Preparation and Reactions of Enantiomerically Pure α-Functionalised Grignard Reagents

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1. Experimental details

1.1 General

Water is distilled water. Brine refers to a saturated aqueous solution of NaCl. All non-aqueous reactions were carried out under oxygen-free Ar using flame-dried glassware. Alkyllithiums were titrated against *N*-benzylbenzamide before use.[1] All diamines and electrophiles were distilled over CaH_2 before use. Et_2O and THF were freshly distilled from sodium and benzophenone ketyl. Petrol refers to the fraction of petroleum ether boiling in the range 40-60 °C.

Flash column chromatography was carried out using Fluka Chemie GmbH silica (220-440 mesh). Thin layer chromatography was carried out using Merck F_{254} aluminium-backed silica plates. ^1H (400 MHz) and ^{13}C (100.6 MHz) NMR spectra were recorded on a Jeol ECX-400 instrument with an internal deuterium lock. Chemical shifts are quoted as parts per million and referenced to $CHCl_3$ (δ_H 7.27) and or $CDCl_3$ (δ_C 77.0, central line of triplet). ^{13}C NMR spectra were recorded with broadband proton decoupling. ^{13}C NMR spectra were assigned using DEPT experiments. Coupling constants (*J*) are quoted in Hertz. IR spectra were recorded on an ATI Matteson Genesis FT-IR spectrometer. Melting points were measured on a Gallenkamp melting point apparatus. Electrospray high and low resolution mass spectra were recorded on a Bruker Daltronics microOTOF spectrometer. Chiral stationary phase HPLC was performed on an Agilent 1200 series instrument and a multiple wavelength, UV/Vis diode array detector; integration was normally performed at 230 nm.

The following compounds were made according to the reported procedures: *O*-alkyl carbamate **8**,[2] *O*-alkyl carbamate **10**,[3] (+)-sparteine surrogate,[4] diamines (*R*,*R*)-**12** and (*S*,*S*)-**12**[5] and isobutyl boronic acid pinacol ester.[6]

1.2 Experimental Procedures and Characterisation Data

General Procedure A: *s*-BuLi/diamine-mediated lithiation-electrophilic trapping of *O*-alkyl carbamate 8 (Table 1, "Normal, A")

s-BuLi (0.92 mL of a 1.3 M solution in hexanes, 1.20 mmol, 1.2 eq.) was added dropwise to a stirred solution of carbamate **8** (263 mg, 1.00 mmol, 1.0 eq.) and diamine (1.20 mmol, 1.2 eq.) in Et_2O (6 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h. Then, the electrophile (2.00 mmol, 2.0 eq.) was added dropwise and the solution was allowed to warm to rt over 2 h and stirred at rt for 16 h. Saturated $NH_4Cl_{(aq)}$ (10 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

General Procedure B: *s*-BuLi/diamine-mediated lithiation-electrophilic trapping of *O*-alkyl carbamate 8 (Table 1, "Normal, B")

s-BuLi (0.92 mL of a 1.3 M solution in hexanes, 1.20 mmol, 1.2 eq.) was added dropwise to a stirred solution of carbamate **8** (263 mg, 1.00 mmol, 1.0 eq.) and diamine (1.20 mmol, 1.2 eq.) in Et_2O (6 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h. Then, the electrophile (2.00 mmol, 2.0 eq.) was added dropwise and the solution was stirred at −78 °C for 5 min. Then, MeOH (2 mL) was added and the resulting solution was allowed to warm to rt over 30 min. The solution was poured into 1 M $HCl_{(aq)}$ (10 mL) and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

General Procedure C: *s*-BuLi/diamine-mediated lithiation-electrophilic trapping of *O*-alkyl carbamate 8 with reverse addition to Andersen's sulfinate (S_s)-3 (Table 1, "Reverse, B")

s-BuLi (0.92 mL of a 1.3 M solution in hexanes, 1.20 mmol, 1.2 eq.) was added dropwise to a stirred solution of carbamate **8** (263 mg, 1.00 mmol, 1.0 eq.) and diamine (1.20 mmol, 1.2 eq.) in Et_2O (6 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h and then added dropwise *via* cannula transfer to a stirred solution of Andersen's sulfinate (S_s)-**3** (589 mg, 2.00 mmol, 2.0 eq.) in THF (4 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 5 min. Then, $MeOH_{(aq)}$ (2 mL) was added and the resulting solution was allowed to warm

to rt over 30 min. The solution was poured into 1 M $HCl_{(aq)}$ (10 mL) and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

General Procedure D: Sulfoxide → Magnesium Exchange Reactions

i-PrMgCl (0.13-0.25 mL of a 2.0 M solution in THF, 0.26-0.50 mmol, 1.3-2.5 eq.) was added dropwise to a stirred solution of the sulfoxide (0.20 mmol, 1.0 eq.) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1-30 min. Then, the electrophile (0.26-0.50 mmol, 1.3-2.5 eq.) was added dropwise and the resulting solution was stirred at rt for 5 min. Saturated $NH_4Cl_{(aq)}$ (7 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

General Procedure E: *s*-BuLi/diamine-mediated lithiation-electrophilic trapping of 4-chloro *N*-Boc piperidine 25 (Table 3, "Normal, A")

s-BuLi (1.69 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.) was added dropwise to a stirred solution of *N*-Boc 4-chloro piperidine **25** (219 mg, 1.0 mmol, 1.0 eq.) and diamine (2.20 mmol, 2.2 eq.) in Et_2O (6 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h. Then, the electrophile (2.20 mmol, 2.2 eq.) was added dropwise. The solution was allowed to warm to rt over 2 h and stirred at rt for 16 h. Saturated $NH_4Cl_{(aq)}$ (10 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

General Procedure F: *s*-BuLi/diamine-mediated lithiation-electrophilic trapping of 4-chloro *N*-Boc piperidine 25 (Table 3, "Normal, B")

s-BuLi (1.69 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.) was added dropwise to a stirred solution of *N*-Boc 4-chloro piperidine **25** (219 mg, 1.0 mmol, 1.0 eq.) and diamine (2.20 mmol, 2.2 eq.) in Et_2O (6 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h. Then, the electrophile (2.20 mmol, 2.2 eq.) was added dropwise and the solution was stirred at −78 °C for 5 min. Then, MeOH (2 mL) was added and the resulting solution was

allowed to warm to rt over 30 min. The solution was poured into 1 M $HCl_{(aq)}$ (10 mL) and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

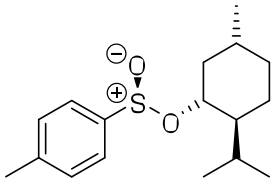
General Procedure G: *s*-BuLi/diamine-mediated lithiation of 4-chloro *N*-Boc piperidine 25 with reverse addition to Andersen's sulfinate (S_S)- 5 (Table 3, "Reverse, B")

s-BuLi (1.69 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.) was added dropwise to a stirred solution of *N*-Boc 4-chloro piperidine **25** (219 mg, 1.0 mmol, 1.0 eq.) and diamine (2.20 mmol, 2.2 eq.) in Et_2O (6 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h and then added dropwise *via* cannula transfer to a stirred solution of Andersen's sulfinate (S_S)-**3** (647 mg, 2.20 mmol, 2.2 eq.) in THF (5 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 5 min. Then, MeOH (2 mL) was added and the resulting solution was allowed to warm to rt over 30 min. The solution was poured into 1 M $HCl_{(aq)}$ (10 mL) and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

General Procedure H: Sulfoxide → Magnesium Exchange Reactions with Transmetallation-Negishi Coupling

i-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.5 mmol, 2.5 eq.) was added dropwise to a stirred solution of sulfoxide *syn*-(*R*,*R*,S_S)-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, $ZnCl_2$ (0.12 mmol of a 1.0 M solution in Et_2O, 0.6 eq.) was added dropwise. The solution was stirred at rt for 30 min. Then, $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and aryl bromide (0.24 mmol, 1.2 eq.) were added sequentially. The resulting brown solution was stirred at rt for 16 h. Then, $NH_4OH_{(aq)}$ (0.1 mL) was added and the resulting solution was stirred for 30 min. The solids were removed by filtration through Celite® and the filtrate was washed with water (5 mL). The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

(*S*)-(−)-Menthyl *p*-toluenesulfinate (S_S)-3

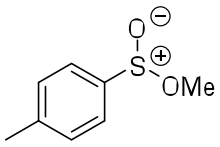


(S_S)-**3**

Thionyl chloride (46.0 mL, 828 mmol, 4.5 eq.) was added dropwise to a stirred suspension of sodium *p*-toluenesulfinate (dried *via* azeotropic distillation from 3 x 75 mL toluene, 32.8 g, 184 mmol, 1.0 eq.) in toluene (110 mL) at 0 °C over 30 min. The resulting solution was then stirred at rt for 2 h. Then, the volatiles were evaporated under reduced pressure and the residue was dissolved in toluene (75 mL). The volatiles were then evaporated under reduced pressure to give the crude sulfinyl chloride. The crude sulfinyl chloride was dissolved in Et_2O (90 mL) and added dropwise over 30 min to a stirred solution of (−)-menthol (35.9 g, 230 mmol, 1.25 eq.) in pyridine (33 mL) and Et_2O (150 mL) at 0 °C. A white precipitate immediately formed and the resulting suspension was stirred at rt for 16 h. Then, the suspension was poured into water (150 mL) and the two layers were separated. The aqueous layer was extracted with Et_2O (2 x 50 mL) and the combined organic layers were washed with 1 M $HCl_{(aq)}$ (3 x 60 mL), dried (Na_2SO_4) and evaporated under reduced pressure. The resulting solid was recrystallised from hot acetone (20 mL). A second recrystallisation of the solid from hot acetone (20 mL) gave Andersen's sulfinate (S_S)-**3** as colourless needles (8.65 g, 16%). Then, 3 drops of conc. $HCl_{(aq)}$ were added to the mother liquor to effect equilibrium of the sulfinate diastereomers. This resulted in crystallisation of Andersen's sulfinate (S_S)-**3**. A recrystallisation of the solid from hot acetone (20 mL) gave Andersen's sulfinate (S_S)-**3** as colourless needles (18.23 g, 34%). Total yield from two crops = 26.88 g (50 %) as colourless needles, mp 107-108 °C (lit.,[7] mp 107-109 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.33 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 4.13 (td, J = 10.5, 4.5 Hz, 1H, CHOS(O)), 2.42 (s, 3H, C_6H_4Me), 2.31-2.26 (m, 1H), 2.14 (dtd, J = 14.0, 7.0, 3.0 Hz, 1H), 1.72-1.66 (m, 2H), 1.50 (m, 1H), 1.36 (ddt, J = 14.0, 10.5, 3.0 Hz, 1H), 1.28-1.24 (m, 1H), 1.10-0.79 (m, 2H), 0.97 (d, J = 8.0 Hz, 3H, Me), 0.87 (d, J = 8.0 Hz, 3H, Me), 0.72 (d, J = 8.0 Hz, 3H, Me); ^{13}C NMR (100.6 MHz,$CDCl_3$) δ 143.1 (*ipso*-Ar), 142.4 (*ipso*-Ar), 129.6 (Ar), 125.0 (Ar), 80.1 (CHO), 47.8 (CH), 42.9 (CH_2), 34.0 (CH_2), 31.7 (CH), 25.2 (CH), 23.1 (CH_2),

22.1 (CH), 21.5 (Me), 20.8 (Me), 14.4 (Me); $[\alpha]_D$ −199.3 (*c* 1.05 in acetone) (lit.,[7] $[\alpha]_D$ −204 (*c* 2.24 in acetone)). Spectroscopic data consistent with those reported in the literature.[7]

Methyl *p*-toluenesulfinate S1

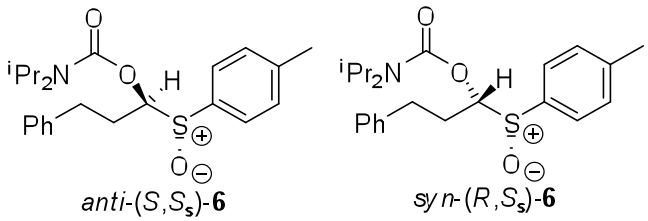


S1

Bromine (4.36 g, 1.40 mL, 27.6 mmol, 3.0 eq.) was added to a stirred suspension of Na_2CO_3 (4.87 g, 46.0 mmol, 5.0 eq.) and *p*-tolyl disulfide (2.27 g, 9.2 mmol, 1.0 eq.) in MeOH (195 mL) at rt. The resulting yellow suspension was stirred at rt for 3 h during which time the suspension became colourless. Then, the solvent was evaporated under reduced pressure. CH_2Cl_2 (100 mL) and water (100 mL) were added to the residue and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with saturated $NH_4Cl_{(aq)}$ (50 mL) and brine (50 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by Kügelrohr distillation gave sulfinate **S1** (2.93 g, 93%) as a colourless oil, bp 91-94 °C/2.0 mmHg (lit.,[8] 129-130°C/16.0 mmHg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.25 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 3.37 (s, 3H, OMe), 2.34 (s, 3H, Me); ^{13}C NMR (100.6 MHz,$CDCl_3$) δ 142.8 (*ipso*-Ar), 140.7 (*ipso*-Ar), 129.7 (Ar), 125.3 (Ar), 49.3 (OMe), 21.4 (Me). Spectroscopic data consistent with those reported in the literature.[9]

(1*S*)-1-(*p*-Tolylsulfinyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate *anti*-(*S*,S_s)-6 and (1*R*)-1-(*p*-tolylsulfinyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate *syn*-(*R*,S_s)-6

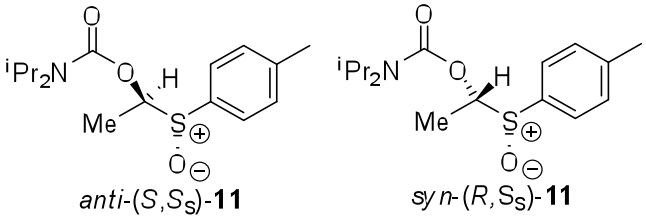
(Scheme 2 and Table 1, Entry 1)



Using general procedure A, *s*-BuLi (0.92 mL of a 1.3 M solution in hexanes, 1.20 mmol, 1.2 eq.), carbamate **8** (263 mg, 1.00 mmol, 1.0 eq.) and TMEDA (139 mg, 1.20 mmol, 1.2 eq.) in Et_2O (5 mL) and a solution of Andersen's sulfinate (S_s)-**3** (382 mg, 1.3 mmol, 1.3 eq.) in THF (1 mL) gave the crude product. Purification by flash column chromatography on silica with 3:1 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *anti-(S,*S_s*)*-**6** (100 mg, 25%, 83:17 er by CSP-HPLC) as a white solid, mp 58-60 °C; R_F (3:1 petrol-EtOAc) 0.3; IR ($CHCl_3$) 2971, 1697 (C=O), 1436, 1370, 1286, 1091, 1035, 910, 812, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.28 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 7.21 (t, J = 7.0 Hz, 2H, *m*-Ph), 7.16 (d, J = 7.0 Hz, 1H, *p*-Ph), 7.02 (d, J = 7.0 Hz, 2H, *o*-Ph), 5.45 (dd, J = 10.0, 3.0 Hz, 1H, OCH), 3.94 (br s, 2H, NCH), 2.74 (ddd, J = 14.0, 10.0, 5.0 Hz, 1H, PhCH_AH_B), 2.56 (ddd, J = 14.0, 10.0, 7.0 Hz, 1H, PhCH_AH_B), 2.40 (s, 3H, Me) 2.36-2.25 (m, 1H, CH), 2.06-1.98 (m, 1H, CH), 1.26 (br s, 12H, NCHMe_2); ^{13}C NMR (100.6 MHz,$CDCl_3$) δ 153.5 (C=O), 141.2 (*ipso*-Ar), 140.3 (*ipso*-Ar), 137.4 (*ipso*-Ar), 129.7 (Ar), 128.3 (Ar), 128.1 (Ar), 126.0 (Ar), 124.4 (Ar), 91.7 (OCH), 46.7 (br, NCH), 46.0 (br, NCH), 31.1 (CH_2), 26.0 (CH_2), 21.3 (Me), 20.2 (br, Me); MS (ESI) *m/z* 424 [(M + Na)$^+$, 100], 402 [(M + H)$^+$, 20]; HRMS *m/z* calcd for $C_{23}H_{31}NO_3S$ (M + Na)$^+$ 424.1917 (+1.3 ppm error), found 424.1911; CSP-HPLC: Chiracel OD (97.5:2.5 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*R*,R_s)-**6** 12.8 min, *anti*-(*S*,S_s)-**6** 14.0 min and sulfoxide *syn-(R,*S_s*)*-**6** (84 mg, 21%, 85:15 er by CSP-HPLC) as a colourless oil, R_F (3:1 petrol-EtOAc) 0.20; IR (film) 2971, 2968, 1707 (C=O), 1434, 1370, 1291, 1136, 1091, 1038, 809 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.28-7.24 (m, 4H, Ar), 7.21-7.14 (m, 3H, Ar), 5.72 (dd, J = 9.5, 4.0 Hz, 1H, OCH), 3.99 (br s, 1H, NCH), 3.57 (br s, 1H, NCH), 2.79-2.75 (m, 2H, PhCH_2), 2.41-2.33 (m, 1H, CH), 2.37 (s, 3H, Me), 2.17-2.08 (m, 1H, CH), 1.21-0.99 (m, 12H, CHMe_2); ^{13}C NMR

(100.6 MHz,$CDCl_3$) δ 152.3 (C=O), 141.5 (*ipso*-Ar), 140.3 (*ipso*-Ar), 136.0 (*ipso*-Ar), 129.5 (Ar), 128.5 (Ar), 128.4 (Ar), 126.3 (Ar), 125.3 (Ar), 86.8 (OCH), 46.3 (br, NCH) 45.9 (br, NCH), 31.7 (CH_2), 30.3 (CH_2), 21.3 (Me), 21.1 (Me), 20.8 (Me), 20.2 (Me), 20.1 (Me); MS (ESI) *m/z* 424 [$(M + Na)^+$, 90], 402 [$(M + H)^+$, 100]; HRMS *m/z* calcd for $C_{23}H_{31}NO_3S$ $(M + Na)^+$ 424.1917, found 424.1905 (+2.7 ppm error); CSP-HPLC: Chiracel OD (97.5:2.5 Hexane-*i*PrOH, 1.0 mL min^{-1}) *syn*-(*S*,R_s)-**6** 21.3 min, *syn*-(*R*,S_s)-**6** 23.8 min.

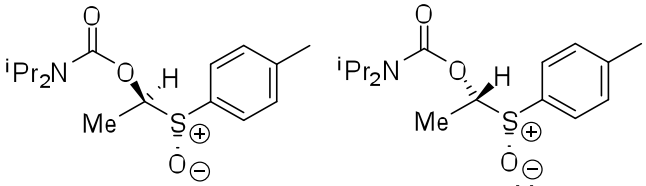
(1*S*)-(*p*-Tolylsulfinyl)-ethyl *N*,*N*-diisopropylcarbamate *anti*-(*S*,S_s)-11 and (1*R*)-(*p*-Tolylsulfinyl)-ethyl *N*,*N*-diisopropylcarbamate *syn*-(*R*,S_s)-11



Using general procedure A, *s*-BuLi (1.85 mL of a 1.3 M solution in hexanes, 2.40 mmol, 1.2 eq.), carbamate **10** (346 mg, 2.00 mmol, 1.0 eq.) and diamine (*S*,*S*)-**12** (744 mg, 2.40 mmol, 1.2 eq.) in Et_2O (12 mL) and a solution of Andersen's sulfinate (S_s)-**3** (1.18 g, 4.0 mmol, 2.0 eq.) in THF (10 mL) gave the crude product. Purification by flash column chromatography on silica with 3:1 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *anti*-(*S*,S_s)-**11** (24 mg, 4%, er not determined) as a colourless oil, R_F (7:3 petrol-EtOAc) 0.4; IR (film) 2971, 2959, 1694 (C=O), 1531, 1475, 1312, 1296, 1050, 910, 854, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.32 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 5.52 (q, J = 6.5 Hz, 1H, OCH), 4.04 (br s, 1H, NCH), 3.86 (br s, 1H, NCH), 2.40 (s, 3H, Me) 1.36 (d, J = 6.5 Hz, 1H, Me), 1.29-1.21 (br m, 12H, NCH*Me*$_2$); ^{13}C NMR (100.6 MHz,$CDCl_3$) δ 153.8 (C=O), 141.2 (*ipso*-Ar), 137.7 (*ipso*-Ar), 129.8 (Ar), 124.3 (Ar), 89.3 (OCH), 46.8 (br, NCH), 45.9 (br, NCH), 21.5 (br, Me), 21.4 (Me), 20.3 (br, Me), 9.4 (Me); MS (ESI) *m/z* 334 [$(M + Na)^+$, 100], 312 [$(M + H)^+$, 80]; HRMS *m/z* calcd for $C_{16}H_{25}NO_3S$ $(M + Na)^+$ 334.1447 (−0.1 ppm error), found 334.1448 and sulfoxide *syn*-(*R*,S_s)-**11** (55 mg, 9%, er not determined) as a colourless oil, R_F (7:3 petrol-EtOAc) 0.30; IR (film) 2992, 2978, 2970, 1700 (C=O), 1530, 1472, 1450, 1390, 1291, 1122, 1078, 910, 730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.29 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 5.80 (q, J = 6.5 Hz, 1H, OCH), 3.90 (br s, 1H, NCH), 3.70 (br s, 1H, NCH), 2.39 (s,

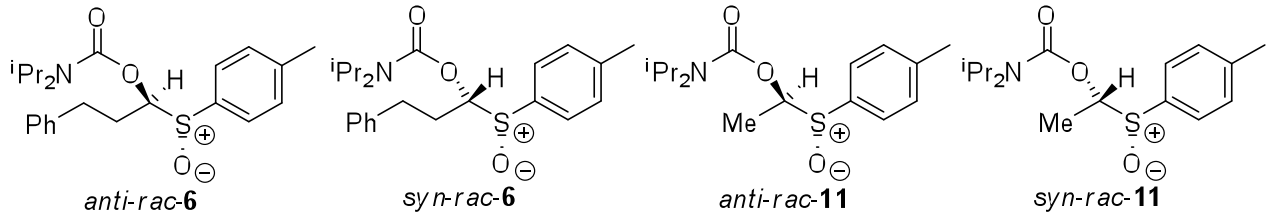
3H, Me), 1.48 (d, J = 6.5 Hz, 1H, Me), 1.15-1.04 (m, 12H, CH*Me*$_2$), ^{13}C NMR (100.6 MHz,$CDCl_3$) δ 152.5 (C=O), 141.7 (*ipso*-Ar), 136.0 (*ipso*-Ar), 129.4 (Ar), 125.4 (Ar), 84.0 (OCH), 47.6 (NCH) 46.1 (NCH), 21.5 (Me), 21.4 (Me), 20.8 (Me), 20.5 (Me), 20.1 (Me), 13.7 (Me); MS (ESI) *m/z* 334 [$(M + Na)^+$, 70], 312 [$(M + H)^+$, 100]; HRMS *m/z* calcd for $C_{16}H_{25}NO_3S$ $(M + Na)^+$ 334.1447, found 334.1447 (+0.1 ppm error).

1-(*p*-Tolylsulfinyl)-ethyl *N*,*N*-diisopropylcarbamate *anti-rac*-11 and 1-(*p*-tolylsulfinyl)-ethyl *N*,*N*-diisopropylcarbamate *syn-rac*-11



Using general procedure A, *s*-BuLi (0.92 mL of a 1.3 M solution in hexanes, 1.20 mmol, 1.2 eq.), carbamate **10** (173 mg, 1.00 mmol, 1.0 eq.) and TMEDA (179 μL, 1.20 mmol, 1.2 eq.) in Et_2O (5 mL) and methyl *p*-tolyl sulfinate **S1** (255 mg, 1.5 mmol, 1.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 3:1 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *anti-rac*-**11** (90 mg, 29%) as a colourless oil and sulfoxide *syn-rac*-**11** (69 mg, 22%) as a colourless oil.

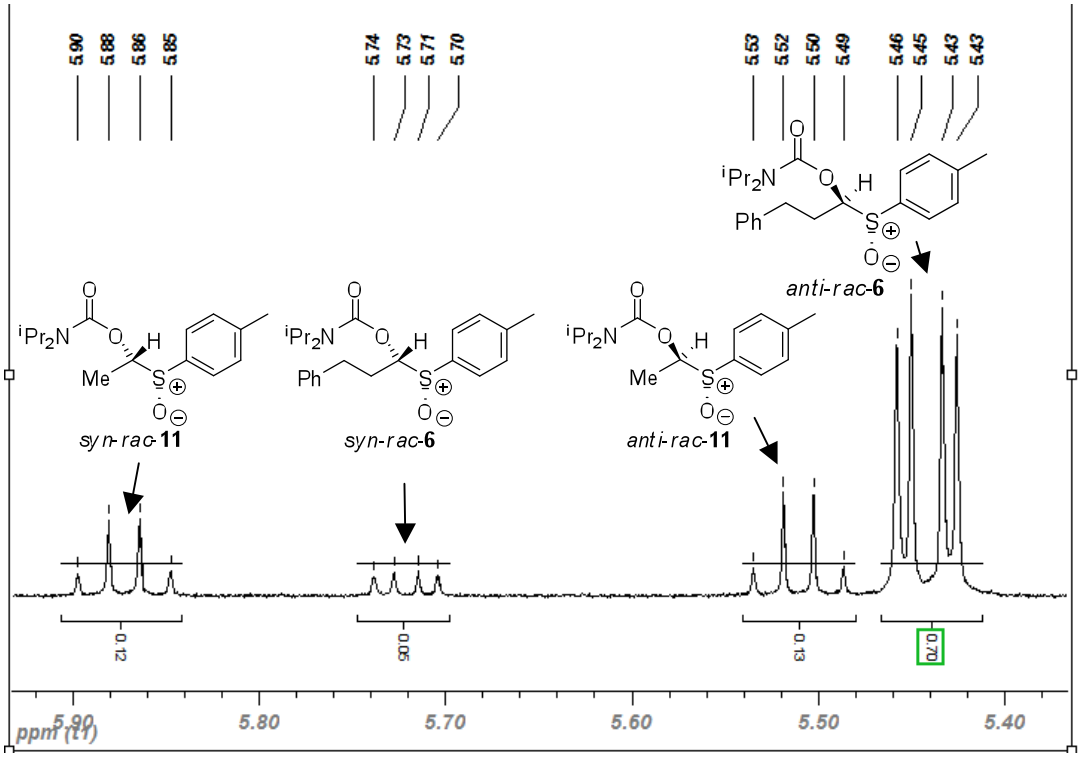
1-(*p*-Tolylsulfinyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate *anti-rac*-6, 1-(*p*-tolylsulfinyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate *syn-rac*-6, 1-(*p*-tolylsulfinyl)-ethyl *N*,*N*-diisopropylcarbamate *anti-rac*-11 and 1-(*p*-tolylsulfinyl)-ethyl *N*,*N*-diisopropylcarbamate *syn-rac* 11 (Scheme 4)



s-BuLi (0.38 mL of a 1.3 M solution in hexanes, 0.50 mmol, 1.0 eq.) was added to a stirred solution of carbamate **10** (87 mg, 0.50 mmol, 1.0 eq.) and TMEDA (75 μL, 0.50 mmol, 1.0 eq.)

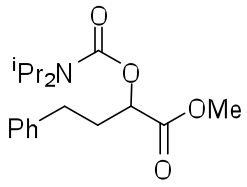
in Et_2O (5 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 h. Then, a solution of sulfoxide *anti-rac*-**6** (200 mg, 0.50 mmol, 1.0 eq.) in Et_2O (2 mL) was added dropwise and the resulting solution was stirred at −78 °C for 1 h. MeOH (1 mL) was added and the solution was warmed to rt over 30 min. The solution was poured into saturated $NH_4Cl_{(aq)}$ (10 mL) and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 4:1-3:1 petrol-EtOAc + 1% Et_3N as eluent gave recovered carbamate **10** (51 mg, 59%) as a colourless oil and a 70:5:13:12 mixture (by ^1H NMR spectroscopy) of sulfoxides *anti-rac*-**6**, *syn-rac*-**6**, *anti-rac*-**11**, *syn-rac*-**11** (180 mg, 66%, 5%, 13%, 12% respectively based on sulfoxide *anti-rac*-**6**) as a pale yellow oil.

Part of the ^1H NMR spectrum of the 70:5:13:12 mixture of sulfoxides *anti-rac*-6, *syn-rac*-6, *anti-rac*-11, *syn-rac*-11

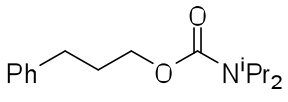


Optimisation of Sulfoxide → Mg Exchange Reaction (Table 2)

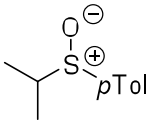
Methyl 2-[(*N*,*N*-diisopropylcarbamoyl)oxy]-4-phenylbutanoate *rac*-13, *O*-alkyl carbamate 8, and *i*-propyl *p*-tolyl sulfoxide *rac*-14



rac-**13**



8



rac-**14**

(Table 2, Entry 1)

Using general procedure D, *i*-PrMgCl (0.13 mL of a 2.0 M solution in THF, 0.26 mmol, 1.3 eq.) and sulfoxide *anti*-*rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 5 min and methyl chloroformate (25 mg, 0.26 mmol, 1.3 eq.) at rt for 5 min gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester *rac*-**46** (27 mg, 48%) as a colourless oil, *O*-alkyl carbamate **8** (9 mg, 14%) as a colourless oil, recovered sulfoxide *anti*-*rac*-**6** (8 mg, 4%) and sulfoxide *rac*-**14** (30 mg, 81%). Full characterisation data is presented later.

(Table 2, Entry 2)

Using general procedure D, *i*-PrMgCl (0.13 mL of a 2.0 M solution in THF, 0.26 mmol, 1.3 eq.) and sulfoxide *anti*-*rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and methyl chloroformate (25 mg, 0.26 mmol, 1.3 eq.) at rt for 5 min gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester *rac*-**13** (37 mg, 65%) as a colourless oil, *O*-alkyl carbamate **8** (4 mg, 6%) as a colourless oil, recovered sulfoxide *anti*-*rac*-**6** (16 mg, 8%) and sulfoxide *rac*-**14** (27 mg, 73%). Full characterisation data is presented later.

(Table 2, Entry 3)

Using general procedure D, *i*-PrMgCl (0.15 mL of a 2.0 M solution in THF, 0.30 mmol, 1.5 eq.) and sulfoxide *anti*-*rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 5 min and methyl

chloroformate (29 mg, 0.30 mmol, 1.5 eq.) at rt for 5 min gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester *rac*-**13** (24 mg, 42%) as a colourless oil, *O*-alkyl carbamate **8** (9 mg, 17%) as a colourless oil and sulfoxide *rac*-**14** (30 mg, 82%). Full characterisation data is presented later.

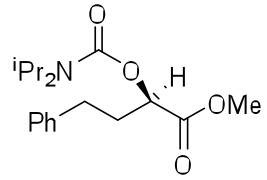
(Table 2, Entry 4)

Using general procedure D, *i*-PrMgCl (0.15 mL of a 2.0 M solution in THF, 0.30 mmol, 1.5 eq.) and sulfoxide *anti*-*rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and methyl chloroformate (29 mg, 0.30 mmol, 1.5 eq.) at rt for 5 min gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester *rac*-**13** (38 mg, 67%) as a colourless oil, *O*-alkyl carbamate **8** (6 mg, 9%) as a colourless oil and sulfoxide *rac*-**14** (31 mg, 84%). Full characterisation data is presented later.

(Table 2, Entry 5)

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti*-*rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and methyl chloroformate (48 mg, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester *rac*-**13** (48 mg, 75%) as a colourless oil, *O*-alkyl carbamate **8** (2.5 mg, 5%) as a colourless oil and sulfoxide *rac*-**14** (31 mg, 84%). Full characterisation data is presented later.

Methyl (2*R*)-[*N*,*N*-(diisopropylcarbamoyl)oxy]-4-phenylbutanoate (*R*)-13

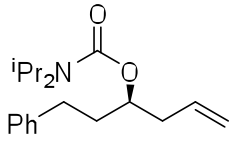


(*R*)-**13**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti*-(*S*,S_S)-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and methyl chloroformate (48 mg, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column

chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester (*R*)-**13** (46 mg, 73%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (9:1 petrol-EtOAc) 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, J = 7.5 Hz, 2H, *m*-Ph), 7.23-7.19 (m, 3H, Ph), 5.08 (t, J = 6.5 Hz, 1H, OCH), 4.11 (br s, 1H, NCH), 3.80 (br s, 1H, NCH), 3.73 (s, 3H, OMe), 2.79-2.75 (m, 2H, $PhCH_2$), 2.21-2.15 (m, 2H, CH), 1.35-1.20 (br m, 12H, NCH*Me*$_2$); ^{13}C NMR (100.6 MHz,$CDCl_3$) δ 171.6 (*C*O_2Me), 154.8 (*i*-Pr_2N*C*=O), 140.7 (*ipso*-Ph), 128.5 (Ph), 128.3 (Ph), 126.2 (Ph), 72.0 (OCH), 52.0 (OMe), 45.4 (br, NCH), 33.3 (CH_2), 31.8 (CH_2), 20.4 (br, Me); $[\alpha]_D$ −17.8 (*c* 0.55 in CH_2Cl_2) [lit.[2], $[\alpha]_D$ −17.3 (*c* 1.0 in CH_2Cl_2) for (*R*)-**13** of 97:3 er)]; CSP-HPLC: Chiracel OD (95:5 Hexane-*i*PrOH, 0.5 mL min^{-1}) (*S*)-**13** 10.7 min, (*R*)-**13** 11.9 min. Spectroscopic data consistent with those reported in the literature.[2]

1-Phenylhex-5-en-(3*R*)-yl *N*,*N*-diisopropylcarbamate (*R*)-16

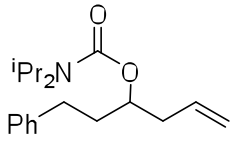


(R)-**16**

i-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) was added dropwise to a stirred solution of sulfoxide *anti*-(*S*,*S*$_s$)-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of CuBr.SMe_2 (8.2 mg, 0.04 mmol, 0.2 eq.) in THF (1.0 mL) and allyl bromide (43 μL, 0.50 mmol, 2.5 eq.) were added sequentially. The solution was stirred at rt for 2 h. Then, saturated $NH_4Cl_{(aq)}$ (10 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1 petrol-Et_2O as eluent gave carbamate (*R*)-**16** (43 mg, 70%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (9:1 petrol-Et_2O) 0.3; IR (film) 3047, 2901, 2874, 1654 (C=O), 1597, 1487, 1301, 1298, 1275, 1117, 1054, 893 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H, Ph), 7.19-7.15 (m, 3H, Ph), 5.85-5.76 (m, 1H, CH_2=C*H*), 5.11-5.04 (m, 2H, C*H*$_2$=CH), 5.00-4.93 (m, 1H, OCH), 4.10 (br s, 1H, NCH), 3.74 (br s, 1H, NCH), 2.74-2.60 (m, 2H, CH), 1.96-1.83 (m, 2H, CH), 1.25-1.21 (br

m, 12H, NCH*Me*$_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.4 (C=O), 142.0 (*ipso*-Ph), 134.1 (CH_2=*C*H), 128.4 (Ph), 128.3 (Ph) 125.8 (Ph), 117.5 (*C*H_2=CH), 73.2 (OCH), 46.2 (br, NCH), 39.0 (CH_2), 35.9 (CH_2), 31.9 (CH_2), 20.8 (br, NCH*Me*$_2$); MS (ESI) *m/z* 326 [$(M + Na)^+$, 100], 304 [$(M + H)^+$, 20]; HRMS *m/z* calcd for $C_{19}H_{29}NO_2$ $(M + Na)^+$ 326.2091, found 326.2082 (+2.5 ppm error). $[\alpha]_D$ +3.0 (*c* 0.45 in $CHCl_3$); CSP-HPLC: Chiracel OD-H (99:1 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*R*)-**16** 5.4 min, (*S*)-**16** 6.7 min.

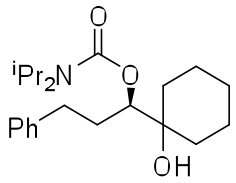
1-Phenylhex-5-en-3-yl *N*,*N*-diisopropylcarbamate *rac*-16



rac-**16**

i-PrMgCl (0.15 mL of a 2.0 M solution in THF, 0.30 mmol, 1.5 eq.) was added dropwise to a stirred solution of sulfoxide *anti-rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of $CuBr.SMe_2$ (8.2 mg, 0.04 mmol, 0.2 eq.) in THF (1.0 mL) and allyl bromide (26 μL, 0.30 mmol, 1.5 eq.) were added sequentially. The solution was stirred at rt for 2 h. Then, saturated $NH_4Cl_{(aq)}$ (10 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1 petrol-Et_2O as eluent gave carbamate *rac*-**16** (31 mg, 51%) as a colourless oil.

(1*R*)-(1-Hydroxycyclohexyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate (*R*)-17



(*R*)-**17**

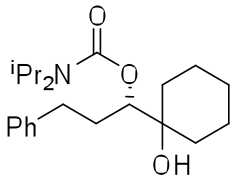
Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-(S,S$_S$)*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and cyclohexanone (52 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 95:5 CH_2Cl_2-Et_2O as eluent gave alcohol (*R*)-**17** (52 mg, 71%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (95:5 CH_2Cl_2-Et_2O) 0.2; IR (film) 3392 (OH), 2920, 2889, 1647 (C=O), 1417, 1347, 1278, 1138, 1117, 1034, 894 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H, Ph), 7.20-7.17 (m, 3H, Ph), 4.88-4.81 (m, 1H, OCH), 4.09 (br s, 1H, NCH), 3.87 (br s, 1H, NCH), 2.75-2.58 (m, 2H, CH), 1.98-1.94 (m, 2H, CH), 1.84 (br s, 1H, OH), 1.63-1.25 (br m, 22H, CH + NCH*Me*$_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.9 (C=O), 142.1 (*ipso*-Ph), 128.4 (Ph), 128.3 (Ph) 125.8 (Ph), 80.1 (OCH), 73.2 (COH), 46.5 (br, NCH), 45.4 (br, NCH), 34.3 (CH_2), 33.2 (CH_2), 32.7 (CH_2), 31.2 (CH_2), 25.8 (CH_2), 21.8 (br, NCH*Me*$_2$), 21.5 (CH_2), 21.4 (CH_2), 20.5 (br, NCH*Me*$_2$); MS (ESI) *m/z* 384 [(M + Na)$^+$, 90], 219 (100), 90 (80); HRMS *m/z* calcd for $C_{22}H_{35}NO_3$ (M + Na)$^+$ 384.2509, found 384.2493 (+4.1 ppm error); $[\alpha]_D$ +29.1 (*c* 0.6 in $CHCl_3$); CSP-HPLC: Chiracel OD (98:2 Hexane-*i*PrOH, 0.5 mLmin^{-1}) (*R*)-**17** 14.5 min, (*S*)-**17** 21.2 min.

(Scheme 8) Using general procedure D, *i*-PrMgCl (0.13 mL of a 2.0 M solution in THF, 0.25 mmol, 2.5 eq.) and sulfoxide *anti-(S,S$_S$)*-**6** (40 mg, 0.10 mmol, 1.0 eq.) in THF (4 mL) at rt for 15 min and cyclohexanone (26 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 95:5 CH_2Cl_2-Et_2O as eluent gave alcohol (*R*)-**17** (12 mg, 34%, 98:2 er by CSP-HPLC) as a colourless oil,

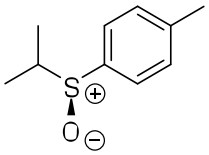
(Scheme 8) Using general procedure D, *i*-PrMgCl (0.13 mL of a 2.0 M solution in THF, 0.25 mmol, 2.5 eq.) and sulfoxide *anti-(S,S$_S$)*-**6** (40 mg, 0.10 mmol, 1.0 eq.) in THF (4 mL) at rt for 30 min and cyclohexanone (26 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash

column chromatography on silica with 95:5 CH_2Cl_2-Et_2O as eluent gave alcohol (*R*)-**17** (8.5 mg, 24%, 98:2 er by CSP-HPLC) as a colourless oil.

(1*S*)-(1-Hydroxycyclohexyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate (*S*)-17 and (*S*)-isopropyl *p*-tolyl sulfoxide (*S*)-14



(*S*)-**17**

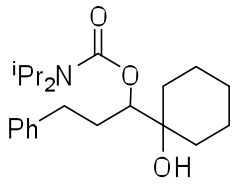


(*S*)-**14**

Using general procedure D, *i*-PrMgCl (0.43 mL of a 2.0 M solution in THF, 0.60 mmol, 2.5 eq.) and sulfoxide *syn-(R,S*$_s$*)*-**6** (96 mg, 0.24 mmol, 1.0 eq.) in THF (9 mL) at rt for 1 min and cyclohexanone (62 μL, 0.60 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 95:5 CH_2Cl_2-Et_2O as eluent gave alcohol (*S*)-**17** (65 mg, 74%, 99:1 er by CSP-HPLC) as a colourless oil, $[\alpha]_D$ −28.6 (*c* 1.0 in $CHCl_3$); CSP-HPLC: Chiracel OD (98:2 Hexane-*i*PrOH, 0.5 mLmin^{-1}) (*R*)-**17** 13.4 min, (*S*)-**17** 21.4 min and sulfoxide (*S*)-**14** (31 mg, 78%) as a colourless oil, R_F (95:5 CH_2Cl_2-Et_2O) 0.05; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.31 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 2.82 (sept, J = 7.0 Hz, 1H, S(O)CH), 2.82 (s, 3H, Me), 1.19 (d, J = 7.0 Hz, 3H, CH*Me*), 1.15 (d, J = 7.0 Hz, 3H, CH*Me*); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.5 (*ipso*-Ar), 138.5 (*ipso*-Ar), 129.6 (Ar), 125.1 (Ar), 54.6 (C*H*Me_2), 21.5 (Me), 15.8 (Me), 14.2 (Me); $[\alpha]_D$ −194.2 (*c* 1.0 in EtOH) [lit.[10], $[\alpha]_D$ −187 (*c* 2.4 in EtOH)]. Spectroscopic data consistent with those reported in the literature.[11]

The isolation of sulfoxide (*S*)-**14** allows assignment of the configuration in sulfoxides *anti-(S,S*$_s$*)*-**6** and *syn-(R,S*$_s$*)*-**6**. Sulfoxide (*S*)-**14** is the expected product of double inversion from Andersen's sulfinate (S_s)-**3**.

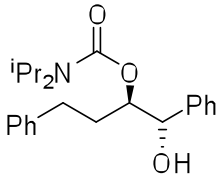
1-(1-Hydroxycyclohexyl)-3-phenylpropyl *N*,*N*-diisopropylcarbamate *rac*-17



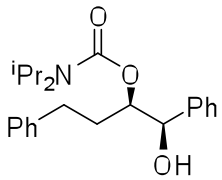
rac-**17**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti*-*rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and cyclohexanone (52 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 95:5 CH_2Cl_2-Et_2O as eluent gave alcohol *rac*-**17** (45 mg, 62%) as a colourless oil.

1-Hydroxy-1,4-diphenylbutan-2-yl *N*,*N*-diisopropylcarbamate (*R*,*S*)-18 and (*R*,*R*)-18



(*R*,*S*)-**18**

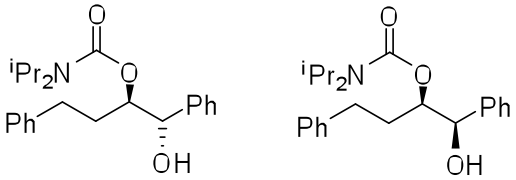


(*R*,*R*)-**18**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti*-(*S*,S_s)-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and benzaldehye (51 μL, 0.50 mmol, 2.5 eq.) gave the crude product which contained a 90:10 mixture of (*R*,*S*)-**18** and (*R*,*R*)-**18** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 95:5-9:1 petrol-EtOAc as eluent gave a 96:4 mixture (by ^{1}H NMR spectroscopy) of alcohols (*R*,*S*)-**18** and (*R*,*R*)-**18** (42 mg, 58%, each diastereoisomer 99:1 er by CSP-HPLC) as a colourless oil, R_F (9:1 petrol-EtOAc) 0.2; IR (film) 3378 (OH), 2923, 2881, 1653 (C=O), 1572, 1451, 1358, 1139, 1118, 943 cm^{-1} ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.32 (m, 4H, Ph), 7.28-7.26 (m, 3H, Ph), 7.21-7.17 (m, 1H, Ph), 7.14-7.12 (m, 2H, Ph), 5.12-5.08 (m,

0.96H, OCH), 5.06-5.01 (m, 0.04H, OCH), 4.89 (d, J = 3.0 Hz, 1H, C*H*OH), 3.98-3.81 (m, 2H, NCH), 2.77-2.70 (m, 1H, PhCH_AH_B), 2.64-2.57 (m, 1H, PhCH_AH_B), 1.94-1.88 (m, 2H, CH), 1.27-1.08 (m, 12H, NCHMe_2), OH not resolved; ^{13}C NMR (100.6 MHz, $CDCl_3$) for (*R*,*S*)-**18** δ 156.1 (C=O), 141.4 (*ipso*-Ph), 140.1 (*ipso*-Ph), 128.4 (Ph), 128.3 (Ph) 128.0 (Ph), 127.5 (Ph), 127.0 (Ph), 126.8 (Ph), 78.6 (OCH), 76.3 (OCH), 46.3 (br, NCH), 32.4 (CH_2), 32.0 (CH_2), 20.4 (br, NCHMe_2); MS (ESI) *m/z* 392 [$(M + Na)^+$, 100], 370 [$(M + H)^+$, 35]; HRMS *m/z* calcd for $C_{19}H_{29}NO_2$ $(M + Na)^+$ 392.2202, found 392.2202 (+0.3 ppm error), CSP-HPLC: Chiracel OD (95:5 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*S*,*S*)-**18** 14.5 min, (*R*,*S*)-**18** 16.7 min, (*R*,*R*)-**18** 18.6 min, (*S*,*R*)-**18** 26.5 min.

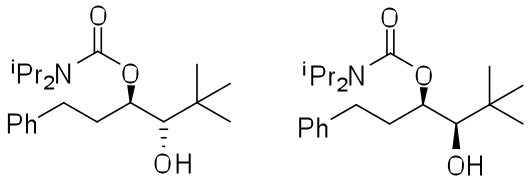
1-Hydroxy-1,4-diphenylbutan-2-yl *N*,*N*-diisopropylcarbamate *anti-rac*-18 and *syn-rac*-18



anti-rac-**18** *syn-rac*-**18**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti*-(*S*,S_s)-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and benzaldehye (51 μL, 0.50 mmol, 2.5 eq.) gave the crude product which contained a 90:10 mixture of (*R*,*S*)-**18** and (*R*,*R*)-**18** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 95:5-9:1 petrol-EtOAc as eluent gave a 92:8 mixture (by ^{1}H NMR spectroscopy) of alcohols (*R*,*S*)-**18** and (*R*,*R*)-**18** (36 mg, 49%) as a colourless oil.

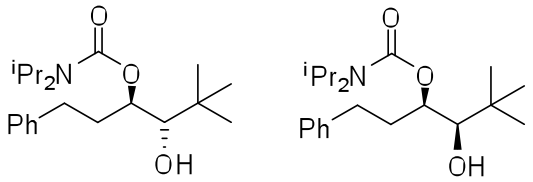
4-Hydroxy-5,5-dimethyl-1-phenylhexan-3-yl *N*,*N*-bis(propan-2-yl)carbamate (*R*,*S*)-19 and (*R*,*R*)-19



(*R*,*S*)-**19** (*R*,*R*)-**19**

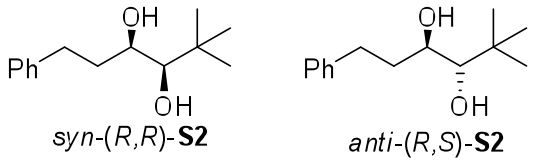
Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-(S,S$_S$)*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and pivaldehyde (54 μL, 0.50 mmol, 2.5 eq.) gave the crude product which contained a 60:40 mixture of (*R*,*S*)-**19** and (*R*,*R*)-**19** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 9:1-8:2 petrol-Et_2O as eluent gave a 70:30 mixture (by ^{1}H NMR spectroscopy) of alcohols (*R*,*S*)-**19** and (*R*,*R*)-**19** (54 mg, 78%, minor diastereoisomer 99:1 er by CSP-HPLC of the diol, major diastereoisomer er not determined) as a colourless oil, R_F (8:2 petrol-Et_2O) 0.2; IR (film) 3383 (OH), 2914, 2889, 1648 (C=O), 1429, 1300, 1271, 1045 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, Ph), 7.22-7.17 (m, 3H, Ph), 5.19 (br t, J = 8.0 Hz, 0.3H, OCH), 4.98 (dt, J = 10.0, 2.5 Hz, 0.7H, OCH), 4.04-3.90 (br m, 2H, NCH), 3.48 (d, J = 2.5 Hz, 0.7H, C*H*OH), 3.24 (d, J = 1.0 Hz, 0.3H, C*H*OH), 2.78 (ddd, J = 14.0, 10.5, 5.0 Hz, 0.7H, CH), 2.68-2.60 (m, 1.3H, CH), 2.32 (br s, 1H, OH), 2.20-2.10 (m, 1H, CH), 2.00-1.91 (m, 1H, CH), 1.28-1.26 (m, 12H, NCH*Me*$_2$), 0.96 (s, 6.3H, C*Me*$_3$), 0.95 (s, 2.7H, C*Me*$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) for (*R*,*S*)-**19** and (*R*,*R*)-**19** δ 155.3 (C=O), 154.3 (C=O), 142.0 (*ipso*-Ph), 141.7 (*ipso*-Ph), 128.4 (Ph), 128.3 (Ph) 128.3 (Ph), 128.3 (Ph), 125.8 (Ph) 125.8 (Ph), 80.9 (OCH), 79.8 (OCH), 76.2 (OCH), 72.8 (OCH), 46.0 (br, NCH), 45.5 (br, NCH), 35.1 (*C*Me$_3$), 34.6 (*C*Me$_3$), 32.41 (CH_2), 32.40 (CH_2), 32.1 (CH_2), 26.6 (C*Me*$_3$), 26.4 (C*Me*$_3$) 21.6 (br, NCH*Me*$_2$), 20.5 (br, NCH*Me*$_2$); MS (ESI) *m/z* 372 [(M + Na)$^+$, 100], 350 [(M + H)$^+$, 50]; HRMS *m/z* calcd for $C_{20}H_{34}NO_3$ (M + Na)$^+$ 372.2509, found 372.2496 (+3.4 ppm error).

4-Hydroxy-5,5-dimethyl-1-phenylhexan-3-yl *N*,*N*-bis(propan-2-yl)carbamate *anti-rac*-19 and *syn-rac*-19



Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and pivaldehyde (54 μL, 0.50 mmol, 2.5 eq.) gave the crude product which contained a 60:40 mixture of *anti-rac*-**19** and *syn-rac*-**19** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 9:1-8:2 petrol-Et_2O as eluent gave a 70:30 mixture (by ^{1}H NMR spectroscopy) of alcohols *anti-rac*-**19** and *syn-rac*-**19** (48 mg, 69%) as a colourless oil.

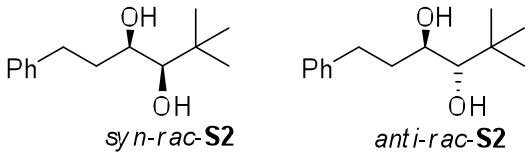
(3*R*,4*R*)-5,5-Dimethyl-1-phenylhexane-3,4-diol *syn*-(*R,R*)-S2 and (3*R*,4S*)*-5,5-dimethyl-1-phenylhexane-3,4-diol *anti*-(*R,S*)-S2



A 70:30 mixture of alcohols *anti*-(*R,S*)-**19** and *syn*-(*R,R*)-**19** (13 mg, 0.037 mmol, 1.0 eq.) in THF (1 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (9 mg, 0.22 mmol, 6.0 eq.) in THF (2 mL) at 0 °C under Ar. The resulting solution was stirred and heated at 70 °C for 1 h. Then, the solution was cooled to 0 °C and water (1 mL), 2 M $NaOH_{(aq)}$ (2 mL) and $MgSO_4$ were added sequentially. The solids were removed by filtration. The filtrate was washed with water (5 mL), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product which contained a 70:30 mixture of *anti*-(*R,S*)-**S2** and *syn*-(*R,R*)-**S2** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 4:1-3:1 petrol-EtOAc as eluent gave diol *syn*-(*R,R*)-

S2 (1.5 mg, 18%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (3:1 petrol-EtOAc) 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H, Ph), 7.23-7.18 (m, 3H, Ph), 3.82 (ddd, J = 8.0, 5.0, 1.0 Hz 1H, C*H*OH), 3.10 (d, J = 1.0 Hz, 1H, C*H*OH), 2.80 (ddd, J = 14.0 10.0, 6.0 Hz, 1H, PhCH_AH_B), 2.70 (ddd, J = 14.0, 9.5, 6.5 Hz, 1H, CH), 1.98 (br s, 2H, OH), 1.93 (dddd, J = 14.0, 9.5, 8.0, 6.0 Hz 1H, CH), 1.80 (dddd, J = 14.0, 10.0, 6.5, 5.0 Hz, 1H, CH), 0.94 (s, 9H, CMe_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.8 (*ipso*-Ph), 128.41 (Ph), 128.37 (Ph) 125.9 (Ph), 79.9 (CHOH), 68.9 (CHOH), 38.5 (CH_2), 35.0 (*C*Me$_3$) 32.1 (CH_2), 26.2 (C*Me*$_3$); MS (ESI) *m/z* 245 [(M + Na)$^+$, 100]; HRMS *m/z* calcd for $C_{14}H_{22}O_2$ (M + Na)$^+$ 245.1512, found 245.1505 (+2.8 ppm error); CSP-HPLC: Chiracel AD-H (98:2 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*R*,*R*)-**S2** 20.5 min, (*S*,*S*)-**S2** 22.2 min and diol *anti*-(*R,S*)-**S2 (**4.5 mg, 55%, er not determined) as a colourless oil, R_F (3:1 petrol-EtOAc) 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H, Ph), 7.24-7.17 (m, 3H, Ph), 3.73 (ddd, J = 10.0, 4.0, 3.0 Hz 1H, C*H*OH), 3.39 (d, J = 4.0 Hz, C*H*OH), 2.92 (ddd, J = 14.0 10.0 (9.5), 5.0 Hz, 1H, PhCH_AH_B), 2.69 (ddd, J = 14.0, 9.5, 7.0 Hz, 1H, CH), 1.96 (dddd, J = 14.0, 9.5, 7.0, 3.0 Hz 1H, CH), 1.89-1.79 (m, 3H, CH + OH), 0.95 (s, 9H, CMe_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.1 (*ipso*-Ph), 128.5 (Ph), 128.4 (Ph) 125.8 (Ph), 82.8 (CHOH), 72.0 (CHOH), 34.3 (*C*Me$_3$), 33.9 (CH_2), 32.2 (CH_2), 26.7 (C*Me*$_3$); MS (ESI) *m/z* 245 [(M + Na)$^+$, 100]; HRMS *m/z* calcd for $C_{14}H_{22}O_2$ (M + Na)$^+$ 245.1512, found 245.1514 (−0.6 ppm error).

5,5-Dimethyl-1-phenylhexane-3,4-diol *syn-rac*-S2 and *anti-rac*-S2

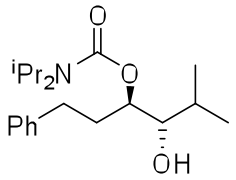


syn-rac-**S2** *anti-rac*-**S2**

An 80:20 mixture of alcohols *anti-rac*-**15** and *syn-rac*-**15** (90 mg, 0.26 mmol, 1.0 eq.) in THF (4 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (60 mg, 1.56 mmol, 6.0 eq.) in THF (5 mL) at 0 °C under Ar. The resulting solution was stirred and heated at 70 °C for 1 h. Then, the solution was cooled to 0 °C and water (2 mL), 2 M $NaOH_{(aq)}$ (4 mL) and $MgSO_4$ were added sequentially. The solids were removed by filtration. The filtrate was washed with water (5 mL), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product which contained

an 80:20 mixture of *anti-rac*-**S2** and *syn-rac*-**S2** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 4:1-3:1 petrol-EtOAc as eluent gave diol *syn-rac*-**S2 (**9 mg, 16%) as a colourless oil and diol *anti-rac*-**S2** (28 mg, 49%) as a colourless oil

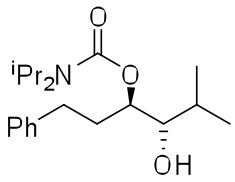
(3*R*,4*S*) 4-Hydroxy-5-methyl-1-phenylhexan-3-yl *N*,*N*-diisopropylcarbamate (*R*,*S*)-20



(*R,S*)-**20**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-(S,S*$_S$*)*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and isobutyraldehyde (46 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 9:1-8:2 petrol-Et_2O as eluent gave alcohol (*R,S*)-**20** (46 mg, 70%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (8:2 petrol-Et_2O) 0.3; IR (film) 3389 (OH), 2923, 2889, 1648 (C=O), 1418, 1348, 1280, 1139, 1118, 1045 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.27 (m, 2H, Ph), 7.20-7.18 (m, 3H, Ph), 4.98 (dt, J = 10.5, 3.5 Hz, 1H, OCH), 4.10-3.89 (br m, 2H, NCH), 3.48 (dd, J = 7.0, 3.5 Hz, 1H, C*H*OH), 2.78 (ddd, J = 14.0, 10.5, 5.0 Hz, 1H, PhCH_AH$_B$), 2.64 (ddd, J = 14.0, 10.5, 6.5 Hz, 1H, PhCH$_A$$H_B$), 2.17 (br s, 1H, OH), 2.06 (dtd, J = 14.5, 10.5, 5.0 Hz, 1H, CH), 1.91 (dddd, J = 14.5, 10.5, 6.5, 3.5 Hz, 1H, CH), 1.70 (oct, J = 7.0 Hz, 1H, C*H*Me$_2$), 1.26 (d, J = 7.0 Hz, 12H, NCH*Me*$_2$), 0.99 (d, J = 7.0 Hz, 3H, CH*Me*$_2$), 0.91 (d, J = 7.0 Hz, 3H, CH*Me*$_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.3 (C=O), 141.9 (*ipso*-Ph), 128.4 (Ph), 128.3 (Ph) 125.9 (Ph), 78.3 (OCH), 76.1 (CHOH), 46.0 (br, NCH), 32.3 (CH_2), 31.0 (CH_2), 30.2 (*C*HMe$_2$), 21.5 (br, NCH*Me*$_2$), 20.5 (br, NCH*Me*$_2$), 19.3 (Me), 18.4 (Me); MS (ESI) *m/z* 358 [(M + Na)$^+$, 100], 336 [(M + H)$^+$, 80]; HRMS *m/z* calcd for $C_{20}H_{34}NO_3$ (M + Na)$^+$ 358.2353, found 358.2347 (+1.5 ppm error); $[\alpha]_D$ +21.22 (*c* 0.40 in $CHCl_3$); CSP-HPLC: Chiracel OD (95:5 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*R,S*)-**20** 5.8 min, (*S,R*)-**20** 7.8 min.

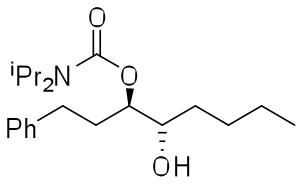
4-Hydroxy-5-methyl-1-phenylhexan-3-yl *N*,*N*-diisopropylcarbamate *anti-rac*-20 and *syn-rac*-20



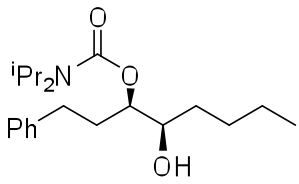
anti-rac-**20**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and isobutyraldehyde (46 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 9:1-8:2 petrol-Et_2O as eluent gave alcohol *anti-rac*-**20** (49 mg, 75%) a colourless oil.

4-Hydroxy-1-phenyloctan-3-yl *N*,*N*-diisopropylcarbamate (*R*,*S*)-21 and (*R*,*R*)-21



(*R*,*S*)-**21**

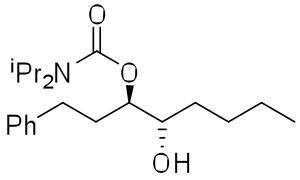


(*R*,*R*)-**21**

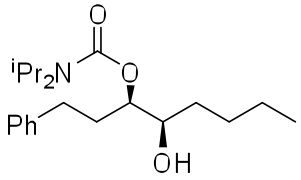
Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-(S,S*$_S$*)*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and valeraldehyde (53 μL, 0.50 mmol, 2.5 eq.) gave the crude product which contained a 90:10 mixture of (*R*,*S*)-**21** and (*R*,*R*)-**21** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 9:1-8:2 petrol-Et_2O as eluent gave a 90:10 mixture (by ^{1}H NMR spectroscopy) of alcohols (*R*,*S*)-**21** and (*R*,*R*)-**21** (45 mg, 65%, each diastereoisomer 99:1 er by CSP:HPLC) as a colourless oil, R_F (8:2 petrol-Et_2O) 0.3; IR (film) 3399 (OH), 2923, 2878, 1647 (C=O), 1428, 1291, 1239, 1117, 1035 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H, Ph), 7.20-7.16 (m, 3H, Ph), 4.87 (dt, J = 8.0, 3.5 Hz, 0.9H, OCH), 4.85-4.80 (m, 0.1H, OCH), 4.06 (br s, 1H, NCH), 3.84 (br s, 1H, NCH), 3.69 (dt, J = 9.0, 3.5 Hz, 0.9H, C*H*OH), 3.65-3.61 (m, 0.1H,

C*H*OH), 2.79-2.59 (m, 2H, CH), 2.04-1.94 (m, 1H, CH), 1.90-1.81 (m, 1H, CH), 1.55-1.24 (m, 18H), 0.88 (t, J = 8.0 Hz, 3H, Me); ^{13}C NMR (100.6 MHz, $CDCl_3$) for (*R,S*)-**21** δ 156.2 (C=O), 141.6 (*ipso*-Ph), 128.4 (Ph), 128.3 (Ph) 126.0 (Ph), 78.6 (OCH), 73.9 (CHOH), 45.6 (br, NCH), 32.5 (CH_2), 32.2 (CH_2), 32.0 (CH_2), 30.2 (*C*HMe_2), 31.9 (CH_2), 22.7 (CH_2), 20.4 (br, NCH*Me*$_2$), 14.0 (Me); MS (ESI) *m/z* 372 [(M + Na)$^+$, 100], 350 [(M + H)$^+$, 30]; HRMS *m/z* calcd for $C_{21}H_{35}NO_3$ (M + Na)$^+$ 372.2509, found 372.2493 (+4.3 ppm error); CSP-HPLC: Chiracel OD (99:1 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*R,R*)-**21** 16.8 min, (*R,S*)-**21** 19.3 min, (*S,S*)-**21** 19.3 min, (*S,R*)-**21** 28.3 min.

4-Hydroxy-1-phenyloctan-3-yl *N,N*-diisopropylcarbamate *anti-rac*-21 and *syn-rac*-21



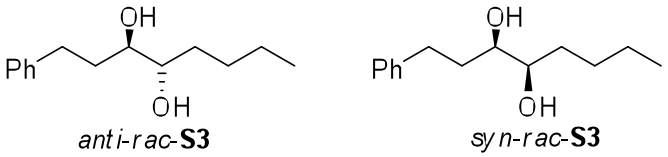
anti-rac-**21**



syn-rac-**21**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *anti-rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min and valeraldehyde (53 μL, 0.50 mmol, 2.5 eq.) gave the crude product which contained a 90:10 mixture of (*R,S*)-**21** and (*R,R*)-**21** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 9:1-8:2 petrol-Et_2O as eluent gave a 90:10 mixture (by ^{1}H NMR spectroscopy) of alcohols *anti-rac*-**21** and *syn-rac*-**21** (37 mg, 53%) as a colourless oil.

1-Phenyloctane-3,4-diol *anti-rac*-S3 and *syn-rac*-S3

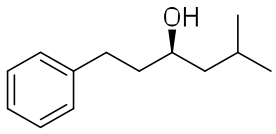


anti-rac-**S3** *syn-rac*-**S3**

A 90:10 mixture of alcohols *anti-rac*-**21** and *syn-rac*-**21** (30 mg, 0.086 mmol, 1.0 eq.) in THF (1 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (20 mg, 0.52 mmol, 6.0 eq.) in THF (2 mL) at 0 °C under Ar. The resulting solution was stirred and heated at 70 °C for 1 h. Then, the solution was cooled to 0 °C and water (1 mL), 2 M $NaOH_{(aq)}$ (2 mL) and $MgSO_4$ were added sequentially. The solids were removed by filtration. The filtrate was washed with water (5 mL), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product which contained a 90:10 mixture of *anti-rac*-**S3** and *syn-rac*-**S3** by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica with 3:1 petrol-EtOAc as eluent gave a 90:10 mixture (by ^{1}H NMR spectroscopy) of diols *anti-rac*-**S3** and *syn-rac*-**S3** (17 mg, 89%) as a colourless oil, R_F (3:1 petrol-EtOAc) 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H, Ph), 7.24-7.18 (m, 3H, Ph), 3.65-3.60 (m, 1.8H, C*H*OH), 3.46-3.44 (m, 0.2H, C*H*OH), 2.93-2.83 (m, 1H, CH), 2.76-2.64 (m, 1H, CH), 2.04-1.94 (m, 1H, CH), 1.81-1.77 (m, 5H, CH + OH), 1.50-1.25 (m, 6H, CH), 0.91 (t, J = 8.0 Hz, 3H, Me); ^{13}C NMR (100.6 MHz, $CDCl_3$) for *anti-rac*-**S3** δ 142.0 (*ipso*-Ph), 128.6 (Ph), 128.5 (Ph) 126.2 (Ph), 74.5 (CHOH), 74.0 (CHOH), 32.9 (CH_2), 32.4 (CH_2), 31.1 (CH_2), 28.2 (CH_2), 22.8 (CH_2), 14.1 (Me). Spectroscopic data for *syn-rac*-**S3** consistent with those reported in the literature.[12]

This experiment enabled the relative stereochemistry of *anti-rac*-**21** to be unequivocably established.

(3*R*)-5-Methyl-1-phenylhexan-3-ol (*R*)-22



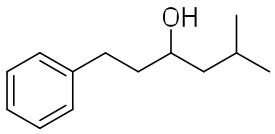
(R)-**22**

i-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) was added dropwise to a stirred solution of sulfoxide *anti*-(*S*,S_s)-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of isobutylboronic acid pinacol ester (107 μL, 0.50 mmol, 2.5 eq.) in THF (1 mL) was added dropwise. The solution was stirred at rt for 30 min and then stirred and heated at 67 °C for 16 h. The reaction mixture was cooled to 0 °C and 3 M $NaOH_{(aq)}$ (0.5 mL) and 30 % $H_2O_{2(aq)}$ (0.25 mL) were added sequentially. The resulting solution was stirred at rt for 2 h and then 2 M $NaOH_{(aq)}$ (7 mL) was added. The two layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 95:5-9:1 petrol-EtOAc as eluent gave alcohol (*R*)-**22** (26 mg, 68%, 94:6 er by CSP-HPLC) as a white solid, mp 44-45 °C (lit.,[6] 45-47 °C); R_F (8:2 petrol-Et_2O) 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H, Ph), 7.23-7.18 (m, 3H, Ph), 3.76-3.70 (m, 1H, C*H*OH), 2.81 (ddd, *J* = 13.5, 10.0, 6.0 Hz, 1H, PhCH_AH$_B$), 2.69 (ddd, *J* = 13.5, 10.0, 6.5 Hz, 1H, PhCH$_A$$H_B$), 1.82-1.68 (m, 3H, $PhCH_2CH_2$ + CH), 1.48-1.40 (m, 2H, CH + OH), 1.30-1.28 (m, 1H, CH), 0.93 (d, *J* = 8.0 Hz, 3H, CHMe_2), 0.91 (d, *J* = 8.0 Hz, 3H, CHMe_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.2 (*ipso*-Ph), 128.4 (4, Ph), 125.8 (Ph) 69.5 (CHOH), 46.8 (CH_2), 39.8 (CH_2), 32.2 (CH_2), 24.8 (CH or Me), 23.6 (CH or Me), 22.2 (CH or Me); $[\alpha]_D$ +16.0 (*c* 0.55 in $CHCl_3$) [lit.[6] , $[\alpha]_D$ +16.00 (*c* 0.70 in $CHCl_3$) for (*R*)-**22** of 97:3 er)]; CSP-HPLC: Chiracel OD (98:2 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*S*)-**22** 13.4 min, (*R*)-**22** 22.2 min. Spectroscopic data consistent with those reported in the literature.[6]

n-BuLi (0.23 mL of a 2.2 M solution in hexanes, 0.50 mmol, 2.5 eq.) was added dropwise to a stirred solution of sulfoxide *anti*-(*S*,S_s)-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 1 min. Then, a solution of isobutylboronic pinacol ester (107 μL, 0.50 mmol, 2.5 eq.) was added dropwise. The solution was stirred at −78 °C for 30 min and then stirred and heated at 67 °C for 16 h. The reaction mixture

was cooled to 0 °C and 3 M $NaOH_{(aq)}$ (0.5 mL) and 30 % $H_2O_{2(aq)}$ (0.25 mL) were added sequentially. The resulting solution was stirred at rt for 2 h and then 2 M $NaOH_{(aq)}$ (7 mL) was added. The two layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave alcohol (*R*)-**22** (28 mg, 72%, 99:1 er by CSP-HPLC) as a white solid, mp 47-48 °C (lit.,[6] 45-47 °C); $[\alpha]_D$ +15.6 (*c* 0.65 in $CHCl_3$) [lit.,[6] $[\alpha]_D$ +16.00 (*c* 0.70 in $CHCl_3$) for (*R*)-**22** of 97:3 er)]; CSP-HPLC: Chiracel OD-H (98:2 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (*S*)-**22** 12.9 min, (*R*)-**22** 21.4 min. Spectroscopic data consistent with those reported in the literature.[6]

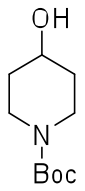
5-Methyl-1-phenylhexan-3-ol *rac*-22



rac-**22**

i-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) was added dropwise to a stirred solution of sulfoxide *anti-rac*-**6** (80 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of isobutylboronic acid pinacol ester (107 μL, 0.50 mmol, 2.5 eq.) in THF (1 mL) was added dropwise. The solution was stirred at rt for 30 min and then stirred and heated at 67 °C for 16 h. The reaction mixture was cooled to 0 °C and 3 M $NaOH_{(aq)}$ (0.5 mL) and 30 % $H_2O_{2(aq)}$ (0.25 mL) were added sequentially. The resulting solution was stirred at rt for 2 h and then 2 M $NaOH_{(aq)}$ (7 mL) was added. The two layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 95:5-90:10 petrol-EtOAc as eluent gave alcohol *rac*-**22** (25 mg, 65%) as a white solid.

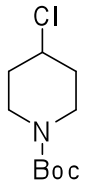
***tert*-Butyl 4-hydroxypiperidine-1-carboxylate S4**



S4

$NaBH_4$ (200 mg, 7.5 mmol, 1.5 eq.) was added to a stirred solution of *N*-Boc piperidin-4-one (1.00 g, 5.0 mmol, 1.0 eq.) in EtOH (5 mL) at 0 °C under Ar. The resulting solution was allowed to warm to rt and stirred at rt for 4 h. Then, the mixture was cooled to 0 °C and saturated $NH_4Cl_{(aq)}$ (20 mL) was added dropwise. The solvent was evaporated under reduced pressure and EtOAc (15 mL) was added. The two layers were separated and the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1 CH_2Cl_2-acetone as eluent gave 4-hydoxy *N*-Boc piperidine **S4** (984 mg, 98%) as a white solid, mp 66-68 °C (lit.,[13] 64.6-66.5 °C); R_F (9:1 CH_2Cl_2-Acetone) 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82-3.72 (m, 3H, NCH_AH$_B$ + C*H*OH), 2.97 (ddd, J = 13.0, 10.0, 3.0 Hz, 2H, NCH$_A$$H_B$), 2.67 (br s, 1H, OH), 1.83-1.78 (m, 2H, NCH$_2$CH_AH$_B$), 1.46-1.37 (m, 2H, NCH$_2$CH$_A$$H_B$), 1.41 (s, 9H, CMe_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 154.7 (C=O), 79.5 (*C*Me$_3$), 67.4 (CHOH), 41.3 (br, NCH_2), 34.0 (NCH$_2$*C*H$_2$), 28.3 (C*Me$_3$*). Spectroscopic data consistent with those reported in the literature.[13]

***tert*-Butyl 4-chloropiperidine-1-carboxylate 25**

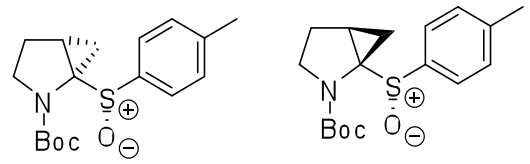


25

A solution of hexachloroethane (7.05 g, 29.8 mmol, 2.0 eq.) in CH_2Cl_2 (25 mL) was added to a stirred solution of 4-hydroxy *N*-Boc piperidine **S4** (3.00 g, 14.9 mmol, 1.0 eq.) and PPh_3 (7.82 g, 29.8 mmol, 2.0 eq.) in CH_2Cl_2 (75 mL) at rt under Ar. The resulting solution was stirred at rt for 16 h. The solvent was evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 4:1 petrol-Et_2O as eluent gave *N*-Boc 4-chloro piperidine **25** (2.13 g, 67%) as a colourless oil, R_F (4:1 petrol-Et_2O) 0.3; IR (film) 2974, 2932, 1696 (C=O), 1477, 1420, 1365, 1277, 1169, 1112, 1002 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.20 (tt, J = 7.5, 3.5 Hz, 1H, CHCl), 3.69 (ddd, J = 13.0, 7.0, 3.5 Hz, 2H, NCH_AH_B), 3.29 (ddd, J = 13.0, 7.5 Hz, 2H, NCH_AH_B), 2.01 (ddt, J = 13.5, 7.0, 3.5 Hz, 2H, $NCH_2CH_AH_B$), 1.78 (dtd, J = 13.5, 7.5, 3.5 Hz, 2H, $NCH_2CH_AH_B$), 1.45 (s, 9H, CMe_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 154.6 (C=O), 79.7 (CMe$_3$), 56.9 (CHCl), 41.2 (br, NCH_2), 34.8 (NCH_2CH_2), 28.3 (CMe_3); MS (ESI) *m/z* 244 [(^{37}M + Na)$^+$, 10], 242 [(^{35}M + Na)$^+$, 30], 166 (30), 164 (100); HRMS *m/z* calcd for $C_{10}H_{18}{}^{35}ClNO_2$ (M + Na)$^+$ 242.0918, found 242.0911 (+3.1 ppm error).

tert-Butyl (1*R*,5*R*)-(*p*-tolylsulfinyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate _syn_-(*R*,*R*,*S*$_S$)-7 and _tert_-Butyl (1*S*,5*S*)-(*p*-tolylsulfinyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate _anti_-(*S*,*S*,*S*$_S$)-7

(Scheme 9 and Table 3, Entry 1)

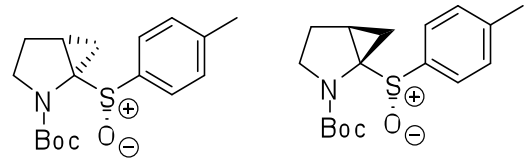


syn-(*R*,*R*,*S*$_S$)-**7** *anti*-(*S*,*S*,*S*$_S$)-**7**

Using general procedure E, *s*-BuLi (1.70 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and TMEDA (256 mg, 2.20 mmol, 2.2 eq.) in Et_2O (6 mL) at −78 °C for 1 h and a solution of Andersen's sulfinate (*S*$_S$)-**3** (647 mg, 2.20 mmol, 2.2 eq.) in THF (2 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R*,*R*,*S*$_S$)-**7** (129 mg, 38%, 58:42 er by CSP-HPLC) as a white solid, mp 163-166 °C; R_F (3:2 petrol-EtOAc) 0.3; IR ($CHCl_3$) 2975, 2931, 1703 (C=O), 1492, 1454, 1393, 1368, 1257, 1168, 1083, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.48 (m, 2H, *m*-C_6H_4Me), 7.28 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 3.47 (br s, 1H, NCH_AH_B), 2.84 (br s, 1H, NCH$_A$$H_B$), 2.41 (s, 3H, Me), 2.28 (br s, 1H, CH), 1.93-1.90 (m, 1H, CH), 1.77-1.74 (m, 2H, CH), 1.52 (br s, 9H, CMe_3), 1.16-1.13 (m, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) (rotamers) δ 155.0 (br, C=O), 141.9 (*ipso*-Ar), 141.6 (*ipso*-Ar), 141.1 (*ipso*-Ar), 139.5 (*ipso*-Ar), 129.7 (br, Ar), 125.5 (Ar), 124.8 (Ar), 81.2 (br, *C*Me$_3$), 61.2 (N*C*S(O)Ar), 61.1 (N*C*S(O)Ar), 52.3 (br, NCH_2), 28.5 (C*Me*$_3$), 26.1 (br, CH_2), 23.7 (CH_2), 22.3 (CH_2), 21.6 (Me), 11.9 (CH), 11.7 (CH); MS (ESI) *m/z* 344 [(M + Na)$^+$, 30], 322 [(M + H)$^+$, 100]; HRMS *m/z* calcd for $C_{17}H_{23}NO_3S$ (M + Na)$^+$ 344.1291, found 344.1286 (+1.5 ppm error); CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S*,*S*,*R*$_S$)-**7** 10.1 min, *syn*-(*R*,*R*,*S*$_S$)-**7** 11.5 min and sulfoxide *anti*-(*S*,*S*,*S*$_S$)-**7** (152 mg, 45%, 70:30 er by CSP-HPLC) as a colourless oil, R_F (3:2 petrol-EtOAc) 0.2; IR (film) 2977, 2932, 1696 (C=O), 1477, 1384, 1335, 1257, 1168, 1083, 1048, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 7.26 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 3.79-3.72 (m, 1H, NCH_AH_B), 3.61 (br s, 1H, NCH$_A$$H_B$), 2.37 (s, 3H, Me), 2.27-2.18 (m, 1H, CH), 2.05 (dtd, J = 8.0, 7.0, 1.5 Hz, 1H, NCC*H*),

1.83-1.75 (m, 1H, CH), 1.49 (s, 9H, CMe_3), 1.09 (t, J = 7.0 Hz, 1H, H), 1.05-1.01 (br m, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.5 (C=O), 141.4 (*ipso*-Ar), 138.0 (*ipso*-Ar), 129.5 (Ar), 124.8 (Ar), 80.9 (CMe_3), 69.9 (br, N*C*S(O)Ar), 52.5 (br, NCH_2), 29.9 (br, CH_2), 28.4 (CMe_3), 26.8 (CH_2), 24.3 (br, CH), 21.3 (Me); MS (ESI) *m/z* 344 [$(M + Na)^+$, 40], 322 [$(M + H)^+$, 100]; HRMS *m/z* calcd for $C_{17}H_{23}NO_3S$ $(M + Na)^+$ 344.1291, found 344.1286 (+1.3 ppm error); CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S,S,S*$_s$)-**7** 9.0 min, *anti*-(*R,R,R*$_s$)-**7** 12.3 min.

***tert*-Butyl (1*R*,5*R*)-(*p*-tolylsulfinyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate *syn*-(*R,R,S*$_s$)-7 and *tert*-Butyl (1*S*,5*S*)-(*p*-tolylsulfinyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate *anti*-(*S,S,S*$_s$)-7**



syn-(*R,R,S*$_S$)-**7** *anti*-(*S,S,S*$_S$)-**7**

(Table 3, Entry 2)

Using general procedure F, *s*-BuLi (1.70 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and TMEDA (256 mg, 2.20 mmol, 2.2 eq.) in Et_2O (6 mL) at −78 °C for 1 h and a solution of Andersen's sulfinate (*S*$_s$)-**3** (647 mg, 2.20 mmol, 2.2 eq.) in THF (2 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R,R,S*$_S$)-**7** (122 mg, 36%, 80:20 er by CSP-HPLC) as a white solid, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S,S,R*$_S$)-**7** 10.7 min, *syn*-(*R,R,S*$_S$)-**7** 12.3 min and sulfoxide *anti*-(*S,S,S*$_S$)-**7** (157 mg, 47%, 78:22 er by CSP-HPLC) as a colourless oil, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S,S,S*$_s$)-**7** 9.4 min, *syn*-(*R,R,R*$_s$)-**7** 13.1 min.

(Table 3, Entry 3)

Using general procedure G, *s*-BuLi (1.70 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and TMEDA (256 mg, 2.20 mmol, 2.2 eq.) in Et_2O (6 mL) and a solution of Andersen's sulfinate (*S*$_s$)-**3** (647 mg, 2.20 mmol, 2.2

eq.) in THF (5 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R*,*R*,S_S)-**7** (132 mg, 39%, 89:11 er by CSP-HPLC) as a white solid, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S*,*S*,R_S)-**7** 13.2 min, *syn*-(*R*,*R*,S_S)-**7** 15.2 min and sulfoxide *anti*-(*S*,*S*,S_S)-**7** (146 mg, 44%, 88:12 er by CSP-HPLC) as a colourless oil, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S*,*S*,S_s)-**7** 11.8 min, *syn*-(*R*,*R*,R_s)-**7** 16.1 min.

(Table 3, Entry 4)

Using general procedure G, *s*-BuLi (1.70 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and (−)-sparteine (504 mg, 2.20 mmol, 2.2 eq.) in Et_2O (6 mL) and a solution of Andersen's sulfinate (S_s)-**3** (647 mg, 2.20 mmol, 2.2 eq.) in THF (5 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R*,*R*,S_S)-**7** (88 mg, 27%, 96:4 er by CSP-HPLC) as a white solid, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S*,*S*,R_S)-**7** 10.2 min, *syn*-(*R*,*R*,S_S)-**7** 11.6 min and sulfoxide *anti*-(*S*,*S*,S_S)-**7** (78 mg, 24%, 89:11 er by CSP-HPLC) as a colourless oil, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S*,*S*,S_s)-**7** 8.7 min, *syn*-(*R*,*R*,R_s)-**7** 11.9 min.

(Table 3, Entry 5)

Using general procedure G, *s*-BuLi (0.85 mL of a 1.3 M solution in hexanes, 1.10 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (110 mg, 0.50 mmol, 1.0 eq.) and (+)-sparteine surrogate (213 mg, 1.10 mmol, 2.2 eq.) in Et_2O (4 mL) and a solution of Andersen's sulfinate (S_s)-**3** (324 mg, 1.10 mmol, 2.2 eq.) in THF (3 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R*,*R*,S_S)-**7** (42 mg, 26%, 99:1 er by CSP-HPLC) as a white solid, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S*,*S*,R_S)-**7** 9.6 min, *syn*-(*R*,*R*,S_S)-**7** 10.9 min and sulfoxide *anti*-(*S*,*S*,S_S)-**7** (43 mg, 27%, 93:7 er by CSP-HPLC) as a colourless oil, CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S*,*S*,S_s)-**7** 8.6 min, *syn*-(*R*,*R*,R_s)-**7** 11.6 min.

(Table 3, Entry 6)

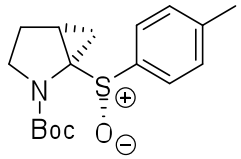
Using general procedure G, *s*-BuLi (1.70 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and diamine (*R*,*R*)-**12** (683 mg, 2.20

mmol, 2.2 eq.) in Et_2O (6 mL) and a solution of Andersen's sulfinate (S_s)-**3** (647 mg, 2.20 mmol, 2.2 eq.) in THF (5 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R,R,S*$_S$)-**7** (163 mg, 51%, 99:1 er by CSP-HPLC) as a white solid, $[\alpha]_D$ −43.7 (*c* 0.65 in $CHCl_3$); CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S,S,R*$_S$)-**7** 9.9 min, *syn*-(*R,R,S*$_S$)-**7** 11.5 min and sulfoxide *anti*-(*S,S,S*$_S$)-**7** (80 mg, 25%, 87:13 er by CSP-HPLC) as a colourless oil, $[\alpha]_D$ +64.6 (*c* 0.9 in $CHCl_3$); CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S,S,S*$_s$)-**7** 8.7 min, *syn*-(*R,R,R*$_s$)-**7** 12.4 min.

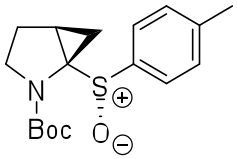
(Table 3, Entry 7)

Using general procedure G, *s*-BuLi (1.70 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and diamine (*S,S*)-**12** (683 mg, 2.20 mmol, 2.2 eq.) in Et_2O (6 mL) and a solution of Andersen's sulfinate (S_s)-**3** (647 mg, 2.20 mmol, 2.2 eq.) in THF (5 mL) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn*-(*R,R,S*$_S$)-**7** (38 mg, 12%, 89:11 er by CSP-HPLC) as a white solid, $[\alpha]_D$ −43.2 (*c* 0.7 in $CHCl_3$); CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*-PrOH, 1.0 mL min^{-1}) *syn*-(*S,S,R*$_S$)-**7** 12.2 min, *syn*-(*R,R,S*$_S$)-**7** 14.2 min and sulfoxide *anti*-(*S,S,S*$_S$)-**7** (174 mg, 54%, 87:13 er by CSP-HPLC) as a colourless oil, $[\alpha]_D$ +86.1 (*c* 0.7 in $CHCl_3$); CSP-HPLC: Chiralcel AD (90:10 Hexane-*i*PrOH, 1.0 mL min^{-1}) *anti*-(*S,S,S*$_s$)-**7** 8.1 min, *syn*-(*R,R,R*$_s$)-**7** 11.4 min.

tert-Butyl 1-(_p_-tolylsulfinyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate _syn-rac_-7 and _anti-rac_-7



syn-rac-**7**



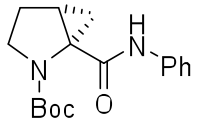
anti-rac-**7**

Using General procedure E, *s*-BuLi (2.11 mL of a 1.3 M solution in hexanes, 2.75 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (275 mg, 1.25 mmol, 1.0 eq.) and TMEDA (319 mg, 2.75 mmol,

2.2 eq.) in Et_2O (8 mL) and methyl *p*-toluenesulfinate **S1** (468 mg, 2.75 mmol, 2.2 eq.) gave the crude product. Purification by flash column chromatography on silica with 3:2 petrol-EtOAc + 1% Et_3N as eluent gave sulfoxide *syn-rac*-**7** (142 mg, 35%) as a white solid, mp 161-163 °C and sulfoxide *anti-rac*-**7** (144 mg, 36%) as a colourless oil.

Investigating the Inherent Enantioselectivity for the Lithiation-Trapping of *N*-Boc 4-chloro piperidine 25

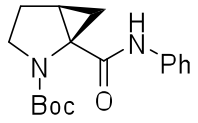
tert-Butyl (1*S*,5*R*)-(phenylcarbamoyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate (*S*,*R*)-35



(S,R)-**35**

Using general procedure E, *s*-BuLi (1.69 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and (−)-sparteine (516 mg, 2.20 mmol, 2.2 eq.) in Et_2O (8 mL) and phenylisocyanate (262 mg, 2.20 mmol, 2.2 eq.) gave the crude product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-Et_2O as eluent gave amide (*S*,*R*)-**35** (283 mg, 94%, 56:44 er by CSP-HPLC) as a pale yellow solid, CSP-HPLC: Chiracel OD (90:10 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (*R*,*S*)-**35** 7.2 min, (*S*,*R*)-**35** 13.6 min. Full characterisation data is presented later.

tert-Butyl (1*R*,5*S*)-(phenylcarbamoyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate (*R*,*S*)-35



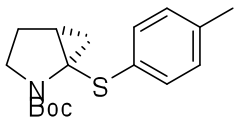
(R,S)-**35**

Using general procedure E, *s*-BuLi (1.51 mL of a 1.3 M solution in hexanes, 1.96 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (194 mg, 0.89 mmol, 1.0 eq.) and (+)-sparteine surrogate (381 mg, 1.96 mmol, 2.2 eq.) in Et_2O (5.5 mL) and phenylisocyanate (233 mg, 1.96 mmol, 2.2 eq.) gave

the crude product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-Et_2O as eluent gave amide (*R*,*S*)-**35** (212 mg, 79%, 54:46 er by CSP-HPLC) as a pale yellow solid, CSP-HPLC: Chiracel OD (90:10 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (*R*,*S*)-**35** 7.4 min, (*S*,*R*)-**35** 14.8 min. Full characterisation data is presented later.

Using general procedure E, *s*-BuLi (1.35 mL of a 1.3 M solution in hexanes, 1.76 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (175 mg, 0.80 mmol, 1.0 eq.) and diamine (*S*,*S*)-**12** (547 mg, 1.76 mmol, 2.2 eq.) in Et_2O (5.0 mL) and phenylisocyanate (124 mg, 1.04 mmol, 1.3 eq.) gave the crude product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-Et_2O as eluent gave amide (*R*,*S*)-**35** (178 mg, 74%, 67:33 er by CSP-HPLC) as a pale yellow solid,); $[\alpha]_D$ +45.5 (*c* 1.1 in $CHCl_3$); CSP-HPLC: Chiracel OD (90:10 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (*R*,*S*)-**35** 7.3 min, (*S*,*R*)-**35** 14.3 min . Full characterisation data is presented later.

tert-Butyl 3-(hydroxymethyl)-1-[(4-methylphenyl)sulfanyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate (1*R*,5*R*)-28

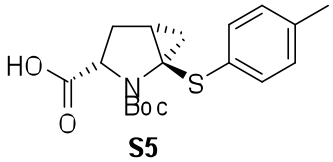


28

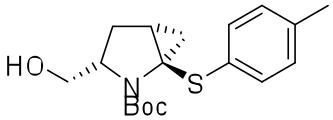
Trifluoroacetic anhydride (318 μL, 2.25 mmol, 3.0 eq.) was added dropwise to a stirred suspension of sulfoxide *syn*-(*R*,*R*,S_S)-**7** (240 mg, 0.75 mmol, 1.0 eq.) and NaI (225 mg, 1.50 mmol, 2.0 eq.) in acetone (9 mL) at −40 °C under Ar. The resulting solution was stirred at −40 °C for 10 min. Then, saturated $Na_2SO_{3(aq)}$ (5 mL) and saturated $NaHCO_{3(aq)}$ (5 mL) were added sequentially and the two layers were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL) The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1-8:2 petrol-EtOAc as eluent gave sulfide **28** (228 mg, 99%) as a pale yellow oil, R_F (8:2 petrol-EtOAc) 0.4; IR (film) 2948, 2912, 2877, 1656 (C=O), 1557, 1552, 1348, 1278, 912, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 7.11 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 3.52-3.48 (m, 2H, NCH_2), 2.34 (s, 3H, Me), 2.11-2.00 (m, 1H, CH), 1.82-1.72 (m,

2H, CH), 1.63 (dd, J = 9.0, 5.0 Hz, 1H, CH), 1.52 (s, 9H, CMe_3), 1.13 (t, J = 5.0 Hz, 1H, CH_AH_B); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.5 (C=O), 137.3 (*ipso*-C_6H_4S), 132.1 (*ipso*-C_6H_4Me), 132.0 (Ar), 129.5 (Ar), 80.0 (CMe_3), 53.7 (NC), 51.2 (NCH_2), 29.1 (CH_2), 28.6 (CMe_3), 28.4 (CH), 26.8 (CH_2), 21.2 (Me); MS (ESI) *m/z* 328 [$(M + Na)^+$, 100], 306 [$(M + H)^+$, 25]; HRMS *m/z* calcd for $C_{17}H_{23}NO_2S$ $(M + Na)^+$ 328.1347, found 328.1347 (0.0 ppm error); $[\alpha]_D$ –45.8 (*c* 0.6 in $CHCl_3$).

tert-Butyl 3-(hydroxymethyl)-1-[(4-methylphenyl)sulfanyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate _cis_-(1_R_,3_S_,5_R_)-29



S5

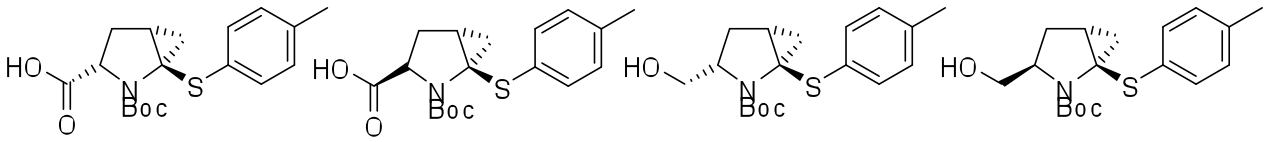


cis-**29**

s-BuLi (0.75 mL of a 1.3 M solution in hexanes, 0.98 mmol, 1.3 eq.) was added dropwise to a stirred solution of sulfide **28** (228 mg, 0.75 mmol, 1.0 eq.) and (+)-sparteine surrogate (191 mg, 0.98 mmol, 1.3 eq.) in Et_2O (5 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 5 min. Then, CO_2 was bubbled through the solution for 10 min and the resulting solution allowed to warm to rt. Water (5 mL) and 1 M $NaOH_{(aq)}$ (10 mL) were added and the two layers were separated. The aqueous layer was acidified (pH 1) with 2 M $HCl_{(aq)}$ and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product which contained a 92:8 mixture (by ^1H NMR spectroscopy) of diastereoisomeric acids **S5** which required no further purification: ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (br s, 1H, OH), 7.28 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 7.12 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 4.55 (br s, 0.92H, NCH), 4.21 (dd, J = 10.0, 5.0 Hz, 0.08H, NCH), 2.68 (br s, 0.08H, 1H, CH), 2.54-2.50 (br m, 0.92H, 1H, CH), 2.34 (s, 2.76H, Me), 2.33 (s, 0.24, Me), 2.07 (dd, J = 13.0, 4.5 Hz, 0.08H, CH_AH_B), 1.99 (dd, J = 13.0, 7.0 Hz, 0.92H, CH_AH_B), 1.78-1.76 (m, 1H, CH), 1.70-1.65 (m, 1H, CH), 1.52-1.43 (m, 1H, CH), 1.47 (br s, 9H, CMe_3). Borane dimethyl sulfide complex (77 μL, 0.82 mmol, 1.3 eq.) was added dropwise to a stirred solution of the crude acids **S5** (218 mg, 0.63 mmol, 1.0 eq.) in THF (5 mL) at 0 °C under Ar. After gas

evolution ceased, the resulting solution was stirred and heated at 66 °C for 1 h. Then, the solution was cooled to rt and MeOH (5 mL) was added dropwise. The solvent was evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1-8:2 petrol-EtOAc as eluent gave alcohol *cis*-(1*R*,3*S*,5*R*)-**29** (211 mg, 84% over two steps) as a colourless oil, R_F (8:2 petrol-EtOAc) 0.3; IR (film) 3315 (OH), 2892, 2877, 1688 (C=O), 1565, 1488, 1258, 912, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 7.14 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 5.32 (br s, 1H, OH), 4.03-3.97 (m, 1H, NCH), 3.52-3.42 (m, 2H, CH_2OH), 2.35 (s, 3H, Me), 2.18-2.11 (m, 1H, CH), 1.64-1.60 (m, 2H, CH), 1.57 (s, 9H, CMe_3), 1.33-1.25 (m, 1H, CH), 1.16-1.14 (m, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.6 (C=O), 138.1 (*ipso*-C_6H_4S), 133.1 (Ar), 131.2 (*ipso*-C_6H_4Me), 129.8 (Ar), 81.1 (*C*Me_3), 70.4 (NCH), 65.0 (CH_2OH), 57.0 (NC), 34.2 (CH_2), 31.9 (CH_2), 28.4 (C*Me*$_3$), 25.7 (CH), 21.1 (Me); MS (ESI) *m/z* 358 [$(M + Na)^+$, 90], 336 [$(M + H)^+$, 40], 280 (100); HRMS *m/z* calcd for $C_{18}H_{25}NO_3S$ $(M + Na)^+$ 358.1447, found 358.1443 (+1.1 ppm error); $[\alpha]_D$ –139.8 (*c* 0.7 in $CHCl_3$).

***tert*-Butyl 3-(hydroxymethyl)-1-[(4-methylphenyl)sulfanyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate *cis-rac*-29 and *tert*-Butyl 3-(hydroxymethyl)-1-[(4-methylphenyl)sulfanyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate *trans-rac*-29**

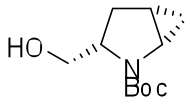


cis-**S5** *trans*-**S5** *cis-rac*-**29** *trans-rac*-**29**

s-BuLi (3.61 mL of a 1.3 M solution in hexanes, 4.69 mmol, 1.3 eq.) was added dropwise to a stirred solution of sulfide *rac*-**28** (1.10 g, 3.61 mmol, 1.0 eq.) and TMEDA (701 μL, 4.69 mmol, 1.3 eq.) in Et_2O (15 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 5 min. Then, CO_2 was bubbled through the solution for 10 min and the resulting solution allowed to warm to rt. Water (5 mL) and 1 M $NaOH_{(aq)}$ (10 mL) were added and the two layers were separated. The aqueous layer was acidified (pH 1) with 2 M $HCl_{(aq)}$ and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product which contained a 68:32 mixture (by ^1H NMR spectroscopy)

of diastereoisomeric acids **S5** which required no further purification. Borane dimethyl sulfide complex (0.36 mL, 3.72 mmol, 1.3 eq.) was added dropwise to a stirred solution of the crude acids **S5** (1.00 g, 2.86 mmol, 1.0 eq.) in THF (20 mL) at 0 °C under Ar. After gas evolution ceased, the resulting solution was stirred and heated at 66 °C for 1 h. Then, the solution was cooled to rt and MeOH (5 mL) was added dropwise. The solvent was evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1-8:2 petrol-EtOAc as eluent gave alcohol *cis*-*rac*-**29** (615 mg, 51% over two steps) as a colourless oil and *trans*-*rac*-**29** (258 mg, 21% over two steps) as a colourless oil, R_F (8:2 petrol-EtOAc) 0.2; IR (film) 3312 (OH), 2901, 2896, 2867, 1698 (C=O), 1495, 1487, 1305, 1132, 915, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H, *o*-C_6H_4Me), 7.17 (d, J = 8.0 Hz, 2H, *m*-C_6H_4Me), 3.88-3.82 (m, 1H, NCH), 3.30 (br s, 1H, OH), 3.25-3.23 (m, 1H, CH_AH_BOH), 2.97 (t, J = 8.5 Hz, 1H, CH_AH_BOH) 2.36 (s, 3H, Me), 2.03-1.98 (m, 1H, CH), 1.76-1.64 (m, 3H, CH), 1.57 (s, 9H, CMe_3), 1.04 (t, J = 5.5 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.0 (C=O), 138.8 (*ipso*-C_6H_4S), 134.5 (Ar), 130.5 (*ipso*-C_6H_4Me), 129.8 (Ar), 81.3 (CMe_3), 66.5 (CH_2OH), 64.7 (NCH), 55.5 (NC), 29.8 (CH_2), 29.7 (CH_2), 28.4 (CMe_3), 27.4 (CH), 21.2 (Me); MS (ESI) *m/z* 358 [$(M + Na)^+$, 100], 336 [$(M + H)^+$, 30], 280 (100); HRMS *m/z* calcd for $C_{18}H_{25}NO_3S$ $(M + Na)^+$ 358.1447, found 358.1449 (−0.5 ppm error).

tert-Butyl 3-(hydroxymethyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate _cis_-(1_S_,3_S_,5_R_)-30

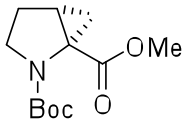


cis-**30**

Raney®-Nickel 2400 (1.5 mL of a 50% suspension in water) was added dropwise to a stirred solution of alcohol (1*R*,3*S*,5*R*)-**29** (211 mg, 0.63 mmol, 1.0 eq.) in 1:2 THF-EtOH (6 mL) at rt under Ar. The resulting solution was stirred at rt for 5 h. Then, CH_2Cl_2 (10 mL) and $MgSO_4$ were added and the solids were removed by filtration through Celite®. The filtrate was evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 9:1-8:2 petrol-acetone as eluent gave alcohol *cis*-(1*S*,3*S*,5*R*)-**30** (98 mg, 73%) as a colourless oil, R_F (8:2 petrol-acetone) 0.3; ^1H NMR (400 MHz, $CDCl_3$) δ 4.32-

4.28 (br m, 1H, CH), 3.51-3.43 (m, 4H, CH + OH), 2.46 (dddd, J = 13.5, 11.0, 6.5, 1.0 Hz, 1H, CH), 1.58-1.52 (m, 1H, CH), 1.50 (s, 9H, CMe_3), 1.50-1.47 (m, 1H, CH_AH_B), 0.80 (dtd, J = 9.0, 6.0, 1.0 Hz, 1H, CH), 0.43-0.40 (br m, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) (rotamers) δ 156.6 (br, C=O), 80.6 (CMe_3), 80.3 (CMe_3), 67.6 (br, N*C*HCH$_2$OH), 54.5 (CH_2OH), 38.8 (NCH), 37.4 (CH_2), 32.0 (CH), 30.6 (CH_2), 28.4 (C*Me*$_3$), 28.4 (C*Me*$_3$), 16.9 (CH_2), 14.7 (CH_2); MS (ESI) *m/z* 236 [(M + Na)$^+$, 100], 213 [(M + H)$^+$, 40]; HRMS *m/z* calcd for $C_{11}H_{19}NO_3$ (M + Na)$^+$ 236.1263, found 236.1263 (0.0 ppm error); $[\alpha]_D$ +6.6 (*c* 0.5 in $CHCl_3$). This compound has been reported in the literature[14a] but characterisation data were not disclosed. Through a personal communication with Professor Hannessian,[14b] the following optical rotation data was provided: $[\alpha]_D$ +12.0 (*c* 0.75 in $CHCl_3$). Our spectroscopic data were also consistent with those provided by Professor Hannessian.[14b]

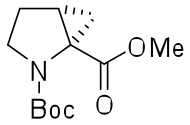
2-*tert*-Butyl (1*S*,5*R*)-1-methyl-2-azabicyclo[3.1.0]hexane-1,2-dicarboxylate (1*S*,5*R*)-32



(*S,R*)-**32**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn*-(*R,R,S*$_S$)-**7** (65 mg, 0.20 mmol, 1.0 eq., 99:1 er) in THF (8 mL) at rt for 1 min and methyl chloroformate (39 μL, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester (*S,R*)-**32** (43 mg, 89%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (9:1 petrol-EtOAc) 0.3; IR ($CDCl_3$) 2979, 1732 (C=O, CO_2Me), 1682 (C=O, Boc), 1529, 1444, 1368, 1164, 908, 881, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (ddd, J = 11.0, 9.5, 6.0 Hz, 1H, NCH_AH_B), 3.73 (s, 3H, OMe), 3.50 (br s, 1H, NCH$_A$*H*$_B$), 2.25 (ddt, J = 13.0, 9.5, 6.0 Hz, 1H, CH), 2.08-2.02 (m, 1H, CH), 1.96 (dd, J = 9.0, 5.5, Hz, 1H, CH), 1.98-1.87 (m, 1H, CH), 1.43 (s, 9H, CMe_3), 1.02 (t, J = 5.5 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.5 (*C*O_2Me) 155.5 (N*C*O_2CMe_3), 80.0 (*C*Me_3), 52.1 (OMe), 50.2 (NCH_2), 47.5 (NC), 31.0 (br, CH_2), 28.4 (CH), 28.3 (C*Me*$_3$), 26.4 (br, CH_2); MS (ESI) *m/z* 264 [(M + Na)$^+$, 100], 186 (20), 142 (30); HRMS *m/z* calcd for $C_{12}H_{19}NO_4$ (M + Na)$^+$ 264.1203, found 264.1206 (+1.3 ppm error); $[\alpha]_D$ −121.05 (*c* 0.20 in $CHCl_3$); CSP-HPLC: Chiracel OD (99:1 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*S,R*)-**32** 13.0 min, (*R*,S)-**32** 15.4 min.

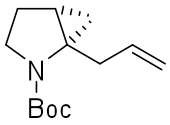
2-*tert*-Butyl 1-methyl-2-azabicyclo[3.1.0]hexane-1,2-dicarboxylate *rac*-32



rac-**32**

Using general procedure D, *i*-PrMgCl (0.15 mL of a 2.0 M solution in THF, 0.30 mmol, 1.5 eq.) and sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq.,) in THF (8 mL) at rt for 1 min and methyl chloroformate (23 μL, 0.30 mmol, 1.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 9:1 petrol-EtOAc as eluent gave ester *rac*-**32** (24 mg, 50%) as a colourless oil.

***tert*-Butyl (1*S*,5*R*)-1-(prop-2-en-1-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate (*S,R*)-33**

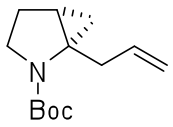


(*S,R*)-**33**

i-PrMgCl (0.25 mL, 0.50 mmol, 2.5 eq.) was added dropwise to a stirred solution of sulfoxide *syn*-(*R,R,S*$_S$)-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of CuBr.SMe$_2$ (8 mg, 20 mol%, 0.2 eq.) in THF (1 mL) was added dropwise. The solution was stirred at rt for 10 min. Then, allyl bromide (63 mg, 0.50 mmol, 2.5 eq.) was added dropwise and the resulting solution was stirred at rt for 2 h. Saturated $NH_4Cl_{(aq)}$ (7 mL) was added and the two were layers separated. The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 95:5 petrol-EtOAc as eluent gave allylated pyrrolidine (*S,R*)-**33** (31 mg, 69%) as a colourless oil, R_F (95:5 petrol-EtOAc) 0.3; IR ($CDCl_3$) 2941, 1685 (C=O), 1519, 1434, 1378, 1164, 1062, 910, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dtd, J = 14.0, 7.0, 6.5 Hz, 1H, C*H*=CH$_2$), 5.10-5.01 (m, 2H, =CH$_2$), 3.62 (ddd, J = 11.0, 9.5, 6.0 Hz, 1H, NC*H*$_A$H$_B$), 3.38 (br s, 1H, NCH$_A$*H*$_B$), 3.21 (br s, 1H, CH), 2.13-2.00 (m, 2H, CH), 1.82-1.75 (m, 1H, CH), 1.47 (s, 9H, CMe$_3$), 1.40-1.34 (m, 1H, CH), 0.91 (dd, J = 8.5, 5.5 Hz, 1H, CH), 0.67 (t, J = 5.5 Hz, 1H, CH) ; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.0 (C=O), 135.2 (*C*H=CH$_2$),

116.7 (CH=*C*H_2), 79.3 (br, *C*Me_3), 50.0 (br, NCH_2), 46.7 (NC), 37.5 (br, *C*H_2CH=), 28.5 (C*Me*$_3$), 25.9 (CH_2), 23.3 (CH), 21.8 (CH_2); MS (ESI) *m/z* 246 [$(M + Na)^+$, 70], 168 (100); HRMS *m/z* calcd for $C_{13}H_{21}NO_2$ $(M + Na)^+$ 246.1466, found 246.1465 (−0.5 ppm error); $[\alpha]_D$ +2.4 (*c* 0.45 in $CHCl_3$); CSP-HPLC: Chiracel AD-H (99.5:0.5 Hexane-*i*PrOH, 0.3 mLmin^{-1}) (*R*,*S*)-**33** 11.0 min, (*S*,*R*)-**33** 11.8 min.

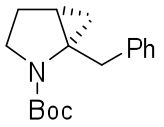
***tert*-Butyl 1-(prop-2-en-1-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate *rac*-33**



rac-**33**

i-PrMgCl (0.15 mL, 0.30 mmol, 1.5 eq.) was added dropwise to a stirred solution of sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) at rt for 1 min at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of CuBr.SMe_2 (8 mg, 20 mol%, 0.2 eq.) in THF (1 mL) was added dropwise. The solution was stirred at rt for 10 min. Then, allyl bromide (38 mg, 0.30 mmol, 1.5 eq.) was added dropwise and the resulting solution was stirred at rt for 2 h. Saturated $NH_4Cl_{(aq)}$ (7 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 95:5 petrol-EtOAc as eluent gave allylated pyrrolidine *rac*-**33** (26 mg, 58%) as a colourless oil.

***tert*-Butyl (1*R*,5*R*)-1-benzyl-2-azabicyclo[3.1.0]hexane-2-carboxylate (*R*,*R*)-34**

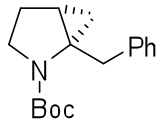


(R,R)-**34**

i-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) was added to a stirred solution of sulfoxide *syn*-(*R*,*R*,S_s)-**7** (65 mg, 0.20 mmol, 1.0 eq., 99:1 er) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of CuBr.SMe_2 (8 mg, 0.04 mmol, 0.2 eq.) in THF (0.5 mL) and benzyl bromide (89 mg, 0.50 mmol, 2.5 eq.) was

added sequentially and the solution was stirred at rt for 2 h. Saturated $NH_4Cl_{(aq)}$ (7 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 4:1 petrol-Et_2O as eluent gave benzylated pyrrolidine (*R*,*R*)-**34** (35 mg, 64%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (4:1 petrol-Et_2O) 0.2; IR ($CDCl_3$) 2985, 2810, 1679 (C=O), 1559, 1487, 1378, 1201, 1164, 908, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H, Ph), 7.22-7.19 (m, 3H, Ph), 3.76 (br s, 1H, NCH_AH_B), 3.42-3.16 (br m, 2H,CH), 2.57 (d, J = 14.0 Hz, 1H, CH), 1.99 (tdd, J = 14.0, 7.0, 2.8 Hz, 1H, CH), 1.77-1.70 (m, 1H, CH), 1.50-1.44 (m, 1H, CH), 1.50 (s, 9H, CMe_3), 0.98 (dd, J = 9.0, 5.0 Hz, 1H, CH) 0.73 (t, J = 5.0 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.9 (C=O), 139.4 (*ipso*-Ph), 129.4 (Ph), 128.2 (Ph), 126.2 (Ph), 79.4 (*C*Me_3), 48.4 (br, NCH_2), 43.5 (br, NC), 41.0 (br Ph*C*H_2), 32.6 (br, CH), 28.6 (C*Me*$_3$), 26.1 (CH_2), 23.7 (CH_2); MS (ESI) *m/z* 296 [(M + Na)$^+$, 70], 218 (100); HRMS *m/z* calcd for $C_{17}H_{24}NO_2$ (M + Na)$^+$ 296.1621, found 296.1611 (+3.2 ppm error); $[\alpha]_D$ −13.6 (*c* 0.2 in $CHCl_3$); CSP-HPLC: Chiracel OD (99:1 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (*R*,*R*)-**34** 5.6 min, (*S*,*S*)-**34** 6.6 min.

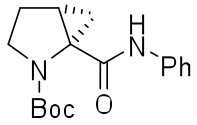
tert-Butyl 1-benzyl-2-azabicyclo[3.1.0]hexane-2-carboxylate _rac_-34



rac-**34**

i-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) was added to a stirred solution of sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq., 99:1 er) in THF (8 mL) at rt under Ar. The resulting solution was stirred at rt for 1 min. Then, a solution of CuBr.SMe_2 (8 mg, 0.04 mmol, 0.2 eq.) in THF (0.5 mL) and benzyl bromide (89 mg, 0.50 mmol, 2.5 eq.) was added sequentially and the solution was stirred at rt for 2 h. Saturated $NH_4Cl_{(aq)}$ (7 mL) was added and the two layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica with 4:1 petrol-Et_2O as eluent gave benzylated pyrrolidine *rac*-**34** (32 mg, 59%) as a colourless oil.

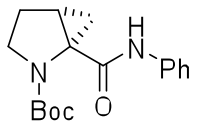
***tert*-Butyl (1*S*,5*R*)-(phenylcarbamoyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate (*S*,*R*)-35**



(S,R)-**35**

Using general procedure D, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn*-(*R*,*R*,S_s)-**7** (65 mg, 0.20 mmol, 1.0 eq., 99:1 er) in THF (8 mL) at rt for 1 min and phenylisocyanate (60 mg, 0.50 mmol, 2.5 eq.) gave the crude product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-Et_2O as eluent gave amide (*S*,*R*)-**35** (31 mg, 67%, 99:1 er by CSP-HPLC) as a pale yellow solid, mp 102-103 °C; R_F (98:2 CH_2Cl_2-Et_2O) 0.2; IR ($CDCl_3$) 3408 (NH), 2979, 1689 (C=O), 1682 (C=O), 1529, 1444, 1368, 1164, 908, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (br s, 1H, NH), 7.49 (d, J = 8.0 Hz, 2H, *o*-Ph), 7.30 (t, J = 8.0 Hz, 2H, *m*-Ph), 7.07 (d, J = 8.0 Hz, 1H, *p*-Ph), 3.75 (ddd, J = 11.5, 9.0, 6.5 Hz, 1H, NCH_AH_B), 3.66 (ddd, J = 11.5, 8.5, 5.5 Hz, 1H, NCH_AH_B), 2.24 (ddt, J = 13.0, 9.0, 6.5 Hz, 1H, CH), 2.17-2.12 (m, 1H,CH), 2.07 (dd, J = 9.0, 5.0 Hz, 1H, CH), 1.94 (dddd, J = 13.0, 8.5, 6.5, 1.5 Hz, 1H, CH), 1.42 (s, 9H, CMe_3), 1.02 (t, J = 5.0 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 168.6 (PhN*C*O) 156.9 (N*C*O_2CMe_3), 137.8 (*ipso*-Ph), 128.9 (Ph), 123.9 (Ph), 119.3 (Ph), 81.2 (*C*Me_3), 51.3 (NCH_2), 50.6 (NC), 31.1 (CH), 28.1 (C*Me*$_3$), 26.4 (CH_2), 24.8 (CH_2); MS (ESI) *m/z* 325 $[(M + Na)^+$, 30], 303 $[(M + H)^+$, 100]; HRMS *m/z* calcd for $C_{17}H_{22}N_2O_3$ $(M + Na)^+$ 325.1523, found 325.1523 (−0.2 ppm error);); $[\alpha]_D$ −58.6 (*c* 0.7 in $CHCl_3$); CSP-HPLC: Chiracel OD (90:10 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (*R*,*S*)-**35** 7.4 min, (*S*,*R*)-**35** 14.5 min..

***tert*-Butyl 1-(phenylcarbamoyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate *rac*-35**

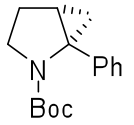


rac-**35**

Using general procedure D, *s*-BuLi (1.69 mL of a 1.3 M solution in hexanes, 2.20 mmol, 2.2 eq.), *N*-Boc 4-chloro piperidine **25** (219 mg, 1.00 mmol, 1.0 eq.) and TMEDA (255 mg, 2.20 mmol, 2.2 eq.) in Et_2O (8 mL) and phenylisocyanate (262 mg, 2.20 mmol, 2.2 eq.) gave the crude

product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-Et_2O as eluent gave amide *rac*-**35** (290 mg, 96%) as a pale yellow solid.

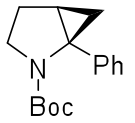
2-*tert*-Butyl (1*S*,5*R*)-1-phenyl-2-azabicyclo[3.1.0]hexane-2-carboxylate (1*S*,5*R*)-36



(1*S*,5*R*)-**36**

Using general procedure H, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn*-(*R*,*R*,S_S)-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and bromobenzene (39 mg, 0.24 mmol, 1.2 eq.) gave the crude product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-petrol as eluent gave arylated pyrrolidine (1*S*,5*R*)-**36** (35 mg, 68%, 99:1 er by CSP-HPLC) as a colourless oil, R_F (98:2 CH_2Cl_2-petrol) 0.3; IR ($CDCl_3$) 2874, 2791, 1681 (C=O) 1540, 1521, 1444, 1368, 908, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.24 (m, 4H, Ph), 7.21-7.16 (m, 1H, Ph), 3.90 (ddd, J = 11.5, 9.5, 6.0 Hz, 1H, NC$H_A$$H_B$), 3.61 (ddd, J = 11.5, 9.0, 6.0 Hz, 1H, NCH$_A$$H_B$), 2.32 (ddt, J = 12.5, 9.5, 6.0 Hz, 1H, CH), 1.97 (dddd, J = 12.5, 9.0, 6.0, 1.0 Hz, 1H, CH), 1.81 (dd, J = 9.0, 5.5 Hz, 1H, CH), 1.62-1.56 (m, 1H, CH), 1.22 (br s, 9H, CMe_3), 1.02 (t, J = 5.5 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 154.7 (C=O), 133.6 (*ipso*-Ph), 132.7 (Ph), 127.9 (Ph), 125.9 (Ph), 79.4 (*C*Me_3), 50.1 (NCH_2), 49.7 (NC), 30.3 (NC*C*H), 28.2 (C*Me*$_3$), 26.7 (CH_2), 22.3 (CH_2); MS (ESI) *m/z* 282 [(M + Na)$^+$, 100], 204 (30); HRMS *m/z* calcd for $C_{16}H_{21}NO_2$ (M + Na)$^+$ 282.1465, found 282.1470 (−2.1 ppm error); $[\alpha]_D$ +8.2 (*c* 0.65 in $CHCl_3$); CSP-HPLC: Chiracel AD-H (99:1 Hexane-*i*PrOH, 0.5 mLmin^{-1}) (1*S*,5*R*)-**36** 8.5 min, (1*S*,5*R*)-**36** 10.0 min.

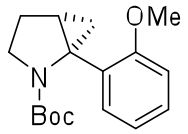
***tert*-Butyl 1-phenyl-2-azabicyclo[3.1.0]hexane-2-carboxylate *rac*-36**



rac-**36**

Using general procedure H, *i*-PrMgCl (0.15 mL of a 2.0 M solution in THF, 0.30 mmol, 1.5 eq.) and sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and bromobenzene (22 mg, 0.14 mmol, 0.7 eq.) gave the crude product. Purification by flash column chromatography on silica with 98:2 CH_2Cl_2-petrol as eluent gave arylated pyrrolidine *rac*-**36** (20 mg, 55%) as a colourless oil.

***tert*-Butyl 1-[2-methoxyphenyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate (1*S*,5*R*)-37**

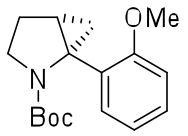


(1*S*,5*R*)-**37**

Using general procedure H, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn*-(*R*,*R*,S_S)-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and methyl 2-bromoanisole (45 mg, 0.24 mmol, 1.20 eq.) gave the crude product. Purification by flash column chromatography on silica with 7:3 petrol-Et_2O as eluent gave arylated pyrrolidine (1*S*,5*R*)-**37** (39 mg, 68%) as a colourless oil, R_F (7:3 petrol-Et_2O) 0.2; IR ($CDCl_3$) 2875, 2782, 1685 (C=O), 1421, 1444, 1368, 913, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (br d, J = 7.5 Hz, 1H, Ar), 7.22 (td, J = 7.5, 2.0 Hz, 1H, Ar), 6.88 (br t, J = 7.5 Hz, 1H, Ar), 6.83 (br d, J = 7.5 Hz, 1H, Ar), 3.97 (td, J = 12.0, 4.5 Hz, 1H, NC$H_A$$H_B$), 3.84 (s, 3H, OMe), 3.60-3.53 (br m, 1H, NC$H_A$$H_B$), 2.37 (dddd, J = 12.5, 7.5, 4.5, 1.5 Hz, 1H, CH), 1.97-1.90 (m, 1H, CH), 1.60-1.53 (m, 2H, CH), 1.22 (br s, 9H, CMe_3), 0.90 (t, J = 4.0 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.8 (C=O), 155.5 (*ipso*-C_6H_4OMe), 131.6 (Ar), 128.7 (Ar), 128.2 (*ipso*-Ar), 119.6 (Ar), 110.1 (Ar), 79.0 (CMe_3), 55.5 (OMe), 50.5

(NCH_2), 46.8 (NC), 28.3 (CMe_3), 27.3 (br, CH), 26.9 (CH_2), 22.8 (CH_2); MS (ESI) *m/z* 312 [$(M + Na)^+$, 100], 234 (70), 190 (30); HRMS *m/z* calcd for $C_{17}H_{23}NO_3$ $(M + Na)^+$ 321.1572, found 312.1570 (−0.5 ppm error); $[\alpha]_D$ −6.9 (*c* 0.65 in $CHCl_3$); CSP-HPLC: Chiracel AD-H (99:1 Hexane-*i*PrOH, 0.5 $mLmin^{-1}$) (1*S,5R*)-**37** 7.5 min, (1*R,5S*)-**37** 8.3 min.

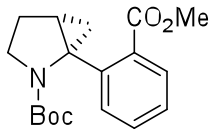
***tert*-Butyl 1-[2-methoxyphenyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate *rac*-37**



rac-**37**

Using general procedure H*, i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and methyl 2-bromoanisole (26 mg, 0.14 mmol, 0.7 eq.) gave the crude product. Purification by flash column chromatography on silica with 7:3 petrol-Et_2O as eluent gave arylated pyrrolidine *rac*-**37** (19 mg, 48%) as a colourless oil.

***tert*-Butyl 1-[2-(methoxycabronyl)phenyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate (1*S*,5*R*)-38**

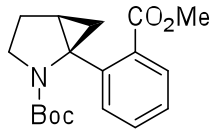


(1*S,5R*)-**38**

Using general procedure H*, i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.), sulfoxide *syn*-(*R,R,S*$_S$)-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL), $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and methyl 2-bromobenzoate (51 mg, 0.24 mmol, 1.2 eq.) gave the crude product. Purification by flash column chromatography on silica with 7:3 petrol-Et_2O as eluent gave arylated pyrrolidine (1*S,5R*)-**38** (47 mg, 74%) as a colourless oil, R_F (7:3 petrol-Et_2O)

0.1; IR ($CDCl_3$) 2874, 1726 (C=O, CO_2Me), 1679 (C=O, Boc), 1532, 1454, 1268, 908, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.0, 1.5 Hz, 1H, *o*-$C_6H_4CO_2Me$), 7.38 (br t, J = 8.0 Hz 1H, *p*-$C_6H_4CO_2Me$), 7.32-7.25 (m, 2H, Ar), 3.87 (s, 3H, OMe), 3.76 (dt, J = 11.0, 4.0 Hz, 1H, NCH_AH_B), 3.37-3.30 (br m, 1H, NCH_AH_B), 2.58-2.49 (m, 1H, CH), 2.00 (dtd, J = 12.0, 9.0, 4.0 Hz, 1H, CH), 1.79-1.74 (m, 1H, CH), 1.81 (dd, J = 9.0, 5.5 Hz, 1H, CH), 1.07 (br s, 9H, CMe_3), 0.90 (t, J = 5.5 Hz, 1H, CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.3 (CO_2Me), 155.9 (NCO_2CMe_3), 134.4 (*ipso*-Ar), 132.1 (Ar), 130.5 (br, Ar), 128.9 (Ar), 128.8 (Ar), 126.5 (Ar), 79.4 (CMe_3), 52.0 (OMe), 48.7 (NC), 48.6 (NCH_2), 30.0 (CH), 27.9 (CMe_3), 25.6 (CH_2), 18.5 (CH_2); MS (ESI) *m/z* 340 [$(M + Na)^+$, 100], 318[$(M + H)^+$, 40], 262 (40), 218 (40); HRMS *m/z* calcd for $C_{18}H_{23}NO_4$ $(M + Na)^+$ 340.1518, found 340.1519 (+0.4 ppm error); $[\alpha]_D$ −46.4 (*c* 1.00 in $CHCl_3$); CSP-HPLC: Chiracel AD-H (99:1 Hexane-*i*PrOH, 1.0 $mLmin^{-1}$) (1*S,5R*)-**38** 9.7 min, (1*R,5S*)-**38** 15.8 min.

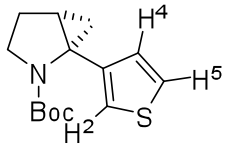
***tert*-Butyl 1-[2-(methoxycabronyl)phenyl]-2-azabicyclo[3.1.0]hexane-2-carboxylate *rac*-38**



rac-**38**

Using general procedure H*, i*-PrMgCl (0.15 mL of a 2.0 M solution in THF, 0.30 mmol, 1.5 eq.) and sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and methyl 2-bromobenzoate (30 mg, 0.14 mmol, 0.7 eq.) gave the crude product. Purification by flash column chromatography on silica with 7:3 petrol-Et_2O as eluent gave arylated pyrrolidine *rac*-**38** (32 mg, 72%) as a colourless oil.

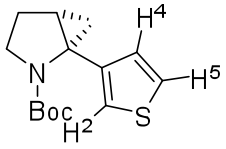
2-*tert*-Butyl (1*S*,5*R*)-1-(thiophen-3-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate (1*S*,5*R*)-39



(1*S*,5*R*)-**39**

Using general procedure H, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn*-(*R*,*R*,S_S)-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$ (3.5 mg, 0.012 mmol, 0.06 eq.) and 3-bromothiophene (23 μL, 0.24 mmol, 1.2 eq.) gave the crude product. Purification by flash column chromatography on silica with 99:1-98:2 CH_2Cl_2-Et_2O as eluent gave arylated pyrrolidine (1*S*,5*R*)-**39** (38 mg, 72%) as a colourless oil, R_F (98:2 CH_2Cl_2-Et_2O) 0.5; IR ($CDCl_3$) 2910, 2874, 1675 (C=O), 1555, 1532, 1268, 908, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, J = 5.0, 3.0 Hz, 1H, H^5), 6.98 (dd, J = 5.0, 1.5 Hz 1H, H^4), 6.94 (dd, J = 3.0, 1.5 Hz, 1H, H^2), 3.86 (ddd, J = 11.5, 9.5, 6.0 Hz, 1H, NC$H_A$$H_B$), 3.55 (ddd, J = 11.5, 9.0, 6.0 Hz, 1H, NC$H_A$$H_B$), 2.34-2.25 (m, 1H, CH), 1.93 (dddd, J = 13.0, 9.0, 6.0, 1.5 Hz, 1H, CH), 1.68-1.60 (m, 2H, CH), 1.28 (br s, 9H, CMe_3), 1.04 (t, J = 5.0 Hz, 1H, NCC$H_A$$H_B$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.2 (C=O), 132.6 (*ipso*-Ar), 126.4 (Ar), 125.0 (br, Ar), 118.7 (Ar), 79.4 (*C*Me_3), 49.9 (NC), 46.6 (NCH_2), 30.8 (br, CH), 28.2 (C*Me*$_3$), 26.5 (CH_2), 23.5 (CH_2); MS (ESI) *m/z* 288 [(M + Na)$^+$, 100], 210 (40); HRMS *m/z* calcd for $C_{14}H_{19}NO_2S$ (M + Na)$^+$ 288.1029, found 288.1027 (+0.6 ppm error); $[\alpha]_D$ −42.0 (*c* 0.5 in $CHCl_3$); CSP-HPLC: Chiracel OD-H (99:1 Hexane-*i*PrOH, 1.0 mLmin^{-1}) (*S*,*R*)-**39** 7.7 min, (*R*,S)-**39** 8.6 min.

***2-tert*-Butyl 1-(thiophen-3-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate *rac*-39**



rac-**39**

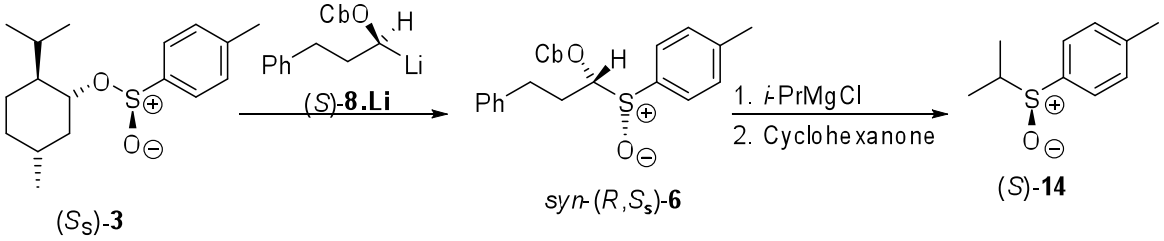
Using general procedure H, *i*-PrMgCl (0.25 mL of a 2.0 M solution in THF, 0.50 mmol, 2.5 eq.) and sulfoxide *syn-rac*-**7** (65 mg, 0.20 mmol, 1.0 eq.) in THF (8 mL) and $ZnCl_2$ (0.12 mL of a 1.0 M solution in Et_2O, 0.12 mmol, 0.6 eq.), $Pd(OAc)_2$ (3 mg, 0.01 mmol, 0.05 eq.), *t*-$Bu_3PH.BF_4$

(3.5 mg, 0.012 mmol, 0.06 eq.) and 3-bromothiophene (23 μL, 0.24 mmol, 1.2 eq.) gave the crude product. Purification by flash column chromatography on silica with 99:1-98:2 CH_2Cl_2-Et_2O as eluent gave arylated pyrrolidine *rac*-**39** (33 mg, 62%) as a colourless oil.

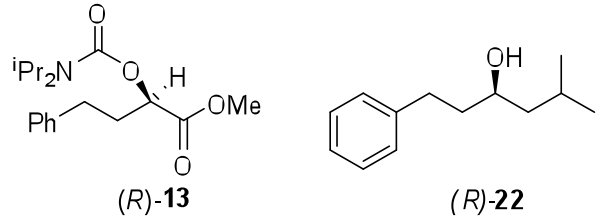
2 Additional Information

2.1 Proof of Configuration of Sulfoxides *anti*-(*S*,S_s)-6 and *syn*-(*R*,S_s)-6

1. For the lithiation-trapping of *O*-alkyl carbamate **8**, the sense of induction using *s*-BuLi and (–)-sparteine,[4,15,16] (+)-sparteine surrogate[4] and diamines (*R*,*R*)-**12** and (*S*,*S*)-**12**[5] is wellprecedented.
2. Inversion of configuration at sulfur when trapping with Andersen's sulfinate is well documented.[7,17,18]
3. (*S*)-Isopropyl *p*-tolyl sulfoxide (*S*)-**14** was isolated as the expected product of a sulfoxide → magnesium exchange reaction. This indicates a double inversion from Andersen's Sulfinate (S_s)-**3** thus confirming the configuration at sulfur in *anti*-(*S*,S_s)-**6** and *syn*-(*R*,S_s)-**6**. The optical rotation for (*S*)-**14** ([α]$_D$ −194.2 (*c* 1.0 in EtOH) (lit.,[10] [α]$_D$ −187 (*c* 2.4 in EtOH)) is in accordance with that reported in the literature.[10]

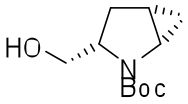


4. Two known products have been synthesized from *anti*-(*S*,S_s)-**6**. Optical rotations for (*R*)-**13** ([α]$_D$ −17.8 (*c* 0.55 in CH_2Cl_2) (lit.,[2] [α]$_D$ −17.3 (*c* 1.0 in CH_2Cl_2) for (*R*)-**13** of 97:3 er)) and (*R*)-**22** ([α]$_D$ +15.59 (*c* 0.65 in $CHCl_3$) (lit.,[6] [α]$_D$ +16.00 (*c* 0.70 in $CHCl_3$) for (*R*)-**22** of 97:3 er)) are in accordance with those reported in the literature.



2.2 Proof of configuration of Sulfoxides *syn*-(*R*,*R*,S_s)-7 and *anti*-(*S*,*S*,S_s)-7

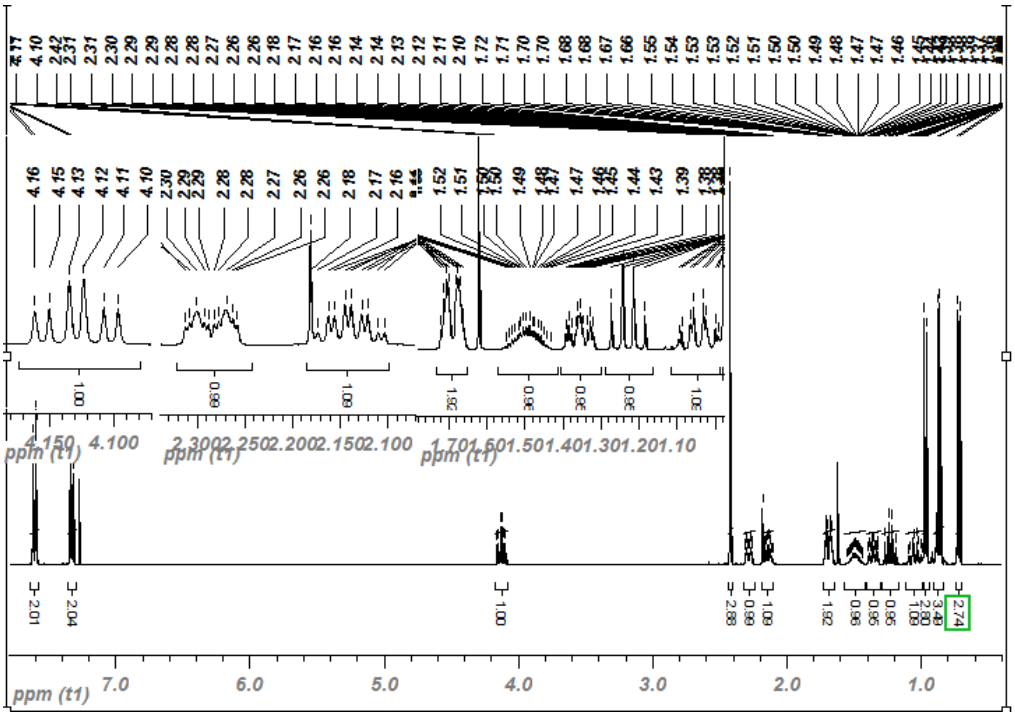
1. For the lithiation-trapping of *N*-Boc 4-chloro piperidine **25** the sense of induction using *s*-BuLi and (–)-sparteine has been established.[19,20] In addition, the sense of induction in the lithiation-trapping of *N*-Boc piperidine is also known.[4,5,20,21]
2. Inversion of configuration at sulfur when trapping with Andersen's sulfinate (S_s)-**3** is well precedented.[7,17,18]
3. Known alcohol *cis*-**30** has been synthesised from *anti*-(*S*,S_s)-**6**. The ^{1}H and ^{13}C NMR spectra for alcohol *cis*-**30** match with those provided by Professor Hannessian and are different to those of alcohol *trans*-**30**.[14b] The optical rotation for *cis*-**30** ($[\alpha]_D$ +6.64 (*c* 0.50 in $CHCl_3$) is in accordance with that provided by Professor Hannessian: $[\alpha]_D$ +12.00 (*c* 0.75 in $CHCl_3$).[14b]

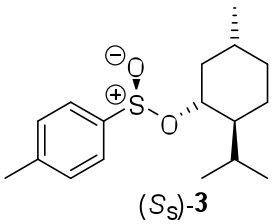


cis-**30**

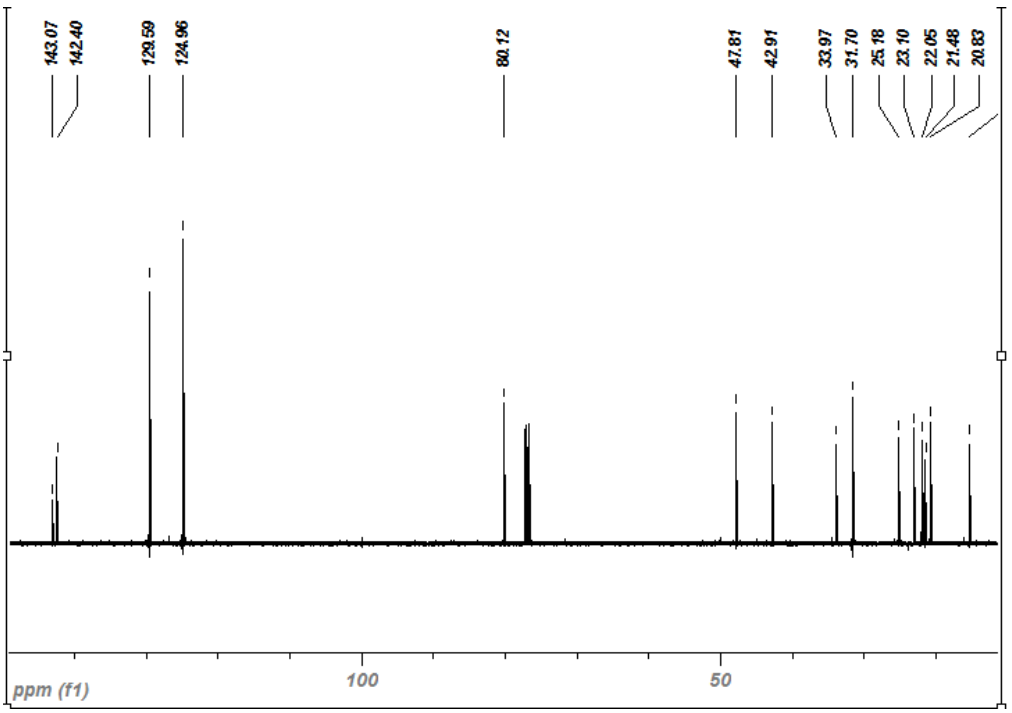
3 $^{1}H/^{13}C$ NMR Spectra and CSP-HPLC Data

400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

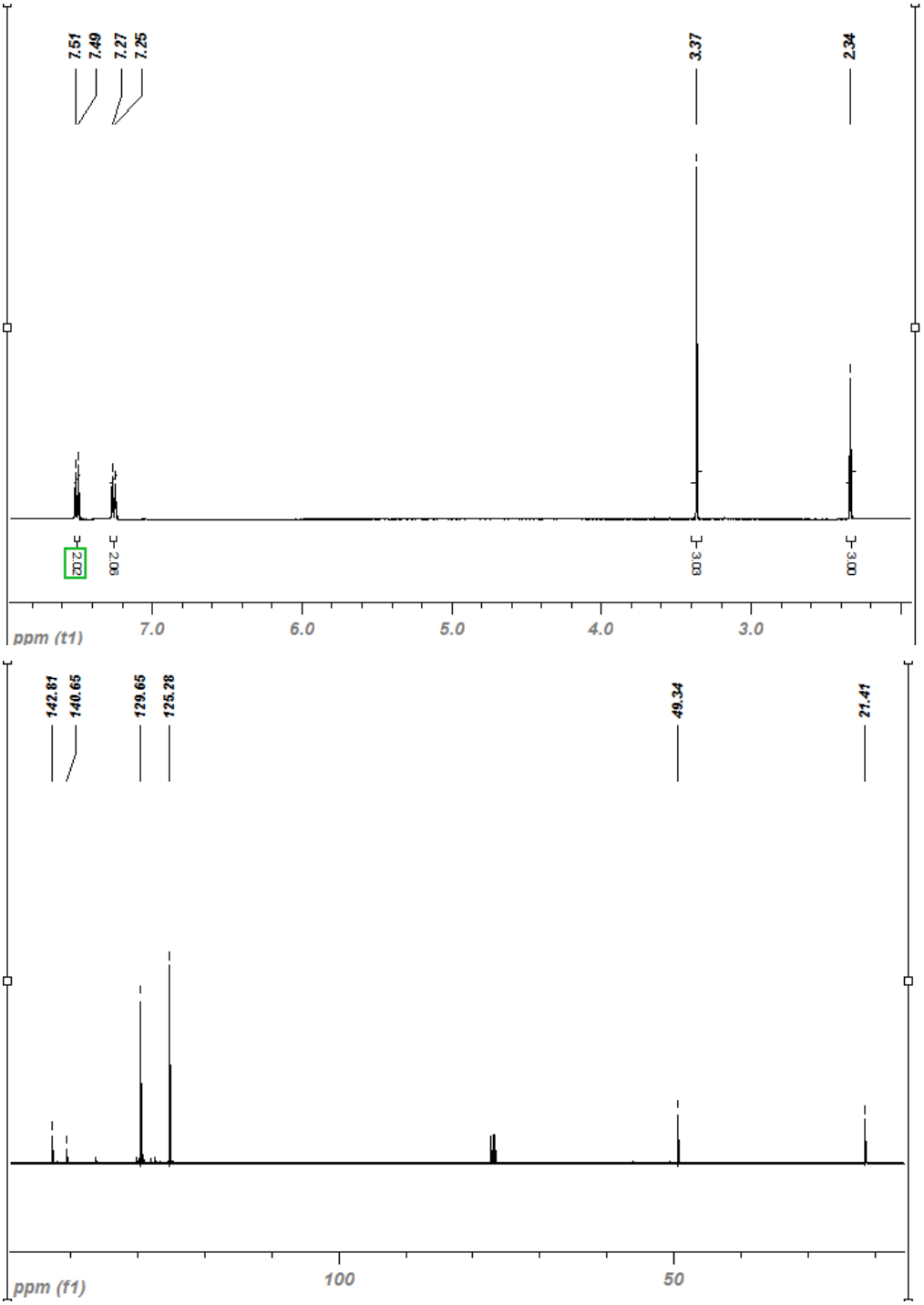


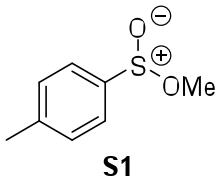


(S_S)-**3**



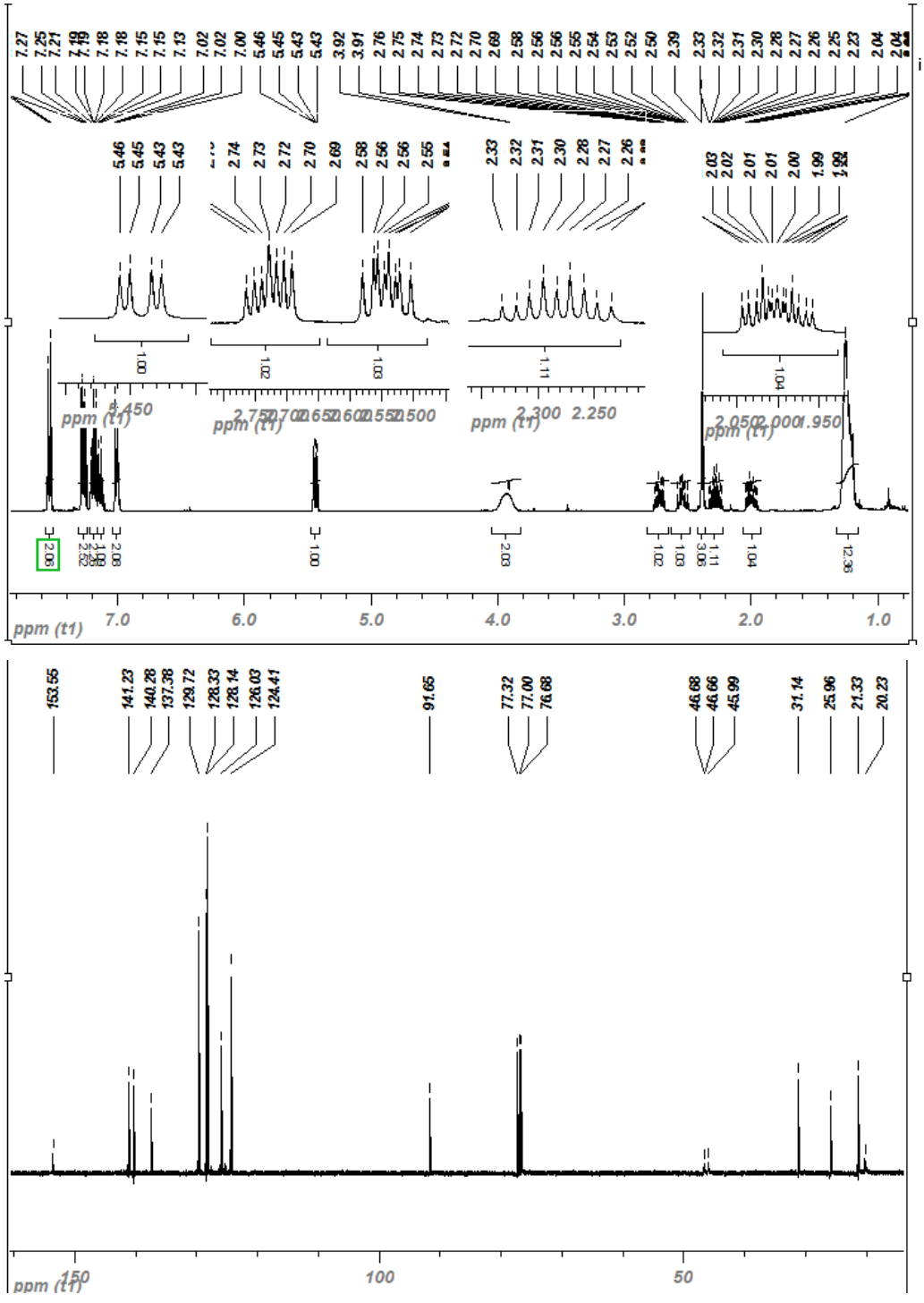
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

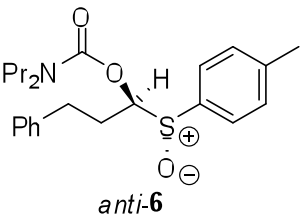




S1

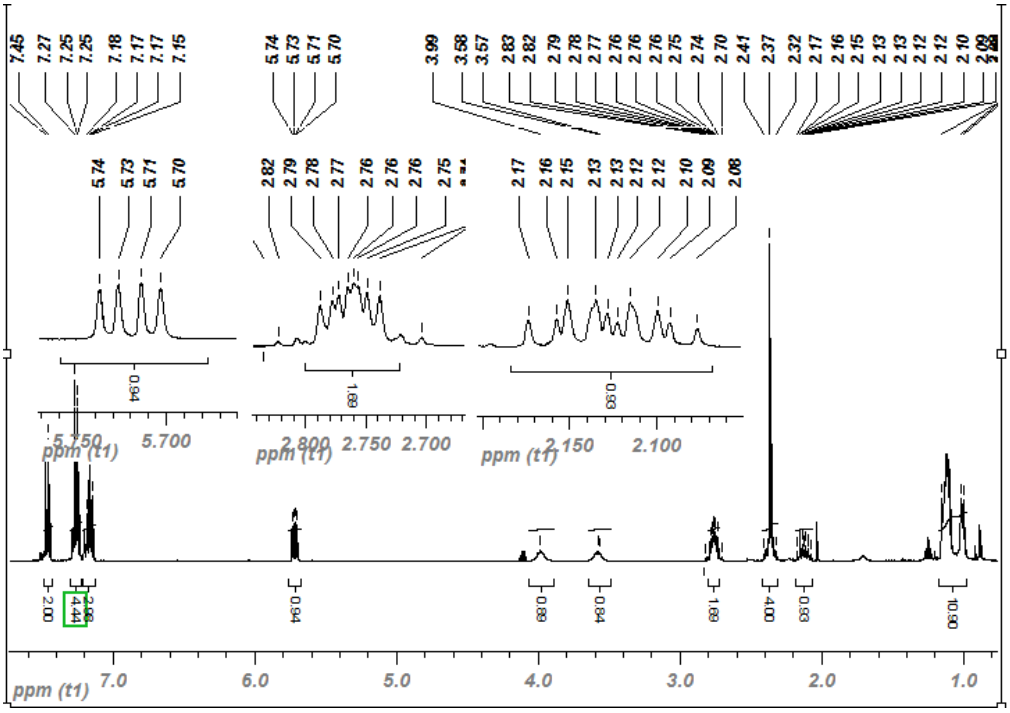
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

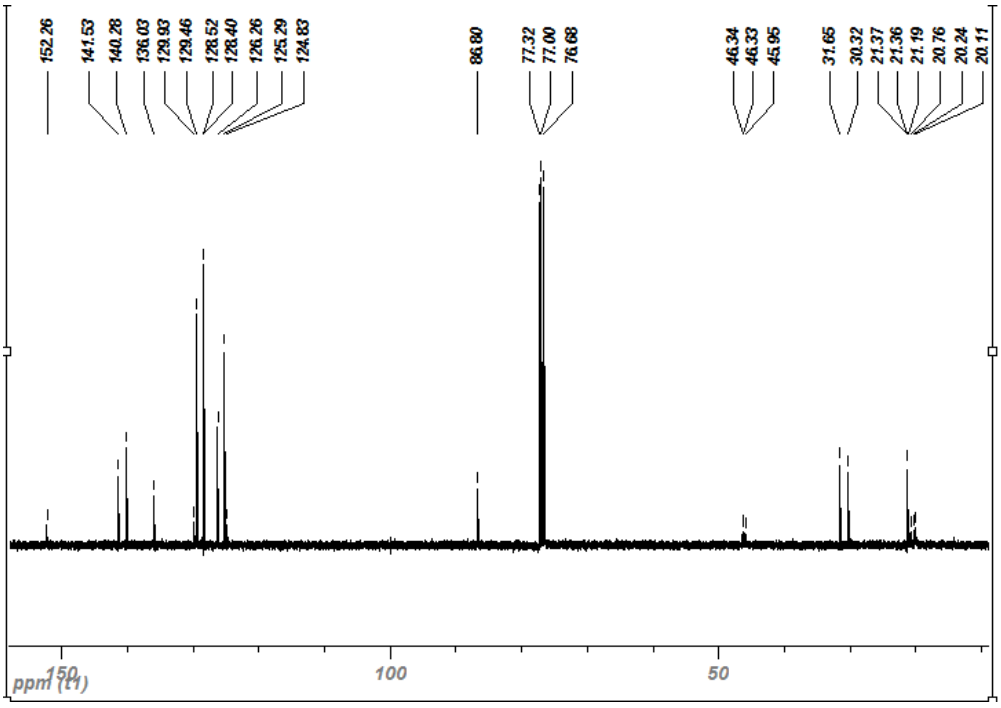


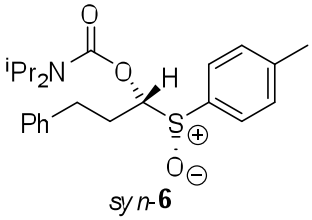


anti-**6**

400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

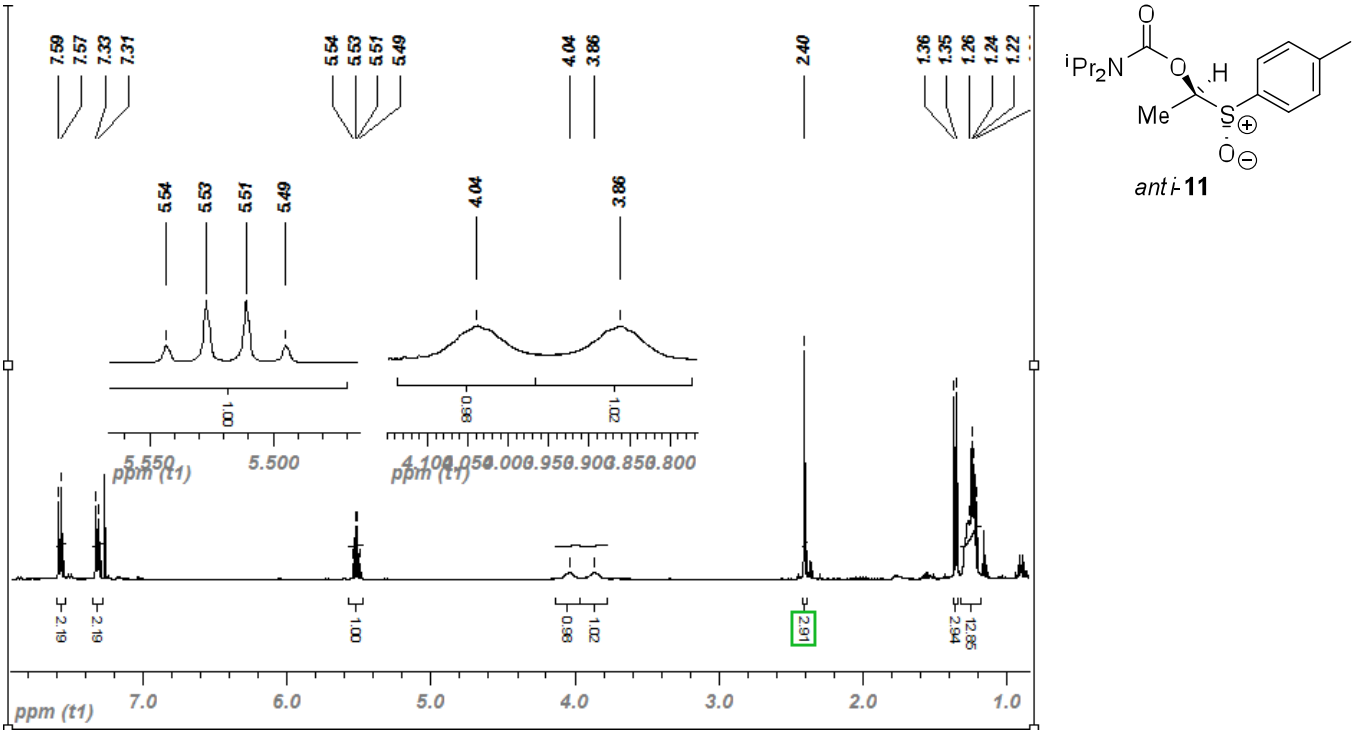




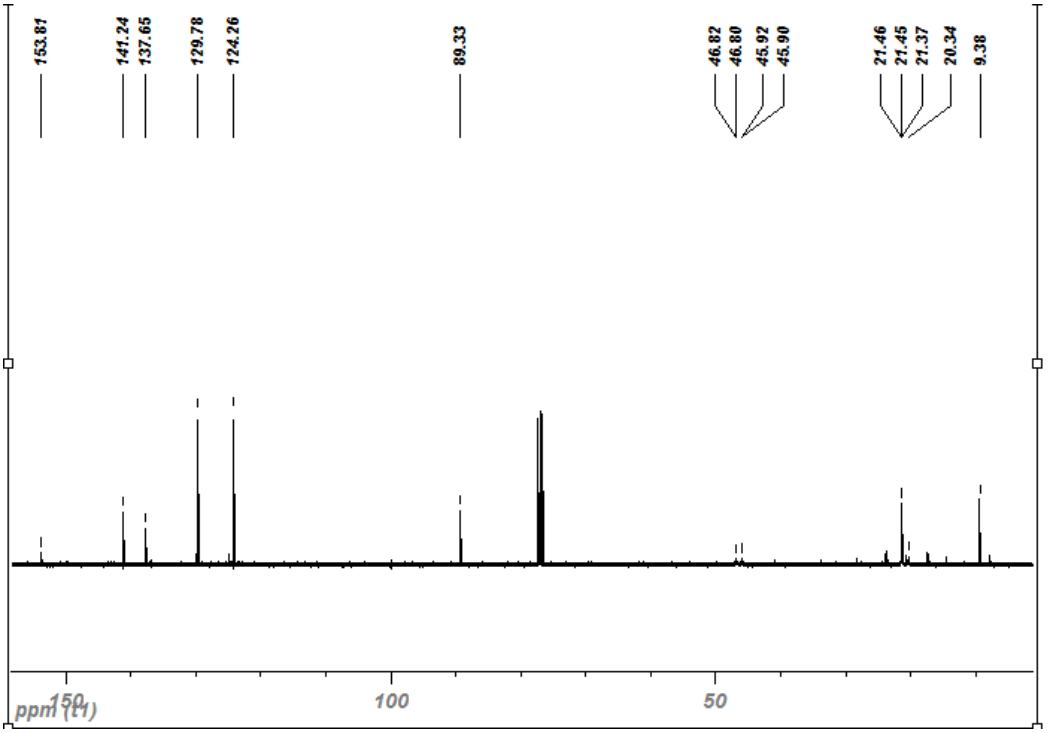


syn-**6**

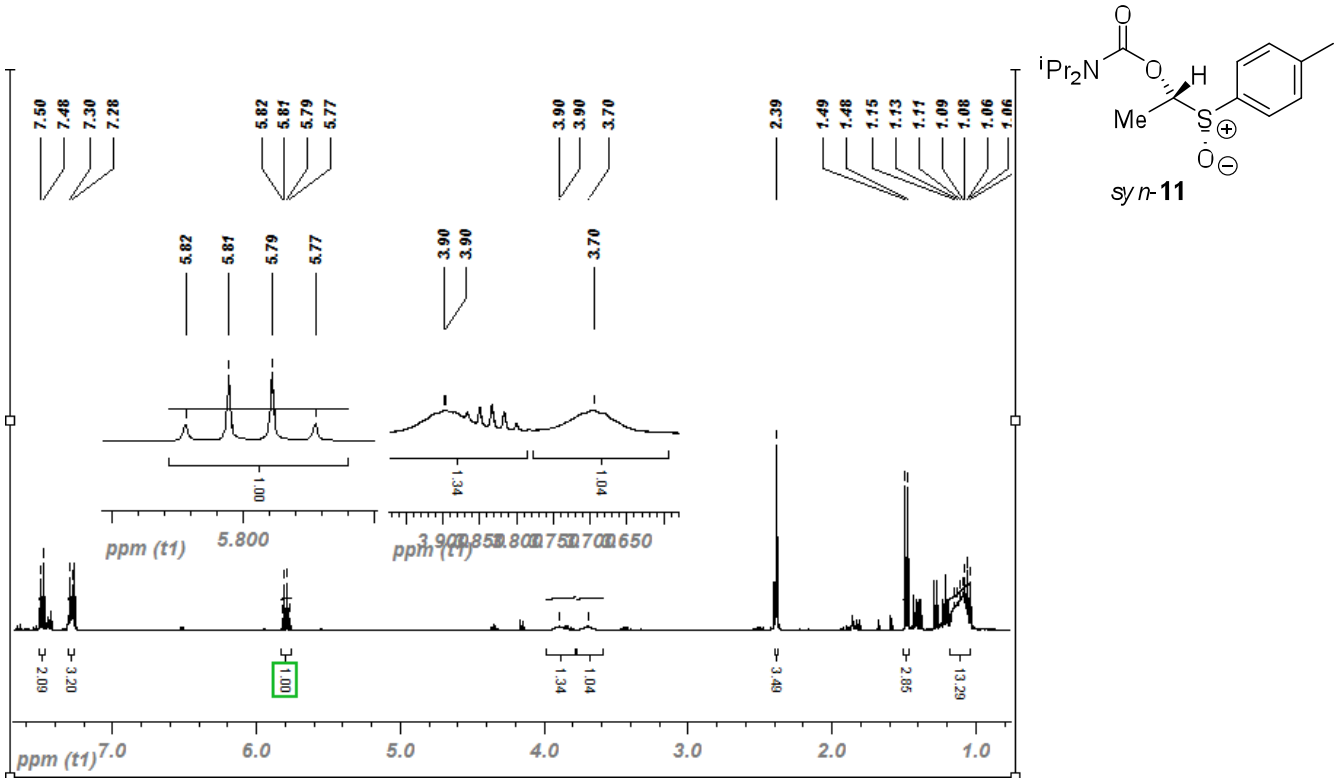
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

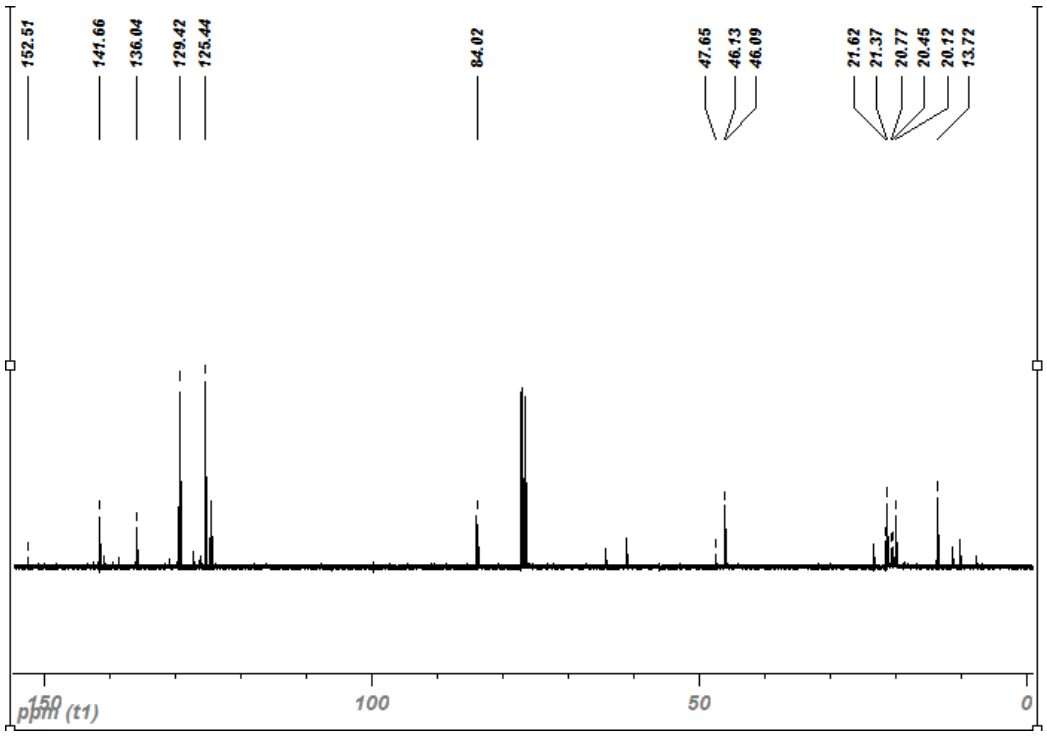


anti-**11**

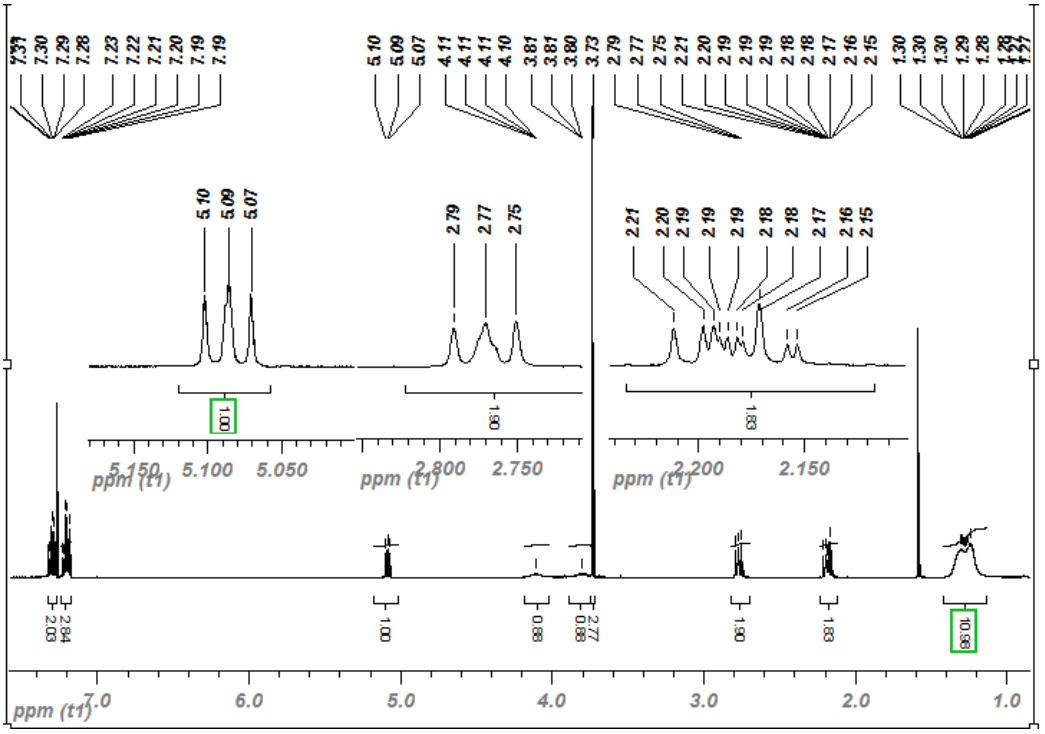


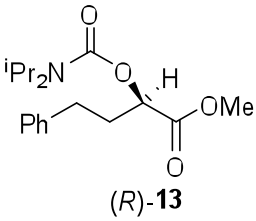
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$



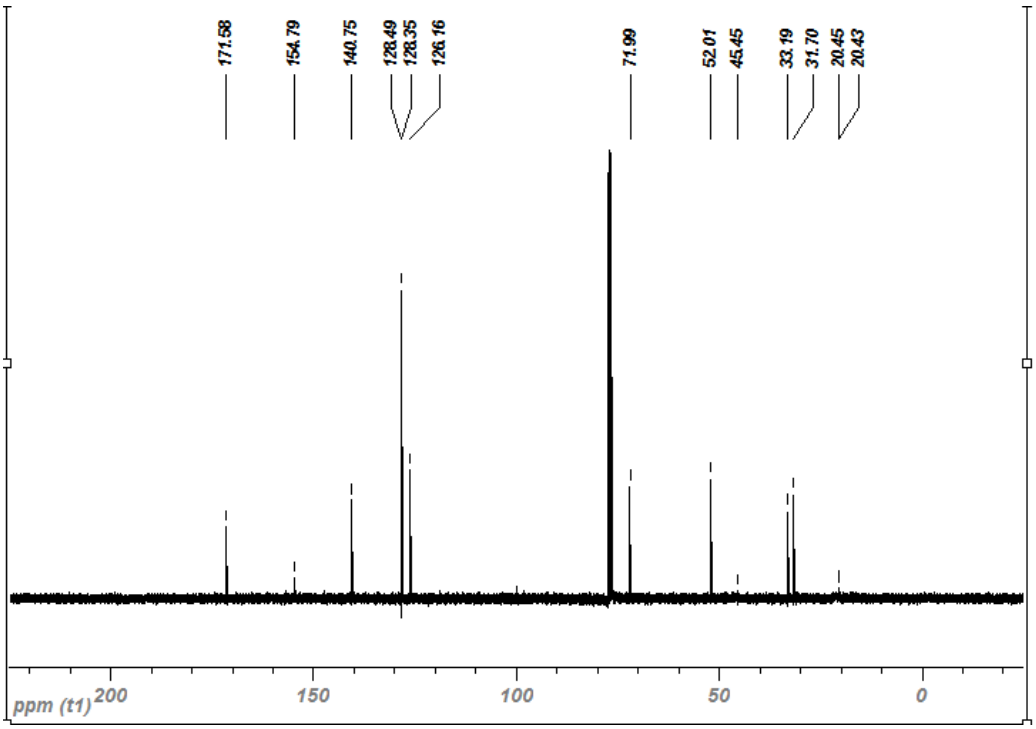


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

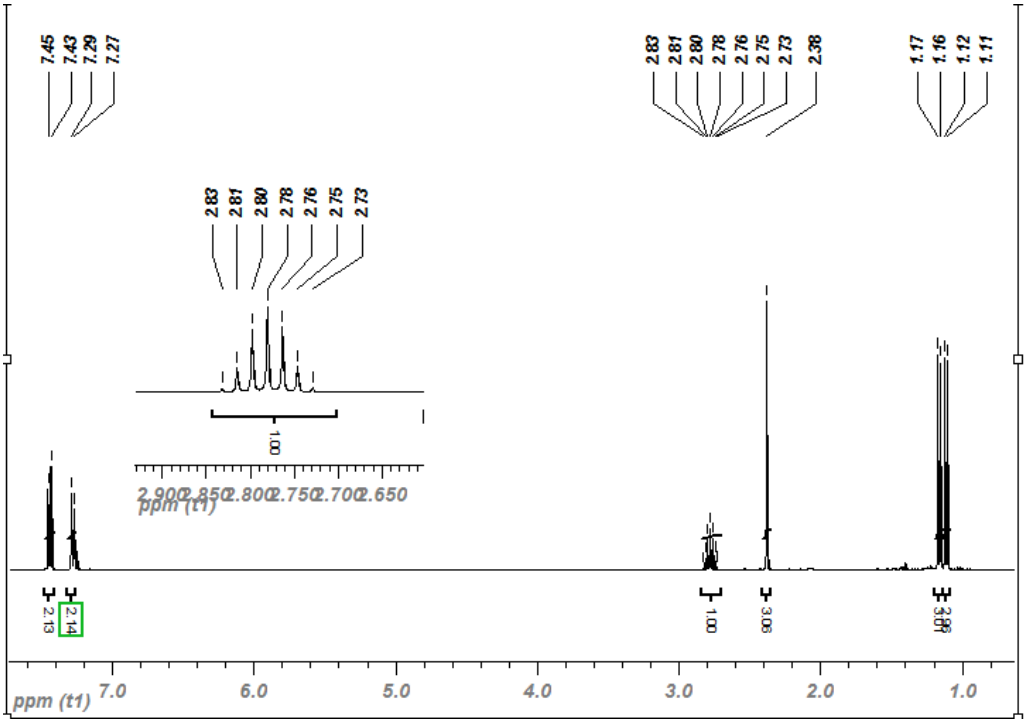


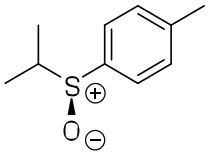


(*R*)-**13**

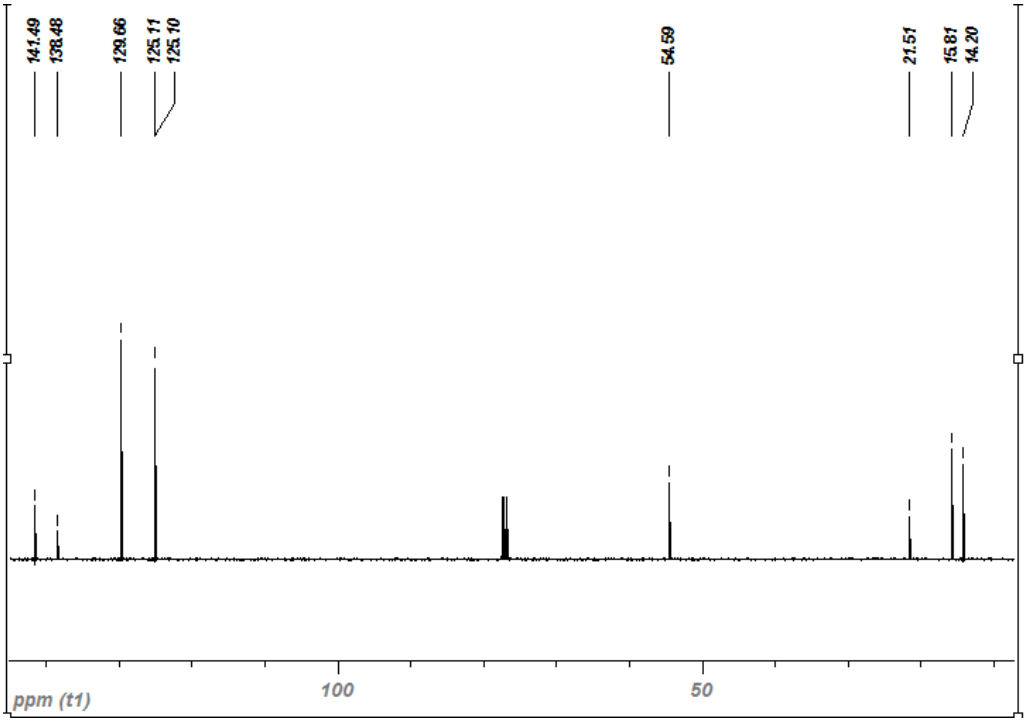


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

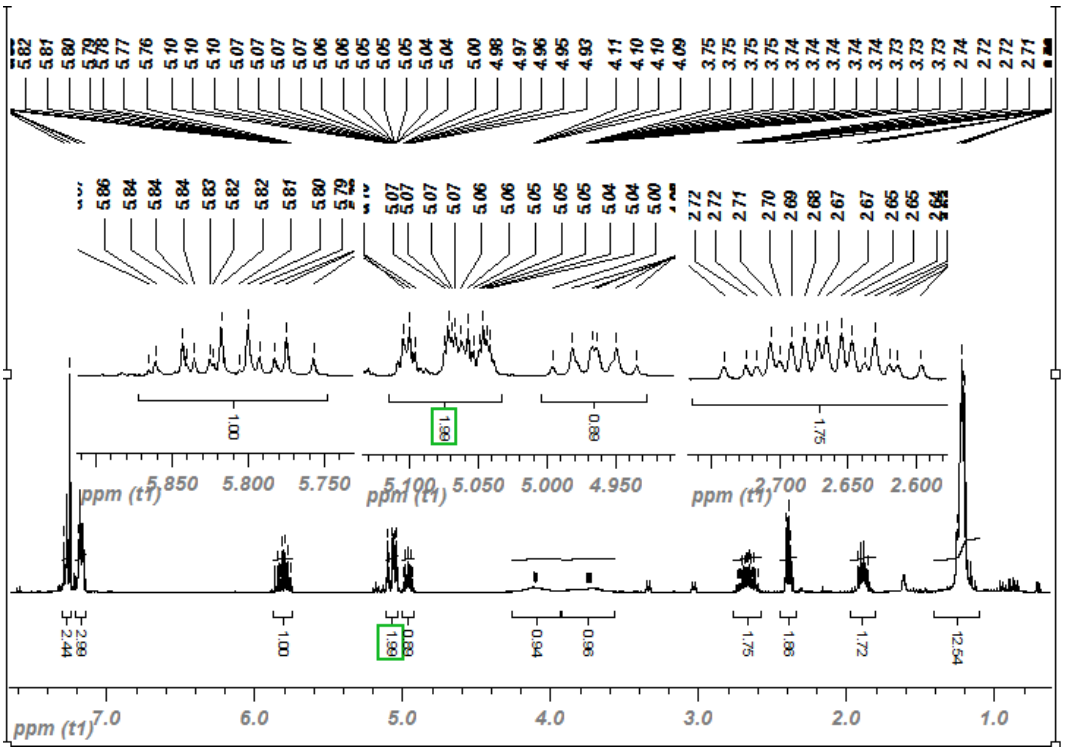


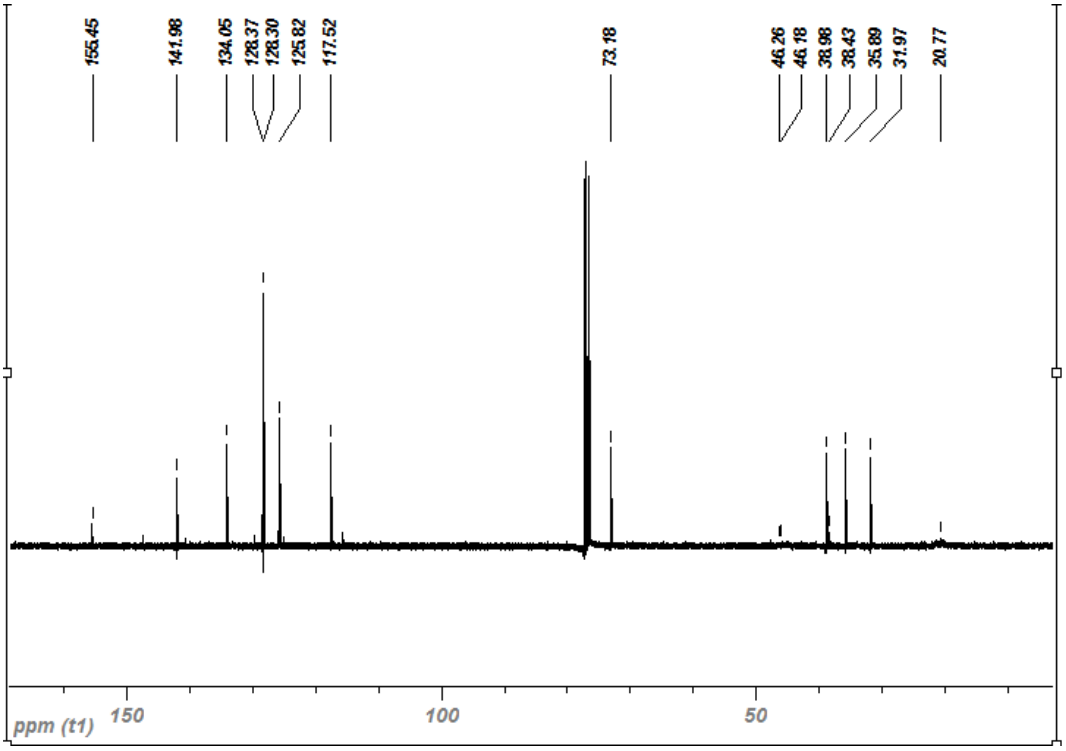


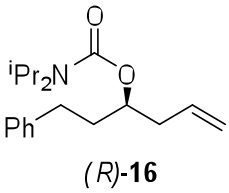
(*S*)-**14**



400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

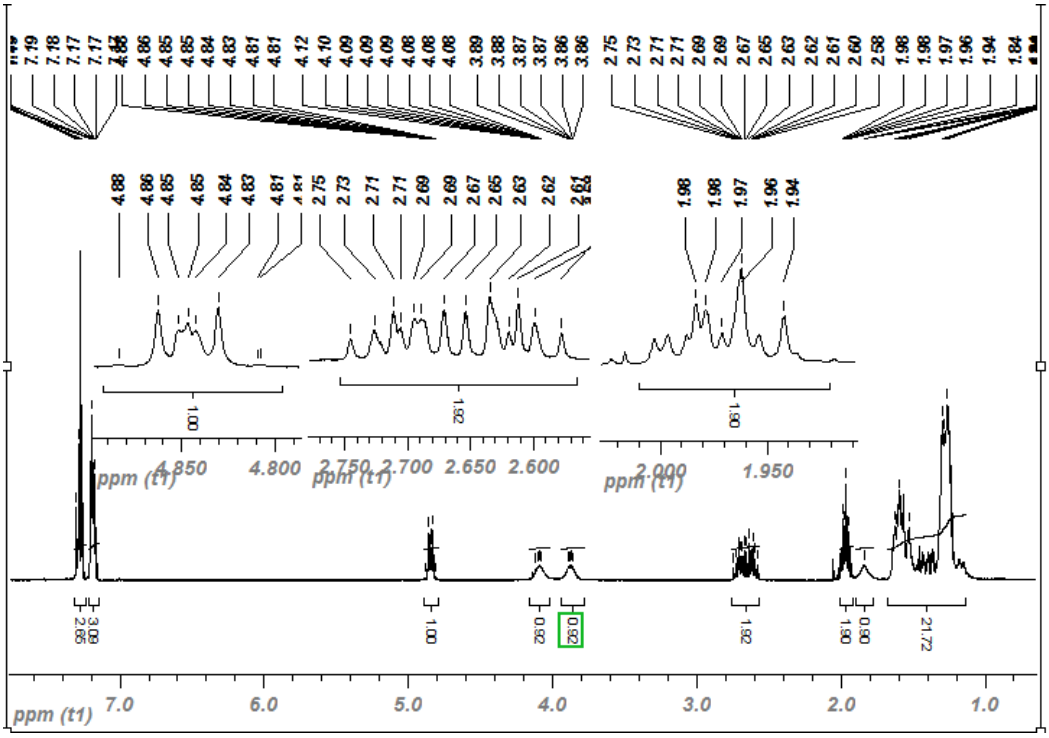


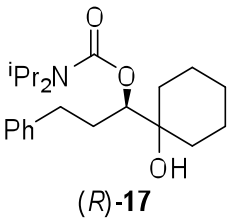




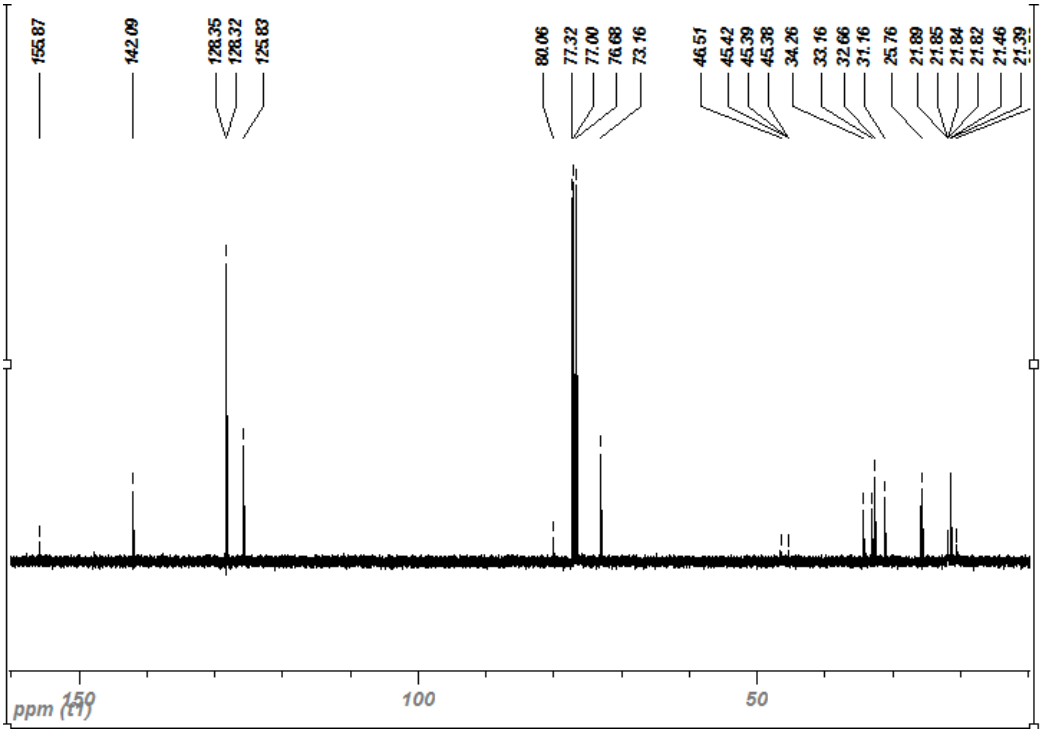
(R)-**16**

400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

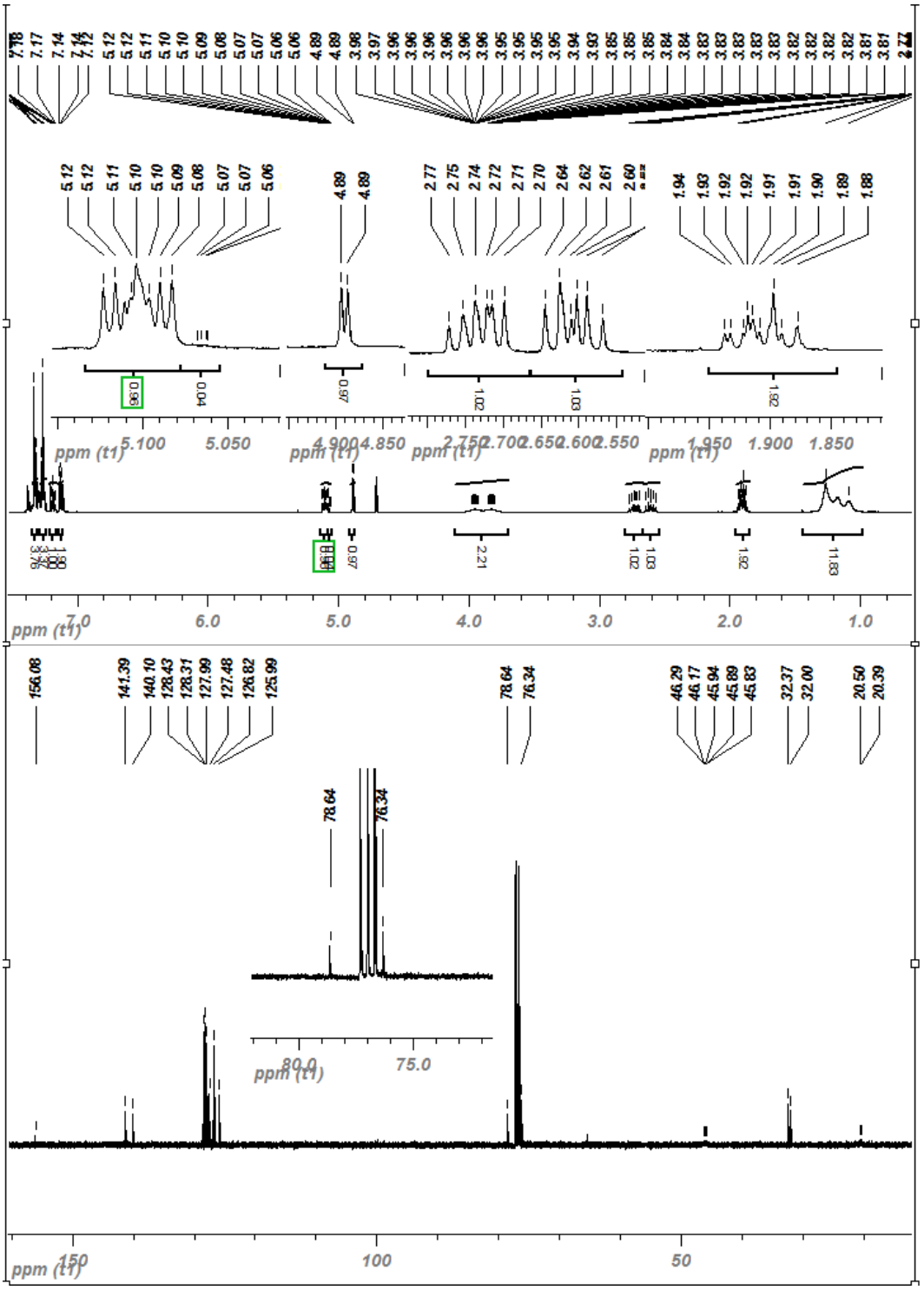


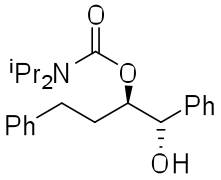


(*R*)-**17**

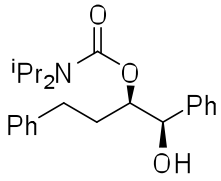


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$



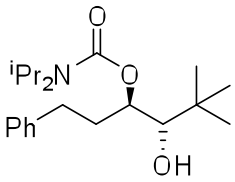


(*R*,*S*)-**18**

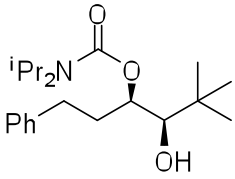


(*R*,*R*)-**18**

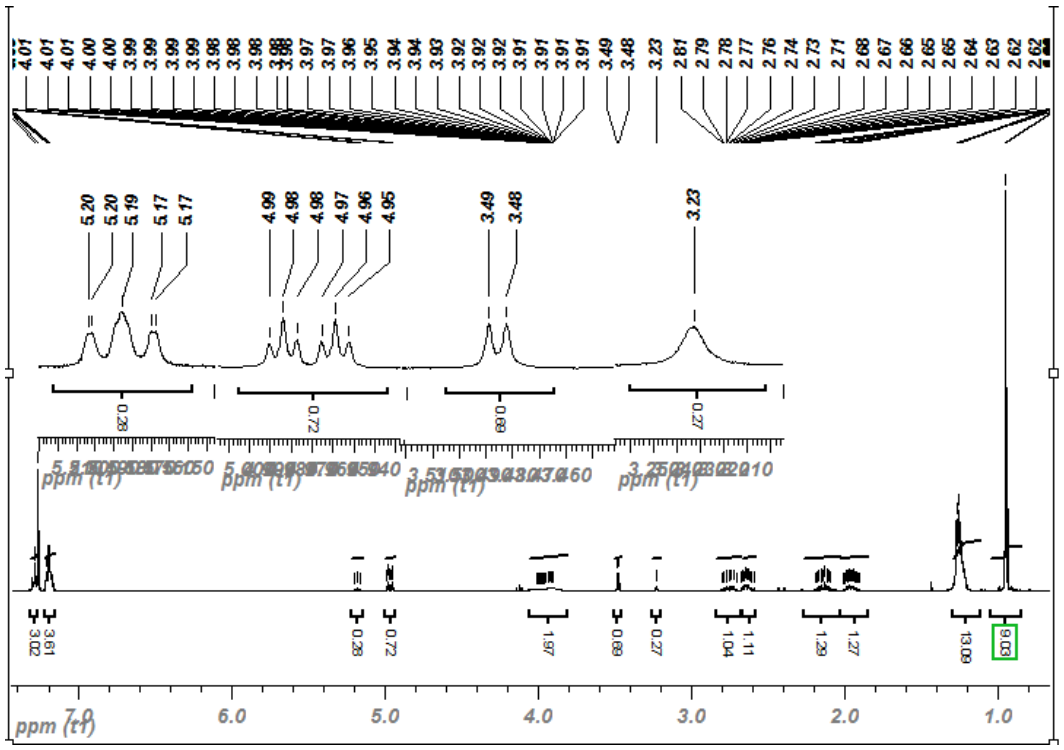
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

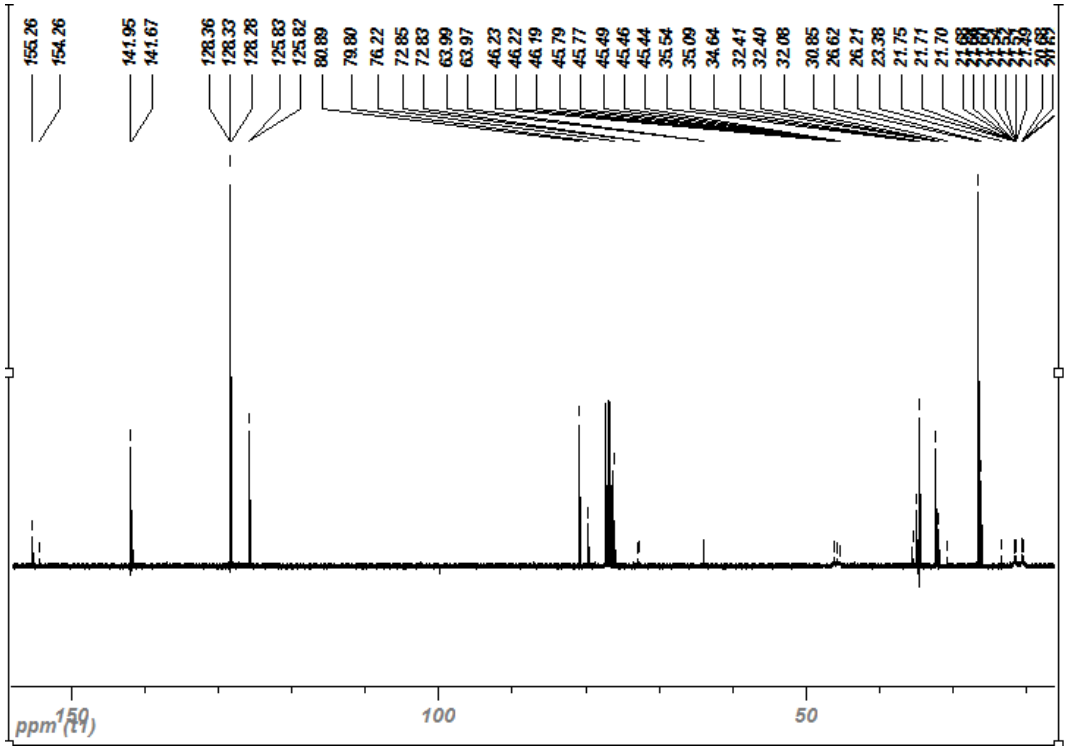


(*R*,*S*)-**19**

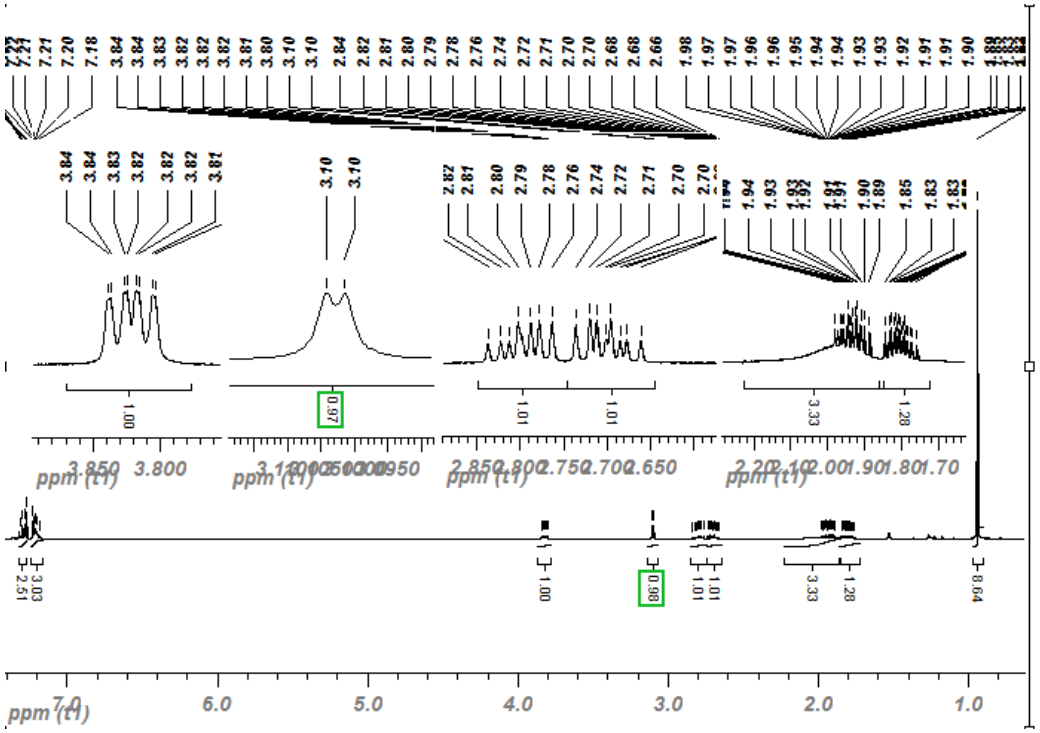


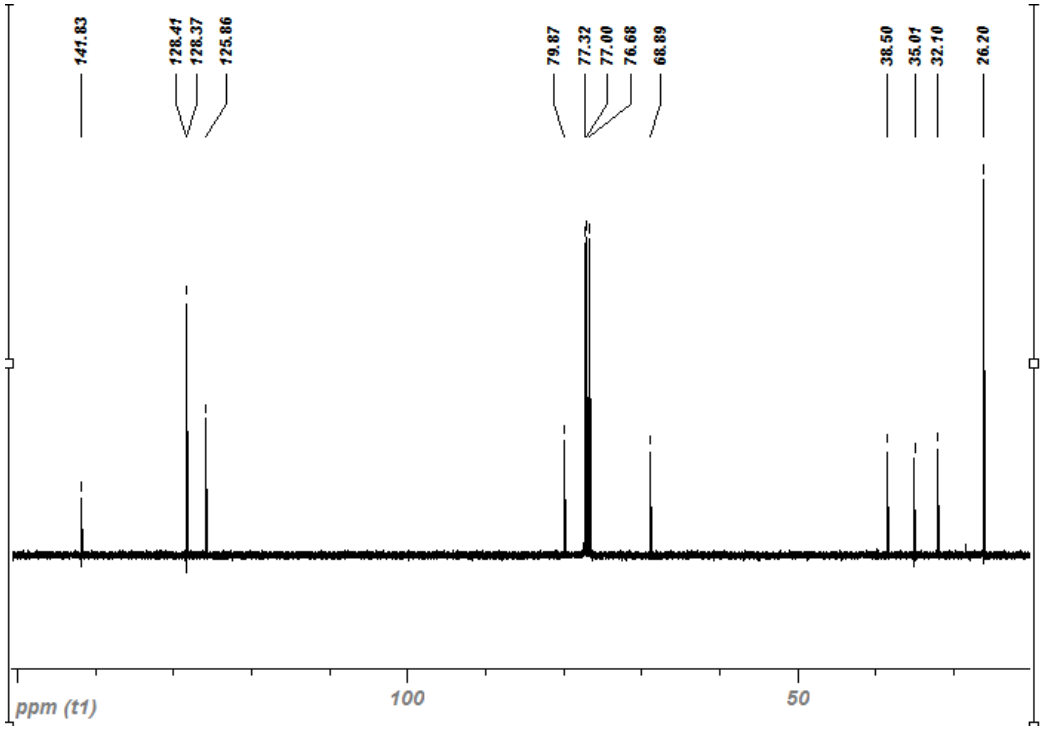
(*R*,*R*)-**19**



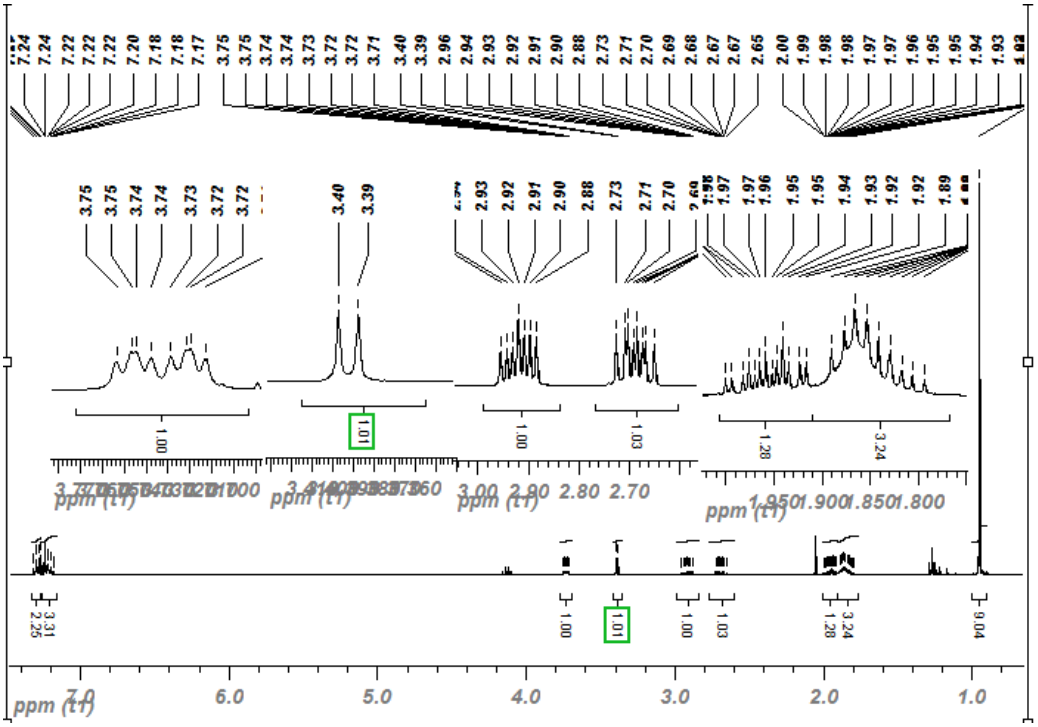


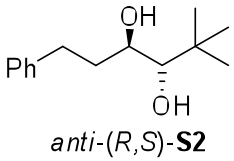
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$



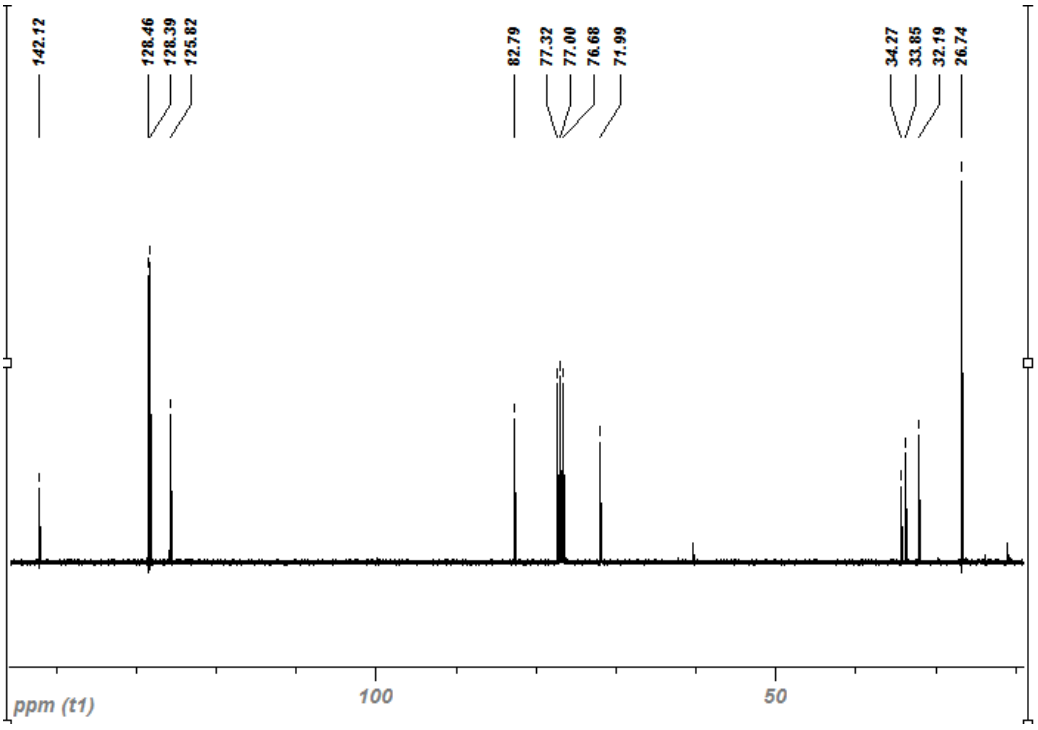


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

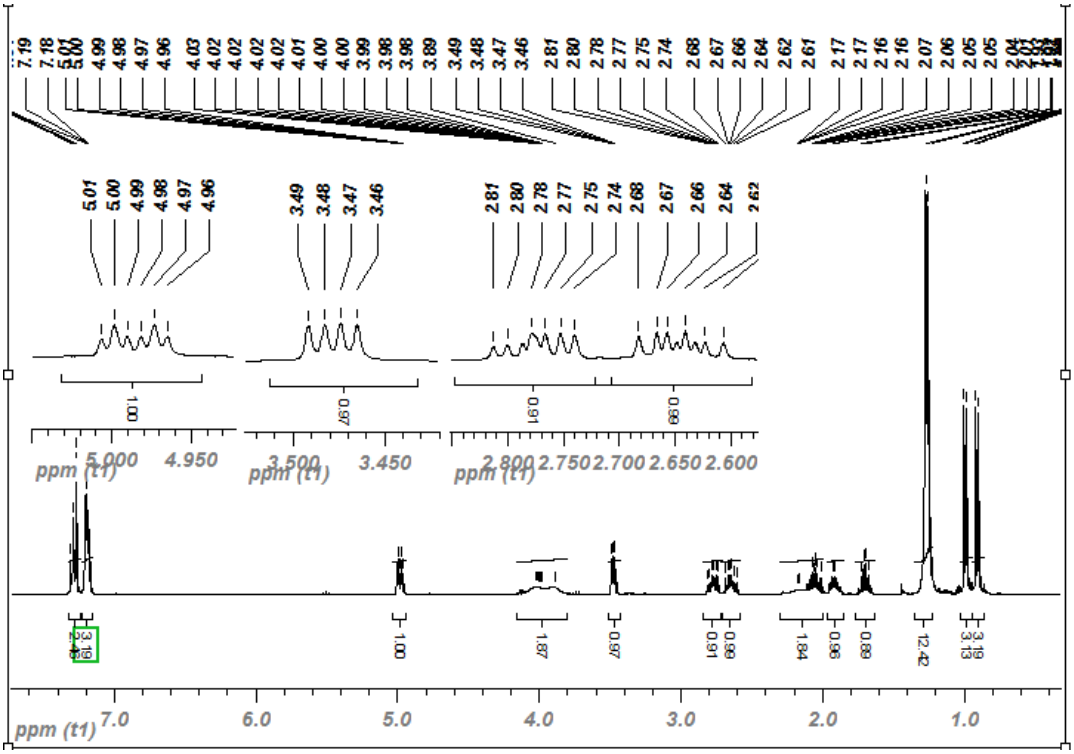


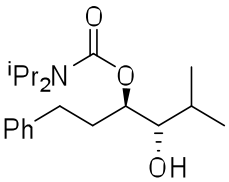


anti-(*R*,*S*)-**S2**

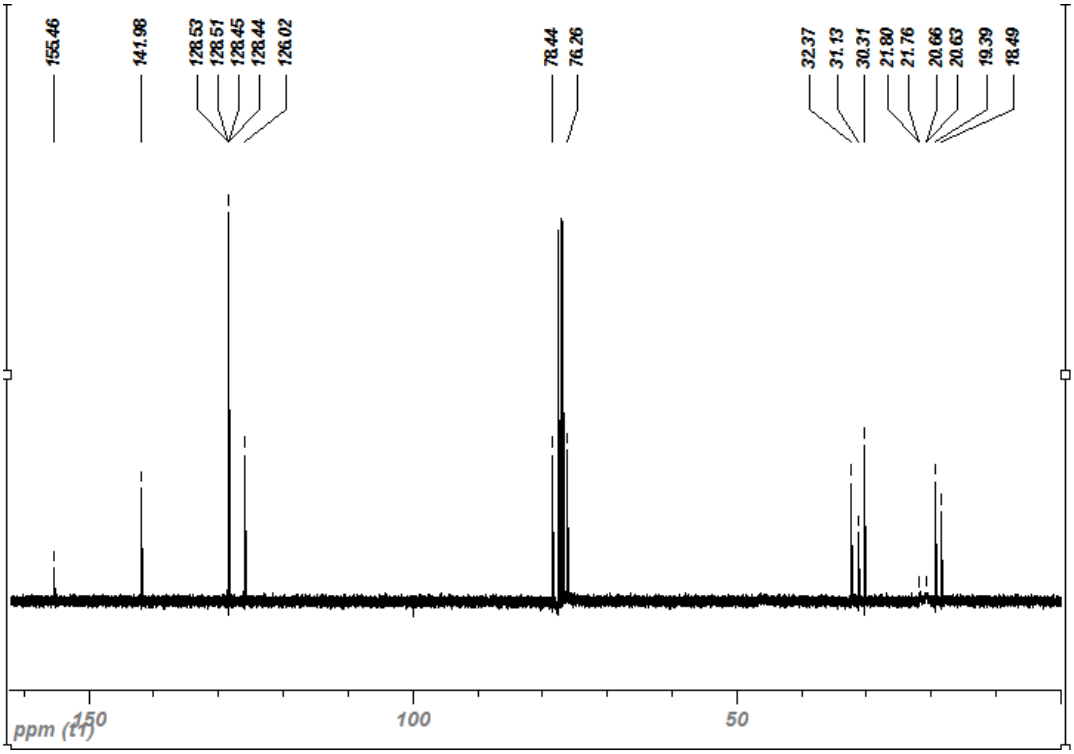


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

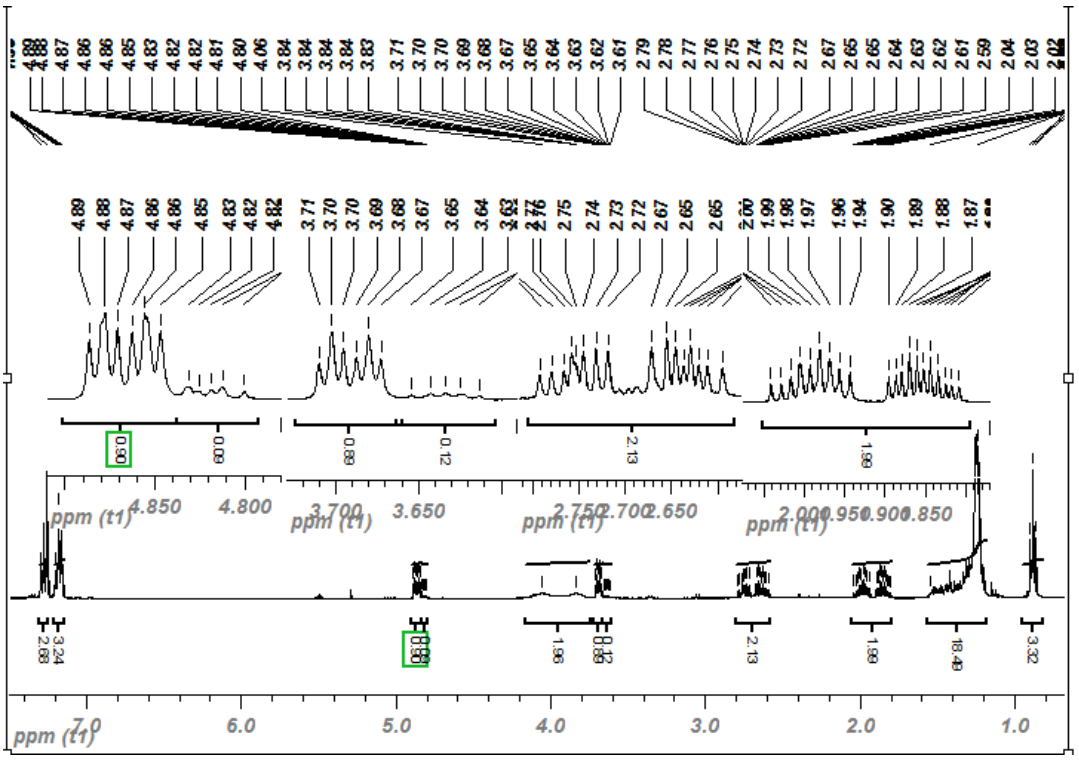


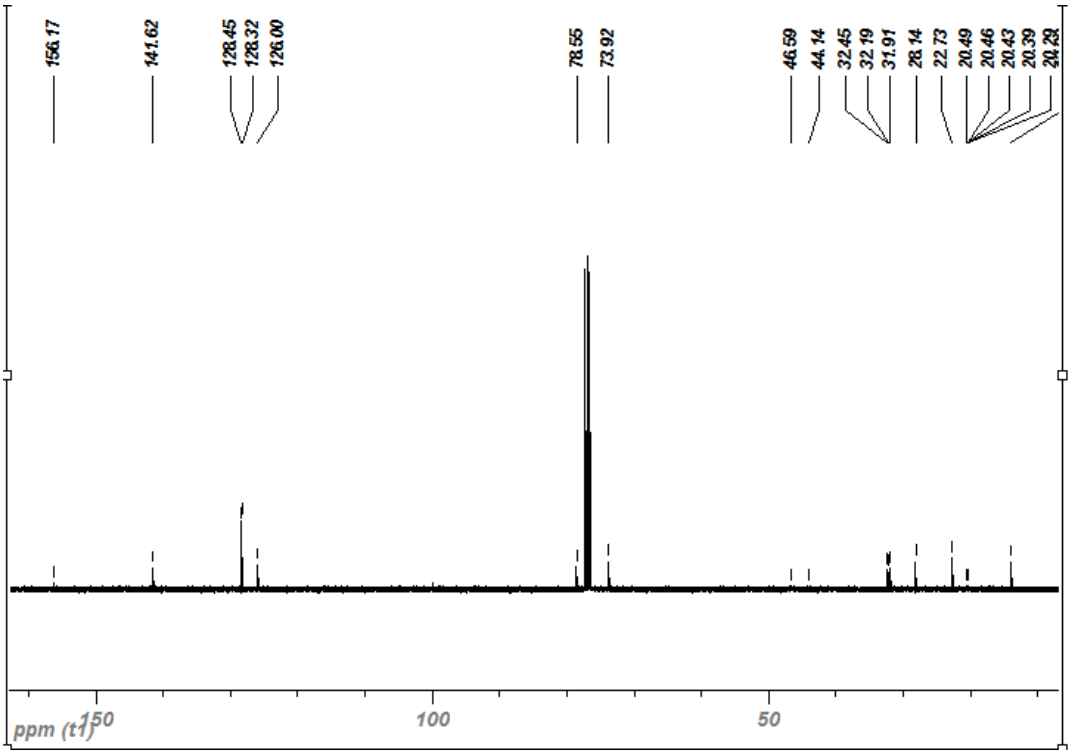


(*R*,*S*)-**20**

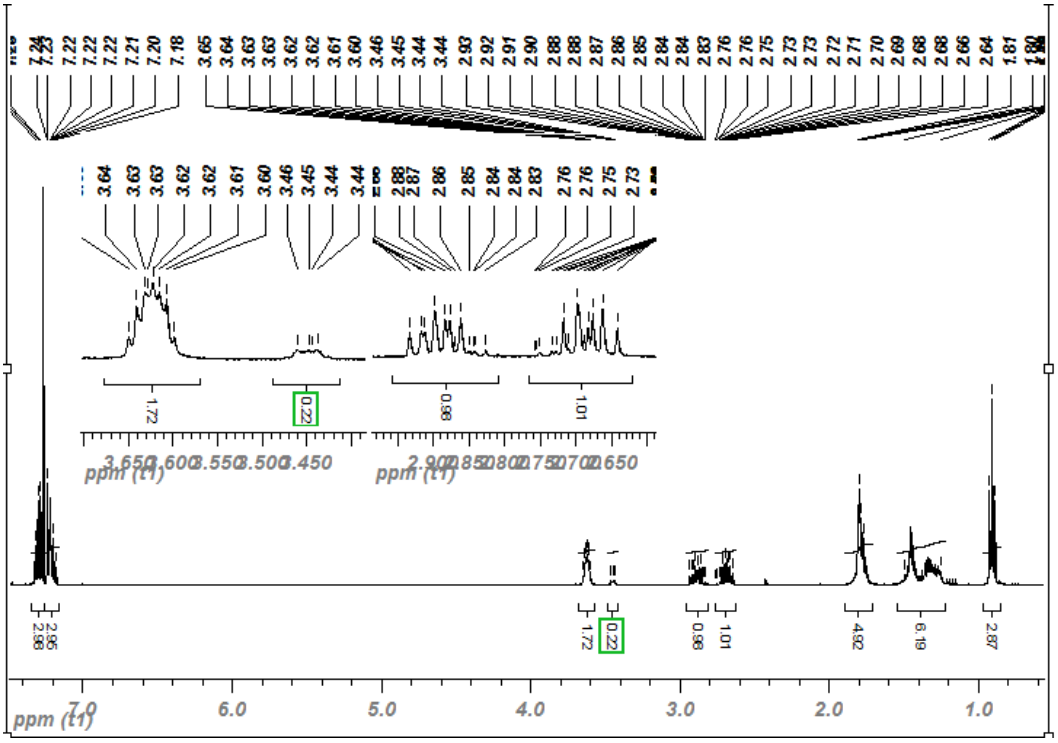


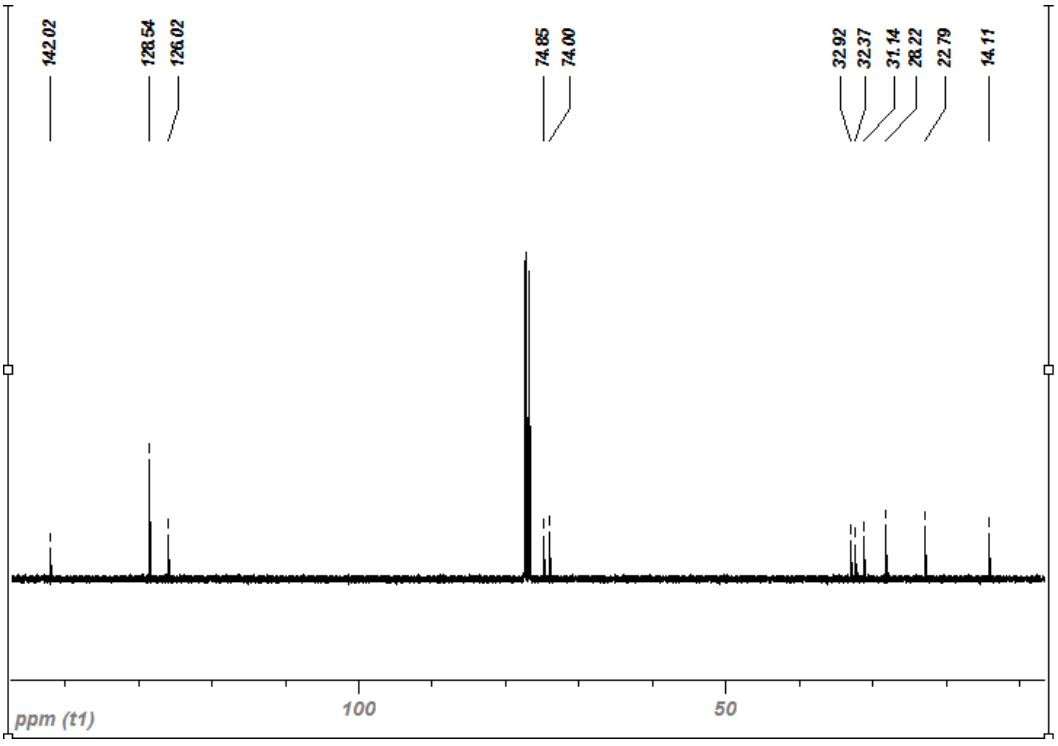
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

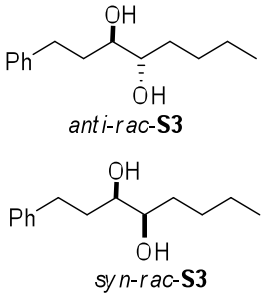




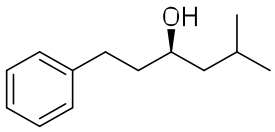
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$



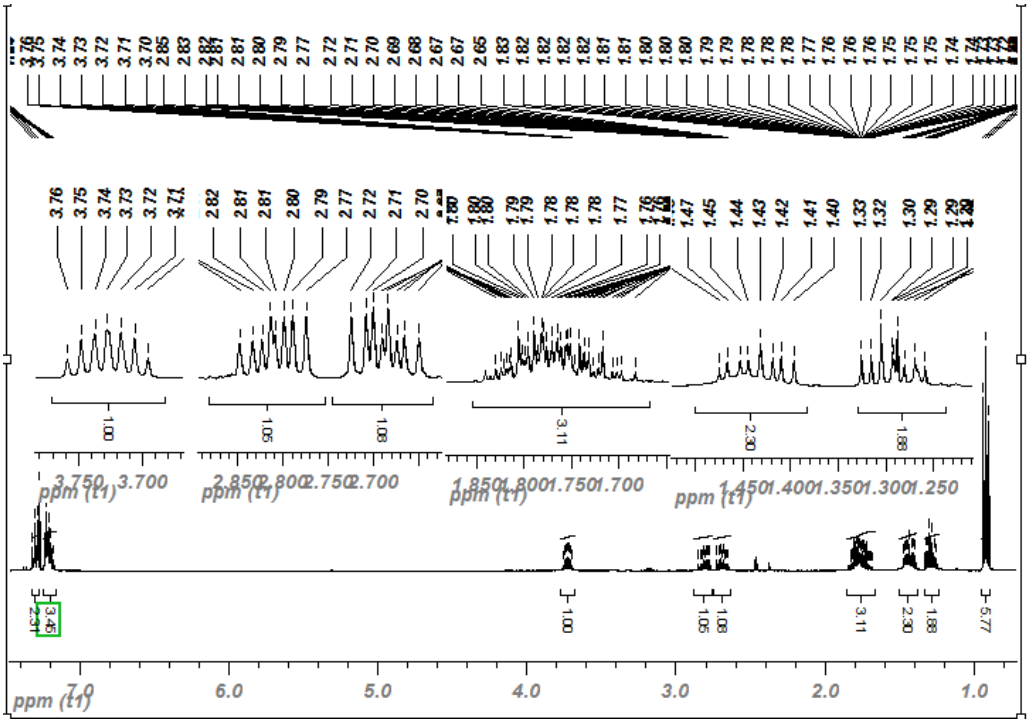


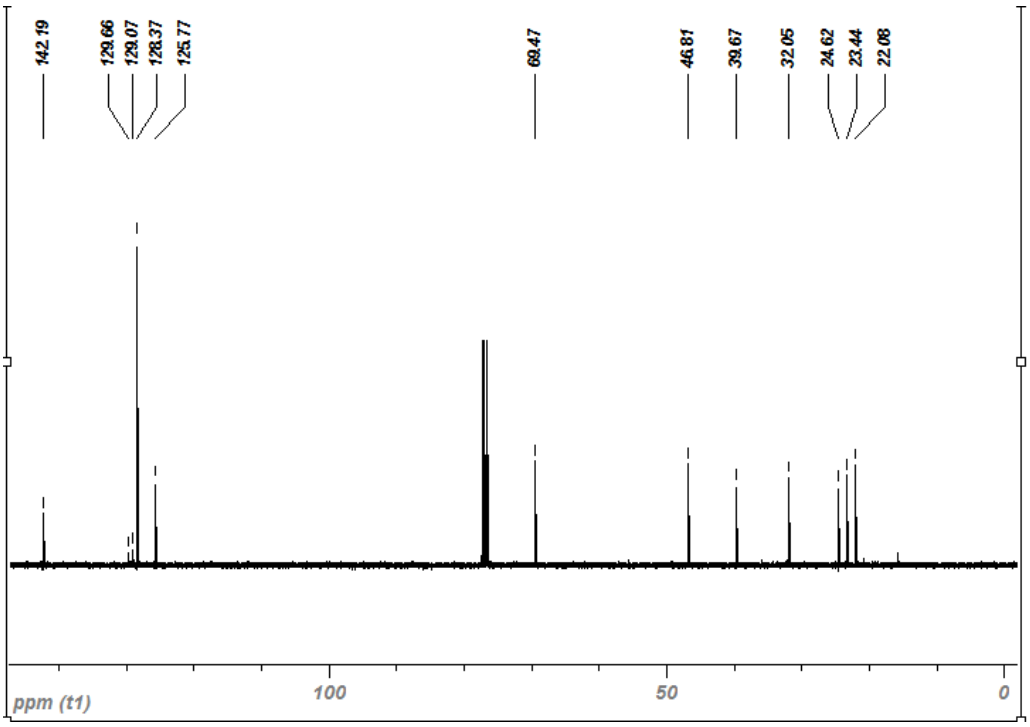


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

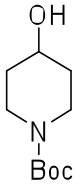


(*R*)-**22**

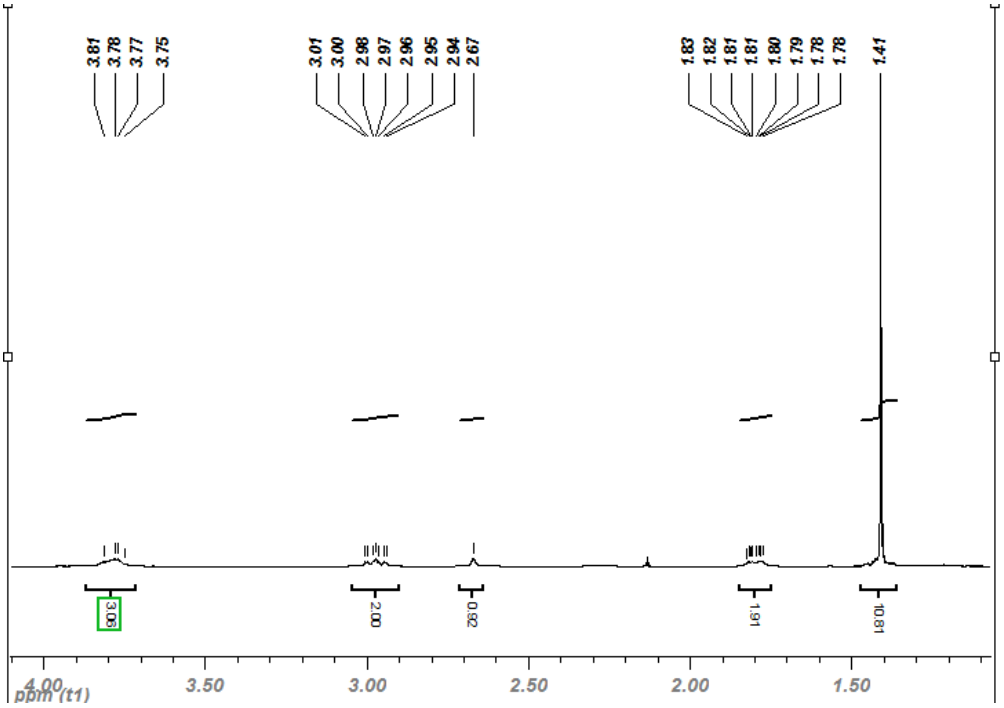


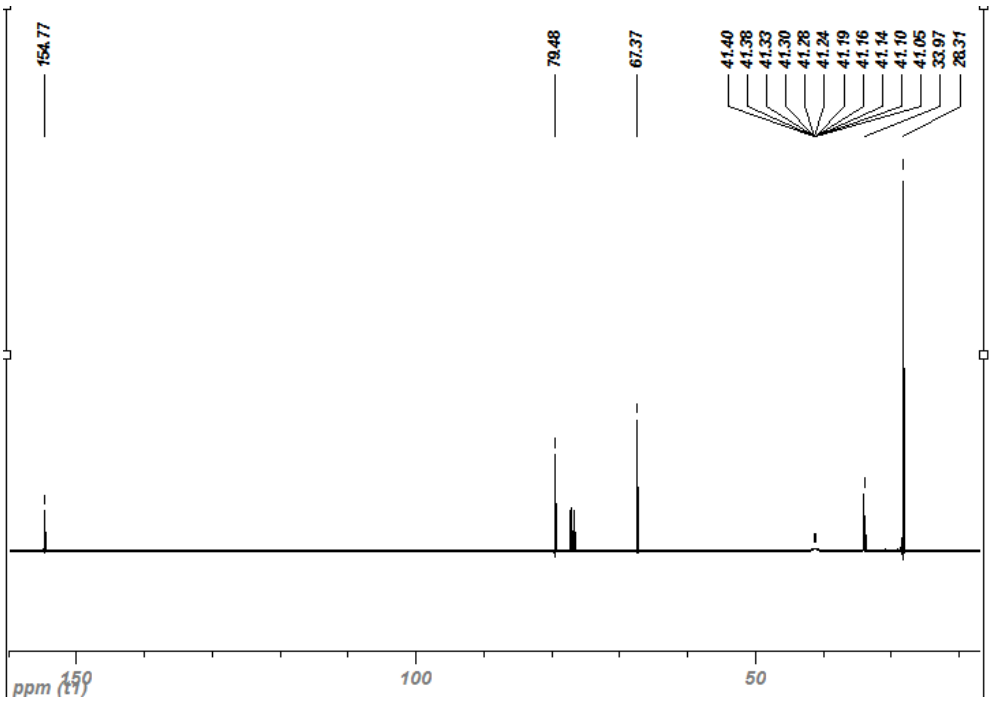


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

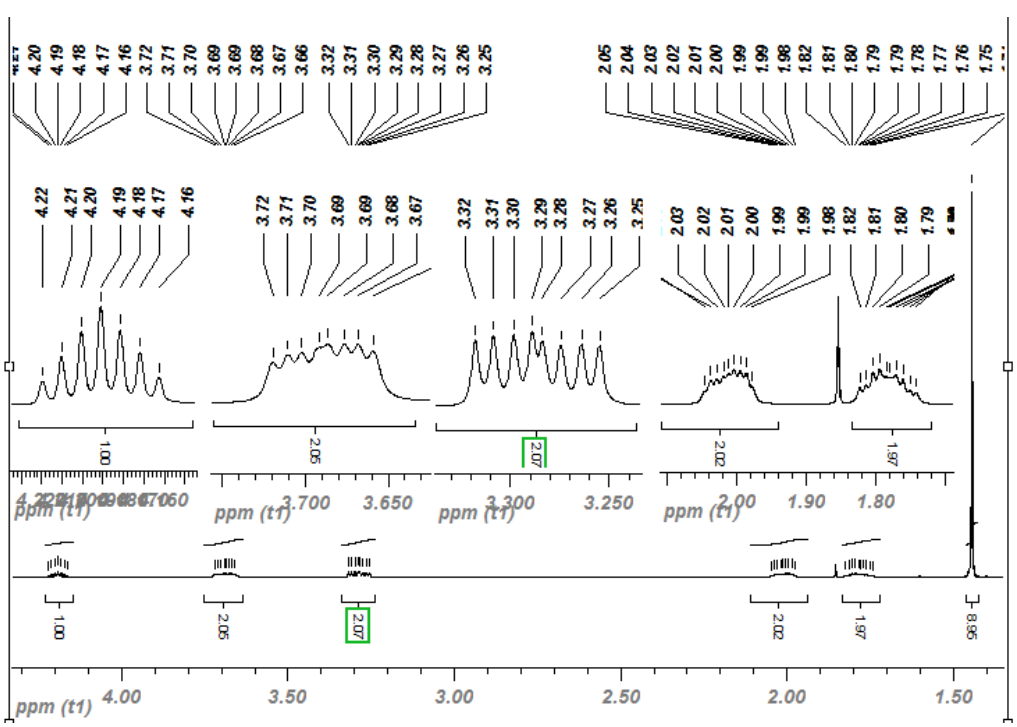


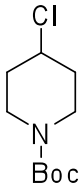
S4



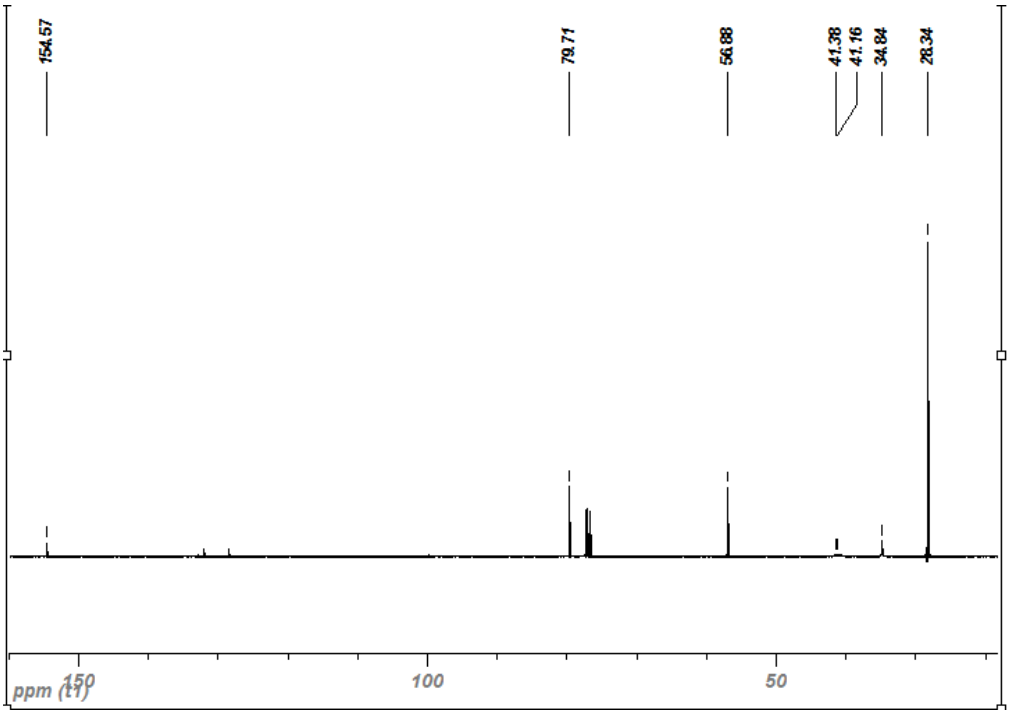


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

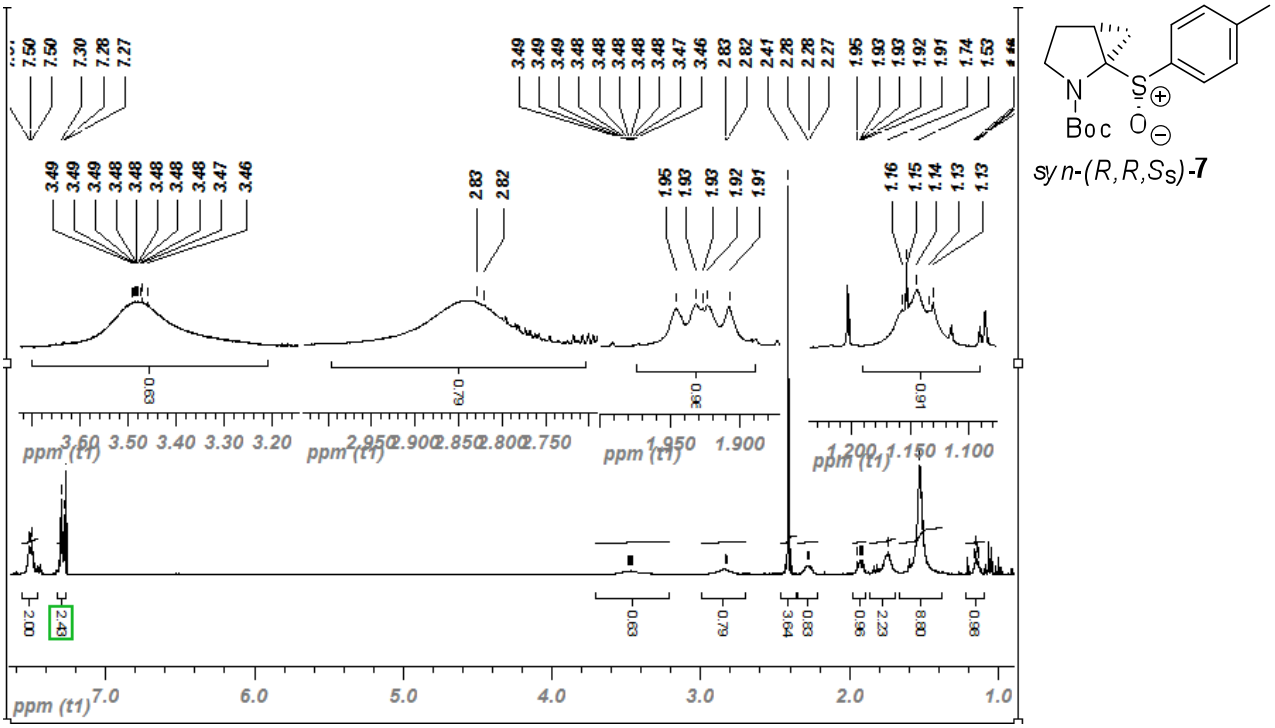


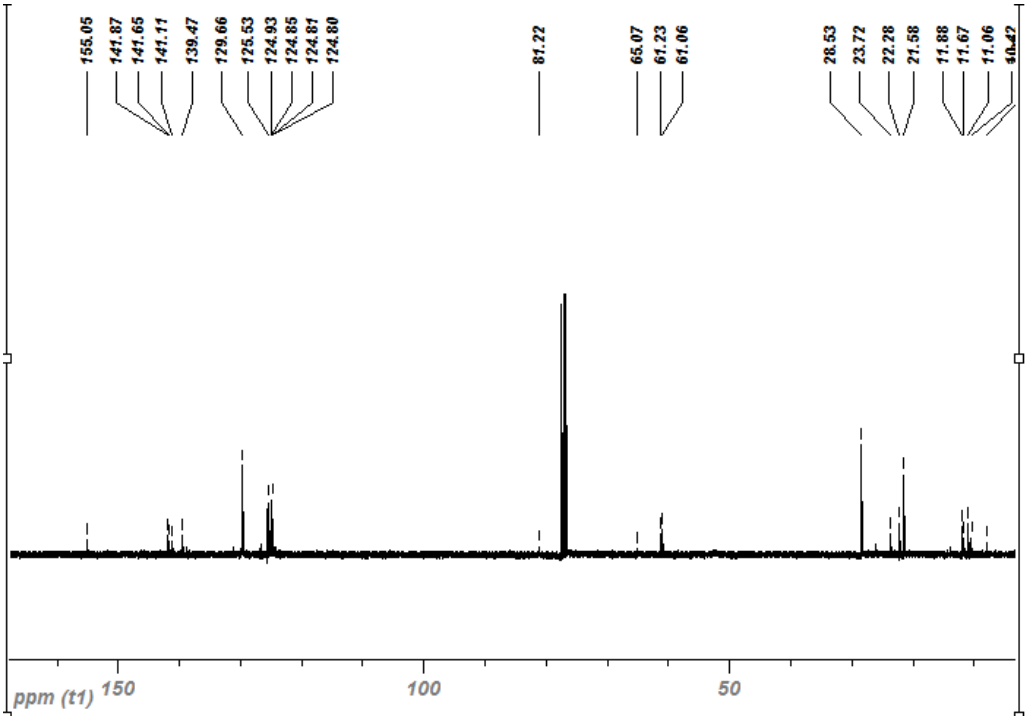


25

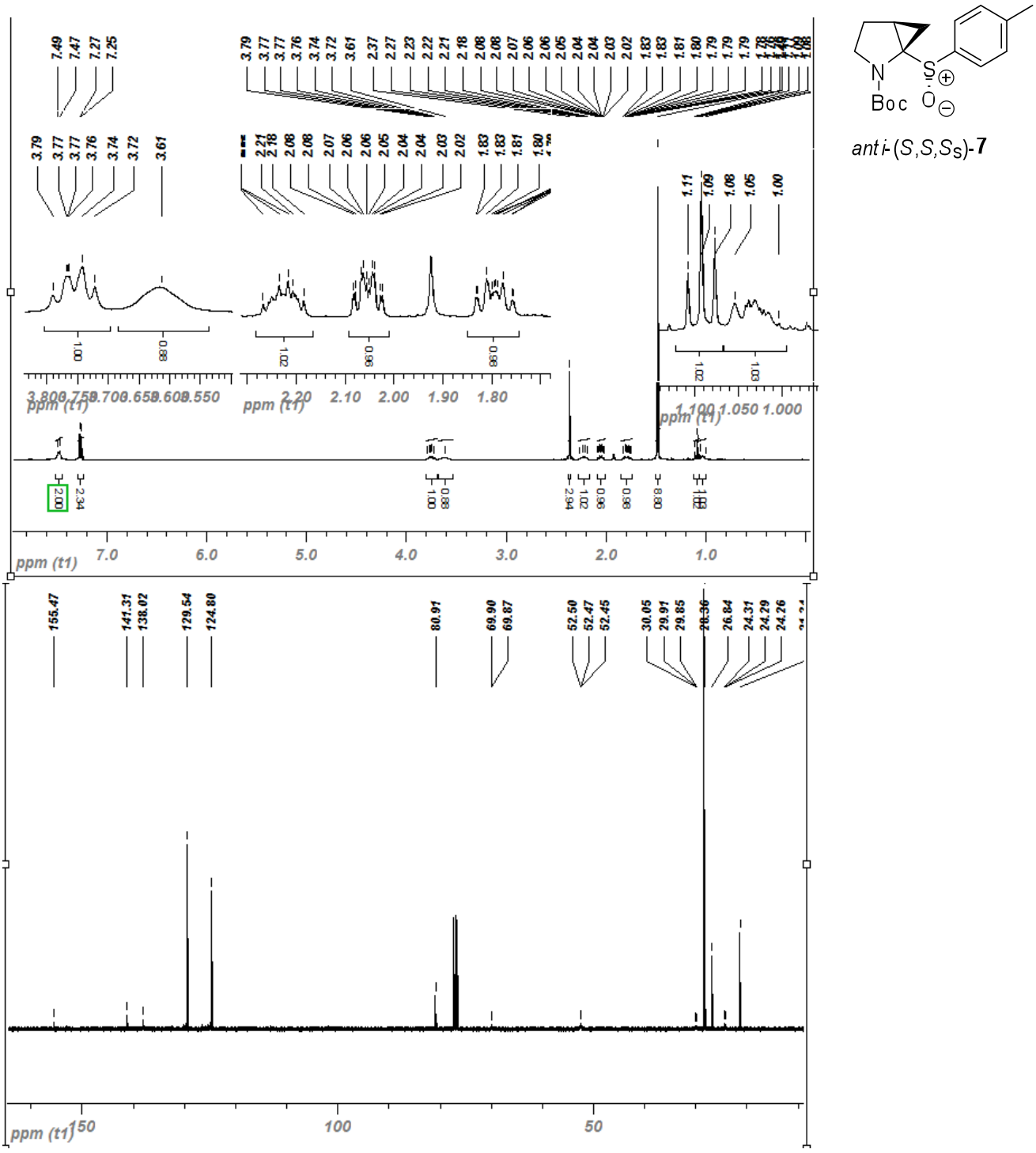


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$



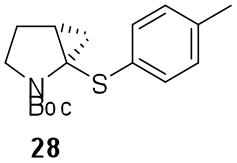


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

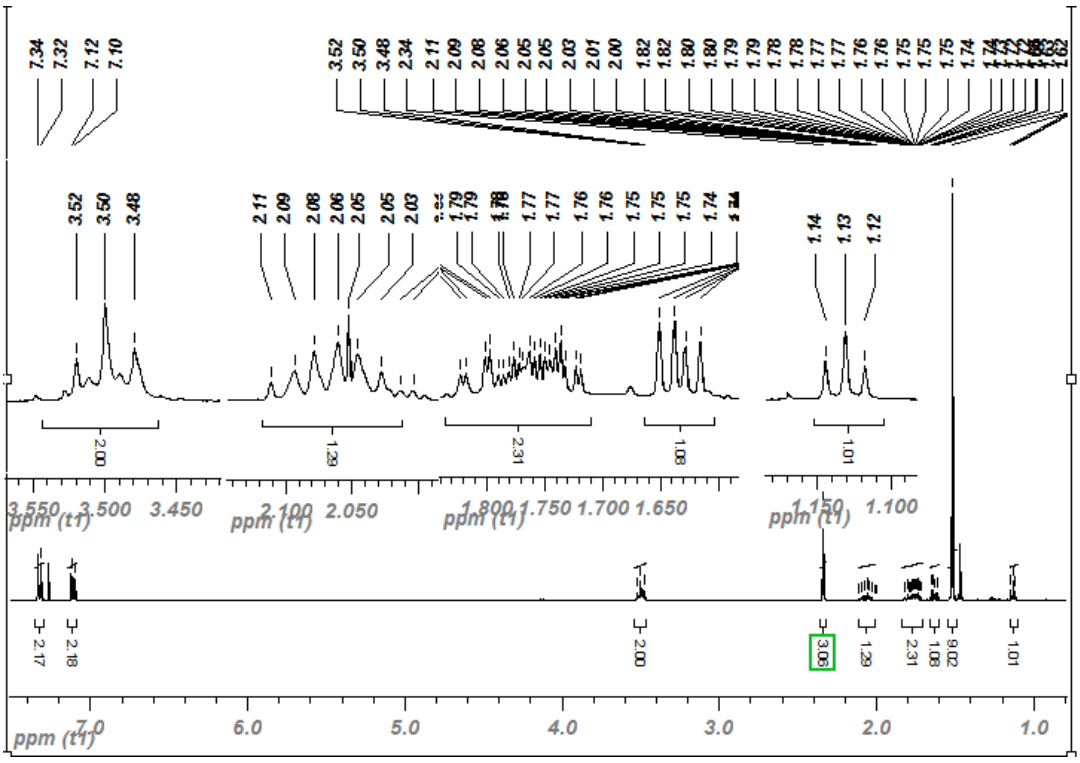


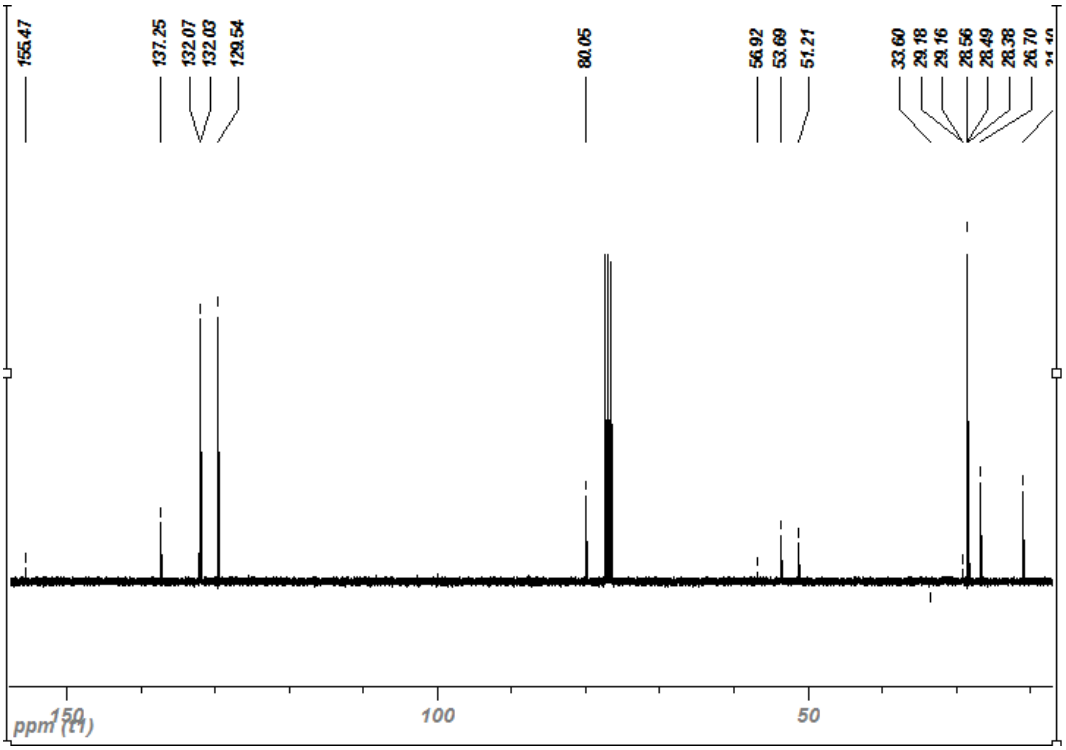
anti-(*S*,*S*,*S*$_S$)-**7**

400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

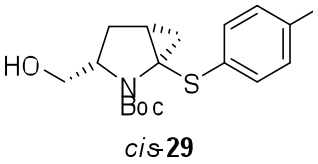


28

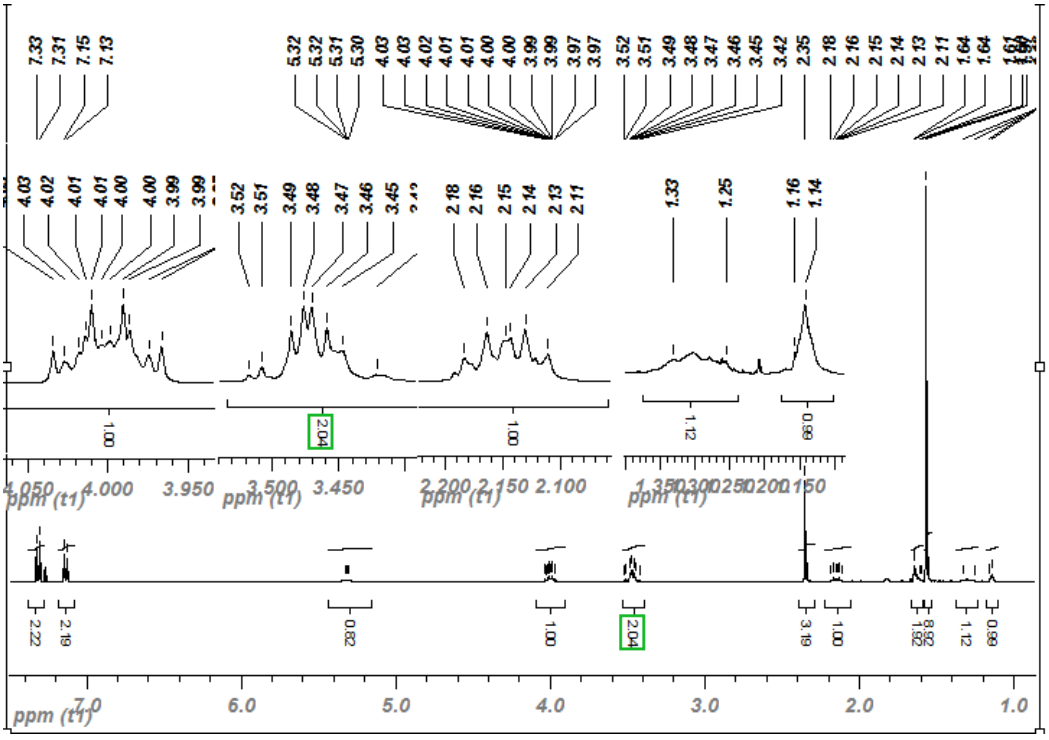


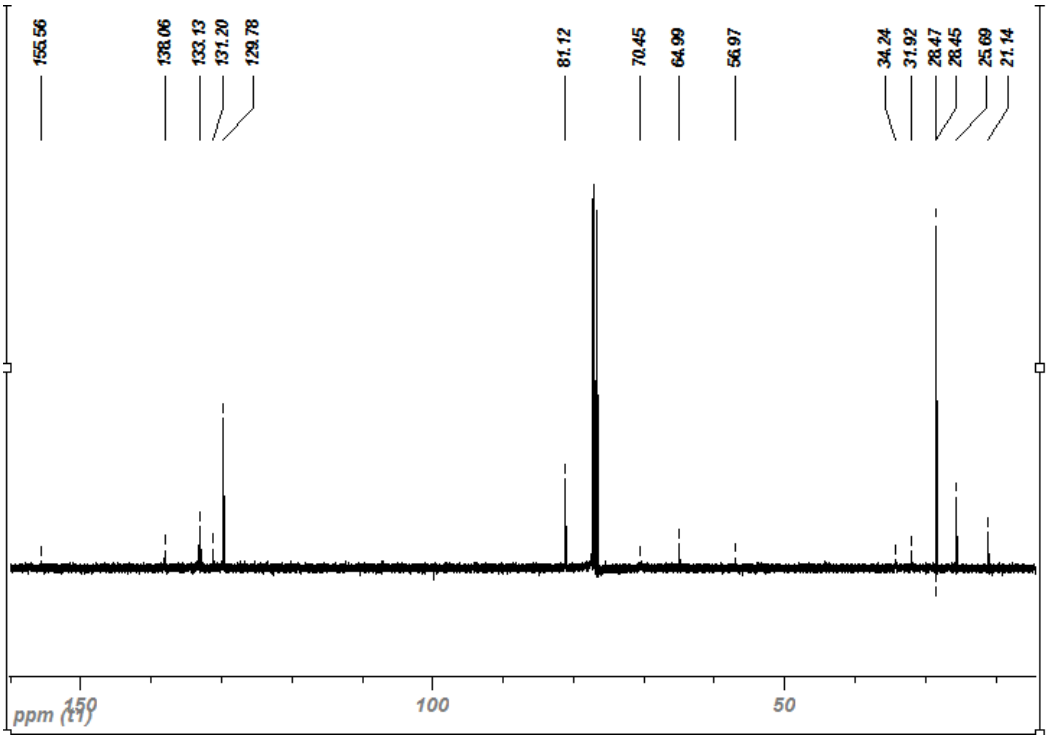


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

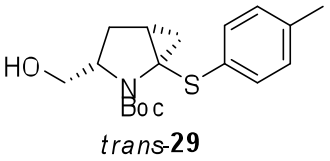


cis-**29**

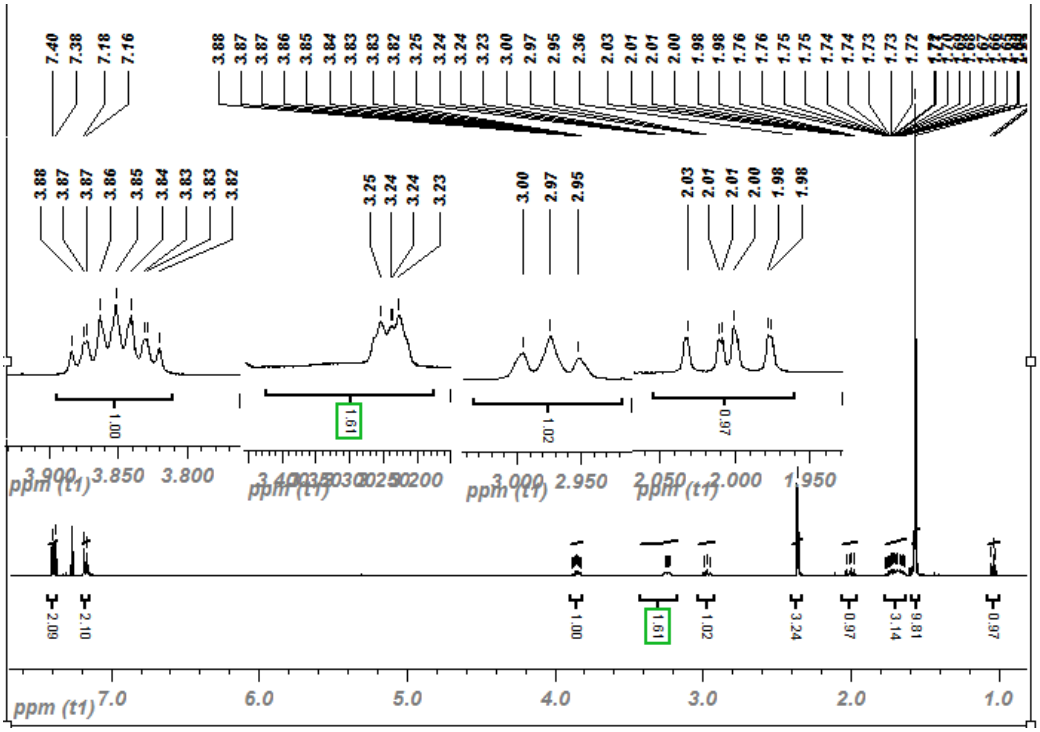


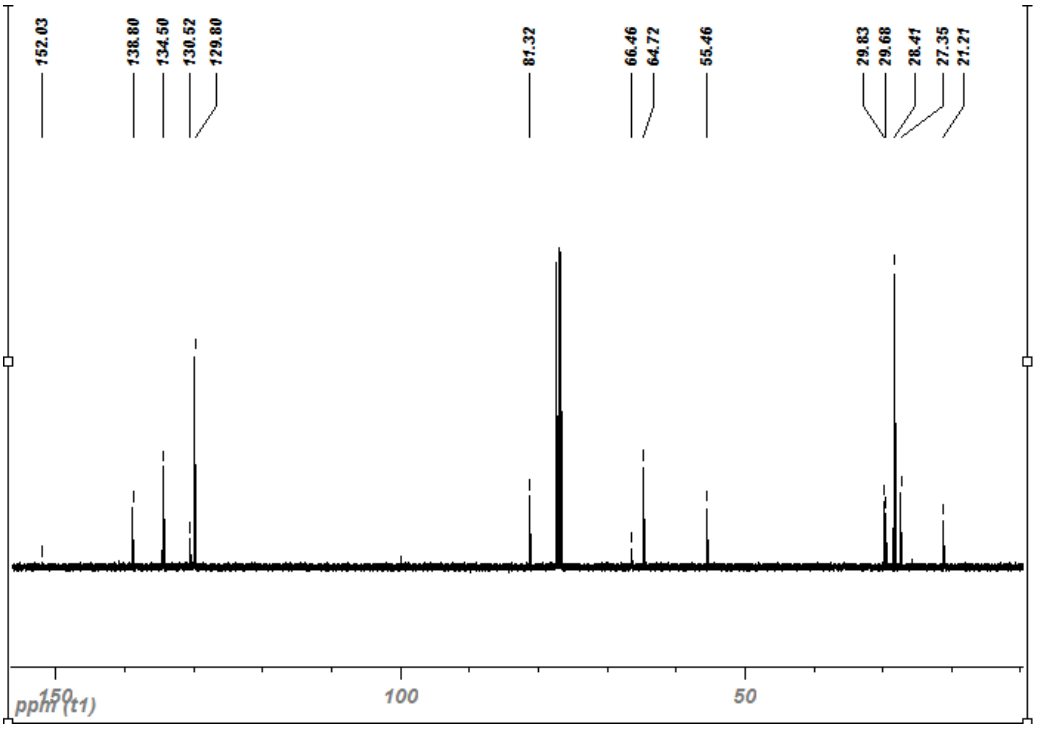


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

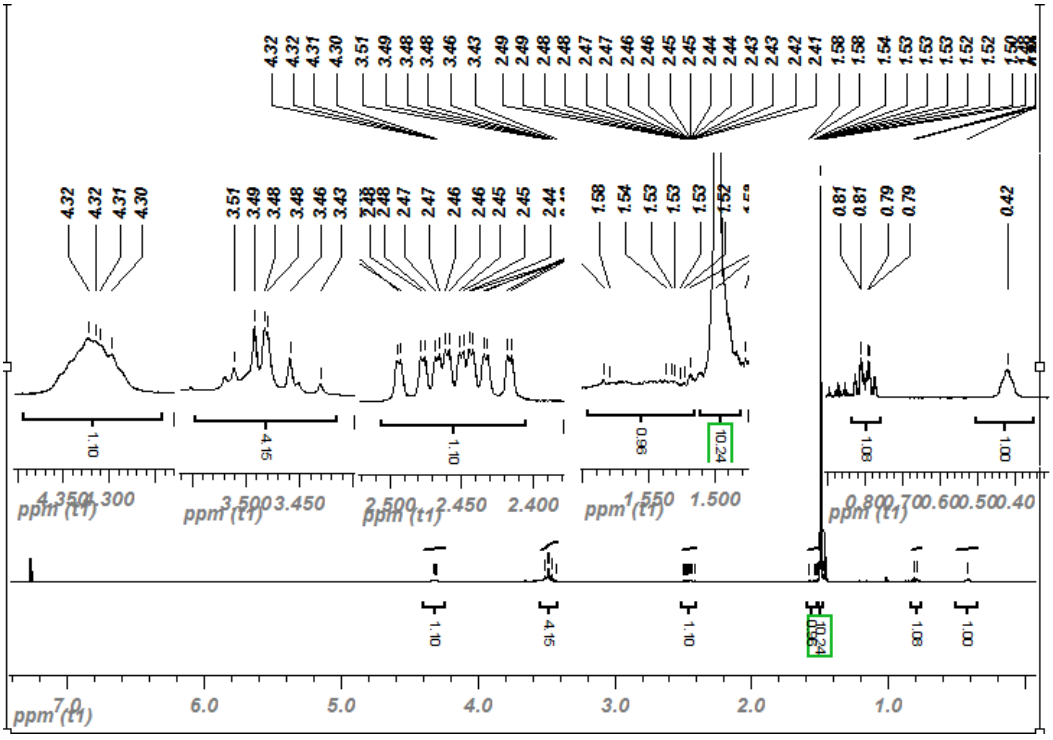


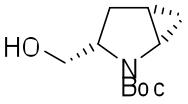
trans-**29**



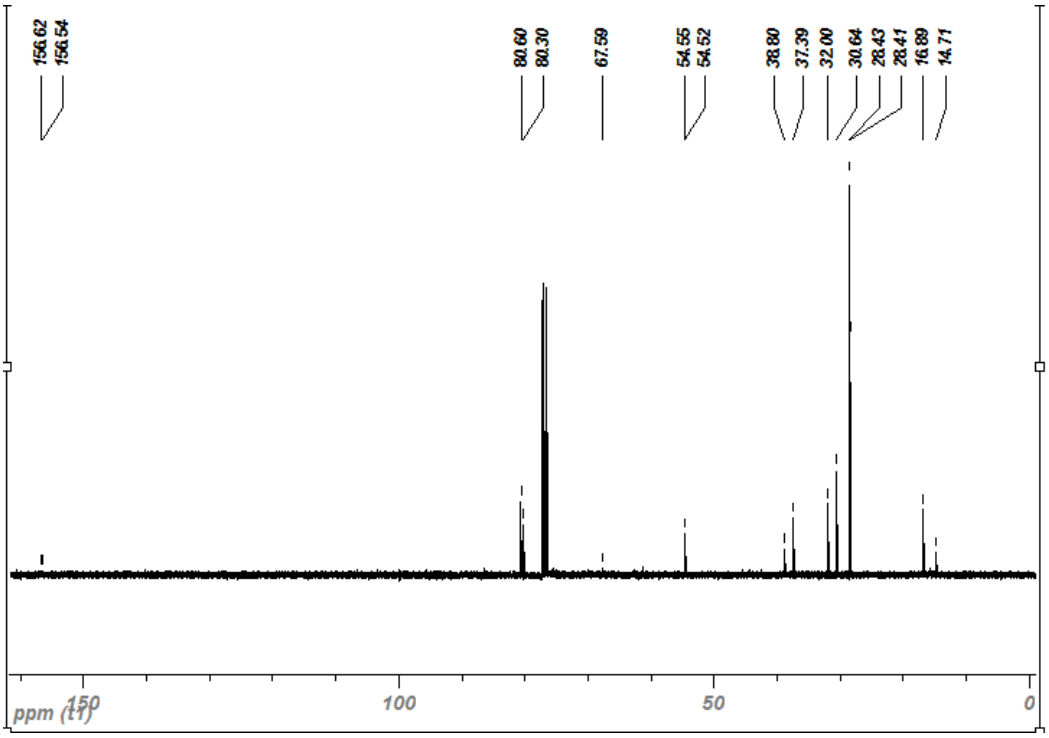


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

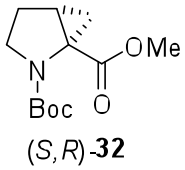




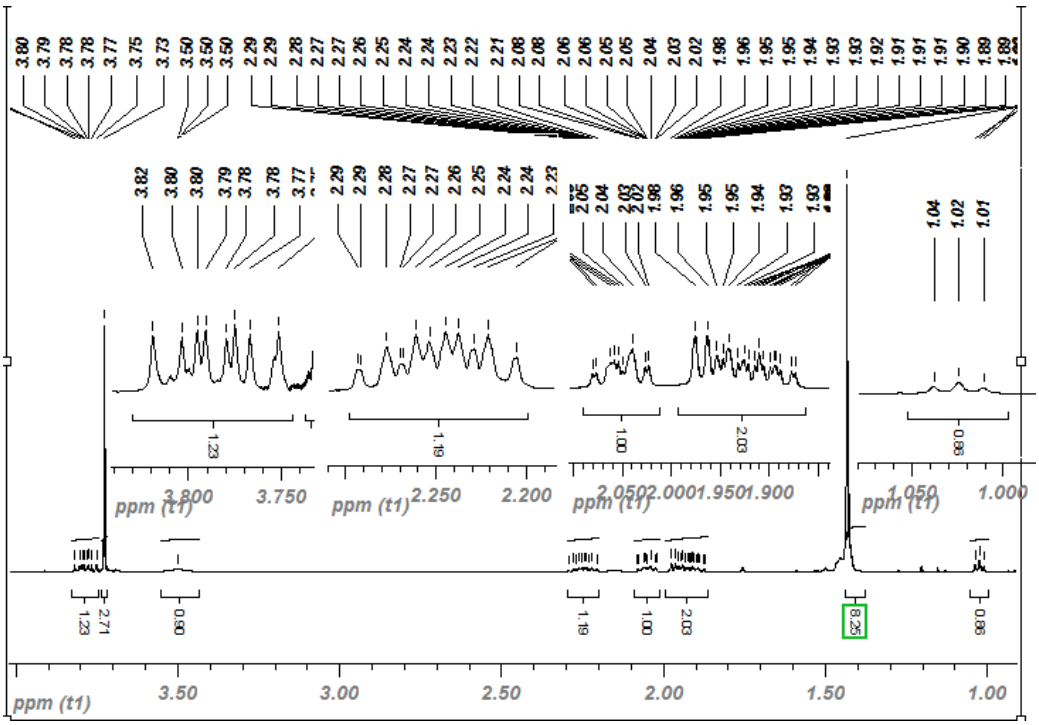
cis-**30**

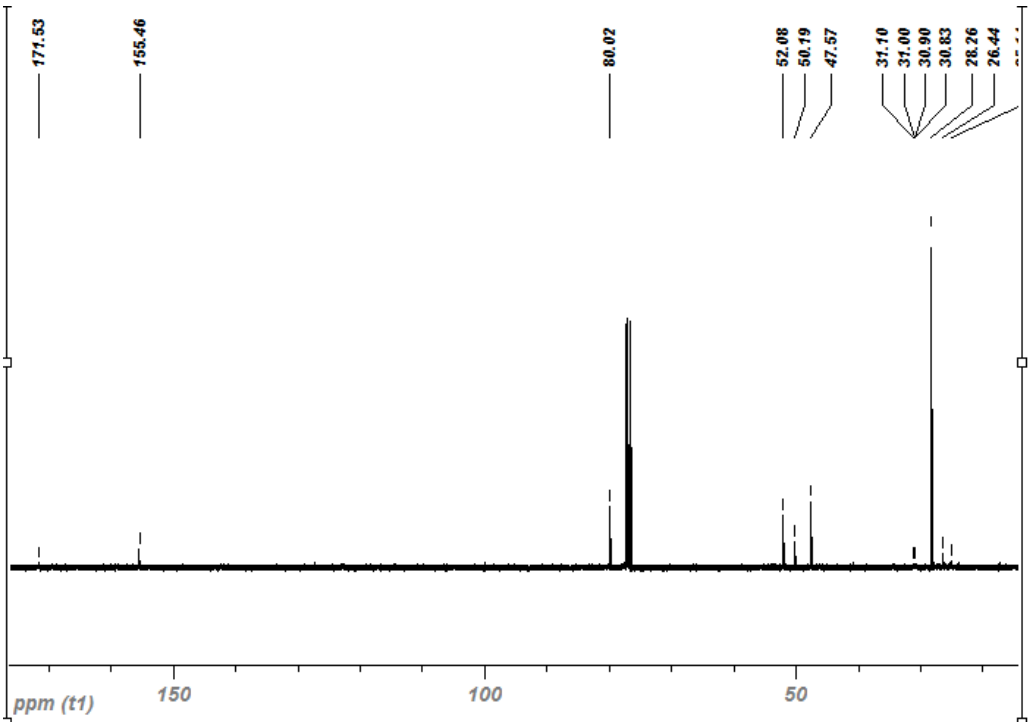


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

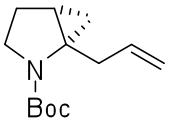


(*S*,*R*)-**32**

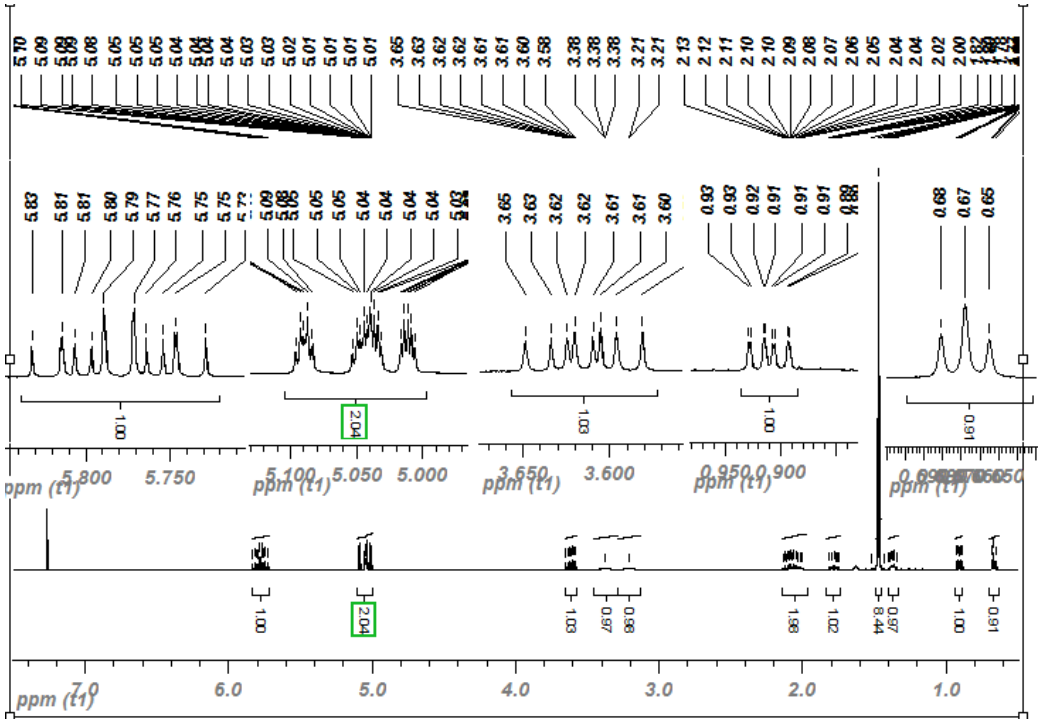


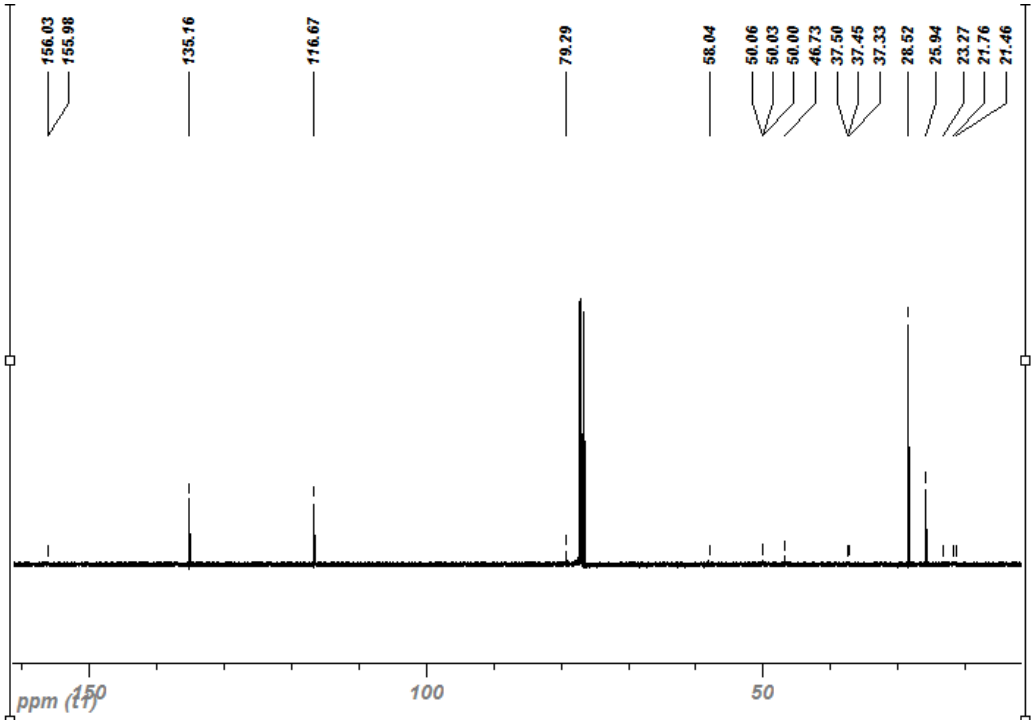


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

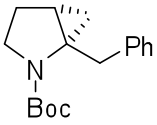


(*S*,*R*)-**33**

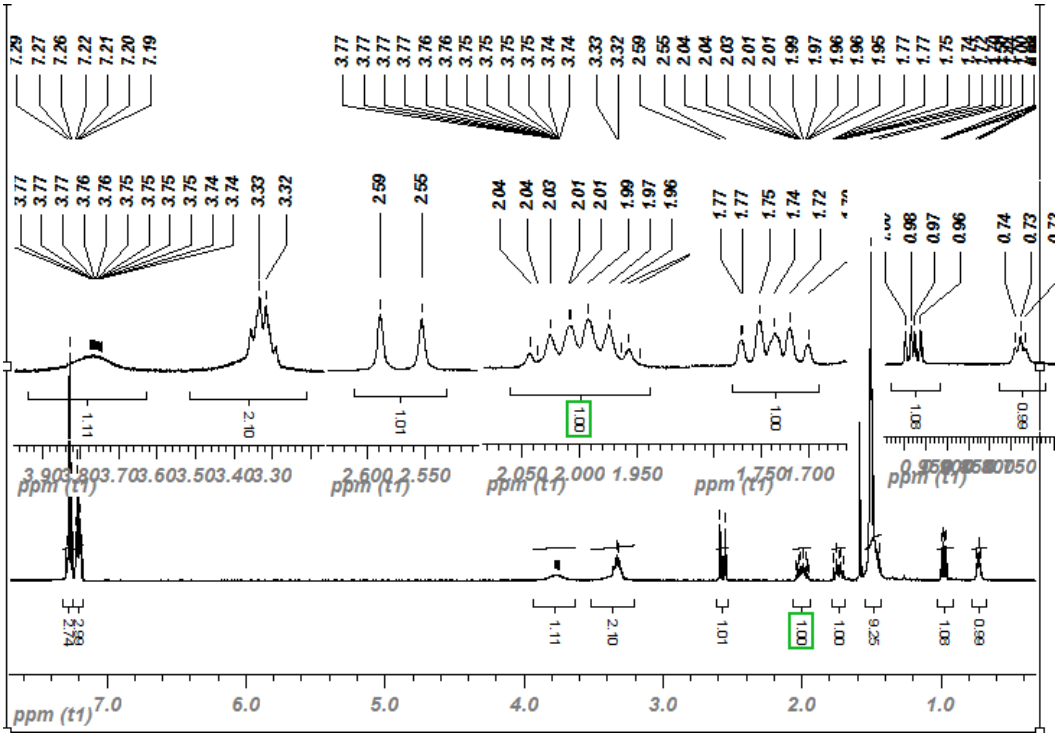


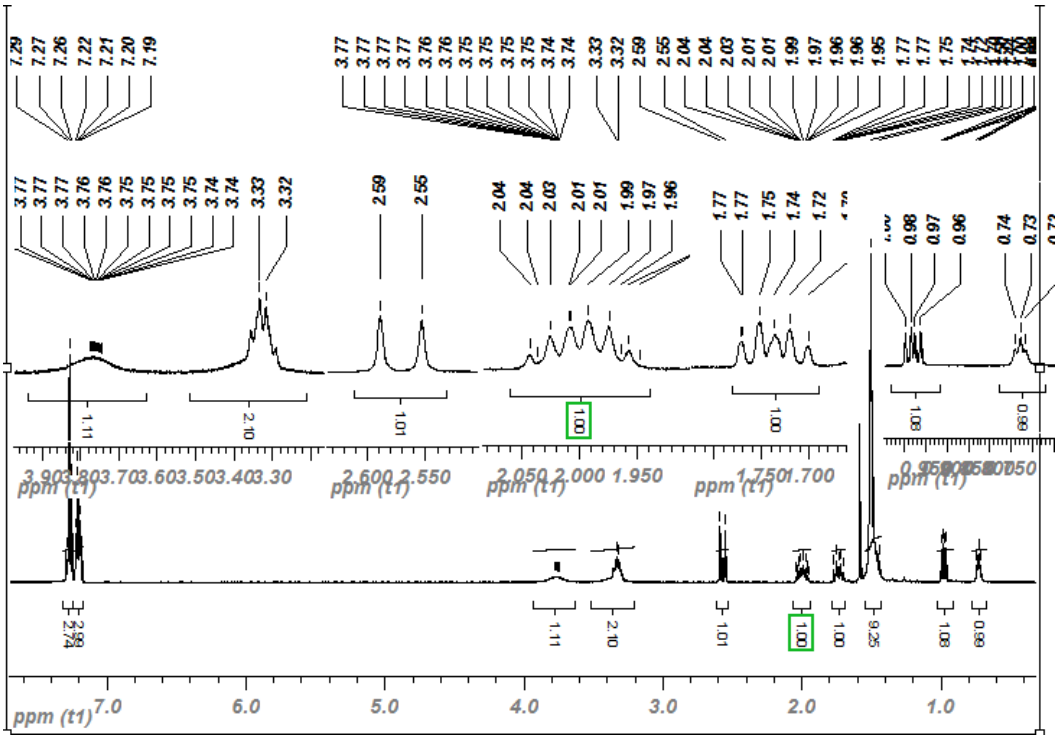


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

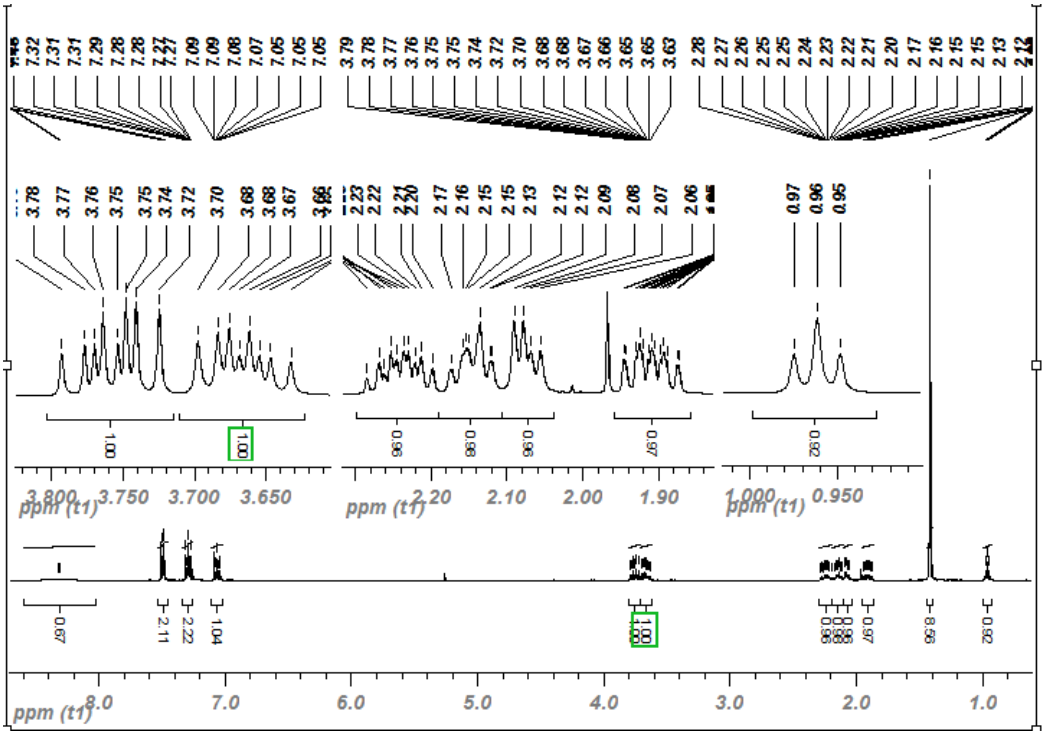


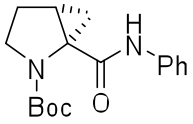
(*R*,*R*)-**34**



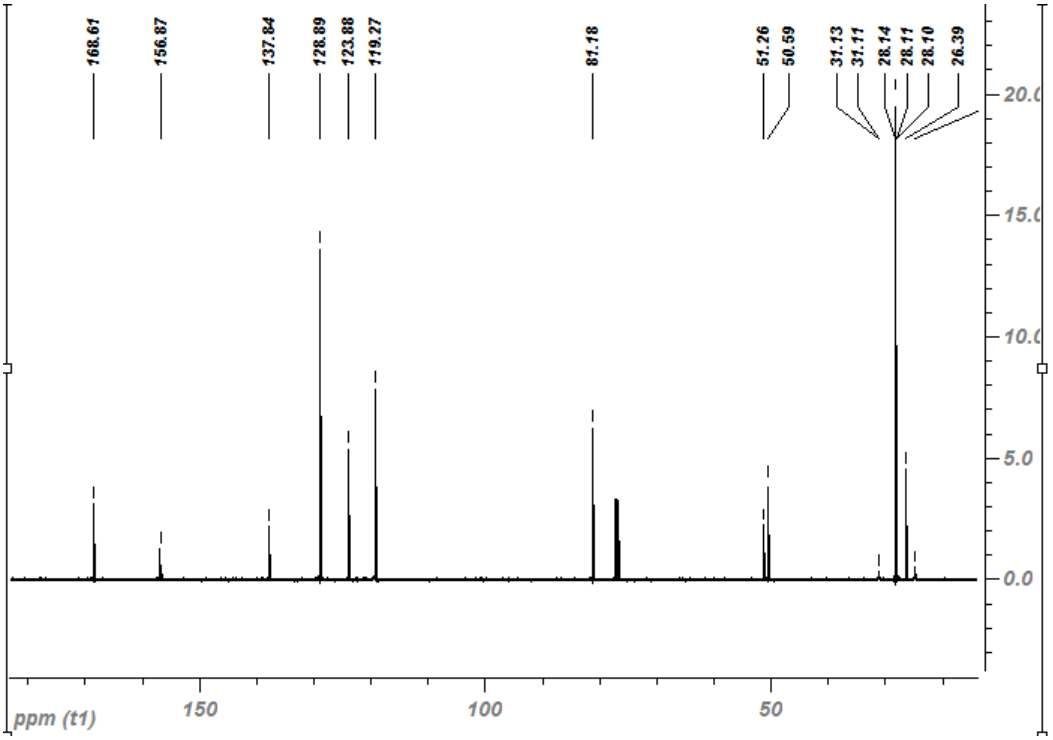


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

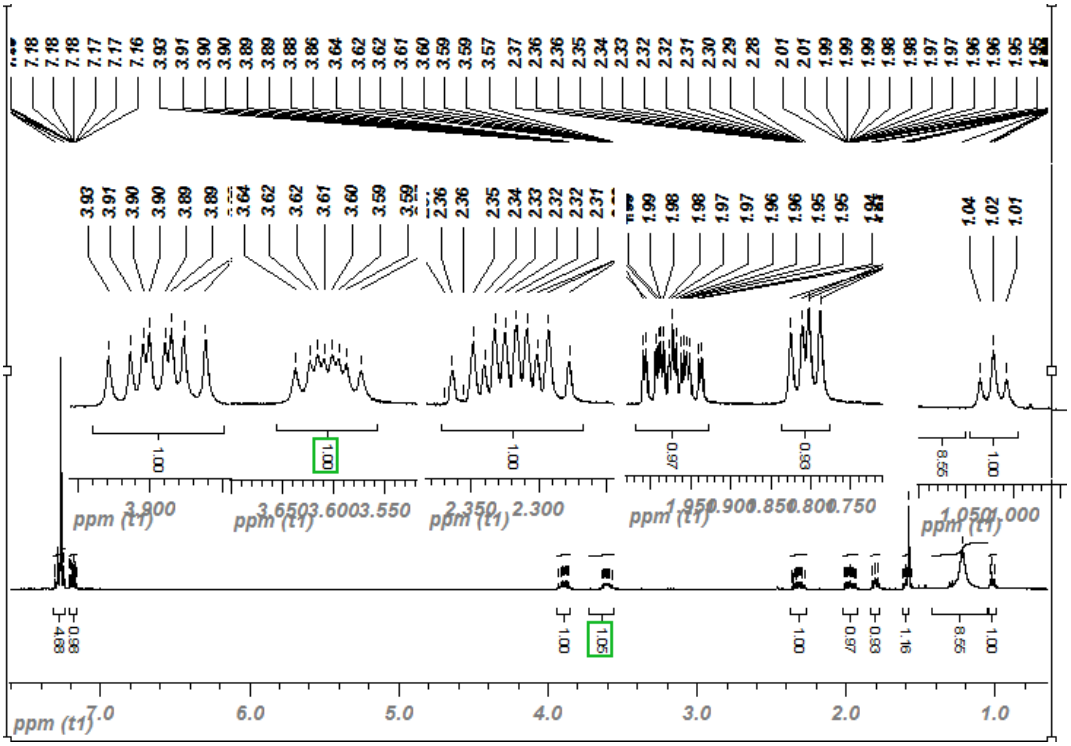


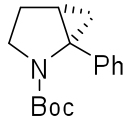


(S,R)-**35**

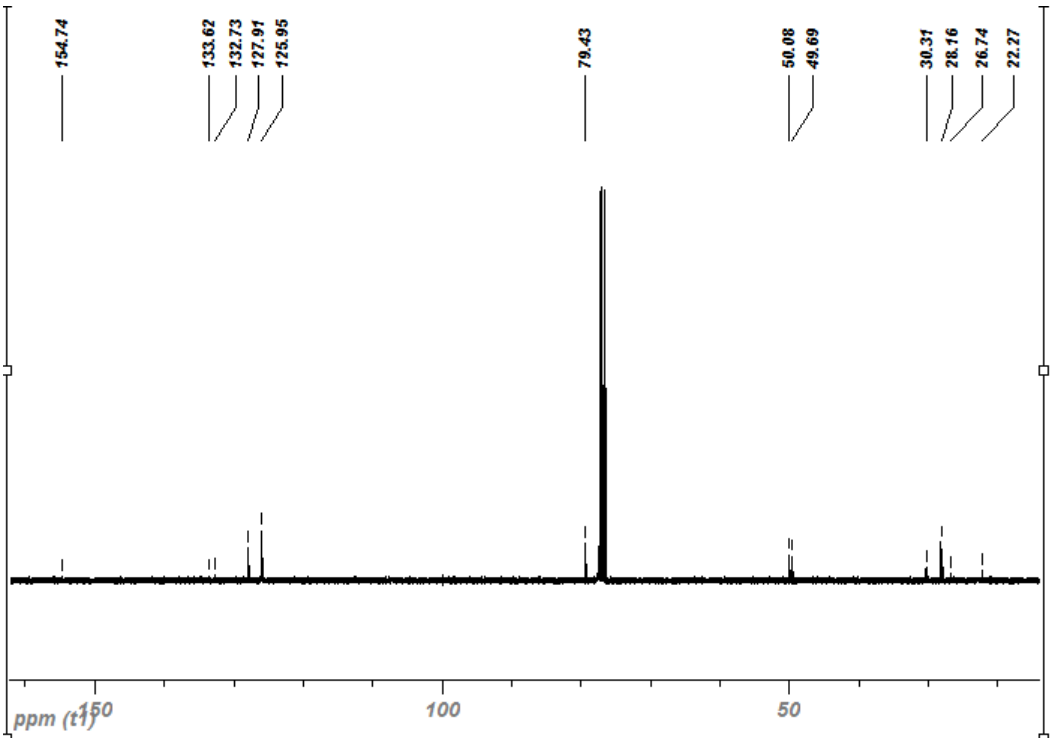


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

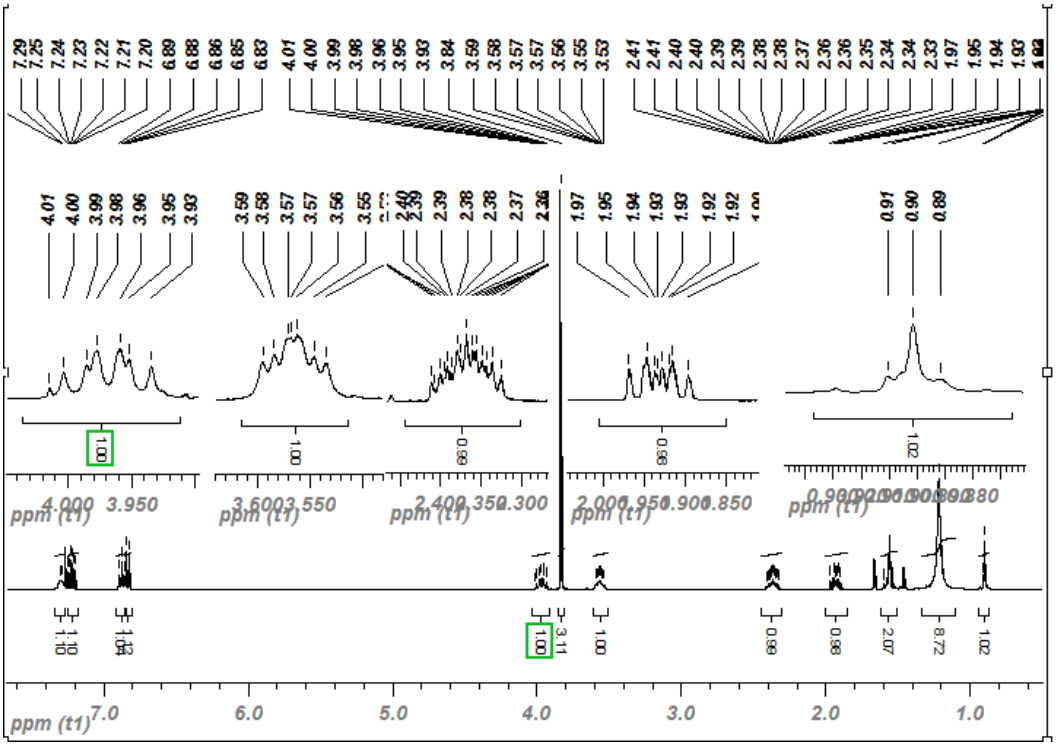


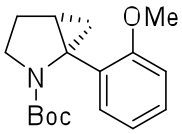


(1*S*,5*R*)-**36**

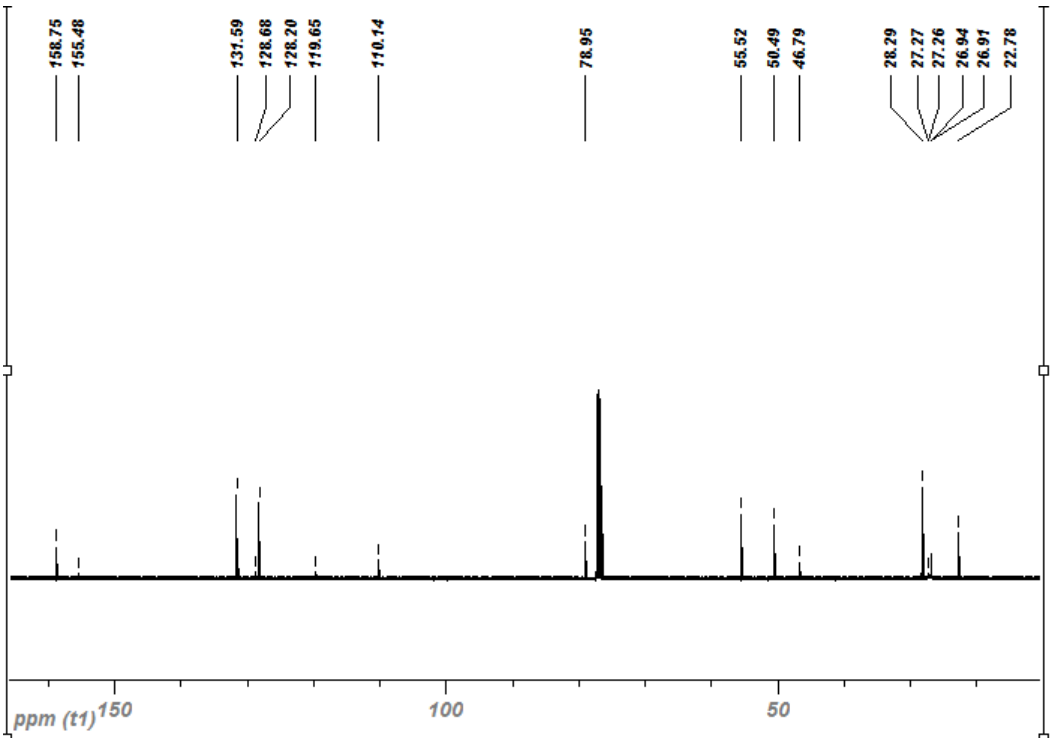


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

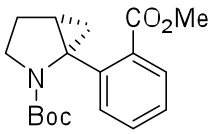




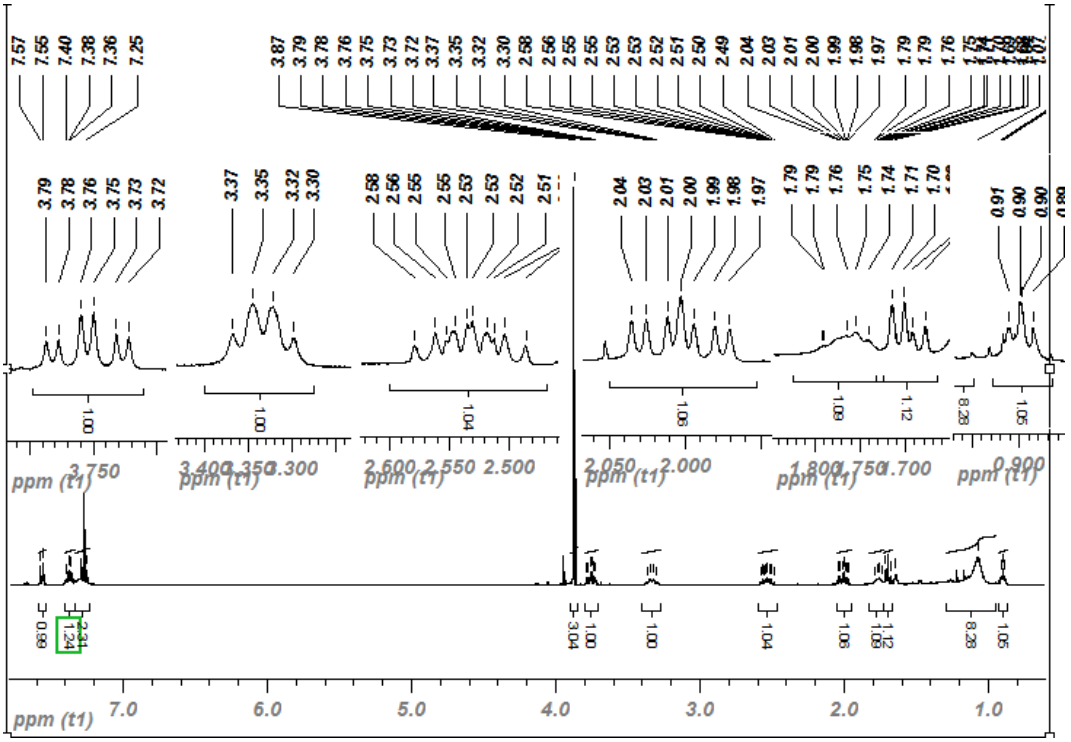
(1*S*,5*R*)-**37**

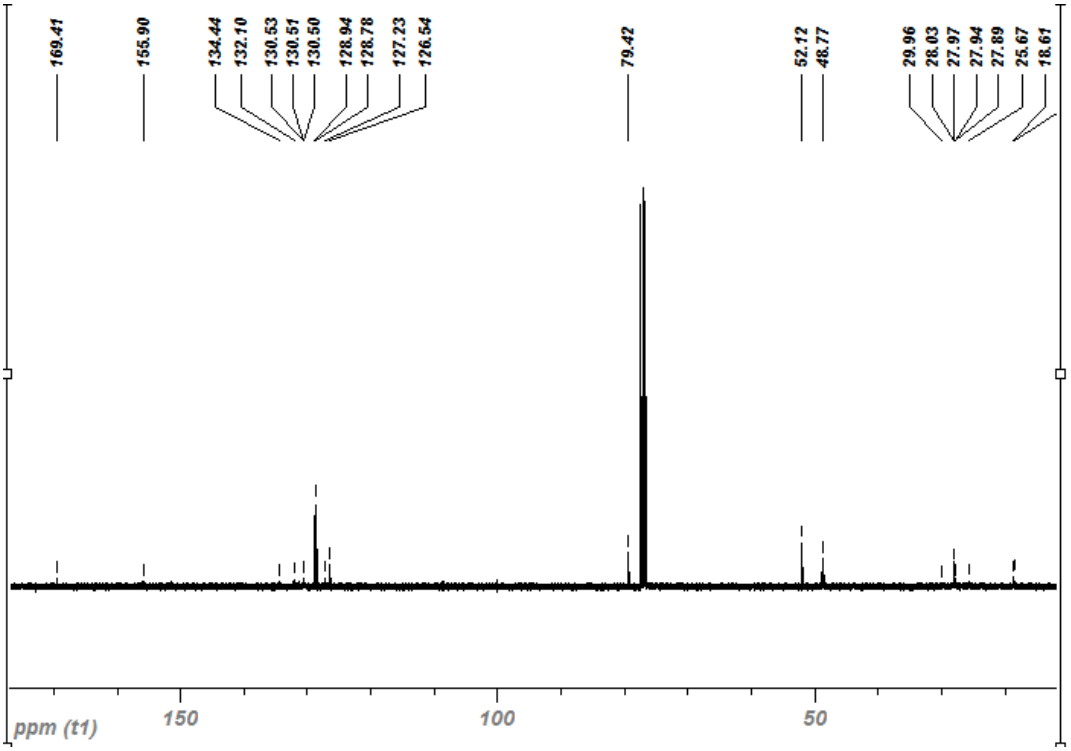


400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

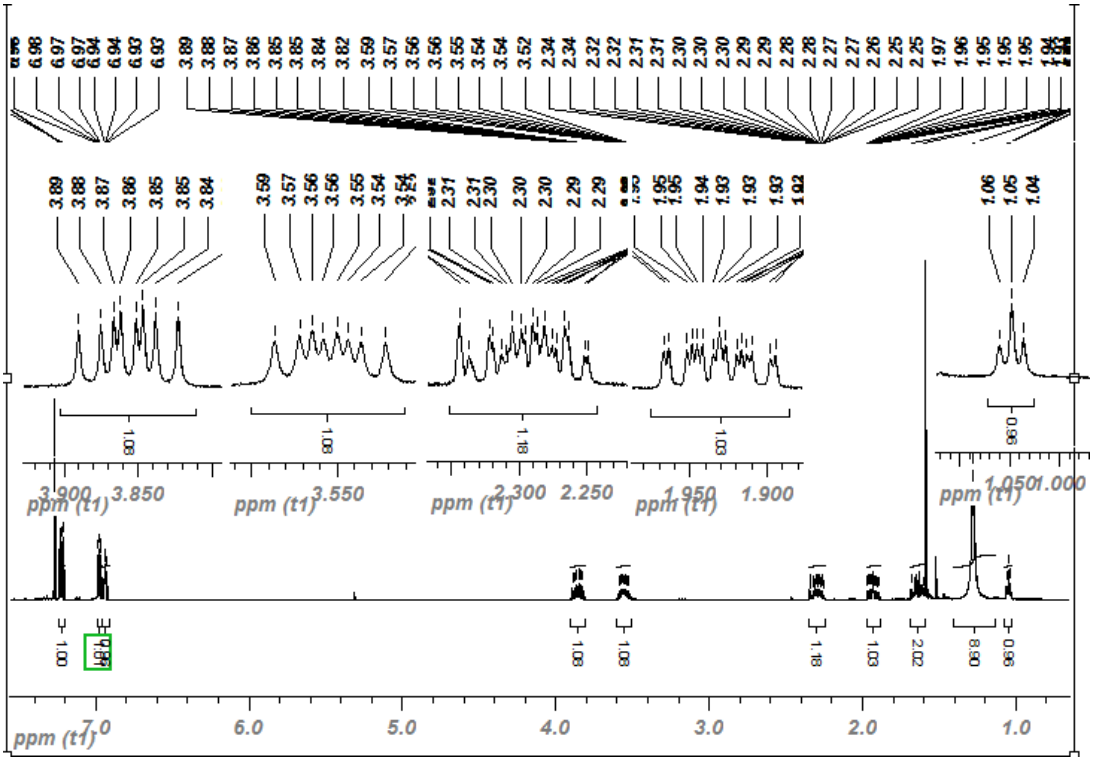


(1*S*,5*R*)-**38**

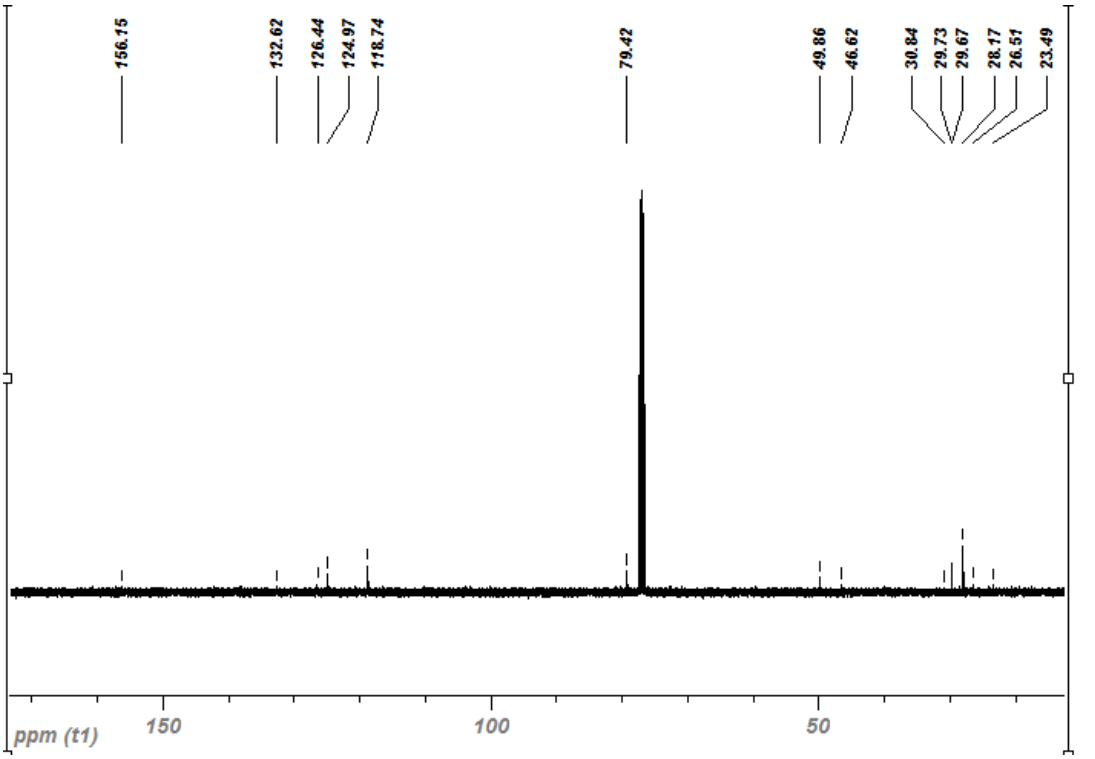




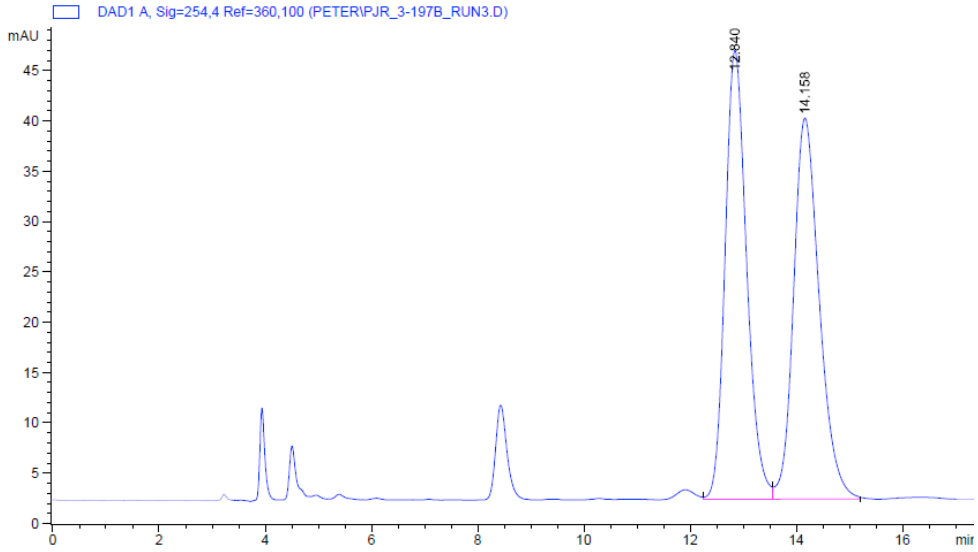
400 MHz ^{1}H NMR spectrum; 100.6 MHz ^{13}C NMR spectrum; $CDCl_3$

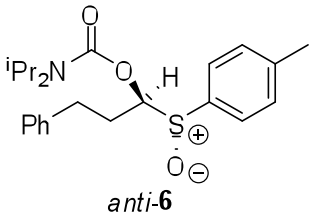


(1*S*,5*R*)-**39**



CSP-HPLC for *anti-rac*-**6**

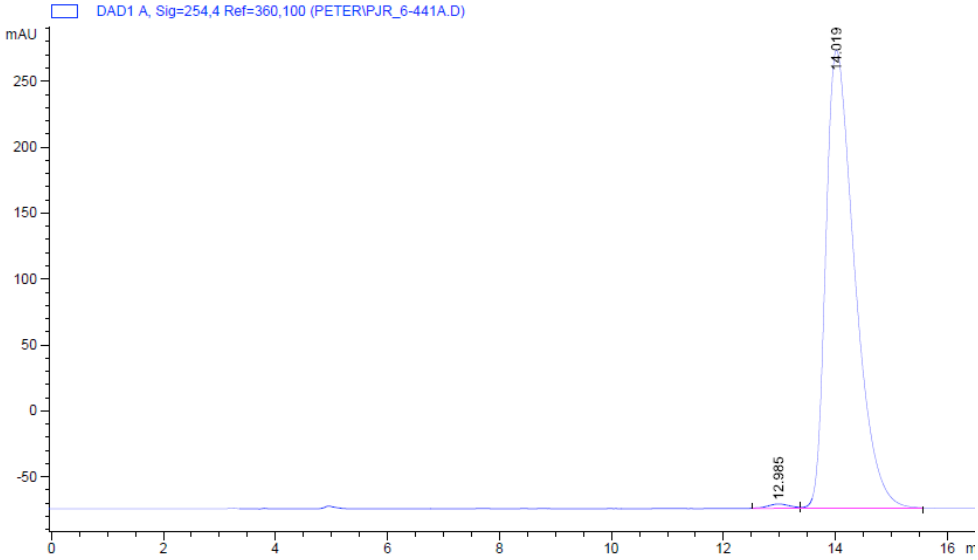


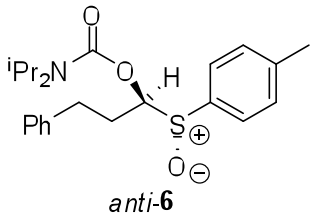


anti-**6**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.840	VV	0.4326	1256.15686	44.59659	49.6726
2	14.158	VB	0.5121	1272.71423	37.86955	50.3274

CSP-HPLC for *anti-(S,S*$_S$*)*-**6** (99:1 er)

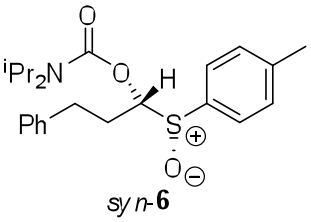




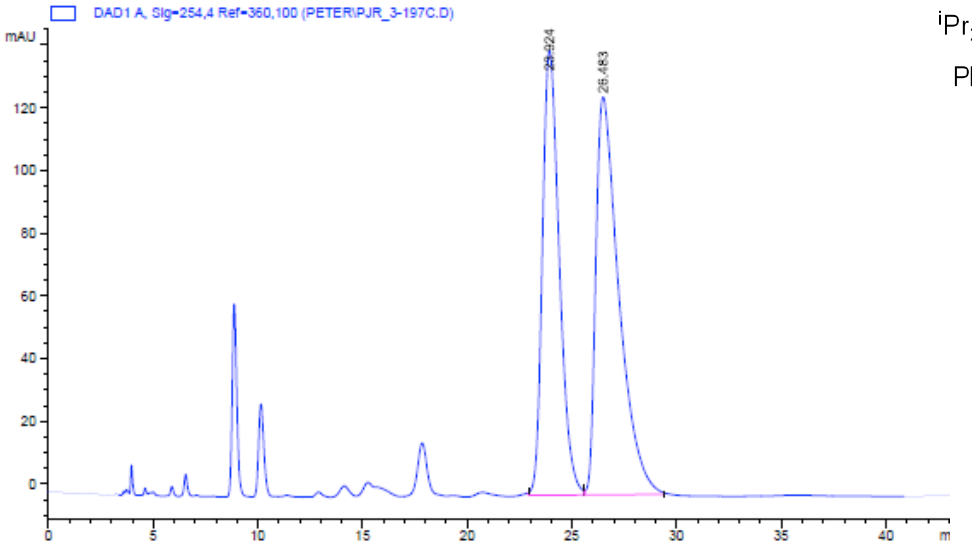
anti-**6**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.985	BV	0.4110	88.44141	3.25492	0.7043
2	14.019	VB	0.5447	1.24698e4	347.48404	99.2957

CSP-HPLC for *syn-rac*-**6**

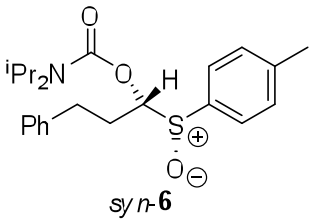


syn-**6**

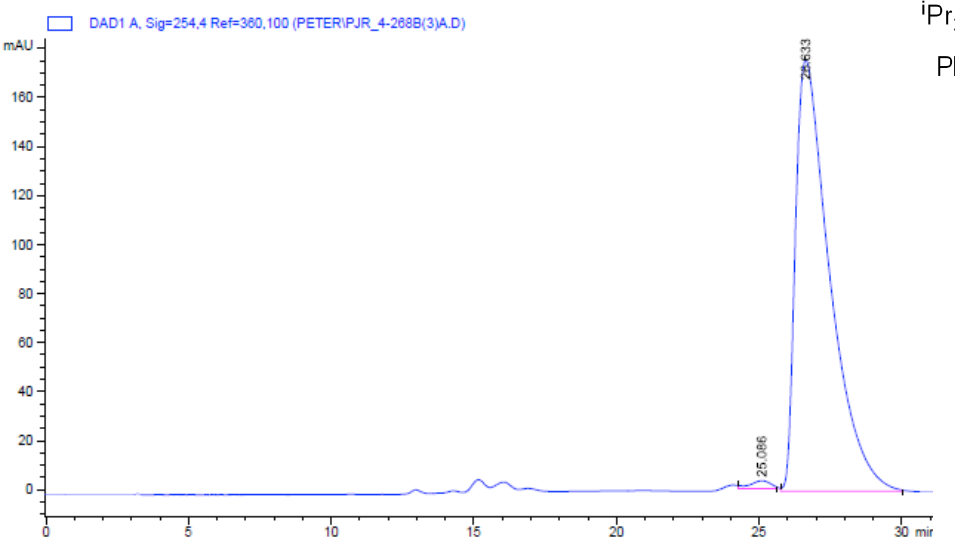


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.924	BV	0.8652	7936.19238	141.74931	44.9044
2	26.483	VB	1.1594	9737.33105	126.87754	55.0956

CSP-HPLC for *syn-(R,S*$_S$*)*-**6** (99:1 er)

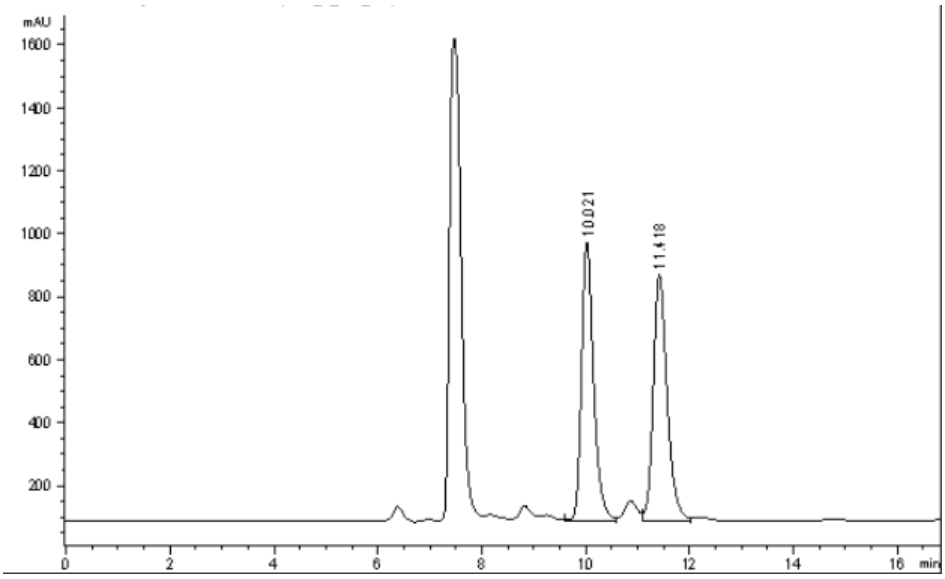


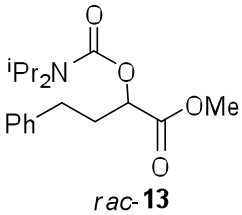
syn-**6**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.086	MM	0.8859	185.51839	3.49031	1.2472
2	26.633	VB	1.2591	1.46898e4	175.75780	98.7528

CSP-HPLC for *rac*-**13**

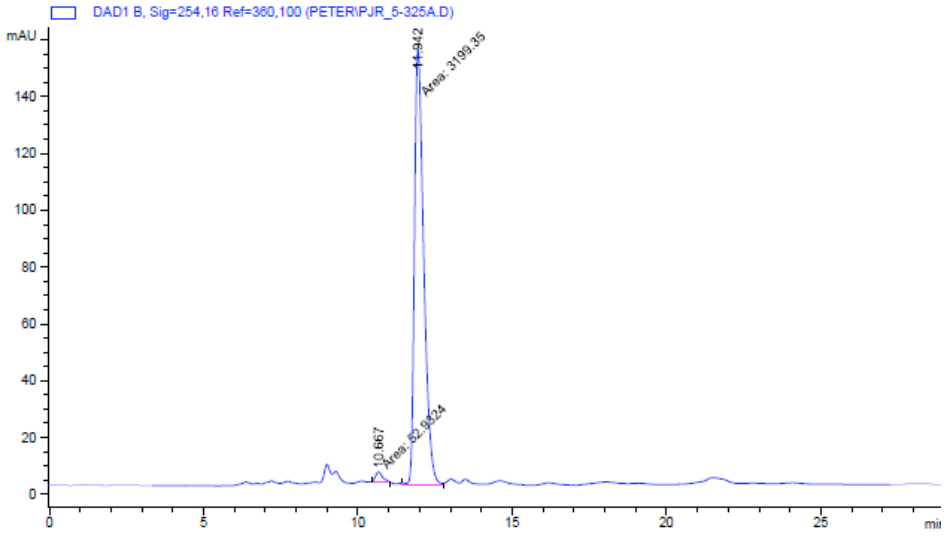


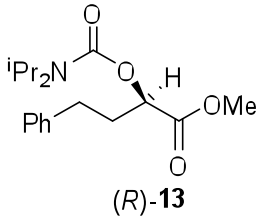


rac-**13**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.021	VV	0.2471	1.43925e4	887.89490	49.8141
2	11.418	VV	0.2804	1.44999e4	781.76660	50.1859

CSP-HPLC for (*R*)-**13** (99:1 er)

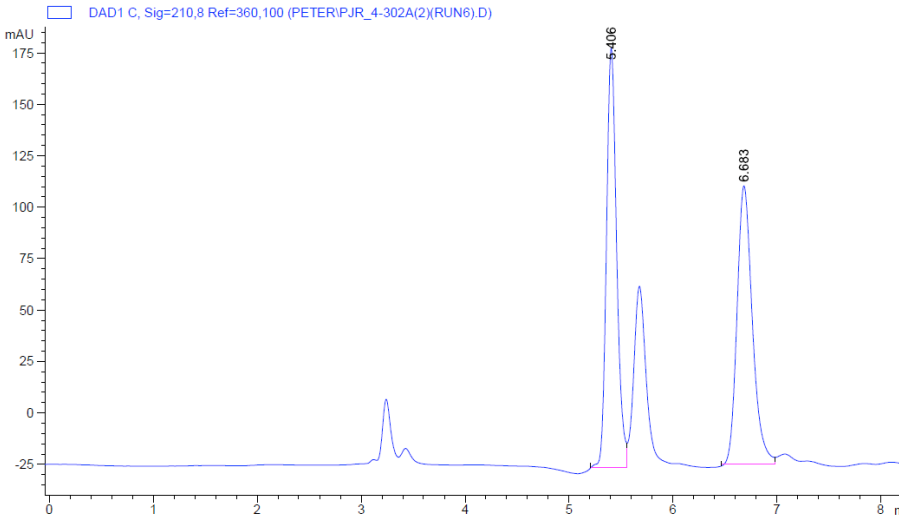


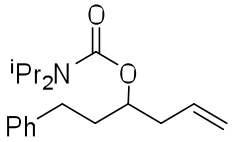


(*R*)-**13**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.667	MM	0.2575	52.93239	3.42662	1.6275
2	11.942	MM	0.3482	3199.34692	153.12131	98.3725

CSP-HPLC for *rac*-**16**

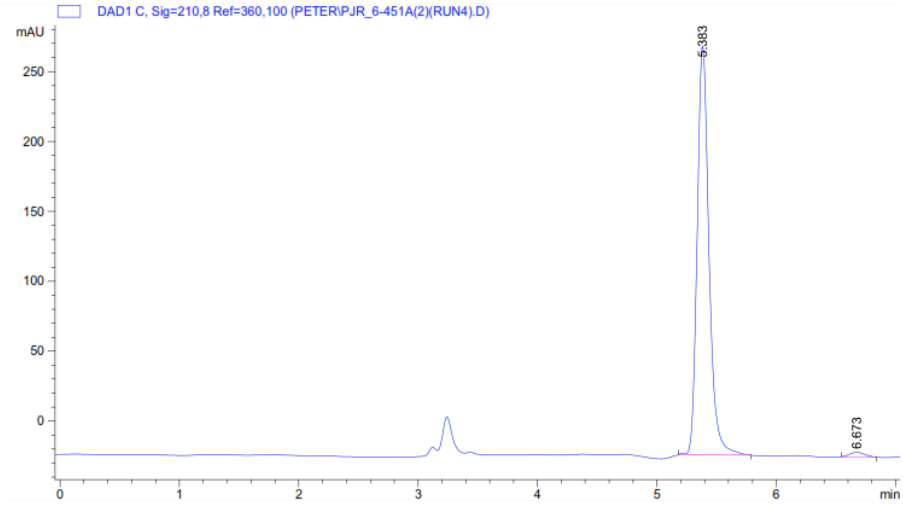


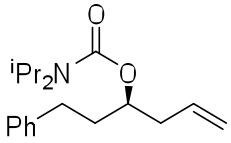


rac-**16**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.406	MM	0.1132	1388.91357	204.45462	50.0454
2	6.683	MM	0.1707	1386.39380	135.34166	49.9546

CSP-HPLC for (*R*)-**16** (99:1 er)

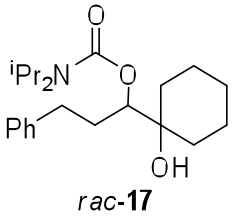




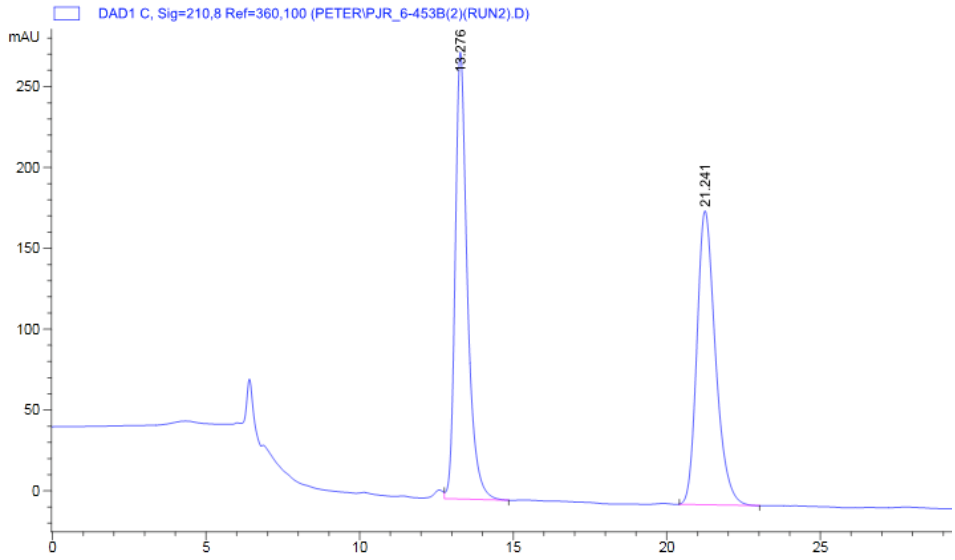
(*R*)-**16**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.383	MM	0.1136	1995.57971	292.86313	98.6153
2	6.673	MM	0.1462	28.02088	3.19376	1.3847

CSP-HPLC for *rac*-**17**

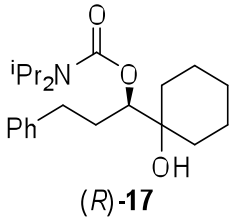


rac-**17**

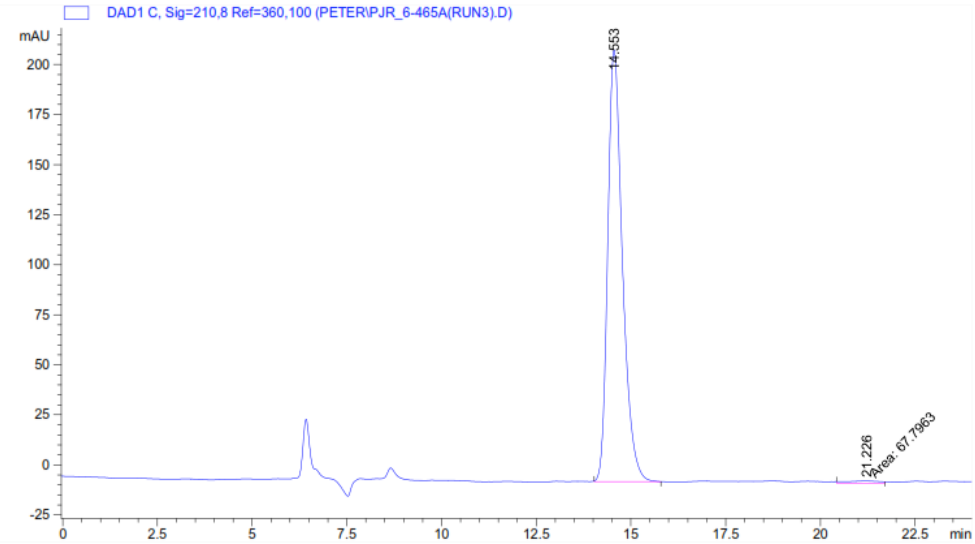


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.276	VB	0.4175	7608.62012	276.09409	49.9043
2	21.241	BB	0.6422	7637.80127	181.76051	50.0957

CSP-HPLC for (*R*)-**17** (99:1 er)

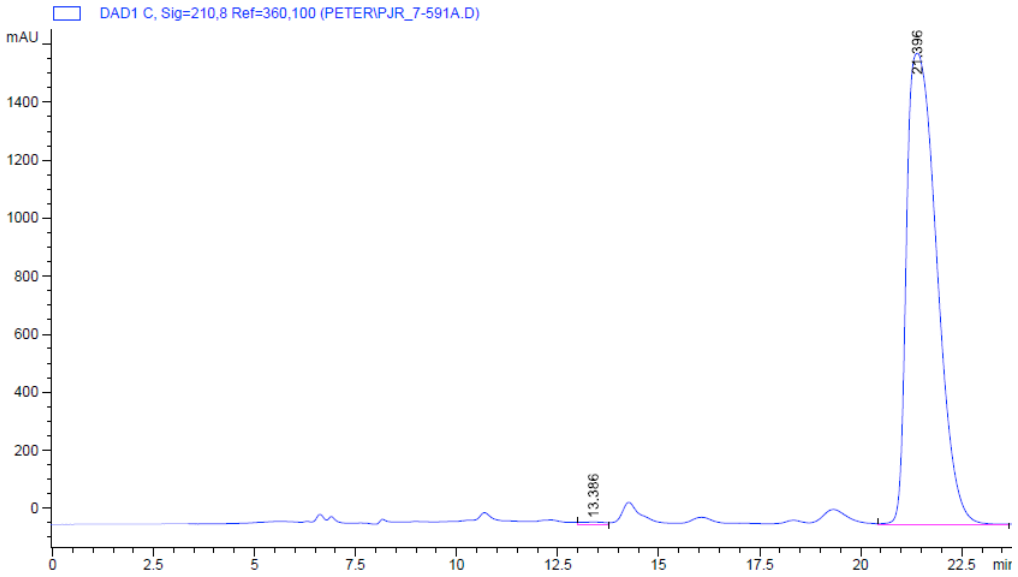


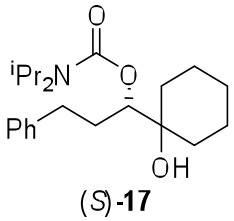
(*R*)-**17**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.553	BB	0.4117	5820.91406	215.13245	98.8487
2	21.226	MM	1.0494	67.79629	1.07678	1.1513

CSP-HPLC for (*S*)-**17** (99:1 er)

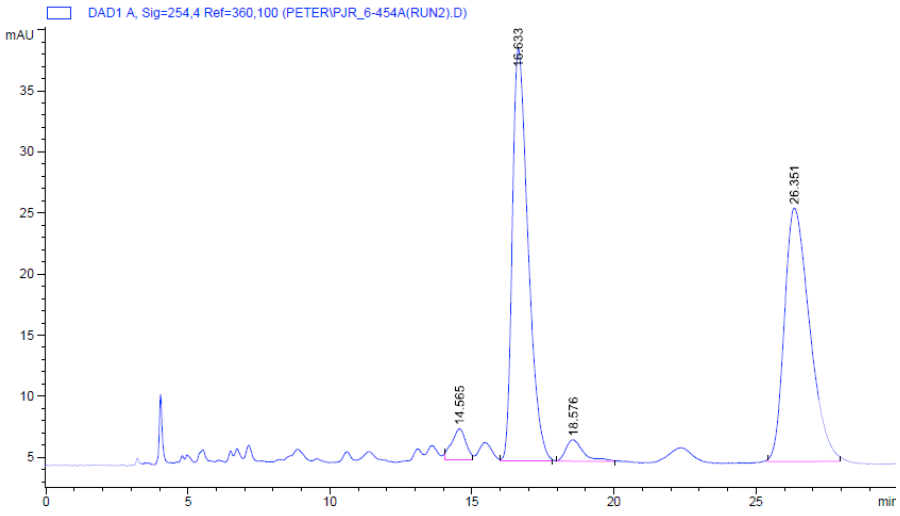




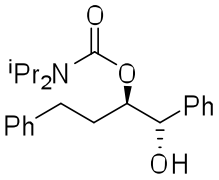
(*S*)-**17**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.386	VV	0.5429	291.95657	7.62147	0.3468
2	21.396	VB	0.8270	8.38875e4	1623.01221	99.6532

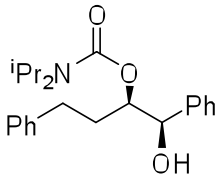
CSP-HPLC for *anti-rac*-**18** and *syn-rac*-**18** (92:8 dr by ^{1}H NMR spectroscopy)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.565	MM	0.5781	89.60790	2.58338	3.2505
2	16.633	VB	0.5705	1304.78772	33.79067	47.3305
3	18.576	BB	0.5267	75.44907	1.75102	2.7369
4	26.351	BB	0.9105	1286.91699	20.78051	46.6822

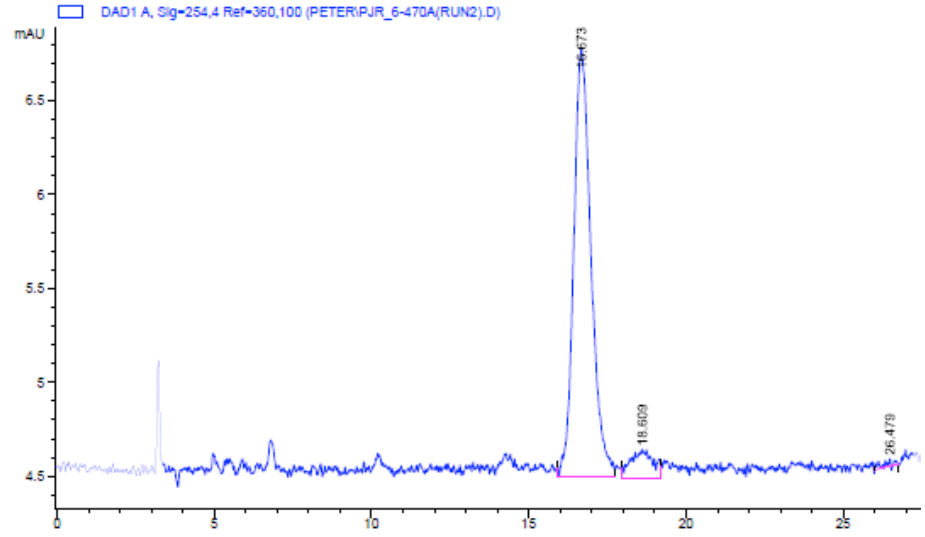


anti-rac-**18**

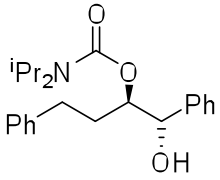


syn-rac-**18**

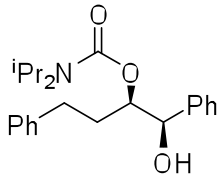
CSP-HPLC for (*R*,*S*)-**18** (99:1 er) and (*R*,*R*)-**18** (99:1 er) (96:4 dr by ^{1}H NMR spectroscopy)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.673	MM	0.6371	87.16567	2.28039	91.7938
2	18.609	MM	0.7833	7.14659	1.52068e-1	7.5260
3	26.479	MM	0.2800	6.45887e-1	3.84520e-2	0.6802

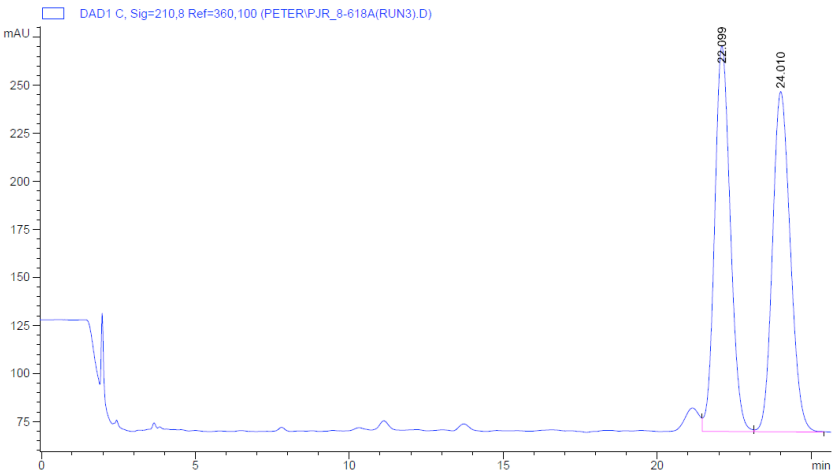


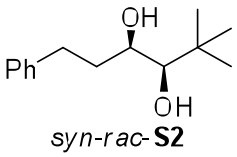
(*R*,*S*)-**18**



(*R*,*R*)-**18**

CSP-HPLC for *syn-rac*-**S2**

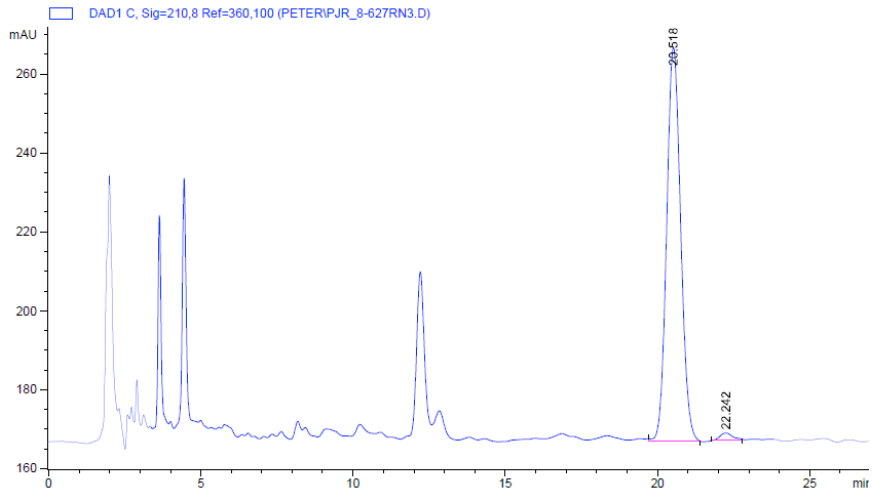


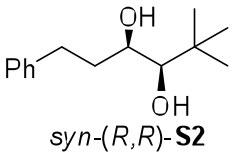


syn-rac-**S2**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.099	VV	0.5499	7109.44775	200.39189	49.9840
2	24.010	VB	0.6292	7113.99951	176.87502	50.0160

CSP-HPLC for *syn*-(*R*,*R*)-**S2** (99:1 er)

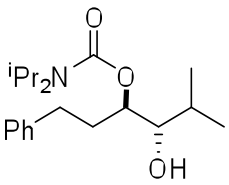




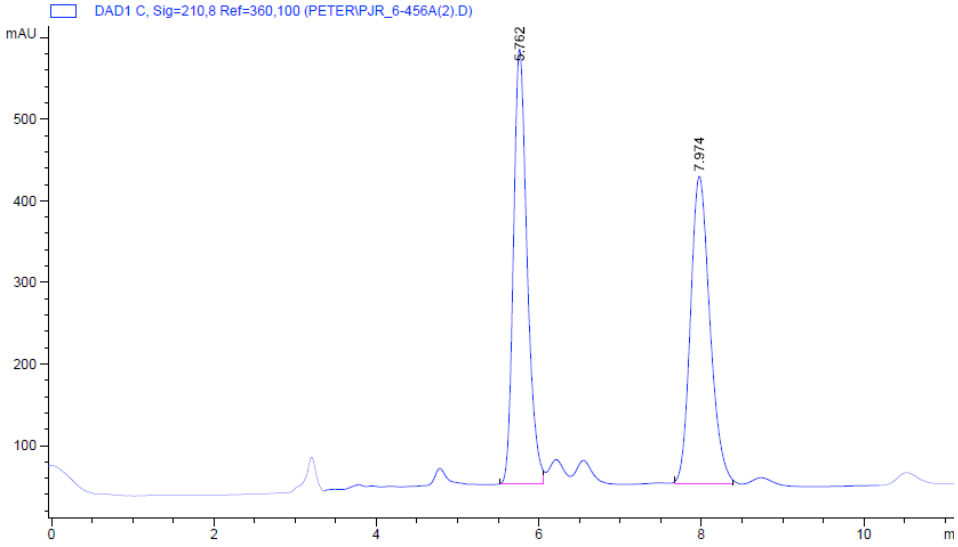
syn-(*R*,*R*)-**S2**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.518	MM	0.5337	3198.96875	99.90102	98.4435
2	22.242	MM	0.4659	50.58067	1.80945	1.5565

CSP-HPLC for *rac*-**20**

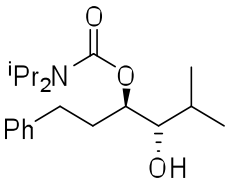


rac-**20**

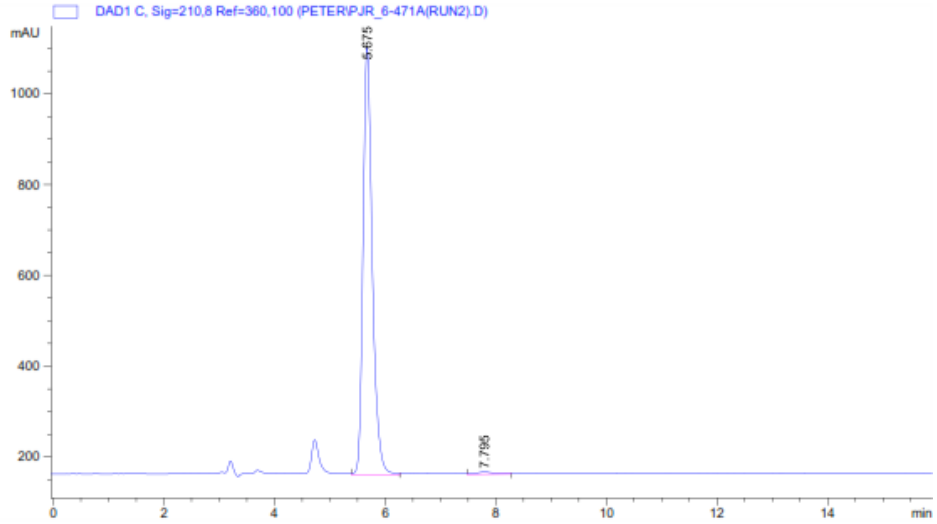


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.762	MM	0.1942	6250.00439	536.40417	49.9423
2	7.974	MM	0.2759	6264.43750	378.48874	50.0577

CSP-HPLC for (*R*,*S*)-**20** (99:1 er)

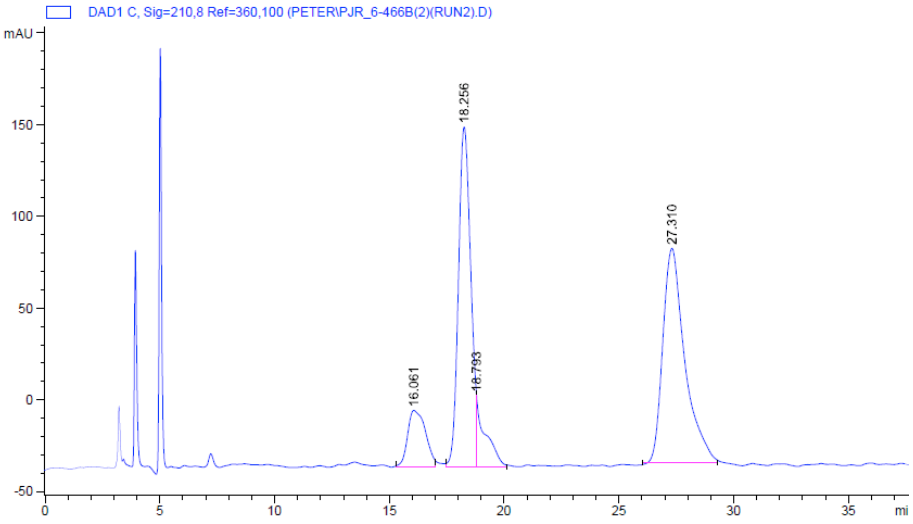


(*R*,*S*)-**20**

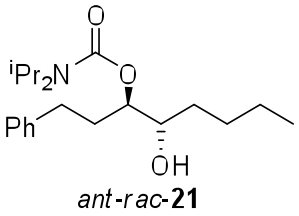


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.675	BV	0.1850	1.10072e4	937.20496	98.9303
2	7.795	BB	0.3494	119.01144	4.86437	1.0697

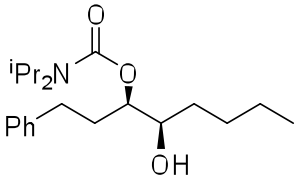
CSP-HPLC for *rac*-**21** (90:10 dr by ^{1}H NMR spectroscopy)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.061	MM	0.9015	1670.50867	30.88497	9.6033
2	18.256	MF	0.6195	6889.58008	185.35547	39.6062
3	18.793	FM	0.4428	1034.77661	38.94897	5.9486
4	27.310	MM	1.1112	7800.33936	116.99807	44.8419

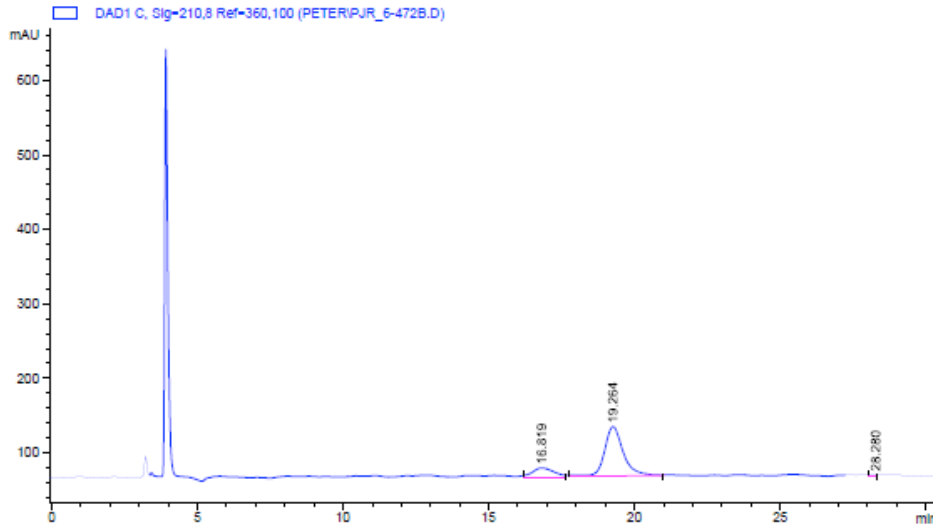


ant-rac-**21**

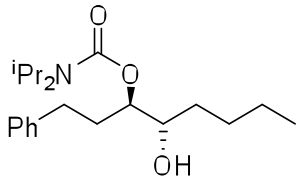


syn-rac-**21**

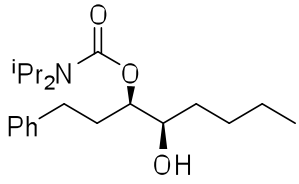
CSP-HPLC for (*R*,*S*)-**21** (99:1 er) and (*R*,*S*)-**21** (99:1 er) (90:10 dr by ^{1}H NMR spectroscopy)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.819	MM	0.8398	628.03522	12.46346	17.1881
2	19.264	VB	0.6770	2985.25220	66.33423	81.7007
3	28.280	MM	0.2979	40.59931	2.27140	1.1111

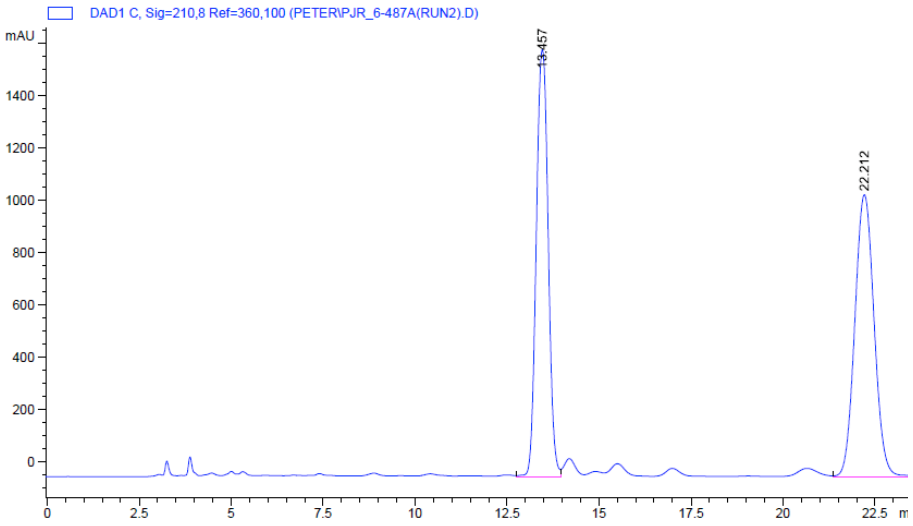


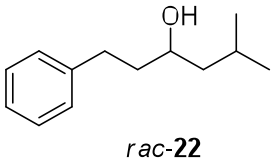
(*R*,*S*)-**21**



(*R*,*R*)-**21**

CSP-HPLC for *rac*-**22**

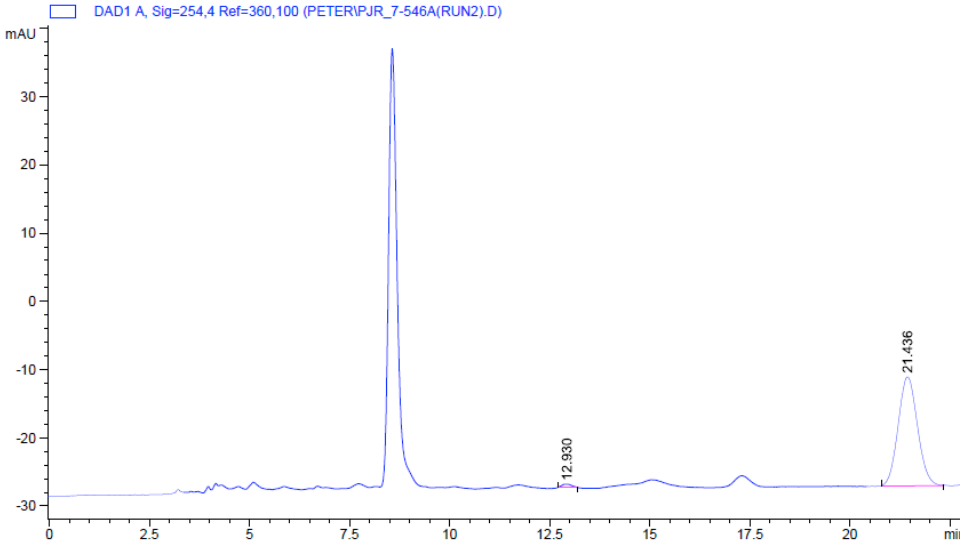


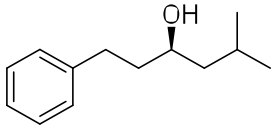


rac-**22**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.457	VV	0.3582	3.67200e4	1633.98254	48.3567
2	22.212	VBA	0.5683	3.92157e4	1078.31128	51.6433

CSP-HPLC for (*R*)-**22** (99:1 er)

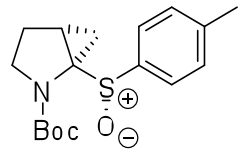




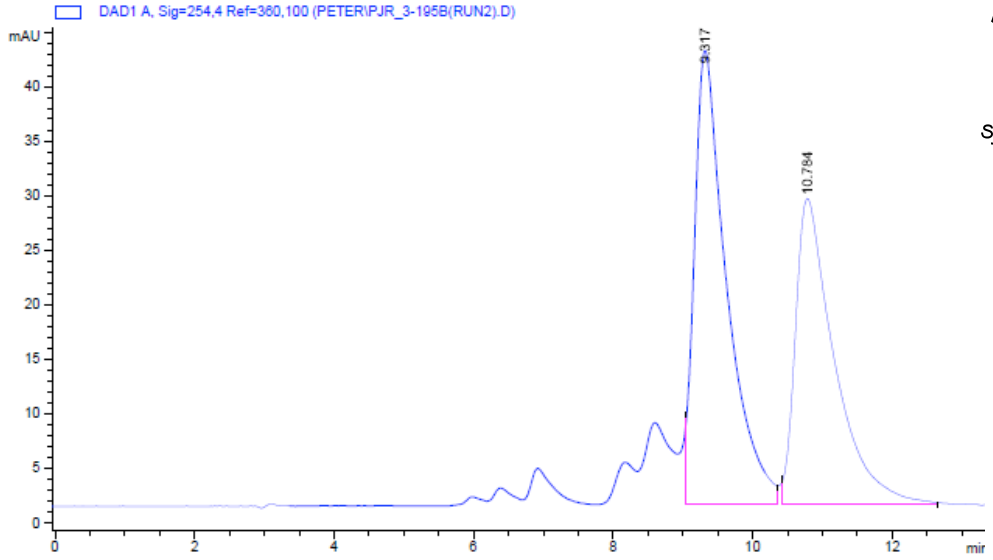
(*R*)-**22**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.930	MM	0.2389	5.58955	3.89917e-1	1.0297
2	21.436	BB	0.5180	537.23975	15.98775	98.9703

CSP-HPLC for *syn-rac*-**7**

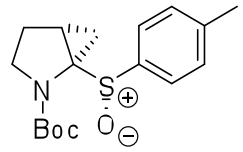


syn-rac-**7**

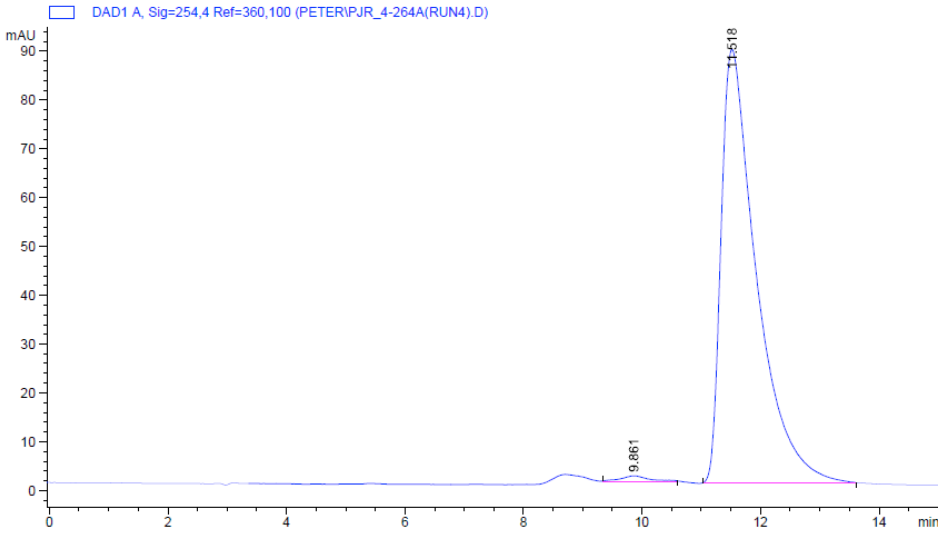


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.317	MM	0.5337	1334.22791	41.66327	55.0223
2	10.784	MM	0.6468	1090.65686	28.10245	44.9777

CSP-HPLC for *syn-(R,R,S*$_S$*)*-**7** (99:1 er)

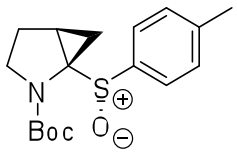


syn-(R,R,S$_S$*)*-**7**

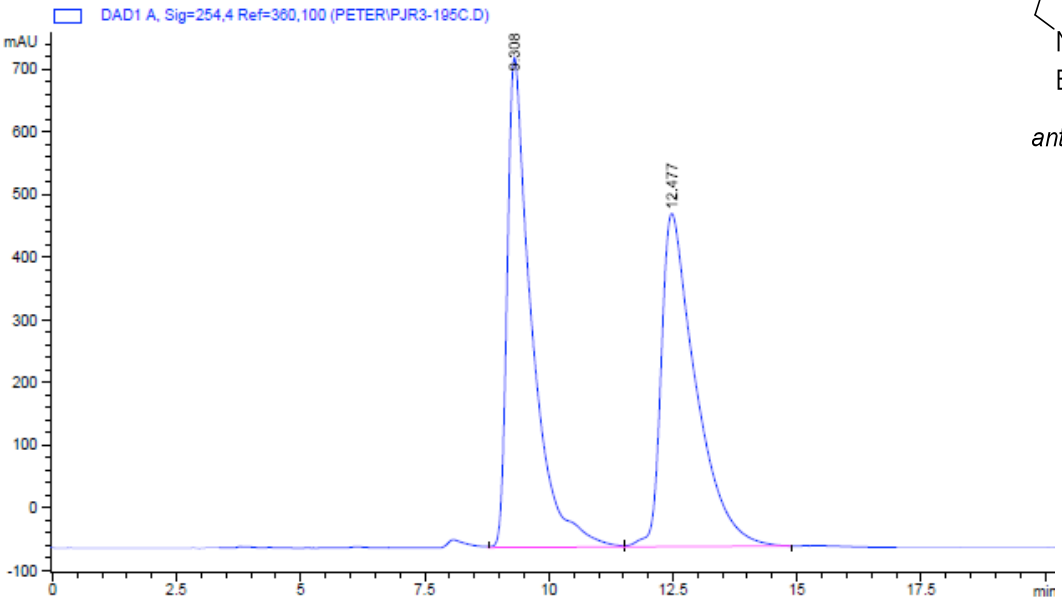


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.861	MM	0.6115	44.94740	1.22496	1.2138
2	11.518	MM	0.6872	3658.00513	88.71557	98.7862

CSP-HPLC for *anti-rac*-**7**

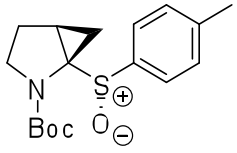


anti-rac-**7**

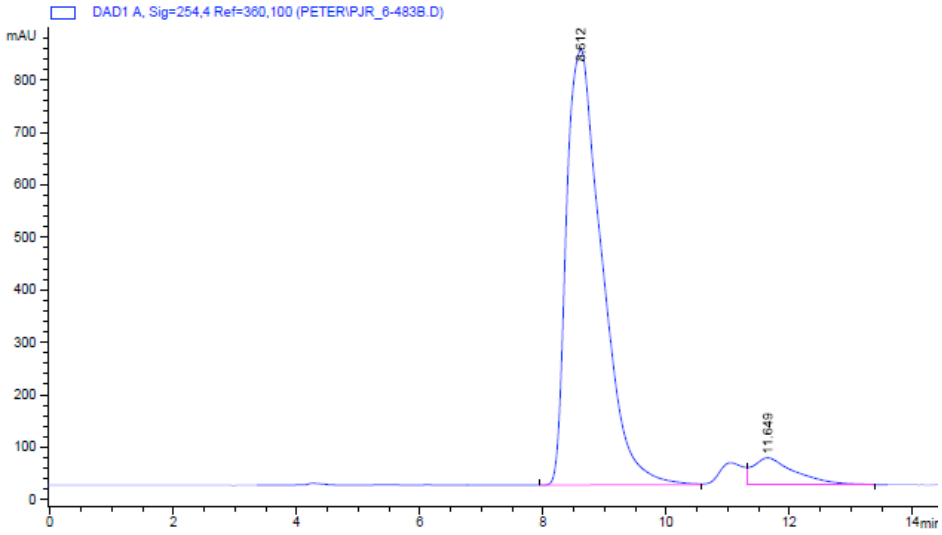


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.308	VV	0.4776	2.67814e4	781.90192	51.1206
2	12.477	VB	0.6883	2.56072e4	531.34259	48.8794

CSP-HPLC for *anti-(S,S,S*$_S$*)*-**7** (93:7 er)

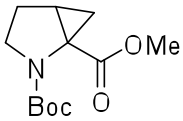


anti-(S,S,S$_S$*)*-**7**

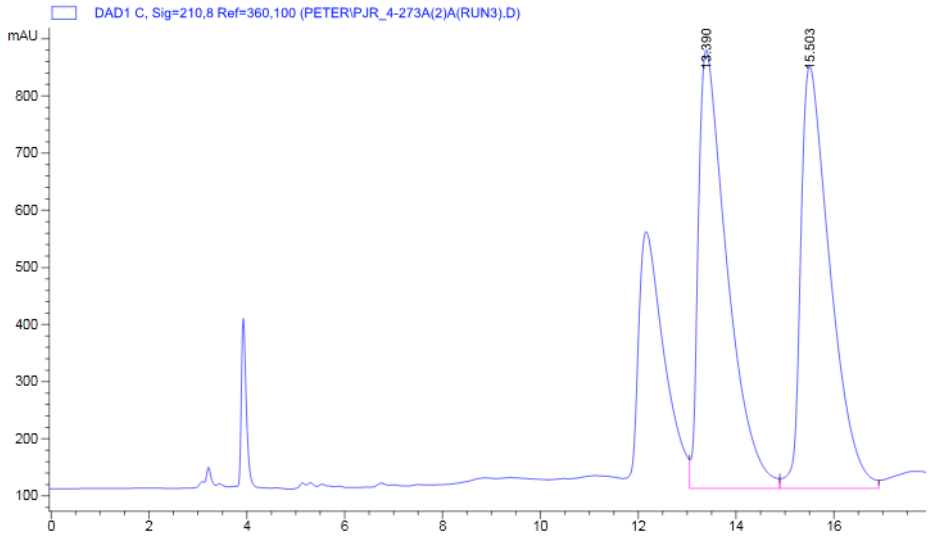


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.612	BV	0.5869	3.30759e4	830.11774	93.0896
2	11.649	VB	0.6572	2455.35596	51.59697	6.9104

CSP-HPLC for *rac*-**32**

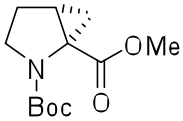


rac-**32**

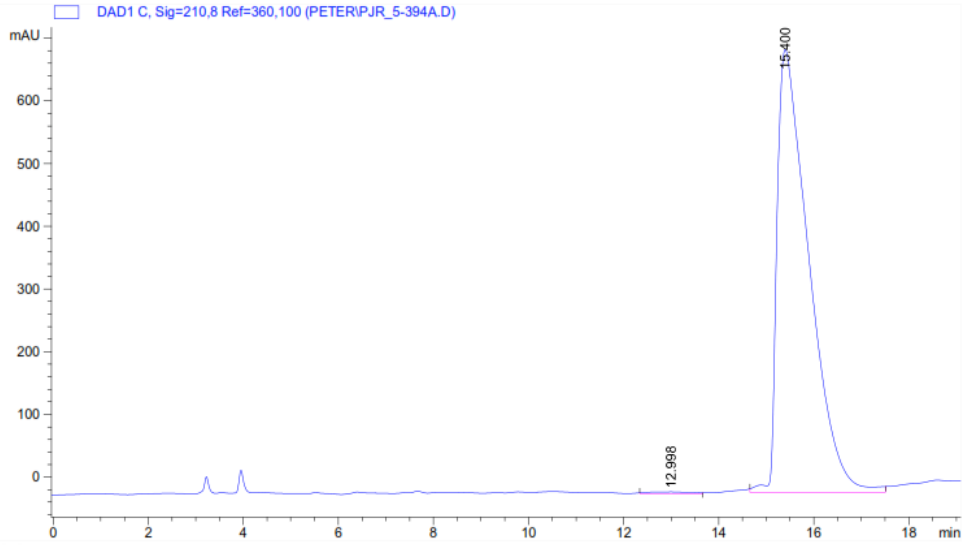


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.390	VV	0.6068	3.14704e4	766.75201	50.4332
2	15.503	VV	0.6242	3.09298e4	739.13617	49.5668

CSP-HPLC for (1*S*,5*R*)-**32** (99:1 er)

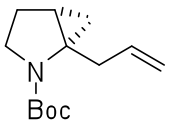


(*S*,*R*)-**32**

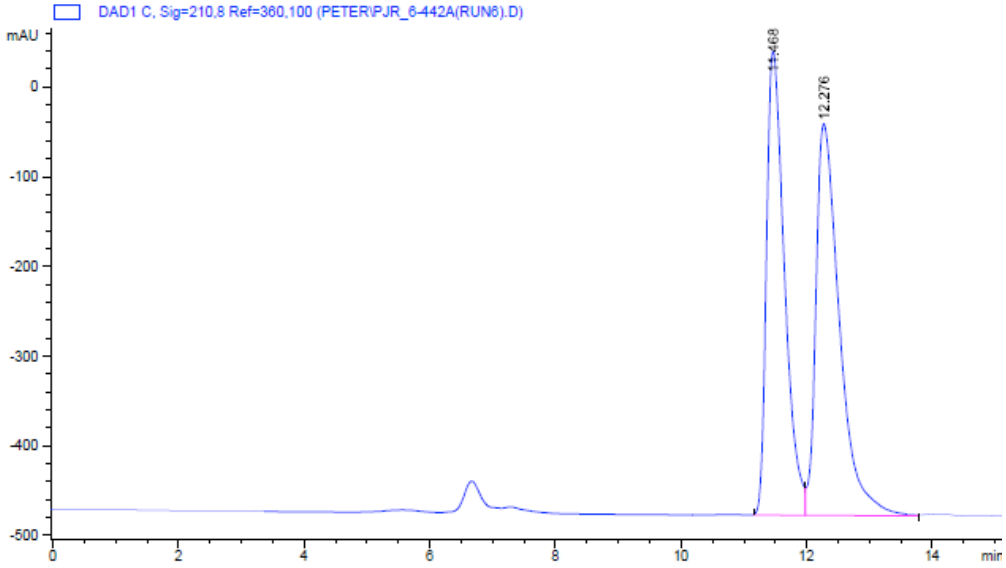


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.998	MM	1.0916	199.18494	3.04122	0.6027
2	15.400	MM	0.7751	3.28479e4	706.27435	99.3973

CSP-HPLC for *rac*-**33**

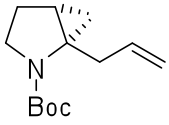


rac-**33**

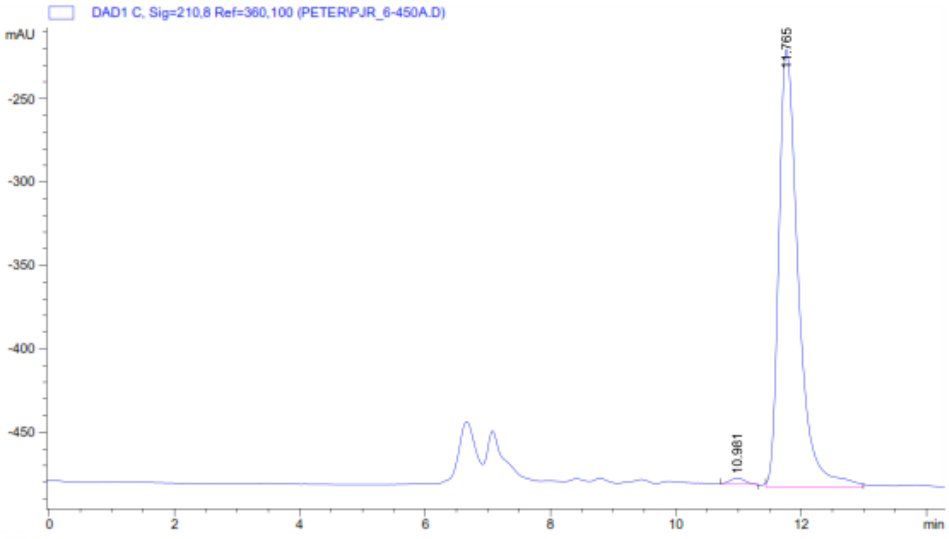


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.468	BV	0.3047	1.02869e4	515.77087	47.4186
2	12.276	VV	0.3929	1.14069e4	436.52994	52.5814

CSP-HPLC for (1*S*,5*R*)-**33** (99:1 er)

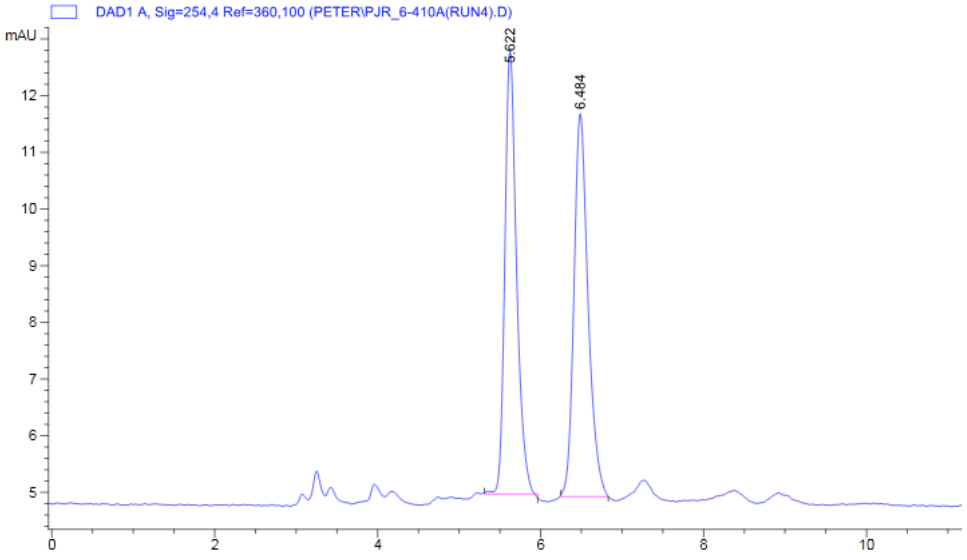


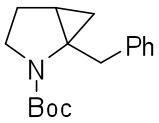
(*S*,*R*)-**33**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.981	MM	0.2737	62.36129	3.79755	1.0850
2	11.765	MM	0.3602	5685.39648	263.05963	98.9150

CSP-HPLC for *rac*-**34**

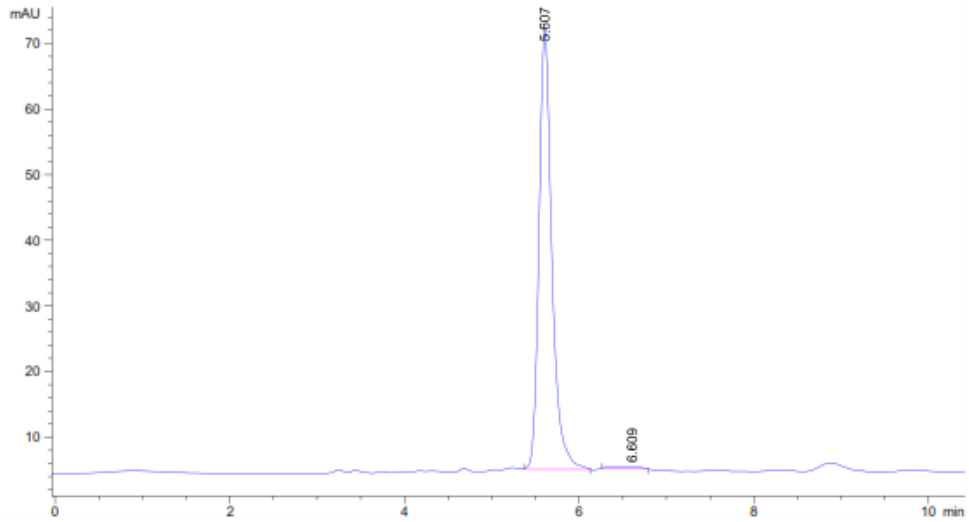


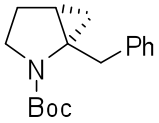


rac-**34**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.622	MM	0.1662	78.10099	7.83157	48.9899
2	6.484	MM	0.2004	81.32155	6.76323	51.0101

CSP-HPLC for (1*R*,5*R*)-**34** (99:1 er)

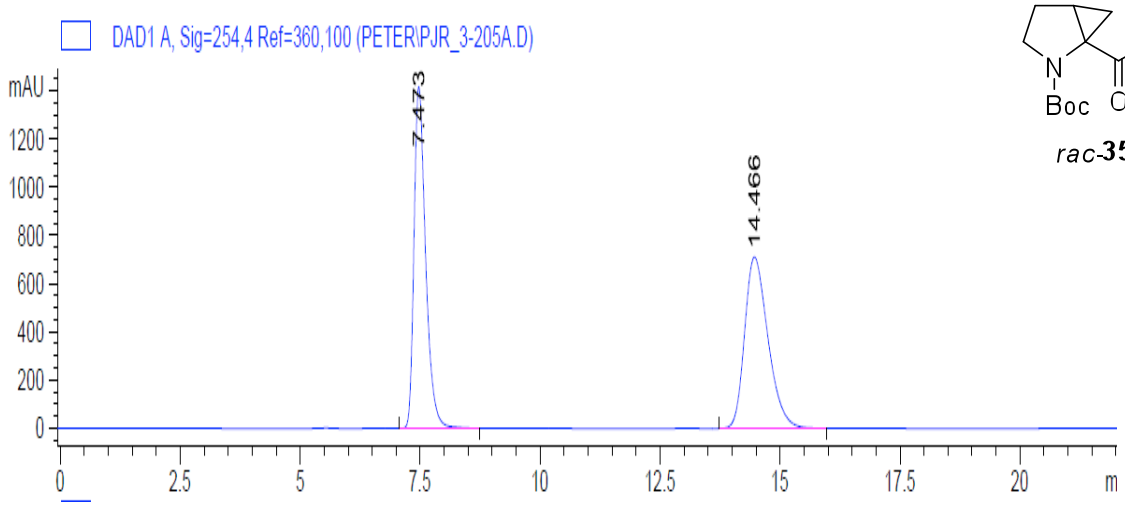


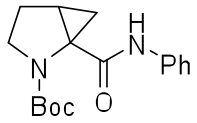


(*R*,*R*)-**34**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.607	MM	0.1713	690.34033	67.15362	98.9961
2	6.609	MM	0.3283	7.00077	3.55392e-1	1.0039

CSP-HPLC for *rac*-**35**

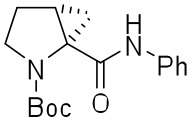




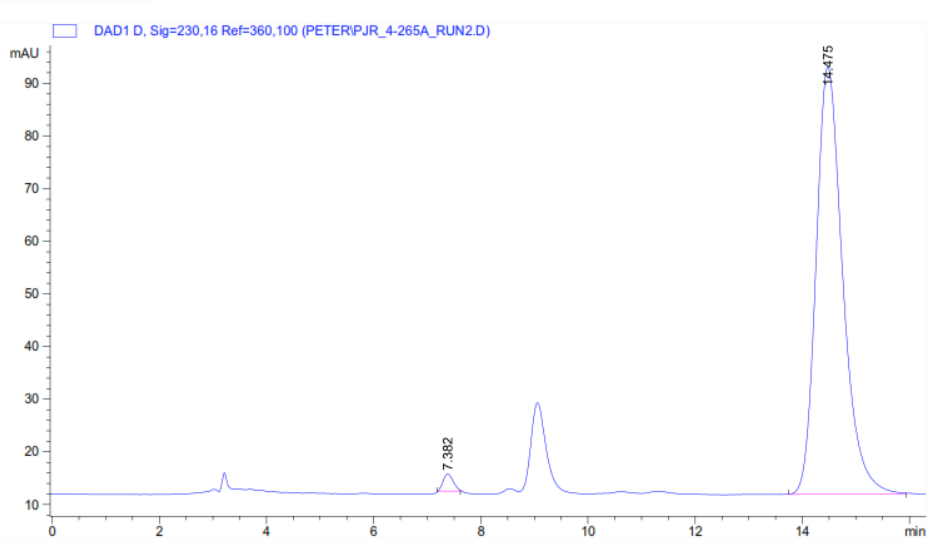
rac-**35**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.473	VB	0.2564	2.38878e4	1419.06726	49.7196
2	14.466	BB	0.5220	2.41572e4	711.78931	50.2804

CSP-HPLC for (1*S*,5*R*)-**35** (99:1 er)

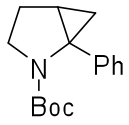


(*S*,*R*)-**35**

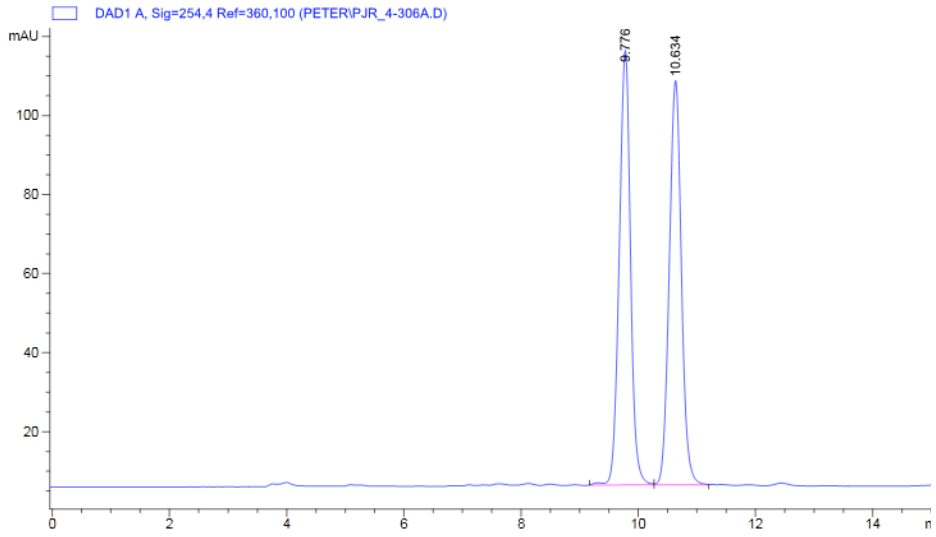


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.382	MM	0.2205	42.72910	3.22954	1.5005
2	14.475	MM	0.5757	2804.94922	81.20789	98.4995

CSP-HPLC for *rac*-**36**

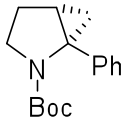


rac-**36**

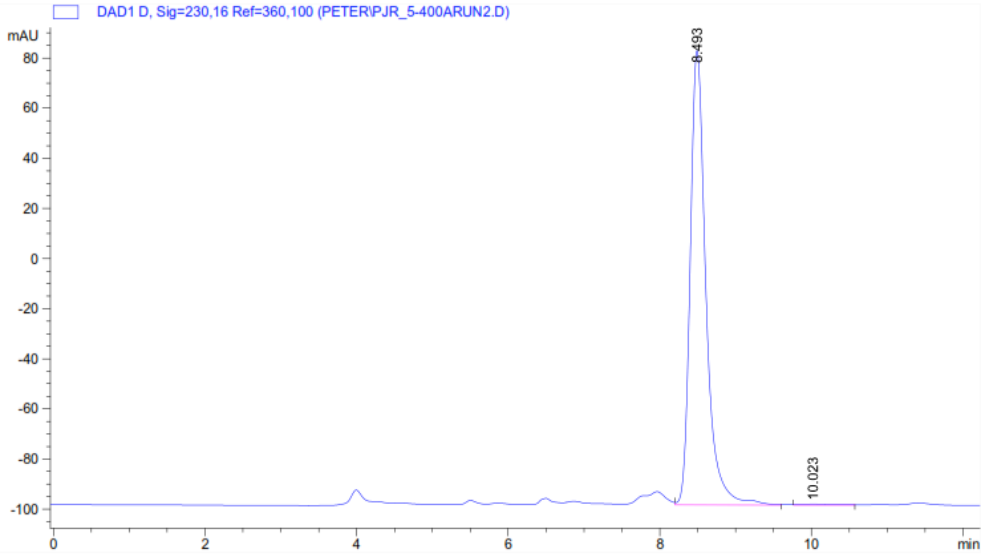


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.776	BV	0.2060	1471.77148	110.05868	50.0249
2	10.634	VB	0.2215	1470.30811	102.42838	49.9751

CSP-HPLC for (1*S*,5*R*)-**36** (99:1 er)

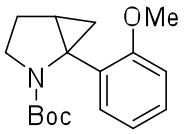


(1*S*,5*R*)-**36**

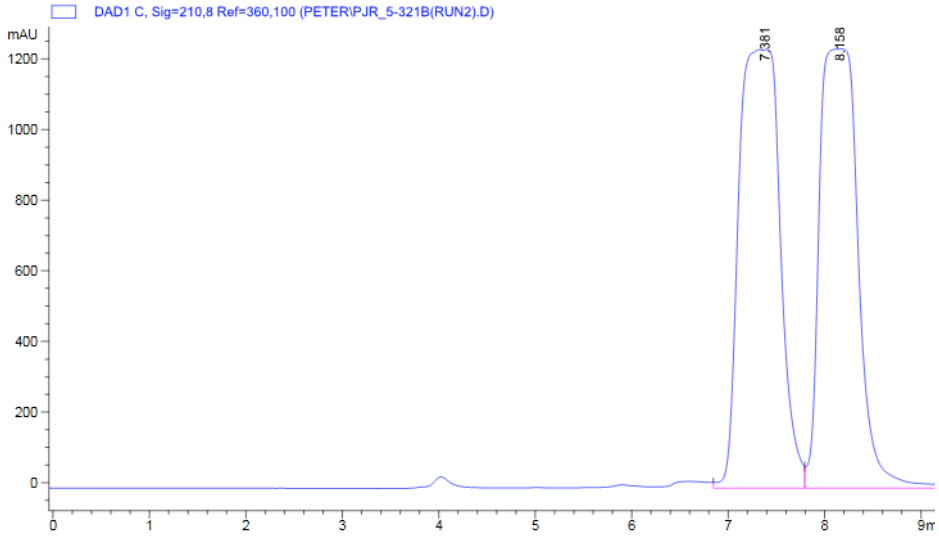


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.493	VB	0.2201	2611.04590	181.20610	99.6176
2	10.023	BB	0.3368	10.02281	4.10539e-1	0.3824

CSP-HPLC for *rac*-**37**

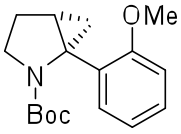


rac-**37**

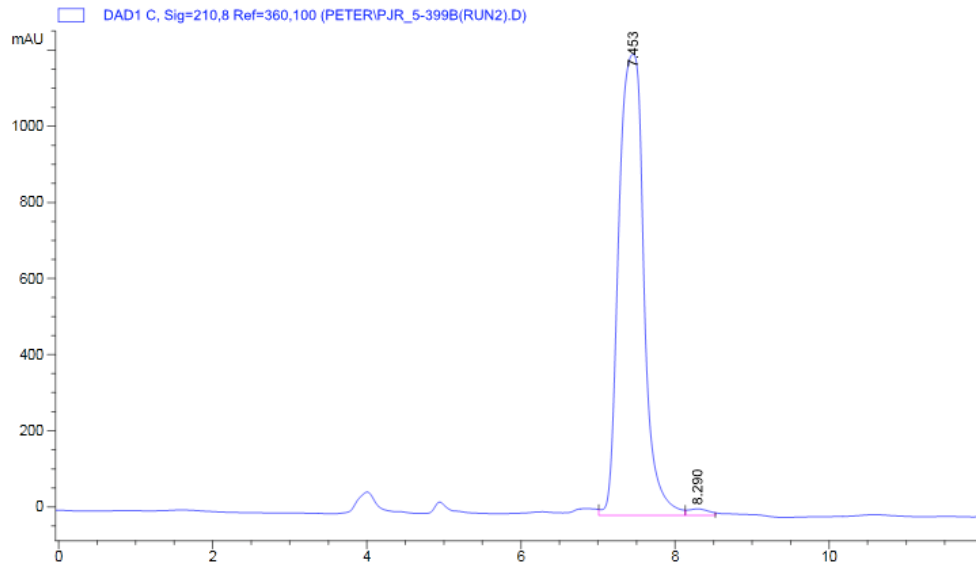


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.381	VV	0.4730	3.67498e4	1242.82227	51.5238
2	8.158	VBA	0.4442	3.45760e4	1244.30042	48.4762

CSP-HPLC for (1*S*,5*R*)-**37** (99:1 er)

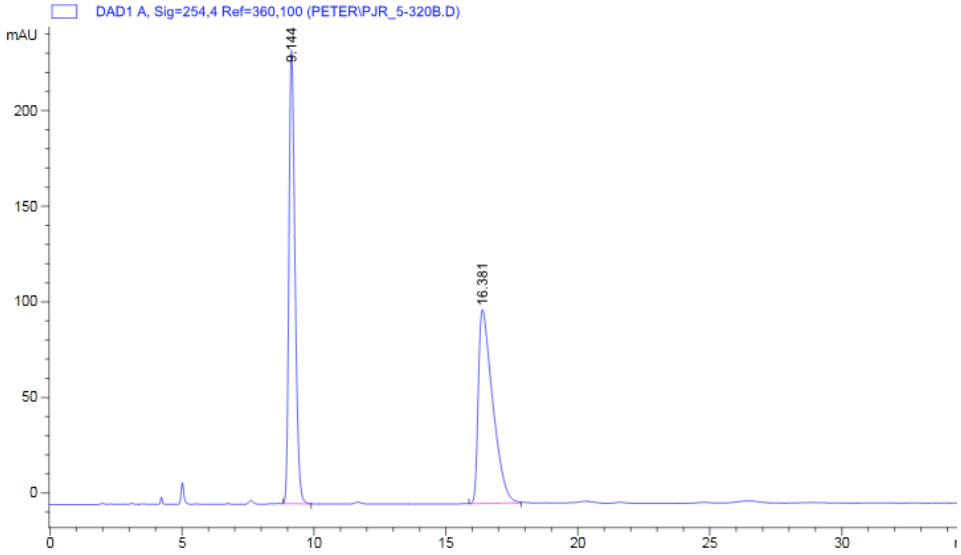


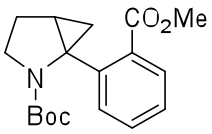
(1*S*,5*R*)-**37**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.453	MM	0.3765	2.74028e4	1212.90356	98.8267
2	8.290	MM	0.3123	325.32260	17.36113	1.1733

CSP-HPLC for *rac*-**38**

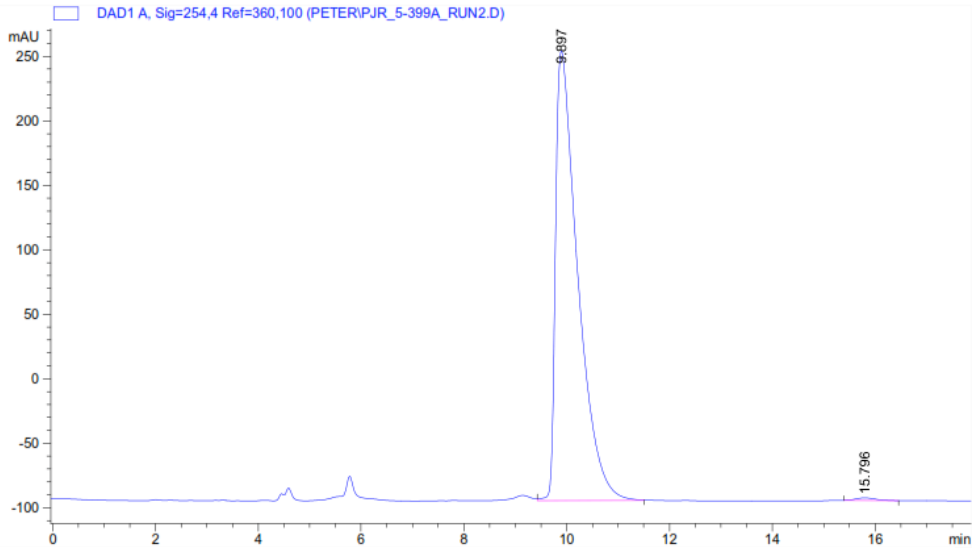


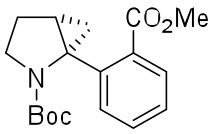


rac-**38**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.144	BB	0.2469	3801.77222	237.34799	49.7029
2	16.381	BB	0.5587	3847.21704	101.37849	50.2971

CSP-HPLC for (1*S*,5*R*)-**38** (99:1 er)

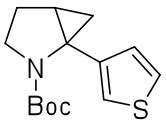




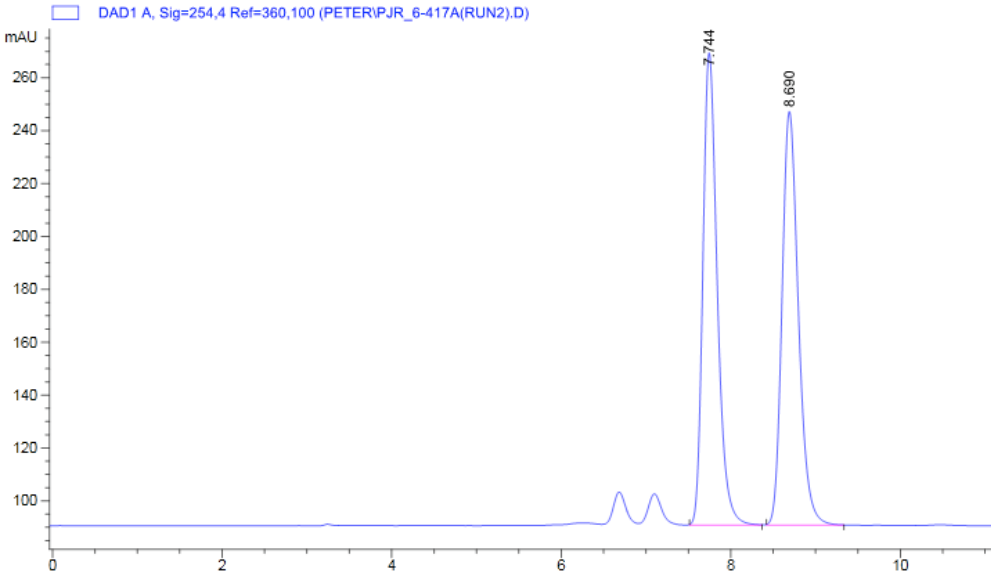
(1*S*,5*R*)-**38**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.897	VB	0.4397	1.04476e4	348.51007	99.4618
2	15.796	BB	0.4093	56.53306	2.09203	0.5382

CSP-HPLC for *rac*-**39**

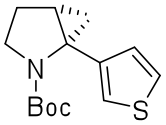


rac-**39**

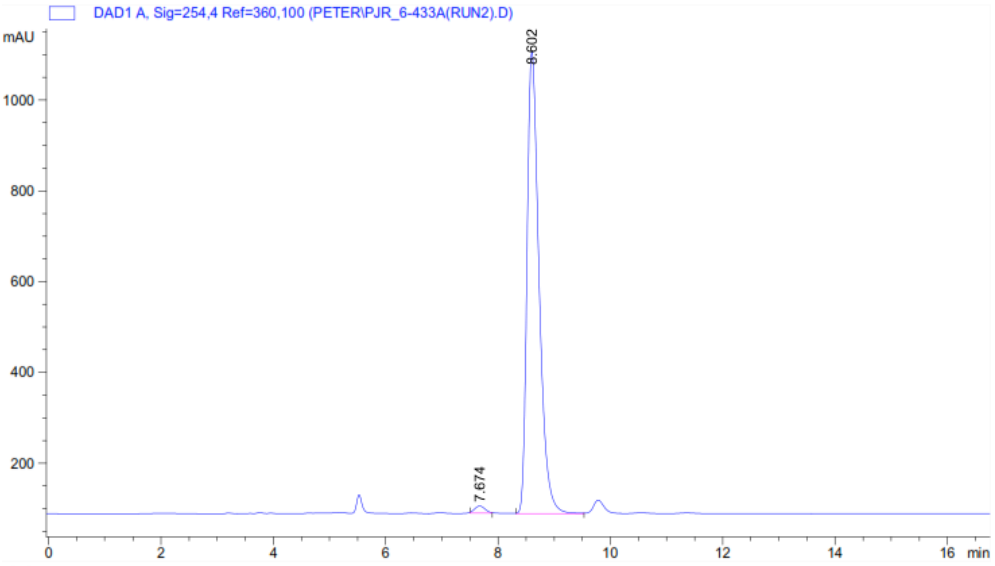


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.744	BB	0.1811	2100.26318	178.78563	50.0488
2	8.690	BB	0.2062	2096.16870	156.55078	49.9512

CSP-HPLC for (1*S*,5*R*)-**39** (99:1 er)



(1*S*,5*R*)-**39**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.674	MM	0.2139	201.09517	15.66800	1.3181
2	8.602	BV	0.2267	1.50554e4	1017.01355	98.6819

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