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Assembly of Indeno[1,2-*c*]chromenes *via* a Palladium-Catalyzed Reaction of 1-Bromo-2-(cyclopropylidenemethyl)benzene with 2-Alkynylphenol

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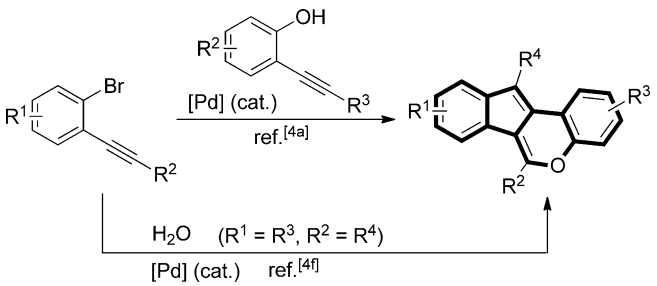
Abstract: 1-Bromo-2-(cyclopropylidenemethyl)benzenes react with 2-alkynylphenols under palladium catalysis, leading to indeno[1,2-*c*]chromenes in moderate to good yields. The molecular complexity and diversity can be introduced efficiently from easily available starting materials.

Keywords: 1-bromo-2-(cyclopropylidenemethyl)-benzenes; 2-alkynylphenols; indeno[1,2-*c*]chromenes; palladium catalysts; tandem reactions

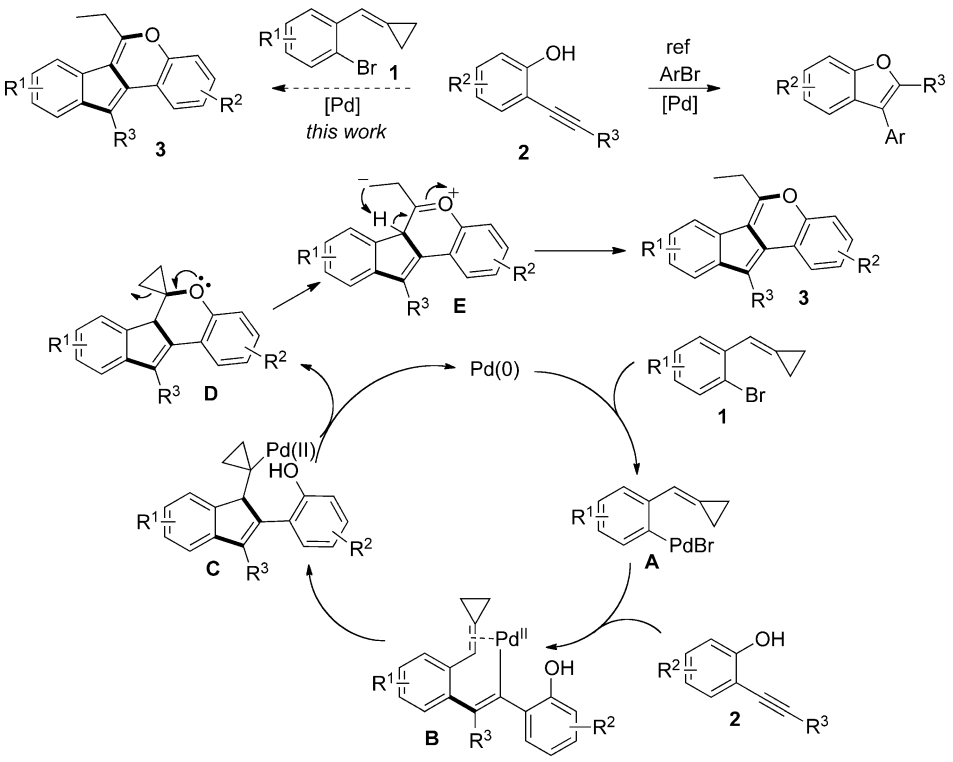
Introduction

Currently, research efforts are documented for the generation of small molecules with privileged scaffolds, which are in great demand in medicinal chemistry and constitute an important target for synthetic chemistry in the drug discovery process.[1] The development of methods for the production of polycycles with molecular complexity and diversity is an essential component in this process.[2] Among the approaches for access to these compounds with functional group diversity, tandem reactions[3] provide an efficient and convenient route, in which several new bonds can be formed in a single step from readily available starting materials.

We are interested in the palladium-catalyzed tandem reactions with the intermolecular double insertion of triple bonds serving as a key step for the formation of heterocyclic compounds from 2-alkynylhalobenzenes.[4] Two tandem reactions have been developed to synthesize indeno[1,2-*c*]chromenes (Scheme 1).[4a,f] Recently, we have found that 1-bromo-2-(cyclopropylidenemethyl)benzenes could be used as an alternative to 1-bromo-2-alkynylbenzenes.[5] Therefore, we conceived that the scaffold of indeno[1,2-*c*]chromene could also be produced *via* a palladium-catalyzed reaction of 1-bromo-2-(cyclopropylidenemethyl)benzenes with 2-alkynylphenols. The proposed synthetic route is presented in Scheme 2. However, this hypothesis is not promising since several competitive reaction pathways are inevitable. For instance, the direct cyclization of 2-alkynylphenol would lead to benzofuran compounds. Moreover, in the presence of aryl bromide, the 3-aryl-substituted benzofuran would be formed (Scheme 2).[6] Encouraged by the reactivity of alkylidenecyclopropanes,[7] we envisioned that the formation of indeno-[1,2-*c*]chromene starting from 2-alkynylphenols and 1-bromo-2-(cyclopropylidenemethyl)benzenes would be feasible. In the presence of palladium(0), an oxidative addition of 1-bromo-2-(cyclopropylidenemethyl)benzene **1** would occur to afford Pd(II) species **A**, which would undergo coordination and insertion of the triple bond of 2-alkynylphenol **2** to generate intermediate **B**. Subsequently, an intramolecular insertion of the double bond of alkylidenecyclopropane with



Scheme 1. Generation of indeno[1,2-*c*]chromenes.



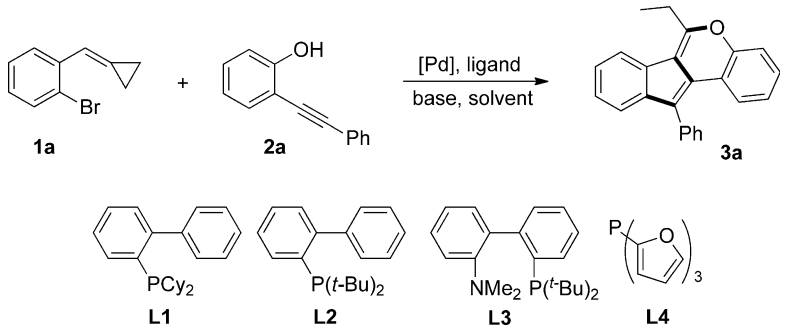
Scheme 2. A possible mechanism for the generation of indeno[1,2-*c*]chromenes.

Pd(II) would occur to afford Pd(II) species **C**, which would then proceed through C–O bond formation to produce compound **D**. After intramolecular rearrangement, compound **3** would be generated. During the reaction process, we believed that the presence of hydroxy group would direct the highly regioselective insertion of the triple bond, and meanwhile minimize the competitive pathways.

Results and Discussion

With the above design in mind, the studies were commenced by reacting 1-bromo-2-(cyclopropylidenemethyl)benzene **1a** and 2-(phenylethynyl)phenol **2a** in the presence of 5 mol% of $PdCl_2(PPh_3)_2$ and 2.0 equivalents of NaO-*t*-Bu in 1,4-dioxane under reflux (Table 1). For the first attempt, the influence of ligands was investigated and the reaction could not proceed to provide the desired product **3a** when **L2**, **L3**, **L4**, PPh_3 and DPPM [methylenebis(diphenylphosphine)] were utilized as a ligand (Table 1, entries 1–5). To our delight, when DPPF [1,1′-bis(diphenylphosphino)ferrocene] was used as a replacement for the above ligands, the reaction proceeded to give rise to indeno[1,2-*c*]chromene **3a** in 21% yield (Table 1, entry 6). The yield was increased to 27% when ligand **L1** was used (Table 1, entry 7). Further exploration revealed that P(*t*-Bu)$_3$ was a more effective ligand with a relatively higher yield of 35% (Table 1, entry 8). Therefore, in the presence of P(*t*-Bu)$_3$, several bases were screened for further optimization of the conditions. As expected, no desired product was detected when weak bases (such as Cs_2CO_3 or K_3PO_4) were employed (Table 1, entries 11 and 12). Further examination showed that other strong bases did not give better results. Lower yields were isolated when *t*-BuOK, KOH or NaOMe was used as replacements for *t*-BuONa (Table 1, entries 9, 10, 13). With these results in hand, we next explored the effect of different palladium catalysts. However, no positive consequence was obtained. The reaction did not happen when catalyzed by $PdCl_2$ or Pd_2dba_3 (Table 1, entries 14 and 15). Also, the yield was reduced to 26% and 30% when $PdCl_2(PhCN)_2$ or $Pd(OAc)_2$ was employed as the catalyst (Table 1, entries 16 and 17). The reaction catalyzed by $PdCl_2[P(t\text{-}Bu)_3]_2$ was examined as well (data not shown in Table 1). However, the yield was inferior (21%) compared with the $Pd(PPh_3)_2Cl_2/P(t\text{-}Bu)_3$ system. We reasoned that the *in situ* generated $\{Pd[P(t\text{-}Bu)_3]_n\}$ species might be more active as the catalyst than $PdCl_2[P(t\text{-}Bu)_3]_2$. The presence of a phosphine ligand in the reaction system would prevent the precipitation of Pd(0) during the reaction process. The screening of solvents showed that diglyme was the best choice for this reaction and the yield was improved to 42% (Table 1, entry 21). Other solvents made no contributions to enhance the final outcome (Table 1, entries 18–20). Interestingly, the amount of the palladium catalyst could affect the

Table 1. Initial studies for the palladium-catalyzed reaction of 1-bromo-2-(cyclopropylidenemethyl)benzenes **1a** with 2-(2-phenylethynyl)phenol **2a**.[a]



Entry	L	[Pd]	Base	Solvent	Yield [%][b]
1	**L2**	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	nr
2	**L3**	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	nr
3	**L4**	$PdCl_2(PPh_3)_2$	*t*BuONa	dioxane	nr
4	PPh_3	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	nr
5	dppm	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	nr
6	dppf	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	21
7	**L1**	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	27
8	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	dioxane	35
9	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuOK	dioxane	21
10	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	KOH	dioxane	22
11	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	Cs_2CO_3	dioxane	nr
12	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	K_3PO_4	dioxane	nr
13	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	NaOMe	dioxane	16
14	P(*t*-Bu)$_3$	$PdCl_2$	*t*-BuONa	dioxane	nr
15	P(*t*-Bu)$_3$	Pd_2dba_3	*t*-BuONa	dioxane	nr
16	P(*t*-Bu)$_3$	$PdCl_2(PhCN)_2$	*t*-BuONa	dioxane	26
17	P(*t*-Bu)$_3$	$Pd(OAc)_2$	*t*-BuONa	dioxane	30
18	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	toluene	trace
19	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	DMSO	nr
20	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	DMF	nr
21	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	diglyme	42
22[c]	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	diglyme	49
23[d]	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	diglyme	65
24[e]	P(*t*-Bu)$_3$	$PdCl_2(PPh_3)_2$	*t*-BuONa	diglyme	51

[a] *Reaction conditions:* 1-bromo-2-(cyclopropylidenemethyl)benzene **1a** (0.4 mmol), 2-alkynylphenol **2a** (0.20 mmol), palladium catalyst (5 mol%), phosphine ligand (10 mol%), base (0.4 mmol), solvent (2.0 mL), reflux, overnight.
[b] Isolated yield based on 2-(2-phenylethynyl)phenol **2a**.
[c] The amount of palladium catalyst: 2.5 mol%.
[d] The reaction was performed at 90 °C.
[e] The reaction was performed at 70 °C.

result of the transformation. Reducing the catalytic amount of $PdCl_2(PPh_3)_2$ to 2.5 mol% resulted in a higher yield (49%, Table 1, entry 22), while increasing the amount led to a slightly lower yield (data not shown in Table 1). Furthermore, it was found that the desired product **3a** could be obtained in 60% yield when the temperature was lowered to 90 °C (Table 1, entry 23). However, the reaction did not perform well at 70 °C (Table 1, entry 24). The structure of compound **3a** has been confirmed by X-ray crystallographic analysis in the meantime (Figure 1).

Under the optimized reaction conditions [2.5 mol% of $PdCl_2(PPh_3)_2$, 5 mol% of P(*t*-Bu)$_3$, 2.0 equiv of *t*-BuONa, diglyme, 90 °C), the scope of this transformation was explored. The results are summarized in Table 2 for the evaluation of various substituted 1-bromo-2-(cyclopropylidenemethyl)benzenes **1** and 2-alkynylphenols **2**. For the R^3 group attached to the triple bond of 2-alkynylphenols **2**, it appeared that electron-withdrawing groups as well as electron-donating groups made no big difference for the final yield. As to the R^2 group, electron-donating groups seemed to give rise to the corresponding products in a slightly higher yield, but not obviously. Additionally, the R^1 groups on the aryl rings affected the reactivity to some extent. The substrates with electron-donating

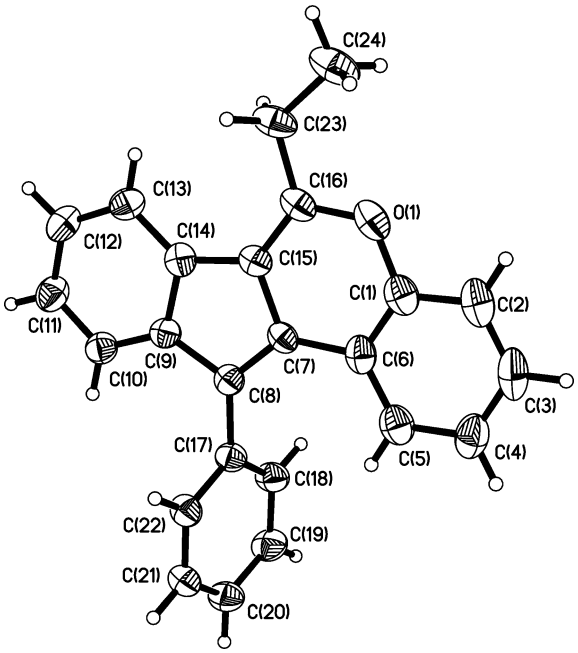


Figure 1. ORTEP illustration of compound **3a** (30% probability ellipsoids).

groups (R^1) were likely to have higher reactivity and these reactions proceeded comparatively well to yield the desired products. Actually, most of the reactions could not give satisfactory results with excellent yields, which might be attributed to the instability of 1-bromo-2-(cyclopropylidenemethyl)benzenes in this reaction.

Conclusions

In summary, we have developed an efficient route for the assembly of indeno[1,2-*c*]chromenes *via* a palladium-catalyzed reaction of 1-bromo-2-(cyclopropylidenemethyl)benzenes with 2-alkynylphenols. This transformation proceeded well, and the diversity and complexity could be easily introduced *via* a simple operation from readily available starting materials. Further exploration of 1-bromo-2-(cyclopropylidenemethyl)benzenes to discover new cascade reactions for the generation of heterocycles is in progress.

Experimental Section

General Procedure for the Synthesis of Indeno[1,2-*c*]chromenes 3 *via* a Palladium-Catalyzed Reaction of 1-Bromo-2-(cyclopropylidenemethyl)benzene 1 with 2-Alkynylphenol 2

1-Bromo-2-(cyclopropylidenemethyl)benzene **1** (0.4 mmol) was added to a mixture of $PdCl_2(PPh_3)_2$ (2.5 mol%), P(*t*-Bu)$_3$ (5 mol%), *t*-BuONa (0.4 mmol), and 2-alkynylphenol **2** (0.20 mmol) in diglyme (2.0 mL). The mixture was heated to 90 °C. After completion of the reaction as indicated by TLC, the reaction was cooled and the solution was diluted with EtOAc (10 mL), washed with saturated brine (2×10 mL), and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by purification on silica gel provided the product **3**.

6-Ethyl-11-phenylindeno[1,2-*c*]chromene (3a): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.96 (m, 1H), 7.64 (dd, J = 8.0, 1.4 Hz, 1H), 7.54–7.53 (m, 4H), 7.47–7.27 (m, 6H), 7.05–7.01 (m, 1H), 3.27 (q, J = 7.6 Hz, 2H), 1.52 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.9, 149.9, 144.1, 136.8, 130.1, 129.7, 128.8, 127.4, 127.3, 126.0, 125.2, 124.9, 124.1, 123.4, 122.9, 121.5, 120.2, 119.5, 117.4, 115.8, 26.0, 11.6; HR-MS (ESI): m/z = 322.1357, calcd. for $C_{24}H_{18}O$: 322.1358 (M^+).

Crystallographic data for the structure **3a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 966489. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif or on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.) +44 -1223/336-033; e-mail: deposit@ccdc.cam.ac.uk].

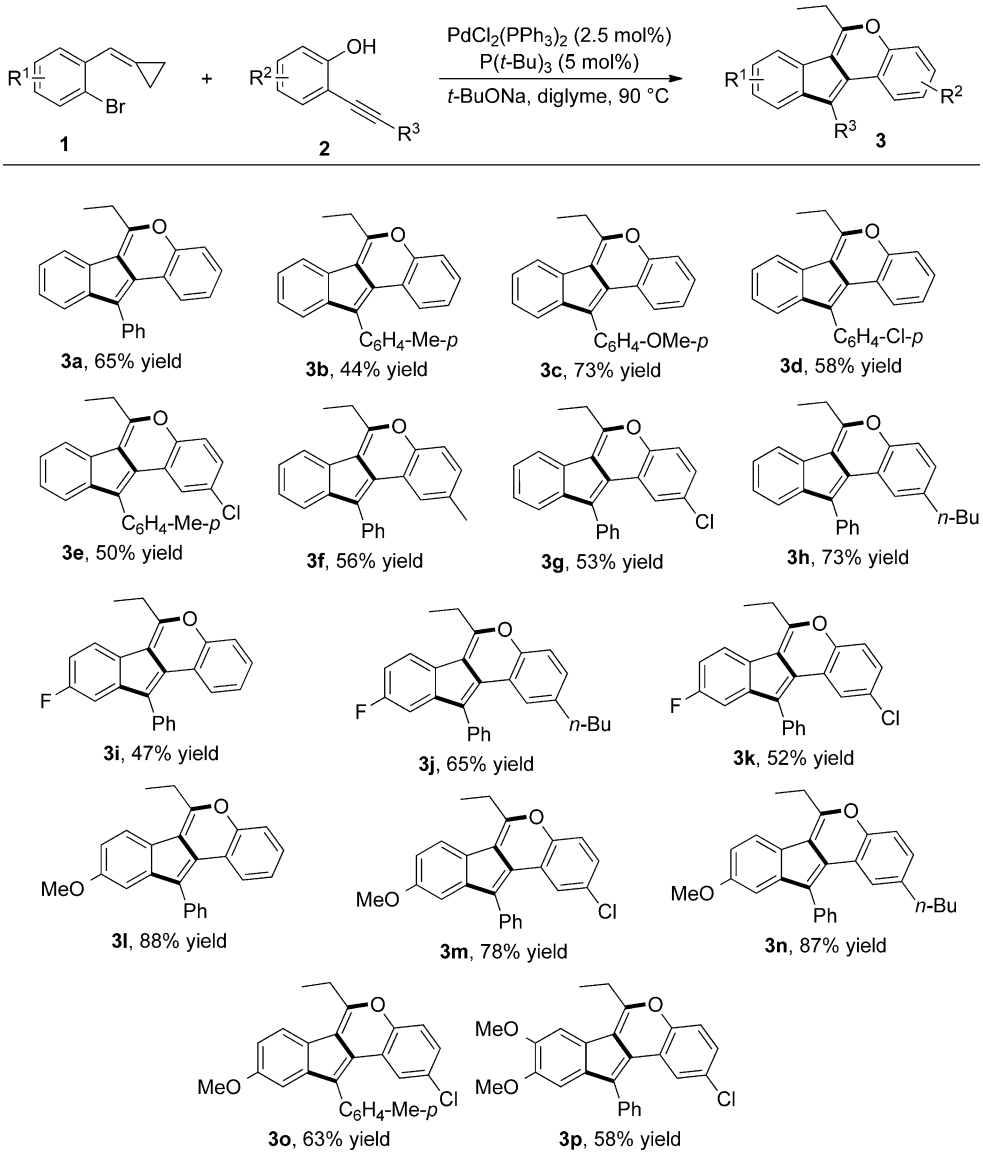
6-Ethyl-11-(*para*-tolyl)indeno[1,2-*c*]chromene (3b): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 6.8 Hz, 1H), 7.69 (dd, J = 8.0, 1.4 Hz, 1H), 7.44–7.27 (m, 9H), 7.06–7.02 (m, 1H), 3.27 (q, J = 7.6 Hz, 2H), 2.48 (s, 3H), 1.52 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.7, 149.9, 144.2, 136.9, 133.7, 129.9, 129.7, 129.6, 127.4, 125.9, 125.3, 124.9, 124.0, 123.3, 122.9, 121.5, 120.4, 119.6, 117.4, 115.8, 26.0, 21.4, 11.6; HR-MS (ESI): m/z = 336.1517, calcd. for $C_{25}H_{20}O$: 336.1514 (M^+).

6-Ethyl-11-(4-methoxyphenyl)indeno[1,2-*c*]chromene (3c): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 7.0 Hz, 1H), 7.68 (dd, J = 8.0, 1.4 Hz, 1H), 7.47–7.29 (m, 8H), 7.09–7.04 (m, 2H), 3.91 (s, 3H), 3.26 (q, J = 7.6 Hz, 2H), 1.52 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 157.7, 150.0, 144.3, 131.2, 129.7, 128.9, 127.4, 125.9, 124.8, 124.0, 123.4, 122.9, 121.5, 120.4, 119.5, 117.4, 114.3, 55.3, 26.0, 11.6; HR-MS (ESI): m/z = 352.1461, calcd. for $C_{25}H_{20}O_2$: 352.1463 (M^+).

11-(4-Chlorophenyl)-6-ethylindeno[1,2-*c*]chromene (3d): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.96 (m, 1H), 7.63–7.61 (m, 1H), 7.52–7.43 (m, 5H), 7.39–7.31 (m, 4H), 7.07 (t, J = 7.2 Hz, 1H), 3.28 (q, J = 7.6 Hz, 2H), 1.53 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2, 150.0, 143.7, 135.4, 133.1, 131.5, 129.6, 129.1, 127.7, 126.1, 124.7, 124.2, 123.8, 123.1, 121.6, 120.0, 119.2, 117.6, 115.8, 26.0, 11.6; HR-MS (ESI): m/z = 356.0973, calcd. for $C_{24}H_{17}ClO$: 356.0968 (M^+).

2-Chloro-6-ethyl-11-(*para*-tolyl)indeno[1,2-*c*]chromene (3e): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.95 (m, 1H), 7.67–7.66 (m, 1H), 7.44–7.33 (m, 8H), 7.24–7.21 (m, 1H), 3.25 (q, J = 7.6 Hz, 2H), 2.49 (s, 3H), 1.51 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 148.3, 144.0, 137.3, 132.8, 129.7, 129.6, 129.2, 127.3, 126.5, 126.1, 124.2, 123.3, 122.0, 121.7, 121.6, 119.9, 118.8, 115.7, 25.9, 21.5, 11.6; HR-MS (ESI): m/z = 370.1120, calcd. for $C_{25}H_{19}ClO$: 370.1124 (M^+).

Table 2. Synthesis of indeno[1,2-*c*]chromenes *via* a Pd-catalyzed reaction of 1-bromo-2-(cyclopropylidenemethyl)benzene **1** with 2-alkynylphenol **2**.[a,b]



[a] *Reaction conditions:* 1-bromo-2-(cyclopropylidenemethyl)benzene **1** (0.4 mmol), 2-alkynylphenol **2** (0.20 mmol), $PdCl_2(PPh_3)_2$ (2.5 mol%), P(*t*-Bu)$_3$ (5 mol%), *t*-BuONa (0.4 mmol), diglyme (2.0 mL), 90 °C, 12 h.

[b] Isolated yield based on 2-alkynylphenol **2**.

6-Ethyl-2-methyl-11-phenylindeno[1,2-*c*]chromene (3f): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.96$ (d, $J = 6.9$ Hz, 1H), 7.56–7.51 (m, 4H), 7.46–7.41 (m, 3H), 7.39–7.31 (m, 3H), 7.12–7.09 (m, 1H), 3.26 (q, $J = 7.6$ Hz, 2H), 2.17 (s, 3H), 1.52 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 157.9, 148.1, 144.0, 136.9, 133.5, 130.1, 129.7, 128.7, 128.5, 127.3, 125.8, 124.8, 123.6, 122.8, 121.5, 119.9, 119.5, 117.1, 115.6, 26.0, 21.2, 11.6; HR-MS (ESI): $m/z = 336.1526$, calcd. for $C_{25}H_{20}O$: 336.1514 (M^+).

2-Chloro-6-ethyl-11-phenylindeno[1,2-*c*]chromene (3g): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.97$–7.95 (m, 1H), 7.58–7.33 (m, 10H), 7.23–7.20 (m, 1H), 3.25 (q, $J = 7.6$ Hz, 2H), 1.51 (t, $J = 8.0$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 157.7, 148.3, 143.8, 136.0, 129.8, 129.7, 129.2, 129.0, 127.7, 127.4, 126.4, 126.2, 124.2, 123.4, 122.2, 121.6, 121.5, 119.8, 118.8, 115.7, 25.9, 11.6; HR-MS (ESI): $m/z = 356.0967$, calcd. for $C_{24}H_{17}ClO$: 356.0968 (M^+).

2-(*tert*-Butyl)-6-ethyl-11-phenylindeno[1,2-*c*]chromene (3h): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.96$ (d, $J = 7.2$ Hz, 1H), 7.68–7.67 (m, 1H), 7.56–7.53 (m, 4H), 7.45–7.43 (m, 2H), 7.38–7.34 (m, 4H), 3.26 (q, $J = 7.6$ Hz, 2H), 1.50 (t, $J =$ 7.6 Hz, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 158.0, 147.9, 146.9, 144.0, 137.1, 130.2, 129.8, 129.4, 128.8, 127.7, 127.2, 125.9, 125.0, 124.8, 124.1, 122.7, 121.5, 119.4,

116.8, 115.7, 34.4, 31.2, 26.0, 11.7; HR-MS (ESI): m/z = 378.1983, calcd. for $C_{28}H_{26}O$: 378.1984 (M^+).

6-Ethyl-9-fluoro-11-phenylindeno[1,2-*c*]chromene (3i): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.60 (m, 2H), 7.53–7.52 (m, 4H), 7.47–7.40 (m, 2H), 7.32–7.28 (m, 2H), 7.12–7.01 (m, 2H), 3.21 (q, J = 7.6 Hz, 2H), 1.52 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2 (d, $J_{C,F}$ = 238.2 Hz), 158.8, 149.8, 140.2, 136.6, 130.0, 128.9, 127.5 (d, $^3J_{C,F}$ = 6.8 Hz), 124.6, 124.3, 120.3, 120.1, 117.5, 113.3 (d, $^2J_{C,F}$ = 23.2 Hz), 108.3 (d, $^2J_{C,F}$ = 24.4 Hz), 25.9, 11.5; HR-MS (ESI): m/z = 340.1269, calcd. for $C_{24}H_{17}FO$: 340.1263 (M^+).

2-(*tert*-Butyl)-6-ethyl-9-fluoro-11-phenylindeno[1,2-*c*]chromene (3j): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.61 (m, 2H), 7.54–7.53 (m, 4H), 7.46–7.43 (m, 1H), 7.34–7.33 (m, 3H), 7.12–7.07 (m, 1H), 3.20 (q, J = 7.6 Hz, 2H), 1.50 (t, J = 7.6 Hz, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1 (d, $J_{C,F}$ = 237.9 Hz), 158.9, 147.8, 147.1, 140.1, 136.8, 130.7 (d, $^3J_{C,F}$ = 8.9 Hz), 130.2, 128.8, 127.3, 125.0, 124.1, 121.3, 120.0, 119.9, 119.5, 116.9, 113.1 (d, $^2J_{C,F}$ = 23.2 Hz), 108.3 (d, $^2J_{C,F}$ = 24.3 Hz), 34.4, 31.1, 25.9, 11.6; HR-MS (ESI): m/z = 396.1888, calcd. for $C_{28}H_{25}FO$: 396.1889 (M^+).

2-Chloro-6-ethyl-9-fluoro-11-phenylindeno[1,2-*c*]chromene (3k): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.59 (m, 1H), 7.56–7.53 (m, 3H), 7.49–7.47 (m, 3H), 7.34–7.31 (m, 2H), 7.24–7.19 (m, 1H), 7.13–7.08 (m, 1H), 3.18 (q, J = 7.6 Hz, 2H), 1.50 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4 (d, $J_{C,F}$ = 239.1 Hz), 158.6, 148.2, 139.9, 135.7, 130.7 (d, $^3J_{C,F}$ = 9.4 Hz), 129.8, 129.4, 129.0, 127.9, 127.4, 125.7, 123.9, 121.5, 120.5 (d, $^3J_{C,F}$ = 8.9 Hz), 118.8, 113.6 (d, $^2J_{C,F}$ = 23.3 Hz), 108.4 (d, $^2J_{C,F}$ = 24.5 Hz), 25.8, 11.5; HR-MS (ESI): m/z = 374.0878, calcd. for $C_{24}H_{16}ClFO$: 374.0874 (M^+).

6-Ethyl-8-methoxy-11-phenylindeno[1,2-*c*]chromene (3l): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (dd, J = 8.0, 1.4 Hz, 1H), 7.55–7.50 (m, 5H), 7.46–7.44 (m, 1H), 7.40–7.37 (m, 1H), 7.31–7.29 (m, 1H), 7.28–7.23 (m, 1H), 7.02–6.97 (m, 2H), 3.91 (s, 3H), 3.21 (q, J = 7.6 Hz, 2H), 1.51 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8, 156.7, 149.8, 138.1, 136.9, 131.1, 130.0, 128.8, 127.2, 127.1, 125.0, 124.5, 124.0, 122.0, 120.5, 120.0, 117.4, 115.8, 112.2, 107.9, 55.9, 25.9, 11.5; HR-MS (ESI): m/z = 352.1475, calcd. for $C_{25}H_{20}O_2$: 352.1463 (M^+).

2-Chloro-6-ethyl-8-methoxy-11-phenylindeno[1,2-*c*]chromene (3m): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.46 (m, 7H), 7.33–7.29 (m, 2H), 7.20–7.17 (m, 1H), 7.00 (dd, J = 8.5, 2.2 Hz, 1H), 3.91 (s, 3H), 3.21 (q, J = 7.6 Hz, 2H), 1.51 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 157.0, 148.2, 137.8, 136.1, 131.1, 129.8, 129.2, 129.0, 127.7, 127.0, 126.2, 123.8, 121.9, 120.8, 120.3, 118.7, 115.7, 112.5, 107.9, 55.9, 25.8, 11.4; HR-MS (ESI): m/z = 386.1073, calcd. for $C_{25}H_{19}ClO_2$: 386.1074 (M^+).

2-(*tert*-Butyl)-6-ethyl-8-methoxy-11-phenylindeno[1,2-*c*]chromene (3n): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.62 (m, 1H), 7.57–7.53 (m, 5H), 7.45–7.42 (m, 1H), 7.34–7.30 (m, 3H), 6.99 (dd, J = 8.5, 2.3 Hz, 1H), 3.91 (s, 3H), 3.20 (q, J = 7.6 Hz, 2H), 1.49 (t, J = 7.6 Hz, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 156.6, 147.8, 146.9, 138.1, 137.2, 131.2, 130.2, 128.7, 127.2, 124.6, 124.5, 122.7, 121.2, 119.8, 119.7, 116.7, 115.6, 112.1, 107.9, 55.9, 34.4, 31.2, 25.9, 11.6; HR-MS (ESI): m/z = 408.2091, calcd. for $C_{29}H_{28}O_2$: 408.2089 (M^+).

2-Chloro-6-ethyl-8-methoxy-11-(*para*-tolyl)indeno[1,2-c]chromene (3o): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.61 (m, 1H), 7.48–7.47 (m, 1H), 7.41–7.39 (m, 2H), 7.36–7.28 (m, 4H), 7.19–7.16 (m, 1H), 6.99 (dd, J = 8.6, 2.3 Hz, 1H), 3.91 (s, 3H), 3.18 (q, J = 7.6 Hz, 2H), 2.48 (s, 3H), 1.49 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 156.6, 147.8, 146.9, 138.1, 137.2, 131.2, 130.2, 128.7, 127.2, 124.6, 124.5, 122.7, 121.2, 129.8, 119.7, 116.7, 115.6, 112.1, 107.9, 55.9, 34.4, 31.2, 25.9, 11.6; HR-MS (ESI): m/z = 400.1233, calcd. for $C_{26}H_{21}ClO_2$: 400.1230 (M^+).

2-Chloro-6-ethyl-8,9-dimethoxy-11-phenylindeno[1,2-*c*]chromene (3p): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.46 (m, 7H), 7.34–7.31 (m, 1H), 7.20–7.17 (m, 1H), 6.91 (s, 1H), 4.02 (s, 3H), 3.87 (s, 3H), 3.21 (q, J = 7.6 Hz, 2H), 1.52 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 157.0, 148.2, 137.9, 137.3, 132.9, 131.1, 129.7, 129.6, 129.1, 126.9, 126.3, 123.8, 122.0, 120.6, 120.4, 118.6, 115.7, 112.4, 107.8, 55.9, 25.8, 21.4, 11.4; HR-MS (ESI): m/z = 416.1177, calcd. for $C_{26}H_{21}ClO_3$: 416.1179 (M^+).

Supporting Information

Experimental procedures, characterization data, as well as ^{1}H and ^{13}C NMR spectra of compounds **3** are available in the Supporting Information.

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References

[1] a) S. L. Schreiber, *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 6699; b) K. Hübel, T. Leßmann, H. Waldmann, *Chem. Soc. Rev.* **2008**, *37*, 1361; c) S. L. Schreiber, *Chem. Eng. News* **2003**, *81*, 51.

[2] a) D. P. Walsh, Y.-T. Chang, *Chem. Rev.* **2006**, *106*, 2476; b) P. Arya, D. T. H. Chou, M.-G. Baek, *Angew. Chem.* **2001**, *113*, 351; *Angew. Chem. Int. Ed.* **2001**, *40*, 339; c) S. L. Schreiber, *Science* **2000**, *287*, 1964; d) M. D. Burke, S. L. Schreiber, *Angew. Chem.* **2004**, *116*, 48; *Angew. Chem. Int. Ed.* **2004**, *43*, 46; e) S. L. Schreiber, *Nature* **2009**, *457*, 153; f) D. S. Tan, *Nat. Chem. Biol.* **2005**, *1*, 74; g) C. Cordier, D. Morton, S. Murrison, A. Nelson, C. O'Leary-Steele, *Nat. Prod. Rep.* **2008**, *25*, 719; h) W. R. J. D. Galloway, A. I. Llobet, D. R. Spring, *Nat. Commun.* **2010**, *1*, 80; i) S. Oh, S. B. Park, *Chem. Commun.* **2011**, *47*, 12754.

[3] For reviews, see: a) J. Montgomery, *Angew. Chem.* **2004**, *116*, 3980; *Angew. Chem. Int. Ed.* **2004**, *43*, 3890; b) J. Panteleev, L. Zhang, M. Lautens, *Angew. Chem.* **2011**, *123*, 9255; *Angew. Chem. Int. Ed.* **2011**, *50*, 9089; c) S. H. Kim, S. H. Park, J. H. Choi, S. Chang, *Chem. Asian J.* **2011**, *6*, 2618; d) P. Lu, Y. Wang, *Chem. Soc. Rev.* **2012**, *41*, 5687; e) T. Miura, M. Murakami, *Chem. Commun.* **2007**, 217; f) M. Malacria, *Chem. Rev.* **1996**, *96*, 289; g) K. C. Nicolaou, T. Montagnon, S. A. Snyder, *Chem.*

Commun. **2003**, 551; h) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem.* **2006**, *118*, 7292; *Angew. Chem. Int. Ed.* **2006**, *45*, 7134; i) D. Enders, C. Grondal, M. R. M. Hüttl, *Angew. Chem.* **2007**, *119*, 1590; *Angew. Chem. Int. Ed.* **2007**, *46*, 1570; j) L. F. Tietze, G. Brasche, K. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; k) L. F. Tietze, M. A. Düfert, T. Hungerland, K. Oum, T. Lenzer, *Chem. Eur. J.* **2011**, *17*, 8452; l) J. Panteleev, L. Zhang, M. Lautens, *Angew. Chem.* **2011**, *123*, 9255; *Angew. Chem. Int. Ed.* **2011**, *50*, 9089; m) S. H. Kim, S. H. Park, J. H. Choi, S. Chang, *Chem. Asian J.* **2011**, *6*, 2618.

[4] For selected examples, see: a) Y. Luo, L. Hong, J. Wu, *Chem. Commun.* **2011**, *47*, 5298; b) Y. Luo, X. Pan, J. Wu, *Org. Lett.* **2011**, *13*, 1150; c) X. Pan, Y. Luo, J. Wu, *Chem. Commun.* **2011**, *47*, 8967; d) Y. Luo, J. Wu, *Chem. Commun.* **2011**, *47*, 11137; e) Y. Luo, X. Pan, J. Wu, *Adv. Synth. Catal.* **2012**, *354*, 3071; f) X. Pan, H. Nie, Y. Luo, Y. Gao, J. Wu, *Org. Biomol. Chem.* **2012**, *10*, 8244. For a review, see: g) Y. Luo, X. Pan, X. Yu, J. Wu, *Chem. Soc. Rev.* **2014**, *43*, 834.

[5] S. Li, Y. Luo, X. Wang, M. Guo, J. Wu, *Chem. Asian J.* **2012**, *7*, 1691, and references cited therein.

[6] For selected examples, see: a) Y. Hu, Y. Zhang, Z. Yang, R. Fathi, *J. Org. Chem.* **2002**, *67*, 2365; b) Y. Nan, H. Miao, Z. Yang, *Org. Lett.* **2000**, *2*, 297; c) Y. Liao, J. Smith, R. Fathi, Z. Yang, *Org. Lett.* **2005**, *7*, 2707; d) Y. Liang, S. Tang, X.-D. Zhang, L.-Q. Mao, Y.-X. Xie, J.-H. Li, *Org. Lett.* **2006**, *8*, 3017; e) C. Martínez, R. Álvarez, J. M. Aurrecoechea, *Org. Lett.* **2009**, *11*, 1083; f) M. Nakamura, L. Ilies, S. Otsubo, *Angew. Chem.* **2006**, *118*, 958; *Angew. Chem. Int. Ed.* **2006**, *45*, 944.

[7] For selected examples, see: a) B. Yao, Y. Li, Z. Liang, Y. Zhang, *Org. Lett.* **2011**, *13*, 640; b) K. Ogata, Y. Atsuumi, S.-i. Fukuzawa, *Org. Lett.* **2010**, *12*, 4536; c) H. Taniguchi, T. Ohmura, M. Suginome, *J. Am. Chem. Soc.* **2009**, *131*, 11298; d) M. Shirakura, M. Suginome, *J. Am. Chem. Soc.* **2009**, *131*, 5060; e) M. Shi, L.-X. Shao, J.-M. Lu, Y. Wei, K. Mizuno, H. Maeda, *Chem. Rev.* **2010**, *110*, 5883; f) J. Terao, M. Tomita, S. P. Singh, N. Kambe, *Angew. Chem.* **2010**, *122*, 148; *Angew. Chem. Int. Ed.* **2010**, *49*, 144; g) S. Saito, K. Maeda, R. Yamasaki, T. Kitamura, M. Nakagawa, K. Kato, I. Azumaya, H. Masu, *Angew. Chem.* **2010**, *122*, 1874; *Angew. Chem. Int. Ed.* **2010**, *49*, 1830; h) C. Su, J. Cao, X. Huang, L. Wu, X. Huang, *Chem. Eur. J.* **2011**, *17*, 1579; i) B.-L. Lu, Y. Wei, M. Shi, *Chem. Eur. J.* **2010**, *16*, 10975; j) K. Chen, Z. Zhang, Y. Wei, M. Shi, *Chem. Commun.* **2012**, *48*, 7696; k) M. Shi, J. Lu, Y. Wei, L. Shao, *Acc. Chem. Res.* **2012**, *45*, 641; l) Q. Xiao, S. Ye, J. Wu, *Org. Lett.* **2012**, *14*, 3430.

