Supporting Information

Asymmetric Homogeneous Hydrogenation of 2-Pyridones

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1. General information

Unless otherwise noted, all reactions were carried out under an atmosphere of argon in flame-dried glassware. Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. The solvents used were purified by distillation over the drying agents indicated in parentheses and were transferred under argon: n-hexane (CaH₂), THF (Na-benzophenone), toluene (CaH₂). DME and DMA were purchased as dry compounds, transferred under argon and stored over 4 Å molecular sieves.

All hydrogenation reactions were carried out in Berghof High Pressure Reactors using hydrogen gas. Commercially available chemicals were obtained from Acros Organics, Aldrich Chemical Co., Strem Chemicals, Alfa Aesar, ABCR and TCI Europe and used as received unless otherwise stated.

Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Flash chromatography was either performed on Merck silica gel (40-63 mesh) by standard technique eluting with solvents as indicated. GC-MS spectra were recorded on an Agilent Technologies 78900A GC-system with an Agilent 5975C VL MSD or an Agilent 5975 inert Mass Selective Detector (EI) and an HP-5MS column (0.25 mm × 30 m, Film: 0.25 μm). The major signals are quoted in m/z with the relative intensity in parentheses. The method used starts with the injection temperature $T_0$; after holding this temperature for 3 min, the column is heated to the temperature $T_1$ (ramp) and this temperature is held for an additional time $t$: Method 50_40: $T_0 = 50 \, ^\circ C$, $T_1 = 290 \, ^\circ C$, ramp = 40 °C/min, $t = 4$ min.

Chiral GC spectra were recorded on a Hewlett Packard 6890 GC-system with a Supelco β-Dex 225 column (0.25 mm × 30 m, Film: 0.25 μm). The method used starts with the injection temperature $T_0$; after holding this temperature for 10 min, the column is heated to the temperature $T_1$ (ramp) and this temperature is held for an additional time $t$: Method 80_10_1_170_30: $T_0 = 80 \, ^\circ C$, $T_1 = 170 \, ^\circ C$, ramp = 1 °C/min, $t = 30$ min.

$^1$H and $^{13}$C-NMR spectra were recorded on a Bruker AV 300 or AV 400 or a Varian Unity plus 600 in solvents as indicated. Chemical shifts ($\delta$) are given in ppm relative to TMS. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl₃: $\delta$H = 7.26 ppm, $\delta$C = 77.16 ppm; CD₂Cl₂: $\delta$H = 5.32 ppm, $\delta$C = 54.00 ppm, (CD₃)₂SO: $\delta$H = 2.50 ppm, $\delta$C = 39.52 ppm). ESI mass spectra were recorded on a Bruker Daltonics MicroTof. Specific rotation was measured on a Perkin Elmer 341 polarimeter at 24 °C using a quartz glass cell (100 mm path length). The enantiomeric ratio (e.r.) was determined by HPLC analysis using chiral column OD-H and OJ-H. No attempts were made to optimize yields for substrate synthesis.
2. Chiral ligands used in the asymmetric hydrogenation of 2-pyridones

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![Chemical structures and reaction scheme](image-url)
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[a] General conditions: 1a (0.3 mmol), [Ru(2-Me-allyl)2(COD)] (0.015 mmol), ligand·HX (0.030 mmol), KOt-Bu (0.045 mmol), H2 (80 bar), hexane (1 mL), 50 °C, 24 h; preformed complex was used. [b] NMR conversions are given. [c] Enantiomeric ratio was determined by HPLC on a chiral stationary phase.
3. Synthesis and characterization of 2-pyridones (3a-3e, 5a-5h)

**Compound 3a: 1,6-dimethyl-2(1H)-pyridone**

In a dry Schlenk tube 6-methyl-2(1H)-pyridone (1) (3.43 g, 31.44 mmol) was dissolved in 50 mL of 1,4-dioxane and KO\textsubscript{t}-Bu (8.69 g, 62.88 mmol) was added. The mixture was stirred at 100 °C for 2 h, then cooled down to rt, MeI (19.6 mL, 314.41 mmol) was added dropwise and the mixture was stirred at 80 °C for 16 h. The solvent was removed under reduced pressure and the residue was separated between DCM and water. The extraction was performed using DCM (3×) and the combined organic phases were dried over MgSO\textsubscript{4}, filtered and evaporated. The residue was transferred to a column chromatography (5% MeOH in DCM) to afford 3a (orange solid), 3.70 g (96%).

R\textsubscript{f} = 0.23 (EtOAc); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.14 (dd, J = 9.1, 6.8 Hz, 1H), 6.38 (d, J = 8.3 Hz, 1H), 5.97 (d, J = 6.2 Hz, 1H), 3.46 (s, 3H), 2.29 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 163.91, 146.39, 138.64, 117.21, 106.50, 31.14, 21.00; GC-MS: R\textsubscript{t} (50_40): 7.2 min; EI: 124 (6), 123 (73), 108 (10), 95 (25), 94 (100), 80 (6), 65 (5), 56 (8), 53 (7), 39 (19); ATR-FTIR (cm\textsuperscript{-1}): 1651, 1547, 1504, 1427, 1397, 1373, 1269, 1157, 1119, 1038, 1011, 856, 787, 729.

**Compound 3b: 1,5-dimethyl-2(1H)-pyridone**

Following the same procedure as for 3a, 5-methyl-2(1H)-pyridone (1b) (662.9 mg, 6.07 mmol) was converted to 1,5-dimethyl-2(1H)-pyridone (yellow oil), (743.4 mg, 99%).

R\textsubscript{f} = 0.20 (EtOAc); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.13 (dd, J = 9.2, 2.6 Hz, 1H), 7.01 (s, 1H), 6.45 (d, J = 9.2 Hz, 1H), 3.45 (s, 3H), 2.01 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 162.37, 142.13, 135.86, 120.24, 114.87, 37.48, 17.00; GC-MS: R\textsubscript{t} (50_40): 7.1 min; EI: 123 (76), 95 (20), 94 (100), 80 (5), 53 (13), 52 (5), 51 (6), 42 (18), 41 (5), 39 (7); ATR-FTIR (cm\textsuperscript{-1}): 2978, 1663, 1574, 1539, 1420, 1366, 1323, 1273, 1211, 1150, 1049, 953, 922, 880, 829, 737, 714.

**Compound 3c: 1,4-dimethyl-2(1H)-pyridone**

Following the same procedure as for 3a, 4-methyl-2(1H)-pyridone (1c) (539.1 mg, 4.94 mmol) was converted to 1,4-dimethyl-2(1H)-pyridone (orange solid), (584.3 mg, 96%).

R\textsubscript{f} = 0.25 (EtOAc); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.08 (d, J = 6.9 Hz, 1H), 6.24 (s, 1H), 5.90 (dd, J = 6.9, 1.9 Hz, 1H), 3.39 (s, 3H), 2.06 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 162.96, 151.07, 137.15, 118.84, 108.31, 37.03, 21.08; GC-MS: R\textsubscript{t} (50_40): 7.1 min; EI: 123 (76), 95 (20), 94 (100), 80 (8), 53 (13), 52 (5), 51 (6), 42 (11), 41 (5), 39 (9); ATR-FTIR (cm\textsuperscript{-1}): 2982, 1659, 1578, 1562, 1539, 1429, 1439, 1415, 1381, 1343, 1319, 1254, 1184, 1126, 1057, 1038, 949, 856, 779, 748, 610.

**Compound 3d: 1,3-dimethyl-2(1H)-pyridone**

Following the same procedure as for 3a, 3-methyl-2(1H)-pyridone (1d) (806.7 mg, 7.39 mmol) was converted to 1,3-dimethyl-2(1H)-pyridone (yellow oil), (831.4 mg, 91%).

R\textsubscript{f} = 0.27 (EtOAc); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.13 (t, J = 6.4 Hz, 2H), 6.02 (t, J = 6.7 Hz, 1H), 3.50 (s, 3H), 2.10 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 163.46, 136.73, 135.67, 129.66, 105.53, 37.76, 17.26; GC-MS: R\textsubscript{t} (50_40): 6.7 min; EI: 123 (52), 95 (18), 94 (100), 80 (10), 53 (9), 52 (6), 51 (8), 42 (8), 39 (8); ATR-FTIR (cm\textsuperscript{-1}): 1647, 1582, 1559, 1508, 1435, 1404, 1377, 1319, 1227, 1103, 1045, 1011, 930, 868, 768.
Compound 3e: 1-methyl-5-(trifluoromethyl)-2(1H)-pyridone

Following the same procedure as for 3a, 5-(trifluoromethyl)-2(1H)-pyridone (1e) (1.63 g, 10.0 mmol) was converted to 1-methyl-5-(trifluoromethyl)-2(1H)-pyridone (yellow solid), (1.42 g, 80%).

R_f = 0.49 (EtOAc); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 7.68 \text{ (s, 1H)}, 7.46 - 7.34 \text{ (m, 1H)}, 6.61 - 6.50 \text{ (m, 1H)}, 3.54 \text{ (s, 3H)}; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta 162.36, 137.99 \text{ (q, } J = 5 \text{ Hz)}, 135.20 \text{ (q, } J = 2 \text{ Hz)}, 123.34 \text{ (q, } J = 270 \text{ Hz)}, 121.07, 109.46 \text{ (q, } J = 36 \text{ Hz)}, 38.14; \) GC-MS: R_t (50_40): 6.2 min; EI: 178 (8), 177 (94), 158 (40), 150 (5), 149 (100), 148 (48), 130 (61), 128 (7), 108 (5), 107 (7), 101 (8), 99 (11), 88 (12), 87 (5), 80 (11), 75 (9), 69 (19), 57 (9), 52 (6), 51 (10), 50 (10); ATR-FTIR (cm\(^{-1}\)): 3048, 2245, 1670, 1616, 1543, 1447, 1389, 1327, 1246, 1157, 1115, 1092, 1030, 949, 907, 833, 795, 729, 637, 613.

Compound 5a: 1-methyl-6-phenyl-2(1H)-pyridone

6-Bromo-1-methyl-2(1H)-pyridone (8a) (422.0 mg, 2.24 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (78.6 mg, 0.11 mmol), PhB(OH)\(_2\) (328.0 mg, 2.69 mmol) and Na\(_2\)CO\(_3\) (1241.1 mg, 8.98 mmol) were placed in a dry Schlenk tube and toluene (32 mL), EtOH (12 mL) and H\(_2\)O (4 mL) were added. The resulted mixture was stirred at 80 °C for 16 h. Toluene and EtOH were removed under reduced pressure and the residual slurry was separated between DCM and water. The extraction was performed using DCM (3×) and the combined organic phases were dried over MgSO\(_4\), filtered and evaporated. The residue was transferred to a column chromatography (2% MeOH in DCM) to afford 5a (orange oil), 397.0 mg (96%).

R_f = 0.34 (EtOAc); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 7.40 - 7.29 \text{ (m, 3H)}, 7.27 - 7.15 \text{ (m, 3H)}, 6.50 \text{ (dd, } J = 9.2, 1.4 \text{ Hz, 1H)}, 6.00 \text{ (dd, } J = 6.9, 1.4 \text{ Hz, 1H)}, 3.26 \text{ (s, 3H)}; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 164.03, 160.39, 150.18, 138.81, 129.89, 127.90, 118.53, 114.22, 108.25, 55.52, 34.62; GC-MS: R_t (50_40): 8.8 min; EI: 186 (7), 185 (64), 184 (100), 157 (12), 156 (22), 129 (5), 128 (7), 115 (14), 77 (11), 51 (6), 39 (11); ATR-FTIR (cm\(^{-1}\)): 3055, 2982, 1647, 1574, 1543, 1489, 1424, 1377, 1339, 1319, 1238, 1180, 1157, 1123, 1061, 1015, 991, 910, 853, 791, 764, 725, 706, 644.

Compound 5b: 6-(4-methoxyphenyl)-1-methyl-2(1H)-pyridone

A procedure similar to that for the preparation of the compound 5a was applied using 4-methoxyphenylboronic acid as the coupling partner. 6-Bromo-1-methyl-2(1H)-pyridone (8a) (300.0 mg, 1.60 mmol) was converted to 6-(4-methoxyphenyl)-1-methyl-2(1H)-pyridone (white solid), (303.0 mg, 88%).

R_f = 0.19 (EtOAc); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.27 \text{ (dd, } J = 9.1, 6.8 \text{ Hz, 1H)}, 7.24 - 7.14 \text{ (m, 2H)}, 6.95 - 6.87 \text{ (m, 2H)}, 6.55 \text{ (dd, } J = 9.2, 1.4 \text{ Hz, 1H)}, 6.04 \text{ (dd, } J = 6.8, 1.4 \text{ Hz, 1H)}, 3.79 \text{ (s, 3H)}, 3.33 \text{ (s, 3H)}; \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta 164.03, 160.39, 150.18, 138.81, 129.89, 127.90, 118.53, 114.22, 108.25, 55.52, 34.62; \) GC-MS: R_t (50_40): 9.4 min; EI: 216 (8), 215 (60), 214 (100), 199 (11), 172 (32), 144 (7), 143 (5), 115 (6); ATR-FTIR (cm\(^{-1}\)): 1647, 1609, 1574, 1508, 1474, 1416, 1288, 1246, 1177, 1158, 1115, 1069, 1011, 841, 795, 725, 698, 656.

Compound 5e: 1-methyl-6-(4-(trifluoromethyl)phenyl)-2(1H)-pyridone
A procedure similar to that for the preparation of the compound 5a was applied using 4-trifluoromethylphenylboronic acid as the coupling partner. 6-Bromo-1-methyl-2(1H)-pyridone (8a) (300.0 mg, 1.60 mmol) was converted to 1-methyl-6-(4-(trifluoromethyl)phenyl)-2(1H)-pyridone (white solid), (384.0 mg, 94%).

\[ R_f = 0.37 \text{ (EtOAc)}; \quad ^1H \text{ NMR (300 MHz, CDCl}_3\):} \delta 7.73 (d, \text{ } J = 8.1 \text{ Hz, 2H}), 7.48 (d, \text{ } J = 8.1 \text{ Hz, 2H}), 7.34 (d, \text{ } J = 9.2, \text{ } 6.8 \text{ Hz, 1H}), 6.61 (d, \text{ } J = 9.4 \text{ Hz, 1H}), 6.08 (dd, \text{ } J = 6.8, \text{ } 1.3 \text{ Hz, 1H}), 3.34 (s, 3H); ^13C \text{ NMR (75 MHz, CDCl}_3\):} \delta 163.58, 148.48, 138.97, 138.54, 131.53 (q, \text{ } J = 33 \text{ Hz}), 129.02, 125.92 (q, \text{ } J = 4 \text{ Hz}), 123.77 (q, \text{ } J = 272 \text{ Hz}), 119.87, 107.97, 34.49; \quad \text{GC-MS:} R_t (50_40): 8.6 \text{ min}; \quad \text{EI:} 254 \text{ (9), 253 \text{ (46), 252 \text{ (100), 234 \text{ (7), 225 (14), 224 (17), 183 (5), 145 (8)}); ATR-FTIR \text{ cm}^{-1}:} 2982, 1647, 1578, 1551, 1512, 1435, 1377, 1319, 1261, 1165, 1111, 1069, 1011, 957, 907, 845, 802, 733, 694, 606.

Compound 5d: 1-methyl-5-phenyl-2(1H)-pyridone

Following the same procedure as for 5a, 5-Bromo-1-methyl-2(1H)-pyridone (8b) (569.4 mg, 3.03 mmol) was converted to 1-methyl-5-phenyl-2(1H)-pyridone (orange oil), (516.2 mg, 92%).

\[ R_f = 0.20 \text{ (EtOAc)}; \quad ^1H \text{ NMR (300 MHz, CDCl}_3\):} \delta 7.62 (dd, \text{ } J = 9.4, \text{ } 2.7 \text{ Hz, 1H}), 7.52 (d, \text{ } J = 2.7 \text{ Hz, 1H}), 7.43 – 7.38 (m, 4H), 7.36 – 7.30 (m, 1H), 6.67 (d, \text{ } J = 9.4 \text{ Hz, 1H}), 3.62 (s, 3H); ^13C \text{ NMR (75 MHz, CDCl}_3\):} \delta 162.33, 139.35, 136.27, 135.70, 129.01, 127.24, 125.67, 120.46, 120.11, 37.94; \quad \text{GC-MS:} R_t (50_40): 9.0 \text{ min}; \quad \text{EI:} 186 \text{ (11), 185 \text{ (100), 184 \text{ (9), 158 \text{ (12), 157 \text{ (69), 156 (23), 142 (9), 131 (5), 129 (7), 128 (8), 116 (11), 115 (34), 114 (7), 89 (9), 63 (11), 42 (7); ATR-FTIR \text{ cm}^{-1}:} 2982, 1655, 1586, 1539, 1497, 1415, 1373, 1327, 1000, 1123, 1076, 1011, 957, 907, 880, 833, 764, 725, 694, 648, 602.

Compound 5e: 5-(4-methoxyphenyl)-1-methyl-2(1H)-pyridone

A procedure similar to that for the preparation of the compound 5a was applied using 4-methoxyphenylboronic acid as the coupling partner. 5-Bromo-1-methyl-2(1H)-pyridone (8b) (587.9 mg, 3.13 mmol) was converted to 5-(4-methoxyphenyl)-1-methyl-2(1H)-pyridone (yellow solid), (650.7 mg, 97%).

\[ R_f = 0.21 \text{ (EtOAc)}; \quad ^1H \text{ NMR (300 MHz, CDCl}_3\):} \delta 7.56 (dd, \text{ } J = 9.4, \text{ } 2.6 \text{ Hz, 1H}), 7.32 – 7.27 (m, 2H), 6.95 – 6.89 (m, 2H), 6.62 (d, \text{ } J = 9.4 \text{ Hz, 1H}), 3.81 (s, 3H), 3.58 (s, 3H); ^13C \text{ NMR (75 MHz, CDCl}_3\):} \delta 162.35, 159.09, 139.51, 135.04, 128.98, 126.99, 120.59, 120.05, 114.51, 55.43, 38.01; \quad \text{GC-MS:} R_t (50_40): 9.7 \text{ min}; \quad \text{EI:} 216 \text{ (13), 215 (100), 201 (8), 200 (58), 172 (26), 145 (6), 144 (9), 115 (6), 102 (6); ATR-FTIR \text{ cm}^{-1}:} 3040, 2978, 2905, 2835, 1659, 1601, 1574, 1535, 1508, 1439, 1408, 1370, 1319, 1277, 1246, 1165, 1115, 1080, 1011, 953, 907, 880, 853, 826, 772, 721, 694, 671, 640.

Compound 5f: 1-methyl-5-(4-(trifluoromethyl)phenyl)-2(1H)-pyridone

A procedure similar to that for the preparation of the compound 5a was applied using 4-trifluoromethylphenylboronic acid as the coupling partner. 5-Bromo-1-methyl-2(1H)-pyridone (8b) (587.9 mg, 3.13 mmol) was converted to 1-methyl-5-(4-(trifluoromethyl)phenyl)-2(1H)-pyridone (yellow solid), (790.4 mg, quant).

\[ R_f = 0.29 \text{ (EtOAc)}; \quad ^1H \text{ NMR (300 MHz, CDCl}_3\):} \delta 7.70 – 7.45 (m, 6H), 6.67 (d, \text{ } J = 10.1 \text{ Hz, 1H}), 3.62 (s, 3H); ^13C \text{ NMR (75 MHz, CDCl}_3\):} \delta 162.40, 140.05, 138.94, 136.50, 129.36 (q, \text{ } J = 32.9 \text{ Hz}), 126.14 (q, \text{ } J = 3.7 \text{ Hz}), 125.99, 124.16 (q, \text{ } J = 272 \text{ Hz}), 121.07, 118.67, 38.18; \quad \text{GC-MS:} R_t (50_40): 9.0 \text{ min}; \quad \text{EI:} 254 (14), 253 (100), 252 (7), 234 (9), 226 (8), 225 (65), 224 (24), 184 (6), 183 (13), 182 (5), 133 (8), 102 (6), 92 (6), 85 (9), 63 (11), 42 (7), 31 (11), 29 (11), 28 (11), 27 (11).
Compound 5g: 1-methyl-4-phenyl-2(1H)-pyridone

Following the same procedure as for 5a, 4-Bromo-1-methyl-2(1H)-pyridone (8e) (999.1 mg, 5.31 mmol) was converted to 1-methyl-4-phenyl-2(1H)-pyridone (white solid), (883.1 mg, 90%).

\[ R_f = 0.23 \ (\text{EtOAc}) \]

\[^1\text{H} \text{NMR (300 MHz, CDCl}_3\]: } \delta 7.59 – 7.48 (m, 2H), 7.49 – 7.35 (m, 3H), 7.31 (d, J = 7.1 Hz, 1H), 6.77 (s, 1H), 6.44 – 6.36 (m, 1H), 3.54 (s, 3H);

\[^13\text{C} \text{NMR (75 MHz, CDCl}_3\]: } \delta 163.27, 151.85, 138.18, 137.45, 129.42, 129.01, 126.71, 116.90, 105.50, 37.35;

\[ \text{GC-MS: } R_f (50_40): 9.1 \text{ min}; \text{ EI: } 186 (13), 185 (100), 184 (41), 158 (7), 157 (61), 156 (22), 142 (5), 129 (5), 128 (10), 127 (5), 116 (8), 115 (37), 102 (5), 93 (7), 89 (7), 77 (7), 63 (7), 51 (8); \text{ ATR-FTIR (cm}^{-1}\): 1651, 1508, 1393, 1343, 1316, 1242, 1188, 1150, 1057, 1015, 926, 853, 791, 756, 721, 698, 606.

Compound 5h: 1-methyl-3-phenyl-2(1H)-pyridone

Following the same procedure as for 5a, 3-Bromo-1-methyl-2(1H)-pyridone (8d) (1093.0 mg, 5.81 mmol) was converted to 1-methyl-3-phenyl-2(1H)-pyridone (white solid), (887.4 mg, 82%).

\[ R_f = 0.40 \ (\text{EtOAc}) \]

\[^1\text{H} \text{NMR (300 MHz, CDCl}_3\]: } \delta 7.68 – 7.63 (m, 2H), 7.43 (dd, J = 7.0, 2.1 Hz, 1H), 7.42 – 7.29 (m, 2H), 7.33 – 7.20 (m, 2H), 6.18 (t, J = 6.8 Hz, 1H), 3.55 (s, 3H);

\[^13\text{C} \text{NMR (75 MHz, CDCl}_3\]: } \delta 161.89, 137.63, 137.52, 136.86, 131.41, 128.59, 128.07, 127.61, 105.81, 38.20;

\[ \text{GC-MS: } R_f (50_40): 8.9 \text{ min}; \text{ EI: } 186 (13), 185 (100), 184 (94), 157 (21), 156 (37), 129 (6), 128 (8), 116 (8), 115 (33), 93 (6), 89 (8), 77 (6), 63 (8), 51 (6); \text{ ATR-FTIR (cm}^{-1}\): 1643, 1578, 1543, 1520, 1435, 1397, 1366, 1319, 1277, 1223, 1188, 1119, 1026, 922, 880, 772, 752, 698.
4. Hydrogenation of 2-pyridones (3a-3e, 5a-5h) to the corresponding 2-piperidones (4a-4e, 6a-6h)

General procedure: In glovebox [Ru(cod)(2-methylallyl)₂] (4.8 mg, 0.015 mmol), imidazolinium salt SINpEt·HBF₄ (14.5 mg, 0.031 mmol) and dry KOt-Bu (5.0 mg, 0.045 mmol) were placed in a flame dried screw-capped Schlenk tube equipped with a magnetic stirring bar. Continuing under argon, the mixture was suspended in 0.5 mL of hexane and stirred at 70 °C for 16 h after which 0.5 mL of t-AmOH was added and stirred at room temperature for 1 h. Then the resulted mixture was transferred under argon to a glass vial containing a 2-pyridone (0.3 mmol) and a magnetic stirring bar. Any applied additive (0.3 mmol) was added at this point. The glass vial was placed in a 150 mL stainless-steel reactor. The autoclave had been purged three times with hydrogen gas before the reaction pressure was set at 120 bar. The hydrogenation reaction was performed at the indicated temperature for 24 h. The autoclave was depressurized and the crude post-reaction mixture was filtered through a plug of silica using 5% MeOH in DCM followed by flash column chromatography (5% MeOH in DCM). The enantiomeric ratio of all compounds was determined by GC with a chiral column or HPLC on a chiral stationary phase.

Compound 4a: 1,6-dimethyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1,6-dimethyl-2(1H)-pyridone (3a) which quantitatively converted the starting material to the corresponding product, while 19.1 mg (50%) of the product 4a could be isolated after column chromatography, e.r. 94:6 (high volatility).

\[ R_f = 0.29 \text{ (10\% MeOH in EtOAc)}; \]
\[ ^1H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta 3.46 (h, J = 6.4 Hz, 1H), 2.92 (s, 3H), 2.37 \text{ (t, } J = 6.5 Hz, 2H), 1.99 – 1.78 \text{ (m, 2H), 1.76 – 1.54 (m, 2H), 1.23 (d, } J = 6.5 Hz, 3H); \]
\[ ^13C \text{ NMR (75 MHz, CDCl}_3\text{): } \delta 170.45, 54.47, 33.05, 32.21, 30.25, 19.95, 17.86; \]
\[ \text{ESI-MS: calculated for [C}_7\text{H}_{13}\text{NONa}^+\text{: 150.0889, found: 150.0889; GC-MS: } R_t \text{ (50}_40\text{): 6.8 min; EI: 127 (25), 113 (7), 112 (100), 84 (12), 72 (24), 57 (7), 56 (9), 55 (33); ATR-FTIR (cm}^{-1}\text{: 1620, 1447, 1397, 1335, 1308, 1246, 1184, 1138, 1099, 1053, 1026, 910, 853, 691, 648).} \]

Compound 4b: 1,5-dimethyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1,5-dimethyl-2(1H)-pyridone (3b) and the starting material was converted to the product 4b (90%, NMR yield, high volatility) of the corresponding product 4b, e.r. 52:48.

\[ R_f = 0.31 \text{ (10\% MeOH in EtOAc)}; \]
\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta 3.22 – 3.13 (m, 1H), 2.87 (s, 3H), 2.42 – 2.35 (m, 1H), 2.33 – 2.22 (m, 1H), 1.98 – 1.85 (m, 1H), 1.82 – 1.72 (m, 1H), 1.48 – 1.32 (m, 1H), 0.96 (d, } J = 6.6 Hz, 3H); \]
\[ \text{GC-MS: } R_f \text{ (50}_40\text{): 6.7 min; EI: 128 (10), 127 (100), 126 (18), 98 (7), 85 (27), 84 (29), 72 (12), 70 (7), 57 (63), 56 (60), 55 (29).} \]

Compound 4c: 1,4-dimethyl-2-piperidone

Following the general procedure (at room temperature), the hydrogenation process has been carried out using 1,4-dimethyl-2(1H)-pyridone (3c) which yielded 34.7 mg (59%) of the corresponding product 4c, e.r. 66:34.

\[ R_f = 0.47 \text{ (10\% MeOH in EtOAc)}; \]
\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta 3.27 – 3.14 (m, 2H), 2.84 (s, 3H), 2.42 – 2.30 (m, 1H), 1.92 – 1.69 (m, 3H), 1.45 – 1.31 (m, 1H), 0.91 (d, } J = 5.9 Hz, 3H); \]
\[ ^13C \text{ NMR (101 MHz, CDCl}_3\text{): } \delta 170.45, 54.47, 33.05, 32.21, 30.25, 19.95, 17.86; \]
\[ \text{ESI-MS: calculated for [C}_7\text{H}_{13}\text{NONa}^+\text{: 150.0889, found: 150.0889; GC-MS: } R_t \text{ (50}_40\text{): 6.8 min; EI: 127 (25), 113 (7), 112 (100), 84 (12), 72 (24), 57 (7), 56 (9), 55 (33); ATR-FTIR (cm}^{-1}\text{: 1620, 1447, 1397, 1335, 1308, 1246, 1184, 1138, 1099, 1053, 1026, 910, 853, 691, 648).} \]
Compound 4d: 1,3-dimethyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1,3-dimethyl-2(1H)-pyridone (1d) and the starting material was converted to the product 4d (82%, NMR yield, high volatility) of the corresponding product 2d, e.r. 82:18.

\[ R_f = 0.43 \text{ (10\% MeOH in EtOAc); } ^1H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta 3.29 \text{ – } 3.13 \text{ (m, 2H), 2.85 (s, 3H), 2.38 – 2.22 (m, 1H), 1.93 – 1.75 (m, 2H), 1.74 – 1.61 (m, 1H), 1.53 – 1.35 (m, 1H), 1.16 (d, } J = 7.2 \text{ Hz, 3H); } \]

\[ GC-MS\text{: } R_t(50_40) \text{: 6.7 min; EI: 128 (8), 127 (100), 126 (31), 85 (11), 84 (29), 72 (7), 71 (22), 70 (7), 69 (33), 58 (9), 57 (46), 56 (36), 55 (18), 53 (6); } ATR-FTIR \text{ (cm}^{-1}\text{): } 1620, 1508, 1454, 1400, 1339, 1242, 1061, 995, 953, 706, 667, 606. \]

Compound 4e: 1-methyl-5-(trifluoromethyl)-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-5-(trifluoromethyl)-2(1H)-pyridone (3e) which yielded 47.8 mg of the corresponding product 4e, e.r. 54:46.

\[ R_f = 0.61 \text{ (EtOAc); } ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta 3.45 \text{ – } 3.31 \text{ (m, 2H), 2.94 (s, 3H), 2.68 – 2.48 (m, 2H), 2.41 – 2.29 (m, 1H), 2.14 – 2.04 (m, 1H), 1.90 – 1.75 (m, 1H); } ^13C \text{ NMR (101 MHz, CDCl}_3\text{): } \delta 168.65, 126.28 \text{ (q, } J = 279 \text{ Hz), 47.83 (q, } J = 3 \text{ Hz), 38.67 (q, } J = 28 \text{ Hz), 34.80, 30.28, 20.70 (q, } J = 3 \text{ Hz); ESI-MS: calculated for [C}_7\text{H}_0\text{F}_3\text{NONa}_+\text{: } 204.0607, \text{ found: } 204.0613; \text{ GC-MS: } R_t(50_40) \text{: 6.3 min, EI: 182 (7), 181 (100), 138 (33), 85 (13), 77 (13), 69 (10), 57 (65), 56 (14), 55 (32), 51 (7); ATR-FTIR (cm}^{-1}\text{): } 1643, 1508, 1470, 1397, 1343, 1261, 1231, 1161, 1107, 1076, 1034, 988, 918, 895, 818, 756, 694, 633. \]

Compound 6a: 1-methyl-6-phenyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-6-phenyl-2(1H)-pyridone (5a) which yielded 93.6 mg of the corresponding product 6a, e.r. 57:43.

\[ R_f = 0.43 \text{ (10\% MeOH in EtOAc); } ^1H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta 7.31 \text{ – } 7.23 \text{ (m, 2H), 7.23 – 7.15 (m, 1H), 7.10 – 7.04 (m, 2H), 4.43 (t, } J = 5.3 \text{ Hz, 1H), 2.71 (s, 3H), 2.52 – 2.29 (m, 2H), 2.16 – 2.01 (m, 1H), 1.80 – 1.48 (m, 3H); } ^13C \text{ NMR (75 MHz, CDCl}_3\text{): } \delta 170.90, 141.34, 128.67, 127.46, 126.35, 63.54, 33.93, 32.21, 32.12, 17.43; \text{ ESI-MS: calculated for [C}_2\text{H}_1\text{ONa}_+\text{: } 212.1046, \text{ found: } 212.1045; \text{ GC-MS: } R_t(50_40) \text{: 8.5 min, EI: 190 (10), 189 (69), 188 (60), 160 (12), 133 (5), 132 (23), 120 (33), 119 (18), 118 (68), 117 (10), 115 (8), 113 (6), 112 (100), 104 (28), 103 (13), 98 (8), 91 (22), 84 (9), 78 (12), 77 (19), 65 (10), 58 (6), 55 (32), 51 (10); ATR-FTIR (cm}^{-1}\text{): } 1628, 1489, 1447, 1397, 1343, 1308, 1246, 1169, 1157, 1123, 1076, 1038, 972, 910, 787, 725, 702, 640, 613. \]

Compound 6b: 6-(4-methoxyphenyl)-1-methyl-2-piperidone
Following the general procedure, the hydrogenation process has been carried out using 6-(4-methoxyphenyl)-1-methyl-2(1H)-pyridone (5b) which yielded 48.1 mg of the corresponding product 6b, e.r. 58:44.

\[ R_f = 0.41 (10\% \text{ MeOH in EtOAc}); \]  
\[ ^1H \text{ NMR (400 MHz, CDCl}_3\]): \delta 7.08 – 7.03 (m, 2H), 6.89 – 6.85 (m, 2H), 4.44 (t, J = 5.4 Hz, 1H), 3.78 (s, 3H), 2.77 (s, 3H), 2.54 – 2.37 (m, 2H), 2.19 – 2.06 (m, 1H), 1.81 – 1.68 (m, 2H), 1.67 – 1.56 (m, 1H); \]  
\[ ^13C \text{ NMR (101 MHz, CDCl}_3\): } \]  
\[ \delta 171.03, 159.03, 133.45, 127.58, 114.14, 63.16, 55.37, 32.41, 32.34, 17.60; \]  
\[ \text{ESI-MS: calculated for } [\text{C}_{13}\text{H}_{17}\text{NO}_2\text{Na}]^+: 242.1151, \text{ found: } 242.1157; \]  
\[ \text{GC-MS: } R_t (50_40) \text{: } 9.2 \text{ min, EI: } 220 (17), 219 (100), 218 (17), 204 (15), 191 (8), 190 (65), 163 (6), 162 (23), 161 (6), 160 (66), 150 (26), 149 (31), 148 (98), 147 (15), 135 (10), 134 (64), 133 (13), 122 (5), 121 (16), 119 (18), 118 (8), 117 (7), 112 (27), 111 (7), 108 (5), 107 (7), 105 (7), 103 (9), 92 (8), 91 (31), 90 (6), 89 (8), 84 (9), 83 (8), 79 (5), 78 (9), 77 (17), 65 (12), 63 (10), 55 (20), 51 (6); \]  
\[ \text{ATR-FTIR (cm}^{-1}\]: 1632, 1586, 1508, 1462, 1443, 1393, 1339, 1304, 1242, 1173, 1153, 1115, 1084, 1034, 972, 814, 768, 721, 698, 656. \]

Compound 6c: 1-methyl-6-(4-(trifluoromethyl)phenyl)-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-6-(4-(trifluoromethyl)phenyl)-2(1H)-pyridone (5c) which yielded 57.9 mg of the corresponding product 6c, e.r. 54:46.

\[ R_f = 0.42 (10\% \text{ MeOH in EtOAc}); \]  
\[ ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.55 (s, 2H), 7.23 – 7.17 (m, 2H), 6.90 (s, 1H), 3.38 – 3.21 (m, 2H), 3.07 – 2.95 (m, 2H), 3.00 – 2.80 (m, 2H), 1.78 – 1.68 (m, 1H); \]  
\[ ^13C \text{ NMR (101 MHz, CDCl}_3\): } \delta 170.95, 145.70, 130.02 (q, J = 33 Hz), 126.88 , 125.88 (q, J = 4 Hz), 124.05 (q, J = 272 Hz), 63.41, 34.12, 32.28, 32.09, 17.52; \]  
\[ \text{ESI-MS: calculated for } [\text{C}_{13}\text{H}_{14}\text{F}_3\text{NONa}]^+: 280.0920, \text{ found: } 280.0921; \]  
\[ \text{GC-MS: } R_t (50_40) \text{: } 8.4 \text{ min, EI: } 258 (14), 257 (100), 256 (91), 242 (8), 238 (28), 229 (5), 228 (6), 201 (10), 200 (31), 189 (5), 188 (60), 187 (15), 186 (74), 185 (6), 173 (5), 172 (28), 171 (5), 160 (12), 159 (28), 153 (6), 152 (5), 151 (14), 146 (7), 145 (22), 133 (5), 132 (5), 131 (9), 128 (6), 127 (11), 125 (6), 119 (5), 118 (7), 115 (8), 113 (6), 112 (64), 109 (7), 103 (14), 102 (5), 98 (15), 95 (6), 84 (11), 77 (7), 75 (5), 69 (12), 55 (21), 51 (5); \]  
\[ \text{ATR-FTIR (cm}^{-1}\]: 1636, 1474, 1412, 1397, 1323, 1246, 1393, 1339, 1304, 1242, 1173, 1153, 1115, 1084, 1034, 972, 829, 814, 768, 721, 698, 656. \]

Compound 6d: 1-methyl-5-phenyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-5-phenyl-2(1H)-pyridone (5d) which yielded 24.4 mg of the corresponding product 6d, e.r. 73:23.

\[ R_f = 0.36 (10\% \text{ MeOH in EtOAc}); \]  
\[ ^1H \text{ NMR (300 MHz, CDCl}_3\): } \delta 7.29 – 7.21 (m, 2H), 7.20 – 7.12 (m, 3H), 3.38 – 3.21 (m, 2H), 3.07 – 2.95 (m, 1H), 2.88 (s, 3H), 2.54 – 2.32 (m, 2H), 2.02 – 1.91 (m, 2H); \]  
\[ ^13C \text{ NMR (75 MHz, CDCl}_3\): } \delta 169.61, 141.78, 128.84, 127.26, 127.05, 56.47, 40.33, 34.79, 31.97, 28.15; \]  
\[ \text{ESI-MS: calculated for } [\text{C}_{12}\text{H}_{15}\text{NONa}]^+: 212.1046, \text{ found: } 212.1050; \]  
\[ \text{GC-MS: } R_t (50_40) \text{: } 8.7 \text{ min, EI: } 190 (7), 189 (49), 117 (9), 115 (9), 105 (9), 104 (100), 103 (11), 91 (10), 78 (10), 77 (8), 57 (8); \]  
\[ \text{ATR-FTIR (cm}^{-1}\]: 1628, 1497, 1462, 1400, 1377, 1346, 1261, 1211, 1084, 1065, 1034, 926, 806, 768, 737, 706, 660. \]

Compound 6e: 5-(4-methoxyphenyl)-1-methyl-2-piperidone
Following the general procedure, the hydrogenation process has been carried out using 5-(4-methoxyphenyl)-1-methyl-2(1H)-pyridone (5e) which yielded 24.4 mg of the corresponding product 6e, e.r. 73:27.

\[ R_f = 0.38 \ (10\% \ MeOH \ in \ EtOAc); \]  \[ ^{1}H \ NMR \ (300 \ MHz, \ CDCl_3): \ \delta \ 7.19 - 7.12 \ (m, \ 2H), \ 6.90 - 6.83 \ (m, \ 2H), \ 3.79 \ (s, \ 3H), \ 3.43 - 3.25 \ (m, \ 2H), \ 3.11 - 2.98 \ (m, \ 1H), \ 2.96 \ (s, \ 3H), \ 2.62 - 2.40 \ (m, \ 2H), \ 2.09 - 1.95 \ (m, \ 2H); \]  \[ ^{13}C \ NMR \ (75 \ MHz, \ CDCl_3): \ \delta \ 169.68, \ 158.70, \ 133.84, \ 128.01, \ 114.19, \ 56.72, \ 55.39, \ 39.53, \ 34.80, \ 32.02, \ 28.38; \]  \[ ESI-MS: \text{calculated for} \ [C_{13}H_{17}NO_2Na]^+: 242.1151, \text{found:} \ 242.1153; \]  \[ GC-MS: \text{R}_f \ (50_40): \ 9.4 \ min; \]  \[ EI: \ 220 (7), \ 219 (47), \ 148 (9), \ 147 (7), \ 134 (100), \ 119 (6), \ 91 (8); \]  \[ ATR-FTIR (cm^{-1}): \ 1636, \ 1586, \ 1512, \ 1462, \ 1400, \ 1373, \ 1343, \ 1281, \ 1130, \ 1111, \ 1072, \ 1030, \ 926, \ 829, \ 814, \ 779, \ 729, \ 644. \]

**Compound 6f**: 1-methyl-5-(4-(trifluoromethyl)phenyl)-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-5-(4-(trifluoromethyl)phenyl)-2(1H)-pyridone (5f) which yielded 57.8 mg of the corresponding product 6f, e.r. 70:30.

\[ R_f = 0.12 \ (EtOAc); \]  \[ ^{1}H \ NMR \ (400 \ MHz, \ CDCl_3): \ \delta \ 7.60 \ (d, \ J = 8.1 \ Hz, \ 2H), \ 7.37 \ (d, \ J = 8.0 \ Hz, \ 2H), \ 3.47 - 3.34 \ (m, \ 2H), \ 3.23 - 3.12 \ (m, \ 1H), \ 2.98 \ (s, \ 3H), \ 2.64 - 2.44 \ (m, \ 2H), \ 2.13 - 2.01 \ (m, \ 2H); \]  \[ ^{13}C \ NMR \ (101 \ MHz, \ CDCl_3): \ \delta \ 169.33, \ 145.85, \ 127.53, \ 129.68 \ (q, \ J = 33 \ Hz), \ 125.86 \ (q, \ J = 4 \ Hz), \ 124.15 \ (q, \ J = 272 \ Hz), \ 56.04, \ 40.26, \ 34.83, \ 31.81, \ 28.10; \]  \[ ESI-MS: \text{calculated for} \ [C_{13}H_{14}F_3NONa]^+: 280.0920, \text{found:} \ 280.0929; \]  \[ GC-MS: \text{R}_f \ (50_40): \ 8.7 \ min; \]  \[ EI: \ 258 (7), \ 257 (47), \ 173 (10), \ 172 (100), \ 171 (5), \ 159 (5), \ 153 (6), \ 151 (9), \ 117 (7), \ 115 (10), \ 103 (14), \ 85 (6), \ 77 (5), \ 57 (15), \ 55 (9); \]  \[ ATR-FTIR (cm^{-1}): \ 1636, \ 1620, \ 1505, \ 1400, \ 1373, \ 1323, \ 1261, \ 1161, \ 1065, \ 1018, \ 841, \ 721, \ 675, \ 606. \]

**Compound 6g**: 1-methyl-4-phenyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-4-phenyl-2(1H)-pyridone (5g) which yielded 93.7 mg of the corresponding product 6g, e.r. 79:21.

\[ R_f = 0.46 \ (10\% \ MeOH \ in \ EtOAc); \]  \[ ^{1}H \ NMR \ (400 \ MHz, \ CDCl_3): \ \delta \ 7.36 - 7.30 \ (m, \ 2H), \ 7.26 - 7.17 \ (m, \ 3H), \ 3.41 \ (ddd, \ J = 12.3, 10.8, 4.8 \ Hz, \ 1H), \ 3.31 \ (ddd, \ J = 12.2, 5.6, 3.3 \ Hz, \ 1H), \ 3.23 - 3.12 \ (m, \ 1H), \ 2.98 \ (s, \ 3H), \ 2.71 \ (ddd, \ J = 17.4, 5.2, 2.2 \ Hz, \ 1H), \ 2.49 \ (dd, \ J = 17.4, 11.1 \ Hz, \ 1H), \ 2.15 - 2.05 \ (m, \ 1H), \ 1.97 \ (ddd, \ J = 13.3, 11.0, 5.6 \ Hz, \ 1H); \]  \[ ^{13}C \ NMR \ (75 \ MHz, \ CDCl_3): \ \delta \ 169.44, \ 143.51, \ 128.82, \ 126.87, \ 126.57, \ 49.16, \ 39.36, \ 38.83, \ 34.54, \ 30.32; \]  \[ ESI-MS: \text{calculated for} \ [C_{12}H_{15}NONa]^+: 212.1046, \text{found:} \ 212.1047; \]  \[ GC-MS: \text{R}_f \ (50_40): \ 8.7 \ min; \]  \[ EI: \ 190 (10), \ 189 (72), \ 188 (9), \ 146 (6), \ 133 (5), \ 132 (6), \ 131 (24), \ 118 (5), \ 117 (10), \ 116 (5), \ 115 (15), \ 112 (5), \ 111 (29), \ 105 (13), \ 104 (60), \ 103 (26), \ 102 (5), \ 91 (22), \ 85 (7), \ 83 (5), \ 78 (19), \ 77 (22), \ 65 (6), \ 63 (5), \ 58 (9), \ 57 (47), \ 56 (6), \ 51 (12); \]  \[ ATR-FTIR (cm^{-1}): \ 1636, \ 1497, \ 1451, \ 1400, \ 1335, \ 1254, \ 1196, \ 1119, \ 1061, \ 976, \ 760, \ 698, \ 613. \]

**Compound 6h**: 1-methyl-3-phenyl-2-piperidone

Following the general procedure, the hydrogenation process has been carried out using 1-methyl-3-phenyl-2(1H)-pyridone (5h) which yielded 47.1 mg of the corresponding product 6h, e.r. rac.

\[ R_f = 0.50 \ (10\% \ MeOH \ in \ EtOAc); \]  \[ ^{1}H \ NMR \ (300 \ MHz, \ CDCl_3): \ \delta \ 7.26 - 7.18 \ (m, \ 2H), \ 7.17 - 7.08 \ (m, \ 3H), \ 3.59 \ (t, \ J = 6.6 \ Hz, \ 1H), \ 3.42 - 3.21 \ (m, \ 2H), \ 2.95 \ (s, \ 3H), \ 2.15 - 2.01 \ (m, \ 1H), \ 1.96 - 1.63 \ (m, \ 3H); \]  \[ ^{13}C \ NMR \ (75 \ MHz, \ CDCl_3): \ \delta \ 170.72, \ 141.77, \ 128.47, \ 128.31, \ 126.56, \ 50.36, \ 48.59, \ 35.11, \ 30.62, \ 20.82; \]
5. Synthesis and characterization of compounds 1, 1b-1e, 7a-7d, 8a-8d.

Compound 1: 6-methyl-2(1H)-pyridone

In a dry Schlenk tube 2-bromo-6-methylpyridine (5.98 g, 35.0 mmol) was dissolved in 100 mL of t-AmylOH and KOt-Bu (39.3 g, 350.0 mmol) was added. The mixture was stirred at 100 °C for 40 h. The solvent was removed under reduced pressure and the residue was dissolved in 50 mL of HCO2H. The solution was stirred for 24 h at rt, then the pH was set to about 6 using 3N aq. KOH solution. The extraction was performed using CHCl3 (3×) and the combined organic phases were washed with brine, dried over MgSO4, filtered and evaporated. The residue was transferred to a column chromatography (8% MeOH in DCM) to afford 1 (white solid), 2.75 g (72%).

\[ R_f = 0.23 \quad (EtOAc); \]

\[ ^1H \text{ NMR (300 MHz, CDCl}_3\): } \delta 13.54 (bs, 1H), 7.30 (dd, \text{ } J = 9.1, 6.9 Hz, 1H), 6.35 (d, \text{ } J = 9.1 Hz, 1H), 6.00 (dt, \text{ } J = 6.8, 0.9 Hz, 1H), \]

\[ 2.30 (s, 3H); \]

\[ ^13C \text{ NMR (75 MHz, CDCl}_3\): } \delta 166.15, 146.01, 141.97, 116.34, 106.14, 19.02; \]

\[ \text{GC-MS: } R_f (50_40): 6.7 \text{ min}; \]

\[ \text{EI: } 109 (58), 81 (28), 80 (100), 73 (8), 66 (17), 53 (14), 51 (7); \]

\[ \text{ATR-FTIR (cm}^{-1}\): 2978, 2924, 2886, 2855, 2793, 1651, 1613, 1551, 1505, 1466, 1435, 1373, 1335, 1254, 1211, 1165, 1080, 995, 922, 872, 795, 737. \]

Compound 1b: 5-methyl-2(1H)-pyridone

Following the same procedure as for 1, 2-bromo-5-methylpyridine (1.88 g, 11.0 mmol) was converted to 4-methyl-2(1H)-pyridone (off-white solid), (680.0 mg, 46%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.33 (dd, \text{ } J = 9.2, 2.6 Hz, 1H), 7.17 – 7.15 (m, 1H), 6.52 (d, \text{ } J = 9.2 Hz, 1H), 2.08 (s, 3H); \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3\): } \delta 164.65, 144.43, 132.43, 119.70, 116.31, 17.09; \]

\[ \text{GC-MS: } R_f (50_40): 6.8 \text{ min}; \]

\[ \text{EI: } 108 (100), 107 (9), 92 (20), 81 (58), 80 (73), 65 (22), 53 (14), 52 (11). \]

Compound 1c: 4-methyl-2(1H)-pyridone

Following the same procedure as for 1, 2-bromo-4-methylpyridine (1.88 g, 11.0 mmol) was converted to 4-methyl-2(1H)-pyridone (off-white solid), (545.0 mg, 46%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.28 (d, \text{ } J = 6.6 Hz, 1H), 6.38 (s, 1H), 6.14 (dd, \text{ } J = 6.6, 1.7 Hz, 1H), 2.22 (s, 3H); \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3\): } \delta 165.57, 153.91, 133.83, 118.72, 109.77, 21.82; \]

\[ \text{GC-MS: } R_f (50_40): 6.8 \text{ min}; \]

\[ \text{EI: } 110 (9), 109 (39), 81 (17), 80 (100), 54 (5), 53 (7), 50 (10). \]

Compound 1d: 3-methyl-2(1H)-pyridone

Following the same procedure as for 1, 2-bromo-3-methylpyridine (1.88 g, 11.0 mmol) was converted to 3-methyl-2(1H)-pyridone (white solid), (810.0 mg, 67%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.33 (d, \text{ } J = 6.3 Hz, 2H), 6.22 (t, \text{ } J = 6.6 Hz, 1H), 2.17 (s, 3H); \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3\): } \delta 165.64, 139.40, 132.19, 129.29, 107.18, 16.81; \]

\[ \text{GC-MS: } R_f (50_40): 6.8 \text{ min}; \]

\[ \text{EI: } 109 (46), 81 (9), 80 (100), 79 (5), 78 (5), 54 (8), 53 (11), 52 (10), 51 (10). \]
Compound 1e: 5-(trifluoromethyl)-2(1H)-pyridone

Following the same procedure as for 1, 2-bromo-5-(trifluoromethyl)pyridine (2.68 g, 15.0 mmol) was converted to 55-(trifluoromethyl)-2(1H)-pyridone (off-white solid), (1692.3 mg, 69%).

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 11.20 (bs, 1H), 7.77 (s, 1H), 7.62 (dd, \(J = 9.6, 2.6\) Hz, 1H), 6.67 (d, \(J = 9.6\) Hz, 1H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 165.31, 137.83 (q, \(J = 2\) Hz), 134.46 (q, \(J = 5\) Hz), 123.29 (q, \(J = 267\) Hz), 121.20, 111.46 (q, \(J = 35\) Hz); GC-MS: R\(_t\) (50_40): 6.2 min; EI: 164 (13), 163 (87), 145 (5), 144 (41), 142 (6), 135 (82), 117 (8), 116 (100), 114 (11), 108 (13), 94 (10), 89 (16), 88 (34), 85 (33), 75 (8), 69 (27), 65 (14), 54 (5), 53 (5), 50 (8).

Compound 7a: 6-bromo-2(1H)-pyridone

Following the same procedure as for 1, 2,6-dibromopyridine (8.05 g, 34.0 mmol) was converted to 6-bromo-2(1H)-pyridone (yellow solid), (3.72 g, 62%).

\(R_f\) = 0.61 (EtOAc); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 12.70 (bs, 1H), 7.43 (dd, \(J = 8.6, 0.8\) Hz, 1H), 6.81 (dd, \(J = 8.6, 0.8\) Hz, 1H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): 165.30, 142.18, 131.93, 116.41, 113.17; GC-MS: R\(_t\) (50_40): 6.6 min; EI: 175 (38), 173 (35), 147 (30), 145 (21), 94 (100), 93 (16), 81 (20), 79 (19), 66 (40), 50 (10); ATR-FTIR (cm\(^{-1}\)): 2643, 2546, 1651, 1597, 1574, 1559, 1474, 1431, 1397, 1331, 1246, 1227, 1153, 1130, 995, 891, 876, 833, 779, 725, 675.

Compound 7b: 5-bromo-2(1H)-pyridone

Following the same procedure as for 1, 2,5-dibromopyridine (1.45 g, 6.1 mmol) was converted to 5-bromo-2(1H)-pyridone (white solid), (712.0 mg, 67%).

\(R_f\) = 0.24 (EtOAc); \(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 10.50 (bs, 1H), 7.56 – 7.49 (m, 2H), 6.57 – 6.49 (m, 1H); \(^13\)C NMR (101 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 164.11, 145.09, 135.38, 121.48, 100.17; GC-MS: R\(_t\) (50_40): 6.8 min; EI: 175 (93), 174 (6), 173 (100), 148 (5), 147 (81), 146 (7), 145 (88), 120 (7), 119 (17), 118 (10), 117 (16), 94 (17), 81 (6), 79 (7), 76 (5), 72 (5), 67 (6), 66 (50), 65 (8), 64 (9), 63 (5), 52 (5), 51 (10), 50 (23).

Compound 7c: 4-bromo-2(1H)-pyridone

In a dry Schlenk tube 4-bromo-2-chloropyridine (3.71 g, 19.3 mmol) was dissolved in 50 mL of t-AmylOH and KO\(_t\)-Bu (10.8 g, 96.5 mmol) was added. The mixture was stirred at 80 °C for 16 h. The solvent was removed under reduced pressure and the residue was dissolved in 20 mL of HCO\(_2\)H. The solution was stirred for 24 h at rt, then the pH was set to about 6 using 3N aq. KOH solution. The extraction was performed using CHCl\(_3\) (3×) and the combined organic phases were washed with brine, dried over MgSO\(_4\), filtered and evaporated. The residue was transferred to a column chromatography (5% MeOH in DCM) to afford 7c (pale brown solid), 2.88 g (86%).

\(R_f\) = 0.19 (EtOAc); \(^1\)H NMR (400 MHz, (CD\(_3\))\(_2\)SO): \(\delta\) 11.89 (bs, 1H), 7.35 (d, \(J = 7.0\) Hz, 1H), 6.64 (d, \(J = 2.1\) Hz, 1H), 6.37 (dd, \(J = 7.0, 2.1\) Hz, 1H); \(^13\)C NMR (101 MHz, (CD\(_3\))\(_2\)SO): \(\delta\) 161.57, 136.36, 136.24, 122.06, 109.01; GC-MS: R\(_t\) (50_40): 7.4 min; EI: 175 (96), 174 (6), 173 (100), 147 (61), 146 (6), 145 (65), 119 (10), 117 (10), 95 (5), 94 (64), 82 (7), 81 (7), 80 (7), 79 (7), 76 (34), 66 (44), 65 (7), 64 (8), 51 (13), 50 (21).
Compound 7d: 3-bromo-2(1H)-pyridone

Following the same procedure as for 7c, 3-bromo-2-chloropyridine (3.71 g, 19.3 mmol) was converted to 3-bromo-2(1H)-pyridone (white solid), (2.32 g, 69%).

\[ \text{Rf} = 0.25 \text{ (EtOAc); } \]
\[ ^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta \text{ 13.62 (bs, 1H), 7.85 (dd, } J = 7.3, 1.9 \text{ Hz, 1H), 7.49 (dd, } J = 6.4, 1.9 \text{ Hz, 1H), 6.23 (dd, } J = 7.3, 6.4 \text{ Hz, 1H); } \]
\[ ^1^3\text{C NMR (75 MHz, CDCl}_3\text{): } \delta \text{ 161.89, 143.92, 134.47, 115.55, 107.67; } \]
\[ \text{GC-MS: Rf (50_40): 7.7 min; EI: 175 (97), 174 (6), 173 (100), 147 (35), 146 (5), 145 (40), 120 (7), 119 (9), 118 (8), 117 (9), 94 (21), 82 (6), 81 (6), 80 (6), 79 (6), 73 (8), 72 (8), 67 (9), 66 (58), 65 (8), 64 (9), 53 (6), 51 (9), 50 (12); ATR-FTIR (cm}^{-1}\text{): 2978, 1640, 1605, 1539, 1508, 1462, 1435, 1397, 1373, 1323, 1300, 1242, 1204, 1157, 1030, 984, 926, 868, 752, 648. \]

Compound 8a: 6-bromo-1-methyl-2(1H)-pyridone

Following the same procedure as for 1, 6-bromo-2(1H)-pyridone (7a) (1.63 g, 10.0 mmol) was converted to 6-bromo-1-methyl-2(1H)-pyridone, (1.42 g, 80%).

\[ ^1\text{H NMR (300 MHz, CD}_2\text{Cl}_2\text{): } \delta \text{ 7.14 (dd, } J = 9.2, 7.2 \text{ Hz, 1H), 6.55 – 6.45 (m, 2H), 3.73 (s, 3H); } \]
\[ ^1^3\text{C NMR (75 MHz, CD}_2\text{Cl}_2\text{): 163.41, 139.11, 128.05, 118.75, 111.12, 36.72; } \]
\[ \text{GC-MS: Rf (50_40): 7.3 min; EI: 189 (27), 187 (27), 161 (7), 159 (7), 109 (6), 108 (100), 93 (10), 80 (6), 65 (5), 64 (8), 53 (6), 52 (5), 51 (6).} \]

Compound 8b: 5-bromo-1-methyl-2(1H)-pyridone

Following the same procedure as for 1, 5-bromo-2(1H)-pyridone (7b) (1176.6 mg, 6.76 mmol) was converted to 5-bromo-1-methyl-2(1H)-pyridone (brown solid), (1182.4 mg, 93%).

\[ \text{Rf} = 0.29 \text{ (EtOAc); } \]
\[ ^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta \text{ 7.39 (d, } J = 2.7 \text{ Hz, 1H), 7.29 (dd, } J = 9.6, 2.7 \text{ Hz, 1H), 6.43 (d, } J = 9.6 \text{ Hz, 1H), 3.47 (s, 3H); } \]
\[ ^1^3\text{C NMR (75 MHz, CDCl}_3\text{): } \delta \text{ 161.46, 142.54, 138.21, 121.78, 97.59, 37.74; } \]
\[ \text{GC-MS: Rf (50_40): 7.5 min; EI: 190 (6), 189 (95), 188 (8), 187 (100), 161 (83), 160 (24), 159 (86), 158 (21), 119 (12), 117 (12), 108 (21), 81 (9), 80 (36), 79 (23), 78 (12), 66 (5), 65 (7), 64 (15), 63 (5), 55 (7), 53 (33), 52 (17), 51 (37), 50 (37); ATR-FTIR (cm}^{-1}\text{): 3044, 2982, 1655, 1582, 1528, 1416, 1358, 1319, 1250, 1235, 1161, 1146, 1103, 1026, 964, 914, 891, 822, 791, 733, 694, 640.} \]

Compound 8c: 4-bromo-1-methyl-2(1H)-pyridone

Following the same procedure as for 1, 4-bromo-2(1H)-pyridone (7c) (1043.9 mg, 6.0 mmol) was converted to 4-bromo-1-methyl-2(1H)-pyridone (white solid), (1041.1 g, 92%).

\[ \text{Rf} = 0.19 \text{ (EtOAc); } \]
\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta \text{ 7.13 (d, } J = 7.2 \text{ Hz, 1H), 6.79 (d, } J = 2.1 \text{ Hz, 1H), 6.29 (dd, } J = 7.2, 2.2 \text{ Hz, 1H), 3.48 (s, 3H); } \]
\[ ^1^3\text{C NMR (101 MHz, CDCl}_3\text{): } \delta \text{ 161.85, 138.10, 135.41, 122.85, 110.24, 37.49; } \]
\[ \text{GC-MS: Rf (50_40): 7.5 min; EI: 190 (6), 189 (98), 188 (8), 187 (100), 161 (59), 160 (18), 159 (64), 158 (15), 119 (5), 117 (5), 108 (34), 81 (6), 80 (33), 79 (17), 78 (12), 67 (7), 66 (5), 64 (9), 53 (26), 52 (14), 51 (25), 50 (24); ATR-FTIR (cm}^{-1}\text{): 3071, 3028, 2978, 1647, 1586, 1528, 1508, 1454, 1412, 1373, 1335, 1296, 1234, 1177, 1142, 1065, 1034, 930, 907, 845, 764, 725, 644.} \]

Compound 8d: 3-bromo-1-methyl-2(1H)-pyridone
Following the same procedure as for 1, 3-bromo-2(1H)-pyridone (7d) (1043.9 mg, 6.0 mmol) was converted to 3-bromo-1-methyl-2(1H)-pyridone (pale brown solid), (1137.3 g, quant).

$R_f = 0.31$ (EtOAc); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.71 (dd, $J = 7.3$, 1.9 Hz, 1H), 7.30 (dd, $J = 6.7$, 1.9 Hz, 1H), 6.05 (d, $J = 6.9$ Hz, 1H), 3.59 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 159.42, 141.62, 137.87, 116.52, 105.90, 38.99; GC-MS: $R_t$ (50-40): 7.8 min; EI: 190 (6), 189 (98), 188 (8), 187 (100), 161 (32), 160 (14), 159 (34), 158 (13), 146 (5), 119 (8), 117 (8), 108 (15), 81 (7), 80 (28), 79 (13), 78 (11), 64 (8), 55 (8), 54 (7), 53 (38), 52 (11), 51 (16), 50 (16); ATR-FTIR (cm$^{-1}$): 1643, 1589, 1524, 1404, 1358, 1300, 1219, 1130, 1080, 1030, 949, 868, 841, 752, 637.
6. NMR Spectra

$^1$H NMR spectrum of 3a

$^{13}$C NMR spectrum of 3a
$^1$H NMR spectrum of 3b

$^{13}$C NMR spectrum of 3b
$^1$H NMR spectrum of 3c

$^{13}$C NMR spectrum of 3c
$^1$H NMR spectrum of 3d

$^{13}$C NMR spectrum of 3d
$^1$H NMR spectrum of 3e

$^{13}$C NMR spectrum of 3e
$^1$H NMR spectrum of 5a

$^{13}$C NMR spectrum of 5a
$^1$H NMR spectrum of 5b

$^{13}$C NMR spectrum of 5b
$^1$H NMR spectrum of 5c

$^{13}$C NMR spectrum of 5c
$^1$H NMR spectrum of 5d

$^{13}$C NMR spectrum of 5d
$^1$H NMR spectrum of **5e**

$^{13}$C NMR spectrum of **5e**
$^1$H NMR spectrum of 5f

$^{13}$C NMR spectrum of 5f
$^1$H NMR spectrum of 5g

$^{13}$C NMR spectrum of 5g
$^1$H NMR spectrum of 5h

$^{13}$C NMR spectrum of 5h
$^1$H NMR spectrum of 4a

$^{13}$C NMR spectrum of 4a
$^1$H NMR spectrum of 4b

$^1$H NMR spectrum of 4c
$^{13}$C NMR spectrum of 4c

$^1$H NMR spectrum of 4d
$^1$H NMR spectrum of 4e

$^{13}$C NMR spectrum of 4e
$^1$H NMR spectrum of 6a

$^{13}$C NMR spectrum of 6a
$^1$H NMR spectrum of 6b

$^{13}$C NMR spectrum of 6b
$^1$H NMR spectrum of 6e

$^{13}$C NMR spectrum of 6e
$^1$H NMR spectrum of 6d

$^{13}$C NMR spectrum of 6d
$^1$H NMR spectrum of 6f

$^{13}$C NMR spectrum of 6f
$^1$H NMR spectrum of 6g

$^{13}$C NMR spectrum of 6g
$^1$H NMR spectrum of 6h

$^{13}$C NMR spectrum of 6h
$^1$H NMR spectrum of 1

$^{13}$C NMR spectrum of 1
$^1$H NMR spectrum of 1c

$^{13}$C NMR spectrum of 1c
$^1$H NMR spectrum of 1d

$^{13}$C NMR spectrum of 1d
$^1$H NMR spectrum of 1e

$^{13}$C NMR spectrum of 1e
$^1$H NMR spectrum of 7a

$^{13}$C NMR spectrum of 7a
$^1$H NMR spectrum of 7b

$^{13}$C NMR spectrum of 7b
$^1$H NMR spectrum of 7c

$^{13}$C NMR spectrum of 7c
$^1$H NMR spectrum of 7d

$^{13}$C NMR spectrum of 7d
$^1$H NMR spectrum of 8a

$^{13}$C NMR spectrum of 8a
$^1$H NMR spectrum of 8b

$^{13}$C NMR spectrum of 8b
$^1$H NMR spectrum of 8c

$^{13}$C NMR spectrum of 8c
$^1$H NMR spectrum of 8d

$^{13}$C NMR spectrum of 8d
7. References