

Sulfoxide-Alkene Hybrids: A New Class of Chiral Ligands for
the Hayashi-Miyaura Reaction

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General

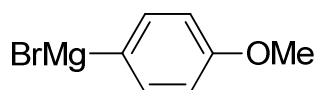
All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. 1,4-Dioxane was predried over KOH and distilled from sodium benzophenone ketyl under nitrogen. Yields refer to isolated yields of compounds estimated to be > 95 % pure as determined by ^1H -NMR (25 °C) and capillary GC. Column chromatography was performed using SiO_2 (0.040 - 0.063 mm, 230 - 400 mesh ASTM) from Merck if not indicated.

Syntheses of the chiral sulfoxide-alkene hybrid ligands:**Preparation of starting materials:****Typical procedure 1: Mg-Insertion:^[1]**

A dry and Ar-flushed 50 mL Schlenk-tube, equipped with a stirring bar and a septum, was charged with anhydrous LiCl (25 mmol; 1.06 g) and heated to 130 °C under high vacuum (1 mbar) for 3 h. After cooling to rt under Ar, Mg turnings (25 mmol; 608 mg), 1,2-dibromoethane (0.1 ml) and freshly distilled THF (20 mL) were added. The reaction mixture was shortly heated to reflux and was cooled to rt under Ar. Under vigorous stirring

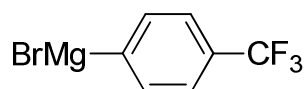
the respective aryl bromide (20 mmol) was slowly added at the appropriate temperature. The reaction mixture was stirred under Ar overnight and was titrated by using a stoichiometric amount of iodine (50 mg) in THF (2 mL).

(4-Methoxyphenyl)magnesium bromide:



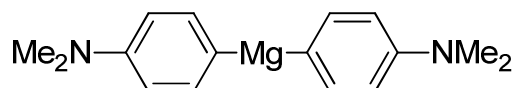
0.81 M in THF (81%); reaction temperature: 40 °C

(4-(Trifluoromethyl)phenyl)magnesium bromide:



0.68 M in THF (68%); reaction temperature: 0 °C. (Caution: Mg filings (no Mg powder) must be used in order to avoid an uncontrollable reaction).

Preparation of bis(4-(dimethylamino)phenyl)magnesium:



A dry and Ar-flushed 250 mL Schlenk-flask, equipped with a stirring bar and a septum, was charged with a solution of 4-bromo-*N,N*-dimethylaniline (4.0 g; 20 mmol) in 20 mL THF. The

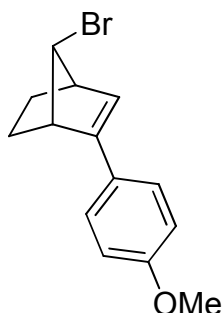
solution was cooled to $-78\text{ }^{\circ}\text{C}$ and $t\text{BuLi}$ (1.89 M in n -pentane; 21.2 mL; 40 mmol) was added dropwise via syringe. The reaction mixture was stirred for 1.5 h at $-78\text{ }^{\circ}\text{C}$, before MgCl_2 (0.5 M in THF; 20 mL; 10 mmol) was added. The mixture was allowed to reach room temperature. The resulting solution was titrated by using a stoichiometric amount of iodine (50 mg) in THF (2 mL) indicating a concentration of 0.31 M (62%).

Preparation of 7-bromo-2-arylbicyclo[2.2.1]hept-2-enes:

A dry and Ar-flushed 500 mL Schlenk-flask, equipped with a stirring bar and a septum, was charged with 7-bromobicyclo[2.2.1]heptan-2-one (3.77 g; 20 mmol) and a solution of $\text{LaCl}_3 \cdot 2\text{ LiCl}$ in THF (0.33 M; 90 mL; 30 mmol).^[2] The mixture was stirred at rt for 1 h. Then, the solution was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of the respective arylmagnesium reagent (30 mmol) was added dropwise. After stirring for 1 h at $-78\text{ }^{\circ}\text{C}$, the cold bath was removed and the mixture was allowed to reach rt within 1 h. The reaction mixture was further stirred for 2 h at room temperature. It was then cooled to $-78\text{ }^{\circ}\text{C}$ and methanesulfonic acid (4.68 mL; 72 mmol) was added dropwise and the mixture was allowed to reach rt. After 1.5 h, the clear yellow solution was quenched with NEt_3 (9.9 mL; 72 mmol). The mixture was filtrated and the precipitate was washed with Et_2O (3x). NH_4Cl sat. solution (250 mL) was added to the filtrate. Phases were separated and the

aqueous phase was extracted with Et₂O (3x 100 mL). The recombined organic phases were dried over Na₂SO₄ and the solvents were evaporated. The crude product was subjected to column-chromatographic purification.

7-Bromo-2-(4-methoxyphenyl)bicyclo[2.2.1]hept-2-ene (5):



yellow oil (67%)

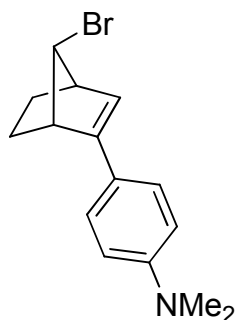
¹H-NMR (300 MHz, CDCl₃) δ : 7.40 (d, J =8.8 Hz, 2 H), 6.89 (d, J =8.8 Hz, 2 H), 6.16 (d, J =2.9 Hz, 1 H), 4.02 (d, J =0.7 Hz, 1 H), 3.82 (s, 3 H), 3.44 (d, J =1.0 Hz, 1 H), 3.17 (br. s., 1 H), 2.00 – 1.85 (m, 2 H), 1.38 – 1.21 (m, 2 H).

¹³C-NMR (75 MHz, CDCl₃) δ : 159.1, 144.9, 127.7, 126.5, 124.1, 114.0, 65.2, 55.3, 50.9, 50.5, 25.0, 23.0.

MS (70 eV, EI) m/z (%): 278 (6) [M⁺], 200 (5), 199 (39), 172 (12), 171 (100), 156 (5), 128 (8), 121 (4).

IR (ATR) $\tilde{\nu}$ (cm⁻¹): 1678 (s), 1610 (s), 1598 (vs), 1570 (s), 1506 (vs), 1306 (s), 1294 (s), 1248 (vs), 1222 (s), 1176 (vs), 1036 (s), 868 (s), 838 (s), 804 (vs), 788 (s), 750 (s), 702 (s), 608 (s).

HRMS (EI) for C₁₄H₁₅BrO (278.0306): 278.0297.

4-(7-bromobicyclo[2.2.1]hept-2-en-2-yl)-*N,N*-dimethylaniline:

slightly red solid (71%)

m.p.: 100.4 – 101.3 °C.

¹H-NMR (400 MHz, C₆D₆) δ: 7.36 (d, *J*=9.0 Hz, 2 H), 6.57 (d, *J*=9.0 Hz, 2 H), 5.97 (d, *J*=2.9 Hz, 1 H), 3.68 (s, 1 H), 3.29 (d, *J*=1.2 Hz, 1 H), 2.90 (br. s., 1 H), 2.51 (s, 6 H), 1.50 – 1.36 (m, 2 H), 1.07 – 0.95 (m, 2 H).

¹³C-NMR (101 MHz, C₆D₆) δ: 150.7, 146.2, 127.1, 124.4, 122.3, 113.2, 65.8, 51.5, 51.1, 40.5, 25.8, 23.6.

MS (70 eV, EI) *m/z* (%): 291 (8) [M⁺], 213 (5), 212 (29), 185 (15), 184 (100), 183 (4), 168 (10), 139 (6), 115 (5), 92 (7), 91 (7), 58 (12), 43 (35).

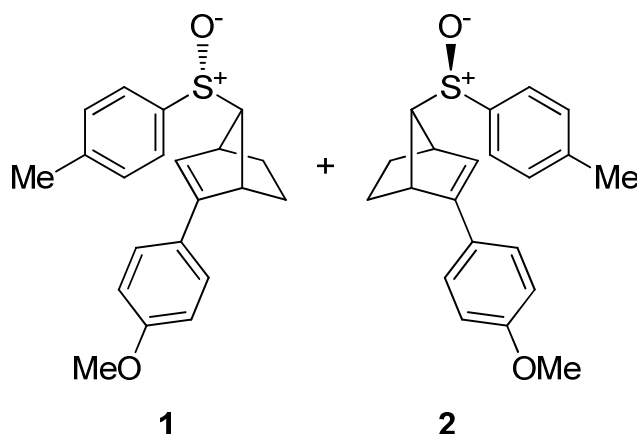
IR (ATR) $\tilde{\nu}$ (cm⁻¹): 2970 (m), 2942 (m), 2870 (m), 2800 (w), 1612 (vs), 1520 (vs), 1480 (m), 1460 (m), 1444 (m), 1364 (s), 1340 (m), 1298 (m), 1284 (w), 1230 (s), 1198 (s), 1188 (s), 1172 (m), 1160 (m), 1116 (s), 1064 (m), 946 (m), 866 (w), 824 (m), 806 (s), 794 (s), 786 (vs), 746 (s), 720 (m), 700 (m).

HRMS (EI) for C₁₅H₁₈BrN (291.0623): 291.0603.

Typical Procedure 2: Preparation of (1*S*,4*R*,7*S*)-2-aryl-7-((*R*)-*p*-tolylsulfinyl)bicyclo[2.2.1]hept-2-enes; quenching with Andersen-sulfinate^[3] ((*S*)-(1*R*,2*S*,5*R*)-2-isopropyl-5-methyl-cyclohexyl 4-methylbenzenesulfinate):

A dry and Ar-flushed 250 mL Schlenk-flask, equipped with a stirring bar and a septum, was charged with a solution of the respective 7-bromo-2-arylbicyclo[2.2.1]hept-2-ene (8 mmol) in THF (16 mL) and cooled to -78 °C. *t*BuLi (1.89 M in *n*-pentane; 9.31 mL; 17.6 mmol) was slowly added via syringe and the mixture was stirred for 2 h. A solution of MgCl₂ in THF (0.5 M; 18 mL; 9 mmol) was added and the mixture was further stirred at -78 °C for 30 min before a solution of the Andersen sulfinate^[3] (2.65 g; 9 mmol) in THF (9 mL) was added dropwise. After 4 h at -78 °C the reaction mixture was allowed to slowly reach rt. H₂O (100 mL) was added. Phases were separated and the aqueous phase was extracted with CH₂Cl₂ (3x 50 mL). The recombined phases were washed with brine (50 mL) and dried over Na₂SO₄. The solvents were evaporated and the crude product was subjected to column chromatography yielding the pure diastereomeric chiral sulfoxides.

(1*R*,4*S*,7*R*)-2-(4-Methoxyphenyl)-7-((*R*)-*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-2-ene (1) and (1*S*,4*R*,7*S*)-2-(4-methoxyphenyl)-7-((*R*)-*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-2-ene (2):



Flash column chromatography: purification/separation of the diastereomeric sulfoxide ligands from byproducts: (a) SiO₂, *n*-pentane : acetone 2 :1; separation of the two diastereomeric sulfoxide ligands: (b) SiO₂, CH₂Cl₂:EtOAc 2:1.

1: white solid (35%)

m.p.: 213.1 – 214.2 °C.

¹H-NMR (300 MHz, C₆D₆) δ: 7.61 (d, *J*=8.0 Hz, 2 H), 7.39 (d, *J*=8.8 Hz, 2 H), 6.95 (d, *J*=7.8 Hz, 2 H), 6.79 (d, *J*=8.8 Hz, 2 H), 5.96 (d, *J*=2.7 Hz, 1 H), 4.07 (d, *J*=1.9 Hz, 1 H), 3.32 (s, 3 H), 2.77 (s, 1 H), 2.45 (br. s., 1 H), 2.01 (s, 3 H), 1.56 – 1.45 (m, 1 H), 1.31 – 1.21 (m, 1 H), 1.12 – 1.03 (m, 1 H), 0.97 – 0.88 (m, 1 H).

¹³C-NMR (75 MHz, C₆D₆) δ: 160.4, 146.4, 144.7, 141.0, 130.2, 127.9, 127.7, 125.0, 124.5, 114.8, 88.0, 55.2, 46.5, 45.4, 27.7, 25.0, 21.5.

MS (70 eV, EI) m/z (%): 338 (6) [M^+], 323 (9), 322 (37), 294 (6), 200 (16), 199 (100), 198 (22), 185 (7), 184 (11), 172 (10), 171 (72), 156 (7), 135 (8), 128 (10), 121 (13), 67 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2974 (w), 2926 (w), 1610 (w), 1594 (w), 1506 (m), 1490 (m), 1466 (m), 1456 (w), 1442 (w), 1296 (w), 1272 (w), 1258 (m), 1246 (m), 1222 (m), 1184 (w), 1176 (m), 1120 (w), 1110 (w), 1080 (m), 1030 (vs), 1012 (s), 992 (m), 972 (w), 840 (m), 828 (w), 808 (s), 800 (s).

HRMS (EI) for $\text{C}_{21}\text{H}_{22}\text{O}_2\text{S}$ (338.1340): 338.1344.

2: white solid (37%)

m.p.: 173.5 – 174.5 °C.

^1H -NMR (300 MHz, C_6D_6) δ : 7.57 (d, $J=8.0$ Hz, 2 H), 7.20 (d, $J=8.8$ Hz, 2 H), 6.89 (d, $J=8.0$ Hz, 2 H), 6.80 (d, $J=8.8$ Hz, 2 H), 6.07 (d, $J=2.9$ Hz, 1 H), 3.66 (br. s., 1 H), 3.33 (s, 3 H), 2.87 – 2.71 (m, 2 H), 1.98 (s, 3 H), 1.60 – 1.49 (m, 1 H), 1.28 – 1.17 (m, 1 H), 1.10 – 1.01 (m, 1 H), 0.94 – 0.84 (m, 1 H).

^{13}C -NMR (75 MHz, C_6D_6) δ : 160.2, 146.0, 144.6, 141.1, 130.2, 127.9, 127.1, 125.3, 124.9, 114.8, 88.3, 55.2, 46.3, 45.8, 27.3, 25.6, 21.5.

MS (70 eV, EI) m/z (%): 338 (19) [M^+], 322 (25), 200 (10), 199 (68), 198 (15), 184 (12), 172 (14), 171 (100), 156 (10), 135 (28), 128 (15), 121 (18).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2982 (vw), 2934 (w), 1612 (w), 1598 (w), 1572 (w), 1508 (m), 1492 (w), 1464 (w), 1446 (w), 1416 (w),

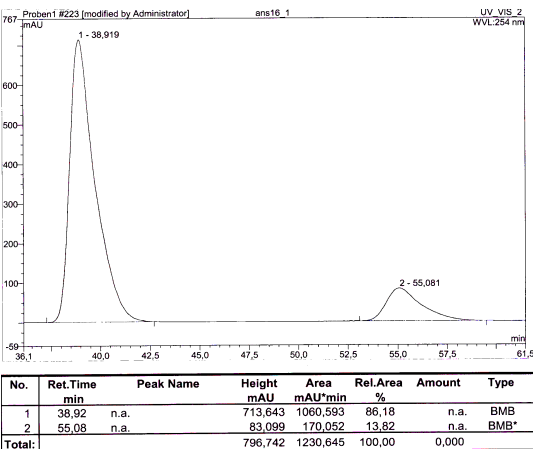
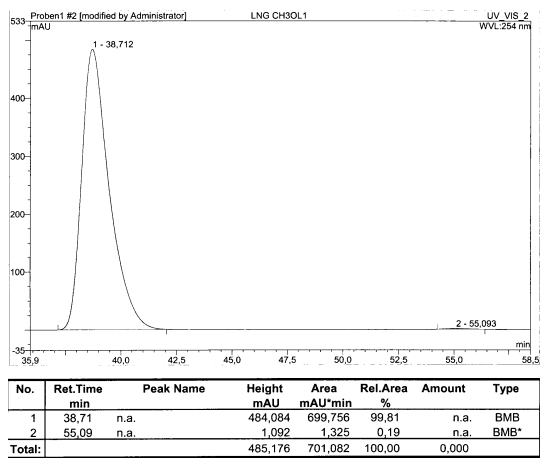
1294 (w), 1276 (w), 1246 (s), 1222 (w), 1210 (w), 1194 (w),
1182 (m), 1124 (w), 1110 (w), 1082 (w), 1030 (vs), 1014 (m),
990 (w), 964 (w), 950 (w), 842 (w), 814 (s), 794 (s), 704 (w).

HRMS (EI) for C₂₁H₂₂O₂S (338.1340): 338.1325.

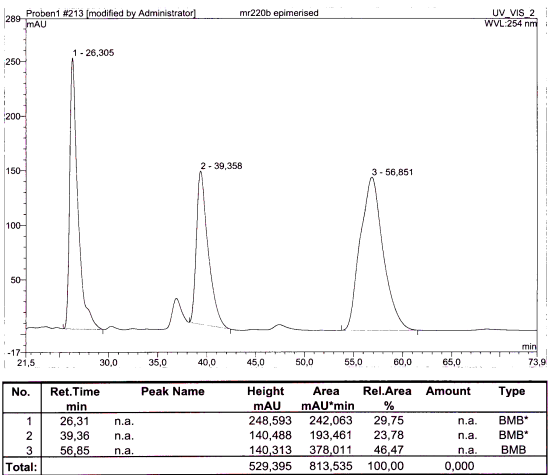
HPLC Data:

Chiralcel AD; *n*-heptane : *i*-propanol 80:20; flow: 0.3 mL/min

1:



without transmetalation to MgCl₂ (72% ee)

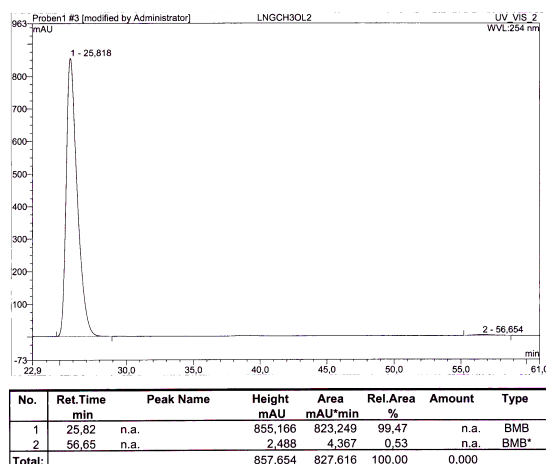


after acidic epimerization of 1 (HCl

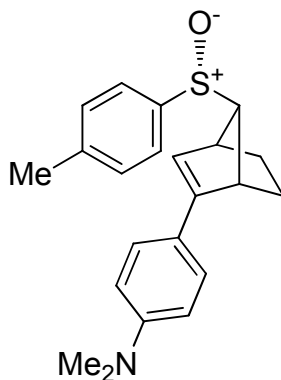
1 M in CH₂Cl₂)

shows 1, 2 and their enantiomers

2:



N,N-Dimethyl-4-((1*R*,4*S*,7*R*)-7-((*R*)-*p*-tolylsulfinyl)bicyclo-[2.2.1]hept-2-en-2-yl)aniline (16):



white solid (28%; only one diastereomer isolated)

m.p.: 224.7 – 226.9 °C.

¹H-NMR (400 MHz, d⁸-THF) δ: 7.50 (d, *J*=8.2 Hz, 2 H), 7.37 (d, *J*=8.8 Hz, 2 H), 7.31 (d, *J*=7.8 Hz, 2 H), 6.70 (d, *J*=9.0 Hz, 2 H), 6.11 (d, *J*=2.5 Hz, 1 H), 3.84 (d, *J*=2.0 Hz, 1 H), 2.94 (s, 6 H), 2.64 (s, 2 H), 2.38 (s, 3 H), 1.91 – 1.80 (m, 1 H), 1.79 – 1.73 (m, 1 H), 1.28 – 1.16 (m, 2 H).

^{13}C -NMR (101 MHz, $\text{d}^8\text{-THF}$) δ : 151.3, 146.9, 145.2, 141.4, 130.3, 127.2, 125.0, 123.9, 122.6, 113.1, 88.2, 46.4, 45.6, 40.6, 30.7, 28.3, 21.4.

MS (70 eV, EI) m/z (%): 351 (5) [M^+], 212 (18), 184 (47), 168 (9), 148 (19), 91 (9), 67 (9), 58 (27), 43 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2924 (w), 2866 (w), 1612 (m), 1520 (m), 1492 (m), 1460 (w), 1444 (w), 1364 (m), 1274 (w), 1234 (w), 1218 (w), 1200 (m), 1190 (m), 1178 (w), 1116 (w), 1078 (m), 1032 (vs), 1014 (m), 976 (w), 952 (w), 868 (w), 826 (m), 812 (s), 794 (vs), 706 (w).

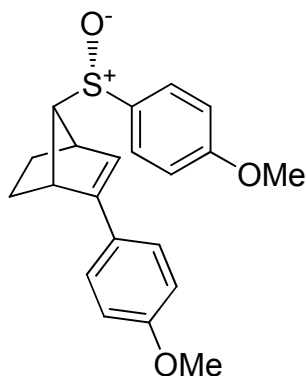
HRMS (EI) for $\text{C}_{22}\text{H}_{25}\text{NOS}$ (351.1657): 351.1644.

Typical Procedure 3: Preparation of chiral sulfoxide-alkene hybrid ligands using (*S*)-TMPOO^[4] (*N*-tosyl-phenyl-methyl-1,2,3-oxathiazolidine-2-oxide):

A dry and Ar-flushed 50 mL Schlenk-tube, equipped with a stirring bar and a septum, was charged with a solution of the 7-bromo-2-(4-methoxyphenyl)bicyclo[2.2.1]hept-2-ene (0.838 g; 3 mmol) in THF (6 mL) and cooled to $-78\text{ }^{\circ}\text{C}$. *t*BuLi (1.89 M in *n*-pentane; 3.49 mL; 6.6 mmol) was slowly added via syringe and the mixture was stirred for 2 h. A solution of MgCl_2 in THF (0.5 M; 13.2 mL; 6.6 mmol) was added. Meanwhile, a dry and Ar-flushed 100 mL Schlenk-flask, equipped with a stirring bar and a septum, was charged with solution of (*S*)-TMPOO^[4] (1.11 g; 3.15 mmol) in THF (8.4 mL) and cooled to $-78\text{ }^{\circ}\text{C}$. The cold

Grignard reagent, which was further kept at $-78\text{ }^{\circ}\text{C}$ was transferred to the (*S*)-TMPPO solution dropwise using a Teflon-cannula. After the addition was finished, the reaction mixture was stirred for further 2 h before the respective second Grignard reagent (3.3 mmol) was added. The reaction mixture was stirred for 1.5 h at $-78\text{ }^{\circ}\text{C}$ and was then allowed to warm to room temperature. The reaction was quenched with NaHCO_3 sat. solution (8 mL). H_2O (20 mL) was added and phases were separated. The aqueous phase was extracted with EtOAc (3x 40 mL). The combined organic layers were washed with brine (50 mL) and dried over Na_2SO_4 . The solvents were evaporated and the crude products were subjected to column chromatography yielding the respective pure diastereomeric chiral sulfoxide.

(1*S*,4*R*,7*S*)-2-(4-methoxyphenyl)-7-((*S*)-(4-methoxyphenyl)-sulfinyl)bicyclo[2.2.1]hept-2-ene (15a):



white solid (31%; only one diastereomer isolated)

m.p.: 184.8 – 186.2 $^{\circ}\text{C}$.

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ : 7.55 (d, $J=8.8\text{ Hz}$, 2 H), 7.34 (d, $J=8.8\text{ Hz}$, 2 H), 6.74 (d, $J=8.8\text{ Hz}$, 2 H), 6.69 (d, $J=8.8\text{ Hz}$, 2 H), 5.92 (d, $J=2.7\text{ Hz}$, 1 H), 4.01 (d, $J=1.8\text{ Hz}$, 1 H), 3.28 (s,

3 H) , 3.16 (s, 3 H), 2.73 (s, 1 H), 2.38 (br. s., 1 H), 1.56 – 1.45 (m, 1 H), 1.30 – 1.21 (m, 1 H), 1.08 – 1.00 (m, 1 H), 0.94 – 0.85 (m, 1 H).

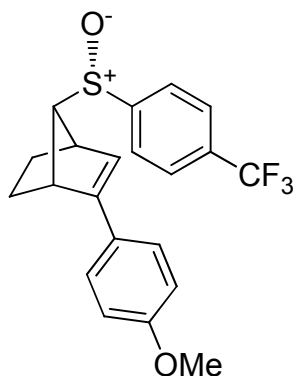
^{13}C -NMR (101 MHz, C_6D_6) δ : 161.5, 159.6, 145.7, 137.9, 127.2, 126.9, 125.9, 123.8, 114.4, 114.1, 87.5, 54.6, 54.5, 45.8, 44.7, 27.0, 24.4.

MS (70 eV, EI) m/z (%): 354 (4) [M^+], 338 (26), 200 (16), 199 (100), 198 (18), 197 (11), 184 (13), 172 (14), 171 (89), 156 (10), 155 (10), 135 (12), 128 (17), 121 (23), 91 (19), 67 (22).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2967 (w), 2945 (vw), 1594 (m), 1577 (w), 1508 (m), 1493 (m), 1307 (w), 1295 (w), 1245 (s), 1176 (m), 1084 (m), 1027 (vs), 1009 (m), 1004 (m), 993 (m), 838 (m), 823 (s), 817 (m), 802 (s), 796 (m), 789 (m), 616 (w), 609 (m).

HRMS (EI) for $\text{C}_{21}\text{H}_{22}\text{O}_3\text{S}$ (354.1290): 354.1282.

(1S,4R,7S)-2-(4-methoxyphenyl)-7-((S)-(4-(trifluoromethyl)-phenyl)sulfinyl)bicyclo[2.2.1]hept-2-ene (15b):



white solid (19%; only one diastereomer isolated)

m.p.: 151.6 – 152.6 °C.

^1H -NMR (300 MHz, C_6D_6) δ : 7.47 (d, $J=8.0$ Hz, 2 H), 7.38 (d, $J=8.8$ Hz, 2 H), 7.30 (d, $J=8.3$ Hz, 2 H), 6.80 (d, $J=8.8$ Hz, 2 H), 5.92 (d, $J=2.7$ Hz, 1 H), 3.99 (d, $J=1.7$ Hz, 1 H), 3.33 (s, 3 H), 2.60 (s, 1 H), 2.30 (br. s., 1 H), 1.53 – 1.42 (m, 1 H), 1.29 – 1.19 (m, 1 H), 1.10 – 1.02 (m, 1 H), 0.97 – 0.88 (m, 1 H).

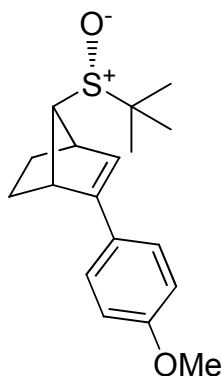
^{13}C -NMR (75 MHz, C_6D_6) δ : 160.5, 152.1 (d, $J=1.3$ Hz), 146.4, 132.7 (q, $J=32.5$ Hz), 127.7, 127.6, 126.3 (q, $J=3.6$ Hz), 125.3, 124.8 (q, $J=272.9$ Hz), 124.2, 114.9, 87.6, 55.2, 46.6, 45.2, 27.7, 24.8.

MS (70 eV, EI) m/z (%): 392 (13) [M^+], 376 (22), 199 (56), 184 (10), 172 (13), 171 (100), 135 (33), 128 (13), 121 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2974 (w), 2960 (w), 2936 (w), 1606 (w), 1596 (w), 1508 (s), 1468 (w), 1458 (w), 1400 (w), 1332 (s), 1306 (m), 1296 (s), 1274 (m), 1258 (m), 1248 (s), 1220 (m), 1174 (s), 1162 (s), 1150 (s), 1122 (vs), 1102 (s), 1084 (m), 1062 (s), 1042 (vs), 1028 (vs), 1012 (s), 974 (m), 870 (w), 832 (s), 818 (m), 804 (s), 712 (w), 702 (m), 610 (w).

HRMS (EI) for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{O}_2\text{S}$ (392.1058): 392.1060.

(1S,4R,7S)-7-((S)-tert-butylsulfinyl)-2-(4-methoxyphenyl)-
bicyclo[2.2.1]hept-2-ene (15c):



white solid (17%; only one diastereomer isolated)

m.p.: 105.4 – 106.6 °C.

$^1\text{H-NMR}$ (400 MHz, C_6D_6) δ : 7.45 (d, $J=8.8$ Hz, 2 H), 6.76 (d, $J=8.8$ Hz, 2 H), 5.95 (d, $J=2.9$ Hz, 1 H), 3.94 (br. s., 1 H), 3.31 (s, 3 H), 2.70 (s, 1 H), 2.61 (br. s., 1 H), 1.66 – 1.51 (m, 2 H), 1.20 – 1.07 (m, 2 H), 1.02 (s, 9 H).

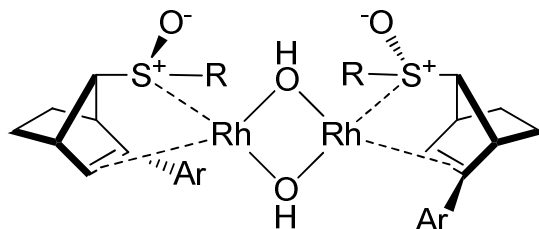
$^{13}\text{C-NMR}$ (101 MHz, C_6D_6) δ : 160.3, 146.6, 128.0, 128.0, 123.9, 114.7, 75.9, 55.2, 52.7, 46.6, 46.5, 28.6, 24.0, 23.5.

MS (70 eV, EI) m/z (%): 304 (9) [M^+], 249 (10), 248 (65), 231 (14), 200 (21), 199 (100), 198 (20), 197 (33), 185 (38), 184 (10), 172 (35), 171 (98), 156 (12), 153 (10), 150 (25), 135 (23), 128 (21), 121 (11), 57 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2944 (w), 2872 (vw), 1612 (vw), 1598 (w), 1510 (m), 1464 (w), 1446 (w), 1364 (w), 1296 (w), 1274 (w), 1262 (w), 1244 (m), 1224 (w), 1186 (m), 1126 (w), 1026 (vs), 994 (w), 878 (w), 846 (m), 816 (s), 804 (m), 786 (w).

HRMS (EI) for $\text{C}_{18}\text{H}_{24}\text{O}_2\text{S}$ (304.1497): 304.1493.

Typical Procedure 4: Preparation of the chiral sulfoxide-alkene hybrid/Rh catalyst:



An Ar-flushed 10 mL Schlenk-tube, equipped with a stirring bar and a septum, was charged with a solution of the respective chiral sulfoxide-alkene ligand (200 μmol) and $[\text{Rh}(\text{coe})_2\text{Cl}]_2$ ^[5] (72 mg; 100 μmol) in 1,4-dioxane (2 mL). $\text{CsOH}\cdot\text{H}_2\text{O}$ (34 mg; 200 μmol) along with 0.8 mL H_2O (HPLC grade) was added. The resulting suspension was stirred overnight at room temperature. The next day, a clear yellow solution had formed.

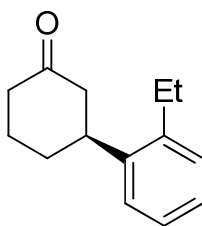
Typical Procedure 5: Enantioselective Hayashi-Miyaura reaction:

An Ar-flushed 10 mL Schlenk-tube, equipped with a stirring bar and a septum, was charged with a solution of the respective electron-deficient alkene (0.5 mmol), the corresponding boronic acid (0.6 mmol) and CsF (0.6 mmol) in 1,4-dioxane (1.5 mL). A solution of the catalyst in 1,4-dioxane (0.036 M; 0.35 mL; 12.5 μmol) was slowly added to the reaction mixture. After the addition was complete, the mixture was warmed to

room temperature. Progress of the reaction was followed via TLC analysis. After all the starting material was consumed, Et₂O (6 mL) was added to the reaction mixture along with SiO₂. The solvents were removed and the product was subjected to column chromatography.

Compounds of Table 1:

(*S*)-3-(2-Ethylphenyl)cyclohexanone (8b):



colorless oil 0.100 g (99%)

¹H-NMR (400 MHz, C₆D₆) δ: 7.14 – 7.04 (m, 2 H), 7.04 – 6.93 (m, 2 H), 3.02 – 2.93 (m, 1 H), 2.48 – 2.42 (m, 1 H), 2.37 (q, *J*=7.5 Hz, 2 H), 2.29 – 2.23 (m, 1 H), 2.15 (t, *J*=13.4 Hz, 1 H), 1.88 (td, *J*₁=13.3 Hz, *J*₂= 6.0 Hz, 1 H), 1.62 – 1.52 (m, 2 H), 1.42 – 1.22 (m, 2 H), 0.99 (t, *J*=7.6 Hz, 3 H).

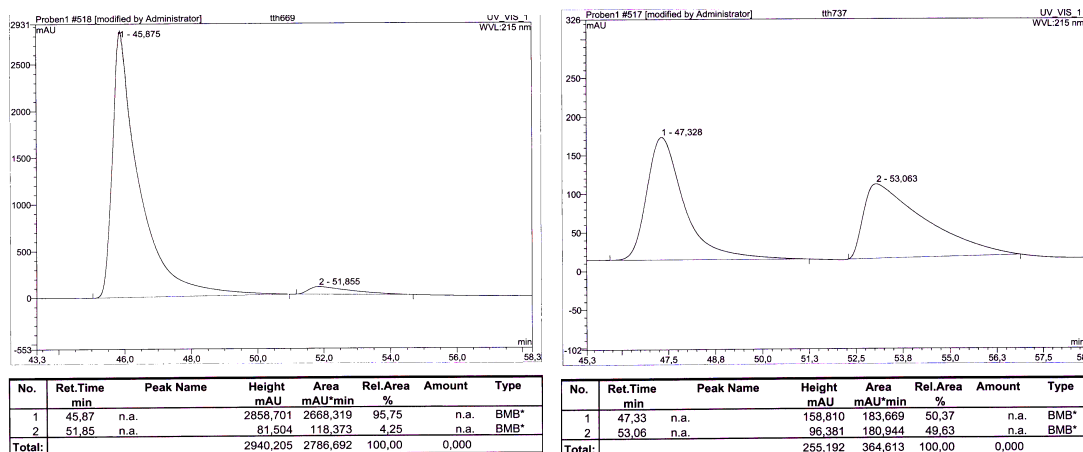
¹³C-NMR (101 MHz, C₆D₆) δ: 207.8, 141.9, 140.7, 128.8, 126.4, 126.2, 125.5, 48.7, 40.8, 39.4, 32.5, 25.5, 25.4, 15.6.

MS (70 eV, EI) *m/z* (%): 202 (86) [M⁺], 173 (33), 160 (12), 159 (100), 145 (45), 145 (32), 132 (12), 131 (17), 129 (14), 128 (10), 118 (12), 117 (54), 115 (20), 91 (11).

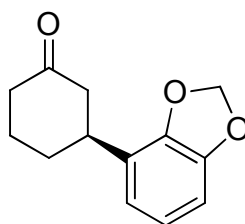
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2962 (m), 2934 (m), 2872 (w), 1708 (vs), 1490 (w), 1448 (m), 1420 (w), 1374 (w), 1364 (w), 1344 (w), 1314 (w), 1286 (w), 1252 (w), 1222 (m), 1182 (w), 1052 (w), 1032 (w), 972 (w), 914 (vw), 884 (vw), 796 (w), 788 (w), 752 (s), 714 (w), 650 (w).

HRMS (EI) for $\text{C}_{14}\text{H}_{18}\text{O}$ (202.1358): 202.1346.

HPLC Data: Chiralcel OD-H; *n*-heptane : *i*-propanol 99:1; flow: 0.3 mL/min



(S)-3-(Benzo[d][1,3]dioxol-4-yl)cyclohexanone (8f):



colorless crystals 0.094 g (86%)

m.p.: 78.8 – 79.9 °C.

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 6.83 – 6.69 (m, 2 H), 6.69 – 6.58 (m, 1 H), 5.93 (s, 2 H), 3.01 – 2.84 (m, 1 H), 2.60 – 2.29 (m, 4 H), 2.20 – 1.97 (m, 2 H), 1.86 – 1.65 (m, 2 H).

^{13}C -NMR (75 MHz, CDCl_3) δ : 210.7, 147.8, 146.1, 138.4, 119.4, 108.2, 106.9, 100.9, 49.2, 44.4, 41.0, 33.0, 25.3.

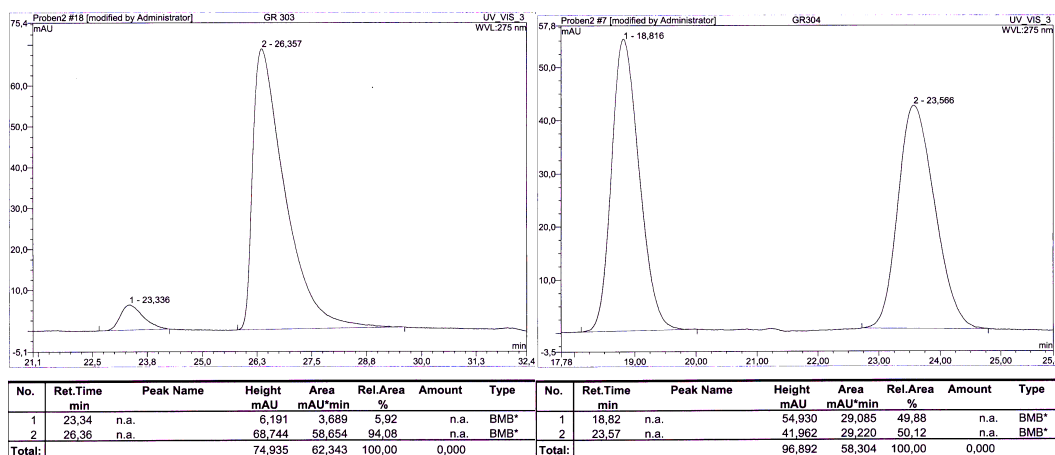
MS (70 eV, EI) m/z (%): 218 (100) [M^+], 175 (14), 162 (10), 161 (57), 148 (36), 147 (14), 135 (22), 103 (11), 89 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (m), 2918 (m), 2852 (m), 1702 (vs), 1608 (w), 1504 (s), 1486 (s), 1440 (s), 1414 (m), 1350 (w), 1250 (m), 1218 (vs), 1188 (s), 1090 (m), 1030 (vs), 974 (m), 928 (vs), 902 (m), 874 (s), 860 (m), 810 (vs), 774 (m), 748 (m).

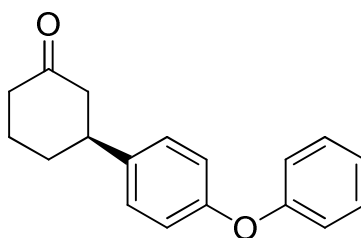
HRMS (EI) for $\text{C}_{13}\text{H}_{14}\text{O}_3$ (218.0943): 218.0952.

HPLC Data:

Chiralcel AS-H; *n*-heptane : *i*-propanol 80:20; flow: 1.0 mL/min



(*S*)-3-(4-Phenoxyphenyl)cyclohexanone (8j):



colorless crystals 0.120 g (90%)

m.p.: 99.3 – 100.5 °C.

¹H-NMR (300 MHz, CDCl₃) δ : 7.34 (t, J =8.0 Hz, 2 H), 7.19 (d, J =8.4 Hz, 2 H), 7.11 (t, J =7.4 Hz, 1 H), 7.02 (d, J =7.9 Hz, 2 H), 6.98 (d, J =8.6 Hz, 2 H), 3.01 (dddd, J_1 =15.5 Hz, J_2 =7.8 Hz, J_3 =3.8 Hz, J_4 =3.7 Hz, 1 H), 2.66 – 2.32 (m, 4 H), 2.24 – 2.03 (m, 2 H), 1.92 – 1.70 (m, 2 H).

¹³C-NMR (75 MHz, CDCl₃) δ : 210.8, 157.2, 155.8, 139.2, 129.7, 127.7, 123.2, 118.9, 118.8, 49.0, 44.0, 41.1, 32.9, 25.4.

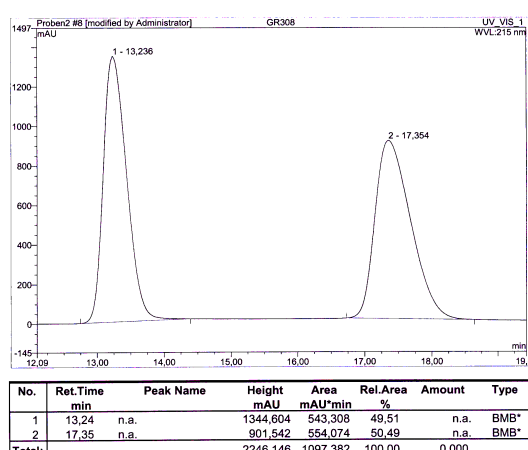
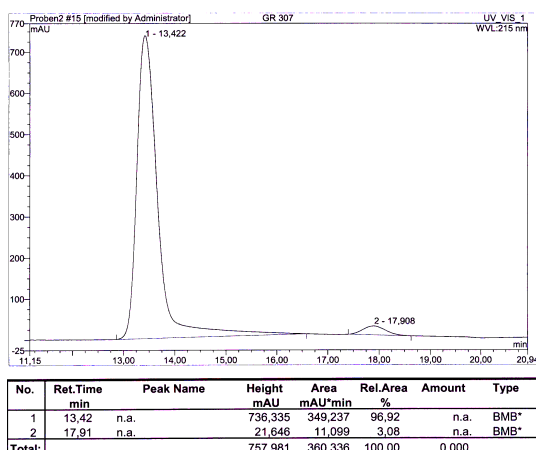
MS (70 eV, EI) m/z (%): 266 (100) [M^+], 223 (16), 210 (11), 209 (79), 196 (25), 183 (12), 116 (22), 115 (27), 97 (14), 85 (16), 83 (11), 77 (16), 71 (24), 69 (14), 57 (32), 43 (14).

IR (ATR) $\tilde{\nu}$ (cm⁻¹): 2944 (w), 2922 (w), 1702 (s), 1588 (m), 1504 (s), 1486 (s), 1456 (m), 1446 (m), 1422 (w), 1366 (w), 1250 (s), 1234 (vs), 1222 (vs), 1198 (s), 1180 (m), 1166 (m), 1110 (w), 1068 (w), 910 (w), 870 (m), 828 (m), 802 (m), 784 (m), 752 (m), 738 (m), 694 (s).

HRMS (EI) for C₁₈H₁₈O₂ (266.1307): 266.1296.

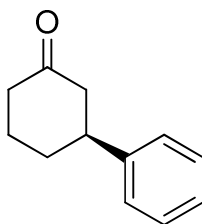
HPLC Data:

Chiralcel AS-H; *n*-heptane : *i*-propanol 80:20; flow: 1.0 mL/min



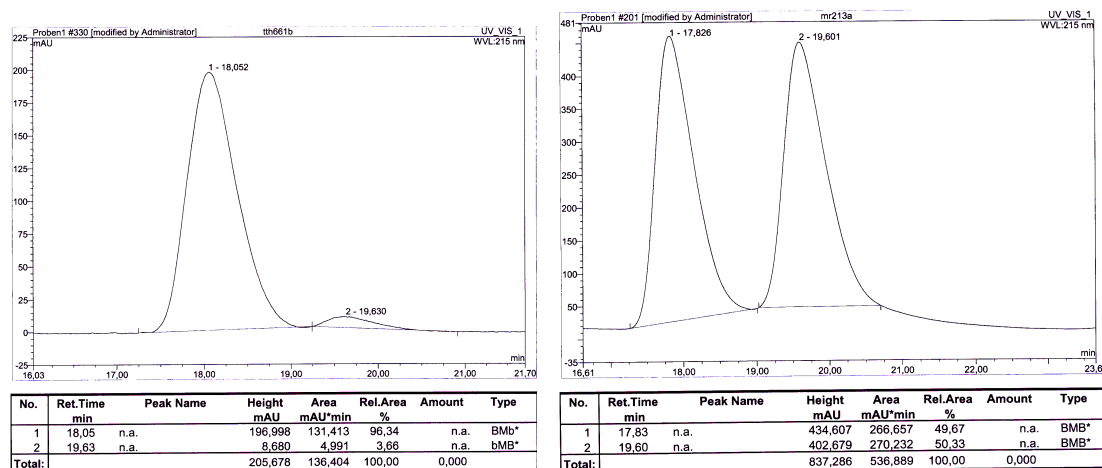
Compounds known in the literature (references [3], [4], [7], [8] and [9] in the manuscript):

(*S*)-3-Phenylcyclohexanone (8a):

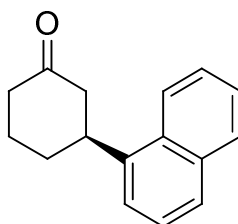


HPLC Data:

Chiralcel AD; *n*-heptane : *i*-propanol 90:10; flow: 0.3 mL/min

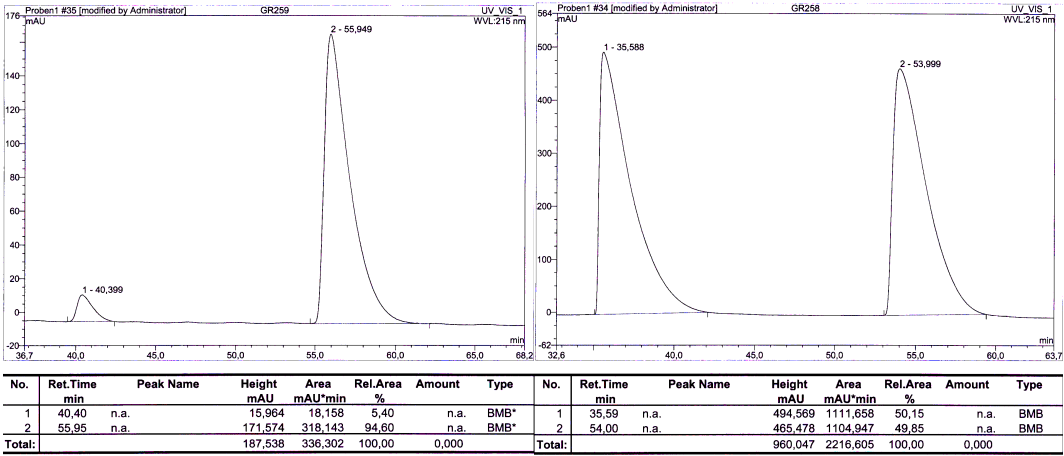


(*S*)-3-(Naphthalen-1-yl)cyclohexanone (8c):

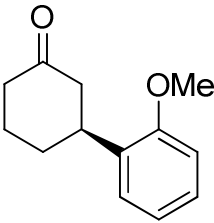


HPLC Data:

Chiralcel OD-H; *n*-heptane : *i*-propanol 95:5; flow: 0.5 mL/min

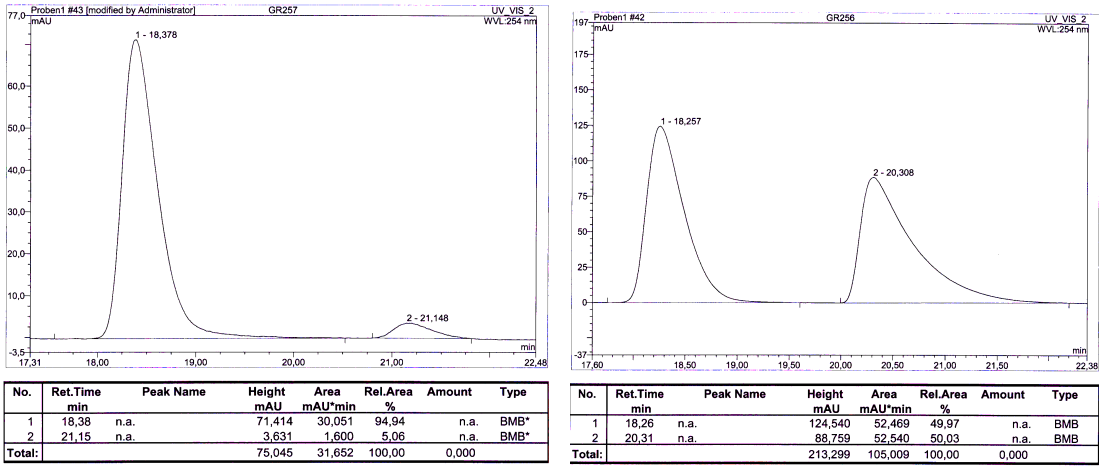


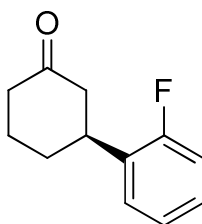
(S)-3-(2-Methoxyphenyl)cyclohexanone (8d):



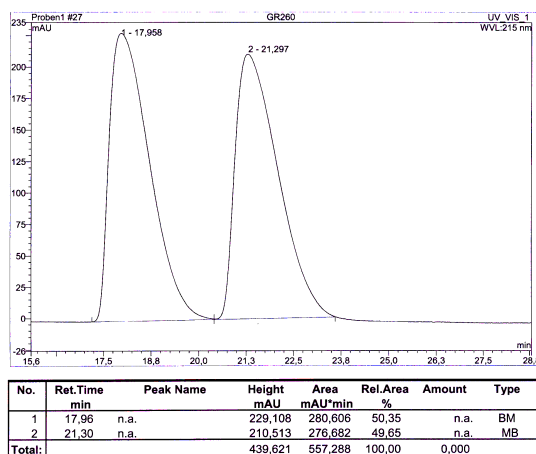
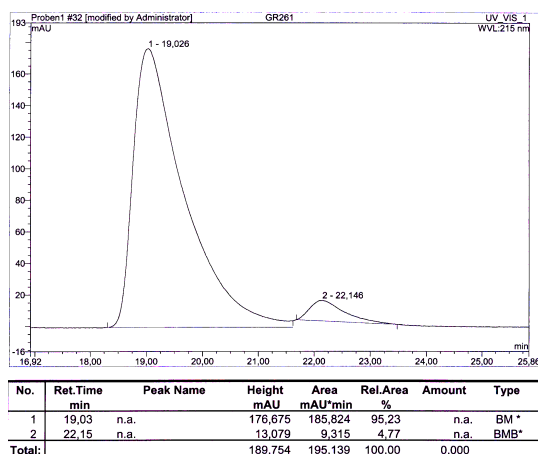
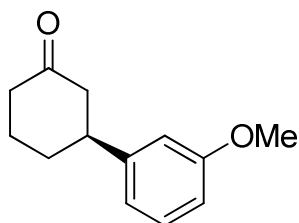
HPLC Data:

Chiralcel OD-H; *n*-heptane : *i*-propanol 95:5; flow: 0.5 mL/min

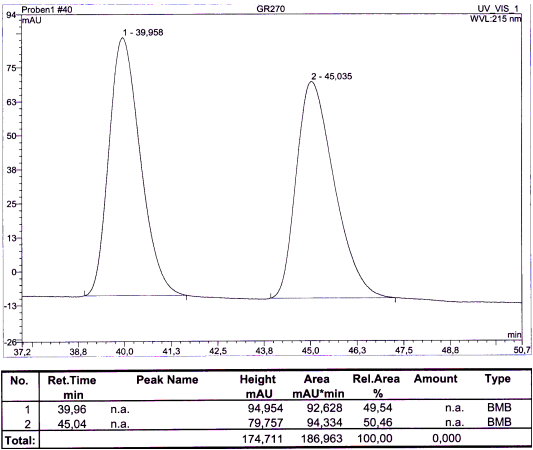
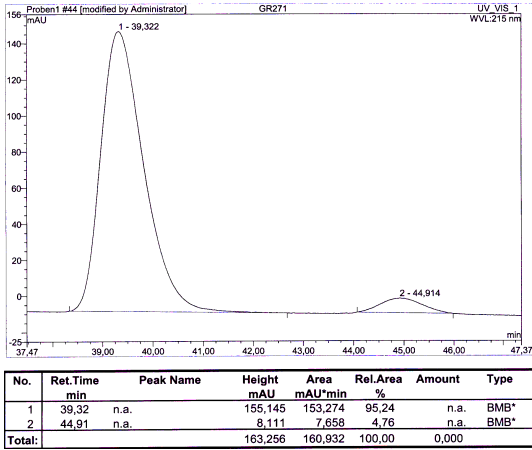


(S)-3-(2-Fluorophenyl)cyclohexanone (8e):**HPLC Data:**

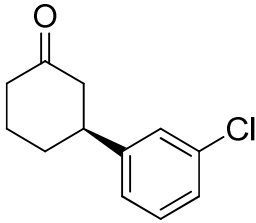
Chiralcel AD; *n*-heptane : *i*-propanol 99.5:0.5; flow: 1.0 mL/min

**(S)-3-(3-Methoxyphenyl)cyclohexanone (8g):****HPLC Data:**

Chiralcel OD-H; *n*-heptane : *i*-propanol 99:1; flow: 1.0 mL/min

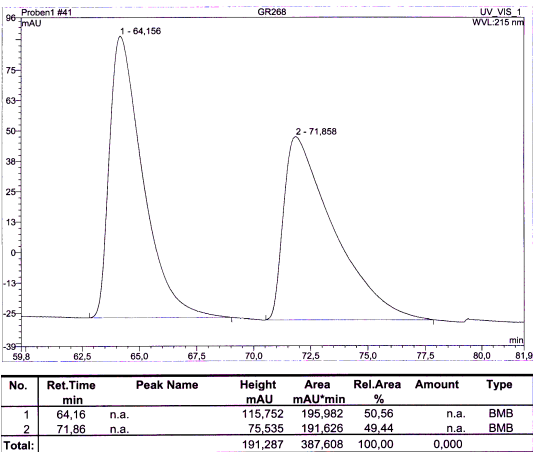
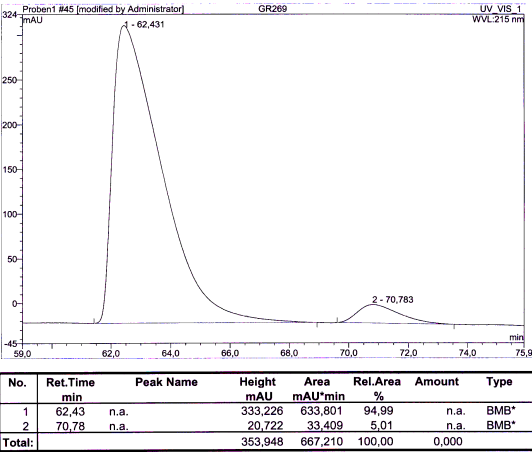


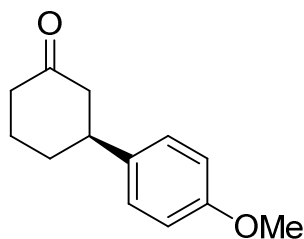
(S)-3-(3-Chlorophenyl)cyclohexanone (8h):



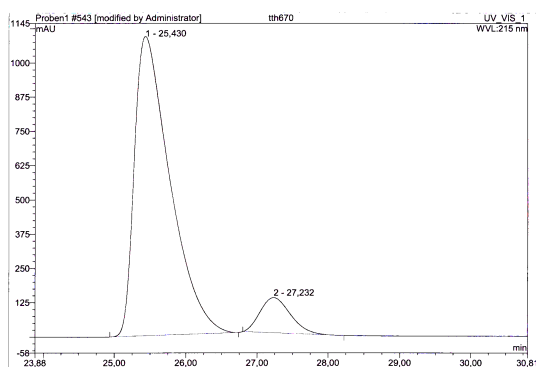
HPLC Data:

Chiralcel OD-H; *n*-heptane : *i*-propanol 99.5:0.5; flow: 0.5 mL/min

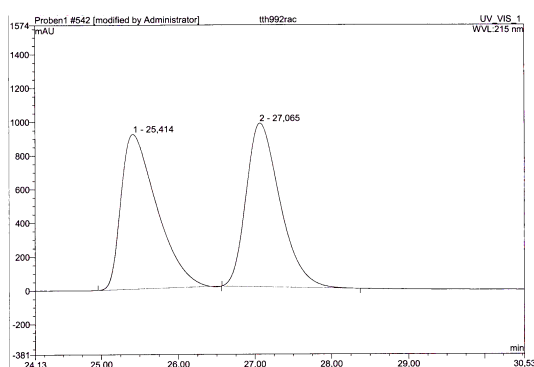


(S)-3-(4-Methoxyphenyl)cyclohexanone (8i):**HPLC Data:**

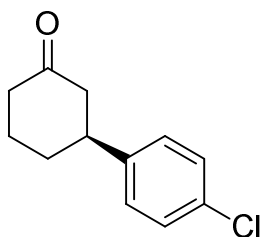
Chiralcel AD-H; *n*-heptane : *i*-propanol 98:2; flow: 0.5 mL/min



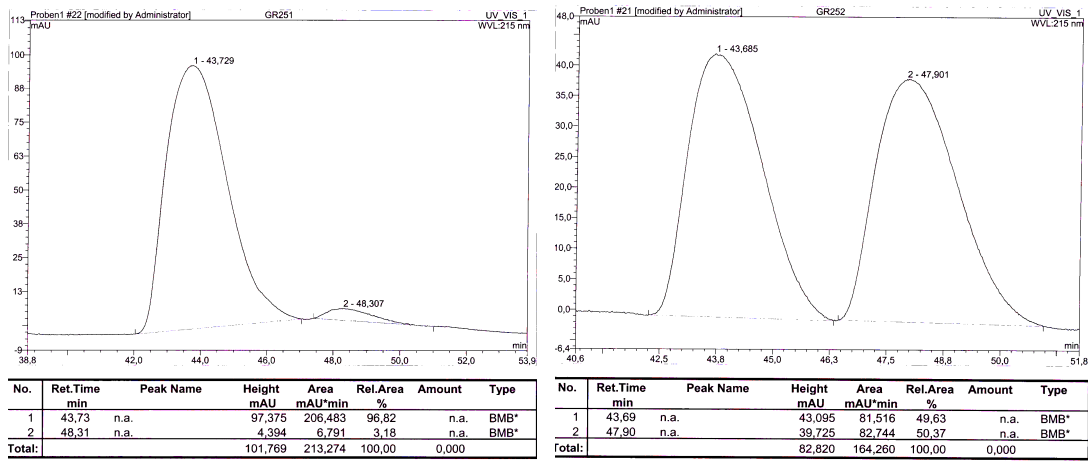
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.43	n.a.	1091,691	628,811	90,85	n.a.	BMB*
2	27.23	n.a.	128,261	63,300	9,15	n.a.	BMB*
Total:			1219,953	692,110	100,00	0,000	



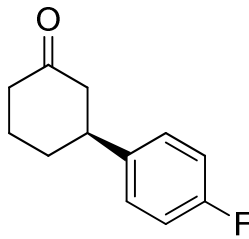
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.41	n.a.	917,254	493,341	49,75	n.a.	BMB*
2	27.06	n.a.	968,955	498,386	50,25	n.a.	BMB*
Total:			1886,209	991,727	100,00	0,000	

(S)-3-(4-Chlorophenyl)cyclohexanone (8k):**HPLC Data:**

Chiralcel OJ; *n*-heptane : *i*-propanol 99:1; flow: 0.5 mL/min

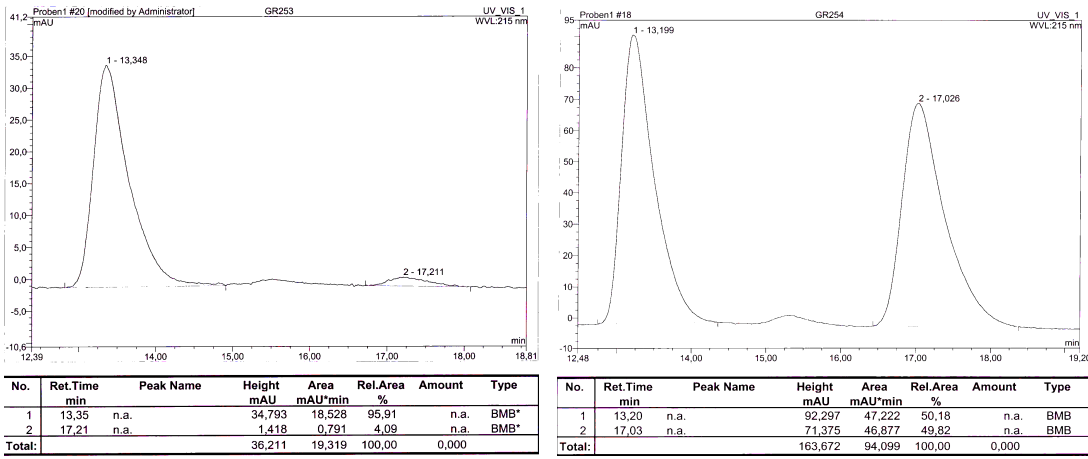


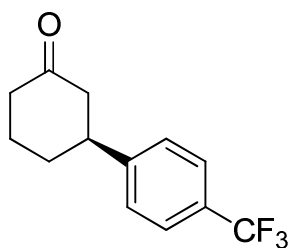
(S)-3-(4-Fluorophenyl)cyclohexanone (81):



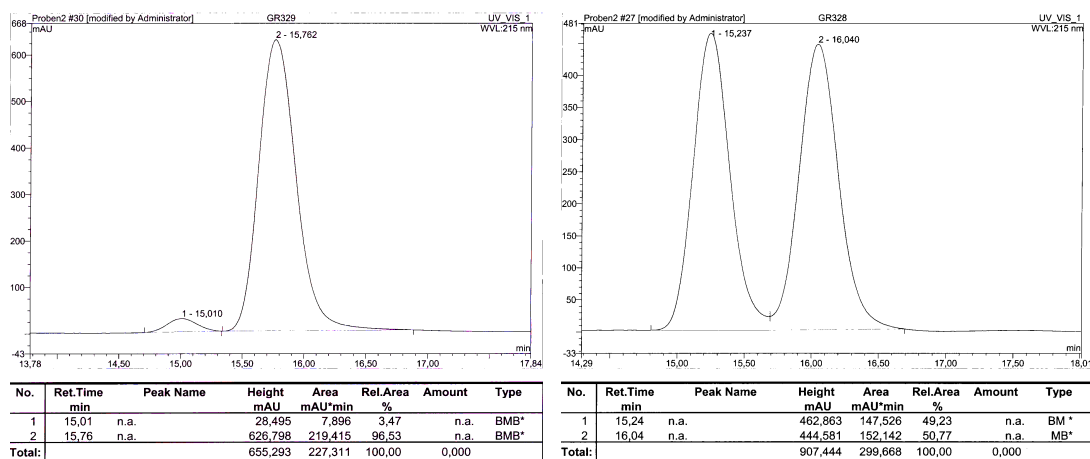
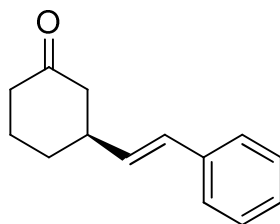
HPLC Data:

Chiralcel AD; *n*-heptane : *i*-propanol 99:1; flow: 1.0 mL/min

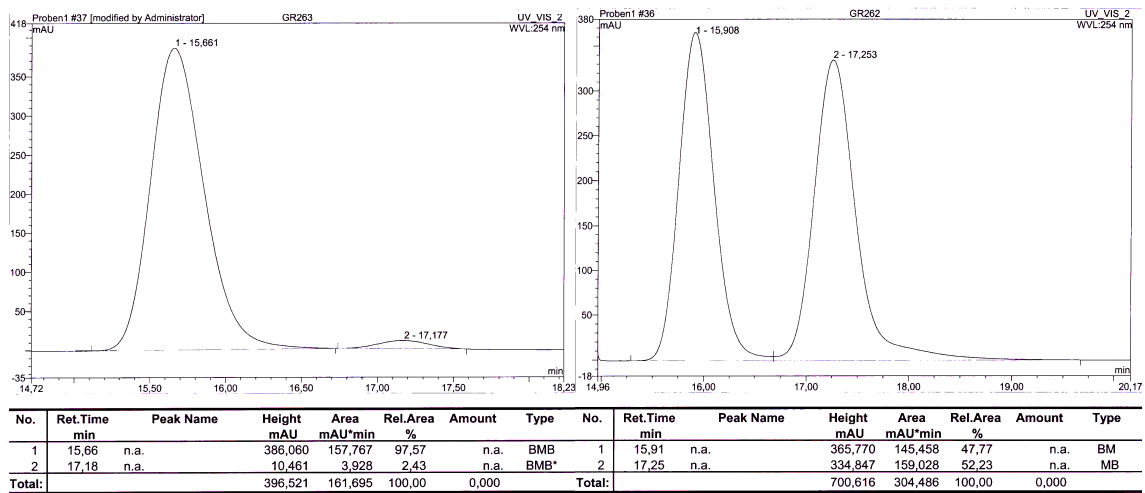


(S)-3-(4-(Trifluoromethyl)phenyl)cyclohexanone (8m):**HPLC Data:**

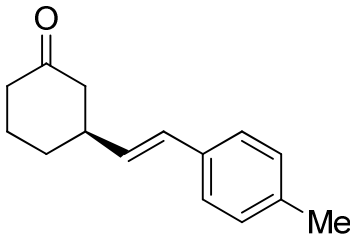
Chiralcel OD-H; *n*-heptane : *i*-propanol 90:10; flow: 0.5 mL/min

**(S,E)-3-Styrylcyclohexanone (8n):****HPLC Data:**

Chiralcel OD-H; *n*-heptane : *i*-propanol 98:2; flow: 1.0 mL/min

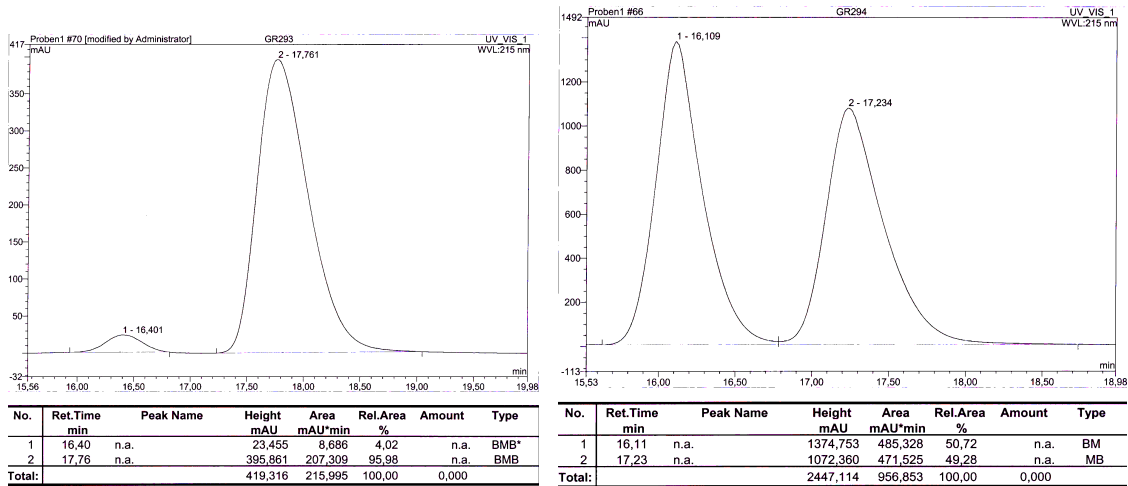


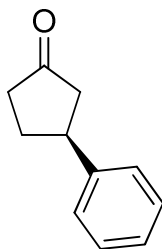
(*S,E*)-3-(4-Methylstyryl)cyclohexanone (8o):



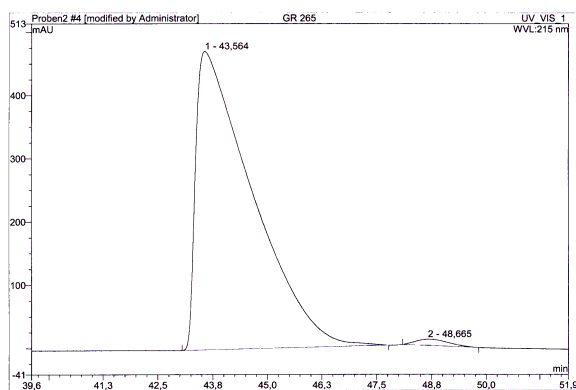
HPLC Data:

Chiralcel OD-H; *n*-heptane : *i*-propanol 99:1; flow: 1.0 mL/min

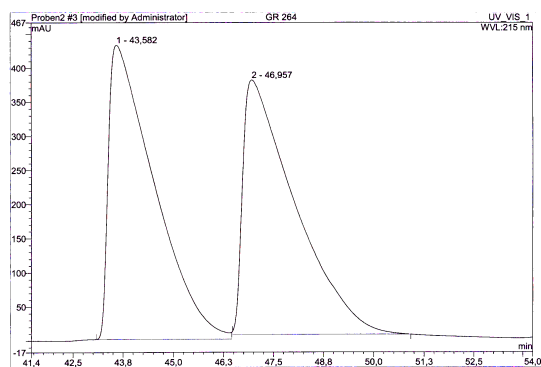


(S)-3-Phenylcyclopentanone (9a):**HPLC Data:**

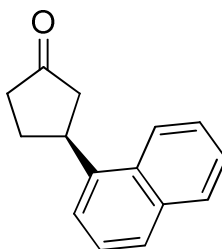
Chiralcel OB-H; *n*-heptane : *i*-propanol 99:1; flow: 0.5 mL/min



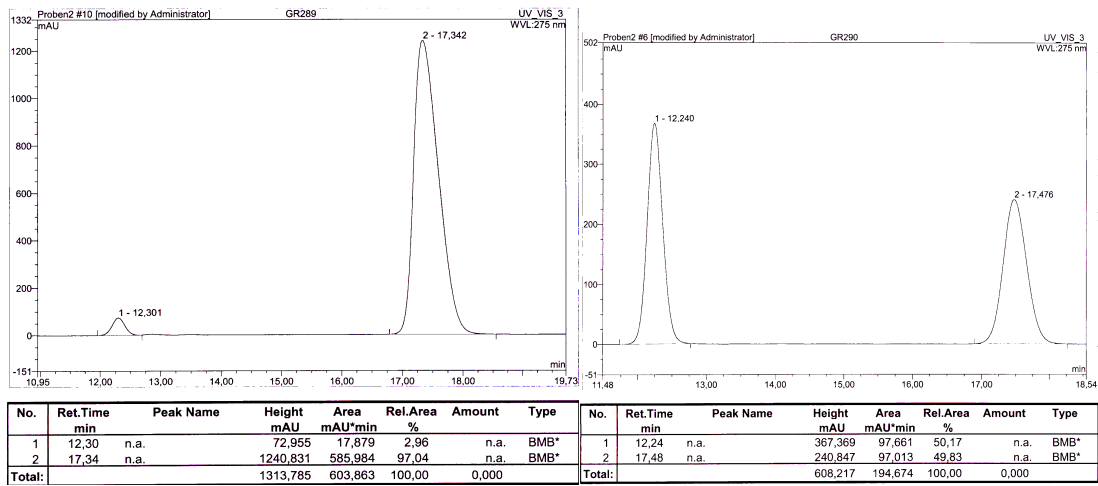
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	43.56	n.a.	472,239	706,999	98,81	n.a.	BMB*
2	48.66	n.a.	9,977	8,500	1,19	n.a.	BMB*
Total:			482,216	715,499	100,00	0,000	



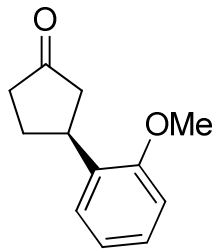
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	43.56	n.a.	431,683	567,373	50,17	n.a.	BM *
2	46.96	n.a.	373,334	563,512	49,83	n.a.	MB*
Total:			805,016	1130,885	100,00	0,000	

(S)-3-(Naphthalen-1-yl)cyclopentanone (9b):**HPLC Data:**

Chiralcel AS-H; *n*-heptane : *i*-propanol 80:20; flow: 0.7 mL/min

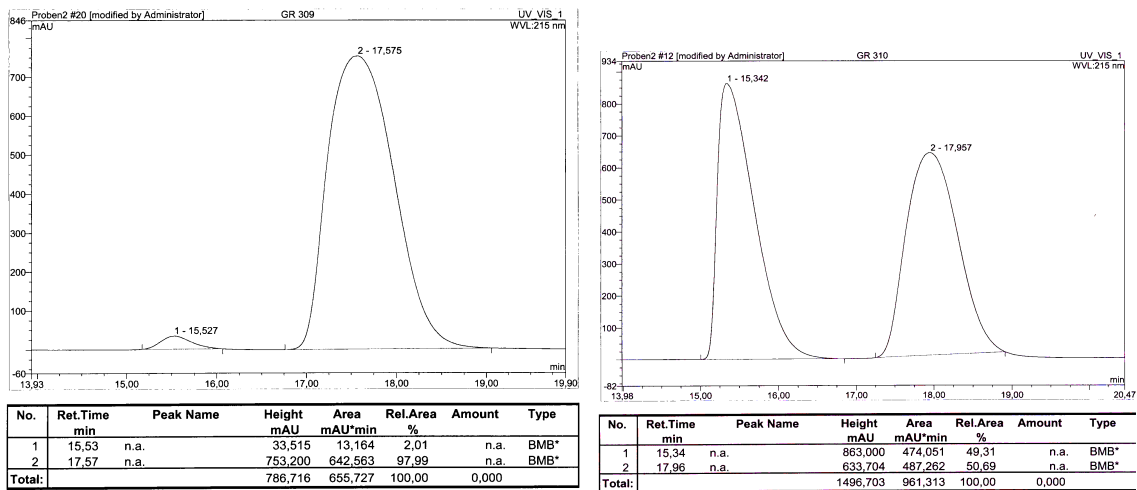


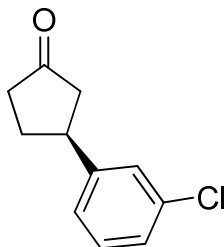
(S)-3-(2-Methoxyphenyl)cyclopentanone (9c):



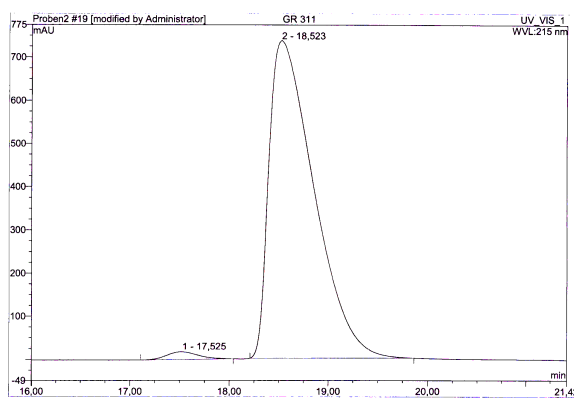
HPLC Data:

Chiralcel OB-H; *n*-heptane : *i*-propanol 90:10; flow: 0.7 mL/min

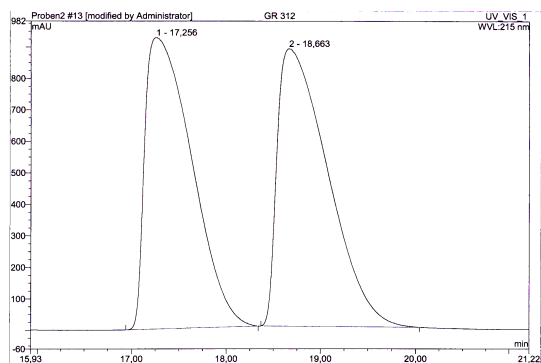


(S)-3-(3-Chlorophenyl)cyclopentanone (9d):**HPLC Data:**

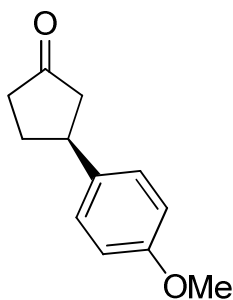
Chiralcel OB-H; *n*-heptane : *i*-propanol 90:10; flow: 0.7 mL/min



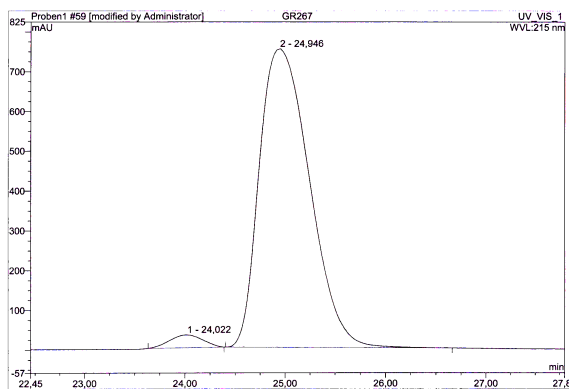
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17,52	n.a.	17,980	6,466	1,64	n.a.	BMB*
2	18,52	n.a.	735,924	388,524	98,36	n.a.	BMB*
Total:			753,804	394,990	100,00	0,000	



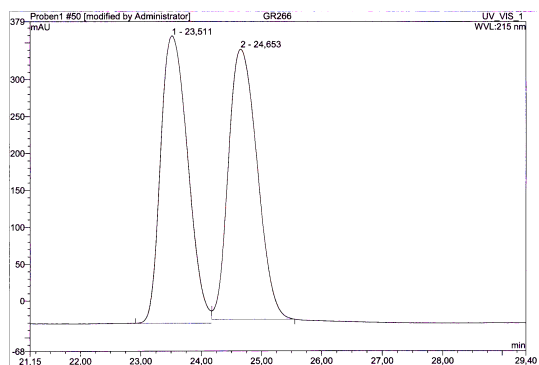
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17,26	n.a.	926,337	530,386	49,20	n.a.	BMB*
2	18,66	n.a.	881,861	547,564	50,80	n.a.	BMB*
Total:			1808,198	1077,950	100,00	0,000	

(S)-3-(4-Methoxyphenyl)cyclopentanone (9e):**HPLC Data:**

Chiralcel OD-H; *n*-heptane : *i*-propanol 95:5; flow: 0.5 mL/min

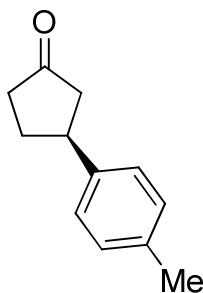


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	24.02	n.a.	32,131	12,270	2.73	n.a.	BMB*
2	24.95	n.a.	750,315	437,335	97.27	n.a.	BMB*
Total:			782,446	449,605	100.00	0.000	



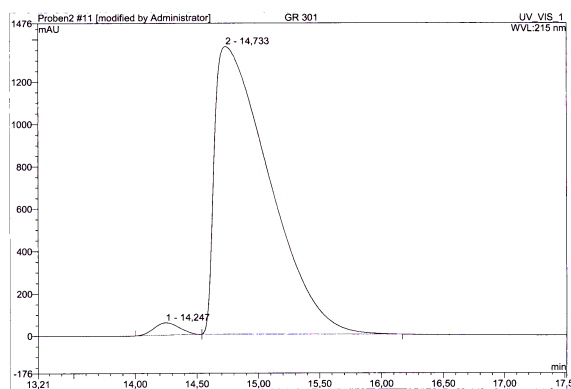
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	23.51	n.a.	390,167	202,315	49.89	n.a.	BM*
2	24.65	n.a.	366,642	203,230	50.11	n.a.	MB*
Total:			756,809	405,545	100.00	0.000	

(S)-3-(p-Tolyl)cyclopentanone (9f):

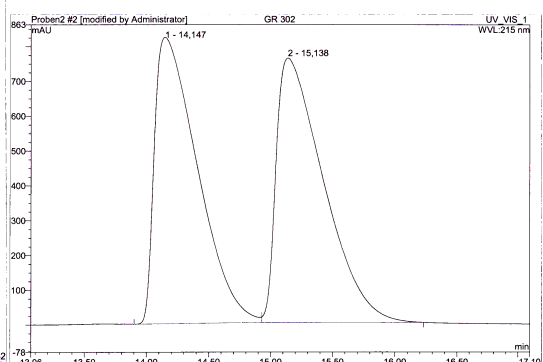


HPLC Data:

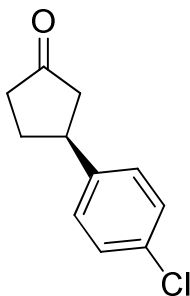
Chiralcel OB-H; *n*-heptane : *i*-propanol 95:5; flow: 0.7 mL/min



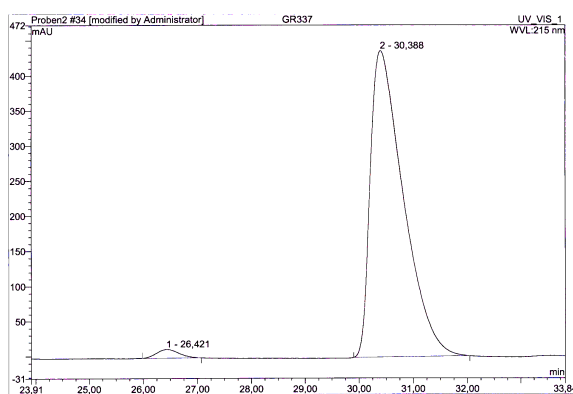
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14.25	n.a.	58,582	13,882	1.94	n.a.	BMB*
2	14.73	n.a.	1359,642	701,284	98.06	n.a.	BMB*
Total:			1418,223	715,166	100.00	0.000	



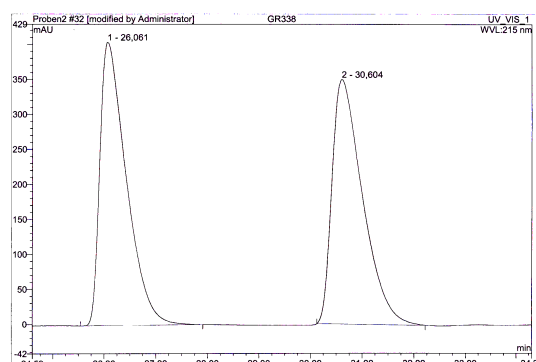
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14.15	n.a.	823,557	329,626	49.49	n.a.	BM*
2	15.14	n.a.	760,584	336,375	50.51	n.a.	MB*
Total:			1584,142	666,002	100.00	0.000	

(S)-3-(4-Chlorophenyl)cyclopentanone (9g):**HPLC Data:**

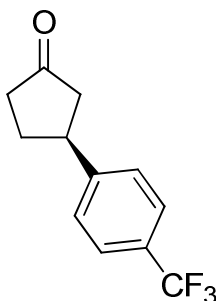
Chiralcel OB-H; *n*-heptane : *i*-propanol 90:10; flow: 0.5 mL/min



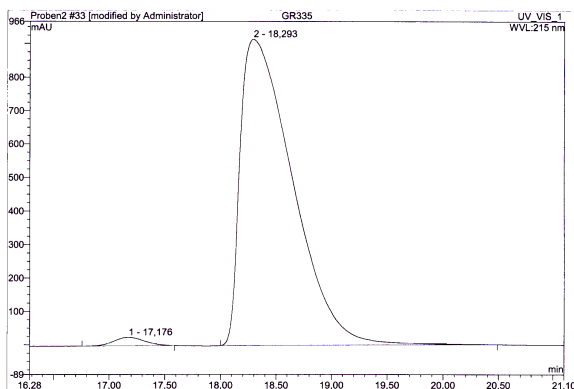
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	26.42	n.a.	12.359	5.858	1.87	n.a.	BMB*
2	30.39	n.a.	436.689	307.479	98.13	n.a.	BMB*
Total:			449.048	313.337	100.00	0.000	



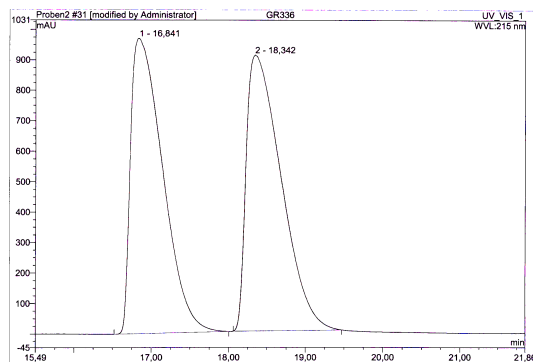
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	26.06	n.a.	404.686	239.906	50.15	n.a.	BMB*
2	30.60	n.a.	349.416	238.456	49.85	n.a.	BMB*
Total:			754.102	478.361	100.00	0.000	

(S)-3-(4-(Trifluoromethyl)phenyl)cyclopentanone (9h):**HPLC Data:**

Chiralcel OB-H; *n*-heptane : *i*-propanol 90:10; flow: 0.5 mL/min

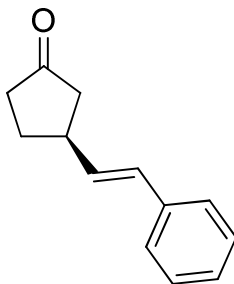


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17,18	n.a.	25,432	8,060	1,58	n.a.	BMB*
2	18,29	n.a.	915,354	501,940	98,42	n.a.	BMB*
Total:			940,786	510,000	100,00	0,000	



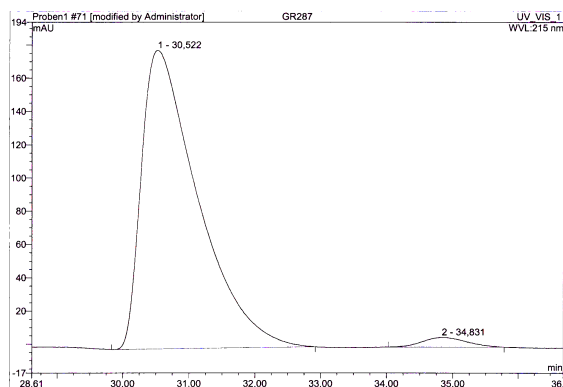
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	16,84	n.a.	970,380	465,800	49,35	n.a.	BMB*
2	18,34	n.a.	906,881	478,027	50,65	n.a.	BMB*
Total:			1877,261	943,828	100,00	0,000	

(*S,E*)-3-Styrylcyclopentanone (**9i**):

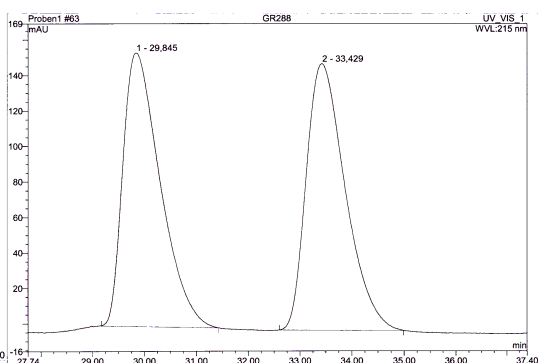


HPLC Data:

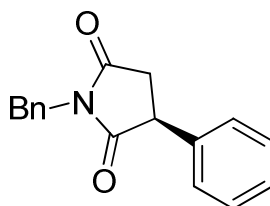
Chiralcel OD-H; *n*-heptane : *i*-propanol 99:1; flow: 1.0 mL/min



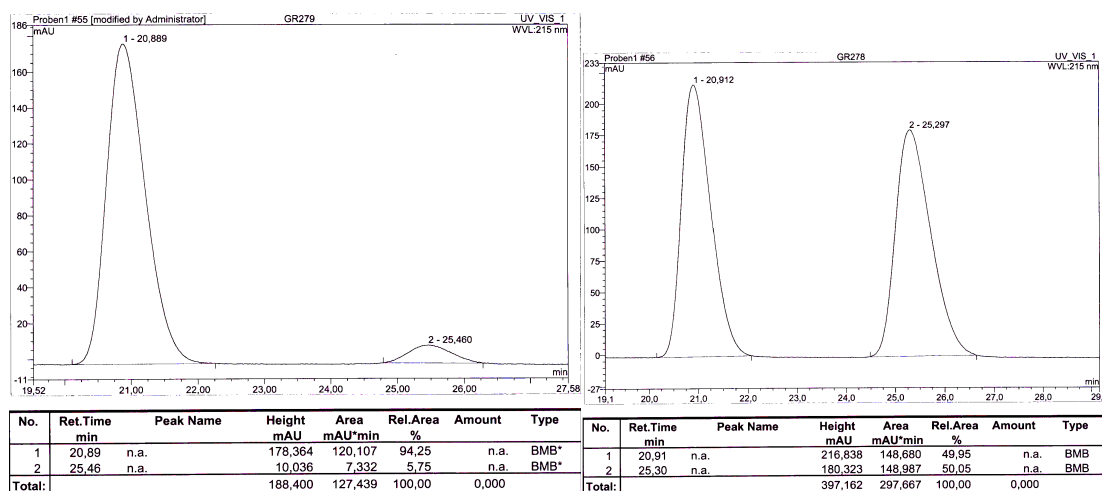
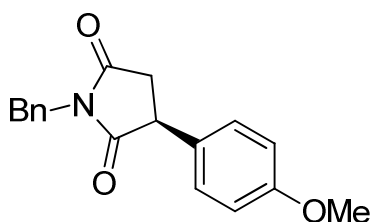
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	30,52	n.a.	179,790	177,514	97,53	n.a.	BMB*
2	34,83	n.a.	5,882	4,505	2,47	n.a.	BMB*
Total:			185,672	182,018	100,00	0,000	



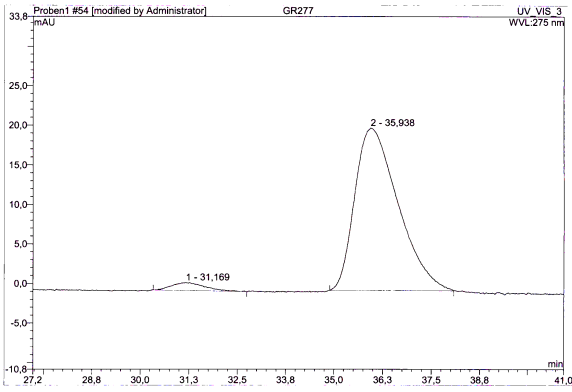
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	29,85	n.a.	154,272	127,953	49,44	n.a.	BMB
2	33,43	n.a.	150,397	130,853	50,56	n.a.	BMB
Total:			304,670	258,806	100,00	0,000	

(S)-1-Benzyl-3-phenylpyrrolidine-2,5-dione (10a):**HPLC Data:**

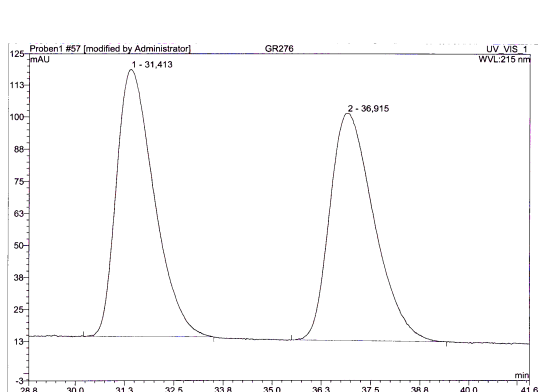
Chiralcel OD-H; *n*-heptane : *i*-propanol 90:10; flow: 1.0 mL/min

**(S)-1-Benzyl-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10b):****HPLC Data:**

Chiralcel OD-H; *n*-heptane : *i*-propanol 90:10; flow: 1.0 mL/min



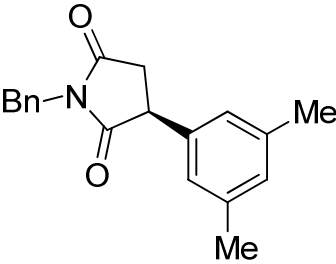
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	31,17	n.a.	1,012	0,983	3,58	n.a.	BMB*
2	35,94	n.a.	20,532	26,454	96,42	n.a.	BMB
Total:			21,545	27,438	100,00	0,000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	31,41	n.a.	104,246	115,257	49,98	n.a.	BMB*
2	36,92	n.a.	88,695	115,361	50,02	n.a.	BMB*
Total:			192,940	230,618	100,00	0,000	

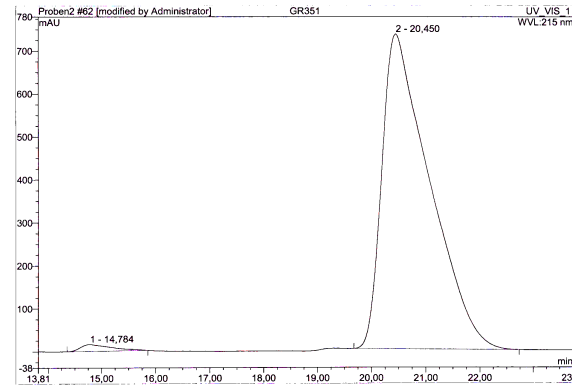
(S)-1-Benzyl-3-(3,5-dimethylphenyl)pyrrolidine-2,5-dione

(10c):

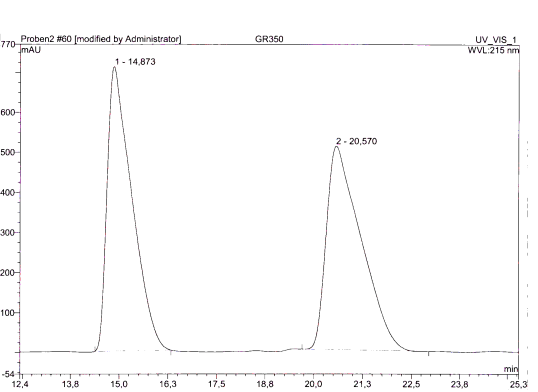


HPLC Data:

Chiralcel AD-H; *n*-heptane : *i*-propanol 95:5; flow: 1.0 mL/min

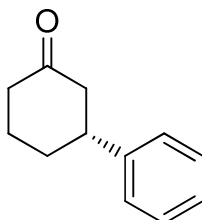


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,78	n.a.	15,824	10,576	1,40	n.a.	BMB*
2	20,45	n.a.	734,654	746,341	98,60	n.a.	BMB*
Total:			750,478	756,917	100,00	0,000	

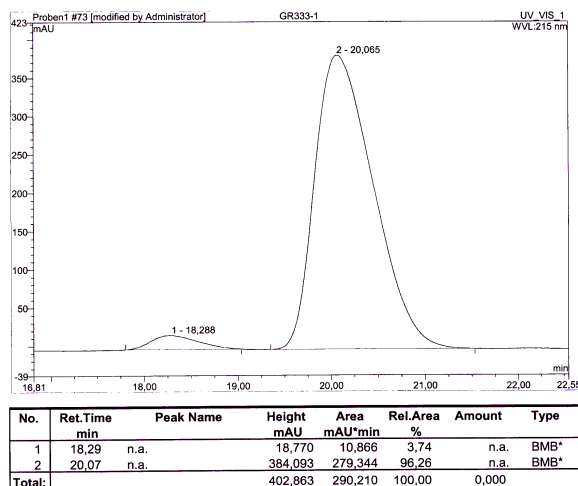
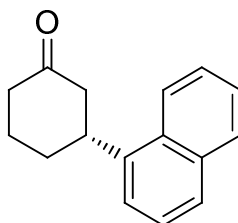


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,87	n.a.	710,604	521,982	49,93	n.a.	BMB*
2	20,57	n.a.	509,225	523,411	50,07	n.a.	BMB*
Total:			1219,829	1045,394	100,00	0,000	

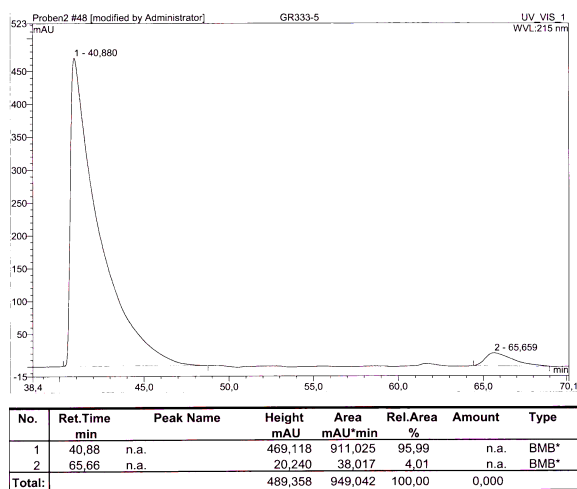
Compounds of Table 2

(*R*)-3-Phenylcyclohexanone (11a):**HPLC Data:**

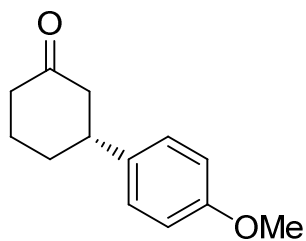
Chiralcel AD; *n*-heptane : *i*-propanol 90:10; flow: 0.3 mL/min

**(*R*)-3-(Naphthalen-1-yl)cyclohexanone (11b):****HPLC Data:**

Chiralcel OD-H; *n*-heptane : *i*-propanol 95:5; flow: 0.5 mL/min



(R)-3-(4-Methoxyphenyl)cyclohexanone (11c):



HPLC Data:

Chiralcel AD-H; *n*-heptane : *i*-propanol 98:2; flow: 0.5 mL/min

