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"Biological Properties, Characterization And Synthesis Of Pyrazolones And Pyrazolones Derivatives – An Overview"

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Abstract :

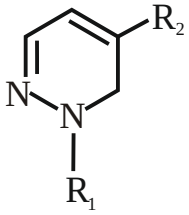
Chemistry very much contributed in the field of agriculture, medicines, industrial technologies, health sectors, pharmaceutical industries etc. Recently inorganic chemistry has gathered an enormous interest from the researchers worldwide.

In recent years nitrogen containing five membered heterocyclic compounds are gained much more attention in the field of chemistry because efficiency in the catalytic activities, biological activities anti-microbial activities, anti-inflammatory activities, anti-viral activities, anti-cancer activities, anti-fungal activities, pyrazole, pyrazolones and pyrazolones derivatives are five membered heterocyclic compounds have attracted the attention of researchers due to their potent biological activities synthesis of various compounds based on the pyrazole and pyrazolone rings. Synthesized compounds were characterized using, FTIR, 'H-NHR, ^{13}C-NMR, chemical analysis and mass spectra. These compounds shows activity against bacteria, fungi, virus etc. The anti-microbial activity of pyrazolone and pyrazolones derivatives shows much more attention of researchers in recent years for the welfare of human being.

Keywords : Pyrazolone, Pyrazolone derivatives, anti-microbial activity, anti-inflammatory activity, anti-virus, anti-cancer bidentate ligand, complex compounds etc.

Introduction :

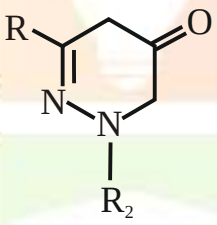
Pyrazole and its derivatives shows various properties. It is five-membered heterocyclic rings with N-atoms surrounded by double bonds. Pyrazoles posses two double bonds and shows aromatic characters and exists in isomeric forms. Pyrazoles and their derivatives shows many biological processes such as catalysis, building materials of compounds agrochemicals, microbial properties and in medicine.



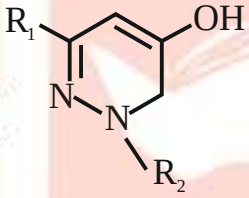
Pyrazole

Pyrazole derivatives shows anti-microbial, anti-glycerin, anti-cancer, anti-inflammatory, anti-allergy, anti-cancer and anti-viral properties.

Pyrazolone is heterocyclic compounds possess two double bonds in five-membered rings exist predominantly in keto form and also exists in enol form.

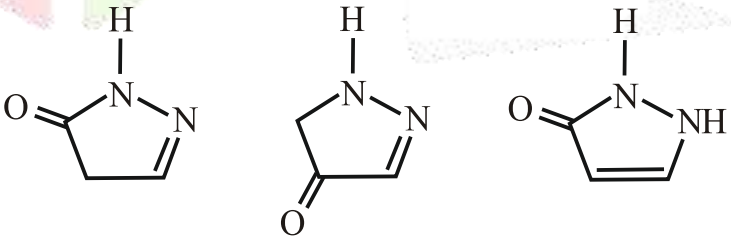


Keto-form



Enol-form

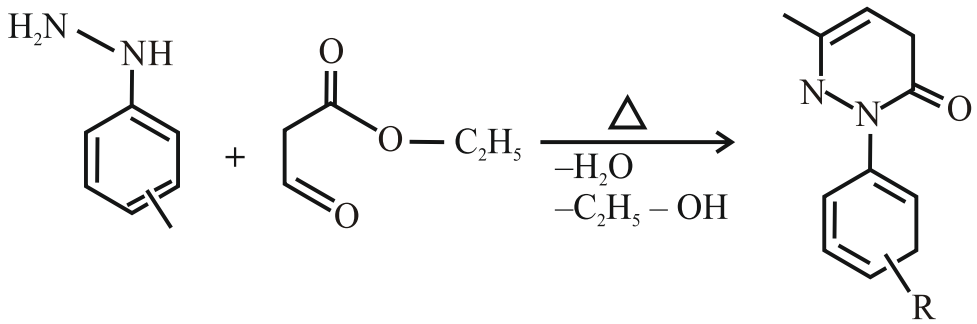
The Keto derivatives known as pyrazolones.



(I) **(II)** **(III)**

Isomers of Pyrazolone

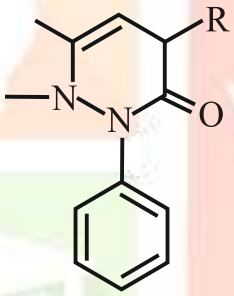
Ludwig knorr first synthesis pyrazolone by the condensation of ethylacetoacetate and phenylhydrazine.



3-methyl-1-phenyl-5-yrazolone synthesis

Pyrazolones ligands use in various biological processes. Sensors, functional materials, catalysis, dyes etc. Many pyrazolone-metal complexes were found to posses potent features like catalytic properties, anti-cancer, anti-oxidant, anti-microbial, anti-fungal, optical properties photoluminescence etc.

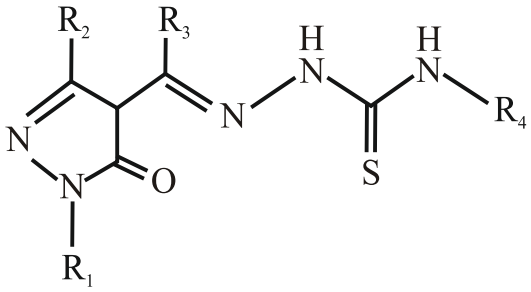
Derivatives of pyrazolone such as aminopyrine, isopropylantipyrine, anti-pyrine, sulpyrine etc. are widely used as anti-inflammatory drugs that exhibits analgesic as well as anti-pyretic properties. Pyrozolones and its derivatives shows allergic reactions and some side effects.



Structure of Pyrazolones

4-thiosemicarbazone-5-pyrazolone :

4-thiosemicarbazone-5-pyrazolone is chelating as well as extracting reagents for metal ions like Zn^{2+}, Cu^{2+}, Fe^{3+}, Ni^{2+}, Na^{+}, Co^{3+} etc. they also shows biological activity and used in co-ordination chemistry widely.

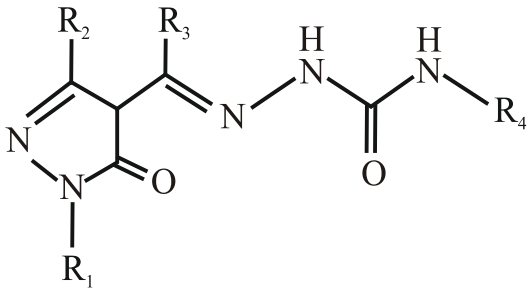


Structure of 4-thiosemicarbazone-5-pyrazolone

4-thiosemicarbazone-5-pyrazolone is a mixture of keto and enol tawtomer forms in the solution. On crystallisation compounds exist in stable forms whereas, during complexation the ligand can exists in enol tautomer and co-ordinates by enolic exygen atom after deprotonation, in the presence of metal ions in solution form.

4-Semicarbazone-5-Pyrazolone :

Due to their superior complex forming ability 4-hydrozone-5-pyrazolones, 4-acythydrazone-5-pyrazolones and 4-thiosemicarbazone-5-pyrazolones compounds are widely uses recently because additional donor atoms in their molecular structure, due to this, pyrazolones and their derivatives shows excellent biological activities.



Structure of 4-semicarbazone-5-pyrazolone

Heterocyclic structure and aromatic character leads to interesting optical properties. Recent studies on pyrazolone derivatives like 4-semicarbazone-5-pyrazolone, 4-thiosemicarbazone-5-pyrazolones have potent biological activities.

4-semicarbazone-5-pyrazolone is synthesised from corresponding 4-acyl pyrazolone and the desired.

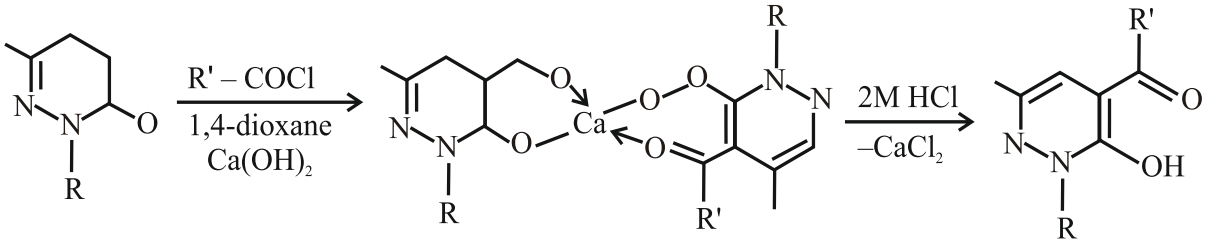
Alkyl or aryl semicarbazide. Jixi et. al in 2011, reported 4-semicarbazone-5-pyrazolone undergo reversible photo colouration and thermal leaching reactions ion pure solid state.

On the irradiation with 365 nm light, the enol form converted to keto form.

4-acyl-5-pyrazolone :

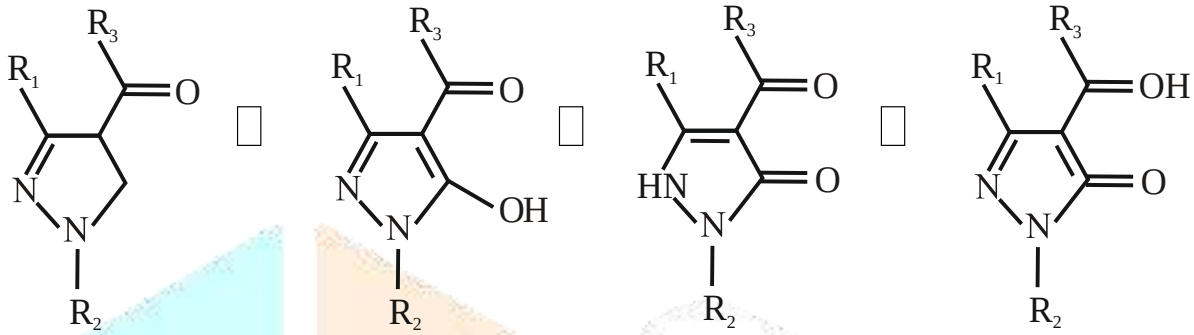
Recently pyrazolone derivatives like dipyrone, antipyrine, propyphenazone and aminopyrine used as an analyesics.

Jensen et al, in 1959, reported that a direct one-step synthesis was effected by treating a solution of 1-phenyl-3-methyl-pyrazol-5-one in dioxane containing suspended calcium hydroxide as a catalyst with an acid chloride or anhydride. Reaction takes place fastly and form calcium complex of 4-acylpyrazolone, which is stable in alkaline medium and protect the wanted derivatives from further reactions. This method was used to prepare the acetyl,butyryl, propionyl, benzoyl, aleryl, chloracetyl, p-bromobenzoyl, p-nitrobenzoyl and ethoxycarbonyl derivatives of 1-phenyl-3-methylpyrazole-5-one and to prepare the benzoyl derivatives of 1-p-nitrophenyl-3-methylpyrazole-5-one. Acylation in pyrazole easily occurs at the C-4 position in the basic medium, dioxane at reflux.



Synthesis of 4-acylpyrazolone

Acylpyrazolones exist in solution as well as in slid-state in several possible tautomeric form. These compounds have versatile complex forming ability with metal ions.



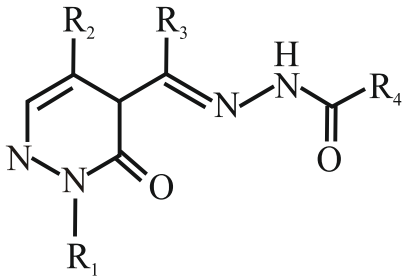
(I) **(II)** **(III)** **(IV)**

Tautomeric structure of acylpyrazole

The spectroscopic characterization of acylpyrazolones ligands through Raman, IR, UV-vis, 'H and ^{13}CNMR, mass spectra and ab initio calculations have been reported factors influencing the equilibrium between the tautomeric forms being mainly explored. Crystallisation of acylpyrazolones are performed in different solvent and medium.

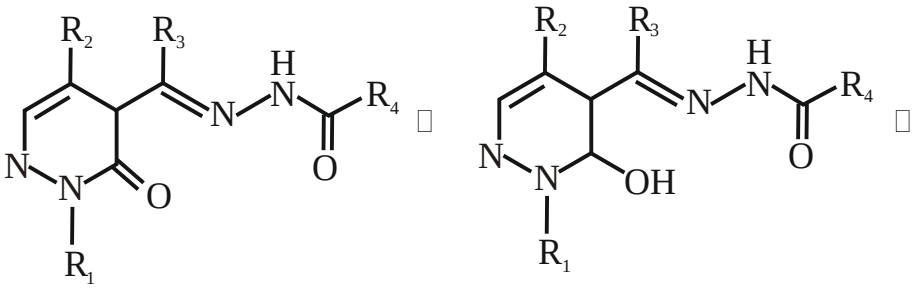
4-acylhydrazone-5-pyrazolone :

Recently, 4-acylhydrazone-5-pyrazolones have much studied because analogy in their structure and many biological properties and applications. It is prepared by reaction of 4-acyl-5-pyrazolones and acylhydrazides.

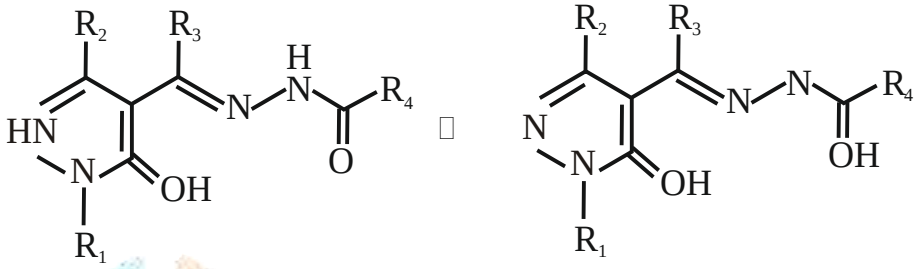


Structure of 4-acylhydrazone-5-pyrazolone

It is reacted as bidentate ligand as well as tridentate ligand in metal complexation. It exist in four tautomeric forms, which is favoured in biological activity and co-ordination chemistry.



(I) **(II)**



(III) **(IV)**

Tautomeric form of 4-acylhydrazone-5-pyrazolone

3-amino-1-phenyl-5-pyrazolone :

It is synthesised from the reaction between acetic acid, phenylhydrazine and ethyl cyanoacetate. Reaction mixture refluxed for 8 hrs and after cooling a viscous product obtained after washing with diethyl ether and recrystallized from benzene to give pure product.

3-amino-1-(2,4-dinitrophenyl)-5-pyrazolone :

It is synthesized from the reaction between acetic acid, dinitrophenyl hydrazine and ethyl cyanoacetate in the flask. After refluxed, cooling and crystallization with the help of suitable solvents and medium pure product is obtained.

1H-pyrazole-3,5-diamine-4-(2-phenyldiazenyl) :

It is synthesized by using aniline (0.01 mole), HCl (5 ml) and water (5 ml) after cooling, sodium nitrite solution (0.01 mole) was added with stirring. Diazonium salt obtained was filtered into a cold solution of sodium acetate (4g) and molonitrile (0.01 mole) in ethanol (25 ml), then after 1h adding hydrazine monohydrate (0.02 ml) a solid product was obtained and recrystallization from ethanol to give pure product.

5-amino-1,3-diphenyl-1H-pyrazolecarbanitrile :

It is synthesized by using ethanol (7 ml) and water (7 ml) phenyl hydrazine (0.01 mole), molonitrile (0.01 mole) and benzaldehyde (0.01 mole). The reaction mixture in flask was stirred at room temperature for 30 min. After completion of reaction solid product is obtained. Collected solid product was recrystallized by ethanol to give pure product.

The chemical structures of the synthesized compounds were confirmed by using different spectroscopic analysis like FTIR, 'H-NMR, ^{13}C-NMR, chemical analysis, Raman, UV-vis. spectroscopy, mass spectra etc.

The anti-microbial activity of synthesized compounds was determined by the disc diffusion technique, preparation of disc containing 1.9-1000 µg/ml of each compound against micro-organisms. The plates were incubated at 37°C for 24h for bacteria and at 28°C for 72h for fungi. The standard anti-biotic ampicillin and anti-fungal colitrimazole were used as references. At the end of the incubation period, the minimum inhibitory concentrations (MIC) values were recorded as the lowest concentration of the substance that had no visible furbidify.

Control experiments with DMSO and unincubated media were run parallel to the test compounds under the same conditions.

Instruments used–

(a) Melting point apparatus

(b) FTIR

(c) 'H-NMR Spectra

(d) ^{13}C-NMR Spectra

(e) Mass Spectra

(f) Elemental micro-analysis

(g) Biological evaluation, and

(h) Incubator

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