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SYNTHESIS AND BIOLOGICAL SIGNIFICANCE OF PYRAZOLONES: A REVIEW

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Keywords:

Pyrazolone, Heterocyclic, Antibacterial, Antifungal and Antitumor

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ABSTRACT: Heterocyclic compounds are acquiring more importance in recent years because of their pharmacological activities. Pyrazolones have a particular value due to their broad spectrum of biological activity and their wide ranging utility as synthetic tools in the design of various bioactive molecules. Pyrazolone is a five membered lactum ring, containing two nitrogen and one ketonic group in its structure. In addition, pyrazolones possess antimicrobial, antifungal, antimycobacterial, antibacterial, anti-inflammatory, antitumor, gastric secretion stimulatory, antidepressant and antifilarial activities. They also serve as precursors for dyes, pigments, pesticides and chelating agents, besides finding applications in the extraction and separation of various metal ions. The high therapeutic properties of the pyrazolone releted drugs have encouraged the medicinal chemists to synthesized a large number of novel chemotherapeutic agents. Numerous methods for the synthesis of pyrazolone and also their various structure reactions offer enormous scope in the field of medicinal chemistry. This articles aims to review the work reported, their chemistry and biological activities of pyrazolone during past years.

INTRODUCTION: Since last two decades a rapid progress in synthetic organic chemistry is associated with a search for new compounds with desired properties. Such compounds are widely used in pharmaceutical industries. Among these, the heterocycles form the largest of the classical division of organic chemistry and are of immense biological and industrial importance. The majority of biologically active compounds are heterocycles also applicative as additives and modifiers used in industries of cosmetics, photography, information storage and plastics. Heterocyclic compounds are also used in pharmacy and agriculture.

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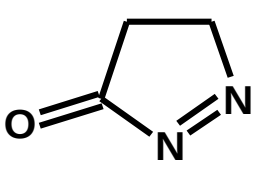
Analysis of scientific papers in the last two decades revealed that there is a general trend in research for new drugs involving modification of existing biologically active matrices and molecular design of the structures of compounds.

In the recent years much attention has been focused on the synthesis of heterocycles containing nitrogen atom because of their biological and medicinal importance including ontological research. They are widely distributed in nature and are essential for life. Pyrazolones is a five member heterocyclic compound containing one ketonic group and two nitrogen atoms adjacent to each other. In 1883, Knorr et al [1] gave the generic name pyrazole to above class of the compounds, which is a five member unsaturated ring compound with two adjacent nitrogen atoms. Antipyrine was the first pyrazolone derivative for clinical use and was synthesized in 1883 [2]. It was used as the first agent to reduce fever and also for arthritis. There are

three possible heteropyrazolines **[1, 2, 3]** in which carbonyl group is adjacent to nitrogen.



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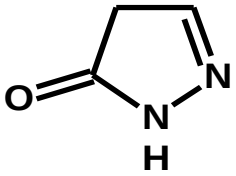
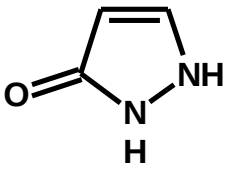
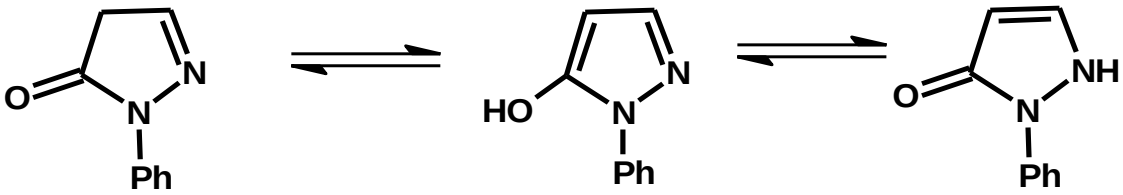


(2)



(3)

The carbonyl at position five leads to 5-hydroxyl pyrazoles **[4]**, since the 5-hydroxy compound exhibits pronounced enol character, tautomeric forms shown below for the 1-phenylderivative are the fundamental structures involved in the pyrazolone reactions.



1-PHENYL-5-PYRAZOLONE (4)

Pyrazolone derivatives are an important class of heterocyclic compounds that occur in many drugs and synthetic products [3, 4]. These compounds exhibit remarkable analgesic [5], antitubercular [6], antifungal, antibacterial [7], anti-inflammatory [8], antioxidant and antitumor activities [9]. Due to their easier preparation and rich biological activity, pyrazolone framework plays an essential role and represents an interesting template for combinatorial and medicinal chemistry.

Pyrazolones are pharmacophores of numerous compounds (**Fig. 1**) that display activities such as analgesic and antipyretic (propylphenazone, phenazone, metamizole etc.) [10], anti-cancer (TELIN) [11], anti-ischemic (edaravone) [12], and anti-anxiolytic [13]. Pyrazolones are gaining importance especially in drug discovery programs towards cerebral ischaemia [14] and cardiovascular diseases [15, 16].

Due to its diverse pharmacological properties, the chemistry of pyrazolones is gaining attention, and there have been numerous novel methodologies reported recently [17]. We describe here in our research findings in this area.

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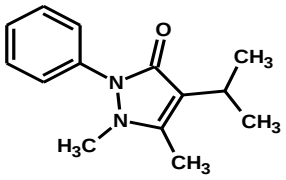
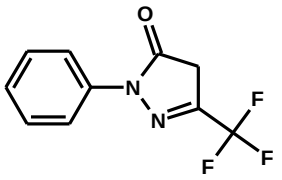


PROPYPHENAZONE



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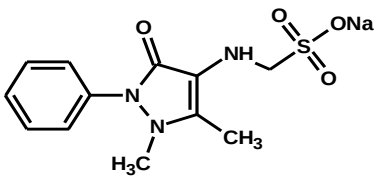
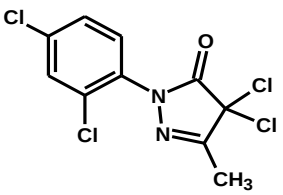
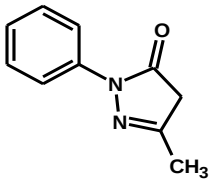


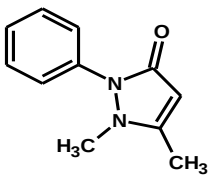
METAMIZOLE SODIUM



TELIN



EDARAVONE



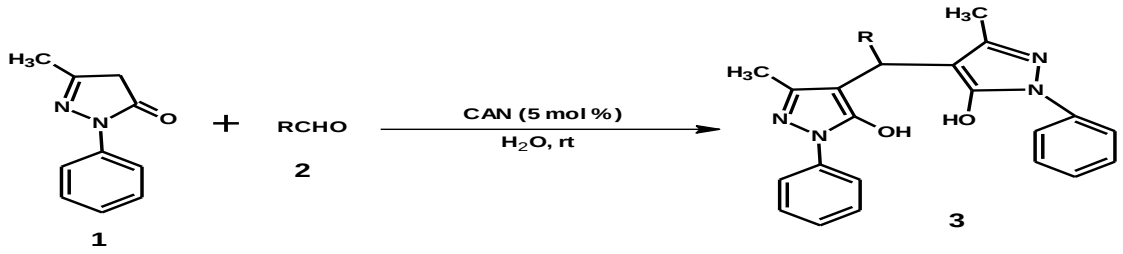
PHENAZONE

FIG. 1: BIOLOGICALLY IMPORTANT PYRAZOLONES

Synthesis of Pyrazolone Derivatives:

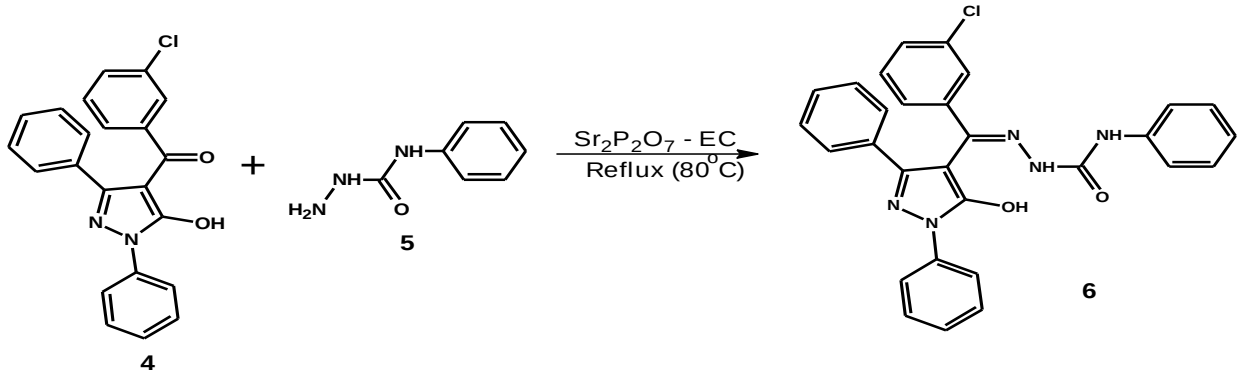
By refluxing methods:

Sujatha et al. [18] have been reported the preparation of 4,4'-(arylmethylene) bis (1*H*-pyrazol-5-ols) **3** has been accomplished by tandem Knoevenagel–Michael reaction of two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one **1** with various aromatic aldehydes **2** catalyzed by ceric ammonium nitrate (CAN) in water.



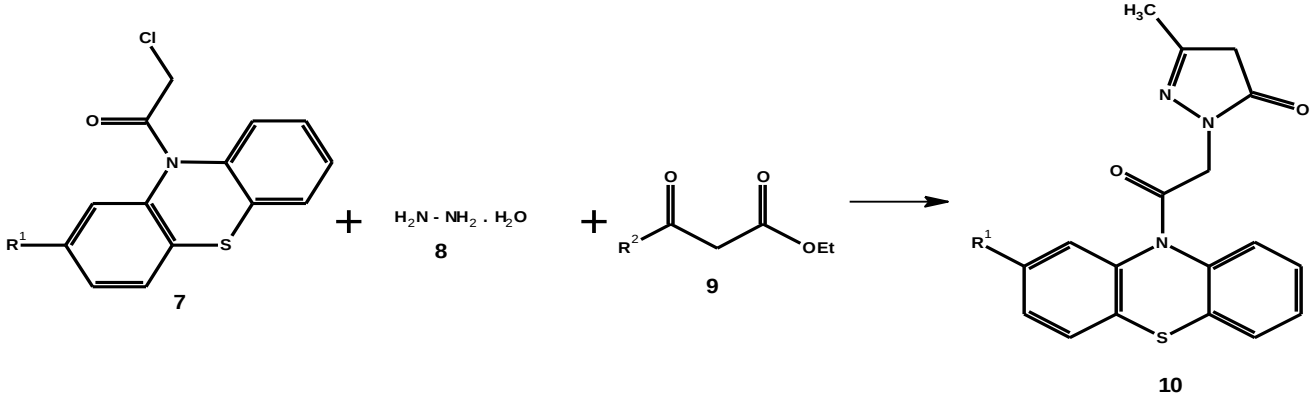
SCHEME 1: SYNTHESIS OF 4,4'-(ARYLMETHYLENE)BIS(1*H*-PYRAZOL-5-OLS) USING CERIC AMMONIUM NITRATE (CAN) AS CATALYST

Liu et al.[19] have been reported a novel solid-state reversible fluorescence photo switching system (FPS) based on photochromism of photochromic pyrazolones has been developed by employing phosphor $Sr_2P_2O_7$ co-doped with europium ion and chlorine ion ($Sr_2P_2O_7$–EC). (3-chlorophenyl)(5-hydroxy-1,3-diphenyl-1*H*-pyrazol-4-yl)methanone **4** react with *N*-phenyl hydrazinecarboxamide **5** to form 1,3-diphenyl-4-(3-chlorobenzal)-5-hydroxypyrazole-4-phenylsemi carbazone **6** as the fluorescence dye and the photochromic compound, respectively.



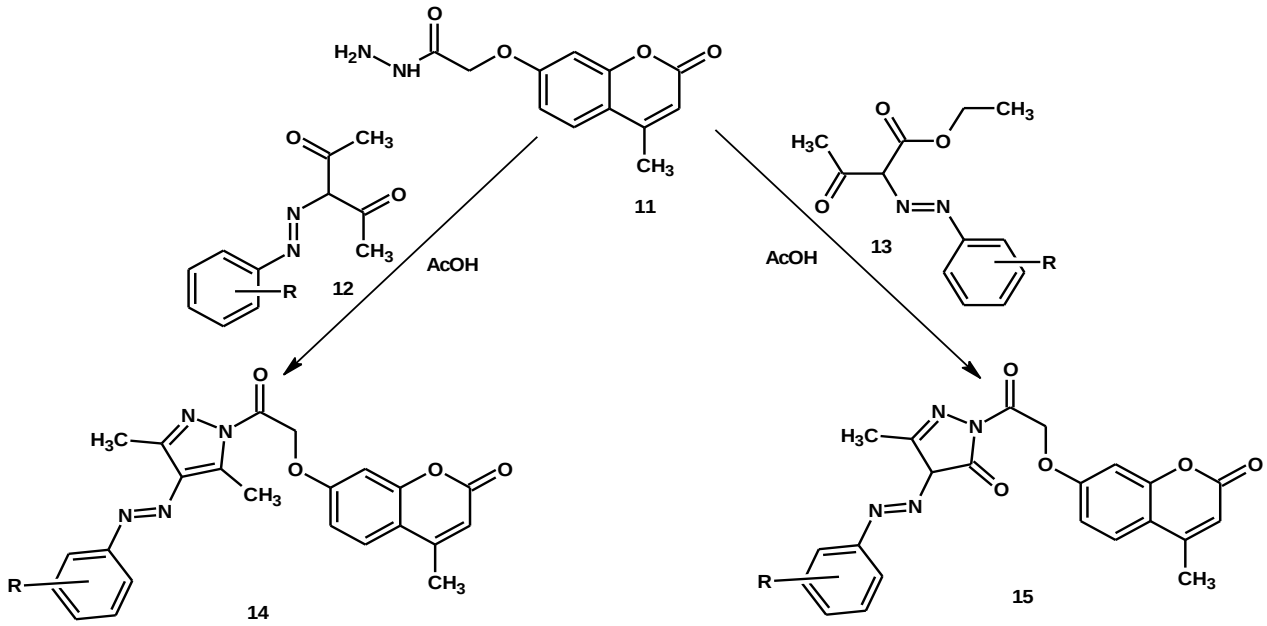
SCHEME 2: SYNTHESIS OF PHOTOCHROMIC PYRAZOLONES BASED ON PHOTOCHROMISM BY EMPLOYING PHOAPHOR $Sr_2P_2O_7$

Baciu-Atudosie et al.[20] have been reported a simple one-pot approach for the synthesis of new 5-substituted-2-[2-(2-substituted-10*H*-phenothiazin-10-yl)-2-oxoethyl]-2,4-dihydro-3*H*-pyrazol-3-one **10** containing a phenothiazine unit by reaction of *N*-chloroacetyl compound **7**, ethyl acetoacetate **9** with hydrazine hydrate **8**.



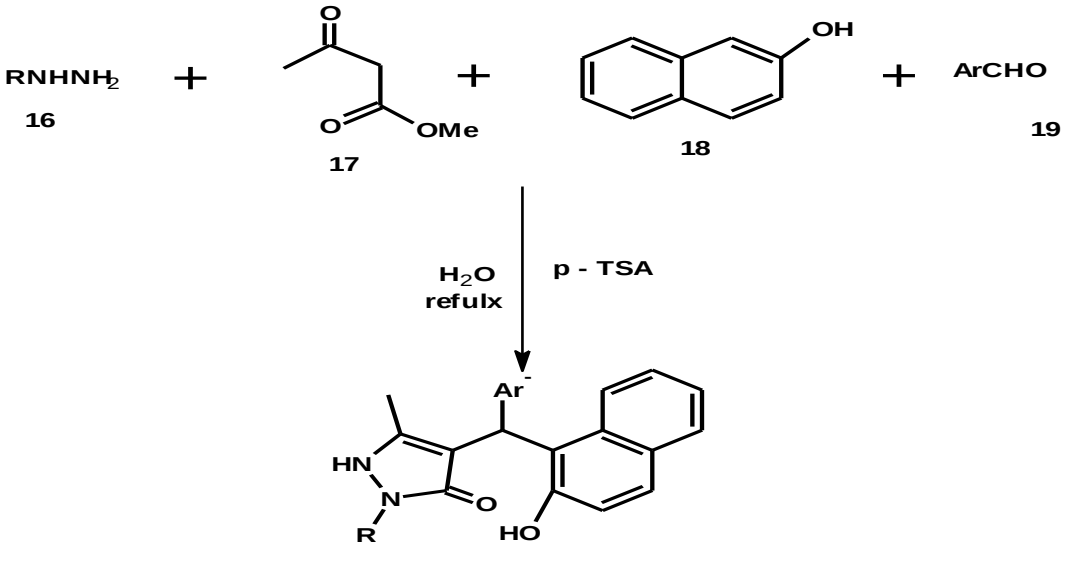
SCHEME 3: SYNTHESIS OF NEW PYRAZOLONES CONTAINING A PHENOTHIAZINE UNIT

Kumar et al.[21] have been reported the synthesis of 1-(4-methylcoumarinyl-7-oxyacetyl)-3,5-dimethyl-4-(arylazo)pyrazoles **14** by reaction of 1,3-diketo-1,3-dimethyl-2-(arylazo)propane **12** and 4-methylcoumarinyl-7-oxyacetic acid hydrazide **11** in glacial acetic acid was refluxed for 10 h. And the synthesis of 1-(4-methylcoumarinyl-7-oxyacetyl)-3-methyl-4-(substituted phenyl) hydrazono-2-pyrazolin-5-one Ethyl-2-(substituted phenyl) hydrazono-3-oxobutyrate **15** was dissolved in glacial acetic acid and 4-methylcoumarinyl-7-oxyacetic acid hydrazide **13** was refluxed for 4 h.



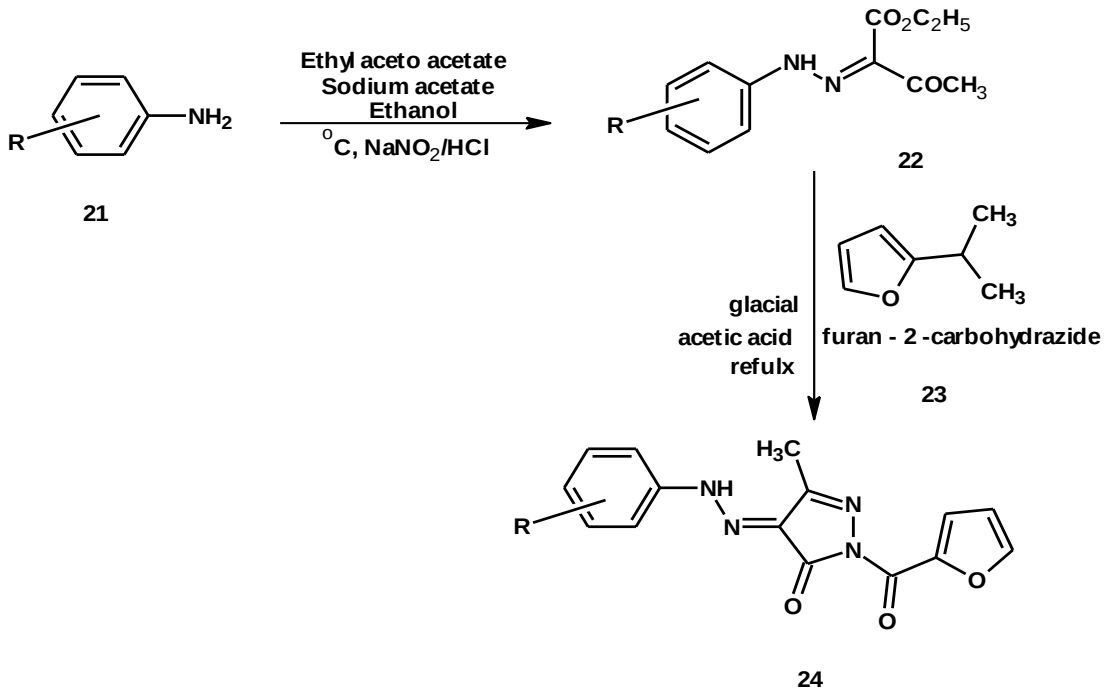
SCHEME 4: SYNTHESIS OF 1-(4-METHYLCOUMARINYL-7-OXYACETYL)-3, 5-DIMETHYL-4-(ARYLAZO) PYRAZOLES AND 1-(4-METHYLCOUMARINYL-7-OXYACETYL)-3-METHYL-4-(SUBSTITUTED PHENYL) HYDRAZONO-2-PYRAZOLIN-5-ONE ETHYL-2-(SUBSTITUTED PHENYL) HYDRAZONO-3-OXOBUTYRATE

Gunasekaran et al.[22] have been reported a series of 2-aryl-5-methyl-2,3-dihydro-1*H*-3-pyrazolones **20** has been synthesized by one-pot, four-component sequential reactions of phenyl hydrazine **16,** methyl acetoacetate **17**, *β*-naphthol **18** and aromatic aldehydes **19** in the presence of *p*-toluenesulphonic acid in water in good yields.



SCHEME 5: SYNTHESIS OF 2-ARYL-5-METHYL-2, 3-DIHYDRO-1*H*-3-PYRAZOLONES IN PRESENCE OF *p*-TSA

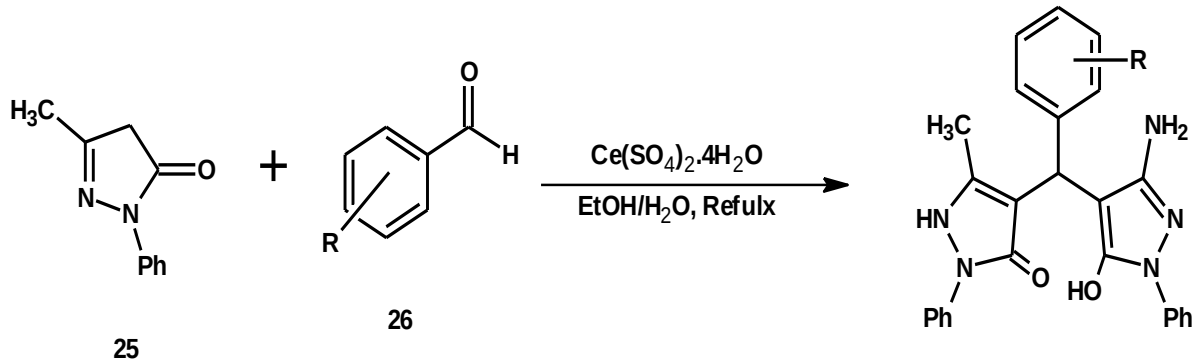
Shah et al.[23] have been reported Mannich reaction of various ethyl-2-substituted phenyl hydrazono-3-oxobutyrates **22** with furan-2-carbohydrazide **23** afforded 1-(furan-2-carbonyl)-3-methyl-4-(2-phenyl hydrazono)-1*H*-pyrazol-5(4*H*)-one **24**.



21 22 23 24

SCHEME 6: SYNTHESIS OF 1-(FURAN-2-CARBONYL)-3-METHYL-4-(2-PHENYL HYDRAZONO)-1*H*-PYRAZOL-5(4*H*)-ONE BY MANNICH REACTION.

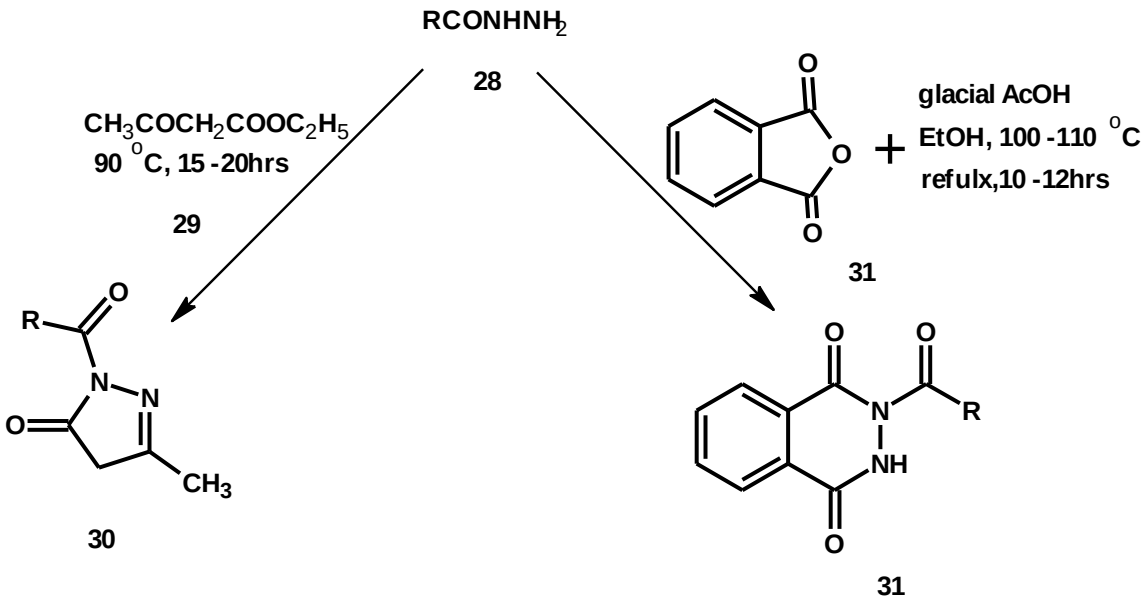
Mosaddegh et al. [24] heve been reported the synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **27** was performed effectively by the reaction of aryl aldehydes **26** and 1-phenyl-3-methyl-5-pyrazolone **25** in the presence of a catalytic amount of $Ce(SO_4)_2.4H_2O$ as reusable and environmentally friendly catalyst in water/ethanol solution. The method has the advantages of high yields, short reaction time, simple work-up and reusability of catalyst.



25 26 27

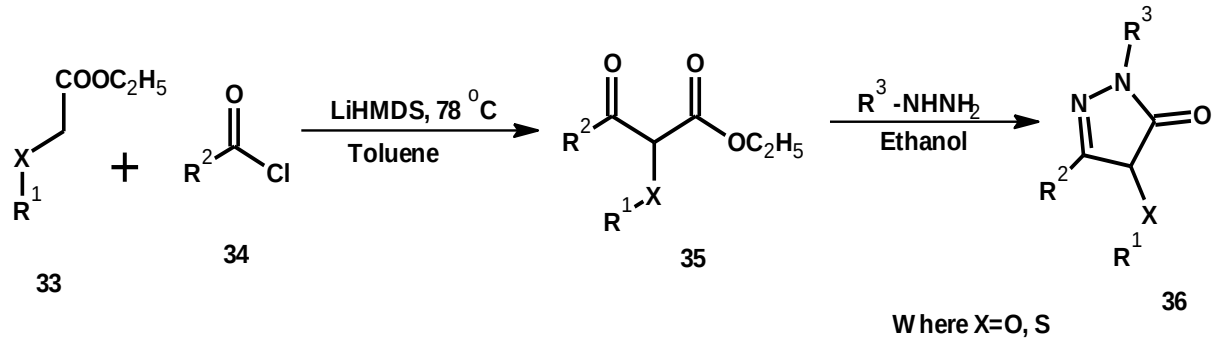
SCHEME 7: SYNTHESIS OF 4,4'-(ARYLMETHYLENE)BIS(3-METHYL-1-PHENYL-1H-PYRAZOL-5-OL) BY USING $Ce(SO_4)_2.4H_2O$

Ahmad et al. [25] have been reported two novel series of 1-long chain alkanoyl/ alkenoyl/ hydroxyalkenoyl-3-methyl-1H-pyrazol-5(4H)-ones **30** and 2-long chain alkenoyl/hydroxyalkenoyl-3H-phthalazin-1,4-diones **32** it is achieved by the reaction of ethylacetoacetate **29** /phthalic anhydride **31** and hydrazides. Compounds **30** were synthesized by the cyclization reaction between ethylacetoacetate and hydrazides. Compounds **32** were synthesized by the reaction of phthalic anhydride and hydrazides in absolute ethanol/glacial AcOH.



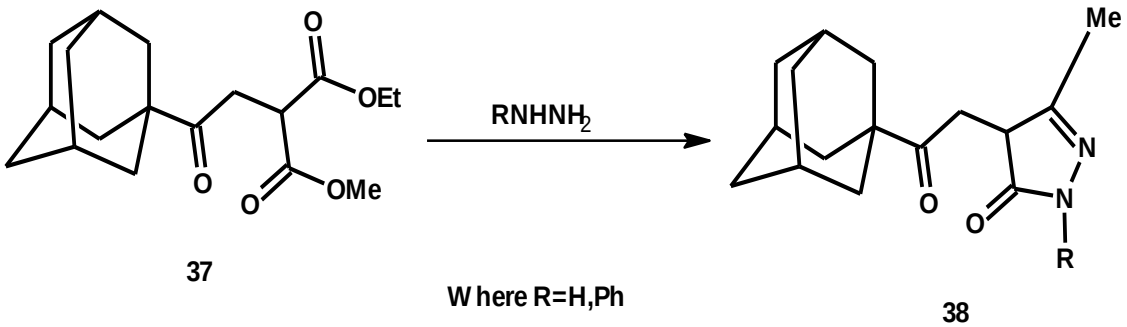
SCHEME 8: SYNTHESIS OF HYDROXYALKENOYL-3-METHYL-1H-PYRAZOL-5(4H)-ONES

Ragavan et al. [26] have been reported Oxy/thio substituted-β-keto esters were synthesized through an efficient cross-Claisen condensation of aryl oxy/thio acetic acid ethyl esters **33** with acid chlorides **34**, they form a intermediate **35** then it is converted into 4-oxy/thio substituted-1 *H* -pyrazol-5(4 *H*)-ones **36** by the addition of hydrazine or hydrazine derivatives.



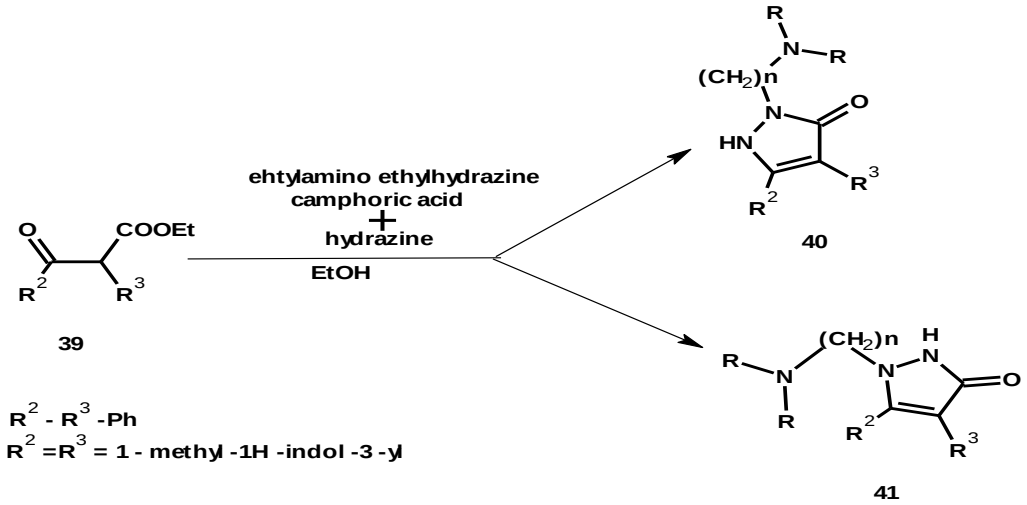
SCHEME 9: SYNTHESIS OF 4-OXY/THIO SUBSTITUTED PYRAZOLONES VIA CROSS-CLAISEN CONDENSATION

Konkov et al.[27] have been reported various pyrazole and dihydropyrazolones containing an adamantane fragment were synthesized from adamantyl-substituted 1,3- and 1,4-diketones, ethyl 4-(1-adamantyl)-2-R-4-oxobutanoates (R=CN, Ac), and ethyl 2-(1-adamantylcarbonyl)-4-oxo-4-phenylbutanoate. Compound **37** reacted with hydrazine and phenylhydrazine to give 4-[2-(1-adamantyl)-2-oxoethyl]-3-methyl-4,5-dihydro-1*H*-pyrazol-5-ones **38**.



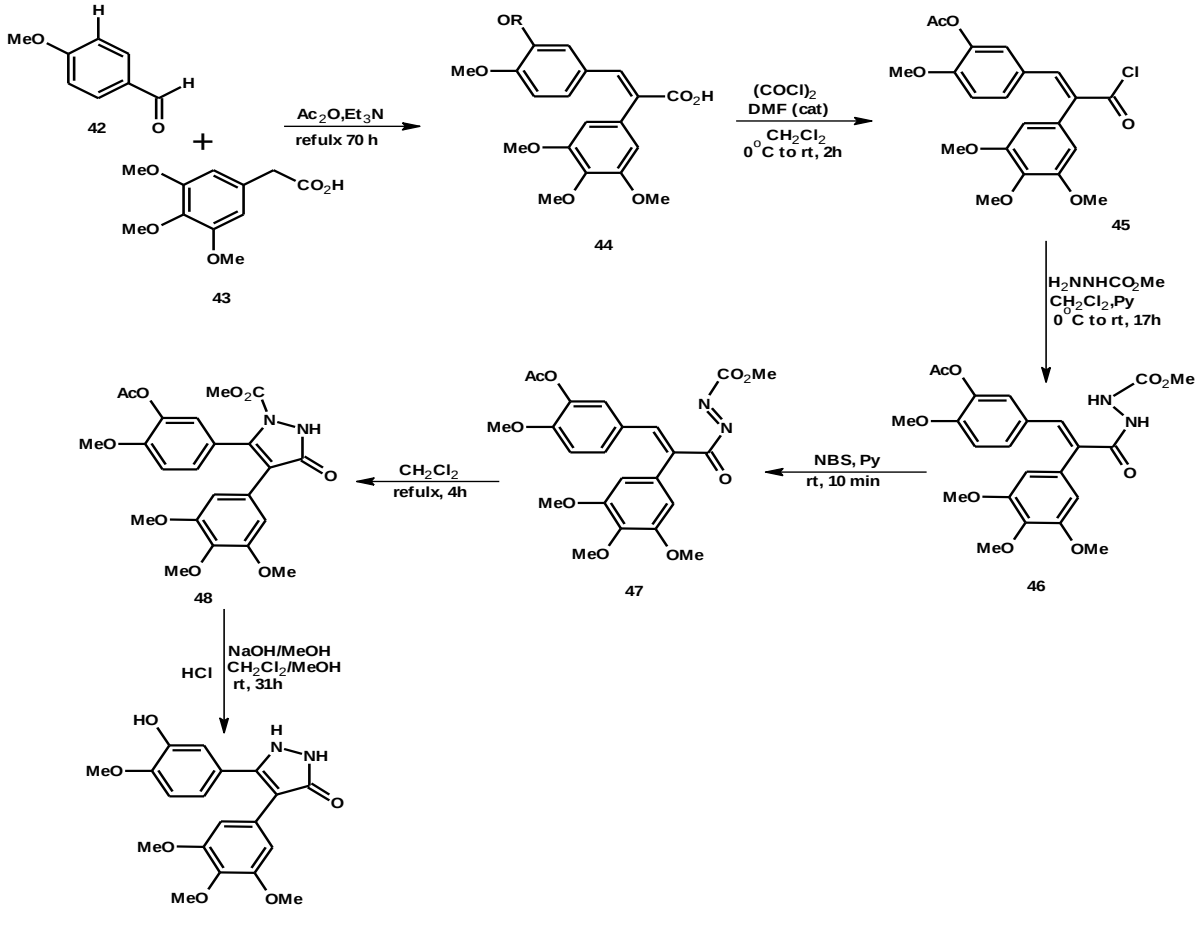
SCHEME10: SYNTHESIS OF DIHYDROPYRAZOLONES CONTAINING AN ADAMANTANE FRAGMENT

Bran et al. [28] have been reported a series of bisindolylpyrazolone **40, 41** derivatives by the reaction of substituted β-ketoester **39**, comphoric acid and ethylaminoethylhydrazine in ethanol medium.



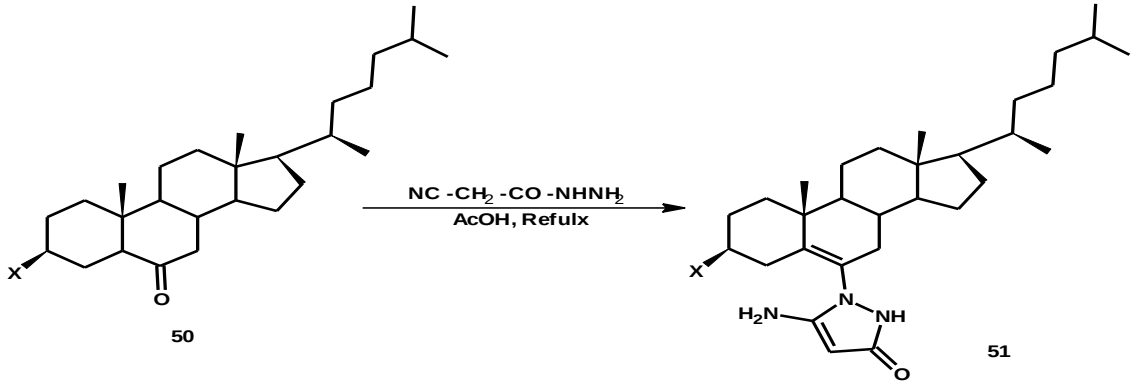
SCHEME11: SYNTHESIS OF BISINDOLYLPYRAZOLONE DERIVATIVES

Burja et al. [29] have been reported a series of pyrazolone-fused combretastatins **49** and their precursors were synthesized by multicomponant reaction method which were completed in multisteps. At the last step methanolic solution of NaOH was added to a stirred mixture of **48** in CH_2Cl_2/MeOH at room temperature.



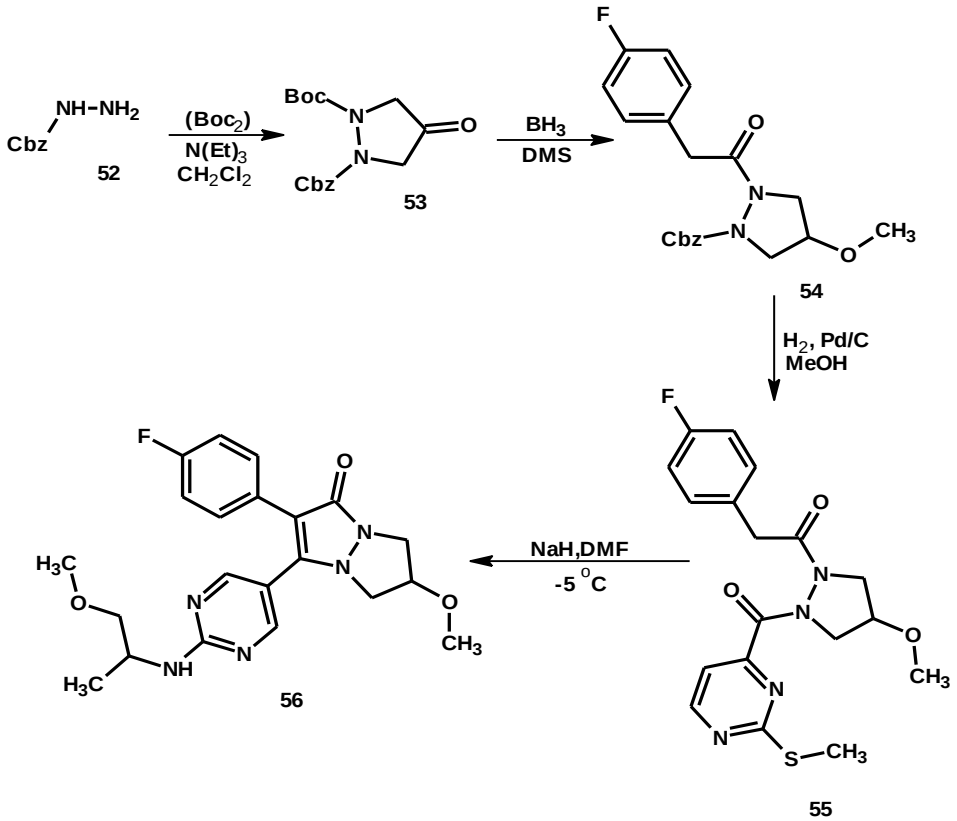
SCHEME12: SYNTHESIS OF THE FIRST PYRAZOLONE-FUSED COMBRETASTSTIN DERIVATIVES AND ITS PRECURSORS

Shamsuzzaman et al. [30] have been reported a convenient synthesis of a new series of nano steroidal pyrazolones **51**, Cyanoacetohydrazide was added in an equimolar ratio to a solution of steroidal ketones **50** in acetic acid. The reaction mixture was stirred under refluxing for 7 h.



SCHEME13: SYNTHESIS OF NANO STEROIDAL PYRAZOLONES

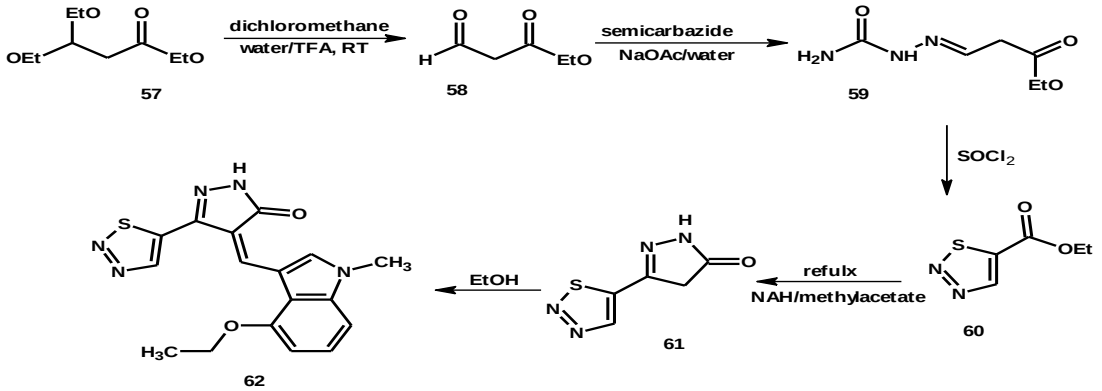
Laufersweiler et al. [31] have been reported novel substituted [5,5]-bicyclic pyrazolones **56** were prepared in multisteps. Reaction start with t-Boc and benzyl carbazate **52** to gave keton. Ketone **53** react with borane dimethylsulfide and gave a intermediate **54**, after that hydrogenolysis followed by acylation with 2-methylsulfanyl- pyrimidine-4-carbonyl chloride gave bis-acylated pyrazolidine **55**. Ring closure proceeded an intramolecular cyclocondensation to form the pyrazolone. This was followed by oxidation of the methyl sulfide and subsequent displacement with an appropriate nucleophile to give the final compounds **56.**



SCHEME14: SYNTHESIS OF NOVEL SUBSTITUTED [5,5]-BICYCLIC PYRZAZOLONES

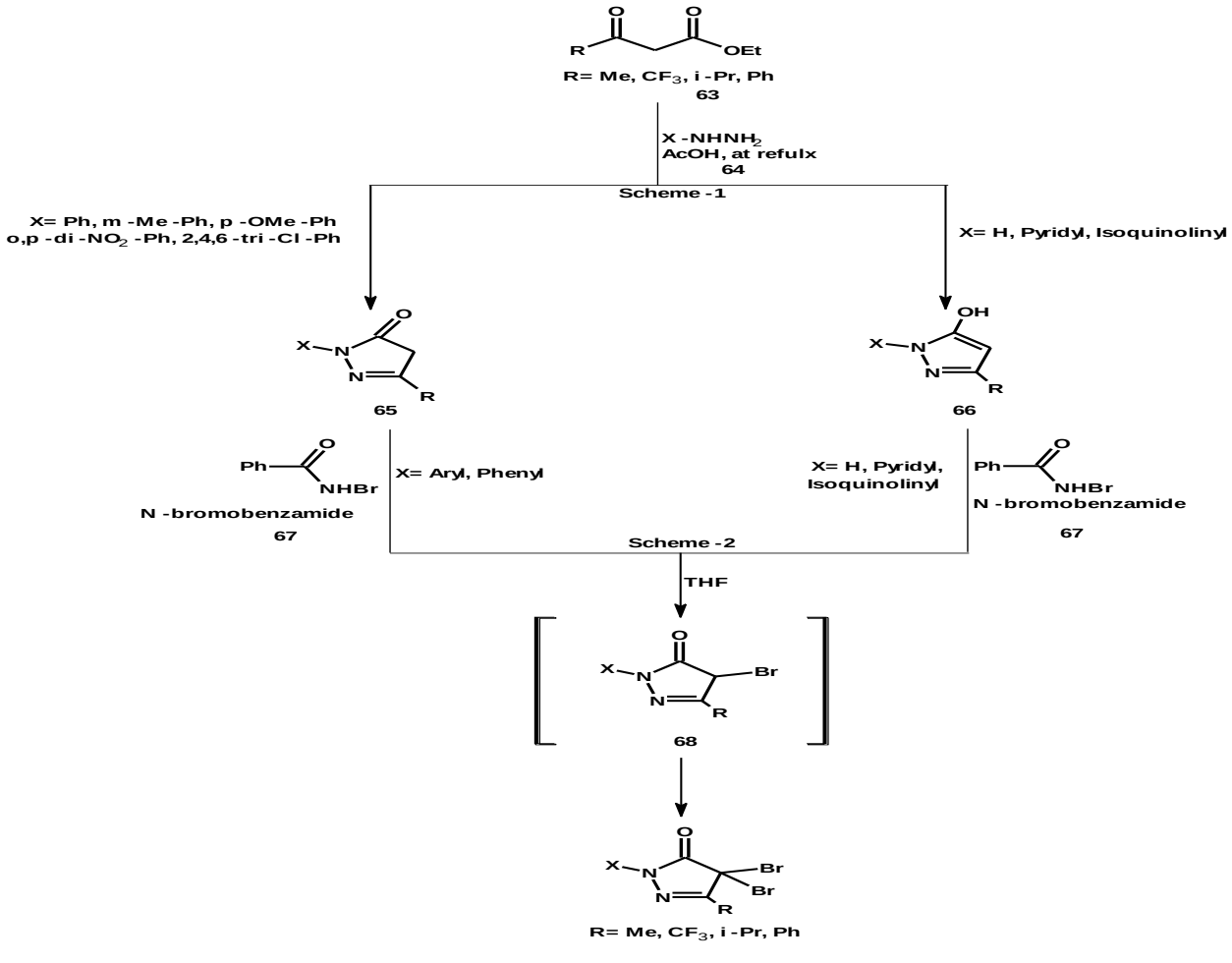
Tripathy et al. [32] have been reported the synthesis of the unsubstituted pyrazolone **61**, accomplished by the reaction of β-ketoester **57** react with semicarbazone which were followed by

rearrangement to 1,2,3-thiadiazole in presence of thionyl chloride to gave 1,2,3-thiadiazole 5-carboxylic acid ethyl ester **60**. Subsequent *β*-ketoester formation followed by cyclization with hydrazine resulted in the pyrazolone **61**. Similar condensation with indole carboxaldehydes resulted in product **62**.



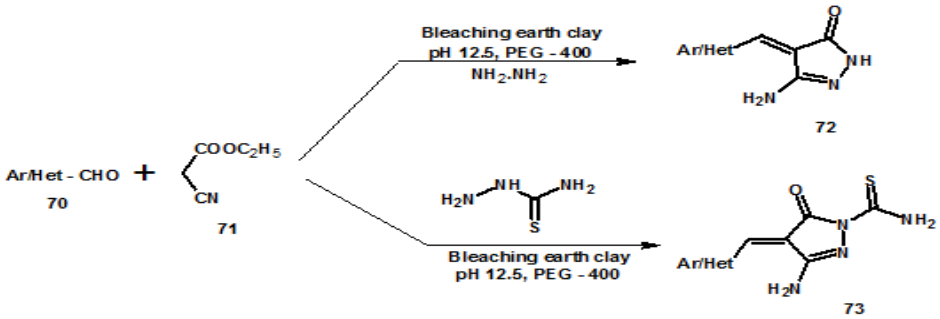
SCHEME15: SYNTHESIS OF UNSUBSTITUTED PYRAZOLONE DERIVATIVES

Huang et al.[33] have been reported an efficient and convenient method for the bromination of pyrazolones **65** and 5-hydroxypyrazoles **66** were developed 1,3-ketoester **63** and hydrazines **64** were added glacial acetic acid by using *N*-bromobenzamide **67** in THF at room temperature. This new method provided di-bromimated pyrazolones in excellent yields.



SCHEME16: SYNTHESIS OF DI-BROMIMATED PYRAZOLONES DERIVATIVES BY USING *N*-BROMOBENZAMIDE IN THF

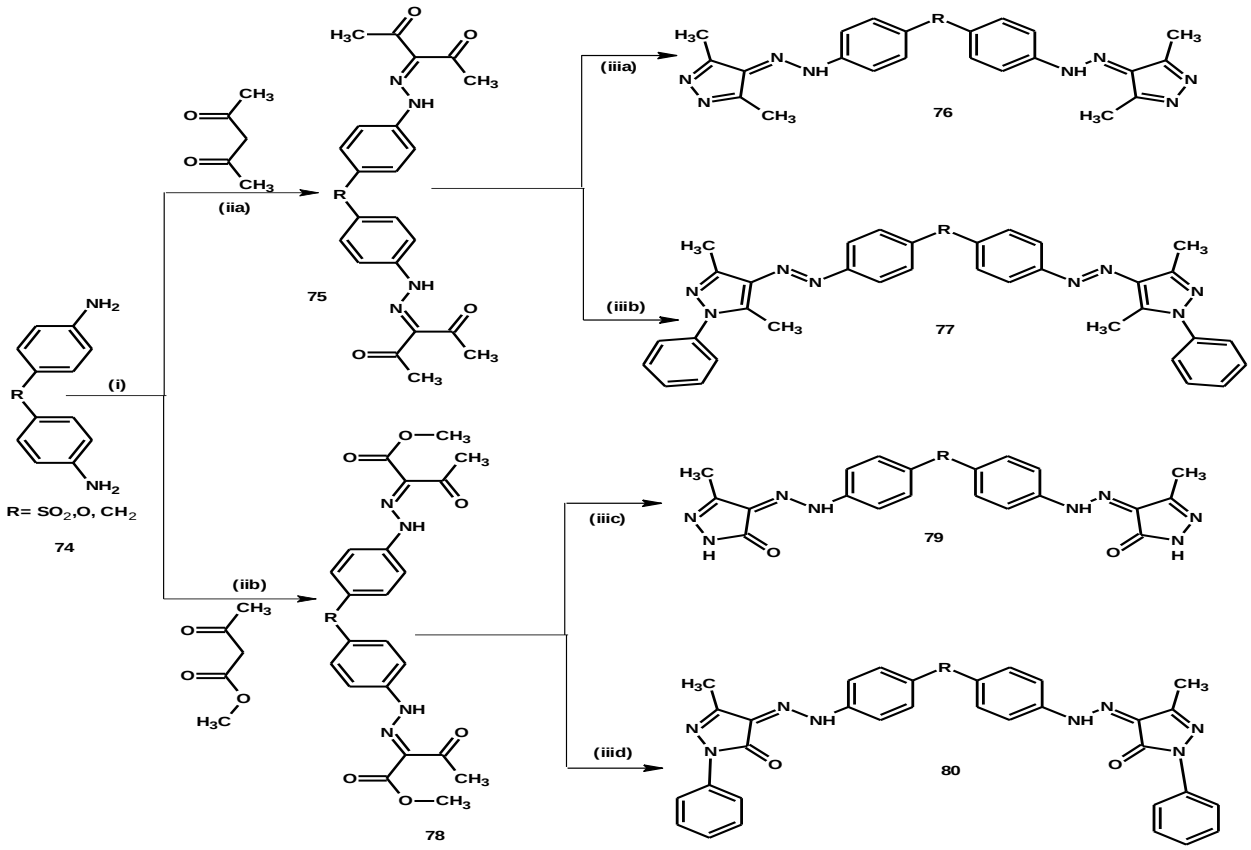
Kadam et al. [34] have been repoted a novel synthesis of 3-amino-4-(4*I*-substituted benzylidene) - 1*H*-pyrazol-5(4*H*)-one derivatives **72** and 3-amino-4-(4I-substitued benzylidene) - 4, 5 - dihydro-5-oxopyrazole-1-carbothioamide derivatives **73** by the reaction of substituted benzaldehyde/ heteroaldehyde **70**, **e**thylcyano acetate **71** and thiosemicarbazide was heated in presence of PEG-400.



SCHEME 17: SYNTHESIS OF TWO TYPE OF PYRAZOLONE DERIVATIVES

Mehta et al. [35]have been reported the synthesis of diphenylic bispyrazole **76, 77** and diphenylic bispyrazolone compounds **79, 80**. According to the method reported in the literature[36], these derivatives have been synthesized by the reaction of 4,4'-sustituted dianiline **74** react with acetylacetone and ethylacetoacetate.

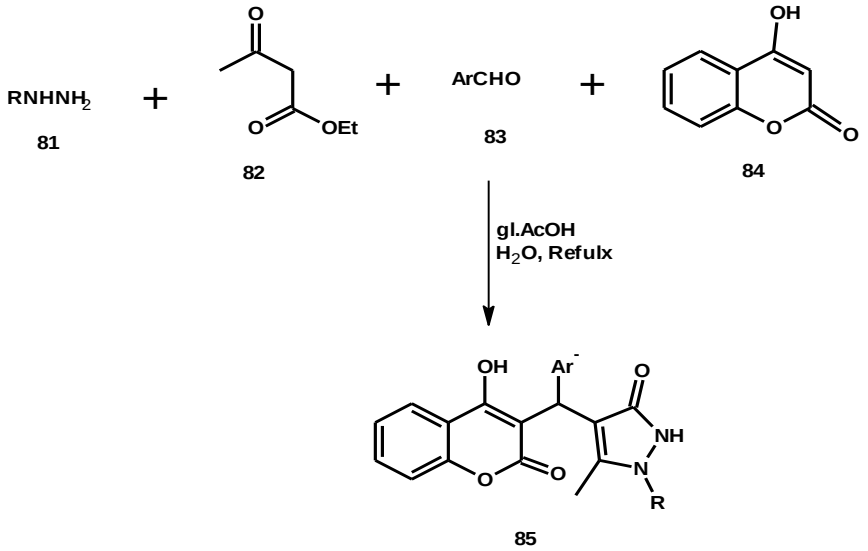
Compound **75** and **78** were reacted with hydrazine hydrate or phenyl hydrazine in CH_3COOH. The reaction mixture was then allowed to reflux for 2 h or 6 h respectively with continuous stirring. After refluxing, it was allowed to cool at room temperature. The yellowish product obtained, was filtered and recrystallized using acetone.



Reagents: (i) $NaNO_2$, H_2SO_4, 0-5^oC (iia) Coupling-acetylacetone, 0-5^oC (iib) Coupling-methyl acetoacetate, 0-5^oC (iiia) Cyclization-hydrazine hydrate, EtOH, MW or Δ (iiib) Cyclization-phenyl hydrazine, AcOH, MW or Δ (iiic) Cyclization-hydrazine hydrate, EtOH, MW or Δ (iiid) Cyclization-phenyl hydrazine, AcOH, MW or Δ

SCHEME18: SYNTHESIS OF DIPHENYLIC BISPYRAZOLE OR BISPYRAZOLONE COMPOUNDS

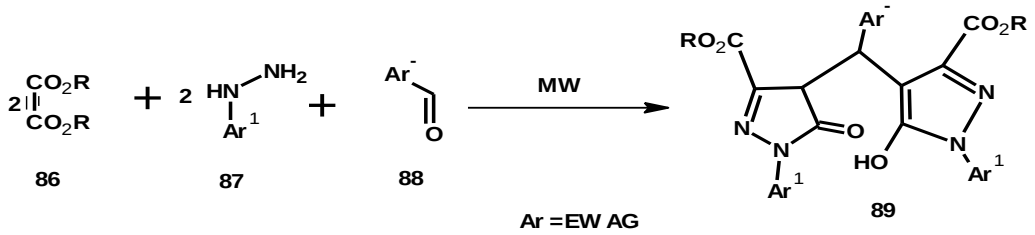
Ghosh et al. [37] have been reported a glacial acetic acid catalyzed reaction for the combinatorial synthesis of highly functionalized benzylpyrazolyl coumarin **85** prepared by a green one-pot four-component reaction between aryl hydrazine/ hydrazine hydrate **81**, ethyl acetoacetate **82**, aromatic aldehydes **83** and 4-hydroxycoumarin **84** in water medium under refluxing conditions.



SCHEME 19: GREEN SYNTHESIS OF BENZYLPYRAZOLYL COUMARINS

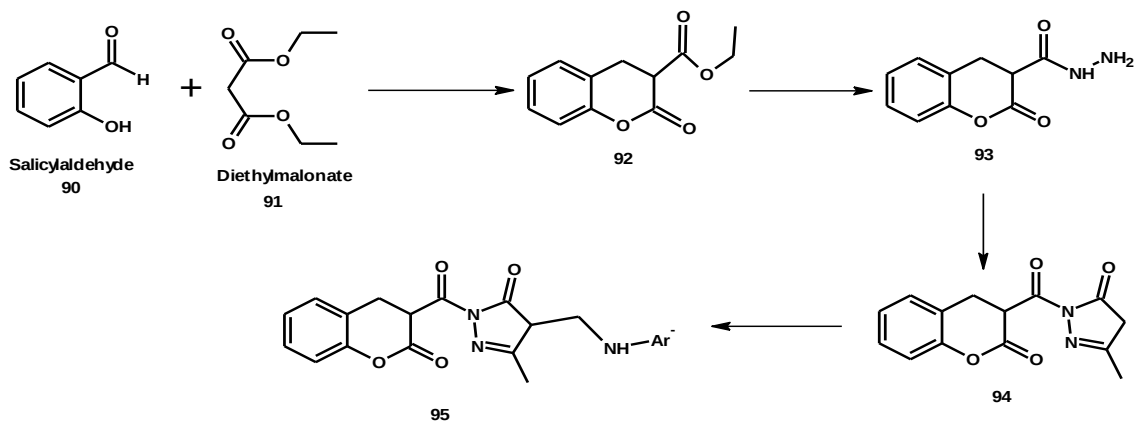
By microwave irradiation:

Tu et al. [38] have been synthesized C-tethered bispyrazol-5-ols **89** via multicomponent domino reactions of acetylenedicarboxylates **86**, phenylhydrazine **87** and aromatic aldehydes **88** under microwave irradiation.



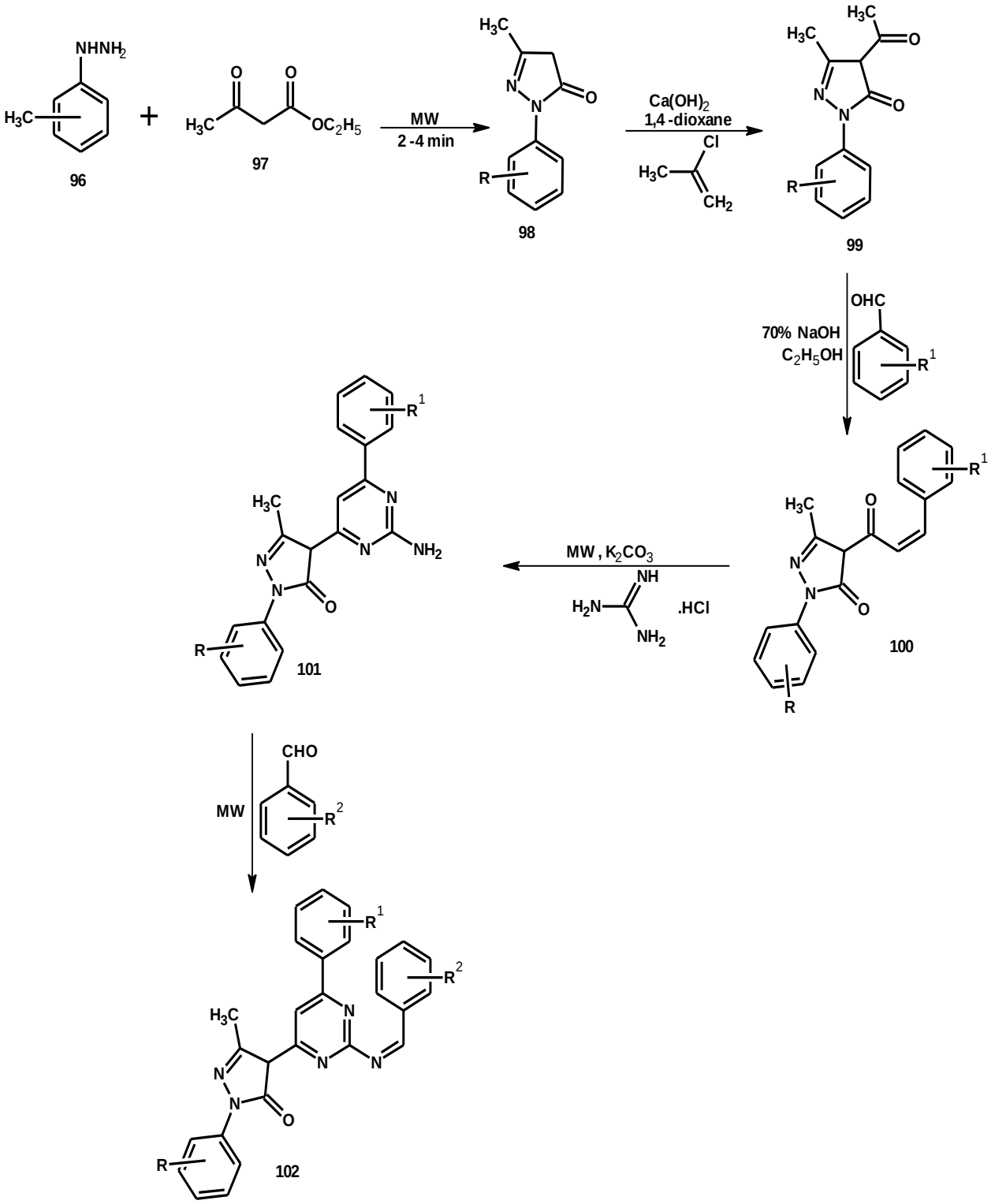
SCHEME 1: SYNTHESIS OF C-TETHERED BISPYRAZOL-5-OLS

Sivakumar et al. [39] have been reported an efficient synthesis of some Mannich base of 5-methyl-2-[(2-oxo-2*H*-chromen-3-yl) carbonyl]-2,4-dihydro-3*H*-pyrazol-3-one **95** have been described by using multicomponant with microwave techniques. Microwave assisted reactions showed that require shorter reaction time and good yield.



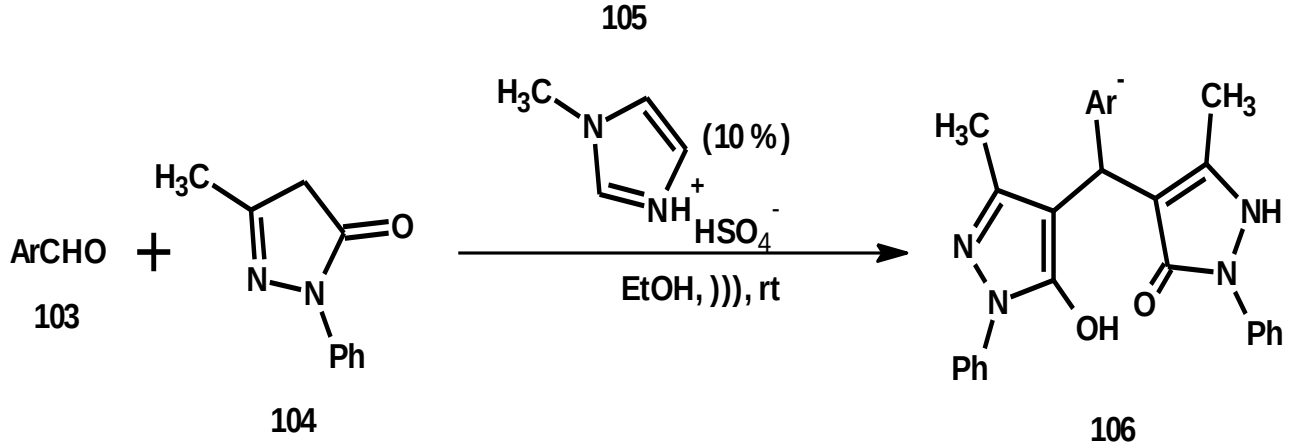
SCHEME 2: SYNTHESIS OF 5-METHYL-2-[(2-OXO-2*H*-CHROMEN-3-YL)CARBONYL]-2,4-DIHYDRO-3*H*-PYRAZOL-3-ONE

Antre et al. [40] have been reported various 4-(2-amino-6-(substituted)pyrimidin-4-yl)-3-methyl-1-(substituted)-1*H*-pyrazol-5(4*H*)-one derivatives **101** and their Schiff bases **102** were synthesized by the reaction of hydrazide **96** and ethylacetoacetate **97** to form pyrazolone derivatives **98**. Compound **98** further react with acetyl chloride and prepared compound **99**, therefore it has react with aromatic aldehyde and guanidine hydrochloride to gave pyrazolone derivatives **100** and **101**. Afterthat pyrazolone derivatives **101** again react with aromatic aldehyde and formed pyrazolone Schiff base derivatives **102**.



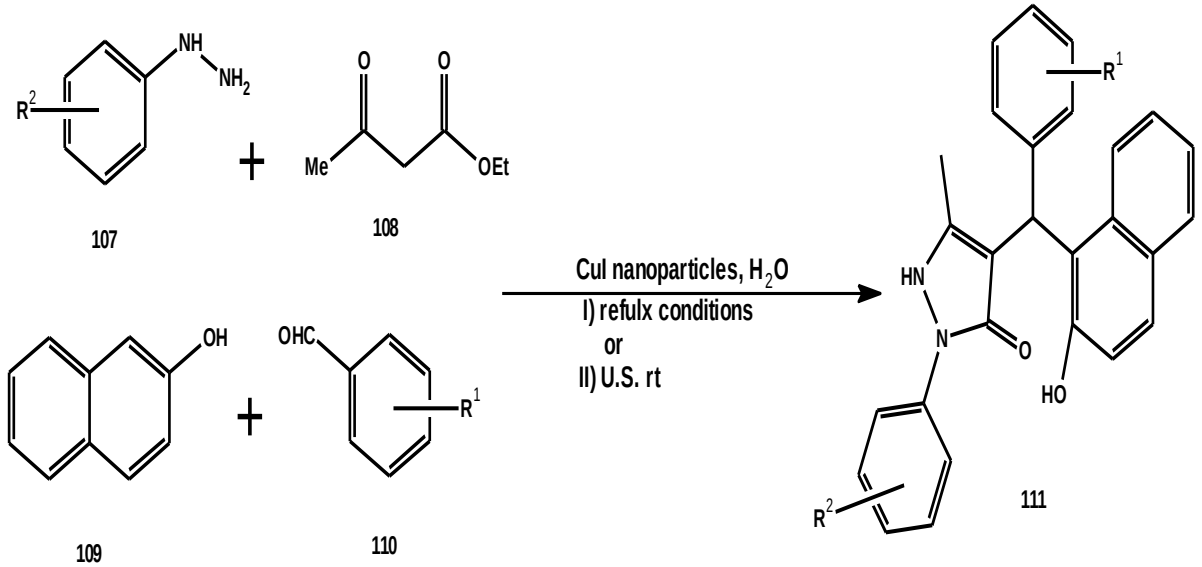
SCHEME 3: SYNTHESIS OF PYRAZOLONE DERIVATIVES AND THEIR SCHIFF BASES

Zang et al. [41] have been reported the synthesis of 4-[(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-phenyl-methyl] – 5 – methyl – 2 - phen-yl-1,2-dihydro-pyrazol-3-ones **106** through the condensation reaction of arylaldehydes **103** and 3-methyl-1-phenyl-5-pyrazolone **104** with Ionic liquid [HMIM]HSO_4 catalyst **105** under ultrasonic irradiation at room temperature. The present methodology offers several advantages such as excellent yields, simple procedure and mild conditions.



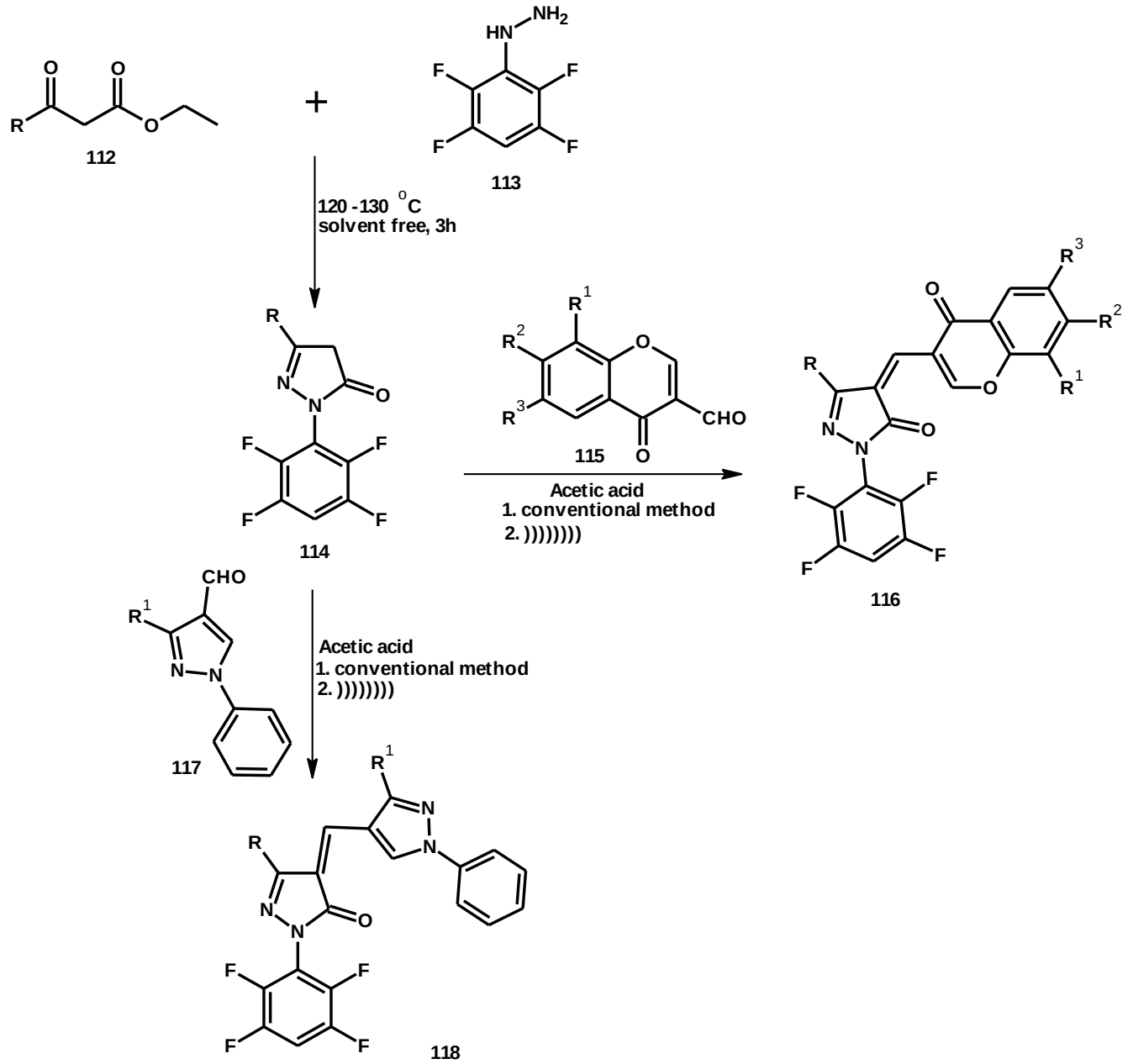
SCHEME 4: SYNTHESIS OF 4-[(5-HYDROXY-3-METHYL-1-PHENYL-1*H*-PYRAZOL-4-YL)-PHENYL-METHYL]-5-METHYL-2-PHEN-YL-1,2-DIHYDRO-PYRAZOL-3-ONES USING [HMIM]HSO_4 CATALYST

Ziarati et al. [42] have been reported simple and green process to prepare copper iodide in nano scale via sonication was carried out. Subsequently, this nanoparticles was used as an efficient catalyst for the synthesis of 2-aryl-5-methyl-2,3-dihydro-1*H*-3-pyrazolones **111** via four-component reaction of hydrazine **107**, ethyl acetoacetate **108**, aldehyde **109** and β-naphthol **110** in water under ultrasound irradiation.



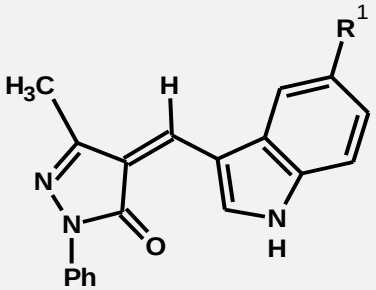
SCHEME 5: SYNTHESIS OF 2-ARYL-5-METHYL-2,3-DIHYDRO-1*H*-3-PYRAZOLONES USING CuI NANOPARTICLES

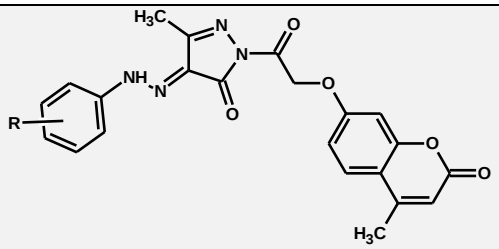
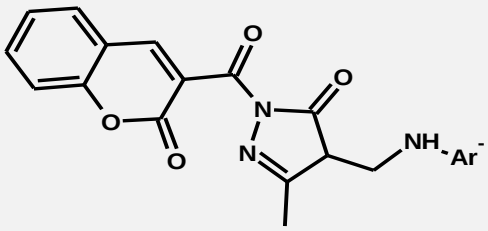
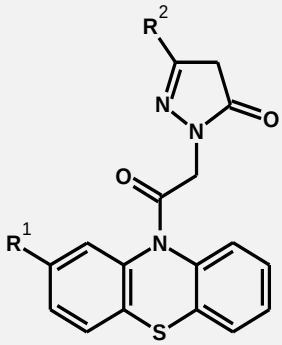
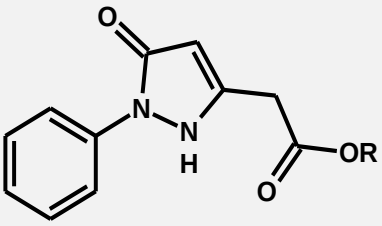
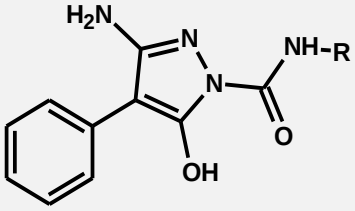
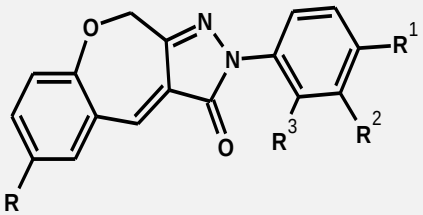
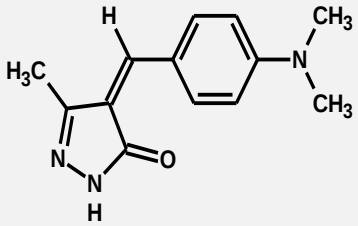
Gadhave et al. [43] have been reported a series of novel fluorine containing pyrazole-pyrazolone **118** and chromone-pyrazolone **116** was synthesized from multifluorinated pyrazolone by the Knoevenagel condensation reaction. All compounds were synthesized by conventional heating as well as ultrasound irradiation technique. It was found that ultrasonication method was more efficient than conventional heating method.

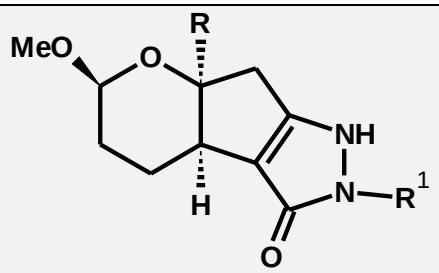
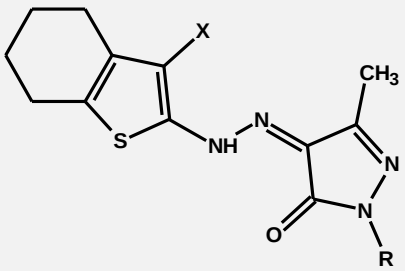
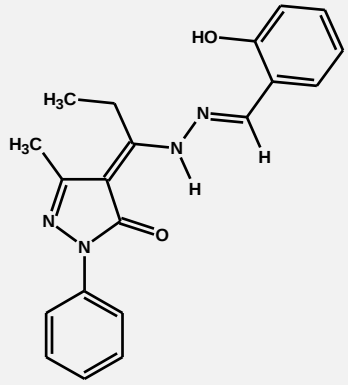
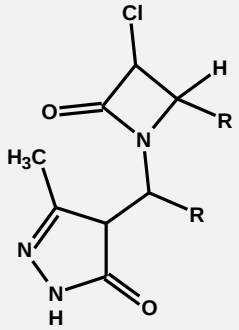
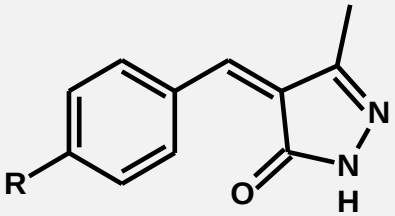
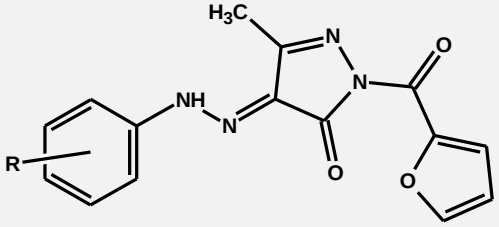


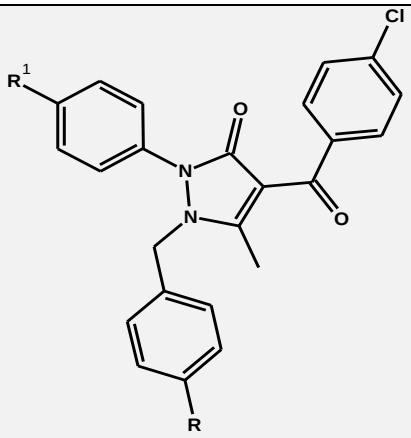
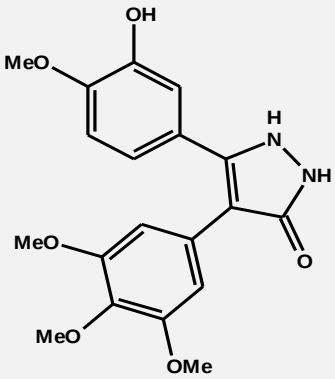
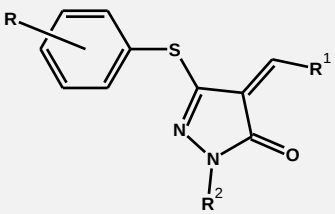
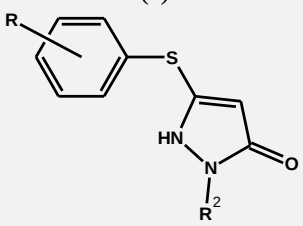
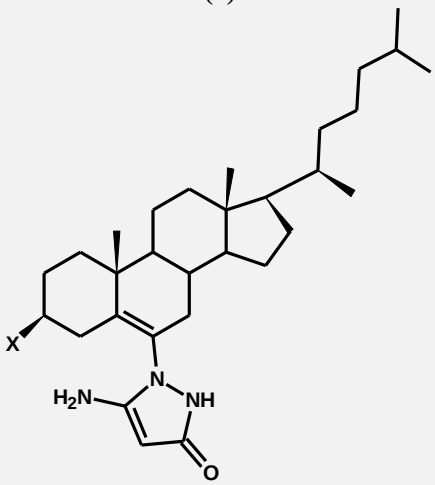
SCHEME 6: SYNTHESIS OF MULTIFLUORINATED PYRAZOLONE CONTAINING PYRAZOLE AND CHROMONE

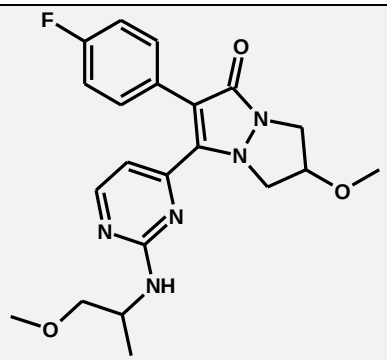
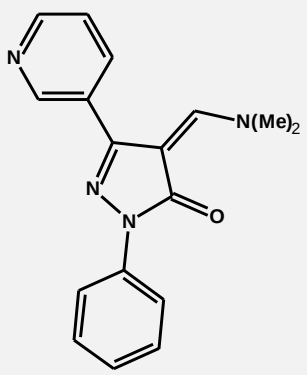
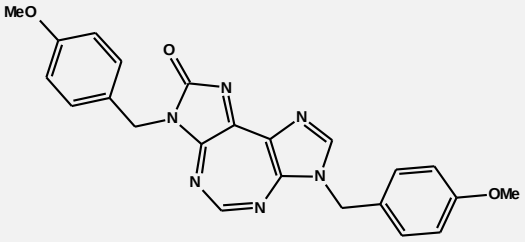
Pharmacological Properties: On the basis of various literature surveys pyrazolone derivatives shows various pharmacological activities.

S.No.	Chemical Structure	Chemical Name	Activity	Ref.
1		(4*Z*)-4-(1*H*-indol-3-ylmethylidene)-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one	anti-bacterial	44

2		(4*E*)-4-[2-(substituted phenyl)hydrazinylidene]-5-methyl-2-{[(4-methyl-2-oxo-2*H*-chromen-7-yl)oxy]acetyl}-2,4-dihydro-3*H*-pyrazol-3-one	antibacterial and antioxidant	21
3		4-[(substituted amino)methyl]-5-methyl-2-[(2-oxo-2*H*-chromen-3-yl)carbonyl]-2,4-dihydro-3*H*-pyrazol-3-one	anti-inflammatory, analgesic, antibacterial	39
4		5-substituted-2-[2-(2-substituted-10*H*-phenothiazin-10-yl)-2-oxoethyl]-2,4-dihydro-3*H*-pyrazol-3-one	antiproliferative	20
5		methyl (5-oxo-1-phenyl-2,5-dihydro-1*H*-pyrazol-3-yl)acetate	antibacterial	45
6		3-amino-5-hydroxy-4-phenyl-1*H*-pyrazole-1-carboxamide	antibacterial	46
7		2-phenyl-2,10-dihydro-3*H*-[1]benzoxepino[3,4-*c*]pyrazol-3-one	anticancer, anti-mycobacterial	47
8		(4*Z*)-4-[4-(dimethylamino)benzylidene]-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one(PYZI)	analgesic, anti-inflammatory, antipyretic	48

9		(3b*R*,6*S*,7a*R*)-2,7a-disubstituted-6-methoxy-1,2,3b,4,5,6,7a,8-octahydro-3*H*-pyrano[3',2':3,4]cyclopenta[1,2-*c*]pyrazol-3-one	anticancer	49
10		(4*Z*)-4-[2-(3-substituted-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)hydrazinylidene]-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one	antitumor	50
11		(4*Z*)-4-{1-[(2*E*)-2-(2-hydroxybenzylidene)hydrazinyl]propylidene}-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one	anticancer	51
12		4-[(3-chloro-2-oxoazetidin-1-yl)methyl]-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one	antibacterial	52
13		(4*Z*)-4-(4-substituted benzylidene)-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one	analgesic	53
14		(4*E*)-4-[2-(4-substituted phenyl)hydrazinylidene]-2-(furan-2-ylcarbonoimidoyl)-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one	antibacterial, antifungal	23

15		1-(4-substituted benzyl)-2-(4-substitutedphenyl)-4-(4-chlorobenzoyl)-5-methyl-1,2-dihydro-3*H*-pyrazol-3-one	mycobacterium tuberculosis	54
16		5-(3-hydroxy-4-methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)-1,2-dihydro-3*H*-pyrazol-3-one	cytotoxicity, antitubulin activity	29
17	 (a)  (b)	(a)(4*E*)-4-(substituted methylidene)-5-[(3-substituted phenyl)sulfanyl]-2-substituted-2,4-dihydro-3*H*-pyrazol-3-one (b) 5-[(3-substituted phenyl)sulfanyl]-2-substituted-2,4-dihydro-3*H*-pyrazol-3-one	amyotrophic lateral sclerosis	55
18		5-Amino-1-[17-(1,5-dimethyl-hexyl)-3,10,13-triethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-trtradecahydro-1*H*-cyclopenta[a]phenanthren-6-yl]-1,2-dihydro-pyrazol-3-one	antimicrobial	30

19		2-fluorobenzene-6-methoxy-3-{2-[(1-methoxypropan-2-yl)amino]pyrimidin-4-yl}-6,7-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazol-1-one	tumor necrosis	31
20		(*E*)-*N*,*N*-dimethyl-1-[5-methylidene-1-phenyl-3-(pyridin-3-yl)-1,5-dihydro-4*H*-pyrazol-4-ylidene]methanamine	antioxidant, antitumor and antimicrobial	56
21		8-(1-(4-methoxybenzyl)-4,5-dihydro-1*H*-imidazole)-3-(4-methoxybenzyl)imidazo[4,5-*d*][1,3]diazepin-2(3*H*)-one	anticancer	57

CONCLUSION: On the basis of literature survey, pyrazolone derivatives exhibits antimicrobial, anti-inflammatory, analgesic, anticancer and antitubercular activities. This review gives an overview of various synthetic routes used to form a biologically rich pyrazolone moiety. The possible improvements in the activity can be further achieved by slight modifications in the substituents on the basic pyrazolone nucleus. This article proves to be helful for further research work on the bioactive pyrazolone ring and as an important tool for the development of better medicinal agents.

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