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Copper-Catalyzed Enantioselective Alkene Carboetherification for the Synthesis of Saturated Six-Membered Cyclic Ethers

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Supporting Information

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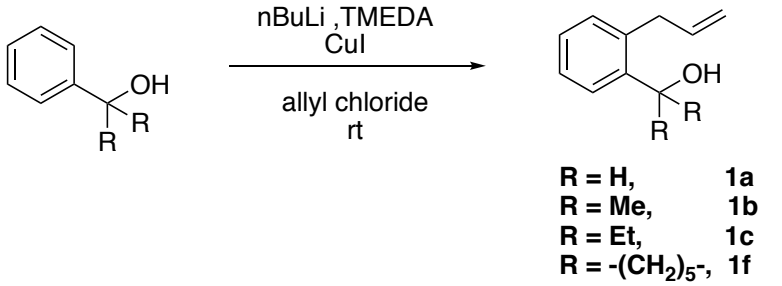
General information: ^{1}H NMR spectra were recorded on 300, 400, or 500 MHz Varian spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on Varian 300 (75 MHz) or 400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0 ppm). Infrared spectra were recorded neat on a Nicolet-Impact 420 FT-IR spectrometer. Wave numbers in cm^{-1} are reported for characteristic peaks. High resolution mass spectra were obtained on a ThermoFinnigan MAT XL spectrometer at the University at Buffalo Mass Spectrometry Facility. Melting points were obtained on an electrothermal melting point apparatus and are reported uncorrected. Optical rotations were measured on a Rudolph Autopol I digital polarimeter fitted with a micro cell with a 1 dm path length and are reported as: $[\alpha]_{\lambda}^{T^{\circ}C}$ (c = g/100 mL, solvent). Enantiomeric excess was determined by gas chromatography (GC) using CP-Chirasil-DEX CB 25 X 0.25 column, or high performance liquid chromatography (HPLC) using Chiralpak AD-RH or Regis (*S*, *S*)-Whelk chiral columns with UV detection.

All experiments were carried out under an argon atmosphere. Unless otherwise noted, all reagents were purchased from Aldrich, Acros, or Strem, and used without further purification. The bisoxazoline ligand, 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole), (achiral box) used to generate racemic samples for GC and HPLC traces, was synthesized as previously described.[1] Manganese (IV) oxide was purchased from Aldrich as an activated, <5 μm powder of 85% purity. Solvents were purified using a solvent filtration system purchased from Contour Glass Co. (Irvine,

California). Trifluorotoluene ($PhCF_3$) was purchased from Acros, 99+ % purity, and distilled over calcium hydride prior to use. All reactions were sensitive to moisture.

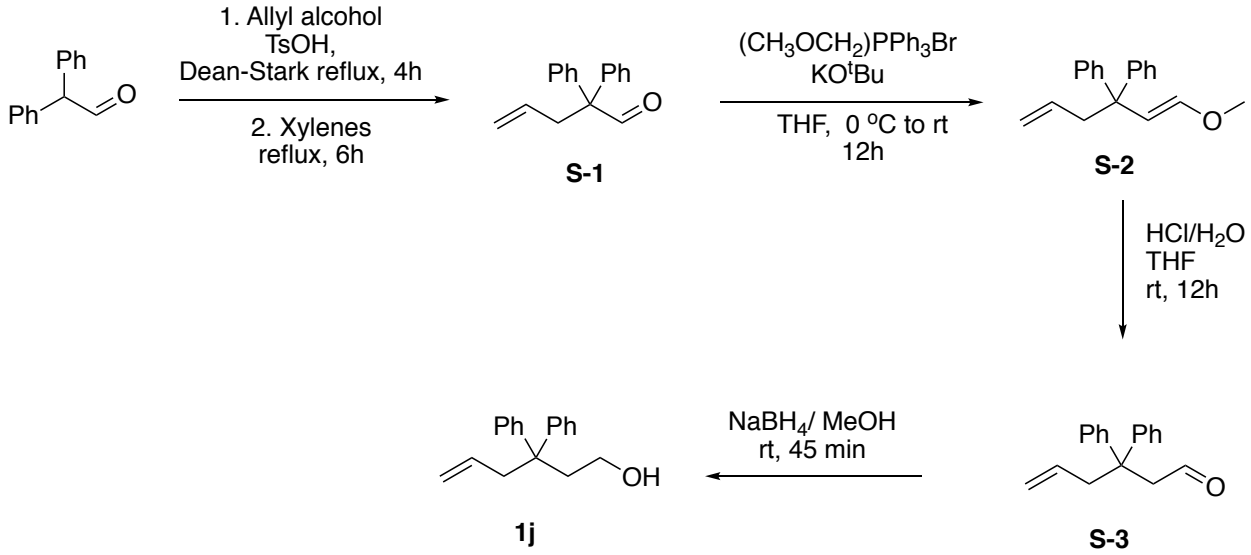
Synthesis of Substrates

2-Allylbenzyl alcohols **1a-1c and 1f** were synthesized as previously reported.[2]



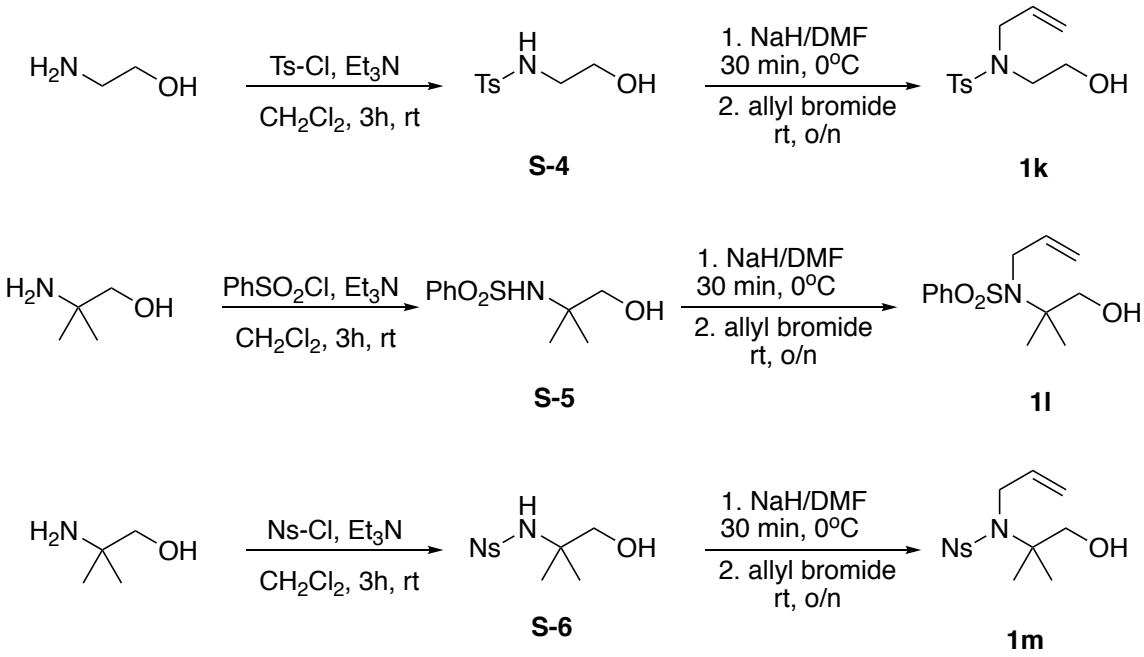
R = H, 1a
R = Me, 1b
R = Et, 1c
R = -$(CH_2)_5$-, 1f

3,3-Diphenylhex-5-en-1-ol (**1j**) was synthesized from 2,2-diphenyl-4-pentenal, **S-1**, as described in the literature.[3] The synthesis of **S-1** from diphenylacetaldehyde also followed a literature procedure.[4]

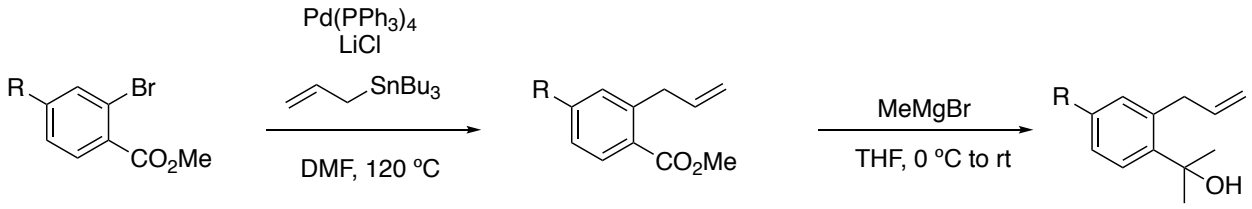


N-Allyl-*N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (**1k**) was synthesized as previously reported.[5] *N*-allyl-N-(1-hydroxy-2-methylpropan-2-yl)benzenesulfonamide (**1l**) and *N*-allyl-*N*-

(1-hydroxy-2-methylpropan-2-yl)-4-nitrobenzenesulfonamide (**1m**) were synthesized as previously described.[2]



The alcohols **1d** and **1e** were synthesized as follows:



Methyl 2-allyl-4-methoxybenzoate (S-7d):

Ester **S-7d** was synthesized following a literature procedure.[6] A 10 mL reaction tube was flame dried, equipped with a stirrer bar, and placed under argon. Lithium chloride (170 mg, 2 equiv.), and tetrakis(triphenylphosphine) palladium (116 mg, 5 mol%) were added to the reaction tube followed by THF (4 mL), allyltributyltin (0.68 mL, 1.1 equiv.), and methyl 2-bromo-4-methoxy benzoate (490 mg, 2 mmol). The reaction tube was sealed, stirred, and heated to 100 ℃ for 12 h. The reaction was then diluted with EtOAc and filtered through a short pad of silica gel mixed with potassium fluoride (10 % by weight) and washed with EtOAc (3 x 20 mL). The organic washings were combined and concentrated *in vacuo*. The crude residue was then purified by flash chromatography (silica gel, 10-20 % EtOAc in hexanes) to give 311.1 mg of **S-7d** as a colorless oil (74 % yield). The ^{1}H NMR of **S-7d** matched the previously reported.[6] ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 9.4 Hz, 1H), 6.77 (d, *J* = 7.2 Hz, 3H), 6.11 – 5.91 (m, 1H), 5.01 (dd, *J* = 7.0, 1.7 Hz, 1H), 3.88 – 3.73 (m, 12H).

2-(2-allyl-4-methoxyphenyl)propan-2-ol (1d):

A 50 mL round bottomed flask was equipped with a magnetic stirrer bar, flame dried and placed under argon. The flask was then charged with a methyl magnesium bromide solution in THF (1M, 3.2 mL, 2.5 equiv.) and placed at 0 ℃ under argon. A solution of ester **S-7d** (311 mg, 1.27 mmol) in THF (4 mL) was then added dropwise and the flask was warmed to rt over two h while being stirred. The reaction was quenched with aqueous NH_4Cl and extracted with EtOAc (3 x 30 mL). The organic extracts were combined and dried over magnesium sulfate, then concentrated *in vacuo*. The crude residue was then purified by flash chromatography (silica gel, 10-30 % EtOAc in hexanes) to give 155.3 mg of **1d** as a colorless oil (50% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.7 Hz, 1H), 6.80 (d, *J* = 2.8 Hz, 1H), 6.72 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.06 (dd, *J* = 16.9, 10.4 Hz, 1H), 5.15 – 4.97 (m, 2H), 3.81 (s, 3H), 3.80 (t, *J* = 1.5 Hz, 1H), 1.66 (s, 6H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 139.7, 139.1, 138.0, 126.7, 117.7, 115.5, 110.7, 73.5, 55.2, 38.3, 31.9.; IR (neat): cm-1 3386.2, 3077.6, 2974.6, 2934.8, 2835.3, 1606.1, 1573.7, 1497.3, 1240.1, 1037.9, 908.8, 810.1, 602.7, 577.9.; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{13}H_{19}O_2Na$: 229.1199, found: 229.1197.

Methyl 2-allyl-4-(trifluoromethyl)benzoate (S-7e):

A 10 mL reaction tube was flame dried, equipped with a stirrer bar, and placed under argon. Lithium chloride (170 mg, 2 equiv.), and tetrakis(triphenylphosphine) palladium (116 mg, 5 mol%) were added to the reaction tube followed by THF (4 mL), allyltributyltin (0.68 mL, 1.1 equiv.), and methyl 2-bromo-4(trifluoromethyl) benzoate (566 mg, 2 mmol). The reaction tube was sealed, stirred, and heated to 100 ℃ for 12 h. The reaction was then diluted with EtOAc and filtered through a short pad of silica gel mixed with potassium fluoride (10 % by weight) and washed with EtOAc (3 x 20 mL). The organic washings were combined and concentrated *in vacuo*. The crude residue was then purified by flash chromatography (silica gel, 10-20 % EtOAc in hexanes) to give 364.4 mg of **S-7e** as a colorless oil (75 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.1 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 2H), 6.07 – 5.90 (m, 1H), 5.16 – 5.01 (m, 2H), 3.94 (s, 3H), 3.81 (d, *J* = 6.5 Hz, 2H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 142.3, 136.2, 133.5 (q, $^{2}J_{CF}$ = 32.5 Hz), 133.1, 130.9, 127.6 (q, $^{3}J_{CF}$ = 3.8 Hz), 125.0, 123.6 (q, $^{1}J_{CF}$ = 270 Hz), 123.02 (q, $^{3}J_{CF}$ = 3.8 Hz), 122.2, 116.6, 52.3, 38.1.; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.17.; IR (neat): 3083.3, 2955.8, 1728.0, 1689.6, 1436.2, 1332.6, 1266.4, 1167.7, 1126.2,

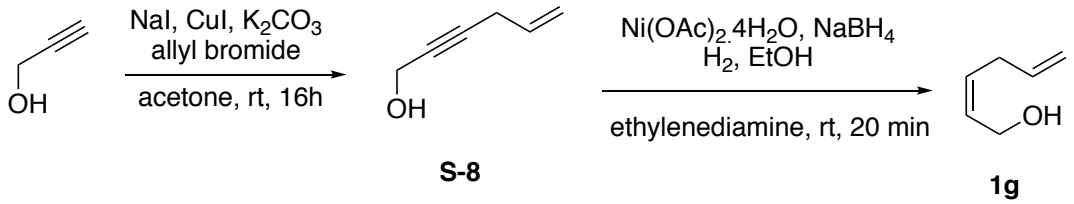
1091.1, 922.3, 813.7, 713.1, 627.1 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{12}H_{11}F_3O_2Na$: 267.0603, found: 267.0602.

2-(2-allyl-4-(trifluoromethyl)phenyl)propan-2-ol (1e):

A flame dried round bottomed flask was charged with a 1 M methyl magnesium bromide solution in THF (3.7 mL, 2.5 equiv) and placed at 0 ℃ under argon. A solution of ester **S-7e** (364 mg, 1.5 mmol) in THF (4 mL) was then added dropwise and the flask was warmed to rt over 2 h while being stirred. The reaction was quenched with aqueous NH_4Cl and extracted with EtOAc (3 x 30 mL). The organic extracts were combined, dried over magnesium sulfate, and then concentrated *in vacuo*. The crude residue was then purified by flash chromatography (silica gel, 10-30 % EtOAc in hexanes) to give 214 mg of **1e** as a colorless oil (59 % yield).

^1H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.80 (m, 1H), 7.62 – 7.39 (m, 3H), 6.06 (ddt, J = 16.5, 10.1, 6.1 Hz, 1H), 5.23 – 4.89 (m, 2H), 3.86 (d, J = 6.1 Hz, 2H), 1.69 (s, 6H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 149.5, 138.8, 138.3, 129.3 (q, $^2J_{CF}$ = 32 Hz), 129.1, 129.0, 128.91 (q, $^3J_{CF}$ = 3.7 Hz), 127.8, 126.1, 125.5, 123.1 (q, $^1J_{CF}$ = 271 Hz) 122.77 (q, $^3J_{CF}$ = 3.7 Hz), 120.4, 116.2, 73.7, 38.2, 31.7, 29.2.; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.61.; IR (neat): 3370.3, 3082.4, 2979.9, 2935.6, 1638.6, 1618.0, 1407.4, 1324.0, 1162.7, 1121.6, 1100.4, 829.8 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{13}H_{15}F_3ONa$: 267.0967, found: 267.0966.

The dienyl alcohol **1g** was synthesized via **S-8** from a previously reported procedure.[7]



(*Z*)-hexa-2,5-dien-1-ol (1g)

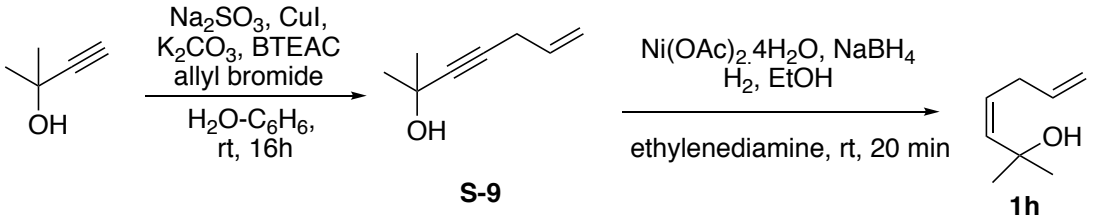
The ^{1}H NMR spectrum for **S-8** matched the previously reported.[7]

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90 – 5.72 (m, 1H), 5.35 – 5.25 (m, 1H), 5.17 – 5.07 (m, 1H), 4.33 – 4.24 (m, 2H), 3.06 – 2.96 (m, 2H), 1.70 (s, 1H).

Compound **1g** was synthesized using a modified protocol of a previously reported procedure.[7] An oven-dried Schlenk flask equipped with a stir bar was connected to a Schlenk line equipped with a hydrogen tank and vacuum pump. The flask was evacuated and back-filled with hydrogen twice. A continuous flow of hydrogen gas through the flask was then maintained. Nickel acetate tetrahydrate (1.3 g, 5.2 mmol) was placed in the flask and then suspended in 100% EtOH (50 mL). Sodium borohydride (197 mg, 5.2 mmol) was then added at rt, which turned the bright green suspension black. The black suspension was stirred for 20 min under hydrogen. Ethylenediamine (1.4 mL, 20.8 mmol) was then added to the solution and the reaction further stirred for 10 min. The intermediate **S-8** (500 mg, 5.2 mmol, diluted in 10 mL EtOH) was then added. After 20 min the reaction was deemed complete (TLC monitoring) and was quenched with Et_2O (50 mL) and filtered through a pad of Celite. The filtrate was washed with brine, dried over Na_2SO_4, and concentrated by short path distillation of solvent at ambient pressure. The crude was purified by flash chromatography (silica gel, 20-25% Et_2O in pentanes) followed by short path distillation of

solvent at ambient pressure to give alcohol **1g** as a colorless oil (298 mg, 58%). ^{1}H NMR matched the previously reported.[8] (**Note :** The dienol **1g** is volatile and was stored at -18 °C.)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 – 5.75 (m, 1H), 5.73 – 5.65 (m, 1H), 5.63 – 5.53 (m, 1H), 5.09 – 4.97 (m, 2H), 4.24 – 4.16 (m, 2H), 2.88 – 2.80 (m, 2H), 1.45 – 1.34 (m, 1H).



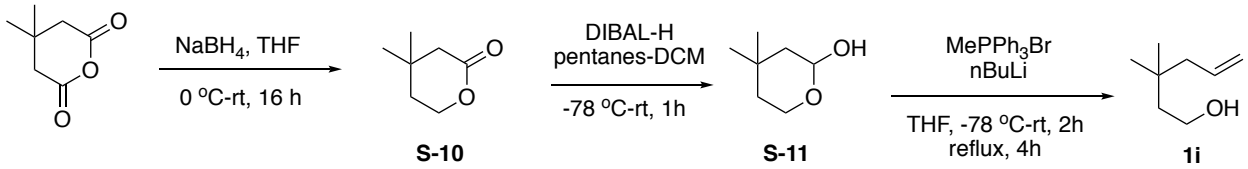
(*Z*)-2-methylhepta-3,6-dien-2-ol (1h)

Propargyl alcohol **S-9** was synthesized as previously reported.[9] Its ^{1}H NMR matched the previously reported spectrum.[9] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 – 5.71 (m, 1H), 5.35 – 5.23 (m, 1H), 5.15 – 5.05 (m, 1H), 3.01 – 2.92 (m, 2H), 1.87 – 1.80 (m, 1H), 1.51 (d, J = 1.9 Hz, 6H).

Nickel acetate tetrahydrate (547 mg, 2.2 mmol) was dissolved in 100% EtOH (25 mL) and placed under H_2 filled balloon. A solution of sodium borohydride (83 mg, 2.2 mmol) in EtOH (2.2 mL) was then added at room temperature, turning the bright green solution black. After 30 min, ethylenediamine (0.6 mL, 8.8 mmol) and the resulting solution was stirred for a further 10 min. The intermediate **S-9** (273 mg, 2.2 mmol, diluted in 4 mL 100% EtOH) was then added. After 20 min of monitoring by TLC, the reaction was quenched with Et_2O (25 mL) and filtered through a pad of Celite, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude was purified by flash chromatography (silica gel, 20% Et_2O in pentanes) to give alcohol **1h** as a colorless oil (110 mg, 40%). (**Note :** Despite our best efforts it was not possible to completely

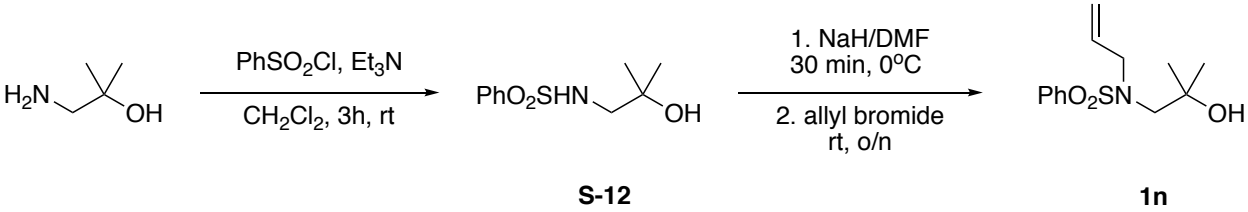
eliminate over-reduced product in the NMR samples. The impurities have been clearly identified in the NMR spectrum.)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 – 5.78 (m, 1H), 5.58 – 5.44 (m, 1H), 5.41 – 5.25 (m, 1H), 5.09 – 4.95 (m, 2H), 3.14 – 3.07 (m, 2H), 1.35 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 137.4, 127.6, 114.7, 77.3, 76.9, 76.7, 71.7, 32.2, 31.1, 31.1; IR (neat): 3387, 2971, 2930, 1712, 1637, 1463, 1363, 1143, 992, 957 cm^{-1}; HRMS (ESI) calc'd for $[M+Ag]^+$ $C_8H_{14}AgO$: 233.0090, found: 233.0090.



3,3-Dimethylhex-5-en-1-ol (1i)

3,3-Dimethylhex-5-en-1-ol (**1i**) was synthesized according to a literature procedure.[10] ^{1}H NMR matched previously reported literature data.[10] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91 – 5.73 (m, 1H), 5.09 – 4.94 (m, 2H), 3.71 (t, J = 7.6 Hz, 2H), 2.00 – 1.94 (m, 2H), 1.57 – 1.47 (m, 2H), 1.21 (s, 1H), 0.91 (s, 7H).

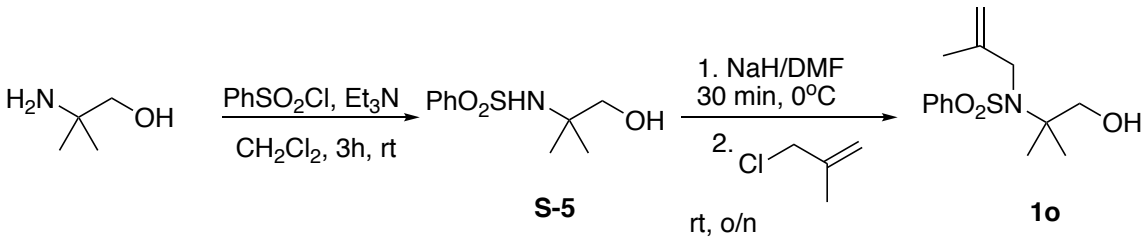


***N*-allyl-*N*-(2-hydroxy-2-methylpropyl)benzenesulfonamide (1n)**

Benzenesulfonyl chloride (0.8 mL, 6.2 mmol) and triethylamine (1.6 mL, 11.2 mmol) were added to a solution of 1-amino-2-methylpropan-2-ol (500 mg, 5.6 mmol) in dichloromethane (5 mL). The reaction was stirred at rt overnight. The reaction was then quenched with water (10 mL) and extracted with CH_2Cl_2 (3 X 25 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated in vacuo to give the crude sulfonamide **S-12**. The crude was used in the next step without further purification.

NaH (98 mg, 4.1 mmol) was added to a solution of crude sulfonamide **S-12** (3.4 mmol) in DMF (7 mL) at 0 °C under argon. After 20 min, allyl bromide (0.4 mL, 4.1 mmol) was added, and the reaction was stirred and allowed to warm to rt for 16 h. The reaction mixture was concentrated and purified by flash chromatography (silica gel, 40% EtOAc in hexanes) to give the alcohol **1n** as a clear oil (776 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, J = 8.4, 1.4 Hz, 2H), 7.63 – 7.44 (m, 3H), 5.60 – 5.38 (m, 1H), 5.20 – 5.00 (m, 2H), 4.01 – 3.84 (m, 2H), 3.12 (s, 2H), 1.24 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 132.9, 132.7, 129.1, 127.3, 119.6, 71.3, 57.6, 53.2, 27.6, 22.8; IR (neat): 3521, 2976, 2930, 1641, 1446, 1326, 1153, 1089, 1045, 970, 924 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{13}H_{19}NNaO_3S$: 292.0978, found: 292.0985.

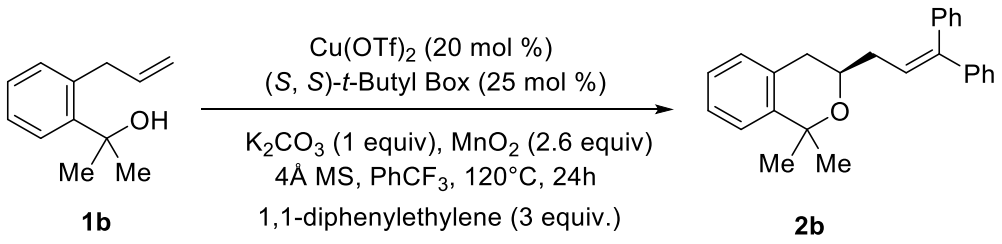


***N*-(1-hydroxy-2-methylpropan-2-yl)-*N*-(2-methylallyl)benzenesulfonamide (1o)**

NaH (374 mg, 15.6 mmol) was added to a solution of crude sulfonamide **S-5** (13.0 mmol) in DMF (26 mL) at 0 °C under argon. After 20 min, 3-chloro-2-methylpropene (1.4 mL, 15.6 mmol) was added, and the reaction was stirred and allowed to warm to rt for 16 h. The reaction mixture was concentrated and purified by flash chromatography (silica gel, 30% EtOAc in hexanes) to give the alcohol **1o** as a waxy solid (552 mg, 15% over two steps).

^{1}H NMR (300 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.75 (m, 2H), 7.61 – 7.39 (m, 3H), 5.08 (s, 1H), 4.93 (s, 1H), 3.98 (s, 2H), 3.64 (s, 2H), 1.76 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 142.5, 132.5, 128.9, 127.0, 111.6, 69.5, 63.9, 52.4, 24.2, 20.0; FTIR (neat, thinfilm) ν 3534, 3069, 2980, 1652, 1446, 1322, 1147, 1322, 1147, 1091 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{14}H_{21}NNaO_3S$: 306.1134, found: 306.1136.

Representative Procedure for Carboetherification Reactions (Conditions A)



1b **2b**

(*R*)-3-(3,3-Diphenylallyl)-1,1-dimethylisochromane (2b)

$Cu(OTf)_2$ (12.9 mg, 0.036 mmol) was flame dried under vacuum in a 12 mL pressure tube until there was no visible blue in the white powder (~1-2 min). Afterwards, the pressure tube was charged with argon before adding a magnetic stir bar, (*S, S*)-*t*Bu-Box (13.2 mg, 0.045 mmol), and 0.9 mL of $PhCF_3$. The pressure tube was flushed with argon for 5 min, sealed, and stirred at 60 °C for 2h. After allowing the reaction to cool to rt, K_2CO_3 (24.7 mg, 0.18 mmol) and MnO_2 (46.7 mg, 0.54 mmol, 2.6 equiv. due to 85 % purity) were added. Alcohol **1b** (31.5 mg, 0.18 mmol) was

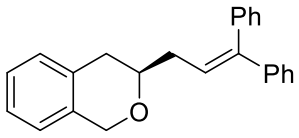
dissolved in 0.9 mL of $PhCF_3$ and added the pressure tube, followed by 1,1-diphenylethylene (0.10 mL, 0.54 mmol) and flame-dried 4Å molecular sieves (~32.0 mg). The pressure tube was flushed with argon for 5 min, sealed, and stirred at 120 °C for 24 h. After allowing it to cool to rt, the reaction mixture was diluted with 10 mL EtOAc and filtered through a pad of silica gel (~5 g). The silica was then washed with EtOAc (3 x 30 mL). The filtrate was concentrated in vacuo. The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give **2b** as a colorless oil (40.9 mg, 64%). The procedure was repeated with the achiral bis(oxazoline) ligand to generate the racemic product for analytical HPLC analysis.

ee = 94%, determined by HPLC analysis [Chiralpak AD-RH, 100% hexanes, 0.1 mL/min, λ = 254 nm, tmin = 38.86 min, tmaj = 33.55 min]; $[\alpha]_D^{21}$ = -54.5 (c 0.22, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 6.99 (m, 14H), 6.28 (t, *J* = 7.3 Hz, 1H), 3.97 – 3.82 (m, 1H), 2.75 – 2.57 (m, 2H), 2.56 – 2.34 (m, 2H), 1.54 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 143.0, 142.7, 140.1, 133.1, 130.0, 128.8, 128.2, 128.1, 127.3, 126.9, 126.1, 125.9, 125.4, 125.2, 75.4, 68.9, 36.4, 35.2, 31.5, 28.7.; IR (neat): 3022, 2973, 2924, 1598, 1491, 1445, 1378, 1363, 1271, 1169, 1109, 1062, 1036, 758, 733, 699 cm^{-1}; HRMS (EI) calc'd for $[M]^+$ $C_{26}H_{26}O_1$: 354.1978, found: 354.1990.

Conditions B for 2b

Reaction was run under similar conditions as the representative procedure except that DCE was used as the solvent and temperature was set at 105 °C. The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give **2b** as a colorless oil (78%)

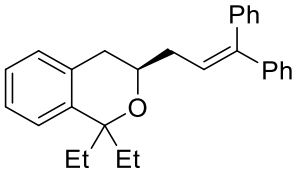
ee > 95%, determined by HPLC analysis [Chiralpak AD-RH, 100% hexanes, 0.1 mL/min, λ = 254 nm, tmin = 38.86 min, tmaj = 33.55 min]; $[\alpha]_D^{27}$ = -40.4 (c 0.1, $CHCl_3$).



2a

(*R*)-3-(3,3-Diphenylallyl)isochromane (2a) (Conditions C)

The isochroman **2a** was synthesized following the representative procedure, using alcohol **1a** except that 1 equiv. of Ag_2CO_3 instead of MnO_2, and the reaction was run in 1, 2-dichloroethane (DCE) at 105 °C for 24 h. The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give 33 mg of the desired product as a colorless oil (50% yield). *ee* = 89 ± 3%, determined by HPLC analysis [Chiralpak AD-RH, 70:30 CH_3CN:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 19.74 min, tmaj = 18.05 min]; $[\alpha]_D^{23}$ = -18.8 (c 0.79, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.19 (m, 10H), 7.18 – 7.12 (m, 2H), 7.11 – 7.04 (m, 1H), 6.99 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.28 (t, *J* = 7.4 Hz, 1H), 4.84 (ABq, J_{ABq} = 15Hz, ν_{ABq} = 9.94 Hz, 2H), 3.83 – 3.73 (m, 1H), 2.79 – 2.64 (m, 2H), 2.57 – 2.40 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 142.5, 140.0, 134.7, 133.2, 129.9, 128.8, 128.2, 128.1, 127.2, 127.0, 126.3, 126.0, 125.0, 124.1, 74.9, 68.3, 36.1, 33.8; IR (neat): 3022, 2839, 1598, 1493, 1444, 1373, 1204, 1095, 1035, 907, 871, 744, 700 cm^{-1}; HRMS (EI) calc'd for $[M]^+$ $C_{24}H_{22}O_1$: 326.1665, found: 326.1673.

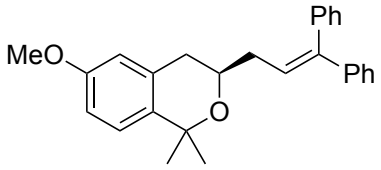


2c

(*R*)-3-(3,3-Diphenylallyl)-1,1-diethylisochromane (2c)

The isochroman **2c** was made from the alcohol **1c** (100 mg, 0.5 mmol) with (*S, S*)-*t*Bu-Box, and 1,1-diphenylethylene in $PhCF_3$ at 120 °C for 24 h (conditions A). The crude was purified by flash chromatography (silica gel, 1% Et_2O in hexanes) to give 120 mg of the desired product as a colorless oil (63% yield).

ee = 87%, determined by HPLC analysis [Chiralpak AD-RH, 0.5% *i*-PrOH in hexanes, 1.0 mL/min, λ = 254 nm, tmin = 19.62 min, tmaj = 13.97 min]; $[\alpha]_D^{27}$ = -18.5 (c 0.1, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 6.97 (m, 14H), 6.32 (t, *J* = 7.4 Hz, 1H), 3.90 – 3.80 (m, 1H), 2.69 – 2.34 (m, 4H), 2.10 – 1.93 (m, 2H), 1.74 – 1.59 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.60 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 142.7, 141.4, 140.1, 134.6, 130.0, 128.5, 128.2, 128.1, 127.2, 126.9, 126.8, 126.1, 125.7, 125.6, 125.1, 79.8, 68.6, 36.5, 35.2, 33.0, 32.2, 8.0, 7.8.; IR (neat): 2966, 2927, 1598, 1491, 1444, 1373, 1260, 1072, 1031, 916, 873, 801, 755, 699 cm^{-1}; HRMS (EI) calc'd for $[M]^+$ $C_{28}H_{30}O_1$: 382.2291, found: 382.2292.

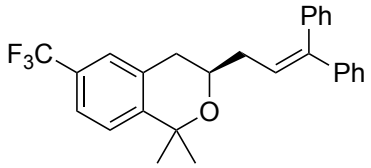


2d

(R)-3-(3,3-diphenylallyl)-6-methoxy-1,1-dimethylisochromane (2d)

The isochroman **2d** was made from the alcohol **1d** (20.6 mg, 0.1 mmol) with (*S, S*)-*t*Bu-Box, and 1,1-diphenylethylene in DCE at 105 °C for 24 h (conditions B). The crude was purified by flash chromatography (silica gel, 3 % EtOAc in hexanes) to give 25.7 mg of the desired product as a colorless oil (67% yield). *ee* >95 %, determined by HPLC analysis [Chiralpak AD-RH, 75:25 *i*-PrOH : H_2O, 0.50 mL/min, column temperature 35 °C, λ = 254 nm, tmin = 11.19 min, tmaj = 12.95 min]; $[\alpha]_D^{22}$ = -48.6 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.37 (m, 2H), 7.37 –

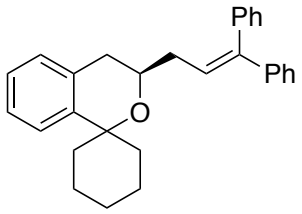
7.20 (m, 9H), 7.04 (d, *J* = 8.6 Hz, 1H), 6.77 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.59 (d, *J* = 2.7 Hz, 1H), 6.29 (dd, *J* = 8.0, 6.6 Hz, 1H), 3.96 – 3.83 (m, 1H), 3.80 (s, 3H), 2.75 – 2.57 (m, 2H), 2.57 – 2.37 (m, 2H), 1.53 (d, *J* = 2.0 Hz, 6H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 143.3, 142.7, 140.1, 135.4, 134.5, 130.0, 128.2, 128.1, 127.3, 127.0, 126.9, 126.3, 125.5, 113.1, 112.6, 75.2, 68.9, 55.2, 36.4, 35.6, 31.6, 28.7.; IR (neat): 2973.4, 2929.5, 1609.9, 1501.1, 1243.1, 1035.0, 700.9, 626.2, 593.9 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{27}H_{28}O_2Na$: 407.1982, found: 407.1982.



2e

(R)-3-(3,3-diphenylallyl)-1,1-dimethyl-6-(trifluoromethyl)isochromane (2e)

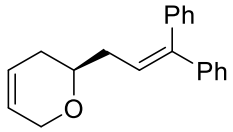
The isochroman **2e** was made from the alcohol **1e** (24.4 mg, 0.1 mmol) with (*S, S*)-*t*Bu-Box, and 1,1-diphenylethylene in DCE at 105 °C for 24 h (conditions B). The crude was purified by flash chromatography (silica gel, 3 % EtOAc in hexanes) to give 28.3 mg of the desired product as a colorless oil (67% yield). *ee* >95%, determined by HPLC analysis [Chiralpak AD-RH, 75:25 IPA:H_2O, 0.40 mL/min, column temperature 30°C, λ = 254 nm, tmin = 9.08 min, tmaj = 7.86 min]; $[\alpha]_D^{22}$ = -42.6 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.08 (m, 14H), 6.18 (dd, *J* = 7.9, 6.7 Hz, 1H), 3.82 (dq, *J* = 8.0, 5.8 Hz, 1H), 2.65 – 2.58 (m, 2H), 2.47 – 2.31 (m, 2H), 1.46 (d, *J* = 2.4 Hz, 7H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.0, 143.6, 142.6, 140.0, 134.0, 129.9, 128.4, 128.3, 128.1, 127.3, 127.0, 125.8, 125.7 (q, J_{CF} = 3.8 Hz), 125.0, 122.9 (q, J_{CF} = 3.7 Hz), 75.3, 68.7, 36.2, 35.1, 31.3, 28.5.; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.50.; IR (neat): 3026.9, 2977.6, 2930.4, 1425.4, 1335.0, 1169.0, 1124.4, 762.1, 700.8, 628.9 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{27}H_{25}F_3ONa$: 445.1750, found: 445.1750.



2f

(*R*)-3'-(3,3-Diphenylallyl)spiro[cyclohexane-1,1'-isochromane (2f)

The isochroman **2f** was made from the alcohol **1f** (43 mg, 0.2 mmol) with (*S, S*)-*i*Pr-Box, and 1,1-diphenylethylene in $PhCF_3$ at 120 °C for 24 h (Conditions A with Ligand **3b**). The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give 66 mg of the desired product as a colorless oil (84% yield). *ee* > 95%, determined by HPLC analysis [Chiralpak AD-RH, 80:20 EtOH:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 13.42 min, tmaj = 11.76 min]; $[\alpha]_D^{23}$ = -38.7 (*c* 1.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 2H), 7.33 – 7.19 (m, 8H), 7.18 – 7.07 (m, 3H), 7.02 (d, *J* = 7.2 Hz, 1H), 6.35 (t, *J* = 7.4 Hz, 1H), 3.87 – 3.77 (m, 1H), 2.74 – 2.56 (m, 2H), 2.55 – 2.38 (m, 2H), 2.12 (d, J = 13.9 Hz, 1H), 1.93 – 1.67 (m, 3H), 1.63 – 1.41 (m, 5H), 1.36 – 1.19 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3, 143.0, 142.8, 140.1, 133.6, 130.0, 128.7, 128.2, 128.1, 127.2, 126.9, 126.8, 126.1, 126.0, 125.8, 125.1, 75.8, 68.0, 39.4, 36.5, 35.4, 35.1, 25.7, 21.8, 21.7; IR (neat): 2966, 2927, 1598, 1491, 1444, 1373, 1260, 1072, 1031, 916, 873, 801, 755, 699 cm^{-1}; HRMS (EI) calc'd for $[M]^+$ $C_{29}H_{30}O_1$: 394.2291, found: 394.2295.

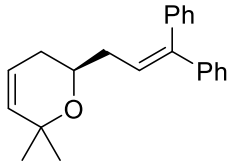


4a

(*S*)-2-(3,3-diphenylallyl)-3,6-dihydro-2H-pyran (4a)

The dihydropyran **4a** was made from the alcohol **1g** (20 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, Ag_2CO_3 and 1,1-diphenylethylene in DCE at 105 °C for 48 h (Conditions C). 2,6-Di-*tert*-butyl-4-methylpyridine was used as the base. Dihydropyran **4a** was isolated by flash chromatography (silica gel, hexanes:Et_2O 99:1) as a colourless oil (24 mg, 44%).

ee = 74 ± 4%, determined by GC analysis [CP-Chirasil-Dex CB column, T_{inj} = 200 ºC, T_{det} = 220 ˚C, flow = 2 mL/min, t_i = 110 ˚C, t_f = 190 ˚C, rate = 1 ˚C/min from 110 ˚C to 140 ˚C, 0.5 ˚C/min thereafter, FID detection, tmin = 187.4 min, tmaj = 186.4 min]; $[\alpha]_D^{23}$ = -32.7 (*c* 0.56, CH_2Cl_2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.14 (m, 10H), 6.21 (t, *J* = 7.4 Hz, 1H), 5.84 – 5.66 (m, 2H), 4.25 – 4.14 (m, 2H), 3.61 (p, *J* = 5.8 Hz, 1H), 2.46 – 2.27 (m, 2H), 2.07 – 1.93 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.9, 128.2, 128.0, 127.2, 126.9, 126.3, 125.3, 124.1, 73.7, 66.0, 36.1, 30.7. IR (neat): 2970, 2923, 1660, 1598, 1493, 1445, 1388, 1259, 1180, 1088, 1014 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{20}NaO$ $[M+Na]^+$: 299.1406, found 299.1406.

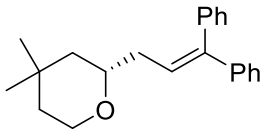


4b

(*S*)-2-(3,3-diphenylallyl)-6,6-dimethyl-3,6-dihydro-2H-pyran (4b)

The dihydropyran **4b** was made from the alcohol **1h** (25 mg, 0.2 mmol) with (*S, S*)-*i*Pr-Box, and 1,1-diphenylethylene in $PhCF_3$ at 120 °C for 24 h (Conditions A with Ligand **3b**). The crude was purified by flash chromatography (silica gel, 1% Et_2O in hexanes) to give 35 mg of the desired product as a colorless oil (58% yield). *ee* = 82%, determined by HPLC analysis [Chiralpak AD-RH, 65:35 iPrOH:H_2O, 0.3 mL/min, λ = 254 nm, tmin = 18.15 min, tmaj = 16.23 min];

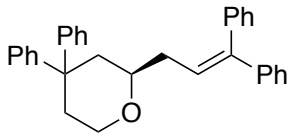
$[\alpha]_D^{22}$ = -18.3 (*c* 0.1, CH_2Cl_2)^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.07 (m, 10H), 6.20 (t, *J* = 7.3 Hz, 1H), 5.72 – 5.55 (m, 2H), 3.75 (q, *J* = 6.5 Hz, 1H), 2.34 (ddp, *J* = 20.8, 14.7, 7.0 Hz, 2H), 1.88 (d, *J* = 7.4 Hz, 2H), 1.25 (d, *J* = 3.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.1, 129.9, 128.1, 128.0, 127.2, 126.9, 125.7, 122.3, 72.8, 68.6, 36.3, 30.5, 29.5, 25.8; FTIR (neat, thinfilm) ν 2972, 1598, 1493, 1440, 1384, 1250, 1058, 759, 700 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{25}O$ $[M+H]^+$: 305.1899, found 305.1899.



5b

(*S*)-2-(3,3-diphenylallyl)-4,4-dimethyltetrahydro-2H-pyran (5b) (Conditions D)

The isochroman **5b** was synthesized following the representative procedure, using alcohol **1i** (26 mg, 0.2 mmol), (*4R, 5S*)-Bis-Ph-Box, and xylenes at 140 °C for 48 h. The crude was purified by flash chromatography (silica gel, 5% Et_2O in hexanes) to give 16 mg of the desired product as a colorless oil (26% yield). *ee* = 13 ± 1%, determined by HPLC analysis [Chiralpak AD-RH, 60:10:30 EtOH:iPrOH:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 16.19 min, tmaj = 17.71 min]; $[\alpha]_D^{23}$ = +1.73 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.12 (m, 10H), 6.19 (dd, *J* = 7.8, 6.9 Hz, 1H), 3.83 (ddd, *J* = 11.7, 5.1, 1.6 Hz, 1H), 3.66 – 3.44 (m, 2H), 2.38 – 2.12 (m, 2H), 1.46 (td, *J* = 13.1, 5.0 Hz, 1H), 1.34 – 1.02 (m, 3H), 1.00 (s, 3H), 0.93 (s, 3H).; ^{13}C NMR (101 MHz, cdcl$_3$) δ 129.92, 128.15, 128.02, 127.22, 126.87, 125.74, 77.31, 76.99, 76.67, 73.38, 64.39, 44.74, 38.77, 36.81, 33.20, 28.85, 24.07; IR (neat): 3060, 2960, 2917, 2849, 1657, 1598, 1578, 1447, 1317, 1276, 1260, 1074, 1014, 941 cm^{-1}, HRMS (EI) calcd for $C_{22}H_{26}NaO$ $[M+Na]^+$: 329.1875, found 329.1874.

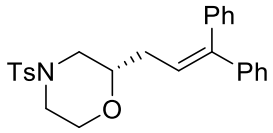


5c

(*R*)-2-(3,3-diphenylallyl)-4,4-diphenyltetrahydro-2*H*-pyran (5c) (Conditions E)

The isochroman **5c** was synthesized following the representative procedure, using alcohol **1j** (25 mg, 0.1 mmol). (*4S, 5R*)-Bis-Ph-Box was used as the ligand and 2,6-di-tert-butyl-4-methylpyridine was used as the base. Reaction was run in DCE at 105 °C for 48 h. The crude was purified by flash chromatography (silica gel, 5% Et_2O in hexanes) to give 17 mg of the desired product as a waxy solid (41% yield). *ee* = 20%, determined by HPLC analysis [Chiralpak AD-RH, 60:40 ACN:H_2O, 1 mL/min, λ = 254 nm, tmin = 17.5 min, tmaj = 14.5 min].

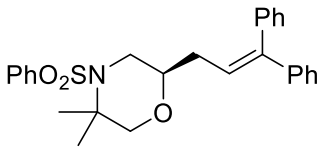
$[\alpha]_D^{23}$ = +4.42 (*c* 0.1, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.05 (m, 20H), 6.21 (t, *J* = 7.3 Hz, 1H), 3.97 (dd, *J* = 11.9, 4.3 Hz, 1H), 3.71 – 3.53 (m, 2H), 2.60 (t, *J* = 11.4 Hz, 2H), 2.47 – 2.32 (m, 2H), 2.26-2.21 (m, 1H), 1.86 (dd, *J* = 14.0, 11.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.1, 144.3, 143.3, 142.4, 140.0, 129.9, 128.6, 128.3, 128.2, 128.0, 127.9, 127.2, 127.0, 126.9, 125.9, 125.8, 125.7, 125.2, 73.7, 64.7, 44.8, 42.0, 36.6, 36.4; FTIR (neat, thin film) ν 3056, 2950, 1597, 1494, 1445, 1099, 761, 699 cm^{-1}; HRMS (EI) calcd for $C_{32}H_{31}O$ $[M+H]^+$: 431.2369, found 431.2368.



7a

(*S*)-2-(3,3-diphenylallyl)-4-tosylmorpholine (7a)

The morpholine **7a** was made from the alcohol **1k** (51 mg, 0.2 mmol) with (4*R,* 5*S*)-Bis-Ph-Box, and 1,1-diphenylethylene in xylenes at 140 °C for 48 h (Conditions D). The crude was purified by flash chromatography (silica gel, 30% EtOAc in hexanes) to give 26 mg of the desired product as a colorless oil (30% yield). *ee* = 55%, determined by HPLC analysis [(*S, S*)-Whelk, 1% iPrOH in hexanes, 1.0 mL/min, λ = 254 nm, tmin = 38.88 min, tmaj = 52.31 min]; $[\alpha]_D^{26}$ = -16.1 (c 0.28, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, J = 7.8 Hz, 2H), 7.42 – 7.08 (m, 14H), 6.09 (t, J = 7.4 Hz, 1H), 3.95 – 3.82 (m, 1H), 3.74 – 3.43 (m, 5H), 2.49 – 2.14 (m, 7H), 2.07 – 1.91 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 143.9, 142.1, 139.6, 132.1, 129.74, 129.7, 128.3, 128.1, 127.8, 127.2, 127.1, 123.5, 75.2, 66.0, 50.1, 45.5, 33.6, 29.7, 21.6; IR (neat): 3000, 2921, 1729, 1658, 1598, 1493, 1448, 1344, 1277, 1165, 1102, 981 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{26}H_{27}NNaO_3S$: 456.1604, found: 456.1611.

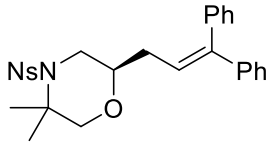


7b

(*R*)-2-(3,3-diphenylallyl)-5,5-dimethyl-4-(phenylsulfonyl)morpholine (7b)

The morpholine **7b** was made from the alcohol **1l** (54 mg, 0.2 mmol) with (*S, S*)-tBu-Box, and 1,1-diphenylethylene in DCE at 105 °C for 24 h. The crude was purified by flash chromatography (silica gel, 20% EtOAc in hexanes) to give 66 mg of the desired product as a colorless oil (74% yield). *ee* > 95%, determined by HPLC analysis [Chiralpak AD-RH, 50:15:35 *i*-PrOH:EtOH:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 25.40 min, tmaj = 22.25 min]; $[\alpha]_D^{25}$ = -47.6 (c 1.51, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 2H), 7.52 (dt, *J* = 15.1, 7.4 Hz, 3H), 7.44 – 7.14 (m, 11H), 6.15 (t, *J* = 7.3 Hz, 1H), 3.69 (dd, *J* = 12.7, 2.7 Hz, 1H), 3.62 – 3.54 (m, 1H) 3.34 (s, 2H),

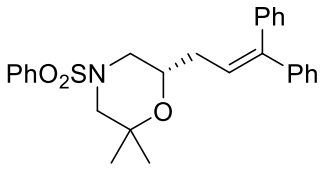
2.89 (dd, J = 12.8, 10.6 Hz, 1H), 2.37 (td, J = 13.0, 11.0, 7.6 Hz, 2H), 1.32 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 142.2, 139.7, 132.4, 129.8, 129.0, 128.3, 128.1, 127.3, 127.2, 127.1, 123.5, 78.0, 76.6, 56.8, 47.2, 33.4, 24.5, 20.0; IR (neat): 2972, 1717, 1659, 1598, 1493, 1446, 1324, 1153, 1091, 1026, 959 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{27}H_{29}NNaO_3S$: 470.1760, found: 470.1768.



7c

(*R*)-2-(3,3-diphenylallyl)-5,5-dimethyl-4-((4-nitrophenyl)sulfonyl)morpholine (7c)

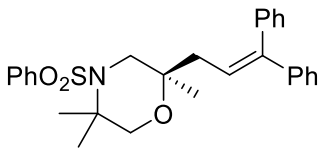
The morpholine **7c** was made from the alcohol **1m** (63 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, and 1,1-diphenylethylene in $PhCF_3$ at 120 °C for 48 h (Conditions A). The crude was purified by flash chromatography (silica gel, 30% EtOAc in hexanes) to give 64 mg of the desired product as a colorless oil (65% yield). *ee* = 89 ± 2%, determined by HPLC analysis [Chiralpak AD-RH, 40:20:40 ACN:iPrOH:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 26.78 min, tmaj = 30.22 min]; $[\alpha]_D^{26}$ = -34.6 (c 0.35, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (dd, J = 8.8, 1.7 Hz, 2H), 7.97 (dd, J = 8.9, 1.8 Hz, 2H), 7.45 – 7.14 (m, 14H), 6.15 (t, J = 7.4 Hz, 1H), 3.69 (d, J = 13.0 Hz, 1H), 3.62 – 3.51 (m, 1H), 3.43 – 3.27 (m, 2H), 2.95 (t, J = 11.9 Hz, 1H), 2.38 (q, J = 6.6, 6.2 Hz, 2H), 1.31 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.8, 148.1, 144.4, 142.1, 139.6, 129.8, 128.4, 128.3, 128.2, 128.16, 127.3, 127.28, 127.2, 124.3, 123.1, 77.7, 76.5, 57.4, 47.3, 33.3, 24.4, 20.7; IR (neat): 2926, 1728, 1658, 1600, 1529, 1446, 1349, 1308, 1278, 1157, 1091, 961 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{27}H_{28}N_2NaO_5S$: 515.1611, found: 515.1623.



7d

(*S*)-6-(3,3-diphenylallyl)-2,2-dimethyl-4-(phenylsulfonyl)morpholine (7d)

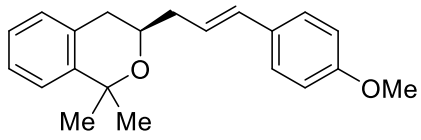
The morpholine **7d** was made from the alcohol **1n** (54 mg, 0.2 mmol) with (4*R,* 5*S*)-Bis-Ph-Box, and 1,1-diphenylethylene in xylenes at 140 °C for 48 h (Conditions D). The crude was purified by flash chromatography (silica gel, 20% EtOAc in hexanes) to give 33 mg of the desired product as a colorless oil (36% yield). *ee* = 26%, determined by HPLC analysis [Chiralpak AD-RH, 40:20:40 ACN:iPrOH:H_2O, 0.3 mL/min, λ = 254 nm, tmin = 22.50 min, tmaj = 25.96 min]; $[\alpha]_D^{26}$ = +43.1 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 2H), 7.65 – 7.49 (m, 4H), 7.39 – 7.10 (m, 11H), 6.08 (t, J = 7.4 Hz, 1H), 3.96 – 3.86 (m, 1H), 3.57 (d, J = 11.4 Hz, 1H), 3.41 – 3.34 (m, 1H), 2.29 – 2.10 (m, 2H), 2.06 – 1.97 (m, 1H), 1.80 (t, J = 10.9 Hz, 1H), 1.38 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 142.2, 139.8, 135.5, 132.9, 129.8, 129.1, 128.3, 128.1, 127.8, 127.6, 127.2, 127.18, 127.1, 123.7, 71.5, 68.7, 54.2, 49.9, 33.9, 27.8, 21.7; IR (neat): 3059, 2978, 1721, 1658, 1598, 1493, 1446, 1347, 1318, 1277, 1166, 1093, 1030, 999, 972 cm^{-1}; HRMS (ESI) calc'd for $[M+H]^+$ $C_{27}H_{30}NO_3S$: 448.1941, found: 448.1946.



7e

(*R*)-2-(3,3-diphenylallyl)-2,5,5-trimethyl-4-(phenylsulfonyl)morpholine (7e)

The morpholine **7e** was made from the alcohol **1o** (28 mg, 0.1 mmol) with (*S, S*)-*t*Bu-Box, and 1,1-diphenylethylene in DCE at 105 °C for 24 h. The crude was purified by flash chromatography (silica gel, 20% EtOAc in hexanes) to give 33 mg of the desired product as a colorless oil (72% yield). *ee* = 93%, determined by HPLC analysis [Chiralpak AD-RH, 50:15:35 iPrOH:EtOH:H_2O, 0.6 mL/min, λ = 254 nm, tmin = 13.1 min, tmaj = 18.0 min]; $[\alpha]_D^{27}$ = +11.1 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.73 (m, 2H), 7.59 – 7.50 (m, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.47 – 7.17 (m, 9H), 7.17 – 7.11 (m, 2H), 6.13 (t, *J* = 7.3 Hz, 1H), 3.28 (q, *J* = 11.9 Hz, 2H), 3.23 (s, 2H), 2.59 (dd, *J* = 15.1, 7.1 Hz, 1H), 2.18 (dd, *J* = 15.1, 7.5 Hz, 1H), 1.28 (s, 3H), 1.20 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 142.4, 141.8, 139.8, 132.4, 129.8, 128.9, 128.3, 128.1, 127.2, 127.1, 127.1, 123.1, 77.3, 76.9, 76.7, 74.1, 71.7, 56.9, 50.2, 36.4, 22.6, 22.3; IR (neat, thin film) ν 3058, 2981, 1726, 1659, 1598, 1493, 1446, 1318, 1277, 1153, 1090, 923 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{28}H_{31}NNaO_3S$: 484.1917, found: 484.1927.

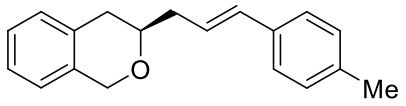


8a

(*R,E*)-3-(3-(4-methoxyphenyl)allyl)-1,1-dimethylisochromane (8a)

The isochroman **8a** was made from the alcohol **1b** (35 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, 2,6-di-*t*Bu-4-methylpyridine, and 4-methoxystyrene in DCE at 105 °C for 24 h (Conditions B but with 2,6-di-t-Bu-4-methylpyridine). The crude was purified by flash chromatography (silica gel, 5% EtOAc in hexanes) to give 33.4 mg of the desired product as a colorless oil (54% yield). *ee* > 95%, determined by HPLC analysis [Chiralpak AD-RH, 60:20:20 iPrOH:EtOH:H_2O, 0.5 mL/min, λ =

254 nm, tmin = 9.44 min, tmaj = 8.54 min]; $[\alpha]_D^{25}$ = -128.6 (c 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H), 7.21 – 7.02 (m, 4H), 6.89 – 6.80 (m, 2H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.19 (ddd, *J* = 15.8, 7.7, 6.5 Hz, 1H), 3.97 – 3.86 (m, 1H), 3.81 (s, 3H), 2.76 – 2.68 (m, 2H), 2.67 – 2.54 (m, 1H), 2.50 – 2.39 (m, 1H), 1.55 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.1, 131.4, 130.5, 128.8, 127.6, 127.2, 126.1, 125.9, 125.2, 124.3, 113.9, 113.7, 75.4, 68.7, 55.3, 39.8, 35.1, 31.5, 28.7; IR (neat): 2973, 2834, 1607, 1577, 1509, 1448, 1378, 1246, 1173, 1111, 1036, 966 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{21}H_{24}NaO_2$: 331.1669, found: 331.1671.



8b

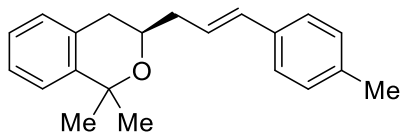
(*R,E*)-3-(3-(p-tolyl)allyl)isochromane (8b)

The isochroman **8b** was made from the alcohol **1a** (30 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, 2,6-di-*t*Bu-4-methylpyridine, Ag_2CO_3, and 4-methylstyrene (1.15mL, 1 mmol, 5 equiv) in DCE at 105 °C for 24 h (Conditions C with 5 eq styrene). The desired product was isolated by flash column chromatography (silica gel, hexanes:Et_2O 95:5) as a colourless oil (30 mg, 57%).

ee = 76%, determined by HPLC analysis [Chiralpak AD-RH, 77:23 ACN:H_2O, 1 mL/min, λ = 254 nm, tmin = 7.8 min, tmaj = 6.40 min].

$[\alpha]_D^{21}$ = -24.4 (c 0.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (dt, *J* = 8.2, 2.9 Hz, 2H), 7.19 – 7.05 (m, 5H), 6.99 (d, *J* = 6.9 Hz, 1H), 6.47 (d, *J* = 15.5 Hζ, 1H), 6.27 (dt, *J* = 14.1, 7.1 Hz, 1H), 4.91 – 4.77 (m, 2H), 3.79 (dt, *J* = 10.7, 5.5 Hz, 1H), 2.85 – 2.70 (m, 2H), 2.61 (dt, *J* = 13.4, 6.5 Hz, 1H), 2.56 – 2.44 (m, 1H), 2.32 (d, *J* = 2.6 Hz, 4H), 2.19 – 2.11 (m, 5H), 1.25 (s, 0H);^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8, 134.6, 133.2, 132.1, 129.1, 128.8, 126.3, 126.0, 125.9, 124.9, 124.1,

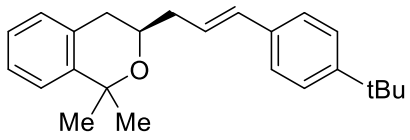
113.7, 77.3, 74.6, 68.2, 39.5, 33.6, 30.9, 21.1; FTIR (neat, thinfilm) ν 3022, 2923, 2844,1607, 1584, 1512, 1448, 1373, 1204, 1098, 968, 744 cm^{-1}; HRMS (EI) calcd. for $[M+Na]^+$ $C_{19}H_{20}NaO$: 287.1406, found 287.1403.



8c

(*R,E*)-1,1-dimethyl-3-(3-(p-tolyl)allyl)isochromane (8c)

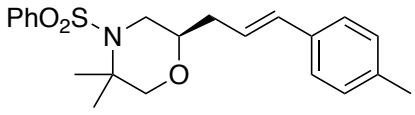
The isochroman **8c** was made from the alcohol **1b** (35 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, 2,6-di-*t*Bu-4-methylpyridine, and 4-methylstyrene in DCE at 105 °C for 24 h (Conditions B but with 2,6-di-t-Bu-4-methylpyridine). The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give 40.8 mg of the desired product as a colorless oil (70% yield). *ee* > 99%, determined by HPLC analysis [Chiralpak AD-RH, 75:25 iPrOH:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 11.00 min, tmaj = 8.40 min]; $[\alpha]_D^{27}$ = -45.9 (c 0.84, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 6.99 (m, 11H), 6.47 (d, *J* = 15.8 Hz, 1H), 6.27 (dt, *J* = 16.4, 7.1 Hz, 1H), 3.95 – 3.87 (m, 1H), 2.79 – 2.53 (m, 3H), 2.45 (dt, *J* = 14.1, 7.0 Hz, 1H), 2.32 (s, 3H), 1.54 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.0, 136.8, 134.9, 133.1, 131.8, 129.2, 128.8, 126.1, 126.0, 125.9, 125.4, 125.2, 76.7, 75.4, 68.7, 39.8, 35.1, 31.53, 31.5, 28.7, 21.2; IR (neat): 2973, 2923, 1512, 1490, 1448, 1379, 1271, 1169, 1104, 1061, 1037, 967 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{21}H_{24}NaO$: 315.1719, found: 315.1727.



8d

(*R,E*)-3-(3-(4-(tert-butyl)phenyl)allyl)-1,1-dimethylisochromane (8d)

The isochroman **8d** was made from the alcohol **1b** (35 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, 2,6-di-*t*Bu-4-methylpyridine, and 4-*tert*butylstyrene in DCE at 105 °C for 24 h (Conditions B but with 2,6-di-t-Bu-4-methylpyridine). The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give 44 mg of the desired product as a colorless oil (65% yield). *ee* > 95%, determined by HPLC analysis [Chiralpak AD-RH, 75:25 *i*-PrOH:H_2O, 0.5 mL/min, λ = 254 nm, tmin = 11.01 min, tmaj = 9.52 min]; $[\alpha]_D^{26}$ = -38.4 (c 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 4H), 7.14 (dt, *J* = 21.8, 7.2 Hz, 3H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 15.8 Hz, 1H), 6.29 (dt, *J* = 16.5, 7.2 Hz, 1H), 3.92 (d, *J* = 8.9 Hz, 1H), 2.82 – 2.53 (m, 3H), 2.46 (m, 1H), 1.54 (s, 3H), 1.52 (s, 3H), 1.34 – 1.28 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.0, 134.9, 133.1, 131.7, 128.8, 126.1, 125.9, 125.8, 125.7, 125.4, 125.2, 75.4, 68.7, 39.8, 35.1, 34.5, 31.5, 31.3, 28.7; IR (neat): 2965, 2928, 1606, 1513, 1490, 1448, 1379, 1363, 1270, 1169, 1105, 1061, 1037, 967 cm-1; HRMS (ESI) calc'd for $[M+H]^+$ $C_{24}H_{31}O$: 335.2369, found: 335.2373.



9

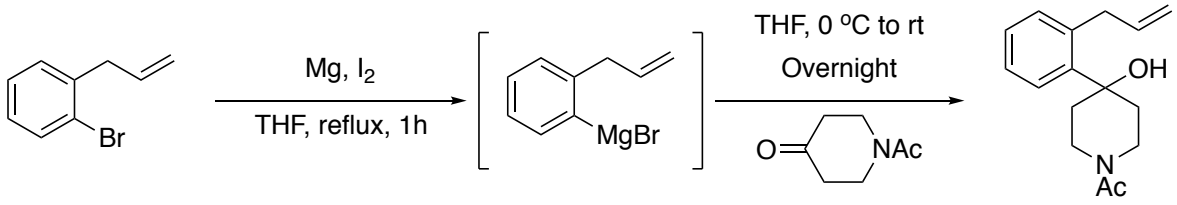
(*R,E*)-5,5-dimethyl-4-(phenylsulfonyl)-2-(3-(p-tolyl)allyl)morpholine (9)

The morpholine **9** was made from the alcohol **1k** (54 mg, 0.2 mmol) with (*S, S*)-*t*Bu-Box, 2,6-di-*t*Bu-4-methylpyridine, and 4-methylstyrene (0.13 mL, 1 mmol, 5 equiv) in DCE at 105 °C for 24

h (Conditions B but with 2,6-di-t-Bu-4-methylpyridine). The crude was purified by flash chromatography (silica gel, 20% EtOAc in hexanes) to give 36 mg of the desired product as a colorless oil (54% yield).

ee > 95%, determined by HPLC analysis [Chiralpak AD-RH, 50:15:35 *i*-PrOH:EtOH:H_2O, 0.6 mL/min, λ = 254 nm, tmin = 15.1 min, tmaj = 13.0 min]; $[\alpha]_D^{26}$ = -1.07 (c 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.76 (m, 2H), 7.59 – 7.43 (m, 3H), 7.29 – 7.20 (m, 2H), 7.10 (dd, *J* = 8.2, 2.1 Hz, 2H), 6.43 (d, *J* = 15.6 Hz, 1H), 6.15 (dtd, *J* = 15.9, 7.2, 2.2 Hz, 1H), 3.77 (dt, *J* = 12.8, 2.6 Hz, 1H), 3.60 (t, *J* = 8.3 Hz, 1H), 3.35 (m, 2H), 3.00 (ddd, *J* = 12.8, 10.5, 2.2 Hz, 1H), 2.53 – 2.29 (m, 2H), 2.31 (s, 3H), 1.30 (s, *J* = 2.2 Hz, 3H), 1.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3, 137.0, 134.4, 132.7, 132.4, 129.2, 128.9, 126.9, 126.0, 123.6, 77.9, 76.4, 56.8, 47.1, 36.7, 24.4, 21.1, 20.1; IR (neat): 2980, 2922, 1720, 1607, 1514, 1447, 1324, 1154, 1091, 958 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{22}H_{27}NNaO_3S$: 408.1604, found: 408.1608.

Formal Synthesis of σ_1 Receptor Antagonist

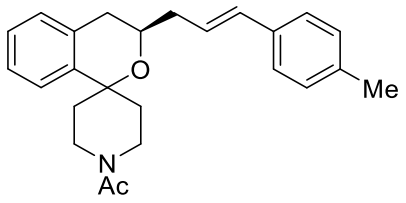


10

1-(4-(2-Allylphenyl)-4-hydroxypiperidin-1-yl)ethan-1-one (10):

Acid washed magnesium turnings (481 mg, 13 equiv.) were flame dried in a round-bottomed flask under vacuum before being placed under an argon atmosphere. The round bottomed flask was equipped with a reflux condenser and several crystals of iodine were added, followed by anhydrous THF (1.5 mL). The mixture was refluxed for approximately 10 min. until the brown color had faded after which the flask was removed from the heat. A solution of 1-allyl-2-bromobenzene (393

mg, 1.3 equiv.) in THF (5 mL) was added dropwise to the reaction flask and then heated to reflux for 1 h before being allowed to cool to rt. A flame-dried round-bottomed flask was charged with a solution of 1-acetyl-4-piperidone (215 mg, 1.53 mmol) in THF (10 mL), and cooled to 0 °C under argon. The Grignard solution was cannulated into the piperidone solution, stirred and allowed to warm to rt overnight. The reaction was quenched with 2,2,2-trifluoroethanol (0.7 mL) and filtered through a pad of Celite. The Celite was washed with CH_2Cl_2 and the washings were concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, 0-6% MeOH in DCM) to give alcohol **10** as white crystals (176.3 mg, 44%). Mp = 135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 1H), 7.28 – 7.17 (m, 3H), 6.08 (ddt, *J* = 16.2, 10.1, 5.9 Hz, 1H), 5.10 (dq, *J* = 10.2, 1.8 Hz, 1H), 4.97 (dq, *J* = 17.2, 2.0 Hz, 1H), 4.49 (d, *J* = 13.1 Hz, 1H), 3.85 (dt, *J* = 6.1, 2.0 Hz, 2H), 3.71 – 3.61 (m, 2H), 3.19 – 3.08 (m, 1H), 2.79 (s, 1H), 2.02 (d, *J* = 36.0 Hz, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 144.3, 139.3, 138.2, 132.6, 127.3, 126.0, 125.1, 115.4, 72.0, 42.4, 38.0, 37.9, 37.4, 37.2, 21.1; IR (neat): 3332, 3072, 3006, 2917, 2850, 2241, 1720, 1615, 1482, 1444, 1426, 1361, 1247, 1130, 1026, 995, 910 cm^{-1}; HRMS (ESI) calc'd for $[M+H]^+$ $C_{16}H_{22}NO_2$: 260.1645, found: 260.1644.



11

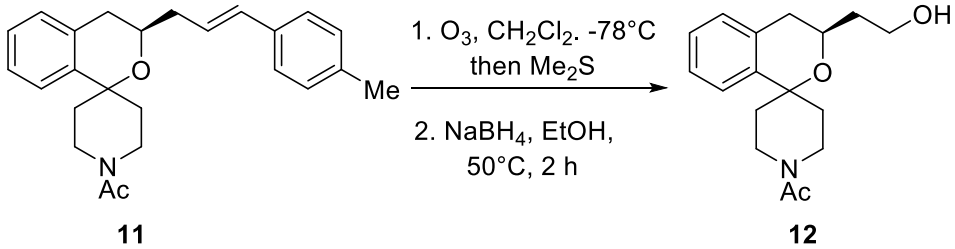
(*R*,*E*)-1-(3-(3-(p-tolyl)allyl)spiro[isochromane-1,4'-piperidin]-1'-yl)ethan-1-one (11)

The isochroman **11** was made from the alcohol **10** (30.2 mg, 0.12 mmol) with (*S, S*)-*i*Pr-Box, 2,6-di-*t*Bu-4-methylpyridine, and 4-methylstyrene in DCE at 105 °C for 24 h (Conditions D). The crude was purified by flash chromatography (silica gel, 3% Et_2O in hexanes) to give 43.2 mg of the isochroman **11** as a colorless oil (58% yield). *ee* = 96%, determined by HPLC analysis [Chiralpak AD-RH, 80:20 CH_3CN:H_2O, 0.7 mL/min, λ = 254 nm, tmin = 6.77 min, tmaj = 4.94 min].

(**Note**: The extra signals in the ^1H and ^{13}C spectra arise out of the presence of rotomers.)

$[\alpha]_D^{26}$ = -36.9 (c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 6.92 (m, 8H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.28 (dt, *J* = 15.7, 7.1 Hz, 1H), 4.73 – 4.37 (m, 1H), 3.83 (d, *J* = 9.4 Hz, 1H), 3.74 – 3.42 (m, 2H), 3.01 (dt, *J* = 60.5, 13.3 Hz, 1H), 2.83 – 2.65 (m, 2H), 2.54 (dq, *J* = 22.6, 8.1, 7.7 Hz, 2H), 2.33 (s, 3H), 2.07 (dd, *J* = 37.7, 17.7 Hz, 5H), 1.73 (dt, *J* = 17.2, 12.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 140.8, 137.0, 133.7, 132.4, 132.3, 129.3, 129.2, 128.9, 126.5, 126.4, 125.9, 125.3, 125.2, 125.0, 74.0, 73.9, 68.6, 68.4, 42.6, 42.5, 39.8, 39.7, 39.6, 38.8, 37.6, 35.2, 34.4, 21.5, 21.1; IR (neat): 2924, 1735, 1621, 1513, 1425, 1371, 1278, 1237, 1117, 1090, 1043, 994, 966 cm^{-1}; HRMS (ESI) calc'd for $[M+Na]^+$ $C_{25}H_{29}NNaO_2$: 398.2091, found: 398.2096.

(**Note**: This reaction was also demonstrated at a 0.8 mmol of alkenol **10**. 149 mg (50%) yield of isochroman **11** was obtained with 92% ee)

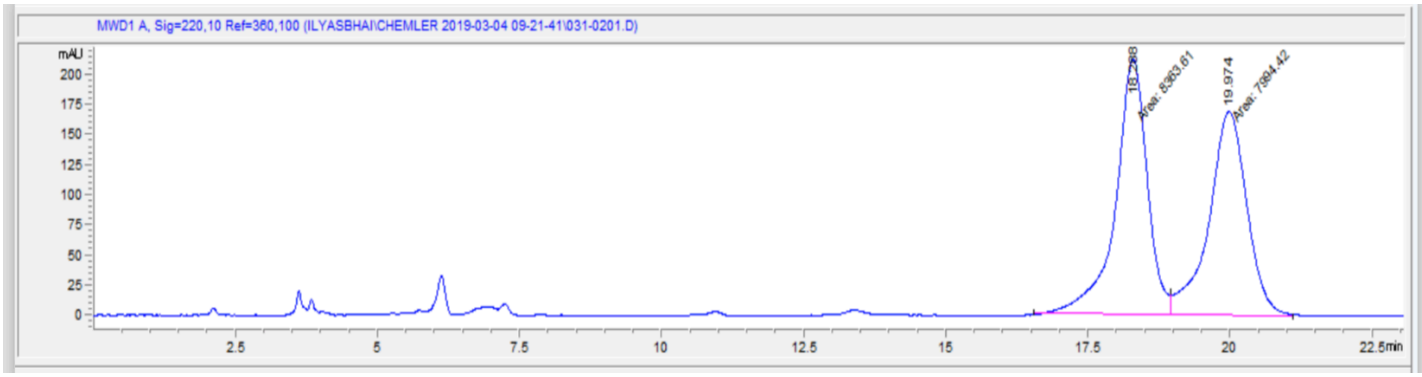


11 **12**

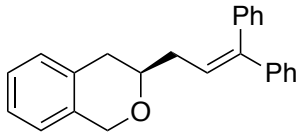
(*S*)-1-(3-(2-hydroxyethyl)spiro[isochromane-1,4'-piperidin]-1'-yl)ethan-1-one (12):

Isochroman **11** (21 mg, 0.06 mmol) was dissolved in 3mL of CH_2Cl_2 and cooled to -78 °C. The solution was then stirred and treated with O_3 until it appeared blue ca. 5 min. The solution was then purged with O_2 until the solution appeared clear. Dimethylsulfide (37 mg, 0.6 mmol) was then added dropwise. The reaction was stirred and allowed to warm to rt overnight. The reaction was concentrated in vacuo to give a crude residue that was used in the next step without further purification. The crude was dissolved in 2 mL of EtOH and treated with sodium borohydride (11 mg, 0.3 mmol). The reaction was stirred at 50 °C for 2h. After cooling to 0 °C, the reaction was quenched with H_2O (5 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude was purified by flash chromatography (silica gel, 50% acetone in hexanes) to give 12.2 mg of the alcohol **12** as a colorless oil (70%, over two steps). $[\alpha]_D^{23}$ = -44.8 (*c* 0.1, MeOH) (lit: $[\alpha]_D^{20}$ = -46 (*c* 0.7, MeOH)[11]; ^{1}H NMR matched the previously reported.[11] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.01 (m, 4H), 4.67 – 4.52 (m, 1H), 4.10 – 3.98 (m, 1H), 3.97 – 3.84 (m, 2H), 3.77 – 3.62 (m, 1H), 3.57 – 3.33 (m, 1H), 2.20 – 1.87 (m, 4H), 1.83 – 1.44 (m, 18H).

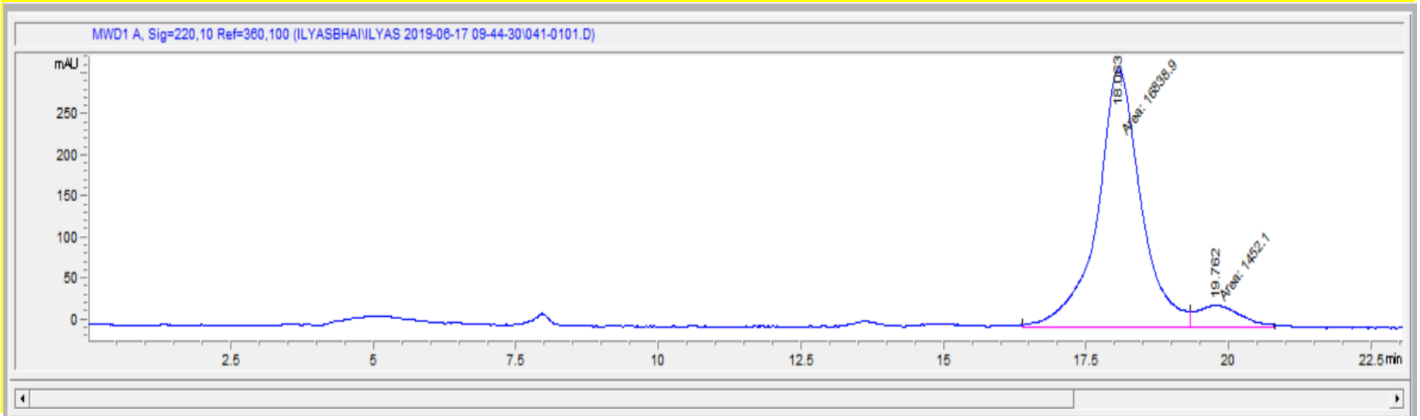
HPLC traces of chiral products



#	Time	Area %
1	18.2	51.1
2	19.9	48.9

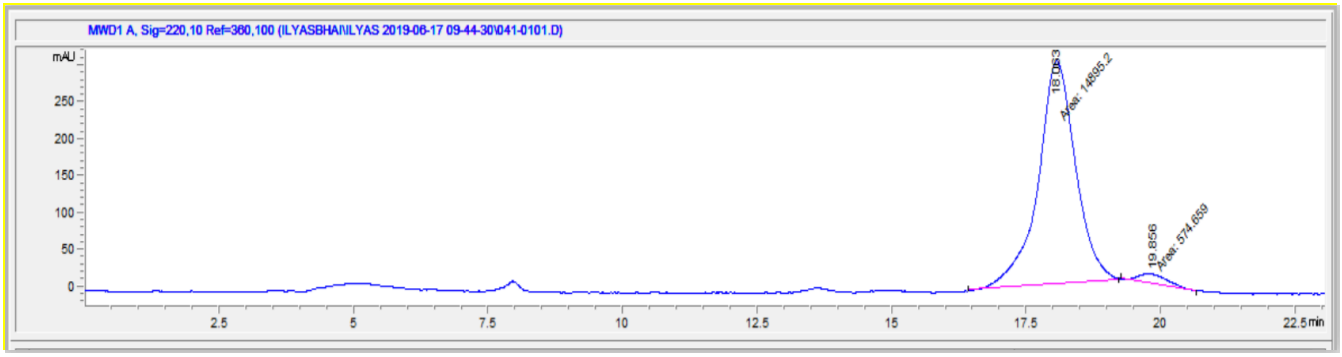


2a



Chiral trace – split peak integration

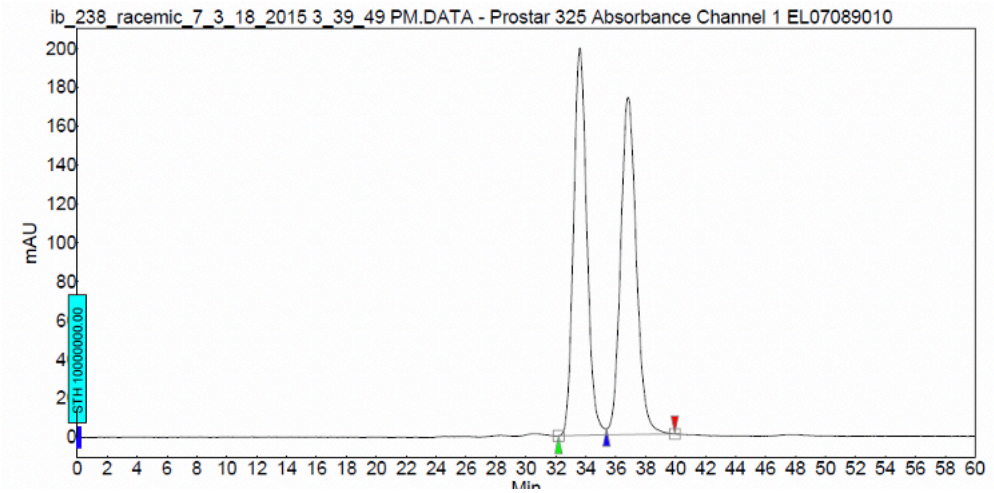
#	Time	Area %
1	18.0	92.0
2	19.8	8.0



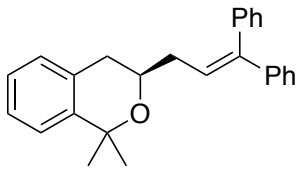
Chiral trace - Valley-to-valley integration

#	Time	Area %
1	18.0	96.2
2	19.8	3.8

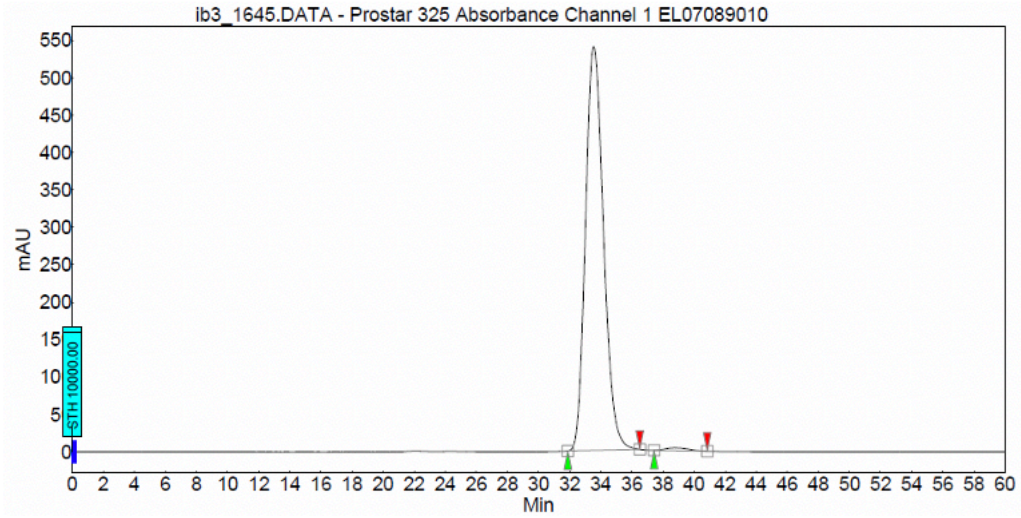
Note : Since the chiral HPLC trace for compound **2a** is not baseline resolved we provide an error value with this ee measurement. The chromatogram obtained was integrated in two ways: (1) valley to valley integration which represents the minimum possible areas of the peaks – this gave an ee value of 92%, and (2) split peak integration, which gave an ee of 86%. The mean ee value is 89% with a std deviation of 3%.



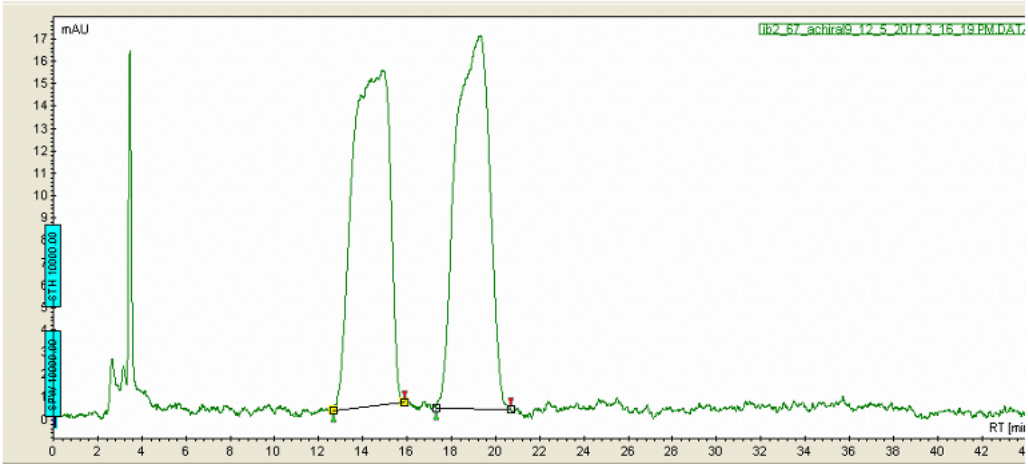
#	Time	Area %
1	33.1	49.2
2	38.0	50.7



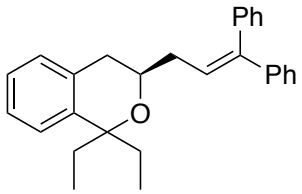
2b



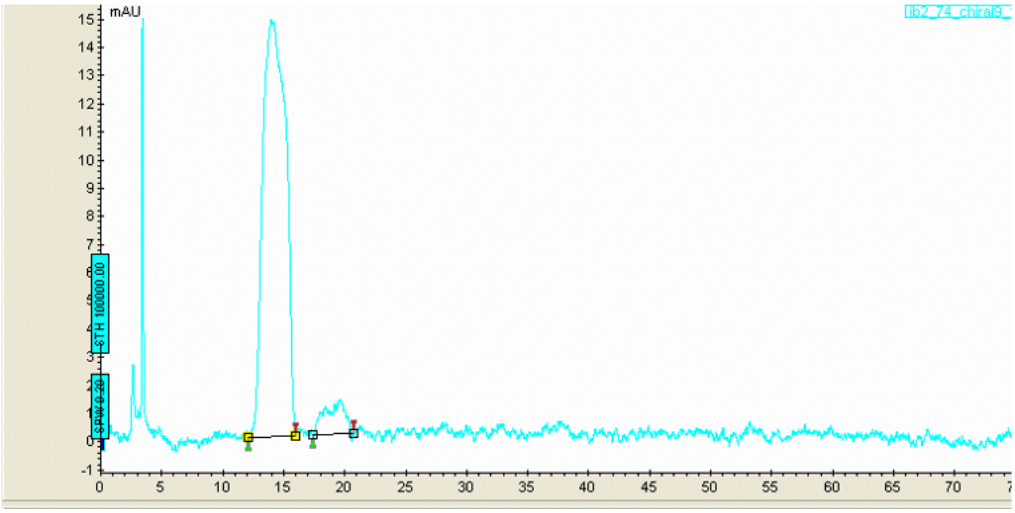
#	Time	Area %
1	33.5	99.2
2	38.8	0.8



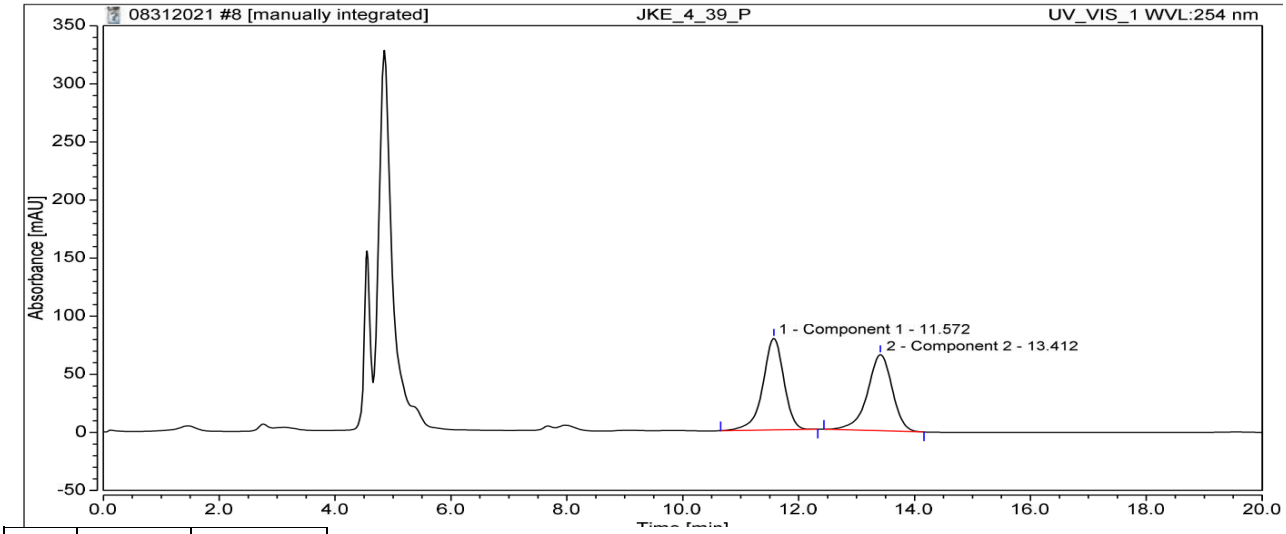
#	Time	Area %
1	14.8	49.8
2	19.3	50.2



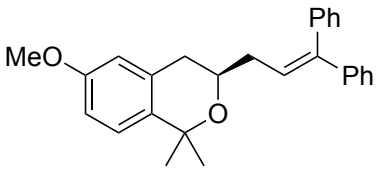
2c



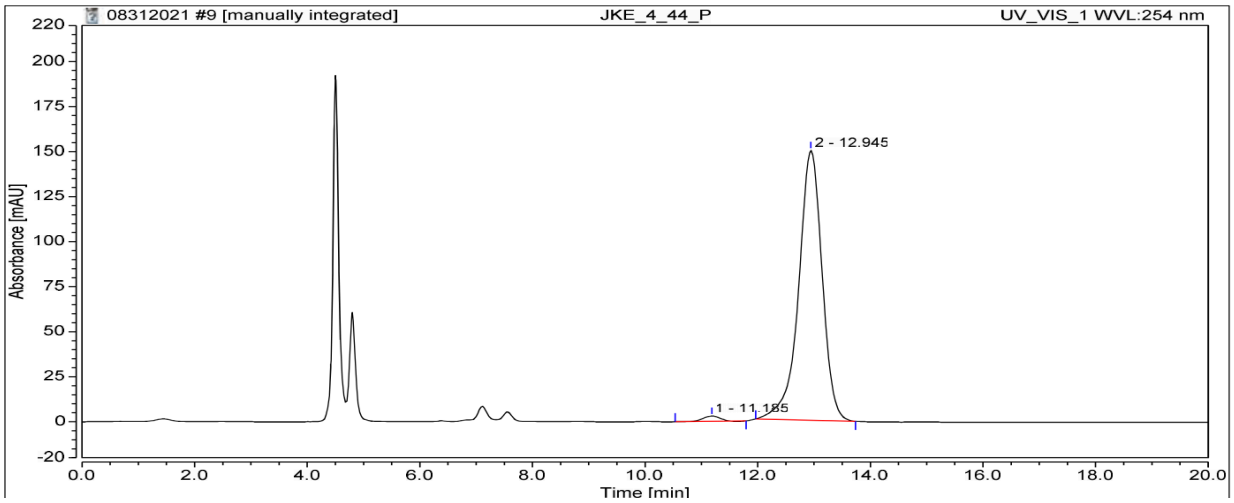
#	Time	Area %
1	14.0	93.7
2	19.6	6.3



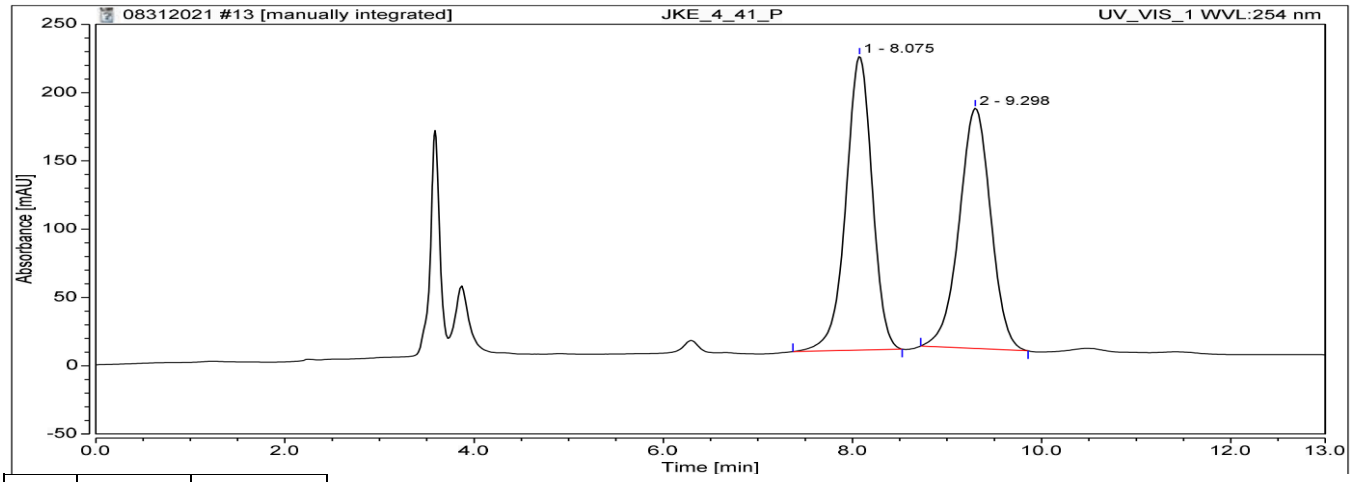
#	Time	Area %
1	11.5	50.4
2	13.4	49.6



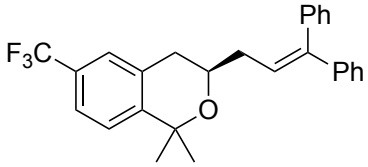
2d



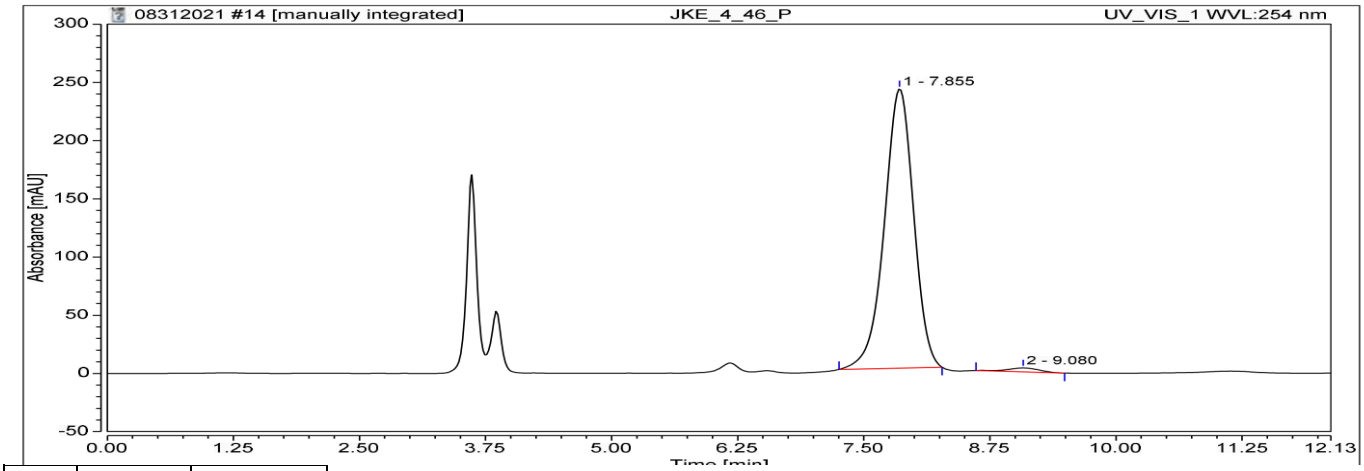
#	Time	Area %
1	11.1	1.8
2	12.9	98.2



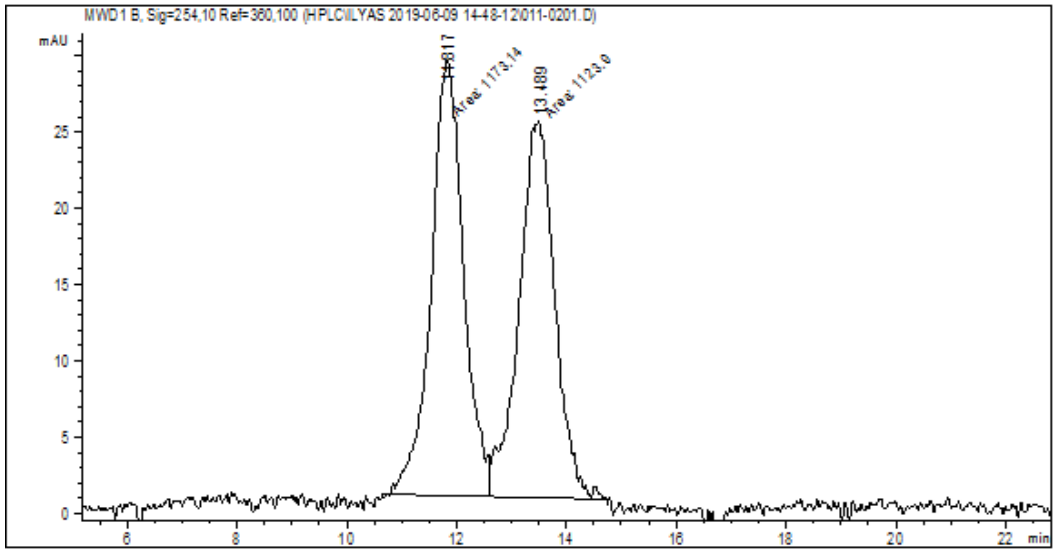
#	Time	Area %
1	8.1	50.5
2	9.3	49.5

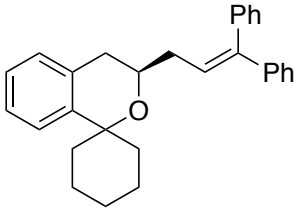


2e



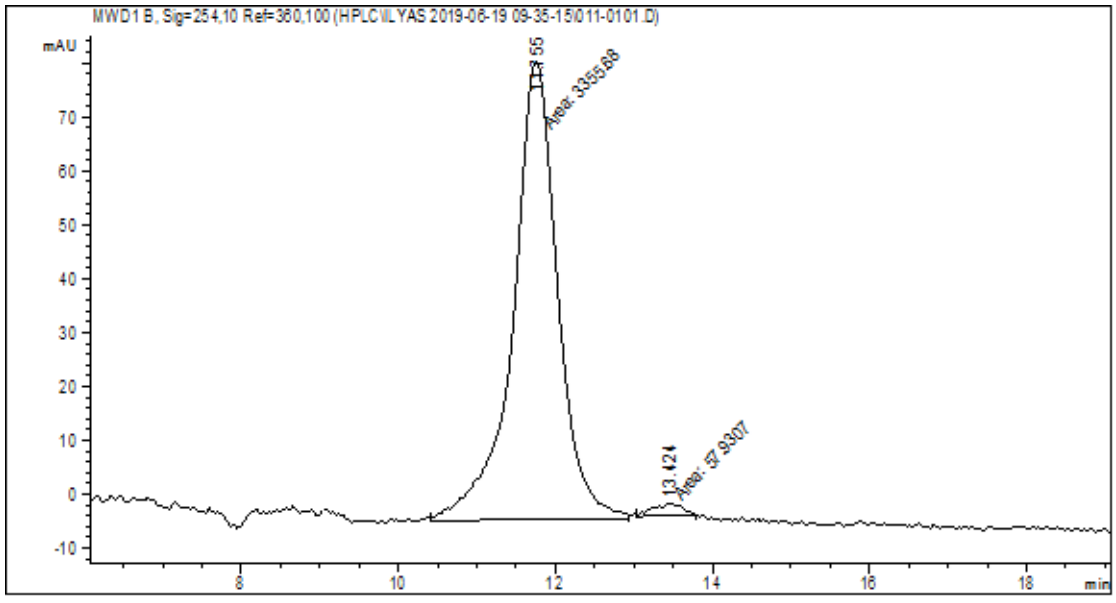
#	Time	Area %
1	7.8	99.5
2	9.1	1.5



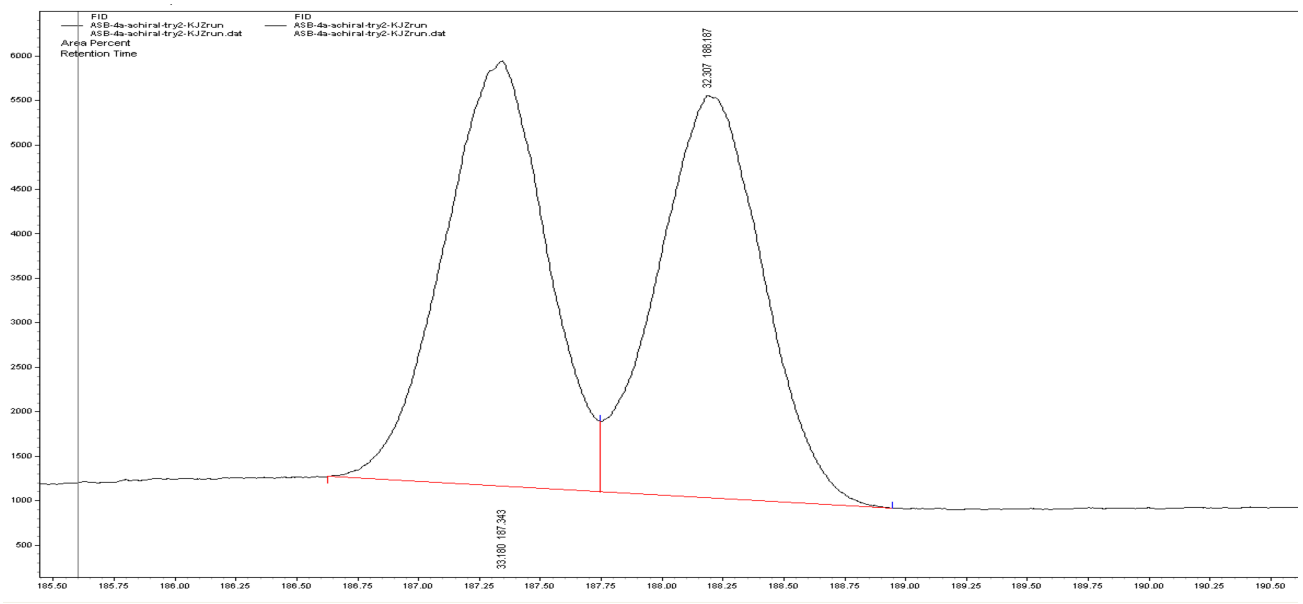


2f

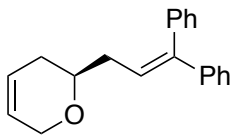
#	Time [min]	Area [%]
1	11.82	51.1
2	13.49	48.9



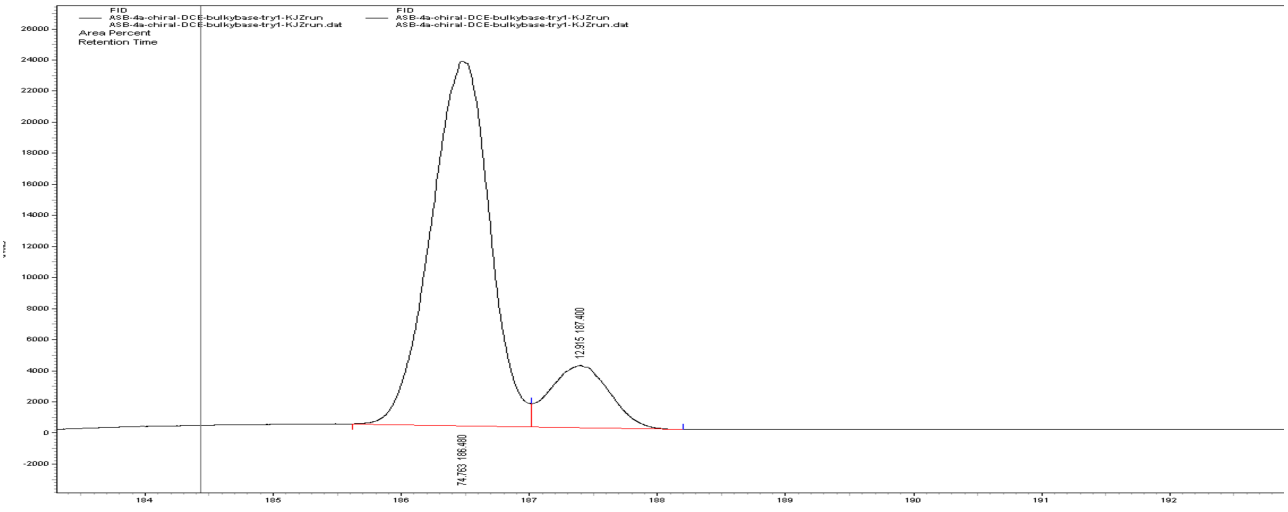
#	Time [min]	Area [%]
1	11.76	98.3
2	13.42	1.7



#	Time	Area %
1	187.3	49.4
2	188.1	50.6

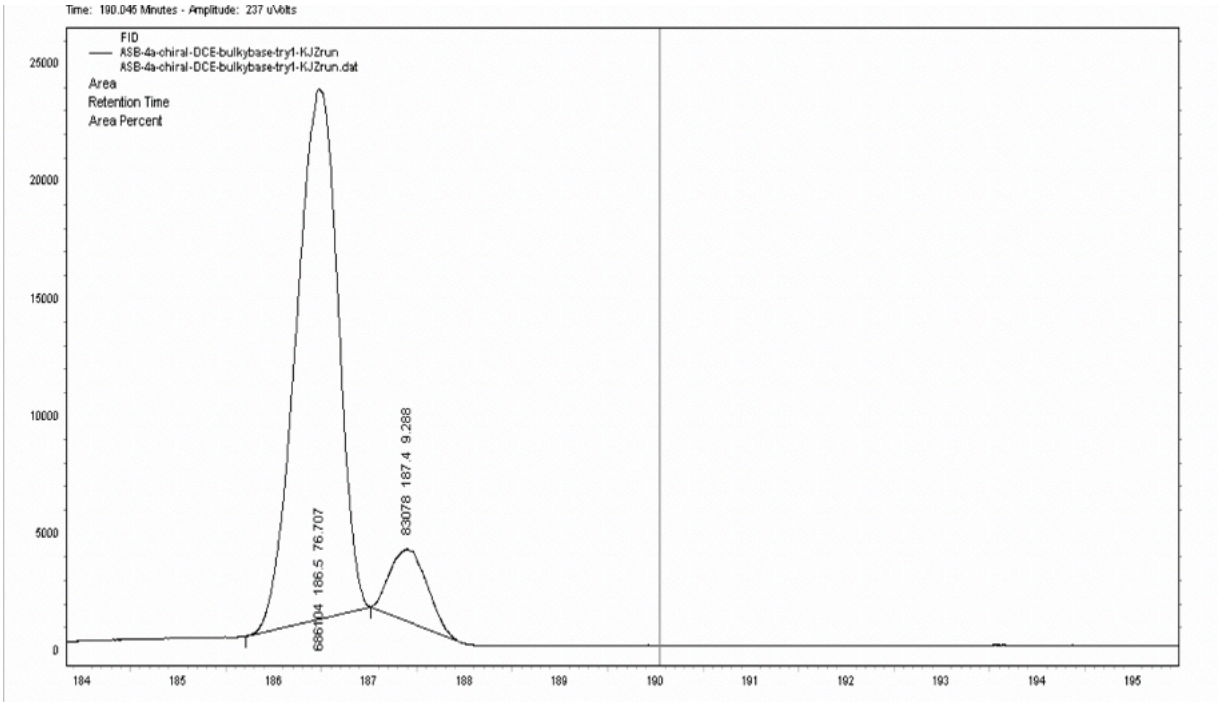


4a



#	Time	Area %
1	186.4	85.3
2	187.4	14.7

Chiral trace – Split peak integration

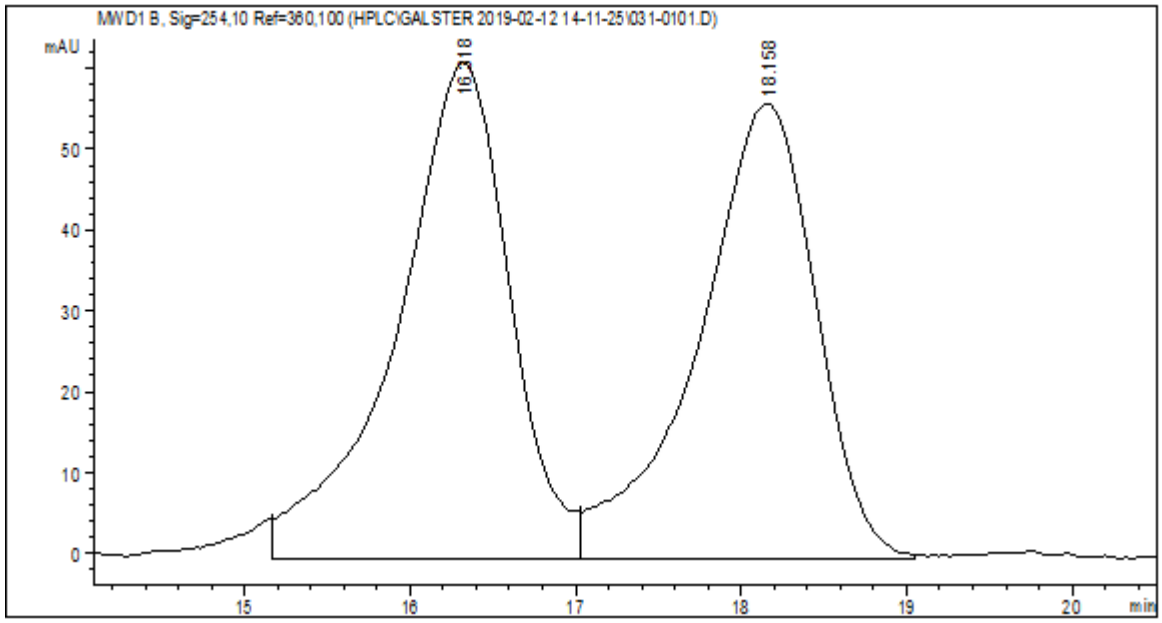


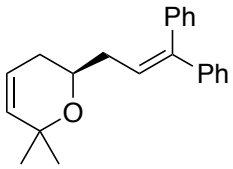
Chiral trace- valley to valley integration

#	Time	Area %
1	186.4	89.1
2	187.4	10.8

Note : Since the chiral HPLC trace for compound **4a** is not baseline resolved we provide an error value with this ee measurement. Error value was calculated as per the procedure described for compound **2a.**

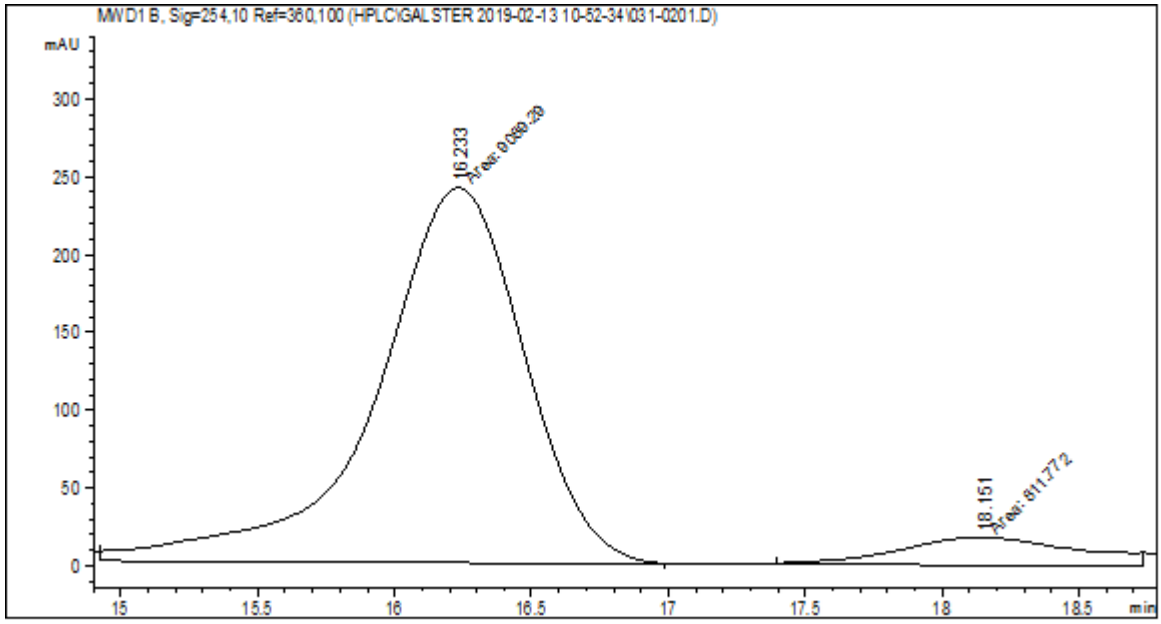
Valley to valley integration yields an ee of 78% while split peak integration yields an ee value of 70%. This gives us a mean ee value of 74% with a standard deviation of 4%. This is reported as the ee of this compound.



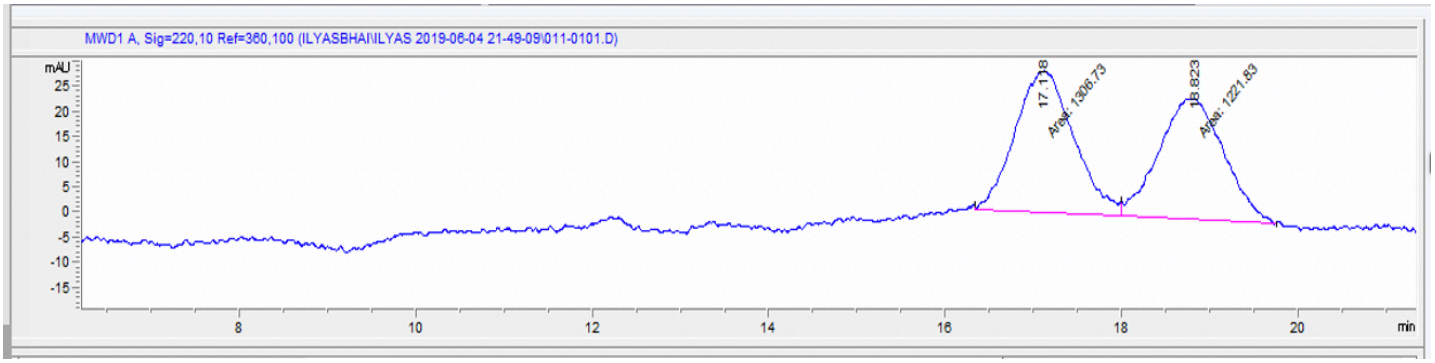


4b

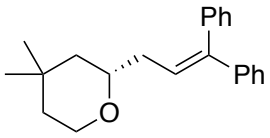
#	Time [min]	Area [%]
1	16.32	51.2
2	18.16	48.8



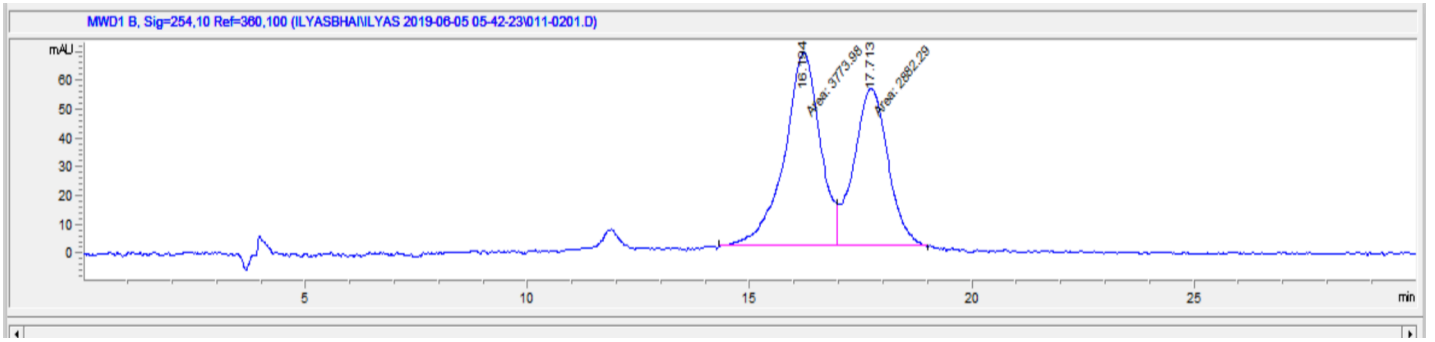
#	Time [min]	Area [%]
1	16.23	91.8
2	18.15	8.2



#	Time	Area %
1	17.1	51.4
2	18.8	48.6

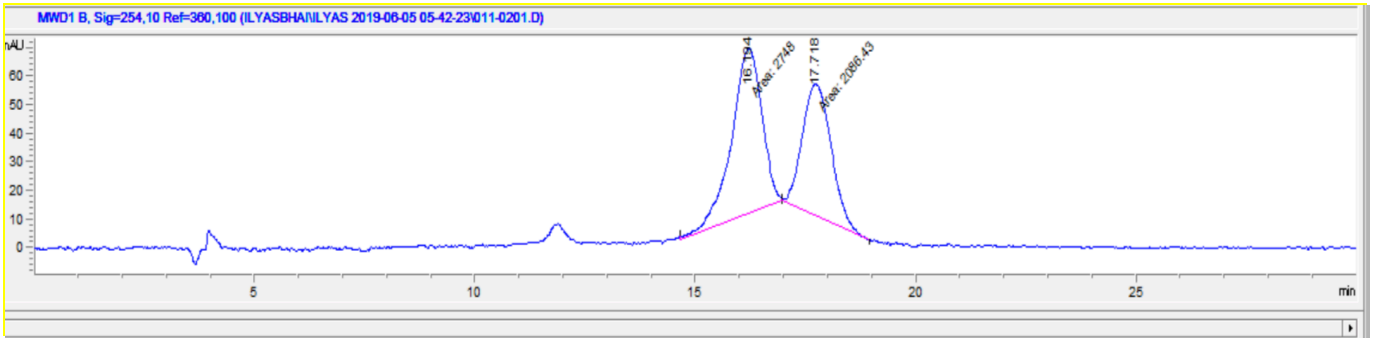


5b



Chiral trace – Split peak integration

#	Time	Area %
1	16.2	56.4
2	17.8	43.6

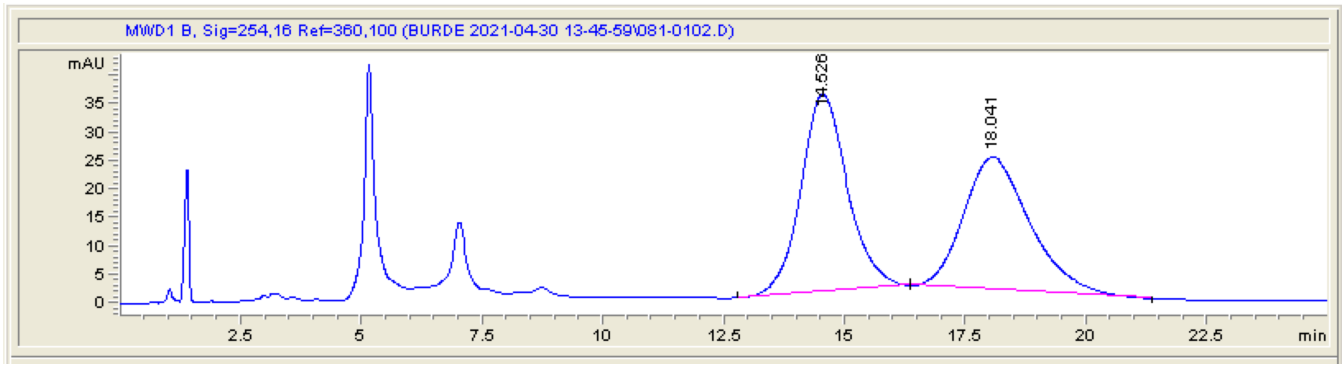


Chiral trace – Valley-to-valley integration

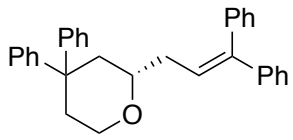
#	Time	Area %
1	16.2	57.4
2	17.8	42.6

Note : Since the chiral HPLC trace for compound **5b** is not baseline resolved we provide an error value with this ee measurement. Error value was calculated as per the procedure described for compound **2a**

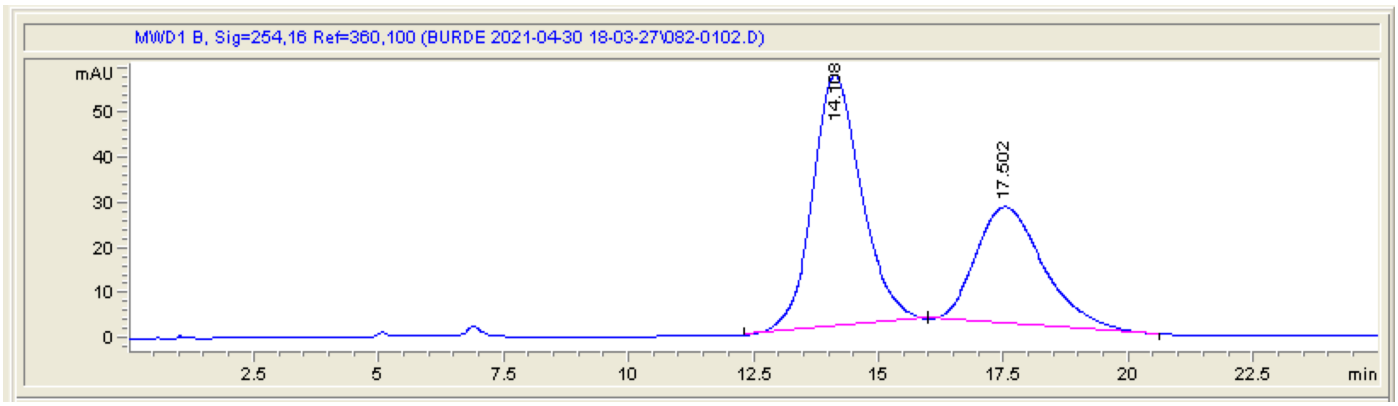
(1) Valley-to-valley integration gives an ee value of 14% and (2) split peak integration gives an ee value of 12%. This is a mean value of 13% with a standard deviation of 1%. This is reported as the ee of this compound.



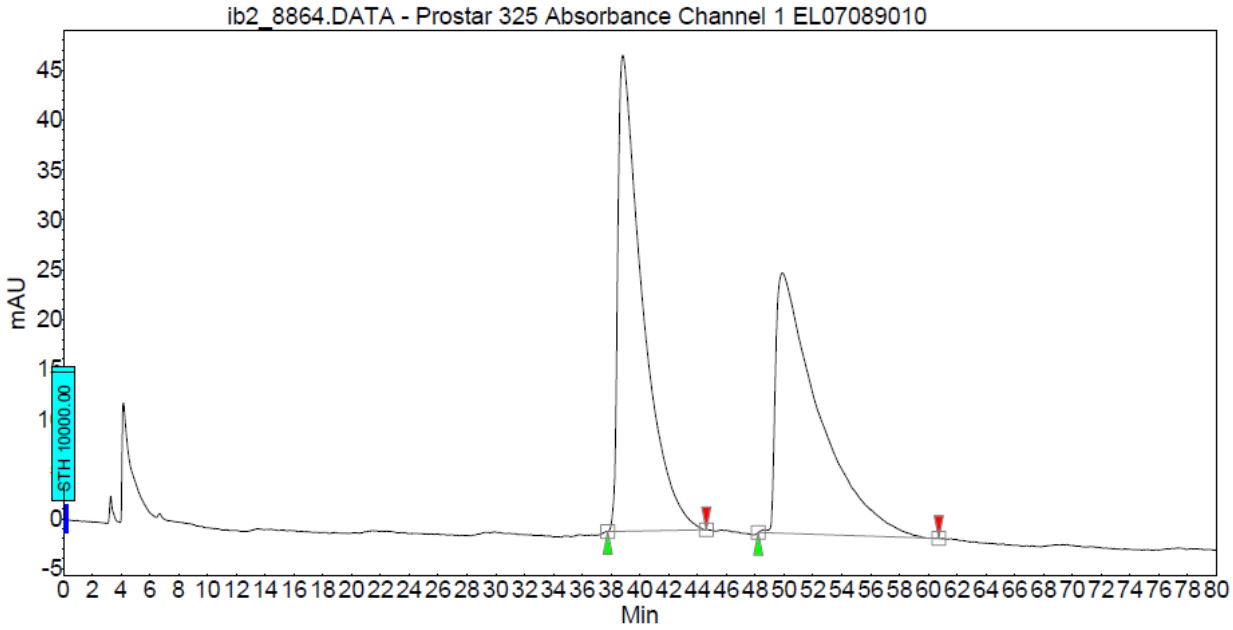
#	Time	Area %
1	14.5	51.2
2	18.0	48.8



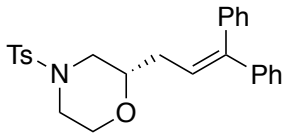
5c



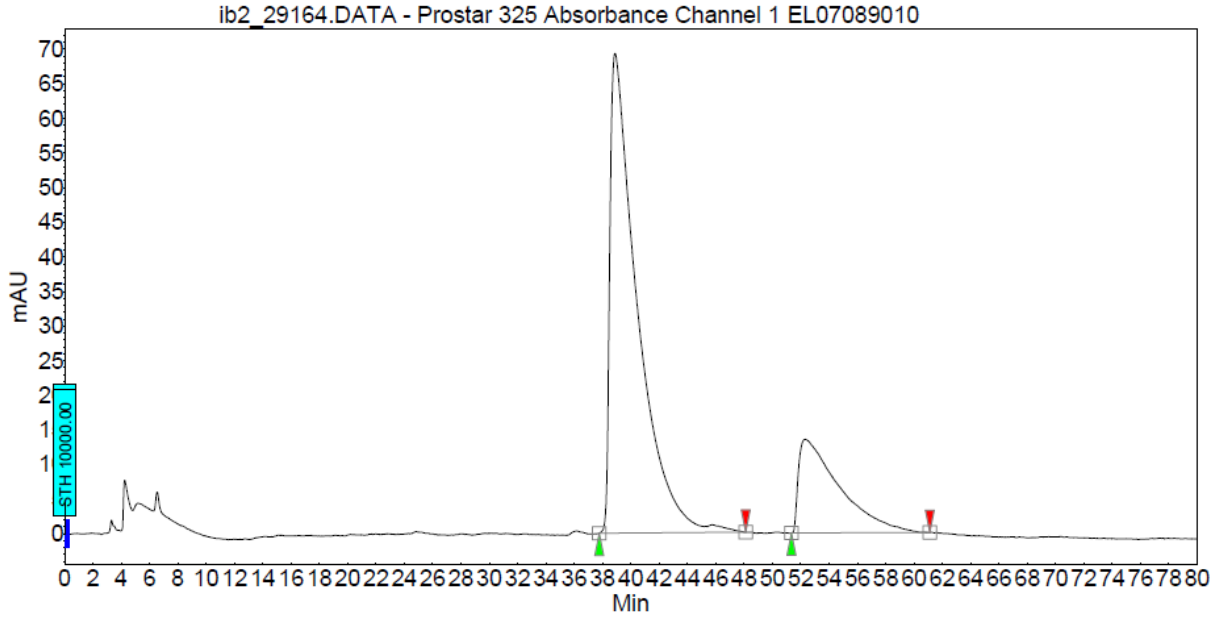
#	Time	Area %
1	14.1	60.2
2	17.5	39.8



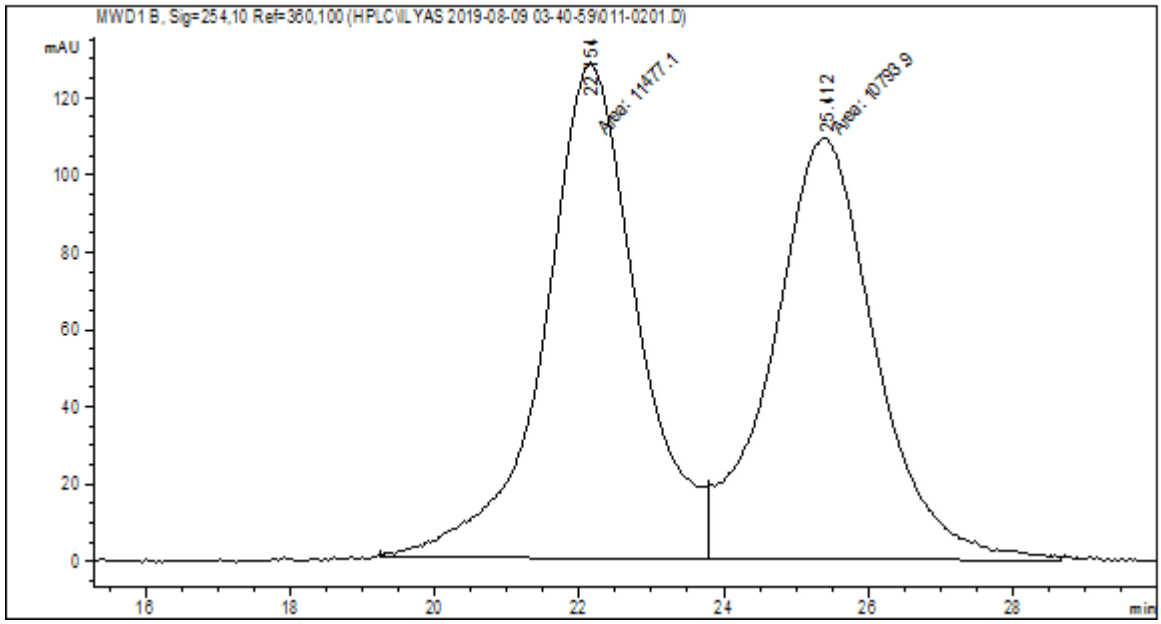
Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	38.81	51.48	47.8	94.9	51.482
2	UNKNOWN	49.88	48.52	26.1	89.4	48.518
Total			100.00	73.9	184.3	100.000

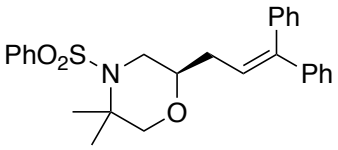


7a



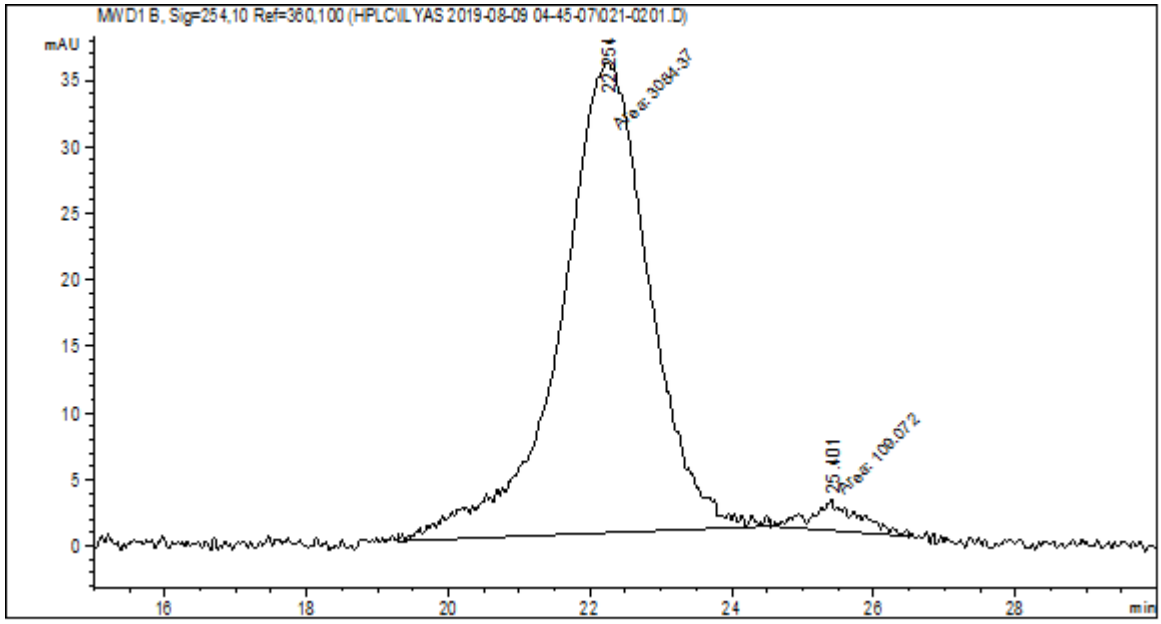
Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	38.88	77.47	69.3	155.0	77.465
2	UNKNOWN	52.31	22.53	13.5	45.1	22.535
Total			100.00	82.8	200.1	100.000



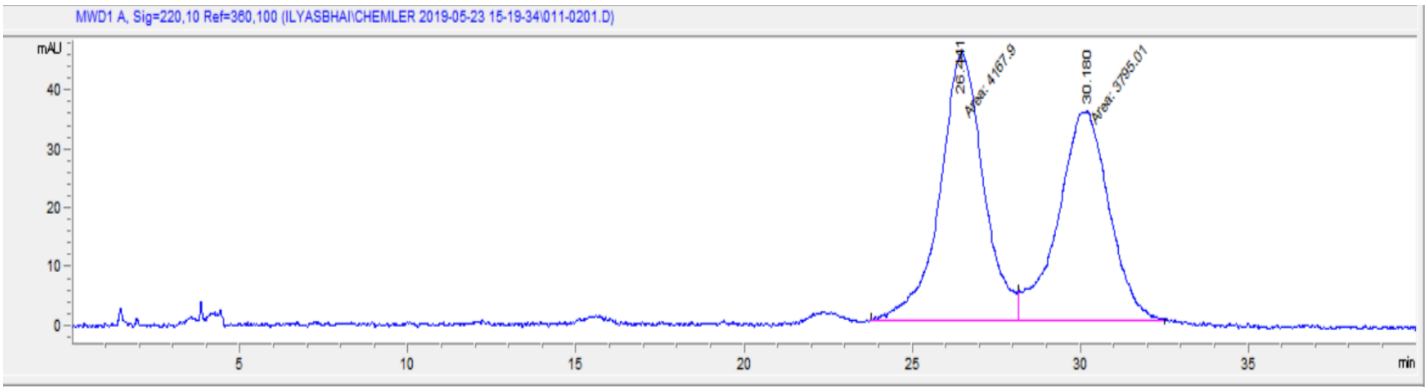


7b

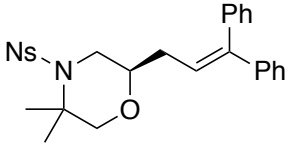
#	Time [min]	Area [%]
1	22.15	51.5
2	25.41	48.5



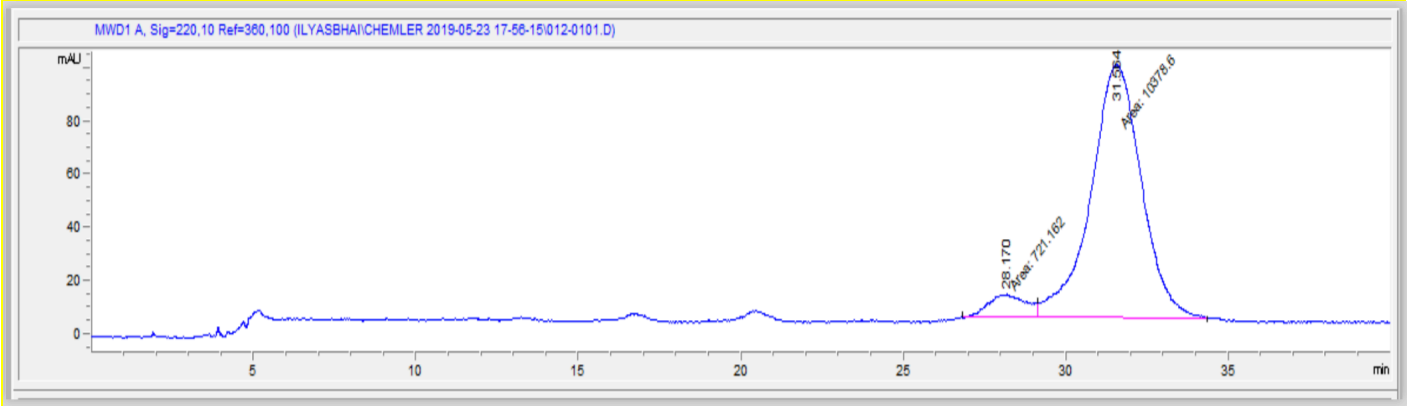
#	Time [min]	Area [%]
1	22.25	96.6
2	25.40	3.4



#	Time	Area %
1	26.4	52.1
2	30.1	47.9

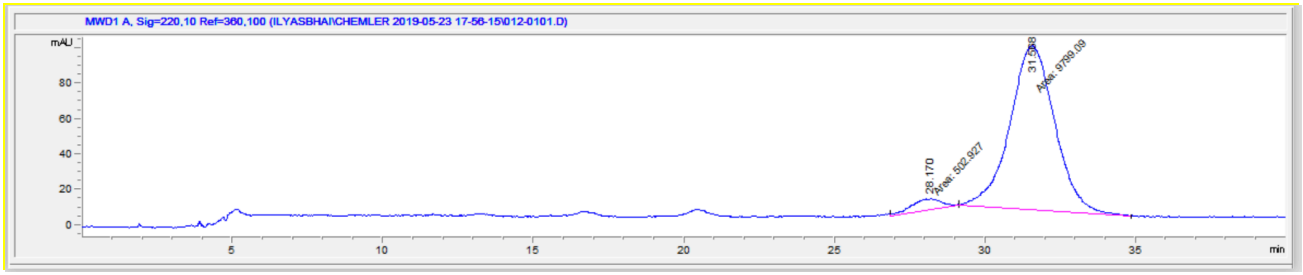


7c



Chiral trace – split peak integration

#	Time	Area %
1	26.1	93.5
2	31.5	6.5

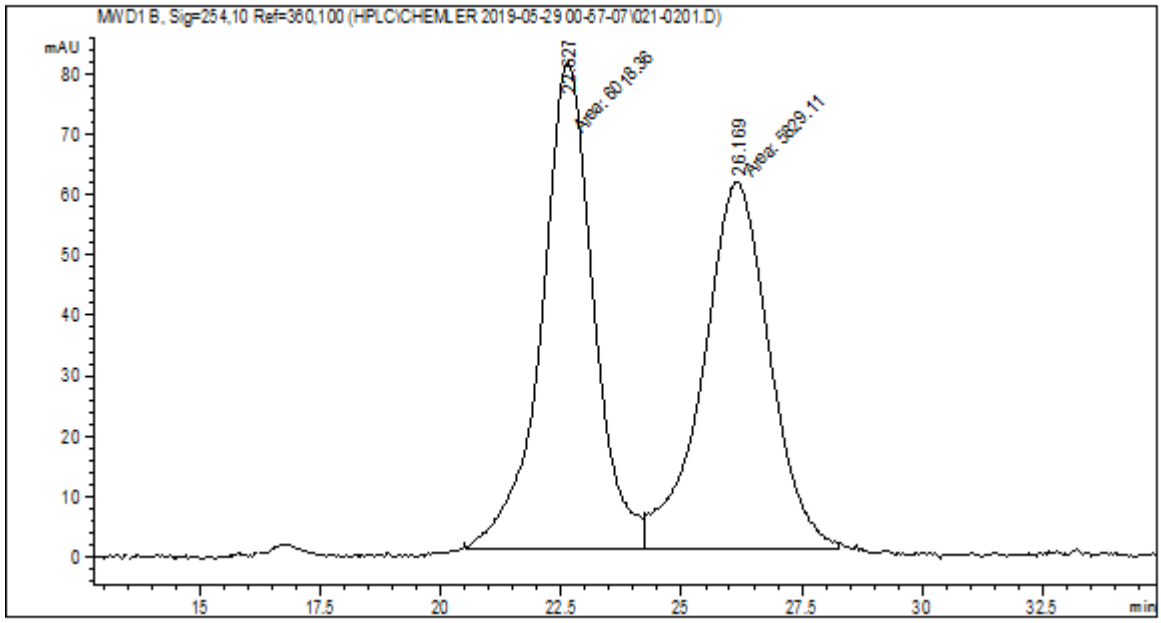


Chiral trace – valley-to-valley integration

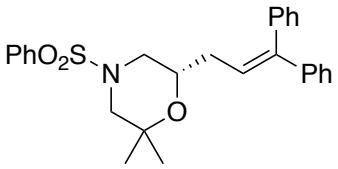
#	Time	Area %
1	26.1	95.1
2	31.5	4.8

Note: Since the chiral HPLC trace is not baseline resolved we provide an error value with this ee measurement. Error value was calculated as per the procedure described for compound **2a**-

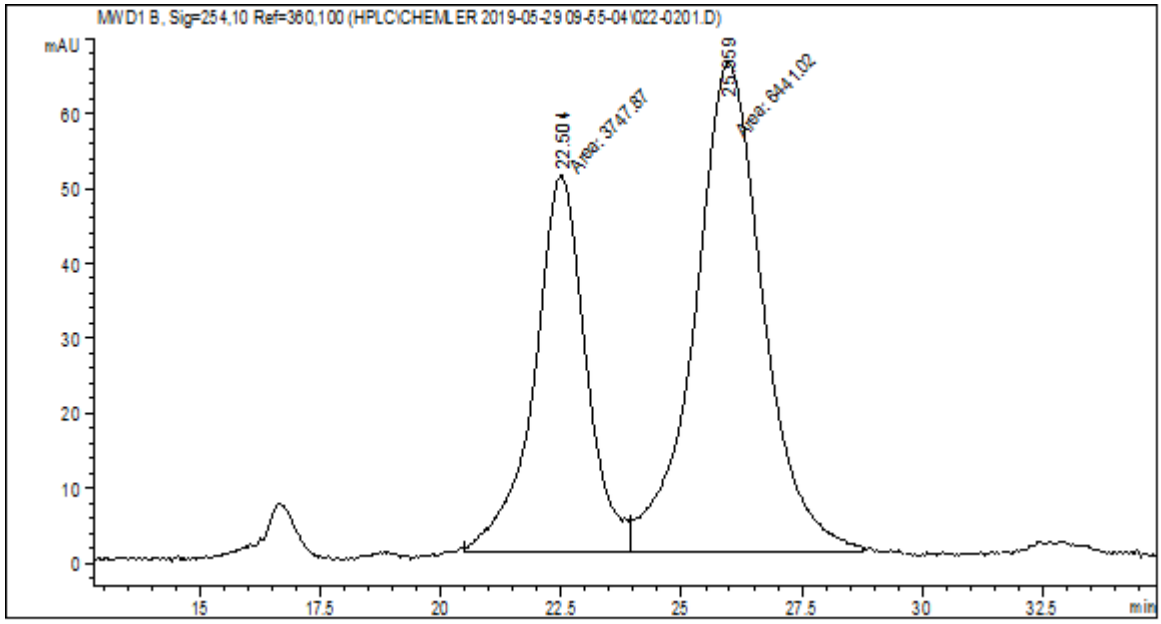
% ee by valley-to-valley integration is 90% and (2) % ee by split peak integration is 87%. Mean % ee (rounded up) is calculated to be 89% with a standard deviation (rounded up) of ± 2%. This is reported as the ee of this compound.



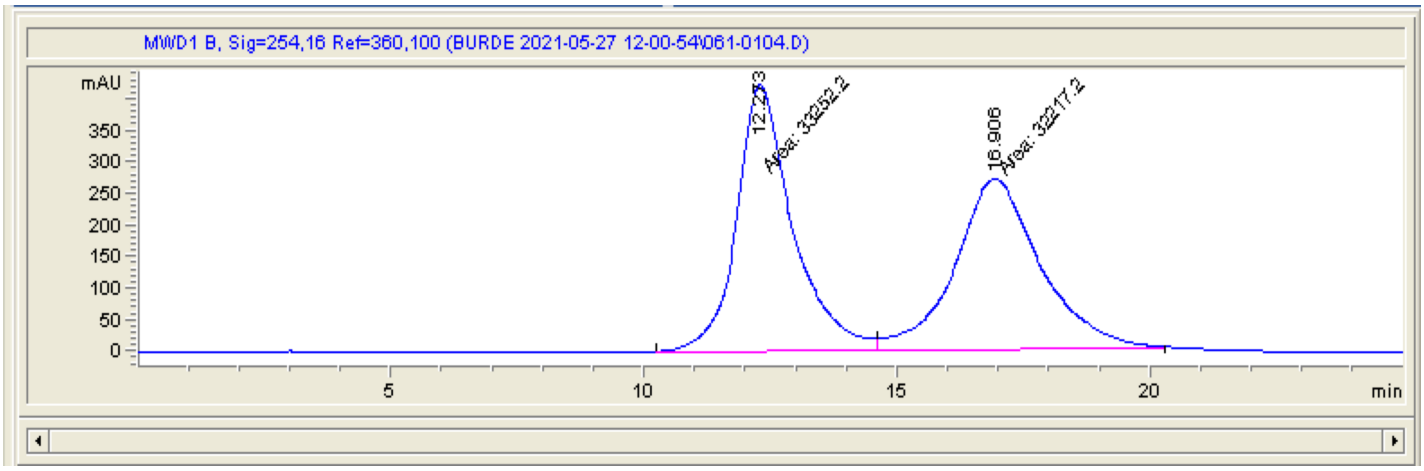
#	Time [min]	Area [%]
1	22.63	50.8
2	26.17	49.2



7d



#	Time [min]	Area [%]
1	22.50	36.8
2	25.96	63.2



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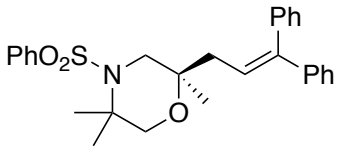
2	16.9	49.7



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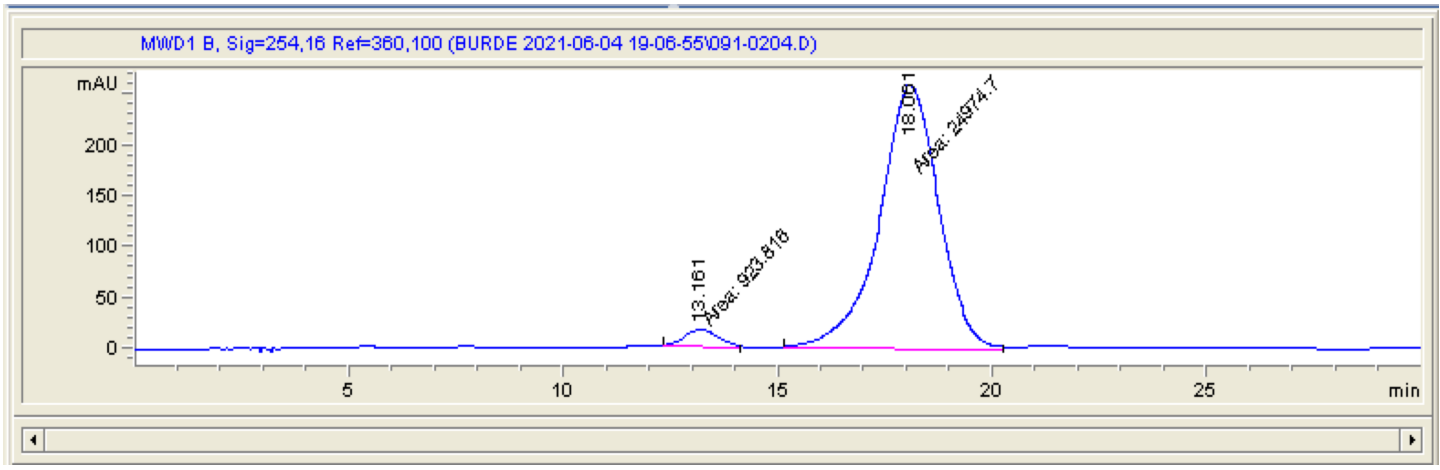

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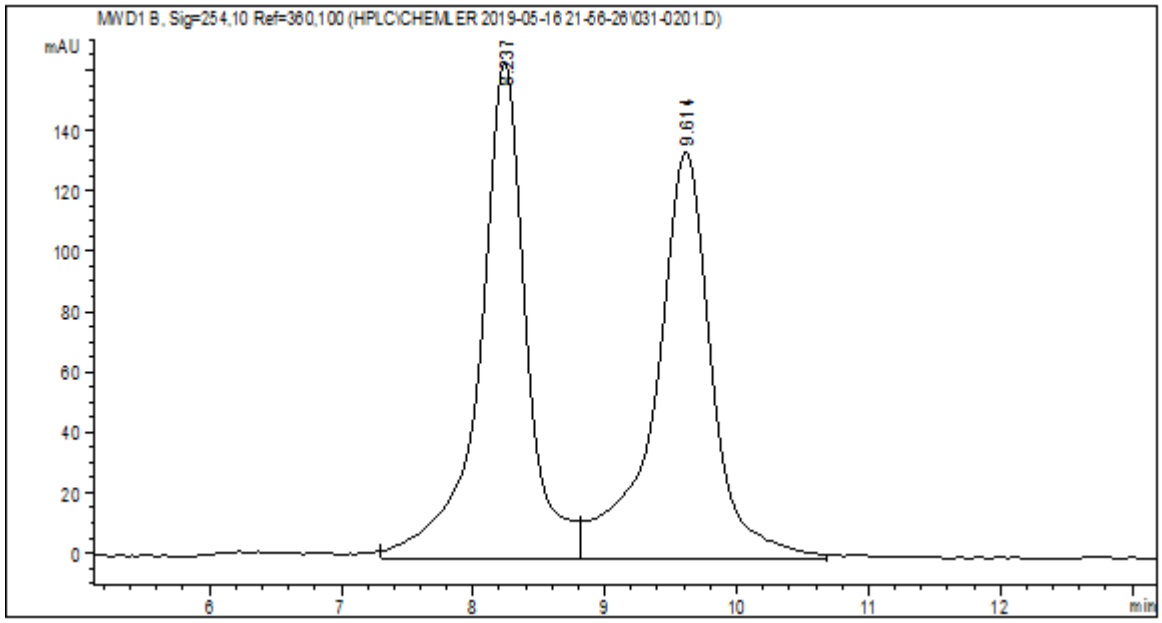

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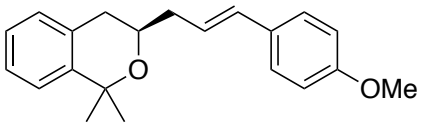
2	9.61	50.0



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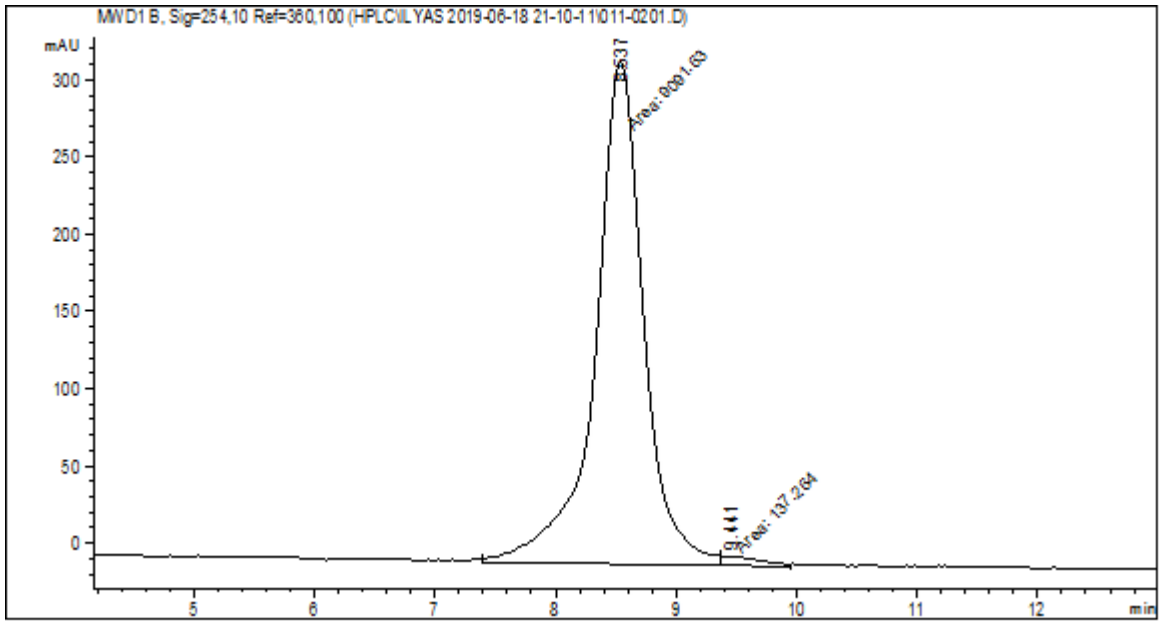

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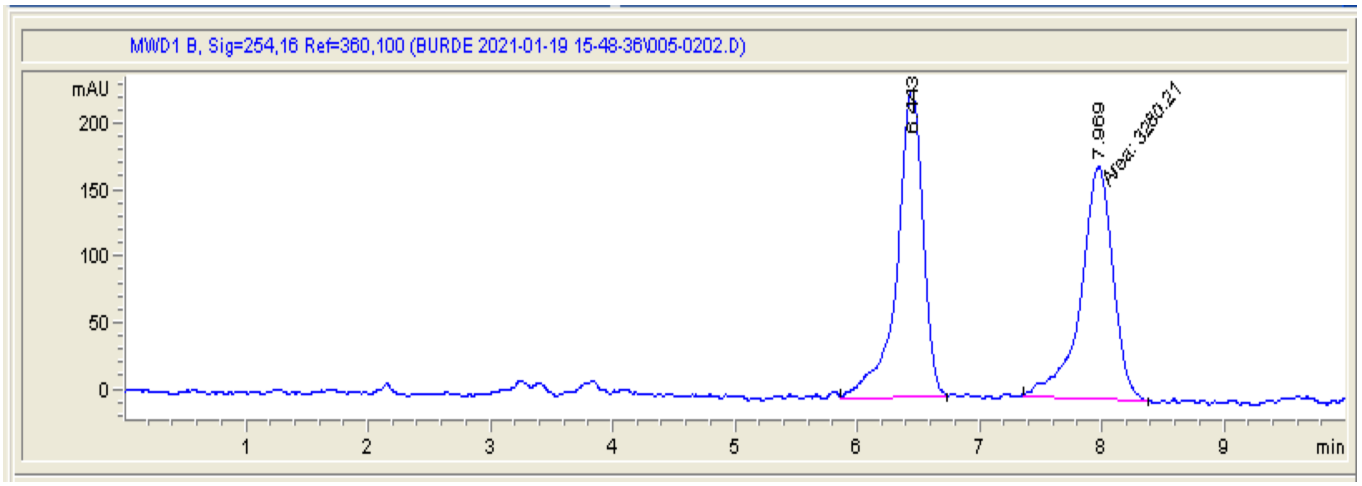
2	9.44	1.5



#	Time	Area %
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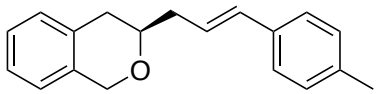
2	7.9	48.8



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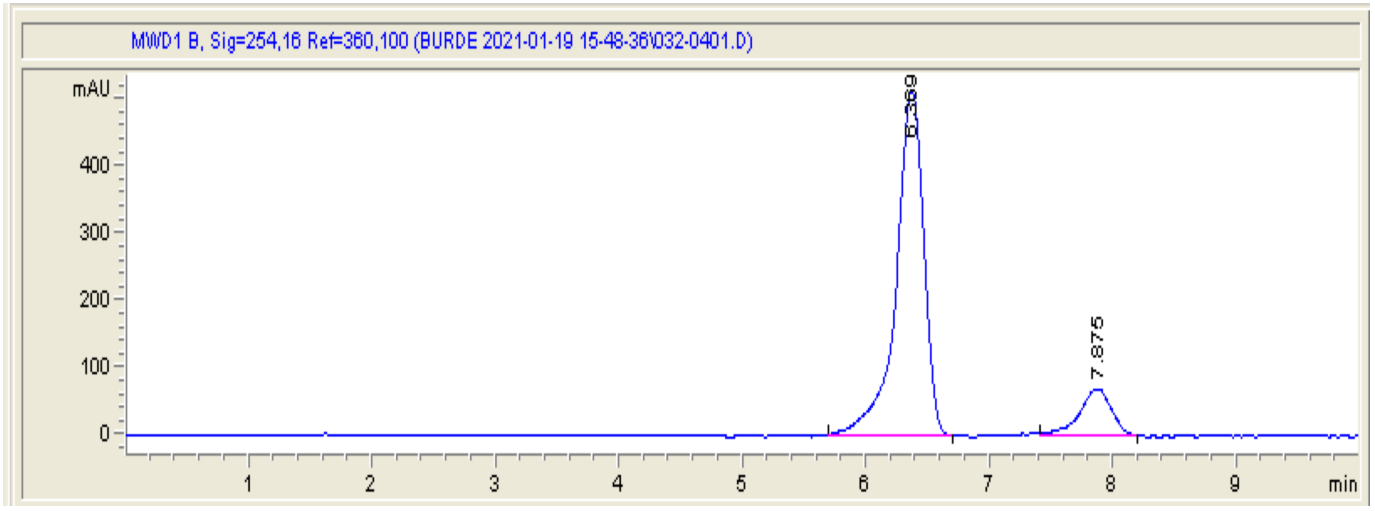

#	Time	Area %
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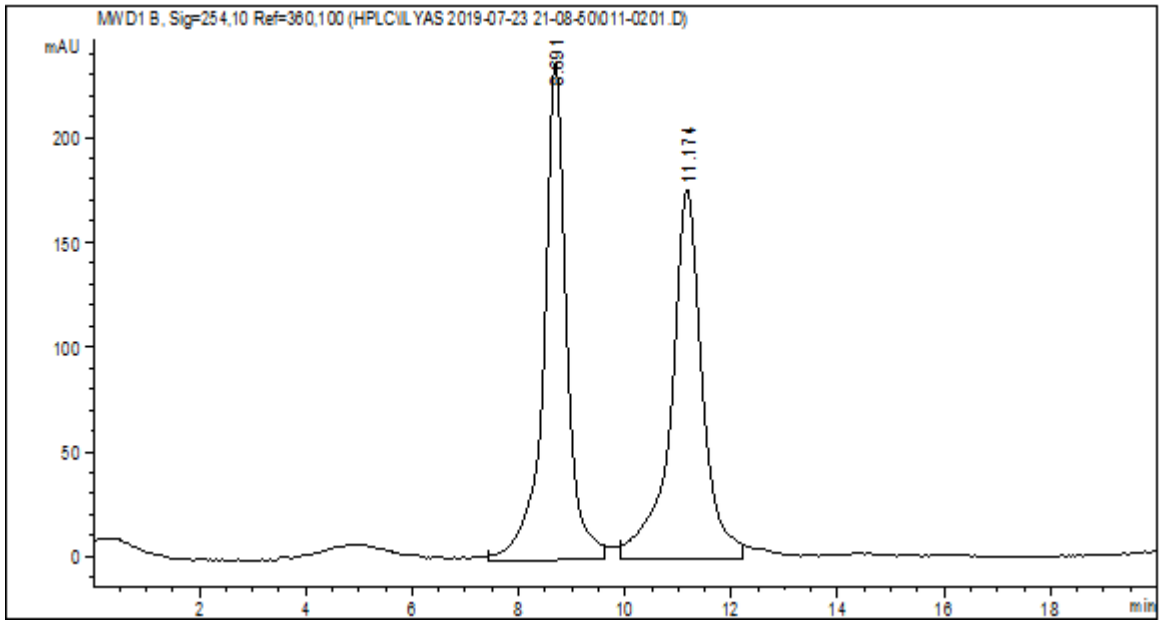

#	Time [min]	Area [%]
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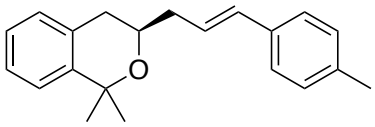

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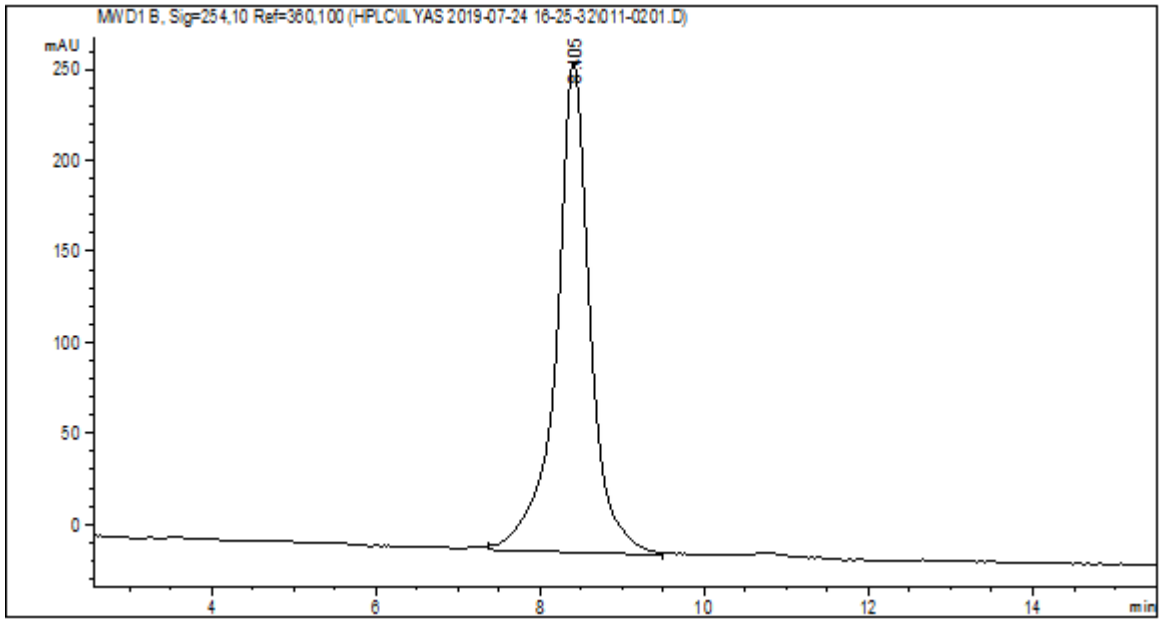

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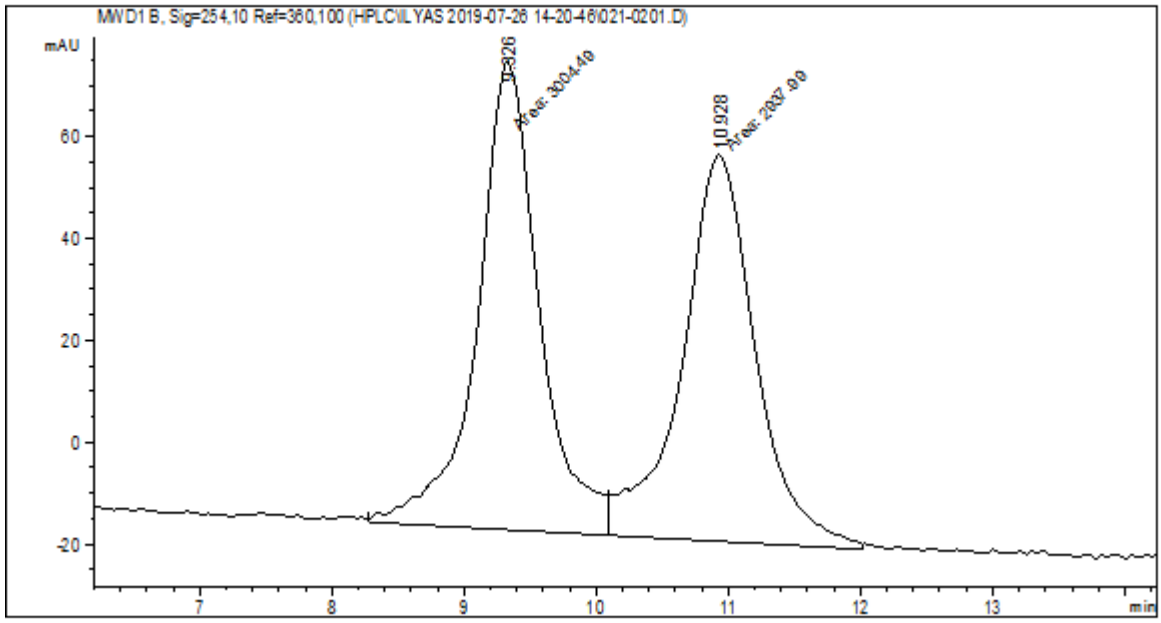

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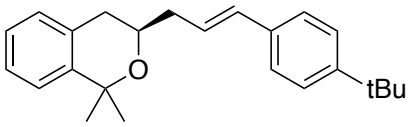
2	10.93	49.4



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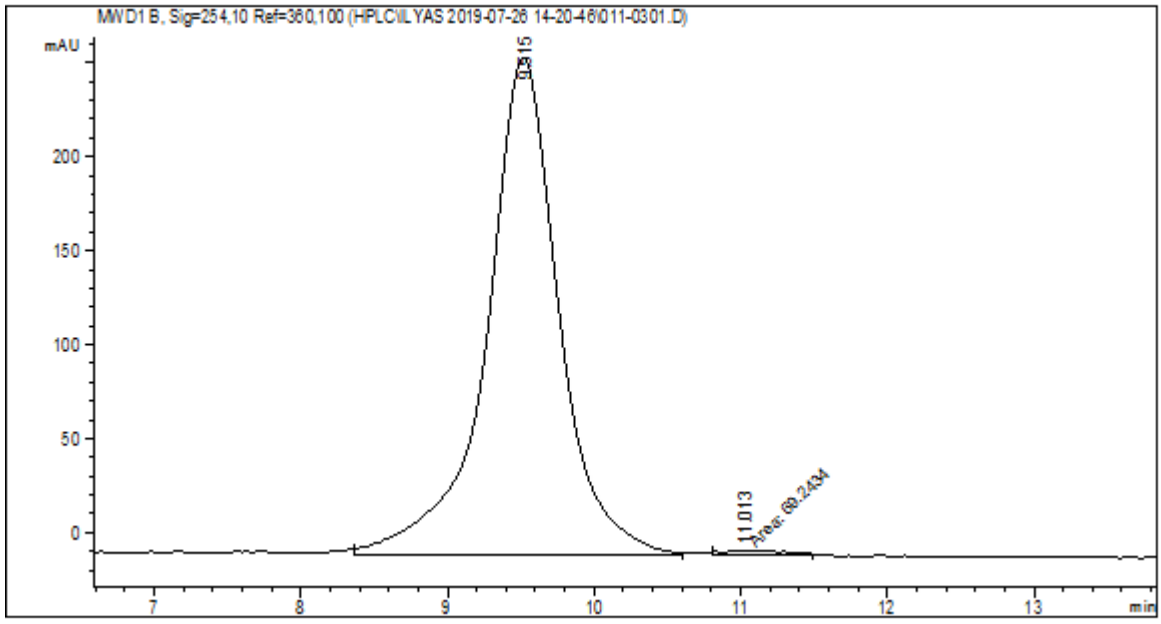

#	Time [min]	Area [%]
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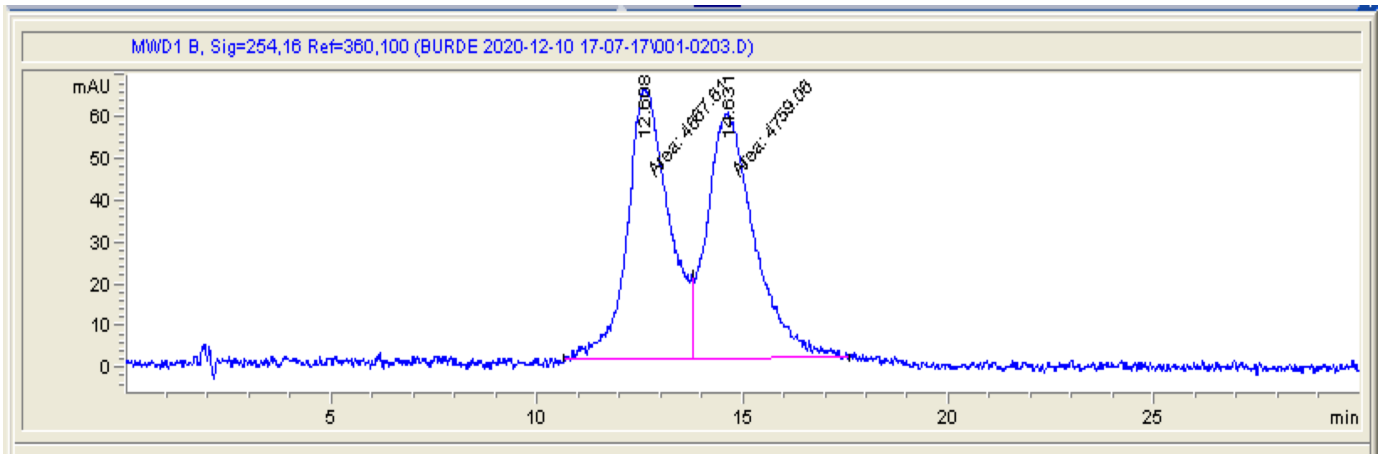
2	11.01	0.8



#	Time	Area %
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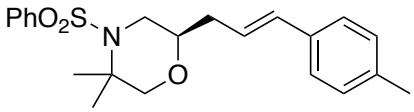

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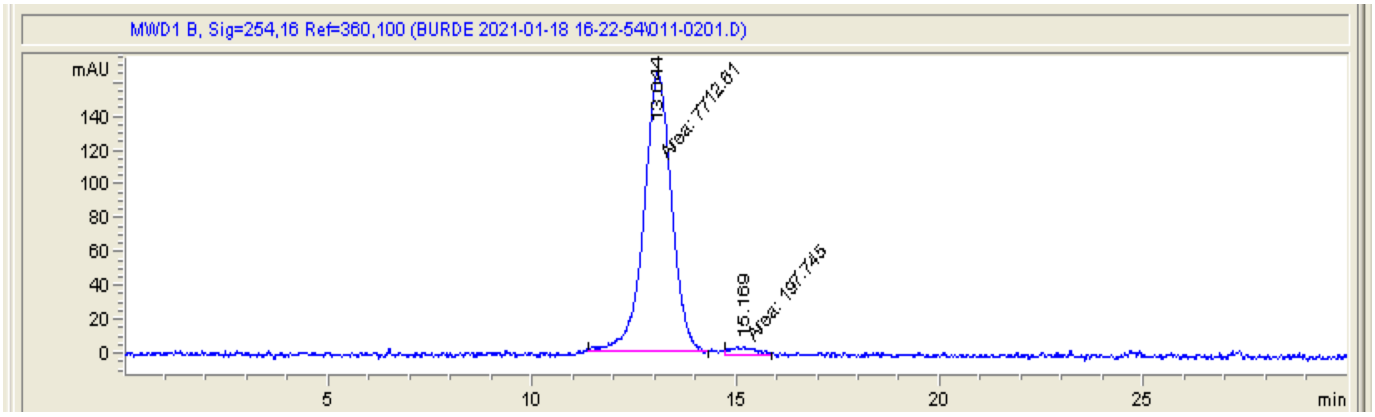
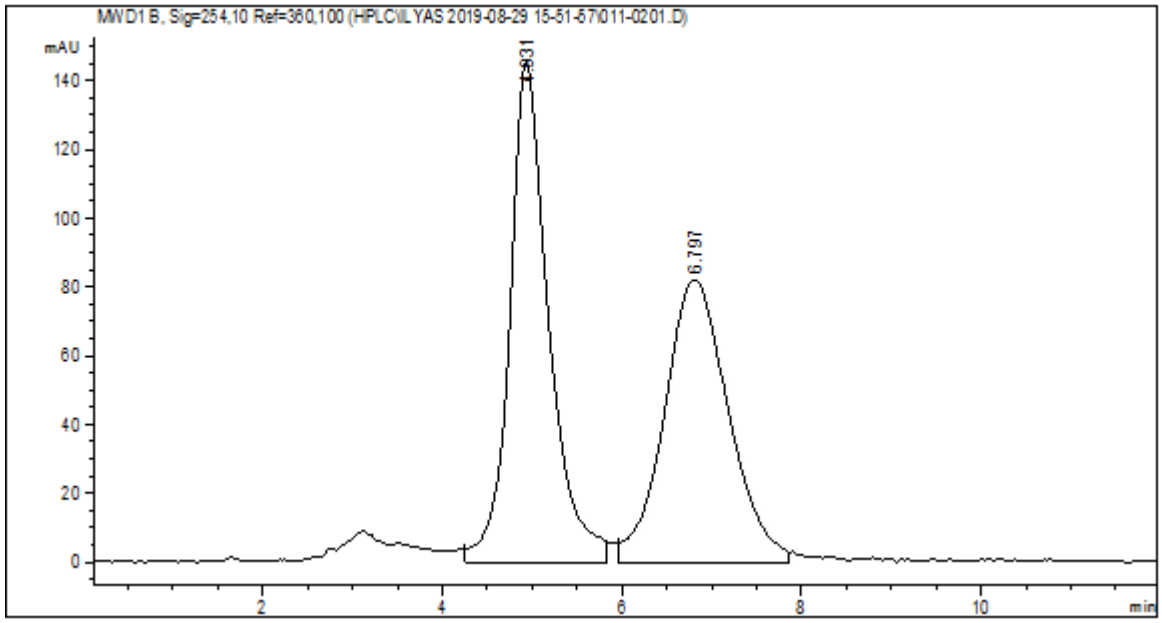
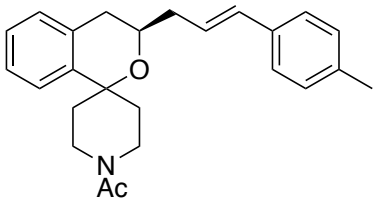


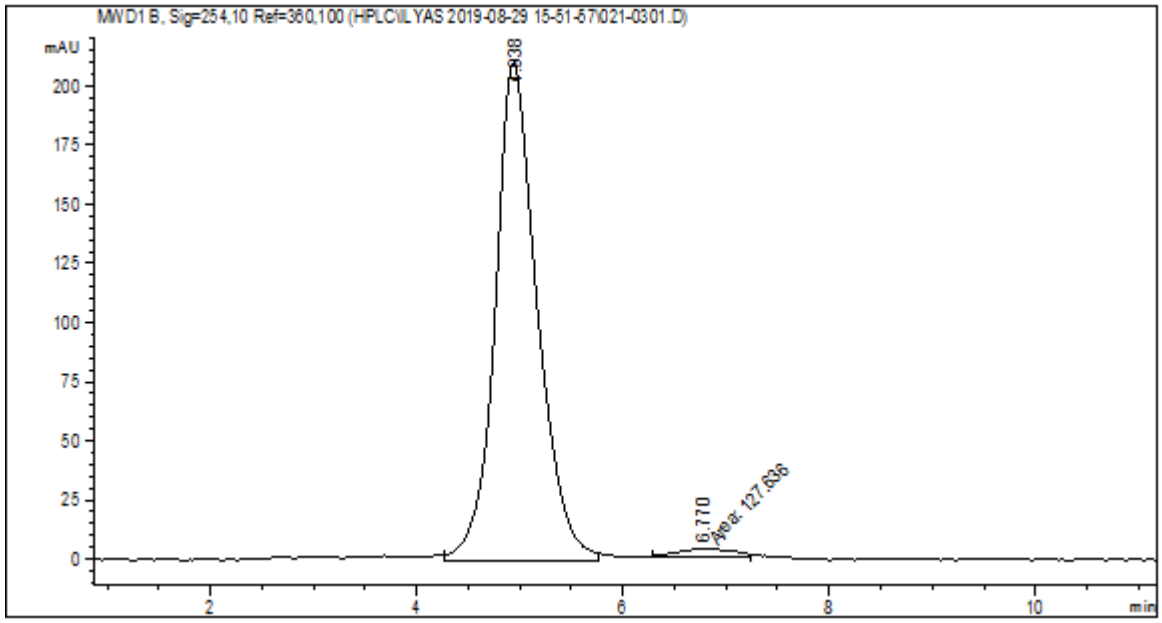
#	Time	Area %
1	13.0	97.6
2	15.1	2.4





10

#	Time [min]	Area [%]
1	4.93	51.8
2	6.80	48.2



#	Time [min]	Area [%]
1	4.94	97.9
2	6.77	2.1

Computational Methods

The Density Functional Theory (DFT) calculations (geometry optimizations, vibrational frequencies and potential energy scans) were performed using the Gaussian 16[12] software package. Geometries of all species involved were optimized using the unrestricted B3LYP[13,14] functional with a def2-SVP[15] basis set on all atoms (i.e. H, C, N, O, Cu). The SMD version of the Integrated Electron Formalism Polarization Continuum Model (IEFPCM)[16] was employed to account for solvation. The calculations were carried out in 1,2-Dichloroethane ($\varepsilon = 10.13$) solvent and the vibrational contributions to the free energy were obtained at 378.15 K (105 °C), to mimic the experimental conditions. Unrestricted single point energies were then performed to obtain the relative energies of the two transition states at the M06[17,18]/def2-TZVP[15] level of theory and test their sensitivity to the functional and basis set employed.

Geometry optimizations of the 3-coordinate starting material (SM), the major (pro-*S*) and minor (pro-*R*) products of the *cis*-oxycupration step were performed. This was followed by a vibrational frequency calculation to ensure the absence of imaginary vibrational frequencies and confirm that the calculated structures were indeed minima. The initial guesses for the transition states (TS) were found by a relaxed potential energy surface scan between the starting material and products by scanning the bond between the oxygen and internal carbon of the terminal alkene. The structure with the highest energy was chosen as the initial guess for the TS optimization. Vibrational frequency calculations were then carried out to confirm both the major and minor TS possessed one imaginary frequency each along the reaction coordinate.

The electronic structure analysis was carried out on calculations performed using the M06/def2-TZVP level of theory. This included natural bond order (NBO) calculations, performed using NBO

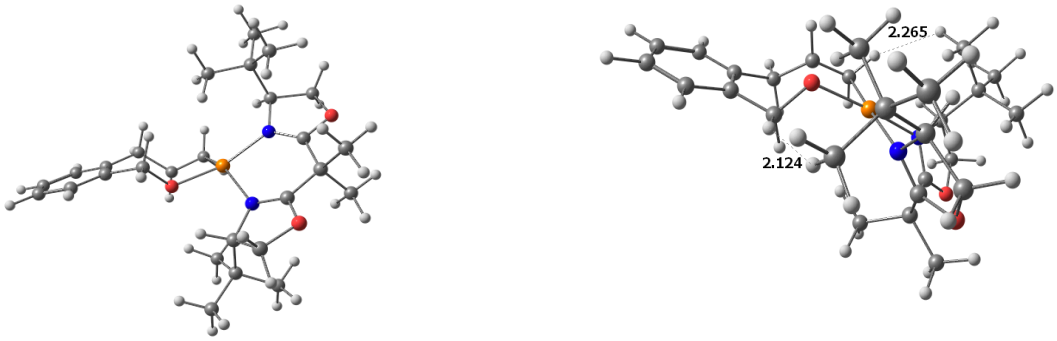
version 3.1[19] as implemented within Gaussian 16, spin density calculations, electrostatic potential and frontier density surfaces (EDS/ FDS), and Mulliken charges.

The 'tetrahedral twist angle', defined in our previous study[20] as the angle between a plane passing through the copper atom and the two nitrogen atoms of the bis(oxazoline) ligand, and a plane passing through the copper atom and the carbon and oxygen directly attached to the copper atom were calculated using Mercury v 4.1.3.[21].

Spin density plots were prepared from Gaussian cube files using Chemcraft v1.8.[22] WebMO[23] was employed to visualize EPS, FDS and select vibrational normal modes.

Computational Results

Geometric Parameters



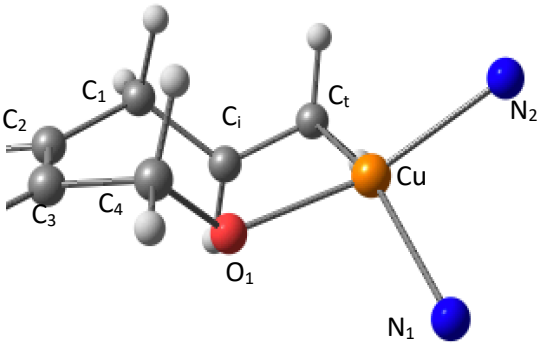
(A) (B)

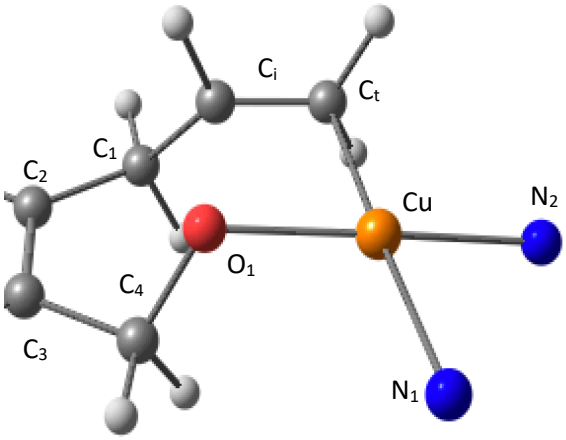
Figure 1. (A) Major (pro-*S*) and (B) minor (pro-*R*) transition states. Color code for atoms is yellow – copper, red – oxygen, blue – nitrogen, gray – carbon, white – hydrogen.

Optimized geometries of the major and minor TS using [Cu(S,S)-t-Bu-Box] as the catalyst are illustrated in Fig 1. At 105 °C and in the solvent 1,2-dichlorethane the pro-*S* TS was preferred by 2.06 kcal/mol and 2.15 kcal/mol at the M06/def2-TZVP and B3LYP/def2-SVP level of theory, respectively, yielding ee values of 88% and 89% respectively. The small difference between the values obtained with the two levels of theory supports the choice of the computational method employed. The computed ee is in excellent agreement with the experimentally obtained ee of 86% (Table 1, Entry 4 in manuscript). As illustrated in Fig 1, an analysis of the TS geometries revealed that the minor TS had two close interatomic H--H distances that measured less than 2.3 Å.

Analysis of the Transition States

Bond Lengths





Cu - C_t	2.153 Å
Ct - C_i	1.401 Å
C_i - C_1	1.506 Å
C_1 - C_2	1.513 Å
C_2 - C_3	1.411 Å
C_3 - C_4	1.511 Å
C_4 - O_1	1.411 Å
O_1 - Cu	1.977 Å
Cu - N_1	2.095 Å
Cu - N_2	2.046 Å

(A)

Cu - C_t	2.176 Å
Ct - C_i	1.393 Å
C_i - C_1	1.503 Å
C_1 - C_2	1.513 Å
C_2 - C_3	1.411 Å
C_3 - C_4	1.512 Å
C_4 - O_1	1.410 Å
O_1 - Cu	1.986 Å
Cu - N_1	2.220 Å
Cu - N_2	2.042 Å

(B)

Figure 2. Zoomed in picture of the first co-ordination sphere around the Cu (II) atom along with bond distances of illustrated atoms in the (A) major and (B) minor TS.

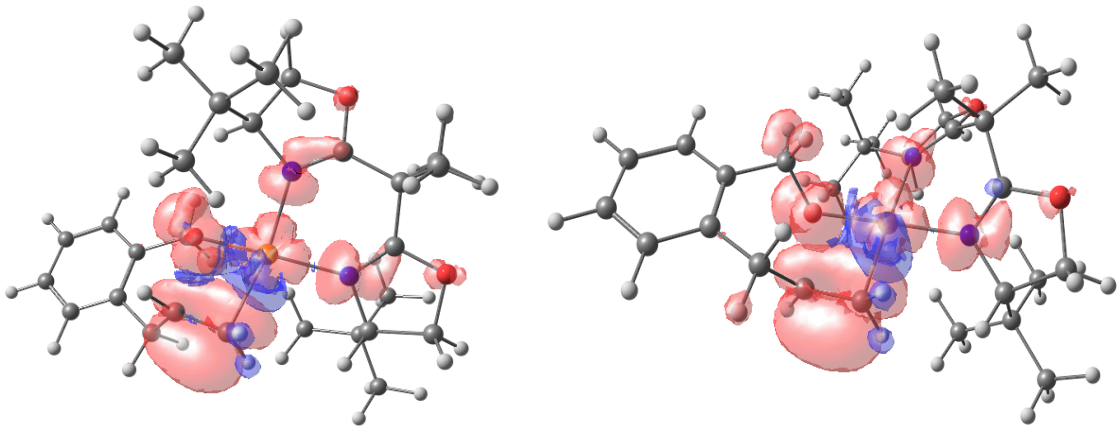
(**Note** -The atomic notations used within this document correspond to the annotations in **Figure 2)**

Spin Analysis

Atom	major TS	minor TS (%)
Cu	49.3%	48.7%
O_1	20.5%	20.8%
C_t	14.8%	10.0%
C_i	5.8%	9.7%
N_1+N_2	2.6+4.5 = 7.1%	5.3+4.4 = 9.7%

Table 1. Spin densities on the important atoms in the TS. O_1 denotes the oxygen bonded to Cu, C_t and C_i are the terminal and internal carbons of the former alkene, N_1 is the nitrogen atom trans to C_t and N_2 is the nitrogen atom trans to O_1, as illustrated in Fig 2.

Isosurface plots of the spin density, and the major contributions to the spin of the SOMO (singly occupied molecular orbital) for the major and minor TS are provided in Fig 3 and Table 1, respectively. In both TS around 98% of the spin is localized on the copper atom, nitrogen, oxygen and carbon atoms bonded to copper, and the internal carbon of the former alkene. In both TS a majority of the spin, ~50%, lies on the copper atom, while around ~20% of the spin lies on the oxygen atom.



(a) (b)

Figure 3. Spin density plots for the (a) major, and (b) minor TS. Isovalue = 0.0008 au

NBO Analysis

An NBO analysis was carried out to determine the main contributions to the stabilization of the major and minor TS in terms of bonding (BD), lone pair (LP) and unoccupied lone pair (LP*) orbitals (Table 2). The N_2-Cu bond distance and N_2(LP) → Cu(LP*) donor-acceptor stabilization energies are essentially the same for the major and minor TS. Both the C_i-Cu and O_1-Cu distances are somewhat shorter and the magnitude of the stabilization energies are slightly larger for the major TS. However, the most striking difference between the two TS is the enhanced stabilization due to the N_1(LP) → Cu(LP*) interaction in the major TS that is coupled with a significantly shorter N_1-Cu bond distance.

Donor Orbital	Acceptor Orbital	Major		Minor		ΔE_{stab} (kcal/mol)	Δd (Å)
		E_{stab} (kcal/mol)	d (Å)	E_{stab} (kcal/mol)	d (Å)		
C_i-O_1 (BD)	Cu (LP*)	26.36	2.153	25.35	2.176	1.01	-0.023
O_1 (LP)	Cu (LP*)	33.22	1.977	29.92	1.986	3.30	-0.009
N_1 (LP)	Cu (LP*)	29.50	2.095	22.98	2.220	6.52	-0.125
N_2 (LP)	Cu (LP*)	45.27	2.046	45.47	2.042	-0.20	0.004

Table 2. Stabilization Energy (E_{stab}) for the most important NBO donor-acceptor contributions to the major and minor TS along with the corresponding bond distances (d). BD - bonding orbital, LP - lone pair orbital, LP*-unoccupied lone pair

The transition states were further characterized by analyzing the Wiberg bond indices[24–26] (WBI). The change in the WBI for a bond between atoms A and B is calculated as[27–29]

$$\Delta BO_{A\text{-}B} = (W_{A-B}^{TS} - W_{A-B}^{R}) / (W_{A-B}^{P} - W_{A-B}^{R}) \qquad \text{(Eq 1)}$$

where W_{A-B}^{TS} is the WBI for the A-B bond in the TS, W_{A-B}^{R} is the WBI for the same bond in the reactant and W_{A-B}^{P} is the WBI in the intermediate product. Since the C_t-C_u and the Ci-O_1 bond do not exist in the Starting material W_{A-B}^{R} is taken to be 0 for these bonds. For the O_1-Cu bond W_{A-B}^{R} is assumed to be 1.

The percent evolution (% EV) for the bond order between atoms A and B is calculated as:[30]

$$\%EV = 100\ \Delta BO_{A\text{-}B} \qquad \text{(Eq2)}$$

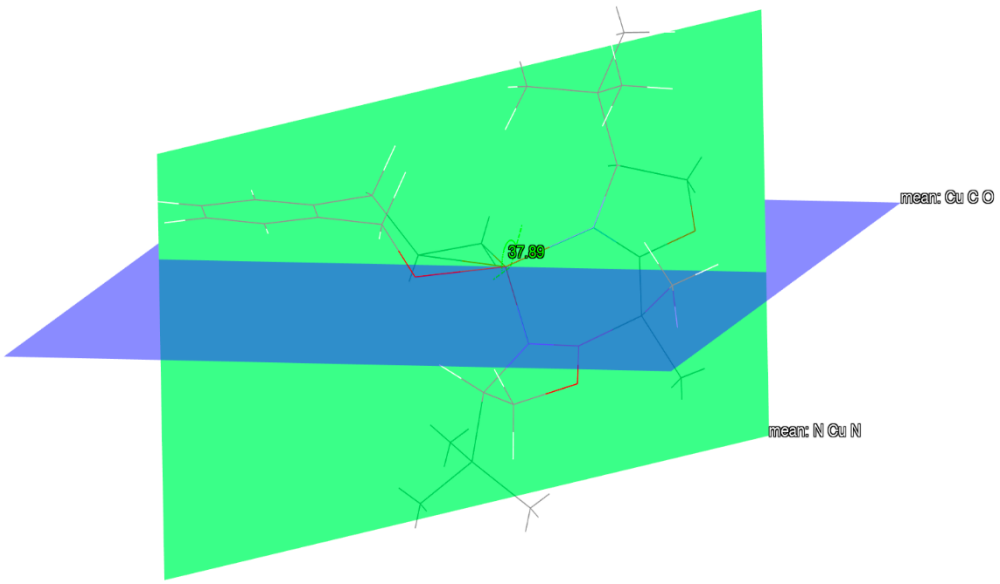
	Major TS			Minor TS		
Bond	W_{A-B}^{TS}	W_{A-B}^{P}	%EV	W_{A-B}^{TS}	W_{A-B}^{P}	%EV
C_t-Cu	0.3069	0.4572	67.1	0.2796	0.4547	61.4
C_i-O_1	0.2962	0.8318	35.6	0.2572	0.8439	30.5
O_1-Cu	0.2931	0.1518	83.3	0.2892	0.1229	81.0

Table 3. Percent evolution (% EV) for the major bonds involved in the TS.

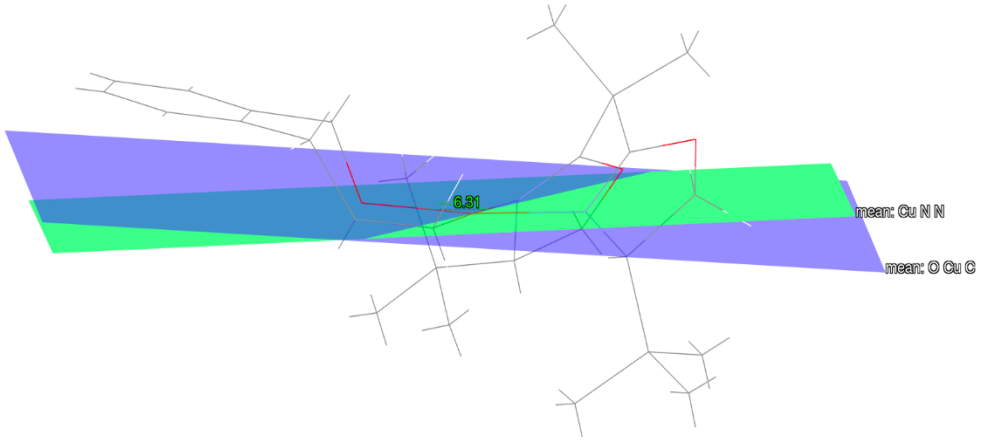
As Table 3 illustrates, in the major TS about 67% of the Cu-Ct and 36% of the Ci-O_1 bond are formed. For the minor TS these values are somewhat lower: 61% and 30%, respectively.

Tetrahedral Twist Angle

The tetrahedral twist angle was calculated by determining the angle between the planes illustrated in Figure 4, as described above in the computational details. This angle was determined to be 37.9° for the major TS, which is about 22° less than the twist angle for a perfect tetrahedron. Therefore, the geometry of this TS can be described as a distorted tetrahedron. For the minor TS the tetrahedral twist angle drops to 6.3°, which is very close to the angle made by a square planar center (0°). Hence, the geometry of the minor TS at the Cu atom may be described as distorted square planar.



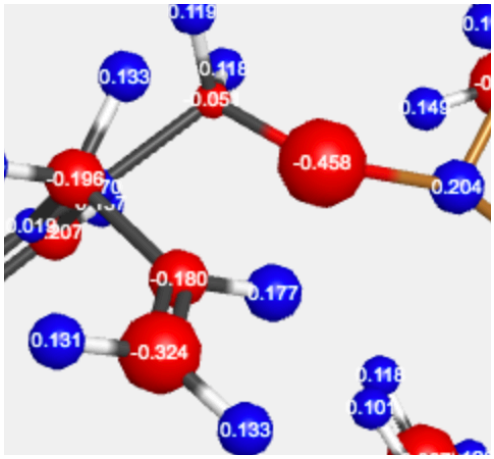
(a)



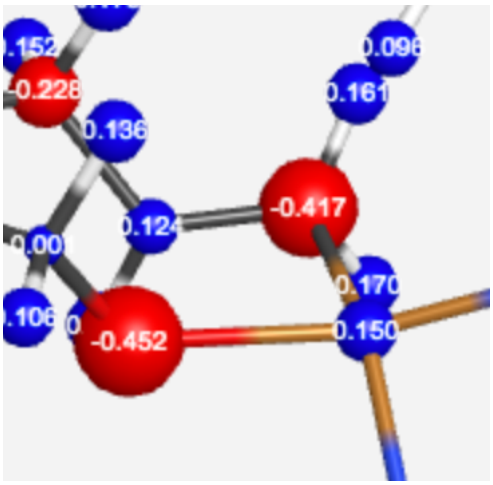
(b)

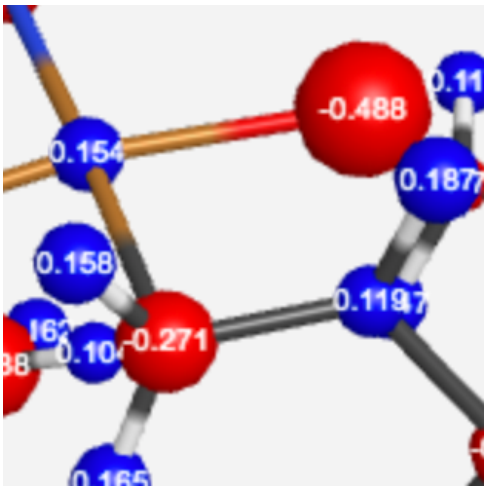
Figure 4. Tetrahedral twist angle measurements for the (a) major and (b) minor TS.

Electronic Structure :



(a)





(b) (c)

Figure 5. Mulliken charge distribution on the (a) starting material, (b) major TS, (c) minor TS.

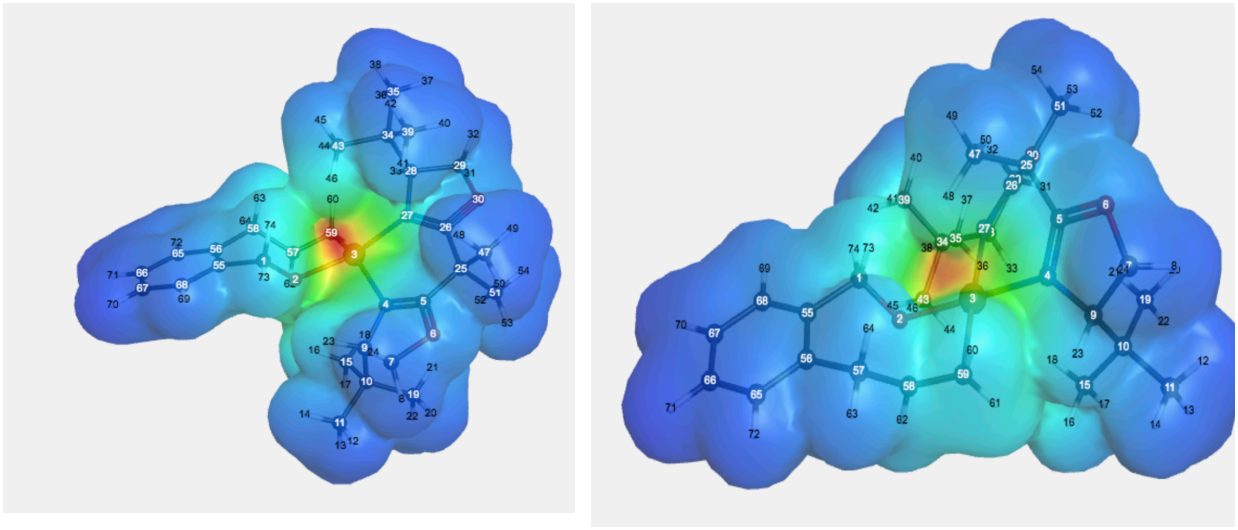
To further interrogate the electronic structure of the transition states, we calculated the Mulliken charges (Figure 5, Table 4). The most striking difference in the charge distribution between the starting material and the TS is that the internal carbon atom of the alkene is negatively charged in the former, and positively charged in the latter. This is consistent with the fact that the end product

of this reaction step is the formation of the C-O bond, in which the carbon would have a partially negative character.

Atom	SM	major TS	minor TS
Cu	+0.204	+0.150	+0.154
O_1	-0.458	-0.452	-0.488
C_t	-0.324	-0.417	-0.271
C_i	-0.180	+0.124	+0.119

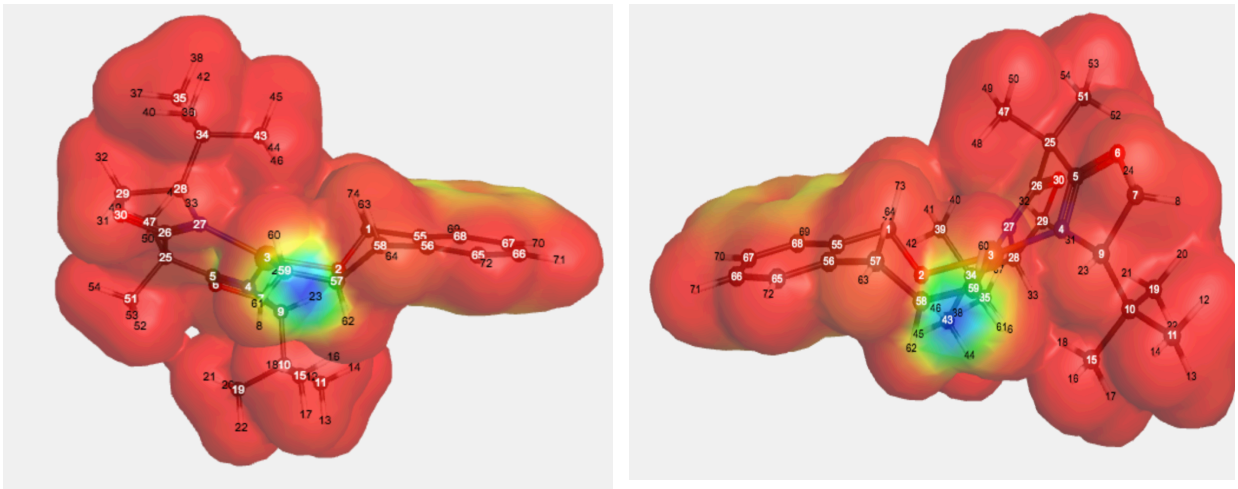
Table 4. Summary of Mulliken charges on the important atoms in the starting material (SM) and transition state (TS).

Isosurfaces of the electrostatic potential, electrophilic, nucleophilic, and radical frontier density surfaces (FDS) for the major and minor TS are illustrated in Figs 6-9.



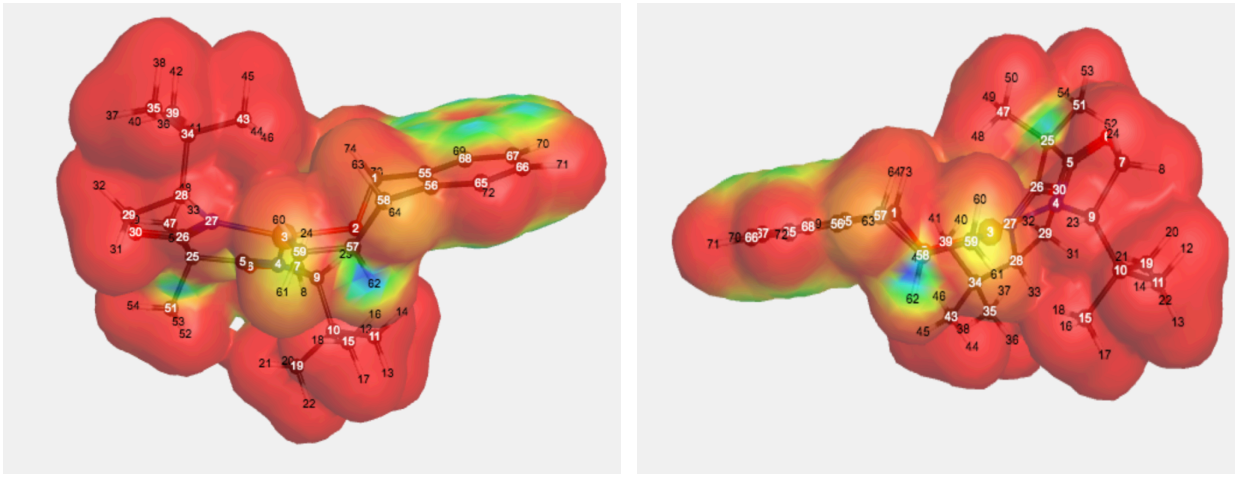
(A) (B)

Figure 6. Electrostatic potential for the (a) major TS and (b) minor TS painted onto an electron density surface (isovalue = 0.003 au) with red indicating negative regions and blue positive regions.



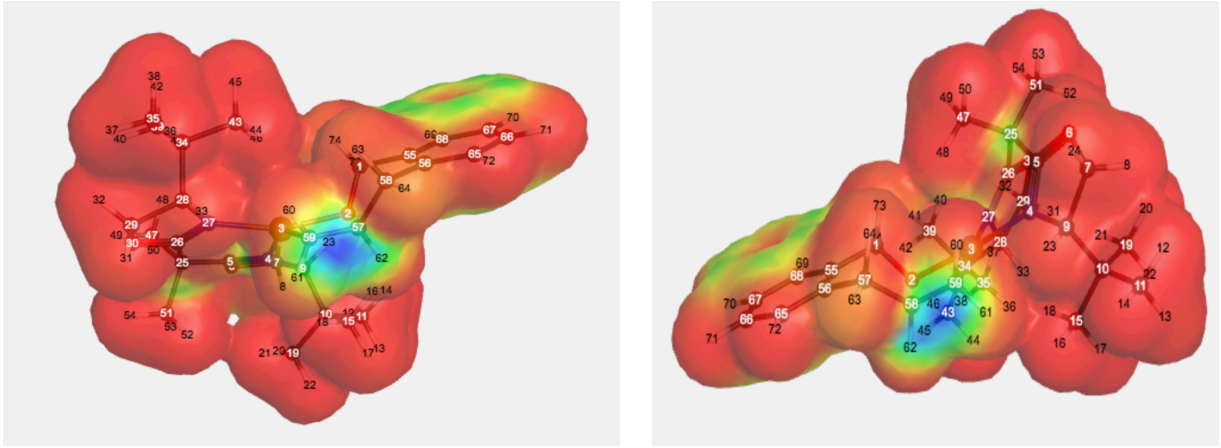
(A) (B)

Figure 7. Electrophilic FDS for (A) major and (B) minor TS. Isovalue = 0.003 au. Blue section shows the atoms most susceptible to nucleophilic attack



(A) (B)

Figure 8. Nucleophilic FDS for (A) major and (B) minor TS. Isovalue = 0.003 au. Blue section shows the atoms most susceptible to electrophilic attack

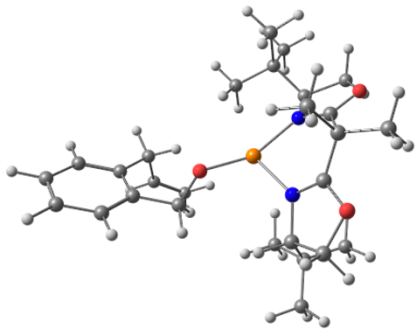


(A) (B)

Figure 9. Radical FDS for (A) major and (B) minor TS. Isovalue = 0.003 au. Blue section shows the atoms most susceptible to radical attack

Cartesian Coordinates of Optimized Geometries

SM (3-coordinate) $[C_{27}H_{41}CuN_2O_3]^+$



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C	0.429458000000	-1.155845000000	0.347034000000
O	1.709319000000	-1.122193000000	0.906729000000
Cu	3.342795000000	-1.589026000000	0.216584000000
N	3.429191000000	-3.589253000000	0.004542000000
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C	6.098851000000	-2.444558000000	0.332553000000
C	2.421865000000	-4.534363000000	-0.527525000000
C	2.914126000000	-5.872770000000	0.070419000000
O	4.266775000000	-5.577919000000	0.529178000000
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C	6.805967000000	-4.746902000000	1.080039000000
C	5.375035000000	-3.274759000000	2.569193000000
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H	4.012691000000	-5.842682000000	-2.480280000000
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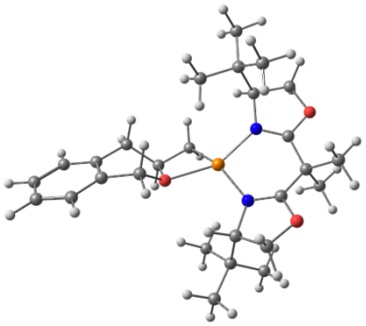
Major Product (proS) (4-coordinate) $[C_{27}H_{41}CuN_2O_3]^+$



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C	-3.119835000000	3.084978000000	-1.474445000000
C	-2.870517000000	1.619119000000	-1.067106000000
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C	-5.258903000000	1.006720000000	-0.578520000000
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C	-3.419756000000	-0.382668000000	0.389426000000
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C	4.149626000000	1.820874000000	-0.335453000000
C	4.753729000000	-0.106359000000	1.169693000000
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H	2.144269000000	-0.201279000000	1.693357000000
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O	0.424540000000	-1.935284000000	-0.206554000000
C	-0.080134000000	-2.349459000000	-1.547435000000
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C	-0.279992000000	-5.996746000000	-0.851459000000
C	0.806968000000	-6.433515000000	1.273535000000
C	0.297139000000	-6.894603000000	0.054674000000
H	-0.819744000000	4.159789000000	2.029981000000
H	-0.916260000000	5.349341000000	0.702356000000
H	0.624943000000	5.094169000000	1.560074000000
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H	-5.284833000000	0.402966000000	-1.500928000000
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H	-4.092167000000	-0.787788000000	1.162869000000
H	-2.392083000000	-0.417916000000	0.783139000000
H	2.502387000000	-0.071458000000	-1.484335000000
H	2.906210000000	-1.428172000000	-0.411099000000
H	4.169582000000	-0.691688000000	-1.433984000000
H	3.380979000000	2.289682000000	-0.969663000000

H	5.019082000000	1.610498000000	-0.978960000000
H	4.474188000000	2.558594000000	0.415334000000
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H	5.068218000000	0.563006000000	1.986570000000
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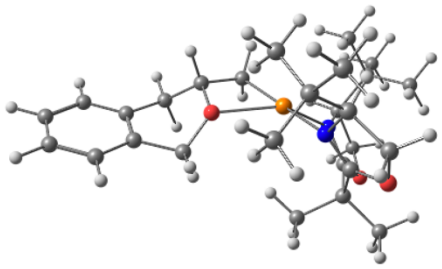
Minor Product (proR) (4-coordinate) $[C_{27}H_{41}CuN_2O_3]^+$



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C	3.667314000000	2.078051000000	4.077064000000
C	3.623265000000	1.879299000000	5.626162000000
C	4.038626000000	3.205300000000	6.290695000000
H	5.077371000000	3.485237000000	6.052625000000
H	3.965494000000	3.120577000000	7.386909000000
H	3.383314000000	4.033780000000	5.974004000000
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H	1.485110000000	2.347335000000	5.780693000000
H	2.133862000000	1.412283000000	7.148219000000
H	1.828543000000	0.609182000000	5.588827000000
C	4.566221000000	0.750224000000	6.077620000000
H	5.616690000000	0.949456000000	5.811099000000
H	4.279070000000	-0.218621000000	5.638500000000
H	4.525186000000	0.639648000000	7.173238000000
H	2.969924000000	2.891807000000	3.829168000000
H	5.057809000000	3.194988000000	2.754381000000
C	4.335086000000	-0.842745000000	1.840541000000
C	3.481859000000	-1.909286000000	2.517579000000
N	2.247926000000	-1.788973000000	2.855210000000

C	1.855257000000	-3.011297000000	3.602275000000
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O	4.080010000000	-3.062979000000	2.804473000000
H	3.482337000000	-4.362956000000	4.304870000000
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H	1.797196000000	-2.727293000000	4.667406000000
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C	0.288396000000	-4.910949000000	4.033413000000
H	0.365191000000	-4.722367000000	5.117367000000
H	1.034028000000	-5.677922000000	3.768165000000
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H	1.119349000000	-4.665772000000	1.397296000000
H	0.537844000000	-3.005883000000	1.118218000000
H	-0.617399000000	-4.312004000000	1.473548000000
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H	6.260482000000	-1.545827000000	2.637856000000
H	6.376865000000	-0.548928000000	1.164328000000
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C	-1.569438000000	0.302331000000	-0.703538000000
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C	-0.815346000000	1.284650000000	1.895112000000
C	0.250902000000	1.760156000000	2.852417000000
H	0.864595000000	2.584331000000	2.456943000000
H	-0.113298000000	1.990015000000	3.863921000000
H	-1.736283000000	1.006215000000	2.434189000000
H	-1.711304000000	3.117494000000	1.200427000000
H	-0.254244000000	2.637086000000	0.312571000000
C	-3.197958000000	2.094808000000	-0.832526000000
C	-3.905429000000	1.377501000000	-1.804666000000
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C	-2.284355000000	-0.418661000000	-1.666433000000
H	-1.930032000000	-1.404180000000	-1.982630000000
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H	0.573432000000	0.339171000000	-0.518091000000
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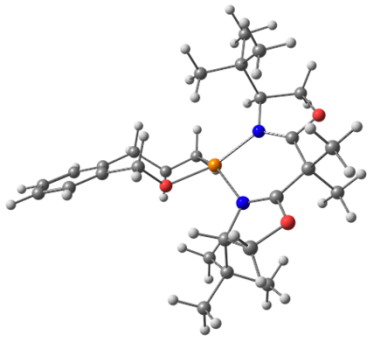
Major TS (proS) $[C_{27}H_{41}CuN_2O_3]^+$



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N	1.993952000000	1.865549000000	2.876323000000
C	3.154359000000	2.339322000000	3.153867000000
O	3.350393000000	3.634298000000	2.889461000000
C	2.174846000000	4.092987000000	2.166364000000
H	1.917248000000	5.090860000000	2.538634000000
C	1.131215000000	2.994980000000	2.446907000000
C	0.045504000000	3.373654000000	3.509759000000
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H	-0.293984000000	5.366634000000	2.621803000000
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H	-1.348505000000	4.086317000000	1.970759000000
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H	-1.245848000000	1.700325000000	2.931772000000
H	-1.641349000000	2.433637000000	4.514819000000
H	-0.229871000000	1.364064000000	4.349827000000
C	0.673185000000	3.908381000000	4.809724000000
H	1.252842000000	4.831827000000	4.652638000000
H	1.333634000000	3.162685000000	5.279932000000
H	-0.120059000000	4.144702000000	5.537437000000
H	0.605239000000	2.700253000000	1.528989000000
H	2.447776000000	4.160089000000	1.102079000000
C	4.319426000000	1.657335000000	3.840843000000
C	4.263384000000	0.142710000000	3.785024000000
N	3.414299000000	-0.646435000000	3.222919000000

C	3.957639000000	-2.031119000000	3.300721000000
C	5.061888000000	-1.872203000000	4.362073000000
O	5.296972000000	-0.440745000000	4.392810000000
H	4.733306000000	-2.176542000000	5.367277000000
H	6.011836000000	-2.364521000000	4.125583000000
H	3.169570000000	-2.703056000000	3.666207000000
C	4.440596000000	-2.569557000000	1.913097000000
C	4.961850000000	-4.005495000000	2.115039000000
H	4.189275000000	-4.653132000000	2.561888000000
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C	5.555549000000	-1.689533000000	1.320248000000
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H	5.893200000000	-2.108760000000	0.358865000000
C	3.258038000000	-2.614159000000	0.930314000000
H	2.470413000000	-3.299123000000	1.281176000000
H	3.597903000000	-2.973488000000	-0.054431000000
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H	6.498525000000	1.631221000000	3.688055000000
H	5.753508000000	3.196354000000	3.268373000000
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H	4.324180000000	3.192977000000	5.398761000000
H	5.176552000000	1.691436000000	5.850759000000
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C	-1.839739000000	-1.657542000000	0.082643000000

C	-0.710398000000	-1.530386000000	2.382519000000
C	-1.102942000000	-2.370427000000	1.195912000000
C	0.380843000000	-1.868009000000	3.194055000000
H	0.983008000000	-2.741115000000	2.928925000000
H	0.358036000000	-1.586325000000	4.252957000000
H	-1.509081000000	-0.921759000000	2.813194000000
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H	-1.736403000000	-3.183028000000	1.594561000000
C	-3.079251000000	-2.107579000000	-0.388937000000
C	-3.716085000000	-1.462603000000	-1.456664000000
C	-3.114274000000	-0.355234000000	-2.060303000000
C	-1.879475000000	0.107087000000	-1.588567000000
H	-1.409519000000	0.980334000000	-2.051176000000
H	-3.607254000000	0.154058000000	-2.892746000000
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H	0.403427000000	0.871518000000	-0.458812000000
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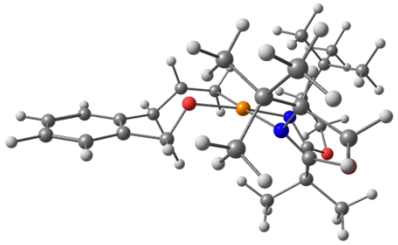
Minor TS (proS) $[C_{27}H_{41}CuN_2O_3]^+$



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N	3.209399000000	0.957496000000	3.215161000000
C	4.265210000000	0.501076000000	2.638341000000
O	5.400578000000	1.149774000000	2.864929000000
C	5.063954000000	2.327416000000	3.654056000000
H	5.802018000000	2.410155000000	4.460089000000
C	3.612550000000	2.063313000000	4.116124000000
C	3.438997000000	1.696403000000	5.625636000000
C	3.849235000000	2.921130000000	6.465104000000
H	4.913372000000	3.177151000000	6.338629000000
H	3.685893000000	2.719478000000	7.535945000000
H	3.252658000000	3.808678000000	6.196176000000
C	1.959870000000	1.377838000000	5.908644000000
H	1.315021000000	2.247291000000	5.702577000000
H	1.825457000000	1.109716000000	6.968907000000
H	1.599004000000	0.533351000000	5.300350000000
C	4.303963000000	0.484534000000	6.015422000000
H	5.378575000000	0.669987000000	5.858132000000
H	4.025258000000	-0.417120000000	5.446763000000
H	4.167981000000	0.253266000000	7.084123000000
H	2.985527000000	2.942278000000	3.912805000000
H	5.148102000000	3.201083000000	2.991319000000
C	4.321712000000	-0.722927000000	1.730936000000
C	3.449512000000	-1.781194000000	2.403007000000

N	2.189656000000	-1.694086000000	2.638525000000
C	1.815665000000	-2.860550000000	3.491278000000
C	3.100799000000	-3.722093000000	3.463683000000
O	4.092401000000	-2.856661000000	2.858437000000
H	3.462686000000	-4.012462000000	4.457983000000
H	3.018906000000	-4.617568000000	2.831593000000
H	1.658271000000	-2.465079000000	4.509778000000
C	0.520251000000	-3.631126000000	3.107250000000
C	0.424677000000	-4.873208000000	4.018461000000
H	0.451398000000	-4.591326000000	5.084520000000
H	1.236388000000	-5.595636000000	3.836562000000
H	-0.526405000000	-5.399436000000	3.837614000000
C	0.543734000000	-4.071955000000	1.634571000000
H	1.373645000000	-4.764741000000	1.420703000000
H	0.643631000000	-3.210246000000	0.957603000000
H	-0.391842000000	-4.595181000000	1.378831000000
C	-0.707134000000	-2.744164000000	3.377034000000
H	-0.752686000000	-2.454136000000	4.440966000000
H	-1.633113000000	-3.297020000000	3.146922000000
H	-0.698025000000	-1.823348000000	2.775968000000
C	3.756199000000	-0.351456000000	0.337173000000
H	2.714113000000	-0.005702000000	0.388387000000
H	3.799011000000	-1.231112000000	-0.322049000000
H	4.367028000000	0.448429000000	-0.106919000000
C	5.771865000000	-1.214719000000	1.576875000000
H	6.231836000000	-1.453496000000	2.544802000000
H	6.374860000000	-0.439735000000	1.085458000000
H	5.790205000000	-2.118138000000	0.952030000000
C	-1.637679000000	0.159140000000	-0.341480000000

C	-1.884368000000	1.545758000000	-0.261232000000
C	-0.877221000000	2.431657000000	0.438827000000
C	-0.578387000000	2.085067000000	1.870933000000
C	0.629987000000	2.412188000000	2.481825000000
H	1.412639000000	2.899126000000	1.890010000000
H	0.647552000000	2.572653000000	3.562491000000
H	-1.448363000000	1.897774000000	2.505516000000
H	-1.250102000000	3.471761000000	0.447139000000
H	0.072226000000	2.452795000000	-0.125748000000
C	-3.034282000000	2.073577000000	-0.861937000000
C	-3.932061000000	1.242896000000	-1.543782000000
C	-3.684187000000	-0.129887000000	-1.625860000000
C	-2.541278000000	-0.666483000000	-1.020501000000
H	-2.348344000000	-1.742170000000	-1.074955000000
H	-4.381934000000	-0.785065000000	-2.154335000000
H	-4.824785000000	1.670312000000	-2.008158000000
H	-3.226662000000	3.148944000000	-0.800665000000
H	0.499185000000	-0.022589000000	-0.222384000000
H	-0.376170000000	-1.483708000000	0.257646000000

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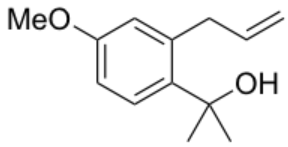

(1d)

	Parameter	Value
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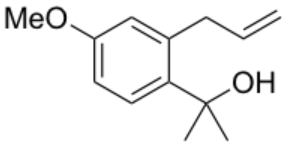
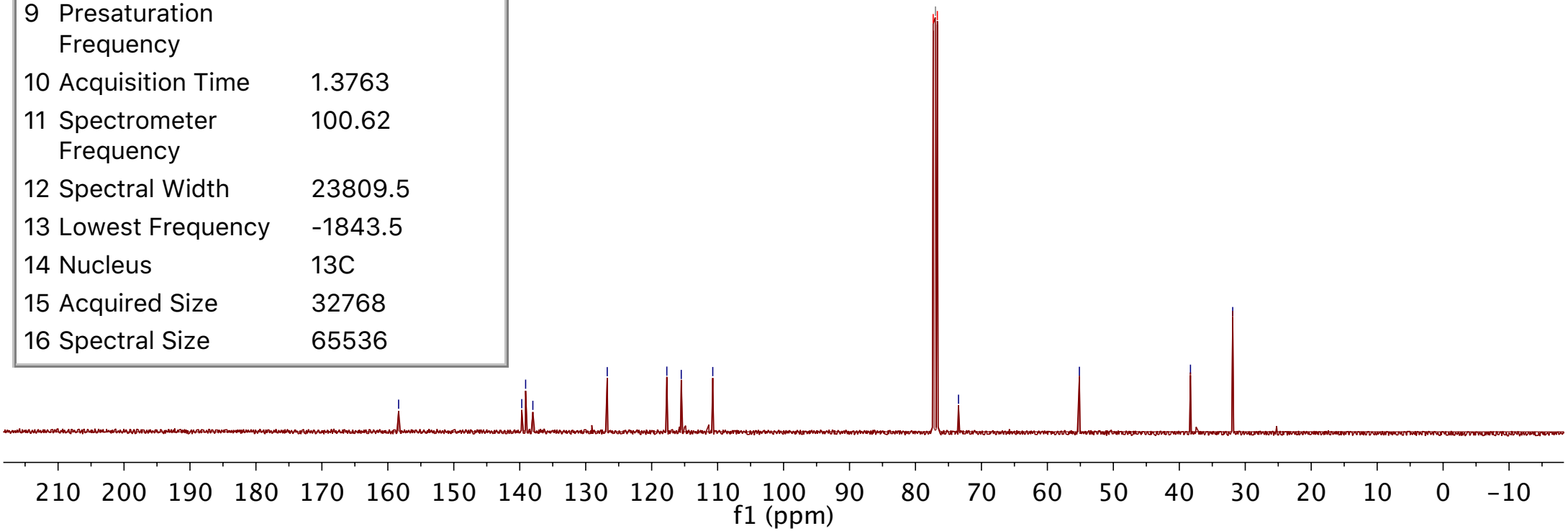
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg30
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	7.8000
9	Presaturation Frequency	
10	Acquisition Time	3.9977
11	Spectrometer Frequency	400.13
12	Spectral Width	8196.7
13	Lowest Frequency	-1627.6
14	Nucleus	1H
15	Acquired Size	32768
16	Spectral Size	65536

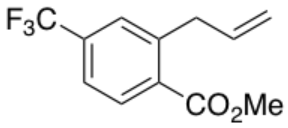


(1d)

158.37
139.70
139.11
138.01
126.74
117.70
115.51
110.73
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
73.48
55.15
38.31
31.90

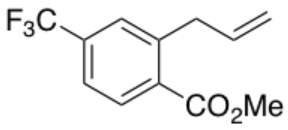
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zgpg30
6	Receiver Gain	101.0
7	Relaxation Delay	2.0000
8	Pulse Width	7.9000
9	Presaturation Frequency	
10	Acquisition Time	1.3763
11	Spectrometer Frequency	100.62
12	Spectral Width	23809.5
13	Lowest Frequency	-1843.5
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536





(S-7e)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg30
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	7.8000
9	Presaturation Frequency	
10	Acquisition Time	3.9977
11	Spectrometer Frequency	400.13
12	Spectral Width	8196.7
13	Lowest Frequency	-1627.6
14	Nucleus	1H
15	Acquired Size	32768
16	Spectral Size	65536



(S-7e)

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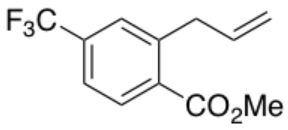
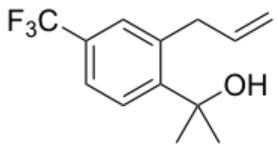
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	11.7000
9	Presaturation Frequency	
10	Acquisition Time	0.7209
11	Spectrometer Frequency	376.46
12	Spectral Width	90909.1
13	Lowest Frequency	-83104.4
14	Nucleus	19F
15	Acquired Size	65536
16	Spectral Size	131072



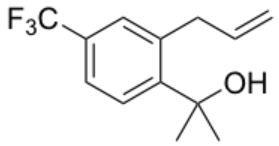
(S-7e)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zgpg30
6	Receiver Gain	101.0
7	Relaxation Delay	2.0000
8	Pulse Width	7.9000
9	Presaturation Frequency	
10	Acquisition Time	1.3763
11	Spectrometer Frequency	100.62
12	Spectral Width	23809.5
13	Lowest Frequency	-1843.5
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



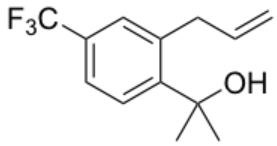
(1e)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg30
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	7.8000
9	Presaturation Frequency	
10	Acquisition Time	3.9977
11	Spectrometer Frequency	400.13
12	Spectral Width	8196.7
13	Lowest Frequency	-1627.6
14	Nucleus	1H
15	Acquired Size	32768
16	Spectral Size	65536



(1e)

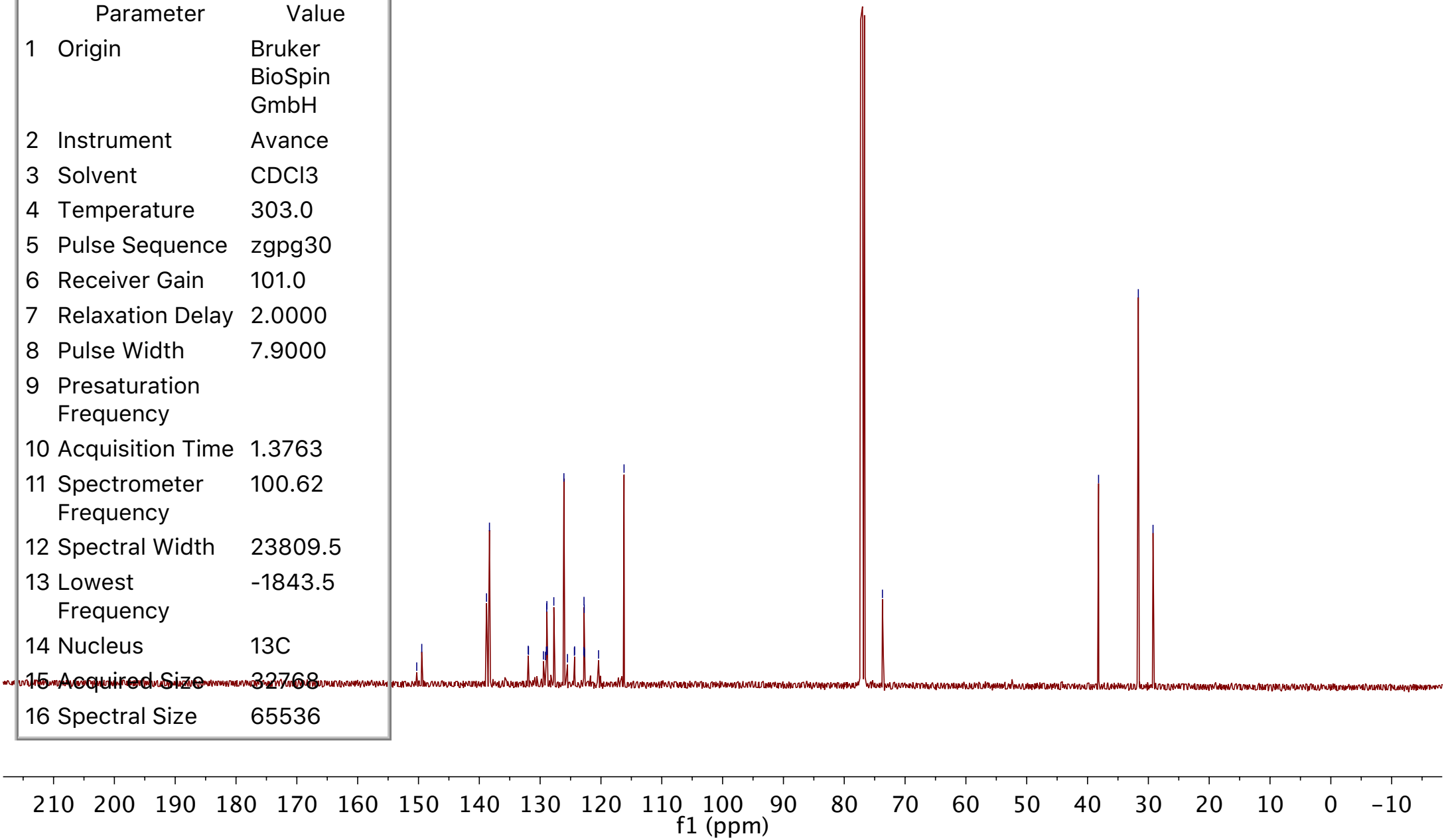
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	11.7000
9	Presaturation Frequency	
10	Acquisition Time	0.7209
11	Spectrometer Frequency	376.46
12	Spectral Width	90909.1
13	Lowest Frequency	-83104.4
14	Nucleus	19F
15	Acquired Size	65536
16	Spectral Size	131072

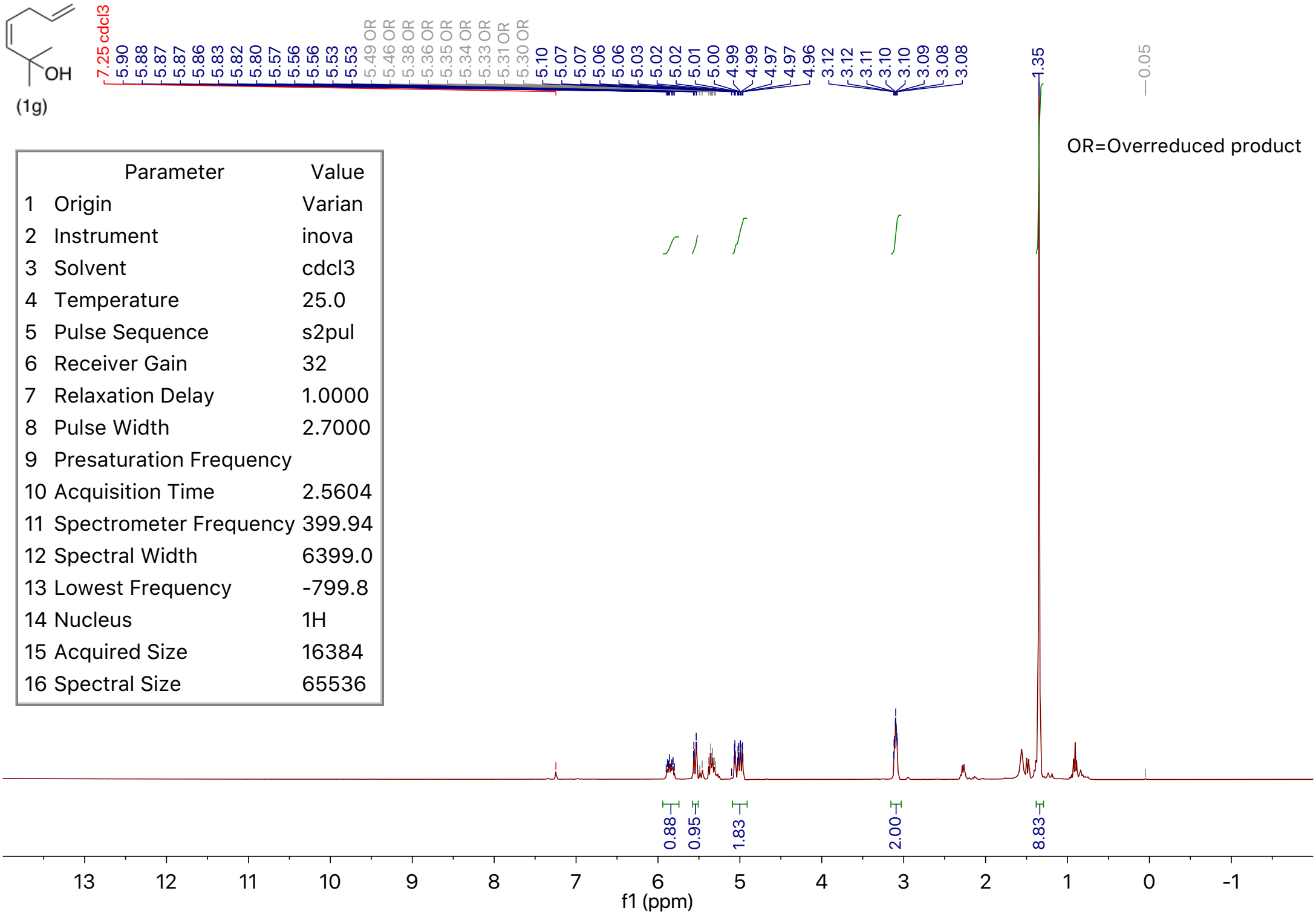


(1e)

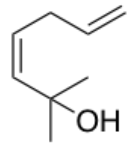
150.29
149.46
138.81
138.33
131.96
131.92
129.46
129.14
128.96
128.93
128.89
128.85
127.75
126.09
125.50
124.37
124.33
122.82
122.79
122.75
122.71
120.39
116.20
73.72
38.19
31.65
29.23

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zgpg30
6	Receiver Gain	101.0
7	Relaxation Delay	2.0000
8	Pulse Width	7.9000
9	Presaturation Frequency	
10	Acquisition Time	1.3763
11	Spectrometer Frequency	100.62
12	Spectral Width	23809.5
13	Lowest Frequency	-1843.5
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536





	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	32
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



(1g)

137.86
137.37
127.57
114.64
77.47 cdcl3
77.05 cdcl3
76.62 cdcl3
71.65
32.17
31.09

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
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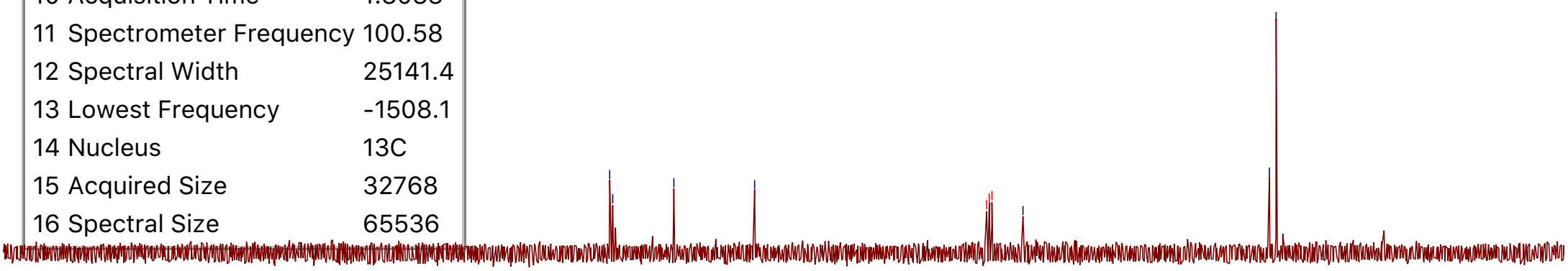
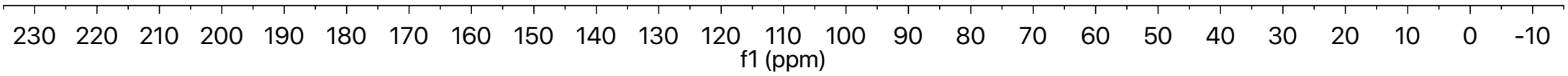
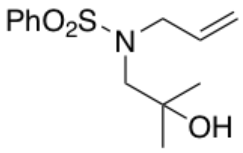
13	Lowest Frequency	-1508.1
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536







(1l)

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4	Temperature	25.0
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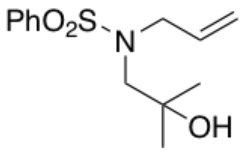
6	Receiver Gain	20
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-795.0
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



(1l)

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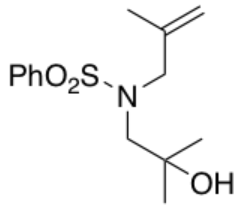
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1512.2
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



(1m)

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6	Receiver Gain	26
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
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13	Lowest Frequency	-792.3
14	Nucleus	1H
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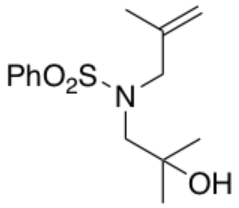
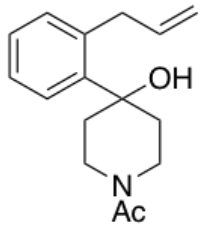
16	Spectral Size	65536



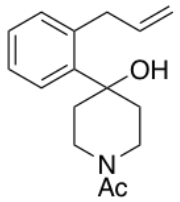
(1m)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1515.0
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



(10)

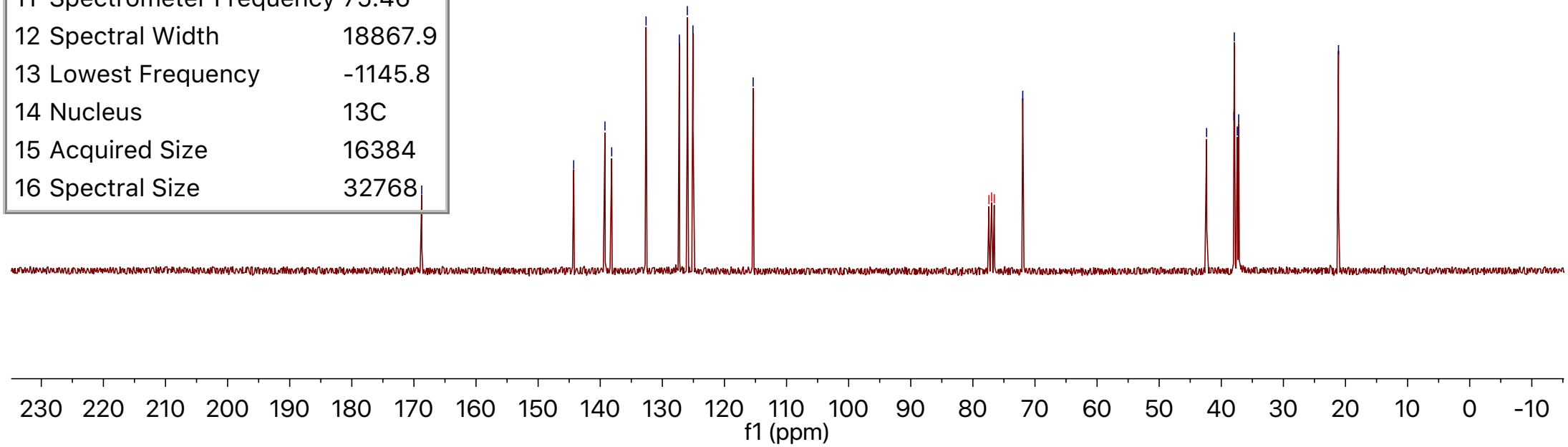
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	26
7	Relaxation Delay	1.0000
8	Pulse Width	2.6500
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-770.4
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536

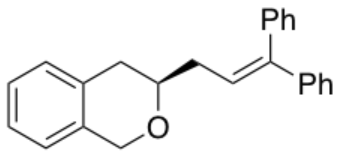


(10)

168.75
144.27
139.24
138.16
132.62
127.26
125.98
125.07
115.38
77.41 cdcl3
76.99 cdcl3
76.56 cdcl3
71.97
42.36
37.96
37.91
37.42
37.20
21.13

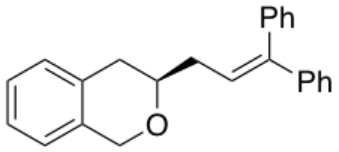
	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	7.3500
9	Presaturation Frequency	
10	Acquisition Time	0.8684
11	Spectrometer Frequency	75.46
12	Spectral Width	18867.9
13	Lowest Frequency	-1145.8
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768





(2a)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	40.0
5	Pulse Sequence	s2pul
6	Receiver Gain	28
7	Relaxation Delay	1.0000
8	Pulse Width	5.7000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-601.6
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536



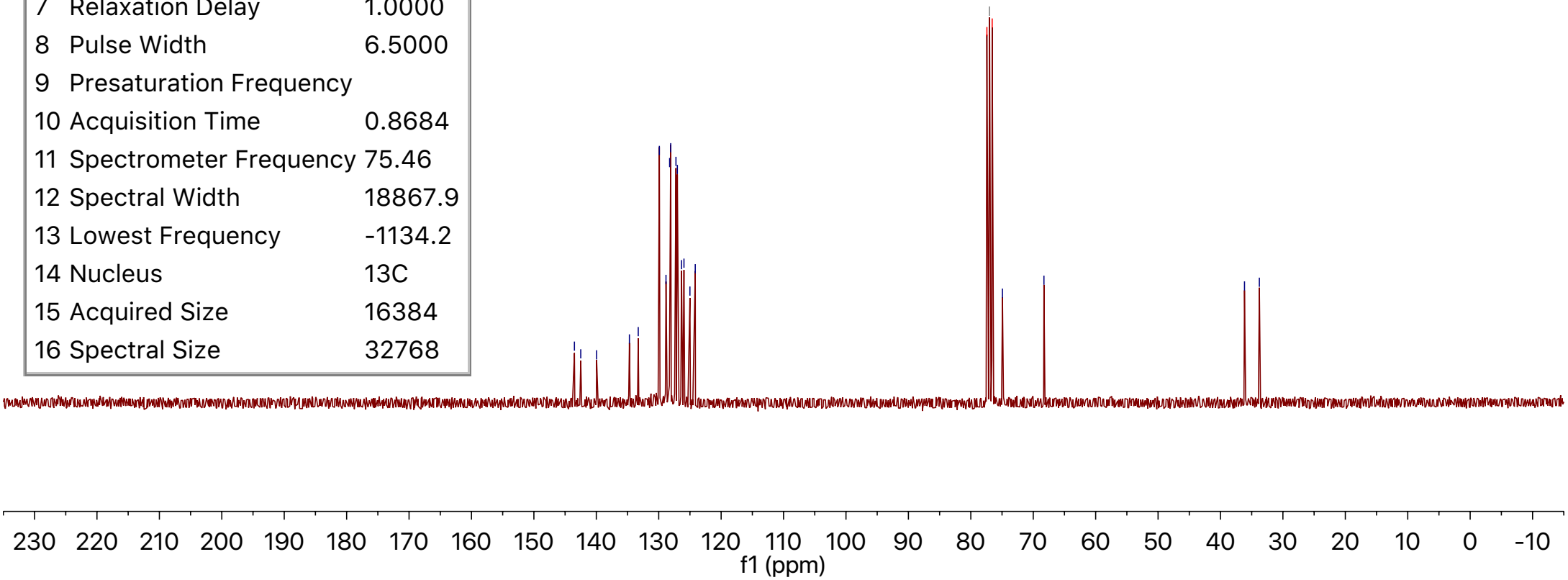
(2a)

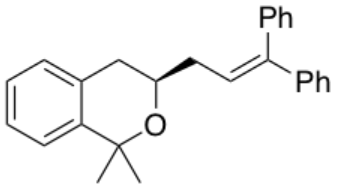
143.51
142.49
139.95
134.70
133.28
129.90
128.84
128.25
128.08
127.24
127.02
126.35
125.96
125.00
124.15

77.42 cdcl3
77.00 CDCl3
76.58 cdcl3
74.93
68.28

36.15
33.77

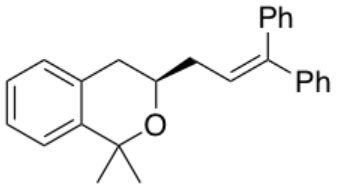
	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	40.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	6.5000
9	Presaturation Frequency	
10	Acquisition Time	0.8684
11	Spectrometer Frequency	75.46
12	Spectral Width	18867.9
13	Lowest Frequency	-1134.2
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768





(2b)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	5.7000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-599.3
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536



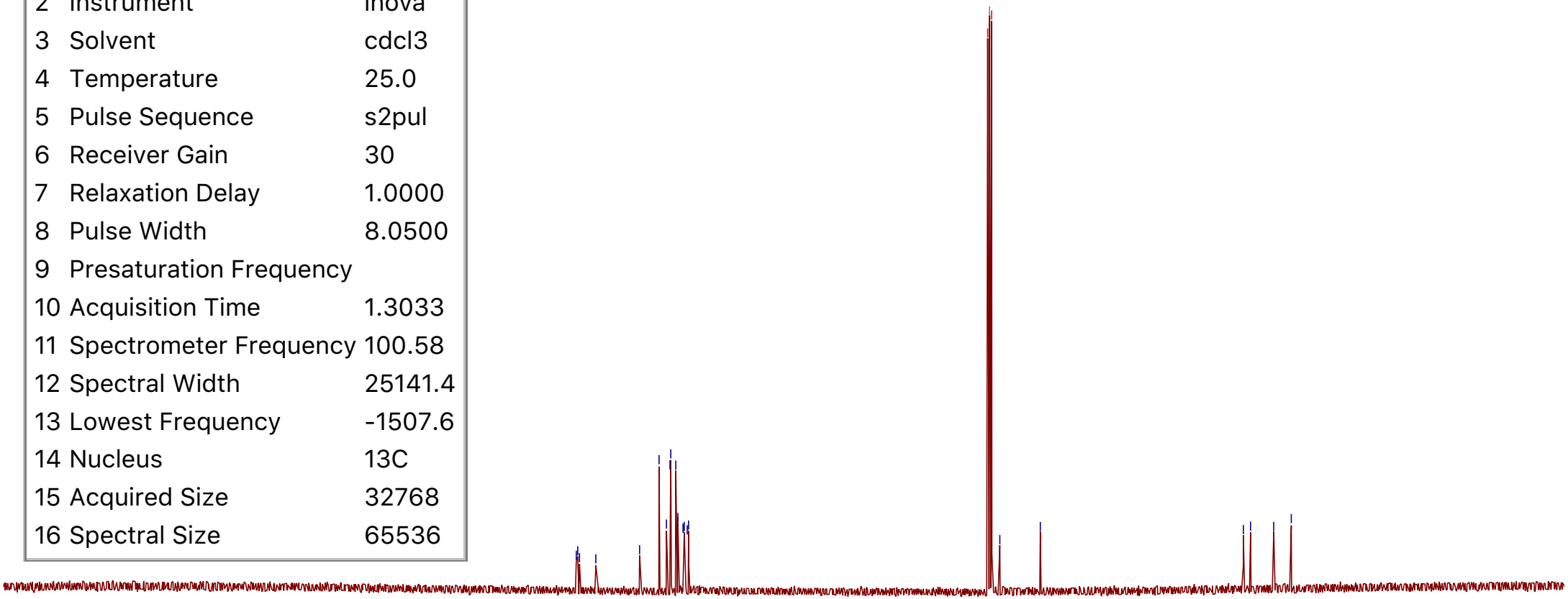
(2b)

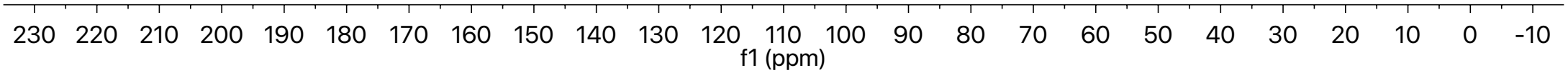
143.22
142.98
142.69
140.08
133.07
129.95
128.77
128.20
128.08
127.27
126.96
126.94
126.11
125.91
125.44
125.23

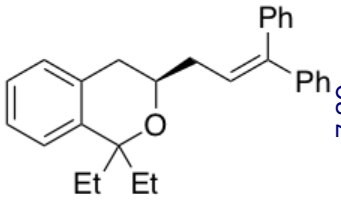
77.32 cdcl3
77.00 CDCl3
76.68 cdcl3
75.37
68.88

36.36
35.20
31.50
28.68

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.0500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1507.6
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536

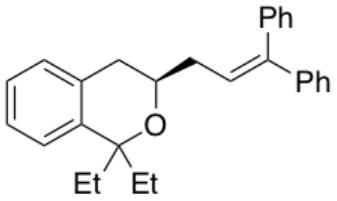






(2c)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	60
7	Relaxation Delay	1.0000
8	Pulse Width	4.0500
9	Presaturation Frequency	
10	Acquisition Time	2.0484
11	Spectrometer Frequency	499.90
12	Spectral Width	7998.4
13	Lowest Frequency	-999.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



(2c)

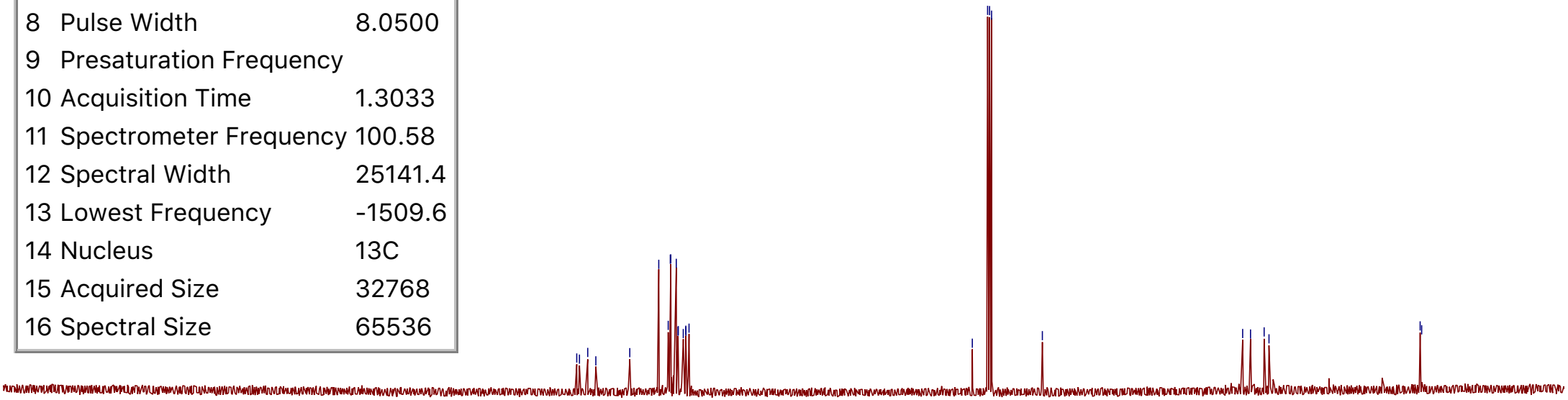
143.12
142.68
141.36
140.06
134.62
129.98
128.47
128.13
128.05
127.18
126.90
126.85
126.06
125.65
125.63
125.13

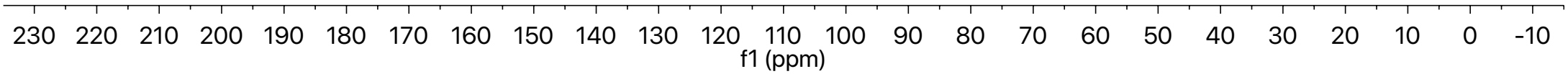
79.76
77.31
76.99
76.67
68.54

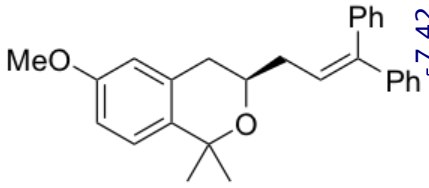
36.45
35.19
33.01
32.24

8.02
7.78

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.0500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1509.6
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536

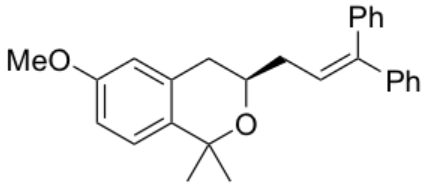






(2d)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg30
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	7.8000
9	Presaturation Frequency	
10	Acquisition Time	3.9977
11	Spectrometer Frequency	400.13
12	Spectral Width	8196.7
13	Lowest Frequency	-1627.6
14	Nucleus	1H
15	Acquired Size	32768
16	Spectral Size	65536



(2d)

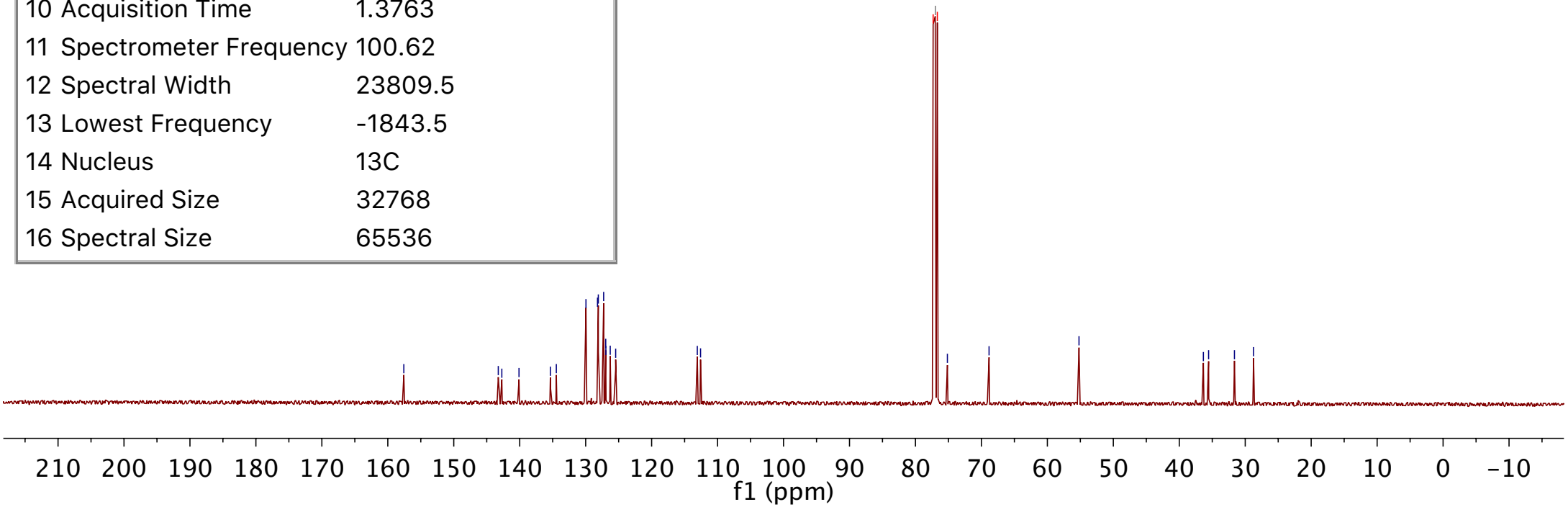
157.57
143.25
142.71
140.11
135.35
134.45
129.96
128.21
128.08
127.27
126.96
126.94
126.28
125.45
113.08
112.58

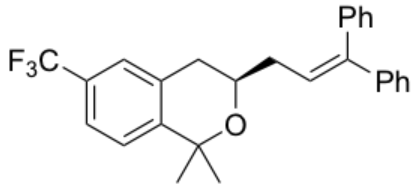
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
75.16
68.84

55.20

36.34
35.55
31.63
28.74

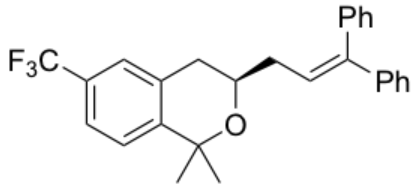
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zgpg30
6	Receiver Gain	101.0
7	Relaxation Delay	2.0000
8	Pulse Width	7.9000
9	Presaturation Frequency	
10	Acquisition Time	1.3763
11	Spectrometer Frequency	100.62
12	Spectral Width	23809.5
13	Lowest Frequency	-1843.5
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536





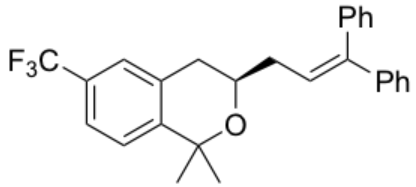
(2e)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg30
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	7.8000
9	Presaturation Frequency	
10	Acquisition Time	3.9977
11	Spectrometer Frequency	400.13
12	Spectral Width	8196.7
13	Lowest Frequency	-1668.4
14	Nucleus	1H
15	Acquired Size	32768
16	Spectral Size	65536



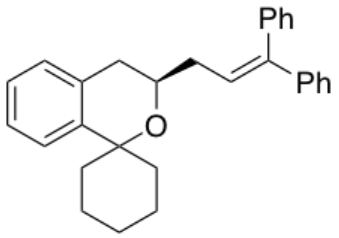
(2e)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zg
6	Receiver Gain	101.0
7	Relaxation Delay	1.0000
8	Pulse Width	11.7000
9	Presaturation Frequency	
10	Acquisition Time	0.7209
11	Spectrometer Frequency	376.46
12	Spectral Width	90909.1
13	Lowest Frequency	-83104.4
14	Nucleus	19F
15	Acquired Size	65536
16	Spectral Size	131072



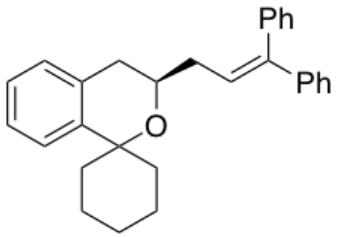
(2e)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	CDCl3
4	Temperature	303.0
5	Pulse Sequence	zgpg30
6	Receiver Gain	101.0
7	Relaxation Delay	2.0000
8	Pulse Width	7.9000
9	Presaturation Frequency	
10	Acquisition Time	1.3763
11	Spectrometer Frequency	100.62
12	Spectral Width	23809.5
13	Lowest Frequency	-1843.5
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



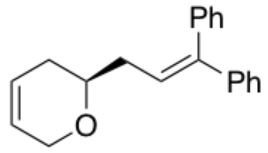
(2f)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	48
7	Relaxation Delay	1.0000
8	Pulse Width	3.3000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-795.1
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



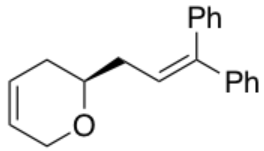
(2f)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.0500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1507.3
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



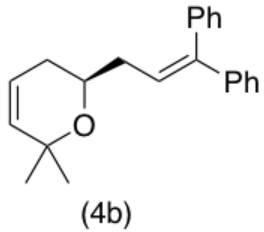
(4a)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	54
7	Relaxation Delay	1.0000
8	Pulse Width	2.6500
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-795.0
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



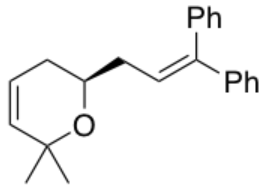
(4a)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	7.3500
9	Presaturation Frequency	
10	Acquisition Time	0.8684
11	Spectrometer Frequency	75.46
12	Spectral Width	18867.9
13	Lowest Frequency	-1134.1
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768



(4b)

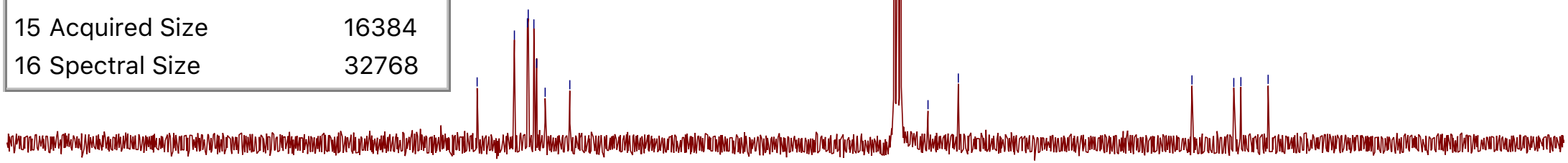
	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	35.0
5	Pulse Sequence	s2pul
6	Receiver Gain	38
7	Relaxation Delay	1.0000
8	Pulse Width	7.3000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-599.9
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536

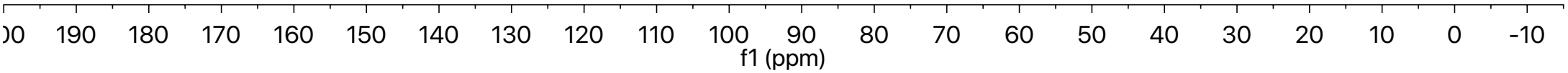


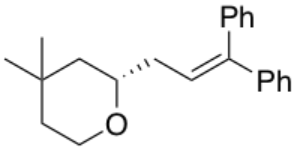
(4b)

135.09
129.94
128.14
128.03
127.25
126.87
125.69
122.29
77.41 cdcl3
76.99 cdcl3
76.56 cdcl3
72.80
68.61
36.33
30.55
29.57
25.80

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	35.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	7.3500
9	Presaturation Frequency	
10	Acquisition Time	1.0093
11	Spectrometer Frequency	75.46
12	Spectral Width	16233.8
13	Lowest Frequency	-1137.4
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768

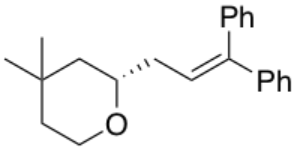






(5b)

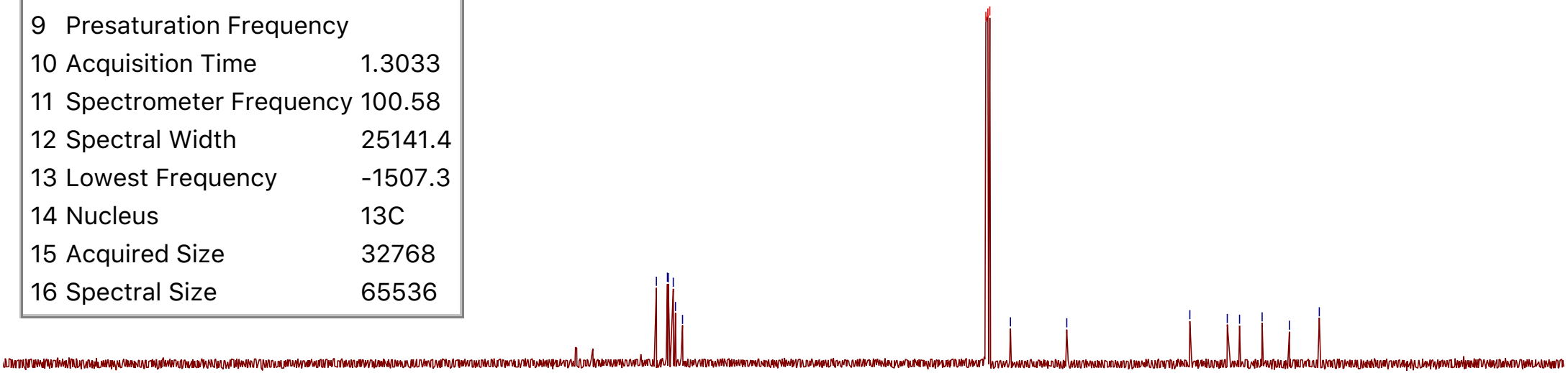
	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	34
7	Relaxation Delay	1.0000
8	Pulse Width	7.3000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-599.9
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536

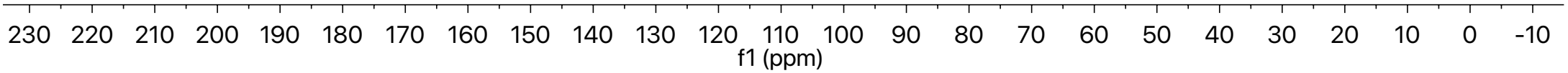


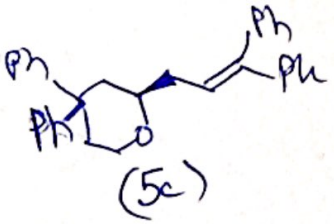
(5b)

129.92
128.15
128.02
127.22
126.87
125.74
77.31 cdcl3
76.99 cdcl3
76.67 cdcl3
73.38
64.39
44.74
38.77
36.81
33.20
28.85
24.07

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5000
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1507.3
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536







(5c)

Agilent Technologies

ASB-5c-PROTON

Sample Name:

Data Collected on:
nmr500c.chem.buffalo.edu-inova500
Archive directory:

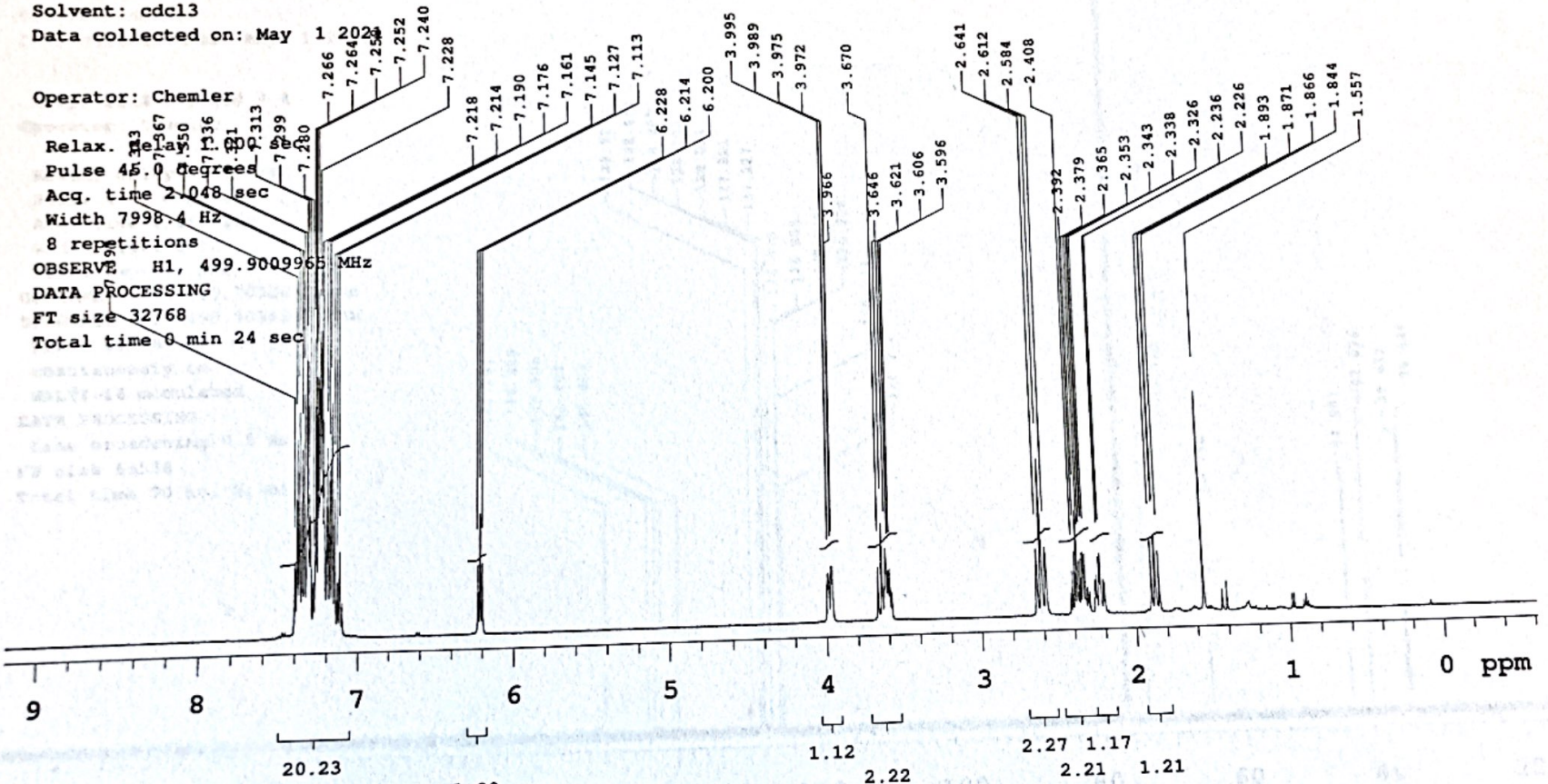
Sample directory:

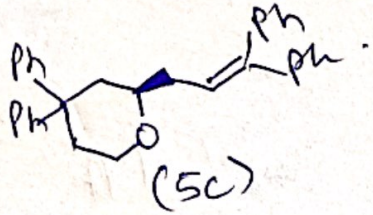
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 1 2024

Operator: Chemler

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 7998.4 Hz
8 repetitions
OBSERVE H1, 499.9009965 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 24 sec





(5c)

ASB-5c-PROTON

Sample Name:

Data Collected on:
nmr500c.chem.buffalo.edu-inova500
Archive directory:

Sample directory:

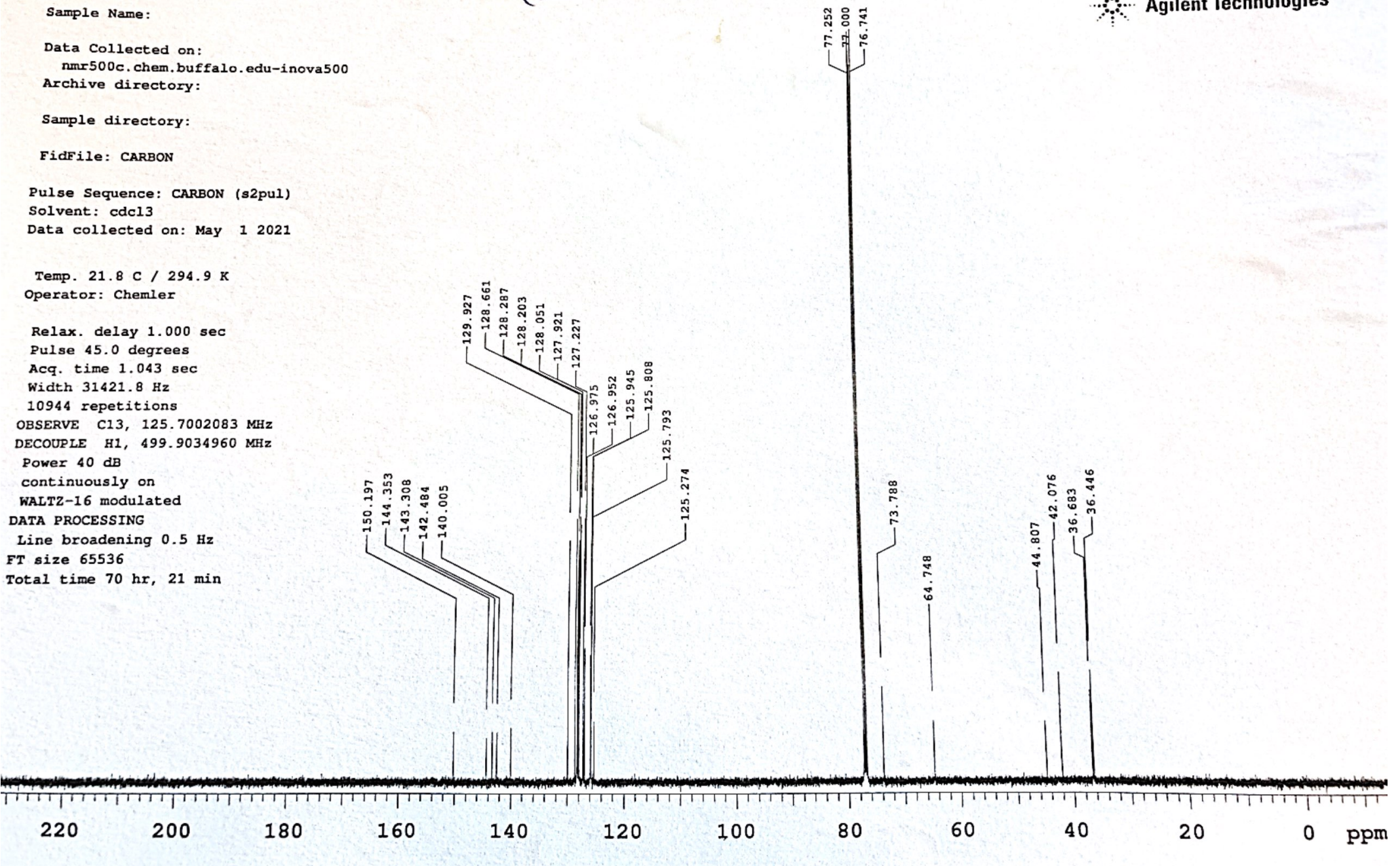
FidFile: CARBON

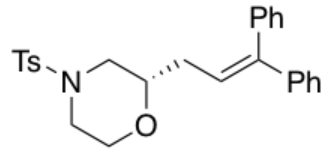
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 1 2021

Temp. 21.8 C / 294.9 K
Operator: Chemler

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31421.8 Hz
10944 repetitions
OBSERVE C13, 125.7002083 MHz
DECOUPLE H1, 499.9034960 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 70 hr, 21 min

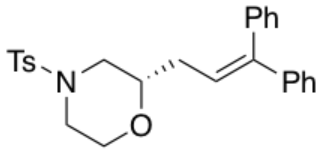
Agilent Technologies





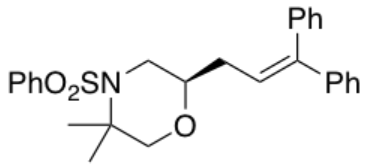
(7a)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	5.7000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-599.3
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536



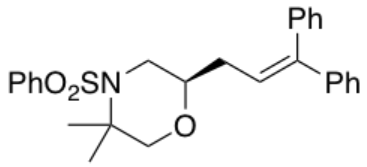
(7a)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	7.3500
9	Presaturation Frequency	
10	Acquisition Time	0.8684
11	Spectrometer Frequency	75.46
12	Spectral Width	18867.9
13	Lowest Frequency	-1134.3
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768



(7b)

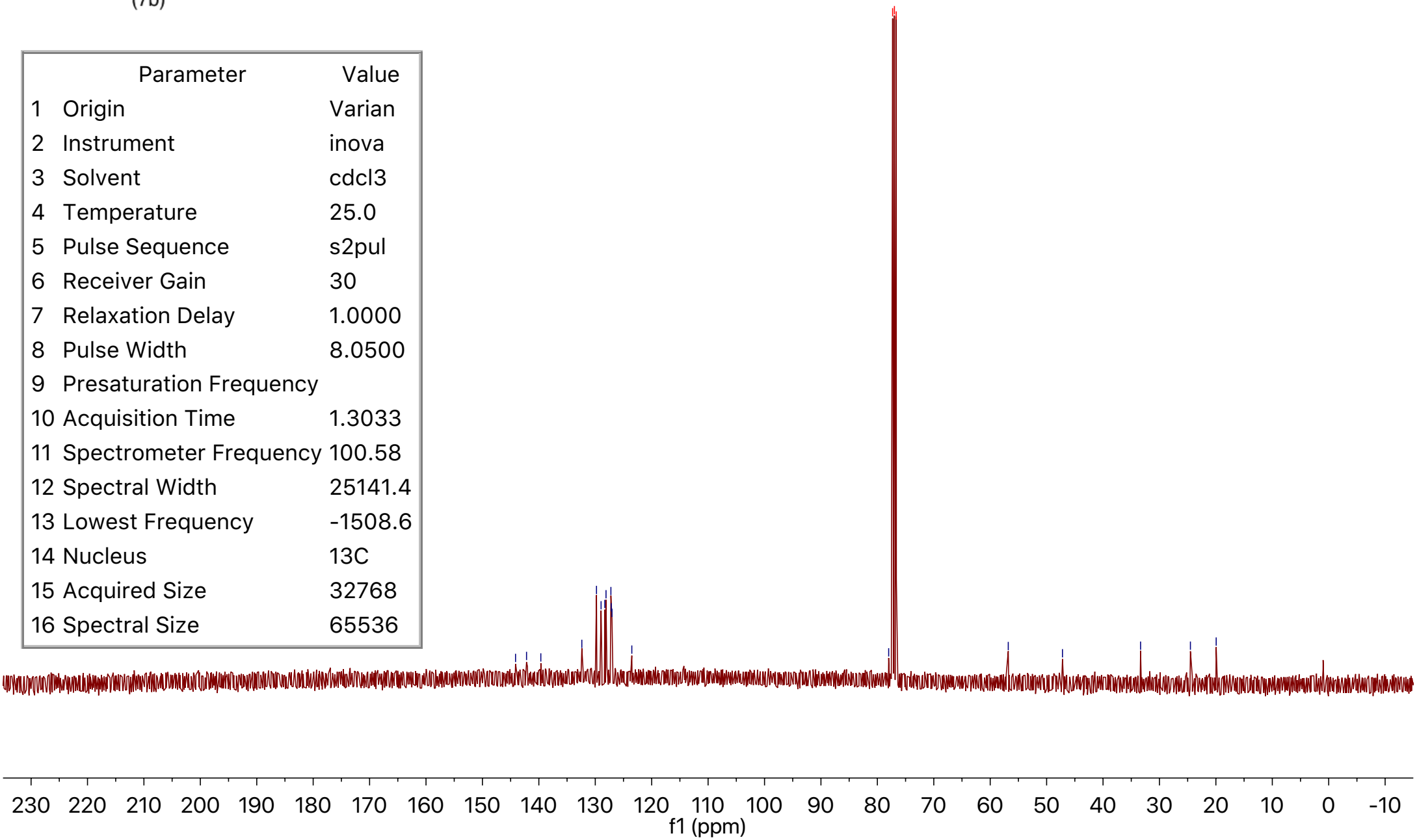
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	60
7	Relaxation Delay	1.0000
8	Pulse Width	3.3000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-794.7
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536

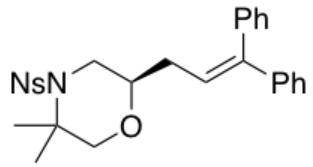


(7b)

144.13
142.18
139.65
132.38
129.78
128.97
128.31
128.09
127.23
127.17
127.04
123.52
77.99
77.30 cdcl3
76.98 cdcl3
76.66 cdcl3
56.80
47.19
33.35
24.51
19.95

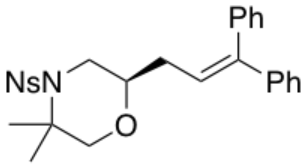
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.0500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1508.6
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536





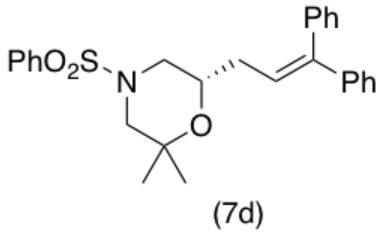
(7c)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	38
7	Relaxation Delay	1.0000
8	Pulse Width	7.3000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-599.3
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536



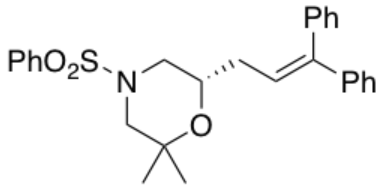
(7c)

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	7.3500
9	Presaturation Frequency	
10	Acquisition Time	0.8684
11	Spectrometer Frequency	75.46
12	Spectral Width	18867.9
13	Lowest Frequency	-1134.3
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768



(7d)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	50
7	Relaxation Delay	1.0000
8	Pulse Width	3.3000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



(7d)

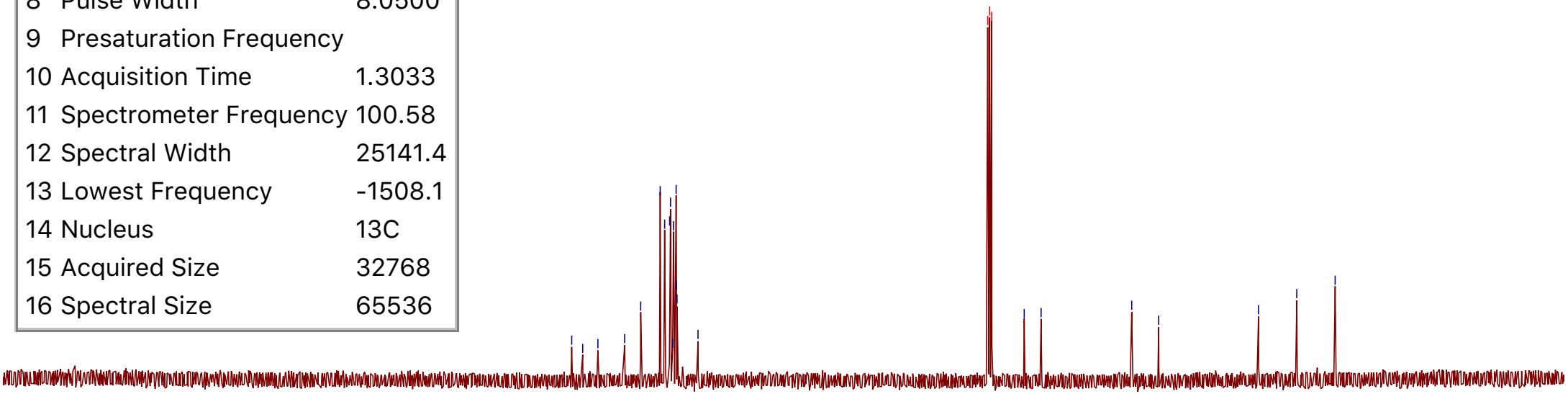
143.94
142.18
139.74
135.45
132.89
129.77
129.05
128.26
128.11
127.78
127.63
127.21
127.17
127.07
123.71

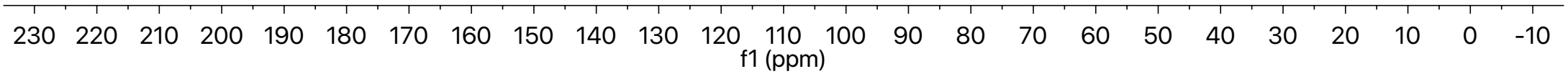
77.31 cdcl3
76.99 cdcl3
76.67 cdcl3
71.46
68.75

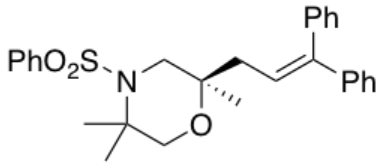
54.24
49.92

33.93
27.80
21.65

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.0500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1508.1
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536

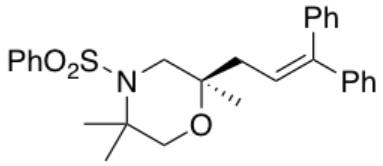






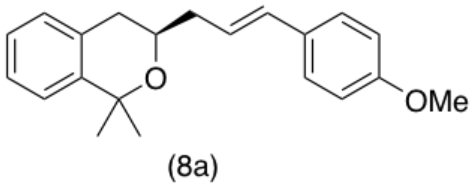
(7e)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	36
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536

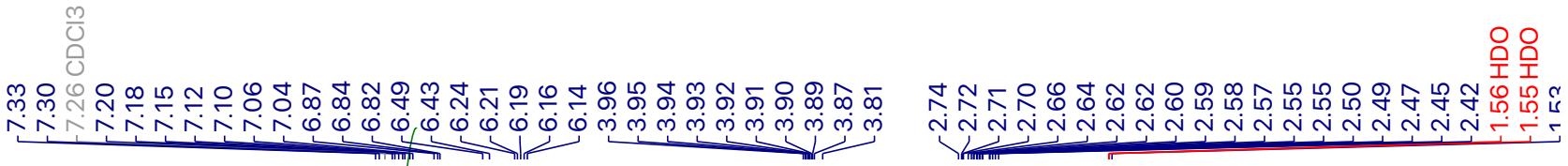


(7e)

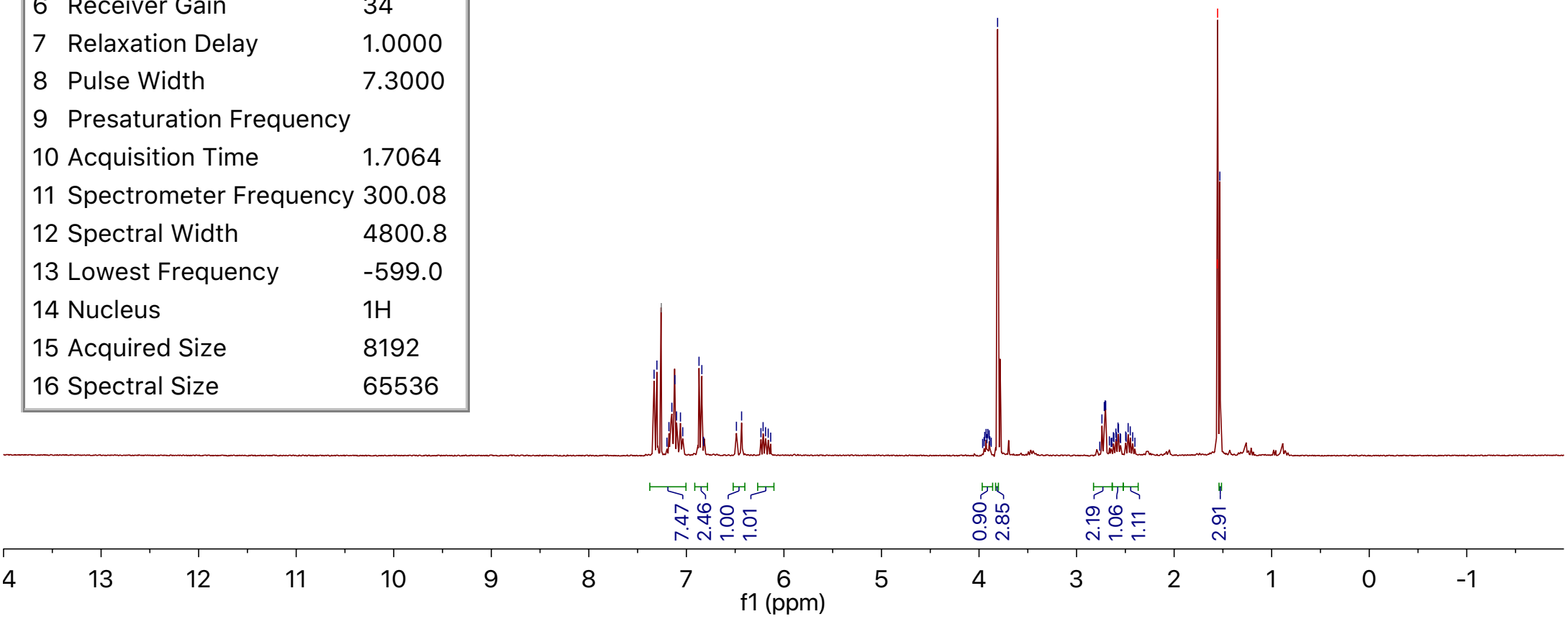
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1510.4
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536

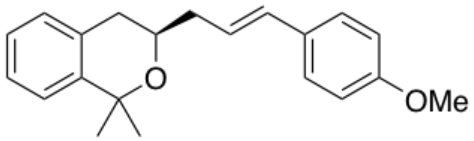


(8a)



	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	34
7	Relaxation Delay	1.0000
8	Pulse Width	7.3000
9	Presaturation Frequency	
10	Acquisition Time	1.7064
11	Spectrometer Frequency	300.08
12	Spectral Width	4800.8
13	Lowest Frequency	-599.0
14	Nucleus	1H
15	Acquired Size	8192
16	Spectral Size	65536





(8a)

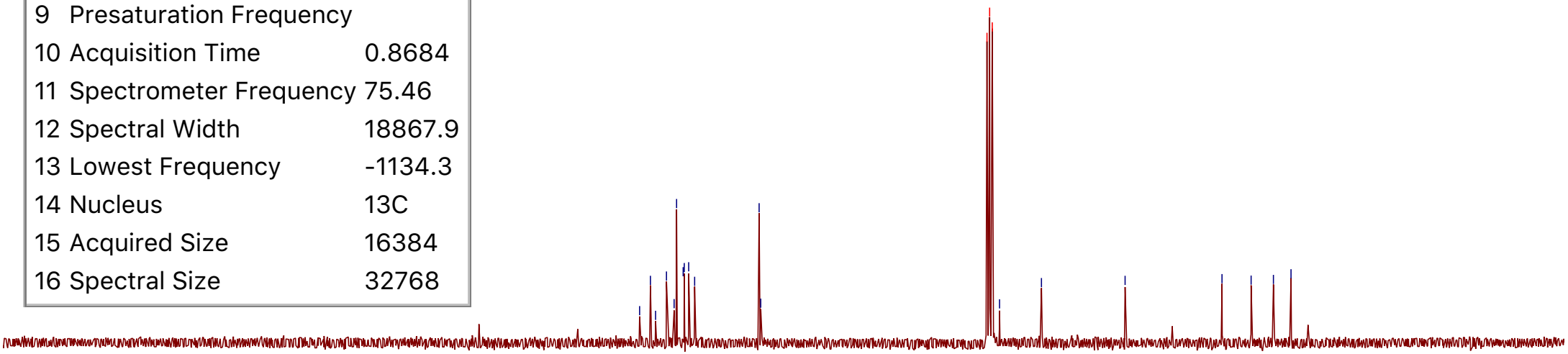
133.06
131.33
130.51
128.76
127.54
127.14
126.08
125.91
125.20
124.25
113.91
113.65

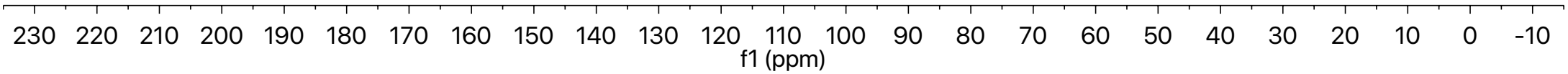
77.41 cdcl3
76.98 cdcl3
76.56 cdcl3
75.40
68.68

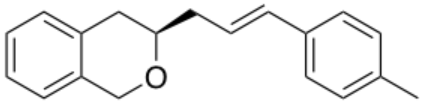
55.28

39.76
35.09
31.52
28.70

	Parameter	Value
1	Origin	Varian
2	Instrument	mercury
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	7.3500
9	Presaturation Frequency	
10	Acquisition Time	0.8684
11	Spectrometer Frequency	75.46
12	Spectral Width	18867.9
13	Lowest Frequency	-1134.3
14	Nucleus	13C
15	Acquired Size	16384
16	Spectral Size	32768

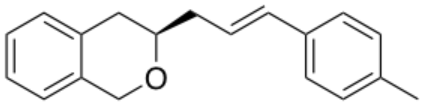






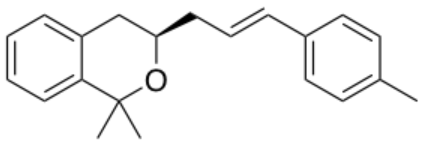
(8b)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	52
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



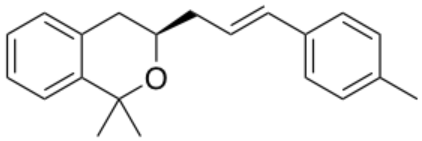
(8b)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1508.6
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



(8c)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	50
7	Relaxation Delay	1.0000
8	Pulse Width	2.6500
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



(8c)

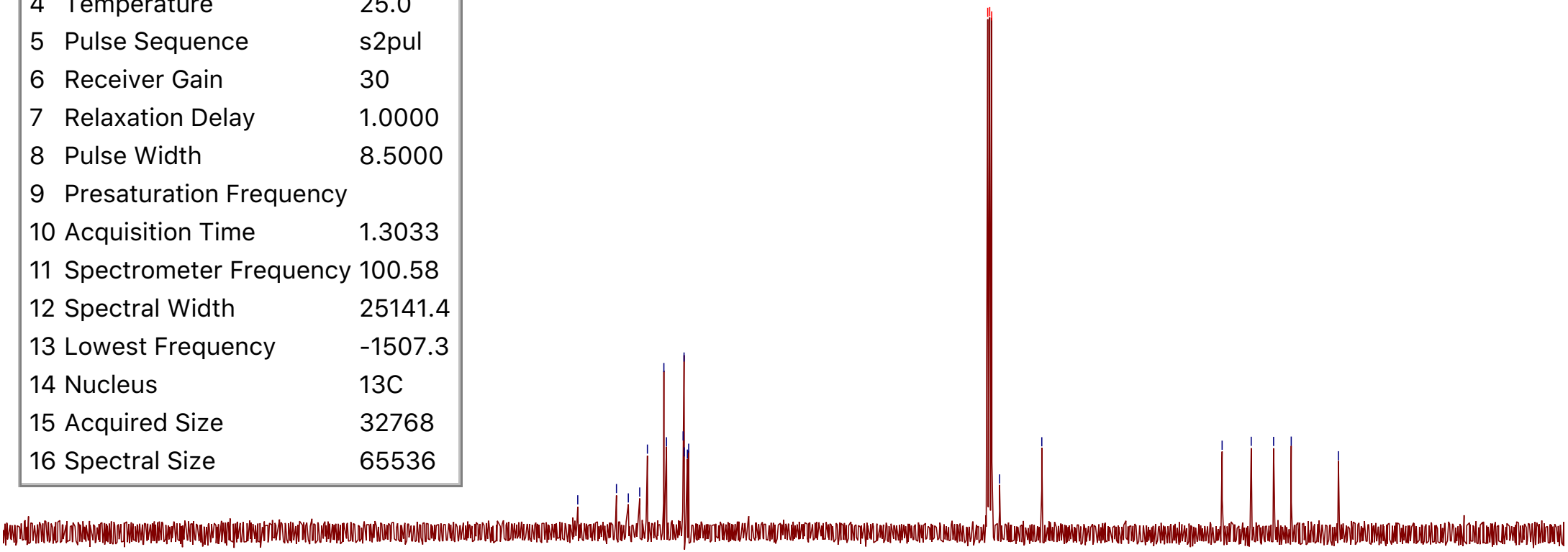
142.98
136.78
134.88
133.06
131.82
129.18
128.77
126.10
125.95
125.92
125.42
125.21

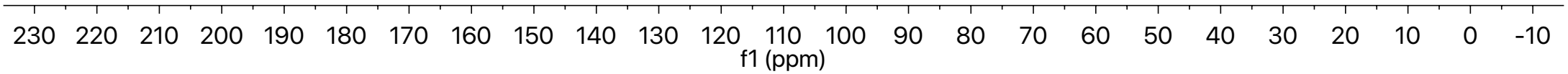
77.31 cdcl3
76.99 cdcl3
76.68 cdcl3
75.41
68.65

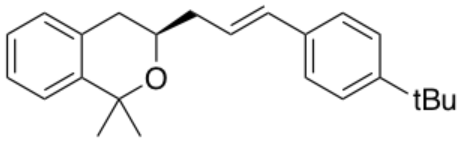
39.77
35.11
31.52
28.70

21.14

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5000
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1507.3
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536

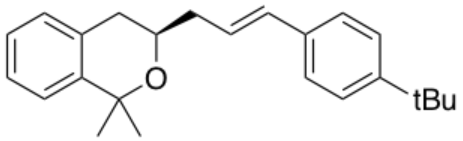






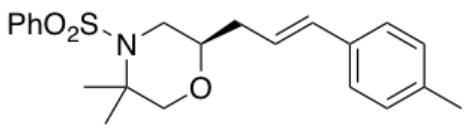
(8d)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	52
7	Relaxation Delay	1.0000
8	Pulse Width	2.6500
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-795.5
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



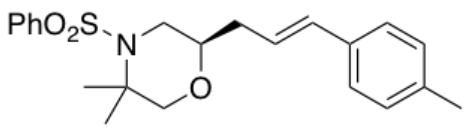
(8d)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5000
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1507.3
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



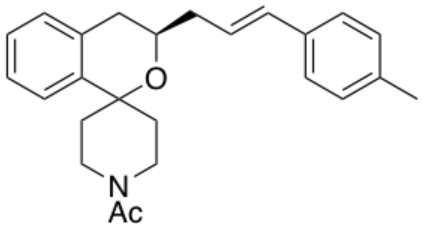
(9)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	44
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



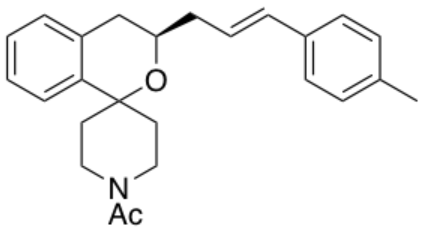
(9)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	1.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1508.8
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536



(10)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	48
7	Relaxation Delay	1.0000
8	Pulse Width	2.7000
9	Presaturation Frequency	
10	Acquisition Time	2.5604
11	Spectrometer Frequency	399.94
12	Spectral Width	6399.0
13	Lowest Frequency	-799.8
14	Nucleus	1H
15	Acquired Size	16384
16	Spectral Size	65536



(10)

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Receiver Gain	30
7	Relaxation Delay	2.0000
8	Pulse Width	8.5500
9	Presaturation Frequency	
10	Acquisition Time	1.3033
11	Spectrometer Frequency	100.58
12	Spectral Width	25141.4
13	Lowest Frequency	-1508.6
14	Nucleus	13C
15	Acquired Size	32768
16	Spectral Size	65536