Journal of Population Therapeutics & Clinical Pharmacology

REVIEW ARTICLE
DOI: 10.53555/jptcp.v30i18.3689

BENIGN AND PROFICIENT PROCEDURE FOR PREPARATION OF QUINOLINE DERIVATIVES

Valarmathy Joshua[1], Shalini.S[2], Janapriya.S[3], Bharath Kumar. R[4], Veeraselvam.S[5], Manickkvasagam.A[6], Sam Solomon. W. D[7], Samuel Joshua.L[8].

[1*,2,3,4,5,6,7]Department of Pharmaceutical Chemistry, PPG College of Pharmacy, Sathyamangalam Main road, Saravanampatti, Coimbatore - 641035, Tamilnadu, India.
[8]Department of Pharmaceutical Chemistry, Padmavathi College of Pharmacy and Research Institute, Krishnagiri main road, Periyanahalli, Dharmapuri-635205, Tamilnadu, India.

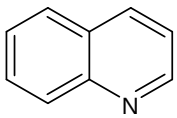
***Corresponding Author:** Valarmathy Joshua
*Department of Pharmaceutical Chemistry, PPG College of Pharmacy, Sathyamangalam Main road, Saravanampatti, Coimbatore - 641035, Tamilnadu, India.

Abstract:
Quinoline is a class of natural mixtures of the aromatic heterocyclic series described by a bicyclic heterocyclic system consistingof a six-membered benzene ring fused with pyridine, reported as an important building block in the field of medicinal chemistry. Among heterocyclic compounds, quinoline is a privileged scaffold that appears as an important construction motif for the development of new drugs. synthetic routes have been developed for the synthesis of quinoline and its derivatives due to its wide range of biological and pharmacological activities. This article covers the synthesis as well as biological activities of quinoline derivatives such as antimalarial, antibacterial, antifungal, antiprotozoal, anthelmintic, local anesthetic, anticancer, antiglaucoma, antipsychotic, antiasthmatic and miscellaneous activities.

Keywords: quinoline, quinoline derivatives, synthesis, biological activity.

1. INTRODUCTION:

Quinoline is a class of natural mixtures of the aromatic heterocyclic series described by a two-fold ring structure made out of benzene and a pyridine ring melded at two nearby carbon atoms, as shown in the figure.



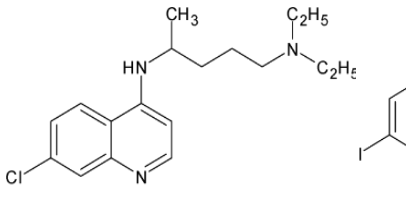
quinoline

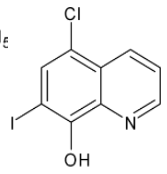
Quinoline or 1-aza-naphthalene or benzo[*b*]pyridine is a nitrogen-containing heterocyclic aromatic compound, acting as a weak tertiary base and can form salts with acids and undergo electrophilic substitution reactions as well as reactions similar to those of pyridine and benzene. It shows both electrophilic and nucleophilic replacement responses. Quinoline is a planner hetero-aromatic compound in which 10π electrons move throughout the structure and have a molecular formula of C_9H_7N. Quinoline is a bicyclic heterocyclic system consisting of six-member benzene ring fused with pyridine, reported as an important building block in the field of medicinal

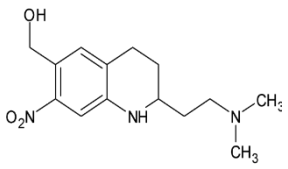
chemistry. Quinoline[1] and its derivatives have both natural and synthetic origins. In addition, quinolines have groups according to their biological action and structural modifications as well as biological activity. With Cinchona alkaloids and other naturally occurring pharmacologically active chemicals, it is one of the most privileged N-containing motifs known to date and tends to occur in a variety of natural products,exhibiting a wide range of biological activities.

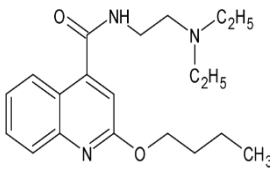
There are several classical synthetic routes available for synthesizing the quinoline structural modification. Synthetic routes which are widely used include the Skraup reaction, Friedlander reaction, Conrad-Limpach-Knorr reaction, Doebner-miller reaction, Skraup-- Doebner-Von Miller reaction, Conrad-–Limpach reaction, and Combes reaction, which majorly utilizes aniline as one of the common reactants. However, several other reactions need special substituted anilines or other substituted reactants to yield quinoline.

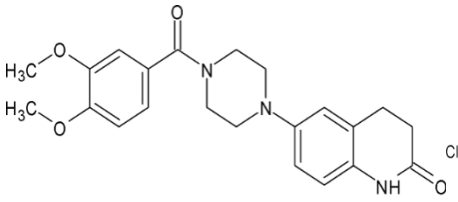
Quinoline core happens in a few regular mixtures (Cinchona Alkaloids) and pharmacologically dynamic substances showing a wide scope of organic action. Quinoline has been found to have antimalarial (Quinine, quinidine, chloroquine, mefloquine, amodiaquine, etc), antibacterial (fluoroquinolone such as ciprofloxacin, sparfloxacin), antifungal, antiprotozoal (Clioquinol), anthelmintic (oxamniquine), a local anesthetic (dibucaine), anticancer (camptothecin, irinotecan, topotecan), antiglaucoma (cartiolol), antipsychotic (Aripiprazole, brexpiprazole), cardiotonic (vesnarinone) and antiasthmatic (montelukast).

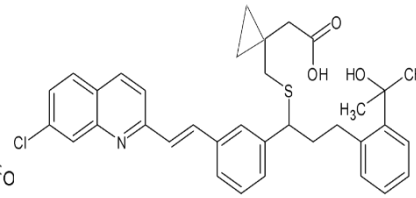

chloroquine

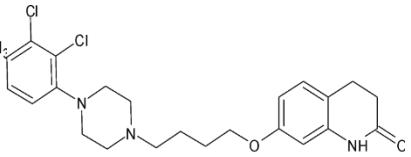

Clioquinol

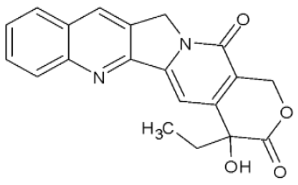

Oxamniquine

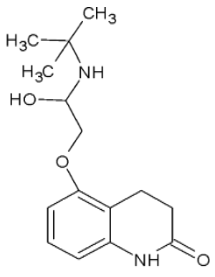

Dibucaine


vesnarinone


Montelukast


Aripiprazole


Camptothecin

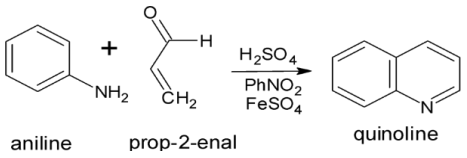

cartiolol

I.SYNTHESIS OF QUINOLINE:

1.QUINOLINE SYNTHESIS NAME REACTION[2]:

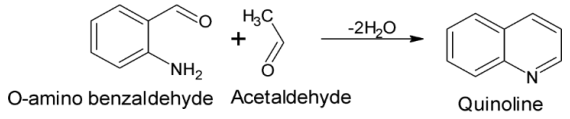
Skraup synthesis:

In this method, aniline, glycerol in the presence of strong acid and an oxidant are heated together to form quinoline.



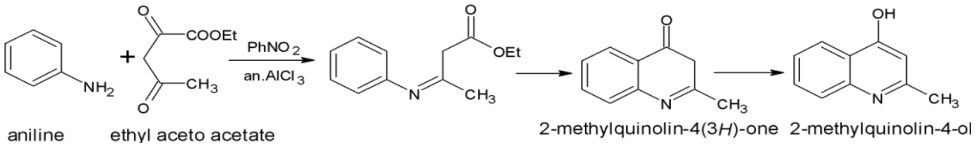
Friedlander synthesis:

In this method, o-aminobezaldehyde or o-amino ketones condenses with another aldehyde or ketone with least methylene α to the carbonyl, that yields substituted quinoline. The reaction can be promoted by acid, base or heat.



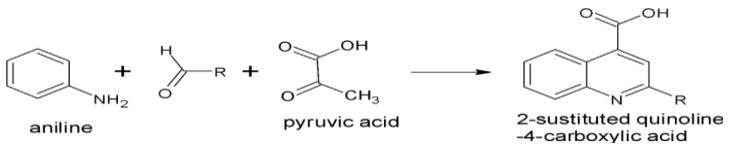
Conrad-Limpach-Knorr synthesis:

In this reaction, formation of 4-hydroxyquinoline takes place via a Schiff's base from β-ketoesters and aniline. The overall reaction type is a combination of both an addition reaction as well as rearrangement reaction.



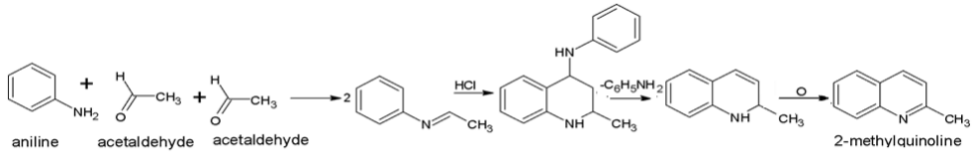
Doebner synthesis:

In this method, three components coupling of an aniline, pyruvic acid and an aldehyde to form quinoline 4-carboxylic acid.



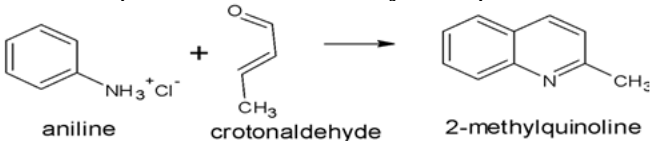
Doebner-miller synthesis:

In this method, aniline with two moles of acetaldehyde are heated in the presence of HCl to form schiff's base. Two molecules of this schiff's base condense to form a 2-methyl quinoline.



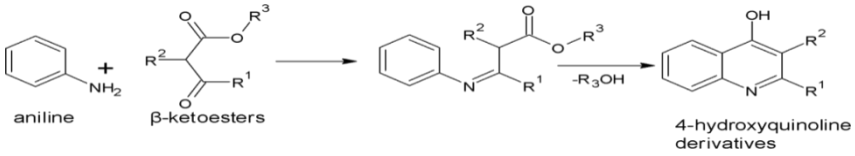
Skraup-Doebner-VonMiller synthesis:

In this way, aniline reacts with α, β-unsaturated carbonyl compounds to form quinolines.



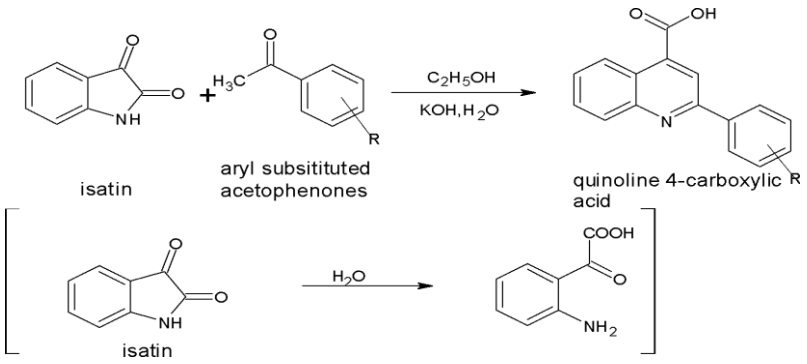
Conrad–Limpach synthesis:

In this system, condensation of anilines with β-ketoesters to form 4- hydroxyquinoline derivatives takes place via a Schiff base. The overall reaction type is a combination of both an addition reaction as well as a rearrangement reaction.



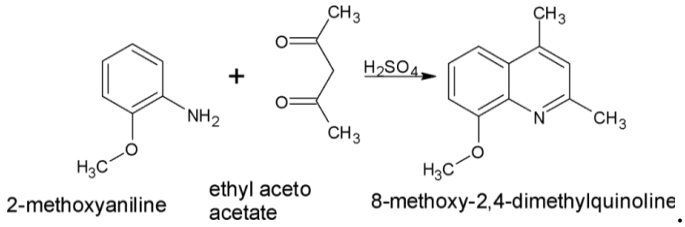
Pfitzinger synthesis:

In this technique, Isatin in the presence of base, converts into isatoic acid which is condensed with a ketone to give quinoline 4-carboxylic acid.



Combes synthesis:

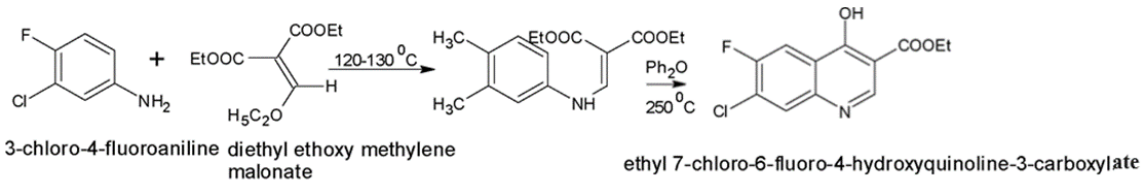
In this process, condensation of 1,3dicarbonyl compounds or keto aldehyde with arylamine gives a β-amino enone which undergoes cyclization with loss of water to give quinoline derivatives.



2. QUINOLINE DERIVATIVES SYNTHESIS WITHOUT CATALYST:

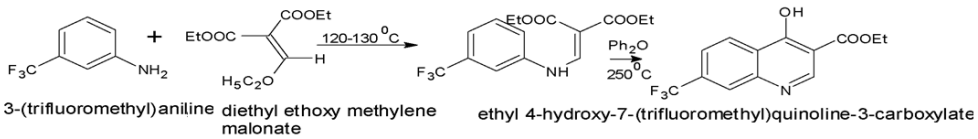
Synthesis of ethyl 7-chloro-6-fluro 4-hydroxyquinoline-3-carboxylate[3]:

3-chloro-4-fluoroaniline is combined with diethylethoxymethylenemalonate (EMME), the matching open chain molecule is produced. This chemical is then cyclized in di-phenylether at 120- 130^{0}C to produce ethyl 7-chloro-4-hydroxy-quinoline 3-carboxylate selectively and with good yield.



Synthesis of diethyl ({[2(trifluoromethyl)phenyl] amino} methylene) malonate[4]:

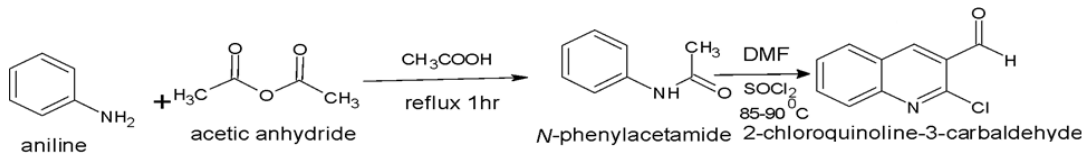
Diethyl ethoxy methylene malonate is suspended in 2- (trifluoromethyl) aniline, which is heated for four hours at 120- 130^{0}C. The reaction mixture was brought to room temperature, and the resulting solid was placed in petroleum ether and agitated for 15 minutes before being filtered to obtain the product.



Synthesis of quinoline-3-carbaldehyde[5]:

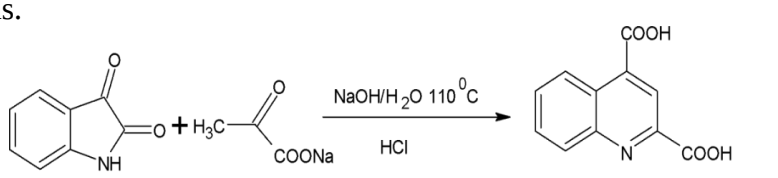
Aniline, acetic anhydride, zinc powder and acetic were added. For one hour, the mixture was reflux-

boiled using a water condenser. It was then allowed to cool to room temperature before being added to ice water. By using suction filtration, the solid product was obtained.



Synthesis of quinoline-2, 4-dicarboxylicacids[6]:

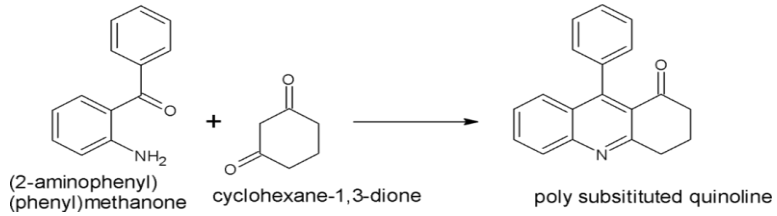
Isatin and sodium pyruvate in water at 110^0C was reported to afford quinoline-2,4-dicarboxylic acid with excellent yields.



3.QUINOLINE DERIVATIVES SYNTHESIS WITH CATALYST:

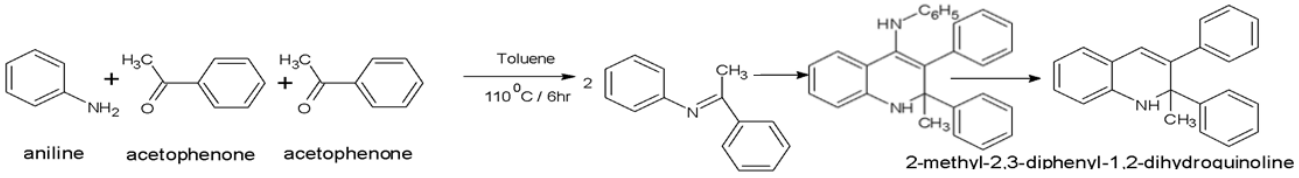
Synthesis of polysubstituted Quinoline Derivative[7]:

An aggregate of 2-aminobenzophenone and cyclohexane 1,3-dione compounds became given 0.1 mmol of $NbCl_5$ in glycerol. At 110^0C, the aggregate became stirred for the recommended amount of response time.



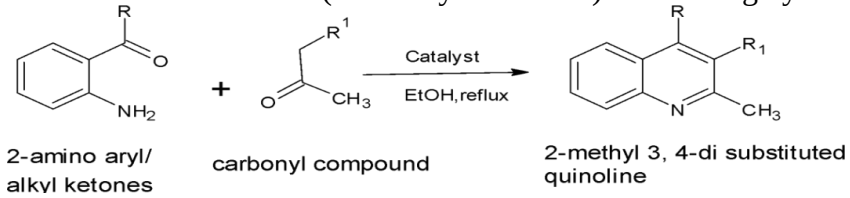
Synthesis of 2, 4-Diphenyl-2-methyl-1, 2-dihydroquinoline derivative[8]:

Aniline condensation with acetophenone followed cyclization with the assist of a zeolite catalyst at 110^0C for 6 hr.



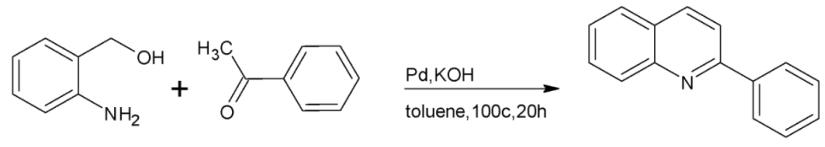
Synthesis of 2-methyl 3,4-disubstituted quinolinederivatives[9]:

2-aminoaryl/alkylketones and carbonyl compounds in the presence of Montmorrilonite K-10, zeolite, nano-crystalline sulfated zirconia (nano- crystalline SZ) leads to high yields.



Synthesis of 2-phenylquinoline derivative[10]:

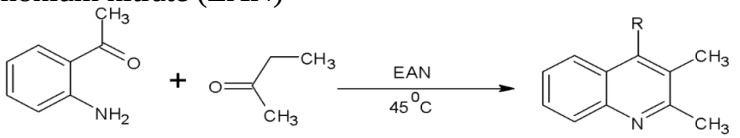
2-aminobenzyl alcohol reacts with acetophenone in toluene or polyethylene glycol (PEG-2000) by employing a palladium catalyst along with KOH to isolate the corresponding quinoline derivative.



2-aminobenzyl alcohol acetophenone 2-phenylquinoline

Synthesis of 2, 3, 4-Trisubstituted quinolones[11]:

2,3,4-Trisubstituted quinolones, have been synthesized by Friedlander annulations of 2-aminosubstituted aromatic ketones and reactive methylene group containing carbonyl compounds in the presence of ethyl ammonium nitrate (EAN)



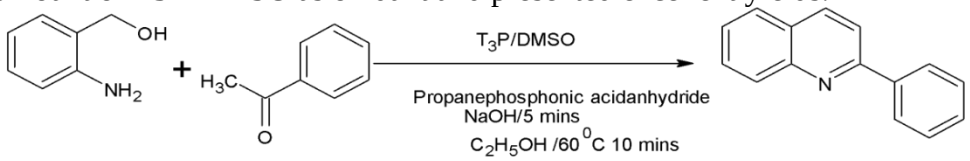
1-(2-aminophenyl) 2-subsitituted methan-1-one butan-2-one 2,3,4-trisubstituted quinolones

4.QUINOLINE SYNTHESIS BY MICROWAVE IRRADIATION:

4.1. MICROWAVE IRRADIATION WITH SOLVENT:

Synthesis of 2-phenylquinolines[12]:

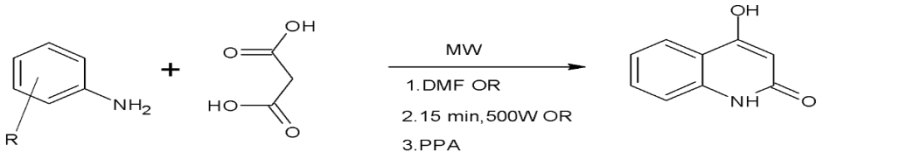
2-aminobenzyl alcohol and acetophenone with a catalytic amount of sodium hydroxide and stoichiometric amount of T3P-DMSO as oxidant and presented excellent yields.



(2-aminophenyl)methanol 1-phenylethan-1-one 2-phenylquinoline

Synthesis of 4-hydroxyquinolin-2(1*H*)-one derivatives[13]:

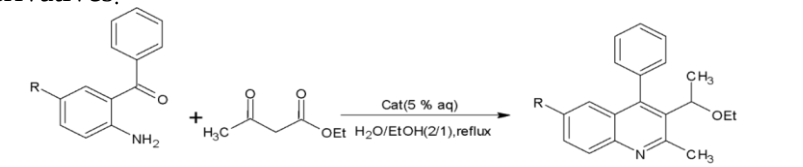
Substituted aromatic amine and malonic acid under microwave irradiation in dimethyl formamide, without employing any solvent and using polyphosphoric acid (PPA) yields 4-hydroxyquinolin-2(1*H*)-one derivatives.



Substituted aromatic amine malonic acid 4-hydroxyquinolin-2(1*H*)-one

Synthesis of 6-substituted -3-(1-ethoxyethyl)-2-methyl-4- phenylquinoline derivatives[14]:

2-amino-5-substituted benzophenone and ketones or β-diketones in the presence of metal dodecyl sulfates or Lewis acid-surfactant catalysts (LASC)/zirconium tetrakisdodecyl sulfate $Zr(DS)_4$ /metal dodecyl sulfates. $Zr(DS)_4$ lead to the formation of 6-substituted -3-(1-ethoxyethyl)-2-methyl-4-phenylquinoline derivatives.

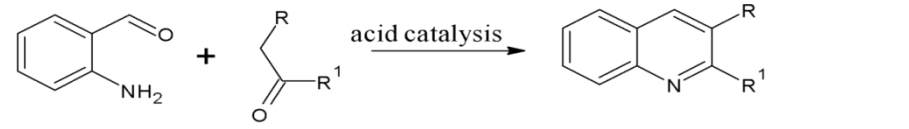


2-amino 5-substituted benzophenone ethyl aceto acetate 6-substituted -3-(1-ethoxyethyl)-2-methyl-4-phenylquinoline

4.2. MICROWAVE IRRADIATION WITHOUT SOLVENT:

Synthesis of 2,3, -disubstituted quinolines derivatives[15]:

O-aminobenzaldehyde and enolisable ketones under acid catalysis, reported yields above 50% in 6 to12 minutes reaction time.

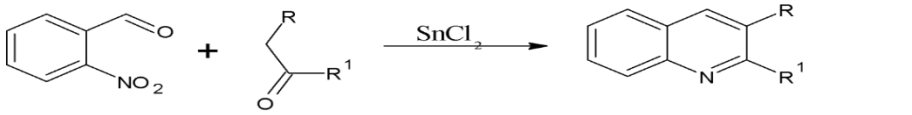


ortho amino benzaldehyde enolisable ketones 2,3-disubsitituted quinolines

SYNTHESIS OF QUINOLINE DERIVATIVES WITH CATALYST:

Synthesis of 2,3, -disubstituted quinolines derivatives[16]:

O-nitrobenzaldehyde and enolisable ketones under the use of $SnCl_2$ as an efficient oxidant toward the synthesis of 2,3-disubstituted quinolines and reported great yields in 2 to 3 minutes reaction time (MV1050v).



2-nitrobenzaldehyde enolisable ketones 2,3-disubsitituted quinolines

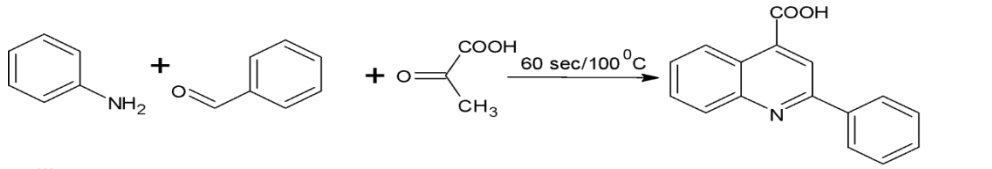
Synthesis of 2,3, -disubstituted quinoline derivatives[17]:

Aniline, aldehydes and acetylene derivatives catalyzed by either rare- earth metal catalysts (YCl3) or triflates $(OTf)_3$. Both catalysts originated excellent yields in 8 minutes reaction time (MV720v,180^{0}C).

aniline

Synthesis of 2-phenylquinoline -4-carboxylic acid[18]:

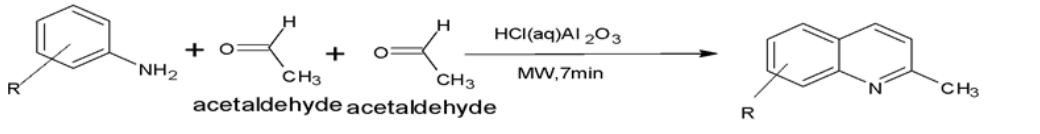
Aniline, benzaldehyde and pyruvic acid reported great yields in 60 sec reaction time at 100^{0}C.



aniline benzaldehyde 2-oxopropanoic acid 2-phenylquinoline-4-carboxylic acic

Synthesis of 3methyl Quinoline derivatives[19]:

Aniline derivatives and acetaldehyde under microwave irradiation without any solvent. In this method they tried different Bronsted acids (Al_2O_3) but found hydrochloric acid appeared to be the best catalyst for this reaction, showing the highest yield.

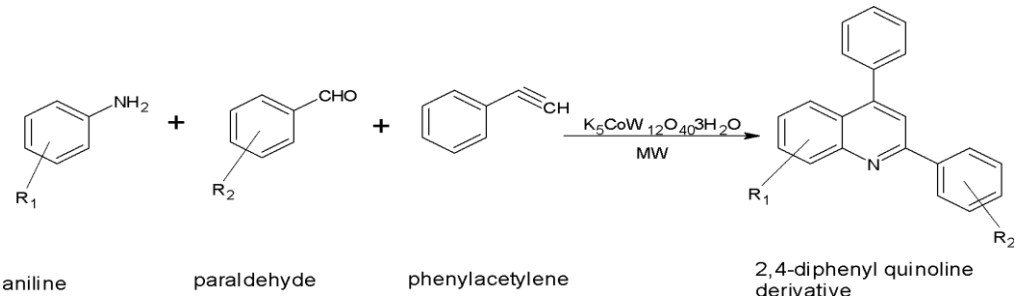


acetaldehyde acetaldehyde

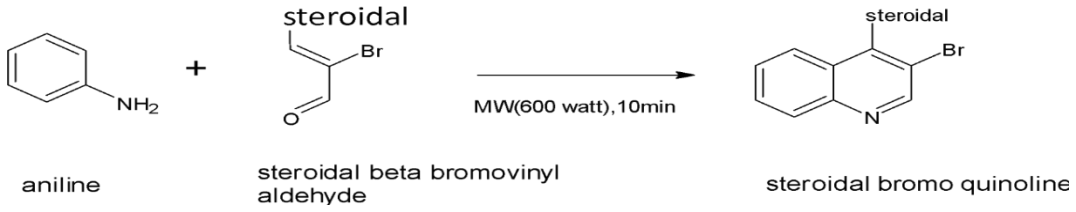
aniline 3-methyl quinoline derivative

Synthesis of 2,4diphenyl Quinoline derivatives[20]:

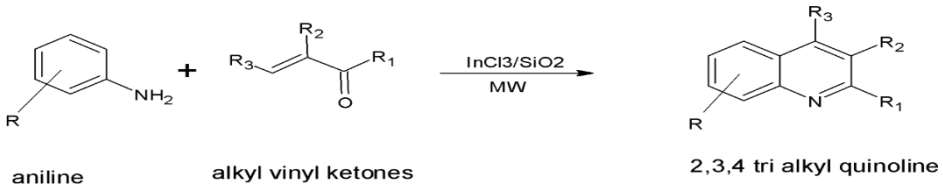
Aromatic amines, aromatic aldehydes and phenylacetylene in the presence of catalytic amounts of potassium dodecatungstocobaltatetrihydrate($K_5CoW_{12}O_{40}\cdot 3H_2O$) for the one-pot three-components synthesis under microwave irradiation.



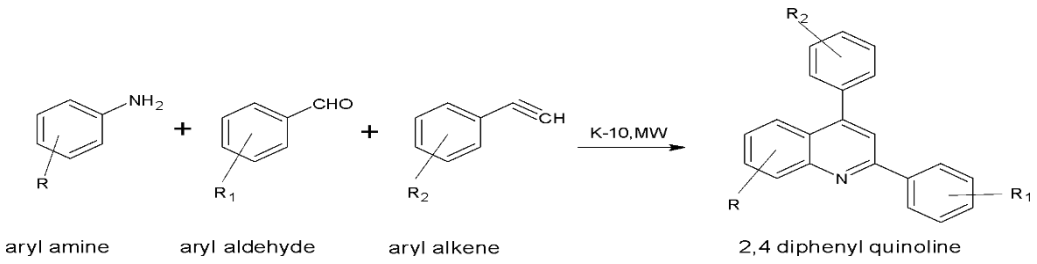
Synthesis of steroidal quinoline derivatives[21]:
In this method steroidal quinoline derivatives were synthesized from a one- pot reaction of steroidal β-bromovinylaldehydes and arylamines in high yield using microwave irradiation without the use of a catalyst and in a solvent-free condition.



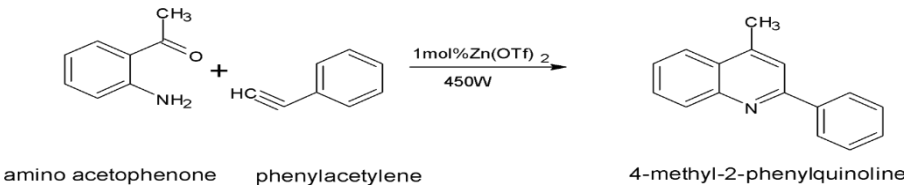
Synthesis of 2,3,4 tri alkylquinoline derivatives[22]:
A one-pot reaction of anilines with alkyl vinyl ketones on the surface of a silica gel inseminated with indium (III) chloride under microwave irradiation without any solvent.



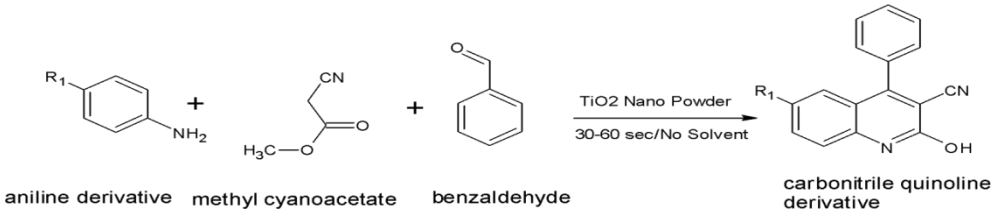
Synthesis of 2,4diphenylquinolinederivatives[23]:
Aniline derivatives, aryl aldehydes and aryl alkynes. The reaction was catalyzed by montmorillonite K-10, a strong and environmentally benign solid acid.



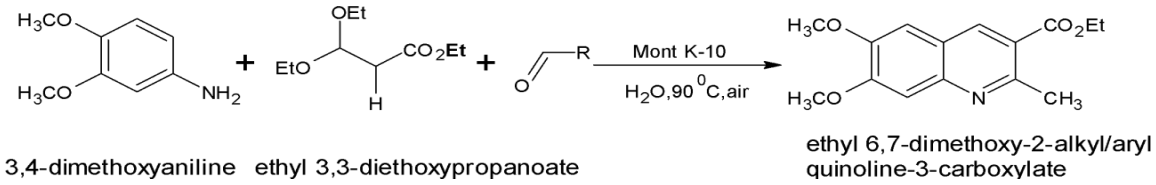
Synthesis of4-methyl-2-phenylquinoline[24]:
Amino acetophenone and phenylacetylene in the presence of Zn $(OTf)_2$ as an effective catalyst under microwave irradiation



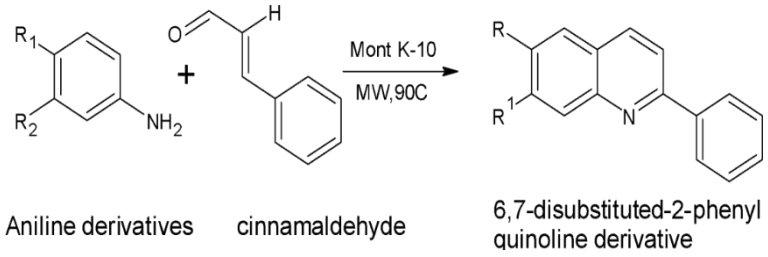
Synthesis of carbonitrile quinoline derivatives[25]:
Benzaldehyde, methyl cyanoacetate and aromatic amine with nano structured TiO_2 photocatalysts under solvent-free conditions and under microwave irradiation.



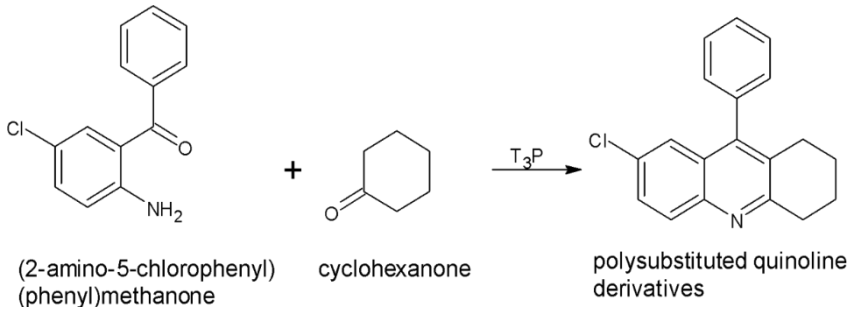
Synthesis of ethyl 6,7-dimethoxy-2-alkyl/aryl quinoline-3-carboxylate derivatives[26]:
A three-component one-pot reaction between 3,4-dimethoxyaniline, aldehydes and ethyl-3,3-diethoxypropionate to a quinoline derivative by using montmorillonite K-10 (Mont K-10) as a green catalyst by utilizing the oxygen of air and water MontmorilloniteK-10 (MontK-10) was found to be more effective compared to other Lewis acids as the expected product was isolated in good yield.



Synthesis of 6,7-disubstituted-2-phenyl quinoline derivatives[27]:
Aniline derivatives and cinnamaldehyde reacts to form a quinoline derivative by using montmorillonite K-10(Mont K-10) clay-catalyzed.

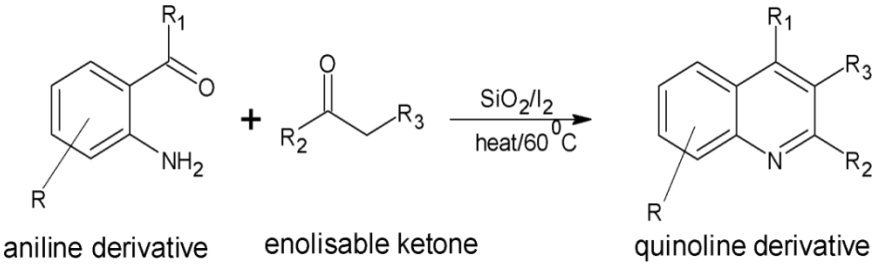


Synthesis of polysubstituted quinoline derivatives[28]:
(2-amino-5-chlorophenyl) (phenyl)methanone and cyclohexanone to a poly substituted quinoline derivative by using propylphosphonic anhydride (T_3P) in short reaction times and in excellent yields. Here T_3P is used as a mild water scavenger catalyst in this coupling reaction.



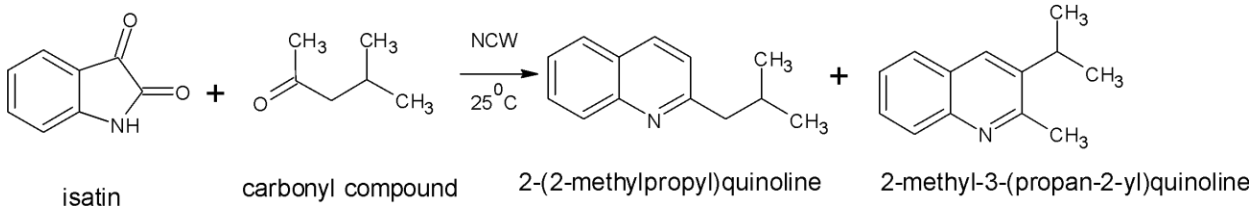
Synthesis of quinoline derivatives[29]:
Enolisable ketone with molecular iodine as a catalyst in ethanol, combining iodine and silica gel under solvent-free conditions, a Friedlander hetero annulation method by using nano ZnO as a mild, non-volatile, non- corrosive and efficient catalyst which provides regiospecific synthesis under

solvent-free conditions, and using ionic liquid [Hbim][BF_4] under ultrasound at room temperature.



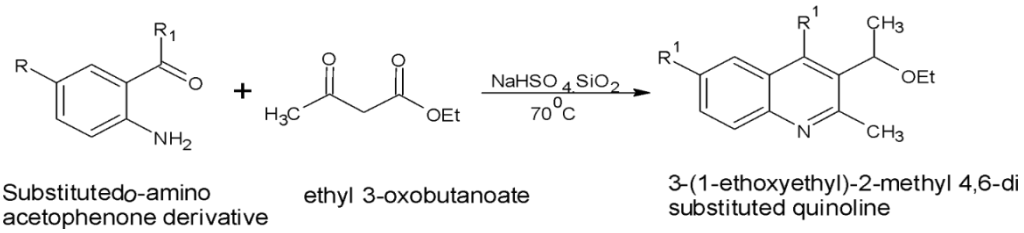
Synthesis of 2-(2-methyl propyl) quinoline and 2-methyl-3- (propan-2- yl) quinolone derivatives[30]:

Carbonyl compound with isatin in NCW form the substituted quinoline derivative via in situ decarboxylation.



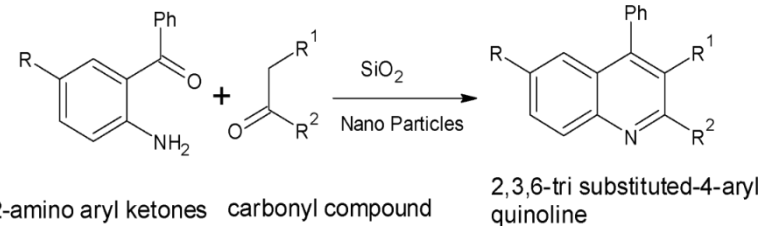
Synthesis of ethyl 6, 7-dimethoxy-2-alkyl/aryl quinoline-3- carboxylate derivatives[31]:

Substituted *o*-amino acetophenone derivative and ethyl 3- oxobutanoate by using $NaHSO_4 \cdot SiO_2$ as a heterogeneous and reusable catalyst.



Synthesis of 2,3,6-trisubstituted-4-aryl quinoline derivatives[32]:

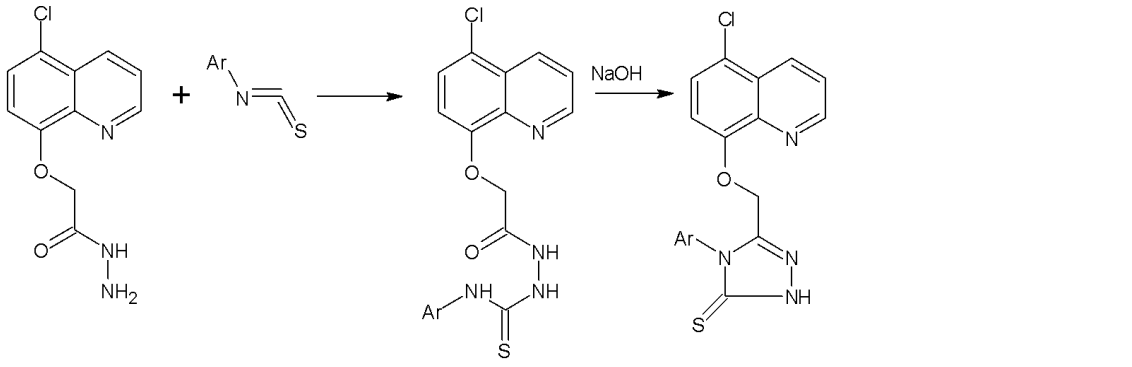
2-amino aryl ketones and carbonyl compounds in the presence of silica nano-particles (NPs) as catalysts under microwave irradiation give high yields of quinoline derivatives. Silica nano-particles gave best results compare to CaO, MgO, Al_2O_3 and SiO2.



II.REACTION OF QUINOLINE:

Synthesis of Quinolinyl Triazole derivatives[33]:

Quinoline hydrazide and aryl-substituted isothiocyanate, was refluxed in methanol to form Quinolinyl Carbothioamide. It reacts with 5 % NaOH (aqueous) at 70°C to form quinolinyltriazole.



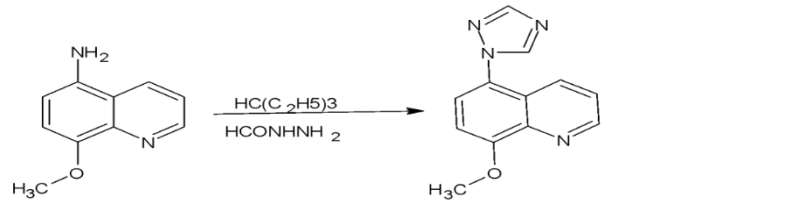
2-[(5-chloroquinolin-8-yl) oxy]acetohydrazide

2-{[(5-chloroquinolin-8-yl)oxy]acetyl} -*N*-aryl hydrazine-1-carbothioamide

5-{[(5-chloroquinolin-8-yl)oxy]methyl} -4-aryl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione

Synthesis of 8-alkoxyquinolin-5-amine derivatives[34]:

A mixture of 8-alkoxyquinolin-5-amine, formyl hydrazine, glacial acetic acid, and triethylorthoformate to form of 8-alkoxy-5-(4H-1,2,4-triazol- 4-yl) quinolines.

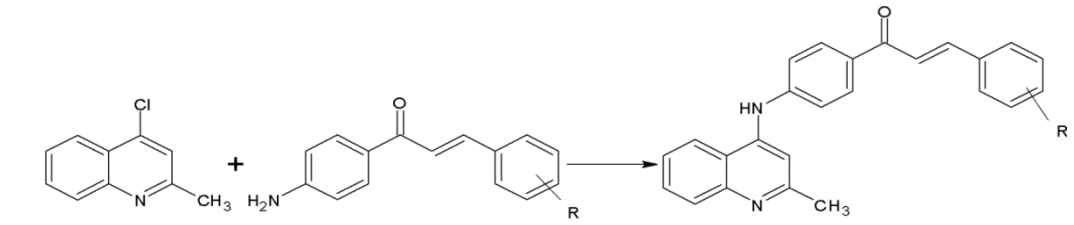


8-aryloxyquinolin -5-amine

8-aryloxy-5-(1*H*-1,2,4-triazol-1-yl) quinoline

Synthesis of quinoline-chalcone derivatives[35]:

Substitution reaction between compounds chalcone derivatives with commercially available 4-chloro-2-methylquinoline gave target compounds quinoline-Chalcone derivatives in the presence of HCl in EtOH at 80 ^{0}C.



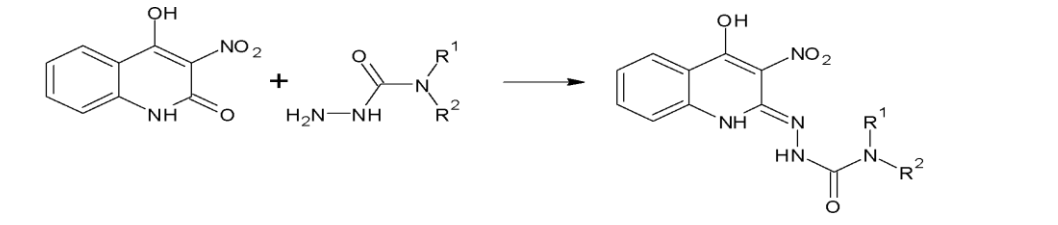
4-chloro-2-methylquinoline

1-(4-aminophenyl) -3-phenylprop-2-en-1-one

1-{4-[(2-methylquinolin-4-yl)amino]phenyl} -3-phenylprop-2-en-1-one

Synthesis of quinoli-ylidene I bearing thiosemicarbazone derivatives[36]:

4-hydroxy-3-nitroquinolin-2 (1*H*)-one reacted with thiosemicarbazide derivatives at 82°C to form 2-(4-hydroxy-3-nitroquinolin-2(1*H*)-ylidene) hydrazine-1-carboxamide.



4-hydroxy-3-nitroquinolin-2(1*H*)-one

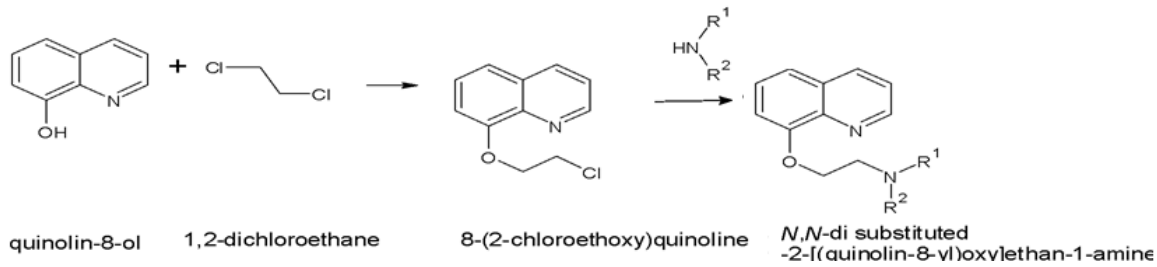
thiosemicarbazide derivatives

2-(4-hydroxy-3-nitroquinolin-2(1*H*)-ylidene) hydrazine-1-carboxamide derivatives

Synthesis of 8-amino substituted quinoline derivatives[37]:

A mixture of 8-hydroxy quinoline,1,2-dichloro ethane and anhydrous potassium carbonate in dry acetone to form 8-(2chloroethanoxy) quinoline. It reacts with amine, anhydrous sodium carbonate

and sodium iodide in dry acetone to form 8-(2-amino-ethanoxy) quinoline.

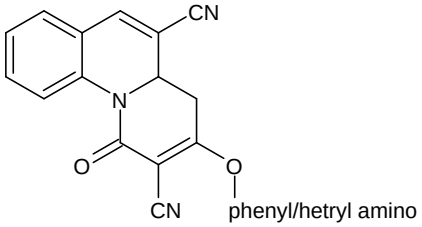


III. Medical application of quinoline derivatives:

Quinoline and its combined heterocyclic subsidiaries tried with assorted pharmacological action established a significant class of mixtures for new medication.

Antimicrobial activities:

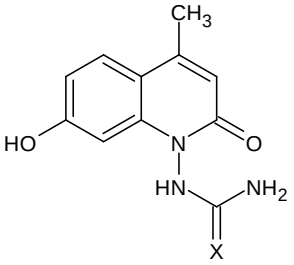
1-oxo-3-phenoxy/hetrylamino-1*H*-pyrimido[1,2-*a*] quinoline-2,5- dicarbonitrile derivatives tested for their antimicrobial[38] activity using disc diffusion technique against *S. aureus, B.Substilis*, the standard antibiotics penicillin and ampicillin showed zones of inhibition against bacterial strains.



1-oxo-3-phenyl/hetryl amino oxy-4,4a-dihydro-1*H*-pyrido[1,2-*a*]quinoline-2,5-dicarbonitrile

Anticancer activity:

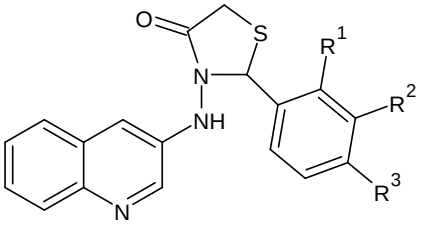
1-(7-Hydroxy-4-methyl-2-oxoquinolin-1(2H)-yl) urea/thiourea derivatives as potential anticancer[39] activity against breast cancer cells (MCF–7), bone marrow cancer cells (K–562) and cervical cancer cells (HeLa) by MTT assay.



N-(7-hydroxy-4-methyl-2-oxoquinolin-1(2*H*)-yl)urea/ thiourea

Anti-inflammatory and analgesic

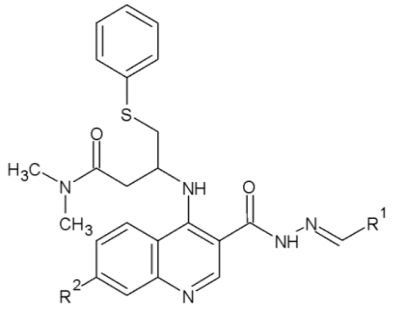
2-(4-substituted phenyl)-3-[(quinolin-2-yl) amino]-1,3-thiazolidin-4- one derivatives are being developed as anti-inflammatory and analgesic[40] activity.



3-[(quinolin-3-yl)amino]-2-(2,3,4-trisubstitutedphenyl)-1,3-thiazolidin-4-one

Anti-tuberculosis activity

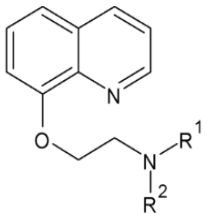
Quinoline derivatives carrying active pharmacophores has been synthesized and evaluated for their invitro anti-tuberculosis[41] activity against *Mycobacterium tuberculosis* H37Rv (MTB), *Mycobacterium smegmatis* (MC2), and *Mycobacterium fortuitum* following the broth micro dilution assay method, when compared with first line drugs are isoniazid (INH) and rifampicin (RIF).



4-amino *N*,*N*-dimethyl-4-(phenylsulfanyl)butanamide
-*N*-[(1*E*)-alkylidene]-7-alkylquinoline-3-carbohydrazide

Anticonvulsant and Antihypertensive activities

A series of 8-substituted quinolines derivatives are tested against seizures induced and antihypertensive[42] activities.



N,*N*-dialkyl-2-[(quinolin-8-yl)oxy]ethan-1-amine

CONCLUSION:

Quinoline derivatives are good in medical applications. Synthesis of different quinoline derivatives with increase in their effectiveness against diseases encourages the continuous attempts towards working on quinoline as well as its derivatives. These are several quinoline synthetic procedures established so far. They include Skraup reaction, Friedlander reaction, Conrad-Limpach-Knorr reaction, Doebner reaction, Doebner-miller reaction, Skraup-Doebner-Von Miller reaction, Conrad–Limpach reaction, Combes reaction, etc. Quinoline and its derivatives are known for their wide spectrum of pharmacological activities, a number of synthetic methods have been developed from time to time for their synthesis by conventional, homogeneous, and heterogeneous without catalyzed methods, with catalyzed methods, microwave-assisted, solvent- free conditions and many more. These quinoline derivatives are very useful to the researcher working in this field, and it would help them to develop new synthetic methods for the potent quinoline derivatives with good or enhanced biological activities for the future.

REFERENCES:

1. Valarmathy Joshua, Shalini S, Janapriya S, Bharath Kumar. R, Veeraselvam. S, Manickkvasagam. A, Sam Solomon. W. D and Samuel Joshua. L, "Synthesis, characterization and biological evaluation of some novel quinoline-4-carboxylic acid derivatives based on Doebner hydrogen transfer reaction", Eur. Chem. Bull. **2023**, 12 (Regular Issue 11), 01–08.
2. Venkat Lingaiah B P, Yakaiah T, Chandra Shekhar A, Ravi Kumar A, Sathaiah G, Raju K, Shanthan Rao P, Narasaiah B, Pranay Kumar K, Murthy U S N, Purushotham U and NaraharíSastry G, "Synthesis of novel α-amino acid functionalized 6-fluoroquinolines, their anti-bacterial activity and molecular docking studies", Indian Journal of Chemistry, 2012;

51(B):969- 980.
3. Sumesh Eswaran, Airody Vasudeva Adhikari and Suchetha Shetty, "Synthesis and antimicrobial activities of novel quinoline derivatives carrying 1,2,4-triazole moiety'', European Journal of Medicinal Chemistry, 2009; 44:4637–4647.
4. Digafie, Zeleke, Rajalakshmanan, Eswaramoorthy, Zerihun, Belay, and Yadessa, Melaku, "Synthesis and Antibacterial, Antioxidant, and Molecular Docking, Analysis of Some Novel Quinoline Derivatives", Hindawi Journal of Chemistry, 2020:16.
5. Zhu H, Yang R F, Yun L H and Li J, "Facile and Efficient Synthesis of Quinoline-4-Carboxylic Acids under Microwave Irradiation", Chin. Chem. Lett, 2010; 21(1):35–38.
6. Mohammad Ali Nasseri, Batolzakerinasab and Sayyedekamayestani, "proficient Procedure for Preparation of Quinoline Derivatives Catalyzed by NbCl5 in Glycerol as Green Solvent", Journal of Applied Chemistry, 2014; 2015:7.
7. Hegedus A, Hell Z, Vargadi T, Potor A and Gresits I, "A new, simple synthesis of 1,2-dihydroquinolines via cyclocondensation using zeolite catalyst", Catalys is Letters, 2007; 117:99-101.
8. Abbas teimouri and Alirezanajafichermahini, "A mild and highly efficient Friedländer synthesis of quinolines in the presence of heterogeneous solid acid nano-catalyst", Arabian Journal of Chemistry, 2016; 9:433-439.
9. Cho C S and Ren W X, "A recyclable palladium-catalyzed modified Friedländerquinoline synthesis", J. Organomet. Chem., 2007; 692:4182-4186.
10. Zhou T, Lin J and Chen Z, "A convenient synthesis of quinolones via ionic liquid-catalysed Friedlander annulations", Letters in Organic Chemistry, 2008; 5:47-50.
11. Bharathkumar H, Mohan C D, Ananda H, Fuchs J E, Li F, Rangappa S, Surender M, Bulusu K C, Girish K S, Sethi G, Bender A, Basappa, and Rangappa K S, "Microwave-Assisted Synthesis, Characterization and Cytotoxic Studies of Novel Estrogen Receptor α Ligands towards Human Breast Cancer Cells", Bioorg. Med. Chem. Lett, 2015; 25(8):1804–1807.
12. Jampilek J, Musiol R, Pesko M, Kralova K, Vejsova M, Carroll J, Coffey A, Finster J, Tabak D and Niedbala H, "Ring-substituted 4-hydroxy-1H- quinolin-2-ones: preparation and biological activity", Molecules, 2009; 14:1145-1159.
13. Zolfigol M A, Salehi P, Ghaderi A, Shiri M and Tanbakouchian Z, "An eco-friendly procedure for the synthesis of polysubstitutedquinolines under aqueous media", J. Mol. Catal. A: Chem., 2006; 259:253-258.
14. Muscia G C, Bollini M, Carnevale J P, Bruno A M and Asís S E, "Microwave-Assisted Friedländer Synthesis of Quinolines Derivatives as Potential Antiparasitic Agent", Tetrahedron Lett, 2006; 47(50):8811-8815.
15. Chaudhuri M K and Hussain S, "An Efficient Synthesis of Quinolines under Solvent-Free Conditions", J. Chem. Sci., 2006; 118(2): 199-202.
16. Zhang L, Wu B, Zhou Y, Xia J, Zhou S and Wang S, "Rare-Earth Metal Chlorides Catalyzed One-Pot Syntheses of Quinolines under Solvent-Free Microwave Irradiation Conditions", Chin. J. Chem, 2013; 31(4):465-471.
17. Bhatt H G, Agrawal Y K and Patel M J, "Amino- and Fluoro-Substituted Quinoline-4-Carboxylic Acid Derivatives: MWI Synthesis, Cytotoxic Activity, Apoptotic DNA Fragmentation and Molecular Docking Studies", Med. Chem. Res, 2015; 24(4):1662-1671.
18. Safari J, Banitaba S H and Samiei S S, "Early Surgical Decompression Restores Neurovascular Blood Flow and Ischemic Parameters in an in Vivo Animal Model of Nerve Compression Injury", J. Chem. Sci, 2009; 121:481-484.
19. Anvar S, Mohammadpoor-Baltork T, Tanges taninejad S, Moghadam M, Mirkhani V, Khosropour A R and Kia R, "Efficient and environmentally- benign three-component synthesis of quinolines and bis-quinolines catalyzed by recyclable potassium dodecatungs to cobaltatetri hydrate under microwave irradiation", RSC Adv, 2012; 2:8713-8720.
20. Gogoi S, Shekarrao K, Duarah A, Bora T C and Boruah R C, Microwave- assisted palladium mediated efficient synthesis of pyrazolo[3,4-b] pyridines, pyrazolo[3,4-b] quinolines,

pyrazolo[1,5-a] pyrimidines and pyrazolo [1,5- a] quinazolines", RSC Adv, 2012; 77:1438-1445.
21. Ranu B C, Hajra A and Jana U, "A simple and green procedure for the synthesis of N, N'-disubstitutedthioureas on the surface of alumina under microwave irradiation", Tetrahedron Letter, 2000; 41:531-533.
22. Kulkarni A and Torok B, "Microwave-assisted multicomponent domino cyclization–aromatization: an efficient approach for the synthesis of substituted quinolines", Green Chem, 2010; 12:875-878.
23. Praveen C, DheenKumar X P, Muralidharan and Perumal P T, "Synthesis, antimicrobial and antioxidant evaluation of quinolines and bis (indolyl) methanes", Bioorg. Med. Chem. Lett., 2010; 20:7292-7296.
24. Prakash Naik H R, BhojyaNaik H S, RavikumarNaik T R, Aravinda T and Lamani T S, "TiO2 Nanopowder Catalyzed Microwave-Induced One- Pot Synthesis of Novel Quinoline/Benzo[h]quinoline3-carbonitrile Under Solvent Free Conditions", Phosphorus, Sulfur Silicon Relat. Elem., 2009; 184:2109-2114.
25. Reddy T R, Reddy L S, Reddy G R, Yarbagi K, Lingappa Y, Rambabu D, Krishna G R, Reddy C M, Kumar K S and Pal M, "Construction of a quinoline ring via a 3-component reaction in water: crystal structure analysis and H-bonding patterns of a 2-aryl quinoline", Green Chem., 2012, 14, 1870—1872.
26. Nagendrappa G, "Applied Clay Science", Science Direct, 2011; 53:106-138.
27. Jida M and Deprez B, "Friedländer synthesis of polysubstitute dquinolines and naphthyridines promoted by propylphosphonic anhydride (T3P®) undermild conditions", New J. Chem., 2012; 36:869.
28. Hosseini Sarvari M, "Synthesis of quinolines using Nano-Flake ZnO as a new catalyst under solvent-free conditions", Journal of the Iranian ChemicalSociety, 2011; 8:119-128.
29. Bryson T A, Gibson J M, Stewart J J, Voegtle H, Tiwari A, Dawson J H, Marley W and Harmon B, "Synthesis of quinolines, pyridine ligands and biological probes in green media", Green Chemistry, 2003; 5:177-180.
30. Vu A T, Cohn S T, Manas E S, Harris H A and Mewshaw R E, "ERbeta ligands Part 4: Synthesis and structure-activity relationships of a series of 2- phenylquinoline derivatives", PubMed, 2005; 15:4520-4525.
31. A. Hasaninejad, M. Shekouhy and A. Zare ,"Silicananoparticlesefficiently catalyzed synthesis of quinolines and quinoxalines", Catalsis Science Technology, 2012; 2:201-214.
32. H. Zhu, R. F. Yang, L. H. Yun and J. Li, "Metal-free synthesis of quinolines by direct condensation of amides with alkynes: revelation of N- aryl nitrilium intermediates by 2D NMR techniques", Chin. Chem. Lett., 2010; 21:35-38.
33. Shi-Ben Wang, Xian-Qing Deng, Yan Zheng, Hong-Jian Zhang and Zhe-Shan Quan, "Synthesis and anticonvulsant activity evaluation of 8-alkoxy-5- (4H-1,2,4-triazol-4-yl) quinoline derivatives", Arch. Pharm. Res, 2013; 36:32-40.
34. Yong-Feng Guan, Xiu-Juan Liu, Xin-Ying Yuan, Wen-Bo Liu, Yin-Ru Li, Guang-Xi Yu, Xin-Yi Tian, Yan-Bing Zhang, Jian Song, Wen Li and Sai- Yang Zhang, "Design, Synthesis, and Anticancer Activity Studies of Novel Quinoline-Chalcone Derivatives", Molecules, 2021; 26:4899.
35. MaciejSerda, Robert Musiol, Jaroslaw and Polanski, "New thiosemicarbazones based on quinoline scaffold as anticancer iron chelators", University of Silesia Institute of Chemistry Szkolna, 9; 40-007.
36. Nithyanantham, Muruganantham, Ramaiah, Sivakumar, Navaneetharaman, Anbalagan, Vedachalam, Gunasekaran, and Joseph Thomas Leonard, "Synthesis, anticonvulsant and antihypertensive activities of 8-Substituted Quinoline Derivatives", Biol. Pharm. Bul, 2004; 27(10):1683-1687.
37. Halikar N K, Jagtap P R, Vartale S P, "Green Synthetic Approach and Antimicrobial Activities of Some Novel Pyrimido[1,2-a] quinoline derivatives",International Journal of Scientific

Research in Science and Technology, 2022; 9(8):117-121.
38. Jamshed Iqbal, Syeda Abida Ejaz, Imtiaz Khan, Elina Ausekle, Mariia Miliutina and Peter Langer, “Exploration of quinolone and quinolone derivatives as potential anticancer agents”, DARU Journal of Pharmaceutical Sciences, 2019; 27:613-626.
39. Mukherjee S and Pal M, “Medicinal chemistry of quinolines as emerginganti-inflammatory: an overview”, Current medicinal chemistry, 2013; 20:4386-4410.
40. Sumesh Eswaran, Airody Vasudeva Adhikari, Nishith Pal K and Imran Chowdhury H, "Design and synthesis of some new quinoline-3- carbohydrazone derivatives as potential antimycobacterial agents”,Bioorganic & Medicinal Chemistry Letters, 2010; 20:1040-1044.
41. Nithyanantham, Muruganantham, Ramaiah, Sivakumar, Navaneetharaman, Anbalagan, Vedachalam, Gunasekaran and Joseph Thomas Leonard, “Synthesis, Anticonvulsant and Antihypertensive Activities of 8-Substituted Quinoline Derivatives”, Biol. Pharm. Bull, 2004; 27(10):1683-1687.