Improved Synthesis of Coumarins by Iron(III)-Catalyzed Cascade Reaction of Propiolic Acids and Phenols

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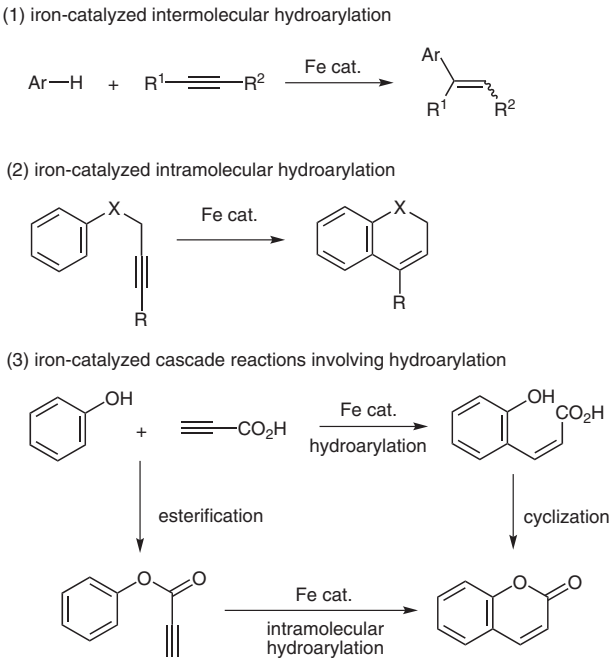
Abstract: The reaction of propiolic acids with phenols in the presence of $FeCl_3$/AgOTf catalyst proceeded efficiently in a mixed solvent of trifluoroacetic acid and 1,2-dichloroethane, and provided coumarins in good to high yields. This iron-catalyzed reaction offers a much-improved synthesis of coumarins.

Key words: iron, hydroarylation, coumarins, propiolic acids, propynoic acids, phenols

Coumarin and its derivatives occur widely in nature and most of them show biological activity.[1] To date, many reactions for coumarin synthesis have been reported,[1] including various named reactions such as the Perkin, Knoevenagel, and Pechmann reactions. Recently, many methods for coumarin synthesis using transition-metal catalysts have also been developed.[2–11] However, most synthetic methods require halogenated substrates such as iodophenols and iodoarenes for the construction of the coumarin skeleton. These synthetic reactions involve bond cleavage of the carbon–halogen bonds by transition metals and produce waste halides. Judging from the atom-economy of the reaction, the use of halogenated substrates is not desirable. If the direct construction of a C–C bond from the C–H bond of a simple arene is possible, this strategy would be a straightforward and efficient process.

Trost and Toste have developed an atom-economic synthesis of coumarins from the reaction of propiolic acids and phenols in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ or $Pd(OAc)_2$ catalyst in formic acid.[7] We have reported the hydroarylation of alkynes with the aid of palladium or platinum catalysts in trifluoroacetic acid[10] and expanded this to the synthesis of coumarins by the reaction of propiolates with phenols.[9a–f] Shi et al. also reported the synthesis of coumarins by the intramolecular reaction of aryl propiolates with $AuCl_3$/AgOTf catalyst.[8]

Iron is an abundant, inexpensive, readily available, nontoxic, and environmentally friendly transition metal, and it shows increasing and promising catalytic ability in many organic syntheses.[12] Until now, however, little attention has been paid to iron as a catalyst for hydroarylation reactions of alkynes. Recently, as an example of intermolecular hydroarylation [Scheme 1, (1)], Lu and coworkers reported the hydroarylation reaction of aryl-substituted alkynes with simple and substituted arenes in the presence of iron(III) chloride in nitromethane without using additives under mild conditions.[13] Aryl-substituted alkynes undergo hydroarylation with electron-rich arenes to afford 1,1-diarylalkenes. To conduct more efficiently the hydroarylation reaction of an electron-deficient propiolic acid, we decided to use iron(III) chloride activated with silver(I) triflate and found that the hydroarylation of propiolic acid with arenes proceeded intermolecularly to give cinnamic acids under catalytic conditions.[14]



Scheme 1

The intramolecular hydroarylation of alkynes occurs effectively [Scheme 1, (2)].[15] Very recently, Komeyama and Takaki demonstrated that iron(III) triflate catalyzes the intramolecular hydroarylation of aryl-substituted alkynes.[15b] Inspired by these successful iron-catalyzed intermolecular and intramolecular reactions, we decided to explore further successive cascade pathways to obtain coumarin derivatives directly from phenols and propiolic acids [Scheme 1, (3)], where there are two possible routes: hydroarylation/cyclization and esterification/intramolecular hydroarylation. Herein, we report for the

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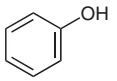
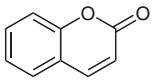
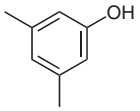
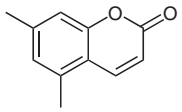
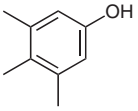
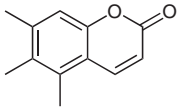
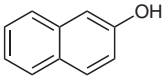
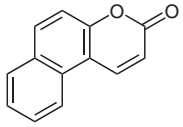
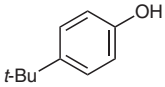
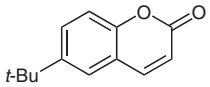
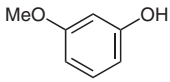
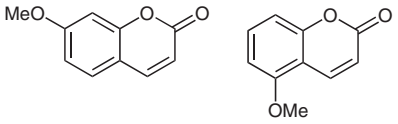
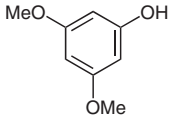
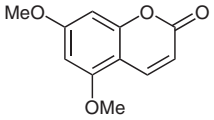
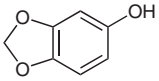
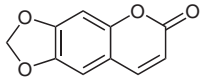
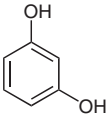
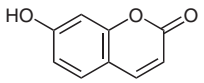
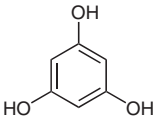
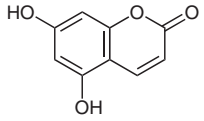
Table 1 Iron-Catalyzed Reaction of **2a** with **1a–j** (Scheme 2)[a]

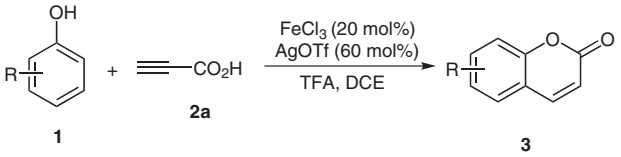
Entry	Phenol **1**	DCE (mL)	Coumarin **3**	Yield[b] (%)	Yield[c] (%) of Pd-catalyzed reaction
1	 **1a**	0.5	 **3a**	33	–
2	 **1b**	0.5	 **3b**	85	49
3[d]	 **1c**	0.5	 **3c**	88	–
4	 **1d**	1	 **3d**	93	67
5	 **1e**	0.5	 **3e**	62	–
6[e]	 **1f**	0.5	 **3f** + **3g** (**3f**/**3g** 79:21)[f]	84	25
7[e]	 **1g**	0.5	 **3h**	65	42
8[e]	 **1h**	0.5	 **3i**	60	53
9[e]	 **1i**	0.5	 **3j**	59	–
10[e]	 **1j**	0.5	 **3k**	95	–

[a] Reaction conditions: $FeCl_3$ (0.4 mmol), AgOTf (1.2 mmol), **1** (4 mmol), **2a** (2 mmol), TFA (0.5 mL), DCE, 60 °C, 15 h.
[b] Isolated yield.
[c] Yield from the previous Pd-catalyzed reaction, see ref. 9d.
[d] **1c** (2 mmol) was used.
[e] The reaction was conducted at 30 °C.
[f] The product ratio was determined by ^{1}H NMR. Coumarins **3f** and **3g** were separated by column chromatography (silica gel).

first time the iron-catalyzed cascade reaction of propiolic acids with phenols directed to the synthesis of coumarins.

As we have already identified good conditions for the iron-catalyzed hydroarylation of propiolic acids in previous studies,[14] the choice of similar conditions was also desirable in this study. Thus, we examined the reaction of phenols **1** and propiolic acid (**2a**) in the presence of $FeCl_3$/AgOTf catalyst in a mixed solvent of trifluoroacetic acid and 1,2-dichloroethane (Scheme 2); the results are given in Table 1.

First, we investigated the reaction of phenol (**1a**) and propiolic acid (**2a**). When the reaction of **1a** (4 mmol) with **2a** (2 mmol) in trifluoroacetic acid (0.5 mL) and 1,2-dichloroethane (0.5 mL) was conducted in the presence of iron(III) chloride (0.4 mmol) and silver(I) triflate (1.2 mmol) at 60 °C for 15 hours, coumarin (**3a**) was obtained in 33% yield (entry 1). The reaction of **2a** with 3,5-dimethylphenol (**1b**) and 3,4,5-trimethylphenol (**1c**) proceeded efficiently to give the corresponding coumarins **3b** and **3c** in 85 and 88% yields, respectively (entries 2 and 3). In the reaction with 2-naphthol (**1d**), coumarin **3d** was obtained in 93% yield (entry 4). A bulky 4-*tert*-butylphenol (**1e**) afforded the corresponding coumarin **3e** in 62% yield (entry 5). In the case of alkoxyphenols, the reaction was carried out at 30 °C because these phenols were reactive and did not give good yields of the products when the reaction was performed at 60 °C. The reaction with 3-methoxyphenol (**1f**) afforded a mixture (79:21) of regioisomers, 7-methoxycoumarin (**3f**) and 5-methoxycoumarin (**3g**), in 84% yield (entry 6). The reaction with 3,5-dimethoxyphenol (**1g**) and 3,4-(methylenedioxy)phenol (**1h**) yielded the corresponding coumarins **3h** and **3i** in 65 and 60% yields, respectively (entries 7 and 8). Similarly, 1,3-dihydroxybenzene (**1i**) and 1,3,5-trihydroxybenzene (**1j**) efficiently reacted with **2a** to give the corresponding coumarins **3j** and **3k** in 59 and 95% yields, respectively (entries 9 and 10).

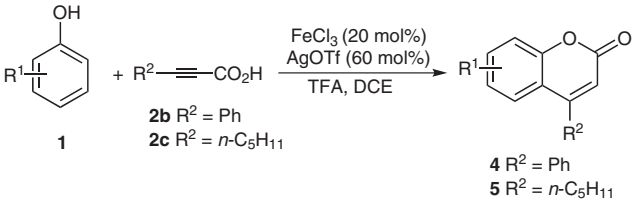


Scheme 2

To understand the efficiency of iron-catalyzed coumarin synthesis, we compared these results with those from the previous palladium-catalyzed reaction of **2a** with **1** in trifluoroacetic acid.[9d] It is clearly understood that the present iron-catalyzed reaction gives better yields of coumarins **2** than that catalyzed by palladium.

We next examined the reaction of substituted propiolic acids with phenols. Under the conditions described above, phenylpropiolic acid (**2b**) and oct-2-ynoic acid (**2c**) were subjected to reaction with phenols **1** in the presence of iron(III) chloride and silver(I) triflate (Scheme 3); the results are given in Table 2. In the reaction of **2b** with phenols **1b** and **1d**, the corresponding 4-phenylcoumarins **4a** and **4b** were obtained in 80 and 90% yields, respectively (entries 1 and 2). For 3-methoxyphenol (**1f**), the reaction proceeded regioselectively to give 7-methoxy-4-phenylcoumarin (**4c**) in 75% yield (entry 3). The reaction of **2b** with **1g** gave the corresponding coumarin **4d** in 62% yield (entry 4). Aliphatic oct-2-ynoic acid (**2c**) underwent the same reaction with **1d** and **1g** to give the corresponding coumarins **5a** and **5b** in 87 and 68% yields, respectively (entries 5 and 6).

The iron-catalyzed reaction using substituted propiolic acids similarly showed improved yields of coumarins compared with the previous palladium-catalyzed examples.

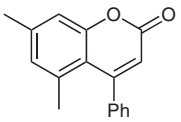
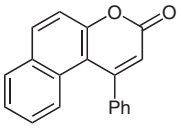
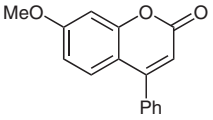
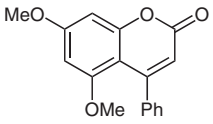
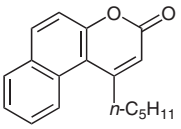
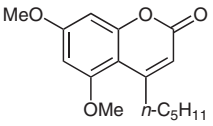


Scheme 3

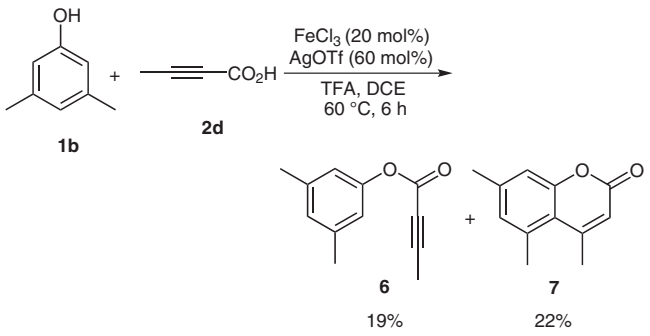
Although the mechanism for the generation of coumarins by the iron catalyst is not clear at present, two pathways may exist from propiolic acids and phenols: (1) intermolecular hydroarylation followed by cyclization, and (2) esterification followed by intramolecular hydroarylation (Scheme 1). As we have already reported,[14] intermolecular hydroarylation of propiolic acid with arenes occurs in the presence of iron catalysts. However, although the yield was low, an aryl propiolate was formed. When the $FeCl_3$/AgOTf-catalyzed reaction of but-2-ynoic acid (**2d**) with 3,5-dimethylphenol (**1b**) was conducted in trifluoroacetic acid and 1,2-dichloroethane at 60 °C for six hours, 3,5-dimethylphenyl but-2-ynoate (**6**) was obtained in 19% yield, together with 4,5,7-trimethylcoumarin (**7**) in 22% yield (Scheme 4). Although this result suggested the esterification/intramolecular hydroarylation process, it was found that the esterification did not proceed efficiently under these conditions because the reaction of propanoic acid with **1b** gave the corresponding 3,5-dimethylphenyl propanoate only in 22% yield ($FeCl_3$/AgOTf, 60 °C, 15 h). In the $FeCl_3$/AgOTf-catalyzed reaction of propiolic acids and phenols, therefore, we propose that the intermolecular hydroarylation/cyclization process occurs along with the esterification/intramolecular hydroarylation process.

In summary, we have demonstrated that iron-catalyzed hydroarylation can be applied to the direct synthesis of coumarin derivatives from phenols and propiolic acids. The reaction of propiolic acids with phenols in the presence of $FeCl_3$/AgOTf catalyst proceeds efficiently in a mixed solvent of trifluoroacetic acid and 1,2-dichloroethane and provides coumarins in good to high yields. The present iron-catalyzed coumarin synthesis is expected to have a high degree of utility for a variety of coumarin de-

Table 2 Iron-Catalyzed Reaction of **2b**,**c** with **1b**,**d**,**f**,**g** (Scheme 3)[a]

Entry	1	2	DCE (mL)	Coumarin 3	Yield (%)[b]	Yield[c] (%) of Pd-catalyzed reaction
1	**1b**	**2b**	0.5	 **4a**	80	–
2	**1d**	**2b**	1	 **4b**	90	69
3	**1f**	**2b**	0.5	 **4c**	75	65
4	**1g**	**2b**	0.5	 **4d**	62	44
5	**1d**	**2c**	1	 **5a**	87	–
6	**1g**	**2c**	0.5	 **5b**	68	57

[a] Reaction conditions: $FeCl_3$ (0.4 mmol), AgOTf (1.2 mmol), **1** (4 mmol), **2** (2 mmol), TFA (0.5 mL), DCE, 60 °C, 15 h.
[b] Isolated yield.
[c] Yield from the previous Pd-catalyzed reaction, see ref. 9d.



Scheme 4

rivatives because it is a highly efficient and economical process.

All solvents and starting materials were commercially available and used as received without further purification. ^1H and ^{13}C NMR spectra were recorded on a Jeol JNM-AL 300 FT-NMR spectrometer (TMS as an internal standard). Melting points were measured with a Yanaco micro melting point apparatus and are uncorrected. Column chromatographic separation was carried out using Silica Gel 60, spherical (Kanto Chemical Co.).

Coumarins by $FeCl_3$/AgOTf-Catalyzed Reaction of Propiolic Acids with Phenols; General Procedure

A mixture of $FeCl_3$ (0.4 mmol) and AgOTf (1.2 mmol) in TFA (0.5 mL) and DCE (0.5–1 mL) was stirred at r.t. for 10 min and then phenol **1** (4 mmol) and propiolic acid **2** (2 mmol) were added and the mixture was stirred at 60 °C or 30 °C for 15 h. The mixture was poured into H_2O (20 mL), neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was washed with 2 M NaOH (10 mL), dried (anhyd Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc–hexane) to give coumarins **3**, **4a**–**d**, or **5a**,**b** as solids, which were recrystallized from the solvents indicated.

Coumarin (3a)[9e,16,17]

Mp 66–67 °C (hexane).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.43 (d, *J* = 9.6 Hz, 1 H, vinyl), 7.28–7.36 (m, 2 H, aryl), 7.47–7.57 (m, 2 H, aryl), 7.71 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 116.67, 116.85, 118.81, 124.38, 127.83, 131.78, 143.38, 154.04, 160.71.

5,7-Dimethylcoumarin (3b)[9e,d,18,19]
Mp 133–135 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 2.48 (s, 3 H, CH_3), 6.35 (d, *J* = 9.6 Hz, 1 H, vinyl), 6.92 (s, 1 H, aryl), 6.98 (s, 1 H, aryl), 7.87 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.06, 21.56, 114.57, 114.91, 115.22, 126.90, 135.61, 140.30, 142.65, 154.64, 161.03.

5,6,7-Trimethylcoumarin (3c)[20]
Mp 159–160 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 6.32 (d, *J* = 9.9 Hz, 1 H, vinyl), 6.97 (s, 1 H, aryl), 7.95 (d, *J* = 9.9 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.80, 15.42, 114.47, 115.31, 115.54, 131.45, 133.44, 140.92, 141.64, 152.42, 161.10.

3*H*-Naphtho[2,1-*b*]pyran-3-one (3d)[7b,9d,e,16]
Mp 117–118 °C (EtOAc–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.59 (d, *J* = 9.6 Hz, 1 H, vinyl), 7.47 (d, *J* = 9.0 Hz, 1 H, aryl), 7.58 (dd, *J* = 6.9, 8.1 Hz, 1 H, vinyl), 7.70 (dd, *J* = 6.9, 8.4 Hz, 1 H, aryl), 7.92 (d, *J* = 8.1 Hz, 1 H, aryl), 8.00 (d, *J* = 9.0 Hz, 1 H, aryl), 8.24 (d, *J* = 8.4 Hz, 1 H, aryl), 8.50 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.79, 115.44, 116.86, 121.20, 125.94, 128.16, 128.83, 128.87, 130.10, 132.95, 138.91, 153.67, 160.74.

6-*tert*-Butylcoumarin (3e)[1b]
Mp 66–67 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9 H, CH_3), 6.41 (d, *J* = 9.6 Hz, 1 H, vinyl), 7.27 (d, *J* = 8.9 Hz, 1 H, aryl), 7.46 (d, *J* = 2.3 Hz, 1 H, aryl), 7.58 (dd, *J* = 2.3, 8.9 Hz, 1 H, aryl), 7.72 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.24, 34.43, 116.26, 116.31, 118.16, 124.08, 129.43, 143.89, 147.48, 151.93, 161.12.

7-Methoxycoumarin (3f)[7b,9c–e]
Mp 117–119 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.38 (s, 3 H, OCH_3), 6.25 (d, *J* = 9.6 Hz, 1 H, vinyl), 6.82–6.86 (m, 2 H, aryl), 7.37 (d, *J* = 8.1 Hz, 1 H, aryl), 7.63 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.75, 100.86, 112.54, 112.57, 113.14, 128.72, 143.35, 155.93, 161.14, 162.85.

5-Methoxycoumarin (3g)[7b,9d,e]
Mp 81–82 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, OCH_3), 6.33 (d, *J* = 9.6 Hz, 1 H, vinyl), 6.71 (d, *J* = 8.4 Hz, 1 H, aryl), 6.91 (d, *J* = 8.4 Hz, 1 H, aryl), 7.44 (t, *J* = 8.4 Hz, 1 H, aryl), 8.10 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.98, 105.12, 109.19, 109.62, 114.52, 132.31, 138.52, 155.11, 156.15, 160.96.

5,7-Dimethoxycoumarin (3h)[9c–e]
Mp 146–148 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.15 (d, *J* = 9.6 Hz, 1 H, vinyl), 6.28 (d, *J* = 2.3 Hz, 1 H, aryl), 6.41 (d, *J* = 2.3 Hz, 1 H, aryl), 7.96 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.74, 55.89, 92.79, 94.75, 103.95, 110.87, 138.66, 156.76, 156.94, 161.43, 163.67.

6,7-(Methylenedioxy)coumarin (3i)[7b,9d,e]
Mp 224–226 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, acetone-d_6): δ = 6.16 (s, 2 H, OCH_2O), 6.24 (d, *J* = 9.6 Hz, 1 H, vinyl), 6.89 (s, 1 H, aryl), 7.10 (s, 1 H, aryl), 7.85 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, acetone-d_6): δ = 98.59, 103.52, 106.18, 113.66, 113.83, 144.66, 145.77, 152.18, 152.22, 160.97.

7-Hydroxycoumarin (3j)[21]
Mp 226.5–228 °C (EtOAc–hexane).

^{1}H NMR (300 MHz, acetone-d_6): δ = 6.16 (d, *J* = 9.5 Hz, 1 H, vinyl), 6.75 (d, *J* = 2.4 Hz, 1 H, aryl), 6.84 (dd, *J* = 2.4, 8.4 Hz, 1 H, aryl), 7.51 (d, *J* = 8.4 Hz, 1 H, aryl), 7.85 (d, *J* = 9.5 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, acetone-d_6): δ = 103.28, 112.81, 112.89, 113.75, 130.41, 144.68, 156.98, 161.05, 162.04.

5,7-Dihydroxycoumarin (3k)[22]
Mp 275–278 °C (EtOAc–hexane).

^{1}H NMR (300 MHz, acetone-d_6): δ = 6.04 (d, *J* = 9.6 Hz, 1 H, vinyl), 6.28 (d, *J* = 2.0 Hz, 1 H, aryl), 6.36 (d, *J* = 2.0 Hz, 1 H, aryl), 8.01 (d, *J* = 9.6 Hz, 1 H, vinyl).

^{13}C NMR (75 MHz, acetone-d_6): δ = 95.46, 99.10, 103.12, 110.30, 139.73, 156.64, 157.92, 161.44, 162.80.

5,7-Dimethyl-4-phenylcoumarin (4a)[9a,c,e]
Mp 94–95 °C (hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.79 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 6.18 (s, 1 H, vinyl), 6.83 (s, 1 H, aryl), 7.08 (s, 1 H, aryl), 7.26–7.29 (m, 2 H, aryl), 7.43–7.45 (m, 3 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.26, 23.27, 115.45, 115.77, 116.08, 127.31, 128.51, 128.67, 129.46, 137.02, 139.55, 142.32, 155.15, 156.74, 160.49.

1-Phenyl-3*H*-naphtho[2,1-*b*]pyran-3-one (4b)[9c–e]
Mp 160–161 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.39 (s, 1 H, vinyl), 7.15 (dd, *J* = 6.6, 8.7 Hz, 1 H, aryl), 7.26 (d, *J* = 8.4 Hz, 1 H, aryl), 7.35–7.43 (m, 3 H, aryl), 7.47–7.55 (m, 4 H, aryl), 7.85 (d, *J* = 8.1 Hz, 1 H, aryl), 8.01 (d, *J* = 9.0 Hz, 1 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.93, 116.71, 117.38, 125.31, 125.82, 126.65, 127.37, 128.93, 129.07, 129.15, 129.24, 131.21, 133.88, 139.47, 154.67, 156.39, 160.26.

7-Methoxy-4-phenylcoumarin (4c)[9c–e]
Mp 111–112 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 6.21 (s, 1 H, vinyl), 6.79 (dd, *J* = 2.4, 9.0 Hz, 1 H, aryl), 6.88 (d, *J* = 2.4 Hz, 1 H, aryl), 7.38 (d, *J* = 9.0 Hz, 1 H, aryl), 7.41–7.45 (m, 2 H, aryl), 7.49–7.52 (m, 3 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.72, 101.02, 111.77, 112.22, 112.42, 127.91, 128.30, 128.75, 129.52, 135.49, 155.73, 155.94, 161.11, 162.72.

5,7-Dimethoxy-4-phenylcoumarin (4d)[7b,9c–e]
Mp 169–171 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.42 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 6.00 (s, 1 H, vinyl), 6.23 (d, *J* = 2.4 Hz, 1 H, aryl), 6.53 (d, *J* = 2.4 Hz, 1 H, aryl), 7.24–7.27 (m, 2 H, aryl), 7.36–7.38 (m, 3 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.33, 55.70, 93.52, 95.68, 103.46, 112.58, 127.04, 127.28, 127.83, 139.69, 155.62, 157.09, 158.16, 160.78, 163.31.

1-Pentyl-3*H*-naphtho[2,1-*b*]pyran-3-one (5a)[9e]
Mp 99–100 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.37–1.56 (m, 4 H, CH_2), 1.77–1.87 (m, 2 H, CH_2), 3.23 (t, *J* = 7.7 Hz, 2 H, CH_2), 6.41 (s, 1 H, vinyl), 7.47 (d, *J* = 9.0 Hz, 1 H, aryl), 7.55 (dd, *J* = 6.9, 8.1 Hz, 1 H, aryl), 7.65 (ddd, *J* = 1.5, 6.9, 8.7 Hz, 1 H, aryl), 7.92 (dd, *J* = 1.5, 8.1 Hz, 1 H, aryl), 7.97 (d, *J* = 9.0 Hz, 2 H, aryl), 8.47 (d, *J* = 8.7 Hz, 1 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.90, 22.33, 28.33, 31.51,.37.47, 113.91, 115.19, 117.90, 124.89, 125.26, 127.76, 129.64, 129.66, 131.30, 133.49, 154.78, 158.17, 160.51.

5,7-Dimethoxy-4-pentylcoumarin (5b)[9c–e]
Mp 102–103 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.34–1.42 (m, 4 H, CH_2), 1.53–1.62 (m, 2 H, CH_2), 2.87 (t, *J* = 7.6 Hz, 2 H, CH_2), 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 5.97 (s, 1 H, vinyl), 6.31 (d, *J* = 2.4 Hz, 1 H, aryl), 6.46 (d, *J* = 2.4 Hz, 1 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.96, 22.42, 29.29, 31.78, 36.44, 55.61, 55.70, 93.57, 95.47, 104.21, 110.55, 157.27, 158.46, 158.59, 161.18, 162.56.

3,5-Dimethylphenyl But-2-ynoate (6) and 4,5,7-Trimethylcoumarin (7) by $FeCl_3$/AgOTf-Catalyzed Reaction of But-2-ynoic Acid (2d) with 3,5-Dimethylphenol (1b)
To a stirred mixture of $FeCl_3$ (0.4 mmol) and AgOTf (1.2 mmol) in TFA (0.5 mL) and DCE (0.5–1 mL) were added **1b** (4 mmol) and **2d** (2 mmol), and then the mixture was stirred at 60 °C for 6 h. The mixture was poured into H_2O (20 mL), neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with 2 M NaOH (10 mL), dried (anhyd Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc–hexane) to give **6** (19%) and **7** (22%).

3,5-Dimethylphenyl But-2-ynoate (6)[23]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 (s, 3 H, CH_3), 2.31 (s, 6 H, CH_3), 6.73 (s, 2 H, aryl), 6.87 (s, 1 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 3.93, 21.20, 72.22, 87.67, 118.93, 128.00, 139.41, 149.96, 152.17.

4,5,7-Trimethylcoumarin (7)[23]
Mp 170–172 °C (CH_2Cl_2–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, CH_3), 2.60 (d, *J* = 0.9 Hz, 3 H, CH_3), 2.68 (s, 3 H, CH_3), 6.16 (s, 1 H, vinyl), 6.88 (s, 1 H, aryl), 7.01 (s, 1 H, aryl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.18, 24.31, 25.15, 115.46, 116.18, 116.79, 129.59, 136.39, 141.85, 154.27, 155.17, 160.76.

References

(1) (a) Hepworth, J. D. In *Comprehensive Heterocyclic Chemistry*, Vol. 3; Katritzky, A. R.; Rees, C. W., Eds.; Pergamon Press: Oxford, **1984**, 737. (b) Matern, U.; Lüer, P.; Kreusch, D. In *Comprehensive Natural Products Chemistry*, Vol. 1; Barton, D. H. R.; Nakanishi, K.; Meth-Cohn, O., Eds.; Pergamon Press: Oxford, **1999**, 623. (c) Hepworth, J. D.; Gabbutt, C. D.; Heron, B. M. In *Comprehensive Heterocyclic Chemistry II*, Vol. 5; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon Press: Oxford, **1996**, Chap. 5.08, 351. (d) Staunton, J. In *Comprehensive Organic Chemistry*, Vol. 4; Barton, D. H. R.; Ollis, W. D., Eds.; Pergamon Press: Oxford, **1979**, Part 18.2, 629.

(2) Pd: (a) An, Z.; Catellani, M.; Chuisoli, G. P. *J. Organomet. Chem.* **1989**, *371*, C51. (b) Deshpande, P. P.; Martin, O. R. *Tetrahedron Lett.* **1990**, *31*, 6313. (c) Catellani, M.; Chuisoli, G. P.; Fagnola, M. C.; Solari, G. *Tetrahedron Lett.* **1994**, *35*, 5919. (d) Catellani, M.; Chuisoli, G. P.; Fagnola, M. C.; Solari, G. *Tetrahedron Lett.* **1994**, *35*, 5923. (e) Cacchi, S. *Pure Appl. Chem.* **1996**, *68*, 45. (f) Catellani, M.; Chuisoli, G. P.; Marzolini, G.; Rossi, E. *J. Organomet. Chem.* **1996**, *525*, 65. (g) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Synlett* **1996**, 568. (h) Cacchi, S.; Fabrizi, G.; Moro, L.; Pace, P. *Synlett* **1997**, 1367. (i) Kadnikov, D. V.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3643. (j) Hesse, S.; Kirsch, G. *Tetrahedron Lett.* **2002**, *43*, 1213. (k) Kadnikov, D. V.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 9423. (l) Kadnikov, D. V.; Larock, R. C. *J. Organomet. Chem.* **2003**, *687*, 425. (m) Palencia, H.; Garcia-Jimenez, F.; Takacs, J. M. *Tetrahedron Lett.* **2004**, *45*, 3849. (n) Battistuzzi, G.; Cacchi, S.; Salve, I. D.; Fabrizi, G.; Parisi, L. M. *Adv. Synth. Catal.* **2005**, *347*, 308. (o) Aoki, S.; Oyamada, J.; Kitamura, T. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 468.

(3) Ru: Chatterjee, A. K.; Toste, F. D.; Goldberg, S. D.; Grubbs, R. H. *Pure Appl. Chem.* **2003**, *75*, 421.

(4) Rh: (a) Yoneda, E.; Sugioka, T.; Hirao, K.; Zhang, S.-W.; Takahashi, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 477. (b) Tollari, S.; Palmisano, G.; Cenini, S.; Cravotto, G.; Giovenzana, G. B.; Penoni, A. *Synthesis* **2001**, 735.

(5) Rh and Co: Park, K. H.; Jung, I. G.; Chung, Y. K. *Synlett* **2004**, 2541.

(6) Ni: Rayabarapu, D. K.; Shukla, P.; Cheng, C.-H. *Org. Lett.* **2003**, *5*, 4903.

(7) (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1996**, *118*, 6305. (b) Trost, B. M.; Toste, F. D.; Greenman, K. *J. Am. Chem. Soc.* **2003**, *125*, 4518.

(8) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669.

(9) (a) Jia, C.; Piao, D.; Kitamura, T.; Fujiwara, Y. *J. Org. Chem.* **2000**, *65*, 7516. (b) Oyamada, J.; Jia, C.; Fujiwara, Y.; Kitamura, T. *Chem. Lett.* **2002**, 380. (c) Kitamura, T.; Yamamoto, K.; Kotani, M.; Oyamada, J.; Fujiwara, Y. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1889. (d) Kotani, M.; Yamamoto, K.; Oyamada, J.; Fujiwara, Y.; Kitamura, T. *Synthesis* **2004**, 1466. (e) Oyamada, J.; Kitamura, T. *Tetrahedron* **2006**, *62*, 6918. (f) Kitamura, T.; Oyamada, J.; Tsubota, T. *Nature Protocols* **2007**, *2*, 845. (g) Li, K.; Zeng, Y.; Neuenswander, B.; Tunge, J. A. *J. Org. Chem.* **2005**, *70*, 6515.

(10) (a) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (b) Jia, C.; Lu, W.; Oyamada, J.; Kitamura, T.; Matsuda, M.; Irie, M.; Fujiwara, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7252. (c) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. (d) Oyamada, J.; Kitamura, T. *Tetrahedron Lett.* **2005**, *46*, 3823. (e) Oyamada, J.; Kitamura, T. *Chem. Lett.* **2005**, *34*, 1430. (f) Oyamada, J.; Kitamura, T. *Tetrahedron* **2007**, *63*, 12754. (g) Oyamada, J.; Hashimoto, T.; Kitamura, T. *J. Organomet. Chem.* **2009**, *694*, 3626.

(11) Tunge, J. A.; Foresee, N. L. *Organometallics* **2005**, *24*, 6440.

(12) Bolm, C.; Legros, J.; Paih, J. L.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217.

(13) Li, R.; Wang, S. R.; Lu, W. *Org. Lett.* **2007**, *9*, 2219.

(14) (a) Hashimoto, T.; Izumi, T.; Kutubi, M. S.; Kitamura, T. *Tetrahedron Lett.* **2010**, *51*, 761. (b) Hashimoto, T.; Kutubi, M. S.; Izumi, T.; Rahman, M. A.; Kitamura, T. *J. Organomet. Chem.* **2011**, *696*, 99.
(15) (a) Zotto, C. D.; Wehbe, J.; Virienx, D.; Campagne, J.-M. *Synlett* **2008**, 2033. (b) Komeyama, K.; Igawa, R.; Takaki, K. *Chem. Commun.* **2010**, *46*, 1748.
(16) Harvey, R. G.; Cortez, C.; Ananthanarayan, T. P.; Schmolka, S. *J. Org. Chem.* **1988**, *53*, 3936.
(17) Dittmer, D. C.; Li, Q.; Avilov, D. V. *J. Org. Chem.* **2005**, *70*, 4682.
(18) Chenault, J.; Dupin, J. F. E. *Heterocycles* **1983**, *20*, 437.
(19) Costa, A. M. B. S. R. C. S.; Dean, F. M.; Jones, M. A.; Varma, R. S. *J. Chem. Soc., Perkin. Trans. 1* **1985**, 799.
(20) Liao, Y.; Hendrata, S.; Bae, S. Y.; Wang, B. *Chem. Pharm. Bull.* **2000**, *48*, 1138.
(21) *The Merck Index*, 13th ed.; Merck & Co., Inc.: Whitehouse Station, **2001**, 1755.
(22) Chang, C.-F.; Yang, L.-Y.; Chang, S.-W.; Fang, Y.-T.; Lee, Y.-J. *Tetrahedron* **2008**, *64*, 3661.
(23) (a) Pastine, S. J.; Youn, S. W.; Sames, D. *Org. Lett.* **2003**, *5*, 1055. (b) Pastine, S. J.; Youn, S. W.; Sames, D. *Tetrahedron* **2003**, *59*, 8859.