



A Brief Overview on One Pot Multi-component Synthesis and Biological Properties of a Class of Nitrogenous Complex Heterocyclic Compounds

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

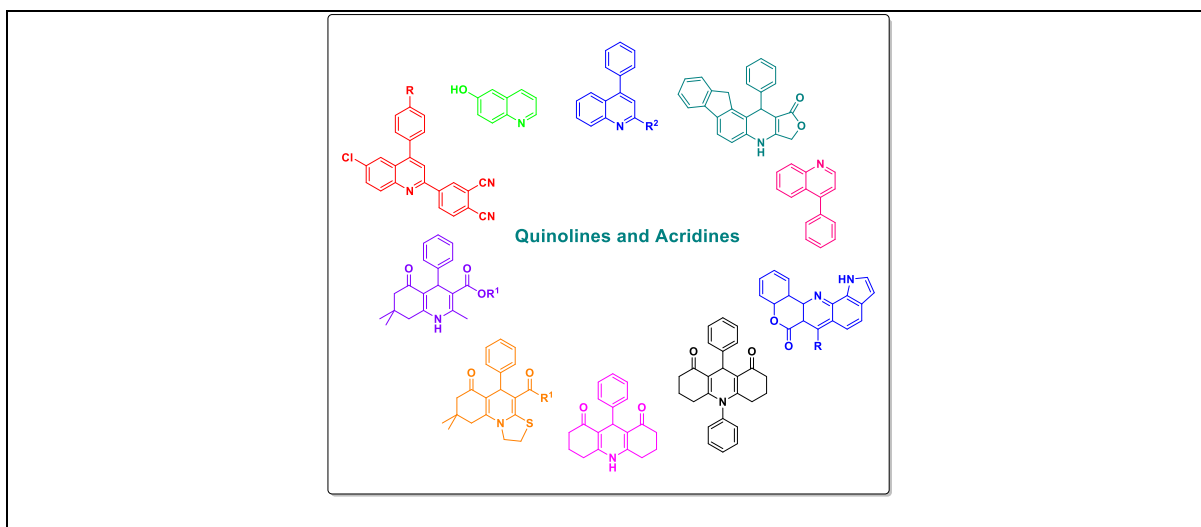
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ABSTRACT

The quinoline and acridine core possesses a vast number of biological activities such as anticancer, anti-malarial, anti-microbial, antifungal, anti-tubercular activities and the conventional classical synthetic methods have harsh conditions having multistep process. Currently scientists are searching new methodology to eliminate the use of chemicals, solvents and catalysts, which are hazardous to human health as well as to environment and so, this review provides a concise overview of new dimensions of one pot multi-component synthetic approaches in designing quinoline and acridine scaffold. This review would give more scientific ideas to synthesis a variety of heterocyclic moieties in a new synthetic way following the one-pot multi-component method.

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Keywords: Quinolines; acridines; 1,4-dihydropyridines; pyrido-pyrimidines; tetrazoloquinazolinones; one-pot reactions; multicomponent synthesis.

1. INTRODUCTION

“Quinoline is a weak tertiary organic base and was discovered in 1834 as a colourless hygroscopic liquid by distillation of coal tar by Friedlieb Ferdinand Runge and in 1871, Dewar observed the chemical similarity between pyridine and quinoline having rigid heterocyclic core of benzene ortho-fused with a pyridine ring. (Fig. 1)” [1] Coal tar is a principal commercial source for quinoline synthesis but numerous reactions have been developed for its laboratory synthesis. Quinoline itself has a few applications but many of its derivatives are useful in various chemical reactions for laboratory synthesis.

There are several reported classical synthetic routes for synthesising the quinoline structural motifs and such classical synthetic routes which are widely used include Skraup reaction, Conrad-Limpach reaction, Doebner reaction, Combes reaction, Povarov reaction, Doebner-Miller reaction, Gould Jacobs reaction and Riehm reaction. Which are majorly utilizes aniline as one of the common reactants (Fig. 2). However, there are several other reactions such as Knorr reaction, Friedländer reaction, Pfitzinger reaction, Niementowski reaction, Meth-Cohn reaction and Camps reaction which requires special substituted anilines or other substituted reactants to yield quinoline structural motifs.

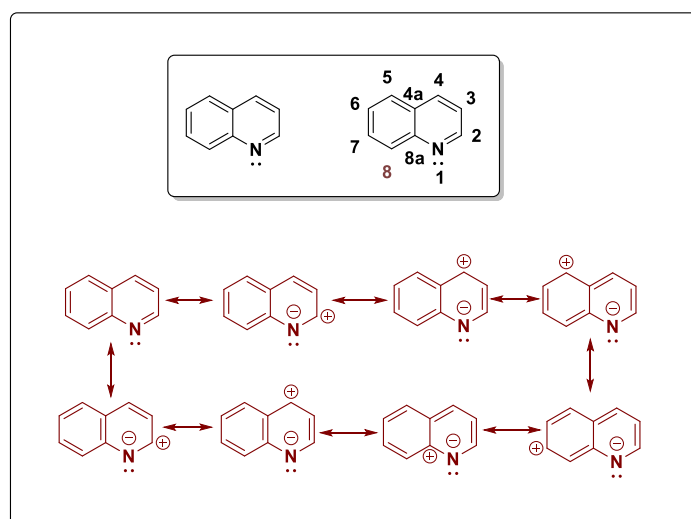


Fig. 1. Chemical structures and resonating structures of quinoline moiety

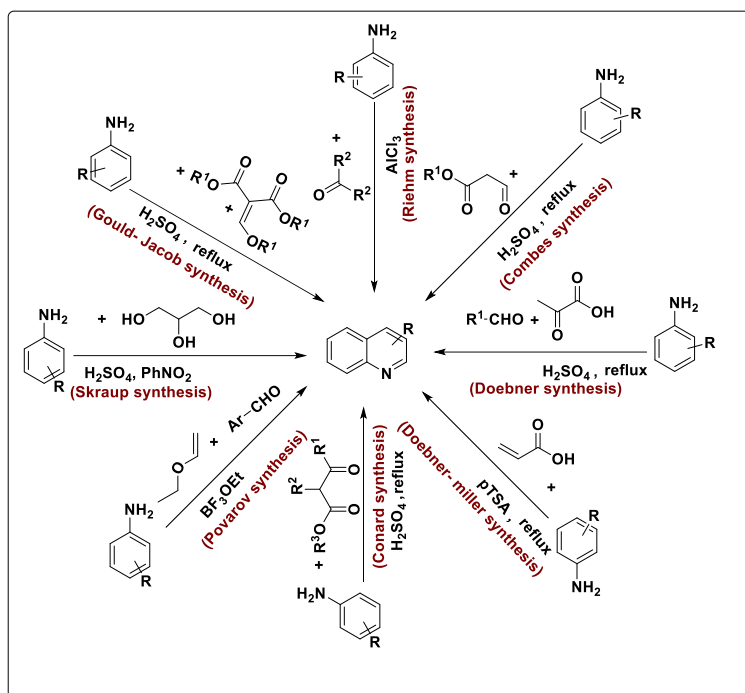


Fig. 2. Diverse synthetic routes for the synthesis of quinoline structures

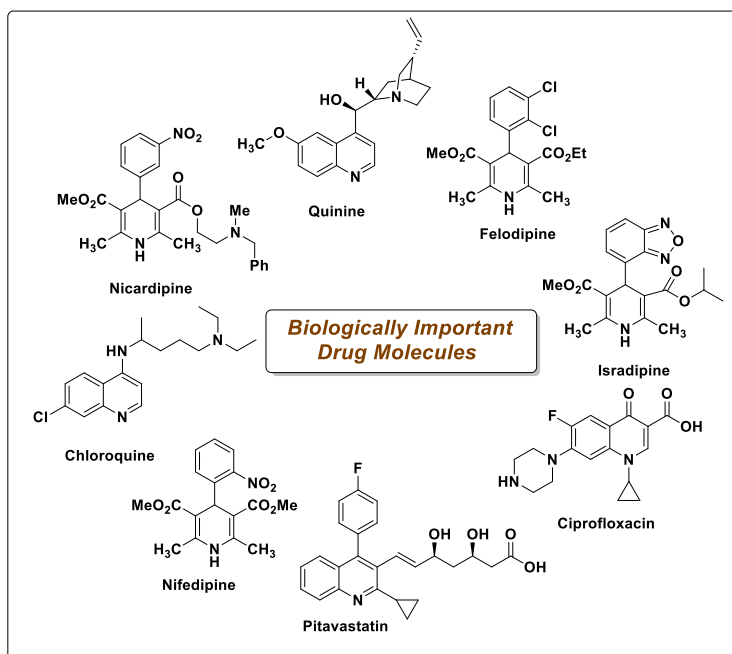


Fig. 3. Some important pharmaceutically active drug molecule

“Quinoline scaffolds are well-known entity under alkaloid class of natural products and is present in various biologically active plants, pharmaceuticals, agrochemicals, dyes etc. and are represented in (Fig. 3)” [2-3]. They are also used as chelating agent due to multiple N-donor ligands and quinoline pharmacophore is a crucial

functionality due to variety of pharmacological activities (Fig. 3) such as anti-malarial, anti-protozoal, anti-tubercular, antibacterial, anticancer, anti-proliferative, antitumor, anti-inflammatory, antifungal, antioxidant, DNA binding, antihypertensive, anti-HIV agents [4-12]. High magnitude of pharmacological importance

of natural or synthesized quinoline derivatives has urged various chemists world-wide to examine the utility and prominence of this scaffold by means of research reviews.

Now, acridine is a nitrogenous heterocyclic compound having planar shaped structural motif and it is also structurally closely resembles to anthracene with one of the central C-H group is replaced by 'N' atom. It is a basic organic compound due to the presence of Sp^2 -hybridised 'N' atom and the unsubstituted compound is generally colourless crystalline solid.[13] In 1870 Carl Grabe and Heinrich Caro first isolated acridine from coal tar by extracting with dil. H_2SO_4 . [14] "Acridines have broad range of research and industrial applications in various fields such as in medicinal chemistry, fluorescent organic dye, chemosensor, photo catalysis, as hole transport materials in solar cell and photovoltaic applications" [15-23]. "Acridinium ions are used as efficient organic photo catalyst for many organic transformations due to their long excited state lifetime and tunable redox potential" [24-25]. There are various procedures [26-35] for the synthesis of acridine structural motifs but at the very first Bernthsen et. al have synthesized it in laboratory by using diphenylamine and carboxylic acid in presence of anhydrous $ZnCl_2$. [36]. There are also other methods (Fig. 4) which have been

developed in recent years and which has opened a broad window for the organic synthesis of acridine structural motifs.

"Acridine derivatives have been used for the preparation of labeled medicinal conjugates such as nucleic acids, peptides, and proteins that exhibit antitumor and DNA-binding properties" [37-39]. "Among other acridine derivatives, substituted 1,8-Dioxo-decahydroacridines and their derivatives have been widely used in medicinal chemistry as can behave as alternative of 1,4-dihydropyridines from a variety of viewpoints such as biological activities and due to close resemblance with 1,4-dihydropyridines in respect of the biological properties 1,8-Dioxo-decahydroacridines have been use as calcium channel blockers for the treatment of defibrillation and hypertension disease" [40-42]. They also possesses antimalarial, antiviral, antibacterial, antiallergic and anticancer properties and recently, acridines showed some inhibition properties for multidrug resistance in tumour cell lines and some of the acridine drugs are exhibiting promising anticancer activity both in vitro and in vivo against a range of murine and human cancers cells [43-46]. And additionally due to having fluorescent properties they are being used as molecular probes for monitoring polymerization processes in biological cells [47].

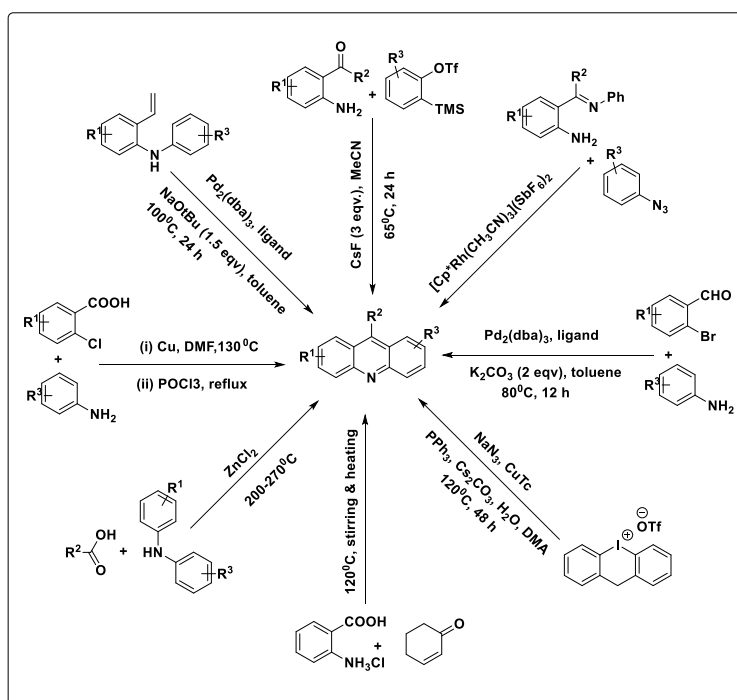


Fig. 4. Diverse synthetic routes for the synthesis of acridine structures

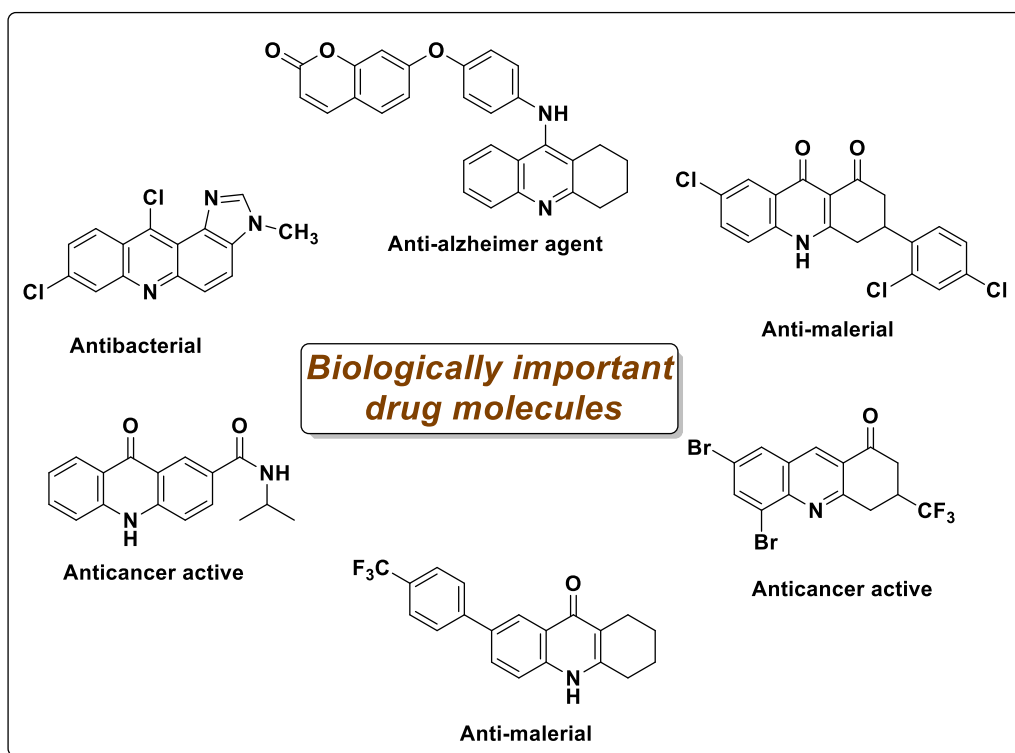
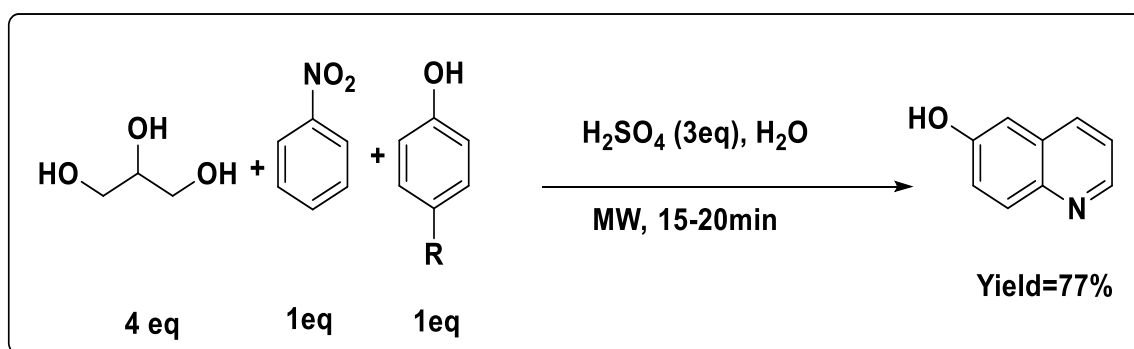


Fig. 5. Some important pharmaceutically active drug molecule

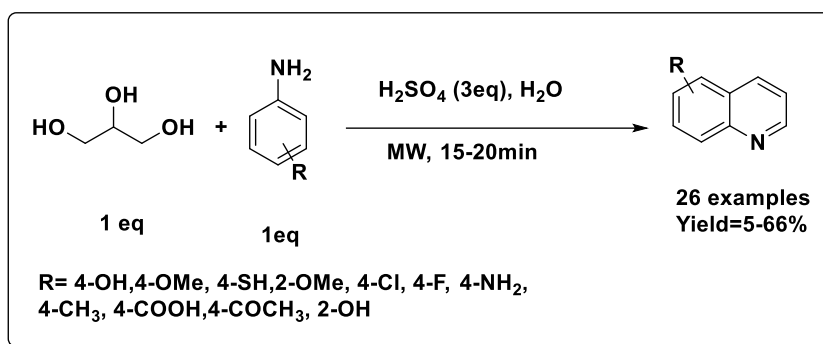
2. METHODS OF SYNTHESIS OF QUINOLINE DERIVATIVES

In 2014, Saggadi. et al. had developed a synthetic method following Skraup reaction and Bamberger rearrangement reaction in water using glycerol, nitrobenzene and *p*-aminophenol or *p*-nitrophenol as reactants. The process involved the presence of sulphuric acid under microwave irradiation condition (Scheme 1.) with yield upto 77% [48].



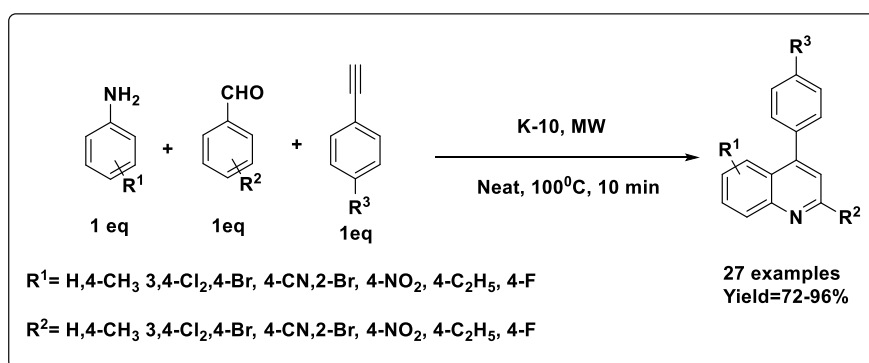
Scheme 1. Microwave assisted regioselective modified Skraup reaction and Bamberger rearrangement reported by Saggadi.et al.

In 2014, Saggadi. et al. had developed a synthetic method following Skraup reaction and Bamberger rearrangement reaction in water using glycerol, nitrobenzene and *p*-aminophenol or *p*-nitrophenol as reactants. The process involved the presence of sulphuric acid under microwave irradiation condition (Scheme 2.) with yield upto 66% [49].



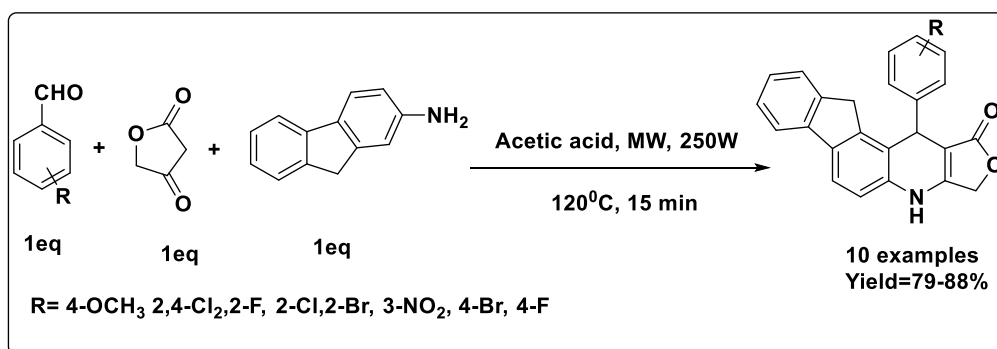
Scheme 2. Green Skraup protocol under microwave irradiation reported by Saggadi.et al.

In 2010, Tork.et al. had developed a synthetic method for the synthesis of quinoline derivatives using aniline derivatives, aldehydes and aromatic alkynes as reactants as reactants under microwave condition. The process involved the presence of K-10, neat condition and 100°C temperature (Scheme 3.) with yield upto 96% [50].



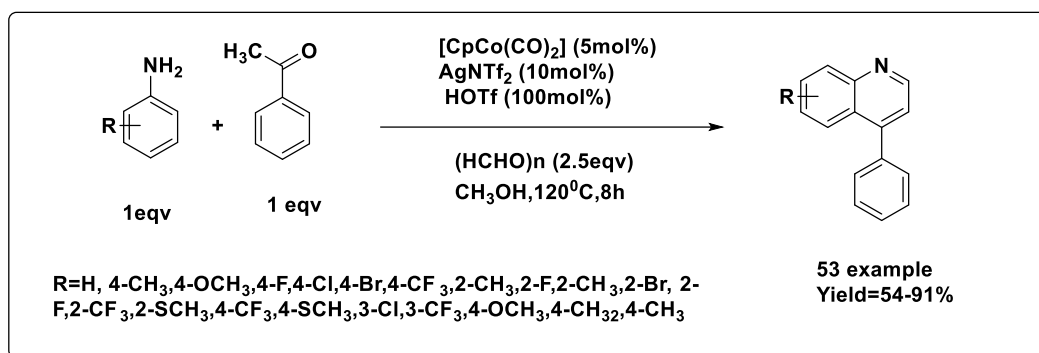
Scheme 3. Microwave assisted solvent free protocol reported by Kulkarni and Tork.et al.

In 2013, Peng.et al. had developed a synthetic method for the synthesis of quinoline derivatives using aniline derivatives using aldehydes, aromatic amine, cyclic 1,3-diketo esters as reactants. The process involved the presence of acetic acid under microwave irradiation condition (Scheme 4.) with yield upto 88% [51].



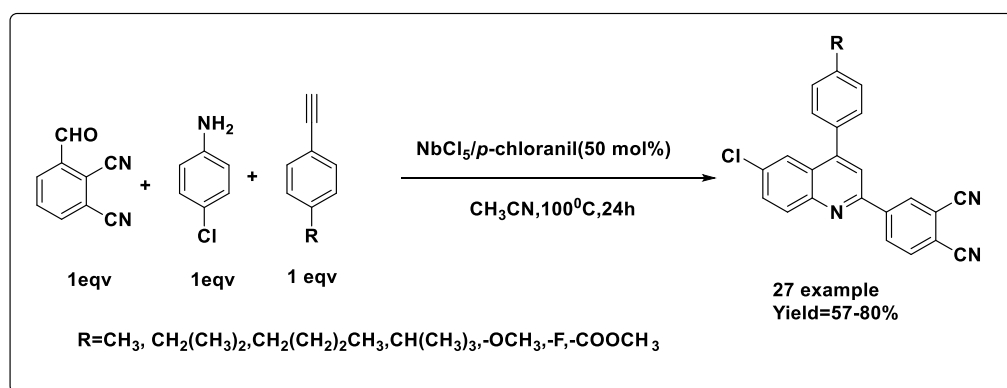
Scheme 4. Microwave influenced solvent free protocol reported by Peng.et al.

In 2017, Xu et al. had developed a synthetic method for the synthesis of quinoline derivatives using aniline derivatives using aldehyde, aromatic amines as reactants. The process involved the presence of PEG and methanol at 120°C temperature (Scheme 5.) with yield upto 91% [52].



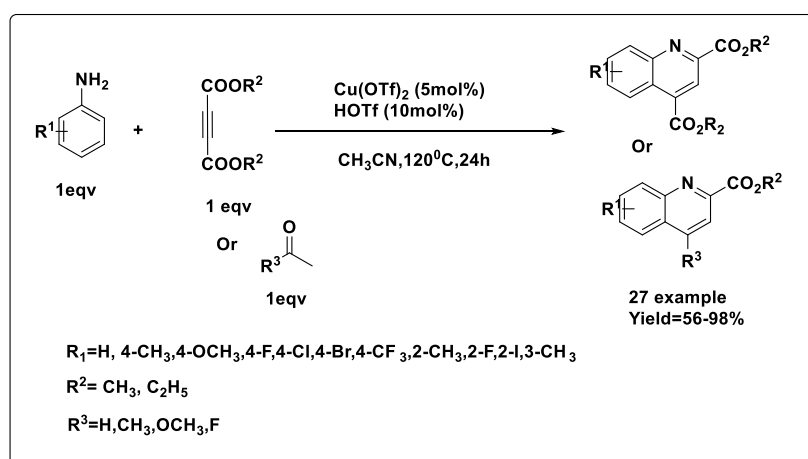
Scheme 5. Cobalt (III) based catalyst for quinolone synthesis reported by Xu et al.

In 2018, Aloisio. et al. had developed a synthetic method for the synthesis of quinoline derivatives using aniline derivatives using aromatic primary amines, cyano-aldehyde, aromatic alkyne and as reactants. The process involved the presence of NbCl_5 / *p*-chloranil in presence of CH_3CN as solvent under 100°C temperature. (Scheme 6.) with yield upto 77% [53].



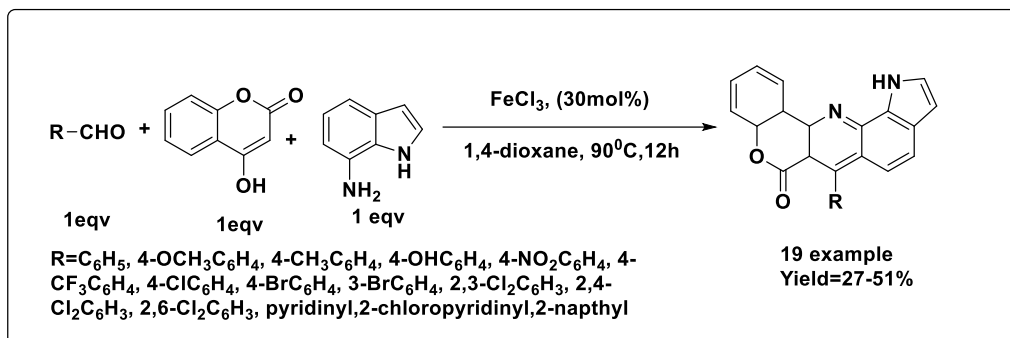
Scheme 6. Multicomponent reaction reported by Aloisio. et al.

In 2018, Wu. et al. had developed a synthetic method for the synthesis of quinoline derivatives using aromatic amine, alkynes and ketones as reactants. The process involved the presence of $\text{Cu}(\text{OTf})_2$, HOTf as catalyst and CH_3CN as solvent under 120°C [54].



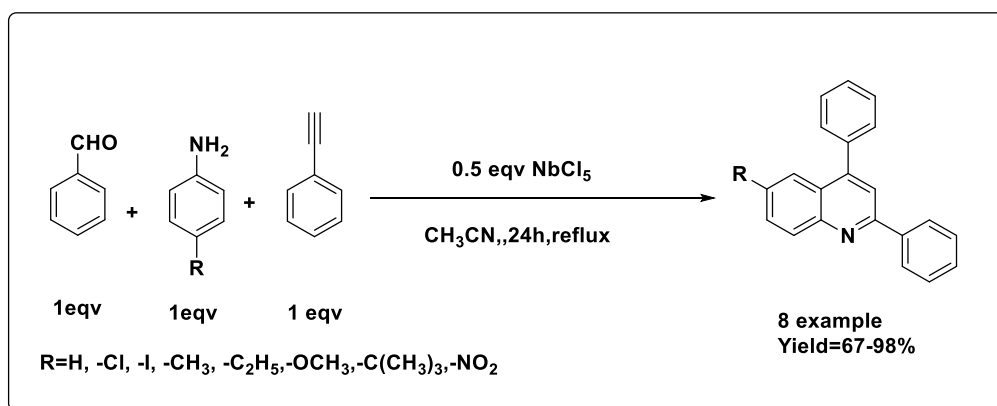
Scheme 7. Regioselective copper catalyzed protocol reported by Wu. et al

In 2017, Thigulla. et al. had developed a synthetic method for the synthesis of quinoline derivatives using aniline derivatives using aldehyde, 4-hydroxycoumarin and 6-aminoindole as reactants. The process involved the presence FeCl_3 as catalyst in 1,4-dioxane solvent under thermal condition (Scheme 8.) with yield upto 51% [55].



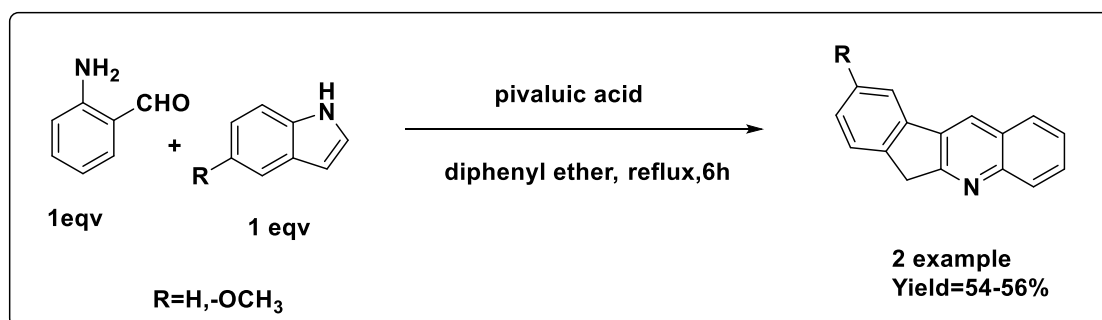
Scheme 8. FeCl_3 catalyzed synthesis of quinolone reported by Thigulla.et al.

In 2015, Andrade.et al. had developed a synthetic method for the synthesis of quinoline derivatives using aniline derivatives, aldehyde and alkyne as reactants. The process involved the presence NbCl_5 as catalyst under thermal condition in CH_3CN solvent (Scheme 9.) with yield upto 98% [56].



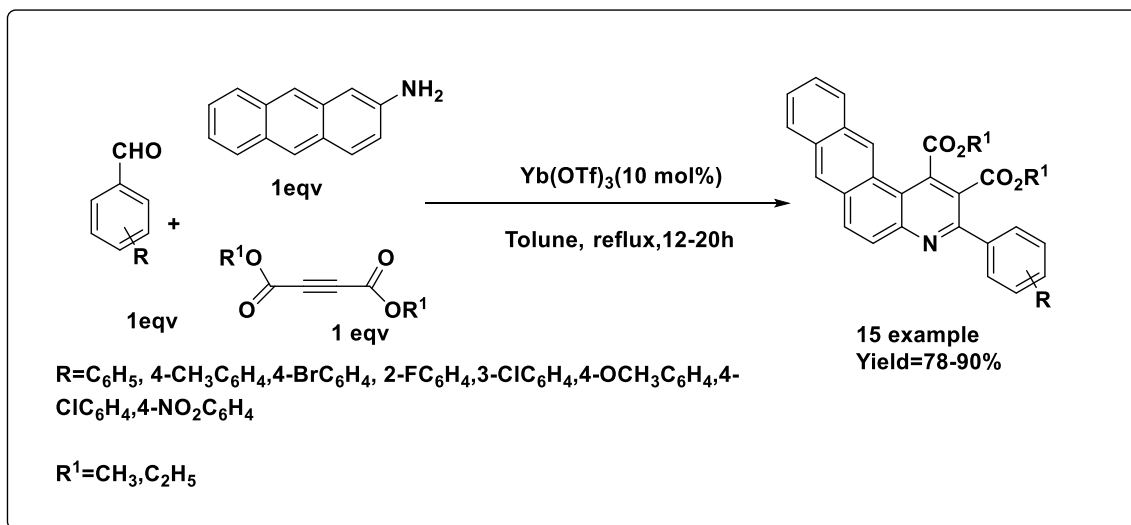
Scheme 9. Niobium pentachloride as catalyst for quinoline synthesis reported by Andrade.et al.

In 2016, Tilve.et al. had developed a synthetic method for the synthesis of quinoline derivatives using 2-aminobenzaldehyde and indole derivatives as reactants. The process involved the presence of pivalic acid under reflux condition (Scheme 10.) with yield upto 56% [57].



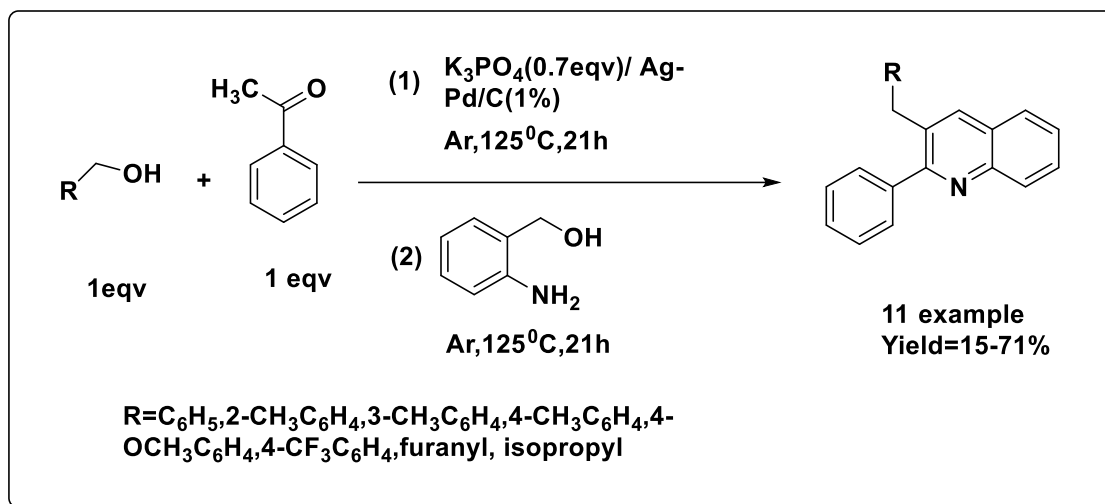
Scheme 10. Pivalic acid catalyzed synthesis reported by Kadam and Tilve.et al.

In 2014, Zhaou.et al. had developed a synthetic method for the synthesis of quinoline derivatives using aldehydes, aromatic primary amines and alkyne diester derivatives as reactants. The process involved the presence of $\text{Yb}(\text{OTf})_3$ in toluene under reflux condition (Scheme 11.) with yield upto 90% [58].



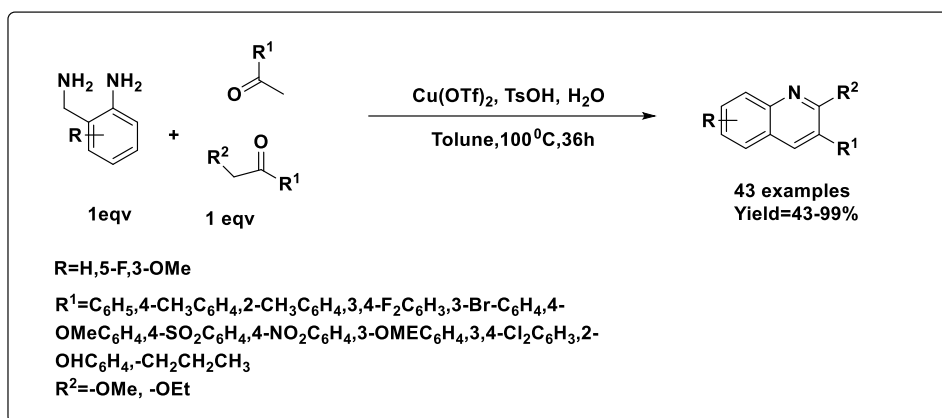
Scheme 11. Ytterbium triflate [$\text{Yb}(\text{OTf})_3$] catalysed synthesis reported by Zhou et al.

In 2013, Chen.et al. had developed a synthetic method for the synthesis of quinoline derivatives using benzaldehyde, alcohols and primary aromatic aminoalcohol derivatives as reactants. The process involved the presence of $\text{K}_3\text{PO}_4/\text{Ag-Pd-C}$ as catalyst under reflux condition (Scheme 12.) with yield upto 71% [59].



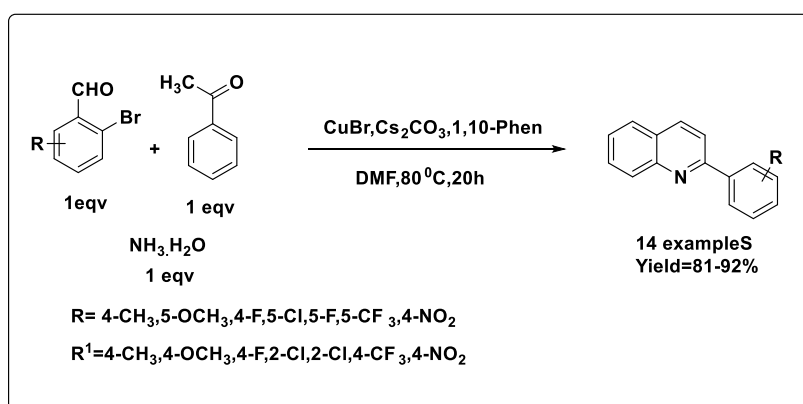
Scheme 12. Synthesis of quinolines reported by Chen.et al

In 2015, Long-Yi.et al. had developed a synthetic method for the synthesis of quinoline derivatives using ketones and amine derivatives as reactants. The process involved the presence of $\text{Cu}(\text{OTf})_2, \text{TsOH}, \text{H}_2\text{O}$ as catalyst in toluene under heating condition (Scheme 13.) with yield upto 99% [60].



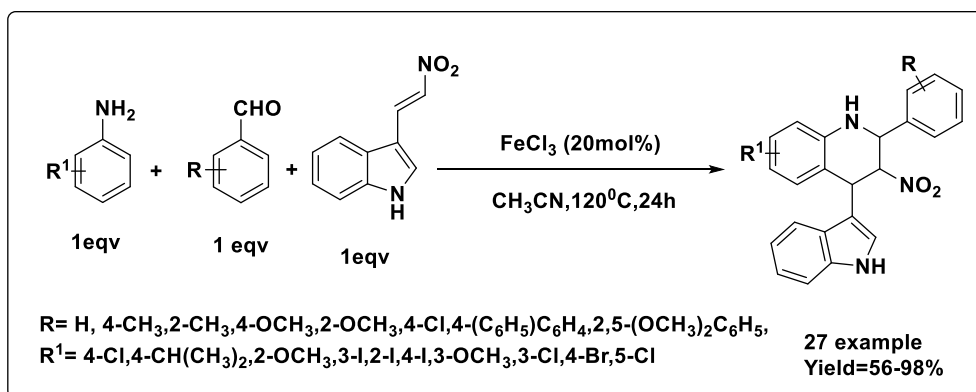
Scheme 13. Copper catalyzed C-N cleavage reported by Long-Yi.et al.

In 2014, Li.et al. had developed a synthetic method for the synthesis of quinoline derivatives using o-bromobenzaldehyde derivatives, acetophenone and ammonia as reactants. The process involved the presence of CuBr, Cs₂CO₃ as catalyst in DMF under heating condition (Scheme 14.) with yield upto 92% [61].



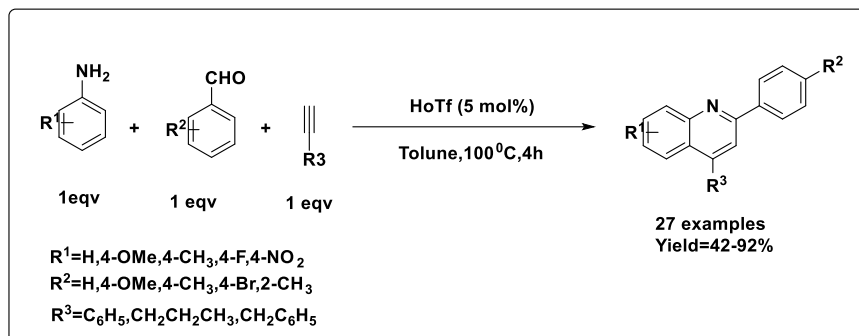
Scheme 14. Copper catalyzed reaction protocol reported by Li.et al.

In 2014, Zanwar.et al had developed a synthetic method for the synthesis of quinoline derivatives using primary aromatic amines, aldehydes and indole derivative as reactants. The process involved the presence of FeCl₃ as catalyst in CH₃CN under heating condition (Scheme 15.) with yield upto 98% [62].



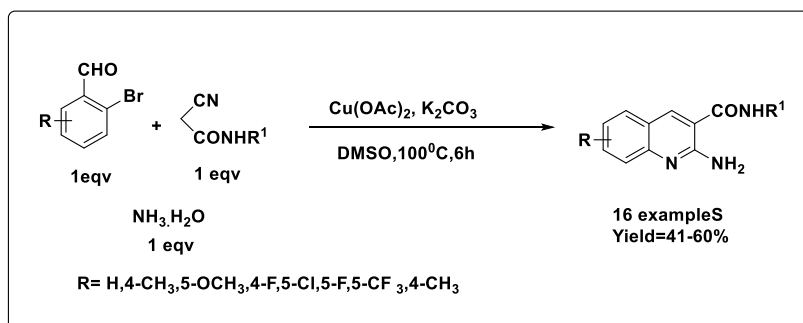
Scheme 15. Mild reaction protocol reported by Zanwar.et al

In 2014, Zhang.et al. had developed a synthetic method for the synthesis of quinoline derivatives using primary aromatic amines, aldehydes and alkyne derivative as reactants. The process involved the presence of HoTf as catalyst in toluene under heating condition (Scheme 16.) with yield upto 92% [63].



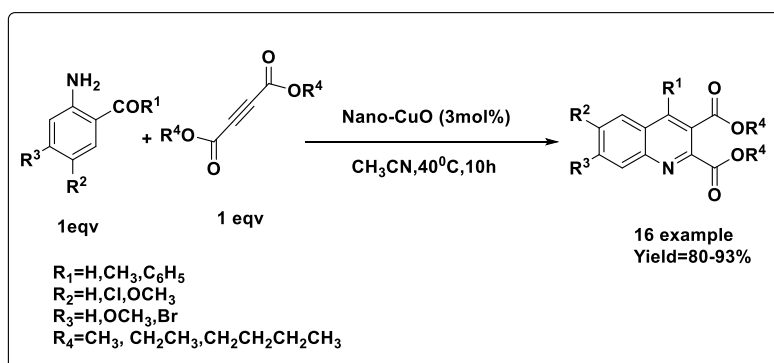
Scheme 16. Mild reaction protocol reported by Zhang et al.

In 2015, Zhang.et al. had developed a synthetic method for the synthesis of quinoline derivatives using o-bromobenzaldehydes derivatives, active methylene compound and ammonia as reactants. The process involved the presence of Cu(OAc)₂, K₂CO₃ as catalyst in DMSO under heating condition (Scheme 17.) with yield upto 60% [64].



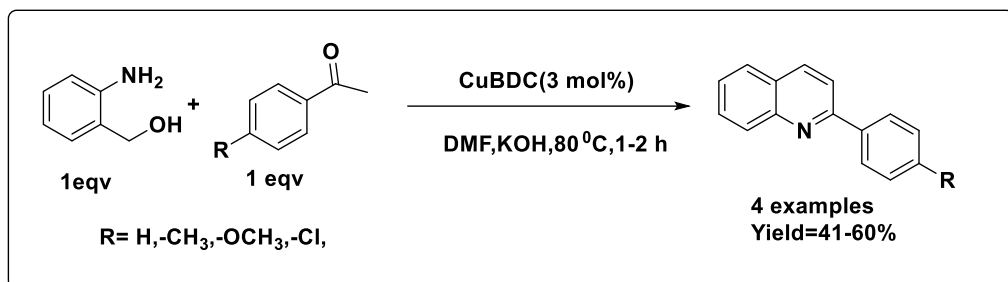
Scheme 17. Mild reaction protocol reported by Zhang et al.

In 2012, Venkanna.et al. had developed a synthetic method for the synthesis of quinoline derivatives using primary aromatic-ketone derivative, and alkyne diester derivatives as reactants. The process involved the presence of Nano-CuO as catalyst in CH₃CN under heating condition (Scheme 18.) with yield upto 93% [65].



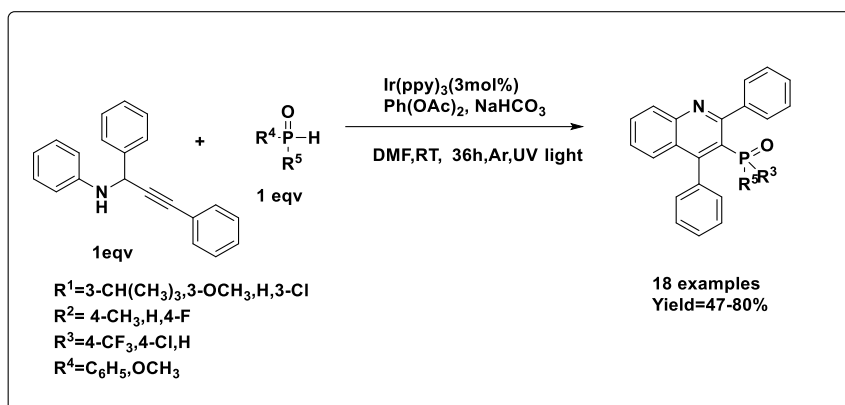
Scheme 18. Mild reaction protocol reported by Venkanna et al.

In 2013, Phan.et al. had developed a synthetic method for the synthesis of quinoline derivatives using primary aromatic aminoalcohol, aromatic ketone derivative as reactants. The process involved the presence of CuBDC as catalyst in alkaline DMF under heating condition (Scheme 19.) with yield upto 60% [66].



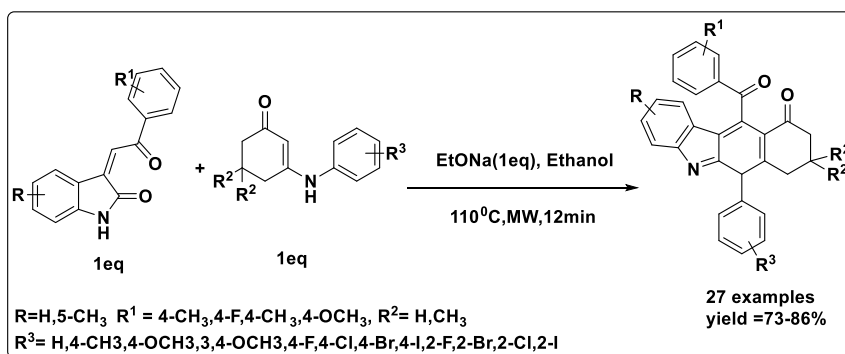
Scheme 19. Cu catalysed reaction reported by Phan et al.

In 2015, Shushizadeh.et al. had developed a synthetic method for the synthesis of quinoline derivatives using primary aromatic aminoalkyne derivatives, dialkyle phosphate derivatives as reactants. The process involved the presence of Ir(ppy)₃, Ph(OAc)₂.NaHCO₃ as catalyst in DMF under room temperature condition with UV light (Scheme 20.) with yield upto 80% [67].



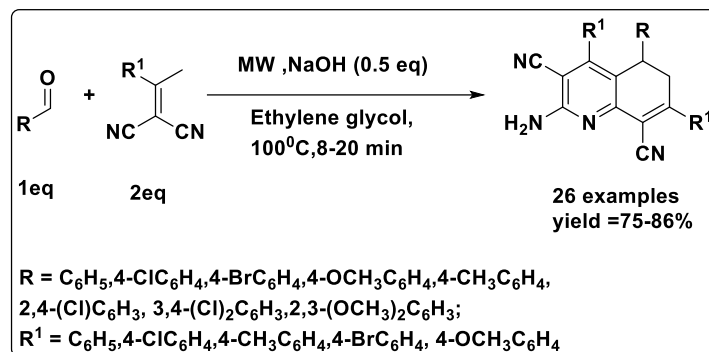
Scheme 20. Iridium catalysed reaction reported by Shushizadeh et al.

In 2014, Li et al. developed a protocol to synthesize biologically active quinolines using 3-arylidene-2-oxindoles with enamines in presence of sodium ethoxide (NaOEt) in ethanol at 110°C under microwave condition with 27 examples having yield 73% to 86% (Scheme 21.) [68].



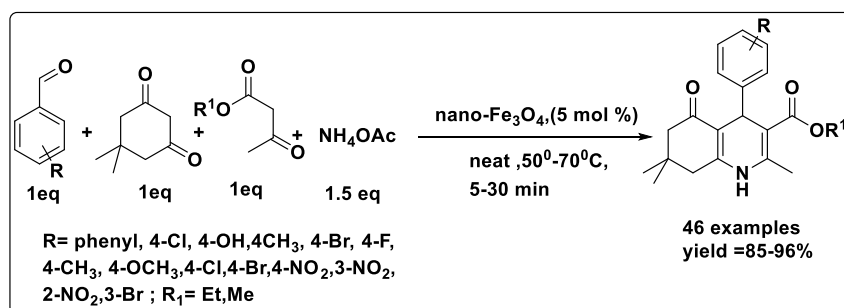
Scheme 21. Base promoted (3+3) Cycloaddition reaction under microwave reported by Li et al.

In 2012, Yu. et al. designed a three component synthesis of polysubstituted dihydroquinoline from aromatic aldehydes and 1-arylethylidenemalononitrile in presence of sodium hydroxide as base in ethylene glycol under microwave irradiation having 26 examples with yield from 75% to 86 % (Scheme 22.) [69].



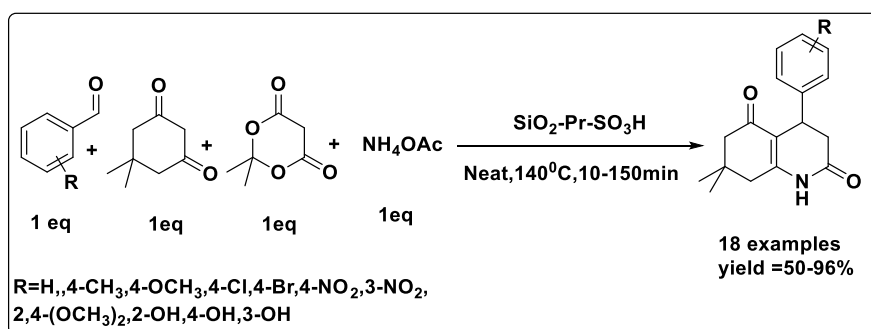
Scheme 22. Base catalyzed Domino reaction under microwave reported by Yu. et al.

In 2014, Esfahani. et al. and Khazaei et al. performed iron (III) oxide nanoparticles catalyzed synthesis of polyhydroquinolines under solvent free conditions using aromatic, cyclic and heterocyclic aldehydes, dimedone, β ketoesters and ammonium acetate at 50°C under solvent free conditions (Scheme 23.) having 46 examples with yield upto 96% [70-71].



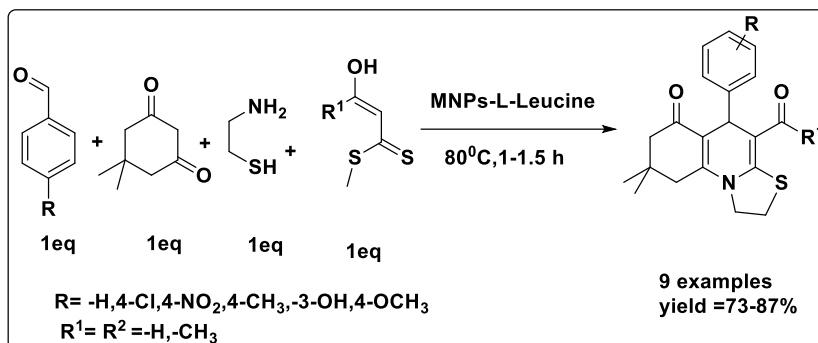
Scheme 23. Solvent free reaction reported by Esfahani. et al.

In 2015, Ziarani. et al synthesized dioxo-octahydroquinolines in one pot method using aromatic aldehydes, dimedone, Meldrum's acid and ammonium acetate and sulfonic acid functionalized SiO_2 -Pr- SO_3H as catalyst under solvent-free condition. (Scheme 24.) [72]. The procedure has some greener advantages having 18 examples with yield up to 96%.



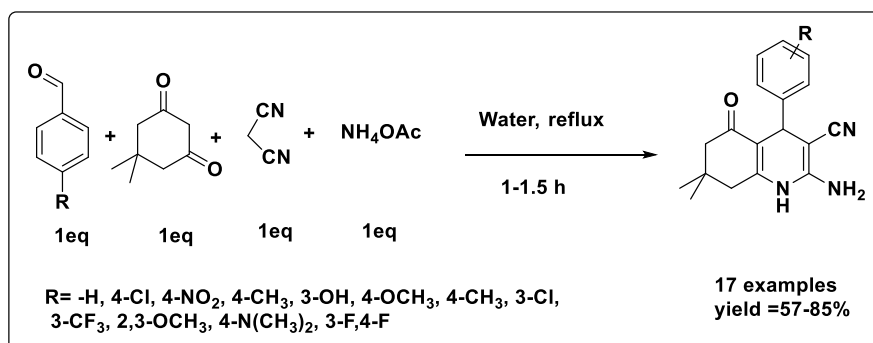
Scheme 24. Microwave assisted silica based catalyst reported for octahydroquinolines by Ziarani. et al.

In 2016, Arabpoor et al. synthesized synthesis of thiazoloquinolines using superparamagnetic silica-encapsulated γ - Fe_2O_3 supported L-Leucine nanoparticles by the four-component reaction of α -enolicdithioesters, cysteamine, aromatic aldehydes and dimedone under thermal solvent-free condition at 80°C in one hour having 9 examples with yield between 73-93% yield (Scheme 25.) [73].



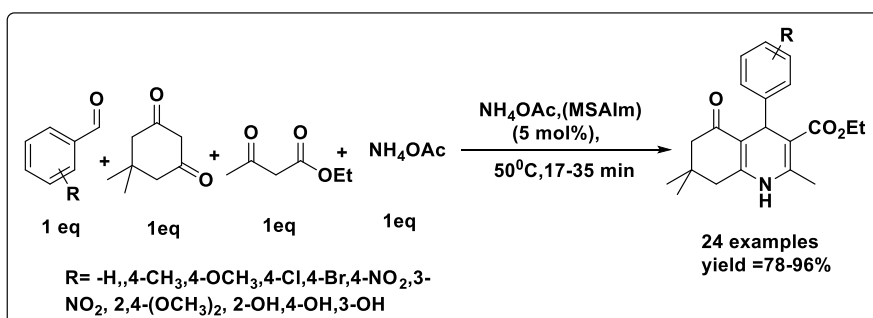
Scheme 25. Biocatalyst based reaction protocol reported by Arabpoor and Shaterian et al.

In 2017, Patil et al. had done a catalyst-free method for the synthesis of hexahydroquinolinones in single pot four component method taking dimedone, ammonium acetate, aryl aldehydes and malanonitrile as substrate in water having 17 examples with yield between 57-85% yield (Scheme 26.) [74].



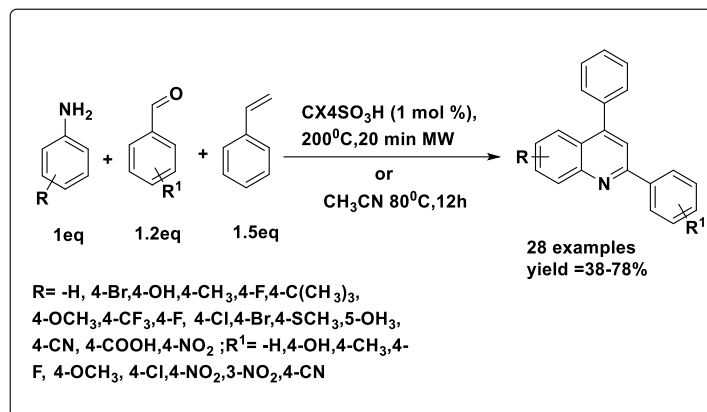
Scheme 26. Catalyst free synthesis protocol reported by Patil et al.

In 2014, Khaligh et al. had done a four-component one-pot synthesis of synthesis of unsymmetrical polyhydroquinoline derivatives from aryl/heteroaryl aldehydes, ethyl acetoacetate, dimedone and ammonium acetate under solvent-free conditions at 50°C . having 24 examples with yield between 78-96% yield (Scheme 27.) [75].



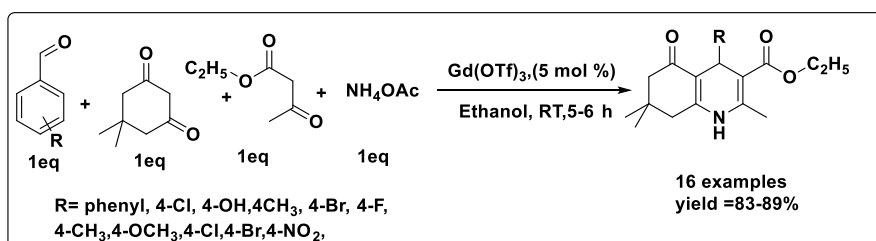
Scheme 27. Solvent free reaction reported by Davoodnia et al. and Khaligh. et al.

In 2017, Liberto et al. has taken a protocol for the synthesis of 2,4-disubstituted quinolines using aromatic aldehydes, aromatic amines, styrene under at 200°C temperature Microwave condition using CX4SO₃H catalyst or at 80°C temperature in acetonitrile solvent having 28 examples with yield between 38-78% yield (Scheme 28.) [76].



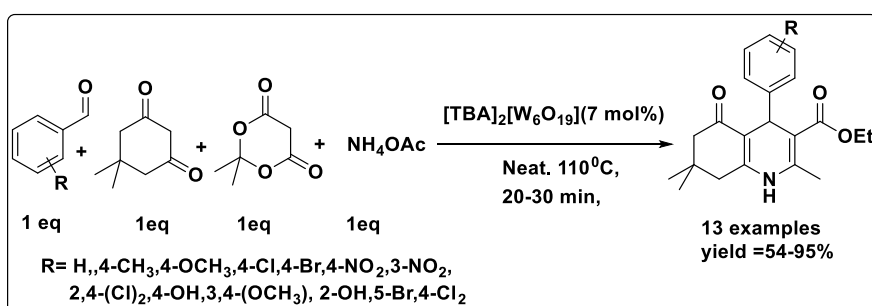
Scheme 28. Microwave assisted solvent free reaction reported by Liberto et al.

In 2017, Mansoor et al. reported a multicomponent method for the synthesis of hexahydroquinolones by using Gd(OTf)₃ as catalyst from aldehydes, 5,5-dimethyl-1,3-cyclohexanedione dimedone, ethyl acetoacetate and ammonium acetate by using Gd(OTf)₃ as catalyst at room temperature. [77]. The procedure has 16 examples with yield between 83-89% yield (Scheme 29.).



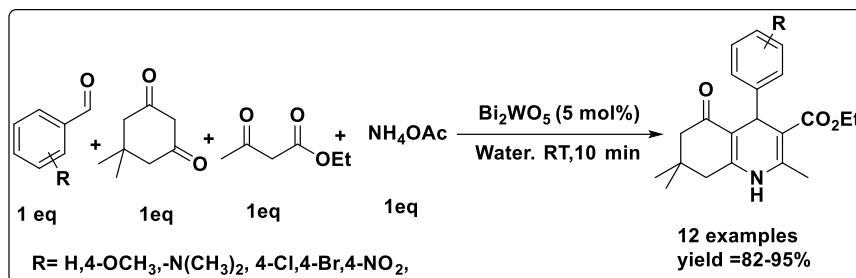
Scheme 29. Mild synthesis protocol for polyhydroquinoline in ethanol reported by Mansoor et al.

In 2011, Khojastehnezhad et al. reported a synthetic method for the synthesis of hexahydroquinolinones in one-pot, four-component method taking dimedone, aldehydes, ethyl acetoacetate and ammonium acetate under solvent-free conditions using [TBA]₂[W₆O₁₉] catalyst [78-79]. The procedure has 13 examples with yield between 54-95% yield (Scheme 30.).



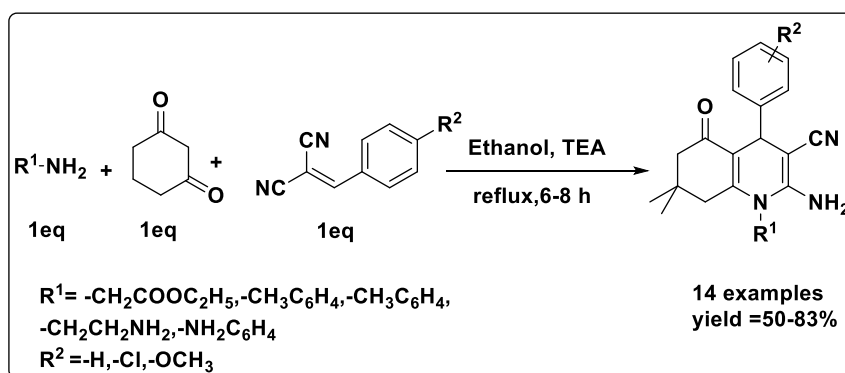
Scheme 30. Solvent free reaction reported by Davoodnia et al. and Khaligh

In 2014, Paplal.et al. synthesized different types of functionalized polyhydroquinolines by reaction of substituted aromatic aldehydes, ethyl acetoacetate, dimedone and ammonium acetate in aqueous medium using Bi_2WO_5 as catalyst having 12 examples with yield between 82-95% yield (Scheme 31.) [80].



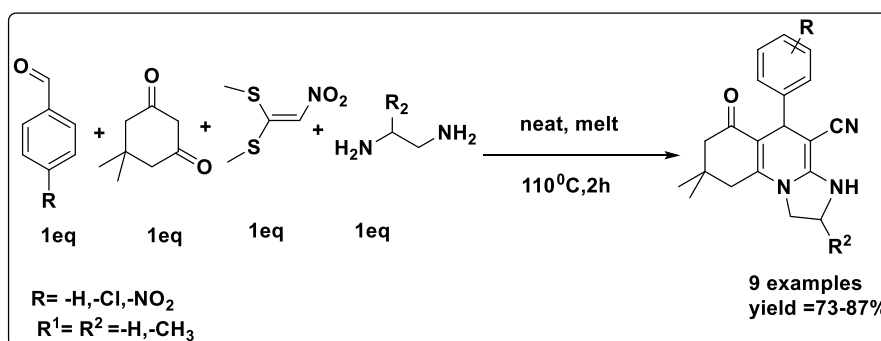
Scheme 31. Synthesis of functionalized polyhydroquinolines reported by Paplal.et al.

In 2017, Abdelhamid.et al. had made a protocol for the three-component cyclocondensation synthetic method of hexahydroquinoline derivatives from 1,3-cyclohexanedione, primary amine in presence of ethanol, TEA under reflux condition having 14 examples with yield between 50-83% yield (Scheme 32.) [81].



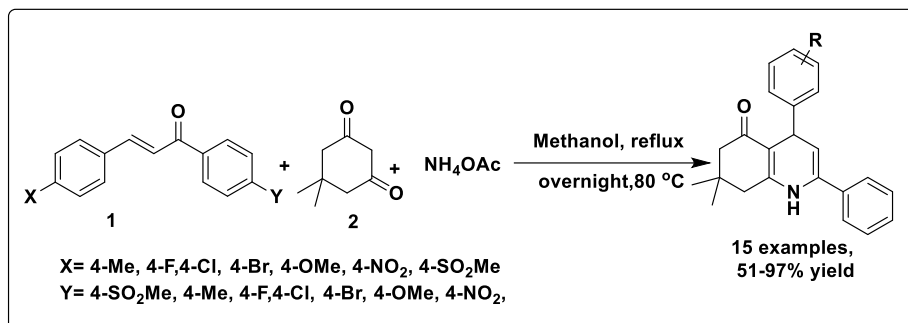
Scheme 32. Three-component cyclocondensation with TEA in ethanol reported by Abdelhamid.et al.

In 2014, Alizadeh.et al. synthesised the octahydro-imidazo[1,2-a]quinoline derivatives under solvent free conditions from aromatic aldehyde, dimidone as amazor component. The advantage of this procedure involve catalyst free reaction having 9 examples with yield between 73-87% yield (Scheme 33.) [82].



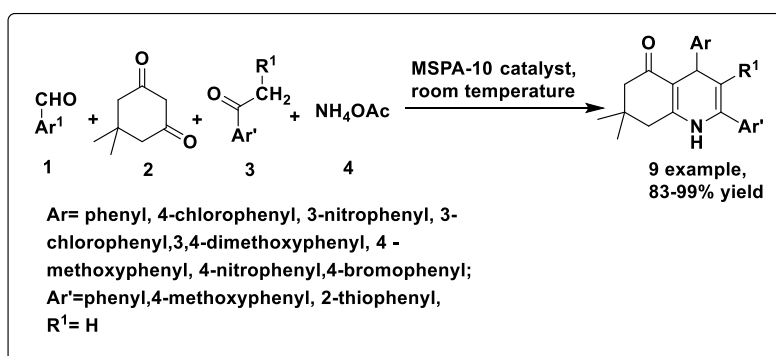
Scheme 33. Solvent free reaction reported by Alizadeh.et al.

In 2014, Zarghia.et al. has reported a synthesis of 2,4-diarylhexahydroquinolines by the one pot reaction between mixture of 5, 5-dimethyl-1,3-cyclohexandion, 1,3-diaryl-2-propen1-one, ammonium acetate in methanol under refluxed condition at 80°C for overnight. This procedure have greener advantageous having 15 examples with yield between 51-97% yield (Scheme 34.) [83].



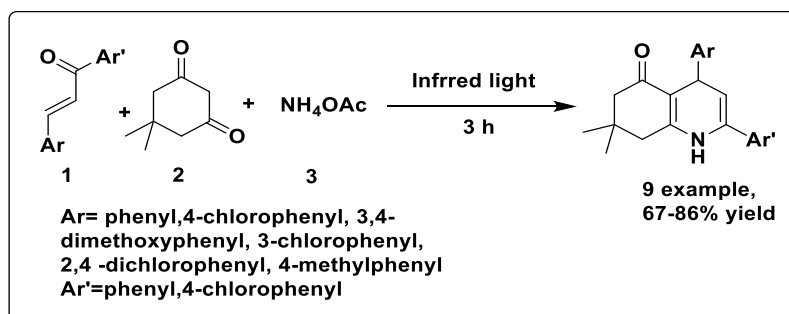
Scheme 34. Synthesis of 2,4-diarylhexahydroquinolines by Zarghia.et al.

In 2013, Ray.et al. has reported a synthesis of 2,4-diarylhexahydroquinolines by carrying out a one pot 4-component reactions between aromatic aldehydes, dimedone and acetophenone and ammonium acetate by using a new heterogeneous MCM-41 silica supported HPF₆ catalyst The procedure have some greener advantageous having 15 examples with yield between 51-97% yield. (Scheme 35.) [84].



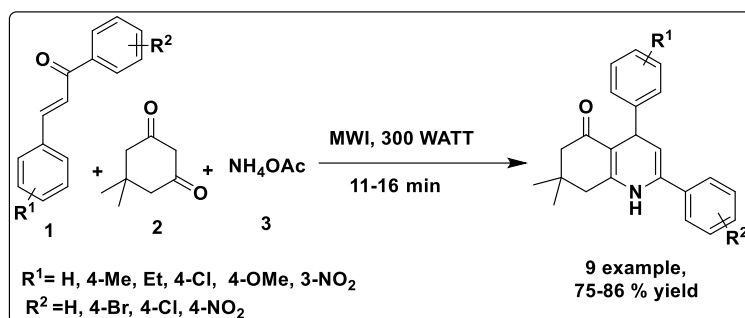
Scheme 35. synthesis of 2,4-diarylhexahydroquinolines by Ray.et al.

In 2006, Wang.et al. reported a synthetic procedure for the synthesis of 2,4-diarylhexahydroquinolines by doing a one pot 3-component reactions between Chalcones, dimedone and ammonium acetate by infrared irradiation (IR) irradiation promoted the synthesis having 9 examples with 67-86% yield (Scheme 36.) [85].



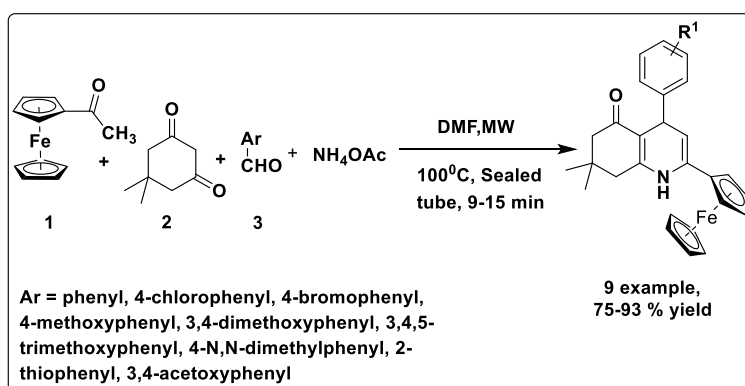
Scheme 36. Synthesis of 2,4-diarylhexahydroquinolines by Wang.et al.

In 2005, Hua.et al. reported a synthetic procedure for the synthesis of 2,4-diarylhexahydroquinolines by doing a one pot 3-component reactions between Chalcones, dimedone and ammonium acetate by microwave irradiation (mwi 300 watt) the synthesis with 75-86% yield.(Scheme 37.) [86].



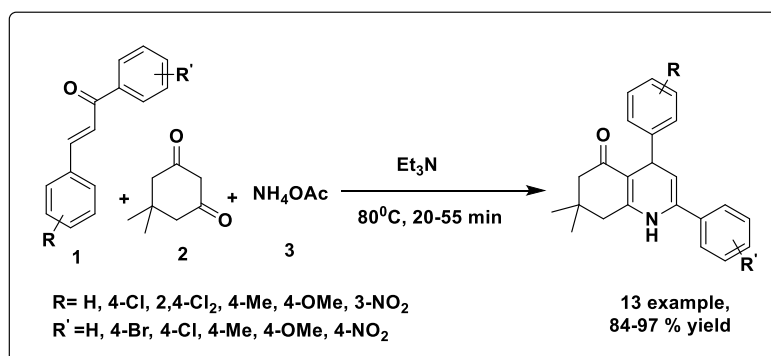
Scheme 37. Synthesis of 2,4-diarylhexahydroquinolines by Hua.et al.

In 2009, Tu.et al. reported a synthetic procedure for the synthesis of 2,4-diarylhexahydroquinolines by doing a one pot 4-component reactions between aromatic aldehydes, dimedone, ammonium acetate and ferrocenyl active methylene compound by microwave irradiation (MW) in presence of DMF solvent with 75-93% yield (Scheme 38.) [87].



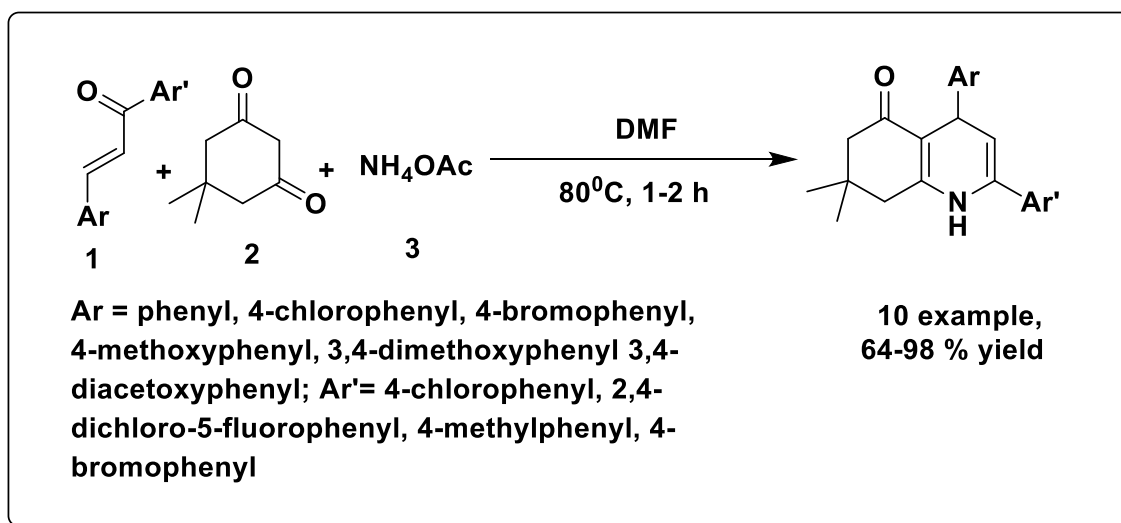
Scheme 38. Synthesis of 2,4-diarylhexahydroquinolines by Tu.et al.

In 2015, Karimi-Jaberi.et al. reported a convenient and efficient protocol for the synthesis of 2,4-diaryl hexahydroquinoline derivatives by a three-component reaction between Chalcones, dimedone and ammonium acetate catalyzed by triethylamine under solvent-free conditions with yield 84-97% (Scheme 39.) [88].



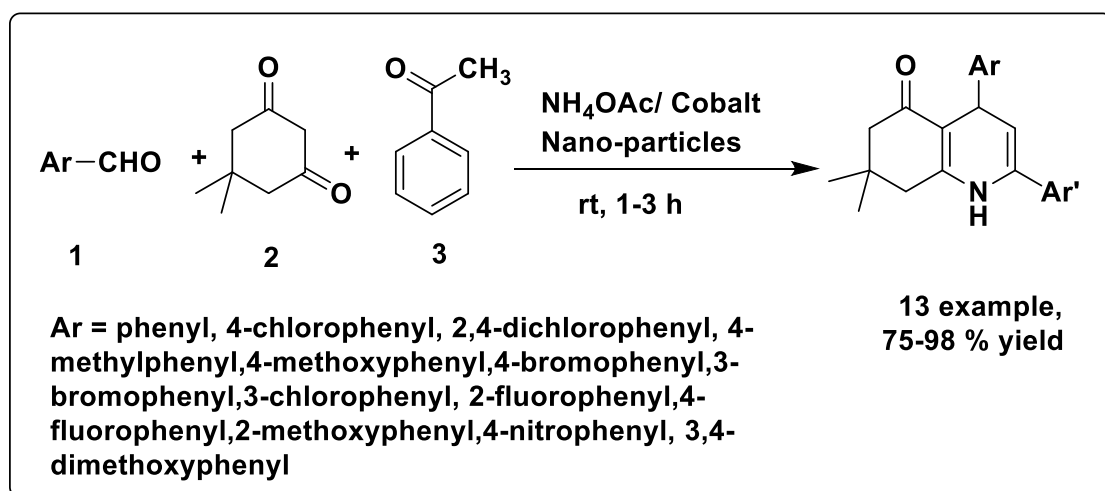
Scheme 39. Synthesis of 2,4-diarylhexahydroquinolines by Karimi-Jaberi et.al.

In 2002, Wang.et al. reported a series of substituted 2,4-diarylhexahydroquinoline derivatives by a 3-component reaction of dimedone ammonium acetate and 1,3-diaryl-2-propen-1-one (Chalcones) in DMF at 80°C temperature with yields 64–98%. (Scheme 40.) [89].



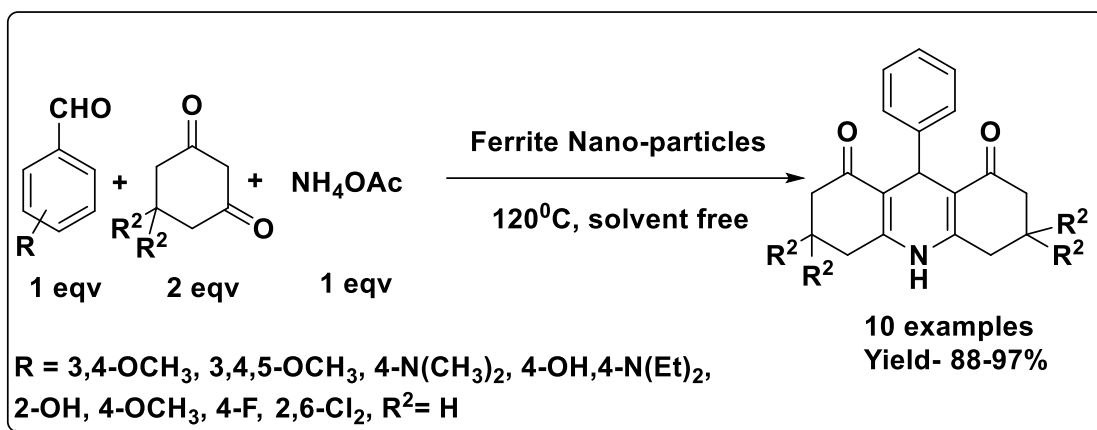
Scheme 40. Synthesis of 2,4-diarylhexahydroquinolines by Wang.et al.

In 2011, Safari.et al. reported a straightforward method for the synthesis of 2,4-diarylhexahydroquinoline derivatives by the reaction between dimedone, acetophenone, aromatic aldehydes, and ammonium acetate in the presence of a catalytic amount of Cobalt nanoparticles at room temperature with 75-98% yield (Scheme 41.) [90].



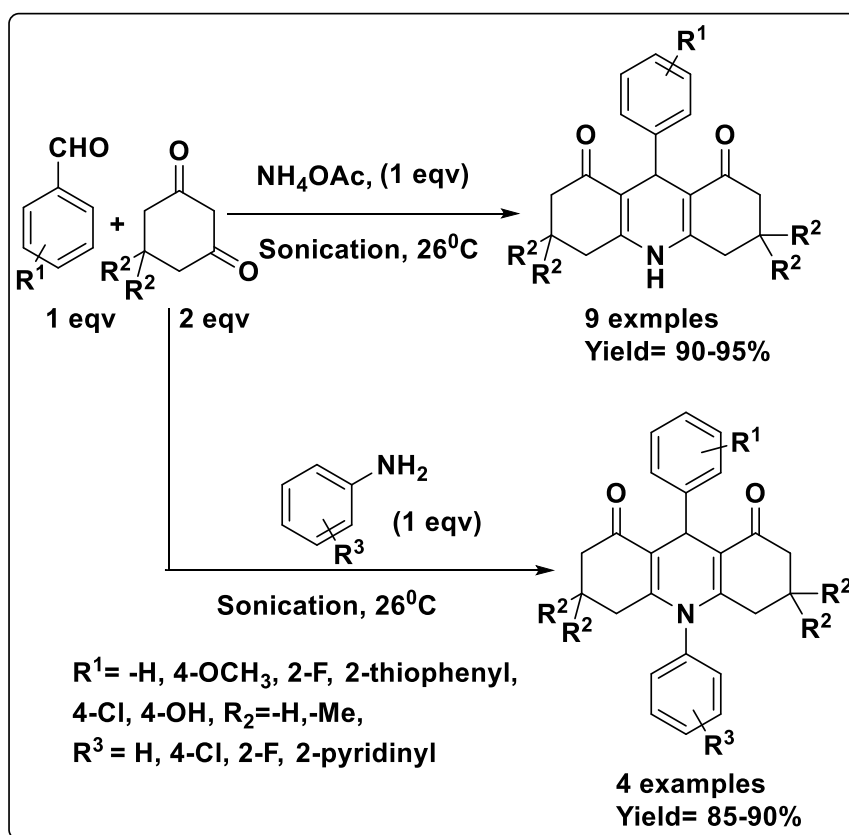
Scheme 41. Synthesis of 2,4-diarylhexahydroquinolines by Safari.et al.

Methods synthesis of acridinedione derivatives: In 2016, Sunkara.et al. had done the synthesis of 9-aryl substituted acridinedione derivatives under solvent free conditions. A one-pot reaction methodology was adopted with the use of 1,3-cyclohexanedione, aldehydes and ammonium acetate using nano ferrite at 120°C for the preparation of acridinediones and their derivatives with yield 88-97% (Scheme 42.) [91].



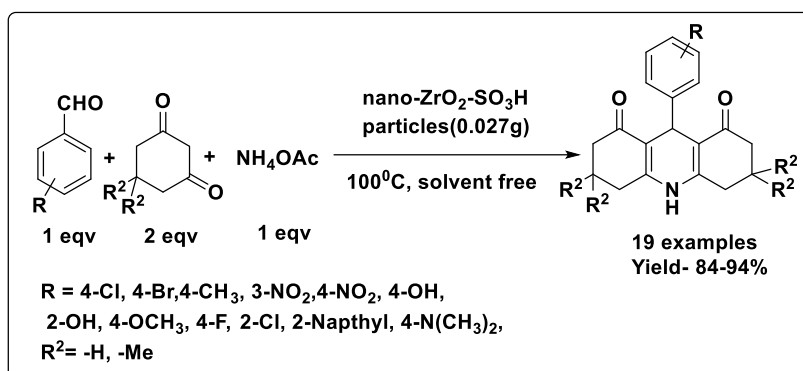
Scheme 42. One-Pot Facile Synthesis of Acridinediones and their Derivatives by Sunkara.et al.

In 2013, A Facile Synthesis of N-H- and N-Substituted Acridine-1,8-diones under Sonic Condition by Sudha.et al. Here ceric ammonium nitrate (CAN) was used along with aromatic aldehydes and aromatic amines or ammonium acetate and dimedone or cyclohexyl-1,3-diones at 26°C under sonic condition with yield 85-90% (Scheme 43.) [92].



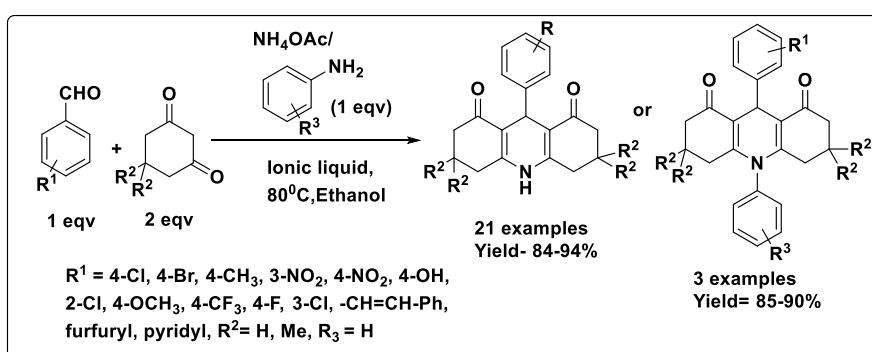
Scheme 43. A facile synthesis of N-H- and N-substituted acridine-1,8-diones by Sudha.et al.

In 2016, Amoozadeh.et al. synthesized 9-arylhexahydroacridines with taking a mixture of various 1,3-cyclic diketone, aromatic aldehydes, and ammonium acetate in presence of n-ZrSA as catalyst at 100°C (in an oil bath) in solvent free conditions with yield 84-94% (Scheme 44.) [93].



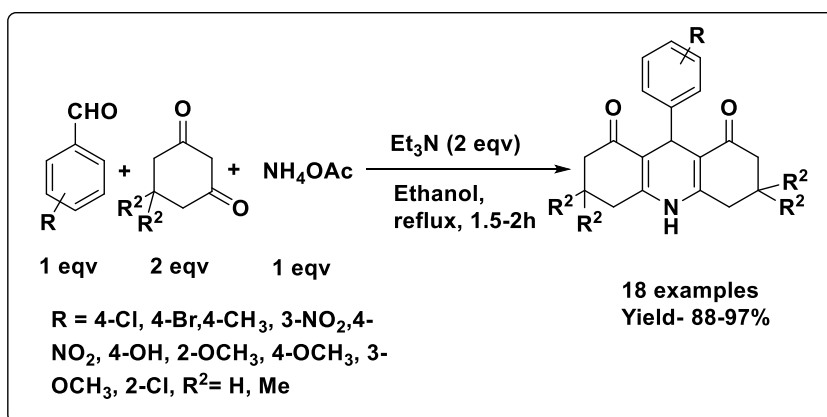
Scheme 44. Synthesis of 9-arylhexahydroacridines Amoozadeh.et al.

In 2017, Zhu.et al. reported the synthesis of 9-arylhexahydroacridines using aromatic aldehyde, 5,5-dimethyl-1,3-cyclohexanedione, NH₄OAc and corresponding amount of ionic liquid were mixed with 1 ml ethanol, and then heated at 80°C by using a series of ionic liquids based on betainium cation (Hbet) with different anions with yield 84-94% (Scheme 45.) [94].



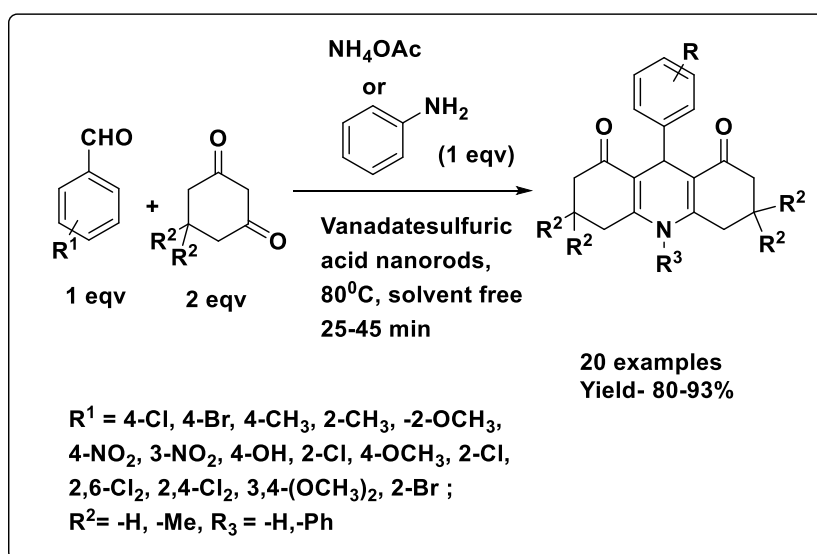
Scheme 45. Synthesis of 9-arylhexahydroacridines Zhu.et al.

In 2018, Djemoui.et al. reported an efficient approach to the synthesis of 1,8-dioxo-decahydroacridines via one-pot multi-component condensation of an aromatic aldehyde, cyclic 1,3-diketones and NH₄OAc in ethanol with use of Triethylamine (TEA) at reflux condition with yield 88-97% (Scheme 46.) [95].



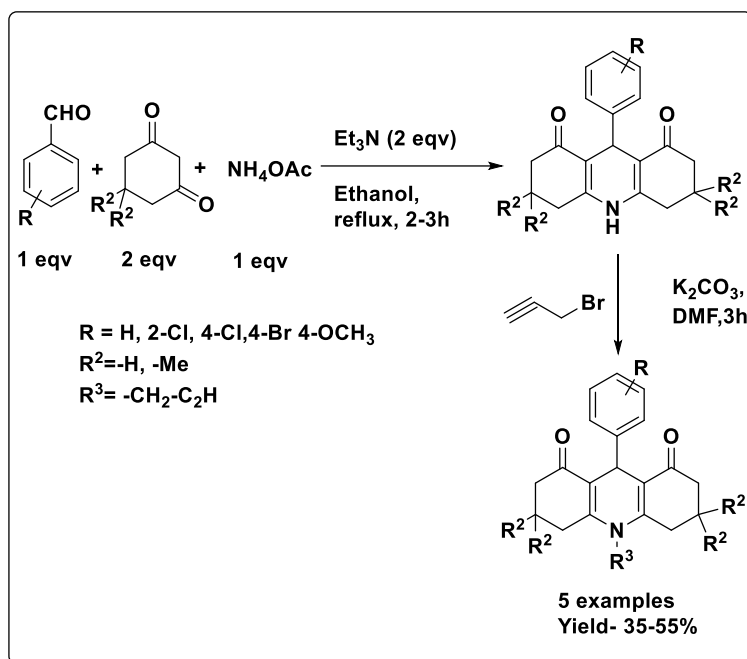
Scheme 46. An efficient synthetic approach to the synthesis of 1,8-dioxo-decahydroacridines by Djemoui.et al.

In 2015, Nasr-Esfahani et al. reported a synthesis of hexahydroacridine-1,8-diones using 1,3-cyclohexanedione derivatives, aldehydes and ammonium acetate or aniline under solvent-free conditions. Nanorod vanadatesulfuric acid (VSA-NRs), was used as catalyst as a novel, recyclable and eco-benign catalyst to synthesis hexahydroacridine-1,8-diones with yield 80-93% (Scheme 47.) [96].



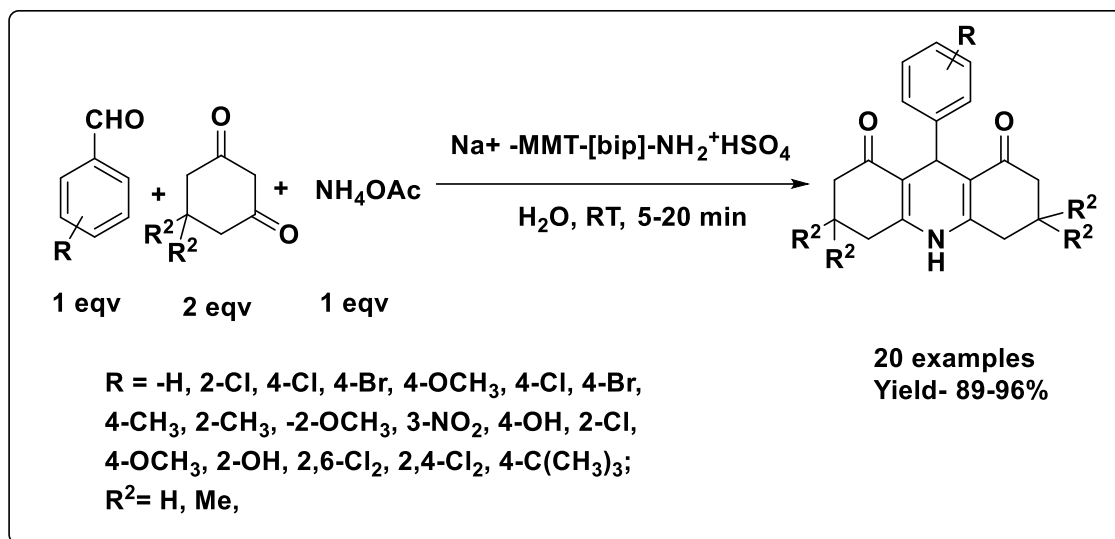
Scheme 47. Nasr-Esfahani et al. reported a synthesis of hexahydroacridine-1,8-diones

In 2020, Naouri et al. reported a procedure for the preparation of 1,8-dioxodecahydroacridine derivatives via a one-pot three-component condensation of aromatic aldehydes, 1,3-cyclohexanedione and ammonium acetate in ethanolic medium under reflux condition catalyzed by triethylamine (TEA) to give the desired product with yield 35-55% (Scheme 48.) [97].



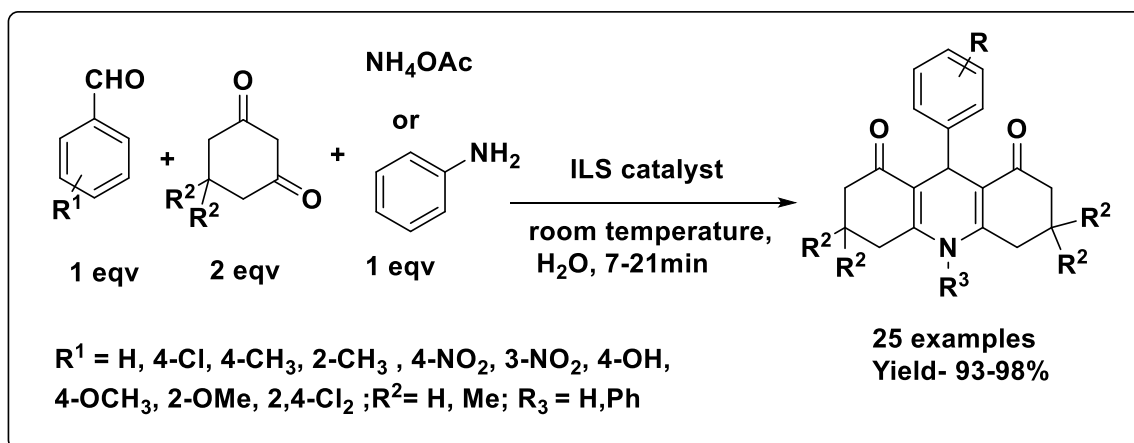
Scheme 48. A one pot multicomponent synthesis of 1,8- dioxodecahydroacridine derivatives by Naouri et al.

In 2020, Mazloumi et al. reported the synthesis of 1,8-dioxo-decahydroacridines via Hantzsch condensations using a new nanoporous catalyst formulated as $\text{Na}^+ \text{-MMT-[bip]-NH}_2^+ \text{HSO}_4$. All reactions were performed under mild reaction conditions taking mixture of a β -ketoester derivative, 1,3-cyclohexanedione derivatives, aldehyde and ammonium acetate with yield 89-96% (Scheme 49.) [98].



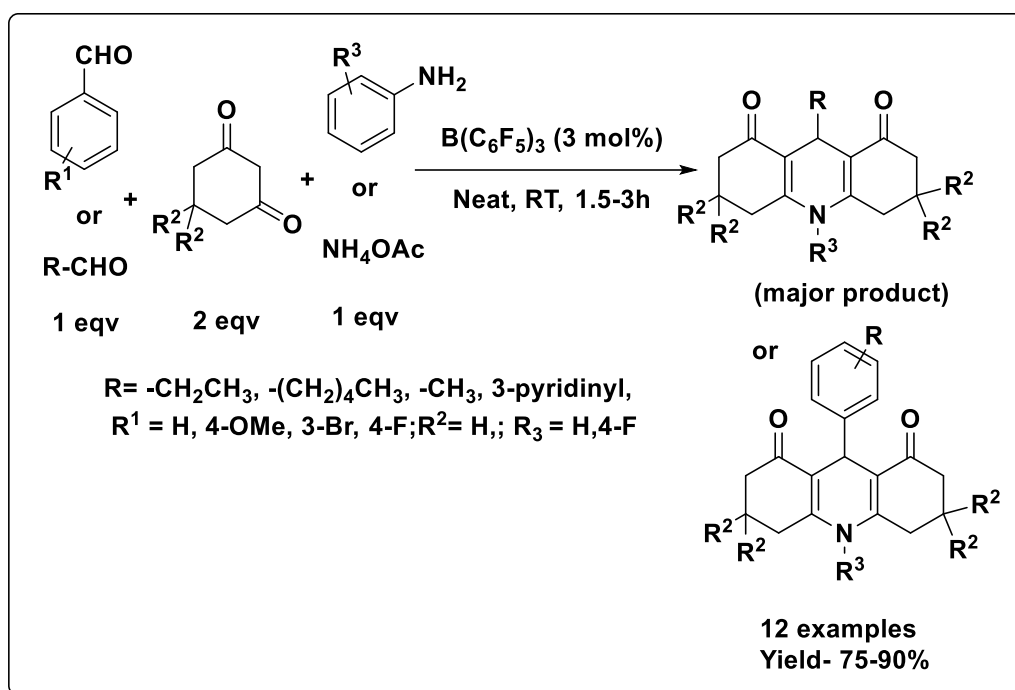
Scheme 49. Synthesis of 1,8-dioxo-decahydroacridines by Mazloumi et al.

In 2011, Vahdat et al. had synthesised 1,8-dioxodecahydroacridines by using ionic liquid with multi-SO₃H groups attached with it via the one-pot method with excellent yield within at room temperature in water medium with yield 93-98% (Scheme 50.) [99].



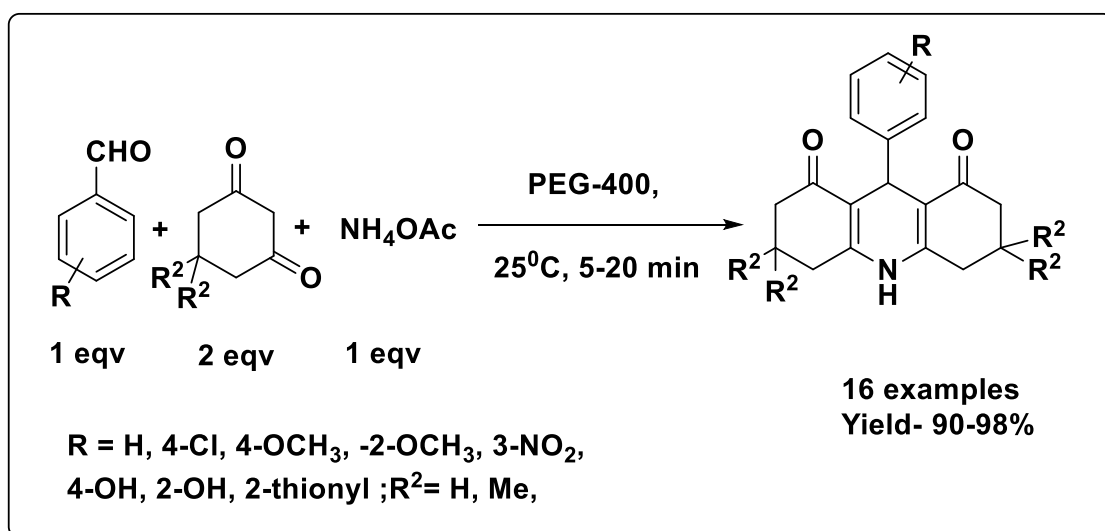
Scheme 50. Synthesis of 1,8-dioxo-decahydroacridines by Vahdat et al.

In 2008, A mild and efficient method for the synthesis of 1,8-dioxodecahydroacridines has been developed by Chandrasekhar et al. via a three-component reaction of a cyclic 1,3-dione, an aldehyde and an amine, under solvent-free conditions, at room temperature catalyzed by tris(pentafluorophenyl)borane $[\text{B}(\text{C}_6\text{F}_5)_3]$ with yield 75-90% (Scheme 51.) [100].



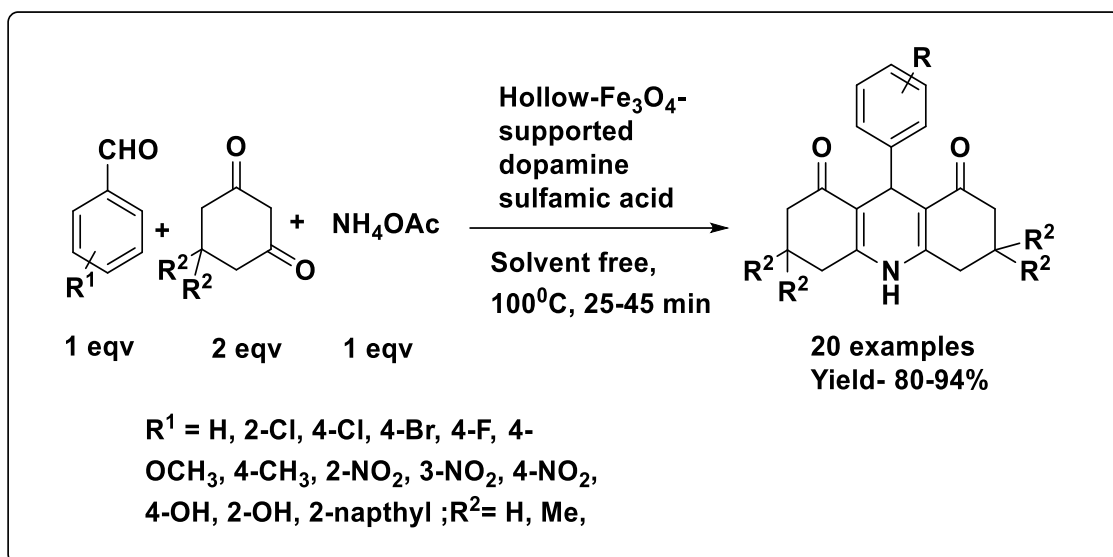
Scheme 51. A mild and efficient method for the synthesis of 1,8-dioxodecahydroacridines by Chandrasekhar.et al.

In 2010, Kidwai.et al. synthesized decahydroacridine-1,8-diones in the presence of polyethylene glycol (PEG) which was found to be an inexpensive non-toxic and effective medium for one pot synthesis of the product with higher yields up to 90-98% (Scheme 52.) [101].



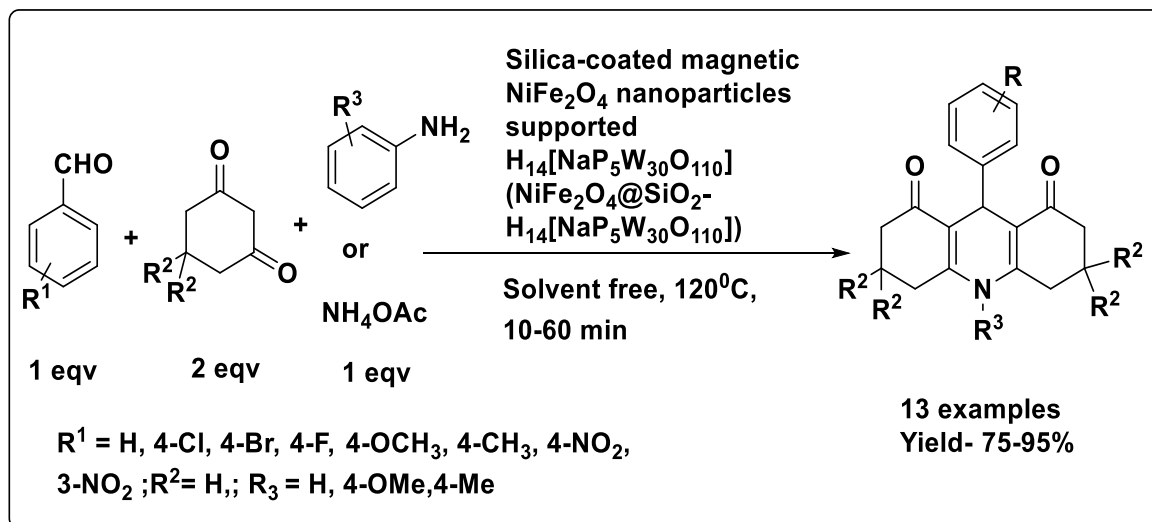
Scheme 52. Synthesis of 1,8-dioxodecahydroacridines has been developed by Kidwai.et al.

In 2017, Mirhosseini.et al. reported the synthesis of 1,8-dioxodecahydroacridine derivatives using H-Fe₃O₄@DA-SO₃H as catalyst by using aldehyde, ethyl acetoacetate or 1,3-cyclohexanedione NH₄OAc at 100°C under solvent-free condition with yield 80-94% (Scheme 53.) [102].



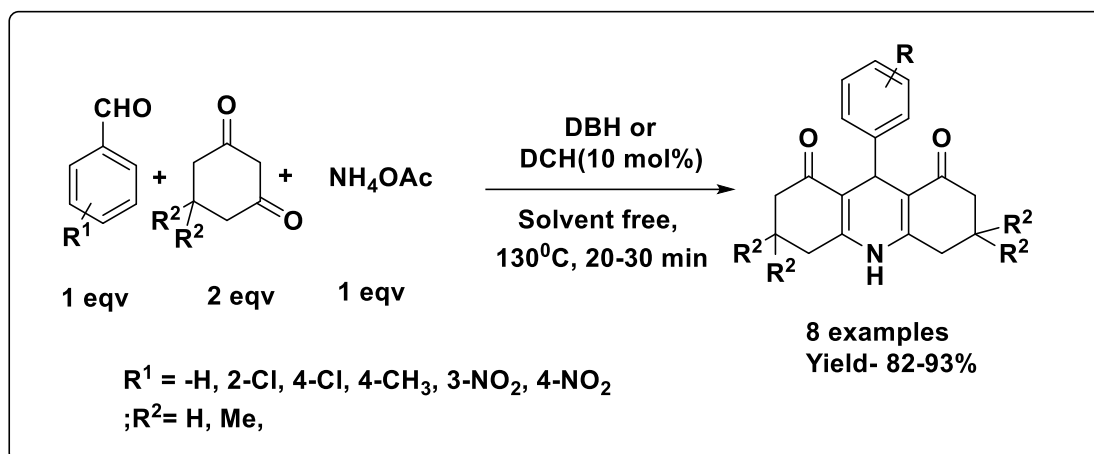
Scheme 53. Synthesis of 1,8-dioxodecahydroacridine derivatives Mirhosseyni.et al.

Malekia.et al. designed a method by using silica-coated magnetic NiFe₂O₄ nanoparticles-supported NiFe₂O₄@SiO₂-H₁₄[NaP₅W₃₀O₁₁₀] as versatile and highly efficient heterogeneous catalyst for one-pot multicomponent synthesis of 1,8-dioxodecahydroacridine derivatives under solvent-free condition. The synthesized catalyst can be magnetically recovered and reused four times without significant loss in catalytic efficiency with yield 75-95% (Scheme 54.) [103].



Scheme 54. Synthesis of 1,8-dioxodecahydroacridine derivatives by Malekia.et al.

Solvent free one pot synthesis of 1,8-dioxodecahydro acridine derivatives have been described by Maleki.et al. via Hantzsch condensation of various aldehydes, ammonium acetate,cyclic 1,3-dicarbonyl compounds in a very simple, efficient and environmentally benign method with excellent yield up to 93% (Scheme 55.) [104].



Scheme 55. Solvent free one-pot synthesis of 1,8-dioxodecahydroacridine derivatives by Malekietr. et al.

3. CONCLUSION

Quinolines, acridines and its derivatives are an imperative heterocyclic ring system, having pharmacological applications in medicinal chemistry. Therefore, there is an unceasing search of environmental-friendly methods to its synthesis. The review compiled and organized most of the newer methods documenting their advantages, limitations and substrate scope and this will help to plan further investigation in this subject. The category wise design and discussions on the advancements will draw a clear picture to the researchers lobby about the advantages and importance of each category and so they could use and improve current methodologies.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Dobbin L. The story of the formula for pyridine. *Journal of Chemical Education*. 1934;11:596.
2. Boyd D R, Sharma ND, Loke PL, Malone JF, McRoberts WC, Hamilton JTG.
3. Cretton S, Breant L, Pourrez L, Ambuehl C, Marcourt L, Ebrahimi S N, Hamburger M, Perozzo R, Karimou S, Kaiser M, Cuendet M, Christen P. Antitrypanosomal quinoline alkaloids from the roots of *Waltheria indica*. *Journal of Natural Products*. 2014;77:2304-2311.
4. Jain S, Chandra V, Kumar Jain P, Pathak K, Pathak D, Vaidya A. Comprehensive review on current developments of quinoline-based anticancer agents. *Arabian Journal of Chemistry*. 2016; 12:4920-4946.
5. Marella A, Tanwar OP, Saha R, Ali MR, Srivastava S, Akhter M, Shaquiquzzaman M, Alam MM. Quinoline A Versatile Heterocyclic. *Saudi Pharmaceutical Journal*. 2013;21:1-12.
6. Afzal O, Kumar S, Haider MR, Ali MR, Kumar R, Jaggi M, Bawa S. A review on anticancer potential of bioactive heterocycle quinoline. *European Journal of Medicinal Chemistry*. 2015;97:871-910.
7. Mandewale MC, Patil UC, Shedge SV, Dappadwad UR, Yamgar RS. A review on quinoline hydrazone derivatives as a new class of potent antitubercular and anticancer agents. *Journal of Basic and Applied Sciences*. 201;6:354-361.
8. Bharate JB, Vishwakarma RA, Bharate SB. Metal-free domino one-pot protocols for quinoline synthesis. *RSC Advances*. 2015;5:42020-42053.

9. Keri RS, Patil SA. Quinoline: A promising antitubercular target. *Biomedicine & Pharmacotherapy*. 2014;68:1161-1175.
10. Mukherjee S, Pal M. Quinolines: A new hope against inflammation. *Drug Discovery Today*. 2013;18:389-398.
11. Hu Y Q, Gao C, Zhang S, Xu L, Xu Z, Feng L S, Wu X, Zhao F. Quinoline hybrids and their antiplasmodial and antimalarial activities. *European Journal of Medicinal Chemistry*. 2017;139:22-47.
12. Khusnutdinov RI, Bayguzina AR, Dzhemilev UM. Metal complex catalysis in the synthesis of quinolines. *Journal of Organometallic Chemistry*. 2014;768:75-114.
13. Schur E, Bernstein J, Price LS, Guo R, Price SL, Lapidus SH, Stephens PW. The (Current) acridine solid form landscape: Eight polymorphs and a hydrate. *Crystal Growth & Design*. 2019;19:4884-4893.
14. Grabe C, Caro H. *Berichte der deutschen chemischen gesellschaft*. 1870;3:746-747.
15. Byvaltsev VA, Bardonova LA, Onaka NR, Polkin RA, Ochkal SV, Shepelev VV, Aliyev MA, Potapov AA. Acridine orange: A review of novel applications for surgical cancer imaging and therapy. *Front. Oncol*. 2019;9:925.
16. Gensicka-Kowalewska M, Cholewiński G, Dzierzbicka K. Recent developments in the synthesis and biological activity of acridine/acridone analogue. *RSC Adv*. 2017;7:15776–15804.
17. Prasher P, Sharma M. Medicinal chemistry of acridine and its analogues. *Med. Chem. Commun*. 2018;9:1589–1618.
18. Galdino-Pitta MR, Pitta MGR, Lima MCA, Galdino LS, Pitta RI. Niche for acridine derivatives in anticancer therapy. *Mini Rev Med Chem*. 2013;13:1256–1271.
19. Mirrett S. Hospital epidemiology and infection control in acute-care settings. *Infection Control & Hospital Epidemiology*. 1982;3:250–253.
20. Geddes CD. Acridine orange stain. *Dyes and Pigments*. 2000;45:243–251.
21. Wang C, Fu J, Yao K, Xue K, Xu K, Pang X. Acridine-based fluorescence chemosensors for selective sensing of Fe³⁺ and Ni²⁺ ions. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2018;199:403–411.
22. Liu X, Karsili T NV, Sobolewski AL, Domcke W. Optical thin film polymeric sensors for the determination of aqueous chloride, bromide and iodide ions at high pH, based on the quenching of fluorescence of two acridinium dyes. *J. Phys. Chem. B*. 2015;119:10664–10672.
23. Qin P, Paek S, Dar MI, Pellet N, Ko J, Grätzel M, Nazeeruddin MK. Perovskite Solar Cells with 12.8% Efficiency by using conjugated quinolizino acridine based hole transporting material. *J. Am. Chem. Soc*. 2014;136:8516–8519.
24. Margrey K A, Nicewicz DA. A general approach to catalytic alkene anti-markovnikov hydrofunctionalization reactions via acridinium photoredox catalysis. *Acc. Chem. Res*. 2016;49:1997–2006.
25. Romero NA, Margrey KA, Tay NE, Nicewicz DA. Site-selective arene C-H amination via photoredox catalysis. *Science*. 2015;349:1326–1330.
26. Dubrovskiy AV, Larock RC. Synthesis of *o*-(Dimethylamino)aryl Ketones, Acridones, Acridinium Salts, and 1*H*-Indazoles by the Reaction of Hydrazones and Arynes. *J. Org. Chem*. 2012;77:11232–11256.
27. Belmont P, Belhadj T. An efficient and simple aminobenzannulation reaction: Pyrrolidine as a trigger for the synthesis of 1-Amino-acridines. *Org. Lett*. 2005; 7:1793– 1795.
28. Kitahara Y, Mizuno T, Kubo A. Synthetic studies of benzo[*b*]pyrrolo[4,3,2 *de*][1,10]phenanthroline. *Tetrahedron*. 2004;60:4283–4288.
29. Zhang J, Chen Y, Chen X, Zheng X, Cao W, Chen J, Zhang M. Synthesis and characterization of oxadisilole-fused acridines, dioxatrisilole-fused acridines and benzo[*b*]acridines. *Tetrahedron*. 2014;70: 5820–5827.
30. Han XD, Zhao YL, Meng J, Ren CQ, Liu Q. Synthesis of acridines and persubstituted phenols from cyclobutenones and active methylene ketones. *J. Org. Chem*. 2012;77:5173–5178.
31. Popp FD. Polyphosphoric acid in the bernthsen reaction. *J. Org. Chem*. 1962;27:2658–2659.
32. Guan Z, Wiechmann S, Drafz M, Hübner E, Schmidt A. Pericyclic rearrangements of N-heterocyclic carbenes of indazole to substituted 9-aminoacridines. *Org. Biomol. Chem*. 2013;11:3558–3567.
33. Bobin M, Kwast A, Wróbel Z. Efficient formation of σ H-adducts as a key step in the synthesis of acridines via Lewis acid-promoted transformations of the nitro

- group. *Tetrahedron*. 2007;63:11048–11054.
34. Y. Kuninobu Y, Tatsuzaki T, Matsuki T, Takai K. Indium-catalyzed construction of polycyclic aromatic hydrocarbon skeletons via dehydration. *J. Org. Chem.* 2011; 76:7005–7009.
 35. Bernthsen A. Die acridine. *Justus Liebigs Annalen der Chemie*. 1884;224:1–56.
 36. Bernthsen A. Bernthsen acridine synthesis. *Ann.* 1878;192:1.
 37. Delfourne E, Roubin C, Bastide J. The first synthesis of the pentacyclic pyridoacridine marine alkaloids: Arnoamines A and B *J. Org. Chem.* 2000;65:5476.
 38. Ferlin M G, Marzano C, Chiarelto G, Baccichetti F, Bordin F. Synthesis and antiproliferative activity of some variously substituted acridine and azacridine derivatives. *Eur. J. Med. Chem.* 2000;39: 827.
 39. Antonini J, Polucci P, Magnano A, Martelli S. Synthesis, Antitumor Cytotoxicity, and DNA-Binding of Novel N-5,2-Di(ω -aminoalkyl)-2,6 dihydropyrazolo[3,4,5-kl]acridine-5-carboxamides. *J. Med. Chem.* 2001;44:3329.
 40. B. Stefanska B, Bontemps-Gracz M M, Antonini I, Martelli S, Arciemiuk M, Piwkowska A, Rogacka D, Borowski E. 2,7-Dihydro-3H-piridazino[5,4,3 k]acridine-3-one derivatives, novel type of cytotoxic agents active on multidrug resistant cell lines. *Synthesis and biological evaluation. Bioorg. Med. Chem.* 2005;13:1969.
 41. Gooch BD, Beal PA. Recognition of duplex RNA by helix-threading peptides. *J. Am. Chem. Soc.* 2004;126:10603.
 42. Janis RA, Silver PJ, Trigg GJ. *Adv. Drug Res.* 1987;16:309.
 43. Ladani NK, Mungra DC, Patel MP, Patel RG. Microwave assisted synthesis of novel Hantzsch 1,4-dihydropyridines, acridine-1,8-diones and polyhydroquinolines bearing the tetrazolo[1,5-a]quinoline moiety and their antimicrobial activity assess. *Chinese Chemical Letters*. 2011; 22:1407.
 44. Demeunynck M, Charmantray F, Martelli A. Interest of acridine derivatives in the anticancer chemotherapy. *Current Pharmaceutical Design*. 2001;17: 1703.
 45. Mazzucco MB, Talarico LB, Vatansever S, Carro AC, Fascio ML, D'Accorso NB, García C C. Antiviral activity of an N-allyl acridone against dengue virus. *Journal of Biomedical Science*. 2015;22:29.
 46. Girault S, Grelhier P, Berecibar A, Maes L, Mouray E, Lemièrre P, Debreu M, Davioud-Charvet E, Sergheraert C. Antimalarial, antitrypanosomal, and antileishmanial activities and cytotoxicity of bis (9-amino-6-chloro-2 methoxyacridines): influence of the linker. *J. Med. Chem.* 2000;43:2646.
 47. Popielarz R, Hu S, Neckers D C. Applicability of decahydroacridine-1, 8 dione derivatives as fluorescent probes for monitoring of polymerization processes. *Journal of Photochemistry and Photobiology A*. 1997;110:79.
 48. Saggadi H, D. Luart D, Thiebault N, Polaert I, Estel L, Len C. Toward the synthesis of 6-hydroxyquinoline starting from glycerol via improved microwave assisted modified Skraup reaction. *Catalysis Communications*, 2014;44:15-18.
 49. Saggadi H, Luart D, Thiebault N, Polaert I, Estel L, Len C. Quinoline and phenanthroline preparation starting from glycerol via improved microwave assisted modified Skraup reaction. *RSC Advances*. 2014;4:21456-21464.
 50. Kulkarni A, Torok B. Microwave-assisted multicomponent domino cyclization aromatization: an efficient approach for the synthesis of substituted quinolines. *Green Chemistry*. 2010;12:875-878.
 51. Peng JH, Jia RH, Ma N, Zhang G, Wu FY, Cheng C, Tu SJ. A facile and expeditious microwave-assisted synthesis of furo[3,4-b]indeno[2,1-f]quinolin-1-one Derivatives via Multicomponent Reaction. *Journal of Heterocyclic Chemistry*. 2013; 50:899- 902.
 52. Xu X, Yang Y, Chen X, Zhang X, Yi W. The one-pot synthesis of quinolines via Co(III)-catalyzed C–H activation/carbonylation/cyclization of anilines. *Organic & Biomolecular Chemistry*. 2017;15:9061-9065.
 53. Bartolomeu A d A, Brocksom TJ, da Silva Filho L C, de Oliveira K T. Multicomponent reactions mediated by NbCl₅ for the synthesis of phthalonitrile quinoline dyads: Methodology, scope, mechanistic insights and applications in phthalocyanine synthesis. *Dyes and Pigments*. 2018;151:391-402.
 54. Wu W, Guo Y, Xu X, Zhou Z, Zhang X, Wu B, Yi W. One-pot regioselective synthesis of 2, 4-disubstituted quinolines via copper(II)-catalyzed cascade annulation. *Organic Chemistry Frontiers*. 2018;5:1713-1718.

55. Thigulla Y, Kumar TU, Trivedi P, Ghosh B, Bhattacharya A. One-Step Synthesis of Fused Chromeno[4,3-*b*]pyrrolo[3,2-*h*]quinolin-7(1*H*)-One Compounds and their Anticancer Activity Evaluation. *ChemistrySelect*. 2017;2:2718-2721.
56. Andrade A, Santos GC, Silva-Filho LC. Synthesis of quinoline derivatives by multicomponent reaction using niobium pentachloride as Lewis acid. *Journal of Heterocyclic Chemistry*. 2015;52:273-277.
57. Kadam H K, Tilve SG. An alternate synthesis of 6*H*-Indolo[2,3-*b*]quinoline via One-Pot Alkylation–Dehydration–cyclization aromatization approach. *Journal of Heterocyclic Chemistry*. 2016; 53:2066-2069.
58. Zhou J X, Wang W, Wang X S. An efficient method for the synthesis of 3-Arylnaphtho[2,3-*f*]quinoline-1,2-dicarboxylate Derivatives Catalyzed by Yb(OTf)₃. *Journal of Heterocyclic Chemistry*. 2014; 51:502-506.
59. Chen BWJ, Chng LL, Yang J, Wei Y, Yang J, Ying JY. Palladium-Based Nanocatalyst for One-Pot Synthesis of Polysubstituted Quinolines. *Chem Cat Chem*. 2013;5:277-283.
60. Xi LY, Zhang RY, Zhang L, Chen SY, Yu XQ. An efficient synthesis of quinolines via copper-catalyzed C–N cleavage. *Organic & Biomolecular Chemistry*. 2015;13:3924-3930.
61. Li B, Guo C, Fan X, Zhang J, Zhang X. Synthesis of substituted quinoline via copper-catalyzed one-pot cascade reactions of 2-bromobenzaldehydes with aryl methyl ketones and aqueous ammonia. *Tetrahedron Letters*. 2014; 55:5944-5948.
62. Zanwar M R, Gawande S D, Kavala V, Kuo C W, Yao C F. Iron(III) chloride catalyzed synthesis of highly substituted indolyl-tetrahydroquinoline derivatives by using indolyl nitroalkene as dienophiles and its application to the synthesis of indolo-benzonaphthyridine derivatives. *Advanced Synthesis & Catalysis*. 2014;356:3849-3860.
63. Zhang X, Xu X, Yu L, Zhao Q. Three-component reactions of aldehydes, amines, and alkynes/ alkenes catalyzed by trifluoromethanesulfonic acid: An efficient route to substituted quinolines. *Asian Journal of Organic Chemistry*. 2014;3:281-284.
64. Zhang X Y, Guo X J, Fan X S. Synthesis of 2-Aminoquinoline-3-carboamides and Pyrimido[4,5-*b*]quinolin-4-ones through Copper-Catalyzed One-pot Multicomponent Reactions. *Chemistry – An Asian Journal*. 2015;10:106-111.
65. Chanda T, Verma RK, Singh MS. InCl₃-driven regioselective synthesis of functionalized/ annulated quinolines: Scope and limitations. *Chemistry – An Asian Journal*. 2012;7:778-787.
66. Phan NTS, Nguyen TT, Nguyen KD, Vo AXT. An open metal site metal–organic framework Cu (BDC) as a promising heterogeneous catalyst for the modified Friedländer reaction. *Applied Catalysis A: General*, 2013;464:128-135.
67. Shushizadeh MR, Mostoufi A, Behfar A, Heidary M. 1, 7-Sigmatropic rearrangement in 1, 2-dihydro and 1, 2, 3, 4-tetrahydroquinoline synthesis using marine sponge/H₂C₂O₄ as a catalyst. *Arabian Journal of Chemistry*. 2015;8:868-872.
68. Li M Y, Xu H W, Fan W, Ye Q, Wang X, Jiang B, Wang SL, Tu SJ. New formal (3+3) cycloaddition of enaminones for forming tetracyclic indolo [2, 3-*b*] quinolines under microwave irradiation. *Tetrahedron*. 2014; 70:1004-1010.
69. Yu Y, Tu MS, Jiang B, Wang SL, Tu SJ. Multicomponent synthesis of polysubstituted dihydroquinoline derivatives. *Tetrahedron Letters*. 2012;53: 5071-5075.
70. Nasr-Esfahani M, Hoseini SJ, Montazerzohori M, Mehrabi R, Nasrabadi. Magnetic Fe₃O₄ nanoparticles: Efficient and recoverable nanocatalyst for the synthesis of polyhydroquinolines and Hantzsch 1,4-dihydropyridines under solvent-free conditions. *Journal of Molecular Catalysis A: Chemical*. 2014; 382:99-105.
71. Khazaei A, Moosavi-Zare AR, Afshar-Hezarkhani H, Khakyzadeh V. Nano-ferric ferric oxide (nano-Fe₃O₄): magnetite catalytic system for the one-pot four-component tandem imine/enamine formation-Knoevenagel–Michael-cyclocondensation reaction of dimedone, aldehydes, β-ketoesters and ammonium acetate under green media. *RSC Advances*. 2014;4:32142-32147.
72. Ziarani GM, Asadi S, Badiei A, Mousavi S, Gholamzadeh P. One-pot four component synthesis of 2, 5-dioxo-1, 2, 3, 4, 5, 6, 7, 8-

- octahydroquinolines catalyzed by silica-based sulfonic acid. *Research on Chemical Intermediates*. 2015;41:637-645.
73. Arabpoor Z, Shaterian H R. *RSC Advances*. 2016; 6:4459- 44468.
 74. Patil D, Chandam D, Mulik A, Jagdale S, Patil P, Deshmukh M. One pot four component sequential synthesis of hexahydroquinoline derivatives in aqueous media via enaminone intermediates: A green protocol. *Journal of Saudi Chemical Society*. 2017;21:S329- S338.
 75. Khaligh NG. Four-component one-pot synthesis of unsymmetrical polyhydroquinoline derivatives using 3-methyl-1-sulfonic acid imidazolium hydrogen sulfate as a catalyst. *Chinese Journal of Catalysis*. 2014;35:1036-1042.
 76. Liberto NA, Simões JB, de Paiva Silva S, da Silva CJ, Modolo LV, de Fátima A, Silva LM, Derita M, Zacchino S, Zuñiga OMP, Romanelli GP, Fernandes SA. Quinolines: Microwave-assisted synthesis and their antifungal, anticancer and radical scavenger properties. *Bioorganic & Medicinal Chemistry*. 2017;25:1153-1162.
 77. Sheik Mansoor S, Aswin K, Logaiya K, Sudhan SPN. An efficient one-pot multi component synthesis of polyhydroquinoline derivatives through Hantzsch reaction catalysed by Gadolinium triflate. *Arabian Journal of Chemistry*. 2017;10:S546-S553.
 78. Davoodnia A, Khashi M, Tavakoli-Hoseini N. Tetrabutylammonium hexatungstate [TBA]₂[W₆O₁₉]: Novel and reusable heterogeneous catalyst for rapid solvent-free synthesis of polyhydroquinoline via unsymmetrical Hantzsch reaction. *Chinese Journal of Catalysis*. 2013;34:1173-1178.
 79. Khojastehnezhad A, Moeinpour F, Davoodnia A. PPA-SiO₂ catalyzed efficient synthesis of polyhydroquinoline derivatives through Hantzsch multicomponent condensation under solvent-free conditions. *Chinese Chemical Letters*. 2011;22:807-810.
 80. Paplal B, Nagaraju S, Veerabhadraiah P, Sujatha K, Kanvah S, Vijaya Kumar B, Kashinath D. Recyclable Bi₂WO₆-nanoparticle mediated one-pot multicomponent reactions in aqueous medium at room temperature. *RSC Advances*. 2014;4:54168-54174.
 81. Abdelhamid AA, Allah OAA, Tamam AHA. An Efficient one-pot three-component synthesis of some new polyhydroquinolines via enaminone intermediates. *Journal of Heterocyclic Chemistry*. 2017;54:2822-2829.
 82. Alizadeh A, Rezvanian A. Catalyst- and solvent-free synthesis of highly functionalized octahydro-imidazo[1,2-a]quinolin-6-ones via a one-pot sequential four-component reaction in melt conditions. *Comptes Rendus Chimie*. 2014;17:103-107.
 83. Zarghia A, Sabakhib I, Topuzuyc V, Hajimahdid Z, Daraie B. Design, synthesis and biological evaluation of 5-Oxo-1,4,5,6,7,8 Hexahydroquinoline Derivatives as Selective Cyclooxygenase-2 Inhibitors. *Ijpr*. 2014;13:61-69.
 84. Ray S, Brown M, Bhaumik A, Dutta A, Mukhopadhyay C. A new MCM-41 supported HPF6 catalyst for the library synthesis of highly substituted 1,4-dihydropyridines and oxidation to pyridines: report of one-dimensional packing towards LMSOMs and studies on their photophysical properties. *Green Chem*. 2013;15:1910-1924.
 85. Wang S, Guo S, Gao M, Li J, Duan Y. E. Infrared Irradiation Synthesis of Substituted 5-Oxo-1, 2, 3, 4, 5, 6, 7, 8-octahydroquinoline Derivatives under Solvent-free Conditions. *Journal of Chemistry*. 2006; 3:159-163.
 86. Hua X, Zhanga X, Fana X, Qu G, Li Y. A facile and green preparation of 2, 4-diarylpolyhydroquinolines. *Journal of Chemical Research*. 2005;697-699.
 87. Tu S, Yan S, Cao X, Wu S, Zhang X, Hao W, Han Z, Shi F. A facile and expeditious microwave-assisted synthesis of 4-aryl-2-ferrocenyl-quinoline derivatives via multi-component reaction. *Journal of Organometallic Chemistry*. 2009;694: 91-96.
 88. Karimi-Jaberi Z, Azadi M. Efficient synthesis of 2, 4-diaryl hexahydroquinoline-5-one derivatives in the presence of triethylamine. *Res Chem Intermed*. 2015;41:6741–6747.
 89. Wang X, Shi D, Tu S. A convenient synthesis of 2, 4 diarylpolyhydroquinoline derivations in the presence of ammonium acetate. *Synthetic Communications*. 2002; 32:3449–3454.
 90. Safari J, Banitaba SH, Khalili SD. Cobalt nanoparticles promoted highly efficient one pot four-component synthesis of 1, 4-dihydropyridines under solvent-free conditions. *Chin. J. Catal*. 2011;32:1850–1855.

91. Sunkara JR, Rallabhandi M, Prasangi S, Palla M. One-pot facile synthesis of acridinediones and their derivatives by nano ferrite as a catalyst. Chem Sci Trans. 2016;5:1001-1007.
92. Sudha S, Pasha MA. Scientific World Journal, A Facile Synthesis of N-H- and N Substituted Acridine-1,8-diones under Sonic Condition. 2013;Article ID 930787:6 DOI:http://dx.doi.org/10.1155/2013/930787
93. Amoozadeh A, Rahmani S, Bitaraf M, Abadi F B, Tabrizian E. Nano-zirconia as an excellent nano support for immobilization of sulfonic acid: A new, efficient and highly recyclable heterogeneous solid acid nanocatalyst for multicomponent reactions. New J.Chem. 2016;40:770 780.
94. Zhu A, Liu R, Du C and Li L. Betainium-based ionic liquids catalyzed multicomponent Hantzsch reactions for the efficient synthesis of acridinediones. RSC Adv. 2017;7:6679–6684.
95. Djemoui A, Ouahrani MR, Naouri A, Souli L, Rahmani S, Boualem LM. Ultrasound-assisted one-pot synthesis of 9-(Substituted heteroaryl) acridinedione derivatives. Heterocyclic Letters. 2018;8: 455-467.
96. Nasr-Esfahani M, Montazerzohori M, Abdizadeh TCR. Nanorod vanadatesulfuric acid (VSA NRs)-catalyzed green synthesis of hexahydroacridine-1, 8-diones in solvent-free conditions. Chimie. 2015; 18:547 553.
97. Naouri A, Djemoui A, Ouahrani MR, Lahrech MB, Lemouari N, Rocha DHA, Albuquerque H, Mendes RF, Paz FAA, Helguero LA, Bachari K, Talhi O, Silvae AMS. Multicomponent and 1,3-dipolar cycloaddition synthesis of triazole- and isoxazole acridinedione/ xanthenedione heterocyclic hybrids: Cytotoxic effects on human cancer cells. Journal of Molecular Structure. 2020;1217:128325
98. Mazloumi M, Shirini F. Introduction of a new catalyst containing an ionic liquid bridge on nanoporous Na⁺-montmorillonite for the synthesis of hexahydroquinolines and 1,8-dioxo decahydroacridines via Hantzsch condensation. Journal of Molecular Structure. 2020;1217:128326
99. Vahdat S M, Akbari M. An efficient one-pot synthesis of 1, 8-dioxo-Decahydroacridines by ionic liquid with multi-SO₃H groups under ambient temperature in water. Oriental Journal of Chemistry. 2011; 27:1573-1580.
100. Chandrasekhar S, Rao YS, Sreelakshmi L, Mahipal B, Reddy CR. Tris (pentafluorophenyl) borane-catalyzed Three-component Reaction for the Synthesis of 1, 8 Dioxodecahydroacridines under Solvent-free Conditions. Synthesis. 2008;11:1737-1740.
101. Kidwai M, Bhatnagar D. Polyethylene glycol-mediated synthesis of decahydroacridine-1, 8-diones catalyzed by ceric ammonium nitrate. Chemical Papers. 2010;64:825-828.
102. Mirhosseyni M S, Nemati F, Elhampour A. An efficient method for the synthesis of dihydropyridine by hantzsch reaction with Fe/SiO₂ nano heterogeneous catalysts. Journal of the Iranian Chemical Society. 2017;14:791-801.
103. Malekia B, Mofrada A V, Tayebbea R, Khojastehnezhad A, Alinezhad H, Rezaei Seresht E. Russian Journal of General Chemistry. 2017;87:2922–2929.
104. Maleki B, Tayebbe R, Kermanian M, Ashrafi SS. Synthesis of quinoline and polyhydroquinoline derivatives using phloroglucinol cored amino functionalized dendritic polymer as catalyst. J. Mex. Chem. Soc. 2013;57:290-297.

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