

An Efficient Carbonized Sugar Catalyzed Entry to 7,8-dihydro-2H-Chromen-5(6H)-ones

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Abstract

The present paper describes a facile entry to various substituted 7,8-dihydro-2H-chromen-5-ones under neat conditions using simple carbonized sugar as a catalyst. The reaction was promoted by visible light under neat or in acetic acid as a solvent with a catalyst to afford the desired products in good to excellent yield. Mild conditions coupled with ease of operation make the protocol synthetically attractive and may find widespread application for the synthesis of chromenone scaffold.

Keywords: Carbonized sugar; Chromenones; Nano; Visible light; Photochemical reaction.

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1. Introduction

Chromanes are represented by a fused core tetrahydropyran ring or pyran unit to a six-membered ring. This basic unit represents a principal synthon for many organic transformations and is entrenched in numerous natural products [1-3]. In recent years, chromenone derivatives have attracted significant interest to organic chemists due to their growing biological and pharmaceutical applications [4-8]. Several graceful synthetic methods exist for these intermediates from α , β -unsaturated iminium salts [9-11] under acidic conditions [12], and by employing tandem Stille-oxa-electrocyclization reaction [13-15]. Also, several synthetic strategies have been reported to construct these skeletons *via* [3+3] cycloaddition of α , β -unsaturated aldehydes and 1,3-dicarbonyl compounds employing different catalysts such as Indium (III) chloride [16], EDDA [17,18], Lewis acid [19], Bronsted acid [20,21], or EDDA/ZnCl₂ co-catalysts [22], Iodine [23], biocatalyst [24], sulfated tin oxide [25].

1,3-Dicarbonyl compounds are versatile synthons for the incorporation of electrophilic and nucleophilic units [26-28]. Further, these derivatives can be converted to

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form a 2*H*-pyran motif by condensation with α , β -unsaturated aldehydes followed by [3+3] cycloaddition [29-31]. This approach allows the facile generation of cyclic rings with new stereogenic centers. The most commonly employed methods to accomplish these cycloadditions include light, heat, sonication, high pressure, or by employing Lewis acids and transition metal as catalysts [32,33].

Recently, the use of visible light as a source of energy to influence reactions under mild conditions has gained importance as a green procedure, and numerous reactions have been described by means of visible light [34-36]. This type of photo-activation of substrate very often minimizes by-products and requires much less time compared to thermal methods. This feature has dramatically improved visible light-mediated photochemical reactions of synthetic importance [37-39].

The inherent ability of carbon materials (CMs) as heterogeneous catalysts could be perceptive. Carbocatalysts are metal-free carbon materials such as activated carbon, single and multi-walled nanotubes, graphene oxide (GO), and fullerene. They have been explored for catalytic properties in a variety of reactions with great success. In particular, carbon-based nanocatalysts are breakthrough materials that exhibit enhanced catalytic performance as a consequence of their characteristic architecture and optoelectronic properties. This has led to replacing several metal catalysts used in organic transformations with graphene oxide-based carbocatalytic systems [40-45]. Herein, we demonstrate the efficient application of carbonized sugar (CS) as a catalyst for synthesizing various substituted 7, 8-dihydro-2*H*-chromen-5-ones under visible light.

2. Experimental

CS-GO Nanoparticles were prepared according to the method given in the literature reference [44,45]. All melting points were determined on an Electrothermal Gallenkamp apparatus. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini Spectrometer 300 and 75 MHz, respectively. IR spectra were recorded on Nicolet Fourier Transform spectrometer. Mass spectra were obtained on a 7070H or VG Autospec Mass spectrometer using the LSIMS technique. Thin-layer chromatography (TLC) was performed on GF-25U (Anal. Tech) plates and silica gel glass-packed plates.

2.1. General experimental procedure for the 7,8 dihydro-2*H* chromen-5(6*H*)-ones

In a typical experimental procedure, a mixture of 1,3-cyclohexanedione (1.0 mmol) and aliphatic α , β -unsaturated aldehyde (1.1 mmol), carbonized sugar (10 %) under neat conditions was stirred for the specified time in the presence of a 100 W tungsten lamp (Philips India Ltd.). The temperature was maintained in the range of 65-70 °C (Table 2). After completing the reaction (as monitored by TLC), the mixture was diluted with methylene dichloride, and the catalyst was removed by filtration. Removal of the solvent under reduced pressure followed by purification over silica gel column with petroleum ether/ethyl acetate (1:3) as eluent afforded the corresponding 7,8- dihydro-2*H*-chromen-5(6*H*)-ones.

3. Results and Discussion

A model reaction was performed with 1,3-cyclohexanedione (1 mmol, 1a) and crotonaldehyde (1.1 mmol, 2a) under different conditions to optimize the reaction conditions and the results are summarized in Table 1.

Table 1. Screening of reaction conditions for cycloaddition reaction.

Entry	Catalyst (%) ^a	(mol)	Solvent	Visible/light (°C)	Time (min)	Yield ^b (%)
1	10		MeOH	65-70	60	0
2	10		CH ₃ CN	65-70	60	0
3	10		(Me) ₂ CHOH	65-70	60	0
4	10		Toluene	65-70	60	68
5	10		AcOH	65-70	60	82
6	10		Neat	Dark reaction conditions	24 h	0
7	0		Neat	65-70	24 h	0
8	5		Neat	65-70	60	80
9	10		Neat	65-70	45	95
10	20		Neat	65-70	45	95
11	10		Neat	100	45	85

^a1.0 mmol (1a), 1.1 mmol (2a), cat. CS-GO NPs.

^bisolated yield. The catalyst can be recycled up to five times.

As is evident from Table 1, the nature of solvent has a significant effect on the product's rate of reaction and yield. The reaction of 1,3-cyclohexanedione (1a) with crotonaldehyde (2a) in MeOH (entry 1), MeCN (entry 2), and (Me)₂CHOH (entry 3) solvents in the presence of visible light (100 W tungsten lamp) at 65-70 °C and 10 % catalyst did not proceed to afford any product. However, the use of toluene (entry 4) and acetic acid (entry 5) as a solvent afforded the desired product 2-methyl-2,6,7,8-tetrahydro-5H-chromen-5-one (3a) in 68 % and 82 % yield, respectively. Further, the effect of visible light was studied in the presence and absence of a 100 W tungsten lamp (Philips India Ltd) at 65-70 °C with 10% of catalyst separately. As expected, in the absence of visible light (dark reaction conditions), the reaction did not proceed to afford the desired product (entry 6). We then decided to study the reaction rate under neat conditions in the absence and presence of a catalyst under visible light (100 W tungsten lamp) irradiation. No product formation was observed without catalyst under visible light conditions even after 24 h stirring (entry 7), while the excellent yield of the product was obtained with 10% catalyst (entry 9). Further increase in catalyst quantity to 20 % did not dramatically affect the yield of the product (entry 10). The reaction temperature of 65-70 °C was maintained by regulating the light source every 10 min. Time interval and a further rise in temperature to 100 °C (entry 11) did not have any desirable effect and led to a reduction in the yield of the product. This observation may be attributed to the instability of the product at a higher temperature under the reaction conditions.

The spectral analysis of compound 3a displays characteristic enone absorption at 1645 cm⁻¹ in the IR spectrum with the expected peaks associated with two vinylic protons of 2H-pyranyl ring at δ 6.48 (d, *J* = 9.8 Hz, 1H) and 5.30 (dd, *J* = 10.3 Hz, 2.6 Hz, 1H) ¹H

NMR spectrum. Mass spectral analysis showed m/z (rel. abund. %) 165.1 ($[M+1]^+$, 100). No xanthene derivative was obtained in this case. Also, studies carried on the effect of catalyst loading for the test reaction using crotonaldehyde and 1,3-cyclohexanedione (mole rate 1.1:1), 5, 10, and 20 % of the catalyst under solvent-free conditions (Table 1, entries 8-10) reveal that 10 % of catalyst afford best results in terms of yield and time (Scheme 1 and Table 1, entry 9) and a further increase in % of catalyst loading did not have any desirable effect in the yield (Table 1, entry 10). The catalyst can be recycled five times after filtration from the reaction mixture with a maximum 5 % variation in yield.

Having optimized reaction parameters (10 % of carbonized sugar, solvent-free conditions in the presence of a 100 W tungsten lamp reaching the temp of 65-70 °C), the general applicability of the reaction conditions was studied with a variety of aliphatic α , β -unsaturated aldehydes such as but-2-enal, 2-methylpent-2-enal, 3-methylbut-2-enal, 4-methylpent-2-enal, pent-2-enal with 1,3-cyclohexanedione (1a) and dimedone (1b). The results are summarized in Table 2. It is heartening to note that, as expected, the desired cyclization proceeded well to afford the corresponding chromenone derivatives within 45-60 min. (Table 2, entries 1-10) in good yield.

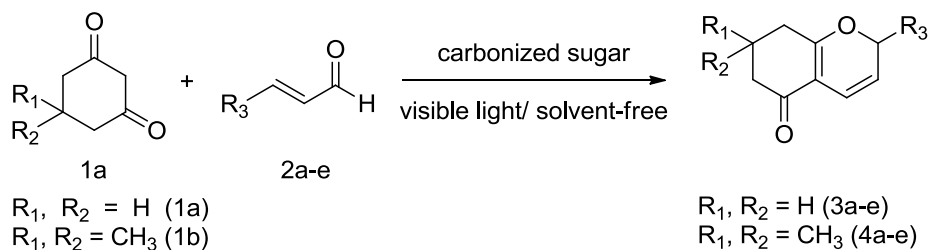
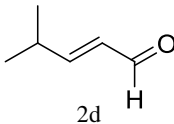
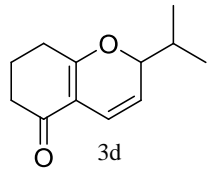
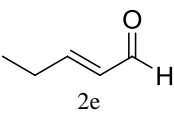
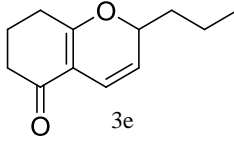
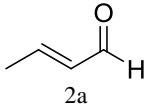
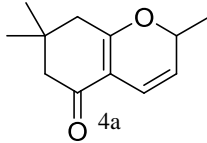
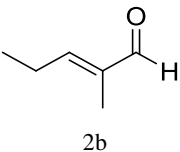
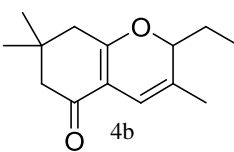
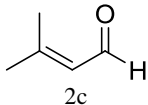
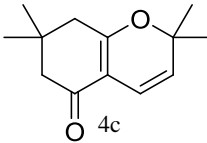
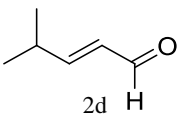
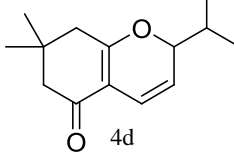
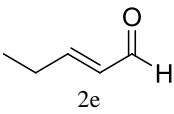
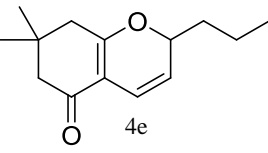


Fig. 1. Synthesis of substituted of 7,8-dihydro-2*H*-chromen-5(6*H*)-ones.

Table 2. Synthesis of 7,8-dihydro-2*H*-chromen-5(6*H*)-ones^a.

Entry	Aldehyde	Product	Time	Yield (%) ^b
1			1 h	95
2			2 h	84
3			1 h	90

Entry	Aldehyde	Product	Time	Yield (%) ^b
4			2 h	88
5			3 h	64
6			1 h	92
7			2 h	94
8			1 h	86
9			2 h	84
10			3 h	71

^aReaction Condition: 1.0 mmol 1,3-cyclohexanedione or dimedone, 1.1 mmol of aliphatic α , β -unsaturated aldehyde, 10 % carbonized sugar under the neat condition in the presence of 100 W tungsten lamp,

^bisolated yield after purification.

4. Reaction Mechanism

We speculate that the reaction proceeds in two steps: In the first step, the catalyst acts as a Lewis acid and facilitates condensation of the active methylene group with an aldehyde to

yield the conjugated enone. In the second step, the enone, in turn, undergoes cyclization to afford the chromen-5-(6*H*)-one.

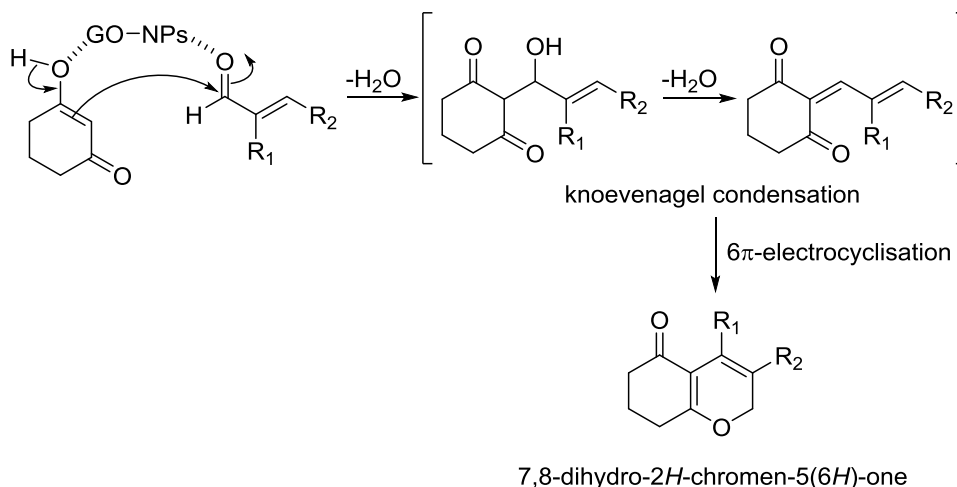


Fig. 2. Plausible mechanism of formation of 7,8-dihydro-2*H*-chromen-5(6*H*)-one.

5. Conclusion

The present paper describes the application of CS-GO NPs as an efficient and green catalyst for one-pot entry to various substituted 7,8-dihydro-2*H*-chromen-5-ones under neat conditions. The protocol has potential merits in terms of simplicity, cost-effectiveness, eco-friendly procedure, and catalyst reusability. The efficiency and nature of catalyst would allow widespread application of this protocol to synthesize sensitive and bioactive compounds bearing 7,8-dihydro-2*H*-chromen-5-one scaffold under mild conditions.

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