

REVIEW ON MULTICOMPONENT SYNTHESIS OF 1H-PYRAZOLO[1,2-b]PHTHALAZINE-5,10-DIONE DERIVATIVES BY NANO CATALYSTS

Koyel Pradhan Department of Chemistry, Gobardanga Hindu College, North 24 Parganas, West Bengal, India; Tel: 91-9051581445 E-mail address: koyelchem@gmail.com

Abstract:

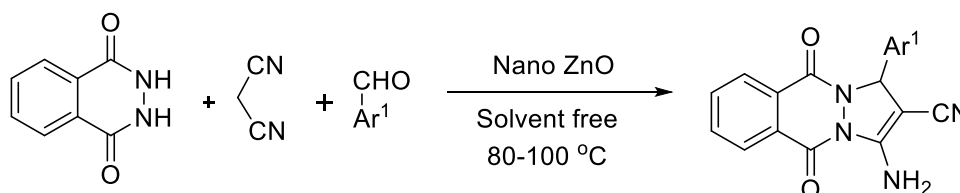
Both pyrazole and phthalazine core-containing compounds are of great biological importance. Use of solid catalysts means easier catalyst separation and recovery. Nano-catalysts mimic homogeneous as well as heterogeneous catalyst systems. This review focuses on the nano material catalyzed synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones derivatives by multicomponent reaction of basic building blocks.

Introduction:

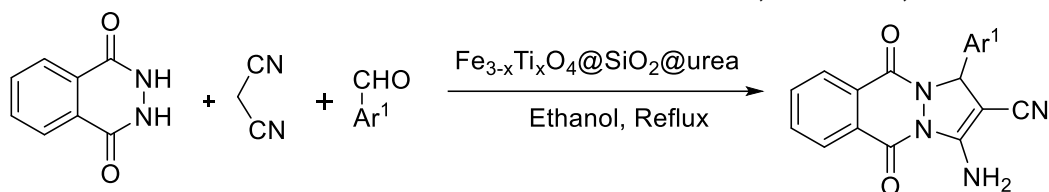
Nitrogen-containing heterocyclic compounds are employed as important skeletons in organic synthesis owing to their tremendous application in biologically active pharmaceuticals, agrochemicals, and functional materials [1-4]. Pyrazole core-containing compounds, including drugs such as celecoxib, viagra, pyrazofurine, and many others, possess a variety of biological activities [5-7]. Celecoxib occupies a unique position as a potent and GI-safe anti-inflammatory and analgesic agent. It is considered as a typical model of the diaryl heterocycles template that is known to inhibit the COX-2 enzyme selectively [8]. On the other hand, much attention has been focused toward pyrazoles as antimicrobial [9], antiviral [10], and anticancer [11, 12] agents after the discovery of the natural pyrazole C-glycoside pyrazofurin. This antibiotic was reported to possess a broad spectrum of antimicrobial and antiviral activities in addition to being active against several tumor cell lines [13]. Phthalazine derivatives exhibit properties such as anticonvulsant [14], cardiogenic [15], vasorelaxant [16], cytotoxic [17, 18], antihypoxic, antipyretic [19], antifungal [20], anticancer [21], and anti-inflammatory [22]. It was thought that molecules containing two active pharmacophores, pyrazole and phthalazine, would produce novel molecular templates that are likely to exhibit interesting biological properties. Quite a good number of methods have already been reported in the literature for the synthesis of pyrazolo[1,2-b]phthalazine derivatives. In this review article synthesis of pyrazolo[1,2-b]phthalazine derivatives catalyzed by nano materials are discussed.

Synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones by nano catalyst:

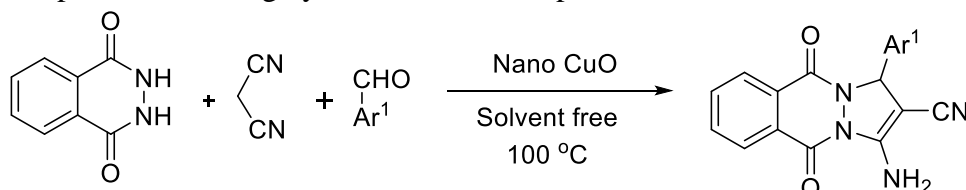
Azarifar et al [23] reported a three component synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones by heating 15 mol% of nano ZnO with phthalhydrazide, aromatic aldehydes, and malononitrile in a mortar.



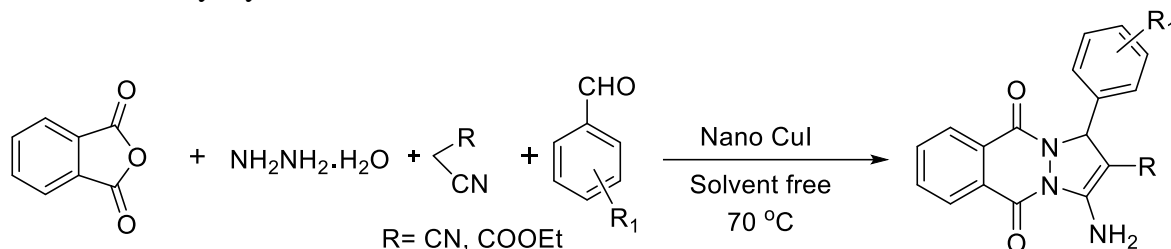
The same group [24] later synthesized Urea-functionalized silica-coated Fe_{3-x}Ti_xO₄ magnetic nanoparticles and applied it for the same reaction to get higher yield.



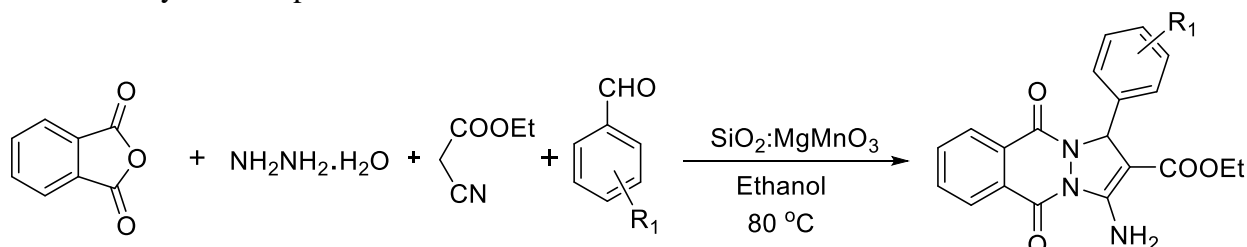
Patil et al [25] developed the synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-dione derivatives via one-pot three-component reaction among phthalhydrazide, malononitrile and aromatic aldehydes under solvent-free conditions using nanostructured CuO. A wide variety of aromatic aldehydes showed tolerance for the protocol with high yield of the desired product.



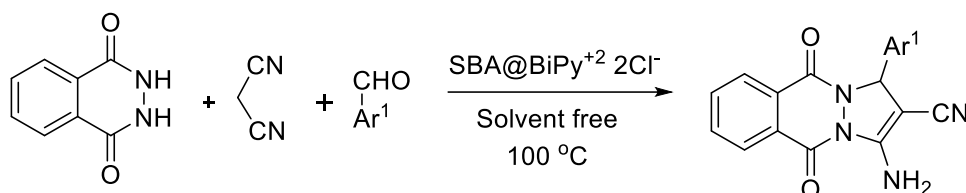
Safaei-Ghomi and group [26] synthesized nano CuI and applied 10 mol% of it for the four-component condensation reaction of phthalic anhydride, hydrazine monohydrate, aromatic aldehydes and malononitrile or ethyl cyanoacetate under solvent-free conditions.



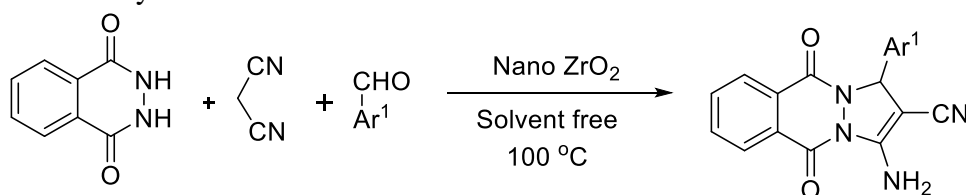
Sagar et al [27] published hydrothermal synthesis of SiO_2 composite MgMnO_3 catalyst and use of this polycrystalline material for the four component synthesis of 1H-pyrazolo[1,2-b]-phthalazine-5,10-dione in presence of ethanol as a solvent at 80 °C. But the procedure restricts the use of malononitrile as active methylene component.



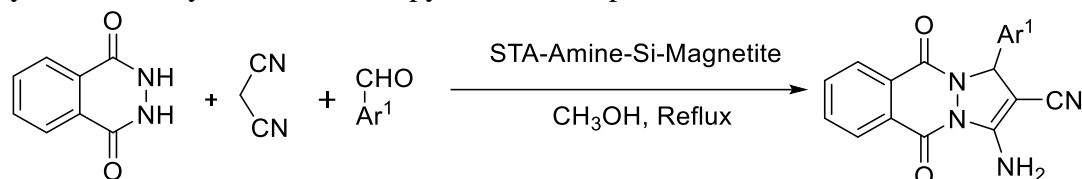
Bashti and colleagues [28] synthesized 1H-pyrazolo[1,2-b]-phthalazine-5,10-dione by one-pot three component reaction in presence of organic-inorganic hybrid nanocomposite, $\text{SBA}@\text{BiPy}^{+2} 2\text{Cl}^-$ without any solvent.



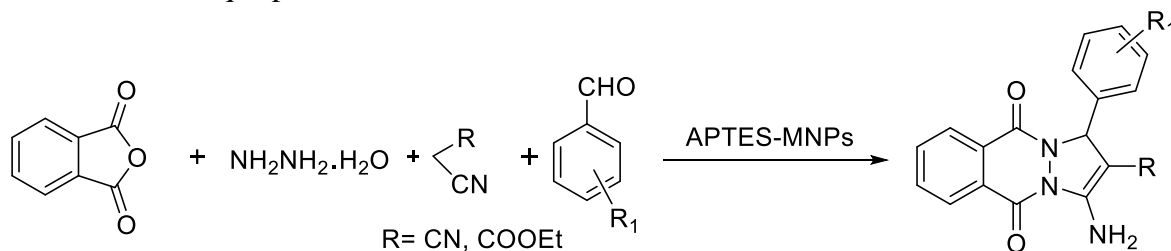
Piltan reported [29] solvent-free preparation of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones using ZrO_2 nanoparticles as a catalyst.



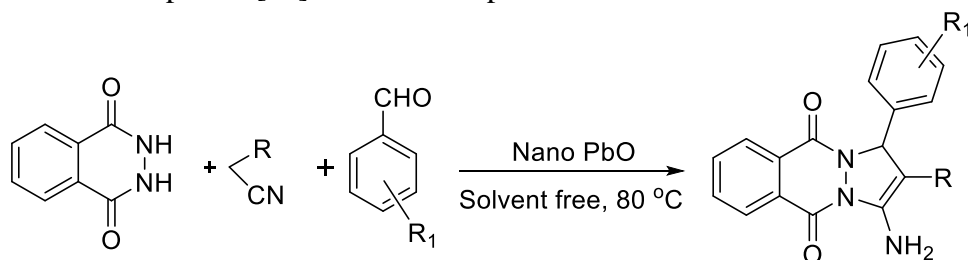
Arora and Rajput reported [30] the same synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones by a completely new nanocatalyst in methanol solvent. They coated silicotungstic acid (STA, $H_4[W_{12}SiO_{40}]$) on aminofunctionalized Si-magnetite nanoparticles and used this for the synthesis of 27 variety of differently substituted 1H-pyrazolo[1,2-b]phthalazine-5,10-diones.



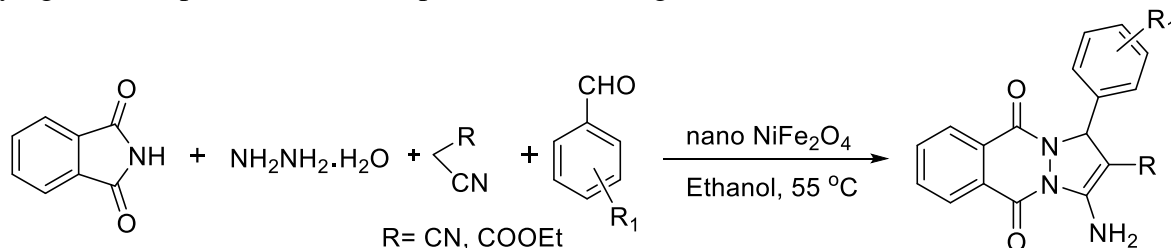
Shaterian and Mohammadnia [31] developed an one-pot quantitative protocol for preparation of 1H-pyrazolo[1,2-b]phthalazine-5,10-dione derivatives from basic building blocks in presence of magnetic Fe_3O_4 nanoparticles coated by (3-aminopropyl)-triethoxysilane as catalyst under solvent-free conditions. As active methylene component both malononitrile and ethyl cyanoacetate tolerated the protocol. Aromatic as well as aliphatic aldehydes are capable to provide products in room temperature which is the most unique part of scheme.



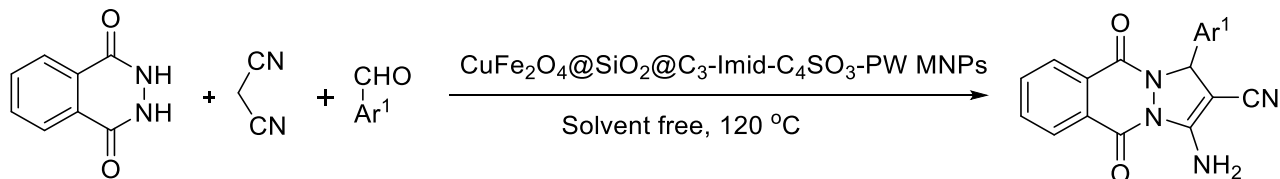
Tayebee and coworker reported [32] the multicomponent reaction with nano PbO .



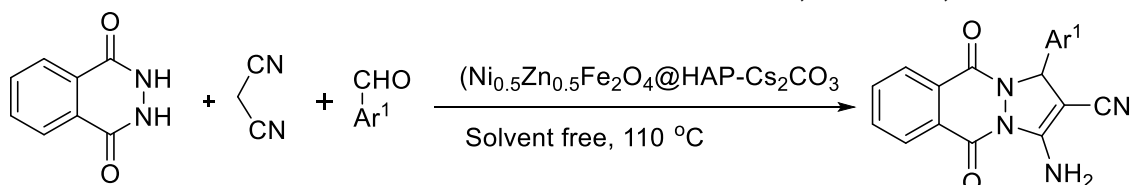
Dabholkar and group reported [33] the synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones applying four component reaction in presence of heterogeneous nano $NiFe_2O_4$ and ethanol solvent.



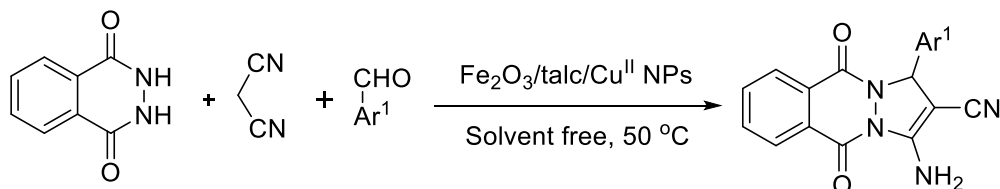
Hosseinasab and group [34] described the synthetic application of heterogeneous acidic ionic liquid based on functionalized imidazolium salt of phosphotungstic acid, immobilized on $CuFe_2O_4@SiO_2$ magnetic nanoparticles to synthesize 1H-pyrazolo[1,2-b]phthalazine-5,10-diones from precursors without any solvent. This protocol needs much higher temperature.



Maleki and group investigated [35] the catalytic activity of caesium carbonate supported on hydroxyapatite-coated $Ni_{0.5}Zn_{0.5}Fe_2O_4$ magnetic nanoparticles on the three-component reaction among phthalhydrazide, malononitrile and aromatic aldehydes under solvent-free heating condition.



Chalaki and Akhlaghinia reported [36] synthetic application of Cu^{II} anchored onto the magnetic talc on the three component synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones at much lower temperature.



Conclusion:

Catalytic processes in aqueous medium are important in many areas of the fine and specialty chemical industries, and the use of solid catalysts means easier catalyst separation and recovery, hence facilitating their reuse. It is widely accepted that a smaller catalyst particle means a higher activity. As a result, both the activity and the stability of a solid catalyst suspended in a liquid media can benefit greatly with the use of these small particles. Nano-catalysts mimic homogeneous (high surface area, easily accessible) as well as heterogeneous (stable, easy to handle) catalyst systems. The main difficulty, however, is that such small particles are almost impossible to separate by conventional means, which can lead to the blocking of valves by the catalyst. To overcome this issue, the use of magnetic nanoparticles has emerged as a viable solution; their insoluble and paramagnetic nature enables easy and efficient separation of the catalysts from the reaction mixture with an external magnet. Other exciting properties of these magnetic materials include their highly active and specific centers; these features serve to encourage this relatively novel but vastly expanding field. They offer a promising option that can meet the requirements of high accessibility with improved reusability. One of the most attractive features of magnetically separable nanoparticles (MSNPs) is their separation properties. Most heterogeneous systems require a filtration or centrifugation step and/or a tedious workup of the final reaction mixture to recover the catalyst. However, magnetically supported catalysts can be recovered with an external magnet due to their paramagnetic character. Magnetically recoverable materials have been applied in a wide range of catalytic reactions, including oxidations, hydrogenations, photocatalysis, and C-C bond formation, as well as in novel applications in asymmetric synthesis, hydration, Knoevenagel condensations, and CO₂ cycloaddition reactions. There has been an increasing trend toward the use of MSNPs in increasingly efficient green chemical synthesis. Multicomponent reactions (MCRs) have emerged as a highly valuable tools for the rapid generation of molecular complexity and diversity with predefined functionality in chemical biology and drug discovery, due to its straightforward reaction design, convergent, and atom efficient nature resulting in substantial minimization of waste, labour, time, and cost.

Acknowledgement

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