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ONE POT SYNTHESIS OF PYRANO[2,3-C]PYRAZOLE: A REVIEW

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ABSTRACT

The synthesis of pyranopyrazole bioactive heterocycles has caught the interest of medicinal and organic chemists due to their biological and therapeutic capabilities. This review summarizes the One Pot Synthetic pathways of pyranopyrazoles. Green approaches, nanoparticulate catalysts, microwave irradiation, ultrasonic irradiations, and other catalysts are among the reaction conditions that can be varied. The present review describes the literature reports for the period 2010 to 2021.

KEYWORDS: One pot synthesis, Microwave irradiation, Pyranopyrazole, Green approach, Ultrasonic irradiation.

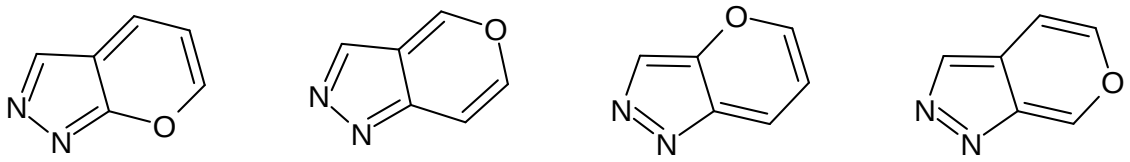
INTRODUCTION

Heterocyclic compounds are widely employed because they have a wide range of applications in pharmaceuticals. The ability to develop diverse structures that are required to fulfil specific significant functions is the primary reason for their versatile application.

In the antibacterial, pharmaceutical, and medicinal sectors, pyran-based heterocyclic chemicals have been extensively used. "Multicomponent Reactions" (MCRs) have recently emerged as an alternative to traditional ways for creating a variety of complex organic compounds by combining three or more initial substrates. Many organic chemists have been drawn to one-pot multicomponent reactions because of their streamlined operation, simplified purification, decreased waste, lowered safety criteria, and reduced duration.[1]

Pyranopyrazoles are a fascinating class of heterocycles due to their synthetic versatility and effective biological activities. Isomer **(1)** is the most studied of the four probable isomeric forms: pyrano[2,3-c]pyrazole **(1)**, pyrano[4,3-c]pyrazole **(2)**, pyrano[3,2-c]pyrazole **(3)**, and

pyrano[3,4-c]pyrazole **(4)**. A variety of pyrano[2,3-c]pyrazole derivatives have been synthesized, derivatized, and biological activities have been described.[2]



1 **2** **3** **4**

Figure 1: Structures of isomeric pyranopyrazoles.

Dihydropyrano[2,3-c]pyrazole is a structurally significant fused heterocyclic molecule obtained when the pyrazole ring is condensed with the 4H-pyran ring.[3]

Otto took the first step in synthesizing these compounds by using a base-catalyzed cyclization of 4-aryliden-5-pyrazolone to start the reaction chain. Otto and Schmelz showed in a subsequent paper that weak bases can also be used for Michael-type cyclization. Klokol et al. built on this work by performing a direct conversion of 3-methyl-3-pyrazolin-5-one with malononitrile in the presence of a weak base.[4]

Dihydropyrano[2,3-c]pyrazole because of its numerous bioactivities, including as anti-inflammatory[5], anticancer[6], anti-oxidant[7], anti-cholinesterase[8], analgesic[9], and anti-microbial[10-12] action, pyrazole nucleus is a rich source of several medicinally relevant chemicals. It also acts as a human checkpoint kinase 1 (Chk1) inhibitor **(5)**.

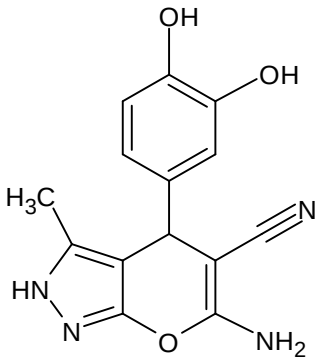


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Figure 2: Potential inhibitor of Human Chk1 kinase.

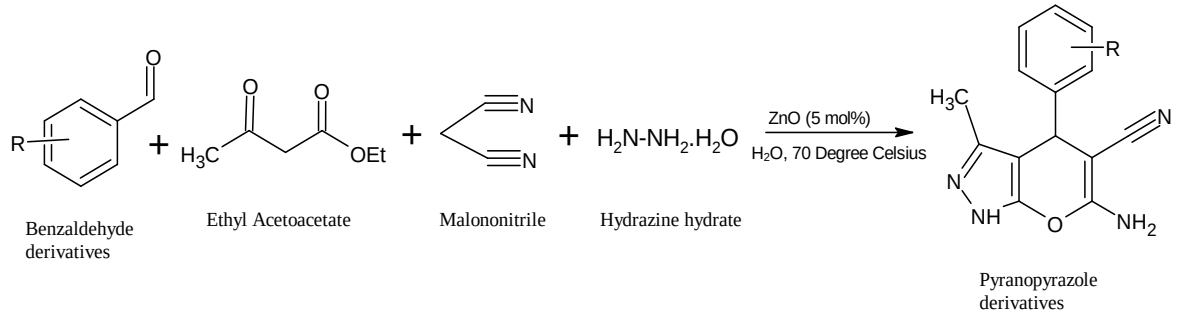
Several types of homogeneous catalysts[13,14], heterogeneous catalysts[15,16], different metal sources[17], micellar catalyst[18], nano ionic liquids[19], enzymatic catalyst[20], and other

catalysts have been reported in the literature for the synthesis of pyrazole using various reaction routes such as ultrasound[21], microwave[22], neat[23], and various substrates.

ONE POT SYNTHESIS OF PYRANOPYRAZOLES:

Scheme 1

Sunil U. Tekale et al. developed an efficient one pot four component synthesis of pyranopyrazoles using 5 mol% of ZnO nanoparticles as catalyst at room temperature in aqueous medium. The coupling reaction of aromatic aldehyde, malononitrile, ethyl acetoacetate and hydrazine hydrate in aqueous medium gives higher yield in short time.[24]

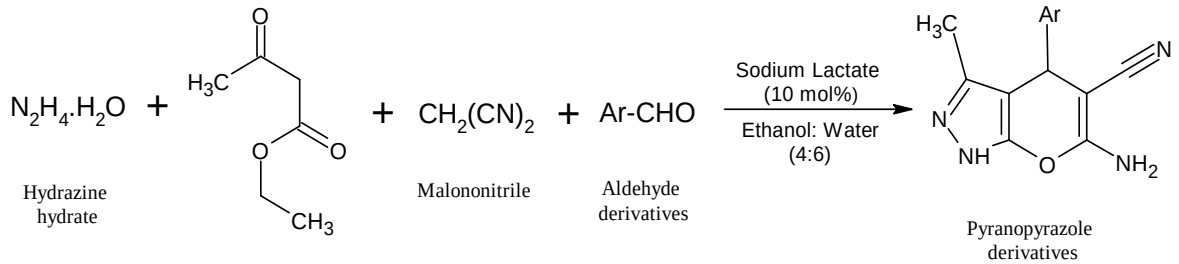


Benzaldehyde derivatives | Ethyl Acetoacetate | Malononitrile | Hydrazine hydrate | Pyranopyrazole derivatives

R= C_6H_5, 4-Cl-C_6H_4, 4-NMe_2-C_6H_4, 4-SMe-C_6H_4, 4-OH-C_6H_4, 2-Cl-C_6H_4, 4-Me-C_6H_4, 4-Br-C_6H_4, 4-NO_2-C_6H_4, 4-OMe-C_6H_4, 3-OMe-4-OH-C_6H_4, 3-$NO_2C_6H_4$, 2-Furyl

Scheme 2

J. P. Sonar, S. D. Pardeshi et.al. developed four-component condensation of hydrazine hydrate, ethyl acetoacetate, aldehydes, and malononitrile in an aqueous ethanolic medium under reflux conditions utilising sodium lactate as a catalyst resulted in an effective one-pot synthesis of pyranopyrazoles. To obtain pyranopyrazoles in a short period of time, a simple and environmentally friendly approach is used. It introduces a new base catalyst that produces product in a wide range of yields, from mediocre to outstanding.[25]

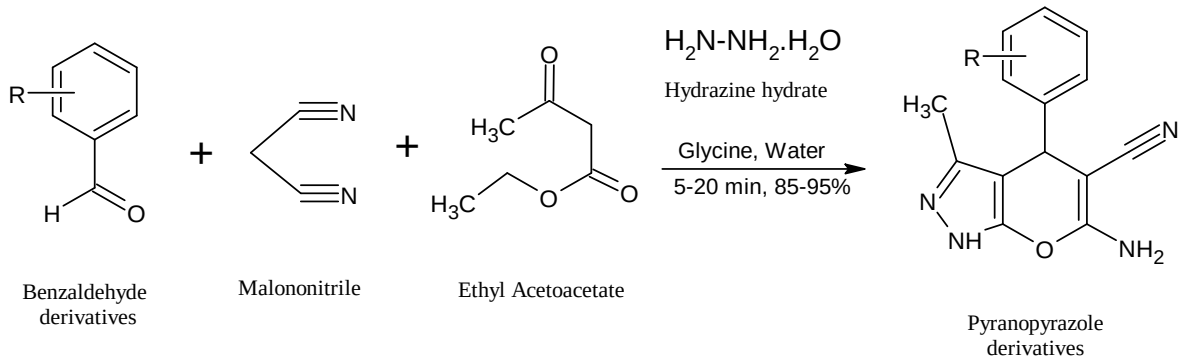


Hydrazine hydrate | Ethyl Acetoacetate | Malononitrile | Aldehyde derivatives | Pyranopyrazole derivatives

Ar = 4-OMe- C_6H_4, 4-Cl-C_6H_4, 2-Cl-C_6H_4, 4-OH-C_6H_4, 4-Br-C_6H_4, 4-NO_2-C_6H_4, 3-NO_2-C_6H_4, 4-Me-C_6H_4, 3-OMe-4-OH-C_6H_3, 2-Furyl, 4-(Piperidin-1-yl)- C_6H_4

Scheme 3

The synthesis of fused pyranopyrazoles from ethyl acetoacetate, hydrazine hydrate, an aldehyde, and malononitrile in the presence of nontoxic, simple, and readily available Glycine organocatalyst in aqueous medium at 25℃.[26]

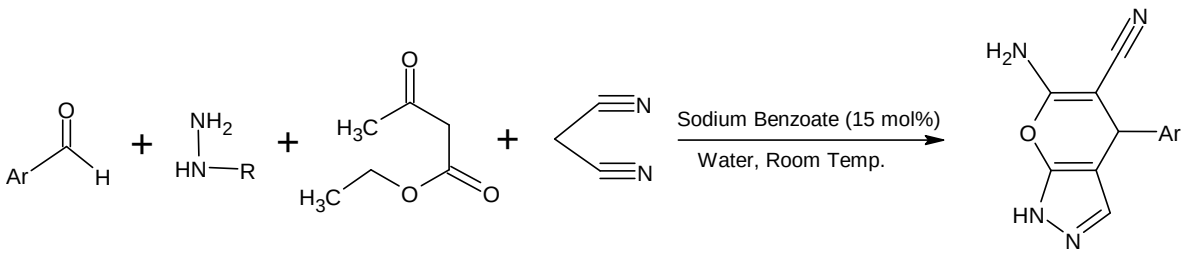


Benzaldehyde derivatives | Malononitrile | Ethyl Acetoacetate | Pyranopyrazole derivatives

R = -Me, -OMe, -NO_2, -Cl, -F, -OH

Scheme 4

The condensation reaction of aryl aldehydes, ethyl acetoacetate, malononitrile, and hydrazine hydrate or phenyl hydrazine in the presence of commercially available organocatalyst sodium benzoate under aqueous conditions results in an efficient, green, and facile four-component reaction for the preparation of pyrano[2,3- c]pyrazole derivatives. The items have excellent yields and are made in a shorter amount of time. It's also gentle, safe, eco-friendly, and non-toxic.[27]



Aryl Aldehydes | Hydrazines | Ethyl Acetoacetate | Malononitrile | Pyrano[2,3-c]pyrazole derivatives

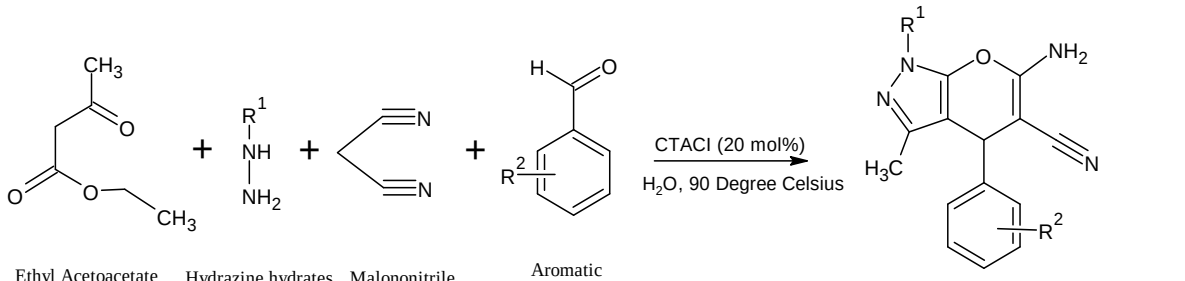
R = H, Ph

Ar = C_6H_5, 4-$NO_2C_6H_4$, 3-$NO_2C_6H_4$, 2-$NO_2C_6H_4$, 4-$CH_3C_6H_4$, 4-$OCH_3C_6H_4$, 4-OHC_6H_4, 4-$(NMe)_2$-C_6H_4, 4-ClC_6H_4

Scheme 5

The synthesis of 6-amino-3-methyl-4-aryl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile has been created using an environmentally friendly four-component reaction in aqueous

medium in the presence of cetyltrimethylammonium chloride (CTACl). The procedure proposed is gentle, ecologically benign, low-cost, and functionally tolerant, yielding good to exceptional results.[28]



Ethyl Acetoacetate | Hydrazine hydrates | Malononitrile | Aromatic aldehydes

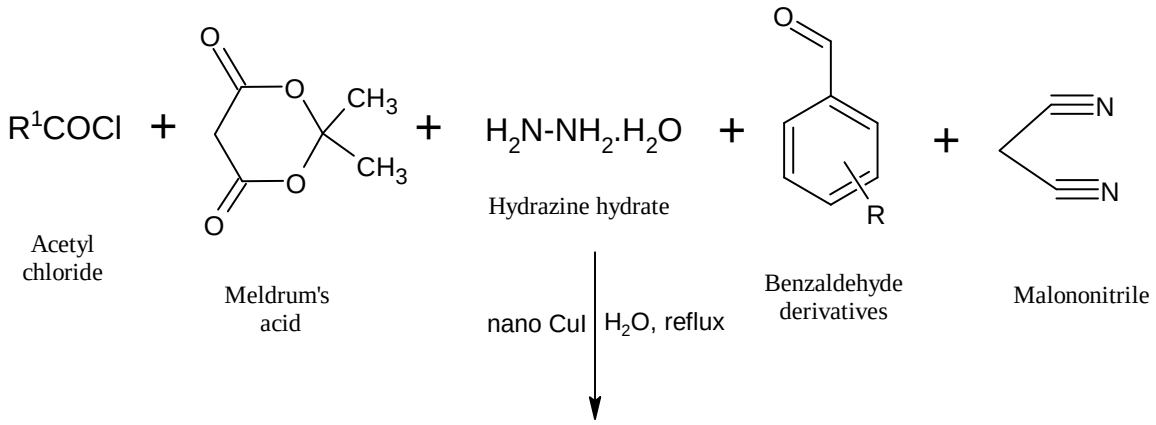
6-Amino-3-methyl-4-aryl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

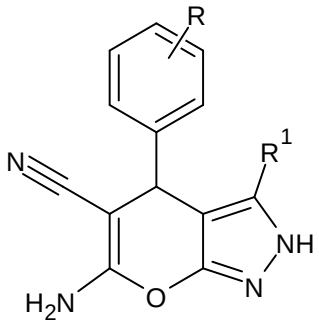
R^1 = C_6H_5, H

R^2 = m-NO_2, p-CH_3, p-OCH_3, p-OH, 3,4-$(Cl)_2$, p-Br, H, p-F, 2,4-$(Cl)_2$, m-NO_2, p-CF_3, P-$N(CH_3)_2$

Scheme 6

In the presence of catalytic amounts of CuI nanoparticles in aqueous media, an unique one-pot, five-component process for the synthesis of highly functionalized pyranopyrazoles from acid chlorides, Meldrum's acid, hydrazine hydrate, aromatic aldehydes, and malononitrile is reported. This process has a number of advantages, including in-situ ketoester preparation, gentle reaction conditions, and an environmentally friendly, waste-free, and straightforward work-up procedure with high yields. With practically constant catalytic activity, the catalyst may be retrieved and reused numerous times.[29]





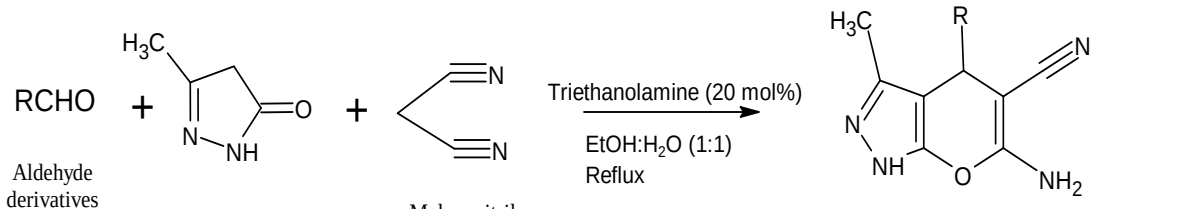
Pyranopyrazole derivatives

R^1 = CH_3, CH_3CH_2, Ph

R = C_6H_5, 4-Cl-C_6H_4, 4-Br-C_6H_4, 4-NO_2-C_6H_4

Scheme 7

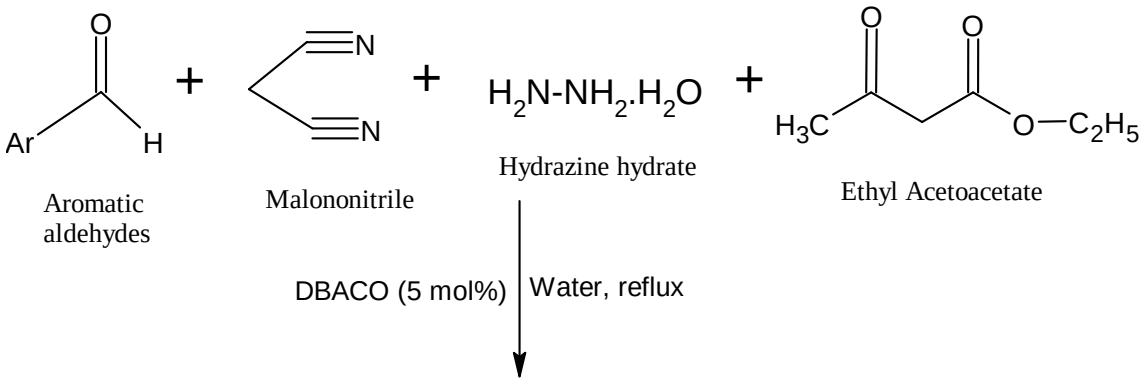
In aqueous medium reflux conditions, triethanolamine is an efficient and environmentally friendly catalyst for the production of 6-amino-1, 4-dihydro-4-substituted-3-methylpyrano[2, 3-c]pyrazole-5-carbonitrile. The technique is simpler, more environmentally friendly, and simple to work up, resulting in a high output of the desired items.[30]

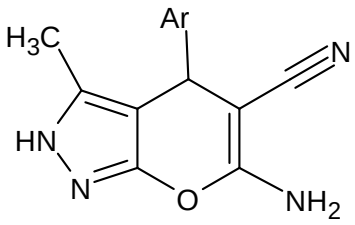


R = 4-OMe-C_6H_4, 4-NO_2-C_6H_4, 4-OH-C_6H_4, 4-Br-C_6H_4, C_6H_4, 4-F-C_6H_4, Furfural

Scheme 8

A one-pot, four-component reaction comprising ethyl acetoacetate, hydrazine hydrate, malanonitrile, and different aldehydes in the presence of a catalytic quantity of DABCO in aqueous medium is devised for the manufacture of dihydropyrano[2,3-c] pyrazole derivatives. This approach has been developed to provide numerous advantages such as high yield, shorter reaction time, benign reaction conditions, operational simplicity, easy work-up procedure, and purification of products using non-chromatographic methods.[31]



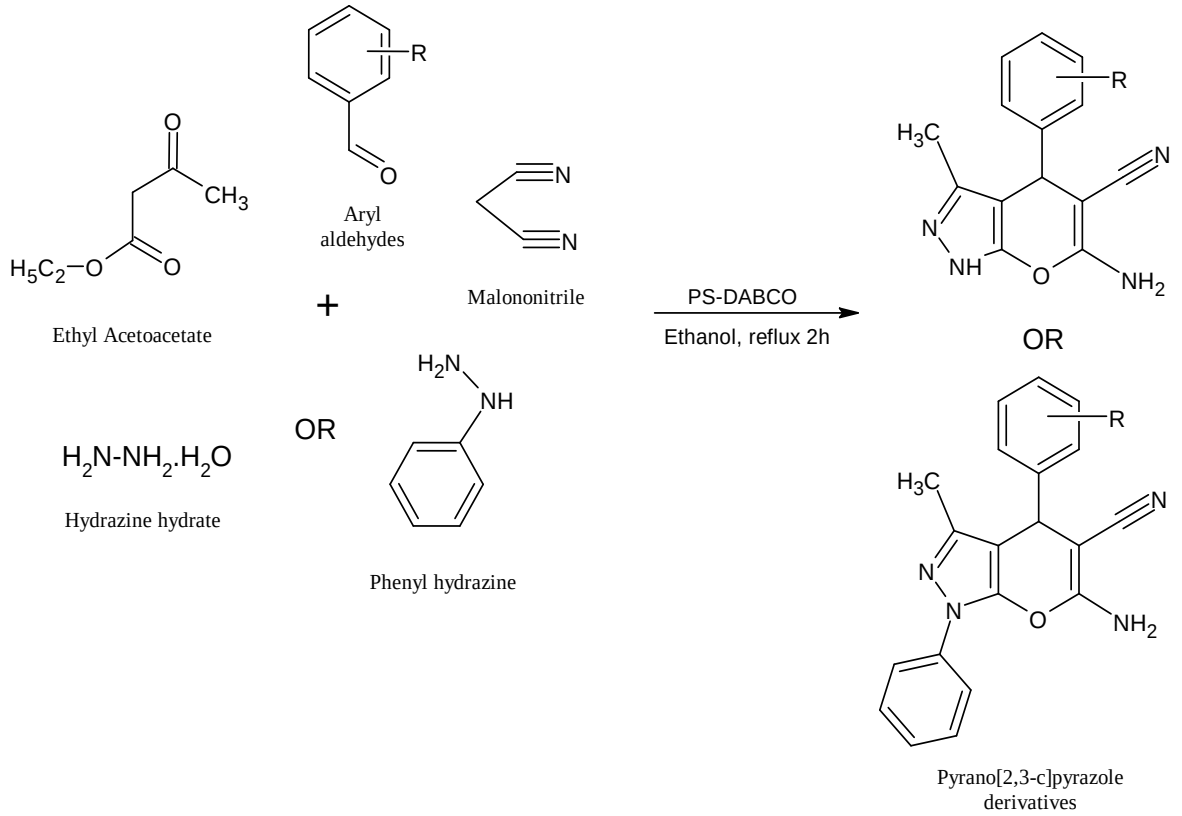


Pyrano[2,3-c]pyrazole derivatives

Ar = 4-Cl-C_6H_4, C_6H_5, 3-NO_2-C_6H_4, 4-OH-C_6H_4, 2-Br-C_6H_4, 4-Me-C_6H_4, 1-naphthyl

Scheme 9

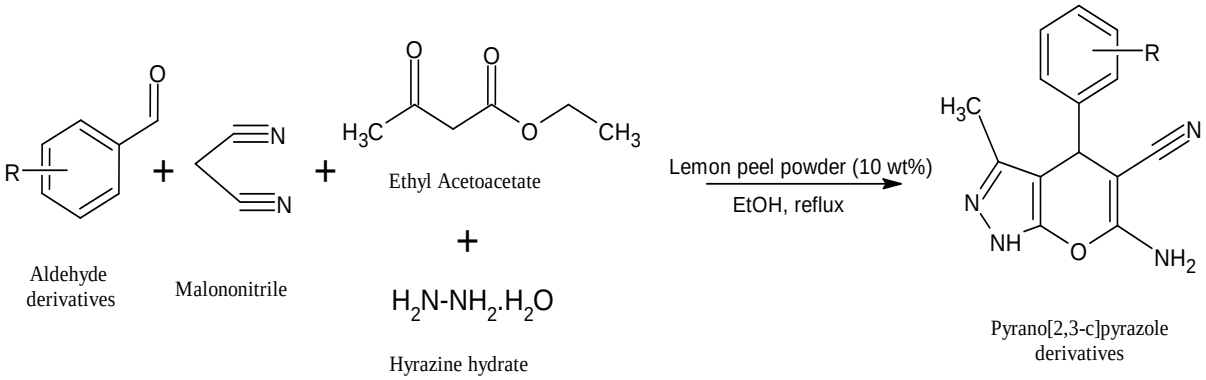
Using PS-DABCO as a green reusable heterogeneous catalyst, a one-pot, four-component, C-C and C-N bond forming reaction of aryl aldehydes, ethyl acetoacetate, malononitrile, and hydrazine hydrate or phenyl hydrazine has been devised for the manufacture of dihydropyrano[2,3-c]pyrazoles derivatives. This protocol is useful, greener, cost effective, and practical for both academic and industrial purposes due to the absence of unwanted products, general applicability, reusability of the catalyst, non-chromatographic purification procedure, green synthesis avoiding toxic reagents, and improved and operational simplicity.[32]



R = H, 2-Cl, 3-Cl, 4-Cl, 4-OMe, 4-F, 2-NO_2, 3-NO_2, 4-NO_2, 3,4-di-OMe

Scheme 10

The condensation of aldehydes, malononitrile, ethyl acetoacetate, and hydrazine hydrate in ethanol under reflux utilising lemon peel powder as a natural catalyst resulted in a straightforward one-pot four-component pyrano[2,3-c]pyrazole synthesis. The advantages of this reaction include a shorter reaction time, a higher yield, easy availability of the catalyst, and the protocol's environmental friendliness.[33]

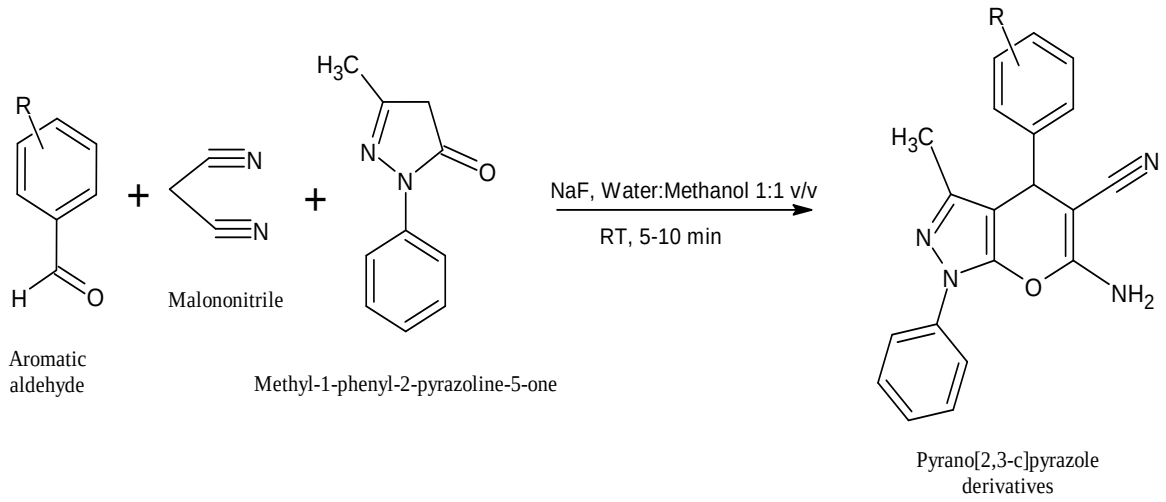


R = 4-NO_2, 4-OH, 4-Cl, 4-F, 4-Br

Scheme 11

The three-component condensation of 3-Methyl-1-phenyl-2-pyrazoline-5-one, aromatic aldehydes, and malononitrile in aqueous methanol at ambient temperature under ultrasonication was identified by Ramaiah Konakanchi et al. as an efficient catalyst for the preparation of series of dihydropyrano [2,3-c]pyrazoles. The affordability and efficacy of the catalyst, as well as the mild reaction conditions, simple workup technique, shorter reaction time, and greater product yields with analytical purity, make this protocol preferable to others previously reported.

All of the compounds' structures were consistent with their spectroscopic (1H NMR, 13C NMR) and elemental (CHN) investigations.[34]



Aromatic aldehyde

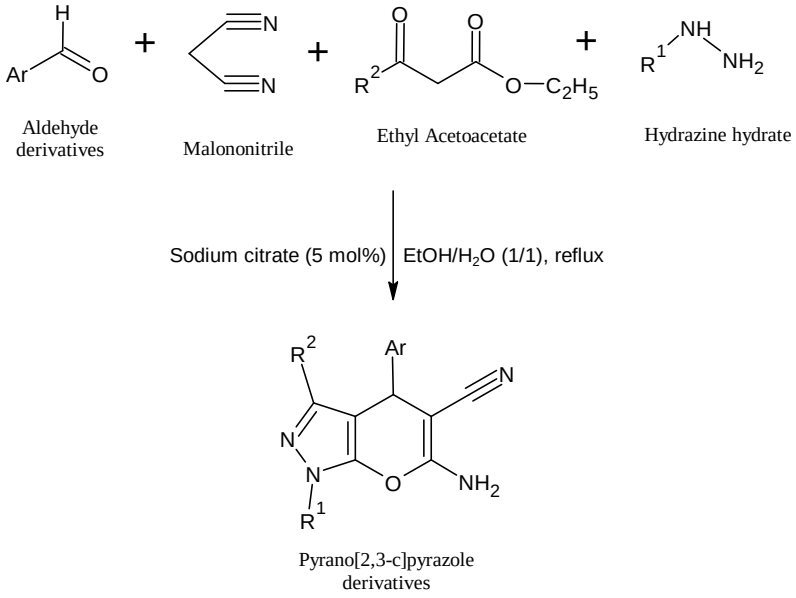
Methyl-1-phenyl-2-pyrazoline-5-one

Pyrano[2,3-c]pyrazole derivatives

R = 4-Cl, 2,4-di-Cl, 4-NO_2, 3-NO_2, 2-NO_2, 4,3-di-CH_3, 4-Br

Scheme 12

Rima Laroum, Abdelmadjid Debache, and colleagues established a one-pot four-component reaction combining commercially available aldehydes, malononitrile, ethyl acetoacetate (or ethyl benzoylacetate), and hydrazine hydrate for the simple synthesis of pyrano[2,3-c] pyrazoles (or phenylhydrazine). In the presence of sodium citrate as a catalyst, the reactions were carried out in aqueous EtOH. Using an eco-friendly four-component one pot reaction, a number of pyrano[2,3-c]pyrazole derivatives were swiftly produced in excellent yields.[35]



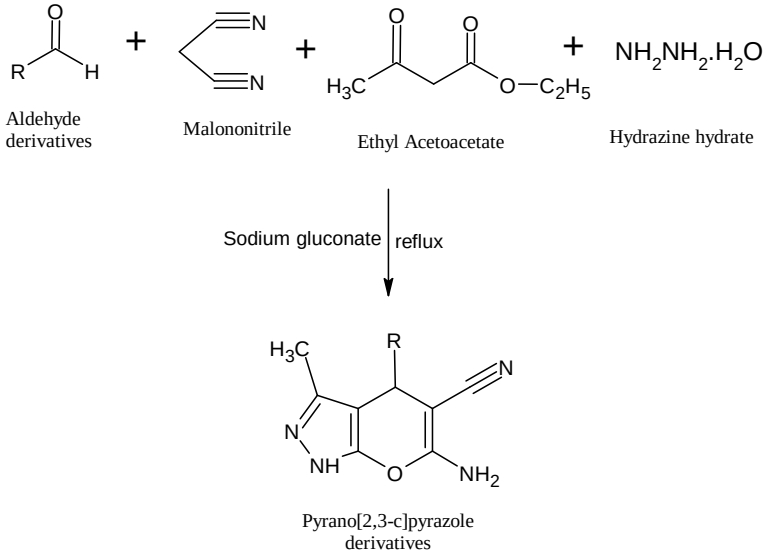
R^1 = H, Ph

R^2 = CH_3, Ph

Ar = C_6H_5, 4-CH_3-C_6H_4, 4-Cl-C_6H_4, 4-NO_2-C_6H_4, 4-OH-C_6H_4, 3-NO_2-C_6H_4

Scheme 13

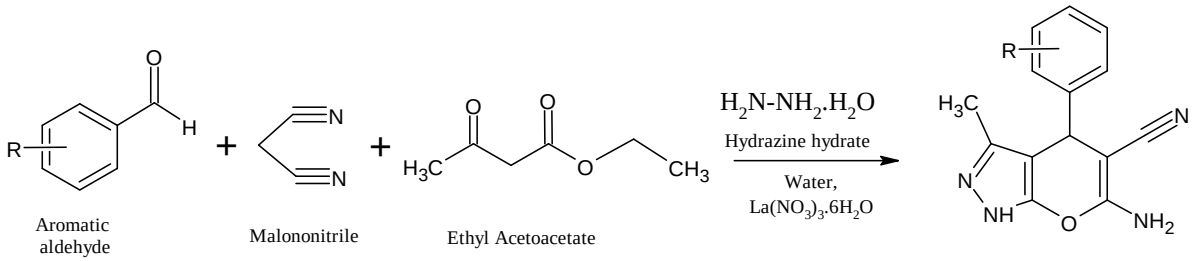
In a one-pot multicomponent reaction involving aryl aldehyde, malononitrile, ethyl acetoacetate, and hydrazine hydrate in water as a solvent, sodium gluconate was discovered to be a capable and recyclable organocatalyst for the synthesis of dihydropyrano[2,3-c]pyrazole derivatives. The catalyst is nontoxic, readily available, biodegradable, and easily removed from the reaction mixture. This methodology is greener since it eliminates the use of heavy metal catalysts, harsh reaction conditions, and catalyst reusability. It also has a broad substrate scope, a simple work-up procedure, and great product yield.[36]



R = Ph, 4-OCH_3-Ph, Thiophene, 4-N, N-dimethyl-Ph, 3-methoxy,4-hydroxy-Ph, 4-Cl-Ph, 4-Br-Ph, Acetaldehyde, 2-methoxy-Ph, 4-Me-Ph, 2-Cl-Ph, 4-OH-Ph, 4-F-Ph

Scheme 14

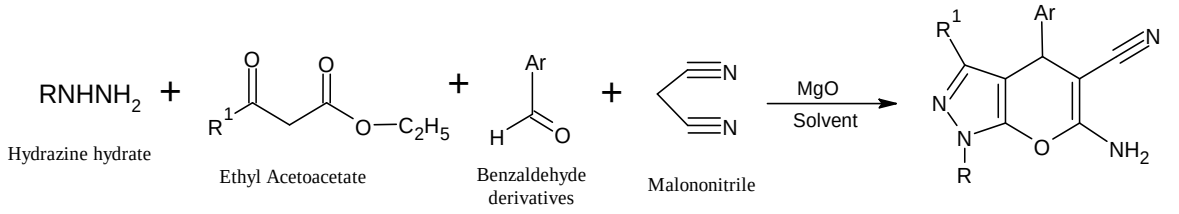
The reaction of aromatic aldehyde, malononitrile, ethyl acetoacetate, and hydrazine hydrate with ultrasonication waves in aqueous medium has been developed into a simple and green one-pot approach for the synthesis of pyranopyrazoles. This technology has the advantages of operational simplicity and an environmentally favourable green approach.[37]



R = 4-Cl-C_6H_4, 4-NO_2-C_6H_4, 4-OH-C_6H_4, 4-Br-C_6H_4, 4-NH_2-C_6H_4, 4-F-C_6H_4

Scheme 15

In the presence of nanosized magnesium oxide as a highly effective heterogeneous base catalyst, a four-component reaction of hydrazine hydrate or phenyl hydrazine, ethyl acetoacetate, aldehydes, and malononitrile resulted in excellent yields and a short experimental time to produce 6-amino-3-alkyl-4-aryl-5-cyano-1,4-dihydropyrano[2,3-c]pyrazole derivatives. This method for concentrating a pyrano ring with a pyrazole ring is easy and quick.[38]



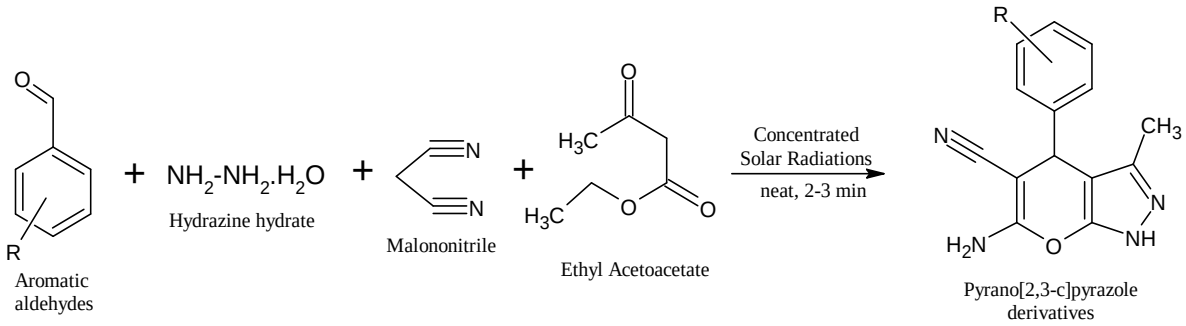
R = H, Ph

R^1 = CH_3, Propyl, Iso-propyl

Ar = C_6H_5, 2-Cl-C_6H_4, 4-Cl-C_6H_4, 3-Br-C_6H_4, 4-NO_2-C_6H_4, 4-CH_3O-C_6H_4, 2,4-Cl_2-C_6H_3

Scheme 16

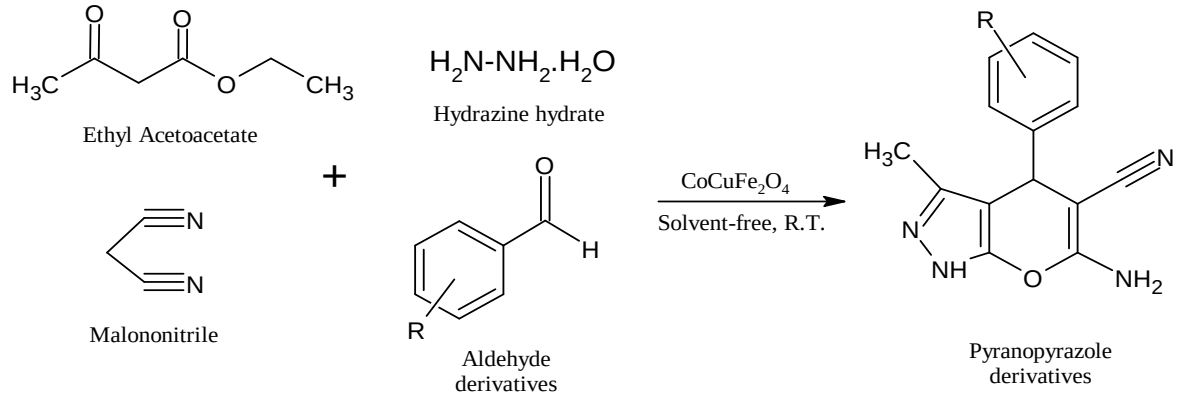
The present protocol describes the use of concentrated sun radiation (CSR) to aid in the synthesis of pyranopyrazole derivatives in a solvent- and catalyst-free environment. The final desired compounds are synthesised in a good yield from aromatic/heteroaldehyde, ethyl acetoacetate, malononitrile, and hydrazine hydrate in a one-pot multicomponent synthesis. The advantages of this operationally easy technology include a green and clean reaction process, simple workup and purification procedures, an exceptionally fast reaction time, atom efficiency, and cost effectiveness. When compared to the traditional way, the present energy-efficient technology saves over 98% of the energy.[39]



R = -Cl, -NO_2, -F, -Me, -OMe, -OH

Scheme 17

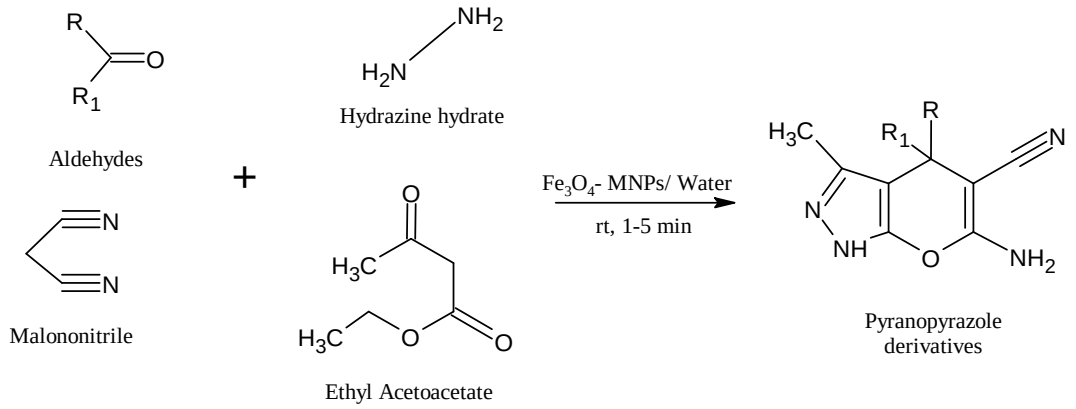
At room temperature and without the use of solvents, an effective and quick four-component reaction of ethyl acetoacetate, hydrazine hydrate, malononitrile, and various aldehydes. The goal of this study was to develop a reusable catalyst for the production of pyranopyrazole derivatives in the presence of CoCuFe2O4 magnetic nanocrystals. Spectroscopic and physical data, such as melting points, FT-IR, and 1H NMR tests, confirmed the products.[40]



R = C_6H_5, 4-Cl-C_6H_4, 4-CH_3-C_6H_4, 4-F-C_6H_4, 3-OMe-C_6H_4, 4-Br-C_6H_4, 4-NO_2-C_6H_4

Scheme 18

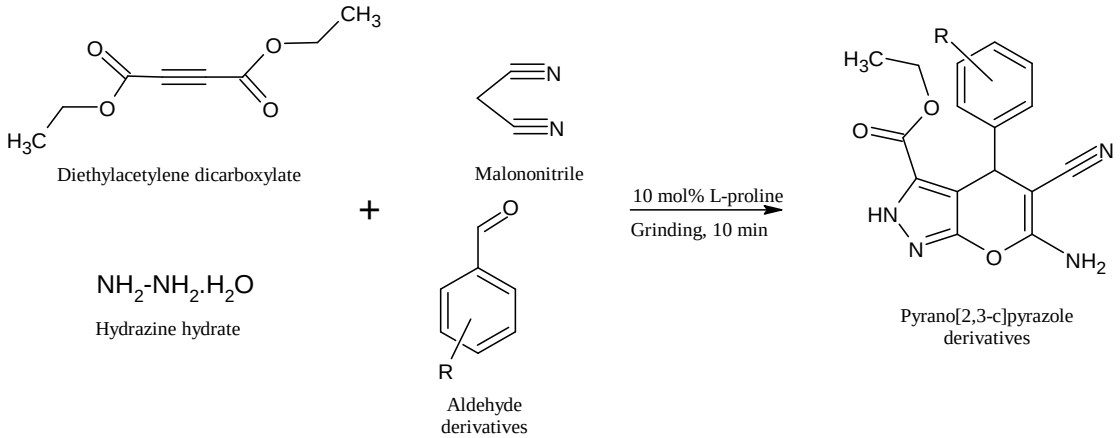
A four-component reaction comprising hydrazine hydrate, ethyl acetoacetate, aldehydes/ketones, and malononitrile in water at room temperature was found to be efficient for the synthesis of a variety of pyranopyrazoles using magnetic Fe3O4 nanoparticles as a heterogeneous catalyst. The catalyst's nano size of roughly 16 nm, which allowed it to serve as a nanoreactor, was blamed for the results. The current approach has the advantages of a clean reaction, a short reaction time, a high yield, ease of purification, and low catalyst costs.[41]



R = Ph, 4-MeO-Ph, 2,5-MeO-Ph, 3,4,5-MeO-Ph, 4-NO_2-Ph, 4-OH-Ph, 4-Cl-Ph, 4-Br-Ph, 4-F-Ph, 4-$(CH_3)_2$N-Ph, 2-OH-Ph, 3-Cl-Ph

Scheme 19

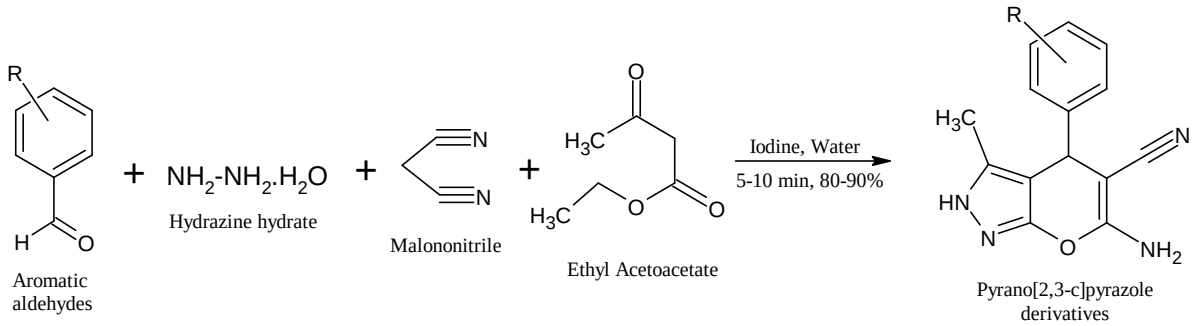
Under solvent-free circumstances, an efficient grinding technique for the synthesis of dihydropyrano[2,3-c]pyrazole derivatives from acetylene ester, hydrazine hydrate, aryl aldehydes, and malononitrile was developed with excellent yields. Spectroscopic techniques were used to deduce the structures of the produced compounds, which were then tested for antioxidant and antibacterial activity in vitro.[42]



R = C_6H_5, 4-CH_3-C_6H_4, 2-Cl-C_6H_4, 4-Cl-C_6H_4, 4-F-C_6H_4, 4-OH-C_6H_4, 4-CH_2CH_3-C_6H_4, 4-NO_2-C_6H_4

Scheme 20

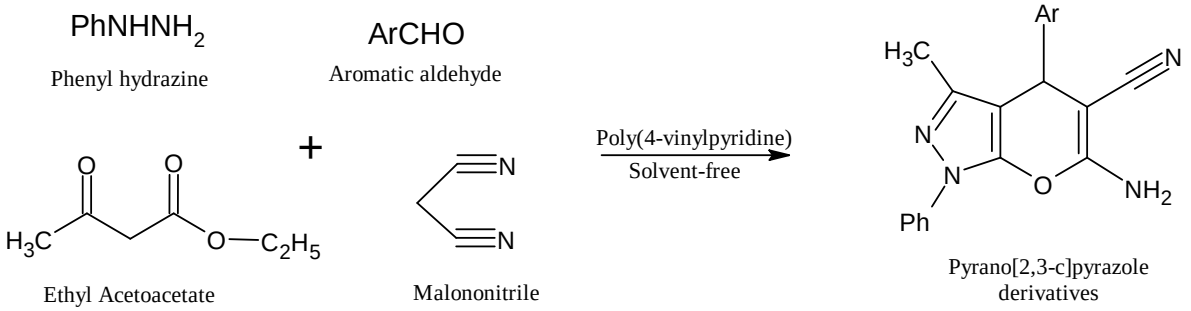
At 25℃ in water, an iodine catalysed four component reaction produces many pyranopyrazoles. The yields are great, and the technique is easy, efficient, and eco-friendly.[43]



R = -Cl, -NO_2, -F, -Me, -OMe, -OH

Scheme 21

The four-component reaction of phenyl hydrazine, ethyl acetoacetate, malononitrile, and aromatic aldehydes, catalysed by poly(4-vinylpyridine), is reported as an effective one-pot synthesis of pyrano[2,3-c]pyrazoles. This process has a number of advantages, including atom-economy, ease of set-up, a clean operation, quick reaction times, and high product yields.[44]

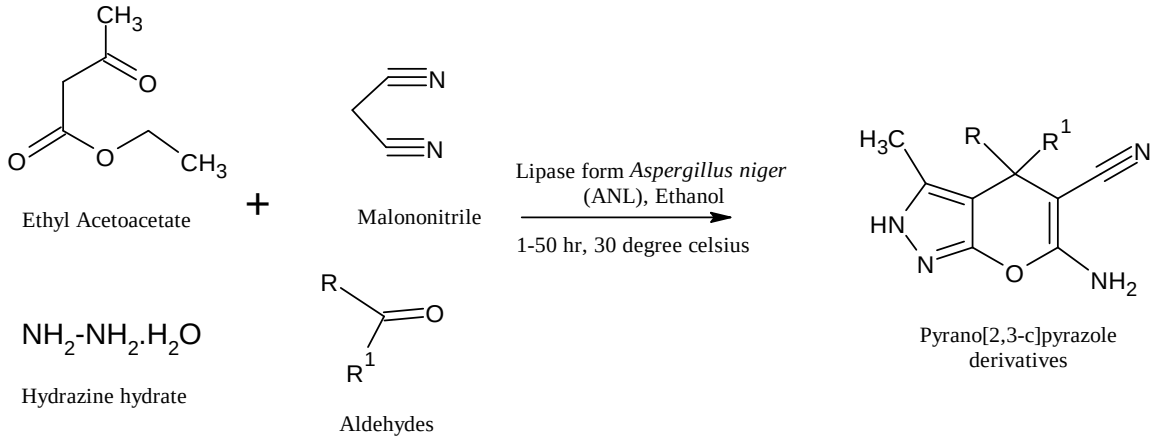


Ar = C_6H_5, 2-Cl-C_6H_4, 3-Cl-C_6H_4, 4-Cl-C_6H_4, 2,4-Cl-C_6H_3, 3-NO_2-C_6H_4, 4-Br-C_6H_4, 4-OMe-C_6H_4

Scheme 22

In a stoichiometric mixture of ethyl acetoacetate, hydrazine hydrate, aldehyde/ketone, and malononitrile in ethanol, lipase from *Aspergillus niger* (ANL) was discovered to be a very

effective catalyst for four-component synthesis of dihydropyrano[2,3-c]pyrazoles. The lipase ANL displayed enzymatic promiscuity for a wide spectrum of aromatic and aliphatic aldehydes, as well as ketones. This protocol's key benefits include the use of an environmentally friendly biocatalyst, reusability of the catalyst, room temperature reaction conditions, no toxic solvent, and outstanding yields.[45]



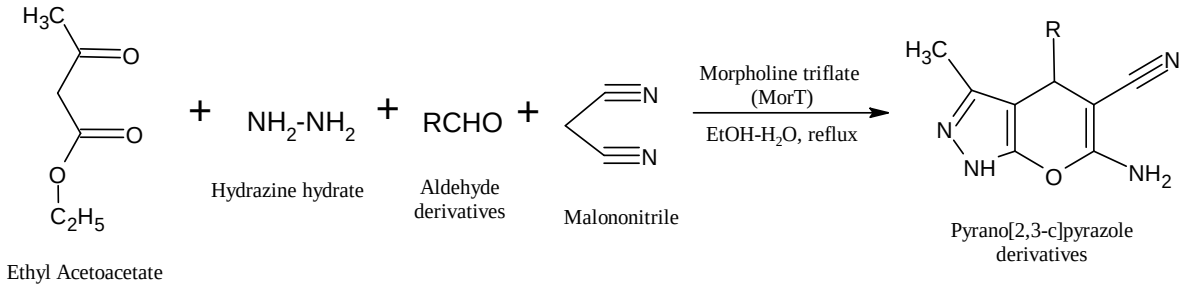
R = H, alkyl, aryl

R^1 = H, alkyl, aryl

Scheme 23

The Lewis acid catalyst morpholine triflate (MorT) was used to catalyse a one-pot, four-component reaction of ethyl acetoacetate, hydrazine hydrate, aldehydes, and malononitrile to yield a series of dihydropyrano[2,3-c]pyrazoles, which were mainly catalysed by organic alkalis.

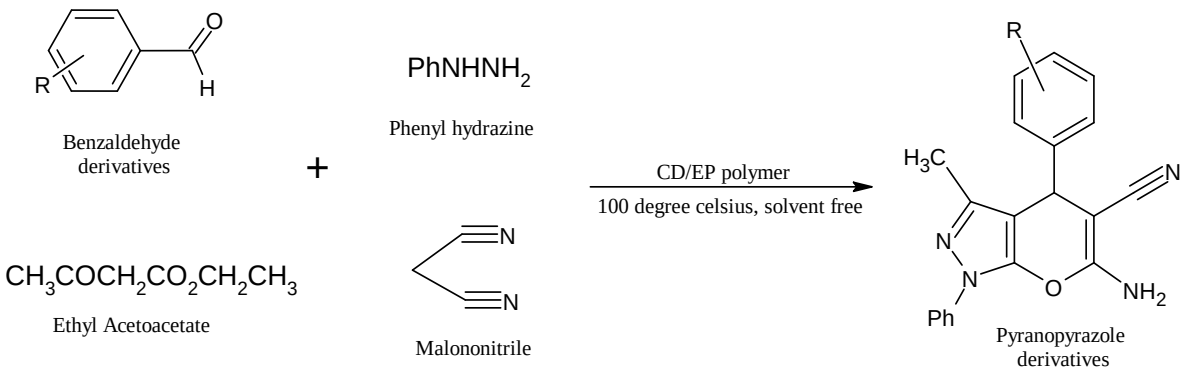
This approach is particularly beneficial for academia and industry because of the moderate to good yields, the lack of chromatographic purification, and the avoidance of ecologically toxic solvents in the reaction process.[46]



R = C_6H_5, 4-F-C_6H_4, 2-Cl-C_6H_4, 4-Br-C_6H_4, 3-OH-C_6H_4, 4-CH_3-C_6H_4, 2-Furan, 3-Pyridine

Scheme 24

FT-IR spectroscopy, thermogravimetric analysis, scanning electron microscopy, and Brunauer–Emmett–Teller were used to describe the □-cyclodextrin-epichlorohydrin nanosponge polymer, □-CD/EP, which was made by stepwise polymerization of □-cyclodextrin with epichlorohydrin under basic circumstances. Using □-CD/EP as a stationary micro-vessel and basic heterogeneous catalyst in a four component reaction under solvent-free conditions, an effective synthesis of spiro[indoline-3,40 -pyrano[2,3-c]pyrazole] and pyranopyrazole derivatives is disclosed.[47]

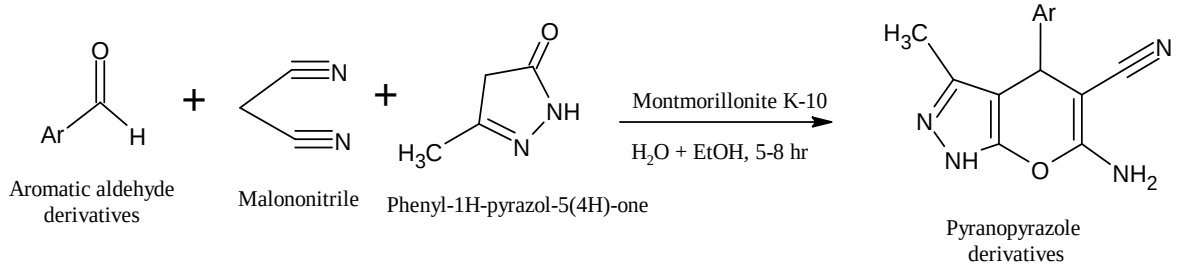


R = H, 4-Me, 4-OMe, 4-OH, 4-Cl, 4-Br, 4-NO_2, 3-Cl, 3-NO_2, 3-Me, 2-OH

Scheme 25

The use of montmorillonite K-10 as a reusable green acid catalyst in the presence of an environmentally acceptable solvent leads to a unique approach for multicomponent pyranopyrazole derivative synthesis.

Furthermore, the catalyst may be utilised for the reaction five times without losing any activity. The goal of this method was to use green catalysis to create new synthetic compounds for subsequent screenings, such as starting molecules for organic electronic materials and biological tests.[48]



Ar = C_6H_5, 4-NO_2-C_6H_4, 4-CH_3-C_6H_4, 4-F-C_6H_4, 4-CF_3-C_6H_4, 4-Cl-C_6H_4, 4-Br-C_6H_4, 2-NH_2-C_6H_4

CONCLUSION

This review has covered the one pot synthetic strategies reported for the synthesis of pyranopyrazole derivatives during the period of 2010 to 2021. Greener protocols, such as sonochemical conditions, MW-assisted technologies, solvent-free conditions, green solvents, particularly water as a solvent, heterogeneous catalysis, particularly nano catalyst, and ionic liquids, have made access to these important heterocyclic compounds possible in recent years. Compounds are reported as antibacterial, antifungal, antioxidant, analgesic, anti-inflammatory, anticancer, anticonvulsant, insecticidal agents.

REFERENCE

1. Yellapurkar, I., Bhabal, S., Ramana, M. M. V., Jangam, K., Salve, V., Patange, S., & More. Magnesium ferrichromate nanoparticles: an efficient and recyclable catalyst in the synthesis of pyrano [2, 3-c] pyrazole derivatives. *Research on Chemical Intermediates*, P., 2021; 1-19.
2. Aslam, N., White, J., Zafar, A. M., Jabeen, M., Ghafoor, A., Sajjid, N., ... & Khan, M. A. 4H-Pyrano [2, 3-c] pyrazoles: a review, 2018.
3. Sikandar, S., & Zahoor, A. F. Synthesis of pyrano [2, 3-c] pyrazoles: A review. *Journal of Heterocyclic Chemistry*, 2021; *58*(3): 685-705.
4. Mamaghani, M., & Hossein Nia, R. A review on the recent multicomponent synthesis of pyranopyrazoles. *Polycyclic Aromatic Compounds*, 2021; *41*(2): 223-291.
5. Kuo, S. C., Huang, L. J., & Nakamura, H. Studies on heterocyclic compounds. 6. Synthesis and analgesic and antiinflammatory activities of 3, 4-dimethylpyrano [2, 3-c] pyrazol-6-one derivatives. *Journal of medicinal chemistry*, 1984; *27*(4): 539-544.
6. Sharma, A., Chowdhury, R., Dash, S., Pallavi, B., & Shukla, P. Fast microwave assisted synthesis of pyranopyrazole derivatives as new anticancer agents. *Current Microwave Chemistry*, 2016; *3*(1): 78-84.
7. Hamed, E. O., Elhoseni, N. K. R., Assy, M. G., Shehab, W., & Abdellattif, M. H. Synthesis and Antioxidant Activity of Some Novel a Zino and Pyranopyrazole Derivative, 2020.
8. Derabli, C., Boualia, I., Abdelwahab, A. B., Boulcina, R., Bensouici, C., Kirsch, G., & Debache, A. A cascade synthesis, in vitro cholinesterases inhibitory activity and docking studies of novel Tacrine-pyranopyrazole derivatives. *Bioorganic & medicinal chemistry letters*, 2018; *28*(14): 2481-2484.

9. Kumar, A., Lohan, P., Aneja, D. K., Gupta, G. K., Kaushik, D., & Prakash, O. Design, synthesis, computational and biological evaluation of some new hydrazino derivatives of DHA and pyranopyrazoles. *European journal of medicinal chemistry*, 2012; *50:* 81-89.
10. Mamaghani, M., Nia, R. H., Shirini, F., Tabatabaeian, K., & Rassa, M. An efficient and eco-friendly synthesis and evaluation of antibactrial activity of pyrano [2, 3-c] pyrazole derivatives. *Medicinal Chemistry Research*, 2015; *24*(5): 1916-1926.
11. Emami, L., Zamani, L., Sabet, R., Zomorodian, K., Rezaei, Z., Faghih, Z., ... & Khabnadideh, S. Molecular Docking and Antimicrobial Evaluation of Some Novel Pyrano [2, 3-C] Pyrazole Derivatives. *Trends in Pharmaceutical Sciences*, 2020; *6*(2): 113-120.
12. Kassem, E. M., El-Sawy, E. R., Abd-Alla, H. I., Mandour, A. H., Abdel-Mogeed, D., & El-Safty, M. M. Synthesis of certain new fused pyranopyrazole and pyranoimidazole incorporated into 8-hydroxyquinoline through a sulfonyl bridge at position 5 with evaluation of their in-vitro antimicrobial and antiviral activities. *Egyptian Pharmaceutical Journal*, 2012; *11*(2): 116.
13. Tang, M., Zhang, W., & Kong, Y. DABCO-promoted synthesis of pyrazoles from tosylhydrazones and nitroalkenes. *Organic & biomolecular chemistry*, 2013; *11*(37): 6250-6254.
14. Zhang, H., Wei, Q., Zhu, G., Qu, J., & Wang, B. A facile and expeditious approach to substituted 1H-pyrazoles catalyzed by iodine. *Tetrahedron Letters*, 2016; *57*(24): 2633-2637.
15. Polshettiwar, V., & Varma, R. S. Greener and rapid access to bio-active heterocycles: room temperature synthesis of pyrazoles and diazepines in aqueous medium. *Tetrahedron Letters*, 2008; *49*(2): 397-400.
16. Nikpassand, M., Mamaghani, M., Tabatabaeian, K., & Abiazi, M. K. KSF: an efficient catalyst for the regioselective synthesis of 1, 5-diaryl pyrazoles using Baylis–Hillman adducts. *Molecular diversity*, 2009; *13*(3): 389-393.
17. Yuan, B., Zhang, F., Li, Z., Yang, S., & Yan, R. AgNO2 as the NO Source for the Synthesis of Substituted Pyrazole N-Oxides from N-Propargylamines. *Organic letters*, 2016; *18*(22): 5928-5931.
18. Pal, G., Paul, S., Ghosh, P. P., & Das, A. R. PhIO promoted synthesis of nitrile imines and nitrile oxides within a micellar core in aqueous media: a regiocontrolled approach to synthesizing densely functionalized pyrazole and isoxazoline derivatives. *RSC Advances*, 2014; *4*(16): 8300-8307.

19. Zolfigol, M. A., Afsharnadery, F., Baghery, S., Salehzadeh, S., & Maleki, F. Catalytic applications of {[HMIM] C (NO 2) 3}: as a nano ionic liquid for the synthesis of pyrazole derivatives under green conditions and a mechanistic investigation with a new approach. *RSC advances*, 2015; *5*(92): 75555-75568.
20. Bora, P. P., Bihani, M., & Bez, G. Multicomponent synthesis of dihydropyrano [2, 3-c] pyrazoles catalyzed by lipase from Aspergillus niger. *Journal of Molecular Catalysis B: Enzymatic*, 2013; *92:* 24-33.
21. Shabalala, N. G., Pagadala, R., & Jonnalagadda, S. B. Ultrasonic-accelerated rapid protocol for the improved synthesis of pyrazoles. *Ultrasonics sonochemistry*, 2015; *27:* 423-429.
22. Polshettiwar, V., & Varma, R. S. Nano-organocatalyst: magnetically retrievable ferrite-anchored glutathione for microwave-assisted Paal–Knorr reaction, aza-Michael addition, and pyrazole synthesis. *Tetrahedron*, 2010; *66*(5): 1091-1097.
23. Shelke, S. N., Bankar, S. R., Mhaske, G. R., Kadam, S. S., Murade, D. K., Bhorkade, S. B., ... & Gawande, M. B. Iron oxide-supported copper oxide nanoparticles (nanocat-Fe-CuO): magnetically recyclable catalysts for the synthesis of pyrazole derivatives, 4-methoxyaniline, and ullmann-type condensation reactions. *ACS Sustainable Chemistry & Engineering*, 2014; *2*(7): 1699-1706.
24. Tekale, S. U., Kauthale, S. S., Jadhav, K. M., & Pawar, R. P. Nano-ZnO catalyzed green and efficient one-pot four-component synthesis of pyranopyrazoles. *Journal of Chemistry*, 2013.
25. Sonar, J. P., Pardeshi, S. D., Dokhe, S. A., Bhavar, G. M., Tekale, S. U., Zine, A. M., & Thore, S. N. One Pot Synthesis of Pyranopyrazoles Using Sodium Lactate as an Efficient Catalyst. *European Chemical Bulletin*, 2019; *8*(6): 207-211.
26. Reddy, M. M., Jayashankara, V. P., & Pasha, M. A. Glycine-catalyzed efficient synthesis of pyranopyrazoles via one-pot multicomponent reaction. *Synthetic Communications®*, 2010; *40*(19): 2930-2934.
27. Kiyani, H., Samimi, H., Ghorbani, F., & Esmaieli, S. One-pot, four-component synthesis of pyrano [2, 3-c] pyrazoles catalyzed by sodium benzoate in aqueous medium. *Current Chemistry Letters*, 2013; *2*(4): 197-206.
28. Wu, M., Feng, Q., Wan, D., & Ma, J. CTACl as catalyst for four-component, one-pot synthesis of pyranopyrazole derivatives in aqueous medium. *Synthetic Communications*, 2013; *43*(12): 1721-1726.

29. Safaei-Ghomi, J., Ziarati, A., & Tamimi, M. A Novel Method for the One-pot Five-component Synthesis Highly Functionalized Pyranopyrazoles Catalyzed by CuI Nanoparticles. *Acta Chimica Slovenica*, 2013; *60*(2): 403-410.
30. Jayant, P. S., Sandeep, D. P., Shrikant, A. D., Ashok, M. Z., & Rajendra, P. P. An Efficient Protocol for the One Pot Synthesis of Pyranopyrazoles in Aqueous Medium using Triethanolamine as a Catalyst. Arc Org Inorg Chem Sci., 2018; 3(1): *AOICS. MS. ID*, *155*.
31. Waghmare, A. S., & Pandit, S. S. DABCO catalyzed rapid one-pot synthesis of 1, 4-dihydropyrano [2, 3-c] pyrazole derivatives in aqueous media. *Journal of Saudi Chemical Society*, 2017; *21*(3): 286-290.
32. Khairnar, B. J., Mane, D. V., & Chaudhari, B. R. Heterogeneous PS-DABCO Catalyzed One pot four-Component Synthesis of Pyranopyrazole. *Journal of Applicable Chemistry*, 2019; *8*(1): 425-434.
33. Ghodke, S. S., Tekale, S. U., Pathrikar, R. D., Khandare, P. M., Kótai, L., & Pawar, R. P. One-pot synthesis of pyrano [2, 3-c] pyrazoles using lemon peel powder as a green and natural catalyst. *European Chemical Bulletin*, 2020; *9*(1): 38-42.
34. Konakanchi, R., Gondru, R., Nishtala, V. B., & Kotha, L. R. NaF-catalyzed efficient one-pot synthesis of dihydropyrano [2, 3-c] pyrazoles under ultrasonic irradiation via MCR approach. *Synthetic Communications*, 2018; *48*(15): 1994-2001.
35. Laroum, R., Boureghda, C., Benhadid, A., Boulcina, R., & Debache, A. Study of the Catalytic Effect of Sodium Citrate on the Four-Component Synthesis of Pyrano [2, 3-c] pyrazole Derivatives: An Eco-Friendly Method. *Indian Journal of Heterocyclic Chemistry*, 2017; *27*(03): 295-302.
36. Khandebharad, A., Sarda, S., Soni, M., & Agrawal, B. Sodium gluconate: An efficient organocatalyst for the synthesis of dihydropyrano [2, 3-c] pyrazole derivatives. *Bulletin of the Chemical Society of Ethiopia*, 2019; *33*(2): 331-340.
37. Khandare, P. M., Ingale, R. D., Taware, A. S., Shisodia, S. U., Pawar, S. S., & Kotai, L., 2017.
38. One pot synthesis and biological evaluation of pyranopyrazoles in aqueous medium. *European Chemical Bulletin*, *6*(9): 410-414.
39. Babaie, M., & Sheibani, H. Nanosized magnesium oxide as a highly effective heterogeneous base catalyst for the rapid synthesis of pyranopyrazoles via a tandem four-component reaction. *Arabian Journal of Chemistry*, 2011; *4*(2): 159-162.

40. Gadkari, Y. U., Hatvate, N. T., & Telvekar, V. N. Concentrated solar radiation-assisted one-pot/multicomponent synthesis of pyranopyrazole derivatives under neat condition. *Research on Chemical Intermediates*, 2021; *47*(10): 4245-4255.
41. Dadaei, M., & Naeimi, H. An Environment-Friendly Method for Green Synthesis of Pyranopyrazole Derivatives Catalyzed by CoCuFe2O4 Magnetic Nanocrystals under Solvent-Free Conditions. *Polycyclic Aromatic Compounds*, 2020; 1-14.
42. Ali, M. A. E. A. A. Synthesis of pyranopyrazoles using magnetic Fe3O4 nanoparticles as efficient and reusable catalyst. *Tetrahedron*, 2014; *70*(18): 2971-2975.
43. Ambethkar, S., Padmini, V., & Bhuvanesh, N. A green and efficient protocol for the synthesis of dihydropyrano [2, 3-c] pyrazole derivatives via a one-pot, four component reaction by grinding method. *Journal of advanced research*, 2015; *6*(6): 975-985.
44. Reddy, M. B., & Pasha, M. A. One-pot, multicomponent synthesis of 4H-pyrano [2, 3-c] pyrazoles in water at 25℃., 2012.
45. Albadi, J., & Mansournezhad, A. Poly (4-vinylpyridine) efficiently catalyzed one-pot four-component synthesis of pyrano [2, 3-c] pyrazoles. *Current Chemistry Letters*, 2014; *3*(4): 221-227.
46. Bora, P. P., Bihani, M., & Bez, G. Multicomponent synthesis of dihydropyrano [2, 3-c] pyrazoles catalyzed by lipase from *Aspergillus niger*. *Journal of Molecular Catalysis B: Enzymatic*, 2013; *92:* 24-33.
47. Zhou, C. F., Li, J. J., & Su, W. K. Morpholine triflate promoted one-pot, four-component synthesis of dihydropyrano [2, 3-c] pyrazoles. *Chinese Chemical Letters*, 2016; *27*(11): 1686-1690.
48. Nasab, M. J., Kiasat, A. R., & Zarasvandi, R. β-Cyclodextrin nanosponge polymer: a basic and eco-friendly heterogeneous catalyst for the one-pot four-component synthesis of pyranopyrazole derivatives under solvent-free conditions. *Reaction Kinetics, Mechanisms and Catalysis*, 2018; *124*(2): 767-778.
49. Reddy, G. M., & Raul Garcia, J. Synthesis of Pyranopyrazoles under Eco-friendly Approach by Using Acid Catalysis. *Journal of Heterocyclic Chemistry*, 2017; *54*(1): 89-94.