WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.041
Volume 6, Issue 1, 465-480 Review Article ISSN 2278 – 4357

RECENT ADVANCES IN THE SYNTHESIS OF 2-CHLORO-3-FORMYL QUINOLINES AND ITS DERIVATIVES: A REVIEW

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Article Received on
08 Nov. 2016,

Revised on 28 Nov. 2016,
Accepted on 18 Dec. 2016

DOI: 10.20959/wjpps20171-8401

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ABSTRACT

In last few years five and six membered heterocyclic compounds containing one or two heteroatoms fused to quinoline ring gains importance in natural products as well as in the synthetic compounds of biological interest.[1a] The substituted quinolines have various annulations, Pyrazolo (3,4-b)Quinolines, quinoline oximes, naphthyridin-4(1H)- one derivatives etc which reviewed here.

INTRODUCTION

Natural compounds and pharmaceutical active substance contains numbers of substituted quinolines like structure, comprising a significant segment of the pharmaceutical market. The classical methods for the synthesis of these heterocyclic skeletons.[1b-d] which require expensive and cheap starting materials and their synthetic methods revived here. The importance of quinolines, its annelated derivatives and Pyrazolo (3,4-b)Quinolines[1e]are well recognized by synthetic and biological chemists.[2-5] Compounds possessing such ring systems have wide applications as drugs and pharmaceuticals.[6-7] Quinolinic acid is a precursor in the synthesis of pesticides, herbicides and 8-hydroxyquinoline is employed in liquid bandages.[8] Likewise, several derivatives having complex structures have been investigated for the use in OLED's, in nano- and chemo-sensors.[9] Quinoline derivatives having potent, pharmacological applications due to their significant antimalarial.[17] anti-inflammatory, antitumor[16-18], antibacterial and antiviral activities[10], anticonvulsant[11], cardiovascular.[12] activities, as well as various central nervous system effects.[13] have also been reported here.

Among the heterocyclic compounds Quinoline structures have unique importance.[14] and many of its derivatives gave activities such as bactericidal.[15] The Quinolines having substitution chlorine at 2ndposition and formyl at 3rd position, which is active site for further

[b]-annelation of wide variety of rings as well as functional group inter conversions.[19-20] Vilsmeier-Haack conditions is favorable for cyclisation of quinoline derivatives reported earlier literatures.[21]The Vilsmeier-Haack reaction is a mild method for the introduction of a formyl group to various activated aromatic and heteroaromatic.[22-23]

The Vilsmeier Haack reagent, i.e halomethylenium salt formed from $POCl_3$ and DMF, has attracted the attention of synthetic organic chemists since 1927.[24a-b]. The Vilsmeier Haack reaction is a mild method for the introduction of formyl group in various activated aromatic and heteroaromatic compounds as mechanism given in fig 1.[25]This reagent is also utilized in the synthesis of a large number of heterocyclic compounds.[26] In continuation of our ongoing work on Vilsmeier Haack reaction,[27] we emphasize to present the utilization of ultrasonic irradiation for the synthetic.[28]

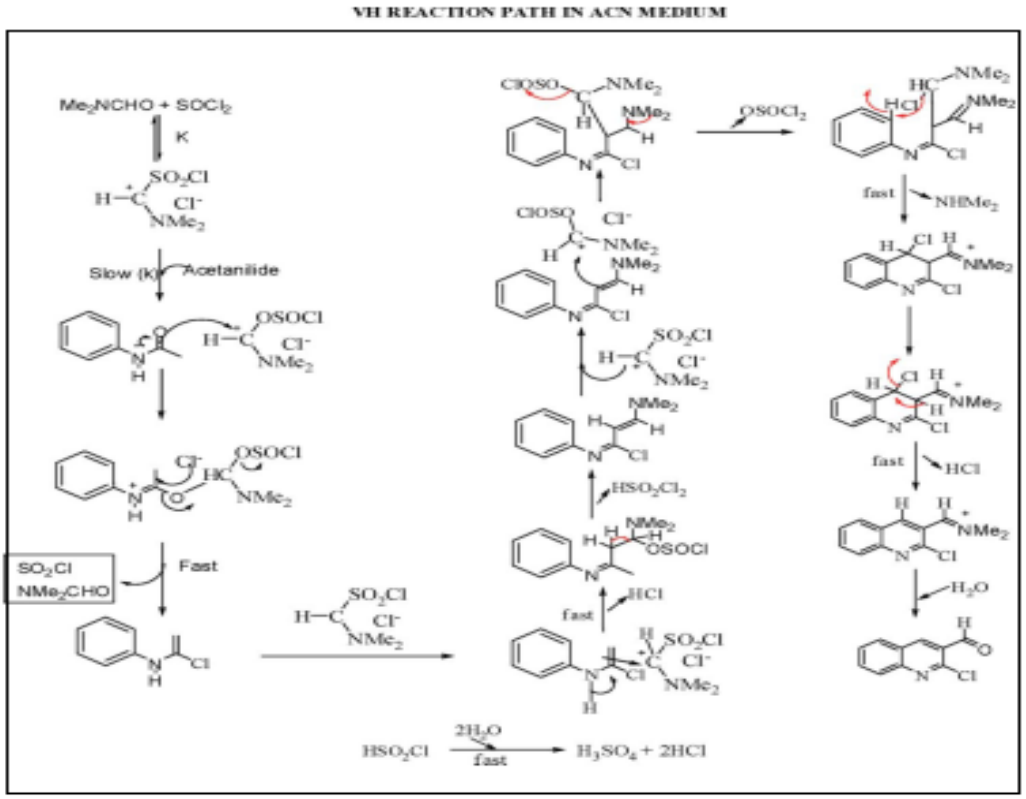
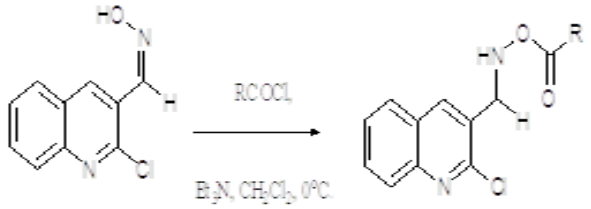


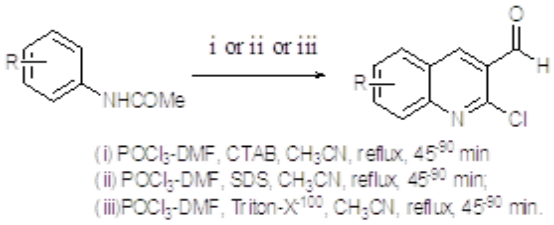
Fig 1: Mechanism for 2-chloro-3-formyl quinoline Synthesis via DMF/$POCl_3$.

P.J. Bindu and its co-workers investigated a novel 2-chloro-3-formyl quinoline oxime esters were synthesized by reacting 2-chloro-3-formyl quinoline oximes with substituted benzoyl chlorides derivatives. The triethyl amine acts mild base and dichloromethane as solvent at 0^oC. They also studied DNA photo cleavage of some new oxime esters were investigated by neutral agarose gel electrophoresis at different concentrations.[29] shown in scheme 1.



Scheme 1: Synthesis of quinoline oxime esters.

Acetanilides efficiently undergo Vilsmeier Haack cyclisation in micellar media to afford 2-chloro-3-formyl quinoline given by M. M. Alireaction is efficiently in CTAB (cetyl trimethyl ammonium bromide).[30] sodium dodecyl sulphate and Triton-X-100 media.[31] shown in scheme 2.



Scheme-2: Cyclisation of acetanilides by Vilsmeier Haack in micellar media.

F. Aneesa and others studied and gave advantage of Vilsmeier Haack reaction according to their rate which can enhance by using transition metal ions such as Cu(II), Ni(II), Co(II), and Cd(II) were used as catalysts in these reactions and the new possible mechanism.[32] shown in fig-2.

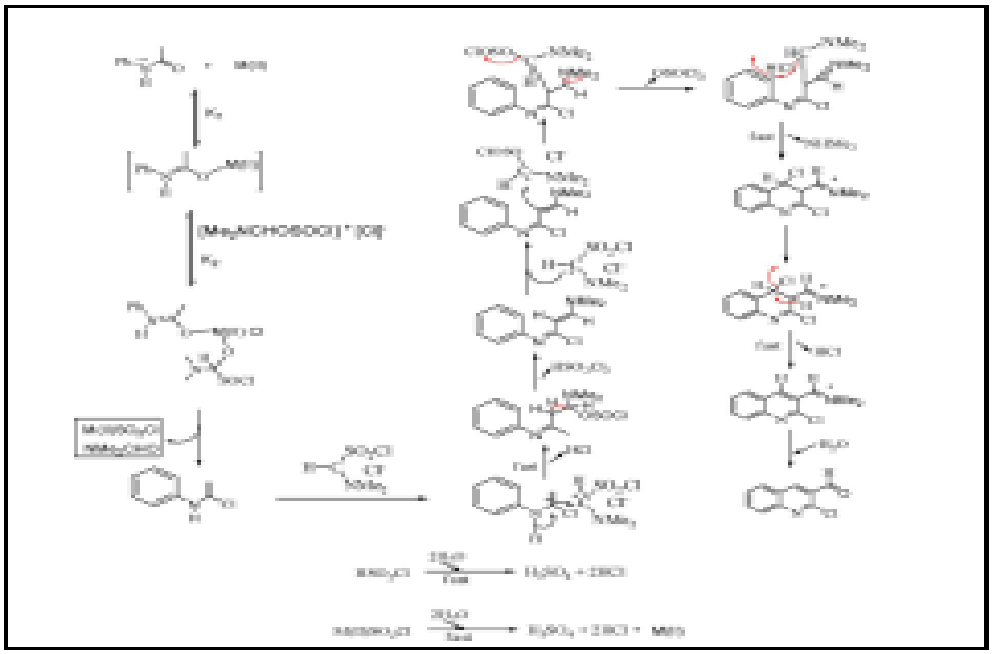
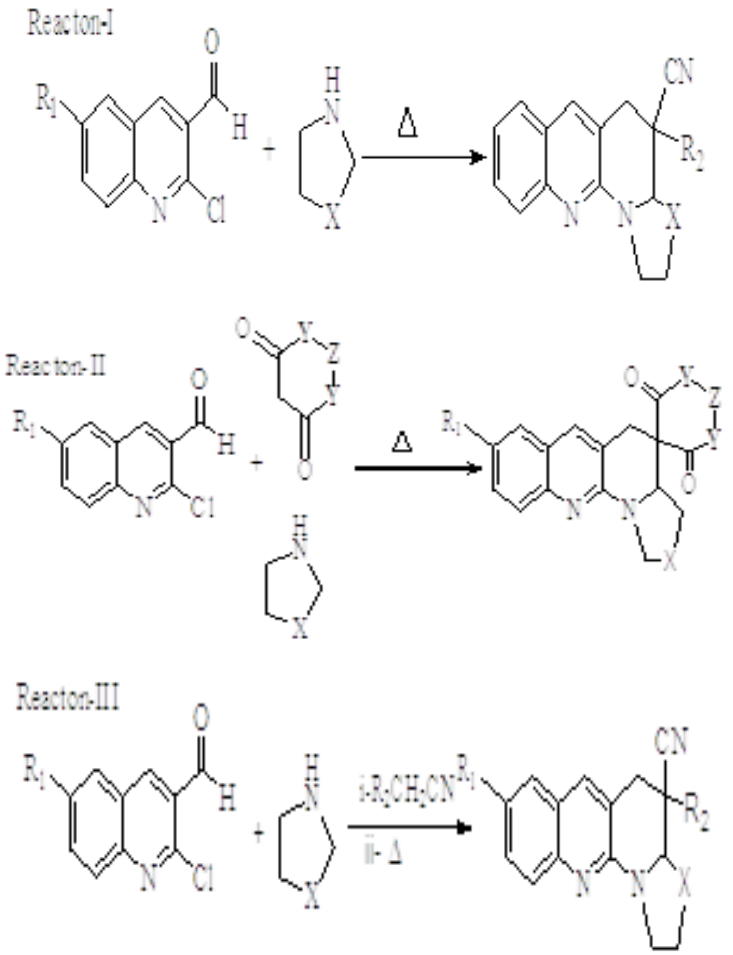


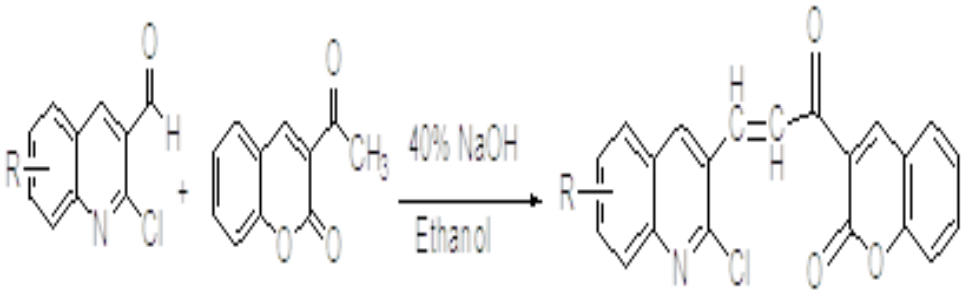
Fig-2: Metal ion catalyzed reaction mechanism in acetonitrile medium.

Ipsita Devi, Biswajita Baruah, and Pulak J. Bhuyan have reported the synthesis of some new types of quinolizine(reaction-I), indolizine(reaction-II) and pyrido-1,4- oxazine-fused complex (reaction-III)quinoline derivatives via a novel three-component reaction without solvent by finding and studied the 'tertiary amine effect' reaction strategy.[33] shown in scheme 4.



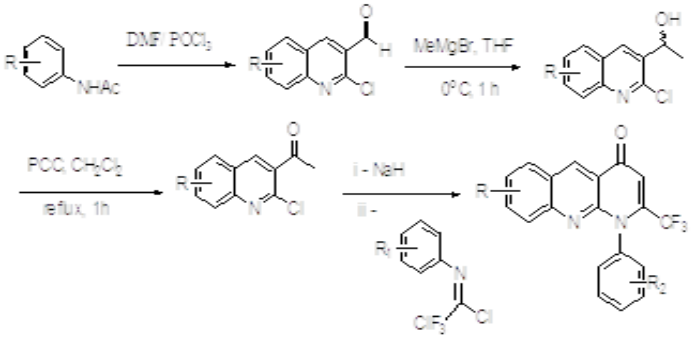
Scheme 4: Quinolizine(reaction-I), Indolizine(reaction-II) and Pyrido-1,4- oxazine-fused complex (reaction-III)quinoline.

N. Pramod et al synthesized coumarin containing quinoline derivatives by both ways i.e. conventional method and microwave techniques. 3-acetyl coumarin was synthesized by treating salicylaldehyde with ethyl acetoacetate in the presence of piperidine using grindstone method and condensation reaction carried out between 3 acetyl coumarin and 2-cholro-3-formyl quinoline derivatives were by dissolving in ethanol in presence of 40% KOH. This reaction was called as crossed Aldol or Clasein Schimdt condensation and it was also done by microwave assisted technique.[34] shown in scheme:5



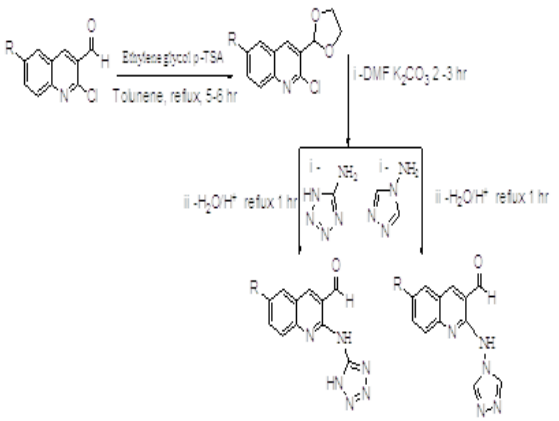
Scheme-5: Synthesis of 3-(3-(2-chloroquinoline-3-yl)acryloyl)-2H-chromen-2-0ne.

Angel H. Romero, José Salazar and Simón E. López gave synthesis of 2 (trifluoromethyl)benzo[b][1,8] naphthyridin-4(1H)- one derivatives. The reaction was carried out between diverse 2-chloro-3-acetyl-quinolines, trifluoroacetimidoyl chlorides using and sodium hydride in THF at room temperature shown in scheme 6.



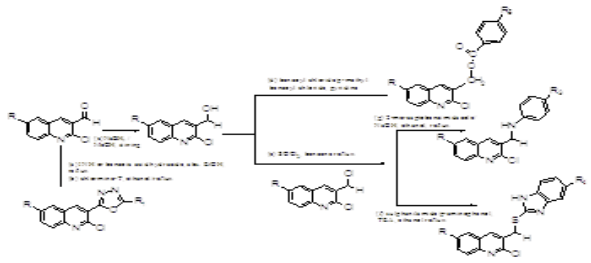
Scheme-6: Synthesis of 2-(trifluoromethyl)benzo[*b*][1,8]naphthyridin-4(1*H*)-one derivatives.

Jayvirsinh D. Gohil, Haresh B. Patel, Manish P. Patelreported a new series of biquinoline derivatives and aromatic trifluoromethyl moiety at *N*-1 position were synthesized by multicomponent reactions of 2-amino triazole/amino tetrazole-3-formyl quinoline with malononitrile/isopropyl cyanoacetate and their β-enaminones.[35] shown in scheme 7.



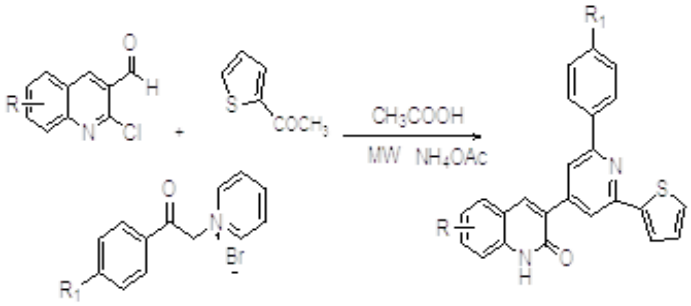
Scheme-7: Synthesis of biquinoline derivatives and aromatic trifluoromethyl

Kumar S, Goel N, Afzal O, Ali MR and Bawa A studied synthesis of differentiated 2-chloroquinoline derivatives having various spacer groups between 2-chloroquinoline and aryl or heteroaryl rings involving nucleophilic addition& substitution, nucleophilic substitution, esterification, cyclization etc.[36] shown in scheme 8.



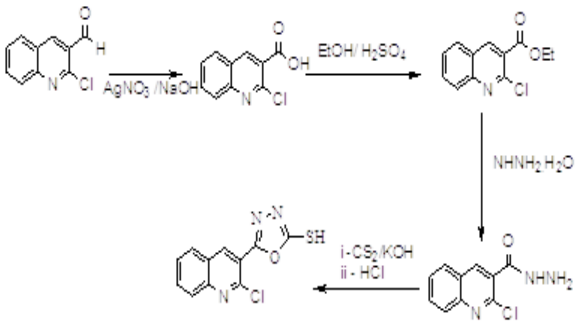
Scheme-8: Various reactions of 2-chloroquinoline.

Niraj K. Ladani, Manish P. Patel, and Ranjan G. Patel gave a series of 3-(2-phenyl-6-(2-thienyl)-4-pyridyl)hydroquinolin-2-ones were synthesized in high yields by one–pot cyclocondensation reaction under Kr¨ohnke's reaction conditions using 2-chloro-3-formyl quinoline, 2-acetyl thiophene, and various *N*-phenacylpyridinium bromides in a mixture of ammonium acetate and acetic acid by microwave irradiation.[37] shown in scheme 9.



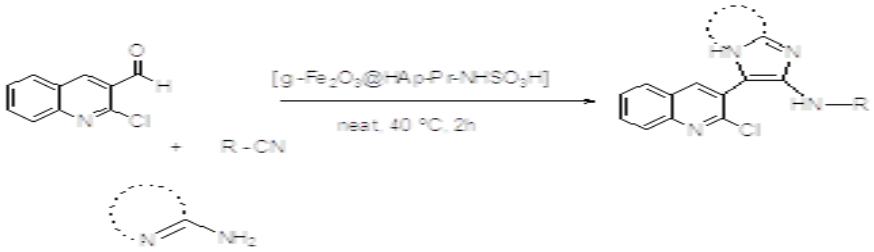
Scheme-9: Synthesis of 3-(2-phenyl-6-(2-thienyl)-4-pyridyl)hydroquinolin-2-ones

Ibrahim Ali M. Radini et al gave a series of new quinoline derivatives prepared using tetrazoloquinoline-3-carbaldehyde as starting material with 2-oxo-1,2-dihydroquinoline-3-carbaldehyde, 2-chloroquinoline-3-carbaldehyde, and 2-(piperidin-1-yl)quinoline-3-carbaldehyde.[38] Shown in scheme 10.



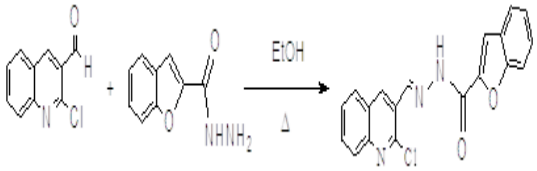
Scheme-10: Synthesis ofquinoliny 1,3,4-oxadiazole

2-chloro-3-formyl-quinoline can undergo a convenient and efficient one-pot reaction with isocyanides and amidines under solvent free condition in the presence of catalytic amount of [γ Fe_2O_3@HAp-Pr-$NHSO_3H$], to provide a verity of N-fused 2-(2-chloro-quinolin-3-yl)-3-aminoimidazoles.[39] shown in scheme 11.



Scheme -11: Synthesis of *N*-fused 2-(2-chloro-quinolin-3-yl)-3-aminoimidazoles.

Mustapha C. Mandewale et al studied series of Co(II), Ni(II), Cu(II), Zn(II) and La(III) complexes of N'-[(E)-(2- hydroxyquinolin-3 yl)methylidene]-1-benzofuran-2-carbohydrazides have been reported. It is synthesized by the condensation of 2-hydroxy-3-formylquinoline with benzofuran-1-carbohydrazide in absolute ethanol.[40] shown in scheme 12.



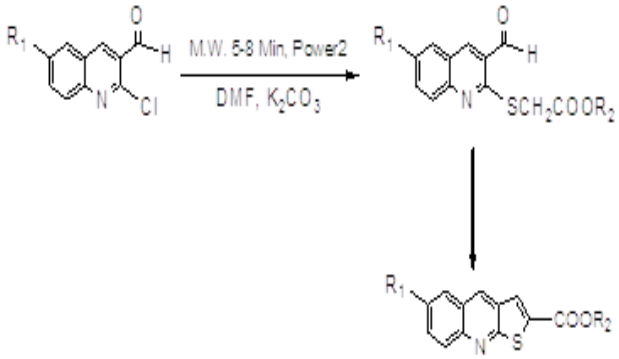
Scheme 12: Synthesis of N'-[(E)-(2- hydroxyquinolin-3 yl)methylidene]-1-benzofuran-2-carbohydrazide

B. M. Prasanna and its coworkers studied the new corrosion inhibitor property shown by 2-Chloro 3-formyl quinolone.[41] with the maximum inhibition about 80 % at 200 ppm conc. The inhibition effect of 2-chloro 3-formyl quinoline is attributed to the adsorption process.

Mechanism of inhibition: The 2-chloro 3-formyl quinoline drug molecules contain N, O and fused benzene rings. They worked on adsorbed phenomenon of the metal surface predominantly by chemisorption. 2-chloro 3-formyl quinoline shows tendency to adsorbed on the mild steel surface as donor–acceptor interactions observed with the vacant d-orbital of metal. An N and O atom of the inhibitor donates a lone pair of electrons forming co-ordinate bond with metal.

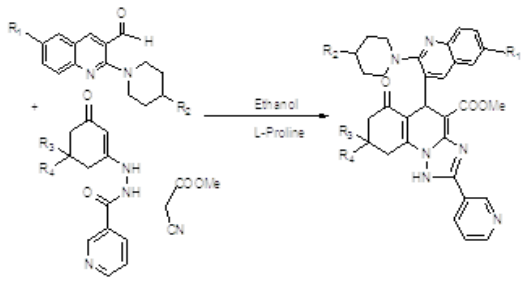
A series of thieno[2,3-b]quinoline-2-carboxylic acids and alkyl esters have been synthesized by the condensation of 2-chloro-3-formyl quinolines with thioglycolic acid/alkyl esters under microwave irradiation using anhydrous potassium carbonate which shoved antibacterial

activity.[42] and TCTA-DMF (2, 4, 6-trichloro-1, 3, 5-triazine / N, N'-dimethyl formamide) adduct has been used as a Vilsmeier - Haack type reagent.[43] as shown in scheme 13.



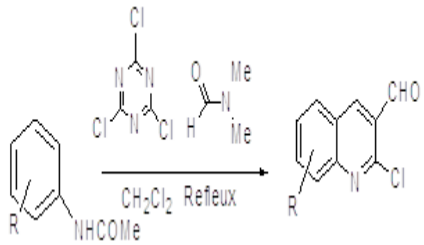
Scheme 13: Synthesis Thieno [2,3-b]quinoline-2-carboxylic acids and alkyl esters.

Gaurav G. found the way of one-pot three-component synthesis of 2- (piperidin-1-yl) quinoline based 1,2,4-triazolo[1,5-a]quinoline derivatives. This has been described by the reaction of aldehyde ethyl 2-cyanoacetate and enaminones.[44] as shown in scheme 14.



Scheme 14: Synthesis of 1,2,4-triazolo[1,5-a]quinoline derivatives.

P. Venkanna studied the catalyst activity of TCTA-DMF(2, 4, 6-trichloro-1, 3, 5-triazine / N, N'-dimethylformamide)[45]adduct as an efficient and modified form of Vilsmeier-Haack reagent for good synthesis of 2-chloro-3-formyl quinolines from starting material as acetanilides. TCTA (2, 4, 6-trichloro-1, 3, 5-triazine) used for the preparation of V-H reagent shown in scheme-15.

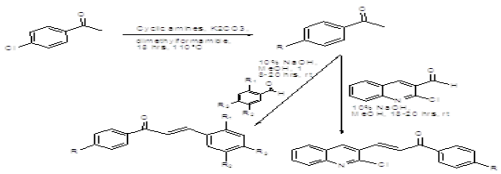


Scheme-15: Synthesis of 2-chloro-3-formyl quinolines.

The thione nucleus formed from 2-chloroquinoline-3-carbaldehyde using sodium sulphide in DMF followed by reaction with various substituted amines to give the corresponding Schiff

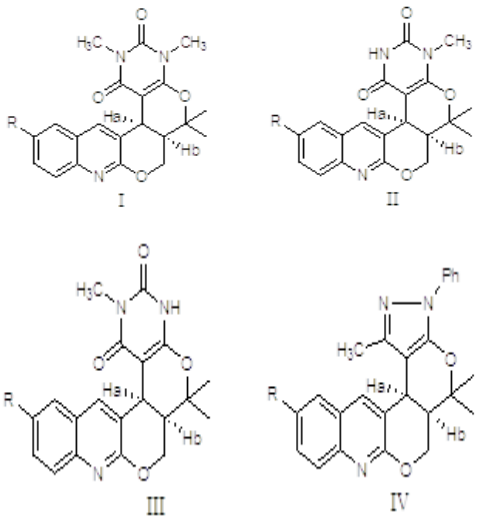
base intermediates. Attempt has been made to derive final azetidinone and thiazolidinone analogues from Schiff bases by using chloroacetyl chloride and 2-mercapto aceticacid.

Neetu Tomar et al gave synthesis of chalcone derivatives via Claisen-Schmidt condensation.[46] method and they were investigated these compounds for in-vitro antiplasmodial activity against P. falciparum isolate. The reaction mechanism as shown in scheme-16.



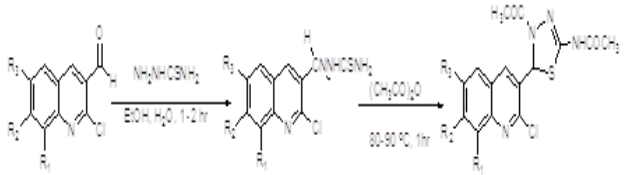
Scheme-16: Chalcone derivatives of 2-chloroquinoline-3-carbaldehyde

Annelated quinoline and its derivatives were studied by Biswajita Baruah and Pulak J. Bhuyan they explore the various synthesis and screening for biological activities.[47] shown in scheme 17. These heterocycles have the following structures.



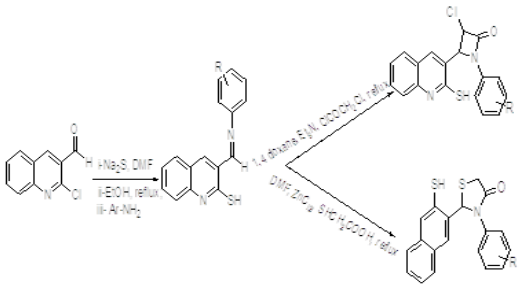
Scheme-17: Various annelated quinoline structures

Sheetal B *et al* synthesized derivatives and studied pharmacological properties of quinoline derivatives[48a] which has 1,3,4-thiadiazole substitution which is shown in scheme 18.



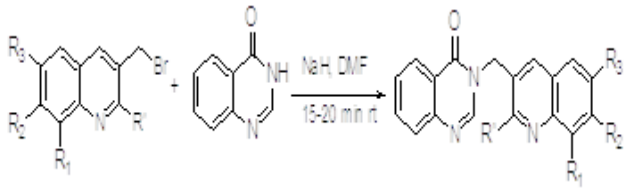
Scheme-18: Synthetic pathway of N-[4-acetyl-5-(6,7,8-substituted-2-chloroquinolin-3-yl)-4,5 dihydro-1,3,4- thiadiazol-2-yl]-acetamides.

Bhupendra M. Mistry gave a novel structures of quinoline-based azetidinone and thiazolidinone [48b]. The thione nucleus made from 2-chloroquinoline-3-carbaldehyde and sodium sulphide as catalyst in DMF solvent with various substituted amine, leads to corresponding Schiff base intermediates as shown in Scheme-19.



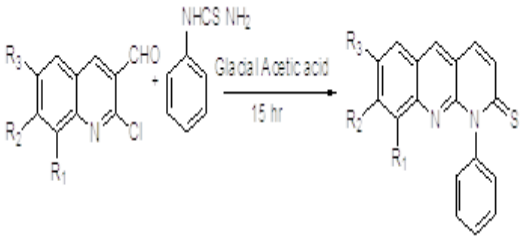
Scheme-19: Structures of quinoline-based azetidinone and thiazolidinone

Priyanka G. Mandhane et al studied various quinazolinone derivatives which were synthesized via 3-(bromomethyl)-2-chloroquinoline or via 2-(ptolyloxy)-(bromomethyl)quinoline that are made from reducing 2-chloroquinoline-3-carbaldehyde or via 2- (p-tolyloxy)quinoline-3-carbaldehyde catalyzed by $NaBH_4$ and methanol yielding (2-chloroquinolin- 3yl)methanol or (2-(p-tolyloxy)quinolin-3yl)methanol as shown in Scheme-20.



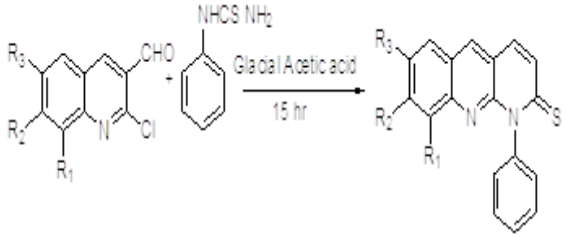
Scheme-20: Synthesis of3-((2-(p-tolyloxy)quinolin-3-yl)methyl)quinazolin-4(3H)-one.

T. Suresh and it's coworkers studied one-step synthesis of substituted pyrimido[4,5-b]quinolines condensation between 2-chloro-3-formyl quinolines and N-phenyl thiourea.[49] as shown in scheme-21.



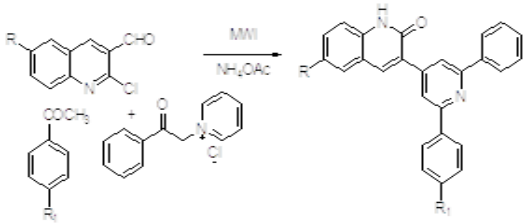
Scheme -21: Synthesis of Pyrimido[4,5-b]quinolines.

Sandhya Bawa and Suresh Kumar have made series of schiff's bases such as 4-substitued-imino-methytetrazolo[1,5-a] quinoline derivatives.[50] These derivatives were synthesized by condensation of 4-formyl-8-methyltetrazolo[1,5-a]quinoline, with selective aromatic amines refluxing in dioxane as shown in scheme-22.



Scheme-22: Synthesis of Schiff's base of 4-substitued-imino-methytetrazolo[1,5-a]quinolone

Niraj K Ladani and its coworkers gave synthesis of Polysubstituted pyridines structures like 3-(2,6-diphenyl-4-pyridyl)hydroqunoline-2-oneunder microwave assistant using 2-choro-3-formyl quinoline, acetophenone, n-phenacylpridinium chloride in presence of ammonium acetate and acetic acid.[51-54]. They have given green method and studied their antimicrobial activities shown in scheme-23.



Scheme-23: Microwave synthesis of 3-(2,6-diphenyl-4-pyridyl)hydroqunoline-2-one

CONCLUSION

Here we have given some latest synthetic methods of synthesis of quinolines. Which includes aldol condensation, organocatalytical reactions, microwave assisted reactions some methods includes ferrite nanoparticals catalyzed reactions which have green chemistry concept, these are environmental being reactions for the synthesis of substituted quinolines and their analogues like oximes, esters, Quinolizine, Indolizine, Pyrido-1,4- oxazine-fused complex quinoline, coumarin, 1,2,4-triazoles and hydroqunoline. Literature survey reveals the importance and utilization of these derivatives as, corrosion inhibitor, pharmaceutical agents, antimicrobial agents and in many fields of organic synthesis.

ACKNOWLEDGEMENTS

We acknowledge Head, Department of Chemistry and The Principal JET's Z.B. Patil College, Dhule for providing the lab facilities and their constant encouragement.

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