Supporting Information

Application of High Pressure Induced by Water-freezing to the Direct Catalytic Asymmetric Three-Component List-Barbas-Mannich Reaction

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Typical experimental procedure

The reaction with 2-naphthaldehyde

To a 1.5 mL Teflon tube¹ was added 2-naphthaldehyde (23.4 mg, 0.15 mmol), L-proline (6.0 mg, 0.052 mmol), *p*-anisidine (20.3 mg, 0.16 mmol), acetone (0.3 mL) and DMSO (1.2 mL), and the tube was capped with exclusion of air. This tube was placed in an autoclave, the inner capacity of which is about 100 mL,² and equipped with a pressure monitor.³ The autoclave was completely filled with water, sealed tightly, and left in a household electric refrigerator at -20 °C. It was found that the internal pressure reached about 200 MPa after 12 h. After 24 h, the autoclave was taken out of the refrigerator, and the Teflon tube was removed from the autoclave. The reaction was quenched with phosphate buffer and the organic materials were extracted with ethyl acetate three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, after which purification by column chromatography with Florisil® (hexane : ethyl acetate = 5 : 1) afforded the Mannich adduct in 64% yield (30.4 mg) with 91% ee. Optical purity was determined by the chiral HPLC analysis.

(*S*)-4-(2-naphthyl)-4-(*p*-anisidino)-butan-2-one⁴

64%, 91% ee.

¹H NMR (400 MHz, CDCl₃): δ 2.10 (3H, s), 2.96 (2H, d, *J* = 6.4 Hz), 3.66 (3H, s), 4.92 (1H, t, *J* = 6.4 Hz), 6.55 (2H, d, *J* = 8.9 Hz), 6.67 (2H, d, *J* = 8.9 Hz), 7.41-7.49 (2H, m), 7.77-7.81 (2H, m);

CHIRALPAK AS-H: hexane : *i*-PrOH = 6 : 1, major 13.9 min, minor 15.8 min, 315 nm 1.0 ml/min.

The reaction of *p*-nitrobenzaldehyde

The product was isolated as a Mannich product.

(*S*)-4-(*p*-nitrophenyl)-4-(*p*-anisidino)-butan-2-one⁴

58%, 91% ee.

¹H NMR (400 MHz, CDCl₃): δ 2.12 (3H, s), 2.92 (2H, d, *J* = 6.3 Hz), 3.67 (3H, s), 4.83 (1H, t, *J* = 6.3 Hz), 6.44 (2H, d, *J* = 8.9 Hz), 6.67 (2H, d, *J* = 8.9 Hz), 7.53 (2H, d, *J* = 8.6 Hz), 8.15 (2H, d, *J* = 8.6 Hz);

CHIRALPAK AD-H: hexane : *i*-PrOH = 3 : 1, major 11.6 min, minor 9.8 min, 280 nm 1.0 ml/min.

The reaction of *p*-bromobenzaldehyde

As the Mannich adduct is unstable, it was immediately reduced to the corresponding alcohol. Yield was referred to the isolated yield of the reduction alcohol with mixtures of *anti* and *syn* isomers. Characterization was performed after separation of the *anti* and *syn* isomers and the enantiomeric excess was determined by the HPLC analysis of the *anti*-isomer.

To a 1.5 mL Teflon tube was added *p*-bromobenzaldehyde (27.8 mg, 0.15 mmol), L-proline (6.0 mg, 0.052 mmol), *p*-anisidine (20.3 mg, 0.16 mmol), acetone (0.3 mL) and DMSO (1.2 mL), and the tube was capped with exclusion of air. This tube was placed in an autoclave, the inner capacity of which is about 100 mL, and equipped with a pressure monitor. The autoclave was completely filled with water, sealed tightly, and left in a household electric refrigerator at -20 °C. After 28 h, the autoclave was taken out of the refrigerator, and the Teflon tube was removed from the autoclave. The reaction was quenched with phosphate buffer and the organic materials were extracted with ethyl acetate three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, the residue was dissolved in THF (2 mL). To the THF solution was added LiAlH₄ (0.45 mmol) at -78 °C. After stirring the mixture for 10 minutes at -78 °C then at rt for 2 h, the reaction was quenched with 1N-NaOH solution (6 mL) and organic materials were extracted with CHCl₃ three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, after which purification by thin-layer chromatography (TLC) (hexane : ethyl acetate = 3 : 1) afforded the *syn* and *anti* mixture of aminoalcohol in 57% yield. To the CH₂Cl₂ solution (0.7 mL) of aminoalcohol (0.09 mmol) was added TBSOTf (0.33 mmol), 2,6-lutidine (0.45 mmol) at 0 °C and the reaction mixture was stirred at rt for 3 h. The reaction was quenched with phosphate buffer and the organic materials were extracted with ethyl acetate three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, after which purification by thin-layer chromatography (TLC) (hexane : ethyl acetate = 1 : 1) afforded the *syn* and *anti* aminosilyl ether in 38%, and 57% yield, respectively. Optical purity was determined by the chiral HPLC analysis of the *anti*-isomer.

(2*R*,4*S*)-4-*p*-anisidino-4-(*p*-bromophenyl)-2-butanol and (2*S*,4*S*)-4-*p*-anisidino-4-(*p*-bromophenyl)-2-butanol

57%, *syn:anti* = 0.4:0.6

¹H NMR (400 MHz, CDCl₃): δ 1.14 (3 x 0.4 H, d, *J* = 6.7Hz), 1.16 (3 x 0.6 H, d, *J* = 6.8Hz), 1.65 – 1.71 (2 x 0.4 H, m), 1.74 – 1.87 (2 x 0.6 H, m), 3.61 (3 H, s), 3.89-3.93 (1 x 0.6 H, m), 3.89-3.93 (1 x 0.4 H, m), 4.33 (1 x 0.4 H, dd, *J* = 4.2, 9.1Hz), 4.46 (1 x 0.6 H, dd, *J* = 4.0, 8.2Hz), 6.38 (2 x 0.6 H, d, *J* = 8.7Hz), 6.54 (2 x 0.4 H, d, *J* = 6.9Hz), 6.60 (2 H, d, *J* = 8.7Hz), 7.08-7.35 (4 H, m);

¹³C NMR (100 MHz, CDCl₃): δ *anti* isomer (major) 24.3, 47.2, 56.1, 59.6, 65.6, 115.2, 116.5, 126.7, 127.3, 128.5, 129.0, 132.1, 143.5, 153.2; *syn* isomer (minor) 24.8, 47.4, 56.1, 60.3, 65.7, 115.3, 116.8, 126.5, 127.3, 128.4, 129.1, 132.2, 144.3, 152.6;

IR (neat): 3388, 2964, 1512, 1236, 1178, 1128, 1036, 820, 702 cm⁻¹;

HRMS (FAB): calcd for C₁₇H₂₀BrNO₂ 349.0677, found 349.0688.

N-((1*S*,3*R*)-3-*tert*-butyldimethylsiloxy-1-(*p*-bromophenyl)-1-butyl)-*p*-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.01(3H, s), 0.04 (3H, s), 0.92 (9H, s), 1.19 (3H, d, *J* = 6.3Hz), 1.79 – 1.81 (2H, m), 3.67 (3H, s), 4.04 (1H, dd, *J* = 4.6, 6.3Hz), 4.39 (1H, t, *J* = 6.2), 4.72 (1H, bs), 6.36 (2H, d, *J* = 8.9Hz), 6.65 (2H, d, *J* = 8.9Hz), 7.21 (2H, d, *J* = 8.3Hz), 7.40 (2H, d, *J* = 8.3Hz);

¹³C NMR (100 MHz, CDCl₃): δ -4.91, -4.35, 23.0, 25.9, 47.9, 55.7, 66.4, 114.4, 114.7, 128.0, 131.7, 141.7, 151.8;

IR (neat): 3374, 2927, 1655, 1512, 1464, 1255, 1240, 1041, 835, 775 cm^{-1} ;
HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{34}\text{BrNO}_2\text{Si}$ 463.1542, found 463.1562;
 $[\alpha]_{\text{D}}^{18.1} +4.2$ ($c = 0.078$, MeOH), 95% ee;
CHIRALPAK AS-H: hexane : *i*-PrOH = 200 : 1, major 14.13 min, minor 13.46 min, 315 nm, 0.3 ml/min.

N-((1*S*,3*S*)-3-*tert*-butyldimethylsilyl-1-(*p*-bromophenyl)-1-butyl)-*p*-anisidine

^1H NMR (400 MHz, CDCl_3): δ 0.01 (3H, s), 0.03 (3H, s), 0.90 (9H, s), 1.14 (3H, d, $J = 6.0\text{Hz}$), 1.67 – 1.73 (1H, m), 1.90 – 1.97 (1H, m), 3.67 (3H, s), 3.87 – 3.96 (1H, m), 4.31 (1H, dd, $J = 6.8, 13.3\text{Hz}$), 6.41 (2H, d, $J = 8.8\text{Hz}$), 6.65 (2H, d, $J = 8.8\text{Hz}$), 7.21 (2H, d, $J = 8.2\text{Hz}$), 7.40 (2H, d, $J = 8.2\text{Hz}$);

^{13}C NMR (100 MHz, CDCl_3): δ -4.91, -4.35, 23.0, 25.9, 47.9, 55.7, 66.4, 114.4, 114.7, 128.0, 131.7, 141.7, 151.8;

IR (neat): 3396, 2927, 1651, 1512, 1464, 1257, 1240, 1039, 835, 775 cm^{-1} .

The reaction of benzaldehyde

As the Mannich adduct is unstable, it was immediately reduced to the corresponding alcohol. Yield was referred to the isolated yield of the reduction alcohol with mixtures of *anti* and *syn* isomers. Characterization was performed after separation of the *anti* and *syn* isomers and the enantiomeric excess was determined by the HPLC analysis of the *anti*-isomer.

(2*R*,4*S*)-4-*p*-anisidino-4-phenyl-2-butanol and (2*S*,4*S*)-4-*p*-anisidino-4-phenyl-2-butanol
99%, *syn:anti* = 0.2:0.8

^1H NMR (400 MHz, CDCl_3): δ 1.20 (3 x 0.2 H, d, $J = 6.2\text{Hz}$), 1.23 (3 x 0.8 H, d, $J = 6.3\text{Hz}$), 1.78 – 1.85 (2 x 0.2 H, m), 1.86 – 1.95 (2 x 0.8 H, m), 3.67 (3 x 0.8 H, s), 3.67 (3 x 0.2 H, s), 3.97-4.02 (1 x 0.8 H, m), 4.02-4.07 (1 x 0.2 H, m), 4.45 (1 x 0.2 H, dd, $J = 4.9, 9.2\text{Hz}$), 4.56 (1 x 0.8 H, dd, $J = 4.9, 7.7\text{Hz}$), 6.49 (2 x 0.8 H, d, $J = 8.9\text{Hz}$), 6.54 (2 x 0.2 H, d, $J = 6.9\text{Hz}$), 6.67 (2 x 0.8 H, d, $J = 8.9\text{Hz}$), 6.67 (2 x 0.2 H, d, $J = 6.9\text{Hz}$), 7.17-7.21 (5 x 0.8 H, m), 7.26-7.36 (5 x 0.2 H, m);

^{13}C NMR (100 MHz, CDCl_3): δ *anti* isomer (major) 23.7, 46.7, 55.7, 56.3, 65.3, 114.8, 115.0, 126.3, 126.9, 128.6, 141.4, 143.9, 152.1; *syn* isomer (minor) 24.3, 47.0, 55.6, 59.9, 68.0, 114.7, 116.4, 126.1, 127.0, 128.7, 141.4, 143.8, 152.1;

IR (neat): 3367, 2964, 1512, 1454, 1236, 1178, 1128, 1036, 820, 702 cm^{-1} ;

HRMS (FAB): calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_2$ 271.1572, found 271.1568.

N-((1*S*,3*R*)-3-*tert*-butyldimethylsiloxy-1-phenyl-1-butyl)-*p*-anisidine

^1H NMR (400 MHz, CDCl_3): δ 0.01 (3H, s), 0.03 (3H, s), 0.92 (9H, s), 1.20 (3H, d, $J = 6.2\text{Hz}$), 1.82 – 1.85 (2H, m), 3.66 (3H, s), 4.02 – 4.06 (1H, m), 4.42 (1H, dd, $J = 5.4, 8.2\text{Hz}$), 6.39 (2H, d, $J = 8.9\text{Hz}$), 6.64 (2H, d, $J = 8.9\text{Hz}$), 7.16 – 7.34 (5H, m);

^{13}C NMR (100 MHz, CDCl_3): δ -4.90, -4.37, 18.0, 23.1, 25.9, 48.2, 55.7, 56.0, 66.4, 114.3, 114.7, 126.2, 126.6, 128.5, 142.1, 145.1, 151.6;

IR (neat): 3380, 2927, 1602, 1511, 1255, 1238, 1039, 835 cm^{-1} ;

HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{35}\text{NO}_2\text{Si}$ 385.2437, found 385.2454;

$[\alpha]_{\text{D}}^{17.4} +6.7$ ($c = 0.021$, MeOH), 93% ee;

CHIRALPAK AS-H: hexane : *i*-PrOH = 200 : 1, major 4.57 min, minor 4.05 min, 254 nm, 1.0 ml/min.

N-((1*S*,3*S*)-3-*tert*-butyldimethylsiloxy-1-phenyl-1-butyl)-*p*-anisidine

^1H NMR (400 MHz, CDCl_3): δ 0.00 (3H, s), 0.05 (3H, s), 0.91 (9H, s), 1.14 (3H, d, $J = 6.0\text{Hz}$), 1.94 – 2.02 (2H, m), 3.67 (3H, s), 3.86 – 3.95 (1H, m), 4.35 (1H, dd, $J = 6.1, 6.9\text{Hz}$), 6.46 (2H, d, $J = 8.9\text{Hz}$), 6.65 (2H, d, $J = 8.9\text{Hz}$), 7.16 – 7.34 (5H, m);

^{13}C NMR (100 MHz, CDCl_3): δ -4.41, -3.99, 18.1, 24.5, 25.9, 48.4, 55.7, 57.4, 67.6, 114.7, 114.8, 126.5, 126.9, 128.6, 141.6, 144.6, 151.8;

IR (neat): 3396, 2929, 1512, 1463, 1375, 1255, 1240, 1138 cm⁻¹.

The reaction of 1-naphthaldehyde

The product was isolated as a Mannich product.

(S)-4-(1-naphthyl)-4-(p-anisidino)-butan-2-one

67%, 93% ee.

¹H NMR (400 MHz, CDCl₃): δ 2.07 (3H, s), 2.87 (1H, dd, *J* = 8.4, 16.2Hz), 3.02 (1H, dd, *J* = 4.0, 16.2Hz), 3.59 (3H, s), 5.51 (1H, dd, *J* = 4.0, 8.4Hz), 6.40 (2H, d, *J* = 8.8Hz), 6.58 (2H, d, *J* = 8.8Hz), 7.30-7.35 (1H, m), 7.38-7.55 (3H, m), 7.68 (1H, d, *J* = 8.1Hz), 7.84 (1H, d, *J* = 7.9Hz), 8.09 (1H, d, *J* = 8.4Hz);

¹³C NMR (100 MHz, CDCl₃): δ 30.7, 50.3, 51.2, 55.7, 114.2, 115.0, 122.1, 123.3, 125.6, 125.7, 126.4, 127.9, 129.3, 130.5, 134.2, 137.5, 140.9, 152.3, 207.2;

IR (neat): 1712, 1597, 1512, 1362, 1240, 1124, 1036, 820, 798, 777, 517 cm⁻¹;

HRMS (FAB): calcd for C₂₁H₂₁NO₂ 319.1572, found 319.1570;

[α]_D^{27.4} +95.7 (*c* = 0.42, MeOH), 93% ee;

CHIRALPAK AD-H: hexane; *i*-PrOH = 3: 1, major 17.8 min, minor 14.6 min, 315 nm, 0.5 ml/min.

The reaction of o-anisaldehyde

As the Mannich adduct is unstable, it was immediately reduced to the corresponding alcohol. Yield was referred to the isolated yield of the reduction alcohol with mixtures of *anti* and *syn* isomers. Characterization was performed after separation of the *anti* and *syn* isomers and the enantiomeric excess was determined by the HPLC analysis of the *anti*-isomer.

(2R,4S)-4-p-anisidino-4-(2-methoxyphenyl)-2-butanol and (2S,4S)-4-p-anisidino-4-(2-methoxyphenyl)-2-butanol

61%, *syn:anti* = 0.2:0.8

¹H NMR (400 MHz, CDCl₃): δ 1.28 (3 x 0.2 H, d, *J* = 6.1Hz), 1.33 (3 x 0.8 H, d, *J* = 6.3Hz), 1.97 – 2.12 (2 H, m), 3.76 (3 H, s), 3.96 (3 x 0.8 H, s), 3.97 (3 x 0.2 H, s), 4.05-4.11 (1 H, m), 4.85 (1 x 0.2 H, dd, *J* = 4.0, 8.9Hz), 4.98 (1 x 0.8 H, dd, *J* = 4.2, 8.3Hz), 6.60 (2 x 0.8 H, d, *J* = 8.9Hz), 6.66 (2 x 0.2 H, d, *J* = 8.9Hz), 6.76 (2 H, d, *J* = 8.9Hz), 6.93-6.96 (2 H, m), 7.27 (1 H, d, *J* = 7.5Hz), 7.34 (1 H, d, *J* = 7.5Hz);

¹³C NMR (100 MHz, CDCl₃): δ *anti* isomer (major) 23.5, 44.2, 51.6, 55.4, 55.6, 110.7, 114.7, 115.1, 120.7, 127.3, 127.8, 141.4, 156.7; *syn* isomer (minor) 23.5, 44.3, 51.6, 55.3, 55.6, 68.0, 110.6, 114.6, 116.5, 121.0, 128.0, 131.2, 152.1;

IR (neat): 3388, 2962, 1599, 1512, 1489, 1236, 1090, 1030, 820, 754 cm⁻¹.

N-((1S,3R)-3-tert-butyltrimethylsiloxy-1-(2-methoxyphenyl)-1-butyl)-p-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.01 (3H, s), 0.02 (3H, s), 0.93 (9H, s), 1.20 (3H, d, *J* = 5.8Hz), 1.75 – 1.81 (1H, m), 1.90 – 1.94 (1H, m), 3.66 (3H, s), 3.86 (3H, s), 4.00 – 4.08 (1H, m), 4.80 (1H, dd, *J* = 5.5, 9.2Hz), 6.41 (2H, d, *J* = 7.0Hz), 6.65 (2H, d, *J* = 7.0Hz), 6.85 (2H, d, *J* = 6.9Hz), 7.15 (1H, d, *J* = 7.5Hz), 7.34 (1H, d, *J* = 7.5Hz);

¹³C NMR (100 MHz, CDCl₃): δ -4.91, -4.35, 18.1, 23.3, 25.9, 45.6, 50.4, 55.2, 55.7, 66.7, 110.4, 114.3, 114.6, 120.7, 127.2, 127.5, 132.4, 142.2, 151.5, 156.6;

IR (neat): 3402, 2929, 1601, 1512, 1489, 1238, 1090, 1030, 835, 775 cm⁻¹;

HRMS (FAB): : calcd for C₂₄H₃₇NO₃Si 415.2543, found 415.2530;

[α]_D^{19.0} +20.8 (*c* = 0.19, MeOH), 97% ee;

CHIRALPAK AD-H: hexane : *i*-PrOH = 30 : 1, major 7.87 min, minor 9.01 min, 315 nm, 0.5 ml/min.

N-((1S,3S)-3-tert-butyltrimethylsiloxy-1-(2-methoxyphenyl)-1-butyl)-p-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.00 (3H, s), 0.05 (3H, s), 0.90 (9H, s), 1.16 (3H, d, *J* = 6.0Hz), 1.85 (2H, t, *J* = 6.5Hz), 3.67 (3H, s), 3.86 (3H, s), 3.97 (1H, q, *J* = 6.0Hz), 4.66

(1H, t, $J = 6.5\text{Hz}$), 6.45 (2H, d, $J = 8.8\text{Hz}$), 6.65 (2H, d, $J = 8.8\text{Hz}$), 6.85 (2H, d, $J = 7.6\text{Hz}$), 7.15 (1H, d, $J = 7.8\text{Hz}$), 7.27 (1H, d, $J = 7.8\text{Hz}$);
 ^{13}C NMR (100 MHz, CDCl_3): δ -4.45, -4.18, 18.1, 24.2, 26.0, 46.4, 52.2, 55.2, 55.7, 67.9, 110.5, 114.6, 114.8, 120.7, 127.3, 127.7, 131.9, 141.8, 151.7, 156.8;
IR (neat): 3381, 2927, 1601, 1512, 1489, 1238, 1090, 1030, 835, 775 cm^{-1} ;
HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{34}\text{BrNO}_2\text{Si}$ 463.1542, found 463.1562;
 $[\alpha]_{\text{D}}^{30.1} +8.2$ ($c = 0.24$, MeOH), 97% ee.

The reaction of *m*-anisaldehyde

As the Mannich adduct is unstable, it was immediately reduced to the corresponding alcohol. Yield was referred to the isolated yield of the reduction alcohol with mixtures of *anti* and *syn* isomers. Characterization was performed after separation of the *anti* and *syn* isomers and the enantiomeric excess was determined by the HPLC analysis of the *anti*-isomer.

(2*R*,4*S*)-4-*p*-anisidino-4-(3-methoxyphenyl)-2-butanol and (2*S*,4*S*)-4-*p*-anisidino-4-(3-methoxyphenyl)-2-butanol

83%, *syn:anti* = 0.32:0.68

^1H NMR (400 MHz, CDCl_3): δ 1.20 (3 x 0.32 H, d, $J = 6.3\text{Hz}$), 1.22 (3 x 0.68 H, d, $J = 6.2\text{Hz}$), 1.80 - 1.95 (2 H, m), 3.67 (3 H, s), 3.75 (3 H, s), 3.95-4.06 (1 H, m), 4.40 (1 x 0.32 H, dd, $J = 3.9, 8.8\text{Hz}$), 4.52 (1 x 0.68 H, dd, $J = 2.9, 7.6\text{Hz}$), 6.49 (2 x 0.68 H, d, $J = 8.7\text{Hz}$), 6.54 (2 x 0.32 H, d, $J = 8.7\text{Hz}$), 6.67 (2 H, d, $J = 8.7\text{Hz}$), 6.74 (1 H, d, $J = 8.0\text{Hz}$), 6.83-6.92 (2 H, m), 7.18 - 7.24 (1 H, m);

^{13}C NMR (100 MHz, CDCl_3): δ *anti* isomer (major) 23.7, 46.7, 55.1, 55.6, 67.9, 111.9, 112.1, 114.8, 114.9, 118.6, 129.6, 141.4, 145.8, 152.1, 159.9; *syn* isomer (minor) 24.2, 46.9, 56.3, 59.8, 65.2, 112.1, 112.2, 114.7, 116.3, 118.5, 129.6, 141.4, 145.8, 152.7, 159.9;

IR (neat): 3388, 2962, 1599, 1512, 1487, 1236, 1126, 1038, 820, 700 cm^{-1} .

N-((1*S*,3*R*)-3-*tert*-butyldimethylsiloxy-1-(3-methoxyphenyl)-1-butyl)-*p*-anisidine

^1H NMR (400 MHz, CDCl_3): δ 0.01 (3H, s), 0.03 (3H, s), 0.92 (9H, s), 1.19 (3H, d, $J = 5.9\text{Hz}$), 1.75- 1.91 (2H, m), 3.66 (3H, s), 3.76 (3H, s), 4.04 (1H, q, 5.9Hz), 4.39 (1H, dd, $J = 5.6, 7.4\text{Hz}$), 6.40 (2H, d, $J = 7.2\text{Hz}$), 6.64 (2H, d, $J = 7.2\text{ Hz}$), 6.72 (1H, d, $J = 8.0\text{Hz}$), 6.87-6.94 (2H, m), 7.17-7.24 (1H, m);

^{13}C NMR (100 MHz, CDCl_3): δ -4.91, -4.36, 18.0, 23.1, 25.9, 48.1, 55.1, 55.7, 56.1, 66.4, 111.8, 112.0, 114.4, 114.7, 118.6, 129.5, 142.1, 147.1, 151.6, 159.9;

IR (neat): 3381, 2929, 1601, 1514, 1487, 1240, 1128, 1030, 837, 820 cm^{-1} ;

HRMS (FAB): calcd for $\text{C}_{24}\text{H}_{37}\text{NO}_3\text{Si}$ 415.2543, found 415.2543;

$[\alpha]_{\text{D}}^{18.4} -5.6$ ($c = 0.11$, MeOH), 97% ee;

CHIRALPAK AD-H: hexane : *i*-PrOH = 100 : 1, major, 31.58 min, minor 34.79 min, 315 nm, 0.2 ml/min.

N-((1*S*,3*S*)-3-*tert*-butyldimethylsiloxy-1-(3-methoxyphenyl)-1-butyl)-*p*-anisidine

^1H NMR (400 MHz, CDCl_3): δ 0.01 (3H, s), 0.05 (3H, s), 0.91 (9H, s), 1.14 (3H, d, $J = 6.0\text{Hz}$), 1.72-1.78 (1H, m), 1.93-2.01 (1H, m), 3.67 (3H, s), 3.76 (3H, s), 3.88-3.95 (1H, m), 4.31 (1H, dd, $J = 5.9, 7.3\text{Hz}$), 6.47 (2H, d, $J = 8.9\text{Hz}$), 6.66 (2H, d, $J = 8.9\text{ Hz}$), 6.74 (1H, dd, $J = 2.4, 8.1\text{Hz}$), 6.88-6.94 (2H, m), 7.18-7.24 (1H, m);

^{13}C NMR (100 MHz, CDCl_3): δ -4.38, -3.99, 18.1, 24.5, 26.0, 48.3, 55.2, 55.7, 57.4, 67.7, 112.1, 112.2, 114.7, 114.8, 118.9, 129.6, 141.7, 146.5, 151.9, 159.9;

IR (neat): 3396, 2929, 1608, 1512, 1485, 1240, 1124, 1043, 835, 820 cm^{-1} .

The reaction of *p*-anisaldehyde

As the Mannich adduct is unstable, it was immediately reduced to the corresponding alcohol. Yield was referred to the isolated yield of the reduction alcohol with mixtures

of *anti* and *syn* isomers. Characterization was performed after separation of the *anti* and *syn* isomers and the enantiomeric excess was determined by the HPLC analysis of the *anti*-isomer.

(2*R*,4*S*)-4-*p*-anisidino-4-(4-methoxyphenyl)-2-butanol and (2*S*,4*S*)-4-*p*-anisidino-4-(4-methoxyphenyl)-2-butanol

99%, *syn:anti* = 0.47:0.63

¹H NMR (400 MHz, CDCl₃): δ 1.19 (3 x 0.47 H, d, *J* = 6.3Hz), 1.21 (3 x 0.63 H, d, *J* = 6.3Hz), 1.77 – 1.90 (2 H, m), 3.67 (3 H, s), 3.74 (3 x 0.47 H, s), 3.75 (3 x 0.63 H, s), 3.91-4.01 (1 H, m), 4.39 (1 x 0.47 H, dd, *J* = 4.9, 9.0Hz), 4.48-4.52 (1 x 0.63 H, m), 6.49 (2 x 0.63 H, d, *J* = 8.8Hz), 6.54 (2 x 0.47 H, d, *J* = 8.8Hz), 6.67 (2H, d, *J* = 8.8Hz), 6.80-6.86 (2H, m), 7.13-7.26 (2H, m);

¹³C NMR (100 MHz, CDCl₃): δ *anti* isomer (major) 23.7, 46.8, 55.2, 55.6, 65.2, 114.0, 114.6, 114.8, 116.5, 127.3, 135.8, 141.4, 152.0, 158.4; *syn* isomer (minor) 24.2, 46.9, 55.7, 59.2, 67.8, 114.7, 115.0, 116.5, 127.1, 135.9, 141.4, 152.7, 158.4;

IR (neat): 3367, 2962, 1610, 1510, 1464, 1240, 1176, 1034, 822, 548 cm⁻¹;

HRMS (FAB): calcd for C₁₈H₂₃NO₃ 301.1678, found 301.1660.

N-((1*S*,3*R*)-3-*tert*-butyldimethylsiloxy-1-(4-methoxyphenyl)-1-butyl)-*p*-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.02 (3H, s), 0.04 (3H, s), 0.93 (9H, s), 1.15 (3H, d, *J* = 6.0Hz), 1.81- 1.87(2H, m), 3.68 (3H, s), 3.77 (3H, s), 3.99-4.08 (1H, m), 4.35-4.42 (1H, m), 6.41 (2H, d, *J* = 8.4Hz), 6.66 (2H, d, *J* = 8.4 Hz), 6.84 (2H, d, *J* = 8.1Hz), 7.21-7.26 (2H, m);

¹³C NMR (100 MHz, CDCl₃): δ -4.89, -4.37, 18.0, 23.1, 25.9, 48.2, 55.2, 55.4, 55.7, 66.4, 114.0, 114.4, 114.7, 127.2, 137.1, 142.2, 151.6, 158.4;

IR (neat): 3381, 2929, 1610, 1512, 1489, 1244, 1128, 1037, 833, 775 cm⁻¹;

HRMS (FAB): calcd for C₂₄H₃₇NO₃Si 415.2543, found 415.2543;

[α]_D^{18.9} -7.4 (*c* = 0.010, MeOH), 94% ee;

CHIRALPAK AS-H: hexane : *i*-PrOH = 30 : 1, major 4.97 min, minor 4.28 min, 315 nm, 1.0 ml/min.

N-((1*S*,3*S*)-3-*tert*-butyldimethylsiloxy-1-(4-methoxyphenyl)-1-butyl)-*p*-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.01 (3H, s), 0.05 (3H, s), 0.92 (9H, s), 1.13 (3H, d, *J* = 6.1Hz), 1.69- 1.76(1H, m), 1.94- 2.01(1H, m), 3.67 (3H, s), 3.76 (3H, s), 3.85-3.90 (1H, m), 4.31 (1H, t, *J* = 6.5Hz), 6.47 (2H, d, *J* = 8.8Hz), 6.66 (2H, d, *J* = 8.8 Hz), 6.83 (2H, d, *J* = 8.6Hz), 7.23-7.26 (2H, m);

¹³C NMR (100 MHz, CDCl₃): δ -4.39, -3.96, 18.1, 24.6, 26.0, 48.4, 55.2, 55.7, 56.7, 67.5, 114.0, 114.7, 114.8, 127.5, 136.6, 141.7, 151.8, 158.5;

IR (neat): 2954, 2929, 1614, 1512, 1471, 1244, 1178, 1038, 833, 775 cm⁻¹.

The reaction of 3,4-dimethoxybenzaldehyde

As the Mannich adduct is unstable, it was immediately reduced to the corresponding alcohol. Yield was referred to the isolated yield of the reduction alcohol with mixtures of *anti* and *syn* isomers. Characterization was performed after separation of the *anti* and *syn* isomers and the enantiomeric excess was determined by the HPLC analysis of the *anti*-isomer.

(2*R*,4*S*)-4-*p*-anisidino-4-(3,4-dimethoxyphenyl)-2-butanol and (2*S*,4*S*)-4-*p*-anisidino-4-(3,4-dimethoxyphenyl)-2-butanol

65%, *syn:anti* = 0.35:0.65

¹H NMR (400 MHz, CDCl₃): δ 1.19 (3 x 0.35 H, d, *J* = 6.2Hz), 1.22 (3 x 0.65 H, d, *J* = 6.2Hz), 1.75 – 1.81 (2 x 0.35 H, m), 1.84 – 1.92 (2 x 0.65 H, m), 3.66 (3H, s), 3.81 (3H, s), 3.95-4.05 (1H, m), 4.36 (1 x 0.35 H, dd, *J* = 4.9, 9.0Hz), 4.47 (1 x 0.65 H, dd, *J* = 5.0, 7.5Hz), 6.49 (2 x 0.65 H, d, *J* = 8.8Hz), 6.54 (2 x 0.35 H, d, *J* = 8.8Hz), 6.66 (2H, d, *J* =

8.8Hz), 6.72-6.94 (4H, m);

¹³C NMR (100 MHz, CDCl₃): δ *anti* isomer (major) 23.7, 46.8, 55.7, 55.8, 56.1, 65.3, 109.5, 114.7, 116.4, 118.1, 136.6, 141.5, 147.8, 149.1, 152.1; *syn* isomer (minor) 24.3, 46.9, 55.6, 55.8, 59.7, 67.8, 109.4, 111.3, 114.6, 118.2, 136.5, 141.1, 148.0, 149.1, 152.8;

IR (neat): 3381, 2962, 1616, 1514, 1464, 1259, 1180, 1028, 912 cm⁻¹.

N-((1*S*,3*R*)-3-*tert*-butyldimethylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-*p*-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.02 (3H, s), 0.04 (3H, s), 0.92 (9H, s), 1.20 (3H, d, *J* = 6.2Hz), 1.79- 1.87(2H, m), 3.67 (3H, s), 3.83 (6H, s), 3.99-4.05 (1H, m), 4.35 (1H, t, *J* = 6.9Hz), 6.41 (2H, d, *J* = 8.8Hz), 6.64 (2H, d, *J* = 8.8Hz), 6.79 (1H, d, *J* = 8.6 Hz), 6.86-6.88 (2H, m);

¹³C NMR (100 MHz, CDCl₃): δ -4.87, -4.35, 18.0, 23.1, 25.9, 48.2, 55.7, 55.9, 55.9, 66.5, 109.4, 111.3, 114.5, 114.7, 118.1, 137.8, 142.2, 147.7, 149.2, 151.7;

IR (neat); 3381,2931, 1593, 1514, 1464, 1238, 1163, 1030, 835, 808 cm⁻¹;

HRMS (FAB): calcd for C₂₅H₃₉NO₄Si 445.2648, found.

[α]_D^{18.0} -3.7 (*c* = 0.12, MeOH), 95% ee;

CHIRALPAK AD-H: hexane : *i*-PrOH = 30 : 1, major 5.72 min, minor 7.05 min, 315 nm, 1.0 ml/min.

N-((1*S*,3*S*)-3-*tert*-butyldimethylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-*p*-anisidine

¹H NMR (400 MHz, CDCl₃): δ 0.01 (3H, s), 0.06 (3H, s), 0.92 (9H, s), 1.14 (3H, d, *J* = 6.1Hz), 1.71- 2.02 (2H, m), 3.68 (3H, s), 3.83 (6H, s), 3.86-3.95 (1H, m), 4.29 (1H, t, *J* = 6.7Hz), 6.49 (2H, d, *J* = 8.9Hz), 6.67 (2H, d, *J* = 8.9Hz), 6.79 (1H, d, *J* = 8.0 Hz), 6.86-6.90 (2H, m);

¹³C NMR (100 MHz, CDCl₃): δ -4.36, -3.97, 18.1, 24.6, 25.9, 26.0, 48.3, 55.7, 55.9, 57.2, 67.6, 109.8, 111.3, 114.5, 114.6, 114.9, 118.4, 137.3, 141.7, 147.9, 149.2, 151.9;

IR (neat): 3388, 2929, 1593, 1512, 1464, 1236, 1161, 1030, 980 cm⁻¹.

The reaction of *N*-acetyl-(4-formyl)aniline

The product was isolated as a Mannich product.

(*S*)-4-(4-acetamidophenyl)-4-(*p*-anisidino)-butan-2-one

82%, 92% ee.

¹H NMR (400 MHz, CDCl₃): δ 2.08 (3H, s), 2.13 (1H, s), 2.86 (2H, d, *J* = 6.3Hz), 3.67 (3H, s), 4.70 (1H, t, *J* = 6.3Hz), 6.47 (2H, d, *J* = 7.8Hz), 6.66 (2H, d, *J* = 7.8Hz), 7.14 (1H, bs), 7.28 (2H, d, *J* = 8.0Hz), 7.41 (2H, d, *J* = 8.0Hz);

¹³C NMR (100 MHz, CDCl₃): δ 24.3, 30.7, 51.2, 54.8, 55.7, 114.7, 115.3, 120.3, 126.9, 137.0, 138.6, 140.9, 152.4, 168.4, 207.2;

IR (neat): 1709, 1668, 1601, 1537, 1514, 1412, 1317, 1240, 1036,822, 731 cm⁻¹;

HRMS (FAB): calcd for C₁₉H₂₂N₂O₃ 326.1630, found 326.1630;

[α]_D^{27.4} -28.4 (*c* = 0.25, MeOH), 92% ee;

CHIRALPAK AS-H: hexane : *i*-PrOH = 3 : 1, major 21.3min, minor 31.3 min, 315 nm, 1.0 ml/min.

The reaction of furylaldehyde

The product was isolated as a Mannich product.

(*S*)-4-(*p*-anisidino)-4-(2-furyl)-butan-2-one

95%, >99% ee.

¹H NMR (400 MHz, CDCl₃): δ 2.07 (3H, s), 2.83-2.98 (2H, m), 3.66 (3H, s), 3.91 (1H, bs), 4.83 (1H, t, *J* = 6.3Hz), 6.07-6.09 (1H, m), 6.20 (1H, dd, *J* = 1.9, 3.3 Hz), 6.55 (2H, d, *J* = 10.1Hz), 6.67 (2H, d, *J* = 10.1Hz), 7.24-7.25 (1H, m);

¹³C NMR (100 MHz, CDCl₃): δ 30.6, 47.3, 49.6, 55.6, 106.3, 110.3, 114.8, 115.9, 140.5, 141.5, 152.9, 155.0, 206.6;

IR (neat): 3367, 1709, 1618, 1512, 1466, 1362, 1269, 1238, 1036, 883 cm⁻¹;

HRMS (FAB): calcd for C₁₅H₁₇NO₃ 259.1208, found 259.1238;

[α]_D^{26.0} -66.2 (*c* = 0.27, MeOH), >99% ee;

CHIRALPAK AS-H: hexane: *i*-PrOH = 30: 1, major 21.7 min, minor 27.3 min, 315 nm, 1.0 ml/min.

The reaction of cyclohexylcarbaldehyde

The product was isolated as a Mannich product.

(*S*)-4-(*p*-anisidino)-4-cyclohexyl-butan-2-one

90%, 84% ee.

¹H NMR (400 MHz, CDCl₃): δ 0.89-1.24 (5H, m), 1.50-1.85 (6H, m), 2.10 (3H, s), 2.49-2.62 (2H, m), 4.00 (1H, q, *J* = 6.1Hz), 3.71 (1H, s), 6.54 (2H, d, *J* = 8.8Hz), 6.73 (2H, d, *J* = 8.8Hz);

¹³C NMR (100 MHz, CDCl₃): δ 26.3, 26.5, 29.4, 29.5, 30.6, 41.9, 45.6, 55.8, 114.8, 115.0, 141.8, 152.1, 208.4;

IR (neat): 2925, 1709, 1512, 1448, 1238, 1180, 1037, 819, 752 cm⁻¹;

HRMS (FAB): calcd for C₁₇H₂₅NO₂ 275.1885, found 275.1861;

[α]_D^{26.8} -6.9 (*c* = 0.57, MeOH), 84% ee;

CHIRALPAK AS-H: hexane: *i*-PrOH = 20: 1, major 8.9 min, minor 13.0 min, 315 nm, 1.0 ml/min.

The reaction of 3,4-dimethoxybenzaldehyde with *tert*-butyldimethylsiloxyaniline

To a 1.5 mL Teflon tube was added 3,4-dimethoxybenzaldehyde (0.155 mmol), L-proline (0.053 mmol), *tert*-butyldimethylsiloxyaniline (0.165 mmol), acetone (0.3 mL) and DMSO (1.2 mL), and the tube was capped with exclusion of air. This tube was placed in an autoclave, the inner capacity of which is about 100 mL, and equipped with a pressure monitor. The autoclave was completely filled with water, sealed tightly, and left in a household electric refrigerator at -20 °C. It was found that the internal pressure reached about 200 MPa after 12 h. After 96 h, the autoclave was taken out of the refrigerator, and the Teflon tube was removed from the autoclave. The reaction was quenched with phosphate buffer and the organic materials were extracted with ethyl acetate three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, the residue was dissolved in THF (2 mL). To the THF solution was added LiAlH₄ (0.45 mmol) at -78 °C. After stirring the mixture for 10 minutes at -78 °C then at rt for 2 h, the reaction was quenched with 1N-NaOH solution (6 mL) and organic materials were extracted with CHCl₃ three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, after which purification by thin-layer chromatography (TLC) (hexane : ethyl acetate = 3 : 1) afforded the *syn* and *anti* mixture (*syn:anti*=0.6:1) of aminoalcohol in 65% yield.

(2*R*,4*S*)-4-(*N*-*tert*-butyldimethylsiloxyphenylamino)-4-(3,4-dimethoxyphenyl)-2-butanol and (2*S*, 4*S*)-4-(*N*-*tert*-butyldimethylsiloxyphenylamino)-4-(3,4-dimethoxyphenyl)-2-butanol
p-anisidino-4-(3,4-dimethoxyphenyl)-2-butanol

¹H NMR (400 MHz, CDCl₃): δ 0.10 (6H, s), 0.92 (9H, s), 1.20 (3 x 0.33 H, d, *J* = 6.3Hz), 1.22 (3 x 0.67 H, d, *J* = 6.3Hz), 1.80-1.83 (2 x 0.33 H, m), 1.87-1.91 (2 x 0.67 H, m), 3.18 (2H, bs), 3.80 (3 x 0.33 H, s), 3.81 (3 x 0.67 H, s), 3.82 (3H, s), 4.00 (1H, dd, *J* = 6.3, 12.4Hz), 4.36 (1 x 0.33 H, dd, *J* = 5.0, 9.0Hz), 4.47 (1 x 0.67 H, dd, *J* = 5.2, 7.2Hz), 6.42 (2 x 0.67 H, d, *J* = 8.7Hz), 6.47 (2 x 0.33 H, d, *J* = 8.7Hz), 6.57 (2 x 0.67

H, d, $J = 2.4\text{Hz}$), 6.59 (2 x 0.33 H, d, $J = 2.3\text{Hz}$), 6.78 (3 x 0.67 H, d, $J = 5.7\text{Hz}$), 6.83 (3 x 0.33 H, d, $J = 2.6\text{Hz}$);

^{13}C NMR (100 MHz, CDCl_3): δ *anti* isomer (major) -4.52, 18.1, 23.7, 24.2, 25.7, 46.8, 55.9, 56.2, 65.4, 67.9, 109.5, 109.6, 111.3, 115.0, 116.4, 118.1, 118.2, 120.4, 136.6, 141.8, 149.2; *syn* isomer (minor) -4.52, 18.1, 23.7, 24.2, 25.7, 46.8, 55.9, 56.2, 65.4, 67.9, 109.5, 109.6, 111.3, 115.0, 116.4, 118.1, 118.2, 120.4, 136.6, 141.8, 149.2;

IR (neat): 2600, 1508, 1464, 1250, 1140, 1028, 922, 908, 839, 781 cm^{-1} ;

HRMS (FAB): calcd for $\text{C}_{24}\text{H}_{37}\text{NO}_4\text{Si}$ 431.2492, found 431.2444.

To the CH_2Cl_2 solution (1.0 mL) of aminoalcohol (0.1 mmol) was added TIPSOTf (0.22 mmol), 2,6-lutidine (0.30 mmol) at 0 °C and the reaction mixture was stirred at rt for 3 h. The reaction was quenched with a phosphate buffer (pH 7.0) and the organic materials were extracted with ethyl acetate three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, after which purification by thin-layer chromatography (TLC) (hexane : ethyl acetate = 1 : 1) afforded the *syn* and *anti* aminosilyl ether in 37%, and 60% yield, respectively. Optical purity was determined by the chiral HPLC analysis of the *anti*-isomer.

N-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-*N*-(4-*tert*-butyldimethylsiloxyphenyl)amine

^1H NMR (400 MHz, CDCl_3): δ 0.10 (3H, s), 0.10 (3H, s), 0.93 (9H, s), 1.02–1.11 (3H, m), 1.07 (18H, bs), 1.28 (3H, d, $J = 6.1\text{Hz}$), 1.82–1.98 (2H, m), 3.83 (3H, s), 3.84 (3H, s), 4.12–4.16 (1H, m), 4.33 (1H, dd, $J = 4.4, 9.3\text{Hz}$), 6.35 (2H, d, $J = 8.1\text{Hz}$), 6.56 (2H, d, $J = 8.1\text{Hz}$), 6.80 (1H, d, $J = 7.9\text{Hz}$), 6.89 (2H, d, $J = 10.1\text{Hz}$);

^{13}C NMR (100 MHz, CDCl_3): δ -4.53, 12.4, 18.1, 18.2, 22.7, 25.7, 48.1, 55.8, 55.9, 56.3, 67.0, 109.4, 111.3, 114.4, 118.2, 120.2, 138.1, 142.5, 147.0, 147.7, 149.2;

IR (neat): 2956, 2866, 1732, 1510, 1464, 1417, 1248, 1138, 1032, 922, 679 cm^{-1} ;

HRMS (FAB): calcd for $\text{C}_{33}\text{H}_{57}\text{NO}_4\text{Si}_2$ 587.3826, found 587.3821;

$[\alpha]_{\text{D}}^{24.6}$ -16.1 ($c = 0.76$, MeOH), 96% ee;

CHIRALPAK AD-H: hexane : *i*-PrOH = 100 : 1, major 17.8 min, minor 21.5 min, 254 nm, 0.3 ml/min.

N-((1*S*,3*S*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-*N*-(4-*tert*-butyldimethylsiloxyphenyl)amine

^1H NMR (400 MHz, CDCl_3): δ 0.10 (3H, s), 0.11 (3H, s), 0.93 (9H, s), 0.98–1.12 (3H, m), 1.07 (18H, bs), 1.12 (3H, d, $J = 5.9\text{Hz}$), 1.77–1.86 (1H, m), 1.98–2.05 (1H, m), 3.82 (3H, s), 3.83 (3H, s), 4.09 (1H, q, $J = 5.9\text{Hz}$), 4.33 (1H, t, $J = 6.0\text{Hz}$), 6.41 (2H, d, $J = 8.0\text{Hz}$), 6.58 (2H, d, $J = 7.4\text{Hz}$), 6.79 (1H, d, $J = 7.7\text{Hz}$), 6.87 (2H, d, $J = 9.4\text{Hz}$);

^{13}C NMR (100 MHz, CDCl_3): δ -4.52, 12.3, 12.4, 12.8, 17.7, 18.1, 18.2, 18.3, 24.4, 25.7, 48.8, 55.8, 55.9, 57.0, 67.5, 109.8, 111.3, 114.7, 118.4, 120.3, 137.3, 142.3, 147.3, 147.9, 149.1;

IR (neat): 2956, 2866, 1732, 1510, 1464, 1417, 1248, 1138, 1032, 922, 679 cm^{-1} ;

HRMS (FAB): calcd for $\text{C}_{33}\text{H}_{57}\text{NO}_4\text{Si}_2$ 587.3826, found 587.3821;

$[\alpha]_{\text{D}}^{24.6}$ -13.8 ($c = 0.64$, MeOH), 96% ee.

To a degassed MeOH (1 mL) solution of *N*-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-*N*-(4-*tert*-butyldimethylsiloxyphenyl)amine (15.9 mg, 0.027 mmol) was added K_2CO_3 (0.135 mmol) at rt and the reaction mixture was stirred at 40 °C for 4 h. After filtration using Florisil® and removal of the volatile materials under reduced pressure, the crude materials were purified with TLC (AcOEt : hexane = 1:2), affording 4-*N*-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-aminophenol 11.5 mg (0.024 mmol, 90%).

4-*N*-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-aminophenol

1H NMR (400 MHz, $CDCl_3$): δ 0.93-1.17 (3H, m), 1.07 (18H, bs), 1.27 (3H, d, J = 6.2Hz), 1.80-1.98 (2H, m), 3.82 (3H, s), 3.83 (3H, s), 4.05-4.18 (1H, m), 4.28-4.35 (1H, m), 6.36 (2H, d, J = 7.2Hz), 6.56 (2H, d, J = 7.2Hz), 6.79 (1H, d, J = 8.0Hz), 6.89 (2H, d, J = 7.5Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 12.4, 18.1, 18.2, 22.6, 48.0, 55.8, 55.9, 56.3, 67.1, 109.3, 111.4, 114.7, 115.9, 118.1, 147.8, 149.3;

IR (neat): 3375, 2958, 2866, 1593, 1512, 1462, 1419, 1257, 1138, 1030, 883, 679 cm^{-1} ;

HRMS (FAB): calcd for $C_{27}H_{43}NO_4Si$ 473.2961, found 473.2937;

$[\alpha]_D^{17.7}$ -6.6 (c = 0.042, MeOH).

N-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-amine

To a mixture of CH_3CN (0.2 mL) and H_2O (0.1 mL) of 4-*N*-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-aminophenol (9.5 mg, 0.02 mmol) was added a solution (CH_3CN (0.2 mL) and H_2O (0.1 mL)) of $PhI(OCOCF_3)_2$ (0.021 mmol) at rt and the reaction mixture was stirred at rt for 20 minutes. The reaction was quenched with phosphate buffer and the organic materials were extracted with ethyl acetate three times. After drying the organic phase, volatile organic materials were removed under reduced pressure, after which purification by TLC ($CHCl_3$: MeOH : Et_3N = 10:1:0.4) afforded *N*-((1*S*,3*R*)-3-triisopropylsiloxy-1-(3,4-dimethoxyphenyl)-1-butyl)-amine in 49% yield (3.7 mg).

1H NMR (400 MHz, $CDCl_3$): δ 0.91-1.10 (3H, m), 1.06 (18H, bs), 1.24 (3H, d, J = 6.0Hz), 1.76-1.82 (1H, m), 1.96-2.04 (1H, m), 3.83 (6H, s), 4.04-4.11 (1H, m), 4.30-4.34 (1H, m), 6.42 (2H, d, J = 8.0Hz), 6.58 (2H, d, J = 8.0Hz), 6.77-6.88 (1H, m);

^{13}C NMR (100 MHz, $CDCl_3$): δ 12.8, 18.2, 18.3, 24.4, 48.9, 55.9, 56.9, 67.6, 109.8, 111.3, 114.9, 115.9, 118.3, 147.9, 149.2;

IR (neat): 3405, 2943, 2866, 1597, 1512, 1461, 1419, 1257, 1137, 1026, 883, 679 cm^{-1} ;

$[\alpha]_D^{18.0}$ -5.1 (c = 0.045, MeOH).

Reference

1 The Teflon tube is made by Hikari Koatu Kiki Co. Ltd. Hiroshima, Japan.

- 2 The autoclave is made by Atlas Co. Ltd. Tokyo, Japan and its size is as follows; 78 mm outside diameter, 340 mm height, 25 mm inside diameter, and 200 mm depth.
- 3 KH78, Naganokeiki Co. Ltd., Tokyo, Japan.
- 4 List, B.; Pojarliev, P.; Biller, W. T.; Martin, H. J. *J. Am. Chem. Soc.* **2002**, *124*, 827.