Green method of synthesis of different derivatives of 2-amino-Chromenes by using CAN as a catalyst

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Abstract Derivatives of chromene are an important group of compound found in plants including fruit and vegetables. chromene are biologically active with wide range of activities such as antimicrobial, mutaginicitical , antviral , antiproliferative and central nervous system activities. In current research work substituted 2-amino 4H-chromenes were synthesized by one pot synthesis method by interaction with substituted benzaldehyde ,β-naphthol , and mlononitrile by using CAN as catalyst. The yield of product is found to be very good. The synthesized compounds were recognized by IR, NMR and mass spectroscopic technique.

Keywords- *2-amino 4H-chromene, benzaldehyde, B-naphthaol, mlononitrile .CAN*

I. INTRODUCTION

Multi-component reactions (MCRs) is one step reaction that combines two or more reagents to form an end product [1]. Since an MCR forms product in one step it generate considerably less waste than a multistep synthesis. Multi-component reactions (MCRs) important for the achievement of high level of brevity and diversity. They allows more than two simple and flexible building blocks to be combine in practical , time saving one pot operation , giving rise to complex structure by simultaneous formation of two or more bond ,according to domino principle [2]. Consenquently from the point of green chemistry, MCRs constitue a very usefull class of tools for the synthesis of new chemicals. MCRs contribute to the requiemrnts of an environmental friendly process by reducing the number of synthetic steps energy consumption and waste production. Researcher have transformed this poewrfull technology into one of the most efficient and economic tools for combinatorial and parallel synthesis [2,3]. Due to their inherent simple experimental procedure and their one pot character they are perfectly suited for Automated synthesis . thus MCRs attracted considerable interwst owing to their exceptional synthetic efficiency [2-4].

Multicomponent reaction are of increasing importance in organic and medicinal chemistry. In times whrere a premium is put on speed , diversity and efficiency in the drugs discovey process MCRs stratergies offer significant advantage over conventional linear type synthesis. In such reactions three or more reactant comes together in a single reaction vessel to form new product that contain portion of all the components. MCRs providing product with the diversity needed for the discovery of new lead compound. Over The last decade industrial and academic researchers have made such powerful MCR strategies into one of the most efficient and co-effective tools for combinatorial and parallel synthesis. [6,7.]

2-amino- 4H-chromenes represent an important class of compounds being the main component of many naturally occurring products. The basic structural frameworks of chromene for example is a common feature of many tannins and polyphenols [8] found in tea , fruits vegetables and red wine .

2-amino chromene and their derivatives are of considerable interest as they possess wide range of biological properties [8] such as spasmolytic ,diuretic ,anticoagulant anticancer and antianaphylactic activity [9].

Several protocols have been reported for the synthesis of 2-amino-4H-chromenes and their derivatives using malononitrile, resorcinol and aldehyde. Various catalysts such as piperidine,9 triethyl amine,10 aqueous K2CO3,11 cetyltrimethylammonium bromide (CTABr),12 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),13 Ca(OH)2,14 HT/MW 15 and basic ionic liquids16 have been used for these reactions. In current work mild reaction condition (Ethanol and waer) and l-proline is used as green and reusable catalyst .Because of its advantages associated with this eco-friendly catalyst, CAN has been explored as a powerful catalyst for MCRs. In recent years, Ceric(IV)Ammonium Nitrate (CAN) has been used for various organic transformations including Lewis acid catalyst

Result and Discussion

At the beginning, multicomponent reaction of benzaldehyde, resorcinol and malononitrile were chosen as the model reaction. Effects of various reaction parameters such as the effect of the solvents, the effect of catalyst concentration and the effect of temperature were studied to optimize the reaction conditions

It was observed that Ceric ammonium nitrate (CAN) with 10 mol% ound to be more influencing catalyst in the synthesis of 2-amino4-H chromene by three component reaction of benzaldehyde, resorcinol and malononitrile resulting into a very good yield of the desired products.

It is reported that in the absence of catalyst no formation of product was observed even in same reaction condition (Table 1, entry 1).

During the research work significant effect of solvent is observed. Solvent play major role in the catalyst activity as express in table 1. We have investigated the effect of protic and aprotic solvent on three component reaction of aromatic aldehyde , malononitrile and resorcinol. It was found that in non polar solvent like toluene the reaction never proceed forward and no

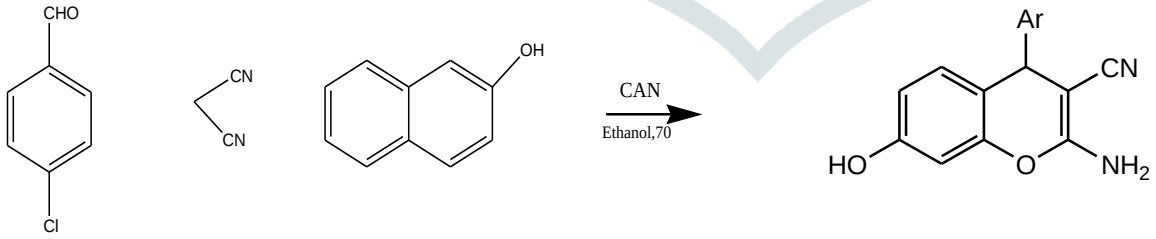
product was formed. Same was observed for solvent free condition and reaction did not takes place.where as in polar aprotic solvent like DMF, Acetonitrile theof the product yield was found to be less (< 20%, Table 1).In Case of polar protic solvent like Water , ethanol yield was found to be good .(< 80% Table 1). Thus polar protic solvent found to more effective.

Use of catalyst in different mole percent found to be more effective. With 5 mol% (entry 2-7, table 1) yield of desir product was found to be less but with increase in loading of catalyst upto 10 mol% yield goes on increasing (entry 7-11, Table 1)

Table 1. Optimization of reaction conditions [a]

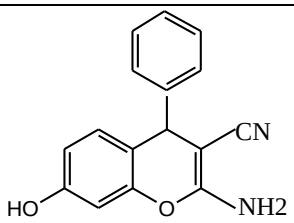
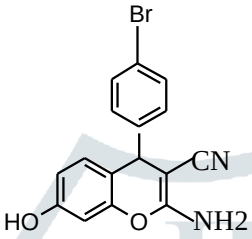
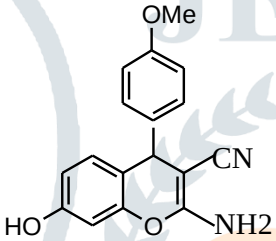
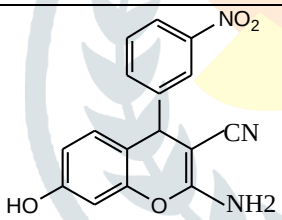
Entry	Reaction condition	Catalyst (mol%) [b]	Time (min)	Yield (%)[c]
1	**H2O, 70 ^{0}C,**	**No catalyst**	24 Hr	00
2	**EtOH, 70 ^{0}C**	**CAN (5)**	5 Hr	82
3	**MeCN 7 0 ^{0}C,**	**CAN (5)**	5 Hr	48
4	**DMF 70 ^{0}C,**	**CAN (5)**	5 Hr	42
5	**Toluene 70 ^{0}C,**	**CAN (5)**	5 Hr	00
6	**EtOH,: H2O(1:1), 70 ^{0}C,**	**CAN (5)**	5 Hr	87
7	**Solvent free ,70 ^{0}C**	**CAN (5)**	5 Hr	00
8	**EtOH, 70 ^{0}C,**	**CAN (10)**	5 Hr	85
9	**MeCN 70 ^{0}C,**	**CAN (10)**	5 Hr	44
10	**DMF 70 ^{0}C,**	**CAN (10)**	5 Hr	46
11	**Toluene 70 ^{0}C**	**CAN (10)**	5 Hr	00
12	**EtOH,: H2O(1:1), 70 ^{0}C,**	**CAN (10)**	5 Hr	90

[a] Reaction condition: benzaldehyde (5 mmol), resorcinol (5 mmol), malononitrile (5 mmol). [b]Weight percentage of the catalyst with respect to resorcinol. [c] Isolated yield



1 2 3 4 a-d

Table 2. 2-Amino-4H-chromene synthesis in Ethanol : Aqueous (1:2) mediuma

Entry	Aldehyde	Product	Code	Time	Yield	M. P. (1C)	
	R	Structure				Found	Reported
1	-H		4a	5 h	85	233–236	234-236[17]
2	-Br		4b	6h	84	224–226	225–227[18]
3	-oMe		4c	7 h	80	112–114	112–114[18]
4	-NO2		4d	5.5h	89	187–189	188–190

Experimental

Materials and Method

All melting points were taken in open capillaries and are uncorrected Infrared (IR) spectra were recorded with a Shimadzu 8400s FT-IR spectrometer using potassium bromide pellets. 500MHz ^{1}HNMR spectra were recorded on a DRX-500 Avance Bruker spectrometer. The chemical shifts are reported in ppm (δ-scale) relative to internal TMS Reagents are obtained from commercial resource. Commercially available regents were used without further purification. Products are all known compounds and were identified by comparing of their physical and spectra data with those reported in the literature.

General procedure for 2-Amino-4H-Chromenes

A mixture of resorcinol(5mmol) ,malononitrile (5mmol) ,and aromatic aldehyde (5mmol) was taken round bottom flask containing 5 mL of water and 5 ml ethanol. (10wt%) catalyst CAN with respect to resorcinol was then added to the reaction flask and the contents were stirred. The reaction mixture was refluxed. The progress of the reaction was monitored by thin layer chromatography (ethyl acetate/pet ether: 30%). After reaction was completed, the reaction mixture was allowed to cool at room temperature. The crude product was extracted with ethyl acetate. The organic layer was washed with water (25 mL), dried with anhydrous Na2SO4, the solvent evaporated under vacuum and the crude product recrystallized from ethanol. Characterization data for selected compounds are provided below:

Selected characterization data

4a: IR (KBr), ν (cm^{-1}): 3400, 3316 ,2180,1645,1590; ^{1}H NMR (DMSO-$d_{6,}$ 500 MHz), δ (ppm): 5.34 (s, 1H, CH), 7.12 (s, 2H, $NH_{2),}$ 7.12-7.22 (d, 2H, J=8.2, ArH), 7.30-7.37 (m, 3H, ArH), 7.40-7. 47 (m, 2H, ArH), 7.81-7.82 (d, 1H, J=8.02, ArH),7.91-7.96 (m, 2H, ArH).

Conclusion

In conclusion, 2-amino-4H-chromenes were prepared in a simple method. The procedure is very simple, efficient and environmentally friendly as it does not use any auxiliary and reasonable catalyst.

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