

Multicomponent Single Step Microwave Induced Organic Synthesis

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ABSTRACT

Substituted 2-amino-4*H*-chromenes have been synthesized by employing one-pot three-component condensation reaction of aromatic aldehyde with malononitrile and activated phenols/diketone with glycine as an inexpensive and effective catalyst. Microwave induced synthesis provides excellent yield, short reaction time and simple work up procedures with the green aspects by avoiding toxic reagents. The advantages of green techniques marked significant environment friendly chemical reactions. The objective of this work is to get better yields with the derivatives of substituted amino chromenes. Deepened literature work facilitated new approach of synthesizing heterocyclic compounds.

Keywords: Multicomponent, Microwave irradiation, Cyclocondensation, Glycine, 2-amino-4*H*-chromenes

I. INTRODUCTION

Development of conventional methods are much tedious which causes major adverse effects on the environment. Use of ultra sound irradiation technique and microwave energy have proved to be one of the stepping stone towards the green synthesis.[1,2]. Green chemistry is a production process that aims at using the existing knowledge and principles of chemistry for developing and implementing the chemical products to reduce the use and generation of substances hazardous to the environment. Choice of inexpensive safe and non-toxic solvents hold the best part of green technique.[3].

Multicomponent reactions (MCRs) are convergent reactions, in which three or more starting materials

react to form a product, where basically all or most of the atoms contribute to the newly formed product.[4]. Nowadays a great number of MCRs are known. In 1850, Strecker reported the first multicomponent reaction for the synthesis of α -amino cyanides.[5]. MW reactions are considered as one of the non-conventional methods which transfer the heat to the reaction mixture directly, thereby saving time and energy required for the process. MW irradiation enables heating the tiny substances throughout their volume rather than their outer surfaces.[6]. This source of energy leads to the minimal use of catalyst or non-catalyzed reactions. Yield obtained have been

reported to be higher than those obtained by conventional method.[7].

Catalysis is the process of increasing the rate of a chemical reaction by adding substance called catalyst. Catalysts are those which alter the rate of reaction by changing the path of reaction. The catalyst generally enters into chemical combination with the reactants but is ultimately regenerated.[8,9].

Among those, glycine due to its environmental compatibility, non-corrosiveness, availability and cost effectiveness properties is being widely used as organocatalyst in various organic syntheses and is one of the highly efficient catalysts in multi-component reactions.[10–15].

Chromene derivatives are an important class of heterocycles, mainly isolated from leaves and stems of plants.[16–18]. Chromene ring consists of a benzene fused to a pyran ring. Hence chromene rings are also known as benzopyran. Structurally, there are important class of chromenes-4*H*-chromene and 2*H*-chromene.[19–22].

These chromenes have diverse biological and chemical importance. Synthetic analogues were developed over the years and recently have emerged as potent anticancer agent.[23]. They also display remarkable effects as pharmaceuticals [24–29], including antifungal [30], anti-HIV [31,32], antitubercular [33] and antimicrobial activity.[34,35].

II. METHODS AND MATERIAL

A. Materials

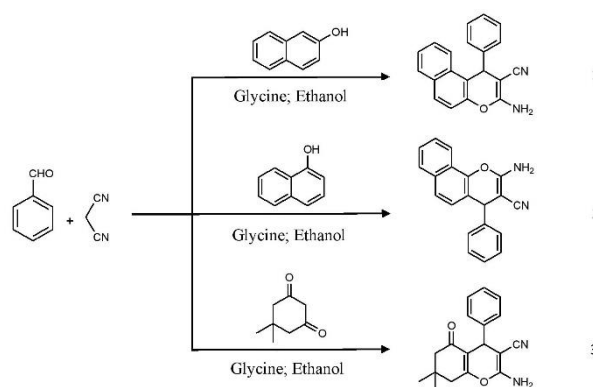
All chemicals were procured from Sigma Aldrich and Loba Chemie Pvt. Ltd. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. ¹H and ¹³C NMR spectrum was recorded using 400 MHz JNM-ECZ400S/L1 Jeol NMR Spectrometer. Chloroform-d solvent containing 99.8 atom% D and 0.03% (v/v) TMS as reference standard were procured from Sigma Aldrich. Perkin Elmer

Spectrum Two Universal ATR device with LiTaO₃ detector was used to record FT-IR Spectrum.

230 V – 50 Hz; 1050 W Microwave instrument was used for irradiation.

B. General Procedure for Preparation of 2-amino chromene derivatives

A mixture of aromatic aldehyde (2mmol), malononitrile (2mmol), diketone or phenol (2mmol) and glycine (3mmol) was irradiated using microwave radiation (Scheme 1). Few drops of Ethanol served as the solvent. After completion of the reaction, crude product was washed successively with water and recrystallized using ethanol.



Scheme 1. Synthesis of compounds 1-3

III. RESULTS AND DISCUSSION

Our synthesis began with the microwave irradiation of benzaldehyde, malononitrile and activated phenol or diketone containing catalytic amount of glycine to give 2-aminochromene derivatives. It was a simple and efficient procedure for the synthesis of 2-amino chromenes.

Spectroscopic data for selected compounds have been given below:

Compound [1]: Pale brown crystals. Yield: 91%.

FT-IR (ν cm^{-1}): 3403, 3288 (primary N-H stretch), 2231 (CN), 1575 (aromatic C=C), 1188 (C-O), 757 (1,2 disubstituted ring). ^1H NMR (400 MHz, CDCl_3): δ_{H} 5.026 (1H, s), 7.307-7.319 (7H, m), 7.428-7.466 (1H, ddt), 7.555-7.592 (1H, ddd), 8.06-8.08 (1H, dddd), 8.426 (1H, ddt). ^{13}C NMR (400 MHz, CDCl_3): δ_{C} 55.61 (1C, s), 60.03 (C-CN, s), 101.49 (1C, s), 126.59 (4C including CN, s), 127.99 (2C, s), 128.32 (2C, s), 128.70 (2C, s), 129.99 (2C, s), 133.17 (1C, s), 143.54 (1C, s), 146.14 (1C, s), 154.03 (C-O, s), 165.59 (C-NH₂, s). MS: m/z calcd for $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}$ 298, found 298 [M^+].

Compound [3]: Orange crystals. Yield: 90%.

FTIR (ν cm^{-1}): 3394, 3323 (primary N-H stretch), 2201 (CN), 1660 (C=O), 1594 (aromatic C=C), 1254 (C-O), 754 (1,2 disubstituted ring). ^1H NMR (400 MHz, CDCl_3): δ_{H} 1.233 (6H, s), 2.214 (1H, d), 2.227 (1H, d), 2.386 (1H, d), 2.397 (1H, d), 4.534 (1H, s), 7.083-7.191 (2H, dtd), 7.216-7.243 (2H, dddd), 7.281-7.283 (1H, tt). ^{13}C NMR (400 MHz, CDCl_3): δ_{C} 27.409 (CH₃, s), 27.678 (CH₃, s), 32.747 (1C, s), 35.521 (1C, s), 40.691 (CH₂, s), 47.06 (CH₂, s), 50.657 (C-CN), 115.585 (1C, s), 125.824 (CN), 127.535 (2C, s), 128.196 (1C, s), 128.579 (2C, s), 143.140 (1C, s), 159.881 (C-NH₂, s), 161.477 (C-O, s), 190.445 (C=O, s). MS: m/z calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$ 294, found 294 [M^+].

First, benzaldehyde, malononitrile and 2-naphthol were irradiated in microwave with catalytic amount of glycine using ethanol as solvent. The completion of reaction was observed within 3 min and product yield was observed to be high. Similarly, benzaldehyde and malononitrile were treated with other activated phenols (1-naphthol and phenol) and diketone (dimedone). The corresponding 2-amino chromene derivatives (Table I) were obtained in good to high yields.

The results found with benzaldehyde, malononitrile and dimedone under the optimal conditions were compared with best ones published so far using inorganic or organic alkali catalysts; the data is listed in Table II. It showed that the glycine was fairly a good catalyst for this reaction.

TABLE I
SYNTHESIS OF SUBSTITUTED 2-AMINO-4H-CHROMENES

Entry	Product	Time /min	Yield (%)	Melting Point (°C)	
				Found	Reported ^l it
1.	1	2.5	91	285-287	287-288 ^[36]
2.	2	1.66	90	215-217	216-217 ^[36]
3.	3	1.33	90	225-226	226-228 ^[37]

TABLE II
DIFFERENT CATALYSTS FOR THE SYNTHESIS OF [1]

Entry	Catalysts	Time/h	Yield (%)
1.	Glycine	0.04	91
2.	Piperazine	0.12	91 ^[38]
3.	$\text{H}_{14}[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$	3	93 ^[39]
4.	p-TSA	3	90 ^[40]
5.	$\text{KF}/\text{Al}_2\text{O}_3$	5	86 ^[41]

IV. CONCLUSION

Microwave irradiation for the synthesis of 2-amino-4H-chromene derivatives is studied in detail. This one-pot condensation reaction using glycine as an organocatalyst offers several advantages such as high yield shorter reaction times and simple work up. The compounds synthesized were evident from the spectroscopic analyses.

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