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REVIEW ARTICLE SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF ISONIAZID BASED PYRAZOLE DERIVATIVES

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ABSTRACT

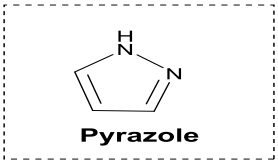
Pyrazole are aromatic compound containing two nitrogen atoms in a five-membered ring. Research attracts and effects the field such as antimicrobial, anti-inflammatory, anticancer, analgesic, anticonvulsant, antioxidant, antiviral, analgesic, and various useful activities. This review based on the synthetic reaction have been applied for the synthesis of pyrazole compound. Review provides up to date synthetic strategies, biological activities. Medicinal chemistry containing pyrazole rings, play an important role in drug. Pyrazole is a lead compound for the design bioactive agents.

The literature survey produce a new source of drug used in the market. Several synthetic routes provide a reaction containing pyrazole in the field of medicinal chemistry. Given data represents pyrazole heterocyclic planer five-membered rings have various pharmacological actions.

Keywords: Antimicrobial, Pyrazole, Isoniazid, Synthesis, Pyridine, Chalcone.

I. INTRODUCTION

Pyrazole is a organic compounds used in medicinal chemistry [1]. Pyrazole refers to the class of simple aromatic ring compounds of the heterocyclic series characterized by a 5-membered ring [2], a structure composed of three carbon atom and two nitrogen atom in an adjacent position [3], Nitrogen important class of natural product and useful biological activity [4]. Drug discovery of compounds based on pyrazole ring [5] and design new heterocyclic compounds [6]. In 1959, the first natural Pyrazole, 1-Pyrazolyl alanine, isolated from the seed of Watermelon [7], typical pyrazole structure are shown in fig [8].



Pyrazole

Pyrazole are apply to block organic synthesis of heterocyclic compound [9-12]. These compound play prime role in medicine [13] and agricultural chemistry [14,15]. Researcher attract[16] and effects the different field [17], such as[18] antimicrobial [19,20], antifungal [21], anticancer [22,23], anti-inflammatory[24], antiviral [25], antitubercular [26-29], antianthelmintics [30], antibacterial [31-34], anticonvulsant [35], MAO inhibitor [36,37], antioxidant [38], antidiabetic[39,40] activity. Antimicrobial resistance treatment of diseases caused by fungi, bacteria, virus [41,42].

The aim of work is the design [43] and synthesis a new heterocyclic compound based on pyrazole moiety [44] and biological evaluation of antimicrobial activities [45]. Pyrazole is an important reagent in organic synthesis and found various applications [46]. Pyrazole compound synthesized by various synthetic route [47] and lead for modification of drug design, development of compounds [48].

Physical and Chemical Properties of pyrazole:

Pyrazole particular stable compound with relative high boiling point. Pyrazole boil at 187-188^{0}C and melt at 70^{0}C, Pyrazole is a colourless solid [49].

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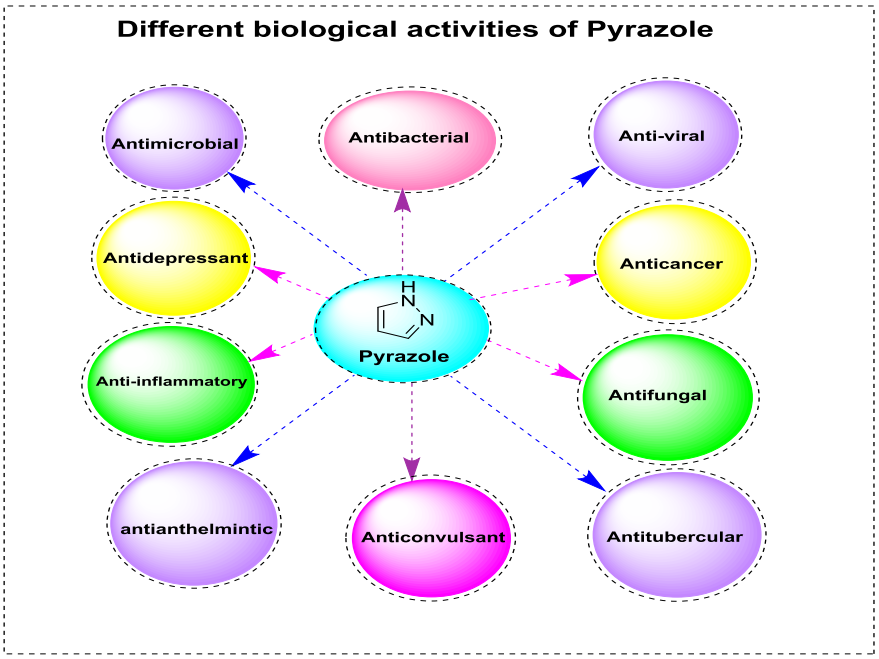
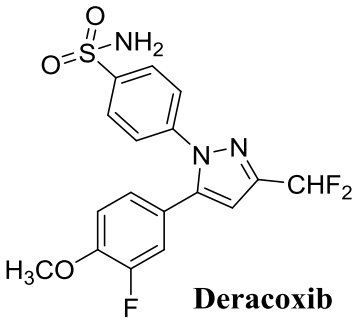
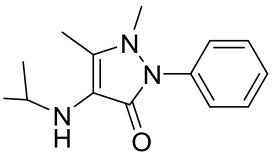


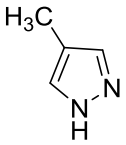
Drugs Containing pyrazole Moiety:



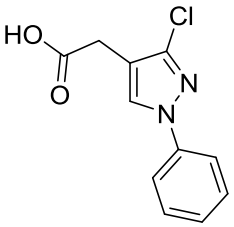
Deracoxib



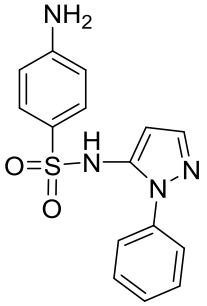
Ramifenazone



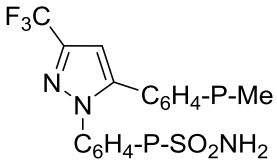
Fomepizole



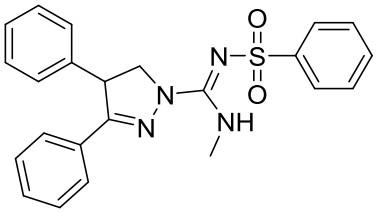
Lonazolac



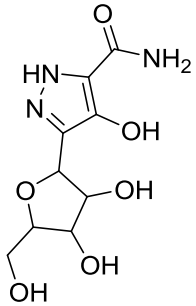
Sulphaphenazole



Celebrex



Ibipinabant



Pyrazofurin

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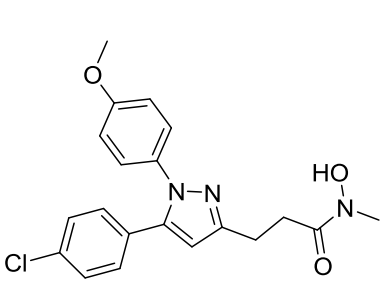
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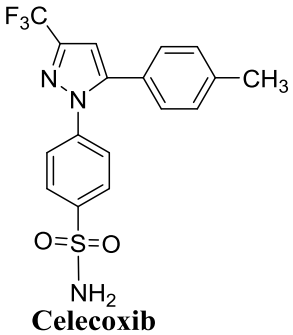
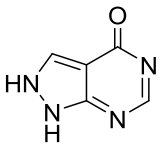
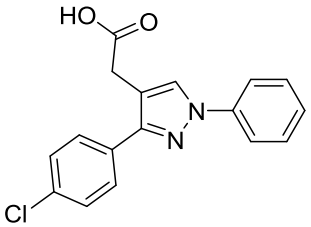
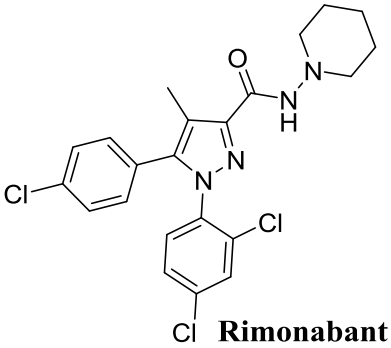
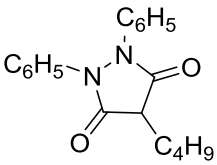

Celecoxib


Allopurinol


Ionazolac


Rimonabant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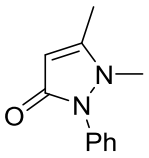
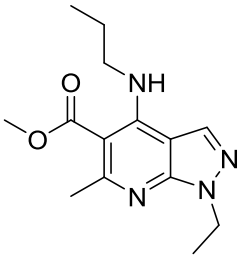
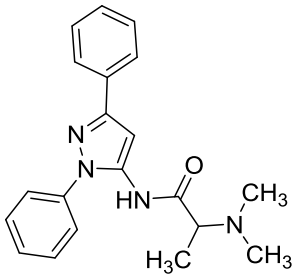
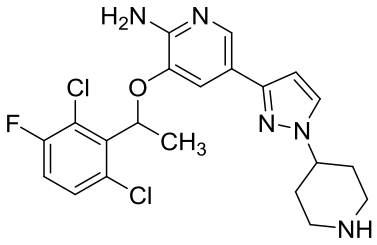
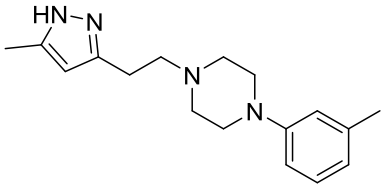
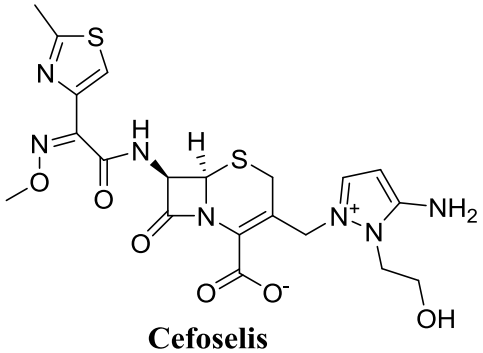

Antipyrine

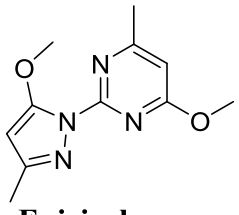

Tracazolate


Difenamizle


Crizotinib


Tolpiprazole


Cefoselis


Epirizole

Number of pharmaceutical drug and natural product based on pyrazole moiety [50] such as Deracoxib (NSAID) [51,52], Ramifenazone (anti-inflammatory) [53], Fomepizole (antidote) [54], Lonazolac (NSAID) [55], Sulphaphenazole (antibacterial) [56,57], Celebrex (NSAID) [58], Ibipinabant (obesity) [59], Pyrazofurin (anticancer) [60], Tepoxalin (NSAID) [61], Celecoxib (anti-inflammatory) [62], Allopuronol [63], Ionazolac (anti-inflammatory) [64], Rimonabant (antiobesity) [65], Phenylbutazone [66], Antipyrine [67], Tracazolate (anxiolytic) [68], Difenoconazole (fungicide) [69], Crizotinib (anticancer) [70], Tolpiprazole (anxiolytic) [71], Cefoselis (antibacterial) [72], Epirizole (anti-inflammatory) [73] .

Physical and Chemical Properties of Isoniazid:

Chemical Name – INH [74]

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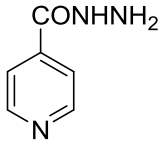
Molecular Weight – 137.14

Molecular formula – $C_6H_7N_3O$

Isoniazid is Colourless and white crystalline powder [75], Melting point 170.0^0-170.8^{0}C [76]

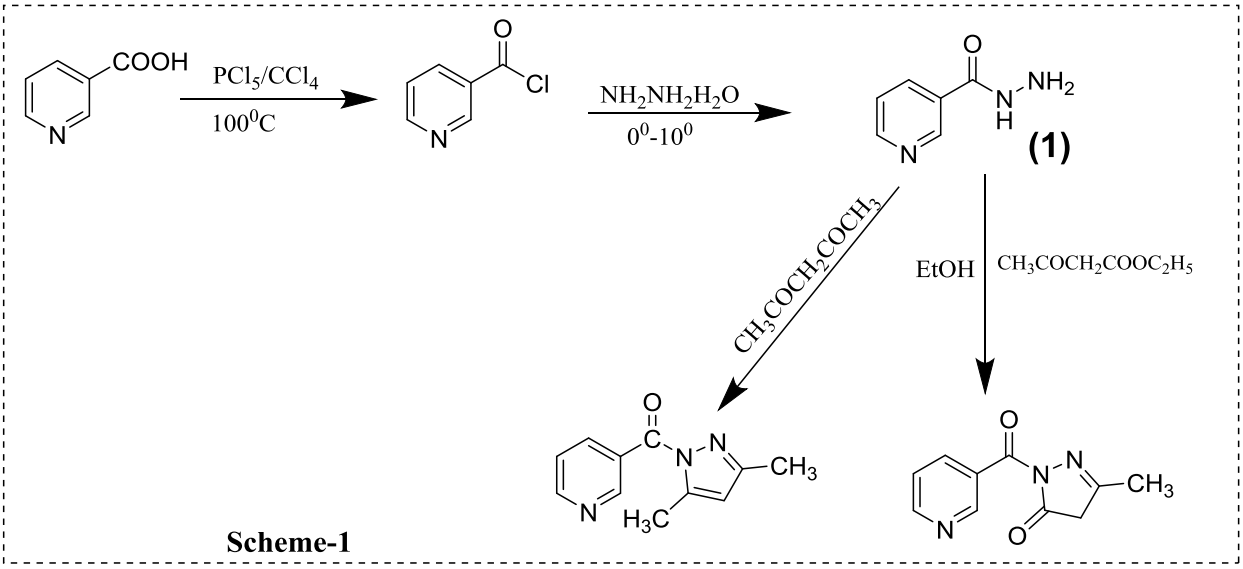
Structure of Isoniazid [77]



Various Synthetic Schemes of Isoniazid based Pyrazole:

Biological activity of compound finds out by synthetic route [78]. The synthetic organic compound finds out using an important drug (Isoniazid), Pyrazole compound synthesis based on the treatment of diseases [79].

[80] Synthesized Isoniazid (1) by using mixture of nicotinic acid and phosphorous pentachloride in anhydrous carbon tetrachloride. The resulted series of (3,5-dimethyl-1H-pyrazol-1-yl)(Pyridine-3-yl)methanone and 3-methyl-1-nicotinoyl-1H-pyrazol-5(4H)-one prepared by using Isoniazid (Scheme-1). Synthesized compound tested for antimicrobial and antimycobacterial activity.



Scheme-1

[81] Synthesis substituted Pyrazole compound i.e (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted benzoyl/ isonicotinoyl/ cinnamoyl-Pyrazol-3-yl)-amine obtained by the cyclocondensation of N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo butyramide with substituted acid hydrazide. Synthesis of butyramide done by react 2,4-diamino-6-methyl-[1,3,5]-triazine with benzaldehyde and condensing the product with ethyl acetoacetate. Microwave irradiative reaction required high yield product (Scheme-2). The synthesize product tested for antimicrobial activity.

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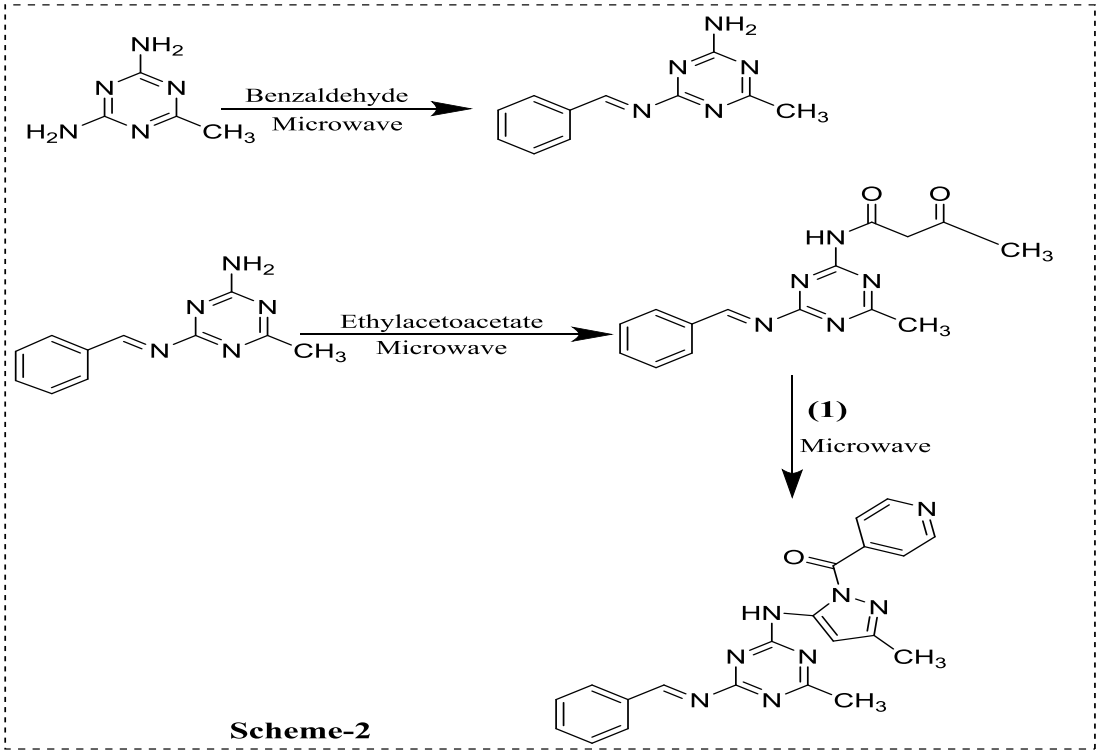
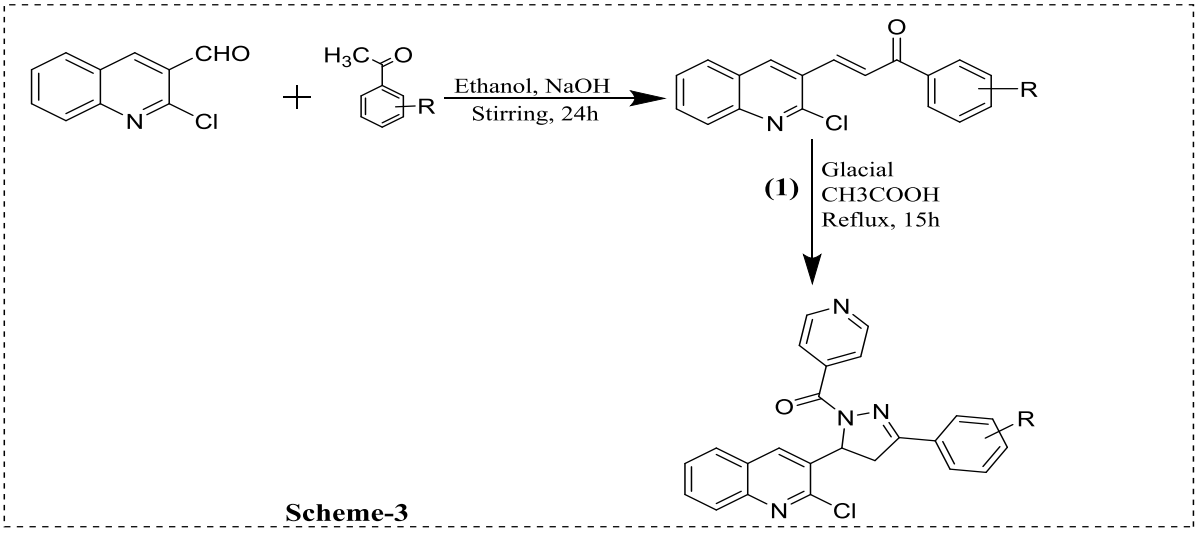


Scheme-2

[82] Vilsmeier-Haack reaction provide synthesis of substituted heterocyclic compound 3-(2-chloro-quinolin-3-yl)-1-(aryl)prop-2-en-1-one, Claisen-schmidt Condensation synthesis different acetophenone derivative and compound 2-chloroquinoline-3-carbaldehyde. Chalcone compound on cyclocondensation with isoniazid final compound (5-(2-chloroquinolin-3-yl)-3-aryl-4,5-dihydro-1H-pyrazol-1-yl)(pyridine-4-yl)methanone (Scheme-3). Compound tested by antibacterial and antifungal activity. The electron withdrawing group enhance the antimicrobial activity of synthesize compound.



Scheme-3

[83] Starting material 3-(4-nitrophenyl)-1-phenyl-1H-Pyrazole-4-carbaldehyde synthesize by condensation with Isoniazid by reflux in 1,4-dioxane for 8h, to produce N-((3-(4-nitrophenyl)-1-phenyl-1H-Pyrazol-4-yl)methylene) isonicotinohydrazide. Cyclization reaction with acetic anhydride under reflux resulting 1-(2-(3-(4-nitrophenyl)-1-phenyl-1H-Pyrazole-4-yl)-5-(Pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone. Claisen-Schmidt condensation of intermediate resulting compound with aldehyde in ethanolic potassium hydroxide under reflux 6-7h , final compound are 1-(2-(3-(4-nitrophenyl)-1-phenyl-1H-Pyrazol-4-yl)-5-(Pyridin-4-yl)-

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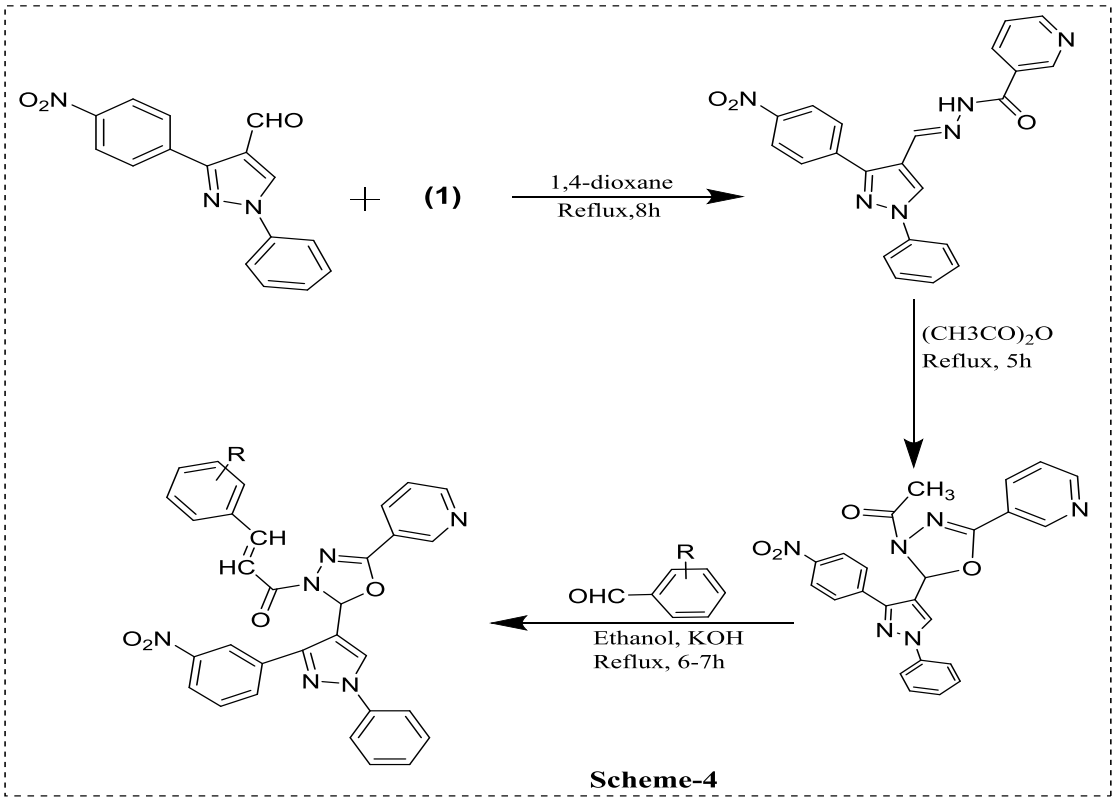
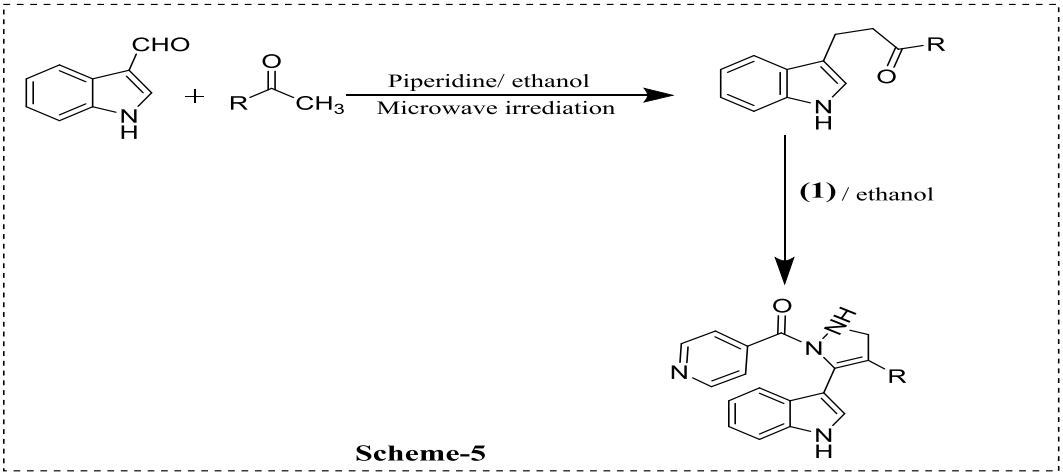
1,3,4-oxadiazol-3(2H)-yl)-3-(aryl)prop-2-en-1-one (Scheme-4). These structure screened for antimicrobial activity.



Scheme-4

[84] Reaction of 3-(1H-indol-3-yl)-(1-methyl/ phenyl) prop-2-en-1-one (chalcone) carried out with hydrazine hydrate, Isoniazid in ethanol contain few drop of glacial acetic acid under microwave irradiation give 1H-indol contain Pyrazole derivative (Scheme-5). Compound tested by antibacterial and antifungal activities.



Scheme-5

[85] A series of (3-(1H-benzoimidazol-2-yl)-5-(aryl)-4,5-dihydro-1H-Pyrazol-1-yl)(Pyridin-4-yl)methanone good yield (Scheme-6), synthesize by the reaction of benzimidazolyl chalcone with Isoniazid. Synthesized compound screened for antimicrobial activity and starting material synthesize by Claisen-Schmidt reaction.

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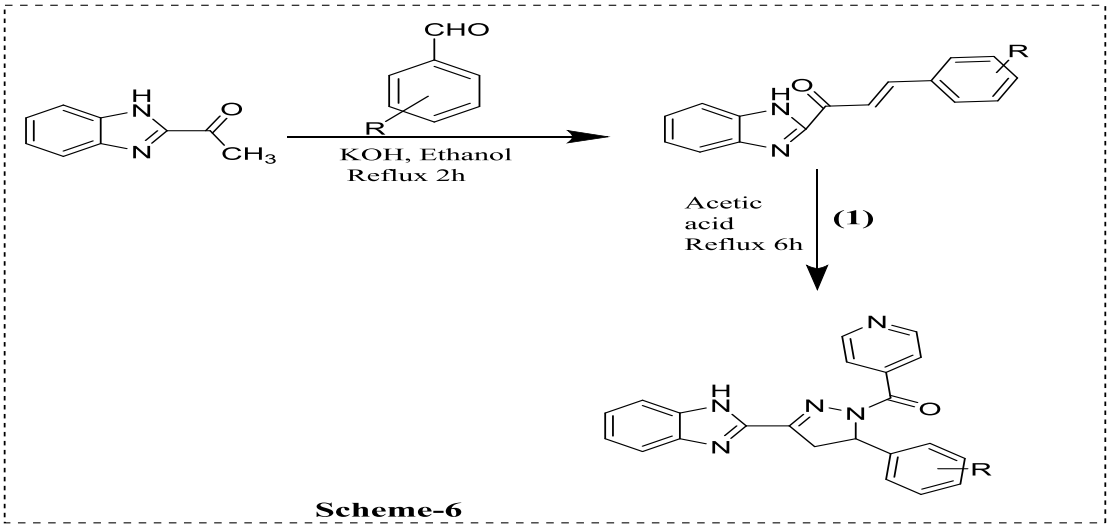
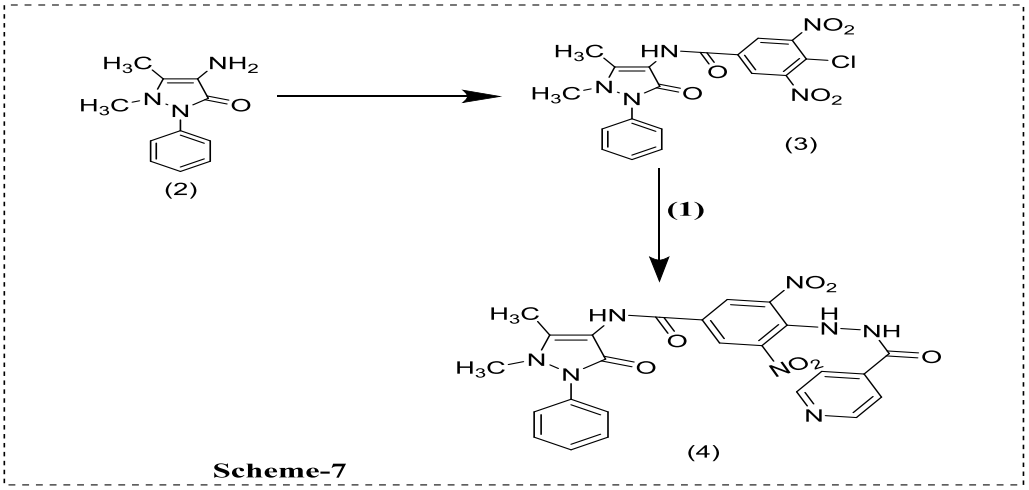


Scheme-6

[86] First compound 4-amino-antipyrine synthesis by using 4-carboxybenzo-15-crown-5 ether and N,N′-dicyclohexylcarbodiimide (DCC) simple coupling reaction. Compound (3) to obtain first the acid chloride from 4-cloro-3,5-dinitrobenzoic acid and further reaction with 4-AAP. Compound (4) gave from using Isoniazid with good yield in simple coupling reaction (Scheme-7). Synthesis compound test for antimicrobial activity.



Scheme-7

[87] Starting material 2,5-disubstituted indol-3-carboxaldehyde obtain from the Vilsmeier Haack reaction of 2,5-disubstituted indole and 3-acetyl-2H-chromen-2-one synthesis by the reaction of Salicylaldehyde with ethyl acetoacetate in the presence of piperidine. [E]-3-(3-(2,5-disubstituted -1H-indol-3-yl)acryloyl)-2H-chromen-2-one obtained by Clainsen-Schmidt condensation with 2,5-disubstituted indol-3-carboxaldehyde presence mixture of piperidin and n-butanol. The resulting compound treated with isoniazid presence of triethylamine in ethanol yield compound 3-[3-(2,5-disubstituted-1H-indol-3-yl)-1-isonicotinoyl-1H-Pyrazol-5-yl]-2H-chromen-2-one (Scheme-8) and biological studies anti-tuberculosis,anti-microbial activity.

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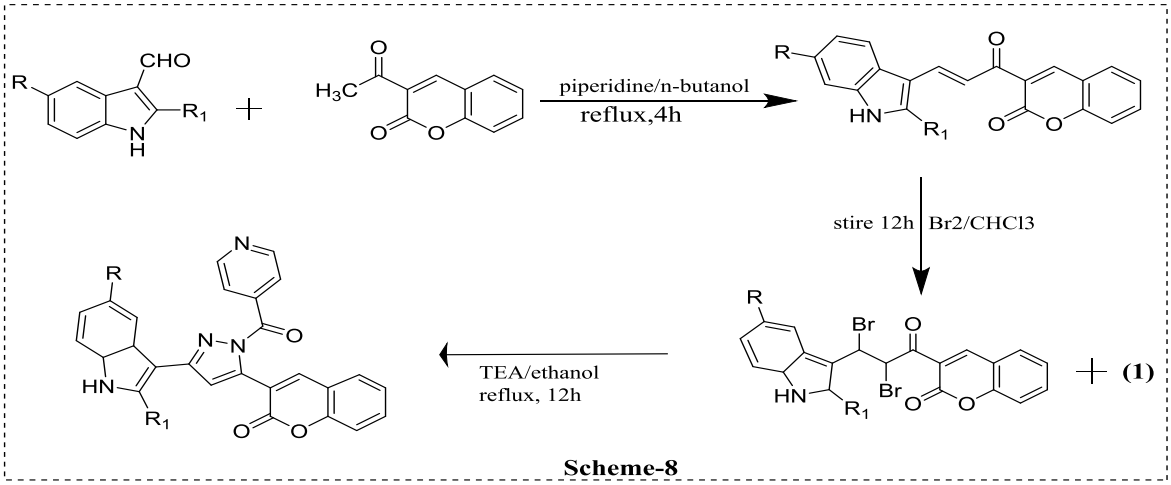
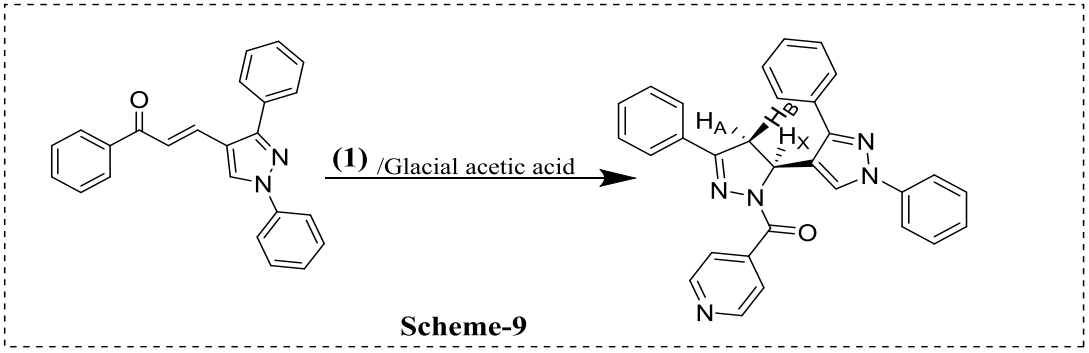


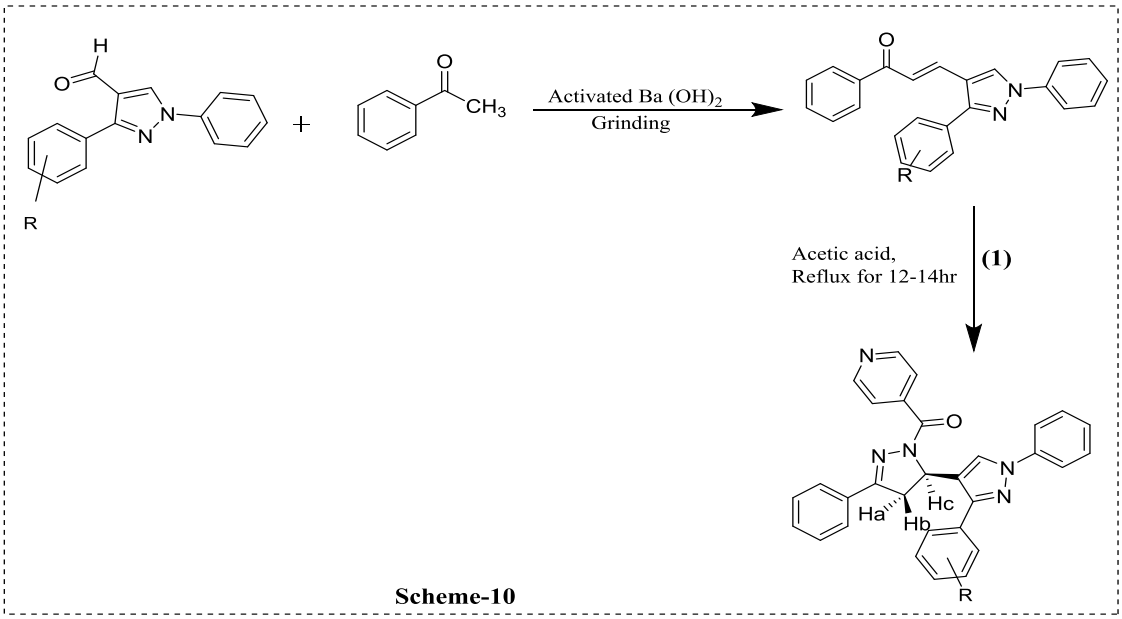
Scheme-8

[88] The compound [5-(1,3-diphenyl-1H-Pyrazol-4-yl)-3-phenyl-4,5-dihydropyrazol-1-yl](pyridine-4-yl)methanone prepared by 3-(1,3-diphenyl-1H-Pyrazol-4-yl)-1-phenylprop-2-en-1-one and Isonicotinic acid hydrazide in glacial acetic acid (Scheme-9).



Scheme-9

[89] A series of (3-phenyl-5-(1-phenyl-3-aryl-1H-Pyrazol-4-yl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridine-4-yl)methanone synthesis by 3-(3-aryl-1-phenyl-1H-pyrazol-4-yl)-1-phenylprop-2-en-1-one with pyrazole aldehyde and acetophenone and activated barium hydroxide (Scheme-10).The compound screened for antimicrobial activity and show good activity.



Scheme-10

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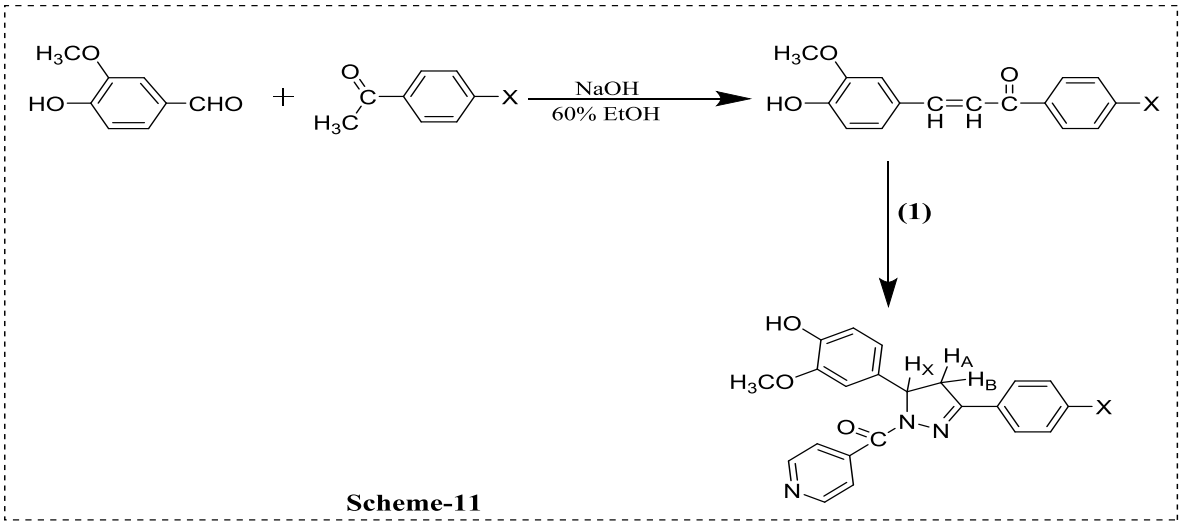
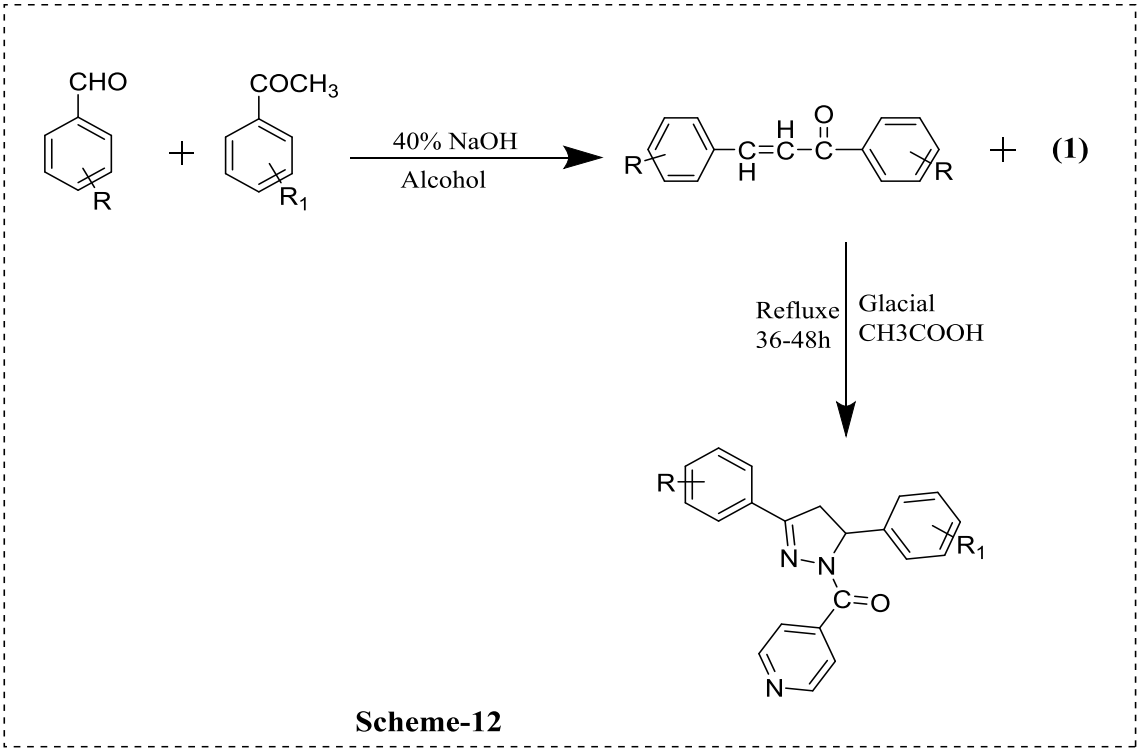
[90] synthesis of chalcone by Claisen-Schmidt condensation in ethanol and acetophenone, 4-hydroxy-3-methoxy-benzaldehyde (Vanillin). Condensation of chalcone with isonicotinic acid hydrazide in ethanol and few drop of acetic acid resulting compound are (5-(4-Hydroxy-3-methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)(pyridine-4-yl)methanone (Scheme-11).The isolated compound test for antimicrobial activity.



Scheme-11

[91] A series of 1,3,5-trisubstituted pyrazoline synthesis by chalcone cyclization in the presence of glacial acetic acid with Isoniazid (Scheme-12). These compound are evaluated for invitro antimicrobial activity.



Scheme-12

[92] Synthesis of α,β-unsaturated keton by condensation of benzyl methyl ketone with p-substituted benzaldehyde in the presence of piperidine. Final compound synthesis by condensation with Isonicotinic acid hydrazide in ethanol contain few drop of acetic acid give 4,5-Dihydro-3-methyl-4-phenyl-5-(p-substituted phenyl)-1-Isonicotinoylpyrazole (Scheme-13) and antimicrobial activity test on isolated compound ,these compound show potent antimicrobial activity.

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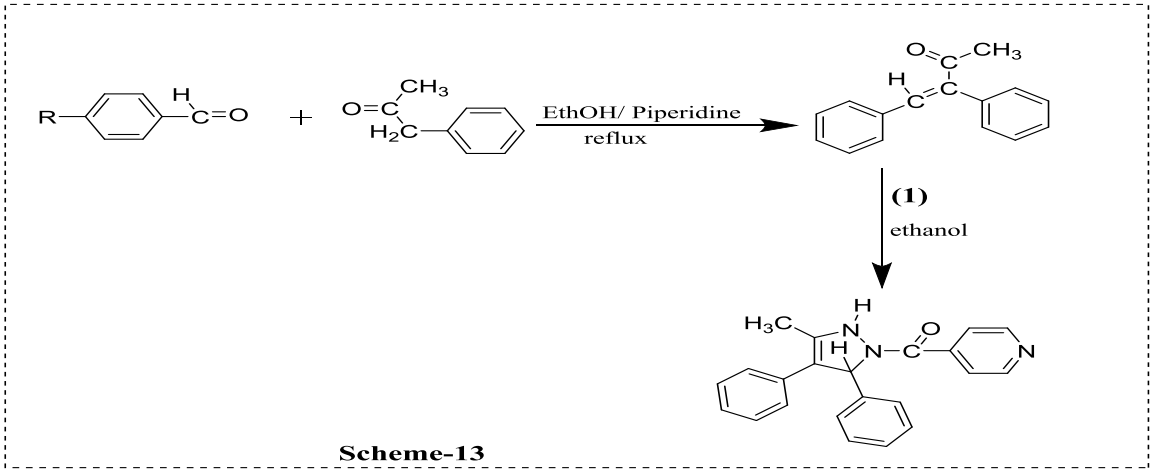
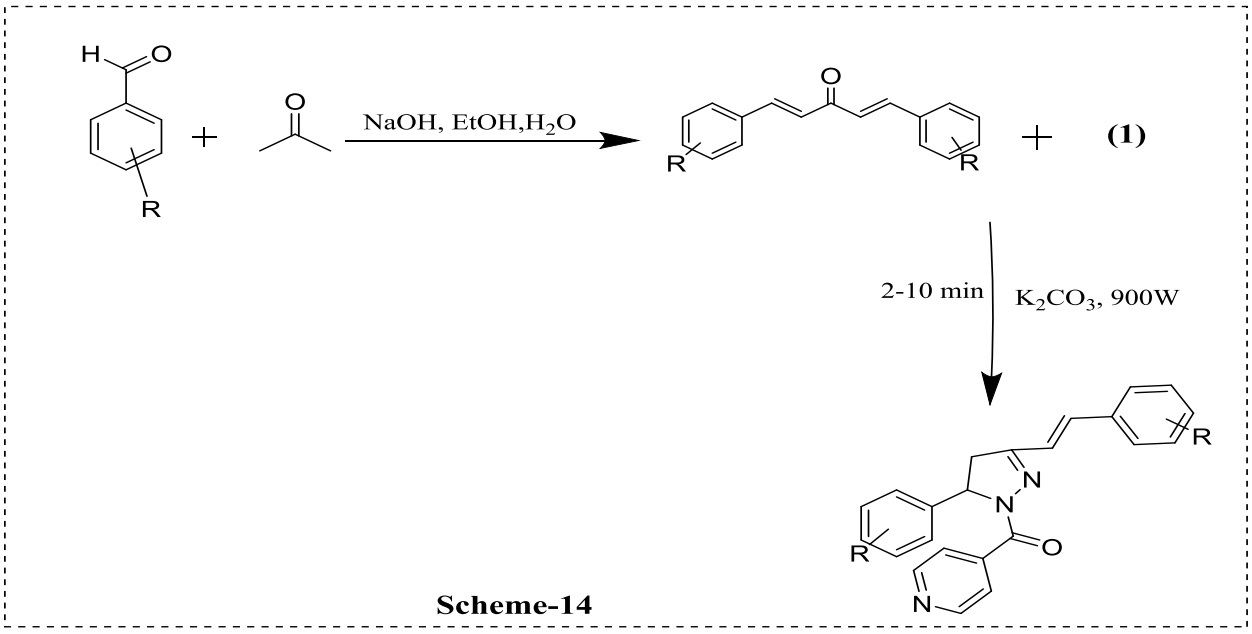


Scheme-13

[93] (1E,4E)-1,5-bis(3-phenyl)penta-1,4-dien-3-one prepare by sodium hydroxide with ethanol and benzaldehyde, aceton. A series of 4-{5-phenyl-3[(E)-2-2 phenylethenyl] 4,5-dihydro-1H-pyrazole-1-carbonyl}pyridine synthesis by dibenzalacetone and Isoniazid, dichloromethane (Scheme-14). The resulted compound show good activity.



Scheme-14

[94] Synthesis Series of 1-(2-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-5-(pyridine-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-3-(aryl)prop-2-en-1-one by first compound 3-(4-fluorophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde with Isoniazid and N′-((3-(4-flurophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)isonicotinohydrazide, reflux with 1-(2-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-5-(pyridine-4-yl)-1,3,4-oxadiazol-3(2Hyl)ethanone (Scheme-15). Synthesis compound test for antimicrobial activity.

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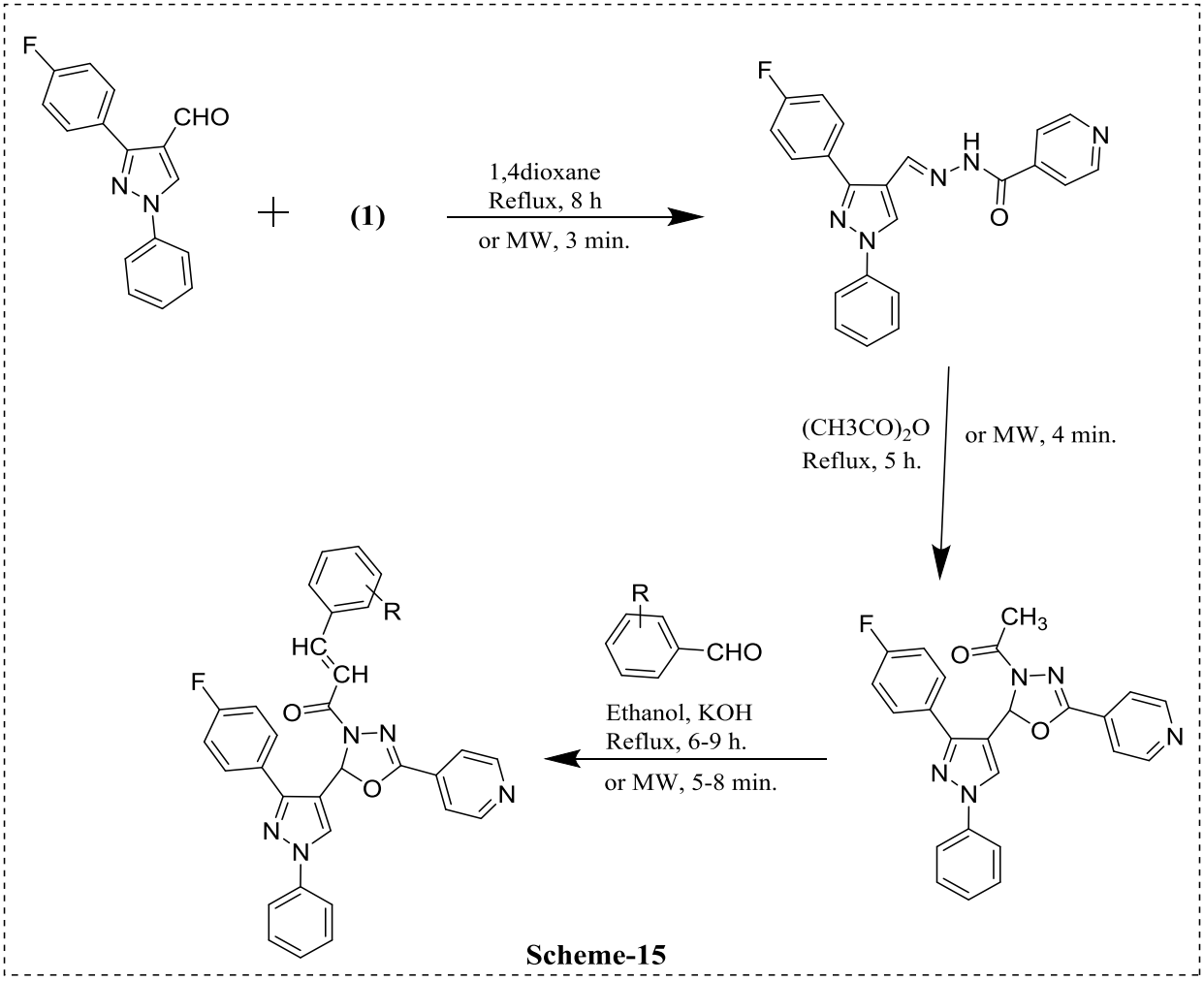
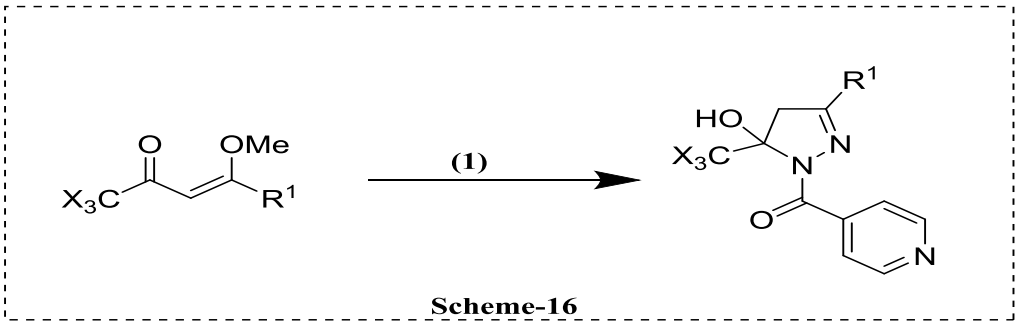


Scheme-15

[95] Synthesis Series of 1-isonicotinoyl-3-alkyl (aryl/heteroaryl)-5-trihalomethyl-5-hydroxy-4,5 dihydro-1H-pyrazole by cyclocondensation reaction 4-alkyl(aryl/heteroaryl)-1,1,1-trihalo-4-alkoxy-3-alken-2-one with isoniazid (Scheme-16). Resulted compound evaluated for antimycobacterial activity.



Scheme-16

[96] 2-isonicotinoyl-5-methyl-2,4-dihydro-3H-pyrazol3-one prepare by isoniazid with ethylacetoacetate in alcohol, presence of sodium ethoxide. These compound perform arylidene treated with 4-substituted benzaldehyde. Arylidene compound react with hydrazine hydrate cyclocondensation reaction give 4-(4-chlorophenyl/4-methoxyphenyl/4-N,N-dimethylaminophenyl/phenyl)-1-isonicotinoyl-3-methyl-3,4-dihydropyrazolo[3,4]-pyrazole.The resulted compound 2-N-ethoxyphthalimido-6-isonicotinoyl-4-methyl-3-(4-substituted phenyl)-3,3-dihydropyrazolo[3,4]pyrazoles react with phthalimidoxy ethy bromide (Scheme-17). Resultant compound evaluated for antibacterial, antimicrobial, antiviral activity.

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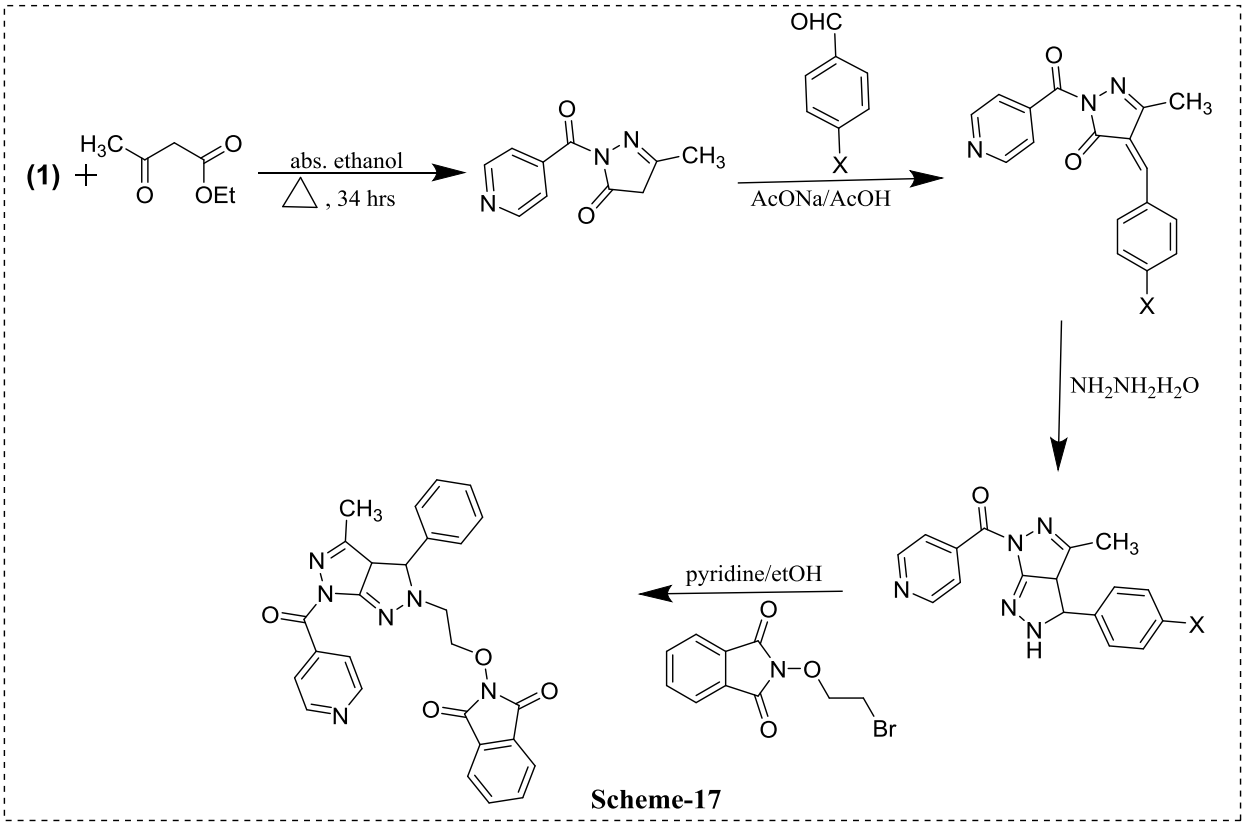
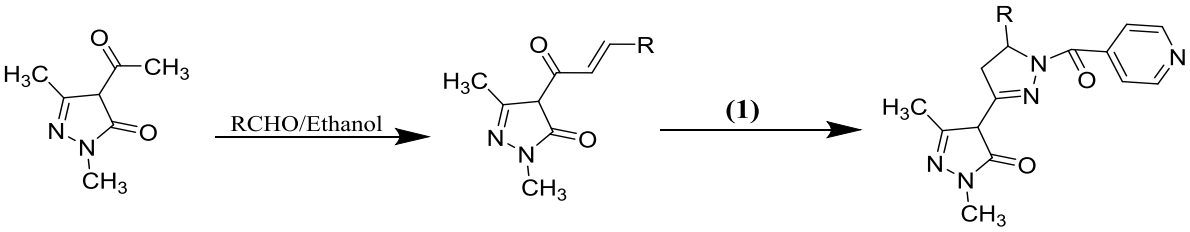


Scheme-17

[97] Series of pyrazole synthesized using mixture of aldehyde and 4-acetyl-3-methyl-1(P-tolyl)-pyrazol-5(4H)-one in ethanol give 3-methyl-1-p-tolyl-4-(3-arylacryloyl)-1H-pyrazol-5(4H)-one. Reaction mixture of given compound and isoniazid reflux to pass 1-isonicotinoyl-3'-methyl-5-aryl-1'-p-tolyl-4,5-dihydro-1H,1'H-3,4'-bipyrazol-5'(4'H)-one (Scheme-18). These compound screened for antimicrobial activity.



Scheme-18

[98] First step condensation of isoniazid with 4-nitroacetophenone presence glacial acetic acid to pass N'-[1-(4-nitrophenyl)ethylidene] benzohydrazide. These compound treated with Vilsmeier Haack reaction to give 3-(4-nitrophenyl)-1-(pyridine-4-ylcarbonyl)-1H-pyrazol-4-carbaldehyde presence aromatic amine and thioglycolic acid, toluene resulted series 2-[3-nitrophenyl-1-(pyridine-4-yl-carbonyl)-1H-pyrazol-4-yl]-3-substituted-1,3-thiazolidin-4-one (Scheme-19) and test for antitubercular and antimicrobial activity.

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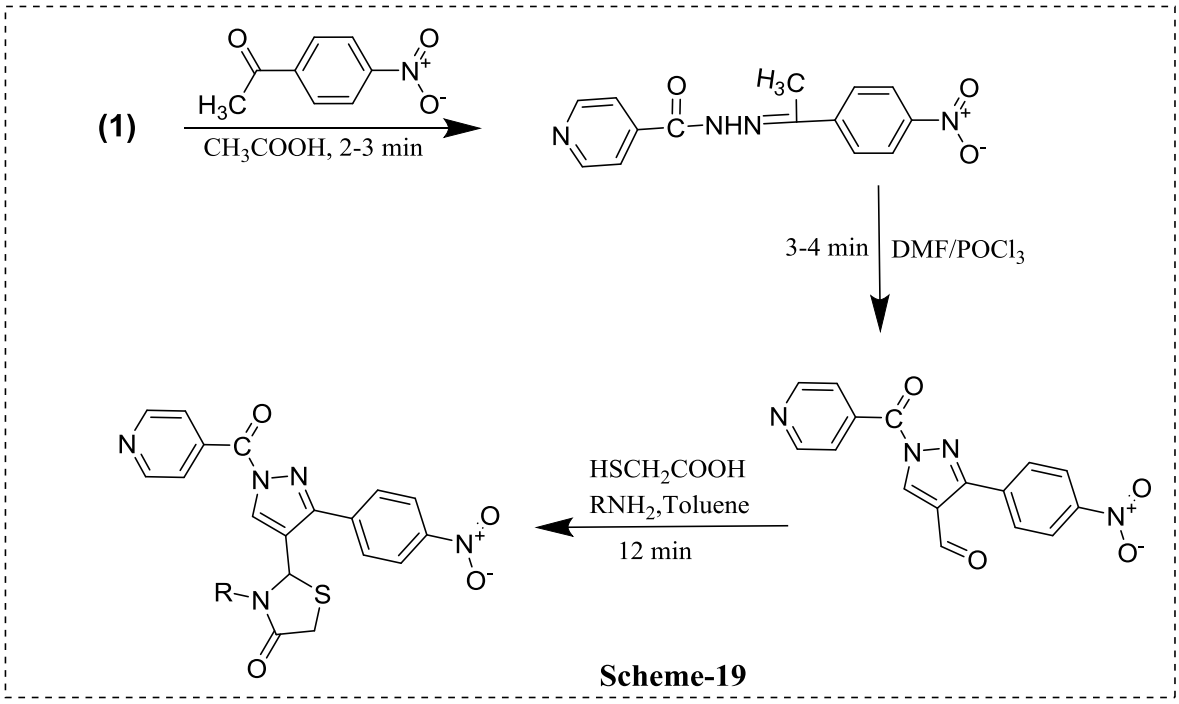

Scheme-19

II. CONCLUSION

The Review survey shows that a number of heterocyclic compounds is known for design and synthesis of the potential area of research. Various heterocyclic derivatives are exhibit a range of pharmacological activities such as antibacterial, antimicrobial, analgesic, anti-inflammatory, and antitubercular, antifungal, anticancer activities. This heterocyclic moiety has a significant pharmacological and medicinal value. This review provides important information for the design of pyrazole skeleton based new microbial agents. Researchers attracted to design more potent pyrazole derivatives having a wide range of biological activities. These derivatives have a long history of application in the agrochemicals and pharmaceutical industries. The synthetic and biological activity of heterocyclic compound help to organize new scheme in medicinal chemistry.

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