Supporting Information

Modular synthesis of 3,3-disubstituted oxindoles from nitrones and acrylic acids

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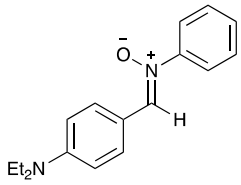
1. General Information

All reactions were performed in an oven-dried flask using standard Schlenk techniques under argon atmosphere, unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECA 500II (500 MHz for ^{1}H, 125 MHz for ^{13}C) spectrometer in $CDCl_3$ or DMSO-d_6. Tetramethylsilane (TMS) served as an internal standard (for ^{1}H, $\delta = 0$) and $CDCl_3$ served as an internal standard (for ^{13}C, $\delta = 77.0$) and DMSO-d_6 served as an internal standard (for ^{13}C, $\delta = 39.6$). IR spectra were recorded on an FT/IR-4600 (JASCO Co., Ltd.). ESI-MS were measured on a Bruker ESI-TOF-MS. Preparative thin-layer chromatography (PTLC) was performed on Wakogel® B-5F. Flash column chromatography was performed on Wakogel® 60N (38–100μm) and Wakogel® C-200 (75–150μm).

Materials. $Cu(OAc)_2$ was purchased from FUJIFILM Wako Pure Chemicals Corporation. *rac*-BINAP was purchased from Tokyo Chemical Industry Co, Ltd. Trimethoxysilane was purchased from Tokyo Chemical Industry Co, Ltd. and used without further purification. Methacrylic acid and crotonic acid were purchased from Tokyo Chemical Industry Co, Ltd. and used without further purification. 2-Methylenepentanoic acid[1] and 2-Methylene-4-[(triisopropylsilyl)oxy]butanoic acid[2] were prepared according to the literature methods. Other nitorones[3] and α,β-unsaturated carboxylic acids[4,5] were prepared according to the literature methods. Toluene was purchased from Nacalai Tesque Inc. and stored with molecular sieves 4Å. Other solvents were purchased from FUJIFILM Wako Pure Chemicals Corporation and Nacalai Tesque Inc. and stored with molecular sieves 4Å.

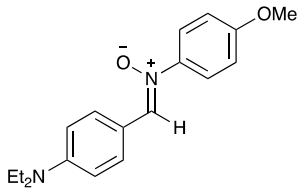
2. Characterisation of New Nitrones and Carboxylic Acids

2.1. Nitrones:



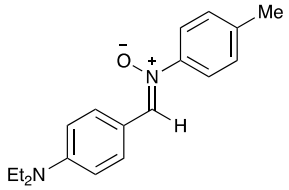
(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-phenylmethanimine oxide (1a):

The title compound was obtained as a yellow solid; mp: 105.5–106.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.31 (d, *J* = 9.2 Hz, 2H), 7.79–7.76 (m, 3H), 7.46–7.37 (m, 3H), 6.71 (d, *J* = 9.2 Hz, 2H), 3.43 (q, *J* = 7.3 Hz, 4H), 1.21 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.5, 148.9, 134.7, 131.5, 128.9, 128.9, 121.4, 118.1, 110.7, 44.4, 12.6; IR (neat): 3063, 2968, 2902, 1568, 1542, 1471, 1456, 1393, 1376, 1360, 1270, 1155, 1058, 818, 766 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{17}H_{21}N_2O^+$: $[M + H]^+$ = 269.1648, found 269.1646.



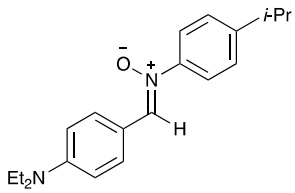
(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(4-methoxyphenyl)methanimine oxide (1b):

The title compound was obtained as a yellow solid; mp: 129.5–130.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.29 (d, *J* = 9.2 Hz, 2H), 7.73–7.68 (m, 3H), 6.95–6.91 (m, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.84 (s, 3H), 3.42 (q, *J* = 7.1 Hz, 4H), 1.20 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.8, 149.3, 142.2, 133.8, 131.3, 122.5, 118.2, 113.8, 110.7, 55.5, 44.3, 12.5; IR (neat): 3090, 2966, 2897, 1515, 1501, 1470, 1442, 1426, 1404, 1389, 1269, 1246, 1184, 1152, 1068, 1028, 827 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{18}H_{23}N_2O_2^+$: $[M + H]^+$ = 299.1754, found 299.1768.



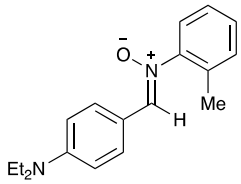
(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(*p*-tolyl)methanimine oxide (1c):

The title compound was obtained as a yellow solid; mp: 126.5–127.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 9.2 Hz, 2H), 7.73 (s, 1H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.43 (q, *J* = 7.1 Hz, 4H), 2.39 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.4, 146.6, 139.0, 134.3, 131.4, 129.4, 121.1, 118.2, 110.7, 44.4, 21.0, 12.5; IR (neat): 2971, 2933, 2870, 1561, 1471, 1446, 1434, 1410, 1375, 1356, 1330, 1279, 1198, 1158, 1127, 1060 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{18}H_{22}N_2NaO^+$: $[M + Na]^+$ = 305.1624, found 305.1623.



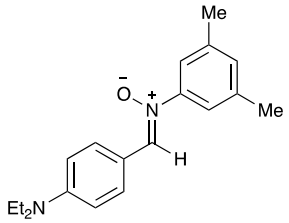
(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(4-isopropylphenyl)methanimine oxide (1d):

The title compound was obtained as a yellow solid; mp: 115.3–116.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 8.6 Hz, 2H), 7.73 (s, 1H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.29–7.26 (m, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.43 (q, *J* = 7.1 Hz, 4H), 3.00–2.91 (m, 1H), 1.27 (d, *J* = 6.9 Hz, 6H), 1.20 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.9, 149.3, 146.8, 134.4, 131.4, 126.8, 121.3, 118.2, 110.7, 44.4, 33.8, 23.9, 12.6; IR (neat): 3053, 2973, 1517, 1470, 1425, 1409, 1378, 1362, 1327, 1269, 1179, 1153, 1066, 832 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{20}H_{27}N_2O^+$: $[M + H]^+$ = 311.2118, found 311.2121.



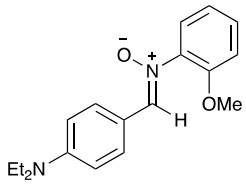
(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(*o*-tolyl)methanimine oxide (1e):

The title compound was obtained as a yellow solid; mp: 97.5–98.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.26 (d, *J* = 9.2 Hz, 2H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.36 (s, 1H), 7.32–7.27 (m, 2H), 7.26–7.22 (m, 1H), 6.71 (d, *J* = 8.6 Hz, 2H), 3.44 (q, *J* = 7.1 Hz, 4H), 2.43 (s, 3H), 1.21 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.3, 148.5, 137.8, 132.0, 131.2, 131.1, 128.8, 126.5, 123.7, 117.7, 110.7, 44.4, 17.1, 12.5; IR (neat): 3053, 3025, 2972, 2933, 1520, 1484, 1465, 1453, 1393, 1372, 1359, 1324, 1270, 1199, 1152, 1120, 1061, 889, 817, 761, 718 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{18}H_{23}N_2O^+$: $[M + H]^+$ = 283.1805, found 283.1806.



(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(3,5-dimethylphenyl)methanimine oxide (1f):

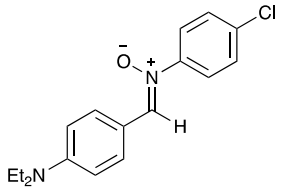
The title compound was obtained as a yellow solid; mp: 87.0–88.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 8.6 Hz, 2H), 7.71 (s, 1H), 7.38 (s, 2H), 7.02 (s, 1H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.43 (q, *J* = 7.1 Hz, 4H), 2.37 (s, 6H), 1.21 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.4, 148.9, 138.8, 134.6, 131.5, 130.5, 119.2, 118.2, 110.7, 44.4, 21.3, 12.6; IR (neat): 2973, 2920, 1603, 1518, 1470, 1361, 1270, 1185, 1142, 1081, 843 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{19}H_{25}N_2O^+$: $[M + H]^+$ = 297.1961, found 297.1967.



(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(2-methoxyphenyl)methanimine oxide (1g):

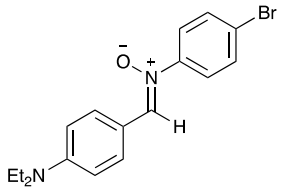
The title compound was obtained as a yellow solid; mp: 118.0–118.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.27 (d, *J* = 9.2 Hz, 2H), 7.64 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.46 (s, 1H), 7.36–7.32 (m, 1H), 7.03–6.99 (m, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.87 (s, 3H), 3.43 (q, *J* = 7.1 Hz, 4H), 1.20 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 151.6,

149.4, 139.4, 138.4, 131.4, 129.8, 125.5, 120.7, 117.9, 112.3, 110.7, 56.1, 44.4, 12.5; IR (neat): 3060, 2968, 2840, 1493, 1470, 1441, 1409, 1392, 1376, 1359, 1326, 1272, 1237, 1194, 1175, 1155, 1121, 1062, 1012, 833, 759 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{18}H_{23}N_2O_2^+$: $[M + H]^+$ = 299.1754, found 299.1741.



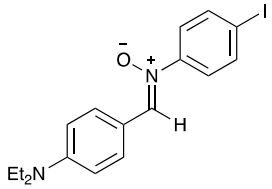
(*Z*)-*N*-(4-Chlorophenyl)-1-[4-(diethylamino)phenyl]methanimine oxide (1h):

The title compound was obtained as a yellow solid; mp: 183.5–184.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 9.2 Hz, 2H), 7.76–7.75 (m, 1H), 7.74–7.73 (m, 2H), 7.43–7.40 (m, 2H), 6.71 (d, *J* = 9.2 Hz, 2H), 3.44 (q, *J* = 7.1 Hz, 4H), 1.22 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.7, 147.2, 134.7, 124.5, 131.7, 129.0, 122.6, 117.8, 110.8, 44.4, 12.5; IR (neat): 2969, 2932, 1564, 1482, 1469, 1410, 1377, 1359, 1328, 1270, 1454, 1059, 1015 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{17}H_{20}ClN_2O^+$: $[M + H]^+$ = 303.1259, found 303.1265.



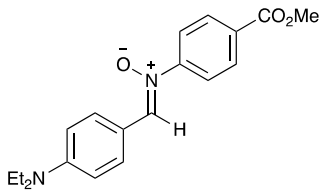
(*Z*)-*N*-(4-Bromophenyl)-1-[4-(diethylamino)phenyl]methanimine oxide (1i):

The title compound was obtained as a yellow solid; mp: 188.0–188.6 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 9.2 Hz, 2H), 7.74 (s, 1H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.6 Hz, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.44 (q, *J* = 7.1 Hz, 4H), 1.21 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.7, 147.7, 134.6, 132.0, 131.7, 122.9, 122.5, 117.8, 110.8, 44.5, 12.6; IR (neat): 3076, 2971, 2889, 1600, 1517, 1408, 1269, 1183, 817, 524 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{17}H_{20}BrNO^+$: $[M + H]^+$ = 347.0754, found 347.0750.



(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-(4-iodophenyl)methanimine oxide (1j):

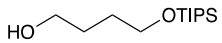
The title compound was obtained as a dark brown solid; mp: 162.9–163.9 °C; ^1H NMR(500 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 9.2 Hz, 2H), 7.78–7.76 (m, 2H), 7.74 (s, 1H), 7.56–7.54 (m, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.43 (q, *J* = 7.1 Hz, 4H), 1.21 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.7, 148.4, 137.9, 134.6, 131.7, 123.0, 117.8, 110.7, 94.0, 44.5, 12.6; IR (neat): 2964.1, 2925.5, 1515.8, 1376.9, 1350.9, 1329.7, 1271.8, 1171.5, 1153.2, 1128.2, 1053.9, 825.4 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{17}H_{20}IN_2O^+$: $[M + H]^+$ = 395.0615, found 395.0607.



(*Z*)-1-[4-(Diethylamino)phenyl]-*N*-[4-(methoxycarbonyl)phenyl]methanimine oxide (1k):

The title compound was obtained as a yellow solid; mp: 145.0–145.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.34 (d, *J* = 9.2 Hz, 2H), 8.12 (d, *J* = 8.6 Hz, 2H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.83 (s, 1H), 6.71 (d, *J* = 9.2 Hz, 2H), 3.94 (s, 3H), 3.44 (q, *J* = 7.1 Hz, 4H), 1.22 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.1, 151.8, 149.9, 135.3, 131.9, 130.5, 130.3, 121.2, 117.7, 110.8, 52.3, 44.5, 12.5; IR (neat): 2973, 2931, 2898, 1517, 1433, 1420, 1379, 1356, 1280, 1171, 1153 1112, 1059, 840, 770 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{19}H_{23}N_2O_3^+$: $[M + H]^+$ = 327.1703, found 327.1707.

2.2. Carboxylic Acid 2b:

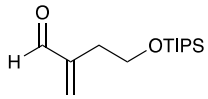


4-[(Triisopropylsilyl)oxy]butan-1-ol:

To an oven-dried round-bottom flask containing a magnetic stirring bar was added 1,4-butanediol (1.36 g, 0.0150 mol) and dissolved in THF (15 mL). The mixture was stirred for 10 min at 0 °C, followed by the addition of a 60% sodium hydride dispersion in paraffin liquid (0.736 g, 0.0184 mol). After stirring at room temperature for 45 min, triisopropylsilyl chloride (0.321 g, 0.0165 mol) was injected into the solution using a syringe. The reaction mixture was stirred at 0 °C for 1 h and then quenched with saturated aqueous $NaHCO_3$ solution (10 mL). The solution was extracted with EtOAc (20 mL × 3), and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The crude mixture was used without further purification in the next step.

The title compound was obtained as a colourless oil.

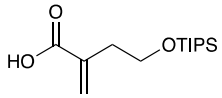
^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.75 (t, J = 5.4 Hz, 2H), 3.66 (t, J = 5.4 Hz, 2H), 2.58 (s, 1H), 1.73–1.63 (m, 4H), 1.15–1.04 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 63.6, 62.8, 30.4, 30.1, 18.0, 11.9. The spectral data matched those reported in the literature.[6]



2-Methylene-4-[(triisopropylsilyl)oxy]butanal:

To an oven-dried round-bottom flask containing a magnetic stirring bar was added 4-[(triisopropylsilyl)oxy]butan-1-ol and dissolved in DMSO (40 mL). Subsequently, triethylamine (8.4 mL) was injected into the solution using syringe. After stirring at room temperature for 10 min, sulfur trioxide pyridine complex (3.19 g, 0.0200 mol) was added as a solid over 20 min. The reaction mixture was stirred at room temperature for 2 h, followed by the addition of *N,N*-dimethylmethyleneiminium chloride (0.936 g, 0.0100 mol) in one portion. The mixture was stirred overnight at room temperature and then poured into a stirred biphasic mixture of cold saturated aqueous $NaHCO_3$ solution and diethyl ether. After stopping the bubbling, the solution was extracted with EtOAc (20 mL × 3), and the combined organic layers were washed with water (50 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated on a rotary evaporator. The residue was purified by flash column chromatography (hexane/EtOAc = 100:1 to 20:1) to give the product as a colourless oil (2.20 g, 86%, 2 steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.54 (s, 1H), 6.39 (s, 1H), 6.07 (s, 1H), 3.79 (t, J = 6.3 Hz, 2H), 2.50 (t, J = 6.6 Hz, 2H), 1.08–1.01 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 194.5, 147.1, 135.9, 61.3, 31.5, 17.9, 11.9; IR (neat): 2944, 2893, 2867, 1739, 1695, 1464, 1382, 1366, 1108, 1070, 1057, 925, 883, 683, 659, cm^{-1}; HRMS (ESI-TOF): calcd for $C_{14}H_{28}NaO_2Si^+$: $[M + Na]^+$ = 279.1751, found 279.1748.



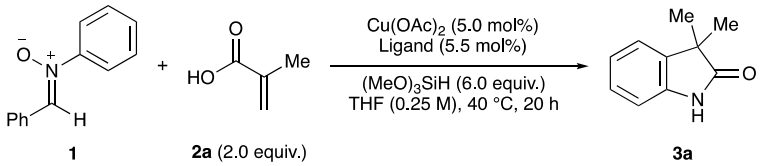
2-Methylene-4-[(triisopropylsilyl)oxy]butanoic acid (2b):

To an oven-dried round-bottom flask containing a magnetic stirring bar was added 2-methylene-4-[(triisopropylsilyl)oxy]butanal (2.20 g, 0.00857 mol) and dissolved in *t*-butyl alcohol (20 mL). Subsequently, 2-methyl-2-butene (6 mL) was added to the solution. After stirring at 0 °C for 10 min, another solution of sodium chlorite (2.74 g, 0.0300 mol) and NaH_2PO_4 (3.63 g, 0.0300 mol) in water (14 mL) was added dropwise over 30 min. The reaction mixture was stirred for 18 h and concentrated using a rotary evaporator to remove *t*-butyl alcohol. The residue was diluted with water and acidified with 50% H_3PO_4 aqueous solution from pH 7 to 3. The solution was extracted with EtOAc (20 mL × 3), and the combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The residue was purified by flash column chromatography (hexane/EtOAc = 50:1) to give the product as a colourless oil (1.30 g, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.34 (d, *J* = 1.1 Hz, 1H), 5.73 (d, *J* = 1.1 Hz, 1H), 3.85 (t, *J* = 6.3 Hz, 2H), 2.57 (t, *J* = 6.3 Hz, 2H), 1.13–1.03 (m, 21H) (one carboxylic proton signal not observed); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.8, 137.4, 129.0, 62.8, 35.3, 17.9, 11.9; IR (neat): 2943, 2893, 2868, 1740, 1698, 1629, 1464, 1440, 1382, 1231, 1174, 1108, 1070, 929, 883, 682 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{14}H_{28}NaO_3Si^+$: $[M + H]^+$ = 295.1700, found 295.1709.

3. Optimisation of Reaction Conditions

3.1. Screening of Ligands[a]

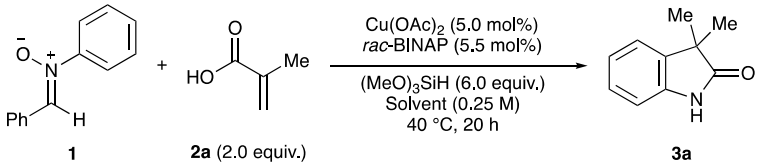


1 **2a** (2.0 equiv.) **3a**

Entry	Ligand	Yield (%)
1	PPh_3[b]	24
2	PCy_3[b]	5
3	dppe	4
4	dppen	Trace
5	*rac*-BINAP	51
6	(*R*)-TolBINAP	36

[a] Reaction Conditions: 1 (0.2 mmol), 2a (0.4 mmol), $Cu(OAc)_2$ (5.0 mol%), ligand (5.5 mol%) and $(EtO)_3SiH$ (1.2 mmol) were reacted in THF (0.8 mL) at 40 °C for 20 h. [b] 11 mol% of ligand was added. dppen: *cis*-1,2-bis(diphenylphosphino)ethylene.

3.2. Screening of Solvents[a]

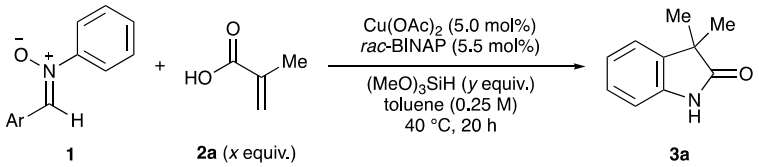


1 **2a** (2.0 equiv.) **3a**

Entry	Solvent	Yield (%)
1	THF	51
2	toluene	57
3	hexane	38
4	mesitylene	42
5	MTBE	49

[a] Reaction Conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $Cu(OAc)_2$ (5.0 mol%), *rac*-BINAP (5.5 mol%) and $(EtO)_3SiH$ (1.2 mmol) were reacted in solvent (0.8 mL) at 40 °C for 20 h. MTBE: *tert*-butyl methyl ether.

3.3. Screening of Other Parameters[a]



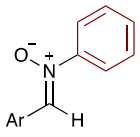
Entry	Ar	*x*	*y*	Yield (%)
1	Ph	2.0	6.0	59
2	4-BrC_6H_4	2.0	6.0	29
3	4-$MeOC_6H_4$	2.0	6.0	71
4	4-$MeOC_6H_4$	2.5	6.0	91
5	4-$MeOC_6H_4$	2.5	5.5	90
6	4-$MeOC_6H_4$	2.5	6.5	85
7	4-$Et_2NC_6H_4$	2.5	6.0	95

[a] Reaction Conditions: **1** (0.2 mmol), **2a**, $Cu(OAc)_2$ (5.0 mol%), *rac*-BINAP (5.5 mol%) and $(EtO)_3SiH$ were reacted in toluene (0.8 mL) at 40 °C for 20 h.

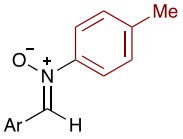
4. Synthesis of 3,3-Disubstituted Oxindoles from Nitrones and Acrylic Acids

Starting Materials for the Oxindole Synthesis:

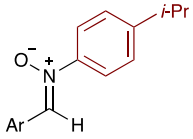
nitrones (Ar = 4-$Et_2NC_6H_4$)



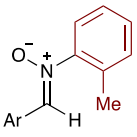
1a



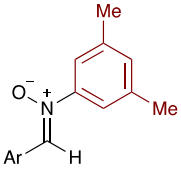
1c



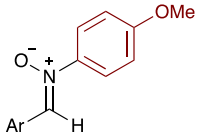
1d



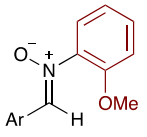
1e



1f



1b



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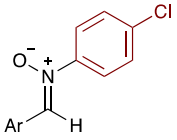
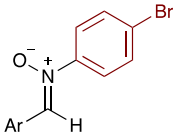
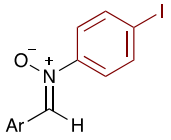


1h



1i



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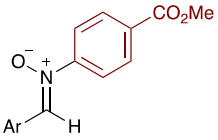

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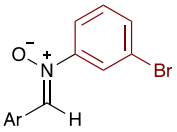
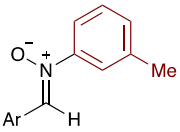
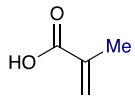


1l

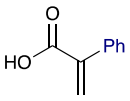


1m

acrylic acids



2a



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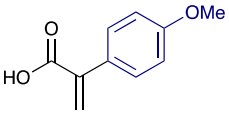

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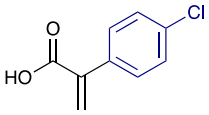

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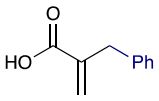

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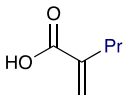

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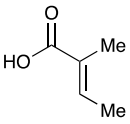
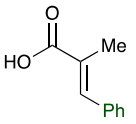


2h



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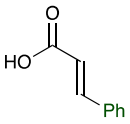

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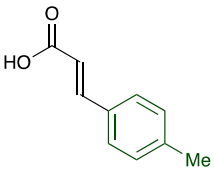

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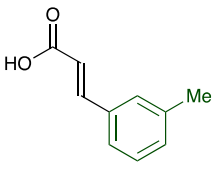

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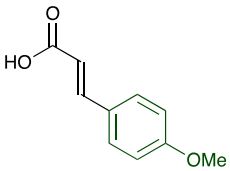

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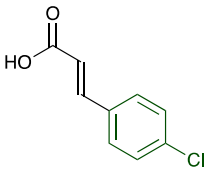
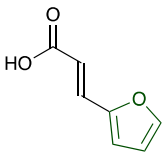
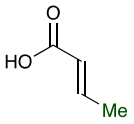


2n



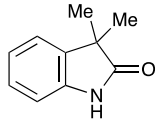
2o



2p

General Procedure for the Synthesis of 3,3-Disubstituted Oxindoles from Nitrones 1 and Acrylic Acids 2:

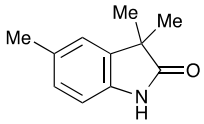
To an oven-dried test tube containing a magnetic stirring bar were added nitrone **1** (0.20 mmol), $Cu(OAc)_2$ (1.8 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol), and dissolved in toluene (0.8 mL). The mixture was stirred for 10 min at room temperature. Subsequently, carboxylic acid **2** (0.50 mmol) and $(MeO)_3SiH$ (146.6 mg, 1.20 mmol) were injected into the solution using a syringe. The reaction mixture was then stirred at 40 °C for 20 h and quenched with 1 M HCl aqueous solution (5 mL). After vigorous stirring for 30 min at room temperature, H_2O (5 mL) was added. The mixture was extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The residue was purified by preparative thin-layer chromatography to give oxindole **3**.



3,3-Dimethylindolin-2-one (3a):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2a** (44.0 mg, 0.511 mmol), $(MeO)_3SiH$ (146.0 mg, 1.20 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3a** (30.7 mg, 95%) as a colourless solid.

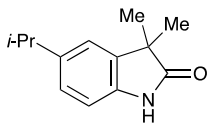
mp: 148.5–149.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.16 (br s, 1H), 7.23–7.17 (m, 2H), 7.07–7.01 (m, 1H), 6.98–6.94 (m, 1H), 1.41 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.4, 139.9, 136.2, 127.6, 122.5, 122.4, 110.0, 44.7, 24.3. The spectral data matched those reported in the literature.[7]



3,3,5-Trimethylindolin-2-one (3b):

The reaction was run with **1c** (56.5 mg, 0.200 mmol), **2a** (43.9 mg, 0.510 mmol), $(MeO)_3SiH$ (142.9 mg, 1.17 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3b** (29.1 mg, 83%) as a pale yellow solid.

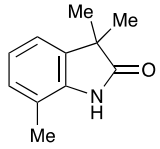
mp: 144.5–145.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.16 (br s, 1H), 7.01–6.99 (m, 2H), 6.85 (d, J = 8.6 Hz, 1H), 2.33 (s, 3H), 1.40 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.4, 137.4, 136.3, 131.8, 127.9, 123.3, 109.7, 44.7, 24.3, 21.1. The spectral data matched those reported in the literature.[8]



5-Isopropyl-3,3-dimethylindolin-2-one (3c):

The reaction was run with **1d** (62.1 mg, 0.200 mmol), **2a** (43.9 mg, 0.510 mmol), $(MeO)_3SiH$ (147.2 mg, 1.21 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40

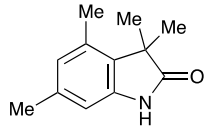
°C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3c** (32.9 mg, 81%) as a colourless solid. mp: 125.0–126.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.99 (br s, 1H), 7.06–7.04 (m, 2H), 6.87 (dd, *J* = 6.9, 1.7 Hz, 1H), 2.93–2.85 (m, 1H), 1.40 (s, 6H), 1.25 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.4, 134.3, 137.7, 136.3, 125.3, 120.7, 109.6, 44.8, 33.9, 24.4, 24.3; IR (neat): 3158, 3036, 2971, 2954, 2928, 2867, 1624, 1488, 1457, 1228, 1215, 833 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{13}H_{17}NNaO^+$: $[M + Na]^+$ = 226.1202, found 226.1203.



3,3,7-Trimethylindolin-2-one (3d):

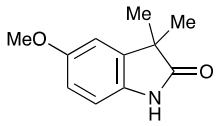
The reaction was run with **1e** (56.6 mg, 0.200 mmol), **2a** (43.2 mg, 0.502 mmol), $(MeO)_3SiH$ (146.5 mg, 1.20 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3d** (27.9 mg, 79 %) as a colourless solid.

mp: 136.1–136.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.52 (br s, 1H), 7.04–7.01 (m, 2H), 6.95 (dd, *J* = 8.0, 6.9 Hz, 1H), 2.33 (s, 3H), 1.40 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.7, 138.8, 135.9, 128.9, 122.3, 119.8, 119.4, 45.0, 24.3, 16.5. The spectral data matched those reported in the literature.[8]



3,3,4,6-Tetramethylindolin-2-one (3e):

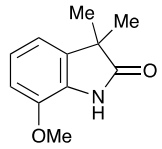
The reaction was run with **1f** (59.3 mg, 0.200 mmol), **2a** (43.2 mg, 0.502 mmol), $(MeO)_3SiH$ (156.1 mg, 1.28 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3e** (18.5 mg, 49%) as a colourless solid. mp: 196.5–197.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.47 (br s, 1H), 6.63 (s, 1H), 6.62 (s, 1H), 2.35 (s, 3H), 2.29 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.1, 140.0, 137.5, 134.1, 130.2, 125.4, 108.4, 45.2, 22.4, 21.3, 17.9; IR (neat): 3220, 2970, 2926, 1714, 1675, 1632, 1596, 1458, 1382, 1334, 1282, 1228, 1157, 851, 768, 726 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{12}H_{15}NNaO^+$: $[M + Na]^+$ = 212.1046, found 212.1040.



5-Methoxy-3,3-dimethylindolin-2-one (3f):

The reaction was run with **1b** (59.7 mg, 0.200 mmol), **2a** (43.6 mg, 0.506 mmol), $(MeO)_3SiH$ (146.8 mg, 1.20 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3f** (33.2 mg, 87%) a colourless solid. mp: 141.1–141.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.19 (br s, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 6.80 (d, *J* = 2.9 Hz, 1H), 6.73 (dd, *J* = 8.3, 2.6 Hz, 1H), 3.80 (s, 3H), 1.40 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.3, 155.8, 137.7,

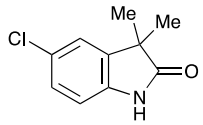
133.2, 111.8, 110.3, 109.9, 55.7, 45.2, 24.3. The spectral data matched those reported in the literature.[7]



7-Methoxy-3,3-dimethylindolin-2-one (3g):

The reaction was run with **1g** (59.7 mg, 0.200 mmol), **2a** (44.4 mg, 0.516 mmol), $(MeO)_3SiH$ (146.0 mg, 1.20 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3g** (30.7 mg, 80%) as a colourless solid.

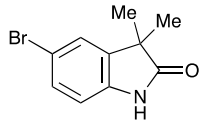
mp: 140.0–141.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.77 (br s, 1H), 7.03–6.99 (m, 1H), 6.84–6.78 (m, 2H), 3.88 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.7, 143.8, 137.1, 128.3, 122.9, 114.9, 110.0, 55.6, 45.3, 24.3. The spectral data matched those reported in the literature.[8]



5-Chloro-3,3-dimethylindolin-2-one (3h):

The reaction was run with **1h** (60.5 mg, 0.200 mmol), **2a** (43.4 mg, 0.504 mmol), $(MeO)_3SiH$ (145.6 mg, 1.19 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3h** (32.2 mg, 82%) as a colourless solid.

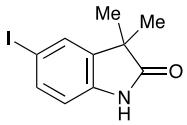
mp: 162.0–162.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.46 (br s, 1H), 7.19–7.16 (m, 2H), 6.90 (d, J = 8.0 Hz, 1H), 1.40 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 174.1, 138.5, 137.9, 127.8, 127.6, 123.1, 111.0, 45.1, 24.1. The spectral data matched those reported in the literature.[7]



5-Bromo-3,3-dimethylindolin-2-one (3i):

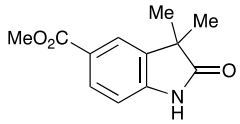
The reaction was run with **1i** (69.5 mg, 0.200 mmol), **2a** (43.9 mg, 0.510 mmol), $(MeO)_3SiH$ (145.9 mg, 1.19 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3i** (38.6 mg, 80%) a colourless solid.

mp: 165.1–166.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.48 (br s, 1H), 7.33–7.31 (m, 2H), 6.86 (d, J = 8.0 Hz, 1H), 1.40 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.0, 138.9, 138.3, 130.5, 125.9, 115.1, 111.5, 45.1, 24.1; IR (neat): 3114, 3054, 2981, 2861, 1723, 1624, 1476, 1223, 1056, 796 cm^{-1}; HRMS (DART): calcd for $C_{10}H_{11}BrNO^+$: $[M + H]^+$ = 240.0019, found 240.0013.



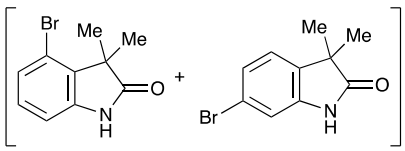
5-Iodo-3,3-dimethylindolin-2-one (3j):

The reaction was run with **1j** (78.9 mg, 0.200 mmol), **2a** (42.0 mg, 0.488 mmol), $(MeO)_3SiH$ (147.0 mg, 1.20 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3j** (45.9 mg, 80%) a colourless solid. mp: 170.1–170.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.46 (br s, 1H), 7.52 (dd, J = 8.0, 1.7 Hz, 1H), 7.47 (d, J = 1.7 Hz, 1H), 6.76 (d, J = 8.6 Hz, 1H), 1.39 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.8, 139.7, 138.7 136.5, 131.5, 112.1, 85.0, 44.9, 24.1; IR (neat): 3132, 2964, 2926, 2868, 1620, 1475, 1384, 1318, 1266, 1224, 1169, 883, 816, 723 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{10}H_{11}INO^+$: $[M + H]^+$ = 287.9880, found 288.9893.



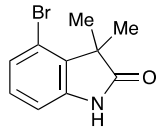
Methyl 3,3-dimethyl-2-oxoindoline-5-carboxylate (3k):

The reaction was run with **1k** (64.9 mg, 0.199 mmol), **2a** (43.9 mg, 0.510 mmol), $(MeO)_3SiH$ (147.6 mg, 1.21 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3k** (29.9 mg, 69%) a white solid. mp: 283.0–284.0 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.72 (br s, 1H), 7.86–7.82 (m, 2H), 6.94 (d, J = 8.0 Hz, 1H), 3.80 (s, 3H), 1.27 (s, 6H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 182.4, 166.2, 145.7, 136.2, 130.1, 123.6, 122.8, 109.3, 51.8, 43.7, 23.7; IR (neat): 3133, 3048, 2961, 2926, 2865, 1626, 1494, 1458, 1436, 1383, 1324, 1290, 1223, 1184, 1107, 768 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{12}H_{13}NNaO_3^+$: $[M + Na]^+$ = 242.0788, found 242.0798.



4-Bromo-3,3-dimethylindolin-2-one/6-Bromo-3,3-dimethylindolin-2-one (3l):

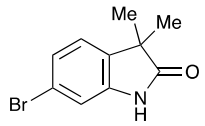
The reaction was run with **1l** (69.6 mg, 0.200 mmol), **2a** (42.2 mg, 0.490 mmol), $(MeO)_3SiH$ (146.2 mg, 1.20 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3l**.



4-Bromo-3,3-dimethylindolin-2-one (3l-major):

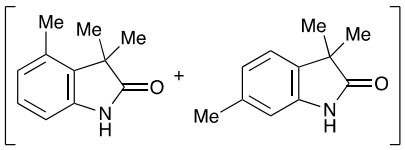
The title compound was obtained as a pale yellow solid (15.4 mg, 32%); mp: 138.0–139.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.29 (br s, 1H), 7.15 (d, J = 7.4 Hz, 1H), 7.08–7.05 (m, 1H), 6.90 (d, J = 6.9 Hz, 1H), 1.56 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.6, 141.9, 133.6, 129.1, 126.6, 118.8, 109.1, 47.0, 21.2; IR (neat): 3183, 3089, 2980,

2873, 1731, 1611, 1464, 1320, 1184, 774 cm^{-1}; HRMS (DART): calcd for $C_{10}H_{11}BrNO^+$: $[M + H]^+$ = 240.0019, found 240.0029.



6-Bromo-3,3-dimethylindolin-2-one (3l-minor):

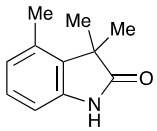
The title compound was obtained as a colourless solid (4.8 mg, 10%); mp: 190.1–190.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.77 (br s, 1H), 7.18 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.12 (d, *J* = 1.7 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 1.39 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.7, 141.0, 135.1, 125.3, 124.0, 121.0, 113.2, 44.5, 24.1. The spectral data matched those reported in the literature.[9]



3,3,4-Trimethylindolin-2-one/3,3,6-Trimethylindolin-2-one (3m):

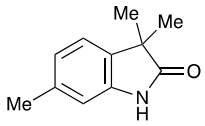
The reaction was run with **1m** (56.5 mg, 0.200 mmol), **2a** (43.8 mg, 0.509 mmol), $(MeO)_3SiH$ (148.1 mg, 1.21 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3m** (21.2 mg, 60%, major:minor = 65:35) as a white solid.

IR (neat): 3177, 2969, 2927, 1676, 1634, 1620, 1599, 1463, 1249, 1233, 1155, 809, 774 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{11}H_{13}NNaO^+$: $[M + Na]^+$ = 198.0889, found 198.0880.



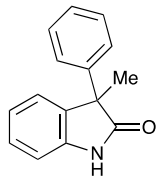
3,3,4-Trimethylindolin-2-one (3m-major):

^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.26–9.06 (m, 1H), 7.12–7.05 (m, 1H), 6.87–6.77 (m, 2H), 2.33 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.70, 139.96, 137.69, 134.29, 122.90, 122.23, 110.81, 44.50, 24.36, 22.25.



3,3,6-Trimethylindolin-2-one (3m-minor):

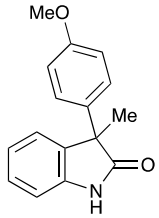
^{1}H NMR(500 MHz, $CDCl_3$) δ: 9.26–9.06 (m, 1H), 7.12–7.05 (m, 1H), 6.87–6.77 (m, 2H), 2.39 (s, 3H), 1.49 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.20, 140.09, 133.35, 133.05, 127.47, 124.81, 107.71, 45.50, 21.54, 18.01;



3-Methyl-3-phenylindolin-2-one (3n):

The reaction was run with **1a** (53.6 mg, 0.200 mmol), **2c** (74.0 mg, 0.499 mmol), $(MeO)_3SiH$ (146.2 mg, 1.20 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC (hexane/EtOAc = 2:1) afforded **3n** (32.7 mg, 73%) as a pale yellow solid.

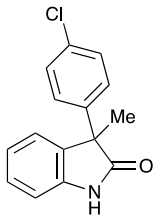
mp: 153.2–154.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.39 (br s, 1H), 7.33–7.28 (m, 4H), 7.26–7.19 (m, 2H), 7.11 (d, J = 6.9 Hz, 1H), 7.05–7.01 (m, 1H), 6.96 (d, J = 8.0 Hz, 1H), 1.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.5, 140.5, 140.5, 135.6, 128.6, 128.0, 127.3, 126.6, 124.2, 122.7, 110.3, 52.7, 23.3. The spectral data matched those reported in the literature.[10]



3-(4-Methoxyphenyl)-3-methylindolin-2-one (3o):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2d** (89.3 mg, 0.501 mmol), $(MeO)_3SiH$ (149.2 mg, 1.22 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3o** (40.3 mg, 79%) as a colourless solid.

mp: 107.5–108.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.26 (br s, 1H), 7.25–7.19 (m, 3H), 7.11 (d, J = 7.4 Hz, 1H), 7.05–7.01 (m, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.85–6.81 (m, 2H), 3.76 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.7, 158.7, 140.5, 135.8, 132.6, 127.9, 127.8, 124.2, 122.7, 113.9, 110.3, 55.2, 52.1, 23.5. The spectral data matched those reported in the literature.[11]

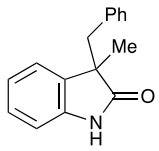


3-(4-Chlorophenyl)-3-methylindolin-2-one (3p):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2e** (91.2 mg, 0.499 mmol), $(MeO)_3SiH$ (146.0 mg, 1.20 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3p** (38.3 mg, 74%) as a white solid.

mp: 150.5–151.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.05 (br s, 1H), 7.32–7.22 (m, 5H), 7.11 (d, J = 6.9 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 6.97 (d, J = 7.4 Hz, 1H), 1.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 181.8, 140.3, 139.0,

135.0, 133.3, 128.7, 128.3, 128.1, 124.3, 122.9, 110.4, 52.2, 23.5. The spectral data matched those reported in the literature.[12]

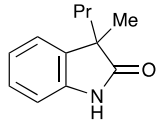


3-Benzyl-3-methylindolin-2-one (3q):

Reaction with 2-benzylacrylic acid: The reaction was run with **1a** (53.7 mg, 0.200 mmol), **2f** (81.0 mg, 0.499 mmol), $(MeO)_3SiH$ (142.5 mg, 1.17 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3q** (43.7 mg, 92%) as a colourless solid.

Reaction with (*E*)-α-methylcinnamic acid: The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2i** (81.0 mg, 0.499 mmol), $(MeO)_3SiH$ (145.2 mg, 1.19 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3q** (15.8 mg, 33%) as a colourless solid.

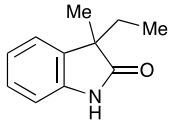
mp: 152.5–153.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.76 (br s, 1H), 7.14–6.99 (m, 6H), 6.90 (dd, *J* = 9.2, 2.9 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 3.11 (d, *J* = 13.2 Hz, 1H), 3.03 (d, *J* = 13.2 Hz, 1H), 1.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.8, 140.3, 136.1, 133.5, 129.9, 127.7, 127.6, 126.5, 123.7, 122.0, 109.7, 50.3, 44.1, 23.0; IR (neat): 3164, 3079, 3027, 2969, 2926, 1704, 1620, 1472, 1451, 1340, 1230, 1182 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{16}H_{15}NNaO^+$: $[M + Na]^+$ = 260.1046, found 260.1047.



3-Methyl-3-propylindolin-2-one (3r):

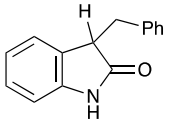
The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2g** (58.7 mg, 0.514 mmol), $(MeO)_3SiH$ (147.7 mg, 1.21 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3r** (33.5 mg, 88%) as a colourless solid.

mp: 87.4–88.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.13 (br s, 1H), 7.21–7.17 (m, 1H), 7.15 (d, *J* = 6.9 Hz, 1H), 7.05–7.02 (m, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 1.93–1.86 (m, 1H), 1.73 (td, *J* = 12.9, 4.4 Hz, 1H), 1.39 (s, 3H), 1.19–1.08 (m, 1H), 0.99–0.88 (m, 1H), 0.80 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.8, 140.6, 134.7, 127.5, 122.8, 122.3, 109.8, 49.1, 40.6, 23.8, 17.8, 14.1; IR (neat): 2961, 2929, 2908, 2870, 2846, 1620, 1483, 1390, 1328, 1247, 1204, 1093, 770, 749, 691 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{12}H_{15}NNaO^+$: $[M + Na]^+$ = 212.1046, found 212.1041.



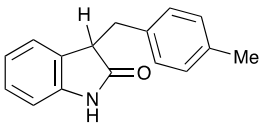
3-Ethyl-3-methylindolin-2-one (3s):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2h** (50.3 mg, 0.502 mmol), $(MeO)_3SiH$ (147.6 mg, 1.21 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3s** (15.5 mg, 44%) as a brown solid. mp: 141.5–142.5 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.67 (br s, 1H), 7.22–7.18 (m, 1H), 7.15 (d, J = 7.4 Hz, 1H), 7.06–7.03 (m, 1H), 6.93 (d, J = 8.0 Hz, 1H), 1.99–1.91 (m, 1H), 1.83–1.77 (m, 1H), 1.39 (s, 3H), 0.67 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.4, 140.6, 134.3, 127.6, 122.8, 122.3, 109.7, 49.5, 31.4, 23.4, 8.8. The spectral data matched those reported in the literature.[13]



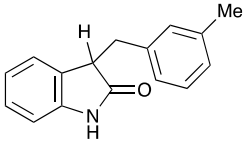
3-Benzylindolin-2-one (3t):

The reaction was run with **1a** (53.7 mg, 0.200 mmol), **2j** (74.2 mg, 0.501 mmol), $(MeO)_3SiH$ (147.1 mg, 1.20 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3t** (18.0 mg, 40%) as a colourless solid. mp: 153.2–154.1 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 9.05 (br s, 1H), 7.27–7.14 (m, 6H), 6.91–6.85 (m, 2H), 6.73 (d, J = 7.4 Hz, 1H), 3.75 (dd, J = 9.2, 4.6 Hz, 1H), 3.50 (dd, J = 13.7, 4.6 Hz, 1H), 2.93 (dd, J = 13.7, 9.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.5, 140.5, 140.5, 135.6, 128.6, 128.0, 127.3, 126.6, 124.2, 122.7, 110.3, 52.7, 23.3. The spectral data matched those reported in the literature.[10]



3-(4-Methylbenzyl)indolin-2-one (3u):

The reaction was run with **1a** (53.6 mg, 0.200 mmol), **2k** (81.1 mg, 0.500 mmol), $(MeO)_3SiH$ (145.8 mg, 1.19 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3u** (32.6 mg, 69%) a yellow solid. mp: 147.3–148.3 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.99 (br s, 1H), 7.18–7.13 (m, 1H), 7.08–7.03 (m, 4H), 6.91–6.87 (m, 1H), 6.85 (d, J = 7.4 Hz, 1H), 6.76 (d, J = 7.4 Hz, 1H), 3.72 (dd, J = 9.2, 4.6 Hz, 1H), 3.45 (dd, J = 13.7, 4.6 Hz, 1H), 2.89 (dd, J = 13.7, 9.2 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 179.9, 141.5, 136.0, 134.6, 129.2, 129.1, 129.0, 127.8, 124.8, 121.9, 109.7, 47.6, 36.2, 21.0. The spectral data matched those reported in the literature.[14]

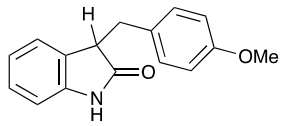


3-(3-Methylbenzyl)indolin-2-one (3v):

The title compound was obtained; The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2l** (81.3 mg, 0.501 mmol), $(MeO)_3SiH$ (147.3 mg, 1.205 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2}

mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3v** (19.2 mg, 40%) as a white solid.

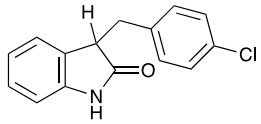
mp: 92.0–92.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.63 (br s, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 7.4 Hz, 1H), 7.05–7.01 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.91–6.87 (m, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 7.4 Hz, 1H), 3.74 (dd, *J* = 9.7, 4.6 Hz, 1H), 3.47 (dd, *J* = 13.7, 4.6 Hz, 1H), 2.86 (dd, *J* = 13.7, 9.7 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 179.5, 141.3, 137.9, 137.8, 130.2, 129.1, 128.2, 127.9, 127.4, 126.4, 124.9, 122.0, 109.6, 47.5, 36.6, 21.4. The spectral data matched those reported in the literature.[15]



3-(4-Methoxybenzyl)indolin-2-one (3w):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2m** (89.2 mg, 0.501 mmol), $(MeO)_3SiH$ (146.0 mg, 1.20 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC (hexane/EtOAc = 2:1) afforded **3w** (36.5 mg, 72%) as a colourless solid.

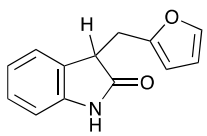
mp: 112.5–113.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.09 (br s, 1H), 7.17–7.14 (m, 1H), 7.08–7.06 (m, 2H), 6.92–6.88 (m, 1H), 6.85 (d, *J* = 7.4 Hz, 1H), 6.78–6.76 (m, 3H), 3.75 (s, 3H), 3.70 (dd, *J* = 9.2, 4.6 Hz, 1H), 3.42 (dd, *J* = 13.7, 4.6 Hz, 1H), 2.90 (dd, *J* = 14.0, 8.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 179.9, 158.2, 141.5, 130.3, 129.7, 129.0, 127.9, 124.7, 121.9, 113.6, 109.7, 55.1, 47.7, 35.7. The spectral data matched those reported in the literature.[16]



3-(4-Chlorobenzyl)indolin-2-one (3x):

The reaction was run with **1a** (53.7 mg, 0.200 mmol), **2n** (91.4 mg, 0.501 mmol), $(MeO)_3SiH$ (147.8 mg, 1.21 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC (hexane/EtOAc = 3:1) afforded **3x** (34.0 mg, 66%) as a white solid.

mp: 137.3–138.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.95 (br s, 1H), 7.19–7.16 (m, 3H), 7.07 (d, *J* = 5.4 Hz, 2H), 6.95–6.91 (m, 1H), 6.84 (dd, *J* = 7.4, 2.9 Hz, 2H), 3.72 (dd, *J* = 8.6, 4.6 Hz, 1H), 3.40 (dd, *J* = 14.0, 4.9 Hz, 1H), 2.99 (dd, *J* = 13.7, 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 179.5, 141.5, 136.0, 132.5, 130.7, 128.5, 128.4, 128.1, 124.6, 122.1, 109.9, 47.3, 35.8. The spectral data matched those reported in the literature.[16]

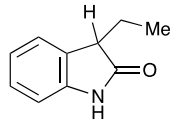


3-(Furan-2-ylmethyl)indolin-2-one (3y):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2o** (69.0 mg, 0.500 mmol), $(MeO)_3SiH$ (144.9 mg, 1.19 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40

°C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3y** (19.2 mg, 45%) as a colourless solid.

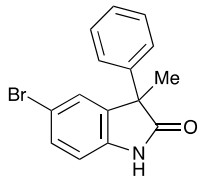
mp: 149.0–149.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.41 (br s, 1H), 7.34 (d, *J* = 1.7 Hz, 1H), 7.21–7.17 (m, 1H), 6.97–6.92 (m, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 6.29 (dd, *J* = 2.9, 1.7 Hz, 1H), 6.03 (d, *J* = 3.4 Hz, 1H), 3.81 (dd, *J* = 9.2, 4.6 Hz, 1H), 3.47 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.99 (dd, *J* = 15.2, 9.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 179.0, 151.9, 141.5, 141.2, 128.7, 128.1, 124.7, 122.3, 110.3, 109.6, 107.3, 45.1, 29.0. The spectral data matched those reported in the literature.[16]



3-Ethylindolin-2-one (3z):

The reaction was run with **1a** (53.8 mg, 0.200 mmol), **2p** (43.0 mg, 0.499 mmol), $(MeO)_3SiH$ (147.6 mg, 1.21 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC (hexane/EtOAc = 2:1) afforded **3z** (13.6 mg, 42%) as a colourless solid.

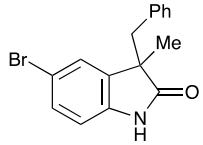
mp: 101.0–101.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.69 (br s, 1H), 7.25–7.19 (m, 2H), 7.05–7.01 (m, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 3.46 (t, *J* = 5.7 Hz, 1H), 2.07–2.01 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 180.5, 141.7, 129.5, 127.8, 124.1, 122.2, 109.6, 47.1, 23.6, 10.0. The spectral data matched those reported in the literature.[16]



5-Bromo-3-methyl-3-phenylindolin-2-one (3aa):

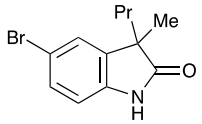
The reaction was run with **1i** (69.5 mg, 0.200 mmol), **2c** (74.1 mg, 0.500 mmol), $(MeO)_3SiH$ (146.9 mg, 1.20 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3aa** (37.0 mg, 61%) as a colourless solid.

mp: 163.0–164.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.36 (br s, 1H), 7.36–7.31 (m, 3H), 7.29–7.25 (m, 3H), 7.22 (d, *J* = 2.3 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 1.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.0, 139.6, 139.4, 137.8, 131.0, 128.8, 127.6, 127.5, 126.5, 115.4, 111.8, 53.0, 23.1; IR (neat): 3166, 3113, 2964, 1616, 1476, 1441, 1305, 1216, 1189, 802, 781, 698 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{15}H_{12}BrNNaO^+$: $[M + Na]^+ = 323.9994$, found 323.9999.



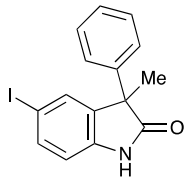
3-Benzyl-5-bromo-3-methylindolin-2-one (3ab):

The reaction was run with **1i** (69.7 mg, 0.200 mmol), **2f** (81.1 mg, 0.500 mmol), $(MeO)_3SiH$ (146.9 mg, 1.20 mmol), $Cu(OAc)_2$ (1.7 mg, 9.4×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ab** (40.8 mg, 64%) as a colourless solid.
mp: 155.0–155.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.80 (br s, 1H), 7.27 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.21 (d, *J* = 1.7 Hz, 1H), 7.12–7.06 (m, 3H), 6.91–6.88 (m, 2H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.10 (d, *J* = 13.2 Hz, 1H), 3.01 (d, *J* = 13.2 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.2, 139.3, 135.7, 135.5, 130.6, 129.9, 127.8, 126.9, 126.7, 114.7, 111.2, 50.6, 44.0, 22.9; IR (neat): 3183, 3028, 2959, 1675, 1622, 1476, 1457, 1438, 1234, 1177, 818, 778, 699 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{16}H_{14}BrNNaO^+$: $[M + Na]^+$ = 338.0151, found 338.0160.



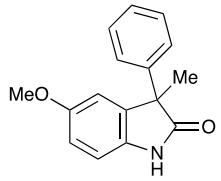
5-Bromo-3-methyl-3-propylindolin-2-one (3ac):

The reaction was run with **1i** (69.5 mg, 0.200 mmol), **2g** (57.4 mg, 0.503 mmol), $(MeO)_3SiH$ (147.1 mg, 1.20 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ac** (26.0 mg, 48%) as a yellow solid.
mp: 133.0–133.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.24 (br s, 1H), 7.33 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.27–7.26 (m, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 1.91–1.85 (m, 1H), 1.70 (td, *J* = 12.9, 4.4 Hz, 1H), 1.38 (s, 3H), 1.16–1.07 (m, 1H), 0.99–0.89 (m, 1H), 0.82 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.3, 139.6, 136.9, 130.4, 126.1, 115.1, 111.3, 49.5, 40.5, 23.7, 17.8, 14.1; IR (neat): 3220, 2962, 2930, 2872, 1615, 1377, 1322, 1284, 1202, 1162, 882, 816, 759, 627 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{12}H_{14}BrNNaO^+$: $[M + Na]^+$ = 290.0151, found 290.0159.



5-Iodo-3-methyl-3-phenylindolin-2-one (3ad):

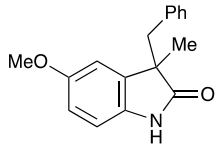
The reaction was run with **1j** (79.0 mg, 0.200 mmol), **2c** (74.2 mg, 0.501 mmol), $(MeO)_3SiH$ (146.8 mg, 1.20 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ad** (34.9 mg, 50%) as a colourless solid.
mp: 218.0–219.0 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.73 (br s, 1H), 7.61 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.53 (d, *J* = 1.1 Hz, 1H), 7.41–7.36 (m, 2H), 7.34–7.27 (m, 3H), 6.84 (d, *J* = 8.0 Hz, 1H), 1.72 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 179.7, 141.2, 140.8, 138.3, 136.5, 132.3, 128.5, 127.1, 126.2, 112.2, 84.8, 52.1, 22.4; IR (neat): 3183, 2962, 2926, 1710, 1616, 1473, 1372, 1346, 1302, 1213, 803, 759, 654 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{15}H_{12}INNaO^+$: $[M + Na]^+$ = 371.9856, found 371.9858.



5-Methoxy-3-methyl-3-phenylindolin-2-one (3ae):

The reaction was run with **1b** (59.8 mg, 0.200 mmol), **2c** (74.4 mg, 0.502 mmol), $(MeO)_3SiH$ (144.3 mg, 1.18 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ae** (23.1 mg, 46%) as a colourless solid.

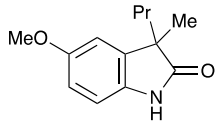
mp: 162.5–163.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.87 (br s, 1H), 7.32–7.29 (m, 4H), 7.28–7.24 (m, 1H), 6.87 (d, J = 8.6 Hz, 1H), 6.78–6.75 (m, 1H), 6.72 (d, J = 2.3 Hz, 1H), 3.75 (s, 3H), 1.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.1, 156.0, 140.4, 137.0, 133.7, 128.6, 127.3, 126.6, 112.6, 111.3, 110.5, 55.7, 53.2, 23.3; IR (neat): 3059, 2964, 2926, 2860, 1614, 1495, 1440, 1303, 1209, 1047, 1032, 804, 650 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{16}H_{15}NNaO_2^+$: $[M + Na]^+$ = 276.0995, found 276.0984.



3-Benzyl-5-methoxy-3-methylindolin-2-one (3af):

The reaction was run with **1b** (59.8 mg, 0.200 mmol), **2f** (81.2 mg, 0.501 mmol), $(MeO)_3SiH$ (147.6 mg, 1.21 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3af** (38.8 mg, 72%) as a colourless solid.

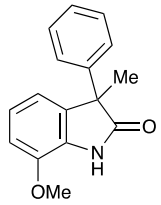
mp: 109.4–109.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.55 (br s, 1H), 7.11–7.05 (m, 3H), 6.93 (dd, J = 7.7, 2.0 Hz, 2H), 6.67 (s, 3H), 3.76 (s, 3H), 3.09 (d, J = 13.2 Hz, 1H), 3.02 (d, J = 13.2 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.5, 155.4, 136.1, 134.9, 133.7, 130.0, 127.6, 126.5, 112.2, 110.9, 110.0, 55.7, 50.7, 44.0, 23.1; IR (neat): 3146, 2960, 2926, 1705, 1666, 1605, 1496, 1308, 1272, 1210, 1031, 800, 701 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{17}H_{17}NNaO_2^+$: $[M + Na]^+$ = 290.1151, found 290.1163.



5-Methoxy-3-methyl-3-propylindolin-2-one (3ag):

The reaction was run with **1b** (59.7 mg, 0.200 mmol), **2g** (58.4 mg, 0.512 mmol), $(MeO)_3SiH$ (148.1 mg, 1.21 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ag** (39.9 mg, 91%) as a colourless solid.

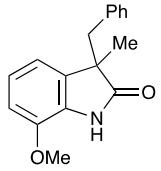
mp: 73.1–73.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.11 (br s, 1H), 6.85 (d, J = 8.6 Hz, 1H), 6.76 (d, J = 2.9 Hz, 1H), 6.72 (dd, J = 8.3, 2.6 Hz, 1H), 3.80 (s, 3H), 1.89 (td, J = 12.6, 4.4 Hz, 1H), 1.69 (td, J = 12.9, 4.4 Hz, 1H), 1.38 (s, 3H), 1.19–1.08 (m, 1H), 0.99–0.89 (m, 1H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.7, 155.8, 136.2, 134.0, 111.6, 110.2, 110.0, 55.7, 49.6, 40.7, 23.9, 17.8, 14.1; IR (neat): 3183, 2960, 2928, 2872, 1604, 1495, 1307, 1270, 1252, 1204, 1166, 1038, 798, 642 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{13}H_{18}NO_2^+$: $[M + H]^+$ = 220.1332, found 220.1338.



7-Methoxy-3-methyl-3-phenylindolin-2-one (3ah):

The reaction was run with **1g** (59.8 mg, 0.200 mmol), **2c** (74.2 mg, 0.501 mmol), $(MeO)_3SiH$ (146.2 mg, 1.20 mmol), $Cu(OAc)_2$ (1.9 mg, 1.0×10^{-2} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ah** (14.1 mg, 28%) as a colourless solid.

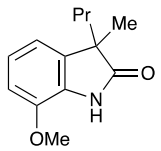
mp: 212.0–213.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.52 (br s, 1H), 7.33–7.22 (m, 5H), 7.03 (t, J = 8.0, 1H), 6.84 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 7.4 Hz, 1H), 3.90 (s, 3H), 1.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 180.4, 143.9, 140.4, 136.1, 128.9, 128.5, 127.2, 126.6, 123.3, 116.7, 110.2, 55.6, 53.2, 23.5; IR (neat): 3165, 3069, 2966, 1698, 1624, 1598, 1497, 1449, 1207, 1037, 693 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{16}H_{15}NNaO_2^+$: $[M + Na]^+$ = 276.0995, found 276.1005.



3-Benzyl-7-methoxy-3-methylindolin-2-one (3ai):

The reaction was run with **1g** (59.6 mg, 0.200 mmol), **2f** (81.1 mg, 0.500 mmol), $(MeO)_3SiH$ (146.8 mg, 1.20 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.9 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3ai** (46.7 mg, 87%) as a brown oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.74 (br s, 1H), 7.09–7.04 (m, 3H), 6.97 (t, J = 7.7 Hz, 1H), 6.93 (dd, J = 7.7, 2.0 Hz, 2H), 6.74 (d, J = 6.9 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 3.76 (s, 3H), 3.13 (d, J = 13.2 Hz, 1H), 3.03 (d, J = 13.2 Hz, 1H), 1.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 181.4, 143.6, 136.2, 134.2, 129.9, 128.9, 127.6, 126.4, 122.5, 116.1, 110.1, 55.5, 51.0, 43.9, 23.3; IR (neat): 3207, 3029, 2966, 2927, 2840, 1632, 1598, 1454, 1399, 1331, 1285, 1257, 1225, 1178, 1071, 1045, 783, 759, 702, 636 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{17}H_{17}NNaO_2^+$: $[M + Na]^+$ = 290.1151, found 290.1164.



7-Methoxy-3-methyl-3-propylindolin-2-one (3aj):

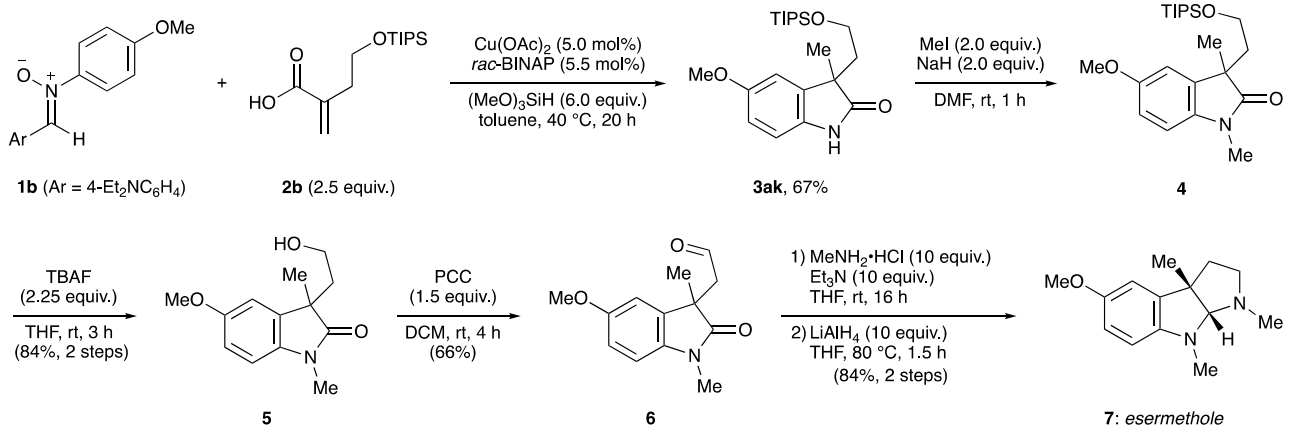
The reaction was run with **1g** (59.8 mg, 0.200 mmol), **2g** (58.5 mg, 0.513 mmol), $(MeO)_3SiH$ (146.7 mg, 1.20 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.8 mg, 1.1×10^{-2} mmol) in toluene (0.8 mL) at 40 °C for 20 h. Purification by preparative TLC ($CHCl_3$/EtOAc = 5:1) afforded **3aj** (21.4 mg, 49%) as a brown solid.

mp: 119.6–119.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.61 (br s, 1H), 7.01 (dd, J = 8.6, 7.4 Hz, 1H), 6.80–6.78 (m, 2H), 3.87 (s, 3H), 1.91–1.85 (m, 1H), 1.73–1.66 (m, 1H), 1.37 (s, 3H), 1.16–1.07 (m, 1H), 0.97–0.87 (m, 1H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 182.0, 143.6, 135.5, 128.9, 122.9, 115.2, 109.9, 55.5, 49.7, 40.6, 23.8, 17.9, 14.1; IR (neat): 3189, 3075, 2961, 2930, 2871, 1633, 1599, 1499, 1464, 1260, 1209, 1081, 1035, 731 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{13}H_{17}NNaO_2^+$: $[M + Na]^+$ = 242.1151, found 242.1162.

5. Gram-Scale Reaction for Synthesis of 3,3-Disubstituted Oxindoles

To an oven-dried round-bottom flask containing a magnetic stirring bar were added nitrone (**1a**, 2.27 g, 10.0 mmol), $Cu(OAc)_2$ (18.7 mg, 0.10 mmol) and *rac*-BINAP (68.5 mg, 0.11 mmol), and dissolved in toluene (40 mL). The mixture was stirred for 10 min at room temperature. Subsequently, carboxylic acid (**2a**, 2.17 g, 25.0 mmol) and $(MeO)_3SiH$ (7.36 g, 60.0 mmol) were injected into the solution using a syringe. The reaction mixture was then stirred at 40 °C for 20 h and quenched with 1 M HCl aqueous solution (20 mL). After vigorous stirring for 30 min at room temperature, H_2O (10 mL) was added. The mixture was extracted with EtOAc (20 mL × 4), and the combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The residue was purified by column chromatography (hexane/EtOAc = 5:1 to 2:1) to give oxindole **3a** (1.40 g, 8.68 mmol, 87%).

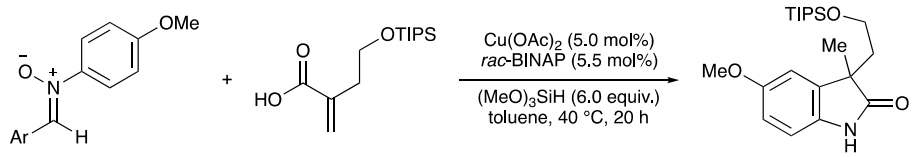
6. Synthesis of (±)-Esermethole



1b (Ar = 4-$Et_2NC_6H_4$) **2b** (2.5 equiv.) **3ak**, 67% **4**

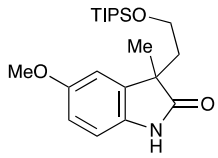
5 **6** **7**: *esermethole*

Synthesis of 3aj



1b (Ar = 4-$Et_2NC_6H_4$) **2b** (2.5 equiv.) **3ak**, 67%

To an oven-dried test tube containing a magnetic stirring bar were added nitrone **1b** (59.7 mg, 0.200 mmol), $Cu(OAc)_2$ (1.8 mg, 9.9×10^{-3} mmol) and *rac*-BINAP (6.7 mg, 1.1×10^{-2} mmol), and dissolved in toluene (0.8 mL). The mixture was stirred for 10 min at room temperature. Subsequently, carboxylic acid **2b** (136.8 mg, 0.502 mmol) and $(MeO)_3SiH$ (147.6 mg, 1.21 mmol) were injected into the solution using a syringe. The reaction mixture was then stirred at 40 °C for 20 h and quenched with 1 M HCl aqueous solution (5 mL). After vigorous stirring for 30 min at room temperature, H_2O (5 mL) was added. The mixture was extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The residue was purified by preparative thin-layer chromatography ($CHCl_3$/EtOAc = 5:1) to give oxindole **3ak** (50.3 mg, 0.133 mmol, 67%).

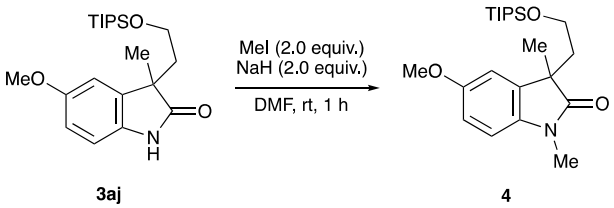


5-Methoxy-3-methyl-3-{2-[(triisopropylsilyl)oxy]ethyl}indolin-2-one (3ak):

The title compound was obtained as a white solid.

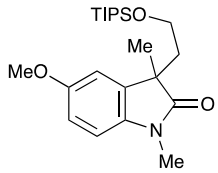
mp: 90.5–91.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.11 (br s, 1H), 6.84 (d, J = 8.0 Hz, 1H), 6.77 (d, J = 2.9 Hz, 1H), 6.72 (dd, J = 8.3, 2.6 Hz, 1H), 3.79 (s, 3H), 3.55–3.44 (m, 2H), 2.32–2.25 (m, 1H), 2.02–1.96 (m, 1H), 1.40 (s, 3H), 0.97–0.91 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.3, 155.7, 135.4, 134.1, 112.1, 110.2, 110.2, 59.7, 55.8, 47.5, 40.5, 24.8, 17.9, 11.9; IR (neat): 3164, 3057, 2960, 2940, 2865, 1709, 1487, 1463, 1206, 1111, 1063, 1034, 885, 798, 767 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{21}H_{35}NNaO_3Si^+$: $[M + Na]^+$ = 400.2278, found 400.2282.

Synthesis of 4



3aj **4**

To an oven-dried round-bottom flask containing a magnetic stirring bar were added oxindole **3aj** (87.0 mg, 0.230 mmol) and dissolved in DMF (2.0 mL). The solution was stirred for 10 min at 0 °C, followed by the addition of a 60% sodium hydride dispersion in paraffin liquid (12.1 mg, 0.303 mmol). The reaction mixture was then stirred at room temperature for 30 min. After cooling to 0 °C, iodomethane (18.6 μL, 0.300 mmol) was added dropwise over 1 min. The reaction mixture was stirred for another hour at room temperature and then quenched with water (5 mL). The aqueous layer was extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The resulting oil was used in the next step without further purification.

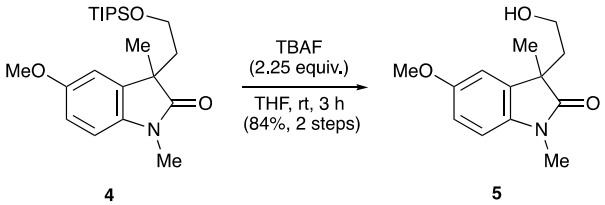


5-Methoxy-1,3-dimethyl-3-{2-[(triisopropylsilyl)oxy]ethyl}indolin-2-one (4):

The title compound was obtained as a colourless oil.

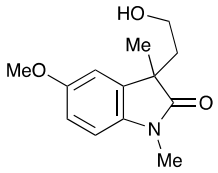
^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.81 (d, *J* = 2.3 Hz, 1H), 6.77 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.50–3.39 (m, 2H), 3.16 (s, 3H), 2.27–2.21 (m, 1H), 2.00–1.94 (m, 1H), 1.36 (s, 3H), 0.97–0.92 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 180.0, 155.9, 136.8, 135.1, 111.7, 110.4, 108.1, 59.7, 55.8, 47.0, 40.6, 26.2, 24.8, 17.9, 11.8; IR (neat): 2943, 2866, 1739, 1715, 1600, 1500, 1471, 1289, 1238, 1118, 1036, 883, 689 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{22}H_{37}NNaO_3Si^+$: $[M + Na]^+$ = 414.2435, found 414.2432.

Synthesis of 5



4 5

To an oven-dried round-bottom flask containing a magnetic stirring bar were added oxindole **4** and dissolved in THF (6 mL). The solution was stirred for 10 min at 0 °C. Subsequently, tetrabutylammonium fluoride (*ca*. 1 mol/L in THF, 517 μL, 0.517 mmol) was injected into the solution using a syringe, and the mixture was stirred at 0 °C for 30 min. After warming to room temperature, the mixture was quenched with H_2O (5 mL) and then extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The residue was purified by preparative thin-layer chromatography (EtOAc) to give alcohol **5** (45.5 mg, 0.193 mmol, 84%, 2 steps).

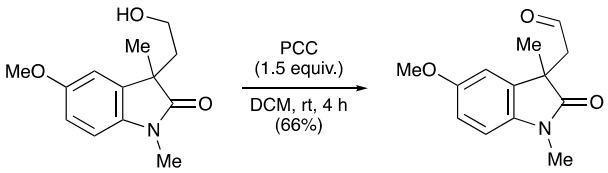


3-(2-Hydroxyethyl)-5-methoxy-1,3-dimethylindolin-2-one (5):

The title compound was obtained as a white solid.

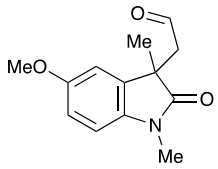
mp: 61.0–61.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.81–6.75 (m, 3H), 3.80 (s, 3H), 3.71–3.66 (m, 1H), 3.52–3.44 (m, 1H), 3.20 (s, 3H), 2.52 (s, 1H), 2.16–2.09 (m, 1H), 2.00–1.93 (m, 1H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 181.2, 156.2, 136.3, 135.6, 111.9, 110.2, 108.6, 59.3, 55.8, 47.4, 40.1, 26.4, 23.5. The spectral data matched those reported in the literature.[17]

Synthesis of 6



5 **6**

To an oven-dried round-bottom flask containing a magnetic stirring bar were added pyridinium chlorochromate (PCC, 48.7 mg, 0.226 mmol) and silica gel (same amount as PCC), and dissolved in dichloromethane (1.0 mL). The solution was stirred for 10 min at 0 °C. Subsequently, alcohol **5** (35.1 mg, 0.150 mmol) was added to the solution. The reaction mixture was stirred at room temperature for 4 h and then filtered through a pad of silica gel. The filtrate was concentrated using a rotary evaporator. The residue was purified by preparative thin-layer chromatography (toluene/EtOAc = 1:1) to give aldehyde **6** (23.1 mg, 9.90×10^{-2} mmol, 66%).

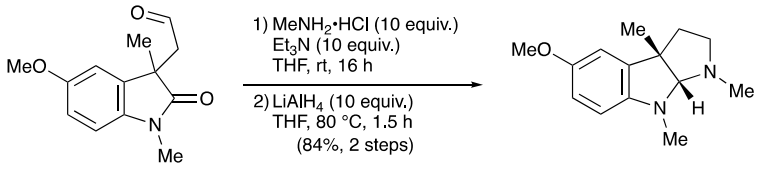


2-(5-Methoxy-1,3-dimethyl-2-oxoindolin-3-yl)acetaldehyde (6):

The title compound was obtained as a white solid.

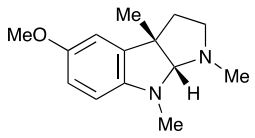
mp: 95.5–96.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.52 (t, J = 1.4 Hz, 1H), 6.81–6.77 (m, 3H), 3.78 (s, 3H), 3.24 (s, 3H), 3.00–2.90 (m, 2H), 1.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 198.7, 179.1, 156.1, 136.6, 134.1, 112.1, 110.3, 108.6, 55.7, 50.5, 45.4, 26.5, 23.9. The spectral data matched those reported in the literature.[18]

Synthesis of 7



6 **7**: *esermethole*

To an oven-dried round-bottom flask containing a stirring bar were added aldehyde **6** (14.5 mg, 6.22×10^{-2} mmol), $MeNH_2 \cdot HCl$ (41.7 mg, 0.618 mmol), triethylamine (62.1 mg, 0.613 mmol) and $MgSO_4$ (60.0 mg), and dissolved in anhydrous THF (3 mL). The mixture was stirred at room temperature for 16 h. Subsequently, $LiAlH_4$ (23.5 mg, 0.619 mmol) was added, and the mixture was refluxed at 80 °C for 1.5 h. After cooling to room temperature, EtOAc (6 mL) and saturated aqueous $NaHCO_3$ solution (6 mL) were added successively. The mixture was extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated using a rotary evaporator. The residue was purified by preparative thin-layer chromatography (dichloromethane/MeOH = 20:1) to afford (±)-esermethole **7** (5.21×10^{-2} mmol, 84%).

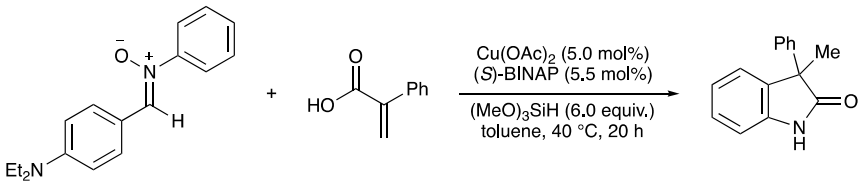


Esermethole (7):

The title compound was obtained as a colourless oil; ^{1}H NMR(500 MHz, $CDCl_3$) δ: 6.67–6.63 (m, 2H), 6.36 (d, J = 8.0 Hz, 1H), 4.05 (s, 1H), 3.75 (s, 3H), 2.89 (s, 3H), 2.75–2.70 (m, 1H), 2.67–2.60 (m, 1H), 2.53 (s, 3H), 1.94 (dd, J = 7.2, 5.4 Hz, 2H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 152.9, 146.6, 138.3, 112.2, 109.8, 107.4, 98.3, 56.0, 53.2, 52.7, 40.8, 38.1, 38.0, 27.4. The spectral data matched those reported in the literature.[17]

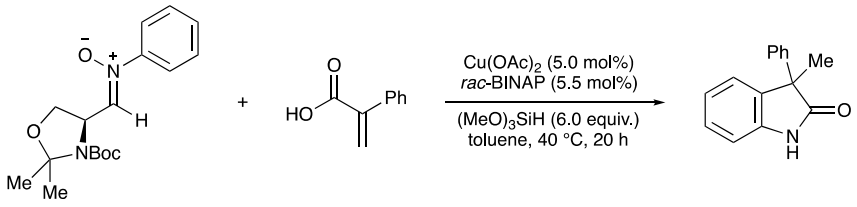
7. Trial for Asymmetric Synthesis of 3,3-Disubstituted Oxindoles

Oxindole Synthesis Using (*S*)-BINAP as a Chiral Ligand



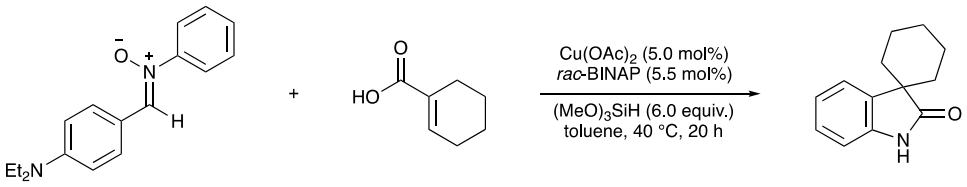
1a **2c** (2.5 equiv.) **3n,** 76%, 0% ee

Oxindole Synthesis Using nitrone 1n containing a chiral auxiliary



1n **2c** (2.5 equiv.) **3n**, trace

8. Trial for Spirooxindole Synthesis



1a **2q** (2.5 equiv.) **3al**, <20%

9. References

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