JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

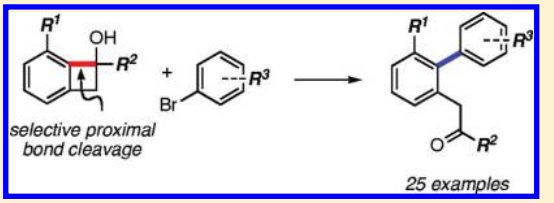
Palladium-Catalyzed Selective Carboelimination and Cross-Coupling Reactions of Benzocyclobutenols with Aryl Bromides

Andrei Chtchemelinine, David Rosa, and Arturo Orellana*

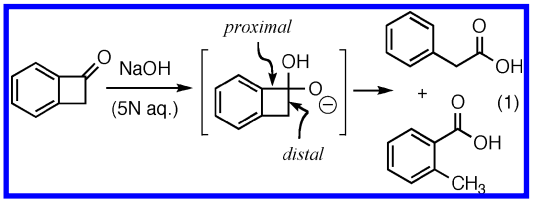
Department of Chemistry, York University, 440 Chemistry Building, 4700 Keele Street, Toronto, ON, Canada M3J 1P3

Supporting Information

ABSTRACT: The palladium-catalyzed selective β-carboelimination and cross-coupling chemistry of benzocyclobutenols is described. In contrast to the base-mediated ring-opening reactions of benzocyclobutenols, this variant proceeds with exclusive cleavage of the proximal bond.



The strain inherent in small ring organic molecules bestows upon them reactivity not observed in the less-strained higher homologues. As a result, strain-releasing reactions of these compounds can be an integral design feature in multistep synthesis. Cyclopropanol and cyclobutanol derivatives have been exploited in the context of synthetic organic chemistry; however, the use of benzocyclobutenols is less common. Nevertheless, the preparation[1−6] and use of benzocyclobutenols have received some attention, and they have proven to be useful intermediates in complex molecule synthesis.[7,8] Furthermore, benzocyclobutenols or the corresponding alkoxides have been postulated as reaction intermediates.[9] By and large, the synthetic use of benzocyclobutenols is dominated by cleavage of the distal bond via thermal cycloreversion to generate α-hydroxyquinonedimethanes[10] that subsequently participate in cycloaddition[11−13] or electrocyclization[14−19] reactions. In 1960, Cava and Muth demonstrated[20] that benzocyclobutenones suffer carbon−carbon bond cleavage at the proximal and distal bonds under basic conditions, presumably through the intermediacy of the corresponding oxyanion (eq 1). This reaction has found significantly less use, likely because of difficulties in controlling the position of carbon−carbon bond cleavage. Although it has been shown that a number of substitutents on the aryl ring favor cleavage of the proximal bond under basic conditions, attempts to intercept the presumed aryl anion intermediate with carbon-based electrophiles have failed, even under anhydrous conditions.[21]



Palladium-catalyzed ring-opening reactions of protected[22−24] and unprotected[25,26] cyclopropanol derivatives have received significant attention since Kuwajima's seminal report.[27] More recently, the palladium-catalyzed[28−30] and rhodium-catalyzed[31−33] desymmetrization of *tert*-cyclobutanols has been developed into a useful synthetic method. In contrast, the palladium-catalyzed chemistry of benzocyclobutenols has not been explored. Our interest in developing synthetic methods based on the palladium-catalyzed chemistry of cyclic[34,35] and acyclic[36] tertiary alcohols[37] and the lack of studies on the transition metal-catalyzed ring opening of benzocyclobutenols prompted us to explore this class of compounds. In particular, we were interested in developing a carbon−carbon bond forming reaction proceeding through a selective palladium-catalyzed proximal bond cleavage of a *tert*-benzocyclobutenol.[38] We envisioned a mechanistic scenario wherein an arylpalladium(II) intermediate (**I**), resulting from oxidative addition of an aryl halide to Pd(0)L$_n$, would undergo ligand exchange with the benzocyclobutenol (Scheme 1, **I** to **II**). We surmised that it should be possible to selectively deprotonate the palladium-bound benzocyclobutenol (**II** to **III**) without deprotonating the free benzocyclobutenol because of their expected pK_a difference, and that this should prevent uncontrolled, base-catalyzed ring-opening reactions. Given the relative bond strengths of Pd−C(sp2) and Pd−C(sp3) bonds,[39] and the ample precedent for selective β-carboelimination leading to alkyl- and arylpalladium(II) intermediates from tertiary alcohols,[22−24,33,40−47] we expected that intermediate **III** would lead selectively to intermediate **IV**, which could be reductively eliminated to generate the desired product.

Initial experiments using an electron-neutral aryl bromide and a simple catalyst system showed formation of the desired cross-coupled product in moderate yield and a significant amount of the ring-opened product (Table 1, entry 1). In addition, the long reaction time required for consumption of most of the starting material proved impractical. After some optimization,[44] it was found that the use of DavePhos as the

Received: August 9, 2011
Published: September 23, 2011

dx.doi.org/10.1021/jo201632c | *J. Org. Chem.* 2011, 76, 9157−9162

Scheme 1. Envisioned Catalytic Cycle for the Cross Coupling of Aryl Halides with Benzocyclobutenols

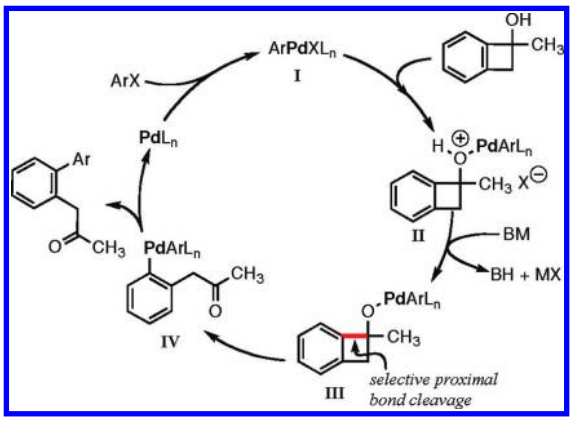
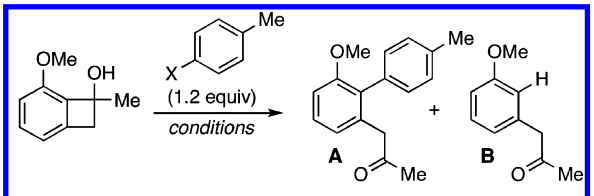


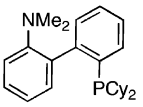
Table 1. Summary of Reaction Optimization



	X	conditions	base	yield	
			1.1 equiv.	A	B
1	Br	*A*	K_2CO_3	42%[a]	38%
2	Br	*B*	Ag_2CO_3	94%[b]	n.a.
3	Br	*B*	Cs_2CO_3	92%[c]	n.a.
4	Cl	*B*	Ag_2CO_3	n.a.	64%
5	I	*B*	Ag_2CO_3	46%	30%
6	OTf	*B*	Cs_2CO_3	n.a.	82%

conditions A
Pd_2dba_3 (5 mol%)
PPh_3 (30 mol%)
THF, 65 °C

conditions B
Pd_2dba_3 (2.5 mol%)
DavePhos (10 mol%)
toluene, 65 °C



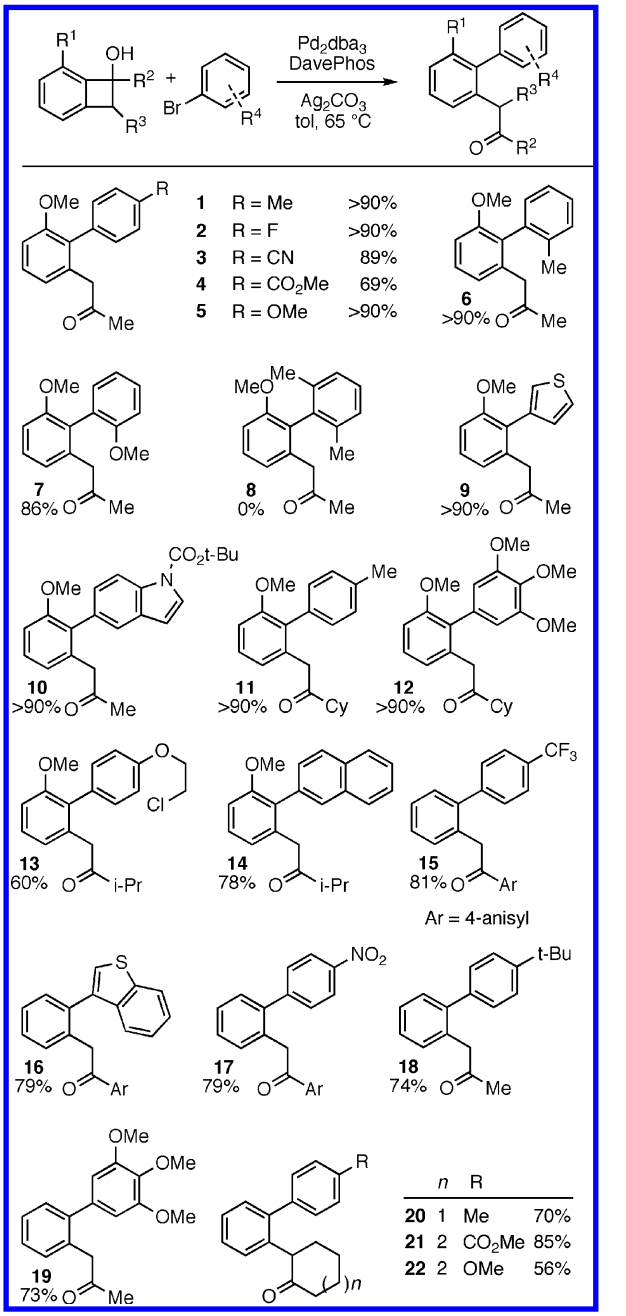
DavePhos

[a]required 3 days for complete conversion. [b]required1.5 hours for complete conversion. [c]required 6 hours for complete conversion.

ligand and Pd_2dba_3 as the palladium source in combination with Ag_2CO_3 provided the cross-coupled product in excellent yield and in a short reaction time (entry 2). Cs_2CO_3 also proved to be a competent base in the process but required a longer reaction time (entry 3). The cross-coupling reaction failed with the corresponding aryl chloride, likely because of a difficult oxidative addition step (entry 4), while the use of the corresponding aryl iodide gave the cross-coupled product along with a significant amount of the ring-opened product (entry 5). It is well-established that silver(I) can promote the generation of cationic palladium intermediates by abstraction of a halide ion. It is reasonable to expect that such cationic palladium complexes may readily coordinate with an alcohol to generate a protonated palladium alkoxide (i.e., intermediate **II** in Scheme 1), especially in nonpolar solvents. To test if this effect is operative, we conducted the reaction with the corresponding aryl triflate. Surprisingly, however, this substrate gave mostly the undesired ring-opened product (entry 6).

Exploration of the substrate scope for this reaction demonstrates that a variety of oxidative addition partners are tolerated (Table 2). Electron-poor (entries 3, 4, 15, 17, and

Table 2. Scope of the Palladium-Catalyzed Cross Coupling of Benzocyclobutenols with Aryl Bromides



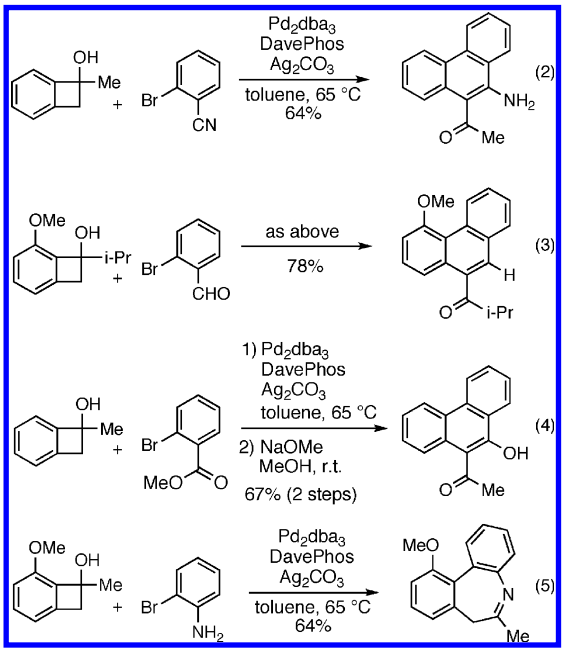
21), electron-neutral (entries 1, 2, 6, 11, 14, 18, and 20), and electron-rich (entries 5, 7, 12, 13, 19, and 22) aryl bromides give the cross-coupled product in good to excellent yield. The diminished yield observed with a substrate bearing a primary alkyl chloride (entry 13) may be due in part to reaction with the electron-rich phosphine ligand. In addition, this reaction tolerates the use of heteroaryl bromides (entries 9, 10, and 16). Furthermore, the use of *ortho*-substituted aryl bromides (entries 6 and 7) does not have a noticeable effect on the reaction;

dx.doi.org/10.1021/jo201632c|*J. Org. Chem.* 2011, 76, 9157–9162

however, the use of a di-*ortho*-substituted aryl bromide fails to deliver cross-coupled product (entry 8). A variety of substituents at the carbinol carbon of the benzocyclobutenol (R^2) are also tolerated, including methyl (entries 1−10, 18, and 19), cyclohexyl (entries 11 and 12), isopropyl (entries 13 and 14), and 4-anisyl (entries 15−17) groups. Although the majority of the examples explored include a benzocyclobutenol bearing a methoxy group (entries 1−14), this substituent is not necessary for the success of the reaction (entries 15−22). It is worth noting that the base-catalyzed ring cleavage of unsubstituted benzocyclobutenols results in mixtures of products arising from proximal and distal bond cleavage. Finally, it is also possible to generate cyclic ketones using this protocol (entries 20−22).

We surmised that using aryl bromides bearing electrophilic functional groups at the ortho position could provide an expedient route to functionalized phenanthrenes[48,49] via condensation with the enolate of the resulting ketone group. Indeed, the use of *ortho*-bromobenzonitrile and *ortho*-bromobenzaldehyde results in the formation of the corresponding phenanthrenes in good yield simply by using an excess of base and allowing the reaction mixture to be stirred for an extended period of time (Scheme 2, eqs 2 and 3). In contrast,

Scheme 2. Synthesis of Phenanthrenes and Cyclic Imines Using a Cross-Coupling and Condensation Sequence



the use of methyl *ortho*-bromobenzoate requires isolation of the cross-coupled product before the phenanthrene synthesis can be conducted (Scheme 2, eq 4). Finally, we have also shown that formation of cylic imines is possible using an *ortho*-bromoaniline as the cross-coupling partner (Scheme 2, eq 5).

In conclusion, we have developed an efficient protocol for the cross-coupling reaction of benzocyclobutenols with aryl bromides. To the best of our knowledge, these are the first examples of carbon−carbon bond-forming processes involving controlled cleavage of the proximal bond of benzocyclobutenols. These reactions proceed in good to excellent yields and tolerate a variety of oxidative addition partners. Finally, this chemistry can be extended to the synthesis of functionalized phenanthrenes and cyclic imines.

EXPERIMENTAL SECTION

General Preparation of Benzocyclobutenols. Benzocyclobutenols were prepared by addition of the required organometallic reagent to the corresponding benzocyclobutenone[19,21] or by addition of ketone enolates to benzyne.[2]

5-Methoxy-7-methylbicyclo[4.2.0]octa-1,3,5-trienol (Table 1, Table 2, entries 1−13, and Scheme 2, eq 5). Isolated as a beige powder (73%) using a 17% solution of EtOAc in hexanes: mp 70−73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, J = 7.8 Hz, 1 H), 6.77 (d, J = 7.8, 1 H), 6.72 (d, J = 7.8 Hz, 1 H), 3.95 (s, 3 H), 3.33 (d, J = 14 Hz, 1 H), 3.21 (d, J = 14.0 Hz, 1 H), 2.39 (s, 1 H), 1.77 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 142.7, 134.5, 130.8, 116.1, 112.8, 77.7, 56.6, 47.9, 26.6; IR 3312, 2922, 1597, 1575, 1263, 1169 cm^{-1}; HRMS (EI) m/z calcd for $C_{10}H_{12}O_2$ (M^+) 164.0837, found 164.0799.

5-Methoxy-7-cyclohexylbicyclo[4.2.0]octa-1,3,5-trienol (Table 2, entries 11 and 12). Isolated as a beige powder (73%) using a 13% solution of EtOAc in hexanes: mp 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 8.0, 8.0 Hz, 1 H), 6.77 (d, J = 8.0 Hz, 1 H), 6.72 (d, J = 8.0 Hz, 1 H), 3.87 (s, 3 H), 3.38 (d, J = 14.0 Hz, 1 H), 2.95 (d, J = 14.0 Hz, 1 H), 2.31 (br s, 1 H), 2.17 (m, 1 H), 1.88−1.07 (m, 5 H), 1.31−1.08 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 143.6, 134.3, 130.5, 116.0, 111.0, 83.6, 55.9, 45.5, 43.3, 27.7, 26.3, 26.2; IR 3436, 2925, 1579, 1477, 1265, 1070 cm^{-1}; HRMS (EI) m/z calcd for $C_{15}H_{20}O_2$ (M^+) 232.1463, found 232.1456.

5-Methoxy-7-(4-anisyl)bicyclo[4.2.0]octa-1,3,5-trienol (Table 2, entries 15−17). Isolated as a clear oil (65%) using a 14% solution of EtOAc in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2 H), 7.37−7.30 (m, 3 H), 7.25 (d, J = 7.2 Hz, 1 H), 6.89 (d, J = 8.4 Hz, 2 H), 3.82 (s, 3 H), 3.66 (d, J = 14.0 Hz, 1 H), 3.59 (d, J = 14.0 Hz, 1 H), 2.60 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 149.2, 142.0, 135.7, 129.5, 127.5, 126.9, 124.1, 121.5, 113.5, 81.2, 55.2, 49.7; IR 3427, 1511, 1248, 1176, 1034 cm^{-1}; HRMS (EI) m/z calcd for $C_{15}H_{14}O_2$ (M^+) 226.0994, found 226.1003.

5-Methoxy-7-isopropylbicyclo[4.2.0]octa-1,3,5-trienol (Table 2, entries 13 and 14, and Scheme 2, entry 3). Isolated as an oil (73%) using a 20% solution of EtOAc in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 8.0, 8.0 Hz, 1 H), 6.78 (d, J = 8.0 Hz, 1 H), 6.71 (d, J = 8.0 Hz), 3.83 (s, 3 H), 3.33 (d, J = 14.0 Hz, 1 H), 2.94 (d, J = 14.0 Hz, 1 H), 2.74 (bs, 1 H), 2.16 (m, J = 6.8 Hz, 1 H), 1.14 (d, J = 6.8 Hz, 1 H), 0.95 (d, J = 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 143.6, 134.4, 130.5, 116.0, 110.9, 84.1, 55.7, 42.7, 33.5, 17.8, 17.6; IR 1602, 1579, 1478, 1435, 1265, 1070 cm^{-1}; HRMS (EI) m/z calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, found 192.1156.

General Procedure for the Cross Coupling of Benzocyclobutenols with Aryl Bromides. *1-(6-Methoxy-4′-methylbiphenyl-2-yl)propan-2-one (entry 1).* A 10 mL round-bottomed flask equipped with a stir bar and condenser was charged with 5-methoxy-7-methylbicyclo[4.2.0]octa-1,3,5-trienol (0.030 g, 1.0 equiv, 0.18 mmol), Dave-Phos (0.007 g, 0.10 equiv, 0.018 mmol), Pd_2dba_3 (0.004 g, 0.025 equiv, 0.005 mmol), Ag_2CO_3 (0.074 g, 1.5 equiv, 0.27 mmol), and toluene. After the mixture had been stirred for 5 min, 4-bromotoluene (0.037 g, 1.2 equiv, 0.22 mmol) was added via syringe and the mixture was heated to 65 °C. Upon completion, the reaction mixture was diluted with EtOAc, filtered through a plug of silica gel, and concentrated. Column chromatography of the crude reaction mixture using an 11% solution of EtOAc in hexanes provided the title compound (0.043 g, 0.017 mmol) as a yellow oil (94%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (dd, J = 7.8, 7.8 Hz, 1 H), 7.25 (d, J = 7.8 Hz, 2 H), 7.08 (d, J = 7.8 Hz, 2 H), 6.93 (d, J = 7.8 Hz, 1 H), 6.88 (d, J = 7.8 Hz, 1 H), 3.74 (s, 3 H), 3.54 (s, 2 H), 2.43 (s, 3 H), 1.96 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.33 (dd, J = 7.8, 7.8 Hz, 1 H), 7.25 (d, J = 7.8 Hz, 2 H), 7.08 (d, J = 7.8 Hz, 2 H), 6.93 (d, J = 7.8 Hz, 1 H), 6.88 (d, J = 7.8 Hz, 1 H), 3.74 (s, 3 H), 3.54 (s, 2 H), 2.43 (s, 3 H), 1.96 (s, 3 H); IR 1717, 1575, 1464, 1352, 1254, 1156, 1076 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{18}O_2$ (M^+) 254.1307, found 254.1301.

1-(4′-Fluoro-6-methoxybiphenyl-2-yl)propan-2-one (entry 2). Isolated as a colorless oil (97%) using a 10% solution of EtOAc in

dx.doi.org/10.1021/jo201632c | J. Org. Chem. 2011, 76, 9157−9162

hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (dd, J = 8.1, 8.1 Hz, 1 H), 7.18−7.08 (m, 4 H), 6.93 (d, J = 8.1 Hz, 1 H), 6.87 (d, J = 8.1 Hz, 1 H), 3.74 (s, 3 H), 3.53 (s, 2 H), 1.97 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2, 162.0 (d, $^1J_{C-F}$ = 244.5 Hz), 157.2, 134.6, 132.7 (d, $^4J_{C-F}$ = 3.0 Hz), 131.6 (d, $^3J_{C-F}$ = 7.5 Hz), 130.2, 128.6, 122.7, 115.1 (d, $^2J_{C-F}$ = 21.0 Hz), 109.7, 55.7, 48.4, 29.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ −114.9; IR 1720, 1468, 1257, 1220, 1159, 1078, 1008 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{15}FO_2$ (M^+) 258.1056, found 258.1047.

2′-Methoxy-6′-(2-oxopropyl)biphenyl-4-carbonitrile (entry 3). Isolated as a pale yellow crystalline solid (69%) using a 15% solution of ethyl acetate in hexanes: mp 74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 2 H), 7.37 (dd, J = 8.1, 8.1 Hz, 1 H), 7.31 (d, J = 8.4 Hz, 2 H), 6.94 (d, J = 8.1 Hz, 1 H), 6.87 (d, J = 8.1 Hz, 1 H), 3.73 (s, 3 H), 3.51 (s, 2 H), 1.99 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 156.7, 142.3, 133.8, 131.9, 131.0, 129.4, 129.4, 122.8, 118.9, 111.1, 109.7, 55.7, 48.3, 29.6; IR 2228, 1718, 1608, 1257, 1078 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{15}NO_2$ (M^+) 265.1103, found 265.1109.

Methyl 2′-Methoxy-6′-(2-oxopropyl)biphenyl-4-carboxylate (entry 4). Isolated as a brown powder (89%) using a 14% solution of ethyl acetate in hexanes: mp 105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2 H), 7.35 (dd, J = 8.1 Hz, 1 H), 7.27 (d, J = 8.4 Hz, 2 H), 6.93 (d, J = 8.1 Hz, 1 H), 6.87 (d, J = 8.1 Hz, 1 H), 3.95 (s, 3 H), 3.72 (s, 3 H), 3.51 (s, 2 H), 1.95 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.0, 167.0, 156.9, 142.2, 134.0, 130.3, 130.1, 129.4, 128.9, 128.9, 122.7, 109.7, 55.7, 52.1, 48.3, 29.6; IR 1722, 1610, 1279, 1257, 1078, 1007 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{18}O_4$ (M^+) 298.1205, found 298.1215.

1-(4′,6-Dimethoxybiphenyl-2-yl)propan-2-one (entry 5). Isolated as a yellow oil (88%) using a 10% solution of ethyl acetate in hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (dd, J = 8.1, 8.1 Hz, 1 H), 7.11 (d, J = 8.7 Hz, 2 H), 6.97 (d, J = 8.7 Hz, 2 H), 6.92 (d, J = 8.1 Hz, 1 H), 6.87 (d, J = 8.1 Hz, 1 H), 3.87 (s, 3 H), 3.74 (s, 3 H), 3.55 (s, 2 H), 1.96 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 158.6, 157.4, 134.9, 131.0, 130.9, 129.0, 128.3, 122.6, 113.6, 109.7, 55.8, 55.2, 48.5, 29.6; IR 1714, 1579, 1288, 1248, 1078, 1018 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{18}O_3$ (M^+) 270.1256, found 270.1266.

1-(6-Methoxy-2′-methylbiphenyl-2-yl)propan-2-one (entry 6). Isolated as a slightly yellow crystalline solid (99%) using a 5% solution of ethyl acetate in hexanes: mp 53 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, J = 8.1, 8.1 Hz, 1 H), 7.29 (m, 2 H), 7.25 (dd, J = 7.8, 7.8 Hz, 1 H), 7.04 (d, J = 7.8 Hz, 1 H), 6.93 (d, J = 8.1 Hz, 1 H), 6.90 (d, J = 8.1 Hz, 1 H), 3.74 (s, 3 H), 3.54 (d, J = 16.2 Hz, 1 H), 3.34 (d, J = 16.2 Hz, 1 H), 2.03 (s, 3 H), 1.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.3, 157.0, 137.0, 136.6, 134.5, 130.4, 129.8, 129.8 128.4, 127.5, 125.6, 122.7, 109.5, 55.7, 48.0, 29.7, 19.5; IR 1720, 1641, 1255, 1078, 1007 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{18}O_2$ (M^+) 254.1307, found 254.1315.

1-(2′,6-Dimethoxybiphenyl-2-yl)propan-2-one (entry 7). Isolated as a clear oil (86%) using a 13% solution of ethyl acetate in hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (dt, J = 8.1, 2.1 Hz, 1 H), 7.34 (dd, J = 7.8, 7.8 Hz, 1 H), 7.08 (dd, J = 8.1, 2.1 Hz, 1 H), 7.04 (dd, J = 8.1 Hz, 1 H), 7.00 (d, J = 8.1 Hz, 1 H), 6.94 (d, J = 7.8 Hz, 1 H), 6.92 (d, J = 7.8 Hz, 1 H), 3.74 (s, 3 H), 3.48 (d, J = 16.2 Hz, 1 H), 3.42 (d, J = 16.2 Hz, 1 H), 2.03 (s, 3 H), 1.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7, 157.5, 156.8, 135.2, 131.7, 129.0, 128.5, 127.7, 125.5, 122.4, 120.5, 110.9, 109.8, 55.9, 55.3, 48.6, 29.2; IR 1711, 1581, 1253, 1078, 1051 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{18}O_3$ (M^+) 270.1256, found 270.1250.

1-[3-Methoxy-2-(thiophen-3-yl)phenyl]propan-2-one (entry 9). Isolated as a clear oil (99%) using an 11% solution of ethyl acetate in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, J = 4.8, 2.4 Hz, 1 H), 7.32 (t, J = 8.0 Hz, 1 H), 7.10 (d, J = 2.4 Hz, 1 H), 6.99 (d, J = 4.8 Hz, 1 H), 6.91 (d, J = 8.0 Hz, 1 H), 6.86 (d, J = 8.0 Hz, 1 H), 3.76 (s, 3 H), 3.60 (s, 2 H), 2.00 (s, 3 H); ^{13}C NMR (282 MHz, $CDCl_3$) δ 206.5, 157.6, 136.4, 135.2, 129.5, 128.5, 126.1, 124.8, 123.5, 122.6, 109.6, 55.7, 48.5, 29.5; IR 1712, 1643, 1360, 1223, 1076 cm^{-1}; HRMS (EI) m/z calcd for $C_{14}H_{14}O_2S$ (M^+) 246.0715, found 246.0721.

tert-Butyl-5-[2-methoxy-6-(2-oxopropyl)phenyl]-1H-indole-1-carboxylate (entry 10). Isolated as a yellow oil (92%) using a 10% solution of ethyl acetate in hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 8.1 Hz, 1 H), 7.66 (d, J = 3.6 Hz, 1 H), 7.38 (s, 1 H), 7.35 (dd, J = 8.1, 8.1 Hz, 1 H), 7.14 (d, J = 8.1 Hz, 1 H), 6.95 (d, J = 8.1 Hz, 1 H), 6.89 (d, J = 8.1 Hz, 1 H), 6.60 (d, J = 3.6 Hz, 1 H), 3.73 (s, 3 H), 3.55 (s, 2 H), 1.93 (s, 3 H), 1.72 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 157.5, 149.8, 134.8, 134.2, 131.6, 131.3, 130.6, 128.3, 126.2, 126.2, 122.5, 122.2, 114.9, 109.6, 107.4, 83.7, 55.8, 48.5, 29.7, 28.2; IR 1730, 1579, 1454, 1255, 1157, 1080, 1024, 735 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{25}NO_4$ (M^+) 379.1784, found 379.1773.

1-Cyclohexyl-2-(6-methoxy-4′-methylbiphenyl-2-yl)ethanone (entry 11). Isolated as a clear oil (91%) using a 4% solution of ethyl acetate in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, J = 8.0, 8.0 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.07 (d, J = 8.0 Hz, 2 H), 6.91 (d, J = 8.0 Hz, 1 H), 6.84 (d, J = 8.0 Hz, 1 H), 3.73 (s, 3 H), 3.57 (s, 2 H), 2.42 (s, 3 H), 2.12 (m, 1 H), 1.71 (m, 2 H), 1.61 (m, 3 H), 1.25−1.17 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1, 157.1, 136.5, 134.8, 133.9, 131.2, 129.8, 128.7, 128.0, 122.7, 109.4, 55.7, 50.2, 45.5, 28.3, 25.7, 25.5, 21.2; IR 2929, 1711, 1468, 1253, 1072 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{26}O_2$ (M^+) 322.1933, found 322.1944.

1-Cyclohexyl-2-(3′,4′,5′,6-tetramethoxybiphenyl-2-yl)ethanone (entry 12). Isolated as a crystalline solid (84%) using a 27% solution of ethyl acetate in hexanes: mp 117 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (dd, J = 8.1, 8.1 Hz, 1 H), 6.91 (d, J = 8.1 Hz, 1 H), 6.82 (d, J = 8.1 Hz, 1 H), 6.38 (s, 2 H), 3.90 (s, 3 H), 3.82 (s, 6 H), 3.76 (s, 3 H), 3.57 (s, 2 H), 2.19 (m, 1 H), 1.70−1.61 (m, 5 H), 1.28−1.14 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.36, 157.0, 152.8, 136.7, 134.9, 132.7, 131.2, 128.3, 122.8, 109.5, 106.9, 60.8, 56.0, 55.8, 50.4, 45.6, 28.4, 25.7, 25.5; IR 2935, 1704, 1581, 1238, 1074 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{30}O_5$ (M^+) 398.2093, found 398.2081.

1-[4′-(2-Chloroethyl)-6-methoxybiphenyl-2-yl]-3-methylbutan-2-one (entry 13). Isolated as a yellow oil (60%) using a 10% solution of ethyl acetate in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, J = 8.0, 8.0 Hz, 1 H), 7.10 (d, J = 8.8 Hz, 2 H), 6.96 (d, J = 8.8 Hz, 2 H), 6.87 (d, J = 8.0 Hz, 1 H), 6.84 (d, J = 8.0 Hz, 1 H), 4.28 (t, J = 6 Hz, 2 H), 3.85 (t, J = 6 Hz, 2 H), 3.72 (s, 3 H), 3.59 (s, 2 H), 2.43 (h, J = 6.8 Hz, 1 H), 0.94 (d, J = 6.8 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.9, 157.2, 157.1, 134.8, 131.1, 130.7, 129.9, 128.1, 122.7, 114.3, 109.4, 67.9, 55.7, 45.3, 41.8, 40.2, 18.1; IR 1708, 1575, 1512, 1463, 1254 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{23}ClO_3$ (M^+) 346.1336, found 346.1325.

1-[3-Methoxy-2-(naphthalen-2-yl)phenyl]-3-methylbutan-2-one (entry 14). Isolated as a yellow oil (78%) using a 12% solution of ethyl acetate in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 2 H), 7.81 (m, 1 H), 7.62 (s, 1 H), 7.50 (m, 2 H), 7.34 (m, 2 H), 6.95 (d, J = 8 Hz, 1 H), 6.88 (d, J = 8 Hz, 1 H), 3.72 (s, 3 H), 3.62 (d, J = 17.0 Hz, 1 H), 3.56 (d, J = 17.0 Hz, 1 H), 2.35 (h, J = 6.8 Hz, 1 H), 0.85 (d, J = 5.0 Hz, 3 H), 0.82 (d, J = 5.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.9, 157.2, 134.7, 134.6, 133.2, 132.4, 131.1, 128.5, 128.4, 128.3, 127.9, 127.6, 127.4, 125.9, 125.7, 122.8, 109.5, 55.7, 45.4, 40.2, 18.0; IR 2963, 2928, 1708, 1575, 1464, 1254, 1085, 1067 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{22}O_2$ (M^+) 318.1620, found 318.1611.

1-(4-Methoxyphenyl)-2-[4′-(trifluoromethyl)biphenyl-2-yl]-ethanone (entry 15). Isolated as a clear oil (81%) using a 10% solution of ethyl acetate in hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.8 Hz, 2 H), 7.62 (d, J = 8.0 Hz, 2 H), 7.43 (d, J = 8.0 Hz, 2 H), 7.39 (m, 2 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.31 (t, J = 8.0 Hz, 1 H), 6.89 (d, J = 8.8 Hz, 2 H), 4.20 (s, 2 H), 3.87 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 163.5, 145.0, 140.9, 132.6, 130.9, 130.4, 130.0 (q, $^2J_{C-F}$ = 32.0 Hz), 129.8, 129.4, 128.1, 127.0, 125.0 (q, $^3J_{C-F}$ = 4.0 Hz), 124.1 (q, $^1J_{C-F}$ = 271.0 Hz), 113.6, 55.3, 42.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.4; IR 1675, 1600, 1324, 1263, 1168, 1068 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{17}F_3O_2$ (M^+) 370.1181, found 370.1169.

2-[2-(Benzo[b]thiophen-3-yl)phenyl]-1-(4-methoxyphenyl)-ethanone (entry 16). Isolated as a yellow oil (76%) using a 10% solution of ethyl acetate in hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 1 H), 7.67 (d, J = 8.7 Hz, 2 H), 7.49 (d, J = 7.8 Hz, 1 H), 7.44−7.29 (m, 7 H), 6.78 (d, J = 8.7 Hz, 2 H), 4.13 (s, 2 H), 3.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 163.3, 139.9,

dx.doi.org/10.1021/jo201632c|J. Org. Chem. 2011, 76, 9157−9162

139.1, 136.5, 135.5, 134.6, 130.8, 130.7, 130.5, 129.6, 128.1, 126.9, 124.7, 124.4, 124.3, 123.0, 122.6, 113.5, 55.4, 42.8; IR 1673, 1599, 1259, 1168, 1027 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{18}O_2S$ (M^+) 358.1028, found 358.1011.

1-(4-Methoxyphenyl)-2-(4′-nitrobiphenyl-2-yl)ethanone (entry 17). Isolated as a yellow oil (79%) using a 13% solution of ethyl acetate in hexanes: ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 2 H), 7.82 (d, J = 8.7 Hz, 2 H), 7.48 (d, J = 8.7 Hz, 2 H), 7.41 (m, 2 H), 7.32 (m, 2 H), 6.89 (d, J = 8.4 Hz, 2 H), 4.20 (s, 2 H), 3.87 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 163.7, 148.3, 147.0, 140.2, 132.6, 131.2, 130.4, 130.1, 129.6, 129.4, 128.6, 127.2, 123.4, 113.8, 55.5 42.7; IR 1664, 1523, 1344, 1225, 1111, 1029 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{17}NO_4$ (M^+) 347.1158, found 347.1149.

1-(4′-tert-Butylbiphenyl-2-yl)propan-2-one (entry 18). Isolated as a white solid (74%) using a 7% solution of ethyl acetate in hexanes: mp 54−57 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 2 H), 7.35−7.31 (m, 3 H), 7.24 (m, 1 H), 7.19 (d, J = 8.4 Hz, 2 H), 3.73 (s, 2 H), 2.01 (s, 3 H), 1.39 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 150.0, 142.3, 138.1, 132.2, 130.4, 130.2, 128.6, 127.3, 127.0, 125.1, 48.3, 34.3, 31.3, 29.6; IR 1712, 1481, 1361 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{22}O$ (M^+) 266.1671, found 266.1663.

1-(3′,4′,5′-Trimethoxybiphenyl-2-yl)propan-2-one (entry 19). Isolated as a white solid (73%) using a 25% solution of ethyl acetate in hexanes: mp 108−111 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 3 H), 7.24 (d, J = 8.4 Hz, 1 H), 6.47 (s, 2 H), 3.92 (s, 3 H), 3.85 (s, 6 H), 3.73 (s, 2 H), 2.10 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 152.8, 142.4, 137.0, 136.8, 132.1, 130.5, 129.8, 127.8, 126.9, 106.1, 60.8, 56.0, 48.4, 29.7; IR 1717, 1575, 1406, 1241 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{20}O_4$ (M^+) 300.1362, found 300.1371.

2-(4′-Methylbiphenyl-2-yl)cyclohexanone (entry 20). Isolated as a white solid (70%) using a 5% solution of ethyl acetate in hexanes: mp 67−69 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.24 (m, 4 H), 7.21 (d, J = 7.8 Hz, 2 H), 7.13 (d, J = 7.8 Hz, 2 H), 3.74 (dd, J = 12.9, 5.4 Hz, 1 H), 2.53−2.47 (m, 1 H), 2.43 (s, 3 H), 2.35−1.61 (m, 7 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 142.0, 138.5, 136.7, 130.0, 128.9, 128.5, 127.2, 126.5, 54.2, 42.3, 35.8, 27.7, 25.6, 21.2; IR 2932, 2856, 1704, 1481, 1446, 1121 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{20}O$ (M^+) 264.1514, found 264.1524.

Methyl 2′-(2-Oxocycloheptyl)biphenyl-4-carboxylate (entry 21). Isolated as a yellow oil (85%) using a 9% solution of ethyl acetate in hexanes: ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2 H), 7.41−7.28 (m, 5 H), 7.21 (d, J = 7.6 Hz, 1 H), 3.97 (s, 3 H), 3.87 (dd, J = 10.0, 3.0 Hz, 1 H), 2.55−2.49 (m, 1 H), 2.44−2.38 (m, 1 H), 2.03−1.84 (m, 5 H), 1.48−1.29 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6, 166.9, 146.4, 140.4, 139.1, 129.5, 129.4, 128.9, 128.2, 128.1, 126.4, 54.1, 52.2, 43.9, 33.3, 29.6, 29.4, 24.0; IR 1717, 1606, 1432, 1277, 1112 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{22}O_3$ (M^+) 322.1569, found 322.1561.

2-(4′-Methoxybiphenyl-2-yl)cycloheptanone (entry 22). Isolated as a yellow oil (56%) using a 6% solution of ethyl acetate in hexanes: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.22 (m, 4 H), 7.19 (d, J = 8.6 Hz, 2 H), 6.97 (d, J = 8.6 Hz, 2 H), 3.98 (dd, J = 11.0, 3.0 Hz, 1 H), 3.88 (s, 3 H), 2.57−2.38 (m, 2 H), 2.03−1.84 (m, 5 H), 1.50−1.28 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.1, 158.6, 141.0, 139.5, 133.8, 130.3, 129.9, 127.9, 127.2, 126.2, 113.4, 55.2, 54.0, 43.8, 33.1, 29.6, 29.3, 24.0; IR 1700, 1609, 1513, 1481, 1441, 1294, 1245, 1175, 1035 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{22}O_2$ (M^+) 294.1620, found 294.1627.

1-(10-Aminophenanthren-9-yl)ethanone (Scheme 2, eq 2). This compound was prepared following the general procedure and using 2.5 equiv of Ag_2CO_3. ^1H and ^{13}C NMR data were identical to that previously reported.[48]

1-(5-Methoxyphenanthren-9-yl)-2-methylpropan-1-one (eq 3). Prepared following the general cross-coupling procedure and using 2.5 equiv of Ag_2CO_3 and isolated as a white solid (78%) using a 17% solution of ethyl acetate in hexanes: mp 54−57 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 9.71 (d, J = 8.0 Hz, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 7.90 (s, 1 H), 7.75 (d, J = 8.0 Hz, 1 H), 7.73 (dd, J = 8.0, 8.0 Hz, 1 H), 7.64 (dd, J = 8.0, 8.0 Hz, 1 H), 7.58 (dd, J = 8.0, 8.0 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 1 H), 4.15 (s, 3 H), 3.57 (h, J = 6.9 Hz, 1 H), 1.31 (d, J = 6.9 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.8, 158.8, 136.8, 131.1, 130.7, 129.0, 128.6, 127.9, 127.5, 127.1, 126.3, 121.3, 118.7, 108.9, 55.7, 40.3, 18.4; IR 1688, 1571, 1445, 1251 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}O_2$ (M^+) 278.1307, found 278.1295

Methyl 2′-(2-Oxopropyl)biphenyl-2-carboxylate (eq 4, first step). Prepared using the general cross-coupling procedure and isolated as a yellow oil (88%) using a 7% solution of ethyl acetate in hexanes: ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 1 H), 7.57 (dd, J = 7.0, 7.0 Hz, 1 H), 7.46 (dd, J = 7.0, 7.0 Hz, 1 H), 7.34 (dd, J = 8.0, 8.0 Hz, 1 H), 7.16 (d, J = 8.0 Hz, 1 H), 6.89 (d, J = 7.0 Hz, 1 H), 6.88 (d, J = 7.0 Hz, 1H), 3.69 (s, 3 H), 3.65 (s, 3 H), 3.50 (d, J = 16.0 Hz, 1 H), 3.40 (d, J = 16.0 Hz, 1 H), 1.95 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 167.3, 156.6, 137.8, 133.4, 131.7, 131.4, 130.9, 130.6, 130.1, 128.3, 127.4, 122.4, 109.1, 55.6, 51.7, 48.5, 29.3; IR 3432.7, 3066.3, 3002.6, 2950.6, 2836.8, 1710.6, 1600.6, 1581.4, 1467.6, 1434.8, 1292.1, 1253.5, 1079.9 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{18}O_4$ (M^+) 298.1205, found 298.1213.

1-(10-Hydroxyphenanthren-9-yl)ethanone (eq 4, second step). The above biaryl was dissolved in a solution of NaOMe (20 equiv) in MeOH. The phenanthrene product was isolated as a yellow solid (76%) using a 17% solution of ethyl acetate in hexanes: mp 106−108 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.24 (s, 1 H), 9.53 (d, J = 8.0 Hz, 1 H), 8.61 (dd, J = 8.0, 1.0 Hz, 1 H), 7.78 (dd, J = 8.0, 8.0 Hz, 1 H), 7.64 (dd, J = 8.0, 8.0 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 1 H), 7.53 (dd, J = 8.0, 8.0 Hz, 1 H), 7.07 (d, J = 8.0 Hz, 1 H), 4.13 (s, 3 H), 2.80 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 161.9, 158.8, 133.6, 132.1, 130.5, 128.5, 127.0, 126.3, 125.6, 124.5, 118.4, 116.6, 112.7, 106.9, 55.6, 31.3; IR 1599, 1579, 1530, 1348, 1254, 1080 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{14}O_3$ (M^+) 266.0943, found 266.0949.

(Z)-11-Methoxy-6-methyl-7H-dibenzo[b,d]azepine (eq 5). Prepared using the general cross-coupling procedure and isolated as a red oil (53%) using a 9% solution of ethyl acetate in hexanes: ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 1 H), 7.39−7.32 (m, 3 H), 7.32 (m, 2 H), 7.17 (dd, J = 7.6, 7.6 Hz, 1 H), 6.95 (d, J = 8.0 Hz, 1 H), 6.91 (d, J = 8.0 Hz, 1 H), 3.83 (s, 3 H), 3.38 (d, J = 11.6 Hz, 1 H), 2.85 (d, J = 11.6 Hz, 1 H), 2.30 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 157.0, 146.9, 139.3, 131.5, 128.8, 127.2, 127.1, 124.9, 124.3, 122.2, 119.1, 109.9, 55.7, 40.5, 26.6; IR 1643, 1592, 1456, 1263, 1076 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{15}NO$ (M^+) 237.1154, found 237.1147.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete reaction optimization and ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: aorellan@yorku.ca.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the support of this work by York University and the Natural Sciences and Engineering Research Council of Canada. We thank Dr. Howard N. Hunter (York University) for assistance in conducting NMR spectroscopy experiments, Professor Michael Organ (York University) for generous sharing of resources, and a previous reviewer for suggested improvements to the manuscript.

■ REFERENCES

(1) Photochemical synthesis: Ito, Y.; Takahashi, H.; Hasegawa, J.-Y.; Turro, N. J. *Tetrahedron* **2009**, *65*, 677.

(2) Addition of ketone enolates to benzynes: Tripathy, S.; Reddy, R.; Durst, T. *Can. J. Chem.* **2003**, *81*, 997.

(3) Intramoleclar reaction of *o*-acylbenzyllithiums: Kobayashi, K.; Kawakita, M.; Uchida, M.; Nishimura, K.; Mannami, T.; Irisawa, S.; Morikawa, O.; Konishi, H. *J. Org. Chem.* **1999**, *64*, 3557.
(4) Intramolecular addition of aryllithiums to ketones: Aidhen, I. S.; Narasimhan, N. S. *Tetrahedron Lett.* **1991**, *32*, 2171.
(5) $Pb(OAc)_4$-mediated decarboxylation of the corresponding carboxylic acids: Macdonald, D. I.; Durst, T. *Tetrahedron Lett.* **1986**, *27*, 2235.
(6) Metallation of *o*-halostyrene oxides: Akguen, E.; Glinski, M. B.; Dhawan, K. L.; Durst, T. *J. Org. Chem.* **1981**, *46*, 2730.
(7) Tambar, U.; Ebner, D. C.; Stoltz, B. *J. Am. Chem. Soc.* **2006**, *128*, 11752.
(8) Macdonald, D. I.; Durst, T. *J. Org. Chem.* **1988**, *53*, 3663.
(9) Tambar, U. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 5340.
(10) Review: Charlton, J. L.; Alauddin, M. M. *Tetrahedron* **1987**, *43*, 2873.
(11) Bogucki, D. E.; Charlton, J. L. *J. Org. Chem.* **1995**, *60*, 588.
(12) Shimada, S.; Osoda, K.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1254.
(13) Choy, W.; Yang, H. *J. Org. Chem.* **1988**, *53*, 5796.
(14) Suzuki, T.; Hamura, T.; Suzuki, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 2248.
(15) Hickman, D. N.; Hodgetts, K. J.; Mackman, P. S.; Wallace, T. W.; Wardleworth, J. M. *Tetrahedron* **1996**, *52*, 2235.
(16) Frimer, A. A.; Weiss, J.; Gottlieb, H. E.; Wolk, J. L. *J. Org. Chem.* **1994**, *59*, 780.
(17) Bradley, J.-C.; Durst, T.; Williams, A. J. *J. Org. Chem.* **1992**, *57*, 6575.
(18) Spangler, L. A.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1986**, 828.
(19) Liebeskind, L. S.; Iyer, S.; Jewell, C. F. *J. Org. Chem.* **1986**, *51*, 3065.
(20) Cava, M. P.; Muth, K. *J. Am. Chem. Soc.* **1960**, *82*, 652.
(21) For a discussion, see: Gokhale, A.; Schiess, P. *Helv. Chim. Acta* **1998**, *81*, 251.
(22) Kuwajima, I.; Nakamura, E. In *Topics in Current Chemistry*; Springer-Verlag: Berlin, 1990; Vol. *155*, p 1.
(23) Kuwajima, I.; Nakamura, E. In *Comprehensive Organic Synthesis*; Trost, B., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. *2*, p 441.
(24) Kuwajima, I. *Pure Appl. Chem.* **1988**, *60*, 115.
(25) Park., S.-B.; Cha, J. K. *Org. Lett.* **2000**, *2*, 147.
(26) Okumoto, H.; Jinnai, T.; Shimizu, H.; Harada, Y.; Mishima, H.; Suzuki, A. *Synlett* **2000**, 629.
(27) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 7360.
(28) Seminal report: Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **1999**, *121*, 11010.
(29) Enantioselective variant: Matsumura, S.; Maeda, Y.; Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **2003**, *125*, 8862.
(30) For a related synthesis of benzolactones from cyclobutanones, see: Matsuda, K.; Shigeno, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 5219.
(31) Seiser, T.; Cramer, N. *Angew. Chem., Int. Ed.* **2011**, *10*, 10163 and references therein.
(32) Seiser, T.; Cathomen, G.; Cramer, N. *Synlett* **2010**, 1699.
(33) For a review on enantioselective metal-catalyzed activation of strained rings, see: Seiser, T.; Cramer, N. *Org. Biomol. Chem.* **2009**, *7*, 2835.
(34) Schweinitz, A.; Chtchemelinine, A.; Orellana, A. *Org. Lett.* **2011**, *13*, 232.
(35) Rosa, D.; Orellana, A. *Org. Lett.* **2011**, *13*, 110.
(36) Rosa, D.; Orellana, A. *Org. Lett.* **2011**, *13*, 3648.
(37) For a review of the palladium-catalyzed chemistry of alcohols, see: Muzart, J. *Tetrahedron* **2005**, *61*, 9423.
(38) Selective cleavage of the proximal bond of $Cr(CO)_3$ benzocyclobutanone complexes has been observed: Brands, M.; Wey, H. G.; Butenschön, H. *J. Chem. Soc., Chem. Commun.* **1991**, 1541.
(39) The bond dissociation energies of Pd−C(sp2) and Pd−C(sp3) bonds have been calculated to be ∼50 and ∼41 kcal/mol, respectively: Siegbahn, P. E. M. *J. Phys. Chem.* **1995**, *99*, 12723.
(40) Terao, Y.; Wakui, H.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2001**, *123*, 10407.
(41) Terao, Y.; Wakui, H.; Nomoto, M.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2003**, *68*, 5236.
(42) Nakano, M.; Satoh, T.; Miura, M. *J. Org. Chem.* **2006**, *71*, 8309.
(43) Terao, Y.; Nomoto, M.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2004**, *69*, 6942.
(44) See the Supporting Information for full details of reaction optimization.
(45) Murakami, M.; Matsuda, T. *Chem. Commun.* **2011**, *47*, 1100.
(46) Satoh, T.; Miura, M. *Top. Organomet. Chem.* **2007**, *24*, 61.
(47) Satoh, T.; Miura, M. *Top. Organomet. Chem.* **2005**, *14*, 1.
(48) Kim, Y. H.; Lee, H.; Kim, Y. J.; Kim, B. T.; Heo, J.-N. *J. Org. Chem.* **2008**, *73*, 495.
(49) Rodrigue, Y.; Rochais, C.; Oliveira, J. S. S.; Dallemagne, P.; Rault, S. *Tetrahedron* **2010**, *66*, 2803.