixture of compound (G3) (0.01 mol) and different aromatic aldehydes (0.01 mol) in absolute ethanol (25ml) and (2 drops) of glacial acetic acid was refluxed in water bath for about (6 h.). The excess solvent was Concentrated Under reduced pressure .The crude product was dried, recrystallized from ethanol . Physical properties of compounds (G4-G10) are listed in Table (3-1).

2.5 Preparation of (E,Z)-3-(4-sub.phenyl)-1-(sub.phenyl)-5-(2-((4-methyl-2-oxo-2H-chromen-7-oxy) oxy) acetyl) formazan[13](G11-G24).

Dissolve aniline derivetave (0.01mol) in dilute solution (HCl (10ml), NaNO2(2.5G)) at (0-5)C^{o} with stirring until form diazonum salt , added solusion to Schiff bases derivative (0.01mol) dissolve in pyrden dry (5ml) , stirring solusion (2h.) at (0-5)C^{o} . filter prespetate and wish with cold water, recrystallized from ethanol . Physical properties of compounds (G11-G24) are listed in Table (3-2).

3. Results and Discussion

This work includes synthesis of new farmazon derivatives as shown in scheme (3-1).



Scheme 3-1

3.1 7-hydroxy 4- methyl coumarin (G1)

Prepare the compound (G1) from reaction equal mole for each recosenol and ethyl chloroacetate. FT-IR spectral data of compound (G1) showed the appearance of characteristic absorption bands at(2810-2950 cm^{-1}) belong to v (CH3) asym. and sym. , characteristic absorption band at (1693 cm^{-1}) belong to v (C=O), absorption band at (1663 cm^{-1}) belong to v (C=C)alph. , absorption band at (1595cm^{-1}) belong to v (C=C)Arom., and absorption band at (3220 cm^{-1}) belong to v (O-H) . 1HNMR spectrum of compound(G1) showed ((δ=2.40 ppm) 3H,CH_3), ((δ=6.11)1H,CH=C), ((δ=7.59 -6.70ppm)3H-Phenyl) , ((δ=10.57ppm) O-H), this shown in figure (3.1).

3.2 ethyle 2-((4-methyl -2-oxo- 2H- chromen -7-yl)oxy) acetat (G2).

Prepare the compound (G2) from reaction7-hydroxy 4-methyl coumarinwith K_2CO3 and ethylchloro acetate. FT-IR spectral data of compound (G2) showed the appearance of characteristic absorption bands at(2876-2993 cm^{-1}) belong to v (CH3) asym. and sym. , characteristic absorption band at (1674-1708 cm^{-1}) belong to v (C=O), absorption band at (1604 cm^{-1}) belong to v (C=C)alph. , absorption band at (1496cm^{-1}) belong to v (C=C)Arom., and disabsorption band at (3220 cm^{-1}) belong to v (O-H) . 1HNMR spectrum of compound (G2) showed ((δ=2.31-1.62ppm) S,3H,CH_3) , ((δ=6.21)1H,CH=C), ((δ=7.59 -6.70ppm) d,3H-CH_3), ((δ=7.83 -6.39ppm)3H-Phenyl) ((S,δ=5.82ppm) 2H,CH_2CO), ((t,δ=5.15ppm) 1H-CH=C).

3.3 2- ((4-methyl-2-oxo- 2H-chromen -7-yl) oxy) acetohydrazide (G3).

The compound (G3) was prepared from reactionone mole ofethyle 2-((4-methyl -2-oxo- 2H- chromen -7-yl)oxy) acetat with two mole hydrazine hydrate. FT-IR spectral data of compound (G3) showed the appearance of characteristic absorption band at (1680-1716 cm^{-1}) belong to v (C=O), absorption band at (1604 cm^{-1}) belong to v (C=C)alph. , absorption band at (1512cm^{-1}) belong to v (C=C)Arom., absorption band at (3134 cm^{-1}) belong to v (N-H) and absorption band at (3245)cm^{-1}) belong to v (NH_2). 1HNMR spectrum of compound (G3) showed((S,δ=2.35 ppm 3H,CH_3), ((δ=6.11 ppm) 2H,CH_2), ((S,δ=6.70) 1H,CH=C), ((δ=7.59 -6.78ppm) 3H-Phenyl) , ((δ=10.52ppm)1H,NH).

3.4 Schiff bases derivetaves from2- ((4-methyl-2-oxo- 2H-chromen -7-yl) oxy) acetohydrazide(G4-G10)

The titled compounds were synthesized from the reaction between compound (G3) and appropriate aldehydes in absolute ethanol and glacial acetic acid. FT-IR spectral data of compounds (G4-G10) showed the appearance of characteristic absorption bands characteristic absorption band at (1676-1735 cm^{-1}) belong to v (C=O), absorption band at (1512-1571 cm^{-1}) belong to v (C=C)alph. , absorption band at (1493-1514cm^{-1}) belong to v (C=C)Arom., absorption band at (3128-3170 cm^{-1}) belong to v (N-H) and absorption band at (1596-1608)cm^{-1}) belong to v (C=N), this shown in table(3.3). 1HNMR spectrum[15] of compound (G4) showed((S, δ=2.36 ppm) 3H,CH_3),((S,δ=6.12 ppm) 2H,CH_2)) , ((δ=6.50 ppm)1H,CH=C),((δ=10.00 ppm)1H,CH=N)(,(t.δ=7.95 -6.70ppm)7H-Phenyl) ((δ=10.53ppm)1H,NH) this shown in figure (3.2). ^{13}C-NMRspectrum of compound (G4) showed ((18.55ppm)CH_3), ((61.20ppm) CH_2), ((110.72ppm)CH)CH=C) (131.62ppmC) (CH=N) (153.98ppm) ((C)) CH=C (155.31ppm) (O-C=O) ((161.64ppm)) N-C=O (102.65 – 160-75ppm), this showen in figure (3.3).

3.5 (E,Z)-3-(4-sub.phenyl)-1-(sub.phenyl)-5-(2-((4-methyl-2-oxo-2H-chromen-7-oxy)oxy)acetyl)formazan(G11-G24)

The titled compounds were synthesized from the reaction betweenSchiff bases derivetaves and diazonyume salt. FT-IR spectral data of compounds (G11-G24) showed the appearance of characteristic absorption bands[14] at (1677-1732 cm^{-1}) belong to v (C=O), absorption band at (1506-1535 cm^{-1}) belong to v (C=C)alph. , absorption band at (1480-1501cm^{-1}) belong to v (C=C)Arom., absorption band at (3128-3170 cm^{-1}) belong to v (N-H) ,absorption band at (1595-1604)cm^{-1} belong to v (C=N) and absorption band at (1444-1450)cm^{-1} belong to v (N=N), this shown in table(3.4) .^{1}H-NMR spectrum of compound((S,δ=3.41-2.19 ppm)3H,CH_3), ((,δ=5.9 PPM)2H,CH_2)) ((S,δ=6.11 PPM1H,CH=C) ((t,δ=8.13 -6.32ppm) 11H-Phenyl) ((S, δ=10.54ppm)1H,NH). ^{13}C-NMR spectrum of compound)(G23((18.54ppm)CH_3) ((32.46ppm)CH_3) ((CH_3-C=O)) (65.20ppm) (CH_2) (87.30ppm (C)) (N-C-N (102.65ppm) ((CH)) CH=C (148.0.2ppm) ((C)) CH=C ((161.64ppm) N-C=O ((185.12ppm)) C=O(CH_3-C=O)153.96ppm) (O-C=O), this showen in figure (3.5).

Table 3.1: Physical properties of compounds (G4-G10)

Comp. No.	G	Molecular Formula	MP $(C)^0$	Yield%	Color
G4	4-Cl	$C_{20}H_{18}O_4N_2Cl$	171-168	93	Yellow
G5	4-OH	$C_{20}H_{19}O_5N_2$	170-167	87	Josie Light
G6	4-NO_2	$C_{20}H_{18}O_6N_3$	147-145	77	Yellow Light
G7	4-Br	$C_{20}H_{18}O_4N_2Br$	177-175	79	Yellow
G8	4-$N(CH_3)_2$	$C_{22}H_{24}O_4N_3$	160-157	88	Orange
G9	4-OH,3-OCH_3	$C_{21}H_{22}O_6N_2$	171-168	67	White
G10	4-OCH_3	$C_{21}H_{21}O_5N_2$	171-168	91	Yellow Light

Table 3.2: Physical properties of compounds (G11-G24)

Comp. No.	X	G	Molecular Formula	MP $(C)^0$	Yield	Color
G11	OCH_3	3-$OCCH_3$	$C_{28}H_{25}N_4O_6Cl$	196	87	Gray
G12	OH,3-OCH_3	3-$OCCH_3$	$C_{28}H_{26}N_4O_7Cl$	201	92	Gray
G13	$N(CH_3)_2$	3-$OCCH_3$	$C_{29}H_{28}N_5O_5Cl$	197	65	Josie Light
G14	Br	3-$OCCH_3$	$C_{27}H_{22}N_4O_5BrCl$	195	73	Josie
G15	NO_2	3-$OCCH_3$	$C_{27}H_{22}N_5O_7Cl$	192	61	Brown
G16	OH	3-$OCCH_3$	$C_{27}H_{23}N_4O_6Cl$	189	79	Broun
G17	Cl	3-$OCCH_3$	$C_{27}H_{22}N_4O_5Cl_2$	175	85	Josie
G18	OCH_3	4-$OCCH_3$	$C_{28}H_{25}N_4O_6Cl$	197-195	90	Josie
G19	OH,3-OCH_3	4-$OCCH_3$	$C_{28}H_{26}N_4O_7Cl$	192	57	Josie Light
G20	$N(CH_3)_2$	4-$OCCH_3$	$C_{29}H_{28}N_5O_5Cl$	193-191	73	Rad light
G21	Br	4-$OCCH_3$	$C_{27}H_{22}N_4O_5BrCl$	140	76	Brown
G22	NO_2	4-$OCCH_3$	$C_{27}H_{22}N_5O_7Cl$	154	85	Brown
G23	OH	4-$OCCH_3$	$C_{27}H_{23}N_4O_6Cl$	113	67	Josie
G24	Cl	4-$OCCH_3$	$C_{27}H_{22}N_4O_5Cl_2$	130	70	Brown

Table 3.3: FTIR spectral data (cm-1) of compounds (G4-G10)

Comp. No.	**G**	**FT-IR cm^{-1}**						
			C=C	C=N	C=O	N-H	Ar-H	**Others**
G4	4-Cl	1500	1529	1600	1680-1706	3166	3020	**744 (C-Cl)**
G5	4-OH	1496	1512	1600	1677-1735	3157	3026	**3300 (OH)**
G6	4-NO_2	1500	1529	1600	1677-1706	3170	3014	**1388 (NO_2)**
G7	4-Br	1493	1525	1596	1677-1730	3153	3026	**2985 (CH_3)**
G8	4-$N(CH_3)_2$	1500	1555	1598	1679-1732	3159	3036	**2954 (CH_3)**
G9	4-OH, 3-OCH_3	1514	1566	1608	1677-1720	3130	3030	**3390 (OH)**
G10	4-OCH_3	1512	1564	1606	1676-1716	3128	3026	**2933 (CH_3)**

Table 3.4: FTIR spectral data (cm-1) of compound (G11-G24)

Comp. No.	G	X	FT-IR cm-1							
			(C=C) Arom.	(C=C) alph.	C=N	C=O	N-H	Ar-H	N=N	others
G11	OCH3	3-OCCH3	1495	1510	1595	1677-1720	3153	3006	1450	2940 (CH3)
G12	OH, 3-OCH3	3-OCCH3	1491	1516	1596	1679-1718	3157	3016	1450	3440 (OH)
G13	N(CH3)2	3-OCCH3	1500	1525	1595	1677-1728	3157	3034	1450	2954 (CH3)
G14	Br	3-OCCH3	1499	1506	1598	1677-1703	3159	3045	1448	2956 (CH3)
G15	NO2	3-OCCH3	1492	1514	1596	1674-1733	3176	3056	1448	1390 (NO2)
G16	OH	3-OCCH3	1501	1520	1595	1677-1707	3145	3012	1446	744 (C-Cl)
G17	Cl	3-OCCH3	1483	1519	1595	1677-1713	3153	3066	1446	2940 (CH3)
G18	OCH3	4-OCCH3	1489	1509	1596	1677-1712	3166	3056	1448	2953 (CH3)
G19	OH, 3-OCH3	4-OCCH3	1490	1519	1595	1677-1712	3155	3014	1446	2955 (CH3)
G20	N(CH3)2	4-OCCH3	1483	1522	1596	1677-1709	3164	3068	1448	2966 (CH3)
G21	Br	4-OCCH3	1483	1529	1596	1677-1713	3126	3076	1448	2956 (CH3)
G22	NO2	4-OCCH3	1483	1518	1600	1677-1703	3155	3016	1444	1388 (NO2)
G23	OH	4-OCCH3	1483	1535	1602	1677-1709	3159	3046	1444	3427 (OH)
G24	Cl	4-OCCH3	1485	1535	1604	1677-1714	3161	3058	1446	750 (C-Cl)

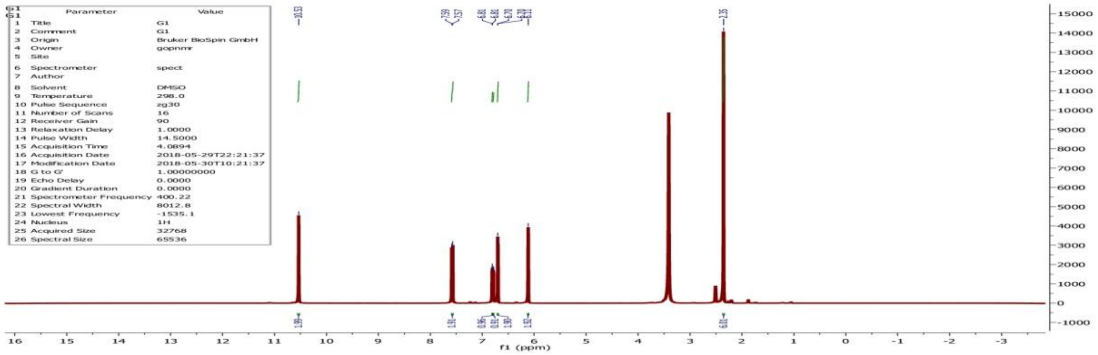


Figure 3.1:1HNMR Spectral of compound (G1)

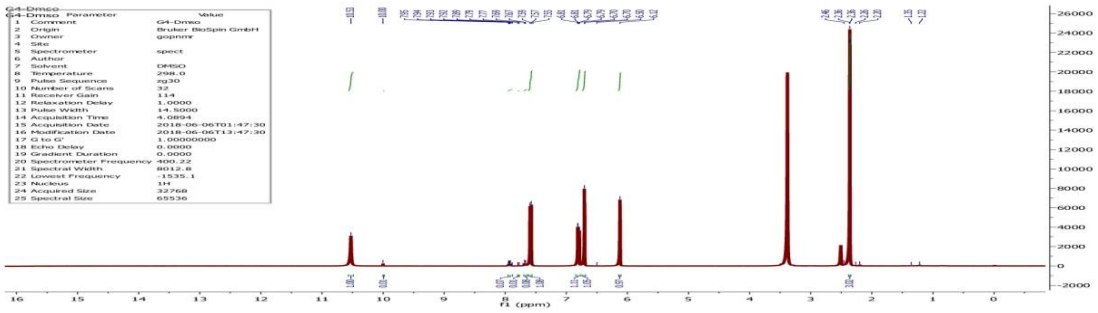


Figure 3.2:1HNMR Spectral of compound (G4)

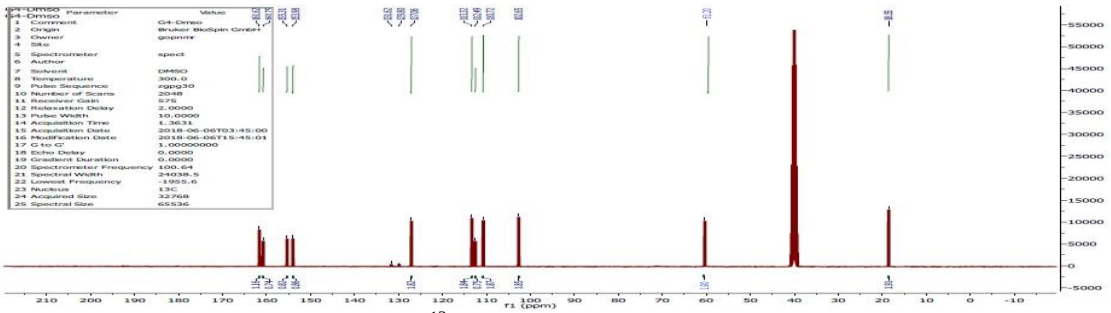


Figure (3.3): ^{13}CNMR Spectral of compound (G4)

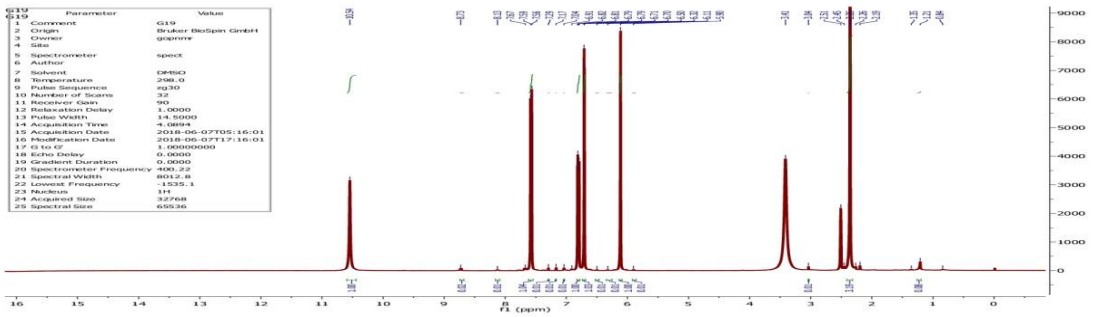


Figure (3.4): ^{13}CNMR Spectral of compound (G20)

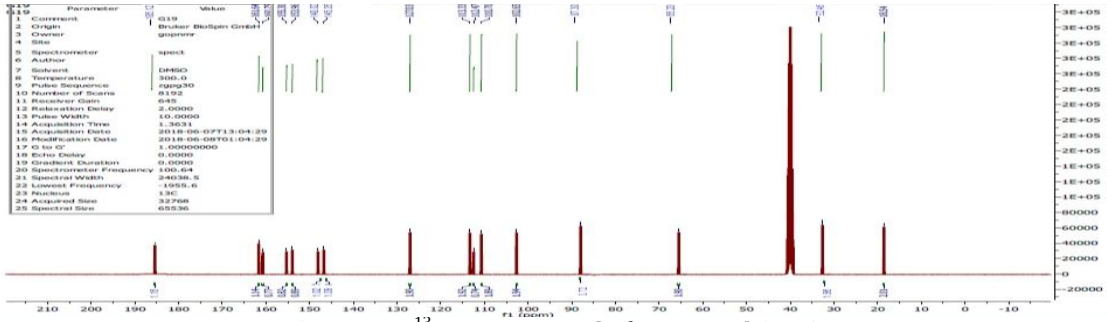


Figure 3.5: ^{13}CNMR Spectral of compound (G23)

4. Biological Activity

The biological activity of some of the prepared compounds was evaluated, with heterogeneous rings having a different biological effect on the Gram-negative and Gram-negative bacteria.The effect of the compounds prepared in this study was evaluated on two types of bacteria, as follows:

1) Pseudomonas aeruginosa.
2) Staphylococcus aureus.

These bacteria have been selected because of their medical importance as they cause many diseases. Moreover, they differ in their resistance to antibiotics. The biological activity of some of the compounds prepared using the drilling method, method of discs and measurement of inhibitory level has been evaluated. The results indicate that the prepared compounds Have the ability to inhibit the growth of bacteria used both positive and negative type different percentages [(16)], this shown in table (4.1).

Table 4.1: Biological activities of some compounds

Comp. No.	Conc. mg/ml	Pseudomonas aeruginosa	Staphylococcus aureus
G_{11}	0.0001	19	13
	0.001	21	19
	0.01	25	24
G13	0.0001	11	11
	0.001	22	17
	0.01	27	21
G_{14}	0.0001	14	20
	0.001	17	22
	0.01	22	24
G_{16}	0.0001	16	13
	0.001	22	24
	0.01	22	24
G_{20}	0.0001	12	15
	0.001	15	20
	0.01	17	22
G_{24}	0.0001	11	13
	0.001	16	19
	0.01	24	25

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