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Research Article

Retro Synthetic Approach on Synthesis of Quinoline Derivative Using Microwave Energy

S Ravichandran[1]*, Sayeeda Sultana[2], G Jagadeeswarao[2] and S Suresh[3]

[1]*Department of Chemistry, Lovely Professional University, Punjab, India*

[2]*St Peter's Institute of Higher Education and Research, Avadi, Chennai, India*

[3]*Department of Chemistry, St. Martin's Engineering College, Secunderabad, India*

***Corresponding Author:** S Ravichandran, Department of Chemistry, Lovely Professional University, Punjab, India.

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Abstract

In the present study an attempt has been made to synthesize quinoline derivative by retrosynthetic method. The fact that every synthesis involves different routes and is reflected in the property of final product The present work replaces conventional heating method by microwave energy to isolate substituted quinolines. The reterosynthesised material is subjected to characterization by spectral techniques and its anti-microbial activities has also been evaluated. Results obtained clearly indicates that retrosynthetic product scores over conventional heating procedure in respect of its purity and anti-microbial activity.

Keywords: Retrosynthetic Products; Quinoline; Antimicrobial Activity

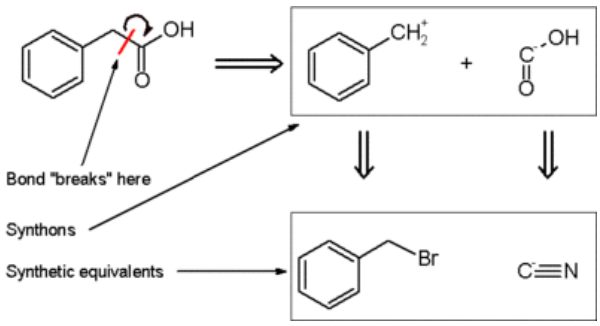
Introduction

Retrosynthetic analysis

Retrosynthetic analysis is a technique for solving various problems in the planning of organic synthesis. Quinoline is a Nitrogen containing heterocyclic aromatic compound which has many biological activities like Antimalarial, Analgesic, Anti-inflammatory, Antineoplastic, Antibacterial, Antifungal, Antiviral activity etc. From the survey of existing literature [1-32], synthesis of quinoline is being reported. Every synthesis is having specific syntheticroute. Retro synthesis is a technique for planning of organic synthesis thus discovering different synthetic routes.

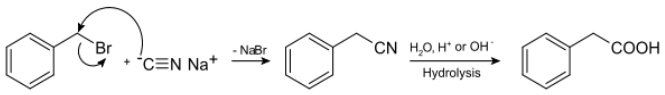
Synthon

A generalized fragment, usually an ion, produced by a disconnection which cannot itself be used, because it is too unstable.



$PhCH_2Br + NaCN \rightarrow PhCH_2CN + NaBr$

$PhCH_2CN + 2\ H_2O \rightarrow PhCH_2COOH + NH_3$



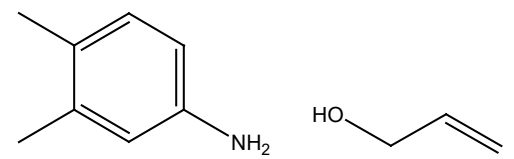
In the present attempt quinoline derivatives are prepared by retro synthetic method instead on conventional heating method. Suitable synthetic equivalents are employed as a source materials. Conventional method takes 2-3 hours which consume lot of fuels. Therefore, in the present study Microwave energy is utilized to heat the reactants using micro-oven. 3,4- dimethyl aniline and acrolein were heated in a micro oven and the product obtained was characterized by analytical methods including melting point, UV-Visible spectrum and Infra-red spectrum.

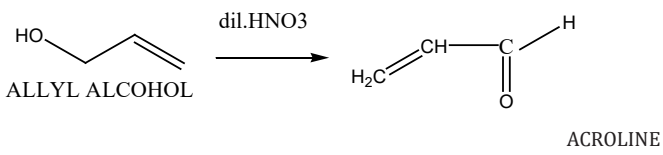
Experimental Methods

Preparation of reaction mixture

4g of 3,4- Dimethyl Aniline was dissolved in 50 ml of acetic acid and 5.8 ml (1 mole) of this solution was taken in a glass beaker and equal molar allyl alcohol (1 mole), 10 ml of 10% dilute nitric acid and 2 ml of concentrated sulphuric acid were added to it. This mixture was kept in a microwave oven with 17% output and subjected to micro wave radiation for 2 minutes. The completion of reaction was verified by TLC. The microwave reaction was continued further two more minutes (totally 4 minutes) and continued the TLC process. Similarly, the heating and TLC identification was carried out for 6 minutes and 8 minutes too. The solution was filtered and the yield was recrystallized using ethanol.

Synthetic equivalents





Disc diffusion method

When a filter paper disc impregnated diffusion will take place into chemical on the agar only around the disc. The solubility of the chemical and its molecular sizes how's the area of chemical infiltration on the disc is known as a "zone of inhibition". Antiseptics are used on living tissue to remove pathogens. When performing disc diffusion susceptibility test certain things are held constant and inhibition is variable. The quantity of organism used is standardized by turbidity standard and incubation is at 35-37°C in ambient air for 24 hours. The Mueller-Hinton agar method is well documented and standard zones of inhibition found for susceptible values. There is also a zone of intermediate resistance indicating that some inhibition occurs using this antimicrobial but it may not be sufficient inhibition toeradicate the organism from the body. The chemical under consideration is used to saturate a filter paper disc. This disc is then used to introduce the chemical to the agar for testing. The actual zone sizes have not been standardized as in the Kirby-Bauer method, but a comparison of zone sizes for the same chemical among organisms will provide a n approximate effectiveness of the chemical.

Results and Discussion

Synthesis of many substituted quinoline by conventional heating methods have been reported. Every synthesis is having more than one possible synthetic route. Retro synthesis is a technique for planning of organic synthesis thus discovering different synthetic routes. In the present attempt, quinoline derivatives are prepared by retro synthetic method using microwave radiation instead of conventional heating method. Suitable synthetic equivalents are employed as a source material. 3,4- Dimethyl aniline and acrolein were heated in a micro-oven and the product obtained was identified by TLC. The product was characterized by analytical methods such as UV- Visible and Infra-red spectrum. Its melting point was found out.

UV-Visible spectrum

The UV-Visible spectrum of the product 5,6 dimethyl quinoline was recorded using Labtronics UV Visible Spectrophotometer (Range 200-1000 nm) using ethanol as solvent and is shown in Figure 1. It showed two prominent peaks at λ_{max}=276.95 nm and λ_{max}= 314.19 nm, indicating the ($n \rightarrow \pi^*$) electronic transition at the higher energy region and a ($\pi \rightarrow \pi^*$) electronic transition in the lower energy region as expected for the product.

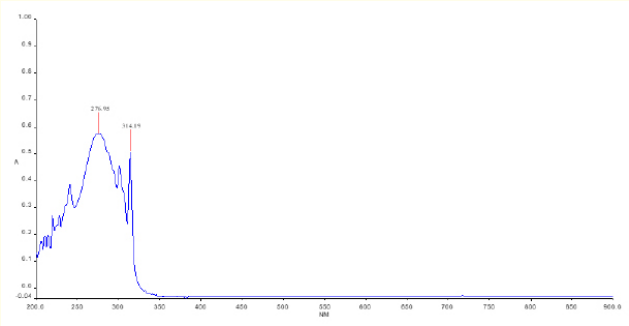


Figure 1: UV-Visible spectrum of 5,6 dimethyl quinoline IR spectrum.

The IR spectrum of the product 5,6 dimethyl quinoline was recorded and is shown in Figure 2. It showed the following characteristic peaks for the product as expected.

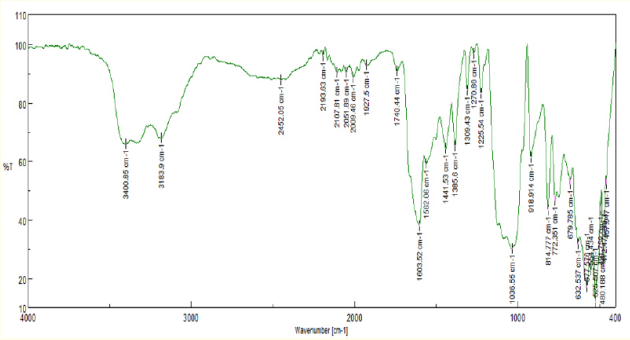
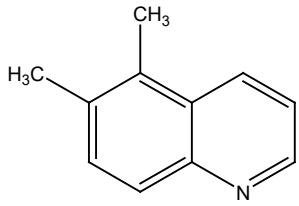


Figure 2: IR Spectrum of 5,6 dimethyl quinoline.

S. No	IR absorption frequency in cm^{-1}	Corresponding bond	Type of vibration
1	1036	C-N	Stretching
2	1603	C=C	Stretching
3	1603	C=N	Stretching
4	1441	Aliphatic C-H	Bending
5	3183	Aromatic C-H	Stretching
6	3400	N-H	Stretching
7	918	C-H	Bending

Table 1: Band assignments - IR spectrum of 5,6 dimethyl quinoline.



5,6-di methyl quinoline

The analytical characteristic studies support the following structure

Kirby-Bauer Antimicrobial Susceptibility Test

Organisms to be tested: *Staphylococcus aureus, E. coli.*

Procedure

- Plate culture got developed for the sample organisms.
- It was mixed thoroughly and made sure that no solid material from the colony was visible.
- This procedure was repeated until the turbidity of the saline solution matches that of the standard available.
- The swab was dipped into the broth culture of the organism. And it was gently squeezed the swab against the inside of the tube to remove excess fluid. The swab was used to streak a Mueller-Hinton agar plate or a nutrient agar plate for a lawn of growth. It was best accomplished by streaking the plate in one direction, then streaking at right angles to the first streaking, and finally streaking diagonally.
- The plates were allowed to dry for about 5 minutes.

Dispenser method

- Dispenser was made containing the correct antibiotic disks for the test sample of organism.
- It was emulsified using a sterile loop in the sterile saline solution.
- Dispenser was placed over the surface of the plate.
- The disks used gently pressed onto the surface of the agar, taking care not to press them into the agar.
- The plates incubated for 24hours at 37° C.

- The zone of inhibition for each antibiotic were measured using metric ruler.
- The collected data are furnished in the following table 2a and 2b.

Species	100 mg	200 mg	500 mg
E. coli	16.63	18.2	20.5
Staphylococcus Aureus	1.2	4.3	4.7

Table 2a: Zone of Inhibition.

Species	100 mg	200 mg	500 mg
E. coli	22.3	25.6	28.2
Staphylococcus aureus	2.3	4.1	9.1

Table 2b: Zone of Inhibition.

Standard: Chloramphenicol

The antibacterial activity of the microwave assisted synthesized compound was tested for a gram negative bacteria (*E. coli*) and gram positive bacteria (*staphylococcus aureus*), using chloramphenicol as standard by disk diffusion method. The zone of inhibition for *E. coli* bacteria was measured in mile meter for different concentration of the sample. The zone of the inhibition for various concentration for the sample was tabulated as above. From the table it is clear that the synthesized compound has antibacterial activity significantly from 100mg onwards.

Summary and Conclusion

Quinoline derivative synthesized by retrosynthetic method. The yield percentage was calculated and compared with that of conventional heating methods. It is concluded the microwave radiation can be utilized for synthesis of quinoline derivatives in better yield than conventional heating methods. The antibacterial activity of the synthesized compound was tested against *E. coli* and *Staphylocaccusaureus* using chloramphenicol as standard by disk diffusion method. It is also reveals that the zone of inhibition linearly varies with concentration. Hence the present project work has wider scope for still more findings.

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