Supporting Information

Ruthenium-Catalyzed Benzylic Substitution of Benzyl Esters with Stabilized Carbon Nucleophiles

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1. General experimental remarks

Commercially available chemicals were purchased from Aldrich, TCI, Kanto, and Wako and used without further purification unless otherwise noted. Benzyl 2,3,4,5,6-pentafluorobenzoates \( \textbf{1a, 1b, 1f, 1h, 1i, 1j, and 1k} \) were prepared according to the our previously reported method.\(^1\) Ruthenium(III) chloride hydrate was purchased from Oakwood chemical. \([\text{Cp}^*\text{RuCl}_2]_2\) was prepared according to the literature.\(^2\) NMR spectra were recorded at 25 °C on a JEOL EX-270 spectrometer (270 MHz for \(^1\)H, 67.9 MHz for \(^{13}\)C) or a JEOL JNM ECP-500 spectrometer (500 MHz for \(^1\)H, 126 MHz for \(^{13}\)C, 471 MHz for \(^{19}\)F). Chemical shifts are reported in δ ppm referenced to an internal tetramethylsilane (0 ppm) for \(^1\)H NMR. Chemical shifts of \(^{13}\)C NMR are given relative to the solvent peak as an internal standard. \(^{19}\)F NMR data are reported relative to external \(\alpha,\alpha,\alpha\)-trifluorotoluene (−63.7 ppm). Multiplicities are indicated as br (broad), s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Coupling constants \((J)\) are reported in Hertz (Hz). Melting points were measured on a Yanako MP-500P. Infrared (IR) spectra were recorded on JASCO FT/IR–400 plus. GC-MS measurements were carried out with JEOL JMS-Q1000GC/K9. HRMS analyses were carried out using a JEOL AccuTOF LCplus for ESI-MS and APCI-MS, Waters G2-S Q-Tof for ESI-MS, and JEOL GCmate for EI-MS. Column chromatography and preparative thin-layer chromatography were conducted with silica gel 60N (KANTO CHEMICAL, spherical, neutral, 40-50 or 63-210 µm) and Wakogel® B-5F (45 µm), respectively. For thin-layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 F254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), phosphomolybdic acid, and I\(_2\)/SiO\(_2\).

2. General procedure for the preparation of benzyl 2,3,4,5,6-pentafluorobenzoates \(1\text{c–e and 1g}\)

\textbf{Scheme S1. Preparation of benzyl 2,3,4,5,6-pentafluorobenzoate 1c}

\[ \begin{align*}
\text{HO} & \quad \text{PivCl (1.2 equiv)} & \quad \text{Et}_3\text{N (10 equiv)} & \quad \text{DMAP (0.05 equiv)} & \quad \text{CH}_2\text{Cl}_2, 0 °C to rt \\
\text{S1} & \quad \text{NaBH}_4 (1.2 equiv) & \quad \text{MeOH, 0 °C to rt} \\
\text{PivO} & \quad \text{1c} & \quad \text{PivO} & \quad \text{1c'} & \quad \text{PivO} & \quad \text{OC(O)C}_6\text{F}_5 \\
\end{align*} \]
Preparation of 6-formylnaphthalen-2-yl pivalate (S1):
6-Hydroxy-2-naphthaldehyde (861 mg, 5.00 mmol) and DMAP (30.5 mg, 0.25 mmol, 0.05 equiv) were charged into a round flask and the flask was refilled with N₂. CH₂Cl₂ (10 mL) and triethylamine (7.0 mL, 50 mmol, 10 equiv) were added to the flask. Pivaroyl chloride (0.74 mL, 6.0 mmol, 1.2 equiv) was added dropwise to the mixture at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was quenched with water and the resulting aqueous phase was extracted with CH₂Cl₂ (70 mL×3). The combined organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography to give 6-formylnaphthalen-2-yl pivalate (S1) as a white solid (1.10 g, 4.29 mmol, 86% yield).

M.p. 98.3–99.6 °C; IR (KBr) 2983, 2876, 1745, 1692, 1472, 1105, 913, 817 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.42 (s, 9H), 7.32 (dd, J = 8.9, 2.2 Hz, 1H), 7.61 (d, J = 2.2 Hz, 1H), 7.89 (d, J = 8.6 Hz, 1H), 7.97 (dd, J = 8.6, 1.6 Hz, 1H), 8.02 (d, J = 8.9 Hz, 1H), 8.34 (s, 1H), 10.1 (s, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 27.1, 39.2, 118.8, 122.5, 123.5, 128.7, 130.4, 131.0, 133.9, 134.1, 137.1, 151.3, 176.9, 192.0; HRMS (APCI/TOF) m/z: [M+H]+ Calcd for C₁₆H₁₇O₃ 257.1178; Found 257.1187.

Preparation of 6-(hydroxymethyl)naphthalen-2-yl pivalate (1c’):
NaBH₄ (174 mg, 4.60 mmol, 1.2 equiv) was added to a solution of 6-formylnaphthalen-2-yl pivalate (S3) (981 mg, 3.8 mmol) in MeOH (13 mL) at 0 °C. The resulting mixture was stirred for 2 h at room temperature. MeOH was removed by evaporation and the resulting mixture was transferred to a separating funnel with EtOAc and water. The aqueous phase was extracted with EtOAc (80 mL×2). The combined organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 5/1, 4/1, 10/3, 20/7) to give 6-(hydroxymethyl)naphthalen-2-yl pivalate (1c’) as a white solid (458 mg, 1.77 mmol, 47% yield).
M.p. 126.3–127.4 °C; IR (KBr) 3326, 2962, 2932, 2871, 1749, 1476, 1279, 1150, 1030, 906, 816 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.40 (s, 9H), 1.72 (bs, 1H), 4.85 (s, 2H), 7.20 (dd, J = 8.9, 2.4 Hz, 1H), 7.48 (dd, J = 8.2, 1.8 Hz, 1H), 7.52 (d, J = 2.4 Hz, 1H), 7.77–7.84 (m, 3H); ¹³C NMR (67.9 MHz, CDCl₃): δ 27.1, 39.1, 65.1, 118.2, 121.4, 125.2, 125.8, 127.9, 129.2, 131.2, 133.2, 138.1, 148.7, 177.3; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₁₆H₁₈O₃Na 281.1154; Found 281.1152.

Preparation of (6-(pivaloyloxy)naphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1c):

6-(Hydroxymethyl)naphthalen-2-yl pivalate (1c') (450 mg, 1.74 mmol) and DMAP (21.3 mg, 0.174 mmol, 0.1 equiv) were charged into a round flask and the flask was refilled with N₂. THF (6 mL) and triethylamine (0.36 mL, 2.60 mmol, 1.5 equiv) were added to the flask. Pentafluorobenzoyl chloride (0.30 mL, 1.91 mmol, 1.1 equiv) was added dropwise to the mixture at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 20 min. The reaction was quenched with water and the resulting aqueous phase was extracted with EtOAc (50 mL × 2). The combined organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 95/5, 92/8, 9/1) to give (6-(pivaloyloxy)naphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1c) as a white solid (643 mg, 1.42 mmol, 84% yield).

M.p. 114.9–115.4 °C; IR (KBr) 2983, 2876, 1756, 1731, 1655, 1498, 1322, 1230, 1140, 1013, 907, 810 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 1.41 (s, 9H), 5.56 (s, 2H), 7.23 (dd, J = 8.5, 2.3 Hz, 1H), 7.53 (dd, J = 8.0, 1.5 Hz, 1H), 7.54 (d, J = 2.3 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H), 7.90 (s, 1H); ¹³C NMR (126 MHz, CDCl₃): δ 27.1, 39.1, 68.4, 108.0 (m), 118.3, 121.8, 126.4, 127.6, 128.3, 129.4, 131.0, 131.7, 133.7, 137.7 (dm, J CF = 256 Hz), 143.3 (dm, J CF = 261 Hz), 145.5 (dm, J CF = 258 Hz), 149.4, 158.9, 177.1; ¹⁹F NMR (471 MHz, CDCl₃): δ -138.7 – -138.8 (m,
2F), -149.1 (tt, J = 21.2, 4.9 Hz, 1F), -161.1 – -161.2 (m, 2F); HRMS (EI) m/z: [M]⁺ Calcd for C₂₃H₁₇O₄F₅ 452.1047; Found 452.1047.

**Scheme S2. Preparation of benzyl 2,3,4,5,6-perfluorobenzoate 1d**

Preparation of tert-butyl (6-formynaphthalen-2-yl) carbonate (S2):
6-Hydroxy-2-naphthaldehyde (861 mg, 5.00 mmol) and DMAP (61.1 mg, 0.50 mmol, 0.1 equiv) were charged into a round flask and the flask was refilled with N₂. CH₂Cl₂ (10 mL) was added to the flask. A solution of Boc₂O (1.09 g, 5.00 mmol, 1.0 equiv) in CH₂Cl₂ was added dropwise to the resulting mixture at 0 °C. After stirring the reaction mixture at room temperature for 1 h, the reaction was quenched with water and the resulting aqueous phase was extracted with CH₂Cl₂ (80 mL×2). The combined organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 9/1, 85/15) to give tert-butyl (6-formynaphthalen-2-yl) carbonate (S2) as a white solid (1.23 g, 4.52 mmol, 90% yield).

**S2**  M.p. 105.7–106.8 °C; IR (KBr) 2979, 2942, 2863, 1751, 1693, 1476, 1374, 1288, 1257, 1147, 899, 823, 778 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.60 (s, 9H), 7.43 (dd, J = 8.9, 2.3 Hz, 1H), 7.73 (d, J = 2.3 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.97 (dd, J = 8.6, 1.4 Hz, 1H), 8.02 (d, J = 8.9 Hz, 1H), 8.34 (s, 1H), 10.1 (s, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 27.7, 84.1, 118.4, 122.2, 123.5, 128.8, 130.4, 131.0, 133.9, 134.0, 137.0, 151.1, 151.5, 191.9; HRMS (APCI/TOF) m/z: [M+H]⁺ Calcd for C₁₆H₁₇O₄ 273.1127; Found 273.1120.
Preparation of (6-((tert-butoxycarbonyl)oxy)naphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1d):

NaBH$_4$ (182 mg, 4.80 mmol, 1.2 equiv) was added to a solution of tert-butyl (6-formylnaphthalen-2-yl) carbonate (S2) (1.10 g, 4.0 mmol) in MeOH (13 mL) at 0 °C. The resulting mixture was stirred overnight at room temperature. MeOH was removed by evaporation and the resulting mixture was transferred to a separating funnel with EtOAc and water. The aqueous phase was extracted with EtOAc (80 mL×2). The combined organic phase was washed with brine and dried over MgSO$_4$. After removal of the solvent, alcohol 1d' was obtained as a crude mixture and this mixture was used next step without further purification. The crude mixture and DMAP (49.0 mg, 0.40 mmol, 0.1 equiv) were placed in a round flask and refilled with N$_2$. THF (12 mL) and triethylamine (0.82 mL, 5.90 mmol, 1.5 equiv) were added to the flask. Pentafluorobenzoyl chloride (0.60 mL, 4.30 mmol, 1.1 equiv) was added dropwise to the mixture at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched with water and the resulting aqueous phase was extracted with EtOAc (80 mL×3). The combined organic phase was washed with brine and dried over MgSO$_4$. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 92/8, 9/1, 88/12) to give (6-((tert-butoxycarbonyl)oxy)naphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1d) as a white solid (1.50 g, 3.20 mmol, 82% yield).

M.p. 107.6–109.8 °C; IR (KBr) 2985, 2936, 1752, 1739, 1651, 1496, 1325, 1226, 1142, 1005, 895 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.59 (s, 9H), 5.55 (s, 2H), 7.35 (dd, $J = 8.5, 2.5$ Hz, 1H), 7.53 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.66 (d, $J = 2.5$ Hz, 1H), 7.84 (d, $J = 9.0$ Hz, 1H), 7.86 (d, $J = 9.0$ Hz, 1H), 7.89 (s, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 27.7, 68.4, 83.8, 108.0 (m), 1105, 1196, 1232, 1264, 127.6, 128.4, 1295, 131.0, 131.8, 133.6, 137.7 (dm, $J_{CF} = 256$ Hz), 143.3 (dm, $J_{CF} = 261$ Hz), 145.5 (dm, $J_{CF} = 262$ Hz), 149.3, 151.8, 158.9; $^{19}$F NMR (471 MHz, CDCl$_3$): $\delta$ -138.7– -138.8 (m, 2F), 149.1 (tt, $J = 20.7, 4.8$ Hz, 1F), -161.1– -161.2 (m, 2F); HRMS (ESI/QTOF) [M+Na]$^+$ Calcd for C$_{23}$H$_{17}$F$_5$O$_5$Na, 491.0894; Found 491.0897.
**Scheme S3. Preparation of benzyl 2,3,4,5,6-perfluorobenzoate 1e**

Preparation of 6-((tert-butyldimethylsilyl)oxy)-2-naphthaldehyde (S3):

6-Hydroxy-2-naphthaldehyde (861 mg, 5.00 mmol), TBSCI (829 mg, 5.50 mmol, 1.1 equiv), and DMAP (24.4 mg, 0.20 mmol, 0.04 equiv) were charged into a round flask and the flask was refilled with N₂. CH₂Cl₂ (17 mL) and triethylamine (0.8 mL, 5.5 mmol, 1.1 equiv) were added to the flask. The resulting mixture was stirred at room temperature for 3 hours. The reaction was quenched with water and the resulting aqueous phase was extracted with CH₂Cl₂ (80 mL × 2). The combined organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 95/5, 9/1) to give 6-((tert-butyldimethylsilyl)oxy)-2-naphthaldehyde (S3) as a white solid (1.29 g, 4.50 mmol, 90% yield).

**S3**

M.p. 46.9–48.1 °C; IR (KBr) 2958, 2928, 2855, 1686, 1622, 1475, 1264, 1168, 873, 816, 778 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 0.28 (s, 6H), 1.03 (s, 9H), 7.17 (dd, J = 8.8, 2.2 Hz, 1H), 7.23 (d, J = 2.2 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.88–7.92 (m, 2H), 8.26 (s, 1H), 10.1 (s, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ -4.36, 18.2, 25.6, 115.1, 123.2, 127.6, 128.1, 131.2, 132.4, 134.4, 138.1, 156.5, 192.0, one peak for aromatic carbon was not found probably due to overlapping; HRMS (ESI/TOF) m/z: [M+H]⁺ Calcd for C₁₇H₂₃O₂Si 287.1467; Found 287.1463.
Preparation of (6-((tert-butyldimethylsilyl)oxy)naphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1e):

NaBH$_4$ (182 mg, 4.80 mmol, 1.2 equiv) was added to a solution of 6-((tert-butyldimethylsilyl)oxy)-2-naphthaldehyde (S3) in MeOH (13 mL) at 0 °C. The resulting mixture was stirred for 2 h at room temperature. MeOH was removed by evaporation and the resulting mixture was transferred to a separating funnel with EtOAc and water. The aqueous phase was extracted with EtOAc (60 mL×2). The combined organic phase was washed with brine and dried over MgSO$_4$. After removal of the solvent, alcohol 1e' was obtained as a crude mixture and this mixture was used next step without further purification. The crude mixture and DMAP (49.0 mg, 0.40 mmol, 0.1 equiv) were placed in a round flask and refilled with N$_2$. THF (13 mL) and triethylamine (0.8 mL, 6.00 mmol, 1.5 equiv) were added to the flask. Pentafluorobenzoyl chloride (0.6 mL, 4.40 mmol, 1.1 equiv) was added dropwise to the mixture at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 30 min. The reaction was quenched with water and the resulting aqueous phase was extracted with EtOAc (100 mL×2). The combined organic phase was washed with brine and dried over MgSO$_4$. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 97/3, 95/5) to give (6-((tert-butyldimethylsilyl)oxy)naphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1e) as a white solid (693 mg, 1.44 mmol, 36% yield).

M.p. 124.4–125.4 °C; IR (KBr) 2930, 2861, 1738, 1525, 1496, 1325, 1219, 1006, 940, 834 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ 0.25 (s, 6H), 1.02 (s, 9H), 5.52 (s, 2H), 7.11 (dd, $J = 8.8$, 2.4 Hz, 1H), 7.20 (d, $J = 2.4$ Hz, 1H), 7.46 (dd, $J = 8.3$, 1.3 Hz, 1H), 7.72 (d, $J = 9.0$ Hz, 1H), 7.74 (d, $J = 9.0$ Hz, 1H), 7.82 (s, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): δ -4.4, 18.2, 25.7, 68.8, 108.1 (m), 114.8, 122.7, 126.2, 127.4, 127.9, 128.8, 129.5, 129.7, 134.6, 137.6 (dm, $J_{CF} = 256$ Hz), 143.2 (dm, $J_{CF} = 261$ Hz), 145.4 (dm, $J_{CF} = 258$ Hz), 154.2, 158.9; $^{19}$F NMR (471 MHz, CDCl$_3$): δ -138.7 – -138.8 (m, 2F), -149.3 (tt, $J = 21.2$, 4.7 Hz, 1F), -161.2 – -161.3 (m, 2F); HRMS (EI) $m/z$: [M]$^+$ Calcd for C$_{24}$H$_{23}$O$_3$F$_5$Si 482.1336; Found 482.1340.
**Scheme S4.** Preparation of benzyl 2,3,4,5,6-perfluorobenzoate 1g

Preparation of 1-(naphthalen-2-yl)propan-1-ol (1g')³:
Magnesium turnings (219 mg, 9.00 mmol) was charged into a two-necked round flask equipped with a condenser and a dropping funnel and the equipment was refilled with N₂. After addition of a small amount of THF, a solution of bromoethane (818 mg, 0.58 mL, 7.50 mmol, 1.5 equiv) in THF (20 mL) was added dropwise to the mixture. The reaction mixture was cooled to room temperature and a solution of 2-naphthaldehyde (781 mg, 5.00 mmol) in THF (20 mL) was added to the mixture at 0 °C. The resulting mixture was stirred at room temperature for 2.5 h. The reaction was quenched with 1N HCl (20 mL) and the resulting aqueous phase was extracted with EtOAc (100 mL x 2). The combined organic phase was washed with brine, dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 85/15, 4/1) to give 1-(naphthalen-2-yl)propan-1-ol (1g') as a pale yellow oil (877 mg, 4.71 mmol, 94% yield).

\[ \text{1H NMR (270 MHz, CDCl}_3): \delta 0.93 \ (t, \ J = 7.4 \text{ Hz, } 3H), 1.75-1.95 \ (m, 2H), 1.98 \ (s, 1H), 4.74 \ (t, \ J = 6.6 \text{ Hz, } 1H), 7.42-7.51 \ (m, 3H), 7.76 \ (d, \ J = 1.4 \text{ Hz, } 1H), 7.80-7.85 \ (m, 3H); ^{13}\text{C NMR (67.9 MHz, CDCl}_3): \delta \ 10.1, 31.7, 76.1, 124.1, 124.7, 125.7, 126.1, 127.6, 127.9, 128.2, 132.9, 133.2, 141.9; \text{GC-MS (EI) m/z: 186 [M]^+}. \]

Preparation of 1-(naphthalen-2-yl)propyl 2,3,4,5,6-pentafluorobenzoate (1g):
1-(Naphthalen-2-yl)propan-1-ol (1g') (689 mg, 3.70 mmol) and DMAP (49.0 mg, 0.40 mmol, 0.1 equiv) were placed in a round flask and refilled with N₂. THF (12 mL) and
triethylamine (0.78 mL, 5.60 mmol, 1.5 equiv) were added to the flask. Pentfluorobenzoyl chloride (0.57 mL, 4.10 mmol, 1.1 equiv) was added dropwise to the mixture at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched with water and the resulting aqueous phase was extracted with EtOAc (60 mL×3). The combined organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 95/5, 9/1) to give 1-(naphthalen-2-yl)propyl 2,3,4,5,6-pentafluorobenzoate (1g) as a white solid (1.10 g, 2.89 mmol, 78% yield).

M.p. 119.0–119.8 °C; IR (KBr) 2978, 2944, 1747, 1655, 1503, 1321, 1227, 995, 957, 818, 752 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 0.99 (t, J = 7.5 Hz, 3H), 2.01–2.08 (m, 1H), 2.11–2.18 (m, 1H), 6.10 (t, J = 6.8 Hz, 1H), 7.47–7.51 (m, 3H), 7.83–7.87 (m, 4H); ¹³C NMR (126 MHz, CDCl₃): δ 9.82, 29.2, 80.7, 108.4 (m), 124.1, 126.1, 126.3 (2C), 127.7, 128.1, 128.5, 133.0, 133.2, 136.4, 137.6 (dm, J_CF = 255 Hz), 143.1 (dm, J_CF = 261 Hz), 145.4 (dm, J_CF = 258 Hz), 158.4; ¹⁹F NMR (471 MHz, CDCl₃): δ -139.0 – -139.1 (m, 2F), -149.7 (tt, J = 21.2, 4.2 Hz, 1F), -161.3 – -161.4 (m, 2F); HRMS (EI) m/z: [M]+ Caled for C₂₀H₁₃O₂F₅ 380.0835; Found 380.0835.

3. General procedure for the ruthenium-catalyzed benzylic substitution of benzyl esters with stabilized carbon nucleophiles

(6-Methoxynaphthalen-2-yl)methyl 2,3,4,5,6-pentafluorobenzoate (1a) (0.25 mmol, 95.6 mg), [Cp*RuCl₂]₂ (3.8 mg, 0.00625 mmol, 0.025 equiv), picolinic acid (L₁) (1.5 mg, 0.0125 mmol, 0.05 equiv), Cs₂CO₃ (89.6 mg, 0.275 mmol, 1.1 equiv) were charged into a screw cap vial. The resulting mixture was carefully evacuated and refilled with N₂ five times. After the addition of CH₃CN (1 mL) and diethyl methylmalonate (2a) (47 µL, 0.275 mmol, 1.1 equiv), the resulting yellow suspension was stirred at 60 °C for 18 h. The reaction was allowed to cool to room temperature and quenched with water (1 mL). The resulting aqueous phase was extracted with EtOAc (3 mL×1). The organic phase was washed with brine and dried over MgSO₄. After removal of the
solvent, the resulting crude mixture was purified by preparative thin-layer chromatography (Hexane/EtOAc = 4/1) to give diethyl 2-((6-methoxynaphthalen-2-yl)methyl)-2-methylmalonate (3aa)¹ as a pale yellow oil (76.8 mg, 0.223 mmol, 89% yield).

![Chemical Structure of 3aa]

¹H NMR (270 MHz, CDCl₃): δ 1.26 (t, J = 7.1 Hz, 6H), 1.37 (s, 3H), 3.36 (s, 2H), 3.91 (s, 3H), 4.21 (q, J = 7.1 Hz, 4H), 7.10-7.14 (m, 2H), 7.21 (dd, J = 8.4, 1.9 Hz, 1H), 7.52 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.65 (d, J = 8.6 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 14.0, 19.8, 41.0, 54.9, 55.2, 61.3, 105.4, 118.7, 126.4, 128.7, 128.8 (2C), 129.0, 131.3, 133.4, 157.4, 172.0; GC-MS (EI): m/z 344 [M⁺].

Diethyl 2-methyl-2-(naphthalen-2-ylmethyl)malonate (3ba)²

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Pentane/Et₂O = 95/5 × 2). Pale yellow oil (70.0 mg, 0.223 mmol, 89% yield); ¹H NMR (270 MHz, CDCl₃): δ 1.26 (t, J = 7.0 Hz, 6H), 1.38 (s, 3H), 3.40 (s, 2H), 4.21 (q, J = 7.0 Hz, 4H), 7.25 (dd, J = 8.4, 1.9 Hz, 1H), 7.40–7.49 (m, 2H), 7.60 (s, 1H), 7.72–7.81 (m, 3H); ¹³C NMR (67.9 MHz, CDCl₃): δ 14.0, 19.8, 41.2, 54.9, 61.3, 125.6, 126.0, 127.5, 127.6 (2C), 128.4, 129.0, 132.4, 133.2, 133.8, 172.0; GC-MS (EI): m/z 314 [M⁺].

Diethyl 2-methyl-2-((6-(pivaloyloxy)naphthalen-2-yl)methyl)malonate (3ca)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 3). White solid (84.1 mg, 0.203 mmol, 81% yield); M.p. 80.5–82.3 °C; IR (KBr) 2983, 2940, 1749, 1731, 1607, 1466, 1286, 1187, 1107, 908 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.25 (t, J = 7.1 Hz, 6H), 1.37 (s, 3H), 1.40 (s, 9H), 3.38 (s, 2H), 4.20 (q, J = 7.1 Hz, 4H), 7.16 (dd, J = 8.8, 2.0 Hz, 1H), 7.26 (dd, J = 8.4,
1.6 Hz, 2H), 7.47 (d, 1H), 7.59 (s, 1H), 7.68 (d, J = 8.6 Hz) 7.76 (d, J = 8.9 Hz, 1H), 7.74 (d, J = 20.3 Hz, 1H); 13C NMR (67.9 MHz, CDCl3): δ 14.0, 19.8, 27.1, 39.1, 41.1, 54.9, 61.3, 118.1, 121.3, 127.3, 128.8, 128.9, 129.0, 131.1, 132.7, 133.6, 148.6, 171.9, 177.2; HRMS (ESI/TOF) [M+Na]⁺ Calcd for C24H30O6Na 437.1940; Found 437.1934.

Diethyl 2-((6-((tert-butoxycarbonyl)oxy)naphthalen-2-yl)methyl)-2-methylmalonate (3da)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 2). Pale yellow oil (102 mg, 0.237 mmol, 95% yield); IR (neat) 2983, 2938, 1732, 1607, 1508, 1463, 1372, 1246, 1021, 899, 862, 813, 781 cm⁻¹; 1H NMR (270 MHz, CDCl3): δ 1.25 (t, J = 7.2 Hz, 6H), 1.37 (s, 3H), 1.58 (s, 9H), 3.38 (s, 2H), 4.20 (q, J = 7.2 Hz, 4H), 7.26 (dd, J = 8.6, 1.6 Hz, 1H), 7.28 (dd, J = 8.8, 2.3 Hz, 1H), 7.59–7.59 (m, 2H), 7.76 (d, J = 8.6 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H); 13C NMR (67.9 MHz, CDCl3): δ 14.0, 19.8, 27.7, 41.1, 54.9, 61.3, 83.6, 117.9, 121.0, 127.4, 128.8, 129.0, 129.1, 131.2, 132.6, 133.7, 148.5, 151.9, 171.9; HRMS (ESI/TOF) [M+Na]⁺ Calcd for C24H30O7Na 453.1889; Found 453.1886.

Diethyl 2-((6-((tert-butyldimethylsilyl)oxy)naphthalen-2-yl)methyl)-2-methylmalonate (3ea)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 3). Pale yellow oil (44.7 mg, 0.101 mmol, 40% yield); IR (neat) 2933, 2858, 1733, 1604, 1473, 1376, 1245, 1022, 976, 937, 781 cm⁻¹; 1H NMR (270 MHz, CDCl3): δ 0.22–0.25 (m, 6H), 0.99–1.03 (m, 9H), 1.25 (t, J = 7.1 Hz, 6H), 1.38 (s, 3H), 3.35 (s, 2H), 4.21 (q, J = 7.1 Hz, 4H), 7.04 (dd, J = 8.8, 2.6 Hz, 1H), 7.14 (d, J = 2.2 Hz, 1H), 7.18 (dd, J = 8.6, 1.8 Hz, 1H), 7.51 (s, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.63 (d, J = 8.8 Hz, 1H); 13C NMR (67.9 MHz, CDCl3): δ -4.37, 14.0, 18.2, 19.8, 25.7, 41.1, 55.0, 61.3, 114.6, 122.2, 126.4, 128.6, 128.7, 129.0, 129.1, 131.5, 133.5, 153.3,
172.0; HRMS (ESI/TOF) [M+Na]^+ Calcd for C_{25}H_{36}O_{5}SiNa 467.2230; Found 467.2224.

Diethyl 2-methyl-2-(1-(naphthalen-2-yl)ethyl)malonate (3fa)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by silica gel column chromatography (Hexane/EtOAc = 99/1, 96/4, 94/6, 92/8) and preparative thin-layer chromatography (Toluene/ EtOAc = 9/1). Pale yellow oil (65.7 mg, 0.200 mmol, 80% yield); ^1H NMR (270 MHz, CDCl$_3$): δ 1.14 (t, $J$ = 7.0 Hz, 3H), 1.27 (t, $J$ = 7.3 Hz, 3H), 1.42 (s, 3H), 1.49 (d, $J$ = 7.1 Hz, 3H), 3.86 (q, $J$ = 7.1 Hz, 1H), 4.04 (q, $J$ = 7.1 Hz, 2H), 4.19–4.28 (m, 2H), 7.37 (dd, $J$ = 8.4, 1.9 Hz, 1H), 7.40–7.47 (m, 2H), 7.68 (d, $J$ = 1.4 Hz, 1H), 7.73–7.81 (m, 3H); ^13C NMR (67.9 MHz, CDCl$_3$): δ 13.8, 14.0, 17.2, 17.3, 43.9, 58.4, 61.1, 61.2, 125.5, 125.8, 127.1, 127.4 (2C), 127.7, 127.9, 132.5, 133.1, 139.2, 171.4, 171.5; GC-MS (EI): m/z 328 [M]^+.

Diethyl 2-(1-(6-methoxynaphthalen-2-yl)ethyl)-2-methylmalonate (3ha)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Pentane/Et$_2$O = 9/1 × 2). Pale yellow oil (74.5 mg, 0.208 mmol, 83% yield); IR (neat) 2976, 2841, 1747, 1633, 1607, 1455, 1393, 1216, 852, 811 cm$^{-1}$; ^1H NMR (270 MHz, CDCl$_3$): δ 1.14 (t, $J$ = 7.0 Hz, 3H), 1.27 (t, $J$ = 7.3 Hz, 3H), 1.41 (s, 3H), 1.47 (d, $J$ = 7.2 Hz, 3H), 3.82 (q, $J$ = 7.2 Hz, 1H), 3.91 (s, 3H), 4.03 (q, $J$ = 7.0 Hz, 2H), 4.17–4.28 (m, 2H), 7.09–7.14 (m, 2H), 7.33 (dd, $J$ = 8.2, 1.8 Hz, 1H), 7.60 (d, $J$ = 1.4 Hz, 1H), 7.62–7.68 (m, 2H); ^13C NMR (67.9 MHz, CDCl$_3$): δ 13.9, 14.0, 17.2, 17.3, 43.7, 55.2, 58.4, 61.1, 61.2, 105.4, 118.7, 126.2, 127.6, 127.7, 128.6, 129.2, 133.5, 136.8, 157.4, 171.4, 171.5; HRMS (ESI/TOF) [M+Na]^+ Calcd for C$_{21}$H$_{26}$O$_{5}$Na 381.1678; Found 381.1672.

S13
Diethyl 2-butyl-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3ab)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 2). Pale yellow oil (77.9 mg, 0.202 mmol, 81% yield); IR (neat) 2959, 2871, 1732, 1606, 1485, 1303, 856, 757 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 0.92 (t, J = 6.8 Hz, 3H), 1.23 (t, J = 7.3 Hz, 6H), 1.28–1.37 (m, 4H), 1.77–1.83 (m, 2H), 3.37 (s, 2H), 3.90 (s, 3H), 4.11–4.27 (m, 4H), 7.08–7.13 (m, 2H), 7.16 (dd, J = 8.6, 1.2 Hz, 1H), 7.47 (d, J = 1.2 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.9 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 13.9, 14.0, 22.8, 26.3, 31.5, 37.9, 55.2, 58.9, 61.1, 105.4, 118.7, 126.5, 128.5 (2C), 128.8, 129.0, 131.5, 133.4, 157.4, 171.4; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₃H₃₀O₅Na 409.1991; Found 409.1977.

Diethyl 2-allyl-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3ac)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 88/15). Colorless oil (74.3 mg, 0.201 mmol, 80% yield); IR (neat) 3060, 2980, 2938, 1732, 1606, 1207, 1034, 856, 757 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.24 (t, J = 7.2 Hz, 6H), 2.60 (d, J = 7.3 Hz, 2H), 3.37 (s, 2H), 3.91 (s, 3H), 4.11–4.27 (m, 4H), 5.14–5.17 (m, 1H), 5.20–5.21 (m, 1H), 5.75–5.90 (m, 1H), 7.08–7.14 (m, 2H), 7.19 (dd, J = 8.5, 1.8 Hz, 1H), 7.51 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 14.0, 36.6, 38.0, 52.2, 58.9, 61.2, 105.5, 118.8, 119.2, 126.6, 128.6, 128.7, 128.8, 129.0, 131.2, 132.7, 133.5, 157.5, 170.8; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₂H₂₆O₅Na 393.1678; Found 393.1679.

Diethyl 2-(2-cyanoethyl)-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3ad)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by silica gel column chromatography...
(Hexane/EtOAc = 9/1, 4/1, 7/3) and preparative thin-layer chromatography (Toluene/EtOAc = 9/1×2). Pale yellow oil (95.5 mg, 0.249 mmol, >99% yield); IR (neat) 2981, 2906, 2249, 1730, 1606, 1485, 1120, 1028, 858, 759 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.28 (t, J = 7.2 Hz, 6H), 2.13–2.19 (m, 2H), 2.44–2.50 (m, 2H), 3.40 (s, 2H), 3.92 (s, 3H), 4.25 (q, J = 7.2 Hz, 4H), 7.09–7.16 (m, 3H), 7.48 (d, J = 0.81 Hz, 1H), 7.65 (d, J = 8.6 Hz, 2H); ¹³C NMR (67.9 MHz, CDCl₃): δ 13.1, 13.9, 28.8, 39.5, 55.2, 57.8, 61.8, 105.4, 119.0, 119.1, 126.9, 128.1, 128.6, 129.0, 129.9, 133.6, 157.6, 170.0; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₂H₂₅NO₅Na 406.1630; Found 406.1630.

Diethyl 2-(3-chloropropyl)-2-(((6-methoxynaphthalen-2-yl)methyl)malonate (3ae)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1×3). Pale yellow oil (95.3 mg, 0.234 mmol, 93% yield); IR (neat) 2979, 2905, 1731, 1606, 1485, 1267, 1030, 857, 758 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.25 (t, J = 7.0 Hz, 6H), 1.78–1.89 (m, 2H), 1.91–1.99 (m, 2H), 3.38 (s, 2H), 3.52 (t, J = 6.1 Hz, 2H), 3.91 (s, 3H), 4.15–4.26 (m 4H), 7.09 (d, J = 2.4 Hz, 1H), 7.12 (dd, J = 8.6, 2.4 Hz, 1H), 7.17 (dd, J = 8.5, 1.6 Hz, 1H), 7.50 (d, J = 1.6 Hz, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 13.1, 13.9, 28.8, 38.3, 44.7, 55.2, 58.5, 61.3, 105.4, 118.9, 126.7, 128.4, 128.5, 128.7, 129.0, 130.9, 133.5, 157.5, 171.0; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₂H₂₅O₃ClNa 429.1445; Found 429.1442.

Diethyl 2-(((6-methoxynaphthalen-2-yl)methyl)-2-(3-oxobutyl)malonate (3af)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by silica gel column chromatography (Hexane/EtOAc = 85/15, 7/3) and preparative thin-layer chromatography (Toluene/EtOAc = 4/1×3). Colorless oil (84.8 mg, 0.212 mmol, 85% yield); IR (neat) 2980, 2905, 1731, 1606, 1485, 1175, 1030, 858, 757 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.24 (t, J = 7.1 Hz, 6H), 2.08–2.14 (m, 5H), 2.50–2.56 (m, 2H), 3.37 (s, 2H), 3.90 (s,
3H), 4.18 (q, J = 7.1 Hz, 4H), 7.08 (d, J = 2.6 Hz, 1H), 7.12 (dd, J = 8.9, 2.6 Hz, 1H), 7.17 (dd, J = 8.5, 1.6 Hz, 1H), 7.49 (d, J = 1.6 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.9 Hz, 1H); $^{13}$C NMR (67.9 MHz, CDCl$_3$): δ 13.9, 26.4, 29.8, 38.8, 39.3, 55.2, 58.1, 61.3, 105.4, 118.8, 126.7, 128.4, 128.6, 128.7, 129.0, 130.8, 133.5, 157.5, 170.9, 207.2; HRMS (ESI/TOF) m/z: [M+Na]$^+$ Calcd for C$_{23}$H$_{28}$O$_6$Na 423.1784; Found 423.1783.

Diethyl 2-benzyl-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3ag)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 2). Pale yellow oil (95.7 mg, 0.228 mmol, 91% yield); IR (neat) 3030, 2980, 2938, 2904, 1730, 1606, 1485, 1265, 1034, 857, 756, 702 cm$^{-1}$; $^1$H NMR (270 MHz, CDCl$_3$): δ 1.14 (t, J = 7.2 Hz, 6H), 3.27 (s, 2H), 3.35 (s, 2H), 3.91 (s, 3H), 4.11 (q, J = 7.2 Hz, 4H), 7.09–7.14 (m, 2H), 7.18–7.21 (m, 2H), 7.24–7.32 (m, 4H), 7.55 (d, J = 1.4 Hz, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H); $^{13}$C NMR (67.9 MHz, CDCl$_3$): δ 13.8, 39.1, 39.2, 55.2, 60.2, 61.2, 105.4, 118.8, 126.5, 126.8, 128.1, 128.7, 128.8, 129.1, 130.1, 131.4, 133.4, 136.3, 157.4, 171.0, one peak for aromatic carbon was not found probably due to overlapping; HRMS (ESI/TOF) m/z: [M+Na]$^+$ Calcd for C$_{26}$H$_{28}$O$_5$Na 443.1834; Found 443.1830.

Diethyl 2-isobutyl-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3ah)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 2). Colorless oil (71.9 mg, 0.186 mmol, 75% yield); IR (neat) 2958, 2871, 1731, 1606, 1229, 1126, 1035, 856 cm$^{-1}$; $^1$H NMR (270 MHz, CDCl$_3$): δ 0.91 (d, J = 6.8 Hz, 6H), 1.22 (t, J = 7.1 Hz, 6H), 1.79 (d, J = 5.9 Hz, 2H), 1.86–2.00 (m, 1H), 3.41 (s, 2H), 3.90 (s, 3H), 4.16 (q, J = 7.1 Hz, 4H), 7.08–7.13 (m, 2H), 7.18 (dd, J = 8.5, 1.6 Hz, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.6 Hz, 1H); $^{13}$C NMR (67.9 MHz, CDCl$_3$): δ 13.9, 23.6, 24.0, 38.7, 40.8, 55.2, 58.3, 61.0, 105.4, 118.7, 126.5,
128.6 (2C), 128.8, 129.0, 131.5, 133.4, 157.4, 171.8; HRMS (ESI/TOF) m/z: [M+Na]^+ Calcd for C_{23}H_{30}O_{5}Na 409.1991; Found 409.1986.

Diethyl 2-((6-methoxynaphthalen-2-yl)methyl)-2-phenylmalonate (3ai)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Pentane/EtOAc = 9/1 and Toluene/EtOAc = 19/1). Pale yellow oil (98.9 mg, 0.243 mmol, 97% yield); IR (neat) 3059, 2980, 2904, 1738, 1606, 1484, 1228, 1033, 857, 755 cm^{-1}; ^1H NMR (270 MHz, CDCl₃): δ 1.20 (t, J = 7.1 Hz, 6H), 3.73 (s, 2H), 3.89 (s, 3H), 4.21 (q, J = 7.1 Hz, 4H), 6.95 (dd, J = 8.4, 1.6 Hz, 1H), 7.05–7.09 (m, 2H), 7.23–7.29 (m, 6H), 7.50 (d, J = 8.1 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H); ^13C NMR (67.9 MHz, CDCl₃): δ 13.8, 42.9, 55.1, 61.5, 64.4, 105.3, 118.5, 125.9, 127.4, 127.8, 128.3, 128.5, 129.1 (2C), 129.2, 131.2, 133.3, 137.0, 157.4, 170.1; HRMS (ESI/TOF) m/z: [M+Na]^+ Calcd for C_{25}H_{26}O_{5}Na 429.1678; Found 429.1677.

Diethyl 2-acetamido-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3aj)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 1/1). White solid (88.8 mg, 0.229 mmol, 91% yield); M.p. 136.7–137.9 °C; IR (KBr) 3266, 3048, 2986, 2941, 1747, 1644, 1515, 1187, 1030, 848, 667, 612 cm^{-1}; ^1H NMR (270 MHz, CDCl₃): δ 1.31 (t, J = 7.2 Hz, 6H), 2.04 (s, 3H), 3.78 (s, 2H), 3.91 (s, 3H), 4.29 (q, J = 7.2 Hz, 4H), 6.52 (brs, 1H), 7.06–7.14 (m, 3H), 7.40 (d, J = 0.81 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H); ^13C NMR (67.9 MHz, CDCl₃): δ 13.9, 22.9, 37.7, 55.2, 62.5, 67.3, 105.4, 118.9, 126.6, 128.2, 128.5, 128.7, 128.9, 130.2, 133.5, 157.5, 167.5, 169.1; HRMS (ESI/TOF) m/z: [M+Na]^+ Calcd for C_{21}H_{25}NO_{6}Na 410.1580; Found 410.1580.
Diethyl 2-fluoro-2-((6-methoxynaphthalen-2-yl)methyl)malonate (3ak)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 3). Yellow oil (35.3 mg, 0.101 mmol, 40% yield); IR (neat) 2983, 2939, 2873, 1751, 1608, 1485, 1250, 1045, 857 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.23 (t, J = 7.1 Hz, 6H), 3.60 (d, JHF = 25.7 Hz, 2H), 3.91 (s, 3H), 4.24 (q, J = 7.1 Hz, 4H), 7.09–7.15 (m, 2H), 7.32–7.36 (m, 1H), 7.65–7.69 (m, 3H); ¹³C NMR (67.9 MHz, CDCl₃): δ 13.9, 40.2 (d, JCF = 20.6 Hz), 55.2, 62.6, 94.8 (d, JCF = 202 Hz), 105.5, 118.9, 126.8, 128.1, 128.7 (2C), 129.1 (d, JCF = 1.1 Hz), 129.2, 133.8, 157.7, 165.8 (d, JCF = 25.1 Hz); ¹⁹F NMR (471 MHz, CDCl₃): δ -165.4 (t, JHF = 25.7 Hz); HRMS (ESI/TOF) m/z: [M+Na⁺] Calcd for C₁₉H₂₁FO₅Na 371.1271; Found 371.1278.

Dimethyl 2-((6-methoxynaphthalen-2-yl)methyl)-2-methylmalonate (3al)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Toluene/EtOAc = 9/1 × 2). White solid (69.5 mg, 0.220 mmol, 88% yield); M.p. 118.0–118.8 °C; IR (KBr) 2990, 2940, 2845, 1733, 1604, 1441, 1232, 1113, 1027, 858, 678 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.39 (s, 3H), 3.36 (s, 2H), 3.74 (s, 6H), 3.91 (s, 3H), 7.09–7.14 (m, 2H), 7.18 (dd, J = 8.2, 1.6 Hz, 1H), 7.50 (d, J = 1.6 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 8.1 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 19.8, 41.2, 52.5, 55.0, 55.2, 105.4, 118.8, 126.5, 128.7 (2C), 129.1, 131.1, 133.5, 157.5, 172.4. one peak for the aromatic carbon was not found probably due to overlapping; HRMS (ESI/TOF) m/z: [M+Na⁺] Calcd for C₁₈H₂₀O₃Na 339.1208; Found 339.1210.

Diisopropyl 2-((6-methoxynaphthalen-2-yl)methyl)-2-methylmalonate (3am)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer
chromatography (Hexane/EtOAc = 9/1 × 2). Pale yellow oil (68.0 mg, 0.183 mmol, 73% yield); IR (neat) 2981, 2938, 1727, 1607, 1485, 1247, 1097, 1033, 854, 757 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.22 (d, J = 6.2 Hz, 6H), 1.27 (d, J = 6.2 Hz, 6H), 1.35 (s, 3H), 3.34 (s, 2H), 3.90 (s, 3H), 5.06 (sep, J = 6.2 Hz, 2H), 7.09–7.13 (m, 2H), 7.23 (dd, J = 8.6, 1.6 Hz, 1H), 7.53 (s, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 19.8, 21.5, 21.6, 40.8, 54.9, 55.2, 68.8, 105.5, 118.7, 126.4, 128.7, 128.8, 129.0 (2C), 131.5, 133.4, 157.4, 171.5; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₂H₂₈O₅Na 395.1834; Found 395.1844.

Ethyl 2-((6-methoxynaphthalen-2-yl)methyl)-2-methyl-3-oxobutanoate (5aa)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by silica gel column chromatography (Hexane/EtOAc = 95/5, 9/1, 85/15). Pale yellow oil (70.4 mg, 0.224 mmol, 90% yield); IR (neat) 2982, 2938, 1712, 1606, 1484, 1231, 1095, 1030, 856, 757 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.25 (t, J = 7.2 Hz, 3H), 1.32 (s, 3H), 2.18 (s, 3H), 3.18 (d, J = 13.8 Hz, 1H), 3.40 (d, J = 13.8 Hz, 1H), 3.91 (s, 3H), 4.14–4.27 (m, 2H), 7.09–7.14 (m, 2H), 7.18 (dd, J = 8.5, 1.6 Hz, 1H), 7.49 (d, J = 1.6 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 13.9, 19.1, 26.5, 40.4, 55.2, 60.9, 61.4, 105.4, 118.8, 126.5, 128.7 (2C), 128.8, 129.0, 131.5, 133.4, 157.4, 172.4, 205.5; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₁₉H₂₂O₄Na 337.1416; Found 337.1404.

Methyl 1-((6-methoxynaphthalen-2-yl)methyl)-2-oxocyclopentanecarboxylate (5ab)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Toluene/EtOAc = 9/1). Light brown solid (76.8 mg, 0.246 mmol, 98% yield); M.p. 92.7–94.4 °C; IR (KBr) 2963, 2946, 2896, 1748, 1720, 1605, 1487, 1230, 1198, 1024, 850, 822 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.51–1.65 (m, 1H), 1.79–1.93 (m, 1H), 1.95–2.09 (m, 2H), 2.32–2.48 (m, 2H), 3.27 (d, J = 13.8 Hz, 1H), 3.33 (d, J = 13.8 Hz, 1H), 3.74 (s, 3H), 3.91 (s, 3H), 7.10 (d, J = 2.4 Hz, 1H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 7.21 (dd, J = 8.4, 1.9 Hz, 1H), 7.52 (s, 1H), 7.64 (d,
$J = 9.2$ Hz, 1H), 7.67 (d, $J = 9.5$ Hz, 1H); $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ 19.4, 31.6, 38.3, 39.0, 52.6, 55.2, 61.6, 105.4, 118.9, 126.8, 128.7 (3C), 129.1, 131.6, 133.3, 157.5, 171.4, 215.0; HRMS (ESI/TOF) $m/z$: [M+Na]$^+$ Calcd for C$_{19}$H$_{20}$O$_4$Na 335.1259; Found 335.1250.

Ethyl 1-((6-methoxynaphthalen-2-yl)methyl)-2-oxocyclohexanecarboxylate (5ac)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Toluene/EtOAc = 9/1 × 2). White solid (62.9 mg, 0.185 mmol, 74% yield); M.p. 81.0–83.0 °C; IR (KBr) 2939, 2862, 1735, 1710, 1606, 1487, 1185, 1125, 1030, 855, 830 cm$^{-1}$; $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ 1.14 (t, $J = 7.2$ Hz, 3H), 1.44–1.77 (m, 4H), 1.96–2.06 (m, 1H), 2.37–2.55 (m, 3H), 3.03 (d, $J = 13.9$ Hz, 1H), 3.42 (d, $J = 13.9$ Hz, 1H), 3.91 (s, 3H), 4.00–4.17 (m, 2H), 7.09–7.13 (m, 2H), 7.23 (dd, $J = 8.4$, 1.4 Hz, 1H), 7.50 (d, $J = 1.4$ Hz, 1H), 7.61 (d, $J = 8.9$ Hz, 1H), 7.65 (d, $J = 9.5$ Hz, 1H); $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ 13.9, 22.5, 27.5, 35.9, 40.3, 41.2, 55.2, 61.2, 62.3, 105.4, 118.6, 126.2, 128.7, 128.8, 129.0, 129.1, 131.8, 133.3, 157.3, 171.1, 207.4; HRMS (ESI/TOF) $m/z$: [M+Na]$^+$ Calcd for C$_{21}$H$_{24}$O$_4$Na 363.1572; Found 363.1572.

Ethyl 2-fluoro-2-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanoate (5ad)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 3). White solid (41.9 mg, 0.132 mmol, 53% yield); M.p. 62.2–64.6 °C; IR (KBr) 2992, 2939, 1752, 1731, 1607, 1192, 1028, 856, 813 cm$^{-1}$; $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ 1.24 (t, $J = 7.2$ Hz, 3H), 2.12 (d, $J_{CF} = 5.4$ Hz, 3H), 3.43–3.65 (m, 2H), 3.92 (s, 3H), 4.17–4.28 (m, 2H), 7.10 (d, $J = 2.5$ Hz, 1H), 7.14 (dd, $J = 8.8$, 2.5 Hz, 1H), 7.29–7.33 (m, 1H), 7.61 (s, 1H), 7.67 (d, $J = 8.4$ Hz, 1H), 7.68 (d, $J = 8.9$ Hz, 1H); $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ 13.9, 26.3, 39.7 (d, $J_{CF} = 20.7$ Hz), 55.2, 62.6, 100.2 (d, $J_{CF} = 200$ Hz), 105.4, 119.0, 126.8, 128.1, 128.7 (d, $J_{CF} = 3.4$ Hz), 128.7, 129.1, 129.2 (d, $J_{CF} = 4.5$ Hz), 133.7, 157.7, 165.7 (d, $J_{CF} = 25.7$ Hz), 202.6 (d, $J_{CF} = 29.6$ Hz); $^{19}$F NMR (471 MHz, CDCl$_3$): $\delta$ -165.3 –
3-((6-Methoxynaphthalen-2-yl)methyl)-3-methylpentane-2,4-dione (5ae)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 9/1 × 2 and Pentane/EtOAc = 4/1 × 2). Colorless oil (53.5 mg, 0.188 mmol, 75% yield); IR (neat) 3058, 2999, 2937, 2841, 1697, 1606, 1484, 1358, 1229, 1031, 855, 756 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.33 (s, 3H), 2.13 (s, 6H), 3.31 (s, 2H), 3.91 (s, 3H), 7.09 (d, J = 2.6 Hz, 1H), 7.13 (dd, J = 8.9, 2.6 Hz, 1H), 7.15 (dd, J = 8.2, 1.6 Hz, 1H), 7.47 (d, J = 1.6 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.9 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 18.3, 27.3, 40.2, 55.2, 67.4, 105.4, 118.9, 126.7, 128.6, 128.7 (2C), 129.1, 131.5, 133.3, 157.5, 207.2; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₁₈H₁₉FO₄Na 341.1165; Found 341.1155.

2-Acetyl-2-((6-methoxynaphthalen-2-yl)methyl)cyclohexanone (5af)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by silica gel column chromatography (Hexane/EtOAc = 95/5, 9/1, 4/1) and preparative thin-layer chromatography (Toluene/EtOAc = 9/1 × 2). Light brown solid (32.1 mg, 0.103 mmol, 41% yield); M.p. 85.3–86.3 °C; IR (KBr) 2960, 2937, 2868, 1690, 1607, 1485, 1265, 1233, 1165, 1121, 1033, 849, 817 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 1.42–1.74 (m, 4H), 1.91–2.03 (m, 1H), 2.12 (s, 3H), 2.20–2.32 (m, 1H), 2.36–2.44 (m, 1H), 2.49–2.57 (m, 1H), 3.25 (s, 2H), 3.91 (s, 3H), 7.08 (d, J = 2.6 Hz, 1H), 7.12 (dd, J = 8.5, 2.6 Hz, 1H), 7.17 (dd, J = 8.4, 1.6 Hz, 1H), 7.47 (d, J = 1.6 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.9 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 22.2, 26.9 (2C), 33.9, 39.8, 42.0, 55.2, 68.8, 105.4, 118.8, 126.5, 128.7, 128.8, 129.0, 129.1, 131.3, 133.3, 157.5, 206.0, 209.5; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₀H₂₂O₃Na 333.1467; Found 333.1456.
5-((6-Methoxynaphthalen-2-yl)methyl)-2,2,5-trimethyl-1,3-dioxane-4,6-dione (5ag)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 4/1). Pale yellow solid (69.9 mg, 0.213 mmol, 85% yield); M.p. 139.1–140.9 °C; IR (KBr) 2994, 2943, 1768, 1736, 1606, 1336, 1284, 1066, 816 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 0.79 (s, 3H), 1.57–1.58 (m, 3H), 1.79 (s, 3H), 3.46 (s, 2H), 3.90 (s, 3H), 7.07 (d, J = 2.7 Hz, 1H), 7.12 (dd, J = 8.9, 2.7 Hz, 1H), 7.25 (dd, J = 8.6, 1.5 Hz, 1H), 7.57 (d, J = 1.5 Hz, 1H), 7.64 (d, J = 9.2 Hz, 1H), 7.68 (d, J = 9.7 Hz, 1H); ¹³C NMR (67.9 MHz, CDCl₃): δ 25.8, 28.3, 29.3, 44.9, 52.2, 55.2, 105.2, 105.3, 119.0, 127.1, 128.3, 128.7, 128.9, 129.4, 130.3, 133.8, 157.7, 169.9; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₁₉H₂₀O₅Na 351.1208; Found 351.1209.

Ethyl 2-cyano-3-(6-methoxynaphthalen-2-yl)-2-((6-methoxynaphthalen-2-yl)methyl)propanoate (5ah)

This compound was prepared according to the same method to 3aa and the desired product was obtained after purification by preparative thin-layer chromatography (Hexane/EtOAc = 85/15 × 2 and Toluene/EtOAc = 9/1 × 2). Brown solid (35.0 mg, 0.0772 mmol, 62% yield); M.p. 106.5–107.7 °C; IR (KBr) 2965, 2939, 2246, 1733, 1606, 1484, 1392, 1237, 1198, 1027, 857 cm⁻¹; ¹H NMR (270 MHz, CDCl₃): δ 0.88 (t, J = 7.1 Hz, 3H), 3.27 (d, J = 13.5 Hz, 2H), 3.50 (d, J = 13.5 Hz, 2H), 3.92 (s, 6H), 3.97 (q, J = 7.1 Hz, 2H), 7.11–7.16 (m, 4H), 7.41 (dd, J = 8.6, 1.6 Hz, 2H), 7.69–7.72 (m, 6H); ¹³C NMR (67.9 MHz, CDCl₃): δ 13.6, 43.3, 53.4, 55.3, 62.6, 105.5, 118.8, 119.1, 127.0, 128.3, 128.7, 128.9, 129.2, 129.3, 134.0, 157.8, 168.4; HRMS (ESI/TOF) m/z: [M+Na]⁺ Calcd for C₂₉H₂₇NO₄Na 476.1838; Found 476.1833.
4. Experimental details for the mechanistic experiments

Scheme S5. Reaction of benzofuran-2-ylmethyl 2,3,4,5,6-pentafluorobenzoate (1i)

Benzofuran-2-ylmethyl 2,3,4,5,6-pentafluorobenzoate (1i) (85.6 mg, 0.25 mmol), [Cp*RuCl₂]₂ (3.8 mg, 0.00625 mmol, 0.025 equiv), picolinic acid (L₁) (1.5 mg, 0.0125 mmol, 0.05 equiv), Cs₂CO₃ (89.6 mg, 0.275 mmol, 1.1 equiv) were charged into a screw cap vial. The resulting mixture was carefully evacuated and refilled with N₂ five times. After the addition of CH₃CN (1 mL) and diethyl methylmalonate (2a) (47 µL, 0.275 mmol, 1.1 equiv), the resulting yellow suspension was stirred at 60 °C for 18 h. The reaction was allowed to cool to room temperature and quenched with water (1 mL). The resulting aqueous phase was extracted with EtOAc (3 mL). The organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the yields of benzylic alkylation product 3ia and aromatic substitution 3ia’ were determined to be 27% and 34%, respectively, by ¹H NMR analyses of the crude reaction mixture. The resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 95/5) and preparative thin-layer chromatography (Pentane/EtOAc = 95/5) to give 3ia in 18% yield (13.4 mg, 0.0440 mmol, 18% yield) and 3ia’ in 19% yield (14.8 mg, 0.0486 mmol, 19% yield), respectively.

Diethyl 2-(benzofuran-2-ylmethyl)-2-methylmalonate (3ia)

¹H NMR (500 MHz, CDCl₃): δ 1.27 (t, J = 7.0 Hz, 6H), 1.46 (s, 3H), 3.41 (s, 2H), 4.19–4.28 (m, 4H), 6.47 (s, 1H), 7.17 (ddd, J = 7.4, 7.4, 1.2 Hz, 1H), 7.21 (ddd, J = 7.6, 7.6, 1.7 Hz, 1H), 7.36–7.38 (m, 1H), 7.48 (dd, J = 7.0, 1.0 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃): δ 14.0, 19.9, 34.5, 53.7, 61.6, 105.3, 110.9, 120.5, 122.5, 123.6, 128.5, 154.1, 154.8, 171.4; GC-MS (EI) m/z: 304 [M]⁺.
Diethyl 2-methyl-2-(2-methylbenzofuran-3-yl)malonate (3ia')

IR (neat) 2983, 2939, 1733, 1603, 1455, 1242, 1110, 1021, 752 \text{ cm}^{-1}; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \delta 1.25 (t, J = 7.0 H, 6H), 1.95 (s, 3H), 2.38 (s, 3H), 4.19–4.32 (m, 4H), 7.14 (ddd, J = 7.8, 7.8, 1.5 Hz, 1H), 7.19 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H); \textsuperscript{13}C NMR (126 MHz, CDCl\textsubscript{3}): \delta 13.9, 22.3, 53.7, 61.9, 110.7, 112.9, 120.5, 122.1, 123.2, 128.1, 151.4, 153.3, 170.9, one peak was not found probably due to overlapping; HRMS (ESI/TOF) m/z: [M+Na]\textsuperscript{+} Calcd for C\textsubscript{17}H\textsubscript{20}O\textsubscript{5}Na 327.1208; Found 327.1211.

Scheme S6. Reaction of (R)-1-(naphthalen-2-yl)ethyl 2,3,4,5,6-pentafluorobenzoate ((R)-1f)

Preparation of (R)-1-(naphthalen-2-yl)ethyl 2,3,4,5,6-pentafluorobenzoate ((R)-1f):
(R)-1f was prepared according to the our previously reported method using (R)-1-(2-naphthyl)methanol as a chiral alcohol.\textsuperscript{1} Pale yellow solid (941 mg, 2.57 mmol, 88% yield, 97% ee). [\alpha]_{D}^{25} = –13.3 (c 1.02, CHCl\textsubscript{3}); HPLC conditions: DAICEL CHIRALPAK AD-H, Hexane/i-PrOH = 99/1, flow rate = 1.0 mL/min, \lambda = 224 nm, retention time; t\textsubscript{R} (major) = 6.34 min, t\textsubscript{R} (minor) = 7.82 min.

Reaction of (R)-1f with diethyl methylmalonate (2a):
(R)-1-(Naphthalen-2-yl)ethyl 2,3,4,5,6-pentafluorobenzoate ((R)-1f) (91.6 mg, 0.25 mmol), [Cp*RuCl\textsubscript{2}]\textsubscript{2} (3.8 mg, 0.00625 mmol, 0.025 equiv), picolinic acid (L1) (1.5 mg, 0.0125 mmol, 0.05 equiv), Cs\textsubscript{2}CO\textsubscript{3} (89.6 mg, 0.275 mmol, 1.1 equiv) were charged into a screw cap vial. The resulting mixture was carefully evacuated and refilled with N\textsubscript{2} five times. After the addition of CH\textsubscript{3}CN (1 mL) and diethyl methylmalonate (2a) (47 \mu L, 0.275 mmol, 1.1 equiv), the resulting yellow suspension was stirred at 60 °C for 18 h. The reaction was allowed to cool to room temperature and quenched with water (1
mL). The resulting aqueous phase was extracted with EtOAc (3 mL × 1). The organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the resulting crude mixture was purified by silica gel column chromatography (Hexane/EtOAc = 97/3, 95/5, 92/8) and preparative thin-layer chromatography (Toluene/EtOAc = 9/1) to give (+)-3fa as a colorless oil (60.1 mg, 0.183 mmol, 73% yield, 97% ee).

(+)-Diethyl 2-methyl-2-(1-(naphthalen-2-yl)ethyl)malonate ((+)-3fa)

[α]₀° = +60.1 (c 0.91, CHCl₃); HPLC conditions: DAICEL CHIRALPAK AD-H, Hexane/i-PrOH = 49/1, flow rate = 1.0 mL/min, λ = 224 nm, retention time; tᵣ (minor) = 7.94 min, tᵣ (major) = 9.19 min.
5. Experimental details for the reaction of non-fused aromatic substrates

**Scheme S7.** Reaction of benzyl 2,3,4,5,6-pentafluorobenzoates (1j):

Benzyl 2,3,4,5,6-pentafluorobenzoate (1j) (75.6 mg, 0.25 mmol), [Cp*RuCl₂]₂ (3.8 mg, 0.00625 mmol, 0.025 equiv), picolinic acid (L1) (1.5 mg, 0.0125 mmol, 0.05 equiv), Cs₂CO₃ (89.6 mg, 0.275 mmol, 1.1 equiv) were charged into a screw cap vial. The resulting mixture was carefully evacuated and refilled with N₂ five times. After the addition of CH₃CN (1 mL) and diethyl methylmalonate (2a) (47 µL, 0.275 mmol, 1.1 equiv), the resulting yellow suspension was stirred at 80 °C for 18 h. The reaction was allowed to cool to room temperature and quenched with water (1 mL). The resulting aqueous phase was extracted with EtOAc (3 mL x 1). The organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the yield of benzylic alkylation product 3ja was determined to be 2% by ¹H NMR analyses of the crude reaction mixture.

**Chart S1.** ¹H NMR spectrum of the reaction of 1j
Scheme S8. Reaction of 4-(trifluoromethyl)benzyl 2,3,4,5,6-pentafluorobenzoates (1k)

4-(Trifluoromethyl)benzyl 2,3,4,5,6-pentafluorobenzoate (1k) (92.6 mg, 0.25 mmol), [Cp*RuCl₂]₂ (3.8 mg, 0.00625 mmol, 0.025 equiv), picolinic acid (L1) (1.5 mg, 0.0125 mmol, 0.05 equiv), Cs₂CO₃ (89.6 mg, 0.275 mmol, 1.1 equiv) were charged into a screw cap vial. The resulting mixture was carefully evacuated and refilled with N₂ five times. After the addition of CH₃CN (1 mL) and diethyl methylmalonate (2a) (47 µL, 0.275 mmol, 1.1 equiv), the resulting yellow suspension was stirred at 80 °C for 18 h. The reaction was allowed to cool to room temperature and quenched with water (1 mL). The resulting aqueous phase was extracted with EtOAc (3 mL × 1). The organic phase was washed with brine and dried over MgSO₄. After removal of the solvent, the yield of benzylic alkylation product 3ka was determined to be 1% by ¹H NMR analyses of the crude reaction mixture.

Chart S2. ¹H NMR spectrum of the reaction of 1k
6. References

7. Copies of NMR spectra (\textsuperscript{1}H, \textsuperscript{13}C, and \textsuperscript{19}F) and HPLC chromatograms
$1c$ ($^1H$, CDCl$_3$)
$S2 \ (^{1}H, CDCl_{3})$
S2 ($^{13}$C, CDCl₃)
1d (1H, CDCl$_3$)
$^{13}$C-NMR Spectrum of Compound 1d (CDCl$_3$)
$1e \ (1H, CDCl_3)$
$^{13}$C, CDCl₃
$1g'$ ($^1H, CDCl_3$)
$1g \ (^{1}H, \ CDCl_{3})$
$^{13}$C NMR spectrum of compound 1g (CDCl$_3$)
3aa (1H, CDC$_3$)
3aa ($^{13}$C, CDCl$_3$)
$\text{3ba} (\text{H, CDCl}_3)$
$3ca \ (^{1}H, \ CDCl_{3})$
$3ca\ (^{13}C, CDCl_3)$
3ea ($^1$H, CDCl$_3$)
$3ea (^{13}C, CDCl_3)$
$\text{3fa (}^{13}\text{C, CDCl}_3\text{)}$
3ha (1H, CDCl₃)
$3ha^{(13C, CDCl_3)}$
$3ab \ (1^H, \text{CDCl}_3)$
3ab (13C, CDCl₃)
$3\text{ac}^{13}\text{C, CDCl}_3$
3ad ($^1$H, CDCl$_3$)
3ad ($^{13}$C, CDCl$_3$)
$3ae \ (^{1}H, CDCl_{3})$
3ae ($^{13}$C, CDCl$_3$)

S71
$3\alpha f \left( {}^{1}H, \text{CDCl}_3 \right)$
S73
3ag (¹H, CDCl₃)
$3\text{ag}^{(13}\text{C}, \text{CDCl}_3)$

$\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}$

X: parts per Million: 13C
3ah (1H, CDCl₃)
$3\text{ah} (^{13}\text{C, CDCl}_3)$
3ai ($^{13}$C, CDCl$_3$)
3aj (1H, CDCl₃)
$3\text{aj} \left( ^{13}\text{C}, \text{CDCl}_3 \right)$
$\text{3ak (}^1\text{H, CCl}_3\text{)}$
3ak$^{(13C, \text{CDCl}_3)}$
$$3\text{a}k \quad (^{19}\text{F}, \text{CDCl}_3)$$
$\text{3al} \left( ^1H, \text{CDCl}_3 \right)$
$3\text{al} (^{13}\text{C, CDCl}_3)$
$3am\ (^{1}H, CDCl_3)$
$3\text{am}^{(13\text{C}, \text{CDCl}_3)$
5aa ($^{13}$C, CDCl$_3$)
$5_{ab} \ (^{1}H, 1.4-2.6 \text{ ppm})$
5ab (\textsuperscript{13}C, CDCl\textsubscript{3})
$5ac\ (1^H, CDCl_3)$
5ac (1H, 1.3–2.7 ppm)
$5\text{ac}$ ($^{13}\text{C}, \text{CDCl}_3$)
$5a d$ ($^1H, CDCl_3$)
$5\text{ad}^{(13}\text{C, CDCl}_3$)
$\text{S101}$
5af (1H, CDCl₃)
5af (\(^1\)H, 1.4–2.6 ppm)
$5af\left(\text{^{13}C, CDCl}_3\right)$
$5_{ag}^{(13}C, \text{CDCl}_3)$
5ah (1H, CDCl₃)
$3\text{ia}$ ($^{13}\text{C}, \text{CDCl}_3$)
$3\text{ia}'{ (}^{1}\text{H, CDCl}_3{)}$