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A new Ni(II) complex as a novel and efficient recyclable catalyst for the synthesis of pyrano[2,3-d]pyrimidines

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ABSTRACT

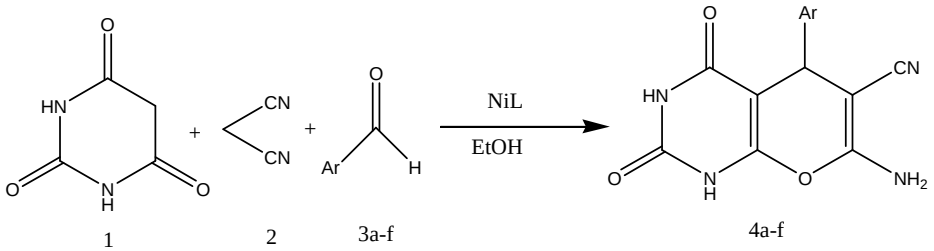
A simple and highly efficient one-pot three-component synthesis of a series of pyrido[2,3-d]pyrimidines from the condensation of barbituric acid, malononitrile and aromatic aldehydes using catalytic amount of a new Ni(II) complex based on 5-nitro-N1-((pyridin-2-yl)methylene) benzene-1,2-diamine (NiL) is reported. This new heterogeneous catalyst has the advantages of being environmentally friendly, simple work-up and high yields character.

Keywords: Pyrido[2,3-d]pyrimidine, Ni(II) complex, multi-component reaction, aromatic aldehyde

INTRODUCTION

During the recent years, the use of reusable catalysts attracted considerable amount of interest in organic synthesis owing their easy work-up procedures, easy filtration and minimization of cost and waste generation due to reuse and recycling of these catalysts [1-3]. Also, much attention has been paid to the development of new methods for the synthesis of heterocyclic compounds, due to their potential importance in the pharmaceutical and agricultural fields. Multicomponent reactions (MCRs) have become important tools in modern preparative synthetic chemistry because they increase the efficiency by combining several operational steps without isolation of intermediates [4,5].Multicomponent reactions have emerged as valuable tools for the preparation of structurally diverse chemical libraries of drug-like heterocyclic compounds [6-8].

Pyrano[2,3-*d*]pyrimidines are very important compounds with a wide range of biological and pharmacological activities [9-14]. The general procedures for the preparation of pyrano[2,3-d]pyrimidines include the condensation of barbituric acid, malononitrile and aromatic aldehydes [15-17]. Many of these methods suffer from some limitations such as long reaction times, drastic reaction conditions and low to moderate yields. Thus, the development of efficient, high-yielding and environmentally friendly method is desirable.



1 2 3a-f 4a-f

Scheme 1

It is therefore of interest to examine the behavior of new Ni(II) complex (NiL) as catalyst for the synthesis of pyrano[2,3-d] pyrimidines. During the course of our studies toward the development of new routes to the synthesis of heterocyclic compounds [18-21], herein we report the catalytic effects of (NiL) for the synthesis pyrano[2,3-d] pyrimidine derivatives (Scheme 1).

Initially, to find the optimal conditions, the reaction of barbituric acid, malononitrile and 4- chlorobenzaldehyde (1 mmol each) in the presence of various amount of catalyst (NiL) was used as a model reaction. The best result has been obtained at (0.05 g) of catalyst in ethanol at reflux temperature (Table1, Entry 3). In the absence of catalyst, the product 4a was obtained in trace amount after 120 min.The generality of this process was demonstrated by the wide range of aromatic aldehydes to synthesize the corresponding products in high to excellent yields (Table 2).

Table 1. Effect of amount of catalyst, solvent and temperature in the model reaction

Entry	Catalyst (g)	Solvent	Temp (°C)	Time (min)	Yield (%)
1	---	EtOH	Reflux	120	30
2	0.03	EtOH	Reflux	40	80
3	0.05	EtOH	Reflux	30	91
4	0.07	EtOH	Reflux	30	92
5	0.03	DMF	Reflux	80	65
6	0.05	DMF	Reflux	70	70
7	0.07	DMF	Reflux	70	71
8	0.03	MeOH	Reflux	60	69
9	0.05	MeOH	Reflux	55	74
10	0.07	MEOH	Reflux	55	76
11	0.03	------	110	60	76
12	0.05	------	110	55	78
13	0.03	------	120	55	78
14	0.05	------	120	50	80

Table 2. Synthesis of pyrano[2,3-d] pyrimidines under optimized conditions

Entry	Ar	Product	Yield (%)	Time (min)	Melting pint (°C)	
					Found	Reported
1	*4-ClC_6H_4*	4a	91	30	232-234	234-237 [22]
2	*3-$NO_2C_6H_4$*	4b	92	30	254-256	255-257 [22]
3	*4-$NO_2C_6H_4$*	4c	93	28	227-228	227-229 [22]
4	*C_6H_5*	4d	89	35	205-227	206-209 [22]
5	*4-MeC_6H_4*	4e	90	38	225-227	226-227 [23]
6	*4-$MeOC_6H_4$*	4f	91	40	283-285	287-288 [22]

MATERIALS AND METHODS

All chemicals were obtained from Merck Company and used as received. Melting points were determined on a SMP3 melting point apparatus. The IR spectra were obtained on a Tensor 27 Bruker spectrophotometer as KBr disks. The ^{1}H- NMR and ^{13}C- NMR (300 MHz) spectra were recorded using Bruker 300 spectrometer. The compounds were identified by the comparison of their physical and spectroscopic data with those of known compounds. The catalyst (NiL) was prepared according to earlier work [24]. All products were known by spectral data and comparison of their melting points with those of authentic sample (Table 2).

General procedure for the synthesis ofpyrano[2,3-d] pyrimidine derivatives (4a-4f)

A mixture of barbituric acid1 (1 mmole), malononitrile 2 (1 mmole), aromatic aldehydes 3a-f (1 mmole) and catalyst (NiL) (0.05 g) was refluxed in ethanol (10 mlit) for 28-40 min. After completion of reaction (monitored by TLC), the mixture was cooled to room temperature and precipitate was filterated and washed with cold ethanol to give products 4a-g in high yields.

Because of solubility of the catalyst in ethanol, the filtrate was evaporated under reduced pressure and catalyst was recycled by a simple filtration. The separated catalyst reused in model reaction without appreciable reduction in the catalytic activity. The results of the first experiment and subsequent experiments were almost consistent in yields (91, 88 and 84%).

Selected Spectral data

7-amino-5-(4-Chlorophenyl)-2,3,4,5-tetrahydro-2,4-dioxo-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4a)

^{1}H NMR (300 MHz, DMSO-d_6): δ 4.23 (s, 1H, CH), 7.14 (s, 2H, NH_2), 7.22 (d, 2H, *J*= 9 Hz, arom-H), 7.32 (d, 2H, *J*= 9 Hz, arom-H), 11.06 (s, 1H, NH), 12.07 (s, 1H, NH). IR (KBr disc): υ 1719, 1677 (C= O), 2198 (C≡N), 3386, 3080 (NH, NH_2) cm^{-1}. ^{13}C NMR (300 MHz, DMSO-d_6):δ 160.19, 160.12 (C=O, amides), 98.62-158.50 (C, aromand C=C), 88.31 (C≡N), 29.58 (CH).

7-amino-5-(4-nitrophenyl)-2,3,4,5-tetrahydro-2,4-dioxo-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4c)
IR (KBr disc): υ 1719, 1651 (C= O), 2273 (C≡N), 3330, 2978 (NH, NH_2) cm^{-1}.

RESULTS AND DISCUSSION

Treatment of barbituric acid, malononitrile and aromatic aldehydes in the presence of a catalytic amount of Ni(II) complex gave products which were identified as pyrano[2,3-d] pyrimidines. All products gave satisfactory spectral data in accord with the assigned structures.

CONCLUSION

In conclusion, a new solid acidic catalyst, Ni(II) complex was prepared according to earlier work [23]. The catalyst showed high catalytic activity in the synthesis pyrano[2,3-d] pyrimidines. Some attractive features of this method are high yields, short reaction times and recyclability and reusability of the catalyst.

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