

REVIEW ON SYNTHESIS OF PYRANOPYRAZOLES DERIVATIVES

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Abstract:

Pyranopyrazole is a heterocyclic organic compound in which the pyran ring substituted by pyrazole in the ortho position. Pyranopyrazole can be synthesized by using Knoevenagel condensation, Michael's addition, and cyclization reaction. Synthesis involves a multicomponent reaction of aldehyde, hydrazine, ethyl acetoacetate, and malononitrile as a precursors. These bioactive heterocycles has attracted the interest of medicinal and organic chemists due to their biological and medicinal properties. This review focuses on the recent developments in multicomponent synthesis of pyranopyrazole. The present review describes the literature reports for the period 2005 to 2018. These reported approaches were performed in the classical and nonclassical conditions, particularly recent reports includes protocols under a green condition such as using catalyst, green solvents, and solvent-free conditions.

Keywords: multicomponent reactions; heterogeneous catalysts; pyranopyrazoles; one-pot process;

1. Introduction

For the sustainable development of chemical enterprises the development of non-hazardous alternatives such as solvent-free syntheses, eco-friendly process and reusable heterogeneous catalysts has given attention due to restrictions on the use, manufacture and disposal of organic solvents. These organic process shows significance such as solvent-free multicomponent reactions with heterogeneous reusable catalysts reduce the consumption of environmentally hazardous solvents.

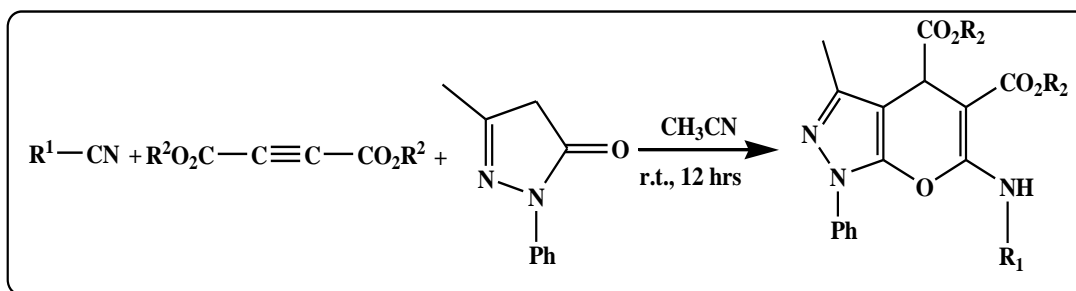
The application of solid acids as heterogeneous catalyst has gained considerable attention in various fields of organic processes. Heteropolyacids (HPAs) have several advantages, such as high flexibility on modification of the acid strength, ease of handling, environmental compatibility, non-toxicity and experimental simplicity [1]. They are found to be highly effective in catalyzing reactions that conventionally use Lewis acids [2] because they shows a strong purely Brønsted acidity. Thus, the process becomes convenient and environment friendly due to the use of HPAs as a catalyst. Heteropolyacids has excellent catalytic properties in the dehydration of diols [3], rearrangements, tetrahydropyranation of alcohols [4], Friedel-Craft alkylation [5], Prins reaction [6], synthesis of dihydroquinolines [7], pyrimidine synthesis [8], Biginelli reaction [9] and Dakin-West reaction [10]. Pyranopyrazoles are reported to possess a wide range of pharmacological properties including anticancer, antimicrobial, anti-inflammatory, insecticidal and molluscicidal activities. So they are prime class of biologically active heterocycles [11-13]. They are also potential inhibitors of human Chk1 kinase [31]. Pyranopyrazoles used in pharmaceutical ingredients and biodegradable agrochemicals. For the synthesis of 6-amino-5-cyanodihydro-pyrano- [2,3-c] pyrazoles various methods has been reported [14]. These compounds can be readily obtained from the reaction of 4-arylmethylene-5-pyrazolone and malononitrile, or 2-pyrazolin-5-ones and benzylidene malononitriles. First time pyranopyrazole was prepared from the reaction between 3-methyl-1- phenylpyrazolin-5-one and tetracyanoethylene [15]. Various 6- amino-5-cyanodihydro-pyrano [2, 3-c] pyrazoles was synthesized by using arylidene malononitrile with 3-methylpyrazoline-5-ones or by the condensation of 4- arylidene pyrazoline-5-one with malononitrile [16-19].

Three-component reaction between pyrazolone, an aldehyde, malononitrile and triethylamine as the catalyst in ethanol was used by Sharanin et al., [10]. Vasuki and coworkers carried out an efficient four-component reaction for the synthesis of pyranopyrazole derivatives with respect to various bases such as pyrrolidine, morpholine, piperidine, and triethylamine at ambient temperature [11]. Solvent-free multicomponent synthesis of pyranopyrazoles using per-6-amino- β -cyclodextrin as a catalyst [20] was developed by Kappusami et al. More recently Myrboh et al. reported the synthesis of pyranopyrazoles using L-proline and γ -alumina as catalyst [21].

2. Synthesis of Pyranopyrazole and its derivatives:

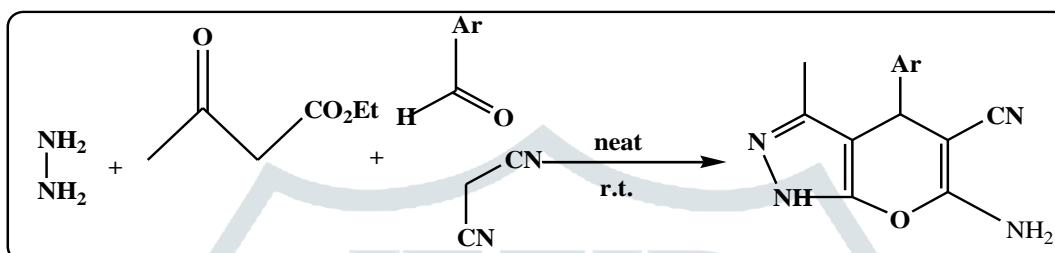
Various types of methods for synthesis of pyranopyrazole and its derivatives are available in literatures which are discussed below.

Shaabani et al. [22] reported a three-component reaction for the preparation of pyranopyrazoles in presence of acetylenedicarboxylate, isocyanides, and 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (Scheme 1.1).



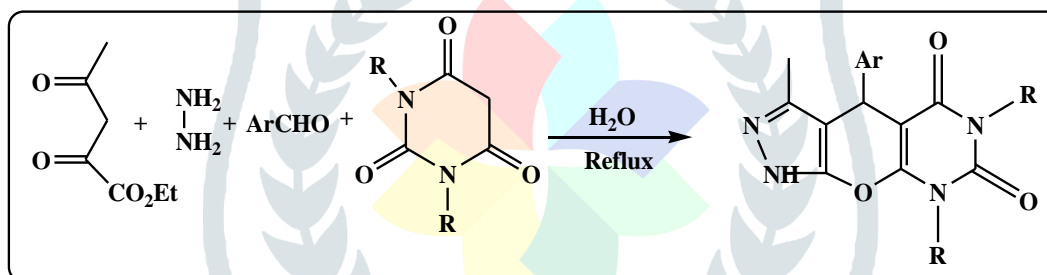
Scheme 1.1

A catalyst-free synthesis of a number of pyranopyrazoles via a four-component reaction between an aromatic aldehyde, hydrazine hydrate, ethyl acetoacetate and malononitrile at room temperature under neat conditions was reported by Nagarajan et.al. [23] (Scheme 1.2).



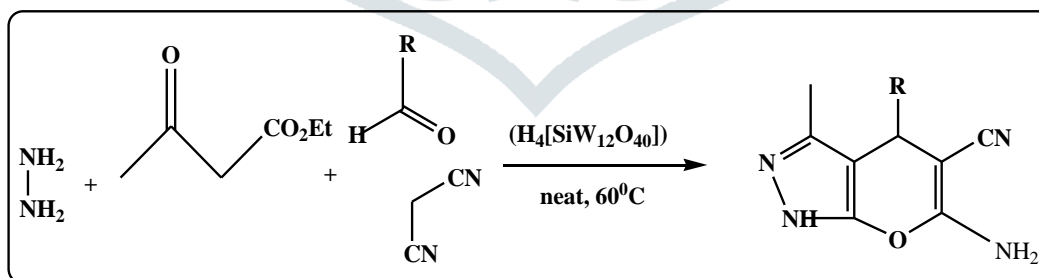
Scheme 1.2

In 2012, Moshtaghi Zonouz et.al. [24] have reported synthesis of methyl 6-amino-5-cyano-4-aryl-2,4-dihydropyrano[2,3-c]pyrazole-3-carboxylates by using four-component catalyst-free reaction between dimethyl acetylene dicarboxylate, hydrazine hydrate, malononitrile, and aromatic aldehydes (Scheme 1.3).



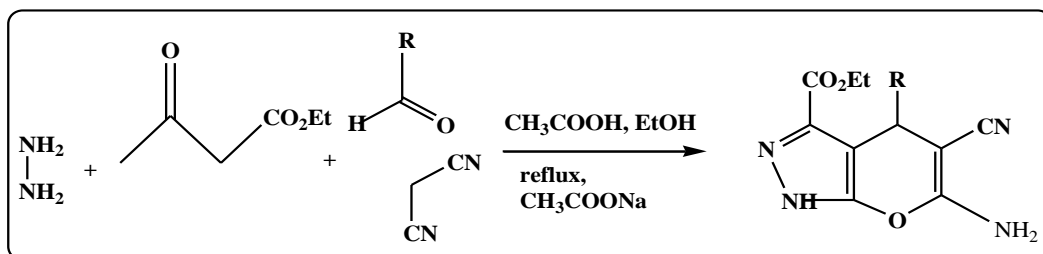
Scheme 1.3

In 2011 Chavan et.al. [25] efficiently synthesized, a series of pyrano[2,3-c]pyrazoles, via one-pot, four component reaction of ethyl acetoacetate, hydrazine hydrate, aldehydes and malononitrile in the presence of environmentally friendly catalyst silico tungstic acid ($H_4[SiW_{12}O_{40}]$) at 60 °C without solvent (Scheme 1.4).



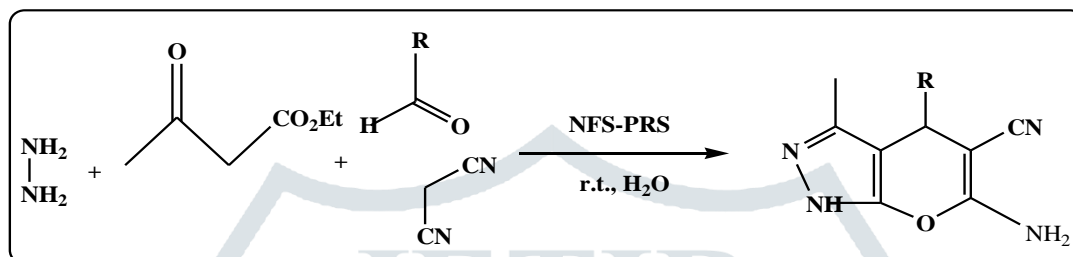
Scheme 1.4

Gein et al. [26] have demonstrated synthesis of ethyl 6-amino-4-aryl-5-cyano-2,4-dihydropyrano [2,3-c] pyrazole-3-carboxylates via a four-component reaction of the sodium salt of diethyl oxaloacetate, an aromatic aldehyde, hydrazine hydrate and malononitrile in EtOH and using acetic acid as a catalyst (Scheme 1.5).



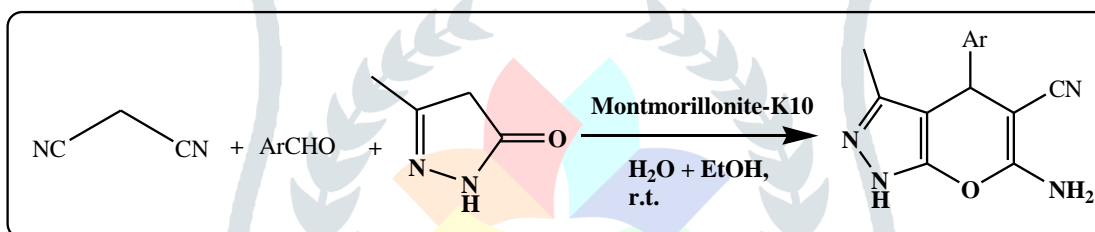
Scheme 1.5

Javid et al. [27] have investigated the preyssler HPA supported onto the silica coated NiFe_2O_4 MNPs ($\text{NiFe}_2\text{O}_4@/\text{SiO}_2$ -Preyssler, abbreviated NFS-PRS) as an efficient and green catalyst for the synthesis of pyrano [2,3-c] pyrazole derivatives via condensation reaction of aromatic aldehydes, hydrazine hydrate, ethyl acetoacetate and malononitrile at room temperature in water (Scheme 1.6).



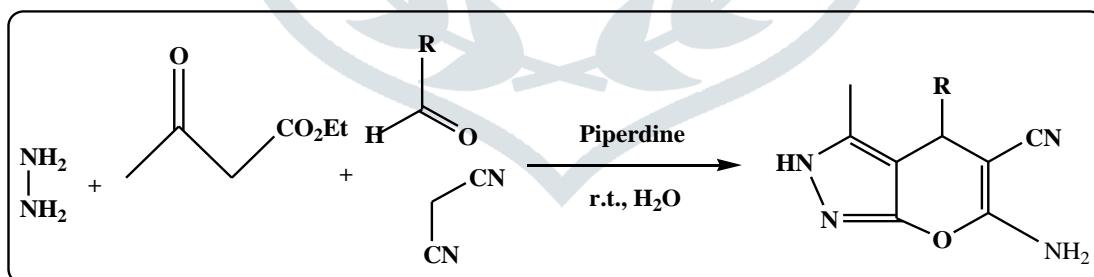
Scheme 1.6

Reddy et.al. [28] demonstrated reusable green heterogeneous acid catalyst Montmorillonite-K10 which was applied under ecofriendly condition to prepare pyrano [2,3-c] pyrazoles (Scheme 1.7).



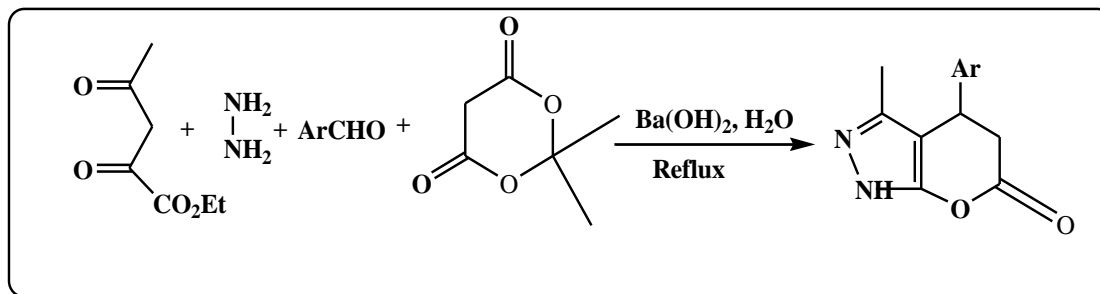
Scheme 1.7

Vasuki and Kumaravel [29] have carried an environmentally benign four-component reaction for the synthesis of 6-amino-5-cyano-3-methyl-4-aryl/heteroaryl-2H,4H-dihydropyrano [2,3-c] pyrazoles in aqueous medium at room temperature by using piperidine as a catalyst (Scheme 1.8).



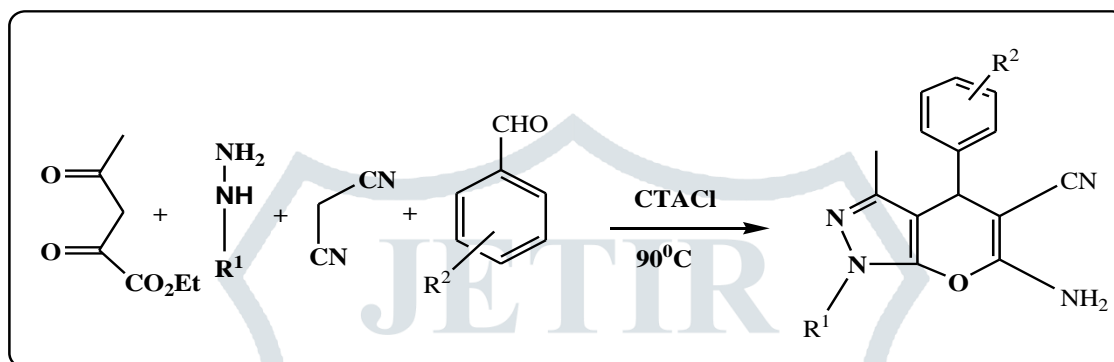
Scheme 1.8

In 2012, Azzam, and Pasha [30] gave $\text{Ba}(\text{OH})_2$ catalyzed one-pot four-component reaction of Meldrums acid, ethyl acetoacetate, hydrazine hydrate, and aromatic aldehydes gives 3-methyl-4-aryl-4,5-dihydro-1H-pyrano[2,3-c]pyrazol-6-ones in refluxing water (Scheme 1.9).



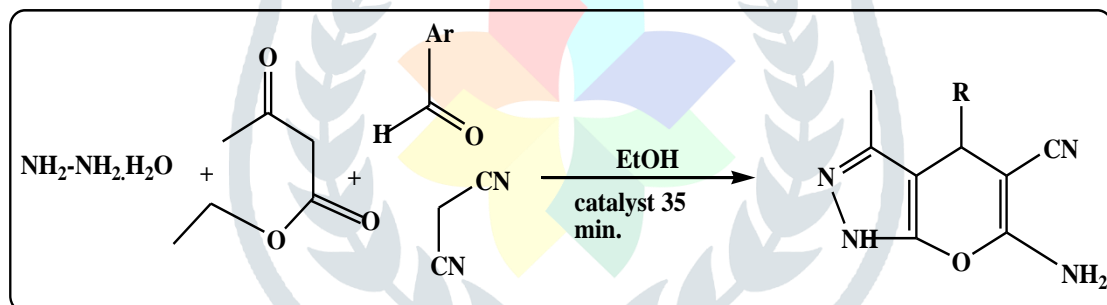
Scheme 1.9

The synthesis of 6-amino-3-methyl-4-aryl-1-phenyl-1,4-dihydropyranopyrazole-5-carbonitriles has been reported by Feng et al. [31]. Four-component reaction between ethyl acetoacetate, hydrazine hydrate or phenyl hydrazine, aromatic aldehydes, and malononitrile in aqueous medium by using cetyltrimethyl ammonium chloride (CTACl) as a catalyst is an eco-friendly synthesis (Scheme-1.10).



Scheme 1.10

Siddekha et al. [32] proposed a one-pot four-component synthesis of pyrano [2,3-c] pyroles from aryl aldehydes, ethyl acetoacetate, malononitrile, and hydrazine hydrate by using catalytic amounts of imidazole in water as medium (Scheme 1.11).



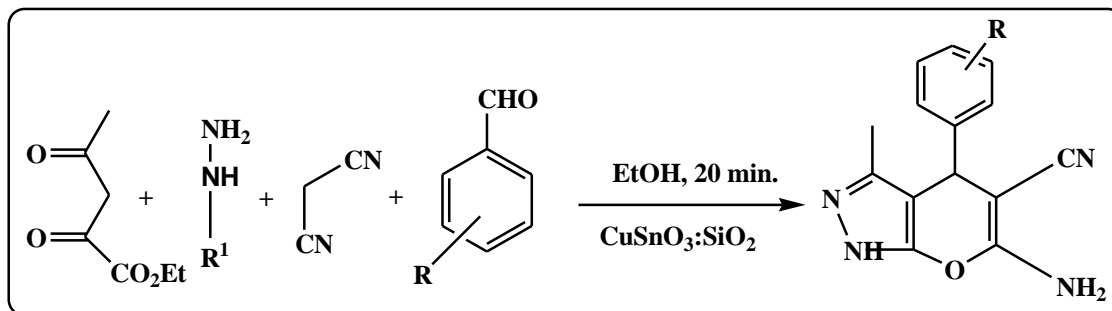
Scheme 1.11

Due to significance of pyranopyrazole, various synthetic routes have been reported to prepare these biologically active heterocycles. The synthetic procedure consists of single or multisteps, and two-component or multicomponent reactions (three or more compound) to obtain pyranopyrazole.

For the preparation of pyranopyrazole derivatives various methods are reported by multicomponent condensation reaction of aromatic aldehyde, ethylacetoacetate, hydrazine hydrate and malononitrile using various catalyst such as Sodium benzoate as the mild basic catalyst [33], triethylamine [34], DMAP (4-dimethylaminopyridine) [35], magnesium oxide [36], Fe₃O₄ nanoparticles [37], ZnS nanoparticles [38], nanosilica from wheat straw (WS-SiO₂ NPs) [39], nano-Fe [phenylsalicylaldiminemethylpyranopyrazole]Cl₂, Schiff base complex, n-Fe₃O₄/PVAm nanocomposite [40], β-Cyclodextrin-epichlorohydrin nanospongepolymer [41], Nd-SM [42], 1-butyl-3-methylimidazolium hydroxide ([bmim][OH]) [43], ZnS nanoparticle [44], molecular sieves (MS4 A⁰) [45].

But these reported methods possess certain disadvantages including low yield of product, lengthy procedure, difficult workup, and tedious reaction conditions. Therefore there is scope to find out new methodology with mild reaction conditions, better yield, short reaction time and environment friendliness. Recently, metal oxides or metals are also used as catalysts in organic reactions.

Perovskite metal oxide nanoparticles was used as a catalyst in organic conversions because of large surface area, high thermal stability, and easy recovery. When the size of catalyst is reduced to nanoregime, it shows higher catalytic activity due to increase in surface area of the catalyst. Hence the use of CuSnO₃:SiO₂ nanoparticles as an efficient and recyclable catalyst for the synthesis of pyranopyrazole derivatives by multicomponent reaction between ethylacetoacetate, aromatic aldehyde, hydrazine hydrate and malononitrile in ethanol (Scheme-1.12).



Scheme 1.12

3. Conclusion:

This review has covered the multicomponent strategies reported for the synthesis of pyranopyrazole during the period of 2005 to 2018. Since the most reports contains synthesis of pyrano[2,3-c]pyrazoles, by using several multicomponent strategies. These reactions were performed in classical and nonclassical conditions. In recent years using greener protocols by employing sonochemical conditions, MW-assisted technologies, and using solvent-free conditions and green solvent especially water as a solvent, heterogeneous catalysis especially nanocatalyst, ionic liquids, have made access to these significant heterocyclic compounds.

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