Current Pharma Research
ISSN-2230-7842
CODEN-CPRUE6
www.jcpronline.in/

Research Article

Grape juice catalyzed synthesis of Bis-coumarin derivatives by Grindstone Technique: A Green chemistry Approach.

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Received 18 December 2018; received in revised form 04 March 2019; accepted 04 March 2019

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ABSTRACT

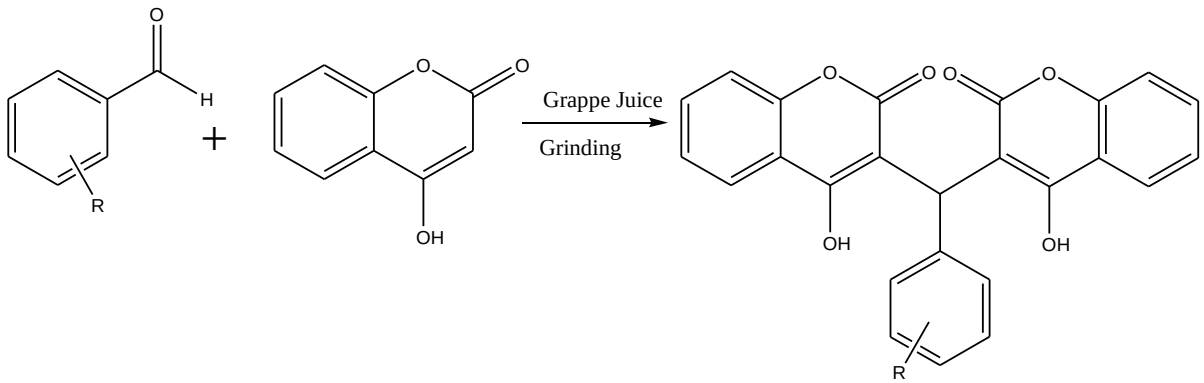
Biscoumarins' properties are similar to those of coumarins and exhibit various biological activities. Bis-coumarins were usually prepared by the condensation of carbonyl compounds with 4-hydroxycoumarin in organic solvents which employs large amounts of hazardous and toxic solvents associated with catalysts. However, these protocols were not environmentally benign. Thus, the introduction of efficient new methods based on green methodology is still in great demand. In the course of our investigation to develop new green synthetic method we wish to report here in a simple, efficient and eco-friendly procedure for the synthesis of bis-coumarin derivatives by grinding the aromatic aldehyde and 4-hydroxy coumarin in the presence of grape juice as a natural catalyst. This is a convenient and facile one pot synthesis of bis-coumarin with a greener approach. Thus facilitating efficient synthesis of bioactive compounds in environmentally benign way with shorter reaction time, mild reaction conditions, easy workup, and more over less expensive with excellent yield of the product.

KEYWORDS

Green chemistry, Grape juice, Multicomponent reaction, Grindstone technique

1. INTRODUCTION

Coumarin derivatives are found in many plants, notably in high concentration in the tonka bean, woodruff and bison grass[1] and Biscoumarins are a relatively unexplored class of compounds, isolated and characterized from different plant species[2]. Biscoumarins' properties are similar to those of coumarins and exhibit various biological activities such as anticoagulants, antioxidants, antitumor, and antifungal agents. Essential and not well studied is their role as inhibitors of various enzymes-urease, anti-HIV-1 protease and integrase, DNA polymerase, and protein kinase [3,4,5,6,7]. Bis-coumarins were usually prepared by the condensation of carbonyl compounds with 4-hydroxycoumarin in organic solvents[8,9] which employs large amounts of hazardous and toxic solvents associated with catalysts. However, these protocols were not environmentally benign, rather this Green Chemistry [10] term was introduced in the year 1998. After this an organic chemist/medicinal chemist has to develop synthetic strategies which should follow principles of Green Chemistry, mainly care should beta ken for atom economy, non hazardous chemical should be released, energy consumption should be minimum, preferably reaction should be completed in aqueous medium or in absence of solvent and last but not the least a catalyst if used should be natural preferably bio-catalysts. As a result of these criteria recently, several methods of synthesis using 4-hydroxycoumarin for preparation of Bis-coumarins in aqueous media have been reported. Despite effectiveness and eco-friendliness of these methods, they use catalysts such as TEBA[11] and I_2[12] and have long reaction times. Thus, the introduction of efficient new methods based on green methodology is still in great demand. In the course of our investigation to develop new green synthetic method we wish to report here in the grape juice catalyzed synthesis of biscoumarin in water just by grinding (Scheme: I)



Scheme I: Synthesis of Bis-coumarin.

2. MATERIALS AND METHODS

All melting points were measured in open capillary and are uncorrected. The products were characterized by IR spectra, 1H NMR. IR spectra were recorded on Perkin–Elmer FT-IR-1710 Instrument. 1H NMR was recorded on Bruker MSL-300 instrument using TMS as an internal

standard. All reagents were purchased from Merck and Loba and used without further purification.

2.1. Experimental

2.1.1. Preparation of aqueous extract of grape juice (Vitisamurensis):

The seed less grapes were purchased from the local market and the (10 g) was crushed in water (50 mL) by grinder, and it was centrifuged using micro centrifuge (REMI RM-12C). The clear portion of the aqueous extract of the grapes was used as catalyst..

2.1.2. General method for series of Bis-coumarin

The mixture of 10 mmol of aldehyde, 20 mmol of 4-hydroxy coumarin, and 5 ml grape juice was grinded using mortar pestle at room temperature with monitoring by TLC. Then the reaction mixture washed with water and was filtered, the crystalline solid recovered by crystallization with ethanol. Its identity was confirmed by IR and NMR and its melting point. This procedure is followed for the synthesis of all the Biscoumarins.

3. RESULTS AND DISCUSSION

A simple, efficient and eco-friendly procedure for the synthesis of bis-coumarin derivatives accomplished by grinding the aromatic aldehyde and 4-hydroxy coumarin by using grape juice as a natural catalyst with excellent yield. The results are presented in Table 1. The probable mechanism of the reaction is depicted in scheme 2. Moreover, fruits are inexpensive and easily available in the market.

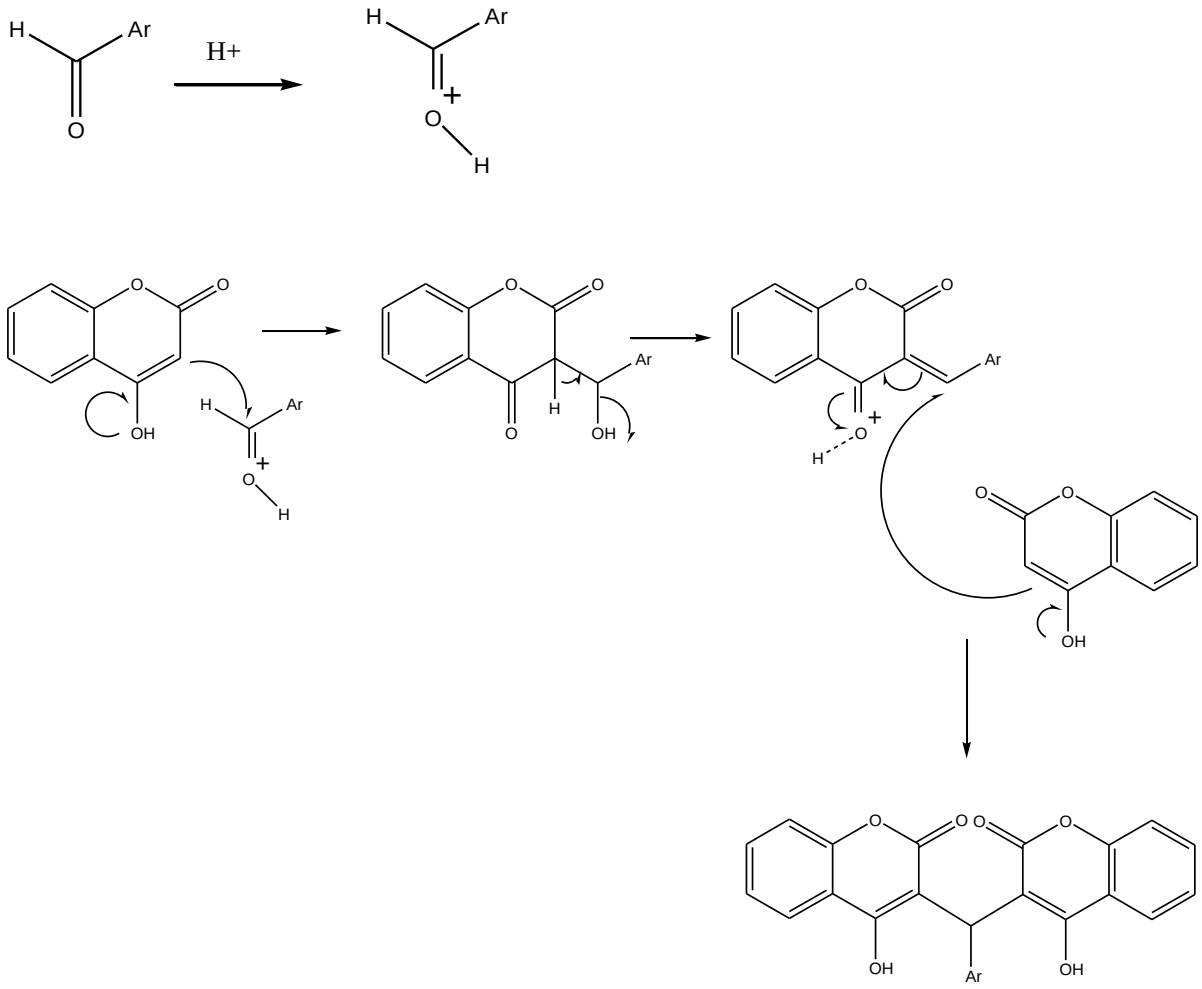
Table 1. Grape juice catalyzed synthesis of biscoumarins just by grinding at ambient condition.

Entry	**R**	**Time(min)**	**Product**	**Yield %**	**MP C^o(observed)**	**MP reported**	**C^o**
1	H	10	3a	86	226-227	226-228[13]	
2	4-NO_2	7	3b	88	233-235	236-237[13]	
3	4-OH	15	3c	85	222-225	220-224[13]	
4	4-Cl	11	3d	79	254-256	256-258[13]	
5	4-OCH_3	12	3e	84	244-245	244-246[13]	

The mechanism of the reaction is depicted in scheme II grape juice plays a complex role in accelerating the coupling reaction and thus promotes the formation of products

3.1. Mechanism

Probable mechanism of the reaction is as under (Scheme-II)



Scheme II. A probable mechanism for the reaction.

Since all the products have been reported previously in the literature so they were characterized by comparison of M.P, IR and NMR spectra with authentic samples.

4. CONCLUSION

This is a convenient and facile one pot synthesis of bis-coumarin with a greener approach. Thus facilitating efficient synthesis of bioactive compounds in environmentally benign way with shorter reaction time, mild reaction conditions, and easy workup, less expensive with excellent yield of the product.

5. ACKOWNOLGEMENT

The authors are thankful to Maharashtra Cosmopolitan Education Society, Pune-411001, Maharashtra, India.

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