Supplementary Information for:

*Copper-catalyzed regioselective dehydrogenative alkoxylation of morpholinonyl alkenols: application to the synthesis of spirotricyclic dihydropyrans and of trans-fused bicyclic morpholines*

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2. Experimental Section

All experiments involving air and moisture sensitive reagents such as organolithium reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 µm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or KMnO₄ stain. Unless otherwise indicated, ¹H, ¹³C, and DEPT-135 NMR spectra were acquired using CDCl₃ solvent at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-EI⁺ data were obtained using either electrospray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx).

The alcohol-bearing allylic lactams employed in these studies (see below) were prepared using our previously reported protocol,¹ with Grignard reagents employed in place of organolithiums in most cases (e.g., allylmagnesium bromide in place of allyllithium). Newly synthesized alcohols were advanced without extensive characterization.

**General Procedure A: Cu-catalyzed enol etherification**

To an oven dried vial equipped with a stir bar was added the alcohol (1.0 mmol) in DMF (5 mL) at room temperature and atmospheric pressure. CuCl (12 mg, 20 mol %) and di-tert-butylperoxide (2 mmol, 2 equiv) were then added to the vial. The vial was sealed with a Teflon-lined cap, placed in an oil bath thermostatted at 100 °C and the contents were stirred for the indicated length of time (usually 12 to 22 h). After complete consumption of the starting material (TLC and GC-MS monitoring), the mixture was cooled to room temperature. It was then diluted with EtOAc:H₂O (50:10) and the contents were transferred to a separatory funnel. A few drops of 1M HCl(aq) were added to the mixture and the layers were separated. The organic layer was washed with brine, dried over MgSO₄, and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was subjected to flash column chromatography.

**General Procedure B: Ring closing metathesis**: To a solution of the corresponding 1,6-diene (1.0 equiv) in dry and degassed CH₂Cl₂ (0.1 M) was added 2nd generation Grubbs catalyst (1.0 mol%). The solution was heated at 40 °C until the starting material was fully consumed, as indicated by TLC (~6 h). The solution was cooled to 23 °C and immediately purified by flash column chromatography on silica eluting with hexanes/EtOAc.
Prepared from alcohol 1a (1.00 mmol) using General Procedure A. Yield = 283 mg, 86%. Data as previously reported by us.¹

Prepared from alcohol 1b (1.00 mmol) using General Procedure A. Yield = 365 mg, 83%. ¹H NMR (400 MHz, Chloroform-δ) δ 7.63 – 7.47 (m, 4H), 7.37 – 7.23 (m, 9H), 7.02 – 6.95 (m, 2H), 5.44 (s, 1H), 4.73 (d, J = 4.7 Hz, 1H), 4.38 (d, J = 4.7 Hz, 1H), 4.36 – 4.16 (m, 3H), 3.38 (q, J = 3.7 Hz, 1H), 1.76 (s, 3H), 1.32 (d, J = 6.9 Hz, 3H), 1.29 (d, J = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 169.2, 145.4, 142.9, 136.9, 136.4, 130.2, 128.9, 128.4, 128.3, 128.1, 127.5, 127.3, 126.8, 126.5, 126.3, 80.3, 78.9, 67.2, 60.4, 48.8, 20.0, 19.4, 13.6. HRMS-EL⁺ (m/z): calc’d for C₂₉H₂₉NO₃ 439.2147; found 439.2150.
Prepared from alcohol 1c (1.00 mmol) using General Procedure A. Yield = 283 mg, 77%.

**HRMS-**<sup>EI</sup> (m/z): calc’d for C<sub>23</sub>H<sub>29</sub>N<sub>3</sub>O<sub>3</sub> 367.2147; found 367.2153.

This compound was advanced to the metathesis reaction without full characterization.

Prepared from alcohol 1d (1.00 mmol) using General Procedure A. Yield = 275 mg, 81%.

<sup>1</sup>H NMR (400 MHz, Chloroform-<i>d</i>) δ 7.35 – 7.25 (m, 5H), 6.11 (dd, <i>J</i> = 17.2, 10.7 Hz, 1H), 6.00 (dd, <i>J</i> = 17.3, 10.6 Hz, 1H), 5.50 (d, <i>J</i> = 17.2 Hz, 1H), 5.41 (d, <i>J</i> = 17.4 Hz, 1H), 5.29 (dd, <i>J</i> = 15.1,
10.8 Hz, 2H), 4.45 – 4.23 (m, 2H), 4.22 (d, $J = 3.2$ Hz, 1H), 4.10 (d, $J = 16.2$ Hz, 1H), 3.69 (d, $J = 3.3$ Hz, 1H), 1.89 (s, 3H), 1.34 – 1.16 (m, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.0, 139.7, 139.3, 137.5, 136.9, 129.6, 128.9, 128.3, 128.2, 127.0, 115.2, 114.9, 79.1, 66.1, 59.9, 48.6, 19.9, 19.6, 14.5. HRMS-EI$^+$ (m/z): calc’d for C$_{21}$H$_{25}$NO$_3$ 339.1834; found 339.1838.
Prepared from alcohol 1e (1.00 mmol) using General Procedure A. Yield = 311 mg, 79%. ¹H NMR (400 MHz, Chloroform-d) δ 7.35 (t, J = 7.6 Hz, 2H), 7.24 (d, J = 6.9 Hz, 2H), 5.85 (dp, J = 21.9, 6.5, 5.3 Hz, 2H), 5.18 (q, J = 6.2, 4.8 Hz, 2H), 5.12 (s, 1H), 4.36 – 4.25 (m, 2H), 4.07 (dd, J = 16.7, 5.6 Hz, 2H), 3.62 (d, J = 4.4 Hz, 1H), 2.44 (q, J = 8.2, 7.4 Hz, 2H), 2.36 – 2.28 (m, 1H), 1.92 – 1.71 (m, 9H), 1.59 – 1.46 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 168.5, 137.2, 136.9, 133.1, 132.7, 129.7, 128.9, 128.3, 128.3, 127.0, 119.6, 119.5, 77.5, 76.8, 76.2, 66.8, 62.5, 59.0, 41.0, 40.3, 28.6, 24.3, 24.2, 14.8. HRMS-ESI⁺ (m/z): calc’d for C₂₅H₃₁NO₃ 393.2304; found 393.2307. FTIR (KBr): 3060.2295, 3027.4261, 2924.038, 1724.2643, 1646.3958, 1494.2931, 1474.3358, 1452.8606, 1432.4058, 1361.9422, 1342.0932, 265.3056, 1205.6142, 1140.2378, 1071.7973, 1028.3461, 996.4523, 924.2151, 735.4288, 700.2396.
Prepared from alcohol 1f (1.00 mmol) using General Procedure A. Yield = 256 mg, 75%. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.3 (d, $J = 7.5$ Hz, 2H), 7.25 (d, $J = 7.9$ Hz, 3H), 4.27 (d, $J = 16.1$ Hz, 1H), 4.19 (d, $J = 5.7$ Hz, 1H), 4.09 (d, $J = 16.1$ Hz, 1H), 3.95 (p, $J = 8.7$ Hz, 1H), 3.51 (d, $J = 5.7$ Hz, 1H), 2.05 – 1.94 (m, 1H), 1.87 (s, 3H), 1.85 – 1.71 (m, 1H), 1.57 – 1.40 (m, 2H), 1.31 (d, $J = 4.1$ Hz, 5H), 1.28 – 1.23 (m, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.4, 136.7, 130.5, 128.9, 128.4, 127.1, 81.0, 72.8, 67.3, 64.2, 59.1, 28.7, 28.6, 26.6, 26.5, 24.5, 14.5. HRMS-El$^+$ ($m/z$): calc’d for C$_{21}$H$_{27}$NO$_3$ 341.1991; found 341.1996.
Prepared from alcohol 1g (1.0 mmol) using General Procedure A. Yield = 312 mg, 82%. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.34 (t, $J = 7.6$ Hz, 2H), 7.21 (t, $J = 9.3$ Hz, 3H), 5.43 (s, 1H), 5.18 (d, $J = 14.3$ Hz, 1H), 5.09 (d, $J = 6.8$ Hz, 2H), 4.62 (t, $J = 5.6$ Hz, 1H), 4.24 (d, $J = 15.9$ Hz, 1H), 4.18 – 4.03 (m, 2H), 1.86 (s, 3H), 1.74 (s, 3H), 1.66 (s, 3H), 1.49 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.2, 145.2, 144.0, 138.3, 137.1, 130.0, 129.2, 128.8, 128.6, 128.5, 128.3, 127.3, 126.9, 114.2, 113.2, 111.9, 83.1, 76.1, 67.8, 59.3, 58.5, 28.8, 19.9, 19.1, 14.2. HRMS-EI$^+$ (m/z): calc’d for C$_{24}$H$_{31}$NO$_3$ 381.2304; found 381.2308.
Prepared from alcohol 1h (0.50 mmol) using General Procedure A. Yield = 184 mg, 80%. $^1$H NMR (400 MHz, Chloroform-d) δ 7.20 – 7.08 (m, 7H), 6.89 – 6.81 (d, 2H), 5.55 (s, 1H), 5.28 (s, 1H), 4.47 (d, $J = 6.6$ Hz, 1H), 4.32 (d, 1H), 4.21 (d, 1H), 3.76 (d, $J = 6.7$ Hz, 1H), 3.64 (s, 3H), 1.64 – 1.53 (m, 15H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.4, 158.5, 137.4, 134.6, 134.5, 132.2, 128.8, 128.6, 128.5, 128.2, 128.1, 127.9, 126.8, 121.4, 114.3, 80.8, 68.1, 67.7, 55.5, 26.9, 26.8, 19.9, 19.8, 14.4. HRMS-EI$^+$ (m/z): calc’d for C$_{29}$H$_{33}$NO$_4$ 459.2410; found 459.2416.
Prepared from alcohol 1i (0.25 mmol) using General Procedure A. Yield = 74 mg, 74%. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.27 – 7.13 (m, 5H), 7.06 – 6.95 (m, 2H), 6.81 – 6.64 (m, 2H), 4.65 – 4.47 (m, 2H), 4.30 (d, $J$ = 16.7 Hz, 1H), 4.03 (d, $J$ = 15.2 Hz, 1H), 3.63 (s, 12H), 2.60 (s, 1H), 2.57 (s, 1H), 1.78 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.4, 158.6, 136.7, 134.0, 132.5, 131.1, 129.0, 128.9, 128.3, 128.2, 128.2, 127.0, 114.4, 82.9, 79.3, 74.7, 74.6, 67.0, 66.1, 65.1, 55.5, 14.6. HRMS-EI$^+$ (m/z): calc’d for C$_{25}$H$_{21}$NO$_4$ 399.1471; found 399.1468.
Prepared from alcohol 1j (0.5 mmol) using General Procedure A. Yield = 195 mg, 83%. $^1$H NMR (400 MHz, Chloroform-d) δ 7.56 (t, $J = 8.9$ Hz, 4H), 7.46 – 7.24 (m, 6H), 7.23 (t, $J = 7.3$ Hz, 1H), 7.06 (d, $J = 8.3$ Hz, 2H), 6.82 (d, $J = 8.3$ Hz, 2H), 5.35 (d, $J = 6.9$ Hz, 1H), 4.72 (d, $J = 2.7$ Hz, 1H), 4.59 (dd, $J = 8.5, 2.7$ Hz, 1H), 4.22 – 4.09 (m, 1H), 4.04 (d, $J = 15.2$ Hz, 1H), 3.79 (s, 3H), 1.41 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.5, 159.5, 145.0, 142.8, 130.4, 129.4, 128.5, 128.3, 127.6, 127.4, 127.3, 126.5, 126.2, 124.7, 114.2, 114.1, 113.7, 83.1, 80.2, 68.4, 57.9, 55.4, 53.6, 28.2. HRMS-El$^+$ (m/z): calc’d for C$_{30}$H$_{32}$NO$_4$ 469.2253; found 469.2249.
Prepared from alcohol 1k (0.5 mmol) using General Procedure A. Yield = 212 mg, 80%. $^1$H NMR (400 MHz, Chloroform- $d$) $\delta$ 7.36 – 7.21 (m, 3H), 7.19 (d, $J = 5.1$ Hz, 2H), 7.12 (d, $J = 15.1$ Hz, 1H), 6.84 (d, $J = 8.3$ Hz, 3H), 6.77 (d, $J = 8.0$ Hz, 1H), 5.46 (d, $J = 6.9$ Hz, 1H), 4.73 – 4.68 (m, 1H), 4.61 (d, $J = 8.1$ Hz, 1H), 4.16 (d, $J = 15.2$ Hz, 1H), 4.03 (d, $J = 15.2$ Hz, 1H), 3.83 – 3.73 (m, 9H), 1.43 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.5, 159.8, 159.6, 159.5, 146.6, 144.5, 130.5, 129.6, 129.5, 129.2, 128.7, 127.6, 118.8, 118.7, 114.1, 112.8, 112.3, 111.8, 83.2, 80.0, 68.3, 57.9, 55.3, 55.3, 55.2, 53.7, 28.3. HRMS-El$^+$ (m/z): calc’d for C$_{32}$H$_{35}$NO$_6$ 529.2464; found 529.2469.
Prepared from alcohol II (1.0 mmol) using General Procedure A. Yield = 244 mg, 72%. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.33 – 7.26 (m, 5H), 6.14 – 5.96 (m, 3H), 5.51 (d, $J = 7.2$ Hz, 1H), 5.44 (d, $J = 17.3$ Hz, 1H), 5.29 (t, $J = 11.9$ Hz, 2H), 4.72 (d, $J = 7.6$ Hz, 1H), 4.22 – 4.06 (m, 1H), 3.98 (d, $J = 15.4$ Hz, 1H), 3.74 (s, 1H), 1.47 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.6, 139.2, 136.0, 131.9, 131.2, 128.7, 128.1, 127.8, 126.4, 115.2, 115.0, 82.9, 78.3, 67.8, 58.1, 53.3, 28.0. HRMS-EI$^+$ (m/z): calc’d for C$_{21}$H$_{25}$NO$_3$ 339.1834; found 339.1837.
Prepared from alcohol 1m (1.0 mmol) using General Procedure A. Yield = 258 mg, 70%. $^1$H NMR (400 MHz, Chloroform-d) δ 7.27 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.1$ Hz, 2H), 6.13 – 5.88 (m, 3H), 5.51 (d, $J = 17.2$ Hz, 1H), 5.42 (d, $J = 7.4$ Hz, 1H), 5.35 – 5.16 (m, 2H), 4.68 (d, $J = 8.0$ Hz, 1H), 4.17 (d, $J = 15.3$ Hz, 1H), 4.06 – 3.93 (m, 1H), 3.80 (s, 3H), 3.76 – 3.71 (m, 1H), 1.45 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.0, 159.6, 140.6, 130.7, 129.6, 128.7, 127.9, 127.6, 116.6, 115.1, 114.1, 85.2, 78.4, 67.8, 58.1, 55.4, 53.2, 28.0. HRMS-El$^+$ (m/z): calc’d for C$_{22}$H$_{27}$NO$_4$ 369.1940; found 369.1945.
Prepared from alcohol In (1.0 mmol) using General Procedure A. Yield = 252 mg, 71%. $^1$H NMR (400 MHz, Chloroform-d) δ 7.28 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.1 Hz, 2H), 6.38 (d, J = 7.9 Hz, 1H), 6.06 (dd, J = 17.3, 10.9 Hz, 1H), 6.01 – 5.89 (m, 2H), 5.39 (d, J = 17.3 Hz, 1H), 5.25 (d, J = 11.8 Hz, 2H), 4.36 – 4.18 (m, 3H), 4.02 (d, J = 15.8 Hz, 1H), 3.79 (s, 3H), 3.66 (d, J = 3.9 Hz, 1H), 1.25 (two d, J = 7.0 Hz, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 159.7, 139.5, 132.3, 129.0, 128.7, 128.2, 127.8, 115.3, 114.8, 114.2, 82.8, 78.3, 66.9, 56.3, 55.3, 47.9, 19.9, 19.7.

HRMS-EI$^+$ (m/z): calc’d for C$_{21}$H$_{25}$NO$_4$ 355.1784; found 355.1788. FTIR (KBr): 3009.7533, 2933.6078, 1647.735, 1607.2444, 1577.183, 1512.0128, 1454.2907, 1427.6278, 1359.8311, 1299.2028, 1250.9581, 1176.0437, 1151.5694, 1119.6948, 1031.3279, 990.3239, 927.8622, 825.4347, 765.0418, 749.7978
Prepared from alcohol 1o (1.0 mmol) using General Procedure A. Yield = 275 mg, 75%. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.40 – 7.20 (m, 5H), 6.39 (d, $J = 8.2$ Hz, 1H), 5.27 (s, 1H), 5.17 (s, 1H), 5.12 (s, 1H), 5.04 (s, 1H), 4.76 (d, $J = 8.2$ Hz, 1H), 4.30 – 4.25 (m, 1H), 4.21 – 4.08 (m, 1H), 4.01 (d, $J = 15.1$ Hz, 1H), 1.73 (ss, 6H), 1.47 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.5, 145.5, 143.9, 136.0, 131.8, 131.4, 128.8, 127.8, 126.5, 113.8, 113.0, 82.8, 78.2, 68.1, 57.9, 53.8, 28.4, 19.2, 18.8. HRMS-ESI$^+ (m/z)$: calc’d for C$_{23}$H$_{29}$N$_3$O$_3$ 367.2147; found 367.2141. FTIR (KBr): 2971.495, 2923.9815, 1644.4038, 1491.4705, 1446.8961, 1429.3142, 1391.6056, 1362.4703, 1318.9377, 1292.671, 1268.871, 1223.0439, 1199.5844, 1151.3831, 1117.7388, 993.1353, 905.3314, 744.2027, 699.8784.
Prepared from alcohol 1p (0.5 mmol) using General Procedure A. Yield = 159 mg, 80%. $^1$H NMR (400 MHz, Chloroform-d) δ 7.27 (d, $J = 8.3$ Hz, 2H), 6.86 (d, $J = 7.8$ Hz, 2H), 6.31 (d, $J = 6.4$ Hz, 1H), 5.25 (s, 1H), 5.16 (s, 1H), 5.11 (s, 1H), 5.02 (d, $J = 8.9$ Hz, 1H), 4.72 (d, $J = 8.2$ Hz, 1H), 4.27 (s, 1H), 4.15 (d, $J = 15.2$ Hz, 1H), 4.01 (d, $J = 15.2$ Hz, 1H), 3.80 (d, $J = 3.2$ Hz, 3H), 1.67 (ss, 6H), 1.45 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.5, 159.4, 145.5, 143.3, 131.8, 130.8, 129.4, 128.6, 127.8, 127.6, 126.5, 114.1, 113.7, 112.0, 82.8, 78.1, 68.2, 68.1, 57.8, 55.4, 53.8, 28.4, 19.0, 18.4. HRMS-El$^+$ (m/z): calc’d for C$_{24}$H$_{31}$NO$_4$ 397.2253; found 397.2256.
Prepared from alcohol 1q (0.5 mmol) using General Procedure A. Yield = 125 mg, 79%. $^1$H NMR (400 MHz, Benzene-$d_6$) $\delta$ 7.22 – 7.07 (m, 5H), 6.48 (d, $J$ = 8.0 Hz, 1H), 4.80 (dd, $J$ = 8.0, 2.4 Hz, 1H), 4.33 (d, $J$ = 15.2 Hz, 1H), 3.88 (d, $J$ = 15.2 Hz, 1H), 3.38 (d, $J$ = 2.4 Hz, 1H), 1.56 (s, 9H), 1.29 (s, 3H), 1.27 (s, 3H). $^{13}$C NMR (101 MHz, C$_6$D$_6$) $\delta$ 171.0, 136.4, 133.1, 130.7, 128.7, 128.7, 128.0, 127.8, 127.5, 84.9, 72.2, 67.9, 57.5, 53.6, 30.2, 27.4, 23.5. HRMS-ESI$^+$ (m/z): calc’d for C$_{19}$H$_{25}$NO$_3$ 315.1834; found 315.1839. FTIR (KBr) 3018.5506, 2924.8333, 1642.2515, 1494.9545, 1448.8548, 1427.0419, 1393.4602 1361.6968, 1328.7144, 1289.7737, 1223.6425, 1198.9141, 1130.0001, 1074.1578, 1030.4745, 988.561, 966.1662, 925.5022, 741.6755, 693.4562.
Prepared in 0.25 mmol scale using General Procedure A. Yield = 108 mg, 83%. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.58 – 7.46 (m, 4H), 7.37 – 7.23 (m, 6H), 7.08 (d, $J = 8.2$ Hz, 2H), 6.83 (d, $J = 8.2$ Hz, 2H), 5.32 (d, $J = 6.1$ Hz, 1H), 4.83 – 4.75 (m, 1H), 4.64 (d, $J = 8.0$ Hz, 1H), 4.15 (p, $J = 6.4$ Hz, 1H), 3.79 (s, 3H), 3.20 (s, 1H), 1.32 – 1.23 (m, 12H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 173.8, 159.5, 145.2, 145.2, 143.3, 130.8, 130.1, 129.8, 128.8, 128.6, 128.4, 128.3, 127.9, 127.5, 127.3, 127.2, 126.8, 126.3, 126.0, 125.6, 125.0, 114.2, 82.9, 80.6, 73.4, 58.3, 56.4, 54.6, 29.8, 16.5.

HRMS-EI$^+$ (m/z): calc’d for C$_{31}$H$_{33}$NO$_4$ 483.2410; found 483.2415.
Prepared in 0.50 mmol scale using General Procedure A. Yield = 172 mg, 90% and 94:6 dr.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.29 – 7.24 (m, 5H), 6.55 (d, $J$ = 7.9 Hz, 1H), 5.89 (tt, $J$ = 16.9, 7.7 Hz, 2H), 5.19 (d, $J$ = 5.9 Hz, 1H), 5.19 – 5.10 (m, 3H), 4.85 (d, $J$ = 7.6 Hz, 1H), 4.00 (q, $J$ = 6.5 Hz, 1H), 3.70 (d, $J$ = 2.4 Hz, 1H), 2.44 (ddt, $J$ = 22.0, 14.1, 7.2 Hz, 2H), 2.28 (dd, $J$ = 14.2, 8.1 Hz, 1H), 2.03 (d, $J$ = 10.1 Hz, 1H), 1.55 – 1.38 (m, 12H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 174.0, 136.1, 133.4, 132.5, 131.8, 130.7, 129.2, 128.7, 127.9, 126.6, 126.4, 119.4, 118.8, 82.1, 76.2, 72.4, 57.9, 54.7, 40.4, 40.0, 28.5, 16.4. HRMS-ESI$^+$ (m/z): calc’d for C$_{24}$H$_{31}$NO$_3$ 381.2304; found 381.2308.
Prepared in 0.5 mmol scale using General Procedure A. Yield = 156 mg, 77% and 95:5 dr. $^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 7.34 – 7.26 (m, 5H), 6.37 (d, $J$ = 7.8 Hz, 1H), 5.31 (s, 1H), 5.15 (d, $J$ = 7.8 Hz, 1H), 5.02 (s, 1H), 4.78 (d, $J$ = 7.8 Hz, 1H), 4.30 (d, $J$ = 2.3 Hz, 1H), 4.07 (q, $J$ = 6.4 Hz, 1H), 1.73 (ss, 6H), 1.45 – 1.36 (m, 12H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 173.8, 145.5, 143.9, 136.1, 132.5, 131.8, 131.4, 128.8, 127.8, 126.5, 126.4, 125.5, 113.7, 113.2, 82.5, 79.2, 72.4, 58.3, 54.1, 28.5, 19.6, 18.6, 16.3. HRMS-EI$^+$ ($m/z$): calc’d for C$_{24}$H$_{31}$NO$_3$ 381.2304; found 381.2308.
Prepared in 0.25 mmol scale using General Procedure A. Yield = 127 mg, 83% and 95:5 dr. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.23 – 6.58 (m, 16H), 4.99 (d, $J = 6.3$ Hz, 1H), 4.92 (d, $J = 6.3$ Hz, 1H), 4.51 (s, 2H), 3.73 – 3.69 (m, 12H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.1, 159.6, 159.4, 158.6, 158.3, 146.7, 143.5, 132.1, 129.3, 129.1, 128.7, 128.6, 118.5, 118.4, 114.2, 113.8, 112.8, 112.5, 112.1, 112.0, 82.7, 79.5, 67.7, 63.3, 55.3, 55.3, 55.2, 55.1. HRMS-EI$^+$ ($m/z$): calc’d for C$_{35}$H$_{32}$ClNO$_7$ 613.1867; found 613.1870.
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Prepared in 0.25 mmol scale using General Procedure A. Yield = 93 mg, 84% and 95:5 dr.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.12 (d, $J = 8.3$ Hz, 2H), 6.83 (d, $J = 8.2$ Hz, 2H), 5.97 (dd, $J = 17.3$, 10.7 Hz, 1H), 5.82 (dd, $J = 17.2$, 10.7 Hz, 1H), 5.43 (d, $J = 17.1$ Hz, 1H), 5.35 (d, $J = 17.3$ Hz, 1H), 5.19 (dd, $J = 14.4$, 10.7 Hz, 2H), 4.61 (d, $J = 4.1$ Hz, 1H), 4.35 (d, $J = 16.1$ Hz, 1H), 4.14 (d, $J = 16.1$ Hz, 1H), 3.77 (s, 3H), 3.63 (d, $J = 4.0$ Hz, 1H), 3.59 (d, $J = 12.1$ Hz, 1H), 1.94 (dt, $J = 20.2$, 11.2 Hz, 1H), 1.58 – 1.18 (m, 11H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.3, 159.1, 139.7, 139.2, 133.6, 129.0, 127.8, 114.8, 114.2, 114.0, 82.4, 78.6, 66.7, 60.1, 57.7, 55.3, 32.4, 32.3,
27.8, 27.4, 27.3, 27.1, 25.6, 25.5, 25.2, 24.9, 24.8. **HRMS-EI**\(^{(m/z)}\): calc’d for C\(_{25}\)H\(_{30}\)ClNO\(_4\) 443.1863; found 443.1869.
Prepared in 0.25 mmol scale using General Procedure A. Yield = 112 mg, 86% and 95:5 dr. $^{1}$H NMR (400 MHz, Chloroform-d) δ 7.50 – 7.23 (m, 4H), 7.19 – 6.97 (m, 6H), 6.49 (d, $J$ = 8.4 Hz, 1H), 6.15 (dd, $J$ = 8.3, 2.1 Hz, 1H), 5.78 (d, $J$ = 2.3 Hz, 1H), 4.66 (d, $J$ = 4.3 Hz, 1H), 4.55 (d, $J$ = 4.3 Hz, 1H), 4.14 – 3.91 (m, 2H), 3.66 (s, 3H), 3.51 (s, 3H), 1.03 (d, $J$ = 6.8 Hz, 3H), 0.72 (d, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.0, 148.8, 148.2, 145.3, 143.0, 134.9, 128.4, 128.3, 127.3, 127.3, 126.4, 126.3, 119.0, 111.0, 110.2, 83.3, 80.2, 67.4, 56.0, 55.9, 48.6, 20.3, 19.9. HRMS-EI$^+$ (m/z): calc’d for C$_{30}$H$_{30}$ClNO$_5$ 519.1813; found 519.1817.
Prepared in 0.25 mmol scale using General Procedure A. Yield = 112 mg, 86% and 95:5 dr. $^1$H NMR (400 MHz, Chloroform-<i>d</i>) δ 7.51 – 7.41 (s, 1H), 7.41 – 7.34 (m, 2H), 7.10 (d, $J$ = 12.9 Hz, 1H), 7.07 – 6.97 (m, 2H), 6.77 (d, 2H), 5.99 (d, 1H), 5.50 (s, 1H), 5.39 (s, 1H), 5.34 (s, 1H), 4.54 (ddd, $J$ = 8.1, 5.4, 0.9 Hz, 1H), 4.38 (d, $J$ = 15.9 Hz, 1H), 4.14 (d, $J$ = 15.9 Hz, 1H), 3.76 – 3.62 (m, 4H), 1.75 – 1.54 (m, 12H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.5, 159.7, 140.7, 137.7, 135.1, 133.2, 131.1, 129.6, 128.6, 128.1, 127.9, 127.7, 127.5, 125.6, 124.3, 124.3, 124.0, 123.9, 114.1, 83.6, 67.7, 61.9, 55.3, 26.8, 26.8, 19.8, 19.7. HRMS-<i>E</i>i<sup>+</sup> (m/z): calc’d for C$_{35}$H$_{30}$F$_3$NO$_6$ 617.2025; found 617.2029.
Prepared in 0.25 mmol scale using General Procedure A. Yield = 134 mg, 87% and 95:5 dr. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.42 – 7.29 (m, 3H), 7.27 (dd, $J = 3.2, 1.6$ Hz, 1H), 7.05 – 6.96 (m, 10H), 6.75 – 6.55 (m, 3H), 4.66 (d, $J = 5.4$ Hz, 1H), 4.55 – 4.42 (m, 1H), 4.30 (d, $J = 15.7$ Hz, 1H), 4.21 (d, $J = 15.7$ Hz, 1H), 3.77 – 3.72 (m, 6H), 3.57 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.5, 159.8, 159.7, 146.2, 143.6, 140.4, 132.8, 130.8, 129.5, 129.5, 129.4, 127.7, 124.7, 124.1, 118.6, 118.5, 113.8, 112.9, 112.6, 112.4, 112.2, 81.8, 79.4, 77.4, 77.4, 67.7, 61.6, 55.3, 55.3, 55.1. HRMS-ESI$^+$ ($m/z$): calc’d for C$_{35}$H$_{30}$F$_3$NO$_6$ 617.2025; found 617.2029.
Prepared from bicycle 2c (0.5 mmol) using General Procedure B. Yield = 156 mg, 92%. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.43 – 7.25 (m, 5H), 5.81 – 5.64 (m, 2H), 4.38 (d, $J = 6.1$ Hz, 1H), 4.31 (d, $J = 15.9$ Hz, 1H), 4.20 – 4.05 (m, 2H), 3.67 (d, $J = 6.0$ Hz, 1H), 2.77 (dt, $J = 17.7$, 2.2 Hz, 1H), 2.70 – 2.46 (m, 2H), 2.46 – 2.35 (m, 1H), 1.93 (s, 3H), 1.38 (d, $J = 6.9$ Hz, 3H), 1.34 – 1.20 (d, $J = 6.9$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.5, 136.7, 136.4, 131.2, 128.8, 128.7, 128.5, 128.4, 128.3, 127.3, 127.2, 83.0, 80.6, 67.6, 63.1, 49.2, 46.3, 44.5, 38.7, 19.8, 19.6, 14.1. **HRMS-El** ($m/z$): calc’d for C$_{21}$H$_{25}$NO$_3$ 339.1834; found 339.1839.
Prepared from bicycle 2d (0.5 mmol) using General Procedure B. Yield = 159 mg, 87%. $^1$H NMR (400 MHz, Chloroform-d) δ 7.36 (q, $J = 7.5$ Hz, 2H), 7.28 (s, 1H), 5.76 – 5.66 (m, 2H), 4.36 – 4.25 (m, 2H), 4.10 (d, $J = 16.0$ Hz, 1H), 3.92 (p, $J = 8.7$ Hz, 1H), 3.66 (d, $J = 6.4$ Hz, 1H), 2.74 (d, $J = 17.6$ Hz, 1H), 2.53 (d, $J = 21.1$ Hz, 2H), 2.36 (d, $J = 16.9$ Hz, 1H), 2.30 (s, 1H), 2.09 – 1.93 (m, 2H), 1.91 (s, 1H), 1.89 (s, 3H), 1.86 – 1.76 (m, 3H), 1.48 (q, $J = 9.1$, 8.1 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.3, 136.7, 135.9, 131.3, 128.9, 128.4, 128.3, 128.2, 127.3, 82.8, 80.4, 67.8, 65.1, 59.1, 46.4, 44.5, 28.7, 28.6, 24.6, 14.2. **HRMS-El** (m/z): calc’d for C$_{23}$H$_{27}$NO$_3$ 365.1991; found 365.1995.
Prepared in 0.25 mmol scale using General Procedure B. Yield = 84 mg, 89%. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.37 (t, $J = 7.5$ Hz, 3H), 7.28 (s, 3H), 5.70 (q, $J = 7.0$ Hz, 2H), 4.40 (d, $J = 7.5$ Hz, 1H), 4.12 (h, $J = 8.8$, 7.9 Hz, 2H), 3.78 (dd, $J = 18.6$, 9.1 Hz, 1H), 3.72 (d, $J = 7.8$ Hz, 1H), 2.72 (d, $J = 17.9$ Hz, 1H), 2.57 – 2.44 (m, 2H), 2.36 (s, 0H), 2.31 (s, 2H), 2.04 (s, 2H), 1.93 (s, 2H), 1.83 (d, $J = 25.6$ Hz, 8H), 1.69 – 1.59 (m, 2H), 1.49 – 1.42 (m, 5H), 1.25 (d, $J = 6.5$ Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.4, 136.7, 135.8, 133.2, 131.9, 129.4, 128.9, 128.5, 128.3, 127.9, 127.2, 82.4, 80.5, 73.8, 66.8, 59.6, 45.8, 43.7, 27.9, 24.3, 18.4, 14.2. HRMS-EI$^+$ ($m/z$): calc’d for C$_{24}$H$_{29}$NO$_3$ 379.2147; found 379.2142.
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![Chemical Shift Graph]

- Normalized intensity vs. Chemical Shift (ppm)
- Two sets of data presented with molecular structures as labels.
LAH reduction

To a 50 mL round-bottomed flask equipped with a magnetic stir bar under a N₂ atmosphere, in a 0 °C ice/water bath, was added bicycle 2b (220 mg, 0.50 mmol) and THF (20 mL). LiAlH₄ (100 mg, 2.70 mmol) was then added portion-wise. The reaction mixture was allowed to warm to room temperature overnight (judged complete by GC-MS analysis). After this time, the reaction mixture was cooled to 0 °C and quenched by slow addition of a solution of 2 N NaOH (aq) (3 mL). The organic layer was decanted and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated in vacuo to yield the tertiary amine as an oil with no purification required. Yield = 189 mg, 89%. ¹H NMR (400 MHz, Chloroform-d) δ 7.77 – 7.70 (m, 2H), 7.42 – 7.05 (m, 13H), 4.39 (d, J = 7.9 Hz, 1H), 4.00 (dt, J = 11.0, 3.1 Hz, 1H), 3.66 (td, J = 10.7, 2.6 Hz, 1H), 3.41 (d, J = 7.9 Hz, 1H), 2.95 (hept, J = 6.6 Hz, 1H), 2.76 (dt, J = 11.5, 2.8 Hz, 1H), 2.54 (td, J = 11.0, 3.4 Hz, 1H), 1.94 (d, J = 1.3 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 145.4, 145.1, 137.3, 131.2, 129.0, 128.0, 127.7, 127.2, 126.8, 126.8, 126.6, 126.6, 81.9, 80.6, 68.1, 67.1, 47.8, 42.0, 21.2, 15.2, 13.3. HRMS-El⁺ (m/z): calc’d for C₂₉H₃₁NO₂ 425.2355; found 425.2359.
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[Two NMR spectroscopy graphs are shown, each with chemical shift values indicated.]
Prepared in the same way as 8a. Yield = 189 mg, 89%. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.74 – 7.57 (m, 4H), 7.49 – 7.13 (m, 9H), 6.97 (ddt, $J = 7.7, 1.7, 0.9$ Hz, 1H), 6.88 – 6.71 (m, 2H), 6.68 (t, $J = 2.1$ Hz, 1H), 6.60 (dd, $J = 8.1, 2.4$ Hz, 1H), 6.39 (d, $J = 6.5$ Hz), 4.53 (d, $J = 1.2$ Hz, 1H), 4.33 (dt, $J = 6.6, 1.4$ Hz, 1H), 3.78 (s, 3H), 3.86 – 3.74 (m, 1H), 3.55 (ddd, $J = 12.2, 6.4, 2.6$ Hz, 1H), 3.44 (ddd, $J = 12.2, 5.9, 2.6$ Hz, 1H), 3.32 (ddd, $J = 10.1, 6.4, 2.6$ Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 159.5, 146.3, 145.2, 144.8, 131.1, 129.7, 128.7, 128.3, 127.7, 127.5, 127.2, 126.8, 125.9, 125.8, 118.2, 115.9, 114.1, 112.1, 86.3, 81.2, 75.8, 62.0, 57.2, 55.4. HRMS-EI$^+$ (m/z): calc’d for C$_{29}$H$_{31}$NO$_2$ 425.2355; found 425.2359.
References