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ISOQUINOLINE DERIVATIVES AND ITS MEDICINAL ACTIVITY: A REVIEW

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ABSTRACT

Isoquinoline is a heterocyclic aromatic compound. This bicyclic compound consist of the fusion of benzene and pyridine ring. Isoquinoline moiety is highly important scaffold for drug development, because it has demonstrated a wide spectrum of pharmacological activities. Isoquinoline are having a varierty of therapeutic uses including antitumor, antibacterial, antimalerial, anti-inflammatory, antiviral, antiarrhythmic, antimicrobial, anti-HIV, antifungal.

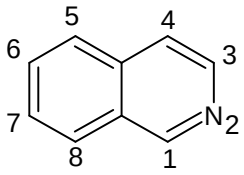
KEYWORDS: Isoquinoline, Medicinal Drugs, Medicinal activity, Synthesis, Chemistry.

INTRODUCTION

Isoquinoline is a heterocyclic aromatic compound. It is structural Isomer of quinoline. Isoquinoline are benzopyridines, which composed of a benzene ring fused to a pyridine ring. Isoquinoline is a colourless hygroscopic liquid at room temperature, unpleasant odor, soluble in organic solvents including ethanol, diethyl ether, acetone carbon disulfide. Isoquinoline ring derive from the aromatic amino acid tyrosine.[1,4] Isoquinoline moiety is highly important scaffold for drug development, because it has demonstrated a wide spectrum of pharmacological activities. Important medicinal activities associated with this class of compounds as reported in current scientific literature are antitumor,[20,22,24,30] antibacterial,[21,29,31] Antimalarial,[23] anti-inflammatory,[25,32] Antiviral,[26] Antiarrhythmic,[27]

antimicrobial,[28] anti-HIV,[29] antifungal.[29] The analogues of isoquinoline and its derivatives have an important role in research area especially medicinal, pharmaceutical industries and synthetic due to of its biological and therapeutic effects.

Isoquinoline was first isolated from coal tar in 1885 by Hoogewerf and W.A. van Dorp.[5] Then it isolated by fractional crystallization of the acid sulfate. In 1914, Weissgerber developed more rapid route for selective extraction of coal tar. Several method are developed for synthesis of isoquinoline. The Pomeranz-Fritsch reaction is efficient method for synthesis of isoquinoline.[6] Another method for synthesis of isoquinoline is Bischler-Napieralski reaction. In this method isoquinoline synthesized from Phenylethylamine. Isoqunoline also synthesized by using Pictet-Gams reaction. A Pictet-Gams reaction is similar to Bischler-Napierlski reaction; the only difference is that an additional hydroxyl group in reactant. In Pictet-Spengler reaction, a condensation of β-phenylethylamine and imine which undergoes a cyclization to give tetrahydroisoquinoline.



Isoquinoline

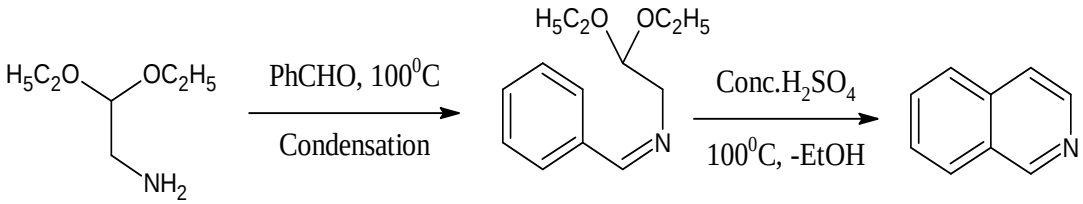
Synthesis of Isoquinoline

Several synthetic methodologies are available for the synthesis of isoquinoline

- Pomeranz-Fritsch synthesis.[6]

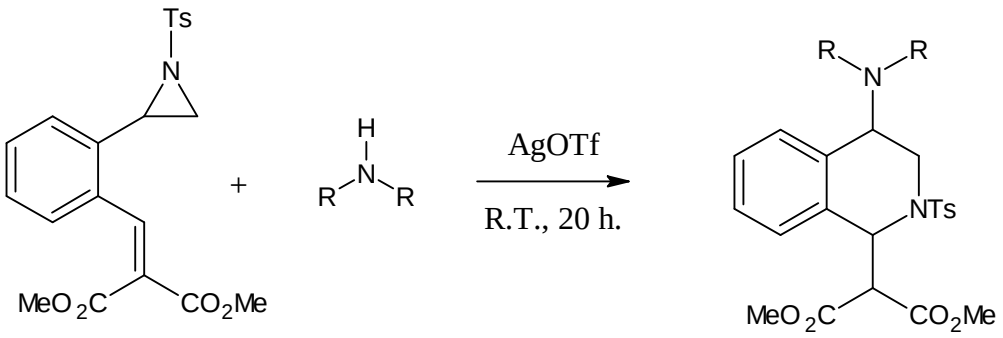
This reaction carried out 2 steps:

Benzaldehyde reacts aminoacetaldehyde diethyl acetal at 100^0C to form an phenylmethylene-ethanamine. Then phenylmethylene-ethanamine reacts with strong acid at 100^0C it give isoquinoline.

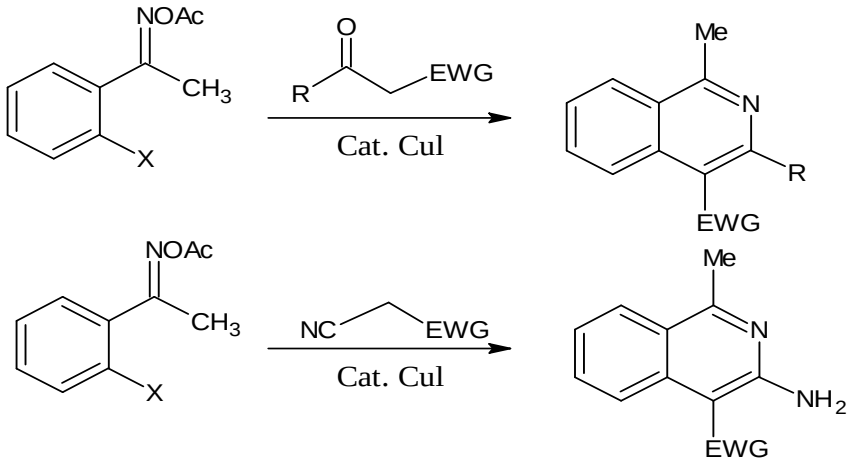


- Siyang Xing et al., Developed a new silver(I) triflate-promoted tandem reaction comprising the ring opening of aziridines and developed Michel reaction. Using

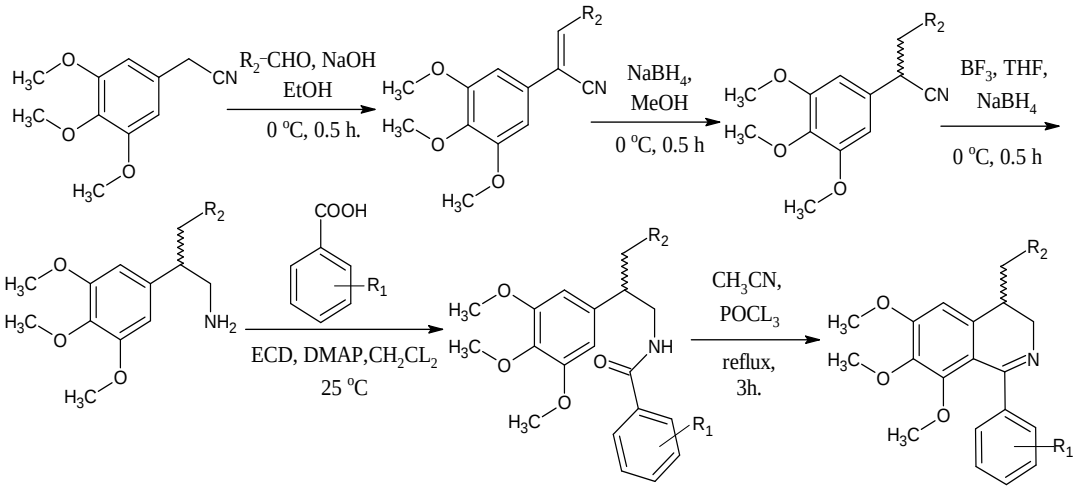
secondary amines as nucleophiles. This method used to synthesis of cis-1-alkyl-4-aminotetrahydroisoquinolines with good yield.[7]



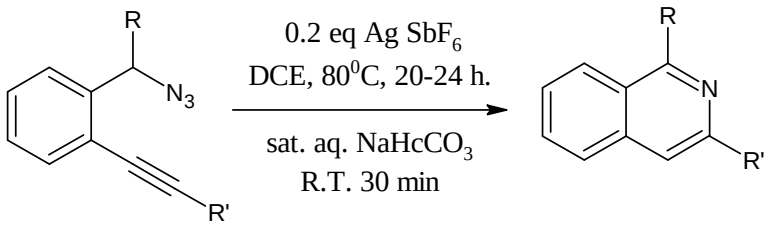
- Huanfeng Jiang et al., Synthesized new series of isoquinoline derivatives, high chemo and regioselectives, via the copper-catalysed cascade reaction of 2-haloaryloxime acetates with β-diketones, β-keto ester, and β-keto nitriles. This scheme have different features includes inexpensive catalysts, no need for additional ligands, and excellent functional group tolerance, which give better synthetic application.[8]



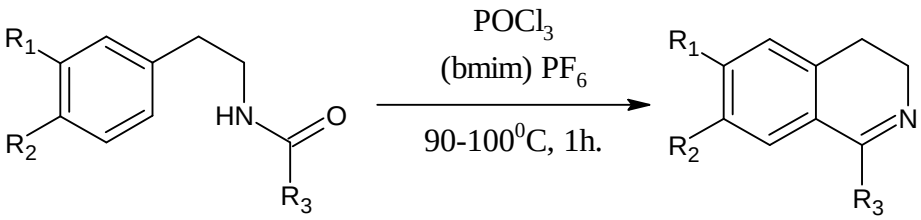
- Ling Zhang et al., Synthesized thirteen new derivative of 1,4-disubstituted -dihydroisoquinoline by Bischler-Napieralski cyclization of corresponding benzamides.[9]



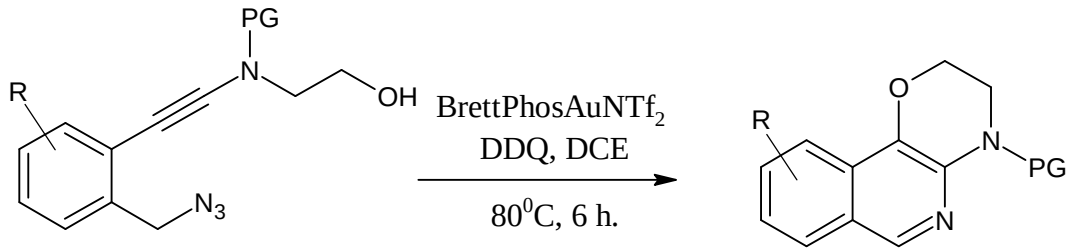
- Yan-Ning Niu et al., It is novel Ag-catalyzed cyclization of 2-alkylbenzyl azides method for synthesis of substituted isoquinoline. The reaction proceeds smoothly in good yields and tolerates various functional groups.[10]



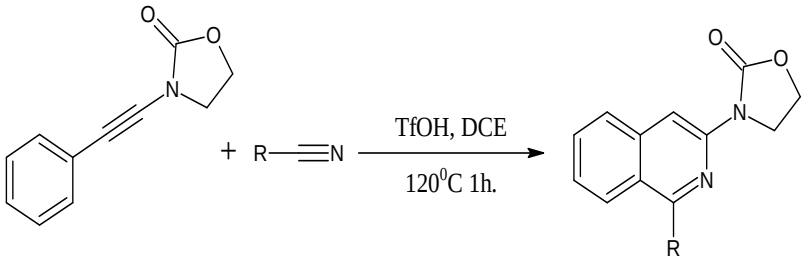
- Zaher M.A. et al., Reported the room temperature ionic liquid, 1-butyl-3-methylimidazoliumhexaflurophosphate [(bmim)PF_6] is environmentally benign solent for preparation of activated 3,4-dihydroisoquinolines derivatives through Bischler-Napieralski cyclization under mild conditions with excellent purity and yields. In this reaction ionic liquid (bmim)PF_6 using phosphorus oxychloride as a dehydrating reagent reacts with N-(3′,4′-dimethoxyphenethyl)-acetamide at 90-100^{0}C for 1 h.[11]



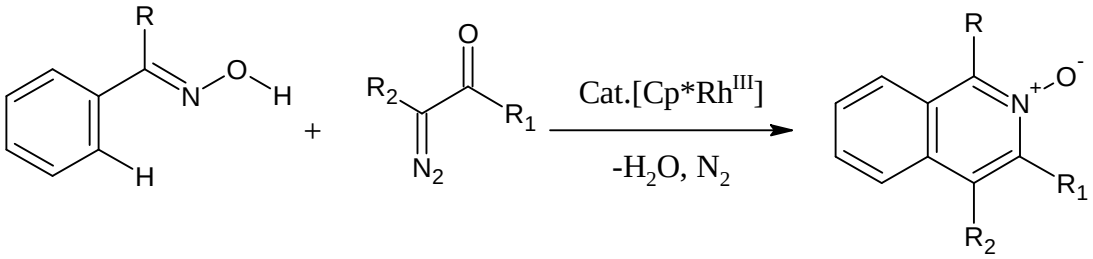
- Yuan Pan et al., Developed a novel gold-catalyzed tandem alkyne amination/ intramolecular O-H insertion. Synthesis variety of [1,4]oxazino[3,2-c]isoquinolines are readily accessed under mild reaction condition, thereby providing an efficient and practical route for the construction of synthetically useful fused isoquinolines.[12]



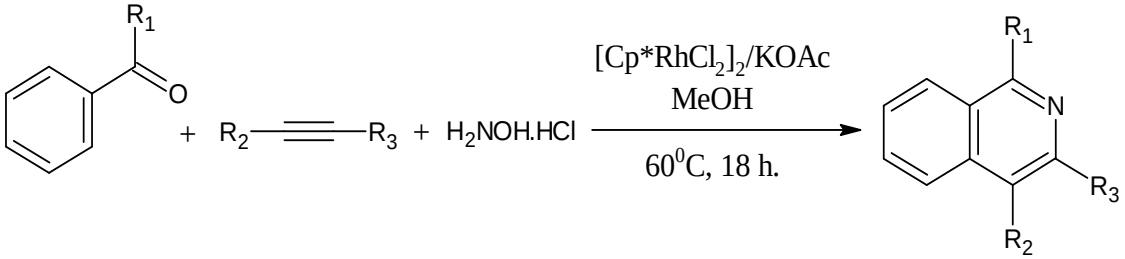
- Lan-Gui Xie et al., Reported metal-free intermolecular formal cycloaddition reactions that enable highly selective and orthogonal access to isoquinolines and pyrimidines by Bronstedacid-mediated regioselective formal cycloaddition of thioalkynes with nitriles.[13]



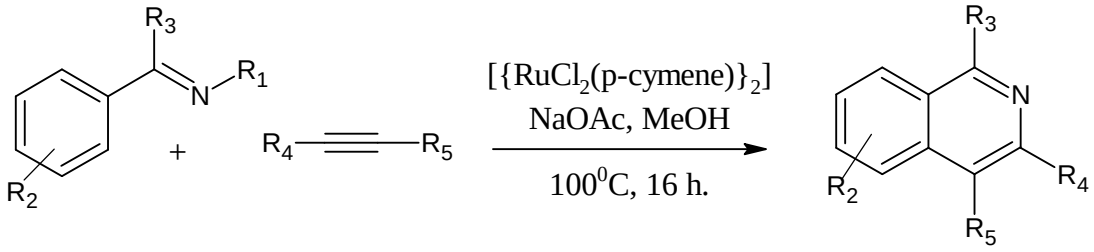
- Zhuangzhi Shi et al., Reported a multisubstituted isoquinoline were prepared by RH(III)-catalyzed cyclization of oximes and diazo compounds, intermolecular cyclization, C-H activation and condensation process under mild condition and used of oxidants, release of byproduct N_2 and H_2O.[14]



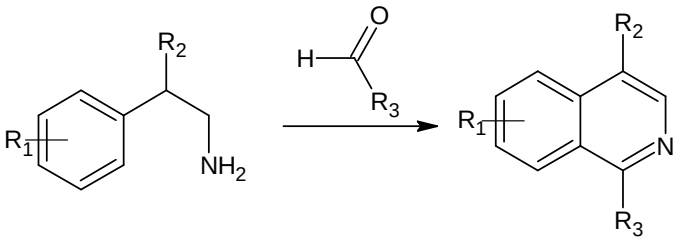
- Liyao Zheng et al., Reported a synthesis of isoquinolines and heterocycle-fused pyridines by three component reaction of aryl ketones, hydroxylamine, and alkynes. The reaction involved in condensation of aryl ketones and hydroxylamine, rhodium(III)-catalyzed C-H bond activation of the in situ generated oxime, and cyclization of internal alkynes.[15]



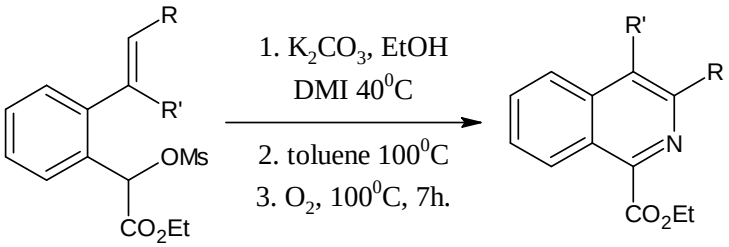
- Ravi K. C. et al., Reported aromatic and heteroaromatic ketoxime underwent cyclization with alkynes in presence of NaOAc, MeOH, and {$RuCl_2$(p-cymene)}$_2$] at 100^0C for 16 h. to give isoquinoline derivatives. [16]



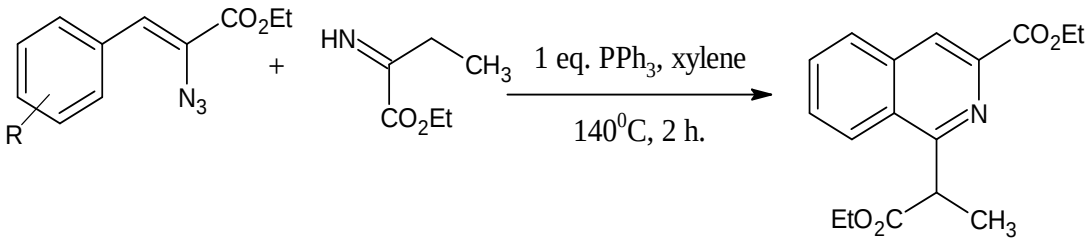
- Emelia A. et al., Reported synthesis based on Bischler-Napieralski or Pictet-Spengler reaction. The dihydroisoquinolines and tetrahydroisoquinolines thus generated could then be oxidized to their corresponding isoquinoline analogues.[17]



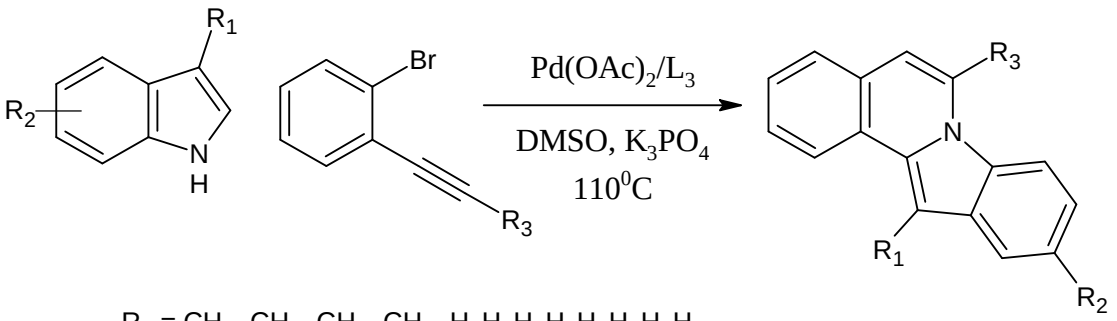
- Benjamin W. et al., Synthesized α-azido carbonyl compounds bearing a 2-alkylaryl moiety at α-position are precursors for synthesis of isoquinoline derivative.[18]



- Y.Y. Yang et al., Reported isoquinolines is synthesized by 2-azido-3-arylacrylate reacts with α-diazocarbonyl compounds and triphenylphosphine to give good yield.[19]



- Singh A. et al., Synthesized indole-and pyrrolo[2,1-α] isoquinolines in good yield by the hydroamination of alkynes followed by intramolecular C-2 arylation.[20]



R_1 = CH_3, CH_3, CH_3, CH_3, H, H, H, H, H, H, H, H,

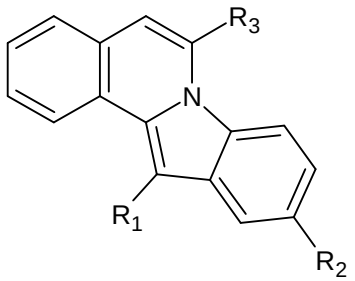
R_2 = H, H, H, H, H, H, H, H, OCH $_3$, OCH_3, OCH_3, OCH_3

R_3 = CH_3, C_2H_5, OCH_3, $CH(CH_3)_3$, CH_3, C_2H_5, OCH_3, H, C_2H_5, C_4H_{10}, CH_3, OCH_3

REVIEW OF LITERATURE

- **Antitumor activity**

Singh A. et al., Synthesis and antitumor activity of indole-and pyrrolo[2,1-α] isoquinolines.[20]

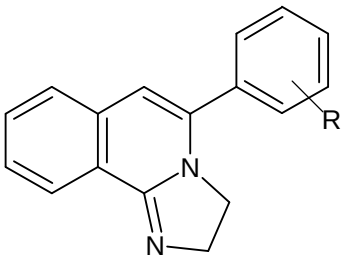


R_1 = CH_3, CH_3, CH_3, CH_3, H, H, H, H, H, H, H, H,

R_2 = H, H, H, H, H, H, H, H, OCH $_3$, OCH_3, OCH_3, OCH_3

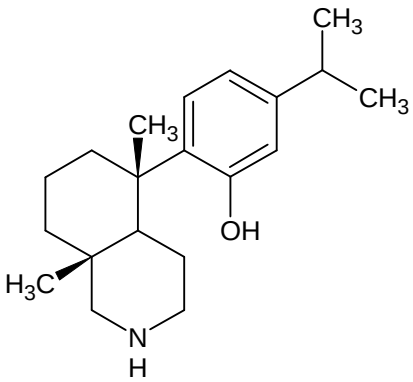
R_3 = CH_3, C_2H_5, OCH_3, $CH(CH_3)_3$, CH_3, C_2H_5, OCH_3, H, C_2H_5, C_4H_{10}, CH_3, OCH_3

Seung H.C. et. al., Synthesis and antitumor activities of some dihydroisoqunoline derivative.[22]

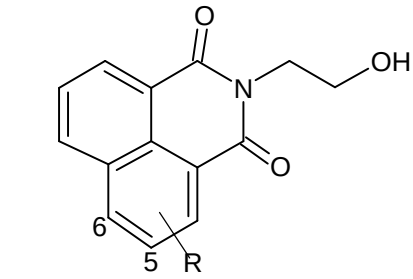


R = 4-CH_3, H

Chao-Xiang L. et al., Synthesized octahydroisoquinoline act as antitumor activity.[24]



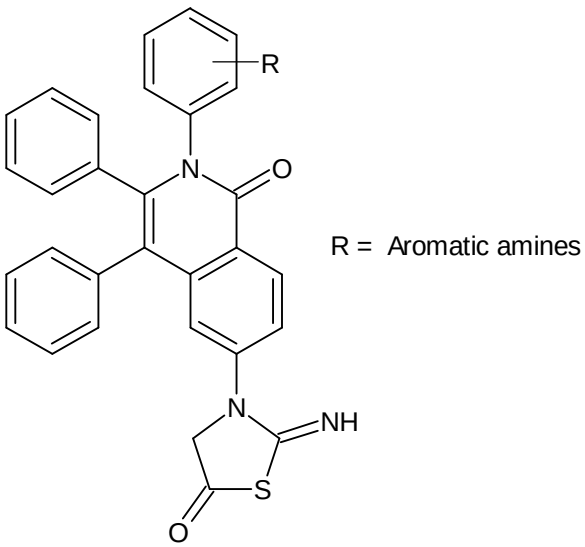
Mukharjee A. et.al., Synthesis of isoquinoline-1,3-dione derivatives for evaluation of anti-tumor activity.[30]



R = H, 6-Br, 6-Cl, 6-NO_2, 5-NO_2

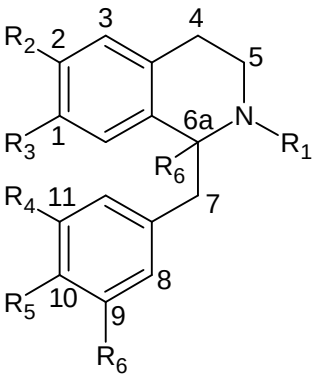
- **Anti-bacterial activity**

Dabholkar V. et al., Synthesis of some isoquinoline derivatives for evaluation of antibacterial activity.[21]



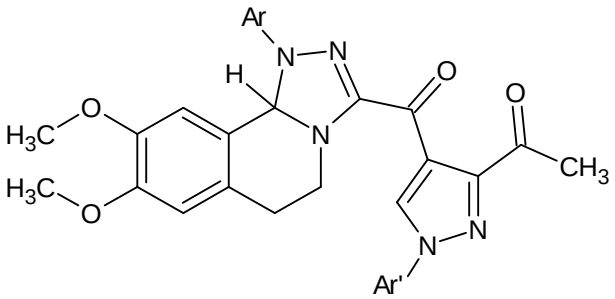
R = Aromatic amines

Qi Tang et al., Synthesis and anti-bacterial activity of some isoquinoline derivatives.[29]



$R_1 = CH_3, CH_3$
$R_2 = OCH_2O, OCH_2O$
$R_3 = OCH_2O, OCH_2O$
$R_4 = H, H$
$R_5 = H, H$
$R_6 = OCH_3, OCH_3$
$C_8 = OH, OH$
$C_3 = OCH_3$

Hassaneen H. et al., Synthesized 3-acetyl(1,2,4)triazolo(3,4-α)isoquinoline act as anti-bacterial activity.[31]

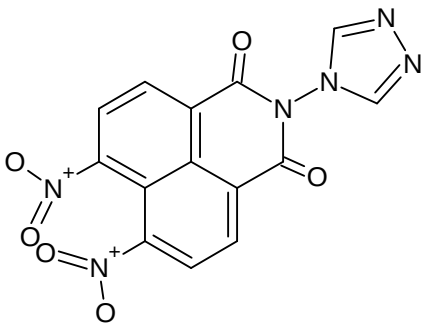


Ar = Ph, Ph, Ph, p-Tol, p-Tol, p-Tol, p-ClC $_6H_4$, p-ClC$_6H_4$, p-ClC$_6H_4$

Ar' = Ph, p-Tol, p-ClC $_6H_4$, Ph, p-Tol, p-ClC $_6H_4$, Ph, p-Tol, p-ClC $_6H_4$

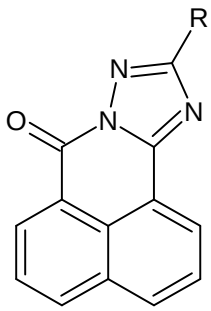
- **Anti-malarial activity**

Rivo Y.B. et.al., Synthesized 6,7-dinitro-2-[1,2,4] triazole -4-yl-benzo[de]isoquinoline-1,3-dione act as anti-malarial activity.[23]



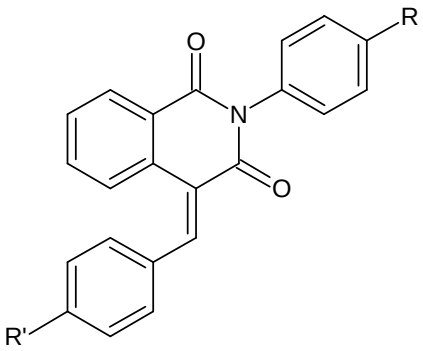
- **Anti-inflammatory activity**

Hatem A. Abuelizz et. al., Synthesis of some isoquinoline derivatives for evaluation of anti-inflammatory activity.[25]



R = SCH_3, O-Ph, SO_2CH_3

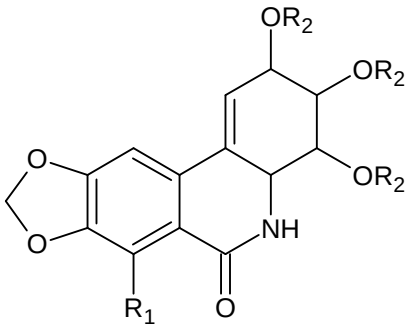
Manikandan A. et.al., Synthesis and anti-inflammatory activity of [N-sunstituted(E)-4-arylidene-isoquinoline-1,3-dione) derivatives.[32]



R = F, Me, Cl, F, Me, Cl, F, Cl,
R' = Br, Br, Br, Me, Me, Me, CN, CN

- **Anti-viral activity**

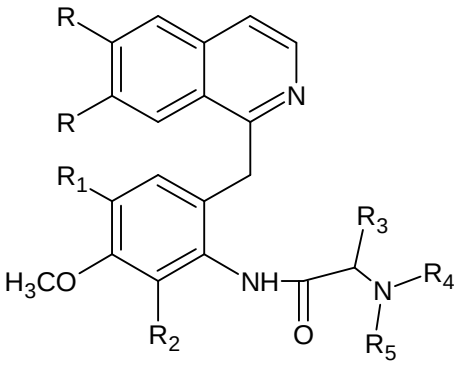
Gabrielsen B. et al., Synthesis and antiviral activity of selected amaryllidaceae isoquinoline derivatives.[26]



R_1 = OH, H, H
R_2 = H, H, Ac

- **Anti-arrhythmic activity**

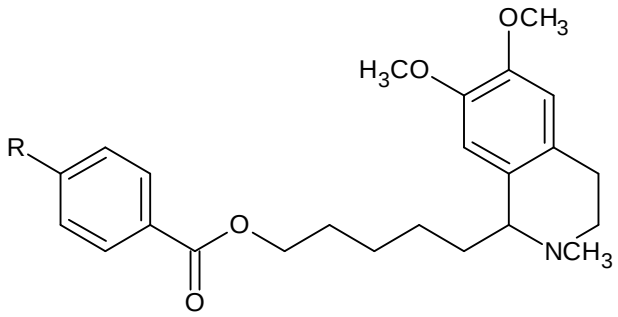
Neumeyer J. L. et al., Synthesis and antiarrhythmic activity of benzylisoquinoline derivatives.[27]



R = OCH_3 , OCH_3, H, H, H, H, H, H
R_1 = OCH_3, OCH_3, OCH_3, H, H, H, H, H
R_2 = H, H, H, H, OCH_3, OCH_3, OCH_3, OCH_3
R_3 = H, H, H, H, H, H, H, CH_3
R_4 = Et, H, Et, Et, Et Et, H, H
R_5 = Et, Et, Et, Et, Et, H, H, H

- **Anti-microbial activity**

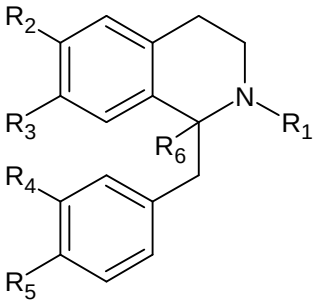
Galan A. et al., Synthesis of novel isoquinoline derivatives as anti-microbial agents.[28]



R = H, F, Cl, OCH_3

- **Anti-HIV activity**

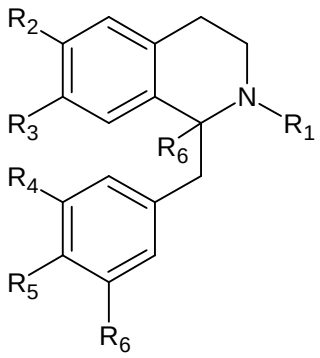
Qi Tang et. al., Synthesis and anti-HIV activity of some isoquinoline derivatives.[29]



R_1 = H, H, CH_3, CH_3, $(CH_3)_2$
R_2 = OH, OCH_3, OCH_3, OCH_3, OH
R_3 = OH, OH, OH, OCH_3, OCH_3
R_4 = H, H, H, H, H
R_5 = OH, OH, OH, OH, OH

- **Anti-fungal activity**

Qi Tang et. al., Synthesis and anti-fungal activity of some isoquinoline derivatives.[29]



R_1 = CH_3, H, H, CH_3, CH_3
R_2 = OCH_2O, OCH_2O, OCH_2O, OCH_2O, OCH_2O
R_3 = OCH_2O, OCH_2O, OCH_2O, OCH_2O, OCH_2O
R_4 = H, H, H, H, H
R_5 = OCH_3, H, H, H, H
R_6 = OH, H, OCH_3, H, H

CONCLUSION

The isoquinoline ring is an important pharmacophore in drug discovery. Some substituted isoquinoline derivative drugs are more potent activity. The synthesis of Isoquinoline derivatives is a privileged is scaffold, having variety of therapeutic uses including antitumor, antibacterial, antimalerial, anti-inflammatory, antiviral, antiarrhythmic, antimicrobial, anti-HIV, antifungal.

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