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Headline Articles

Pd^{II}-Catalyzed Reaction of Phenols with Propiolic Esters. A Single-Step Synthesis of Coumarins

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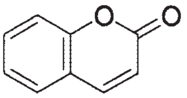
The intermolecular reaction of phenols with propiolic esters in TFA in the presence of a $Pd(OAc)_2$ catalyst, affording coumarin derivatives, is described. An exclusive formation of 5,6,7-trimethoxy-4-phenylcoumarin was observed in the reaction of 3,4,5-trimethoxyphenol and ethyl phenylpropiolate with a catalytic amount of $Pd(OAc)_2$. The reaction in the absence of $Pd(OAc)_2$ did not give any coumarin at all. Coumarin derivatives were obtained in high yields in the cases of electron-rich phenols, such as 3,4-methylenedioxyphenol, 3-methoxyphenol, 2-naphthol, and 3,5-dimethoxyphenol. Furthermore, the reaction of some phenols with various 2-alkynoates or with diethyl acetylenedicarboxylate gave the corresponding coumarins in good-to-high yields.

Coumarin **1** (Fig. 1) and its derivatives occur widely in nature, particularly in plants; most of them show wide biological activities.[1] To date, many synthetic methods for coumarins have been extensively reported,[1] including the Perkin reaction, the Knoevenagel reaction and the Pechmann–Duisberg reaction. The latter method has been widely used to synthesize coumarin derivatives.[2] However, there are still limitations, such as severe reaction conditions, the need for a stoichiometric amount of a condensing agent, and a difficulty to obtain the starting 2-hydroxybenzaldehyde derivatives.

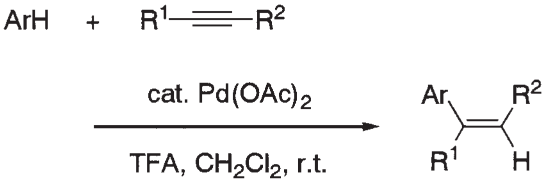
Recently, several studies on coumarin synthesis concerning palladium-catalyzed reactions of phenols have been reported. These involve inter- and intramolecular reactions of 2-iodophenol or its *O*-acyl derivatives in the presence of CO,[3] intramolecular reactions of (2-hydroxyphenyl)alkenes or -alkynes,[4] reactions of phenols and ethyl propioloates,[5] and reactions of 2-iodophenol and alkynes in the presence of CO.[6] In these reactions, however, a Pd(0) species acts as the actual catalyst. To accomplish a catalytic cycle, these reactions need iodides or triflates as substrates,[3,4,6] or formic acid to re-oxidize the Pd(0) species.[5]



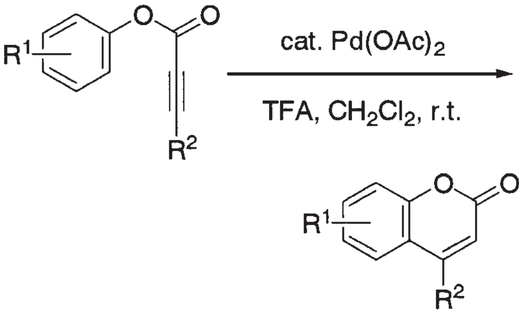
1

Fig. 1.

Very recently, we reported on Pd^{II}-catalyzed hydroarylations of alkynes by simple arenes at room temperature in a mixed solvent containing trifluoroacetic acid (TFA), as shown in Scheme 1.[7] Also, we have demonstrated that the intramolecular hydroarylation of aryl propiolates provides coumarin derivatives in high yields.[7d] This Pd^{II}-catalyzed intramolecular reaction in Scheme 2 proceeds with high efficiency under mild



Scheme 1.



Scheme 2.

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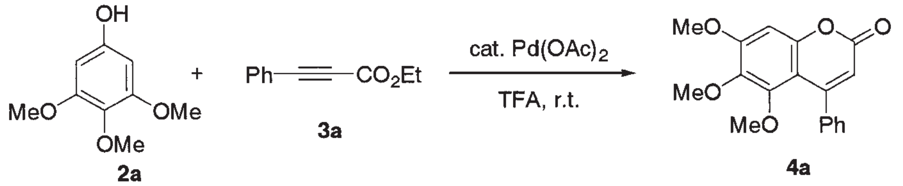
Table 1. Pd^{II}-Catalyzed Reaction of **2a** with **3a**[a)]



Entry	$Pd(OAc)_2$/mmol	**2a**/mmol	**3a**/mmol	Time/h	Yield of **4a**/%[b)]
1	0.025	1	1	6	66
2	0.025	2	1	6	76
3	0.025	1	1.5	6	76
4	0.025	1	2	6	87
5	0	2	1	6	0
6	0.01	2.5	2.5	6	60[c)]
7	0.01	1	2	18	93[d)]
8	0.01	1	1.2	18	91[e)]
9	0.01	1	1.2	6	78[e)]
10	0.01	1	1.2	6	80[f)]

a) All reactions were carried out at room temperature using **2a**, **3a**, $Pd(OAc)_2$, and TFA (1.5 cm^3). b) GC yield based on the least amount of the substrate. c) TFA (3.7 cm^3) and $Pd(OAc)_2$ (0.025 mmol) were used. d) TFA (1.0 cm^3) was used. e) TFA (0.6 cm^3) was used. f) TFA (0.5 cm^3) was used.

conditions. In this reaction, however, the starting aryl propiolates must be prepared by the condensation of propiolic acids and phenols.

If we can synthesize coumarins directly from phenols and propiolic esters without using aryl propiolates, the procedure for coumarin synthesis becomes much simpler and more convenient. We thus examined a direct synthesis of coumarin derivatives from phenols and propiolic esters.

Results and Discussion

Reaction of 3,4,5-Trimethoxyphenol (2a) with Ethyl Phenylpropiolate (3a). We examined the reaction of **2a** with **3a** in TFA to optimize the reaction conditions. A solution of $Pd(OAc)_2$, **2a**, and **3a** in TFA was stirred at room temperature for 6 or 18 h and then neutralized with aqueous $NaHCO_3$. The product, 5,6,7-trimethoxy-4-phenylcoumarin (**4a**), was extracted with CH_2Cl_2 and analyzed by GC. The results are given in Table 1.

An exclusive formation of **4a** was observed in the reaction with a catalytic amount of $Pd(OAc)_2$ (Entries 1–4 and 6–10). The reaction in the absence of $Pd(OAc)_2$ did not give **4a** at all (Entry 5). The reaction using an excess amount of **3a**, rather than **2a**, gave a better yield of **4a** (Entries 2–4). The use of a smaller amount of TFA as the solvent increased the yield of **4a** to 91%, even though the amount of **3a** was reduced to 1.2 equivalent to that of **2a** (Entry 8). This result suggests that a higher concentration of the substrates promotes the reaction effectively.

Reaction of 3a with Various Phenols 2. In order to investigate the scope and limitations of this coumarin synthesis, we examined reactions with various phenols **2**. The results are summarized in Table 2.

Table 2 indicates that coumarins **4** were obtained in high yields in the cases of electron-rich phenols **2**, such as 3,4-methylenedioxyphenol (**2b**), 3-methoxyphenol (**2c**), 2-naphthol (**2d**), and 3,5-dimethoxyphenol (**2e**). In the case of 3,5-dimethoxylphenol (**2e**), a subsequent hydroarylation of **4e** took place to yield 8-(2-ethoxycarbonyl-1-phenylvinyl]-5,7-dimethoxy-4-phenylcoumarin (**5**). This result shows that a coumarin derivative also undergoes the hydroarylation of an alkyne. It is considered to be due to a high concentration of the substrates and an excess amount of alkyne **3a**.

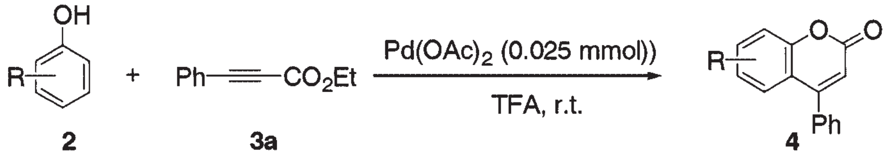
Moderately activated 3,4- and 3,5-dimethylphenols, **2f** and **2g**, were also useful for the hydroarylation of **3a** to give the corresponding coumarins, **4f** and **4g**, in moderate yields, respectively. In the case of 3,5-dimethylphenol (**2g**), interestingly, the hydroarylation of **3a** occurred, even at the *para* position of **2g**, to afford ethyl (*Z*)-3-(4-hydroxy-2,6-dimethylphenyl)cinnamate (**6a**) in 37% yield.

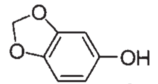
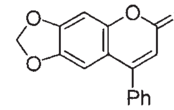
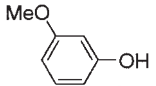
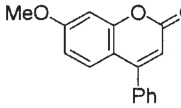
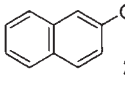
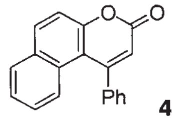
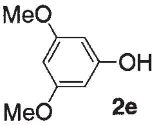
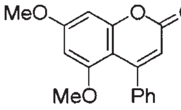
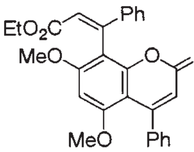
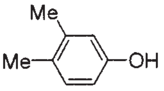
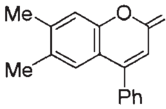
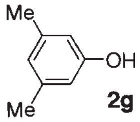
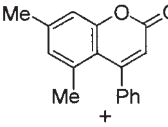
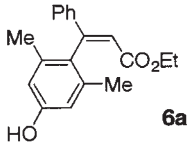
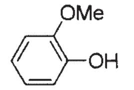
In the reaction of phenols **2**, however, the hydroarylation of **3a** occurred at the *ortho* position of the phenols with extremely high selectivity. In addition, only the less-hindered *ortho* position took part in the hydroarylation during the reactions of phenols **2a**, **2c**, **2d**, and **2f**, which have two possible *ortho* positions. Such a high regioselectivity of phenols favors coumarin synthesis.

Reaction of 2 with Various 2-Alkynoates 3. Furthermore, we examined the reaction of some phenols **2** with various 2-alkynoates **3**, including ethyl propiolate (**3b**), 2-butynoate (**3c**), 2-octynoate (**3d**), and diethyl acetylenedicarboxylate (**3e**). The results are given in Table 3. In the reaction of 3,5-dimethoxyphenol (**2e**), all 2-alkynoates, including ethyl propiolate (**3b**), 2-butynoate (**3c**), and 2-octynoate (**3d**) gave the corresponding coumarins **4** in good-to-high yields (Entries 1–4). 3-Methoxyphenol (**2c**) and 4-methoxyphenol (**2i**) gave the corresponding coumarins **4**, but the yields were low compared with that of **2e** (Entries 6 and 7). Although diethyl acetylenedicarboxylate (**3e**) also reacted with 3,5-dimethoxyphenol (**2e**) to give coumarin **4k** in 47% yield, it was found that coumarin formation competed with hydroarylation at the *para* position of **2e** (Entry 5).

Mechanistic Consideration. We have already reported and discussed the hydroarylation of arenes catalyzed by the Pd^{II} species.[7] In the coumarin synthesis from phenols and pro-

Table 2. Pd^{II}-Catalyzed Reaction of **3a** with Various Phenols **2**[a)]



Entry	Phenol **2**	**2**/mmol	**3a**/mmol	TFA/cm^3	Time/h	Product	Yield/%
1	 **2b**	1	2	1.5	6	 **4b**	60
2	**2b**	1	1.2	0.5	18	**4b**	93[b)]
3	 **2c**	1	2	1.0	20	 **4c**	85
4	 **2d**	2	4	2.0	20	 **4d**	88
5	 **2e**	2	4	0.75	21	 **4e** +  **5**	56 18
6	 **2f**	2	4	0.5	24	 **4f**	44[c)]
7	 **2g**	1	2	1.0	22	 **4g** +  **6a**	35 37
8	 **2h**	2	4	1.0	24	—[d)]	

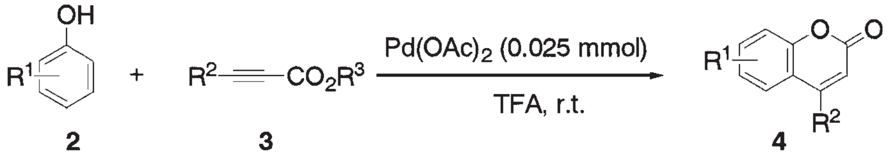
a) All reactions were carried out at room temperature using **2**, **3a**, $Pd(OAc)_2$ (0.025 mmol), and TFA. b) $Pd(OAc)_2$ (0.01 mmol) was used and the yield was determined by GC. c) $Pd(OAc)_2$ (0.05 mmol) was used. d) No coumarins were detected by GC.

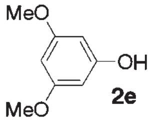
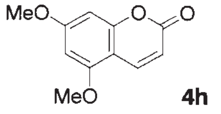
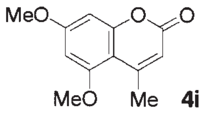
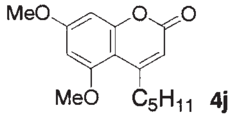
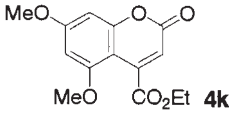
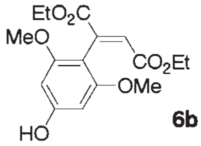
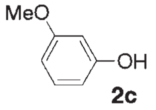
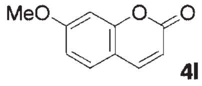
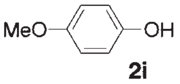
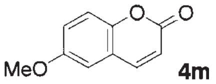
piolates, Trost et al. reported a different catalytic system in formic acid from our reaction.[5] In their reaction, $Pd(OAc)_2$ does not provide the coupling product between phenol **2e** and ethyl propiolate **3b** in acetic acid, but $Pd_2(dba)_3$ affords coumarin **4h** in high yield in formic acid. Therefore, they have concluded that a Pd(0) species acts as the actual catalyst, and that formic acid plays an important role in the catalytic cycle. In our case, a Pd(II) species catalyzed the hydroarylation of 2-alkynoates in TFA. Therefore, no additives were required for this reaction.

Lately, we have reported on coumarin formation by the intramolecular hydroarylation of aryl 2-alkynoates, as shown in Scheme 2. Because this intramolecular process is very efficient, it is supposed that the present reaction involves the intramolecular hydroarylation of aryl 2-alkynoates generated in situ by transesterification of 2-alkynoates with phenols.

We then examined whether aryl 2-alkynoates are formed or not during coumarin formation. In the reaction of **3a** with phenols **2a** and **2c**, the formation of aryl 2-alkynoates **7a** and **7b**

Table 3. Pd^{II}-Catalyzed Reaction of **2** with Various 2-Alkynoates **3**[a)]



Entry	Phenol **2**	**2** mmol	2-Alkynoate **3**	R^2	R^3	**3** mmol	TFA cm^3	Time h	Product	Isolated Yield/%
1	 **2e**	2	**3b**	H	Et	3	1.0	18	 **4h**	59
2	**2e**	2	**3c**	Me	Et	3	1.0	20	 **4i**	97
3	**2e**	2	**3d**	n-C_5H_{11}	Me	3	1.0	21	 **4j**	60
4	**2e**	2	**3d**	n-C_5H_{11}	Me	3	1.0	77	**4j**	96[b)]
5	**2e**	2	**3e**	EtO_2C	Et	3	1.0	66	 **4k**	47
									 **6b**	20
6	 **2c**	2	**3b**	H	Et	4	1.5	37	 **4l**	34
7	 **2i**	2	**3b**	H	Et	4	1.5	37	 **4m**	24

a) All reactions were carried out at room temperature using **2**, **3**, $Pd(OAc)_2$ (0.025 mmol), and TFA. b) GC yield.

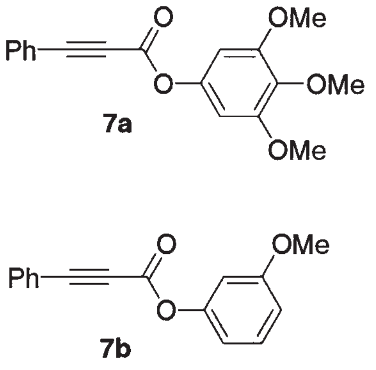
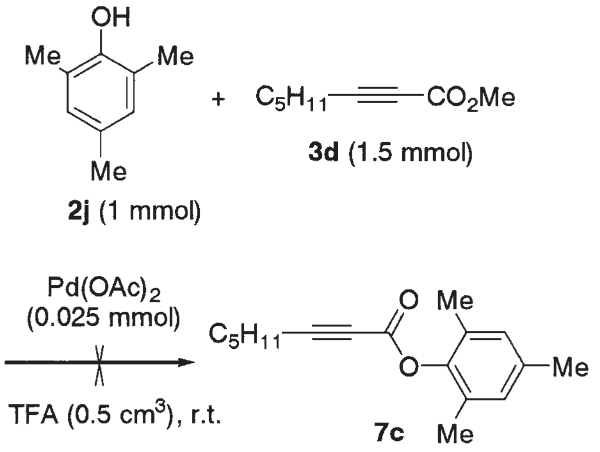
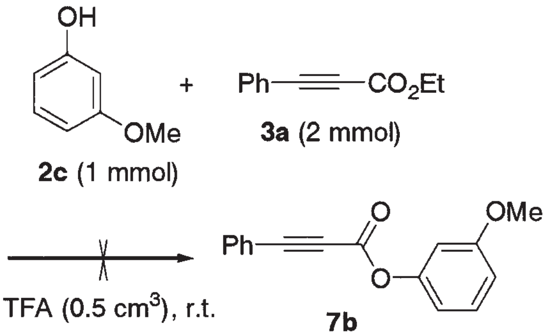

7a
7b

Fig. 2.



Scheme 3.

(Fig. 2) was checked, respectively. However, no aryl 2-alkynoates, **7a** and **7b**, were detected under the reaction conditions employed in the coumarin synthesis. Even in the case of the phenol blocked at the *ortho* position with a substituent, no aryl 2-alkynoates were formed. For example, the reaction of 2,4,6-trimethylphenol (**2j**) with methyl 2-octynoate (**3d**) in the presence of $Pd(OAc)_2$ (0.025 mmol) in TFA did not give the corresponding 2,4,6-trimethylphenyl 2-octynoate (**7c**) at all (Scheme 3). Similarly, the ester exchange of 3-methoxyphenol



Scheme 4.

(**2c**) and ethyl phenylpropiolate (**3a**) did not undergo in TFA without Pd(OAc)$_2$, and the starting materials were recovered unchanged (Scheme 4).

We could not obtain any evidence for the intervention of aryl 2-alkynoates **7** in coumarin formation. Therefore, at the present time, we consider that a possible mechanism for coumarin formation from phenols and 2-alkynoates involves the *ortho* palladation of a phenol by a Pd(II) species, probably Pd(OCOCF$_3$)$_2$, followed by the hydroarylation of an alkynoate, and finally cyclization (intramolecular transesterification) to afford a coumarin, as shown in Scheme 5.

In a few cases, we observed the products produced by the hydroarylation of 2-alkynoates **3** arising from the *para* palladation of phenols **2** (Table 2, Entry 7 and Table 3, Entry 5). A mechanism proposed by Trost et al.[5] cannot explain the formation of these products. Furthermore, the reaction of an aryl methyl ether and ethyl phenylpropiolate, giving a hydroarylation product, supports our mechanism.[7]

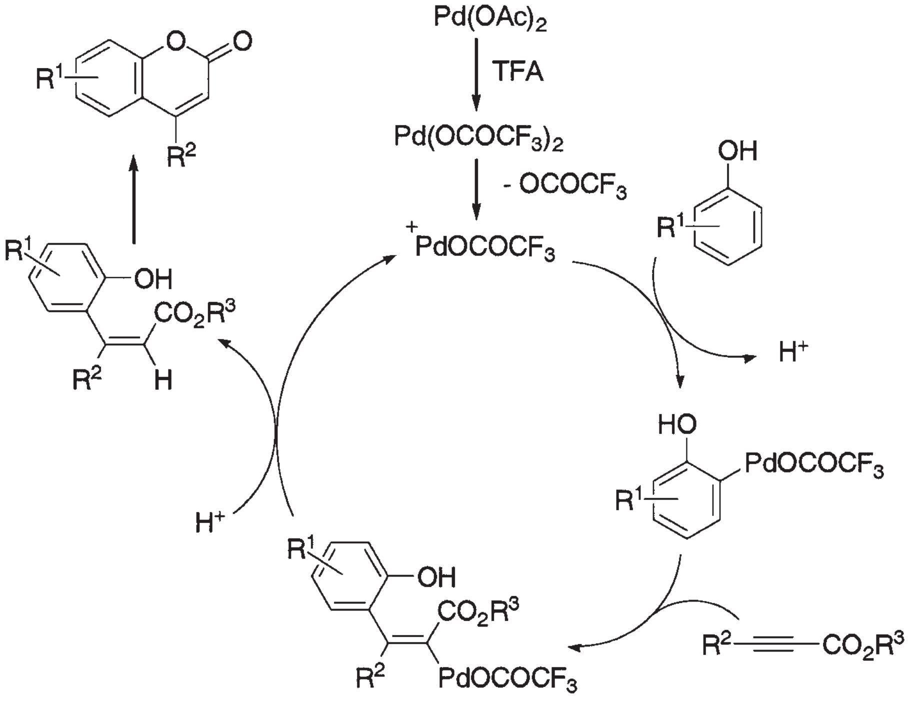
In the sulfonation of phenol by 77.8 wt % H$_2$SO$_4$ at 25 °C, *ortho* and *para* partial rate factors are 3400 and 7300, respectively.[8] This means that the *ortho*/*para* selectivity is low. In the present case, most phenols employed in this study showed a high *ortho* selectivity for the hydroarylation, suggesting that a Pd species may be stabilized by coordination with the oxygen atom.[9]

Conclusion

We have demonstrated a simple and direct synthesis of coumarins from phenols and propiolic esters by using Pd(OAc)$_2$ as an efficient catalyst. This process involves the hydroarylation of propiolic esters and subsequent cyclization to coumarins. This reaction proceeds at room temperature and does not need any additives or special conditions, such as an inert atmosphere. Because of its simplicity and convenience, the present method will be widely utilized. This method is especially useful for alkoxy-substituted coumarin derivatives, most of which show biological activities.

Experimental

General. All of the reactions were performed in a Pyrex tube with a glass cap under an ambient atmosphere. The regio- and stereochemistry of the product were determined by differential NOE experiments. Analytical GLC evaluations of the product mixtures were performed with a Shimadzu GC-17A having a flame ionization detector using a 30 m × 0.25 mm capillary column (DB-1-30N-STD, J&W Scientific) under the conditions of the injection temperature (280 °C) and the detector temperature (280 °C). A GC/MS analysis was performed with a Shimadzu GCMS-QP5050A. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-A1300 spectrometer, and the chemical shifts were expressed in parts per million downfield from tetramethylsilane. IR spectra were obtained on a HORIBA FT-200 spectrometer. The melting points were measured with a YANACO micro-melting apparatus, and were not corrected. Elemental analyses were conducted by the Service Center of the Elemental Analysis of Organic Compounds, Faculty of Science, Kyushu University.



Scheme 5.

Palladium(II) acetate was prepared from a palladium sponge and acetic acid according to a method of Wilkinson et al.[11] All chemicals were used as received without further purification.

Pd^{II}-Catalyzed Reaction of 3,4,5-Trimethoxyphenol (2a) and Ethyl Phenylpropiolate (3a) in TFA. To a cold mixture of $Pd(OAc)_2$, 3,4,5-trimethoxyphenol (**2a**), and TFA in an ice/water bath was added ethyl phenylpropiolate (**3a**). After stirring at the same temperature for 5 min, the mixture was stirred at room temperature for an appropriate time, described in Table 1. The reaction mixture was then neutralized with an aqueous $NaHCO_3$ solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4, and concentrated. Flash column chromatography on silica gel with hexane and ethyl acetate as an eluent gave 5,6,7-trimethoxy-4-phenylcoumarin (**4a**)[7d] as colorless crystals. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.26 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.94 (s, 3 H, OMe), 6.07 (s, 1H, =CH), 6.73 (s, 1H, ArH), 7.34 (m, 2H, Ph), 7.40 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 56.22, 60.88, 61.01, 96.23, 107.23, 114.02, 127.17, 127.46, 127.98, 138.98, 139.41, 151.04, 151.64, 155.35, 156.86, 160.58. IR (KBr, cm^{-1}) 1726 (C=O).

General Procedure for Synthesis of Coumarins 4. To a cold mixture of $Pd(OAc)_2$, a phenol **2**, and TFA in an ice/water bath was added 2-alkynoate **3**. After stirring at 0 °C for 5 min, the mixture was stirred at room temperature under the conditions described in Tables 2 and 3. The reaction mixture was then neutralized with an aqueous $NaHCO_3$ solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4, and concentrated. Flash column chromatography on silica gel with hexane and ethyl acetate as an eluent gave a coumarin **4**.

6,7-Methylenedioxy-4-phenylcoumarin (4b). Mp 144–146 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.05 (s, 2 H, OCH_2O), 6.24 (s, 1H, =CH), 6.83 (s, 1H, ArH), 6.90 (s, 1 H, ArH), 7.43 (m, 2H, Ph), 7.52 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 98.56, 102.34, 104.35, 112.21, 112.84, 128.22, 128.87, 129.58, 135.66, 144.81, 151.13, 151.33, 155.87, 161.17. IR (KBr, cm^{-1}) 1708 (C=O). Anal. Calcd for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79%. Found: C, 72.38; H, 3.81%.

7-Methoxy-4-phenylcoumarin (4c). Mp 110–111 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.89 (s, 3H, OMe), 6.23 (s, 1H, =CH), 6.80 (dd, $J = 2.7$, 9.0 Hz, 1H, ArH), 6.90 (d, $J = 2.7$ Hz, 1H, ArH), 7.40 (d, $J = 9.0$ Hz, 1 H, ArH), 7.45 (m, 2H, Ph), 7.51 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 55.79, 101.05, 111.85, 112.33, 112.50, 127.97, 128.36, 128.81, 129.57, 135.55, 155.82, 156.00, 161.24, 162.78. IR (KBr, cm^{-1}) 1733 (C=O). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79%. Found: C, 76.02; H, 4.88%.

1-Phenyl-3*H*-naphtho[2,1-*b*]pyran-3-one (4d). Mp 159–161 °C (MeOH). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (s, 1H, =CH), 7.13–7.54 (m, 9H, ArH), 7.85 (d, $J = 8.1$ Hz, 1H, ArH), 8.01 (d, $J = 9$ Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 112.99, 116.77, 117.45, 125.35, 125.87, 126.68, 127.41, 128.98, 129.12, 129.20, 129.28, 131.26, 133.94, 139.51, 154.71, 156.46, 160.36. IR (KBr, cm^{-1}) 1726 (C=O). Anal. Calcd for $C_{19}H_{12}O_2$: C, 83.81; H, 4.44%. Found: C, 83.56; H, 4.46%.

5,7-Dimethoxy-4-phenylcoumarin (4e). Mp 168–170 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.43 (s, 3H, OMe), 3.87 (s, 3H, OMe), 6.01 (s, 1H, =CH), 6.23 (d, $J = 2.1$ Hz, 1H, ArH), 6.53 (d, $J = 2.1$ Hz, 1H, ArH), 7.27 (m, 2H, Ph), 7.38 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 55.37, 55.76, 93.50, 95.73, 103.51, 112.66, 127.08, 127.33, 127.88, 139.73, 155.67, 157.14, 158.18, 160.88, 163.32. IR (KBr, cm^{-1}) 1716 (C=O). Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00%. Found: C, 72.21; H, 5.01%.

8-(2-Ethoxycarbonyl-1-phenylvinyl)-5,7-dimethoxy-4-phenylcoumarin (5). Mp 185–187 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.19 (t, $J = 7.2$ Hz, 3H, Me), 3.49 (s, 3H, OMe), 3.78 (s, 3H, OMe), 4.07 (q, $J = 7.2$ Hz, 2H, OCH_2), 5.94 (s, 1H, =CH), 6.34 (s, 1H, ArH), 6.64 (s, 1H, =CH), 7.30–7.40 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.08, 55.28, 56.03, 59.82, 91.28, 103.13, 108.87, 112.79, 120.28, 126.81, 127.02, 127.25, 127.67, 128.39, 129.24, 139.11, 139.97, 147.24, 152.81, 155.43, 158.12, 159.72, 160.42, 165.33. IR (KBr, cm^{-1}) 1720 (C=O). Anal. Calcd for $C_{28}H_{24}O_6$: C, 73.67; H, 5.30%. Found: C, 73.61; H, 5.31%. The stereochemistry was determined by NOE experiment.

6,7-Dimethyl-4-phenylcoumarin (4f). Mp 142.5–145.5 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.23 (s, 3H, Me), 2.36 (s, 3H, Me), 6.29 (s, 1H, =CH), 7.19 (s, 1H, ArH), 7.20 (s, 1H, ArH), 7.45 (m, 2H, Ph), 7.53 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.32, 20.15, 114.06, 116.58, 117.80, 126.88, 128.37, 128.77, 129.48, 132.90, 135.54, 142.00, 152.56, 155.59, 161.24. IR (KBr, cm^{-1}) 1714 (C=O). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64%. Found: C, 81.37; H, 5.67%.

5,7-Dimethyl-4-phenylcoumarin (4g).[7d] Mp 93.5–95 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.79 (s, 3H, Me), 2.39 (s, 3H, Me), 6.18 (s, 1H, =CH), 6.81 (s, 1H, ArH), 7.08 (s, 1H, ArH), 7.29 (m, 2H, Ph), 7.45 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.27, 23.29, 115.42, 115.75, 116.06, 127.29, 128.50, 128.66, 129.45, 137.00, 139.53, 142.31, 155.12, 156.73, 160.49. IR (KBr, cm^{-1}) 1726 (C=O).

Ethyl (*Z*)-3-(4-Hydroxy-2,6-dimethylphenyl)-3-phenylpropenoate (6a). Mp 170–171 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15 (t, $J = 7.2$ Hz, 3H, Me), 2.01 (s, 6 H, Me), 4.07 (q, $J = 7.2$ Hz, 2H, OCH_2), 4.81 (s, 1H, OH), 6.53 (s, 2H, ArH), 6.64 (s, 1H, =CH), 7.34 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.01, 19.90, 60.19, 114.24, 117.68, 126.98, 128.66, 129.59, 130.29, 136.37, 138.52, 154.81, 155.40, 166.27. IR (KBr, cm^{-1}) 3293 (OH), 1672 (C=O). Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80%. Found: C, 76.93; H, 6.80%. The stereochemistry was determined by NOE experiment.

5,7-Dimethoxycouamrin (4h). Mp 140.5–142 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 3H, OMe), 3.89 (s, 3H, OMe), 6.16 (d, $J = 9.9$ Hz, 1H, =CH), 6.29 (d, $J = 2.1$ Hz, 1H, ArH), 6.42 (d, $J = 2.1$ Hz, 1H, ArH), 7.97 (d, $J = 9.9$ Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 55.77, 55.91, 92.76, 94.79, 103.97, 110.91, 138.71, 156.78, 156.94, 161.51, 163.67. IR (KBr, cm^{-1}) 1726 (C=O). Anal. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89%. Found: C, 63.88; H, 4.98%.

5,7-Dimethoxy-4-methylcoumarin (4i). Mp 170.5–172 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.53 (d, $J = 1.2$ Hz, 3H, Me), 3.85 (s, 3H, OMe), 3.86 (s, 3H, OMe), 5.95 (d, $J = 1.2$ Hz, 1H, =CH), 6.29 (d, $J = 2.4$ Hz, 1H, ArH), 6.44 (d, $J = 2.4$ Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.18, 55.67, 55.71, 93.35, 95.42, 104.87, 111.36, 154.46, 156.98, 159.10, 161.07, 162.75. IR (KBr, cm^{-1}) 1729 (C=O). Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49%. Found: C, 65.28; H, 5.48%.

5,7-Dimethoxy-4-pentylcoumarin (4j). Mp 102–103 °C (CH_2Cl_2/hexane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (m, 3H, Me), 1.37 (m, 4H, $2CH_2$), 2.38 (m, 2H, CH_2), 2.86 (m, 2H, CH_2), 3.84 (s, 3H, OMe), 3.87 (s, 3H, OMe), 5.96 (s, 1H, =CH), 6.30 (s, 1H, ArH), 6.45 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.00, 22.44, 29.31, 31.80, 36.48, 55.63, 55.72, 93.55, 95.49, 104.23, 110.56, 157.27, 158.53, 158.59, 161.25, 162.56. IR (KBr, cm^{-1}) 1718 (C=O). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30%. Found: C, 69.56; H, 7.34%.

4-Ethoxycarbonyl-5,7-dimethoxycoumarin (4k). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.40 (t, $J = 7.2$ Hz, 3H, Me), 3.85 (s, 3H, OMe), 3.87 (s, 3H, OMe), 4.40 (q, $J = 7.2$ Hz, 2H, OCH_2), 6.09 (s, 1H, =CH), 6.31 (s, 1H, ArH), 6.48 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.15, 55.89, 56.33, 62.15, 93.62, 95.66, 100.57, 109.37, 145.33, 156.63, 157.01, 160.26, 164.13, 166.46. IR (KBr, cm^{-1}) 1733 (C=O). Anal. Calcd for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07%. Found: C, 60.40; H, 5.14%.

Ethyl (*Z*)-3-Ethoxycarbonyl-3-(4-hydroxy-2,6-dimethoxyphenyl)propenoate (6b). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.19 (t, $J = 7.2$ Hz, 3H, Me), 1.27 (t, $J = 7.2$ Hz, 3H, Me), 3.66 (s, 6H, OMe), 4.12 (q, $J = 7.2$ Hz, 2H, OCH_2), 4.24 (q, $J = 7.2$ Hz, 2H, OCH_2), 5.94 (s, 2H, ArH), 6.27 (bs, 1H, OH), 6.87 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.97, 14.07, 55.43, 60.62, 61.61, 92.23, 104.02, 128.25, 138.21, 158.10, 159.00, 166.27, 168.17. IR (KBr, cm^{-1}) 3405 (OH), 1720 (C=O). This sample did not give a satisfactory analysis because of the presence of inseparable impurities.

7-Methoxycoumarin (4l). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.88 (s, 3H, OMe), 6.26 (d, $J = 9.6$ Hz, 1H, =CH), 6.92 (d, $J = 2.7$ Hz, 1H, ArH), 7.11 (dd, $J = 2.7$, 8.9 Hz, 1H, ArH), 7.38 (d, $J = 8.9$ Hz, 1H, ArH), 7.65 (d, $J = 9.6$ Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 55.75, 100.77, 112.47, 112.58, 113.04, 128.72, 143.43, 155.86, 161.21, 162.78. IR (KBr, cm^{-1}) 1712 (C=O). Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58%. Found: C, 68.08; H, 4.69%.

6-Methoxycoumarin (4m). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 3H, OMe), 6.43 (d, $J = 9.3$ Hz, 1H, =CH), 6.92 (d, $J = 2.7$ Hz, 1H, ArH), 7.11 (dd, $J = 2.7$, 9.3 Hz, 1H, ArH), 7.27 (d, $J = 2.7$ Hz, 1H, ArH), 7.67 (d, $J = 9.3$ Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 55.77, 109.91, 117.02, 117.84, 119.11, 119.43, 143.21, 148.38, 156.00, 160.99. IR (KBr, cm^{-1}) 1700 (C=O). Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58%. Found: C, 68.06; H, 4.59%.

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9 A referee has suggested the intermediacy of an ArO–Pd species. Although Trost et al. favor a mechanism involving a palladium(0) and a hydridopalladium phenoxide, we cannot abandon a mechanism depicted in Scheme 5 for the following reasons. (i) Coumarin formation readily takes place in case of electron-rich phenols. According to Trost's mechanism, the coumarin formation should be independent or weakly dependent upon the substituent of phenols. (ii) A phenoxide complex suggested by Trost et al. is supposed to be difficult to form easily under our reaction system (in a strong acid, TFA). (iii) Although there is a possibility that a phenoxide complex undergoes O-alkenylation of phenols,[11] we have not observed any products derived from O-alkenylation of phenols.

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