Introduction

1.1 Quinoline:

Is a heterocyclic aromatic organic compound with the chemical formula C9H7N. Quinoline structure composed of benzene and pyridine ring at two adjacent carbon atoms.

1.2 Quinolines:

Quinoline derivatives are prevalent in variety of pharmacologically active synthetic and natural compounds.

1.3 Occurrence and isolation:

Quinoline is present in small amount in crude oil within the virgin diesel fraction. It can be removed by hydro treating often with nickel-molybdenum and alumina.

Quinoline was first extracted from coal tar (is brown or black liquid of extremely high viscosity).

In 1834 by Friendlier Ferdinand Rung. Coal tar remains the principle source of commercial quinoline.

1.4 Physical properties of quinoline:

Is colorless aged sample, if exposed to light, becomes yellow and later brown.

Hydroscopic liquid with strong odor.

Slightly soluble in cold water but dissolve in hot water and most organic solvent.
1.5 Synthetic methods for preparation quinoline:

1.5.1 CONRAD-LIMPACH SYNTHESIS:

Is the condensation of aniline with B-keto ester to form 4-hydroxy quinoline via a Schiff base. The overall reaction type is a combination of both an addition reaction as well as rearrangement reaction was discovered by Max Conrad (1848-1920) and Leonhard Limpach (1852-1933) in 1887 while they were studying the synthesis of quinoline derivatives.
The mechanism begins with an attack of aniline on the keto group of the keto group of B-keto ester, the newly formed oxide is then twice protonated to form the Schiff base, which then undergoes keto-enol tautomerization before an electro cyclic ring closing. The mechanism concludes with the removal of an alcohol, a series of proton transfers, and a keto–enol tautomerization to form a 4-hydroxy quinoline, the final product of Conrad–Limpach synthesis.

**1.5.2 Doebner – Miller Reaction:**

The Doebner–Miller reaction is the organic reaction of an aniline with a B-unsaturated carbonyl compounds to form quinoline
The reaction is also known as Skarup – Doebner – Von Miller quinolines synthesis

1.5.3 Gould - Jacobs reaction:

The Gould – Jacobs reaction is an organic synthesis for the preparation of quinolines. In this reaction aniline or an aniline derivative first reacts with malonic acid derivative ethyl ethoxymethylene. A benzannulation takes place by application of heat to quinoline. The ester group is hydrolyzed by sodium hydroxide to the carboxylic acid and de carboxylation again by application of heat to 4-hydroxy quinoline.
1.5.4 Skarup reaction:

Is a chemical reaction used to synthesized quinoline. Aniline is heated with sulfuric acid, glycerol, and an oxidizing agent such as nitro benzene to yield quinoline.
1.5.5 Knorr quinoline synthesis:

Is an intra molecular organic reaction converting a B- keto anilide to a 2-hydroxyl quinoline using sulfuric acid. This reaction was first described by Ludwig Knorr.

The reaction is a type of electrophilic substitution accompanied by elimination of water.
1.5.6 Combes quinoline synthesis:

Also known as the (Combes cyclization) is a chemical reaction where by an O-acyl amino acetophenone is transformed into two different hydroxyl quinolines using hydroxide ion. The relative proportions of the hydroxyl quinoline produced are dependent upon the reaction conditions and structure of the starting material. Although the reaction product is commonly depicted that the keto form predominated in both the solid state and in solution making the compound quinoline.

Pathway A:
**Pathway B:**

![Chemical Pathway Diagram]

**1.5.7 Friedlander synthesis:**

Is a chemical reaction of 2-amino benzaldehyde with ketones to form quinoline derivatives.

![Chemical Reaction Diagram]

This reaction has been catalyzed by trifluoro acetic acid, toluene, sulfonic acid, iodine and Lewis acids.
1.5.8 Pfitzinger` reaction:

Also known as the Pfitzinger-Borsche reaction is the chemical reaction of stain with base and carbonyl compound to yield substituted quinoline 4-carboxylic acids.

1.5.9 Doebner reaction:

The Doebner reaction is the chemical reaction of an aniline with an aldehyde and pyruvic acid to form quinoline-4-carboxylic acids.
1.5.10 Povarov reaction:

The Povarov reaction is an organic reaction described as a formal cycloaddition between an aromatic imine and an alkene.

\[
\text{phenyl imine} + \text{alkene} \rightarrow \text{cycloaddition product}
\]

1.5.11 Niementowski Quinoline synthesis:

The Niementowski quinoline synthesis is the chemical reaction of anthranilic acids and ketones or aldehyde to form \( \alpha \)-hydroquinoline derivatives.

\[
\text{anthranilic acid} + \text{ketone} \rightarrow \text{quinoline derivative}
\]
1.6 Biological activities of Quinolines:

Quinolines and its fused heterocyclic derivatives tested with diverse pharmacological activity functional groups constitute an important class of compounds for new drug developments, therefore many experiments have synthesized these compounds as target structures and evaluated their biological activities covering anti cancers, antibacterial, anticonvulsants, anti malarial, anti inflammatory plus cardiovascular activities. quinolines are a family of synthetic broad-spectrum antibacterial drugs. first generation of quinolines began with the introduction of nalidixic acid in 1962 for treatment of urinary tract infections in humans.

Nalidixic acid was discovered by George lesher and coworkers in a distillate during an attempt at chloroquine synthesis which is a famous antimalarial derivative.

These derivatives compounds exerts their antibacterial effect by preventing bacterial DNA from unwinding and duplicating in bacterial cell, however the majority of quinolones in clinical use belong to the subset fluoroquinolones, which have fluorine atom attached to benzene ring.
1.6.1 Examples for these pharmaceuticals:

Ceprofloxacin is an antibiotic that used for decades in treating bacterial infections, the quinoline core playing the major role in its activity.

A chemotherapeutic agent that is a topoisomerase inhibitor.

Although the assortment of antifungal drugs is broad, the most commonly used agents have major drawbacks. Toxicity, serious side effects or the emergence of drug resistance are amongst them, new drugs and drugs candidates under clinical trials do not guarantee better pharmacological parameters. These new medicines may appear effective, however they may cause serious side effects. This current review is focused on the recent findings seems to be especially interesting as 8-hydroxy quinoline and its metal Complexes have been well known as
antifungals for years structural similarities between quinoline based antifungal and allylammines or homoallylammines.

Laquinimod A derivative that used to treat multiple sclerosis disease.

An antimalarial quinoline alkaloid found in *cinchona officinalis* tree, it is insoluble in water so used as a salicylate salt in medication.

As a result of diversity of these compounds in nature as well as synthesis, combination in therapeutic properties interactions may occur. For example the antimalarial Quinoline derivative its trade name is LARIAM but must be carefully used because of serious mental side effects that results from its CNS activity, it crosses the blood brain barrier predicting antidepressant quinoline derivatives, anticonvulsants, as well as anti HIV.
This quinoline derivative demonstrated the highest anti-proliferative activity, most active compound makes it promising for further development; In cancer researcher field.

8-hydroxyquinoline a monoprotic bidentate chelating agent.

The complexes as well as the heterocycle itself exhibit antiseptic, disinfectant, and pesticide properties.
1.7 QUINOLINE REACTIONS:

Benzene ring fused with pyridine in an aromatic heterocyclic compound is Quinoline, benzene is more electron rich than pyridine that is because of the electronegative heteroatom of Nitrogen.

They undergo many reactions and have a rich chemistry, starting from hydrogenation, EAS, the famous Reissert reaction, oxidative cleavage, nucleophilic substitution as they are in the form of N-oxides, halogenations, etc.

Quinoline reacts slowly and some reactions take days to be achieved.

**Reduction by hydrogen gas which occurs in pyridine ring as follows:**

Using THF as a solvent… hydrogenation occurred at the hetero ring.
Quinoline undergo oxidative cleavage with alkali potassium permangunate to give pyridine-2,3-dicarboxylic acid. However, pyridine-2,3-dicarboxylic acid is not stable and undergoes decarboxylation to give nicotinic acid.

Another characteristic reaction is electrophilic substitution or EAS. Pyridine is less reactive towards electrophilic aromatic substitution than benzene; therefore, the substitution will occur on the benzene ring of quinoline. The resonance effect experienced from the pyridine ring decreases electron density at carbon 5 but not at carbon 8; therefore, the substitution will occur at carbon 8 as in Nitration:

There is an important reaction that observed in quinolines also called Reissert reaction in which an acyl chloride and KCN are used to give Reissert product, in the last step hydrolysis occurred as followed:
The Cyanide group makes the neighboring proton extremely acidic.

Since quinolines undergoes electrophilic substitution the possesses an ability to undergo nucleophilic substitution:
In position 2 the Lewis base nucleophiles are added in pyridine. Nucleophilic substitution include halogenation, adding bases such as methoxide nucleophile and others happened. But in the case of isoquinolines it occurs in position 1.
(1-8) Aim and Objectives:

To synthesize four quinoline derivatives using the starting materials: Phenylpyruvic acid, Benzaldehyde, Furfural aldehyde, and 4-aminobenzenesulfonamide Using ethanol as a solvent upon reflux for 3 hrs. and Calculate the percentage yield for each compound, weight in gram, melting points.

Then to identify these compounds by IR spectroscopy and UV spectroscopy.
Materials and Methods

2.1 Materials:

Absolute ethanol (National Distillation Company).

Benzaldehyde (Assay, 98%, loba chemicals ltd, India).

Concentrated Hydrochloric acid

Dichloro methane

Furfuraldehyde (98%, loba chemicals ltd, India).

Phenyl pyruvic acid

Saturated Sodium Hydroxide

Sulfanilamide (Techmopharm. Chemistry)

2.2 Instrumentation:

2.2.1 TLC:

TLC analyses were performed on pre-coated silica gel (E-Merck Kieselged 60 f254) plates and visualisation was done by exposing to iodine vapour. Solvents were purified by standard procedures before use. Column chromatography was conducted by using silica gel with different solvent systems as elutes.

2.2.2 Infra Red (IR) spectra:

IR spectra were recorded in KBr on Perkin_Elmer spectrum BX series FT_IR spectrometer

Name of instrument: FT_IR spectrometer
Make: SHIMADZUE.Model No.(FT-IR-8400).

Date of issue: June 2009

Made: In Japan

2.2.3 Ultra Violet (UV) Spectra:

Name of instrument: UV\ Visible spectrometer

Made: SHIMADZU

Date of issue: June 2009

Mode No.: UV-1800

Made: In Japan

2.3 General Equipments:

Beakers (250 ml, 400ml)
Glass rode: India
Capillary tubes
Condenser: India
Conical flask: India
Funnel: India
Heating mantel: BOECO Germany lab heat
Measuring cylinder: India
Round bottom flask ( RBF) : (250 ml) India
Sensitive balance: BOECO Germany
Separation funnel: India
All of glasses wire were Pyrex type
2.4 Methods:

2.4.1 Synthesis of 2,3-diphenyl-6-sulfamoyl quinoline-4-carboxylic acid:

A mixture of benzaldehyde (0.118mol) and (0.00134mol ) of phenyl pyruvic acid in 2ml of ethanol , (0.00131mol, 0.226g) of sulfanilamide in 0.13 ml of ethanol added, was heated for 1 hour ( all the amount of sulfanilamide solution was added gradually) , the mixture was cooled to room temperature, the precipitate that separated was collected by removal of the solvent in vacuo , the resulting precipitate collected , dried and weighted.(A)

2.4.2 Synthesis of ethyl 2,3-diphenyl-6-sulfamoyl quinoline -4-carboxylate:

The reaction was performed from compound (A) (0.1g ,0.00269 mol) ,10 ml ethanol and( 1 ml) concentrated hydro chloric acid was refluxed for 2 hours . After cooling at room temperature , the mixture was poured into saturated Na2CO3 , and extracted the organic layer , the solvent was removed in vacuo , dried and weighted.(B)

2.4.3 Synthesis of 2-(furan-2-yl)-3-phenyl-6- sulfanilamoyl quinoline-4-carboxylic acid:

A mixture of fur fural aldehyde 1ml (0.012 mol) , (0.21g , 0.0012mol) of phenyl pyruvic acid in 2ml of ethanol , was refluxed for 1 hour , which at these hour all the amount of sulfanilamide dissolve in ethanol was completely added gradually , the mixture was refluxed for 3 hours . Then cooled after that to room temperature , the precipitate that separated was collected by removal of the solvent in vacuo, the resulting precipitate collected , dried and weighted .(C)
2.4.4 Synthesis of ethyl2-(furan-2-yl)-3-phenyl -6- sulfamoyl quinoline-4-carboxylate:

The precipitate was formed from compound (c) , (0.1g ,0.0025 mol) 10 ml of ethanol and concentrated hydro chloric acid was refluxed for 3 hours , after cooling at room temperature , the mixture was poured into saturated Na2CO3 , and extracted the organic layer , the solvent was removal in vacuo, dried and weighted.

2.5 Reaction Conditions:

Table (2.1): Reaction conditions of the prepared quinoline derivatives compounds::

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Reaction temp(°C)</th>
<th>Time(h)</th>
<th>Rec.solvent</th>
<th>Yield(%)</th>
<th>Yield(g)</th>
<th>m.p.(°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td><img src="Image1" alt="image" /></td>
<td>70</td>
<td>3</td>
<td>Ethanol</td>
<td>32.053%</td>
<td>3</td>
<td>&gt;300</td>
</tr>
<tr>
<td>II</td>
<td><img src="Image2" alt="image" /></td>
<td>70</td>
<td>3</td>
<td>Ethanol</td>
<td>44.722%</td>
<td>2.1574</td>
<td>&gt;300</td>
</tr>
</tbody>
</table>
Table (2.2) Reaction Condition of the prepared quinoline derivatives compounds:

![Chemical structure of the quinoline derivative](image)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Reaction temp(°C)</th>
<th>Time(h)</th>
<th>Rec.solvent</th>
<th>Yield(%)</th>
<th>Yield(g)</th>
<th>m.p(°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td>70</td>
<td>1</td>
<td>Ethanol</td>
<td>33.75</td>
<td>0.2963</td>
<td>&gt;300</td>
</tr>
<tr>
<td>II</td>
<td></td>
<td>70</td>
<td>1</td>
<td>Ethanol</td>
<td>46.62</td>
<td>0.2145</td>
<td>300&gt;</td>
</tr>
</tbody>
</table>
2.6 Chemical names of the prepared compounds:

Table (2.3) Chemical Names of quinoline derivatives:

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Chemical name</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>🍃</td>
<td>2,3-Diphenyl-6-sulphamoylquinoline-4-carboxylic acid.</td>
</tr>
<tr>
<td>II</td>
<td>🍃</td>
<td>2-Furyl-3-phenyl-6-sulphamoylquinoline-4-carboxylic acid.</td>
</tr>
</tbody>
</table>

Table (2.4): Chemical names of quinoline derivatives:

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Chemical name</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>🍃</td>
<td>Ethyl 2,3-diphenyl-6-sulphamoyl quinoline-4-carboxylate</td>
</tr>
<tr>
<td>II</td>
<td>🍃</td>
<td>Ethyl 2-(furan-2-yl)-3-phenyl-6-sulphamoyl quinoline-4-carboxylate</td>
</tr>
</tbody>
</table>
Table (2.5): Infra-red spectral data of quinoline derivatives:

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>C=C_CarO \text{st.vib}</th>
<th>C-N \text{st.vib}</th>
<th>C=O \text{st.vib}</th>
<th>N-H \text{st.vib}</th>
<th>SO \text{2st.vib}</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td>1591.16</td>
<td>1209</td>
<td>1743</td>
<td>Asym.3311.55</td>
<td>Asym.1307.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sym.3263.33</td>
<td>Sym.1105.14</td>
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<tr>
<td>II</td>
<td></td>
<td>1691.46</td>
<td>1280</td>
<td>1691.46</td>
<td>Asym. 3361.69</td>
<td>Asym.1328.86</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sym. 3261.40</td>
<td>Sym. 1328.86</td>
</tr>
</tbody>
</table>

Table (2.6): Infra-red spectral data of quinoline derivatives:

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>C=C_CarO \text{st.vib}</th>
<th>C-N \text{st.vib}</th>
<th>C=O \text{st.vib}</th>
<th>N-H \text{st.vib}</th>
<th>SO \text{2st.vib}</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td>1448.44</td>
<td>1220</td>
<td>1758.96</td>
<td>Asym.3380</td>
<td>Asym.1409.8</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sym.3300.98</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sym.1159.14</td>
<td>Sym.1159.14</td>
</tr>
<tr>
<td>II</td>
<td></td>
<td>1616.24</td>
<td>1278</td>
<td>1919.04</td>
<td>Asym.3407.98</td>
<td>Asym.1325.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sym.3220</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sym.1210</td>
<td></td>
</tr>
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</table>
Table (2.7) UV – Visible spectral data:

<table>
<thead>
<tr>
<th>Compounds structure</th>
<th>R</th>
<th>Number of peaks</th>
<th>λ&lt;sub&gt;max&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="化合物结构1" /></td>
<td><img src="image2.png" alt="R" /></td>
<td>Six peaks</td>
<td>1013</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>908</td>
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<tr>
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<td>808.50</td>
</tr>
<tr>
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<td></td>
<td>741</td>
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<td></td>
<td>581</td>
</tr>
<tr>
<td><img src="image3.png" alt="化合物结构2" /></td>
<td><img src="image2.png" alt="R" /></td>
<td>Seven peaks</td>
<td>1013</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>908</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>805</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>741</td>
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<td>278</td>
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<tr>
<td><img src="image4.png" alt="化合物结构3" /></td>
<td><img src="image2.png" alt="R" /></td>
<td>Five peaks</td>
<td>1013</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>908</td>
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<tr>
<td></td>
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<td>812</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td>671</td>
</tr>
<tr>
<td><img src="image5.png" alt="化合物结构4" /></td>
<td><img src="image2.png" alt="R" /></td>
<td>Four peaks</td>
<td>1013</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>908</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>805</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>741</td>
</tr>
</tbody>
</table>
Results & Discussion

(3-1) General chemical background:

In this present work reverse synthesis ideas were derived from functional group interchange, functional group removal. Using p-sulfanilamido aniline as starting material in all four prepared quinoline derivatives. Criteria of cyclization was doebner-miller reaction upon condensation between aniline, phenylpyruvic acid and benzaldehyde as in compound (1) its ester is compound (2).

A reaction was pfitzinger like occurred in forming of compound(3) which is a condensation between aniline, phenylpyruvic acid and furfural aldehyde. Estrification reactions were done for acid derivatives using ethanol, concentrated hydrochloric acid and saturated sodium carbonate.
(3.2) spectral data:

(3-2-a) 2,3 diphenyl -6-sulfamoylquinoline-4-carboxylic acid:

Mp. = 300-320 °C
yield = 32.05%  
MW = 362 g/mol

Yield in gram = 3 g

IR(KBr) : v=, (c=0)= 1683.74 strong peak, 1640 for aromatic (c=c), two peaks for (N-H) stretching vibration at 3263.33 and 3311.55, broad peak for (O-H) at 3739.72, (C-H) stretching vibration at 3070.46, (C-O) stretching vibration at 1222.79, (S=O) stretching vibration at 1105.14, 1029, 902.62, 757.97, 638.39 \text{ \text{ cm}^{-1}}

UV-VIS(absolute ethanol): 6 peaks, (\text{lambda max}= 1013 )

(3-2-b) 2,3 diphenyl-6-sulfamoylquinoline-4-carboxylate:

Mp. = 298-320 °C
yield = 44.72%  
MW = 369 g/mol

Yield in gram = 2.1574 g

IR(KBr): v=, (c=0) intense peak at 1758.96, (c=c) aromatic at 1664.45, (N-H) stretching vibration gives two peaks at 3355 and 3385.95, (C-H) stretching vibration at 2979, (C-O) at 1159, 904.55, 865.98 \text{ \text{ cm}^{-1}}.
UV-VIS(ethanol): 4 peaks, (lambda max)= 1013

(3-2-c)  2-(furan-2-yl)-3-phenyl-6-sulfamoylquinoline-4-carboxylic acid:

Mp.=301-322 °C   yield = 33.75%   yield in gram= 0.3692g  
MW=348g\mol

IR(KBr): v=, (c=o) strong peak at 1691.46, (c=c) aromatic at 1591, (N-H) stretching vibration gives to peaks to indicate the primary amine functional group at 3361.61 and 3261.40, (C-H) stretching vibration at 3122.54, (O-H) at 3732.00,(C-O) at 1226.56, 2354.92, 1328.86, 1155.28, 1099, 1018, 918.05, 885.27 l\cm

UV-VIS(ethanol): 4 peaks, (lambda max= 1013)

(3-2-d) ethyl2- (furan-2-yl) -3- phenyl-6-sulfamoylquinoline -4-carboxylate:

Mp.=300-325 °C   yield = 46.62%   MW=360g\mol
yield in gram= 0.5412g

IR(KBr): v=, (c=o) at 1787, (c=c) aromatic at 1616.24, (N-H) stretching vibration gives two peaks to indicate primary amine group at 3220 and 3407.98, (C-H) stretching vibration at 3086.08, (C-O) at 1159.14, 1099,2364.57, 1325.01, 1037.63, 999.06,835.12

UV-VIS (ethanol): 4 peaks, (lambda max= 1013)
(3-3) Synthesis methods:

The prepared quinoline derivatives have general skeleton in synthesis of:

\[ X = \text{SO}_2\text{NH}_2 \]

(3-3-a) 2,3 diphenyl-6-sulfamoylquinoline-4-carboxylic acid:
(TM)

(i)

(ii)

(iii)

and

1,3 dicarbonyl compound

FGI

+SO₂Cl + "NH₂NH₂"
In the case of ester of this prepared compound, disconnection of (C-O) leads to primary reactants of acid and alcohol.
(3-3-b) 2-(furan-2-yl)-3-phenyl-6-sulfamoylquinoline-4-carboxylic acid:

\[
\begin{align*}
\text{H}_2\text{N}&\text{SO}_2\text{NH}_2 \quad + \quad \text{H}_2\text{FO} &\quad + \quad \text{H}_2\text{FCA} \quad \rightarrow \\
\text{H}_2\text{N}&\text{SO}_2\text{C} &\quad \text{OH} \quad \text{H}_2\text{FO} &\quad \text{N} \quad \text{O} &\quad \text{H} \\
\end{align*}
\]

**Essential disconnections:**

Disconnection of (C=N) (i) leads to –NH2 group and carbonyl (C=O) which corresponds to condensation, disconnection of (C-C) (ii) between benzene and carbon attached to carboxylic group leads to negative synthon of benzene and electron deficient carbon in carbonyl (C=O),
\[
\text{benzyne intermediate}
\]
(3-4) Estrification reactions:

The prepared esters quinoline derivatives compound (2) and compound (4) are: 2,3 diphenyl-6-sulfamoylquinoline-4-carboxylate and 2-(furan-2-yl)-3-phenyl-6-sulfamoylquinoline-4-carboxylic acid were synthesized from their acids by acid catalyzed fisher estrification using ethanol and solid sodium carbonate:

(3-4-a)

(3-4-b)
(3-5) **Anti-microbial activity of quinoline core in a general discussion:**

Researchers in pharmaceutical organic synthesis field are interested in quinoline derivatives because of their inhibition ability and/or destruction of bacterial cell, the quinoline skeleton is playing the major role in this biochemical process. Such as in the case of other five-membered heterocycles like: imidazoles, pyrazoles, pyrazolones, lactams,…etc

All these derivatives are effective pharmacologically because the existence of the parent core as well as type of substituents presents.

(3-6) **conclusion and results:**

After preparation of the four quinoline derivatives it is found that the percentage yields were:

For 2,3 diphenyl-6-sulfamoylquinoline-4-carboxylic acid was 32.05% , and 2,3 diphenyl-6-sulfamoylquinoline-4-carboxylate was 44.72% , for 2-(furan-2-yl)-3-phenyl-6-sulfamoylquinoline-4-carboxylic acid was 33.75% , for ethyl2-(furan-2-yl)-3-phenyl-6-sulfamoylquinoline-4-carboxylate was 46.62% ,

And the weights in grams were : 3 , 2.1754 , 0.3692 , 0.5412 respectively.
References:

- Quinoline. Encylopaedia Britannica. 1911.