

# Synthesis of coumarins by Pt-catalyzed hydroarylation of propiolic acids with phenols

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**Abstract**—Synthesis of coumarins from phenols and propiolic acids was examined by using a Pt catalyst such as PtCl<sub>2</sub>/AgOTf, K<sub>2</sub>PtCl<sub>4</sub>/AgOTf, and K<sub>2</sub>PtCl<sub>4</sub>/AgOAc. Propiolic acid reacted even with less reactive phenols in trifluoroacetic acid to give coumarins and dihydrocoumarins. In the case of substituted propiolic acids, phenylpropionic acid and 2-octynoic acid, the reactions proceeded selectively to afford coumarins in good to high yields.

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## 1. Introduction

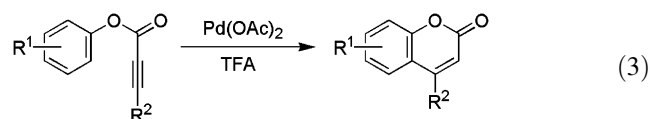
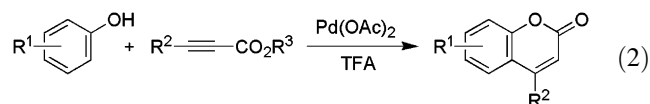
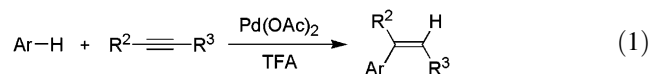
Coumarin derivatives exist widely in nature, especially in plants, and many of them show a wide range of biological activities.<sup>1,2</sup> To date, many synthetic methods for coumarins have been developed due to their useful properties.<sup>1,3</sup> The representative methods are the Perkin, Pechmann and Knoevenagel reactions. However, there are still limitations such as severe reaction conditions, requirement of a stoichiometric amount of condensing agents, and difficulty of getting the starting materials.

Much effort has been paid to the development of coumarin synthesis through the reaction utilizing a transition metal catalyst.<sup>4–11</sup> However, most of the syntheses require halogenated substrates such as iodophenols and iodoarenes as starting materials for the construction of the coumarin skeleton. These synthetic reactions involve bond cleavage of the C–X bonds by transition metals and produce waste halides. When the atom-economy of the reaction is considered, the use of halogenated substrates is not favorable. If a direct construction of a C–C bond from the C–H bond in simple arenes is possible then this strategy will become a straightforward efficient process.

Trost et al. have developed an atom-economic synthesis of coumarins from the reaction of propiolic acids and phenols in the presence of Pd<sub>2</sub>(dba)<sub>3</sub>CHCl<sub>3</sub> or Pd(OAc)<sub>2</sub> catalysts in formic acid.<sup>9</sup> Their reaction did not need any halogenated

phenols. Shi and He also reported a direct synthesis of coumarins by the reaction of aryl propiolates with AuCl<sub>3</sub>/AgOTf catalyst.<sup>10</sup>

We have reported that the hydroarylation of alkynes proceeded by using Pd(OAc)<sub>2</sub> or PtCl<sub>2</sub>/AgOAc catalyst in trifluoroacetic acid (TFA) to give aryl-substituted alkenes (Eq. 1).<sup>12</sup> This direct functionalization of the C–H bonds in arenes was expanded to the synthesis of coumarins by the intra- or intermolecular hydroarylation of propiolates with phenols (Eqs. 2 and 3).<sup>11</sup> Recently, PtCl<sub>2</sub>/AgOTf and K<sub>2</sub>PtCl<sub>4</sub>/AgOTf were found to be effective catalysts for hydroarylation of propiolic acids, affording the corresponding cinnamic acids selectively.<sup>13</sup> Especially, the K<sub>2</sub>PtCl<sub>4</sub>/AgOTf catalyst was the most effective in application to the hydroarylation of propiolic acid with less reactive benzene. The effectiveness of the Pt catalysts encouraged us to investigate the synthesis of coumarin.



**Keywords:** Coumarin; Hydroarylation; Propiolic acid; Platinum catalyst; Silver triflate; C–H bond functionalization; Trifluoroacetic acid.

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## 2. Results and discussion

First, we examined the reaction of propiolic acid (**2a**) ( $R^2=H$ ,  $R^3=H$ ) or ethyl propiolate (**2b**) ( $R^2=H$ ,  $R^3=Et$ ) under similar conditions to the previous reports (Eq. 4, Table 1).<sup>13</sup> The reaction with 2-naphthol (**1a**) proceeded at room temperature to give coumarin **3a** selectively in high yield (entries 1 and 2). 3,4-Dimethylphenol (**1b**) gave 6,7-dimethylcoumarin (**3b**) and 5,6-dimethylcoumarin (**3c**) in 46

and 31% yields, respectively (entry 3). In the case of 3,5-dimethylphenol (**1c**), (2*Z*)-cinnamic acid derivative **4a** was obtained as the major product along with coumarin **3d** (entry 4). *p*-Cresol (**1d**) also reacted to give 6-methylcoumarin (**3e**) and dihydrocoumarin **5a** although the reaction was slow at room temperature and required higher temperature (entries 5–7). Furthermore, a small amount of dihydrocoumarin **5b** was formed, which might be derived from the further reaction of **5a** and **2a**. The reaction using an excess

**Table 1.** The reaction of propiolic acid (**2a**) or its ethyl ester (**2b**) with phenols **1**<sup>a</sup>

Entry	Phenol	R <sup>3</sup>	Cat. <sup>b</sup>	Temp (°C)	Time (h)	Products and yields/% <sup>c</sup>	
1		H	A	rt	25		86 <sup>d,e</sup>
2		H	B	rt	25		86 <sup>e</sup>
3		Et	A	rt	45		46 <sup>f</sup>
							31 <sup>f</sup>
4		Et	A	rt	26		37
							50
5		Et	A	50	48		35
6		H	C	40	48		51
7		H	C	rt	90		51
							44
							24
							21
8		H	C	40	12		27 <sup>g</sup>
							15 <sup>g</sup>
9		H	C	rt	25		18 <sup>f,h</sup>
							17 <sup>f,h</sup>
10		H	C	40	48		33
11		H	C	40	90		7
							34

<sup>a</sup> Reaction conditions: phenol **1** (4 mmol), **2a** or **2b** (2 mmol), catalyst, and TFA (1 mL).

<sup>b</sup> Catalyst A: PtCl<sub>2</sub> (0.05 mmol) and AgOTf (0.10 mmol). B: K<sub>2</sub>PtCl<sub>4</sub> (0.05 mmol) and AgOTf (0.10 mmol). C: K<sub>2</sub>PtCl<sub>4</sub> (0.02 mmol) and AgOTf (0.08 mmol).

<sup>c</sup> Isolated yields based on **2**.

<sup>d</sup> Compound **1a** (3 mmol) was used.

<sup>e</sup> CH<sub>2</sub>Cl<sub>2</sub> (0.75 mL) was added.

<sup>f</sup> The products were obtained as a mixture of the isomeric coumarins. The product ratios were determined by <sup>1</sup>H NMR.

<sup>g</sup> Compound **1d** (2 mmol) and **2a** (3 mmol) were used.

<sup>h</sup> Compound **5c** was also isolated in 27% yield.

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