

Recent Developments for Eco-compatible And Environmentally Benign Synthesis of Pyranopyrazole Derivatives: A Review

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Abstract: Owing to biological and medicinal properties of pyranopyrazoles, synthesis of these bioactive heterocycles has attracted the interest of medicinal and organic chemists. This review focuses on the recent advances in greener and one-pot synthesis of pyranopyrazole derivatives. The present review describes the literature reports for the period 2011 to 2025. The reported methodologies encompass both conventional and alternative reaction conditions, with recent studies predominantly emphasizing environmentally sustainable protocols. These include the application of microwave and ultrasound irradiation, the use of catalytic systems, eco-friendly solvents, and solvent-free approaches.

Key Words: Pyranopyrazoles, one-pot synthesis, energy efficient synthesis, solvent-free condition

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1. Introduction:

To develop safer and more sustainable organic synthetic protocols, methodologies addressing the principles of green chemistry have received considerable attention in recent years. This approach emphasizes the use of environmentally acceptable chemicals and solvents, long-lifetime and recyclable catalysts, and atom-efficient procedures. [1–3] With growing awareness of environmental issues, the need for clean and sustainable synthetic approaches has become increasingly important in modern research. In this regard, heterogeneous organic reactions have attracted significant attention due to their practical benefits, such as convenient handling, straightforward separation of products, reusability of catalysts, and reduced environmental impact. [4–9]

Heterocyclic compounds are widely distributed in nature and play an essential role in various biological processes. [10,11] Heterocyclic compounds play a pivotal role in medicinal chemistry due to their unique structural features and diverse physicochemical characteristics. [12,13] During the last two to three decades, significant progress has been

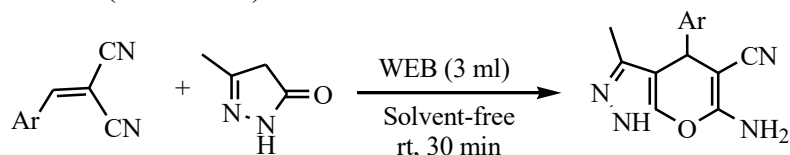
made in heterocyclic chemistry, with considerable attention directed toward the synthesis and diverse applications of medium-sized ring systems. [14–16]

In recent years, pyranopyrazoles and their derivatives have gained considerable attention as an important class of heterocyclic compounds owing to their wide range of biological activities, such as antioxidant, anticancer, antimicrobial, anti-inflammatory, antifungal, insecticidal, antitumor, antipyretic, antidepressant, and anti-HIV properties [17–22]. Furthermore, certain pyranopyrazole-based compounds have demonstrated potential applications in the agricultural sector. As a result, the construction of heterocyclic systems incorporating both pyran and pyrazole moieties has become an area of significant research interest. To address environmental concerns, a variety of eco-friendly synthetic approaches have been developed, particularly those employing heterogeneous and recyclable nanocatalysts. For instance, zwitterionic sulfamic acid-functionalized nanoclay has been reported as an efficient catalyst for the synthesis of dihydropyrano[2,3-c]pyrazoles and spiro-pyranopyrazole derivatives under green reaction conditions [79]. Consequently, due to the presence of these valuable structural motifs in biologically active molecules, extensive efforts have been directed toward the development of sustainable and efficient synthetic methodologies for pyranopyrazole derivatives.

2. Synthesis of pyranopyrazoles

2.1 Using solvent free condition

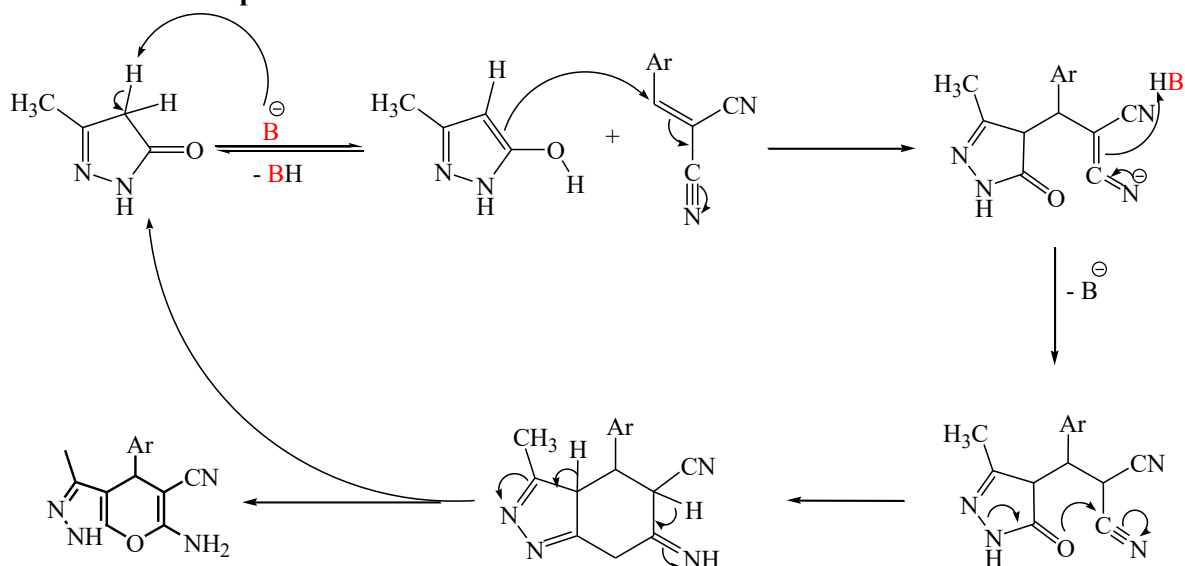
Dwivedi et al. [23] reported an environmentally friendly and efficient method for synthesizing pyrano[2,3-c] pyrazoles at ambient temperature, employing WEB as the reaction medium. (Scheme1-2)



Scheme1. An efficient solvent-free approach was employed for the synthesis of pyrano[2,3-c] pyrazole derivatives at ambient temperature using WEB.

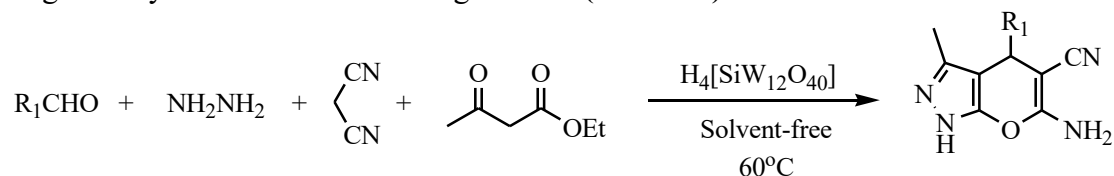
Entry	Solvent	T°C	Time (min)	Yield (%)
1	MeOH	R.T.	300	5
2	EtOH	R.T.	300	5
3	MeOH + WEB (1:1)	R.T.	240	20
4	EtOH + WEB (1:1)	R.T.	120	25
5	MeOH + WEB (2:8)	R.T.	120	55
6	EtOH + WEB (2:8)	R.T.	120	60
7	DCM + WEB (1:1)	R.T.	240	25
8	DCM + WEB (2:8)	R.T.	120	40
9	WEB	R.T.	30	96

Table 1. Optimization of the solvent system for the efficient synthesis of pyrano[2,3-c]pyrazoles using WEB at ambient temperature



Scheme 2. A plausible reaction mechanism for the formation of pyrano[2,3-c]pyrazole derivatives in the WEB medium.

Chavan et al. [24] reported the synthesis of pyranopyrazoles under solvent-free conditions using a catalytic amount of silicotungstic acid (Scheme 3)

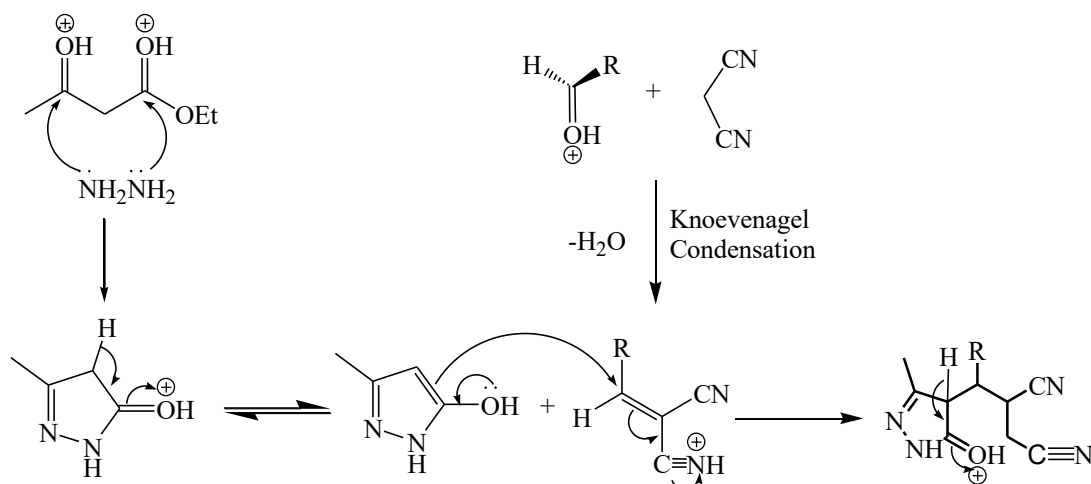


$R_1 = \text{Ph, 2-NO}_2\text{Ph, 3-NO}_2\text{Ph, 4-NO}_2\text{Ph, 3-ClPh, 2,4-diClPh, 2,6-diClPh, 3-BrPh, 4-BrPh, 4-FPh, 2-OMePh, 3,4-diOMePh, 2-OHPh, 2,4-diFPh, 4-OMePh, 4-OHPh, 4-MePh, 2-Furanyl, 2-Thiophenyl, Propyl, n-Hexyl}$

Scheme 3. A one-pot multicomponent strategy was employed for the synthesis of pyrano[2,3-c]pyrazole derivatives using $\text{H}_4[\text{SiW}_{12}\text{O}_{40}]$ as a catalyst under solvent-free conditions at 60 °C

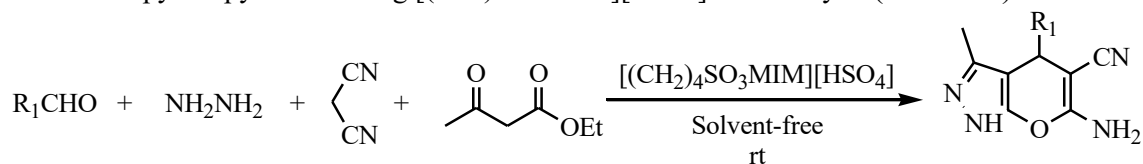
Entry	Catalyst	Catalyst (mol %)	Time (min)	Yield (%)
1	None	-	180	-
2	FeCl_3	2	10	20
3	SnCl_4	2	10	38
4	ZnCl_2	2	10	25
5	P_2O_5	2	10	32
6	CAN	2	10	15
7	$\text{H}_4[\text{SiW}_{12}\text{O}_{40}]$	2	10	96
8	$\text{H}_4[\text{SiW}_{12}\text{O}_{40}]$	0.5	10	34
9	$\text{H}_4[\text{SiW}_{12}\text{O}_{40}]$	1	10	68
10	$\text{H}_4[\text{SiW}_{12}\text{O}_{40}]$	5	10	95

Table 2. Screening of catalysts and optimization of catalyst loading for the synthesis of pyrano[2,3-c]pyrazoles.



Scheme 4. A plausible reaction mechanism for the formation of pyrano[2,3-c]pyrazoles via Knoevenagel condensation is proposed.

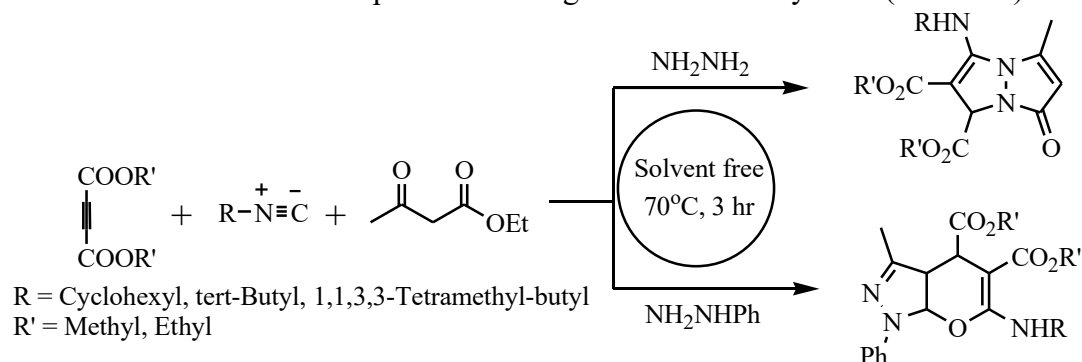
Ebrahimi et al. [25] reported an efficient and environmentally benign method for synthesizing substituted pyranopyrazoles using $[(\text{CH}_2)_4\text{SO}_3\text{MIM}][\text{HSO}_4]$ as a catalyst. (Scheme 5)



$R_1 = \text{Ph}, 3\text{-NO}_2\text{Ph}, 4\text{-NO}_2\text{Ph}, 2\text{-ClPh}, 3\text{-ClPh}, 4\text{-ClPh}, 3\text{-BrPh}, 4\text{-BrPh}, 4\text{-OMePh}, 4\text{-MePh},$

Scheme 5. Pyrano[2,3-c]pyrazoles were synthesized under solvent-free conditions using $[(\text{CH}_2)_4\text{SO}_3\text{HMIm}][\text{HSO}_4]$ as a catalyst

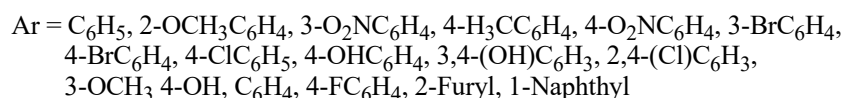
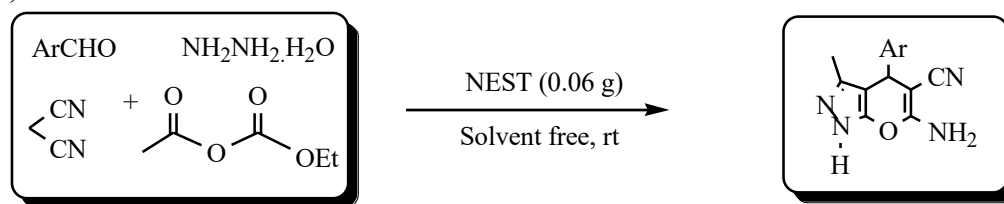
Shaabani et al. [26] reported a straightforward and efficient four-component reaction involving dialkyl acetylenedicarboxylates, isocyanides, and ethyl acetoacetate with hydrazine hydrate or phenylhydrazine, affording pyrazolo[1,2-a]pyrazoles and pyrano[2,3-c]pyrazoles under solvent-free conditions at mild temperatures with good to excellent yields. (Scheme 6)



Scheme 6. A one-pot, solvent-free approach for the synthesis of pyrazolo[1,2-a]pyrazoles and pyrano[2,3-c]pyrazoles

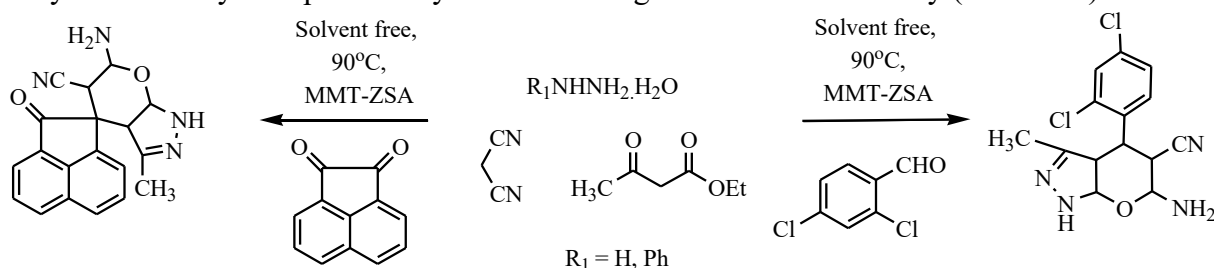
Mirjalili et al. [27] reported the synthesis of a nano-eggshell/Ti(IV) (NEST) catalyst and demonstrated its application as a heterogeneous natural nanocatalyst for the efficient synthesis of dihydropyrano[2,3-c]pyrazoles at ambient temperature under solvent-free conditions through the

condensation of hydrazine hydrate, ethyl acetoacetate, malononitrile, and aromatic aldehydes.(
Scheme 7)



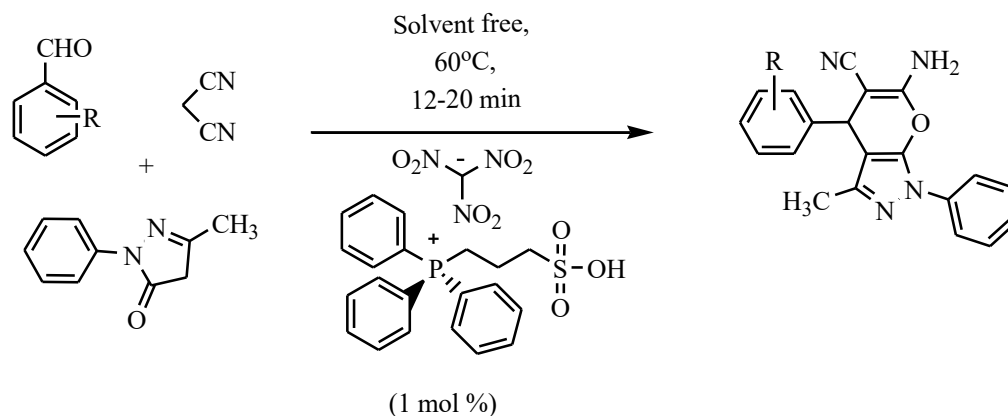
Scheme 7. One-pot multicomponent synthesis of dihydropyrano[2,3-c]pyrazoles under solvent-free conditions.

Safari et al. [28] reported the synthesis and characterization of MMT-ZSA as a non-toxic and environmentally benign zwitterionic catalyst for the preparation of pyrano[2,3-c]pyrazole and spiro[indoline-3,4'-pyrano[2,3-c]pyrazole] derivatives. They developed a novel methodology for heterocycle synthesis employing a heterogeneous zwitterionic sulfamic acid catalytic system based on MMT-ZSA nanoclay. The catalyst demonstrated excellent reusability, maintaining its catalytic efficiency for up to five cycles without significant loss of activity.(**Scheme 8)**



Scheme 8. One-pot multicomponent synthesis of pyrano[2,3-c]pyrazole and spiro[indoline-3,4'-pyrano[2,3-c]pyrazole] derivatives.

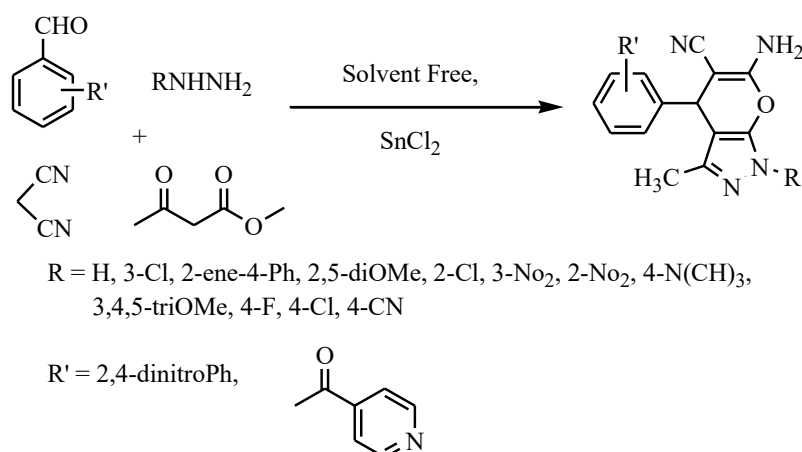
Yarie et al. [29] reported the synthesis of a novel nanosized molten salt and its application in the preparation of dihydropyrano[2,3-c]pyrazole derivatives through a three-component reaction. The developed protocol offers several advantages, including mild reaction conditions, high catalytic efficiency, simple work-up, shorter reaction times, and excellent yields.(**Scheme 9)**



R = 4-Cl, 2-Cl, 2,4-Cl₂, 4-Br, 4-F, 2,6-F₂, 3,4-F₂, 3,5-F₂, 4-CF₃, 3,5-(CF₃)₂, 4-CN, 2-NO₂, 3-NO₂, 4-NO₂, H, 4-Me, 2-OMe, 4-OMe, 4-OH, 3-OEt, 1-cinnamaldehyde, 1-naphthaldehyde

Scheme 9. One-pot multicomponent synthesis of dihydropyrano[2,3-c]pyrazole derivatives.

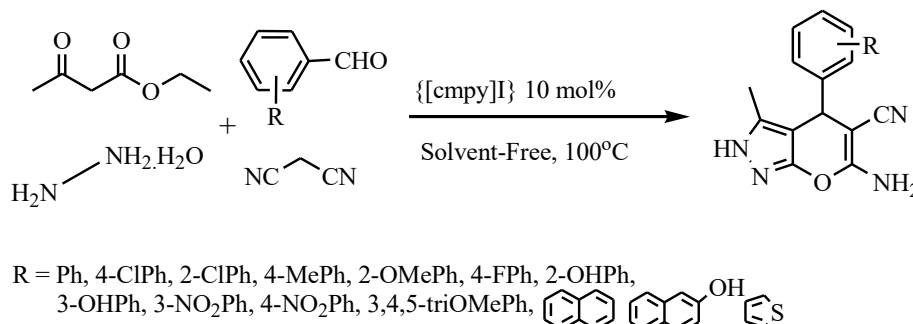
Vasava et al. [30] reported the synthesis of a series of novel and biologically active 6-amino-1-(2,4-dinitrophenyl)-4-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile derivatives via a multicomponent reaction involving various substituted aromatic aldehydes, 2,4-dinitrophenylhydrazine, ethyl acetoacetate, and malononitrile in the presence of SnCl₂ as an efficient catalyst. The reaction was carried out using both microwave irradiation and conventional methods. The synthesized compounds were evaluated for *in vitro* antibacterial, antitubercular, and cytotoxic activities using the MTT assay. Additionally, *in silico* ADME pharmacokinetic studies were performed to assess their bioavailability. Furthermore, molecular docking studies with enoyl-ACP reductase (oxidoreductase) were conducted to determine the binding affinity of the compounds. (Scheme 10)



Scheme 10. One-pot multicomponent synthesis of 6-amino-1-(2,4-dinitrophenyl)-4-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile derivatives

A.R. Moosavi-Zare et al. [31] investigated an acetic acid-functionalized pyridinium salt, 1-(carboxymethyl)pyridinium iodide {[cmpy]I}, as a reusable catalyst for the green, simple, and efficient synthesis of 6-amino-4-(4-methoxyphenyl)-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazoles. The reaction was carried out via a one-pot tandem four-component condensation of aryl aldehydes, ethyl acetoacetate, malononitrile, and hydrazine

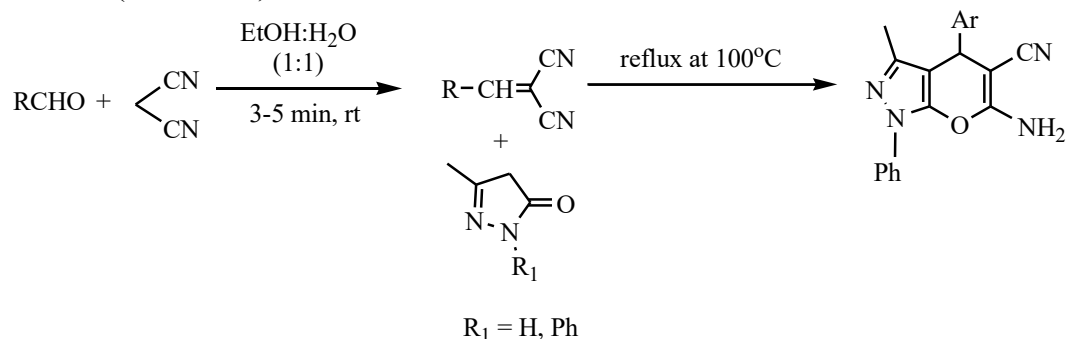
hydrate at 100 °C under solvent-free conditions. This methodology offers several advantages, including high efficiency, broad applicability, excellent yields, shorter reaction times, cost-effectiveness, a cleaner reaction profile, simple product isolation, and adherence to green chemistry principles. (Scheme 11)



Scheme 11. One-pot synthesis of 6-amino-4-(4-methoxyphenyl)-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole.

2.2 Using green solvent

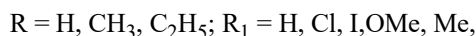
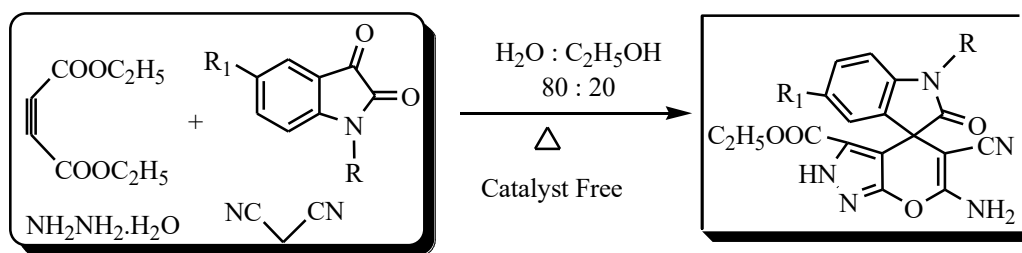
Mandha et al. [32] reported an efficient, cost-effective, and environmentally friendly multicomponent approach for the synthesis of pyrano[2,3-c]pyrazoles under catalyst-free conditions. (Scheme 12)



R = 3-OH-C₆H₄, 4-Br-C₆H₄, 4-CH₃-C₆H₄, 4-OH-C₆H₄, C₆F₅, 3-C₅H₄N, 2-C₄H₃S, 4-C₁₁H₅Cl₃NO, 3-OC₆H₅-C₆H₄, 3-C₁₁H₅Cl₃NO, C₆H₅, 4-OH-C₆H₄, 4-OCH₃-C₆H₄, 4-NO₂-C₆H₄, 3-OC₆H₅-C₆H₄, 3-C₅H₄N, 3-C₁₁H₅Cl₃NO

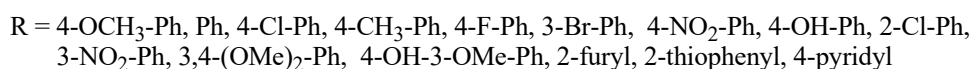
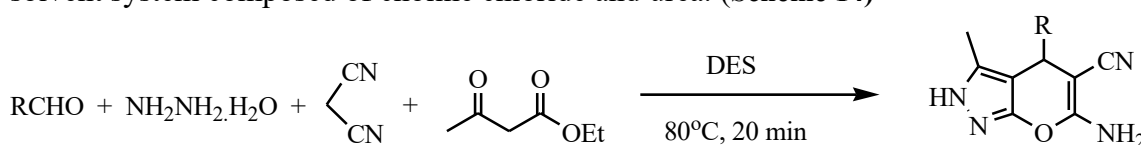
Scheme 12. Preparation of pyrano[2,3-c]pyrazoles in ethanol without the use of a catalyst.

D.M. Pore et al. [33] reported a catalyst-free multicomponent reaction (MCR) for the synthesis of spiro pyranopyrazole derivatives via the reaction of acetylenic esters with hydrazine hydrate, followed by their interaction with isatin and malononitrile in water as a green solvent at room temperature. (Scheme 13)



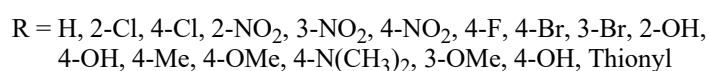
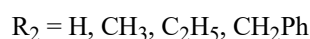
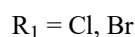
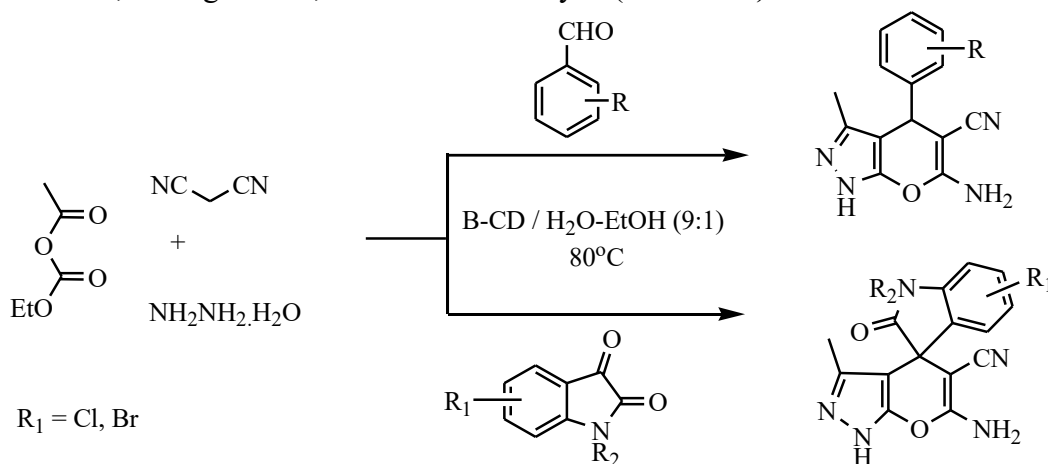
Scheme 13. Preparation of spiro pyranopyrazole derivatives using ethanol as the solvent in the absence of a catalyst.

Bhosle et al. [34] reported a facile and environmentally friendly method for the synthesis of biologically active substituted pyranopyrazoles via a one-pot cyclocondensation of various aromatic aldehydes, ethyl acetoacetate, hydrazine hydrate, and malononitrile using a deep eutectic solvent system composed of choline chloride and urea. (Scheme 14)



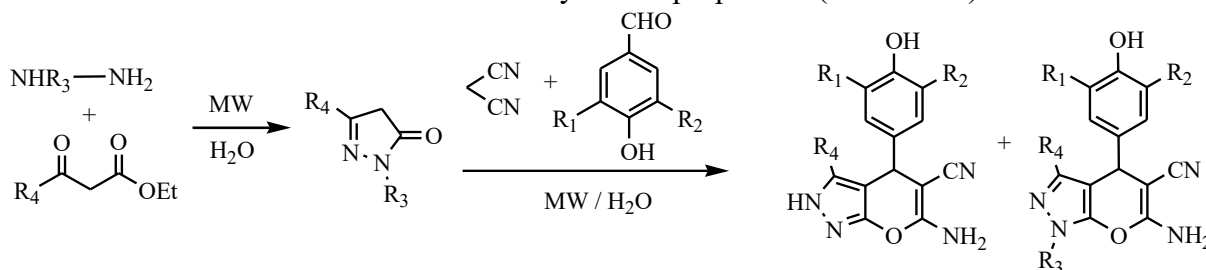
Scheme 14. Synthesis of biologically active substituted pyranopyrazoles malononitrile in a deep eutectic solvent, choline chloride: urea.

Dalal et al. [35] investigated the synthesis of pyranopyrazole derivatives through a one-pot four-component reaction involving aldehydes or isatins, hydrazine hydrate, malononitrile, and a β -keto ester in an H₂O–EtOH (9:1) system at 80 °C. This study represents the first report of such a transformation under neutral conditions using supramolecular β -cyclodextrin (β -CD) as an efficient, biodegradable, and reusable catalyst. (Scheme 15)



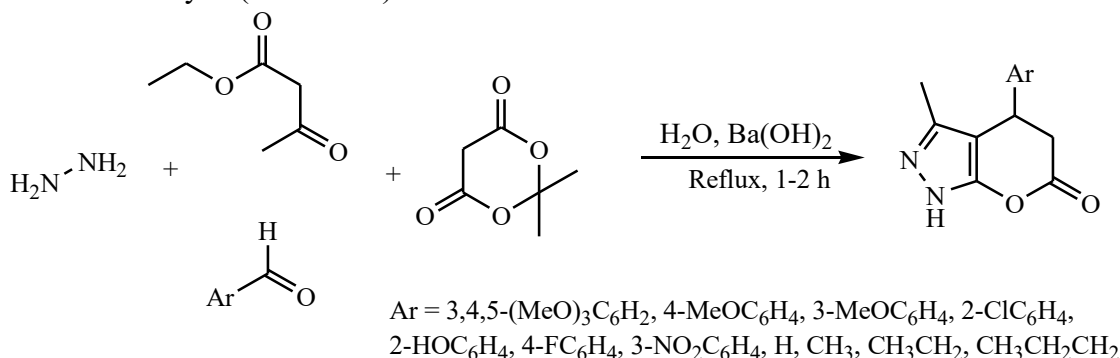
Scheme 15. A green approach for the synthesis of pyranopyrazole derivatives using β -cyclodextrin (β -CD) as a supramolecular, biodegradable, and recyclable catalyst.

Yang et al. [36] developed a green method for the synthesis of novel dihydropyrano[2,3-c]pyrazoles employing lignin-derived aromatic aldehydes, and the resulting compounds were assessed for their in vitro antioxidant and cytotoxic properties. (Scheme 16)



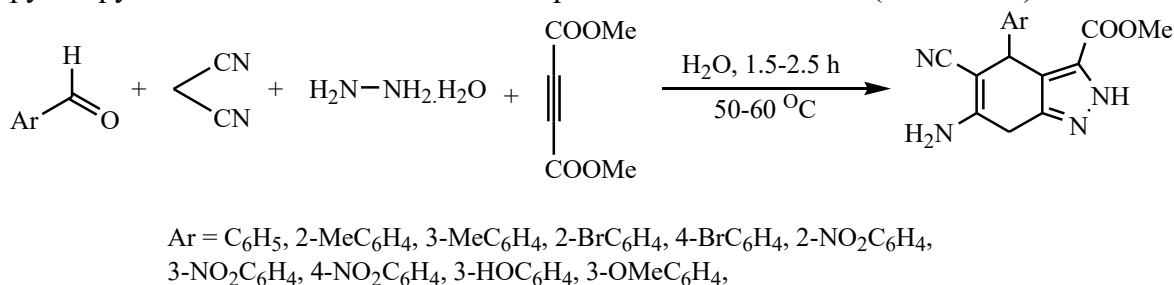
Scheme 16. An efficient approach for the synthesis of dihydropyrano[2,3-c]pyrazoles.

Azzam et al. [37] demonstrated a simple and novel one-pot four-component synthesis of pyranopyrazol-6-one derivatives via the reaction of Meldrum's acid, ethyl acetoacetate, hydrazine hydrate, and aromatic aldehydes in water, using Ba(OH)₂ as a readily available, inexpensive, and efficient catalyst. (Scheme 17)



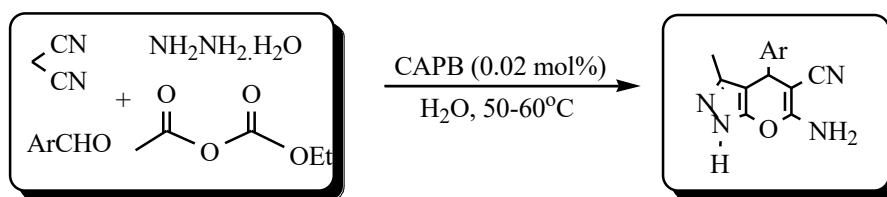
Scheme 17. Synthesis of pyranopyrazol-6-one derivatives in water using Ba(OH)₂ as a catalyst.

Zonouz et al. [38] reported a green and catalyst-free approach for the synthesis of novel pyranopyrazole derivatives via a four-component reaction in water. (Scheme 18)



Scheme 18. Synthesis of pyranopyrazole derivatives in an aqueous medium at 50–60 °C.

Tamaddon et al. [39] reported a protocol for the rapid multicomponent synthesis of dihydropyrano[2,3-c]pyrazoles using cocamidopropyl betaine (CAPB) as a biodegradable surfactant in a novel water-based worm-like micellar medium at 50–60 °C. (Scheme 19)

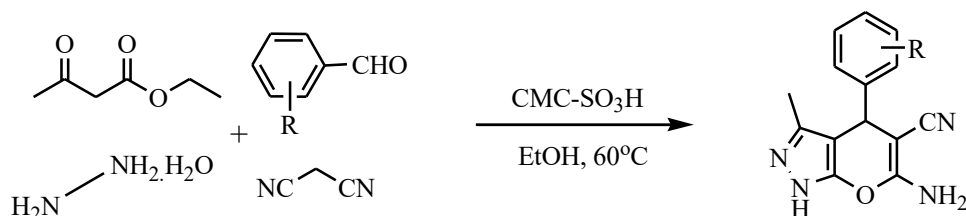


Ar = 2-furyl, 2-C₆H₅, 3,4-O₂NC₆H₄, 2-O₂NC₆H₄, 3-O₂NC₆H₄, 4-ClC₆H₄, 2-ClC₆H₄, 3-ClC₆H₄, 4-FC₆H₄, 3-BrC₆H₄, 4-H₃CC₆H₄, 3-H₃CC₆H₄, 4-MeOC₆H₄, 4-HOC₆H₄, 2-HOC₆H₄, 3-HOC₆H₄, CH₃, CH₃CH₂CH₂

Scheme 19. Synthesis of dihydropyrano[2,3-c]pyrazoles using cocamidopropyl betaine (CAPB) in an aqueous worm-like micellar medium

2.3 Using green catalyst

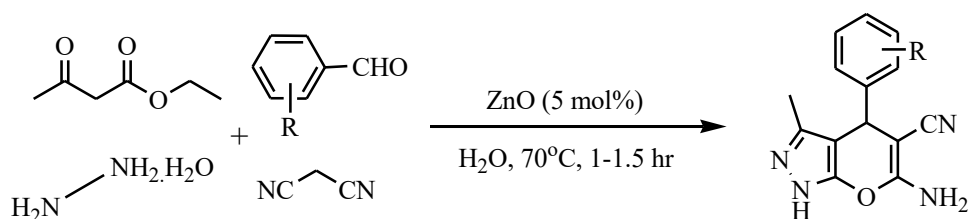
Ali et al. [40] reported sulfonated carboxymethylcellulose (SCMC), a biopolymer-derived solid acid, as a green heterogeneous catalyst for the one-pot multicomponent synthesis of pyrano[2,3-c] pyrazole derivatives. The reaction involved ethyl acetoacetate, hydrazine hydrate, malononitrile, and various aldehydes in ethanol, serving as a green solvent. (Scheme 20)



R = H, 4-Cl, 2-Cl, 4-OH, 2-Cl, 4-Br, 4-NO₂, 3, 4-diOMe, 3-OMe, 4-OH, 3-NO₂, 4-F

Scheme 20. Synthesis of pyrano[2,3-c] pyrazole derivatives using sulfonated carboxymethylcellulose (SCMC) as a catalyst.

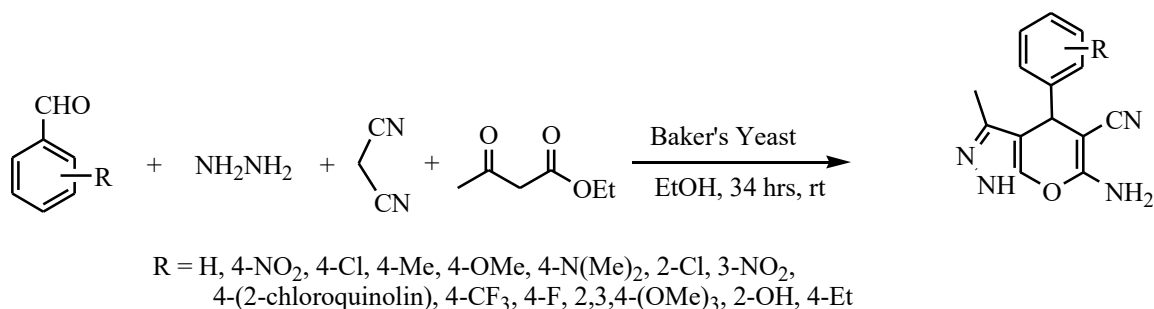
Tekale et al. [41] reported a one-pot four-component synthesis of dihydropyrano[2,3-c]pyrazoles in an aqueous medium using zinc oxide nanoparticles as an efficient catalyst. (Scheme 21)



R = H, 4Cl, 4-NMe₂, 4-SMe, 4-OH, 2-Cl, 4-Me, 4-Br, 4-NO₂, 4-OMe, 3-OMe, 4-OH, 3-NO₂, 2-Furyl

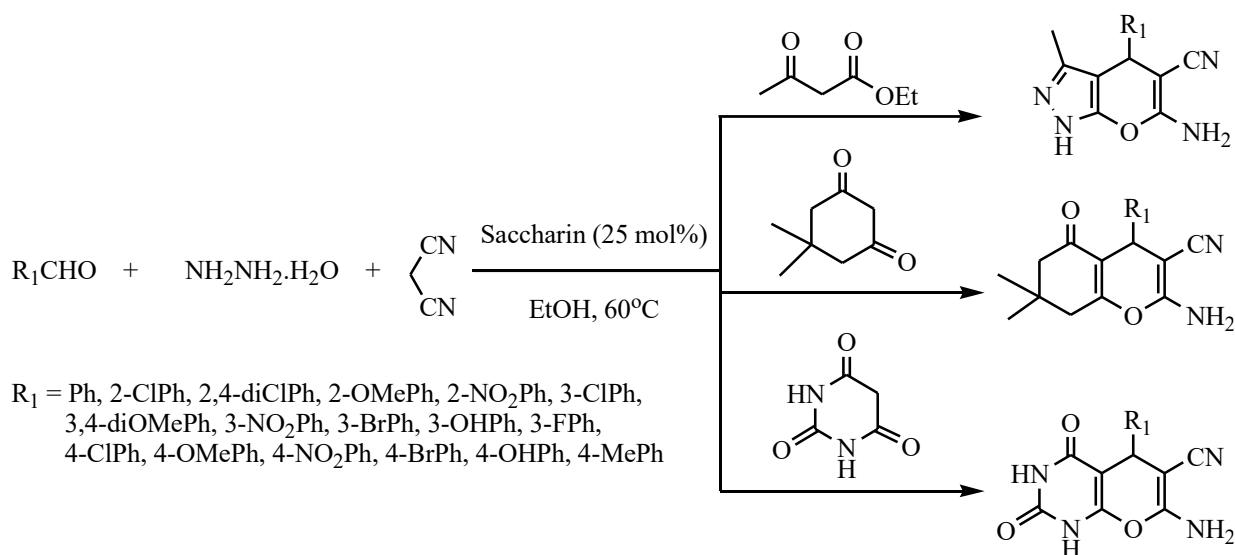
Scheme 21. Preparation of dihydropyrano[2,3-c]pyrazoles catalyzed by zinc oxide nanoparticles.

Shrinivas et al. [42] demonstrated an efficient green approach for the one-pot four-component synthesis of pyranopyrazoles in a non-aqueous medium using baker's yeast at room temperature under neutral pH conditions. (Scheme 22)



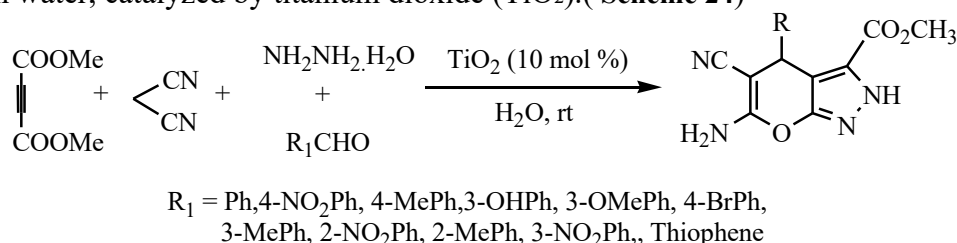
Scheme 22. Preparation of pyranopyrazoles in non-aqueous medium using a baker's yeast

Mohamadpour et al. [43] developed a green and facile saccharin-catalyzed method for the convenient one-pot synthesis of pyranopyrazole derivatives via a multicomponent tandem Knoevenagel–cyclocondensation reaction. (Scheme 23)



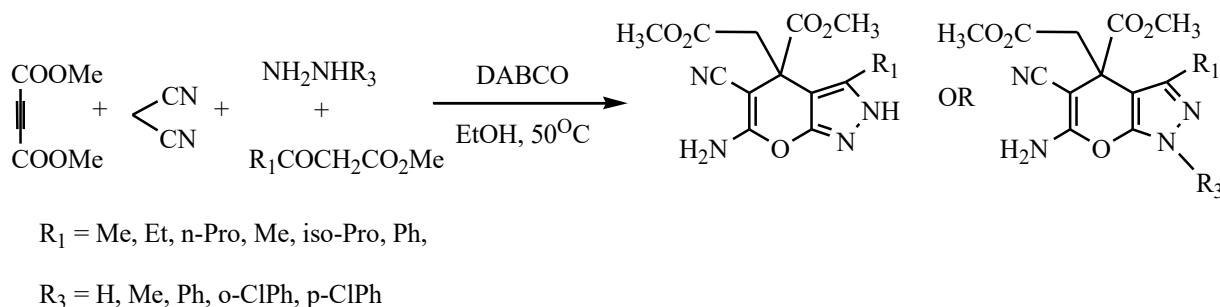
Scheme 23. An efficient synthesis of pyranopyrazole derivatives via Knoevenagel cyclocondensation

Sangshetti et al. [44] described a green and eco-friendly protocol for the one-pot, four-component synthesis of methyl 6-amino-5-cyano-4-aryl-2,4-dihydropyranopyrazole-3-carboxylates in water, catalyzed by titanium dioxide (TiO₂). (Scheme 24)



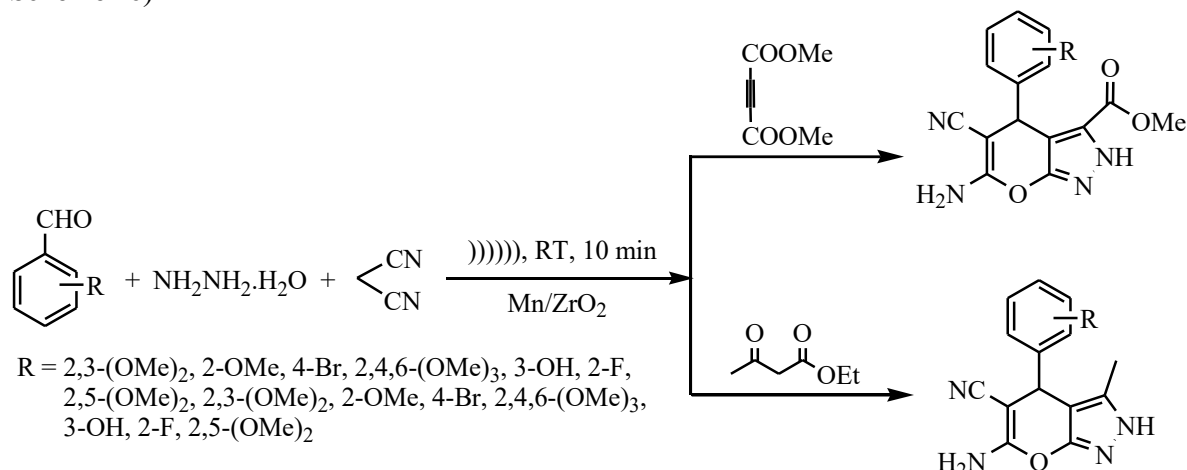
Scheme 24. Preparation of methyl 6-amino-5-cyano-4-aryl-2,4-dihydropyranopyrazole-3-carboxylates using TiO₂ as a catalyst.

Keyume et al. [45] reported an efficient and straightforward one-pot method for the synthesis of functionalized, multisubstituted 2,4-dihydropyrano[2,3-c]pyrazole dicarboxylates from β -ketoesters, hydrazine, dimethyl acetylenedicarboxylate, and malononitrile in ethanol. (Scheme 25)



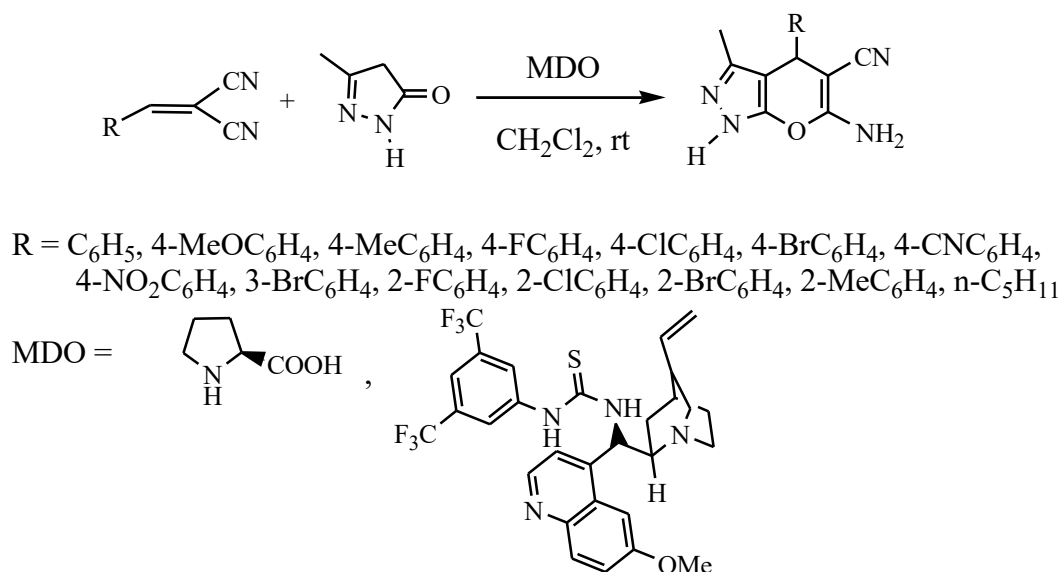
Scheme 25. An efficient synthesis of 2,4-dihydro-pyrano[2,3-c]pyrazole dicarboxylates

Lavanya et al. [46] reported a rapid, clean, and highly efficient method for the green synthesis of pyrano[2,3-c]pyrazole-3-carboxylate and pyrano[2,3-c]pyrazole-5-carbonitrile derivatives via a one-pot four-component reaction catalyzed by Mn/ZrO₂ under ultrasonication. (Scheme 26)



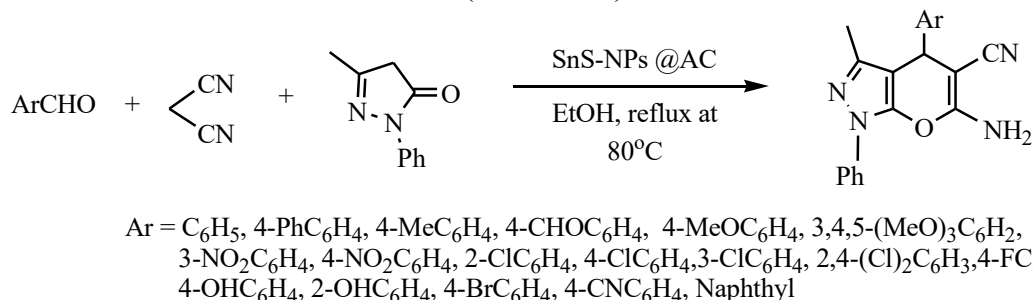
Scheme 26. One-pot synthesis of pyrano[2,3-c]pyrazole-3-carboxylate and pyrano[2,3-c]pyrazole-5-carbonitrile derivatives.

Muramulla et al. [47] demonstrated a novel catalytic role of MDOs, where they function as Lewis base catalysts in a tandem Michael addition–cyclization reaction between 3-methyl-2-pyrazolin-5-one and benzylidene malononitriles. (Scheme 27)



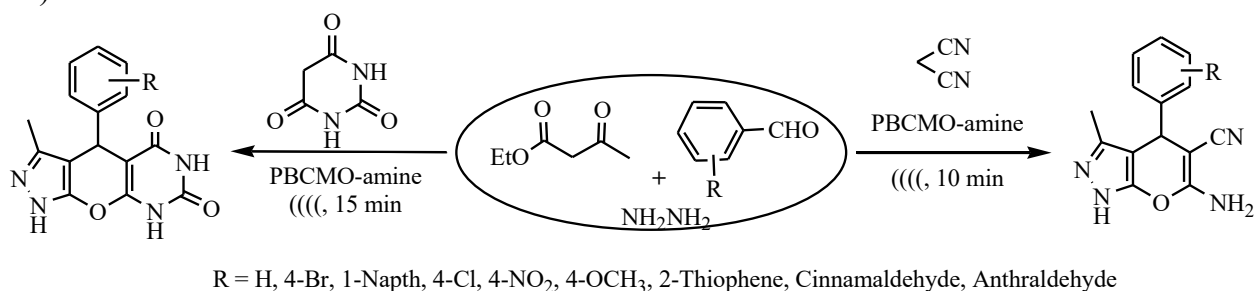
Scheme 27. MDO-catalyzed tandem Michael addition–cyclization reaction between 3-methyl-2-pyrazolin-5-one and benzylidene malononitriles.

Iravani et al. [48] synthesized tin sulfide nanoparticles (SnS-NPs) on activated carbon (AC) in an aqueous medium at room temperature and utilized the resulting nanocomposite as a heterogeneous Lewis acid catalyst for the one-pot three-component synthesis of 4H-pyrano[2,3-c]pyrazole derivatives in ethanol at 80 °C. (Scheme 28)



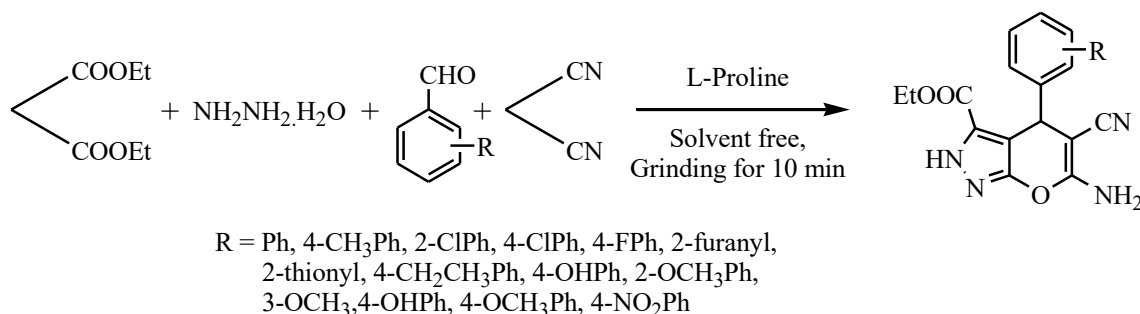
Scheme 28. Synthesis of 4H-pyrano [2,3-c]pyrazole derivatives in ethanol at 80°C.

Krishnapillai et al. [49] synthesized a novel porphyrin-initiated amine-functionalized poly(BCMO) dendritic polymer and evaluated its catalytic performance in the one-pot, four-component solvent-free synthesis of pyrazolopyranopyrimidinones and pyranopyrazoles. (Scheme 29)



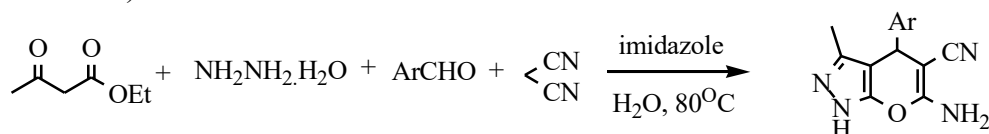
Scheme 29. Preparation of pyrazolopyrano pyrimidinone and pyranopyrazole

Padmini et al. [50] demonstrated an efficient grinding-assisted protocol for the synthesis of dihydropyrano[2,3-c]pyrazole derivatives from acetylenic esters, hydrazine hydrate, aryl aldehydes, and malononitrile under solvent-free conditions, affording excellent yields. (Scheme 30)



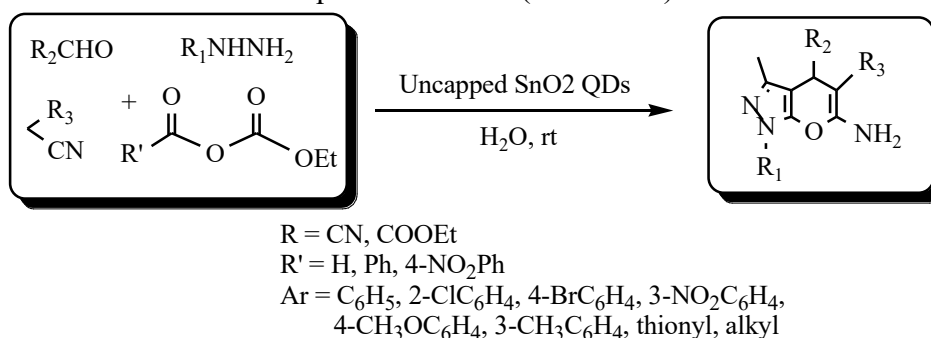
Scheme 30. Preparation of dihydropyrano[2,3-c]pyrazole derivatives

Siddekha et al. [51] reported an efficient and practical protocol for the synthesis of pyranopyrazoles, employing imidazole as an organocatalyst in aqueous medium, affording high yields. (Scheme 31)



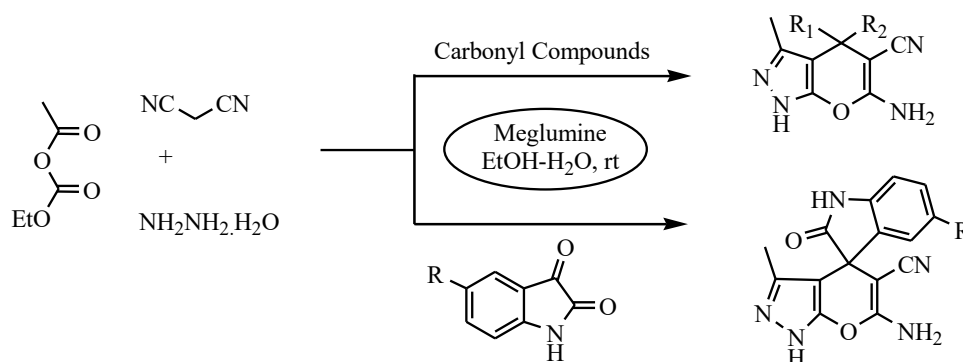
Scheme 31. Preparation of pyranopyrazoles employing imidazole as an organocatalyst.

Paul et al. [52] developed a novel strategy utilizing uncapped SnO₂ quantum dots (QDs) as catalysts for the one-pot multicomponent synthesis of substituted pyrano[2,3-c]pyrazole and spiro-2-oxindole derivatives in an aqueous medium. (Scheme 32)



Scheme 32. An efficient SnO₂ quantum dot-catalyzed synthesis of pyrano[2,3-c]pyrazole and spiro-2-oxindole derivatives.

Zhang *et al.* [53] developed a highly efficient and greener approach for the one-pot, four-component synthesis of pyranopyrazole derivatives using meglumine as an inexpensive, biodegradable and reused catalyst. (Scheme 33)



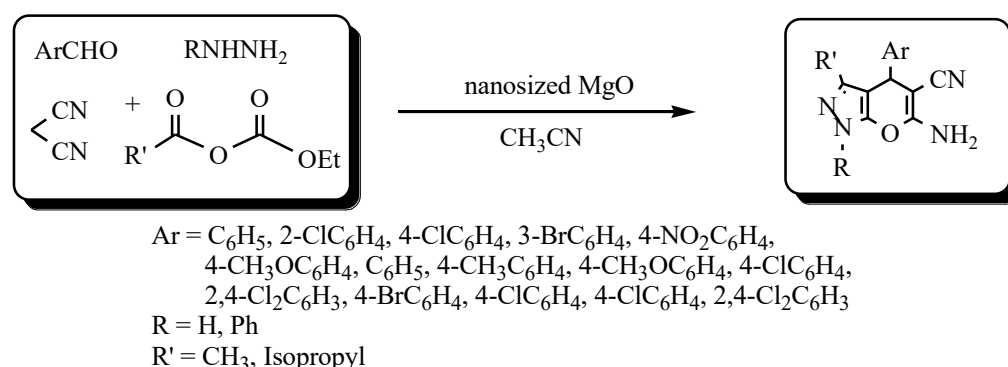
Carbonyl Compounds

R = H, CH₃, F, Cl, Br, NO₂

PhCHO, 2-OCH₃C₆H₄CHO, 4-OCH₃C₆H₄CHO, 4-CH₃(CH₂)₂OC₆H₄CHO, 4-CH₃(CH₂)₄OC₆H₄CHO, 2-OMe-5-CHMe₂C₆H₃CHO, 2,3,4-(OMe)₃C₆H₂CHO, 3-CH₃C₆H₄CHO, 4-C(CH₃)₃C₆H₄CHO, 4-SCH₃C₆H₄CHO, 4-OHC₆H₄CHO, 2-FC₆H₄CHO, 3-FC₆H₄CHO, 4-FC₆H₄CHO, 2-ClC₆H₄CHO, 3-ClC₆H₄CHO, 4-ClC₆H₄CHO, 2,4-Cl₂C₆H₃CHO, 2-NO₂C₆H₄CHO, 4-NO₂C₆H₄CHO, 3-CF₃C₆H₄CHO, 4-CF₃C₆H₄CHO, 4-((4-Nitrobenzyl)oxy) benzaldehyde, Furan-2-carbaldehyde, Thiophene-2-carbaldehyde, Pyridine-4-carbaldehyde, 1-Naphthaldehyde, Decanal, Cyclohexanecarbaldehyde

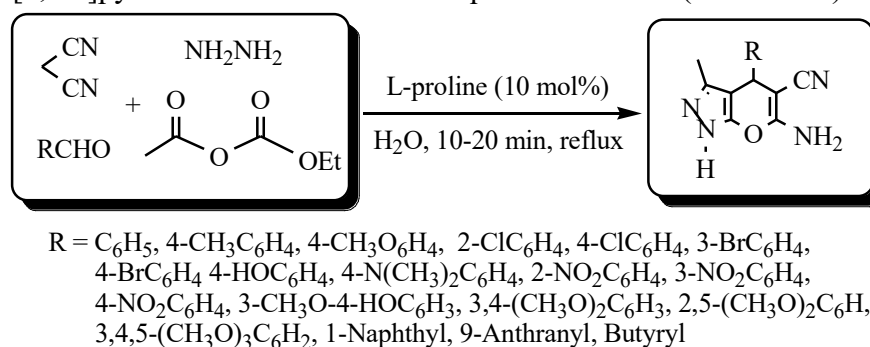
Scheme 33. Synthesis of pyranopyrazole derivatives using meglumine as a biodegradable and reused catalyst.

Babaie et al. [54] reported a four-component reaction involving hydrazine hydrate or phenylhydrazine, ethyl 3-alkyl-3-oxopropanoate, aldehydes, and malononitrile in the presence of a highly efficient heterogeneous nanosized magnesium oxide catalyst, leading to the formation of 6-amino-3-alkyl-4-aryl-5-cyano-1,4-dihydropyranopyrazole derivatives in excellent yields within a short reaction time. (**Scheme 34**)



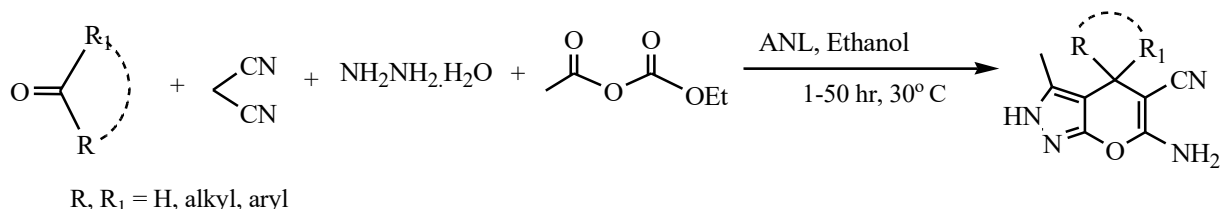
Scheme 34. Preparation of 6-amino-3-alkyl-4-aryl-5-cyano-1,4-dihydropyranopyrazole derivatives.

Mecadon et al. [55] demonstrated that L-proline (10 mol%) serves as an effective organocatalyst for the four-component synthesis of 6-amino-4-alkyl/aryl-3-methyl-2,4-dihydropyranopyrazole-5-carbonitriles in aqueous medium. (**Scheme 35**)



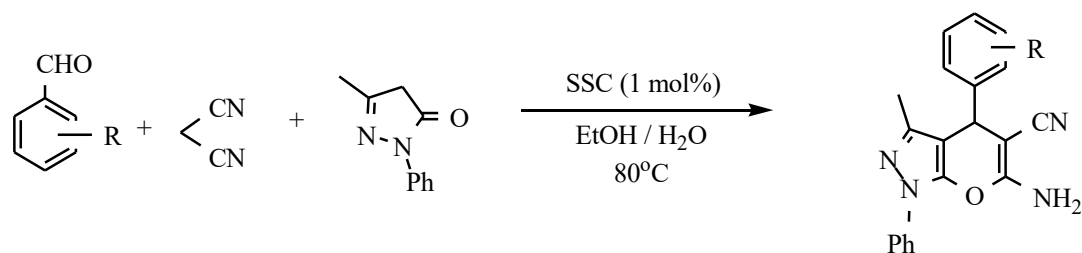
Scheme 35. A green approach for the synthesis of 6-amino-4-alkyl/aryl-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitriles in water.

Bora et al. [56] reported an environmentally friendly and efficient protocol for the four-component synthesis of dihydropyrano[2,3-c]pyrazoles in ethanol using a catalytic amount of the biocatalyst ANL (lipase from *Aspergillus niger*) at room temperature. (Scheme 36)



Scheme 36. An efficient biocatalytic synthesis of dihydropyrano[2,3-c]pyrazoles in ethanol using ANL derived from *Aspergillus niger*.

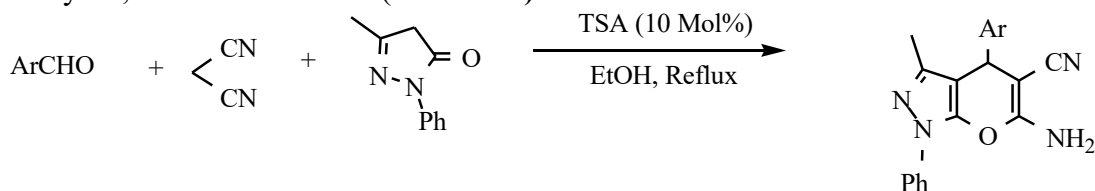
Karami et al. [57] examined first application of SSC (silica sodium carbonate) as a green, highly efficient and recyclable catalyst to synthesis of new 1,4-dihydropyrano[2,3-c]pyrazoles. (Scheme 37)



R = H, 2-Cl, 3-Br, 4-CH₃, 4-OMe, 4-OH, 3-OEt, 4-CH(CH₃)₂, 4-Ph, 4-OCH₂Ph

Scheme 37. An efficient synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles using SSC as a recyclable green catalyst.

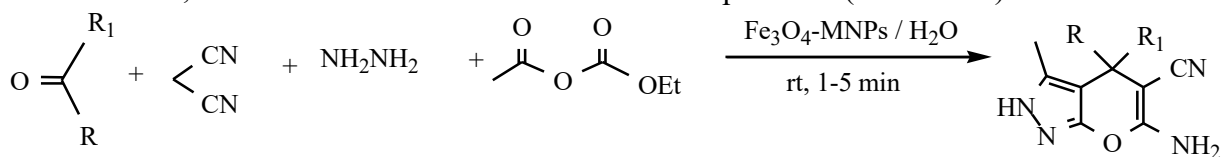
Farahi et al. [58] described tungstate sulfuric acid as an efficient and environmentally friendly catalyst for the synthesis of 6-amino-4-aryl-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazoles via the reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one, aromatic aldehydes, and malononitrile. (Scheme 38)



Ar = C₆H₅, 2-Cl-C₆H₄, 3-Br-C₆H₄, 3-NO₂-C₆H₄, 4-MeO-C₆H₄, 4-Me-C₆H₄, 4-Br-C₆H₄, 4-NO₂-C₆H₄, 4-Iso-propyl-C₆H₄, 4-Bisphenyl-C₆H₄, 4,-Benzyloxy-C₆H₄ 1-Naphthyl, 2,4-Cl₂-C₆H₃, 3-OEt-4-HO-C₆H₃

Scheme 38. Preparation of 6-amino-4-aryl-5-cyano-1,4-dihydropyrano[2,3-c]pyrazoles via the reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one, aromatic aldehydes, and malononitrile.

Remaily et al. [59] reported a one-pot four-component synthesis of a series of pyranopyrazoles using magnetically recoverable Fe₃O₄ nanoparticles as a heterogeneous catalyst. The reaction involved hydrazine hydrate, ethyl acetoacetate, aldehydes or ketones, and malononitrile, and was carried out in water at room temperature. (**Scheme 39**)

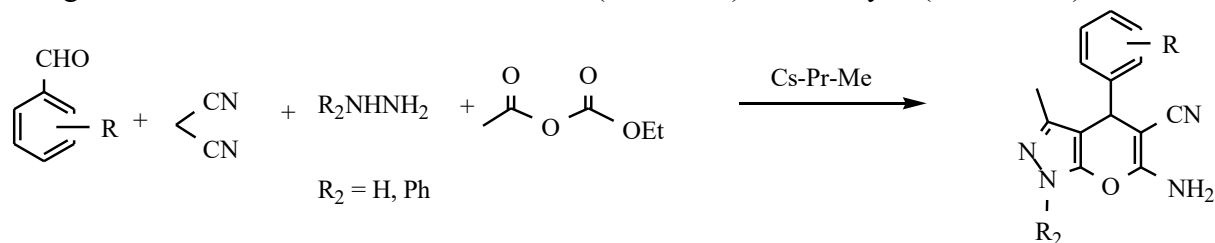


R₁ = H, CH₃, Ph

R = H, 2-NO₂, 4-NO₂, 2-Cl, 4-Cl, 2,4-DiCl, 4-F, 3-Br, 4-CH₃, 4-OMe, 2-OMe, 2-OH, 4-OH, 3-OH, 4-N(Me)₂, 2,5-di OMe, 3,4,5-tri OMe,

Scheme 39. Synthesis of pyranopyrazoles using magnetically recoverable Fe₃O₄ nanoparticles as a heterogeneous catalyst in aqueous medium at room temperature.

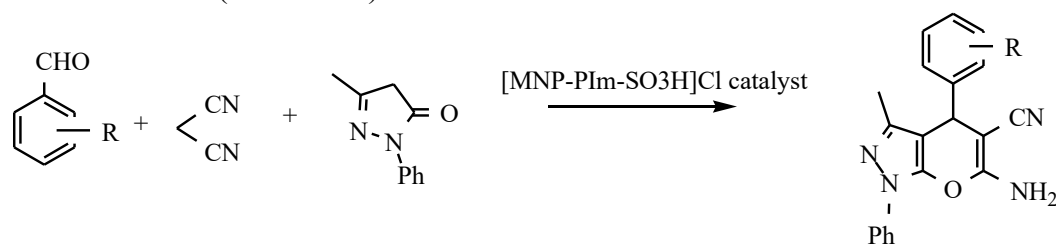
Valiey et al. [60] developed an environmentally benign organocatalytic protocol for the synthesis of functionalized dihydropyrano[2,3-c]pyrazole and benzylpyrazolyl coumarin scaffolds using bio-based melamine-modified chitosan (Cs-Pr-Me) as a catalyst. (**Scheme 40**)



R = H, 2-NO₂, 4-NO₂, 2-Cl, 4-Cl, 2,4-DiCl, 4-F, 3-Br, 4-CH₃, 4-OMe, 2-OMe, 2-OH, 4-OH, 3-OH, 4-N(Me)₂

Scheme 40. Synthesis of dihydropyrano[2,3-c]pyrazole and benzylpyrazolyl coumarin scaffolds using Cs-Pr-Me as a catalyst.

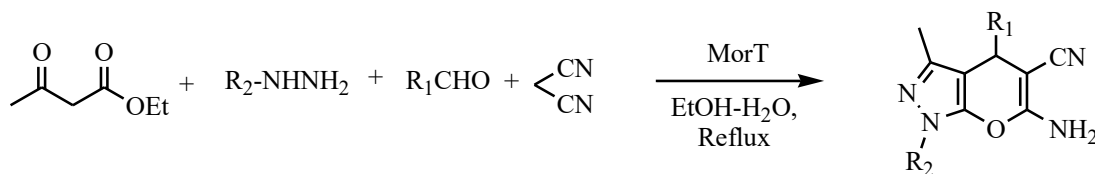
Zolfigol et al. [61] reported the use of an environmentally benign [nano-Fe₃O₄@SiO₂@(CH₂)₃-Imidazole-SO₃H]Cl catalyst for the efficient synthesis of 1,8-dioxooctahydroxanthenes and dihydropyrano[2,3-c]pyrazole derivatives under mild and solvent-free conditions. (**Scheme 41**)



R = H, 2-NO₂, 3-NO₂, 4-NO₂, 2-Cl, 3-Cl, 4-Cl, 2,4-DiCl, 4-F, 3-F, 4-Br, 2-Br, 4-CH₃, 4-OMe, Naphthalene-2-carbaldehyde, Naphthalene-1-carbaldehyde, 4-N,N-Dimethylaminobenzaldehyde, 2-Hydroxy-3,5-dichlorobenzaldehyde

Scheme 41. Efficient synthesis of 1,8-dioxooctahydroxanthenes and dihydropyrano[2,3-c]pyrazoles using Fe₃O₄@SiO₂@(CH₂)₃-imidazole-SO₃H]Cl.

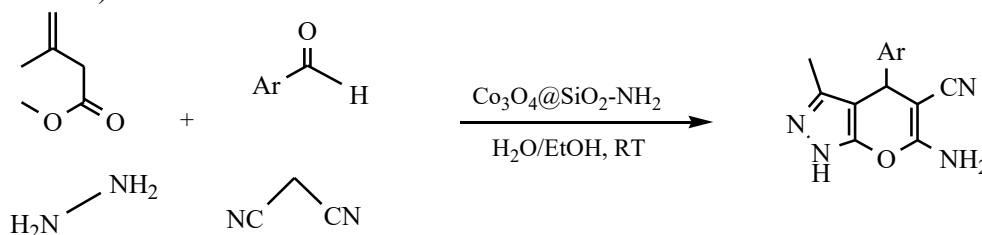
Zhou et al. [62] have developed an efficient method for the synthesis of a diverse range of dihydropyrano[2,3-c]pyrazoles using Lewis acid MorT as an eco-friendly catalyst. (**Scheme 42**)



$R_1 = C_6H_5, 4-F-C_6H_4, 2-Cl-C_6H_4, 4-Cl-C_6H_4, 2-Br-C_6H_4, 4-Br-C_6H_4, 2-HOC_6H_4, 3-HOC_6H_4, 3-CH_3C_6H_4, 4-CH_3C_6H_4, 3-CH_3OC_6H_4, 4-CH_3OC_6H_4, 4-CF_3C_6H_4, 4-NO_2C_6H_4, 4-iPrC_6H_4, 4-(CH_3)_2NC_6H_4, 2-F-6-Cl-C_6H_3, 2,4-Cl_2C_6H_3, 3,4-(CH_3)_2C_6H_3, 2,4,5-(CH_3O)_3C_6H_2, 3-C_6H_5O, 4-F-C_6H_3, CH_3CH_2CH_2, (CH_3)_2CH, (CH_3)_3C, 2-Furan, 3-Pyridine$
 $R_2 = H, Ph$

Scheme 42. Synthesis of dihydropyrano[2,3-c]pyrazoles using eco-friendly Lewis acid MorT catalyst.

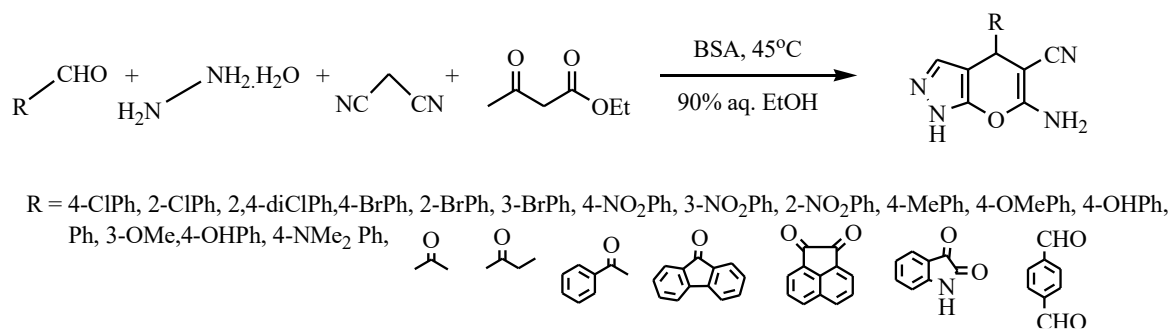
Shahbazi et al. [63] demonstrated that the $Co_3O_4@SiO_2-NH_2$ nanocomposite functions as a green, efficient, and robust heterogeneous nanocatalyst for multicomponent reactions involving ethyl acetoacetate, hydrazine hydrate, aldehydes, and malononitrile. This approach offers several advantages, including excellent yields, short reaction times, facile separation, catalyst recyclability, simple purification, and environmentally benign reaction conditions. Furthermore, the synthesized pyranopyrazole nanocomposites were evaluated for their antibacterial and antifungal activities against Gram-positive bacteria such as *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA), Gram-negative bacteria including *Escherichia coli* and *Pseudomonas aeruginosa*, as well as *Candida albicans*, using disc diffusion and minimum inhibitory concentration (MIC) methods. The results indicated that derivatives bearing (4-Br), (4-F), and (2,4-Cl) substituents exhibited the most significant activity against *S. aureus*. (Scheme 43)



$Ar = 4-BrPh, 4-OMePh, 4-ClPh, 4-OHPh, 4-NO_2Ph, 4-CH_3Ph, 4-SCH_3Ph, 3-NO_2Ph, 2-ClPh, 4-FPh, 2,4-diClPh, 2-NO_2Ph, 4-N(CH_3)_2Ph, 4-CNPh$

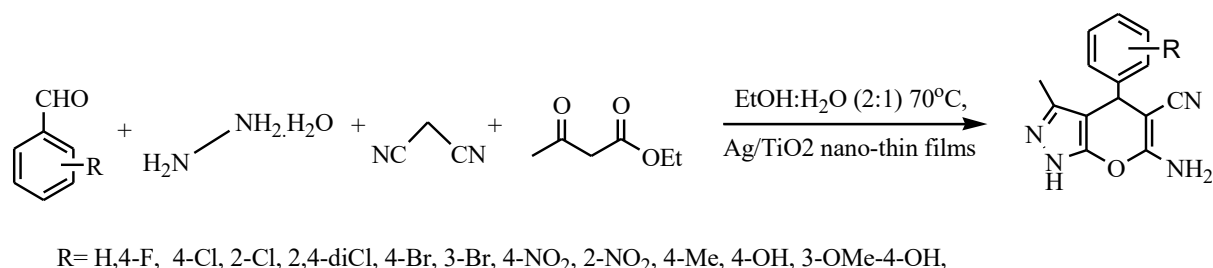
Scheme 43. Synthesis of pyranopyrazoles using $Co_3O_4@SiO_2-NH_2$ nanocomposite as a green heterogeneous catalyst.

Xingtian Huang et al. [64] developed a novel, efficient, and environmentally friendly protocol employing BSA as a reusable biocatalyst for the synthesis of a wide range of pyrano[2,3-c]pyrazole derivatives. This method offers several advantages, including eco-compatibility, mild reaction conditions, shorter reaction times, high yields, and operational simplicity. (Scheme 44)



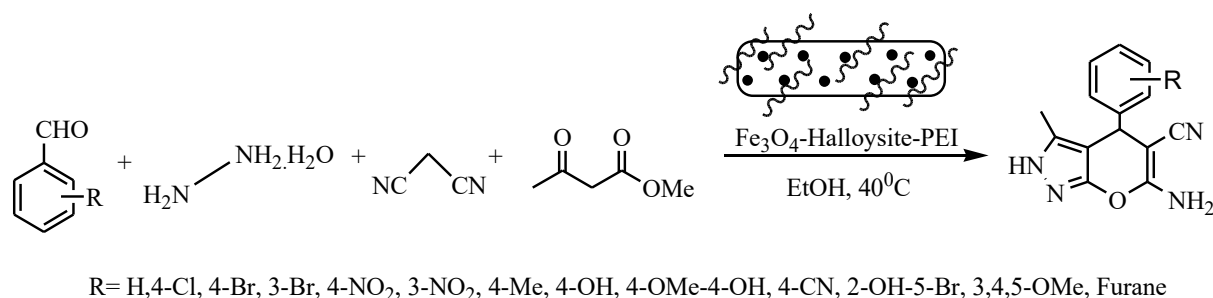
Scheme 44. Synthesis of pyrano[2,3-c]pyrazole derivatives using BSA as a reusable biocatalyst

Fatahpour et al. [65] reported a simple and environmentally friendly method for the cascade synthesis of biologically significant dihydropyrano[2,3-c]pyrazole scaffolds, employing Ag/TiO₂ nano-thin films as a durable and recyclable catalyst in a one-pot multicomponent process. (Scheme 45)



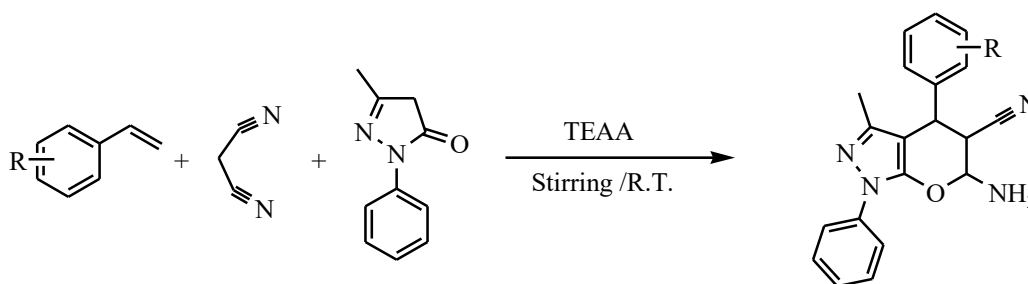
Scheme 45. Preparation of dihydropyrano[2,3-c]pyrazoles employing Ag/TiO₂ nano-thin films as an eco-friendly and reusable catalyst.

Hajizadeh et al. [66] synthesized a novel, environmentally benign, stable, magnetically retrievable, and reusable poly(ethyleneimine)-functionalized magnetic halloysite nanotube nanocomposite (Fe₃O₄@HNTs-PEI). The catalytic performance of this material was evaluated in the synthesis of dihydropyrano[2,3-c] pyrazole derivatives. The nanocomposite exhibits notable features, including nanotubular morphology, high thermal stability, well-defined crystalline structure, and magnetic properties. (Scheme 46)



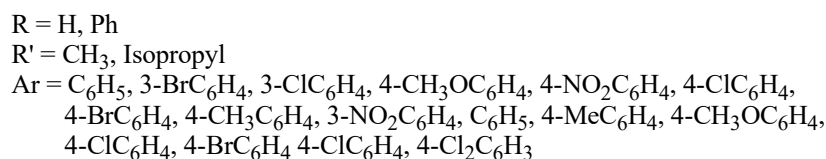
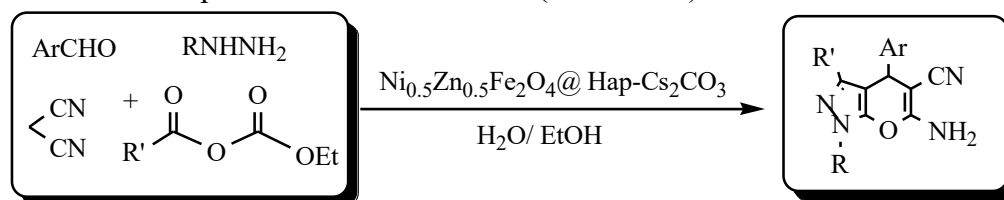
Scheme 46. A green and sustainable approach for the synthesis of dihydropyrano[2,3-c]pyrazoles using Fe₃O₄@HNTs-PEI as a reusable magnetic catalyst.

Balaskar et al. [67] introduced an alternative route for the synthesis of 1,4-dihydropyrano[2,3-c]pyrazol-5-yl cyanide derivatives using triethylammonium acetate (TEAA) as a catalyst in a green reaction medium. The method offers several advantages, including solvent-free conditions, low cost, ease of handling, and recyclability of the catalyst. (Scheme 47)



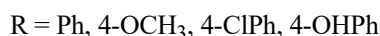
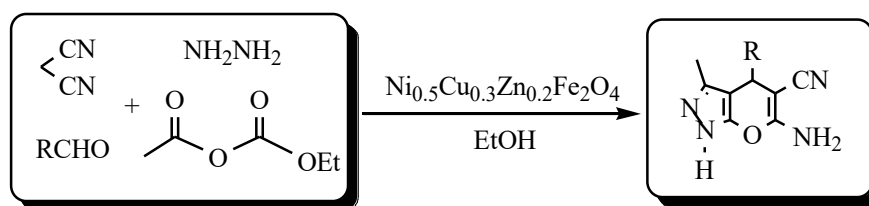
Scheme 47. Synthesis of 1,4-dihydropyrano[2,3-c]pyrazol-5-yl cyanide derivatives using TEAA as catalyst.

Moeinpour *et al.* [68] had reported $\text{Ni}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4@ \text{Hap-Cs}_2\text{CO}_3$ as a basic green nanocatalyst for the new efficient and green synthesis of 5-cyano-1,4-dihydropyrano[2,3-c]pyrazoles at room temperature in water/ethanol. (**Scheme 48**)



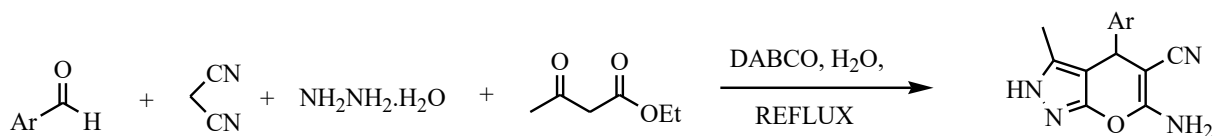
Scheme 48. Preparation of 5-cyano-1,4-dihydropyrano[2,3-c]pyrazoles using $\text{Ni}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4@ \text{HAp-Cs}_2\text{CO}_3$ as a green nanocatalyst

Mandle *et al.* [69] developed magnetically recoverable Cu^{2+} doped Ni-Zn Nano Ferrite catalyst for efficient one pot multicomponent synthesis of Pyrano (2,3-C) Pyrazoles from ethyl acetoacetate, hydrazine hydrate, aromatic aldehydes and malononitrile. (**Scheme 49**)



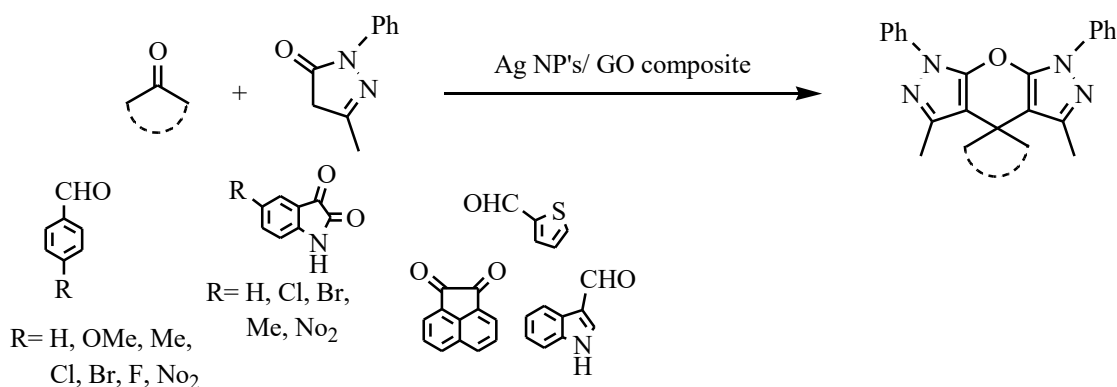
Scheme 49. An efficient synthesis of pyrano[2,3-c]pyrazoles using Cu^{2+} -doped Ni-Zn nano ferrite as an efficient catalyst.

Pandit *et al.* [70] reports DABCO as an efficient catalyst to promote rapid one-pot multicomponent reaction between aromatic aldehydes, malanonitrile, ethyl acetoacetate and hydrazine hydrate in aqueous media to give substituted pyrano[2,3-c]pyrazole. (**Scheme 50**)



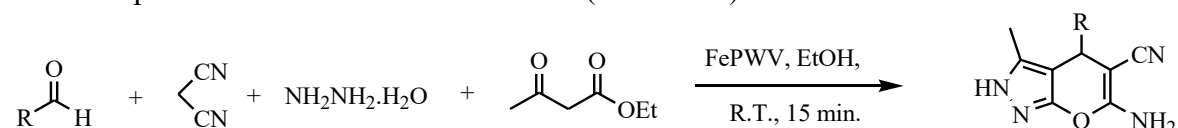
Scheme 50. Synthesis of substituted pyrano[2,3-c]pyrazoles via rapid one-pot multicomponent reaction in aqueous medium.

Dandia *et al.* [71] reports ‘on-water’ chemoselective synthesis of pyranodipyrzolonones *via* the reaction of various carbonyl compounds with 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one using Ag NPs decorated reduced graphene oxide (Ag NPs/GO) composite which is a facile, leach free and easily recyclable heterogeneous catalyst at room temperature. (**Scheme 51**)



Scheme 51. Synthesis of pyranodipyrzolonones using Ag NPs/rGO as a catalyst.

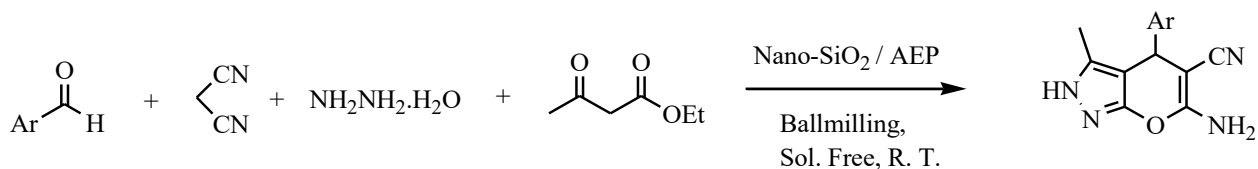
Subrahmanyam *et al.* [72] designed and utilized a highly effective and cost-effective protocol for the synthesis of pyranopyrazole analogues via one-pot multi-component reaction using iron-doped heteropoly acid [(Fe₅(PW₁₀V₂O₄₀)₃] (FePWV) as an efficient catalyst at room temperature and ethanol as the solvent. (**Scheme 52**)



R = 2,3-OMe-C₆H₃, 2,4,6-OMe-C₆H₂, 2,4-OMe-C₆H₃, 2-Br-C₆H₄, 2-Cl-C₆H₄, 2-NO₂-C₆H₄, 3-OMe-C₆H₄, 4-Cl-C₆H₄, 3-OH-C₆H₄, C₆H₅, C₄H₄S, C₄H₄O

Scheme 52. Synthesis of pyranopyrazole analogues via one-pot multicomponent reaction using FePWV as an efficient catalyst.

Mirjalili *et al.* [73] has been reported an efficient approach for the synthesis of pyranopyrazoles (PPzs) using ball milling and metal-free nano-catalyst (Nano-silica/aminoethylpiperazine [AEP]), under solvent-free conditions. (**Scheme 53**)

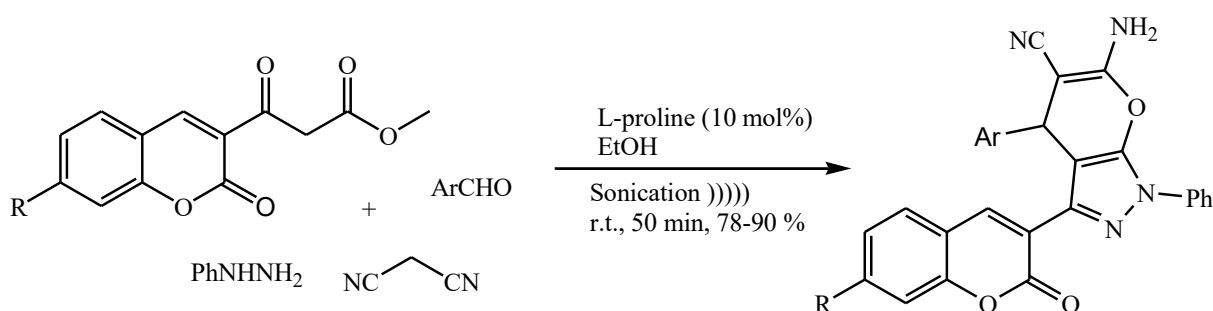


Ar = 4-NO₂-C₆H₄, 4-Cl-C₆H₄, 2,4-diCl-C₆H₃, 4-F-C₆H₄, 4-Br-C₆H₄, 3-OMe-4-OH-C₆H₃, 4-OH-C₆H₄, 4-CH₃-C₆H₄, C₆H₅, 3,4-diOH-C₆H₃, Furan-2-Carbaldehyde, Pyrole-2-Carbaldehyde, 2-OMe-C₆H₄

Scheme 53. Synthesis of pyranopyrazoles using Nano-silica/AEP as a metal-free nanocatalyst under solvent-free ball-milling conditions

2.4 Using energy resources

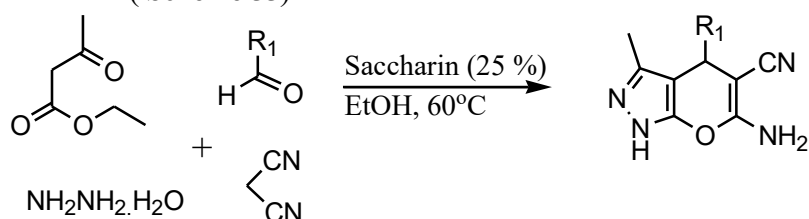
Mengnisa Seydimemet *et al.* [74] discussed an environmentally benign simple and novel four component synthesis of coumarin based dihydropyrano[2,3-*c*] pyrazoles by the reaction of β -dicarbonyl compound, phenylhydrazine, aromatic aldehydes and malononitrile in ethanol in presence of L-proline as catalyst under ultrasonic irradiation. (Scheme 54)



R = OH, OCH₃, N(Et)₂
 Ar = 2,4-Cl₂C₆H₃, 2,3-Cl₂C₆H₃, 2-BrC₆H₄, C₆H₅,
 2-ClC₆H₄, 3-NC₅H₄, 4-BrC₆H₄, 4-ClC₆H₄,

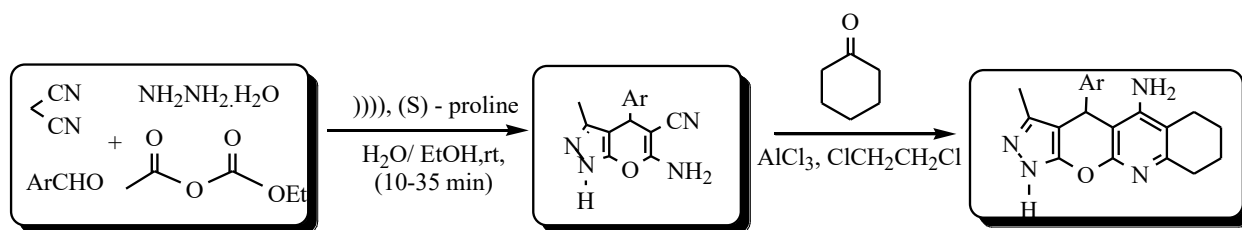
Scheme 54. Synthesis of coumarin-based dihydropyrano[2,3-*c*]pyrazoles using L-proline in ethanol under ultrasonic irradiation.

Mohamadpour *et al.* [75] developed an atom economic and facial synthesis of dihydropyrano[2,3-*c*]pyrazole via multi-component tandem Knoevenagel cyclo-condensation reaction. (Scheme 55)



Scheme 55. Synthesis of dihydropyrano[2,3-*c*] pyrazoles via atom-economical multicomponent Knoevenagel cyclo condensation.

Khoobi *et al.* [76] designed a novel series of tacrine-based compounds consisting pyrano[2,3-*c*]pyrazole substructure. The poly-functionalized hybrid molecules were efficiently synthesized through multi-component reaction and subsequent Friedländer reaction between the obtained pyrano[2,3-*c*]pyrazoles and cyclohexanone using ultrasonic irradiation. (Scheme 56)

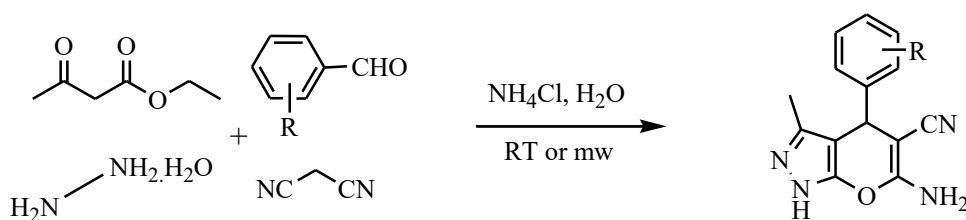


Ar = Naphthalen-1-yl, Thiophen-2-yl, 4-tolyl, 2-F Ph, 4-F Ph, 3-NO₂Ph, 4-MeOPh, 2-MeOPh, 2,5-diMeOPh, 3,4-diMeOPh, 3,4,5-triMeOPh,

Scheme 56. Synthesis of tacrine-based pyrano[2,3-c]pyrazole hybrids via multicomponent and Friedländer reactions under ultrasonic irradiation.

2.5 Miscellaneous condition

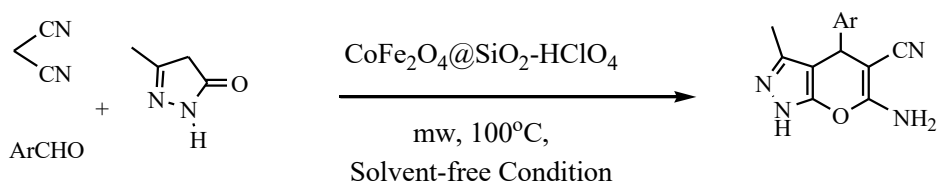
Pawar et al. [77] developed a green protocol for the synthesis of pyranopyrazoles using energy-efficient microwave irradiation or room-temperature stirring in the presence of ammonium chloride as a mild, cost-effective, and eco-friendly catalyst, with water serving as the green solvent. (Scheme 57)



R = H, 4-Cl, 2-Cl, 4-OH, 2-Cl, 4-Br, 4-NO₂, 3, 4-diOMe, 3-OMe, 4-OH, 3-NO₂, 4-F

Scheme 57. Preparation of pyranopyrazoles employing NH₄Cl as an eco-friendly catalyst in aqueous medium under microwave or ambient conditions.

Thakare et al. [78] developed a novel magnetically recoverable CoFe₂O₄@SiO₂-HClO₄ nanocatalyst for the synthesis of pyranopyrazoles and their derivatives under solvent-free conditions using microwave irradiation. (Scheme 58)



Ar = C₆H₅, 3-NO₂-C₆H₄, 4-Cl-C₆H₄, 4-OH-C₆H₄, 3-OC₂H₅, 4-OH-C₆H₄, 4-OCH₃-C₆H₅, 3,4-OCH₃-C₆H₄, 3,4,5-OCH₃-C₆H₃, 4-CH₃-C₆H₅, 4-(CH₃)₂CH-C₆H₅, 4-(CH₃)₂N-C₆H₅, 2-furyl-C₆H₅, 2-Thiophene-C₆H₅, 3-Indolyl-C₆H₅, Terephthalaldehyde

Scheme 58. Microwave-assisted, solvent-free synthesis of pyrano[2,3-c]pyrazoles employing CoFe₂O₄@SiO₂-HClO₄ as a recyclable magnetic nanocatalyst.

3 Conclusion

This review summarizes recent green and efficient strategies reported for the synthesis of pyranopyrazole derivatives during the period from 2011 to 2025. The focus is on environmentally friendly protocols, including sonochemical methods, microwave-assisted techniques, solvent-free conditions, and the use of green solvents, particularly water. In addition, the application of heterogeneous catalysts such as nanocatalysts, heteropoly acids, and ionic liquids has significantly enhanced the accessibility of these important heterocyclic compounds. Pyranopyrazole derivatives have been reported to exhibit a wide range of biological activities, including antibacterial, antifungal, antioxidant, anti-inflammatory, anti-ulcerogenic, analgesic, anticonvulsant, and insecticidal properties. Structural characterization of these compounds has been carried out using spectroscopic and analytical techniques such as NMR, mass spectrometry, IR spectroscopy, elemental analysis, and X-ray diffraction to confirm their structures and the position of hydrogen atoms in the pyrazolone ring.

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5 Conflict of interest

The authors declare that there are no conflicts of interest.

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