Stereoselective Synthesis of γ-Amino Alcohols

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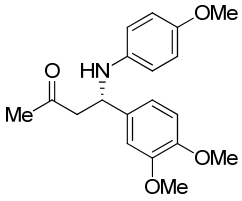
Contents

General remarks

All chemicals were obtained from commercial sources and used without further purification unless stated otherwise. All reactions were carried out under ambient atmosphere unless stated otherwise. R_f values were obtained using thin layer chromatography (TLC), which was carried out on silica gel-coated plates (Merck 60 F254). Column chromatography was carried out using silica gel. Melting points were analysed with Büchi melting point B-545. IR spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer, or a Bruker Tensor 27 FTIR spectrometer. NMR spectra were recorded on a Bruker DMX300, Varian Inova 400 or Bruker DPX200 spectrometer. ^{1}H NMR chemical shifts are reported in parts per million (ppm) relative to a residual proton peak of the NMR solvent (δ = 7.26 ppm for $CHCl_3$, δ = 3.31 ppm for CD_3OD, δ = 2.50 ppm for DMSO-d_6. δ = 4.79 ppm for D_2O. ^{13}C NMR chemical shifts are reported in ppm relative to $CDCl_3$ (77.0 ppm), CD_3OD (49.0 ppm) or DMSO-d_6 (39.5 ppm). Optical rotation were determined with a Perkin Elmer 241 polarimeter. High resolution mass spectra were recorded on a JEOL AccuTOF-CS or JEOL AccuTOF-GCv spectrometer. HPLC analysis was carried out on various Shimadzu HPLC-configurations using the stated columns and eluents. Detection was carried out using UV light.

Synthesis of substrates (*S*)-**1**, (*S*)-**6**, (*S*)-**7**, (*R*)-**8**, (*S*)-**9**

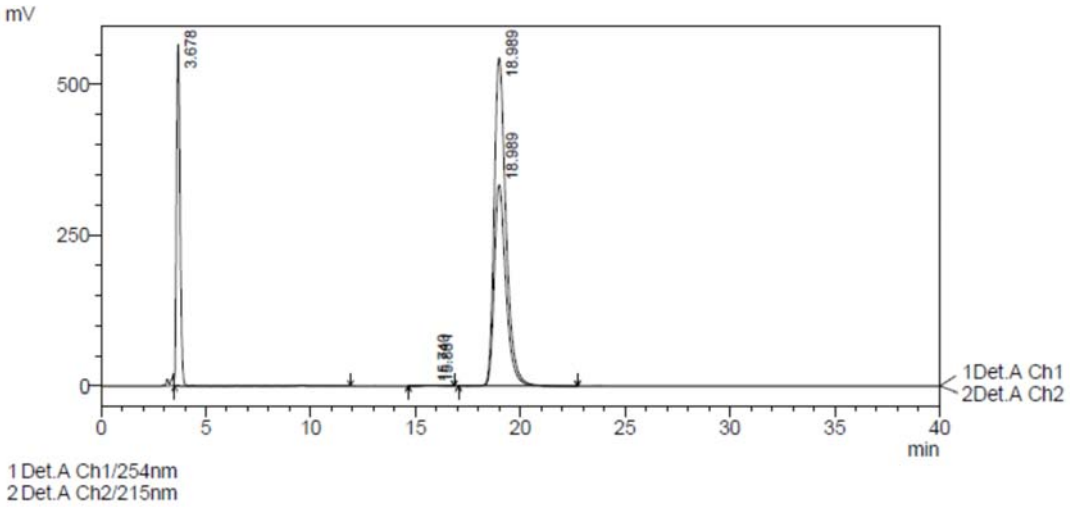
(*S*)-4-(3,4-Dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-one ((*S*)-1)



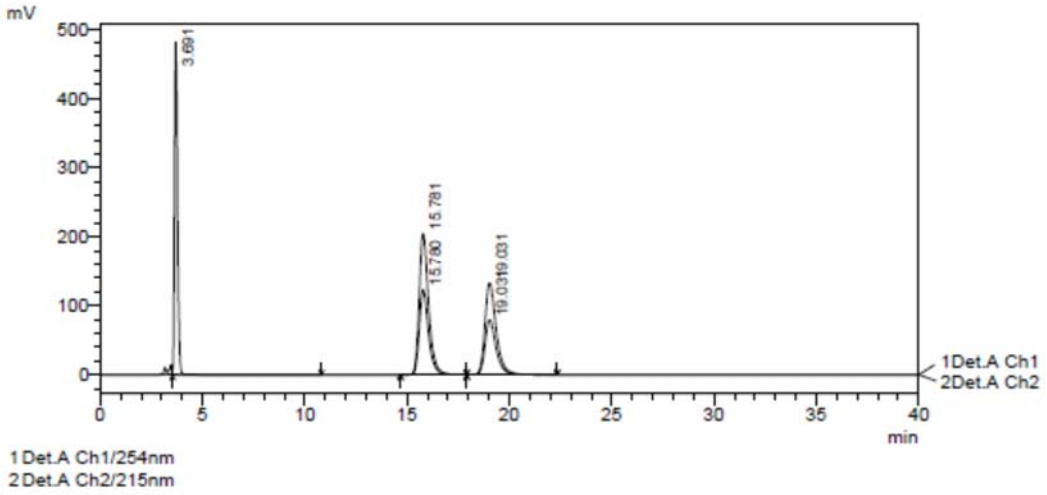
To a mixture of DMSO (45 mL) and acetone (180 mL) was added 3,4-dimethoxybenzaldehyde (10.5 g, 63.2 mmol), *p*-anisidine (7.78 g, 63.2 mmol) and L-proline. The resulting reaction mixture was stirred for 23 h. The reaction mixture was quenched with 100 mL potassium phosphate buffer (0.5 M, pH 7, 100 mL). Subsequently, a total of 150 mL of potassium phosphate buffer (0.5 M, pH 7) was added in portions. The reaction mixture was cooled to 0 °C and the flask was scratched with a spatula, which induced precipitation. After stirring for 20 min, the suspension was filtered off and the residue was washed with water (0 °C, 50 mL). The product was dried *in vacuo*. The product was obtained as an off-white powder (12.7 g). The product was recrystallised from EtOAc and obtained as off-white crystals (10.2 g, 31.0 mmol, 49%).^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.92–6.86 (m, 2H), 6.84–6.77 (m, 1H), 6.73–6.65 (m, 2H), 6.57–6.48 (m, 2H), 4.69 (t, *J* = 6.5 Hz, 1H), 3.85 (s, 6H), 3.70 (s, 3H), 2.89 (d, *J* = 6.5 Hz, 2H), 2.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 207.4, 152.4, 149.2, 148.1, 141.0, 135.4, 118.2, 115.4, 114.7, 111.3, 109.5, 55.9 (2C), 55.7, 55.2, 51.4, 30.8; HRMS [ESI$^+$ (m/z)]: calcd for $C_{19}H_{23}NO_4Na$ (M+Na$^+$) 352.15248, found 352.15249; HPLC: ee: >99%, Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol 80/20, retention time: major enantiomer 19.0 min, minor enantiomer: 15.8 min.

HPLC traces

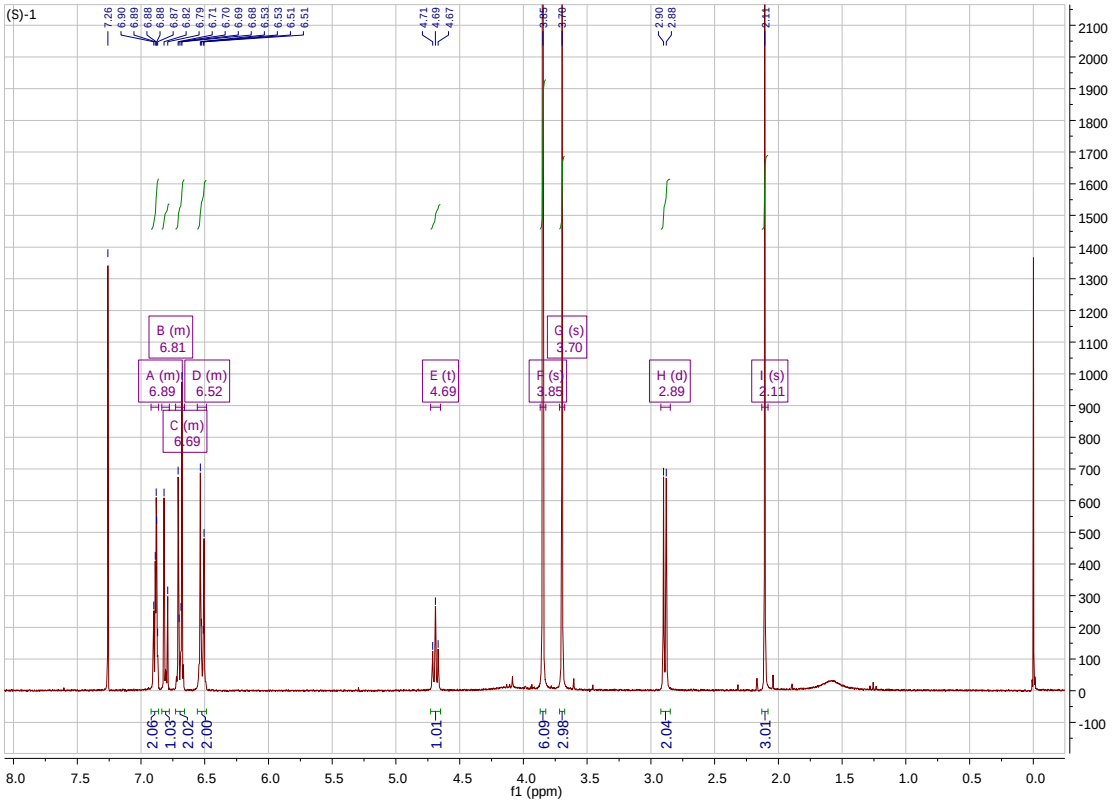
((*S*)-1)



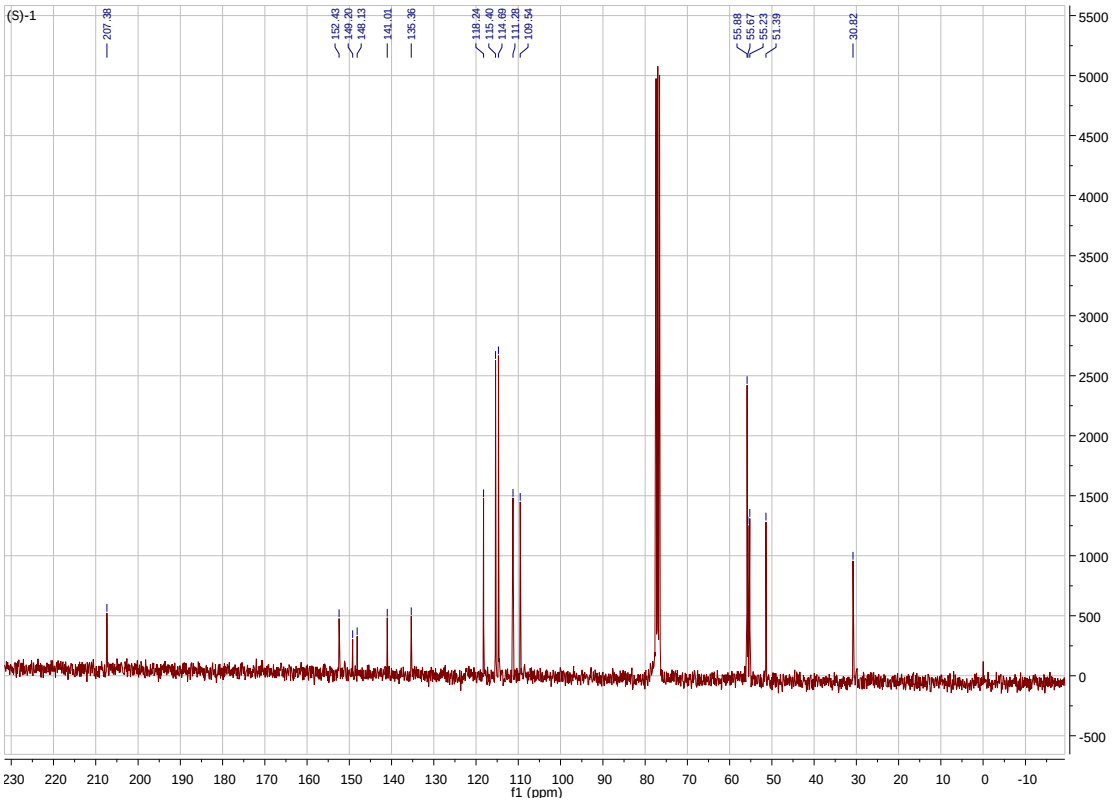
((*RS*)-1)


mV
500
400
300
200
100
0
3.691
15.781
15.780
19.031
19.031
1Det.A Ch1
2Det.A Ch2
0
5
10
15
20
25
30
35
40
min
1 Det.A Ch1/254nm
2 Det.A Ch2/215nm

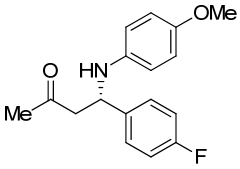
^{1}H NMR (*S*)-1


(S)-1
B (m)
6.81
A (m)
6.89
D (m)
6.52
C (m)
6.69
E (t)
4.69
G (s)
3.70
F (s)
3.85
H (d)
2.89
I (s)
2.11
2.06
1.03
2.02
2.00
1.01
6.09
2.98
2.04
3.01
f1 (ppm)

^{13}C NMR (*S*)-1



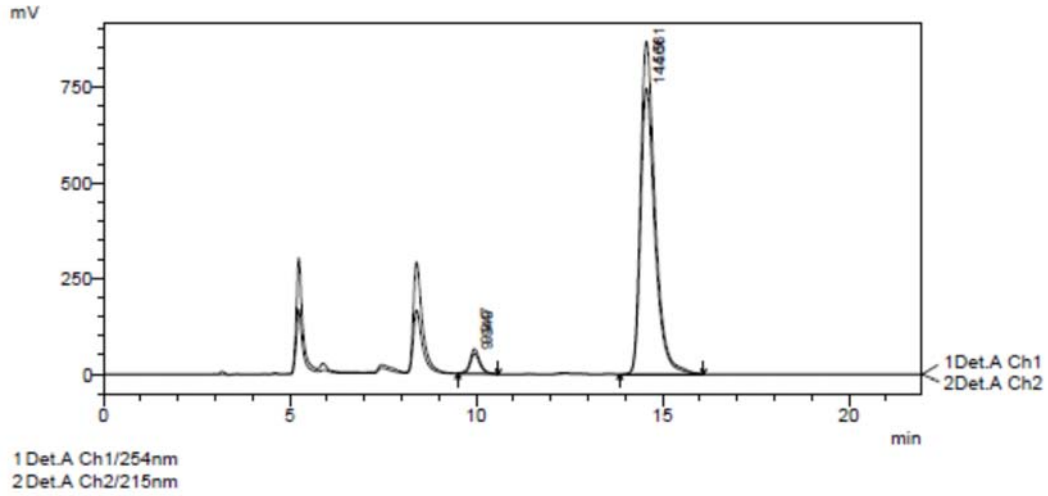
(*S*)-4-(4-Fluorophenyl)-4-((4-methoxyphenyl)amino)butan-2-one (6)



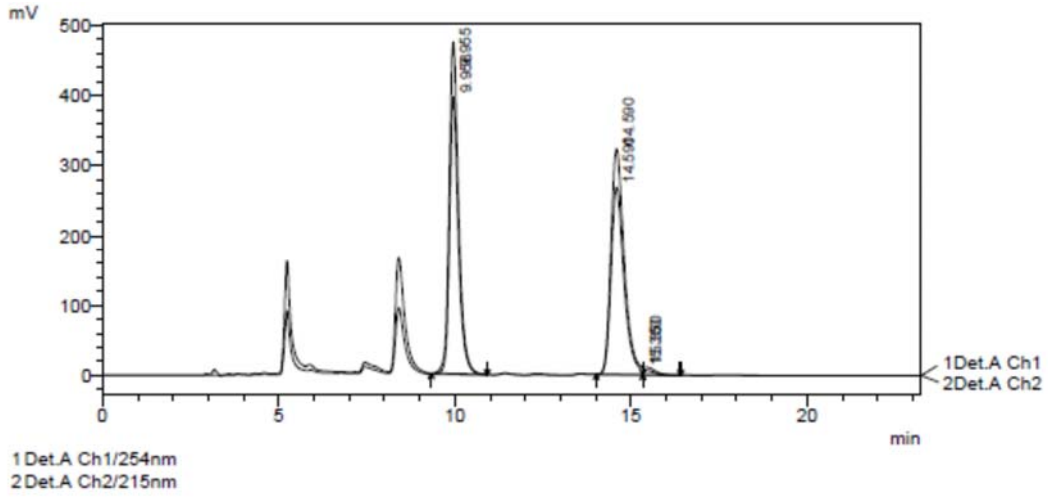
p-Anisidine (2.00 g, 16.2 mmol) was dissolved in DMSO (20 mL) and 4-fluorobenzaldehyde (1.74 mL, 2.00 g, 16.2 mmol) and L-proline (373 mg, 3.24 mmol) were added. After 2 h of stirring, acetone was added (80 mL). The resulting mixture was stirred for 22 h and quenched with saturated aqueous $NaHCO_3$ (100 mL). It was subsequently extracted with a mixture of EtOAc and heptane (1:1, 2 × 100 mL) The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified using column chromatography (1st column: EtOAc/heptane 1/9 → 1/4 → 1/3, 2nd column: EtOAc/heptane 1/9 → 1/4). Yield: 1.40 g (4.87 mmol, 30%) of an orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.38–7.29 (m, 2H), 7.05–6.95 (m), 6.72–6.65 (m, 2H), 6.53–6.46 (m, 2H), 4.74 (t, *J* = 6.5 Hz, 1H), 4.15 (bs, 1H), 3.70 (s, 3H), 2.89 (d, *J* = 6.5 Hz, 2H), 2.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 206.9, 161.91 (d, *J* = 245.4 Hz), 152.5, 140.7, 138.4, 127.90 (d, *J* = 8.0 Hz), 115.59 (d, *J* = 21.5 Hz), 115.4, 114.7, 55.6, 54.6, 51.3, 30.7; IR (cm^{-1}): 3383, 3003, 2833, 1710, 1509, 1235, 820; HRMS [ESI$^+$ (m/z)]: calcd for $C_{17}H_{18}FNO_2Na$ (M+Na$^+$) 310.12193, found 310.12059; HPLC: ee: 91%, Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol 80/20, retention time: major enantiomer 14.6 min,; minor enantiomer: 9.9 min. R_f 0.26 (EtOAc/heptane 1/2).

HPLC traces

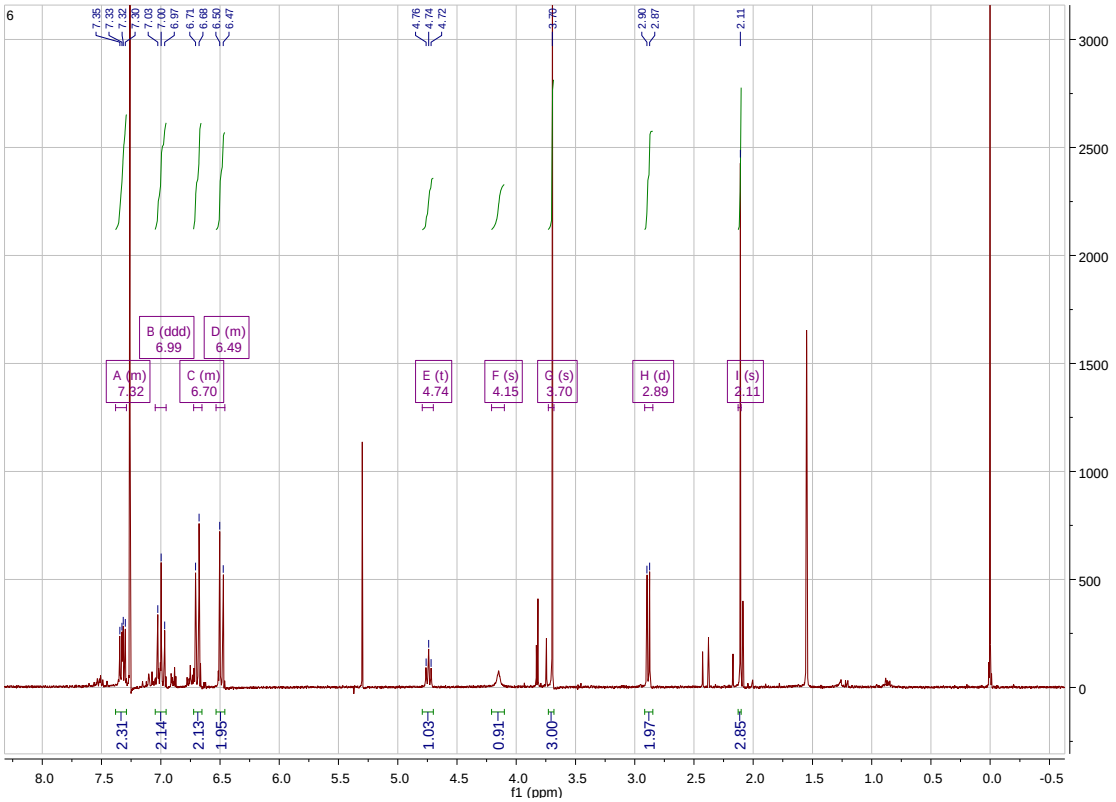
(*S*)-6



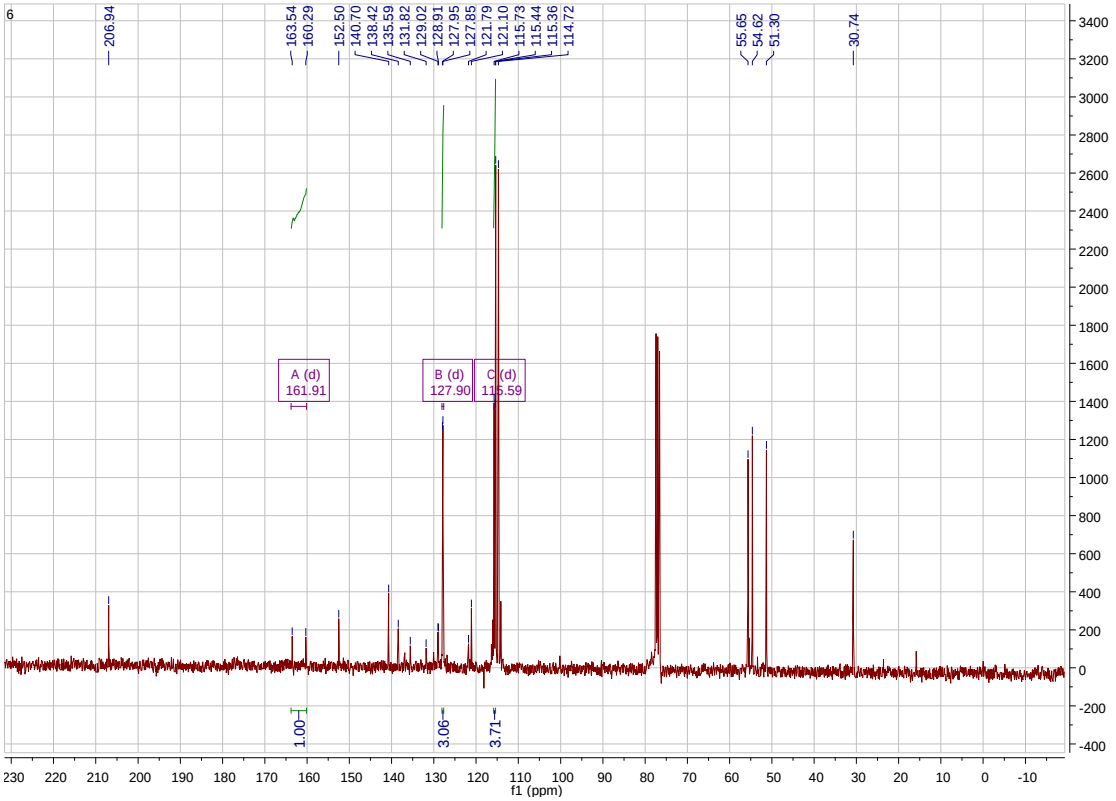
(*RS*)-6



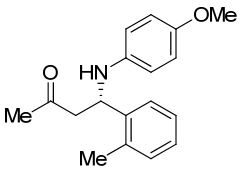
^{1}H NMR **6**



^{13}C NMR **6**



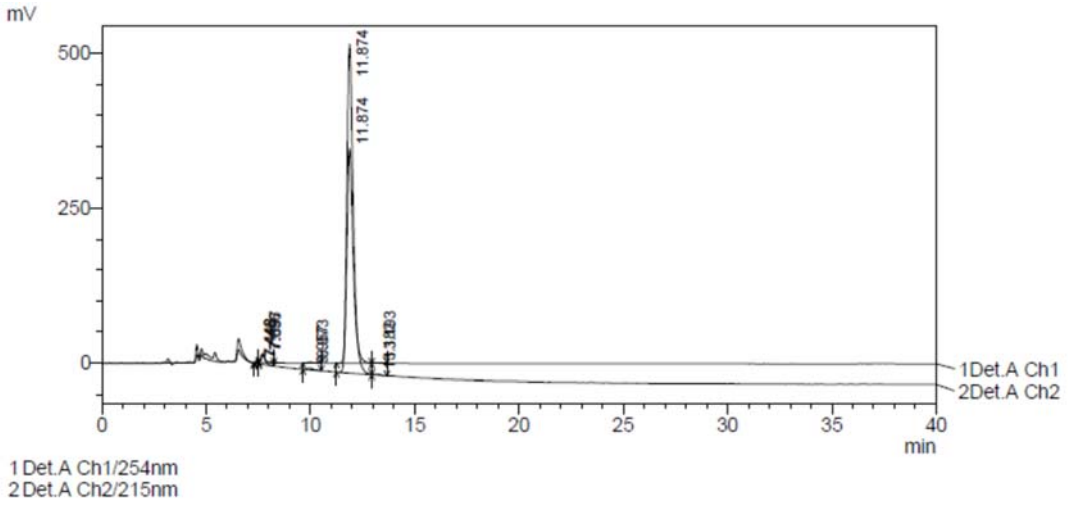
(*S*)-4-((4-Methoxyphenyl)amino)-4-(*o*-tolyl)butan-2-one (**7**)



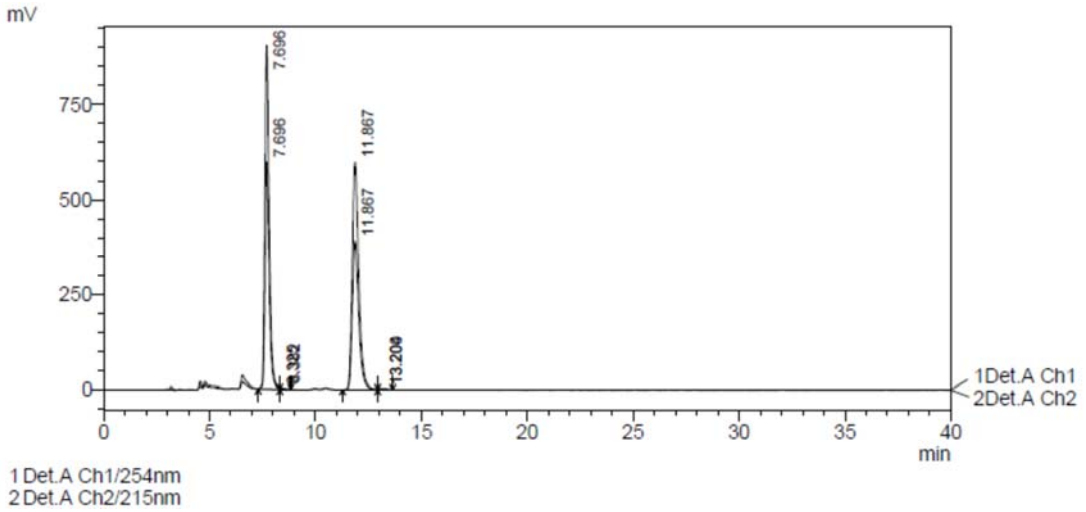
p-Anisidine (2.00 g, 16.2 mmol) was dissolved in DMSO (20 mL) and *o*-tolualdehyde (1.88 mL, 2.00 g, 16.2 mmol) and L-proline (373 mg, 3.24 mmol) were added. After 2 h of stirring, acetone was added (80 mL). The resulting mixture was stirred for 19 h and quenched with saturated aqueous $NaHCO_3$ (100 mL). It was subsequently extracted with a mixture of EtOAc and heptane (1:1, 2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified using column chromatography (EtOAc/heptane 1/9 → 1/4). Yield 2.34 g (8.26 mmol, 51%) of an orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.41–7.33 (m, 1H), 7.19–7.12 (m, 3H), 6.73–6.65 (m, 2H), 6.50–6.40 (m, 2H), 4.96 (dd, *J* = 7.9, 5.3 Hz, 1H), 4.07 (bs, 1H), 3.69 (s, 3H), 2.87 (dd, *J* = 15.7, 5.1 Hz, 1H), 2.80 (dd, *J* = 15.9, 7.9 Hz, 1H), 2.45 (s, 3H), 2.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 207.3, 152.3, 141.0, 140.4, 134.7, 130.8, 127.1, 126.6, 125.2, 115.0, 114.8, 55.7, 51.6, 49.8, 30.5, 19.1, 10.0; IR (cm^{-1}) 3383, 3022, 2947, 2831, 1708, 1510, 1237; HRMS [ESI$^+$ (m/z)]: calcd for $C_{18}H_{21}NO_2Na$ (M+Na$^+$) 306.14700, found 306.14873; HPLC: ee: 96%, Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol 80/20, retention time: major enantiomer 11.9 min, minor enantiomer: 7.7 min.; R_f 0.33 (EtOAc/heptane 1/2).

HPLC traces

(*S*)-7



(*RS*)-7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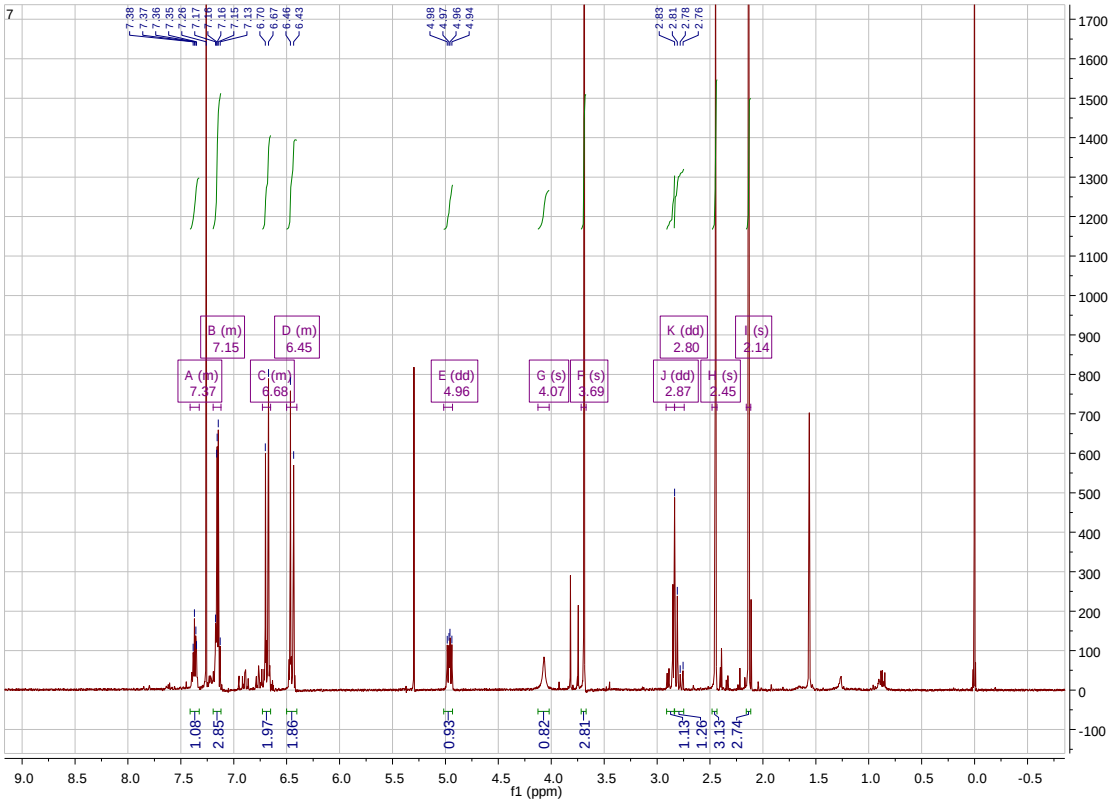
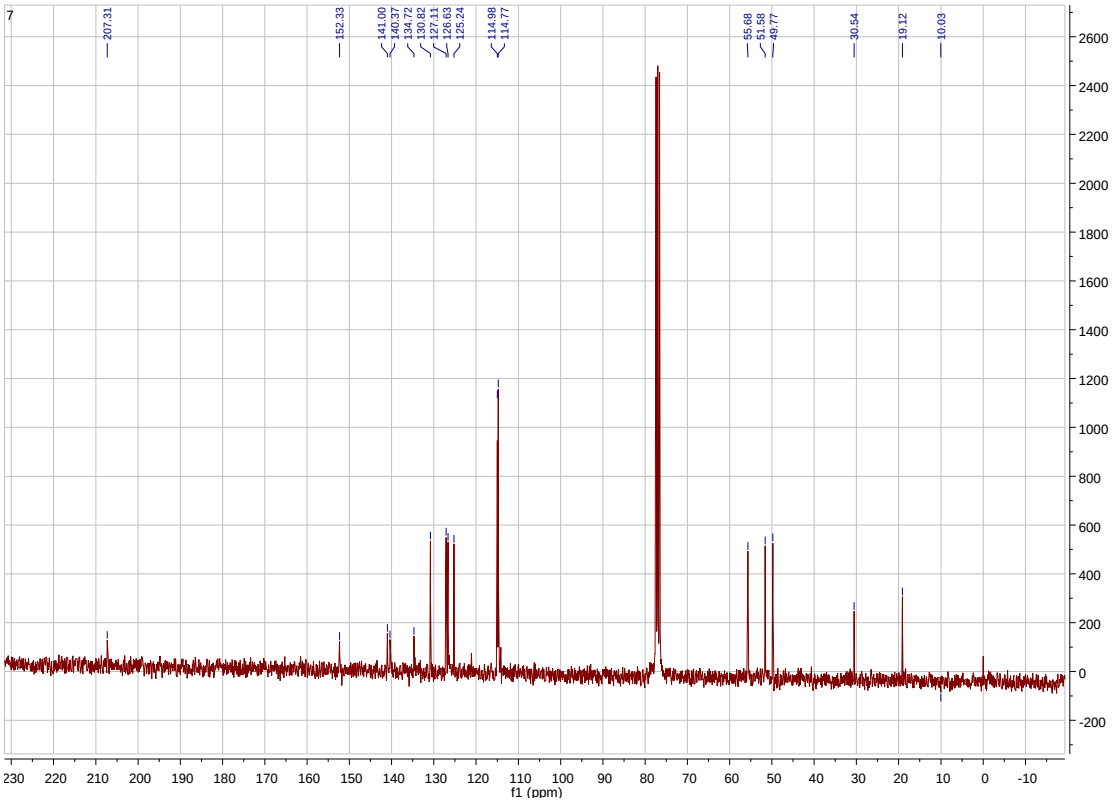
500
250
0
7.696
7.696
11.867
11.867
13.206
0
5
10
15
20
25
30
35
40
min
1Det.A Ch1
2Det.A Ch2
1 Det.A Ch1/254nm
2 Det.A Ch2/215nm

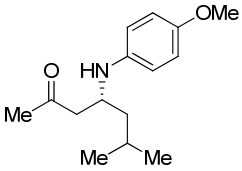
^{1}H NMR **7**


7
B (m) 7.15
D (m) 6.45
A (m) 7.37
C (m) 6.68
E (dd) 4.96
G (s) 4.07
F (s) 3.69
K (dd) 2.80
J (dd) 2.87
H (s) 2.45
I (s) 2.14
1.08
2.85
1.97
1.86
0.93
0.82
2.81
1.13
1.26
3.13
2.74
f1 (ppm)

^{13}C NMR **7**



(*R*)-4-((4-Methoxyphenyl)amino)-6-methylheptan-2-one (8)

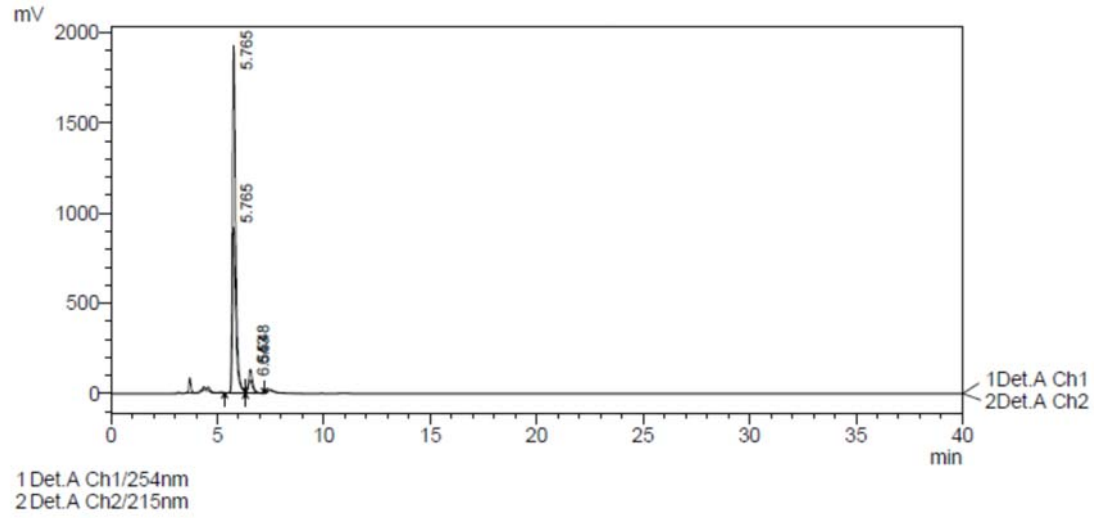


p-Anisidine (2.00 g, 16.2 mmol) was dissolved in DMSO (20 mL) and isovaleraldehyde (1.74 mL, 2.00 g, 16.2 mmol) and L-proline (373 mg, 3.24 mmol) were added. After 2 h of stirring, acetone was added (80 mL). The resulting mixture was stirred for 18 h and quenched with saturated aqueous $NaHCO_3$ (100 mL). It was subsequently extracted with a mixture of EtOAc and heptane (1:1, 2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified using column chromatography (EtOAc/heptane 1/9 → 1/4). Yield: 2.16 g (8.66 mmol, 53%) of a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz,) δ (ppm) 6.80–6.73 (m, 2H), 6.62–6.54 (m, 2H), 3.85–3.75 (m, 1H), 3.73 (s, 3H), 2.65 (dd, *J* = 16.1, 5.0 Hz, 1H), 2.54 (dd, *J* = 16.2, 6.5 Hz, 1H), 2.12 (s, 3H), 1.83–1.65 (m, 1H), 1.47 (ddd, *J* = 14.2, 8.2, 6.1 Hz, 1H), 1.32 (ddd, *J* = 13.7, 8.0, 5.7 Hz, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 208.4, 152.2, 141.3, 115.0, 114.9, 55.7, 49.1, 48.1, 44.7, 31.0, 25.0, 22.9, 22.3; HPLC: ee: 84%, Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol 80/20, retention time: major enantiomer 5.8 min, minor enantiomer: 6.5 min.

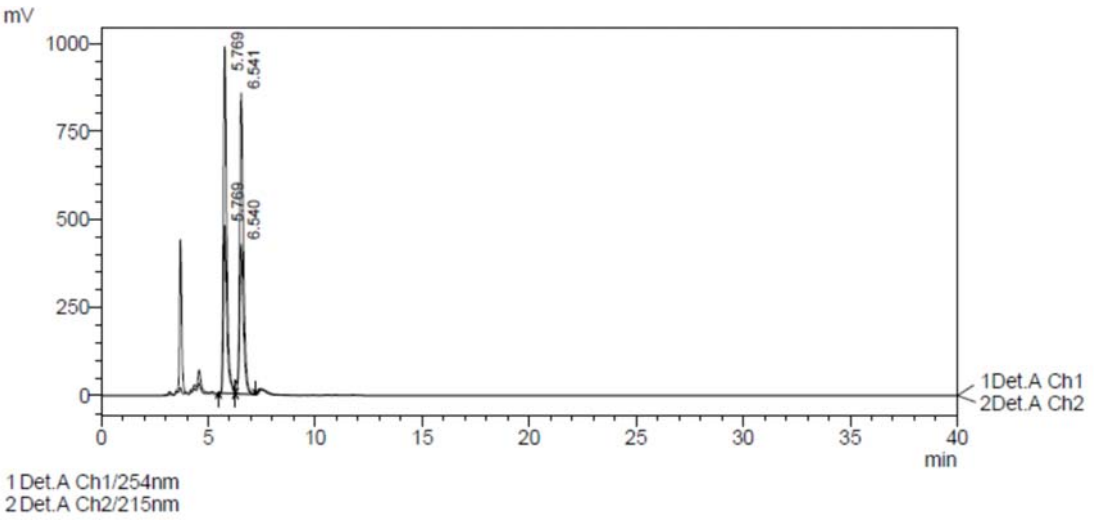
Spectral data are in accordance with literature values.[1]

HPLC traces

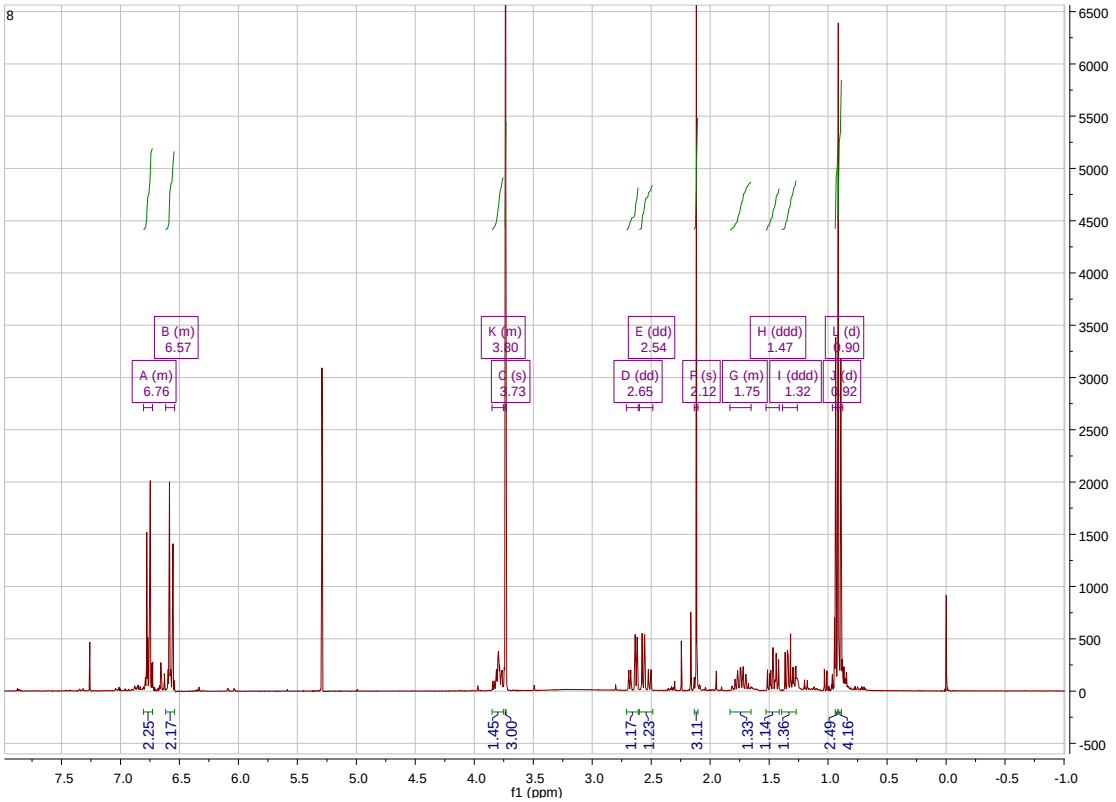
(*S*)-8



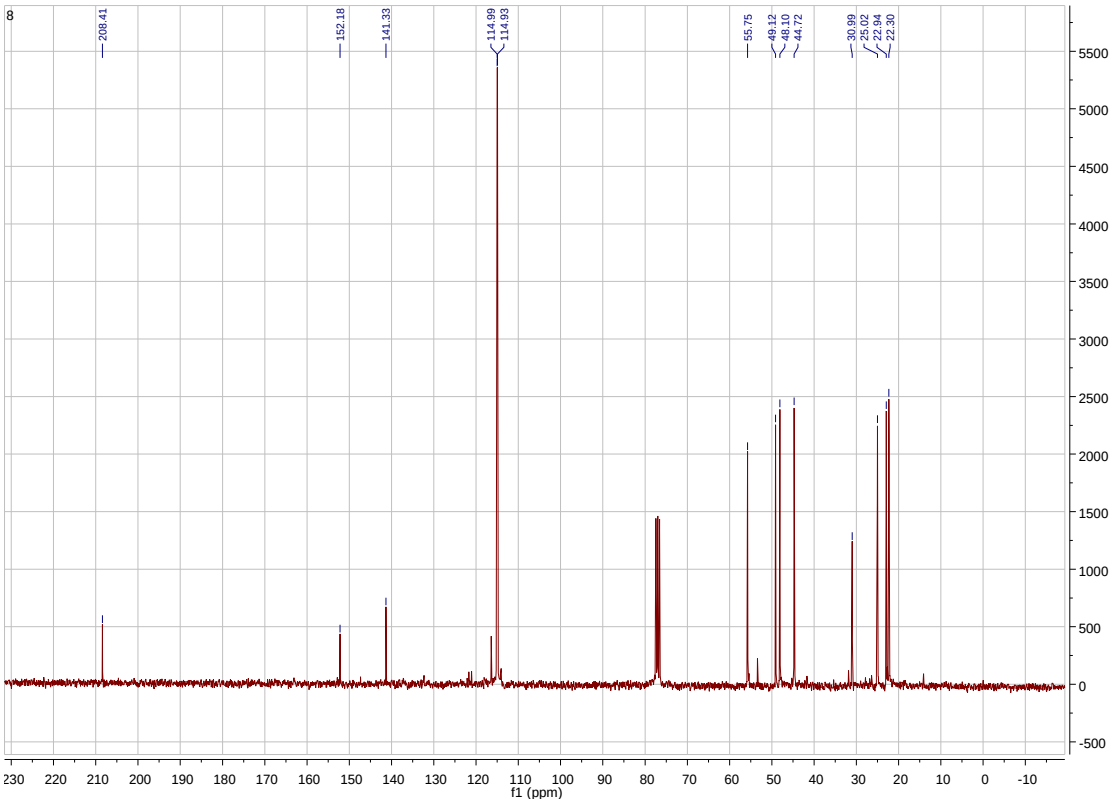
(*RS*)-8



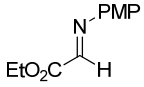
^{1}H NMR **8**



^{13}C NMR **8**



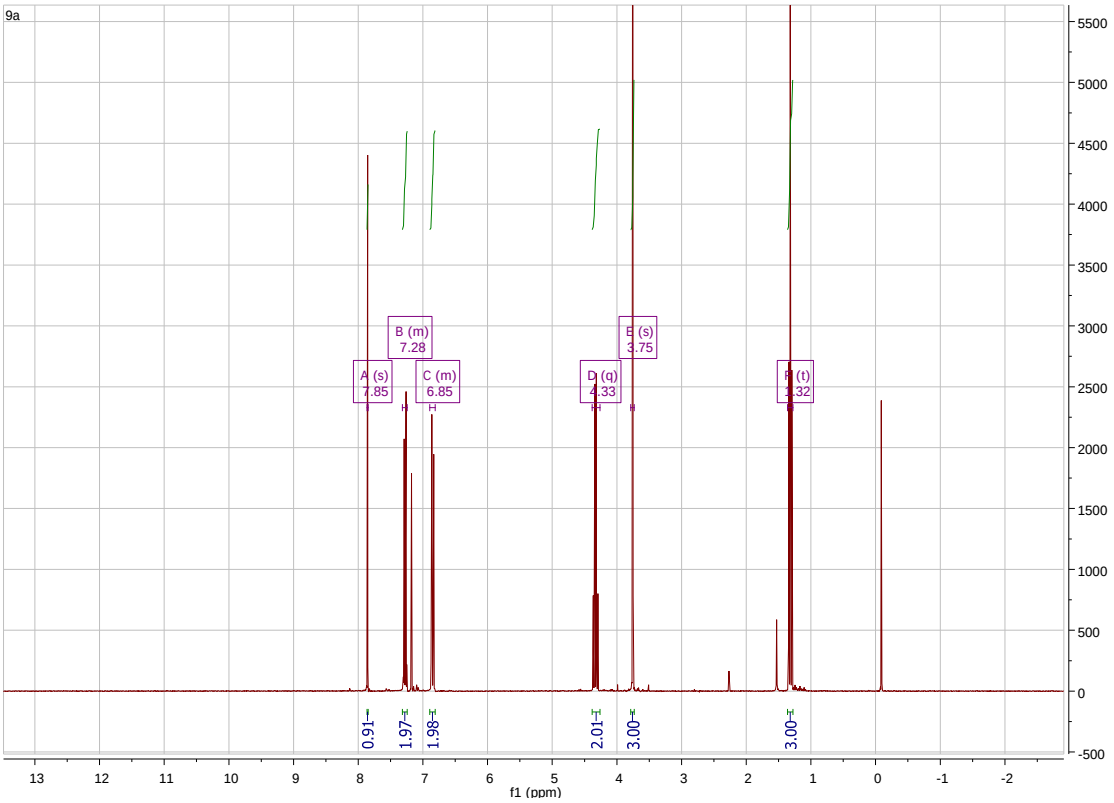
(*E*)-Ethyl 2-((4-methoxyphenyl)imino)acetate (9a)



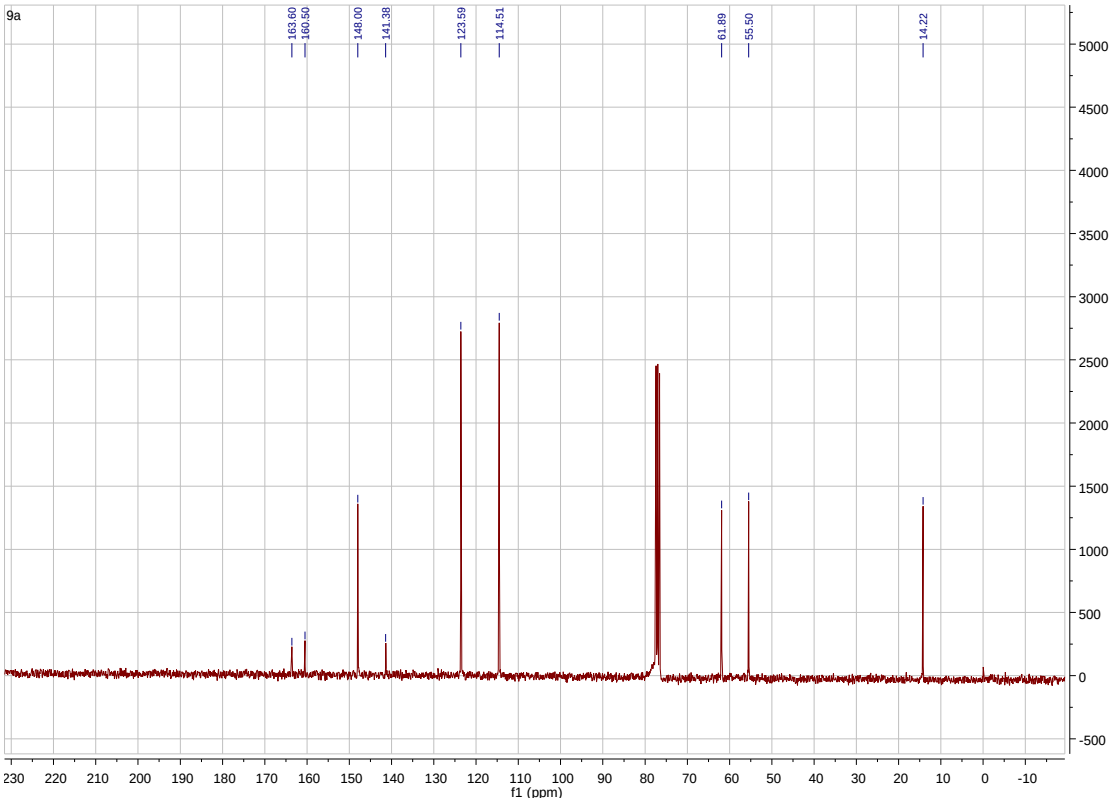
Under an atmosphere of argon, ethyl glyoxylate (10 mL, ~50% in toluene) was dissolved in anhydrous toluene (250 mL). Molsieves (4Å, 50 g) and *p*-anisidine (5.54 g, 45 mmol) were added. The mixture was stirred for 22 h and filtered over celite. The filtrate was concentrated. The product was obtained as a dark yellow oil (9.28 g, 44.8 mmol, quant.) ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.94 (s, 1H), 7.40–7.33 (m, 2H), 6.98–6.89 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 163.6, 160.5, 148.0, 141.4, 123.6, 114.5, 61.9, 55.5, 14.2.

Spectral data are in accordance with literature values.[2]

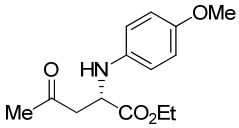
^{1}H NMR **9a**



^{13}C NMR **9a**



(*S*)-Ethyl 2-((4-methoxyphenyl)amino)-4-oxopentanoate (9)

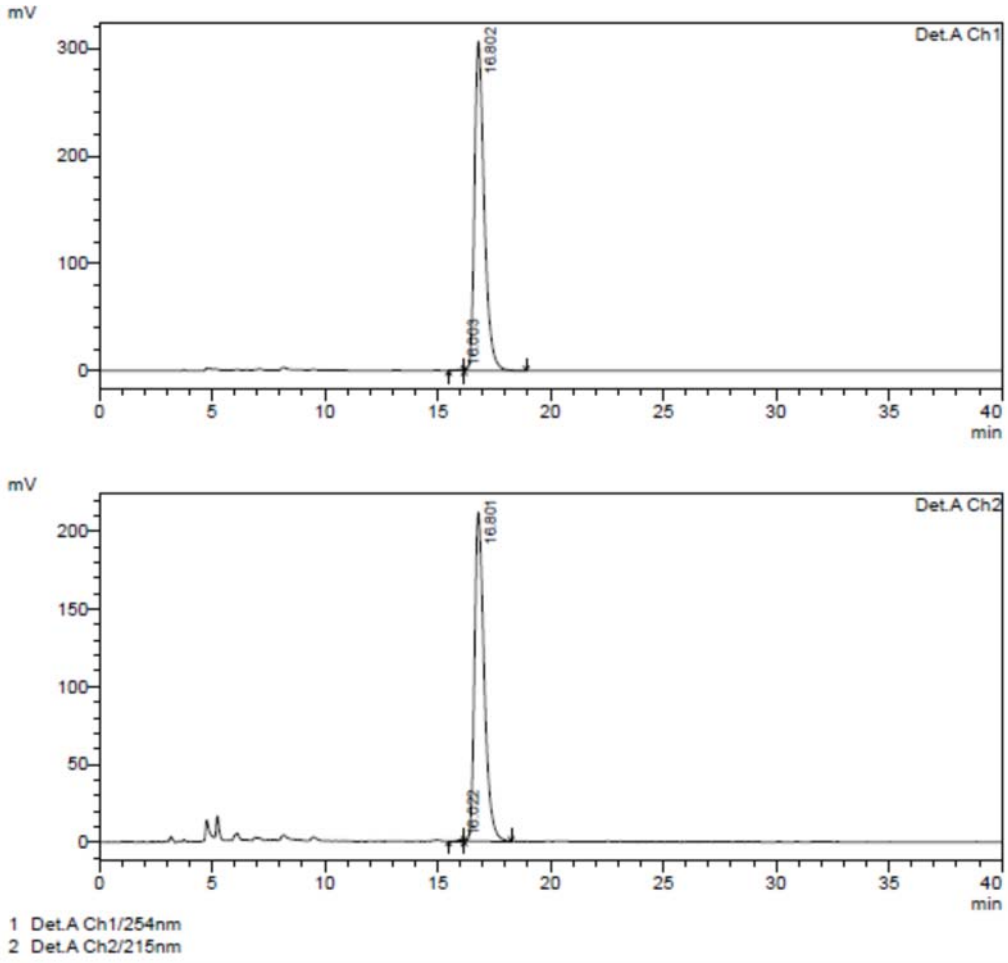


(*E*)-Ethyl 2-((4-methoxyphenyl)imino)acetate (**9a**) (3.36 g, 16.2 mmol) was dissolved in DMSO (20 mL) and acetone (80 mL) and L-proline were added. The resulting mixture was stirred for 18 h and quenched with aqueous $NaHCO_3$. The resulting mixture was extracted with a mixture of EtOAc and heptane (1:1, 2 × 200 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was taken up in diisopropyl ether (20 mL) and washed with water (2 × 50 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4) and concentrated. The product could be obtained as an orange oil in pure form without further purification (3.16 g, 11.9 mmol, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.83–6.71 (m, 2H), 6.70–6.57 (m, 2H), 4.33 (t, *J* = 5.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 2.96 (d, *J* = 5.6 Hz, 2H), 2.18 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 205.8, 173.0, 153.1, 140.5, 115.8, 114.8, 61.4, 55.7, 54.3, 45.8, 30.4, 14.1; HPLC: ee: >99%, Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol/ethanol 80/10/10, retention time: major enantiomer 16.8 min; minor enantiomer: 16.0 min.

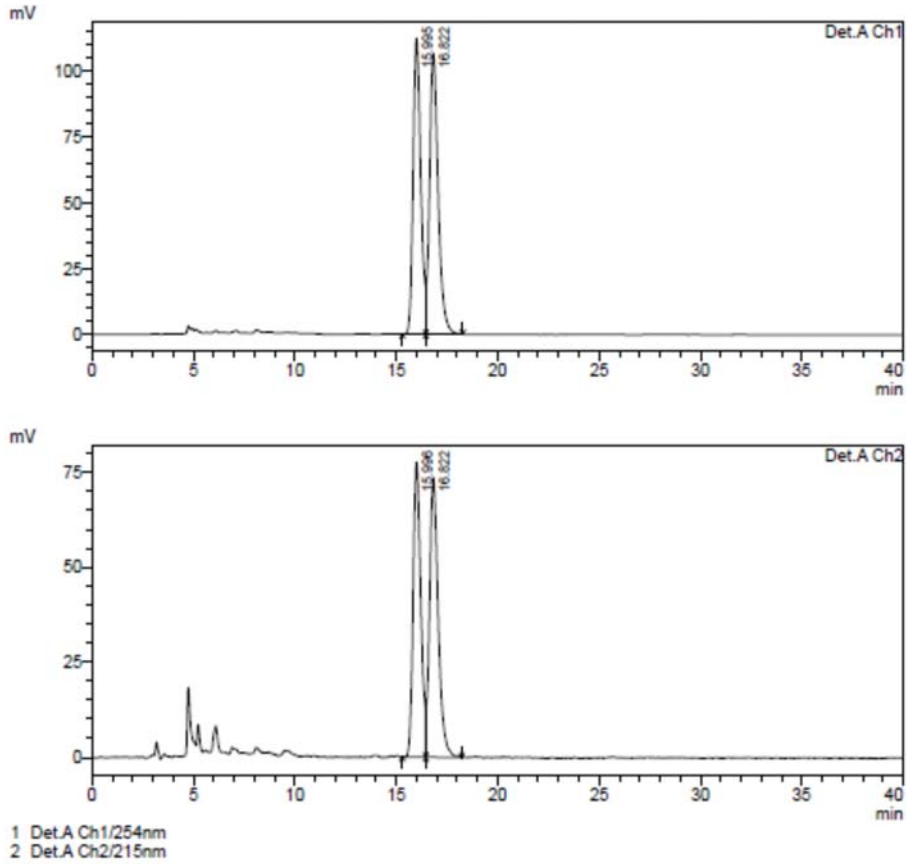
Spectral data are in accordance with literature values.[3]

HPLC traces

(*S*)-9



(*RS*)-9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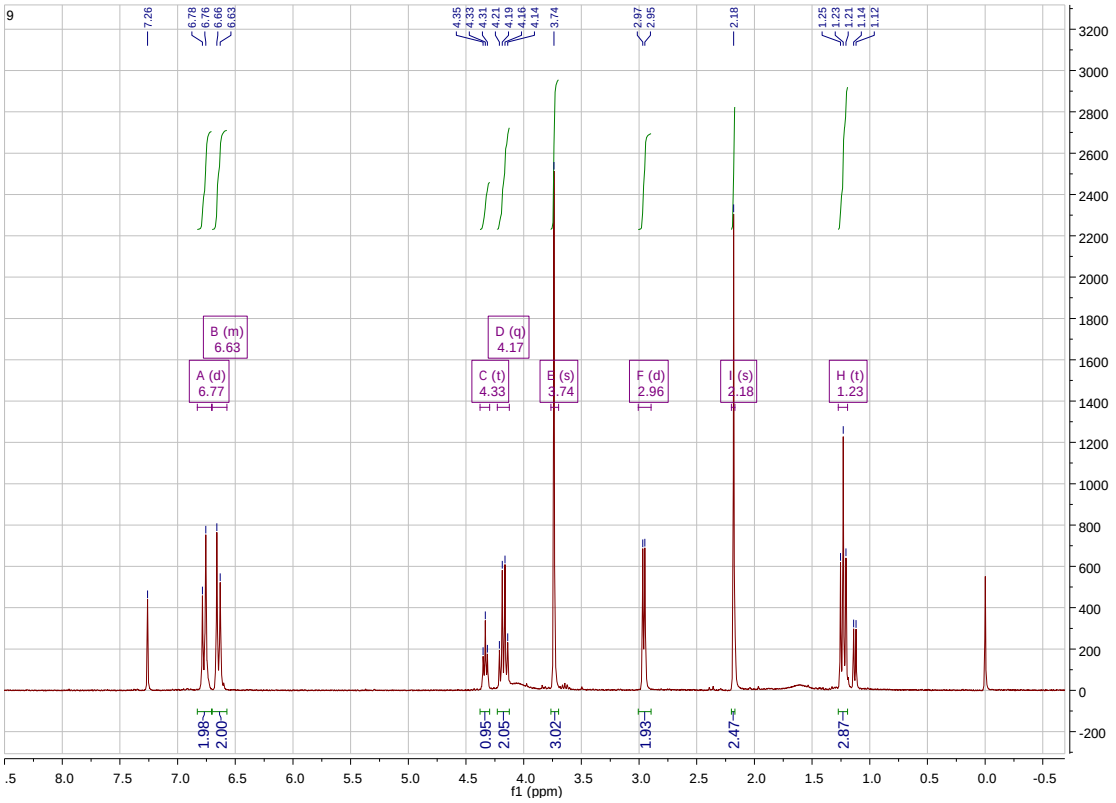
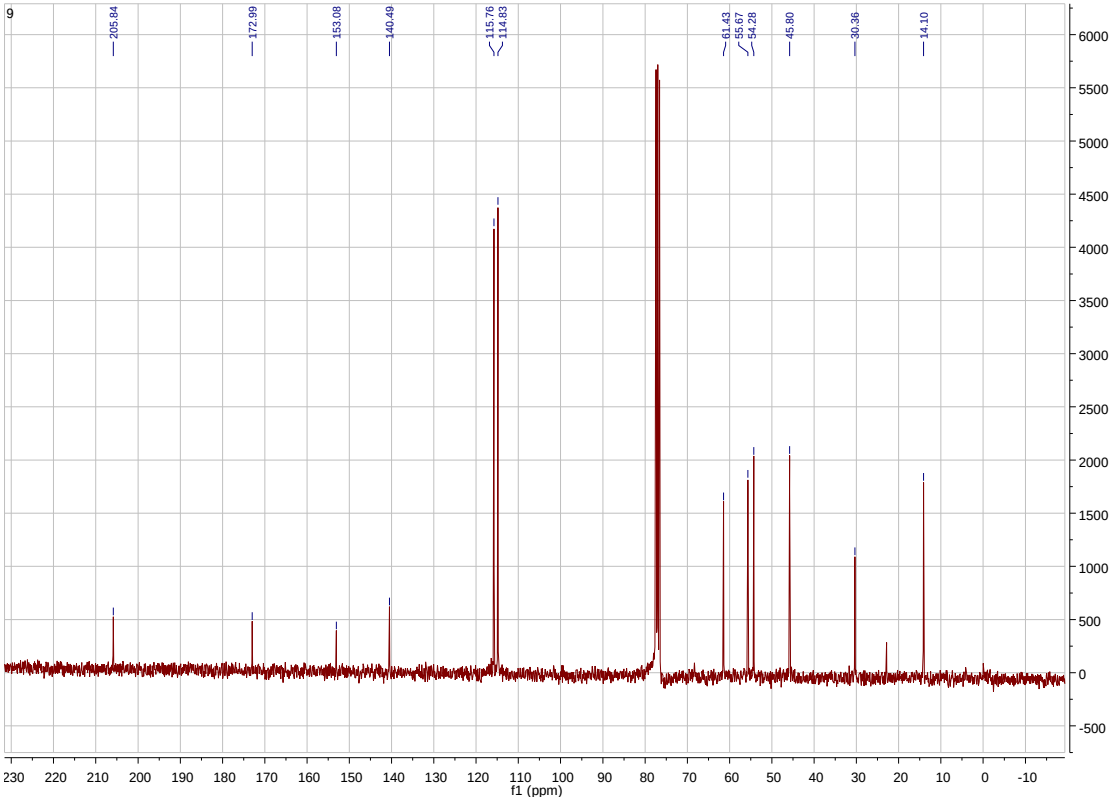
16.822
100
75
50
25
0
0
5
10
15
20
25
30
35
40
min
mV
Det.A Ch2
15.996
16.822
75
50
25
0
0
5
10
15
20
25
30
35
40
min
1 Det.A Ch1/254nm
2 Det.A Ch2/215nm

^{1}H NMR **9**

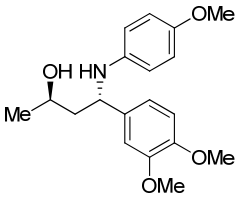

9
7.26
6.78
6.76
6.66
6.63
4.35
4.33
4.31
4.21
4.19
4.16
4.14
3.74
2.97
2.95
2.18
1.25
1.23
1.21
1.14
1.12
B (m)
6.63
A (d)
6.77
D (q)
4.17
C (t)
4.33
E (s)
3.74
F (d)
2.96
I (s)
2.18
H (t)
1.23
1.98
2.00
0.95
2.05
3.02
1.93
2.47
2.87
f1 (ppm)

^{13}C NMR **9**


9
205.84
172.99
153.08
140.49
115.76
114.83
61.43
55.67
54.28
45.80
30.36
14.10
f1 (ppm)

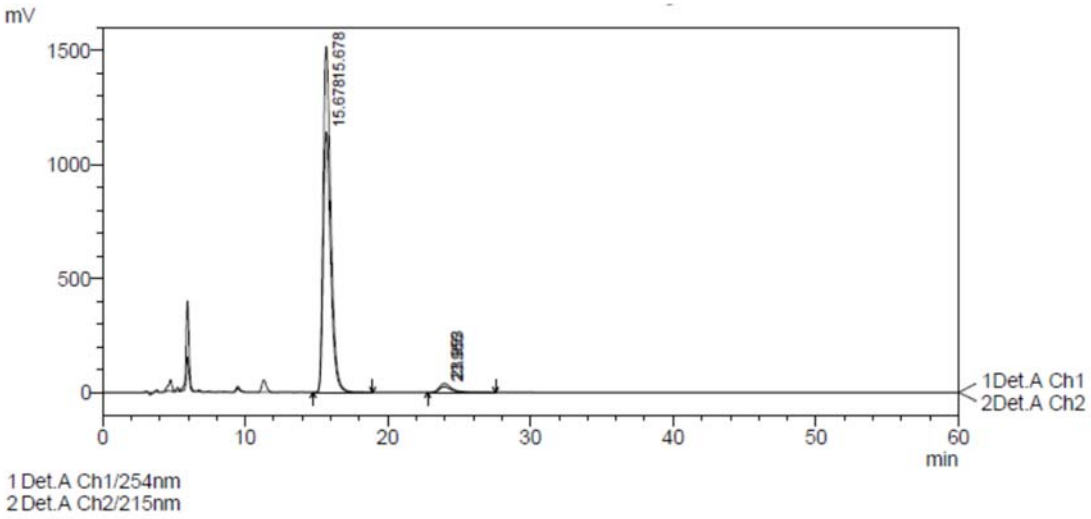
Synthesis of products **2** and **10**–**13** via Ir-based transfer hydrogenation (Table 2)

(2*R*,4*S*)-4-(3,4-Dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-ol (2) (Table 2, entry 1)

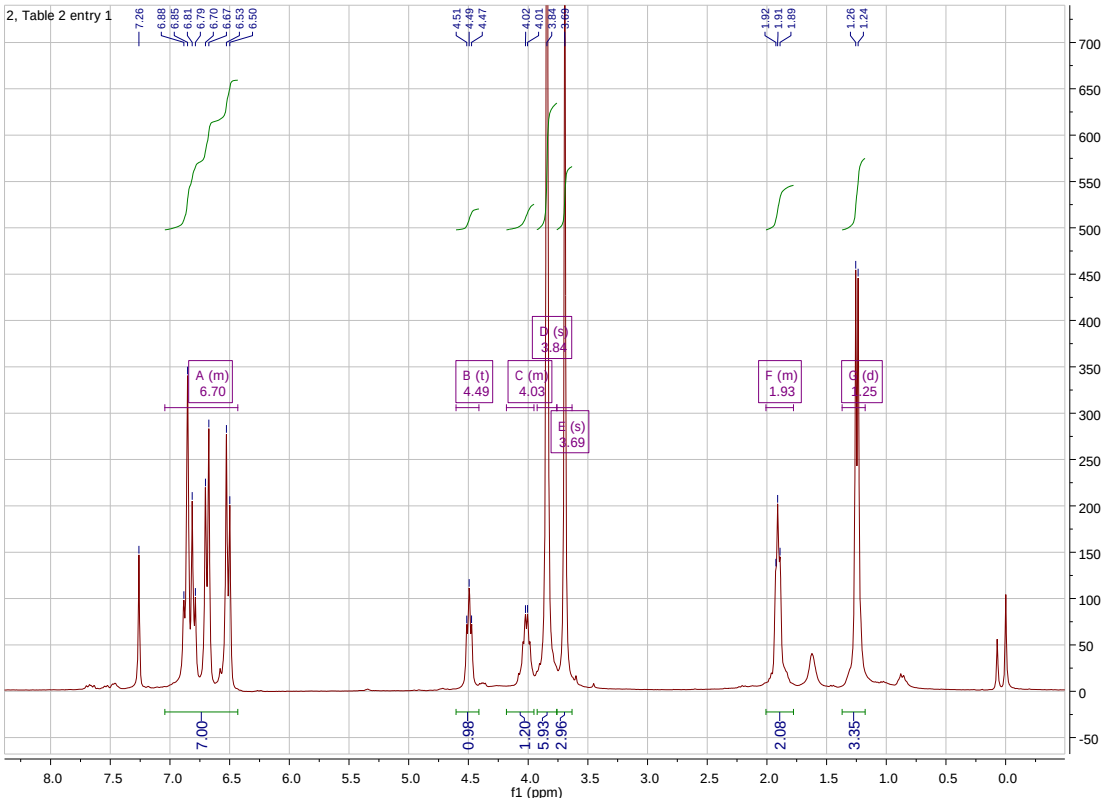


D-α-Methylphenylglycinamide (4.12 mg, 0.025 mmol), K_2CO_3 (50 mg, 0.361 mmol) and $[IrCp^*Cl_2]_2$ (2 mg, 2.51 µmol) were taken up in MeCN (dry, 5 mL). The mixture was stirred for 30 min at 70 °C and cooled to 0 °C. The solution was filtered and concentrated. (*S*)-4-(3,4-Dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-one ((*S*)-**1**) (41 mg, 0.125 mmol) was added to the catalyst together with dry 2-propanol (10 mL). The resulting reaction mixture was stirred for 20 h under argon, poured out in a mixture of saturated aqueous $NaHCO_3$ (20 mL) and DCM (20 mL). The aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (EtOAc in heptane, 1/9 → 3/7). The product was obtained as an off-white sticky oil (quant. yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.04–6.43 (m, 7H), 4.49 (t, *J* = 6.1 Hz, 1H), 4.18–3.95 (m, 1H), 3.84 (s, 6H), 3.69 (s, 3H), 2.01–1.78 (m, 2H), 1.25 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 152.1, 149.1, 147.8, 141.4, 136.5, 118.1, 115.1, 114.7, 111.2, 109.4, 65.3, 56.2, 55.8 (2C), 55.7, 46.7, 23.7. IR (cm^{-1}) 3383, 2933, 2832, 1511, 1234; HRMS [ESI$^+$ (m/z)]: calcd for $C_{19}H_{25}NO_4$ (M+H$^+$) 332.18618, found 332.18626; HPLC: d.r.: 96.4 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, heptane/2-propanol 80/20, retention time: major diastereomer 15.7 min, minor diastereomer: 24.0 min. R_f 0.17 (EtOAc/heptane 1:1).

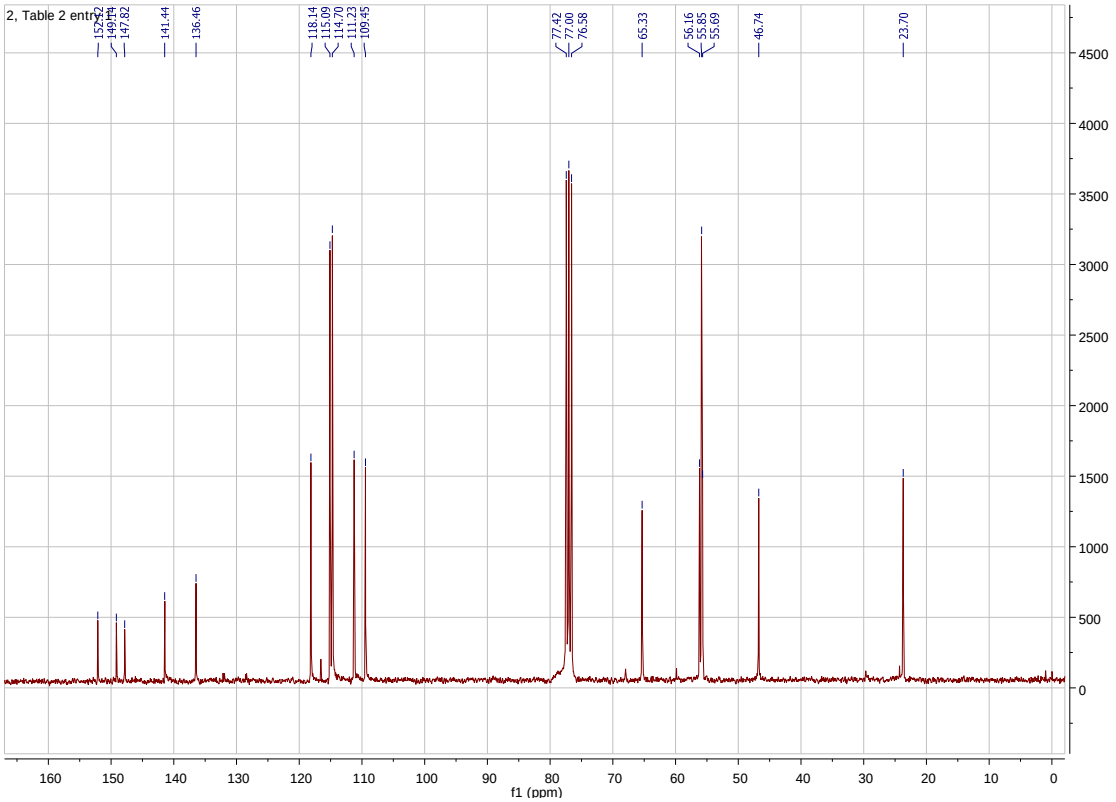
HPLC trace



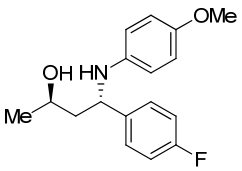
^{1}H NMR **2,** Table 2 entry 1



^{13}C NMR **2**, Table 2 entry 1

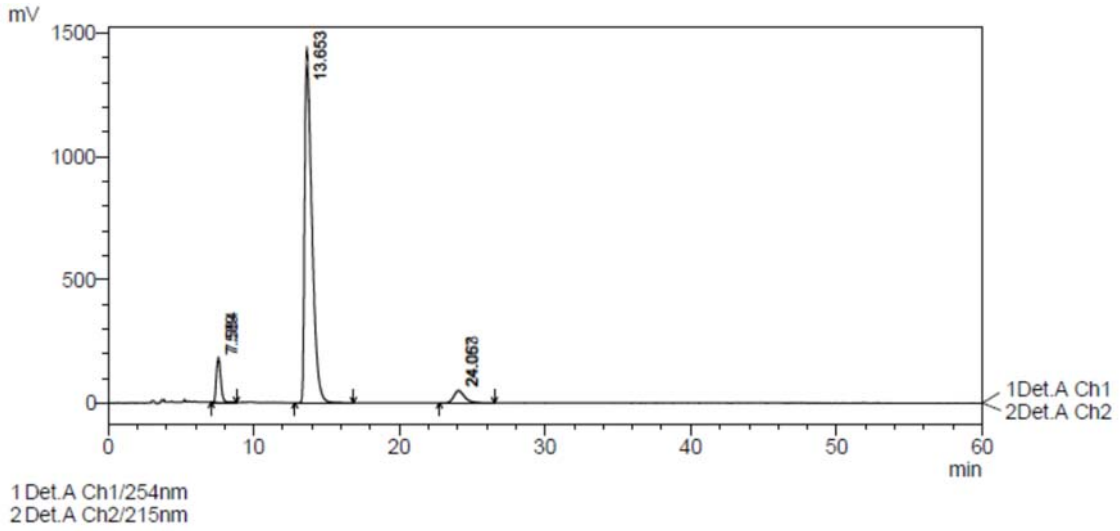


(2*R*,4*S*)-4-(4-Fluorophenyl)-4-((4-methoxyphenyl)amino)butan-2-ol (10)

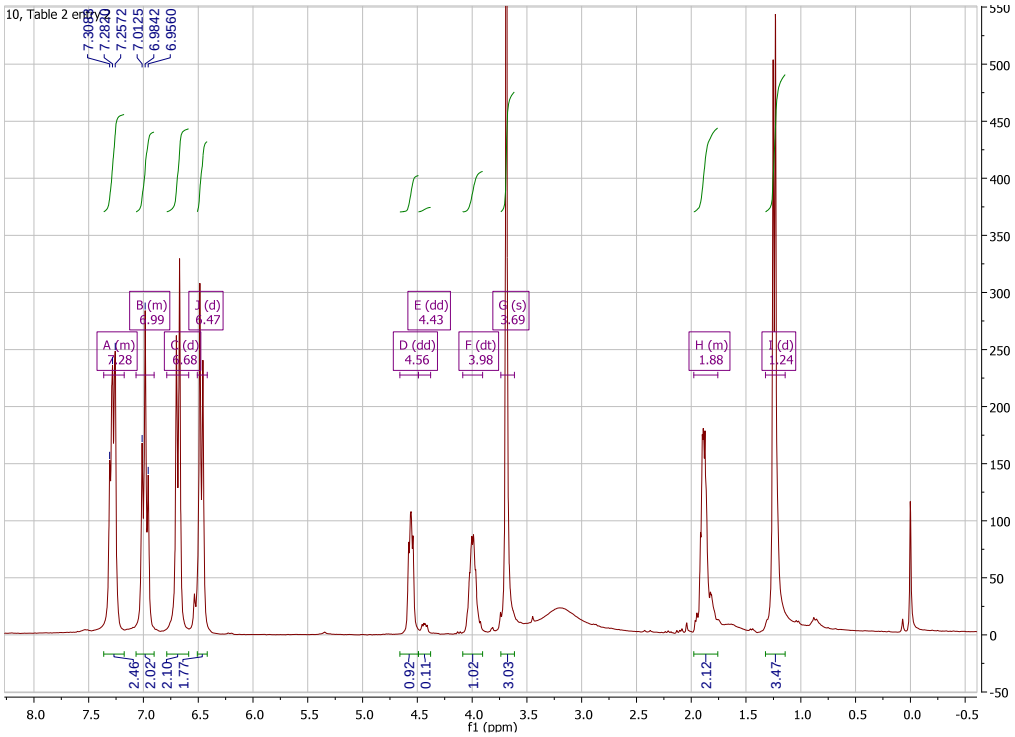


D-α-Methylphenylglycinamide (8.24 mg, 0.050 mmol), K_2CO_3 (100 mg, 0.723 mmol) and $[IrCp^*Cl_2]_2$ (4 mg, 5.02 µmol) were taken up in MeCN (dry, 5 mL). The mixture was stirred for 30 min at 70 °C and cooled to 0 °C. The solution was filtered and concentrated. The residue was taken up in 4 mL dry 2-propanol. (*S*)-4-(4-Fluorophenyl)-4-((4-methoxyphenyl)amino)butan-2-one (**6**) (36 mg, 0.125 mmol) was dissolved in dry 2-propanol (8 mL), followed by addition of 2 mL of the catalyst mixture. The resulting reaction mixture was stirred under argon for 2 h and poured out in a mixture of a half-saturated aqueous $NaHCO_3$ (20 mL) and DCM (20 mL). The aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (EtOAc/*n*-heptane, 1/9 → 3/7). The product was obtained as an off-white solid (32 mg, 0.111 mmol, 88%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.36–7.18 (m, 2H), 7.09–6.89 (m, 2H), 6.68 (d, *J* = 8.6 Hz, 2H), 6.47 (d, *J* = 8.7 Hz, 2H), 4.56 (dd, *J* = 6.9, 5.1 Hz, 0.9H), 4.43 (dd, *J* = 8.8, 5.0 Hz, 0.1H), 4.10–3.90 (dt, *J* = 19.0, 9.5 Hz, 1H), 3.69 (s, 3H), 1.98–1.76 (m, 2H), 1.24 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 161.69 (d, *J* = 244.5 Hz), 152.11 (s), 141.16 (s), 139.51 (s), 127.71 (d, *J* = 7.9 Hz), 115.41 (d, *J* = 21.3 Hz), 114.91 (s), 114.76 (s), 65.24 (s), 55.70 (s), 55.58 (s), 46.74 (s), 23.81 (s); IR (cm^{-1}) 3381, 2969, 1510, 1235; HRMS [ESI$^+$ (m/z)]: calcd for $C_{17}H_{21}FNO_2$ ($M+H^+$) 290.15563, found 290.15600 HPLC d.r. 95:5 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol 80/20, retention time: major diastereomer 13.7 min, minor diastereomer: 24.1 min. R_f 0.17 (EtOAc/heptane 1/2).

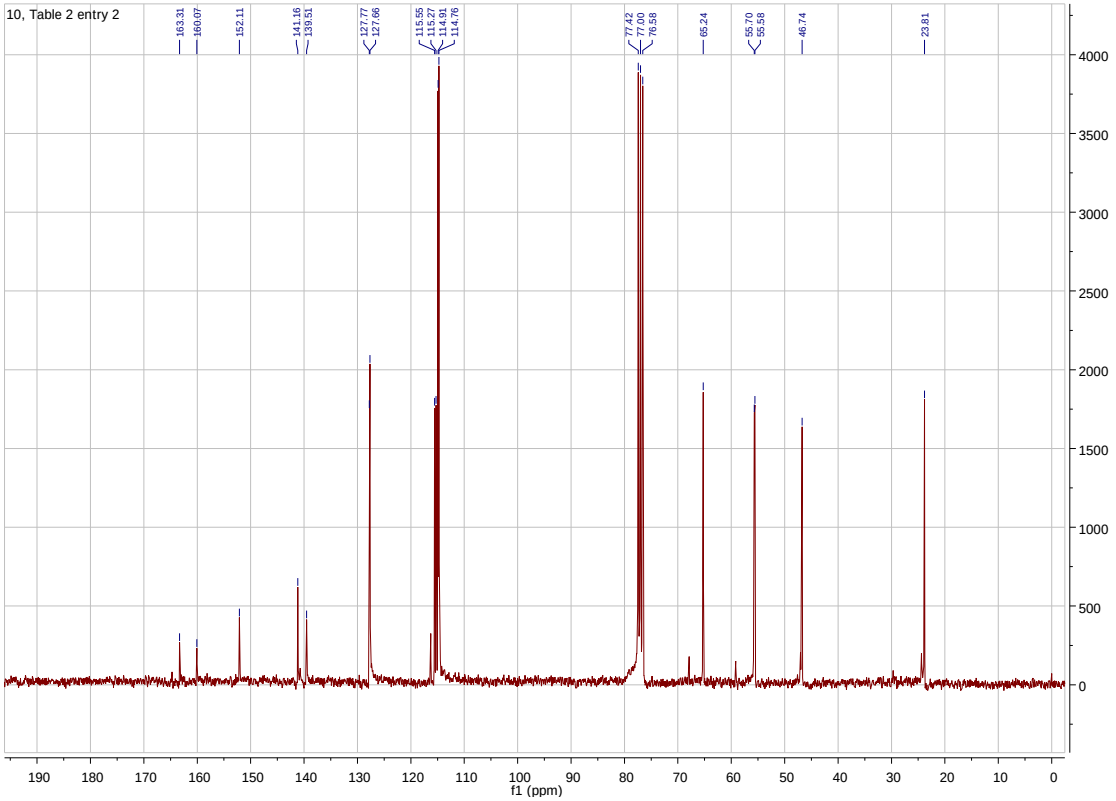
HPLC trace



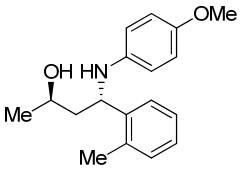
^{1}H NMR **10,** Table 2 entry 2



^{13}C NMR **10,** Table 2 entry 2

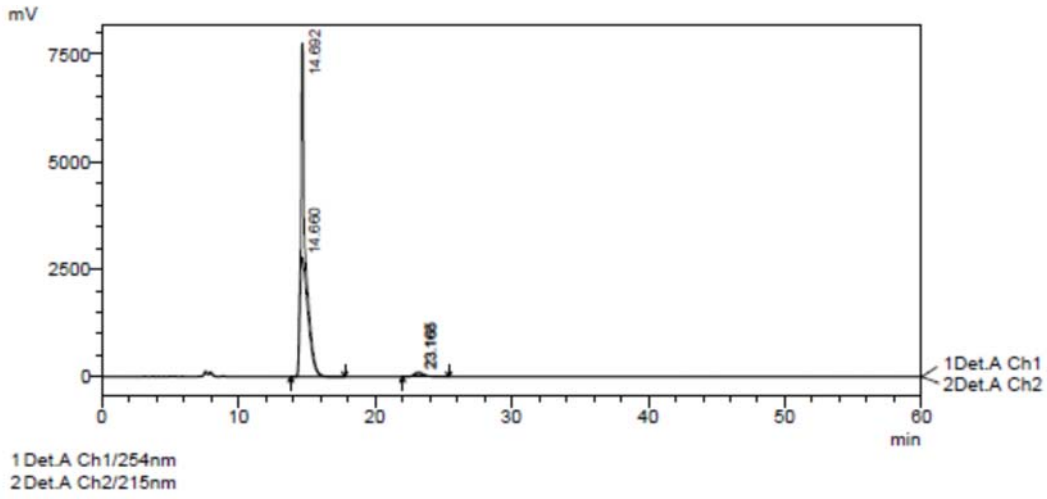


(2*R*,4*S*)-4-((4-Methoxyphenyl)amino)-4-(o-tolyl)butan-2-ol (11)

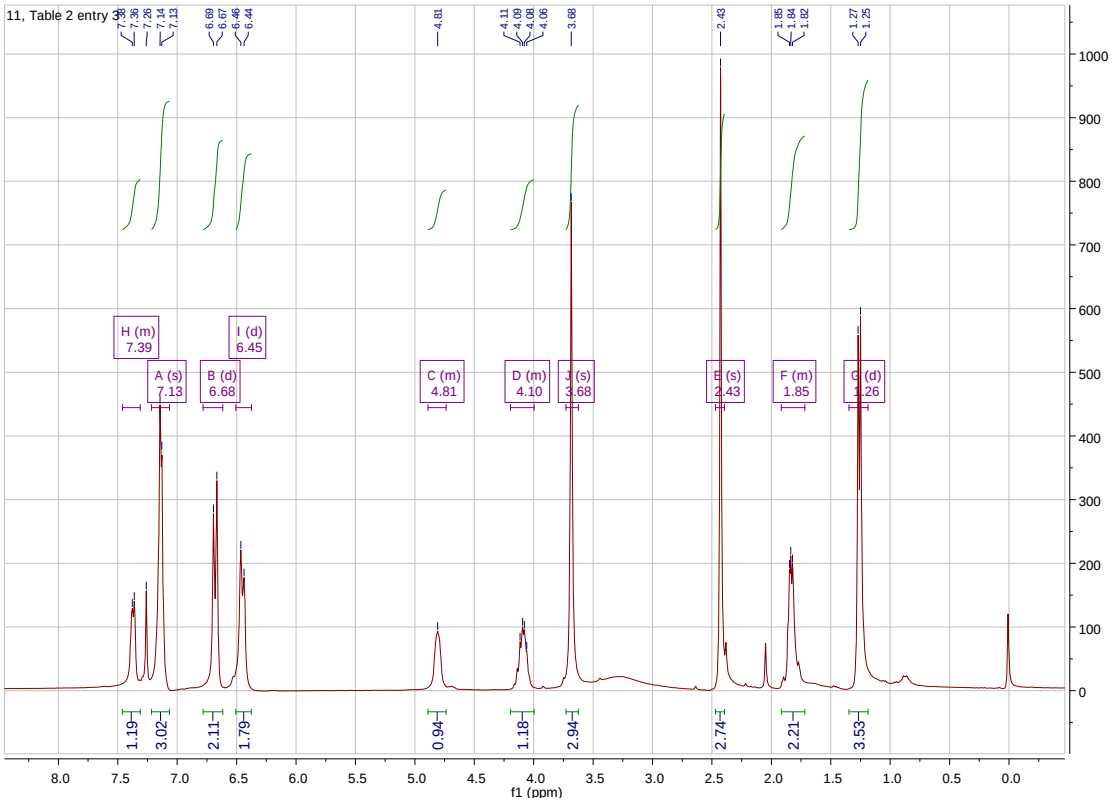


D-α-Methylphenylglycinamide (8.24 mg, 0.050 mmol), K_2CO_3 (100 mg, 0.723 mmol) and $[IrCp^*Cl_2]_2$ (4 mg, 5.02 µmol) were taken up in MeCN (dry, 5 mL). The mixture was stirred for 30 min at 70 °C and cooled to 0 °C. The solution was filtered and concentrated. The residue was taken up in 4 mL dry 2-propanol. (*S*)-4-((4-Methoxyphenyl)amino)-4-(*o*-tolyl)butan-2-one (**7**) (35 mg, 0.125 mmol) was dissolved in dry 2-propanol (8 mL), followed by addition of 2 mL of the catalyst mixture. The resulting reaction mixture was stirred for 1.5 h under argon and quenched with half-saturated aqueous $NaHCO_3$ (30 mL) and DCM (30 mL). After separation, the aqueous layer was extracted with DCM (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (EtOAc/heptane, 1/9 → 3/7) The product was obtained as a yellow oil (27 mg, 0.095 mmol, 76%).^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.50–7.33 (m, 1H), 7.22–7.06 (m, 3H), 6.68 (d, *J* = 8.6 Hz, 2H), 6.45 (d, *J* = 8.0 Hz, 2H), 4.94–4.72 (m, 1H), 4.20–4.00 (m, 1H), 3.68 (s, 3H), 2.43 (s, 3H), 1.92–1.72 (m, 2H), 1.26 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 152.1, 141.5, 141.3, 134.5, 130.7, 126.6, 126.4, 125.2, 114.8, 65.5, 55.7, 52.3, 45.0, 23.8, 19.1; IR (cm^{-1}) 3391, 2966, 1511, 1235, 1040, 819; HRMS [ESI$^+$ (m/z)]: calcd for $C_{18}H_{24}NO_2$ (M+H$^+$) 286.18070, found 286.18151; HPLC d.r. 97:3 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, heptane/2-propanol 80/20, retention time: major diastereomer 14.7 min; minor diastereomer: 23.2 min; R_f 0.17 (EtOAc/heptane 1:1).

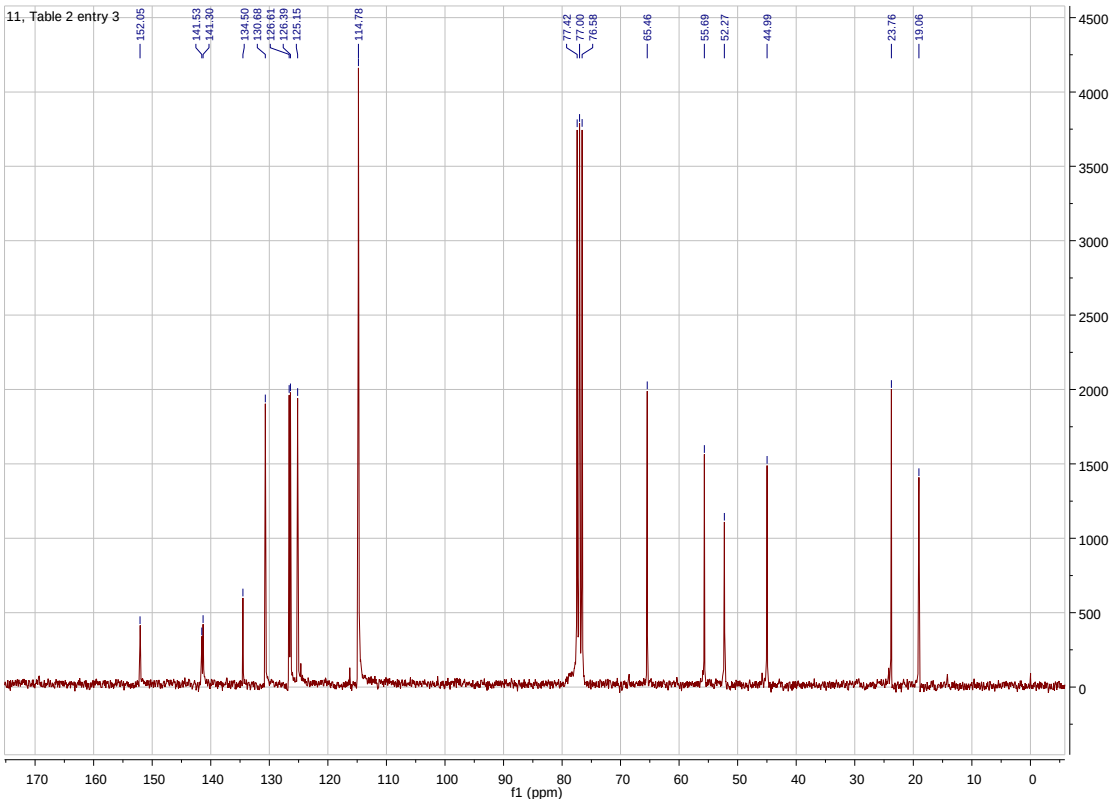
HPLC trace



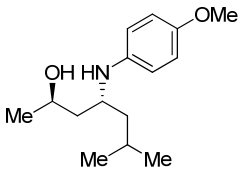
^{1}H NMR **11,** Table 2 entry 3



^{13}C NMR **11,** Table 2 entry 3

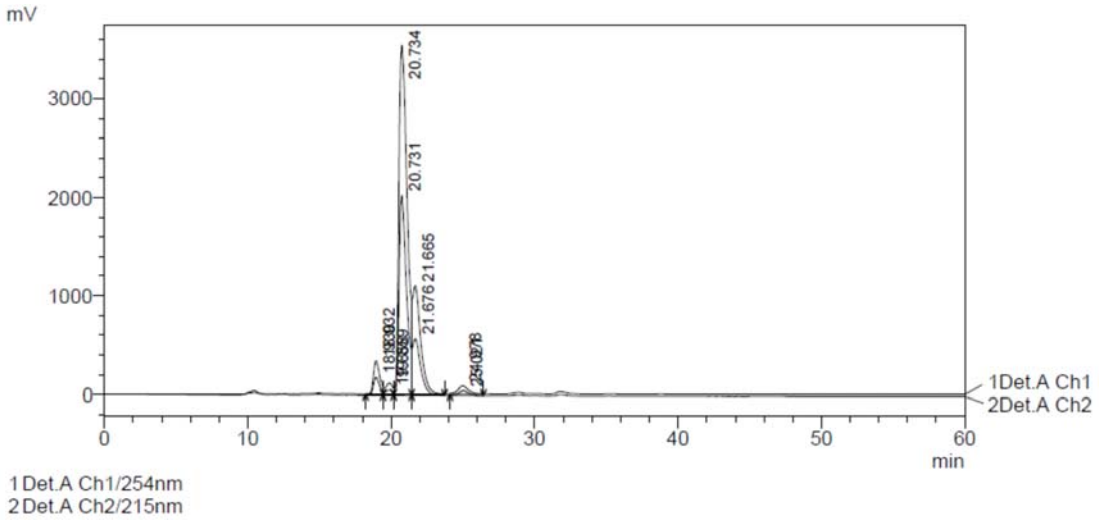


(2*R*,4*R*)-4-((4-Methoxyphenyl)amino)-6-methylheptan-2-ol (12)

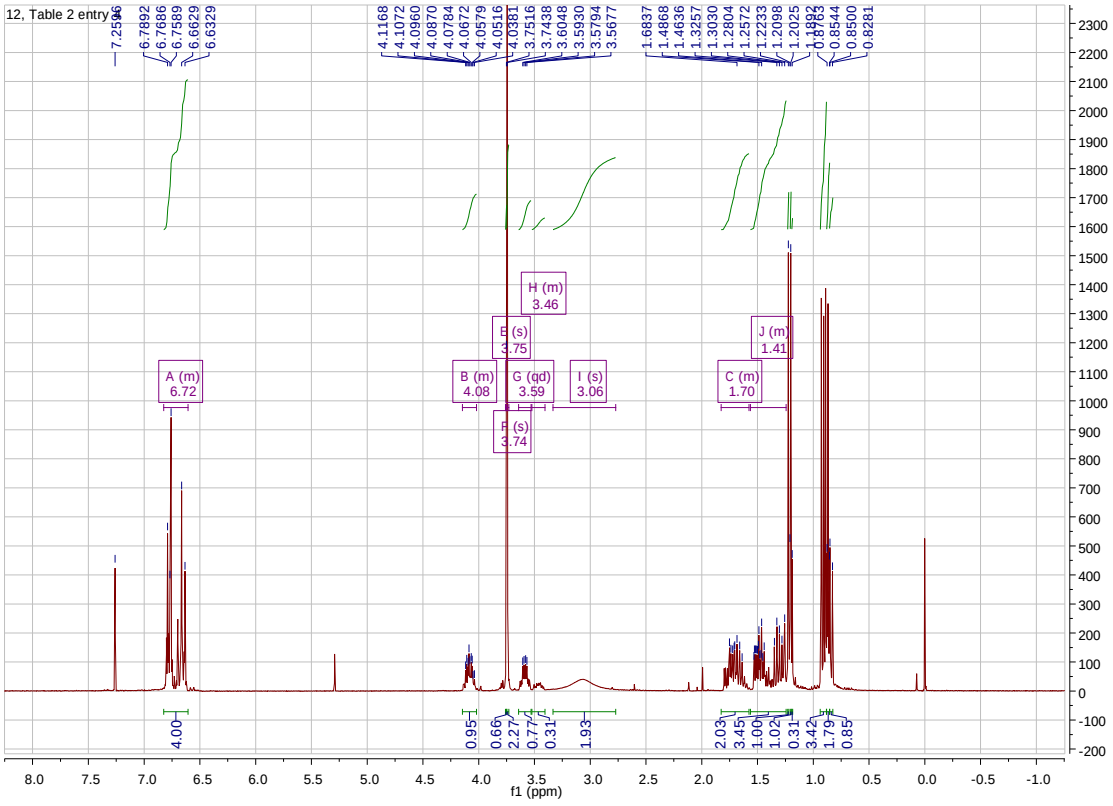


Under an atmosphere of argon, D-α-methylphenylglycinamide (8.24 mg, 0.050 mmol), K_2CO_3 (100 mg, 0.723 mmol) and $[IrCp^*Cl_2]_2$ (4 mg, 5.02 μmol) were taken up in MeCN (dry, 5 mL). The mixture was stirred for 30 min at 70°C and cooled to 0°C. The solution was filtered and concentrated. The residue was taken up in 4 mL dry 2-propanol. (*R*)-4-((4-Methoxyphenyl)amino)-6-methylheptan-2-one (**8**) (33 mg, 0.125 mmol) was placed under argon and dissolved in dry 2-propanol (8 mL). 2 mL of the catalyst solution was added and the mixture was stirred for 18 h. The reaction mixture was poured out in a mixture of a an aqueous half-saturated solution of $NaHCO_3$ (20 mL) and DCM (20 mL). After separation, the aqueous phase was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (EtOAc/heptane 1/9 → 1/4). The product was obtained as a yellow oil (31 mg, 0.123 mmol, 99%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.82–6.61 (m, 4H, both diastereomers), 4.14–4.02 (m, 1H, both diastereomers), 3.75 (s, 3/5H, minor diastereomer), 3.74 (s, 12/5H, major diastereomer), 3.59 (qd, *J* = 7.0, 3.5 Hz, 4/5H, major diastereomer), 3.52–3.41 (m, 1/5H, minor diastereomer), 3.40–2.75 (bs, 2H, both diastereomers), 1.83–1.58 (m, 2H, both diastereomers), 1.56–1.24 (m, 3H,both diastereomers), 1.21 (d, *J* = 6.3 Hz, 12/5H, major diastereomer), 1.20 (d, *J* = 6.2 Hz, 3/5H, minor diastereomer), 0.92 (d, *J* = 6.6 Hz, 12/5H), 0.88 (d, *J* = 6.5 Hz, 12/5H), 0.87 (d, *J* = 6.6 Hz, 3/5H), 0.84 (d, *J* = 6.6 Hz, 3/5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 153.3 (minor diastereomer), 152.5 (major diasteromer), 141.8 (major diastereomer), 140.7 (minor diastereomer), 117.1 (minor diastereomer), 115.5 (major diastereomer), 114.9 (major diastereomer), 114.8 (minor diastereomer), 68.6 (minor diastereomer), 65.3 (major diastereomer), 55.7 (major diastereomer), 55.6 (minor diastereomer), 54.9 (minor diastereomer), 50.4 (major diastereomer), 45.6 (minor diastereomer), 44.9 (major diastereomer), 43.2 (minor diastereomer), 42.9 (major diastereomer), 25.0 (major diastereomer), 24.9 (minor diastereomer), 24.0 (both diastereomers), 23.3 (minor diastereomer), 23.0 (major diastereomer), 22.5 (major diastereomer), 22.0 (minor diastereomer). IR (cm^{-1}, film from DCM) 3367, 2955, 1510, 1236; HRMS [ESI$^+$ (m/z)]: calcd for $C_{12}H_{26}N_1O_2$ ($M+H^+$) 252.19635, found 252.19628; HPLC: d.r. 76:24 (Chiralpak AD-H (250 × 4.6 mm), flow 0.3 mL/min, *n*-heptane/2-propanol/ethanol 80/15/5, retention time: major diastereomer 20.7 min; minor diastereomer 21.7 min; R_f 0.29 (EtOAc/heptane 1/2).

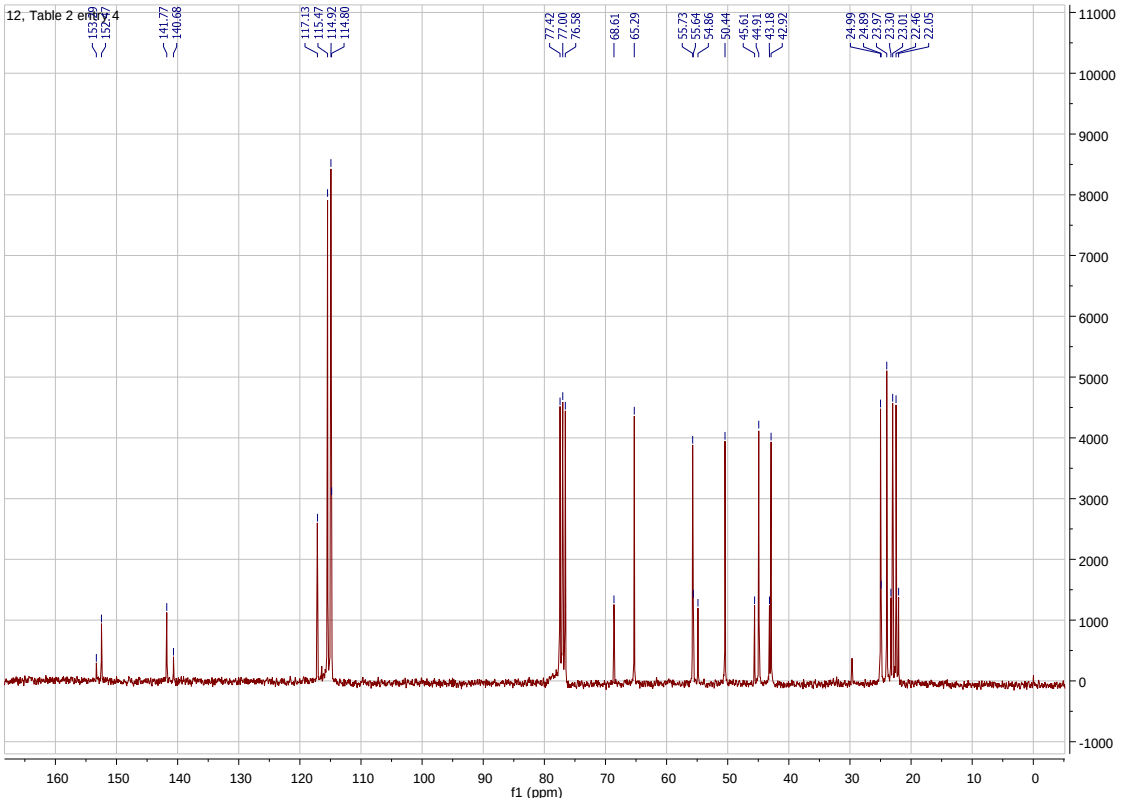
HPLC trace



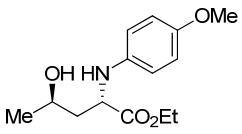
^{1}H NMR **12,** Table 2 entry 4



^{13}C NMR **12,** Table 2 entry 4



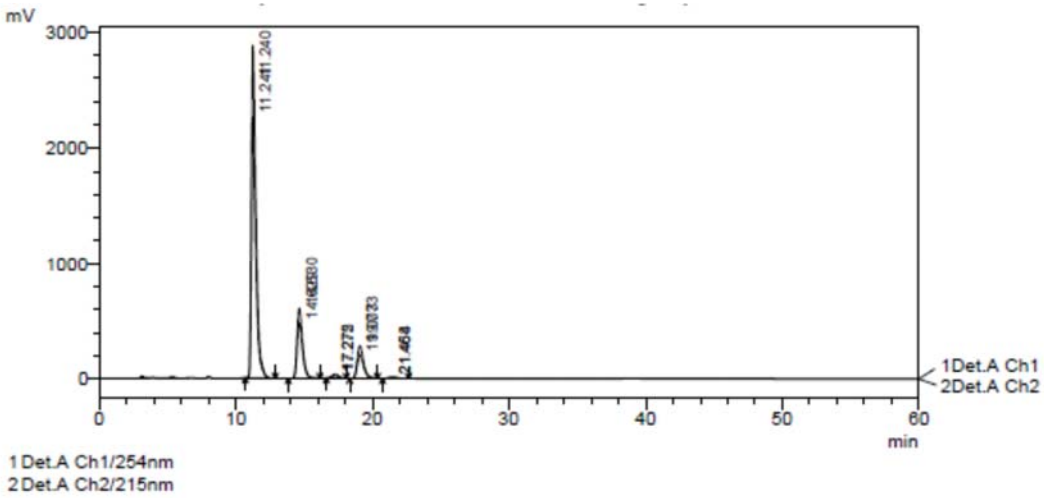
(2*S*,4*R*)-Ethyl 4-hydroxy-2-((4-methoxyphenyl)amino)pentanoate (13)



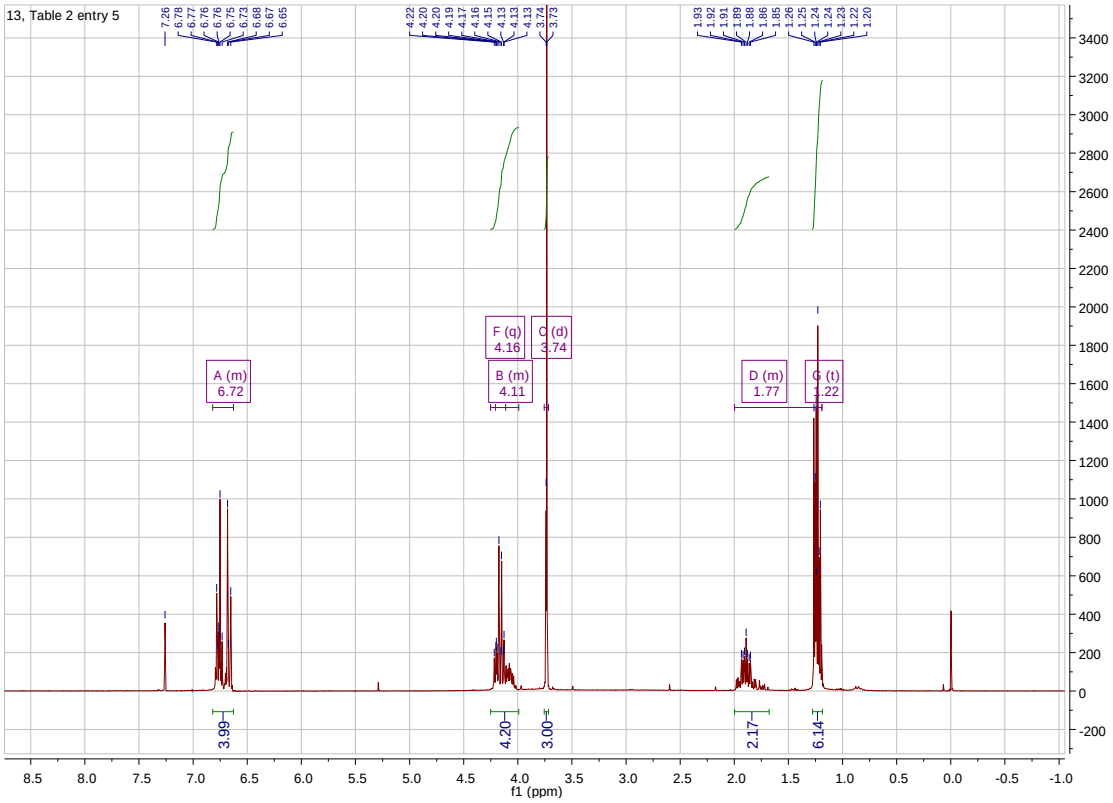
Under an atmosphere of argon, D-α-methylphenylglycinamide (8.24 mg, 0.050 mmol), K_2CO_3 (100 mg, 0.723 mmol) and $[IrCp^*Cl_2]_2$ (4 mg, 5.02 μmol) were taken up in MeCN (dry, 5 mL). The mixture was stirred for 30 min at 70°C and cooled to 0°C. The solution was filtered and concentrated. The residue was taken up in 4 mL dry 2-propanol. (*R*)-4-((4-Methoxyphenyl)amino)-6-methylheptan-2-one (**9**) (33 mg, 0.12 mmol) was placed under argon and dissolved in dry 2-propanol (8 mL). 2 mL of the catalyst solution was added and the mixture was stirred for 18 h. The reaction mixture was poured out in a mixture of a an aqueous half-saturated solution of $NaHCO_3$ (20 mL) and DCM (20 mL). After separation, the aqueous phase was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (EtOAc/heptane 1/9 → 1/4 → 1/2). The product was obtained as a yellow oil (33 mg, 0.12 mmol, 100%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.82–6.63 (m, 4H, both diastereomers), 4.25–3.99 (m, 2H), 4.16 (q, *J* = 7.0 Hz, 2H, both diastereomers, 3.74 (s, 0.18 × 3H, minor diastereomer), 3.73 (s, 0.82 × 3H, major diastereomer), 2.00–1.68 (m, 2H, both diastereomers), 1.25 (d, *J* = 6.3 Hz, 3H, both diastereomers), 1.23 (t, *J* = 7.1 Hz, 0.82 × 3H, major diastereomer), 1.22 (t, *J* = 7.1 Hz, 0.18 × 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 174.4 (major diastereomer), 173.7 (minor diastereomer), 154.0 (minor diastereomer), 153.2 (major diastereomer), 140.9 (major diastereomer), 140.2 (minor diastereomer), 117.4 (minor diastereomer), 115.9 (major diastereomer), 114.8 (major diastereomer), 114.8 (minor diastereomer) , 67.6 (minor diastereomer), 65.2 (major diastereomer), 61.2 (minor diastereomer), 61.2

(major diastereomer), 59.2 (minor diastereomer), 56.2 (major diastereomer), 55.6 (major diastereomer), 55.6 (minor diastereomer), 41.2 (both diastereomers), 23.8 (major diastereomer), 23.6 (minor diastereomer), 14.2 (both diastereomers); IR (cm^{-1}) 3368, 2968, 1728, 1513, 1238; HRMS [ESI^+ (m/z)]: calcd for $C_{14}H_{22}N_1O_4$ ($M+H^+$) 268.15488, found 268.15511 HPLC: d.r. 79:21 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, heptane/2-propanol/ethanol 80/10/10, retention time: major diastereomer 11.2 min; minor diastereomer: 14.6 min; R_f 0.12 (EtOAc/heptane 1/2).

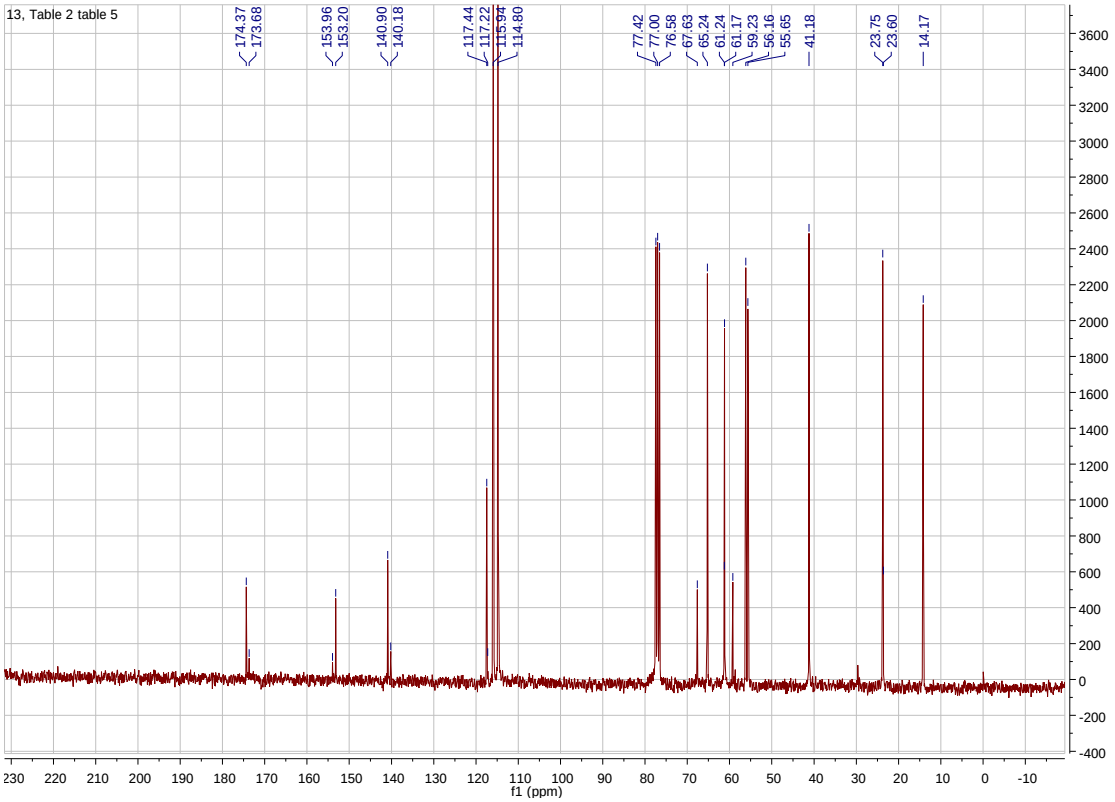
HPLC trace



^{1}H NMR **13,** Table 2 entry 5



^{13}C NMR **13,** Table 2 entry 5

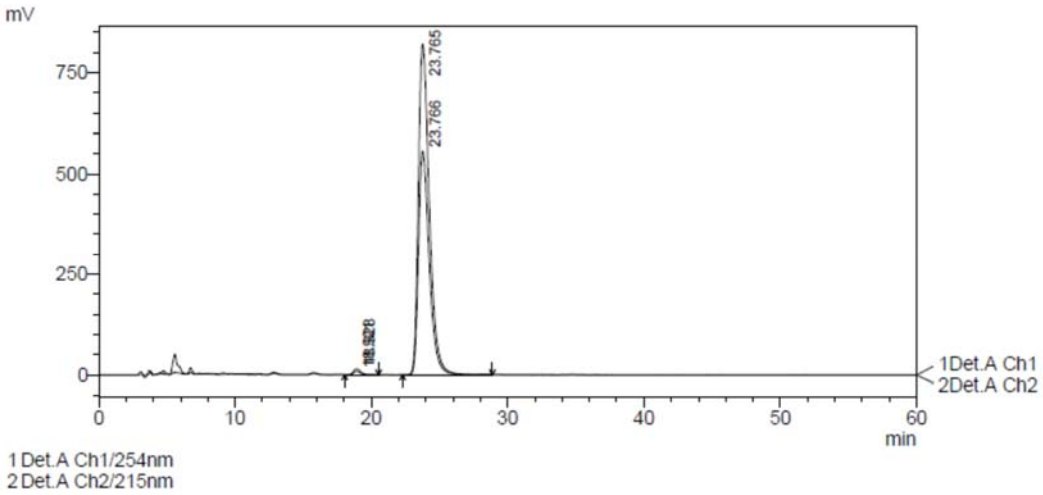


Synthesis of products **2** and **10**–**13** via Rh-based hydrogenation (Table 3)

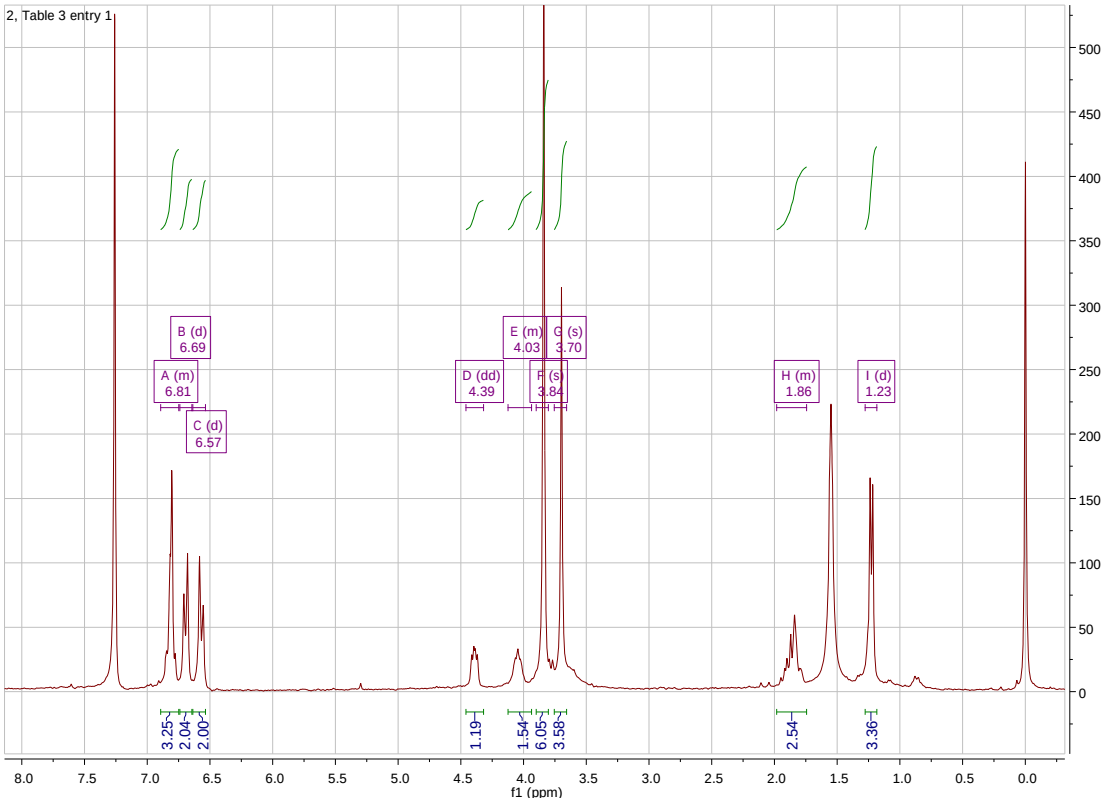
(2*S*,4*S*)-4-(3,4-Dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-ol (2)

$Rh(COD)_2BF_4$ (16.24 mg, 0.040 mmol) and (*R*)-BINAP (25 mg, 0.040) were taken up in 2 mL DCM and heated to 50°C for 30 min. The catalyst solution was added to a solution of (*S*)-4-(3,4-dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-one ((*S*)-**1**) (41 mg, 0.125 mmol) in DCM (10 mL) in an autoclave. Hydrogen pressure was applied (25 bar) and the mixture was heated to 50°C and stirred for 19 h. The mixture was diluted with DCM (20 mL) and aqueous $NaHCO_3$ (20 mL). After separation, the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (EtOAc/heptane 1/9 → 3/7).Yield: 32 mg (77%) of a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.89–6.75 (m, 3H), 6.69 (d, *J* = 8.6 Hz, 2H), 6.57 (d, *J* = 8.6 Hz, 2H), 4.39 (dd, *J* = 8.5, 5.1 Hz, 1H), 4.18–3.94 (m, 1H), 3.84 (s, 6H), 3.70 (s, 3H), 1.98–1.74 (m, 2H), 1.23 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 152.9, 149.2, 141.0, 136.5, 125.9, 118.1, 116.6, 114.6, 111.2, 109.3, 68.0, 59.9, 55.9 (2C), 55.7, 46.9, 24.3; IR (cm^{-1}) 3367, 2934, 2834, 1511, 1234, 1028; HRMS [ESI$^+$ (m/z)]: calcd for $C_{19}H_{25}NO_4Na$ (M+Na$^+$) 354.16813, found 354.16781; HPLC d.r. >99:1 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, heptane/2-propanol 80/20, retention time: major diastereomer 23.8 min; minor diastereomer: n/a. (see (*R,S*)-**2**) R_f 0.21 (EtOAc/heptane 1/1).

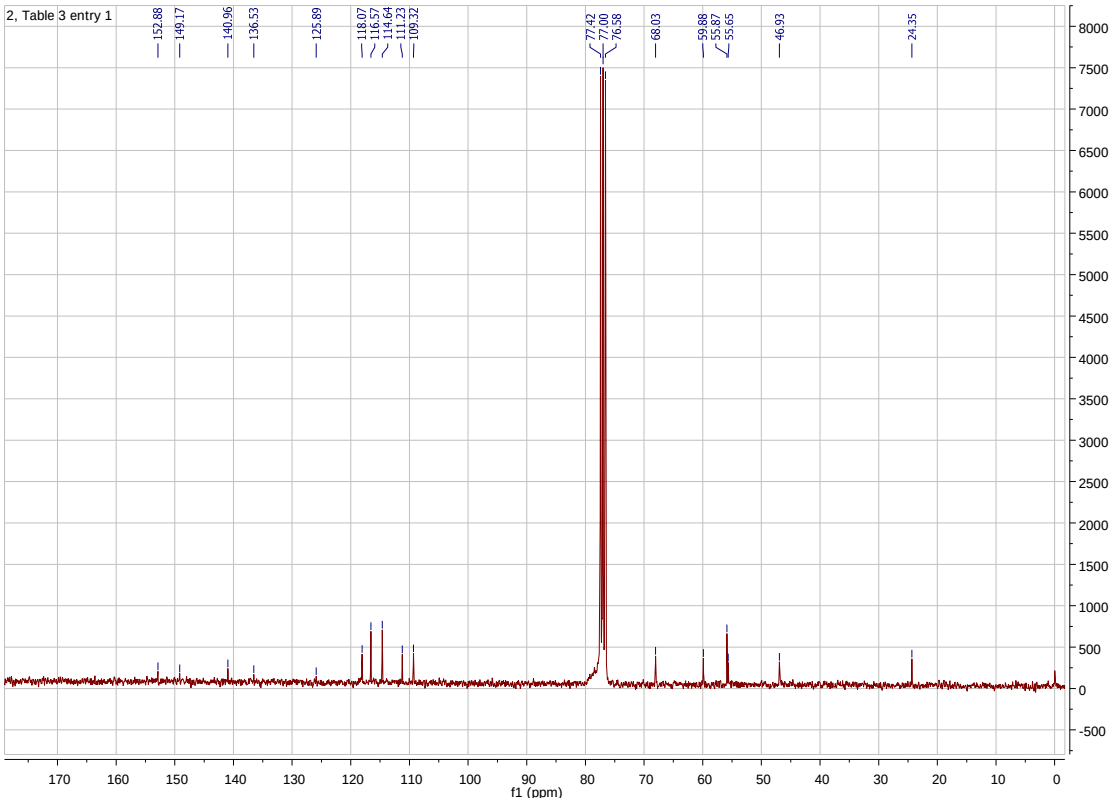
HPLC trace



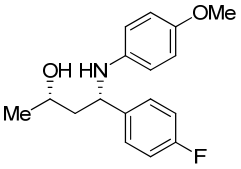
^{1}H NMR **2,** Table 3 entry 1



^{13}C NMR **2,** Table 3 entry 1

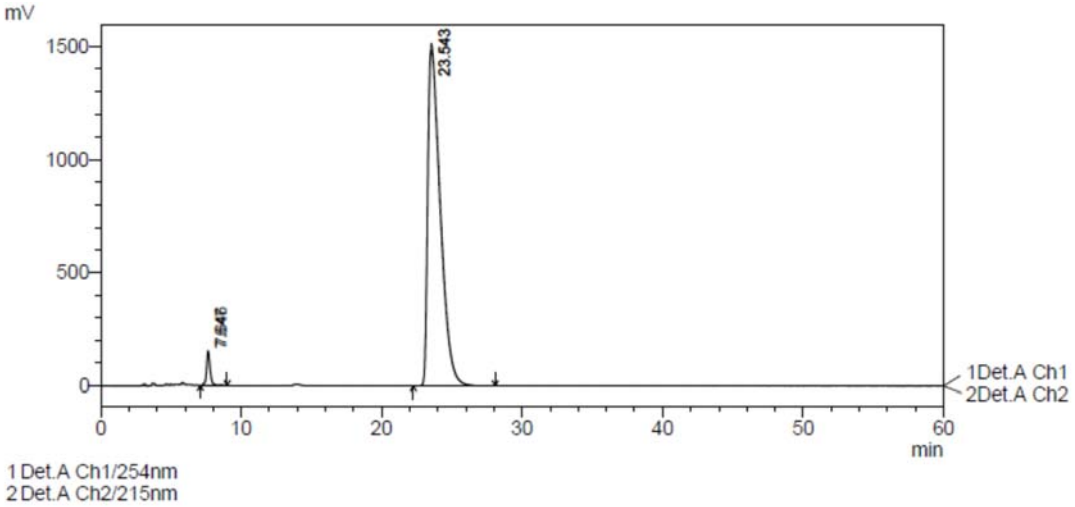


(2*S*,4*S*)-4-(4-Fluorophenyl)-4-((4-methoxyphenyl)amino)butan-2-ol (10)

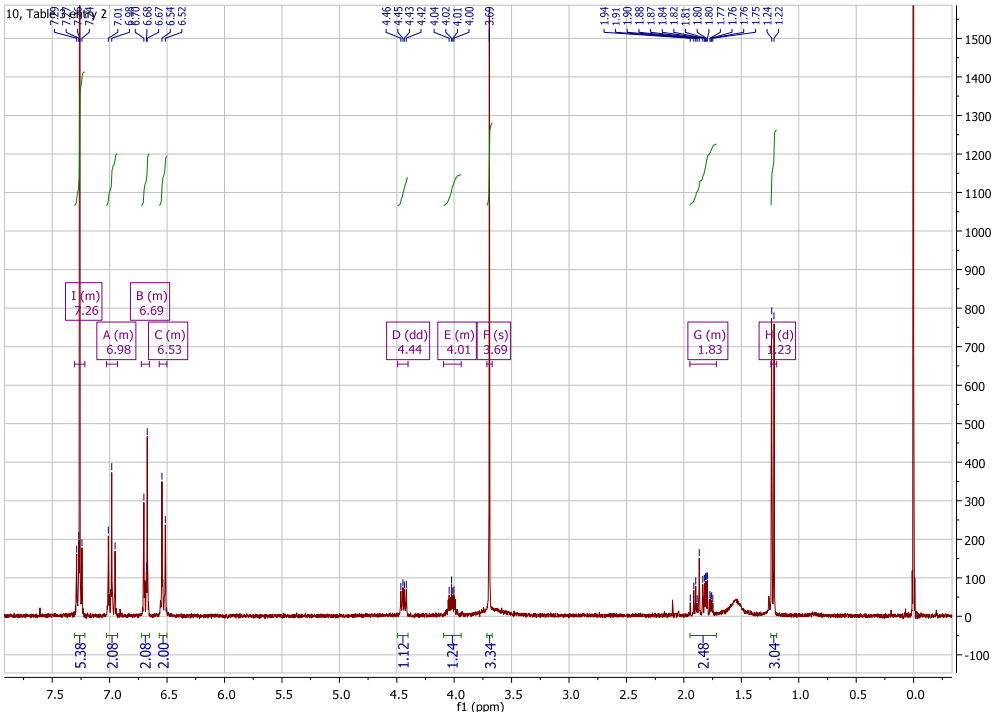


$Rh(COD)_2BF_4$ (15.2 mg, 0.037 mmol) and (*R*)-BINAP (23.35 mg, 0.037 mmol) were taken up in 2 mL DCM. 0.33 mL of the catalyst solution was added to a tube, containing (*S*)-4-(4-fluorophenyl)-4-((4-methoxyphenyl)amino)butan-2-one (**6**) (36 mg, 0.125 mmol) in DCM (5 mL). Hydrogen pressure was applied (25 bar) and the mixture was stirred at 300K for 44 h. The reaction mixture was concentrated and the crude product was purified by column chromatography (heptane → 22% EtOAc in heptane). Yield: 27 mg (76%) of an off-white solid). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.31–7.22 (m, 2H), 7.03–6.93 (m, 2H), 6.72–6.65 (m, 2H), 6.57–6.50 (m, 2H), 4.44 (dd, *J* = 9.0, 5.0 Hz, 1H), 4.09–3.94 (m, 1H), 3.69 (s, 3H), 1.95–1.72 (m, 2H), 1.23 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 161.84 (d, *J* = 245.5 Hz), 160.2, 153.0, 140.3, 139.3, 127.73 (d, *J* = 7.9 Hz), 116.6, 115.51 (d, *J* = 21.4 Hz), 114.7, 67.9, 59.4, 55.6, 46.9, 24.4 IR (cm^{-1}) 3366, 2966, 2931, 1510, 1234; HRMS [ESI$^+$ (m/z)]: calcd for $C_{17}H_{21}F_1N_1O_2$ ($M+H^+$) 299.15563, found 290.15677; HPLC: d.r. >99:1 (*syn/anti*) Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, heptane /2-propanol 80/20, retention time: major diastereomer 23.5 min; minor diastereomer: n/a. (see (*R*,*S*)-**10**); R_f 0.38 (EtOAc/heptane 1/1).

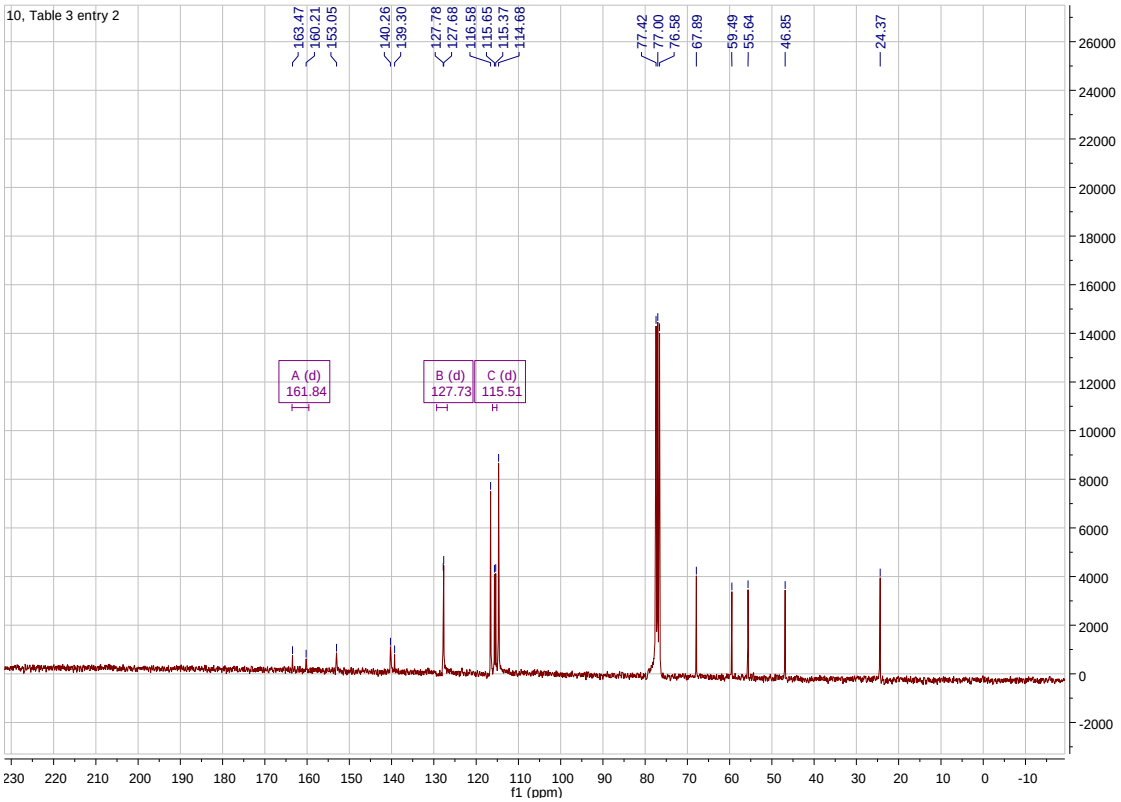
HPLC trace



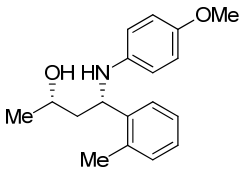
^{1}H NMR **10,** Table 3 entry 2



^{13}C NMR **10,** Table 3 entry 2

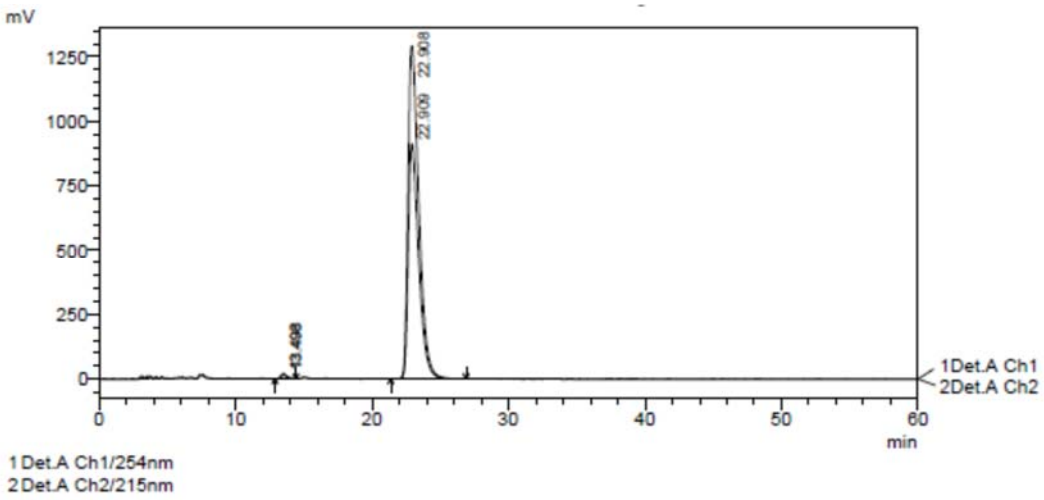


(2*S*,4*S*)-4-((4-Methoxyphenyl)amino)-4-(*o*-tolyl)butan-2-ol (11)

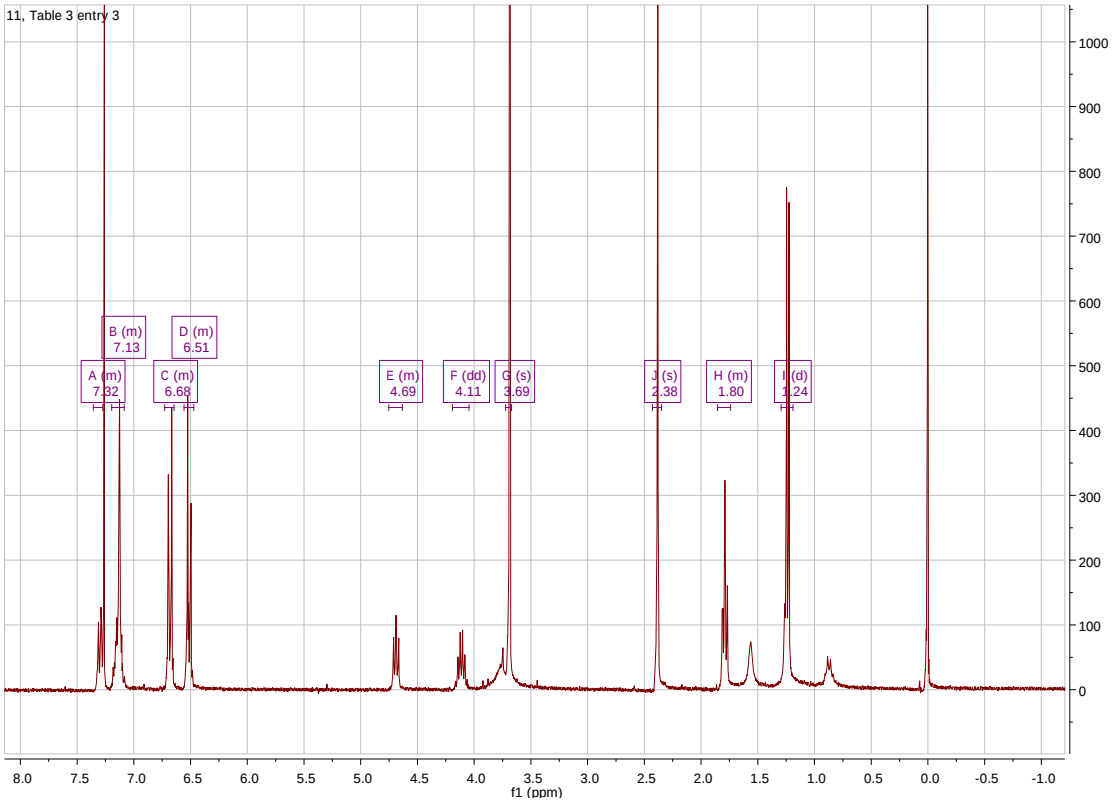


$Rh(COD)_2BF_4$ (15.2 mg, 0.037 mmol) and (*R*)-BINAP (23.35 mg, 0.037 mmol) were taken up in 2 mL DCM. Catalyst solution (0.33 mL) was added to a tube, containing (*S*)-4-((4-methoxyphenyl)amino)-4-(*o*-tolyl)butan-2-one (**7**) (36 mg, 0.125 mmol) in DCM (5 mL). Hydrogen pressure was applied (25 bar) and the mixture was stirred at 300 K for 44 h. The reaction mixture was concentrated and purified by column chromatography (heptane → 30% EtOAc in heptane). Yield: 29 mg (81%) of colorless wax. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.37–7.27 (m, 1H), 7.19–7.09 (m, 3H), 6.73–6.65 (m, 2H), 6.56–6.47 (m, 2H), 4.75–4.63 (m, 1H), 4.11 (dd, *J* = 12.2, 6.1 Hz, 1H), 3.69 (s, 3H), 2.38 (s, 3H), 1.85–1.74 (m, 2H), 1.24 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 152.8, 141.7, 140.8, 134.5, 130.7, 126.7, 126.6, 124.6, 116.2, 114.7, 68.6, 56.0, 55.6, 45.9, 24.2, 19.2; IR (cm^{-1}) 3671, 2985, 2900, 1406, 1393, 1066, 1055; HRMS [ESI$^+$ (m/z)]: calcd for $C_{18}H_{24}NO_2$ (M+H$^+$) 286.18070, found 286.18105; HPLC: d.r. > 99:1 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, *n*-heptane/2-propanol 80/20, retention time: major diastereomer 22.9 min, minor diastereomer: n/a. (see (*R*,*S*)-**11**); R_f 0.45 (EtOAc/heptane 1/1).

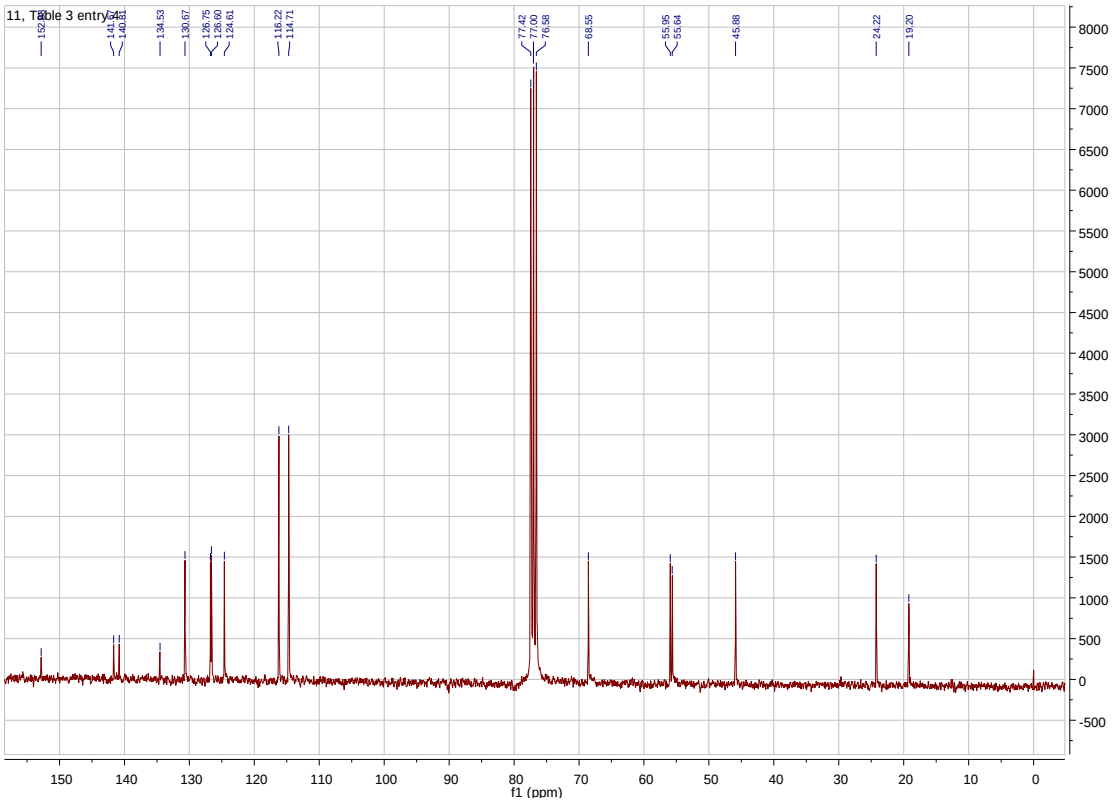
HPLC trace



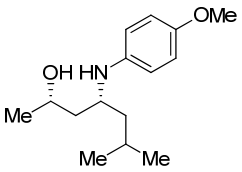
^{1}H NMR **11,** Table 3 entry 3



^{13}C NMR **11,** Table 3 entry 3

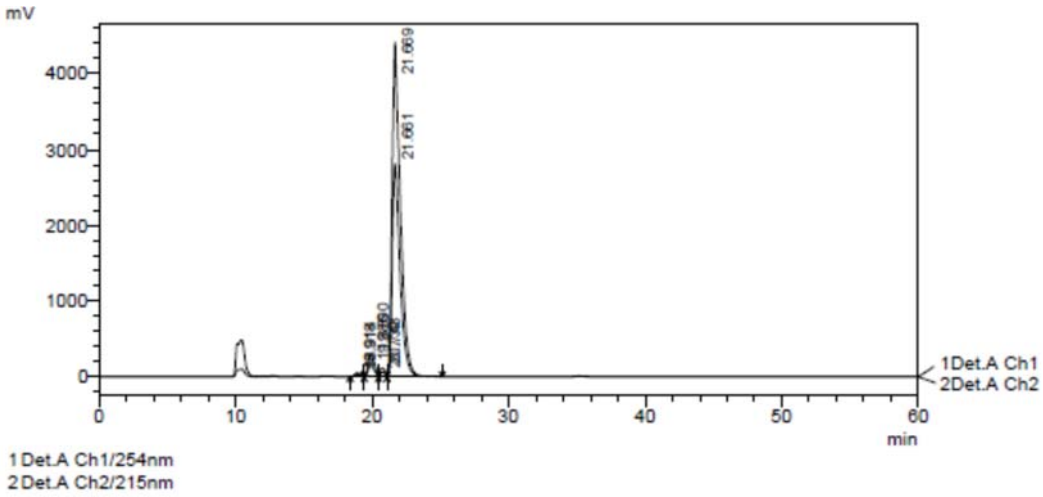


(2*S*,4*R*)-4-((4-Methoxyphenyl)amino)-6-methylheptan-2-ol (12)

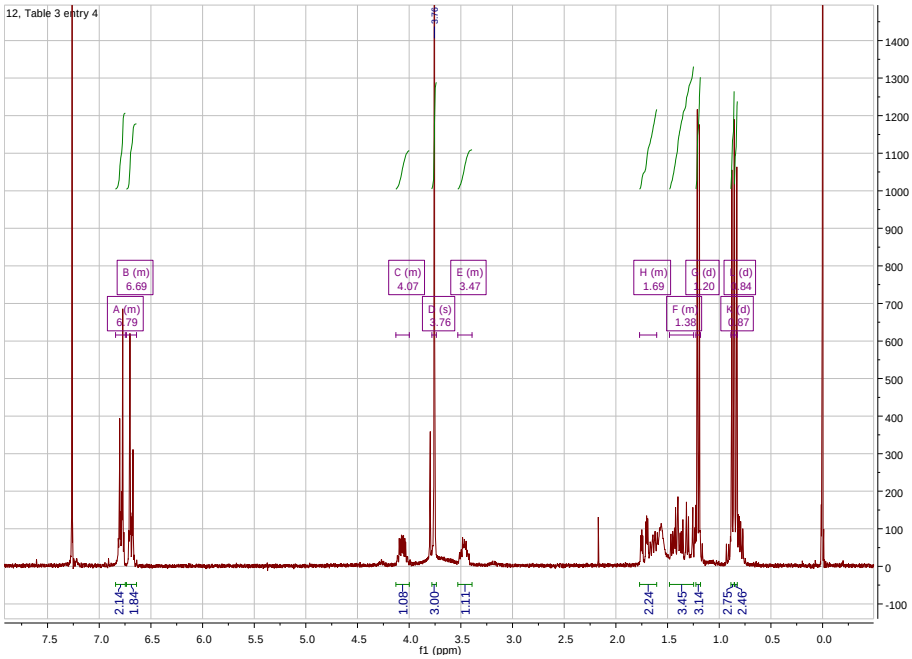


$Rh(COD)_2BF_4$ (16.24 mg, 0.040 mmol) and (*R*)-BINAP (25 mg, 0.040) were taken up in 2 mL DCM and heated to 50°C for 30 min. The catalyst solution was added to a solution of (*R*)-4-((4-methoxyphenyl)amino)-6-methylheptan-2-one (**8**) (41 mg, 0.125 mmol) in DCM (10 mL) in an autoclave. Hydrogen pressure was applied (25 bar) and the mixture was heated to 50 °C and stirred for 15 h. The mixture was diluted with DCM (20 mL) and an aqueous solution of $NaHCO_3$ (20 mL). After separation, the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The product was purified by column chromatography (EtOAc/heptane 1/9 → 3/7) and obtained as a brown oil. Yield: 77%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.84–6.75 (m, 2H), 6.74–6.64 (m, 2H), 4.13–4.00 (m, 1H), 3.76 (s, 3H), 3.53–3.39 (m, 1H), 1.78–1.16 (m, 5H), 1.20 (d, *J* = 6.2 Hz, 3H), 0.94–0.76 (m, 1H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 153.3, 140.7, 117.2, 114.8, 68.7, 55.7, 54.9, 45.7, 43.2, 24.9, 24.0, 23.3, 22.1; IR (cm^{-1}) 3367, 2954, 2929, 1510, 1236; HRMS [ESI$^+$ (m/z)]: calcd for $C_{12}H_{26}NO_2$ ($M+H^+$) 252.19635, found 252.19470; R_f 0.50 (EtOAc/heptane 1/1) HPLC: d.r. 98:2 Chiralpak AD-H (250 × 4.6 mm), flow 0.3 mL/min, heptane/2-propanol/ethanol 80/15/5, retention time: major diastereomer 21.7 min, minor diastereomer: 20.7 min.

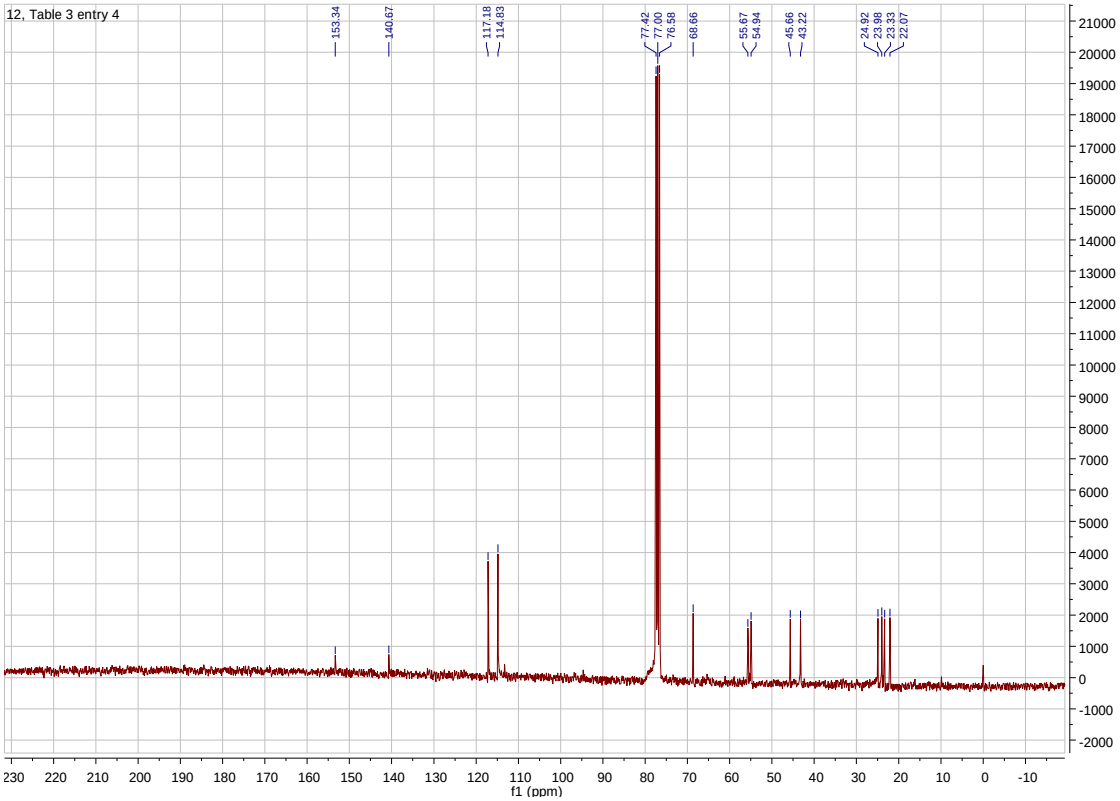
HPLC trace



^{1}H NMR **12,** Table 3 entry 4

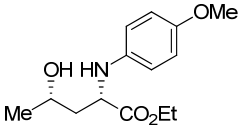


^{13}C NMR **12,** Table 3 entry 4

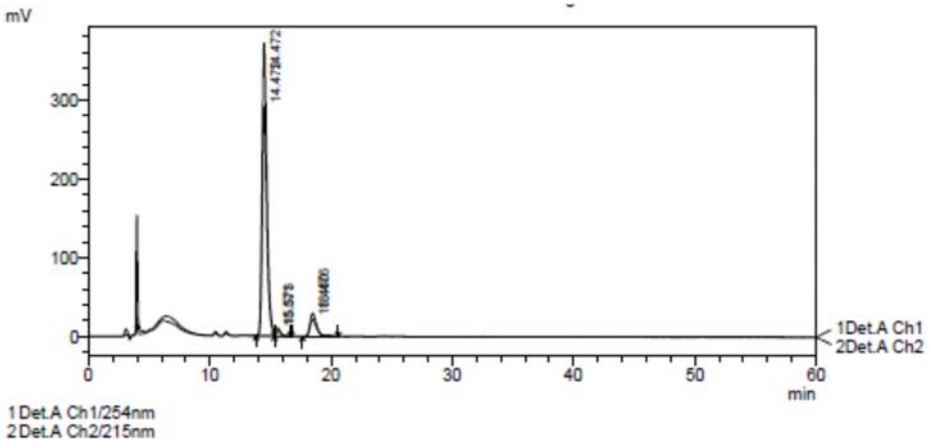


(2*S*,4*S*)-Ethyl 4-hydroxy-2-((4-methoxyphenyl)amino)pentanoate (13)

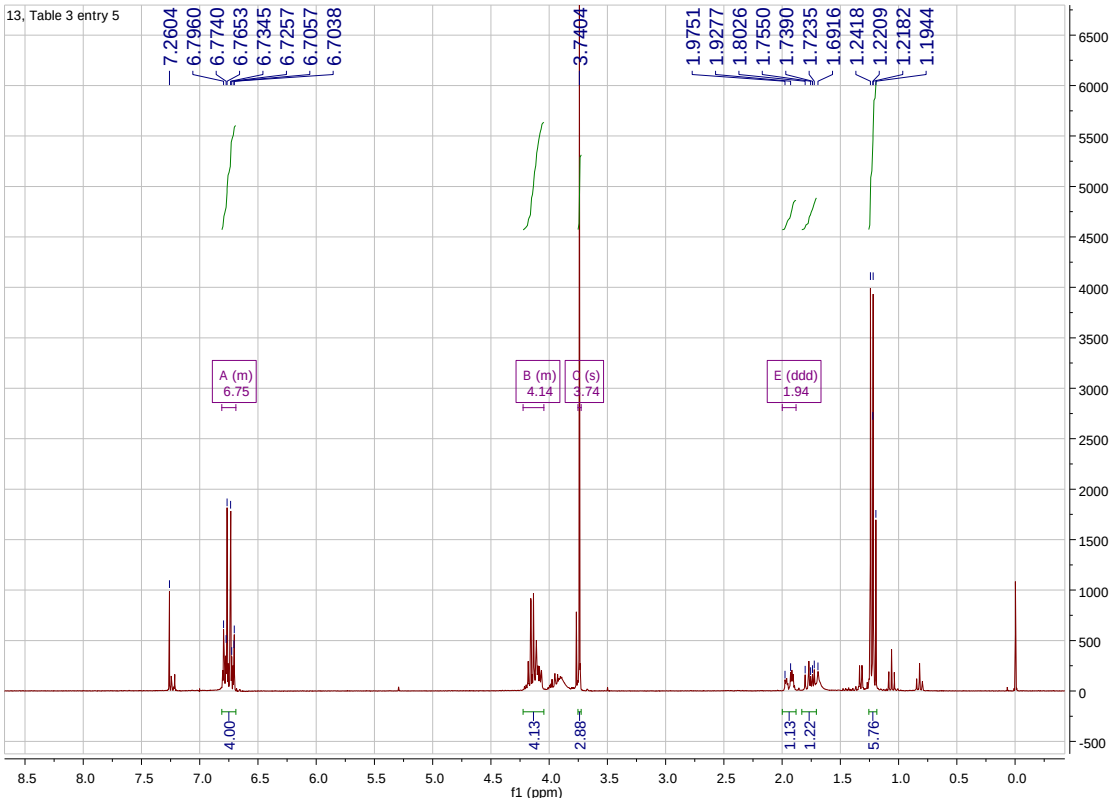
$Rh(COD)_2BF_4$ (16.24 mg, 0.040 mmol) and (*R*)-BINAP (25 mg, 0.040) were taken up in 2 mL DCM and heated to 50°C for 30 min. The catalyst solution was added to a solution of (*S*)-ethyl 2-((4-methoxyphenyl)amino)-4-oxopentanoate (**9**) (33 mg, 0.125 mmol) in DCM (10 mL) in an autoclave. Hydrogen pressure was applied (25 bar) and the mixture was heated to 50 °C and stirred for 17 h. The mixture was diluted with DCM (20 mL) and aqueous $NaHCO_3$ (20 mL). After separation, the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The product was purified by column chromatography (EtOAc/heptane 1/9 → 3/7) and obtained as an off-white solid. Yield: 19 mg (0.070 mmol, 56%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.81–6.69 (m, 4H), 4.22–4.04 (m, 4H), 3.74 (s, 3H), 1.94 (ddd, *J* = 14.2, 4.3, 2.5 Hz, 1H), 1.78 (dt, *J* = 14.3 Hz, 9.5 Hz, 1H,), 1.23 (d, *J* = 6.3 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 173.7, 154.0, 140.2, 117.5, 114.8, 67.7, 61.3, 59.3, 55.6, 41.2, 23.6, 14.1; IR (cm^{-1}) 3367, 2967, 2932, 1728, 1511, 1236; HRMS [ESI$^+$ (m/z)]: calcd for $C_{14}H_{22}NO_4$ (M+H$^+$) 268.15488, found 268.15450; HPLC: d.r. >99:1 Chiralpak AD-H (250 × 4.6 mm), flow 1.0 mL/min, heptane/2-propanol/ethanol 80/10/10, retention time: major diastereomer 14.5 min, minor diastereomer: n/a. (see (*R*,*S*)-**13**), R_f 0.30 (EtOAc/heptane 1/1).



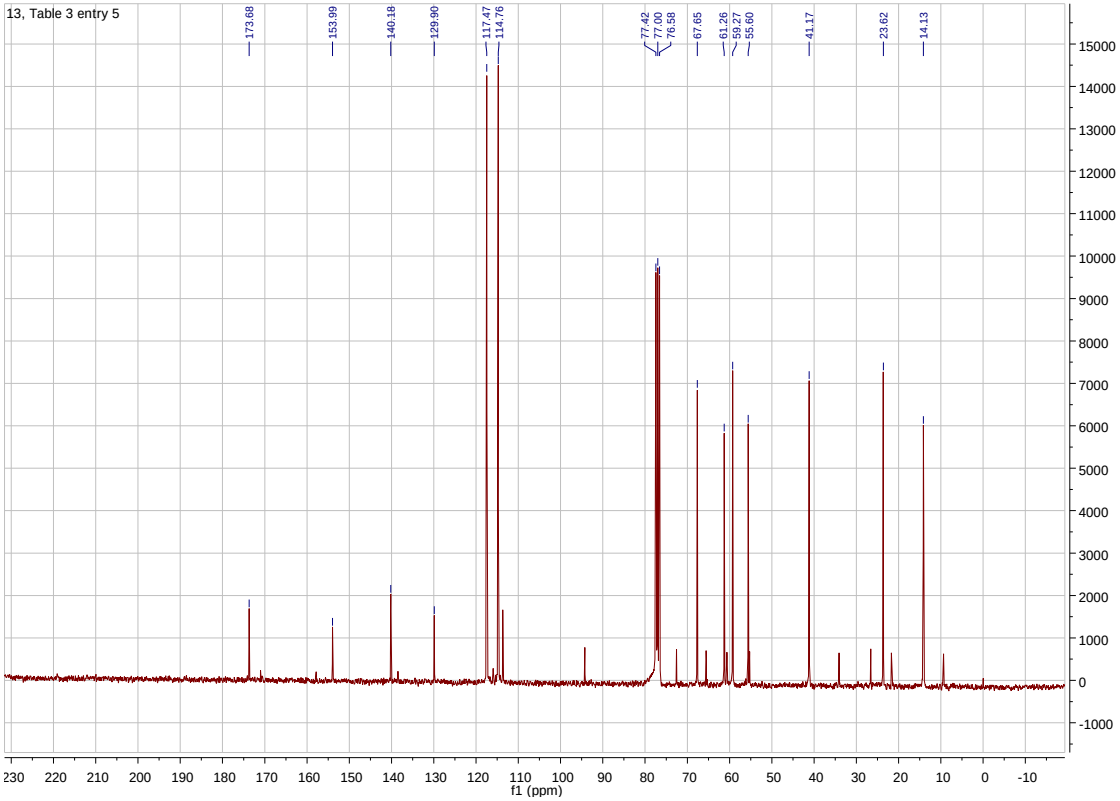
HPLC trace



^{1}H NMR **13,** Table 3 entry 5

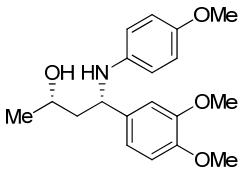


^{13}C NMR **13,** Table 3 entry 5



Larger scale synthesis of (*S,S*)-**2**

(2*S*,4*S*)-4-(3,4-Dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-ol (2)



$Rh(COD)_2BF_4$ (31 mg, 0.076 mmol) and (*R*)-BINAP (47 mg, 0.076 mmol) were dissolved in DCM (5 mL). (*S*)-4-(3,4-dimethoxyphenyl)-4-((4-methoxyphenyl)amino)butan-2-one (*S*)-**1** (500 mg, 1.52 mmol) was added and the mixture was put under H_2 (autoclave, 25 bar) and stirred for 3 days. After release of the H_2 pressure, the reaction mixture was diluted with DCM (50 mL) and washed with saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (silica eluted with EtOAc/heptane 1/2 → 1/1), which yielded an off-white solid (211 mg, 0.64 mmol, 42%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ (ppm) 6.86–6.76 (m, 3H), 6.73–6.66 (m, 2H), 6.61–6.53 (m, 2H), 4.39 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.11–3.99 (m, 1H), 3.84 (s, 3H), 3.84 (s, 3H), 3.70 (s, 3H), 1.96–1.76 (m, 2H), 1.23 (d, *J* = 6.2 Hz, 3H). ^{1}H NMR data in accordance with data obtained from (*S,S*)-**2**.

Suitable crystals for X-ray analysis were grown from EtOAc. The resulting crystals were analysed by X-ray analysis (Table 1).

Table 1 Crystal data and structure refinements for (*S*,*S*)-**2**.

Crystal colour		translucent colourless
Crystal shape		regular rod
Crystal size		0.50 × 0.29 × 0.25 mm
Empirical formula		$C_{19}H_{25}NO_4$
Formula weight		331.40
Temperature		208(2) K
Radiation / Wavelength		MoKa (graphite mon.) / 0.71073 Å
Crystal system, space group		Orthorhombic, P 21 21 21
Unit cell dimensions,	a	5.8467(2) Å
528 reflections,	b	17.0069(5) Å
2.340 < θ < 27.500	c	17.3740(9) Å
	α	90°
	β	90°
	γ	90°
Volume		1727.57(12) $Å^3$
Z, Calculated density		4, 1.274 Mg/m^3
Absorption coefficient		0.089 mm^{-1}
Diffractometer / scan		Nonius KappaCCD with area detector f and w scan
F(000)		712
θ range for data collection		2.34 to 27.50°.
Index ranges		-7<=h<=7, -22<=k<=22, -22<=l<=22
Reflections collected / unique		37079 / 3975 [R(int) = 0.0237]
Reflections observed		3510 ([Io>2σ(Io)])
Completeness to 2θ = 27.50		100.0%
Absorption correction		SADABS multiscan correction (Sheldrick, 1996)
Refinement method		Full-matrix least-squares on F^2
Computing		SHELXL-97 (Sheldrick, 1997)
Data / restraints / parameters		3975 / 0 / 222
Goodness-of-fit on F^2		1.079
SHELXL-97 weight parameters		0.0365, 0.4031
Final R indices [I>2σ (I)]		R1 = 0.0358, wR2 = 0.0793
R indices (all data)		R1 = 0.0445, wR2 = 0.0841
Largest diff. peak and hole		0.199 and -0.210 $e.A^{-3}$

References

1 B. List, *J. Am. Chem. Soc*. 2000, **122**, 9336.

2 Y. Niwa and M. Shimizu, *J. Am. Chem. Soc*. 2003, **125**, 3720.

3 W. Wang, J. Wan and H. Li, *Tetrahedron Lett.* 2004, **45**, 7243.