# Palladium-Catalyzed Cycloaromatization/Alkylation of *o*-(Alkynyl)styrenes

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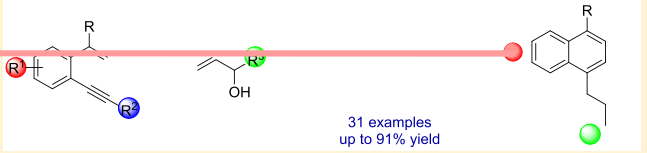
Supporting Information



deficient alkenes as well as the environment-friendly allylic alcohols[20] to form the (alkenyl)naphthalenes, indenes, or $\beta$-arylketone products (Scheme 1c, 1d). Another work on platinum-catalyzed cycloaromatization and [3 + 2] cycloaddition of -(alkynyl)styrenes with silyl enol ethers was successfully developed by Iwasawa and co-workers to make the five-membered-ring-fused naphthalenes.[21] Comparing with the extensive studies on the cycloaromatization of -(alkynyl)-biaryls and -(alkynyl)heterobiaryls for construction of fused ring compounds,[22] so far only rare examples have been explored to prepare the highly functionalized naphthalenes via transition-metal-catalyzed cycloaromatization of -(alkynyl)-styrenes.[18,21] Herein, we would like to describe a palladium-catalyzed tandem cycloaromatization and alkylation reactions of -(alkynyl)styrenes for the synthesis of functionalized naphthalenes (Scheme 1e).

## RESULTS AND DISCUSSION

We began our study by investigating the -(alkynyl)styrene **1a** to couple with 3-buten-2-ol **2a** (Table 1). As illustrated in the previous work, the substituent locations at alkenyl double bonds are crucial for the regioselective cyclization of 1,3-dien-5-ynes.[23] It was found that the desired product **3a** could be formed in 9% yield and along with mainly recovering the starting material with using $Pd(OAc)_2$ as catalyst, $CuCl_2$ as oxidant in DMSO at 30 °C under oxygen atmosphere (Table 1, entry 1). To improve the conversion of this reaction, the temperature was elevated to 80 °C, and the yield of the desired product was then increased up to 70% (Table 1, entry 2). With this promising result, different catalysts, oxidants, solvents, and additives were further screened in sequence. It was found that the combination of $Pd(OAc)_2$ with $CuCl_2$ more favored the formation of product in a high yield in DMSO solution (Table 1, entries 4−11). Next, to further improve the product yield, different additives were examined. The product **3a** was obtained in 76% when 10 equiv of $H_2O$ were used as additive (Table 1, entries 12−14). Decreasing the $Pd(OAc)_2$ catalyst loading to 5 mol %, the desired product **3a** still could be obtained in 73% isolated yield (Table 1, entry 15). Finally, the control experiments show that palladium catalyst and copper oxidant are necessary to afford the desired product **3a** in a good yield (Table 1, entries 16−18).

With the optimized reaction conditions at hand, the substrate scope of -(alkynyl)styrenes was tested (Table 2). It was noticed that all the substrates with an electron-donating or electron-withdrawing group on the phenyl ring ($R^4$) could be smoothly transformed to the corresponding desired products in good to high yields (**3b−3h**). Comparing with electron-donating group, it was observed that the electron-withdrawing group at

result of the easy protodemetalation of electron-rich carbopalladium intermediate generated in situ.

Following, we probed the generality of different allylic alcohols as the coupling partners. The results are summarized in Table 3. When the prop-2-en-1-ol was subjected to this reaction, a naphthalenyl propanal product **4a** was isolated only in 31% yield. A similar result was observed when the (*E*)-but-2-en-1-ol was used as the coupling partner (**4d**). Installing a methyl group at the 2-position of allylic alcohol will significantly increase the yield of product (**4e**). Unfortunately, no desired product was detected with using the 3-methylbut-2-en-1-ol as coupling partner possibly due to its steric hindrance (**4h**). Interestingly, the 1,1-dimethyl substituted allylic alcohol could afford the (alkenyl)naphthalene product **4f** in moderate yield. When the side chain of the allylic alcohol was prolonged, the corresponding desired products could be obtained in moderate to good yields (**4b**, **4c**). Unfortunately, the hexa-1,5-dien-3-ol and 1-phenylprop-2-en-1-ol failed to give the desired product.

releasing the Pd(0), which could be activated again by using $CuCl_2$ and molecular oxygen as oxidants.

## CONCLUSION

In conclusion, a palladium-catalyzed tandem cycloaromatization/alkylation reaction of -(ethynyl)styrenes has been developed. Under mild reaction conditions, the multifunctionalized naphthalenes were obtained in moderate to high yields with using the abundant and environmentally friendly allylic alcohols as alkylation reagent. This tandem reaction provides a simple, cost-effective route for the regioselective synthesis of alkyl naphthalenes.

## EXPERIMENTAL SECTION

**General Information.** $PdCl_2$, $CuCl_2$, and the allylic alcohols were purchased from commercial suppliers and used as received unless otherwise noted. All reactions were performed under oxygen environment unless otherwise specified. All commercial solvents and reagents were employed without further purification. Reactions were monitored through analytical thin layer chromatography ($SiO_2$ 60 F-254 plates). The spots visualization was performed under UV radiation (254 nm), further visualization was possible using basic solution of potassium permanganate. Flash chromatography was carried out using 200−300 mesh silica gel ($SiO_2$ 60) with distilled solvents. Proton nuclear magnetic resonance ($^1$H NMR) and carbon nuclear magnetic resonance ($^{13}$C{$^1$H} NMR) spectra were recorded on Bruker Advance 400 M NMR spectrometers. Chloroform-*d* was used as the solvent and $SiMe_4$ (TMS) as internal standard. Chemical shifts for $^1$H NMR spectra are reported as $\delta$ in units of parts per million (ppm) downfield from TMS ($\delta$ 0.00 ppm) and relative to the signal of chloroform-*d* ($\delta$ 7.260 ppm, singlet). Multiplicities are recorded as (singlet); *d* (doublet); (triplet); (quartet); *dd* (doublets of doublet); *m* (multiplets). Coupling constants are expressed as a *J* value in Hz. $^{13}$C{$^1$H} NMR are reported as $\delta$ in units of parts per million (ppm) downfield from TMS ($\delta$ 0.00 ppm) and relative to the signal of chloroform-*d* ($\delta$ 77.03 ppm, triplet). HRMS spectra were recorded on XEVO-G2 Q-TOF (Waters Corporation). The starting materials of **1a−1v** were prepared according to the reported procedures, and the NMR spectroscopic data of these compounds are identified with the literatures.[26]

**Procedure for the Synthesis of Products (3a−3v), (4a−4f).** A 35 mL sealed tube equipped with a stirring bar was charged with $Pd(OAc)_2$ (5 mol %, 3.4 mg) and $CuCl_2$ (10 mol %, 4.0 mg), and a septum cap was affixed. The sealed tube was evacuated and refilled with oxygen two times, and then a needle connected to an oxygen balloon was inserted through the septum cap. DMSO (1.5 mL) was added into the sealed tube by a syringe. To the resulting mixture, substrate **1** (0.3 mmol), **2** (0.9 mmol), and water (3.0 mmol, 54 $\mu$L) were added. The reaction mixture was allowed to stir at 80 °C (oil bath) for 12 h. Then the mixture was cooled to room temperature, diluted with diethyl ether (5 mL), and filtered through a Celite pad. The filtrate was washed with water three times (3 × 30 mL), dried over $Na_2SO_4$, and concentrated in vacuo. The residue was purified by thin layer chromatography on silica gel (300−400 mesh) using (petroleum ether/ethyl acetate = 20/1) as eluting solvent to afford the desired product.

**Procedure for the Synthesis of Product 3a on a 5 mmol Scale.** A 100 mL Schlenk tube equipped with a stirring bar was charged with $Pd(OAc)_2$ (5 mol %, 56.1 mg) and $CuCl_2$ (10 mol %, 67.2 mg), and a septum cap was affixed. The sealed tube was evacuated and refilled with oxygen two times, and then a needle connected to an oxygen balloon was inserted through the septum cap. DMSO (25.0 mL) was added into the sealed tube by a syringe. To the resulting mixture, substrate **1a** (5.0 mmol), **2** (15.0 mmol), and water (50.0 mmol, 900.0 $\mu$L) were added. The reaction mixture was allowed to stir at 80 °C (oil bath) for 15 h. Then the mixture was cooled to room temperature, diluted with diethyl ether (80 mL), and filtered through a Celite pad. The filtrate was washed with water three times (3 × 100 mL), dried over $Na_2SO_4$, and concentrated in vacuo. The residue was purified via column chromatography on silica gel (eluents: petroleum ether/ethyl acetate = 50:1−20:1) to afford the desired product **3a** (1056.8 mg, 3.664 mmol, 73%) as yellow solid.

*4-(4-Methyl-2-phenylnaphthalen-1-yl)butan-2-one (**3a**).* Yellow solid; 63.2 mg, 0.219 mmol, yield 73%; mp 87−89 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.03 (t, *J* = 8.3 Hz, 2H), 7.60−7.50 (m, 2H), 7.46−7.29 (m, 5H), 7.20 (s, 1H), 3.26 (t, *J* = 8.1 Hz, 2H), 2.70−2.63 (m, 5H), 2.02 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 208.0, 142.6, 139.3, 132.5, 132.4, 132.1, 131.8, 129.2, 129.2, 128.3, 127.1, 126.4, 125.5, 125.1, 124.6, 45.1, 29.8, 23.2, 19.4; HRMS (ESI, *m*/ ) Calcd for $C_{21}H_{20}NaO$ [M + Na]$^+$: 311.1412, found 311.1407.

*4-(2-(4-Methoxyphenyl)-4-methylnaphthalen-1-yl)butan-2-one (**3b**).* Yellow solid; 64.0 mg, 0.201 mmol, yield 67%; mp 115−117 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (td, *J* = 7.5, 1.8 Hz, 2H), 7.61−7.53 (m, 2H), 7.31−7.20 (m, 3H), 7.00 (d, *J* = 8.5 Hz, 2H), 3.89 (s, 3H), 3.31 (t, *J* = 8.2 Hz, 2H), 2.73−2.67 (m, 5H), 2.07 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 158.7, 138.9, 134.9, 132.4, 132.4, 132.2, 131.8, 130.3, 129.6, 126.3, 125.4, 125.0, 124.6, 113.8, 55.4, 45.1, 29.8, 23.2, 19.4. HRMS (ESI, *m*/ ) Calcd for $C_{22}H_{22}NaO_2$ [M + Na]$^+$: 341.1517, found 341.1510.

*4-(4-Methyl-2-(p-tolyl)naphthalen-1-yl)butan-2-one (**3c**).* Yellow solid; 73.5 mg, 0.243 mmol, yield 81%; mp 89−91 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07−8.01 (m, 2H), 7.55 (tt, *J* = 6.9, 5.1 Hz, 2H), 7.25−7.19 (m, 5H), 3.28 (t, *J* = 8.2 Hz, 2H), 2.71−2.65 (m, 5H), 2.43 (s, 3H), 2.05 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$208.1, 139.6, 139.3, 136.7, 132.5, 132.4, 132.1, 131.8, 129.5, 129.1, 129.0, 126.3, 125.4, 125.1, 124.6, 45.2, 29.8, 23.2, 21.3, 19.5; HRMS (ESI, *m*/ ) Calcd for $C_{22}H_{22}NaO$ [M + Na]$^+$: 325.1568, found 325.1567.

*4-(2-([1,1′-Biphenyl]-4-yl)-4-methylnaphthalen-1-yl)butan-2-one (**3d**).* Yellow solid; 85.3 mg, 0.234 mmol, yield 78%; mp 115−117 °C;$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (t, *J* = 9.3 Hz, 2H), 7.67 (d, *J* = 7.8 Hz, 4H), 7.61−7.53 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 3H), 7.25 (s, 1H), 3.32 (t, *J* = 8.1 Hz, 2H), 2.74−2.68 (m, 5H), 2.06 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 141.6, 140.9, 140.0, 138.9, 132.6, 132.2, 131.8, 129.7, 129.3, 129.0, 127.5, 127.2, 127.1, 126.4, 125.6, 125.1, 124.7, 45.2, 29.9, 23.3, 19.5; HRMS (ESI, *m*/ ) Calcd for $C_{27}H_{24}NaO$ [M + Na]$^+$: 387.1725, found 387.1725.

*4-(2-(4-Fluorophenyl)-4-methylnaphthalen-1-yl)butan-2-one (**3e**).* Yellow solid; 63.4 mg, 0.207 mmol, yield 69%; mp 92−94 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.09−8.00 (m, 2H), 7.62−7.53 (m, 2H), 7.31−7.25 (m, 2H), 7.14 (dd, *J* = 16.0, 7.6 Hz, 3H), 3.25 (t, *J* = 8.1 Hz, 2H), 2.71−2.63 (m, 5H), 2.06 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 207.9, 162.1 (d, *J* = 245.9 Hz), 138.5 (d, *J* = 3.4 Hz), 138.2, 132.6, 132.6, 132.3, 131.8, 130.8 (d, *J* = 7.9 Hz), 129.2, 126.5, 125.7, 125.1, 124.6, 115.3 (d, *J* = 21.3 Hz), 45.0, 29.9, 23.2, 19.5; $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ −115.62 (ddd, *J* = 14.3, 8.9, 5.4 Hz); HRMS (ESI, *m*/ ) Calcd for $C_{21}H_{19}FNaO$ [M + Na]$^+$: 329.1318, found 329.1315.

*4-(2-(4-Chlorophenyl)-4-methylnaphthalen-1-yl)butan-2-one (**3f**).* Yellow solid; 66.8 mg, 0.207 mmol, yield 69%; mp 110−112 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.08−8.00 (m, 2H), 7.61−7.53 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.15 (s, 1H), 3.25 (t, *J* = 8.2 Hz, 2H), 2.70−2.63 (m, 5H), 2.06 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 207.8, 141.0, 138.0, 133.2, 132.8, 132.6, 132.2, 131.8, 130.6, 129.0, 128.6, 126.5, 125.8, 125.1, 124.6, 45.0, 29.9, 23.1, 19.5; HRMS (ESI, *m*/ ) Calcd for $C_{21}H_{19}ClNaO$ [M + Na]$^+$: 345.1022, found 345.1018.

*4-(2-(2-Methoxyphenyl)-4-methylnaphthalen-1-yl)butan-2-one (**3g**).* Yellow solid; 79.3 mg, 0.249 mmol, yield 83%; mp 34−35 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (dd, *J* = 9.7, 6.9 Hz, 2H), 7.57 (qd, *J* = 6.8, 3.5 Hz, 2H), 7.40 (td, *J* = 7.9, 1.7 Hz, 1H), 7.19 (q, *J* = 2.3, 1.6 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 3.77 (s, 3H), 3.26 (ddd, *J* = 14.3, 11.1, 5.2 Hz, 1H), 3.10 (ddd, *J* = 14.1, 10.9, 5.8 Hz, 1H), 2.80−2.60 (m, 5H), 2.04 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 208.5, 156.6, 135.6, 133.2, 132.6, 132.3, 131.7, 131.1, 131.1, 129.5, 128.9, 126.1, 125.3, 125.1, 124.6, 120.6,



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110.9, 55.5, 44.6, 29.7, 23.7, 19.5; HRMS (ESI, *m/z*) Calcd for $C_{22}H_{22}NaO_2$ $[M + Na]^+$: 341.1517, found 341.1513.

*4-(4-Methyl-2-(o-tolyl)naphthalen-1-yl)butan-2-one* (**3h**). Yellow solid; 77.1 mg, 0.255 mmol, yield 85%; mp 34−35 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.13−8.06 (m, 2H), 7.61 (qd, $J$ = 7.2, 3.5 Hz, 2H), 7.36−7.27 (m, 3H), 7.20 (d, $J$ = 7.3 Hz, 1H), 7.15 (s, 1H), 3.36 (ddd, $J$ = 15.2, 11.0, 5.1 Hz, 1H), 2.93 (ddd, $J$ = 14.0, 10.7, 6.0 Hz, 1H), 2.78−2.56 (m, 5H), 2.12 (s, 3H), 2.04 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 141.7, 138.6, 135.8, 132.6, 132.5, 132.2, 131.8, 130.2, 129.4, 128.7, 127.5, 126.2, 125.7, 125.4, 125.1, 124.5, 44.6, 29.7, 23.3, 20.3, 19.5; HRMS (ESI, *m/z*) Calcd for $C_{22}H_{22}NaO$ $[M + Na]^+$: 325.1568, found 325.1569.

*4-(2-(2-Fluorophenyl)-4-methylnaphthalen-1-yl)butan-2-one* (**3i**). Yellow solid; 62.5 mg, 0.204 mmol, yield 68%; mp 78−80 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.10−8.02 (m, 2H), 7.61−7.55 (m, 2H), 7.42−7.34 (m, 1H), 7.30−7.14 (m, 4H), 3.21 (t, J = 8.2 Hz, 2H), 2.80−2.62 (m, 5H), 2.05 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 159.8 (d, $J$ = 244.6 Hz), 133.5, 132.9, 132.7, 132.6, 131.8, 131.7, 129.6 (d, $J$ = 17.3 Hz), 129.4 (d, $J$ = 8.0 Hz), 129.0, 126.4, 125.8, 125.1, 124.7, 124.2 (d, $J$ = 3.7 Hz), 115.8 (d, $J$ = 22.4 Hz), 44.5 (d, $J$ = 1.5 Hz), 29.8, 23.7, 19.5; $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ −114.34 (d, $J$ = 4.3 Hz); HRMS (ESI, *m/z*) Calcd for $C_{21}H_{19}FNaO$ $[M + Na]^+$: 329.1318, found 329.1323.

*4-(2-(2-Chlorophenyl)-4-methylnaphthalen-1-yl)butan-2-one* (**3j**). Yellow solid; 56.2 mg, 0.174 mmol, yield 58%; mp 34−35 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.11−8.02 (m, 2H), 7.61−7.56 (m, 2H), 7.54−7.49 (m, 1H), 7.34 (dt, $J$ = 7.7, 3.9 Hz, 2H), 7.30−7.25 (m, 1H), 7.12 (s, 1H), 3.25−3.15 (m, 1H), 3.14−3.04 (m, 1H), 2.79−2.57 (m, 5H), 2.03 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 140.9, 136.4, 133.5, 132.9, 132.8, 132.7, 131.7, 131.3, 129.7, 129.0, 128.5, 126.8, 126.4, 125.8, 125.2, 124.6, 44.4, 29.8, 23.5, 19.5; HRMS (ESI, *m/z*) Calcd for $C_{21}H_{19}ClNaO$ $[M + Na]^+$: 345.1022, found 345.1011.

*4-(2-Butyl-4-methylnaphthalen-1-yl)butan-2-one* (**3k**). Yellow solid; 58.8 mg, 0.219 mmol, yield 73%; mp 36−38 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.00−7.94 (m, 2H), 7.54−7.44 (m, 2H), 7.16 (s, 1H), 3.35 (t, $J$ = 8.2 Hz, 2H), 2.80−2.71 (m, 4H), 2.66 (s, 3H), 2.20 (s, 3H), 1.67−1.57 (m, 2H), 1.45 (h, $J$ = 7.4 Hz, 2H), 0.97 (t, $J$ = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.4, 137.8, 132.6, 132.2, 131.8, 131.5, 129.4, 125.9, 125.0, 124.7, 124.0, 44.9, 34.2, 33.6, 30.1, 23.1, 22.0, 19.5, 14.2; HRMS (ESI, *m/z*) Calcd for $C_{19}H_{24}NaO$ $[M + Na]^+$: 291.1725, found 291.1727.

*4-(2-Cyclopropyl-4-methylnaphthalen-1-yl)butan-2-one* (**3l**). Yellow solid; 56.0 mg, 0.222 mmol, yield 74%; mp 40−41 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.03−7.95 (m, 2H), 7.51 (dtd, $J$ = 15.9, 7.4, 6.0 Hz, 2H), 7.00 (s, 1H), 3.58 (d, $J$ = 8.2 Hz, 2H), 2.82 (d, $J$ = 8.2 Hz, 2H), 2.66 (s, 3H), 2.22 (s, 3H), 2.11 (td, $J$ = 8.6, 4.3 Hz, 1H), 1.09−1.00 (m, 2H), 0.78 (h, $J$ = 4.5 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.6, 137.3, 133.7, 132.7, 131.9, 131.6, 126.0, 125.4, 124.9, 124.8, 123.8, 44.3, 30.1, 22.2, 19.6, 13.6, 7.6; HRMS (ESI, *m/z*) Calcd for $C_{18}H_{20}NaO$ $[M + Na]^+$: 275.1412, found 275.1411.

*4-(2-(2-(Benzyloxy)ethyl)-4-methylnaphthalen-1-yl)butan-2-one* (**3m**). Yellow solid; 56.1 mg, 0.162 mmol, yield 54%; mp 48−49 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.99 (d, $J$ = 8.6 Hz, 1H), 7.95 (d, $J$ = 7.8 Hz, 1H), 7.53−7.46 (m, 2H), 7.35−7.27 (m, 5H), 7.18 (s, 1H), 4.53 (s, 2H), 3.72 (t, $J$ = 7.3 Hz, 2H), 3.34 (t, $J$ = 8.2 Hz, 2H), 3.08 (t, $J$ = 7.3 Hz, 2H), 2.74 (t, $J$ = 8.1 Hz, 2H), 2.65 (s, 3H), 2.11 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.3, 138.4, 133.6, 132.7, 132.1, 132.1, 129.5, 128.5, 127.8, 127.7, 126.0, 125.0, 124.1, 73.2, 71.2, 44.7, 34.2, 30.1, 22.0, 19.5; HRMS (ESI, *m/z*) Calcd for $C_{24}H_{26}NaO_2$ $[M + Na]^+$: 369.1830, found 369.1828.

*4-(4-Methyl-2-vinylnaphthalen-1-yl)butan-2-one* (**3n**). Yellow solid; 21.4 mg, 0.09 mmol, yield 30%; mp 40−41 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.01 (t, $J$ = 9.1 Hz, 2H), 7.56−7.47 (m, 3H), 7.19 (dd, $J$ = 17.3, 11.1 Hz, 1H), 5.77 (d, $J$ = 17.3 Hz, 1H), 5.42 (d, $J$ = 11.0 Hz, 1H), 3.42 (t, $J$ = 8.1 Hz, 2H), 2.75 (t, $J$ = 8.1 Hz, 2H), 2.68 (s, 3H), 2.18 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.2, 134.8, 133.0, 132.9, 132.9, 132.2, 132.0, 126.3, 125.6, 125.0, 124.8, 124.4, 116.6, 44.4, 30.1, 21.8, 19.7; HRMS (ESI, *m/z*) Calcd for $C_{17}H_{18}NaO$ $[M + Na]^+$: 261.1255, found 261.1259.

*4-(6-Methoxy-4-methyl-2-phenylnaphthalen-1-yl)butan-2-one* (**3o**). Yellow solid; 66.9 mg, 0.210 mmol, yield 70%; mp 140−142 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.95 (d, $J$ = 9.2 Hz, 1H), 7.43 (t, $J$ = 7.4 Hz, 2H), 7.39−7.28 (m, 4H), 7.23 (d, $J$ = 9.1 Hz, 1H), 7.18 (s, 1H), 3.97 (s, 3H), 3.23 (t, $J$ = 8.0 Hz, 2H), 2.68−2.61 (m, 5H), 2.02 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 157.4, 142.6, 137.2, 133.8, 132.1, 131.2, 129.9, 129.4, 128.3, 127.0, 126.3, 118.3, 103.9, 55.5, 45.3, 29.8, 23.3, 19.7; HRMS (ESI, *m/z*) Calcd for $C_{22}H_{22}NaO_2$ $[M + Na]^+$: 341.1517, found 341.1514.

*4-(4,6-Dimethyl-2-phenylnaphthalen-1-yl)butan-2-one* (**3p**). Yellow solid; 71.7 mg, 0.237 mmol, yield 79%; mp 127−128 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.94 (d, $J$ = 8.6 Hz, 1H), 7.83 (s, 1H), 7.47−7.31 (m, 6H), 7.18 (s, 1H), 3.26 (t, $J$ = 8.2 Hz, 2H), 2.70−2.64 (m, 5H), 2.58 (s, 3H), 2.03 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 142.6, 138.4, 135.1, 132.7, 131.9, 131.8, 129.9, 129.3, 129.3, 128.5, 128.3, 127.0, 124.5, 124.2, 45.2, 29.8, 23.2, 21.9, 19.5; HRMS (ESI, *m/z*) Calcd for $C_{22}H_{22}NaO$ $[M + Na]^+$: 325.1568, found 325.1559.

*4-(6-Fluoro-4-methyl-2-phenylnaphthalen-1-yl)butan-2-one* (**3q**). Yellow solid; 40.4 mg, 0.132 mmol, yield 44%; mp 113−115 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (dd, $J$ = 9.3, 5.8 Hz, 1H), 7.65 (dd, $J$ = 10.9, 2.6 Hz, 1H), 7.48−7.30 (m, 6H), 7.24 (s, 1H), 3.26 (t, $J$ = 8.0 Hz, 2H), 2.69−2.60 (m, 5H), 2.05 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 207.8, 160.5 (d, $J$ = 246.0 Hz), 142.2, 138.6 (d, $J$ = 2.5 Hz), 133.8 (d, $J$ = 8.1 Hz), 132.3, 131.9 (d, $J$ = 5.2 Hz), 130.3, 129.2, 128.8, 128.4, 127.2 (d, $J$ = 8.8 Hz), 127.2, 116.2 (d, $J$ = 24.6 Hz), 108.7 (d, $J$ = 20.6 Hz), 45.1, 29.8, 23.3, 19.4; $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ −114.86. HRMS (ESI, *m/z*) Calcd for $C_{21}H_{19}FNaO$ $[M + Na]^+$: 329.1318, found 329.1311.

*4-(6-Chloro-4-methyl-2-phenylnaphthalen-1-yl)butan-2-one* (**3r**). Yellow solid; 48.4 mg, 0.150 mmol, yield 50%; mp 150−151 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.02 (d, $J$ = 2.1 Hz, 1H), 7.96 (d, $J$ = 9.0 Hz, 1H), 7.50 (dd, $J$ = 9.1, 2.1 Hz, 1H), 7.45 (t, $J$ = 7.3 Hz, 2H), 7.39 (d, $J$ = 7.0 Hz, 1H), 7.31 (d, $J$ = 7.8 Hz, 2H), 7.23 (s, 1H), 3.24 (t, $J$ = 8.1 Hz, 2H), 2.66−2.61 (m, 5H), 2.03 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 207.8, 142.1, 139.6, 133.5, 132.3, 131.8, 131.6, 130.4, 130.2, 129.2, 128.4, 127.3, 127.0, 126.4, 124.2, 45.0, 29.8, 23.2, 19.4; HRMS (ESI, *m/z*) Calcd for $C_{21}H_{19}ClNaO$ $[M + Na]^+$: 345.1022, found 345.1010.

*4-(4-Ethyl-2-phenylnaphthalen-1-yl)butan-2-one* (**3s**). Yellow solid; 74.4 mg, 0.246 mmol, yield 82%; mp 91−92 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.16−8.12 (m, 1H), 8.08−8.04 (m, 1H), 7.60−7.53 (m, 2H), 7.46 (t, $J$ = 7.3 Hz, 2H), 7.40 (d, $J$ = 6.5 Hz, 1H), 7.35 (d, $J$ = 7.5 Hz, 2H), 7.24 (s, 1H), 3.29 (t, $J$ = 8.2 Hz, 2H), 3.13 (q, $J$ = 7.5 Hz, 2H), 2.70 (t, $J$ = 8.2 Hz, 2H), 2.05 (s, 3H), 1.40 (t, $J$ = 7.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.1, 142.7, 139.4, 138.4, 132.0, 131.7, 129.3, 128.4, 127.5, 127.1, 126.3, 125.5, 124.8, 124.7, 45.1, 29.8, 25.9, 23.3, 15.1; HRMS (ESI, *m/z*) Calcd for $C_{22}H_{22}NaO$ $[M + Na]^+$: 325.1568, found 325.1567.

*4-(2,4-Diphenylnaphthalen-1-yl)butan-2-one* (**3t**). Yellow solid; 95.7 mg, 0.273 mmol, yield 91%; mp 67−69 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.12 (d, $J$ = 8.6 Hz, 1H), 8.02 (d, $J$ = 8.5 Hz, 1H), 7.60 (t, $J$ = 7.7 Hz, 1H), 7.56−7.38 (m, 11H), 7.36 (s, 1H), 3.39 (t, $J$ = 8.1 Hz, 2H), 2.78 (t, $J$ = 8.1 Hz, 2H), 2.09 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 207.9, 142.3, 140.6, 139.2, 138.6, 133.5, 132.0, 131.5, 130.3, 129.5, 129.3, 128.4, 128.4, 127.4, 127.2, 127.1, 126.6, 125.7, 124.4, 45.0, 29.8, 23.4; HRMS (ESI, *m/z*) Calcd for $C_{26}H_{22}NaO$ $[M + Na]^+$: 373.1568, found 373.1565.

*4-(3,4-Dimethyl-2-phenylnaphthalen-1-yl)butan-2-one* (**3u**). Yellow solid; 24.5 mg, 0.081 mmol, yield 27%; mp 84−86 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.15 (d, $J$ = 8.2 Hz, 1H), 7.99 (d, $J$ = 8.1 Hz, 1H), 7.57−7.44 (m, 4H), 7.42−7.37 (m, 1H), 7.19 (d, $J$ = 8.0 Hz, 2H), 3.06 (t, $J$ = 8.1 Hz, 2H), 2.67 (s, 3H), 2.61 (t, $J$ = 8.1 Hz, 2H), 2.11 (s, 3H), 2.00 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 208.2, 142.2, 140.7, 132.6, 132.4, 132.2, 130.2, 123.0, 129.2, 128.6, 127.0, 125.6, 125.4, 124.8, 124.4, 45.0, 29.7, 24.3, 18.9, 15.4; HRMS (ESI, *m/z*) Calcd for $C_{22}H_{22}NaO$ $[M + Na]^+$: 325.1568, found 325.1572.

*N-Methyl-N-(4-methyl-1-(3-oxobutyl)naphthalen-2-yl)-methanesulfonamide* (**3v**). Yellow solid; 10.5 mg, 0.033 mmol, yield



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11%; mp 129−130 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.00 (dt, $J$ = 8.0, 4.2 Hz, 2H), 7.57 (dd, $J$ = 6.7, 3.2 Hz, 2H), 7.17 (s, 1H), 3.56−3.37 (m, 2H), 3.28 (s, 3H), 3.13−2.97 (m, 4H), 2.78 (ddd, $J$ = 17.6, 10.9, 5.8 Hz, 1H), 2.68 (s, 3H), 2.20 (s, 3H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 208.5, 136.2, 136.0, 135.1, 132.8, 132.6, 126.8, 126.6, 125.4, 125.1, 124.7, 44.2, 39.4, 37.4, 30.1, 21.6, 19.6; HRMS (ESI, $m/z$) Calcd for $C_{17}H_{21}NNaO_3S$ $[M + Na]^+$: 342.1140, found 342.1140.

*3-(4-Methyl-2-phenylnaphthalen-1-yl)propanal (**4a**).* Yellow solid; 25.5 mg, 0.093 mmol, yield 31%; mp 35−36 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.69 (s, 1H), 8.10−8.07 (m, 1H), 8.05−8.02 (m, 1H), 7.62−7.54 (m, 2H), 7.48−7.43 (m, 2H), 7.40 (d, $J$ = 7.0 Hz, 1H), 7.34 (d, $J$ = 7.3 Hz, 2H), 7.23 (s, 1H), 3.35 (t, $J$ = 8.0 Hz, 2H), 2.75−2.69 (m, 5H); $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$) $\delta$ 201.6,

Yang, C.-W.; Liu, R.-S. Short and efficient synthesis of coronene derivatives via ruthenium-catalyzed benzannulation protocol. *J. O . C em.* **2005**, *70*, 10113−10116. (d) Yamamoto, Y.; Matsui, K.; Shibuya, M. A combined experimental and computational study on the cycloisomerization of 2-ethynylbiaryls catalyzed by dicationic arene ruthenium complexes. *C em. - E . J.* **2015**, *21*, 7245−7255. (e) Lian, J.-J.; Odedra, A.; Wu, C.-J.; Liu, R.-S. Ruthenium-catalyzed regioselective 1,3-methylene transfer by cleavage of two adjacent σ-carbon−carbon bonds: an easy and selective synthesis of highly subsituted benzenes. *J. Am. C em. S c.* **2005**, *127*, 4186−4187.

(5) (a) Shibata, T.; Takayasu, S.; Yuzawa, S.; Otani, T. Rh(III)-catalyzed C−H bond activation along with "rollover" for the synthesis of 4−azafluorenes. *O . L .* **2012**, *14*, 5106−5109. (b) Shibata, T.; Takayasu, S. Synthesis of multicyclic heterocycles initiated by C−H bond activation along with "Rollover" using a Rh(III) catalyst. *H a . C em.* **2014**, *25*, 379−388. (c) Seo, B.; Jeon, W. H.; Kim, J.; Kim, S.; Lee, P. H. Synthesis of fluorenes via tandem copper-catalyzed [3 + 2] cycloaddition and rhodium-catalyzed denitrogenative cyclization in a 5- mode from 2−ethynylbiaryls and *N*−sulfonyl azides in one pot. *J. O . C em.* **2015**, *80*, 722−732.

(6) (a) Chernyak, N.; Gevorgyan, V. Exclusive 5- -dig hydroarylation of -alkynyl biaryls proceeding via C−H activation pathway. *J. Am. C em. S c.* **2008**, *130*, 5636−5637. (b) Chernyak, N.; Gevorgyan, V. Synthesis of fluorenes via the palladium-catalyzed 5- -dig annulation of -alkynylbiaryls. *Ad . S . Ca a .* **2009**, *351*, 1101−1114. (c) Kadoya, N.; Murai, M.; Ishiguro, M.; Uenishi, J.; Uemura, M. Palladium(II)-catalyzed asymmetric cycloisomerization of enynes for axially chiral biaryl construction. *T a ed L .* **2013**, *54*, 512−514. (d) Hwang, J. H.; Jung, Y. H.; Hong, Y. Y.; Jeon, S. L.; Jeong, I. H. Synthesis of novel 2-trifluoromethyl-1-methylene-3-phenylindene derivatives via carbocyclization reaction of 2-trifluoromethyl-1,1-diphenyl-1,3-enynes. *J. F C em.* **2011**, *132*, 1227−1231.

(7) (a) Liu, L.; Zhang, J. Selectivity control in Lewis acid catalyzed regiodivergent tandem cationic cyclization/ring expansion terminated by pinacol rearrangement. *A . C em., I . Ed.* **2009**, *48*, 6093−6096. (b) Liu, L.; Wei, L.; Lu, Y.; Zhang, J. One-pot tandem catalysis: a concise route to fused bicyclic scaffolds from acyclic β-ketoesters and alkynyl aldehydes. *C em. - E . J.* **2010**, *16*, 11813−11817. (c) Fürstner, A.; Mamane, V. Concise total synthesis of the aporphine alkaloid 7,7′-bisdehydro-O-methylisopiline by an $InCl_3$ mediated cycloisomerization reaction. *C em. C mm .* **2003**, *17*, 2112−2113.

(8) (a) Maeyama, K.; Iwasawa, N. $W(CO)_5$•THF-catalyzed endo-selective cyclization of ω-acetylenic silyl enol ethers. *J. Am. C em. S c.* **1998**, *120*, 1928−1929. (b) Maeyama, K.; Iwasawa, N. $W(CO)_5$•THF-catalyzed electrocyclizations of aromatic enynes via vinylidene intermediates. *J. O . C em.* **1999**, *64*, 1344−1346.

(9) (a) Xu, J.; Wang, Y.; Burton, D. J. Site-specific preparation of 3-Fluoro-1-substituted-naphthalenes via a novel base-catalyzed cyclization reaction from (*E*)-monofluoroenynes. *O . L .* **2006**, *8*, 2555−2558. (b) Wang, Y.; Xu, J.; Burton, D. J. A simple, two-step, site-specific preparation of fluorinated naphthalene and phenanthrene derivatives from fluorobromo-substituted alkenes. *J. O . C em.* **2006**, *71*, 7780−7784. (c) Wang, Y.; Burton, D. J. Site-specific preparation of 2-carboalkoxy-4-substituted naphthalenes and 9-alkylphenanthrenes and evidence for an allene intermediate in the novel base-catalyzed cyclization of 2-alkynylbiphenyls. *O . L .* **2006**, *8*, 5295−5298. (d) Zhou, H.; Xing, Y.; Yao, J.; Chen, J. Sulfur-assisted propargyl−allenyl isomerizations and electrocyclizations for the convenient and efficient synthesis of polyfunctionalized benzenes and naphthalenes. *O . L .* **2010**, *12*, 3674−3677. (e) Zhou, H.; Xing, Y.; Yao, J.; Lu, Y. Heteroatom as a promotor: synthesis of polyfunctionalized benzenes and naphthalenes. *J. O . C em.* **2011**, *76*, 4582−4590. (f) Zhao, G.; Zhang, Q.; Zhou, H. Propargyl−allenyl isomerizations and electrocyclizations for the functionalization of phosphonium salts: one-pot synthesis of polysubstituted vinylbenzenes and naphthalenes. *Ad . S . Ca a .* **2013**, *355*, 3492−3496.

(10) (a) Goldfinger, M. B.; Swager, T. M. Fused polycyclic aromatics via electrophile-induced cyclization reactions: application to the synthesis of graphite ribbons. *J. Am. C em. S c.* **1994**, *116*, 7895−7896. (b) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. Directed electrophilic cyclizations: efficient methodology for the synthesis of fused polycyclic aromatics. *J. Am. C em. S c.* **1997**, *119*, 4578−4593. (c) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. Synthesis of ethynyl-substituted quinquephenyls and conversion to extended fused-ring structures. *J. O . C em.* **1998**, *63*, 1676−1686.

(11) (a) Mohamed, R. K.; Mondal, S.; Gold, B.; Evoniuk, C. J.; Banerjee, T.; Hanson, K.; Alabugin, I. V. Alkenes as alkyne equivalents in radical cascades terminated by fragmentations: overcoming stereoelectronic restrictions on ring expansions for the preparation of expanded polyaromatics. *J. Am. C em. S c.* **2015**, *137*, 6335−6349. (b) Mondal, S.; Gold, B.; Mohamed, R. K.; Phan, H.; Alabugin, I. V. Rerouting radical cascades: intercepting the homoallyl ring expansion in enyne cyclizations via C−S scission. *J. O . C em.* **2014**, *79*, 7491−7501. (c) Mondal, S.; Gold, B.; Mohamed, R. K.; Alabugin, I. V. Design of leaving groups in radical C−C fragmentations: through-bond 2c−3e interactions in self-terminating radical cascades. *C em. - E . J.* **2014**, *20*, 8664−8669. (d) Pati, K.; Michas, C.; Allenger, D.; Piskun, I.; Coutros, P. S.; dos Passos Gomes, G.; Alabugin, I. V. Synthesis of functionalized phenanthrenes via regioselective oxidative radical cyclization. *J. O . C em.* **2015**, *80*, 11706−11717.

(12) (a) Liu, J.; Li, B.-W.; Tan, Y.-Z.; Giannakopoulos, A.; SanchezSanchez, C.; Beljonne, D.; Ruffieux, P.; Fasel, R.; Feng, X.; Müllen, K. Toward cove-edged low band gap graphene nanoribbons. *J. Am. C em. S c.* **2015**, *137*, 6097−6103. (b) Yamamoto, K.; Oyamada, N.; Xia, S.; Kobayashi, Y.; Yamaguchi, M.; Maeda, H.; Nishihara, H.; Uchimaru, T.; Kwon, E. Equatorenes: synthesis and properties of chiral naphthalene, phenanthrene, chrysene, and pyrene possessing bis(1-adamantyl) groups at the peri-position. *J. Am. C em. S c.* **2013**, *135*, 16526−16530. (c) Sharma, H.; Sanchez, T. W.; Neamati, N.; Detorio, M.; Schinazi, R. F.; Cheng, X.; Buolamwini, J. K. Synthesis, docking, and biological studies of phenanthrene β-diketo acids as novel HIV-1 integrase inhibitors. *B . M ed. C em. L .* **2013**, *23*, 6146−6151.

(13) Dankwardt, J. W. Transition-metal-promoted 6- *d* -dig cyclization of aromatic enynes: rapid synthesis of functionalized naphthalenes. *T a ed L .* **2001**, *42*, 5809−5812.

(14) Shibata, T.; Ueno, Y.; Kanda, K. Cationic Au(I)-catalyzed cycloisomerization of aromatic enynes for the synthesis of substituted naphthalenes. *S* **2006**, *2006*, 411−414.

(15) Kinoshita, H.; Tohjima, T.; Miura, K. Hydroalumination-triggered cyclization of silylated 1,3-dien-5-ynes to polysubstituted benzenes. *O . L .* **2014**, *16*, 4762−4765.

(16) Liu, Y.; Guo, J.; Liu, Y.; Wang, X.; Wang, Y.; Jia, X.; Wei, G.; Chen, L.; Xiao, J.; Cheng, M. Au(I)-catalyzed triple bond alkoxylation/dienolether aromaticity-driven cascade cyclization to naphthalenes. *C em. C mm .* **2014**, *50*, 6243−6345.

(17) Crone, B.; Kirsch, S. F.; Umland, K.-D. Electrophilic cyclization of 1,5-enynes. *A . C em., I . Ed.* **2010**, *49*, 4661−4664.

(18) Feng, C.; Loh, T.-P. Palladium-catalyzed bisolefination of C−C triple bonds: a facile method for the synthesis of naphthalene derivatives. *J. Am. C em. S c.* **2010**, *132*, 17710−17712.

(19) Liu, X.-W.; Li, S.-S.; Dai, D.-T.; Zhao, M.; Shan, C.-C.; Xu, Y.-H.; Loh, T.-P. Palladium-catalyzed dialkylation of C−C triple bonds: access to multi-functionalized indenes. *O . L .* **2019**, *21*, 3696−3700.

(20) (20) Weiss, M.; Peters, R. Catalytic direct dehydrogenative cross-couplings of C−H (Pro)nucleophiles and allylic alcohols without an additional oxidant. *ACS Ca a .* **2015**, *5*, 310−316.

(21) Saito, K.; Sogou, H.; Suga, T.; Kusama, H.; Iwasawa, N. Platinum(II)-catalyzed generation and [3 + 2] cycloaddition reaction of α,β-unsaturated carbene complex intermediates for the preparation of polycyclic compounds. *J. Am. C em. S c.* **2011**, *133*, 689−691.

(22) Komeyama, K.; Igawa, R.; Takaki, K. Cationic iron-catalyzed intramolecular alkyne-hydroarylation with electron-deficient arenes. *C em. C mm .* **2010**, *46*, 1748−1750.

(23) (a) Yeh, M.-C. P.; Liang, C.-J.; Chen, H.-F.; Weng, Y.-T. Indium(III)-catalyzed cyclization of aromatic 5-enynamides: facile



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synthesis of 2-aminonaphthalenes, 2-amino-1*H*-indenes, and 2,3-dihydro-1*H*-indeno[2,1-b]pyridines. *Ad . S . Ca a .* **2015**, *357*, 3242−3254. (b) Please see refs 2c, d, 19.

(24) (a) Yasuhara, A.; Kaneko, M.; Sakamoto, T. Synthesis of 2-substituted 3-alkenyl-indoles by the palladium-catalyzed cyclization followed by alkenylation (Heck Reaction). *He c c* **1998**, *48*, 1793−1799. (b) Shen, Z.; Lu, Xi Palladium(II)-catalyzed tandem intramolecular aminopalladation of alkynylanilines and conjugate addition for synthesis of 2,3-disubstituted indole derivatives. *Te a d* **2006**, *62*, 10896−10899. (c) Wang, Q.; Huang, L.; Wu, X.; Jiang, H. Nucleopalladation triggering the oxidative Heck Reaction: a general strategy to diverse *β*-indole ketones. *O . Le .* **2013**, *15*, 5940−5943. (d) Martínez, C.; Álvarez, R.; Aurrecoechea, J. M. Palladium-catalyzed sequential oxidative cyclization/coupling of 2-alkynylphenols and alkenes: a direct entry into 3-alkenylbenzofurans. *O . Le .* **2009**, *11*, 1083−1086. (e) Álvarez, R.; Martínez, C.; Madich, Y.; Denis, J. G.; Aurrecoechea, J. M.; De Lera, A. R. A general synthesis of alkenyl-substituted benzofurans, indoles, and isoquinolones by cascade palladium-catalyzed heterocyclization/oxidative Heck coupling. *C em. - E . J.* **2010**, *16*, 12746−12753. (f) Please see refs 2c, d, 18, 19.

(25) (a) Franzén, J.; Löfstedt, J.; Dorange, I.; Bäckvall, J.-E. Allenes as carbon nucleophiles in palladium-catalyzed reactions: observation of anti attack of allenes on (*π*-allyl)palladium complexes. *J. Am. C em. S c.* **2002**, *124*, 11246−11247. (b) Smidt, J.; Hafner, W.; Jira, R.; Sieber, R.; Sedlmeier, J.; Sabel, A. The oxidation of olefins with palladium chloride catalysts. *A . C em., I . Ed. E .* **1962**, *1*, 80−88.

(26) (a) Sanjuán, A. M.; Rashid, M. A.; García-García, P.; Martínez-Cuezva, A.; Fernández-Rodríguez, M. A.; Rodríguez, F.; Sanz, R. Gold(I)-catalyzed cycloisomerizations and alkoxycyclizations of ortho-(alkynyl)styrenes. *C em. - E . J.* **2015**, *21*, 3042−3052. (b) Thomé, I.; Besson, C.; Kleine, T.; Bolm, C. Base-catalyzed synthesis of substituted indazoles under mild, transition-metal-free conditions. *A . C em., I . Ed.* **2013**, *52*, 7509−7513. (c) Cheng, J.-K.; Loh, T. P. Copper- and cobalt-catalyzed direct coupling of $sp^3$ *α*-carbon of alcohols with alkenes and hydroperoxides. *J. Am. C em. S c.* **2015**, *137*, 42−45. (d) Hu, L.; Xu, S.; Zhao, Z.; Yang, Y.; Peng, Z.; Yang, M.; Wang, C.; Zhao, J. Ynamides as racemization-free coupling reagents for amide and peptide synthesis. *J. Am. C em. S c.* **2016**, *138*, 13135−13138.



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