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CHEMISTRY AND BIOLOGICAL PROPERTIES OF PYRAZOLE DERIVATIVES: A REVIEW

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ABSTRACT

Ludwig Knorr was the first to discover the name "pyrazole" in 1883, while Edward Buchner is credited with being the first to synthesis it in 1889. The present review was based on the chemistry and biological properties of pyrazole derivatives for which an extensive literature survey was done using Scopus, Springer Nature, and Google Scholar. Two atoms of vicinal nitrogen, acidic pyrrole-like nitrogen with a single pair of aromatic electrons, simple sp2-hybridized nitrogen-like pyridine, and three carbon atoms make up the five-membered aromatic ring structure of pyrazole. The pyrazole has the chemical formula: $C_3H_4N_2$, IUPAC name: 1,2-Diazacyclopenta-2,4-diene, molar mass: 68.079g/mol, melting point: 66 to 70°C and boiling point: 186 to 188°C. Pyrazole protonation results in pyrazolium cations that are more susceptible to an electrophilic attack at C-3 but less likely to experience one at C-4. While the pyrazole anion is more reactive with electrophiles, it is significantly less reactive with nucleophiles. There are some of the pyrazole molecule's reactions characteristics i.e., Acylation, Oxidation, Reduction, Halogenation, Nitration and Sulphonation. In conclusion, numerous pharmacological properties have been reported for the novel derivatives of pyrazoles including anti-

inflammatory, analgesic, anti-diabetic, anti-viral, anti-diarrheal, anti-cancer, anti-tubercular, anti-leishmanial, anti-cholinesterase, antibacterial, antioxidant anti-Parkinson, and neuroprotective. Different nuclei added to pyrazole derivatives have been observed to exhibit a range of pharmacological profiles. The chemical pyrazole can be utilized to increase biological activity in a variety of heterocyclic systems. Pyrazole derivatives may be a rich source of potential entities in the study of a new generation of physiologically active molecules.

KEYWORDS: Design, Chemistry, Pyrazole derivatives, Pharmacological properties, anti-cancer.

INTRODUCTION

Interest in pyrazole chemistry has grown significantly over the last ten years, mostly due to the discovery of intriguing features shown by a large number of pyrazole derivatives. Ludwig Knorr was the first to discover the name "pyrazole" in 1883[1], while Edward Buchner is credited with being the first to synthesis it in 1889.[2] As heterocycles with five members, pyrazoles are a type of molecules that are highly prized in chemical synthesis. They are one of the most researched classes of chemicals in the azole family. Numerous synthetic analogues and synthesis techniques have been reported over time, underscoring their critical role in both research and applications. A basic component found in many small compounds, pyrazole has a wide range of applications in both agriculture and medicine.[3] They are specifically categorized as protein glycation inhibitors and have anti-inflammatory, antibacterial, antifungal, anticancer, antidiabetic, antioxidant, antidepressant, anti-tuberculosis, and antiviral characteristics.[4][5][6] Pyrazole derivatives have been used in the formulation of a number of FDA-approved and commercially accessible medications in recent years, both patented and non-patented.[7] Because of their structures and distinct pharmacological effects on humans, they are referred to as alkaloids. In 1959, 1-pyrazolyl-alanine was the first naturally occurring pyrazole to be extracted from watermelon seeds.[8][9]

Chemistry of Pyrazole

Two atoms of vicinal nitrogen, acidic pyrrole-like nitrogen with a single pair of aromatic electrons, simple sp2-hybridized nitrogen-like pyridine, and three carbon atoms make up the five-membered aromatic ring structure of pyrazole. These combined characteristics need to be carefully taken into account when evaluating reactivity.[10] In the first case, because of the nitrogen, N-unsubstituted pyrazoles have amphoteric characteristics, functioning as both

bases and acids.[11] The simple pyridine-like nitrogen may take protons even more easily than the acidic pyrrole-like NH group, which is why the basic character is usually more common. However, ring substitutions can alter these characteristics; for example, it has been demonstrated that electron-donating groups intensify the acidity of the pyrrole-like -NH group.[12][13]

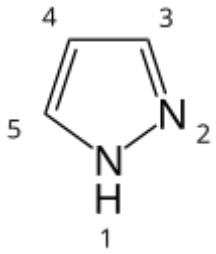


Fig. 1: Basic structure of pyrazole.

Chemical formula: $C_3H_4N_2$

IUPAC Name: 1,2-Diazacyclopenta-2,4-diene

Molar mass: 68.079g/mol

Melting point: 66 to 70°C

Boiling point: 186 to 188°C

Basicity: 11.5

Individual atoms' effects can be used to describe the pyrazole molecule's chemical characteristics. Because it is basic, the two-electron N-atom at position two reacts with electrophiles. Despite being unreactive, the N-atom at position 1 loses its proton when a base is present. By lowering the charge density at C-3 and C-5, the two N-atoms work together to open up C-4 for electrophilic assault. Ring-opening can result from deprotonation at C-3 when a strong base is present. Pyrazole protonation results in pyrazolium cations that are more susceptible to an electrophilic attack at C-3 but less likely to experience one at C-4. While the pyrazole anion is more reactive with electrophiles, it is significantly less reactive with nucleophiles.[14] The following are some of the pyrazole molecules' more general chemical characteristics:

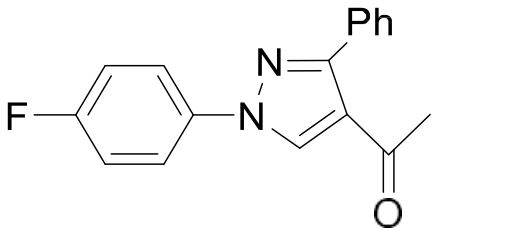
- Acylation
- Oxidation
- Reduction
- Halogenation

- Nitration
- Sulphonation

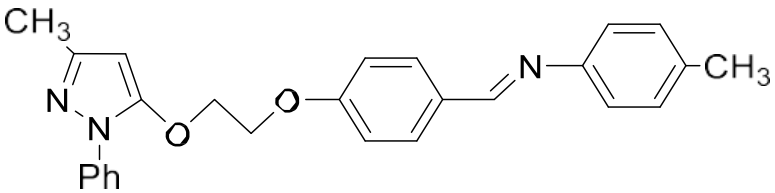
Biological properties

Anti-inflammatory

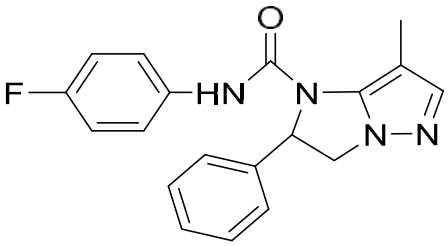
The anti-inflammatory and analgesic properties of several 1-(4-substituted-phenyl)-3-phenyl-1H-pyrazole-4-carbaldehydes were synthesized and evaluated. showed the strongest anti-inflammatory effect among the compounds that were synthesized.[15] Tewari et al. (2014) reported a novel series of pyrazole derivatives and assessed their anti-inflammatory properties in vivo. Comparable anti-inflammatory properties were demonstrated by N-(4-(2-(3-methyl-1-phenyl-1H-pyrazol-5-yloxy)benzylidene)-4-methylbenzenamine.[16] The anti-inflammatory evaluation of novel 2,3-dihydro-imidazo[1,2-b]pyrazole derivatives was reported and synthesized by Brullo et al. (2012). Of these, compound N-(4-fluorophenyl)-2,3-dihydro-7-methyl-2-phenylimidazo[1,2-b]pyrazole-1-carboxamide demonstrated an intriguing dual activity, inhibiting both Fmlp-Ome and IL8-induced chemotoxis with IC50 values of 3.8 and 1.2 Nm, respectively.[17]



1-(1-(4-fluorophenyl)-3-phenyl-1H-pyrazol-4-yl)ethanone

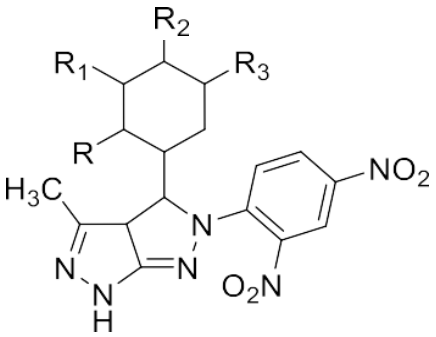


(E)-N-(4-(2-(3-methyl-1-phenyl-1H-pyrazol-5-yloxy)ethoxy)benzylidene)-4-methylbenzenamine

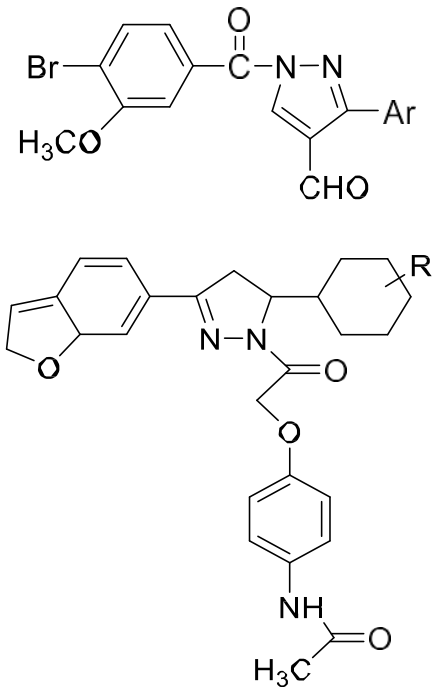


N-(4-fluorophenyl)-2,3-dihydro-7-methyl-2-phenylimidazo[1,2-b]pyrazole-1-carboxamide

The series of 1-(3-bromo-4-methoxybenzyl)-4-formyl-3-(substituted phenyl) pyrazoles and their anti-inflammatory properties were produced by Freddy et al. (2001).[18] The synthesis of 4,5-disubstituted-3-methyl-1,3a,4,5-tetrahydropyrazolo[3,4-c] pyrazoles and their anti-inflammatory properties were documented by Bhaskar et al. (2007).[19] N-phenyl-5-substituted aryl-3-P-(fluorophenyl) pyrazoline and fluorinated phenyl styryl ketones were assessed by Nargund et al. (1992), who also demonstrated anti-inflammatory efficacy in vivo.[20]



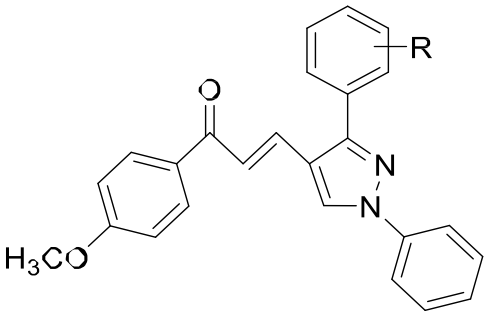
4,5-disubstituted-3-methyl-1,3a,4,5-tetrahydropyrazolo[3,4-c] pyrazoles



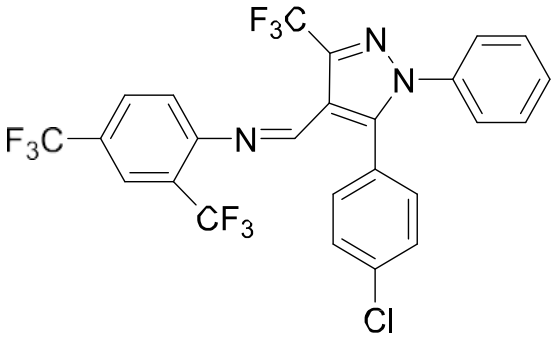
N-Phenyl-5-substituted aryl-3-P-(fluorophenyl) pyrazoline

Sayed et al. (2012) described a number of new pyrazole derivatives defined as N-((5-(4-chlorophenyl)-1- phenyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)methylene)- 3,5bis (trifluoromethyl) aniline which showed optimal anti-inflammatory activity when compared

with reference medications diclofenac sodium and celecoxib.[21] By using the Claisen-Schmidt condensation of 1-(2,4-dimethoxy-phenyl)-ethanone and substituted 1,3-diphenyl-1H-pyrazole-4-carbaldehyde, Bandgar et al. (2009) assessed the series of unique 1-(2,4-dimethoxy-phenyl)-3-(1,3-diphenyl-1H-pyrazol-4-yl)-propenone. Every synthetic compound's anti-inflammatory properties were assessed.[22]



1,3-diphenyl-1H-pyrazole-4-carbaldehyde

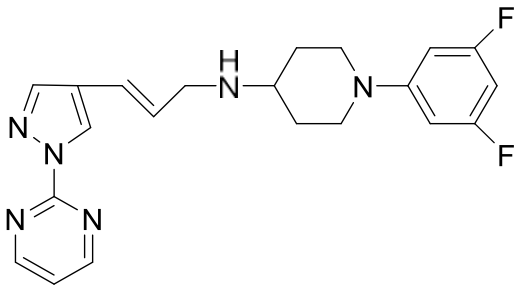


N-((5-(4-chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)methylene)-3,5bis (trifluoromethyl) aniline

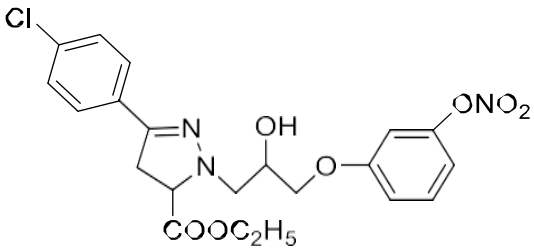
Anti-cancer

Different derivatives of pyrazole are generated by linking pyrimidine, carboxyhydrazide, as well as ferrocenyl molecule with pyrazole cap and all that are particularly effective against carcinoma of lung cells. Ohki et al (2002) synthesized the pyrimidinyl pyrazole derivatives 1-(3,5- difluorophenyl)-N-(E)-3-(1-pyrimidin-2-yl)-1H-pyrazol-4- yl)piperidin-4-amine as a new scaffold of an anti-tumor agent, which also showed antiproliferative activity against human lung cancer cell lines and inhibited tubulin polymerization.[23] Wei et al (2006) reported a series of novel small molecules of compound ethyl1-[20-hydroxy- 30-aroxypropyl]-3-aryl-1H-pyrazole-5-carboxylate derivatives which have its potency to suppress lungs cancer cell growth.[24] Xia et al (2007) prepared a series of novel 1-arylmethyl-3-aryl-1H-pyrazole-5-carbohyrazide derivatives which had inhibitory effects on the growth of A549 cells and induced the cell apoptosis.[25] Fan et al (2008) reported a series

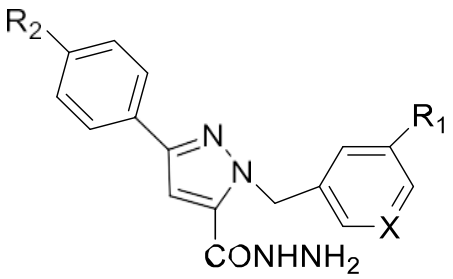
of novel 1-(3-(4-chlorophenoxy)phenyl)- 3-(4-chlorophenyl)-1H-pyrazole-5-carbohydrazide which is inhibiting the growth of A549 cells.[26]



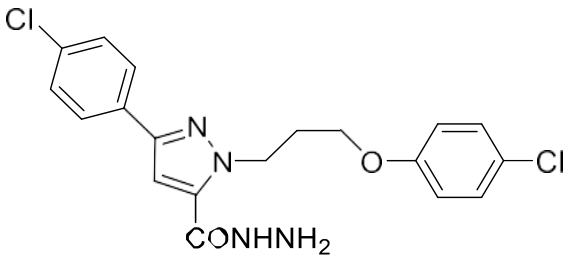
1-(3,5-Difluorophenyl)-N-((E)-3-(1-(pyrimidin-2-yl)-1H-pyrazol-4-yl)allyl)piperidin-4-amine



Ethyl1-[20-hydroxy-30-aroxypropyl]-3-aryl-1H-pyrazole-5-carboxylate



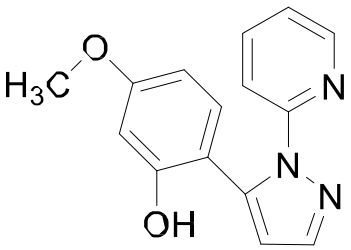
1-Arylmethyl-3-aryl-1H-pyrazole-5-carbohyrazide



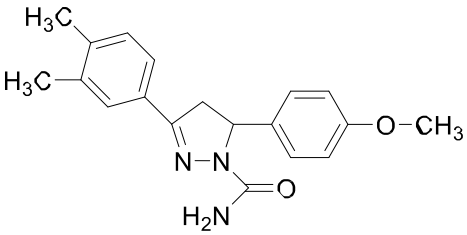
1-(3-(4-chlorophenoxy)propyl)-3-(4-chlorophenyl)-1H-pyrazole-5-carbohydrazide

A new pyrazole derivative, 5-methoxy-2-(1-(pyridine-2-yl)-1H-pyrazol-5-yl)phenol, was synthesized by Balbi et al. (2011) and its antiproliferative activity was found in human lung carcinoma A549 cells, human ovarian adenocarcinoma A2780 cells, and murine P388

leukemia cells.[27] Two series of pyrazole derivatives, 4,5-dihydro-5-(4-methoxyphenyl)-3-(3,4-dimethylphenyl)pyrazole-1-caboxamide, were reported and synthesized by Lv et al. (2010). These derivatives are being designed for potential EGFR kinase inhibitors and have antiproliferative activity against MCF-7 with strong inhibitory activity in tumor growth inhibition, which could be an anticancer activity.[28] A novel class of 3, 5-diaryl pyrazole compounds was created by Bandgar et al. (2010). the anticancer properties of 1-(3,5-dichlorophenyl)-4-(4,5-dihydro-1H-imidazol-2-yl)- 1H-pyrazol-5-amine.[29]

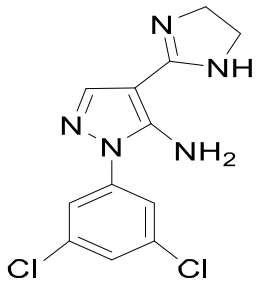


5-methoxy-2-(1-(pyridin-2-yl)-1H-pyrazol-5-yl)phenol

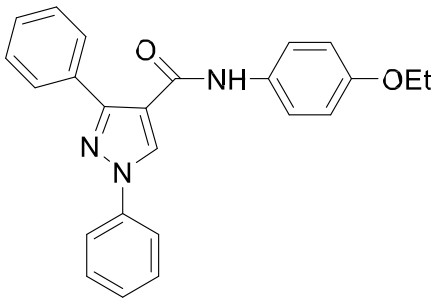


4,5-dihydro-5-(4-methoxyphenyl)-3-(3,4-dimethylphenyl)pyrazole-1-carboxamide

A series of 1H-pyrazole-4-carboxamide derivatives were created by Li et al. (2012), who also reported on their possible antiproliferation and Aurora-A kinase inhibitory properties. With IC50 values of 0.39 and 0.46 µM, respectively, N-(4-ethoxyphenyl)-1,3-diphenyl-1H-pyrazole-4-carboxamide demonstrated the strongest biological activity against the HCT116 and MCF-7 cell lines among the compounds.[30]



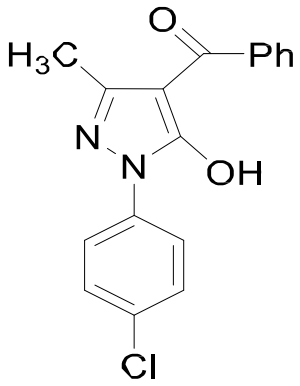
1-(3,5-dichlorophenyl)-4-(4,5-dihydro-1H-imidazol-2-yl)-1H-pyrazol-5-amine



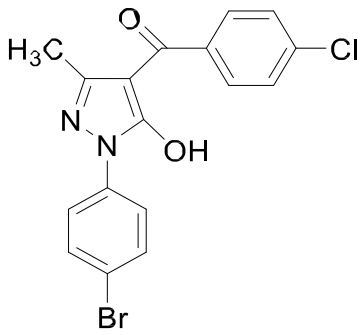
N-(4-ethoxyphenyl)-1,3-diphenyl-1H-pyrazole-4-carboxamide

Anti-tubercular

In 2006, Manetti et al. created novel Mycobacterium tuberculosis inhibitors. With a MIC value of 25 µM/mL, the compound (1-(- chlorophenyl)-5-hydroy-3-methyl-1H-pyrazol-4-yl)(phenyl)methanone was determined to be the most active agent.[31] The compound (1-(4-bromophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)(4-chlorophenyl)methanone of pyrazole derivatives was synthesized by Castagnolo et al. (2008) and tested as an inhibitor of M. tuberculosis H37Rv, continuing our earlier work that focused on the identification of antimycobacterial compounds with novel structures. It was demonstrated that the pyrazole compounds containing the p-bromophenyl group at the N1 position were very active.[32] Shelki et al. (2012) reported and screened a novel family of fluorinated pyrazoles for their anti-tubercular properties against Mycobacterium TB H37Rv in vitro. With respect to the M. tuberculosis H37Rv strain, the chemical 4-(5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-3-(4-fluorophenyl)-1-phenyl-1H-pyrazole shown notable anti-tubercular properties (MIC=6.25 µg/mL).[33]



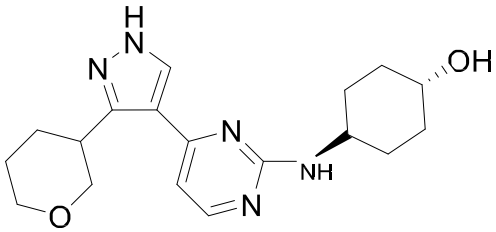
(1-(4-chlorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)(phenyl)methanone



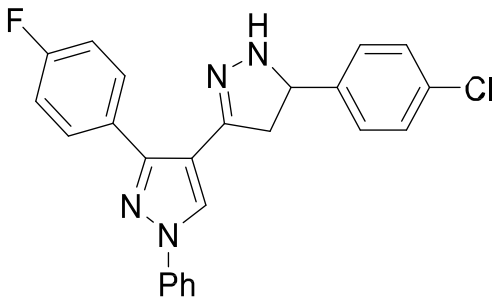
(1-(4-bromophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)(4-chlorophenyl)methanone

Anti-diabetic

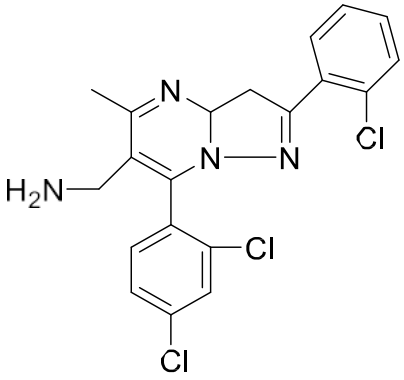
In order to inhibit c-Jun-N-terminal kinases, Humphries et al. (2009) developed a series of new 4-pyrazolyl-2- aminopyrimidines. The molecule (1s,4s)-4-(4-(3-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4- yl)pyrimidin-2-ylamino)cyclohexanol was identified as a result of this investigation, and it demonstrated good selectivity across a panel of different proteins and lipids.[34] A number of pyrazolopyrimidines were described by Brigance et al. and assessed as dipeptidyl peptidase-4 (DPP4) inhibitors. Seven-(2,4- dichlorophenyl)-2-(2-chlorophenyl) is one of the compounds that has been reported. 5, methylpyrazolo-3,3a-dihydro[1,5-a]pyrimidin-6-yl) Compared to the other dipeptidyl peptidase, methanamine showed the highest potency (Ki=20 Nm) and superior selectivity.[35]



(1s,4s)-4-(4-(3-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)pyrimidin-2-ylamino)cyclohexanol



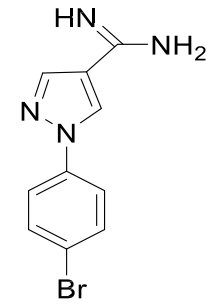
4-(5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-3-(4-fluorophenyl)-1-phenyl-1H-pyrazole



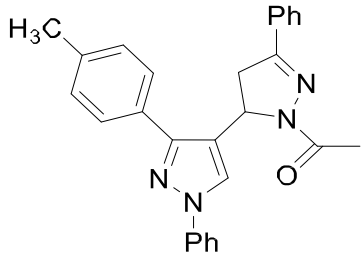
(7-(2,4-dichlorophenyl)-2-(2-chlorophenyl)-3,3a-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl)methanamine

Anti-leishmanial

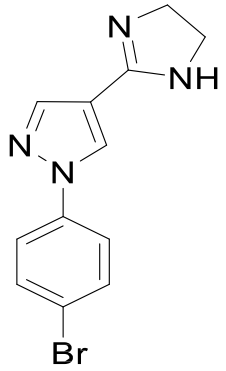
New 1-Aryl-1H-pyrazole-4-carboximimidamide derivatives were synthesized and their anti-leishmanial properties assessed in vitro by Dos Santos et al. (2011a). Medicinal chemistry techniques can be used to enhance the activity profile of compound 1-(4-bromophenyl)-1H-pyrazole-4-carboxamide.[36] The novel 1-aryl-4-(4,5-dihydro-1H-imidazol-2-yl)-1H-pyrazole series was described by Dos Santos et al. (2011b) and tested in vitro against three Leishmania species: L. amazonensis, L. braziliensis, and L. infantum. With an IC50 value of 15 µM, 1-(4-bromophenyl)-4-(4,5-dihydro-1H-imidazol-2-yl)-1H-pyrazole was shown to be the most active molecule among those that were evaluated on promastigotes forms of L. amazonensis.[37]



1-(4-Bromophenyl)-1H-pyrazole-4-carboxamidine

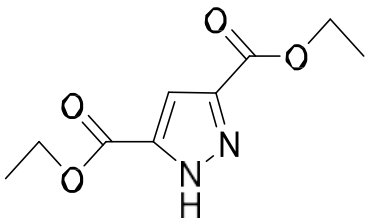


1-(4,5-dihydro-3-phenyl-5-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)pyrazol-1-yl)ethanone



1-(4-Bromophenyl)-4-(4,5-dihydro-1H-imidazol-2-yl)-1H-pyrazole

Tuha et al were developed a new series of pyrazole derivatives and tested *in vitro* for their anti-leishmanial activity. Compound 1- (4,5-dihydro-3-phenyl-5-(1-phenyl-3-p-tolyl-1H-pyrazol-4- yl)pyrazol-1-yl)ethenone was found to be the most active than the standard multefosine and amphotericin B deoxycholate for Leishmania donovani.[38] Reviriego et al (2017) reported the synthesis of some simple dialkyl pyrazole-3,5-dicarboxylates against *Trypanosoma cruzi, Leishmania infantum* and *Leishmania braziliensis.* The compound diethyl-1H-pyrazole-3,5-dicarboxylate showed high efficiency against the mentioned protozoa.[39]

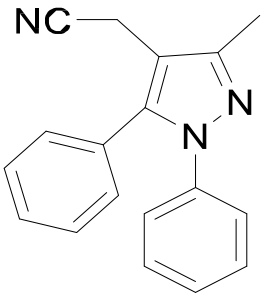


Diethyl 1H-pyrazole-3,5-dicarboxylate

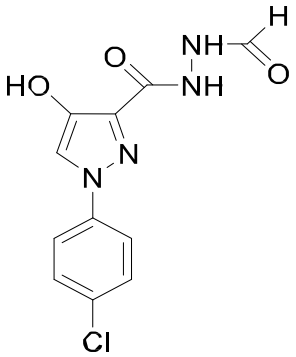
Anti-viral

A new class of HIV-1 nonnucleoside reverse transcriptase inhibitors, the 1,5-diphenylpyrazole class, was created by Genin et al. (2000). In comparison to both wild-type and delaviridine-resistant P236L reverse transcriptase, compound 2-(3-methyl-1,5-diphenyl-1H-pyrazol-4-yl)acetonitrile was shown to exhibit good performance.[40] Using the reverse transcriptase-polymerase chain reaction technique, Rostom et al. (2003) reported a new series of 1-(4-chlorophenyl)-4-hydroxy-1H-pyrazole-3-carboxylic acid hydrazide analogs and evaluated their in vitro impact on the replication of the hepatitis-C virus (HCV) in HepG2 hepatocellular carcinoma cell line infected with the virus. The findings showed that, at concentrations between 10 and 100µg/ml, chemical 1-(4-chlorophenyl)-N- formyl-4-hydroxy-1H-pyrazole-3-carbohydrazide may block the replication of both the HCV RNA(+)

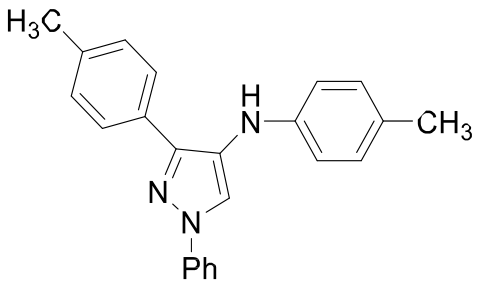
and (-).[41] The series of N-((1,3-diphenyl-1H-pyrazol-4-yl)methyl)anilines was described by Fioravanti et al. (2015), who also assessed the compounds' cytotoxicity and antiviral activity against a wide range of viruses in vitro. At micromolar concentrations, the majority of the examined substance 1-phenyl-N,3-dip-tolyl-1H-pyrazol-4-amine inhibited RSV replication.[42]



2-(3-Methyl-1,5-diphenyl-1H-pyrazol-4-yl)acetonitrile



1-(4-Chlorophenyl)-N'-formyl-4-hydroxy-1H-pyrazole-3-carbohydrazide

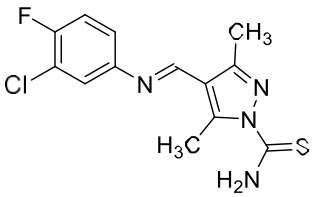


1-Phenyl-N,3-dip-tolyl-1H-pyrazol-4-amine

Anti-Parkinson

Several new pyrazole derivatives containing a quinolone moiety were synthesized and tested for their anti- inflammatory and ulcerogenic effect. Hussain et al (2015) synthesized pyrazole derivatives and investigated them for their, anti-inflammatory and analgesic

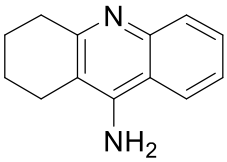
activity. Results indicated that (E)-4-(((3-chloro-4-fluorophenyl)imino)methyl)-3,5-dimethyl-1H-pyrazole-1- carbothioamide showed anti-inflammatory activities.[43][44]



(*E*)-4-(((3-chloro-4-fluorophenyl)imino)methyl)-3,5-dimethyl-1*H*-pyrazole-1-carbothioamide

Anti-cholinesterase

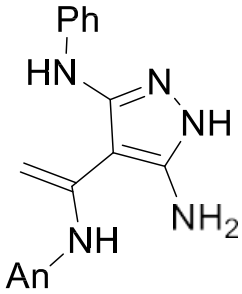
The anti-cholinesterase activity of the target compound was assessed *in vitro* against AchE from Electrophorus electrics and horse serum butyrylcholinesterase in comparison to tacrine as the reference drug.[45]



Tacrine

Antimicrobial

Bondock et al (2008) reported the synthesis and antimicrobial activity of some new heterocycles incorporating antipyrine moiety. 2-cyano-N-(1,5-dimethyl- 3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) acetamide was utilized as a key intermediate for the synthesis of some new coumarin, pyridine, pyrrole, thiazole, pyrido, pyrazolo triazine and amino pyrazole.[46]

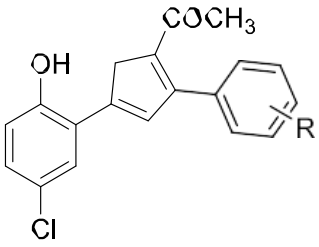


2-cyano-N-(1,5-dimethyl- 3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) acetamide

Analgesic

Rajasekaran et al. (2012) synthesized novel [1-(3-(5-chloro-2-hydroxy phenyl)-5-aryl-4,5-

dihydro pyrazol-1-yl] ethanone derivatives and used the acetic acid-induced writhing inhibition method to test for analgesic efficacy. When compared to a typical medicine, the results indicated that all of the synthesized compounds had considerable activity.[47][48]

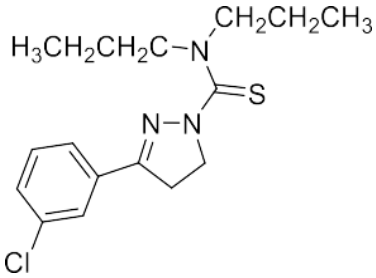


R=C_6H_5, 2-Furyl, 4-$NO_2C_6H_5$

[1-(3-(5-chloro-2-hydroxy phenyl)-5-aryl-4,5-dihydro pyrazol-1-yl] ethanone

Anti-amoebic

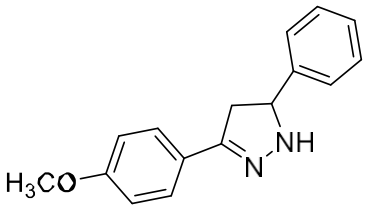
Abid et al 2005, examined the anti-amoebic properties of a number of novel 1-N-substituted cyclized pyrazolines that were synthesized and compared to thiosemicarbazole.[49]



1-N-substituted cyclized pyrazolines

Neuroprotective

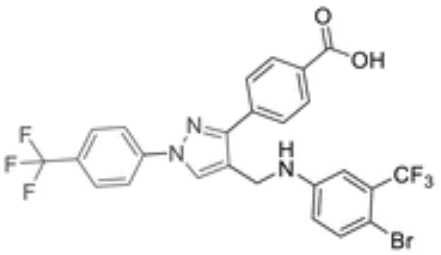
Cocconcelli et al (2008), have explained how aryl azoles are synthesized in parallel. Here, acetic acid was employed as a catalyst to cause the regioselective synthesis of 4,5-dihydro-1H-pyrazole through the reaction of substituted phenylhydrazine with an α, β-unsaturated ketones. Compounds have strong neuroprotective properties.[50]



4,5-dihydro-1H-pyrazole

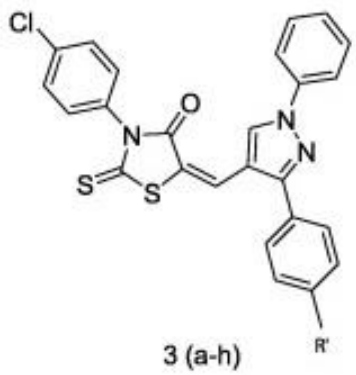
Anti-bacterial

The N-(trifluoromethyl)phenyl substituted pyrazole derivative effectively limit the growth of Gram-positive bacteria that are resistant to antibiotics and stop methicillin-resistant Staphylococcus aureus (MRSA) and Enterococcus faecalis from forming biofilms. These substances were found to be more effective than the control antibiotic, vancomycin, at eliminating the preformed biofilms. Strong substances exhibited a selectivity factor of >20 and minimal toxicity to human embryonic kidney cells in vitro. The most promising chemical is highly effective against clinical isolates of Enterococcus fecium that are resistant to vancomycin, oxacillin, and meropenem. Macromolecular synthesis inhibition tests revealed a wide variety of inhibitory effects, indicating targets that impact bacterial cell activity globally.[51]



N-(trifluoromethyl)phenyl substituted pyrazole

The 3-(4-chlorophenyl)-5-((1-phenyl-3-aryl-1H-pyrazol-4-yl)methylene) is a class of new derivative. They have synthesized 2-thioxothiazolidin-4-one (3a-h). Using widely available antibiotics like ampicillin as a benchmark medication, these newly synthesized compounds were tested for in vitro antibacterial activity against Escherichia coli (MTCC 443), Pseudomonas aeruginosa (MTCC 1688), Staphylococcus aureus (MTCC 96), and Staphylococcus pyogenes (MTCC 442). While compounds 3a, 3d, and 3g were found to be effective against S. aureus and 3d against S. pyogenes, compound 3c was found to be effective against E. coli. Using griseofulvin as a reference medication, these compounds were evaluated for their in vitro antifungal efficacy against Aspergillus niger (MTCC 282), Candida albicans (MTCC 227), and Aspergillus clavatus (MTCC 1323). It was discovered that compounds 3b and 3d exhibited very excellent efficacy against Candida albicans. Variable and mild activity were noted against the bacterial and fungal strains under investigation.[52]



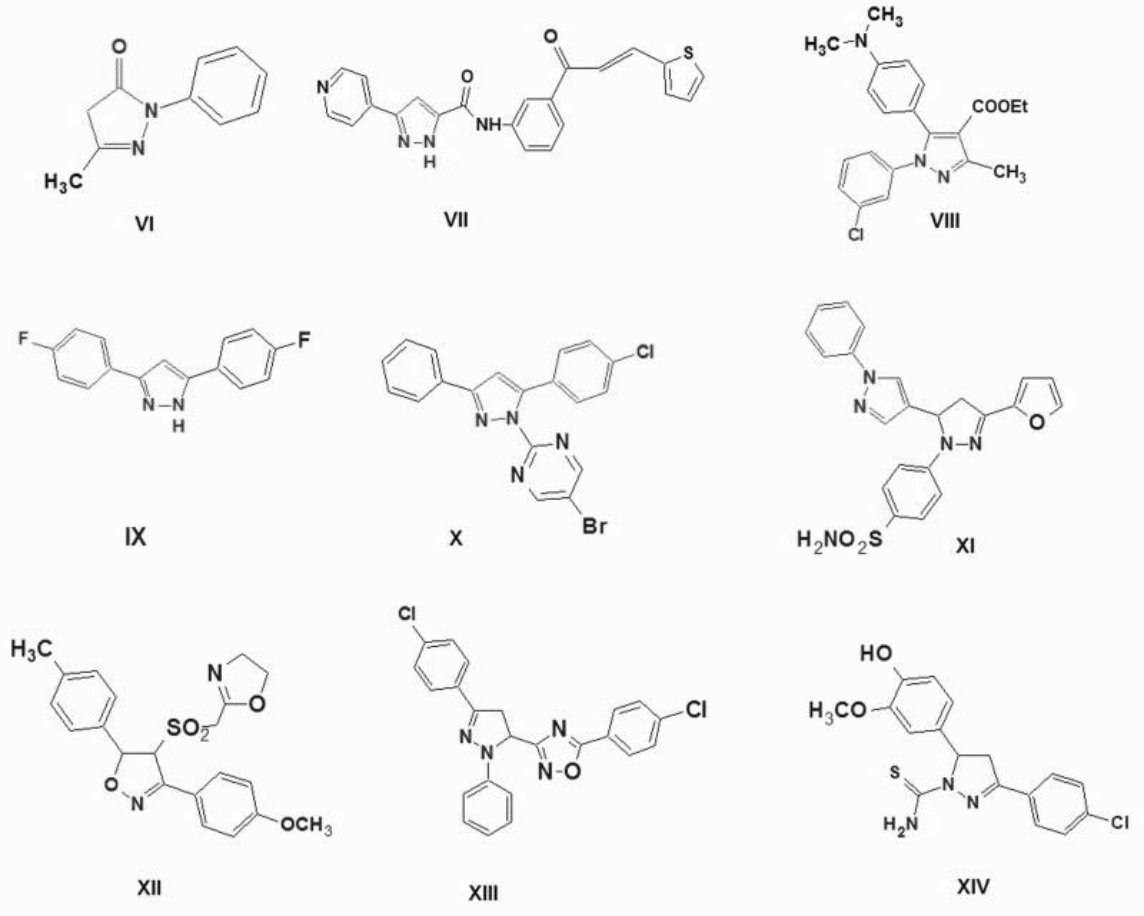
3 (a-h)

	3a	3b	3c	3d	3g	3h
R`	-H	$-CH_3$	-OH	$-NO_2$	-Cl	$-OCH_3$

3-(4-chlorophenyl)-5-((1-phenyl-3-aryl-1H-pyrazol-4-yl)methylene)

Antioxidant

By boosting antioxidant enzymes like GPx and slowing down the lipid peroxidation process, the pyrazole (1,2-diazole) exhibits antioxidant activity and can stop oxidative stress. Examples of 1,2-diazole's or its related medications' pharmacological effects. It was discovered that 1,2-Diazole effectively prevented nephrotoxicity brought on by the anti-neoplastic medication cisplatin. A new antioxidant called edaravone VI has been used as a stroke support treatment for patients who have had cerebral infarction. Among the synthetic pyrazoles that have been reported: Strong radical scavenging activity (RSA) was demonstrated by 3-(Pyridin-4-yl)-1H-pyrazole-5-carboxamide chalcones VII against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. Moreover, 1,5-diarylpyrazoles VIII shown good DPPH RSA when compared to the usual ascorbic acid. It was discovered that 3,5-diarylpyrazole IX also exhibited strong RSA. Furthermore, employing DPPH, the 3,5-diarylpyrazoline derivative X demonstrated outstanding RSA. In the DPPH experiment, bipyrazole XI and other pyrazole derivatives shown good scavenging performance (19%, BHT7=20%) at 10−4 M concentration. Additionally, when compared to ascorbic acid33, bis-isoxazoline XII shown good RSA utilizing DPPH, NO, and H2O2 techniques. Moreover, DPPH RSA was strong in Pyrazolyl-1,2,4-oxadiazoles XIII. In the DPPH technique, derivative XIV of 4,5-Dihydropyrazole-1-carbothioamide shown strong antioxidant activity at low concentrations (0.25mg/ml).[53]



Diverse derivatives of pyrazole (1,2-diazole)

CONCLUSION

Pyrazoles are a type of heterocyclic compounds with two nitrogen atoms and five members. They are vital hit molecules for creating novel pharmacological treatments that target a range of clinically significant infections, which is why they are so important in drug development. Pyrazole synthesis techniques have advanced quickly due to the wide range of pharmaceutical uses for pyrazoles. A variety of efficient and adaptable methods have emerged in the past ten years, including the utilization of transition-metal catalysts and photoredox reactions, one-pot multicomponent processes, new reactants, and unique reaction modalities.

In conclusion, Numerous pharmacological properties have been reported for the novel derivatives of pyrazoles including anti-inflammatory, analgesic, anti-diabetic, anti-viral, anti-diarrhoeal, anti-cancer, anti-tubercular, anti-leishmanial, antibacterial, antioxidant, anti-cholinesterase, anti-Parkinson, and neuroprotective. Different nuclei added to pyrazole derivatives have been observed to exhibit a range of pharmacological profiles. The chemical

pyrazole can be utilized to increase biological activity in a variety of heterocyclic systems. Pyrazole derivatives may be a rich source of potential entities in the study of a new generation of physiologically active molecules.

CONFLICT OF INTEREST

None.

FUNDING

Nil.

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