

Preparation , Characterazation, With Study Biological Activities With Some Newchalcone Derivatives.

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Abstract:

A variety of novel Chalcone derivatives were synthesized, described, and evaluated for their biological activity in this work. Terephthaldehyde and p-hydroxy acetopheneone were used to make Chalcone [A1]. Chalcone is treated with a medication that contains a primary1amino group in order to make schiffe base [A2] (Ampciline trihydraete). When all of this is done, additional derivatives [A3-A11] may be formed by reacting with other materials (Tetrazole, Thiazole idenones, Beta-lactam, and Oxazepine, and other chalcone derivatives). The melting point, FTIR, and 1HNMR were used to describe the compounds. In certain cases, these compounds have already been tested for their ability to affect human health..

Keywords: chalcone, schiff bases, tetrazole, oxazepene, thiazolidinone

Introduction:

Heterocyclic compounds are cyclic organic molecules that contain heteroatoms For example nitrogen, oxygen, sulfur, as well as other elements furthermore to the carbon framework. The heterocyclic compounds have a wide range of pharmacological properties and are used to treat a wide range of disorders. The heterocyclic ring is a significant structural component of the majority of medicinal drugs used in today's therapy. Although these compounds are very easy to synthesize, nitrogen-containing heterocyclic rings stand out among them due to their wide dispersion and biological properties ⁽¹⁾. One of the flavonoid secondary metabolites found in plants is chalcone (1,3-diphenyl-2-propen-1-one). Benzene rings A and B are joined by unsaturated benzene rings in the form of Chalcone. ketones ⁽²⁾.figure 1

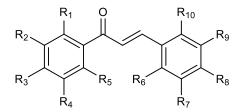


figure (1): Chalcone formula

The Claisen1-Schmidt condensation technique may be used to make chalcone derivatives. The derivatives come in a variety of substituent groups and ring types. These derivatives have a variety of biological actions as a result of their variations. Antibacterial, antimicrobial, antimalarial, antidepressant, antihistaminic, antitubercular , anti-inflammatory, antioxidant , anticancer ⁽¹⁻³⁾, and anti-invasion activities in glioblastoma cells ⁽⁴⁾.Schiff bases are a significant family of chemical compounds with a wide range of biological activity, includingantimalarial⁽⁵⁾, antitumar⁽⁶⁾, antifungal⁽⁷⁾, antibacterial⁽⁸⁾, anticorrosion⁽⁹⁾, and antiviral properties ⁽¹⁰⁾. It prepares in the reaction of an aldehyde, according to the principle. (respectively a ketone) with the use of a primary amine $^{(11)}$. An oxyazepine is a seven-membered ring that contains oxygen in the first position and nitrogen in the third, in addition to the five carbon atoms. It is a heterocyclic oxazepine known as 1,3-oxazepine that may be found in a number of forms^(12,13). The synthesis of oxazepine has been studied and reported over the years. Anhydrides maleic and phthalic react with Schiff base or hydrazone to form $it^{(14-18)}$. Antibacterial, antifungal, hypnotic muscle relaxant, inflammatory, antagonistic, antiepileptic, and antibacterial properties have all been discovered in oxazepine derivatives ^(12,18).Compounds with the five-member ring tetrazoles have four nitrogen and one carbon atoms in them⁽¹⁹⁾. Tetrazoles are a kind of heterocyclic scaffold that has a wide range of uses, particularly in the realm of medicinePharmaceutical chemistry is a branch of chemistry that deals with the production of pharmaceuticals. They're also useful in organic chemistry, coordination chemistry, photography, and agriculture ⁽²⁰⁾. photosensitive agents, polymers, energy materials, as well as speciality explosives, among other materials science applications ⁽²¹⁾. Due to its many biological actions, thiazolidinone is an extremely powerful heterocyclic ring. This nucleus is constantly being investigated in order to develop and manufacture new chemicals. Thiazolidinone is a tetrahydro derivative of thiazole and a tetrahydro derivative of thiazole ⁽²²⁾. The compound thiazolidine 2,4-dione is commonly employed in the development of new anti-diabetic medicines. This scaffold has anti-diabetic, anti-arthritic, anti-cancer, anti-anti-microbial, inflammatory, as well as anti-melanoma properties ⁽²³⁾. The heterocyclic amide ring B-lactam is made up of three carbon atoms and one nitrogen atom ⁽²⁴⁾. The four-membered cyclic amide -lactam (2-Azetidinone) is produced from 3-amino-propanoic acid. The (N) atom is attached to the -

3766

carbon atom adjacent to the carbonyl, thus the name. The -lactam ring is found in various antibiotic families, the most notable of which being cephalosporins, penicillins, and carbapenems. Monobactams (also known as -lactam antibiotics) are a kind of antibiotic ⁽²⁵⁾.

Materials and Methods:

A wide range of firms, including Thomas Baker, Merck, BDH, GCC, and Scharlau, contributed the chemicals that were used in the study. further purification is not required Uncorrected electrothermal melting point equipment was used to get the melting point values (Stuart Germany). The end of all chemicals' purity and reactivity. TLC plates 60 F245 (E. Merck) were coated with aluminum and iodine vapor was used as a mobile phase. The FTIR Shimadzu was used to acquire infrared spectra on a KBrb disk in the 400-4000 cm-1 band (Japan). A Bruker DMX-500 spectrophotometer was used to investigate the NMR spectra of the chemicals produced (500 bMHZ, solvent DMSO-d6).

Synthesis of Chalcone compound [A1]⁽²⁶⁾

The chalcone compound [A1] was made by dissolving Terephthaldehyde (0.0372mol,5g) and P-hydoxyacetophenone (0.0367mol,5g) in 20 mL pure ethanol, adding 10 mL sodium hydroxide aqueous solution (25%) and stirring for 4-6 hours at room temperature. After examining the solid, T.L.C. ,cold water was used to rinse and filter it out. The solid then filtered and dried then purified from Ethanol, which was likewise dry.

4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl) benzaldehyde [A1]

FT-IR (KBr)/cm⁻¹): 3479 (OH phenol), 3005 (C-H aromatic), 2902, 2869 (C-H aliphatic), 1780 (C=O), 1693 (C=C aliphatic), 1463 (C=C aromatic), 1093 (C-O).

| Comp. No | Structure of compound | Yield % | Color | M.P °C |
|-------------|---|------------|-------|-------------|
| A1 | HC HC C H | 51 | White | 112- 114 |

| Table 1: Physica | I properties | of compound | [A1] |
|------------------|--------------|-------------|------|
|------------------|--------------|-------------|------|

Synthesis of Schiff Bases Compound [A2]⁽²⁷⁾

An ethanol solution of 20 ml was used to combine compound [A1] (0.0277 mole, 7.gm) and the principal amine drug (Ampciline trihydraete) (0.0277 mole, 9.8 gm) together, then glacial acetic acid was added and the mixture was heated for nine to ten hours. After the response was over, T.L.C. examined it. Filtered, 1dried, and purified from Ethanol, the final solid was also dry.

6-(2-((4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)benzylidene)amino)-2-phenylacetamido)-3,3-

dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A2]

FT-IR (KBr)/cm⁻¹): 3671 (OH phenol), 3391 (NH), 3000 (C-H aromatic), 2918, 2850 (C-H aliphatic), 1725 (C=O carboxyl),1700 (C=O), 1675 (C=O amide), 1651 (C=N), 1593 (C=C aliphatic), 1468 (C=C aromatic), 1384 (C-N), 1019 (C-S).

Table 2: Physical properties of compound [A2]

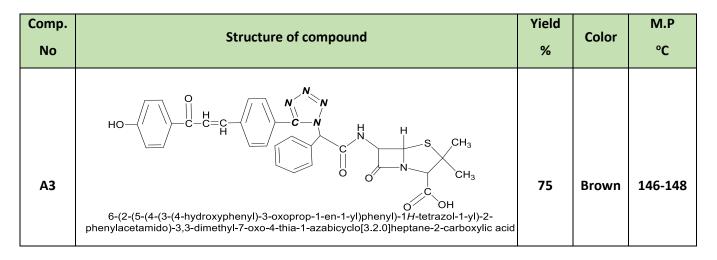
| Comp. No | Structure of compound | Yield % | Color | M.P °C |
|-------------|---|------------|------------|-----------|
| A2 | HO HO HO HO HO HO HO HO HO HO HO HO HO H | 83 | Orang e | 192-194 |

Synthesis of Tetrazole Compound[A3]⁽²⁸⁾

The Schiff base [A2] (0.00137 mole, 0.8g) was dissolved in (10) milliliters of tetrahydrofuran [THF], then sodiumazide (0.00137 mole, 0.1 gm) was added. T.L.C. evaluated the combination after it had been heated in a water bath for 9-11 hours at 60-70 degrees Celsius. The reaction mixturewas filtered, and the solidi that formed were purified with Ethanol before being dried..

6-(2-(5-(4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)phenyl)-1H-tetrazol-1-yl)-2-phenylacetamido)-3, 3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A3] FT-IR (KBr)/cm⁻¹): 3500 (OH phenol),3307 (NH), 3000 (C-H aromatic), 2918, 2850 (C-H aliphatic), 2111,2000 (N=N-N), 1735 (C=O carboxyl),1725 (C=O), 1650 (C=O amide), 1576 (C=C aliphatic), 1476 (C=C aromatic), 1384 (C-N), 1017 (C-S).

 Table 3: Physical properties of compound [A3]



Synthesis of Thiazolidinone Compound [A4]⁽²⁹⁾

Schiff base [A2] (0.00137mole, 0.8g) was dissolved in dry benzene (5ml), then Mercaptoacetic acid (0.00137mole, 0.2 ml) wasadded. T.L.C. was used to evaluate the mixture after it had been refluxed for 12-14 hours. The reaction mixture2 was filtered., and the solidi that formed were recrystallized from acetone, then. dried.

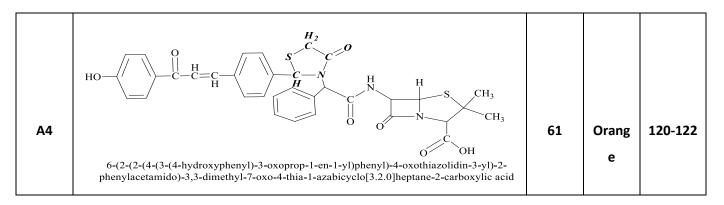
6-(2-(2-(4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)phenyl)-4-oxothiazolidin-3-yl)-2-phenylacetamido)-

3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid[A4]

FT-IR (KBr)/cm⁻¹): 3600 (OH phenol),3401 (NH), 3000 (C-H aromatic), 2918, 2850 (C-H aliphatic), 1724 (C=O carboxyl),1600 (C=O amide), 1576 (C=C aliphatic), 1435 (C=C aromatic), 1300 (C-N), 1035 (C-S).

Table 4: Physical properties of compound [A4]

| Comp. | Structure of compound | Yield | Color | M.P |
|-------|-----------------------|-------|-------|-----|
| No | Structure of compound | % | Color | °C |



Synthesis of β–Lactam Compound [A5]⁽³⁰⁾

Schiff bases [A2] (0.00137 mole, 0.8g) and triethyl amine (0.5 ml) were dissolved in dimethyl formamide (10 ml). Add 0.2 ml of -chloroacetyl chloride (0.2 ml) to the mixture at room temperature and stir for (6-7) hours. (48) hours at room temperature. After that, it was placed in a container filled with ice cubes and chilled. Filtration and washing of the solid precipitate in water followed by purification with ethanol/H2O (1:1) were performed prior to drying.

6-(2-(3-chloro-2-(4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)phenyl)-4-oxoazetidin-1-yl)-2phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid[A5]

FT-IR (KBr)/cm⁻¹): 3670 (OH phenol),3400 (NH), 3000 (C-H aromatic), 2920, 2800 (C-H aliphatic), 1724 (C=O carboxyl),1605 (C=O amide), 1576 (C=C aliphatic), 1459 (C=C aromatic), 1303 (C-N), 1020 (C-S), 964 (C-Cl).

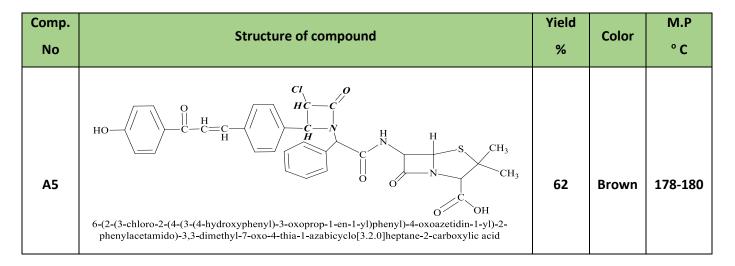


Table 5: Physical properties of compound [A5]

Synthesis of Oxazepine Compounds [A6, A7, A8]⁽³¹⁾

In 7ml of dry benzene, a mixture of Schiff base [A2] (0.00137mol) and various anhydrides (3-Nitrophathalic anhydride, maleic anhydride, succinic anhydride) (0.00137mol) was dissolved. For 5–6 hours, the mixture was refluxed. When the response was complete, T.L.C. went back and examined it. A filter was used to collect the reaction mixture, and the resulting solids were crystallized from acetone and dried.

6-(2-(3-(4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)phenyl)-1,5-dioxobenzo[e][1,3]oxazepin-

4(1H,3H,5H)-yl)-2-phenylacetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A6]

FT-IR (KBr)/cm⁻¹): 3600 (OH phenol),3400 (NH), 3058 (C-H aromatic), 2920, 2850 (C-H aliphatic), 1700 (C=O carboxyl),1700 (C=O lactone), 1606 (C=O lactam), 1571 (C=O amide), 1551 (C=C aliphatic), 1466 (C=C aromatic), 1252 (C-O-C), 1170 (C-O), 1017 (C-S).

6-(2-(2-(4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)phenyl)-4,7-dioxo-1,3-oxazepin-3(2H,4H,7H)-yl)-2phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A7]

FT-IR (KBr)/cm⁻¹): 3650 (OH phenol), 3401 (NH), 3000 (C-H aromatic), 2918, 2850 (C-H aliphatic), 1750 (C=O carboxyl),1700 (C=O lactone), 1655 (C=O lactam), 1576 (C=O amide), 1541 (C=C aliphatic), 1467 (C=C aromatic), 1243 (C-O-C), 1141 (C-O), 1019 (C-S).

6-(2-(2-(4-(3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)phenyl)-4,7-dioxo-1,3-oxazepan-3-yl)-2phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A8]

FT-IR (KBr)/cm⁻¹): 3650 (OH phenol), 3400 (NH), 3000 (C-H aromatic), 2918, 2850 (C-H aliphatic), 1724 (C=O carboxyl),1684 (C=O lactone), 1665 (C=O lactam), 1630 (C=O amide), 1575 (C=C aliphatic), 1467 (C=C aromatic), 1246 (C-O-C), 1141 (C-O), 1018 (C-S).compound Characterization [A6] was donevia 1H-NMR spectra which gave [A6] δ (10.12)ppm due to (s,1H,OH_{carboxlic acid}), δ (8.24) ppm due to (s,1H,NH_{amide}), δ (7.0-8.1) ppm due to (m,17H,Ar-H), δ (6.88)ppm due to (d,2H,CH=CH), δ (4.31) ppm due to (s,1H,OH_{aromatic}), δ (4.12) ppm as (d,2H,CH_{methine}), δ (2.49)ppm (DMSO),and δ (1.55)ppm due to(s,2H,CH_{methyl}).

Table 6: Physical properties of compounds[A6, A7, A8]

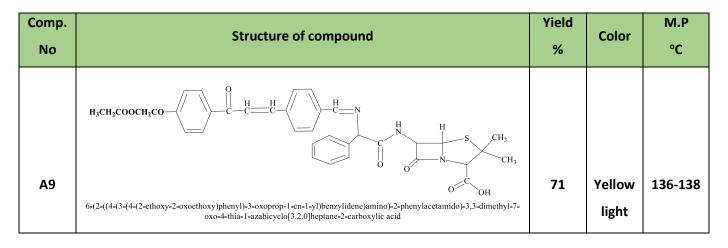
| Comp. | Structure of compounds | Yield | Color | M.P |
|-------|------------------------|---------|-------|-----|
| No | Structure of compounds | % Color | Color | °C |

| A6 | $HO \longrightarrow C \longrightarrow $ | 60 | Yellow pale | 150- 152- |
|----|--|----|----------------|--------------|
| А7 | HO-C-C=C-H-C-C-H-H-H-H-H-H-S-CH ₃ HO-C-C-C-C-H-H-H-H-H-H-H-S-CH ₃ O-C-C-C-H-H-C-C-C-C-C-H-H-H-H-H-H-S-CH ₃ O-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C | 68 | Brown | 175-177 |
| A8 | HO- C - C - C = C - H | 66 | Brown | 148-150 |

Synthesis of 6-(2-((4-(3-(4-(2-ethoxy-2-oxoethoxy)phenyl)-3-oxoprop-1-en-1-yl)benzylidene)amino)-2phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A9]⁽³²⁾ Anhydrous potassium carbonate (5.6 mmol), Schiff base [A2] (0.0102mol,6g), and ethyl chloroacetate (1.2 ml) were dissolved in dry acetone (10 ml) for 12 hours with steady stirring. After filtration, the solid product was re-crystallized from ethaol after being concentrated under high pressure, vacuum, and drying.

6-(2-((4-(3-(4-(2-ethoxy-2-oxoethoxy)phenyl)-3-oxoprop-1-en-1-yl)benzylidene)amino)-2phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A9] FT-IR (KBr)/cm⁻¹): 3369 (NH), 3000 (C-H aromatic), 2920, 2851 (C-H aliphatic), 1724 (C=O ester),1700 (C=O carboxyl), 1650 (C=N), 1576 (C=O amide), 1540 (C=C aliphatic), 1433 (C=C aromatic), 1141 (C-O), 1099 (C-S).





Synthesisof 6-(2-((4-(3-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)-3-oxoprop-1-en-1-yl)benzylidene)amino)-2-phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A10]⁽³³⁾ The chemical compound [A9] (0.00702 mole, 4.6gm) was dissolved in ten milliliters of absolute ethanol, stirred for ten minutes at room temperature, and a few drops of hydrazine hydrate 80 percent were gently added (0.00702 mole). The mixture was then refluxed for 10 hours. The resulting solid was purified with ethanol/H2O after the reaction mixture was filtered (1:1).

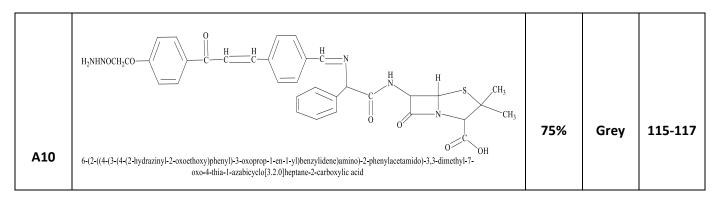
6-(2-((4-(3-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)-3-oxoprop-1-en-1-yl)benzylidene)amino)-2-

phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [A10]

FT-IR (KBr)/cm⁻¹): 3550,3467 (NH₂), 3329 (NH), 3000 (C-H aromatic), 2920, 2851 (C-H aliphatic), 1724 (C=O carboxyl), 1676 (C=O amide), 1663 (C=N), 1540 (C=C aliphatic), 1434 (C=C aromatic), 1141 (C-O), 1020 (C-S).Compound Characterization [A10] was done by 1H-NMR spectra which gave [A10] δ (11.33)ppm due to (s,1H,OH_{carboxlic acid}), δ (8.68) ppm due to (s,1H,NH_{amide}), δ (7.11-8.38) ppm due to (m,13H,Ar-H), δ (6.54)ppm due to (d,2H,CH=CH), δ (4.49) ppm owing to (d,2H,CH_{methine}), δ (2.13) ppm because of (s,2H,NH₂), δ (2.49)ppm as (DMSO),and δ (1.22)ppm due to(s,2H,CH_{methyl}).

Table 8: Physical properties of compound [A10]

| Comp. | Structure of compound | Yield | Color | M.P |
|-------|-----------------------|-------|-------|-----|
| No | | % | | °C |



Synthesis of 6-(2-((4-(3-(4-(2-(2-(4-hydroxybenzylidene)hydrazinyl)-2-oxoethoxy)phenyl)-3-oxoprop-1en-1-yl)benzylidene)amino)-2-phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid [A11]⁽²⁷⁾

Benzaldehyde,4-hydroxybenzaldehyde (0.6g) and different aldehydes (0.00534 mole, 3.5gm) were combined with (10ml of pure alcohol and Few drops of glacial acetic acid were added to the mixture before it was refluxed for 8 to 10 hours. When the response was complete, T.L.C. went back and examined it. The solid was filtered, dried, and purified with ethanol and water (1:1).

6-(2-((4-(3-(4-(2-(2-(4-hydroxybenzylidene)hydrazinyl)-2-oxoethoxy)phenyl)-3-oxoprop-1-en-1-

yl)benzylidene)amino)-2-phenylacetamido)-3,3- dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2carboxylic acid [A11]

FT-IR (KBr)/cm⁻¹):3646 (OH phenol), 3307 (NH), 3000 (C-H aromatic), 2920, 2851 (C-H aliphatic), 1724 (C=O ester),1700 (C=O amide), 1670 (C=N), 1540 (C=C aliphatic), 1433 (C=C aromatic), 1247 (C-O), 1099 (C-S).

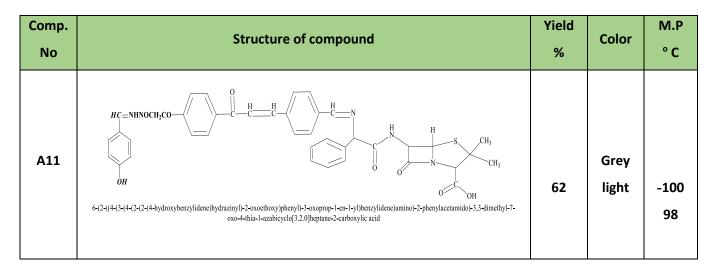
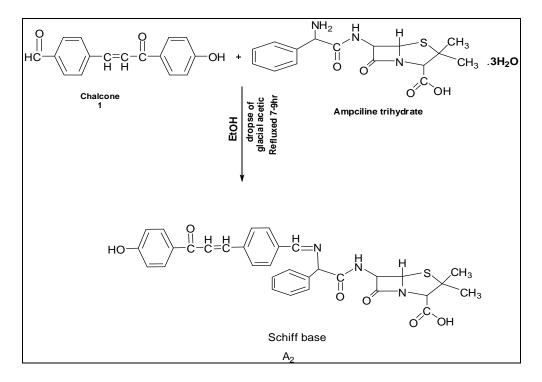
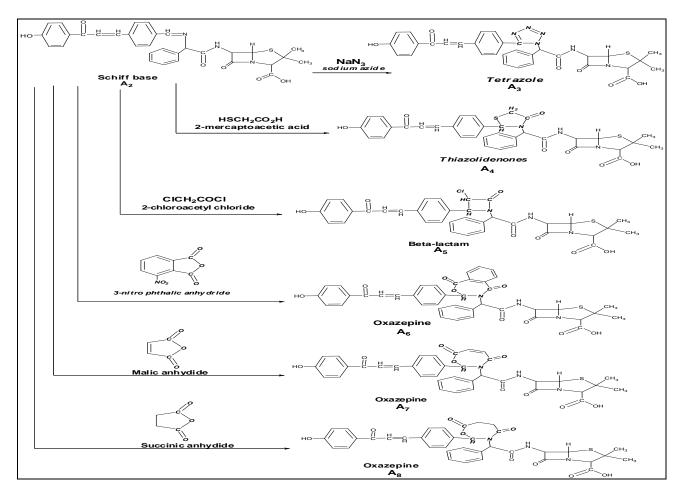


Table 9: Physical properties of compound [A11]

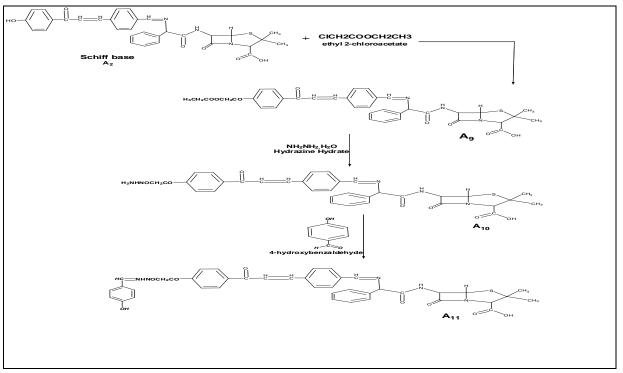
The sequence of reactions that has led to the synthesis of final products is shown in scheme 1,2, and 3.



Scheme (1)



Scheme (2)



Scheme (3)

Biological Part

The biological activities of a manufactured chemical (A5) were investigated against bacterial and fungal strains. The agar well diffusion method was used to test E. coli, Staphylococcus aureus, Klebsiella pneumoniae, Candida albicans, and Proteus vulgaris, as shown in the table (10).

Table (10) biological activity for synthesized compound (A5).

| | zone of Inhibition (6mm.) | | | | | | | |
|-------------|---|----|-----------|----|----------|--|--|--|
| Compound | Compound E.coli S.aureus Klebsiella Candida | | | | | | | |
| No.1000 ppm | | | pnoumonia | | Proteus | | | |
| | | | | | vulgaris | | | |
| A5 | 21 | 20 | 22 | 35 | 23 | | | |
| DMSO | - | - | | - | | | | |

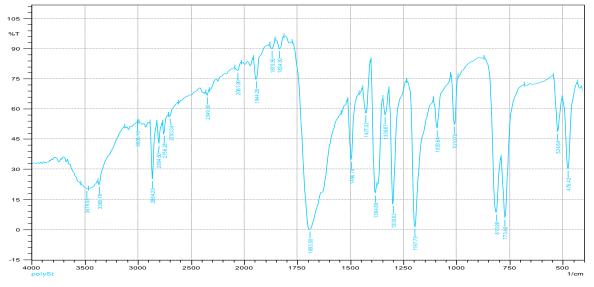


Figure (1) FT-IR spectrum for compound[A1]

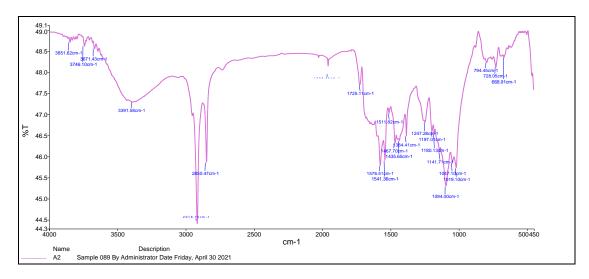


Figure (2) FT-IR spectrum for compound[A2]

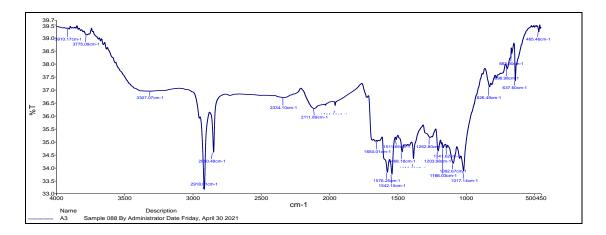


Figure (3) FT-IR spectrum for compound[A3]

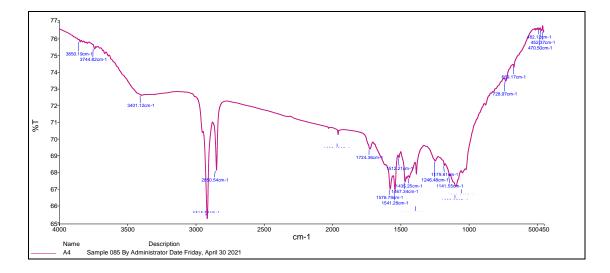


Figure (4) FT-IR spectrum for compound[A4]

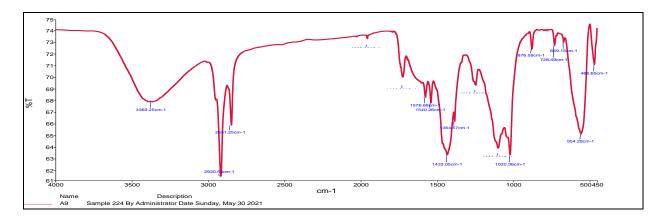


Figure (4) FT-IR spectrum for compound[A9]

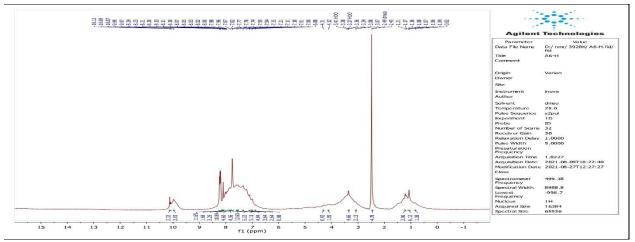


Figure (5):The¹H-NMR of compound [A6]

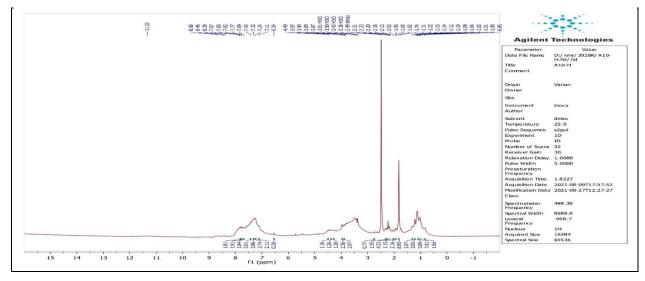


Figure (6):The¹H-NMR of compound [A10]

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