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Synthesis, Characterization and Polymerization of 1,3,4- Oxadiazole Derivatives of Amoxicillin and Evaluation Antibacterial Activities

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A B S T R A C T

A new series of 1,3,4-oxadiazoles, have been synthesized from amoxicillin on treatment with various chemicals, the prepared 1,3,4-oxadaizoles derivatives(9-13) reacted with acryloyl chloride to prepared acryl monomers (14-18) that polymerized to acryl polymers of amoxicillin derivatives (19-23). The structures of compounds (2-23) have been elucidated by FT-IR and ^{1}HNMR, furthermore some compounds (9-13) and (19-23) were screened for in vitro antibacterial activity against gram positive and gram negative bacteria. The compounds show inhibitory action against test organism.

Introduction

Oxadiazole is five member heterocyclic compound containing an oxygen atom and two nitrogen atoms, oxadiazole have four isomers, 1,3,4-oxadiazole (1),1,2,4-oxadiazole (2), 1,2,5-oxadiazole (3) and 1,2,3-oxadiazole (4), figure-1 (1).

Heterocyclic compounds containing 1,3,4-oxadiazole are associated with diverse pharmacological activities such as antimicrobial (2), anti-intiflammatory (3), analgesic (4), anticancer (5), anticonvulsant (6). The rapid development of resistance to existing antimicrobial drugs generates a serious challenge to the scientific community.

The synthesis of new 1,3,4-oxadiazole derivatives and investigation of their biological behavior in last years has increase (7). In addition 1,3,4-oxadiazole have played a crucial part.in the development of theory in heterocyclic chemistry and also used extensively in organic chemistry (8-10).

Antimicrobial polymers class of insecticides are becoming increasingly important as alternative to the existing insecticides and in some cases even to the antibiotics. Mechanism action of large number of different polymers structurally often do not fully understand. However, it is known that some of them low potential of building

microbial resistant strains (11).

Acrylate homo and copolymers are used in different applications such as films, coating, fibers, adhesives, filaments, printing inks, lacquers and binders (12-14). Homo and copolymers are a class of reactive polymers that used extensive fields (15).

Experimental Section

Materials

All chemicals used were of analytical reagent grade and they were available from Aldrich and Fluka Companies and amoxicillin trihydrate standard material was provided from state company for drug industries and medical appliance (SDI) Samaraa – Iraq.

Instruments

Melting points were determined in an open capillary tube and are uncorrected.

Infrared spectra were recorded in KBr on Shimadzu spectrophotometer.

The ^{1}HNMR were measured in DMSO solutions on a Bruker-400 MHz spectrometer using TMS as internal reference (chemical shift in ppm).

All reactions was monitored by thin layer chromatography (TLC) and spots were visualized using iodine chamber.

The antibacterial activity was determined by Agar-well diffusion method.

Synthesis Methods of Prepared Compounds

Synthesis of methyl-6-(2-amino-2-(4-hydroxyphenyl) acetamido)-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0) heptane-3-carboxylate 2 (16).

In 250mL round bottom flask was place a mixture of amoxicillin**1** (0.05mole) and an excess of absolute methanol (150mL) with (5-7) drops of concentrate sulfuric acid. The mixture was refluxed for (3-4)hrs. The solution was cooled and poured into crushed ice. Precipitate obtained filtered, dried and recrystallized from ethanol.

Synthesis of 2-amino-N-((2-acidhydrazide)-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)-2-(4-hydroxy phenyl)acetamide 3 (17).

In 100mL round bottom flask was place a mixture of (0.05mole) ester **2**, (0.05mole) hydrazine hydrate and (50mL) ethanol refluxed for (5-8)hrs. The resultant mixture was concentrated, cooled and poured into crushed ice. The solid mass thus separated out was dried and recrystallized from ethanol.

Synthesis of 2-substituted-N-((2,2-dimethyl-3-(benzyl ideneacidhydrazino)-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)acet amide acid hydrazones (4-8) (18).

In 100mL round bottom flask was place a solution of acid hydrazide **3** (0.01mole) in methanol (50mL) with different aliphatic and aromatic aldehyde (0.02mole) and (4-5) drops of glacial acetic acid as a catalyst. The mixture was refluxed for (3-6)hrs., the resultant allowed to cool and poured into cold water. Solid was collected after filtration and recrystallized from ethanol to give the pure product.

Synthesis of 2-substuted-N-2,2-dimethyl-5-oxo-3-(5-phenyl)-1,3,4-oxadiazol-2 -yl)}-1-thia-4-azabicyclo (3.2.0)heptan-6-yl)acetamides(9-13) (19).

To compounds (4-8) (0.01mole) were added glacial acetic acid (40mL) and lead dioxide (0.01mole) with stirring to the homogenous

solution. The mixture was stirred at 25ºC for 1hr. poured in to ice water (100ml) and left to stand for 24hrs., filtered and recrystallized from ethanol.

Synthesis of acryl monomers of 2-substuted-N-2,2-dimethyl-5-oxo-3-(5-phenyl)-1,3,4-oxadiazol-2 -yl)}-1-thia-4-azabicyclo (3.2.0)heptan-6-yl)acetamides (14-18) (20).

In 50mL round bottom flask dissolve (0.002mole) of hydrazones**(9-13)** in THF (5mL) with (0.002mole) of Et_3N and (0.002mole) and acryloyl chloride in THF (5mL) was added drop wise with stirring at 0ºC for (4-6)hrs. The Et_3N-HCl salt was precipitated and filtered. The filterate was poured with stirring into (100mL) water to precipitate the product, filtered and recrystallization from ethanol.

Synthesis of acryl polymers of 2-substuted-N-2,2-dimethyl-5-oxo-3-(5-phenyl)- 1,3,4-oxadiazol-2-yl)-1-thia-4-azabicyclo (3.2.0) heptan-6-yl) acetamides (19-23) (21).

In a screw-capped polymerization bottle dissolve (0.001mole) of monomers (14-18) in (5mL) THF, DMF or DMSO. An amount equal to 0.02% of the monomers wt. of AIBN added. bottle was flushed with nitrogen gas about few min. and firmly stoppered. The maintained at (70-80)ºC in constant temperature water bath for (1-2)hrs. Then the solution was poured into about 50mL of water or methanol. The precipitate was collected by filterate, washed with methanol several time and dried

Results and Discussion

In the current study a novel series of amoxicillin based on 1,3,4- oxadiazoles were synthesized using compound 1 (amoxicillin) as starting material for synthesis. the synthesis of compounds (2-23) were performed according to the outline given in scheme-1.

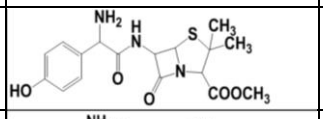
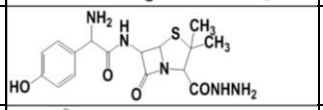
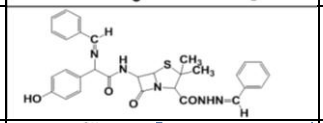
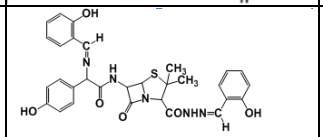
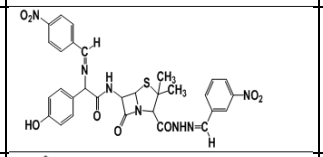
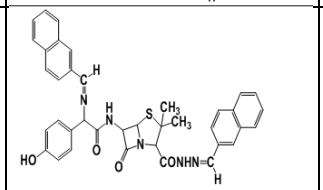
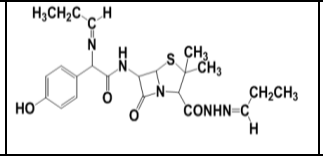
Compounds (9-13) were prepared by treatment compounds(4-8) with lead dioxide in glacial acetic acid affords intramolecular cyclization to give 1,3,4-oxadiazoled,then reacted with acryloly chloride to give drug containing acryl monomers (14-18). The polymerization of monomers were carried out in DMF, using AIBN as initiator. physical properties for compounds(2-23) are listed in table -1

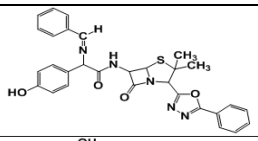
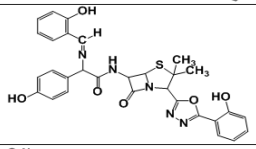
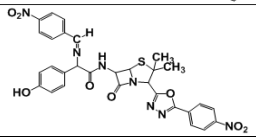
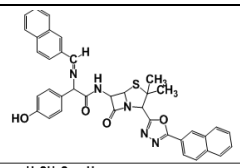
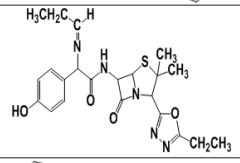
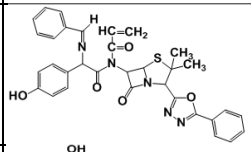
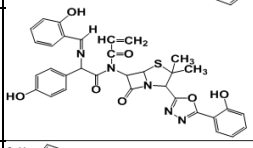
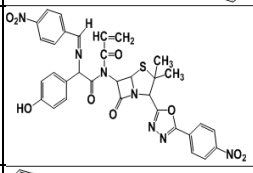
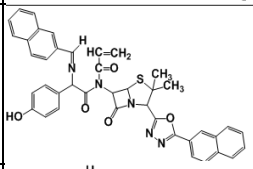
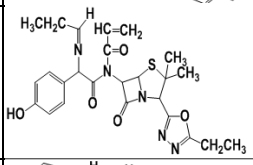
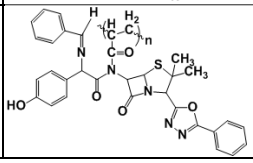
The structures of all compounds were confirmed by FT-IR and ^{1}HNMR spectroscopy that showed absorption bands at (3221-3283), (1609-1626), (1742-1758) and (1659-1686) cm^{-1} regions, confirming the presence of ν(N-H), ν(CH=N), ν(C=O) azetidinone and ν(C=O) amide respectively The FT-IR spectrum of compound 2 characteristic absorption bands at (3526,3462) and 1740 cm^{-1} for ν(NH_2) and ν(C=O) ester respectively, the absorption bands of ν(C=O) and ν(NH_2) disappearance in compound 3 and appearance absorption bands at (1607-1622)cm^{-1} for ν(CH=N) of compounds (4-8). FT-IR spectra of the compounds (9-13) showed absorption bands at (1224-1242)cm^{-1} confirming the presence ν (C-O-C), while the compounds (14-18) appearance absorption bands at (1695-1702) cm^{-1} for ν(C=O) imide and at (1604-1614) cm^{-1} for ν(C=C) olefinic that disappearance in compounds (19-23) due to polymerized, all details FT-IR spectral data for compounds are listed in table -2.

The chemical shifts in the ^{1}HNMR spectra of the respective derivatives verified their structures. The spectra of compounds (2-23) showed the characteristic protons of benzene, 2-CH_3, CH-CH-S, CH-CH-S and -OH phenolic at around δ (6.51-7.95), (1.35-1.55), (4.83-4.89)., (5.16-5.34) and (5.32-

5.39) ppm respectively. The ^{1}HNMR spectra of compound 2 exhibited characteristic 3H protons of $COOCH_3$ at δ 3.68 ppm and the characteristic 1H proton of δ –CHCOOCH$_3$ at δ 4.68 ppm. ^{1}HNMR spectra of compound 3 exhibited characteristic 3H protons of NH-NH_2, 1H of NH-NH_2,and CH-NH_2 at δ 2.01, at δ 8.02 ppm and δ 4.81 ppm respectively. 1HNMR spectra of compounds (4,5) exhibited characteristic 1H proton of CH-N=CH and 1H proton of NH-N=CH at around δ (8.13-8.26) and at around δ (8.48-8.73) ppm respectively. 1HNMR spectra of compounds (9,10) exhibited characteristic 1H proton of CH-N=CH and 1H proton of NH-amide around δ 5.34 and at δ (8.03-8.09) pp respectively. 1HNMR spectrum of compound 14 exhibited characteristic 1H proton of CH-Oxa,2H protons of CH_2=CH and 1H proton CH_2=CH at δ 5.72 ppm, at δ 4.68 ppm and at δ 6.268 ppm ,while 1HNMR spectrum of compound 19 exhibited characteristic 2H protons of –(CH_2-CH-)$_n$- and 1H proton of –(CH_2-CH-)$_n$- at δ 1.657 ppm and at δ 2.615 ppm respectively. All details ^{1}HNMR spectral data are listed in table-3, figures (2-9).

Table.1 Physical Properties of Synthesized Compounds(2-23)

Comp. Code	Physical properties			
	Compound structure	Compound name	Dec.p ^oC	Yield %
2		Methyl-6-(2-amino-2-(4-hydroxyphenyl)acetamido)-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0)heptane-3-carboxylate	196	87
3		2-amino-N-((2-acidhydrazide)-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0)heptan-6-yl)-2-(4-hydroxy phenyl)acetamide	184	89
4		2-((benzylidene amino)-(4-hydroxy phenyl))-N-((2,2-dimethyl-3-(benzyl ideneacidhydrazino)-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)acet amide	170	75
5		2-((2-hydroxy benzylidene amino) (4-hydroxyphenyl)) -N-(2,2-dimethyl-2 –hydroxybenzyl ideneacid)hydrazine-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl) acetamide	172	85
6		N-((2,2-dimethyl-3-(nitrobenzyl ideneacidhydrazino)-5-oxo-1-thia-4-azabicyclo(3.2.0)heptan-6-yl))-2-(4-hydroxyphenyl)-2-((4-nitrobenzyl idene)amino) acetamide	166	71
7		N-((2,2-dimethyl-3-(2-naphthalen-2-ylmethyleneacid hydrazineco)-5-oxo-1-thia-4-aza bicyclo(3.2.0) heptan-6-yl))-2-((4-hydroxyphenyl) -2-(naphthalen-2-ylmethylene)amino)acetamide	176	89
8		N-((2,2-dimethyl-5-oxo-2-(2-propyl ideneacidhydrazino)-1-thia-4-aza bicyclo(3.2.0)heptan-6-yl))-2-((4-hydroxyphenyl)-3-(propylideneamino))acetamide	160	68

9		2-({benzylideneamino)(4-hydroxyphenyl)}-N-2,2-dimethyl-5-oxo-3-(5-phenyl)-1,3,4-oxadiazol-2 -yl)}-1-thia-4-azabicyclo (3.2.0)heptan-6-yl)acetamide	154	86
10		2-((2-hydroxybenzylidene)amino)(4-hydroxyphenyl))-N-(3-(5-(2-hydroxy phenyl)-1,3,4-oxadiazol-2-yl)-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)acetamide	160	75
11		N-(2,2-dimethyl-3-(5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)-2-((4-hydroxyphenyl)(4-nitrobenzylidene)amino)acetamide	158	85
12		N-(2,2-dimethyl-3-(5-(naphthalen-2-yl)-1,3,4-oxadiazol-2-yl)-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)-2-((4-hydroxyphenyl)(2-naphthalen-2-ylmethylene)amino) acetamide	166	76
13		N-3-(5-ethyl-1,3,4-oxadiazol-2-yl)-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0)heptan-6-yl)-2-((4-hydroxyphenyl)(propylideneamino))acetamide	140	73
14		N-((2-{(benzylidene amino)(4-hydroxy phenyl)}acetyl)-N-{2,2-dimethyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-5-oxo -1-thia-4-azabicyclo (3.2.0)heptan-6-yl} acrylamide	162	53
15		N-((2-{(2-hydroxybenzylidene)amino)(4-hydroxyphenyl)} acetyl)-N-{3-(5-(2-hydroxyphenyl-1,3,4-oxadiazol-2-yl)}-{2, 2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0)heptan-6-yl} acrylamide	158	61
16		N-(2,2-dimethyl-3-(5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-5-oxo -1-thia-4-azabicyclo (3.2.0)heptan-6-yl)-N-(2-{(4-hydroxyphenyl) ((4-nitrobenzylidene) amino}acetyl) acrylamide	160	58
17		N-{2,2-dimethyl-3-(5-(naphthalen-2-yl)-1,3,4-oxadiazol-2-yl}-5-oxo-1-thia-4-azabicyclo(3.2.0)heptan-6-yl)-N-(2-{(4-hydroxyphenyl) ((naphthalen-2-ylmethylene)amino}acetyl)acrylamide	166	66
18		N-({3-(5-ethyl-1,3,4-oxadiazol-2-yl}-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo (3.2.0)heptan-6-yl)-N-(2-{(4-hydroxyphenyl) (propylideneamino} acetyl)acrylamide	156	59
19		Poly(N-((2-{(benzylideneamino)(4-hydroxyphenyl) }acetyl)-N-{2,2-dimethyl-3-(5-phenyl-1,3,4-oxa diazol-2-yl)-5-oxo-1-thia-4-azabicyclo (3.2.0)heptan-6-yl} acrylamide)	Oily	70

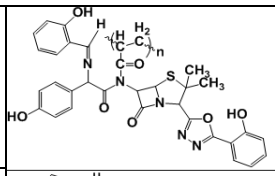
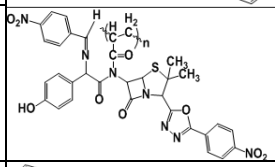
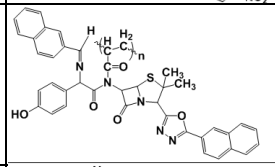
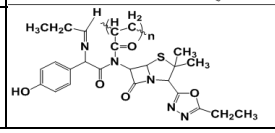
20		Poly(N-((2-{(2-hydroxy benzylidene)amino)(4-hydroxyphenyl) }acetyl)-N-{3-(5-(2-hydroxyphenyl)-1,3,4-oxadiazol-2-yl)}-{2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl} acrylamide)	Oily	65
21		Poly(N-(2,2-dimethyl-3-(5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)-N-(2-{(4-hydroxyphenyl)((4-nitrobenzyl idene)amino}acetyl)acrylamide)	132	71
22		Poly(N-{2,2-dimethyl-3-(5-(naphthalen-2-yl)-1,3,4-oxadiazol-2-yl}-5-oxo-1-thia-4-azabicyclo(3.2.0) heptan-6-yl)-N-(2-{(4-hydroxyphenyl)((naphthalen-2-ylmethylene)amino}acetyl) acrylamide)	Oily	69
23		Poly(N-({3-(5-ethyl-1,3,4-oxadiazol-2-yl}-2,2-dimethyl-5-oxo-1-thia-4-azabicyclo(3.2.0)heptan-6-yl)-N-(2-{(4-hydroxyhenyl) (propylideneamino}acetyl) acrylamide)	Oily	62

Table.2 Ft-Ir Spectral Data of Synthesized Compounds(2-23)

Comp. Code	**Major FT-IR absorption cm^{-1}**								
	ν(NH_2)	**ν(N-H) Amide**	**ν(C-H) Arom.**	**ν(C-H) Aliph.**	**ν(C=C) Arom.**	**ν(C=O) 1.azetidinone 2.ester(imide) 3.amide**	**ν(CH=N) Imine**	**ν(C-O-C)**	**ν(C=C) Olefinic-Vinylic**
2	3526 3462	3169	3042	2970 2936	1584 1518	1.1776 2.1740 3.1688	-	-	-
3	3527 3443	3219	3053	2969 2930	1599 1514	1. 1770 2. - 3.1668	-	-	-
4	-	3233	3032	2967 2930	1585 1514	1.1742 2.- 3.1667	1614	-	-
5	-	3215	3048	2970 2930	1578 1514	1.1744 2. – 3.1665	1622	-	-
6	-	3241	3080	2970 2932	1587 1520	1.1752 2. – 3.1688	1607	-	-
7	-	3221	3055	2969 2928	1586 1514	1.1748 2. – 3.1680	1613	-	-
8	-	3229	3044	2970 2932	1590 1516	1.1758 2. – 3.1659	1613	-	-
9	-	3221	3030	2951 2931	1585 1518	1.1742 2. – 3.1670	1626	1236	-
10	-	3262	3033	2972 2932	1576 1514	1.1744 2. – 3.1659	1616	1242	-

11	-	3283	3077	2967 2930	1588 1520	1.1752 2. – 3.1686	1609	1234	-
12	-	3268	3055	2967 2929	1596 1512	1.1748 2. – 3.1684	1613	1229	-
13	-	3269	3063	2969 2932	1590 1524	1.1758 2. – 3.1686	1613	1224	-
14	-	-	3063	2970 2928	1543 1514	1.1756 2.(1695) 3.1655	1620	1229	1614
15	-	-	3078	2959 2928	1578 1514	1.1765 2.(1702) 3.1653	1617	1231	1604
16	-	-	3073	2963 2930	1598 1520	1.1759 2.(1698) 3.1659	1611	1225	1606
17	-	-	3071	2957 2928	1596 1510	1.1766 2.(1701) 3.1657	1611	1226	1607
18	-	-	3063	2969 2932	1590 1524	1.1748 2.(1697) 3.1659	1612	1227	1605
19	-	-	3063	2965 2922	1541 1514	1.1744 2.(1672)	1605	1231	
20	-	-	3069	2967 2924	1573 1516	1.1745 2.(1655)	1613	1236	
21	-	-	3073	2967 2926	1599 1520	1.1765 2.(1676)	1619	1236	
22	-	-	3057	2965 2924	1596 1512	1.1759 2.(1682)	1609	1226	
23	-	-	3064	2960 2924	1590 1513	1.1764 2.(1643)	1611	1224	

Figure.1

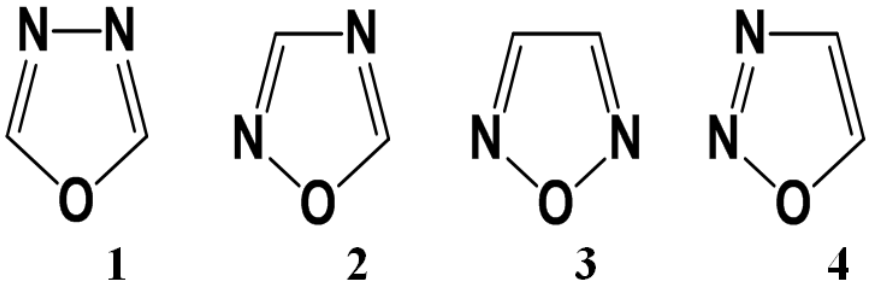


Table.3 1HNMRspectral Data of Selected Synthesized Compounds

Comp. No.	^{1}HNMR Spectral data(δ ppm)
2	6.63-7.37(m,4H,Ar-H); 1.55(s,6H,2CH_3); 3.68(s,3H,-COOCH_3); 4.68(s,1H,-N-CH-$COOCH_3$); 4.75(s,1H,-CH-NH_2); 4.82(d,1H,CH-CH-S)Azet; 5.30(s,2H,-NH_2); 5.34(d,1H,CH-CH-S) Azet.; 5.35(s,1H,-OH); 8.06(s,1H,-NH amide).
3	6.70-7.68(m,4H,Ar-H); 1.55(s,6H,2CH_3); 2.01(s,2H,NH-NH_2); 4.75(s,1H,-CH-CONH-NH_2); 4.83(s,1H,CH-CH-S); 5.13(s,2H,-CH-NH_2); 5.24(d,1H,CH-CH-S)Azet.; 5.39(s,1H,-OH); 8.02(s,1H,-NH-NH_2); 8.05(s,1H,NH-amide)
4	6.51-7.40(m,14H,Ar-H); 1.64(s,6H,2-CH_3); 4.62(s,1H,-CH-C(CH_3)$_2$); 4.86(s,1H,C-CH-S)Azet.; 5.16(d,1H,CH-CH-S)Azet.; 5.36(s,1H,-OH); 5.46(s,1H,-CH-N=CH); 8.00(s,1H,NH-N=CH); 8.05(s,1H,-NH Amide); 8.13(s,1H,CH-N=CH); 8.48(s,1H,NH-N=CH-)
5	6.69-7.53(m,12H,Ar-H); 1.56(s,6H,2CH_3); 4.79(s,1H,-CH-C(CH_3)$_2$); 4.86(s,1H,-CH-CH-S)Azet.; 5.19(d,1H-CH-CH-S)Azet.; 5.32(s,1H,-OH); 5.33(s,1H,-CH-N=CH); 8.01(s,1H,NH-N=CH); 8.06(s,1H,-NH)Amide; 8.27(s,1H,CH-N=CH); 8.73(s,1H,NH-N=CH-)
9	6.88-7.91(m,14H,Ar-H); 1.36(s,6H,2CH_3); 4.85(d,1H,-CH-CH-S)Azet.; 5.11(s,1H,-CH-oxa); 5.17(d,1H,-CH-CH-S)Azet.; 5.33(s,1H,-OH); 5.34(s,1H,-CH-N=CH); 8.09(s,1H,-NH) Amide; 8.17(s,1H,CH-N=CH)
10	6.70-7.53(m,13H,Ar-H); 1.37(s,6H,2CH_3); 4.86(d,1H,-CH-CH-S)Azet.; 5.12(s,1H,-CH-oxa); 5.16(d,1H,-CH-CH-S)Azet.; 5.33(s,1H,-OH); 5.34(s,1H,-CH-N=CH); 8.03(s,1H,-NH)Amide; 8.27(s,1H,CH-N=CH)
14	7.175-7.778(m,14H,Ar-H); 1.354(s,6H,2CH_3); 4.897(d,1H,-CH-CH-S)Azet; 5.146(s,1H,-CH-Oxa); 5.196(d,1H,-CH-CH-S)Azet; 5.386(s,1H,OH phenolic); 5.455(s,1H,CH-N=CH); 5.720(s,2H,-CH_2=CH-); 6.268(s,1H,CH_2=CH-); 8.014(s,1HCH,-N=CH)
19	6.925-7.957(m,14H,Ar-H); 1.392(s,6H,2CH_3); 1.657(d,2H,-(-CH_2-CH-)n-); 2.615(t,1H,-(-CH_2-CH-)n-); 4.847(d,1H,-CH-CH-S)Azet; 5.145(s,1H,-CH-Oxa); 5.202(d,1H,-CH-CH-S)Azet; 5.352(s,1H, OH phenolic); 5.385(s,1H,CH-N=CH); 8.226(s,1HC-H,-N=CH)

Table.4 Antibacterial Activities of Compounds (9-13) and (19-23)

Comp. No.	*Inhibition zone diameter(mm)*			
	Staphylococcus aurous	***Bacillus subtitles'***	***Escherichia coli***	***Pseudomonas Aeruginosa***
9	15	11	9	5
10	14	12	8	-
11	15	11	9	4
12	14	12	8	-
13	16	13	5	6
19	16	13	7	5
20	15	12	6	-
21	16	13	8	5
22	16	14	7	-
23	14	12	6	-
Amoxicillin(A)	14	11	5	-
DMSO	-	-	-	-

Figure.2 1HNMR Spectrum for Compound(2)

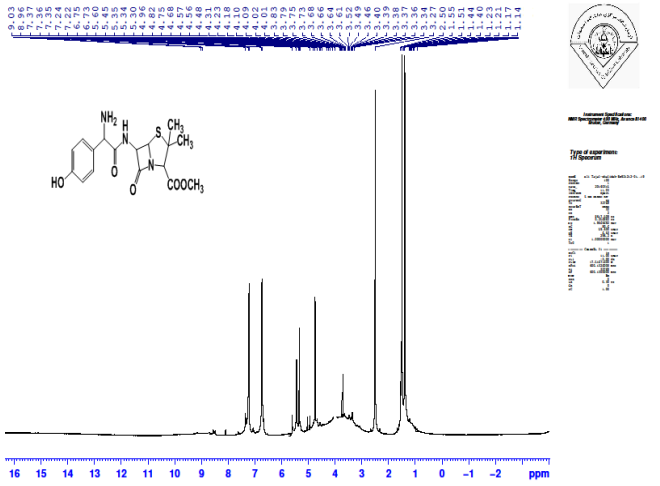


Figure.3 1HNMR Spectrum for Compound(3)

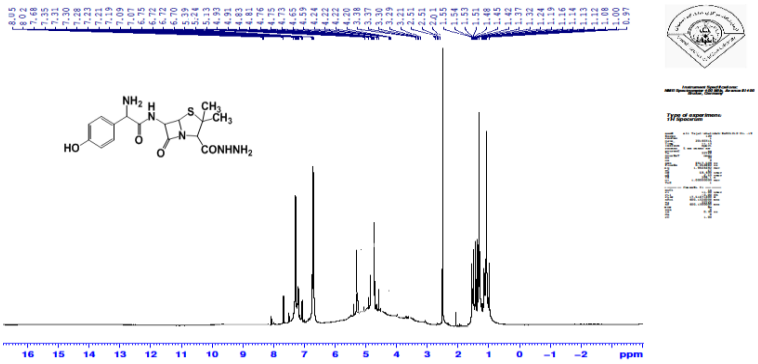


Figure.4 1HNMR Spectrum for Compound(4)

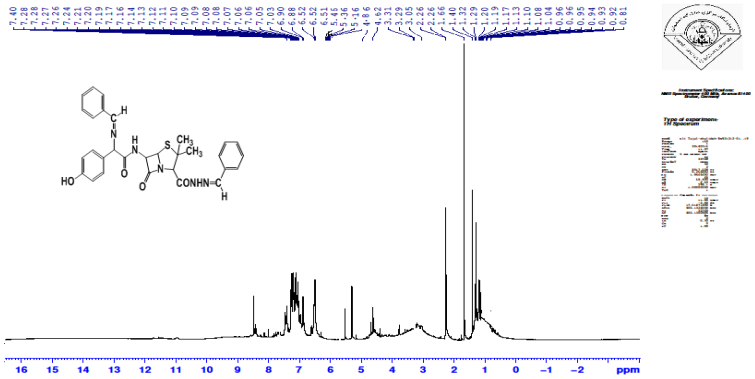


Figure.5 1HNMR Spectrum for Compound(5)

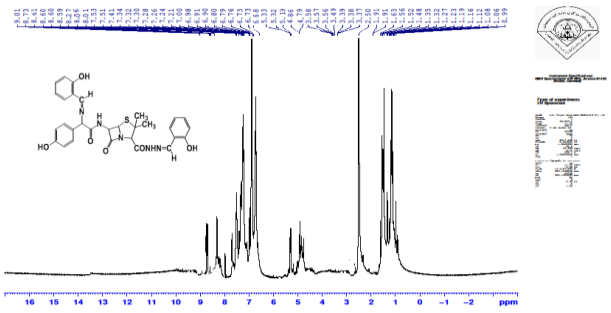


Figure.6 1HNMR Spectrum for Compound(9)

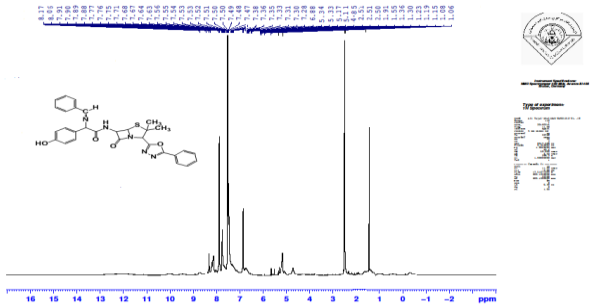


Figure.7 1HNMR Spectrum for Compound(10)

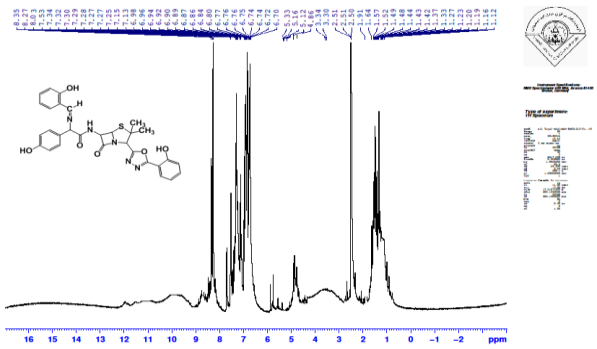


Figure.8 1HNMR Spectrum for Compound(14)

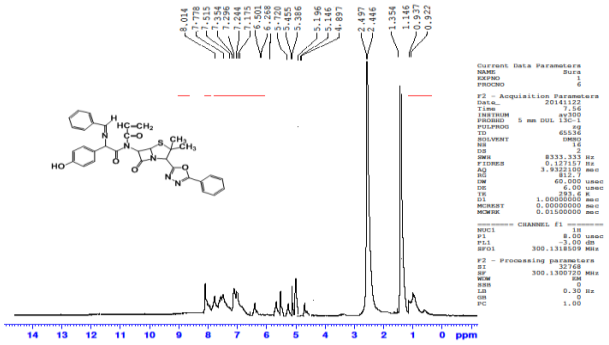
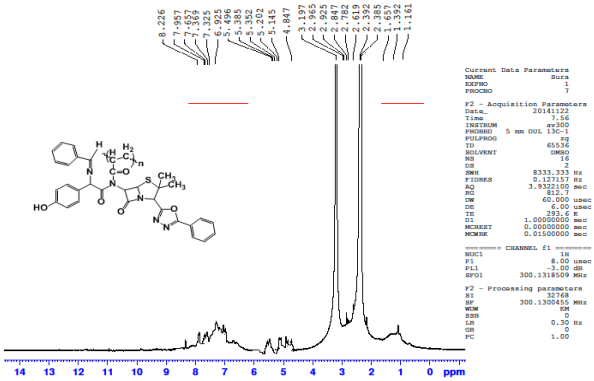
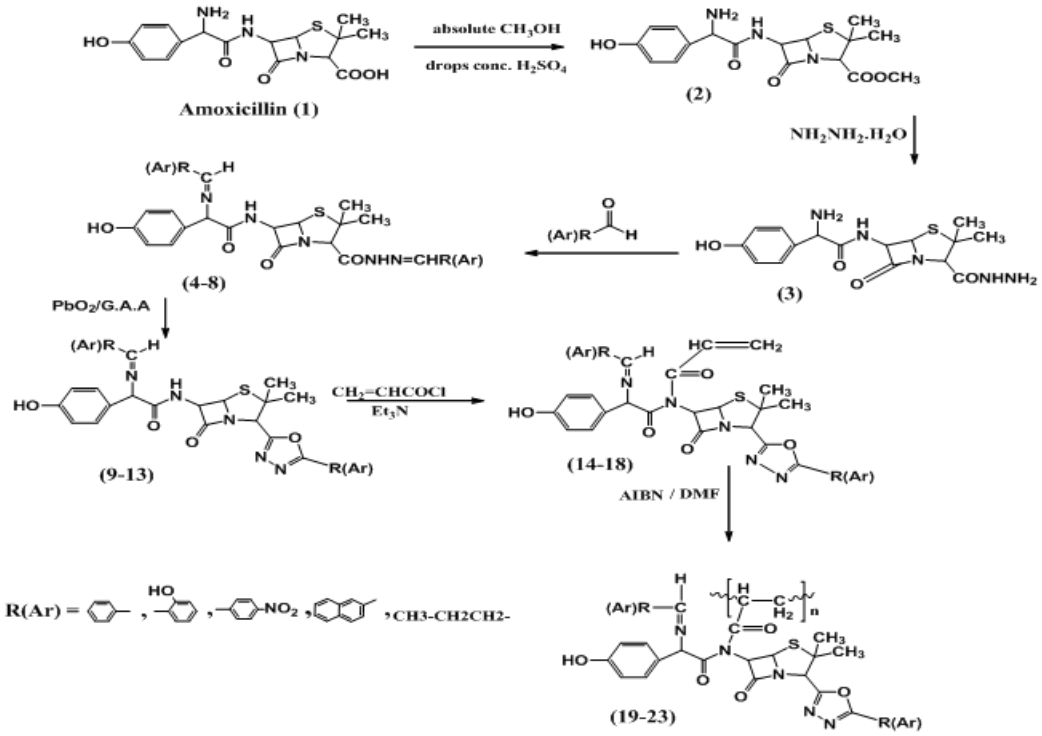


Figure.9 1HNMR Spectrum for Compound(19)



Scheme.1



Antibacterial Activity (22)

The compounds (9-13) and compounds (19-23) were evaluated their antibacterial activity in comparison to the control antibacterial drug amoxicillin against some bacterial species positive gram bacterial (*Staphylococcus aureus* and *Bacillus*) and negative gram bacterial (*Escherichia coli* and *Pseudomonas aeruginosa*) using DMSO as solvent to get desired concentration (1mg/ml) by agar diffusion method, the plates were incubated at 37 ºC for 24 hours, the inhibition zone measured in (mm). Synthesized compounds (9-13) were screened antibacterial activity and showed varying degree of inhibition zone against the tested gram positive and gram negative bacteria and observed that gram positive bacteria show better activity than gram negative bacteria, the compounds(9,11 and 13) show antibacterial activity against

Pseudomonas aeruginosa compared with drugs that show no change in the growth of this bacteria. All compounds (19-23) showed antibacterial activity against the tested organisms. The compounds (19,21) showed antibacterial activity better than drugs and other derivatives. The results of activity listed in table-4.

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