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Efficient Multi-component Synthesis of New Quinolines Derivatives †

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Abstract: Quinolines have become important compounds because of their variety of applications in medicinal, synthetic organic chemistry and industrial chemistry. In recent years there are greater societal expectations that chemists should produce greener and more sustainable chemical processes. Multi-component reaction (MCRs) are useful methods for the construction of nitrogen heterocyclic compounds, syntheses of quinoline derivatives via MCRs have attracted considerable attention. In this work, we present the synthesis of new series of quinoline derivatives with good yieldsvia One-pot three-component reaction including aniline derivatives, malononitrile, and aromatic aldehydes using mild conditions.

Keywords: heterocycles; quinoline derivatives; multi-component reaction

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1. Introduction

Heterocyclic compounds constitute the largest and most varied of organic compounds and have a role in most fields of science such as medicinal chemistry, biochemistry, and other sciences [1]. There are a lot of heterocycle compounds, especially Nitrogen-heterocyclic [2], which represent a wide class of organic molecules broadly distributed in nature and generally known for their ability to attract biological and therapeutical properties within this class quinoline [3].

Quinoline scaffold is one of remarkable nitrogen-containing bicyclic compounds that are widely found throughout nature in various form shave [4], recently attracted a lot of attention due to their uses in the areas of medicine, food, catalysts, dyes, materials, refineries, electronics, etc. Furthermore, the quinoline core exhibits several biological and therapeutical activities [5–6] as anti-tuberculosis [5], anti-malarial [6], anti-microbial [7], anti-cancer [8], anti-viral [9], and anti-inflammatory [10].

Due to the inherent biological importance of quinoline derivatives and their various medicinal and commercial applications, a multitude of methodologies were investigated for their synthesis [10].

In our work, we describe a simple and convenient protocol for the synthesis of quinoline derivatives (Figure 1) via One-pot multi-component reaction.

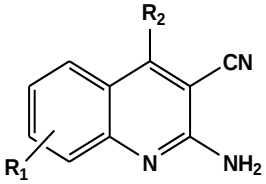
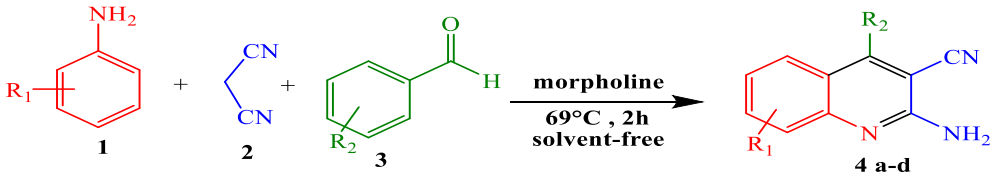


Figure 1. General structure of quinoline derivatives.

2. Results and Discussion

In this paper, we report a general and efficient One-pot three-component synthesis of new series of substituted quinoline derivatives **4a–d**, utilizing aniline derivatives **1**, malononitrile **2**, and aromatic aldehydes **3**in the presence of morpholine as base and under solvent–free conditions at high temperature, this strategy led to the quinoline derivatives in good yields. The structure of the synthesized compounds was confirmed by spectroscopic analyses (Table 1).

Table 1. Synthesis of quinoline derivatives **4a–d.**



R_1	R_2	Yields %
H	H	61
	4-NO_2	73
2,4-Cl	4-NO_2	56
	OH	53

The synthesized compounds **4a–d** were obtained with good yields and were confirmed by spectral analysis. The IR spectra (KBr, ν, cm^{-1}) showed the appearance of CN at 2218–222 cm^{-1} and NH_2 at 3361-3377 cm^{-1}, the $_1H$ NMR showed the appearance of NH_2 stretch at δ_H 6-6.2 ppm and OH stretch at 10.9-11.1 ppm.

3. Experimental Procedures

The products **4a-d** was prepared using aniline derivatives (0.01 mol), malononitrile (0.01 mol) and aromatic aldehydes (0.01 mol), the reaction mixture heated and stirred at 69 °C during 2 h, the progress of the reaction is monitored by TLC, the mixture is cooled, a precipitate is formed, the latter is filtered and washed with diethyl ether and ethanol and dried under reduced pressure.

4. Conclusion

In the summary, we have developed a novel, efficient, rapid, and environmentally friendly approach for the One-pot multi-component synthesis of new diversely quinoline derivatives with high yields, the present process includes some important advantages like easy operation mild reaction condition, facile accessibility of reactants, simple workup procedure.

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