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GREEN SYNTHESIS OF SOME QUINOLINE DERIVATIVES: A REVIEW

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ABSTRACT

Microwave assisted organic synthesis has emerged as a new “lead” in field of organic synthesis which makes the chemistry to follow approaches of green chemistry. The green chemistry links with safer approaches for process and product development. This technique has provided the excellent momentum for many chemists to switch from conventional methods to microwave assisted chemistry. There has been a dramatic uptake in the use of microwaves as an energy source to promote synthetic transformations. Microwave-assisted synthesis is clearly a method by which the medicinal chemist can achieve goals in a lesser fraction of the time as compared to traditional conductive heating methods. In the present article an attempt was made to focus on basics of microwave assisted synthesis and its improvisations in recent synthetic development of quinolone derivatives. Quinoline is one of the most important N-based heterocyclic aromatic compounds. Quinoline recently is one of the priorities in lead selection by researchers because of its broad range of activities and also for their wide applications.

KEYWORDS: Green Chemistry, Microwave, Quinoline, microwave irradiation, Microwave energy.

INTRODUCTION

Microwave synthesis is a method which is used as the source of heating in the organic synthetic reactions. Many organic reactions *can* be conducted very rapidly under microwave irradiation was demonstrated by Gedye et aL4 and Giguere et al.5 In 1986.[1] Microwaves are in the form of electromagnetic energy which lies in electromagnetic spectrum which corresponds to wavelength of 1cm to 1m and frequency of 30GHz to 300MHz .This places it between infrared radiation and radiowaves. For the industrial applications the typical bands are 915±15 and 2450 ±50 MHz The shorter wavelength in the range 1-25cm is for radar, whereas remaining section are devoted to telecommunication. The entire microwave region is therefore not available for heating applications and equipment operating at 2.45GHz is most commonly used. Microwave energy consist of both electric as well as magnetic field.[2] The difference between microwave energy and other forms of radiation, such as X- and γ-rays, is that microwave energy is non-ionizing and therefore does not alter the molecular structure of the compounds being heated – it provides only thermal activation. Dielectric polarization causes the heating effect utilized in microwave assisted organic transformations. When a molecule is irradiated with microwaves, it aligns itself with the applied field. The rapidly changing electric field (2.45 x 109 Hz) affects the molecule and consequently the molecule continually attempts to align itself with the changing field and energy is absorbed.[3]

Advantage

Uniform heating occurs throughout the material

Process speed is increased

High efficiency of heating

Reduction in unwanted side reaction

Purity in final product

Improve reproducibility

Environmental heat loss can be avoided

Disadvantages

Heat force control is difficult

Closed container is difficult because it could burst

In-situ monitoring

Expensive setup MV4

In the early **1970s** the first application in chemical research was reported**,** when gas-phase discharge was applied to realise decomposition of simple organic compound. By the early **1980s,** two patents had appeared concerning polymer chemistry and one concerning starch derivatisation.[4]

The present review article will give an idea about microwave assisted synthesis of quinoline derivatives.

Quinoline is one of the most important N-based heterocyclic aromatic compounds. Quinoline recently having the attention of researchers because of their broad range of activities and also for their wide applications.[5]

The main sources of quinoline include petroleum, coal processing, wood preservation and shale oil. The quinoline derivatives occur in various natural products, especially in alkaloids. In 1820, quinine (1) was isolated from the bark of the cinchona tree which replaced the use of crude bark for the treatment of malaria.[6]

Silvia E. Asis et.al proposed a series of substituted quinolines was developed by the Friedlander reaction employing microwave irradiation (MW), in the presence of a catalytic amount of hydrochloric acid in 1.5–12 min. The products were obtained in good yield.[7]

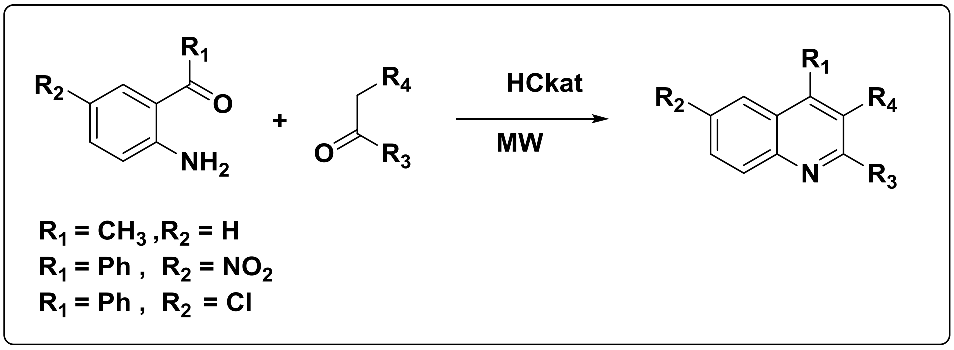


Figure 1.

Tae Woo Kwan et.al was synthesized a minilibrary of 12 quinoline derivatives in the presence of 0.1–0.5 equiv. of diphenyl phosphate in solvent free condition. Each compound was obtained with high yield in 4 min of microwave irradiation.[8]

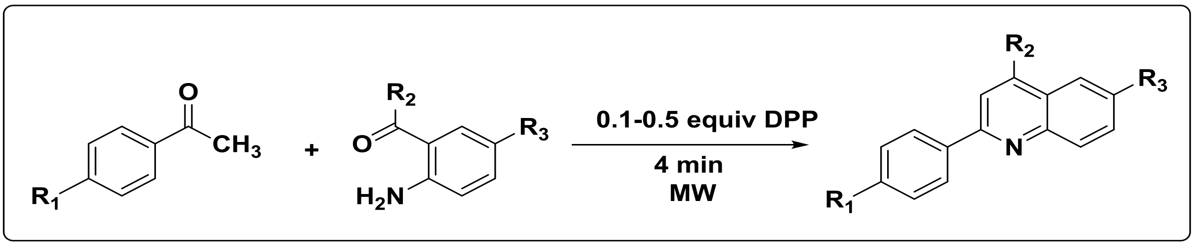


Figure 2.

The microwave procedure for 2,4-diphenylquinoline: Acetophenone (0.36, 3.0 mmol), 2-aminobenzophenone (0.59 g, 3.0 mmol) and 0.5 equiv. of DPP (0.38 g, 1.50 mmol, purchased from Aldrich) were mixed in the absence of any organic solvent and then submitted to microwave irradiation for 4 min inside a domestic microwave oven (Sam Sung, RE-555 TCW).[9]

Brindaban C. Ranu et.al proposed the synthesis of quinolines and dihydroquinolines a convenient and efficient procedure has been developed by a simple onepot reaction of anilines with alkyl vinyl ketones on the surface of silica gel impregnated with indium(III) chloride under microwave irradiation without any solvent.[10]

The microwave procedure for the synthesis of 4,6-dimethylquinoline: A mixture of 4-methyl aniline (214 mg, 2 mmol) and methyl vinyl ketone (175 mg, 2.5 mmol) was added to silica gel impregnated with indium(III) chloride (132 mg, 0.6 mmol) and it was prepared by adding a solution of $InCl_3$ in minimum amount of THF to silica gel (HF254, E-Merck, which is activated by heating for 3 h at 150°C under reduced pressure) followed by complete evaporation of solvent under vacuum. Then the mixture was stirred for 5 min for uniform mixing and it was irradiated by microwave in a domestic microwave oven (BPL, India) at 600 W (50% of total power) for 10 min (5þ5 min with an intermission of 10 min in between) as required to complete the reaction (TLC).[11]

Noel S. Wilson et.al described a solid acid-catalyzed microwave-assisted synthesis of substituted quinolines. The quinolines were synthesized by a multicomponent domino reaction of anilines, aldehydes and terminal aryl alkynes. The reaction is catalyzed by montmorillonite K-10, a strong, environmentally benign solid acid. It yields the products with nearly 90% atom economy in excellent yields in a matter of minutes. The use of microwave activation reduces the reaction time significantly.

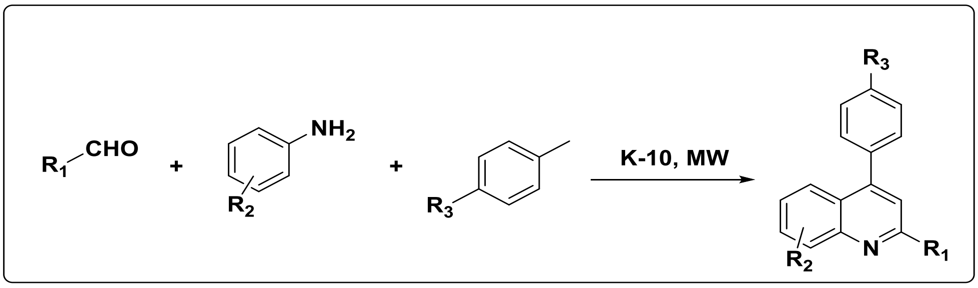


Figure 3.

Noel S. Wilson et.al suggest an improved method for the synthesis of 2-aminoquinolines utilizing microwave-assisted synthesis. The process involves rapid microwave irradiation of secondary amines and aldehydes to form enamines followed by the addition of 2-azidobenzophenones with subsequent irradiation to produce the 2-aminoquinoline derivatives.[12]

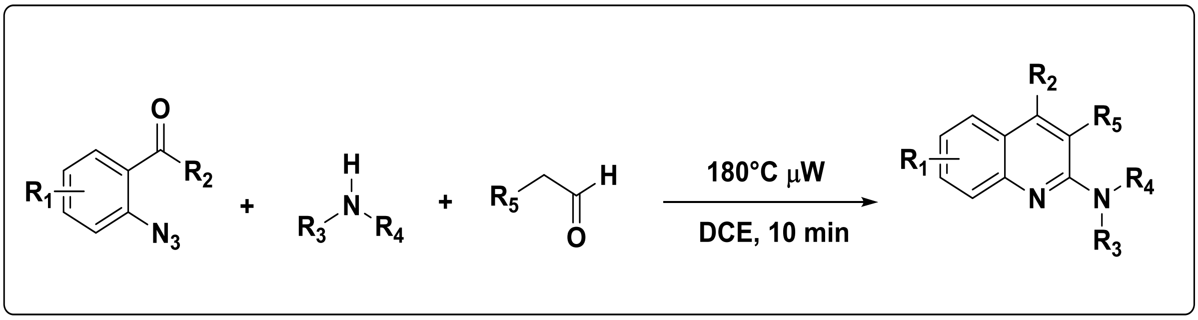


Figure 4.

Table 1.

Entry	R1, R2	R3, R4	R5	Yield (%)
1	4-Me, Ph	Me, Bz	4-Ethoxyphenyl	76
2	4-Me, Ph	Me, 3,4-Dimethoxyphenyl	4-Ethoxyphenyl	62
3	4-Me, Ph	Methylisonipecotate	4-Ethoxyphenyl	72
4	4-Me, Ph	4-Furoylpiperazine	4-Ethoxyphenyl	71
5	4-NO_2, Ph	Pyrrolidine	3,4-Dimethoxyphenyl	100
6	5-Cl, *o*-F Ph	Methylisonipecotate	2-Fluorophenyl	64
7	4-Br, *o*-F Ph	Morpholine	3,4-Dichlorophenyl	57

In a typical procedure, the enamine was prepared in situ by adding N-methylcyclohexylamine (1 mmol) and phenylacetaldehyde (1.1 mmol) to a Smith Process VialTM (glass vessel) containing 4 mL of DCE. The vial was sealed and the mixture was heated in the Smith SynthesizerTM microwave at 180°C for 3 min, cooled to room temperature, and added to a second capped Smith Process VialTM containing 2-azido-5-nitrobenzophenone9 (0.8 mmol). The mixture was then heated a second time in the microwave at 180°C for 7 min and cooled to room temperature. The crude mixture was purified by filtering through a Varian SCX cartridge with DCE or DCM as the eluent to remove the impurities followed by 1% HCl /MeOH to release the 2-aminoquinoline. The 1% HCl/MeOH fractions are combined and the solvent removed on a rotary evaporator to furnish the desired material as a solid.[13]

Brindaban C. Ranu et.al suggest a simple and efficient procedure for the synthesis of 4-alkylquinolines by a one-pot reaction of anilines with alkyl vinyl ketones on the surface of silica gel impregnated with indium(III) chloride under microwave irradiation without any solvent.[14]

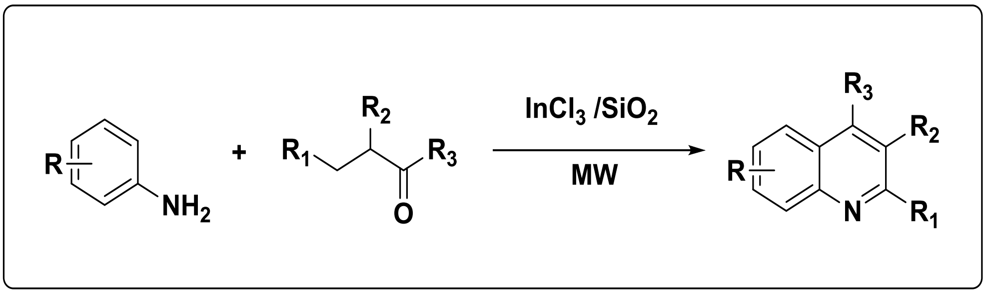
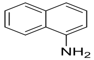
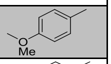
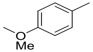


Figure 5.

Table 2.

Entry	Aniline R	R1	R2	R3
1	H	H	H	Me
2	o-Me	H	H	Me
3	*m*-Me	H	H	Me
4	*p*-Me	H	H	Me
5	*o*-Me	H	H	Me
6	*o*-OMe	H	H	Me
7	*p*-OMe	H	H	Me
8	*m*-OH	H	H	Me
9	*m*-Cl	H	H	Me
10	*p*-Cl	H	H	Me
11	*o*-Me, *p*-I	H	H	Me
12		H	H	Me
13	H	Me	H	
14	*m*-Cl	Me	H	
15	H	n-Pr	Et	Me

In a typical procedure, a mixture of aniline (1 mmol) and alkyl vinyl ketone (1 mmol) was added to silica gel impregnated with indium (III) chloride5 and the whole mixture was stirred for 5 min for uniform mixing. This mass was then irradiated by microwave in a domestic microwave oven at 600 W for a few minutes as required to complete the reaction. The reaction mixture was then eluted with ethyl acetate and the extract was washed with brine, dried over Na2SO4 and evaporated to leave the crude product which was purified by column chromatography over silica gel. Gram-scale reactions with 3–5 g of anilines (2.5 g of silica gel used per 1 g of aniline) have also been carried out in a few cases and found to give analogously good yields of corresponding products.[15]

Belalakatte P. Nandeshwarappa et.al proposed a novel and efficient method for the synthesis of substituted thienoquinolines. A simple one-pot reaction of 3-formyl-2-mercaptoquinolines with 1-chloroacetone, 2-chloroacetamide, ethyl chloroacetate and 2-chloro-1-phenylethanone in presence of catalytic amount of potassium carbonate under microwave irradiation and solvent-free conditions gave thienoquinolin-2-ylethanone derivatives thienoquinoline-2-carboxamide derivatives, ethyl thienoquinoline-2-carboxylate and phenyl(thienoquinolin-2-yl)methanone derivatives respectively.[16]

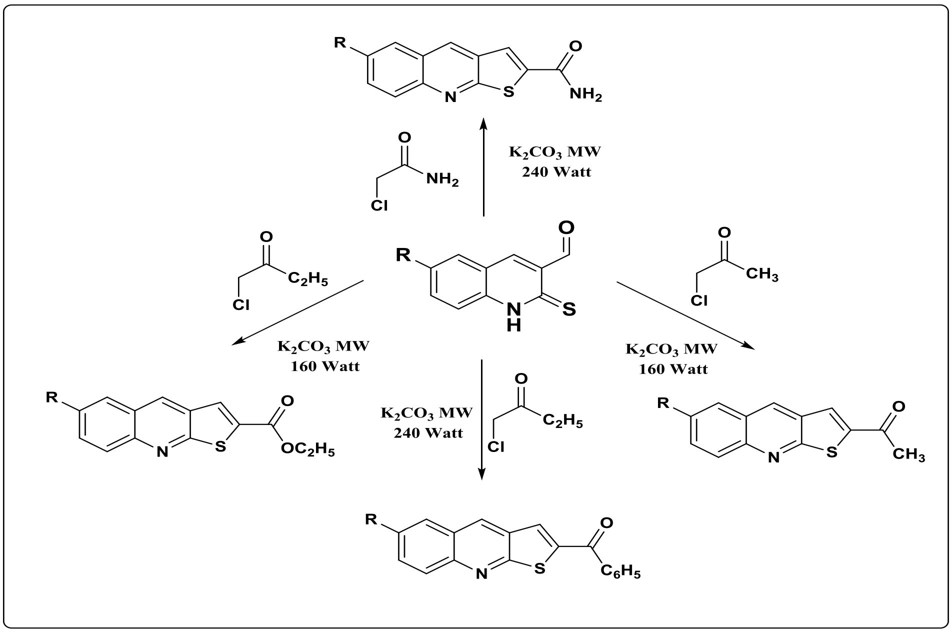


Figure 6.

A wide range of substituted thienoquinolines were prepared by treating 3-formyl-2-mercaptoquinolines with 1-chloroacetone, 2-chloroacetamide, ethyl chloroacetate and 2-chloro-1-phenylethanone in the presence of potassium carbonate under microwave irradiation as shown in scheme. 3-Formyl-2- mercaptoquinolines were prepared from 3-formyl-2-chloroquinolines. The structural elucidation of the newly synthesised compounds was established on the basis of their IR, 1H NMR and mass spectral data.[17]

3.1 Preparation of methyl ketones: A mixture of Starting material (1800 mg, 10 mmol), 1-chloroacetone (920 mg, 10 mmol) and potassium carbonate (690 mg, 10 mmol) were ground for uniform mixing. The mixture was then irradiated by microwave radiation in a domestic microwave oven for 10 min at an interval of 1 min at 160 Watt as required to complete the reaction (TLC). The reaction mixture was then poured into water, stirred, filtered and dried. The crude product was purified by column chromatography on silica gel with ethyl acetate-benzene (9:1) as eluent to gave 1900 mg.

3.7 Preparation of carboxamides: A mixture of Starting material (1800 mg, 10 mmol), 2-chloroacetamide (935 mg, 10 mmol) and potassium carbonate (690 mg, 10 mmol) were ground for uniform mixing. It was irradiated by microwave radiation in a domestic microwave oven for 8 min at an interval of 1 min at 240 Watt. The reaction mixture was poured into ice cold water, the resulting brown solid was collected by filtration, dried and recrystallized from ethyl acetate-chloroform (8:2) to provide desired product (1710 mg, 75%).

A mixture Starting material (1800 mg, 10 mmol), ethyl chloroacetate (1220 mg, 10 mmol) and potassium carbonate (690 mg, 10 mmol) were ground for uniform mixing. The mixture was irradiated by microwave radiation in a domestic microwave oven for 12 min at an interval of 1 min at 160 Watt as required to complete the reaction. The yellow solid was filtered off, washed with water and dried. The obtained product was purified by column chromatography on silica gel with ethyl acetate-chloroform (7:3) as eluent to gave 2133 mg (83%) of product.

Preparation of phenyl ketones: A mixture of Starting material (1800 mg, 10 mmol), 2-chloro-1-phenylethanone (1540 mg, 10 mmol) and potassium carbonate (690 mg, 10 mmol) were ground for uniform mixing. The mixture was then irradiated by microwave radiation in a domestic microwave oven for 8 min at an interval of 1 min at 240 Watt. The reaction mixture was then poured into water, stirred, filtered and dried. The crude product was recrystallized from DMF to provide 1900 mg (69%).

Shujiang Tu et.al developed a sequential three-component reaction of an aromatic aldehyde with an equimolar amount of 2-aminoanthracene and cyclic 1,3-dicarbonyl compounds (such as tetronic acid, 5,5-dimethyl,3-cyclohexanedione, 1,3- indanedione, 3H-chromene-2,4-dione, quinoline-2,4-dione and barbituric acid) in acidic medium under microwave irradiation. In this one-pot reaction, a series of unusual fused heterocyclic compounds, naphtho[2,3-]quinoline derivatives, were synthesized. This method has the advantages of operational simplicity, increased safety for small-scale fast synthesis, and minimal environmental impact. Most distinctively, this new class of naphtho[2,3-]quinoline derivatives exhibit good luminescent properties in the ethanol solution, which can be used potentially as organic electroluminescent (EL) media.[18]

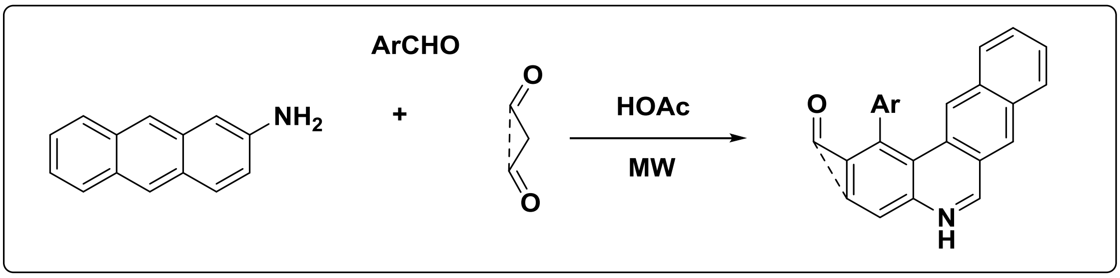


Figure 7.

General Procedure. The reactions were performed in a monomodalEmrys Creator from Personal Chemistry, Uppsala, Sweden. In a 10 mL Emrys reaction vial, aldehyde (0.05 mmol) and 2-aminoanthracene (0.05 mmol), with an equimolar amount of cyclic 1,3-dicarbonyl compounds separately (tetronic acid 3, 5,5-dimethyl-1,3-cyclohexanedione 5, barbituric acid 7, 3H-chromene-2,4-dione 9, quinoline2,4(1H, 3H)-dione 10, and barbituric acid 13) and glacial acetic acid (3 mol), were mixed and then capped. The mixture was irradiated for a desired time (monitored by TLC) at 200 W and at 120 °C. The reaction mixture was cooled to room temperature and then poured into water. The solid products were filtered, washed with water and EtOH (95%), and recrystallized from EtOH to give the pure products.[19]

Hitesh D. Patel et.al suggest that Quinolines have become important compounds because of their variety of applications in medicinal, synthetic organic chemistry as well as in the field of industrial chemistry. In recent years there are greater societal expectations that chemists should produce greener and more sustainable chemical processes. This review article gives information about the green and clean syntheses using alternative reaction methods for the synthesis of quinoline derivatives. The article includes synthesis by microwave, using clay or some other catalyst which could be recycled and reused, one-pot reaction, solvent-free reaction conditions, using ionic liquids, ultrasound promoted synthesis and photocatalytic synthesis (UV radiation).[20]

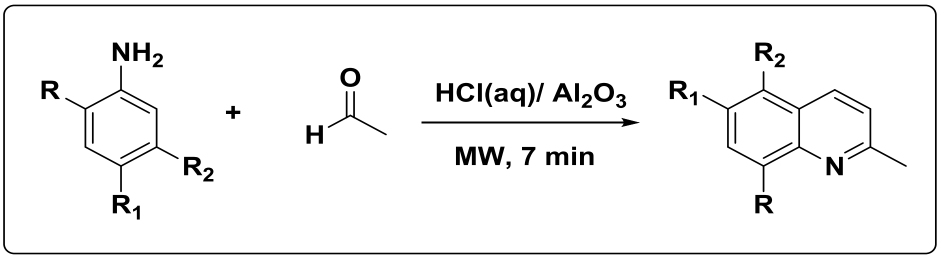


Figure 8.

Safari et al. described a procedure for preparation of quinaldine derivatives from aniline derivatives and acetaldehyde under microwave irradiation without any solvent. In this method they tried different Bronsted acids but found hydrochloric acid appeared to be the best catalyst for this reaction, showing the highest yield. Moreover the yield of the product was not affected by the nature of substituent in this reaction.[21]

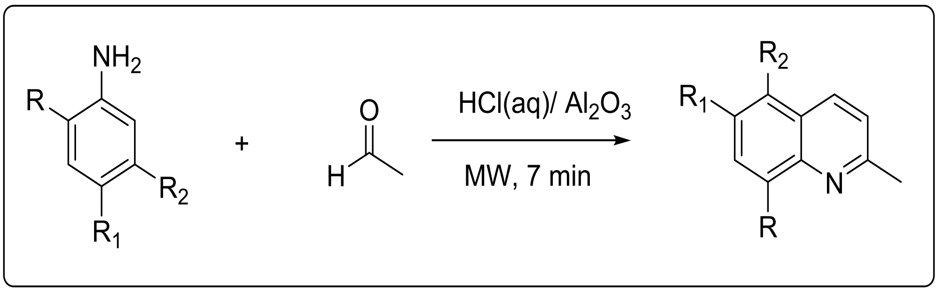


Figure 9.

Ranu et al. developed a simple and efficient procedure for the synthesis of 4-alkylquinoline derivatives by a one-pot reaction of anilines with alkyl vinyl ketones on the surface of a silica gel inseminated with indium(III) chloride under microwave irradiation without any solvent The main advantages of this procedure are: operational simplicity, fast reaction, high yield and general applicability. These advantages accommodate a variety of substitution patterns.[22]

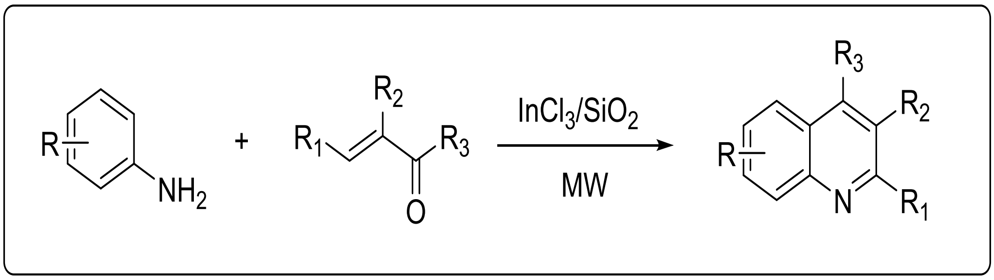


Figure 10.

Microwave-assisted solid acid-catalyzed syntheses of substituted quinoline derivatives have been discussed by Kulkarni and his colleagues. The quinoline derivatives were synthesized by a multicomponent reaction of anilines, aldehydes and terminal aryl alkynes. The reaction was catalyzed by montmorillonite K-10, a strong and environmentally benign solid acid. The multicomponent approach yields products with nearly 90% atom economy in excellent yields in a matter of minutes. The use of microwave activation reduces the reaction time signicantly.[23]

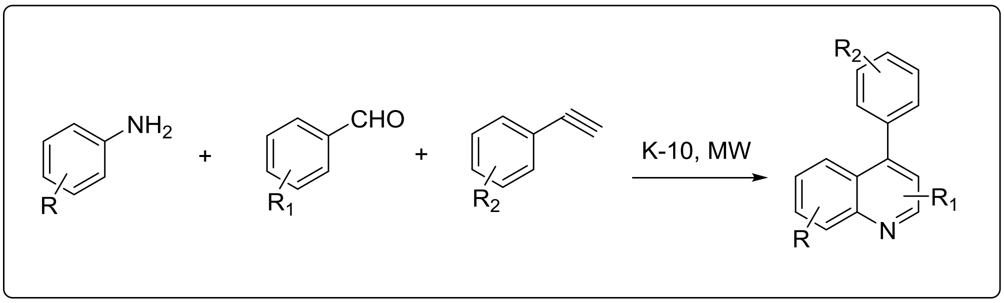


Figure 11.

Quinoline derivatives were synthesized by employing amino acetophenone and phenylacetylene in the presence of $Zn(OTf)_2$ as an effective catalyst under microwave irradiation, as presented by Praveen and co-workers.[24]

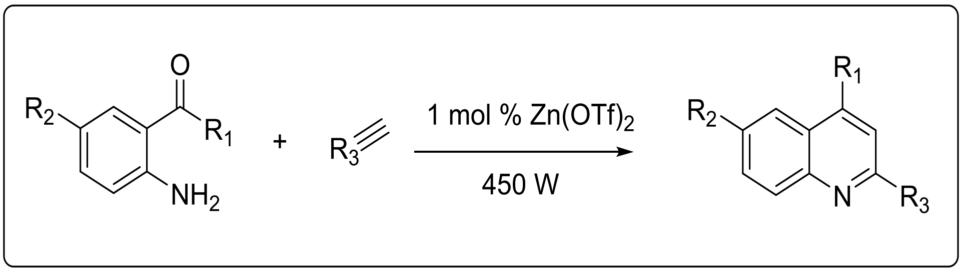


Figure 12.

Naik et al. have reported a rapid and efficient method for the synthesis of various carbonitrilequinoline/benzoquinoline derivatives by utilizing benzaldehyde, methyl cyanoacetate and aromatic amine with nanostructured TiO_2 photocatalysts under solvent-free conditions under microwave irradiation.[25]

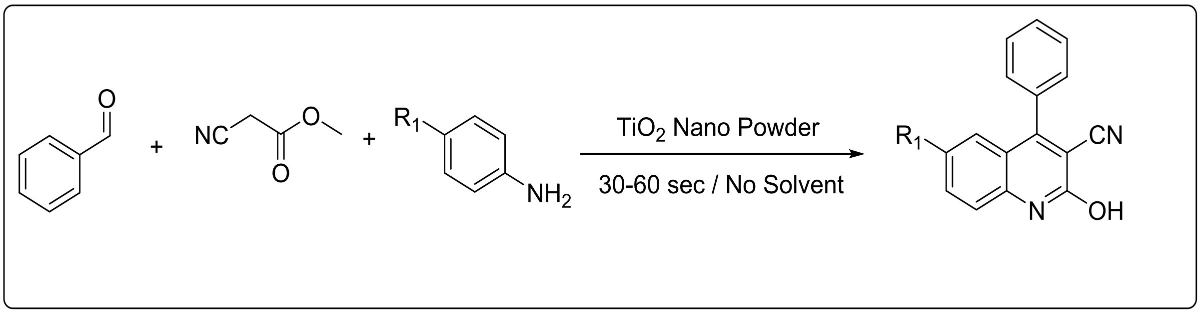


Figure 13.

3-Unsubstituted 4-hydroxyquinolin-2-one was synthesized using substituted aromatic amine and malonic acid under microwave irradiation in dimethylformamide, without employing any solvent and using polyphosphoric acid (PPA). Operational simplicity and high yield in signicantly very short reaction time make this procedure a useful and attractive alternative to the currently available methods.[26]

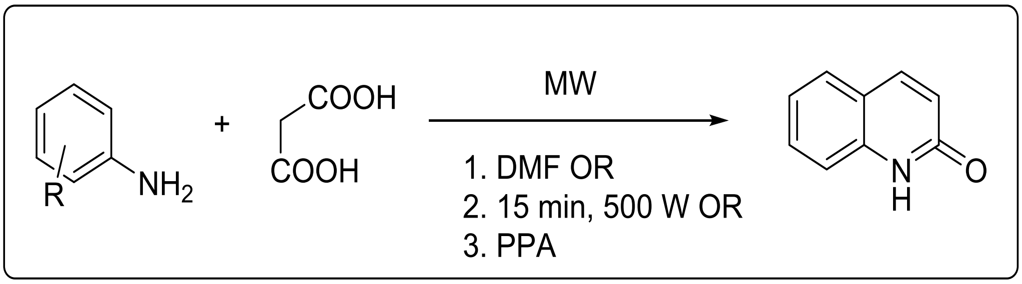


Figure 14.

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