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Recent advances in heterogeneous catalysts for the green synthesis of pyrazole and pyrano pyrazole derivatives

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Abstract
Pyrazole and pyranopyrazole derivatives represent an important class of nitrogen-containing heterocyclic compounds which display diverse biological and pharmaceutical activities such as antimicrobial, anti-inflammatory, anticancer, antiviral and antioxidant properties. The development of sustainable and environmentally benign synthetic methodologies for these compounds has been the focus of considerable attention in recent years. Heterogeneous catalysts, especially magnetic nanocatalysts and functionalised metal oxide nanomaterials, have been shown to be efficient alternatives to traditional homogeneous catalysts owing to their high catalytic activity, easy separation, reusability, thermal stability, and low environmental impact. This review summarises recent advances in the heterogeneous catalysis synthesis of pyrazole and pyranopyrazole derivatives through one-pot multicomponent reactions under green reaction conditions. A critical review of various catalyst systems like Fe_3O_4-based magnetic nanoparticles, silica supported catalysts, carbon nanotube supported catalysts, graphene oxide composites, biopolymer supported nanocatalysts and metal oxide nanomaterials are performed with respect to their synthesis, catalytic performance, reaction conditions, substrate scope, product yields and recyclability. Special emphasis is placed on solvent-free protocols, aqueous media, mild reaction conditions, fast reaction rates and catalyst reusability, all of which contribute to greener and more sustainable synthetic processes.

Keywords: Nanocatalyst, heterocyclic compound, green chemistry

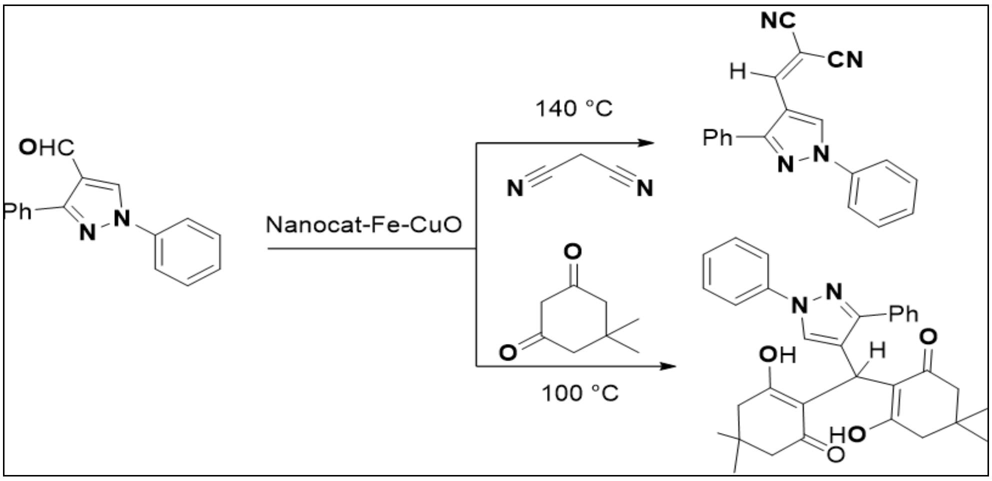
Introduction

Heterogeneous catalysis has become a prominent field of research in recent years, driven by the unique properties of catalyst materials and their wide-ranging applications in various industrial processes. Several desirable features, including high thermal stability, diverse structural configurations, ease of modification, elevated absorption capacities, and low toxicity characterize the materials used in heterogeneous catalysts. These attributes enable the development of efficient, durable, and environmentally friendly catalytic systems. Continued advancements in material design and understanding of catalytic mechanisms are expanding the potential uses of heterogeneous catalysts, contributing significantly to areas such as energy production, environmental protection, and chemical manufacturing [1-4]. Compared with homogeneous catalysts, heterogeneous catalysts offer several advantages, including ease of separation and recovery via simple filtration. This property makes them highly attractive for energy-related applications such as biodiesel production [5-11], where they can be reused multiple times, reducing production costs. Furthermore, heterogeneous catalysts have proven to be highly effective in dye removal [12] and biomass conversion [13, 14], where they play a crucial role in improving process efficiency. The structural diversity and adaptability of heterogeneous catalysts allow for their customization to suit a wide range of applications and operating conditions, which makes them highly valuable for industrial processes. A variety of polymer supports, differing in composition, properties, size, and features, have demonstrated effectiveness either as catalysts themselves or as supporting materials for catalysts. Additionally, numerous bioactive heterocyclic compounds have been synthesized using polymers derived from various sources, including organic, inorganic, and hybrid origins [15]. Moreover, modern catalysts come in various morphological forms, such as nanoparticles, nanocomposites, nanosheets, and nanotubes, which have shown great effectiveness. The structural diversity and flexibility of heterogeneous catalysts enable their customization for diverse applications and operating conditions, making them highly valuable in industrial processes. A wide range of polymer supports varying in composition, properties, size, and features have proven effective either as catalysts themselves or as supporting materials for catalysts. Additionally, many bioactive heterocyclic compounds have been synthesized using polymers derived from various sources, including organic, inorganic, and hybrid origins nanocatalysts [16].

Researchers have long faced challenges in developing composites and non-toxic materials that can selectively anchor, remain catalytically active, and be recycled. Consequently, many scientists have focused on overcoming the technical hurdles in creating solid-supported, functionalized metal oxides as effective catalysts. Over the past two decades, metal oxides have gained popularity in synthetic chemistry because of their diverse surface-active sites, which include metal cations, oxyanions, and hydroxyl groups. These sites enable metal oxides to interact with reactants and promote catalytic reactions.

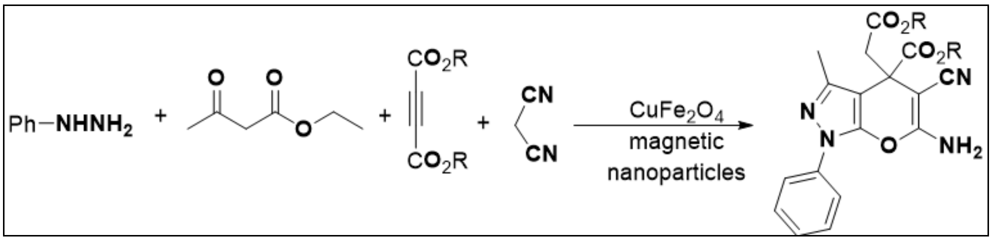
The synthesis of important heterocyclic compounds with pharmacological applications has been a key research area, utilizing various catalysts supported on different solid materials. Common heterocycles include five- and six-membered rings that incorporate heteroatoms like nitrogen, sulfur, or oxygen. Heterogeneous catalysts are essential in producing these compounds, particularly pyrazole, which is prevalent in pharmaceuticals. pyrazole features a five-membered ring with two nitrogen atoms, and its production has been widely studied using nanoparticle-based heterogeneous catalysts.

In 2014, Shelke *et al*. reported on the synthesis of pyrazole derivatives using magnetite-supported copper nanoparticles, specifically nanocat-Fe-CuO, under moderate reaction conditions. This process is illustrated in Scheme 1.1. The study emphasizes that nanocatalysts present a promising alternative to traditional catalytic methods, offering several notable advantages. One of the key benefits of nanocatalysts is their magnetic property, which allows for easy separation from reaction mixtures using an external magnet. This magnetic separability makes recovery and reuse straightforward, enhancing the overall efficiency of the catalytic process. In their experiments, the nanocatalyst could be effectively recovered from the reaction mixture simply by applying a magnetic field, thereby significantly simplifying the separation process. Moreover, the nanocatalyst maintained its catalytic activity after multiple cycles of reuse, demonstrating its high stability and durability throughout repeated applications, which is critical for practical and sustainable catalytic processes [17].



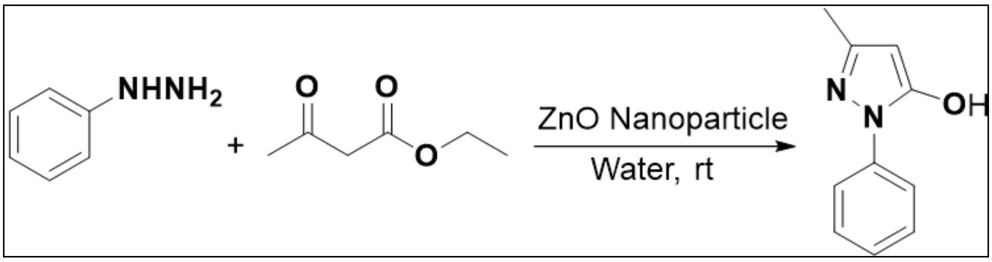
Scheme 1.1

Pradhan *et al*. employed CuFe2O4 magnetic nanoparticles as an efficient catalyst for the one-pot, multi-component synthesis of dihydropyrano[2,3-c] pyrazole scaffolds. This method utilizes ethyl acetoacetate, hydrazine, cyanoacetonitrile, and dialkyl acetylenedicarboxylates at moderate temperatures, yielding a high proportion of the desired products (Scheme 1.2). An important feature of this catalytic system is its remarkable reusability and recyclability, maintaining its catalytic activity over multiple cycles. This innovative approach offers a practical, economical, and environmentally friendly strategy for large-scale production of dihydropyrano[2,3-c] pyrazole frameworks, which serve as essential building blocks in various fields of organic synthesis and pharmaceutical development [18].



Scheme 1.2

Girish *et al*. conducted a study in which they employed nano zinc oxide (ZnO) as a catalyst to synthesize the pyrazole moiety. This synthesis was achieved through a condensation reaction between 1,3-diketone and phenylhydrazines conducted at ambient temperature, as detailed in Scheme 1.3. The method proved to have several significant advantages: it yielded high product quantities, involved a rapid reaction process, and featured an uncomplicated workup procedure, making it practical for laboratory applications. Additionally, the researchers found that the nano ZnO catalyst exhibited excellent reusability, maintaining consistent catalytic activity even after multiple cycles of use. These findings suggest that nano ZnO not only serves as an effective and efficient catalyst for the large-scale production of pyrazole derivatives but also offers considerable benefits in terms of cost-effectiveness and environmental sustainability. Its reusability and eco-friendly nature make it a promising candidate for sustainable chemical manufacturing processes involving pyrazole synthesis [19].



Scheme 1.3

Paul and colleagues employed an innovative approach for the one-pot multi-component synthesis of substituted pyrano[2,3-c] pyrazole derivatives, as illustrated in Scheme 1.4, Method 1. Their methodology involved using an uncapped SnO2 quantum dots (QDs) as a catalyst within an aqueous solvent system. The researchers designed this process to utilize a minimal amount of catalyst, which contained phenylhydrazine, ethyl acetylacetate, benzaldehyde, and dicyanomethane as key reactants. The nanocatalyst used in this study proved to be highly effective, demonstrating excellent catalytic activity that facilitated the synthesis of the desired products in high yields. Furthermore, the catalyst could be easily recovered from the reaction mixture after completion and was capable of being reused multiple times without any significant loss in its catalytic performance, underscoring its potential for sustainable and cost-effective applications [20].

In 2015, Moeinpour and colleagues reported the synthesis of pyrano pyrazole derivatives using cesium carbonate attached to hydroxyapatite-coated Ni0.5Zn0.5Fe2O4 magnetic nanoparticles (Ni0.5Zn0.5Fe2O4@Hap-Cs2CO3). This reaction was performed at room temperature in a 1:1 ethanol/water mixture, employing phenylhydrazine, ethyl acetylacetate, aryl aldehyde, and dicyanomethane (Scheme 1.4, Method 2). The nanocatalyst Ni0.5Zn0.5Fe2O4@Hap-Cs2CO3 exhibited outstanding catalytic efficiency, magnetic separability, and reusability without loss of activity. This approach underscores the promise of cesium carbonate bound to magnetic nanoparticles as a versatile tool for the efficient synthesis of complex organic compounds [21].

Saha and colleagues reported the synthesis of a biologically active compound featuring a pyrano[2,3-c] pyrazole moiety (Scheme 1.4, Method 3) via a multi-component, one-pot reaction. This procedure was conducted at ambient temperature, employing ZrO2 nanoparticles as a catalyst, with ethyl acetoacetate, hydrazine monohydrate, benzaldehyde, and dicyanomethane as starting materials. The reaction proceeded rapidly and achieved high yield. Furthermore, the catalytic activity of the ZrO2 nanoparticles remained stable after extended use, demonstrating their robustness [22].

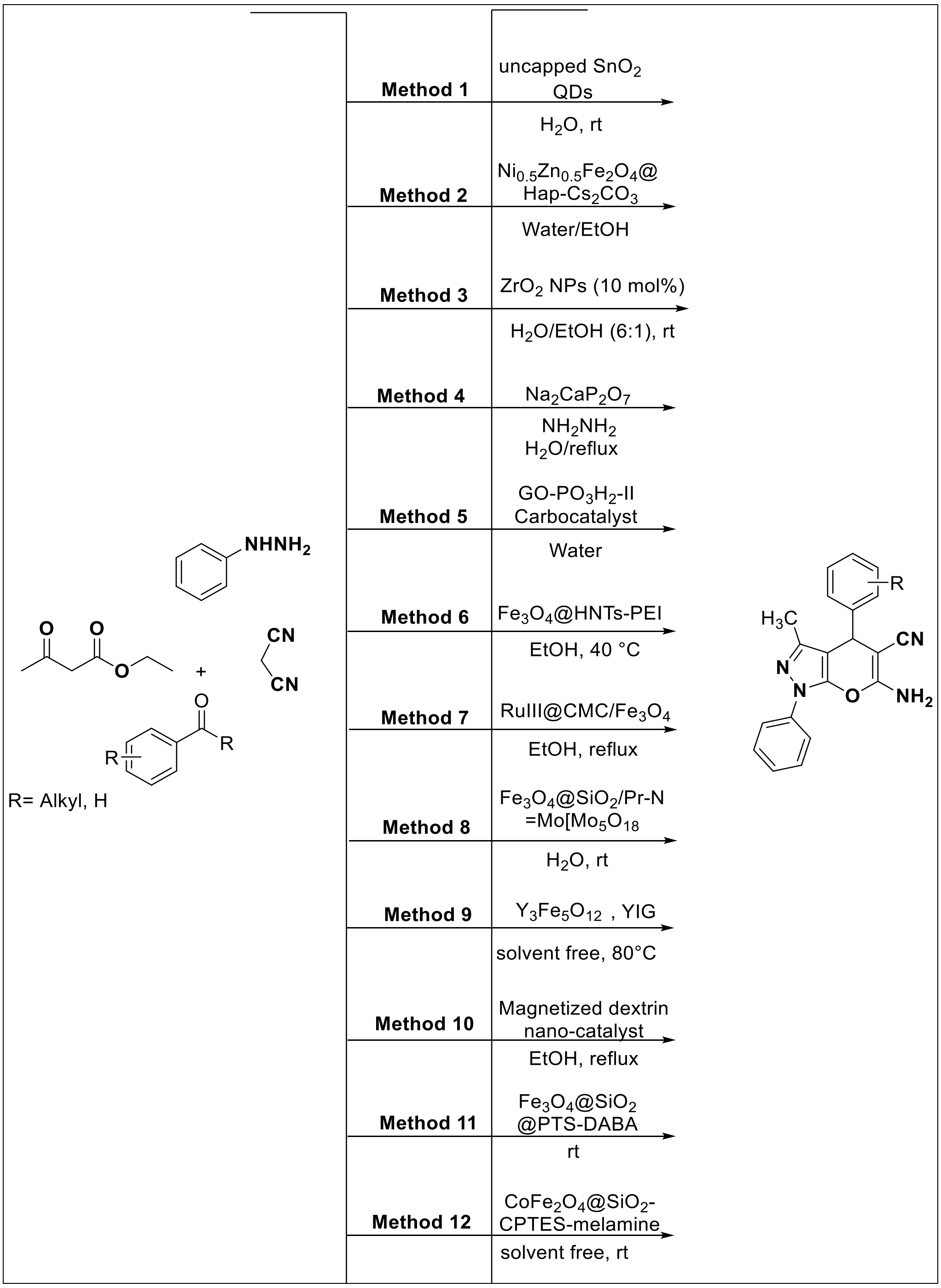
Maleki *et al.* reported the synthesis of nano-structured diphosphate (Na2CaP2O7) and its utilization as a catalyst in the synthesis of pyrano[2,3-c] pyrazole derivatives via a multi-component reaction (Scheme 1.4, Method 4). The reaction was conducted in an aqueous medium employing aldehyde, dicyanomethane, hydrazine hydrate, and ethyl acetylacetate as starting materials. The nano-structured diphosphate catalyst demonstrated several advantageous properties, including reusability, operational simplicity, high catalytic efficiency, and environmental compatibility. The catalyst could be readily recovered and reused without a significant decline in activity. Moreover, the recovered catalyst maintained consistent catalytic performance over multiple cycles, underscoring its robustness and stability [23].

In 2017, Zakeri *et al.* synthesized a carbon-based phosphonic acid-functionalized carbo-catalyst for the production of pyrazole derivatives via a multi-component reaction (Scheme 1.4 Method 5). This process employed aqueous media and involved aryl aldehydes, dicyanomethane, ethyl acetylacetate, and hydrazine monohydrate as reactants. The nano-catalyst demonstrated several advantageous characteristics, including straightforward preparation, high catalytic efficiency, excellent yields, and reusability without performance degradation over multiple cycles. The utilization of water as the solvent further contributed to the environmentally friendly nature of the methodology [24].

Hajizadeh *et al.* synthesized a natural, clay-based green magnetic nano-catalyst, Fe_3O_4@HNTs-PEI, for the synthesis of pyrano pyrazole derivatives via a multi-component reaction (Scheme 1.4 Method 6). The catalyst facilitated the reaction of ethyl acetoacetate, hydrazine monohydrate, aryl aldehyde, and dicyanomethane in an environmentally friendly solvent. The nano-catalyst was efficiently recovered from the reaction mixture using an external magnet and demonstrated recyclability for at least eight consecutive cycles without significant loss of catalytic activity [25].

Chen *et al.* developed a new nanocatalyst, RuIII@CMC/Fe_3O_4, for the efficient synthesis of pyrano pyrazole scaffolds via a multi-component reaction (Scheme 1.4 Method 7). The reaction was carried out using ethyl acetoacetate, hydrazine, dicyanomethane, and various carbonyl compounds, and it showed excellent yields with high purity of the products. Additionally, the reaction conditions are mild, and the energy consumption is low, making it an eco-friendly and sustainable approach. The RuIII@CMC/Fe_3O_4 nano-catalyst exhibited excellent catalytic activity, and the products could be easily isolated due to their magnetic properties. Furthermore, the nano-catalyst could be quickly recovered and reused for multiple cycles without losing its catalytic activity, making it a cost-effective and efficient approach for large-scale synthesis [26].

A novel core-shell structured propylamine/molybdate complex supported on magnetic silica, Fe_3O_4@SiO_2/Pr-N=Mo [Mo_5O_{18}], was synthesized and employed as a catalyst for the synthesis of pyrano- pyrazole derivatives through a multi-component reaction (Scheme 1.4 Method 8). The reaction involved aryl aldehyde, 1,3-dicarbonyl compound, hydrazine monohydrate, and dicyanomethane under mild conditions. The nano-catalyst demonstrated high efficiency and excellent selectivity, yielding superior results. These findings underscore the potential of this innovative nano-catalyst as an effective and sustainable option for pyrano- pyrazole synthesis [27].



Scheme 1.4

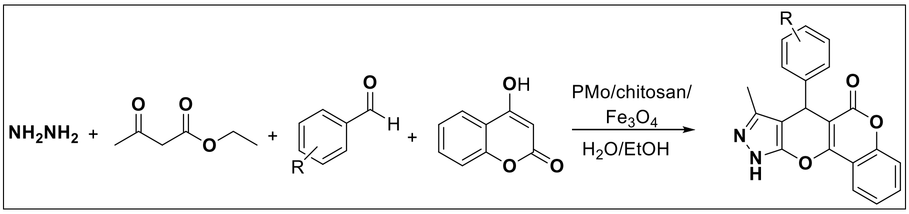
Sedighinia *et al*. described a solvent-free synthesis of pyrano[2,3-c] pyrazole scaffolds utilizing a superparamagnetic yttrium iron garnet (YIG) nano-catalyst in a one-pot procedure. The reaction involved aryl aldehyde, dicyanomethane, ethyl acetoacetate, and hydrazine (Scheme 1.4 Method 9). This protocol offers several advantages, including the elimination of organic solvents, a clean reaction profile, facile catalyst recovery, reduced reaction times, high product yields, and catalyst recyclability. The employment of a superparamagnetic YIG nano-catalyst facilitates straightforward separation through an external magnetic field. The YIG nano-catalyst demonstrated excellent catalytic performance and could be reused multiple times with minimal activity loss. The solvent-free conditions and catalyst reusability render this method an environmentally friendly and sustainable strategy for synthesizing pyrano[2,3-c] pyrazoles [28].

The eco-friendly biopolymer-based magnetized dextrin nano-catalyst was synthesized and employed in the multi-component synthesis of dihydropyrano[2,3-c] pyrazole frameworks through a reaction involving hydrazine monohydrate, ethyl acetoacetate, aryl aldehydes, and dicyanomethane (Scheme 1.4 Method 10). This innovative methodology offers several advantages, including the use of a biocompatible nano-catalyst, simplicity of the procedure, rapid reaction kinetics, and the capacity for catalyst reuse over four consecutive cycles without any significant loss of catalytic activity [29].

Karami *et al*. reported the development of a novel nanocatalyst, $Fe_3O_4@SiO_2$@PTS-DABA, designed for the environmentally friendly synthesis of pyrano pyrazole frameworks under mild reaction conditions. This nanocatalyst features a core-shell magnetic silica structure functionalized with 3,4-diaminobenzoic acid. Its synthesis involves the reaction of hydrazine monohydrate, 1,3-diketones, aldehydes, and dicyanomethane in the presence of the nanocatalyst (Scheme 1.4, Method 11). Conducted at moderate temperatures, this method yields higher product quantities compared to conventional approaches. The catalyst exhibits notable advantages, including low toxicity, thermal stability, cost-effectiveness, and high catalytic efficiency. Additionally, it maintains its activity over multiple cycles without significant performance decline [30].

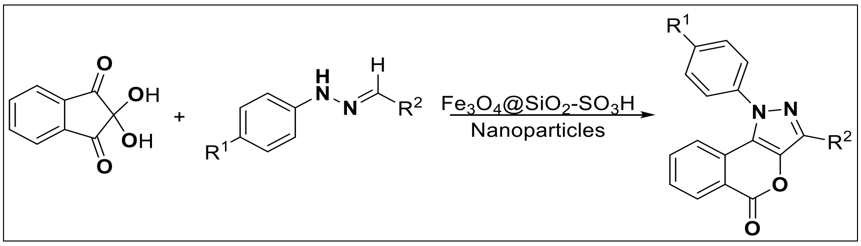
Dadai and colleagues devloped an eco-friendly and effective approach for synthesizing dihydropyrano[2,3-c] pyrazoles by utilizing a heterogeneous nano-catalyst composed of melamine-containing cobalt ferrite silica-supported nanoparticles ($CoFe_2O4@SiO_2$-CPTES-melamine). The process was conducted under mild conditions, involving 1,3-diketone, benzaldehyde, hydrazine hydrate, and dicyanomethane, achieving excellent yields (Scheme 1.4 Method 12). The employed nano-catalyst demonstrated notable efficiency, ease of use, and non-toxicity, requiring only a minimal amount to produce high yields within short reaction times. Its reusability was also verified, indicating its potential as a valuable tool in the synthesis of complex molecules [31].

In 2016, Ayati and colleagues introduced a novel one-pot multi-component synthetic method for constructing pyrano-pyrazole frameworks (Scheme 1.5). The process employed four distinct reactants: ethyl acetylacetate, hydrazine monohydrate, 4-hydroxycoumarin, and an aryl aldehyde. The reaction was catalyzed by a unique nanomagnetic composite heteropolyacid immobilized on chitosan/Fe_3O_4, serving as a nanocatalyst. This immobilized nanocatalyst offered several advantages over conventional catalysts, including ease of recovery and reuse, thereby enhancing the process's environmental sustainability. Moreover, it improved reaction yields and selectivity, demonstrating its effectiveness in promoting the multi-component transformation [32].



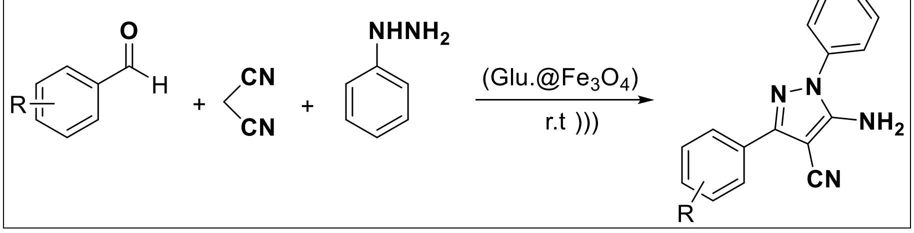
Scheme 1.5

In 2016, Mukherjee *et al*. introduced an innovative synthetic method for producing pyrazole-fused isocoumarins utilizing $Fe_3O_4@SiO_2-SO_3H$ nanoparticles as a nanocatalyst (Scheme 1.6). The procedure involved the reaction between ninhydrin and aryl hydrazones in a solvent-free environment. The employment of $Fe_3O_4@SiO_2-SO_3H$ nanoparticles conferred multiple advantages over conventional catalysts. Notably, the nanocatalyst demonstrated high thermal stability, rendering it suitable for high-temperature reactions. Additionally, its facile recovery and recyclability contributed to decreased waste production and enhanced environmental sustainability. [33]

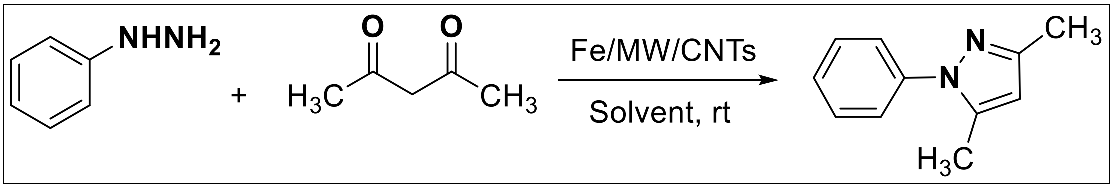


Scheme 1.6

In 2017, Esfandiary and colleagues introduced a novel synthetic method for constructing the pyrazole moiety utilizing a heterogeneous superparamagnetic glucose-coated catalyst (Glu.@Fe_3O_4). The procedure involved combining dicyanomethane, an aldehyde, and phenylhydrazine in the presence of the Glu.@Fe_3O_4 catalyst (Scheme 1.7). This catalyst demonstrated several benefits over conventional options, including high catalytic efficiency, which resulted in enhanced yields and selectivity. Its relatively low cost further favored large-scale applications. Additionally, the catalyst was environmentally benign and user-friendly, thereby minimizing exposure to toxic or hazardous substances [34].



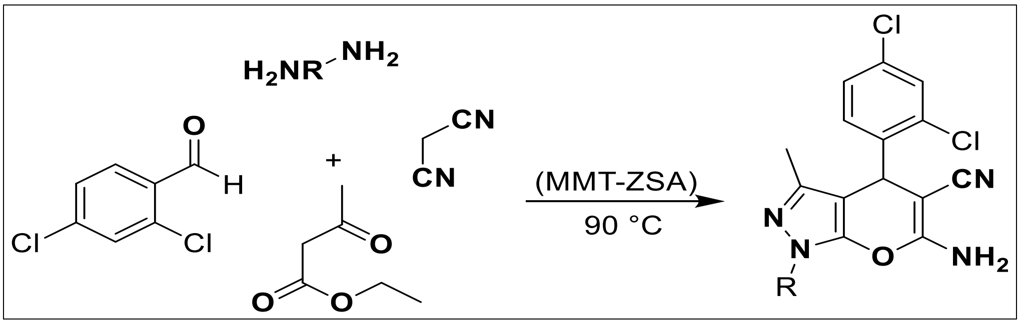
Scheme 1.7



Scheme 1.8

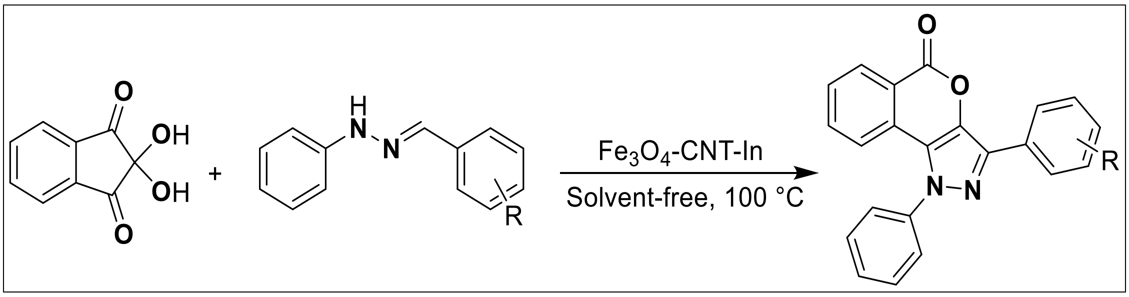
Safari *et al*. employed a nano-catalyst comprising zwitterionic sulfamic acid-functionalized nano clay (MMT-ZSA) to synthesize dihydropyrano[2,3-c] pyrazoles through a multi-component reaction involving hydrazine hydrate, dicyanomethane, β-keto ester, and carbonyl compounds under solvent-free conditions. This methodology yielded excellent results, characterized by high efficiency, rapid reaction times, and heterogenous conditions. It also offered the advantages of milder reaction parameters, minimal workup and purification requirements, and catalyst reusability. Furthermore, this strategy reduces the use of toxic reagents and solvents, presenting a more environmentally sustainable alternative to traditional approaches [36].

Sharghi and colleagues investigated the application of iron-doped multi-walled carbon nanotubes (Fe/MWCNTs) as a highly efficient and environmentally benign heterogeneous nanocatalyst for the one-pot synthesis of pyrazole scaffolds. This process achieved good to excellent yields at room temperature through the condensation of 1,3-diketones with hydrazine (see Scheme 1.8). The method offers several advantages, including mild and eco-friendly reaction conditions, rapid reaction times, clean reaction profiles, straightforward operation, simple purification procedures, and high product yields facilitated by the reusable heterogeneous catalyst. Furthermore, the catalyst retained its catalytic activity over ten consecutive cycles [35].



Scheme 1.9

In this study, an indium nano-catalyst supported on magnetic carbon nanotube (Fe_3O_4-CNT-In) was prepared and employed for the synthesis of chromeno[4,3-c] pyrazole-5(1H)-one scaffold (Scheme 1.10). The reaction was carried out under solvent-free conditions, using aryl hydrazones and ninhydrin as starting materials. The synthesis of chromeno[4,3-c] pyrazole-5(1H)-one scaffold using the Fe_3O_4-CNT-In catalyst is a highly efficient process, with several advantages over traditional methods. One of the most significant benefits is the environmentally friendly nature of the reaction, which eliminates the use of hazardous solvents and reduces the generation of waste. This is a crucial factor in achieving sustainable and eco-friendly synthetic processes [37].



Scheme 1.10

Amirnejat *et al*. synthesized a novel nanocatalyst, Fe3O4@Alg@CPTMS@Arg, and employed it in the single-pot synthesis of pyrazole derivatives using phenylhydrazine, dicyanomethane, and various aryl aldehydes in ethanol solvent (Scheme 1.11). The nanocatalyst exhibited remarkable catalytic efficiency, yielding high quantities of the pyrazole product. Additionally, the hybrid nanocatalyst demonstrated excellent recyclability, underscoring its potential for sustainable catalytic applications [38].

Sameri and colleagues have effectively synthesized derivatives of dihydropyrano[2,3-c] pyrazoles employing a core/shell CaO@SiO_2-SO_3H nano-catalyst within a one-pot multi-component reaction. This process involved the use of benzaldehyde, malononitrile, and 3-methyl-1-phenyl-2-pyrazolin-5-one under ambient conditions (refer to Scheme 1.12, Method 1). The CaO@SiO_2-SO_3H nano-catalyst exhibited remarkable catalytic efficiency, yielding high quantities of the target derivatives. Its application facilitated straightforward workup procedures, reduced reaction durations, and eliminated the need for volatile or hazardous organic solvents, thereby aligning with principles of eco-friendliness and sustainability [39].

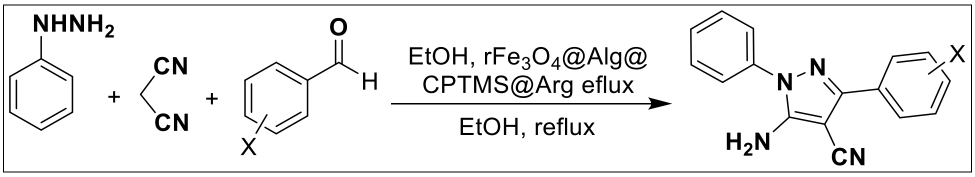
Zolfigol and colleagues utilized a nano-catalyst comprising an imidazole-based ionic liquid stabilized on silica-coated Fe3O4 magnetic nanoparticles [nano-Fe_3O_4@SiO_2@$(CH_2)_3$-Imidazole-SO_3H]Cl for the one-pot, three-component synthesis of dihydropyrano- pyrazole derivatives. The process involved the condensation of aldehydes, 3-methyl-1-phenyl-2-pyrazoline-5-one, and dicyanomethane under solvent-free conditions at ambient temperature (Scheme 1.12 Method 2). The employment of this nano-catalyst conferred several benefits, including high product yields, short reaction times, catalyst recyclability, straightforward workup procedures, and elimination of organic solvents, thereby presenting an environmentally sustainable approach for the synthesis of these compounds [40].

Azarifar and colleagues employed Fe_3-xTixO$_4$@SO_3H as a nano-catalyst in a one-pot, three-component synthesis of 1,4-dihydropyrano[2,3-c] pyrazoles. The process involved the condensation of dicyanomethane, aldehyde, and 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one under solvent-free conditions (Scheme 1.12 Method 3). The acidic nano-catalyst demonstrated excellent catalytic efficiency, with the added advantages of facile recovery and reuse without activity loss. This method yielded high product yields, short reaction times, and straightforward product separation, offering an effective approach for the synthesis of these compounds [41].

Azarifar *et al*. developed a one-pot synthesis process for pyrano pyrazole employing a nanocatalyst composed of titanomagnetite and an amino acid ionic liquid (Fe_3-xTixO$_4$@TMSP@TBAAsp). The reaction occurred in the presence of aldehyde, malononitrile, and 3-methyl-1-phenyl-1H-2-pyrazol-5(4H)-one under moderate conditions (Scheme 1.12 Method 4). The nanocatalyst exhibited notable catalytic efficiency, facilitating the formation of 1,4-dihydropyrano[2,3c] pyrazole derivatives. Additionally, the catalyst could be easily recovered and reused for at least six cycles without a significant decline in activity. This study underscores the potential of titanomagnetite-based nanocatalysts for the sustainable and efficient synthesis of valuable organic compounds [42].

Azarifar and colleagues introduced a novel methodology for synthesizing dihydropyran[3,2c] pyrazoles employing a nanocatalyst composed of γ-Fe_2O_3@Cu_3Al-LDH-TUD MNPs under mild, solvent-free conditions. This reaction involved aldehyde, dicyanomethane, and 4-hydroxycoumarin in a one-pot, multi-component system (Scheme 1.12, Method 5). The method provides several advantages, including high product yield, straightforward product isolation, and the elimination of hazardous organic solvents. Moreover, the catalyst exhibits versatility, can be easily separated via its magnetic properties, and can be reused across multiple cycles with minimal performance loss [43].

A novel magnetic nano-catalyst was synthesized through the immobilization of tungstic acid onto TiO_2-coated Fe_3O_4 nanoparticles grafted with 3-chloropropyl groups. This nano-catalyst facilitated the synthesis of pyrano[2,3-c] pyrazole derivatives via the reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one, dicyanomethane, and aryl aldehydes (Scheme 1.12, Method 6). The advantages of this nano-catalyst include its non-toxic nature, thermal stability, cost-effectiveness, and the capacity for rapid reuse and recovery without any loss in catalytic activity [44].



Scheme 1.11

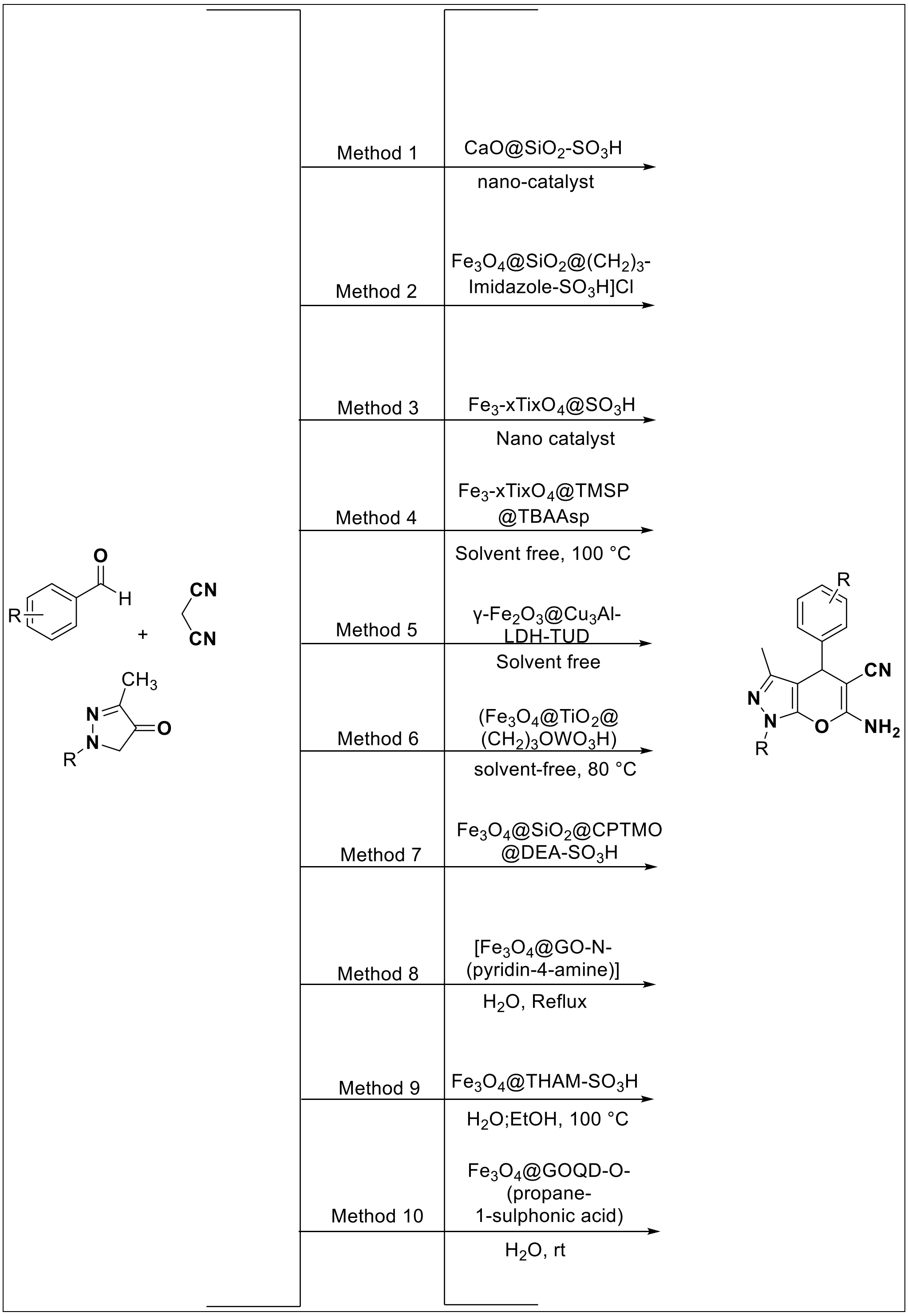
Eftekhari Far and colleagues employed a nano-bentonite (NB) Fe_3O_4@SiO_2@CPTMO@DEA-SO_3H nano-catalyst to synthesize dihydropyrano[2,3c] pyrazole scaffolds using dicyanomethane, 3-methyl-1-phenyl-5-pyrazolone, and aldehyde (Scheme 1.12 Method 7). The synthesis of the nano-catalyst was characterized by its efficiency, cost-effectiveness, and environmental compatibility, along with high magnetic properties. This method offers several advantages, including straightforward catalyst separation, reusability, high yield, and rapid reaction times [45].

Azarifar and colleagues establishing a one-pot, three-component synthesis of the dihydropyrano[2,3-c] pyrazole framework. This method employs a magnetic amine-functionalized graphene oxide nanocatalyst, specifically [Fe_3O_4@GO-N-(pyridin-4-amine)], alongside aldehyde, malononitrile, and 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one to produce the target compound (Scheme 1.12, Method 8). The strategy offers several advantages, including enhanced product yields, reduced reaction durations, the utilization of water as an eco-friendly solvent, and a streamlined workup process. Furthermore, the catalyst exhibits recyclability for up to six cycles without a decline in catalytic efficiency, thereby contributing to the overall sustainability of the process [46].

Niya and colleagues developed a novel approach for synthesizing the dihydropyrano[2,3-c] pyrazole core, employing sulphuric acid-functionalized Fe_3O_4 nanoparticles conjugated with tris(hydroxymethyl)aminomethane (THAM) as the catalytic agent (Scheme 1.12, Method 9). This technique is distinguished by its high catalytic efficiency and non-toxic profile. The reaction entails the coupling of aryl aldehyde, malononitrile, 1,3-diketone, and hydrazine monohydrate. The catalyst can be readily isolated from the reaction mixture via an external magnetic field, facilitating its reuse. The method's simplicity and effectiveness position it as a compelling alternative to conventional procedures [47].

Abbasabadi and colleagues presented a one-pot synthesis of dihydropyrano[2,3-c] pyrazole derivatives utilizing a catalyst composed of magnetized graphene oxide quantum dots functionalized with sulfonic acid-modified ferric oxide, conducted under moderate conditions (Scheme 1.12, Method 10). The reaction employed aryl aldehyde, dicyanomethane, and 3-methyl-1-phenyl-1H-pyrazol-5(4H)-

one as starting materials. This methodology offers several advantages over conventional approaches, including reduced reaction times, resulting in a shorter synthesis process. Furthermore, the process achieves high product yields, demonstrating its efficiency. Additionally, the reaction setup is straightforward and facile [46].



Scheme 1.12

Conclusion

Heterogeneous catalysts have transformed the synthesis of pyrazole and pyrano pyrazole derivatives offering eco-friendly, efficient and sustainable alternatives to the conventional homogeneous catalytic systems. Recent advances in magnetic nanocatalysts, metal oxide nanoparticles, carbon-based materials, silica supported catalysts and biopolymer-functionalized nanomaterials have been reported with significant improvements in the reaction efficiency, product selectivity and catalyst recyclability. These catalysts are preferred in one pot multicomponent reactions under mild or solvent free conditions leading to high yields of products, decreased reaction times, simplified work-up procedures and less waste generation. Their easy separation and reusability make the synthetic processes economically and environmentally viable. The surveyed literature has indicated that heterogeneous nanocatalysts have become essential tools in green organic synthesis, especially in the synthesis of biologically important pyrazole derivatives. Their excellent catalytic performance and their compliance with the principles of green chemistry make them highly attractive for both laboratory-scale and industrial applications. However, challenges such as large-scale catalyst production, long-term structural stability, catalyst deactivation, and cost-effective commercialisation need to be addressed.

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