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Review Article

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A Review on Quinoline: Diverse Pharmacological Agent

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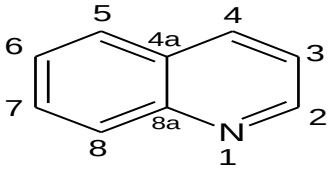
Abstract Quinoline is a heterocyclic aromatic organic & fused ring compound with the Chemical formula C_9H_7N. Quinoline is an important pharmacophore in medicinal chemistry, since a large number of its derivatives possess useful biological properties. Also, Quinolones are known for their formation of conjugated molecules and polymers that combine enhanced electronic, optoelectronic, or nonlinear optical properties with excellent mechanical properties. They have a crucial role in the synthesis of various new therapeutic agents. For new drug development, quinoline and its derivatives constitute a significance role play. Different synthetic procedure has been emphasized by the researchers for the synthesis of quinoline derivatives. This review focuses on detailed work done so far on the quinoline and its derivatives in the search of new therapeutic agents. The review covers the general methods for synthesis as well as biological activities of quinoline derivatives such as antimalarial, anticancer, antibacterial, antihelmintic, antiviral, antiprotozoal, antifungal, anti-inflammatory, analgesic, cardiovascular, reproductive, antiplasmodium, antidermatophytic.

Keywords Quinoline, Synthesis, Biological activity

1. Introduction

Quinoline is a heterocyclic aromatic organic & fused ring compound with the Chemical formula C_9H_7N. Quinine was extracted from the Cinchona trees bark as an active ingredient in 1820 and consecutively follow the crude bark for the treatment of malaria. Benzo pyridine is a nitrogen-containing heterocyclic compound that was first isolated from coal tar, in 1834 by Friedlieb Ferdinand Runge. In poison cracking, catalysts quinoline is used and catalysts for hydrogenation acetylenes [4]. Quinoline itself has useful applications, most of the industrial organic compounds are synthesized starting from quinolone, for instance 8-hydroxyquinoline as the chelating agent used in organic light-emitting diodes, and quinolinic acid as the biosynthetic precursor of niacin. Naturally, occurring quinoline is liberated from the thoracic glands of Oreophoetes Peruana, take part in the function of chemically protecting against spiders, cockroaches, ants, and frog exit as a degeneracy product from quinine, strychnine, and cinchonine. As it was extracted from quinine, so it is called quinoline.



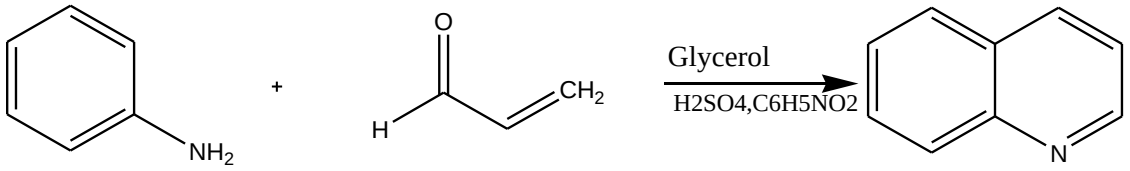
Structures of Quinoline

Quinoline is a very crucial pharmacophore in medicinal chemistry since quinoline moiety is widely used for the synthesis of many synthetic compounds with various pharmacological properties. Quinoline has been contain antimalarial, anticancer, antibacterial, anticonvulsant, cardiotonic, antifungal, antihelmintic, anti-inflammatory and analgesic, anti-dermatophytic, antiplasmodium agents.

2. Synthesis

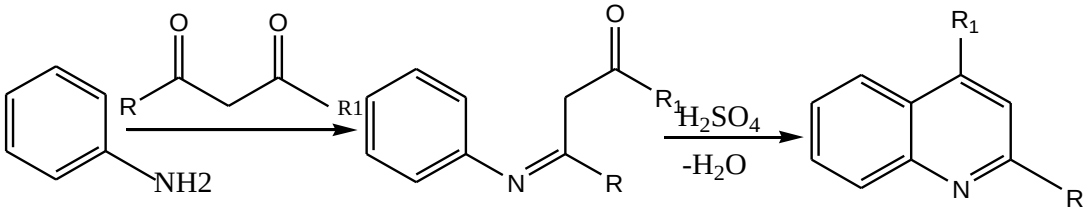
Skraup Synthesis

Zdenko Hans Skraup synthesized quinoline by mixing and gently heating Aniline, glycerol, nitrobenzene, iron (II) sulphate and sulphuric acid. The reaction starts with vigorous exotherm and completed by further heating after removal of residual nitrobenzene via steam-distillation. Quinoline is separated by basification of reaction mixture. The reaction involves dehydration of glycerol to propenal, further acid-catalysed cyclisation and dehydrogenation by nitrobenzene [6].



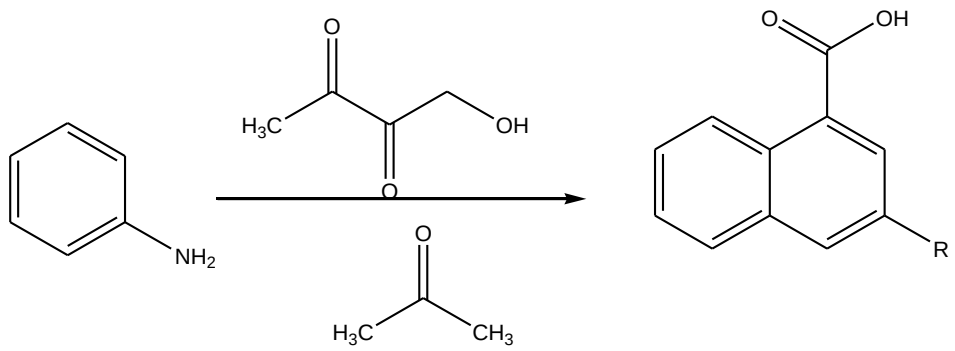
Combe's quinoline Synthesis

Combes first revealed this quinoline synthesis in 1988. It includes condensing an arylamine with β-diketones (1,3-dicarbonyl compounds) to provide substituted quinolines through an acid-catalyzed ring closure reaction. The synthesis guarantees to form a desired regioisomer as the product [7].



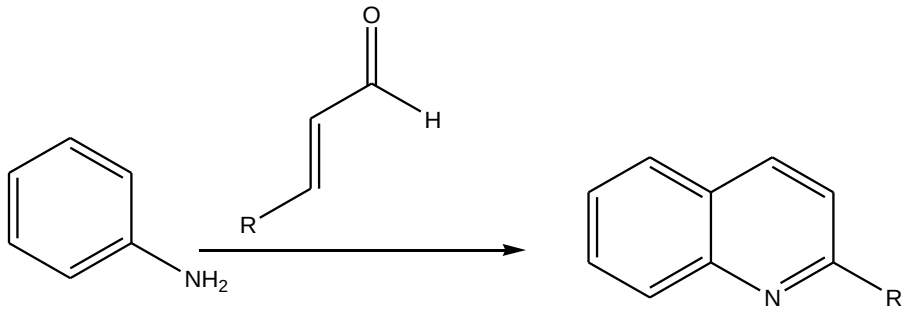
Doebner Reaction

Aniline when reacted with an aldehyde first forms the Schiff base further succeeding reaction with pyruvic acid (enol form) yield quinoline 4-carboxylicacids.



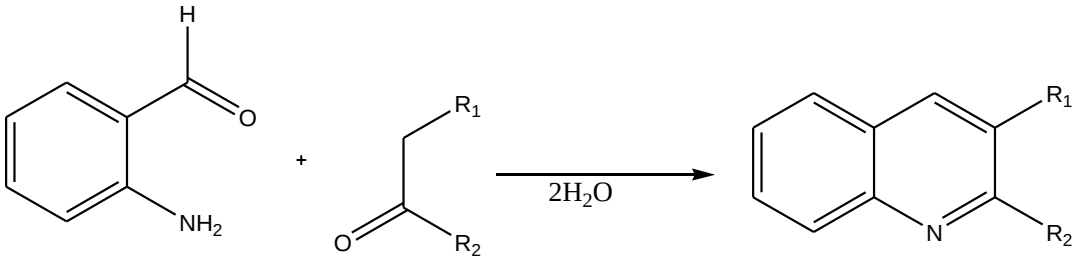
Doebner-Miller Synthesis

This synthesis involves formation of quinoines by aniline and α,β-unsaturated carbonyls, discovered by the Germans chemist Oscar Doebner and Wilhelm Miller. The reaction uses α,β-unsaturated carbonyls which provide alkyl and aryl substituents in the pyridine ring of quinoline. An intermediate β-aminocarbonyl compound is forms which then it will be subsequently cyclised under a variety of conditions to form quinoline.



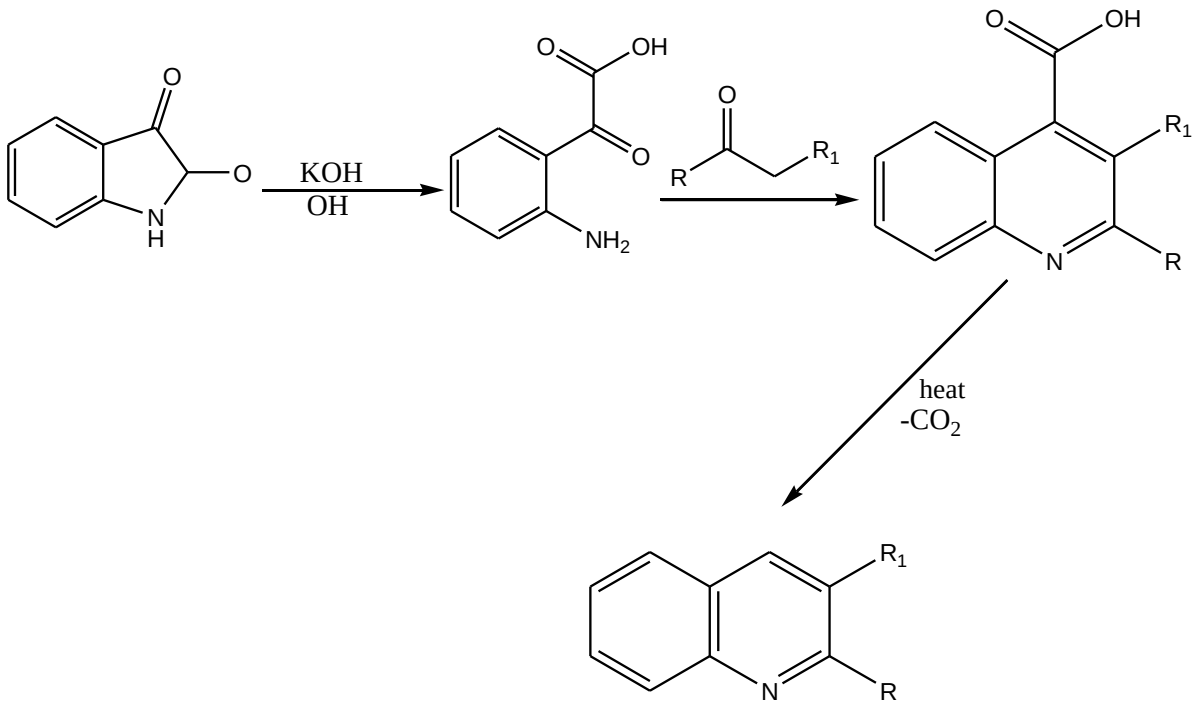
Friedlander Synthesis

This synthesis was given by German chemist Paul Friedlander (1857–1923), the synthesis involves the reaction of *o*-aminobenzaldehyde with a carbonyl compound in an alkaline medium to gives imine by dehydrative cyclization.



Pfitzinger Synthesis

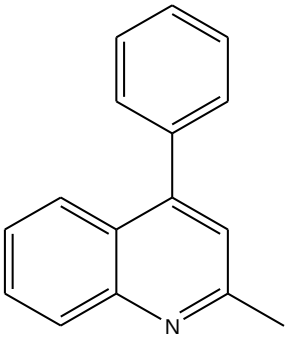
This synthesis is the modification of Friedlaender's quinoline synthesis and it employs isatin on the place of *o*-aminobenzaldehyde. The reaction is named after Wilhelm Pfitzinger and involves synthesis of substituted quinoline-4-carboxylic acids with isatin, base and carboxyl group. Thermally the carbonyl compound removed thereafter.[8]



3. Biological Activity

Anti-dermatophytic

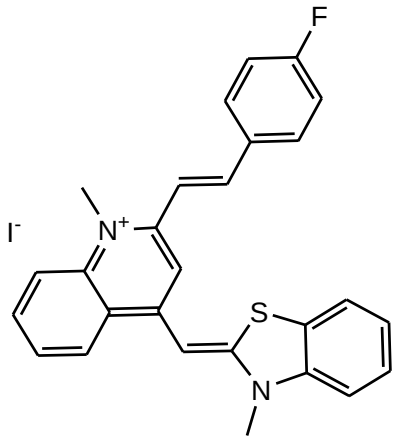
Machado Monte Rosa Gabriella da. *et al.* (2020) synthesized a series of substituted 2 methyl- 4 –phenyl quinoline derivative by skaraup & Doebner-von Miller. It is performed by reacting the aniline with the α,β-unsaturated ketone. At C-4 position on 4- phenyl quinoline contain phenyl substituent, it is responsible to the action of anti-dermatophytic. It found that 2- methyl quinoline & 2- methyl 4- ethyl quinoline show anti-Candida action. G.D.R.M Machado found that quinoline derivative like 2 methyl-4 phenyl quinoline represented as potential toxicological profile act as strong candidate for new efficiency & saver compound for dermatophytosis. [9]



Anti-bacterial activity

Liua Hua Zhi*et al.* (2018) production a new quinolinumderivatives, a styryl substituent at the orthoposition of 1-methylquinolinium and their in vitro antibacterial activities were examined thoroughly. Resulting that quinolinum derivatives shows own important antibacterial activity opposing tested pathogens includes the drug-resistant strains of MRSA, VRE, and NDM-1 E. coli.2-((E)-4-fluorostyryl)-1-methyl-4-((E)-(3-methylbenzo[d]thiazol2(3H)-ylidene)methyl)quinolin-1-ium iodide shows a excellent antibacterial activity and methicillin and vancomycin are found higher than its MICs to the drug-resistant strains. Quinolinium derivatives can obstruct the GTPase activity

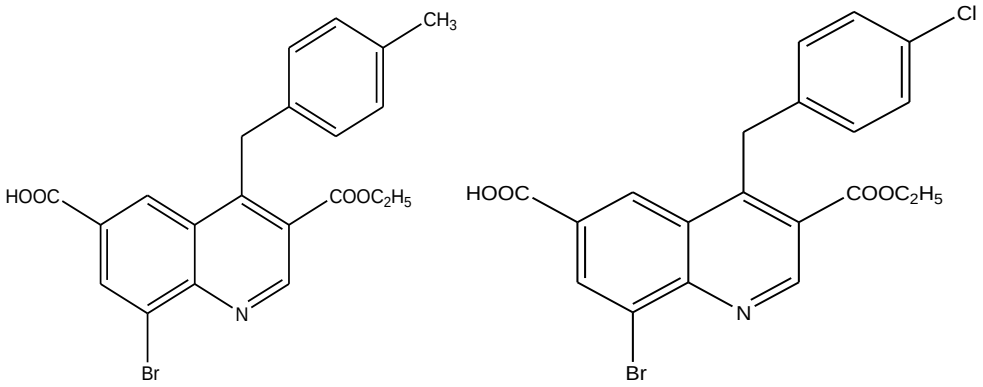
and dynamic assembly of FtsZ, and hence bacterial cell division retard and bacterial cell death. Further evaluation of these compound for the development of new antibacterial agents targeting FtsZ [11].



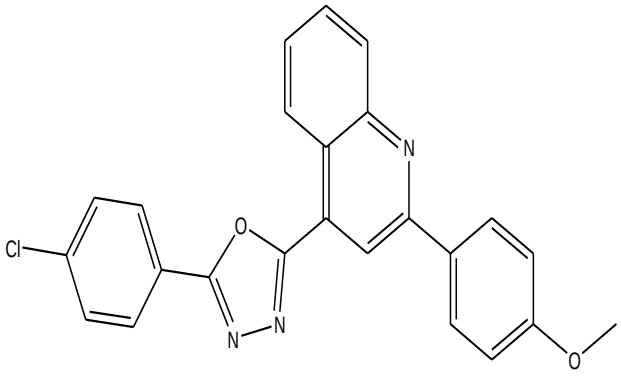
2-((E)-4-fluorostyryl)-1-methyl-4-((E)-(3-methylbenzo[d]thiazol2(3H)-ylidene)methyl)quinolin-1-ium iodide

Anticancer activity

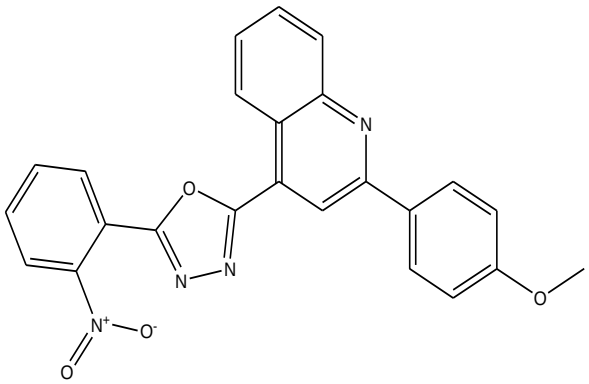
Abdellatif K.R.A. *et al.* (2017) synthesize novel series of 4-(4-substituted-anilino)quinoline derivative from amine derivatives via Gould–Jacobs reaction and evaluated for their cytotoxic activity against two human cancer cell lines viz. breast carcinoma (MCF-7) and non-small cell lung cancer (A549) which were maintained in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum, penicillin/ streptomycin. The literature revealed that compounds **2a** and **2b** have greater potency for non-small cell lung cancer cell line (A549) than breast carcinoma (MCF-7) and may exhibit their cytotoxicity in a similar manner to erlotinib [12].



Dofe S. Vidya *et al.* (2017) produce a series of quinoline-based oxadiazole derivatives and evaluated their *in vitro* cytotoxic effectiveness against human breast cancer MCF-7 cell line. 4-(5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl)-2-(4-methoxyphenyl)quinoline,2-(4-Methoxyphenyl)-4-(5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl)quinoline and 4-(4-Acetyl-4,5-dihydro-5-(2-(4-methoxyphenyl)quinolin-4-yl)-1,3,4-oxadiazol-2-yl)- 2-methoxyphenyl acetate showed excellent activity and retard the growth of breast cancer cell MCF-7 with 50% inhibitory concentration (IC_{50}) of 8.31, 9.81, and 9.96 lM, respectively. Apoptosis evaluated by using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) also indicate that this compound cause cell death by apoptosis [13].



. 4-(5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl)-2-(4-methoxyphenyl)quinoline

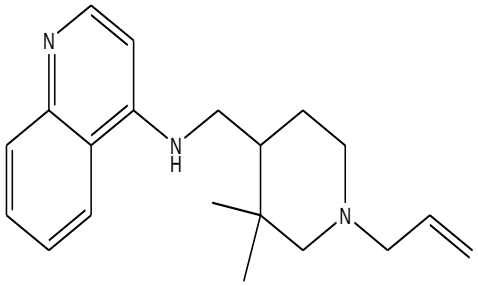


2-(4-Methoxyphenyl)-4-(5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl)quinoline

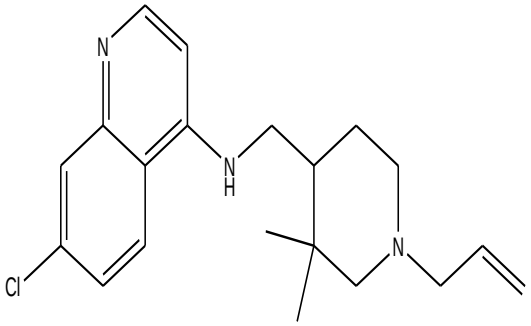
Hamdy Rania *et al.* (2019) Bcl-2 inhibitory aromatic heterocycles are inhibition with Bcl-2–Bim peptide binding and demonstrate potential anti-proliferative activity against Bcl-2 expressing human cancer cell lines. Target compounds were synthesized by aryl-substituted quinoline-4-carbonyl-N-arylhydrazine-1-carbothioamide intermediate, through simple dissimilarity of the basic cyclisation conditions. Quinoline-based oxadiazole analogues were found to display sub-micromolar anti-proliferative activity in Bcl-2-expressing cancer cell lines, Bcl2-Bim peptide ELISA assay found sub-micromolar IC_{50} activity. The Bcl-2 targeted anticancer activity was further justify via computational molecular modeling [14].

Antiplasmodium agents

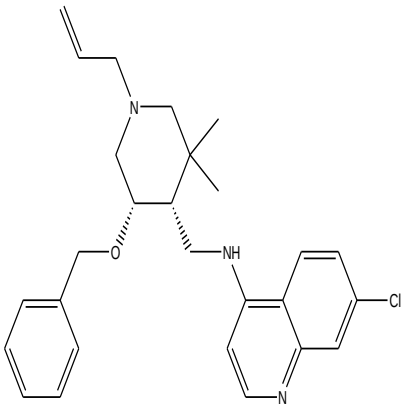
Walle de Van Tim *et al.* (2020) Piperidine moieties like a bicyclic 1-azabicyclo heptane and a 4-substituted monocyclic piperidine, were combined with different quinoline cores by an addition-elimination reaction or a reductive amination method , provide a total four different series of quinoline piperidines. Antiplasmodium action assay against a CQ-sensitive (NF54) and a CQ-resistant (K1) strain of P. falciparum disclose a propitious activity for almost all compounds. Five novel analogues belonging to the class of 4-aminoquinoline-piperidines (7-chloro-N-[(4-phenyl-1-azabicyclo[2.2.1]heptan-2-yl)methyl]quinolin-4-amine, N-[(4-Phenyl-1-azabicyclo[2.2.1]heptan-2-yl)methyl]quinolin-4-amine, N-[(cis-1-Allyl-5-benzyloxy-3,3-dimethylpiperidin-4-yl)methyl]-7-chloroquinolin-4-amine, N-[(1-Allyl-3,3-dimethylpiperidin-4-yl)methyl]-7-chloroquinolin-4-amine, N-[(1-Allyl-3,3-dimethylpiperidin-4-yl)methyl]quinolin-4-amine denote superior *in vitro* antiplasmodium activity.[15]



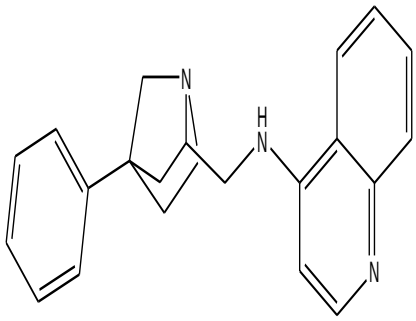
N-[(1-Allyl-3,3-dimethylpiperidin-4-yl)methyl]quinolin-4-amine



N-[(1-Allyl-3,3- dimethylpiperidin-4-yl)methyl]-7- chloroquinolin-4-amine



N-[(cis-1-Allyl-5-benzyloxy-3,3-dimethylpiperidin-4-yl)methyl]-7-chloroquinolin-4-amine

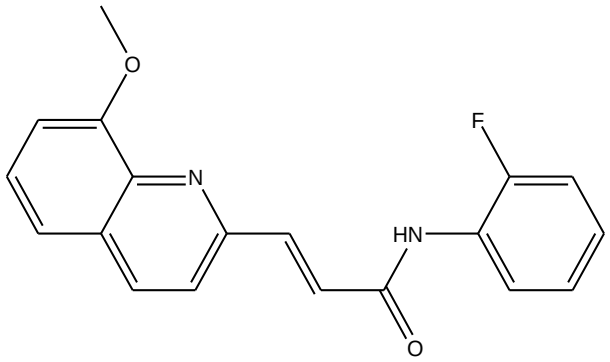


N-[(4-Phenyl-1-azabicyclo[2.2.1]heptan-2-yl)methyl]quinolin-4-amine

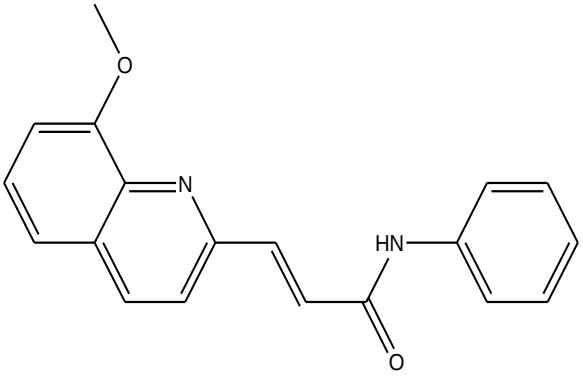
AntiHIV-1 agents

Shahapurv*iet al.* (2018) Quinolines such as 2-styrylquinolines and 8-hydroxyquinolines are considerably evaluated, found to be act through HIV-1 integrase enzyme inhibition for their anti-HIV-1 activity. Thirty-one quinoline derivatives with distinct linkers to ancillary phenyl ring were produce and analyzed by using TZM-bl assay for in vitro anti-HIV-1 activity. N-(2-fluorophenyl)-3-(8-methoxyquinolin-2-yl)acrylamide exhibit higher activity in TZM-bl cell line against HIV-1VB59 and HIV-1UG070 cell correlated virus (IC50 3.35 ± 0.87 and 2.57 ± 0.71 μM) as refer to other derivatives. N-(2-fluorophenyl)-3-(8-methoxyquinolin-2-yl)acrylamide compound to be test against against HIV1VB51 in activated peripheral blood mononuclear cells (PBMCs), resulting that their activity to be confirmed.

N-phenyl-3-(8-methoxyquinolin-2-yl)acrylamide, N-(2-fluorophenyl)-3-(8-methoxyquinolin-2-yl)acrylamide, 2-(8-Methoxyquinolin-2-yl)-5-(4-methoxyphenyl)-1,3,4- oxadiazole compounds were exhibit highest TI values against both the HIV-1 strains [16].



(E)-N-(2-fluorophenyl)-3-(8-methoxyquinolin-2-yl)acrylamide

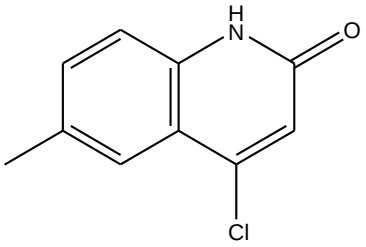


(E)-N-phenyl-3-(8-methoxyquinolin-2-yl)acrylamide

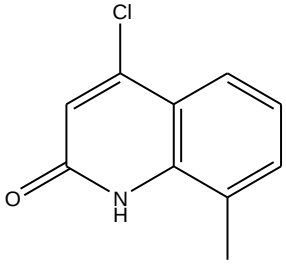
Antifungal activities

Murugavel.S.*et al.* (2018) Novel compound 4-chloro-6- methylquinoline-2(1H)-one (4C6MQ) and its isomer 4-chloro-8-methylquinoline-2(1H)-one (4C8MQ) have been assay by means of experimental and computational quantum chemical process like density functional theory (DFT). These two isomer compounds are characterized spectroscopically by FTIR, FT-Raman, UV-Vis, and NMR spectrum and comparison with DFT results. By using DFT/B3LYP method with the 6-311G++(d,p) basis sets the geometries of the isomer compounds have been optimized. After that geometric parameter (bond lengths, bond angles, and torsion angles); vibrational analysis; chemical shifts; and electronic absorption of the isomer compounds have been computed and comparison with the practical result. The *in silico* (absorption, distribution, metabolism, excretion and toxicity) studies were examined to

identify the potential drug likeliness of the isomer compounds. Inhibitory activity of isomer compounds against DNA gyrase and lanosterol 14 α-demethylase enzyme by molecular docking are evaluated, these isomer compounds were screened for their antibacterial and antifungal activities [17].

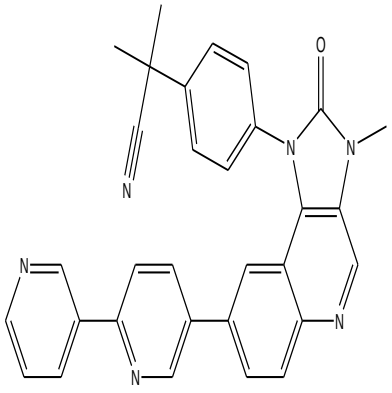


4-chloro-6- methylquinoline-2(1H)-one

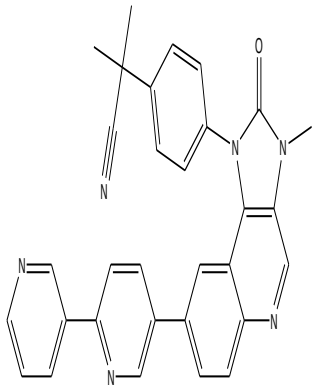


4-chloro-8-methylquinoline-2(1H)-one

Yanjie LI *et al.* (2017) a series of imidazo[4,5-c]quinoline derivatives were synthesized via various step. As starting material 2-amino-5-bromobenzoicacid, 4-nitrophenylacetonitrile and 6-bromo-4-chloro-3-nitroquinoline as intermediate and Suzuki reaction occurs. Imidazolinone ring with triphosgene as the keystep.2-(4-(8-([2,3'-Bipyridin]-5-yl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]quinolin-1-yl)phenyl)-2-methylpropanenitrile and2-Methyl-2-(4-(3-methyl-2-oxo-8-(6-phenylpyridinyl-3-yl)-2,3-dihydro-1H-imidazo[4,5-c]quinolin-1yl)phenyl) propane nitrile compounds are display dual PI3Kα/mTOR inhibition, both supply good starting points to explore the probability of developing dual PI3K/mTOR inhibitors [18].

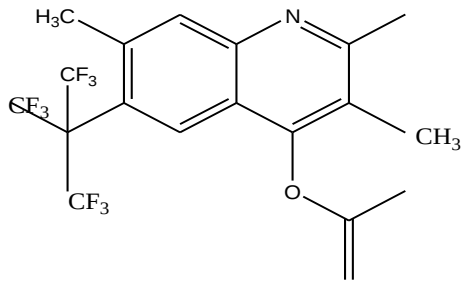


2-(4-(8-([2,3'-Bipyridin]-5-yl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]quinolin-1-yl)phenyl)-2-methylpropanenitrile



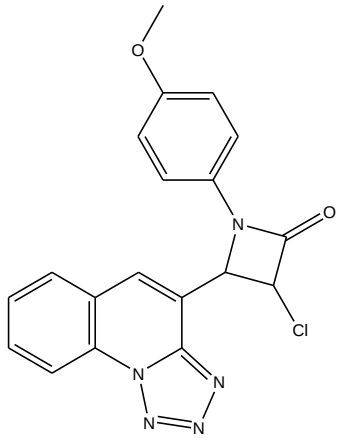
2-(4-(8-([2,3'-Bipyridin]-5-yl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]quinolin-1-yl)phenyl)-2-methylpropanenitrile

Zai Zhang Minhua Liu *et al*. (2019) synthesized a series of perfluoropropan 2-yl based novel quinoline derivative as fungicidal activities against Erysiphe graminis. Tetrahydrofuran-3-yl (2,3,8-trimethyl-6-(perfluoropropan-2-yl)quinolin-4-yl) Carbonate is found high potential fungicidal activity. This compound has 50% maximal effect values (EC_{50}) 1.48mg/L against Erysiphe graminis. This compound is most excellent than the tebufloquin [19].



Tetrahydrofuran-3-yl (2,3,8-trimethyl-6-(perfluoropropan-2-yl)quinolin-4-yl)

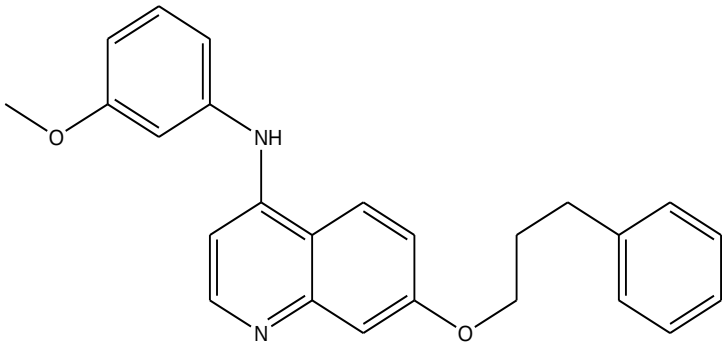
Gupta S.K. *et al.* (2016) synthesized a series of 3-chloro-1-(substituted)-4-(tetrazolo[1,5-a]quinolin-4-yl) azetidine-2-one derivatives. It was synthesized via various steps. First of all, acetanilide reacting with the Vilsmeier-Hack reagent to produce 2-chloro-3-formyl quinoline. After that, it reacts with p-toluene sulphonic acid and sodium azide which give Tetrazolo [1,5-1] quinoline-4-carbaldehyde. Various substituted amines reaction with formyl group formed Schiff base intermediates. These intermediates are further reaction with chloroacetyl chloride to produce 3-chloro-1-(substituted)-4-(tetrazolo[1,5-a]quinolin-4-yl) azetidine-2-one derivatives. By using the carrageenan-induced rat paw model and Eddy's hot plate method corresponding, synthesized compounds were screened for anti-inflammatory and analgesic activities. 3-chloro-1-(4-methoxy-phenyl)-4-(tetrazolo[1,5-a]quinoline-4-yl)azetidine-2-one compound found to potential anti-inflammatory and analgesic activities [20].



3-chloro-1-(4-methoxy-phenyl)-4-(tetrazolo[1,5-a]quinoline-4-yl)azetidine-2-one

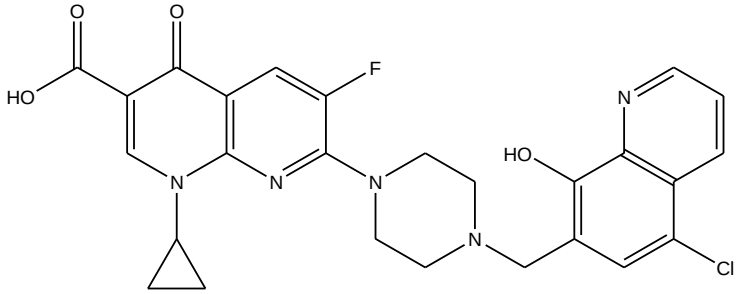
Antitumor Drug

Chang Z.J. *et al.* (2019) synthesized a series of new quinolines that carry an alkoxy group in position-7 and 4-aniline substituent in position-4 of quinoline ring. Compounds N-(3-fluorophenyl)-7-(octyloxy)quinolin-4-amine,7-(benzyloxy)-N-(3-nitrophenyl)quinoline-4-amine,7-((4-fluorobenzyl)oxy)-N-(3-nitrophenyl)quinoline-4-amine and ((7-(3-Phenylpropoxy)quinoline-4-yl)amino)phenyl nitrate were found to broad-spectrum antiproliferative activity . These compounds were values of IC_{50} lower than 10 mM against seven human tumor cell lines. Among these compounds, N-(3-methoxyphenyl)-7-(3-phenylpropoxy)quinolin-4-amine compound established most potential antiproliferative agents against HCT-116, RKO, A2780, and Hela cell lines with IC_{50} values of 2.56, 3.67, 3.46, and 2.71 mM. N-(3-methoxyphenyl)-7-(3-phenylpropoxy)quinoline-4- amine compound inhibited tumor growth and decreased tumor weight in animal models (mice). The mode of action of this compound inhibits colorectal cancer growth through the ATG5-dependent autophagy pathway. Resulting this quinoline derivative was found the potential to be developed as a new antitumor drug [21].



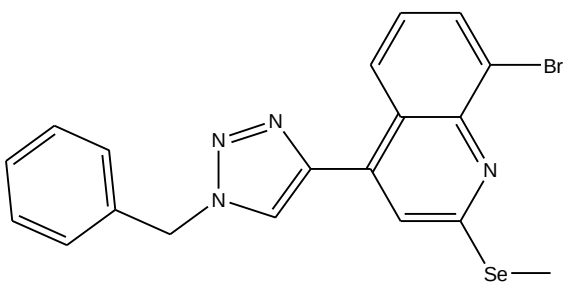
N-(3-methoxyphenyl)-7-(3-phenylpropoxy)quinolin-4- amine

Fu Hai-Gen *et al.* (2019) synthesized nineteen new quinoline derivatives via the Mannich reaction. Their antibacterial activities evaluation against both Gram-positive (G+) and Gram-negative (G−) bacteria.
7-{4-[(5-Chloro-8-hydroxyquinolin-7-yl)methyl]piperazin-1-yl}-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid compound employed potent effect against G+ and G− strains with MIC values of 0.125–8 μg/mL. By molecular-docking study that compound might target both bacterial LptA and Top IV proteins, thereby exhibit a broad-spectrum antibacterial effect.[22]

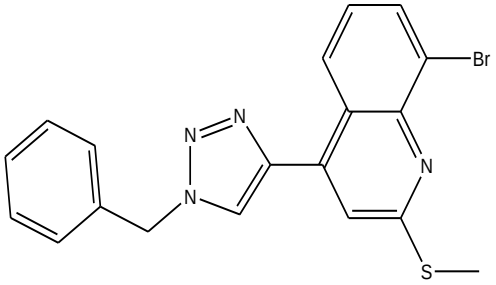


7-{4-[(5-Chloro-8-hydroxyquinolin-7-yl)methyl]piperazin-1-yl}-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid

Krzysztof M. *et al.* (2017) synthesized methylthio- or methylselenoquinolyl-linked 1,4-disubstituted 1,2,3-triazole conjugates from the halogenopropargylthio- or halogenopropargyl seleno-quinolines by one-pot click reaction. These compounds were inhibiting the proliferation of the C-32, T-47D, and SNB-19 cell line. It was determined by using the WST-1 assay. Modified derivatives of quinolyl-triazoles, their cytotoxic properties were compared to cisplatin. 1-benzyl-4-[methylseleno-(6-chloro-4-quinolyl)]-1H-1,2,3-triazole and 1-benzyl-4-[methylseleno- (8-bromo-4-quinolyl)]-1H-1,2,3-triazole compounds were exhibit consequential activity on the C-32 and SNB-19 cell lines [23].

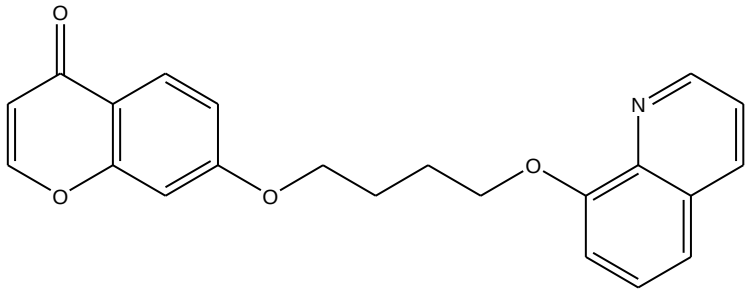


1-Benzyl-4-[methylseleno-(8-bromo-4-quinolyl)]-1H-1,2,3-triazole

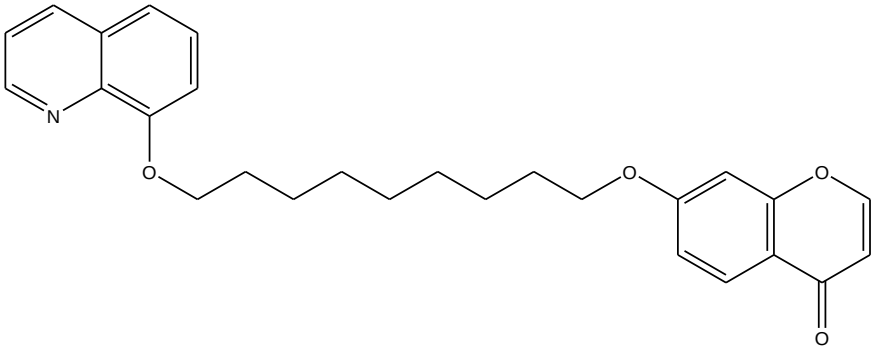


1-Benzyl-4-[methylthio-(8-bromo-4-quinolyl)]-1H-1,2,3-triazole (2e)

Juan C.C. *et al.* (2017) synthesized and leishmanicidal, trypanocidal and cytotoxic activities of quinoline-chalcone and quinoline-chromone hybrid. The most active compounds are 7-[4-(quinolin-8-yloxy)butoxy]-4H-chromen-4-one and 7-{[9-(quinolin-8-yloxy)nonyl]oxy}-4H-chromen-4-one are both Leishmania (V) panamensis and Trypanosoma cruzi with EC_{50} of 6.11 ± 0.26 μg mL−1 (16.91 μM) and 4.09 ± 0.24 (11.32 μM), respectively. These compounds are exhibit higher activity than benznidazole, the current anti-trypanosomal drug. These compounds express toxicity for mammalian U-937 cells, they regard as antileishmanial or trypanocydal drug development [24].



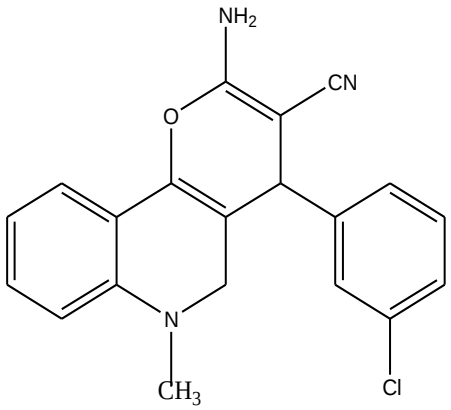
7-[4-(quinolin-8-yloxy)butoxy]-4H-chromen-4-one



7-{[9-(quinolin-8-yloxy)nonyl]oxy}-4H-chromen-4-one

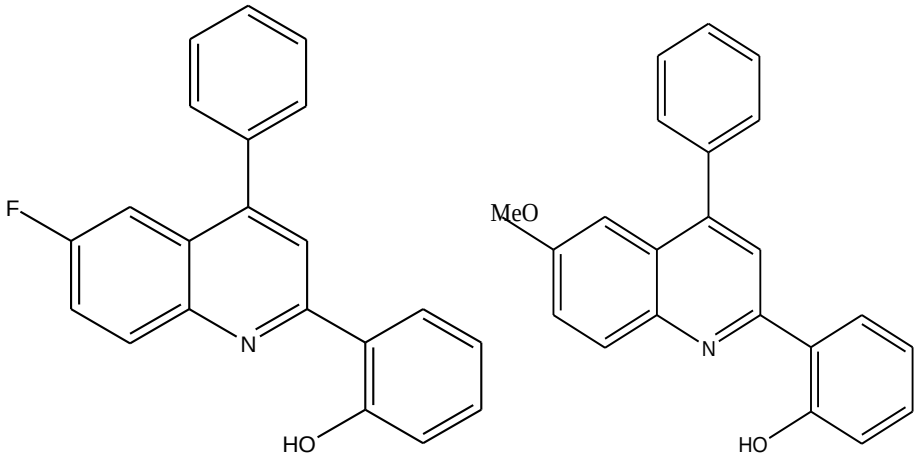
Anti-inflammatory activity

Upadhyay K.D. *et al.* (2018), synthesized a series of pyrano[3,2-c]quinoline based structural analogues It was prepared by reaction between 2,4-dihydroxy-1-methylquinoline, malononitrile, and un(substituted) aromatic aldehydes. By the structure−activity relationship was studied that if 3-substitution on the aryl ring at C4 position of the pyrano[3,2-c]quinolone structural was significant position for both TNF-α and IL-6 inhibition and anticancer activity. Synthesized compound to inhibit TNF-α production in the human peripheral blood mononuclear cells (hPBMC) assay. Structural variety with electron withdrawing, electron donating, sterically hindered, and heteroaryl substitution sincerely affected both the inflammation and cancer activity. The screening results revealed that compounds 4c, 4f, 4i, and 4j were found as most active candidates of the series against both anti-inflammatory and anticancer activity [25].

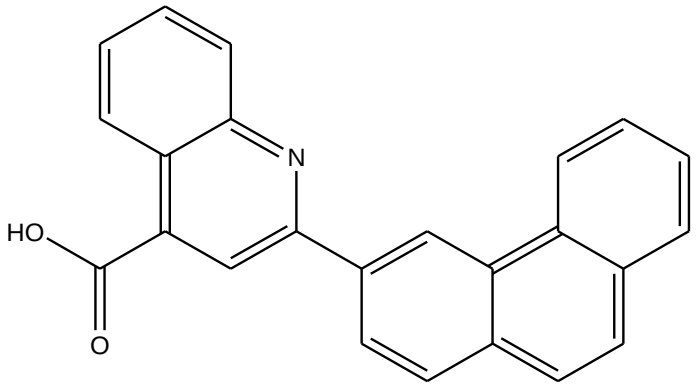


Manikandan A. *et al.* (2017) a new series of analgesic and anti-inflammatory agents was reported by which are gaining lots of attraction because of their importance in management of acute pain and inflammation as well as their utility in early phases of many serious disorders like Alzheimer's dementia, cancer, heart vascular disease etc. In literature 2-(4-phenylquinoline-2-yl)phenol derivatives are reported to possess interesting profile of analgesic and

anti-inflammatory activity with COX-2 enzyme inhibition and antipyretic potentials. The reported compounds **$3a_1$** (IC_{50} 0.026 lM) and **$3b_1$** (IC_{50} 0.102 lM) were found as most potent COX-2 inhibitors [26].



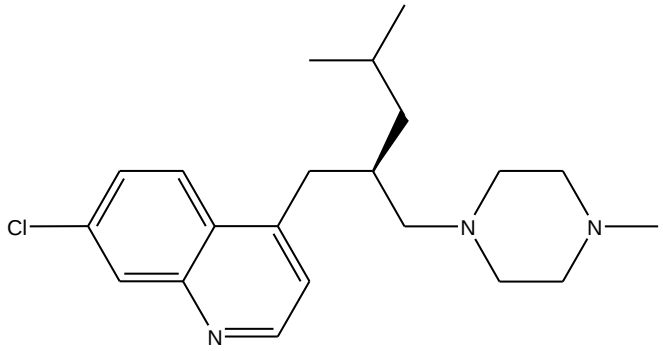
Muscia C. Gisela *et al.* (2018) Under microwave irradiation by use of Beyer and Friedlander methods, reaction times are too short and yield result very good. To prepare 2,4-di-arylquinolines, homogeneous and heterogeneous acid catalysts were used and compare the use of catalyst then trifluoroacetic acid (TFA) reached the higher yields. The synthesis of a series of polycyclic analogous led to six new active compounds and a Quantitative Structure Activity Relationship study (QSAR) study was estimated. All the synthesized compounds were examined *in vitro* against M. tuberculosis (Mtb) H37Rv. 2-(phenanthren-3-yl)quinoline-4-carboxylic acid 14 compound had a higher potential inhibition against the ofloxacin resistant strain (OFX-R), lacked of bactericidal activity, was not active under low oxygen conditions and exhibited percentages of viability comparable to rifampicin at low and mid concentrations, so it was not toxic to macrophages. Considering the established minimal structural requirements supported by theoretical calculations, it is worthy to note that the introduction of a sulfonamide moiety at C6 of the quinoline ring in future series could improve the anti-TB activity and diminish the cytotoxicity [27].



2-(phenanthren-3-yl)quinoline-4-carboxylic acid

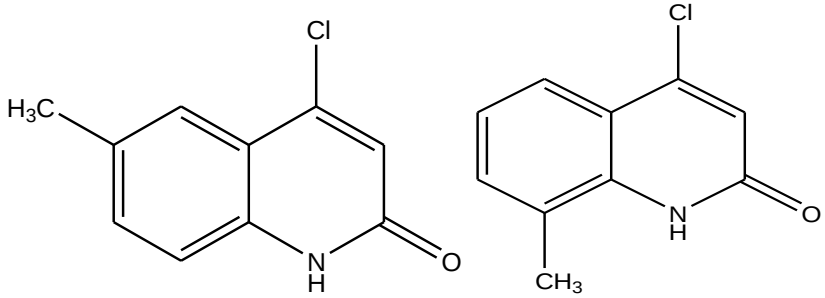
Antimalarial activity

Dola V.R. *et al.* (2017) reported to synthesize a 4-aminoquinoline derivative series exhibiting curative activity against chloroquine-resistant malaria parasites as blood schizonticidal agent. The structures of these compounds have been established by means of IR, proton NMR, Mass spectral analysis and elemental analysis. The reported compound (S)-7-chloro-N-(4-methyl-1-(4-methylpiperazin-1-yl)pentan-2-yl)-quinolin-4-amine **4a** found to be most potent.[28]



Antimicrobial activity

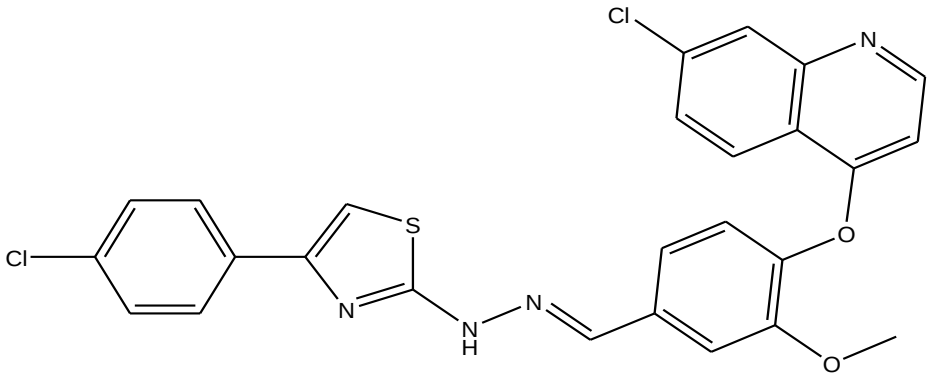
Murugavel S. *et al.* (2018) reported novel isomer quinoline derivatives, 4-chloro-6- methylquinoline-2(1*H*)-one **5a** and its isomer 4-chloro-8-methylquinoline-2(1*H*)-one **5b** and examined it by means of experimental and computational quantum chemical methods like density functional theory and also spectroscopically by FTIR, FT-Raman, UV-Vis, and NMR spectrum. The screening of compounds for antimicrobial activity reported to give excellent performance in treatment of multidrug resistant infections and also shows good docking scores for the isomer ligand protein complexes which reveal the inhibition nature of the isomer compounds against DNA gyrase and lanosterol 14 α-demethylase enzymes [29].



5a 5b

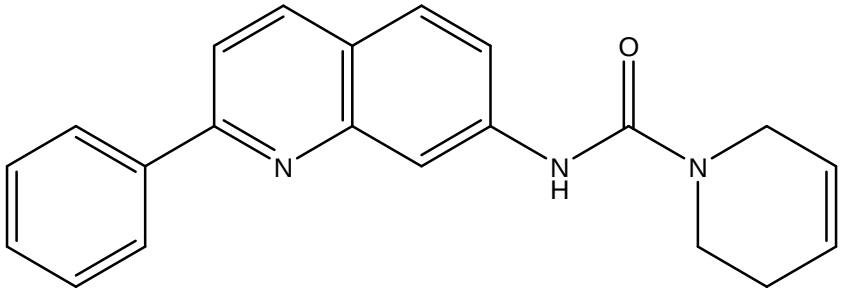
Antitubercular activity

Salve P.S. *et al.* (2018) reported new series of 7-chloro-4-phenoxyquinoline analogs, which is synthesized by synthesizing the intermediate, 4-(7-chloroquinolin-4-yloxy)-3-methoxy benzaldehyde via reaction between 4, 7-dichloroquinoline and 4-hydroxy-3- methoxybenzaldehyde. 4-(7-chloroquinolin-4-yloxy)-3-methoxy benzaldehyde and para- substituted acetophenones were condensed to afford corresponding chalcones. Desired compound was obtained via cyclocondensation of chalcones. The antitubercular activity of reported compounds **6a** against *mycobacterium tuberculosis* H37Rv strain reveals that the compound shows satisfactory result [30].



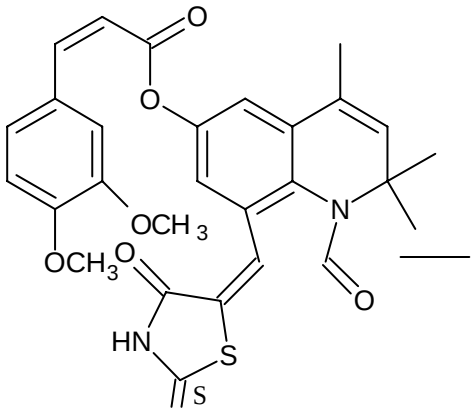
Antiparasitic activity

Nefertiti A.S.G. *et al.* (2018) reported a novel series if trypanocidal agents to develop therapies for human African trypanosomiasis and Chagas disease, caused by *Trypanosoma brucei* and *Trypanosoma cruzi*. The reported quinolone derivative **7a** was found to havemore potency than marketed drug benznidazole [Bz] and were characterized by elemental analysis, IR and ^{1}H NMR spectroscopy [31].



Anticoagulant activity

Medvedeva S.M. *et al.* (2018) synthesized a series of pyrrolo clubbed quinoline-1, 2-diones substituted by condensation at the -carbonyl with rhodanine, arylamines, and H-tryptamines. The reported compounds were identified using elemental analysis and PMR spectroscopy and evaluated for their anticoagulant activity as serine protease factor-Xa inhibitor which are key enzyme in the blood coagulation cascade. The reported derivative **9a** was found to have highest potency as anticoagulant agent when evaluated *in vitro* in buffer and human blood plasmamore potency than marketed drug benznidazole [Bz] and were characterized by elemental analysis, IR and ^{1}H NMR spectroscopy [32].



3. Conclusions

In Medicinal Chemistry, various quinoline derivatives are take part in the develop of organic synthesis. By using different procedure recently researchers have synthesized hybrid quinoline compound. Various researchers have synthesized quinoline and its fused heterocyclic derivatives. Their research work has been guiding for the development of new quinoline derivatives that contain various biological activities i.e., anticancer, antimycobacterial, antimicrobial, anticonvulsant, anti-inflammatory and cardiovascular activities, antiplasmodium, A lot of work has been done and more to go. Synthesized of newer quinolines have immense possibilities and scope for drug development scientist. We have represented a brief collection of this work to aid in present knowledge and to help researchers to survey an interesting quinoline class.

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