# Synthesis, Characterization and Biological Activity Study of Some New Schiff Bases Derived From Phenyl quinoline-2(1H)-one

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## Abstract

This research comprises the preparation of new phenyl quinoline derivatives. The cinnamic acid was reacted with aniline derivatives in absolute ethanol to produce the substituted of4-phenylquinolin-2(1*H*)-one (1a-c). Treatment of (1a-c) with hydrazine hydrate to give hydrazone (2a-c), then the hydrazone (2a-c) was used to react with formic acid and different aromatic aldehydes to obtain the1,2,4-triazole derivatives (3a-c) and azomethines (4,5a-c) respectively via Schiff bases formation. The compounds obtained were characterized by such spectroscopy means namely FT-IR, U.V and $^1$H-NMRanalysis. Biological activity for some of the prepared compound were evaluated against two types of bacteria (*Escherichia Coli and Staphylococcus aureus).* The results in general showed that all the tested compounds possess good biological activity against the tested organisms.

# تحضير، تشخيص ودراسة الفعالية البايولوجية لبعض قواعد شيف الجديدة المشتقة من فنيل كوينولين -2- (1H)- ون

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## الخلاصة

يشمل هذا البحث تحضير مشتقات جديدة للفنيل كوينولين. تم مفاعلة حامض السينامك مع مشتقات الانيلين بوجود الايثانول المطلق لإنتاج 4-فنيل كوينولين-2-ون المعوض (1a-c). معاملة المركبات (1a-c) مع الهايدرازين المائي (99%) لإعطاء الهايدرازون (2a-c)، ثم الهايدرازون (2a-c) استعمل للتفاعل مع حامض الفورميك والديهايدات اروماتية مختلفة للحصول على مشتقات1, 2, 4- ترايازول (3a-c) وازوميثين (4,5a-c) على التوالي عن طريق تكوين قواعد شيف. المركبات المكتسبة شخصت بواسطة الطرائق الطيفية: طيف الاشعة فوق البنفسجية (UV)، طيف الاشعة تحت الحمراء (FT-IR) والرنين النووي المغناطيسي ($^1$H-NMR) لعدة مركبات. قيمت الفعالية البايولوجية لبعض المركبات المحضرة ضد نوعين من البكتيريا (الاشريشياكولاي والستافيلوكوكس اوريوس). وقد بينت الدراسة أن اغلب المركبات المحضرة ذات فعالية بايولوجية جيدة ضد الميكروبات قيد الدراسة.

## Introduction

Quinoline is a heterocyclic scaffold of paramount importance to human race. Several quinoline derivatives isolated from natural resources or prepared synthetically are significant with respect to medicinal chemistry and biomedical use. Indeed quinoline derivatives are some of the oldest compounds which have been utilized for the treatment of a variety of diseases (1). Quinoline derivatives have been known to possess a variety of biological activities such as antitumor (2), anti-malarial (3), anti-platelet (4), antidepressant (5), antiulcer (6) and cardiac stimulant (7). Various 1,2,4-triazole derivatives have aroused considerable interest of chemistry due to their versatile practical applications as well as their wide range of biological properties (8-12).

Therefore it was thought to combine phenyl quinolone moiety with 1,2,4-Trizoloring together in amolecular framework to see the additive effects of these rings towards biological activity(13-16).The compounds containing azomethine (-CH=N-) group are known as Schiff bases constitute an important class of compounds for new drug development(17). Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities. These observations have been guiding for the development of new hydrazones that possess varied biological activities (18).

## Experimental

- **General:** All reactions were monitored by thin-layer chromatography (TLC) using 0.25 mm pre-coated silica-gel F254 plates, spots were detected with iodine vapor. The IR spectra were recorded on (SHIMDZU) FT-IR 8400 spectrophotometer; solid samples were run in KBr discs, Liquid samples were run as smears. UV spectra were recorded with UV-Visible spectrophotometer (CARY)UV-100 Conc. Melting point were determined on a Gallenkamp meting point apparatus with sample contained in open capillary glass tube in an electrically heated metal block apparatus and were un corrected.$^{1}$H-NMR spectra were recorded on ultra shield300 MHz NMR spectrophotometer in Jordan, with tetra methyl silane (TMS) as an internal standard and acetone-$d_6$ solutions was used as solvent.
- **Preparation of 4-phenylquinolin-2(1*H*)-one (1a-c):** A mixture of cinnamic acid (0.05 mole) and appropriate aromatic amine (0.05 mol)were taken in a round bottom flask. Then to it (15 ml) of absolute ethanol was added. Then it was refluxed for about (6hrs). Then the whole concentrate was transferred to a beaker by filtration. Then a clear liquid was obtained and it was kept for overnight which produced white solid transparent flakes of crystals, after draining out the mother liquor. Then it was recrystallized from a suitable solvent afford compounds(1a-c).
- **Preparationof4-phenylquinolin-2(1*H*)-onehydrazone(2a-c):** To a solution of compound1(0.05 mol) in absolute ethanol (20 ml), hydrazine hydrate (99%) (0.08 mol) was added then the resulting mixture was refluxed for(5 hrs). The mixture was poured into an ice-water, the solid product was filtered and recrystallized from an appropriate solvent to give the hydrazone derivatives (2a-c).
- **Preparation of5-phenyl-3,3a-dihydro[1, 2, 4]triazolo[4,3-a]quinoline(3a-c):** A mixture of compound 2 (0.05 mol) and absolute ethanol (20 ml) in a round bottom flask. Formic acid (10 ml) was added with continuous stirring. It was refluxed for (7 hrs), then the mixture was poured into an ice-water. The resulting solid was filtered and recrystallized from a suitable solvent afford compounds (3a-c).
- **Preparation of 4-phenylquinolin-2(1*H*)-one azomethine (4,5a-c):** A mixture of compound 2 (0.01 mol), aromatic aldehyde (0.01 mol) and (2-3) drops of glacial acetic acid in absolute ethanol (20 ml) was refluxed for (6 hrs). After cooling the obtained precipitate was filtered then washed with cold ethanol, dried and recrystallized from an appropriate solvent to give compounds (4,5a-c). Table (1) represent the physical data of compounds (1a-5c).Characteristic absorption bands of FT-IR and U.V spectra of compounds (1c-5c) are listed in Table (2). Table (3) represent the$^{1}$H-NMR spectra for compounds (3a,3b,4b,5c).

## Results and Discussion

A new series of quinoline derivatives were synthesized according to the Scheme. The required starting material for the synthesis of the targeted compounds is 4-phenyl quinoline-2(1H)-one (1a-c) which was prepared by the reaction of cinnamic acid with appropriate aromatic amine in absolute ethanol with good yield. The IR spectra showed the N-H amide stretching absorption between (3248-3325)cm$^{-1}$ and the C=O amide

stretching (1661-1670)$cm^{-1}$, which was indicated by the disappearance of the broad band for OH stretching absorption for COOH group in cinnamic acid. Condensation of (1a-c) with hydrazine hydrate (99%) to obtain the hydrazone (2a-c) was confirmed by its IR spectra that showed bands (3221-3414)$cm^{-1}$ and (1664-1677)$cm^{-1}$ due to $NH_2$ and C=N groups respectively, then the hydrazone (2a-c) was used to prepare two types of derivatives via Schiff bases formation. The first type was prepared from ring cyclization of (2a-c) with formic acid in the presence of absolute ethanol afforded 1,2,4-triazole derivatives (3a-c) was characterized by IR spectra and $^1$H-NMR. IR spectra showed absorption bands between (3226-3377)$cm^{-1}$ and (1667-1680)$cm^{-1}$ attributed to the N-H and C=N groups respectively. The $^1$H-NMR spectrum of compound (3a) showed two signals at (9.1)ppm and (8.7)ppm assigned to the N-H and C-H protons of the triazole ring respectively, signals between (7.1-8.4) ppm due to aromatic protons and a signal at (5.8) p.pm assigned to the olefinic proton(C<u>H</u>=C). The second type for derivatives included was prepared via reaction(2a-c) with different primary aromatic aldehydes to give azomethine compounds (4,5 a-c), the formation of these Schiff bases was indicated by the presence in their IR spectra of the azomethine C=N stretching bands between (1667-1675)$cm^{-1}$, combined with the disappearance of the $NH_2$ stretching band. Further, its $^1$H-NMR spectra for compound (4c) showed a signal at (8.3) ppm attributed to the (C<u>H</u>=N) proton in the azomethin moiety ,two signals at (9.4) ppm and (9.2) ppm assigned to the N-H and O-H protons respectively ,signal at (5.1) ppm due to olefinic proton (C<u>H</u>=C) and a multiplet at (7.2-8.1) p.pm assigned to the aromatic protons.

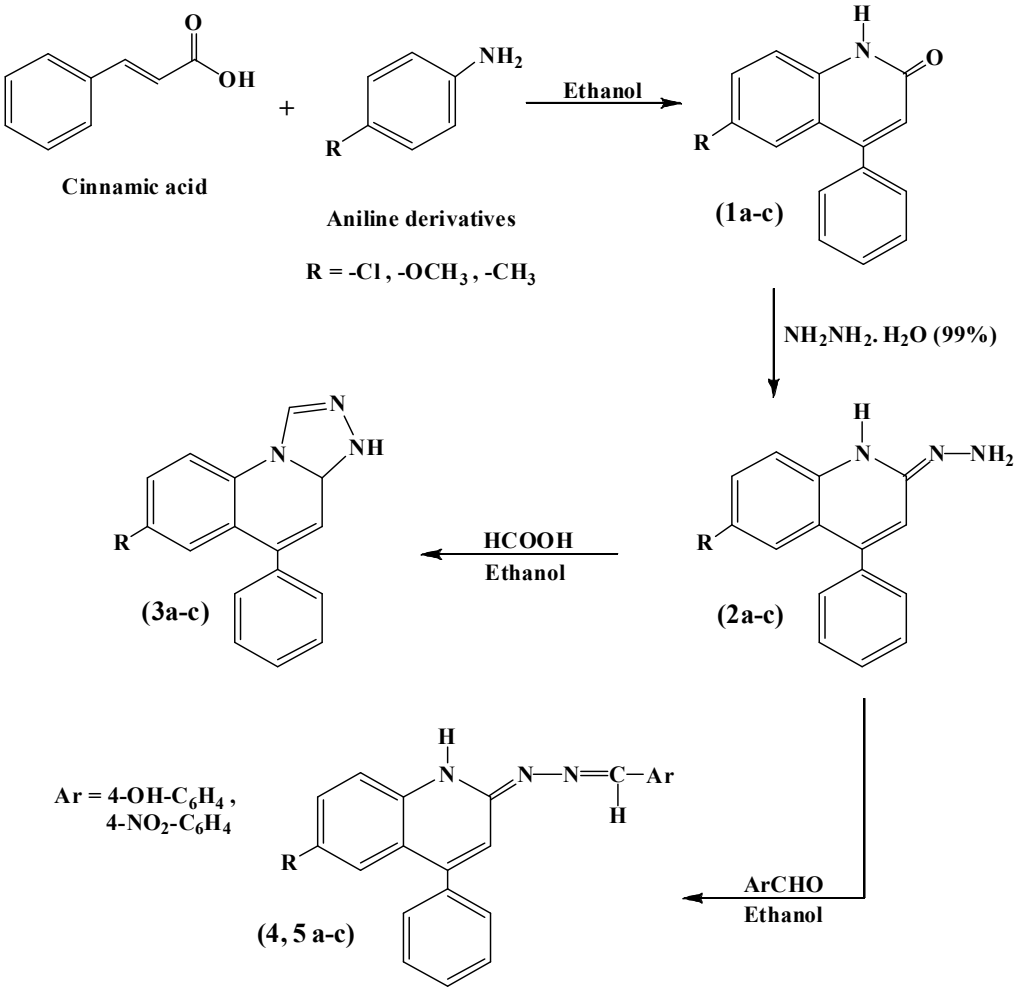


**Table (1) Represent the physical data of compounds (1a-5c)**

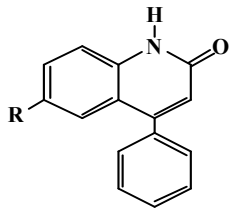
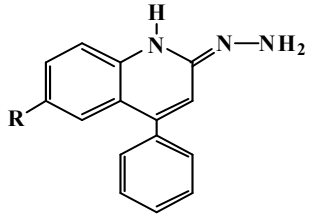
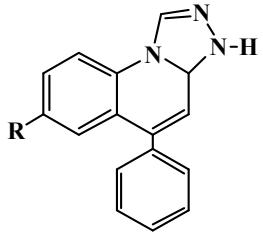
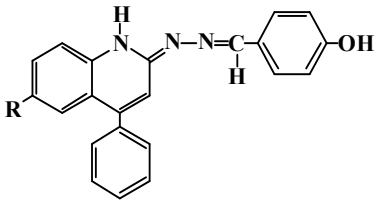
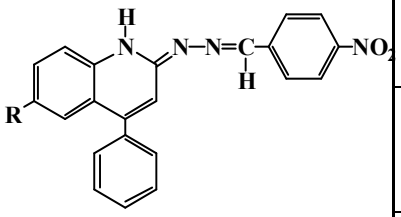
| Compound structure | Comp. No. | R | Scientific name | Color of crystal | m.p. °C | Yield % | Solvent of Rec. |
|---|---|---|---|---|---|---|---|
|  | **1a** | Cl | 6-Chloro-4-phenylquinolin-2(1*H*)-one | Yellow | 177-179 | 72 | Benzene |
| | **1b** | $OCH_3$ | 6-Methoxy-4-phenylquinolin-2(1*H*)-one | Gray | 97-99 | 77 | Benzene |
| | **1c** | $CH_3$ | 6-Methyl-4-phenylquinolin-2(1*H*)-one | Brown | 113-115 | 74 | Toluene |
|  | **2a** | Cl | 6-Chloro-4-phenylquinolin-2(1*H*)-one hydrazone | Pale-yellow | 102-104 | 71 | Benzene |
| | **2b** | $OCH_3$ | 6-Methoxy-4-phenylquinolin-2(1*H*)-one hydrazone | Gray | 126-128 | 71 | Toluene |
| | **2c** | $CH_3$ | 6-Methyl-4-phenylquinolin-2(1*H*)-one hydrazone | Brown | 145-147 | 71 | Benzene |
|  | **3a** | Cl | 7-Chloro-5-phenyl-3,3a-dihydro[1,2,4]triazolo[4,3-a]quinoline | Yellow | 153-155 | 76 | n-hexane |
| | **3b** | $OCH_3$ | 7-Methoxy-5-phenyl-3,3a-dihydro[1,2,4]triazolo[4,3-a]quinoline | Light-brown | 161-163 | 70 | Toluene |
| | **3c** | $CH_3$ | 7-Methyl-5-phenyl-3,3a-dihydro[1,2,4]triazolo[4,3-a]quinoline | Pale-brown | 105-107 | 75 | Toluene |
|  | **4a** | Cl | 6-Chloro-4-phenylquinolin-2(1*H*)-one-(4-hydroxy-benzylidene)-hydrazone | Dark-yellow | 125-127 | 69 | Benzene |
| | **4b** | $OCH_3$ | 6-Methoxy-4-phenylquinolin-2(1*H*)-one-(4-hydroxy-benzylidene)-hydrazone | Dark-brown | 88-90 | 75 | Benzene |
| | **4c** | $CH_3$ | 6-Methyl-4-phenylquinolin-2(1*H*)-one-(4-hydroxy-benzylidene)-hydrazone | Pale-brown | 174-176 | 77 | Dioxane |
|  | **5a** | Cl | 6-Chloro-4-phenylquinolin-2(1*H*)-one-(4-nitro-benzylidene)-hydrazone | Yellow | 127-129 | 66 | Dioxane |
| | **5b** | $OCH_3$ | 6-Methoxy-4-phenylquinolin-2(1*H*)-one-(4-nitro-benzylidene)-hydrazone | Light-brown | 194-196 | 68 | Benzene |
| | **5c** | $CH_3$ | 6-Methyl-4-phenylquinolin-2(1*H*)-one-(4-nitro-benzylidene)-hydrazone | Brown | 181-183 | 66 | Toluene |

**Table (2) Characteristic absorption bands of FT-IR and U.V spectra of compounds (1a-5c)**

| Comp. No. | FTIR spectral data $cm^{-1}$ | | | | | | | | U.V. ($\lambda_{max}$) nm |
|---|---|---|---|---|---|---|---|---|---|
| | υ(N-H) | υ(C-H) Aromatic | υ(C-H) Aliphatic | υ(C=C) Aromatic | υ(C=C) Olefinic | υ(C-H) Olefinic | υ(C=N) Imine | Others (υ) | |
| **1a** | 3248 | 3057 | - | 1563 | 1641 | 2955 | - | 1661(C=O)<br>1088 (C-Cl) | 308 |
| **1b** | 3325 | 3062 | 2893 | 1546 | 1619 | 2943 | - | 1667 (C=O)<br>1229, 1072 (C-O-C) | 311 |
| **1c** | 3315 | 3055 | 2889 | 1527 | 1626 | 2961 | - | 1670 (C=O) | 305 |
| **2a** | 3353-3277 | 3056 | - | 1561 | 1640 | 2949 | 1673 | 1084 (C-Cl) | 318 |
| **2b** | 3351-3238 | 3065 | 2887 | 1506 | 1629 | 2909 | 1677 | 1229,1112 (C-O-C) | 325 |
| **2c** | 3414-3221 | 3059 | 2920 | 1589 | 1639 | 2951 | 1664 | - | 319 |
| **3a** | 3226 | 3051 | - | 1559 | 1647 | 2959 | 1669 | 1087 (C-Cl) | 336 |
| **3b** | 3347 | 3063 | 2884 | 1526 | 1634 | 2921 | 1680 | 1225, 1101 (C-O-C) | 346 |
| **3c** | 3377 | 3066 | 2893 | 1593 | 1631 | 2947 | 1667 | - | 337 |
| **4a** | 3277 | 3049 | - | 1552 | 1649 | 2988 | 1673 | 3455 (O-H)<br>1081 (C-Cl) | 341 |
| **4b** | 3297 | 3079 | 2891 | 1564 | 1651 | 2964 | 1672 | 3511 (O-H)<br>1219,1114 (C-O-C) | 347 |
| **4c** | 3371 | 3069 | 2955 | 1558 | 1631 | 2993 | 1668 | 3543 (O-H) | 338 |
| **5a** | 3297 | 3069 | - | 1586 | 1639 | 2971 | 1667 | 1530, 1348 ($NO_2$) | 346 |
| **5b** | 3341 | 3055 | 2918 | 1579 | 1649 | 2991 | 1675 | 1551, 1348 ($NO_2$)<br>1220,1115 (C-O-C) | 341 |
| **5c** | 3265 | 3097 | 2858 | 1570 | 1627 | 2958 | 1667 | 1544, 1342 ($NO_2$) | 339 |

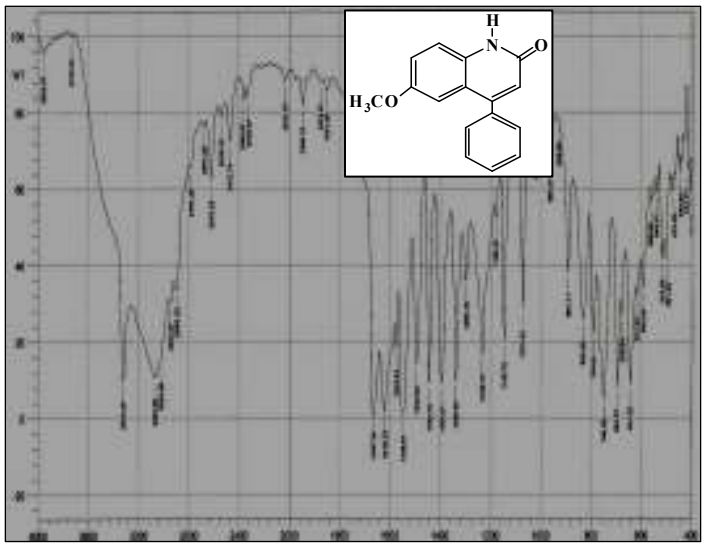



Fig.(1) FT-IR spectrum for compound (1b)

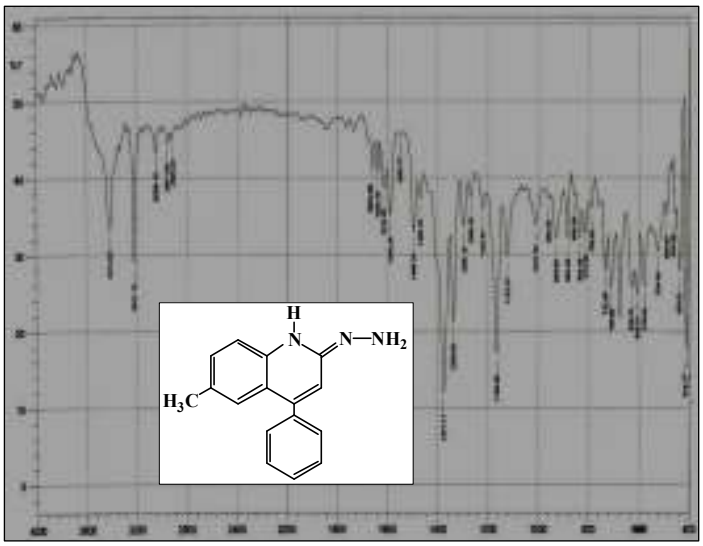



Fig.(2) FT-IR spectrum for compound (2c)

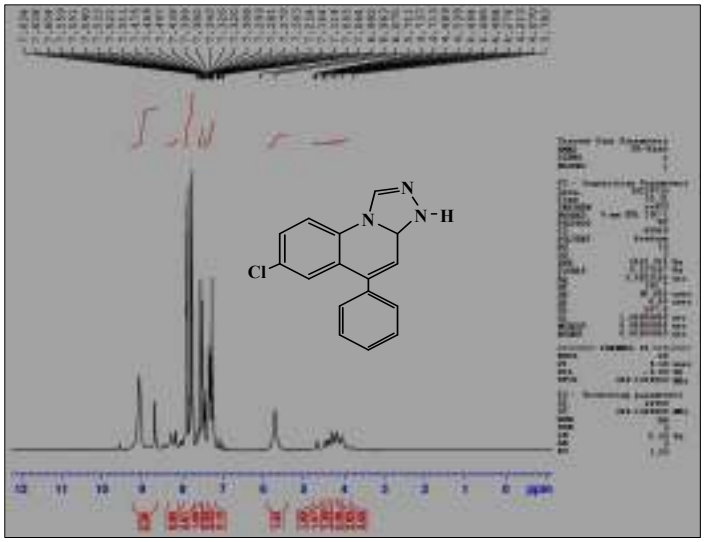



Fig.(3) $^{1}$H-NMR spectrum for compound (3a)

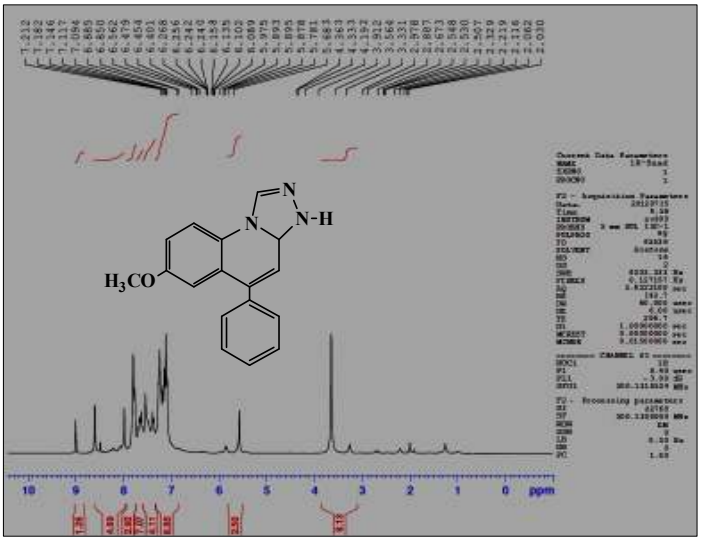



Fig.(4) $^{1}$H-NMR spectrum for compound (3b)

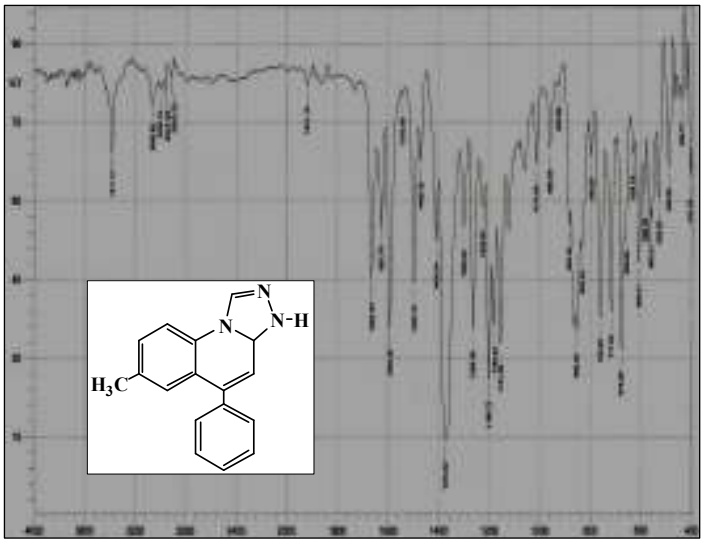



Fig.(5) FT-IR spectrum for compound (3c)

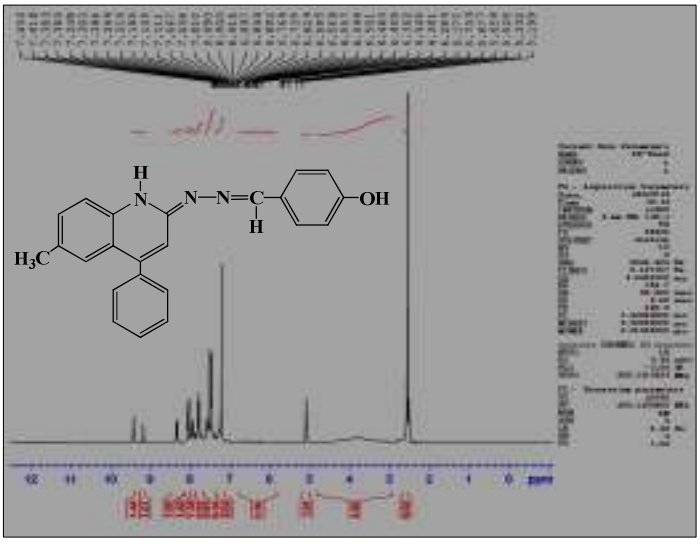



Fig.(6) $^{1}$H-NMR spectrum for compound (4c)

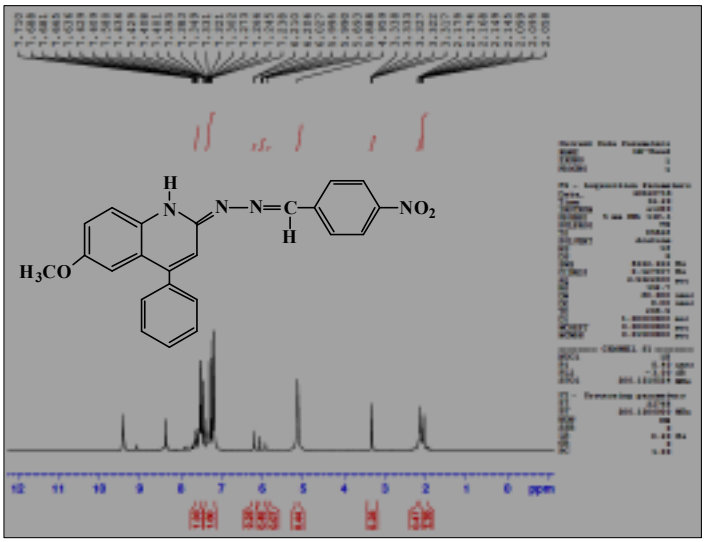


Fig.(7) $^{1}$H-NMR spectrum for compound (5b)

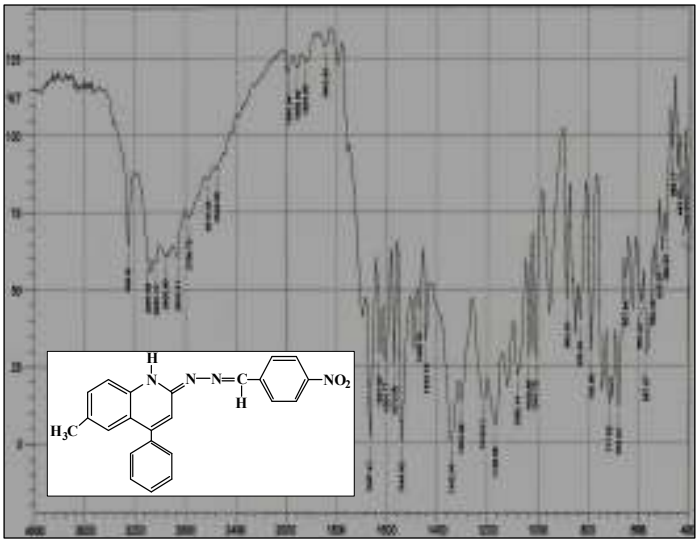
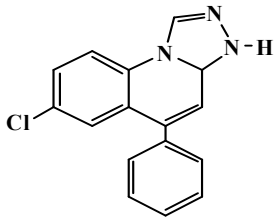
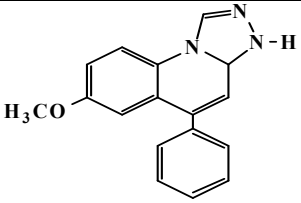
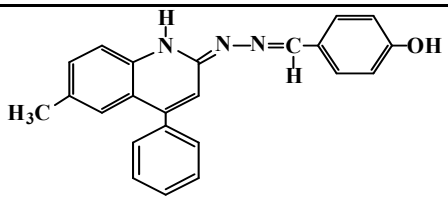
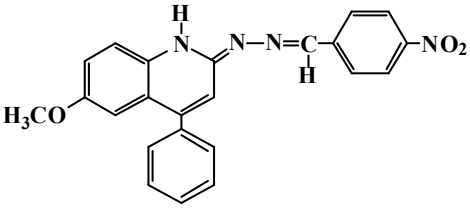


Fig.(8) FT-IR spectrum for compound (5c)

**Table (3) $^{1}$H-NMR spectra for compounds (3a, 3b, 3c and 5b)**

| Comp. No. | Compound structure | δH aromatic ppm | δH other bands ppm |
|---|---|---|---|
| 3a |  | 7.1-8.4(m,8H,Ar-H) | 9.1 (s,1H,NH)<br>8.7(s,1H,CH=N)<br>5.8 (s,1H,CH=C) |
| 3b |  | 7.0-8.2 (m,8H,Ar-H) | 9.0(s,1H,NH)<br>3.8(s,3H,$OCH_3$)<br>8.6(s,1H,CH=N)<br>5.7 (s,1H,CH=C) |
| 4c |  | 7.2-8.1 (m,12H,Ar-H) | 9.4 (s,1H,NH)<br>9.2(s,1H,OH)<br>2.6(s,3H, $CH_3$)<br>8.3(s,1H,CH=N)<br>5.1 (s,1H,CH=C) |
| 5b |  | 7.1-7.8 (m,12H,Ar-H) | 9.5 (s,1H,NH)<br>3.4(s,1H,$OCH_3$)<br>8.4(s,1H,CH=N)<br>5.1 (s,1H,CH=C) |

**Test of the biological activity:** To study the biological activity effects of the phenyl quinoline-2(*1H*)-one derivatives that correspond to the wells assay, the solution of the prepared compounds in (conc.=1 mg/ml)in DMSO (70%) were applied to the selected agar medium that has been inoculated with suitable test culture. The antimicrobial agent diffuses in an over-colony circle around the wells of application, the radial growth of the colony was recorded before the completion of incubation and the mean diameters of the zones of inhibition were recorded to represent the degree of the anti microbial agent. The prepared derivatives in this work were expected to possess biological activity since they have starting material (Quinoline) and two active moieties in their molecules (Azomethine and 1,2,4-Triazole) that were tested against two types of bacteria *Escherichia coli* (gram-negative) and *Staphylococcus aureus* (gram-positive), the experiment was conducted by using Muller Hinton Agar. The plates were incubated at37ºC for 24 hrs. The results showed that most of the tested derivatives possess anti-bacterial activity as shown in Table (4).

**Table (4) : Anti-bacterial activity for some phenyl quinoline-2(*1H*)-one derivatives**

| Comp. No. | Gram-positive bacteria | Gram-negative bacteria |
|---|---|---|
| | *Staphylococcus aureus* | *Escherichia coli* |
| 3a | ++ | ++ |
| 3b | + | + |
| 3c | + | + |
| 4a | ++ | ++ |
| 4b | ++ | - |
| 5a | ++ | - |
| 5b | ++ | + |
| 5c | +++ | +++ |

**Note: (-) = No inhibition = Inactive , (+) = (1-5) mm = Weak activity (++) = (6-10) mm = Moderate activity , (+++) = (11-15) mm = High activity**

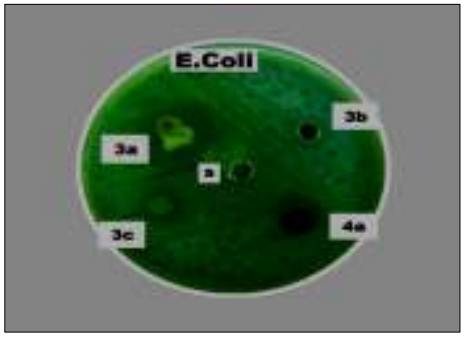



**Fig.(9) Effect of compounds [3a], [3b], [3c], [4a] on *Escherichia coli***

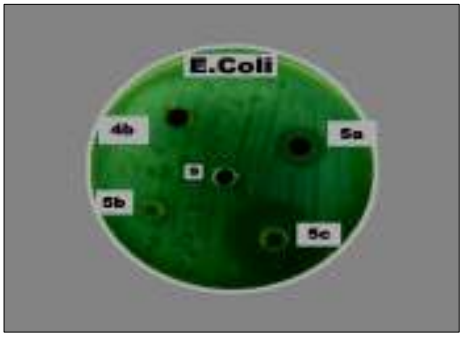



**Fig.(10) Effect of compounds [4b], [5a], [5b], [5c] on *Escherichia coli***

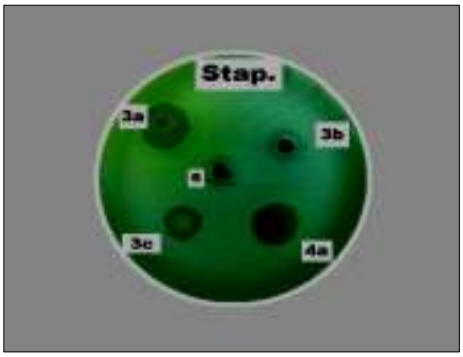



**Fig.(11) Effect of compounds [3a], [3b],[3c], [4a] on *Staphylococcus aureus***

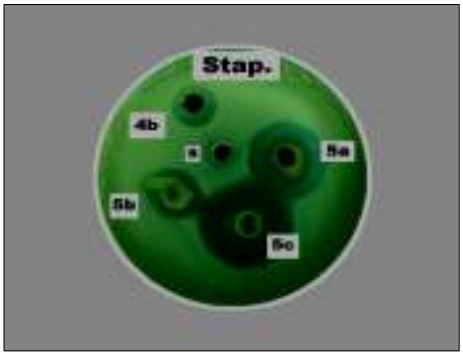



**Fig.(12) Effect of compounds [4b], [5a], [5b], [5c] on *Staphylococcus aureus***

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