Practical and Highly Selective Sulfur Ylide-Mediated Asymmetric Epoxidations and Aziridinations Using an Inexpensive, Readily Available Chiral Sulfide. Applications to the Synthesis of Quinine and Quinidine

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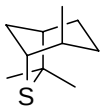
General Experimental

^{1}H-NMR and ^{13}C-NMR are reported in ppm relative to tetramethylsilane. Chiral phase HPLC was carried out using Daicel Chiralcel® OD, AD, OJ and ODH columns (length 25 cm, diameter 0.46 cm) and a Chromtech chiral-AGP column (length 10 cm, diameter 4.0 mm) equipped with UV–VIS-detectors. Chiral phase GC was carried out using a SupelCo cyclodextrin-α column (α-Dex, 30 m, i. d. 0.25 mm), equipped with a FID (Flame Ionization Detector) at 250 °C.

Synthesis of (*1R,4R,5R*)-Isothiocineole [(1*R*,4*R*,5*R*)-4,7,7-trimethyl-6-thiabicyclo[3.2.1]-octane], (*R*)-1.[1]



(*R*)-Limonene (10 ml, 0.062 mol, 99:1 e.r.) were placed in a round bottom flask equipped with a reflux condenser. Elemental sulfur (2.32 g, 0.07 mol) and γ-terpinene (9.6 ml, 0.06 mol) or 1,4-cyclohexadiene (5.8 ml, 0.06 mol) were added. The reaction mixture was heated to 110 °C (internal temperature) overnight (the oil bath was set to a higher temperature – 130 °C on this scale). After that, the reaction mixture was allowed to cool down and a distillation apparatus with a Vigreux column was connected. After separation of various volatiles, isothiocineole (3.75 g, 36% yield, 99:1 e.r.) was distilled at 85–90 °C/5 mm Hg.

Description of the distillation procedure:

The oil bath was heated up to approximately 70 °C to make sure all the volatiles were removed (not only limonene but also cymene, and other very smelly by-products, all of which were colorless). Then, the oil bath temperature was increased up to approximately 110 °C, and a yellow material started condensing in the Vigreux column. Isothiocineole was distilled at 85–90 °C/5 mmHg. A first fraction of this distillate was collected until the temperature of the distillate had stabilized. Then the main fraction was collected (85–90 °C/5 mmHg). After that there was still isothiocineole remaining in the crude mixture but as it was very viscous, the temperature of the oil bath needed to be increased to 140 °C to complete the distillation. When a very sticky orange material was seen in the Vigreux column (presumably polysulfides) the distillation was stopped. The fractions were analyzed by GC for purity and combined if appropriate (see below

for GC conditions; see page 83-84 for chromatograms of the reaction carried out in the absence and the presence of γ-terpinene).

Yellow oil; b.p. 85–90 °C/5 mm Hg [Lit.[1] 79 °C (5 mm Hg)]; ^{1}H-NMR (270 MHz, $CDCl_3$): 1.05 (d, 3H, J = 7.3 Hz, axial CH_3), 1.14 (dd, 1H, J = 13.9 Hz, 5.3 Hz), 1.37 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.57–1.60 (m, 2H), 1.80–1.81 (m, 1H), 1.86–1.90 (m, 1H), 2.04–2.07 (m, 2H), 2.23–2.38 (m, 1H), 3.29–3.31 (m, 1H, CHS); ^{13}C-NMR (67.5 MHz, $CDCl_3$): 18.8 (CH_3), 23.9 (CH_2), 24.4 (CH_2), 25.5 (CH_3), 34.5 (CH_2), 35.0 (CH_3), 35.5 (CH), 47.4 (CH), 52.7 (C), 53.1 (CH); IR (cm^{-1}, film): 2950, 2923, 1454, 1383, 1360, 1136, 1043; HRMS (CI) $C_{10}H_{18}SH^+$ ($M+H^+$) requires: 171.1207; found: 171.1204; $[\alpha]_D^{20}$ –57.4 (c = 1.32, $CHCl_3$) [lit.[1] $[\alpha]_D^{25}$ –69.1° (neat)]; Chiral-phase GC conditions: α-Dex column, oven temperature: 110 °C; R_t 20.85 min (*R*), 21.39 min (*S*); Injection/detector temperatures: 250 °C; GC conditions, supelco-SLB5MS, 15 m × 0.25 mm i.d., Injection 250 °C; detector temperature 280 °C; oven temperature: 70 °C (3 min), increase by 25 °C/min to 200 °C, followed by temperature ramp to 300 °C, R_t isothiocineole (**1**) 5.8 min, (1*R*,5*R*)-4,7,7-trimethyl-6-thiabicyclo[3.2.1]oct-3-ene (**3**) 5.5 min.

3

(1*S*,4*S*,5*S*)-Isothiocineole, (*S*)-1

Starting from (*S*)-limonene (approx. 90:10 e.r.) using the procedure described above the sulfide (**(*S*)-1**) obtained had an e.r. of 90:10. To increase the enantiopurity up to 99:1, pentane (slightly less than the volume of distillate) was added and the mixture was placed in a bath and then cooled to –50 °C and held at that temperature for several hours. Crystallization has to be slow to give an enrichment of the enantiopurity. Filtration of the crystals was carried out at low temperature (–50 °C) and the crystals were washed with cold pentane (–50 °C). We carried out the filtration using a cannula with filter paper secured around one end with Teflon tape. One to two recrystallizations were required to obtain an e.r. of 99:1. Yields of **(*S*)-1** (e.r. = 99:1) were in the region of 10%.

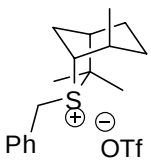
Chiral phase GC conditions for limonene: α-Dex column; oven temperature: 50 °C; injector/detector temperatures: 250 °C; R_t: 40 min (*S*), 41 min (*R*);

General Procedures for the synthesis of Sulfonium Salts A-D

General Procedure 1: from alkyl halides

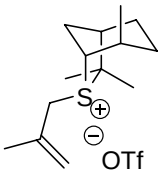
Sulfide (1 eq.) was dissolved in dichloromethane (1 ml for each 2.4 mmol of sulfide) and then the appropriate bromide (2 eq) and a solution of lithium triflate (5 eq.) in water (1 ml for each 5 mmol of LiOTf) were added. The resulting biphasic mixture was stirred at r.t. for 1 day. Water (same amount as starting volume) and dichloromethane (same amount as starting volume) were added and the layers were separated. The aqueous organic layer was extracted with dichloromethane (3 × half the amount of starting volume). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was dissolved in the minimum amount of dichloromethane and added drop-wise to rapidly stirred diethyl ether (at least 10 times the volume of dichloromethane used to dissolve the crude). The precipitate was filtered and washed several times with diethyl ether (same amount as used to precipitate the salt).

(*1R,4R,5R,6R*)-6-Benzyl-4,7,7-trimethyl-6-thioniabicyclo[3.2.1]octane trifluoromethanesulfonate (A)



Using general procedure 1, sulfide **1** (1.00 g, 5.9 mmol), yielded sulfonium salt **A** as a white solid (1.57 g, 65% yield); m.p. 142–145 °C (Et_2O/CH_2Cl_2); ^{1}H-NMR (400 MHz, $CDCl_3$): 1.05 (d, 3H, J = 7.3 Hz, axial CH_3), 1.40–1.80 (m, 4H, 2 × CH_2), 1.73 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.02-2.08 (m, 1H, C*H*Me), 2.34 (m, 2H, C*H*CS and C*H*H of 5-membered ring), 2.71–2.76 (m, 1 H, CH*H* of 5-membered ring), 3.79–3.81 (m, 1H, CHS), 4.52 (d, 1H, J = 12.5 Hz, SC*H*H), 4.88 (d, 1H, J = 12.5 Hz, SCH*H*), 7.33–7.36 (m, 3H, ArH), 7.57–7.62 (m, 2H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 17.8 (CH_3), 22.2 (CH_2), 23.2 (CH_3), 25.2 (CH_2), 25.5 (CH_3), 31.7 (CH_2), 32.1 (CH), 42.2 (CH_2), 50.5 (CH), 63.9 (CH), 72.5 (C), 120.9 (q, J = 321, CF_3), 129.1 (C), 129.7 (CH), 129.8 (CH), 130.6 (CH); IR (cm^{-1}, film): 3017, 2875, 1456, 1262, 1216, 1158, 1030, 756; HRMS (ESI^+) $C_{17}H_{25}S^+$ ($M–CF_3SO_3^-$) requires: 261.1671; found: 261.1664; $[\alpha]_D^{20}$ –142 (c = 1.01, $CHCl_3$);

(*1R,4R,5R,6R*)-4,7,7-Trimethyl-6-(2-methylallyl)-6-thioniabicyclo[3.2.1]octane trifluoromethanesulfonate (B)

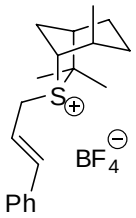


Using general procedure 1, sulfide **1** (0.500 g, 2.9 mmol) yielded sulfonium salt **B** as a white solid (450 mg, 41% yield); m.p. 97–98 °C (Et_2O/CH_2Cl_2); ^{1}H-NMR (270 MHz, $CDCl_3$): 1.18 (d, 3H, J = 6.9 Hz, axial CH_3), 1.57–1.75 (m, 4H, 2 × CH_2), 1.71 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 1.93 (s, 3H, C*H*$_3$C=CH_2), 2.26–2.39 (m, 3H), 2.58–2.64 (m, 1H), 3.90-3.92 (m, 1H, CHS), 4.03 (d, 1H, J = 12.9 Hz, SC*H*H), 4.32 (d, 1H, J = 12.9 Hz, SCH*H*), 5.20 (s, 1H, CH_2C(Me)=C*H*$_2$), 5.35 (s, 1H, CH_2C(Me)=C*H*$_2$); ^{13}C-NMR (67.5 MHz, $CDCl_3$): 17.8 (CH_3), 21.4 (CH_3), 22.3 (CH_2), 23.4 (CH_3), 25.2 (CH_3), 25.5 (CH_2), 31.9 (CH_2), 32.2 (CH), 45.2 (CH_2), 50.5 (CH), 64.6 (CH), 72.2 (C), 121.6 (C), 135.1 (CH_2); IR (cm^{-1}, film): 3018, 2942, 1463, 1265, 1216, 1161, 1031, 756; HRMS (ESI$^+$) $C_{14}H_{25}S^+$ (M–$CF_3SO_3^-$) requires: 225.1671; found: 225.1665; $[\alpha]_D^{20}$ – 86.0 (c = 1.07, $CHCl_3$);

General Procedure 2: from alcohols

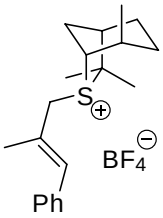
Sulfide (1 eq.) was dissolved in anhydrous diethyl ether (1 ml for each 0.58 mmol of sulfide), then the appropriate alcohol (3 eq.) was added. The mixture was placed in an ice-water bath and $HBF_4.Et_2O$ (3 eq., 54% wt) was added slowly. When the addition was finished the ice bath was removed and the resulting mixture was stirred at r.t. for 1 day. Water was added (same amount as starting volume of diethyl ether) and the layers were separated. The aqueous organic layer was extracted with diethyl ether (3 × half the amount of starting volume). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was dissolved in the minimum amount of dichloromethane and added drop wise to rapidly stirred diethyl ether (at least 10 times the volume used to dissolve the sulfonium salt). The precipitate was filtered and washed several times with diethyl ether (approximately with the same volume as used to precipitate sulfonium salt).

(*1R,4R,5R,6R*)-6-Cinnamyl-4,7,7-trimethyl-6-thioniabicyclo[3.2.1]octane tetrafluoroborate (C)



Using general procedure 2 sulfide **1** (1.00 g, 5.9 mmol) yielded sulfonium salt **C** as a pinkish solid (662 mg, 30% yield); m.p. 124–126 °C (Et_2O/CH_2Cl_2); ^{1}H-NMR (400 MHz, $CDCl_3$): 1.13 (d, 3H, J = 7.1 Hz, axial CH_3), 1.44–1.60 (m, 2H, CH_2), 1.69 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 1.64–1.78 (m, 2H), 2.21–2.27 (m, 1H, C*H*Me), 2.35–2.49 (m, 2H), 2.55–2.64 (m, 1 H), 3.94–3.96 (m, 1H, CHS), 4.08 (dd, 1H, J = 12.0 Hz, J = 9.0 Hz, CH*H*Ph), 4.34 (d, 1H, J = 12.0 Hz, J = 6.6 Hz, C*H*HPh), 6.24 (ddd, 1 H, J = 15.8 Hz, J = 9.0 Hz, J = 6.6 Hz, CH_2C*H*=), 7.05 (d, 1 H, J = 15.8 Hz, CH=C*H*Ph), 7.28–7.31 (m, 3H, ArH), 7.41–7.43 (m, 2H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 17.8 (axial CH_3), 22.3 (CH_2), 23.2 (CH_3), 25.3 (CH_2 and CH_3), 31.9 (CH_2), 32.1 (CHMe), 41.4 (*C*H_2CH=CHPh), 50.3 (*C*HCMe$_2$), 63.9 (CHS), 71.9 (C), 115.8 (*C*H=CHPh), 127.3 (CH), 128.8 (CH), 129.21 (CH), 135.2 (C), 141.3 (CH=*C*HPh); IR (cm^{-1}, film): 3020, 1216, 1031, 1067, 757; HRMS (ESI$^+$) for $C_{19}H_{27}S^+$ (M–BF_4^-) requires: 287.1828; found: 287.1820; $[\alpha]_D^{20}$ –165 (c = 0.66, $CHCl_3$);

(*1R,4R,5R,6R*)-4,7,7-Trimethyl-6-((*E*)-2-methyl-3-phenylallyl)-6-thioniabicyclo[3.2.1]octane tetrafluoroborate (D)



Using general procedure 2, sulfide **1** (1.00 g, 5.9 mmol) yielded sulfonium salt **D** as a white solid (1.13 g, 49% yield); m.p. 150–152 °C (Et_2O/CH_2Cl_2); ^{1}H-NMR (400 MHz, $CDCl_3$): 1.15 (d, 3H, J = 7.1 Hz, axial CH_3), 1.58–1.60 (m, 1H, CH*H*), 1.74 (s, 3H, CH_3), 1.71–1.77 (m, 3H), 1.82 (s, 3H, CH_3), 2.07 (s, 3H, C*H*$_3$C=), 2.20–2.28 (m, 1H), 2.37–2.41 (m, 2H), 2.65–2.68 (m, 1 H), 3.90–3.94 (m, 1H, CHS), 4.10 (d, 1H, J = 12.3 Hz, SCH*H*), 4.32 (d, 1H, J = 12.3 Hz, SC*H*H),

6.87 (s, 1 H, *H*C=), 7.23–7.33 (m, 5 H, Ar); ^{13}C-NMR (100 MHz, $CDCl_3$): 17.3 (*C*H_3C=), 17.8 (axial CH_3), 22.3 (CH_2), 23.3 (CH_3), 25.0 (CH_3), 25.5 (CH_2), 31.9 (CH_2), 32.3 (*C*HMe), 48.7 (SCH_2), 50.5 (*C*HCMe_2), 64.2 (CHS), 72.5 (C), 126.8 (Me*C*=CHPh), 127.9 (CH), 128.5 (CH), 129.3 (CH), 135.9 (C), 135.9 (CH_3C=*C*HPh); IR (cm^{-1}, film): 3020, 2941, 2975, 1469, 1216, 1071, 756; HRMS (ESI^+) for $C_{20}H_{29}S^+$ ($M–BF_4^-$) requires: 301.1984; found: 301.1977; $[\alpha]_D^{20}$ – 209 (c = 0.88, $CDCl_3$);

General Methods for Epoxidation Reactions

Commercially available aldehydes were distilled before use.

General Epoxidation Method A

Sulfonium salt (0.3–0.5 mmol, 1 eq.) was dissolved in a 9:1 mixture of acetonitrile and water (2 ml for every 0.37 mmol of sulfonium salt). Then the aldehyde (1.1 eq.) was added. The solution was then placed in a 0 °C bath and freshly ground KOH (1.1 eq.) was added. The solution was stirred at 0 °C overnight. Acetonitrile was then evaporated under reduced pressure and dichloromethane (5 ml) and water (5 ml) were added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 5 ml). The organic phases were then combined, dried with $MgSO_4$ and the solvent evaporated under reduced pressure. Products were purified by flash chromatography on silica gel (unless stated otherwise). For unstable vinyl epoxides the yield was determined by ^{1}H NMR after addition of an internal standard.

General Epoxidation Method B

Sulfonium salt (0.3–0.5 mmol, 1 eq.) was dissolved in a 15:1 mixture of acetonitrile and *tert*-butanol (2 ml for every 0.37 mmol of sulfonium salt). Then the aldehyde (2 eq.) was added. The solution was then placed in a 0 °C bath and freshly ground KOH (1.1 eq.) was added. The solution was stirred at 0 °C overnight. Acetonitrile and *tert*-butanol were then evaporated under reduced pressure and dichloromethane (5 ml) and water (5 ml) was added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 5 ml). The organic phases were then combined, dried with $MgSO_4$ and the solvent evaporated under reduced pressure. Products were purified by flash chromatography on silica gel (unless stated otherwise). For unstable vinyl epoxides the yield was determined by ^{1}H NMR after addition of an internal standard.

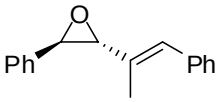
Characterization data for Epoxides

In each case the chiral-phase HPLC R_t given is for the major enantiomer obtained using salts derived from **(*R*)-1**.

2,3-Diphenyloxirane (Tab1e 1, entry 1)[2]

trans-2,3-Diphenyloxirane was isolated as a white solid; R_f 0.40 (5% EtOAc/PE); m.p. 65–66 °C (Et_2O) [lit.[3] 65–67 °C (petrol)]; ^{1}H-NMR (270 MHz, $CDCl_3$): 3.86 (s, 2H, 2 × CH), 7.33–7.38 (m, 2 × 5H, Ar*H*); HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1 ml/min, 8.5 min ((*S,S*), minor), 17.3 ((*R,R*), major);

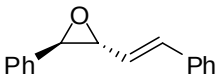
2-Phenyl-3-[(*E*)-1-methyl-2-phenyl-1-ethenyl] oxirane (Tab1e 1, entry 2)[4]



trans-2-Phenyl-3-[(*E*)-1-methyl-2-phenyl-1-ethenyl] oxirane was obtained as a colorless oil; A racemic sample was obtained by reaction of 2-methylcinnamaldehyde with 1-benzyltetrahydrothiophenium tetrafluoroborate.[5] Using sulfonium salt **A** or **D** and the appropriate aldehyde only the *trans*-isomer was formed. The yield was determined by ^{1}H NMR after addition of 1,3,5-trimethoxybenzene as an internal standard.

^{1}H-NMR (270 MHz, $CDCl_3$): 1.86 (d, J = 0.7 Hz, 1H, CH_3), 3.48 (dd, J = 2.0, 0.7 Hz, 1H, OCH), 3.89 (d, J = 2.0 Hz, 1H, OCHPh), 6.66 (s, 1H, CMe=C*H*Ph), 7.30–7.37 (m, 10H, ArH); HPLC conditions: OD column, 1% *i*PrOH/Hexane, 10 °C, 1 ml/min, R_t: 10.60 min (minor (*S,S*)), 17.64 min (major (*R,R*));

2-Phenyl-3-[(*E*)-2-phenyl-1-ethenyl] oxirane (Tab1e 1, entry 3)[2]



Using general epoxidation method A and 1-benzyltetrahydrothiophenium tetrafluoroborate[5] and cinnamaldehyde, racemic epoxide was obtained as a colorless oil (0.3:1 mixture of *cis*- and *trans*

isomers); R_f 0.42 (10% EtOAc/PE). Using sulfonium salt **A** and cinnamaldehyde only the *trans*-isomer was formed (method A). Using sulfonium salt C and benzaldehyde an 80:20 (*trans*:*cis*) mixture of epoxides was formed (method A). The yield was determined by ^{1}H NMR after addition of 1,3,5-trimethoxybenzene as an internal standard.

trans-2-Phenyl-3-[(*E*)-2-phenyl-1-ethenyl] oxirane was obtained as a colorless oil; R_f 0.42 (10% EtOAc/PE); ^{1}H-NMR (270 MHz, $CDCl_3$): 3.52 (dd, J = 7.7, 2.0 Hz, 1H, OCH), 3.89 (d, J = 2.0 Hz, 1H, OCHPh), 6.06 (dd, J = 15.9, 7.7 Hz, 1H, C*H*CHPh), 6.81 (d, J = 15.9 Hz, 1H, CHC*H*Ph), 7.15–7.50 (m, 10H, ArH);

cis-2-Phenyl-3-[(*E*)-2-phenyl-1-ethenyl] oxirane; R_f 0.42 (10% EtOAc/PE); ^{1}H-NMR (270 MHz, $CDCl_3$): 3.84 (ddd, J = 8.7, 4.2 Hz, 1H, OCH), 4.31 (d, J = 4.2 Hz, 1H, OCHPh), 5.72 (dd, J = 16.1, 8.7 Hz, 1H, C*H*CHPh), 6.84 (d, J = 16.1 Hz, 1H, CHC*H*Ph), 7.05–7.25 (m, 10H, ArH);

HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1 ml/min, <u>*trans*</u>: 12.89 min ((*S,S*), minor), 14.78 min ((*R,R*), major), <u>*cis*</u>: 8.22 min and 8.54 min;

2-Phenyl-3-[(*E*)-1-propenyl] oxirane (Tab1e 1, entry 4)[2]

Using general epoxidation method A and 1-benzyltetrahydrothiophenium tetrafluoroborate[5] and crotonaldehyde, racemic epoxide was obtained as a colorless oil (0.3:1 mixture of *cis*- and *trans* isomers); R_f 0.30 (5% EtOAc/PE + 1% Et_3N). Using sulfonium salt **A** and crotonaldehyde only the *trans*-isomer was formed (method A). The yield was determined by NMR after addition of 1,3,5-trimethoxybenzene as an internal standard.

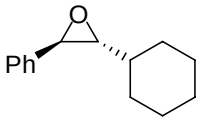
trans-2-Phenyl-3-[(*E*)-1-propenyl] oxirane was obtained as a colorless oil; R_f 0.30 (5% EtOAc/PE + 1% Et_3N); ^{1}H-NMR (400 MHz, $CDCl_3$): 1.80 (dd, J = 6.7, 1.7 Hz, 3H, CH_3), 3.34 (dd, J = 8.1, 2.1 Hz, 1H, PhCHC*H*), 3.78 (d, J = 2.1 Hz, 1H, PhC*H*CH), 5.38 (ddq, J = 15.5, 8.1, 1.7 Hz, 1H, C*H*CHCH$_3$), 6.01 (dq, J = 15.5, 6.7 Hz, 1H, CHC*H*CH$_3$), 7.29–7.39 (m, 5H, ArH);

cis-2-Phenyl-3-[(*E*)-2-phenyl-1-ethenyl] oxirane; R_f 0.30 (5% EtOAc/PE + 1% Et_3N); ^{1}H-NMR (400 MHz, $CDCl_3$): 1.67 (dd, J = 6.6, 1.6 Hz, 3H, CH_3), 3.67 (dd, J = 8.8, 4.3 Hz, 1H, PhCHC*H*), 4.24 (d, J = 4.3 Hz, 1H, PhC*H*CH), 5.05 (ddq, J = 15.2, 8.8, 1.6 Hz, 1H, C*H*=CHCH$_3$), 5.99–6.09

(m, 1H, CHC*H*CH_3), 7.29–7.39 (m, 5H, ArH);

HPLC conditions: OD column, 0.5% *i*PrOH/Hexane, 0.5 ml/min, R_t <u>*trans*</u>: 15.77 min ((*S,S*), minor), 31.15 min ((*R,R*), major), <u>*cis*</u>: 13.31 min and 21.1 min;

2-Cyclohexyl-3-phenyloxirane (Tab1e 1, entry 5)[6]



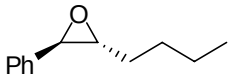
2-Cyclohexyl-3-phenyloxirane was obtained as a colorless oil; R_f 0.41 (5% EtOAc/PE); (mixture of *cis* and *trans* isomers).

trans-2-Cyclohexyl-3-phenyloxirane: ^{1}H-NMR (270 MHz, $CDCl_3$): 0.76–2.09 (m, 11H), 2.76 (dd, *J* = 6.8, 2.2 Hz, 1H, CH*c*Hx), 3.65 (d, *J* = 2.2 Hz, 1H, CHPh), 7.15–7.23 (m, 5H, ArH).

cis-2-Cyclohexyl-3-phenyloxirane: ^{1}H-NMR (270 MHz, $CDCl_3$): 0.76–2.09 (m, 11H), 2.90 (dd, *J* = 8.7, 4.3 Hz, 1H, CH*c*Hx), 4.05 (d, *J* = 4.3 Hz, 1H, CHPh), 7.15–7.23 (m, 5H, ArH).

HPLC conditions: OJ column, 0.5% *i*PrOH/Hexane, 1.5 ml/min, *cis*: 4.48 min, 4.66 min. *trans*: 11.6 min ((*S,S*), minor), 13.5 min ((*R,R*), major);

2-Butyl-3-phenyloxirane (Tab1e 1, entry 6) [4]

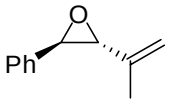


2-Butyl-3-phenyloxirane was obtained as a colorless oil as a mixture of *cis*- and *trans*-isomers; HPLC conditions: OD column, 0.5% *i*PrOH/Hexane, 1 ml/min, R_t <u>*trans*</u>: 34.86 min ((*S,S*), minor), 42.59 min ((*R,R*), major), <u>*cis*</u>: 18.04 min and 20.61 min;

<u>*trans*-Isomer</u>: R_f 0.57 (10% EtOAc/PE); ^{1}H-NMR (400 MHz, $CDCl_3$): 0.74–0.98 (3H, m (overlapping with *cis*), CH_3), 1.18–1.76 (6H, m (overlapping with *cis*), 3 × CH_2), 2.96 (1H, td, *J* = 5.5, 2.0 Hz, CH_2C*H*), 3.60 (1H, d, *J* = 2.0 Hz, PhC*H*), 7.23–7.39 (5H, m (overlapping with *cis*), Ar*H*);

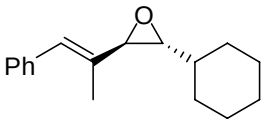
cis-isomer: R_f 0.53 (10% EtOAc/PE); ^{1}H-NMR (400 MHz, $CDCl_3$): 0.74–0.98 (3H, m (overlapping with *trans*), CH_3), 1.18–1.76 (6H, m (overlapping with *trans*), 3 × CH_2), 3.17–3.23 (m, CH_2CH), 4.07 (1H, d, J = 4.0 Hz, PhC*H*), 7.23–7.39 (5H, m (overlapping with *trans*), Ar*H*);

2-Phenyl-3-(prop-1-en-2-yl)oxirane (Tab1e 2, entry 3)[4]



trans-2-Phenyl-3-(prop-1-en-2-yl)oxirane was obtained as a colorless oil; A racemic sample was obtained by reaction of 2-methylpropenal with 1-benzyltetrahydrothiophenium tetrafluoroborate.[5] The epoxide was unstable to column chromatography. The yield was determined by NMR after addition of 1,3,5-trimethoxybenzene as an internal standard. ^{1}H-NMR (270 MHz, $CDCl_3$): 1.75 (3H, d, J = 1.5 Hz, CH_3), 3.37 (1H, d, J = 2.0 Hz, PhCHC*H*), 3.81 (1H, d, J = 2.0 Hz, PhCH), 5.04–5.08 (1H, m, C=CH*H*), 5.17–5.20 (1H, m, C=CH*H*), 7.27–7.41 (5H, m, Ar*H*); HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1 ml/min, R_t 4.75 min ((*S,S*), minor), 6.42 min ((*R,R*), major);

(2*R*,3*R*)-2-cyclohexyl-3-((*E*)-1-phenylprop-1-en-2-yl)oxirane (Tab1e 2, entry 4)



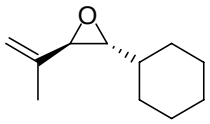
A racemic sample of 2-cyclohexyl-3-((*E*)-1-phenylprop-1-en-2-yl)oxirane was obtained as a mixture of *cis*- and *trans*-epoxides (1.5:1) by reaction of cyclohexylcarboxaldehyde with (*E*)-1-(2-methyl-3-phenylallyl)tetrahydro-1*H*-thiophenium tetrafluoroborate. Use of sulfonium salt **D** and method B gave enantioenriched *trans*-epoxide. The yield and dr were determined by NMR after addition of 1,3,5-trimethoxybenzene as an internal standard. Careful column chromatography (R_f 0.78, 5% EtOAc/PE, alumina) of a racemic sample gave a clean sample of a mixture of the *cis*- and *trans*-epoxides as an oil for characterization purposes.

HRMS (EI) for $C_{22}H_{21}NO_3S$ (M^+) requires: 242.1664; found: 242.1671; HPLC conditions: OD column, 1% IPA/Hexane, 1 ml/min, R_t *trans*: 6.98 min ((*R,R*), major), 9.29 min ((*S,S*), minor), *cis*: 4.80 min;

trans-Isomer: ^{1}H-NMR (400 MHz, $CDCl_3$): 1.10–1.41 (8H, m, *c*Hx), 1.66–1.79 (3H, m, *c*Hx), 1.80 (3H, s, CH_3), 2.78 (1H, dd, *J* = 6.9, 2.3 Hz, OC*H*cHx), 3.31 (1H, dd, *J* = 2.3, 0.5 Hz, OC*H*C=), 6.62 (1H, s, PhC*H*=C), 7.22–7.40 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.0 (CH_3), 25.5–30.6 (5 × CH_2), 40.5 (C*H* *c*Hx), 61.4 (OC*H*C=), 63.2 (OC*H*cHx), 125.8 (CH), 126.7 (CH), 128.3 (CH), 126.6 (Ph*C*H=C), 134.8 (PhCH=*C*), 137.4 (C);

cis-Isomer: ^{1}H-NMR (400 MHz, $CDCl_3$): 1.10–1.41 (8H, m, *c*Hx), 1.66–1.79 (3H, m, *c*Hx), 1.98 (3H, s, CH_3), 2.88 (1H, dd, *J* = 8.6, 4.4 Hz, OC*H*cHx), 3.53 (1H, ddd, *J* = 4.4, 1.2, 0.7 Hz, OC*H*C=), 6.50 (1H, s, PhC*H*C=C), 7.22–7.40 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 16.3 (CH_3), 25.5–30.6 (5 × CH_2), 35.2 (C*H* *c*Hx), 59.9 (OC*H*C=), 64.1 (OC*H*cHx), 125.8 (CH), 126.7 (CH), 129.1 (CH), 127.5 (Ph*C*H=C), 131.6 (PhCH=*C*), 137.4 (C);

2-Cyclohexyl-3-(prop-1-en-1-yl)oxirane (Tab1e 2, entry 5)



A racemic sample of 2-cyclohexyl-3-(prop-1-en-1-yl)oxirane was obtained as a mixture of *cis*- and *trans*-epoxides (1.1:1) by reaction of cyclohexylcarboxaldehyde with 1-(2-methylallyl)tetrahydro-1*H*-thiophenium tetrafluoroborate.[7,8] Use of sulfonium salt **B** and method B gave enantioenriched *trans*-epoxide. The yield and dr were determined by NMR after addition of 1,3,5-trimethoxybenzene as an internal standard. Careful column chromatography (R_f 0.66, 5% EtOAc/PE, alumina (neutral, grade1)) of a racemic sample gave a clean sample of a mixture of the *cis*- and *trans*-epoxides as a colorless oil for characterization purposes.
HRMS (EI) for $C_{11}H_{19}O$ ($M+1^+$) requires: 167.1442; found: 167.1436; Chiral GC conditions: α-Dex column, oven temperature: 70 °C for 100 min and then ramp with 25 °C/min until 200 °C, R_t *trans*: 103.21 ((*S,S*), minor), 103.34 ((*R,R*), major), *cis*: 93.78 and 95.00 min;

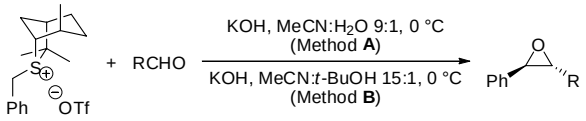
trans-Isomer: ^{1}H-NMR (400 MHz, $CDCl_3$): 1.04–1.23 (6H, m, *c*Hx), 1.41–1.46 (1H, m, *c*Hx), 1.60–1.76 (3H, m, *c*Hx), 1.60 (3H, dd, *J* = 1.5, 0.9 Hz, CH_3), 1.84–1.88 (1H, m, *c*Hx), 2.62 (1H, dd, *J* = 6.8, 2.2 Hz, OC*H*cHx), 3.13 (1H, d, *J* = 2.2 Hz, OCHC=), 4.91–4.92 (1H, m, CH*H*=C), 5.05 (1H, dq, *J* = 2.6, 0.9 Hz, C*H*H=C); ^{13}C-NMR: 17.1 (CH_3), 25.5–30.5 (5 × CH_2), 40.4 (C*H*

*c*Hx), 59.7 (OCHC=), 62.9 (OC*H*cHx), 113.3 (*C*H_2=C), 142.0 (CH_2=*C*).

<u>*cis*-Isomer</u>: ^{1}H-NMR (400 MHz, $CDCl_3$): 1.04–1.23 (6H, m, *c*Hx), 1.60–1.76 (4H, m, *c*Hx), 1.76 (3H, ddd, *J* = 1.5, 0.9 Hz x 2, CH_3), 1.84–1.88 (1H, m, *c*Hx), 2.73 (1H, dd, *J* = 8.3, 4.4 Hz, OC*Hc*Hx), 3.31 (1H, ddd, *J* = 4.4, 0.7, 0.7 Hz, OC*H*C=), 4.88–4.90 (1H, m, C*H*H=C), 4.92–4.95 (1H, m, CH*H*=C); ^{13}C-NMR: 20.2 (CH_3), 25.5–30.5 (5 × CH_2), 34.9 (*C*H *c*Hx), 58.6 (O*C*HC=), 63.3 (O*C*H*c*Hx), 111.7 (*C*H_2=C), 138.8 (CH_2=*C*).

Comparison between sulfide 1 and sulfide 2 in epoxidation reactions

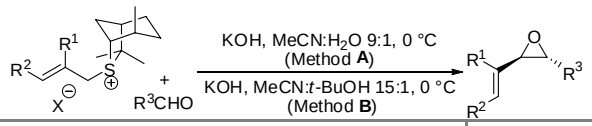
Table 1. Comparison of results in this paper with previous results with sulfide **2**. Reactions of benzyl sulfonium salt with aldehydes.



Entry	Aldehyde	Sulfide **1**				Catalytic with Sulfide **2** [d]			Stoichiometric with Sulfide **2** [e]		
		Method	Yield (%)	*d.r.* [a]	*e.r.* [b]	Yield (%)	*d.r.* [a]	*e.r.*	Yield (%)	*d.r.* [a]	*e.r.*
1	Benzaldehyde	A	77	>95:5	99:1	87	98:2	97:3	75	98:2	99:1
2	(*E*)-PhCH=C(Me)CHO	A	84[c]	>95:5	98:2						
3	(*E*)-Cinnamaldehyde	A	88[c]	>95:5	99:1	70[c]	>98:2	93.5:6.5			
4	(*E*)-Crotonaldehyde	A	86[c]	>95:5	97:3				72	98:2	95:5
5	*c*-C_6H_{11}CHO	B	62	93:7	99:1	58	88:12	95:5			
6	*n*-C_4H_9CHO	B	56	91:9	99:1	46	75:25	94.5:5.5	58	60:40	95:5

[a] *trans*:*cis*. [b] Determined by chiral HPLC. [c] Determined by ^{1}H NMR with an internal standard; [d] Obtained using sulfide **2** as a catalyst (5-20 mol%); see Aggarwal, V. K.; Alonso, E.; Bae, I.; Hynd, G.; Lydon, K. M.; Palmer, M. J.; Patel, M.; Porcelloni, M.; Richardson, J.; Stenson, R. A.; Studley, J. R.; Vasse, J.-L.; Winn, C. L. *J. Am. Chem. Soc.* **2003**, *125*, 10926 and Aggarwal, V. K.; Aragoncillo, C.; Winn, C. L. *Synthesis* **2005**, 1378 for details. [e] Obtained using the benzyl sulfonium salt derived from sulfide **2** with method **A**, see Aggarwal, V. K.; Bae, I.; Lee, H.-Y.; Richardson, J.; Williams, D. T. *Angew. Chem. Int. Ed.* **2003**, *42*, 3274.

Table 2. Comparison of results in this paper with previous results with sulfide **2**. Reactions of allylic sulfonium salts with aldehydes.



R^1	R^2	R^3	Sulfide **1**				Sulfide **2** [g]		
			Method	Yield (%) [a]	*d.r.* [b]	*e.r.*	Yield (%) [a]	*d.r.* [b]	*e.r.*
H[c]	Ph	Ph	A	65	80:20	85:15[d]			
Me[c]	Ph	Ph	A	97	>95:5	99:1[d]	96	96:4	95:5
Me[e]	H	Ph	A	80	>95:5	99:1[d]	37	97:3	98.5:1.5
Me[c]	Ph	*c*-C_6H_{11}	B	77	>95:5	98:2[d]			
Me[e]	H	*c*-C_6H_{11}	B	77	>95:5	97:3[f]			

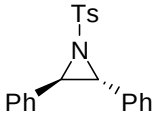
[a] Determined by ^{1}H NMR with an internal standard. [b] *trans*:*cis*. [c] X = BF_4. [d] Determined by chiral HPLC. [e] X = OTf. [f] Determined by chiral GC. [g] Obtained using allylic sulfonium salt derived from sulfide **2** using method **A**, see Aggarwal, V. K.; Bae, I.; Lee, H.-Y.; Richardson, J.; Williams, D. T. *Angew. Chem. Int. Ed.* **2003**, *42*, 3274.

General Procedure for Aziridination Reactions

In a typical experimental procedure sulfonium salt (0.3–0.5 mmol, 1 eq.) was dissolved in acetonitrile (2 ml for every 0.244 mmol of sulfonium salt). Then the imine (1.0 eq.) was added. The solution was then placed in a 0 °C bath and K_2CO_3 (2.0 eq.) was added. The solution was stirred at room temperature overnight. Acetonitrile was then evaporated under reduced pressure and 5 ml of dichloromethane were added. This solution was washed with a saturated solution of $NaHSO_3$ (5 ml), aq. NaOH (5 ml, 1M) and finally brine (5 ml). The organic layer was dried with $MgSO_4$ and the solvent evaporated under reduced pressure. The dr was determined by ^{1}H NMR at this point. The products were isolated by stirring rapidly in hexanes followed by filtration. If further purification was needed flash chromatography was carried out using silica gel (unless otherwise stated).

Characterization data for Aziridines

(*2R, 3R*)-2,3-Diphenyl-1-Tosylaziridine (Tab1e 3, entry 1)[9,10]

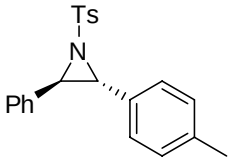


A mixture of *cis*- and *trans*-2,3-diphenyl-1-tosylaziridine was isolated as a white solid (*trans*:*cis* 5.8:1); IR (cm^{-1}, solution of $CHCl_3$): 3031, 3013, 1599, 1498, 1452, 1327; HRMS (EI) for $C_{21}H_{19}NO_2S$ (M^+) requires: 349.1137; found: 349.1126; The mixture had $[\alpha]_D^{20}$ +4.3 (*c* = 0.94, $CHCl_3$); HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t <u>*trans*</u>: 28.53 min ((*S,S*), minor), 33.20 min ((*R,R*), major).

<u>*trans*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.38 (s, 3H, CH_3), 4.26 (2H, s, 2 × CHN), 7.20 (2H, d, *J* = 7.9 Hz, ArH), 7.33–7.43 (10H, m, ArH), 7.63 (2H, d, *J* = 8.3 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 21.7 (CH_3), 50.5 (2 × CHN), 127.7 (CH), 128.4 (CH), 128.6 (CH), 128.8 (CH), 129.5 (CH), 133.2 (C), 137.2 (C), 144.1 (C);

<u>*cis*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.44 (s, 3H, CH_3), 4.21 (2H, s, 2 × C*H*N), 7.00–7.12 (10H, m, ArH), 7.33–7.43 (2H, m, ArH), 7.96 (2H, d, *J* = 8.3 Hz, ArH);

(*2R,3R*)-2-Phenyl-3-*p*-tolyl-1-tosylaziridine (Tab1e 3, entry 2)[11,12]

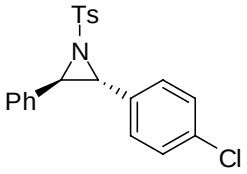


A mixture of *cis*- and *trans*-2-phenyl-3-*p*-tolyl-1-tosylaziridine was isolated as a white solid (*trans*:*cis* 6:1); IR (cm^{-1}, solution of $CHCl_3$): 3027, 3010, 1600, 1327, 1161; HRMS (EI) for $C_{22}H_{21}NO_2S$ (M^+) requires: 363.1293; found: 363.1278; The mixture had $[\alpha]_D^{20}$ +7.7 (*c* = 0.90, $CHCl_3$);

<u>*trans*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.34 (3H, s, CH_3), 2.37 (3H, s, CH_3), 4.18 (1H, d, *J* = 4.6 Hz, C*H*N), 4.28 (1H, d, *J* = 4.6 Hz, C*H*N), 7.13–7.20 (4H, m, ArH), 7.30–7.41 (7H, m, ArH), 7.63 (2H, d, *J* = 8.3 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 21.4 (CH_3), 21.7 (CH_3), 50.0 (CHN), 50.1 (CHN), 127.6 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 129.3 (CH), 129.5 (CH), 133.6 (C), 137.4 (C), 138.8 (C), 144.0 (C); HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t <u>*trans*</u>: 25.22 min ((*S,S*), minor), 27.44 min ((*R,R*), major);

<u>*cis*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.19 (3H, s, CH_3), 2.43 (3H, s, CH_3), 4.18–4.19 (2H, m, 2 × CHN), 7.00–7.41 (11H, m, ArH), 7.94 (2H, d, *J* = 8.3 Hz, ArH);

(*2R,3R*)-2-(4-Chlorophenyl)-3-phenyl-1-tosylaziridine (Tab1e 3, entry 3)[11,12]



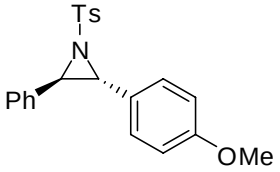
A mixture of *cis*- and *trans*-2-(4-chlorophenyl)-3-phenyl-1-tosylaziridine was isolated as a white solid (*trans*:*cis* 3.0:1); IR (cm^{-1}, solution of $CHCl_3$): 3026, 1600, 1495, 1363, 1329, 1161; HRMS (EI) for $C_{21}H_{18}ClNO_2S$ (M^+) requires: 383.0747; found: 383.0739; The mixture had $[\alpha]_D^{20}$ +8.7 (*c* = 0.46, $CHCl_3$);

<u>*trans*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.38 (3H, s, CH_3), 4.18 (1H, d, *J* = 4.6 Hz, CHN), 4.22 (1H, d, *J* = 4.6 Hz, CHN), 7.21 (2H, d, *J* = 8.3 Hz, ArH), 7.32–7.40 (9H, m, ArH), 7.62 (2H, d, *J* = 8.3 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 21.7 (CH_3), 21.7 (CH_3), 49.9 (CHN), 50.5 (CHN), 127.6 (CH), 128.3 (CH), 128.7 (CH), 128.8 (CH), 129.6 (CH), 129.8 (CH), 131.7 (C),

132.9 (C), 134.8 (C), 137.0 (C), 144.3 (C); HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t <u>*trans*</u>: 26.13 min ((*S,S*), minor), 31.75 min ((*R,R*), major).

<u>*cis*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.44 (3H, s, CH_3), 4.16 (1H, d, J = 7.3 Hz, CHN), 4.20 (1H, d, J = 7.3 Hz, CHN), 6.94–7.14 (9H, m, ArH), 7.32–7.40 (2H, m, ArH), 7.92 (2H, d, J = 8.3 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 21.8 (CH_3), 46.8 (CHN), 47.7 (CHN), 127.8 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 128.9 (CH), 129.2 (CH), 130.0 (CH), 130.8 (C), 131.8 (C), 133.8 (C), 145.1 (C);

(*2R,3R*)-2-(4-Methoxyphenyl)-3-phenyl-1-tosylaziridine (Tab1e 3, entry 4)[11-14]

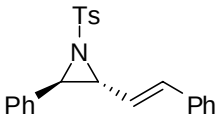


A mixture of *cis*- and *trans*-2-(4-methoxyphenyl)-3-phenyl-1-tosylaziridine was isolated as a white solid (*trans*:*cis* 4.8:1); IR (cm^{-1}, solution of $CHCl_3$): 3023, 1600, 1516, 1418, 1363; HRMS (EI) for $C_{22}H_{21}NO_3S$ (M^+) requires: 379.1242; found: 379.1237; The mixture had $[\alpha]_D^{20}$ +19.5 (*c* = 0.41, $CHCl_3$);

<u>*trans*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.40 (3H, s, CH_3), 3.83 (3H, s, OCH_3), 4.15 (1H, d, J = 4.8 Hz, CHN), 4.33 (1H, d, J = 4.8 Hz, CHN), 6.89 (2H, d, J = 8.9 Hz, ArH), 7.20 (2H, d, J = 7.9 Hz, ArH), 7.30–7.42 (7H, m, ArH), 7.64 (2H, d, J = 8.6 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): 21.7 (CH_3), 49.5 (CHN), 51.4 (CHN), 55.4 (OCH_3), 114.0 (CH), 127.6 (CH), 127.6 (CH), 128.0 (CH), 128.6 (CH), 129.5 (CH), 130.1 (CH), 124.5 (C), 133.8 (C), 137.4 (C), 144.0 (C); HPLC conditions: Chiral AGP column, 1% *i*PrOH:10 mM phosphate buffer pH=7, 0.75 ml/min, R_t <u>*trans*</u>: 4.07 min ((*R,R*), major), 20.24 min ((*S,S*), minor);

<u>*cis*-Isomer</u>: ^{1}H-NMR (270 MHz, $CDCl_3$): 2.45 (3H, s, CH_3), 3.70 (3H, s, OCH_3), 4.17 (1H, d, J = 7.3 Hz, CHN), 4.20 (1H, d, J = 7.3 Hz, CHN), 6.66 (2H, d, J = 8.9 Hz, ArH), 7.14 (2H, d, J = 7.9 Hz, ArH), 7.30–7.42 (7H, m, ArH), 7.96 (2H, d, J = 8.3 Hz, ArH);

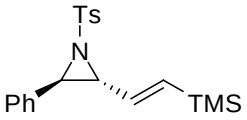
(*2R,3R*)-2-Phenyl-3-[(*E*)-2-phenyl-1-ethenyl]-1-tosylaziridine (Tab1e 3, entry 5) [11,15]



trans-2-Phenyl-3-[(*E*)-2-phenyl-1-ethenyl]-1-tosylaziridine was isolated as a white solid; m.p. 124–126 °C (PE); ^{1}H-NMR (270 MHz, $CDCl_3$): 2.38 (3H, s, CH_3), 3.43 (1H, dd, *J* = 9.2, 4.2 Hz, NC*H*CH=), 4.15 (1H, d, *J* = 4.2 Hz, NCHPh), 6.65 (1H, dd, *J* = 15.8, 9.2 Hz, C*H*=CHPh), 6.79 (1H, d, *J* = 15.8 Hz, CH=C*H*Ph), 7.19–7.45 (12H, m, Ar*H*), 7.82 (2H, d, *J* = 8.6 Hz, Ar*H*); ^{13}C-NMR (100 MHz, $CDCl_3$): 21.7 (CH_3), 48.8 (NCHPh), 55.4 (N*C*HCH=), 122.3 (CH=*C*HPh), 126.4 (CH), 126.9 (CH), 127.7 (CH), 128.4 (CH), 128.5 (CH), 128.7_5 (CH), 128.8_0 (CH), 129.7 (CH), 125.2 (C), 136.1 (C), 137.0 (C), 137.6 (*C*H=CHPh), 144.4 (C); IR (cm^{-1}, solution of $CHCl_3$): 3029, 3010, 1711, 1600, 1497, 1328; HRMS (EI) for $C_{23}H_{21}NO_2S$ (M^+) requires: 375.1293; found: 375.1278; $[\alpha]_D^{20}$ +8.9 (*c* = 0.90, $CHCl_3$); HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t: 29.56 min ((*S,S*), minor), 52.77 min ((*R,R*), major);

The aziridination was also carried out starting from 14 mmol of sulfonium salt using the general procedure described above to give the desired aziridine in 77% yield after precipitation. The sulfide was recovered from the filtrate in 70% yield by simple distillation.

(*2R,3R*)-2-Phenyl)-1-tosyl-3-((*E*)-2-trimethylsilyl)vinyl)aziridine (Tab1e 3, entry 6)[15]



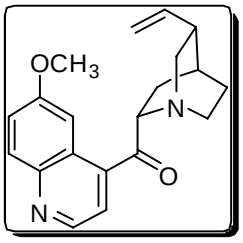
trans-2-Phenyl)-1-tosyl-3-((*E*)-2-trimethylsilyl)vinyl)aziridine was isolated as a white solid; m.p. 115–116 °C (PE); ^{1}H-NMR (270 MHz, $CDCl_3$): 0.11 (9H, s, $Si(CH_3)_3$), 2.39 (3H, s, CH_3), 3.26 (1H, dd, *J* = 9.2, 4.2 Hz, NC*H*CH=), 4.07 (1H, d, *J* = 4.2 Hz, NCHPh), 6.19 (1H, d, *J* = 18.3 Hz, CH=C*H*TMS), 6.41 (1H, dd, *J* = 18.3, 9.2 Hz, C*H*=CHTMS), 7.16–7.27 (7H, m, ArH), 7.81 (2H, d, *J* = 8.6 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): –1.4 ($Si(CH_3)_3$), 21.7 (CH_3Ar), 48.5 (NCHPh), 57.0 (N*C*HCH=), 126.5 (CH), 127.7 (CH), 128.3 (CH), 128.7 (CH), 129.7 (CH), 135.2 (C), 137.1 (C), 137.8 (*C*H=CHTMS), 140.6 (CH=*C*HTMS), 144.3 (C); IR (cm^{-1}, solution of $CHCl_3$): 3031, 2958, 1600, 1497, 1456, 1404, 1322, 1254; HRMS (EI) for $C_{20}H_{26}NO_2SiS$ (M^+)

requires: 372.1454; found: 372.1460; $[\alpha]_D^{20}$ +6.0 (*c* = 0.67, $CHCl_3$); HPLC conditions: OJ column, 1% *i*PrOH/Hexane, 1.5 ml/min, R_t: 8.27 ((*S,S*), minor), 12.13 min ((*R,R*), major);

The aziridination was also carried out starting from 12 mmol of sulfonium salt using the general procedure described above. Following precipitation and chromatography (silica, petrol/EtOAc 95:5) to remove traces of unreacted imine, the desired aziridine was obtained in 69% yield. The sulfide was recovered from the filtrate in 95% yield by chromatography (Petrol/EtOAc 5:1).

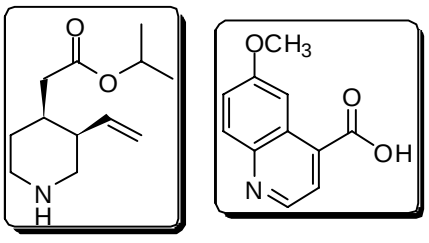
Characterization data for precursors to Quinine and Quinidine 6-15

Preparation of 6-methoxyquinoline-4-yl)((2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)- methanone [16]



Anhydrous (–)-quinine (25.0 g, 77.2 mmol) was taken in a three neck 2 litre round bottom flask and anhydrous toluene (500 ml) was added, and the mixture was stirred for 5 minute under a nitrogen atmosphere. Benzophenone (28.0 g, 154 mmol) and potassium *tert*-butoxide (21.7 g, 194 mmol) were added. The reaction mixture was refluxed for 16 h under a nitrogen atmosphere. The resulting orange viscous material was cooled to 0 °C and 3 M HCl (200 ml) was added slowly with stirring at such a rate that the temperature was maintained below 30 °C. The yellow aq. layer was separated and the orange toluene layer was extracted with additional 3 M HCl (3 × 150 ml). The combined aq. extracts were cooled to 0 °C and basified by the dropwise addition of conc. ammonia solution (50 ml). The aqueous phase was saturated with solid NaCl and extracted with CH_2Cl_2 (5 × 200 ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by silica column chromatography (Et_2O/acetone 4:1→3:2) to afford quininone (24.0 g, 96%) as a pale yellow solid; R_f(CH_2Cl_2/MeOH/NH_3 9:1:0.1) 0.49; δ_H (400 MHz; $CDCl_3$) 8.82 (1 H, d, *J* 4.5, ArH), 8.01 (1 H, d, *J* 9.0, ArH), 7.63–7.62 (2 H, m, ArH), 7.38 (1 H, dd, *J* 9.0, 3.0, ArH), 5.95 (1 H, ddd, *J* 17.2, 10.3, 7.4, =CH), 5.05 (1 H, ddd, *J* 10.3, 1.6, 1.2, =CH*H*), 5.03 (1 H, ddd, *J* 17.2, 1.6, 1.3, =C*H*H), 4.17 (1 H, t, *J* 9.0, COCHN), 3.91 (3 H, s, OCH_3), 3.09 (1 H, m), 2.92–2.84 (2 H, m), 2.60 (1 H, ddd, *J* 14.0, 7.5, 2.5), 2.33 (1 H, m), 2.25 (1 H, ddd, *J* 13.5, 7.5, 1.0), 1.86 (1 H, m), 1.71–1.63 (2 H, m), 1.51 (1 H, m).

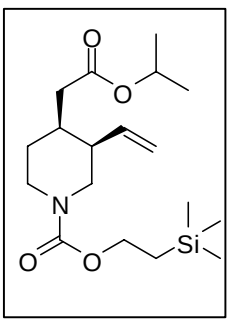
Preparation of isopropyl 2-((3*R*,4*S*)-3-vinylpiperidin-4-yl)acetate and 6-methoxy- quinoline-4-carboxylic acid (9) [16,17]



Isopropanol (7.5 ml) was added to a solution of potassium *tert*-butoxide (1.85 g, 16.5 mmol) in THF (15 ml) at 0 °C. The solution was saturated by bubbling oxygen through it for 1 h. A solution of quininone (2.12 g, 6.6 mmol) in THF (15 ml) was added at such a rate that maintains the reaction temperature below 20 °C. Oxygen bubbling was continued through the stirred reaction mixture at

0 °C to RT for 3 h. Conc. acetic acid (2 ml) was added slowly at 0 °C and resulting yellow slurry was stirred well and concentrated under vacuum. Water (10 ml) was added and the aqueous mixture was basified by slowly adding conc. ammonia solution (5 ml). The basic aq. phase was extracted with ether (5 × 20 ml). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude oily material was purified by short path vacuum distillation (fraction boiling at 110–115 °C / 5 mmHg) to get the pure meroquinene isopropyl ester (0.83 g, 60%) as colorless oil; bp 110–115 °C (5 mmHg); R_f(CH_2Cl_2/MeOH/NH_3 9:1:0.1) 0.24; δ_H (400 MHz, $CDCl_3$) 6.01 (1 H, ddd, *J* 17.0, 10.5, 9.0, C*H*=CH_2), 5.09–4.90 (3 H, m, CH=C*H*$_2$ and OC*H*Me_2), 3.00 (1 H, td, *J* 12.5, 4.0), 2.86 (2 H, dq, *J* 12.5, 3.5), 2.64 (1 H, ddd, *J* 12.5, 10.5, 3.5), 2.24 (1 H, dd, *J* 8.5, 3.5), 2.20–2.04 (4 H, m), 1.47–1.31 (2 H, m), 1.17 (6 H, d, *J* 6.5, OCH(*CH*$_3$)$_2$); δ_C (100 MHz, $CDCl_3$) 172.5 (-OC=O), 137.2 (CH), 116.8 (CH_2), 67.4 (CH), 51.4 (CH_2), 46.2 (CH_2), 43.1 (CH), 38.7 (CH_2), 35.8 (CH), 29.0 (CH_2), 21.9 (CH_3), 21.9 (CH_3).

The basic aq. layer was acidified by conc. acetic acid (2 ml, pH=5). Quininic acid was precipitated out as a pale yellow solid, which was separated by vacuum filtration, washed with cold water and dried in air for overnight and in an oven (80–90 °C) for 24 h to afford quininic acid **9** (1.21 g, 90%) as pale yellow needles (MeOH); mp decomposed >285 °C; R_f(CH_2Cl_2/MeOH, 7:3 + 5 drops of conc. AcOH) 0.39; δ_H (400 MHz, DMSO-d_6) 8.86 (1 H, d, *J* 4.5 ArH), 8.17 (1 H, d, *J* 3.0 ArH), 8.02 (1 H, d, *J* 9.0, ArH), 7.93 (1 H, d, *J* 4.5 ArH), 7.49 (1 H, dd, *J* 9.0, 3.0, ArH), 3.90 (3 H, s, OCH_3); δ_C (100 MHz, DMSO-d_6) 168.3 (CO_2H), 158.9 (4° C), 148.1 (CH), 145.4 (4° C), 134.7 (4° C), 131.7 (CH), 126.5 (4° C), 123.2 (CH), 122.6 (CH), 104.3 (CH), 56.0 (OCH_3).

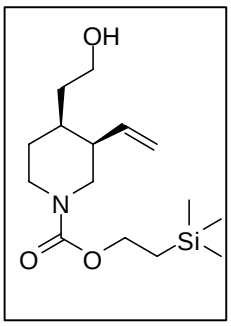


Preparation of (3*R*,4*S*)-2-(trimethylsilyl)ethyl-4-(2-isopropoxy-2-oxoethyl)-3-vinyl- piperidin-1-carboxylate (13)

Anhydrous K_2CO_3 (25.5 g, 185 mmol) was added to a stirred solution of 2-(trimethylsilyl)ethanol (7.94 ml, 55.5 mmol) in toluene (60 ml) at 0 °C under nitrogen atmosphere. The mixture was stirred at 0 °C for 20 minutes and

slowly added a solution of triphosgene (5.5 g, 18.5 mmol) in toluene (60 ml) and the resulting mixture was stirred at RT for 1 h. Reaction mixture was again cooled to – 10 °C and a solution of meroquinene isopropyl ester (3.90 g, 18.5 mmol) in toluene (30 ml) was added dropwise with stirring. After complete addition, the reaction mixture was stirred at RT for 16 h. Reaction was quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc (3 × 50 ml). The combined organic layers were washed again with sat. aq. $NaHCO_3$ and dried over $MgSO_4$, filtered and concentrated in vacuum to get the crude oily material, which was purified by flash silica gel column chromatography (acetone/pet. ether 1:9) to afford **13** (5.60 g, 85%) as a colorless viscous oil; R_f (acetone/pet. ether 1:9) 0.38; $[\alpha]_D^{24}$ = +10.0 (*c* 1.3, $CHCl_3$); IR (cm^{-1}, neat) 2953, 1728, 1695, 1435, 1283, 1235, 1169, 1104, 998, 919, 858; δ_H (300 MHz; $CDCl_3$) 5.76 (1 H, ddd, *J* = 17.0, 10.5, 9.0 Hz, C*H*=CH_2), 4.93–5.14 (3 H, m, CH=C*H*$_2$ and –C*H*$(CH_3)_2$), 4.11–4.17 (2 H, m, $NCO_2CH_2CH_2Si$), 3.90–4.02 (2 H, m, NCH_2CH_2), 3.06 (1 H, dd, *J* = 13.5, 3.0 Hz, NC*H*HCH), 2.90 (1 H, m, NCH*H*CH), 2.11–2.42 (4 H, m, CO_2CH_2, ring CH and C*H*-CH=CH_2), 1.37–1.52 (2 H, m, ring CH_2), 1.21 (6 H, d, *J* = 6.5 Hz, CH(CH_3)$_2$), 0.94–0.99 (2 H, m, $NCO_2CH_2CH_2Si$), 0.01 (9 H, s, Si(CH_3)$_3$); δ_C (100 MHz, $CDCl_3$) 172.3 (OC=O), 156.1 (N[O]C=O), 135.2 (CH), 117.8 (CH_2), 67.7 (CH), 63.6 (CH_2), 48.3 (CH_2), 43.6 (CH_2), 42.4 (CH), 38.2 (CH_2), 35.7 (CH), 27.9 (CH_2), 22.0 (CH_3), 21.9 (CH_3), 17.9 (CH_2), –1.3 (CH_3 × 3); HRMS(CI) calcd. for $C_{18}H_{34}NO_4Si$ $[M+1]^+$ 356.2257, found 356.2254.

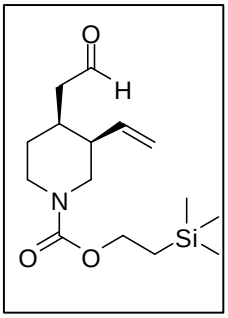
Preparation of (3*R*,4*S*)-2-(trimethylsilyl)ethyl-4-(2-hydroxyethyl)-3-vinylpiperidine-1-carboxylate (14) [18]



A 1.0 M solution of $LiAlH_4$ in THF (3.89 ml, 3.89 mmol) was added dropwise over 30 min. to a 0 °C cooled stirred solution of *N*-Teoc protected meroquinene isopropyl ester **13** (1.84 g, 5.18 mmol) in THF (100 ml) under argon atmosphere. After complete addition, the reaction mixture was stirred at 0 °C for 30 min. The reaction was quenched by the dropwise addition of 0.15 ml water, 0.15 ml 15% aq. NaOH and 0.45 ml water, which resulted in a solid granular mass. The mixture was filtered through a plug of Celite by suction followed by washing the residue with EtOAc. The combined filtrate and washing were washed with brine,

dried over $MgSO_4$, filtered and evaporated in vacuum to get the crude oily material, which was purified by flash silica gel column chromatography (acetone/pet. ether 1:4) to afford alcohol **14** (1.1 g, 71%) as a colorless viscous oil; R_f (acetone/pet. ether, 1:4) 0.24; $[\alpha]_D^{22}$ = +31.1 (*c* 1.2, $CHCl_3$); IR (cm^{-1}, neat) 3415, 2952, 1674, 1438, 1394, 1247, 1177, 1059, 858, 836, 752; δ_H (300 MHz; $CDCl_3$) 5.81 (1 H, m, C*H*=CH_2), 5.08–5.13 (2 H, m, CH=C*H*$_2$), 4.13–4.20 (2 H, m, $NCO_2CH_2CH_2Si$), 3.90–4.10 (2 H, m, NCH_2CH_2), 3.69 (2 H, t, *J* = 6.5 Hz, CH_2OH), 3.04 (1 H, dd, *J* = 13.0, 3.0 Hz, NC*H*HCH), 2.88 (1 H, m, NCH*H*CH), 2.32 (1 H, br. s., OH), 1.83 (1 H, m, CH), 1.35-1.70 (6 H, m, CH_2, ring CH_2, CH, CH), 0.96-1.02 (2 H, m, $NCO_2CH_2CH_2CH_2Si$), 0.03 (9 H, s, $Si(CH_3)_3$); δ_C (75 MHz, $CDCl_3$) 156.2 (N[O]C=O), 135.8 (CH), 117.2 (CH_2), 63.6 (CH_2), 60.4 (CH_2), 48.8 (CH_2), 43.8 (CH_2), 42.6 (CH), 35.8 (CH_2), 35.1 (CH), 27.6 (CH_2), 17.9 (CH_2), −1.3 (CH_3 × 3); HRMS(CI) calcd. for $C_{15}H_{30}NO_3Si$ $[M + 1]^+$ 300.1995, found 300.2001.

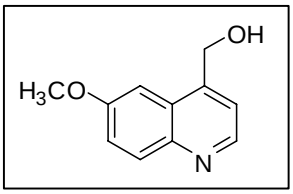
Preparation of (3*R*,4*S*)-2-(trimethylsilyl)ethyl-4-(2-oxoethyl)-3-vinylpiperidine-1-carboxylate (6)[18]



A solution of anhydrous DMSO (0.71 ml, 10.0 mmol) in dry CH_2Cl_2 (15 ml) was added dropwise into a stirred solution of oxalyl chloride (0.42 ml, 5.0 mmol) in dry CH_2Cl_2 (10 ml) at −78 °C under argon atmosphere. The mixture was stirred at this temperature for 20 minutes and a solution of **14** (1.04 g, 3.46 mmol) in dry CH_2Cl_2 (15 ml) was added slowly followed by stirring the mixture at −78 °C for 40 minutes. Anhydrous Et_3N (1.56 ml) was added and stirring was continued for further 40 minutes at the same low temperature. Additional Et_3N (1.0 ml) was added and the reaction flask was transferred to a crushed ice bath (0 °C) and the reaction mixture was stirred for 1 h. The reaction was quenched by adding water (50 ml). Organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 ml). The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuum. The crude oily material was purified by flash silica gel column chromatography (acetone/pet. ether 1:9) to afford aldehyde **6** (0.997 g, 97%) as a colorless viscous oil; R_f (acetone/pet. ether, 1:9) 0.23; $[\alpha]_D^{20}$ = +44.0 (*c* 1.0, $CHCl_3$); IR (cm^{-1}, neat): 2952, 2720, 1723, 1690, 1435, 1238, 1180, 1145, 920, 858; δ_H (500 MHz; DMSO-d_6 80 °C) 9.66 (1 H, br. s. CHO), 5.75 (1 H, ddd, *J* = 17.2, 10.5, 8.4

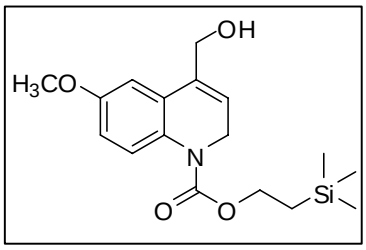
Hz, C*H*=CH_2), 5.06–5.12 (2 H, m, CH=CH_2), 4.06–4.14 (2 H, m, $NCO_2CH_2CH_2Si$), 3.83 (1 H, dtd, *J* = 13.4, 4.3, 1.2 Hz, $CH_2NCHHCH_2$), 3.76 (1 H, ddd, *J* = 13.1, 4.3, 1.2 Hz, $CHCHHNCH_2$), 3.16 (1 H, dd, *J* = 13.3, 3.0 Hz, NC*H*HCH), 3.00 (1 H, ddd, *J* = 13.4, 10.4, 3.4 Hz, $NCHHCH_2$), 2.26–2.43 (4 H, m, CH_2, ring CH, CH), 1.49 (1 H, m, ring C*H*H), 1.35 (1 H, m, ring CH*H*), 0.92–0.96 (2 H, m, $CH_2Si(CH_3)_3$), 0.03 (9 H, s, $Si(CH_3)_3$; δ_C (100 MHz; DMSO-d_6) 203.4 (H-C=O), 155.4 (N[O]C=O), 136.4 (CH), 117.8 (CH_2), 63.2 (CH_2), 47.7 (CH_2), 46.5 (CH_2), 43.3 (CH_2), 42.1 (CH), 32.8 (CH), 27.6 (CH_2), 17.8 (CH_2), –0.86 (CH_3 × 3); HRMS(CI) calcd. for $C_{15}H_{28}NO_3$ $[M + 1]^+$ 298.1838, found 298.1849.

Preparation of (6-methoxyquinolin-4-yl)methanol (15)[19]



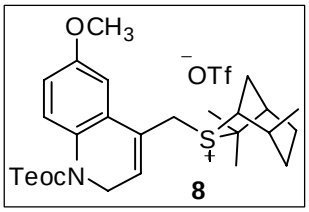
BH_3·THF 1.0 M solution in THF (53 ml, 53.0 mmol) was slowly added to a stirred suspension of quininic acid **9** (2.7 g, 13.3 mmol) in THF (80 ml) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred overnight at RT after complete addition. Reaction mixture was then quenched by the dropwise addition of H_2O (10 ml) and concentrated until 50% of the volume. A solution of NaOH (6 M, 45 ml) was added and the reaction mixture was refluxed for 1 h. The THF was evaporated and the reaction mixture was diluted with H_2O (100 ml) and extracted with EtOAc (3 × 75 ml). Organic fraction was dried over $MgSO_4$, filtered by suction and concentrated in vacuum. The resulting crude yellow material was purified by flash silica gel column chromatography (EtOAc/pet. ether 1:3→1:0), which afforded pure alcohol **15** (1.62 g, 69%) as light yellow needles, mp 132-134 °C (MeOH); R_f (EtOAc) 0.32; IR (cm^{-1}, neat): 3184, 2961, 2838, 1622, 1595, 1509, 1342, 1241, 1226, 1132, 1087, 1069, 825; δ_H (300 MHz; CD_3OD) 8.64 (1 H, d, *J* = 4.5 Hz, ArH), 7.99 (1 H, d, *J* = 9.0 Hz, ArH), 7.45 (1 H, d, *J* = 4.5 Hz, ArH), 7.34 (1 H, dd, *J* = 9.0, 3.0 Hz, ArH), 7.14 (1 H, d, *J* = 3.0 Hz, ArH), 5.13 (2 H, s, CH_2OH), 3.91 (3 H, s, OCH_3), 3.53 (1 H, br. s. OH); δ_C (75 MHz; CD_3OD) 157.9 (C), 147.7 (C), 145.2 (C), 143.8 (C), 131.2 (CH), 127.0 (C), 121.8 (CH), 117.7 (CH), 102.2 (CH), 61.9 (CH_2), 55.7 (CH_3); HRMS(EI) calcd. for $C_{11}H_{11}NO_2$ (M^+) 189.0790, found 189.0791.

Preparation of 2-(trimethylsilyl)ethyl-4-(hydroxymethyl)-6-methoxyquinoline-1(2*H*)-carboxylate (10)



K_2CO_3 (4.14 g, 30.0 mmol) was charged in an oven-dried Schlenk flask and after cycles of vacuum-nitrogen, THF (7 ml) was added and the flask was transferred to an ice bath. 2-(Trimethylsilyl)ethanol (1.31 ml, 9.0 mmol) was added and the mixture was stirred at 0 °C for 20 minutes. A solution of triphosgene (0.89 g, 3.0 mmol) in THF (7 ml) was added slowly and the resulting mixture was stirred at RT for 1 h. Teoc-Cl (trimethylsilylethoxycarbonyl chloride) thus formed was transferred via cannula into another flask containing a solution of substrate alcohol **15** (0.57 g, 3.0 mmol) in THF (7 ml) at RT. The resulting mixture was stirred for 20 minutes and then $NaBH_4$ (0.23 g, 6.0 mmol) was added followed by the careful addition of water (1.2 ml, over 10 min.). The reaction mixture was stirred at RT for 4 h, quenched with water and extracted with EtOAc (3 × 30 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (EtOAc/pet. ether 1:2) to afford alcohol **10** (0.79 g, 79%) as yellow viscous oil. Note: The flash column chromatography has to be done very quickly. R_f (EtOAc/pet. ether 3:7) 0.27; IR (cm^{-1}, neat) 3414, 2955, 2901, 1691, 1607, 1574, 1496, 1394, 1247, 1198, 1175, 1147, 1056, 858, 836; δ_H (400 MHz, $CDCl_3$) 7.52 (1 H, br. s. ArH), 6.88 (1 H, d, J = 2.8 Hz, ArH), 6.81 (1 H, dd, J = 8.9, 2.8 Hz, ArH), 6.10 (1 H, t, J = 4.4 Hz, ArH), 4.48 (2 H, s, CH_2OH), 4.36 (2 H, d, J = 4.4 Hz, N CH_2CH), 4.22–4.30 (2 H, m, $NCO_2CH_2CH_2Si$), 3.81 (3 H, s, OCH_3), 2.07 (1 H, br. s. OH), 1.02–1.10 (2 H, m, CH_2Si), 0.04 (9 H, s, $Si(CH_3)_3$); δ_C (100 MHz, $CDCl_3$) 156.2 (C), 154.4 (N[O]C=O), 135.1 (C), 129.8 (C), 128.4 (CH), 125.1 (CH), 123.2 (CH), 112.4 (CH), 108.6 (CH), 64.3 (CH_2), 62.4 (CH_2), 55.5 (CH_3), 42.8 (CH_2), 17.7 (CH_2), –1.6 (CH_3 × 3); HRMS(EI) calcd. for $C_{17}H_{25}NO_4Si$ (M^+) 335.1553, found 335.1543.

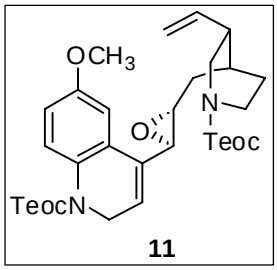
Preparation of (1*R*,4*R*,5*R*,6*R*)-6-((6-methoxy-1-((2-(trimethylsilyl)ethoxy)carbonyl)-1,2-dihydroquinolin-4-yl)methyl)-4,7,7-trimethyl-6-thioniabicyclo[3.2.1]octane-trifluoromethanesulfonate (8)



8

Trifluoromethanesulfonic anhydride (0.1 ml, 0.61 mmol) was added dropwise to a –45 °C cooled solution of 2,6-di-*tert*-butylpyridine (0.15 ml, 0.67 mmol) in CH_2Cl_2 (2 ml) under argon atm. and the resulting solution was stirred for 20 minutes at same low temperature. A solution of alcohol **10** (0.19 g, 0.56 mmol) in CH_2Cl_2 (2 ml) was added slowly followed by the addition of (–) sulfide **1** (0.28 g, 1.67 mmol). The reaction mixture was stirred from –45 °C to RT for 16 h. Water (10 ml) was added and the aqueous layer was extracted with CH_2Cl_2 (4 × 10 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was re-dissolved in CH_2Cl_2 (5 ml) and passed through a short silica plug eluting first with CH_2Cl_2 to remove unreacted sulfide **1** and then with 10% MeOH in CH_2Cl_2 to afford sulfonium salt **8** (0.253 g, 71%) as a yellow foam; R_f (CH_2Cl_2/MeOH 9:1) 0.39; $[\alpha]_D^{20}$ = –145.0 (*c* 1.1, $CHCl_3$); IR (cm^{-1}, neat): 2953, 1697, 1608, 1574, 1498, 1396, 1248, 1223, 1148, 1028, 857, 836; δ_H (400 MHz; $CDCl_3$) 7.50 (1 H, br. s. ArH), 7.00 (1 H, d, *J* = 2.7 Hz, ArH), 6.86 (1 H, dd, *J* = 9.0, 2.7 Hz, ArH), 6.69 (1 H, t, *J* = 4.4 Hz, C=CH), 4.77 (1 H, d, *J* =13.2 Hz, SC*H*H), 4.48–4.60 (2 H, m, SCH*H* and NC*H*H), 4.18–4.28 (2 H, m, $CO_2CH_2CH_2Si$), 3.88 (4 H, s. OCH_3 and NCH*H*), 3.63 (1 H, dt, *J* = 17.0, 2.7 Hz, SC*H*CH_2), 2.80 (1 H, d, *J* = 13.7 Hz), 2.41 (1 H, br. s), 2.35 (1 H, d, *J* = 14.3 Hz), 2.06 (1 H, m), 1.87 (3 H, s, CH_3), 1.81 (3 H, s, CH_3), 1.60–1.77 (4 H, m, CH_2, CH_2), 1.53 (1 H, m), 1.11 (3 H, d, *J* = 7.1 Hz, CH_3), 0.99–1.07 (2 H, m, CH_2Si), 0.03 (9 H, s, $Si(CH_3)_3$); δ_C (125 MHz; $CDCl_3$) 156.9 (C), 154.0 (N[O]C=O), 133.4 (CH), 130.0 (C), 126.0 (C), 126.0 (C), 125.7 (CH), 120.6 (q, *J* 320, CF_3), 115.2 (CH), 107.9 (CH), 73.2 (C), 64.7 (CH), 64.5 (CH_2), 56.2 (CH_3), 50.6 (CH), 42.9 (CH_2), 39.0 (CH_2), 31.9 (CH), 31.9 (CH_2), 25.3 (CH_2), 25.3 (CH_3), 23.3 (CH_3), 22.1 (CH_2), 17.7 (CH_2), 17.7 (CH_3), –1.6 (CH_3 × 3); HRMS(ESI) calcd. for $C_{27}H_{42}NO_3SSi$ $[M - TfO]^+$ 488.2649, found 488.2659.

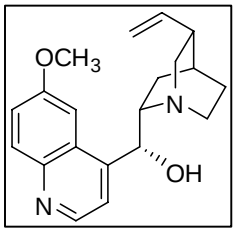
Preparation of 2-(trimethylsilyl)ethyl 6-methoxy-4-((2*S*,3*S*)-3-(((3*R*,4*S*)-1-((2-(trimethylsilyl)ethoxy)carbonyl)-3-vinylpiperidin-4-yl)methyl)oxiran-2-yl)-quinoline-1(2*H*)-carboxylate (11)



11

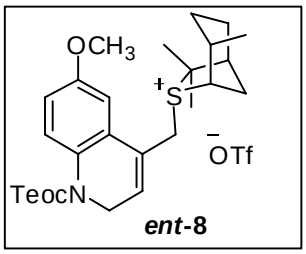
Manually ground KOH (0.021 g, 0.37 mmol) was added to a solution of sulfonium salt **8** (0.178 g, 0.28 mmol) in CH_3CN:*t*-BuOH (15:1) (1.0 ml, 0.28 M) containing meroquinene aldehyde **6** (0.167 g, 0.56 mmol) at 0 °C under argon atm. The resulting turbid yellow solution was stirred at 0 °C for 24 h. CH_3CN was evaporated under vacuum and water (10 ml) was added and the aq. layer was extracted with EtOAc (3 × 10 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material (dr 89:11 *trans:cis*) was purified by flash silica gel column chromatography (Et_2O/pentane 1:4) to afford the pure *trans* epoxide **11** (0.123 g, 72%) as a light yellow gum; R_f (Et_2O/pentane 2:3) 0.33; $[\alpha]_D^{24}$ = +35.0 (*c* 0.8, $CHCl_3$); IR (cm^{-1}, neat): 2952, 1692, 1608, 1575, 1495, 1433, 1394, 1245, 1222, 1148, 858, 830; δ_H (400 MHz; $CDCl_3$) 7.53 (1 H, br. s, ArH.), 6.75–6.84 (2 H, m, ArH), 6.01 (1 H, t, *J* = 4.0 Hz), 5.82 (1 H, ddd, *J* = 17.0, 10.3, 9.2 Hz, CH_2=C*H*-CH), 5.07–5.19 (2 H, m, C*H*$_2$=CH), 4.52 (1 H, dd, *J* = 16.7, 4.6 Hz, N*H*H), 4.21–4.29 (2 H, m, $CO_2CH_2CH_2Si$), 4.12–4.20 (3 H, m, $CO_2CH_2CH_2Si$ and NCH*H*), 3.92–4.12 (2 H, m, NCH_2), 3.80 (3 H, s, OCH_3), 3.43 (1 H, br. s, OCH), 3.08 (1 H, dd, *J* = 13.1, 2.5 Hz, NC*H*H), 2.94 (1 H, m, NCH*H*), 2.84 (1 H, dt, *J* = 7.2, 2.8 Hz, OC*H*-CH_2), 2.42 (1 H, m, CH_2=CH-C*H*), 1.95 (1 H, m, CH), 1.84 (1 H, m, CH), 1.46–1.65 (2 H, m, CH_2), 1.39 (1 H, m, CH), 1.01–1.09 (2 H, m, $CO_2CH_2CH_2Si$), 0.93–1.01 (2 H, m, $CO_2CH_2CH_2Si$), 0.03 (9 H, s, $Si(CH_3)_3$), 0.02 (9 H, s, $Si(CH_3)_3$); δ_C (100 MHz; $CDCl_3$) 156.2 (C), 156.0 (N(O)C=O), 154.3 (N(O)C=O), 135.4 (CH), 132.6 (C), 129.6 (C), 128.4 (C), 125.2 (CH), 122.0 (CH), 117.6 (CH_2), 112.1 (CH), 108.8 (CH), 64.3 (CH_2), 63.5 (CH_2), 59.7 (CH), 55.8 (CH), 55.5 (CH_3), 48.4 (CH_2), 43.5 (CH_2), 42.8 (CH_2), 42.5 (CH), 37.0 (CH), 35.3 (CH_2), 27.7 (CH_2), 17.7 (CH_2× 2), −1.5 (CH_3 × 3); −1.6 (CH_3 × 3); HRMS(ESI) calcd. for $C_{32}H_{50}N_2O_6Si_2Na$ $[M + Na]^+$ 637.3100, found 637.3123.

Quinine



CsF (288 mg, 1.90 mmol) was added to a solution of epoxide **11** (115 mg, 0.187 mmol) in DMF (1.5 ml) and the mixture was irradiated at 180 °C using a microwave for 15 minutes. The resulting yellow solution was stirred in oxygen atm. at RT for 24 h. The reaction mixture was diluted with water (10 ml), basified with aq. NaOH (6 M) and extracted with EtOAc (4 × 10 ml). The combined organic layer was washed with water (4 × 20 ml), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (CH_2Cl_2/MeOH 20:1 containing 0.75% Et_3N) to afford quinine (44 mg, 73%) as a colorless solid, with spectral (^{1}H NMR, ^{13}C NMR, HRMS) properties matching to the reported data[20] and an authentic sample from Aldrich. R_f (CH_2Cl_2/MeOH/NH_3 9:1:0.1) 0.31; mp = 164–166 °C (EtOH) [Lit.[20] mp = 172-175 °C]; $[\alpha]_D^{21}$ = –139 (*c* 0.4, EtOH) [Lit.[20] $[\alpha]_D^{26}$ = –154.1 (*c* 1.0, EtOH)]; IR (cm^{-1}, neat) 3271, 2926, 1620, 1590, 1508, 1469, 1430, 1239, 1227, 1102, 1030, 823; δ_H (400 MHz; $CDCl_3$), 8.68 (1 H, d, *J* = 4.4 Hz, ArH), 7.98 (1 H, d, *J* = 9.3 Hz, ArH), 7.52 (1 H, d, *J* = 4.4 Hz, ArH), 7.32 (1 H, dd, *J* = 9.3, 2.7 Hz, ArH), 7.23 (1 H, d, *J* = 2.7 Hz, ArH), 5.74 (1 H, ddd, *J* = 17.3, 10.1, 7.6 Hz, C*H*=CH_2), 5.61 (1 H, d, *J* = 3.7 Hz, C*H*-OH), 4.90–5.02 (2 H, m, CH=C*H*$_2$), 3.89 (3 H, s, OCH_3), 3.51 (1 H, m, NCH), 3.07–3.22 (2 H, m, NCH_2), 2.65–2.76 (2 H, m, NCH_2), 2.31 (1 H, br. s, C*H*-CH=CH_2), 1.85 (1 H, m, CH), 1.70–1.81 (2 H, m, CH_2), 1.47–1.62 (2 H, m, CH_2); δ_C (125 MHz; $CDCl_3$) 157.8 (C), 147.6 (CH), 147.2 (C), 144.3 (C), 141.5 (CH), 131.6 (CH), 126.6 (C), 121.5 (CH), 118.4 (CH), 114.6 (CH_2), 101.2 (CH), 71.7 (CH), 60.0 (CH), 56.8 (CH_2), 55.7 (CH_3), 43.2 (CH_2), 39.8 (CH), 27.8 (CH), 27.4 (CH_2), 21.8 (CH_2); HRMS(CI) calcd. for $C_{20}H_{25}N_2O_2$ $[M + 1]^+$ 325.1916, found 325.1914.

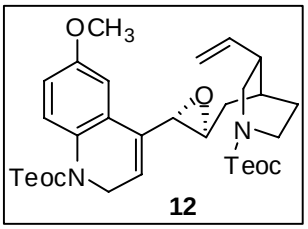
Preparation of (1*S*,4*S*,5*S*,6*S*)-6-((6-methoxy-1-((2-(trimethylsilyl)ethoxy)carbonyl)-1,2-dihydroquinolin-4-yl)methyl)-4,7,7-trimethyl-6-thioniabicyclo[3.2.1]octane-trifluoromethanesulfonate (*ent*-8)



***ent*-8**

Trifluoromethanesulfonic anhydride (0.081 ml, 0.48 mmol) was added dropwise to a –45 °C cooled solution of 2,6-di-*tert*-butyl-4-methylpyridine (0.1 g, 0.48 mmol) in CH_2Cl_2 (5 ml) under argon atm. and the resulting solution was stirred for 5 minutes. A solution of alcohol **10** (0.145 g, 0.44 mmol) in CH_2Cl_2 (5 ml) was added slowly followed by the addition of (+) sulfide **1** (0.22 g, 1.3 mmol). The reaction mixture was stirred from –45 °C to RT for 16 h. Water (10 ml) was added and the aqueous layer was extracted with CH_2Cl_2 (4 × 10 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (CH_2Cl_2/MeOH, 1:20) to afford sulfonium salt ***ent*-8** (0.174 g, 62%) as a yellow foam; R_f (CH_2Cl_2/MeOH, 9:1) 0.35; $[\alpha]_D^{20}$ = +150.0 (*c* 1.2, $CHCl_3$); IR (cm^{-1}, neat): 2988, 2901, 1698, 1497, 1394, 1249, 1224, 1148, 1065, 1028, 859, 836; δ_H (400 MHz; $CDCl_3$) 7.49 (1 H, br. d. *J* = 7.0 Hz, ArH), 7.00 (1 H, d, *J* = 2.6 Hz, ArH), 6.85 (1 H, dd, *J* = 9.0, 2.8 Hz, ArH), 6.68 (1 H, t, *J* = 4.3 Hz, =CH), 4.77 (1H, d, *J* = 13.4 Hz, SC*H*H), 4.47–4.58 (2 H, m, NCH_2), 4.19–4.26 (2 H, m, $CO_2CH_2CH_2Si$), 3.89 (4 H, s. OCH_3 and SCH*H*), 3.63 (1 H, dd, *J* = 16.9, 2.6 Hz), 2.79 (1 H, d, *J* = 13.8 Hz), 2.41 (1 H, br. s, CH), 2.35 (1 H, d, *J* = 14.3 Hz, CH), 2.05 (1 H, m, CH), 1.86 (3 H, s, CH_3), 1.80 (3 H, s, CH_3), 1.49–1.74 (4 H, m, CH_2, CH_2), 1.11 (3 H, d, *J* = 7.2 Hz, CH_3), 0.99–1.06 (2 H, m, CH_2Si), 0.03 (9 H, s, $Si(CH_3)_3$); δ_C (100 MHz; $CDCl_3$) 157.0 (C), 154.0 (N(O)C=O), 133.5 (CH), 130.2 (C), 126.0 (C), 126.0 (C), 125.7 (CH), 120.6 (q, *J* 320, CF_3), 115.3 (CH), 107.9 (CH), 73.2 (C), 64.6 (CH). 64.5 (CH_2), 56.2 (CH_3), 50.6 (CH), 42.9 (CH_2), 39.0 (CH_2), 31.9 (CH), 31.9 (CH_2), 25.3 (CH_2), 25.3 (CH_3), 23.3 (CH_3), 22.1 (CH_2), 17.7 (CH_2), 17.7 (CH_3), –1.6 (CH_3 × 3); HRMS(ESI) calcd. for $C_{27}H_{42}NO_3SSi$ $[M - TfO]^+$ 488.2649, found 488.2668.

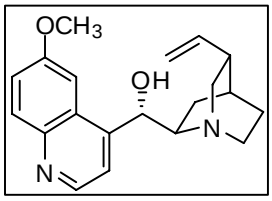
Preparation of 2-(trimethylsilyl)ethyl 6-methoxy-4-((2*R*,3*R*)-3-(((3*R*,4*S*)-1-((2-(trimethylsilyl)ethoxy)carbonyl)-3-vinylpiperidin-4-yl)methyl)oxiran-2-yl)-quinoline-1(2*H*)-carboxylate (12)



12

Manually ground KOH (10 mg, 0.17 mmol) was added to a solution of sulfonium salt ***ent*-8** (90 mg, 0.14 mmol) in CH_3CN:*t*-BuOH (15:1) (0.6 ml, 0.23 M) containing meroquinene aldehyde **6** (83 mg, 0.28 mmol) at 0 °C under argon atm. The resulting turbid yellow solution was stirred at 0 °C for 24 h. CH_3CN was evaporated under vacuum and water (10 ml) was added and the aq. layer was extracted with EtOAc (3 × 10 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material (dr 84:16 *trans:cis*) was purified by flash silica gel column chromatography (Et_2O/pentane 1:4) to afford the pure *trans* epoxide **12** (53 mg, 61%) as a light yellow gum; R_f (Et_2O/pentane 2:3) 0.33; $[\alpha]_D^{24}$ = +49.0 (*c* 0.8, $CHCl_3$); IR (cm^{-1}, neat): 2970, 2901, 1692, 1495, 1394, 1247, 1076, 859, 835; δ_H (400 MHz; $CDCl_3$) 7.54 (1 H, br. s, ArH.), 6.80–6.85 (2 H, m, ArH), 6.02 (1 H, t, *J* = 4.4 Hz), 5.83 (1 H, ddd, *J* = 17.8, 10.0, 9.0 Hz, CH_2=C*H*-CH), 5.13–5.20 (2 H, m, C*H*$_2$=CH), 4.51 (1 H, ddd, *J* = 16.8, 4.9, 1.0 Hz, N*H*HCH$_2$), 4.24–4.30 (2 H, m, $CO_2CH_2CH_2Si$), 4.15–4.22 (3 H, m, $CO_2CH_2CH_2Si$ and NCH*H*), 3.95–4.14 (2 H, m, NCH_2), 3.82 (3 H, s, OCH_3), 3.46 (1 H, m, OCH), 3.07 (1 H, dd, *J* = 13.2, 2.2 Hz, NC*H*H), 2.93 (1 H, m, NCH*H*), 2.85 (1 H, td, *J* = 5.9, 2.2 Hz, OC*H*-CH_2), 2.37 (1 H, m, CH_2=CH-C*H*), 1.96 (1 H, m, CH), 1.84 (1 H, m, CH), 1.58–1.63 (3 H, m, CH and CH_2), 1.50 (1 H, m, CH), 1.03–1.10 (2 H, m, $CO_2CH_2CH_2Si$), 0.95-1.03 (2 H, m, $CO_2CH_2CH_2Si$), 0.04 (9 H, s, $Si(CH_3)_3$), 0.03 (9 H, s, $Si(CH_3)_3$); δ_C (100 MHz; $CDCl_3$) 156.2 (C), 155.9 (N(O)C=O), 154.2 (N(O)C=O), 135.1 (CH), 132.5 (C), 129.5 (C), 128.3 (C), 125.2 (CH), 121.9 (CH), 117.6 (CH_2), 112.0 (CH), 108.7 (CH), 64.3 (CH_2), 63.4 (CH_2), 59.7 (CH), 56.3 (CH), 55.5 (CH_3), 48.3 (CH_2), 43.5 (CH_2), 42.9 (CH), 42.7 (CH_2), 36.7 (CH), 35.6 (CH_2), 27.1 (CH_2), 17.7 (CH_2× 2), −1.5 (CH_3 × 3), −1.6 (CH_3 × 3); HRMS(ESI) calcd. for $C_{32}H_{50}N_2O_6Si_2Na$ $[M + Na]^+$ 637.3100, found 637.3094.

Quinidine



CsF (148 mg, 0.98 mmol) was added to a solution of epoxide **12** (60 mg, 0.098 mmol) in DMF (1.5 ml) and the mixture irradiated at 180 °C using a microwave for 15 minutes. The resulting yellow solution was stirred in O_2 atm. at RT for 19 h. The reaction mixture was diluted with water (10 ml), basified with NaOH (6 M) and extracted with EtOAc (4 × 10 ml). The combined organic layer was washed with water (4 × 20 ml), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (CH_2Cl_2/MeOH 20:1 containing 0.75% Et_3N) to afford the target quinidine (25 mg, 78%) as a colorless solid, with spectral (^{1}H NMR, ^{13}C NMR, HRMS) properties matching the reported data[20] and an authentic sample from Aldrich. R_f (CH_2Cl_2/MeOH/NH_3 9:1:0.1) 0.31; mp = 172–174 °C (EtOH) [Lit.[20] mp = 170-172 °C]; $[\alpha]_D^{21}$ = +233 (*c* 0.9, EtOH) [Lit.[20] $[\alpha]_D^{26}$ = +236 (*c* 1.0, EtOH)]; IR (cm^{-1}, neat) 3218, 2988, 2901, 1621, 1508, 1242, 1228, 1076, 1028, 828; δ_H (400 MHz; $CDCl_3$, 21 mg) 8.61 (1 H, d, *J* = 4.6 Hz, ArH), 7.93 (1 H, d, *J* = 9.2 Hz, ArH), 7.53 (1 H, d, *J* = 4.6 Hz, ArH), 7.27 (1 H, dd, *J* = 9.2, 2.8 Hz, ArH), 7.15 (1 H, d, *J* = 2.8 Hz, ArH), 6.03 (1 H, ddd, *J* = 17.5, 10.0, 7.5 Hz, C*H*=CH_2), 5.68 (1 H, d, *J* = 3.8 Hz, C*H*-OH), 5.08 (1 H, m, CH=C*H*H), 5.04 (1 H, m, CH=CH*H*), 3.82 (3 H, s, OCH_3), 3.42 (1 H, m, NCH), 3.07 (1 H, td, *J* = 9.2, 3.7 Hz, NC*H*H-CH_2), 2.86–2.97 (2 H, m, NC*H*$_2$-CH), 2.78 (1 H, m, NCH*H*CH_2), 2.25 (1 H, m, C*H*-CH-CH_2), 2.07 (1 H, m, CH), 1.77 (1 H, m, CH), 1.44–1.61 (2 H, m, CH_2), 1.12 (1 H, m); δ_C (100 MHz; $CDCl_3$) 157.6 (C), 147.4 (CH), 147.4 (C), 144.0 (C), 140.2 (CH), 131.4 (CH), 126.4 (C), 121.5 (CH), 118.4 (CH), 114.8 (CH_2), 101.1 (CH), 71.4 (CH), 59.7 (CH), 55.6 (CH_3), 50.0 (CH_2), 49.4 (CH_2), 39.8 (CH), 28.1 (CH), 26.1 (CH_2), 20.8 (CH_2); HRMS(CI) calcd. for $C_{20}H_{25}N_2O_2$ $[M + 1]^+$ 325.1916, found 325.1910.

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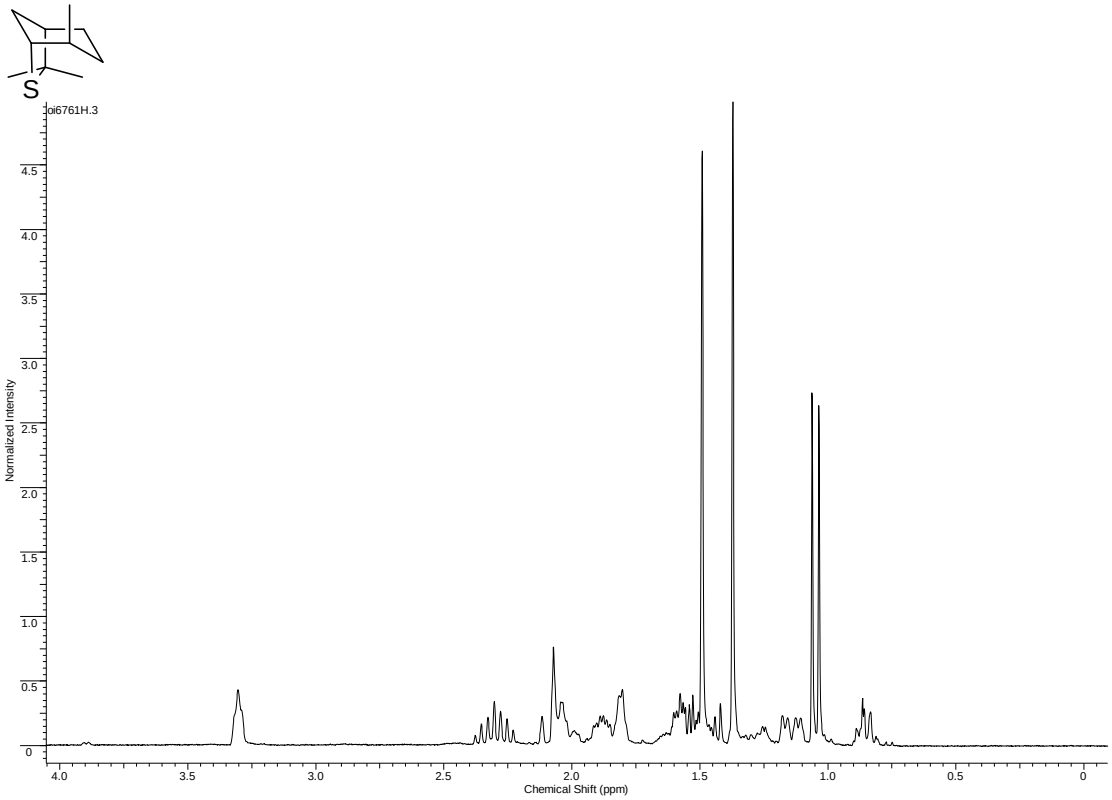
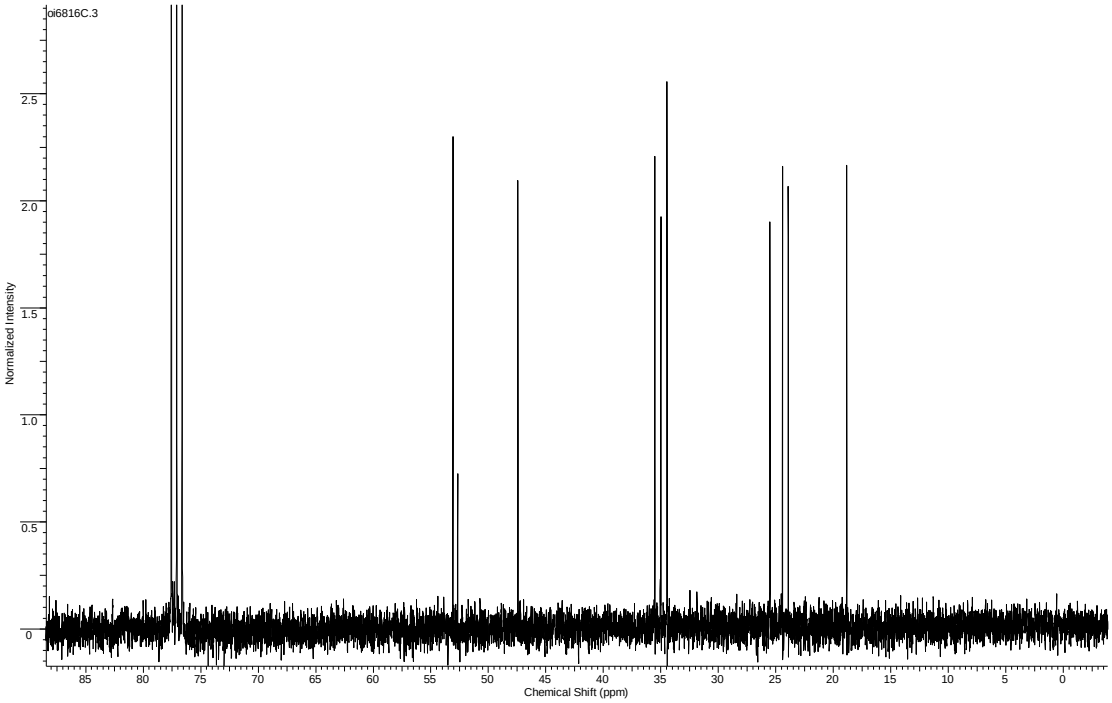
NMR Spectra for Sulfide 1 and Sulfonium Salts

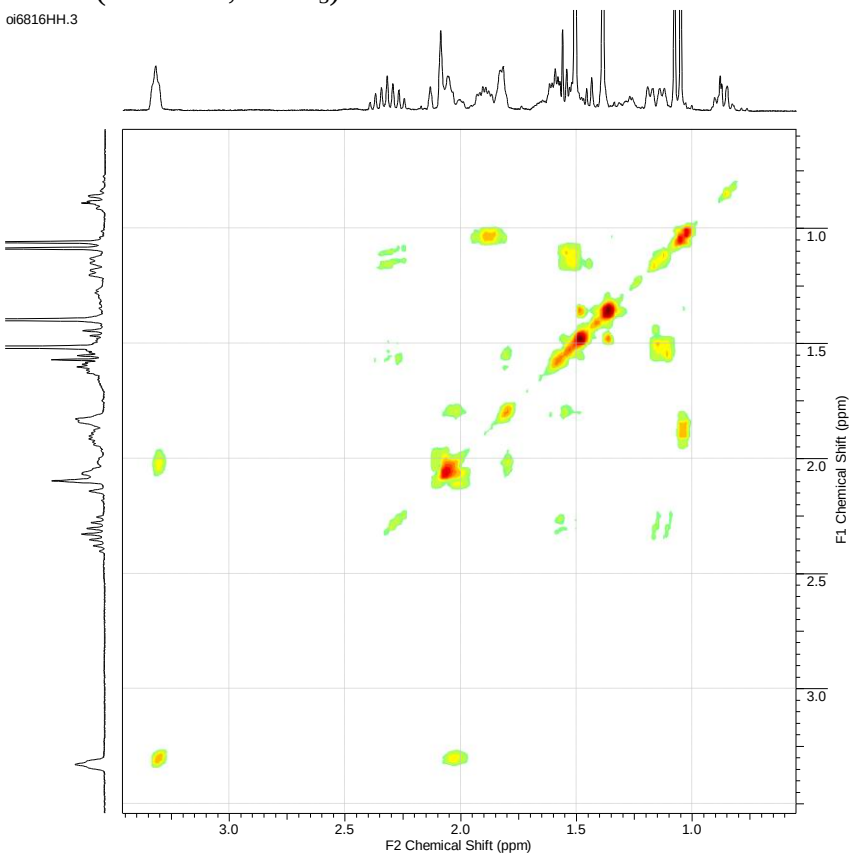
^{1}H-NMR (270 MHz, $CDCl_3$)



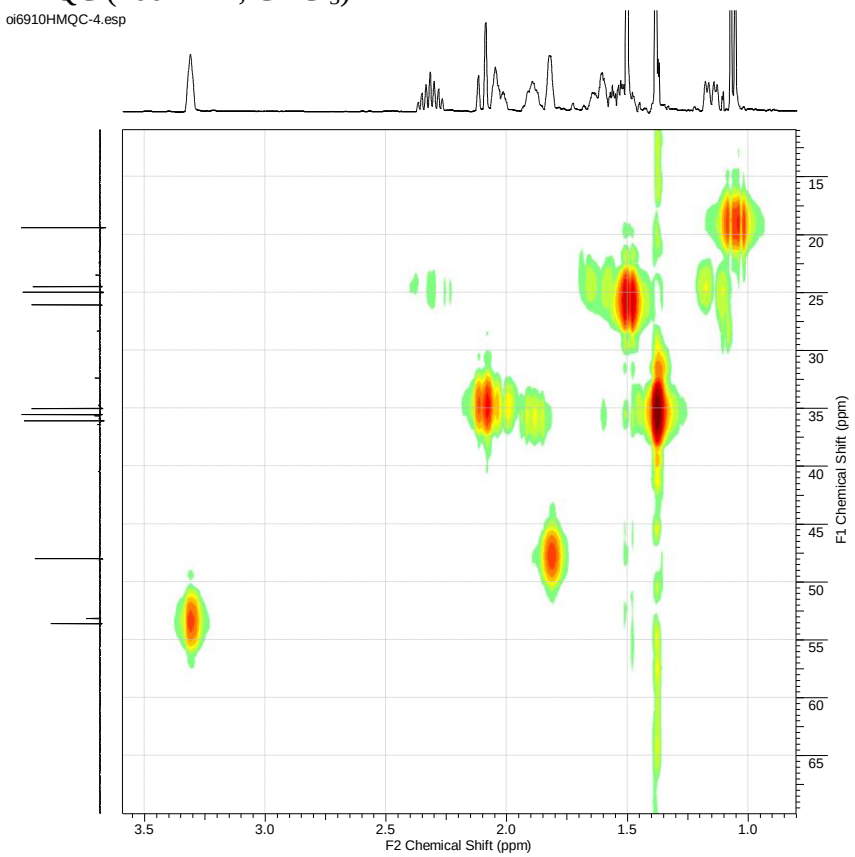
^{13}C-NMR (67.5 MHz, $CDCl_3$)



COSY (270 MHz, $CDCl_3$)



HMQC (400 MHz, $CDCl_3$)



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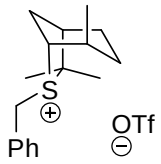

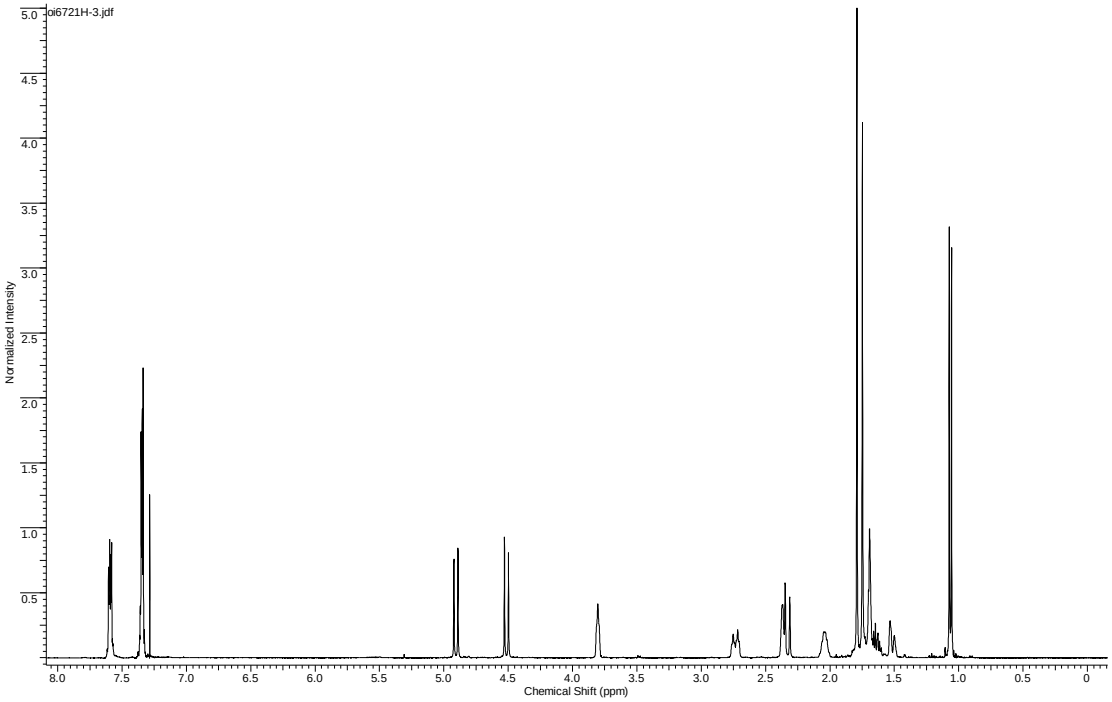

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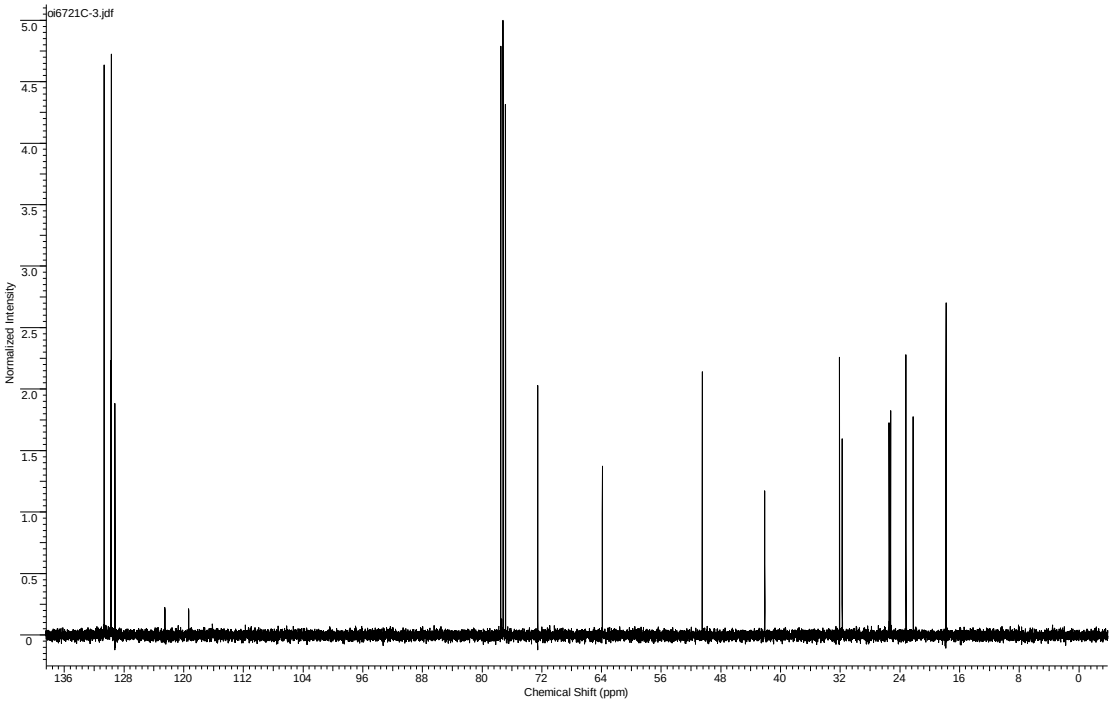
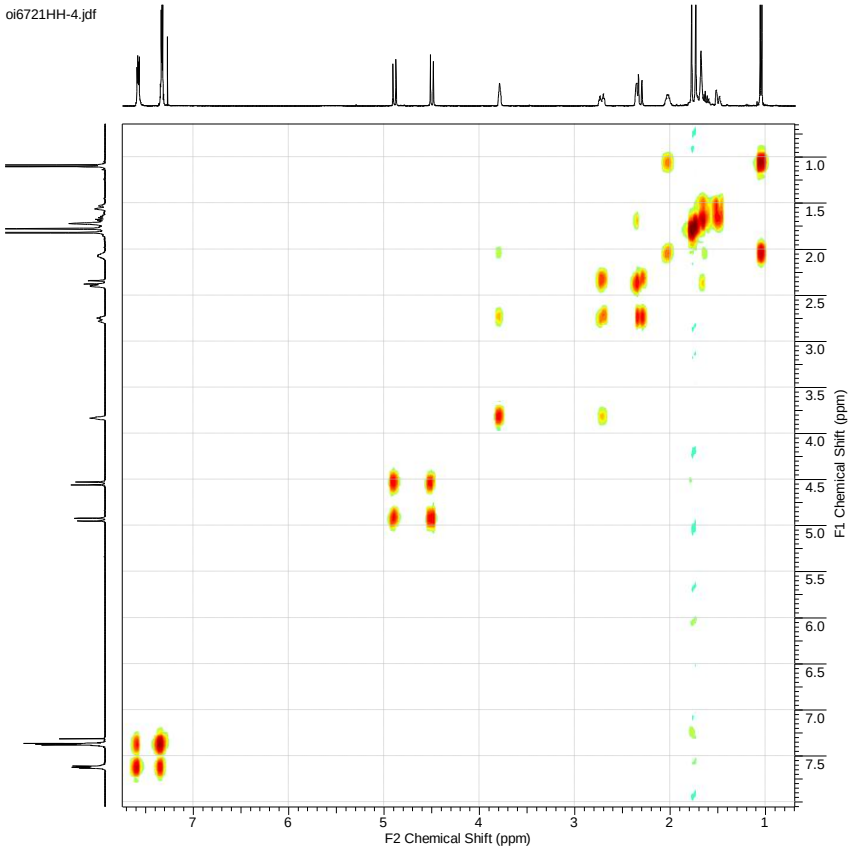
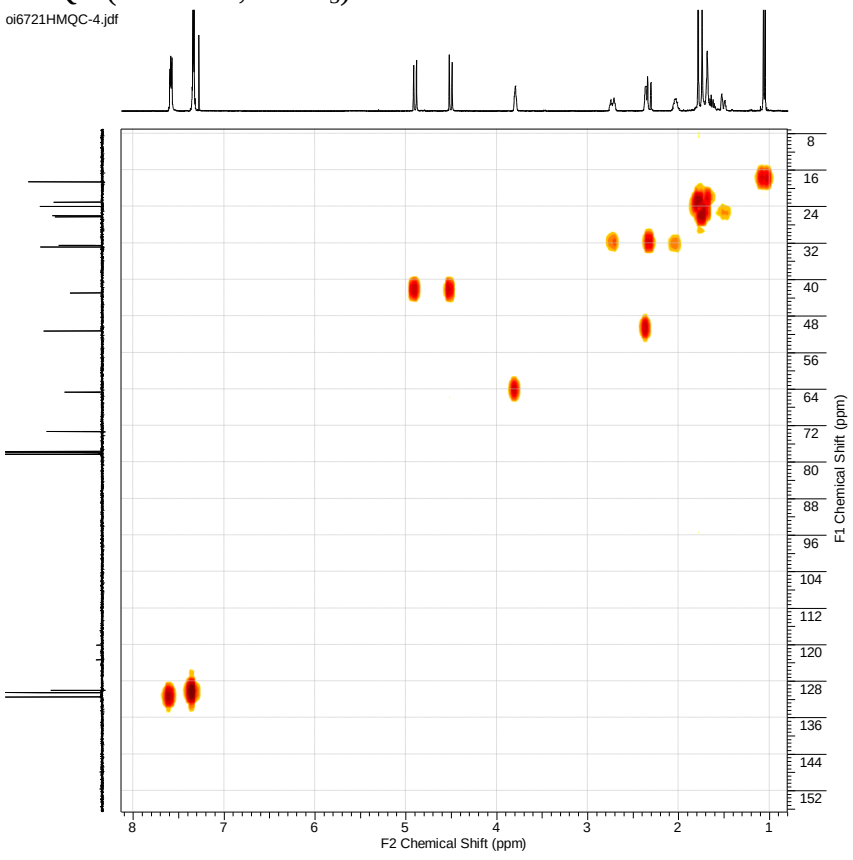


COSY (400 MHz, $CDCl_3$)



HMQC (400 MHz, $CDCl_3$)



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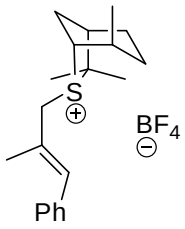
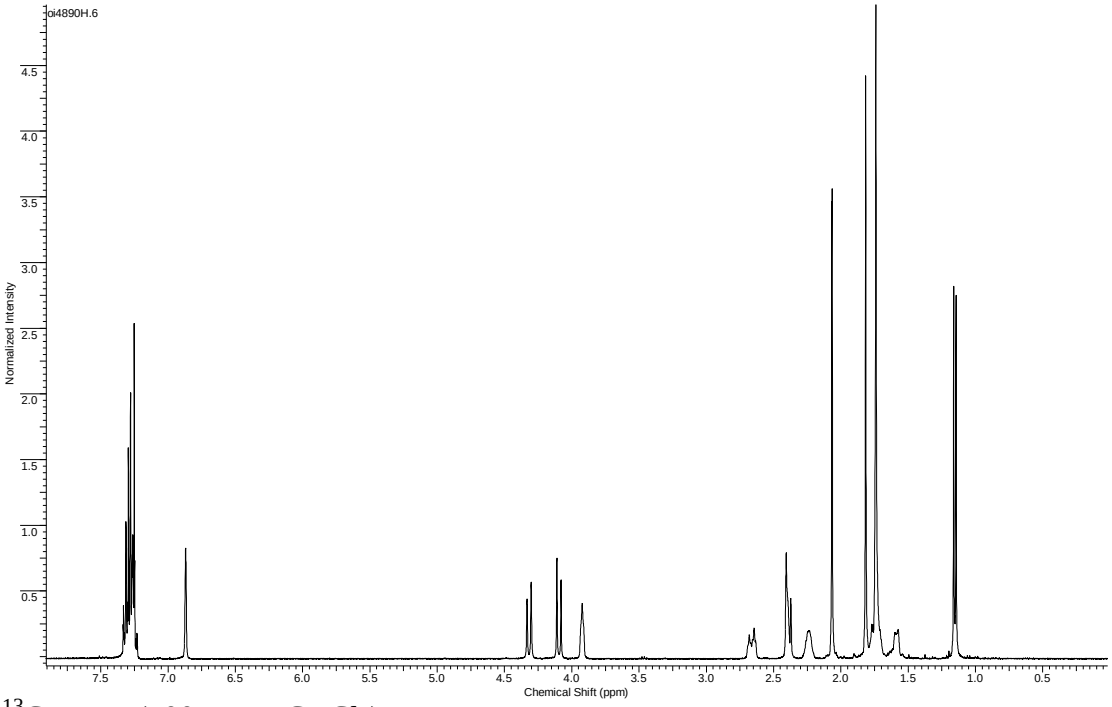
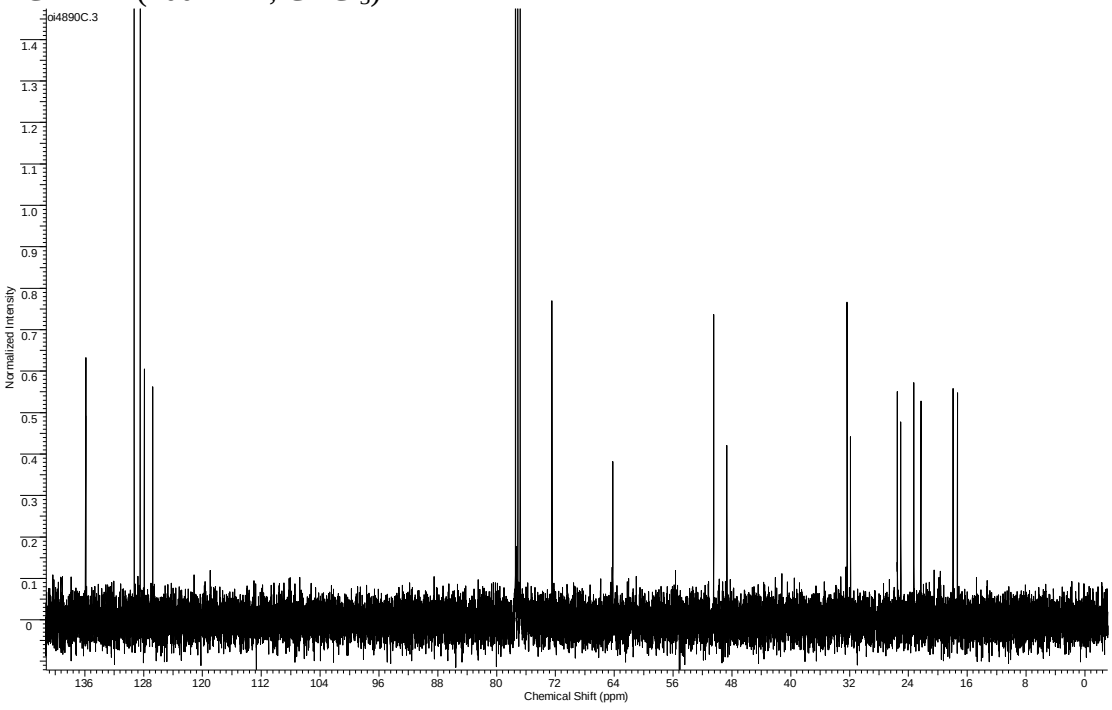
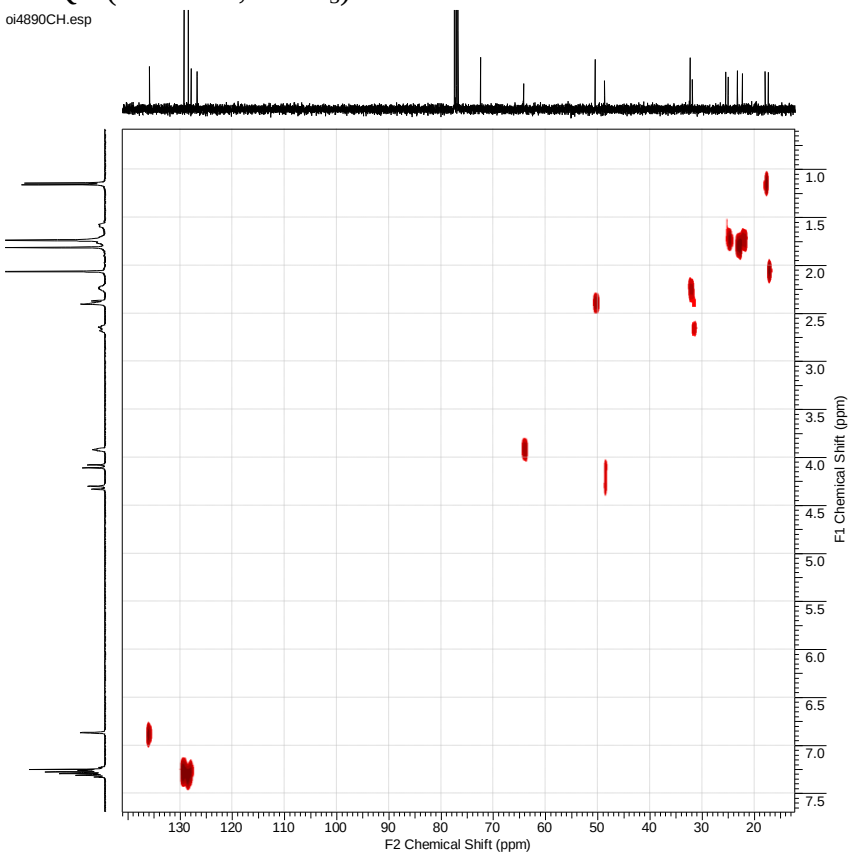




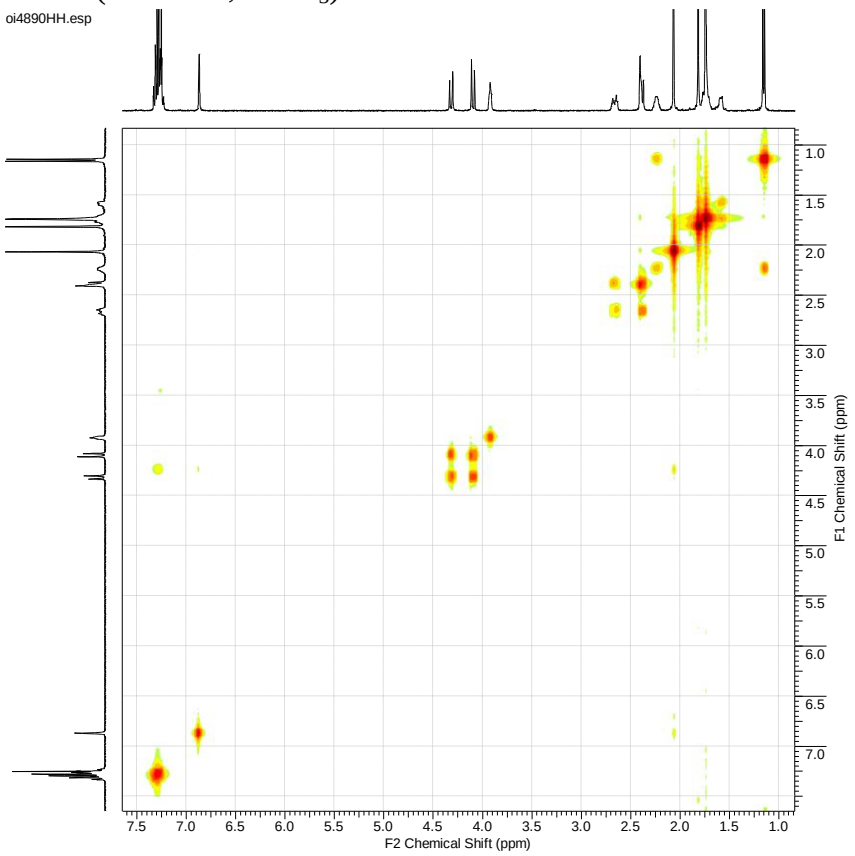
^{13}C-NMR (100 MHz, $CDCl_3$)



HMQC (400 MHz, $CDCl_3$)



COSY (400 MHz, $CDCl_3$)



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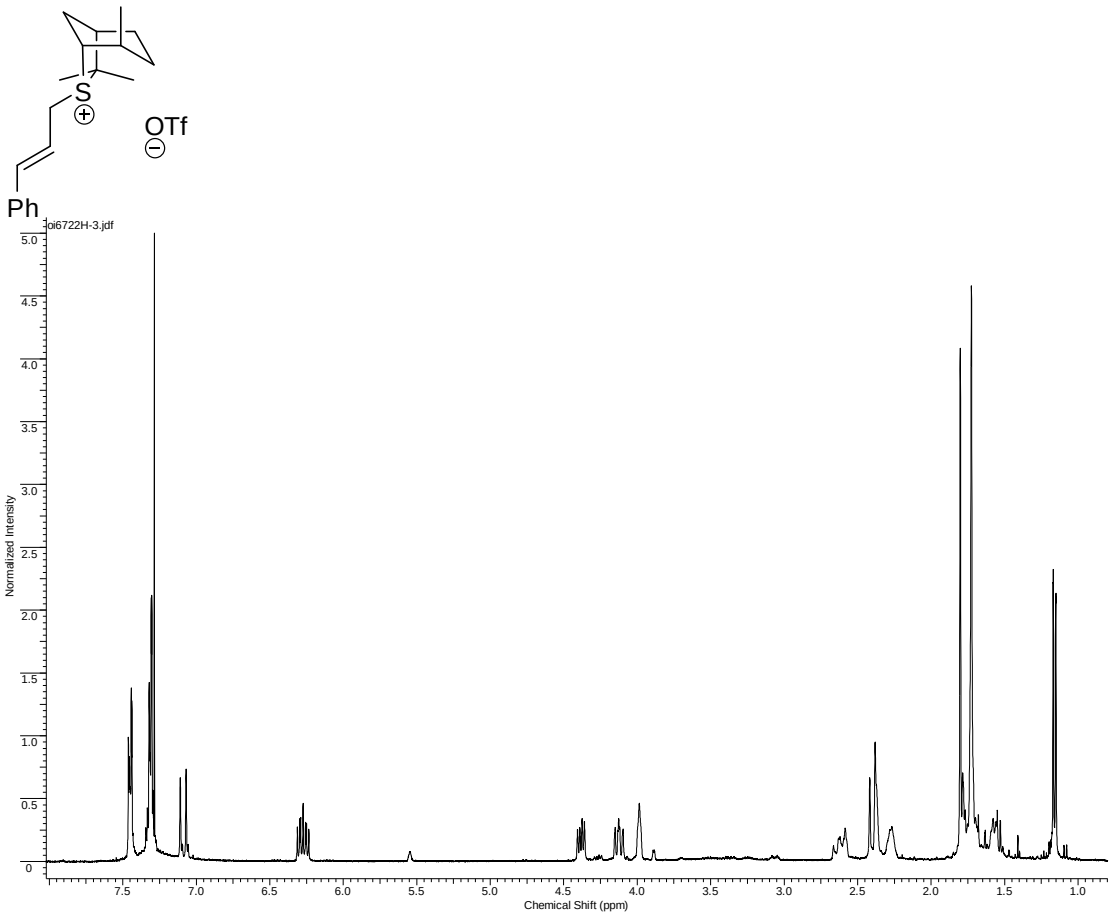

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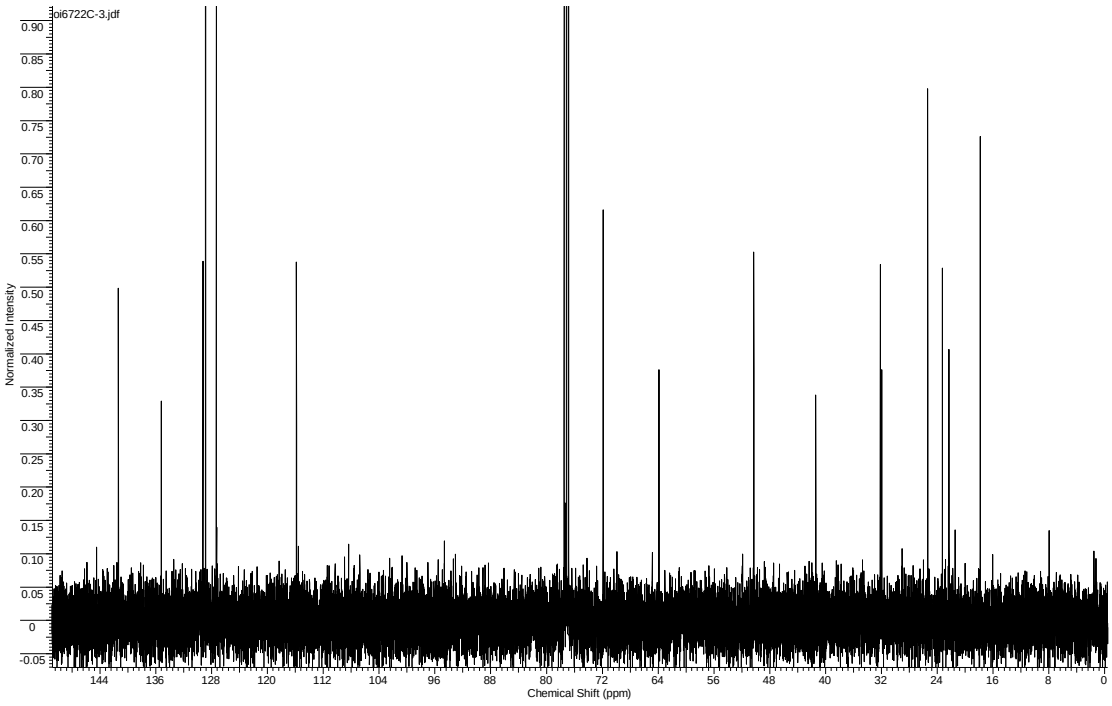
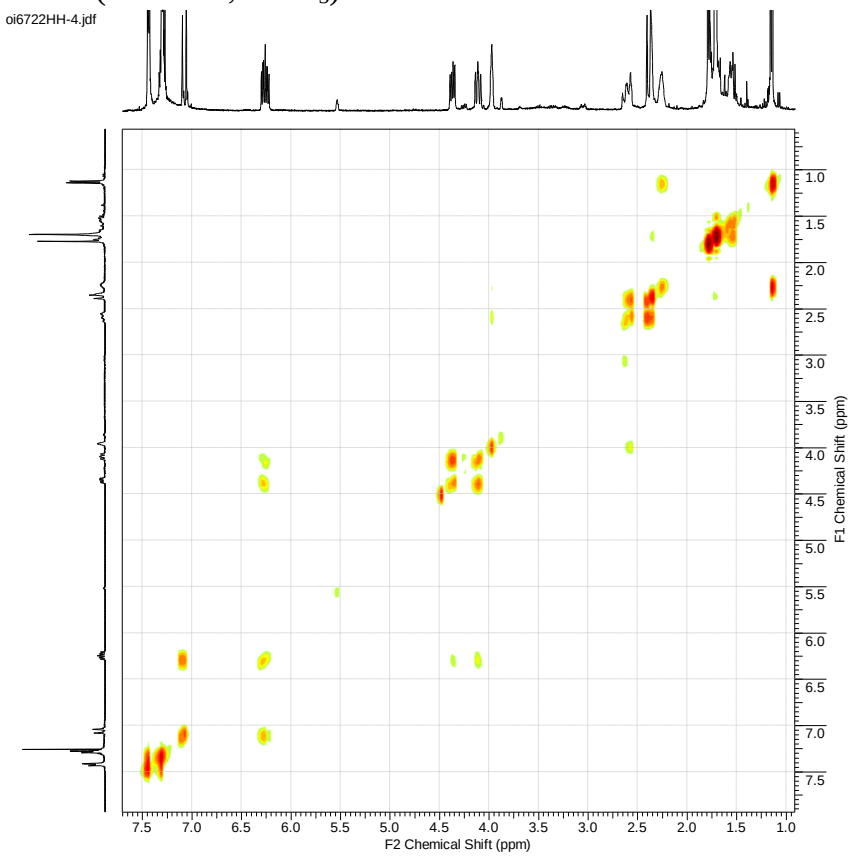


COSY (400 MHz, $CDCl_3$)



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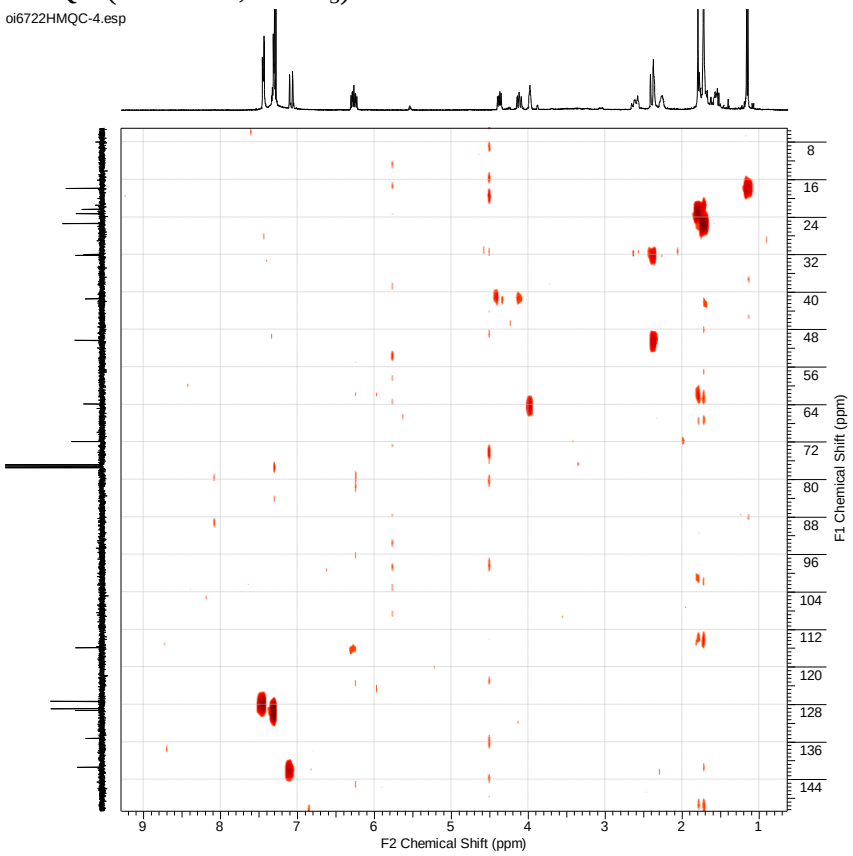
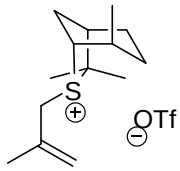
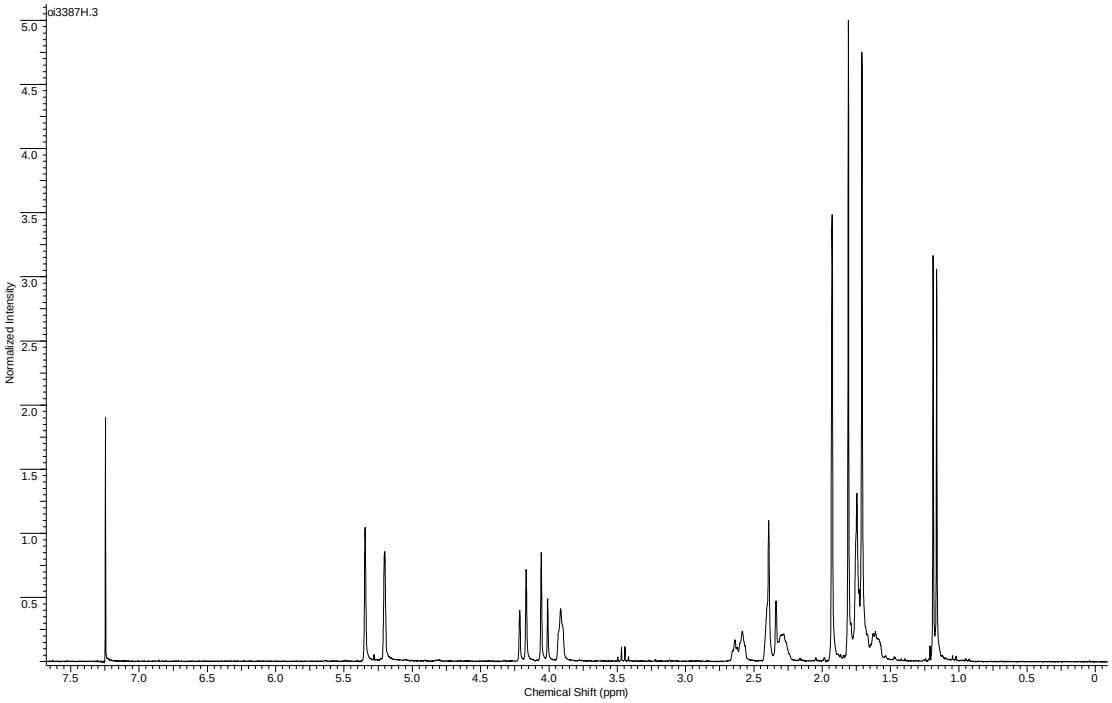
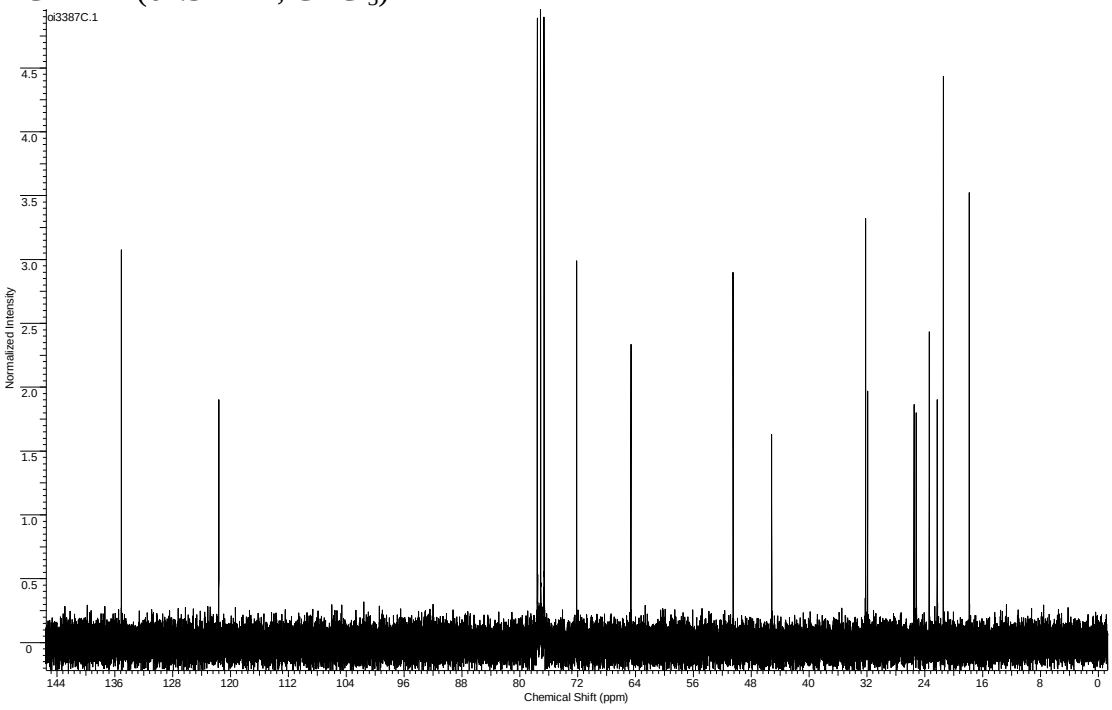


^{1}H-NMR (270 MHz, $CDCl_3$)

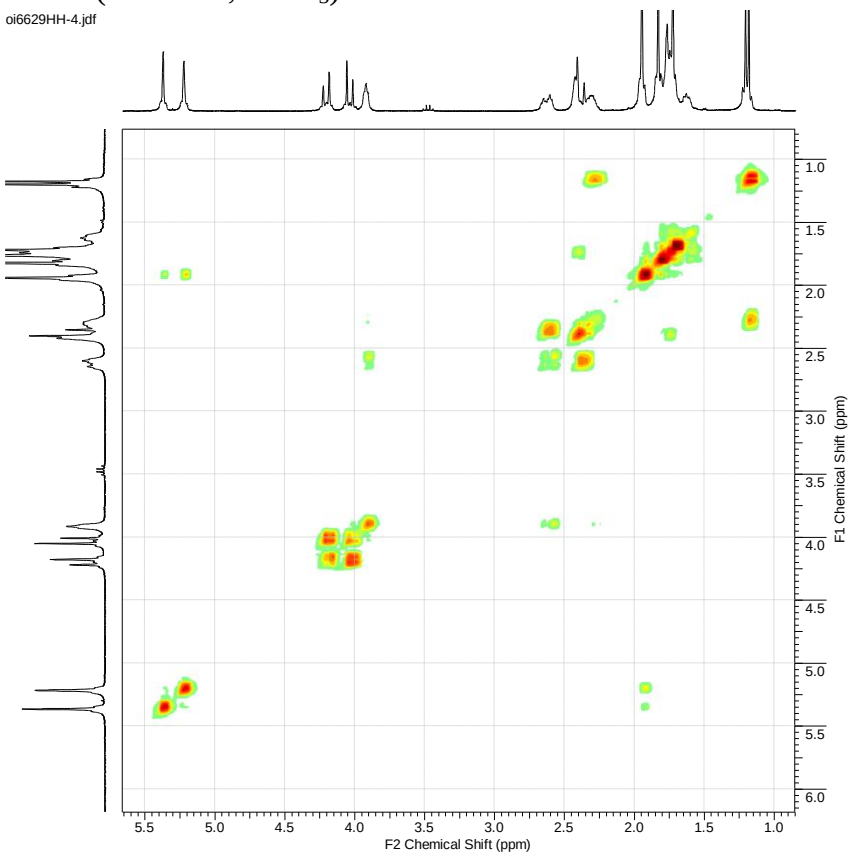




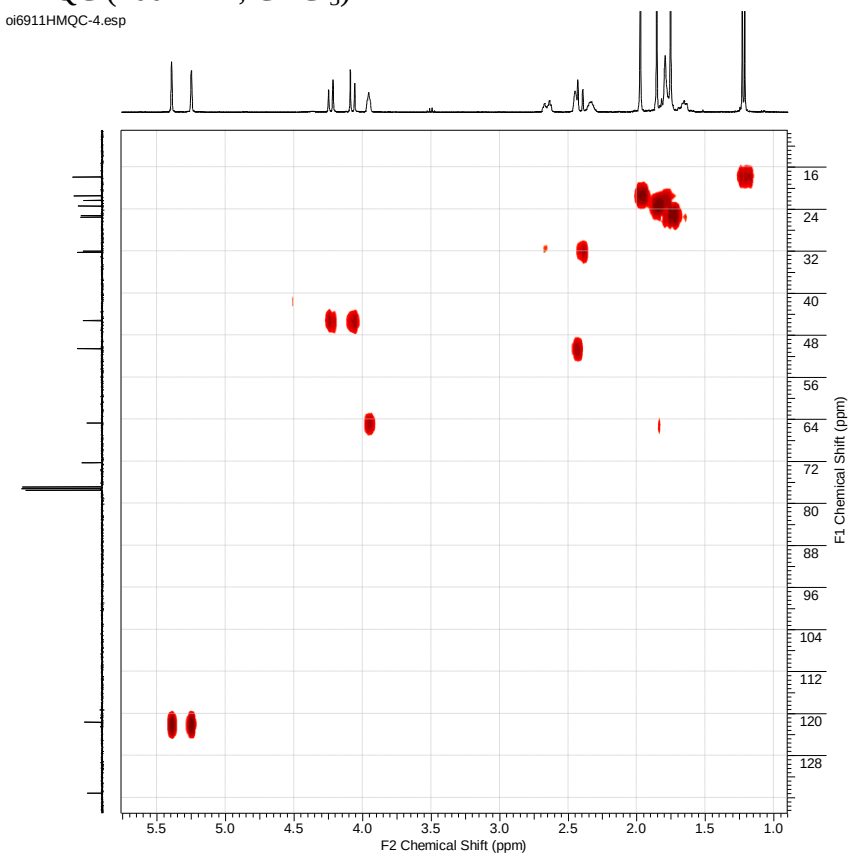
^{13}C-NMR (67.5 MHz, $CDCl_3$)



COSY (300 MHz, $CDCl_3$)

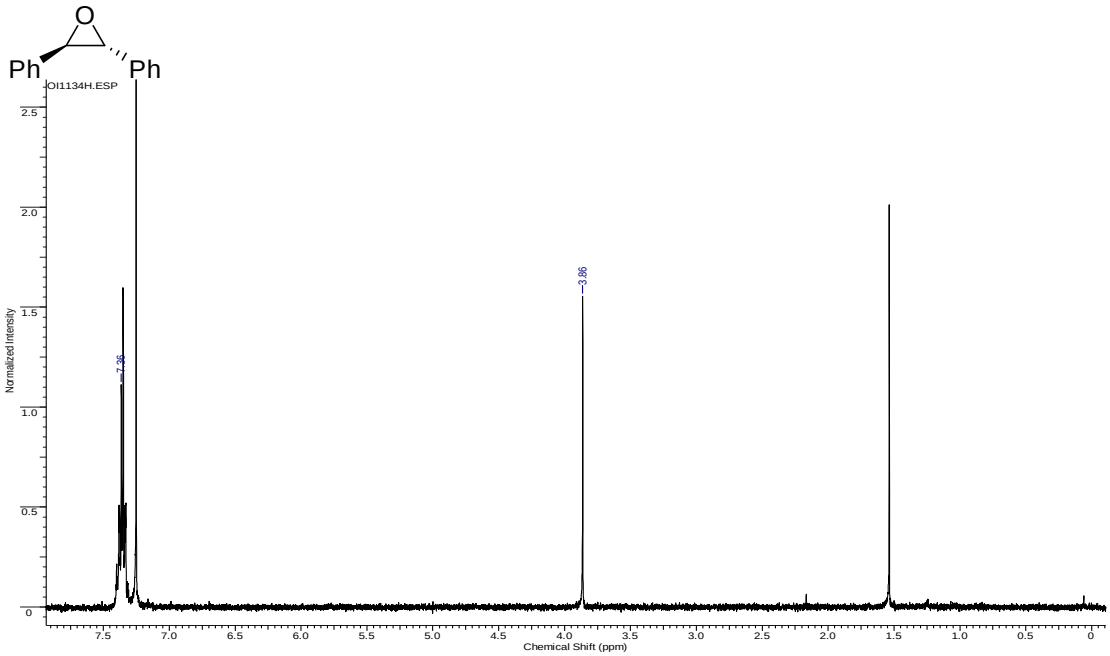


HMQC (400 MHz, $CDCl_3$)

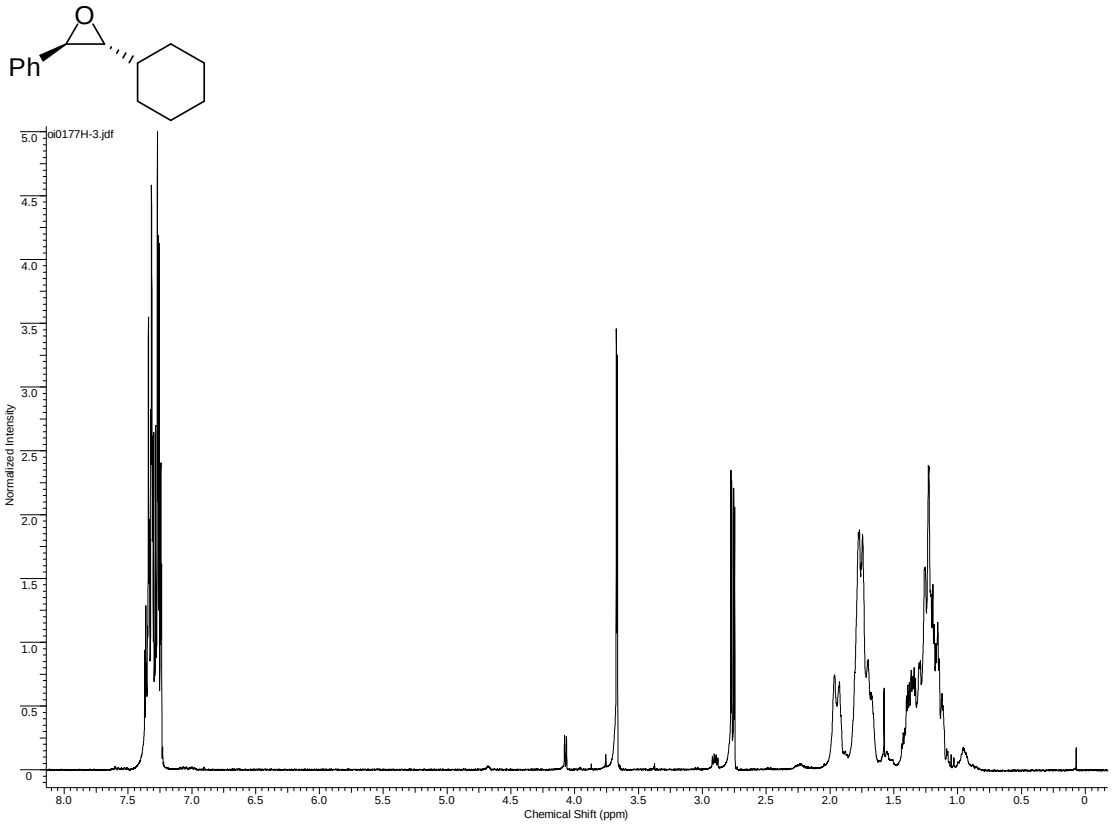


NMR Spectra for Epoxides

^{1}H-NMR (270 MHz, $CDCl_3$)

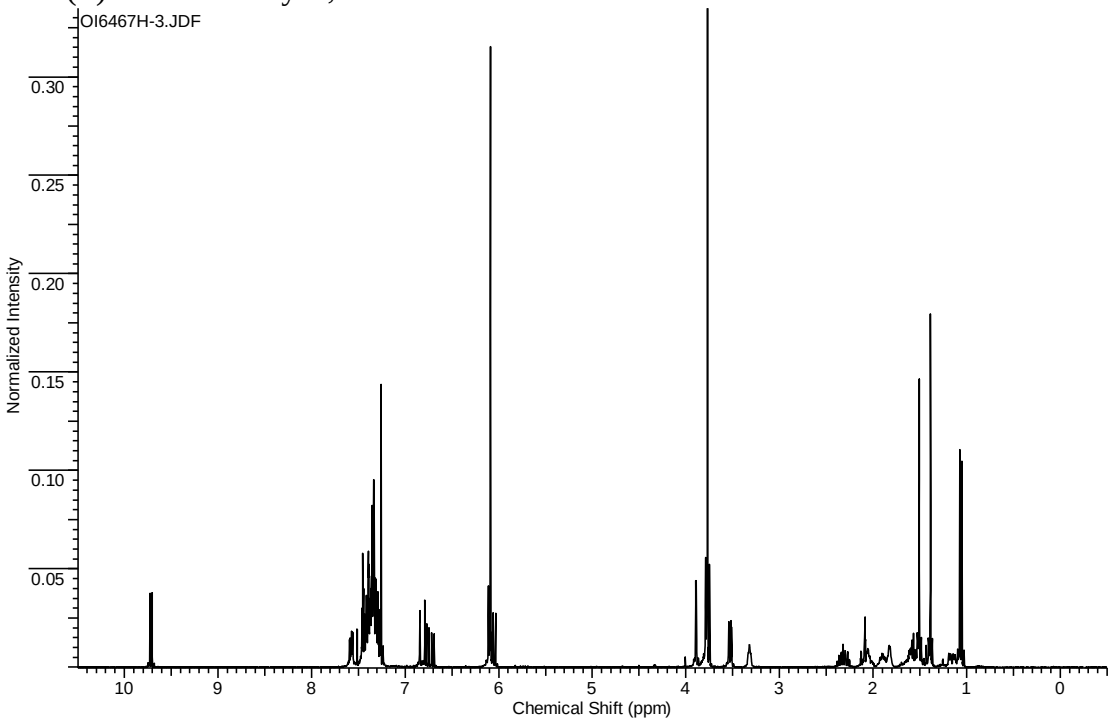


^{1}H-NMR (300 MHz, $CDCl_3$) mixture *trans*:*cis*



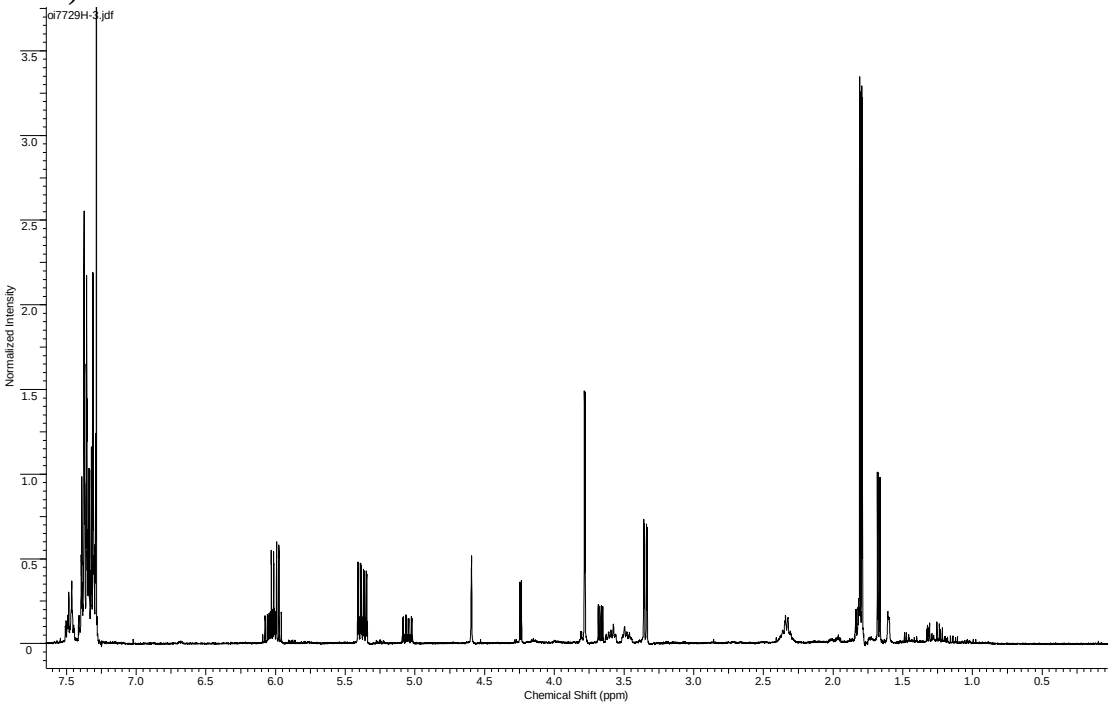
^{1}H-NMR ($CDCl_3$)

Crude ^{1}H NMR (270 MHz) spectrum from reaction of chiral benzyl sulfonium salt **A** with (*E*)-cinnamaldehyde; *trans*:*cis* >95:5

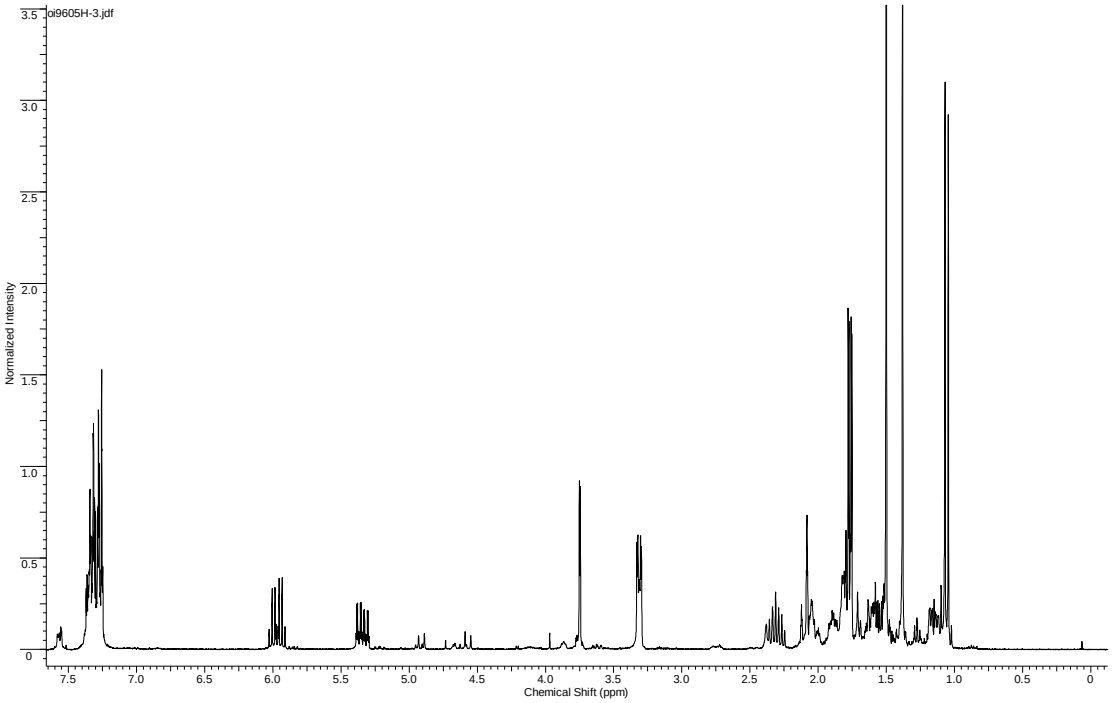


^{1}H-NMR ($CDCl_3$)

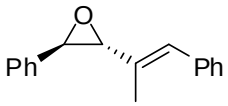
crude NMR: 1:0.3 *trans*:*cis* mixture from reaction with achiral sulfonium salt (400 MHz)



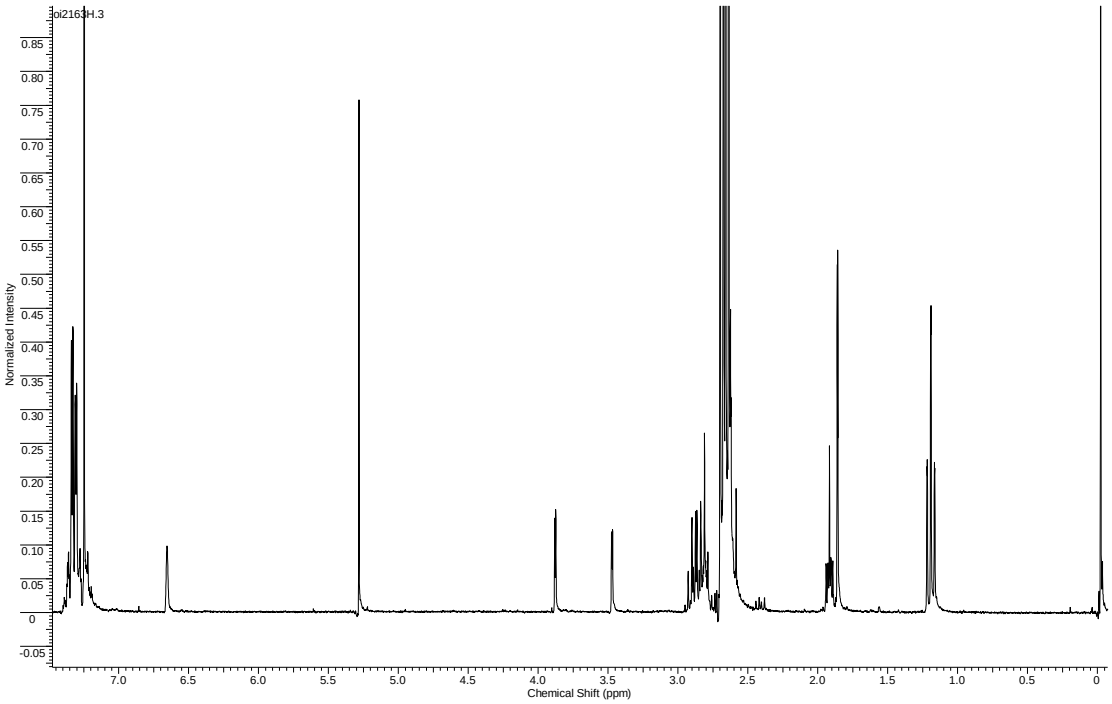
crude NMR: only *trans* epoxide from reaction with chiral sulfonium salt (300 MHz)



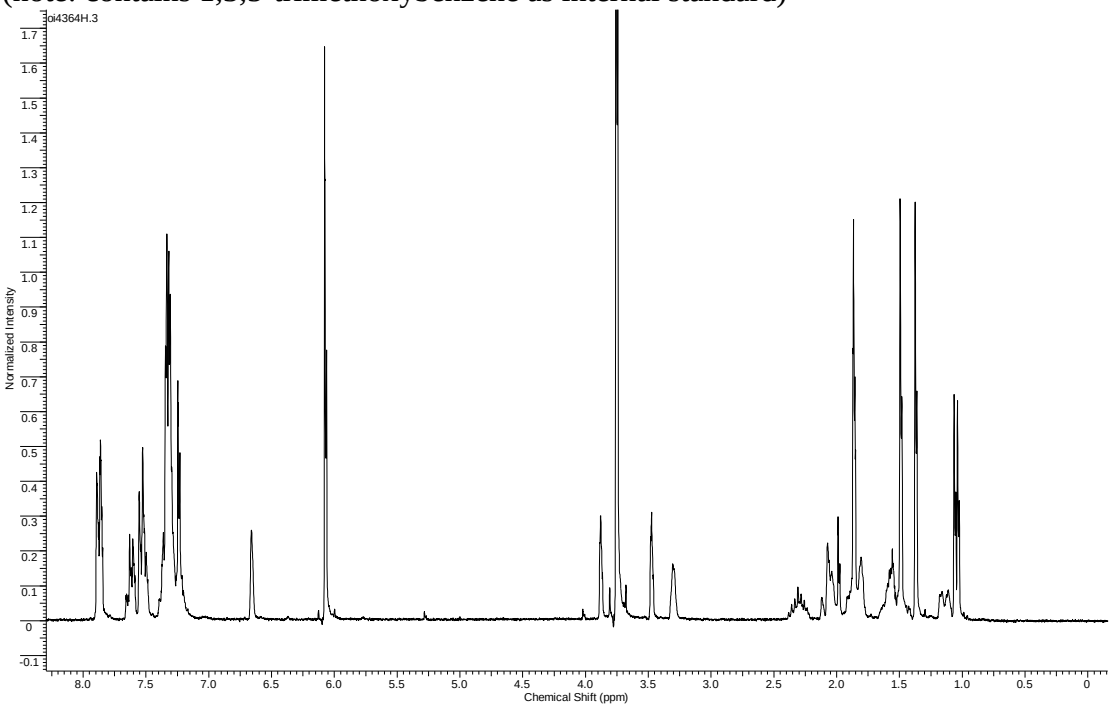
^{1}H-NMR ($CDCl_3$)



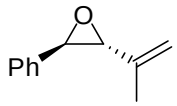
crude NMR: *trans* epoxide from reaction with achiral sulfonium salt (270 MHz)



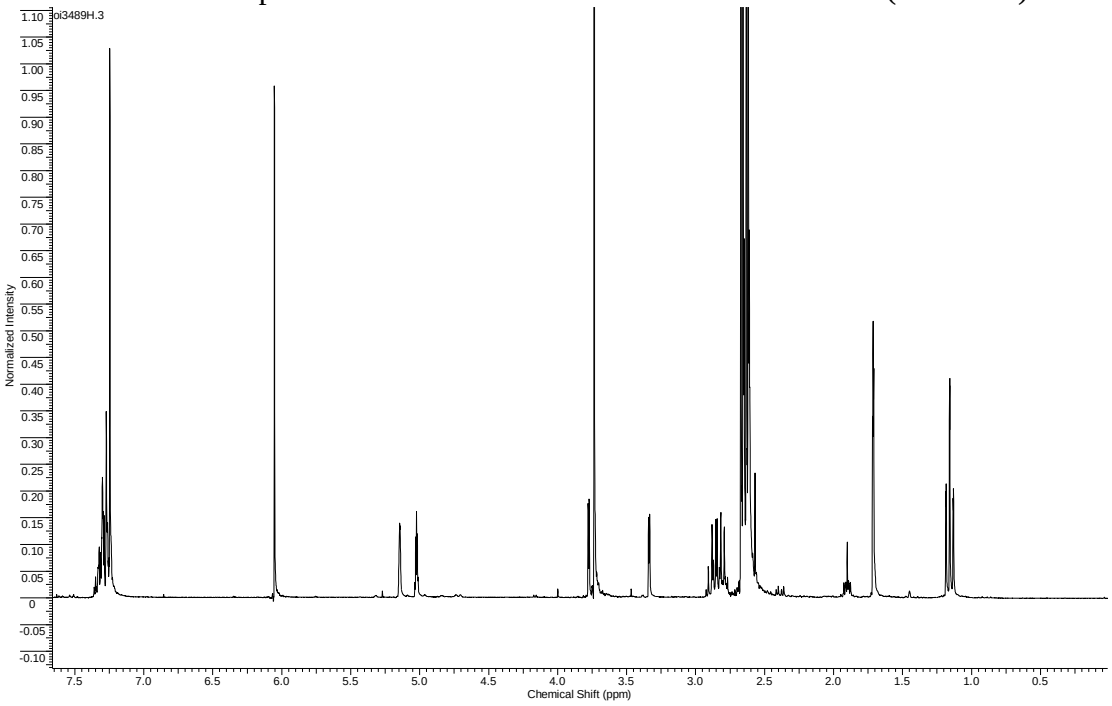
crude NMR: only *trans* epoxide from reaction with chiral sulfonium salt (300 MHz)
(note: contains 1,3,5-trimethoxybenzene as internal standard)



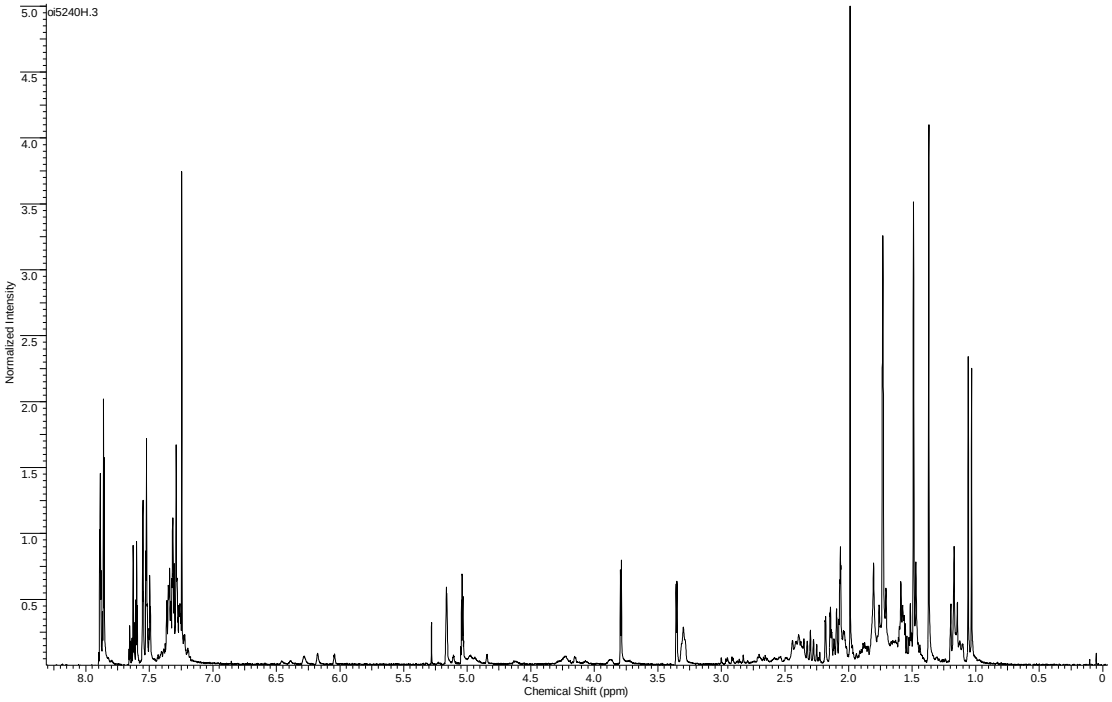
^{1}H-NMR ($CDCl_3$)



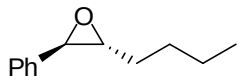
crude NMR: *trans* epoxide from reaction with achiral sulfonium salt (270 MHz)



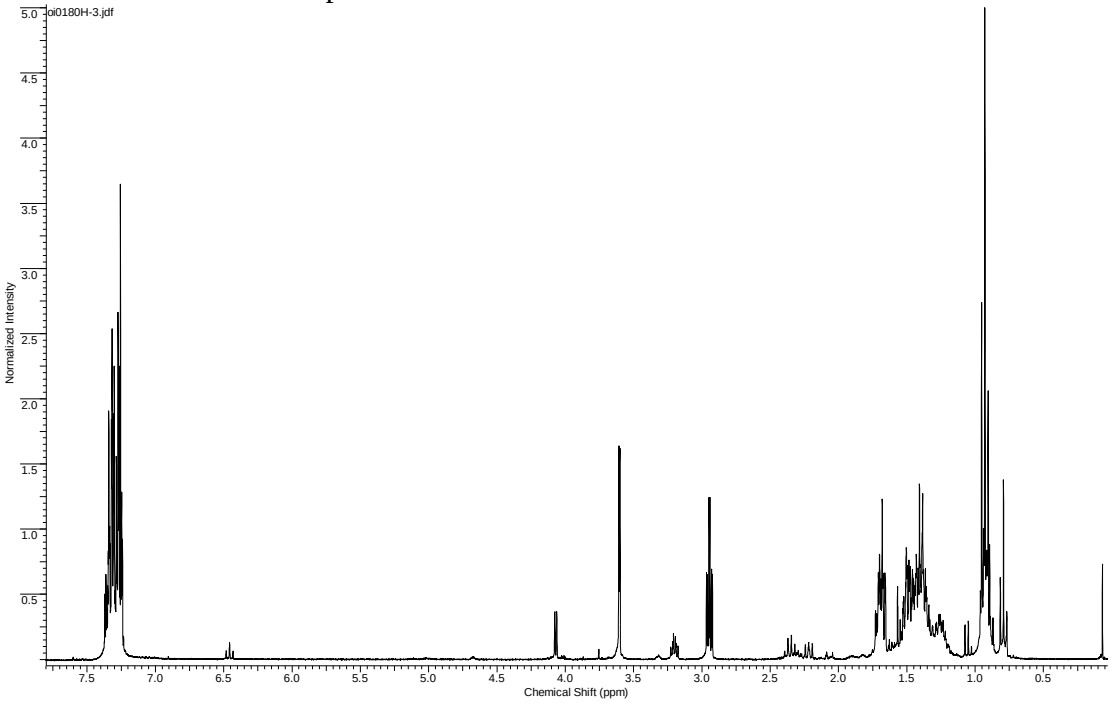
crude NMR: only *trans* epoxide from reaction with chiral sulfonium salt (270 MHz)



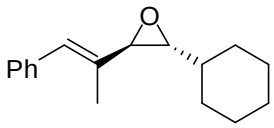
^{1}H-NMR (300 MHz, $CDCl_3$)



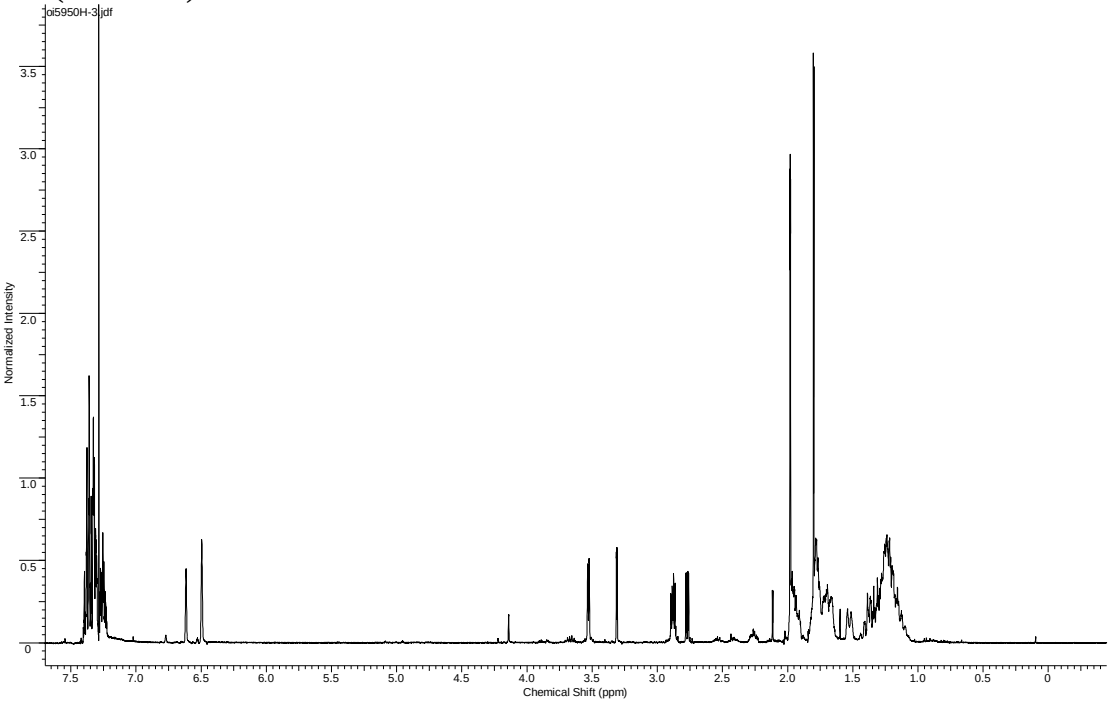
4:1 mixture of *trans*:*cis* epoxide from reaction with achiral sulfonium salt



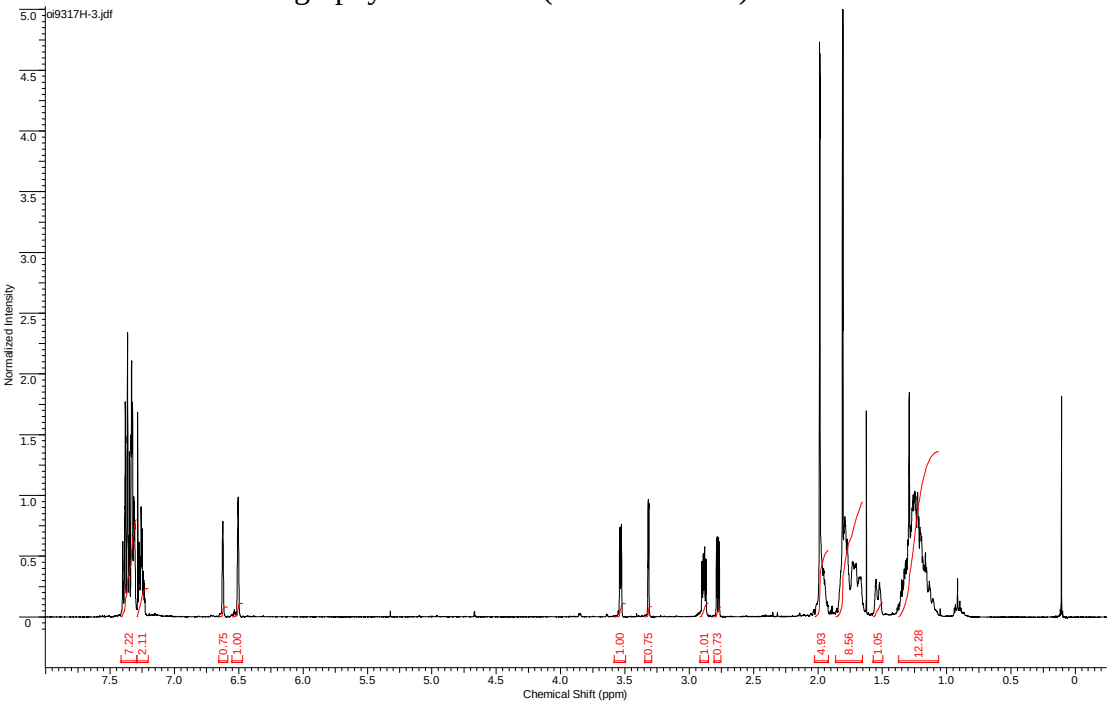
^{1}H-NMR (400 MHz, $CDCl_3$)



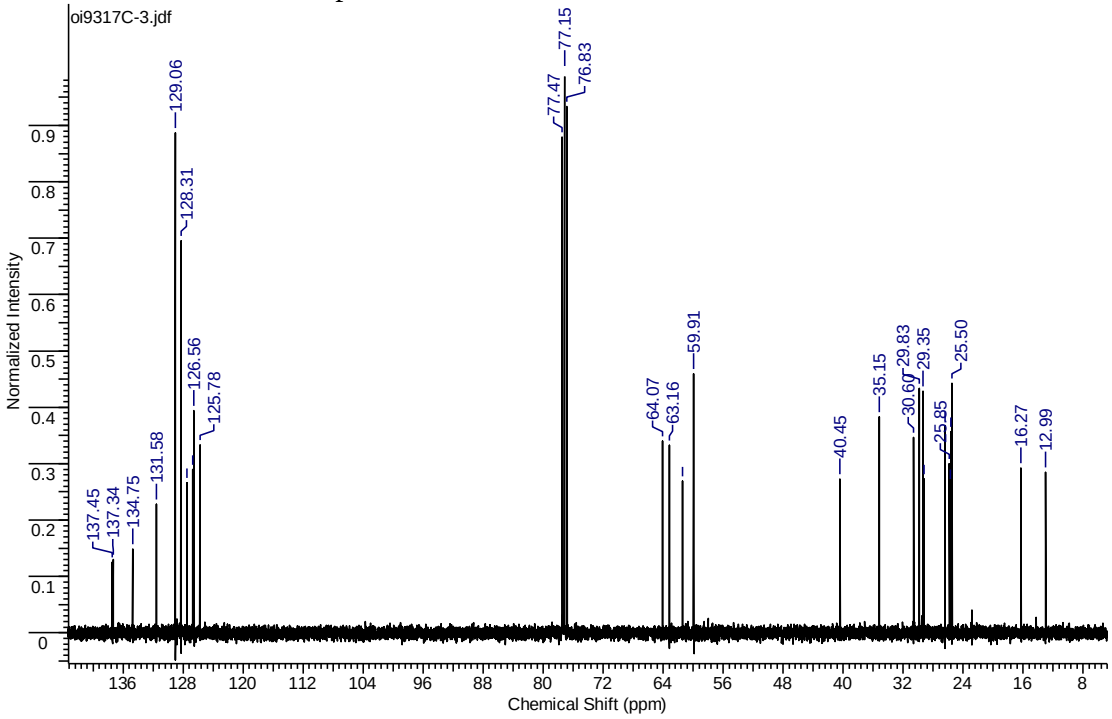
crude NMR: 1:1.5 mixture of *trans*:*cis* epoxide from reaction with achiral sulfonium salt (400 MHz)



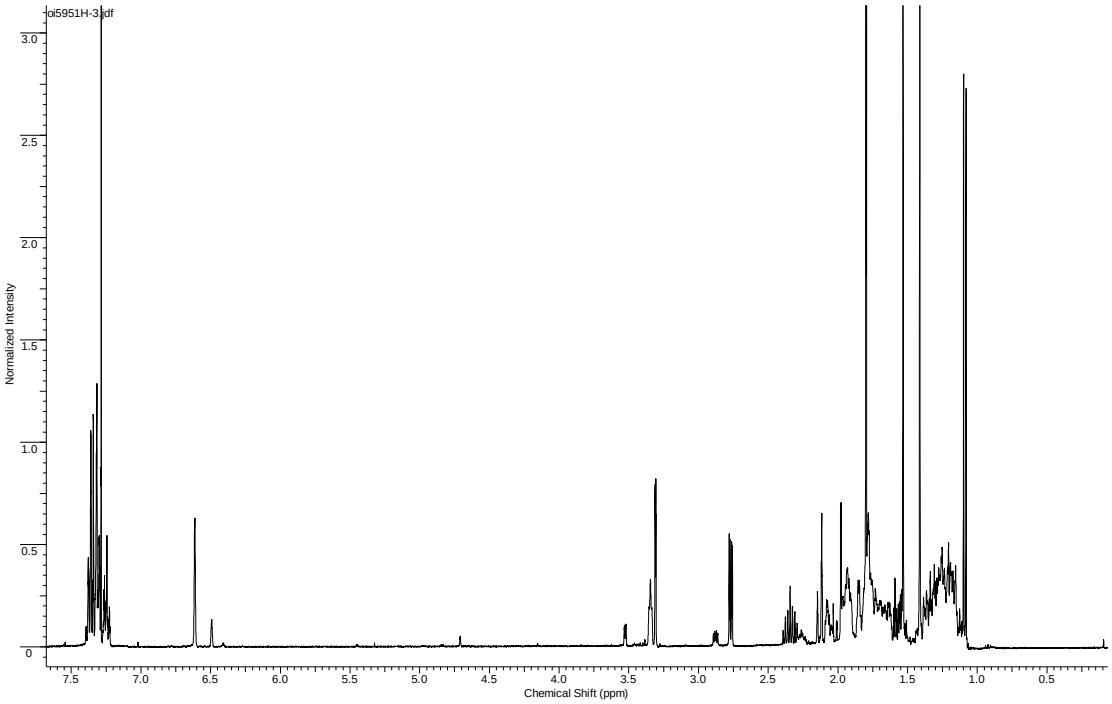
After careful chromatography on alumina (5% EtOAc/PE).



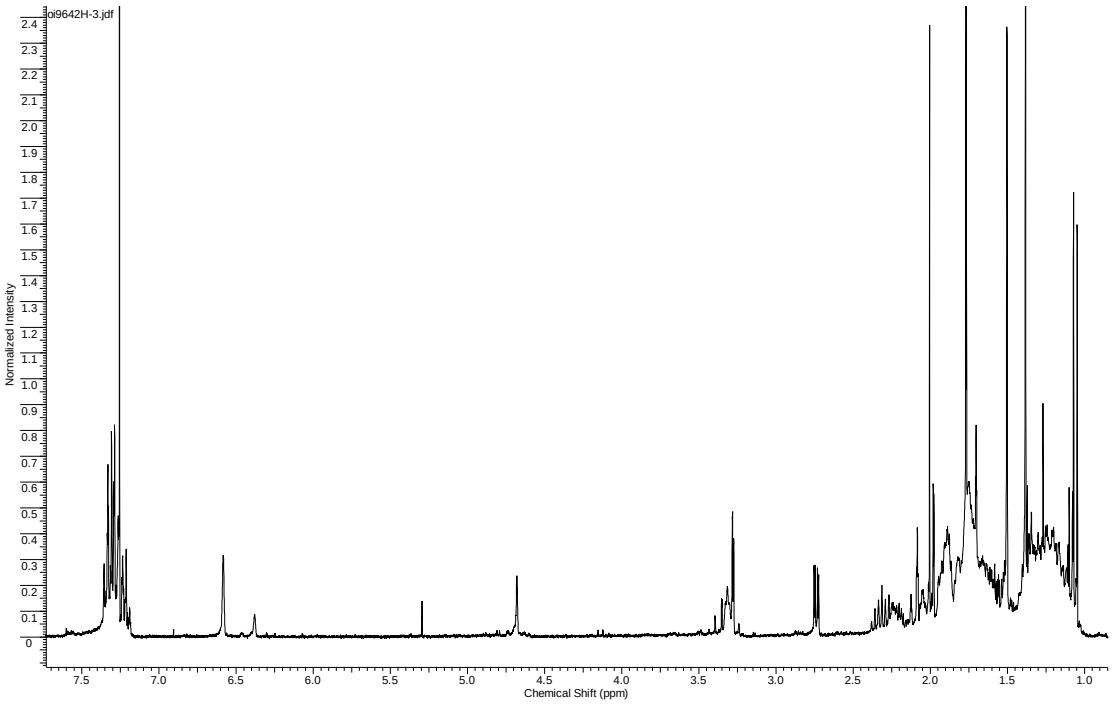
^{13}C NMR ($CDCl_3$, 100 MHz)
Mixture of *cis* and *trans*-epoxides



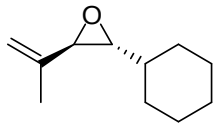
crude NMR: 1:0.2 mixture of *trans*:*cis* epoxides from reaction with chiral sulfonium salt ($CDCl_3$, 400 MHz) Method A



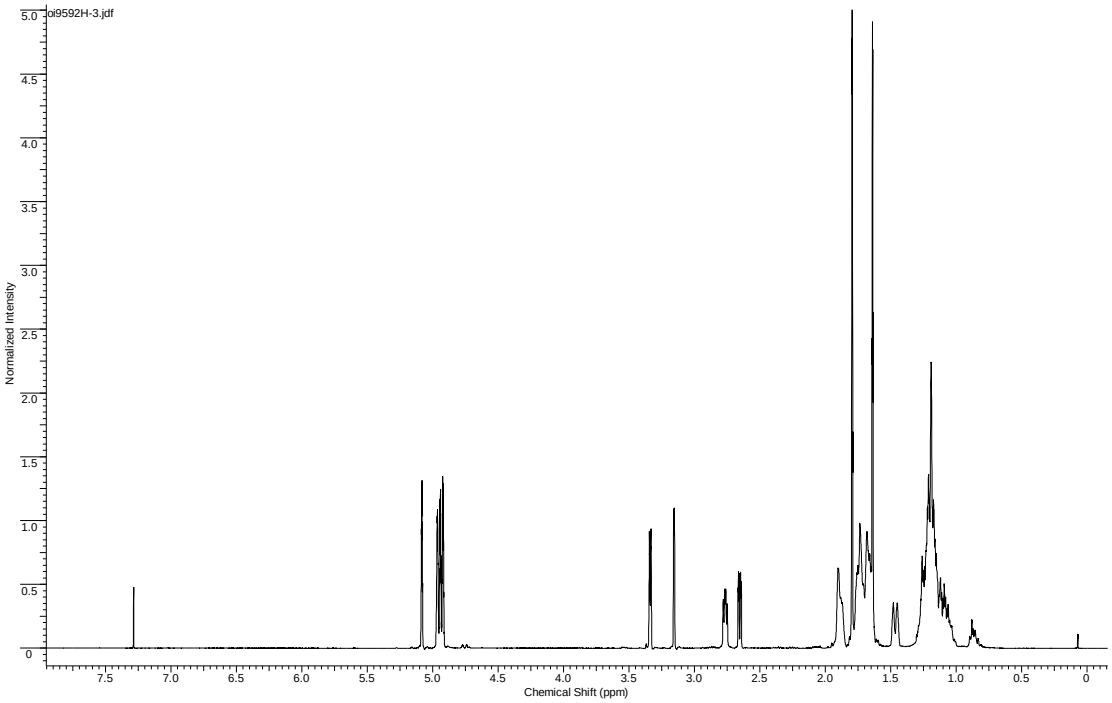
crude ^1H NMR: *trans* epoxide from reaction with chiral sulfonium salt (400 MHz, $CDCl_3$) Method B

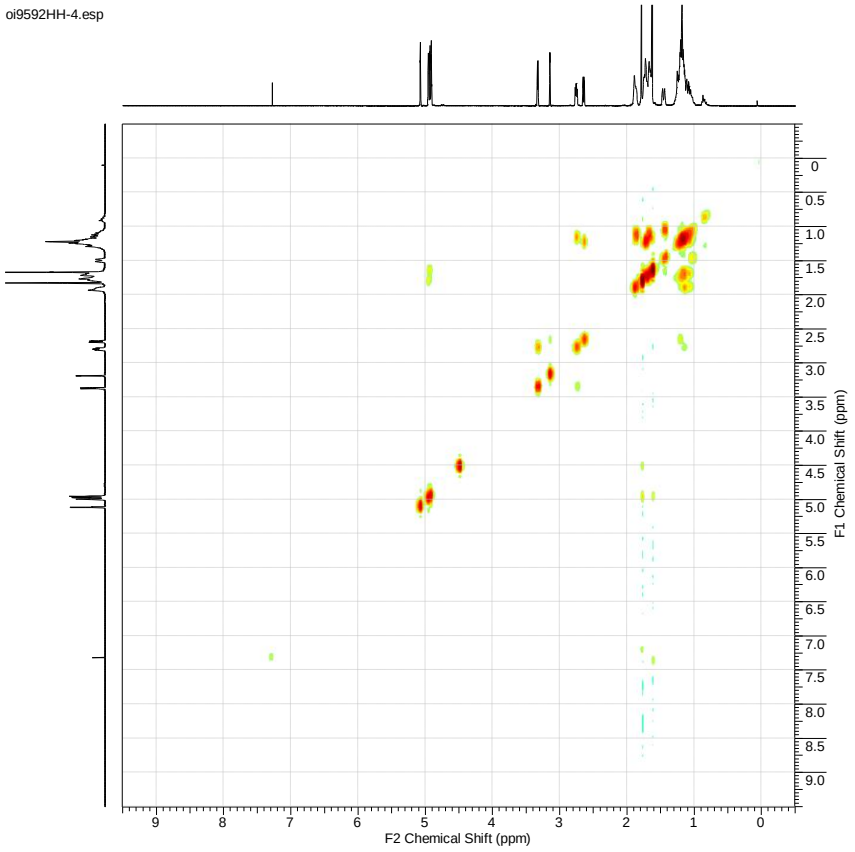


^{1}H-NMR (400 MHz, $CDCl_3$)

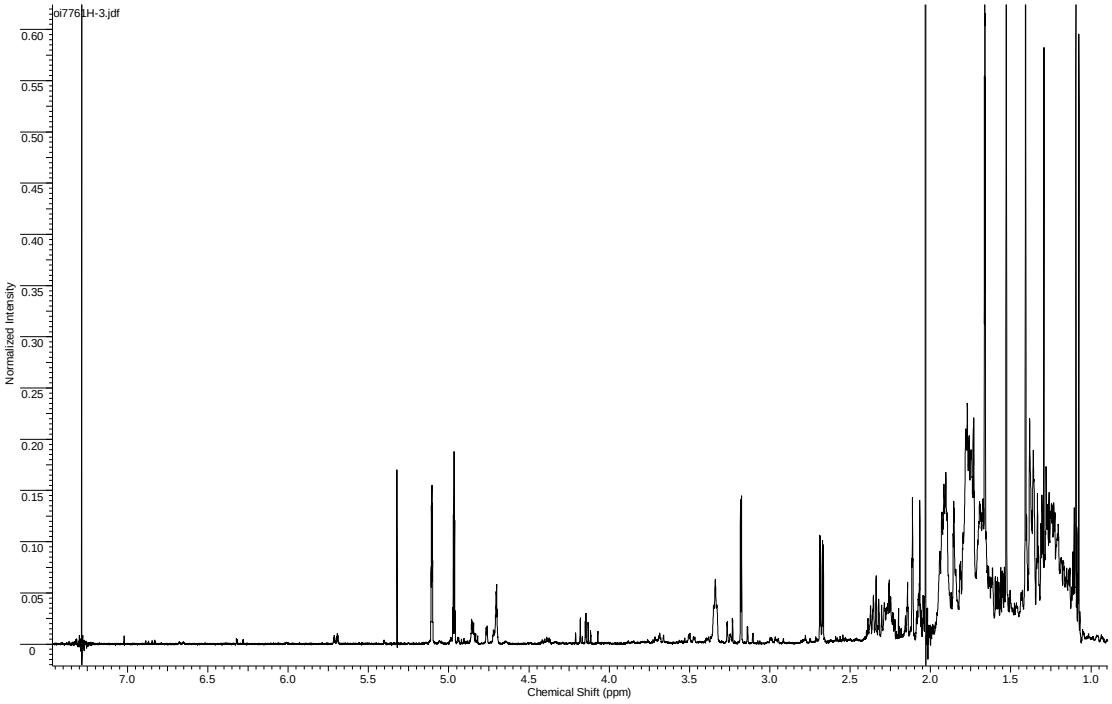


crude NMR: 1:1.1 mixture of *trans*:*cis* epoxide from reaction with achiral sulfonium salt



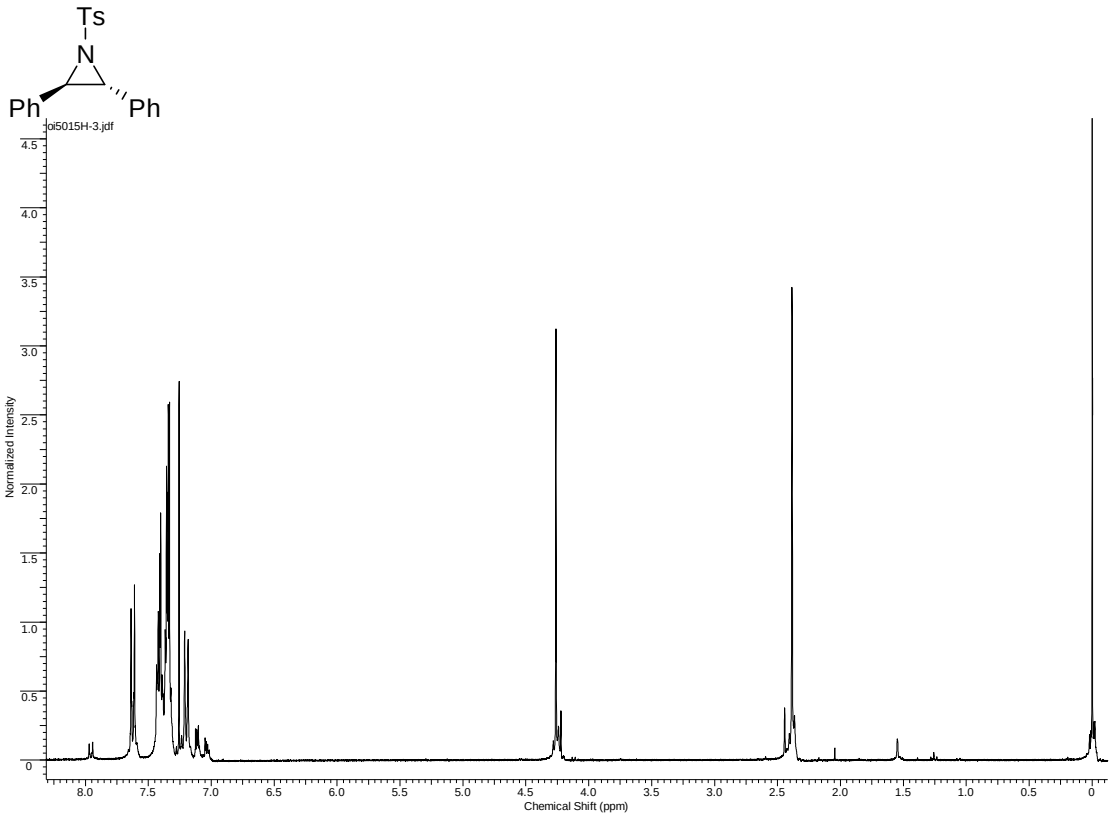


crude NMR: *trans* epoxide from reaction with chiral sulfonium salt (400 MHz)

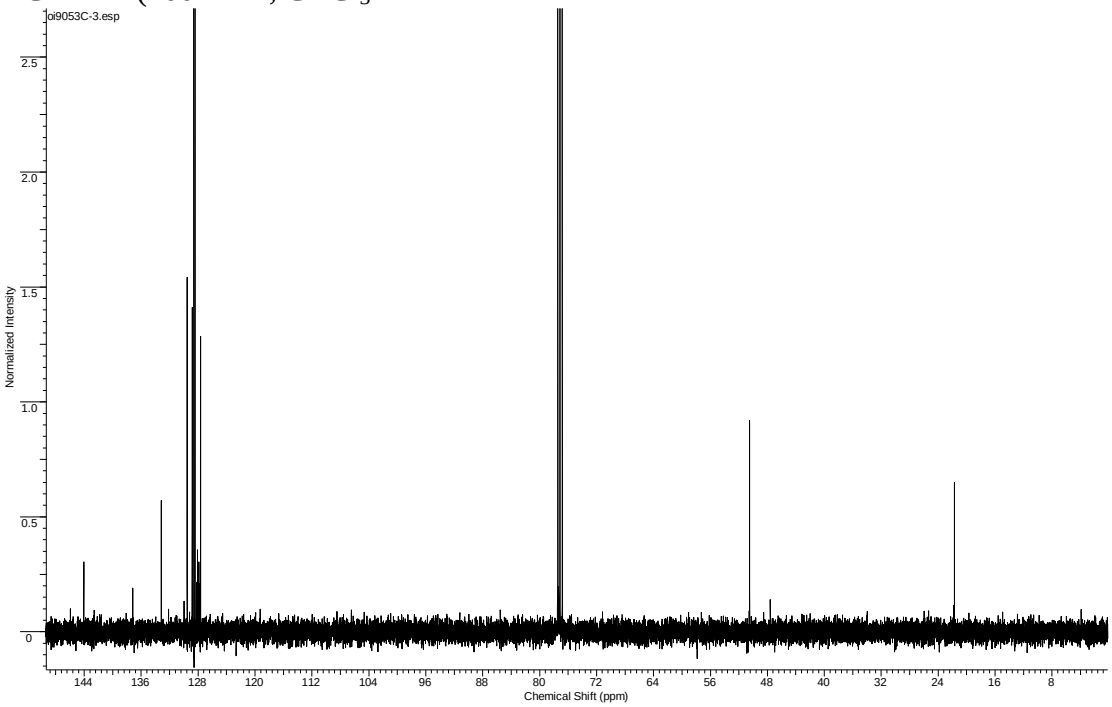


NMR Spectra for Aziridines

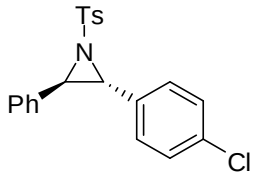
^{1}H-NMR (300 MHz, $CDCl_3$) mixture *trans*:*cis* 6:1

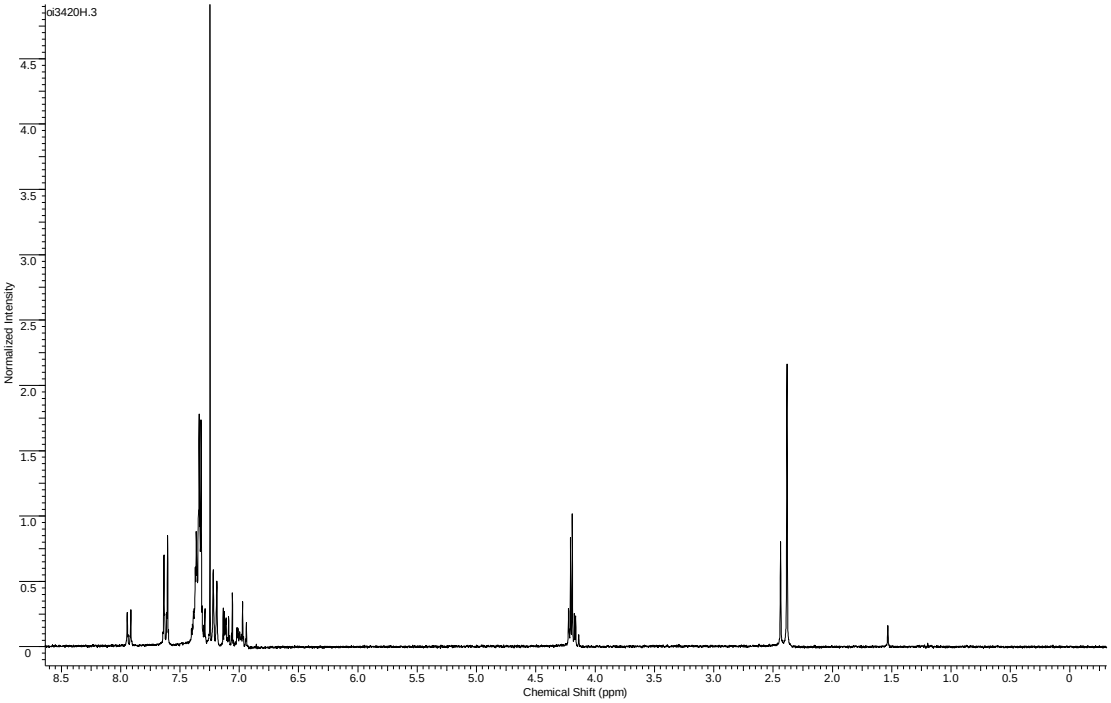


^{13}C-NMR (100 MHz, $CDCl_3$

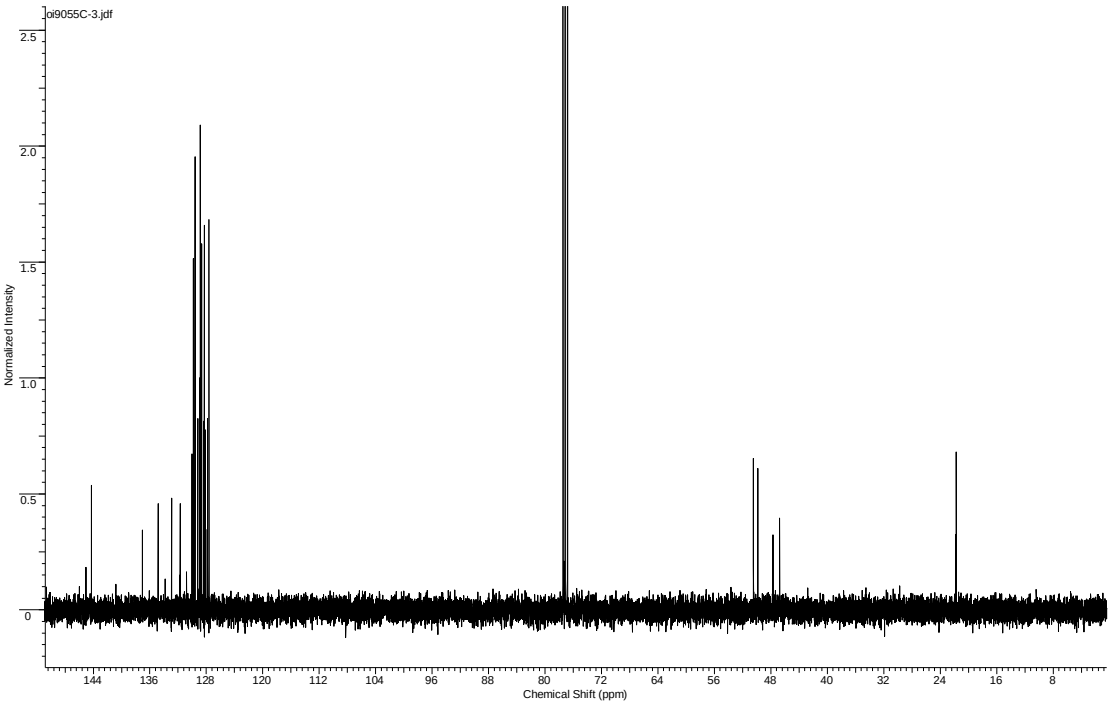


^{1}H-NMR (270 MHz, $CDCl_3$) mixture *trans*:*cis* 2.6:1

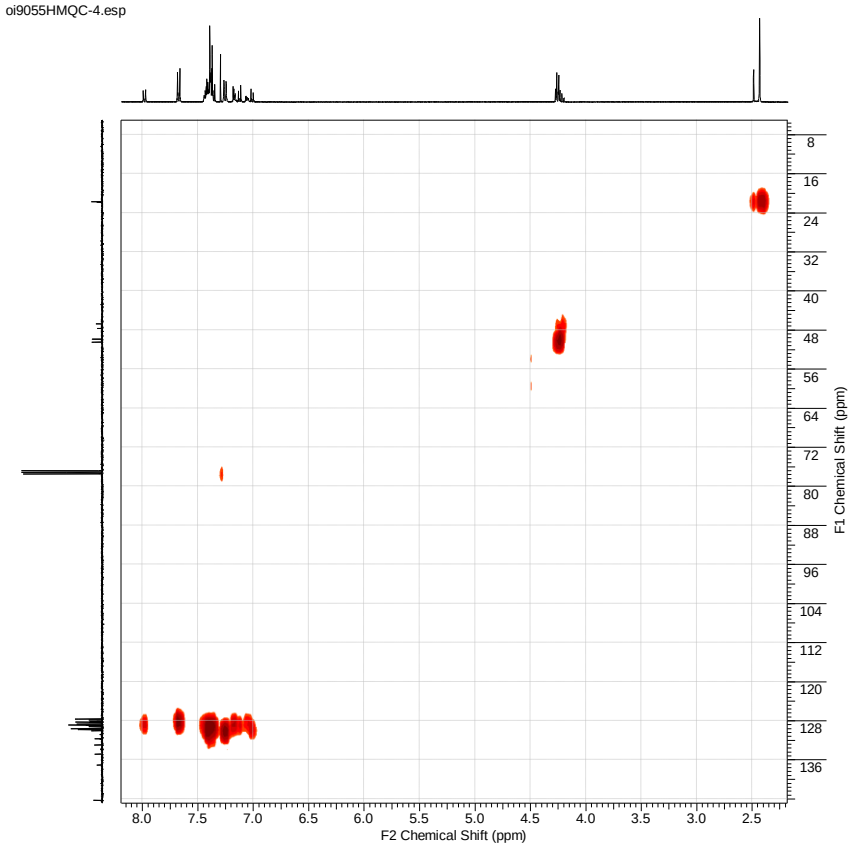




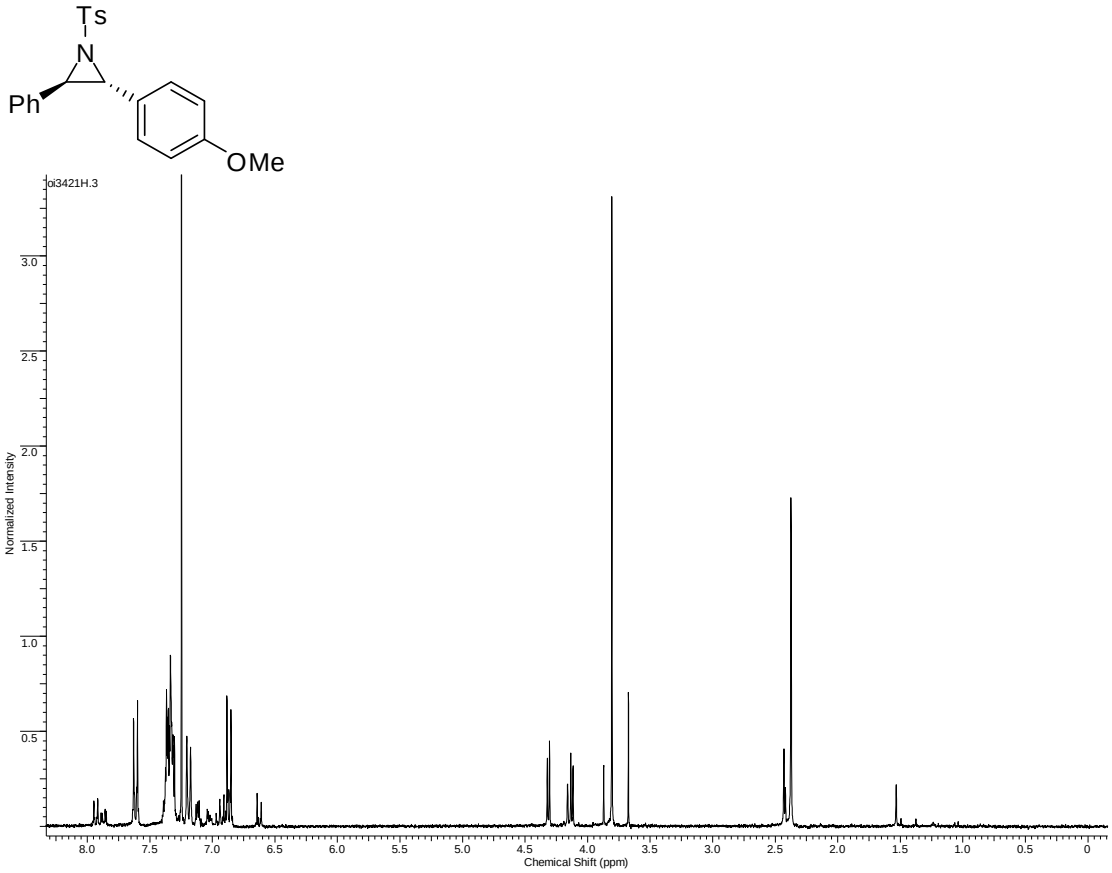
^{13}C-NMR (100 MHz, $CDCl_3$)



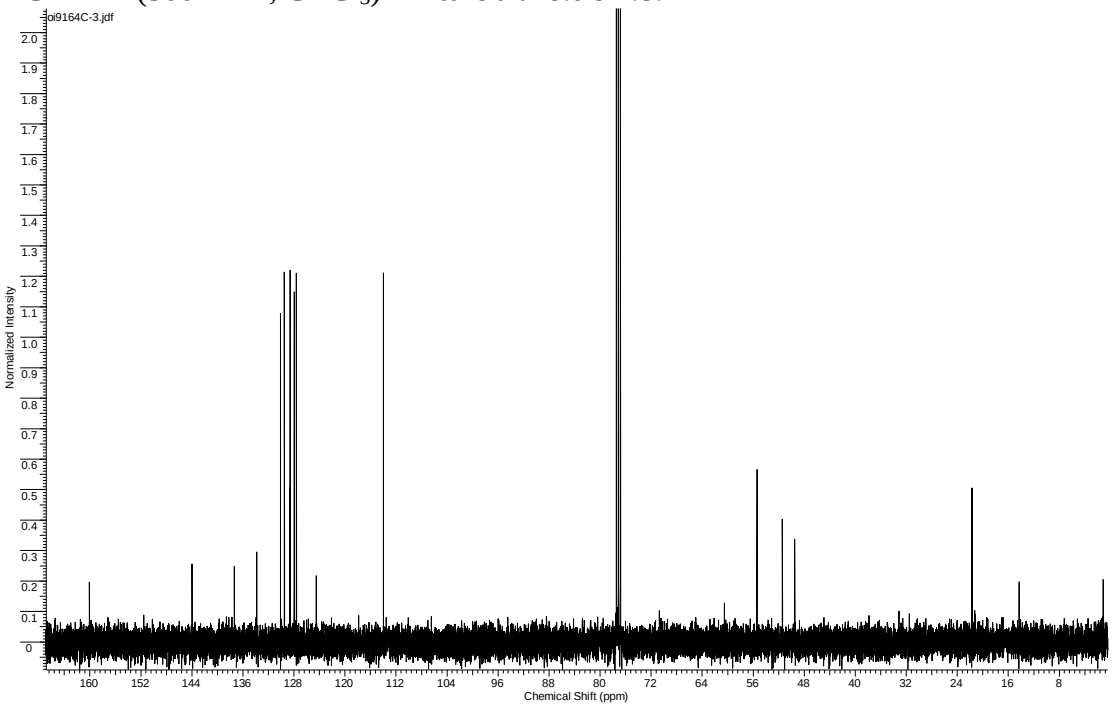
HMQC (400 MHz, $CDCl_3$)



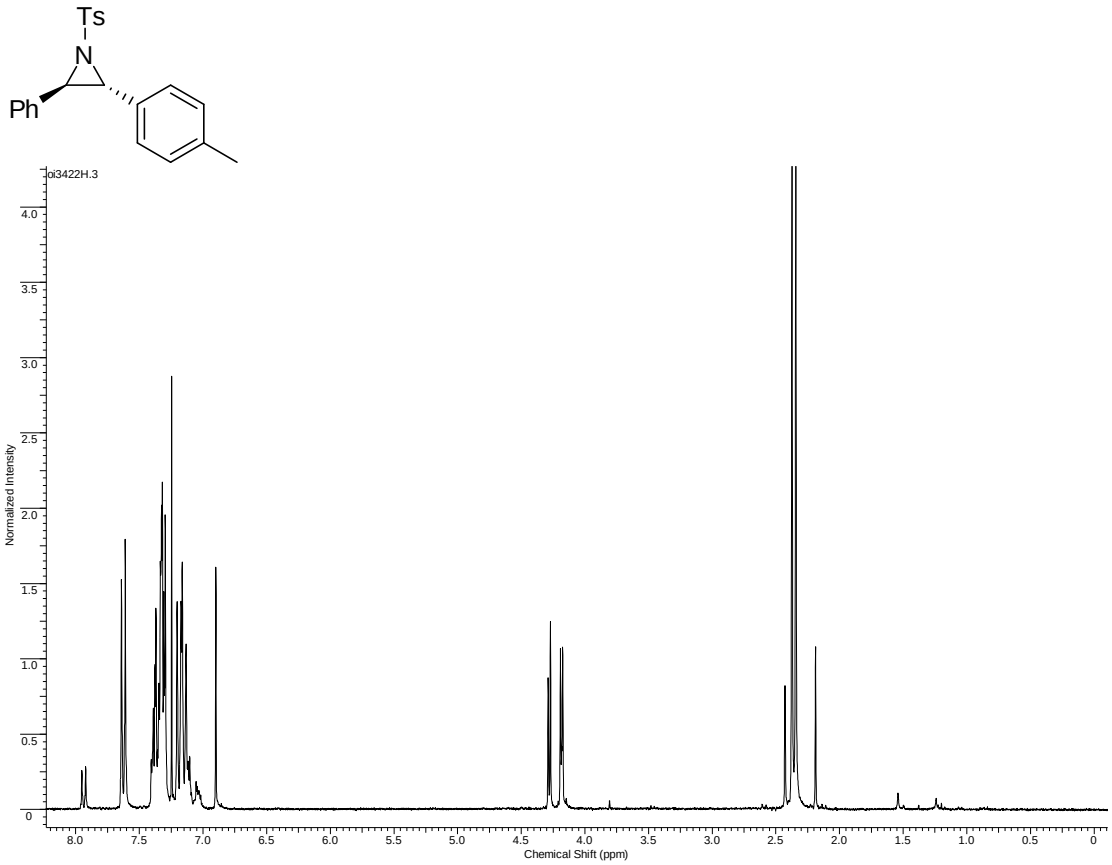
^{1}H-NMR (300 MHz, $CDCl_3$) mixture *trans*:*cis* 4.8:1



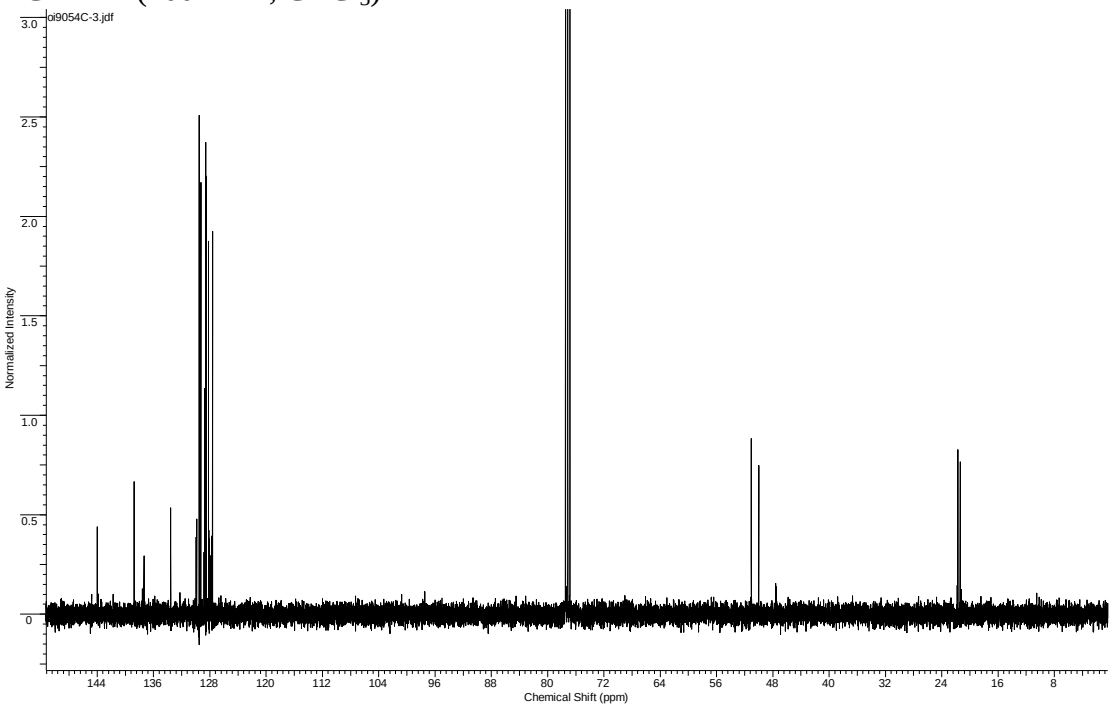
^{13}C-NMR (300 MHz, $CDCl_3$) mixture *trans*:*cis* 4.8:1



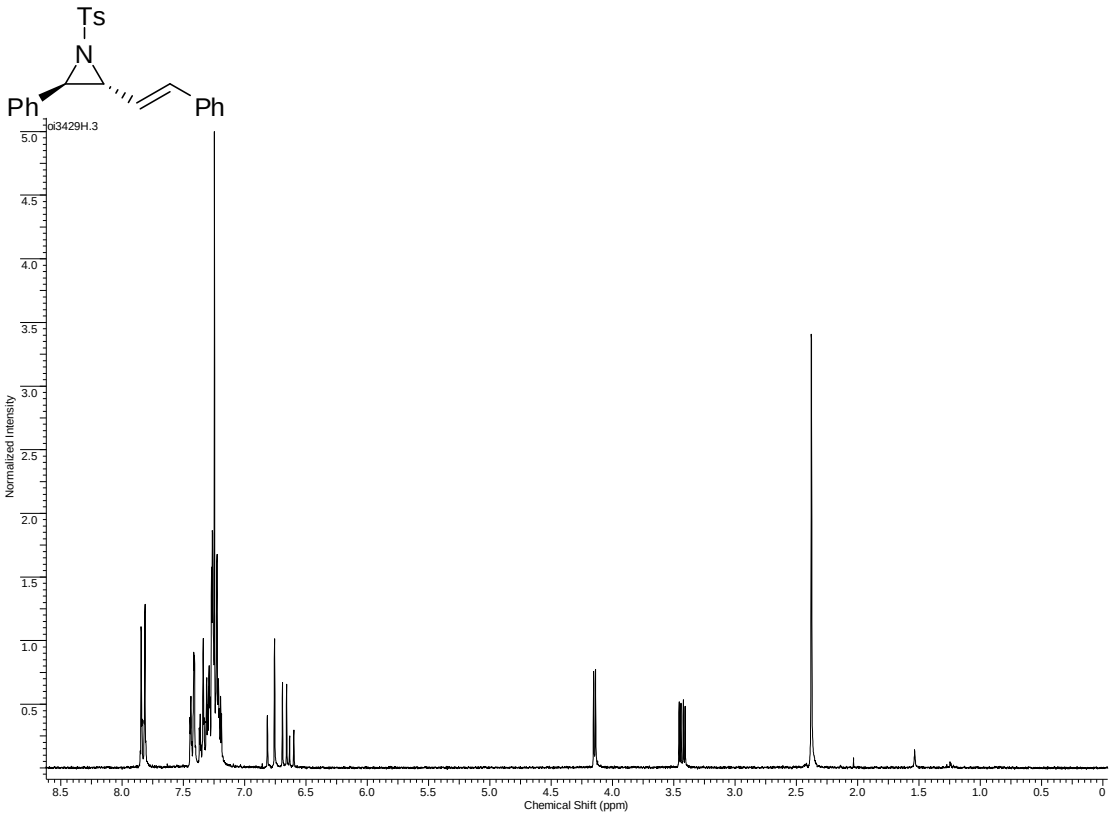
^{1}H-NMR (270 MHz, $CDCl_3$) mixture *trans*:*cis* 6:1



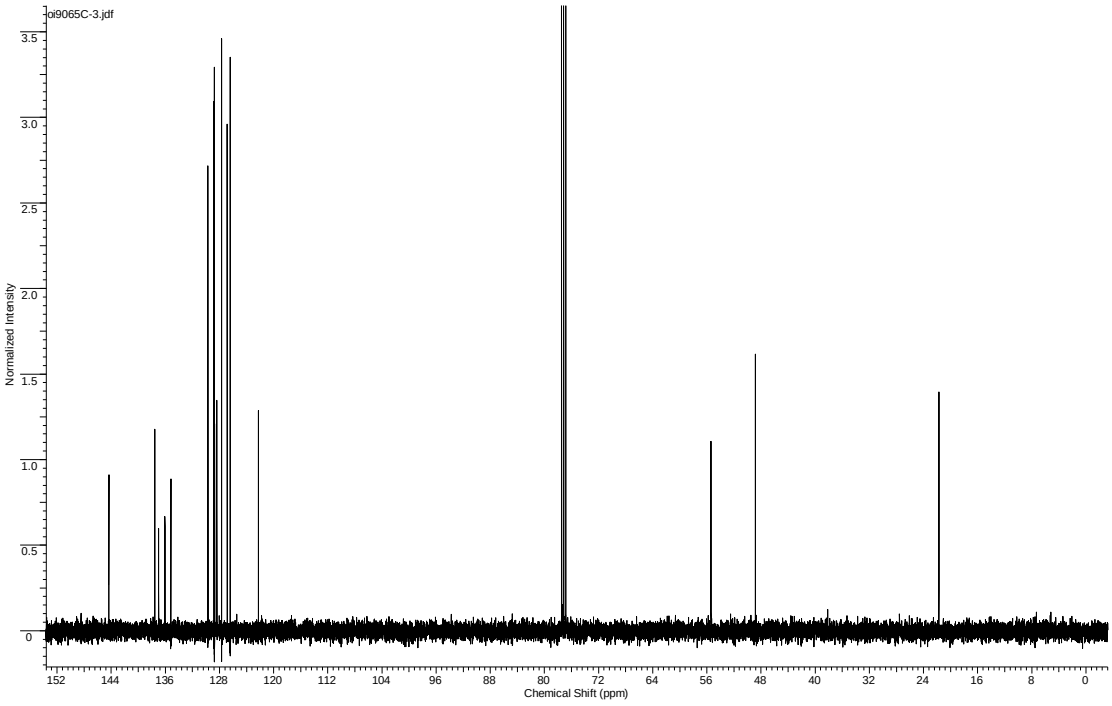
^{13}C-NMR (100 MHz, $CDCl_3$)



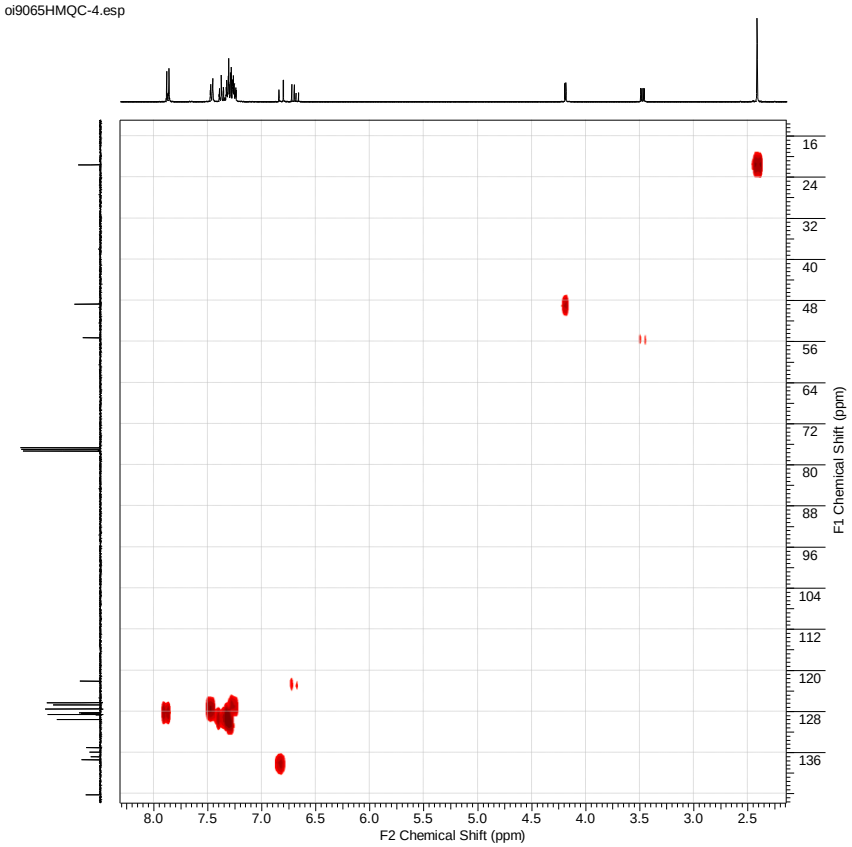
^{1}H-NMR (270 MHz, $CDCl_3$)



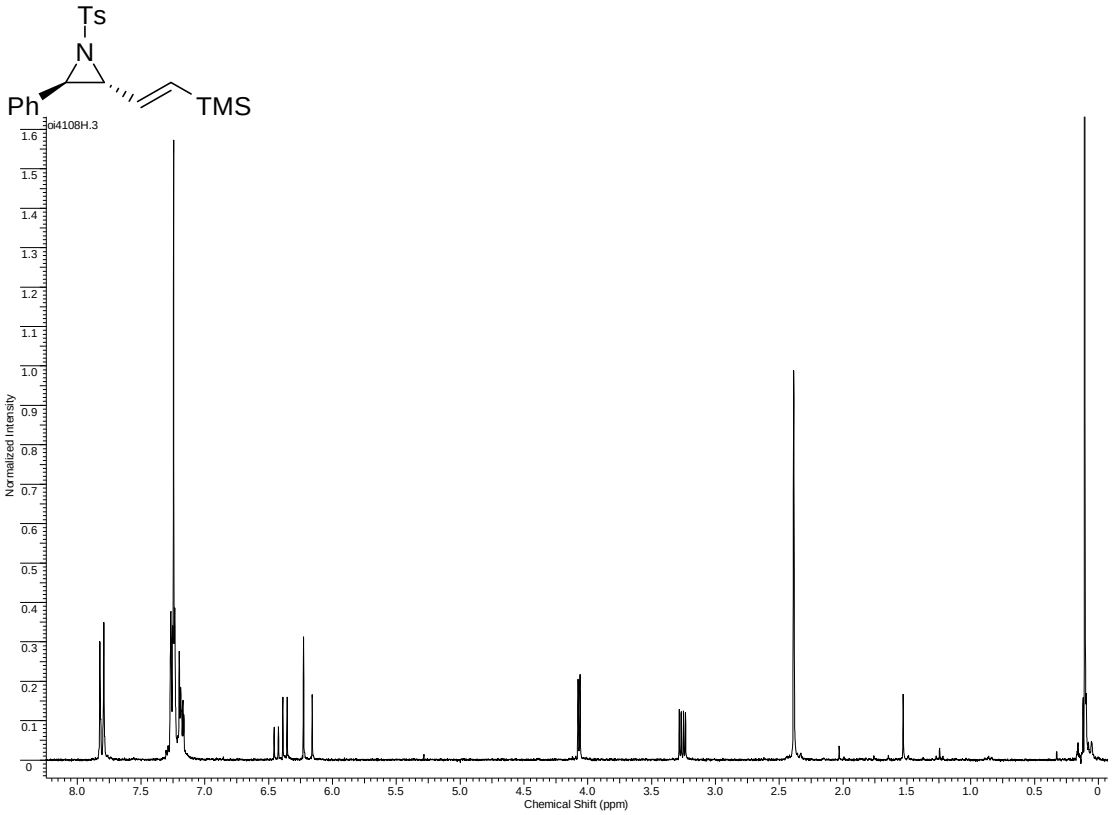
^{13}C-NMR (100 MHz, $CDCl_3$)



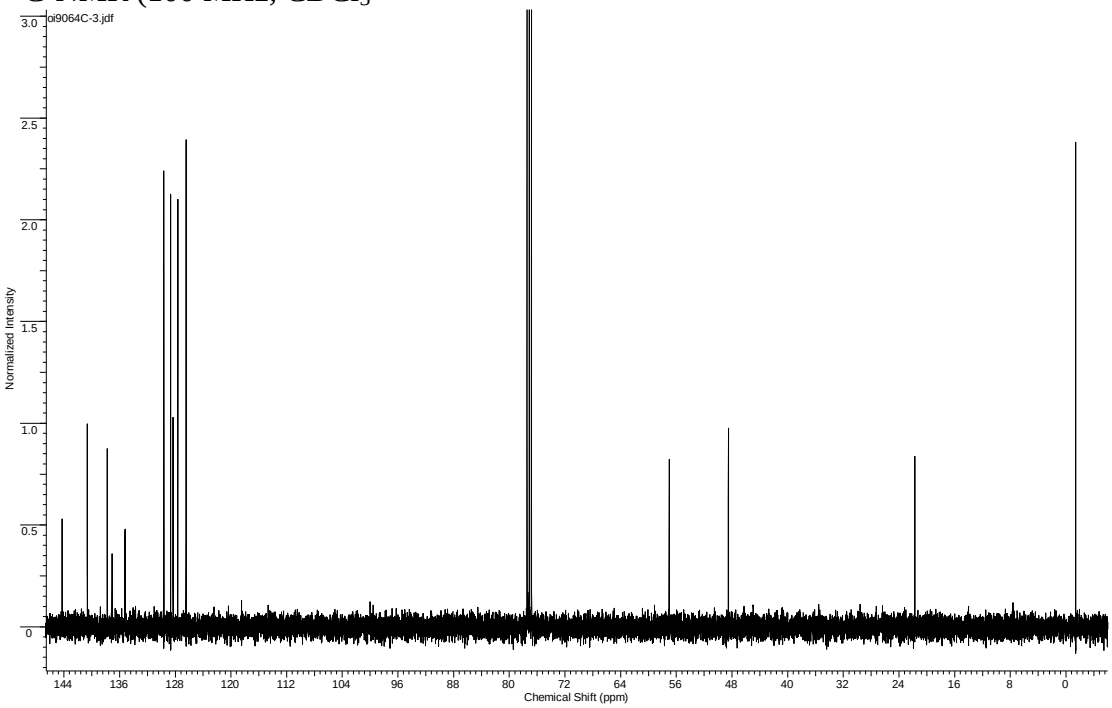
HMQC (400 MHz, $CDCl_3$)



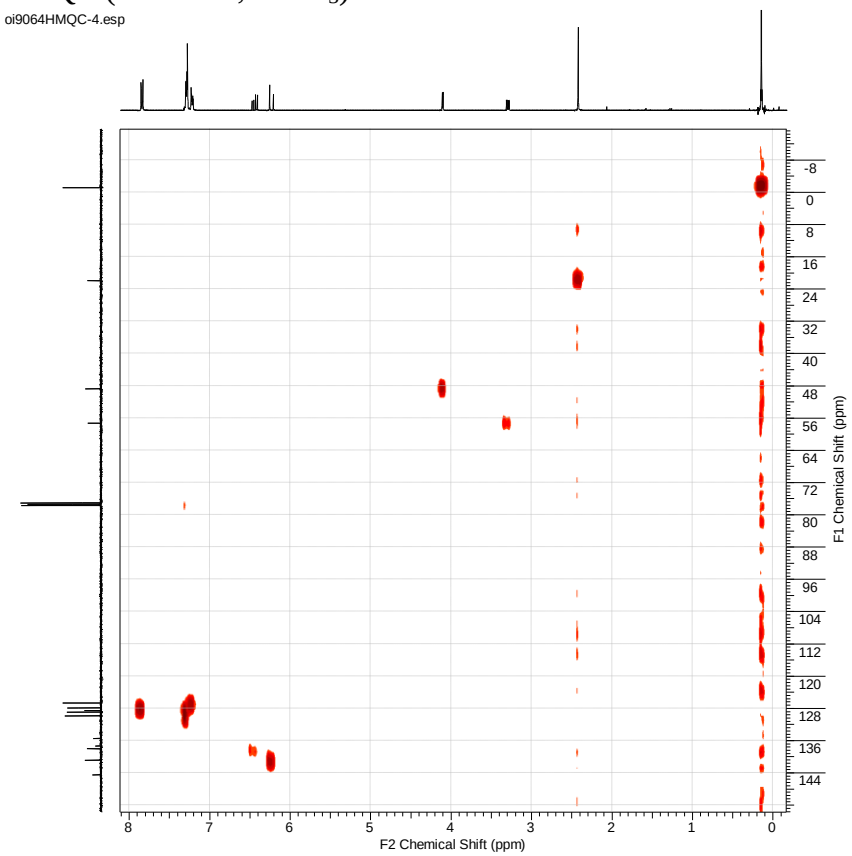
^{1}H-NMR (270 MHz, $CDCl_3$)



^{13}C-NMR (100 MHz, $CDCl_3$

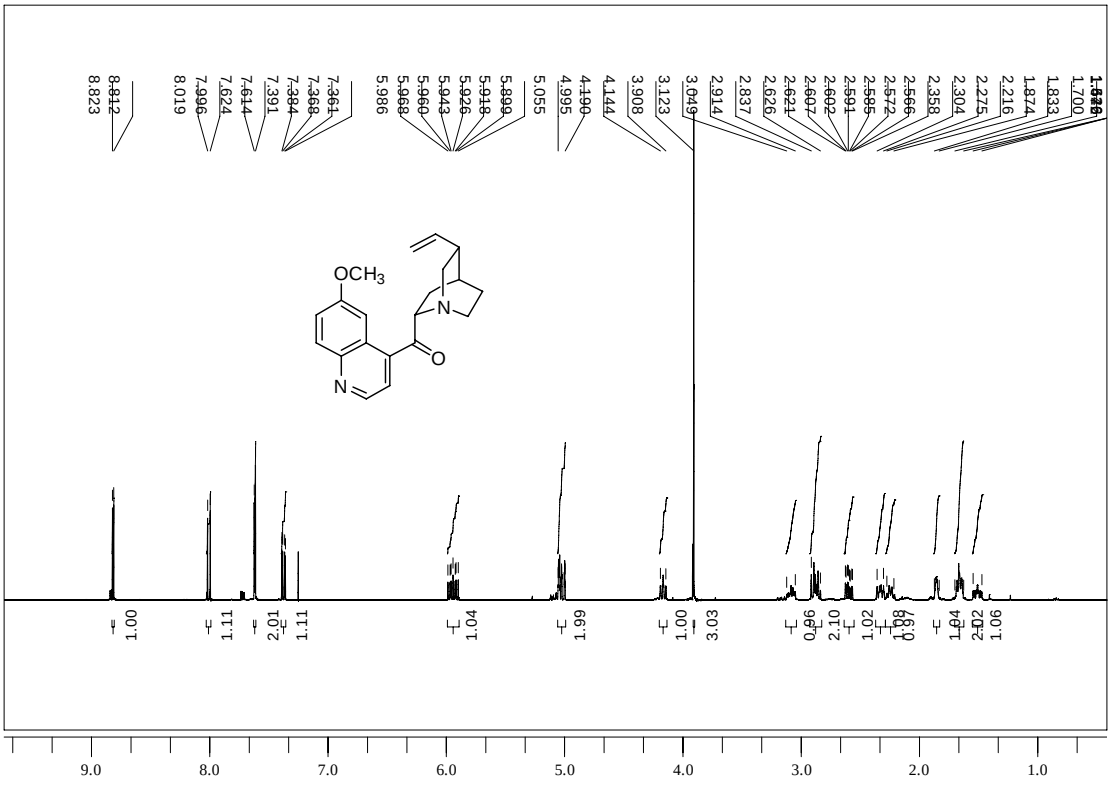


HMQC (400 MHz, $CDCl_3$)

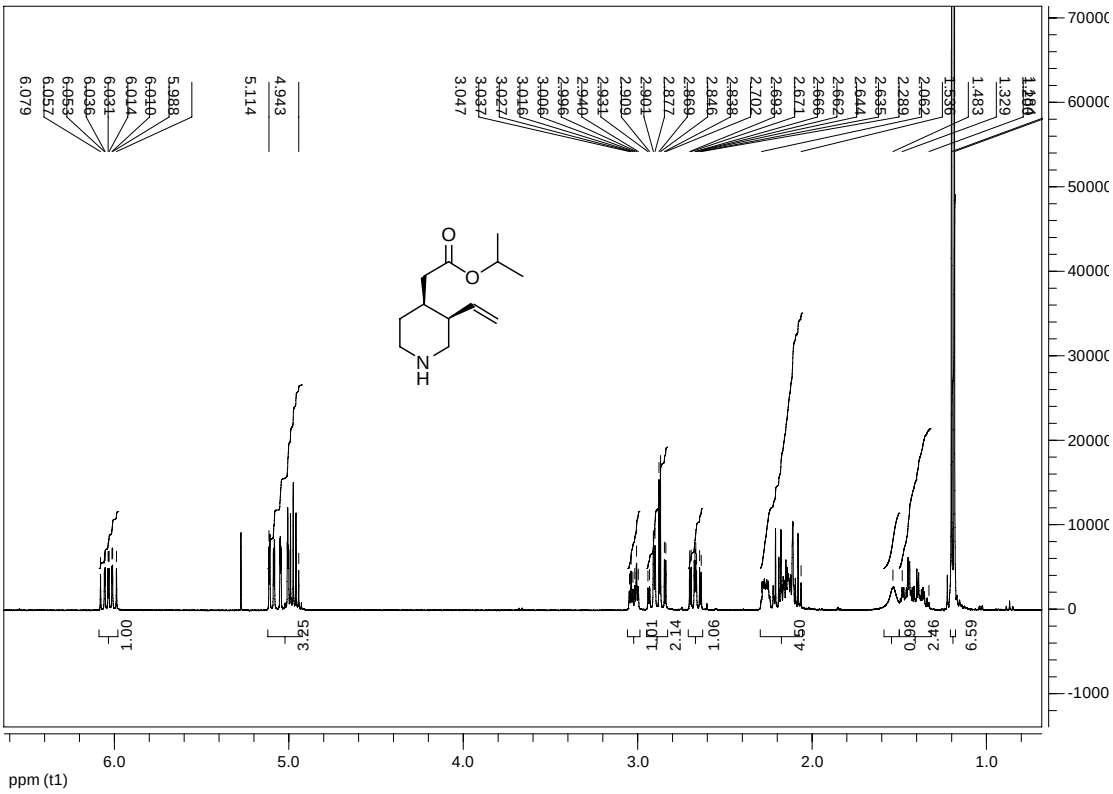


NMR Spectra for precursors to Quinine and Quinidine 6-15

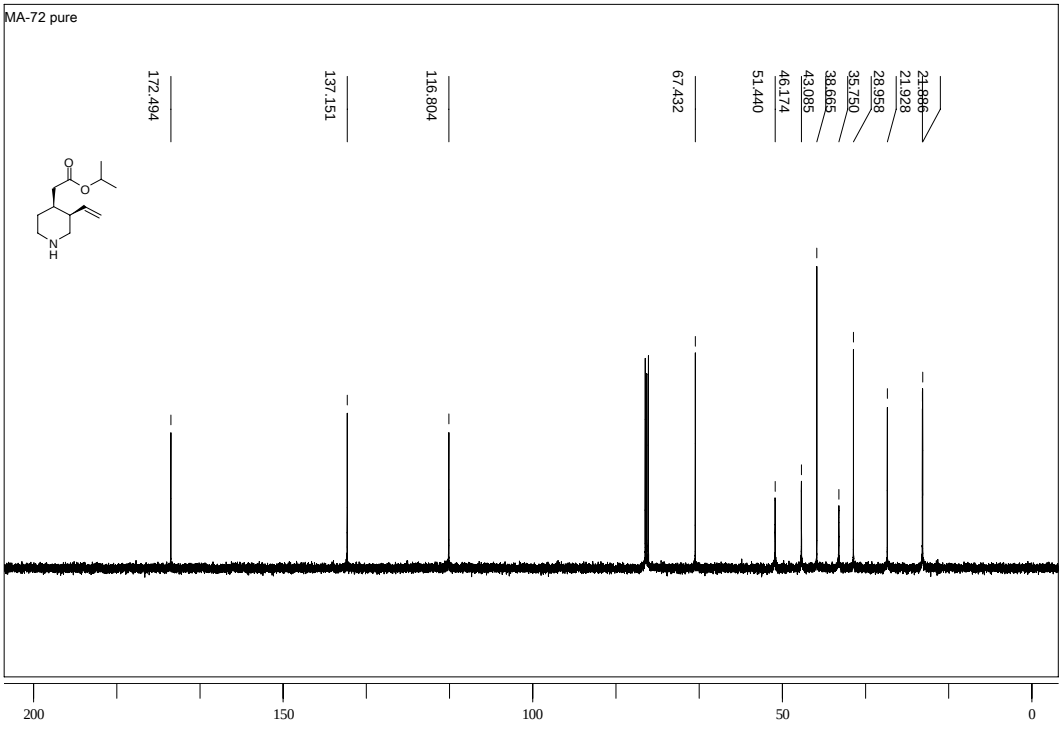
^{1}H NMR (400 MHz, $CDCl_3$)



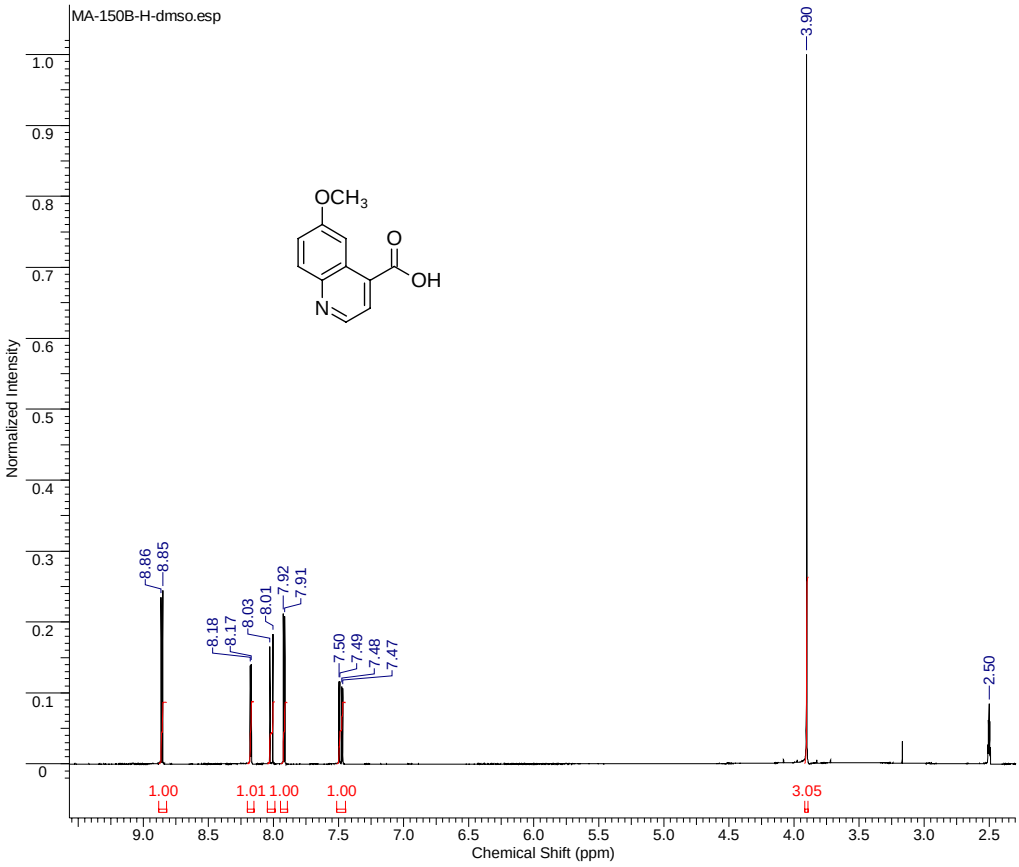
^{1}H NMR (400 MHz, $CDCl_3$)



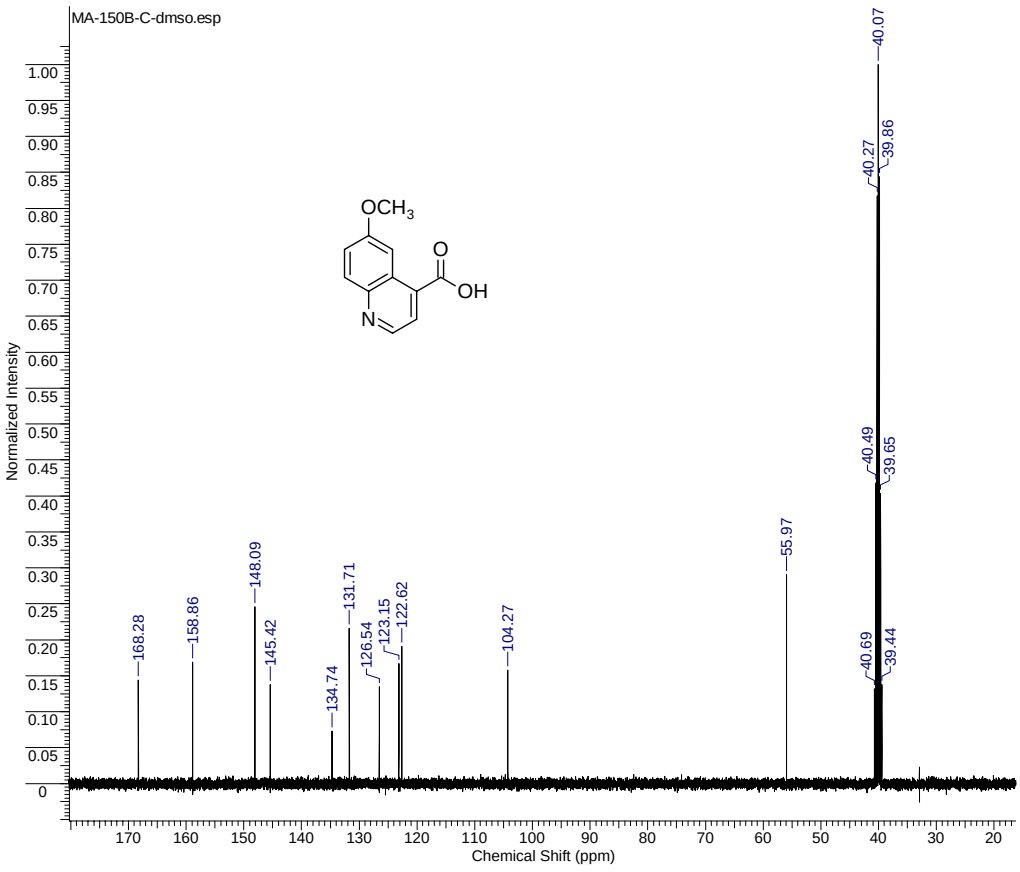
^{13}C NMR (100 MHz, $CDCl_3$)



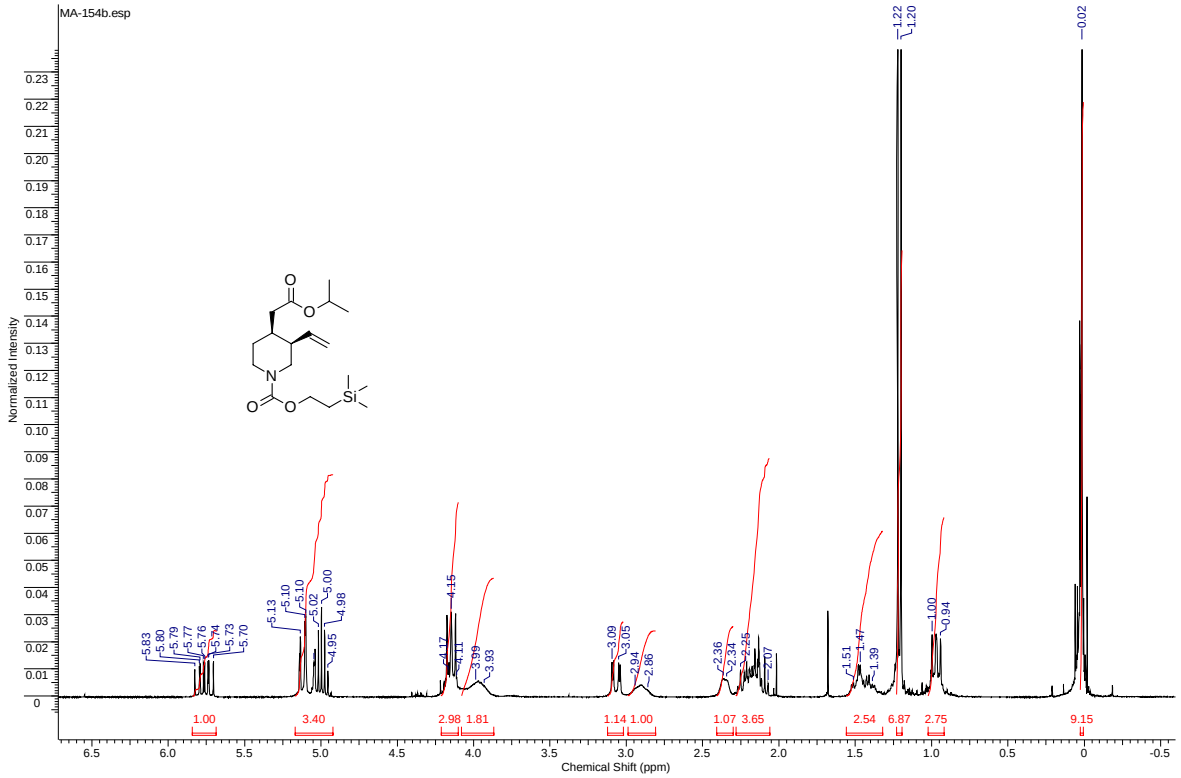
^{1}H NMR (400 MHz, DMSO-d_6)



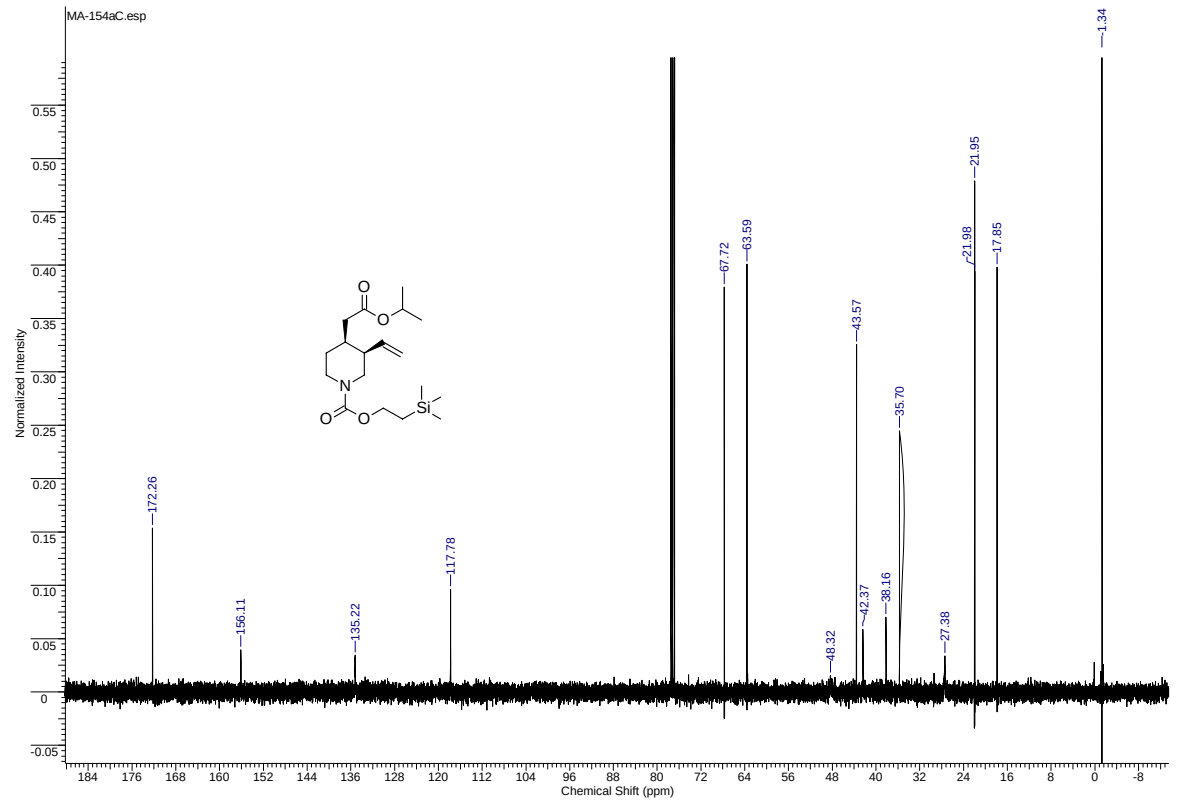
^{13}C NMR (100 MHz, DMSO-d_6)



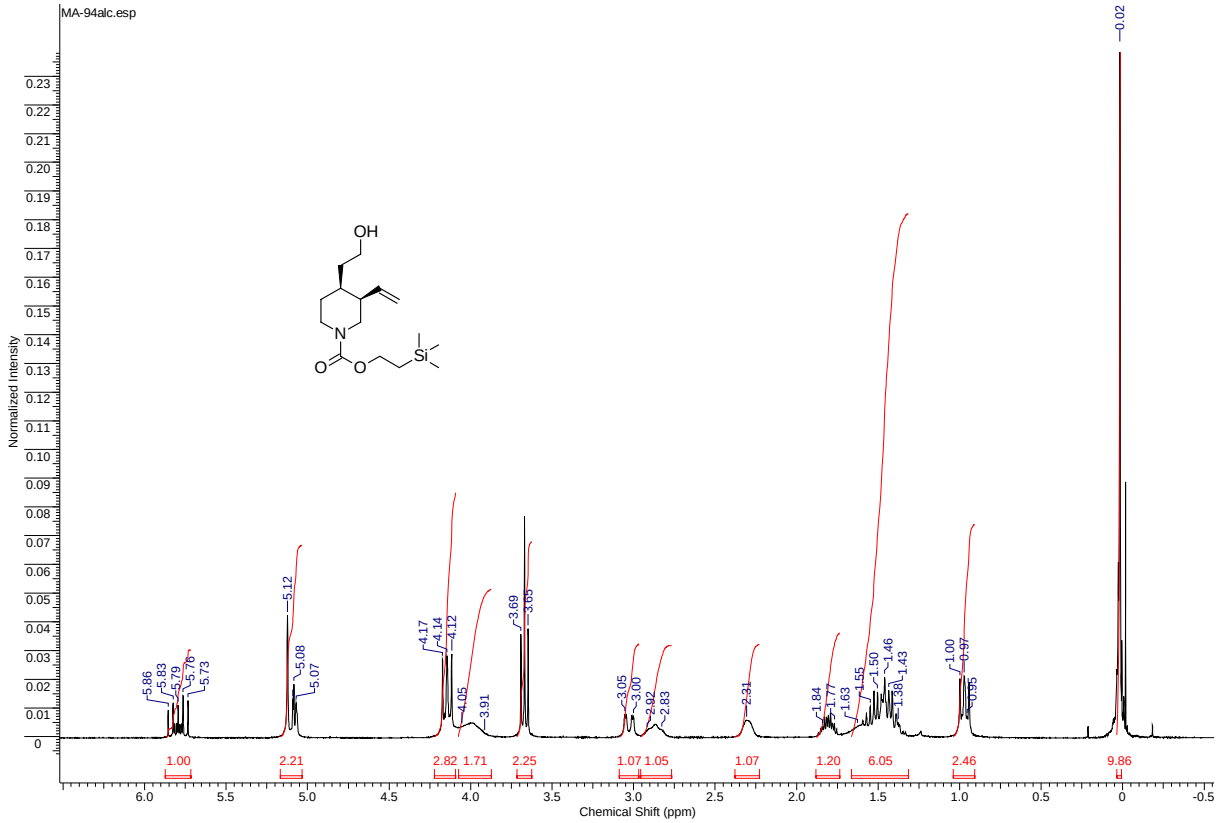
^{1}H-NMR (300 MHz, $CDCl_3$)



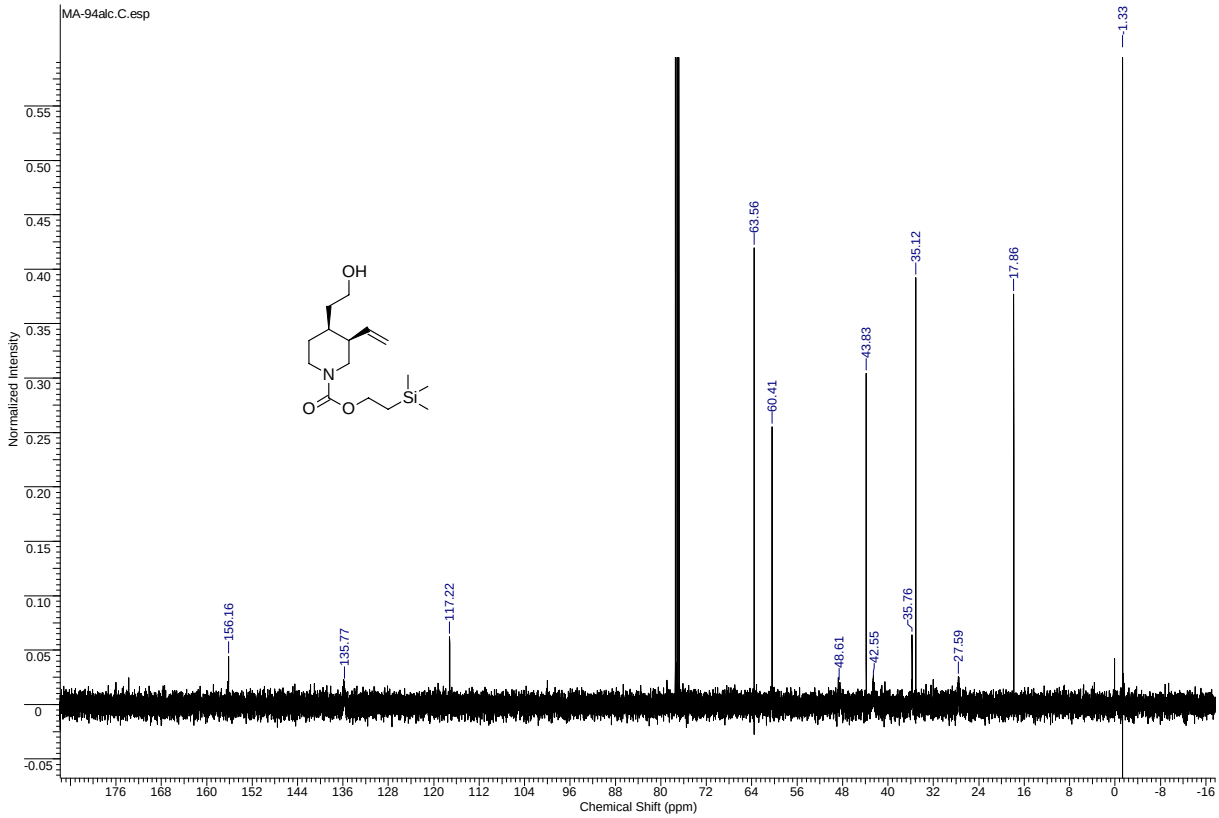
^{13}C-NMR (100 MHz, $CDCl_3$)



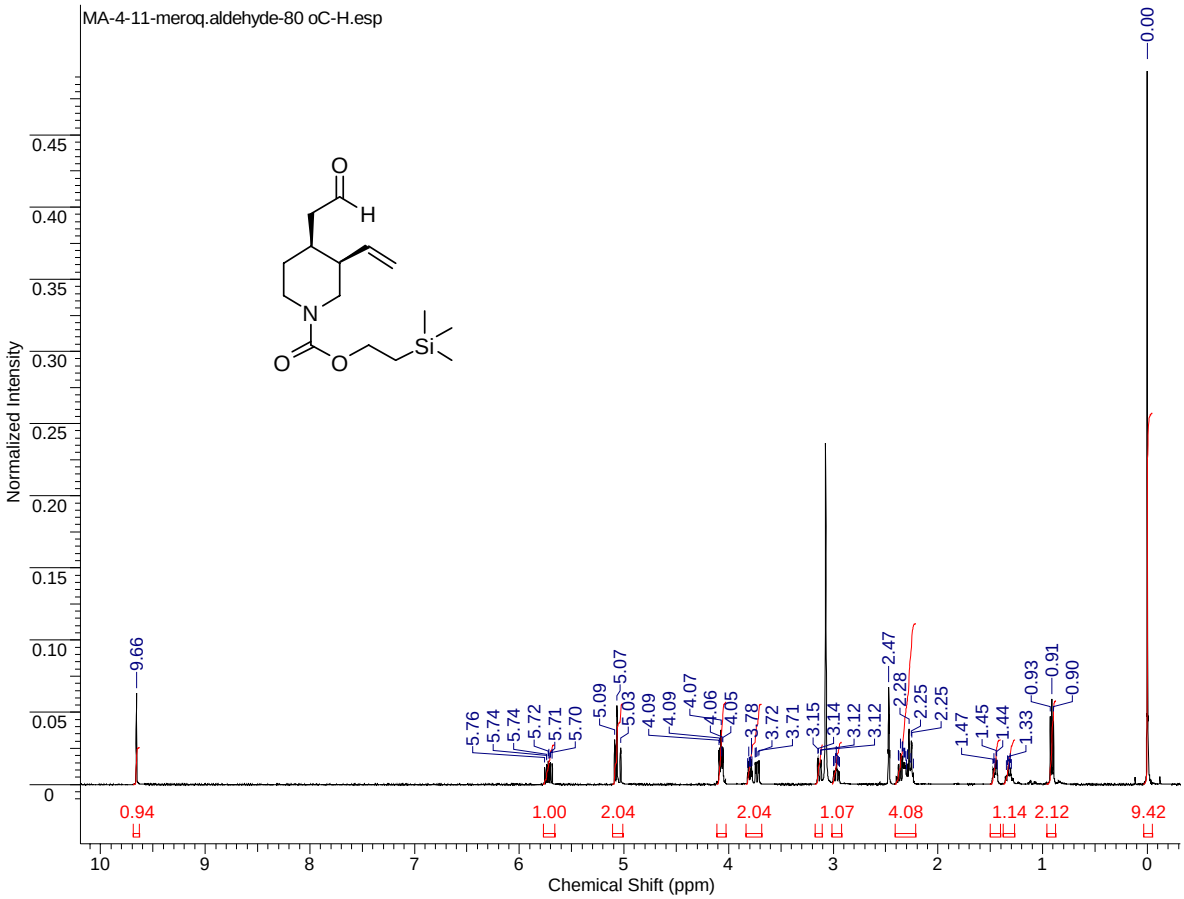
^{1}H-NMR (300 MHz, $CDCl_3$)



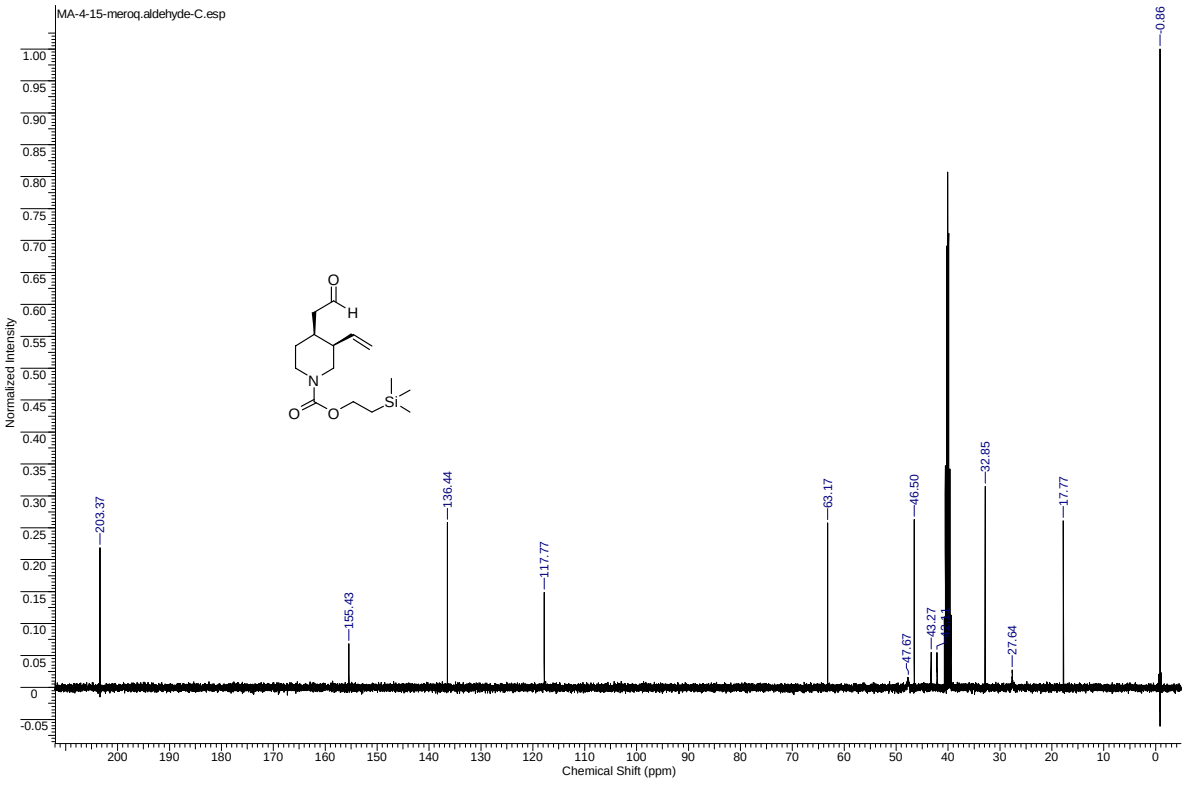
^{13}C-NMR (75 MHz, $CDCl_3$)



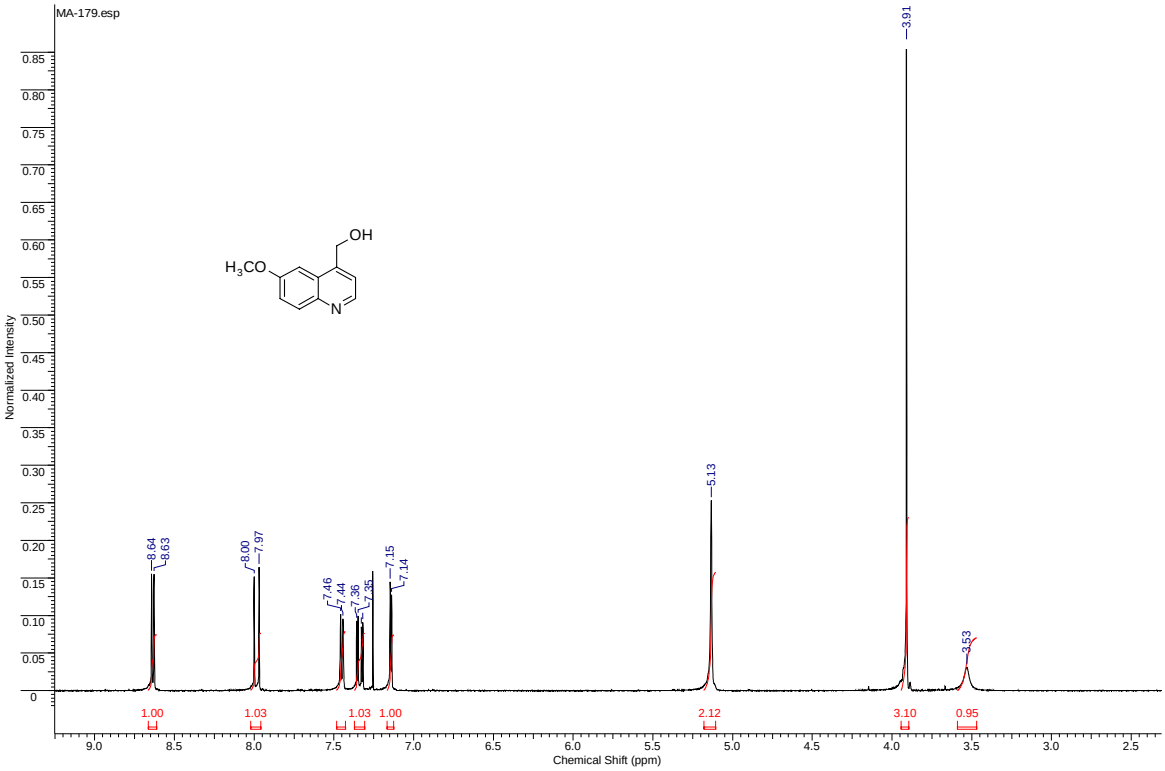
^{1}H-NMR (500 MHz, d_6-DMSO, 80 °C)



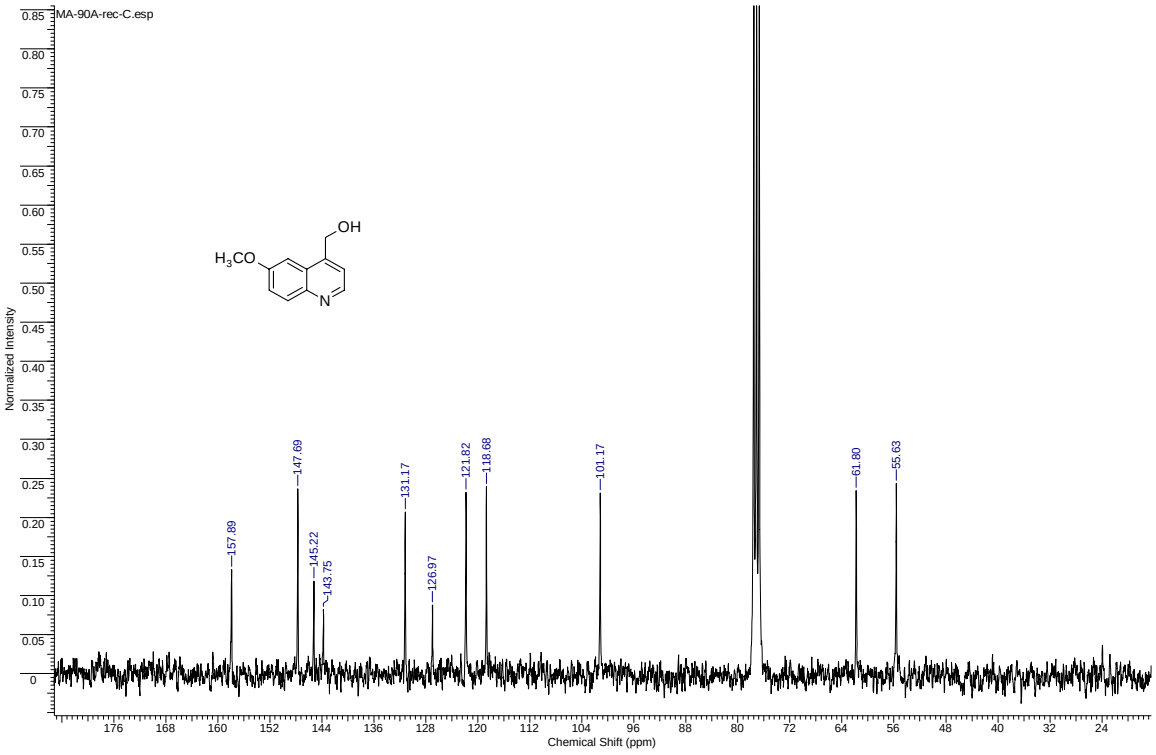
^{13}C-NMR (100 MHz, $CDCl_3$)



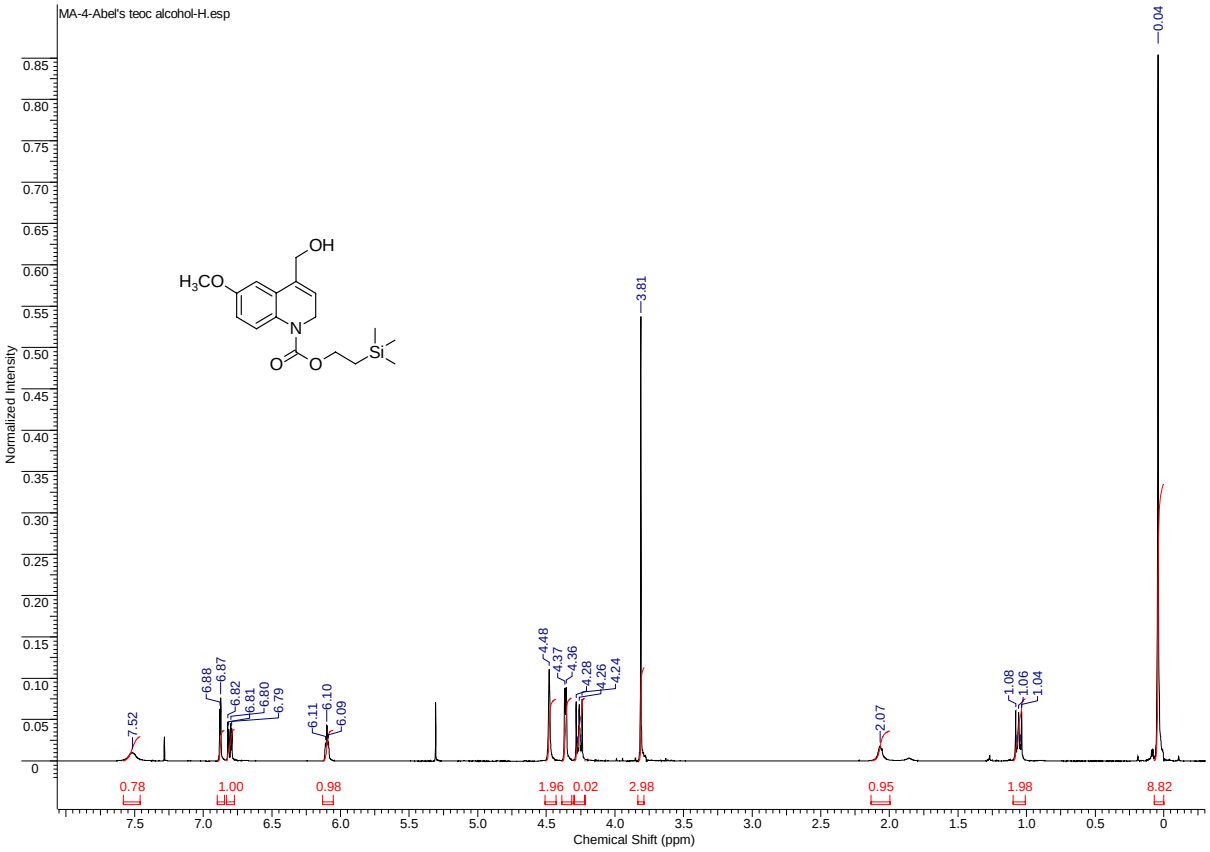
^{1}H-NMR (300 MHz, CD_3OD)



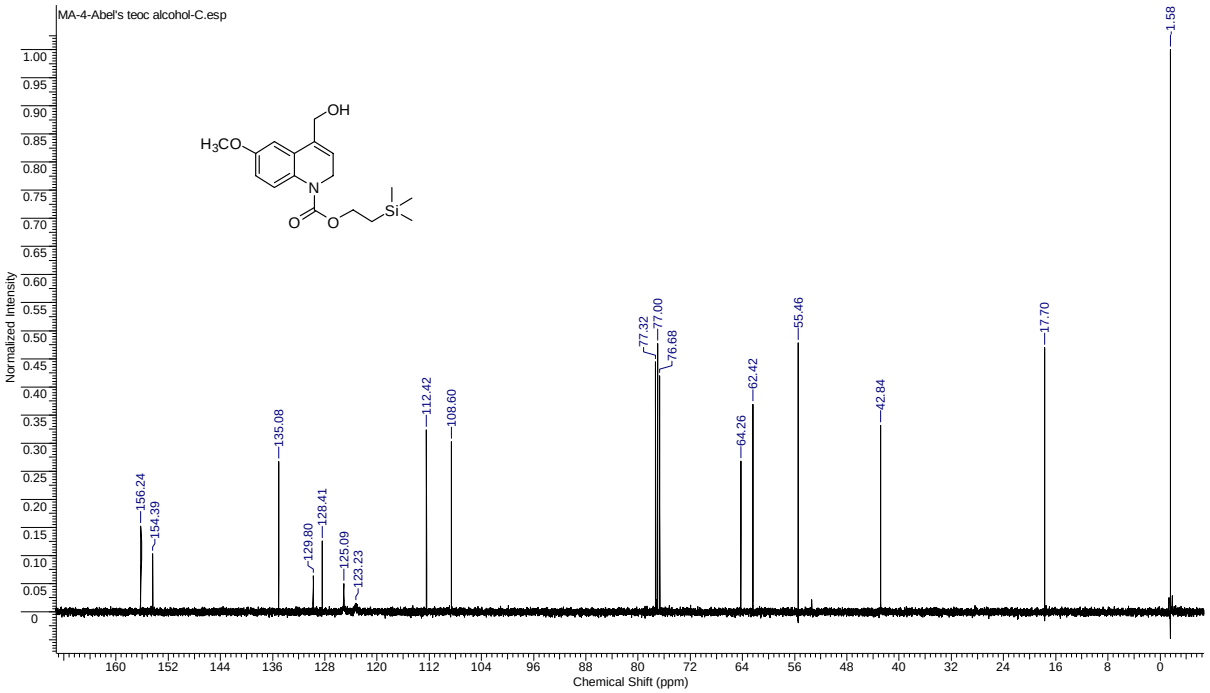
^{13}C-NMR (75 MHz, CD_3OD)



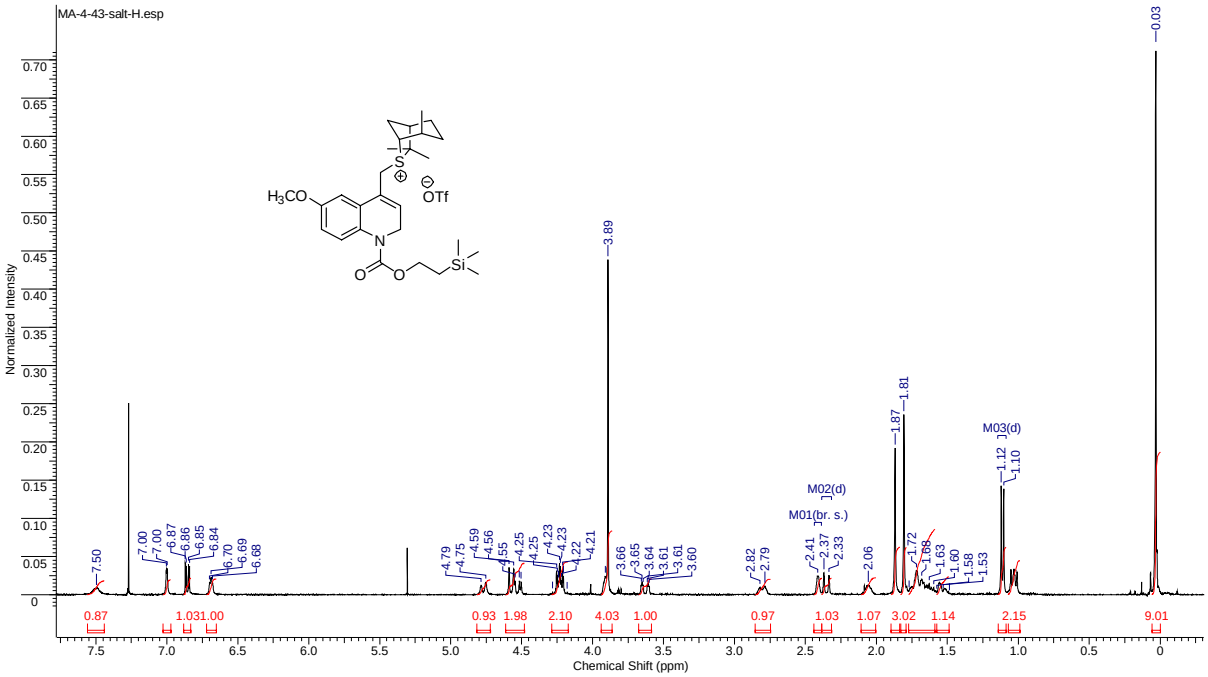
^{1}H-NMR (400 MHz, $CDCl_3$)



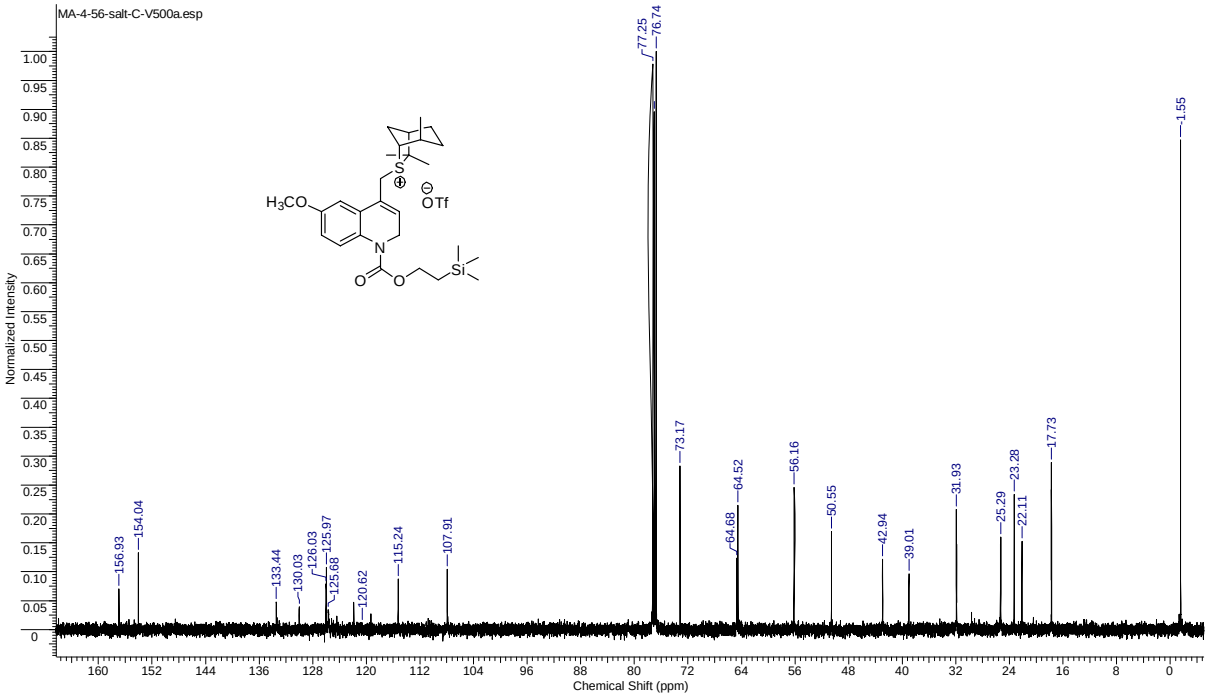
^{13}C-NMR (100 MHz, $CDCl_3$)



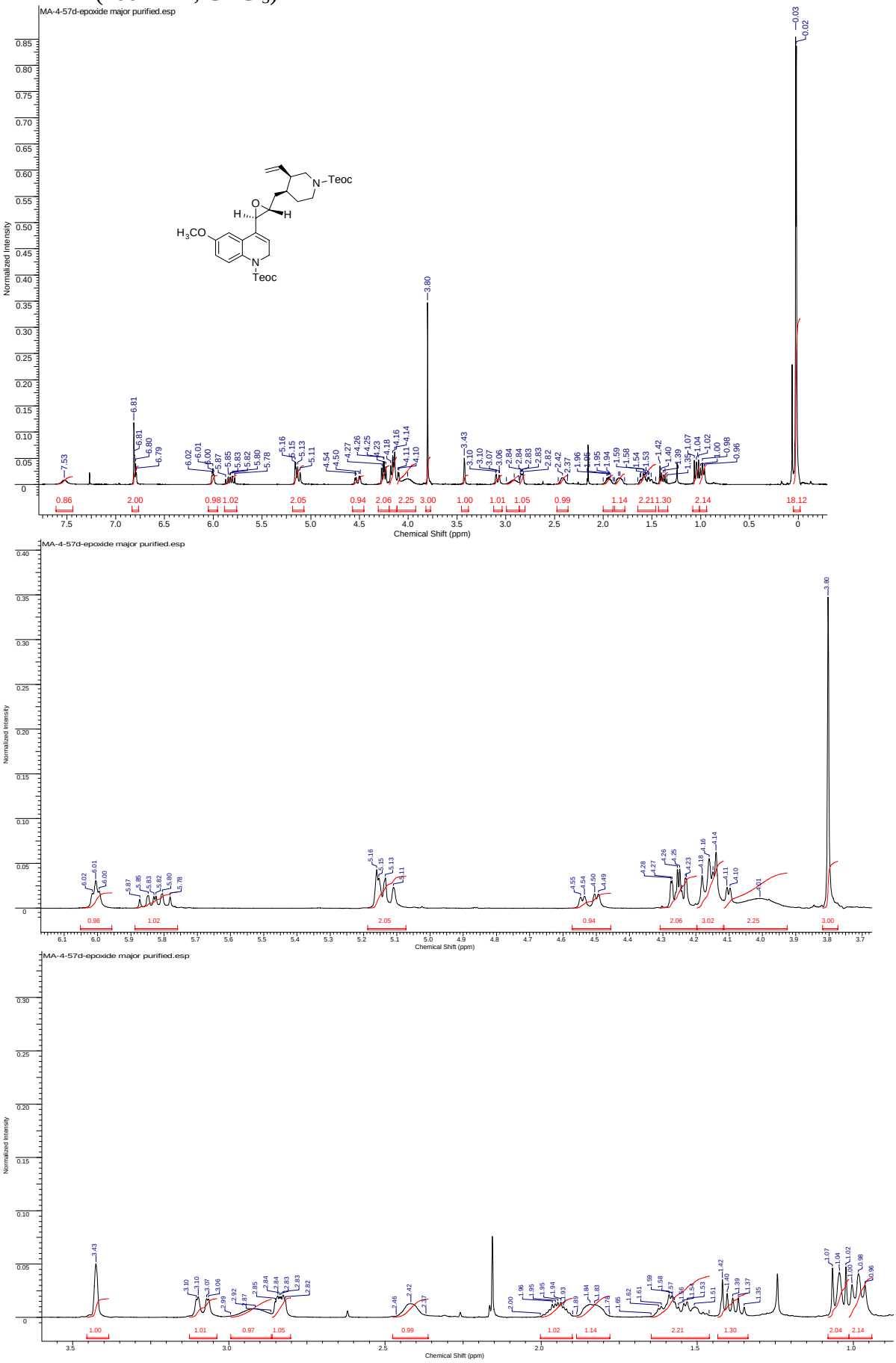
^{1}H-NMR (400 MHz, $CDCl_3$)



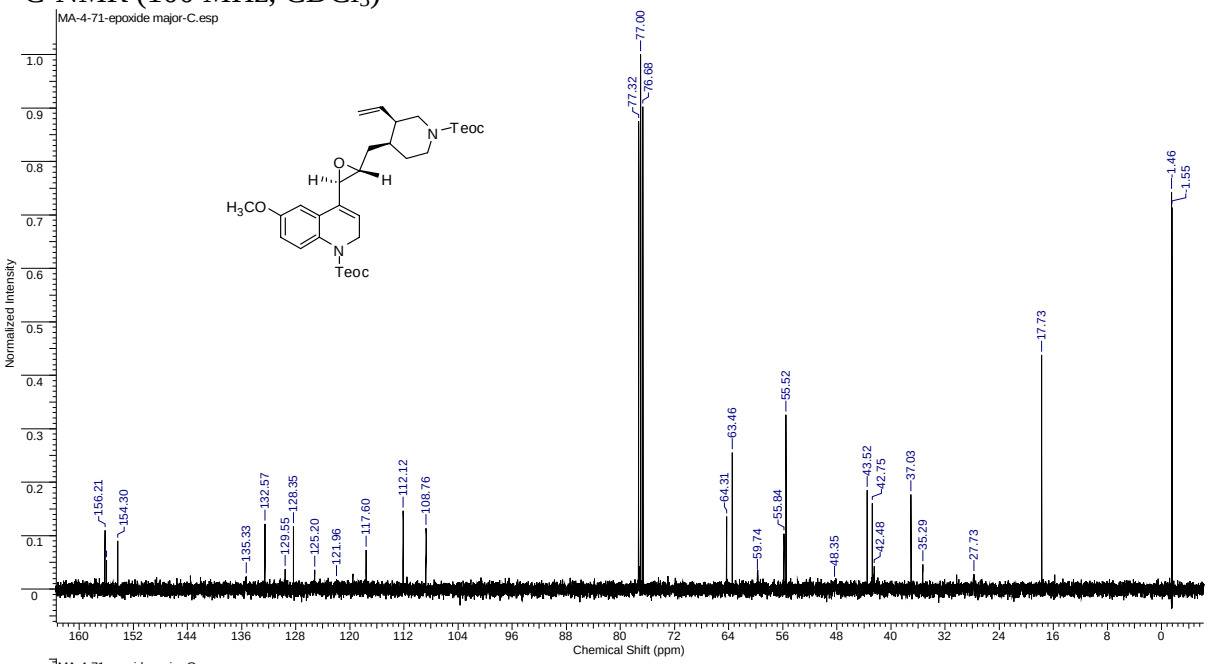
^{13}C-NMR (125 MHz, $CDCl_3$)

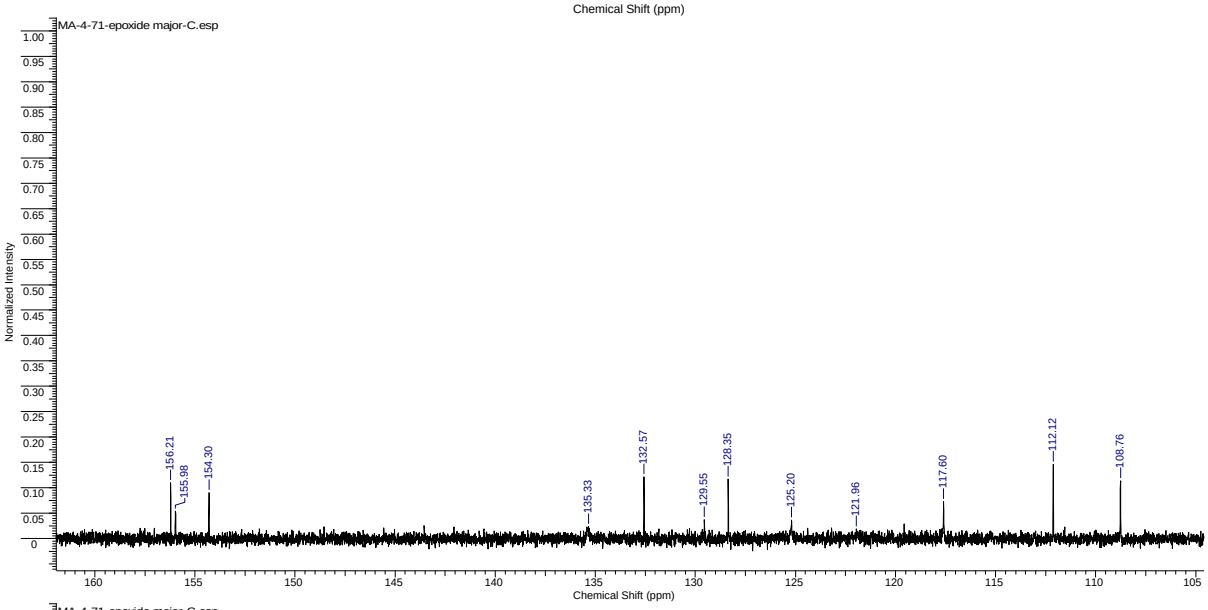


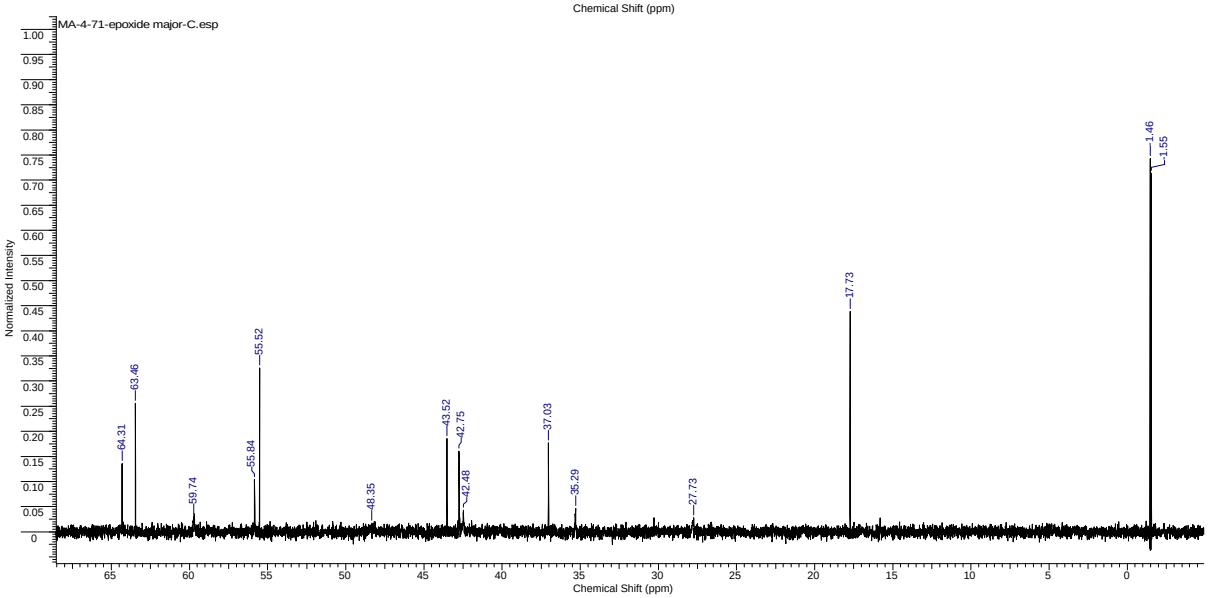
^{1}H-NMR (400 MHz, $CDCl_3$)



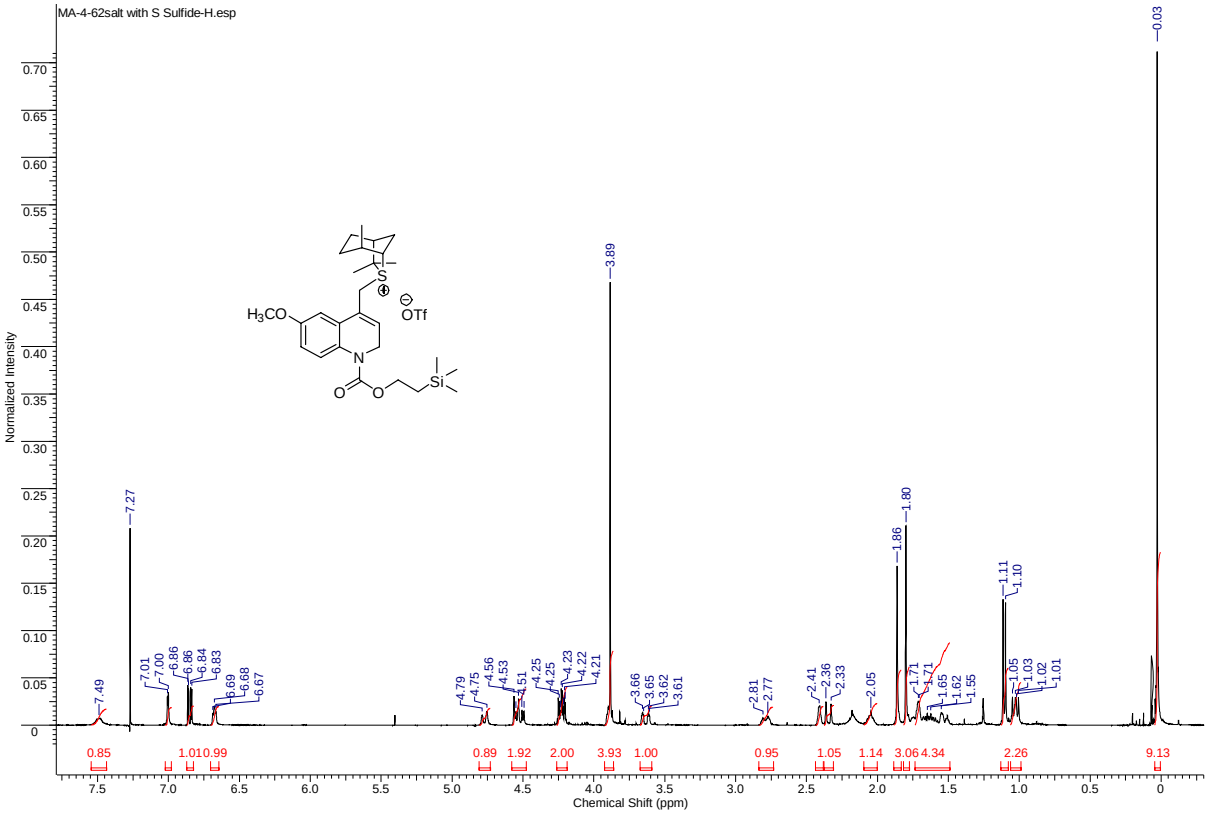
^{13}C-NMR (100 MHz, $CDCl_3$)



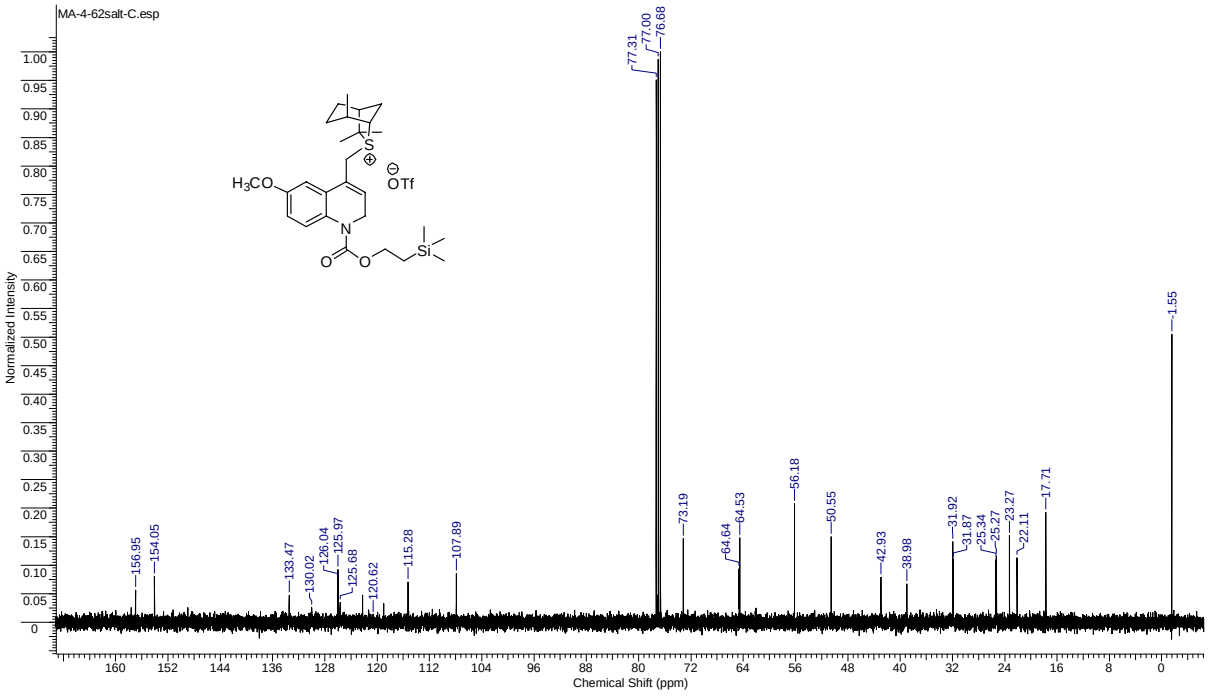




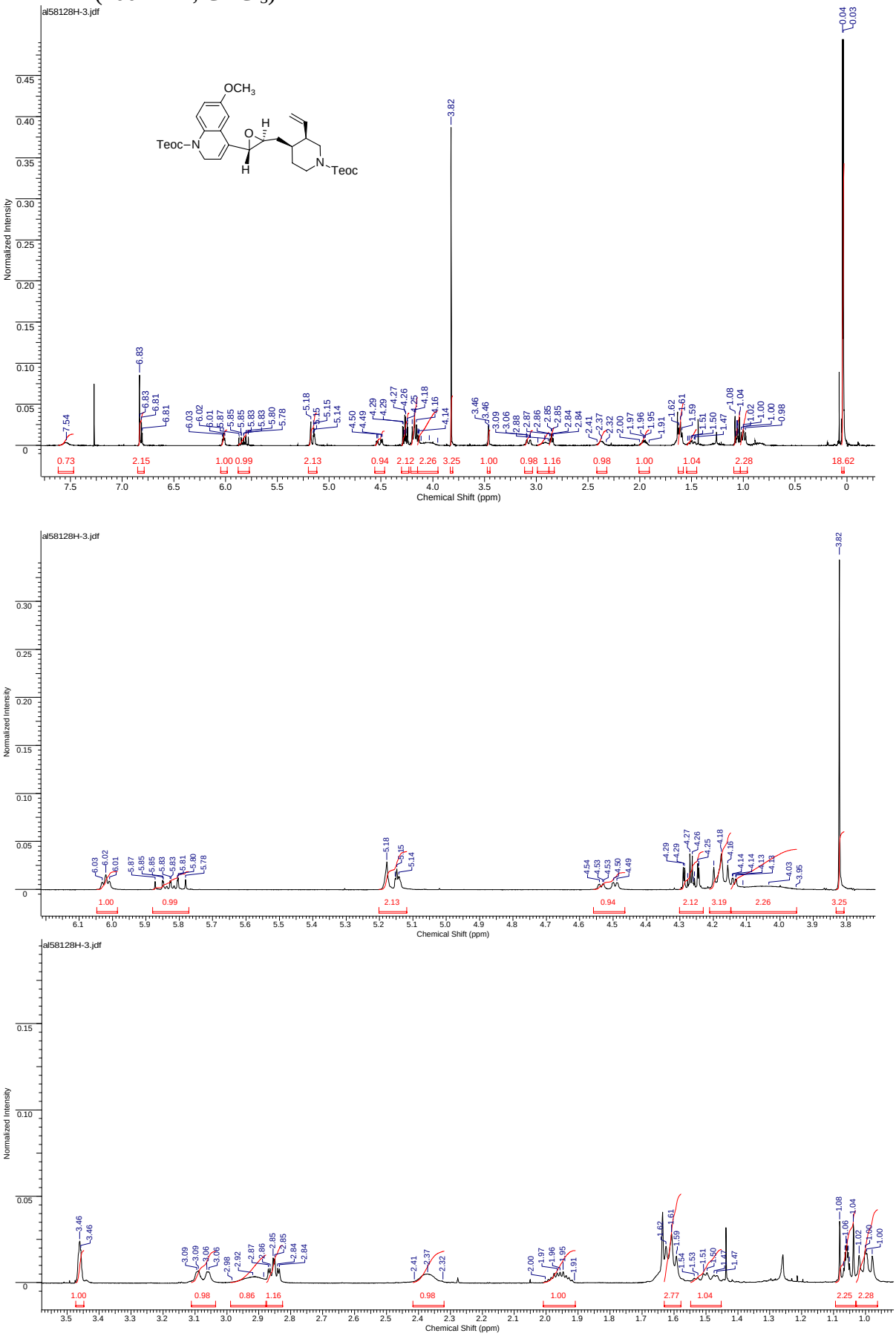
^{1}H-NMR (400 MHz, $CDCl_3$)



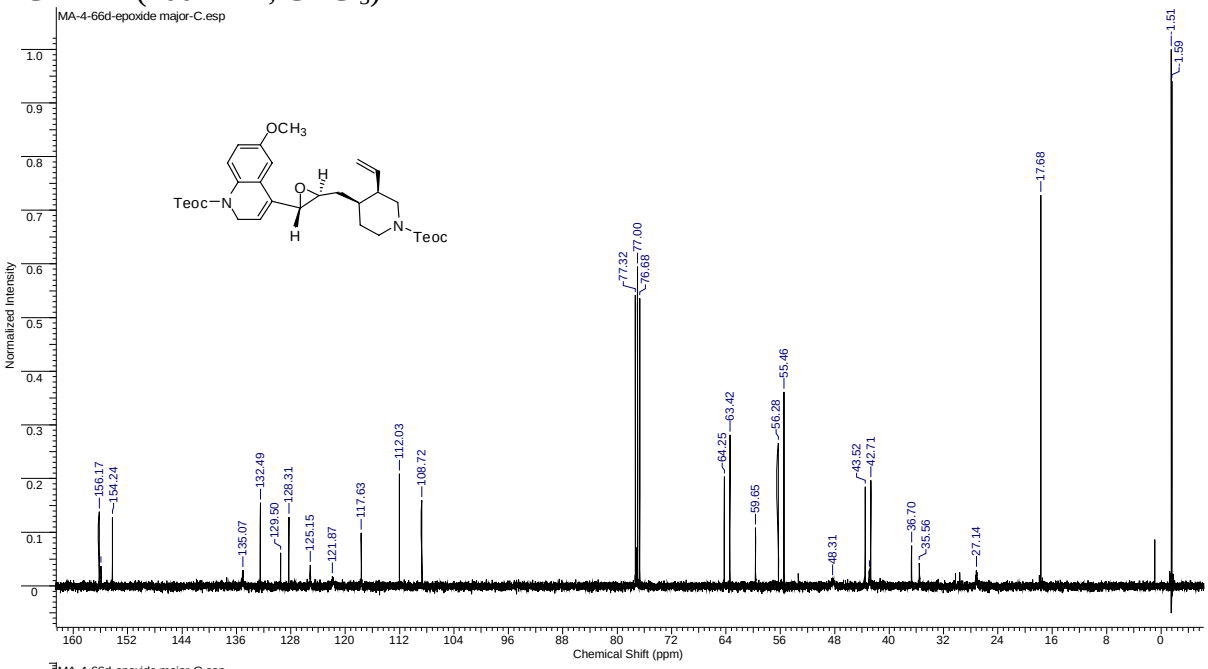
^{13}C-NMR (100 MHz, $CDCl_3$)

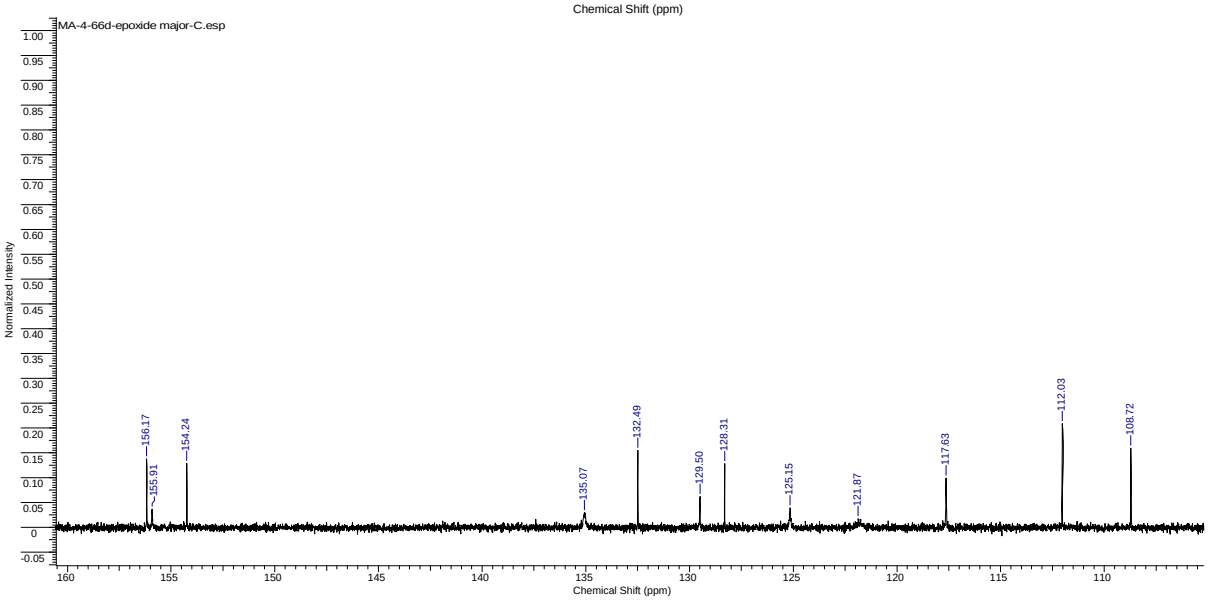


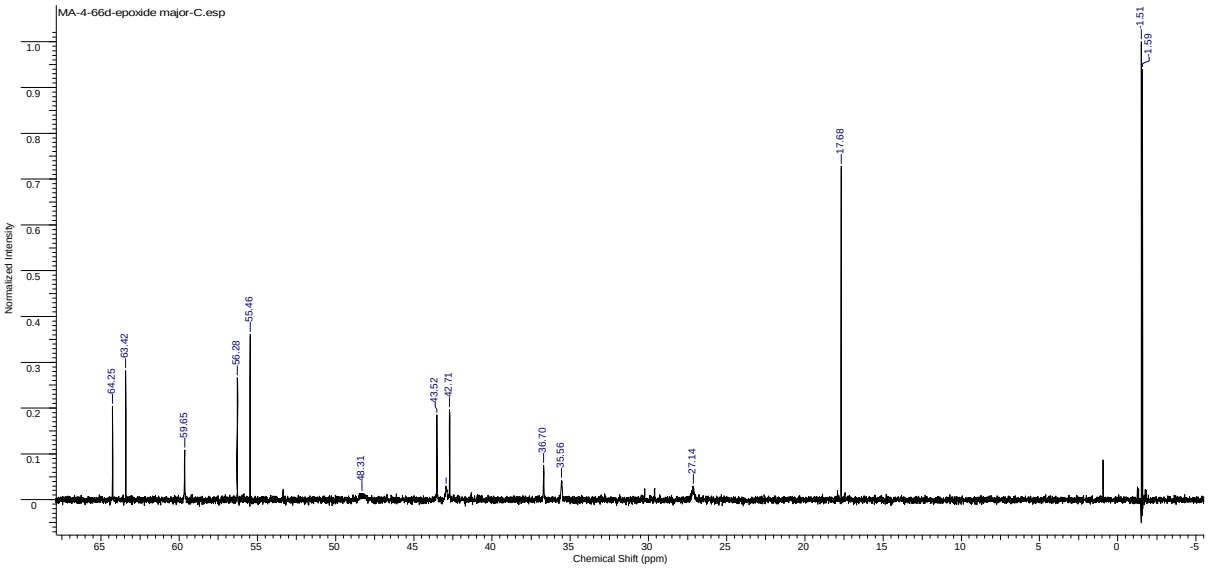
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (100 MHz, $CDCl_3$)

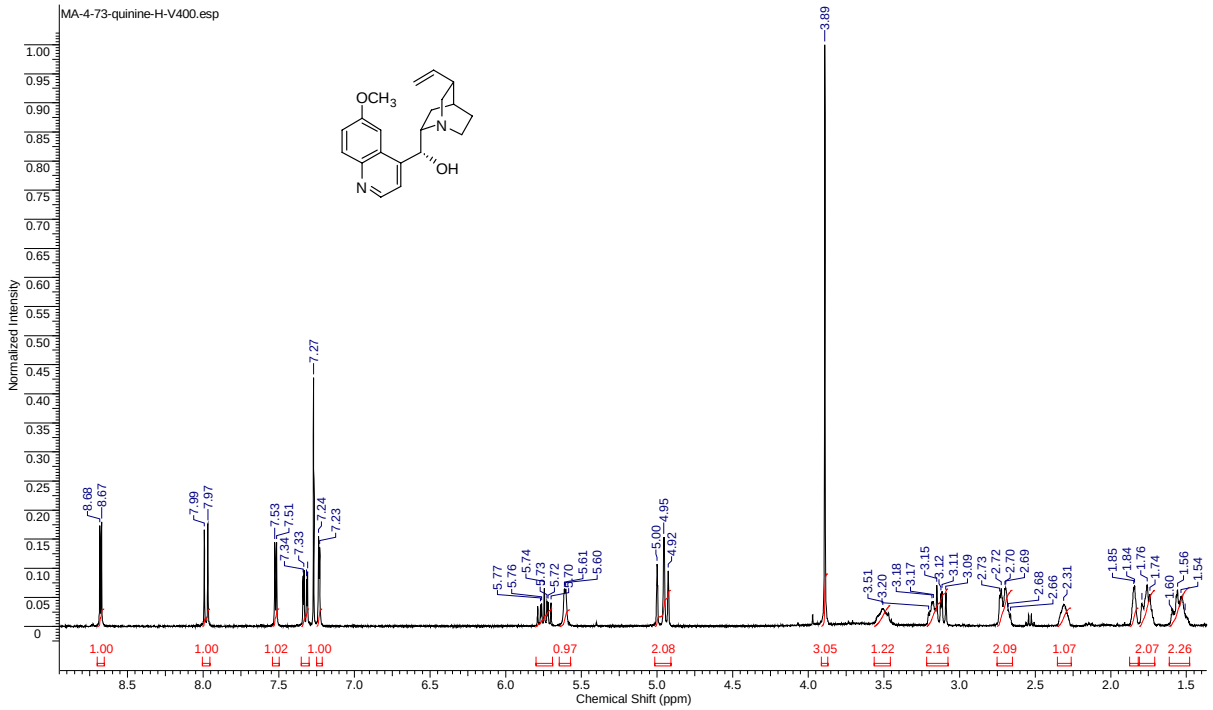




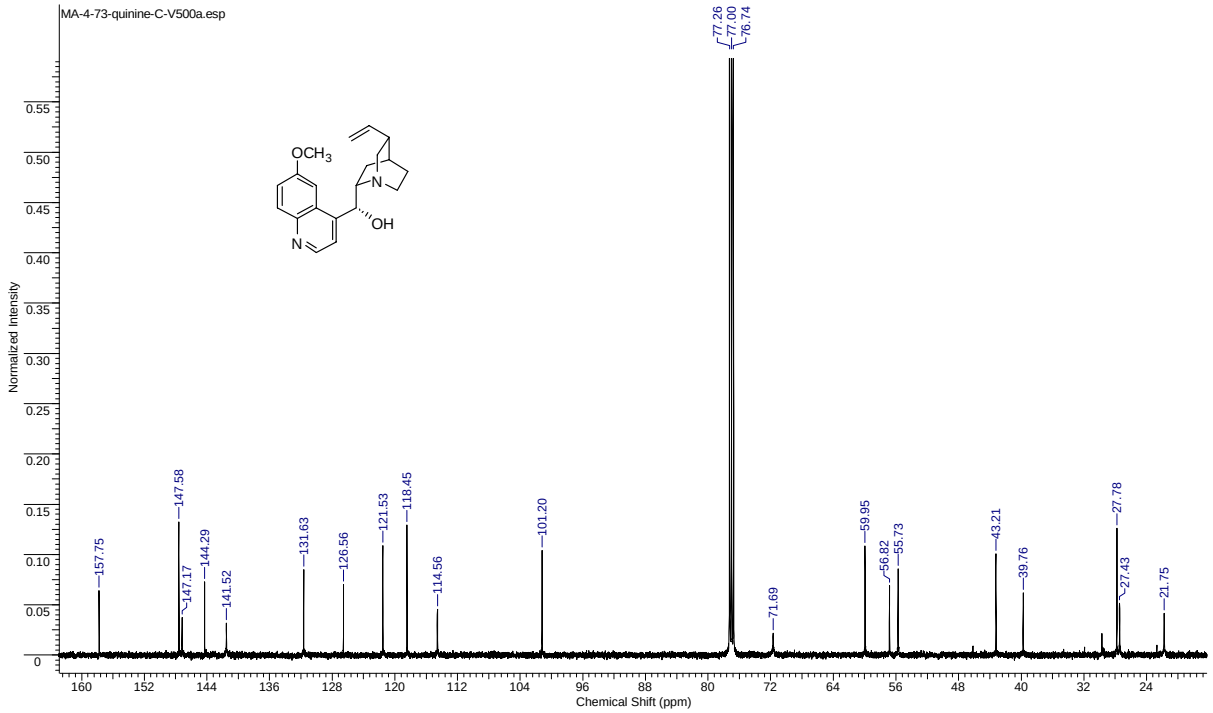


NMR Spectra for Quinine and Quinidine

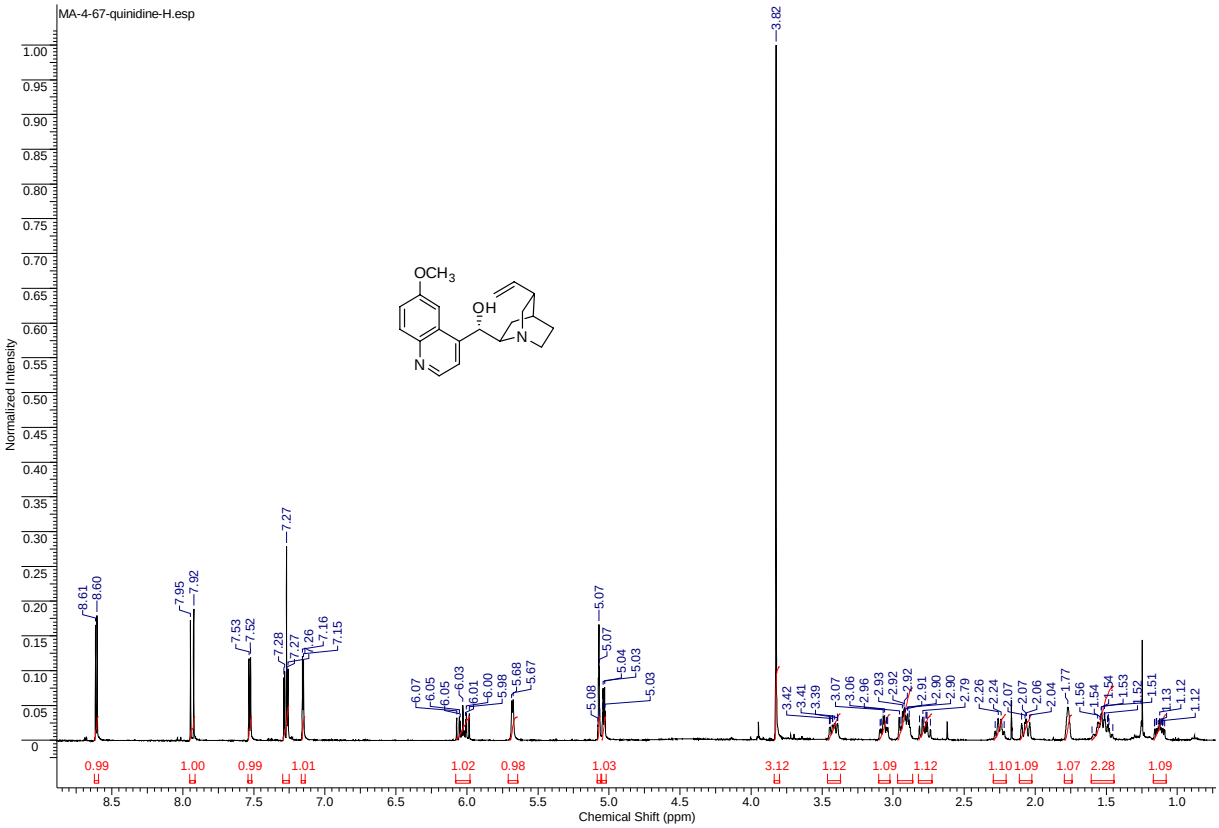
^{1}H-NMR (400 MHz, $CDCl_3$) Quinine



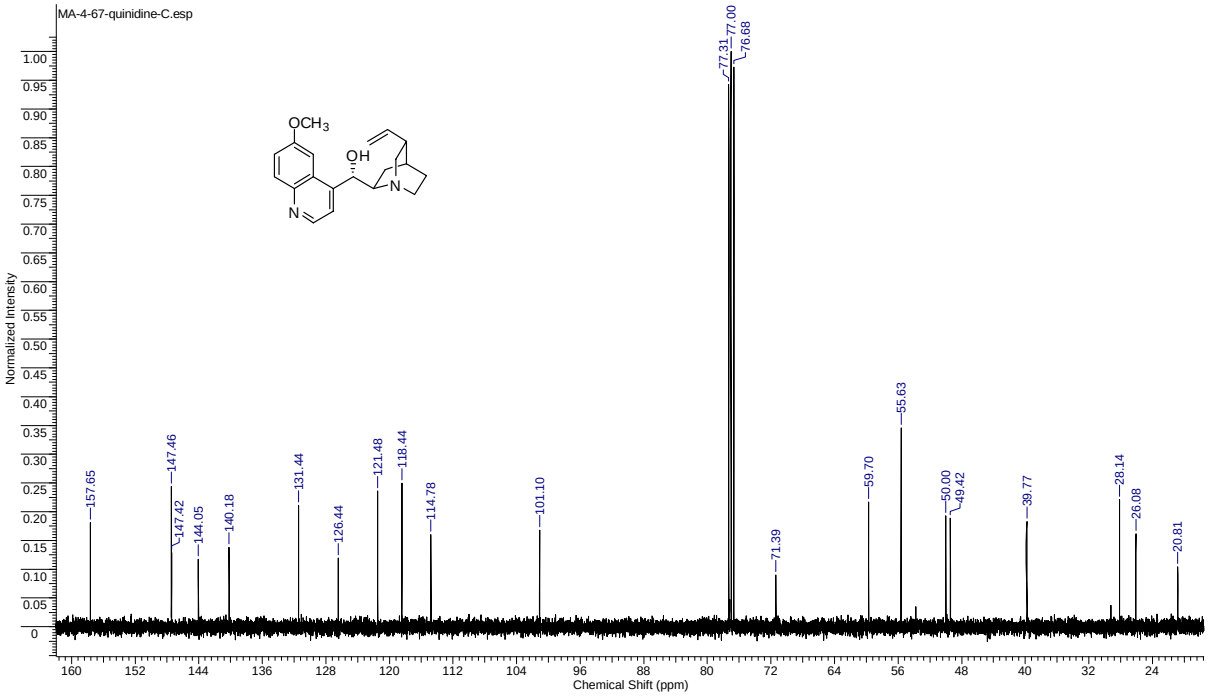
^{13}C-NMR (125 MHz, $CDCl_3$) Quinine



^{1}H-NMR (400 MHz, $CDCl_3$) Quinidine



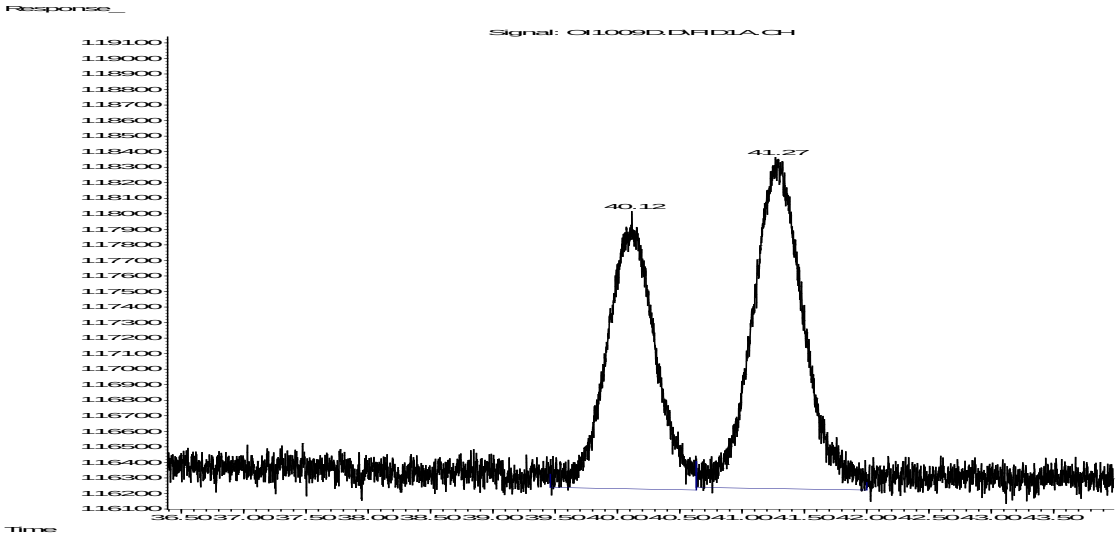
^{13}C-NMR (100 MHz, $CDCl_3$) Quinidine



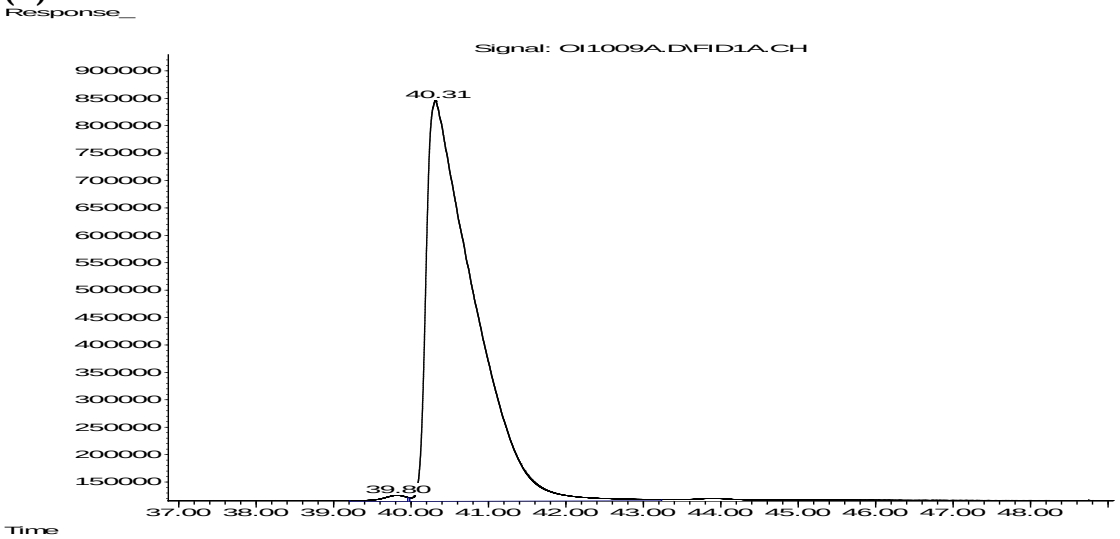
Gas Chromatograms for Isothiocineole 1 and Limonene

Limonene α-Dex column; oven temperature: 50 °C; injector/detector temperatures: 250 °C;

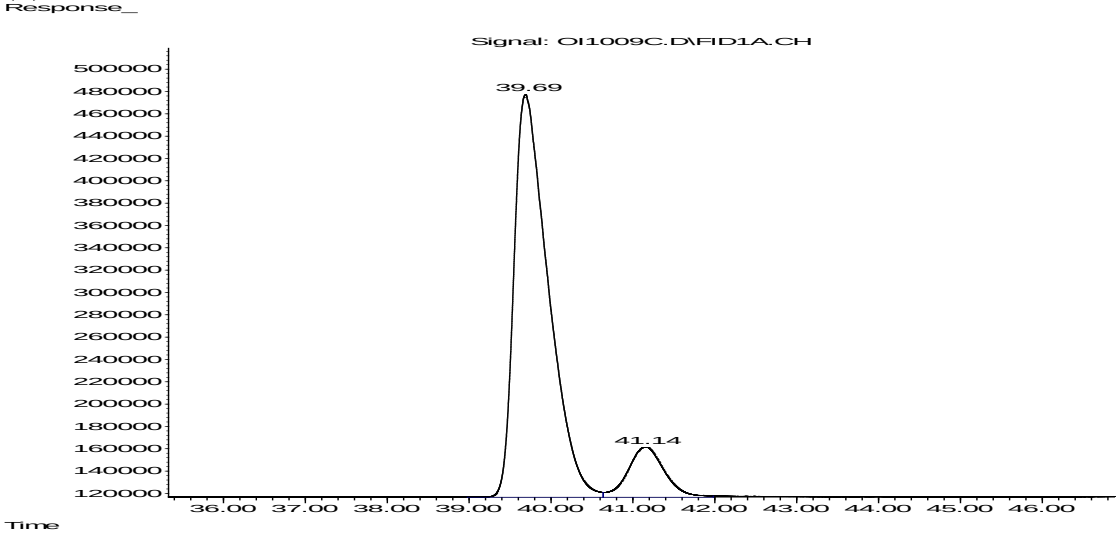
Racemic Limonene



(*R*)-Limonene



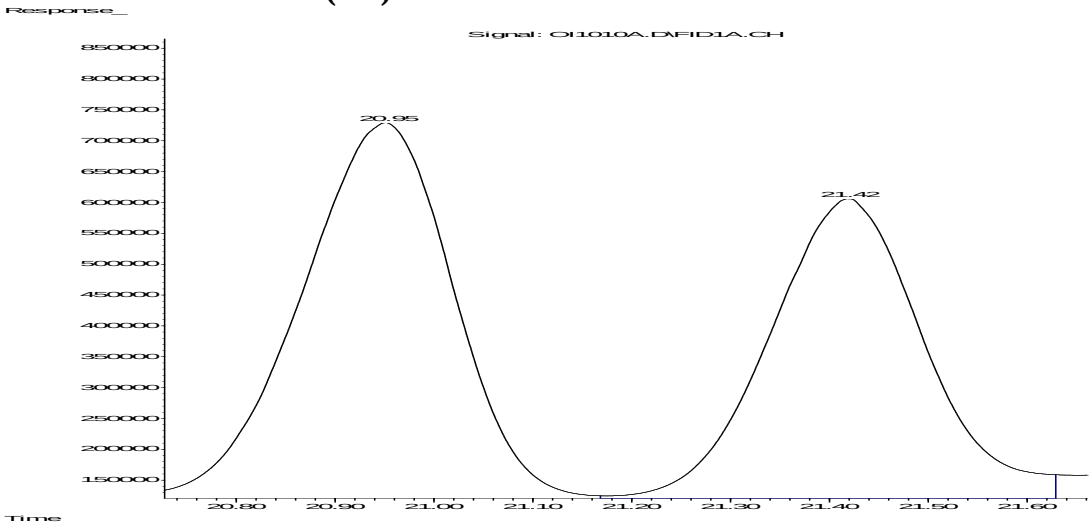
(*S*)-Limonene


Response_
Signal: OI1009C.D\FID1A.CH
39.69
41.14
500000
480000
460000
440000
420000
400000
380000
360000
340000
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
36.00
37.00
38.00
39.00
40.00
41.00
42.00
43.00
44.00
45.00
46.00
Time

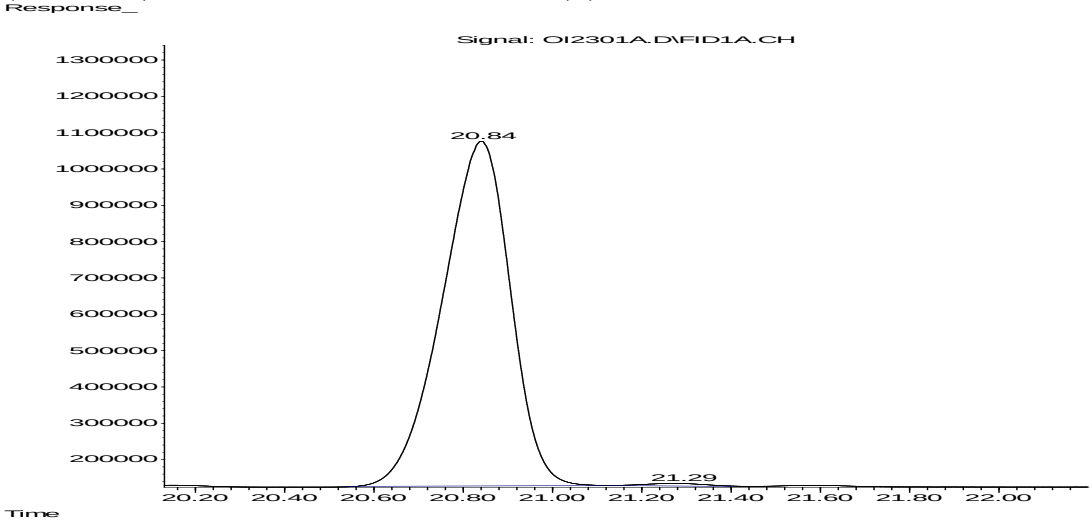
Isothiocineole (1)

Chiral-phase GC conditions: α-Dex column, oven temperature: 110 °C; R_t 20.85 min (*R*), 21.39 min (*S*); Injection/detector temperatures: 250 °C;

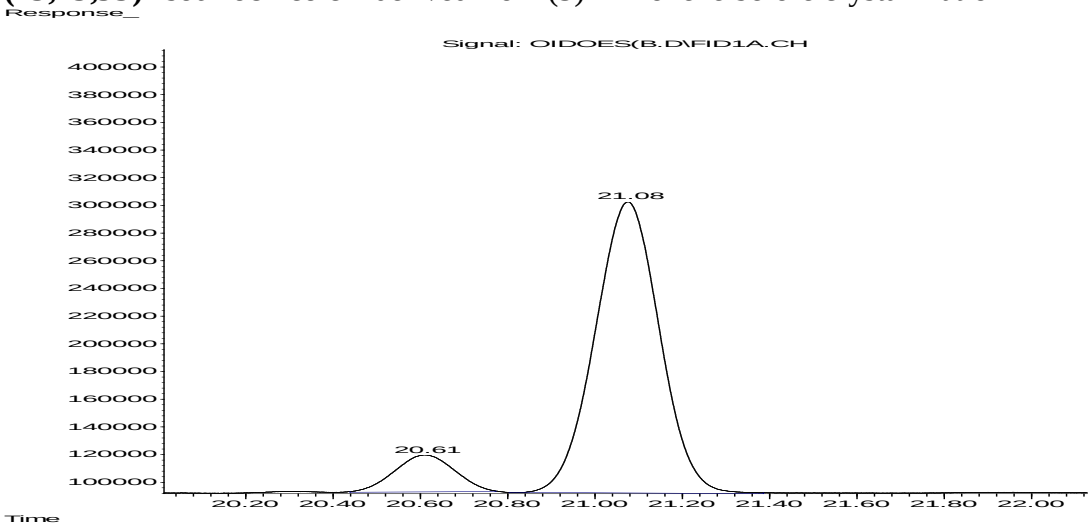
Racemic Isothiocineole (±-1)



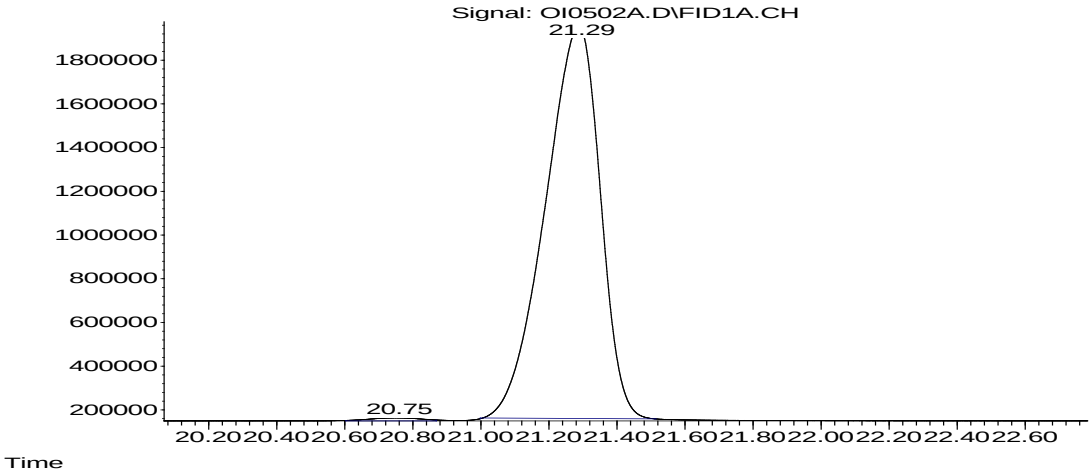
(*1R,4R,5R*)-Isothiocineole 1 derived from (*R*)-Limonene



(*1S,4S,5S*)-Isothiocineole 1 derived from (*S*)-Limonene before crystallization

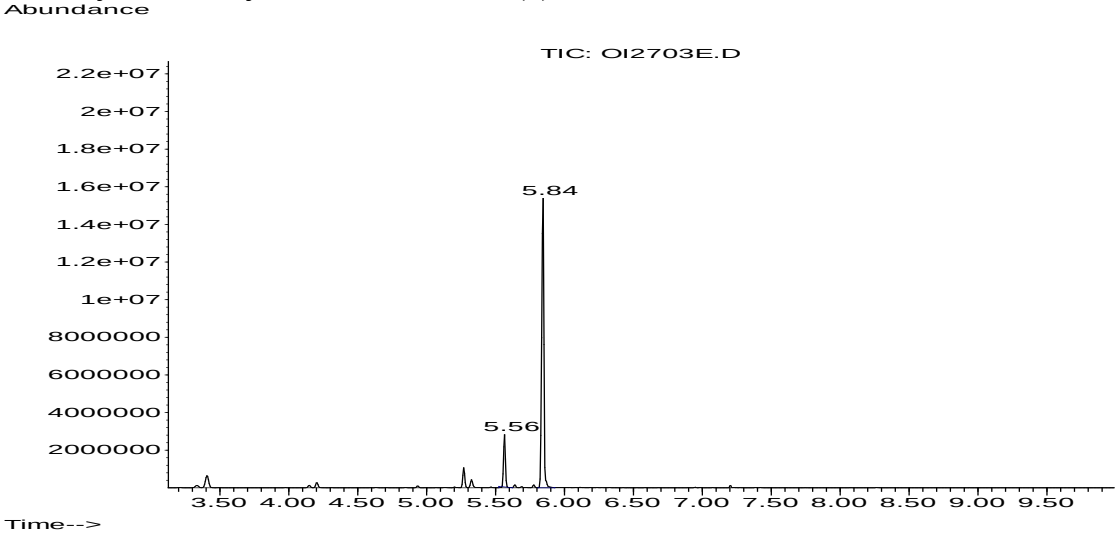


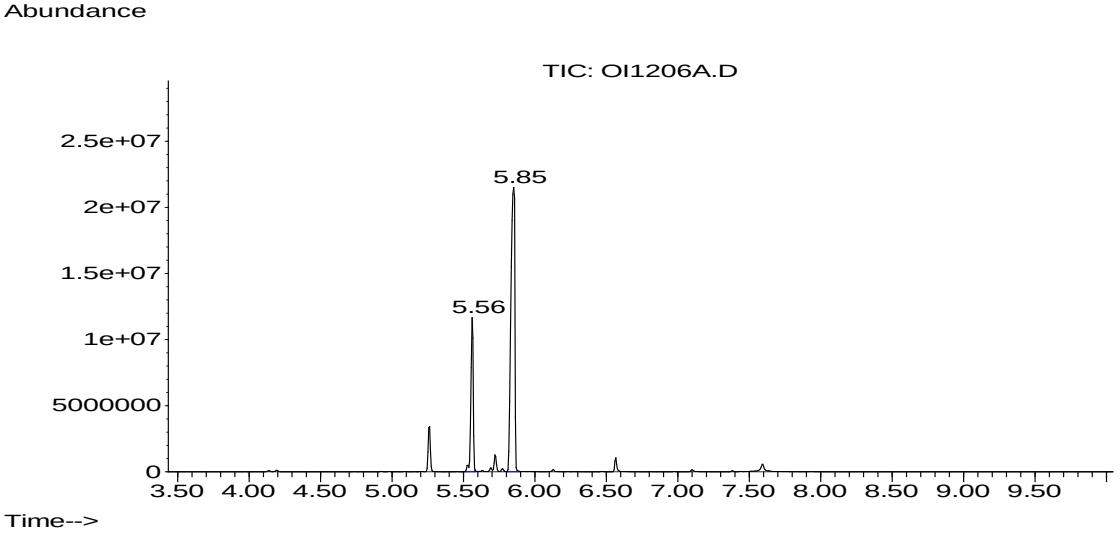
(*1S,4S,5S*)-Isothiocineole 1 derived from (*S*)-Limonene after crystallization



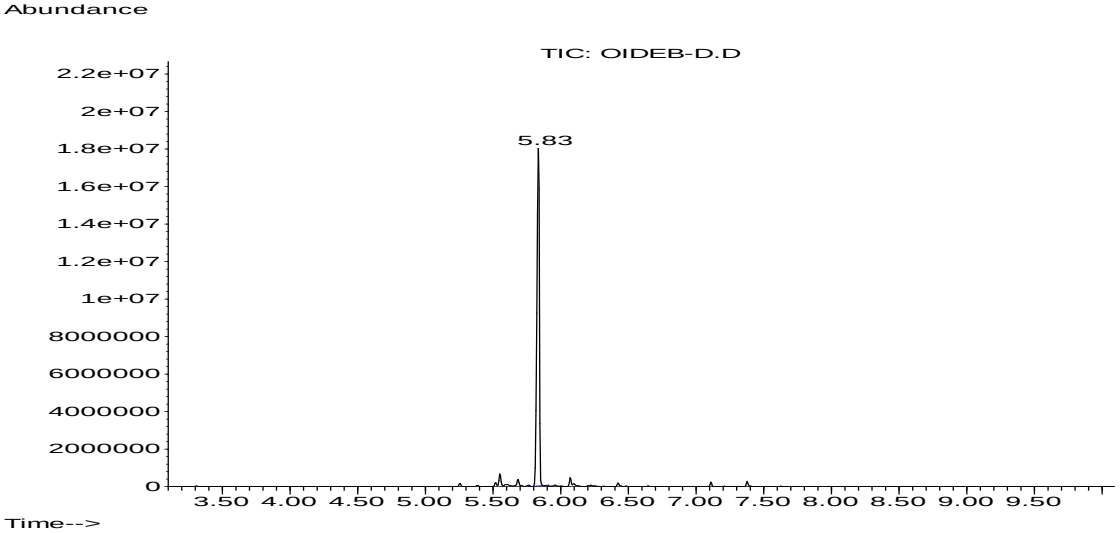
GC Chromatogram of Distillate from Initial Method for synthesis of isothiocineole (reaction carried out in the absence of γ-terpinene/1,4-cyclohexadiene)

GC conditions, supelco-SLB5MS, 15 m × 0.25 mm i.d., Injection 250 °C; detector temperature 280 °C; oven temperature: 70 °C (3 min), increase by 25 °C/min to 200 °C, followed by temperature ramp to 300 °C, R_t isothiocineole (**1**) 5.8 min, (1*R*,5*R*)-4,7,7-trimethyl-6-thiabicyclo[3.2.1]oct-3-ene (**3**) 5.5 min.

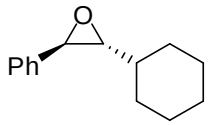




GC Chromatogram of Distillate from Improved Method for synthesis of isothiocineole (carried out in the presence of γ-terpinene)

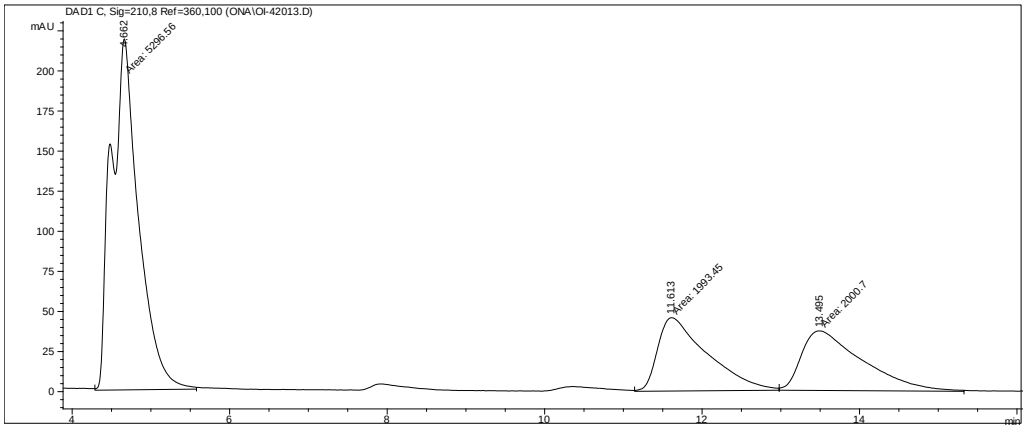


Chiral Phase Chromatograms for Epoxides

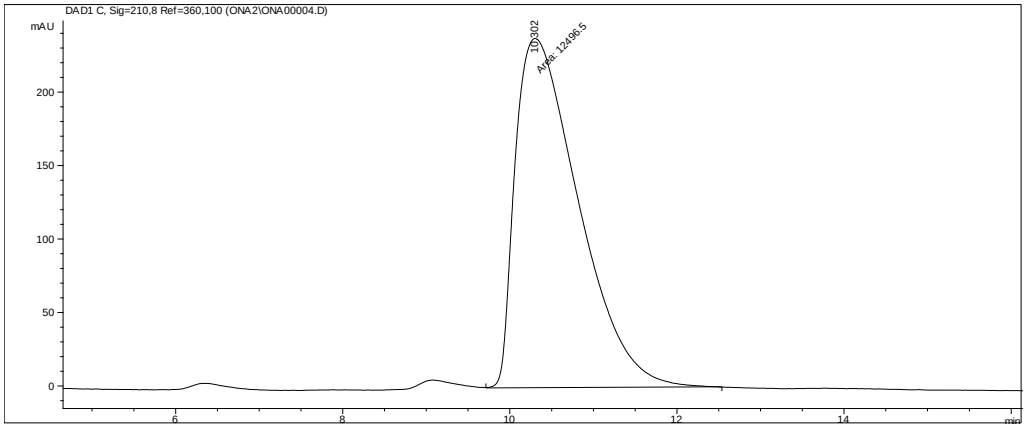


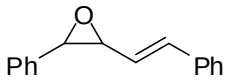
HPLC conditions: OJ column, 0.5% *i*PrOH/Hexane, 1.5 ml/min, *cis*: 4.48 min, 4.66 min. *trans*: 11.6 min ((*S*,*S*), minor), 13.5 min ((*R*,*R*), major);

Racemic



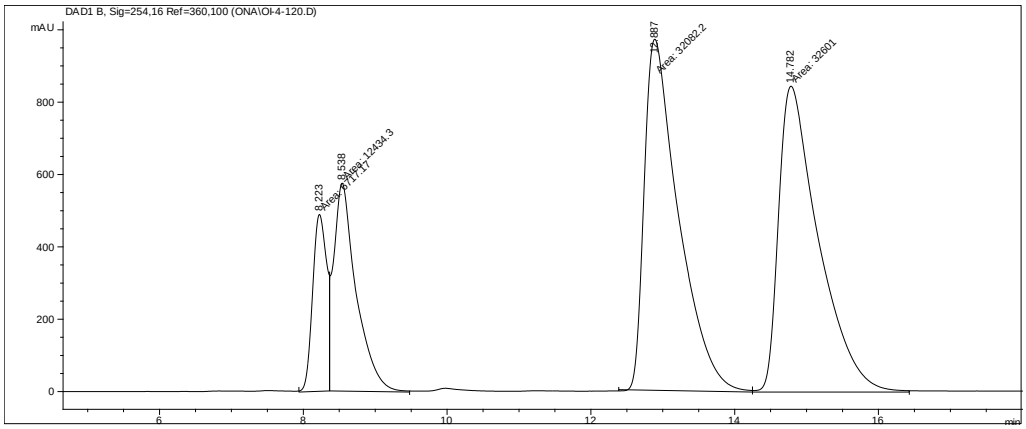
Enantioenriched



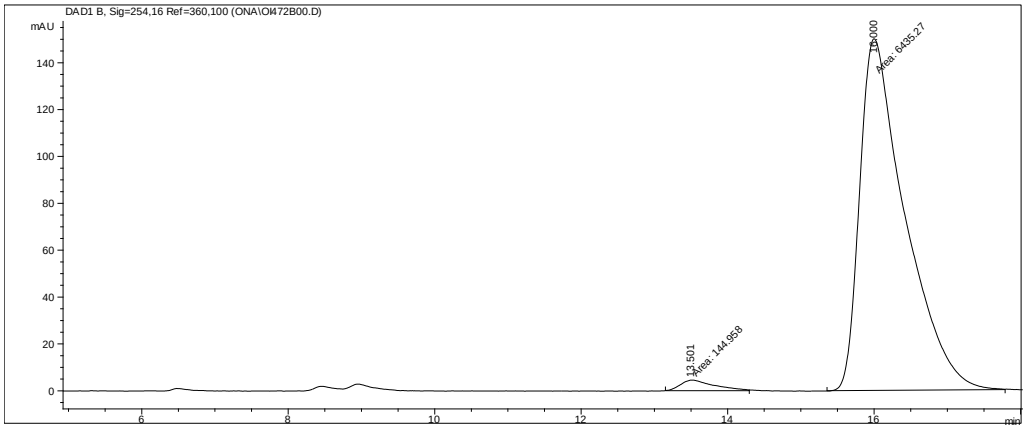


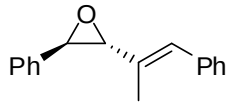
HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1 ml/min, <u>*trans*</u>: 12.89 min ((*S*,*S*), minor), 14.78 min ((*R*,*R*), major), <u>*cis*</u>: 8.22 min and 8.54 min;

Racemic



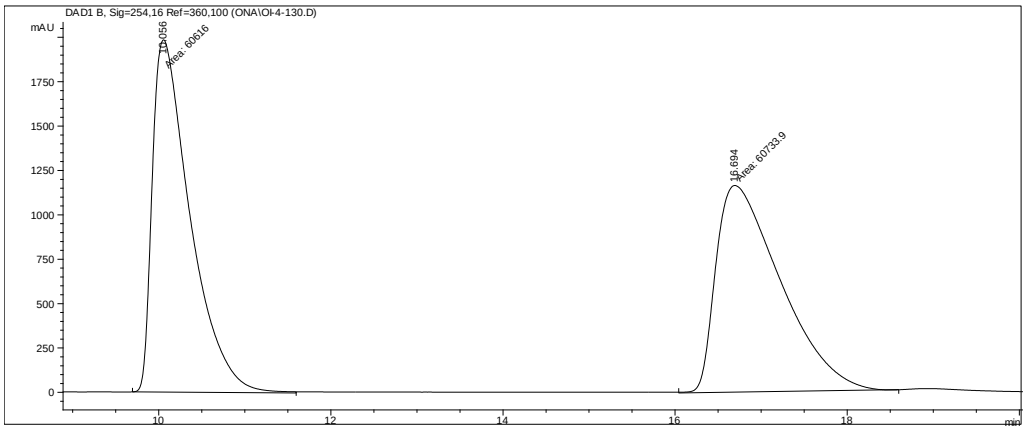
Enantioenriched:



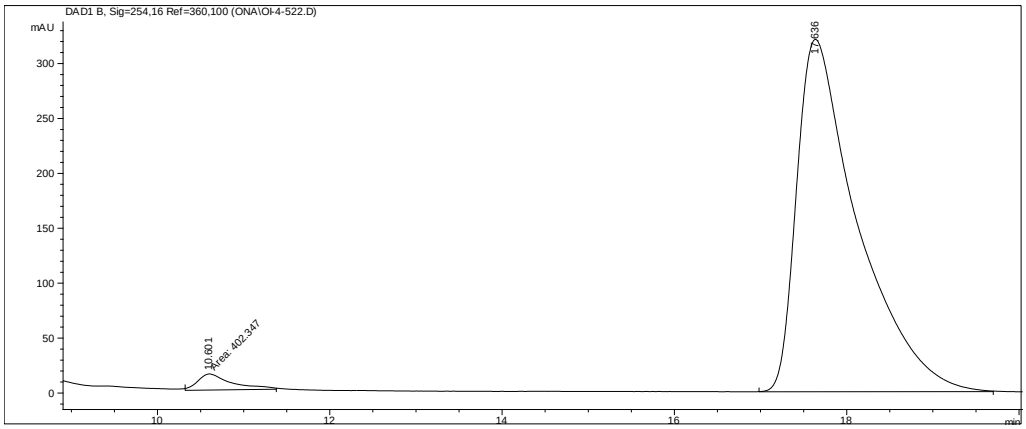


HPLC conditions: OD column, 1% *i*PrOH/Hexane, 10 °C, 1 ml/min, R_t: 10.60 min (minor (*S*,*S*)), 17.64 min (major (*R*,*R*));

Racemic

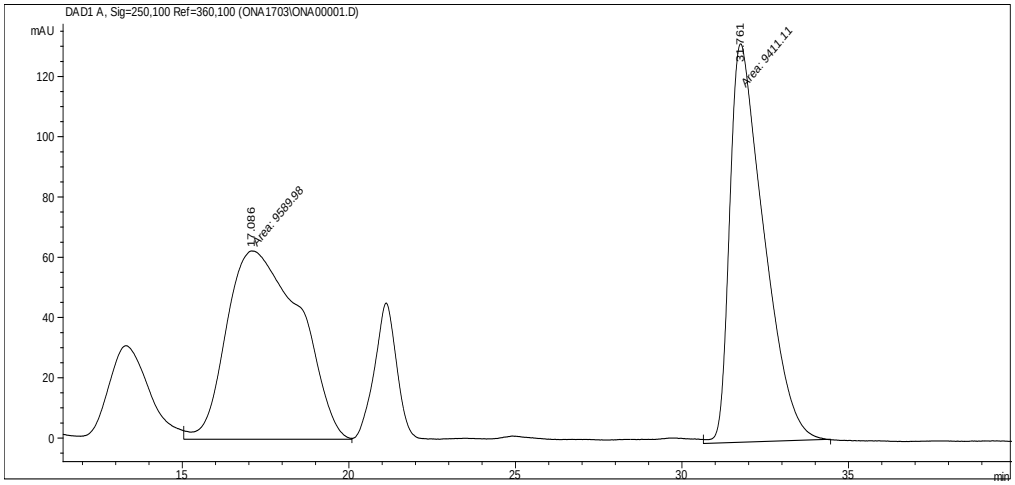


Enantioenriched

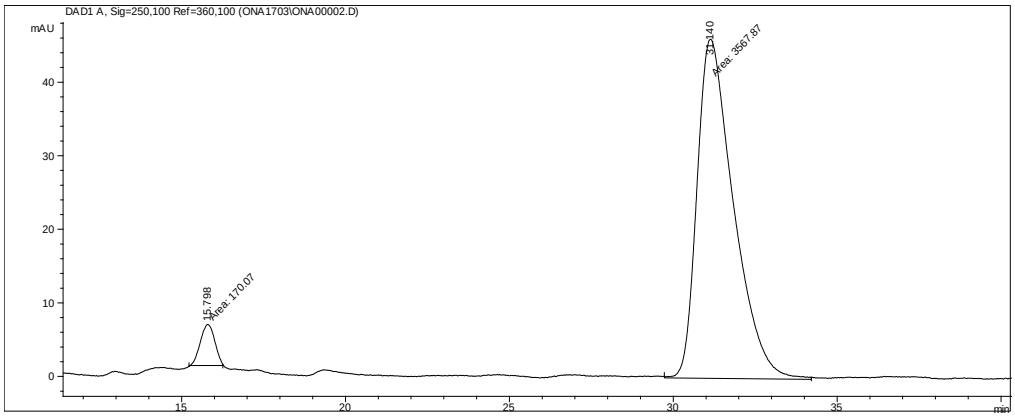


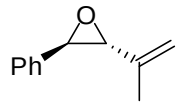
HPLC conditions: OD column, 0.5% *i*PrOH/Hexane, 0.5 ml/min, R_t <u>*trans*</u>: 15.77 min ((*S*,*S*), minor), 31.15 min ((*R*,*R*), major), <u>*cis*</u>: 13.31 min and 21.1 min;

Racemic



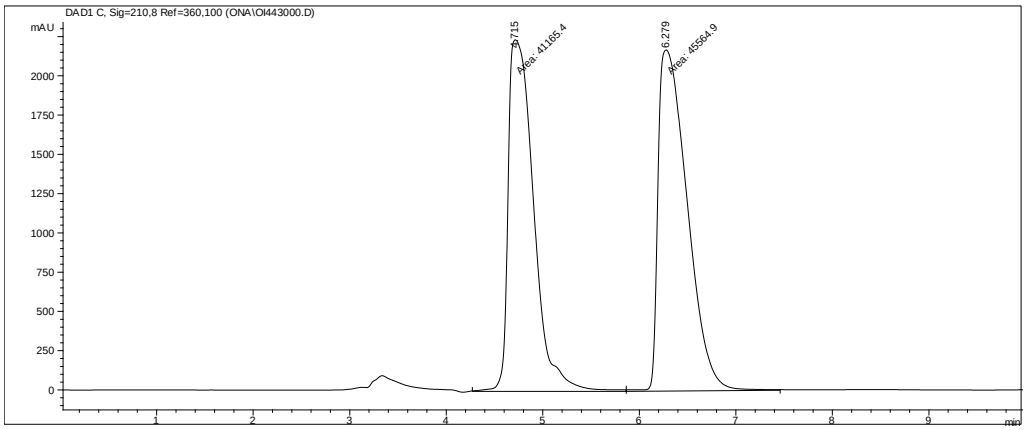
Enantioenriched:



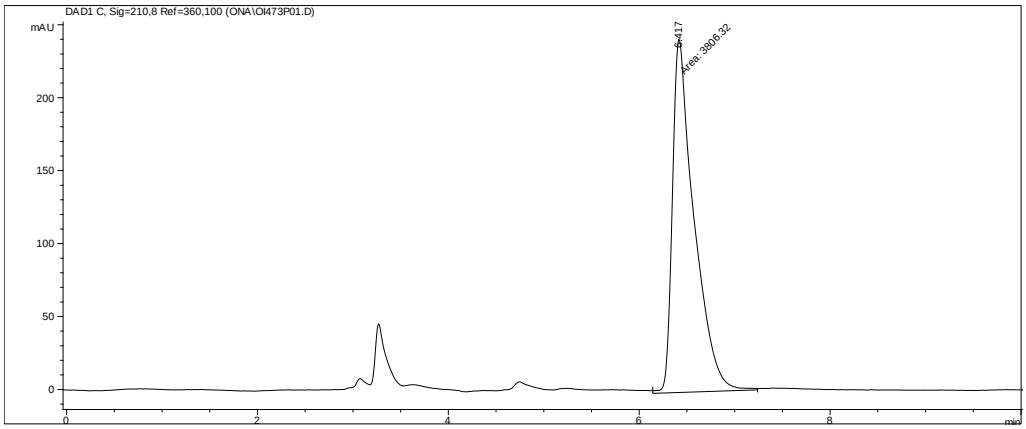


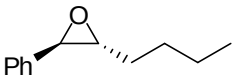
HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1 ml/min, R_t 4.75 min ((*S*,*S*), minor), 6.42 min ((*R*,*R*), major);

Racemic



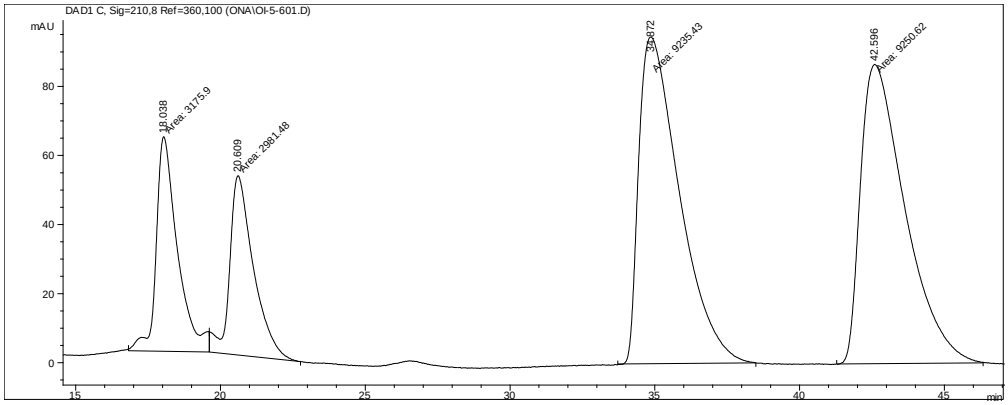
Enantioenriched



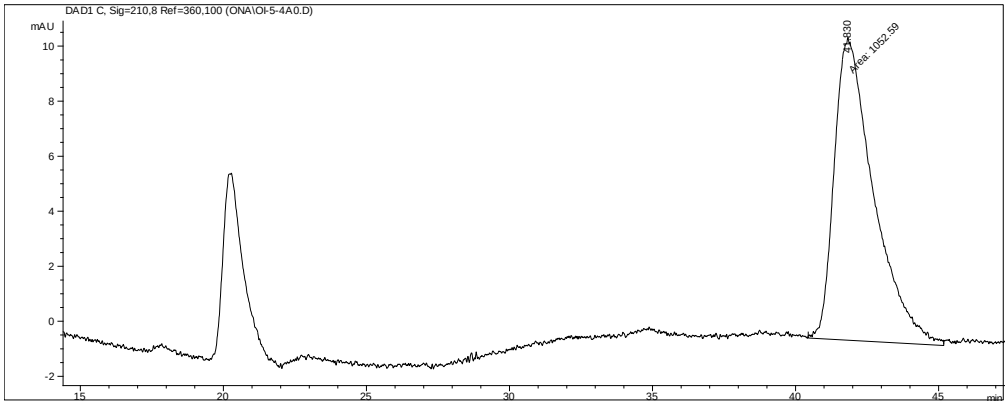


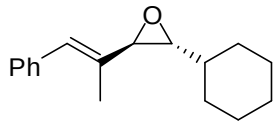
HPLC conditions: OD column, 0.5% *i*PrOH/Hexane, 1 ml/min, R_t <u>*trans*</u>: 34.86 min ((*S*,*S*), minor), 42.59 min ((*R*,*R*), major), <u>*cis*</u>: 18.04 min and 20.61 min;

Racemic



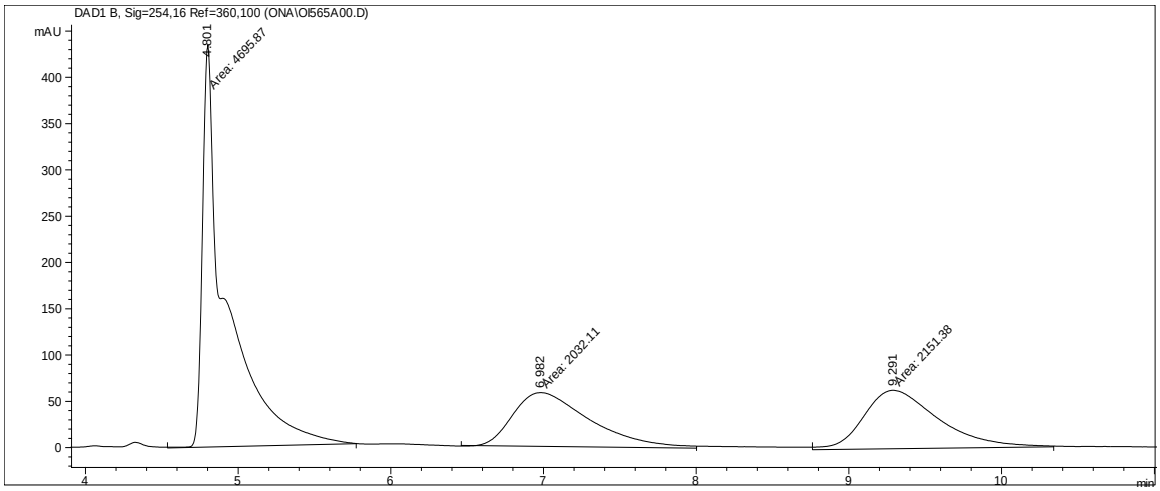
Enantioenriched



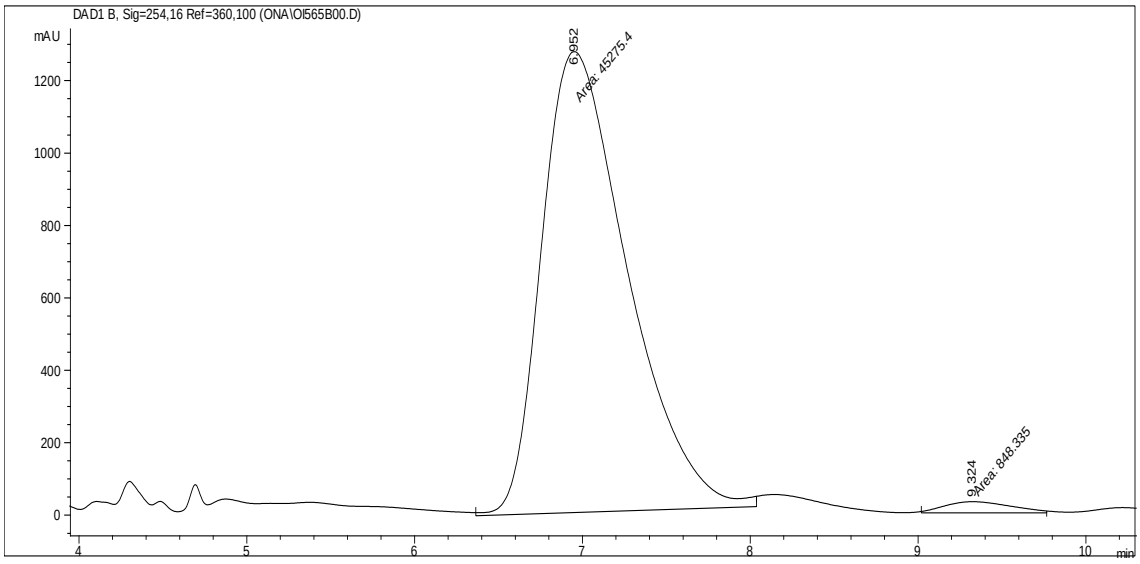


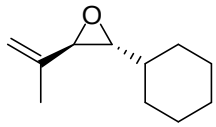
HPLC conditions: OD column, 1% IPA/Hexane, 1 ml/min, R_t <u>*trans*</u>: 6.98 min ((*R*,*R*), major), 9.29 min ((*S*,*S*), minor), <u>*cis*</u>: 4.80 min;

Racemic



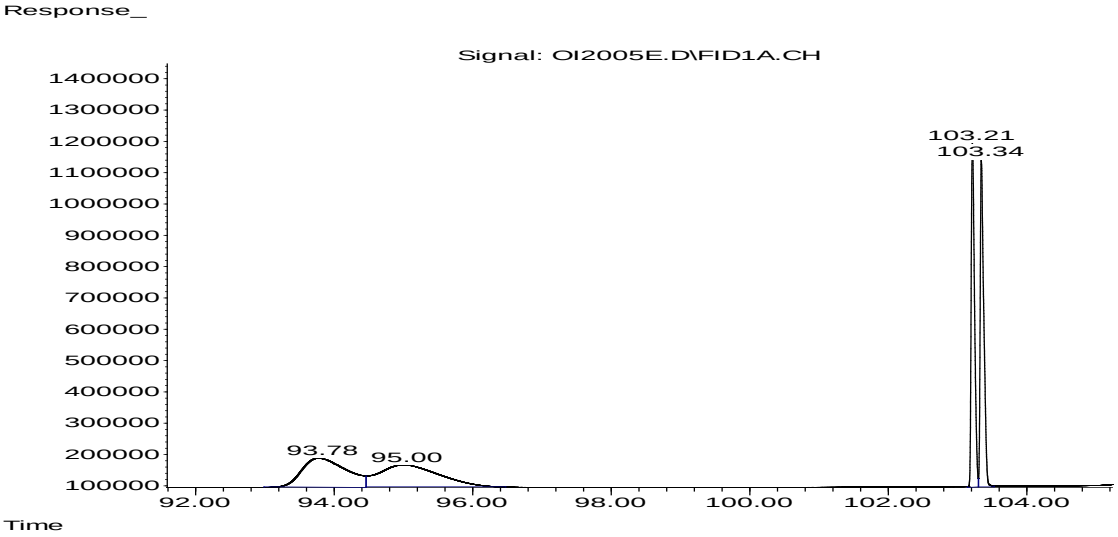
Enantioenriched



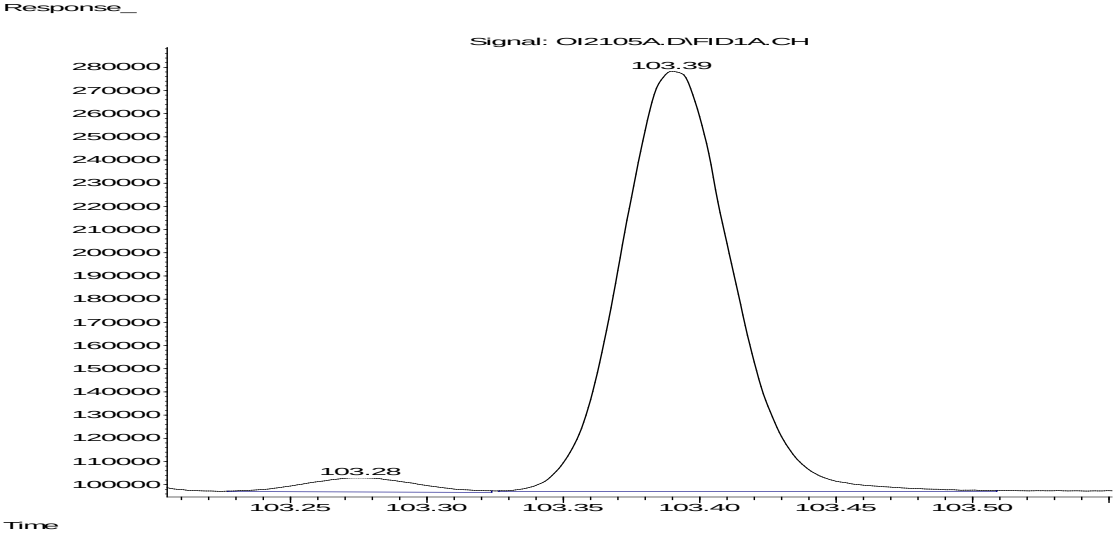


Chiral GC conditions: α-Dex column, oven temperature: 70 °C for 100 min and then ramp with 25 °C/min until 200 °C, R_t <u>*trans*</u>: 103.21((*S*,*S*), minor), 103.34((*R*,*R*), major), <u>*cis*</u>: 93.78 and 95.00 min;

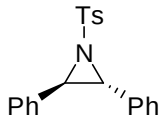
Racemic



Enantioenriched

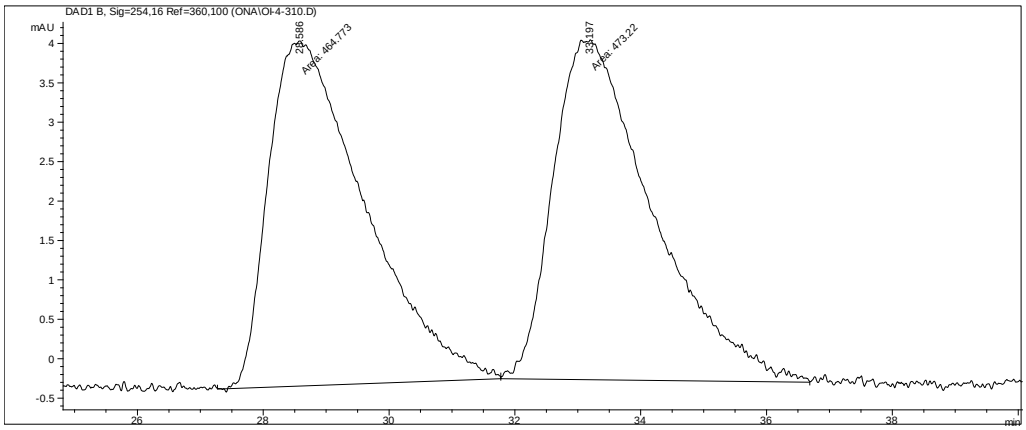


Chiral Phase Chromatograms for Aziridines

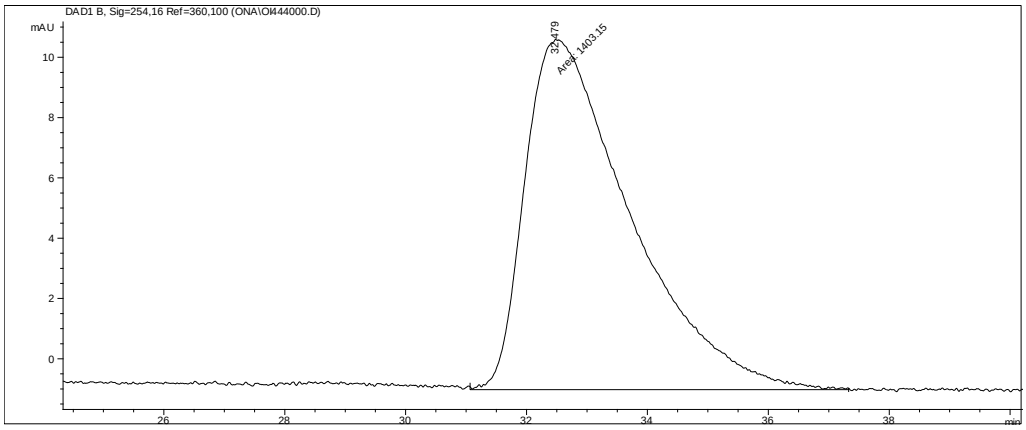


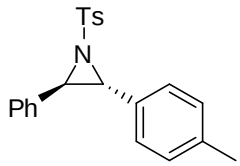
OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t <u>*trans*</u>: 28.53 min ((*S*,*S*), minor), 33.20 min ((*R*,*R*), major).

Racemic



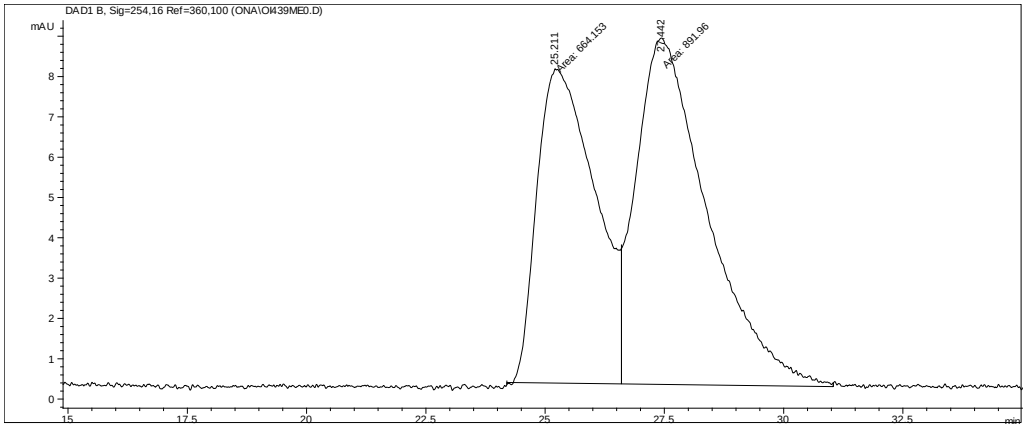
Enantioenriched



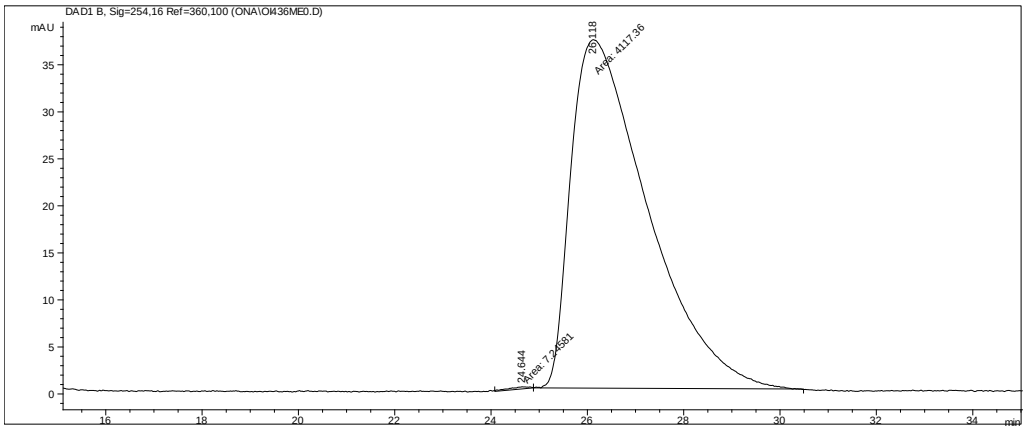


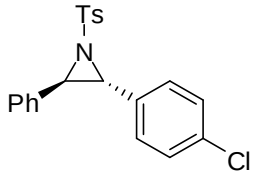
HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t <u>*trans*</u>: 25.22 min ((*S*,*S*), minor), 27.44 min ((*R*,*R*), major);

Racemic



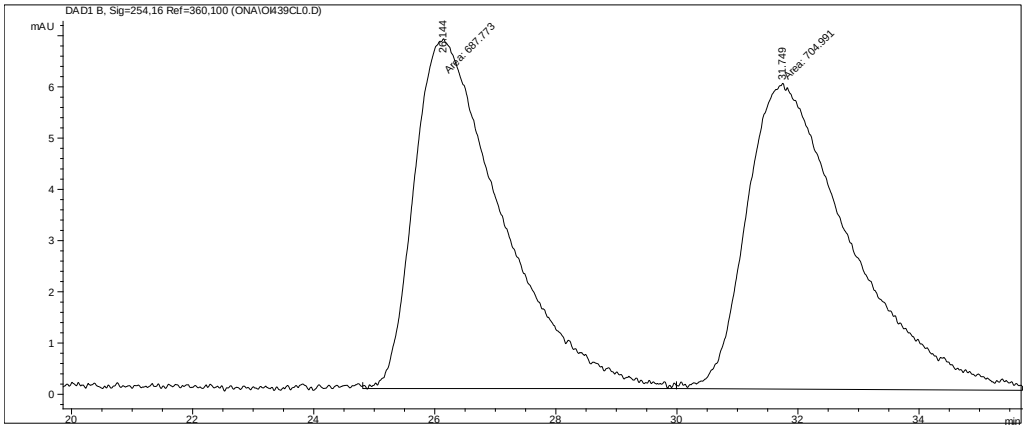
Enantioenriched



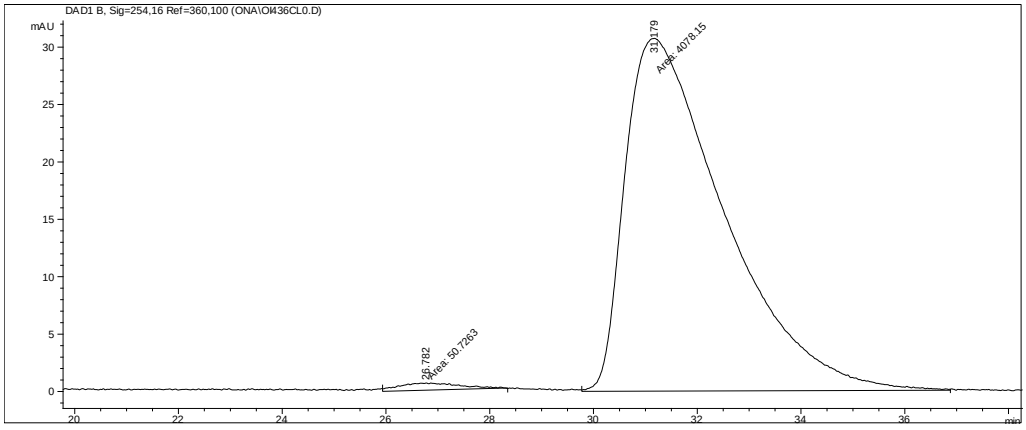


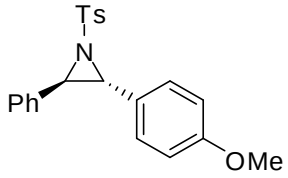
HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t <u>*trans*</u>: 26.13 min ((*S*,*S*), minor), 31.75 min ((*R*,*R*), major).

Racemic



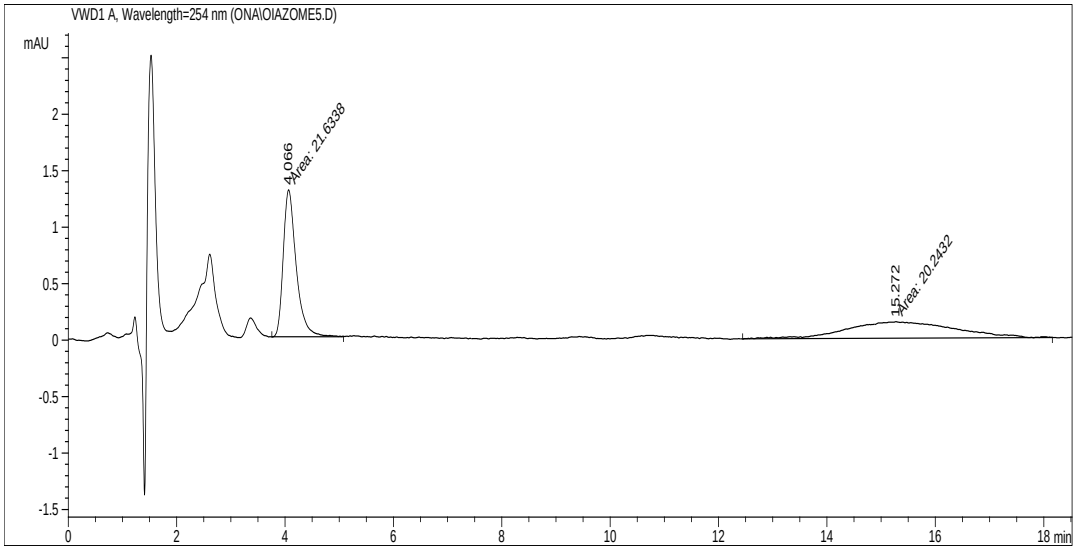
Enantioenriched



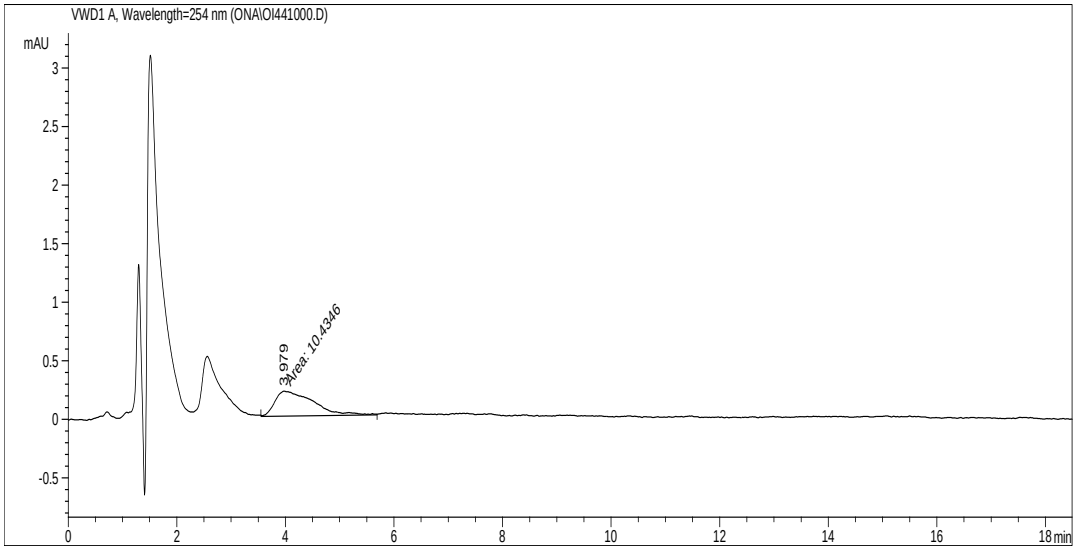


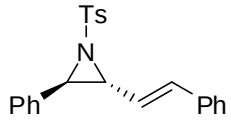
HPLC conditions: Chiral AGP column, 1% *i*PrOH:10mM phosphate buffer pH=7, 0.75 ml/min, R_t <u>*trans*</u>: 4.07 min ((*R*,*R*), major), 20.24 min ((*S*,*S*), minor);

Racemic



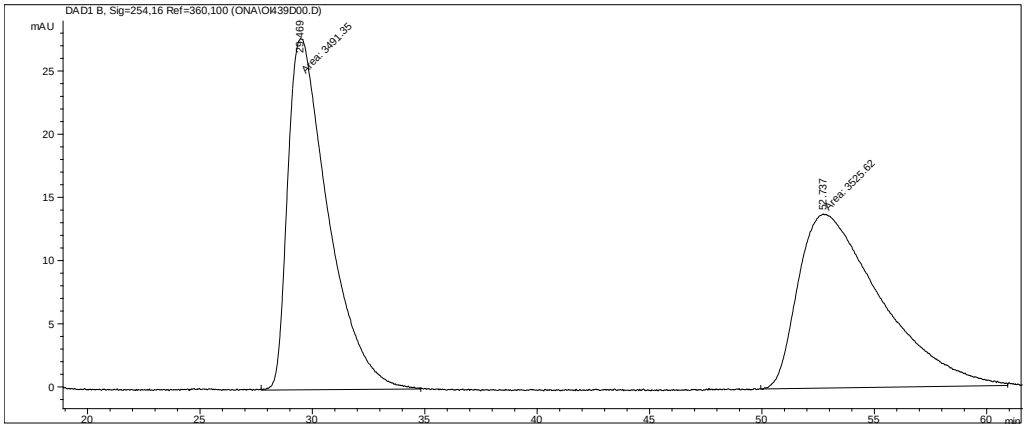
Enantioenriched



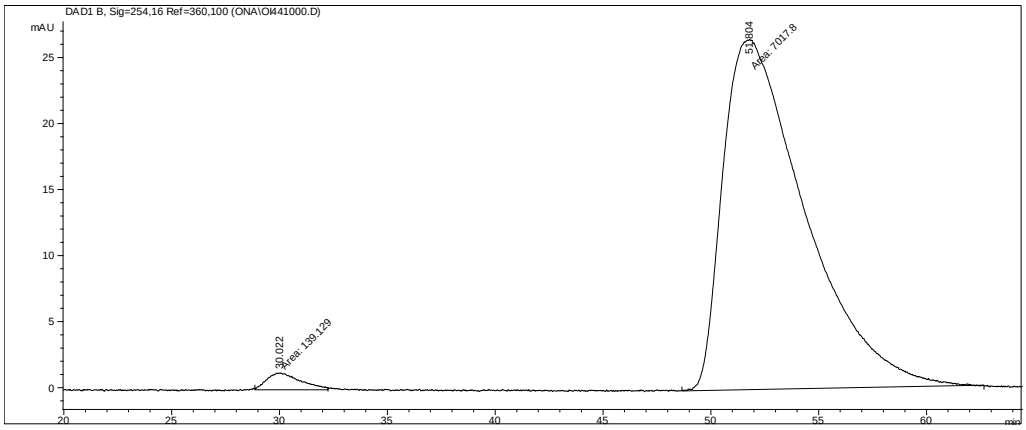


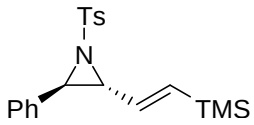
HPLC conditions: OD column, 2% *i*PrOH/Hexane, 1.5 ml/min, R_t: 29.56 min ((*S*,*S*), minor), 52.77 min ((*R*,*R*), major);

Racemic



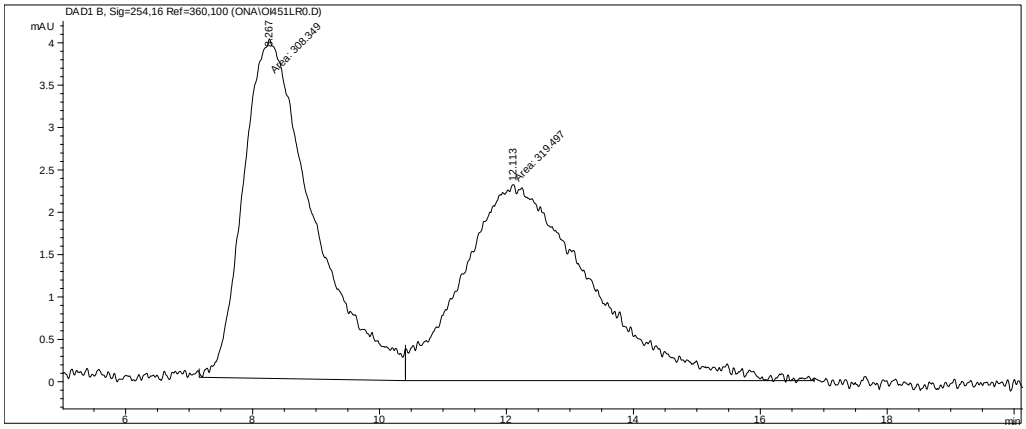
Enantioenriched





HPLC conditions: OJ column, 1% *i*PrOH/Hexane, 1.5 ml/min, R_t: 8.27 ((*S*,*S*), minor), 12.13 min ((*R*,*R*), major);

Racemic



Enantioenriched from salt derived from (*S*)-limonene