Multi-component Synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazoles in the presence of Co_3O_4@SiO_2-NH_2 nanocomposites as catalyst

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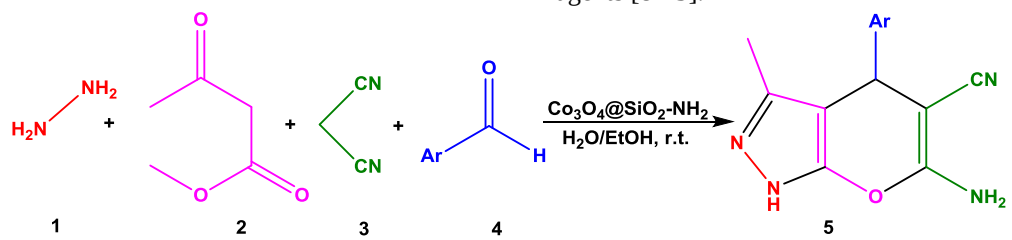
Abstract
In this research a series of pyranopyrazoles were efficiently synthesized via the one-pot four-component reactions of ethyl acetoacetate, hydrazinehydrate, aldehydes and malononitrile in the presence of Co_3O_4@SiO_2-NH_2 nanocomposites as catalyst. This study offers many advantages including short reaction times, excellent yields, environmental friendly nature, simple purification techniques and economic availability of the catalyst. The structure and magnetic characteristics of the nanocatalyst were fully characterized by spectral techniques including TEM, FE-SEM, EDX, XRD, FT-IR and VSM analysis.
Key words: Multi-component ،1,4-dihydropyrano[2,3-*c*]pyrazoles، Co_3O_4@SiO_2-NH_2 nonocomposites

Introduction
Recently, four- component synthesis of pyrano[2,3-c]pyrazoles have been done via the reaction of hydrazine hydrate, ethyl acetoacetate, malononitrile, and aromatic aldehydes using various catalysts such as: L-prolin [14], cesium fluoride [15], silicotungstic acid [16], sodium bisulfite[17], piperidine [18], Glycine [19] and γ-Alumina [20].
In continue of our efforts into the improvement of the synthetic approaches using heterogeneous catalysts [21-23], here we report and efficient pathway for the preparation of dihydropyrano[2,3-c]pyrazoles via multi-component reactions of aryl aldehydes, molononitrile, ethyl acetoacetate and hydrazine hydrate using Co_3O_4@SiO_2-NH_2 nanocomposite (Scheme 1).

Multi-component reactions (MCRs) are procedures that more than two reactants mixed together to afford heterocyclic structures that almost applied in the preparation of some drugs with anti-bacterial, anti-cancer, anti-asthma, anti-HIV, anti-tumor, anti-Parkinson and anti-fungal activities [1,2]. In recent years, nanoscience and nanotechnology have been one of the most important research fields between scientists. [3].
Cobalt oxide has been significantly used because of their exclusive properties and diverse applications such as p-type semi-conductor, gas sensor, catalytst, elecrochromic devices and lithium batteries. [4-6]. Co_3O_4 nanoparticles are in nature hydrophilic due to the being of hydroxyl groups on the particle surfaces. While, theses nanoparticles incline to aggregate in the reaction mixture of organic
reactions, so the silica coating on the surface of cobalt oxide nanoparticles can hinder their aggregation and stay their chemical stability. [7].
Furthermore, with the existence of numerous hydroxyl groups on SiO_2 shell, the Co_3O_4@SiO_2 can easily react with some organosilanes such as 3-aminopropyltriethyloxysilane (APTES) via formation of Si-O-Si bonds. The presence of NH_2 groups on the terminal shell of the prepared Fe_3O_4@SiO_2–NH_2 nanocomposite can be act as Brønsted basic catalysts to promote organic reactions.
Pyranopyrazoles are an important class of heterocyclic compounds, that have shown analgesic activity, anti-cancer agent, inhibitor of human chk1 kinase agent, anti-tumor agent, anti-inflammatory activity, as vasodilators and hypotensive and hypoglycemic agents [8-13].



Scheme 1: Co_3O_4@SiO_2-NH_2 nanocomposites catalyzed one-pot four-component synthesis of pyrano[2,3-c]pyrazoles.