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Pd-Catalyzed Selective Arylative Cascade Cyclization of 1,6-Diynes and Dibenzoxaborins for Fused Naphthalene Derivatives

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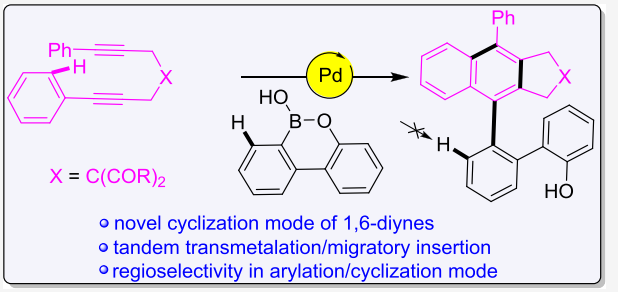
ABSTRACT: A palladium-catalyzed new mode of cascade arylative cyclization of 1,6-diynes is disclosed using dibenzoxaborin as an arylating agent featuring transmetalation and selective migratory insertion as the key steps. This process enables the efficient construction of polysubstituted fused naphthalene skeletons via the formation of three new C−C bonds through dual regioselectivity in both arylation as well as C−H functionalization. Some control experiments and kinetic isotope effect (KIE) studies were conducted to elucidate the reaction mechanism, and some product diversifications were achieved to showcase the synthetic potential.



INTRODUCTION

1,6-Diynes are versatile synthons for the construction of polycyclic fused architectures in an efficient and convergent manner while accounting for high atom economy.[1−4] They effortlessly generate carbometallacycles with various metals including Ir, Rh, Ru, Pd, Ni, Co, and Mn opening numerous avenues for [2 + 2 + 2] annulations. A vast study has been dedicated to the annulation of diynes with a wide range of coupling partners (viz. alkynes, alkenes, nitriles, isocyanates, ketenes, allenes, etc.) inter and intramolecularly. Recently, this area has attracted significant attention due to the development of innovative methodologies that allow for the synthesis of complex polycyclic carbo and heterocyclic aromatic structures. The versatile reactive nature of these diynes provides enormous scope for exploring new cyclization modes.

One such new mode is the coupling of diynes with dual inert aromatic vicinal C−H bonds[3] (Scheme 1a), through migratory insertions, assisted by appropriate directing groups (DGs). This strategy is particularly valuable for constructing fused polycyclic aromatic compounds in an expeditious manner. 1,2-Aromatic annulations with these diynes through interesting dehalogenative[4a] and decarboxylative[4b] (traceless directing groups) pathways also appeared recently for building complementary architectures.

Further, aryl diynes have also been shown to undergo cyclizations/cycloisomerizations reactions, particularly through formal [3 + 2] nucleophilic cyclization functionalizing an aryl C−H bond for differently fused scaffolds.[5−8] On this line, Liu and co-workers[5] disclosed an Au-catalyzed formal [3 + 2] cycloaddition (cycloisomerization) reaction of aryl diynes to achieve fused tricyclic compounds (Scheme 1b). On the same line, later, Schipper and co-workers[6] reported a copper-mediated nucleophilic addition-cyclization strategy for the similar but selectively substituted tricyclic scaffolds (Scheme 1c). Further, iodide or hydride initiated cyclizations were reported by Wang and co-workers[7a] and Lautens and co-workers[7b] respectively. Along this line, as part of our investigations on C−H annulations with unsaturated systems,[9] we disclose herein a novel mode of cyclization of aryl diynes; a palladium-catalyzed arylative cascade cyclization between 1,6-diynes and dibenzoxaborins, to access newly fused scaffolds. This finding differs from the earlier disclosures, with a 5-*exo*-*dig* mode of cyclization through cis−trans isomerization toward novel migratory insertion to afford complementary fused patterns of the rings. This transformation which produces fused naphthalene derivatives, enables the formation of three new C−C bonds through dual regioselectivity in both arylation and C−H functionalization. Naphthalene-based scaffolds are a privileged class of core structures, widely represented in functional materials, natural products, and pharmaceuticals.[10]

RESULTS AND DISCUSSION

Our investigations commenced with the optimization of reaction conditions with dibenzoxaborin **1a** and 1,6-diyne **2a** as model substrates (Table 1). After examining several reaction parameters (screening through various catalysts, ligands, additives and oxidants) we found that 10 mol % of $Pd(OAc)_2$

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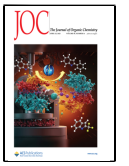

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Scheme 1. Cascade Cyclizations of 1,6-Diynes

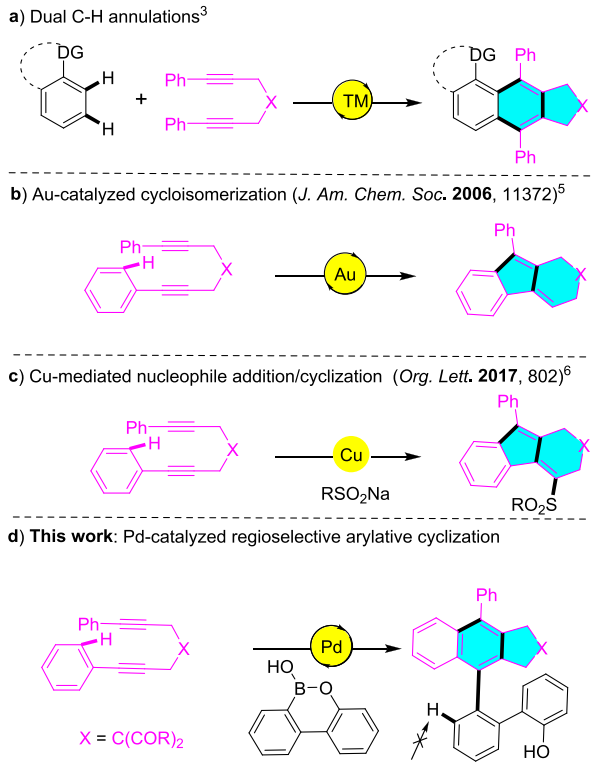
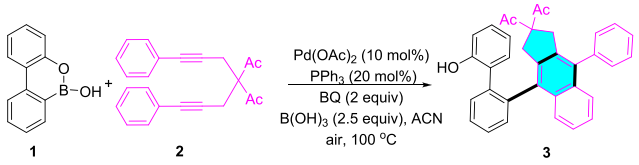


Table 1. Optimization Studies[a]



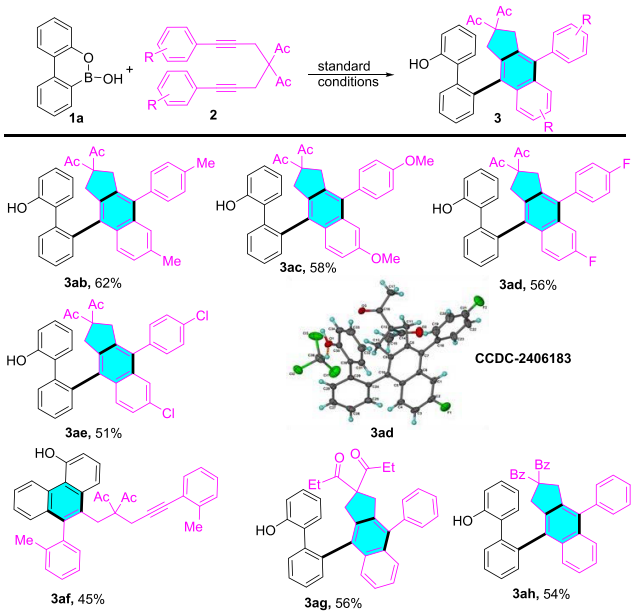
entry	variation from standard conditions	yield[b]
1	none	65%
2	$Pd(TFA)_2$ instead of $Pd(OAc)_2$	trace
3	$[RuCl_2(p\text{-cymene})]_2$ instead of $Pd(OAc)_2$	...
4	tri(*P*-Tolyl)Phosphine instead of PPh_3	40%
5	DPPF instead of PPh_3	20%
6	*rac*-BINAP instead of PPh_3	5%
7	$Cu(OAc)_2{\cdot}H_2O$ instead of benzoquinone	5%
8	AcOH instead of $B(OH)_3$	...
9	PivOH instead of $B(OH)_3$	...
10	DCE instead of ACN	10%
11	at room temperature	...
12	60 °C instead of 100 °C	20%

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), catalyst (10 mol %) ligand (20%), oxidant (2 equiv), additive (2.5 equiv), ACN (3 mL), 100 °C for 12 h under air balloon. [b]Isolated yield.

along with 20 mol % PPh_3 with benzoquinone as an oxidant and $B(OH)_3$ as an additive in ACN as a solvent at 100 °C under air was the suitable condition to get the desired product **3aa** in 65% yield (entry-1). Other catalysts based on palladium and ruthenium, which are well-known for C−H functionalization, were found to be ineffective for this transformation (entries 2−3). The use of tri(*p*-tolyl)phosphine DPPF, or *rac*-BINAP instead of PPh_3 led to erosion of the yield (entries 4−6). Copper acetate was found to be unsuitable as an oxidant (entry-7). Acetic acid, PivOH in place of $B(OH)_3$[10d] totally failed to give any desired product (entries 8−9). DCE as a solvent gave only a lower yield of the product (entry 10). Temperature has a significant impact on this process. There was no reaction at room temperature, and a slow transformation was observed at 60 °C (entries 11−12). More details of optimization studies are provided in the Supporting Information.

Having optimized the reaction conditions, we explored the scope and generality of this selective arylative cyclization of 1,6-diynes. *Para*-substitution of aryl diynes (**2b−2e** with methyl, methoxy, fluoro, and chloro groups) allowed smooth cyclization with **1a**, affording desired products **3ab-3ae** in 51−62% yields. *Ortho*-methylated diyne **2f** produced phenanthrene **3af** in somewhat lower yield, perhaps due to steric congestion. Substitution of the acyl group in 1,6-diyne with propionyl and benzoyl groups (**2g** and **2h** Scheme 2) did not affect the course

Scheme 2. Scope of 1,6-Diynes



of the reaction, producing **3ag−3ah** in 54−56% yield. The structure of **3ad** was unambiguously confirmed by a single-crystal X-ray diffraction (CCDC-2406183).

Next, the general applicability of this transformation was investigated by treating **2a** with various dibenzoxaborins **1**, which were readily prepared from corresponding biphenols.[11] **1b−1c** bearing methyl and ethyl substituents at the 8-position (Scheme 3) smoothly reacted with **2a** (**3ba−3ca** in 60−56% yields). Halogenated precursors **1d−1e** showed slightly lower productivity (**3da−3ea** in 51−57% yields). Dibenzoxaborins **1f−1g** with varied substitution at the 9-position (fluoro, chloro) reacted smoothly with **2a** to furnish the respective cyclized adducts **3fa−3ga** in 50−52% yields.

Later, we synthesized precursors **1h−1m** with substitutions (like Me, Cl, and F) on the phenol ring of dibenzoxaborin. Delightfully, they all underwent the desired cyclization with **2a** to deliver the relevant products **3ha−3ma** in moderate to good yields (46−56% Scheme 4).

To expand the synthetic utility of the reaction, we performed some scale-up and downstream transformations (Scheme 5). The reaction of **1a** at a 5 mmol scale yielded 1.19 g (48% yield) of **3aa**. Compound **3** was acylated and trifluoromethane

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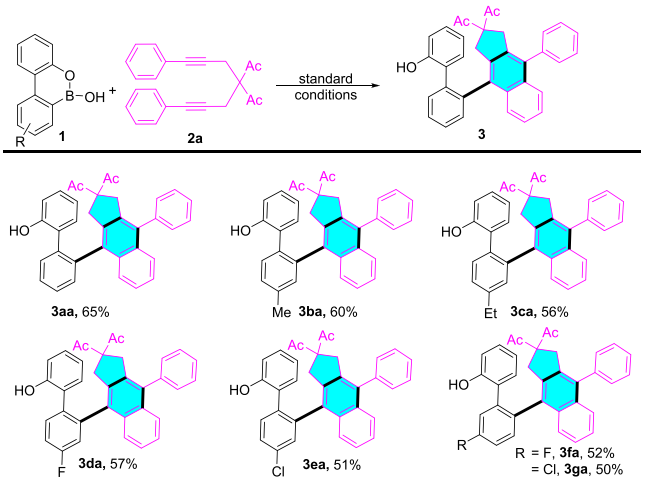
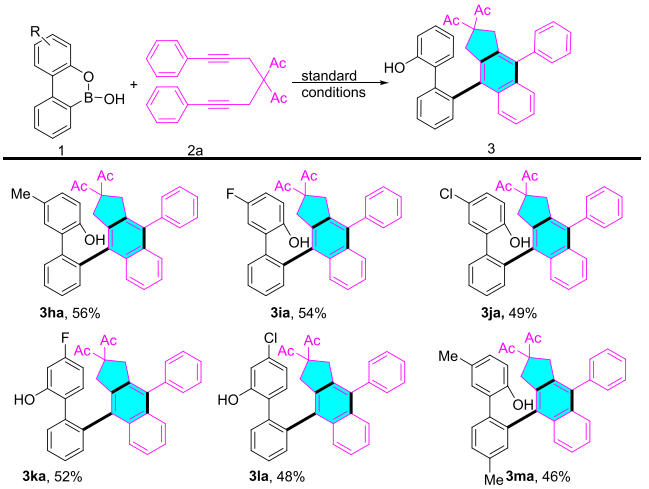
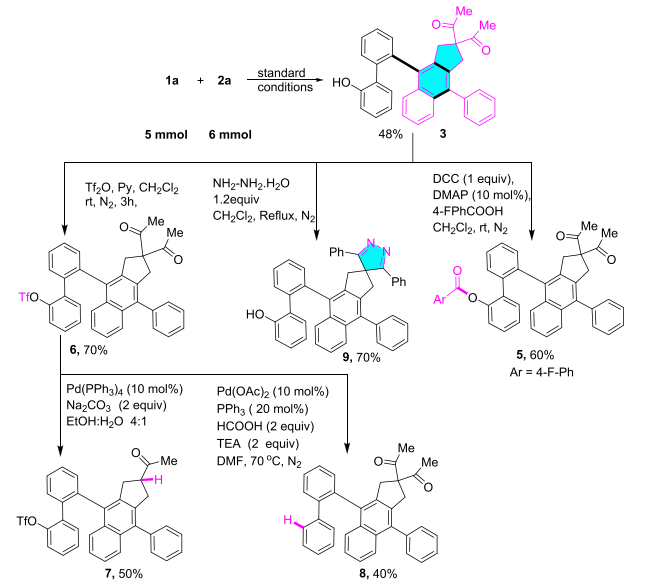
Scheme 3. Scope of Dibenzoxaborins



Scheme 4. Extended Scope of Dibenzoxaborins



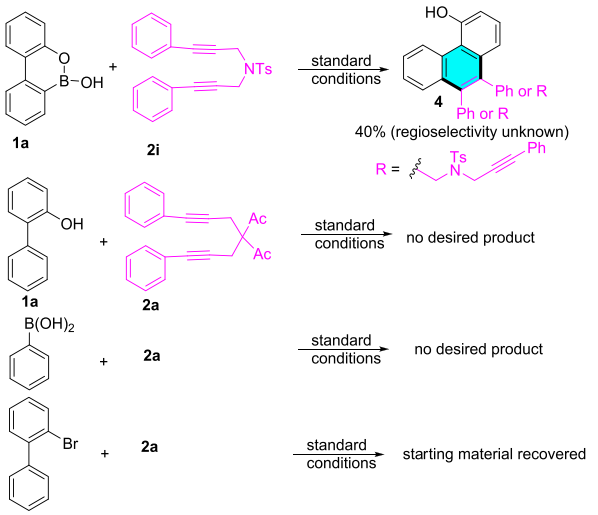
Scheme 5. Product Diversifications



sulfonylated to obtain compounds **5** and **6** in 60% and 70% yields, respectively. An initial attempt for the reductive removal of the triflate group in **6** with $Pd(PPh_3)_4$ surprisingly ended up with retro Claisen condensation[12a,b] to afford deacylated adduct **7** in 50% yield. Later, the triflate group was successfully removed with the assistance of $Pd(OAc)_2$ to get the desired **8** in 50% yield.[12c] Treatment of **3ah** with hydrazine hydrate delivered the spiro pyrazole adduct 9 in 70% yield.[12d]

To gain insights into the reaction mechanism, we carried out some control experiments and KIE studies (Scheme 6). A

Scheme 6. Control Experiments



reaction between **1a** and N-tethered 1,6-diyne **2i** under standard conditions surprisingly delivered the phenanthrene derivative **4** (as of now, we were unable to establish the regioselectivity of it even with the help of NOE) in 40% yield through a rollover cyclometalation. Some Thorpe-Ingold effect (C alpha-tetrasubstitution) might be playing a crucial role in selective migratory insertion. Efforts to react biphenol with **2a** (under optimal conditions) failed to produce any desired product, indicating that the transmetalation between palladium and boron was essential. Phenyl boronic acid or biaryl bromide did not show any similar reactivity with diyne **2a** under standard conditions, suggesting that the phenolic ligand played an equally important role in carrying out the title transformation. A KIE value of **2.37** was determined from the parallel reactions of **2a** and its deuterated counterpart **2a**-d_{10}, as shown in Scheme 7. Additionally, a competitive reaction revealed a kH/kD ratio of **2.33**, indicating that the C−H bond cleavage is probably the rate-determining step.

We thus propose a plausible mechanistic pathway for this transformation based on the above results and some literature precedents (Scheme 8). The reaction initiated through a transmetalation of **1a**, generating intermediate **A**. Regioselective insertion of diyne **2a** into **A** generated **B**. This large palladacycle, succumbing to steric repulsions arose at *o,o'*-protons, underwent solvolysis and subsequent cis−trans isomerization, followed by intramolecular carbopalladation through 5-*exo*-*dig* manner to deliver intermediate **D**. Transmetalation through C(sp^2)-H activation (**E**) followed by reductive elimination furnished the desired product **3aa** along with Pd(0). The oxidation of Pd(0) with the aid of benzoquinone generated Pd(II) for the next catalytic cycle.

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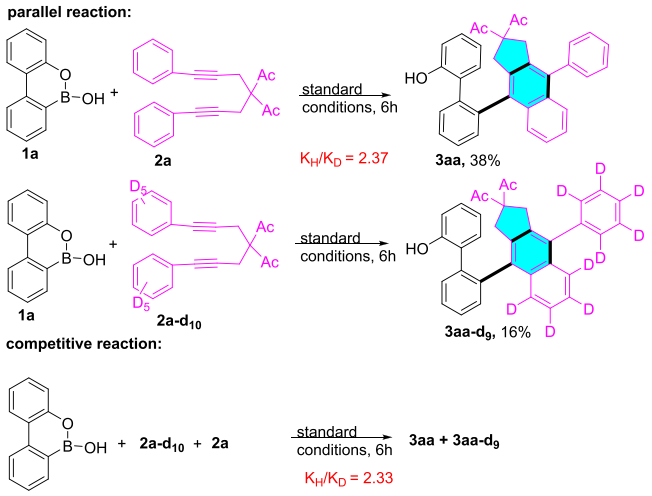
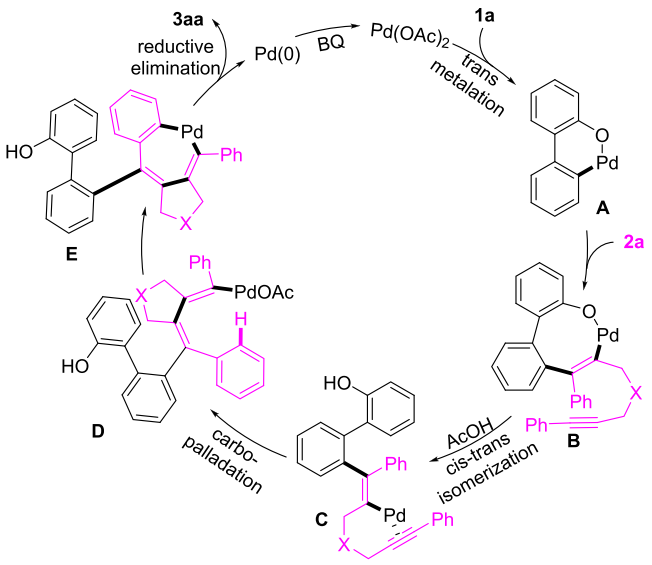
Scheme 7. KIE Studies



Scheme 8. Proposed Mechanism



CONCLUSIONS

In summary, we have demonstrated a new mode of cascade cyclization of 1,6-diyne with dibenzoxaborins for arylated fused naphthalene scaffolds. This Pd-catalyzed assembly displayed dual regioselectivity with respect to both arylation as well as terminating C−H functionalization. Pd−B transmetalation and selective migratory insertion of palladium were key to this realization. Some downstream modifications were accomplished to show the potential of the transformation. The reaction mechanism has been elucidated through a combination of control experiments and KIE studies.

EXPERIMENTAL SECTION

General Information and Methods. All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300, 400, or 500 MHz spectrometer for ^{1}H NMR, 75, 100, or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethyl silane in $CDCl_3$ or deuterated solvent $CDCl_3$ for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), and multiplet (m). HRMS were recorded using a qToF mass spectrometer. Column chromatography was performed with silica gel (100−200 mesh) as the stationary phase. All reactions were monitored by using TLC.

General Procedure for Title Compound 3 and Their Characteristic Data. *General Procedure for Title Compounds Taking **3aa** As an Example.* To a mixture of **1a** (98 mg, 0.5 mmol), 1,6-diyne **2a** (197 mg, 0.6 mmol) in ACN, $Pd(OAc)_2$ (11.2 mg, 10 mol %), PPh_3 (26.2 mg, 20 mol %), benzoquinone (108 mg, 2 equiv), $B(OH)_3$ (77.5 mg, 2.5 equiv) were introduced and the reaction mixture was stirred at 100 °C (oil bath) for 12 h under air balloon. After completion of the reaction (TLC), the reaction mixture was cooled to room temperature the solvent was evaporated. The resulting crude compound was dissolved in water and extracted using ethyl acetate and dried over MgSO4 before concentrating under vacuum. The residue was purified by column chromatography (R_f = 0.50) (SiO_2, EtOAc:Hexane, 15:85) to get **3aa** as an off-white solid (161.2 mg, 65% yield, mp 113−118 °C).

*1,1′-(4-(2′-Hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3aa**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (t, J = 3.9 Hz, 3H), 7.53 (dd, J = 9.7, 5.8 Hz, 3H), 7.49−7.40 (m, 3H), 7.38−7.28 (m, 4H), 7.03−6.94 (m, 1H), 6.77 (t, J = 7.6 Hz, 2H), 6.54 (d, J = 7.4 Hz, 1H), 5.31 (s, 1H), 3.39 (d, J = 17.2 Hz, 1H), 3.32−3.19 (m, 2H), 3.05 (d, J = 17.2 Hz, 1H), 2.02 (s, 3H), 1.81 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 206.0, 205.3, 152.4, 138.7, 138.6, 137.0, 136.8, 136.4, 135.0, 133.7, 133.0, 132.4, 132.2, 130.9, 130.7, 130.0, 129.8, 129.0, 128.7, 128.5, 128.4, 127.5, 127.2, 126.1, 125.9, 125.5, 125.2, 120.2, 115.9, 73.7, 37.7, 37.6, 27.0, 26.3. HRMS (ESI) calcd for $C_{35}H_{29}O_3$ $[M + H]^+$ 497.2117, found 497.2120.

*1,1′-(9-(2′-Hydroxy-[1,1′-biphenyl]-2-yl)-6-methyl-4-(p-tolyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ab**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2b** (214 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ab** as a white solid (162.4 mg, 62% yield), mp 114−118 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61−7.56 (m, 2H), 7.54 (ddd, J = 7.4, 5.1, 3.8 Hz, 1H), 7.50 (d, J = 8.6 Hz, 1H), 7.44−7.38 (m, 1H), 7.35−7.29 (m, 3H), 7.19 (ddd, J = 10.2, 5.9, 1.7 Hz, 3H), 7.00 (ddd, J = 8.1, 7.4, 1.7 Hz, 1H), 6.78 (dd, J = 17.5, 7.5 Hz, 2H), 6.54 (t, J = 7.4 Hz, 1H), 3.35 (d, J = 17.1 Hz, 1H), 3.29−3.17 (m, 2H), 3.00 (d, J = 17.1 Hz, 1H), 2.47 (s, 3H), 2.35 (s, 3H), 2.01 (s, 3H), 1.78 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 206.2, 205.5, 152.4, 138.7, 137.0, 136.7, 136.5, 136.0, 135.8, 134.8, 134.5, 133.3, 132.9, 132.5, 131.3, 130.9, 130.7, 129.8, 129.7, 129.4, 129.0, 128.4, 128.3, 127.7, 127.2, 125.7, 125.2, 120.3, 115.9, 73.5, 37.8, 37.5, 27.0, 26.3, 21.8, 21.4. HRMS (ESI) calcd for $C_{37}H_{33}O_3$ $[M + H]^+$ 525.2430, found 525.2434.

*1,1′-(9-(2′-Hydroxy-[1,1′-biphenyl]-2-yl)-6-methoxy-4-(4-methoxyphenyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis-(ethan-1-one) (**3ac**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2c** (233 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ac** as a off-white solid (161 mg, 58% yield), mp 104−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 11.2, 3.8 Hz, 3H), 7.50 (d, J = 9.2 Hz, 1H), 7.40 (d, J = 7.2 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.06−6.95 (m, 4H), 6.90 (d, J = 2.3 Hz, 1H), 6.76 (d, J = 8.3 Hz, 2H), 6.54 (t, J = 7.3 Hz, 1H), 5.27 (s, 1H), 3.90 (s, 3H), 3.69 (s, 3H), 3.34 (d, J = 17.1 Hz, 1H), 3.31−3.17 (m, 2H), 3.00 (d, J = 17.0 Hz, 1H), 2.02 (s, 3H), 1.80 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.2, 205.5, 158.9, 157.1, 152.4, 138.7, 137.3, 136.8, 134.7, 133.7, 133.6, 133.5, 132.4, 131.0, 130.9, 130.8, 130.7, 129.0, 128.4, 128.3, 127.5, 127.2, 120.2, 117.3, 116.2, 115.9, 114.2, 105.1, 73.7, 55.4, 55.2, 37.9, 37.4, 27.0, 26.3. HRMS (ESI) calcd for $C_{37}H_{33}O_5$ $[M + H]^+$ 557.2328, found 557.2327.

*1,1′-(6-Fluoro-4-(4-fluorophenyl)-9-(2′-hydroxy-[1,1′-biphenyl]-2-yl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ad**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2d** (218 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ad** as a white solid (149

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mg, 56% yield), mp 120−125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.52 (m, 4H), 7.40 (d, J = 7.1 Hz, 1H), 7.30−7.26 (m, 2H), 7.21 (dd, J = 5.8, 2.7 Hz, 2H), 7.11−7.06 (m, 2H), 6.98 (dd, J = 11.3, 4.1 Hz, 1H), 6.74 (d, J = 8.0 Hz, 2H), 6.53 (t, J = 7.5 Hz, 1H), 5.21 (s, 1H), 3.39 (d, J = 17.2 Hz, 1H), 3.31−3.18 (m, 2H), 3.07 (d, J = 17.2 Hz, 1H), 2.04 (s, 3H), 1.87 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 205.3, 204.8, 163.4, 161.5, 161.4, 159.5, 152.3, 140.5, 138.2, 137.9, 137.8, 137.6, 137.4, 136.9, 136.4, 134.1, 134.0, 133.3, 133.3, 132.8, 132.1, 131.6, 131.5, 131.4, 131.3, 131.0, 130.6, 130.0, 129.2, 129.1, 128.9, 128.7, 128.5, 128.5, 128.2, 127.0, 120.2, 116.0, 115.8, 115.5, 115.3, 109.8, 109.4, 109.2, 74.0, 37.6, 37.4, 26.9, 26.4. $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −114.38, (s, 1F) −115.25. (s, 1F). HRMS (ESI) calcd for $C_{35}H_{27}F_2O_3$ $[M + H]^+$ 533.1928, found 533.1983.

*1,1′-(6-Chloro-4-(4-chlorophenyl)-9-(2′-hydroxy-[1,1′-biphenyl]-2-yl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ae**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2e** (238 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ae** as a white solid (144 mg, 51% yield), mp 136−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.54 (m, 3H), 7.53−7.47 (m, 3H), 7.43 (d, J = 1.9 Hz, 1H), 7.38 (d, J = 6.7 Hz, 1H), 7.24 (d, J = 2.5 Hz, 3H), 7.03−6.97 (m, 1H), 6.74 (d, J = 8.3 Hz, 2H), 6.54 (t, J = 7.1 Hz, 1H), 5.14 (s, 1H), 3.39 (d, J = 17.3 Hz, 1H), 3.30−3.16 (m, 2H), 3.07 (d, J = 17.3 Hz, 1H), 2.03 (s, 3H), 1.88 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 205.1, 204.7, 152.3, 137.9, 137.4, 136.9, 136.4, 134.3, 133.9, 132.9, 132.8, 132.0, 131.6, 131.3, 131.2, 131.0, 130.6, 129.2, 129.1, 128.8, 128.5, 127.8, 127.0, 126.2, 124.5, 120.3, 115.9, 74.0, 37.5, 37.4, 26.9, 26.3. HRMS (ESI) calcd for $C_{35}H_{27}Cl_2O_3$ $[M + H]^+$ 565.1337, found 565.1338.

*3-((5-Hydroxy-10-(o-tolyl)phenanthren-9-yl)methyl)-3-(3-(o-tolyl)prop-2-yn-1-yl)pentane-2,4-dione (**3af**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2f** (214 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 12:88) gave pure product **3af** as white solid (118 mg, 45% yield), mp 94−99 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.72 (dd, J = 8.5, 1.1 Hz, 1H), 8.29 (d, J = 7.3 Hz, 1H), 7.64−7.57 (m, 1H), 7.56−7.49 (m, 1H), 7.34 (d, J = 3.0 Hz, 3H), 7.21 (dd, J = 9.8, 6.1 Hz, 2H), 7.17−7.11 (m, 2H), 7.10−7.05 (m, 2H), 6.99−6.95 (m, 1H), 6.84 (dd, J = 8.2, 0.9 Hz, 1H), 5.91 (s, 1H), 4.34 (d, J = 15.2 Hz, 1H), 3.48 (d, J = 15.1 Hz, 1H), 2.82 (q, J = 17.5 Hz, 2H), 2.23 (s, 3H), 1.94 (s, 3H), 1.86 (s, 3H), 1.84 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 206.0, 205.2, 154.1, 140.0, 139.5, 138.8, 137.3, 134.4, 132.2, 132.1, 131.4, 131.0, 130.6, 129.3, 128.4, 128.1, 128.0, 126.5, 126.3, 126.2, 126.1, 126.1, 125.4, 123.0, 121.7, 120.7, 119.7, 113.7, 89.6, 82.8, 70.4, 30.5, 27.9, 27.3, 24.1, 20.7, 20.0. HRMS (ESI) calcd for $C_{37}H_{32}O_3Na$ $[M + Na]^+$ 547.2249, found 547.2258.

*1,1′-(4-(2′-Hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(propan-1-one) (**3ag**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2g** (214 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ag** as colorless solid (147 mg, 56% yield), mp 98−103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.55 (m, 4H), 7.51 (dd, J = 15.3, 7.6 Hz, 3H), 7.46−7.41 (m, 2H), 7.35−7.27 (m, 4H), 7.01−6.96 (m, 1H), 6.77 (dd, J = 14.8, 7.7 Hz, 2H), 6.52 (t, J = 7.3 Hz, 1H), 5.28 (s, 1H), 3.38 (d, J = 17.0 Hz, 1H), 3.27 (s, 2H), 3.07 (d, J = 17.0 Hz, 1H), 2.32−2.17 (m, 3H), 2.08−1.98 (m, 1H), 0.97−0.88 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 208.7, 208.2, 152.4, 138.7, 138.6, 137.2, 136.9, 136.5, 134.9, 133.5, 132.9, 132.4, 130.9, 130.6, 130.0, 129.9, 128.9, 128.6, 128.5, 128.4, 127.5, 127.2, 126.1, 125.9, 125.3, 125.2, 120.1, 115.8, 73.7, 37.8, 37.7, 32.4, 32.0, 8.3, 8.1. HRMS (ESI) calcd for $C_{37}H_{33}O_3$ $[M + H]^+$ 525.2430, found 525.2440.

*(4-(2′-Hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(phenylmethanone) (**3ah**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2h** (271 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.60, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ah** as a pale gray solid (167.4 mg, 54% yield), mp 135−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.7 Hz, 4H), 7.53 (dd, J = 13.4, 8.1 Hz, 4H), 7.46 (dd, J = 15.1, 7.4 Hz, 4H), 7.40 (t, J = 7.2 Hz, 3H), 7.36−7.32 (m, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.26−7.21 (m, 3H), 7.10 (dd, J = 13.7, 8.5 Hz, 1H), 6.90 (t, J = 7.0 Hz, 1H), 6.75 (d, J = 6.7 Hz, 1H), 6.44 (t, J = 7.4 Hz, 2H), 4.97 (s, 1H), 4.01 (d, J = 17.4 Hz, 1H), 3.86 (d, J = 17.3 Hz, 1H), 3.64 (t, J = 13.6 Hz, 1H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.7, 197.4, 152.1, 138.9, 138.7, 137.2, 136.6, 135.4, 135.3, 134.7, 133.5, 133.2, 132.3, 130.8, 130.6, 130.2, 130.0, 129.4, 129.3, 128.7, 128.6, 128.6, 128.2, 127.3, 125.9, 125.7, 125.0, 124.9, 120.1, 115.7, 69.3, 41.2, 40.8. HRMS (ESI) calcd for $C_{45}H_{33}O_3$ $[M + H]^+$ 621.2430, found 621.2437.

*1,1′-(4-(2′-Hydroxy-4-methyl-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ba**).* The title compound was prepared from **1b** (105 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 16:84) gave pure product **3ba** as a pale brown solid (153 mg, 60% yield), mp 132−136 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.3 Hz, 1H), 7.57−7.48 (m, 3H), 7.48−7.38 (m, 3H), 7.38−7.27 (m, 4H), 7.24 (s, 1H), 6.98 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 7.6 Hz, 2H), 6.51 (t, 1H), 3.40 (d, J = 17.2 Hz, 1H), 3.25 (q, J = 17.2 Hz, 2H), 3.02 (d, J = 17.2 Hz, 1H), 2.48 (s, 3H), 2.03 (s, 3H), 1.79 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 206.0, 205.3, 152.5, 138.7, 138.4, 138.2, 136.9, 136.4, 134.9, 133.8, 133.6, 133.0, 132.2, 130.7, 130.0, 129.8, 129.4, 128.9, 128.7, 127.5, 127.1, 126.1, 125.9, 125.4, 125.2, 120.2, 115.7, 73.6, 37.7, 37.5, 27.0, 26.2, 21.3. HRMS (ESI) calcd for $C_{36}H_{31}O_3$ $[M + H]^+$ 511.2273, found 511.2280.

*1,1′-(4-(4-Ethyl-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ca**).* The title compound was prepared from **1c** (112 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 16:84) gave pure product **3ca** as a white solid (147 mg, 56% yield), mp 118−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.3 Hz, 1H), 7.58−7.47 (m, 4H), 7.44 (t, J = 7.1 Hz, 2H), 7.36 (d, J = 6.9 Hz, 1H), 7.33 (d, J = 6.5 Hz, 3H), 7.26 (d, J = 1.9 Hz, 1H), 6.98 (t, J = 7.1 Hz, 1H), 6.77 (d, J = 7.7 Hz, 2H), 6.52 (t, J = 7.4 Hz, 1H), 5.29 (s, 1H), 3.41 (d, J = 17.2 Hz, 1H), 3.31−3.19 (m, 2H), 3.03 (d, J = 17.2 Hz, 1H), 2.78 (q, J = 7.5 Hz, 2H), 2.03 (s, 3H), 1.79 (s, 3H), 1.34 (t, J = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.1, 205.4, 152.5, 144.5, 138.7, 138.4, 137.0, 136.4, 134.9, 134.0, 133.8, 133.1, 132.2, 131.9, 130.7, 130.0, 129.8, 128.8, 128.7, 128.1, 127.5, 127.1, 126.1, 126.0, 125.5, 125.2, 120.2, 115.7, 73.6, 37.7, 37.6, 28.7, 27.0, 26.3, 15.5. HRMS (ESI) calcd for $C_{37}H_{33}O_3$ $[M + H]^+$ 525.2430, found 525.2438.

*1,1′-(4-(4-Fluoro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3da**).* The title compound was prepared from **1d** (107 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.6, SiO_2, EtOAc:Hexane, 16:84) gave pure product **3da** as a white solid (146.5 mg, 57% yield), mp 125−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.1 Hz, 1H), 7.55 (dd, J = 10.9, 5.1 Hz, 2H), 7.50 (dd, J = 6.2, 4.9 Hz, 2H), 7.46−7.42 (m, 1H), 7.36 (dd, J = 11.2, 4.0 Hz, 1H), 7.34−7.26 (m, 4H), 7.14 (dd, J = 9.2, 2.7 Hz, 1H), 7.01−6.94 (m, 1H), 6.78 (d, J = 6.6 Hz, 1H), 6.75−6.69 (m, 1H), 6.52 (t, J = 7.4 Hz, 1H), 5.31 (s, 1H), 3.40 (d, J = 17.2 Hz, 1H), 3.26 (s, 2H), 3.10 (d, J = 17.2 Hz, 1H), 2.04 (s, 3H), 1.82 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.1, 205.1, 163.5, 161.0, 152.5, 140.6, 140.5, 138.5, 137.0, 136.3, 135.3, 133.2, 133.0, 132.9, 132.7, 132.1, 130.9, 129.8, 129.8, 129.0, 128.7, 128.7, 127.6, 126.4, 126.1, 125.7, 125.6, 125.3, 120.3, 118.9, 118.7, 115.9, 115.5, 115.3, 73.7, 37.6, 37.4, 27.0, 26.4. $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −114.0, (s, 1F). HRMS (ESI) calcd for $C_{35}H_{28}FO_3$ $[M + H]^+$ 515.2022, found 515.2021.

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*1,1′-(4-(4-Chloro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ea**).* The title compound was prepared from **1e** (115 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.5, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ea** as a white solid (135 mg, 51% yield), mp 128−133 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 7.1 Hz, 1H), 7.56−7.53 (m, 2H), 7.53−7.47 (m, 3H), 7.44 (dd, J = 11.6, 4.3 Hz, 2H), 7.36 (dd, J = 11.1, 4.0 Hz, 1H), 7.33−7.28 (m, 3H), 6.99 (td, J = 8.1, 1.6 Hz, 1H), 6.79 (d, J = 6.6 Hz, 1H), 6.72 (d, J = 8.1 Hz, 1H), 6.54 (t, J = 7.5 Hz, 1H), 5.18 (s, 1H), 3.39 (d, J = 17.2 Hz, 1H), 3.26 (s, 2H), 3.10 (d, J = 17.2 Hz, 1H), 2.05 (s, 3H), 1.81 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.0, 205.1, 152.4, 140.2, 138.5, 137.1, 136.4, 135.8, 135.4, 134.0, 132.7, 132.6, 132.2, 131.9, 130.8, 129.8, 129.8, 129.2, 128.7, 128.7, 128.5, 127.6, 126.4, 126.2, 125.7, 125.4, 120.4, 116.0, 77.4, 37.6, 37.5, 27.0, 26.3. HRMS (ESI) calcd for $C_{35}H_{28}O_3Cl$ $[M + H]^+$ 531.1727, found 531.1738.

*1,1′-(4-(5-Fluoro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3fa**).* The title compound was prepared from **1f** (107 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.51, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3fa** as a white solid (134 mg, 52% yield), mp 115−120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.1 Hz, 1H), 7.51 (dd, J = 13.8, 7.5 Hz, 3H), 7.45 (d, J = 6.9 Hz,1), 7.40−7.37 (m, 2H), 7.32 (dd, J = 13.8, 7.4 Hz, 4H), 7.24 (d, J = 12.2 Hz, 1H), 6.99 (t, J = 7.2 Hz, 1H), 6.80 (d, J = 7.5 Hz, 1H), 6.72 (d, J = 8.1 Hz, 1H), 6.54 (t, J = 7.4 Hz, 1H), 5.26 (s, 1H), 3.37 (d, J = 17.2 Hz, 1H), 3.25 (s, 2H), 3.08 (d, J = 17.2 Hz, 1H), 2.03 (s, 3H), 1.82 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.1, 205.1, 164.0, 160.7, 152.3, 140.8, 139.4, 139.3, 138.6, 138.3, 137.4, 136.3, 135.2, 134.1, 133.7, 133.6, 133.1, 132.9, 132.6, 132.4, 132.2, 130.7, 129.9, 129.8, 129.3, 128.7, 127.6, 126.5, 126.4, 126.1, 125.8, 125.5, 125.3, 120.3, 118.2, 117.9, 116.1, 115.7, 115.4, 115.2, 115.1, 73.8, 37.6, 37.6, 27.0, 26.4. ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ −109.35, (s, 1F). HRMS (ESI) calcd for $C_{35}H_{28}FO_3$ $[M + H]$+ 515.2022, found 515.2006.

*1,1′-(4-(5-Chloro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(Nethan-1-one) (**3ga**).* The title compound was prepared from **1g** (115 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.51, SiO_2, EtOAc:Hexane, 1:4) gave pure product **3ga** as a pale gray solid (132 mg, 50% yield), mp 126−130 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.52 (dd, J = 16.6, 8.2 Hz, 5H), 7.36 (s, 1H), 7.30 (d, J = 6.7 Hz, 5H), 7.05−6.94 (m, 1H), 6.81 (d, J = 7.7 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 6.55 (t, J = 7.1 Hz, 1H), 5.18 (s, 1H), 3.37 (d, J = 17.1 Hz, 1H), 3.26 (s, 2H), 3.09 (d, J = 17.1 Hz, 1H), 2.03 (s, 3H), 1.83 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 206.0, 205.1, 152.4, 139.1, 138.6, 137.2, 136.8, 136.3, 135.3, 134.0, 133.3, 132.8, 132.7, 132.2, 131.2, 130.8, 129.9, 129.8, 129.3, 128.7, 128.3, 127.6, 126.4, 126.2, 125.7, 125.5, 125.3, 120.4, 116.1, 73.8, 37.6, 37.5, 27.0, 26.4. HRMS (ESI) calcd for $C_{35}H_{28}ClO_3$ $[M + H]^+$ 531.1727, found 531.1756.

*1,1′-(4-(2′-Hydroxy-5′-methyl-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ha**).* The title compound was prepared from **1h** (105 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.52, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ha** as a white solid (143 mg, 56% yield), mp 98−103 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (t, J = 8.5 Hz, 3H), 7.56−7.47 (m, 4H), 7.47−7.41 (m, 2H), 7.34 (d, J = 7.4 Hz, 2H), 7.30 (d, J = 6.6 Hz, 2H), 6.76 (d, J = 6.7 Hz, 1H), 6.66−6.56 (m, 2H), 5.01 (s, 1H), 3.40 (d, J = 17.2 Hz, 1H), 3.34−3.21 (m, 2H), 3.09 (d, J = 17.2 Hz, 1H), 2.03 (s, 3H), 1.90 (s, 3H), 1.84 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 205.9, 205.3, 150.2, 138.7, 138.5, 137.1, 137.0, 136.3, 135.0, 133.8, 132.9, 132.1, 131.2, 131.0, 129.9, 129.8, 129.4, 129.1, 128.7, 128.5, 128.2, 127.5, 127.0, 126.0, 125.9, 125.3, 125.2, 115.5, 73.8, 37.7, 27.0, 26.3, 20.1. HRMS (ESI) calcd for $C_{36}H_{31}O_3$ $[M + H]^+$ 511.2273, found 511.2281.

*1,1′-(4-(5′-Fluoro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ia**).* The title compound was prepared from **1i** (107 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 1:4) gave pure product **3ia** as a white solid (139 mg, 54% yield), mp 133−138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (tdd, J = 6.3, 5.3, 3.0 Hz, 4H), 7.51 (dd, J = 7.7, 2.5 Hz, 3H), 7.44 (ddd, J = 7.4, 3.9, 2.2 Hz, 2H), 7.34 (dd, J = 6.4, 1.5 Hz, 2H), 7.32−7.27 (m, 2H), 6.69 (d, J = 1.6 Hz, 1H), 6.67 (d, J = 1.4 Hz, 1H), 6.53 (d, J = 8.8 Hz, 1H), 3.40 (d, J = 17.1 Hz, 1H), 3.30 (s, 2H), 3.12 (d, J = 17.1 Hz, 1H), 2.04 (s, 3H), 1.91 (s, 3H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 205.8, 205.1, 157.5, 155.1, 148.6, 138.6, 138.5, 137.0, 136.3, 136.0, 135.2, 133.2, 132.8, 132.3, 132.2, 130.7, 130.0, 129.8, 128.8, 128.7, 128.6, 128.4, 128.4, 127.6, 126.2, 125.6, 125.6, 125.4, 116.9, 116.8, 116.7, 116.3, 115.5, 115.3, 74.0, 37.6, 37.6, 27.0, 26.4. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −124.57, (s, 1F). HRMS (ESI) calcd for $C_{35}H_{28}FO_3$ $[M + H]^+$ 515.2022, found 515.2031.

*1,1′-(4-(5′-Chloro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ja**).* The title compound was prepared from **1j** (115 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO2, EtOAc:Hexane, 1:4) gave pure product **3ja** as a white solid (130 mg, 49% yield), mp 104−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 2.9 Hz, 2H), 7.52 (dd, J = 16.1, 8.3 Hz, 5H), 7.46 (s, 2H), 7.33 (d, J = 6.9 Hz, 2H), 7.28 (d, J = 16.0 Hz, 2H), 6.89 (d, J = 7.0 Hz, 1H), 6.79 (s, 1H), 6.62 (d, J = 8.5 Hz, 1H), 5.37 (s, 1H), 3.42 (d, J = 17.1 Hz, 1H), 3.36−3.25 (m, 2H), 3.13 (d, J = 17.1 Hz, 1H), 2.05 (s, 3H), 1.93 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 205.8, 205.1, 151.3, 138.7, 138.5, 137.1, 136.2, 135.9, 135.3, 133.2, 132.6, 132.1, 130.8, 130.3, 130.0, 129.8, 128.8, 128.7, 127.6, 126.2, 125.6, 125.4, 124.7, 117.1, 74.1, 37.7, 26.9, 26.5. HRMS (ESI) calcd for $C_{35}H_{28}ClO_3$ $[M + H]^+$ 531.1727, found 531.1735.

*1,1′-(4-(4′-Fluoro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1Hcyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ka**).* The title compound was prepared from **1k** (107 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ka** as a colorless solid (134 mg, 52% yield), mp 102−117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 17.0, 7.4 Hz, 5H), 7.51 (d, J = 7.9 Hz, 2H), 7.45 (t, J = 7.2 Hz, 2H), 7.31 (dd, J = 13.9, 7.8 Hz, 4H), 6.79−6.68 (m, 1H), 6.50 (d, J = 8.7 Hz, 1H), 6.24 (t, J = 7.3 Hz, 1H), 5.58 (s, 1H), 3.37 (d, J = 17.1 Hz, 1H), 3.29 (s, 2H), 3.09 (s, 1H), 2.03 (s, 3H), 1.89 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 205.9, 205.1, 163.7, 161.8, 153.7, 153.6, 140.5, 140.1, 139.1, 138.8, 138.6, 138.3, 138.0, 137.0, 136.3, 136.1, 135.2, 133.5, 132.3, 132.2, 131.6, 131.5, 131.0, 130.0, 129.8, 128.8, 128.7, 128.6, 128.6, 127.7, 127.6, 126.2, 125.7, 125.6, 125.5, 125.3, 123.3, 107.3, 107.1, 103.4, 103.2, 74.0, 37.7, 37.6, 26.9, 26.4. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −112.53, −112.74.(d, 1F). HRMS (ESI) calcd for $C_{35}H_{28}FO_3$ $[M + H]^+$ 515.2022, found 515.2035.

*1,1′-(4-(4′-Chloro-2′-hydroxy-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3la**).* The title compound was prepared from **1l** (115 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3la** as a off-white solid (127 mg, 48% yield), mp 121−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (td, J = 7.1, 1.7 Hz, 2H), 7.56−7.53 (m, 2H), 7.53−7.50 (m, 3H), 7.49−7.45 (m, 1H), 7.43 (dd, J = 7.4, 1.4 Hz, 1H), 7.37−7.34 (m, 1H), 7.32 (dd, J = 6.6, 5.0 Hz, 2H), 7.30−7.27 (m, 1H), 6.79 (s, 1H), 6.73 (d, J = 8.2 Hz, 1H), 6.52 (d, J = 8.1 Hz, 1H), 3.38−3.34 (m, 1H), 3.28 (dd, J = 13.8, 5.0 Hz, 2H), 3.07 (d, J = 17.1 Hz, 1H), 2.03 (s, 3H), 1.88 (s, 3H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.1, 205.1, 153.2, 138.6, 137.1, 136.3, 136.0, 135.2, 133.9, 133.4, 132.9, 132.3, 132.2, 131.5, 130.9, 130.0, 129.8, 128.7, 128.6, 127.6, 126.2, 126.0, 125.7, 125.6, 125.3, 120.4, 116.3, 73.9, 37.7, 37.6, 27.0, 26.4.

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HRMS (ESI) calcd for $C_{35}H_{28}ClO_3$ $[M + H]^+$ 531.1727, found 531.1766.

*1,1′-(4-(2′-Hydroxy-4,5′-dimethyl-[1,1′-biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**3ma**).* The title compound was prepared from **1m** (112 mg, 0.5 mmol) and **2a** (197 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.53, SiO_2, EtOAc:Hexane, 15:85) gave pure product **3ma** as an off-white solid (120 mg, 46% yield), mp 113−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.9 Hz, 1H), 7.50 (d, J = 8.3 Hz, 3H), 7.45 (d, J = 7.0 Hz, 2H), 7.39 (d, J = 7.7 Hz, 1H), 7.31 (dd, J = 22.9, 17.0 Hz, 5H), 6.76 (d, J = 8.1 Hz, 1H), 6.60 (d, J = 8.4 Hz, 2H), 5.00 (s, 1H), 3.41 (d, J = 17.2 Hz, 1H), 3.33−3.21 (m, 2H), 3.06 (d, J = 17.4 Hz, 1H), 2.48 (s, 3H), 2.04 (s, 3H), 1.89 (s, 3H), 1.82 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.0, 205.4, 150.3, 138.8, 138.3, 138.1, 136.9, 136.3, 134.9, 134.0, 133.0, 132.7, 132.1, 131.3, 130.8, 129.9, 129.8, 129.3, 129.1, 128.7, 127.5, 126.8, 126.0, 125.9, 125.3, 125.2, 115.4, 73.7, 37.7, 27.0, 26.3, 21.3, 20.1. HRMS (ESI) calcd for $C_{37}H_{33}O_3$ $[M + H]^+$ 525.2430, found 525.2435.

*N-((4-Hydroxy-10-phenylphenanthren-9-yl)methyl)-4-methyl-N-(3-phenylprop-2-yn-1yl)benzenesulfonamide (**4**).* The title compound was prepared from **1a** (98 mg, 0.5 mmol) and **2i** (239 mg, 0.6 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.51, SiO_2, EtOAc:Hexane, 15:85) gave pure product **4** as a pale gray solid (113 mg, 40% yield), mp 145−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77−9.68 (m, 1H), 8.87−8.81 (m, 1H), 7.75−7.67 (m, 4H), 7.26−7.21 (m, 3H), 7.19 (dd, J = 7.8, 4.4 Hz, 3H), 7.15 (d, J = 6.7 Hz, 3H), 7.09 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 6.9 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 6.66 (d, J = 7.1 Hz, 2H), 5.84 (s, 1H), 4.84 (s, 2H), 3.87 (s, 2H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.0, 143.4, 141.0, 138.8, 135.5, 134.7, 131.6, 131.4, 130.8, 130.7, 130.4, 129.5, 129.3, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.3, 126.9, 126.7, 126.6, 126.1,125.9, 122.6, 121.5, 120.1, 114.0, 86.1, 82.7, 76.9, 47.1, 36.0, 21.5. HRMS (ESI) calcd for $C_{37}H_{28}NO_3S$ $[M-H]^-$ 566.1790, found 566.1805.

General Procedure and Characteristic Data of Synthetic Transformations. *2′-(2,2-Diacetyl-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalen-4-yl)-[1,1′-biphenyl]-2-yl 4-fluorobenzoate (**5**).* An oven-dried round-bottom flask was charged with **3aa** (50 mg, 0.1 mmol, 1 equiv) and DMAP (1.2 mg, 0.01 mmol, 10 mol %) and purged with argon for 10 min. The contents were dissolved in CH_2Cl_2 before the 4-Fluorobenzoic acid (15.5 mg, 0.11 mmol, 1.1 equiv) was added. The mixture was cooled to 0 °C, and a CH_2Cl_2 solution of DCC (20.7 mg, 0.1 mmol, 1.0 equiv) was added dropwise, and the reaction was warmed to room temperature and stirred overnight (approximately 12 h). The resulting crude compound was added with water and extracted using CH_2Cl_2 and dried over $MgSO_4$, concentrated under vacuum. The residue was purified by column chromatography, R_f = 0.50 (SiO_2, EtOAc:Hexane, 1:9), to get **5** as a colorless solid in 60% (37 mg) yield, mp 130−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 5.7 Hz, 2H), 7.65−7.49 (m, 5H), 7.49−7.40 (m, 3H), 7.38−7.24 (m, 5H), 7.21−7.10 (m, 4H), 6.94 (s, 1H), 6.83 (s, 1H), 3.33 (t, J = 15.1 Hz, 2H), 3.20 (d, J = 16.9 Hz, 2H), 2.02 (s, 3H), 1.77 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 205.3, 167.2, 165.2, 164.5, 147.8, 138.7, 137.6, 137.1, 136.5, 135.0, 133.9, 133.4, 132.9, 132.8, 132.2, 131.6, 131.5, 131.1, 129.9, 129.9, 128.5, 128.1, 127.5, 126.2, 126.0, 125.7, 125.4, 125.3, 123.2, 116.0, 115.8, 37.6, 27.0, 26.3. ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ −104.32, (s, 1F). HRMS (ESI) calcd for $C_{42}H_{32}O_4F$ $[M + H]^+$ 619.2285, found 619.2293.

*2′-(2,2-Diacetyl-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalen-4-yl)-[1,1′-biphenyl]-2-yltrifluoromethanesulfonate (**6**).* A round-bottomed flask was charged with compound **3aa** (50 mg, 0.1 mmol), pyridine (16 mg, 0.2 mmol) in dichloromethane, and triflic anhydride (57 mg, 0.2 mmol) was added dropwise at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. The solvent was removed before 10 mL of water was added. The aqueous layer was extracted with ethyl acetate (2 × 10 mL), the organic layer was concentrated, and the residue was purified by column chromatography. A colorless solid was **6** obtained in 70% (44 mg) yield. R_f = 0.50 (SiO_2, EtOAc:Hexane, 10:90), mp 122−127 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62−7.56 (m, 3H), 7.54−7.46 (m, 4H), 7.45−7.40 (m, 2H), 7.33−7.23 (m, 4H), 7.22−7.08 (m, 3H), 7.03 (d, J = 16.2 Hz, 1H), 3.43 (d, J = 17.0 Hz, 1H), 3.29 (s, 2H), 3.15 (d, J = 16.8 Hz, 1H), 2.04 (s, 3H), 1.94 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 205.1, 146.9, 138.6, 138.1, 137.1, 135.2, 134.1, 133.4, 132.5, 132.0, 131.5, 131.4, 129.9, 129.8, 129.2, 129.1, 128.7, 128.6, 127.9, 127.5, 127.4, 126.3, 125.8, 125.3, 121.0, 74.2, 37.5, 26.7, 26.6. ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ −74.19, (s, 3F). HRMS (ESI) calcd for $C_{36}H_{28}O_5F_3S$ $[M + H]^+$ 629.1610, found 629.1645.

*2′-(−2-Acetyl-9-phenyl-2,3-dihydro-1H-cyclopenta[b]-naphthalen-4-yl)-[1,1′-biphenyl]-2-yltrifluoromethanesulfonate (**7**).* The compound **6** (50 mg, 0.079 mmol) in ethanol:water (4:1) was add sodium carbonate (17 mg, 2 equiv) followed by $Pd(PPh_3)_4$ (9 mg, 10 mol %) and the reaction mixture and stirred at 80 °C (oil bath temperature) for 8 h. The reaction progress was monitored by TLC. After completion of the reaction, water was added to the reaction mixture, and the contents were extracted with ethyl acetate (3 × 15 mL). Combined organic layers were dried over sodium sulfate and concentrated on rotary evaporation. The obtained crude product was purified by using flash column chromatography. R_f = 0.50 (SiO_2, EtOAc:Hexane, 7:93) gave sticky solid **7**, which was obtained in 50% (23 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.55 (m, 2H), 7.54−7.50 (m, 1H), 7.50−7.41 (m, 5H), 7.39 (d, J = 7.4 Hz, 1H), 7.33 (d, J = 7.4 Hz, 1H), 7.24 (d, J = 7.7 Hz, 2H), 7.19 (d, J = 5.2 Hz, 2H), 7.13−7.08 (m, 1H), 7.02 (d, J = 7.8 Hz, 2H), 3.27 (s, 1H), 3.10 (t, J = 10.7 Hz, 3H), 2.90 (d, J = 7.9 Hz, 1H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 209.6, 147.0, 139.0, 138.6, 135.5, 134.8, 134.5, 133.0, 132.4, 131.9, 131.7, 131.4, 131.1, 130.1, 130.0, 129.0, 129.0, 128.6, 128.2, 127.8, 127.3, 126.1, 125.8, 124.8, 124.7, 120.6, 52.7, 35.5, 34.8, 28.9. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −73.68, (s, 3F). HRMS (ESI) calcd for $C_{34}H_{26}O_4F_3S$ $[M + H]^+$ 587.1504, found 587.1500.

*1,1′-(4-([1,1′-Biphenyl]-2-yl)-9-phenyl-2,3-dihydro-1H-cyclopenta[b]naphthalene-2,2-diyl)bis(ethan-1-one) (**8**).* The compound **6** (60 mg, 0.095 mmol) in DMF was added with $Pd(OAc)_2$ (2.1 mg, 10 mol %), PPh_3 (5 mg, 20 mol %), triethylamine (29 mg, 3 equiv) and formic acid (9 mg, 2 equiv) and the reaction mixture was stirred at 70 °C (oil bath) for 3 h under nitrogen balloon. After completion of the reaction, the reaction mixture was cooled to room temperature before ice water was added to it. The aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated under reduced pressure. The crude residue was purified by column chromatography (R_f = 0.50) (SiO_2, EtOAc:Hexane, 1:9) to get **8** as an off-white solid (18 mg, 40% yield, mp 90−94 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.67 (m, 1H), 7.60−7.55 (m, 3H), 7.51 (dd, J = 13.6, 6.2 Hz, 3H), 7.47−7.44 (m, 1H), 7.37−7.30 (m, 5H), 7.10 (dt, J = 11.2, 4.7 Hz, 5H), 3.30 (d, J = 17.4 Hz, 1H), 3.23 (s, 2H), 2.79 (d, J = 17.4 Hz, 1H), 2.00 (s, 3H), 1.62 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 205.8, 205.4, 141.6, 141.2, 138.8, 136.8, 136.5, 135.0, 134.5, 133.3, 132.3, 131.6, 130.7, 130.0, 129.9, 128.9, 128.7, 128.3, 128.1, 127.5, 127.0, 126.3, 126.1, 125.5, 125.3, 73.3, 37.8, 37.7, 27.1, 25.9. HRMS (ESI) calcd for $C_{35}H_{28}O_2Na$ $[M + Na]^+$ 503.1987, found 503.1960.

*2′-(3′,4,5′-Triphenyl-1,3-dihydrospiro[cyclopenta[b]-naphthalene-2,4′-pyrazol]-9-yl)-[1,1′-biphenyl]-2-ol (**9**).* The compound **3ah** (50 mg, 0.08 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added hydrazine hydrate (3.09 mg, 0.09 mmol, 1.2 equiv) in a dropwise manner. The reaction was stirred at 45 °C in an oil bath overnight. After the reaction, the reaction mixture was cooled to room temperature before ice water was added to it. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated under reduced pressure. The crude mixture was purified using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 1:1) to get **9** as a white solid obtained in 70% yield (34.5 mg), mp 279−284 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 1H), 7.71 (d, J = 7.4 Hz, 2H), 7.67 (d, J = 8.2 Hz, 1H), 7.54−7.47 (m, 3H), 7.47−7.43 (m, 3H), 7.43−7.40 (m, 2H), 7.38 (d, J = 8.6 Hz, 2H), 7.35−7.28 (m, 5H), 7.22 (dd, J = 6.7, 4.3 Hz, 2H), 7.10 (t, J = 7.6 Hz,

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2H), 6.97−6.90 (m, 1H), 6.83 (dd, J = 7.6, 1.4 Hz, 1H), 6.62 (d, J = 7.9 Hz, 1H), 6.52 (t, J = 7.3 Hz, 1H), 3.63 (d, J = 18.7 Hz, 1H), 3.37 (dt, J = 18.6, 16.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.9, 152.7, 138.3, 138.0, 137.9, 137.5, 137.2, 136.7, 136.2, 133.5, 132.6, 131.6, 131.5, 131.2, 130.8, 130.4, 129.5, 129.3, 129.2, 129.0, 128.9, 128.8, 128.3, 128.2, 127.7, 127.5, 127.2, 127.0, 126.4, 126.2, 125.9, 125.8, 119.7, 116.3, 63.6, 41.7, 40.9. HRMS (ESI) calcd for $C_{45}H_{33}ON_2$ $[M + H]^+$ 617.2593, found 617.2590.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and in its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.5c00034.

Optimization studies; KIE studies; and characterization of related compounds (PDF)

Accession Codes

Deposition Number 2406183 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe Access Structures service.

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Notes

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