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Synthesis and Characterization of Some Pyrazole Based Heterocyclic Compounds

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ABSTRACT

The reaction of phenyl hydrazine with ethyl acetoacetate gave 3-methyl-1-phenyl-5-pyrazolone(1), which then treated with malonitrile and benzaldehyde to give 6-amino-3-methyl-1,4-dihydropyrano [2,3-b]pyrazole-5-carbonitrile(2) which considered assynthone for prepare some new pyrazole derivatives (3a-j).The structure of the prepared compounds was suggested in the IR , 1 H-NMR, 13 C-NMR and UV Spectroscopy. Many steps starting from esterification of isophthalic acid to yield diester compound [I] which was converted to their acid hydrazide [II], then the later compound reacted with ethylacetoacetate to yield pyrazol-5-one compound [III]. Afterword added acetyl chloride to give the compound [IV], there action of this compound with theiosemicarbazide ledto produce a new carbothioamide compound [V], Which was reacted with ethyl chloro acetate to yield thethioxoimidazolidin compound [VI]. The condensation reaction of this compound with different substituted aldehyde give new alkene derivatives[VII]a-d. The synthesized compounds were characterized by melting points , FT-IR ,1H-NMR and Mass spectroscopy.

KEYWORDS: *pyrazole, synthesis, characterization, heterocyclic, compounds, spectroscopy, melting points*

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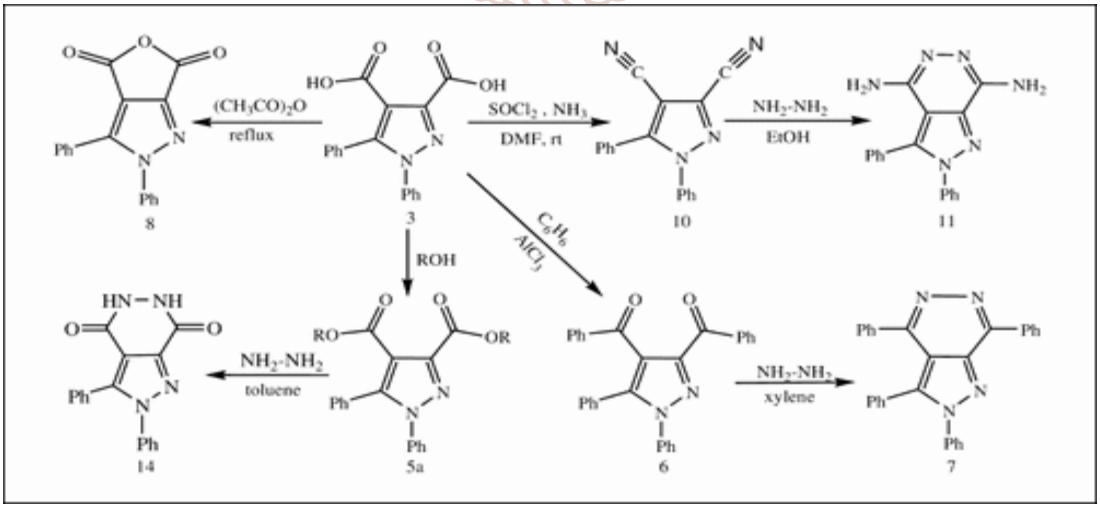
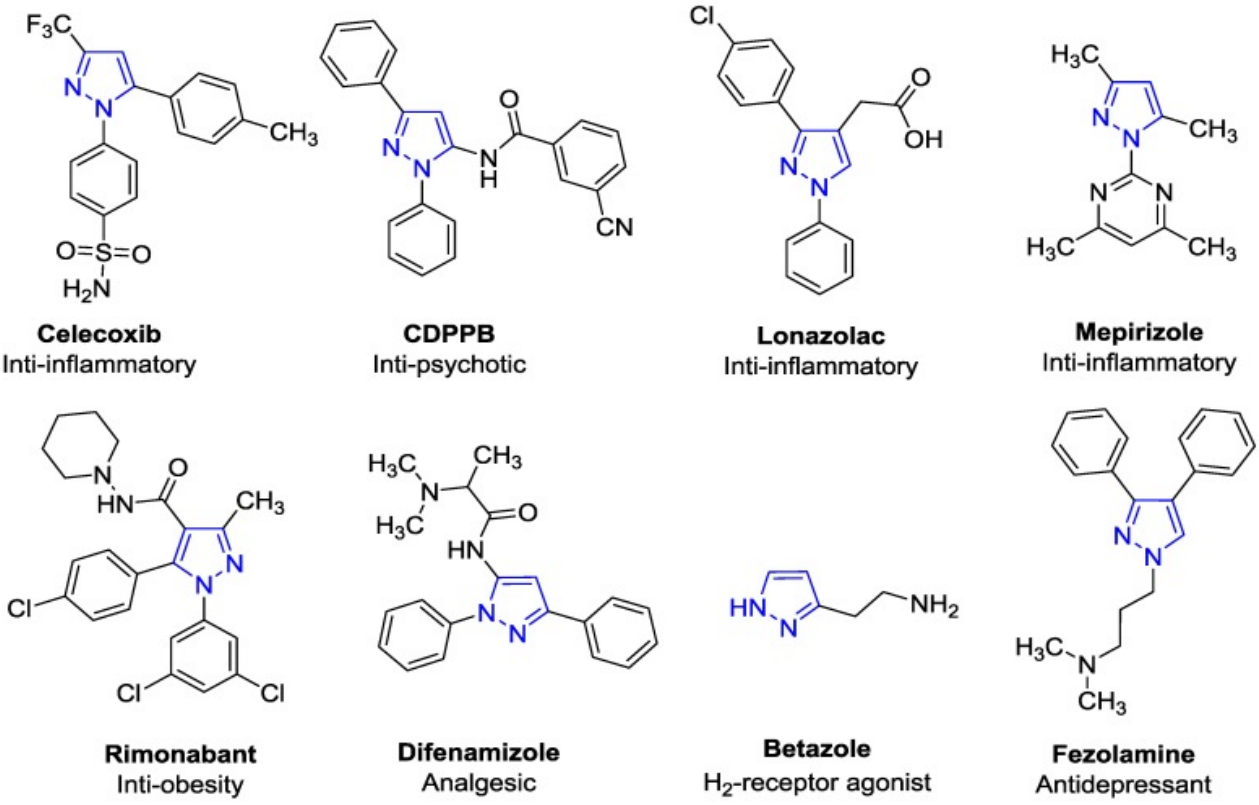
INTRODUCTION

Compound of 4-(ethoxycarbonyl)-1,5-diphenyl-1*H*-pyrazole-3-carboxylic acid 2 was obtained from the reaction of ethyl 4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate and 1-benzylidene-2-phenylhydrazine. A number of substitute pyrazole dicarboxylic acid derivatives were synthesized from 1, 5-diphenyl-1*H*-pyrazole-3, 4-dicarboxylic acid 3 which was prepared from basic hydrolysis[1,2]



Pyrazole and its derivatives are considered a pharmacologically important active scaffold that possesses almost all types of pharmacological activities. The presence of this nucleus in pharmacological agents of diverse therapeutic categories such as celecoxib, a potent anti-inflammatory, the antipsychotic CDPPB, the anti-obesity drug rimonabant, difenamizole, an analgesic, betazole, a H2-receptor agonist and the antidepressant agent fezolamide have proved the pharmacological potential of the pyrazole moiety. Owing to this diversity in the

biological field, this nucleus has attracted the attention of many researchers to study its skeleton chemically and biologically. This review highlights the different synthesis methods and the pharmacological properties of pyrazole derivatives. Studies on the synthesis and biological activity of pyrazole derivatives developed by many scientists around the globe. [3,4]



Low quality of life and life-threatening conditions often demand pharmacological screening of lead compounds. A spectrum of pharmacological activities has been attributed to pyrazole analogs. The substitution, replacement, or removal of functional groups on a pyrazole ring appears consistent with diverse molecular interactions, efficacy, and potency of these analogs.

Series of methyl 3- and 5-(*N*-Boc-piperidinyl)-1*H*-pyrazole-4-carboxylates were developed and regioselectively synthesized as novel heterocyclic amino acids in their *N*-Boc protected ester form for achiral and chiral building blocks. In the first stage of the synthesis, piperidine-4-carboxylic and (*R*)- and (*S*)-piperidine-3-carboxylic acids were converted to the corresponding β-keto esters, which were then treated with *N*,*N*-dimethylformamide dimethyl acetal. The subsequent reaction of β-enamine diketones with various *N*-mono-substituted hydrazines afforded the target 5-(*N*-Boc-piperidinyl)-1*H*-pyrazole-4-carboxylates as major products, and tautomeric NH-pyrazoles prepared from hydrazine hydrate were further *N*-alkylated with alkyl halides to give 3-(*N*-Boc-piperidinyl)-1*H*-pyrazole-4-carboxylates.[5,6]

Discussion

Pyrazole are potent medicinal scaffolds and exhibit a full spectrum of biological activities. This review throws light on the detailed synthetic approaches which have been applied for the synthesis of pyrazole. This has been followed by an in depth analysis of the pyrazole with respect to their medical significance. This follow-up may help the medicinal chemists to generate new leads possessing pyrazole nucleus with high efficacy. Pyrazole is a five-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions as represented by the molecular formula $C_3H_4N_2$. It is a weak base, with pKb 11.5 (pKa of the conjugated acid 2.49 at 25°C). The term pyrazole was first coined by Ludwig Knorr in 1883. Due to its composition and unique pharmacological effects on human beings, they are classified as alkaloids. 1-pyrazolyl-alanine was the first natural pyrazole isolated from watermelon seeds in the year 1959. Pyrazoles are reported to possess a wide range of biological activities in literature such as anti-microbial, anti-fungal, anti-tubercular, anti-inflammatory, anti-convulsant, anticancer, anti-viral, angiotensin converting enzyme (ACE) inhibitory, neuroprotective, cholecystokinin-1 receptor antagonist, and estrogen receptor (ER) ligand activity, etc. Many pyrazole derivatives has already found their application as nonsteroidal anti-inflammatory drugs clinically, such as anti-pyrine or phenazone (analgesic and antipyretic), metamizole or dipyrone (analgesic and antipyretic), aminopyrine or aminophenazone (anti-inflammatory, antipyretic, and analgesic), phenylbutazone (anti-inflammatory, antipyretic

mainly used in osteoarthritis, rheumatoid arthritis, spondylitis, Reiter's disease), sulfinpyrazone (chronic gout), and oxyphenbutazone (antipyretic, analgesic, anti-inflammatory, mild uricosuric).[7,8]

For a very long time, the usefulness and great therapeutic value of pyrazole nucleus have been recognized and widest range of activities of this nucleus evaluated. However, as the first synthetic organic compound having pyrazoline-5-one nucleus, to find use as an important drug. Phenylbutazone as a prototype of pyrazolidinedione is a very potent anti-inflammatory agent, but its use is now banned in some countries. Later on, many modifications of pyrazole nucleus were attempted and several compounds have been synthesized which serves as the basis for the treatment of different diseases like-inflammation, pain, cancer, tuberculosis, and diseases caused by bacteria.

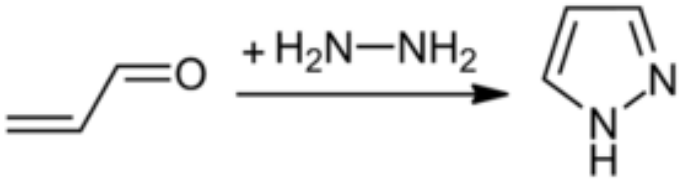
The designing and synthesis of new pyrazole derivatives is very important for biological and pharmacological activities. This derivative is behaving as anti-cancer, antiinflammatory, anti-oxidant, anti-fungal, anti-glycemis, anti-amoebic and anti-depressive. Pharmacological activities of some of the drug molecules improved due to pyrazole nucleus directly attached to heterocyclic moieties. Most of the pyrazole containing heterocyclic compounds existed in market as drugs like cartazolate, zaleplon, sildenafil, allopurinol, indiplon, etazolate, etc. Fused pyrazole derivatives, particularly pyrazoloazines were reported to mimic purine bases, present in DNA and RNA because of their close structure resemblance. Pyrazole is a five membered heteroaromatic compound which contains two adjacent nitrogen atoms. NH-Pyrazoles as weak bases and moderately weak acids because of having a pyridine type proton acceptor nitrogen atom (C=N) and proton donating behaviour of one pyrrole-type nitrogen atom (N-H). The metal complex is prepared with different type of pyrazoles derivatives due to pyridine -like N-atom present in the respective ligand. Pyrazoles compounds can react with electrophilic reagents at fourth position easily and will react to nucleophiles poorly at position of 3 and 5 due to π-excess aromatic heterocyclic. However, pyrazole reactivity can be increased in both electrophiles and nucleophiles by introducing electron withdrawing (EWG) or electron donating groups (EDG) attached to pyrazole derivative. Physicochemical properties of pyrazole are mainly depends on nitrogen atoms and electronic effects of substituents attached to the ring system[9,10]

We can synthesize more conjugated compounds like as substituted phenyl, fluorene, anthracene, and pyrene based pyrazole derivatives with good yield. All the compounds were thoroughly characterized by various spectral techniques such as NMR and mass analysis. Further, we studied the photophysical behavior of some strained/sterically hindered pyrazole derivatives (hybrids) upon the addition of analytes using UV-visible spectroscopic techniques. All the hybrid compounds are good colorimetric sensor for copper(II) ion. AS1, AS2 and AS3 hybrid compounds limit of detections are 0.62 mM, 0.47 mM, and 4.4 mM respectively. The Binding constant of the hybrid compounds of AS1, AS2 and AS3 are 3.1 x 10-2 M, 2.3 x 10-2 M and 3.9 x 10-2 M respectively. The detection limit and binding constant of anthracene based hybrid AS2 are superior when compared to AS1 and AS3. In addition to that we found ligand to metal charge transfer in AS1 and AS2. Further, ligand to the metal charge transition of the probe with analyte were confirmed by density function theory (DFT) through Gaussian 09 Software.[11]

Results

The 4-acetyl-5-methyl-2-(4-methylphenyl)-2,4-dihydro-3H-pyrazol-3-one condense with various substituted aromatic aldehyde were yield various chalcone. Further this chalcone converted into pyrazole by condensation of various synthesized chalcone with isoniazide. In the present research article a new series of pyrazole derivatives have been synthesized. The structures of newly synthesized compounds are characterized on the basis of IR, 1HNMR, Mass spectroscopies and elemental analysis. The newly synthesized compounds were studied for antimicrobial activity. The 4-acetyl-5-methyl-2-(4-methylphenyl)-2,4-dihydro-3H-pyrazol-3-one was prepared by reported method. The IR spectra were recorded by a Perkin-Elmer 237 spectrophotometer and 1H NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker AM 400 instrument (at 400MHz). Mass spectra (MS) were recorded on M S route JMS 600-H. Melting points were determined in open capillary tubes and were uncorrected. All the synthesized compounds were purified by recrystallization method. The reactions were followed up and the purity of compounds was checked on pre-coated TLC plates. In results, in present we can prepare new pyrazoline derivatives says, 1-isonicotinoyl-3'-methyl-5-aryl-1'-p-tolyl4,5-dihydro-1H,1'H-3,4'-bipyrazol-5'(4'H)-one. All the synthesized compounds were studied for antimicrobial activity which shows good activity.

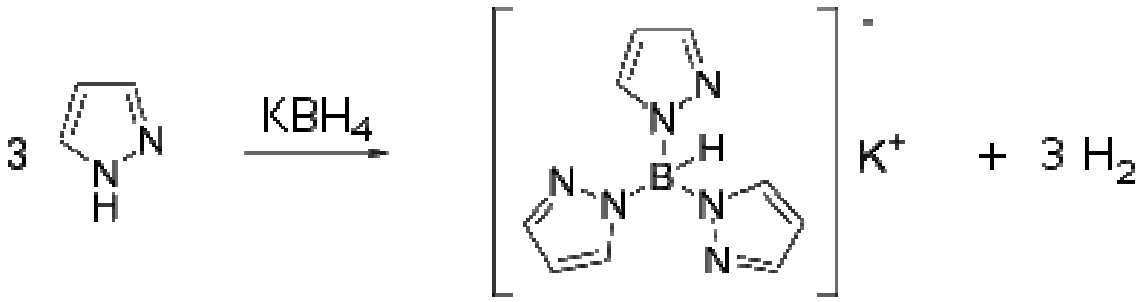
Pyrazoles are synthesized by the reaction of α, β-unsaturated aldehydes with hydrazine and subsequent dehydrogenation:



Substituted pyrazoles are prepared by condensation of 1,3-diketones with hydrazine (Knorr-type reactions). For example, acetylacetone and hydrazine gives 3,5-dimethylpyrazole:

$$CH_3C(O)CH_2C(O)CH_3 + N_2H_4 \rightarrow (CH_3)_2C_3HN_2H + 2\ H_2O$$

Pyrazoles react with potassium borohydride to form a class of ligands known as scorpionate. Pyrazole itself reacts with potassium borohydride at high temperatures (~200 °C) to form a tridentate ligand known as Tp ligand:



Stanozolol, also known as 17α-methyl-2'*H*-androst-2-eno[3,2-*c*]pyrazol-17β-ol, is a synthetic 17α-alkylated and rostane steroid and a derivative of 5α-dihydrotestosterone (DHT) with a methyl group at the C17α position and a pyrazole ring attached to the A ring of the steroid nucleus. Stanozolol is subject to extensive hepatic biotransformation by a variety of enzymatic pathways. The primary metabolites are unique to stanozolol and are detectable in the urine for up to 10 days after a single 5–10 mg oral dose. Methods for detection in urine specimens usually involve gas chromatography-mass spectrometry or liquid chromatography-mass spectrometry.[12,13] Stanozolol has been investigated in the treatment of a number of dermatological conditions including urticaria, hereditary angioedema, Raynaud's phenomenon, cryofibrinogenemia, and lipodermatosclerosis

Conclusions

3,5-Dimethylpyrazole is an organic compound with the formula $(CH_3C)_2CHN_2H$. It is one of several isomeric derivatives of pyrazole that contain two methyl substituents. The compound is unsymmetrical but the corresponding conjugate acid (pyrazolium) and conjugate base (pyrazolide) have C_{2v} symmetry. It is a white solid that dissolves well in polar organic solvents.

It is a precursor to a variety of ligands that are widely studied in coordination chemistry including trispyrazolylborate, a trispyrazolylmethane, and a pyrazolyldiphosphine.

Condensation of acetylacetone and hydrazine gives 3,5-dimethylpyrazole:

$$CH_3C(O)CH_2C(O)CH_3 + N_2H_4 \rightarrow (CH_3C)_2CHN_2H + 2\ H_2O$$

It has found use as a blocking agent for isocyanates

Pyrazolidine can be produced by cyclization of 1,3-dichloropropane or 1,3-dibromopropane with hydrazine [14,15]

References

[1] C. H. Lakshmi Praveena, V. Esther Rani, Y. N. Spoorthy and L. K. Ravindranath, Journal of Chemical and Pharmaceutical Research, 2013, 5(5), 280-292.

[2] P. J. Shah, P. N. Patel, K. D. Patel and H. S. Patel, heteroletters, 2014, 4(4), 537-547.

[3] N. V. Kavitha, K. Divekar, Der pharma chemical, 2011, 3(4), 55-62.

[4] K. Karrouchi, Y. Charkaoui, K. Benlafya, Y. Ramli, J. Taoufik, S. Radi and M. Ansar, J. of Chemical and Pharmaceutical Research, 2013, 5(3), 1-6.

[5] P J Shah, H S Patel and B P Patel, Journal of Saudi Chemical Society, 2013, 17, 307-313.

[6] A. Goyal, S. Jain, Der chemica sinica, 2012, 3(1), 249-254.

[7] P J Shah, H S Patel and B P Patel, Orbital – The Electronic Journal of Chemistry, 2010, 2(3), 303-310.

[8] S. Kucukguzel, S. Rollas, European Journal Medicinal Chemistry, 2000, 35, 761-771.

[9] P J Shah, H S Patel and B P Patel, Bulgarian Chemical Communications, 2010, 42(4), 274.

[10] Satyanarayana M., Tiwari P., Tripathi B. K., Sriwastava A. K., Pratap R., Bioorg. Med. Chem., 2004, 12, 883.

[11] S. Mukherjee, N. Kumar, A. K. Parasad, H. G. Raj, M. E. Bracke, C. E. Olsen, S. C. Jain, V. S. Parmar, Bioorg. Med. Chem, 2001, 9, 337.

[12] S. B. Zangade, J. D. Jadhav, Y. B. Vibhute, B. S. Dawane, J. Chem. Pharm. Res. , 2010, 2, 310e314.

[13] K. L. Lahtchev, D. I. Batovska, St. P. Parushev, V. M. Ubiyvovk and A. A. Sibirny, Eur. J. Med. Chem. , 2008, 43, 2220e2228.

[14] J. Wu, J. Li, Y. Cai, Y. Pan, F. Ye, Y. Zhang, Y. Zhao, S. Yang, X. Li and G. Liang, Journal of Medicinal chemistry, 2011, 54, 8110.

[15] P. J. Shah and J. D. Patel, Asian Journal of Chemistry, 2010, 22(4), 3069-3075.