Note

Ruthenium-Catalyzed C-H Arylation of 1-Naphthol with Aryl and Heteroaryl Halides

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Ruthenium-Catalyzed C-H Arylation of 1-Naphthol with Aryl and Heteroaryl Halides

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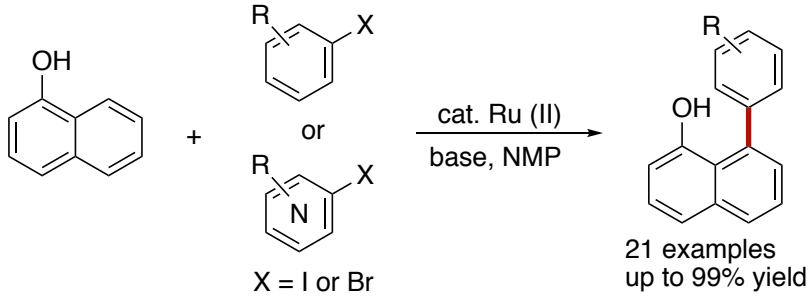
ABSTRACT While 8-aryl-1-napthols are promising dye molecules and useful intermediates in the synthesis of polycyclic aromatic hydrocarbons, they can be difficult to access. A new, ruthenium-catalyzed method for *peri* C-H arylation of 1-naphthol with a variety of aryl and heteroaryl halides (iodides, bromides) is reported that overcomes the limitations of previous palladium-catalyzed approaches. Yields for the 21 examples range from 16-99%, with an average of 71%, and the reaction tolerates a variety of functional groups: pyridine, pyrimidine, primary aniline, aldehyde, and ester.

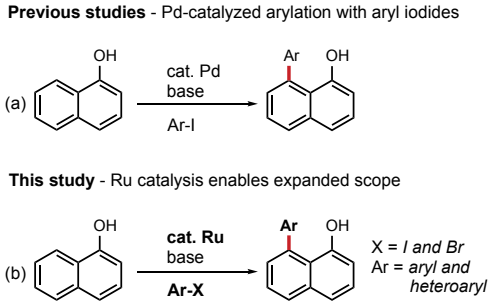


Transition metal catalyzed C-H arylation can streamline synthesis by avoiding the need for prefunctionalization, but selective reaction with one C-H out of many can be challenging.[1,2] Directed C-H arylation has proven to be one of the most robust approaches to solving this

problem.[2] Methods that rely upon innate functional groups as directing groups rather than the introduction and removal of specialized groups can be especially efficient, albeit often at the expense of more narrow applicability.[3] These methods can nonetheless open up new chemical space for exploration. For example, the development of a method to access 8-aryl-1-naphthol derivatives from 1-naphthol by Miura (Scheme 1a)[4] enabled exploration of these derivatives for organic light emitting diode (OLED) applications.[5] In addition, easy access to these 8-arylated naphthols simplified access to fluoranthenes.[6,7]

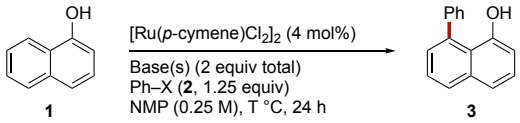
While the palladium-catalyzed C-H arylation procedure was a powerful advance, the method only provided high yields with aryl iodides and functional-group tolerance was limited: no examples with aniline functional groups or heteroaromatic halides were provided.[8] This is problematic because the more promising 8-aryl-1-naphthol dyes contain heteroaromatic or highly substituted aryl groups, requiring lengthy cross-coupling approaches involving protection/deprotection steps.[5] Ruthenium-catalyzed C-H arylation in some cases has been demonstrated to be superior to the analogous palladium-catalyzed methods.[2c,g,3g] For example, our group, along with Gooßen, Ackermann, and Larossa, found that ruthenium catalysts are more tolerant of heteroaromatic halides and less reactive aryl halides in the *ortho*-arylation of benzoic acids.[9] *peri*-Arylation with naphthols has not been reported, but *ortho*-alkylation of phenols and naphthols[10] and *ortho*-arylation of 2-pyridyl-protected phenols has been reported.[11] We show here how standard ruthenium C-H arylation conditions allow the use of aryl bromides and heteroaromatic halides in 1-naphthol *peri*-C-H arylation (Scheme 1b).

Scheme 1. Synthesis of 8-(Hetero)Aryl-1-Naphthols.



The optimal conditions (Table 1, entries 1, 10, and 12) do not require an ancillary ligand, but , similar to what Miura reported with palladium catalysis, both a carbonate and acetate base are essential.[4,12] Aryl bromides and iodides are both coupled under essentially the same conditions, but at lower temperature with cesium carbonate, activated aryl iodides can be coupled while aryl bromides provide low yields (entries 1, 6, 7, and 12). In cases with challenging aryl iodides, the higher-temperature conditions worked best, and these conditions appear to be the most general (Scheme 2). See the Supporting Information for additional details on the conditions tested. Even though unactivated aryl bromides could be coupled, chlorobenzene could not be coupled (entry 13).

Table 1. Optimization of Intermolecular C–H Arylation of 1-Naphthol with Halobenzenes



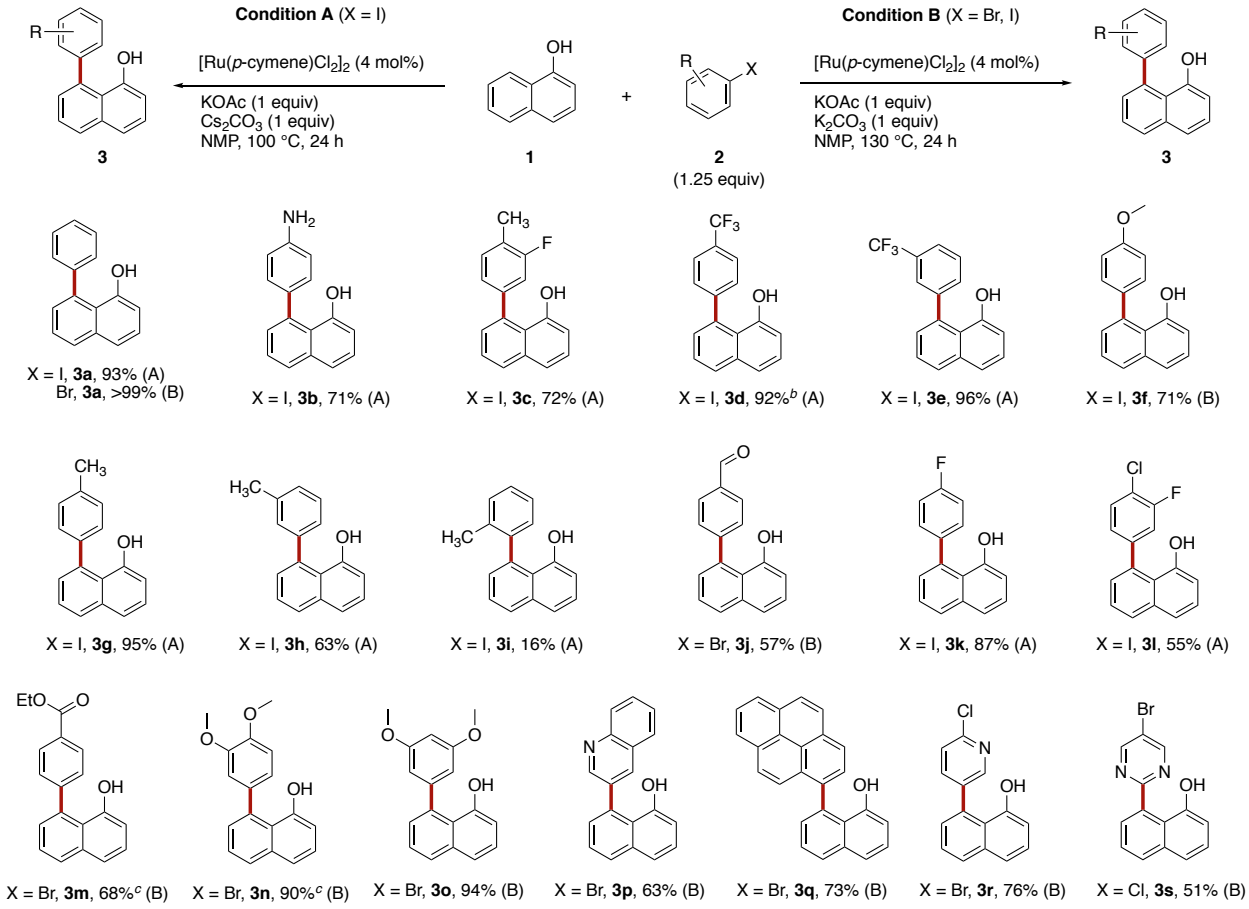
entry[a]	X	base(s)[b]	T (°C)	yield[c] (%)
1	I	Cs_2CO_3, KOAc	100	98 (93)
2	I	KOAc	100	45
3	I	Cs_2CO_3	100	50
4	I[d]	Cs_2CO_3, KOAc	100	96
5	I[e]	Cs_2CO_3, KOAc	100	0

6	Br	Cs_2CO_3, KOAc	100	35
7	Br	K_2CO_3, KOAc	130	72
8	Br	KOAc	130	12
9	Br	K_2CO_3	130	71
10	Br[d]	K_2CO_3, KOAc	130	84
11	Br[e]	K_2CO_3, KOAc	130	0
12	I	K_2CO_3, KOAc	130	96
13	Cl	K_2CO_3, KOAc	130	6

[a] Reactions were run on a 0.25 mmol scale in 1 mL of solvent for 24 h. [b] A total of 2 equiv of base was used in each case. When two bases were used together, 1 equiv of each was used. [c] GC yield vs internal standard (dodecane), isolated yields in parenthesis. [d] 1.5 equiv of aryl halide used. [e] Ruthenium catalyst omitted.

Application of these conditions to a variety of aryl halides is demonstrated in Scheme 2. Both electron-rich and electron-poor aryl iodides and bromides can be coupled in useful yields, but for electron-rich aryl iodides the higher temperature conditions were found to be optimal. Important improvements over previously reported methods are tolerance for reactive functional groups: an unprotected aniline (**3b**), an ester (**3m**), and an aldehyde (**3j**); and the ability to couple heteroaryl halides (**3p**, **3r, 3s**). Substitution at the *ortho*-position of the aryl halide generally resulted in diminished yields (compare **3g** to **3i**), but bromopyrene was coupled in 73% yield (**3q**). In addition, dihalide substrates were also tolerated, with the more reactive carbon-halide bond being selectively arylated (**3l**, **3r**, **3s**), although selectivity was not always perfect, resulting in diminished yields (**3s**). While chlorobenzene had been unsuccessful (Table 1, entry 13), 2-chloropyrimidine was reactive (**3s**). This selectivity allows for the use of different halides as orthogonal functional group handles for further chemical elaboration. Finally, the reaction could be scaled to 10 mmol scale without difficulty using standard Schlenk techniques (**3d**, 2.66 g of product).

Scheme 2. Intermolecular C–H Arylation of 1-Naphthol with (Hetero)aromatic Halides[a]



[a] Reactions were run on a 0.5 mmol scale in 2 mL of solvent for 24 h. [b] Reaction was run on a 10.0 mmol scale using standard Schlenk line techniques on the benchtop. [c] Product was inseparable from a small amount (<8%) of naphthol impurity. The yield has been adjusted based upon NMR.

Although we have not conducted any mechanistic investigations on this system, it appears to proceed in analogy to other, related, palladium and ruthenium catalyzed methods.[4,9,13] Deprotonation of the phenol, coordination to ruthenium, and concerted metalation deprotonation activates the C-H bond and sets the regioselectivity. Subsequent oxidative addition of the aryl halide and reductive elimination to form the new C-C bond would then complete the cycle.

This new approach to *peri*-substituted naphthols expands the pool of 8-arylated naphthol derivatives that can be accessed in a single step to include nitrogen-substitution, a common component in some of the most promising dyes.[5] This result mirrors our findings for the arylation

of benzoic acids,[9] demonstrating again how ruthenium C-H arylation is a useful complement to palladium catalyzed methods.[2c,3g] While we have no plans to further investigate this methodology, it is likely that other electrophiles could be used in this chemistry as well.

Experimental Section

General Methods. Dry NMP (1-Methyl-2-pyrrolidinone, anhydrous, 99.5%) was purchased and used without purification. ^{1}H nuclear magnetic resonance (NMR) spectroscopy chemical shifts are reported in ppm and referenced to TMS (tetramethylsilane) in $CDCl_3$ (δ = 0 ppm) or the residual solvent peak for $CDCl_3$ (δ = 7.26 ppm). For ^{13}C NMR and ^{19}F NMR chemical shifts, the residual solvent peak ($CDCl_3$, δ= 77.00 ppm) and TMS (δ = 0 ppm) were used as references. Chemical shifts are reported in parts per million (ppm), multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Coupling constants (J) are reported in Hertz. GC analyses were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m × 180 μm × 0.18 μm), dual FID detectors, and hydrogen as the carrier gas. Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques or on 40 g HP Silica column (catalog 69-2203-347) using a Teledyne Isco Rf- 200 (detection at 210 nm and 340 nm). Products were visualized by UV-vis. GCMS data was collected with a Shimadzu GCMS-2010S. For non-volatile compounds, high resolution mass spectra (HRMS) data was collected on a Thermo Q Exactive Plus (ESI-Q-IT-MS) (thermofisher.com) via flow injection with electrospray ionization. An ASAP-MS source (ionSence, Saugus, MA) on the Thermo Q Exactive Plus was used to obtain HRMS for volatile compounds analyzed by GCMS. This HRMS data was acquired by the chemistry mass spectrometry facility at the University of Wisconsin – Madison.

General Procedure for the Arylation of 1-Naphthol and Aryl Iodides (Condition A)

Glovebox procedure: On the bench, an oven-dried 1-dram vial fitted with a Teflon-coated stir-bar was charged with [Ru(*p*-cymene)Cl_2]$_2$ (12.3 mg, 0.02 mmol, 4 mol%), 1-naphthol (72.1 mg, 0.50 mmol, 1.0 equiv), and potassium acetate (49.1 mg, 0.50 mmol, 1.0 equiv). The vial was moved into a nitrogen filled glove box and Cs_2CO_3 (162.9 mg, 0.50 mmol, 1.0 equiv), dodecane (as an internal standard, 10.0 μL), aryl iodide (0.625 mmol, 1.25 equiv), and NMP (2.00 mL) were sequentially added. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, removed from the glove box, and heated in a reaction block set to 100 °C on the benchtop with stirring at 1250 rpm until the reaction was judged complete (<5% 1-naphthol or aryl iodide remaining) by GC analysis, typically 24 h.

Benchtop procedure: An oven-dried 100 mL Schlenk flask containing a PTFE-coated stir-bar was charged with [Ru(*p*-cymene)Cl_2]$_2$ (0.24 g, 0.4 mmol, 4 mol %), 1-naphthol (1.44 g, 10.0 mmol, 1.0 equiv), potassium acetate (0.98 g, 10.0 mmol, 1.0 equiv), and Cs_2CO_3 (3.26 g, 10.0 mmol, 1.0 equiv). 50 mL of anhydrous NMP was then added to the flask, which was subsequently attached to a nitrogen manifold. The headspace was purged with N_2 (through the stopcock with venting through a needle in the septa). After 10 min, the vent needle was removed from the septa and 4-iodobenzotrifluoride (1.47 mL, 12.5 mmol, 1.25 equiv) was added via syringe. The flow of N_2 into the vessel was turned off and the sealed (septum) reaction vessel was stirred (1250 rpm) in a 100 °C oil bath for 24 h.

General Procedure for the Arylation of 1-Naphthol and Aryl Bromides (Condition B)

Glovebox procedure: As for condition A, except that K_2CO_3 (69.1 mg, 0.50 mmol, 1.0 equiv) and aryl bromide (0.625 mmol, 1.25 equiv), and NMP (2.00 mL) were used in place of Cs_2CO_3 and aryl iodide. The reaction was stirred at 130 °C instead of 100 °C.

Isolation and purification

Upon reaction completion, the reaction mixture was diluted with dichloromethane (50 mL). The mixture was poured into a separatory funnel and the organic layer was washed with 1 M $LiBr_{aq}$ (50 mL), 1 M HCl_{aq} (50 mL), and saturated $NaCl_{aq}$ (50 mL). The combined aqueous layers were then extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford the pure product.

8-Phenylnaphthalen-1-ol (3a)[6] Condition A from iodobenzene (127.5 mg, 69.7 µL): 93% yield (102.4 mg). Yellow oil. Condition B from bromobenzene (98.1 mg, 66.6 µL): >99% yield (110.1 mg). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.3, 1.3 Hz, 1H), 7.52 (m, 6H), 7.43 (dt, J = 17.2, 7.6 Hz, 2H), 7.21 (dd, J = 7.1, 1.3 Hz, 1H), 6.91 (dd, J = 7.6, 1.3 Hz, 1H), 5.40 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.0, 141.4, 136.2, 135.7, 129.5, 129.0, 128.7, 128.6, 128.5, 126.9, 124.8, 121.3, 121.0, 111.8. HRMS (ESI) *m/z* calculated for $C_{16}H_{11}O$ $[M - H]^-$ 219.0815, found 219.0814. Our characterization data is consistent with those previously reported.

8-(4-Aminophenyl)naphthalen-1-ol (3b) Condition A from 4-iodoaniline (136.9 mg): 71% yield (83.5 mg). Brick red oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 8.3, 1.2 Hz, 1H), 7.47 (dd, J = 8.2, 1.2 Hz, 1H), 7.39 (dt, J = 15.3, 7.5 Hz, 2H), 7.32 – 7.27 (m, 2H), 7.17 (dd, J = 7.0, 1.3 Hz, 1H), 6.90 (dd, J = 7.5, 1.2 Hz, 1H), 6.83 – 6.77 (m, 2H), 5.93 (s, 1H), 3.87 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.4, 146.9, 136.3, 135.7, 130.6, 130.3, 128.7, 128.3, 126.8, 124.9, 121.6, 120.7, 115.2, 111.4. HRMS (ESI) *m/z* calculated for $C_{16}H_{12}NO$ $[M - H]^-$ 234.0924, found 234.0923.

8-(3-Fluoro-4-Methylphenyl)naphthalen-1-ol (3c) Condition A from 2-fluoro-4-iodotoluene (147.5 mg): 72% yield (90.8 mg). Amber oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 8.2, 1.3 Hz, 1H), 7.51 (dd, J = 8.2, 1.2 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.33 (t, J = 7.8 Hz, 1H), 7.21 – 7.18

(m, 2H), 7.18 – 7.17 (m, 1H), 6.93 (dd, J = 7.6, 1.3 Hz, 1H), 5.41 (s, 1H), 2.38 (d, J = 2.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 161.0 (d, J = 248.2 Hz), 152.8, 140.7 (d, J = 7.5 Hz), 135.6, 134.9 (d, J = 1.8 Hz), 131.9 (d, J = 5.7 Hz), 128.9, 128.5, 126.9, 125.4 (d, J = 17.2 Hz), 124.8, 124.8, 121.2, 121.1, 116.3 (d, J = 22.4 Hz), 111.9, 14.4 (d, J = 3.4 Hz). $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ 9.42. HRMS (ASAP-MS) *m/z* calculated for $C_{17}H_{12}FO$ $[M - H]^-$ 251.0878, found 251.0878.

8-(4-Trifluoromethylphenyl)naphthalen-1-ol (3d)[6] Condition A, benchtop procedure (10.0 mmol scale) from 4-iodobenzotrifluoride (3.4 g, 1.84 mL): 92% yield (2.66 g). Brown solid. Mp. 71.4-74.1 °C (lit.[6] 72.8-74.0 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, J = 8.3, 1.3 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.54 (dd, J = 8.2, 1.2 Hz, 1H), 7.48 (d, J = 7.0 Hz, 1H), 7.47 (d, J = 7.0 Hz, 0H), 7.41 (t, J = 7.8 Hz, 1H), 7.21 (dd, J = 7.0, 1.3 Hz, 1H), 6.90 (dd, J = 7.5, 1.2 Hz, 1H), 5.00 (s, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 152.4, 146.16, 146.15, 135.8, 135.4, 130.5 (q, J = 32.6 Hz), 129.8, 129.1, 128.8, 127.4 (q, J = 274.5 Hz), 126.9, 125.3 (q, J = 3.8 Hz), 125.2, 125.0, 121.5, 121.2, 112.0, 29.7. $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ 62.52. HRMS (ESI) *m/z* calculated for $C_{17}H_{10}F_3O$ $[M - H]^-$ 287.0689, found 287.0688. Our characterization data is consistent with those previously reported.

8-(3-Trifluoromethylphenyl)naphthalen-1-ol (3e)[6] Condition A from 3-iodobenzotrifluoride (170.0 mg, 90.1 µL): 96% yield (136.4 mg). Dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, J = 8.3, 1.1 Hz, 1H), 7.77 (dd, J = 7.3, 1.2 Hz, 1H), 7.70 (dd, J = 15.6, 7.7 Hz, 2H), 7.60 (t, J = 7.7 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.48 (d, J = 7.1 Hz, 1H), 7.46 (d, J = 6.9 Hz, 0H), 7.40 (t, J = 7.9 Hz, 1H), 7.22 (dd, J = 5.9, 1.2 Hz, 1H), 6.88 (dd, J = 7.6, 1.2 Hz, 1H), 4.92 (s, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 152.5, 143.4, 140.2, 136.0, 135.4, 132.8, 130.8 (q, J = 32.4 Hz), 129.2, 129.1, 128.8, 126.9, 126.4 (q, J = 3.8 Hz), 125.2, 124.7 (q, J = 3.8 Hz), 124.4 (q, J = 273.9 Hz),

121.6, 121.4, 112.0. $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ 62.39. HRMS (ESI) *m/z* calculated for $C_{17}H_{10}F_3O$ $[M - H]^-$ 287.0688, found 287.0689. Our characterization data is consistent with those previously reported.

8-(4-Methoxyphenyl)naphthalen-1-ol (3f)[6] Condition B from 4-iodoanisole (146.3 mg): 71% yield (88.9 mg). Brick red solid. Mp. 114.2-116.4 °C (lit.[6] 114.1-114.9 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 8.2, 1.4 Hz, 1H), 7.49 (dd, J = 8.1, 1.3 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.42 – 7.36 (m, 1H), 7.18 (dd, J = 7.0, 1.3 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.91 (dd, J = 7.6, 1.2 Hz, 1H), 5.65 (s, 1H), 3.89 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 159.9, 153.2, 135.8, 135.7, 133.0, 130.7, 128.7, 128.5, 126.8, 124.9, 121.5, 120.9, 114.4, 111.6, 55.4. HRMS (ESI) *m/z* calculated for $C_{17}H_{13}O_2$ $[M - H]^-$ 249.0921, found 249.0922. Our characterization data is consistent with those previously reported.

8-(4-Methylphenyl)naphthalen-1-ol (3g)[6] Condition A from 4-iodotoluene (136.3 mg): 95% yield (111.3 mg). Brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.41 (p, *J* = 8.5, 7.9 Hz, 4H), 7.33 (d, *J* = 7.7 Hz, 2H), 7.22 – 7.16 (m, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 5.55 (s, 1H), 2.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 153.4, 138.8, 138.3, 136.3, 135.9, 129.9, 129.5, 128.8, 128.7, 127.0, 125.0, 121.6, 121.1, 111.9, 21.5. HRMS (ESI) *m/z* calculated for $C_{17}H_{13}O$ $[M - H]^-$ 233.0972, found 233.0972. Our characterization data is consistent with those previously reported excepting morphology (lit.[6] reports a yellow solid).

8-(3-Methylphenyl)naphthalen-1-ol (3h)[6] Condition A from 3-iodotoluene (136.3 mg, 80.3 µL): 63% yield (73.6 mg). Amber solid. Mp. 81.6-84.0. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, J = 8.2, 1.3 Hz, 1H), 7.51 – 7.42 (m, 2H), 7.42 – 7.31 (m, 5H), 7.12 (dd, J = 6.9, 1.3 Hz, 1H), 6.87 (dd, J = 7.6, 1.2 Hz, 1H), 5.54 (s, 1H), 2.08 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 153.4, 140.3, 137.6, 135.6, 135.4, 130.6, 130.0, 129.2, 128.6, 127.6, 126.8, 126.5, 125.1, 121.6, 121.0,

111.4, 20.1. HRMS (ESI) *m/z* calculated for $C_{17}H_{13}O$ $[M - H]^-$ 233.0972, found 233.0971. Our characterization data is consistent with those previously reported excepting morphology (lit.[6] reports a yellow oil).

8-(2-Methylphenyl)naphthalen-1-ol (3i) Condition A from 2-iodotoluene (136.3 mg, 79.5 µL): 59% yield (69.1 mg). Amber oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, J = 8.2, 1.3 Hz, 1H), 7.37 (dd, J = 8.2, 1.2 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.30 – 7.25 (m, 2H), 7.25 – 7.18 (m, 2H), 7.00 (dd, J = 7.0, 1.3 Hz, 1H), 6.77 (dd, J = 7.6, 1.2 Hz, 1H), 5.45 (s, 1H), 1.96 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.4, 140.3, 137.6, 135.7, 135.4, 130.7, 130.0, 129.2, 128.6, 127.3, 126.9, 126.5, 125.2, 121.7, 121.0, 111.4, 20.2. HRMS (ESI) *m/z* calculated for $C_{17}H_{13}O$ $[M - H]^-$ 233.0972, found 233.0972.

4-(8-hydroxynaphthalen-1-yl)benzaldehyde (3j) Condition B from 4-bromobenzaldehyde (115.6 mg): 57% yield (71 mg). Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 – 7.98 (m, 2H), 7.85 (dd, J = 8.3, 1.2 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.49 (dd, J = 8.1, 1.1 Hz, 1H), 7.43 (dd, J = 8.3, 7.0 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.18 (dd, J = 7.0, 1.3 Hz, 1H), 6.90 (dd, J = 7.6, 1.2 Hz, 1H), 5.75 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 200.4, 162.9, 137.2, 136.3, 130.6, 129.3, 128.1, 127.3, 126.4, 126.3, 124.9, 124.3, 123.5, 116.8, 111.5. HRMS (ASAP-MS) *m/z* calculated for $C_{17}H_{11}O_2$ $[M - H]^-$ 247.0765, found 247.0764.

8-(4-Fluorophenyl)naphthalen-1-ol (3k) Condition A from 4-fluoroiodobenzene (138.8 mg, 72.1 µL): 87% yield (103.6 mg). Brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, J = 8.3, 1.2 Hz, 1H), 7.39 (dd, J = 8.2, 1.2 Hz, 1H), 7.37 – 7.31 (m, 3H), 7.29 (t, J = 7.3 Hz, 1H), 7.12 – 7.04 (m, 3H), 6.79 (dd, J = 7.6, 1.2 Hz, 1H), 5.21 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.8 (d, J = 248.6 Hz), 152.9, 137.5 (d, J = 3.6 Hz), 135.8, 135.3, 131.3 (d, J = 8.1 Hz), 128.9 (d, J = 1.2 Hz),

127.0, 125.0, 121.4, 121.2, 115.8 (d, J = 21.5 Hz), 111.9. $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ -113.13. HRMS (ESI) *m/z* calculated for $C_{16}H_{10}FO$ $[M - H]^-$ 237.0721, found 237.0722.

8-(2-Fluoro-4-bromophenyl)naphthalen-1-ol (3l) Condition A from 1-chloro-2-fluoro-4-iodobenzene (160.3 mg, 79.8 μL): 55% yield (74.9 mg). Brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, J = 8.3, 1.2 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.37 (t, J = 7.8 Hz, 1H), 7.25 (dd, J = 9.5, 2.0 Hz, 1H), 7.17 (dt, J = 7.9, 1.8 Hz, 2H), 6.86 (dd, J = 7.6, 1.2 Hz, 1H), 5.18 (s, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 157.5 (d, J = 250.8 Hz), 152.3, 135.8, 134.6, 130.3, 129.1, 128.7, 126.8, 125.8 (d, J = 3.6 Hz), 125.0, 121.4, 121.2, 117.8 (d, J = 21.2 Hz), 111.9. $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ -114.70. HRMS (ESI) *m/z* calculated for $C_{16}H_9ClOF$ $[M - H]^-$ 271.0331, found 271.0331.

8-(4-Ethylbenzoate)naphthalen-1-ol (3m) Condition B from ethyl 4-bromobenzoate (143.2 mg, 102.0 μL): 68% yield (99.4 mg). This compound could not be separated from a small amount of 1-naphthol. The yield reported has been adjusted to account for this impurity based upon ^{1}H NMR integration. Light brown solid. Mp. 132.4-133.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.13 (m, 2H), 7.88 (dd, J = 8.2, 1.2 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.55 – 7.51 (m, 1H), 7.46 (dd, J = 8.3, 7.0 Hz, 1H), 7.41 (t, J = 7.9 Hz, 1H), 7.21 (dd, J = 7.0, 1.3 Hz, 1H), 6.91 (dd, J = 7.5, 1.2 Hz, 1H), 5.12 (s, 1H), 4.43 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 166.2, 152.6, 146.7, 135.7, 135.6, 130.2, 129.8, 129.7, 129.4 (d, J = 3.5 Hz), 129.1, 128.5, 126.9, 124.9, 121.3, 121.2, 112.0, 61.2, 14.4. HRMS (ASAP-MS) *m/z* calculated for $C_{19}H_{15}O_3$ $[M - H]^-$ 291.1027, found 291.1026.

8-(3,4-dimethoxyphenyl)naphthalen-1-ol (3n) Condition B from 4-bromoveratrole (135.7 mg, 89.9 μL): 90% yield (126.0 mg). This compound could not be separated from a small amount of 1-naphthol. The yield reported has been adjusted to account for this impurity based upon ^{1}H NMR

integration. Amber oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, J = 8.3, 1.3 Hz, 1H), 7.49 (dd, J = 8.2, 1.2 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.22 (dd, J = 6.9, 1.3 Hz, 1H), 6.93 (dd, J = 7.6, 1.2 Hz, 1H), 6.62 (d, J = 2.3 Hz, 2H), 6.57 (t, J = 2.3 Hz, 1H), 5.84 (s, 1H), 3.82 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.2, 149.3, 149.1, 135.8, 135.7, 133.3, 128.64, 128.58, 126.9, 124.8, 121.6, 120.9, 112.6, 111.7, 111.3, 56.02, 55.99. HRMS (ESI) *m/z* calculated for $C_{18}H_{15}O_3$ $[M - H]^-$ 279.1027, found 279.1026.

8-(3,5-dimethoxyphenyl)naphthalen-1-ol (3o) Condition B from 1-bromo-3,5-dimethoxybenzene (135.7 mg): 94% yield (131.7 mg). Brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.46 – 7.37 (m, 2H), 7.27 – 7.20 (m, 1H), 6.93 (dd, *J* = 7.6, 1.1 Hz, 1H), 6.63 (d, *J* = 2.3 Hz, 2H), 6.57 (t, *J* = 2.3 Hz, 1H), 5.81 (s, 1H), 3.82 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 161.0, 153.0, 143.3, 136.0, 135.6, 128.8, 127.9, 126.9, 124.8, 121.2, 120.9, 112.0, 107.4, 100.7, 55.5. HRMS (ASAP-MS) *m/z* calculated for $C_{18}H_{15}O_3$ $[M - H]^-$ 279.1027, found 279.1027.

8-(Quinolin-3-yl)naphthalen-1-ol (3p) Condition B from 3-bromoquinoline (130.0 mg, 84.8 µL): 63% yield (85.5 mg). Amber oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 9.0 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 8.3 Hz, 3H), 7.60 (t, J = 7.8 Hz, 1H), 7.52 (t, J = 8.1 Hz, 2H), 7.43 (q, J = 8.0 Hz, 2H), 7.36 (d, J = 7.3 Hz, 1H), 7.12 (d, J = 8.9 Hz, 1H). ^{13}C{^{1}H} (126 MHz, $CDCl_3$) δ 162.2, 149.9, 146.6, 140.0, 135.0, 129.8, 128.0, 127.9, 127.5, 127.3, 126.4, 126.1, 125.73, 125.70, 125.0, 124.9, 122.1, 117.3, 112.1. HRMS (ASAP-MS) *m/z* calculated for $C_{19}H_{14}NO$ $[M + H]^+$ 272.1070, found 272.1067.

8-(Pyren-2-yl)naphthalen-1-ol (3q) Condition B from 1-bromopyrene (175.7 mg): 73% yield (125.7 mg). Off-white solid. Mp. 90.4-91.6 °C; ^{1}H NMR (500 MHz, benzene-d6) δ 8.46 (d, J = 9.2 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.92 (d, J = 7.6 Hz, 2H), 7.89 – 7.78 (m, 6H), 7.78 – 7.66

(m, 4H), 7.61 (d, J = 8.9 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, benzene-d6) δ 131.23 131.2, 131.0, 130.6, 129.9, 129.8, 129.0, 127.9, 127.74, 127.68, 127.6, 127.5, 126.3, 126.0, 125.9, 125.7, 125.6, 125.5, 124.93, 124.91, 124.2, 119.9. HRMS (ASAP-MS) *m/z* calculated for $C_{26}H_{15}O$ $[M - H]^-$ 343.1128, found 343.1127. The product was not sufficiently soluble in $CDCl_3$ to obtain a ^{13}C NMR spectrum with sufficient signal to noise.

8-(2-Chloro-pyridin-5-yl)naphthalen-1-ol (3r) Condition B from 5-bromo-2-chloropyridine (120.3 mg): 76% yield (97.2 mg). Amber oil. ^{1}H (500 MHz, Chloroform-d) δ 8.19 (d, J = 2.5 Hz, 1H), 7.93 (dd, J = 8.4, 1.2 Hz, 1H), 7.88 (dd, J = 8.1, 1.3 Hz, 1H), 7.79 – 7.70 (m, 2H), 7.55 – 7.40 (m, 3H), 7.22 (dd, J = 7.5, 1.0 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H, O**H**, exchangeable in D_2O). $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-d) δ 163.1, 149.6, 148.6, 142.0, 135.0, 128.0, 127.3, 126.5, 126.3, 125.7, 125.4, 121.8, 117.2, 113.5, 112.4. HRMS (ESI) *m/z* calculated for $C_{15}H_9ClNO$ $[M - H]^-$ 254.0378, found 254.0380.

8-(3-Bromo-pyrimidin-5-yl)naphthalen-1-ol (3s) Condition B from 5-bromo-2-chloropyrimidine (120.9 mg): 51% yield (65.5 mg). Amber oil. ^{1}H NMR (500 MHz, Chloroform-d) δ 8.55 (s, 2H), 7.93 – 7.86 (m, 2H), 7.82 – 7.77 (m, 1H), 7.51 (ddd, J = 8.5, 7.1, 1.7 Hz, 2H), 7.46 (ddd, J = 8.2, 6.8, 1.3 Hz, 1H), 7.30 (dd, J = 7.5, 1.0 Hz, 1H). $^{13}C\{^{1}H\}$ (126 MHz, Chloroform-d) δ 164.4, 160.2, 148.7, 134.8, 128.1, 126.9, 126.5, 126.5, 126.1, 125.6, 121.5, 117.7, 113.2. HRMS (ASAP-MS) *m/z* calculated for $C_{14}H_{10}BrN_2O$ $[M + H]^+$ 300.9971, found 300.9977.

ASSOCIATED CONTENT

Supporting Information. Copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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