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SYNTHESIS AND HARACTERIZATION OF QUINOLINE DERIVATIVES CATALYSED BY β-CYCLODEXTRINE

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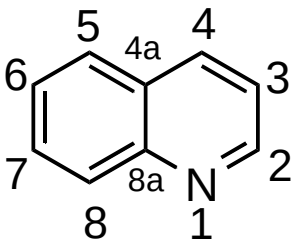
Abstracts: Synthesis of substituted quinolines has been accomplished in a one-pot reaction from an aryl amine, aryl aldehyde and a pyruvic acid using beta dextrin as a catalyst.

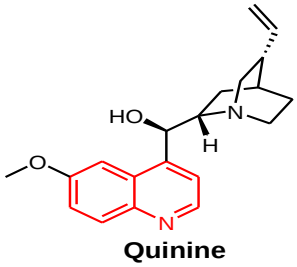
Keywords*:* Quinoline, aromatic aldehyde, beta cyclodextine.

Introduction:

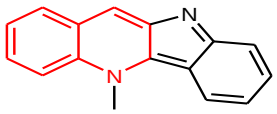
Quinoline is a heterocyclic aromatic organic compound having molecular formula C9H7N, characterized by a double-ring structure that contains a benzene ring fused to pyridine at two adjacent carbon atoms.

Quinoline is also known as, **benzopyridine**, **benzo[b]pyridine**, **1-benzazine** and **benzazine**. It is a hygroscopic, yellowish oily liquid, slightly soluble in water, soluble in alcohol, ether and many other organic solvents.

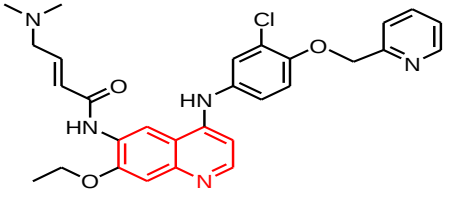




Quinine



Cryptolepine



Neratinib

Quinoline as anti-cancer agents:

Cancer is one of the second leading causes of mortality. It is of great concern to mankind. Due to negative lifestyle and food habits people are prone to cancer risk, more and more people around the globe are diagnosed with this disease.[1,2] Therefore, the discovery and development of promising new antitumor agents with high efficiency and low toxicity to healthy cells and tissues have become urgent and are key focuses of pharmaceutical chemists worldwide. To acheive this goal, a great deal of attention is being focused on molecules that act synchronously on multiple targets by combining two/more active pharmacophores covalently in a single-hybrid molecule with dual/multiple antitumor effects.[3,4]

Quinoline and its derivatives display a variety of powerful biological activities including inhibition of cellular proliferation and developmental changes,[5–7] which make the quinoline ring a valuable versatile synthetic scaffold for new antitumor agents. Among the various existing active scaffolds of quinolines, chloroquinoline is a type of alkaloid, which is as abundant as quinoline. Previous studies have indicated that chloroquinoline derivatives display preferable biological activities such as anticancer and antiproliferation activities.[8,9]

Chloroquinoline scaffold is thus chosen in the present study as an active antitumor pharmacy core, and some structural modifcations are designed to explore the antitumor activity. In addition, a bicyclic compound, namely, benzimidazole, which is the fusion of benzene and imidazole, which act as a pharmacophore possessing wide range of biological activities.[10]

EXPERIMENTAL

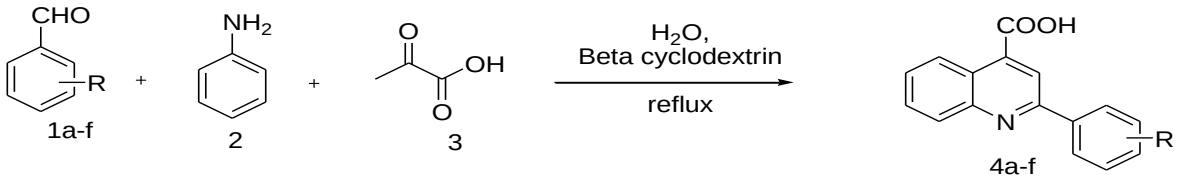
Solvents were employed as commercial anhydrous grade. The column chromatography was done over the silica gel (100-120 mesh). Melting points were determined in open capillary tube and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker advance II-400 MHz spectrometer. The molar conductivity measurements of complexes in (1 × 10−3 M) DMSO solution were measured at 25 ^{0}C with a Bibby conduct meter.

Material and Methods:

All solvents were labouring as commercial anhydrous mark without further Refining. The column chromatography was carried out over silica gel (100120esh). Melting points determined by open capillary tube. ^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer in DCl3 solvent TMS as internal standard. The crude product was recrystallizing from 80 percentage ethanol.

General procedure for the Synthesis of substituted Quinoline (4a-f) :

Substituted aromatic aldehyde (1 mmol), pyruvic acid (1.1 mmol) and aniline (1 mmol) were taken in the rbf ,water was used as a solvent and Beta cyclodextrin as a catalyst. Then the mixture was stirred for 10 to 24 hours under refluxing. On completion of the reaction (monitored by TLC), water was poured to the mixture and the formed precipitate was filtrated, washed with water several times and dried to yield substituted quinoline derivatives 4a-f. The compound was identified by IR and ^{1}H NMR. Compound also purify by silica gel column chromatography eluent ethyl acetate hexane reaction was. Monitored by TLC & spot were visualized in iodine.



1a	Benzaldehyde
1b	4-Chlorobenzaldehyde
1c	4-OMe Benzaldehyde
1d	2-NitroBenzaldehyde
1e	3-NitroBenzaldehyde
1f	4-NitroBenzaldehyde

1a	2-Phenylquinolone-4-carboxylic acid
1b	2-(4-ChloroPhenyl)Quinoline--4-carboxylic acid
1c	2-(4-methoxyPhenyl)Quinoline--4-carboxylic acid
1d	2-(2-NitroPhenyl)Quinoline--4-carboxylic acid
1e	2-(3-NitroPhenyl)Quinoline--4-carboxylic acid
1f	2-(4-NitroPhenyl)Quinoline--4-carboxylic acid

Scheme: 1

Table 1. Synthesized derivatives of 2-Phenylquinoline-4-carboxylic acid

Sr. No.	Name	M. Formula	M. Weight	M. P °C	Time (Hrs)	Yield % [b]
1	2-Phenylquinoline-4-carboxylic acid	$C_{16}H_{11}NO_2$	249.264	208	24	60
2	2-(4-ChloroPhenyl) quinoline-4-carboxylic acid	$C_{16}H_{10}ClNO_2$	283.709	234	30	55
3	2-(4-methoxyPhenyl)quinoline-4-carboxylic acid	$C_{17}H_{13}NO_3$	279.29	220	24	55
4	2-(2-NitroPhenyl)quinoline-4-carboxylic acid	$C_{16}H_{10}N_2O_4$	294.262	244	24	60
5	2-(3-NitroPhenyl)quinoline-4-carboxylic acid	$C_{16}H_{10}N_2O_4$	294.262	190	10	50
6	2-(4-NitroPhenyl)quinoline-4-carboxylic acid	$C_{16}H_{10}N_2O_4$	294.262	198	26	45

Table 2. Spectral Data of Synthesised 4a, 4b, 4c of 2-Phenylquinoline-4-carboxylic acid derivatives:

Compound	IR	^{1}HNMR
4a	1540 cm^{-1} for C=N Stretch, 1690 cm^{-1} for C=O Stretch, 2870 cm^{-1} for C-H Stretch, 3260 cm^{-1} for O-H Stretch,	δ7.35 – 9.11 m for 10H (Ar-H), δ 10.44 S for 1H (– COOH)
4b	715 cm^{-1} for C-Cl Stretch, 1580 cm^{-1} for C=N Stretch, 1730 cm^{-1} for C=O Stretch, 2910 cm^{-1} for C-H Stretch, 3320 cm^{-1} for O-H Stretch,	δ7.89 – 10.56 m for 10H (Ar-H), δ 11.44 S for 1H (– COOH)
4c	1150 cm^{-1} for C-O Stretch, 1460 cm^{-1} for C=N Stretch, 1650 cm^{-1} for C=O Stretch, 2840 cm^{-1} for C-H Stretch, 3230 cm^{-1} for O-H Stretch,	δ 2.5 s for 3H δ7.22 – 9.36 m for 10H (Ar-H), δ 10.02 S for 1H (– COOH)

Result and Discussion

In summary, irrespective of mechanism, we have developed an efficient and general route to 2-Phenylquinoline-4-carboxylic acid in a one-pot synthesis from an aryl amine, an aldehyde and a pyruvic acid. This methodology appears very attractive for a combinatorial synthesis of quinolines for which exertions are in progress in our laboratory. All the Synthesised Compound will screened for their biological activity.

Conclusion:

The quinoline ring system is found in medicinal plant alkaloids and constitutes a key structural component of pharmaceuticals, agrochemical, dyestuffs, and materials. Because of its unique pharmaceutical importance, a continuous development in the synthesis of new quinoline derivatives is a growing area research. An impressively diverse range of efficient quinoline synthesis based on new metal-catalyzed coupling cyclizations or acid catalyzed cycloaddition of appropriate precursors have been developed during past years that proves practical importance of this heterocyclic system. However, having a plethora of new synthetic methods for preparing quinoline derivatives including classical syntheses, a clean, efficient, large-scale and cheap technology is still needed to obtain useful polyfuntionalizated quinolines.

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