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Regioselective synthesis of flavone derivatives via DMAP-catalyzed cyclization of *o*-alkynoylphenols

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This paper is dedicated to Professor Gilbert Stork on the occasion of his 90th birthday

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ABSTRACT

A catalytic amount of DMAP promoted cyclization of *o*-alkynoylphenols via a 6-*endo* cyclization mode leading to flavone derivatives in high yields without forming 5-*exo* cyclized aurone derivatives. Utilizing this method, methoxy substituted flavone and alkyl substituted γ-benzopyranone derivatives were synthesized.

1. Introduction

Flavonoids, a major class of polyphenolic natural products found in plants, possess a wide range of biological activities such as anti-tumor and anti-inflammatory.[1] In their families, flavones (**1**) exhibit interesting biological properties such that nobiletin enhances PKA-mediated phosphorylation of GluR1,[2] and baicalin shows the strongest induction of alkaline phosphatase (ALP) activity in the cultured rat osteoblasts and promotes osteoblastic differentiation via the activation of Wnt/β-catenin signaling pathway.[3] The flavone derivatives consist of a γ-benzopyranone ring system with aromatics at the C-2 position and can be synthesized by 6-*endo*-*digonal* cyclization of *o*-alkynoylphenols. In general, the 6-*endo*-*digonal* cyclization is a favorable process that has been reported as a Baldwin's rule in 1976.[4] However, it is well known that 5-*exo*-*digonal* cyclization proceeds competitively against a 6-*endo*-*digonal* mode that leads to benzofuranone derivatives, aurones (**2**), especially, in the cyclization of *o*-alkynoylphenols under basic conditions in protic media.[5] To overcome this problem, several research groups have developed efficient methods[6] such as secondary amine-promoted cyclization,[7] KF-promoted cyclization[8] and iodonium cation-mediated cyclization.[9] Recently, we have demonstrated that trifluoromethanesulfonic acid promoted cyclization of *o*-alkynoylphenols proceeds regioselectively leading to a variety of flavone derivatives.[10] These methods, however, required stoichiometric amount of the reagents. We are therefore interested in a catalytic reaction toward highly regioselective cyclization of *o*-alkynoylphenols (Fig. 1).

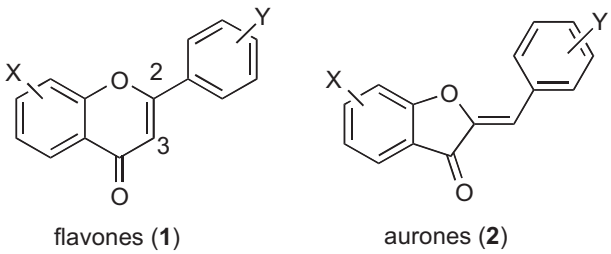

Fig. 1. Structures of flavones and aurones.

We focused on Morita–Baylis–Hillman reaction in an ynone system. Morita–Baylis–Hillman reaction, found by Morita in 1968[11] and also by Baylis and Hillman in 1972,[12] is an efficient method for the preparation of α-(hydroxyalkyl)acrylates from acrylates and can be carried out as follows: (1) nucleophilic addition of tertiary amine or phosphine to the β-carbon of an acrylate, (2) addition of the resulting enolate to an electrophile such as aldehyde

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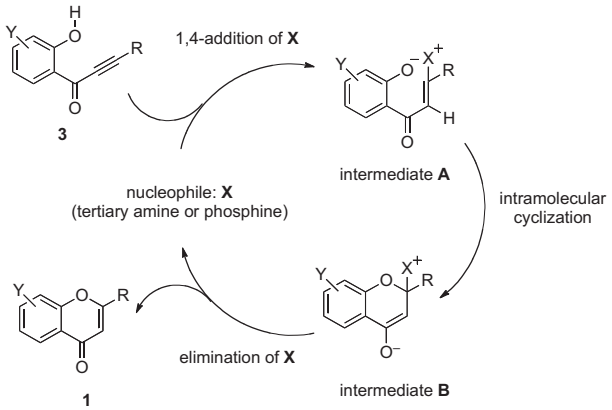
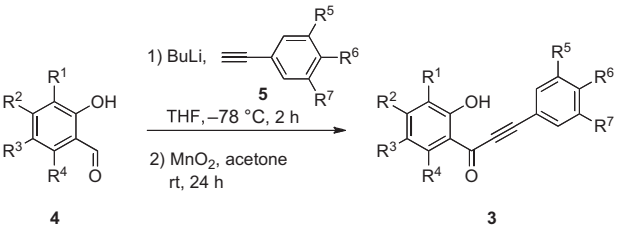
or imine at the α-carbon, and (3) elimination of the initial nucleophile to regenerate the acrylate.[13] Despite of numerous reports for the reaction of α,β-alkenyl carbonyl compounds, a few examples applied to an α,β-acetylenic carbonyl system have been reported.[14] We assumed that the reaction sequence of Morita–Baylis–Hillman reaction could be applicable to the regioselective synthesis of flavone derivatives from *o*-alkynoylphenols. Our synthetic outline is illustrated in Scheme 1. Synthesis of flavone (**1**) can be initiated by 1,4-addition of a nucleophile **X**, such as tertiary amine or phosphine to the β-carbon in an ynone system **3**. The corresponding allenoate initially formed could be rapidly protonated to generate the intermediate **A**. Intramolecular Michael addition of the phenoxide in the resulting enone **A**, followed by elimination of the nucleophile **X** in the intermediate **B** would exclusively provide 6-*endo* cyclized product **1**,[4b,15] and **X** regenerated should be employed as a catalyst. This integrated synthesis of flavone derivatives could be useful because the above reactions can be performed in a one-pot catalytic operation.[16] We herein report that 4-(dimethylamino)pyridine (DMAP) efficiently catalyzed the regioselective cyclization of *o*-alkynoylphenols in the synthesis of flavone derivatives.



Scheme 1. A catalytic cycle in the regioselective synthesis of **1** from **3**.

2. Results and discussion

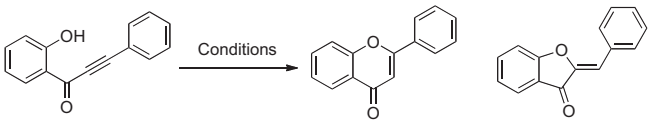
Facile preparation of *o*-alkynoylphenols **3** is illustrated in Scheme 2. 1,2-Addition of lithiated arylacetylenes **5** to salicylaldehydes **4**, followed by mild oxidation of the resulting ynols with MnO_2 afforded *o*-alkynoylphenols **3** in good to moderate yields.



Scheme 2. Preparation of *o*-alkynoylphenols **3**.

We initially investigated the cyclization of *o*-alkynoylphenol **3a** in DMF with a catalytic amount of various tertiary amines and phosphines (Table 1). It was found that DMAP exclusively induced 6-*endo* cyclization to provide the corresponding cyclized product flavone (**1a**) in 96% yield (entry 1). The 5-*exo* cyclized product aurone (**2a**) was not observed under the reaction conditions. DABCO often used in Morita–Baylis–Hillman reaction is not as effective as DMAP (entry 2) though the desired **1a** was obtained in good regioselectivity (93%). Using phosphine reagents, PPh_3 and PBu_3, poor results in both regioselectivity and yield were observed

Table 1
Investigation of regioselective cyclization of **3a** catalyzed by various tertiary amines and phosphines



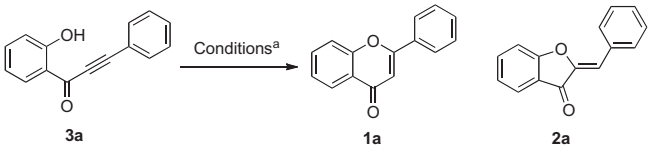
Entry	Reagent[a]	Solvent	Temp (°C)	Time (h)	Ratio of **1a**/**2a**[b]	Yield of **1a**[c] (%)
1	DMAP	DMF	30	1.5	>99:1	96
2	DABCO	DMF	30	3	93:7	72
3	PPh_3	DMF	30	3	42:58	31
4[d]	PPh_3	Toluene	70	24	43:57	13
5	PBu_3	DMF	30	3	24:76	19
6	PCy_3	DMF	30	3	94:6	89
7	K_2CO_3	Acetone	Reflux	4	87:13	80
8	K_2CO_3	EtOH	rt	4	23:77	18

[a] Reagent (10 mol %) was used.
[b] The ratio of **1a** and **2a** was determined on the basis of ^1H NMR of the crude products.
[c] Isolated yield.
[d] The reaction was not completed.

(entries 3–5). On the other hand, PCy_3 preferably promoted the 6-*endo* cyclization yielding **1a** in 89% yield with 94% regioselectivity (entry 6). The phosphine reagents could act as a base[17] to deprotonate the phenolic hydroxy group and the resulting phenoxide would employ 5-*exo* cyclization. In the use of PPh_3 and PBu_3, the vinyl carbanion of **2a** initially formed was readily protonated by the protonated phosphines such as $H-P^+Ph_3$ or $H-P^+Bu_3$ to provide **2a**. On the other hand, in the use of PCy_3, the vinyl carbanion of **2a** would not be rapidly protonated due to the steric bulkiness of $H-P^+Cy_3$, therefore, the carbanion of **2a** would be back to **3a** to form more stable vinyl carbanion of **1a** in a reversible process, eventually providing **1a**.[5] In the use of K_2CO_3–acetone, a 6-*endo* mode was predominant (87% selectivity, 80% yield, entry 7), whereas a 5-*exo* mode was preferred using K_2CO_3–EtOH (entry 8).[5]

We next investigated solvent effects on the DMAP-catalyzed cyclization of **3a** (Table 2). Polar non-protic solvents, DMSO and CH_3CN as well as DMF promoted the 6-*endo* cyclization in good regioselectivity (>94%) and a small amount of 5-*exo* product **2a** was detected (entries 2–3 vs entry 1). In THF, 1,4-dioxane, and 1,2-dichloroethane, the reactions proceeded slower than in DMF with

Table 2
Solvent effects in the DMAP-catalyzed cyclization of **3a**



Entry	Solvent	Time (h)	Ratio of **1a**/**2a**[b]	Yield of **1a**[c] (%)
1	DMF	3	>99:1	96
2	DMSO	3	98:2	93
3	CH_3CN	3	94:6	75
4	THF	16	92:8	84
5	1,4-Dioxane	24	93:7	87
6	$(CH_2Cl)_2$	16	98:2	91
7	Toluene	22	90:10	81
8	EtOH	3	87:13	68

[a] The reaction was performed in the presence of 10 mol % of DMAP at 30 °C.
[b] The ratio of **1a** and **2a** was determined on the basis of ^1H NMR of the crude products.
[c] Isolated yield.

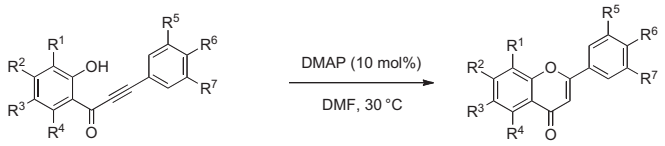
good regioselectivities and yields (entries 4–6). In toluene, less regioselectivity (90%) was observed (entry 7). Interestingly, the 6-*endo* product was still dominant in EtOH (87% selectivity) (entry 8) although protic solvents usually induce 5-*exo* product, aurone, as a major product (see Table 1, entry 8).

With the optimal reaction conditions in hand, cyclization of various 2-propyn-1-ones **3b**–**3p** possessing either a methoxy group on the left benzene ring or 1–3 methoxy groups on the right benzene ring was investigated. The results are depicted in Table 3. When a methoxy group is attached on the left benzene ring at either R^1, R^2, R^3 position, the reaction of **3b**–**3n** proceeded smoothly leading to the corresponding flavones **1b**–**1n**, exclusively, regardless of the number of the methoxy groups on the right benzene ring. On the other hand, when R^4 is the methoxy group, the reaction resulted in poor regioselectivity (25% for **3o** and 50% for **3p**).

conceivable that the electron-donating R^4 group would decrease the electron-deficiency of the carbonyl group to suppress 1,4-addition of DMAP, resulting in the formation of 5-*exo* cyclized product. Interestingly, when the R^2 group is OMe, excellent regioselectivity for **3e** was observed (entry 5 in Table 3) compared with poor selectivity for **3o** (entry 15 in Table 3). IR absorptions for the carbony groups were found to be 1588 cm^{-1} for **3e** and 1563 cm^{-1} for **3o**, respectively. Thus, the lower shift of the wavenumber in **3o** indicated the resonance effect by the electron-donating group in the *o*-position is stronger than that in the *p*-position.[18]

Further extension of this regioselective cyclization was investigated (Table 5). 3-Alkyl-2-propyn-1-ones **6a**–**6c** underwent 6-*endo* regioselective cyclization leading to **7a**–**7c** in good yields without forming 5-*exo* products. Cyclization of **6d** possessing a 1-naphthol moiety also exclusively provided **7d**. Therefore, this method is applicable to the synthesis of a wide range of flavones and related derivatives.

Table 3
Scope of the DMAP-catalyzed regioselective cyclization of substituted 1-(2-hydroxyphenyl)-3-phenyl-2-propyn-1-one **3**



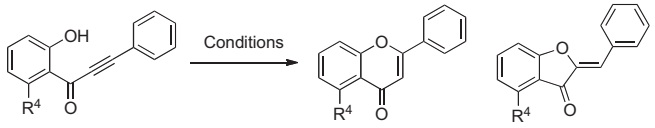
3 1

Entry	Substrate	R^1	R^2	R^3	R^4	R^5	R^6	R^7	Product	Time (h)	Regioselectivity[a] (%)	Yield[b] (%)
1	**3a**	H	H	H	H	H	H	H	**1a**	1.5	>99	96
2	**3b**	H	H	H	H	H	OMe	H	**1b**	2	>99	93
3	**3c**	H	H	H	H	OMe	OMe	H	**1c**	1	>99	87
4	**3d**	H	H	H	H	OMe	OMe	OMe	**1d**	1.5	99	89
5	**3e**	H	OMe	H	H	H	H	H	**1e**	4	>99	74
6	**3f**	H	OMe	H	H	H	OMe	H	**1f**	10	>99	72
7	**3g**	H	OMe	H	H	OMe	OMe	H	**1g**	7	99	90
8	**3h**	H	OMe	H	H	OMe	OMe	OMe	**1h**	3	>99	84
9	**3i**	H	H	OMe	H	H	H	H	**1i**	4	>99	92
10	**3j**	H	H	OMe	H	H	OMe	H	**1j**	4	>99	93
11	**3k**	H	H	OMe	H	OMe	OMe	H	**1k**	5	>99	86
12	**3l**	H	H	OMe	H	OMe	OMe	OMe	**1l**	2	>99	93
13	**3m**	OMe	H	H	H	H	H	H	**1m**	3.5	>99	91
14	**3n**	OMe	H	H	H	OMe	OMe	H	**1n**	4	>99	91
15	**3o**	H	H	H	OMe	H	H	H	**1o**	4	25	20
16	**3p**	H	H	H	OMe	OMe	OMe	H	**1p**	2.5	50	45

[a] The regioselectivity was determined on the basis of the ^1H NMR spectrum of the crude products.
[b] Isolated yield.

To elucidate the effect of a substituent as the R^4 group, the cyclization of **3q**–**3s** was performed (Table 4). Electron-donating groups like OMe, Ph, and Me groups significantly decrease regioselectivity in the 6-*endo* cyclization when they were attached to the *o*-position for the alkynoyl group (entries 1–3). In contrast, the cyclization of **3s** (R^4=OTf) retained excellent regioselectivity. It is

Table 4
Effects of the R^4 substituent in the DMAP-catalyzed cyclization



3 1 2

Entry	Substrate	R^4	Time (h)	Ratio of **1**/**2**[a]	Yield of **1**[b] (%)
1	**3o**	OMe	4	25:75	20
2	**3q**	Ph	4	56:44	50
3	**3r**	Me	3	14:86	13
4	**3s**	OTf	1	>99:1	83

[a] The regioselectivity was determined on the basis of the ^1H NMR spectrum of the crude products.
[b] Isolated yield.

3. Summary

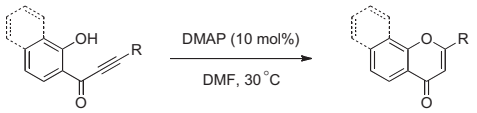
We have demonstrated DMAP-catalyzed 6-*endo* selective cyclization of 3-substituted 1-(2-hydroxyphenyl)-2-propyn-1-ones. This method mostly induces exclusive formation of 6-*endo* products, flavones, without formation of 5-*exo* cyclized products, aurones, except an electron-donating group is attached on the *o*-position of the alkynoyl group. Further functionalization of flavonoid derivatives on the basis of this method is underway in our laboratory.

4. Experimental section

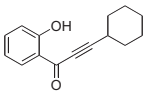
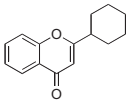
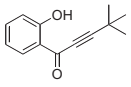
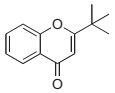
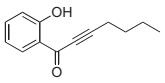
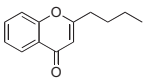
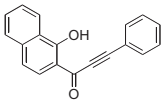
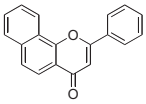
4.1. General

All commercially available reagents were used as received. Dry THF (Kanto Chemical Co.) was obtained by passing commercially available pre-dried, oxygen-free formulations. DMF was purchased from Wako (for peptide synthesis, grade: 99.5%). All reactions in solution-phase were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light, and visualized with anisaldehyde, 10% ethanolic

Table 5
DMAP-catalyzed regioselective cyclization of **6**



6 **7**

Entry	Substrate	Product	Time (h)	Yield[a] (%)
1	 **6a**	 **7a**	4.5	89
2	 **6b**	 **7b**	7	89
3	 **6c**	 **7c**	1	94
4	 **6d**	 **7d**	2	93

[a] Isolated yield.

phosphomolybdic acid. Silica gel 60 N (Kanto Chemical Co. 100–210 μm) was used for column chromatography. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were recorded on JEOL JNM-Al400 spectrometers in the indicated solvent. Chemical shifts (δ) are reported in units parts per million (ppm) relative to the signal for internal tetramethylsilane (0 ppm for ^{1}H) for solutions in $CDCl_3$. NMR spectral data are reported as follows: chloroform (7.26 ppm for ^{1}H) or chloroform-*d* (77.0 ppm for ^{13}C), when internal standard is not indicated. Multiplicities are reported by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (double doublet), dt (double triplet), ddd (double double doublet), ddt (double double triplet), dddd (double double double doublet), br s (broad singlet), br d (broad doublet), *J* (coupling constants in hertz). Mass spectra and high-resolution mass spectra were measured on JEOL JMS-DX303 and MS-AX500 instruments. IR spectra were recorded on a Shimadzu FTIR-8400. Only the strongest and/or structurally important absorption are reported as the IR data afforded in cm^{-1}. All Melting points were measured with Yazawa Micro Melting Point BY-2 and are not corrected.

4.2. General procedure for the synthesis of *o*-alkynoylphenols 3

To a solution of phenylacetylene derivative **5** (2.2 equiv) in dry THF (4 mL/mmol) was added BuLi (1.60 M in hexane solution, 2.2 equiv) dropwise at −78 °C under argon. After stirring at the same temperature for 1 h, a solution of aldehyde **4** in dry THF (1 mL/mmol) was added to the reaction mixture dropwise at −78 °C under argon. After being stirred at the same temperature for 1 h and at 0 °C for additional 30 min, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 °C. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo to afford the propargylic alcohol. The crude alcohol was used for the next reaction without further purification.

To a solution of the crude alcohol in acetone (1 mL/mmol) was added MnO_2 (5 equiv) at room temperature under argon. After being stirred at the same temperature, the reaction mixture was filtered through a pad of Celite® and the filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to afford *o*-alkynoylphenol derivatives **3**. Alkynoylphenols **6** were also prepared in a similar manner. Spectral data of **3a**–**3p** and **6a**–**6c** have been reported previously.[10]

*4.2.1. 3-Phenyl-2-(3-phenylpropynoyl)phenol (**3q**).* Yellow solid: mp 67–68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.7 (s, 1H), 7.50–7.20 (m, 9H), 7.04 (m, 3H), 6.88 (d, 1H, *J*=7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.3, 162.6, 145.8, 140.9, 135.2, 133.1, 130.5, 130.1, 128.3, 128.2, 128.1, 122.8, 120.5, 119.8, 117.1, 98.7, 88.8. FTIR (neat) 3586, 3369, 2197, 1609, 1582, 1237 cm^{-1}. HRMS [FAB] calcd for $C_{21}H_{15}O_2$ $(M+H)^+$ 299.1072, found 299.1072.

*4.2.2. 3-Methyl-2-(3-phenylpropynoyl)phenol (**3r**).* Yellow solid: mp 80–82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.5 (s, 1H, e), 7.62 (m, 2H), 7.42 (m, 4H), 6.86 (d, 1H, *J*=8.4 Hz), 6.75 (d, 1H, *J*=7.6 Hz), 2.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.8, 164.5, 141.2, 136.1, 132.7, 131.2, 128.8, 123.1, 120.6, 116.7, 97.9, 90.3, 23.4. FTIR (neat) 3589, 2926, 2199, 1610, 1583, 1198 cm^{-1}. HRMS [FAB] calcd for $C_{16}H_{13}O_2$ $(M+H)^+$ 237.0916, found 237.0911.

*4.2.3. 2-(3-Phenylpropynoyl)-3-trifluoromethanesulfonyloxy phenol (**3s**).* Yellow solid: mp 62–64 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.2 (s, 1H), 7.64 (dt, 2H, *J*=7.2, 1.2 Hz), 7.52 (t, 1H, *J*=8.0 Hz), 7.46 (m, 3H), 7.07 (d, 1H, *J*=8.0 Hz), 6.93 (d, 1H, *J*=8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 164.2, 148.6, 136.0, 133.5, 131.5, 128.6, 119.4, 119.0, 118.7 (q, *J*=320 Hz), 114.8, 112.4, 99.0, 88.4. FTIR (neat) 3587, 3369, 2202, 1631, 1580 cm^{-1}. HRMS [EI] calcd for $C_{16}H_9F_3O_5S$ 370.0123, found 370.0118.

*4.2.4. 1-(1-Hydroxy-2-naphthalenyl)-3-phenyl-2-propyn-1-one (**6d**).* Yellow solid: mp 113–115 °C (lit.[19] 110–111 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.5 (s, 1H), 8.48 (d, 1H, *J*=7.6 Hz), 8.03 (d, 1H, *J*=8.8 Hz), 7.79 (d, 1H, *J*=8.4 Hz), 7.73 (m, 2H), 7.67 (dt, 1H, *J*=7.2, 0.8 Hz), 7.52 (m, 4H), 7.34 (d, 1H, *J*=8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.8, 163.6, 137.7, 133.1, 132.2, 131.1, 130.7, 128.8, 128.6, 127.6, 126.4, 126.1, 124.9, 124.6, 120.0, 118.9, 114.8, 96.7, 86.1. FTIR (neat) 2201, 1588, 1283, 1058 cm^{-1}. HRMS [EI] calcd for $C_{19}H_{12}O_2$ 272.0837, found 272.0819.

4.3. General procedure for DMAP-catalyzed regioselective cyclization of *o*-alkynoylphenols 3 and 6

To a solution of *o*-alkynoylphenol **3** or **6** in DMF (4 mL/mmol) was added DMAP (10 mol %) at 0 °C under argon. After being stirred at 30 °C, the reaction mixture was diluted with water. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 1 M HCl, saturated aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and then the resulting residue was purified by column chromatography on silica gel to afford flavone **1** or **7**. Spectral data of flavones **1a**–**1n** and **7a**–**7c** have been reported previously.[10]

*4.3.1. 5-Methoxy-2-phenyl-4H-chromen-4-one (**1o**).* Yield: 20%, white solid: mp 131–133 °C (lit.[20] 130–134 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 2H), 7.58 (t, 1H, *J*=8.4 Hz), 7.50 (m, 3H), 7.14 (dd, 1H, *J*=8.4, 0.8 Hz), 6.83 (d, 1H, *J*=8.4 Hz), 6.74 (s, 1H), 4.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 161.1, 160.0, 158.3, 133.7, 131.5, 131.3, 129.0, 126.1, 114.6, 110.2, 109.1, 106.4, 56.5. FTIR (neat) 3584, 3413, 2924, 1646,

1603, 1267 cm^{-1}. HRMS [EI] calcd for $C_{16}H_{12}O_3$ 252.0786, found 252.0774.

*4.3.2. 5-Methoxy-2-(3,4-dimethoxy)phenyl-4H-chromen-4-one (**1p**).* Yield: 45%, white solid: mp 212–214 °C (lit.[21] 204–206 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (t, 1H, J=3.2 Hz), 7.54 (dd, 1H, J=8.8, 2.4 Hz), 7.55 (d, 1H, J=2.4 Hz), 7.14 (dd, 1H, J=8.4, 1.2 Hz), 6.98 (d, 1H, J=8.8 Hz), 6.83 (d, 1H, J=8.4 Hz), 6.69 (s, 1H), 4.01 (s, 3H), 3.98 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 161.0, 159.7, 151.8, 151.7, 149.2, 133.5, 123.8, 119.6, 114.4, 111.0, 108.6, 107.9, 106.3, 56.4, 56.0. FTIR (neat) 3423, 2922, 1632, 1601, 1263, 1100 cm^{-1}. HRMS [EI] calcd for $C_{18}H_{16}O_5$ 312.0998, found 312.0989.

*4.3.3. 2,5-Diphenyl-4H-chromen-4-one (**1q**).* Yield: 50%, white solid: mp 152–153 °C (lit.[22] 152–154 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (m, 2H), 7.66 (t, 1H, J=8.0 Hz), 7.58 (d, 1H, J=8.0 Hz), 7.52 (m, 3H), 7.39 (m, 3H), 7.34 (m, 2H), 7.21 (d, 1H, J=8.0 Hz), 6.68 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 161.8, 157.4, 143.2, 141.2, 132.4, 131.6, 131.4, 129.0, 128.6, 126.3, 127.4, 127.0, 126.2, 121.3, 117.7, 108.8. FTIR (neat) 3582, 3402, 3068, 1648, 1597, 1367 cm^{-1}. HRMS [FAB] calcd for $C_{21}H_{15}O_2$ $(M+H)^+$ 299.1072, found 299.1090.

*4.3.4. 5-Methyl-2-phenyl-4H-chromen-4-one (**1r**).* Yield: 13%, white solid: mp 133–135 °C (lit.[23] 129–130 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.51 (m, 4H), 7.39 (d, 1H, J=8.4 Hz), 7.13 (d, 1H, J=8.0 Hz), 6.73 (s, 1H), 2.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.6, 161.5, 157.7, 141.0, 132.6, 131.6, 131.3, 128.9, 127.7, 126.1, 122.3, 116.0, 108.8, 22.7. FTIR (neat) 3586, 3392, 2923, 1653, 1295 cm^{-1}. HRMS [FAB] calcd for $C_{16}H_{13}O_2$ $(M^+ + H)$ 237.0916, found 237.0914.

*4.3.5. 2-Phenyl-5-trifluoromethanesulfonyloxy-4H-chromen-4-one (**1s**).* Yield: 83%, white solid: mp 121–122 °C (lit.[22] 122–123 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 2H), 7.72 (t, 1H, J=8.4 Hz), 7.65 (dd, 1H, J=8.4, 0.8 Hz), 7.54 (m, 3H), 7.23 (d, 1H, J=8.4 Hz), 6.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 162.8, 157.2, 146.8, 133.3, 132.1, 130.8, 129.2, 126.3, 119.1, 118.9 (q, J=322 Hz), 118.8, 117.8, 108.7. FTIR (neat) 3582, 3362, 2922, 1646, 1624, 1207 cm^{-1}. HRMS [EI] calcd for $C_{16}H_9F_3O_5S$ 370.0123, found 370.0120.

*4.3.6. 2-Phenyl-4H-naphtho[1,2-b]pyran-4-one (**7d**).* Yield: 93%, white solid: mp 158–160 °C (lit.[24] 159–161 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (m, 1H), 8.18 (d, 1H, J=8.6 Hz), 8.04 (m, 2H), 7.95 (m, 1H), 7.79 (d, 1H, J=8.6 Hz), 7.72 (m, 2H), 7.59 (m, 3H), 6.98 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 162.7, 153.6, 136.0, 132.0, 131.0, 129.2, 129.1, 128.5, 127.2, 126.5, 125.4, 124.5, 122.3, 120.8, 120.3, 108.8. FTIR (neat) 3446, 1642, 1388, 1020 cm^{-1}. HRMS [ESI] calcd for $C_{19}H_{12}O_2Na$ 295.0730 $(M+Na)^+$, found 295.0712.

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