

Synthesis of 2-Amino-7-hydroxy-4-(4-methoxyphenyl)-4H-chromene-3-carbonitrile by using dealuminated mesolite as a heterogenous catalyst

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Abstract

In order to investigate optimum loading of catalyst and reaction condition, 4-OCH₃ benzaldehyde (1mmol), resorcinol (1mmol), were reacted with malononitrile (1mmol) as model reaction with different amount of dealuminated mesolite as catalyst under reflux condition and results are summarized in (Table 1.1). In the absence of catalyst the reaction did not gave satisfactory yield of desired product (4c), which indicate crucial role of catalyst 0.1 g of dealuminated mesolite is suitable to catalyze reaction smoothly. The same reaction was carried out under different protic and aprotic solvents and it is observed that the reaction proceeds faster in protic solvent such as water and ethanol with maximum yield in reduced time as compare to non protic solvents such as tetrahydrofuran and acetonitrile which gave lower yield.

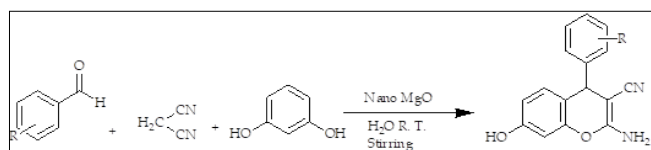
Keywords: Synthesis, 4-OCH₃ benzaldehyde, 4H-chromenes, malononitrile, mesolite and Yield etc

Introduction

In recent years 2-Amino-4H-chromenes and their derivatives have attracted strong research interest because of their potent biological and pharmacological significance such as antimicrobial, anti-angiogenesis, antioxidant and antitumor activities [1, 6]. 4H-chromenes are building blocks of number of oxygen contain heterocyclic natural products like tannin and polyphenol which is present in green tea, fruits and vegetables [7]. Chromene heterocycles is an important constituent in cosmetics, pigments and biodegradable agrochemicals [8]. In addition dihydropyranochromens are well known spasmolytic, diuretic, anti-coagulant agents; furthermore they are utilized as cognitive enhancers, for the treatment of neurodegenerative disease including Alzheimer's disease, Parkinson's diseases, Down's syndrome schizophrenia and myoclonus [9]. Besides this 2-amino-4H-chromenes and pyran derivatives are used as photoactive material to construct the solar cell. [10]. Considering these wide applications of chromene scaffold several catalytic methods were developed for synthesis of 2-amino-4H-chromene derivatives.

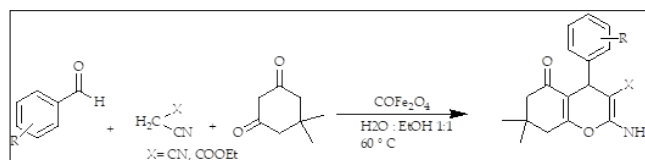
Literature Review on 2-Amino-4h-Chromens

J Safari *et al* [11], have used nanocrystalline MgO as heterogeneous base catalyst for one pot synthesis of 2-amino-4H-chromen derivatives at room temperature in water to give yield 80-95% in 20 min. (Scheme 1)



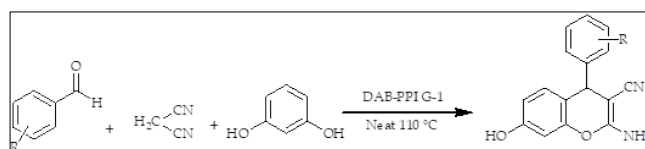
Scheme-1

J. K. Rajput *et al* [12], developed CoFe₂O₄ reported catalyzed efficient synthesis of tetrahydro [b] pyran derivatives in H₂O:EtOH (1:3) solvent system at 60 °C with 90-95 % yield in 5-10 min. (Scheme-2)



Scheme-2

Behrooz *et al* [13], have developed nanopolypropylenimine dendrimer (DAB-PPI-G₁) polymer base catalyst for one pot synthesis of 2-amino-4H-chromen derivatives under solvent free condition at 110 °C with 82-98% yield in 20-30 min. (Scheme-3)

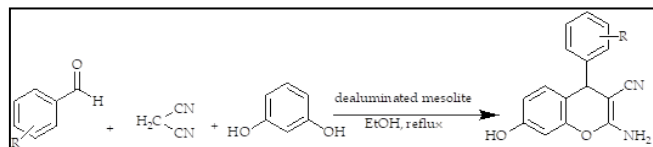


Scheme-3

Although, reported methods have excellent yield and minimum reaction time but some of them suffers from one or other kind of drawbacks such as long reaction time, use of volatile carcinogenic organic solvents, low yield non reusable and expensive catalyst and hence in order to overcome these limitations it is necessary to develop simple, cost effective and environmentally benign protocol for the synthesis of 2-Amino-4H-chromenes derivatives.

Present Work

In present work, dealuminated mesolite was found to be an active catalyst for one pot synthesis of 2-amino-4H-chromene derivatives via cyclocondensation of aromatic aldehydes, malononitrile and resorcinol in ethanol under reflux condition (Scheme 4). Present method offer several advantages over reported protocols such as simple work up procedure, short reaction time, mild reaction conditions, excellent yield and reusability of catalyst.



Scheme-4

Results and Discussion

In order to investigate optimum loading of catalyst and reaction condition, 4-OCH₃ benzaldehyde (1mmol), resorcinol (1mmol), were reacted with malononitrile (1mmol) as model reaction with different amount of dealuminated mesolite as catalyst under reflux condition and results are summarized in (Table 1.1). In the absence of catalyst the reaction did not give satisfactory yield of desired product (4c), which indicate crucial role of catalyst 0.1 g of dealuminated mesolite is suitable to catalyze reaction smoothly. The same reaction was carried out under different protic and aprotic solvents and it is observed that the reaction proceeds faster in protic solvent such as water and ethanol with maximum yield in reduced time as compare to non protic solvents such as tetrahydrofuran and acetonitrile which gave lower yield (Table 1.1).

Table 1: Optimization of catalyst loading with different solvents for the synthesis of (4c)

Entry	Solvent	Catalyst amount (g)	Time (min)	Yield(%) ^a
1	Ethanol	-	120	30
2	Methanol	-	120	25
3	Acetonitrile	-	120	23
4	1,4-dioxane	-	120	27
5	Tetrahydrofuran	-	120	21
6	Water	-	120	40
7	Ethanol	0.05	30	80
8	Ethanol	0.1	30	85
9	Ethanol	0.15	30	85
10	Ethanol	0.2	30	85

In order to explore the scope and importance of the present method, different aromatic aldehydes were tested under optimum reaction conditions for the synthesis of 2-amino-4H-chromene derivatives and the results are summarized in (Table 1.2). After optimizing reaction conditions, efforts have been made towards the recovery and reusability of the catalyst. The catalyst was separated after completion of reaction by diluting reaction mixture by hot ethanol and filtration. The recovered catalyst was washed with acetone and dried at 100 °C for 1 hour before the next catalytic run. Reusability of the catalyst was also investigated for three times and it was found that the catalyst has retained almost consistent activity (Table 1.2, entry 4c).

Table 2: Dealuminated mesolite catalyzed cyclocondensation reaction of aromatic aldehyde, malononitrile and resorcinol. (°C)

Entry	R	Time (min)	Yield (%) ^a	Melting point (°C)	
				Observed	Reported
4a	H	30	93	235-237	233-235 [11]
4b	4-Cl	30	92	161-163	162-164 [11]
4c	4-OCH ₃	30	85 (85, 85, 80) ^c	110-112	111-112 [11]

Reaction conditions: benzaldehyde (1 mmol), resorcinol (1 mmol), malononitrile, (1 mmol), catalyst 0.1g, and ethanol 15 ml. ^a Isolated yields. ^cYield after consecutive cycle

To specify the advantages of proposed method, results of different reported methods are compared with our results and are summarized in (Table 1.3) It is found from tabulated results that, dealuminated mesolite promotes reaction more effectively than other reported method.

Table 3: Catalytic performance of different catalyst for synthesis of 2-Amino-7-hydroxy-4-(4-methoxyphenyl)-4H-chromene-3-carbonitrile

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Lit.
1	Nano MgO	H ₂ O, R. T. stirring	20	95	[11]
2	(DAB-PPI-G ₁)	Solvent free 110 °C	03	95	[13]
3	Clinoptilolite	H ₂ O, reflux	20	90	[14]
4	Na ₂ CO ₃ (30 mol %)	H ₂ O: MeOH (95:5) 25 °C	600	75	[15]
5	PPI	H ₂ O, reflux	20	96	[17]
6	Polyamine/SiO ₂	H ₂ O:Ethanol, reflux	80	88	[18]
7	Dealuminated mesolite	reflux in ethanol	30	85	Our results

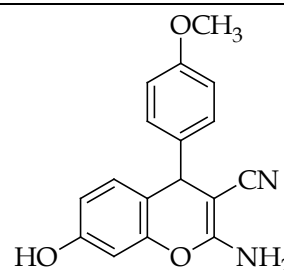
General Procedure

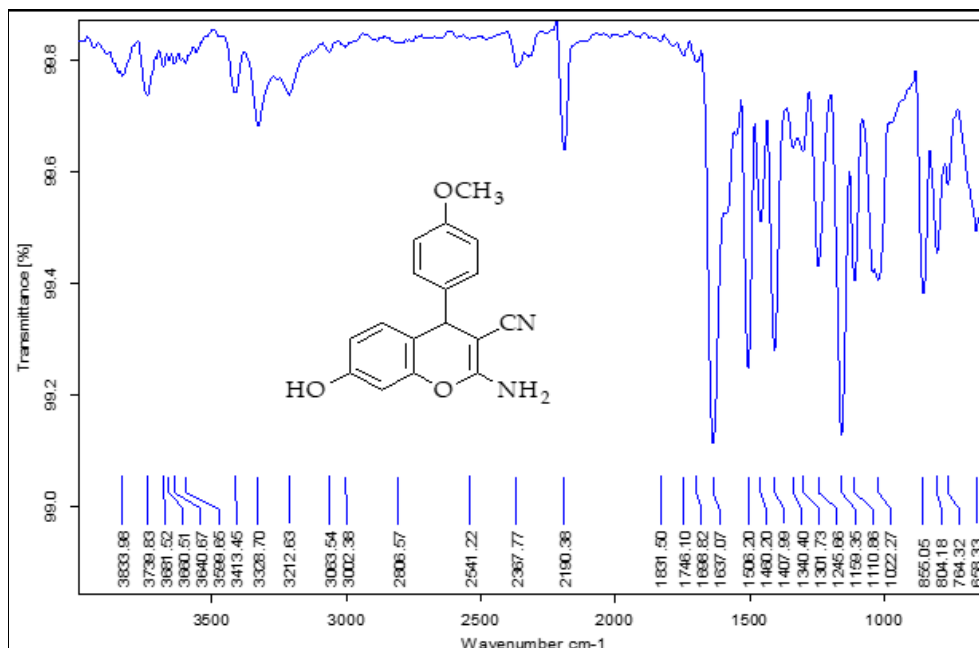
A mixture of aromatic aldehyde (1 mmol), resorcinol 0.110 g (1 mmol), malononitrile 0.066 g (1 mmol), and catalytic amount dealuminated mesolite (0.1g) was refluxed in ethanol (15 ml) for the time shown in (Table 1.2). The progress of the reaction was monitored by thin layer chromatography using ethyl acetate: pet ether (7:3) as a solvent system. After completion of the reaction, the reaction mass was filtered, the filtrate was concentrated, and the crude product obtained was recrystallised from ethanol to afford pure products (4a-c).

Spectral Data of Representative Compound

2-Amino-7-hydroxy-4-(4-methoxyphenyl)-4H-chromene-3-carbonitrile (4c): White solid, M. P. 110-112 °C

FT-IR (cm⁻¹) 3413 (OH), 3328 (NH₂), 2190 (CN), 1506, 1159





FT-IR spectrum of 2-Amino-7-hydroxy-4-(4-methoxyphenyl)-4H-chromene-3-carbonitrile.

Conclusions

- In summary, an efficient catalytic system has been developed for the synthesis of 2-Amino-4H-chromene derivatives via one pot cylocon cyclocondensation of benzaldehyde, malononitrile and resorcinol using dealuminated mesolite type natural zeolite as heterogeneous catalyst.
- The reaction takes place in short time with excellent yield of the product.
- The present method shows several advantages over reported method such as such as inexpensive, non-toxic and non-corrosive nature of catalyst. Simple recovery and reusability of the catalyst makes the reaction more successful under environmental benign conditions.

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