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Novelty of the work

“This review article gives information about the recent advances in the synthesis of quinoline derivatives by various eco-friendly, green and clean protocols.”
RECENT ADVANCES IN SYNTHESIS OF QUINOLINES: A REVIEW

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ABSTRACT

Quinolines have become important compounds because of their variety of applicability 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 synthesis 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 recycle and reuse, one pot reaction, solvent free reaction condition, using ionic liquids, ultrasound promoted synthesis and photo catalytic synthesis (UV radiations).
INRODUCTION

Quinoline is one of the most important N-based heterocyclic aromatic compound. Quinolines recently have been caught attention of researchers because of their broad range of activities and of course for their wide applications too.

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 Cinchona tree which replace the use of crude bark for the treatment of malaria. Other quinoline derivatives (2-9) having various activities were also isolated from different plant species.¹ (Figure 1)

Quinoline was first extracted from coal tar in 1834 by Friedlieb Ferdinand Runge. Coal tar remains the principal source of commercial quinoline.²
ACTIVITIES AND APPLICATIONS

Quinoline derivatives in general are known to have a broad range of applications in medicinal, bioorganic, industrial as well as in the fields of synthetic organic chemistry. Their derivatives have been found to possess various biological activities like antimalarial, anti-bacterial, anti-fungal, anti-asthmatic, antihypertensive, anti-inflammatory, and anti-platelet activity. They also exhibit anti-tubercular and immune depressant activities. Few promising compounds with the quinoline ring system like, Pamaquine (10), chloroquine (11), Tafenoquine (12), Bulaquine (13), Quinine (14) and Mefloquine (16) as an antimalarial agent, Amodiaquine (15) as an antimalarial and anti-inflammatory agent (Figure 2).

![Quinoline derivatives](image)

Figure 2 Few promising compounds with quinoline ring system.

The 2-arylquinoline derivatives (17a) and (17b) shows selectivity in binding to the estrogen receptor β (ER β), which plays an important role in the development, maintenance, and function of the mammalian reproductive system, as well as non-sexual tissues.
4-[2-(Diethylamino) ethylamino] quinolin-7-ol (18) containing nitrogen at position 4 exhibits antiplasmodial activity.\textsuperscript{9} Polysubstituted quinoline derivatives such as 8-hydroxyquinoline and quinoline-8-thiol have been used to produce metal complexes which emit light.\textsuperscript{10} 2-(4-Bromo-5-ethylthiophen-2-yl)-6-ethynyl-4-phenylquinoline (19) has been applied in sensors and light emitting diodes.\textsuperscript{11}

Some quinoline derivatives such as quinalidine (20) and quinaldic acid (21) shows their activity as corrosion inhibitors for mild steel in hydrochloric acid.\textsuperscript{4} (Figure 3)

![Chemical Structures](image)

Figure 3 Some important quinoline derivatives

In recent years some Quinoline derivatives (22) shown below, which are explored structural modification of Sorafenib, where synthesized as novel Raf kinase inhibitors with more potent and selective antitumor activities.\textsuperscript{12}

![Chemical Structure](image)

Aziridine–isoquinoline hybrids and their ring-opening products shown in below figure exhibits potent antiplasmodial activity.\textsuperscript{13}
A new series of hybrid conjugates of N-(7-chloroquinolin-4-yl) piperazine-1-carbothioamide and 1,3,5-triazine derivatives have considerable antimalarial activity against both wild and mutant parasites with marked variation on changing the pattern of substitution. Such derivatives also show excellent Antibacterial activity against several Gram-positive and Gram-negative microorganisms.\textsuperscript{14,15}

4-arylquinoline-2-carboxylate derivatives show antiprotozoal activity against the pathogenic parasite Toxoplasma gondii.\textsuperscript{16}

Many quinoline derivatives are found to have applications as agrochemicals\textsuperscript{37} as well as in the study of bio-organic and bio-organometallic\textsuperscript{3} processes. They are also used in manufacturing dyes, food colorants, pH indicators and other organic compounds. In additional to this they have also been used as ligands for the preparation of OLED phosphorescent complexes\textsuperscript{18} and with conjugated polymers used as a selective chemo sensors of the fluoride and metal ions.\textsuperscript{19,20}

Due to such a wide range of applicability, there has been increasing interest in the development of efficient methodologies for the synthesis of quinoline derivatives.

CONVENTIONAL METHODS OF SYNTHESIS
A number of preparations have been known since the late 1800s for the synthesis of quinoline and its derivatives.

Figure 5 Various conventional routes for the synthesis of quinoline derivatives

The structural core of quinoline has been generally synthesized by various conventional named reactions such as Skraup, Doebner-von Miller, Friedlander, Pfitzinger, Conrad-Limpach, Combes synthesis.\(^1\)

Though many of these methods are very effective, they often involve the use of various acids or reagents that are not environmentally compatible, produce a large amount of waste and require longer reaction times.\(^{17}\) Moreover, many of these methods give relatively large amounts of undesirable by-products whose removal is tedious and often wasteful and are also not satisfactory with respect to operational simplicity to isolate yield. Thus, it has become very important to follow methods which could be considered as a better and eco friendly viable ‘green synthetic methods’.

This green chemistry approach provides a way to design products in a simplified manner and has less feedstock, minimum waste, low energy consumption, less hazardous, renewable materials, high atom economy, reduce reaction steps and green catalysts that improves the efficiency of the reaction.

Clean chemical synthesis using alternative reaction methods includes:
1) Alternative reaction media for synthesis using Supercritical fluids, Ionic liquids, Water, Polyethylene glycol and Solvent free or grinding method.

2) Alternative energy sources like Microwave (fast and homogeneous heating by microwave irradiation), Ultrasound and Sunlight/UV.

3) Catalysts which may be Clay or other green catalysts which could be recycle and reuse.

VARIOUS REACTION SCHEMES

Scheme 1

Safari et al. described a procedure for preparation of quinaldine derivatives (35) from aniline derivatives (33) and acetaldehyde (34) under microwave irradiation without any solvent (Scheme 1). In this method they tried different best bronsted acids but found hydrochloric acid appeared to be the best catalyst for this reaction, showing the highest yield. Moreover yield of the product was not affected by the nature of substituent in this reaction.

The method presents a simple and useful synthetic process for quinaldines because of high yield, short reaction time, straight forward, easy work-up procedure, the use of microwave irradiation is the novel efficient source of energy and use of molecular oxygen as a green oxidant.

Scheme 2

A method for the synthesis of quinoline derivatives and bis-quinoline derivatives (39) includes microwave-assisted, one-pot-three-component reaction between aromatic amines, (36) aromatic aldehydes (37) and phenylacetylene (38) in the presence of
catalytic amounts of potassium dodecatungstocobaltate trihydrate (K₅CoW₁₂O₄₀·₃H₂O) have been acquainted by Anvar and his co-workers (Scheme 2). They were first to report the use of polyoxometalates (POM) as catalyst for the one-pot three-component synthesis of quinolines and bis-quinolines under microwave irradiation.

The catalyst could be easily recovered by simple filtration and could be reuse for several cycles without any significant loss of its catalytic activity. Moreover no metal was detected in the final product which confirms the green nature of the present method. This makes the method useful and attractive for the synthesis of quinoline derivatives.

Scheme 3

A synthesis of steroidal and nonsteroidal quinoline derivatives (41) has been established by Gogoi et al. (Scheme 3). In this method steroidal quinoline derivatives were synthesized from one-pot reaction of steroidal β-bromovinyl aldehydes (40) and arylamines in high yield using microwave irradiation without use of catalyst and in a solvent-free condition. This methodology offers an environment friendly ‘green’ alternative organic synthesis.

Scheme 4

Facile microwave-assisted processes suitable for the preparation of a series of quinoline-4-carboxylic acids (44) have been introduced by Zhu and co-workers (Scheme 4). In this Pfitzinger type of reaction condensation reaction between isatins (42) and sodium pyruvate to give quinoline-2,4-dicarboxylic acid (QDC) (43) is carried out under the microwave conditions which optimise reaction solvent, time and temperature. The subsequent decarboxylation reaction of QDCs in water instead of toxic nitrobenzene under MW was also promoted succesfully.

Scheme 5
Ranu et al. developed a simple and efficient procedure for the synthesis of 4-alkylquinoline derivatives (46) by a one-pot reaction of anilines (36) with alkyl vinyl ketones (45) on the surface of silica gel inseminated with indium (III) chloride under microwave irradiation without any solvent (Scheme 5).\textsuperscript{25} The main advantages of this procedure are: operational simplicity, fast reaction, high yield and general applicability. These advantages accommodate a variety of substitution patterns.

Scheme 6

Microwave-assisted solid acid-catalyzed syntheses of substituted quinoline derivatives (48) have been discussed by Kulkarni and his colligues (Scheme 6).\textsuperscript{26} The quinoline derivatives were synthesized by a multicomponent reaction of anilines (36), aldehydes (37) and terminal aryl alkynes (49). The reaction was catalyzed by montmorillonite K-10, a strong and environmentally benign solid acid. The multicomponent approach 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.

Scheme 7

Quinoline derivatives (51) were synthesized by employing amino acetophenone (41) and phenylacetylene (50) in the presence of Zn(OTf)\textsubscript{2} as an effective catalyst under microwave irradiation have been acquainted by Praveen and co-workers (Scheme 7).\textsuperscript{27}
Advantage of this method is that the reaction is amenable to alkynes containing alkyl, aromatic and heteroaromatic groups. Good yield, short reaction time, operational simplicity, low catalyst loading and wide substrate scope are the significant advantages of this reaction from synthetic viewpoint.

Scheme 8

Naik et al. have been reported a rapid and efficient method for the synthesis of various carbonitrile quinoline/benzo[h]quinoline derivatives (55) by utilizing benzaldehyde (52), methyl cyanoacetate (53) and aromatic amine (54) with nanostructured TiO\(_2\) photocatalyst in solvent-free conditions under microwave irradiation (Scheme 8).\(^{28}\)

Scheme 9

3-Unsubstituted 4-hydroxyquinolin-2(1H)-one (57) was synthesized using substituted aromatic amine (36) and melonic acid (56) under microwave irradiation in dimethylformamide\(^{29}\), without employing any solvent\(^{25}\) and using polyphosphoric acid (PPA)\(^{126}\) have been reported (Scheme 9). Operational simplicity and high yield in significantly very short reaction time can impose this procedure as a useful and attractive alternative to the currently available methods.

Scheme 10

Reddy et al. introduced 3-component one-pot reaction between 3,4-dimethoxyaniline (58), aldehydes and ethyl-3,3-diethoxypropionate (59) to quinoline derivative (60) by using montmorillonite K-10 (Mont K-10) as a green catalyst by utilizing oxygen of air
and water (Scheme 10). Montmorillonite K-10 (Mont K-10) was found to be more effective compared to other Lewis acids as the expected product was isolated in good yield. Moreover, montmorillonite K-10 was recovered by simple filtration and reused easily. While the use of water as solvent makes this reaction eco-friendly.

Scheme 11

Montmorillonite K10 clay catalyzed synthesis of quinoline derivative (63) has been enclosed by Paolis et al. by employing aniline derivatives (61) and cinnamaldehyde (62) (Scheme 11). As a mechanism, domino process involving cyclization followed by dehydration and then after oxidation to deliver quinolines. The reaction was carried out under solvent-free condition and with the assistance of microwave irradiation.

Scheme 12

A new, convenient, efficient and eco-friendly protocol for the synthesis of polysubstituted quinoline derivative (66) under mild condition has been described by Mouhamad Jida et al. (Scheme 12). A wide variety of new products were readily prepared in the presence of propylphosphonic anhydride (T3P) in short reaction times and excellent yield. Here T3P is used as a mild water scavenger catalyst in this coupling reaction. In addition, this non toxic T3P offers several advantages over traditional reagents, such as low toxicity, commercial scale availability, low price, low epimerization tendency, high selectivity yields, excellent purity, broad functional group, easy work up procedures. Simplicity and cost-effectiveness of this methodology attract for large scale synthesis.
Scheme 13

A mild and efficient route for the synthesis of quinoline derivative and polycyclic quinoline derivative (46) by utilizing substituted o-amino acetophenone derivative (67) and enolisable ketone (68) with molecular iodine as a catalyst in ethanol\textsuperscript{34}, combined iodine and silica gel under solvent free condition\textsuperscript{35}, Friedlander heteroannulation method by using of nano ZnO as a mild, non-volatile, non-corrosive and efficient catalyst which provides regiospecific synthesis under solvent free condition\textsuperscript{36}, ionic liquid [Hbim][BF\textsubscript{4}] under ultrasound at room temperature\textsuperscript{37}. These methods avoid the use of hazardous acids or bases and harsh reaction conditions. The advantage of this method includes good substrate generality, the use of inexpensive reagents and catalysts under mild conditions, and experimental operational ease (Scheme 13).

Scheme 14

Gibson et al. used near critical water (NCW) as a medium for the organic synthesis of nitrogen heterocyclic compounds. The potential for solvent recycling was also demonstrated. In this method carbonyl compound with isatin (69) in NCW form the substituted quinoline derivative (70-71) via in situ decarboxylation (Scheme 14).\textsuperscript{38} Hot pressurized NCW get more ionized and is a very good dehydrating media suited for isatin opening, condensation and cyclodehydration with carbonyls.
A highly efficient, cost-effective and environmentally benign protocol for the synthesis of 2, 4, 6-trisubstituted quinoline derivative (73) by using NaHSO₄·SiO₂ as a heterogeneous and reusable catalyst have been enclosed by Mitragotri and co-workers (Scheme 15). This procedure is operationally simple and can be an alternative to the existing protocols for the synthesis of tri-substituted quinoline derivatives. From the practical point of view, the catalyst is easier to prepare from the readily available reagents and like other heterogeneous catalysts, it can also be reused.

Scheme 16

A Microwave-assisted procedure for quinoline derivative (76) has been reported by Shekouhy and co-workers (Scheme 16). Reaction between 2-aminaryl ketones (74) and carbonyl compounds (75) in the presence of silica nanoparticle (NPs) as catalysts under microwave irradiation give high yields of quinoline derivatives. Silica nanoparticle gave best results compared to CaO, MgO, Al₂O₃ and SiO₂. Silica NPs, highly microporous solid, offer a wide range of active sites and often can be regenerated if deactivated during reaction. On the other hand, reducing catalytic substances to nanometers in size greatly increases the surface area available per gram and ultimately the catalytic activity. The NPs catalyst can be reused without loss of activity even after recycling fourteen times.

Scheme 17

A one-pot, mild, efficient, and environmentally benign protocol have been developed by Chermahini et al. for the synthesis of quinoline derivative (78) catalyzed by Montmorrilonite K-10, zeolite, nano-crystalline sulfated Zirconia (nano-crystalline SZ) in
high yields (Scheme 17).\(^{40}\) The mild reaction conditions, easy work-up, clean reaction profiles, lower catalyst loading and cost efficiency makes this approach an interesting alternative to the existing methods.

**Scheme 18**

Ren et al. have enclosed a method in which 2-aminobenzyl alcohol (79) reacts with ketones (80) in toluene or poly ethylene glycol (PEG-2000) by employing a palladium catalyst along with KOH to isolate corresponding quinoline derivative (81) in good yields (Scheme 18).\(^{41}\) The catalytic system could be recovered and reused five times without any loss of catalytic activity.

**Scheme 19**

Uses of some new metal dodecyl sulfates as a catalyst in the synthesis of quinoline derivative (83) by Friedlander protocol in aqueous media have been developed by Salehi et al. (Scheme 19).\(^{42}\) In which metal dodecyl sulfates were used in reaction between o-aminoaryl ketones (82) and ketones or β-diketones (72). They prepare some combined Lewis acid-surfactant catalysts (LASC) and tried to use them for the synthesis. They found zirconium tetrakis(dodecyl) sulfate Zr(DS)\(_4\) superior to all other prepared metal dodecyl sulfates. Zr(DS)\(_4\) was recovered easily through separation by a centrifuge and reused in aqueous media.

**Scheme 20**

Air-mediated metal free one-pot and three component green synthetic method for quinoline derivative (86) by utilizing 4-substituted aniline (54), aldehyde derivative (84),
ethynylbenzene (85) with molecular iodine as a catalyst have been reported by Li et al. (Scheme 20). Here molecular iodine acts as a mild Lewis acid.

Scheme 21

Synthesis of quinoline derivatives and polycyclic quinoline derivatives (88-89) via Friedlander condensation between 2-aminoarylketones (87) with enolisable ketones by using recyclable heterogeneous catalyst sulfamic acid have been described by Rao and colleagues (Scheme 21). The ease of recovery and reuse of this novel catalyst makes this method quite simple, convenient and environmentally benign for the synthesis of highly functionalized quinoline derivatives.

Scheme 22

One-pot synthesis of 2- or 3-mono-substituted, 2,3-disubstituted quinoline derivatives and also other bi- or tricyclic quinoline derivatives have been synthesized by Li et al. (Scheme 22). The reaction was applicable to a wide variety of ketones and aldehydes, The most advantage of this method is use of inexpensive, readily available reagents and solvents that do not require oxygen or moisture free conditions.

Scheme 23
Motokura et al. have given one-pot processes for the synthesis of quinoline derivative (93) by using (2-aminophenyl)methanol (79) and enolisable ketone (68) with Ru-grafted hydrotalcite (Ru/HT), a multifunctional heterogeneous catalyst (Scheme 23). The presented catalytic system overcome previously reported catalytic system by the advantages like high catalytic activity, wide applicability to various carbonyl compounds, no need for homogeneous bases and the use of molecular oxygen as a green oxidant. This is the first reported one-pot quinoline synthesis using heterogeneous catalysts.

**Scheme 24**

One-pot, solvent free, microwave-assisted, multi component reaction for the synthesis of quinoline derivative (95) without any solvent by utilizing substituted aniline (94), acetone and benzaldehyde (52) on the surface of alumina impregnated with hydrochloric acid have been developed by Mirza et al. (Scheme 24). Hydrochloric acid appeared to be the best catalyst for this reaction, showing the highest yield and was preferred compare to sulfuric acid because of its higher, safety, more environmental friendliness and lower price. The advantages like high yield, short reaction time, straight forward and easy work-up procedure makes the method completely eco friendly, fast, simple, and highly efficient.

**Scheme 25**

An efficient microwave assisted, one-pot, solvent free synthesis of substituted quinoline derivative (96) from o-nitrobenzaldehyde (90) and enolizable ketones (65) using SnCl$_2$.2H$_2$O as the reductant have been introduced by Chaudhuri and co-workers.
This method is relatively faster and it affords the desired products in respectable yields.

Scheme 26

Yao et al. have described a novel application of highly stable Fe(OTf)$_3$ as an efficient catalyst for carbon–carbon bond formation via the activation of a terminal alkyne C–H bond under solvent-free conditions for the synthesis of quinoline derivative (48) (Scheme 26). Furthermore, the catalyst was easily recovered from the reaction mixture and reused many times with only a little loss of activity. Other catalyst such as FeCl$_3$, Fe(OTf)$_2$, FeSO$_4$, Fe(NO$_3$)$_3$ and Fe$_2$(SO$_4$)$_3$ were examined in this reaction, but they did not efficient as like Fe(OTf)$_3$ in terms of yield of the products. It was also noted that, reaction in solvent free condition was more favorable compare to reaction with various organic solvents.

Scheme 27

Synthesis of quinoline-2- carboxylate derivative (98) by Cu(OTf)$_2$ catalyst via intermolecular addition of alkyne (50) onto imines (99) and subsequent intermolecular ring closure by arylation have been described by Huang et al. (Scheme 27). In addition, Various catalyst such as Cu(OAc)$_2$, Cu(acac)$_2$, Cu(tmhd)$_2$, CuI, Cu(OTf)$_2$ were examined by authors in this reaction with different organic solvents like DCM, 1,4-dioxane, toluene, furan, DMSO and DMF. However the best result was obtained when reaction was carried out using Cu(OTf)$_2$ in DCM. The efficiency of this system allowed the reactions to be carried out at room temperature.
Method for quinoline derivative (100) using ultrasound and ionic liquid have established by Kowsari et al. Two-component, one-pot, condensation reaction of isatin (69) with enolisable ketone (68) yields Quinoline derivative (100) (Scheme 28). Authors examined the various solvents effect on the reaction. The results showed that the reaction is favored in water. Also, the ionic liquid could be recovered and reused many times without loss of its activity. In addition, simple process, high selectivity, short reaction time, use of cheap and environmentally benign solvent and the reusability of the aqueous media are the superior advantages of this protocol.

Austin et al. have described the photosynthesis of substituted annulated quinoline derivative (102-104) from (101) and (103) (Scheme 29). This photocyclisation–elimination process provides a convenient route for the synthesis of the variety of substituted 2,3-dihydro-1Hcyclopenta[b] quinoline derivatives from readily accessible precursors. Reactions of meta-substituted precursors were highly regioselective, with alkyl substituents, which afforded 5-substituted 2,3-dihydro-1H-cyclopenta[b]quinolines.
In addition, substrates containing powerful electron-donating substituents, that generally affording 7-substituted products in high yield.

**Scheme 30**

Photochemical cyclization method for the synthesis of 2, 4-diiodoquinoline derivative (105) by cyclization of o-alkynylaryl isocyanide (106) with iodine has been developed by Mitamura and co-workers (Scheme 30).\(^{53}\) Which are difficult to synthesize by using other existing methods. For comparative study authors employed various organic solvents such as chloroform, methanol, acetone, acetonitrile, ethyl acetate, tetrahydrofuran, toluene, n-hexane and triethyl amine. However the best results were obtained in terms of yield of the products, when chloroform was used as a solvent. This photochemical reaction was also carried out with various cyclizing agents such as Br\(_2\), Nz-chlorosuccinimide (NCS), Nz-bromosuccinimide (NBS) and Nz-iodosuccinimide (NIS) but they were not found an efficient catalyst for this protocol. This eco-friendly green reaction proceeds under mild conditions and readily affords the appropriate products in high to excellent yield.

**Scheme 31**

One pot synthesis of 4-ethoxy-1,2,3,4-tetrahydroquinoline (109) from a heterogeneous solution of nitroarene (107), ethanol and TiO\(_2\) upon irradiation of UV light have been reported by Joo and colleagues (Scheme 31).\(^{54}\) In addition, substrates have either oxygen or amino substituents like m-nitroanisole etc., in such cases the reaction proceeds rather slowly compared to those having alkyl substituent under the same reaction conditions. An added advantage of this protocol is that, quinoline derivatives were directly synthesized from the nitro nitroarenes instead of aminoarenes using environmentally friendly conditions.
Selvam et al. have given the photo catalytic conversion of nitrobenzene (110) to 2-methylquinoline derivative (113) in absolute ethanol using TiO$_2$ as a photo catalyst. In this reaction exited electrons are trapped by the metal which is used to dope TiO$_2$, this enhances the charge separation between hole and electron. Holes causes the oxidation of alcohol (112) to aldehyde (111) and the trapped electrons are consumed for the reduction of nitrobenzene to aniline by H$^+$ formed during the oxidation of alcohol. Further reaction of aniline and aldehyde gives quinaldine. This photo reaction is only possible in the presence of TiO$_2$. In 2009 Selvam et al. prepared substituted quinoline derivatives and other heterocycles by TiO$_2$ nanoparticles by this photo catalytic process. In 2010 they synthesized quinaldines Au-loaded TiO$_2$. In 2011 they synthesized nanosized silver particles loaded TiO$_2$ to get materials with enhanced adsorption and photo catalytic performance. In 2012 N-Doped TiO$_2$ using a new nitrogen precursor hydrazine hydrate has been synthesized by a simple wet method by Selvam et al. (Scheme 32). They concluded that N-TiO$_2$ is more efficient than other metal doped catalysts in quinaldine synthesis under visible light. Therefore, this process has the potential to enable a more sustainable quinaldine synthesis from nitrobenzene in UV and visible light.

Conclusion:

Since Quinoline and its derivatives possess a wide spectrum of pharmacological activities and are also utilized as ligands in various biologically modelled transition metal
complexes, a number of methods have been developed from time to time for their synthesis by microwave assisted, ultrasound promoted, heterogeneous acid catalyzed, in Uv light, solvent free condition and many more. We have made here efforts to compile most of these methods that have been reported in the literature. This review will be very useful to the researcher, working in this field. And it would help them to develop a new eco-friendly, efficient and economical method. This is necessary from today’s point of view as we need an environmentally clean protocol for the large scale production of such an important biological moiety, which may be used further in many reactions to develop a potent pharmacophore for the future.

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