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Iodine catalyzed synthesis of the chromene derivatives in one-pot

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Abstract

Iodine catalyzed one-pot reactions of salicylaldehyde and dimolecular 1*H*-indene-1,3(2*H*)-dione, barbituric acids, 4-hydroxycoumarin, or 4-hydroxy-6-methylpyran-2-one were performed and provided a rapid, convenient and general approach to synthesize the chromene derivatives. 2-(11-Oxo-10,11-dihydroindeno[1,2-*b*]chromen-10-yl)-1*H*-indene-1,3(2*H*)-diones **P1**–**P4** and 10-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-3-methylpyrano[4,3-*b*]chromen-1(10*H*)-ones **P8**–**P9** were unprecedentedly prepared and structurally identified by NMR and Mass. The confirmation of structure by single crystal X-ray crystallography is reported for **P3**.

Keywords: Chromene; Iodine; MCRs; Salicylaldehyde; 1*H*-Indene-1,3(2*H*)-dion

Compared to stepwise process, multicomponent reactions (MCRs) are more efficient and particularly useful to generate high levels of diversity. The intrinsic atom economy, time and energy savings, as well as environmental friendliness underlying the MCRs abstracted the scientists in both academia and industry [1–3]. Simultaneously, iodine, as a mild, less-toxic, cheap and readily available Lewis-acid, has been successfully utilized to promote MCRs in our previous studies. Several novel heterocyclic compounds have been smoothly obtained in a manner of iodine catalyzed MCRs [4,5].

The approach of iodine catalyzed MCRs is even more useful when they provide access to ‘‘privileged medicinal scaffolds’’. As one of the privileged scaffolds, the chromene moiety is frequently found in biologically active molecules [6–8] and naturally occurring products [9,10]. Numbers of publications were devoted to the synthesis of the chromene derivatives. One efficient strategy is to introduce the salicylaldehyde into the construction of chromene core, wherein the oxygen in the chromene core is contributed by salicylaldehyde [11–15]. Keeping in view of above point we designed a synthetic route of iodine catalyzed one-pot condensation (Scheme 1) of salicyldaldehyde **A1**, 1*H*-indene-1,3(2*H*)-dione **B1** and malononitrile **C** aiming at preparing compound **M**. Unfortunately, we failed to construct molecule **M**. According to the analysis of NMR and MS, structure **P1**, a novel chromene derivative similarly originated from **A1**, was formed unexpectedly. Herein, we would like to present our work on applying the protocol of iodine catalyzed MCRs to the preparation of novel chromene derivatives conveniently.

1. Results and discussion

A careful literature survey indicates that limited work on the synthesis of chromene core was reported from salicylaldehyde and dimolecular 1,3-dicarbonyl compounds [11,13,16], especially **B1**, to the best of our knowledge,

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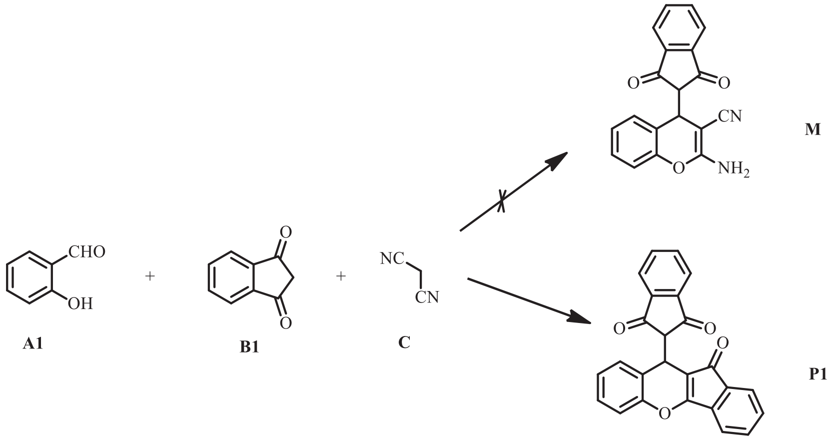
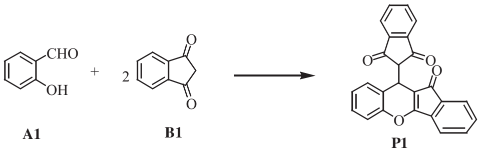


Scheme 1. Newly synthesis of chromene derivative.

have never been reported to synthesize **P1** before. Thereby, we were triggered to investigate this iodine catalyzed three-component reaction. Initially, the iodine was evaluated, the results collected in Table 1 implied that iodine markedly promoted the transformation in terms of both yield and reaction time, since poor yield of expected product (31%) along with an unknown byproduct were formed within 5 h without iodine, while heating the EtOH solution containing reactants and 20 mol% of iodine for 8 min provide 73% yield of product **P1** (Table 1, entries 2 and 4). Further optimization of reaction condition suggested that 10 mol% of iodine catalyzed three-component reaction of **A1** and dimolecular **B1** in refluxing EtOH was favored (Table 1, entry 4).

To explore the limitation and scope, substituted salicylaldehydes were subjected to the optimized reaction conditions. The results outlined in Table 2, entries 1–4 denoted that both electronic-withdrawing and electronic-donating substrates were tolerated, and all the transformations were completed in good yields within 1 h. Encouraged by the above success, we attempt to apply this protocol to other 1,3-dicarbonyl compounds. Barbituric acids, constituted the basic moiety of a number of clinically used hypnotic drugs such as Veronal, Phenobarbital and Luninal [17], was primarily considered. The coupling of barbituric acids **B2** and **B3** with salicylaldehyde was carried out respectively under the standard reaction conditions, the data shown in Table 2, entries 6 and 7 validated the availability

Table 1
The conditional optimization of the synthesis of chromene **P1**[a].



Entry	Iodine	Solvent	*T* (min)	Yield (%)[b]
1	20	EtOH	8	73
2	0	EtOH	5 h	31[c]
3	15	EtOH	10	79
4	10	EtOH	10	85
5	5	EtOH	20	82
6	10	MeCN	2 h	32
7	10	AcOEt	50	46
8	10	*i*-PrOH	30	78

[a] The reaction conditions: salicylaldehyde **A1** (1 mmol, 0.122 g), 1*H*-indene-1,3(2*H*)-dione **B1** (2 mmol, 0.292 g) and iodine were added in EtOH (2 mL) and heated to refluxing temperature.

[b] Isolated yield.

[c] An unknown product was obtained along with the target product.