Supporting Information

Catalytic Friedel–Crafts Reactions of Unactivated Secondary Alcohols:
Site-Selective Alkylation of Phenols

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1. General Information

   i) Solvents and reagents

Commercial reagents were purchased from MilliporeSigma, Acros Organics, Chem-Impex, TCI, Oakwood, and Alfa Aesar, and used without additional purification. Solvents were purchased from Fisher Scientific, Acros Organics, Alfa Aesar, and Sigma Aldrich. Tetrahydrofuran (THF), diethyl ether (Et₂O), acetonitrile (MeCN), dichloromethane (CH₂Cl₂), benzene, 1,4-dioxane, and triethylamine (Et₃N) were sparged with argon and dried by passing through alumina columns using argon in a Glass Contour (Pure Process Technology) solvent purification system. Dimethylformamide (DMF), dimethyl sulfoxide
(DMSO), and dichloroethane (DCE) were purchased in Sure/Seal or AcroSeal bottling and dispensed under N₂. Deuterated solvents were obtained from Cambridge Isotope Laboratories, Inc. or MilliporeSigma.

ii) Reaction setup, progress monitoring, and product purification

In general, the catalytic reactions are not air- or moisture-sensitive; however, the iron and zinc salts are hygroscopic and quickly change color when being weighed and added to the reaction vessel. This influences how much metal catalyst is being added because their molecular weights increase on hydration. For consistency and rigor, the iron and zinc salts were weighed and added to vials inside a nitrogen-filled glovebox. All other reagents, including the solvent, were added outside the glovebox under open air. Reaction progresses were monitored using thin-layer chromatography (TLC) on EMD Silica Gel 60 F254 or Macherey–Nagel SIL HD (60 Å mean pore size, 0.75 mL/g specific pore volume, 5–17 μm particle size, with fluorescent indicator) silica gel plates. Visualization of the developed plates was performed under UV light (254 nm). Purification and isolation of products were performed via silica gel chromatography (both column and preparative thin-layer chromatography). Organic solutions were concentrated under reduced pressure on IKA® temperature-controlled rotary evaporator equipped with an ethylene glycol/water condenser.

iii) Analytical instrumentation

Melting points were measured with the MEL-TEMP melting point apparatus.

Proton nuclear magnetic resonance (¹H NMR) spectra, carbon nuclear magnetic resonance (¹³C NMR) spectra and fluorine nuclear magnetic resonance (¹⁹F NMR) spectra were recorded on Bruker Avance NEO 400 (not ¹H decoupled) or Bruker Avance 600 MHz spectrometers (¹H decoupled). Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ 7.26 for ¹H NMR, δ 77.16 for ¹³C NMR in CDCl₃).¹ Data for ¹H NMR spectroscopy are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets), coupling constant (Hz), integration. Data for ¹³C and ¹⁹F NMR spectroscopy are reported in terms of chemical shift (δ ppm).

IR spectroscopic data were recorded on a NICOLET 6700 FT-IR spectrophotometer using a diamond attenuated total reflectance (ATR) accessory. Samples are loaded onto the diamond surface either neat or as a solution in organic solvent and the data acquired after the solvent had evaporated.

High resolution accurate mass (ESI) spectral data were obtained from the Analytical Chemistry Instrumentation Facility at the University of California, Riverside, on an Agilent 6545 Q-TOF LC/MS instrument (supported by NSF grant CHE-1828782).
2. Selected Reaction Optimization Data for Alkylation of 3-tert-butylphenol

![Chemical structure of 3-tert-butylphenol and cyclohexanol reacting to form 3aa]

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[^a]: Conditions: All reactions performed on 0.2 mmol scale, 3-tert-butylphenol 1a (1 equiv), cyclohexanol 2a (3 equiv), 1 M PhCl, 140 °C, 18 h.  
[^b]: Determined by NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as the internal standard, unless otherwise specified.  
[^c]: Isolated yield.  
[^d]: with 0 equiv (R)-CSA•H₂O, 0% yield.

3. Preparation of Secondary Alcohols

i) General Procedure A: Reductions of Ketones with LiAlH₄

To a 50 mL RBF (flame-dried, stir bar) was added LiAlH₄ (1 equiv) before purging with N₂ and suspending in dry Et₂O (to produce a 0.2 M suspension). The mixture was cooled to 0 °C before adding dropwise a solution of ketone (1 equiv) in dry Et₂O (1 M). The resulting suspension was allowed to stir at 0 °C for 4 h. The reaction mixture was quenched via the Fieser–Fieser workup conditions: diluted with Et₂O (30 mL), then cooled to 0 °C and dropwise added distilled water (dH₂O) (2 equiv), 15% (w/v) NaOH(aq) (2 equiv), and dH₂O (3 equiv). The mixture was warmed to room temperature and stirred for 15 min, then added anhydrous MgSO₄ was and stirred for an additional 15 min. The solids were removed by
filtration and the filtrate concentrated under reduced pressure to obtain the secondary alcohol product. The alcohols were subsequently used without further purification.

ii) Product Characterization

Cycloheptanol (2b)

Prepared using General Procedure A with LiAlH₄ (76.2 mg, 2.01 mmol, 1 equiv), Et₂O (10 mL, 0.2 M), and cycloheptanone (0.24 mL, 2 mmol, 1 equiv) in Et₂O (2 mL, 1 M) to afford 2b (0.10 g, 44%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 3.85 (tt, J = 8.5, 4.3 Hz, 1H), 1.95–1.87 (m, 2H), 1.69–1.61 (m, 2H), 1.59–1.51 (m, 6H), 1.43–1.36 (m, 2H). The spectral data recorded are consistent with those previously reported.¹

1,2,3,4-Tetrahydronapthalen-2-ol (2c)

Prepared using General Procedure A with LiAlH₄ (0.19 g, 5 mmol, 1 equiv), Et₂O (25 mL, 0.2 M), and 2-tetralone (0.66 mL, 5 mmol, 1 equiv) in Et₂O (5 mL, 1 M) to afford 2c (470.0 mg, 63%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.16–7.06 (m, 4H), 4.21–4.13 (m, 1H), 3.10 (dd, J = 16.2, 5.0 Hz, 1H), 2.96 (dt, J = 17.0, 5.7 Hz, 1H), 2.85 (ddd, J = 16.6, 9.3, 6.0 Hz, 1H), 2.78 (dd, J = 16.2, 7.9 Hz, 1H), 2.11–2.02 (m, 1H), 1.83 (ddt, J = 12.7, 9.2, 5.8 Hz, 1H). The spectral data recorded are consistent with those previously reported.²

Norbornan-2-ol (2g)

In a glovebox, to a non-dry 50 mL round-bottomed flask equipped with a stir bar was added norbornene (2.06 g, 21.9 mmol, 1 equiv) before removing from the glovebox and adding 33% H₂SO₄(aq) (21 mL, 1 M) followed by non-anhydrous DCM (2.1 mL, ~1 M final concentration). The reaction mixture was stirred at 80 °C for 4 h under a reflux condenser. After the flask was cooled to rt, the layers were separated, and the aqueous layer was extracted with DCM (3 × 10 mL) before the combined organic extracts were washed with sat. NaHCO₃(aq) (30 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure to afford 2g (2.16 g, 88%) as a white solid exclusively as the exo product, according to literature.³ ¹H NMR (500 MHz, CDCl₃) δ 3.76 (d, J = 6.9 Hz, 1H), 2.28–2.22 (m, 1H), 2.14 (d, J = 4.8 Hz, 1H), 1.66 (ddd, J = 13.2, 6.9, 2.5 Hz, 1H), 1.56 (dt, J = 9.9, 2.0 Hz, 1H), 1.52–1.44 (m, 2H), 1.43–1.36 (m, 1H),
1.31–1.24 (m, 1H), 1.13–1.09 (m, 1H), 1.05–0.95 (m, 2H). The spectral data recorded are consistent with those previously reported.\(^3\)

1-(Adamant-1-yl)ethanol (2h)

Prepared using General Procedure A with LiAlH\(_4\) (0.19 g, 5 mmol, 1 equiv), Et\(_2\)O (25 mL, 0.2 M), and adamant-1-yl methyl ketone (0.89 g, 5 mmol, 1 equiv) in Et\(_2\)O (5 mL, 1 M) to afford 2h (470.0 mg, 63%) as a colorless solid. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 3.24 (q, \(J=6.5\) Hz, 1H), 1.96 (s, 3H), 1.68 (d, \(J=12.3\) Hz, 3H), 1.65–1.52 (m, 6H), 1.45 (d, \(J=12.3\) Hz, 3H), 1.38 (s, 1H), 1.06 (d, \(J=6.6\) Hz, 3H). The spectral data recorded are consistent with those previously reported.\(^4\)

4. Reactions of Unactivated Secondary Alcohols

\(i\) General Procedure B: Alkylations with cyclohexanol

A one-dram vial equipped with a stirring bar was sequentially added ZnCl\(_2\) or FeCl\(_3\) (2–10 \(\mu\)mol, 1–5 mol%), arene derivative (0.2 mmol, 1 equiv), PhCl (0.2 mL, 1 M), cyclohexanol (62.5 \(\mu\)L, 0.6 mmol, 3 equiv), and (\(R\))-camphor sulfonic acid monohydrate (\(R\)-CSA•H\(_2\)O) (37.6 mg, 0.15 mmol, 75 mol%) or (\(S\))-camphor sulfonic acid (\(S\)-CSA) (35 mg, 0.15 mmol, 75 mol%). The reaction mixture was heated at 140 °C for 18 h, at which time the solution was filtered through a 5” pipette plug of silica gel (approximately one-third filled) and eluted with hexanes/EtOAc (3:1). The solution was concentrated \textit{in vacuo} and purified via silica gel chromatography to obtain the alkylation product.

\(ii\) General Procedure C: Alkylations with 2-adamantanol

A one-dram vial equipped with a stirring bar was sequentially added ZnCl\(_2\) or FeCl\(_3\) (10 \(\mu\)mol, 5 mol%), arene derivative (0.2 mmol, 1 equiv), PhCl (0.2 mL, 1 M), 2-adamantanol (33.5 mg, 0.22 mmol, 1.1 equiv), (\(R\))-camphor sulfonic acid monohydrate (\(R\)-CSA•H\(_2\)O) (37.6 mg, 0.15 mmol, 75 mol%) or (\(S\))-camphor sulfonic acid (\(S\)-CSA) (35 mg, 0.15 mmol, 75 mol%). The reaction mixture was heated at 140 °C for 18 h, at which time the solution was filtered through a silica gel plug (packed in a 5” glass pipette, approximately one-third filled) and eluted with hexanes/EtOAc (3:1). The solution was concentrated \textit{in vacuo} and purified via silica gel chromatography to obtain the alkylation product.

\(iii\) General Procedure D: Alkylations with other secondary alcohols

A one-dram vial equipped with a stirring bar was sequentially added ZnCl\(_2\) (0.01 mmol, 5 mol%), 3-\textit{tert}-butylphenol (0.2 mmol, 1 equiv), PhCl (0.2 mL, 1 M), secondary alcohol (0.22–1.0 mmol, 1.1–5 equiv), and (\(R\))-camphor sulfonic acid monohydrate (\(R\)-CSA•H\(_2\)O) (37.6 mg, 0.15 mmol, 75 mol%). The reaction mixture was heated at 140 °C for 18 h, at which time the solution was filtered through a silica gel plug (packed in a 5” glass pipette, approximately one-third filled) and eluted with hexanes/EtOAc (9:1) or
EtOAc. The solution was concentrated in vacuo and purified via silica gel chromatography to obtain the alkylation product.

iv) Product Characterization

5-(tert-Butyl)-2-cyclohexylphenol (3aa)

Prepared using General Procedure B with 3-tert-butylphenol (30.2 mg, 0.2 mmol, 1 equiv), ZnCl₂ (1.5 mg, 0.055 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3 equiv), and CSA•H₂O (37.6 mg, 0.150 mmol, 0.75 equiv).

Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc) afforded 3aa (34.5 mg, 74%) as a yellow-orange oil. Rₜ: 0.33 (19:1 hexanes/EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 7.12 (d, J = 8.1 Hz, 1H), 6.95 (dd, J = 8.1, 2.0 Hz, 1H), 6.81 (d, J = 2.2 Hz, 1H), 4.74 (s, 1H), 2.77 (qt, J = 6.3, 2.5 Hz, 1H), 1.94–1.83 (m, 5H), 1.82–1.74 (m, 1H), 1.51–1.38 (m, 4H), 1.31 (s, 9H); ¹³C NMR (151 MHz, CDCl₃) δ 152.4, 150.2, 130.5, 126.5, 118.0, 112.7, 37.2, 34.4, 33.3, 31.4, 27.2, 26.4; IR (ATR): 3380, 2925, 2855, 1617, 1577, 1504, 1460, 1415, 1362, 1292, 1264, 1233, 1203, 1168, 1128, 1089, 931, 863, 814, 738, 705, 651, 576, 485, 458, 451, 440, 404 cm⁻¹; HRMS (ESI⁺): m/z [M+H]⁺ calculated for C₁₆H₂₅O: 233.1900; found: 233.1902.

5-(tert-Butyl)-2-cycloheptylphenol (3ab)

Prepared using General Procedure D with 3-tert-butylphenol (30.2 mg, 0.201 mmol, 1 equiv), ZnCl₂ (1.7 mg, 0.012 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), cycloheptanol (69.6 mg, 0.609 mmol, 3 equiv), and CSA•H₂O (37.8 mg, 0.151 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc × 2) afforded 3ab (34.0 mg, 69%) as an orange oil. Rₜ: 0.33 (19:1 hexanes/EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 7.09 (d, J = 8.0 Hz, 1H), 6.91 (dd, J = 8.1, 1.5 Hz, 1H), 6.78 (d, J = 2.0 Hz, 1H), 2.95–2.83 (m, 1H), 1.96–1.87 (m, 2H), 1.85–1.77 (m, 2H), 1.72–1.52 (m, 8H), 1.28 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 151.8, 150.0, 132.4, 126.8, 118.0, 112.7, 39.3, 35.5, 34.4, 31.5, 28.1, 27.6; IR (ATR): 3380, 2923, 2855, 1617, 1577, 1504, 1460, 1415, 1362, 1292, 1264, 1233, 1203, 1168, 1128, 1089, 931, 863, 814, 738, 705, 651, 576, 554, 485, 458, 451, 440, 404 cm⁻¹; HRMS (ESI⁺): m/z [M+H]⁺ calculated for C₁₇H₂₇O: 247.2056; found: 247.2061.

5-(tert-Butyl)-2-(1,2,3,4-tetrahydronaphthalen-1-yl)phenol (3ac)

Prepared using General Procedure D with 3-tert-butylphenol (30.2 mg, 0.201 mmol, 1 equiv), ZnCl₂ (1.5 mg, 0.011 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), 2-tetralol (2c) (53.5 µL, 0.399 mmol, 2 equiv), and CSA•H₂O (37.5 mg, 0.150 mmol, 0.75
equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3ac (45.4 mg, 81%) as an orange oil. Rf: 0.27 (19:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.18–7.12 (m, 2H), 7.10–7.04 (m, 1H), 6.89–6.84 (m, 2H), 6.81 (d, J = 1.8 Hz, 1H), 4.48 (s, 1H), 4.28 (dd, J = 8.8, 5.7 Hz, 1H), 2.97–2.80 (m, 2H), 2.17–2.08 (m, 1H), 1.99–1.90 (m, 2H), 1.82–1.73 (m, 1H), 1.29 (s, 9H); 13C NMR (151 MHz, CDCl3) δ 152.9, 151.0, 138.3, 137.9, 130.5, 129.6, 129.5, 126.5, 126.3, 117.9, 113.6, 40.9, 34.5, 31.5, 30.9, 29.9, 21.7; IR (ATR): 3312, 2971, 1379, 1087, 1045, 879, 653 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C20H23O: 279.1754; found 279.1765.

5-(tert-Butyl)-2-isopropylphenol (3ad)

Prepared using General Procedure D with 3-tert-butylphenol (30.1 mg, 0.2 mmol, 1 equiv), ZnCl2 (1.5 mg, 0.011 mol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), sec-butanol (76.5 µL, 1.0 mmol, 5 equiv), and CSA•H2O (37.5 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3ad (26.7 mg, 70%) as a light-yellow-white solid. M.p. 53–56 °C; Rf: 0.34 (19:1 hexanes/EtOAc); 1H NMR (500 MHz, CDCl3) δ 7.15 (d, J = 8.0 Hz, 1H), 6.97 (dd, J = 8.0, 2.0 Hz, 1H), 6.81 (d, J = 1.9 Hz, 1H), 4.69 (s, 1H), 3.18 (h, J = 6.9 Hz, 1H), 1.32 (s, 9H), 1.28 (d, J = 6.9 Hz, 6H); 13C NMR (151 MHz, CDCl3) δ 152.4, 150.3, 131.3, 126.0, 118.0, 112.7, 34.3, 31.5, 26.9, 22.8; IR (ATR): 3349, 2960, 2869, 1415, 1156, 1082, 932, 817, 739 cm⁻¹; HRMS (ESI+): m/z [M+H]⁺ calculated for C13H21O: 193.1587; found: 193.1583.

2-(sec-Butyl)-5-(tert-butyl)phenol (3ae)

Prepared using General Procedure D with 3-tert-butylphenol (30.1 mg, 0.2 mmol, 1 equiv), ZnCl2 (1.5 mg, 0.011 mol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), sec-butanol (920 µL, 1 mmol, 5 equiv), and CSA•H2O (37.5 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3ae (22.1 mg, 54%) as a colorless oil; 1H NMR (600 MHz, CDCl3) δ 7.07 (d, J = 8.0 Hz, 1H), 6.92 (dt, J = 8.0, 1.5 Hz, 1H), 6.78 (t, J = 1.5 Hz, 1H), 4.57 (s, 1H), 2.89 (sextet, J = 7.0 Hz, 1H), 1.70–1.63 (m, 1H), 1.58 (dq, J = 13.9, 6.9 Hz, 2H), 1.29 (s, 9H), 1.23 (dd, J = 6.9, 1.1 Hz, 3H), 0.88 (td, J = 7.4, 1.1 Hz, 3H); 13C NMR (151 MHz, CDCl3) δ 157.2, 152.7, 150.2, 126.7, 118.0, 112.7, 34.4, 33.9, 31.5, 30.0, 20.5, 12.4; IR (ATR): 3312, 2968, 1417, 1087, 1045, 879, 655 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C14H23O: 205.1598; found: 205.1601.
2-[(1-Adamant-1-yl)ethyl]-5-(tert-butyl)phenol (3a)

Prepared using General Procedure D with 3-tert-butylphenol (30.1 mg, 0.2 mmol, 1 equiv), ZnCl₂ (1.6 mg, 0.012 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), adamant-1-yl methyl ketone (2f) (72.7 mg, 0.40 mmol, 2 equiv), and CSA•H₂O (37.8 mg, 0.151 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3a (54.7 mg, 87%) as an orange oil. Rf: 0.37 (19:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl₃) δ 7.02 (d, J = 8.1 Hz, 1H), 6.92–6.87 (m, 1H), 6.78 (d, J = 2.1 Hz, 1H), 4.60 (s, 1H), 2.74 (q, J = 7.3 Hz, 1H), 1.93 (s, 3H), 1.67–1.62 (m, 5H), 1.57 (d, J = 12.6 Hz, 4H), 1.50–1.45 (m, 3H), 1.29 (s, 9H), 1.18 (d, J = 7.2 Hz, 3H); 13C NMR (151 MHz, CDCl₃) δ 153.0, 150.0, 129.0, 127.0, 117.3, 117.0, 112.4, 41.1, 39.7, 37.3, 36.3, 34.4, 31.5, 28.9, 14.4; IR (ATR): 3314, 2971, 1379, 1087, 1045, 879, 657 cm⁻¹; HRMS (ESI−): m/z [M−H]⁻ calculated for C₂₂H₃₁O: 311.2380; found: 311.2395.

2-[(norborn-2-yl)-5-(tert-butyl)phenol (3a)

Prepared using General Procedure D with 3-tert-butylphenol (30 mg, 0.2 mmol, 1 equiv), ZnCl₂ (1.5 mg, 0.055 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), norbornan-2-ol (24.7 mg, 0.22 mmol, 1.1 equiv), and CSA•H₂O (37.6 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc) afforded 3a (40.2 mg, 82%) as a yellow-orange oil. Rf: 0.37 (19:1 hexanes/EtOAc); 1H NMR (400 MHz, CDCl₃) δ 7.14 (d, J = 8.1 Hz, 1H), 6.93 (dd, J = 8.1, 2.0 Hz, 1H), 6.84 (d, J = 2.0 Hz, 1H), 4.73 (s, 1H), 2.82 (dd, J = 9.1, 5.3 Hz, 1H), 2.45–2.24 (m, 2H), 1.81 (dd, J = 11.7, 8.8, 2.3 Hz, 1H), 1.75–1.51 (m, 4H), 1.47–1.35 (m, 2H), 1.31 (s, 9H), 1.24 (dd, J = 9.7, 2.3, 1.5 Hz, 1H); 13C NMR (151 MHz, CDCl₃) δ 153.1, 150.2, 129.9, 125.7, 117.4, 112.7, 41.1, 40.4, 38.2, 37.0, 36.3, 34.4, 31.5, 30.4, 29.2; IR (ATR): 3314, 2971, 1379, 1087, 1045, 879, 657 cm⁻¹; HRMS (ESI+): m/z [M+H]⁺ calculated for C₁₇H₂₅O: 245.1900; found: 245.1901.

2-[(adamantan-2-yl)-5-(tert-butyl)phenol (3a)

Prepared using General Procedure C with 3-tert-butylphenol (30.1 mg, 0.2 mmol, 1 equiv), ZnCl₂ (1.5 mg, 0.011 mol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), adamantan-2-ol (33.9 mg, 0.2 mmol, 1.1 equiv), and CSA•H₂O (37.48 mg, 0.151 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc) afforded 3a (43 mg, 76%) as a pale-yellow-white solid. M.p. 135–139 °C; Rf: 0.35 (19:1 hexanes/EtOAc); 1H NMR (500 MHz, CDCl₃) δ 7.37 (d, J = 8.1 Hz, 1H), 6.94 (dd, J = 8.1, 2.0 Hz, 1H), 6.78 (d, J = 2.0 Hz, 1H), 4.67 (s, 1H), 3.15 (s, 1H), 2.38–2.33 (m, 2H), 2.05 (dd, J = 12.8, 2.9 Hz, 2H), 2.02–1.92 (m, 5H), 1.88 (p, J = 3.2 Hz, 1H), 1.82–1.77 (m, 2H), 1.68–1.63 (m, 2H), 1.30 (s, 9H); 13C NMR (151 MHz, CDCl₃)
δ 153.6, 150.2, 128.5, 127.9, 117.3, 113.0, 43.9, 40.1, 38.1, 34.3, 33.0, 31.4, 31.2, 28.3, 27.9; IR (ATR): 3301, 2899, 2849, 1615, 1450, 1411, 1192, 1092, 935, 859, 827, 731, 650 cm\(^{-1}\); HRMS (ESI\(+\)): \(m/z [\text{M}+\text{H}]^+\) calculated for C\(_{20}\)H\(_{29}\)O: 285.2213; found 285.2223.

2-cyclohexyl-5-isopropylphenol (3ba)

Prepared using General Procedure B with 3-isopropylphenol (27.5 µL, 0.2 mmol, 1 equiv), ZnCl\(_2\) (1.4 mg, 0.01 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3 equiv), and CSA•H\(_2\)O (37.4 mg, 0.15 mmol, 0.75 equiv).

Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc) afforded 3ba (21.5 mg, 49%) as an orange oil. R\(_f\): 0.27 (9:1 hexanes/EtOAc); \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ 7.10 (d, \(J = 7.9\) Hz, 1H), 6.79 (dd, \(J = 7.9, 1.8\) Hz, 1H), 6.64 (t, \(J = 2.0\) Hz, 1H), 4.74 (s, 1H), 2.84 (h, \(J = 6.9\) Hz, 1H), 2.79–2.70 (m, 1H), 1.93–1.81 (m, 4H), 1.81–1.72 (m, 1H), 1.49–1.35 (m, 4H), 1.34–1.24 (m, 1H), 1.23 (d, \(J = 6.9\) Hz, 6H); \(^13\)C NMR (151 MHz, CDCl\(_3\)) δ 152.7, 147.8, 130.9, 126.8, 119.1, 113.5, 37.2, 33.7, 33.3, 27.2, 26.5, 24.1; IR (ATR): 3390, 2923, 2850, 1579, 1423, 738 cm\(^{-1}\); HRMS (ESI\(+\)): \(m/z [\text{M}+\text{H}]^+\) calculated for C\(_{15}\)H\(_{23}\)O: 219.1743; found: 219.1744.

2-(Adamant-2-yl)-5-isopropylphenol (3bh)

Prepared using General Procedure C with 3-isopropylphenol (27.5 µL, 0.2 mmol, 1 equiv), ZnCl\(_2\) (1.7 mg, 0.012 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), adamantan-2-ol (33.6 mg, 0.22 mmol, 1.1 equiv), and CSA•H\(_2\)O (37.6 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc) afforded 3bh (46.0 mg, 85%) as a yellow-white solid. M.p. 115–118 °C; R\(_f\): 0.41 (9:1 hexanes/EtOAc); \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ 7.34 (d, \(J = 7.9\) Hz, 1H), 6.78 (dd, \(J = 7.8, 1.2\) Hz, 1H), 6.62 (d, \(J = 1.4\) Hz, 1H), 4.59 (s, 1H), 3.13 (s, 1H), 2.83 (dt, \(J = 13.4, 6.3\) Hz, 1H), 2.33 (s, 2H), 2.03 (d, \(J = 12.4\) Hz, 2H), 1.96 (d, \(J = 5.4\) Hz, 5H), 1.78 (s, 2H), 1.64 (d, \(J = 12.7\) Hz, 2H), 1.23 (d, \(J = 6.9\) Hz, 6H); \(^13\)C NMR (151 MHz, CDCl\(_3\)) δ 153.9, 147.9, 128.9, 128.1, 118.5, 113.7, 44.0, 40.2, 38.2, 33.6, 33.0, 31.3, 28.3, 27.9, 24.1; IR (ATR): 3411, 2901, 2844, 1619, 1420, 1210, 1094, 947, 854, 830, 729, 645 cm\(^{-1}\); HRMS (ESI\(--\)): \(m/z [\text{M}–\text{H}]^-\) calculated for C\(_{19}\)H\(_{25}\)O: 269.1911; found 269.1922.

2-cyclohexyl 5-phenylphenol (3ca)

Prepared using General Procedure B with 3-phenylphenol (90% technical grade, 37.8 mg, 0.200 mmol, 1 equiv), ZnCl\(_2\) (1.5 mg, 0.011 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.600 mmol, 3 equiv), and CSA•H\(_2\)O (37.5 mg, 0.150 mmol,
0.75 equiv). Purification by preparative TLC (eluting with 9:1 hexanes/EtOAc) afforded 3ca (16 mg, 32%) as a yellow-white solid. M.p. 120–124 °C; Rf: 0.35 (19:1 hexanes/EtOAc); 1H NMR (500 MHz, CDCl3) δ 7.58–7.53 (m, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.36–7.29 (m, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.15 (dd, J = 8.0, 1.8 Hz, 1H), 6.99 (d, J = 1.8 Hz, 1H), 4.76 (s, 1H), 2.87–2.79 (m, 1H), 1.94–1.84 (m, 4H), 1.78 (d, J = 13.1 Hz, 1H), 1.49–1.42 (m, 4H), 1.31–1.24 (m, 1H); 13C NMR (151 MHz, CDCl3) δ 153.1, 140.8, 140.0, 132.8, 128.8, 127.5, 127.3, 127.1, 119.9, 114.1, 37.3, 33.3, 27.2, 26.4; IR (ATR): 3391, 2922, 2849, 1564, 1484, 1447, 1407, 1305, 1197, 907, 862, 823, 758, 695 cm⁻¹; HRMS (ESI+): m/z [M+H]⁺ calculated for C18H21O: 253.1587; found 253.1585.

2-(Adamant-2-yl)-5-phenylphenol (3ch)

Prepared using General Procedure C with 3-phenylphenol (90% technical grade, 37.9 mg, 0.200 mmol, 1 equiv), ZnCl₂ (1.3 mg, 9.5 µmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), adamantan-2-ol (33.6 mg, 0.221 mmol, 1.1 equiv), and CSA•H₂O (37.8 mg, 0.151 mmol, 0.75 equiv). Purification by flash chromatography (eluting with 0–20% EtOAc in hexanes) afforded 3ch (43.0 mg, 64%) as a light orange-white solid. M.p. 104–107 °C; Rf: 0.34 (9:1 hexanes/EtOAc); 1H NMR (500 MHz, CDCl₃) δ 7.60–7.55 (m, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 7.16 (dd, J = 8.8, 1.1 Hz, 1H), 6.99 (d, J = 1.9 Hz, 1H), 4.77 (s, 1H), 3.22 (s, 1H), 2.39 (s, 2H), 2.07 (d, J = 12.8 Hz, 2H), 2.01–1.98 (m, 4H), 1.90 (s, 1H), 1.80 (s, 2H), 1.68 (d, J = 12.5 Hz, 2H), 1.25 (s, 1H); 13C NMR (151 MHz, CDCl₃) δ 154.3, 140.7, 139.9, 130.8, 128.8, 128.7, 127.3, 127.0, 119.2, 114.3, 44.1, 40.1, 38.1, 33.0, 31.3, 28.3, 27.9; IR (ATR): 3510, 2897, 2845, 1563, 1485, 1448, 1406, 1172, 1108, 857, 758, 694 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C₂₂H₂₃O: 303.1765; found 303.1765.

The reaction was performed using General Procedure B with 2-ethylphenol (23.5 µL, 0.20 mmol, 1 equiv), ZnCl₂ (1.4 mg, 0.01 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3.0 equiv), and CSA (35 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3da as the major product (6.5 mg, 16%) and S-3da as the minor product (6.3 mg, 11%).

S10
2-Cyclohexyl-6-ethylphenol (3da): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.06 (dd, $J = 7.7$, 1.7 Hz, 1H), 7.00 (dd, $J = 7.4$, 1.7 Hz, 1H), 6.87 (t, $J = 7.7$ Hz, 1H), 4.71 (s, 1H), 2.77 (qd, $J = 7.2$, 3.2 Hz, 1H), 2.63 (q, $J = 7.6$ Hz, 2H), 2.07–1.91 (m, 4H), 1.84–1.70 (m, 2H), 1.49–1.35 (m, 4H), 1.26 (t, $J = 7.6$ Hz, 3H); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 150.7, 133.1, 129.2, 126.4, 124.5, 120.7, 37.7, 33.4, 27.2, 26.4, 23.3, 14.0. IR (ATR): 3574, 3038, 2963, 1448, 1187, 774 cm$^{-1}$; HRMS (ESI+): $m/z$ [M+H]$^+$ calculated for C$_{14}$H$_{21}$O: 205.1587; found: 205.1579.

2,4-Dicyclohexyl-6-ethylphenol (S-3da): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 6.89 (d, $J = 2.2$ Hz, 1H), 6.84 (d, $J = 2.2$ Hz, 1H), 4.56 (s, 1H), 2.80 (qd, $J = 7.2$, 3.2 Hz, 2H), 2.77 (qd, $J = 7.2$, 3.2 Hz, 1H), 2.63 (q, $J = 7.6$ Hz, 2H), 2.07–1.91 (m, 4H), 1.84–1.70 (m, 2H), 1.49–1.35 (m, 4H), 1.26 (t, $J = 7.6$ Hz, 3H); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 148.7, 140.3, 132.8, 128.8, 124.7, 122.8, 44.3, 37.8, 35.0, 33.4, 27.3, 27.2, 26.5, 26.4, 23.5, 14.1. IR (ATR): 3574, 3038, 2963, 1448, 1187, 774 cm$^{-1}$; HRMS (ESI+): $m/z$ [M+H]$^+$ calculated for C$_{20}$H$_{31}$O: 287.2369; found: 287.2359.

The reaction was performed using General Procedure C with 2-ethylphenol (23.5 µL, 0.20 mmol, 1 equiv), ZnCl$_2$ (1.4 mg, 0.01 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), 2-adamantanol (33.5 mg, 0.22 mmol, 1.1 equiv), and CSA (35 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 50% overall yield of two alkylation products with ortho-3dh being the major product (16.9 mg, 33%) and dialkylated S-3dh (13.2 mg, 17%) as the minor product. The mono-para-substituted product was not observed.

2-(Adamantan-2-yl)-6-ethylphenol (3dh): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.32 (d, $J = 7.8$ Hz, 1H), 7.03 (d, $J = 7.5$ Hz, 1H), 6.87 (t, $J = 7.6$ Hz, 1H), 4.70 (s, 1H), 3.17 (s, 1H), 2.62 (q, $J = 7.6$ Hz, 2H), 2.34 (s, 2H), 2.08–1.93 (m, 7H), 1.92–1.84 (m, 2H), 1.79 (s, 2H), 1.67 (d, $J = 12.6$ Hz, 2H) 1.25 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 150.7, 131.1, 129.2, 126.5, 125.8, 120.0, 44.4, 40.3, 38.2, 33.0, 31.4, 28.3, 27.9, 23.2, 14.0. IR (ATR): 3600, 3046, 2901, 1450, 1187, 735 cm$^{-1}$; HRMS (ESI+): $m/z$ [M+H]$^+$ calculated for C$_{18}$H$_{25}$O: 257.1900; found: 257.1892.
2,4-(Diadamantan-2-yl)-6-ethylphenol (S-3dh): \(^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.29 (d, \(J = 2.2\) Hz, 1H), 6.98 (d, \(J = 2.2\) Hz, 1H), 4.55 (s, 1H), 2.96 (s, 1H), 2.62 (q, \(J = 7.6\) Hz, 2H), 2.34 (s, 4H), 2.08–1.93 (m, 16H), 1.79 (s, 4H), 1.67 (d, \(J = 12.6\) Hz, 4H) 1.25 (t, \(J = 7.5\) Hz, 3H); \(^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) 149.2, 135.4, 130.5, 128.6, 124.9, 124.2, 46.5, 44.5, 40.3, 39.4, 38.2, 33.2, 33.0, 32.1, 31.5, 31.4, 28.4, 28.3, 28.0, 27.9, 23.7, 14.3. IR (ATR): 3600, 3046, 2901, 1450, 1187, 735 cm\(^{-1}\); HRMS (ESI+): \(m/z\) [M+H]\(^+\) calculated for C\(_{28}\)H\(_{39}\)O: 391.2995; found: 391.2985.

2-(Adamantan-2-yl)-6-benzylphenol (3eh)

Prepared using General Procedure C with 2-benzylphenol (36.8 mg, 0.20 mmol, 1 equiv), ZnCl\(_2\) (1.4 mg, 0.01 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), 2-adamantanol (33.5 mg, 0.22 mmol, 1.1 equiv), and CSA (35 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/Et\(_2\)O) afforded 3eh (38.7 mg, 60%) as a yellow oil. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.38 (dd, \(J = 7.6, 1.4\) Hz, 1H), 7.33–7.27 (m, 2H), 7.24–7.18 (m, 3H), 7.01 (dd, \(J = 7.6\) Hz, 1H), 4.65 (s, 1H), 4.00 (s, 2H), 3.14 (s, 1H), 2.30 (q, \(J = 2.9\) Hz, 2H), 2.14–1.92 (m, 7H), 1.88 (dt, \(J = 6.5, 3.2\) Hz, 1H), 1.78 (d, \(J = 3.3\) Hz, 2H), 1.65 (dt, \(J = 12.7, 2.5, 1.2\) Hz, 2H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 152.4, 139.7, 132.0, 128.9, 128.7, 128.5, 126.7, 126.6, 126.4, 120.1, 44.3, 40.2, 38.1, 37.2, 33.0, 31.4, 28.3, 27.8. IR (ATR): 3544, 2898, 1449, 1187, 730 cm\(^{-1}\); HRMS (ESI+): \(m/z\) [M+H]\(^+\) calculated for C\(_{23}\)H\(_{27}\)O: 319.2056; found: 319.2055.

2-(Adamantan-2-yl)-6-phenylphenol (3fh)

Prepared using General Procedure C with 2-phenylphenol (34 mg, 0.20 mmol, 1 equiv), ZnCl\(_2\) (1.4 mg, 0.01 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), 2-adamantanol (33.5 mg, 0.22 mmol, 1.1 equiv), and CSA (35 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/Et\(_2\)O) afforded 3fh (33.9 mg, 55%) as a yellow oil. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.53–7.43 (m, 5H), 7.40 (t, \(J = 7.0\) Hz, 1H), 7.09 (dd, \(J = 7.5, 1.7\) Hz, 1H), 6.97 (t, \(J = 7.6\) Hz, 1H), 5.32 (s, 1H), 3.31 (s, 1H), 2.30 (q, \(J = 2.9\) Hz, 2H), 2.14–1.92 (m, 7H), 1.88 (dt, \(J = 6.5, 3.2\) Hz, 3H), 1.78 (d, \(J = 3.3\) Hz, 1H), 1.65 (dt, \(J = 12.7, 2.5, 1.2\) Hz, 1H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 150.7, 137.6, 132.4, 129.5, 128.0, 127.9, 127.5, 126.3, 125.8, 119.9, 44.4, 40.2, 38.2, 33.2, 31.3, 28.4, 28.0. IR (ATR): 3547, 2900, 2847, 1467, 1196, 907, 733 cm\(^{-1}\); HRMS (ESI+): \(m/z\) [M+H]\(^+\) calculated for C\(_{22}\)H\(_{25}\)O: 305.1900; found: 319.1900.
2-Cyclohexyl-4-ethylphenol (3ga)

Prepared using General Procedure B with 4-ethylphenol (25.3 mg, 0.2022 mmol, 1 equiv), ZnCl$_2$ (0.3 mg, 2.2 µmol, 0.01 equiv), PhCl (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3 equiv), and CSA•H$_2$O (37.6 mg, 0.150 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3ga (16.9 mg, 41%) as a yellow oil. $R_f$: 0.26 (19:1 hexanes/EtOAc); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.03 (d, $J = 2.2$ Hz, 1H), 6.91 (dd, $J = 8.1$, $2.2$ Hz, 1H), 6.70 (d, $J = 8.1$ Hz, 1H), 4.75 (s, 1H), 2.81 (tt, $J = 11.5$, 3.0 Hz, 1H), 2.59 (q, $J = 7.6$ Hz, 2H), 1.93–1.84 (m, 4H), 1.82–1.76 (m, 1H), 1.52–1.39 (m, 4H), 1.35–1.26 (m, 1H), 1.23 (t, $J = 7.6$ Hz, 3H); $^{13}$C NMR (151 MHz, CDCl$_3$) δ 150.7, 136.7, 133.5, 126.5, 125.8, 115.3, 37.5, 33.3, 28.4, 27.2, 26.5, 16.1; IR (ATR): 3341, 2923, 2850, 1504, 1447, 813 cm$^{-1}$; HRMS (ESI+): $m/z$ [M+H]$^+$ calculated for C$_{14}$H$_{21}$O: 205.1587; found: 205.1581.

2-(Adamant-2-yl)-4-fluorophenol (3hh)

Prepared using General Procedure C with 3-phenylphenol (22.5 mg, 0.200 mmol, 1 equiv), ZnCl$_2$ (1.7 mg, 0.012 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), adamantan-2-ol (33.7 mg, 0.221 mmol, 1.1 equiv), and CSA•H$_2$O (37.4 mg, 0.150 mmol, 0.75 equiv). Purification by preparatory TLC (eluting with 9:1 hexanes/EtOAc) afforded 3hh (15.2 mg, 31%) as a yellow solid. M.p. 90–93 ºC; $R_f$: 0.32 (9:1 hexanes/EtOAc); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.15 (dd, $J = 10.6$, 3.0 Hz, 1H), 6.76 (td, $J = 8.2$, 3.1 Hz, 1H), 6.66 (dd, $J = 8.7$, 5.0 Hz, 1H), 4.60 (s, 1H), 3.14 (s, 1H), 2.32 (s, 2H), 2.09 (d, $J = 11.6$ Hz, 1H), 2.00–1.95 (m, 6H), 1.88 (s, 1H), 1.78 (s, 2H), 1.65 (d, $J = 12.8$ Hz, 2H); $^{13}$C NMR (151 MHz, CDCl$_3$) δ 157.4 (d, $J = 236.7$ Hz), 149.9, 133.6, 115.9 (d, $J = 8.3$ Hz), 115.3 (d, $J = 23.8$ Hz), 112.5 (d, $J = 23.2$ Hz), 44.3, 40.0, 38.0, 32.8, 31.1, 28.2, 27.7; $^{19}$F NMR (564 MHz, CDCl$_3$) δ –124.0; IR (ATR): 3406, 2900, 2847, 1698, 1502, 1427, 1341, 1252, 1178, 1165, 1115, 983, 956, 871, 821, 803, 746, 570, 473 cm$^{-1}$; HRMS (ESI–): $m/z$ [M–H]$^-$ calculated for C$_{16}$H$_{18}$FO: 245.1347; found 245.1359.

2-(Adamant-2-yl)-4-chlorophenol (3ih)
Prepared using General Procedure C with 4-chlorophenol (26.1 mg, 0.203 mmol, 1 equiv), ZnCl₂ (1.4 mg, 0.10 mmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), adamantan-2-ol (33.6 mg, 0.221 mmol, 1.1 equiv), and CSA•H₂O (37.8 mg, 0.151 mmol, 0.75 equiv).
Purification by flash chromatography (eluting with 0–20% EtOAc in hexanes) afforded 3ih (21.4 mg, 41%) as a yellow. Rf: 0.30 (9:1 hexanes/EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 7.37 (d, J = 2.5 Hz, 1H), 7.04 (dd, J = 8.5, 2.5 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 4.70 (s, 1H), 3.13 (s, 1H), 2.32 (s, 2H), 2.01–1.94 (m, 7H), 1.89 (s, 1H), 1.78 (s, 2H), 1.65 (d, J = 12.8 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 153.3, 134.0, 128.3, 126.1, 124.8, 116.4, 44.1, 40.0, 38.1, 32.9, 30.9, 28.2, 27.8; IR (ATR): 3411, 2898, 2847, 1697, 1491, 1409, 1341, 1212, 1166, 1111, 919, 972, 806, 721, 657, 472 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C₁₆H₁₈ClO: 261.1052; found 261.1063.

2-(Adamant-2-yl)-4-bromophenol (3jh)
Prepared using General Procedure C with 4-bromophenol (34.7 mg, 0.200 mmol, 1 equiv), ZnCl₂ (1.5 mg, 0.11 mmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), adamantan-2-ol (33.7 mg, 0.221 mmol, 1.1 equiv), and CSA•H₂O (37.4 mg, 0.150 mmol, 0.75 equiv).
Purification by preparatory TLC (eluting with 9:1 hexanes/EtOAc) afforded 3jh (18.6 mg, 35%) as an orange-brown oil. Rf: 0.38 (9:1 hexanes/EtOAc); ¹H NMR (600 MHz, CDCl₃) δ 7.50 (d, J = 2.5 Hz, 1H), 7.20–7.15 (m, 1H), 6.62 (dd, J = 8.6, 1.6 Hz, 1H), 4.68 (s, 1H), 3.14 (s, 1H), 2.32 (s, 2H), 2.02–1.92 (m, 7H), 1.89 (s, 1H), 1.78 (s, 2H), 1.65 (d, J = 12.7 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 153.2, 134.2, 131.3, 129.4, 117.2, 113.0, 44.2, 40.0, 38.0, 32.8, 31.0, 28.1, 27.8; IR (ATR): 3299, 2900, 1411, 1087, 1045, 879, 627 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C₁₆H₁₈BrO: 305.0547; found 305.0551.

2-Cyclohexyl-6-isopropyl-3-methylphenol (3ka)
Prepared using General Procedure B with thymol (30 mg, 0.20 mmol, 1 equiv), ZnCl₂ (1.4 mg, 0.01 mmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3.0 equiv), and CSA (35 mg, 0.15 mmol, 0.75 equiv). Purification by preparative TLC (eluting with 19:1 hexanes/EtOAc) afforded 3ka (14.5 mg, 31%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 6.94 (d, J = 7.9 Hz, 1H), 6.73 (d, J = 7.7 Hz, 1H), 4.84 (s, 1H), 3.05 (p, J = 6.8 Hz, 1H), 2.90 (s, 1H), 2.32 (s, 3H), 2.04 (q, J = 9.9 Hz, 2H), 1.86 (d, J = 12.5 Hz, 2H), 1.74 (dd, J = 24.5, 12.1 Hz, 3H), 1.38 (q, J = 12.5 Hz, 3H), 1.26 (d, J = 6.8 Hz, 6H); ¹³C NMR (151 MHz, CDCl₃) δ 152.0, 134.7, 132.2, 130.9, 123.1, 120.6, 39.9, 34.4, 30.3, 27.0, 26.5, 22.9
21.0. IR (ATR): 3620, 2922, 1574, 1486, 767 cm\(^{-1}\); HRMS (ESI\(^{+}\)): \(m/z\) [M+H]\(^+\) calculated for C\(_{16}\)H\(_{25}\)O: 233.1900; found: 233.1908.

2-(Adamant-2-yl)-4,5-dimethylphenol (3lh)

Prepared using General Procedure C with 3,4-xylene (24.5 mg, 0.200 mmol, 1 equiv), ZnCl\(_2\) (1.3 mg, 9.5 µmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), adamantane-2-ol (33.6 mg, 0.221 mmol, 1.1 equiv), and CSA•H\(_2\)O (37.5 mg, 0.150 mmol, 0.75 equiv). Purification by preparatory TLC (eluting with 9:1 hexanes/EtOAc) afforded 3lh (26.9 mg, 52%) as a light brown-white solid. M.p. 105–107 °C; \(R_f\): 0.38 (19:1 hexanes/EtOAc); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.17 (s, 1H), 6.55 (s, 1H), 4.42 (s, 1H), 3.13 (s, 1H), 2.34–2.30 (m, 2H), 2.20 (s, 3H), 2.18 (s, 3H), 2.07–2.01 (m, 2H), 1.99–1.94 (m, 5H), 1.88–1.86 (m, 1H), 1.78 (s, 2H), 1.64 (d, \(J = 12.6\) Hz, 2H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 151.8, 134.7, 129.5, 128.7, 128.0, 117.0, 43.9, 40.2, 38.2, 33.0, 31.3, 28.3, 27.9, 19.4, 19.3; IR (ATR): 3313, 2898, 2847, 1617, 1449, 1407, 1275, 1198, 1084, 878, 576, 474 cm\(^{-1}\); HRMS (ESI\(^{+}\)): \(m/z\) [M+H]\(^+\) calculated for C\(_{18}\)H\(_{25}\)O: 257.1900; found 257.1898.

4-(Adamant-2-yl)-2,6-dimethylphenol (3mh)

Prepared using General Procedure C with 2,6-xylene (24.6 mg, 0.201 mmol, 1 equiv), ZnCl\(_2\) (1.3 mg, 9.5 µmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), adamantane-2-ol (33.6 mg, 0.221 mmol, 1.1 equiv), and CSA•H\(_2\)O (37.7 mg, 0.151 mmol, 0.75 equiv). Purification by flash chromatography (eluting with 0–20% EtOAc in hexanes) afforded 3mh (34.2 mg, 68%) as a white solid. M.p. 135–139 °C; \(R_f\): 0.44 (9:1 hexanes/EtOAc); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 6.95 (s, 2H), 4.45 (s, 1H), 2.89 (s, 1H), 2.40 (s, 2H), 2.25 (s, 6H), 2.16 (d, \(J = 7.9\) Hz, 1H), 1.98 (d, \(J = 13.0\) Hz, 3H), 1.88 (dd, \(J = 22.6, 12.6\) Hz, 4H), 1.76 (d, \(J = 7.8\) Hz, 3H), 1.52 (s, 1H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 149.8, 136.1, 127.1, 122.6, 46.2, 39.3, 38.1, 32.1, 31.2, 28.2, 28.0, 16.3; IR (ATR): 3379, 2897, 2844, 1486, 1447, 1200, 1144, 869, 765, 699, 631 cm\(^{-1}\); HRMS (ESI\(^–\)): \(m/z\) [M–H]\(^–\) calculated for C\(_{18}\)H\(_{23}\)O: 255.1754; found 255.1764.
The reaction was performed using General Procedure C with phenol (19.1 mg, 0.203 mmol, 1 equiv), ZnCl\(_2\) (1.4 mg, 0.10 mmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), adamantan-2-ol (33.7 mg, 0.221 mmol, 1.1 equiv), and CSA•H\(_2\)O (37.7 mg, 0.151 mmol, 0.75 equiv). Purification by preparatory TLC (eluting with 9:1 hexanes/EtOAc) afforded 47% overall yield of three products with \(\text{o-3nh}\) (12.8 mg, 25%) as an orange oil, \(\text{o/o-3nh}\) (10.1 mg, 14%) as a yellow-white solid, and \(\text{p-3nh}\) (4.3 mg, 8%) as a light tan solid.

\(\text{2-(Adamant-2-yl)phenol (o-3nh)}\): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.44 (d, \(J = 7.7\) Hz, 1H), 7.11–7.06 (m, 1H), 6.91 (t, \(J = 7.6\) Hz, 1H), 6.75–6.72 (m, 1H), 4.69 (s, 1H), 3.18 (s, 1H), 2.35 (s, 2H), 2.05–1.93 (m, 8H), 1.79 (s, 2H), 1.65 (d, \(J = 12.6\) Hz, 2H). \(^{13}\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 154.0, 131.7, 128.4, 126.8, 120.5, 115.6, 44.1, 40.1, 38.1, 33.0, 31.2, 28.3, 27.9. The spectral data recorded are consistent with those previously reported.xix

\(\text{2,6-Bis(adamant-2-yl)phenol (o/o-3nh)}\): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.33 (d, \(J = 7.7\) Hz, 2H), 6.90 (t, \(J = 7.7\) Hz, 1H), 4.76 (s, 1H), 3.13 (s, 2H), 2.33–2.29 (m, 4H), 2.05 (d, \(J = 12.9\) Hz, 4H), 2.01–1.95 (m, 10H), 1.78 (s, 4H), 1.65 (d, \(J = 12.7\) Hz, 4H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 152.3, 131.0, 125.5, 119.5, 44.5, 40.3, 38.1, 33.0, 31.5, 28.3, 27.8; IR (ATR): 3589, 2899, 2847, 1732, 1467, 1451, 1437, 1359, 1340, 1316, 1249, 1217, 1183, 1165, 1116, 1095, 1086, 1061, 1048, 995, 953, 934, 877, 840, 826, 802, 767, 752, 735, 698, 638, 627, 559, 539 cm\(^{-1}\); HRMS (ESI\(^+\)): \(m/z\) [M+\(\text{H}\)]\(^+\) calculated for C\(_{26}\)H\(_{35}\)O: 363.2682; found 363.2672.

\(\text{4-(Adamant-2-yl)phenol (p-3nh)}\): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.21 (d, \(J = 8.3\) Hz, 2H), 6.80 (d, \(J = 8.3\) Hz, 2H), 4.63 (s, 1H), 2.93 (s, 1H), 2.40 (s, 2H), 2.02–1.88 (m, 8H), 1.83 (d, \(J = 12.8\) Hz, 2H), 1.76 (s, 2H). The spectral data recorded are consistent with those previously reported.xix

The reaction was performed using General D with estrone (54.3 mg, 0.201 mmol, 1 equiv), ZnCl\(_2\) (1.5 mg, 0.011 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), isopropanol (76.5 \(\mu\)L, 1.0 mmol, 3 equiv), and CSA (37.6 mg, 0.150 mmol, 0.75 equiv). Purification by flash chromatography (eluting with 5–30% EtOAc in hexanes) afforded 31% overall yield of two alkylation products with 5a being the minor product (7.9 mg, 13%) and 5b (11.9 mg, 19%) as the major product. The di-alkylated product was not observed.
(8R,9S,13S,14S)-3-hydroxy-2-isopropyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (5a): M.p. 137–140 °C; Rf: 0.56 (4:1 hexanes/EtOAc); 1H NMR (400 MHz, CDCl3) δ 7.12 (s, 1H), 6.50 (s, 1H), 3.16 (p, J = 6.9 Hz, 1H), 2.86–2.74 (m, 2H), 2.50 (dd, J = 18.8, 8.7 Hz, 1H), 2.46–2.40 (m, 1H), 2.30–2.20 (m, 1H), 2.19–2.09 (m, 1H), 2.09–1.92 (m, 3H), 1.67–1.39 (m, 6H), 1.25 (dd, J = 6.9, 5.9 Hz, 6H), 0.91 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 221.8, 151.1, 134.9, 132.1, 131.8, 123.4, 115.5, 50.5, 48.2, 44.3, 38.6, 36.0, 31.7, 29.2, 27.4, 26.7, 26.1, 22.9, 21.7, 14.0; IR (ATR): 3317, 2929, 2869, 1720, 1614, 1586, 1510, 1454, 1421, 1375, 1357, 1337, 1264, 1233, 1208, 1162, 1087, 1055, 1034, 1012, 912, 889, 820, 800, 734, 703, 580, 519, 493, 474, 450, 429, 417, 403 cm⁻¹; HRMS (ESI+): m/z [M+H]⁺ calculated for C21H29O2: 313.2162; found 313.2175.

(8R,9S,13S,14S)-3-hydroxy-4-isopropyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (5b): M.p. 137–140 °C; Rf: 0.56 (4:1 hexanes/EtOAc); 1H NMR (400 MHz, CDCl3) δ 7.04 (d, J = 8.6 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 3.31 (q, J = 7.1 Hz, 1H), 2.86–2.74 (m, 2H), 2.50 (dd, J = 18.8, 8.7 Hz, 1H), 2.40–2.34 (m, 1H), 2.30–2.20 (m, 1H), 2.19–2.10 (m, 1H), 2.09–1.92 (m, 3H), 1.67–1.39 (m, 6H), 1.36 (dd, J = 7.1, 2.0 Hz, 6H), 0.90 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 214.9, 153.0, 151.1, 135.2, 132.3, 131.7, 123.8, 114.2, 50.6, 48.1, 48.0, 44.7, 37.4, 36.1, 27.5, 27.1, 26.4, 22.9, 21.7, 20.4, 13.9; IR (ATR): 3317, 2929, 2869, 1720, 1614, 1586, 1510, 1454, 1421, 1375, 1357, 1337, 1264, 1233, 1208, 1162, 1087, 1055, 1034, 1012, 912, 889, 820, 800, 734, 703, 580, 519, 493, 474, 450, 429, 417, 403 cm⁻¹; HRMS (ESI+): m/z [M+H]⁺ calculated for C21H29O2: 313.2162; found 313.2175.

The reaction was performed using General Procedure B with estrone (54.2 mg, 0.201 mmol, 1 equiv), ZnCl₂ (1.5 mg, 0.011 mmol, 0.05 equiv), PhCl (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3 equiv), and CSA (37.7 mg, 0.151 mmol, 0.75 equiv). Purification by flash chromatography (eluting with 5–30% EtOAc in hexanes) afforded 60% overall yield of two alkylation products with 6a being the major product (29.6 mg, 42%) and 6b (12.9 mg, 18%) as the minor product. The di-alkylated product was not observed.
(8R,9S,13S,14S)-2-cyclohexyl-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (6a): M.p. 126–129 °C; Rf: 0.31 (7:3 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.10 (s, 1H), 6.51 (s, 1H), 4.52 (s, 1H), 2.87–2.80 (m, 3H), 2.50 (dd, J = 19.1, 8.7 Hz, 1H), 2.45–2.40 (m, 1H), 2.28–2.22 (m, 1H), 2.18–2.10 (m, 1H), 2.09–1.92 (m, 3H), 1.89–1.81 (m, 4H), 1.78–1.70 (m, 1H), 1.68–1.23 (m, 11H), 0.91 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 221.5, 150.9, 134.9, 132.0, 131.3, 124.0, 115.5, 50.5, 48.2, 44.3, 38.6, 37.4, 36.0, 33.4, 31.7, 29.2, 27.2, 26.7, 26.4, 26.2, 21.7, 14.0; IR (ATR): 3408, 2926, 2852, 1727, 1614, 1508, 1450, 1420, 1374, 1341, 1274, 1264, 1207, 1189, 1088, 1054, 1008, 909, 882, 870, 816, 647, 581, 534, 479, 451, 417, 402 cm⁻¹; HRMS (ESI+): m/z [M+NH4]⁺ calculated for C24H36NO2: 370.2741; found 370.2740.

(8R,9S,13S,14S)-4-cyclohexyl-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (6b): M.p. 126–129 °C; Rf: 0.31 (7:3 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.03 (d, J = 8.5 Hz, 1H), 6.54 (d, J = 8.4 Hz, 1H), 4.52 (s, 1H), 2.87–2.80 (m, 3H), 2.50 (dd, J = 19.1, 8.7 Hz, 1H), 2.40–2.33 (m, 1H), 2.18–2.10 (m, 1H), 2.09–1.92 (m, 3H), 1.89–1.81 (m, 4H), 1.78–1.70 (m, 1H), 1.68–1.23 (m, 11H), 0.91 (s, 3H); IR (ATR): 3408, 2926, 2852, 1727, 1614, 1508, 1450, 1420, 1374, 1341, 1264, 1207, 1189, 1088, 1054, 1036, 1008, 909, 882, 870, 816, 647, 581, 534, 479, 451, 417, 402 cm⁻¹; HRMS (ESI+): m/z [M+NH4]⁺ calculated for C24H36NO2: 370.2741; found 370.2740.

To a one-dram vial (oven-dried, 1.5 × 8 mm stir bar) was added phenol 3ah (28.7 mg, 0.101 mmol, 1 equiv) followed by Cs₂CO₃ (39.4 mg, 0.121 mmol, 1.2 equiv) and the vial was brought into a glovebox. To the solids were added via auto-pipette DMSO (170. µL, 0.6 M) and 2-fluoropyridine (10.0 µL, 0.116 mmol, 1.15 equiv) before capping and removing from the glovebox. The solution was allowed to stir at 80 °C for 16 h. Initial white solid (Cs₂CO₃) stirring in a light-yellow solution turns into a yellow-orange heterogeneous solution. The reaction was diluted in DCM (0.5 mL) and the solution was washed with water (3 × 0.5 mL) and sat. brine (0.5 mL) before drying over MgSO₄, filtering, and concentrating under reduced pressure to afford 8 (31.2 mg, 86%) as a pale yellow/colorless oil. 1H NMR (600 MHz, CDCl3) δ 8.19 (d, J = 5.0 Hz, 1H), 7.64 (tt, J = 8.3, 1.6 Hz, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.21 (dt, J = 8.1, 1.6 Hz, 1H), 7.03 (t, J = 1.7 Hz, 1H), 6.95 (dd, J = 7.1, 5.0 Hz, 1H), 6.76 (d, J = 8.3 Hz, 1H), 3.02 (s, 1H), 2.33 (s, 2H), 2.04 (d, J = 12.8 Hz, 2H), 1.84 (d, J = 14.2 Hz, 4H), 1.74 (d, J = 8.8 Hz, 4H), 1.61 (d, J = 12.7
Hz, 2H), 1.29 (s, 9H); $^{13}$C NMR (151 MHz, CDCl$_3$) δ 164.0, 152.3, 150.1, 148.1, 139.3, 134.6, 128.3, 121.8, 119.6, 117.9, 110.6, 44.0, 40.0, 38.1, 34.5, 32.9, 31.4, 31.3, 28.1, 27.9; IR (ATR): 3053, 2902, 2849, 1596, 1574, 1501, 1467, 1451, 1428, 1403, 1362, 1343, 1285, 1264, 1244, 1223, 1206, 1190, 1135, 1099, 1092, 1069, 990, 969, 943, 910, 887, 851, 831, 776, 734, 703, 679, 627, 598, 513, 475, 443, 413 cm$^{-1}$; HRMS (ESI+): m/z [M+H]$^+$ calculated for C$_{25}$H$_{32}$NO: 362.2478; found 362.2494.

Mechanistic Studies

1-(Cyclohexyl)-4-methoxybenzene ($p$-10)

Prepared using General Procedure B with anisole (22 µL, 0.20 mmol, 1 equiv), ZnCl$_2$ (1.4 mg, 0.01 mmol, 0.05 equiv), chlorobenzene (0.2 mL, 1.0 M), cyclohexanol (62.5 µL, 0.6 mmol, 3.0 equiv), and CSA (35 mg, 0.15 mmol, 0.75 equiv). Purification by flash chromatography (eluting with 0–20% EtOAc in hexanes) afforded 5 (2.0 mg, 5%) as a colorless oil. $^1$H NMR (500 MHz, Chloroform-$d$) δ 7.15 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 3.81 (s, 3H), 2.47 (t, 1H), 1.86 (dd, J = 11.5, 7.6 Hz, 4H), 1.76 (d, J = 13.1 Hz, 1H), 1.48–1.35 (m, 4H), 0.92–0.83 (m, 2H). The spectral data recorded are consistent with those previously reported.$^5$

80 ºC: A one-dram vial equipped with a stirring bar was sequentially added ZnCl$_2$ (1.4 mg, 0.010 mmol, 5 mol%), 2-ethylphenol (24.0 µL, 0.200 mmol, 1 equiv), PhCl (0.2 mL, 1 M), tert-butanol (21.0 µL, 0.22 mmol, 1.1 equiv), and (R)-camphor sulfonic acid monohydrate (R-CSA•H$_2$O) (37.5 mg, 0.150 mmol, 75 mol%). The reaction mixture was heated at 80 ºC for 18 h, at which time the solution was filtered through a silica gel plug (packed in a 5” glass pipette, approximately one-third filled) and eluted with hexanes/EtOAc (9:1), and the solution was concentrated in vacuo. Purification by preparatory TLC (19:1 hexanes/EtOAc) afforded mixtures of a 4:1 ratio of $o$-11 to $o$/$p$-11 (7.5 mg, 20%) as a pale-yellow oil, and a 1.25:1 ratio of $p$-11 to 2-ethylphenol (0.5 mg, <1%) as a yellow oil.

140 ºC: A one-dram vial equipped with a stirring bar was sequentially added ZnCl$_2$ (1.3 mg, 9.5 µmol, 5 mol%), 2-ethylphenol (24.0 µL, 0.200 mmol, 1 equiv), PhCl (0.2 mL, 1 M), tert-butanol (21.0 µL, 0.22 mmol, 1.1 equiv), and (R)-camphor sulfonic acid monohydrate (R-CSA•H$_2$O) (37.8 mg, 0.151 mmol, 75 mol%). The reaction mixture was heated at 140 ºC for 18 h, at which time the solution was filtered through a silica gel plug (packed in a 5” glass pipette, approximately one-third filled) and eluted with hexanes/EtOAc (9:1), and the solution was concentrated in vacuo. Purification by preparatory TLC (19:1...
hexanes/EtOAc × 2) afforded mixtures of a 1:3.4 ratio of o-11 to o/o-11 (6.8 mg, 15%) as a bright yellow oil, and 6.7:1 p-11 to 2-ethylphenol (15.7 mg, 40%) as a bright yellow-orange oil.

2-tert-Butyl-6-ethylphenol (o-11): Rr: 0.45 (19:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.17 (dd, J = 7.9, 1.6 Hz, 1H), 7.03 (d, J = 7.5 Hz, 1H), 6.84 (t, J = 7.7 Hz, 1H), 4.86 (s, 1H), 2.61 (q, J = 7.6 Hz, 2H), 1.43 (s, 9H), 1.28 (t, J = 7.6 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 152.4, 135.8, 129.1, 126.7, 125.0, 120.2, 34.7, 30.0, 23.0, 13.9; IR (ATR): 3618, 2959, 2871, 1654, 1591, 1479, 1437, 1391, 1361, 1318, 1283, 1265, 1248, 1190, 1150, 1128, 1106, 1060, 932, 877, 834, 820, 794, 763, 746, 721, 649, 597, 573 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C12H17O: 177.1285; found 177.1287.

2,4-Di-tert-butyl-6-ethylphenol (o-o-11): Rr: 0.45 (19:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.20 (d, J = 2.5 Hz, 1H), 7.03 (d, J = 7.6 Hz, 1H), 4.72 (s, 1H), 2.64–2.59 (m, 2H), 1.44 (s, 9H), 1.31 (s, 9H), 1.29 (t, J = 7.6 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 150.0, 142.4, 135.0, 128.4, 123.6, 122.1, 34.9, 34.5, 31.8, 30.1, 23.5, 14.1; IR (ATR): 3618, 2959, 2871, 1654, 1591, 1479, 1437, 1391, 1361, 1318, 1283, 1265, 1190, 1150, 1128, 1106, 1060, 932, 877, 834, 820, 794, 763, 746, 721, 649, 597, 573 cm⁻¹; HRMS (ESI–): m/z [M–H]⁻ calculated for C16H25O: 233.1911; found 233.1915. The spectral data recorded are consistent with those previously reported. ²xx²

4-tert-Butyl-2-ethylphenol (p-11): Rr: 0.25 (19:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.16 (d, J = 2.4 Hz, 1H), 7.10 (dd, J = 8.3, 2.3 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 4.59 (s, 1H), 2.64 (q, J = 7.6 Hz, 2H), 1.30 (s, 9H), 1.25 (t, J = 7.6 Hz, 3H). The spectral data recorded are consistent with those previously reported. ²xx²

5. Kinetic Experiments

Kinetic experiments were carried out using the system depicted above. 3-tert-Butylphenol (1a) was chosen because little-to-no side products form over the course of the reaction. No products of decomposition were observed, therefore simplifying the data analysis. The kinetic profile of the reaction was examined using the method of initial rates and by varying the concentrations of 1a, 2h, ZnCl₂ catalyst, and (R)-CSA•H₂O. The conversions to product 3ah were monitored by SFC analysis.
Table S1. Kinetic Data for Arene Alkylation with adamant-2-ol

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<th>Entry</th>
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<th>[2h] / M</th>
<th>[ZnCl₂] / M</th>
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<th>initial rate[^a] / M·s⁻¹</th>
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<td>4.1 × 10⁻¹</td>
<td>2.5 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>2.27 × 10⁻⁵</td>
</tr>
<tr>
<td>12</td>
<td>5.0 × 10⁻¹</td>
<td>6.9 × 10⁻¹</td>
<td>2.5 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>3.43 × 10⁻⁵</td>
</tr>
<tr>
<td>13</td>
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<td>8.3 × 10⁻¹</td>
<td>2.5 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>3.38 × 10⁻⁵</td>
</tr>
<tr>
<td>14</td>
<td>5.0 × 10⁻¹</td>
<td>9.6 × 10⁻¹</td>
<td>2.5 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>3.52 × 10⁻⁵</td>
</tr>
<tr>
<td>15[^b]</td>
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<td>2.5 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>3.17 × 10⁻⁵</td>
</tr>
<tr>
<td>16</td>
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<td>5.5 × 10⁻¹</td>
<td>0</td>
<td>3.8 × 10⁻¹</td>
<td>5.76 × 10⁻⁶</td>
</tr>
<tr>
<td>17[^b]</td>
<td>5.0 × 10⁻¹</td>
<td>5.5 × 10⁻¹</td>
<td>1.3 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>2.29 × 10⁻⁵</td>
</tr>
<tr>
<td>18[^b]</td>
<td>5.0 × 10⁻¹</td>
<td>5.5 × 10⁻¹</td>
<td>5.0 × 10⁻²</td>
<td>3.8 × 10⁻¹</td>
<td>2.58 × 10⁻⁵</td>
</tr>
<tr>
<td>19[^b]</td>
<td>5.0 × 10⁻¹</td>
<td>5.5 × 10⁻¹</td>
<td>2.5 × 10⁻²</td>
<td>1.9 × 10⁻¹</td>
<td>1.77 × 10⁻⁵</td>
</tr>
<tr>
<td>20[^b]</td>
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<td>5.5 × 10⁻¹</td>
<td>2.5 × 10⁻²</td>
<td>7.5 × 10⁻¹</td>
<td>3.08 × 10⁻⁵</td>
</tr>
</tbody>
</table>

[^a] Average value from 2 independent experiments.  
[^b] Experiments ran for 8 h. See plots on next few pages.
Initial rates under standard conditions:

Initial rates varying [phenolic 1a]:
Initial rates varying [alcohol 2h]:

- [product 3ah] with respect to time using 1.0 × 10⁻⁸ M (2 equiv) phenol 1a (Table S1, entry 7)
  - Trial 1 Initial Rates: y = 0.00003103x + 0.03600461, R² = 0.9999775
  - Trial 2 Initial Rates: y = 0.00003221x + 0.02772281, R² = 0.9999908

- [product 3ah] with respect to time using 1.4 × 10⁻⁸ M (0.25 equiv) alcohol 2h (Table S1, entry 8)
  - Trial 1 Initial Rates: y = 0.0000091x + 0.00843132, R² = 0.9905296
  - Trial 2 Initial Rates: y = 0.0000090x + 0.00900309, R² = 0.9772692

- [product 3ah] with respect to time using 1.8 × 10⁻⁸ M (0.33 equiv) alcohol 2h (Table S1, entry 9)
  - Trial 1 Initial Rates: y = 0.00001052x + 0.00620401, R² = 0.9619136
  - Trial 2 Initial Rates: y = 0.00000924x + 0.00640720, R² = 0.9924121

- [product 3ah] with respect to time using 2.8 × 10⁻⁸ M (0.5 equiv) alcohol 2h (Table S1, entry 10)
  - Trial 1 Initial Rates: y = 0.00001745x + 0.00491945, R² = 0.9929777
  - Trial 2 Initial Rates: y = 0.00001342x + 0.00276678, R² = 0.9815949

- [product 3ah] with respect to time using 4.1 × 10⁻⁸ M (0.75 equiv) alcohol 2h (Table S1, entry 11)
  - Trial 1 Initial Rates: y = 0.00002357x + 0.00186485, R² = 0.9784476
  - Trial 2 Initial Rates: y = 0.00002177x + 0.00110627, R² = 0.9995640
Initial rates varying [ZnCl$_2$]:

**[product 3ah] with respect to time using 6.9 \times 10^{-1} \text{ M (1.25 equiv) alcohol 2h (Table S1, entry 12)}**

- **Trial 1 Initial Rates**
  
  \[ y = 0.00003373x - 0.01457344 \]

  \[ R^2 = 0.99653360 \]

- **Trial 2 Initial Rates**
  
  \[ y = 0.00003484x - 0.00493146 \]

  \[ R^2 = 0.97198014 \]

**[product 3ah] with respect to time using 8.3 \times 10^{-1} \text{ M (1.5 equiv) alcohol 2h (Table S1, entry 13)}**

- **Trial 1 Initial Rates**
  
  \[ y = 0.00003547x - 0.01739314 \]

  \[ R^2 = 0.99490348 \]

- **Trial 2 Initial Rates**
  
  \[ y = 0.00003209x - 0.01397305 \]

  \[ R^2 = 0.99828669 \]

**[product 3ah] with respect to time using 9.6 \times 10^{-1} \text{ M (1.75 equiv) alcohol 2h (Table S1, entry 14)}**

- **Trial 1 Initial Rates**
  
  \[ y = 0.00003722x - 0.03806779 \]

  \[ R^2 = 0.99932418 \]

- **Trial 2 Initial Rates**
  
  \[ y = 0.00003314x - 0.03224498 \]

  \[ R^2 = 0.9998144 \]

**[product 3ah] with respect to time using 1.1 \times 10^{-1} \text{ M (2 equiv) alcohol 2h (Table S1, entry 15)}**

- **Trial 1 Initial Rates**
  
  \[ y = 0.00003579x - 0.04708591 \]

  \[ R^2 = 0.99993814 \]

- **Trial 2 Initial Rates**
  
  \[ y = 0.00002754x - 0.02917755 \]

  \[ R^2 = 0.99989550 \]

**[product 3ah] with respect to time using 0 \text{ M (0 equiv) ZnCl$_2$ (Table S1, entry 16)}**

- **Trial 1 Initial Rates**
  
  \[ y = 0.00000699x - 0.00274046 \]

  \[ R^2 = 0.97852142 \]

- **Trial 2 Initial Rates**
  
  \[ y = 0.00000453x + 0.00462684 \]

  \[ R^2 = 0.98989511 \]

**[product 3ah] with respect to time using 1.3 \times 10^{-3} \text{ M (2.5 mol%) ZnCl$_2$ (Table S1, entry 17)}**

- **Trial 1 Initial Rates**
  
  \[ y = 0.00002604x - 0.01853098 \]

  \[ R^2 = 0.99625682 \]

- **Trial 2 Initial Rates**
  
  \[ y = 0.00001969x - 0.01001802 \]

  \[ R^2 = 0.99973957 \]
Initial rates varying [(R)-CSA•H₂O]:

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6. References


NMR Spectra

AP-ELN2-246-1_cycloheptanol_crude.1.fid
600 MHz, CDCl3

2b
($^1$H, CDCl3)
$2c$ 
($^1H$, CDCl$_3$)

$2g$ 
($^1H$, CDCl$_3$)
$\mathbf{2h}$

($^1\text{H}, \text{CDCl}_3$)

$\mathbf{3aa}$

($^1\text{H}, \text{CDCl}_3$)
3aa  
$^{13}$C, CDCl$_3$  

3ab  
$^1$H, CDCl$_3$
3ab
($^{13}$C, CDCl$\textsubscript{3}$)

3ac
($^{1}$H, CDCl$\textsubscript{3}$)
3ac
($^{13}$C, CDCl$_3$)

3ad
($^1$H, CDCl$_3$)
3ad
($^{13}$C, CDCl$_3$)

3ae
($^1$H, CDCl$_3$)
3ae
($^{13}$C, CDCl$_3$)
3af
(\(^1\)H, CDCl\(_3\))

3af
(\(^{13}\)C, CDCl\(_3\))
3ag (\textsuperscript{1}H, CDCl\textsubscript{3})

3ag (\textsuperscript{13}C, CDCl\textsubscript{3})

S36
3ah
\((^{1}H, \text{CDCl}_3)\)

3ah
\((^{13}C, \text{CDCl}_3)\)
$\text{3ba}$

($^1\text{H, CDCl}_3$)

$\text{3ba}$

($^{13}\text{C, CDCl}_3$)
3bh
($^1$H, CDCl$_3$)

3bh
($^{13}$C, CDCl$_3$)
3ca
$\left(^1H, \text{CDCl}_3\right)$

3ca
$\left(^{13}C, \text{CDCl}_3\right)$
3da
($^1$H, CDCl$_3$)

$^{13}$C, CDCl$_3$
3dh
($^1$H, CDCl$_3$)

3dh
($^{13}$C, CDCl$_3$)
3fh
($^1$H, CDCl$_3$)

3fh
($^{13}$C, CDCl$_3$)
3ga
\((^1H, CDCl_3)\)

3ga
\((^{13}C, CDCl_3)\)
3hh
($^1$H, CDCl$_3$)

3hh
($^{13}$C, CDCl$_3$)
$3\text{hh}$
($^{19}\text{F}, \text{CDCl}_3$)

$3\text{ih}$
($^1\text{H}, \text{CDCl}_3$)
$\textbf{3jh}$

($^{13}$C, CDCl$_3$)

$\textbf{3jh}$

($^1$H, CDCl$_3$)
3jh
($^{13}$C, CDCl$_3$)

3ka
($^1$H, CDCl$_3$)
3ka
({}^{13}\text{C}, \text{CDCl}_3)

3lh
({}^1\text{H}, \text{CDCl}_3)
3lh
\((^{13}\text{C}, \text{CDCl}_3)\)

3mh
\((^1\text{H}, \text{CDCl}_3)\)
3mh
\((^{13}\text{C}, \text{CDCl}_3)\)

\[ \text{Me} \]
\[ \text{Me} \]

\(\text{o-3nh}
\((^{1}\text{H}, \text{CDCl}_3)\)

S53
o-3nh
\(^{13}\text{C, CDCl}_3\)

\(\text{o, o-3nh \quad \text{CDCl}_3}\)

S54
$o, o$-$3nh$

($^{13}\text{C}, \text{CDCl}_3$)

$\rho$-$3nh$

($^1\text{H}, \text{CDCl}_3$)
5a/b
($^1$H, CDCl$_3$)

5a/b
($^{13}$C, CDCl$_3$)
$^6\text{a/b}$

($^1\text{H, CDCl}_3$)

$^13\text{C, CDCl}_3$
8

\(^{1}\text{H}, \text{CDCl}_3\)

\[\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{N} & \quad \text{O}
\end{align*}\]

8

\(^{13}\text{C}, \text{CDCl}_3\)

\[\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{N} & \quad \text{O}
\end{align*}\]
p-10
($^1$H, CDCl$_3$)

[Chemical structure image with NMR spectrum]
$^{13}$C, CDCl$_3$)
$^1$H, CDCl$_3$