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One-pot multicomponent synthesis of pyrano[2,3-*d*]pyrimidine derivatives catalyzed by supported magnetic nanoparticles

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Abstract: A series of pyrano[2,3-*d*]pyrimidine derivatives were synthesized via the three-component reaction of aromatic aldehyde, active methylene compounds and barbituric or thiobarbituric acid in the presence of supported magnetic nanocomposite at room temperature. This method has been found to be eco-friendly, simple and economical.

Keywords: Cellulose, Nanocatalyst, Multicomponent reactions, Pyrimidine, Pyran, Magnetic.

Introduction

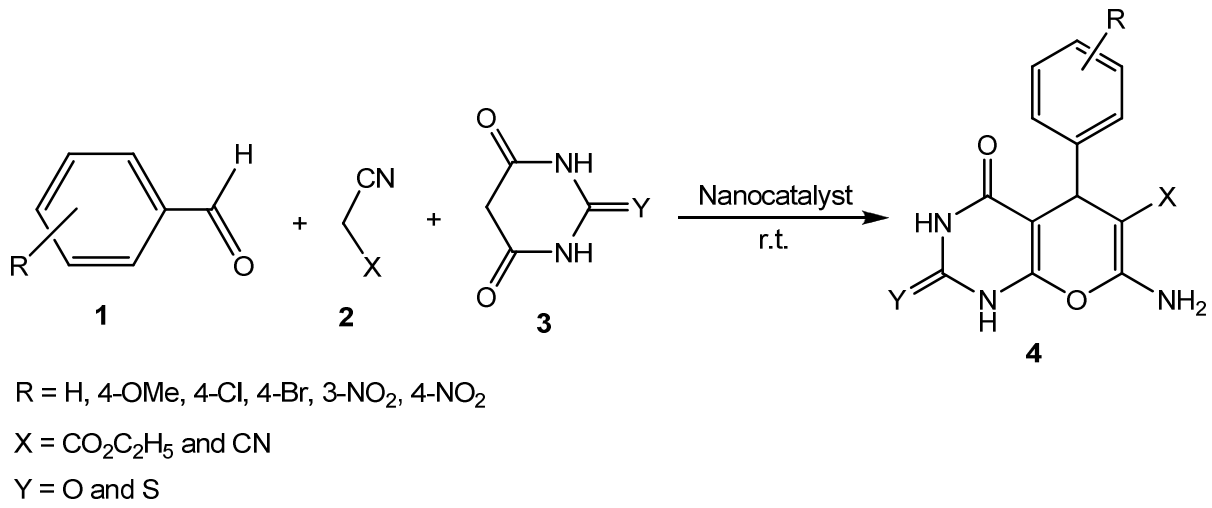
Pyranopyrimidine is one of the fused heterocycles that exhibit diverse biological properties. Compounds with such annulated uracils have antitumor, antibacterial, antihypertensive, vasodilator, hepatoprotective, bronchiodilators cardiotonic, and antiallergic activities. Furthermore, some of them exhibit antimalarial, antifungal, analgesics and herbicidal properties. Preparation of these molecules containing a uracil ring possesses significant synthetic challenges. A number of reports have appeared in literature, which usually requires harsh reaction conditions, long reaction times, complex synthetic

pathways and involved organic solvents and wastes. Thus, new routes for the synthesis of these molecules have attracted considerable attention in the search for a rapid entry to these heterocycles [1,2].

Recently, one-pot multicomponent reactions of aromatic aldehyde, active methylene compounds and barbituric or thiobarbituric acid has produced pyrano[2,3-*d*]pyrimidines in the presence of a few catalysts. But the design of efficient and recoverable catalyst is important for both economical and environmental points of view [3-5].

Nowadays, metal nanoparticles and functionalized magnetic nanoparticles, especially supported superparamagnetic metal nanoparticles, have attracted considerable interest in both academic and industrial researches because of their potential applications in chemical, biomedical and materials science. They have emerged as viable alternatives to conventional materials, as robust, readily available, high-surface-area heterogeneous catalyst supports, magnetically separable, thereby eliminating the requirement of catalyst filtration after completion of the reaction. Other important features of these catalysts are high catalytic activity, simple separation of them using an external magnet, high degree of chemical stability in various organic and inorganic solvents, reusability and benign character in the context of green chemistry. As a result, they have enabled researchers to apply nanocatalysts as greener and sustainable options for organic transformations [6,7].

Herein, we have developed a synthetic route for the one-pot three-component synthesis of annulated fused pyrano[2,3-*d*]pyrimidines **4** from condensation of aromatic aldehydes **1**, active methylene compounds **2** and barbituric or thiobarbituric acid **3** in the presence of a catalytic amount of supported metal nanoparticles at room temperature (Scheme 1).



Scheme 1. Synthesis of pyrano[2,3-*d*]pyrimidine derivatives.

Experimental

General

All solvents, chemicals and reagents were purchased from Merck, Fluka and Aldrich chemical companies. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected.

Synthesis of pyrano[2,3-d]pyrimidine derivatives (**4a-h)**

A solution of an aldehyde **1** (1 mmol), malononitrile or ethyl cyanoacetate **2** (1 mmol), barbituric or thiobarbituric acid **3** (1 mmol) in the presence of a catalytic amount of supported metal nanoparticles was stirred at room temperature for appropriate times according to Table 1. After completion of the reaction, the catalyst was removed by an external magnet and the solid product was collected by filtration and washed with ethanol.

Results and discussion

In this article, we have performed condensation reaction between an aldehyde, active methylene compounds such as ethyl cyanoacetate or malononitrile and barbituric or thiobarbituric acid with catalytic activity of metal nanoparticles at room temperature. As is evident from Table 1, different kinds of aldehydes have employed in the reaction and pyranopyrimidines **4a-h** were obtained as sole products in high yields. The workup procedure of the product was easy as the nanocatalyst can be separated simply by an external magnet. So, this process offer attractive advantages like operational simplicity and environmentally benign nature.

Table 1. Synthesis of pyrano[2,3-*d*]pyrimidine derivatives.

Product	R	X	Y	Mp (°C)	
				Observed	Reported
4a	H	CO_2Et	O	216-218	206-210 [8]
4b	4-OMe	CO_2Et	O	296-298	290-293 [8]
4c	4-Cl	CO_2Et	O	297-300	295-300 [8]
4d	H	CN	O	206-207	205-207 [5]
4e	4-Br	CN	O	228-230	230-231 [1]
4f	3-NO_2	CN	O	266-268	268-270 [1]
4g	4-NO_2	CN	O	244-245	239-240 [1]
4h	4-MeO	CN	S	115-118	116-118 [5]

Conclusions

In summary, we have introduced an attractive catalyst for three component synthesis of pyrano[2,3-*d*]pyrimidine derivatives. This efficient catalyst for the preparation of biologically and pharmaceutically pyrano[2,3-*d*]pyrimidine derivatives includes some important aspects like the easy workup procedure, reusability of catalyst as well as high atom economy, excellent yields, and mild reaction conditions.

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