Review article

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A review on Pyrazole derivatives of pharmacological potential

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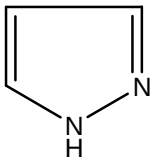
Abstract

Pyrazole is five membered heterocyclic rings which is versatile lead compound for designing potent bioactive agent. The interesting groups of this compound has diverse biological activities such as antimicrobial, anti-inflammatory, anticancer, analgesic, anticonvulsant, anthelmintic, antioxidant and herbicidal. Given data represents that pyrazole being heterocyclic planar five membered rings have various pharmacological actions. These derivatives of pyrazzole are analyzed here for pharmacological activities.

Keywords: Pyrazole, Antimicrobial, Ant-inflammatory, Analgesic, Anticonvulsant, Anticancer.

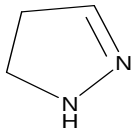
Introduction:

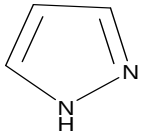
Pyrazole refer to both to class of simple aromatic ring organic compound of heterocyclic diazole series characterized by a 5- member ring structure composed of three carbon atom and two nitrogen atom in the adjacent position and to unsaturated parent compound. Being so composed and have pharmacological effect on humans, they classified as alkaloids, although they are rare in nature.



Pyrazole unsubstituted in 1- position show NH- acidity. The pKa value of Pyrazole is 14.21 and equal to that of imidazole.

Pyrazoline is basic in nature. An intermolecular conjugated charge transfer process has been reported to exist in it in excited state. The conjugated part (-N1-N2-C3-) of the ring, the nitrogen atom at the 3 position is, respectively electron donating and withdrawing moieties. The carbon atoms at 4- and 5- position do not conjugated with remaining part of the ring.





Pyrazole
Pyrazoline / 4,5 - dihydropyrazole

Pharmacological and biological evolution:

Pyrazole as Antimicrobials

Vijay v. Dabholkar et al. [1] synthesized a series of fused isooxazole and pyrazole and the newly synthesized compound were screened for antibacterial activity against *Escherichia coli, Staphyllococcus aureus, Corynebacterium diphtheriae and Proteus aeruginosa.* All the synthesized compounds showed good activity against *S. aureus* and against *C. diphtheriae* as compared to other derivatives.

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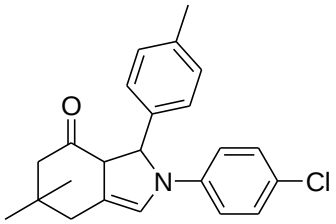
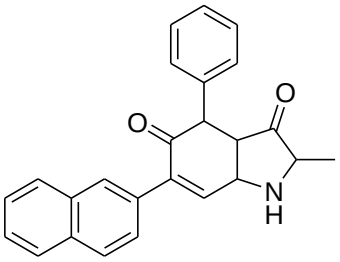
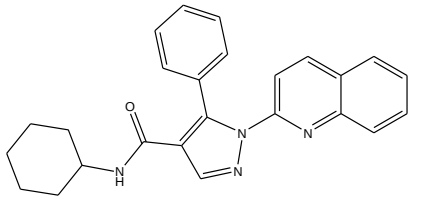


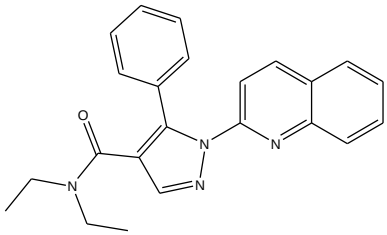
M.M Yousef et al. [2] synthesized a series of some new thiazole and pyrazole derivatives using diarylpoxylpropanone as precursor. The antimicrobial activity of compound considered was tested on *Escheria coli, Pseudomonas puticle, Bacillus subtilis, Streptococcus lactus and Aspergillus niger.* The entire synthesized compounds showed good activity.



B. Chankantha et al.[29], synthesized N-cyclohexyl-5-phenyl-1-(quinolin-2-yl)-1H-pyrazole-4-carboxamide, N-(2,6-dimethylphenyl)-5-phenyl-1-9quinolin-2-yl)-1H-pyrazole-4-carboxamide and N,N-diethyl-5-phenyl-1-(quinolin-2-yl)-1H-pyrazole-4-carboxamide and these compounds showed good antibacterial activity.



N-cyclohexyl-5-phenyl-1-(quinolin-2-yl)-1H-pyrazole-4-carboxamide



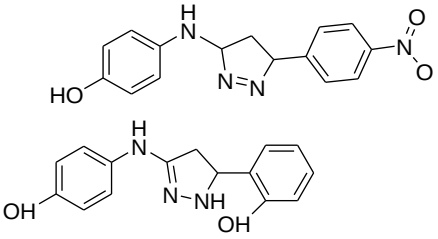
N,N-diethyl-5-phenyl-1-(quinolin-2-yl)-1H-pyrazole-4-carboxamide

K. Karrouchi et al. [31] found that N'[(aryl) methyl]-5-substituted-1H pyrazole-3-carbohydrazide derivatives did not showed good activity against *Pseudomonas aeruginosa* and *Bacillus subtilis.*

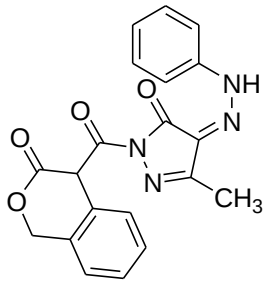
N. D. Gaikwad et al. [34] showed that 1-[4-(2,3,4-substituted-phenyl)thiazol-2yl]-3-(2,3,4-substituted-phenyl)-1H-pyrazole-4-carbaldehyde derivatives are having good antibacterial activity.

Pyrazole as Analgesic Agents

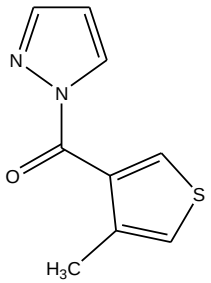
S.K Sahu et al. [3] synthesized a series of Pyrazole derivative and screened for their analgesic activity.



K.K. Sivakumar et al. [4] synthesized a series of (4Z)- 3 methyl-1-[2 oxo-2H- chromen-4yl) carbonyl] – 1H pyrazole -4, 5-dione4-[(4- substituted phenyl) hydra zone). The entire compounds were screened for anti-inflammatory and analgesic activity.

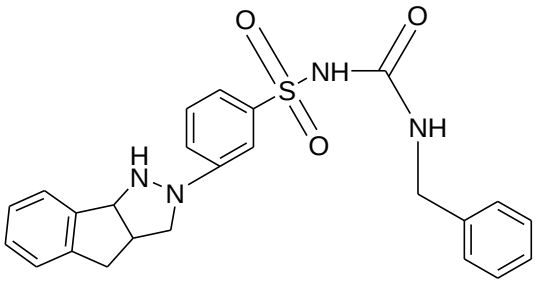


L. R. S. Dias et al. [33] synthesized and showed (4-methylthiophen-3-yl) (1H-pyrazol-1-yl) methanone contains good analgesic activity.

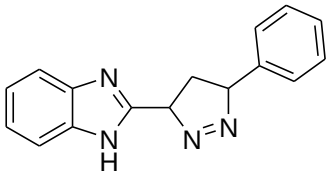


Pyrazole as Anticancer Agents

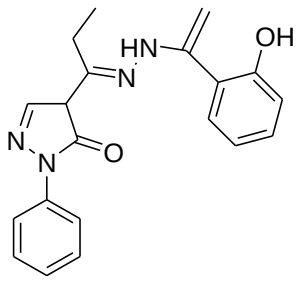
Mohammad S.M. Al-Saadi, et al. [5] synthesized a series of pyrazole and pyrazoline fused ring systems substituted with variable biologically- active chemical species.



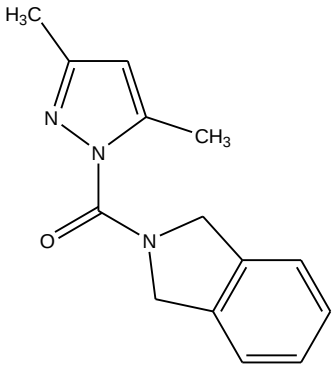
R. Kalirajan, et al. [6] synthesized a series of pyrazole derivatives and these derivatives showed anticancer activity.



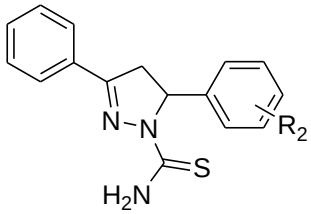
Xiao Hong Wang et al. [7] synthesized a series of pyrazole derivatives. Derivatives were reported to have potent cytotoxicity against some tumour cells.



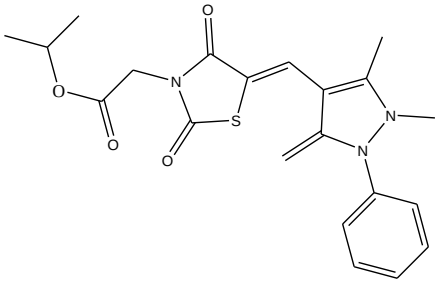
L. R. S. Dias et al. [33] synthesized (isoindolin-2-yl) (3, 5-dimethyl-1H-pyrazol-1-yl) methanone and the synthesized compound showed good antitumour activity.



Peng-cheng LV et al. [14] synthesized a series of pyrazole derivatives. The compounds showed high antiproliferative activity against MCF-7 with IC_{50} 0.08 µM.

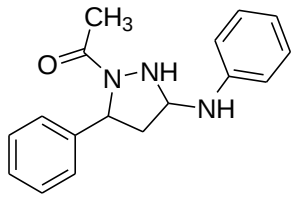


S. Nishida et al.[35] worked on isopropyl-2-[(10Z)-5-{(2,5-dihydro-2,3-dimethyl-5-methyl-1-phenyl-1H-pyrazol-4-yl)methylene}-2,4-dioxothiazolidin-3-l]acetate and showed that it contains good anticancer activity.



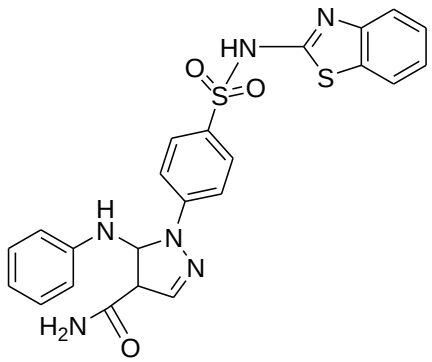
Pyrazole as Anticonvulsant Activity

Anoop Singh, et al. [8], synthesized a series of 1- [(4, 5 – dihydro- 5 phenyl -3 phenyl amino) pyrazole -1 yl)] ethanone and evaluated for anticonvulsant activity against electric shock induced convulsion method.



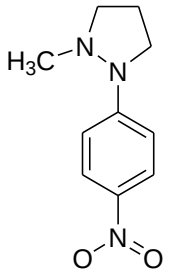
Pyrazole as Antihelmintic Agents

Sreenivara G.M, et al. [9], synthesized a series of pyrazole derivative and evaluated for their antihelminitic activity. Synthesized compound of pyrazole derivative were tested for antihelminitic activity against earthworms, Perituma poshuma and were compared to std. Albendazole.

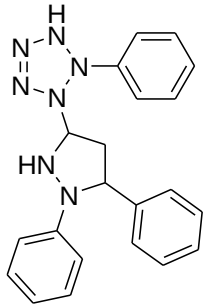


Pyrazole as Anti-inflammatory Agents

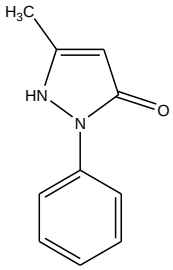
Shilpa Ailawadi et al.[10] synthesized a series of new substituted 3,5- dimethyl pyrazole, 3-methyl pyrazole 5-one derivative , 3- methyl- 1- (substituted phenyl) pyrazole- 5 ones and 2,3 di methyl -1-(substituted phenyl) pyrazole 5-ones derivatives. All the newly synthesized compounds tested for their in vivo anti inflammatory and analgesic activity by bioassay namely Corragenan induced paw Edema method and acetic acid induced method respectively. Compound exhibited promising and significant inhibitory activity against COX-2 enzyme.



V. H. Bhaskar, et al. [11] synthesized a series of pyrazole derivatives and examined for their anti-inflammatory activity. All the compounds exhibited weak to potent anti-inflammatory activity. Some derivatives bearing a methoxy group exhibited very good anti-inflammatory.

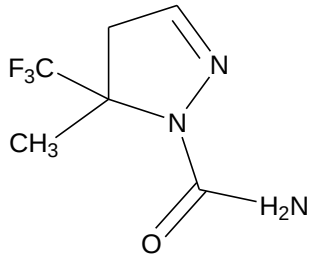


L. R. S. Dias et al. [33] showed that 1, 2-dihydro-5-methyl-2-phenylpyrazol-3-one contains good anti-inflammatory activity.



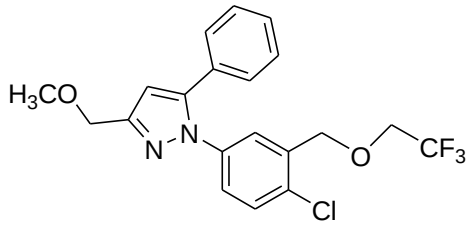
Pyrazole as Antioxidant activity:

J.S.M. Pasin et al. [12] synthesized a series of pyrazole derivatives and screened for antioxidant activity. All compound showed good activity.



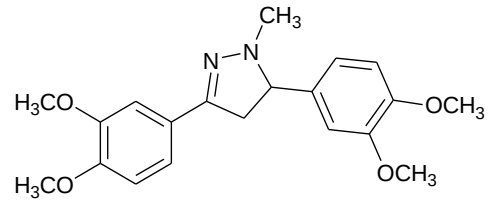
Pyrazole as Herbicidal

Noriaki kudo et al. [13] synthesized a series of 1, 5 Diarylpyrazole derivative. Some of these compounds showed noticeable pre- emergent herbicide activities against various kinds of weeds. The synthesized compound, .methyl 4-chloro-1-(2,5-diflurophenyl)-5-(4-flurophenyl)-pyrazole-3-carboxylate exhibited good activity.

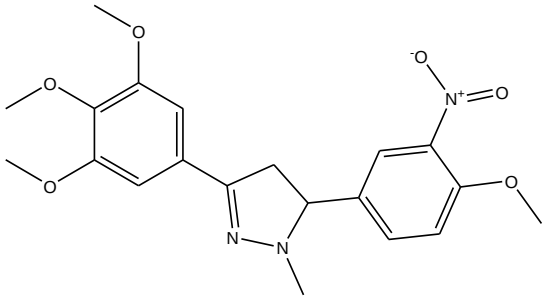


Pyrazole as ACE- Inhibitors

Macro Bonesi et al. [15] synthesized a series of pyrazole derivatives and investigated their potential activity as Angiotensin-I-converting enzymes inhibitory activity by performing assay. This derivative of pyrazole showed effective ACE-inhibitory activity with 0.123 mM IC50 value.

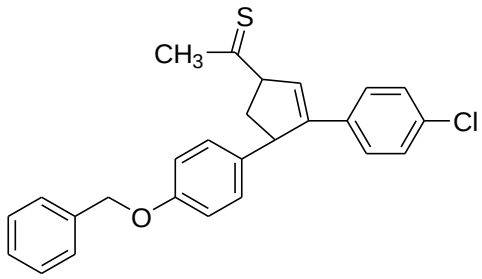


P. K. Arora and A. Chauhan[38] showed that 4,5-dihydro-5-(4-methoxy-3-nitrophenyl)-3-(3,4,5-trimethoxyphenyl)-1-methyl-1H-pyrazole is having promising ACE inhibitory activity.

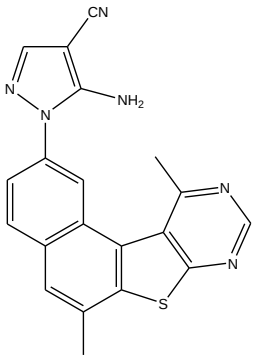


Pyrazole as Antiviral Agents

Osama I, et al. [16] synthesized 4, 5-disubstituted pyrazole derivatives. The derivative containing R=Cl group (Fig. 16) showed the potent antiviral activity against a broad panel of viruses in different cell culture (HEL Cell cultures).



Aymn E. Rashad, et al. [17] synthesized substituted pyrazole derivatives. These derivatives showed promising antiviral activity against Hepatitis A virus and Herpes Simplex virus type-1 using plaque infective assay.

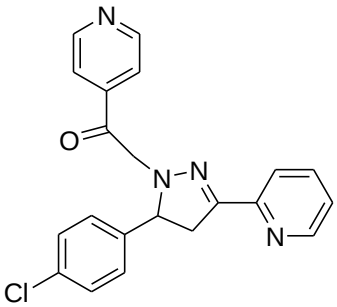


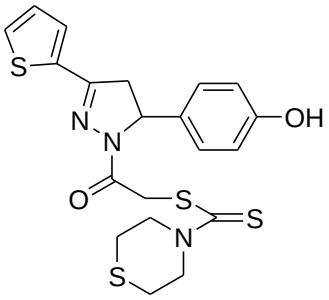
Pyrazole as Antimycobacterial Agents

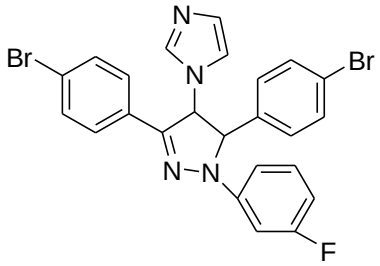
Mamolo et al. [18] synthesized 5 –Aryl – isonicotionyl- 3-(pyridine-2-yl)- 4, 5 – dihydro-1 H pyrazole derivatives and tested for their in vitro antimycobacterial activity.

Ozdemir et al. [19] synthesized new 1-[(N, N- -disubstituted thiocaramoylthio) acetyl] - 3 – (2 thienyl)-5 aryl-2- pyrazoline derivatives and evaluated for in vitro antimycobacterial activity against M. tuberculosis H37 Rv.

Zampieri et al. [20], synthesized several 1-(3, 5-Diaryl-4, 5- dihydro – H – pyrazol- 4 yl)-1 h– imidazole derivatives and tested for their in vitro antifungal and antimycobacterial activities. These imidazole derivatives showed an excellent antifungal activity against clinical strain of *C. albicans* and an interesting antitubercular activity against M. tuberculosis H37R.

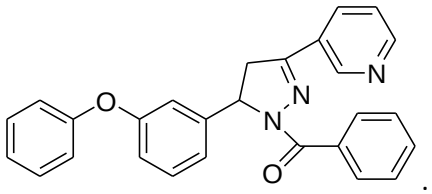




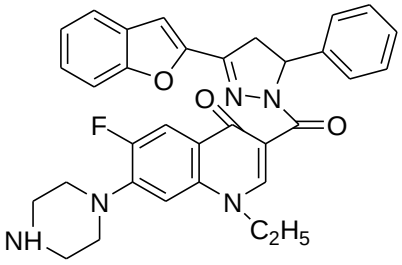


Pyrazole as Antitubercular Agents

Kini et al. [21], synthesized a novel series of heterocyclic o/m/p- substituted diphenyl ether derivatives and determined their activity against H37Rv strain of *Mycobacterium.* All 10 compounds inhibited the growth at concentration as low as 1 ugml^{-1}.



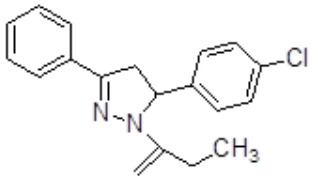
Babu et al. [22] synthesized and evaluated a biological activity of 1, 3, 5 Trisubstituted pyrazolines bearing benzofuran. They found to be anti tubercular, antimicrobial and antiinflamatory in nature.



Pyrazole as MAO Inhibitors

Chimenti et al. [23] synthesized a series of N - propanoyl – 3, 5- diphenyl-4, 5-dihydro- (1H)- pyrazole derivatives and assayed as inhibitors of MAO- A and MAO-B isoforms. These showed inhibitor activity with micromolar values and MAO-A selectivity and found to

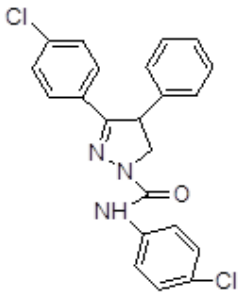
be useful as co – adjuvants in the treatment of Parkinson's disease (PD) and Alzhemer's disease.

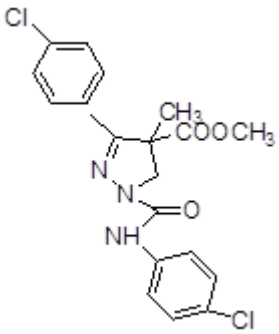


U. Salgin-Goksen et al.[37] synthesized a series of 1-[2-{(5-methylchloro)-2-benzoxazolinone-3-yl}acetyl]-3,5-diaryl-4,5-dihydro-1H-pyrazole derivatives and these compounds were found to inhibit human MAO-A selectivity.

Pyrazole as Insecticidal Agents

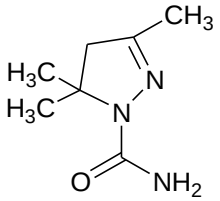
Silver et al. [24] synthesized pyrazoline- type insecticides and examined the mechanism of action of these compounds based on available electrophysiological, pharmacological and toxicological information and found to act at neuronal target sites.



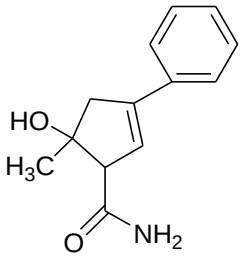


Pyrazole as Antinociceptive Activity

Godoy et al.[25] investigated whether spinal noradrenogenic and seretogenic systems are involved in antinociception induced by novel pyrazolines MPCA and PPCA .The result suggested that spinal 5-HT receptors and a2 – adrenoreceptors are involved and induced by MPCA and PPCA, but not in the elicited by dipyrone.



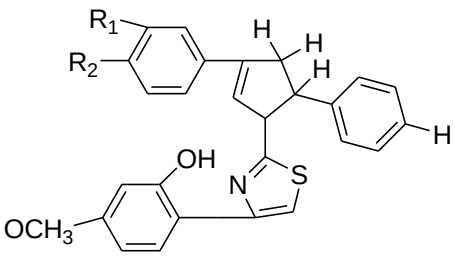
MPCA



PPCA

Pyrazole as Hypotensive Agents

Turan –Zitouni et al. [26] synthesized some 1-(4-Arylthiazol-2-yl)-3, 5- diaryl -2 – pyrazoline derivatives and investigated their hypotensive activity by tail-cuff method using clonidine as reference standard. All examined compounds shows appreciable hypotensive activities.

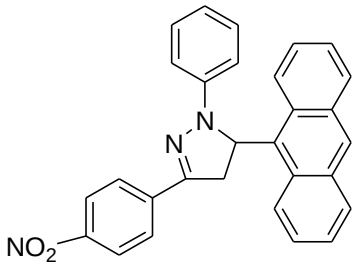


2-(2-(3,5-diphenyl-2-pyrazolin-1-yl)thiazol-4yl)-5-methoxyphenol,where R1=R2=R3=H
and, 5-methoxy-2-(2-(5-(4-methoxyphenyl)-3phenyl-2-pyrazoline-1-yl)thiazol-4-yl)phenol,where, R1=R2=R3=OCH3

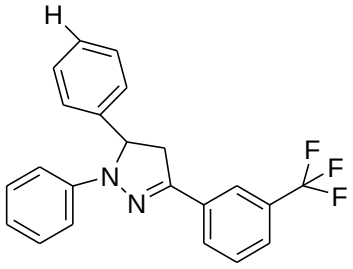
Pyrazole as Photoluminescence (PL) Activity

Wang et al. [27] synthesized 5- (9 Anthryl-3- (4 nitro phenyl) -1 – phenyl-2- pyrazoline (ANPP) and screened its photoluminescence property. Photo induced intermolecular energy transfer from anthryl to pyrazoline moiety exists simultaneously with the charge

transfer from N1 to C3 in the pyrazoline moiety in the excited state and both compete with each other.

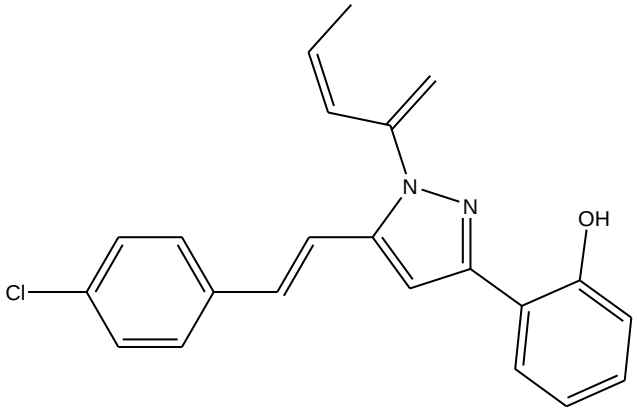


Jin et al. [28] synthesized Triphenyl pyrazoline derivatives (TPPs) bearing electron withdrawing and pushing substituents and investigated photo luminescent property in the solution and doped into the poly (N- vinylcarbazole) (PVK) thin films. When TPPs were doped into PVK films the photoluminescence intensity was enhance with increased TPPs concentration.

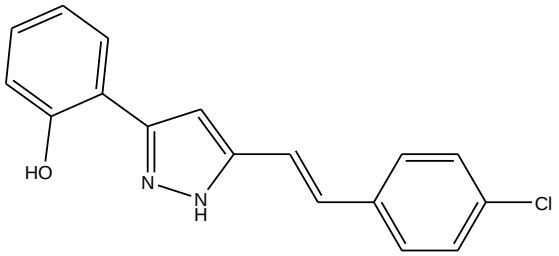


Pyrazole as Antifungal Agents

P. Priyadersini et al. [30] synthesized 3-(2-hydroxyphenyl)-5-(4-chlorostyryl)-1-phenylpyrazole and 3-(2-hydroxyphenyl)-5-(4-chlorostyryl)-1H-pyrazole and found them to be having good activity against *Aspergillus niger*.

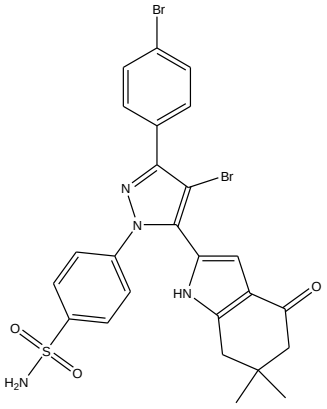


3-(2-hydroxyphenyl)-5-(4-chlorostyryl)-1-phenylpyrazole



3-(2-hydroxyphenyl)-5-(4-chlorostyryl)-1H-pyrazole

S. Y. Hassan et al.[32] found that 4-[4-Bromo-3-(4-bromophenyl)-5-(6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-1H-indol-2-yl)-1H-pyrazol-1-yl]benzenesulphonamide is having good activity against *Candida albicans*.



Pyrazole as Anthelmintic Agents

S. M. A. El-Badwi et al. [36] showed that pyrazole alkaloids obtained from *Withania somnifera* are having good anthelmintic activity.

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