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Microwave induced synthesis of 4-hydroxy-3-methyl-7, 8-dihydroquinoline-5(6H)-one using proline catalyst

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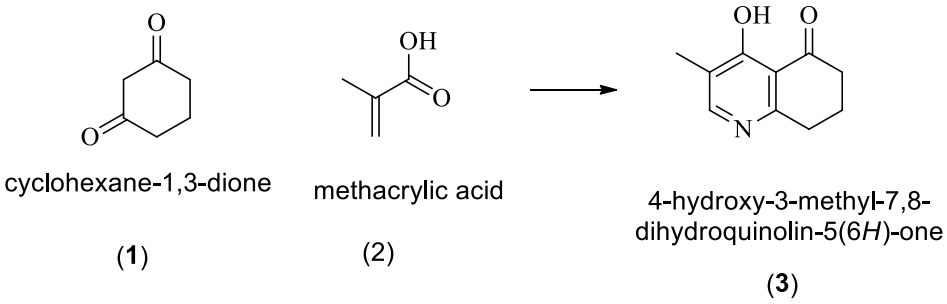
Abstract

In the present investigation synthesis of 4-hydroxy-3-methyl-7,8-dihydroquinolin-5(6H)-one was successfully demonstrated from cyclohexane-1,3-dione using microwave heating using proline catalyst. The synthesis of Hexa-Hydro-Quinolone derivatives, carried out by sequential in situ, Michael Addition, Cyclisation, and Aromatization. A new protocol for one step synthesis of 4-hydroxy-3-methyl-7,8-dihydroquinolin-5(6H)-one was successfully demonstrated from cyclohexane-1,3-dione with 98% yield.



cyclohexane-1,3-dione (**1**) + methacrylic acid (2) → 4-hydroxy-3-methyl-7,8-dihydroquinolin-5(6*H*)-one (**3**)

Keywords: Microwave reactions; Michael addition reaction; Quinolone; Proline

1. Introduction

The chemical formula of Benzo[b]pyridine or 1-azanaphthalene, or quinolone is C_9H_7N. The molecular weight of an aromatic nitrogen-containing heterocyclic molecule is 129.16. As an inert tertiary base, it reacts similarly to benzene and pyridine and forms salts with acids.

Quinoline pharmacophore is an important feature because it has been reported to have a wide range of pharmacological activities, including anticancer, antimalarial, antitubercular, antibacterial, antiprotozoal, antiproliferative, antitumor, anti-inflammatory, antifungal, antioxidant, DNA binding, antihypertensive, anti-HIV agents, and anti-HIV agents for the treatment of lupus and neurodegenerative diseases[1-9].

A variety of quinoline derivatives considerably support the development of organic synthesis along with their use in medicinal chemistry. The development of hybrid quinoline scaffolds has recently occurred by scientists, utilizing various techniques and molecules including other heterocyclic chemicals. For instance, modified named processes can be utilized to create a variety of noble and useful quinoline derivatives employing multicomponent one-pot synthesis,

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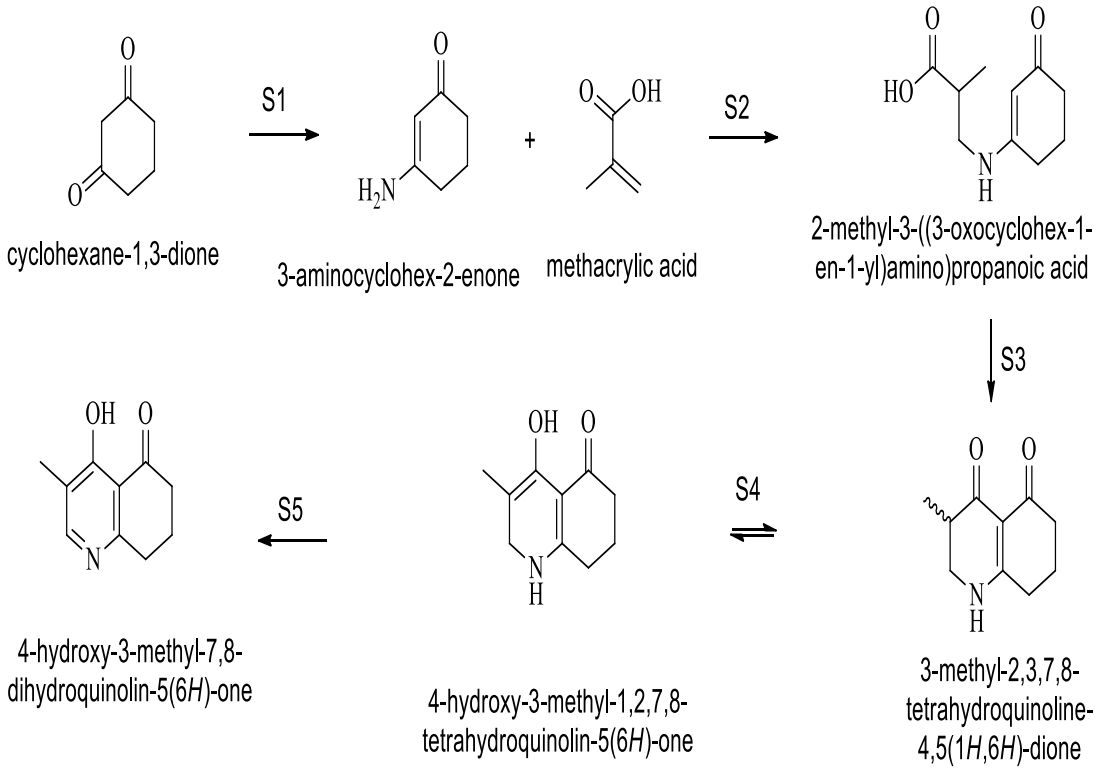
ultrasonic irradiation, or metal-free or transitional metal-catalyzed processes. Now a day's research examines environmentally friendly reaction processes as well as the production of quinoline and its byproducts. Common solvent-free, ionic liquid- and metal-free aqueous media-catalyzed processes are examples of green methods. Quinoline and its derivatives have shown potential in treating a variety of human diseases, including cancer, malaria, fungal infections, and bacterial infections.

2. Synthesis of 4-hydroxy-3-methyl-7,8-dihydroquinoline-5(6H)-one



Where:
S1: In Situ Amination: Heat/Ammonium Acetate/MW
S2: In Situ Microwave assisted Proline catalyzed Michael addition: Proline (1%)/MW
S3: In Situ Microwave assisted Proline catalyzed cyclisation: MW
S4: In Situ Tautomerisation: MW
S5: In Situ Aromatization: MW

As shown above the synthesis of Hexa-Hydro-Quinolone derivatives, carried out by sequential in situ, Michael Addition, Cyclisation, and Aromatization.

- Ammonium acetate on MW-heating with cyclohexane-1, 3-dione (S1), provides, 3-aminocyclohex-2-enone which on microwave assisted Proline catalyzed addition (S2) with Methacrylic acid yields, an adduct 2-methyl-3-((3-oxocyclohex-1en-1-yl) amino) propanoic acid.
- This adducts on heating under Microwave irradiation, undergoes cyclo-addition (S3) to get 3-methyl-2,3 7, 8-tetrahydro quinoline-4, 5(1H, 6H)-dione. This intermediate can be used as scaffold.
- 3-methyl-2,3 7, 8-tetrahydro quinoline-4, 5(1H, 6H)-dione, scaffold on derivatization yields, 4-hydroxy-3-methyl-1,2,7,8-tetrahydro quinoline-5(6H)-dione and 4-hydroxy-3-methyl-7,8- dihydroquinolin-5(6H)-one, as shown in the reactions S4 and S5.

2.1. Practical Details

The solution of cyclohexane-1,3-dione (1) (1.15 g, 10 mol) in THF (100 mL) Ammonium Acetate (1 g, 10 mole, 1 eq) had been administered at 0 °C & agitated at the room temperature. Following half an hour, methacrylic acid (0.8 g, 10 mol, 1eq.) and catalytic amount of Proline (1 mole %) had been incorporated and reaction continued with microwave

irradiation for 20 min. TLC tracked the reaction's development. ^{1}H NMR spectra of 4-hydroxy-3-methyl-7,8-dihydroquinolin-5(6H)-one were recorded Bruker AC 200 using $CDCl_3$.

3. Conclusion

A new protocol for one step synthesis of 4-hydroxy-3-methyl-7, 8-dihydroquinolin-5(6H)-one was successfully demonstrated from cyclohexane-1, 3-dione with 98% yield.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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