

Supporting Information

Direct Transformation of Aryl 2-Pyridyl Esters to Secondary Benzylidic Alcohols by Nickel Relay Catalysis

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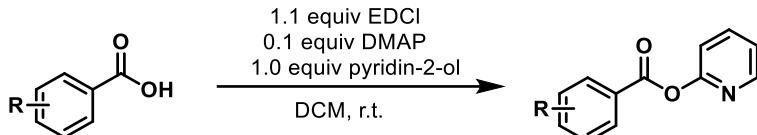
General Experimental

All reactions were carried out under nitrogen atmosphere and anhydrous conditions unless otherwise indicated. All manipulations of air- sensitive or moisture-sensitive compounds were performed in a glovebox under an atmosphere of nitrogen. Unless otherwise noted, all catalytic reactions were run in dried glassware. Toluene and THF were distilled from sodium/benzophenone. DCM was distilled over CaH₂. Ni(acac)₂ (CAS 3264-82-2) was purchased from Energy Chemical; ZnCl₂ (CAS 7646-85-7) was purchased from Strem; *N,N*-Dimethylformamide (DMF, CAS 68-12-2) was purchased from Adamas (99.8%, SafeDry, with molecular sieves, Water ≤ 50 ppm (by K.F.), SafeSeal); ⁷BuLi (CAS 109-72-8, 2.5 M in hexane) was purchased from Acros; Cyclohexylmagnesium bromide (CAS 931-50-0, 1.0 M in THF) was purchased from Energy Chemical. Zinc dust (325 mesh) and LiCl were purchased from Geneal Reagent. All Negishi reagents were titrated according to Knochel's procedure.^[1] Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.20 mm Huanghai silica gel plates (HSGF 254) using UV light as the visualizing agent and an acidic solution of Phosphomolybdic Acid (PMA) with heat as the developing agent. All new compounds were characterized by means of GC, ¹H-NMR, ¹³C-NMR, and HR-MS. GC analysis was performed on Agilent Technologies 7820A GC system. GC runs were performed with the following method: GC; HP-5 column; inlet temperature 100 °C; column temperature 100 °C for 1 min, then 50 °C/min to 280 °C, then 280 °C for 6 min. NMR spectra were recorded using a Bruker AVANCE III 400 MHz NMR spectrometer and can be found at the end of the paper. High-resolution mass spectra (HRMS) were recorded on a Waters GCT Premier mass spectrometer using EI-TOF (electron ionization-time of flight). Melting points were obtained for all crystalline solids on a X-4 Melting-Point Apparatus with microscope (from Shanghai Jingsong company). All ¹H-NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual chloroform (7.26 ppm) in deuteriochloroform (CDCl₃). All ¹³C-NMR data are reported in ppm relative to CDCl₃ (77.16 ppm) and were obtained with ¹H decoupling. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sep = septet.

Experimental Procedures and Characterization Data for Substrates

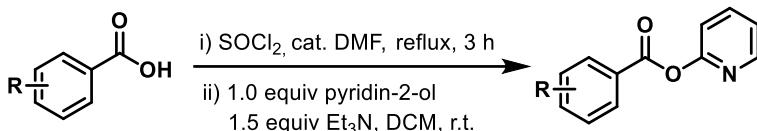
Compounds **1a**,^[2] **1b**,^[2] **1g**,^[3] **1i**,^[2] **1j**,^[2] **1o**,^[2] **1q**,^[3] **1r**,^[3] **1s**,^[2] **1ab**,^[4] **1ac**,^[5] **1ad**,^[6] **1ae**,^[7] **1ag**,^[8] **4**,^[9] **5**,^[10] **6**,^[11] **8**,^[12] **9**,^[13] were synthesized according to the published procedures.

General procedure A for substituted aryl 2-pyridyl esters synthesis



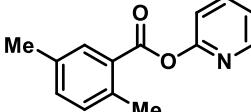
To a round-bottomed flask with the carboxylic acid (1.0 equiv) were added pyridin-2-ol (1.0 equiv), DMAP (0.1 equiv), EDC·HCl (1.1 equiv) and DCM (0.3 M). The reaction mixture was monitoring by TLC. When the starting material was consumed, the reaction was quenched with sat. aq. NaHCO₃ and extracted three times with DCM. The combined organic layer was washed with brine, dried over Na₂SO₄, and then filtered. The filtrate was concentrated in *vacuo* and the residue was purified by recrystallization or flash column chromatography to afford the corresponding aryl 2-pyridyl esters.

General procedure B for substituted aryl 2-pyridyl esters synthesis



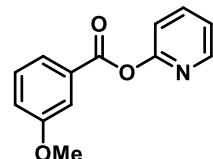
To a solution of carboxylic acid (1.0 equiv) in DCM were added thionyl chloride (2.0 equiv) and 1 drop of DMF and the mixture was refluxed for 3h. The solution was then concentrated in *vacuo*. Pyridin-2-ol (1.0 equiv) and DCM (0.5 M) were added to the residue. After cooling the mixture to 0 °C, Et₃N (1.5 equiv) was slowly added, then the reaction mixture was warmed to room temperature and stirred overnight. Then reaction was quenched with water extracted three times with DCM. The combined organic layer was washed with brine, dried over Na₂SO₄, and then filtered. The filtrate was concentrated in *vacuo* and the residue was purified by recrystallization or flash column chromatography to afford the corresponding aryl 2-pyridyl esters.

pyridin-2-yl 2,5-dimethylbenzoate (1c)

 General procedure A was followed on 2 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 5/1) afforded **1c** as a colorless oil (216.4 mg, 48%). R_f = 0.53 (PE/EtOAc = 5/1); ¹H NMR (400 MHz, CDCl₃): δ 8.52 (dd, *J* = 4.8, 2.0 Hz, 1H), 8.11 (s, 1H), 7.88 (ddd, *J* = 8.4, 7.6, 2.0 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.30 (ddd, *J* = 7.2, 4.8, 0.4 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 2.70 (s,

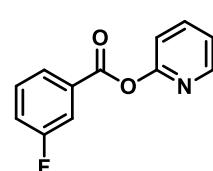
3H), 2.44 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 165.4, 158.3, 148.7, 139.5, 138.6, 135.5, 133.9, 131.9, 131.9, 127.5, 122.0, 116.8, 21.5, 20.8; **HRMS (EI)**: Calcd for C₁₄H₁₃NO₂: 227.0946; found: 227.0947.

pyridin-2-yl 3-methoxybenzoate (1d)



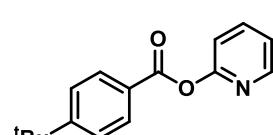
General procedure A was followed on 10 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 5/1) afforded **1d** as a white solid (1.087 g, 47%). M.P. = 45–46 °C; **R_f** = 0.50 (PE/EtOAc = 3/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.50 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.90–7.86 (m, 2H), 7.77 (dd, *J* = 2.4, 1.6 Hz, 1H), 7.45 (t, *J* = 8.4 Hz, 1H), 7.31 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 2H), 7.26–7.21 (m, 2H), 3.91 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 164.8, 159.8, 158.3, 148.8, 139.7, 130.4, 129.7, 122.9, 122.3, 120.7, 116.8, 114.5, 55.6; **HRMS (EI)**: Calcd for C₁₃H₁₁NO₃: 229.0739; found: 229.0738

pyridin-2-yl 3-fluorobenzoate (1e)



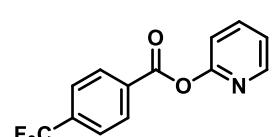
General procedure A was followed on 5 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 8/1) afforded **1e** as a colorless oil (894.7 mg, 83%). **R_f** = 0.50 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.32 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.77 (dt, *J* = 9.2, 2.4 Hz, 1H), 7.68 (td, *J* = 8.0, 2.0 Hz, 1H), 7.34 (td, *J* = 8.0, 5.6 Hz, 1H), 7.20 (dt, *J* = 8.4, 2.8 Hz, 1H), 7.12 (dd, *J* = 7.2, 4.8 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃): δ 163.4 (d, *J*_{C-F} = 3.1 Hz), 162.3 (d, *J*_{C-F} = 246 Hz), 157.7, 148.4, 139.4, 131.0 (d, *J*_{C-F} = 7.6 Hz), 130.1 (d, *J*_{C-F} = 7.7 Hz), 125.8 (d, *J*_{C-F} = 3.1 Hz), 122.1, 120.7 (d, *J*_{C-F} = 21.1 Hz), 116.8 (d, *J*_{C-F} = 23.2 Hz), 116.3. **¹⁹F NMR** (376 MHz, CDCl₃): -111.8 (td, *J* = 8.6, 5.3 Hz, 1F); **HRMS (EI)**: Calcd for C₁₂H₈FNO₂: 217.0539; found: 217.0540.

pyridin-2-yl 4-(tert-butyl)benzoate (1f)



General procedure A was followed on 2 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 10/1) afforded **1f** as a white solid (420 mg, 82%). M.P. = 58–59 °C; **R_f** = 0.38 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.45 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.17 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.80 (ddd, *J* = 8.0, 7.6, 2.0 Hz, 1H), 7.53 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.24 (ddd, *J* = 7.2, 4.8, 0.4 Hz, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 1.35 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃): δ 164.8, 158.3, 157.7, 148.6, 139.5, 130.3, 126.3, 125.6, 122.1, 116.8, 35.2, 31.1; **HRMS (EI)**: Calcd for C₁₆H₁₇NO₂: 255.1259; found: 255.1260.

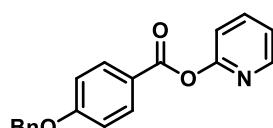
pyridin-2-yl 4-(trifluoromethyl)benzoate (1h)



General procedure B was followed on 2 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 5/1) afforded **1h** as a white solid (422 mg, 79%). M.P. = 40–41 °C; **R_f** = 0.43 (PE/EtOAc = 5/1); **¹H NMR** (400

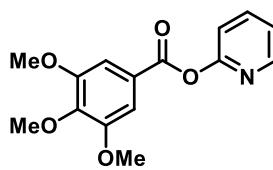
MHz, CDCl_3): δ 8.47 (dd, $J = 4.8, 2.0$ Hz, 1H), 8.34 (d, $J = 8.0$ Hz, 2H), 7.86 (ddd, $J = 8.0, 7.6, 2.0$ Hz, 1H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.29 (ddd, $J = 7.2, 4.8, 0.8$ Hz, 1H), 7.22 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 163.7, 157.9, 148.9, 139.9, 135.3 (q, $J_{\text{C}-\text{F}} = 32.5$ Hz), 132.5, 130.8, 125.7 (q, $J_{\text{C}-\text{F}} = 3.7$ Hz), 123.6 (q, $J_{\text{C}-\text{F}} = 271.4$ Hz), 122.6, 116.6; ^{19}F NMR (376 MHz, CDCl_3): -63.2; HRMS (EI): Calcd for $\text{C}_{13}\text{H}_8\text{F}_3\text{NO}_2$: 267.0507; found: 267.0506.

pyridin-2-yl 4-(benzyloxy)benzoate (1k)



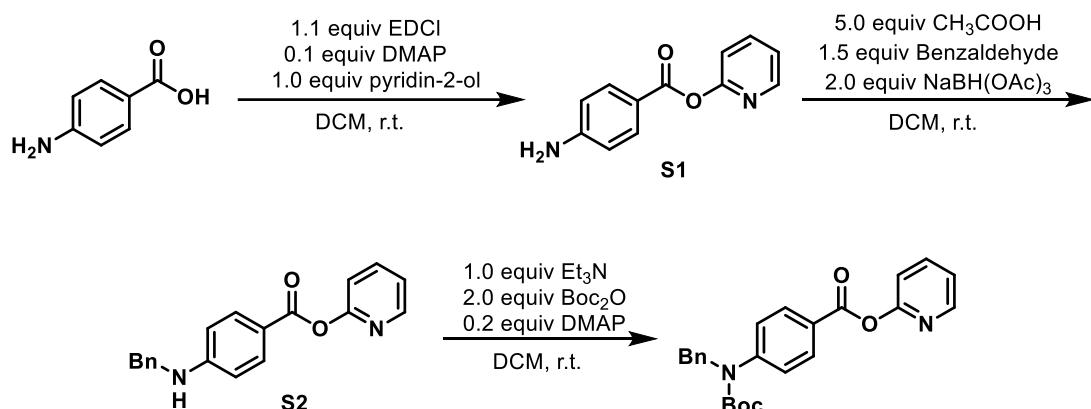
General procedure A was followed on 1 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 5:1) afforded **1k** as a white solid (241 mg, 79%). M.P. = 120–121 °C; $\text{R}_f = 0.52$ (PE/EtOAc = 2/1); ^1H NMR (400 MHz, CDCl_3): δ 8.46 (d, $J = 3.2$ Hz, 1H), 8.19 (d, $J = 8.8$ Hz, 2H), 7.83 (ddd, $J = 8.0, 7.6, 2.0$ Hz, 1H), 7.46–7.33 (m, 5H), 7.26 (t, $J = 6.0$ Hz, 1H), 7.21 (d, $J = 8.0$ Hz, 1H), 7.06 (d, $J = 8.8$ Hz, 2H), 5.16 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 164.6, 163.4, 158.5, 148.7, 139.6, 136.2, 132.7, 128.8, 128.4, 127.7, 122.1, 121.7, 116.9, 114.8, 70.3; HRMS (EI): Calcd for $\text{C}_{19}\text{H}_{15}\text{NO}_3$: 305.1052; found: 305.1054.

pyridin-2-yl 3,4,5-trimethoxybenzoate (1l)



General procedure A was followed on 10 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 5:1) afforded **1l** as a white solid (1.8753 g, 65%). M.P. = 119–120 °C; $\text{R}_f = 0.35$ (PE/EtOAc = 2/1); ^1H NMR (400 MHz, CDCl_3): δ 8.44 (dd, $J = 5.2, 2.0$ Hz, 1H), 7.82 (td, $J = 8.0, 2.0$ Hz, 1H), 7.46 (s, 2H), 7.25 (dd, $J = 7.2, 4.8$ Hz, 1H), 7.19 (d, $J = 8.0$ Hz, 1H), 3.92 (s, 3H), 3.91 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 164.5, 158.2, 153.1, 148.7, 143.0, 139.6, 123.9, 122.2, 116.8, 107.6, 61.0, 56.4; HRMS (EI): Calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_5$: 289.0950; found: 289.0951.

pyridin-2-yl 4-(benzyl(tert-butoxycarbonyl)amino)benzoate (1m)

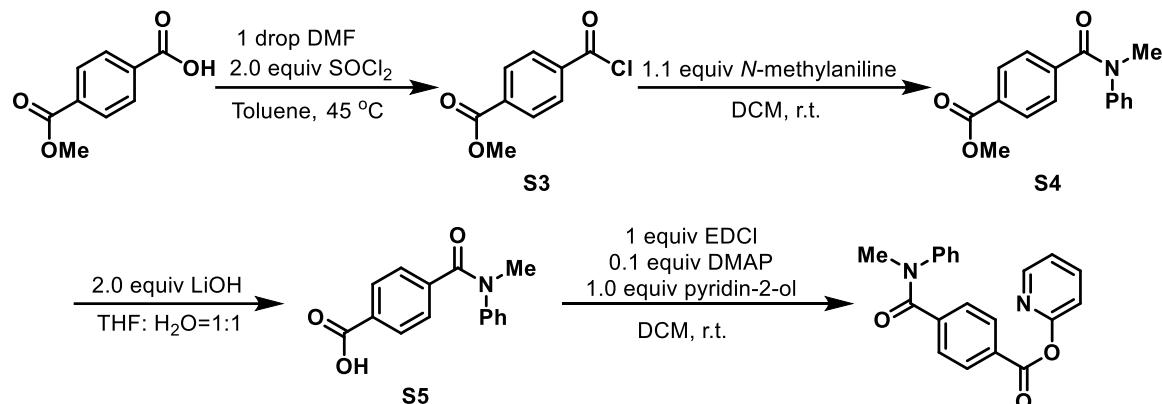


S1 was synthesized according to the General procedure A in 38% yield. A Schlenk tube charged with Pyrenin-2-yl 4-aminobenzoate (2.0 mmol, 428 mg) and $\text{NaBH}(\text{OAc})_3$ (4.0 mmol, 848 mg) was subsequently added DCM (10 mL),

benzaldehyde (3.0 mmol, 0.31 mL), and CH₃COOH (10.0 mmol, 0.57 mL) and the reaction mixture was stirred overnight. The reaction was quenched with sat. aq. NaHCO₃ and extracted three times with DCM. The combined organic layer was washed with brine, dried over Na₂SO₄, and then filtered. The filtrate was concentrated in *vacuo* and the crude product was purified by column chromatography (silica gel, PE/EtOAc/DCM = 8/1/1) to afford the product **S2** as white solid (549 mg, 90%).

To a round-bottomed flask with **S2** (1.8 mmol, 548.7 mg), DMAP (0.36 mmol, 44 mg), (Boc)₂O (3.6 mmol, 785.7 mg) in DCM (12 mL) was added Et₃N (1.8 mmol, 0.25 mL), and the reaction mixture was stirred overnight. The reaction was quenched with sat. aq. NaHCO₃ and extracted three times with DCM. The combined organic layer was washed with brine, dried over Na₂SO₄, and then filtered. The filtrate was concentrated in *vacuo* and the crude product was purified by column chromatography (silica gel, PE/EtOAc = 20/1–10/1–5/1) to afford the product **1m** as a colorless oil (452.6 mg, 62%). **R_f** = 0.63 (PE/EA = 3/1); ¹H NMR (400 MHz, CDCl₃): δ 8.45 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 7.83 (ddd, *J* = 8.0, 7.2, 2.0 Hz, 1H), 7.35–7.30 (m, 4H), 7.28–7.18 (m, 5H), 4.92 (s, 2H), 1.44 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 164.4, 158.3, 154.2, 148.8, 148.1, 139.7, 138.1, 131.1, 128.7, 127.4, 127.1, 125.7, 125.5, 122.2, 116.8, 81.6, 53.6, 28.3; HRMS (EI): Calcd for C₂₄H₂₄N₂O₄: 404.1736; found: 404.1734.

pyridin-2-yl 4-(methyl(phenyl)carbamoyl)benzoate (**1n**)



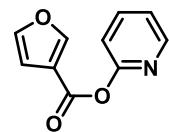
To a round-bottomed flask with 4-(methoxycarbonyl)benzoic acid (5.0 mmol, 0.9 g) in toluene (15 mL) was added SOCl₂ (10.0 mmol, 0.73 mL) and a drop of DMF, then the reaction mixture was stirred at 45 °C for 3 h. After completion, the solvent was removed under reduced pressure to give the crude product **S3**, which was dissolved in DCM (12 mL) and placed in an ice water bath, followed by adding N-methylaniline (5.5 mmol, 0.59 mL), and the mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with water and washed with hexane, dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, PE/EtOAc = 5/1) to afford the product **S4** as a white solid (1.075 g, 80%).

To a round-bottomed flask with **S4** (1.075 g, 4 mmol) in THF (10 mL)/H₂O (10 mL) was added LiOH (8.0 mmol, 191.5 mg) and the resulted mixture was stirred at room temperature overnight. The mixture was acidified with 1.0 M HCl to pH = 1 and

extracted with EtOAc (3×10 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 , and then filtered. The filtrate was concentrated in *vacuo* and the residue was purified by flash column chromatography (silica gel, PE/EtOAc = 2/1–1/1) to afford the product **S5** as a white solid (930.3 mg, 91 %).

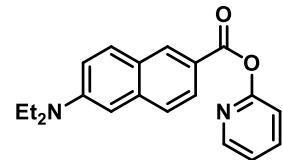
General procedure A was followed with **S5** and purification by flash column chromatography (silica gel, PE/EtOAc = 3/1) afforded **1n** as a white solid (810.6 mg, 67%). M.P. = 122–123 °C; R_f = 0.36 (PE/EtOAc = 2/1); ^1H NMR (400 MHz, CDCl_3): δ 8.41 (dd, J = 4.8, 1.6 Hz, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.81 (td, J = 8.0, 2.0 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.26–7.21 (m, 3H), 7.17–7.14 (m, 2H), 7.02 (t, J = 7.6 Hz, 2H), 3.51 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.6, 164.2, 158.1, 148.8, 144.2, 141.3, 139.7, 129.9, 129.8, 129.5, 128.8, 127.1, 127.0, 122.3, 116.6, 38.3; HRMS (EI): Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_3$: 332.1161; found: 332.1158.

pyridin-2-yl furan-3-carboxylate (1p)



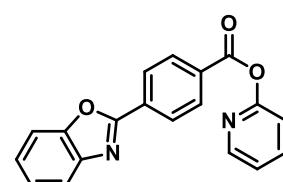
General procedure A was followed on 5 mmol scale and purification by flash column chromatography (silica gel, PE/EtOAc = 8:1) afforded **1p** as a white solid (493.1 mg, 52%). M.P. = 41–42 °C; R_f = 0.46 (PE/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 8.33 (d, J = 3.6 Hz, 1H), 8.14 (s, 1H), 7.70 (td, J = 8.0, 2.0 Hz, 1H), 7.40 (t, J = 2.0 Hz, 1H), 7.14 (dd, J = 7.2, 4.8 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 6.78 (d, J = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 160.7, 157.5, 148.9, 148.4, 144.1, 139.4, 122.0, 118.3, 116.4, 109.8; HRMS (EI): Calcd for $\text{C}_{10}\text{H}_7\text{NO}_3$: 189.0426; found: 189.0425.

pyridin-2-yl 4-(diethylamino)benzoate (1t)



General procedure A was followed on 1.28 mmol from 6-(diethylamino)-2-naphthoic acid **S6**.^[14–15] Purification by flash column chromatography on silica gel (PE/EtOAc = 10/1) afforded **1t** as a yellow solid (150.2 mg, 43%). M.P. = 135–136 °C; R_f = 0.42 (PE/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 8.63 (s, 1H), 8.47 (dd, J = 4.8, 1.6 Hz, 1H), 8.05 (dd, J = 8.4, 1.2 Hz, 1H), 7.84 (td, J = 8.0, 2.0 Hz, 1H), 7.80 (d, J = 9.2 Hz, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.28–7.24 (m, 2H), 7.12 (dd, J = 9.2, 2.0 Hz, 1H), 6.85 (s, 1H), 3.50 (q, J = 7.2 Hz, 4H), 1.25 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 165.4, 158.6, 148.6, 148.0, 139.4, 138.5, 132.3, 131.0, 126.1, 125.8, 124.6, 121.8, 121.0, 116.9, 116.0, 104.2, 44.6, 12.7; HRMS (EI): Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2$: 320.1525; found: 320.1526.

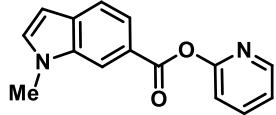
pyridin-2-yl 4-(benzo[d]oxazol-2-yl)benzoate (1u)



General procedure A was followed on 0.5 mmol from 4-(benzo[d]oxazol-2-yl)benzoic acid **S7**.^[16] Purification by flash column chromatography on silica gel (PE/EtOAc = 3/1) afforded **1u** as a white solid (90.2 mg, 57%). M.P. = 187–188 °C; R_f = 0.35 (PE/EtOAc = 3/1); ^1H NMR (400 MHz, CDCl_3): δ 8.48 (dd, J = 4.8, 1.2 Hz, 1H), 8.42–8.37 (m, 4H), 7.88 (td, J = 8.0, 2.0 Hz, 1H), 7.83–7.81 (m, 1H), 7.64–7.62 (m, 1H), 7.44–7.38 (m, 2H), 7.31 (ddd, J = 7.6, 5.2, 0.8 Hz,

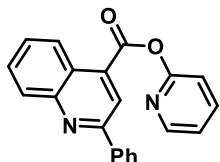
1H), 7.26 (d, J = 8.0 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃): δ 164.3, 157.8, 156.7, 149.3, 148.9, 139.9, 138.5, 134.0, 130.4, 130.2, 130.0, 129.0, 128.3, 127.5, 125.3, 124.1, 122.6, 121.1, 116.7; **HRMS (EI)**: Calcd for C₁₉H₁₂N₂O₃: 316.0848; found: 316.0851.

pyridin-2-yl 1-methyl-1H-indole-6-carboxylate (1v)



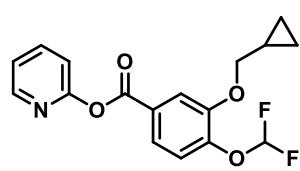
General procedure A was followed on 2.7 mmol from 1-methyl-1H-indole-6-carboxylic acid **S8**.^[17] Purification by flash column chromatography on silica gel (PE/EtOAc = 8/1–3/1) afforded **1v** as a white solid (526.9 mg, 77%). M.P. = 85–86 °C; **R_f** = 0.35 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.42 (dd, J = 4.8, 1.6 Hz, 1H), 8.25 (s, 1H), 7.97 (dd, J = 8.8, 1.2 Hz, 1H), 7.78 (ddd, J = 8.4, 7.6, 2.0 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.17 (ddd, J = 7.2, 6.0, 0.8 Hz, 2H), 6.50 (dd, J = 3.2, 0.8 Hz, 1H), 3.72 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 165.7, 158.3, 148.3, 139.3, 135.7, 132.7, 132.7, 121.7, 121.4, 120.7, 120.4, 116.7, 112.4, 101.3, 32.7; **HRMS (EI)**: Calcd for C₁₅H₁₂N₂O₂: 252.0899; found: 252.0900.

pyridin-2-yl 2-phenylquinoline-4-carboxylate (1w)



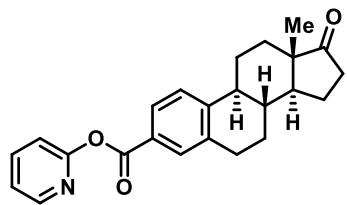
General procedure A was followed on 1.0 mmol from 2-phenylquinoline-4-carboxylic acid **S9**.^[18] Purification by flash column chromatography on silica gel (PE/EtOAc = 10/1–5/1) afforded **1w** as a white solid (153.0 mg, 47%). M.P. = 116–117 °C; **R_f** = 0.26 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.90 (dd, J = 8.8, 0.8 Hz, 1H), 8.70 (s, 1H), 8.51 (dd, J = 4.8, 1.2 Hz, 1H), 8.28–8.24 (m, 3H), 7.86 (td, J = 8.0, 2.0 Hz, 1H), 7.79 (ddd, J = 8.0, 6.8, 1.2 Hz, 1H), 7.64 (ddd, J = 8.8, 7.2, 1.2 Hz, 1H), 7.56–7.46 (m, 3H), 7.31–7.28 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃): δ 164.3, 157.8, 156.7, 149.3, 148.8, 139.9, 138.5, 134.0, 130.4, 130.2, 130.0, 129.0, 128.3, 127.5, 125.3, 124.1, 122.6, 121.1, 116.7; **HRMS (EI)**: Calcd for C₂₁H₁₄N₂O₂: 326.1055; found: 326.1056.

pyridin-2-yl 3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzoate (1am)



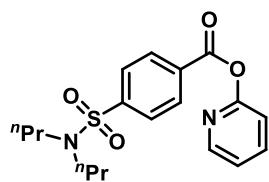
General procedure A was followed on 0.3 mmol scale and purification by flash column chromatography (silica gel, PE/EtOAc = 4/1) afforded **1am** as a colorless oil (76.5 mg, 76%). **R_f** = 0.33 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.44 (dd, J = 5.2, 1.6 Hz 1H), 7.86–7.81 (m, 2H), 7.76 (d, J = 2.0 Hz, 1H), 7.27 (ddd, J = 7.2, 4.8, 0.8 Hz, 2H), 7.23 (d, J = 8.8 Hz, 1H), 6.75 (t, J_{H-F} = 74.8 Hz, 1H), 3.94 (d, J = 7.2 Hz, 2H), 1.35–1.26 (m, 1H), 0.68–0.63 (m, 2H), 0.38–0.34 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃): δ 164.0, 158.1, 150.3, 148.8, 144.9 (t, J_{C-F} = 3.1 Hz), 139.7, 127.1, 123.9, 122.4, 121.8, 116.7, 115.8 (t, J_{C-F} = 259.4 Hz), 115.8, 74.2, 10.1, 3.3; **¹⁹F NMR** (376 MHz, CDCl₃): δ -81.9 (d, J = 74.8 Hz, 2F); **HRMS (EI)**: Calcd for C₁₇H₁₅F₂NO₄: 335.0969; found: 335.0970.

estrone 2-pyridyl esters (1an)



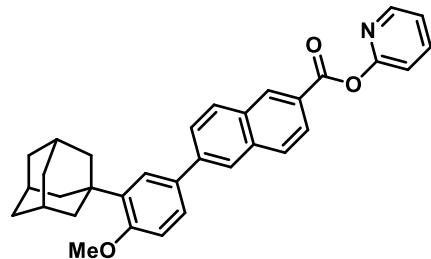
General procedure A was followed on 1.4 mmol from 3-deoxyestrone -3-carboxylic acid **S10**.^[19-20] Purification by flash column chromatography on silica gel (PE/EtOAc = 3/1) afforded **1an** as a white solid (74.6 mg, 14%). M.P. = 192–193 °C; R_f = 0.26 (PE/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 8.42 (dd, J = 4.8, 1.6 Hz, 1H), 7.95 (d, J = 10.4 Hz, 2H), 7.81 (td, J = 8.0, 2.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.24 (dd, J = 6.8, 5.2 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 2.98–2.94 (m, 2H), 2.53–2.42 (m, 2H), 2.34 (td, J = 10.4, 3.6 Hz, 1H), 2.18–2.01 (m, 3H), 1.99–1.95 (m, 1H), 1.67–1.41 (m, 6H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): ^{13}C NMR (100 MHz, CDCl_3): 220.7, 165.0, 158.4, 148.7, 146.5, 139.7, 137.2, 131.2, 127.8, 126.6, 125.8, 122.2, 116.9, 50.7, 48.0, 44.9, 37.9, 36.0, 31.7, 29.3, 26.4, 25.7, 21.7, 14.0; HRMS (EI): Calcd for $\text{C}_{24}\text{H}_{25}\text{NO}_3$: 375.1834; found: 375.1831.

pyridin-2-yl 4-(N,N-dipropylsulfamoyl)benzoate (1ao)



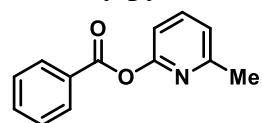
General procedure A was followed and purification by flash column chromatography on silica gel (PE/EtOAc = 10/1) afforded **1ao** as a white solid (482.1 mg, 66%). M.P. = 69–70 °C; R_f = 0.52 (PE/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 8.42 (d, J = 3.2 Hz, 1H), 8.30 (d, J = 8.8 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.83 (ddd, J = 8.0, 2.0 Hz, 1H), 7.27 (dd, J = 6.8, 4.8 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 3.09 (t, J = 7.6 Hz, 4H), 1.52 (sext, J = 7.6 Hz, 4H), 0.83 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 163.5, 157.8, 148.7, 145.1, 139.9, 132.4, 131.0, 127.1, 122.6, 116.5, 49.8, 21.8, 11.1; HRMS (EI): Calcd for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_4\text{S}$: 362.1300; found: 362.1304.

pyridin-2-yl 6-(3-((3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)-2-naphthoate (1ap)



General procedure A was followed and purification by flash column chromatography on silica gel (PE/EtOAc = 10/1–5/1) afforded **1ap** as a white solid (54.4 mg, 37%). M.P. = 171–172 °C; R_f = 0.43 (PE/DCM = 1/2); ^1H NMR (400 MHz, CDCl_3): δ 8.84 (s, 1H), 8.51 (dd, J = 5.2, 2.0 Hz, 1H), 8.23 (dd, J = 8.4, 1.6 Hz, 1H), 8.06 (s, 1H), 8.03 (d, J = 8.8 Hz, 1H), 7.98 (d, J = 8.8 Hz, 1H), 7.89–7.83 (m, 2H), 7.63 (d, J = 2.0 Hz, 1H), 7.56 (dd, J = 8.4, 2.4 Hz, 1H), 7.31–7.28 (m, 2H), 7.01 (d, J = 8.4 Hz, 1H), 3.91 (s, 3H), 2.20 (s, 6H), 2.12 (s, 3H), 1.82 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3): δ 165.1, 159.1, 158.4, 148.8, 142.0, 139.7, 139.1, 136.5, 132.5, 132.2, 131.3, 130.0, 128.6, 126.8, 126.1, 125.9, 125.8, 124.9, 122.2, 116.8, 112.2, 55.3, 40.7, 37.3, 37.2, 29.2; HRMS (EI): Calcd for $\text{C}_{33}\text{H}_{31}\text{NO}_3$: 489.2304; found: 489.2308.

6-methylpyridin-2-yl benzoate (7)



General procedure A was followed on 3 mmol scale and purification by flash column chromatography on silica gel (PE/EtOAc = 6/1) afforded **1c** as a white solid (474 mg, 74%). **R_f** = 0.53 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.13 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 2.44 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 164.6, 157.9, 157.2, 139.4, 133.6, 130.1, 128.9, 128.3, 121.4, 113.1, 23.8.

Experimental Procedures and Characterization Data for Products

Preparation of ZnCl₂ Solution (1.0 M in THF).

Zinc chloride (1.0 M in THF): Finely powdered anhydrous ZnCl₂ (0.68 g, 5.0 mmol) was weighed into a 25-mL, flame-dried Schlenk tube in the glove box in an inert atmosphere. The tube was taken out of the glove box and heated with a heat gun for 2 min under vacuum and then back filled with nitrogen (This process was repeated for 3 times.). After cooling, the flask was backfilled with N₂, and THF (anhydrous, 5.0 mL) was added. The suspension was vigorously stirred for 30 min before it was used.

General procedure A for preparation of "BuZnCl from transmetallation of "BuLi to ZnCl₂.

To a solution of ZnCl₂ (1.0 M, 1.0 mmol, 1.0 mL) in THF (0.6 mL) was added "BuLi (2.5 M, 1.0 mmol, 0.4 mL) at 0 °C. The mixture was vigorously stirred at the same temperature for 30 min. The concentration of alkylzinc reagents prepared by this method is from 0.39 M to 0.45M

General procedure B for Preparation of CyZnCl from transmetallation of CyMgBr to ZnCl₂.

To a solution of ZnCl₂ (1.0 M, 1.0 mmol, 1.0 mL) in THF (0.3 mL) was added CyMgBr solution (0.58 M, 1.0 mmol, 1.7 mL) at 0 °C. The mixture was vigorously stirred at the same temperature for 30 min. The concentration of CyZnCl₂ is 0.33 M.

General procedure C for the preparation of organozinc reagents via direct insertion of zinc

This method is modified from the reported literature.^[2] Anhydrous LiCl (10 mmol, 2.0 equiv) was placed in an N₂-flushed sealed tube and dried for 10 min under the vacuum with heat gun. Zinc powder (10 mmol, 2.0 equiv, 325 mesh) was added under N₂ and the heterogeneous mixture of Zn and LiCl was dried again for 10 min under the vacuum with heat gun. The sealed tube was backfilled with N₂ (This process was repeated for three times). THF (5 mL) was added and the Zn was activated with BrCH₂CH₂Br (5 mol%) under the reflux condition for 20 min. After cooling, Me₃SiCl (1 mol%) and I₂ (0.5 mol%) was added under N₂, then the mixture was refluxed for another 20 min. Alkyl bromide (5 mmol) was then added neat at room temperature and the reaction mixture was stirred at 65 °C for 12–48 h (checked by GC analysis of reaction aliquots, the conversion was higher than 98%). The concentration of Negishi reagents ranges from 0.39 M to 0.8M.

General procedure for the Ni-Catalyzed tandem reaction of 2-pyridyl ester

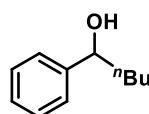
An oven-dried Schlenk tube charged with aryl 2-pyridyl ester (1.0 equiv) and Ni(acac)₂ (10 mol%) was evacuated and backfilled with N₂ (This process was repeated for three times) and cooled to 0 °C. Negishi reagent (3.0 equiv) and DMF (0.2 M) were subsequently added into the reaction mixture. The tube was sealed with Parafilm,

equipped with a balloon filled with N₂, and allowed to stir overnight (2–22 h) at 50 °C. The mixture was quenched with sat. aq. NH₄Cl and extracted with EtOAc. The separated organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography.

Note: The reverse addition sequence of Negishi reagent and DMF sometimes cause diminished yield.

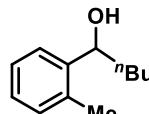
Characterization Data for products

1-Phenylpentan-1-ol (2a)



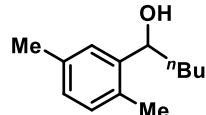
General procedure was followed with pyridin-2-yl benzoate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 1.0 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 20/1) to afford **2a** as a colorless oil (143.3 mg, 87%). **R_f** = 0.31 (PE/EtOAc = 10/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.29–7.25 (m, 4H), 7.22–7.18 (m, 1H), 4.57 (dd, *J* = 7.2, 6.0 Hz, 1H), 1.87 (s, 1H), 1.77–1.58 (m, 2H), 1.37–1.13 (m, 4H), 0.81 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 145.0, 128.5, 127.6, 126.0, 74.8, 38.9, 28.1, 22.7, 14.1. The spectral data are consistent with those reported in the literature.^[21]

1-(*o*-tolyl)pentan-1-ol (2b)



General procedure was followed with pyridin-2-yl 2-methylbenzoate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.5 mmol scale with a reaction time of 16 hours. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 20/1) to afford **2b** as a colorless oil (51.9 mg, 58%). **R_f** = 0.57 (PE/EtOAc = 6/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.47 (d, *J* = 7.6 Hz, 1H), 7.24 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (td, *J* = 7.2, 1.2 Hz, 1H), 7.15–7.13 (m, 1H), 4.92 (dd, *J* = 7.6, 5.2 Hz, 1H), 2.35 (s, 3H), 1.98 (s, 1H), 1.80–1.65 (m, 2H), 1.52–1.29 (m, 4H), 0.93 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 143.2, 134.5, 130.4, 127.2, 126.3, 125.2, 70.7, 38.0, 28.3, 22.8, 22.6, 19.2, 14.2. **HRMS (EI)**: Calcd for C₁₂H₁₈O: 178.1358; found: 178.1359. The spectral data are consistent with those reported in the literature.^[22]

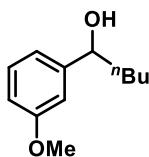
1-(2,5-dimethylphenyl)pentan-1-ol (2c)



General procedure was followed with pyridin-2-yl 2,5-dimethylbenzoate, and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.3 mmol scale with a reaction time of 16 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2c** as a white solid (34.4 mg, 60%). M.P. = 46–47 °C; **R_f** = 0.46 (PE/EtOAc = 6/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.29 (s, 1H), 7.04–6.97 (m, 2H), 4.90 (dd, *J* = 8.0, 5.2 Hz, 1H), 2.34 (s, 3H), 2.30 (s, 3H), 1.79–1.64 (m, 3H), 1.53–1.27 (m, 4H), 0.92 (t, *J* = 6.8 Hz, 3H); **¹³C NMR**

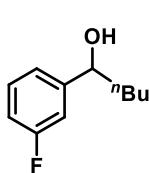
(100 MHz, CDCl_3): δ 143.0, 135.8, 131.3, 130.4, 127.9, 125.8, 70.8, 38.1, 28.4, 22.8, 21.3, 18.7, 14.2; **HRMS (EI)**: Calcd for $\text{C}_{13}\text{H}_{20}\text{O}$: 192.1514; found: 192.1510.

1-(3-methoxyphenyl)pentan-1-ol (2d)



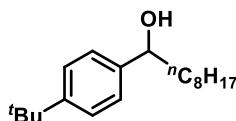
General procedure was followed with pyridin-2-yl 3-methoxybenzoate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.5 mmol scale with a reaction time of 18 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2d** as a colorless oil (74.7 mg, 77%). \mathbf{R}_f = 0.50 (PE/EtOAc = 3/1); **1H NMR** (400 MHz, CDCl_3): δ 7.26 (t, J = 8.0 Hz, 1H), 6.93–6.91 (m, 2H), 6.83–6.80 (m, 1H), 4.62 (dd, J = 7.2, 6.0 Hz, 1H), 3.81 (s, 3H), 2.30 (s, 1H), 1.84–1.65 (m, 2H), 1.45–1.22 (m, 4H), 0.90 (t, J = 7.2 Hz, 3H); **13C NMR** (100 MHz, CDCl_3): δ 159.7, 146.8, 129.4, 118.3, 112.9, 111.5, 74.6, 55.2, 38.8, 28.0, 22.7, 14.1. The spectral data are consistent with those reported in the literature.^[23]

1-(3-fluorophenyl)pentan-1-ol (2e)



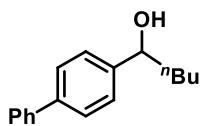
General procedure was followed with pyridin-2-yl 3-fluorobenzoate and *n*-butylzinc chloride (0.38 M, prepared according to the general procedure A) on 0.2 mmol scale with a reaction time of 15 hours. The reaction mixture was purified by and purification by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2e** as a colorless oil (28.1 mg, 77%). \mathbf{R}_f = 0.43 (PE/EtOAc = 10/1); **1H NMR** (400 MHz, CDCl_3): δ 7.26–7.20 (m, 1H), 7.04–6.98 (m, 2H), 6.89 (td, J = 8.4, 2.8 Hz, 1H), 4.60 (dd, J = 7.2, 6.0 Hz, 1H), 1.92 (s, 1H), 1.75–1.58 (m, 2H), 1.36–1.15 (m, 4H), 0.83 (t, J = 6.8 Hz, 3H); **13C NMR** (100 MHz, CDCl_3): δ 163.1 (d, $J_{\text{C-F}}$ = 244.4 Hz), 147.8 (d, $J_{\text{C-F}}$ = 6.6 Hz), 130.0 (d, $J_{\text{C-F}}$ = 8.1 Hz), 121.6 (d, $J_{\text{C-F}}$ = 2.8 Hz), 114.4 (d, $J_{\text{C-F}}$ = 21.1 Hz), 112.9 (d, $J_{\text{C-F}}$ = 21.6 Hz), 74.2, 39.0, 27.9, 22.7, 14.1 ppm; **19F NMR** (376 MHz, CDCl_3) δ -113.1 (td, J = 9.4, 5.6 Hz, 1F); **HRMS (EI)**: Calcd for $\text{C}_{11}\text{H}_{15}\text{O}$: 182.1107; found: 182.1106. The spectral data are consistent with those reported in the literature.^[24]

1-(4-(*tert*-butyl)phenyl)nonan-1-ol (2f)



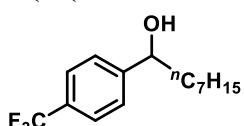
General procedure was followed with pyridin-2-yl 4-(*tert*-butyl)benzoate and *n*-octylzinc bromide (0.58 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 9 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20:1) to afford **2f** as a colorless oil (40.4 mg, 73%). \mathbf{R}_f = 0.39 (PE/EtOAc = 10:1); **1H NMR** (400 MHz, CDCl_3): δ 7.38 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 4.63 (dd, J = 7.6, 5.6 Hz, 1H), 1.89 (s, 1H), 1.85–1.67 (m, 2H), 1.49–1.39 (m, 1H), 1.33 (s, 9H), 1.30–1.27 (m, 11H), 0.89 (t, J = 7.2 Hz, 3H); **13C NMR** (100 MHz, CDCl_3): δ 150.5, 142.1, 125.8, 125.4, 74.6, 39.1, 34.6, 32.0, 31.5, 29.7, 29.7, 29.4, 26.1, 22.8, 14.2; **HRMS (EI)**: Calcd for $\text{C}_{19}\text{H}_{32}\text{O}$: 276.2453; found: 276.2452.

1-([1,1'-biphenyl]-4-yl)pentan-1-ol (2g)



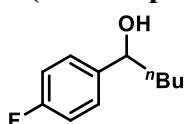
General procedure was followed with pyridin-2-yl [1,1'-biphenyl]-4-carboxylate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.3 mmol scale with a reaction time of 22 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 15/1) to afford **2g** as a white solid (61.7 mg, 86%). M.P. = 77–78 °C; R_f = 0.42 (PE/EtOAc = 8/1); **1H NMR** (400 MHz, CDCl₃): δ 7.61–7.58 (m, 4H), 7.47–7.41 (m, 4H), 7.35 (t, J = 7.2 Hz, 1H), 4.72 (t, J = 6.8 Hz, 1H), 1.90–1.72 (m, 3H), 1.48–1.27 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 144.1, 140.9, 140.4, 128.9, 127.3, 127.2, 127.1, 126.5, 74.5, 38.9, 28.1, 22.7, 14.2; **HRMS (EI)**: Calcd for C₁₇H₂₀O: 240.1514; found: 240.1513.

1-(4-(trifluoromethyl)phenyl)octan-1-ol (2h)



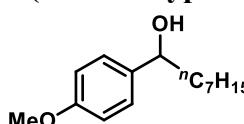
General procedure was followed with pyridin-2-yl 4-(trifluoromethyl)benzoate and *n*-heptylzinc bromide (0.61 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 15 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2h** as a colorless oil (49.7 mg, 91%). R_f = 0.6 (PE/EtOAc = 2/1); **1H NMR** (400 MHz, CDCl₃): δ = 7.61 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 4.73 (dd, J = 7.2, 6.0 Hz, 1H), 2.02 (bs, 1H), 1.82–1.65 (m, 2H), 1.44–1.26 (m, 10H), 0.89 (t, J = 6.8 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 149.0, 129.7 (q, J_{C-F} = 32.3 Hz), 126.3, 125.5 (q, J_{C-F} = 3.7 Hz), 124.3 (q, J_{C-F} = 270.2 Hz), 74.2, 39.4, 31.9, 29.6, 29.3, 25.8, 22.8, 14.2; **19F NMR** (376 MHz, CDCl₃): δ -62.4 (s, 3F); **HRMS (EI)**: Calcd for C₁₅H₂₁F₃O: 274.1544; found: 274.1545.

1-(4-fluorophenyl)pentan-1-ol (2i)



General procedure was followed with pyridin-2-yl 4-fluorobenzoate and *n*-butylzinc chloride (0.45 M, prepared according to the general procedure A) on 0.5 mmol scale with a reaction time of 18 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2i** as a colorless oil (67.3 mg, 74%). R_f = 0.47 (PE/EtOAc = 6/1); **1H NMR** (400 MHz, CDCl₃): δ = 7.31–7.26 (m, 2H), 7.02 (t, J = 8.8 Hz, 2H), 4.62 (t, J = 6.8 Hz, 1H), 2.04 (s, 1H), 1.81–1.61 (m, 2H), 1.41–1.17 (m, 4H), 0.88 (t, J = 6.8 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 162.2 (d, J_{C-F} = 243.7 Hz), 140.8 (d, J_{C-F} = 3.1 Hz), 127.6 (d, J_{C-F} = 8.0 Hz), 115.3 (d, J_{C-F} = 21.2 Hz), 74.1, 39.0, 28.0, 22.7, 14.1; **19F NMR** (376 MHz, CDCl₃): δ -115.4 (tt, J = 8.6, 5.3 Hz, 1F); **HRMS (EI)**: Calcd for C₁₁H₁₅FO: 182.1107; found: 182.1108.

1-(4-methoxyphenyl)octan-1-ol (2j)



General procedure was followed with pyridin-2-yl 4-methoxybenzoate and *n*-heptylzinc bromide (0.61 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 15 hours. The reaction mixture was purified by

flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2j** as a colorless oil (33 mg, 70%). R_f = 0.45 (PE/EtOAc = 2/1); **1H NMR** (400 MHz, CDCl₃): δ = 7.18 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 4.52 (t, J = 6.8 Hz, 1H), 3.72 (s, 3 H), 1.81 (s, 1H), 1.71–1.55 (m, 2H), 1.37–1.18 (m, 10H), 0.79 (t, J = 6.8 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 159.1, 137.2, 127.3, 113.9, 74.4, 55.4, 39.1, 31.9, 29.6, 29.4, 26.0, 22.8, 14.2; **HRMS (EI)**: Calcd for C₁₅H₂₄O₂: 236.1776; found: 236.1773. The spectral data are consistent with those reported in the literature.^[25]

1-(4-(benzyloxy)phenyl)octan-1-ol (**2k**)

General procedure was followed with pyridin-2-yl 4-(benzyloxy)benzoate and *n*-heptylzinc bromide (0.60 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2k** as a white solid (40.2 mg, 64%). M.P. = 48–49 °C; R_f = 0.33 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, CDCl₃): δ = 7.46–7.38 (m, 4H), 7.34 (ddt, J = 8.4, 6.0, 1.2 Hz, 1H), 7.27 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 5.07 (s, 2H), 4.61 (t, J = 6.8 Hz, 1H), 1.85–1.65 (m, 3H), 1.44–1.27 (m, 10H), 0.89 (t, J = 6.8 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 158.3, 137.5, 137.1, 128.7, 128.1, 127.6, 127.3, 114.8, 74.4, 70.1, 39.1, 31.9, 29.6, 29.3, 26.0, 22.8, 14.2; **HRMS (EI)**: Calcd for C₂₁H₂₈O₂: 312.2089; found: 312.2092.

1-(3,4,5-trimethoxyphenyl)pentan-1-ol (**2l**)

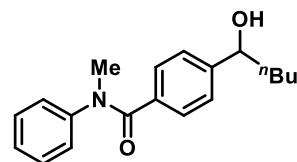
General procedure was followed with pyridin-2-yl 3,4,5-trimethoxybenzoate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.3 mmol scale with a reaction time of 21 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 3/1) to afford **2l** as a yellow oil (64.5 mg, 85%). R_f = 0.12 (PE/EtOAc = 6/1); **1H NMR** (400 MHz, CDCl₃): δ = 6.55 (s, 2H), 4.56 (dd, J = 7.6, 5.6 Hz, 1H), 3.84 (s, 6H), 3.81 (s, 3H), 2.01 (s, 1H), 1.81–1.63 (m, 3H), 1.44–1.22 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 153.2, 141.0, 137.1, 102.7, 74.9, 60.9, 56.1, 39.0, 28.2, 22.7, 14.1; **HRMS (EI)**: Calcd for C₁₄H₂₂O₄: 254.1518; found: 254.1519.

tert-butyl benzyl(4-(1-hydroxyoctyl)phenyl)carbamate (**2m**)

General procedure was followed with pyridin-2-yl 4-(benzyl(tert-butoxycarbonyl)amino)benzoate and *n*-heptylzinc bromide (0.61 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 15 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **2m** as a colorless oil (68.8 mg, 84%). R_f = 0.38 (PE/EtOAc = 2/1); **1H NMR** (400 MHz, CDCl₃): δ = 7.31–7.22 (m, 7H), 7.12 (d, J = 7.6 Hz, 2H), 4.82 (s, 2H), 4.59 (t, J = 6.8 Hz, 1H), 2.04 (bs, 1H), 1.77–1.58 (m, 2H), 1.42 (s, 9H), 1.30–1.25 (m, 10H), 0.87 (t, J = 6.8 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ 154.9, 142.5, 142.0, 138.7, 128.4, 127.3, 127.1, 126.4, 126.3, 80.7, 74.2, 54.0, 39.1,

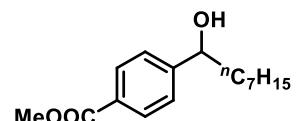
31.9, 29.6, 29.3, 25.9, 22.7, 14.2; **HRMS (EI)**: Calcd for C₂₆H₃₇NO₃: 411.2773; found: 411.2769.

4-(1-hydroxypentyl)-N-methyl-N-phenylbenzamide (2n)



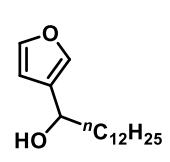
General procedure was followed with pyridin-2-yl 4-(methyl(phenyl)carbamoyl)benzoate and *n*-butylzinc chloride (0.41 M, prepared according to the general procedure A) on 0.2 mmol scale with a reaction time of 8 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 2/1) to afford **2n** as a colorless oil (55.8 mg, 94%). **R_f** = 0.2 (PE/EtOAc = 2/1); **¹H NMR** (100 MHz, CDCl₃): δ = 7.22–7.17 (m, 4H), 7.12–7.07 (m, 3H), 7.00 (d, *J* = 7.2 Hz, 2H), 4.53 (t, *J* = 6.8 Hz, 1H), 3.45 (s, 3H), 2.40 (s, 1H), 1.71–1.51 (m, 2H), 1.27–1.07 (m, 4H), 0.82 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 170.7, 146.7, 144.9, 134.8, 129.2, 128.9, 126.9, 126.6, 125.3, 74.0, 38.8, 38.5, 27.8, 22.6, 14.1; **HRMS (EI)**: Calcd for C₁₉H₂₃NO₂: 297.1729; found: 297.1730.

methyl 4-(1-hydroxyoctyl)benzoate (2o)



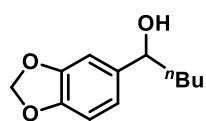
General procedure was followed with methyl pyridin-2-yl terephthalate and *n*-heptylzinc bromide (0.65 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2o** as a colorless oil (37.7 mg, 71%). **R_f** = 0.44 (PE/EtOAc = 10/1); **¹H NMR** (400 MHz, CDCl₃): δ = 7.98 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 4.70 (dd, *J* = 7.2, 6.0 Hz, 1H), 3.89 (s, 3H), 2.18 (s, 1H), 1.80–1.64 (m, 2H), 1.38–1.24 (m, 10H), 0.86 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 167.1, 150.3, 129.8, 129.2, 125.9, 74.3, 52.2, 39.3, 31.9, 29.6, 29.3, 25.8, 22.7, 14.2; **HRMS (EI)**: Calcd for C₁₆H₂₄O₃: 264.1725; found: 264.1732.

1-(furan-3-yl)tridecan-1-ol (2p)



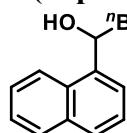
General procedure was followed with methyl pyridin-2-yl furan-3-carboxylate and *n*-dodecylzinc bromide (0.58 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 2 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2p** as a brown oil (17.9 mg, 34%). **R_f** = 0.44 (PE/EtOAc = 10/1); **¹H NMR** (400 MHz, CDCl₃): δ = 7.39–7.38 (m, 2H), 6.40 (t, *J* = 1.2 Hz, 1H), 4.65 (t, *J* = 6.8 Hz, 1H), 1.81–1.70 (m, 2H), 1.64 (s, 1H), 1.45–1.25 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ = 143.5, 139.1, 129.4, 108.6, 67.2, 38.0, 32.1, 29.8, 29.7, 29.6, 29.5, 25.8, 22.8, 14.3; **HRMS (EI)**: Calcd for C₁₇H₃₀O₂: 266.2246; found: 266.2247.

1-(benzo[d][1,3]dioxol-5-yl)pentan-1-ol (2q)



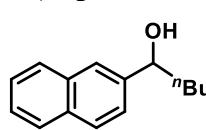
General procedure was followed with methyl pyridin-2-yl benzo[d][1,3]dioxole-5-carboxylate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.5 mmol scale with a reaction time of 22 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 8/1) to afford **2q** as a colorless oil (78.3 mg, 75%). **R_f** = 0.38 (PE/EtOAc = 8/1); **¹H NMR** (400 MHz, CDCl₃): δ 6.83 (s, 1H), 6.77–6.72 (m, 2H), 5.92 (s, 2H), 4.52 (t, *J* = 6.8 Hz, 1H), 2.18 (s, 1H), 1.79–1.58 (m, 2H), 1.39–1.15 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 147.7, 146.8, 139.1, 119.4, 108.0, 106.4, 100.9, 74.5, 38.8, 28.0, 22.6, 14.1; **HRMS (EI)**: Calcd for C₁₂H₁₆O₃: 208.1099; found: 208.1100.

1-(naphthalen-1-yl)pentan-1-ol (2r)



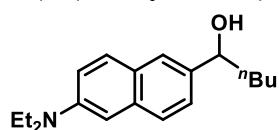
General procedure was followed with methyl pyridin-2-yl-1-naphthoate and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.3 mmol scale with a reaction time of 15 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 15/1) to afford **2r** as a white solid (40 mg, 62%). M.P. = 62–63 °C; **R_f** = 0.35 (PE/EtOAc = 8/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.13–8.10 (m, 1H), 7.90–7.88 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.55–7.46 (m, 3H), 5.45 (dd, *J* = 8.0, 4.8 Hz, 1H), 2.08 (s, 1H), 2.01–1.85 (m, 2H), 1.59–1.30 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 140.7, 133.9, 130.5, 129.0, 127.9, 126.0, 125.6, 125.6, 123.3, 122.9, 71.4, 38.2, 28.5, 22.8, 14.2. The spectral data are consistent with those reported in the literature.^[26]

1-(naphthalen-2-yl)pentan-1-ol (2s)



General procedure was followed with methyl pyridin-2-yl-2-naphthoate and *n*-butylzinc chloride (0.40 M, prepared according to the general procedure A) on 0.3 mmol scale with a reaction time of 14 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2s** as a white solid (53.3 mg, 83%). M.P. = 43–44 °C; **R_f** = 0.51 (PE/EtOAc = 6/1); **¹H NMR** (400 MHz, CDCl₃): 87.86–7.82 (m, 3H), 7.76 (s, 1H), 7.53–7.47 (m, 3H), 4.79 (t, *J* = 6.8 Hz, 1H), 2.38 (s, 1H), 1.93–1.76 (m, 2H), 1.46–1.24 (m, 4H), 0.92 (t, *J* = 7.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 142.3, 133.3, 133.0, 128.2, 128.0, 127.7, 126.1, 125.7, 124.7, 124.2, 74.7, 38.7, 28.0, 22.7, 14.1. The spectral data are consistent with those reported in the literature.^[27]

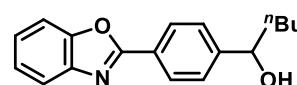
1-(6-(diethylamino)naphthalen-2-yl)pentan-1-ol (2t)



General procedure was followed with methyl pyridin-2-yl 6-(diethylamino)-2-naphthoate and *n*-butylzinc chloride (0.36 M, prepared according to the general procedure A) on 0.2 mmol scale with a reaction time of 14 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 15/1) to afford **2t** as

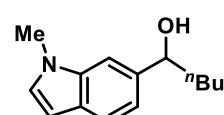
a white solid (39 mg, 68%). M.P. = 47–48 °C; **R_f** = 0.50 (PE/EtOAc = 10/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.67 (d, *J* = 9.2 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.59 (s, 1H), 7.36 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.11 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.88 (s, 1H), 4.74 (t, *J* = 6.8 Hz, 1H), 3.47 (q, *J* = 6.8 Hz, 4H), 1.97 (s, 1H), 1.92–1.74 (m, 2H), 1.43–1.27 (m, 4H), 1.23 (t, *J* = 7.2 Hz, 6H), 0.89 (t, *J* = 7.2 Hz, 6H); **¹³C NMR** (100 MHz, CDCl₃): δ 146.0, 137.8, 135.0, 129.0, 126.4, 126.0, 124.6, 116.3, 105.6, 75.1, 44.7, 38.6, 28.2, 22.8, 14.2, 12.8; **HRMS (EI)**: Calcd for C₁₉H₂₇NO: 285.2093; found: 285.2094.

1-(4-(benzo[d]oxazol-2-yl)phenyl)pentan-1-ol (2u)



General procedure was followed with methyl pyridin-2-yl 6-(diethylamino)-2-naphthoate and *n*-butylzinc chloride (0.40 M, prepared according to the general procedure A) on 0.1 mmol scale with a reaction time of 14 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 8/1) to afford **2u** as a white solid (20.5 mg, 73%). M.P. = 65–66 °C; **R_f** = 0.33 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 8.21 (d, *J* = 8.4 Hz, 2H), 7.79–7.74 (m, 1H), 7.60–7.56 (m, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.38–7.33 (m, 2H), 4.75 (dd, *J* = 6.0 Hz, 1H), 2.16 (s, 1H), 1.87–1.70 (m, 2H), 1.46–1.25 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 163.1, 150.8, 149.0, 142.0, 127.9, 126.6, 126.2, 125.3, 124.8, 120.0, 110.7, 74.3, 39.0, 27.9, 22.7, 14.1; **HRMS (EI)**: Calcd for C₁₈H₁₉NO₂: 281.1416; found: 281.1414.

1-(1-methyl-1H-indol-6-yl)pentan-1-ol (2v)



General procedure was followed with pyridin-2-yl 1-methyl-1H-indole-6-carboxylate and *n*-butylzinc chloride (0.41 M, prepared according to the general procedure A) on 0.2 mmol scale with a reaction time of 20 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 8/1) to afford **2v** as a green solid (22.4 mg, 51%). M.P. = 39–40 °C; **R_f** = 0.4 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.34 (s, 1H), 7.09 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.06 (d, *J* = 2.8 Hz, 1H), 6.48 (d, *J* = 3.2 Hz, 1H), 4.80 (t, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 1.95–1.76 (m, 3H), 1.47–1.24 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 138.8, 136.8, 129.2, 128.1, 120.9, 117.9, 106.6, 100.9, 75.6, 39.2, 32.9, 28.3, 22.8, 14.2; **HRMS (EI)**: Calcd for C₁₄H₁₉NO: 217.1467; found: 217.1468.

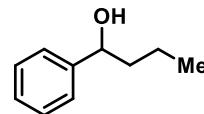
1-(2-phenylquinolin-4-yl)nonan-1-ol (2w)



General procedure was followed with pyridin-2-yl 2-phenylquinoline-4-carboxylate and *n*-octylzinc(II) bromide (0.53 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2w** as a pale yellow solid (35.5 mg, 51%). M.P. = 73–74 °C; **R_f** = 0.51 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ = 8.19 (d, *J* = 8.0 Hz, 1H), 8.03–8.01 (m, 2H), 7.83 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.67 (ddd, *J* = 7.6, 6.8, 1.2 Hz, 1H), 7.48–7.40 (m, 4H), 5.28 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.06 (s, 1H), 1.88–1.71 (m, 2H), 1.57–1.38 (m, 2H), 1.33–1.25 (m, 10H), 0.87 (t, *J* =

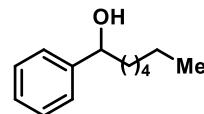
6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 157.0, 151.7, 148.1, 139.3, 130.2, 129.5, 129.4, 128.8, 127.6, 126.2, 124.5, 122.9, 115.2, 70.2, 38.5, 32.0, 29.6, 29.4, 26.2, 22.8, 14.2; **HRMS (EI)**: Calcd for C₂₄H₂₉NO, 347.2249; found: 347.2245.

1-phenylbutan-1-ol (2x)



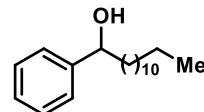
General procedure was followed with pyridin-2-yl benzoate and propylzinc bromide (0.63 M, prepared according to the general procedure C) on 0.3 mmol scale with a reaction time of 17 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2x** as a colorless oil (33.4 mg, 74%). **R_f** = 0.43 (PE/EtOAc = 7/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.29–7.25 (m, 4H), 7.23–7.17 (m, 1H), 4.59 (dd, *J* = 7.6, 6.0 Hz, 1H), 1.89 (s, 1H), 1.76–1.56 (m, 2H), 1.40–1.20 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 145.0, 128.5, 127.6, 126.0, 74.5, 41.3, 19.1, 14.1. The spectral data are consistent with those reported in the literature.^[28]

1-phenylheptan-1-ol (2y)



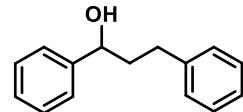
General procedure was followed with pyridin-2-yl benzoate and hexylzinc bromide (0.59 M, prepared according to the general procedure C) on 0.3 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2y** as a colorless oil (52 mg, 89%). **R_f** = 0.30 (PE/EtOAc = 8/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.30–7.23 (m, 4H), 7.22–7.18 (m, 1H), 4.56 (dd, *J* = 7.6, 6.0 Hz, 1H), 2.06 (s, 1H), 1.76–1.58 (m, 2H), 1.37–1.15 (m, 8H), 0.81 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 145.1, 128.5, 127.5, 126.0, 74.7, 39.2, 31.9, 29.3, 25.9, 22.7, 14.2. The spectral data are consistent with those reported in the literature.^[29]

1-phenyltridecan-1-ol (2z)



General procedure was followed with pyridin-2-yl benzoate and dodecylzinc bromide (0.57 M, prepared according to the general procedure C) on 0.3 mmol scale with a reaction time of 17 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2z** as a colorless oil (63.4 mg, 77%). **R_f** = 0.55 (PE/EtOAc = 7/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.29–7.25 (m, 4H), 7.23–7.17 (m, 1H), 4.57 (dd, *J* = 7.6, 6.0 Hz, 1H), 1.88 (s, 1H), 1.77–1.59 (m, 2H), 1.35–1.18 (m, 20H), 0.82 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 145.1, 128.5, 127.6, 126.0, 74.8, 39.2, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 26.0, 22.8, 14.3. The spectral data are consistent with those reported in the literature.^[30]

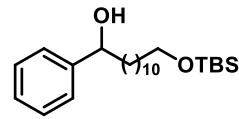
1,3-diphenylpropan-1-ol (2aa)



General procedure was followed with pyridin-2-yl benzoate, and phenethylzinc bromide (0.63 M, prepared according to the general procedure C) on 0.3 mmol scale with a reaction time of 10 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2aa** as a colorless oil (52.5 mg, 83%). **R_f** = 0.3 (PE/EtOAc

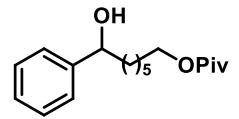
= 10/1) ; **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ 7.29–7.25 (m, 4H), 7.23–7.19 (m, 3H), 7.14–7.11 (m, 3H), 4.57 (dd, $J = 8.0, 5.6$ Hz, 1H), 2.70–2.54 (m, 2H), 2.08 (s, 1H), 2.06–1.90 (m, 2H); **$^{13}\text{C NMR}$** (100 MHz, CDCl_3): δ 144.6, 141.9, 128.6, 128.5, 128.5, 127.7, 126.0, 125.9, 73.9, 40.5, 32.1. The spectral data are consistent with those reported in the literature.^[31]

12-((tert-butyldimethylsilyl)oxy)-1-phenyldodecan-1-ol (2ab)



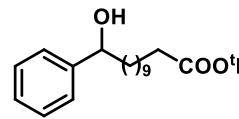
General procedure was followed with pyridin-2-yl benzoate and (11-((tert-butyldimethylsilyl)oxy)undecyl)zinc bromide (0.4 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2ab** as a colorless oil (57.9 mg, 74%). **$\text{R}_f = 0.44$** (PE/EtOAc = 10/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ 7.29–7.25 (m, 4H), 7.23–7.17 (m, 1H), 4.57 (dd, $J = 7.2, 6.0$ Hz, 1H), 3.52 (t, $J = 6.8$ Hz, 1H), 1.88 (s, 1H), 1.76–1.58 (m, 2H), 1.43 (quin, $J = 6.8$ Hz, 2H), 1.31–1.18 (m, 16H), 0.83 (s, 9H), –0.02 (s, 6H); **$^{13}\text{C NMR}$** (100 MHz, CDCl_3): δ 145.1, 128.5, 127.6, 126.0, 74.8, 63.5, 39.2, 33.0, 29.7, 29.7, 29.7, 29.6, 26.1, 26.0, 25.9, 18.5, -5.1; **HRMS (EI)**: Calcd for $\text{C}_{24}\text{H}_{44}\text{O}_2\text{Si}$: 392.3111; found: $[\text{M}-\text{C}_4\text{H}_9]^+ = 335.2394$.

7-hydroxy-7-phenylheptyl pivalate (2ac)



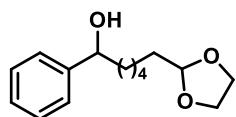
General procedure was followed with pyridin-2-yl benzoate and (6-(pivaloyloxy)hexyl)zinc bromide (0.54 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 19 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2ac** as a colorless oil (44.4 mg, 76%). **$\text{R}_f = 0.47$** (PE/EtOAc = 5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ 7.27–7.25 (m, 4H), 7.22–7.17 (m, 1H), 4.58 (dd, $J = 7.6, 6.0$ Hz, 1H), 3.95 (t, $J = 6.8$ Hz, 2H), 1.91 (bs, 1H), 1.75–1.51 (m, 4H), 1.39–1.19 (m, 6H), 1.11 (s, 9H); **$^{13}\text{C NMR}$** (100 MHz, CDCl_3): δ 178.8, 145.0, 128.5, 127.6, 126.0, 74.7, 64.5, 39.1, 38.8, 29.2, 28.6, 27.3, 25.9, 25.8; **HRMS (EI)**: Calcd for $\text{C}_{18}\text{H}_{28}\text{O}_3$: 292.2038; found: 292.2037.

tert-butyl 12-hydroxy-12-phenyldodecanoate (2ad)



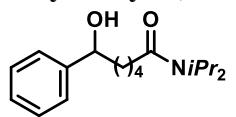
General procedure was followed with pyridin-2-yl benzoate, and (11-(tert-butoxy)-11-oxoundecyl)zinc bromide (0.58 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 2 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2ad** as a colorless oil (51.8 mg, 74%). **$\text{R}_f = 0.44$** (PE/EtOAc = 10/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ 7.29–7.25 (m, 4H), 7.22–7.17 (m, 1H), 4.57 (dd, $J = 7.6, 6.0$ Hz, 1H), 2.12 (t, $J = 7.2$ Hz, 2H), 2.05 (bs, 1H), 1.76–1.59 (m, 2H), 1.49 (quin, $J = 7.2$ Hz, 2H), 1.37 (s, 9H), 1.19–1.18 (m, 14H); **$^{13}\text{C NMR}$** (100 MHz, CDCl_3): δ 173.5, 145.1, 128.5, 127.5, 126.0, 80.0, 74.7, 39.2, 35.7, 29.6, 29.5, 29.4, 29.2, 28.2, 25.9, 25.2; **HRMS (EI)**: Calcd for $\text{C}_{22}\text{H}_{36}\text{O}_3$, 348.2664, found: 348.2657.

6-(1,3-dioxolan-2-yl)-1-phenylhexan-1-ol (2ae)



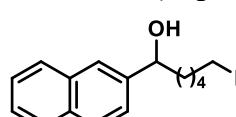
General procedure was followed with pyridin-2-yl benzoate, and (5-(1,3-dioxolan-2-yl)pentyl)zinc bromide (0.48 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 12 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 6/1) to afford **2ae** as a colorless oil (42 mg, 84%). R_f = 0.37 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, CDCl₃): δ 7.29–7.25 (m, 4H), 7.23–7.17 (m, 1H), 4.75 (t, J = 4.8 Hz, 1H), 4.58 (dd, J = 7.2, 6.0 Hz, 1H), 3.89–3.83 (m, 2H), 3.80–3.74 (m, 2H), 1.78–1.53 (m, 5H), 1.39–1.19 (m, 6H); **13C NMR** (100 MHz, CDCl₃): δ 145.0, 128.5, 127.6, 126.0, 104.7, 74.7, 64.9, 39.1, 33.9, 29.5, 25.8, 24.1; **HRMS (EI)**: Calcd for C₁₅H₂₂O₃: 250.1569; found: 250.1568.

6-hydroxy-N,N-diisopropyl-6-phenylhexanamide (2af)



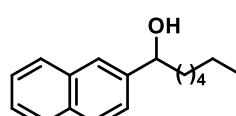
General procedure was followed with pyridin-2-yl benzoate, and (5-(diisopropylamino)-5-oxopentyl)zinc bromide (0.34 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 7 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 2/1) to afford **2af** as a yellow oil (31.7 mg, 54%). R_f = 0.31 (PE/EtOAc = 2/1); **1H NMR** (400 MHz, CDCl₃): δ = 7.27–7.23 (m, 4H), 7.19–7.15 (m, 1H), 4.63 (dd, J = 8.0, 5.6 Hz, 1H), 3.85 (sep, J = 6.4 Hz, 1H), 3.37 (s, 1H), 2.56 (s, 1H), 2.20 (t, J = 7.6 Hz, 2H), 1.78–1.48 (m, 4H), 1.43–1.30 (m, 2H), 1.27 (d, J = 6.4 Hz, 6H), 1.09 (d, J = 6.4 Hz, 6H); **13C NMR** (100 MHz, CDCl₃): δ 172.1, 145.1, 128.5, 127.4, 126.0, 74.2, 45.8, 38.9, 35.1, 25.7, 25.0, 21.1, 20.8; **HRMS (EI)**: Calcd for C₁₈H₂₉NO₂: 291.2198; found: 291.2199.

6-fluoro-1-(naphthalen-2-yl)hexan-1-ol (2ag)



General procedure was followed with pyridin-2-yl benzoate and (5-fluoropentyl)zinc bromide (0.57 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 8 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 9/1) to afford **2ag** as a white solid (32.3 mg, 66%). M.P. = 44–45 °C; R_f = 0.28 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, CDCl₃): δ 7.85–7.83 (m, 3H), 7.76 (s, 1H), 7.52–7.45 (m, 3H), 4.83 (t, J = 6.8 Hz, 1H), 4.47 (t, J = 2.0 Hz, 1H), 4.36 (t, J = 2.0 Hz, 1H), 2.01 (bs, 1H), 1.94–1.76 (m, 2H), 1.74–1.61 (m, 2H), 1.54–1.28 (m, 4H); **13C NMR** (100 MHz, CDCl₃): δ 142.2, 133.4, 133.1, 128.4, 128.0, 127.8, 126.3, 125.9, 124.7, 124.1, 84.2 (d, J_{C-F} = 163.1 Hz), 74.7, 38.9, 30.4 (d, J_{C-F} = 19.3 Hz), 25.5, 25.2 (d, J_{C-F} = 5.3 Hz); **19F NMR** (376 MHz, CDCl₃): -218.1 (tt, J = 47.8, 25.2 Hz, 1F); **HRMS (EI)**: Calcd for C₁₆H₁₉FO: 246.1420; found: 246.1422.

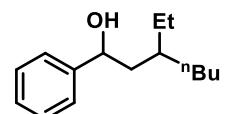
8-methyl-1-(naphthalen-2-yl)non-7-en-1-ol (2ah)



General procedure was followed with pyridin-2-yl benzoate and (7-methyloct-6-en-1-yl)zinc bromide (0.56 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 13 hours. The reaction mixture was

purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2ah** as a white solid (46.6 mg, 83%). M.P. = 43–44 °C; R_f = 0.32 (PE/EtOAc = 10/1); **1H NMR** (400 MHz, CDCl₃): δ 7.84–7.82 (m, 3H), 7.77 (s, 1H), 7.52–7.45 (m, 3H), 5.11 (ddt, J = 8.4, 7.2, 1.2 Hz, 1H), 4.81 (t, J = 6.8 Hz, 1H), 2.05 (bs, 1H), 1.97–1.95 (m, 2H), 1.91–1.75 (m, 2H), 1.70 (d, J = 0.4 Hz, 3H), 1.59 (s, 3H), 1.48–1.41 (m, 1H), 1.33–1.26 (m, 5H); **13C NMR** (100 MHz, CDCl₃): δ 142.4, 133.4, 133.1, 131.4, 128.3, 128.0, 127.8, 126.2, 125.9, 124.9, 124.7, 124.2, 74.9, 39.1, 29.9, 29.3, 28.1, 25.9, 25.8, 17.8; **HRMS (EI)**: Calcd for C₂₀H₂₆O: 282.1984; found: 282.1982.

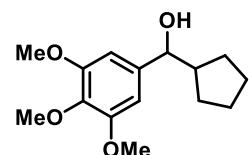
ethyl-1-phenylheptan-1-ol (2ai)



General procedure was followed with pyridin-2-yl benzoate and (2-ethylhexyl)zinc bromide (0.45 M, prepared according to the general procedure C) on 0.3 mmol scale with a reaction time of 21 hours.

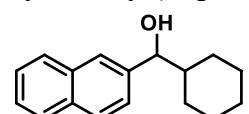
The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2ai** as a colorless oil (31.7 mg, 71%). R_f = 0.5 (PE/EtOAc = 8/1); **1H NMR** (400 MHz, CDCl₃): δ 7.27–7.26 (m, 3H), 7.22–7.17 (m, 1H), 4.66 (dd, J = 8.4, 5.6 Hz, 1H), 1.75 (s, 1H), 1.67 (ddt, J = 14.0, 8.1, 6.0 Hz, 1H), 1.54–1.46 (m, 1H), 1.38–1.14 (m, 10H), 0.83–0.74 (m, 6H); **13C NMR** (100 MHz, CDCl₃): δ 145.5, 145.5, 128.6, 127.6, 126.0, 126.0, 72.9, 72.8, 43.5, 35.5, 35.4, 33.1, 32.5, 28.8, 28.6, 26.3, 25.5, 23.2, 14.3, 10.7, 10.4; **HRMS (EI)**: Calcd for C₁₅H₂₄O: 220.1827; found: 220.1829.

cyclopentyl(3,4,5-trimethoxyphenyl)methanol (2aj)



General procedure was followed with pyridin-2-yl 3,4,5-trimethoxybenzoate and cyclopentylzinc bromide (0.61 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 18 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 3/1) to afford **2aj** as a yellow solid (32.5 mg, 61%). M.P. = 69–70 °C; R_f = 0.12 (PE/EtOAc = 6/1); **1H NMR** (400 MHz, CDCl₃): δ 6.56 (s, 2H), 4.31 (d, J = 8.4 Hz, 1H), 3.85 (s, 6H), 3.82 (s, 3H), 2.17 (sext, J = 8.0 Hz, 1H), 1.92–1.84 (m, 2H), 1.68–1.36 (m, 6H), 1.24–1.12 (m, 1H); **13C NMR** (100 MHz, CDCl₃): δ 153.2, 140.4, 137.2, 103.3, 79.5, 60.9, 56.2, 47.8, 29.7, 29.6, 25.7, 25.5; **HRMS (EI)**: Calcd for C₁₅H₂₂O₄: 266.1518; found: 266.1517.

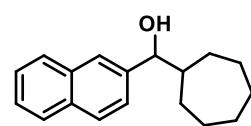
cyclohexyl(naphthalen-2-yl)methanol (2ak)



General procedure was followed with pyridin-2-yl-2-naphthoate and cyclohexylzinc bromide (0.33 M, prepared according to the general procedure B) on 0.2 mmol scale with a reaction time of 14 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2ak** as a white solid (30 mg, 63%). M.P. = 65–66 °C; R_f = 0.32 (PE/EtOAc = 10/1); **1H NMR** (400 MHz, CDCl₃): δ 7.84–7.82 (m, 3H), 7.73 (s, 1H), 7.51–7.44 (m, 3H), 4.53 (d, J = 7.2 Hz, 1H), 2.05–2.02 (m, 2H), 1.81–1.65 (m, 4H), 1.42–1.38 (m, 1H), 1.28–1.08 (m, 4H), 1.05–0.89 (m, 1H); **13C NMR** (100 MHz, CDCl₃): δ 141.2, 133.2, 133.1, 128.1, 128.0, 127.8, 126.2, 125.8, 125.6, 124.8, 79.6,

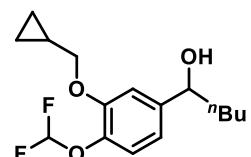
45.0, 29.5, 29.0, 26.5, 26.2, 26.1; **HRMS (EI)**: Calcd for $C_{17}H_{20}O$: 240.1514; found: 240.1510. The spectral data are consistent with those reported in the literature.^[32]

cycloheptyl(naphthalen-2-yl)methanol (2al)



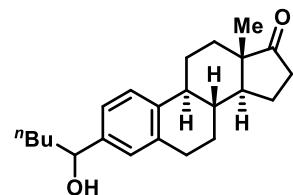
General procedure was followed with pyridin-2-yl-2-naphthoate and cycloheptylzinc bromide (0.65 M, prepared according to the general procedure C) on 0.2 mmol scale with a reaction time of 4 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **2al** as a white solid (30.2 mg, 59%). M.P. = 46–47 °C; R_f = 0.36 (PE/EtOAc = 10/1); **1H NMR** (400 MHz, $CDCl_3$): δ 7.85–7.81 (m, 3H), 7.75 (s, 1H), 7.52–7.45 (m, 3H), 4.62 (d, J = 6.4 Hz, 1H), 2.03 (s, 1H), 1.99–1.91 (m, 2H), 1.73–1.35 (m, 10H), 1.29–1.18 (m, 1H); **13C NMR** (100 MHz, $CDCl_3$): δ 141.4, 133.2, 133.0, 128.1, 128.0, 127.8, 126.2, 125.8, 125.6, 124.8, 79.4, 46.3, 31.3, 29.3, 28.6, 28.4, 26.8, 26.7; **HRMS (EI)**: Calcd for $C_{18}H_{22}O$: 254.1671; found: 254.1669.

1-(3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl)pentan-1-ol (2am)



General procedure was followed with **1am** and *n*-butylzinc chloride (0.39 M, prepared according to the general procedure A) on 0.17 mmol scale with a reaction time of 13 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 10/1) to afford **2am** as a colorless oil (37.5 mg, 74%). R_f = 0.5 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, $CDCl_3$): δ = 7.10 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 6.84 (dd, J = 8.4, 2.0 Hz, 1H), 6.61 (t, J_{H-F} = 76.0 Hz, 1H), 4.61 (dd, J = 7.6, 6.0 Hz, 1H), 3.87 (d, J = 6.8 Hz, 2H), 2.03 (bs, 1H), 1.78–1.61 (m, 2H), 1.41–1.20 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H), 0.66–0.61 (m, 2H), 0.36–0.33 (m, 2H), 0.07 (s, 1H); **13C NMR** (100 MHz, $CDCl_3$): δ 150.6, 143.9, 139.6, 122.6, 118.6, 116.4 (t, J_{C-F} = 257.7 Hz), 111.9, 74.3, 74.0, 39.0, 28.0, 22.7, 14.1, 10.3, 3.3, 1.1; **19F NMR** (376 MHz, $CDCl_3$): δ -81.6 (d, J = 75.6 Hz, 2F); **HRMS (EI)**: Calcd for $C_{16}H_{22}F_2O_3$: 300.1537; found: 300.1534.

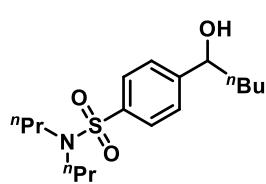
(8R,9S,13S,14S)-3-(1-hydroxypentyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (2an)



General procedure was followed with **1an** and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.08 mmol scale with a reaction time of 14 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **2an** as a colorless oil (15.2 mg, 56%). R_f = 0.39 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, $CDCl_3$): δ 7.29 (s, 0.4H), 7.27 (s, 0.8H), 7.14–7.09 (m, 2H), 4.60 (dd, J = 7.6, 6.0 Hz, 1H), 2.93 (dd, J = 8.8, 4.0 Hz, 2H), 2.54–2.41 (m, 2H), 2.30 (td, J = 11.2, 4.0 Hz, 1H), 2.19–1.94 (m, 4H), 1.84–1.25 (m, 13H), 0.91 (s, 3H), 0.89 (t, J = 7.2 Hz, 3H); **13C NMR** (100 MHz, $CDCl_3$): 221.1, 142.6, 139.1, 136.7, 136.7, 126.6, 126.6, 125.6, 125.6,

123.5, 123.5, 74.6, 74.5, 50.6, 48.1, 44.5, 38.8, 38.8, 38.3, 38.3, 36.0, 31.7, 29.6, 29.6, 28.3, 26.7, 25.9, 22.8, 21.7, 14.2, 14.0; **HRMS (EI)**: Calcd for $C_{23}H_{32}O_2$: 340.2402; found: 340.2410.

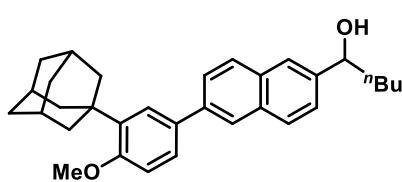
4-(1-hydroxypentyl)-N,N-dipropylbenzenesulfonamide (2ao)



General procedure was followed with **1ao** and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.2 mmol scale with a reaction time of 6 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **2ao** as a colorless oil (56.1 mg, 86%).

R_f = 0.36 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 4.70 (dd, J = 7.2, 6.0 Hz, 1H), 3.02 (t, J = 8.0 Hz, 4H), 2.42 (s, 1H), 1.78–1.61 (m, 2H), 1.51 (sext, J = 7.2 Hz, 4H), 1.38–1.19 (m, 4H), 0.85 (t, J = 7.2 Hz, 3H), 0.83 (t, J = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 149.8, 138.7, 127.1, 126.5, 73.8, 50.1, 39.0, 27.8, 22.6, 22.1, 14.0, 11.2; **HRMS (EI)**: Calcd for $C_{17}H_{29}NO_3S$: 327.1868; found: 327.1870.

1-(6-(3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)pentan-1-ol (2ap)



General procedure was followed with **1ap** and *n*-butylzinc chloride (0.42 M, prepared according to the general procedure A) on 0.095 mmol scale with a reaction time of 11 hours. The reaction mixture was purified by flash column chromatography (silica gel,

PE/EtOAc = 10/1) to afford **2ap** as a white solid (34.2 mg, 79%). M.P. = 132–133 °C; R_f = 0.29 (PE/EtOAc = 5/1); **1H NMR** (400 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.88 (dd, J = 8.4, 4.8 Hz, 2H), 7.78 (s, 1H), 7.75 (dd, J = 8.4, 1.6 Hz, 1H), 7.62 (d, J = 2.4 Hz, 1H), 7.54 (dd, J = 8.4, 2.4 Hz, 1H), 7.50 (dd, J = 8.4, 1.6 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 4.84 (t, J = 6.8 Hz, 1H), 3.91 (s, 3H), 2.21 (s, 6H), 2.13 (s, 3H), 1.96–1.88 (m, 3H), 1.83 (s, 6H), 1.46–1.26 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): 8158.7, 142.0, 139.0, 139.0, 133.4, 133.2, 132.2, 128.5, 128.4, 126.1, 126.0, 125.7, 124.9, 124.6, 124.5, 112.2, 75.0, 55.3, 40.7, 38.8, 37.3, 37.3, 29.2, 28.1, 22.8, 14.2; **HRMS (EI)**: Calcd for $C_{32}H_{38}O_2$: 454.2872; found: 454.2873.

Mechanistic Studies

Dynamic experiment for tandem nickel-catalyzed cross-coupling reaction of 2-pyridyl ester with alkyl zinc reagent

A flame-dried Schlenk tube was charged with aryl 2-pyridyl ester (0.3 mmol, 1.0 equiv) and $\text{Ni}(\text{acac})_2$ (0.03 mmol, 10 mol%), dodecane (10.0 μL , 0.044 mmol) subjected to three evacuation/backfilling cycles under vacuum and cooled to 0 $^{\circ}\text{C}$. A solution of $^{\text{t}}\text{BuZnCl}$ (0.9 mmol, 3.0 equiv) and DMF (1.5 mL) was added in sequence. The reaction mixture was stirred at 0 $^{\circ}\text{C}$ for 5 min, moved to room temperature to stir for 5 min and then heated under 50 $^{\circ}\text{C}$ for 6 h. The reaction was started to be monitored at 1 min, 3 min, 5 min, 10 min, 30 min, 60 min, 2 h, 3 h (checked by GC analysis of reaction aliquots). The corresponding curves of ketone intermediate (**3a**), and desired product 1-phenylpentan-1-ol (**2a**) were depicted in the following graph (Figure S1). The starting material was consumed within 1 min to generate the ketone intermediate **3a**, which was converted into **2a** when extending the reaction time as observed by GC.

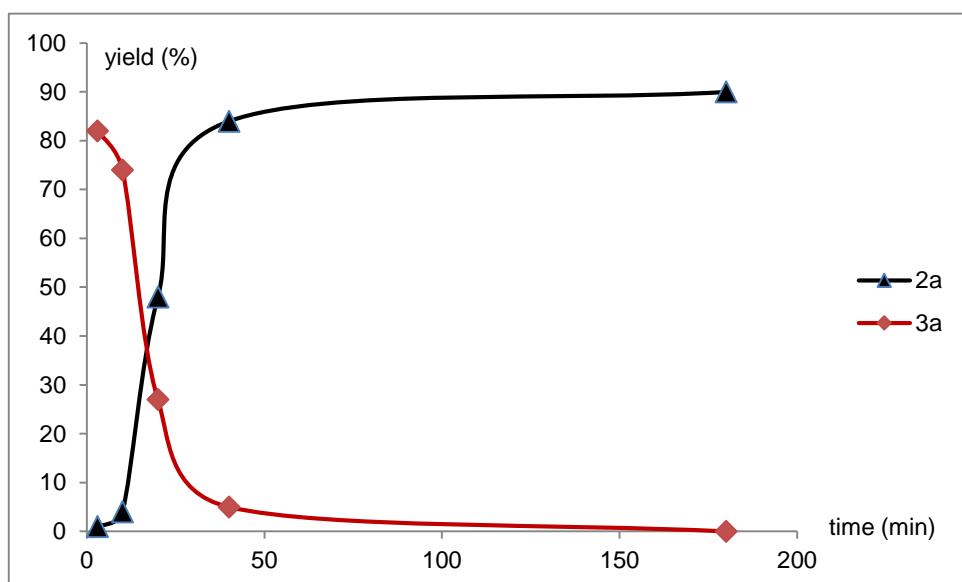


Figure S1. Curves of dynamic experiment via normal addition sequence

To observe the variation of starting material in the reaction mixture, the addition sequence of Negishi reagent and DMF is reversed to slow down the reaction rate. The reaction was started to be monitored at 20 s, 50 s, 80 s, 2 min, 3 min, 6 min, 10 min, 30 min, 1 h, 3 h (checked by GC analysis of reaction aliquots). The corresponding curves of aryl 2-pyridyl ester (**1a**), ketone intermediate (**3a**), and desired product 1-phenylpentan-1-ol (**2a**) were depicted in the following graph (Figure S2). The starting material could be observed within 1 min and consumed all after 1 min. In contrast to the above result, reversing the addition sequence of Negishi reagent and DMF could somehow diminished the yield.

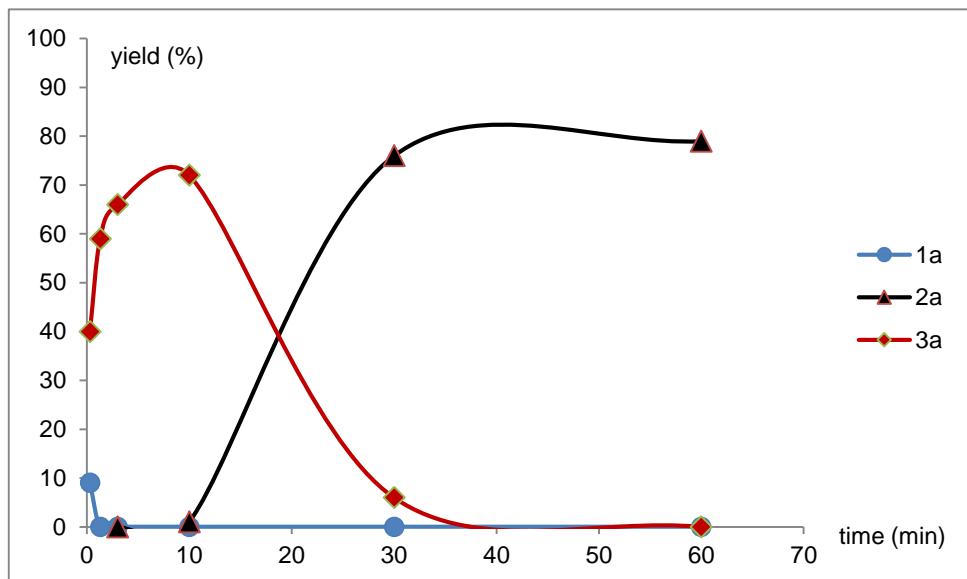
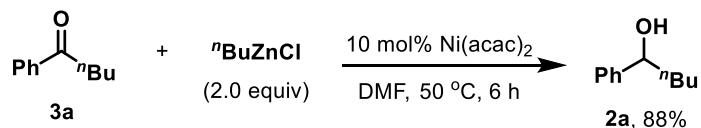


Figure S2. Curves of dynamic experiment via reversing addition sequence

The kinetic data reveals that Negishi cross coupling proceeds extremely fast even at lower temperature. The transformation of ketone **3a** to secondary benzylic alcohol **2a** excludes the possibility of aldehyde intermediate formation as depicted in scheme 1c in the text.

Control reaction without addition of Ni(acac)₂ or ZnCl₂

1) The directed reduction of ketone using ⁿBuZnCl as Ni-H precursor



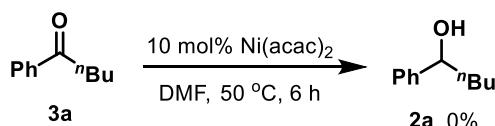
A flame-dried Schlenk tube was charged with 1-phenylpentan-1-one **3a** (0.1 mmol, 1.0 equiv) and Ni(acac)₂ (0.01 mmol, 10 mol%), subjected to three evacuation/backfilling cycles under vacuum and cooled to 0 °C. A solution of ⁿBuZnCl (0.2 mmol, 2.0 equiv) and DMF (1.5 mL) was added in sequence. Dodecane (10.0 μL, 0.044 mmol) as the internal standard was added to determine the GC yield. Then the tube was sealed with parafilm, equipped with a balloon filled with N₂, and allowed to stir 6 h at 50 °C. The mixture was quenched with sat. aq. NH₄Cl and diluted with EtOAc. GC analysis was conducted by using an aliquot of the resulting organic phase. The product **2a** was obtained in 88% GC corrected yield, suggesting the highly possibility for ketone intermediate **3a** in the reaction process

2) Control reaction without addition of Ni(acac)₂



A flame-dried Schlenk tube was charged with 1-phenylpentan-1-one **3a** (0.1 mmol, 1.0 equiv) and subjected to three evacuation/backfilling cycles under vacuum and cooled to 0 °C. A solution of ⁿBuZnCl (0.2 mmol, 2.0 equiv) and DMF (1.5 mL) was added in sequence. Dodecane (10.0 μL, 0.044 mmol) as the internal standard was added to determine the GC yield. Then the tube was sealed with Parafilm, equipped with a balloon filled with N₂, and allowed to stir 6 h at 50 °C. The mixture was quenched with sat. aq. NH₄Cl and diluted with EtOAc and was conducted on GC by using an aliquot of the resulting organic phase. The product **2a** was not observed on the GC analysis, implying the importance of the nickel catalyst in the reduction step.

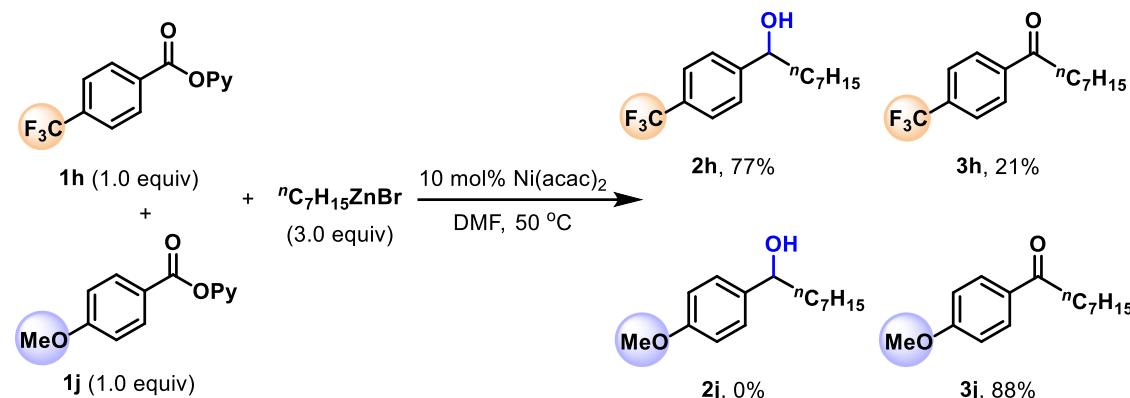
3) Control reaction without addition of ZnCl₂



A flame-dried Schlenk tube was charged with 1-phenylpentan-1-one **3a** (0.1 mmol, 1.0 equiv) and Ni(acac)₂ (0.01 mmol, 10 mol%), subjected to three evacuation/backfilling cycles under vacuum and DMF (1.5 mL) was added. Dodecane (10.0 μL, 0.044 mmol) as the internal standard was added to determine the GC yield. Then the tube was sealed with Parafilm, equipped with a balloon filled with N₂, and allowed to stir 6 h at 50 °C. The mixture was quenched with sat. aq. NH₄Cl, diluted

with EtOAc, and conducted on GC by using an aliquot of the resulting organic phase. The product **2a** was not observed on the GC analysis, indicating that the hydride species likely arise from the Negishi reagents.

Competition experiment using electron-rich and electron-deficient aromatic 2-pyridyl ester



To a flame-dried Schlenk tube was added pyridin-2-yl 4-(trifluoromethyl)benzoate (**1h**, 26.7 mg, 0.10 mmol), pyridin-2-yl 4-methoxybenzoate (**1j**, 22.9 mg, 0.10 mmol), $\text{Ni}(\text{acac})_2$ (5.2 mg, 0.02 mmol). Dodecane (10.0 μL , 0.044 mmol) as the internal standard was added to determine the GC yield. The tube was placed at 0 $^\circ\text{C}$, evacuated and refilled with N_2 (repeat three times). Then $n\text{C}_7\text{H}_{15}\text{ZnBr}$ (0.59 M, 0.52 mL, 0.30 mmol) was added, following by DMF (1.6 mL). Then the tube was sealed with Parafilm, equipped with a balloon filled with N_2 , and allowed to stir 5 h at 50 $^\circ\text{C}$. The mixture was quenched with sat. aq. NH_4Cl and extracted with EtOAc , GC analysis was conducted by using an aliquot of the resulting organic phase. The separated organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated under the vacuum to give the crude mixture. To the mixture was added CH_2Br_2 (7.0 μL , 0.10 mmol) as an internal standard. ^1H NMR analysis was conducted by using this crude mixture.

As depicted in the GC spectrum, the characteristic peaks of **2h**, **3h**, **3j**, dodecane and homocoupling product $\text{C}_{14}\text{H}_{30}$ from Negishi reagent were observed on GC analysis (Figure S3). ^1H NMR's result shows that benzylic alcohol product **2h** was formed with a yield of 77% while benzylic alcohol **2j** was not observed; moreover, ketone intermediate **3j** resulting from ester **1j** was the main product yielding 88% whereas **3h** was obtained with a yield of 21% (Figure S4). These distributions suggested that Ni-H reduction step preferred the electron deficient substituted aryl ketone intermediate.

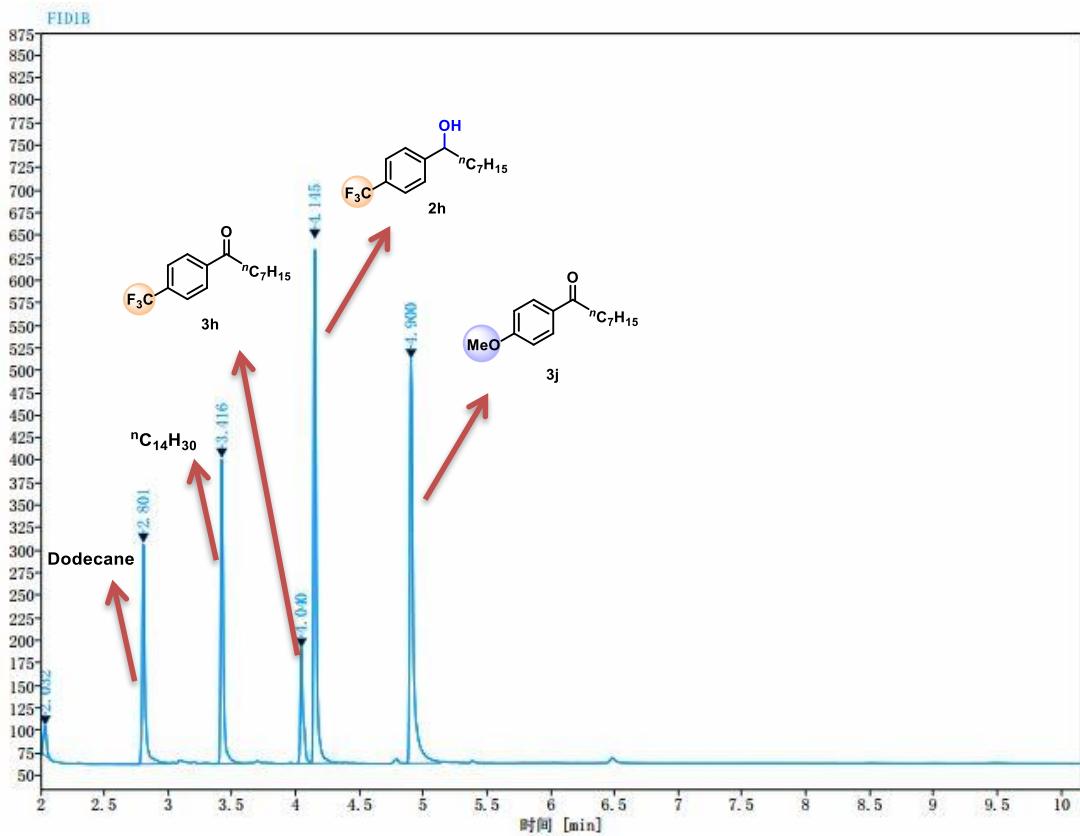


Figure S3. GC spectrum of a reaction mixture in EtOAc

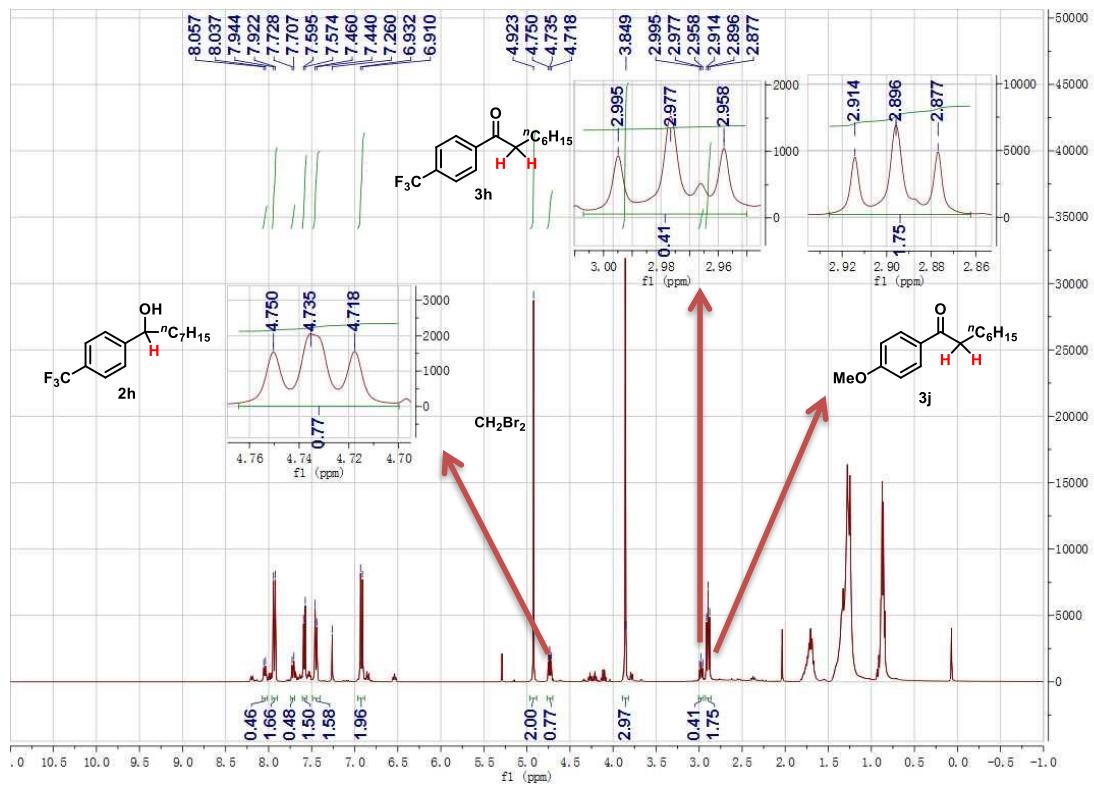
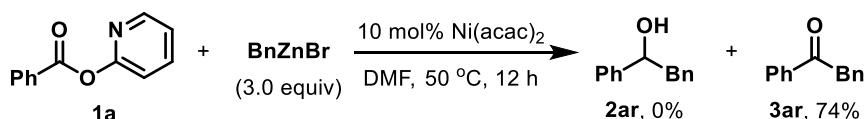


Figure S4. ^1H NMR spectrum of a reaction mixture in CDCl_3

Verification of the formation and identity of the Ni–H intermediate



To check whether β -H functioned in the reduction process, BnZnBr was used as nucleophile: An oven-dried Schlenk tube equipped with a stir bar was charged with aryl 2-pyridyl ester (0.2 mmol, 1.0 equiv) and Ni(acac)₂ (0.02 mmol, 10 mol%), subjected to three evacuation/backfilling cycles under vacuum and cooled to 0 °C. A solution of BnZnBr (0.6 mmol, 3.0 equiv) and DMF (1.0 mL) was added in sequence. Then the tube was sealed with Parafilm, equipped with a balloon filled with N₂, and allowed to stir 12 h at 50 °C. The mixture was quenched with sat. aq. NH₄Cl and extracted with EtOAc. The separated organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated under the vacuum to give the crude mixture. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 60/1) to afford **3ar** as a colorless oil (29.3 mg, 74%). R_f = 0.50 (PE/EtOAc = 20/1); **1H NMR** (400 MHz, CDCl₃): δ 8.0 (d, J = 7.2 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.2 Hz, 2H), 7.23–7.26 (m, 3H), 4.27 (s, 2H); **13C NMR** (100 MHz, CDCl₃): δ 197.6, 136.7, 134.6, 133.3, 129.6, 128.8, 128.8, 128.7, 127.0, 45.6; The spectral data are consistent with those reported in the literature.^[33] The result that benzyl ketone **3ar** was formed as the single product, while the desired product **2ar** was not observed demonstrated that lack of a β -H in the benzyl nucleophile precludes β -H elimination, which is necessary for formation of the Ni–H species.

Reference

- (1) Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890.
- (2) Tatamidani, H.; Kakiuchi, F.; Chatani, N. *Org. Lett.* **2004**, *6*, 3597.
- (3) Nakanishi, J.; Tatamidani, H.; Fukumoto, Y.; Chatani, N. *Synlett* **2006**, 869.
- (4) Peduto, A.; Scuotto, M.; Krauth, V.; Roviezzo, F.; Rossi, A.; Temml, V.; Esposito, V.; Stuppner, H.; Schuster, D.; D'Agostino, B.; Schiraldi, C.; De Rosa, M.; Werz, O.; Filosa, R. *Eur J Med Chem.* **2017**, *127*, 715.
- (5) Kirchhoff, J. H.; Netherton, M. R.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662.
- (6) Wilson, M. R.; Solà, J.; Carbone, A.; Goldup, S. M.; Lebrasseur, N.; Leigh, D. A. *Nature* **2016**, *534*, 235.
- (7) MacMillan, J. B.; Molinski, T. F. *J. Am. Chem. Soc.* **2004**, *126*, 9944.
- (8) Yang, B.; Lu, Z. *J. Org. Chem.* **2016**, *81*, 7288.
- (9) Guo, L.; Chatupheeraphat, A.; Rueping, M. *Angew. Chem., Int. Ed.* **2016**, *55*, 11810.
- (10) Kaithal, A.; Chatterjee, B.; Gunanathan, C. *Org. Lett.* **2016**, *18*, 3402.
- (11) Giudice, M. R. D.; Settimj, G. Delfini, M. *Tetrahedron* **1984**, *40*, 4067.
- (12) Fife, T. H.; Przystas, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 7297.
- (13) Sharada, D. S.; Muresan, A. Z.; Muthukumaran, K.; Lindsey, J. S. *J. Org. Chem.* **2005**, *70*, 3500.
- (14) Chen, P.-Z.; Weng, Y.-X.; Niu, L.-Y.; Chen, Y.-Z.; Wu, L.-Z.; Tung, C.-H.; Yang, Q.-Z. *Angew. Chem., Int. Ed.* **2016**, *55*, 2759.
- (15) Gensini, M.; Altamura, M.; Dimoulas, T.; Fedi, V.; Giannotti, D.; Giuliani, S.; Guidi, A.; Harmat, N. J. S.; Meini, S.; Nannicini, R.; Pasqui, F.; Tramontana, M.; Triolo, A.; Maggi, C. A. *ChemMedChem.* **2010**, *5*, 65.
- (16) Kalsi, D.; Barsu, N.; Sundararaju, B. *Chem. Eur. J.* **2018**, *24*, 2360.
- (17) Szczepankiewicz, B. G.; Liu, G.; Jae, H.-S.; Tasker, A. S.; Gunawardana, I. W.; Von Geldern, T. W.; Gwaltney, S. L.; Wu-Wong, J. R.; Gehrke, L.; Chiou, W. J.; Credo, R. B.; Alder, J. D.; Nukkala, M. A.; Zielinski, N. A.; Jarvis, K.; Mollison, K. W.; Frost, D. J.; Bauch, J. L.; Hui, Y. H.; Claiborne, A. K.; Li, Q.; Rosenberg, S. H. *J. Med. Chem.* **2001**, *44*, 4416.
- (18) Nicolaï, E.; Güngör, T.; Goyard, J.; Cure, G.; Fouquet, A.; Teulon, JM.; Delchambre, C.; Cloarec, A. *Eur J Med Chem.* **1992**, *27*, 977.
- (19) Van der Born, D.; Sewing, C.; Herscheid, J. (Koos) D. M.; Windhorst, A. D.; Orru, R. V. A.; Vugts, D. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 11046.
- (20) Cacchi, S.; Lupi, A. *Tetrahedron Lett.* **1992**, *33*, 3939.
- (21) Shing, K.-P.; Liu, Y.; Cao, B.; Chang, X.-Y.; You, T.; Che, C.-M. *Angew. Chem., Int. Ed.* **2018**, *57*, 11947.
- (22) Smith III, A. B.; Tong, R.; Kim, W.-S.; Maio, W. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 8904.
- (23) Paptchikhine, A.; Itto, K.; Andersson, P. G. *Chem. Commun.* **2011**, *47*, 3989.
- (24) Chen, T.; Jiang, J.-J.; Xu, Q.; Shi, M. *Org. Lett.* **2007**, *9*, 865.
- (25) Freitag, F.; Irrgang, T.; Kempe, R. *Chem. Eur. J.* **2017**, *23*, 12110.
- (26) Bouffard, J.; Itami, K. *Org. Lett.* **2009**, *11*, 4410.

(27) Yang, J.; Chen, X.; Wang, Z. *Tetrahedron Lett.* **2015**, *56*, 5673.

(28) Jakhar, V. K.; Barman, M. Kr.; Nembenna, S. *Org. Lett.* **2016**, *18*, 4710.

(29) Wang, Q.; Wu, K.; Yu, Z. *Organometallics* **2016**, *35*, 1251.

(30) Almeida, A. R.; Dias, R. D.; Monteiro, C. J. P.; Abreu, A. R.; Gois, P. M. P.; Bayon, J. C.; Pereira, M. M. *Adv. Synth. Catal.* **2014**, *356*, 1223.

(31) Xu, Q.; Chen, J.; Tian, H.; Yuan, X.; Li, S.; Zhou, C.; Liu, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 225.

(32) Yang, Y.-X.; Liu, Y.; Zhang, L.; Jia, Y.-E.; Wang, P.; Zhuo, F.-F.; An, X.-T.; Da, C.-S. *J. Org. Chem.* **2014**, *79*, 10696.

(33) Su, Y.; Petersen, J. L.; Gregg, T. L.; Shi, X. *Org. Lett.* **2015**, *17*, 1208.

NMR Spectras

