Electronic Supplementary Information

Enantio- and diastereoselective palladium catalysed arylative and vinylative allene carbocyclisation cascades

Meiling Li,[a] Alison Hawkins,[a] David M. Barber,[a] Patrick Bultinck,[b] Wouter Herrebout[c] and Darren J. Dixon*[a]

[a] *Department of Chemistry, Chemistry Research Laboratory, University of Oxford, 12 Mansfield Road, Oxford, OX1 3TA, U.K.*
darren.dixon@chem.ox.ac.uk

[b] *Department of Inorganic and Physical Chemistry, Ghent University, Krijgslaan 281-S3, 9000 Gent, Belgium*

[c] *Department of Chemistry, University of Antwerp, Groenenborgerlaan 171, 2020 Antwerp, Belgium*

Contents

1. General experimental

All reactions were performed without special precautions to avoid the presence of moisture unless otherwise stated. For reactions conducted under anhydrous conditions glassware was dried in an oven at 100 °C and carried out under a nitrogen atmosphere.

Bulk solutions were evaporated under reduced pressure using a Büchi rotary evaporator. Solvents used were dry solvents. Petroleum ether refers to distilled light petroleum of fraction 30 - 40 °C. Dimethyl sulfoxide was dried over molecular sieves. THF was distilled over sodium using benzophenone as an indicator of dryness. Toluene was distilled over CaH_2. All other solvents were used as supplied without any further purification.

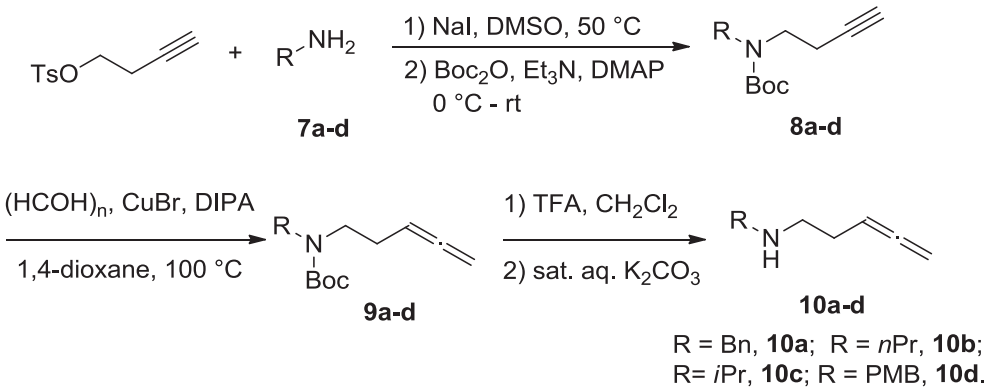
Commercial reagents were used as supplied without any further purification. Aminol alcohols were prepared according to literature procedures.[1] (*E*)-(2-iodovinyl)benzene,[2] (*Z*)-1-chloro-4-(2-iodovinyl)benzene,[3] (*Z*)-1-(2-iodovinyl)-4-methoxybenzene,[3] (*Z*)-methyl 4-(2-iodovinyl)benzoate,[3] (*Z*)-1-(2-iodovinyl)-3-nitrobenzene,[3] (*Z*)-2-(2-iodovinyl)furan,[3] (*Z*)-2-(2-iodovinyl)thiophene[3] were prepared according to the corresponding literature procedures.

Column chromatography was carried out using Merck Kieselgel 60 silica gel (230-400 mesh). All reactions were followed by thin-layer chromatography (TLC) where practical, using Merck Kieselgel 60 F_{254} (230-400 mesh) fluorescent treated silica which were visualised under UV light (254 nm) or by staining with aqueous basic potassium permanganate solutions as appropriate.

All ^{1}H and ^{13}C NMR spectra were recorded using a Bruker 500 MHz and Bruker 400 MHz spectrometers with residual protic solvents used as the internal standard. Unless otherwise stated all experiments were carried out using $CDCl_3$ and d_6-DMSO as the solvent. Chemical shifts (δ) are given in parts per million (ppm) and coupling constants (J) are given in Hertz (Hz). The ^{1}H NMR spectra are reported as follows: δ/ppm (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, m = multiplet), number of protons, coupling constants *J*/Hz (where appropriate)). The NMR spectra are reported as how the spectra are observed and do not take into account the theoretical NMR splitting. DEPT 135, and two-dimensional (COSY, HMQC, HMBC) NMR spectroscopy was used where appropriate to assist the assignment of signals in the ^{1}H and ^{13}C NMR spectra. IR spectra were recorded on an ATI Mattson: Genesis Series FT-IR spectrometer or a Bruker Tensor 27 FT-IR spectrometer, from a thin film deposited on a sodium chloride plate. Only selected maximum absorbances are reported. Low resolution mass spectrometry (ESI) was recorded on a Fissions VG Trio 2000 quadrupole mass spectrometer or a Waters LCT premier XE mass spectrometer. High resolution mass spectra (accurate mass) were recorded on a Thermo Finnigan Mat 95XP mass spectrometer or a Bruker MicroTof mass spectrometer (electrospray technique). Melting points were recorded on a Leica Galen III apparatus, at ambient pressure and are uncorrected. Enantiomeric excesses were determined using high performance liquid chromatography (HPLC) performed on a Hewlett-Packard Series 1050 series system (column and

eluent conditions are given with the compounds). Optical rotations were recorded using a Perkin-Elmer 241 polarimeter; Specific rotation (SR) ($[\alpha]_D$) are reported in 10^{-1} deg cm^2 g^{-1}; concentrations (*c*) are quoted in g/100 mL; *D* refers to the D-line of sodium (589 nm); temperatures (*T*) are given in degrees Celsius (°C).

2. Synthesis of aminoallenes 10



General procedure for the synthesis of Boc-protected amines 8

Amine **7a-d** (2.0 equiv) and sodium iodide (2.5 mol%) were added to a solution of but-3-yn-1-yl 4-methylbenzenesulfonate (1.0 equiv) in DMSO. After being stirred for 40 h at 45 ºC, the reaction mixture was poured into 2 % aq. NaOH and extracted with Et_2O (×3). The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2. Di-*tert*-butyl dicarbonate (2.0 equiv), Et_3N (2.0 equiv) and DMAP (3.0 mol%) were added at 0 ºC. The reaction mixture was stirred at ambient temperature for 16 h and was then poured into water. The reaction mixture was seperated, and extracted with CH_2Cl_2 (×2). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The resulting residue was subjected to column chromatography (PE/Et_2O) to afford the desired Boc-protected amine **8a-d**.[4]

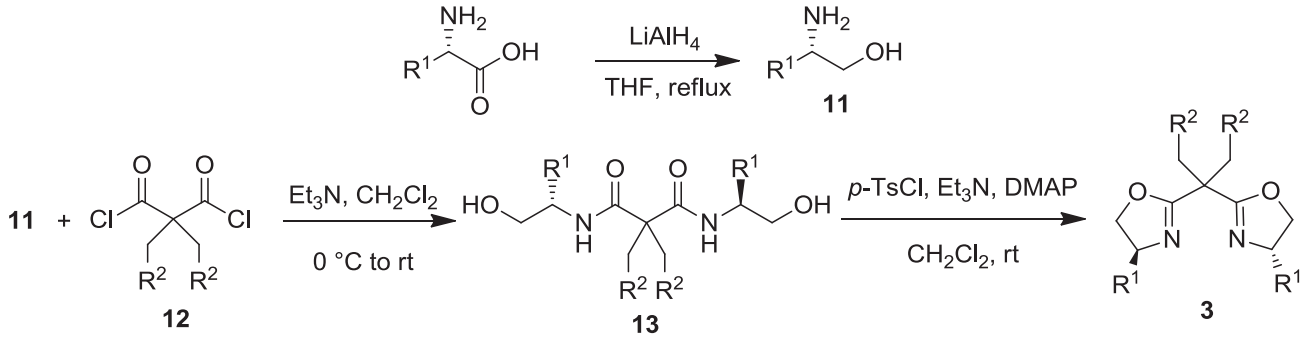
General procedure for the synthesis of Boc-protected allenes 9

A solution of compound **8a-d** (1.0 equiv), cuprous bromide (0.5 equiv), paraformaldehyde (2.5 equiv) and DIPEA (2.0 equiv) in 1,4-dioxane (0.67 mmol/mL) was heated at reflux for 12 h. The reaction mixture cooled to room temperature, diluted with water and Et_2O and then acidified with aqueous 1.0 N HCl until the mixture became clear. The organic layer was separated and the aqueous layer was further extracted with Et_2O (×2). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography on silica gel (PE/Et_2O) to afford the desired Boc-protected allene **9a-d**.[5]

General procedure for the synthesis of amino allenes 10

Boc-protected allene **9a-d** was stirred with TFA in CH_2Cl_2 (1:1, v/v) and monitored by TLC. Upon completion, the reaction mixture was basified with saturated aqueous K_2CO_3 to pH 8. The mixture was extracted with CH_2Cl_2 (×3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated to afford the desired crude amino allene **10a-d**. The crude amino allenes **10** were used in the next step without further purification.[5]

3. Synthesis of bis(oxazoline) ligands 3



Bis(oxazoline) ligands **3c**, **3d**, **3e**, and **3f** are commercially available and were used as supplied. Bis(oxazoline) ligands **3g**, **3h** and **3i** were synthesised using the following procedures.

General procedure for the synthesis of aminols 11

In a dry flask under nitrogen, $LiAlH_4$ (5.44 equiv) was suspended in THF (1.7 mL/mmol amino acid). The suspension was cooled to 0 °C and the amino acid (1.00 equiv) was added in small portions. Once all the amino acid was added, the suspension was stirred at 0 °C for 15 minutes and then allowed to warm to room temperature for 1 h. The flask was then mounted with a condenser and the mixture was refluxed for 16 h. The resulting suspension was then allowed to cool to room temperature and diluted with Et_2O (1.5 mL/mmol of starting amino acid). The excess $LiAlH_4$ was quenched by slow addition of sodium sulfate decahydrate (100 mg/mmol of amino acid) and then the resulting mixture was stirred for 1 h at room temperature. The suspension was filtered through a pad of silica gel (which was eluted with EtOAc) and the filtrate was concentrated to afford the desired crude aminols **11**. The aminols **11** were used in the next step without further purification.[1,6]

General procedure for the synthesis of bis(amides) 13

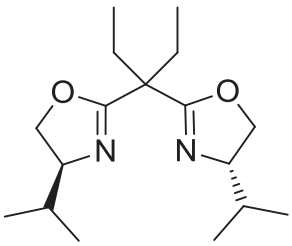
To an ice-cooled solution of aminols **11** (2.25 equiv) in CH_2Cl_2 (1 mL/mmol **12**) was added Et_3N (5.00 equiv) and a solution of malonyl dichloride **12** (1.00 equiv) in CH_2Cl_2 (1 mL/mmol **12**) dropwise. The reaction mixture was warmed to room temperature, stirred for 2 h and then diluted with CH_2Cl_2 (8 mL/mmol **12**). The organic layer was separated and then washed with aqueous 1.0 N HCl, saturated aqueous $NaHCO_3$ solution and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated to afford the desired crude (*S*,*S*)-bis(amides) **13**. The (*S*,*S*)-bis(amides) **13** were used in the next step without further purification.[1,6]

General procedure for the synthesis of bis(oxazolines) 3

To an ice-cooled solution of the (*S*,*S*)-bis(amides) **13** (1.0 equiv) and DMAP (0.1 equiv) in CH_2Cl_2 (3.8 mL/mmol **13**) was added Et_3N (6.0 equiv) and a solution of *p*-TsCl (2.0 equiv) in CH_2Cl_2 (2 mL/mmol **13**). The cooling bath was then removed and the reaction was monitored by TLC analysis. Upon completion, the reaction was quenched by the addition of saturated aqueous NH_4Cl solution. The organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (×3). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated. Purification

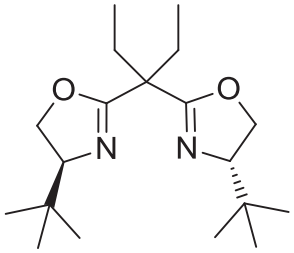
by flash column chromatography on silica gel (PE/EtOAc) afforded the desired (*S*,*S*)-bis(oxazolines) **3**.[1,6]

Synthesis and characterisation of (4*S*,4'*S*)-2,2'-pentane-3,3-diylbis[4-(propan-2-yl)-4,5-dihydro-1,3-oxazole] 3g



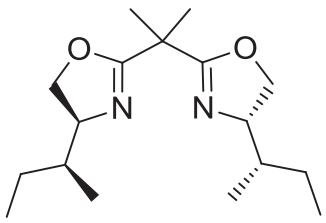
Synthesised on a 1.6 mmol scale of diethylmalonyl dichloride (314 mg). Purification by flash column chromatography on silica gel (PE/EtOAc 20:1 to 10:1) afforded **3g** (282 mg, 60% over two steps) as a colourless oil. $[\alpha]_D^{25}$ = –108.0 (*c* 1.75, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.11-4.19 (m, 2H), 3.89-3.98 (m, 4H), 1.89-2.08 (m, 4H), 1.76-1.87 (m, 2H), 0.91 (d, 6H, *J* = 6.8 Hz), 0.80-0.88 (m, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 167.7 (2C), 71.9 (2C), 69.5 (2C), 46.6, 32.3 (2C), 25.2 (2C), 18.7, 17.6, 8.3 (2C). The data was in agreement with that previously reported in the literature.[6]

Synthesis and characterisation of (4*S*,4'*S*)-2,2'-pentane-3,3-diylbis(4-*tert*-butyl-4,5-dihydro-1,3-oxazole) 3h



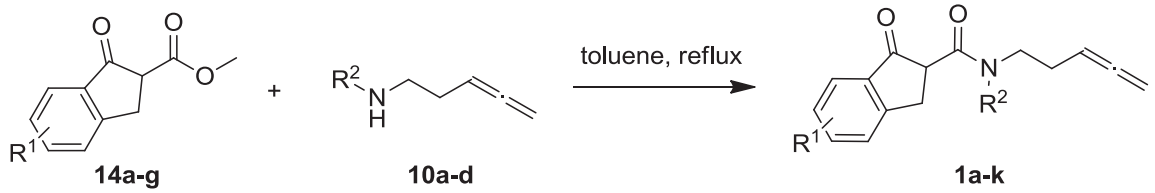
Synthesised on a 0.80 mmol scale of diethylmalonyl dichloride (157 mg). Purification by flash column chromatography on silica gel (PE/EtOAc 20:1 to 10:1) afforded **3h** (122 mg, 50% over two steps) as a colourless solid. $[\alpha]_D^{25}$ = –128.0 (*c* 1.75, $CHCl_3$); **Mp** 36 - 37 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.13 (dd, 2H, *J* = 10.1 Hz, *J* = 8.7 Hz), 4.03 (t, 2H, *J* = 8.4 Hz), 3.87 (dd, 2H, *J* = 10.1 Hz, *J* = 7.4 Hz), 2.02-2.11 (m, 2H), 1.88-1.97 (m, 2H), 0.83-0.88 (m, 24H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 167.2 (2C), 75.5 (2C), 68.4 (2C), 47.5, 33.8 (2C), 30.9 (2C), 25.8 (6C), 8.4 (2C). The data was in agreeement with that previouosly reported in the literature.[6]

Synthesis and characterisation of (4*S*,4'*S*)-2,2'-propane-2,2-diylbis{4-[(2*S*)-butan-2-yl]-4,5-dihydro-1,3-oxazole} 3i



Synthesised on a 2.0 mmol scale of dimethylmalonyl dichloride (338 mg). Purification by flash column chromatography on silica gel (PE/EtOAc 20:1 to 10:1) afforded **3i** (282 mg, 41% over two steps) as a colourless oil. $[\alpha]_D^{25}$ = –120.0 (*c* 1.00, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.17 (t, 2H, *J* = 7.6 Hz), 4.06-4.11 (m, 2H), 3.98 (t, 2H, *J* = 7.2 Hz), 1.63-1.69 (m, 2H), 1.50 (s, 6H), 1.36-1.47 (m, 2H), 1.09-1.20 (m, 2H), 0.90 (t, 6H, *J* = 7.2 Hz), 0.78 (d, 6H, *J* = 6.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 168.7 (2C), 70.0 (2C), 69.3 (2C), 38.5 (2C), 26.0 (2C), 24.4, 13.6 (2C), 11.7 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2950 (C-H), 1660 (C=N); **MS** (ESI+) *m/z* (rel. intensity %) 317.24 (M+Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{17}H_{30}N_2NaO_2$ $[M + Na]^+$ 317.2205, found 317.2206.

4. Synthesis of starting materials 1

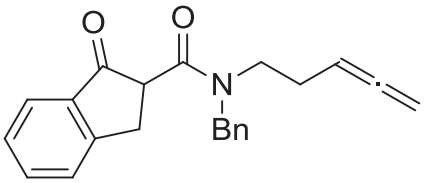


14a-g **10a-d** **1a-k**

R^1 = H, **14a**; R^1 = 6-Me, **14b**; R^1 = 6-OMe, **14c**; R^1 = 4-CF_3, **14d**;
R^1 = 5-F, **14e**; R^1 = 5-Br, **14f**; R^1 = 5-Cl, **14g**.

The starting materials **1a-k** were prepared from the corresponding esters **14a-g** (1.0 equiv) and secondary amines **10a-d** (1.5 equiv) in toluene at reflux until the reaction was complete by TLC analysis. The reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (PE/EtOAc) to afford the desired products **1a-k**.[5]

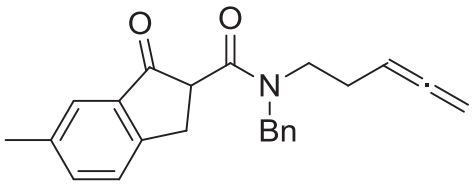
Synthesis and characterisation of *N*-benzyl-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1a



Synthesised from ethyl methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate **14a** (950 mg, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1a** was obtained as a yellow oil (1.49 g, 90%) after purification by flash column chromatography on silica gel (PE/EtOAc 1:2).

Two rotamers in a 1.6:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.59-7.73 (m, both, 6H), 7.39-7.47 (m, both, 4H), 7.32-7.36 (m, both, 4H), 7.23-7.27 (m, both, 4H), 5.24 (qu, major, 1H, J = 6.9 Hz), 5.12 (qu, minor, 1H, J = 6.8 Hz), 5.03 (d, minor, 1H, J = 17.0 Hz), 4.85 (d, major, 1H, J = 15.4 Hz), 4.73-4.77 (m, both, 5H), 4.41 (dd, major, 1H, J = 7.6 Hz, J = 3.9 Hz), 4.37 (d, major, 1H, J = 15.5 Hz), 4.30 (dd, minor, 1H, J = 7.8 Hz, J = 3.6 Hz), 3.83 (td, major, 1H, J = 15.3 Hz, J = 7.7 Hz), 3.43-3.47 (m, minor, 1H), 3.37-3.40 (m, major, 3H), 3.28-3.37 (m, minor, 2H), 3.15-3.24 (m, minor, 1H), 2.28-2.34 (m, major, 2H), 2.07-2.21 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 203.0 (both, 2C), 170.2 (minor), 169.9 (major), 155.8 (major), 155.5 (minor), 138.6 (major), 138.4 (minor), 136.2 (major), 136.1 (minor), 129.5 (both, 2C), 129.3 (both, 2C), 128.5 (both, 2C), 128.2 (both, 2C), 127.9 (both, 2C), 127.8 (both, 2C), 127.7 (both, 2C), 127.6 (both, 2C), 124.4 (both, 2C), 87.7 (minor), 87.4 (major), 76.4 (major), 76.3 (minor), 51.8 (minor), 50.9 (both, 2C), 48.7 (major), 46.0 (minor), 47.6 (major), 31.9 (both, 2C), 28.1 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2927 (C-H), 1955 (C=C=C), 1710 (C=O), 1641 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 354.17 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{22}H_{21}NNaO_2$ [M + Na]$^+$ 354.1470, found 354.1462.

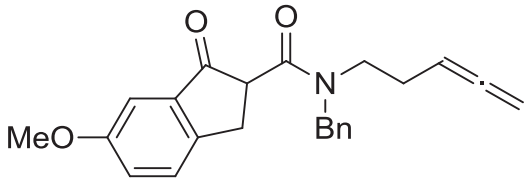
Synthesis and characterisation of *N*-benzyl-6-methyl-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1b



Synthesised from compound **14b** (1.02 g, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1b** was obtained (1.60 g, 93%) as a yellow oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:2).

Two rotamers in a 1.5:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.25-7.52 (m, both, 16H), 5.24 (qu, major, 1H, J = 6.8 Hz), 5.12 (qu, minor, 1H, J = 6.8 Hz), 5.02 (d, minor, 1H, J = 17.0 Hz), 4.84 (d, major, 1H, J = 15.4 Hz), 4.71-4.77 (m, both, 5H), 4.34-4.40 (m, major, 2H), 4.27 (dd, minor, 1H, J = 7.8 Hz, J = 3.6 Hz), 3.83 (td, major, 1H, J = 15.3 Hz, J = 7.7 Hz), 3.41-3.49 (m, minor, 1H), 3.27-3.40 (m, both, 4H), 3.14-3.25 (m, minor, 2H), 2.37 (s, major, 3H), 2.36 (s, minor, 3H), 2.28-2.32 (m, major, 2H), 2.11-2.18 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 203.2 (major), 203.0 (minor), 170.2 (minor), 170.0 (major), 153.2 (major), 152.9 (minor), 138.7 (both, 2C), 138.0 (both, 2C), 137.3 (major), 137.2 (minor), 136.4 (minor), 136.3 (major), 129.5 (both, 2C), 129.2 (both, 2C), 128.2 (both, 2C), 127.9 (both, 2C), 127.8 (both, 2C), 127.3 (both, 2C), 124.2 (both, 2C), 87.7 (minor), 87.4 (major), 76.4 (major), 76.3 (minor), 51.8 (minor), 51.2 (both, 2C), 48.7 (major), 47.6 (major), 46.0 (minor), 31.5 (both, 2C), 28.1 (major), 26.6 (minor), 21.4 (both, 2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2924 (C-H), 1955 (C=C=C), 1708 (C=O), 1642 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 368.18 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{23}H_{23}NNaO_2$ [M + Na]$^+$ 368.1621, found 368.1614.

Synthesis and characterisation of *N*-benzyl-6-methoxy-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1c

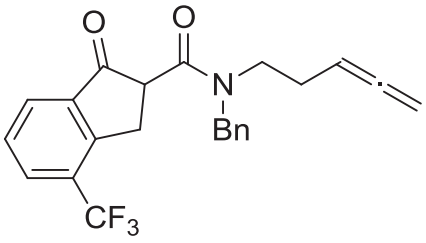


Synthesised from compound **14c** (1.02 g, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1c** was obtained (1.51 g, 84%) as a yellow oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Two rotamers in a 1.6:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.50-7.52 (m, both, 2H), 7.40-7.42 (m, both, 2H), 7.25-7.35 (m, both, 10H), 7.10-7.13 (m, both, 2H), 5.24 (qu, major, 1H, J = 6.8 Hz), 5.12 (qu, minor, 1H, J = 6.8 Hz), 5.01 (d, minor, 1H, J = 17.0 Hz), 4.85 (d, major, 1H, J = 15.4 Hz), 4.73-4.77 (m, both, 5H), 4.42 (dd, major, 1H, J = 7.4 Hz, J = 3.7 Hz), 4.37 (d, major, 1H, J = 15.4 Hz), 4.30 (dd, minor, 1H, J = 7.6 Hz, J = 3.4 Hz), 3.84-3.86 (m, major, 1H), 3.81 (s, major, 3H), 3.80 (s, minor, 3H), 3.41-3.48 (m, minor, 1H), 3.25-3.37 (m, both, 4H), 3.15-3.23 (m, minor, 2H), 2.30-2.32 (m, major, 2H), 2.11-2.18 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 203.0 (major), 202.8 (minor), 170.2 (minor), 170.0 (major), 160.0 (both, 2C), 148.4 (major), 148.1 (minor), 138.7 (major), 138.4 (minor), 137.4 (minor), 137.3 (major), 129.5 (both, 2C), 129.2 (both, 2C), 128.4 (major), 128.3 (minor), 128.2 (both, 2C), 128.0 (major), 127.9 (minor), 127.8 (minor), 127.7 (major), 124.9 (major), 124.7 (minor), 106.1 (both, 2C), 87.7 (minor), 87.4 (major),

76.4 (major), 76.3 (minor), 56.4 (both, 2C), 51.8 (minor), 51.6 (both, 2C), 48.7 (major), 47.6 (major), 46.0 (minor), 31.2 (both, 2C), 28.1 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2930 (C-H), 1955 (C=C=C), 1708 (C=O), 1641 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 384.18 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{23}H_{23}NNaO_3$ [M + Na]$^+$ 384.1570, found 384.1566.

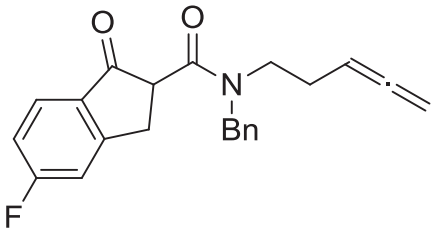
Synthesis and characterisation of *N*-benzyl-1-oxo-*N*-(penta-3,4-dien-1-yl)-4-(trifluoromethyl) indane-2-carboxamide 1d



Synthesised from compound **14d** (1.29 g, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1d** was obtained (1.59 g, 80%) as a yellow oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Two rotamers in a 1.6:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 8.08 (t, both, 2H, J = 7.9 Hz), 7.94-7.99 (m, both, 2H), 7.69 (dd, both, 2H, J = 14.4 Hz, J = 7.3 Hz), 7.41 (t, both, 2H, J = 7.5 Hz), 7.34 (dd, both, 4H, J = 13.2 Hz, J = 5.1 Hz), 7.26 (d, both, 4H, J = 6.9 Hz), 5.24 (qu, major, 1H, J = 6.9 Hz), 5.11 (qu, minor, 1H, J = 6.8 Hz), 5.03 (d, minor, 1H, J = 17.0 Hz), 4.85 (d, major, 1H, J = 15.4 Hz), 4.72-4.78 (m, both, 5H), 4.54-4.56 (m, major, 1H), 4.43 (dd, minor, 1H, J = 7.6 Hz, J = 3.6 Hz), 4.38 (d, major, 1H, J = 15.4 Hz), 3.83 (td, major, 1H, J = 15.3 Hz, J = 7.7 Hz), 3.36-3.51 (m, both, 6H), 3.16-3.23 (m, minor, 1H), 2.32-2.36 (m, major, 2H), 2.13-2.16 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 201.9 (major), 201.7 (minor), 169.5 (minor), 169.2 (major), 152.4 (major), 152.2 (minor), 138.5 (major), 138.2 (minor), 137.8 (minor), 137.7 (major), 132.9 (major), 132.8 (minor), 129.7 (both, 2C), 129.5 (both, 2C), 129.3 (both, 2C), 128.8 (both, 2C), 128.3 (both, 2C), 127.9 (both, 2C), 127.8 (both, 2C), 127.7 (both, 2C), 127.5 (both, 2C), 87.7 (minor), 87.3 (major), 76.4 (major), 76.3 (minor), 51.8 (minor), 50.7 (both, 2C), 48.8 (major), 47.7 (major), 46.1 (minor), 30.9 (both, 2C), 28.0 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2935 (C-H), 1956 (C=C=C), 1722 (C=O), 1644 (C=O); **MS** (ESI+) *m/z* (rel. intensity %) 422.15 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{23}H_{20}F_3NNaO_2$ [M + Na]$^+$ 422.1338, found 422.1335.

Synthesis and characterisation of *N*-benzyl-5-fluoro-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1e

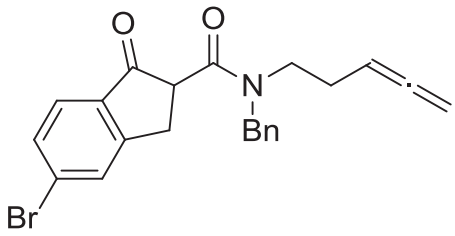


Synthesised from compound **14e** (1.04 g, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1e** was obtained (1.48 g, 85%) as a yellow oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:2).

Two rotamers in a 1.6:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO): δ_H 7.70-7.76 (m, both, 2H), 7.45-7.51 (m, both, 2H), 7.40-7.42 (m, both, 2H), 7.25-7.35 (m, both, 10H), 5.24 (qu, major, 1H, J = 6.8 Hz), 5.11 (qu, minor, 1H, J = 6.8 Hz), 5.02 (d, minor, 1H, J = 17.0 Hz), 4.85 (d, major, 1H, J = 15.4 Hz), 4.72-4.77 (m, both, 5H), 4.45 (dd, major, 1H, J = 7.6 Hz, J = 3.8 Hz),

4.36 (d, major, 1H, *J* = 15.5 Hz), 4.32-4.34 (m, minor, 1H), 3.82 (td, major, 1H, *J* = 15.3 Hz, *J* = 7.8 Hz), 3.26-3.47 (m, both, 6H), 3.14-3.21 (m, minor, 1H), 2.30-2.32 (m, major, 2H), 2.09-2.18 (m, 2H, minor); **^{13}C NMR** (100 MHz, d_6-DMSO): δ_C 209.1 (major), 209.0 (minor), 201.5 (major), 201.2 (minor), 169.9 (minor), 169.7 (major), 159.0 (major), 158.8 (minor), 138.6 (both, 2C), 132.8 (both, 2C), 129.5 (both, 2C), 129.3 (both, 2C), 128.3 (both, 2C), 127.9 (both, 2C), 127.8 (both, 2C), 127.2 (major), 127.1 (both, 2C), 127.0 (minor), 116.8 (major), 116.6 (minor), 114.4 (major), 114.2 (minor), 87.7 (minor), 87.4 (major), 76.4 (major), 76.3 (minor), 51.8 (both, 2C), 51.2 (both, 2C), 48.7 (major), 47.6 (major), 46.0 (minor), 31.9 (both, 2C), 28.0 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2929 (C-H), 1955 (C=C=C), 1714 (C=O), 1642 (NC=O); **MS** (ES+) *m/z* (rel. intensity %) 372.16 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{22}H_{20}FNNaO_2$ [M + Na]$^+$ 372.1370, found 372.1357.

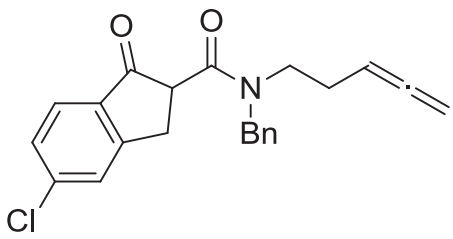
Synthesis and characterisation of *N*-benzyl-5-bromo-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1f



Synthesised from compound **14f** (1.33 g, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1f** was obtained (1.75 g, 86%) after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Two rotamers in a 1.6:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.91 (d, both, 2H, *J* = 13.5 Hz), 7.61 (td, both, 4H, *J* = 18.1 Hz, *J* = 8.3 Hz), 7.41 (t, both, 2H, *J* = 7.7 Hz), 7.31-7.34 (m, both, 4H), 7.25 (dd, both, 4H, *J* = 4.9 Hz, *J* = 2.9 Hz), 5.23 (qu, major, 1H, *J* = 6.8 Hz), 5.11 (qu, minor, 1H, *J* = 6.8 Hz), 5.01 (d, minor, 1H, *J* = 17.0 Hz), 4.83 (d, major, 1H, *J* = 15.5 Hz), 4.72-4.77 (m, both, 5H), 4.43 (dd, major, 1H, *J* = 7.6 Hz, *J* = 3.9 Hz), 4.37 (d, major, 1H, *J* = 15.4 Hz), 4.31 (dd, minor, 1H, *J* = 7.8 Hz, *J* = 3.6 Hz), 3.80 (td, major, 1H, *J* = 15.2 Hz, *J* = 7.7 Hz), 3.25-3.49 (m, major, 6H), 3.14-3.21 (m, minor, 1H), 2.29-2.32 (m, major, 2H), 2.09-2.17 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 202.2 (major), 202.0 (minor), 169.8 (minor), 169.6 (major), 157.8 (major), 157.5 (minor), 138.6 (major), 138.3 (minor), 135.3 (minor), 135.2 (major), 131.8 (both, 2C), 130.8 (major), 130.7 (minor), 130.5 (both, 2C), 130.4 (both, 2C), 129.5 (both, 2C), 129.3 (both, 2C), 127.9 (both, 2C), 127.8 (both, 2C), 126.1 (both, 2C), 87.7 (minor), 87.3 (major), 76.4 (both, 2C), 51.8 (minor), 51.0 (both, 2C), 48.7 (major), 47.6 (major), 46.0 (minor), 31.7 (both, 2C), 28.0 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2926 (C-H), 1955 (C=C=C), 1714 (C=O), 1641 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 432.08, 434.07 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{22}H_{20}BrNNaO_2$ [M + Na]$^+$ 432.0570, 434.0550, found 432.0570, 434.0556.

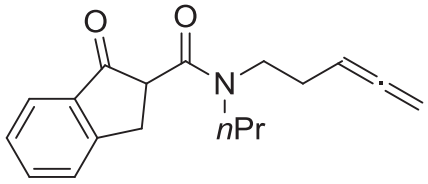
Synthesis and characterisation of *N*-benzyl-5-chloro-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1g



Synthesised from compound **14g** (1.12 g, 5.00 mmol) and amine **10a** (1.30 g, 7.50 mmol) according to the general procedure. Compound **1g** was obtained (1.55 g, 85%) after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Two rotamers in a 1.6:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.75 (d, both, 2H, J = 13.5 Hz), 7.67 (t, both, 2H, J = 9.2 Hz), 7.50 (t, both, 2H, J = 7.4 Hz), 7.41 (t, both, 2H, J = 7.6 Hz), 7.31-7.3 (m, both, 4H), 7.25 (d, both, 4H, J = 6.5 Hz), 5.23 (qu, major, 1H, J = 6.8 Hz), 5.11 (qu, minor, 1H, J = 6.8 Hz), 5.01 (d, minor, 1H, J = 17.0 Hz), 4.84 (d, major, 1H, J = 15.4 Hz), 4.72-4.77 (m, major, 5H), 4.45 (dd, major, 1H, J = 7.5 Hz, J = 3.9 Hz), 4.37 (d, major, 1H, J = 15.5 Hz), 4.32-4.34 (m, minor, 1H), 3.81 (td, major, 1H, J = 15.2 Hz, J = 7.7 Hz), 3.25-3.49 (m, both, 6H), 3.14-3.21 (m, minor, 1H), 2.30-2.32 (m, major, 2H), 2.07-2.17 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 202.0 (major), 201.8 (minor), 169.9 (minor), 169.6 (major), 157.6 (major), 157.4 (minor), 141.1 (major), 141.0 (minor), 138.6 (major), 138.3 (minor), 135.0 (minor), 134.9 (major), 129.5 (both, 2C), 129.3 (both, 2C), 129.0 (both, 2C), 128.3 (both, 2C), 127.9 (both, 2C), 127.7 (both, 2C), 126.1 (both, 2C), 126.0 (both, 2C), 87.7 (minor), 87.3 (major), 76.4 (major), 76.3 (minor), 51.8 (minor), 51.1 (both, 2C), 48.7 (major), 47.6 (major), 46.0 (minor), 31.7 (both, 2C), 28.0 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2928 (C-H), 1955 (C=C=C), 1714 (C=O), 1643 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 388.13 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{22}H_{20}ClNNaO_2$ [M + Na]$^+$ 388.1075, found 388.1075.

Synthesis and characterisation of 1-oxo-*N*-(penta-3,4-dien-1-yl)-*N*-propylindane-2-carboxamide 1h

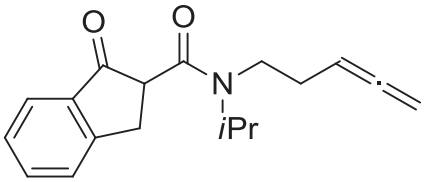


Synthesised from compound **14a** (950 mg, 5.00 mmol) and amine **10b** (937 mg, 7.50 mmol) according to the general procedure. Compound **1h** was obtained (1.10 g, 78%) after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Two rotamers in a 1.2:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.70 (t, both, 2H, J = 7.4 Hz), 7.63 (t, both, 4H, J = 7.9 Hz), 7.44 (t, both, 2H, J = 7.4 Hz), 5.25 (qu, minor, 1H, J = 6.9 Hz), 5.15 (qu, major, 1H, J = 6.8 Hz), 4.75-4.79 (m, both, 4H), 4.24-4.28(m, both, 2H), 3.79 (td, minor, 1H, J = 15.1 Hz, J = 7.6 Hz), 3.58-3.68 (m, major, 1H), 3.22-3.67 (m, both, 9H), 3.06-3.13 (m, minor, 1H), 2.26-2.37 (m, minor, 2H), 2.10-2.19 (m, major, 2H), 1.56-1.72 (m, major, 2H), 1.41-1.54 (m, minor, 2H), 0.89 (t, major, 3H, J = 7.3 Hz), 0.81 (t, minor, 3H, J = 7.4 Hz); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.2 (major), 209.1 (minor), 203.2 (both, 2C), 169.6 (major), 169.3 (minor), 155.7 (minor), 155.6 (major), 136.3 (minor), 136.1 (major), 128.4 (both, 2C), 127.6 (both, 2C), 124.4 (both, 2C), 124.3 (both, 2C), 87.8 (major), 87.5 (minor), 76.3 (minor), 76.2 (major), 50.9 (major), 50.7 (minor), 50.3 (major), 47.9 (minor), 47.8 (minor), 46.1 (major), 31.9 (both, 2C), 28.5 (major), 27.0 (minor), 23.0 (major), 21.4 (minor), 11.9 (minor), 11.8 (major); **FT-IR** ν_{max}(NaCl)/cm^{-1}

2932 (C-H), 1955 (C=C=C), 1711 (C=O), 1637 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 306.18 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{18}H_{21}NNaO_2$ $[M + Na]^+$ 306.1465, found 306.1474.

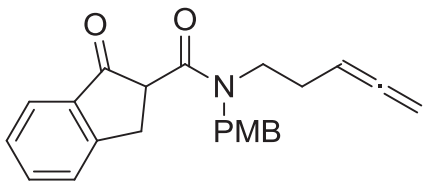
Synthesis and characterisation of *N*-isopropyl-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1i



Synthesised from compound **14a** (950 mg, 5.00 mmol) and amine **10c** (937 mg, 7.50 mmol) according to the general procedure. Compound **1i** was obtained (707 mg, 50%) as a yellow solid after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Mp 44 - 46 °C; two rotamers in a 1.5:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.70 (t, both, 2H, J = 7.4 Hz), 7.62 (t, both, 4H, J = 7.7 Hz), 7.44 (t, both, 2H, J = 7.4 Hz), 5.27 (qu, minor, 1H, J = 6.8 Hz), 5.17 (qu, major, 1H, J = 6.8 Hz), 4.75-4.81 (m, both, 4H), 4.39-4.51 (m, both, 2H), 4.36 (dd, major, 1H, J = 7.9 Hz, J = 3.6 Hz), 4.15 (t, minor, 1H, J = 5.7 Hz), 3.62-3.70 (m, major, 1H), 3.11-3.48 (m, both, 7H), 2.30-2.32 (m, minor, 2H), 2.07-2.16 (m, major, 2H), 1.30 (d, major, 3H, J = 6.5 Hz), 1.18 (d, major, 3H, J = 6.6 Hz), 1.11-1.14 (m, minor, 6H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.0 (minor), 208.9 (major), 203.4 (minor), 203.0 (major), 168.7 (both, 2C), 155.8 (minor), 155.5 (major), 136.2 (major), 136.1 (minor), 136.0 (both, 2C), 128.4 (both, 2C), 127.6 (both, 2C), 124.4 (both, 2C), 88.1 (major), 87.5 (minor), 76.5 (minor), 76.3 (major), 51.5 (minor), 51.1 (major), 49.2 (major), 46.8 (minor), 43.6 (major), 41.1 (minor), 32.1 (minor), 31.7 (major), 30.4 (minor), 28.2 (major), 22.1 (major), 22.0 (major), 21.0 (minor), 20.9 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2974 (C-H), 1955 (C=C=C), 1713 (C=O), 1637 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 306.18 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{18}H_{21}NNaO_2$ $[M + Na]^+$ 306.1465, found 306.1471.

Synthesis and characterisation of *N*-(4-methoxybenzyl)-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1j

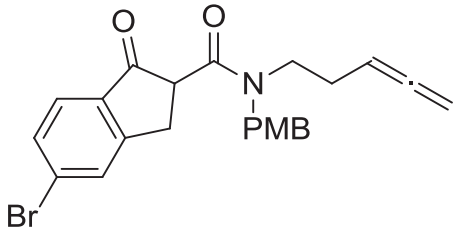


Synthesised from compound **14a** (950 mg, 5.00 mmol) and amine **10d** (1.52 g, 7.50 mmol) according to the general procedure. Compound **1j** was obtained (1.57 g, 87%) as a yellow oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Two rotamers in a 1.5:1 ratio, **^{1}H NMR** (400 MHz, d_6-DMSO) δ_H 7.60-7.73 (m, both, 6H), 7.45 (dd, both, 2H, J = 12.6 Hz, J = 7.1 Hz), 7.29 (d, minor, 2H, J = 8.4 Hz), 7.19 (d, major, 2H, J = 8.4 Hz), 6.96 (d, minor, 2H, J = 8.4 Hz), 6.89 (d, major, 2H, J = 8.4 Hz), 5.23 (qu, major, 1H, J = 6.8 Hz), 5.11 (qu, minor, 1H, J = 6.8 Hz), 4.92 (d, minor, 1H, J = 16.6 Hz), 4.74-4.79 (m, both, 5H), 4.67 (d, minor, 1H, J = 16.6 Hz), 4.37 (dd, major, 1H, J = 7.7 Hz, J = 3.9 Hz), 4.33-4.35 (m, minor, 1H), 4.30 (d, major, 1H, J = 15.0 Hz), 3.70-3.82 (m, major, 1H), 3.75 (s, minor, 3H), 3.73 (s, major, 3H), 3.26-3.43 (m, both, 6H), 3.14-3.21 (m, minor, 1H), 2.26-2.31 (m, major, 2H), 2.06-2.18 (m, minor, 2H); **^{13}C NMR** (100 MHz, d_6-DMSO) δ_C 209.1 (major), 209.0 (minor), 203.3 (major), 203.1 (minor), 170.0 (minor), 169.9 (major), 159.5 (minor), 159.2 (major), 155.8 (major), 155.5 (minor), 136.2 (both, 2C),

136.1 (both, 2C), 130.5 (both, 2C), 130.0 (both, 2C), 129.5 (both, 2C), 129.2 (both, 2C), 128.5 (both, 2C), 127.7 (major), 127.6 (minor), 124.5 (major), 124.4 (minor), 114.9 (minor), 114.7 (major), 87.7 (minor), 87.4 (major), 76.4 (major), 76.3 (minor), 55.9 (minor), 55.8 (major), 51.3 (minor), 50.9 (both, 2C), 48.0 (major), 45.7 (minor), 47.3 (major), 31.9 (both, 2C), 28.0 (major), 26.6 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2930 (C-H), 1955 (C=C=C), 1709 (C=O), 1639 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 384.18 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{23}H_{23}NNaO_3$ [M + Na]$^+$ 384.1570, found 384.1563.

Synthesis and characterisation of 5-bromo-*N*-(4-methoxybenzyl)-1-oxo-*N*-(penta-3,4-dien-1-yl)indane-2-carboxamide 1k



Synthesised from compound **14f** (1.33 g, 5.00 mmol) and amine **10d** (1.52 g, 7.50 mmol) according to the general procedure. Compound **1k** was obtained (1.76 g, 81%) as a yellow solid after purification by flash column chromatography on silica gel (PE/EtOAc 1:1).

Mp 70 - 73 °C; two rotamers in a 1.5:1 ratio, **^{1}H NMR** (400 MHz, *d*$_6$-DMSO) δ_H 7.90 (d, both, 2H, *J* = 10.3 Hz), 7.64 (t, both, 2H, *J* = 6.4 Hz), 7.58 (dd, both, 2H, *J* = 8.1 Hz, *J* = 5.2 Hz), 7.27 (d, both, 2H, *J* = 8.4 Hz), 7.17 (d, both, 2H, *J* = 8.3 Hz), 6.95 (d, both, 2H, *J* = 8.4 Hz), 6.88 (d, both, 2H, *J* = 8.4 Hz), 5.22 (qu, major, 1H, *J* = 6.8 Hz), 5.10 (qu, minor, 1H, *J* = 6.8 Hz), 4.89 (d, minor, 1H, *J* = 16.6 Hz), 4.72-4.77 (m, both, 5H), 4.65 (d, minor, 1H, *J* = 16.6 Hz), 4.33-4.39 (m, both, 2H), 4.29 (d, major, 1H, *J* = 15.0 Hz), 3.75 (s, minor, 3H), 3.73 (s, major, 3H), 3.67-3.77 (m, both, 2H), 3.28-3.37 (m, both, 5H), 3.13-3.20 (m, minor, 1H), 2.27-2.29 (m, major, 2H), 2.10-2.12 (m, minor, 2H); **^{13}C NMR** (100 MHz, *d*$_6$-DMSO) δ_C 209.1 (major), 209.0 (minor), 202.3 (major), 202.1 (minor), 169.7 (minor), 169.6 (major), 159.5 (minor), 159.2 (major), 157.8 (major), 157.5 (minor), 135.3 (minor), 135.2 (major), 131.8 (both, 2C), 130.8 (both, 2C), 130.5 (both, 2C), 130.4 (both, 2C), 129.9 (both, 2C), 129.5 (both, 2C), 129.2 (both, 2C), 126.1 (both, 2C), 114.9 (minor), 114.7 (major), 87.7 (minor), 87.4 (major), 76.4 (major), 76.3 (minor), 55.9 (both, 2C), 51.2 (minor), 51.0 (both, 2C), 48.1 (major), 47.3 (major), 45.7 (minor), 31.7 (both, 2C), 28.0 (major), 26.5 (minor); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2928 (C-H), 1955 (C=C=C), 1714 (C=O), 1639 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 462.09, 464.08 (M + Na$^+$, 80); **HRMS** (ESI+) calcd. for $C_{23}H_{22}BrNNaO_3$ [M + Na]$^+$ 462.0675, 464.0656, found 462.0670, 464.0651.

The *N*-tosylated γ-lactam-derived pro-nucleophile **1l** was synthesised using a previously reported procedure.[5]

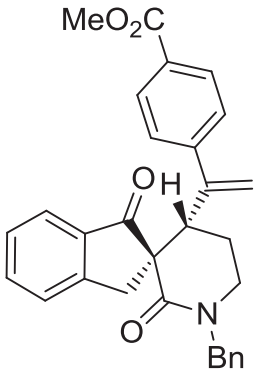
5. Synthesis of spirolactams 2 and 4

General procedure for the synthesis of spirolactams 2a-q and 4a-m

$Pd(OAc)_2$ (10 mol%) and bis(oxazoline) **3i** (20 mol%) were stirred for 1 h in DCE (4 mL) at room temperature. Then the corresponding allene **1a-k** (0.20 mmol), aromatic/vinyl iodide (0.30 mmol) and Ag_3PO_4 (0.10 mmol) were added. The reaction mixture was stirred in a sealed tube at 70 °C and monitored by TLC analysis. Upon completion, the reaction mixture was filtered through a short pad of silica gel, eluting with Et_2O several times. The combined organic washings were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (PE/EtOAc) to afford the desired products **2a-q** and **4a-m**.

Racemic samples were synthesised in an analogous manner to the general procedure without ligand **3i** and by replacing Ag_3PO_4, $Pd(OAc)_2$ and DCE with K_2CO_3, $PdCl_2(dppf)$ and DMF respectively.

Synthesis and characterisation of methyl 4-{1-[(2*R*,4'*S*)-1'-benzyl-1,2'-dioxo-1,3-dihydrospiro [indene-2,3'-piperidin]-4-yl]vinyl}benzoate 2a

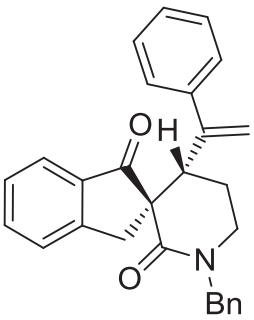


Synthesised from substrate **1a** (66 mg, 0.20 mmol) and methyl 4-iodobenzoate (79 mg, 0.30 mmol) according to the general procedure. Compound **2a** was obtained (single diastereomer, 78 mg, 84%) as a colourless oil after flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a >99:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 8.16 min, minor t_R = 11.14 min (85% *ee*). $[\alpha]_D^{25}$ = –4.8 (*c* 1.3, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.67 (d, 2H, *J* = 8.4 Hz), 7.49-7.53 (m, 1H), 7.30-7.39 (m, 6H), 7.14-7.22 (m, 2H), 6.89 (d, 2H, *J* = 8.4 Hz), 5.28 (s, 1H), 5.14 (s, 1H), 4.70 (d, 1H, *J* = 14.6 Hz), 4.59 (d, 1H, *J* = 14.6 Hz), 3.89 (s, 3H), 3.71 (dd, 1H, *J* = 10.5 Hz, *J* = 2.0 Hz), 3.49-3.58 (m, 2H), 3.38-3.43 (m, 1H), 3.33 (d, 1H, *J* = 17.0 Hz), 2.35 (ddd, 1H, *J* = 13.1 Hz, *J* = 6.9 Hz, *J* = 4.0 Hz), 1.91 (dtd, 1H, *J* = 13.7 Hz, *J* = 10.4 Hz, *J* = 5.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.8, 170.4, 166.7, 153.9, 148.3, 145.4, 136.7, 136.4, 134.9 (2C), 129.0 (2C), 128.7 (2C), 128.1 (2C), 127.5, 127.3, 126.9 (2C), 125.8, 124.2, 117.2, 60.0, 52.1, 50.6, 45.7, 43.9, 36.5, 24.9; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2928 (C-H), 1718 (C=O), 1632 (NC=O), 1595 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 488.21 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{27}NNaO_4$ $[M + Na]^+$ 488.1832, found 488.1833.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-(1-phenylvinyl)-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2b

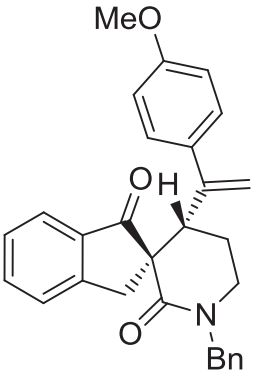


Synthesised from substrate **1a** (66 mg, 0.20 mmol) and iodobenzene (61 mg, 0.30 mmol) according to the general procedure. Compound **2b** was obtained (single diastereomer, 67 mg, 82%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 3:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 45:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 5.53 min, minor t_R = 14.41 min (87% *ee*); $[\alpha]_D^{25}$ = –16.6 (*c* 1.34, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.49-7.53 (m, 1H), 7.27-7.39 (m, 7H), 7.18 (t, 1H, *J* = 7.4 Hz), 7.08-7.11 (m, 1H), 7.00-7.04 (m, 2H), 6.86-6.88 (m, 2H), 5.24 (s, 1H), 5.05 (s, 1H), 4.65 (s, 2H), 3.68 (dd, 1H, *J* = 10.1 Hz, *J* = 2.1 Hz), 3.58 (d, 1H, *J* = 16.9 Hz), 3.49-3.54 (m, 1H), 3.39-3.44 (m, 1H), 3.36 (d, 1H, *J* = 17.0 Hz), 2.39-2.45 (m, 1H), 1.83-1.92 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.9, 170.5, 154.1, 149.0, 140.8, 136.8, 136.3, 134.7, 128.7 (2C), 128.1 (2C), 127.7 (2C), 127.5, 127.4, 127.1, 126.9 (2C), 125.8, 124.3, 115.6, 60.0, 50.7, 45.7, 44.1, 36.7, 24.6; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2926 (C-H), 1717 (C=O), 1631 (NC=O), 1590 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 430.19 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{28}H_{25}NNaO_2$ $[M + Na]^+$ 430.1778, found 430.1777.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(4-methoxyphenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2c

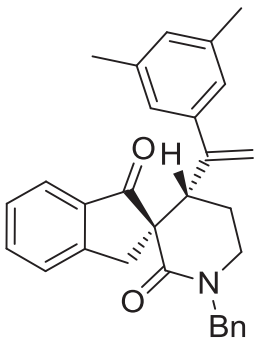


Synthesised from substrate **1a** (66 mg, 0.20 mmol) and 1-iodo-4-methoxybenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **2c** was obtained (single diastereomer, 74 mg, 85%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 56:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 6.30 min, minor t_R = 8.70 min (87% *ee*); $[\alpha]_D^{25}$ = +1.4 (*c* 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.48-7.52 (m, 1H), 7.30-7.37 (m, 7H), 7.17 (t, 1H, *J* = 7.4 Hz), 6.78 (dd, 2H, *J* = 9.2 Hz, *J* = 2.5 Hz), 6.53-6.55 (m, 2H), 5.18 (s, 1H), 4.99 (s, 1H), 4.63 (s, 2H), 3.73 (s, 3H), 3.65 (dd, 1H, *J* = 10.2 Hz, *J* = 1.4 Hz), 3.49-3.56 (m, 2H), 3.39-3.43 (m, 1H), 3.35 (d, 1H, *J* = 16.9 Hz), 2.38 (ddd, 1H, *J* = 12.9 Hz, *J* = 7.4 Hz, *J* = 4.3 Hz), 1.87 (dtd, 1H, *J* = 15.1 Hz, *J* = 10.1 Hz, *J* = 5.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.1, 170.7, 159.0, 154.2, 148.5, 136.8, 136.4, 134.6, 133.1, 128.7 (2C), 128.2 (2C), 128.1 (2C), 127.4, 126.9, 125.7 124.2, 114.4, 113.1 (2C), 60.1, 55.2, 50.7, 45.8, 44.3, 36.6, 24.7; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2928 (C-H), 1716 (C=O), 1631 (NC=O), 1607 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 460.21 (M + Na$^+$, 70); **HRMS** (ESI+) calcd. for $C_{29}H_{27}NNaO_3$ $[M + Na]^+$ 460.1883, found 460.1881.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2d

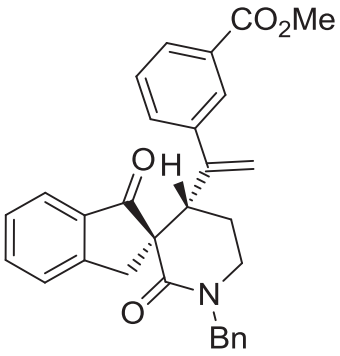


Synthesised from substrate **1a** (66 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **2d** was obtained (single diastereomer, 66 mg, 76%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 39:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 4.34 min, minor t_R = 14.92 min (89% *ee*); $[\alpha]_D^{25}$ = –9.8 (*c* 1.84, CH_2Cl_2).

Mp 106 - 109 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.50-7.54 (m, 1H), 7.23-7.39 (m, 7H), 7.20 (t, 1H, *J* = 7.4 Hz), 6.73 (s, 1H), 6.45 (s, 2H), 5.20 (s, 1H), 5.00 (s, 1H), 4.71 (d, 1H, *J* = 14.6 Hz), 4.58 (d, 1H, *J* = 14.6 Hz), 3.63 (dd, 1H, *J* = 9.9 Hz, *J* = 2.5 Hz), 3.57 (d, 1H, *J* = 17.0 Hz), 3.49-3.53 (m, 1H), 3.38-3.41 (m, 1H), 3.34 (d, 1H, *J* = 17.0 Hz), 2.38-2.45 (m, 1H), 2.11 (s, 6H), 1.85 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.0, 170.6, 154.2, 149.3, 140.8, 137.1 (2C), 136.9, 136.3, 134.4, 129.1, 128.7 (2C), 128.1 (2C), 127.4, 127.0, 125.8, 125.1 (2C), 124.2, 114.9, 60.0, 50.7, 45.6, 44.5, 36.8, 24.5, 21.1 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2920 (C-H), 1718 (C=O), 1631 (NC=O), 1590 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 458.23 (M + Na$^+$, 80); **HRMS** (ESI+) calcd. for $C_{30}H_{29}NNaO_2$ $[M + Na]^+$ 458.2091, found 458.2087.

Synthesis and characterisation of methyl 3-{1-[(2*R*,4'*S*)-1'-benzyl-1,2'-dioxo-1,3-dihydrospiro[indene-2,3'-piperidin]-4'-yl]vinyl}benzoate 2e



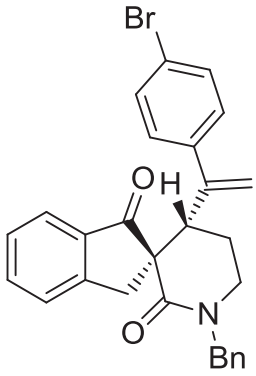
Synthesised from substrate **1a** (66 mg, 0.20 mmol) and methyl 3-iodobenzoate (79 mg, 0.30 mmol) according to the general procedure. Compound **2e** was obtained (single diastereomer, 80 mg, 86%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 41:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 6.31 min, minor t_R = 17.26 min (86% *ee*); $[\alpha]_D^{25}$ = –0.32 (*c* 2.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.75 (d, 1H, *J* = 7.5 Hz), 7.49 (t, 1H, *J* = 7.3 Hz), 7.30-7.40 (m, 7H), 7.20 (d, 1H, *J* = 7.6 Hz), 7.06-7.15 (m, 3H), 5.26 (s, 1H), 5.12 (s, 1H), 4.70 (d, 1H, *J* = 14.6 Hz), 4.59 (d, 1H, *J* = 14.6 Hz), 3.85 (s, 3H), 3.69-3.72 (m, 1H), 3.50-3.59 (m, 2H), 3.39-3.44 (m, 1H), 3.35 (d, 1H, *J* = 17.0 Hz), 2.36 (ddd, 1H, *J* = 13.0 Hz, *J* = 6.9 Hz, *J* = 3.9 Hz), 1.91 (ddt, 1H, *J* = 15.6 Hz, *J* = 10.5 Hz, *J* = 5.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.9, 170.5, 166.6, 153.9, 148.3, 141.1, 136.8, 136.4, 134.7, 131.4, 129.5, 128.7 (2C), 128.6, 128.5, 128.1 (2C), 127.7, 127.5, 127.1, 125.9, 124.1, 116.7, 59.9, 52.0, 50.6, 45.7, 44.2, 36.5, 24.8; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2918 (C-H), 1719 (C=O), 1631

(NC=O), 1589 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 488.21 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{27}NNaO_4$ $[M + Na]^+$ 488.1832, found 488.1826.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(4-bromophenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2f

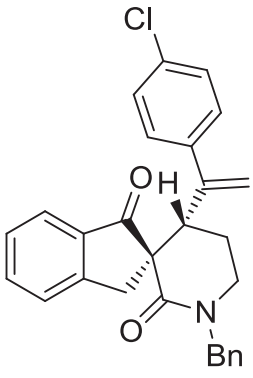


Synthesised from substrate **1a** (66 mg, 0.20 mmol) and 1-bromo-4-iodobenzene (85 mg, 0.30 mmol) according to the general procedure. Compound **2f** was obtained (single diastereomer, 76 mg, 79%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 25:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 5.88 min, minor t_R = 8.62 min (86% *ee*); $[\alpha]_D^{25}$ = +24.8 (*c* 2.68, CH_2Cl_2).

Mp 58 - 62 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.49-7.53 (m, 1H), 7.27-7.39 (m, 7H), 7.21 (t, 1H, *J* = 7.4 Hz). 7.10 (dd, 2H, *J* = 8.8 Hz, *J* = 2.1 Hz), 6.68 (dd, 2H, *J* = 8.8 Hz, *J* = 2.1 Hz), 5.21 (s, 1H), 5.08 (s, 1H), 4.68 (d, 1H, *J* = 14.6 Hz), 4.61 (d, 1H, *J* = 14.6 Hz), 3.65 (dd, 1H, *J* = 10.8 Hz, *J* = 1.5 Hz), 3.48-3.57 (m, 2H), 3.39 (td, 1H, *J* = 12.3 Hz, *J* = 4.5 Hz), 3.31 (d, 1H, *J* = 17.0 Hz), 2.32 (ddd, 1H, *J* = 13.2 Hz, *J* = 6.9 Hz, *J* = 4.0 Hz), 1.90 (dtd, 1H, *J* = 13.5 Hz, *J* = 10.6 Hz, *J* = 5.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.1, 170.6, 154.0, 148.1, 139.5, 136.7, 136.5, 134.8, 130.7 (2C), 128.7 (2C), 128.6 (2C), 128.1 (2C), 127.5, 127.1, 125.8, 124.3, 121.6, 116.3, 60.0, 50.6, 45.8, 44.1, 36.5, 24.9; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2924 (C-H), 1716 (C=O), 1631 (NC=O), 1588 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 508.10, 510.11 (M + Na^+, 80); **HRMS** (ESI+) calcd. for $C_{28}H_{24}BrNNaO_2$ $[M + Na]^+$ 508.0883, 510.0864, found 508.0877, 510.0863.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(4-chlorophenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2g



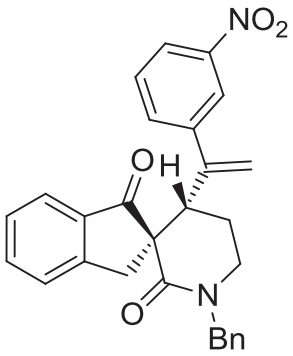
Synthesised from substrate **1a** (66 mg, 0.20 mmol) and 1-chloro-4-iodobenzene (71 mg, 0.30 mmol) according to the general procedure. Compound **2g** was obtained (single diastereomer, 74 mg, 84%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 33:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 5.72 min, minor t_R = 8.47 min (87% *ee*); $[\alpha]_D^{25}$ = +14.8 (*c* 3.1, CH_2Cl_2).

Mp 58 - 60 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.52 (dd, 1H, *J* = 10.8 Hz, *J* = 3.9 Hz), 7.27-7.39 (m, 7H), 7.20 (t, 1H, *J* = 7.4 Hz), 6.95 (d, 2H, *J* = 8.4 Hz), 6.74 (d, 2H, *J* = 8.4 Hz), 5.20 (s, 1H), 5.08 (s, 1H), 4.68 (d, 1H, *J* = 14.6 Hz), 4.61 (d, 1H, *J* = 14.6 Hz), 3.66 (dd, 1H, *J* = 10.6 Hz, *J* = 1.5 Hz), 3.49-3.57 (m, 2H), 3.39 (td, 1H, *J* = 12.3 Hz, *J* = 4.6 Hz), 3.32 (d, 1H, *J* = 17.0 Hz), 2.32 (ddd, 1H, *J* =

13.1 Hz, *J* = 6.8 Hz, *J* = 3.8 Hz), 1.85-1.95 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.0, 170.6, 154.0, 148.1, 139.1, 136.5, 134.8 (2C), 133.4, 128.7 (2C), 128.3 (2C), 128.1 (2C), 127.7 (2C), 127.5, 127.1, 125.8, 124.3, 116.2, 60.0, 50.6, 45.8, 44.1, 36.5, 24.9; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2925 (C-H), 1716 (C=O), 1631 (NC=O), 1589 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 464.15 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{28}H_{24}ClNNaO_2$ [M + Na]$^+$ 464.1388, found 464.1384.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3-nitrophenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2h

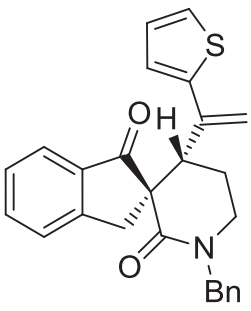


Synthesised from substrate **1a** (66 mg, 0.20 mmol) and 1-iodo-3-nitrobenzene (75 mg, 0.30 mmol) according to the general procedure. Compound **2h** was obtained (single diastereomer, 69 mg, 77%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:2). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 35:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 7.34 min, minor t_R = 19.96 min (86% *ee*); $[\alpha]_D^{25}$ = –8.2 (*c* 1.34, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.89-7.94 (m, 1H), 7.50 (ddd, 1H, *J* = 8.2 Hz, *J* = 5.8 Hz, *J* = 2.6 Hz), 7.24-7.42 (m, 9H), 7.08-7.12 (m, 2H), 5.30 (s, 1H), 5.23 (d, 1H, *J* = 0.7 Hz), 4.73 (d, 1H, *J* = 14.6 Hz), 4.57 (d, 1H, *J* = 14.6 Hz), 3.73-3.75 (m, 1H), 3.59 (dt, 1H, *J* = 11.8 Hz, *J* = 4.3 Hz), 3.48 (d, 1H, *J* = 17.0 Hz), 3.42 (ddd, 1H, *J* = 12.3 Hz, *J* = 5.1 Hz, *J* = 3.1 Hz), 3.33 (d, 1H, *J* = 17.0 Hz), 2.26-2.31 (m, 1H), 1.94-2.04 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.0, 170.4, 153.8, 147.4, 147.3, 142.3, 136.6, 136.5, 135.2, 132.9, 129.0, 128.7, 128.4, 128.1, 127.6, 127.2, 126.0, 123.9, 122.5 (2C), 122.3, 118.2, 59.9, 50.6, 45.9, 44.2, 36.3, 25.2; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2927 (C-H), 1716 (C=O), 1630 (NC=O), 1592 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 475.18 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{28}H_{24}N_2NaO_4$ [M + Na]$^+$ 475.1628, found 475.1630.

Synthesis and characterisation of (2*R*,4'*R*)-1'-benzyl-4'-[1-(2-thienyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2i



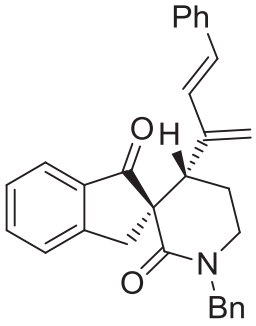
Synthesised from substrate **1a** (66 mg, 0.20 mmol) and 2-iodothiophene (63 mg, 0.30 mmol) according to the general procedure. Compound **2i** was obtained (single diastereomer, 58 mg, 70%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 40:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 6.47 min, minor t_R = 16.80 min (75% *ee*); $[\alpha]_D^{25}$ = –42.8 (*c* 1.96, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.53 (ddd, 2H, *J* = 10.5 Hz, *J* = 5.9 Hz, *J* = 2.0 Hz), 7.23-7.40 (m, 7H), 7.01 (dd, 1H, *J* = 4.5 Hz, *J* = 1.6 Hz), 6.82-6.84 (m, 2H), 5.49 (s, 1H), 4.94 (s, 1H), 4.73 (d, 1H, *J*

= 14.6 Hz), 4.61 (d, 1H, *J* = 14.7 Hz), 3.73 (d, 1H, *J* = 17.0 Hz), 3.56 (dd, 1H, *J* = 8.2 Hz, *J* = 3.3 Hz), 3.38-3.51 (m, 2H), 3.32 (d, 1H, *J* = 17.1 Hz), 2.59-2.66 (m, 1H), 1.84-1.92 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.9, 169.9, 154.3, 143.8, 141.3, 136.8, 135.6, 134.9, 128.7 (2C), 128.1 (2C), 127.5, 127.3, 127.1, 125.9, 124.9, 124.6, 124.5, 114.0, 60.1, 50.8, 45.2, 44.4, 37.2, 24.1; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2926 (C-H), 1714 (C=O), 1632 (NC=O), 1590 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 436.15 (M + Na^+, 75); **HRMS** (ESI+) calcd. for $C_{26}H_{23}NNaO_2S$ [M + Na]$^+$ 436.1342, found 436.1345.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*E*)-4-phenylbuta-1,3-dien-2-yl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2j

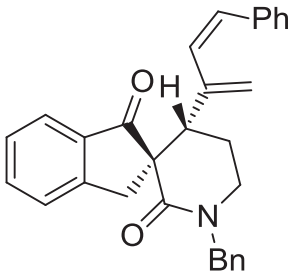


Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*E*)-(2-iodovinyl)benzene (69 mg, 0.30 mmol) according to the general procedure. Compound **2j** was obtained (single diastereomer, 53 mg, 61%) as a yellow oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 21:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 6.13 min, minor t_R = 8.74 min (53% *ee*); $[\alpha]_D^{25}$ = –10.1 (*c* 0.68, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.65 (d, 1H, *J* = 7.7 Hz), 7.53 (t, 1H, *J* = 7.4 Hz), 7.21-7.42 (m, 12H), 6.36-6.49 (m, 2H), 5.32 (s, 1H), 4.94 (s, 1H), 4.66 (dd, 2H, *J* =14.6 Hz, *J* = 9.6 Hz), 3.72 (d, 1H, *J* = 17.1 Hz), 3.35-3.50 (m, 3H), 3.26 (d, 1H, *J* = 17.1 Hz), 2.56-2.63 (m, 1H), 1.82-1.90 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.3, 170.0, 154.3, 145.3, 136.9, 136.7, 135.9, 135.0, 129.7, 129.3 128.7 (2C), 128.5 (2C), 128.1 (2C), 127.7, 127.4, 127.3, 126.5 (2C), 126.1, 124.6, 115.9, 59.9, 50.7, 45.3, 41.7, 37.1, 23.8; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2926 (C-H), 1712 (C=O), 1631 (NC=O), 1589 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 456.23 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{27}NNaO_2$ [M + Na]$^+$ 456.1934, found 456.1925.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*Z*)-4-phenylbuta-1,3-dien-2-yl)spiro [indene-2,3'-piperidine]-1,2'(3*H*)-dione 2k

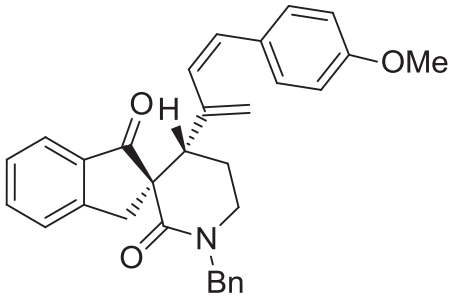


Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-(2-iodovinyl)benzene (69 mg, 0.30 mmol) according to the general procedure. Compound **2k** was obtained (single diastereomer, 63 mg, 72%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 23:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 220 nm, major t_R = 6.14 min, minor t_R = 10.20 min (77% *ee*); $[\alpha]_D^{25}$ = –8.0 (*c* 0.20, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.77 (d, 1H, *J* = 7.7 Hz), 7.51-7.54 (m, 1H), 7.20-7.42 (m, 12H), 6.18 (d, 1H, *J* =12.5 Hz), 5.69 (d, 1H, *J* = 12.5 Hz), 5.15 (s, 1H), 4.97 (s, 1H), 4.73 (d, 1H, *J* = 14.6 Hz), 4.46 (d, 1H, *J* = 14.6 Hz), 3.52 (d, 1H, *J* = 17.0 Hz), 3.34-3.42 (m, 2H), 3.22-3.27 (m, 2H), 2.15-2.19 (m, 1H), 1.83-1.95 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 205.2, 170.6, 154.1, 143.6, 136.8, 136.7, 134.9, 131.0, 130.2, 128.7, 128.6 (2C), 128.3 (2C), 128.0, 127.9 (2C), 127.5, 127.4, 126.9, 126.5, 126.3, 124.5, 117.4, 60.1, 50.4, 45.8, 44.8, 36.5, 24.6; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2925 (C-H), 1714 (C=O), 1632 (NC=O), 1590 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 456.23 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{27}NNaO_2$ [M + Na]$^+$ 456.1934, found 456.1927.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*Z*)-4-(4-methoxyphenyl)buta-1,3-dien-2-yl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2l

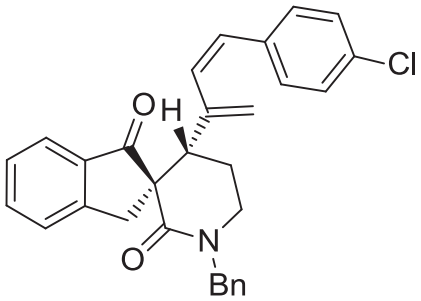


Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-1-(2-iodovinyl)-4-methoxybenzene (78 mg, 0.30 mmol) according to the general procedure. Compound **2l** was obtained (single diastereomer, 62 mg, 67%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 20:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 220 nm, major t_R = 7.59 min, minor t_R = 14.06 min (65% *ee*); $[\alpha]_D^{25}$ = –10.7 (*c* 1.23, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.64 (d, 1H, *J* = 7.7 Hz), 7.51-7.54 (m, 1H), 7.24-7.41 (m, 7H), 7.17 (dd, 2H, *J* = 9.3 Hz, *J* = 2.3 Hz), 6.79-6.81 (m, 2H), 6.32 (br s, 2H), 5.27 (s, 1H), 4.88 (s, 1H), 4.69 (d, 1H, *J* = 14.6 Hz), 4.61 (d, 1H, *J* = 14.6 Hz), 3.80 (s, 3H), 3.71 (d, 1H, *J* = 17.1 Hz), 3.36-3.44 (m, 3H), 3.26 (d, 1H, *J* = 17.1 Hz), 2.56-2.62 (m, 1H), 1.81-1.87 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 205.4, 170.2, 159.3, 154.3, 145.4, 136.9, 135.9, 134.9, 129.5, 128.8, 128.6 (2C), 128.0 (2C), 127.7 (2C), 127.6, 127.4, 127.2, 126.0, 124.6, 114.9, 113.9 (2C), 59.9, 55.2, 50.7, 45.3, 41.7, 37.1, 23.8; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2923 (C-H), 1718 (C=O), 1633 (NC=O), 1589 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 486.23 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{29}NNaO_3$ [M + Na]$^+$ 486.2040, found 486.2030.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*Z*)-4-(4-chlorophenyl)buta-1,3-dien-2-yl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2m

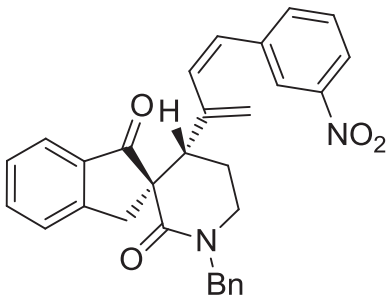


Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-1-chloro-4-(2-iodovinyl)benzene (79 mg, 0.30 mmol) according to the general procedure. Compound **2m** was obtained (single diastereomer, 73 mg, 78%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 18:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 70:30, 1.0 mL/min, λ = 230 nm, major t_R = 8.33 min, minor t_R = 20.44 min (76% *ee*); $[\alpha]_D^{25}$ = –13.4 (*c* 0.53, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.76 (d, 1H, *J* = 7.7 Hz), 7.54 (dt, 1H, *J* = 7.5 Hz, *J* = 1.2 Hz), 7.27-7.41 (m, 7H), 6.99-7.02 (m, 2H), 6.81-6.84 (m, 2H), 6.09 (d, 1H, *J* = 12.5 Hz), 5.70 (dd, 1H, *J* = 12.5 Hz, *J* = 0.8 Hz), 5.14 (s, 1H), 5.00 (s, 1H), 4.77 (d, 1H, *J* = 14.6 Hz), 4.42 (d, 1H, *J* = 14.6 Hz), 3.49 (d, 1H, *J* = 17.1 Hz), 3.33-3.43 (m, 3H), 3.24 (dd, 1H, *J* = 11.6 Hz, *J* = 2.4 Hz), 2.09-2.15 (m, 1H), 1.87-1.97 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.2, 170.6, 153.9, 143.2, 136.8, 136.7, 135.2, 134.9, 132.5, 130.9, 129.6, 129.5 (2C), 128.7, 128.6, 128.1 (2C), 128.0 (2C), 127.6, 127.5, 126.3, 124.5, 117.7, 60.1, 50.4, 45.8, 44.8, 36.4, 24.7; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2931 (C-H), 1713 (C=O), 1631 (NC=O), 1596 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 490.15 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{26}ClNNaO_2$ $[M + Na]^+$ 490.1544, found 490.1540.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*Z*)-4-(3-nitrophenyl)buta-1,3-dien-2-yl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2n



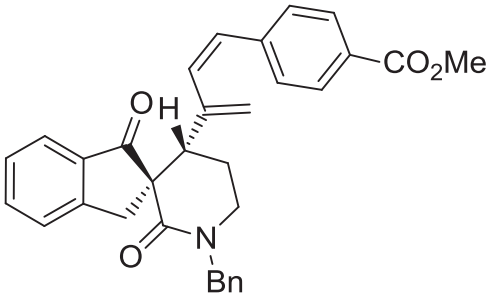
Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-1-(2-iodovinyl)-3-nitrobenzene (82 mg, 0.30 mmol) according to the general procedure. Compound **2n** was obtained (single diastereomer, 74 mg, 77%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 16:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 10.62 min, minor t_R = 21.64 min (73% *ee*); $[\alpha]_D^{25}$ = –11.9 (*c* 0.87, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.02 (d, 1H, *J* = 1.7 Hz), 7.92-7.95 (m, 1H), 7.72 (d, 1H, *J* = 7.7 Hz), 7.19-7.46 (m, 10H), 6.12 (d, 1H, *J* = 12.5 Hz), 5.82 (d, 1H, *J* = 12.5 Hz), 5.21 (s, 1H), 5.11 (s, 1H), 4.79 (d, 1H, *J* = 14.6 Hz), 4.40 (d, 1H, *J* = 14.6 Hz), 3.37-3.51 (m, 4H), 3.30 (dd, 1H, *J* = 11.7 Hz, *J* = 1.9 Hz), 2.14-2.19 (m, 1H), 1.93-2.05 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.3, 170.5, 153.7, 147.8, 143.2, 138.0, 136.8, 136.6, 134.8, 134.7, 133.5, 128.9, 128.7 (2C), 128.1 (3C), 127.6, 127.5, 126.4, 124.4, 122.7, 121.7, 118.0, 60.0, 50.4, 45.9, 44.8, 36.4, 24.7; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2919 (C-

H), 1716 (C=O), 1631 (NC=O), 1589 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 501.20 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{26}N_2NaO_4$ $[M + Na]^+$ 501.1785, found 501.1787.

Synthesis and characterisation of methyl 4-((*Z*)-3-((2*R*,4'*S*)-1'-benzyl-1,2'-dioxo-1,3-dihydrospiro[indene-2,3'-piperidin]-4'-yl)buta-1,3-dien-1-yl)benzoate 2o

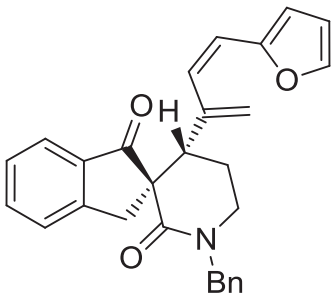


Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-methyl 4-(2-iodovinyl)benzoate (86 mg, 0.30 mmol) according to the general procedure. Compound **2o** was obtained (single diastereomer, 67 mg, 68%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 17:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 70:30, 1.0 mL/min, λ = 230 nm, major t_R = 12.16 min, minor t_R = 25.43 min (82% *ee*); $[\alpha]_D^{25}$ = −7.9 (*c* 2.36, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.71-7.77 (m, 3H), 7.52-7.55 (m, 1H), 7.42 (d, 1H, *J* = 7.7 Hz), 7.26-7.34 (m, 6H), 6.95 (d, 2H, *J* = 8.2 Hz), 6.17 (d, 1H, *J* = 12.5 Hz), 5.78 (d, 1H, *J* = 12.4 Hz), 5.11 (s, 1H), 4.99 (s, 1H), 4.75 (d, 1H, *J* = 14.6 Hz), 4.43 (d, 1H, *J* = 14.6 Hz), 3.89 (s, 3H), 3.49 (d, 1H, *J* = 17.0 Hz), 3.33-3.39 (m, 3H), 3.24 (dd, 1H, *J* = 11.6 Hz, *J* = 2.1 Hz), 2.09-2.14 (m, 1H), 1.89-1.97 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 205.2, 170.6, 166.8, 153.9, 143.1, 141.6, 136.8, 136.7, 135.0, 132.2, 129.9, 129.3 (2C), 128.7 (2C), 128.3, 128.2 (2C), 128.0 (2C), 127.7, 127.5, 126.3, 124.5, 118.0, 60.1, 52.0, 50.4, 45.9, 44.8, 36.3, 24.7; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2950 (C-H), 1717 (C=O), 1632 (NC=O), 1608 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 492.24 (M + H^+, 100); **HRMS** (ESI+) calcd. for $C_{32}H_{30}NO_4$ $[M + H]^+$ 492.2169, found 492.2168.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*Z*)-4-(furan-2-yl)buta-1,3-dien-2-yl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2p



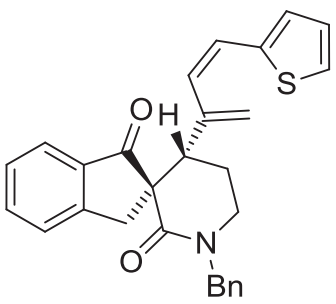
Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-2-(2-iodovinyl)furan (66 mg, 0.30 mmol) according to the general procedure. Compound **2p** was obtained (single diastereomer, 59 mg, 70%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 19:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 70:30, 1.0 mL/min, λ = 230 nm, major t_R = 6.47 min, minor t_R = 9.42 min (71% *ee*); $[\alpha]_D^{25}$ = –8.2 (*c* 0.60, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.67 (d, 1H, *J* = 7.6 Hz), 7.29-7.38 (m, 6H), 7.20 (dd, 2H, *J* = 15.3 Hz, *J* = 7.6 Hz), 7.04 (d, 1H, *J* = 1.8 Hz), 6.14 (dd, 1H, *J* = 3.3 Hz, *J* = 1.8 Hz) 6.08 (d, 1H, *J* = 3.3 Hz), 5.78 (d, 1H, *J* = 12.6 Hz), 5.51 (d, 1H, *J* = 12.6 Hz), 5.34 (s, 1H), 5.16 (s, 1H), 4.77 (d, 1H, *J* = 14.6 Hz), 4.45 (d, 1H, *J* = 14.6 Hz), 3.35-3.50 (m, 4H), 3.31 (dd, 1H, *J* = 11.2 Hz, *J* = 2.3 Hz), 2.21-

2.27 (m, 1H), 1.88-1.95 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.9, 170.8, 154.1, 151.4, 143.8, 141.2, 136.8, 136.7, 134.3, 128.6 (2C), 128.1 (2C), 127.7, 127.4, 127.1, 126.1, 124.1, 118.4, 116.6, 110.9, 110.5 60.1, 50.5, 45.9, 45.1, 36.5, 24.4; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2925 (C-H), 1713 (C=O), 1629 (NC=O), 1593 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 446.20 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{28}H_{25}NNaO_3$ [M + Na]$^+$ 446.1727, found 446.1730.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-((*Z*)-4-(thiophen-2-yl)buta-1,3-dien-2-yl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 2q

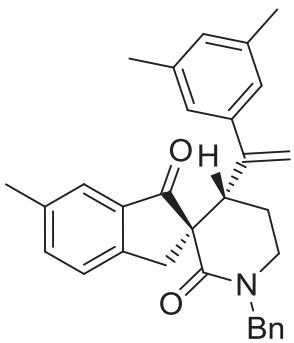


Synthesised from substrate **1a** (67 mg, 0.20 mmol) and (*Z*)-2-(2-iodovinyl)thiophene (71 mg, 0.30 mmol) according to the general procedure. Compound **2q** was obtained (single diastereomer, 57 mg, 65%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 18:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 8.17 min, minor t_R = 11.25 min (75% *ee*); $[\alpha]_D^{25}$ = –14.3 (*c* 0.50, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.69 (d, 1H, *J* = 7.7 Hz), 7.28-7.36 (m, 6H), 7.22 (dd, 1H, *J* = 11.0 Hz, *J* = 3.8 Hz), 7.16 (d, 1H, J = 7.6 Hz), 7.01 (d, 1H, *J* = 5.1 Hz), 6.77 (dd, 1H, *J* = 5.1 Hz, *J* = 3.6 Hz), 6.67 (d, 1H, *J* = 3.6 Hz), 6.15 (d, 1H, *J* = 12.2 Hz), 5.51 (d, 1H, *J* = 12.3 Hz), 5.48 (s, 1H), 5.23 (s, 1H), 4.76 (d, 1H, *J* = 14.6 Hz), 4.45 (d, 1H, *J* = 14.6 Hz), 3.37-3.48 (m, 4H), 3.30 (dd, 1H, *J* = 10.9 Hz, *J* = 2.3 Hz), 2.27-2.32 (m, 1H), 1.92-2.00 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.8, 170.6, 153.9, 144.1, 138.6, 136.8, 134.4, 129.9, 128.6 (2C), 128.2, 128.1 (2C), 128.0, 127.4, 127.1, 126.3, 126.0, 125.1, 124.1, 123.9, 117.8, 60.1, 50.5, 45.9, 45.1, 36.7, 24.5; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2924 (C-H), 1714 (C=O), 1630 (NC=O), 1590 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 440.20 (M + H$^+$, 100); **HRMS** (ESI+) calcd. for $C_{28}H_{26}NO_2S$ [M + H]$^+$ 440.1679, found 440.1674.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-6-methyl-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4a

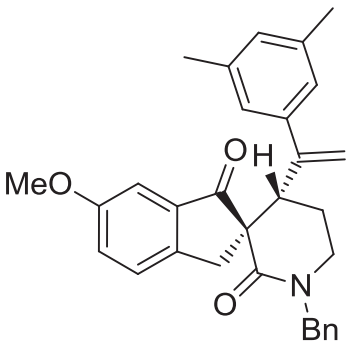


Synthesised from substrate **1b** (69 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4a** was obtained (single diastereomer, 75 mg, 84%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 26:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 4.21 min, minor t_R = 6.47 min (86% *ee*); $[\alpha]_D^{25}$ = –23.4 (*c* 2.1, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.26-7.39 (m, 7H), 7.11 (s, 1H), 6.75 (s, 1H), 6.44 (s, 2H), 5.19 (s, 1H), 4.99 (s, 1H), 4.73 (d, 1H, *J* = 14.6 Hz), 4.56 (d, 1H, *J* = 14.6 Hz), 3.62 (dd, 1H, *J* = 9.9 Hz, *J* = 2.4 Hz), 3.48-3.54 (m, 2H), 3.40 (td, 1H, *J* = 12.2 Hz, *J* = 5.0 Hz), 3.29 (d, 1H, *J* = 16.8 Hz), 2.40 (ddd, 1H, *J* = 12.8 Hz, *J* = 7.7 Hz, *J* = 4.5 Hz), 2.32 (s, 3H), 2.12 (s, 6H), 1.79-1.89 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.0, 170.6, 151.5, 149.3, 141.0, 137.1 (2C), 136.9 136.7, 136.6, 135.8, 128.9, 128.7 (2C), 128.1 (2C), 127.4, 125.5, 125.1 (2C), 124.1, 114.9, 60.4, 50.6, 45.6, 44.5, 36.4, 24.6, 21.1 (2C), 20.9; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2920 (C-H), 1716 (C=O), 1632 (NC=O), 1600 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 472.24 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{31}NNaO_2$ [M + Na]$^+$ 472.2247, found 472.2244.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-6-methoxy-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4b

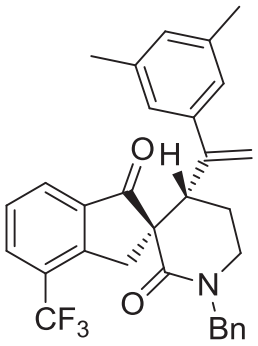


Synthesized from substrate **1c** (72 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4b** was obtained (single diastereomer, 76 mg, 82%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 42:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 4.54 min, minor t_R = 6.35 min (89% *ee*); $[\alpha]_D^{25}$ = –31.0 (*c* 2.8, CH_2Cl_2).

Mp 55 - 57 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.30-7.39 (m, 5H), 7.26 (d, 1H, *J* = 8.0 Hz), 7.13 (dd, 1H, *J* = 8.3 Hz, *J* = 2.5 Hz), 6.73 (s, 1H), 6.69 (d, 1H, *J* = 2.3 Hz), 6.42 (br s, 2H), 5.18 (s, 1H), 5.00 (s, 1H), 4.76 (d, 1H, *J* = 14.6 Hz), 4.54 (d, 1H, *J* = 14.6 Hz), 3.74 (s, 3H), 3.63-3.65 (m, 1H), 3.52 (m, 1H), 3.44 (d, 1H, *J* = 16.8 Hz), 3.37-3.41 (m, 1H), 3.25 (d, 1H, *J* = 16.6 Hz), 2.32-2.36 (m, 1H), 2.13 (s, 6H), 1.87 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.9, 170.7, 159.0, 149.3, 147.1, 140.9, 137.8, 137.1 (2C), 136.9, 129.0, 128.7 (2C), 128.1 (2C), 127.4, 126.5, 125.1 (2C), 124.1, 115.1, 105.2, 60.9, 55.4, 50.6, 45.8, 44.5, 36.0, 24.9, 21.1 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2929 (C-H), 1715 (C=O), 1632 (NC=O), 1600 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 488.24 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{31}NNaO_3$ [M + Na]$^+$ 488.2196, found 488.2198.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-4-(trifluoromethyl)-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4c

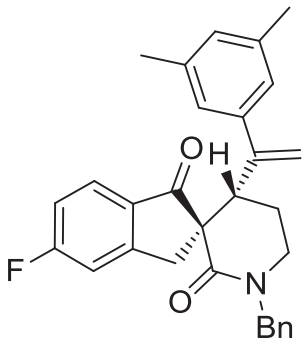


Synthesised from substrate **1d** (79 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4c** was obtained (single diastereomer, 80 mg, 80%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:2). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 28:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 4.10 min, minor t_R = 10.68 min (86% *ee*); $[\alpha]_D^{25}$ = –2.7 (*c* 2.88, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.74 (d, 1H, *J* = 7.5 Hz), 7.30-7.40 (m, 6H), 7.23-7.27 (m, 1H), 6.64 (s, 1H), 6.37 (s, 2H), 5.21 (s, 1H), 5.07 (s, 1H), 4.70 (d, 1H, *J* = 14.6 Hz), 4.60 (d, 1H, *J* = 14.6 Hz), 3.75 (d, 1H, *J* = 11.1 Hz), 3.58-3.62 (m, 1H), 3.55 (d, 2H, *J* = 4.0 Hz), 3.39-3.44 (m, 1H), 2.29 (dd, 1H, *J* = 13.4 Hz, *J* = 2.9 Hz), 2.06 (s, 6H), 1.89-2.01 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.4, 170.4, 151.7, 149.1, 140.2, 137.9, 137.0 (2C), 136.6, 130.6, 130.5, 129.2, 128.8 (2C), 128.1 (2C), 127.6, 127.3, 127.2, 125.4 (2C), 125.2, 115.5, 59.9, 50.7, 46.0, 44.6, 35.4, 25.2), 21.0 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2920 (C-H), 1726 (C=O), 1633 (NC=O), 1596 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 526.21 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{28}F_3NNaO_2$ [M + Na]$^+$ 526.1964, found 526.1968.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-5-fluoro-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4d



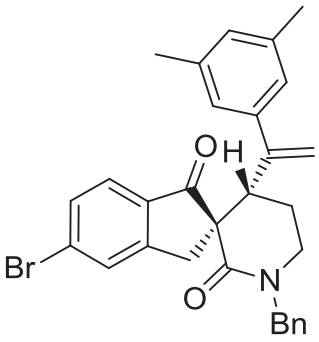
Synthesised from substrate **1e** (70 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4d** was obtained (single diastereomer, 72 mg, 80%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 21:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 4.70 min, minor t_R = 12.89 min (87% *ee*); $[\alpha]_D^{25}$ = –15.3 (*c* 2.8, CH_2Cl_2).

Mp 122 - 126 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.33 (m, 6H), 7.04 (dd, 1H, *J* = 8.4 Hz, *J* = 0.9 Hz), 6.88 (dt, 1H, *J* = 8.7 Hz, *J* = 2.0 Hz), 6.73 (s, 1H), 6.47 (s, 2H), 5.22 (s, 1H), 5.01 (s, 1H), 4.70 (d, 1H, *J* = 14.6 Hz), 4.58 (d, 1H, *J* = 14.6 Hz), 3.66 (dd, 1H, *J* = 10.1 Hz, *J* = 2.0 Hz), 3.49-3.56 (m, 2H), 3.38-3.43 (m, 1H), 3.31 (d, 1H, *J* = 17.2 Hz), 2.35-2.41 (ddd, 1H, *J* = 12.8 Hz, *J* = 7.2 Hz, *J* = 4.2 Hz), 2.13 (s, 6H), 1.85 (dtd, 1H, *J* = 15.1 Hz, *J* = 10.1 Hz, *J* = 5.1 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 203.1, 170.4, 165.8, 157.2, 149.2, 140.6, 137.2 (2C), 136.8, 132.9, 129.2, 128.7 (2C), 128.1 (2C), 127.5, 126.4, 125.1 (2C), 115.3, 115.1, 112.4, 60.4, 50.7, 45.7, 44.4, 36.5, 24.7 19.4 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2921 (C-H), 1719 (C=O), 1632 (NC=O), 1594 (C=C); **MS** (ESI+) *m/z* (rel. intensity

%) 476.21 (M + Na^+, 85); **HRMS** (ESI+) calcd. for $C_{30}H_{28}FNNaO_2$ $[M + Na]^+$ 476.1996, found 476.2000.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-5-bromo-4'-[1-(3,5-dimethylphenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4e

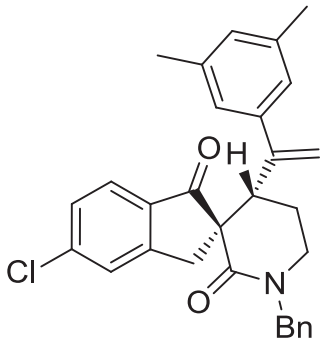


Synthesised from substrate **1f** (81 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4e** was obtained (single diastereomer, 60 mg, 58%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 32:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 5.23 min, minor t_R = 13.95 min (86% *ee*); $[\alpha]_D^{25}$ = +37.7 (*c* 0.98, CH_2Cl_2).

Mp 131 - 135 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.55 (s, 1H), 7.35-7.39 (m, 2H), 7.27-7.32 (m, 4H), 7.10 (d, 1H, *J* = 8.1 Hz), 6.71 (s, 1H), 6.43 (s, 2H), 5.21 (s, 1H), 5.01 (s, 1H), 4.70 (d, 1H, *J* = 14.6 Hz), 4.57 (d, 1H, *J* = 14.6 Hz), 3.66 (dd, 1H, *J* = 10.5 Hz, *J* = 1.5 Hz), 3.52-3.57 (m, 1H), 3.48 (d, 1H, *J* = 17.3 Hz), 3.40 (td, 1H, *J* = 12.2 Hz, *J* = 4.6 Hz), 3.30 (d, 1H, *J* = 17.2 Hz), 2.31-2.37 (m, 1H) 2.12 (s, 6H), 1.86 (ddt, 1H, *J* = 15.6 Hz, *J* = 10.5 Hz, *J* = 5.1 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.0, 170.4, 155.8, 149.2, 140.4, 137.2 (2C), 136.7, 135.4, 130.5, 129.7, 129.1, 128.9, 128.7 (2C), 128.1 (2C), 127.5, 125.3 (2C), 125.1, 115.2, 60.2, 50.7, 45.8, 44.5, 36.3, 24.9, 21.1 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2921 (C-H), 1720 (C=O), 1633 (NC=O), 1597 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 536.14, 538.13 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{28}BrNNaO_2$ $[M + Na]^+$ 536.1196, 538.1177, found 536.1201, 538.1175.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-5-chloro-4'-[1-(3,5-dimethylphenyl) vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4f



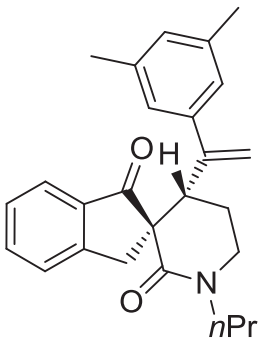
Synthesised from substrate **1g** (73 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4f** was obtained (single diastereomer, 75 mg, 80%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 53:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 4.95 min, minor t_R = 13.48 min (84% *ee*); $[\alpha]_D^{25}$ = +32.0 (*c* 3.35, CH_2Cl_2).

Mp 170 - 174 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.36-7.39 (m, 3H), 7.29-7.33 (m, 3H), 7.13-7.19 (m, 2H), 6.72 (s, 1H), 6.44 (s, 2H), 5.22 (s, 1H), 5.02 (s, 1H), 4.70 (d, 1H, *J* = 14.6 Hz), 4.58 (d, 1H, *J* = 14.6 Hz), 3.67 (dd, 1H, *J* = 10.6 Hz, *J* = 1.8 Hz), 3.52-3.57 (m, 1H), 3.48 (d, 1H, *J* = 17.2 Hz), 3.36-3.43 (m, 1H), 3.31 (d, 1H, *J* = 17.2 Hz), 2.32-2.38 (m, 1H), 2.13 (s, 6H), 1.82-1.91 (m, 1H); **^{13}C NMR**

(100 MHz, $CDCl_3$) δ_C 203.7, 170.4, 155.7, 149.2, 140.9, 140.5, 137.2 (2C), 136.7, 135.0, 129.2, 128.7 (2C), 128.1 (2C), 127.7, 127.5, 125.9, 125.3 (2C), 125.1, 115.2, 60.3, 50.7, 45.8, 44.5, 36.4, 24.8, 21.1 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2920 (C-H), 1719 (C=O), 1632 (NC=O), 1600 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 492.19 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{30}H_{28}ClNNaO_2$ $[M + Na]^+$ 492.1701, found 492.1700.

Synthesis and characterisation of (2*R*,4'*S*)-4'-[1-(3,5-dimethylphenyl)vinyl]-1'-propyl-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4g

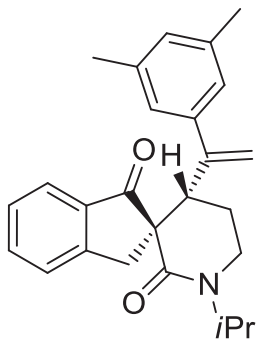


Synthesised from substrate **1h** (57 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4g** was obtained (single diastereomer, 56 mg, 72%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 40:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 3.81 min, minor t_R = 11.82 min (89% *ee*), $[\alpha]_D^{25}$ = –3.2 (*c* 2.4, CH_2Cl_2).

Mp 106 - 109 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.47-7.51 (m, 1H), 7.36 (d, 1H, *J* = 7.7 Hz), 7.29 (t, 1H, *J* = 8.3 Hz), 7.17 (t, 1H, *J* = 7.4 Hz), 6.72 (s, 1H), 6.46 (s, 2H), 5.22 (s, 1H), 5.02 (s, 1H), 3.57-3.63 (m, 2H), 3.43-3.52 (m, 2H), 3.33-3.39 (m, 2H), 3.29 (d, 1H, *J* = 17.0 Hz), 2.43-2.49 (m, 1H), 2.11 (s, 6H), 1.83-1.93 (m, 1H), 1.63 (qt, 2H, *J* = 14.2 Hz, *J* = 7.0 Hz), 0.93 (t, 3H, *J* = 7.4 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.1, 170.0, 154.3, 149.4, 140.9, 137.1 (2C), 136.3, 134.3, 129.1, 126.8, 125.7, 125.1 (2C), 124.1, 114.8, 59.9, 49.4, 46.3, 44.5, 36.7, 24.6, 21.1 (2C), 20.2, 11.3; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2929 (C-H), 1718 (C=O), 1632 (NC=O), 1588 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 410.23 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{26}H_{29}NNaO_2$ $[M + Na]^+$ 410.2091, found 410.2088.

Synthesis and characterisation of (2*R*,4'*S*)-4'-[1-(3,5-dimethylphenyl)vinyl]-1'-isopropyl-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4h

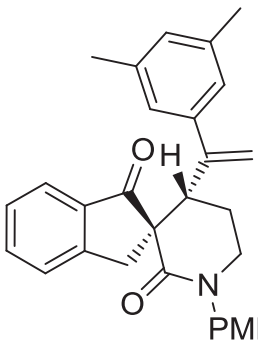


Synthesised from substrate **1i** (57 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4h** was obtained (single diastereomer, 65 mg, 84%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 2:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 29:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 3.74 min, minor t_R = 5.52 min (86% *ee*); $[\alpha]_D^{25}$ = +0.4 (*c* 3.9, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.46-7.50 (m, 1H), 7.35 (d, 1H, *J* = 7.7 Hz), 7.28 (d, 1H, *J* = 7.8 Hz), 7.15 (t, 1H, *J* = 7.4 Hz), 6.71 (s, 1H), 6.45 (s, 2H), 5.21 (s, 1H), 5.02 (s, 1H), 4.83 (sept., 1H, *J* = 6.8 Hz), 3.58 (dd, 1H, *J* = 2.0 Hz, *J* = 10.1 Hz), 3.41-3.49 (m, 3H), 3.28 (d, 1H, *J* = 17.0 Hz), 2.42-2.49 (m, 1H), 2.10 (s, 6H), 1.78-1.88 (m, 1H), 1.21 (d, 3H, *J* = 6.9 Hz), 1.14 (d, 3H, *J* = 6.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.2, 169.7, 154.3, 149.6, 140.9, 137.1 (2C), 136.4, 134.3, 129.1, 126.8, 125.7, 125.1 (2C), 124.1, 114.7, 60.2, 44.8, 44.2, 39.3, 36.9, 24.8, 21.1 (2C), 19.3, 19.0; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2923 (C-H), 1718 (C=O), 1624 (NC=O), 1586 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 410.24 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{26}H_{29}NNaO_2$ [M + Na]$^+$ 410.2091, found 410.2097.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4i

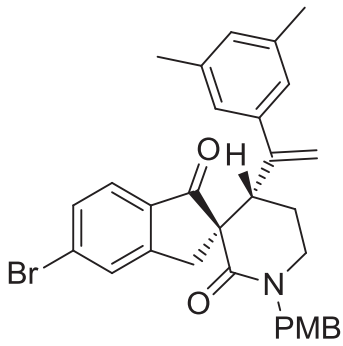


Synthesised from substrate **1j** (72 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4i** was obtained (single diastereomer, 67 mg, 72%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 41:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ= 230 nm, major t_R = 5.02 min, minor t_R = 16.60 min (88% *ee*); $[\alpha]_D^{25}$ = –13.2 (*c* 2.26, CH_2Cl_2).

Mp 135 - 139 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.52 (t, 1H, *J* = 7.4 Hz), 7.38 (d, 1H, *J* = 7.6 Hz), 7.33 (d, 1H, *J* = 7.6 Hz), 7.25-7.27 (m, 2H), 7.19 (t, 1H, *J* = 7.4 Hz), 6.90 (d, 2H, *J* = 8.5 Hz), 6.73 (s, 1H), 6.44 (s, 2H), 5.19 (s, 1H), 4.99 (s, 1H), 4.64 (d, 1H, *J* = 14.4 Hz), 4.51 (d, 1H, *J* = 14.4 Hz), 3.82 (s, 3H), 3.62 (dd, 1H, *J* = 10.0 Hz, *J* = 2.5 Hz), 3.55 (d, 1H, *J* = 17.0 Hz), 3.46-3.52 (m, 1H), 3.37-3.42 (m, 1H), 3.32 (d, 1H, *J* = 17.0 Hz), 2.37-2.43 (m, 1H), 2.11 (s, 6H), 1.78-1.88 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 205.0, 170.4, 159.0, 154.2, 149.3, 140.8, 137.1 (2C), 136.3, 134.4, 129.5 (2C), 129.1, 129.0, 126.9, 125.8, 125.1 (2C), 124.2, 114.9, 114.0 (2C), 60.0, 55.3, 50.1, 45.4, 44.4, 36.8, 24.6, 21.1 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2930 (C-H), 1955 (C=C=C), 1717 (C=O), 1630 (C=O); **MS** (ESI+) *m/z* (rel. intensity %) 488.24 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{31}NNaO_3$ [M + Na]$^+$ 488.2196, found 488.2191.

Synthesis and characterisation of (2*R*,4'*S*)-1'-benzyl-5-bromo-4'-[1-(3,5-dimethylphenyl) vinyl]-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4j

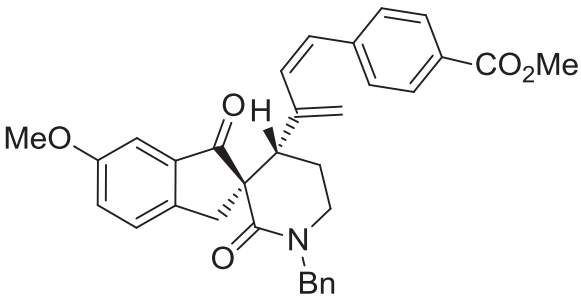


Synthesised from substrate **1k** (88 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4j** was obtained (single diastereomer, 78 mg, 72%) as a colourless solid after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 41:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 7.05 min, minor t_R = 15.30 min (81% *ee*); $[\alpha]_D^{25}$ = –33.5 (*c* 1.68, CH_2Cl_2).

Mp 124 - 127 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.54 (s, 1H), 7.24-7.31 (m, 3H), 7.10 (d, 1H, *J* = 8.1 Hz), 6.90 (d, 2H, *J* = 8.6 Hz), 6.71 (s, 1H), 6.43 (s, 2H), 5.20 (s, 1H), 5.00 (s, 1H), 4.63 (d, 1H, *J* = 14.4 Hz), 4.49 (d, 1H, *J* = 14.4 Hz), 3.82 (s, 3H), 3.63-3.65 (m, 1H), 3.50-3.55 (m, 1H), 3.46 (d, 1H, *J* = 16.4 Hz), 3.36-3.45 (m, 1H), 3.28 (d, 1H, *J* = 17.2 Hz), 2.30-2.35 (m, 1H), 2.12 (s, 6H), 1.79-1.89 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 204.0, 170.2, 159.1, 155.9, 149.3, 144.4, 137.2, 135.4, 130.5 (2C), 129.7, 129.5 (2C), 129.1, 128.9, 128.8, 125.3 (2C), 125.1, 115.1, 114.1 (2C), 60.2, 55.3, 50.1, 45.6, 44.5, 36.3, 24.9, 21.1 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2920 (C-H), 1719 (C=O), 1631 (NC=O), 1597 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 566.15, 568.15 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{30}BrNNaO_3$ $[M + Na]^+$ 566.1301, 568.1283, found 566.1297, 568.1284.

Synthesis and characterisation of methyl 4-((*Z*)-3-((2*R*,4'*S*)-1'-benzyl-6-methoxy-1,2'-dioxo-1,3-dihydrospiro[indene-2,3'-piperidin]-4'-yl)buta-1,3-dien-1-yl)benzoate 4k



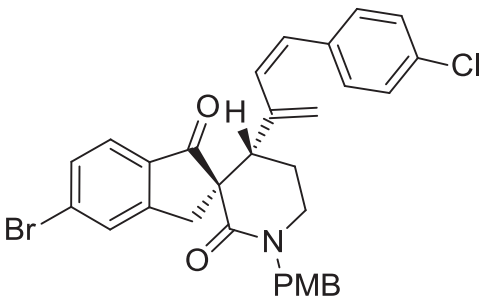
Synthesised from substrate **1c** (73 mg, 0.20 mmol) and (*Z*)-methyl 4-(2-iodovinyl)benzoate (86 mg, 0.30 mmol) according to the general procedure. Compound **4k** was obtained (single diastereomer, 59 mg, 81%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 18:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 70:30, 1.0 mL/min, λ = 230 nm, major t_R = 11.80 min, minor t_R = 20.80 min (76% *ee*); $[\alpha]_D^{25}$ = –13.9 (*c* 0.54, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.72-7.74 (m, 2H), 7.25-7.36 (m, 6H), 7.18 (d, 1H, *J* = 2.5 Hz), 7.10-7.13 (m, 1H), 6.99-7.01 (m, 2H), 6.19 (d, 1H, *J* = 12.5 Hz), 5.79 (d, 1H, *J* = 12.5 Hz), 5.12 (s, 1H), 5.00 (s, 1H), 4.77 (d, 1H, *J* = 14.6 Hz), 4.40 (d, 1H, *J* = 14.6 Hz), 3.90 (s, 3H), 3.80 (s, 3H), 3.28-3.39 (m, 4H), 3.25 (dd, 1H, *J* = 11.6 Hz, *J* = 2.1 Hz), 2.06-2.11 (m, 1H), 1.88-1.96 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 205.1, 170.6, 166.7, 159.6, 146.8, 143.2, 141.6, 138.0, 136.7, 132.3, 129.8, 129.7, 129.3 (2C), 128.7 (2C), 128.4, 128.2, 128.1 (2C), 127.4, 127.0, 124.5, 117.9, 105.5, 60.8, 55.6, 52.0

50.4, 45.9, 44.7, 35.7, 29.7; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2924 (C-H), 1715 (C=O), 1632 (NC=O), 1590 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 544.23 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{33}H_{31}NNaO_5$ [M + Na]$^+$ 544.2094, found 544.2094.

Synthesis and characterisation of (2*R*,4'*S*)-5-bromo-4'-((*Z*)-4-(4-chlorophenyl)buta-1,3-dien-2-yl)-1'-(4-methoxybenzyl)spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4l

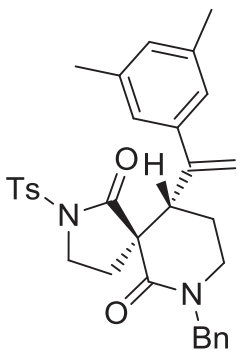


Synthesised from substrate **1k** (88 mg, 0.20 mmol) and (*Z*)-1-chloro-4-(2-iodovinyl)benzene (79 mg, 0.30 mmol) according to the general procedure. Compound **4l** was obtained (single diastereomer, 91 mg, 79%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:1). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 16:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 70:30, 1.0 mL/min, λ = 230 nm, major t_R = 11.43 min, minor t_R = 16.76 min (71% *ee*); $[\alpha]_D^{25}$ = –18.8 (*c* 0.90, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.58 (d, 1H, *J* = 8.2 Hz), 7.50 (d, 1H, *J* = 0.8 Hz), 7.43-7.45 (m, 1H), 7.20 (d, 2H, *J* = 8.6 Hz), 7.05-7.08 (m, 2H), 6.86-6.92 (m, 4H), 6.06 (d, 1H, *J* = 12.5 Hz), 5.67 (d, 1H, *J* = 12.5 Hz), 5.19 (s, 1H), 5.03 (s, 1H), 4.67 (d, 1H, *J* = 14.4 Hz), 4.33 (d, 1H, *J* = 14.4 Hz) 3.81 (s, 3H), 3.20-3.42 (m, 5H), 2.08-2.13 (m, 1H), 1.83-1.92 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 204.1, 170.1, 159.1, 155.4, 143.4, 135.7, 134.9, 132.9, 131.2, 130.9, 130.4, 129.8, 129.6 (3C), 129.5 (2C), 128.7, 128.2 (2C), 125.5, 117.7, 114.0 (2C), 60.2, 55.3, 49.8, 45.6, 44.7, 36.0, 24.6; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2931 (C-H), 1717 (C=O), 1631 (NC=O), 1596 (C=C); **MS** (ESI+) *m/z* (rel. intensity %) 598.10, 600.11 (M + Na$^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{27}BrClNNaO_3$ [M + Na]$^+$ 598.0755, 600.0735 found 598.0745, 600.0718.

Synthesis and characterisation of (5*S*,10*S*)-7-benzyl-10-[1-(3,5-dimethylphenyl)vinyl]-2-[(4-methylphenyl)sulfonyl]-2,7-diazaspiro[4.5]decane-1,6-dione 4m



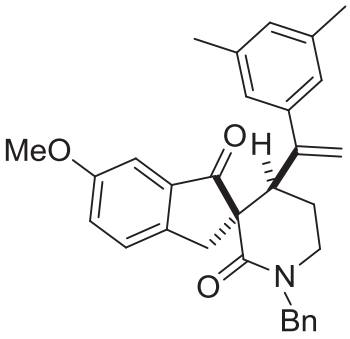
Synthesised from substrate **1l** (88 mg, 0.20 mmol) and 1-iodo-3,5-dimethylbenzene (70 mg, 0.30 mmol) according to the general procedure. Compound **4m** was obtained (single diastereomer, 65 mg, 60%) as a colourless oil after purification by flash column chromatography on silica gel (PE/EtOAc 1:2). Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed a 33:1 dr.

The *ee* was determined by HPLC analysis using a Chiralcel AD column, hexane/isopropanol 60:40, 1.0 mL/min, λ = 230 nm, major t_R = 5.72 min, minor t_R = 8.07 min (83% *ee*); $[\alpha]_D^{25}$ = –23.4 (*c* 1.80, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.89 (d, 2H, *J* = 8.3 Hz), 7.26-7.31 (m, 5H), 7.07-7.09 (m, 2H), 6.94 (s, 1H), 6.87 (s, 2H), 5.36 (s, 1H), 4.80 (s, 1H), 4.68 (d, 1H, *J* = 14.7 Hz), 4.31 (d, 1H, *J* = 14.8 Hz), 4.05 (q, 1H, *J* = 8.3 Hz), 3.91 (dt, 1H, *J* = 8.9 Hz, *J* = 2.6 Hz), 3.43 (t, 1H, *J* = 4.8 Hz), 3.27-3.34 (m, 1H), 3.17-3.23 (m, 1H), 2.64-2.72 (m, 2H), 2.40 (s, 3H), 2.32 (s, 6H), 2.18 (td, 1H, *J* = 13.3 Hz, *J* = 8.6 Hz), 1.48-1.56 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 172.9, 168.5, 147.3, 144.9, 141.0, 138.1 (2C), 136.4, 134.6, 129.8, 129.5 (2C), 128.6 (2C), 128.1 (2C), 127.7 (2C), 127.4, 124.5 (2C), 114.6, 55.8, 50.5, 45.8, 44.2, 44.1, 28.5, 22.6, 21.7, 21.3 (2C); **FT-IR** ν_{max}(NaCl)/cm^{-1} 2950 (C-H), 1720 (NC=O), 1638 (NC=O), 1359 (SO_2), 1112 (SO_2); **MS** (ESI+) *m/z* (rel. intensity %) 565.24 (M + Na^+, 100); **HRMS** (ESI+) calcd. for $C_{32}H_{34}N_2NaO_4S$ $[M + Na]^+$ 565.2137, found 565.2138.

6. Synthesis of diastereomer 4b′

Synthesis and characterisation of *rac*-(2*R*,4'*R*)-1'-benzyl-4'-[1-(3,5-dimethylphenyl)vinyl]-6-methoxy-2'*H*-spiro[indene-2,3'-piperidine]-1,2'(3*H*)-dione 4b′

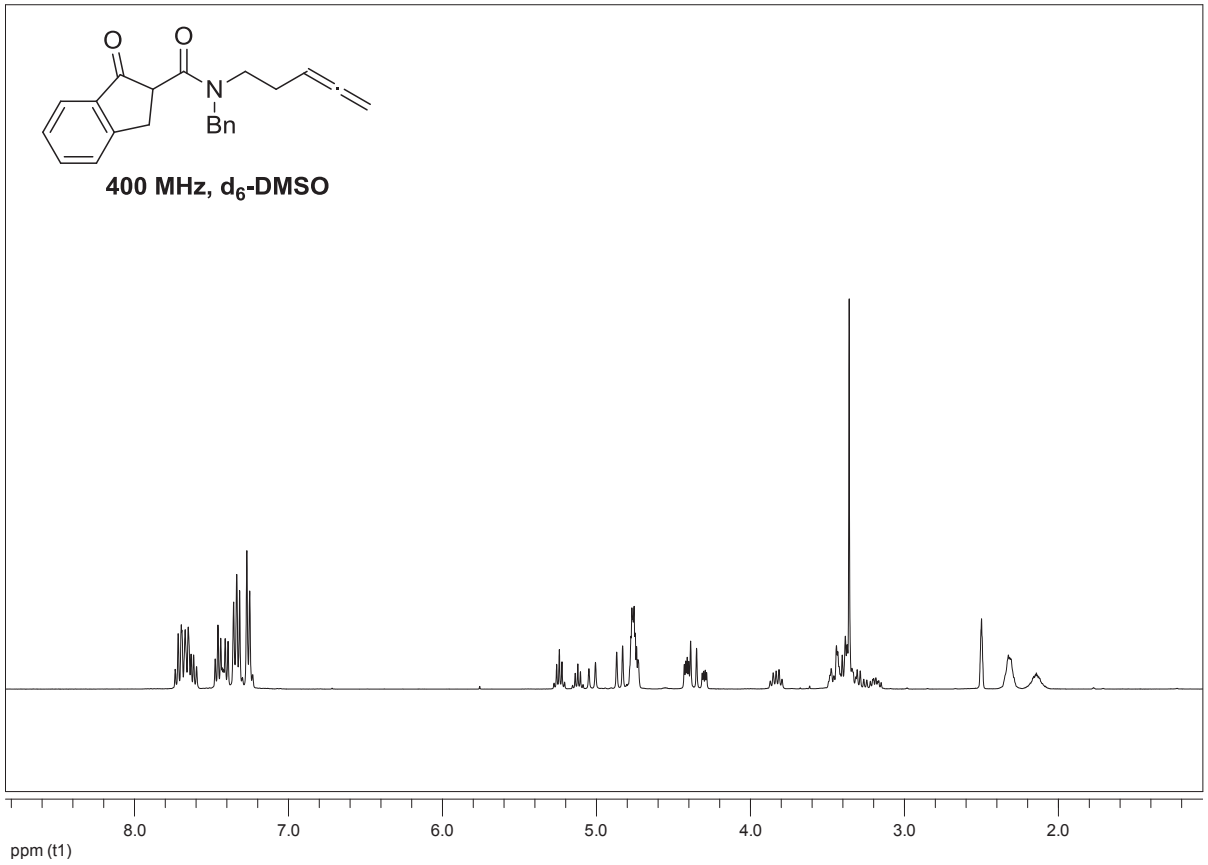


To a solution of **1c** (42 mg, 0.160 mmol) in dioxane (0.30 mL) was added LiHMDS (1.0 M in cyclohexanes, 0.14 mL, 0.140 mmol) at room temperature. After 20 minutes a solution of 1-iodo-3,5-dimethylbenzene (40 mg, 0.170 mmol) and Pd(dppf)Cl_2 (10 mg, 0.012 mmol) in 1,4-dioxane (0.30 mL) was added and the reaction mixture was stirred at 90 °C for 16 h. The reacton mixture was cooled to room temperature and concentrated. The crude residue (dr 3:1 **4b**:**4b′**) was purified by flash column chromatography on silica gel (PE/EtOAc 4:1 to 1:1) to afford **4b′** (10 mg, 19%) as a yellow oil. $[\alpha]_D^{25}$ = –8.0 (*c* 0.30, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.34-7.41 (m, 4H), 7.27-7.33 (m, 1H), 7.08-7.13 (m, 2H), 6.90-6.95 (m, 1H), 6.85 (s, 1H), 6.34 (br s, 2H), 4.92-5.03 (m, 3H), 4.38 (d, 1H, *J* = 14.8 Hz), 3.86 (s, 3H), 3.71 (d, 1H, *J* = 16.7 Hz), 3.47-3.54 (m, 2H), 3.32 (dd, 1H, *J* = 13.4 Hz, *J* = 2.4 Hz), 3.07-3.20 (m, 1H, *J* = 11.2 Hz, *J* = 6.8 Hz), 2.56 (d, 1H, *J* = 16.7 Hz), 2.19 (s, 6H), 1.81-1.89 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 204.7, 169.4, 159.3, 148.6, 148.1, 143.5, 137.4, 137.1 (2C), 136.9, 129.0, 128.7 (2C), 127.9 (2C), 127.3, 126.7, 124.4 (2C), 124.0 (2C), 116.4, 104.9, 61.7, 55.6, 50.8, 46.8 (2C), 38.0, 24.7, 21.2; **FT-IR** ν_{max}(NaCl)/cm^{-1} 2956 (C-H), 1713 (C=O), 1628 (NC=O); **MS** (ESI+) *m/z* (rel. intensity %) 466.30 ($M + H^+$, 90), 488.29 ($M + Na^+$, 100); **HRMS** (ESI+) calcd. for $C_{31}H_{31}NNaO_3$ $[M + Na]^+$ 488.2196, found 488.2183.

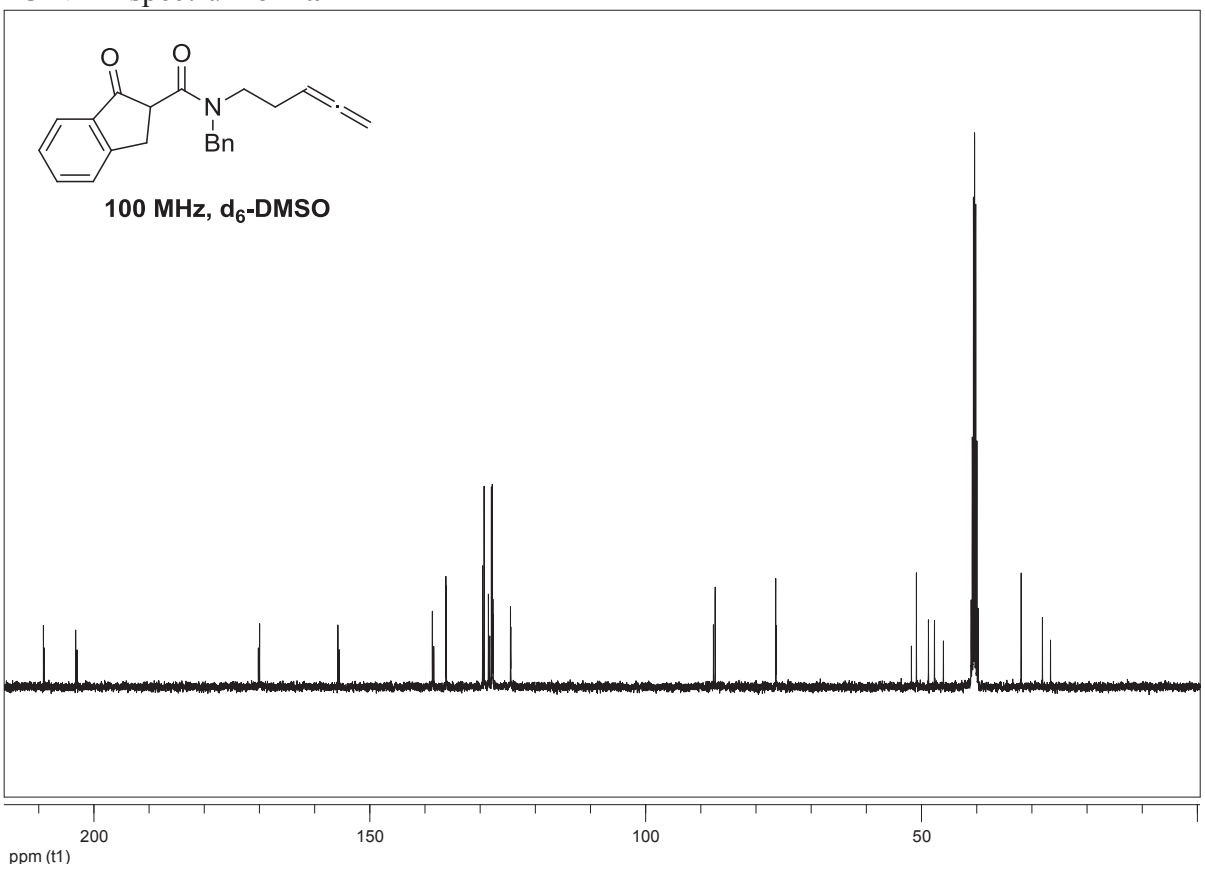
7. References

[1] M. Korner, M. Hiersemann, *Org. Lett.* **2007**, *9*, 4979.
[2] N. A. Petasis, I. A. Zavialov, *Tetrahedron Lett*, **1996**, *37*, 567.
[3] L. L. W. Cheung, A. K. Yudin, *Org. Lett.* **2009**, *11*, 1281.
[4] Y. Hirai, T. Terada, T. Yamazaki, T. Momose, *J. Chem. Soc., Perkin Trans 1*, **1992**, 509.
[5] M. Li, D. J. Dixon, *Org. Lett.* **2010**, *12*, 3784.
[6] S. E. Denmark, N. Nakajima, O. J.-C. Nicaise, A.-M. Faucher, J. P. Edwards, *J. Org. Chem.* **1995**, *60*, 4884.

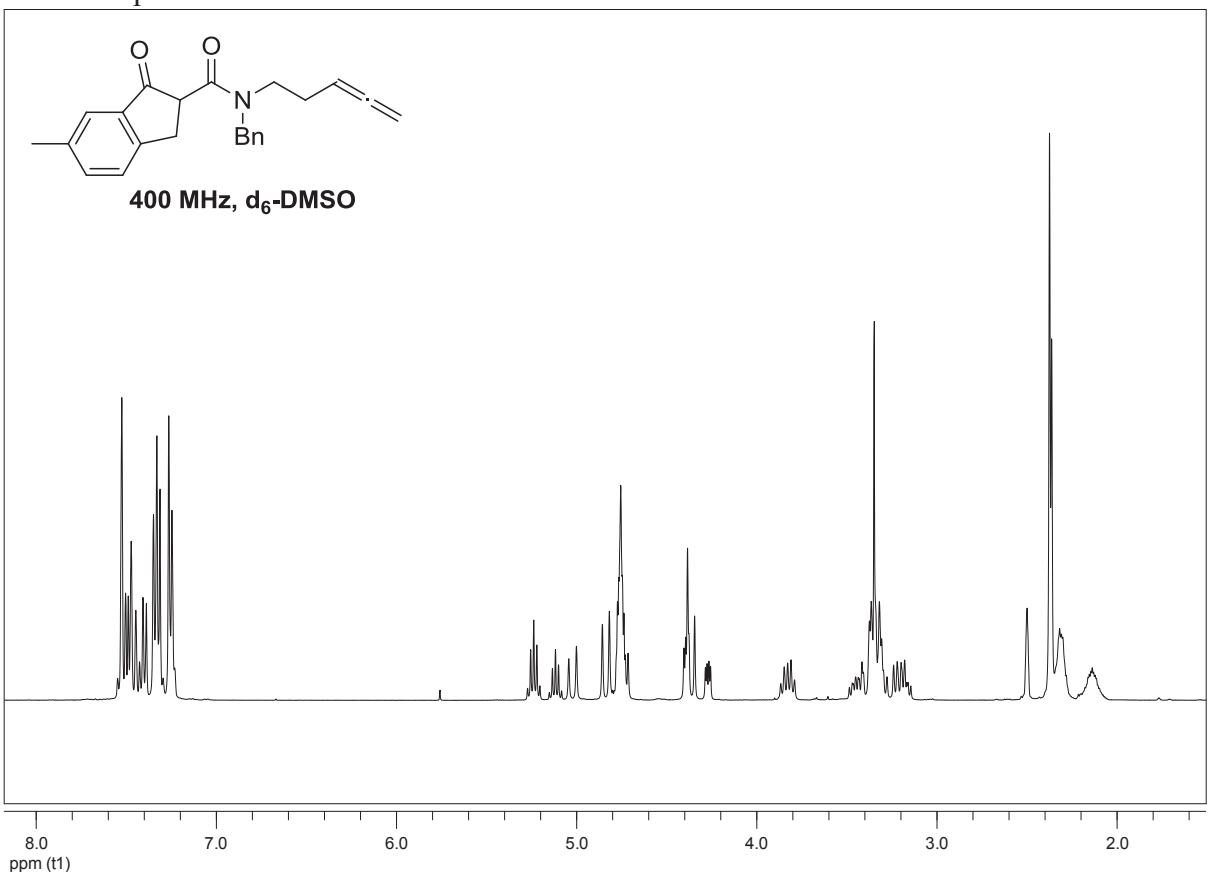
^{1}H NMR spectrum of **1a**



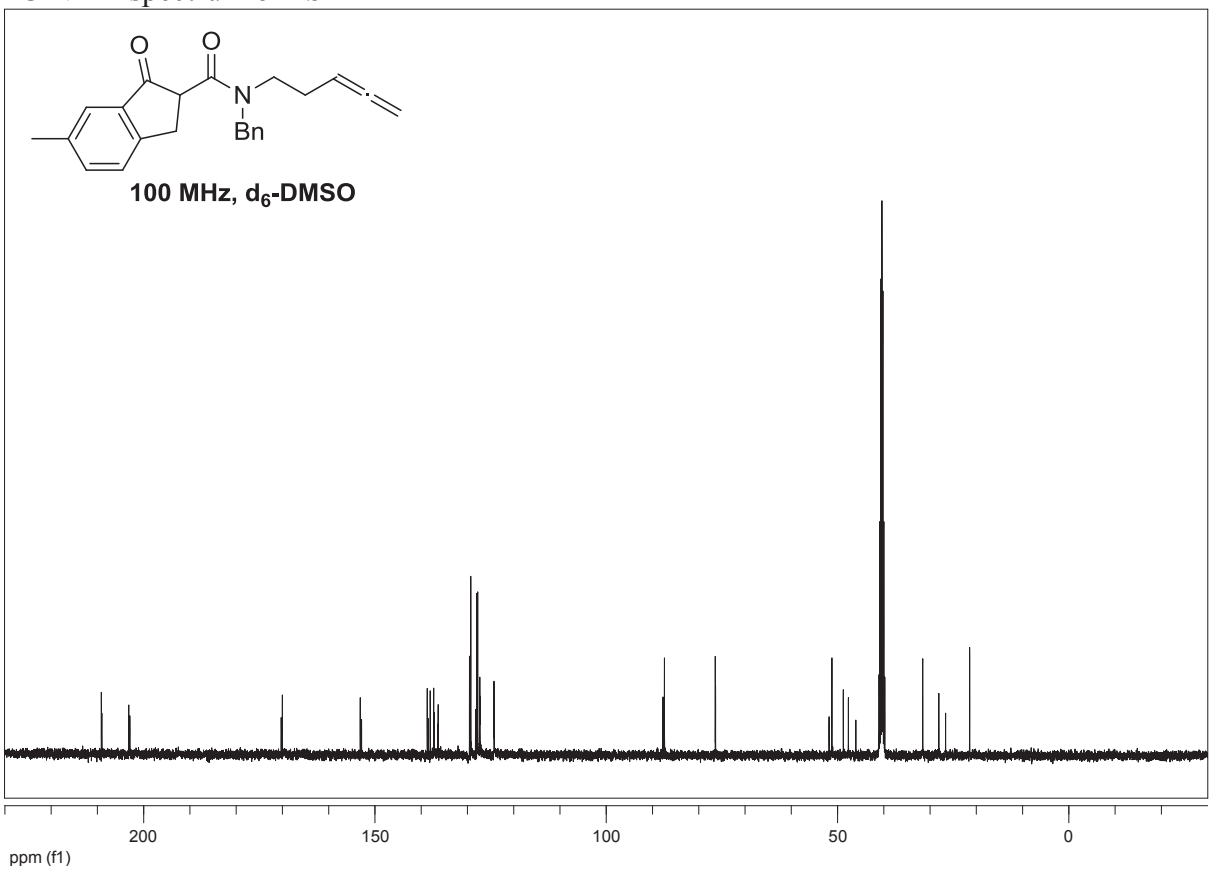
^{13}C NMR spectrum of **1a**



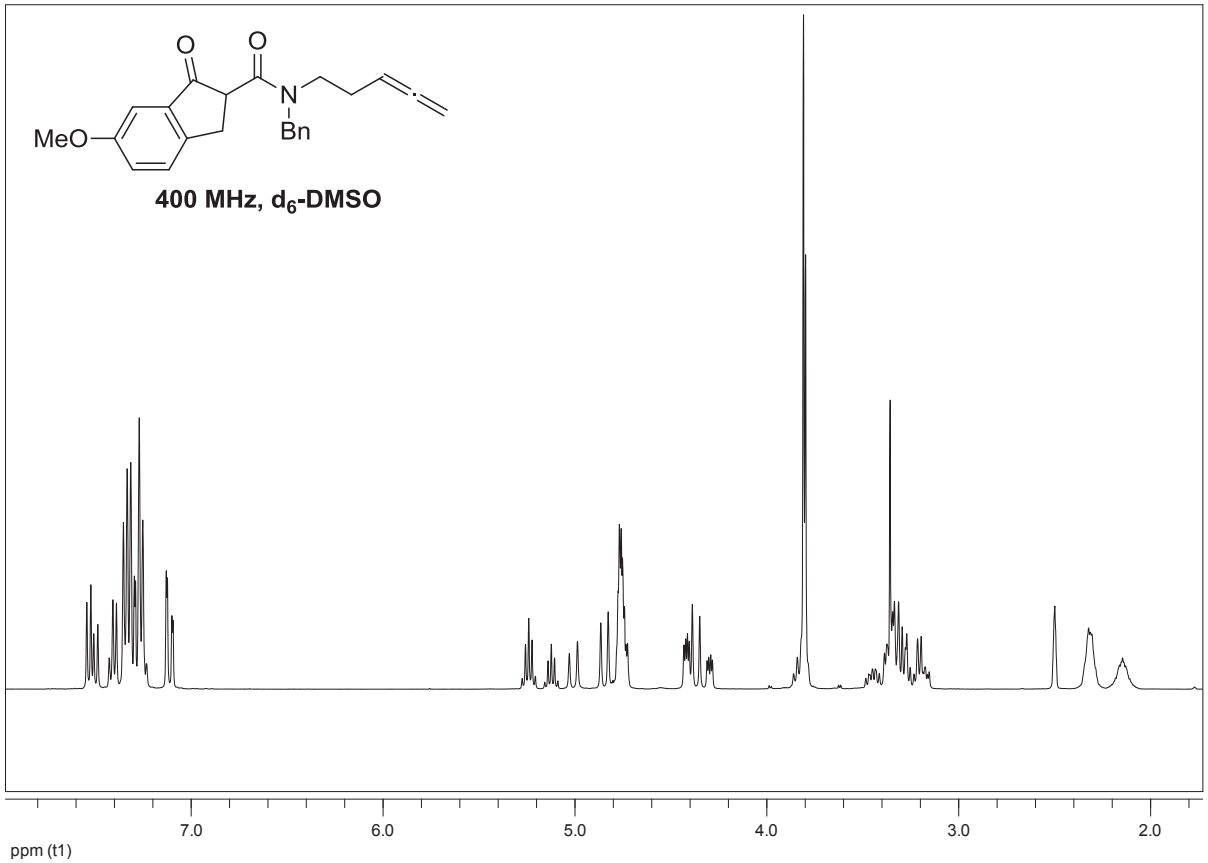
^{1}H NMR spectrum of **1b**



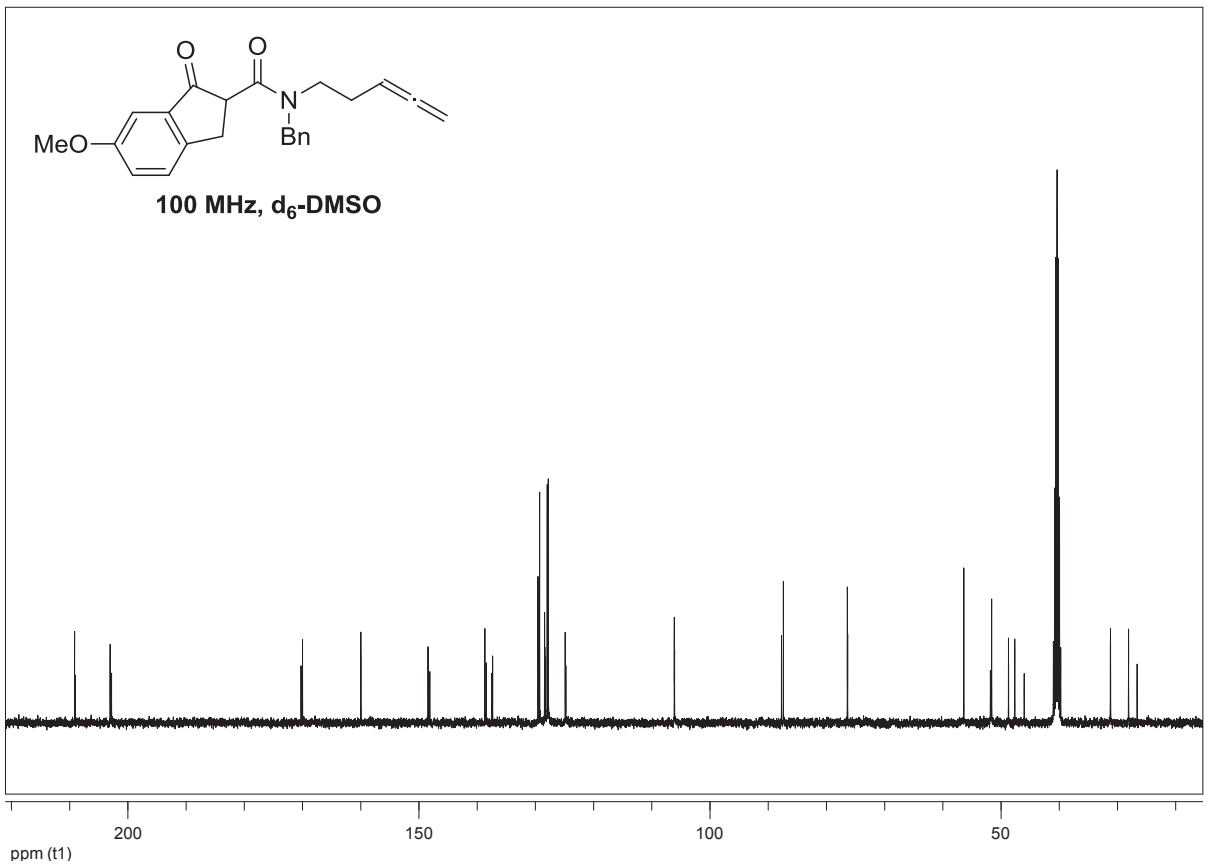
^{13}C NMR spectrum of **1b**



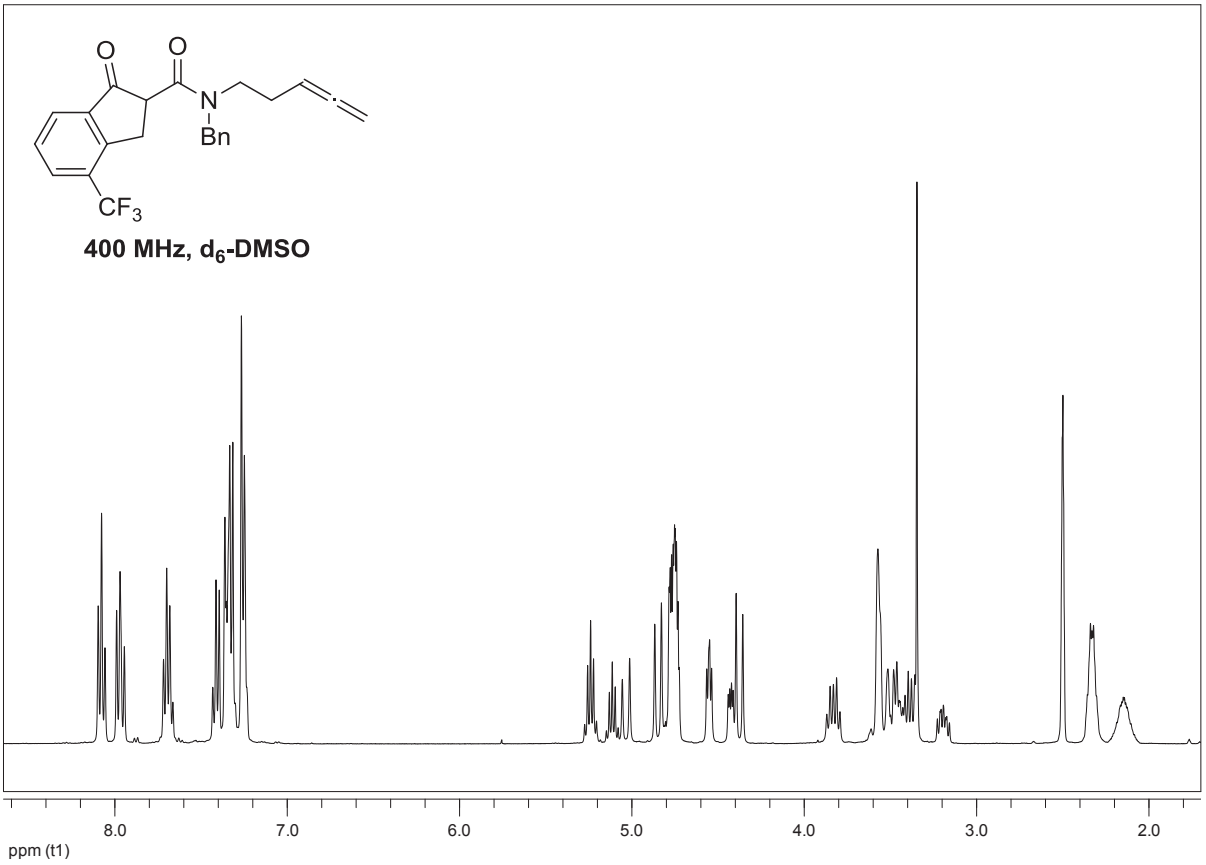
^{1}H NMR spectrum of **1c**



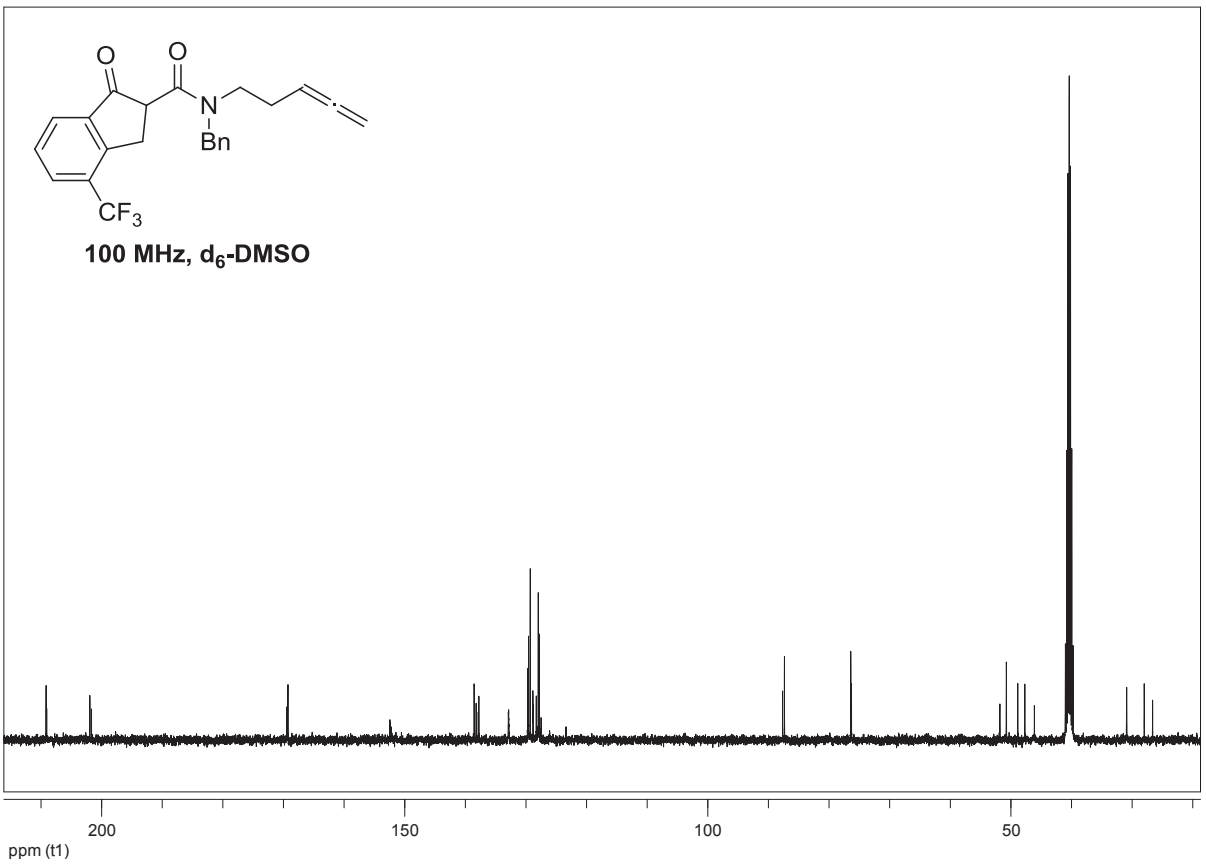
^{13}C NMR spectrum of **1c**



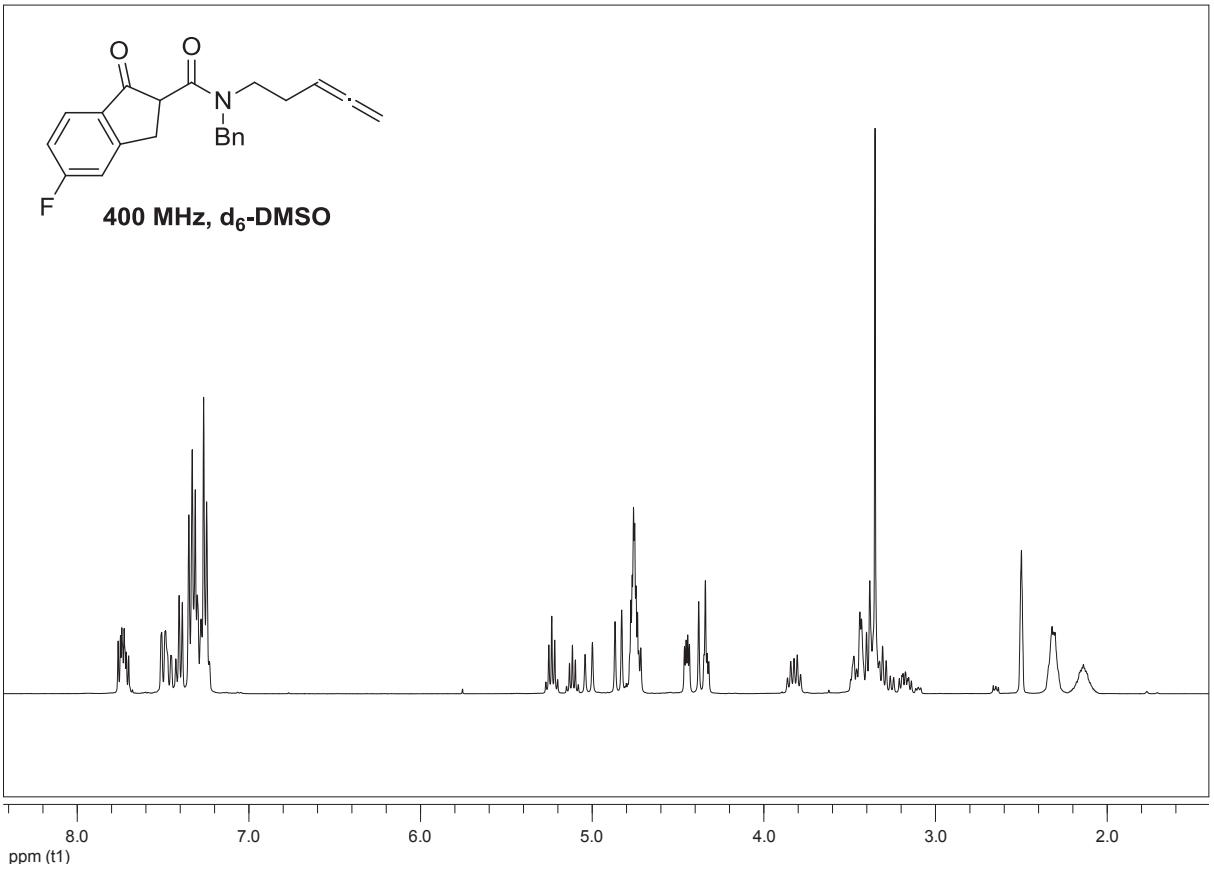
^{1}H NMR spectrum of **1d**



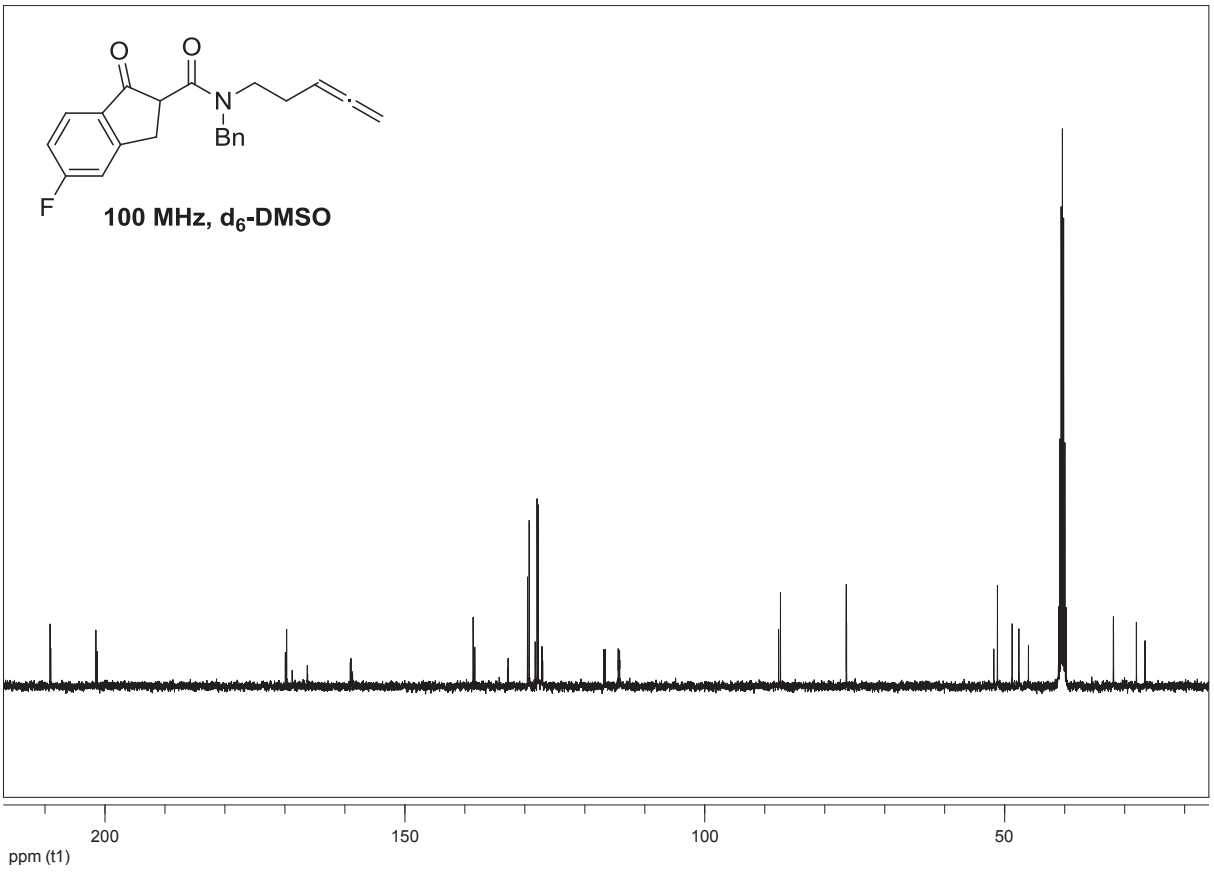
^{13}C NMR spectrum of **1d**



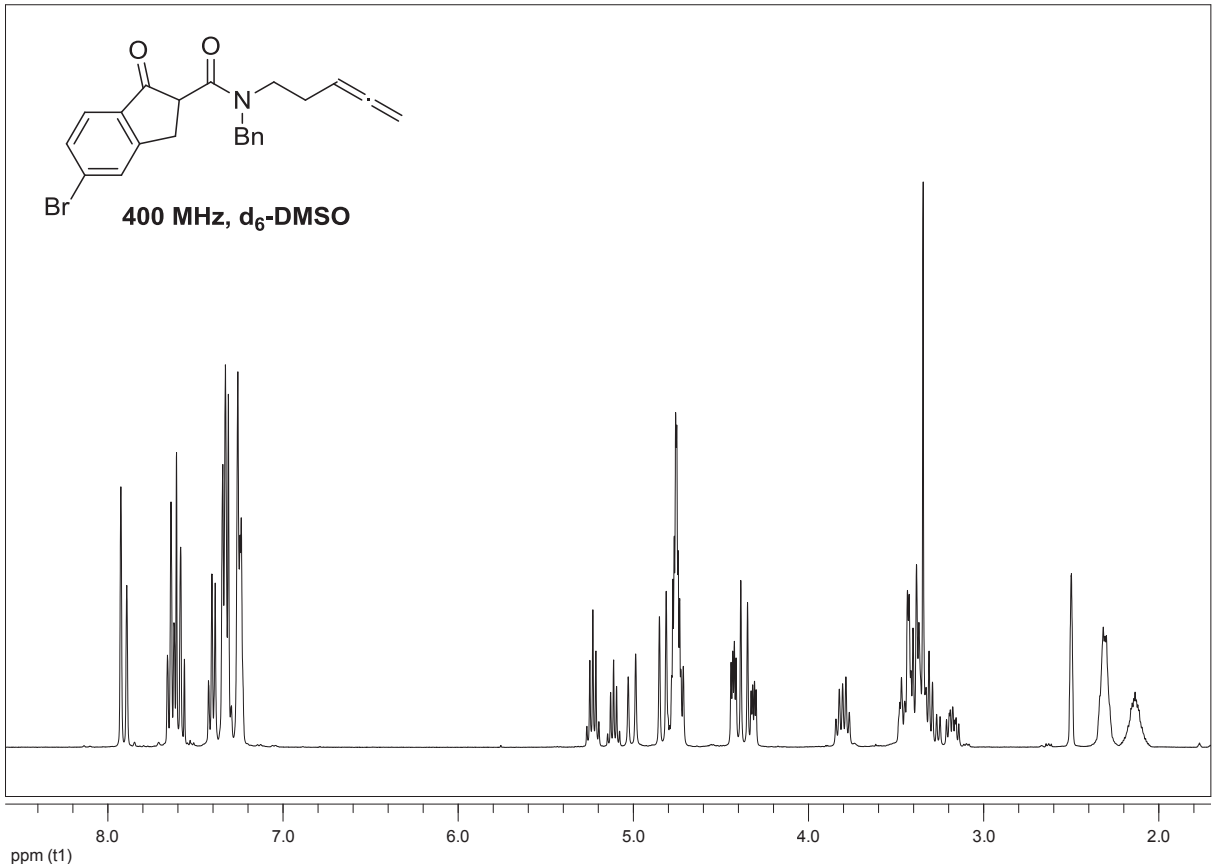
^{1}H NMR spectrum of **1e**



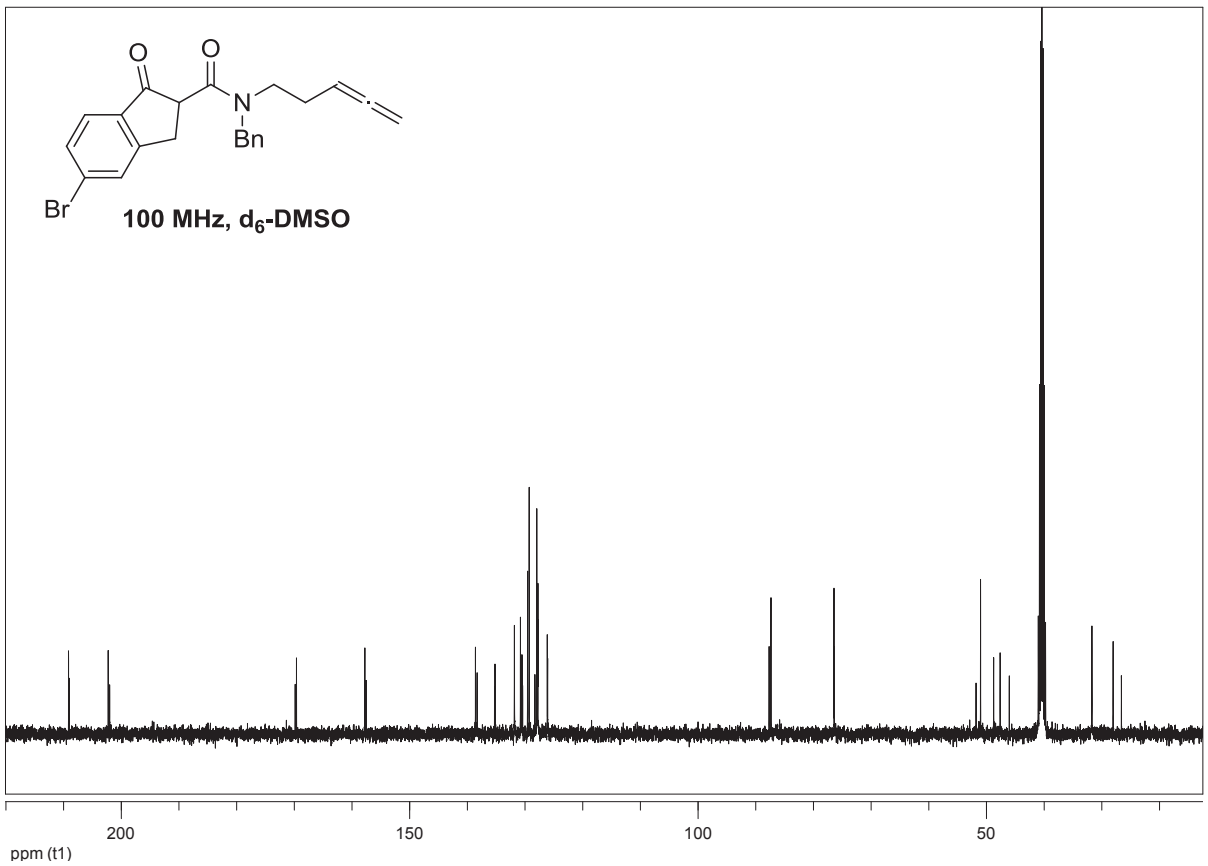
^{13}C NMR spectrum of **1e**



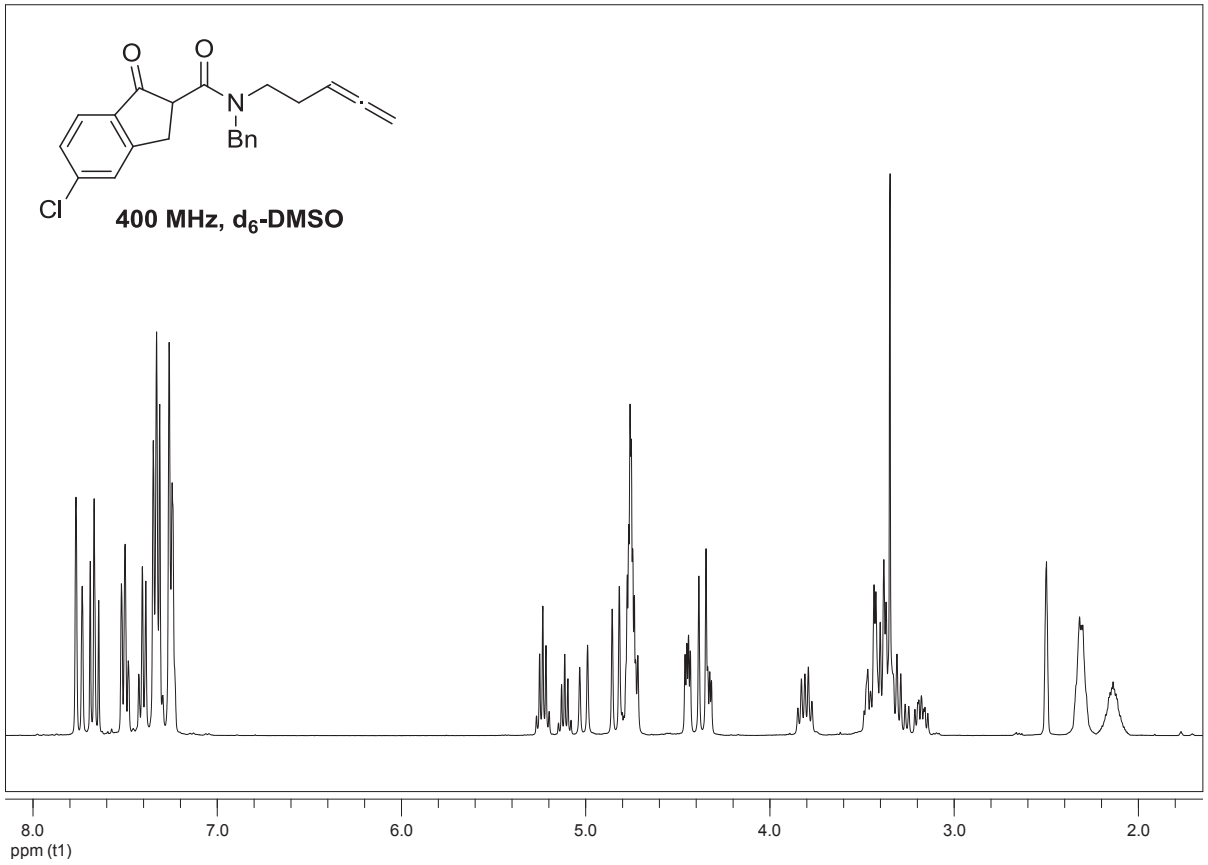
^{1}H NMR spectrum of **1f**



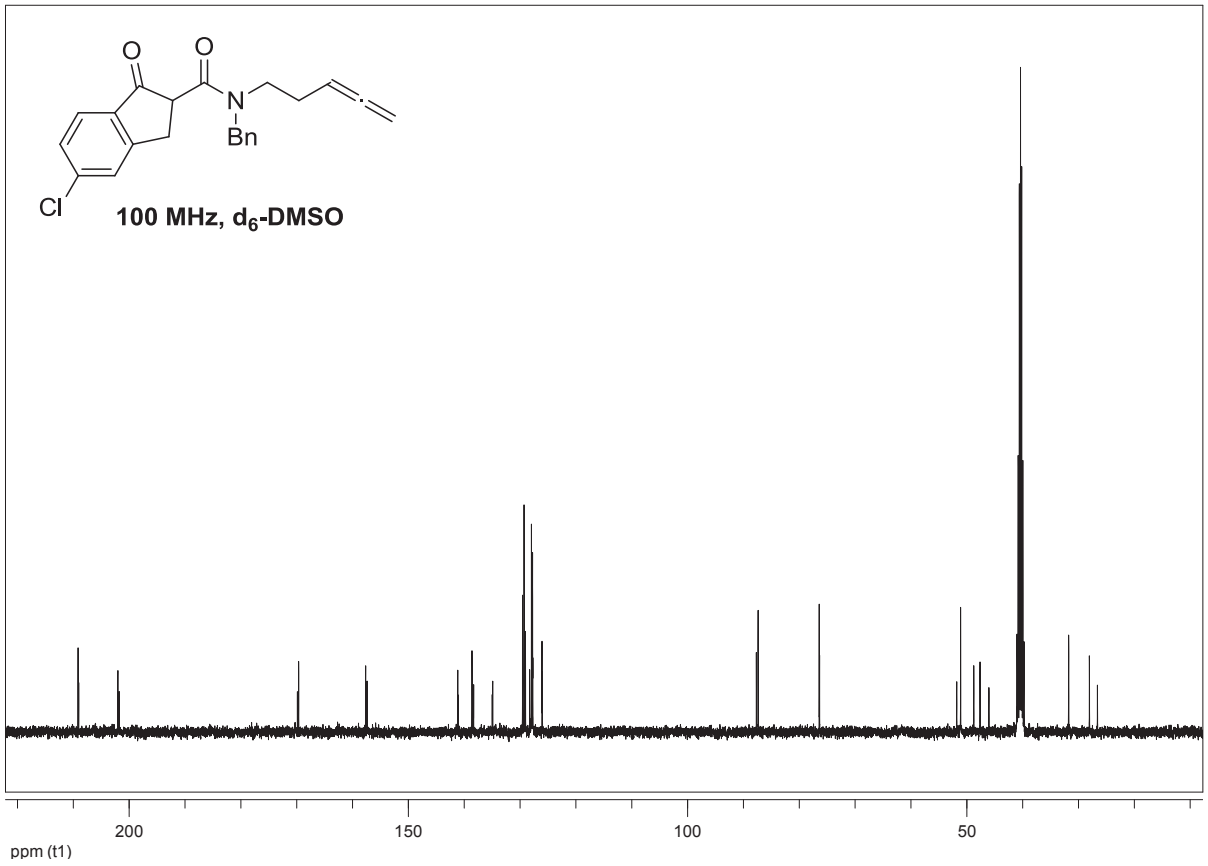
^{13}C NMR spectrum **1f**



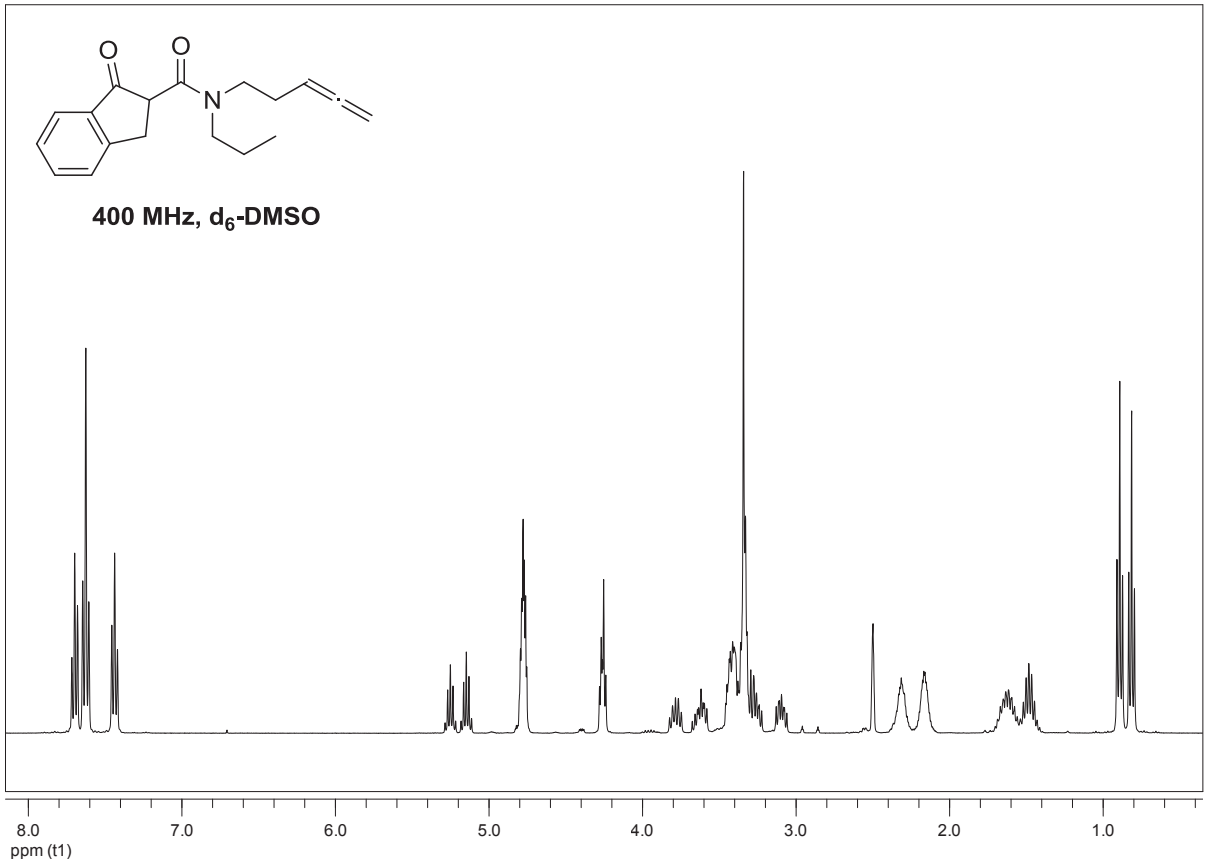
^{1}H NMR spectrum of **1g**



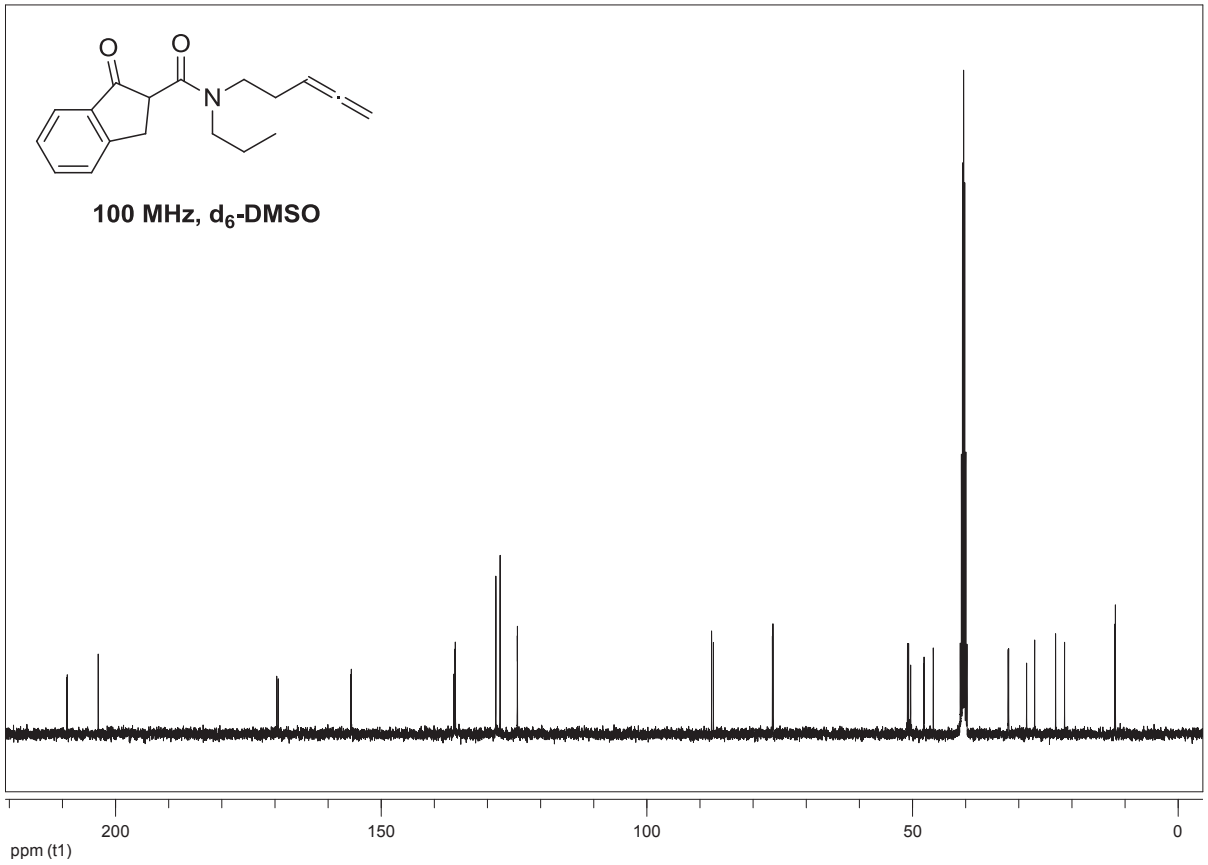
^{13}C NMR spectrum of **1g**



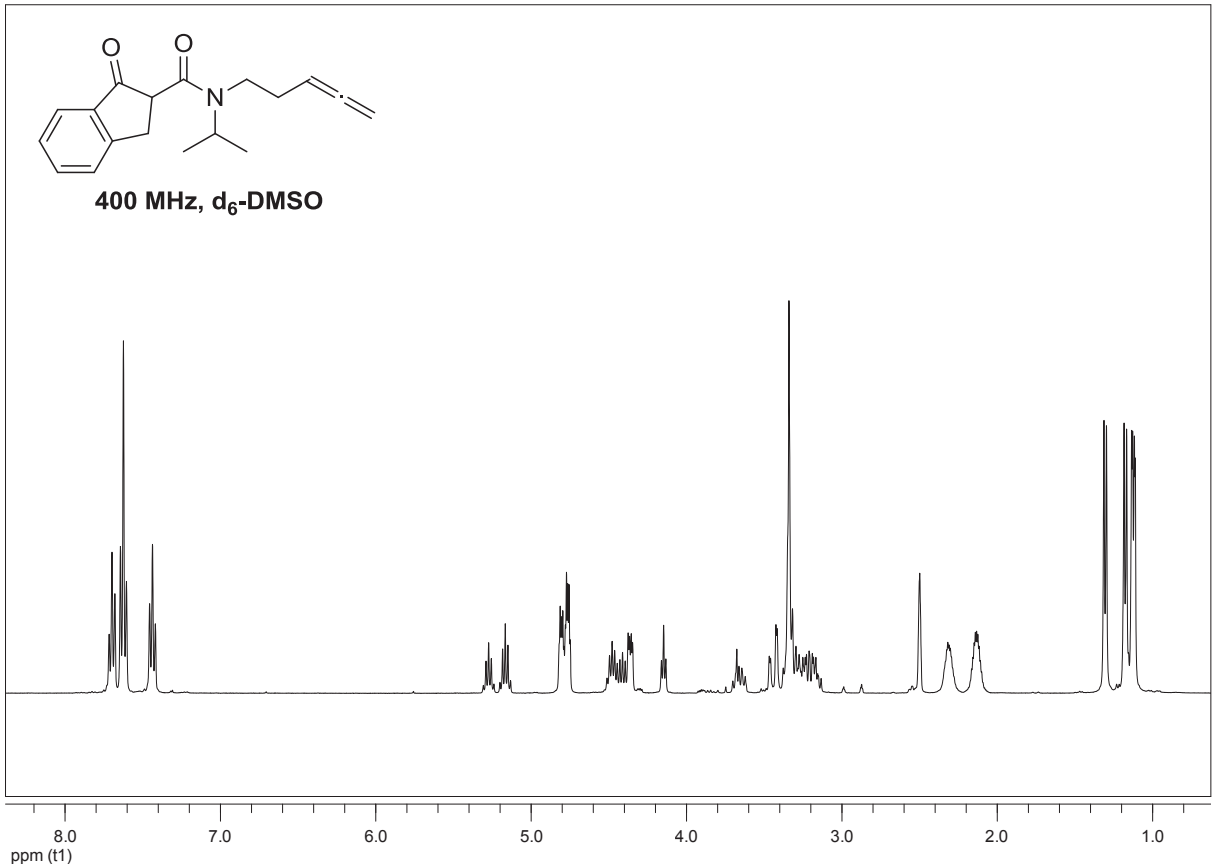
^{1}H NMR spectrum of **1h**



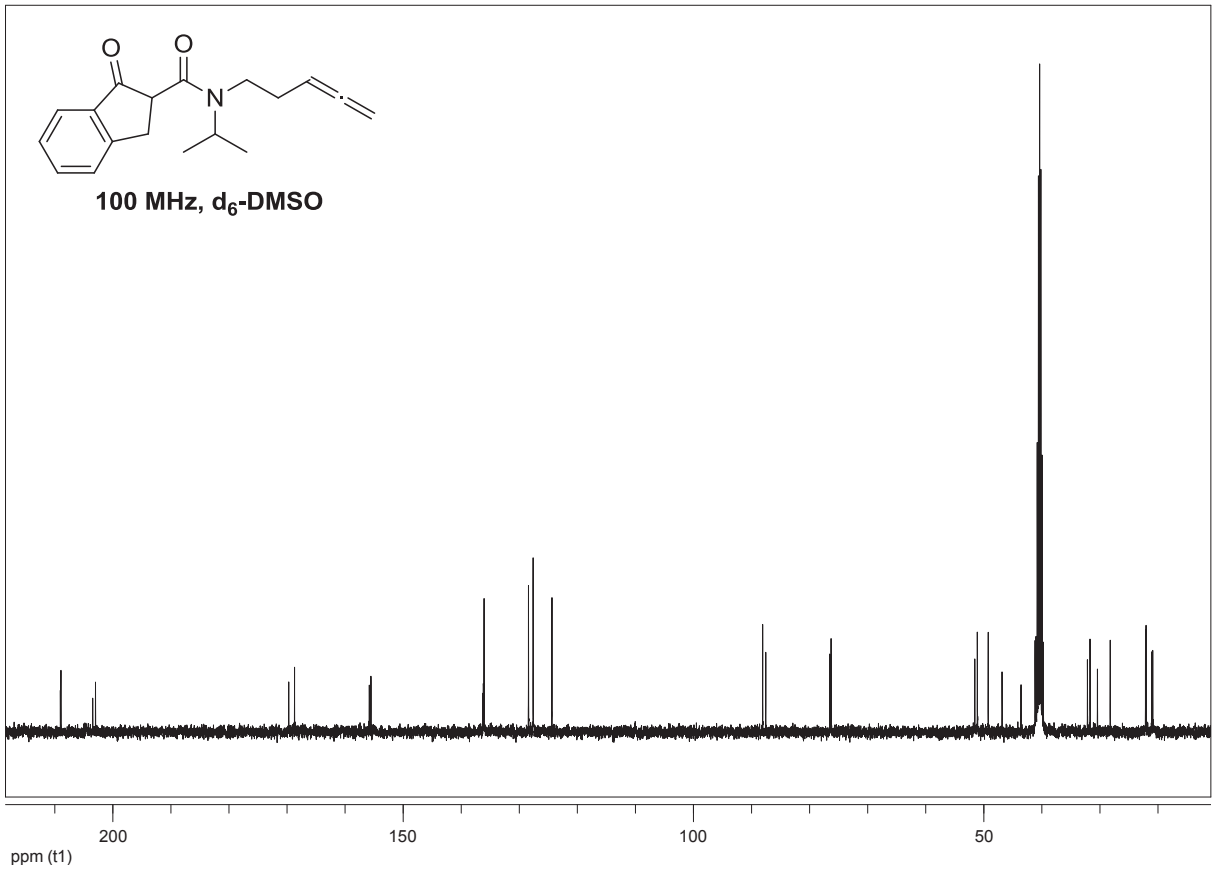
^{13}C NMR spectrum of **1h**



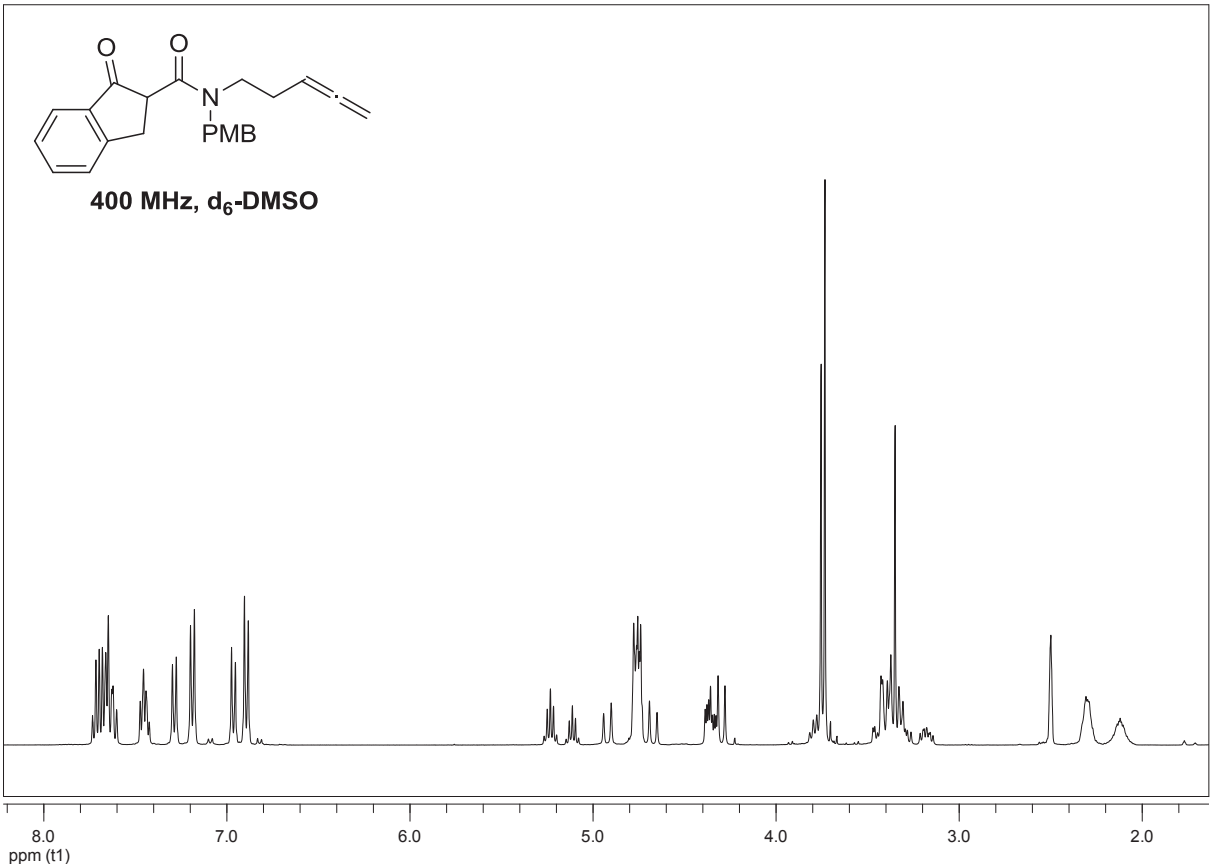
^{1}H NMR spectrum of **1i**



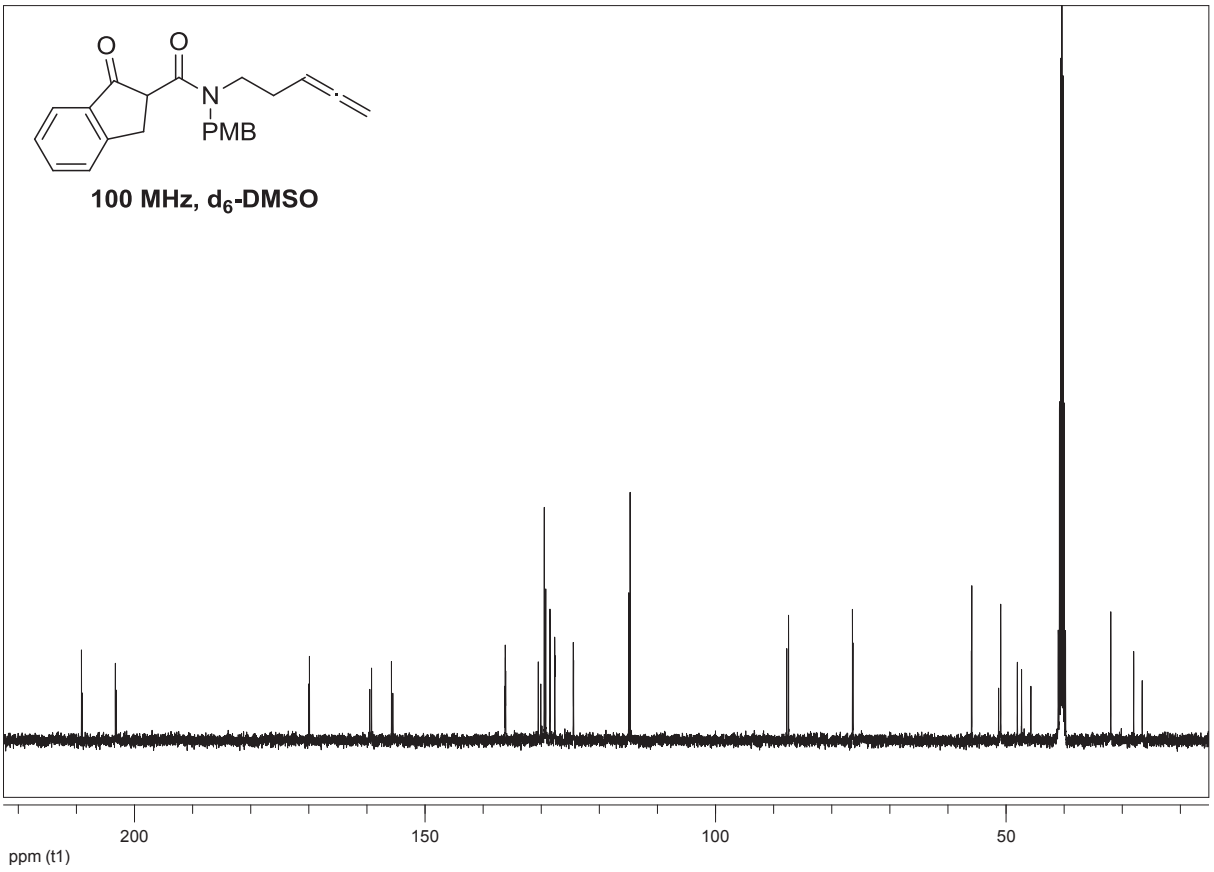
^{13}C NMR spectrum of **1i**



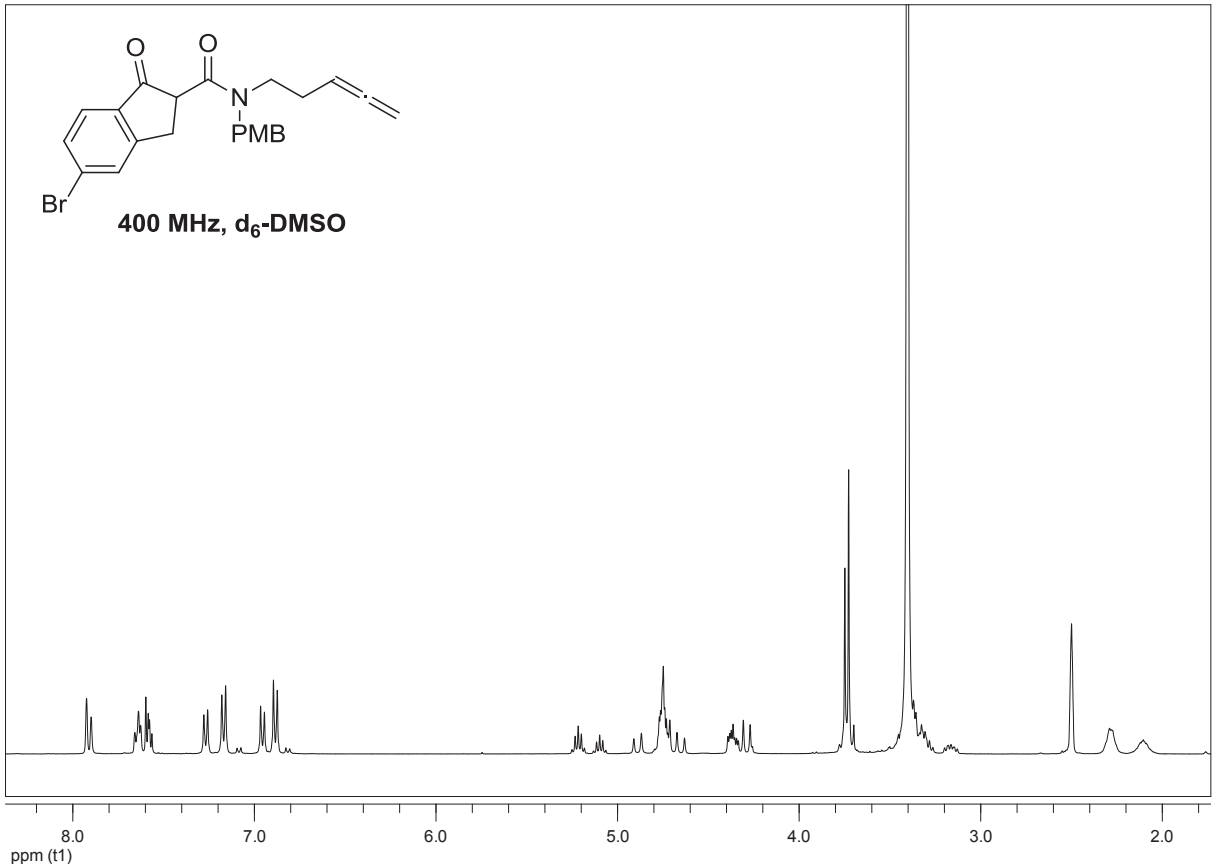
^{1}H NMR spectrum of **1j**



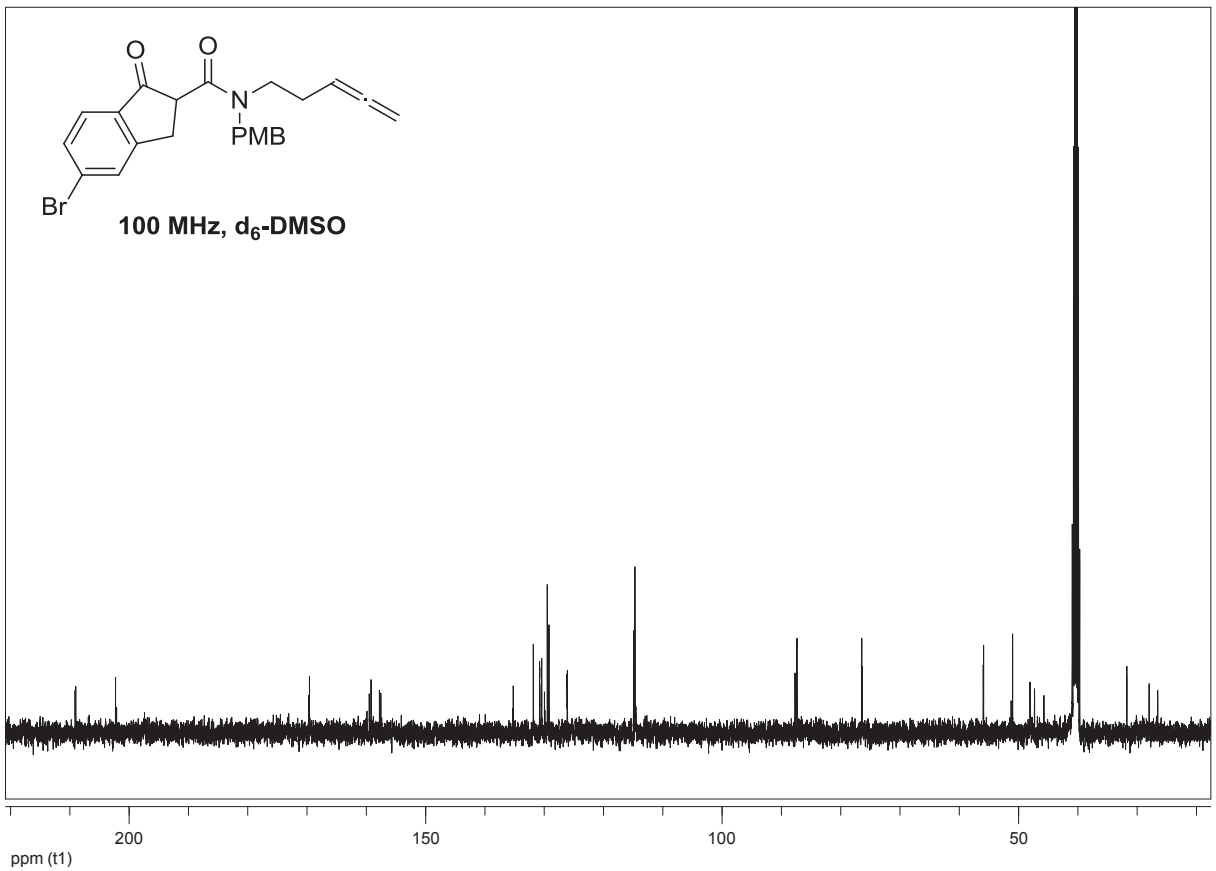
^{13}C NMR spectrum of **1j**



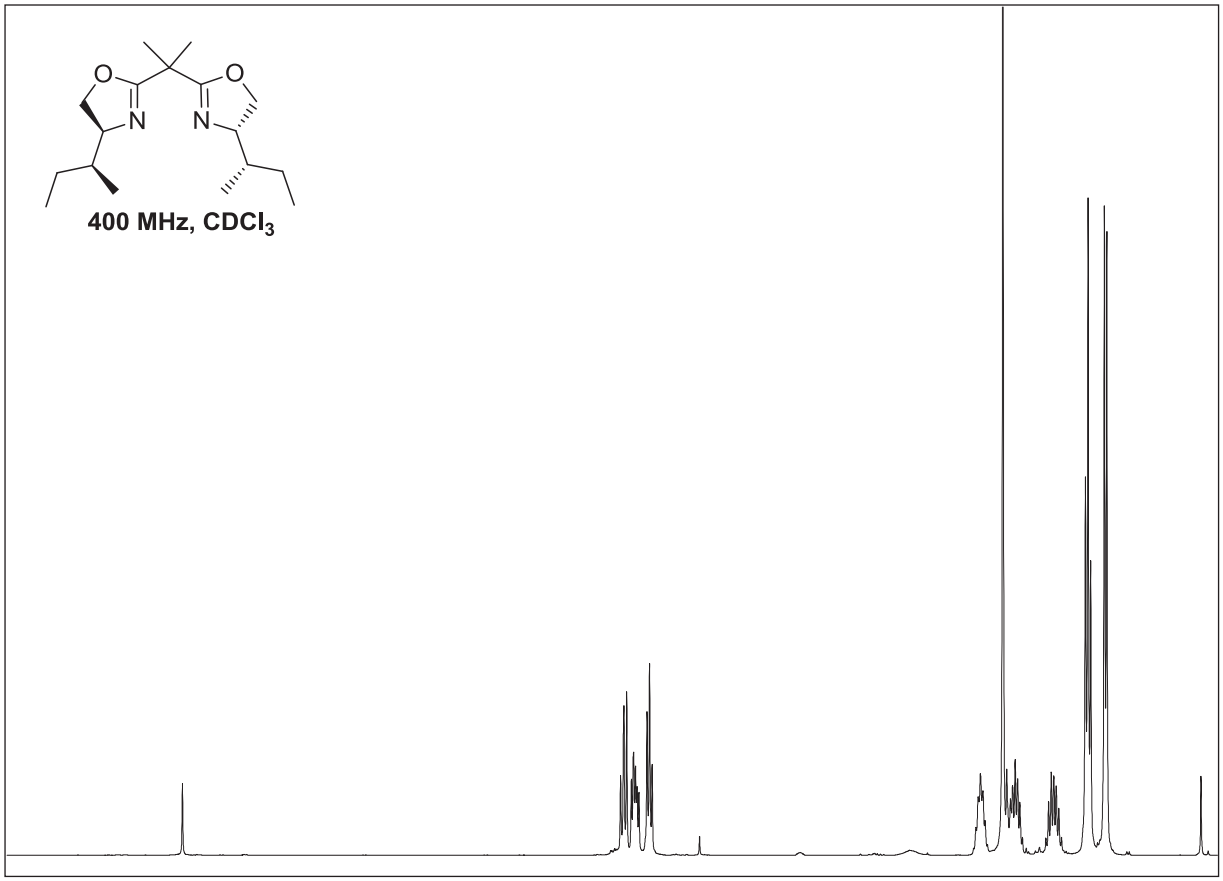
^{1}H NMR spectrum of **1k**



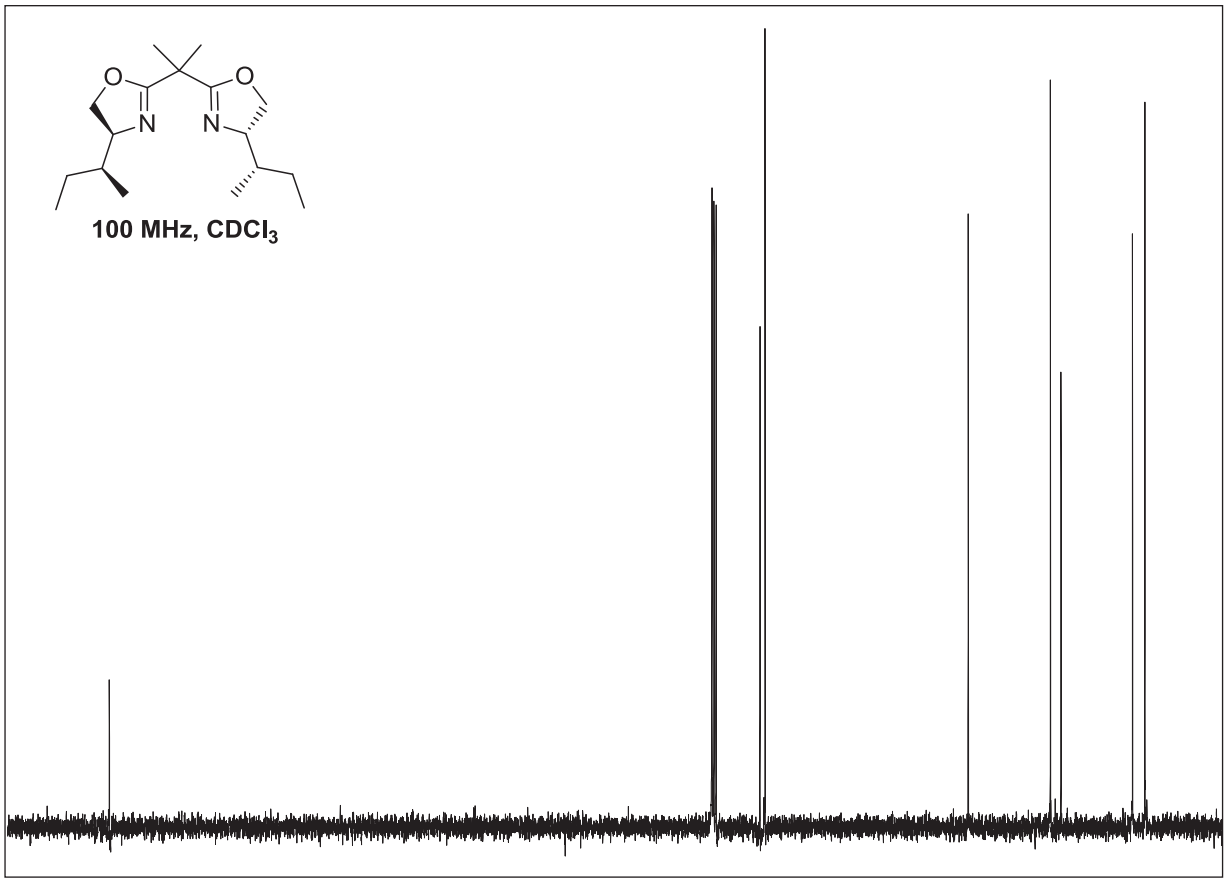
^{13}C NMR spectrum of **1k**



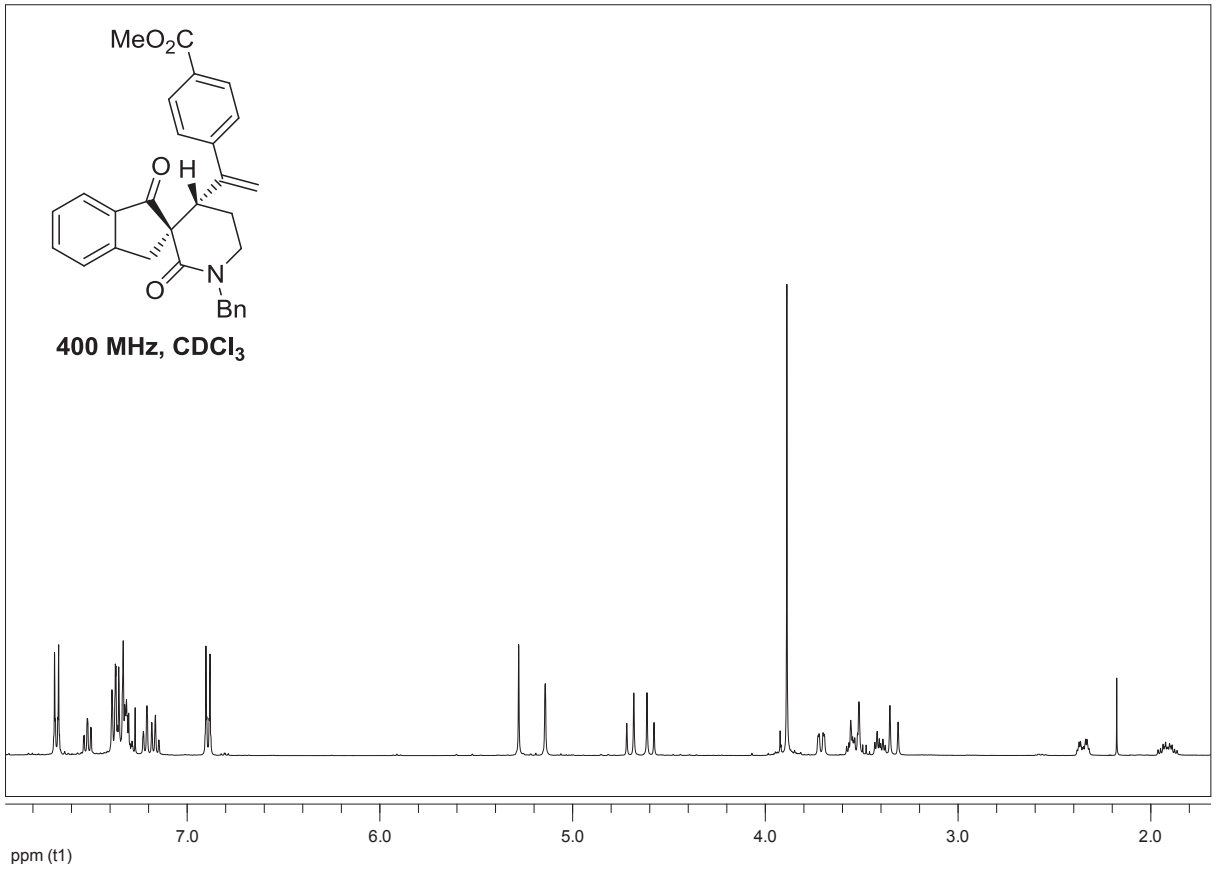
^{1}H NMR spectrum of **3i**



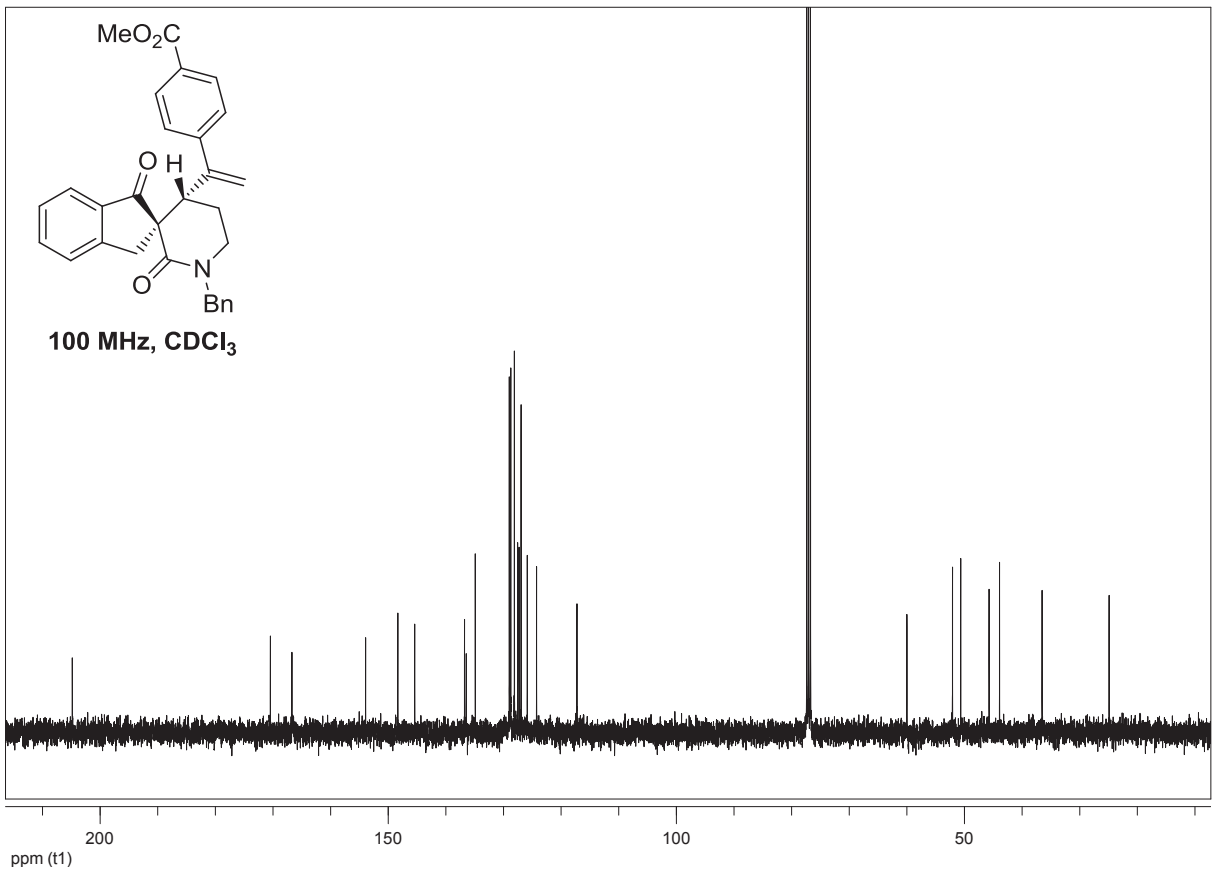
^{13}C NMR spectrum of **3i**



^{1}H NMR spectrum of **2a**

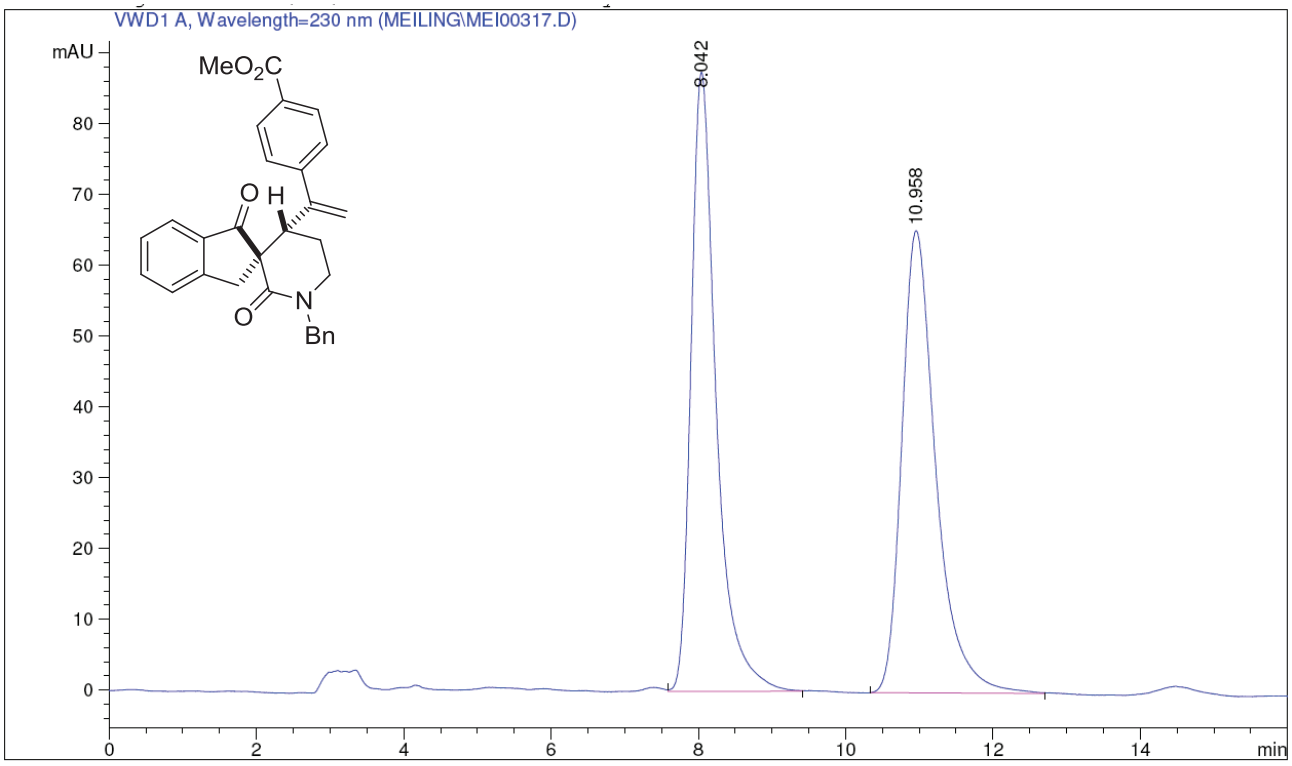


^{13}C NMR spectrum of **2a**



2a **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

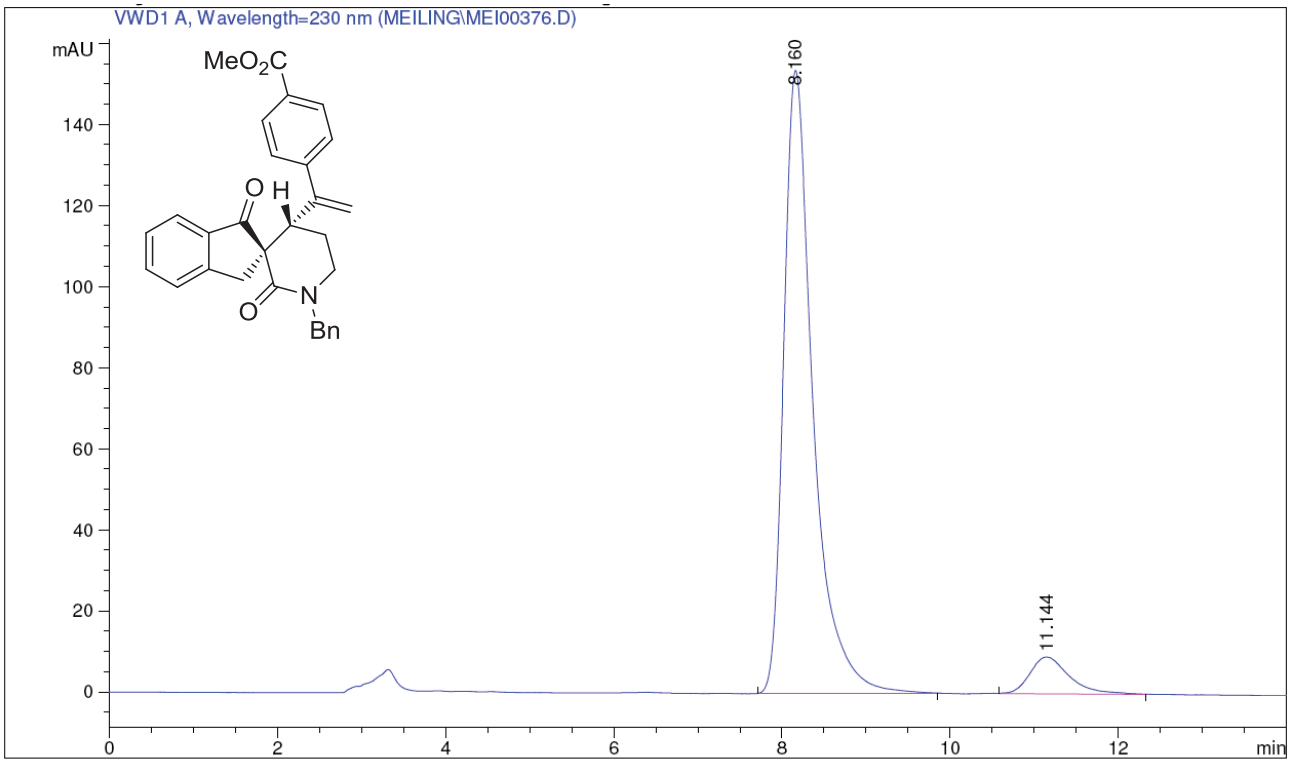
Racemic




```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.042 VB    0.3566 2074.07861   87.48759  49.6621
   2  10.958 BB    0.4854 2102.30078   65.32774  50.3379

Totals :                  4176.37939  152.81533

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

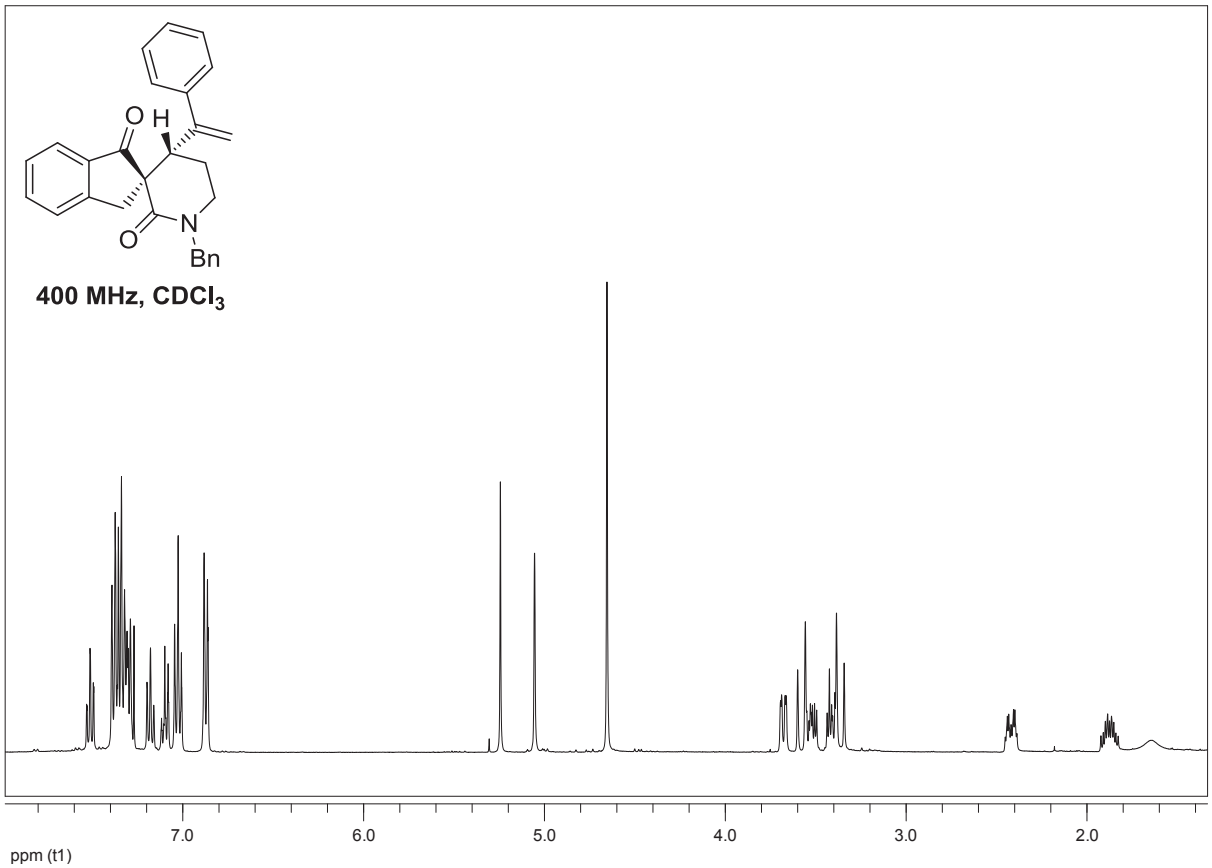
2a **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

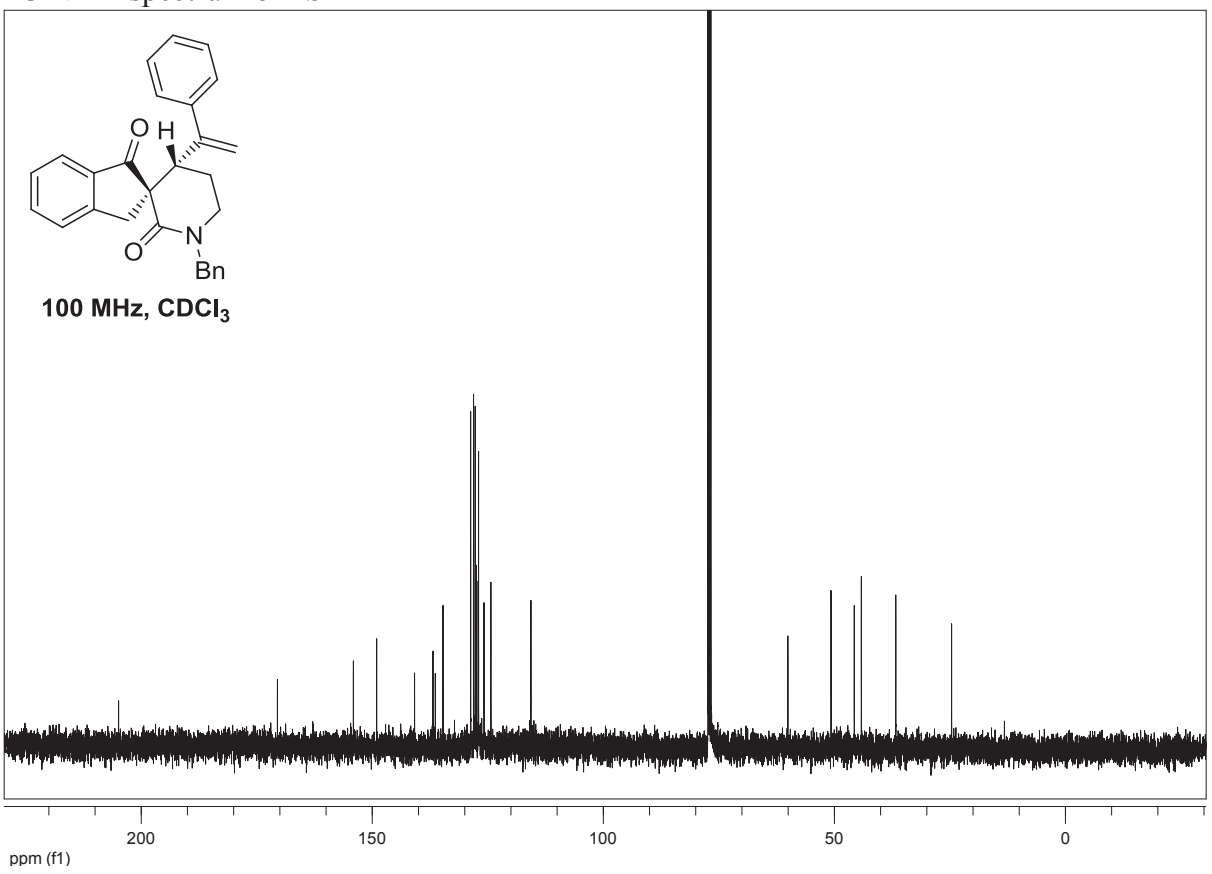



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.160 BB    0.3632 3729.39600  153.66104  92.6855
   2  11.144 BB    0.4848  294.31284    9.06500   7.3145

Totals :                  4023.70883  162.72604

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

^{1}H NMR spectrum of **2b**

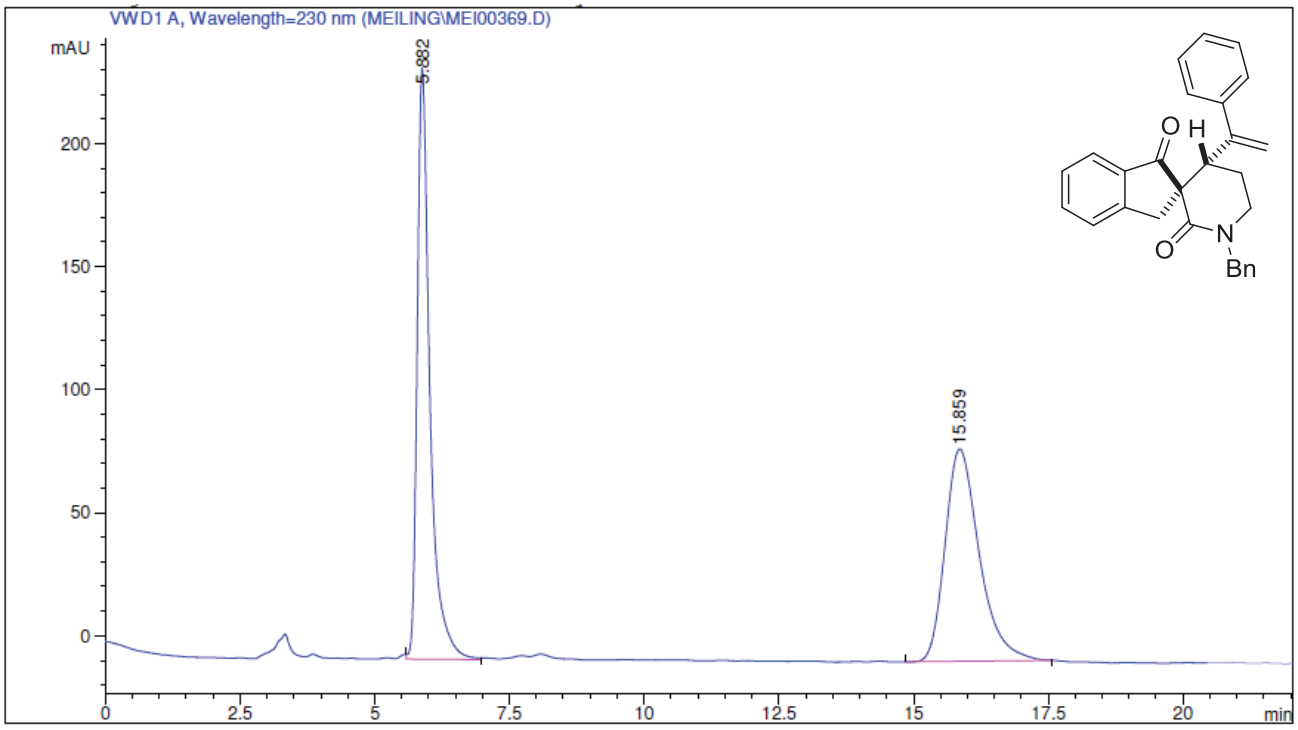


^{13}C NMR spectrum of **2b**



2b **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

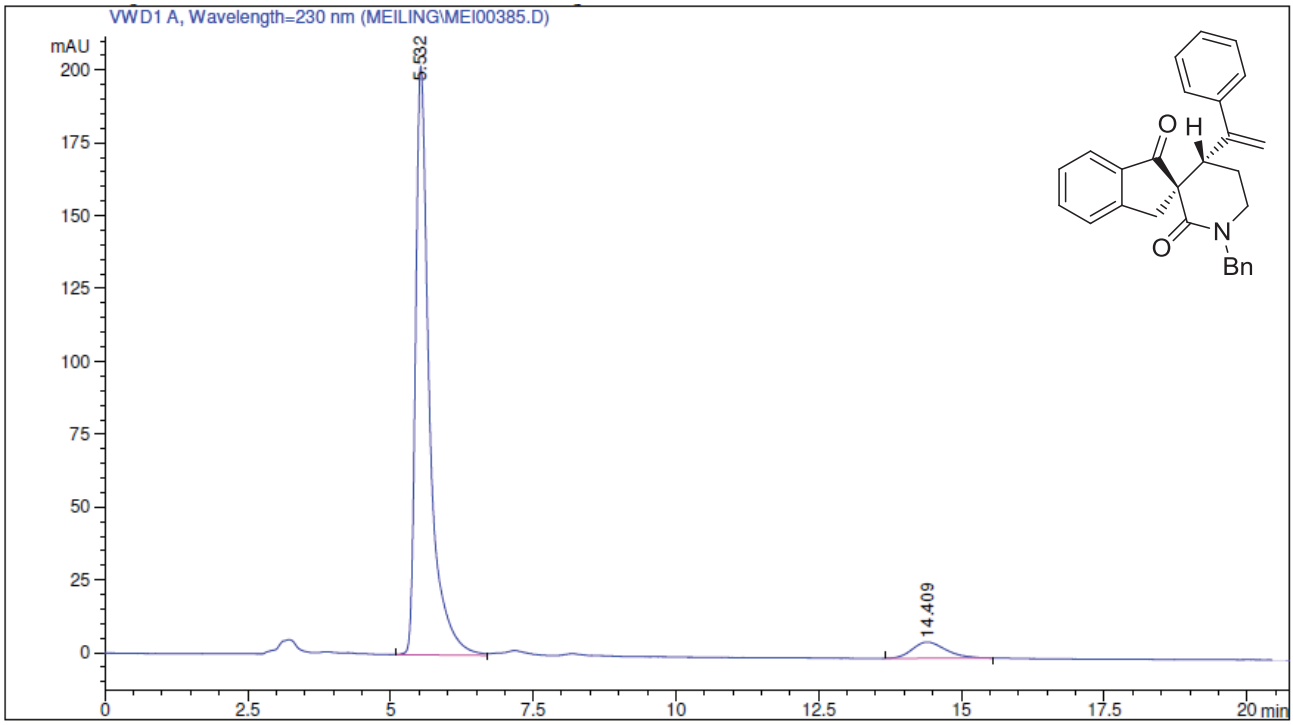
Racemic




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.882 VB    0.2430 3934.46606  240.37802  50.7733
   2  15.859 PB    0.6056 3814.61450   86.31119  49.2267

Totals :                  7749.08057  326.68921
```

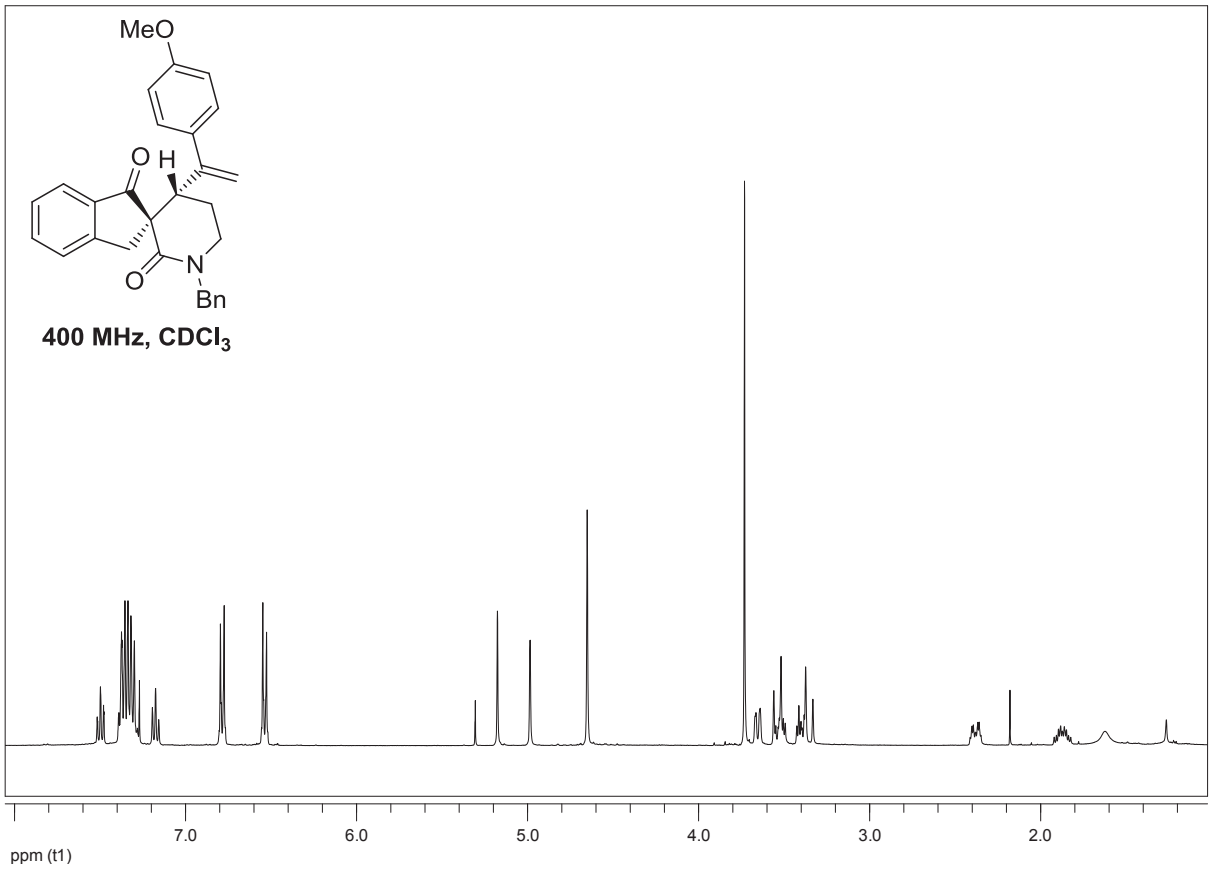
2b **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

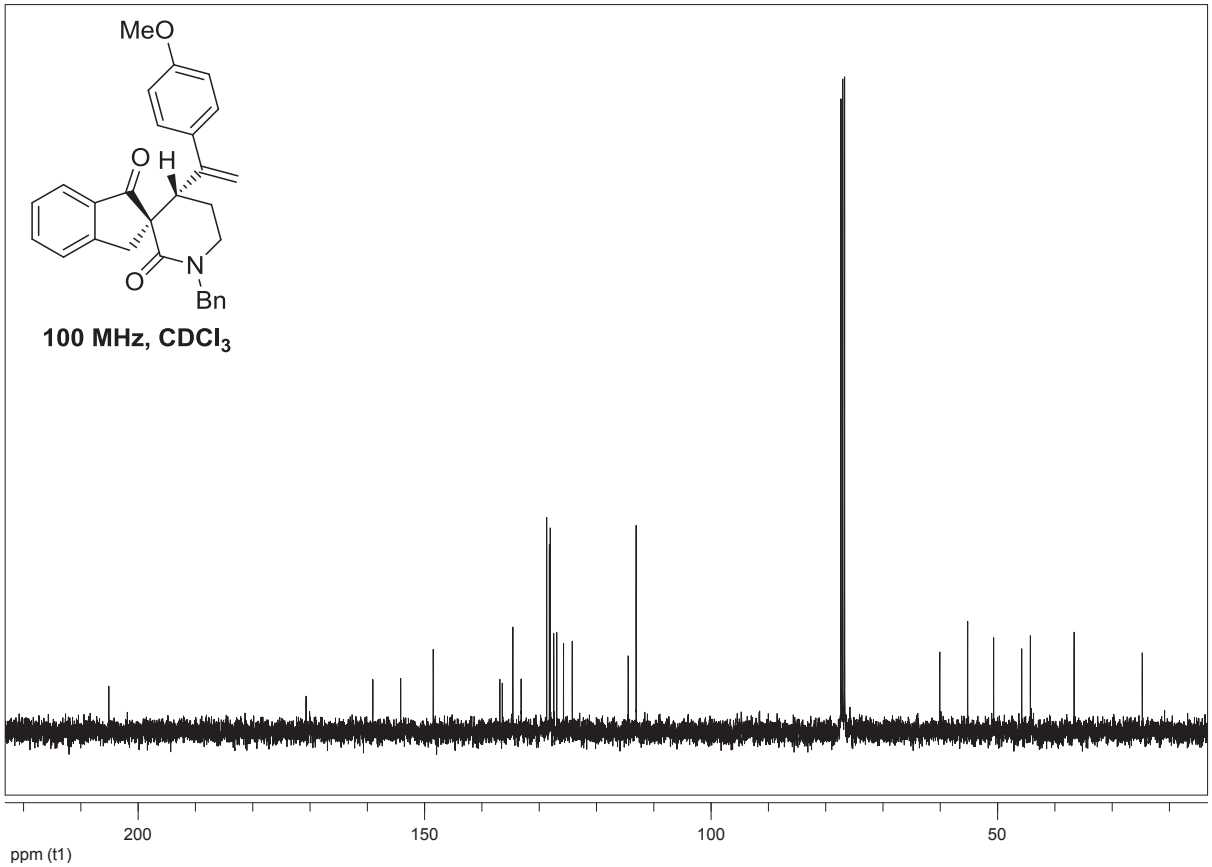



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.532 BV    0.2489 3409.95728  202.02847  93.7336
   2  14.409 BB    0.4820  227.96500    5.54135   6.2664

Totals :                  3637.92227  207.56982
```

^{1}H NMR spectrum of **2c**

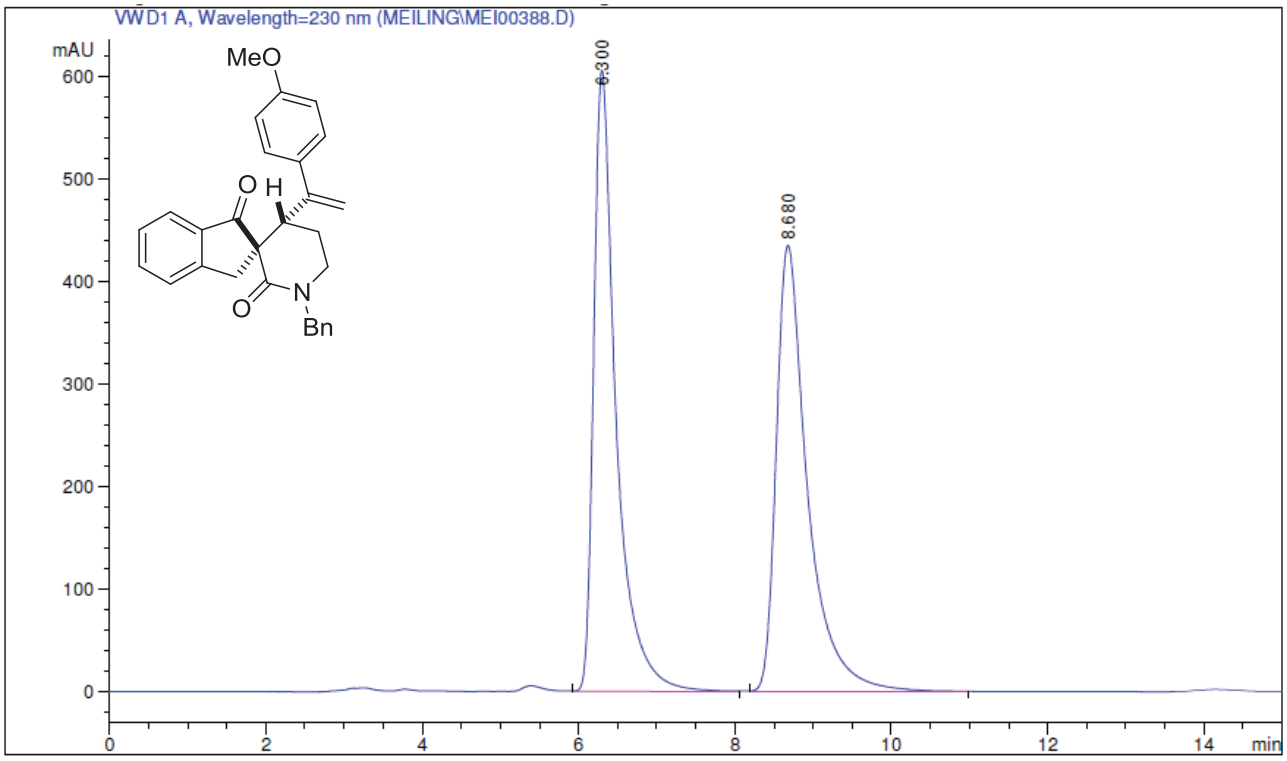


^{13}C NMR spectrum of **2c**



2c **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

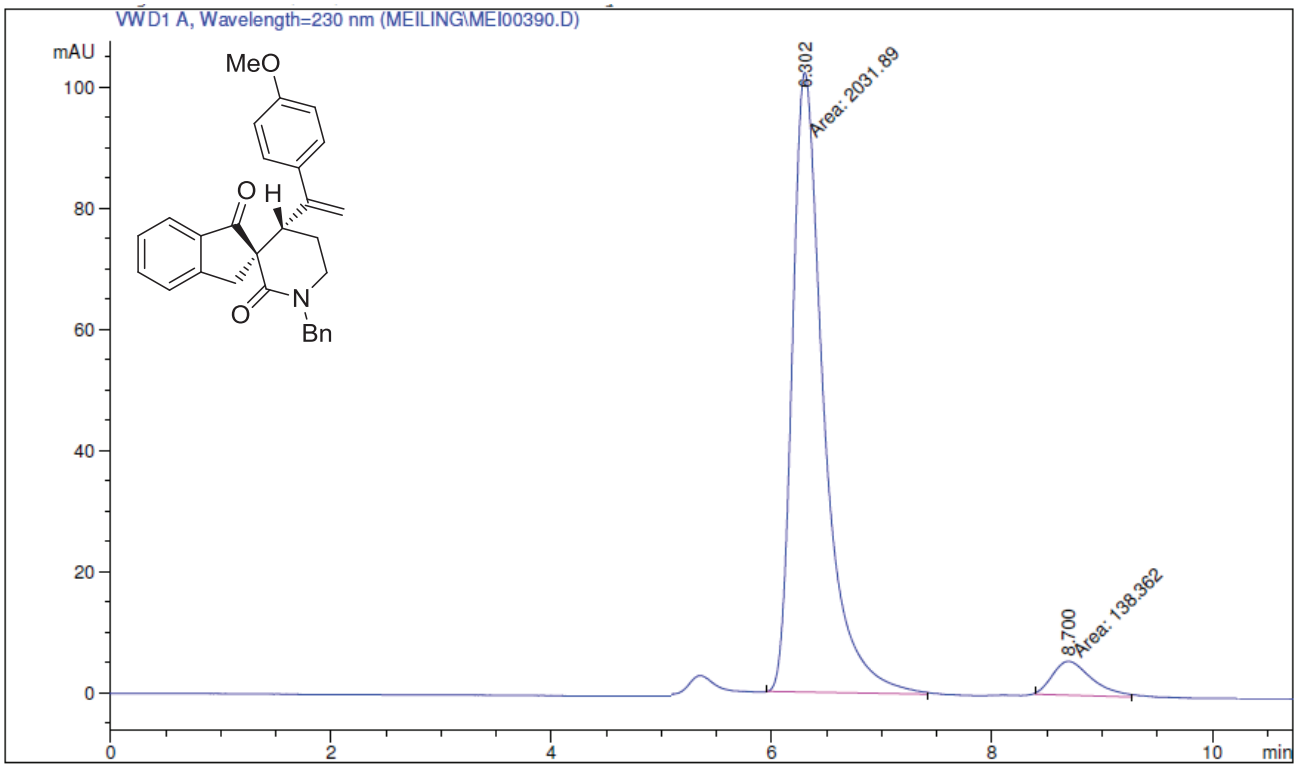
Racemic




```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.300 VB    0.2925 1.20695e4   605.66840  49.9327
   2   8.680 BB    0.4104 1.21021e4   435.17255  50.0673

Totals :                  2.41716e4  1040.84094
```

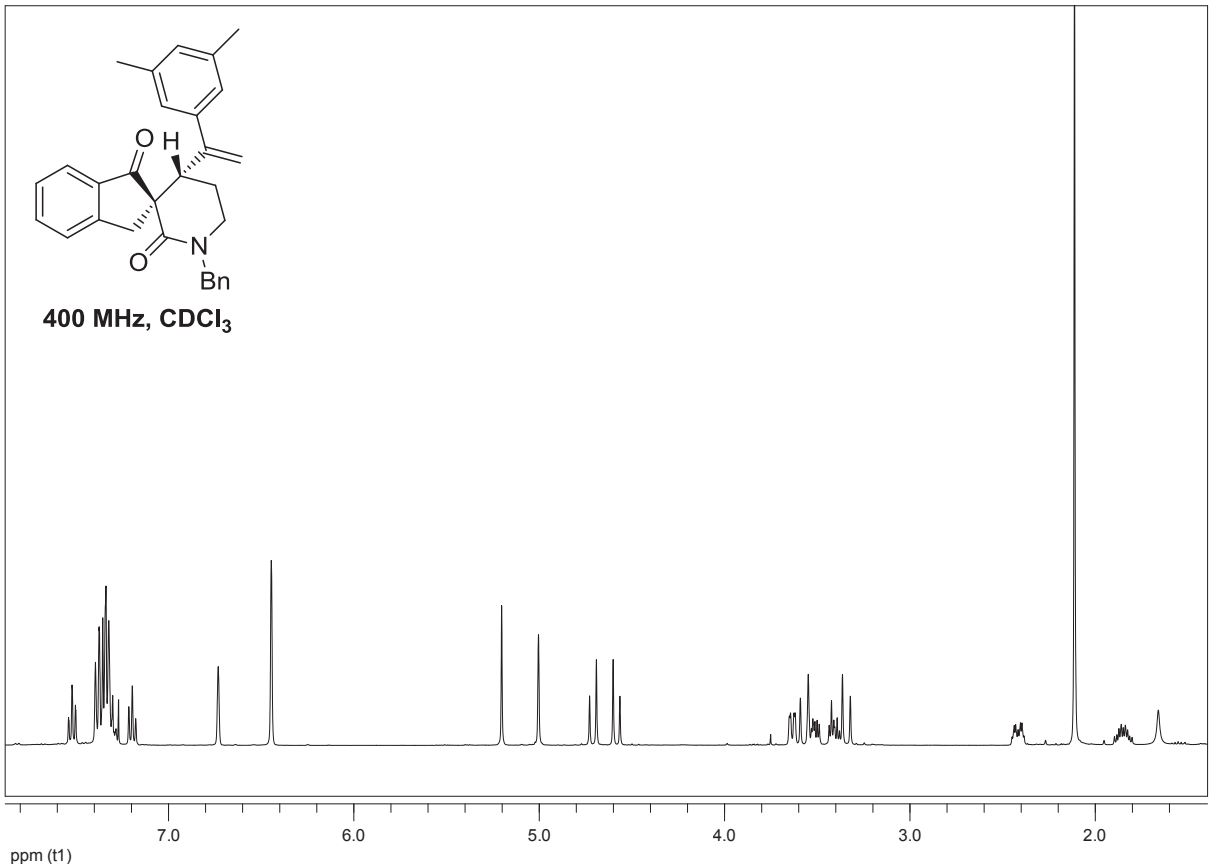
2c **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

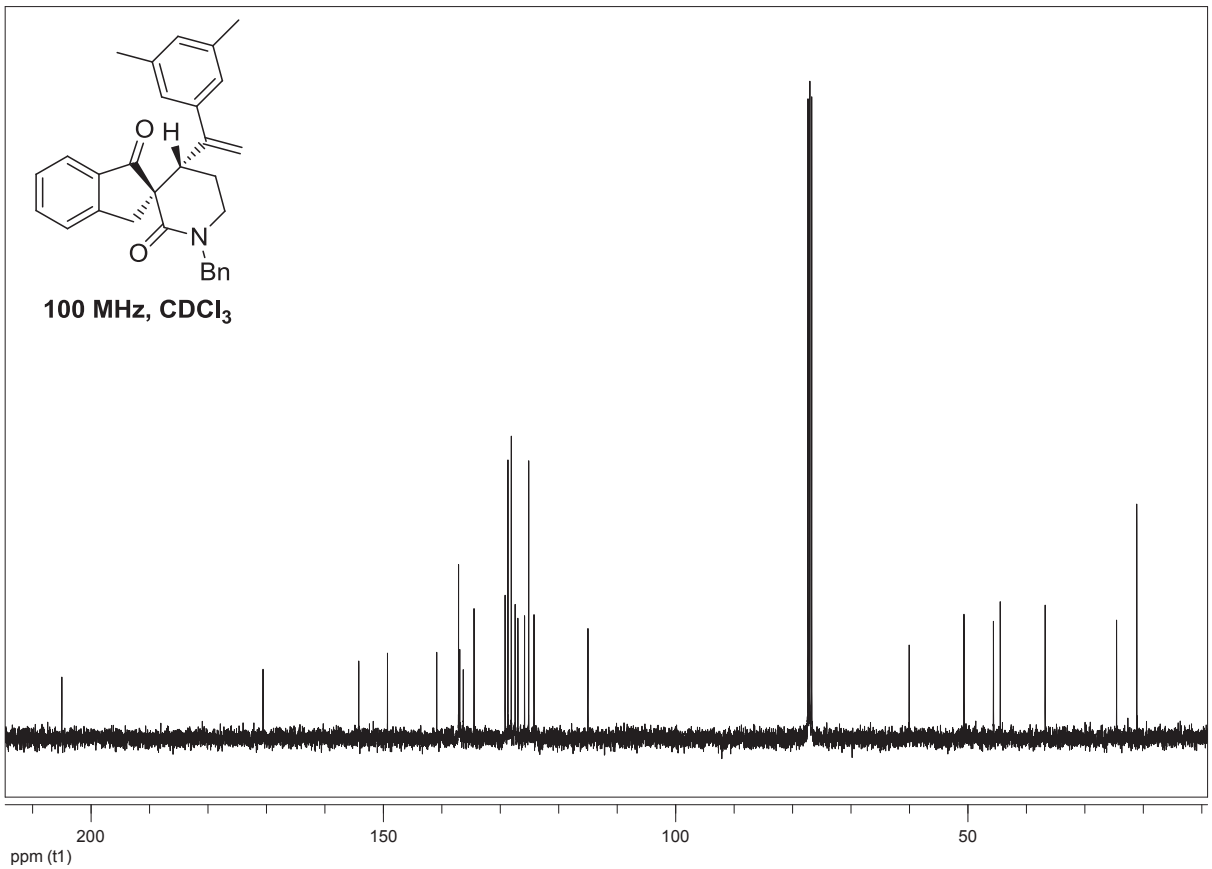



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.302 MM    0.3313 2031.89417  102.21532  93.6246
   2   8.700 MM    0.4136  138.36247    5.57573   6.3754

Totals :                  2170.25664  107.79106

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **2d**

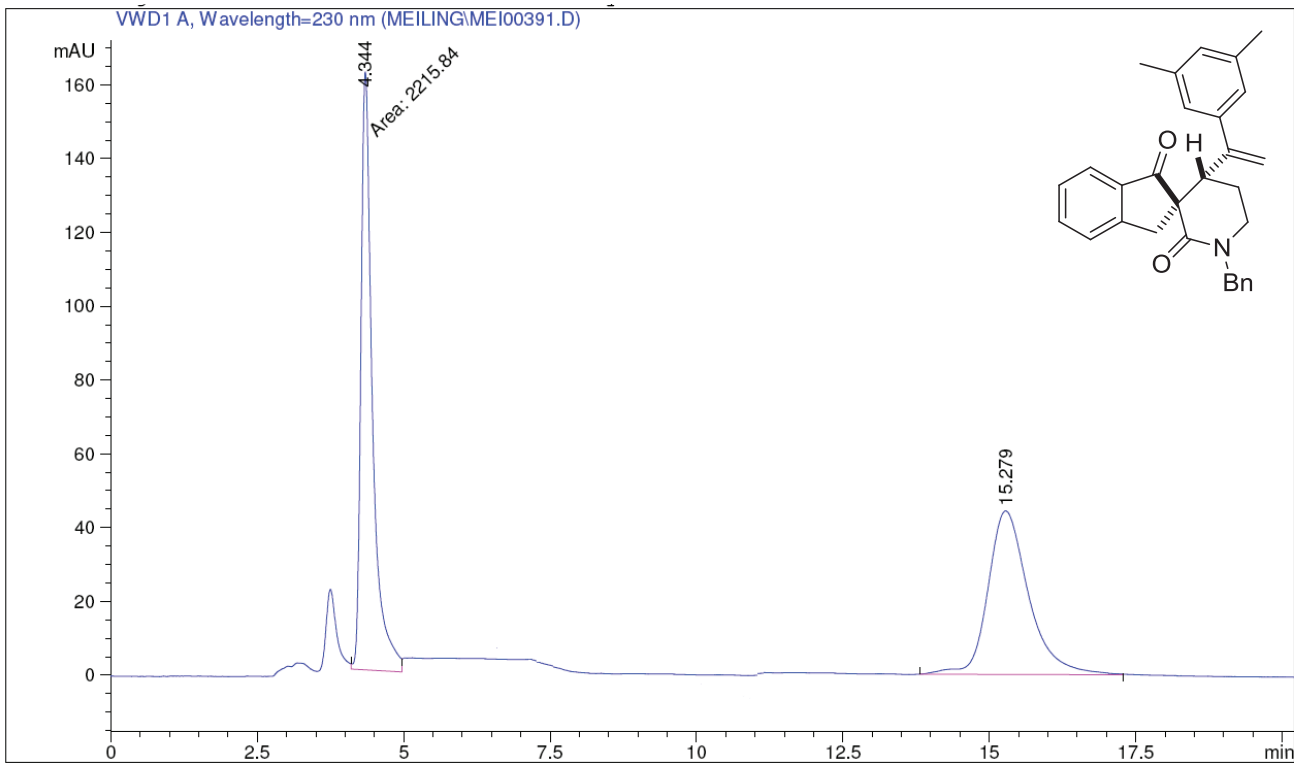


^{13}C NMR spectrum of **2d**



2d **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

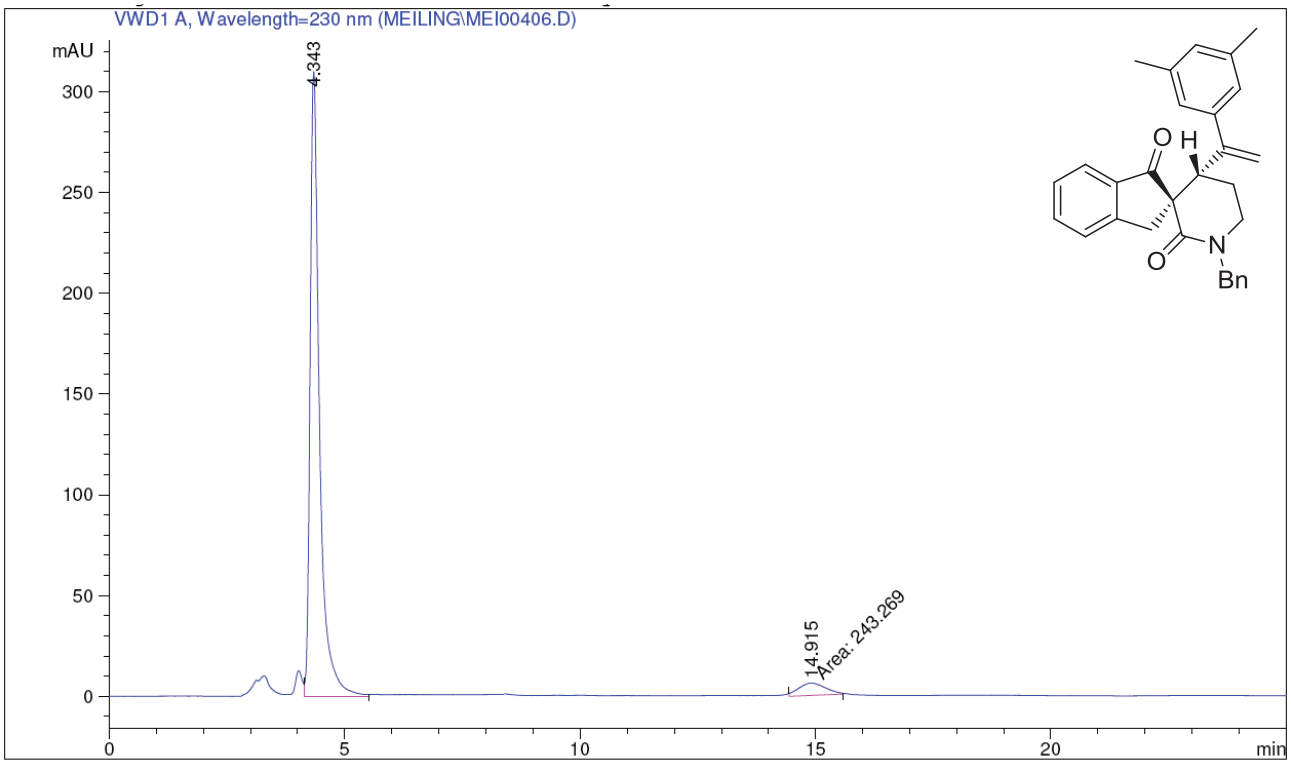
Racemic




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.344 MM    0.2278 2215.84448  162.14415  50.7536
   2  15.279 BB    0.7299 2150.04419   44.32693  49.2464

Totals :                  4365.88867  206.47108

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

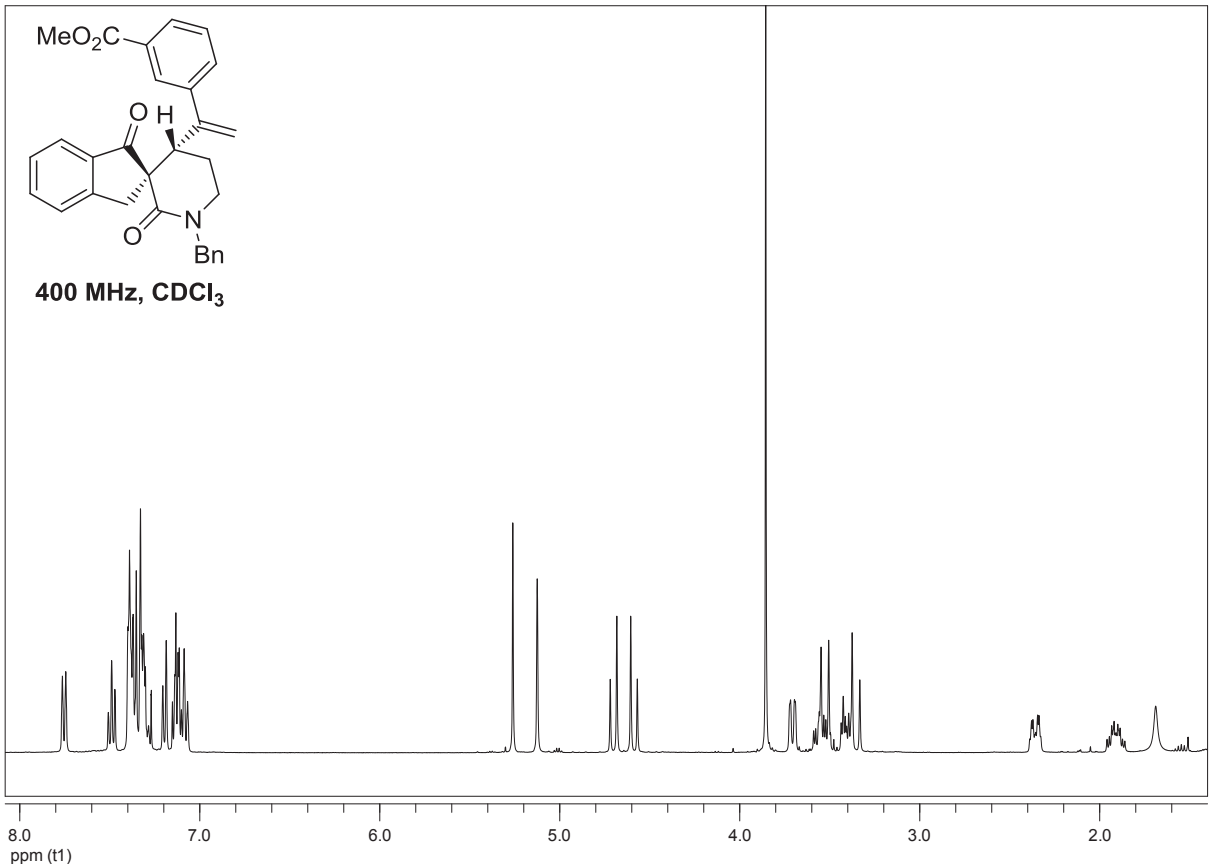
2d **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

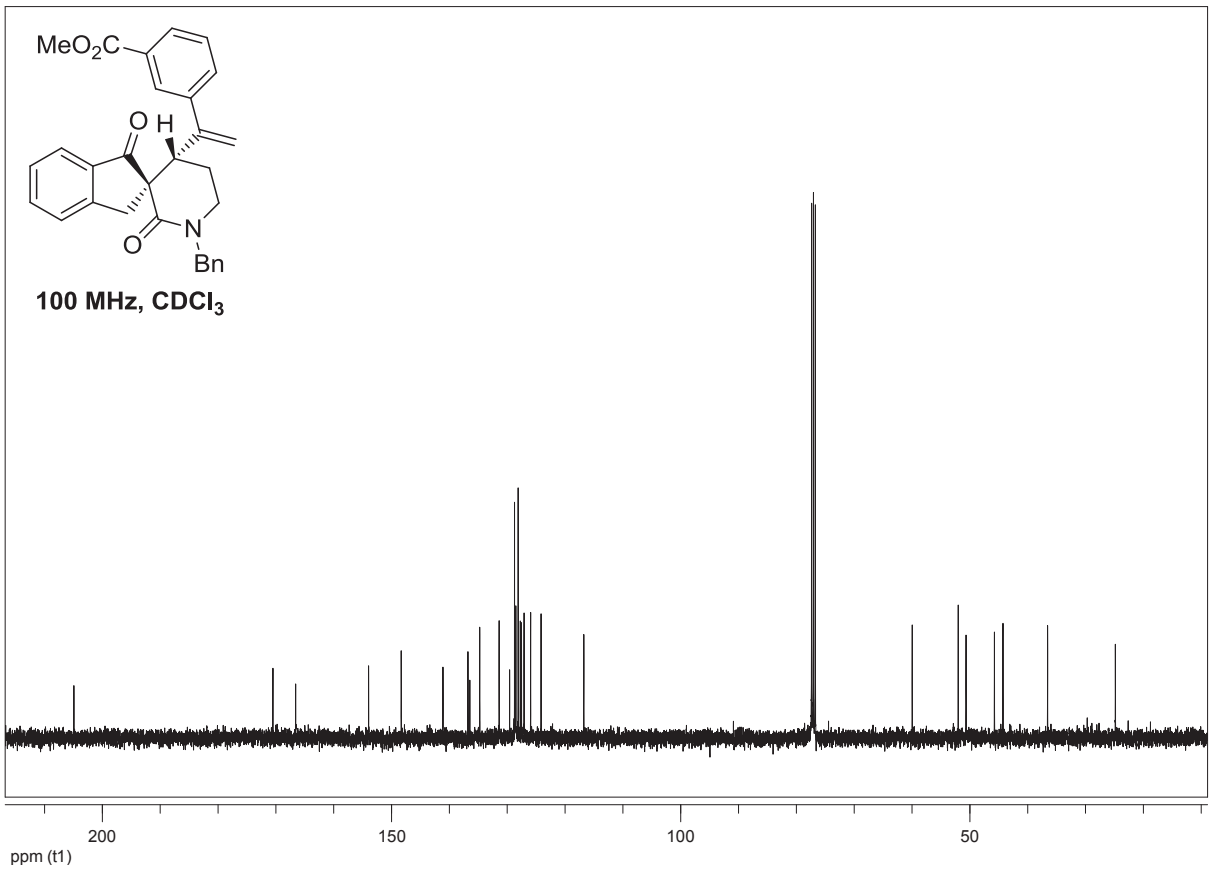



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.343 VB    0.2061 4306.41846  309.92630  94.6531
   2  14.915 MM    0.4766  243.26886    6.07218   5.3469

Totals :                  4549.68732  315.99848

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

^{1}H NMR spectrum of **2e**

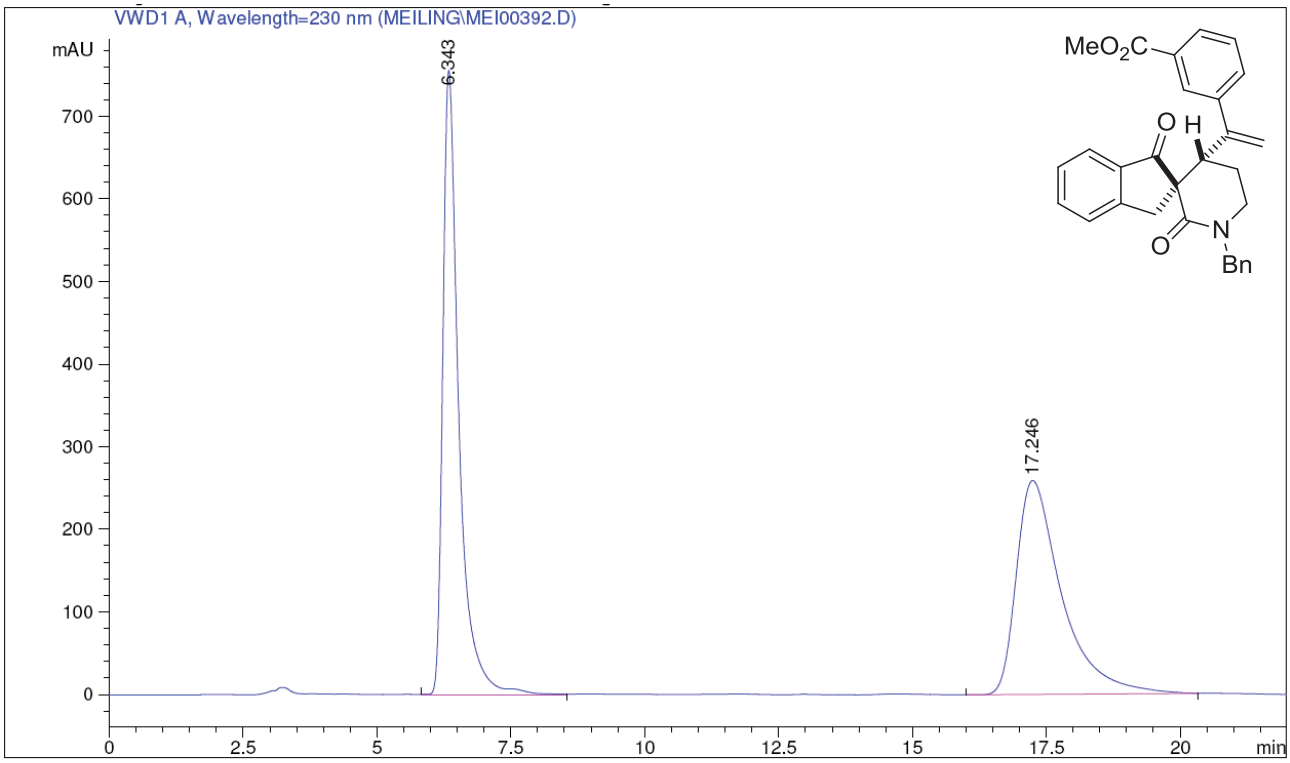


^{13}C NMR spectrum of **2e**



2e **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

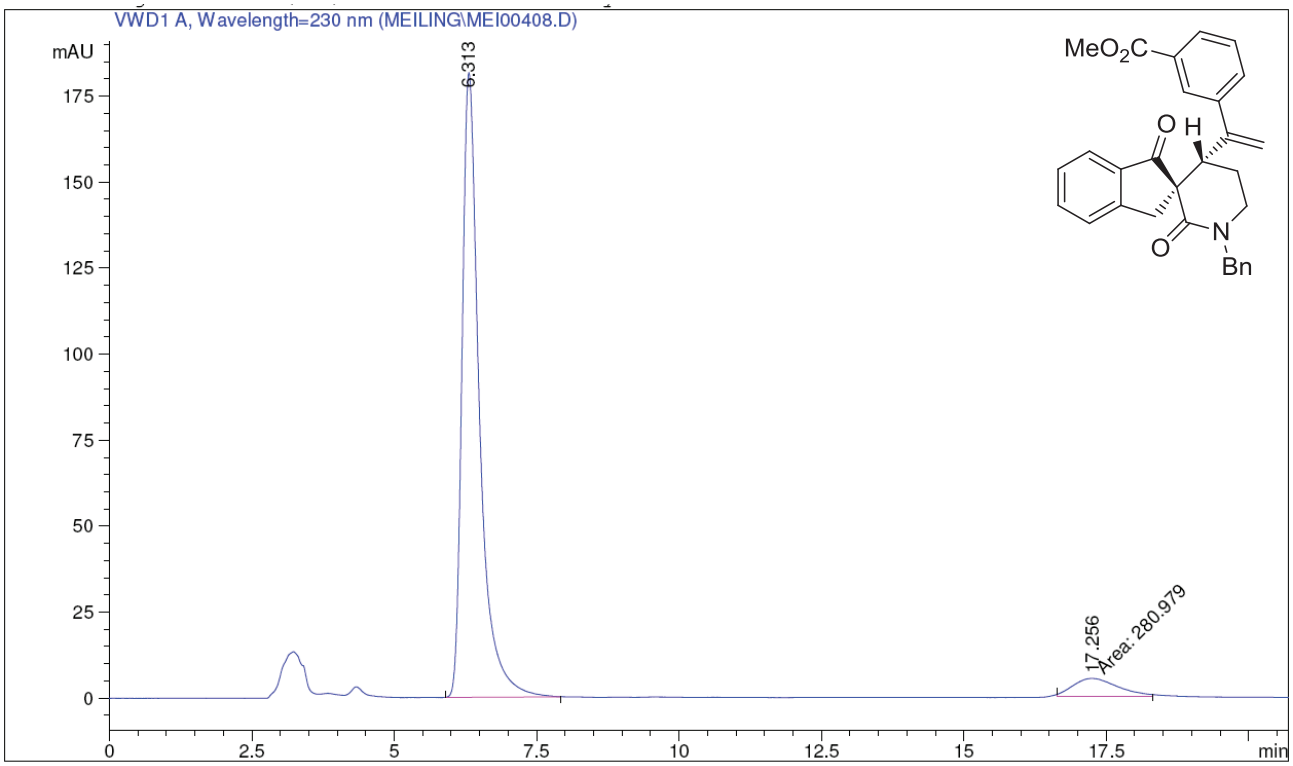
Racemic




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.343 BB    0.3087 1.57139e4   755.40088  50.7575
   2  17.246 VB    0.8770 1.52449e4   258.88623  49.2425

Totals :                  3.09588e4  1014.28711

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

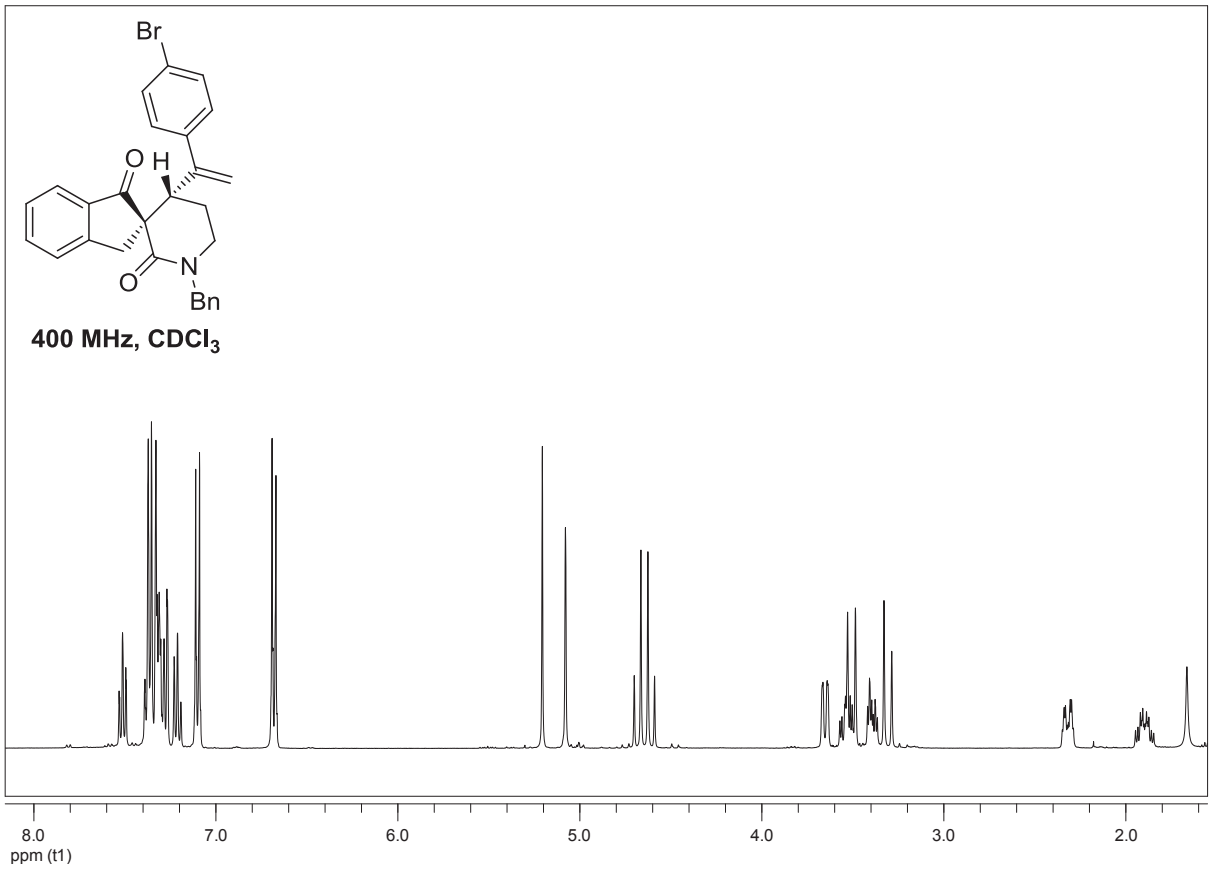
2e **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

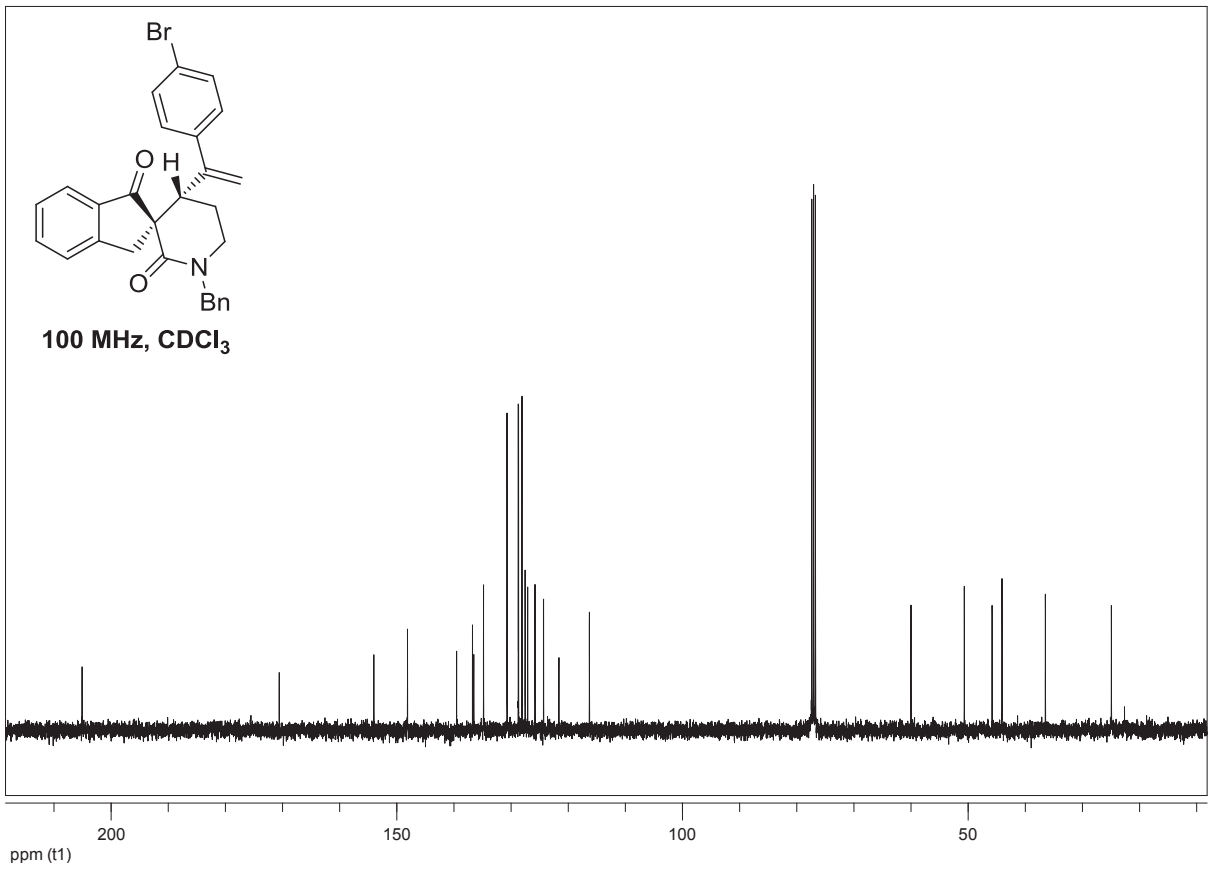



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.313 BB    0.3181 3860.28247  181.52113  93.2151
   2  17.256 MM    0.9065  280.97888    5.16583   6.7849

Totals :                  4141.26135  186.68697

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **2f**

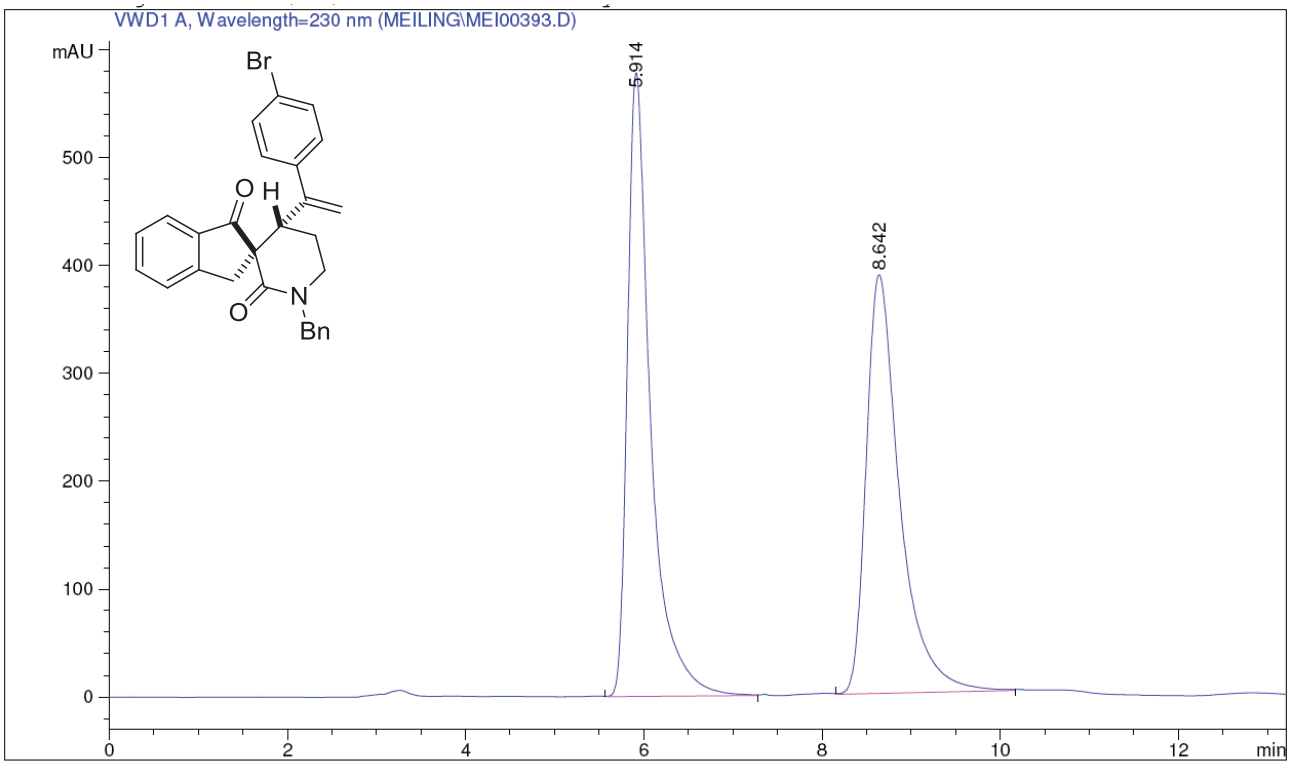


^{13}C NMR spectrum of **2f**



2f **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

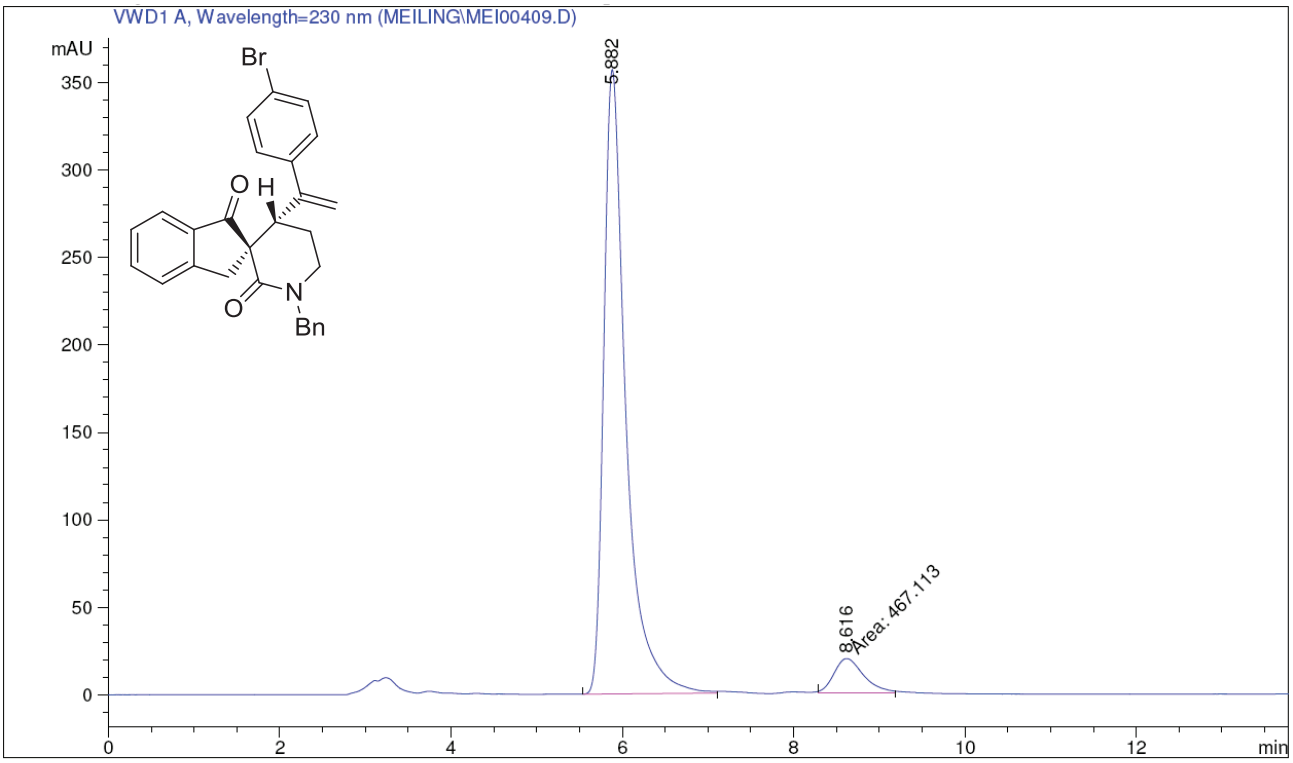
Racemic




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.914 VV    0.2673 1.04774e4   578.38678  50.7740
   2   8.642 VB    0.3914 1.01580e4   388.08847  49.2260

Totals :                  2.06354e4   966.47525

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

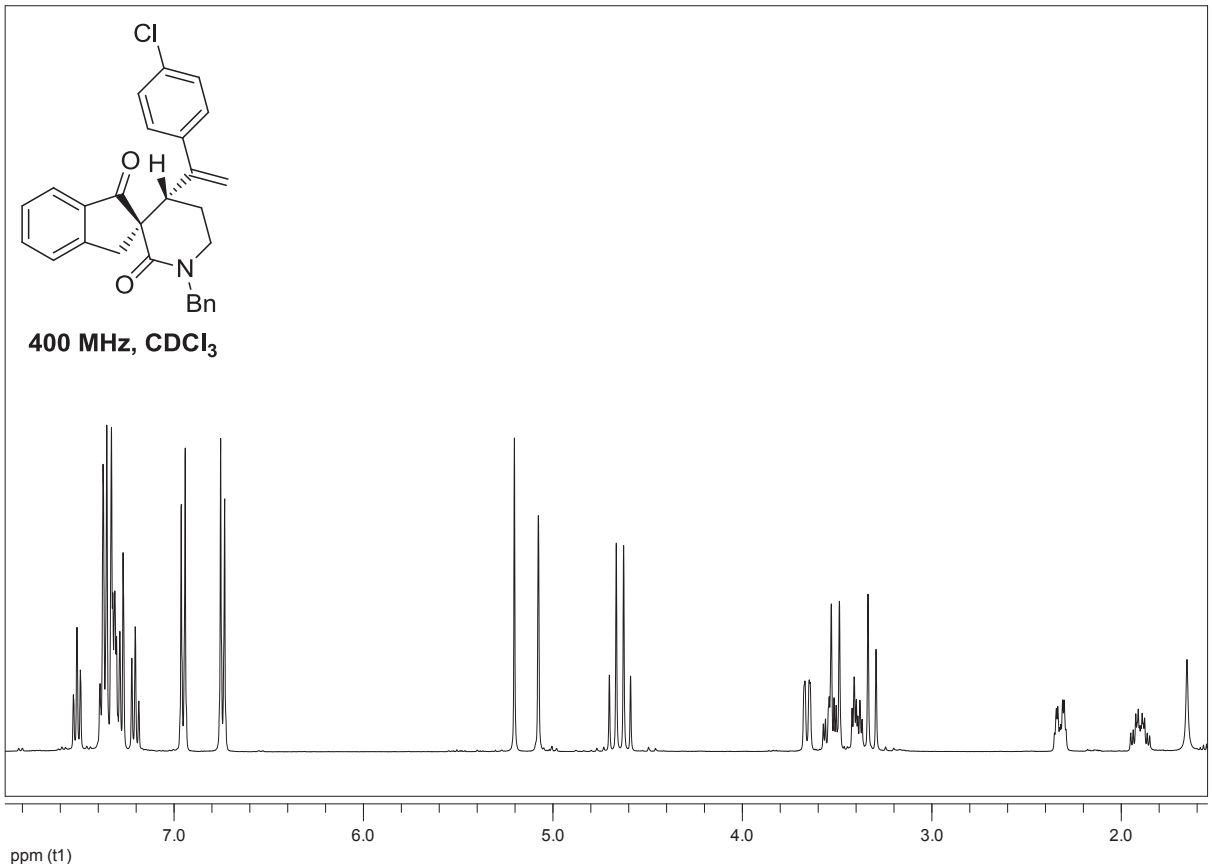
2f **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

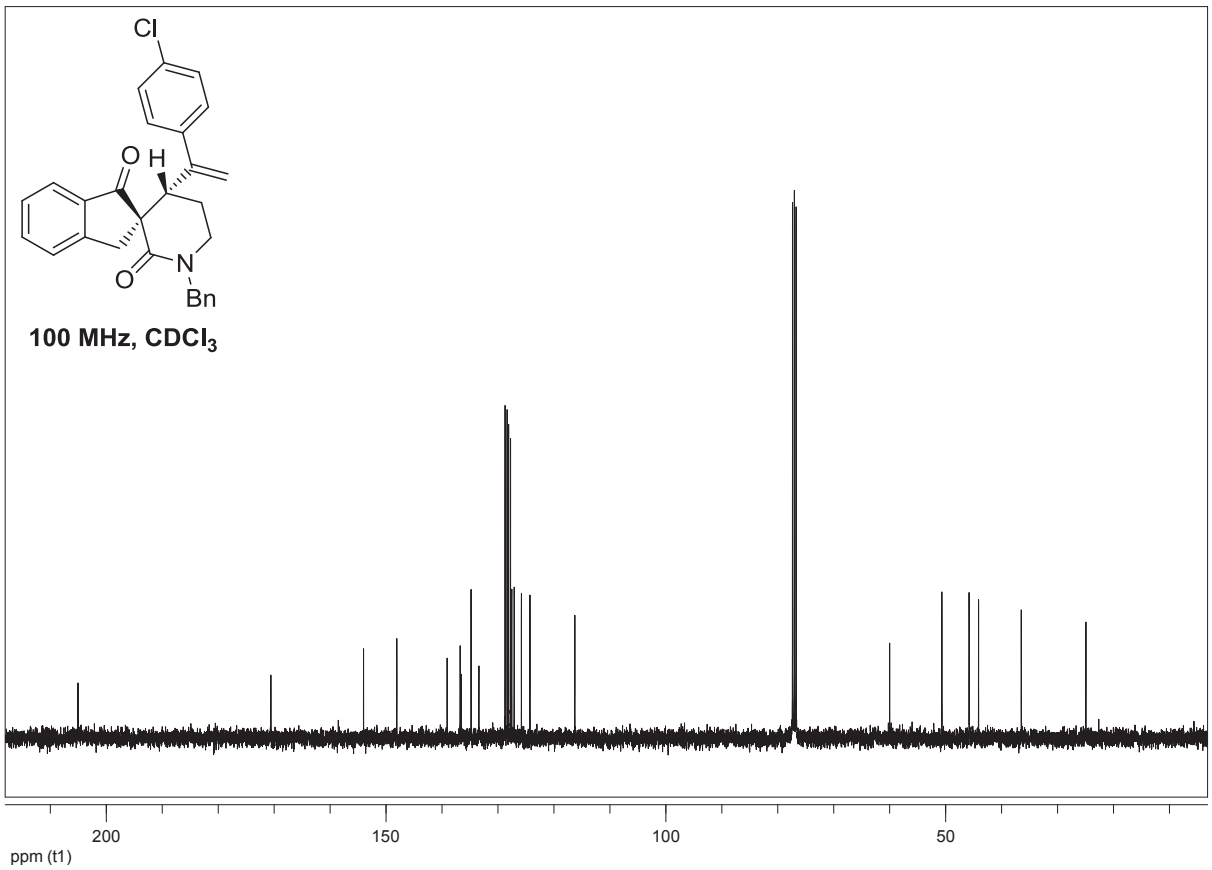



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.882 PB    0.2678 6414.06738  356.68668  93.2117
   2   8.616 MM    0.3993  467.11343   19.49923   6.7883

Totals :                  6881.18082  376.18590

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

^{1}H NMR spectrum of **2g**

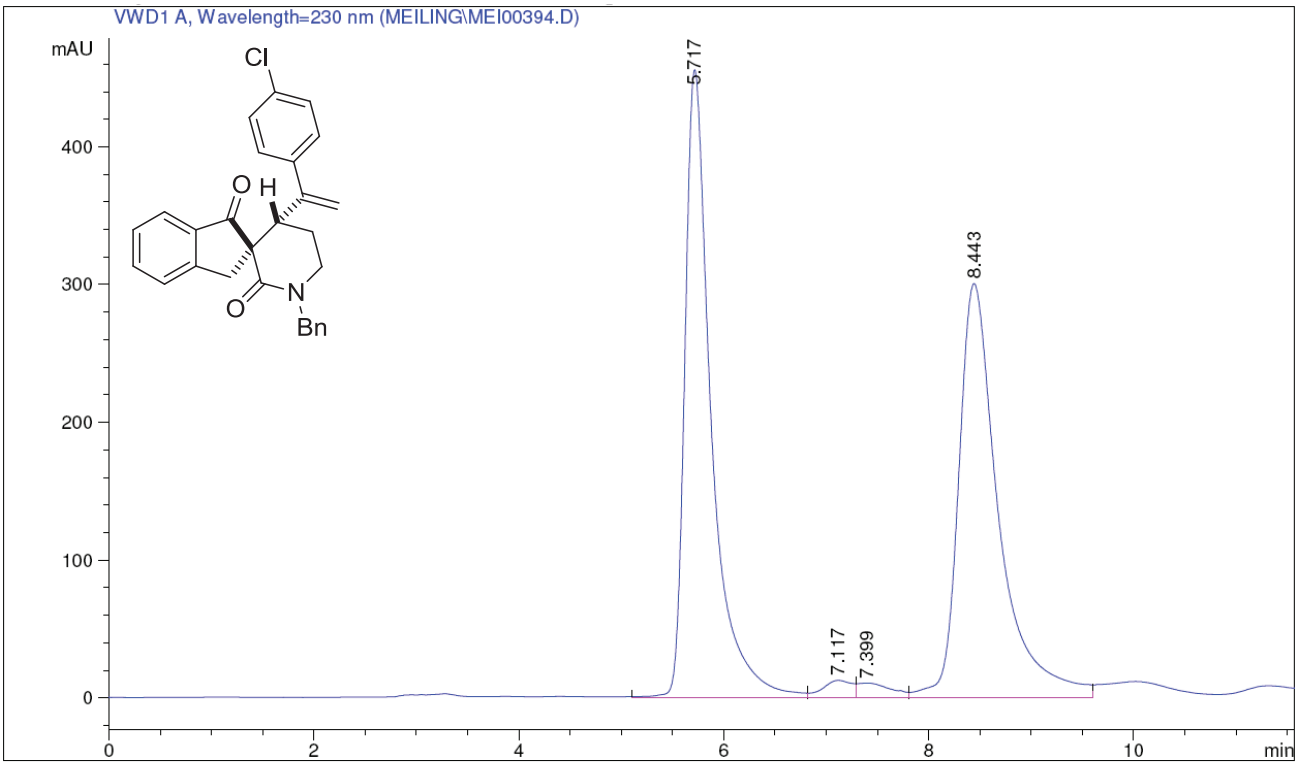


^{13}C NMR spectrum of **2g**



2g **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

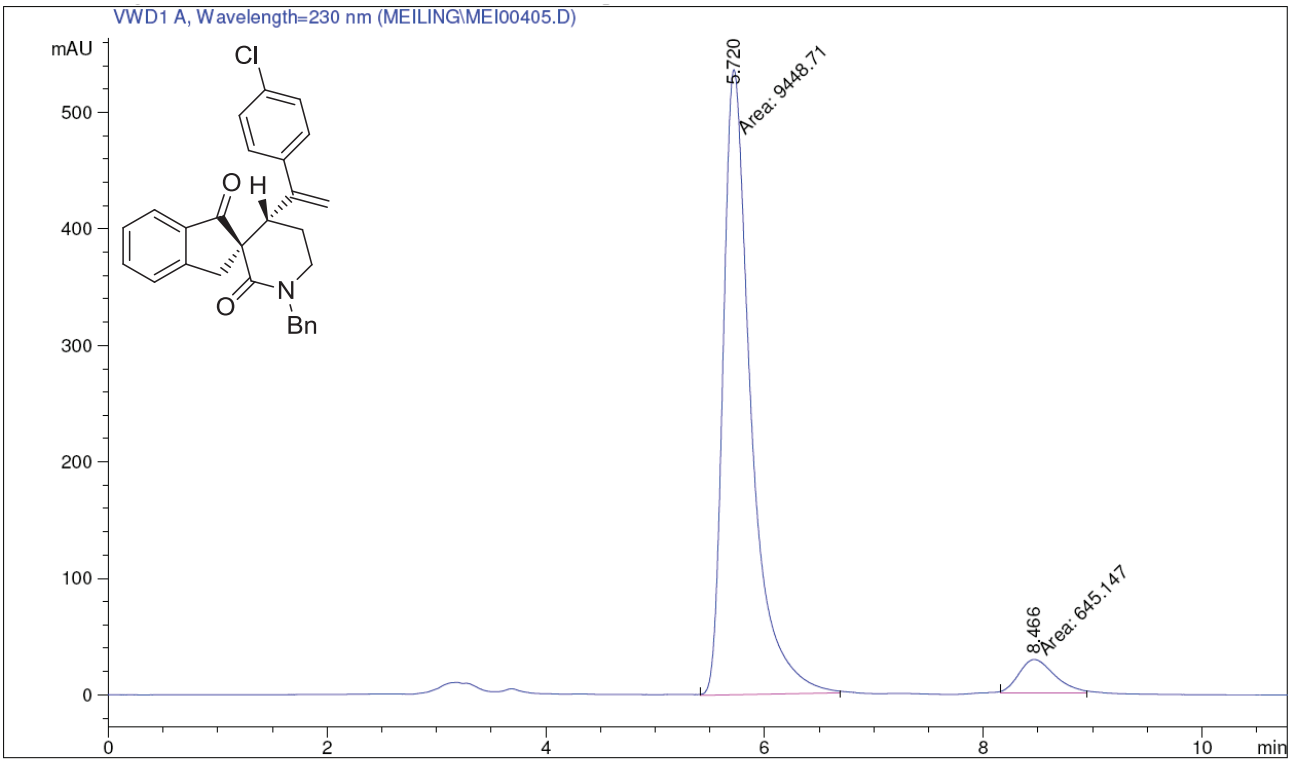
Racemic: Mixture of 2 diastereomers




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.717 BV    0.2623 8136.26270  455.67233  48.5110
   2   7.117 VV    0.2897  247.10759   12.44256   1.4733
   3   7.399 VV    0.3291  237.97835   10.47460   1.4189
   4   8.443 VV    0.3985 8150.64746  300.48026  48.5968

Totals :                  1.67720e4   779.06975

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

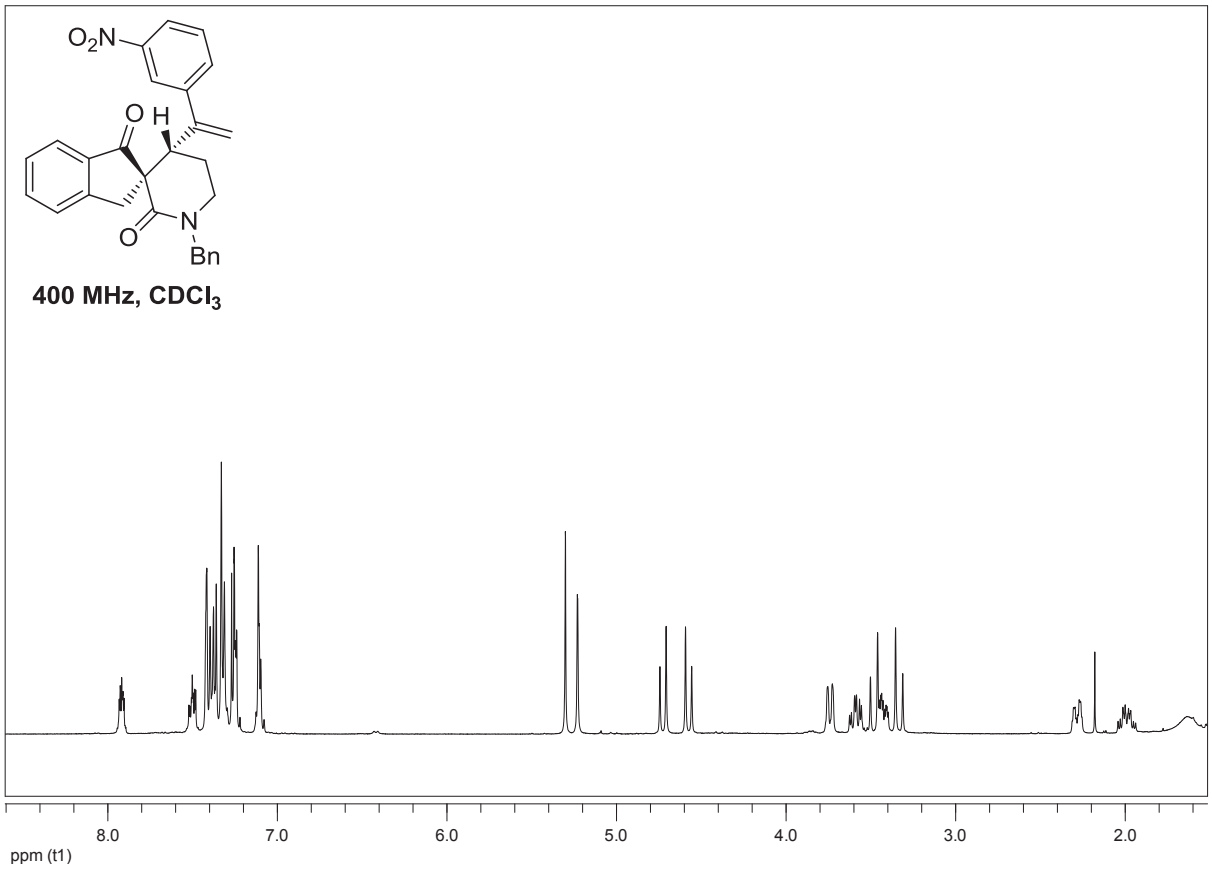
2g **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched: Major diastereomer

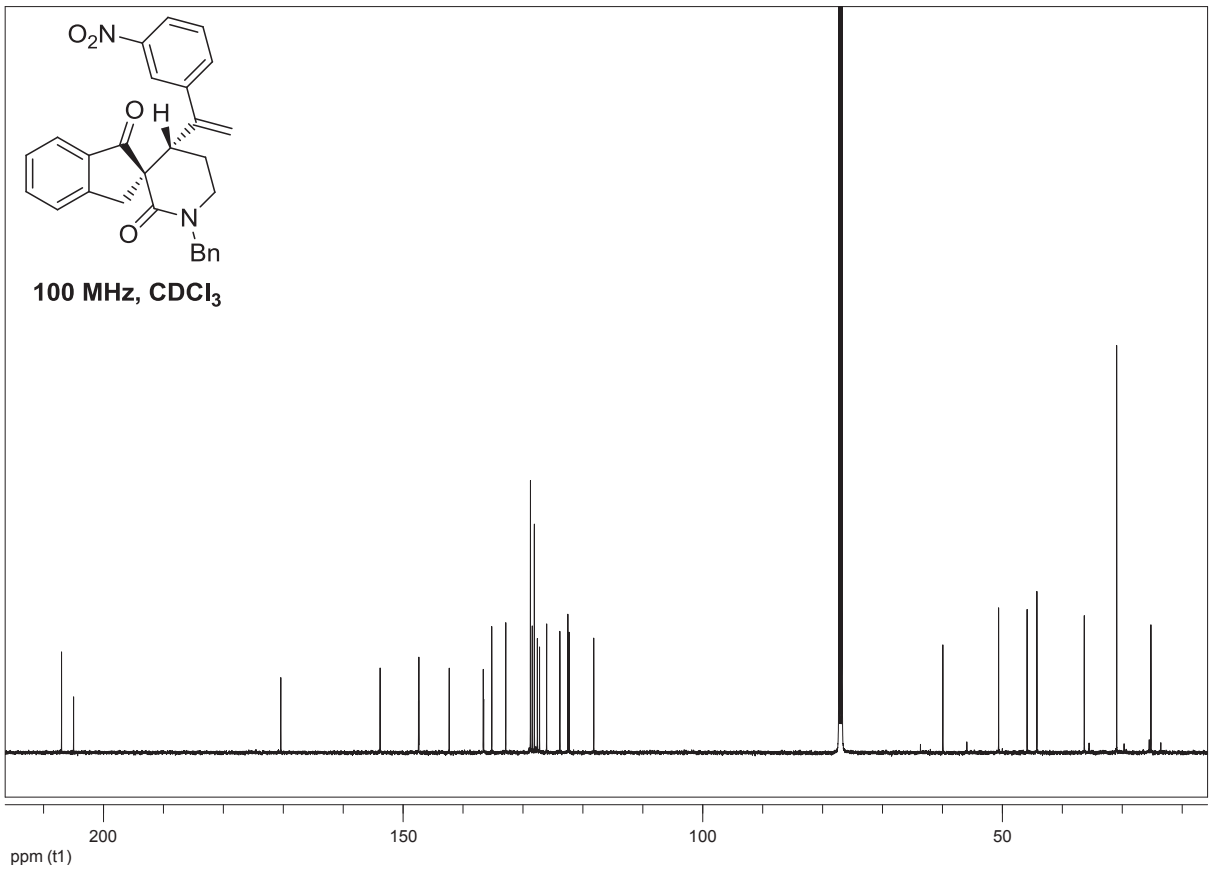



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.720 MM    0.2934 9448.71191  536.76563  93.6085
   2   8.466 MM    0.3775  645.14722   28.48247   6.3915

Totals :                  1.00939e4   565.24809

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **2h**

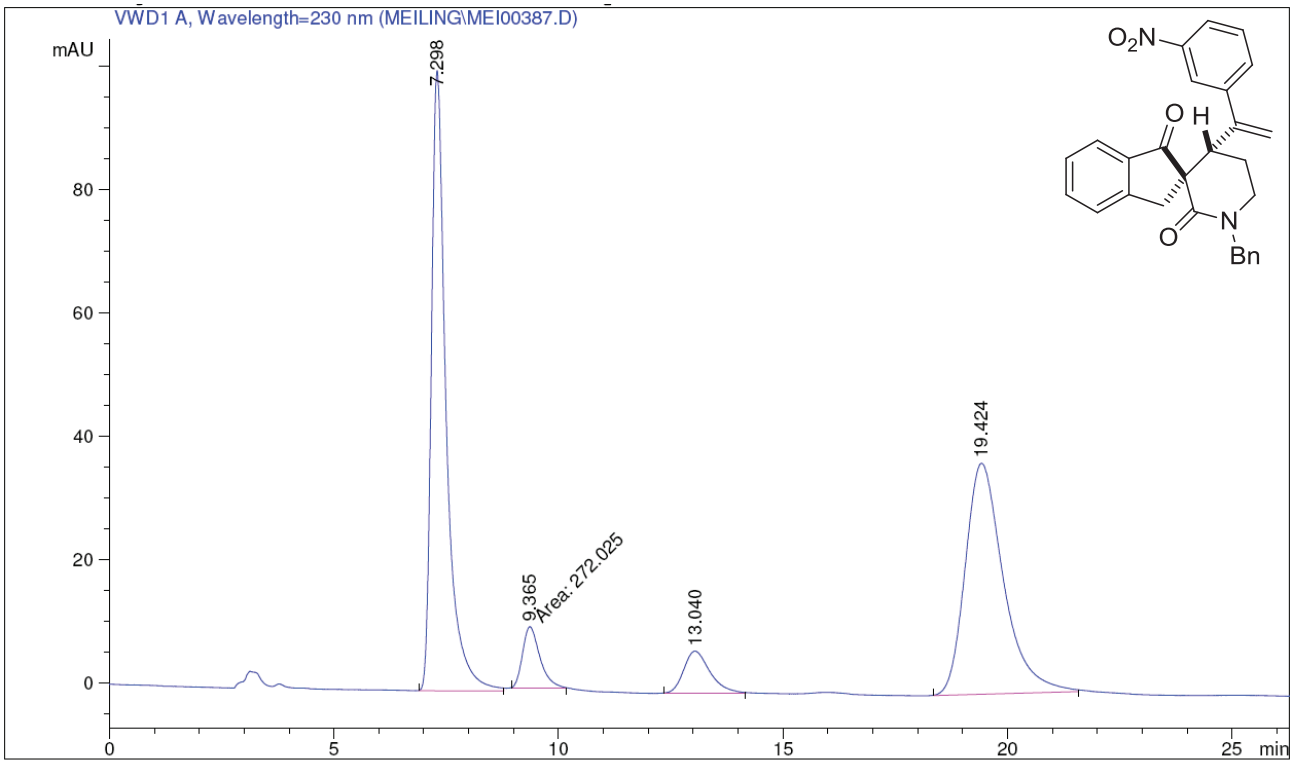


^{13}C NMR spectrum of **2h**



2h **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

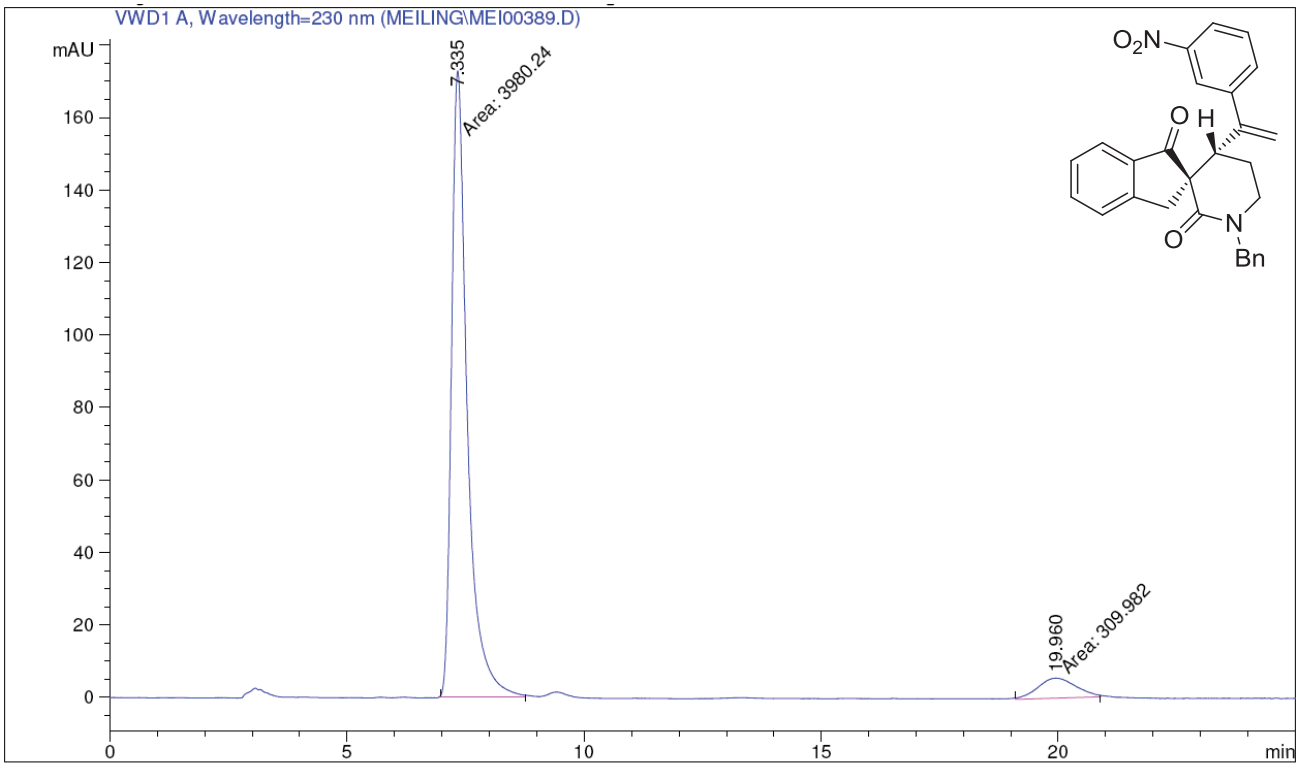
Racemic: Mixture of 2 diastereomers




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.298 BB    0.3416 2305.01953  100.48466  45.4246
   2   9.365 MM    0.4529  272.02536   10.01124   5.3607
   3  13.040 BB    0.6059  278.71246    6.83253   5.4925
   4  19.424 BB    0.8876 2218.63403   37.42518  43.7222

Totals :                  5074.39139  154.75362

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

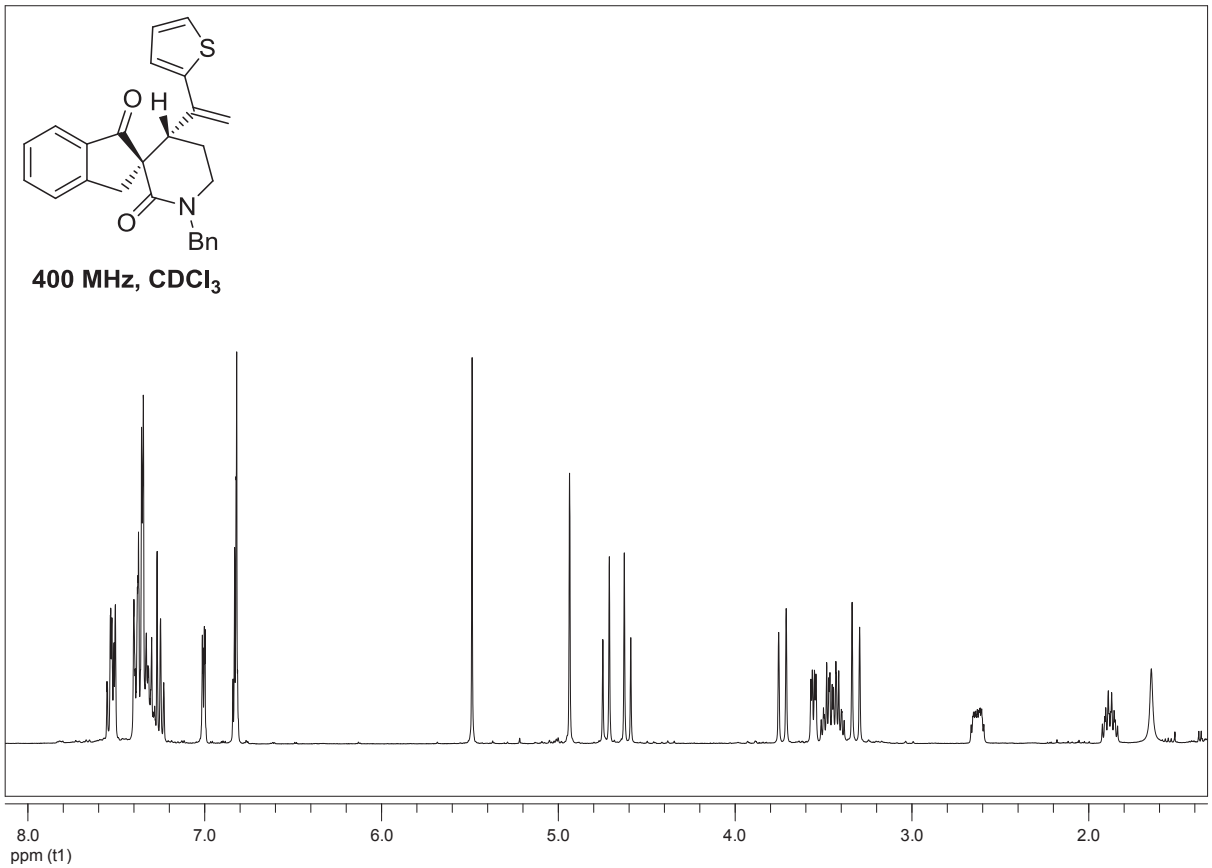
2h **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched: Major diastereomers

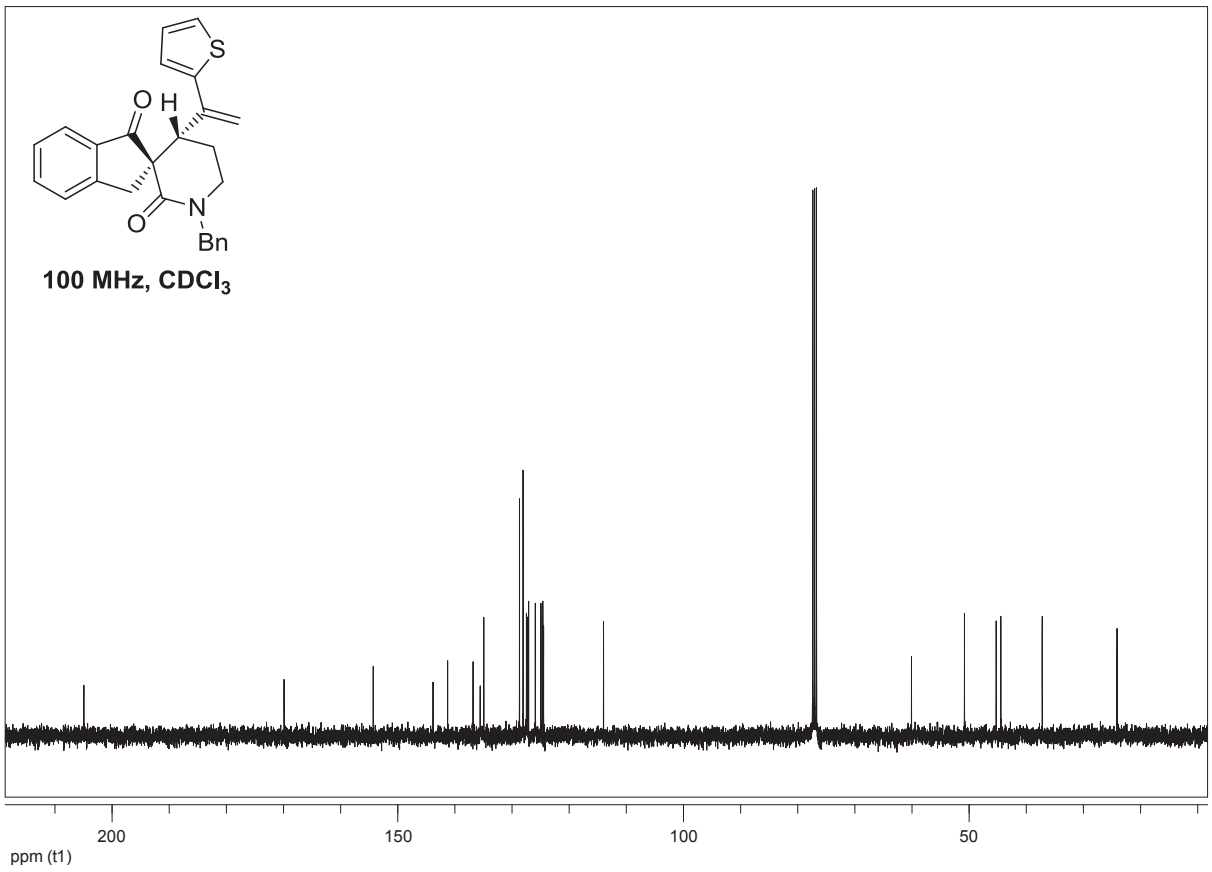



```
==================================================================================
                              Area Percent Report
==================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.335 MM    0.3840 3980.24463  172.73393  92.7747
   2  19.960 MM    0.9304  309.98196    5.55270   7.2253

Totals :                  4290.22659  178.28663

 Results obtained with enhanced integrator!
==================================================================================
                            *** End of Report ***
```

^{1}H NMR spectrum of **2i**

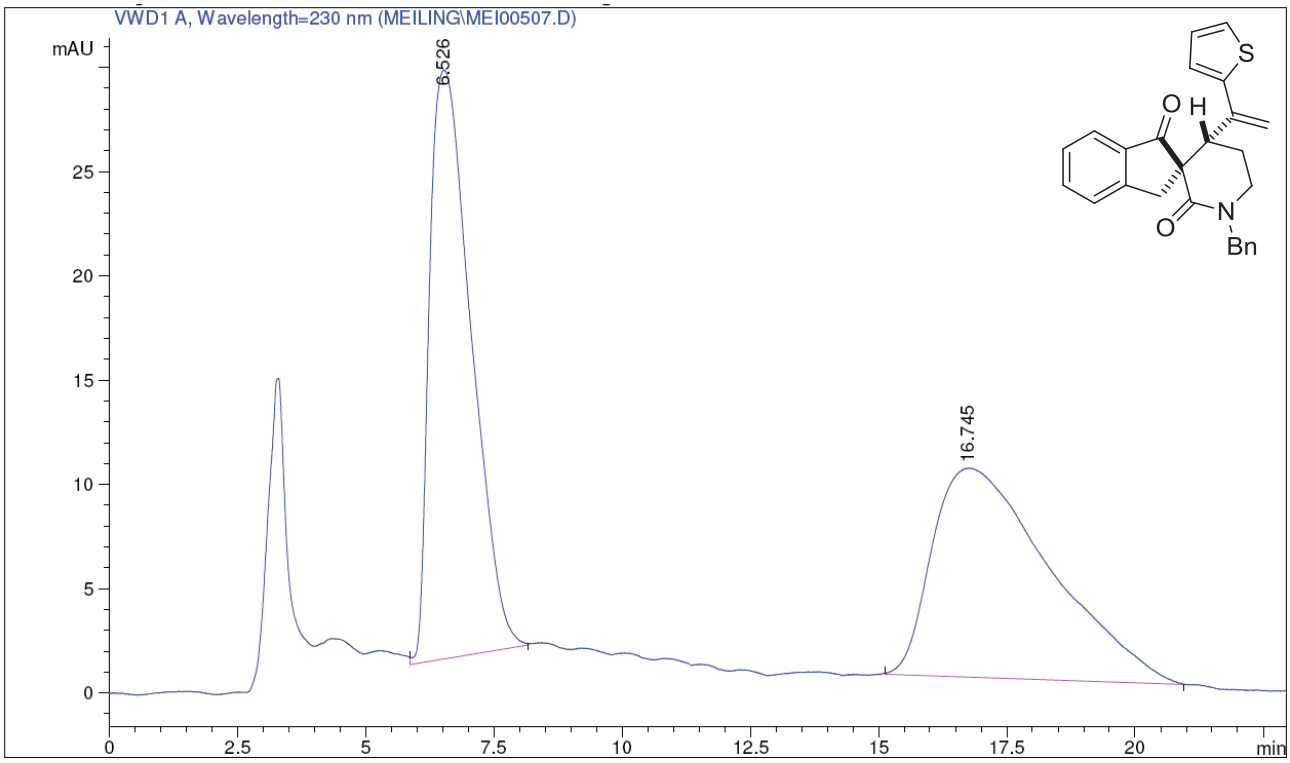


^{13}C NMR spectrum of **2i**



2i **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

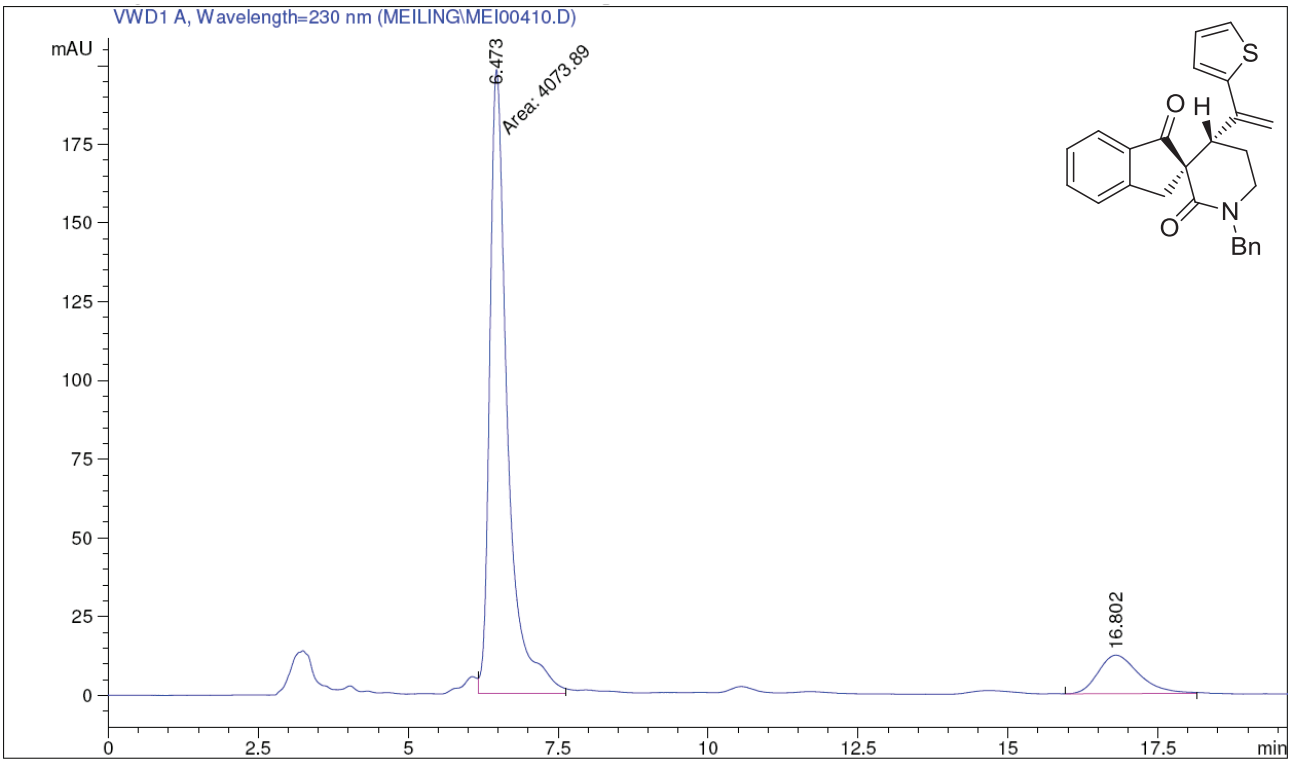
Racemic




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.526 BB    0.8490 1590.69617   28.24532  49.8209
   2  16.745 BB    1.8760 1602.13586   10.02752  50.1791

Totals :                  3192.83203   38.27284

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

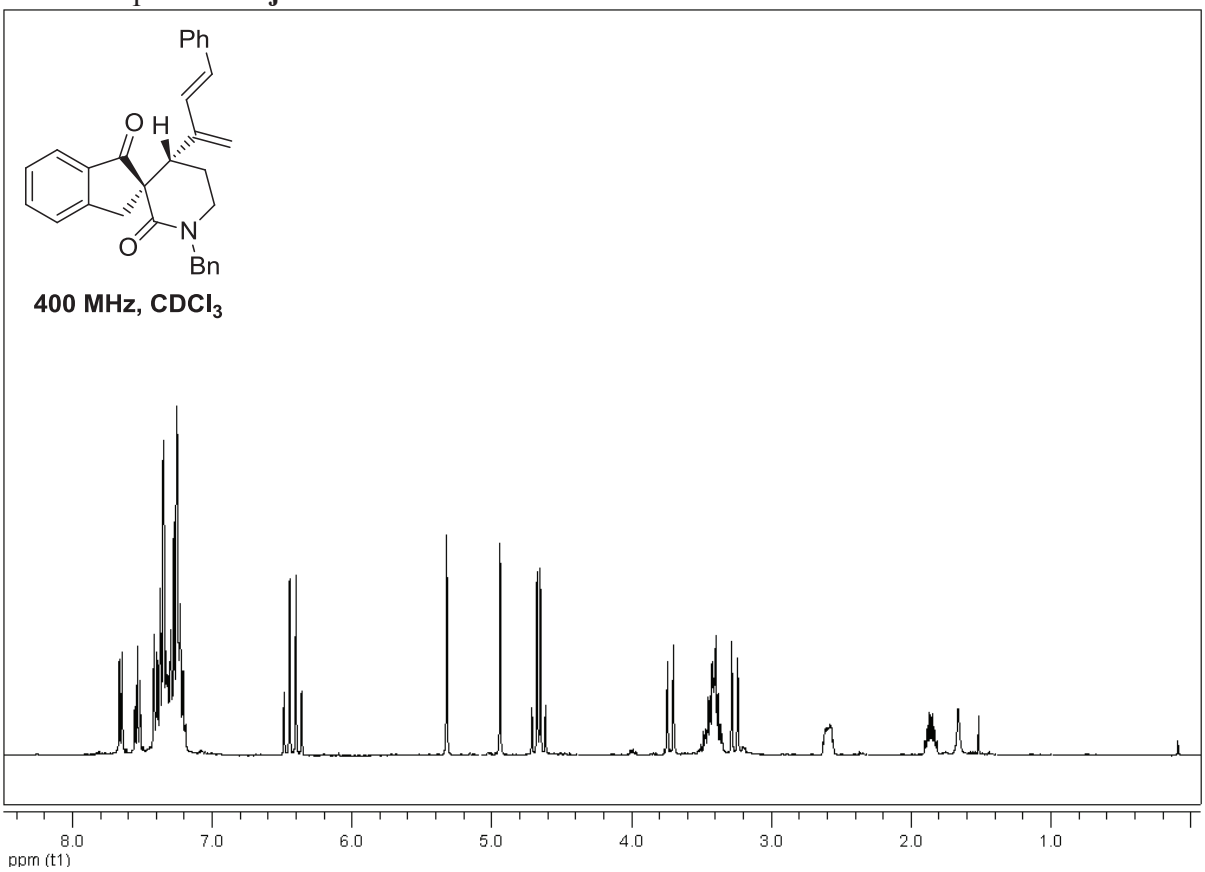
2i **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

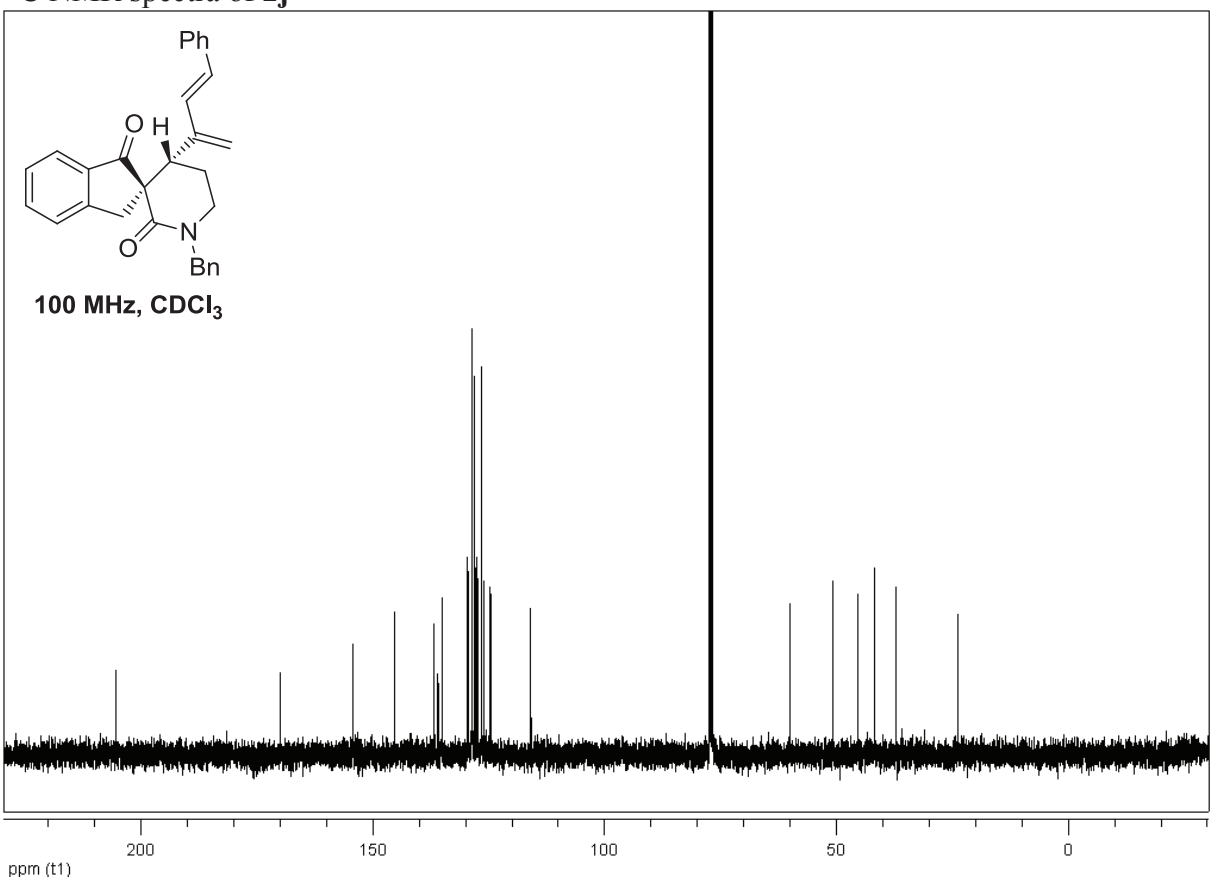



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.473 MM    0.3428 4073.88989  198.09509  87.5908
   2  16.802 BB    0.7108  577.15833   12.18167  12.4092

Totals :                  4651.04822  210.27676

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

^{1}H NMR spectra of **2j**

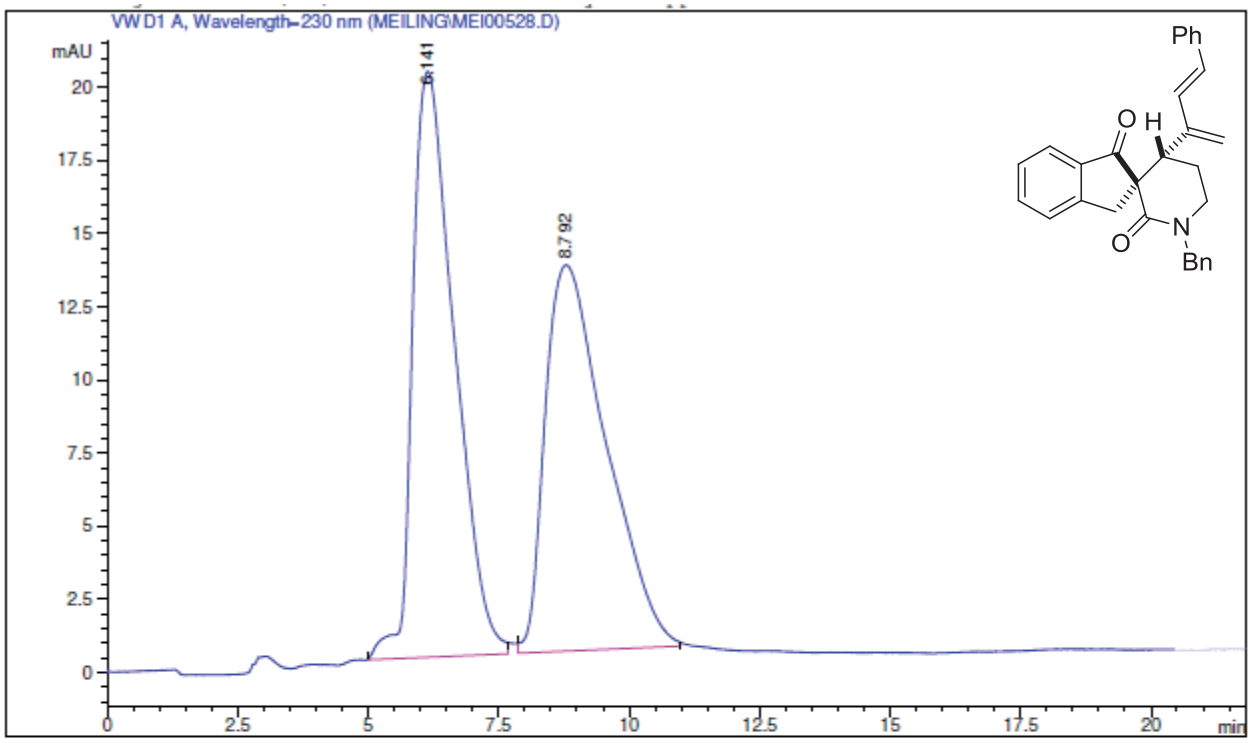


^{13}C NMR spectra of **2j**



2j **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

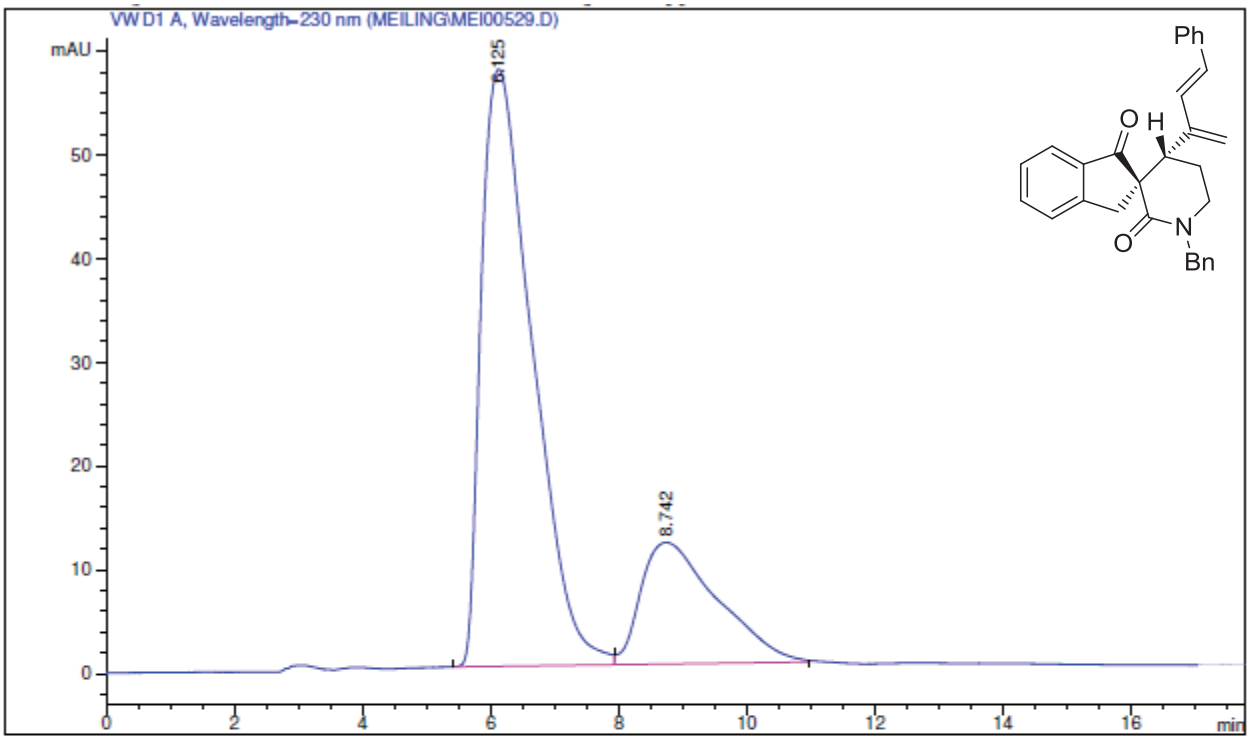
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.141	BB	0.8308	1113.48547	20.02211	50.8738
2	8.792	BB	1.1848	1075.23462	13.19364	49.1262
Totals :				2188.72009	33.21574	

Results obtained with enhanced integrator!

*** End of Report ***

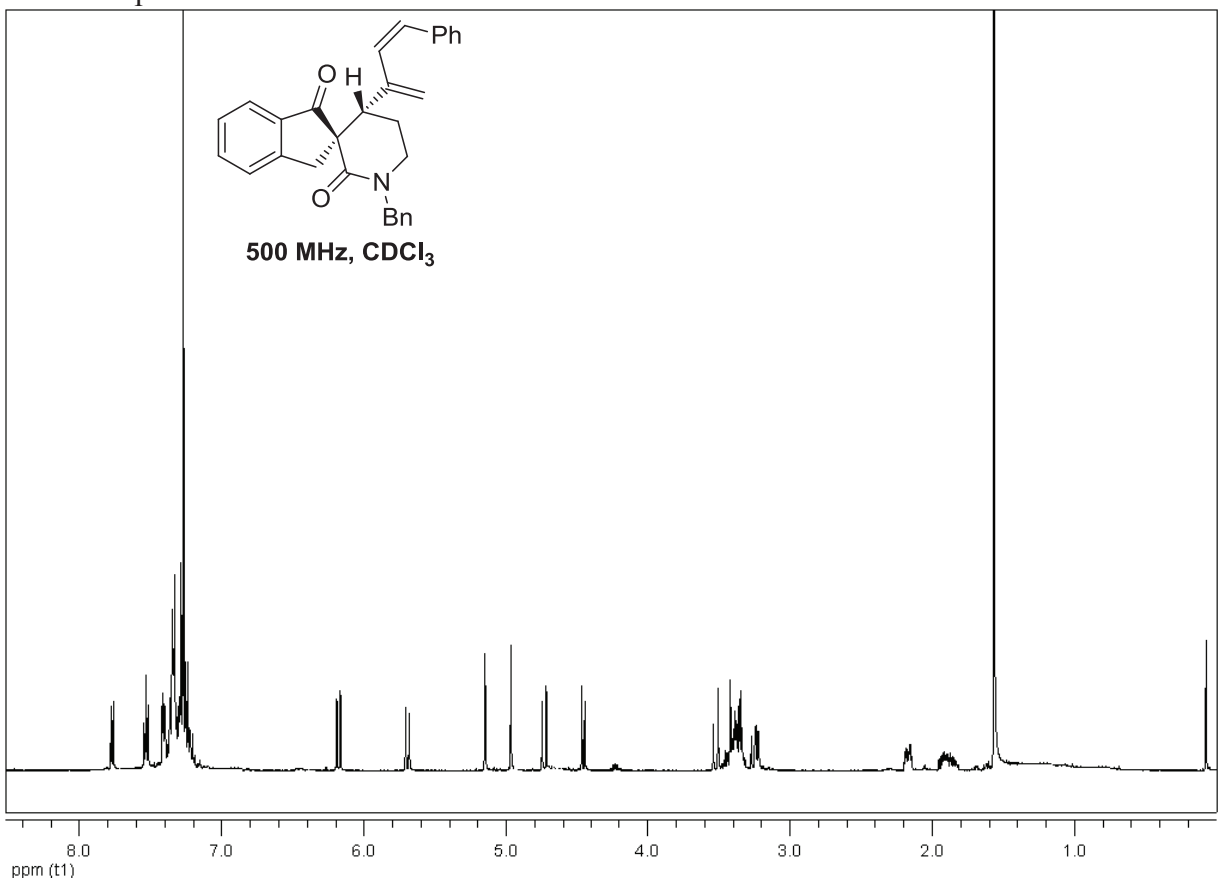
2j **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

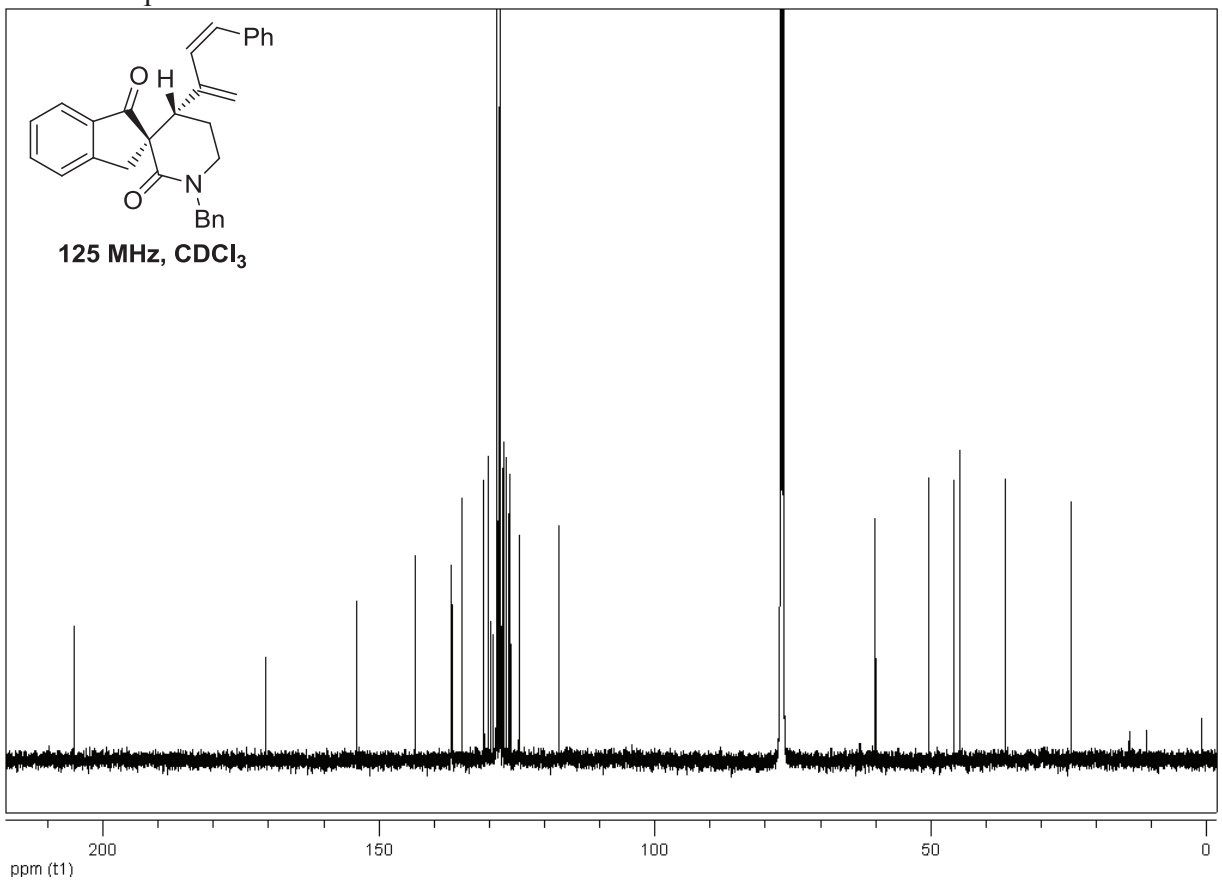



```
------------------------------------------------------------------------
                        Area Percent Report
------------------------------------------------------------------------

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.125 BV    0.8209 3181.31592   57.54797  76.5919
   2   8.742 VB    1.1703  972.27789   11.71471  23.4081

Totals :                  4153.59381   69.26268

 Results obtained with enhanced integrator!
------------------------------------------------------------------------
                        *** End of Report ***
```

^{1}H NMR spectra of **2k**

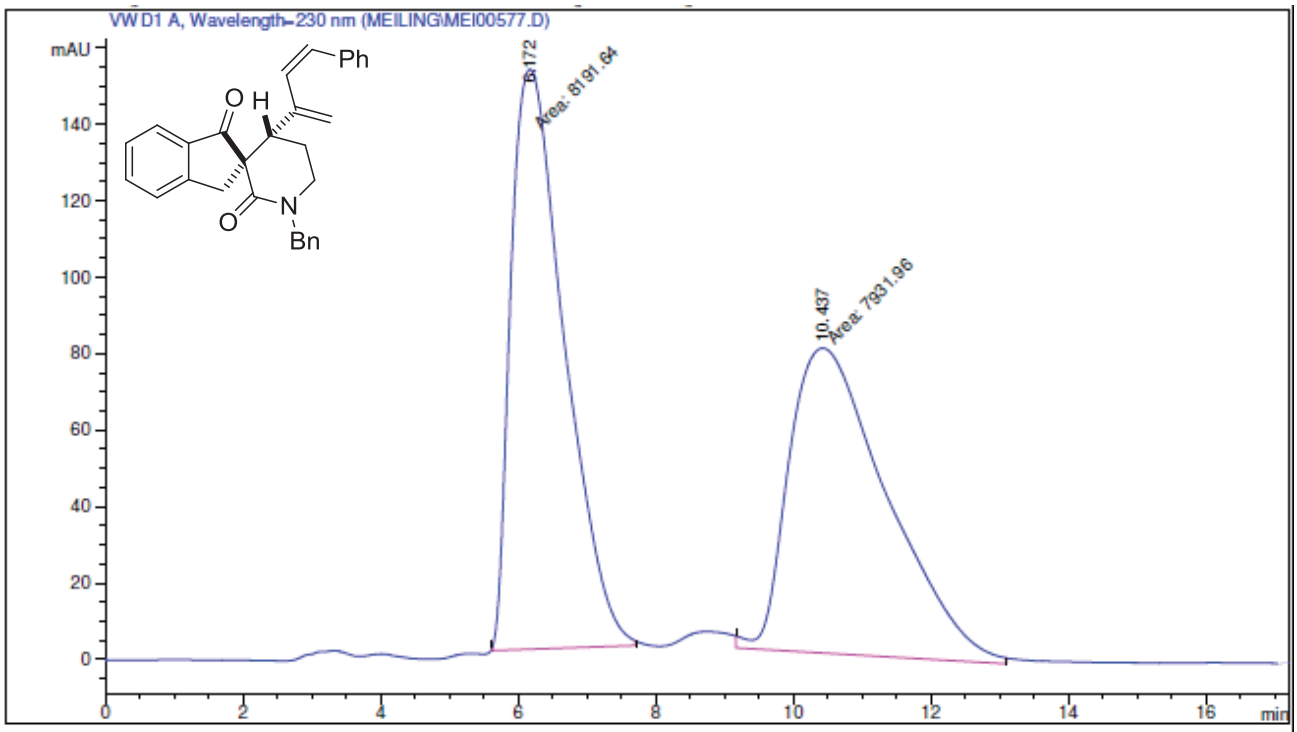


^{13}C NMR spectra of **2k**



2k **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.172	MM	0.9001	8191.64355	151.67474	50.8053
2	10.437	MM	1.6574	7931.95605	79.76170	49.1947

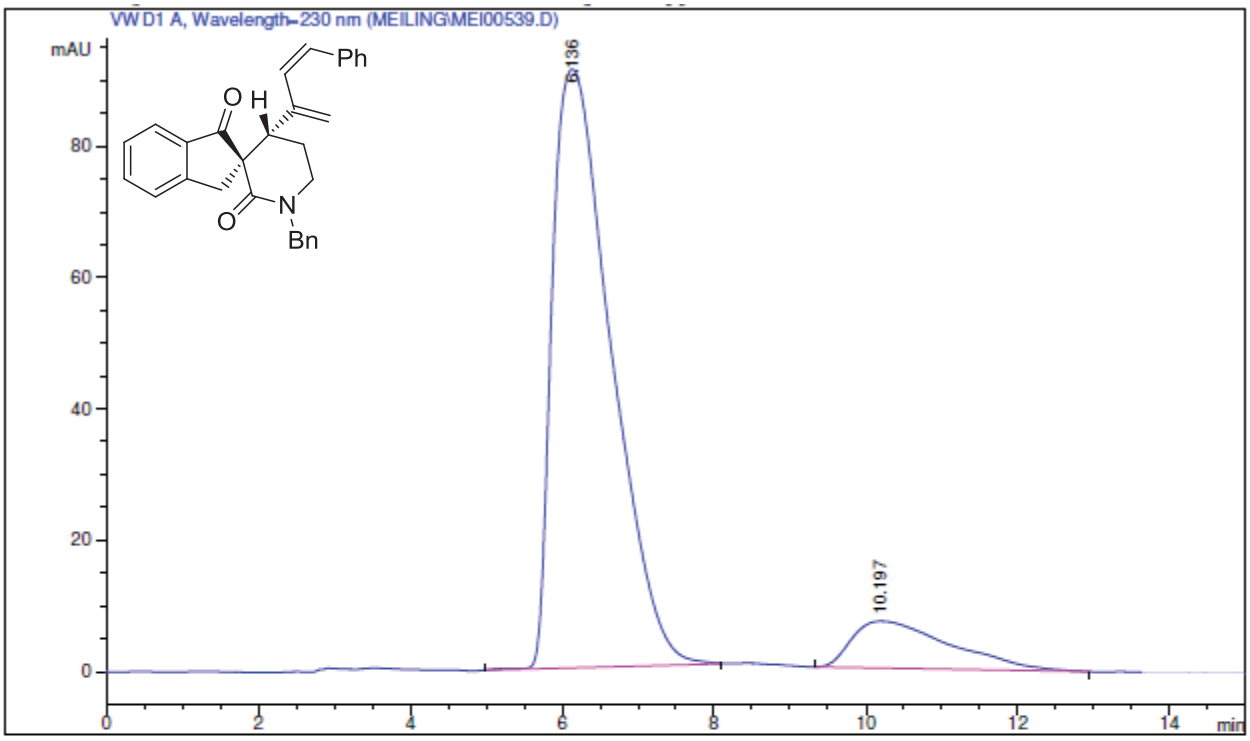
Totals : 1.61236e4 231.43644

Results obtained with enhanced integrator!

*** End of Report ***

2k **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

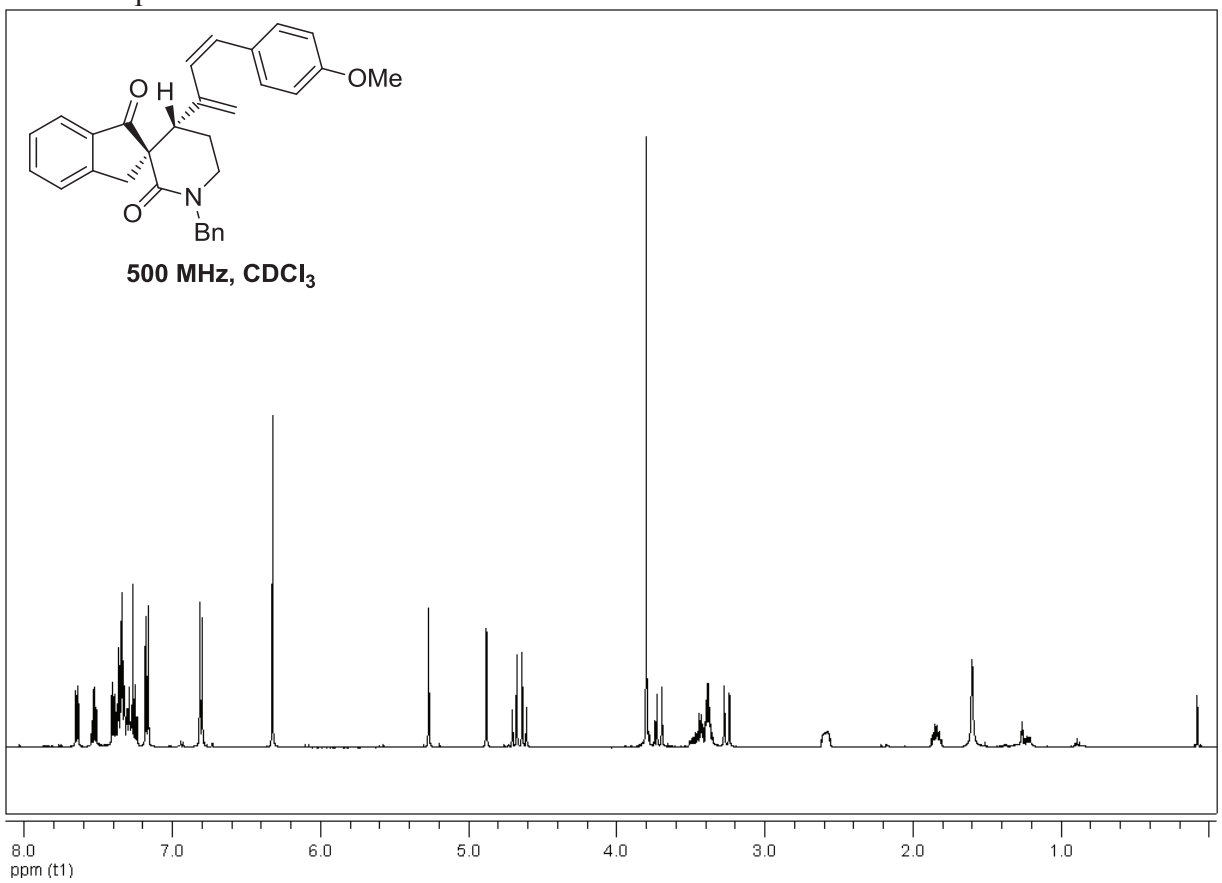
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.136	PB	0.8137	4887.21973	91.12161	88.3431
2	10.197	PP	1.0749	644.87280	7.15886	11.6569

Totals : 5532.09253 98.28047

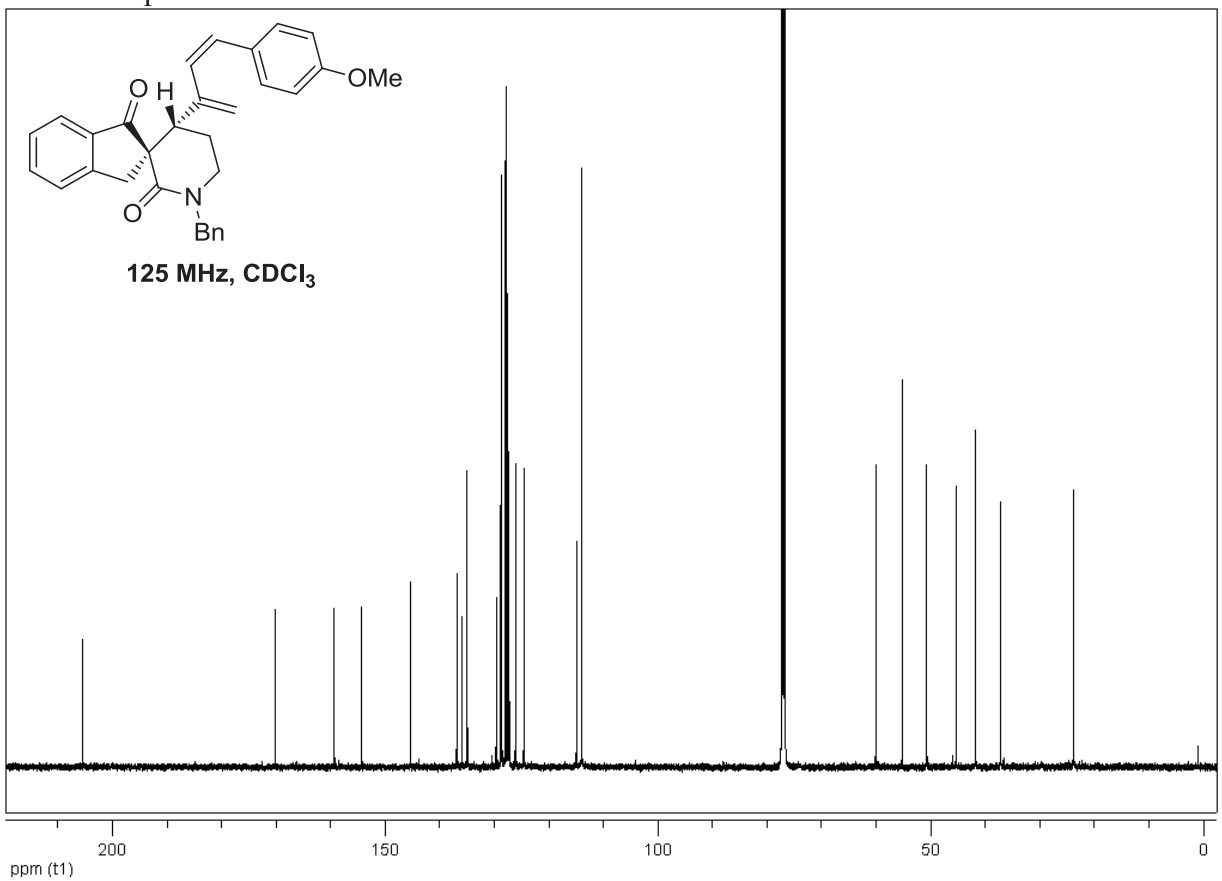
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectra of **2l**

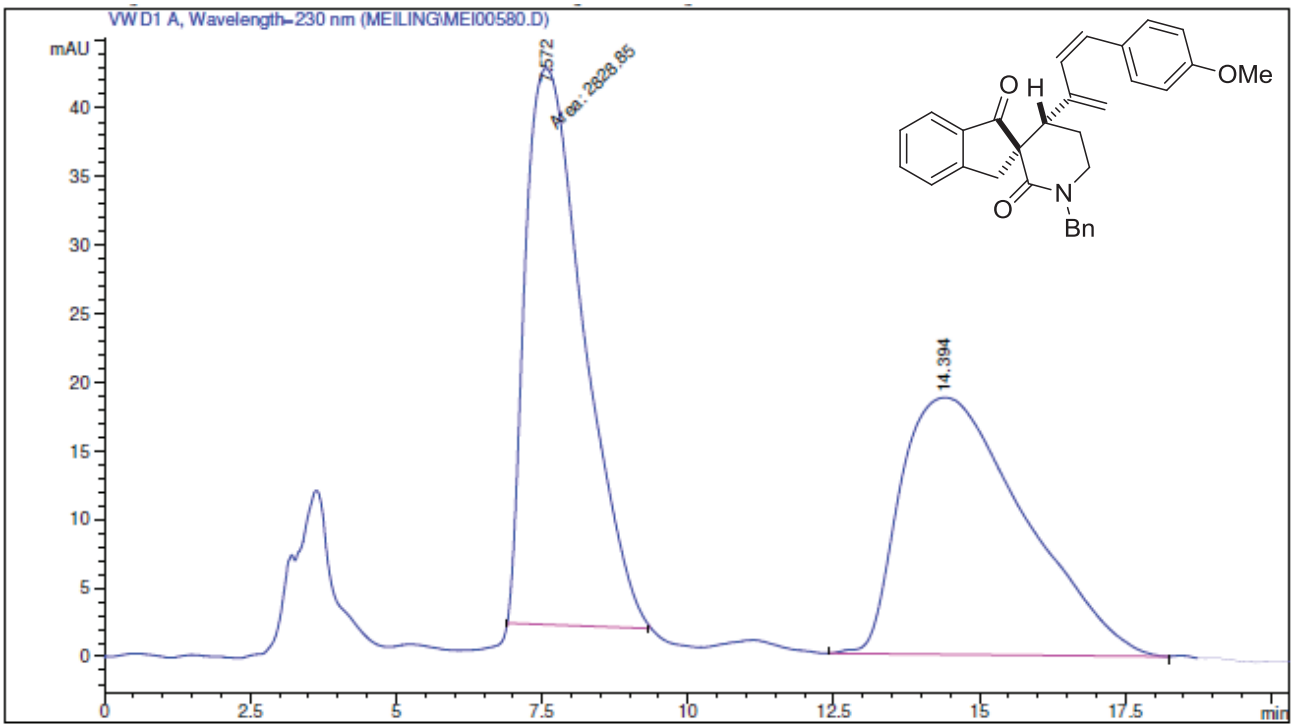


^{13}C NMR spectra of **2l**



2l **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.572	MM	1.1623	2828.85156	40.56512	50.4575
2	14.394	PP	1.7396	2777.55273	18.73517	49.5425

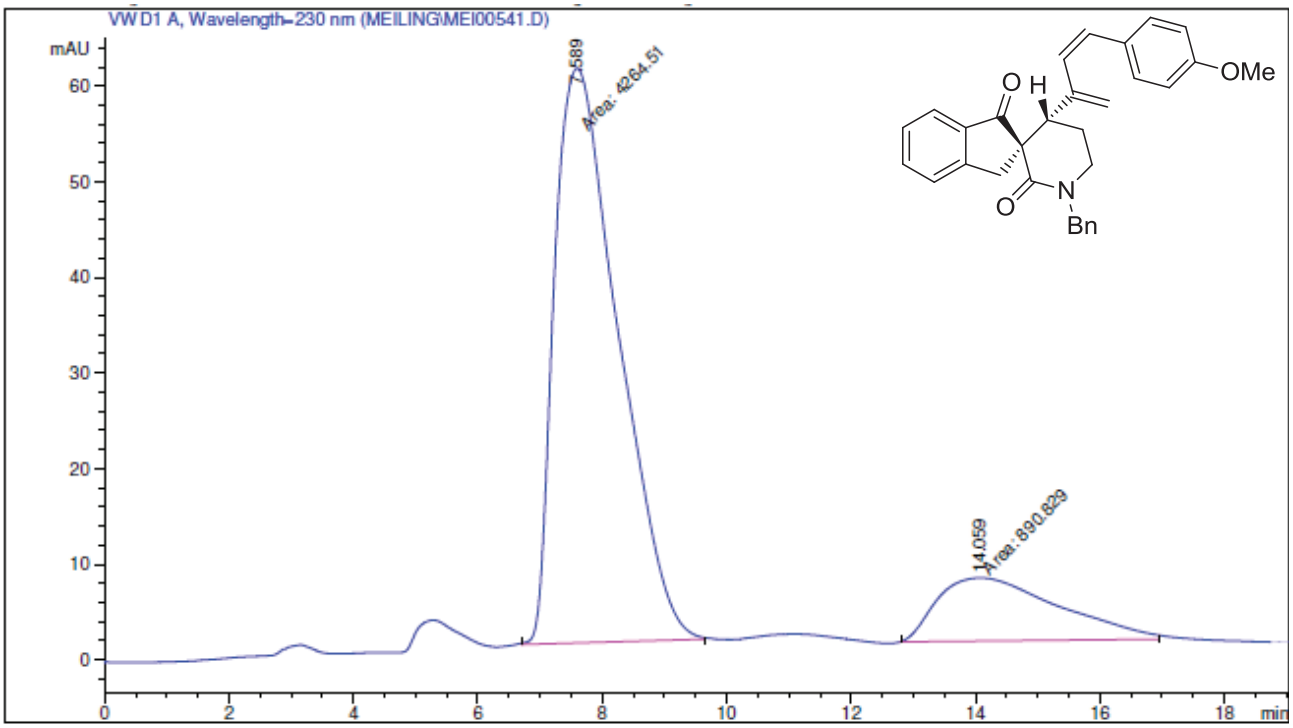
Totals : 5606.40430 59.30029

Results obtained with enhanced integrator!

*** End of Report ***

2l **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

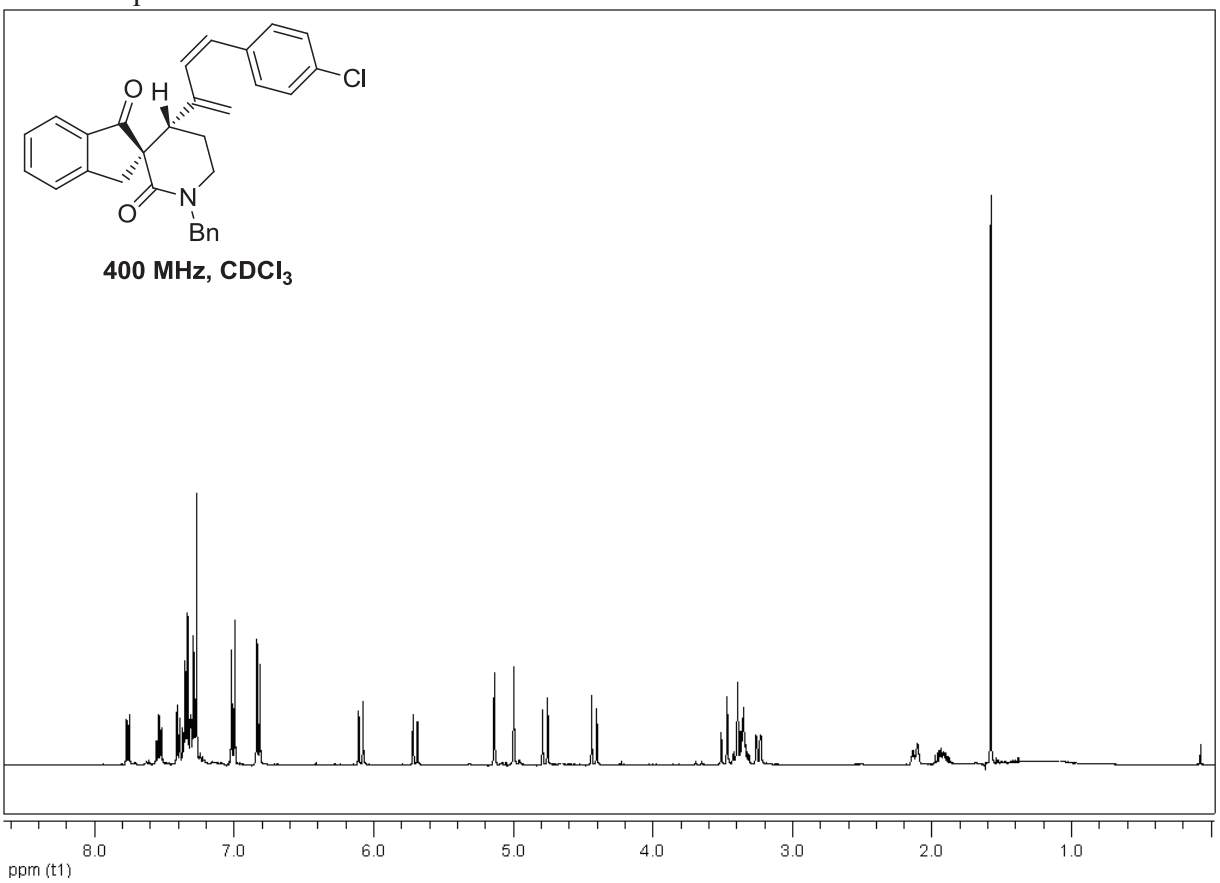
Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.589	MM	1.1834	4264.51367	60.05998	82.7203
2	14.059	MM	2.2504	890.82867	6.59764	17.2797
Totals :				5155.34235	66.65762	

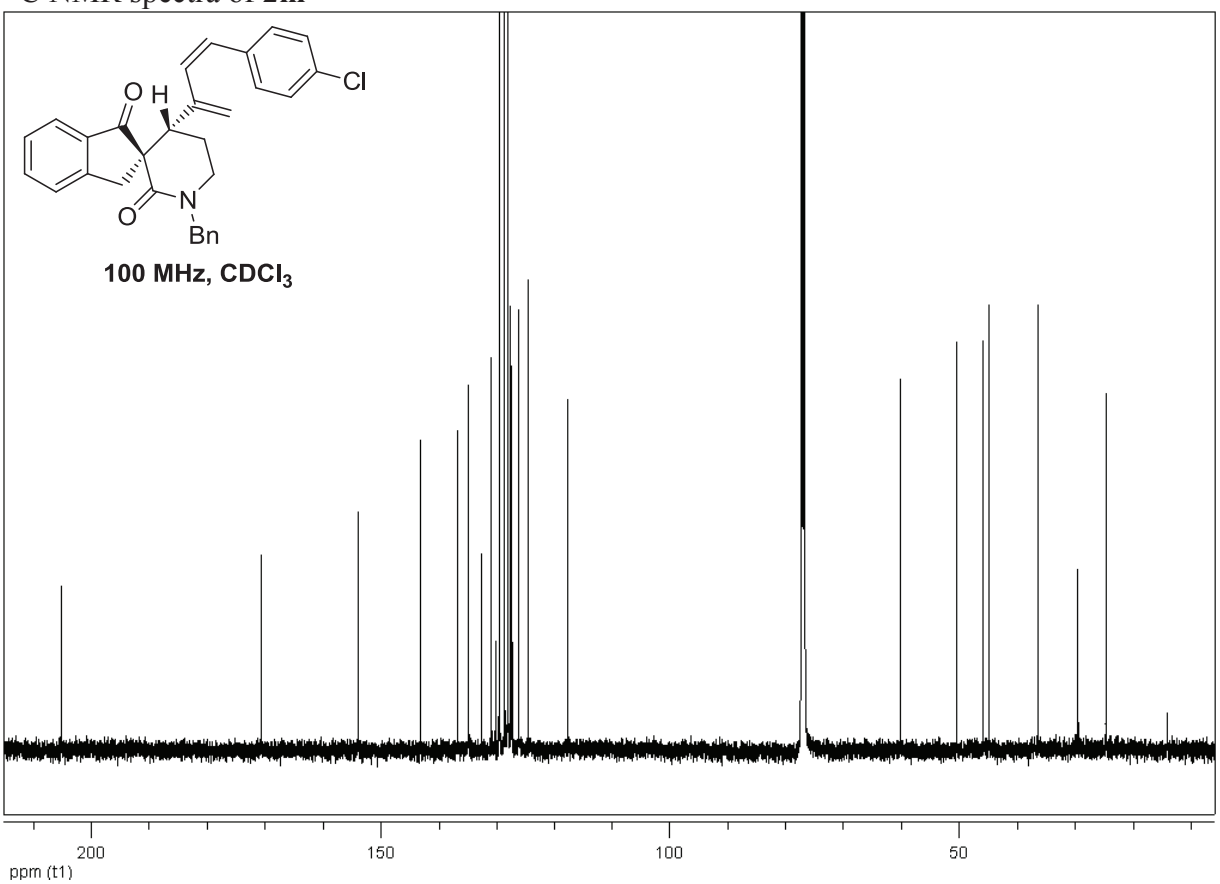
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectra of **2m**

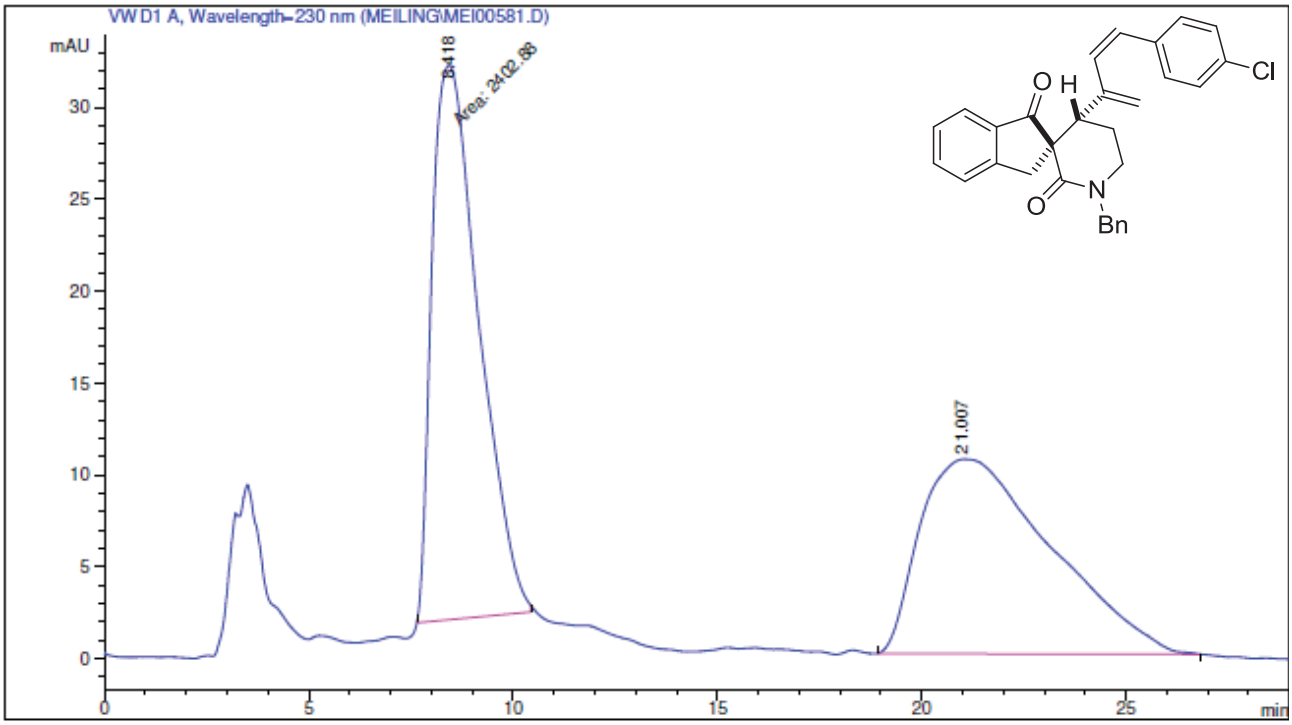


^{13}C NMR spectra of **2m**



2m **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.418	MM	1.3267	2402.87817	30.18527	50.4327
2	21.007	BB	2.6005	2361.64941	10.60714	49.5673

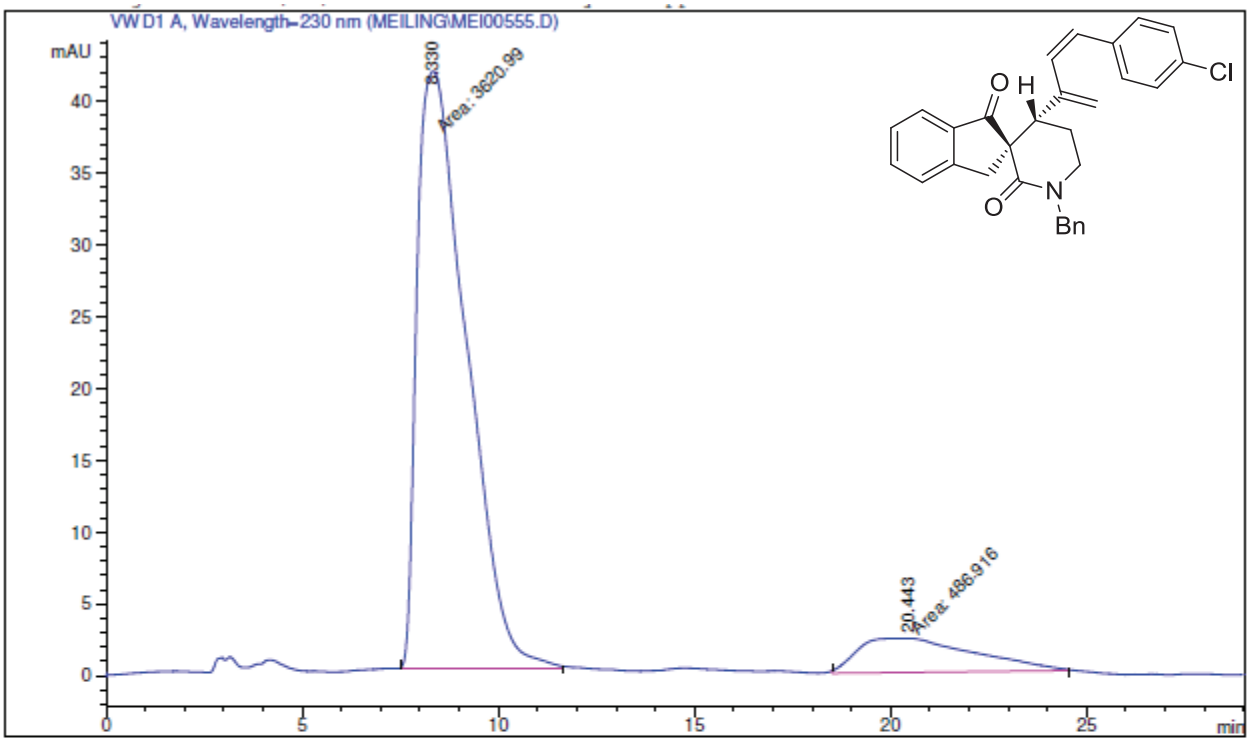
Totals : 4764.52759 40.79241

Results obtained with enhanced integrator!

*** End of Report ***

2m **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

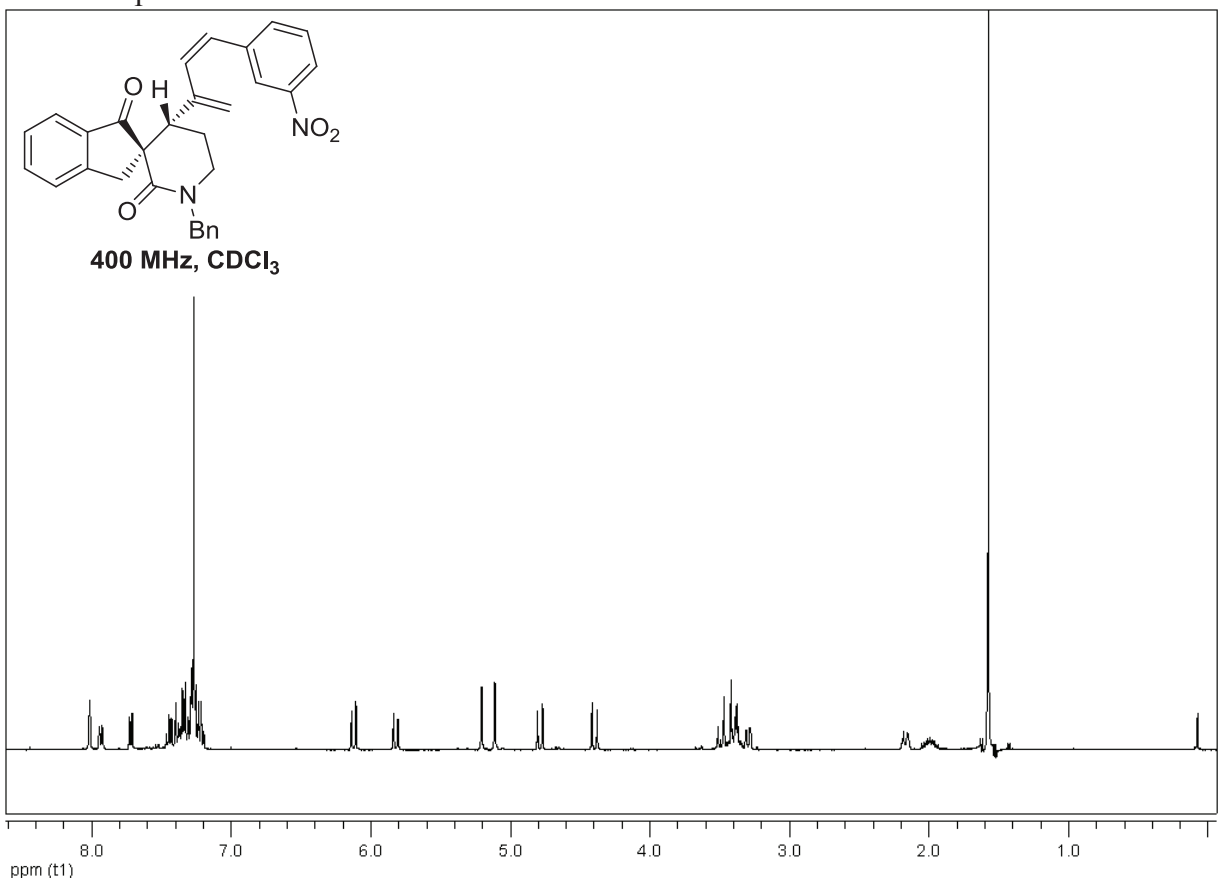
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.330	MM	1.4546	3620.98975	41.48933	88.1469
2	20.443	MM	3.4284	486.91556	2.36707	11.8531

Totals : 4107.90530 43.85640

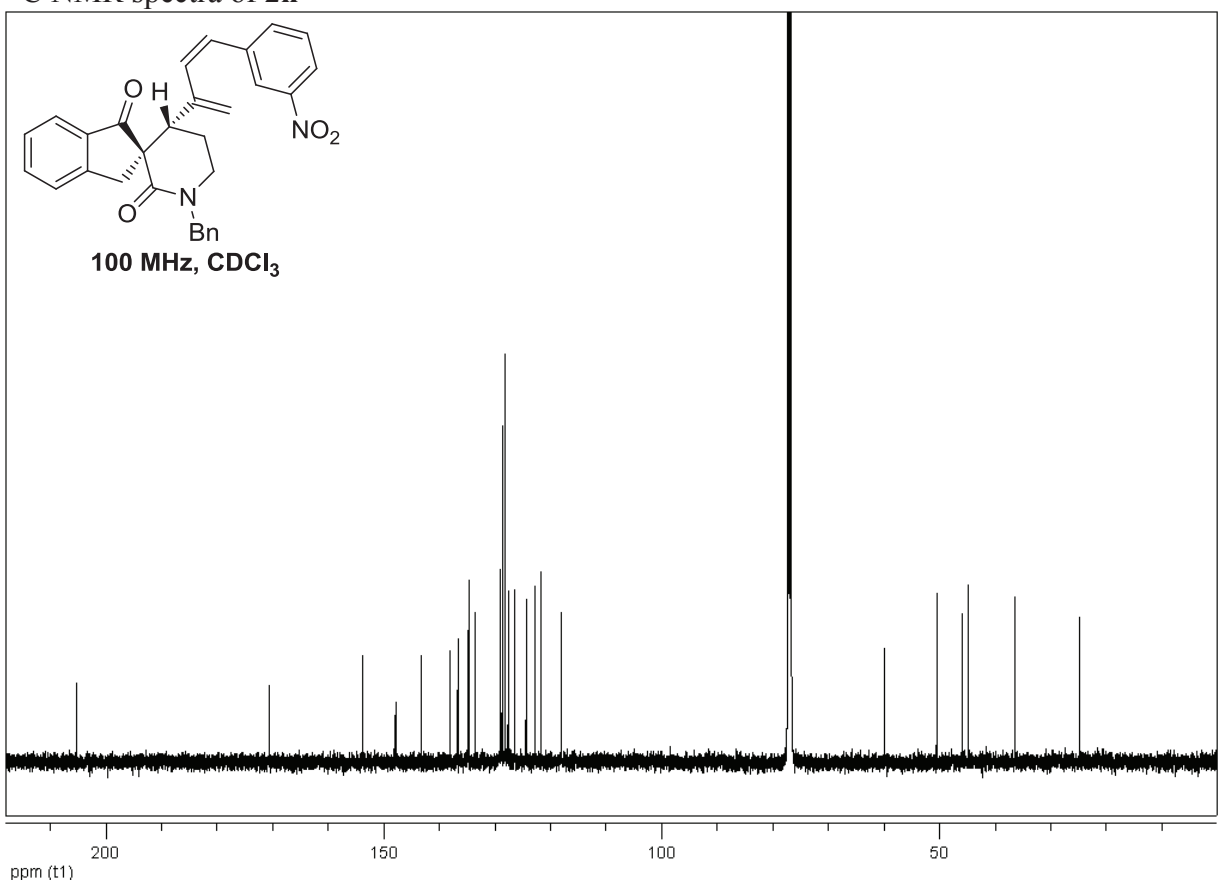
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectra of **2n**

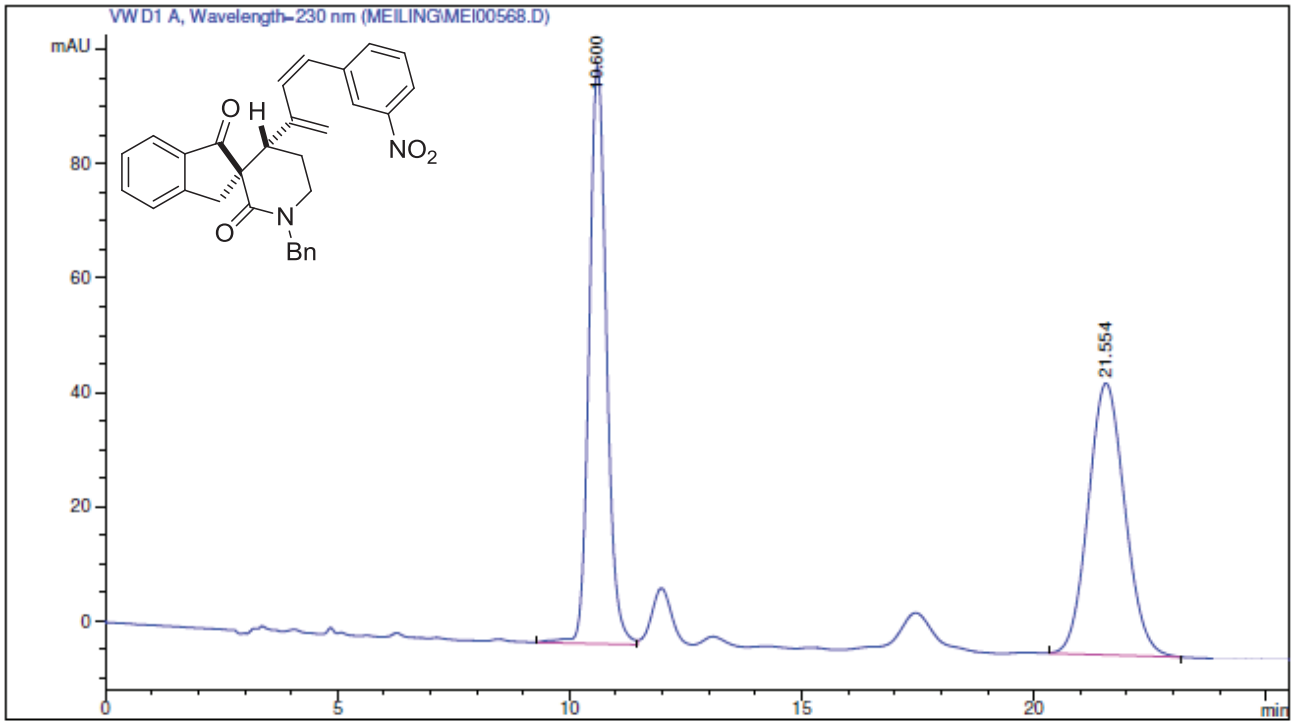


^{13}C NMR spectra of **2n**



2n **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

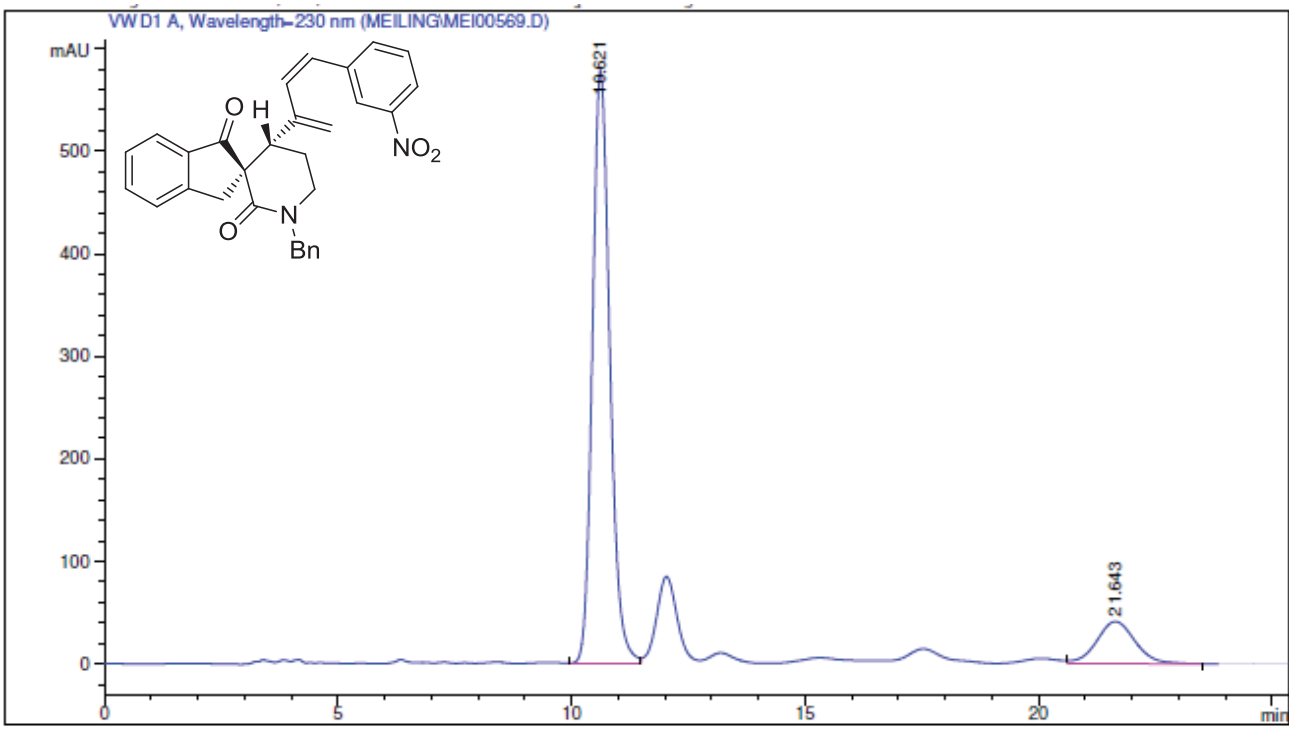
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.600	BB	0.3945	2634.79565	101.28857	50.2120
2	21.554	BB	0.6805	2612.54712	47.58736	49.7880
Totals :				5247.34277	148.87593	

Results obtained with enhanced integrator!

*** End of Report ***

2n **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

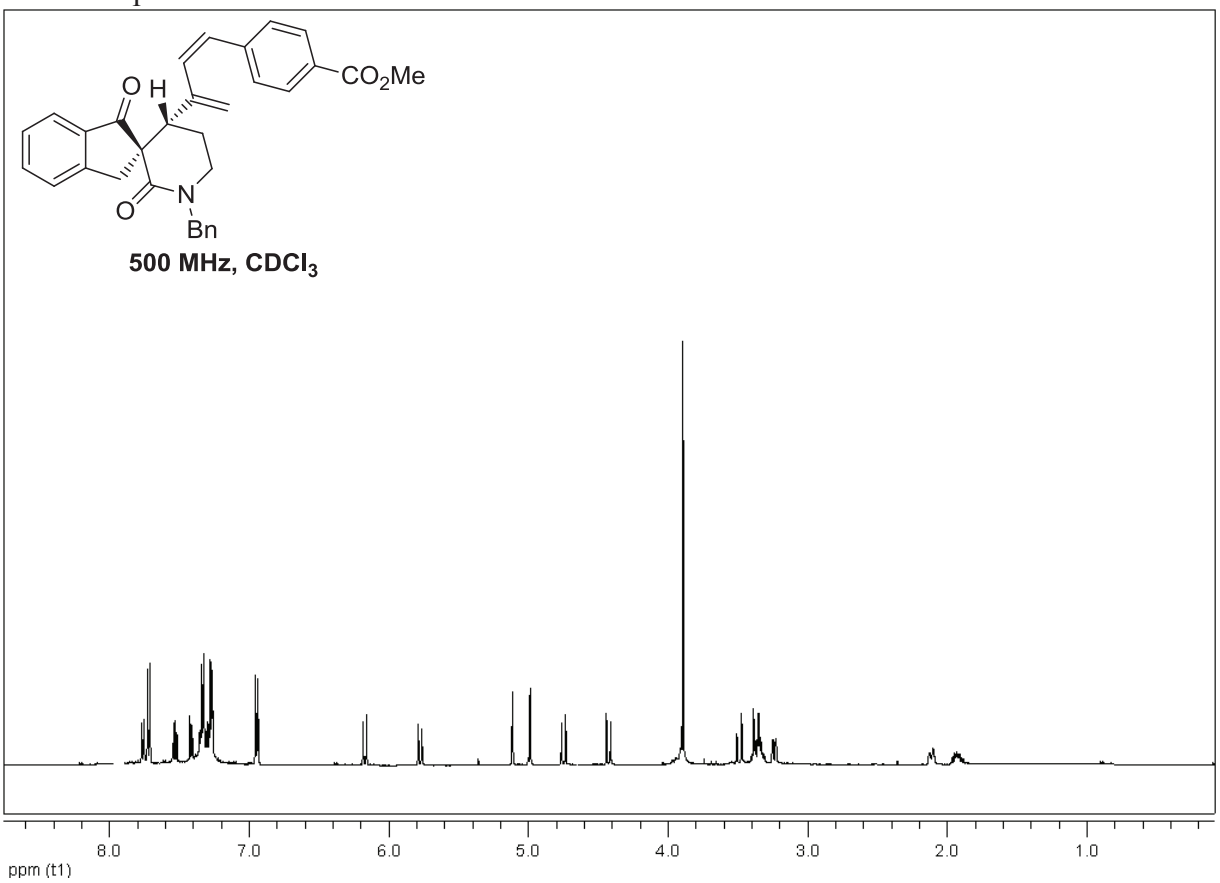
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.621	VV	0.4020	1.50271e4	578.69391	86.3312
2	21.643	VB	0.7034	2379.22778	41.28006	13.6688

Totals : 1.74063e4 619.97397

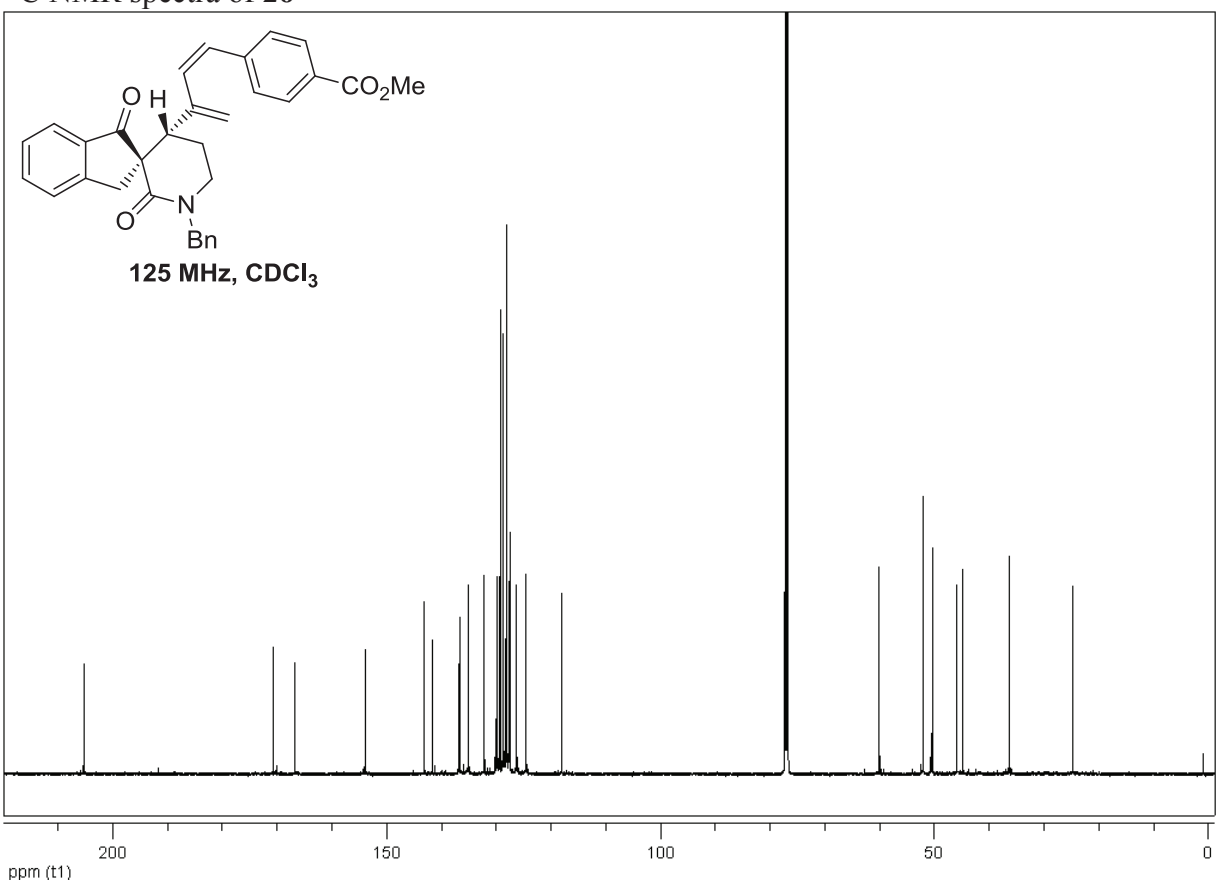
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectra of **2o**

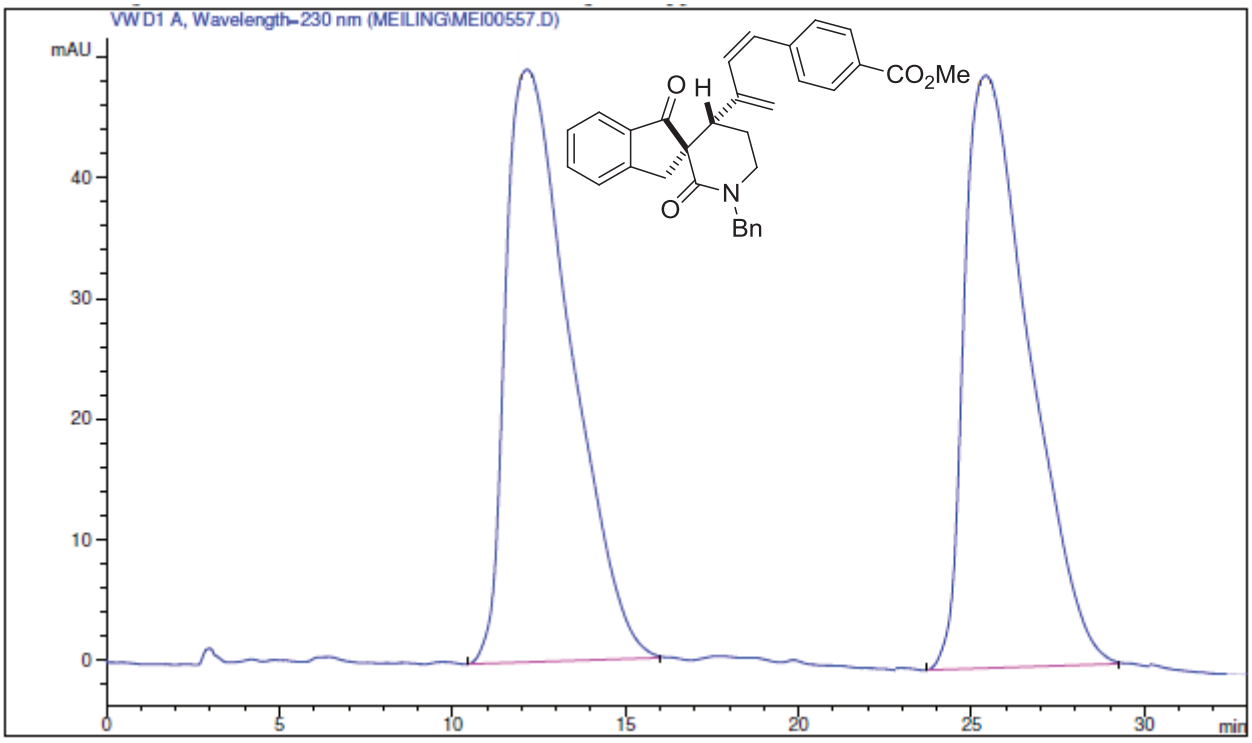


^{13}C NMR spectra of **2o**



2o **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

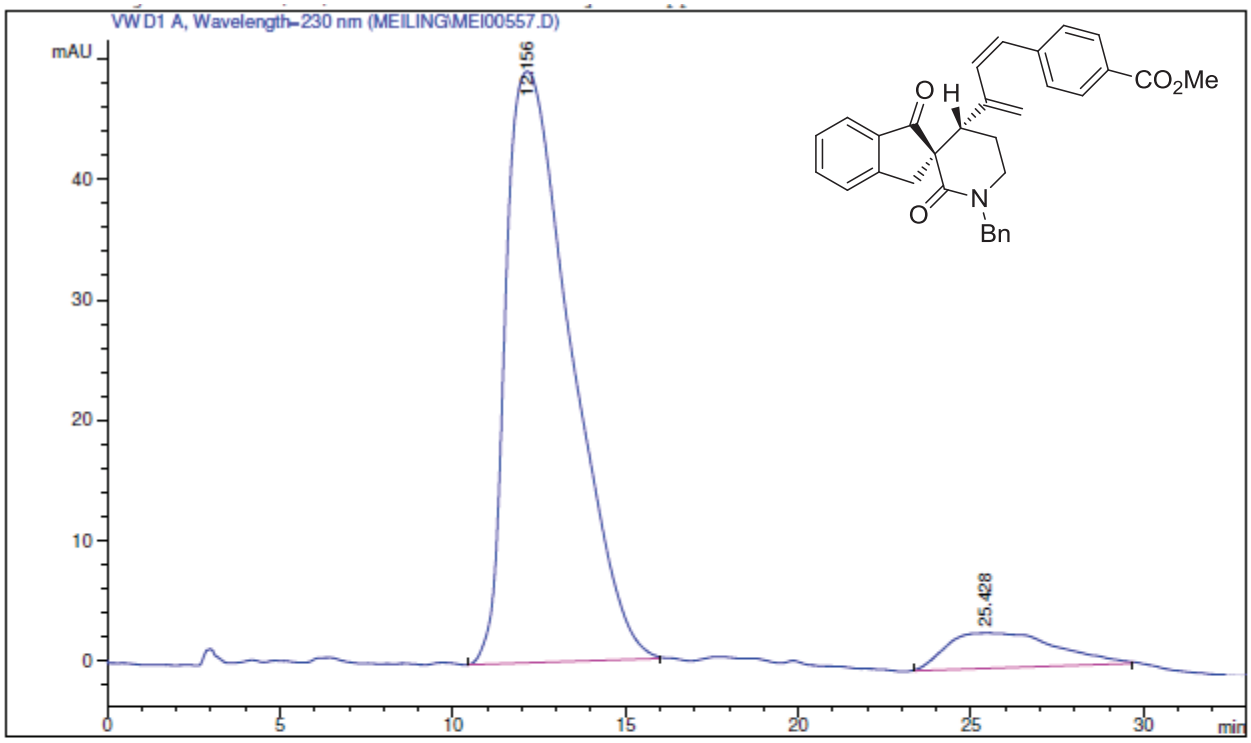
Racemic




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.156 PB    1.8330 3500.56494   49.09288  50.7575
   2  25.428 BB    2.5722  3510.34579   49.10059  49.2425

Totals :                  7070.05457   52.02750

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

2o **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

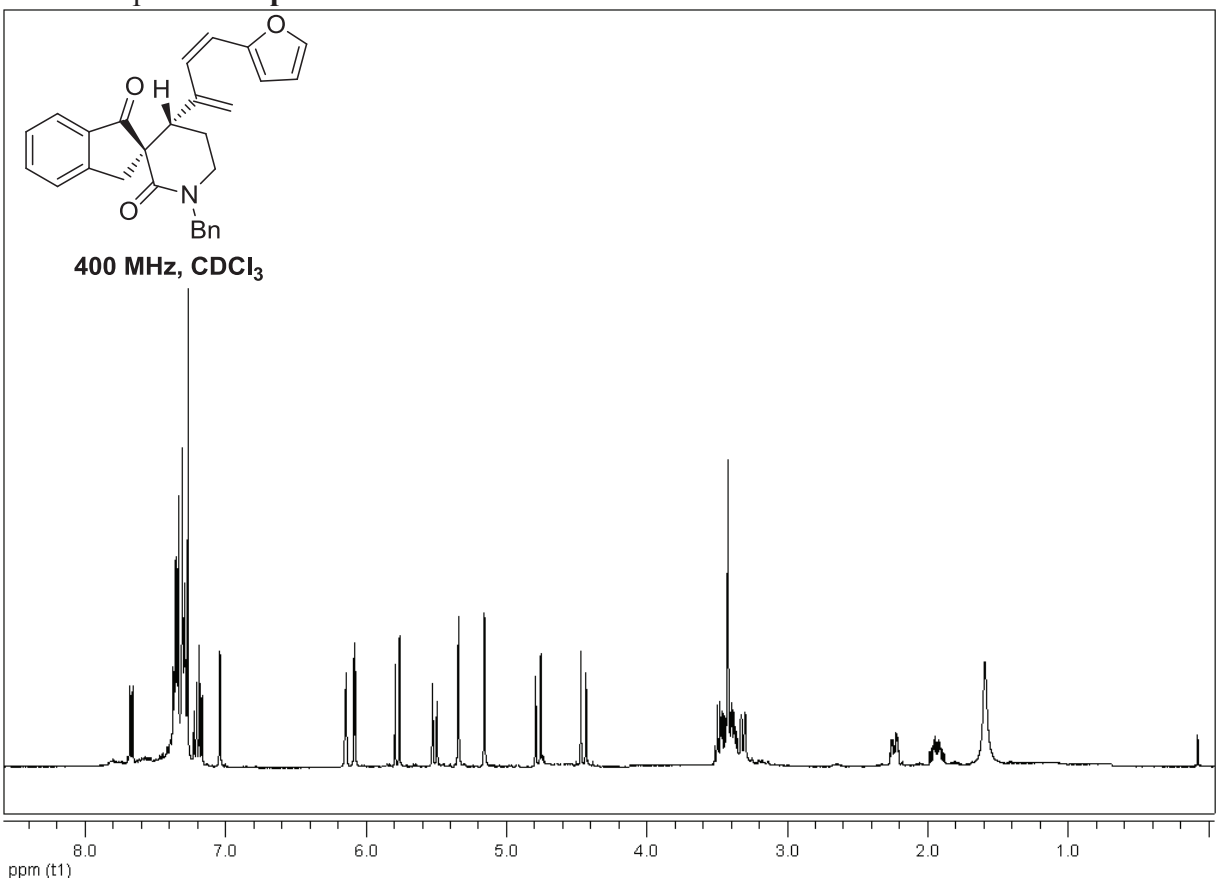
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.156	PB	1.8330	6425.56494	49.09288	90.8842
2	25.428	BB	2.5722	644.48962	2.93461	9.1158

Totals : 7070.05457 52.02750

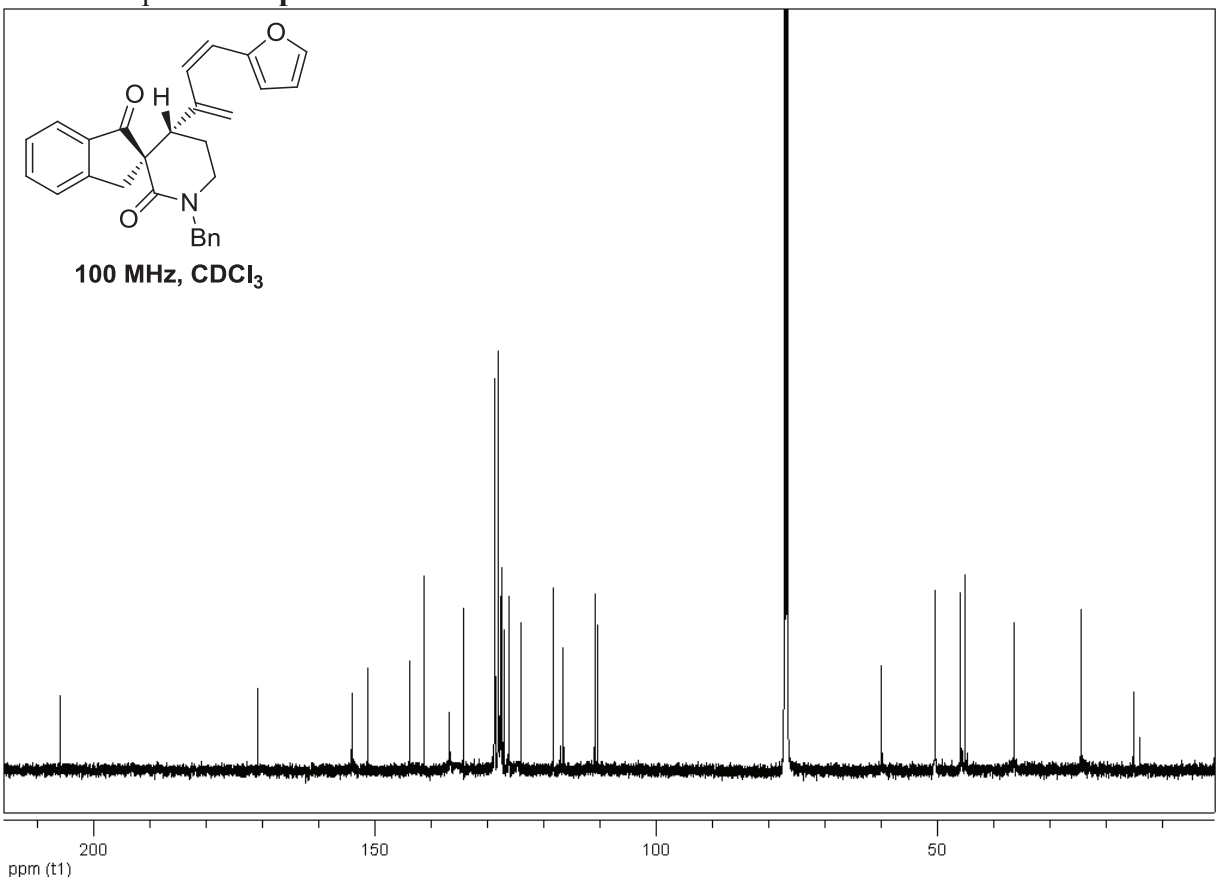
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectra of **2p**

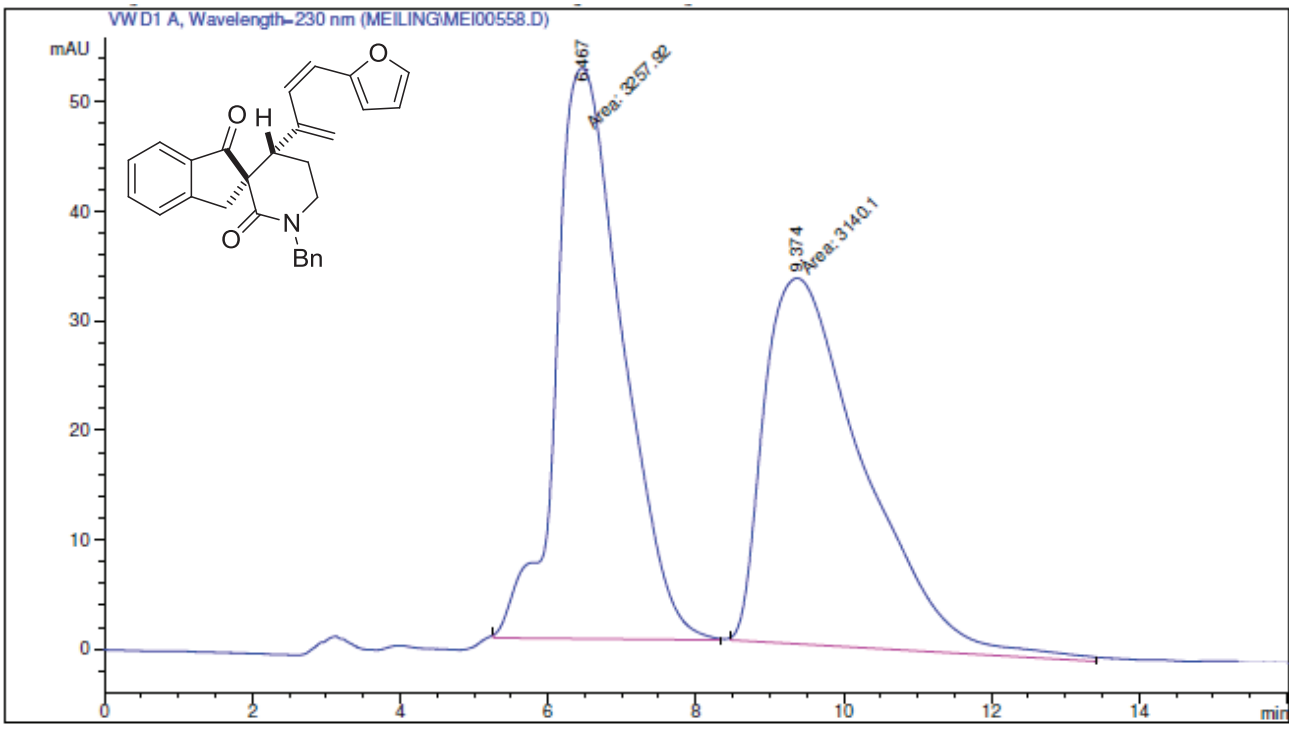


^{13}C NMR spectra of **2p**



2p **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.467	MM	1.0422	3257.91797	52.10023	50.9207
2	9.374	MM	1.5662	3140.09937	33.41520	49.0793

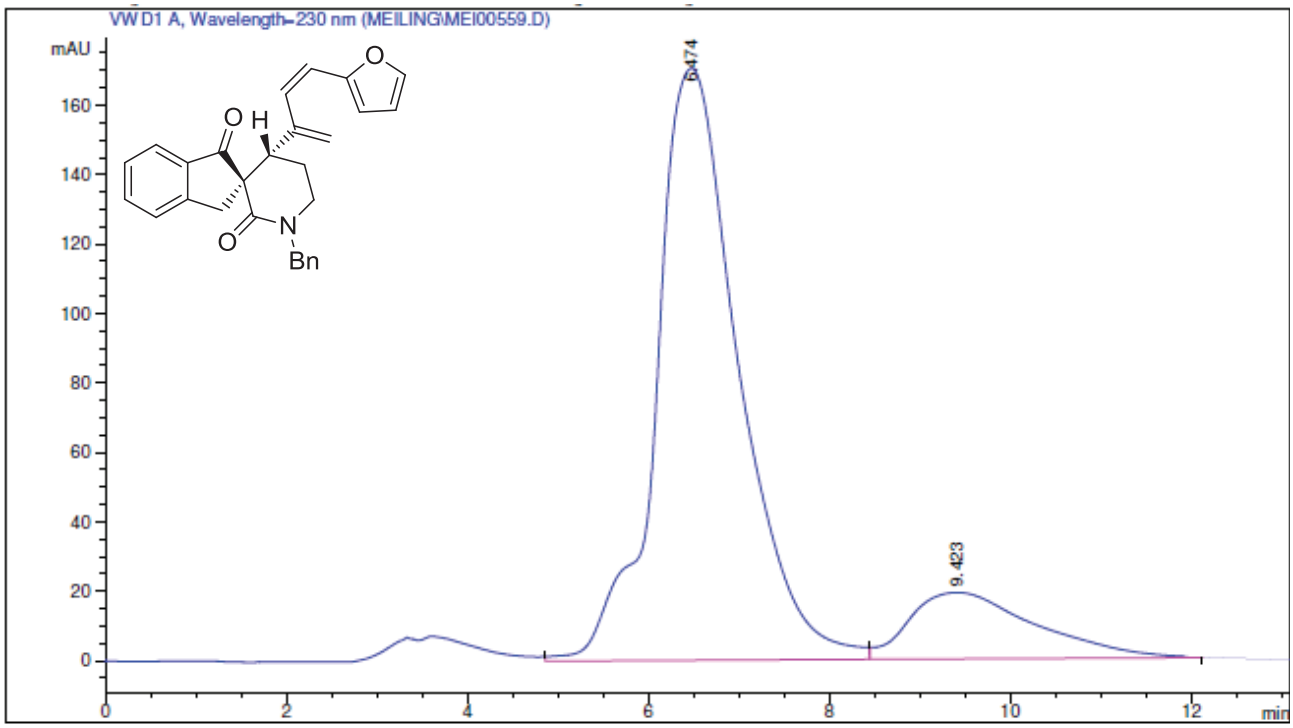
Totals : 6398.01733 85.51543

Results obtained with enhanced integrator!

*** End of Report ***

2p **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

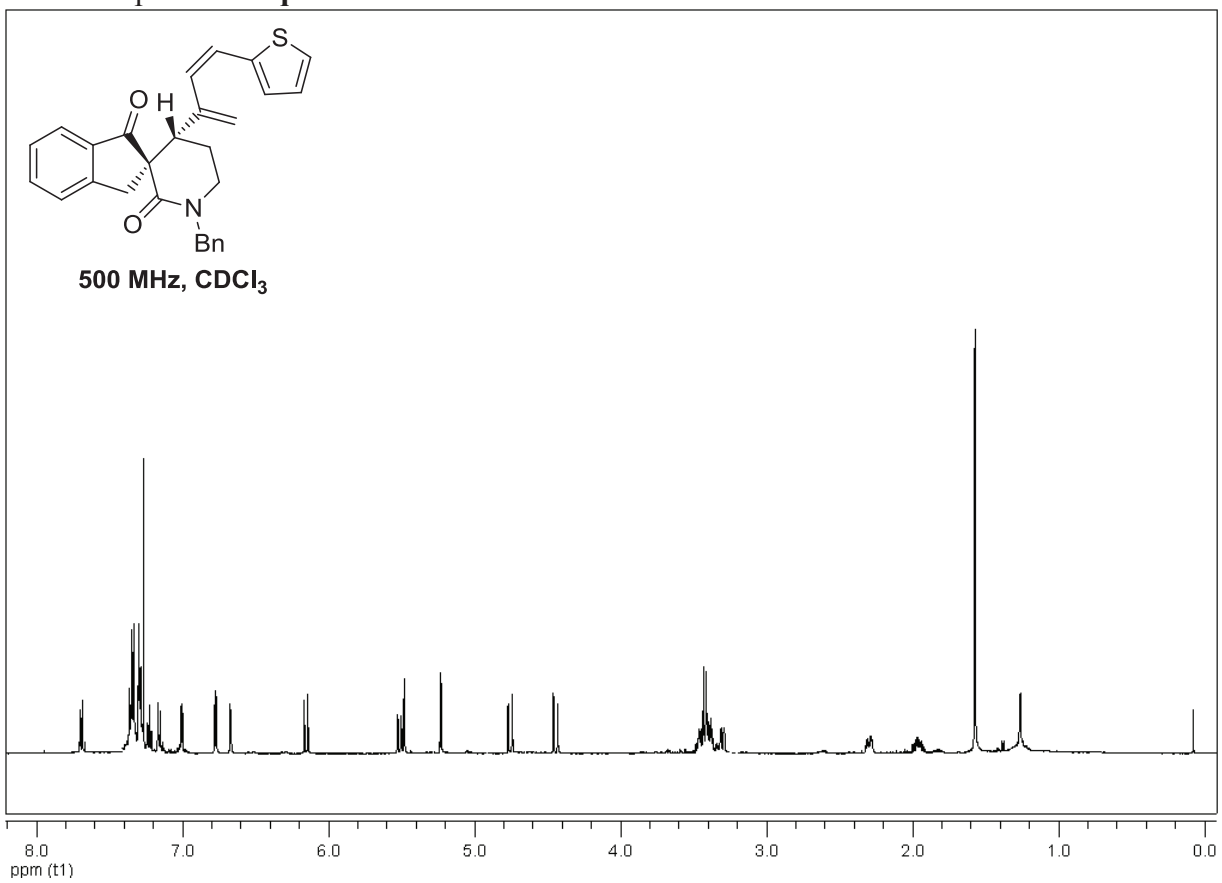
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.474	BB	0.8909	1.08010e4	170.53583	85.3514
2	9.423	BB	1.1337	1853.75073	19.12747	14.6486

Totals : 1.26548e4 189.66330

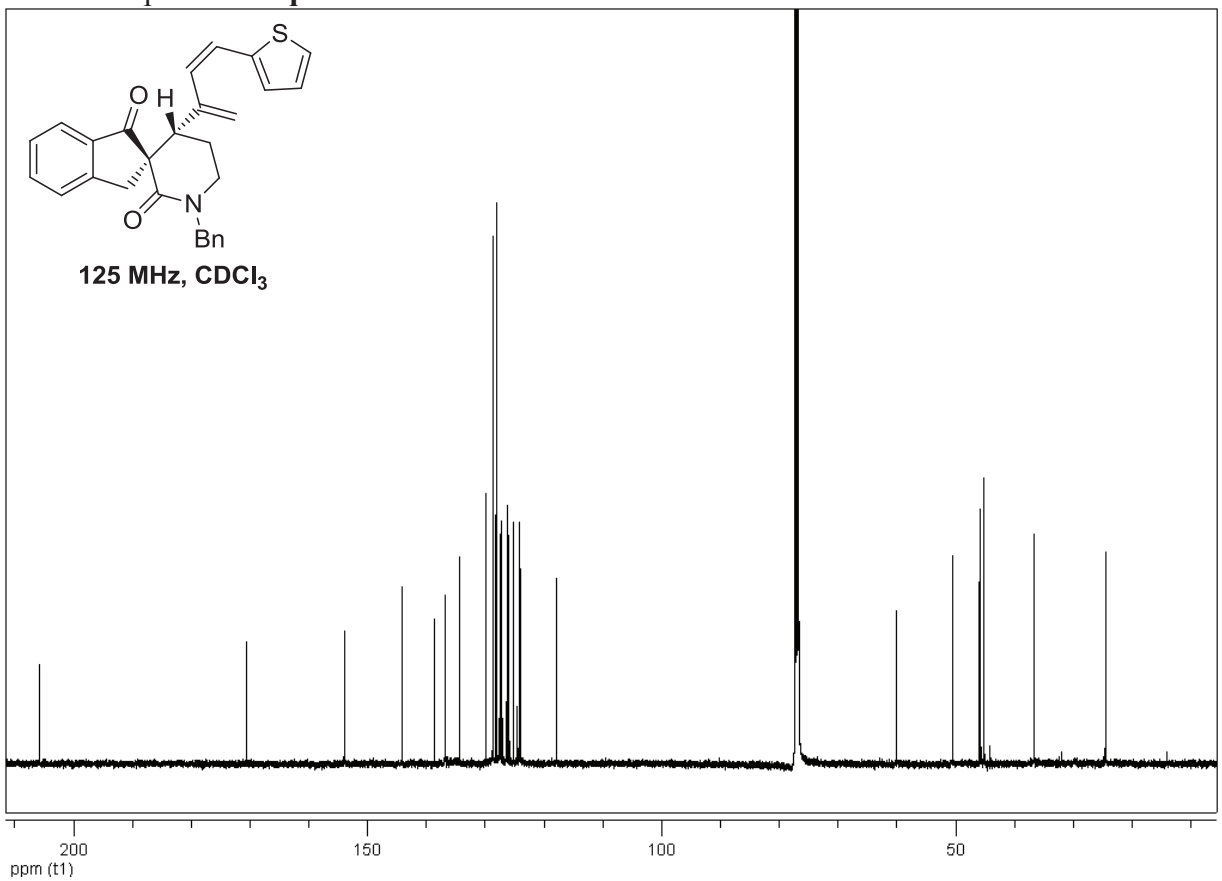
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectra of **2q**

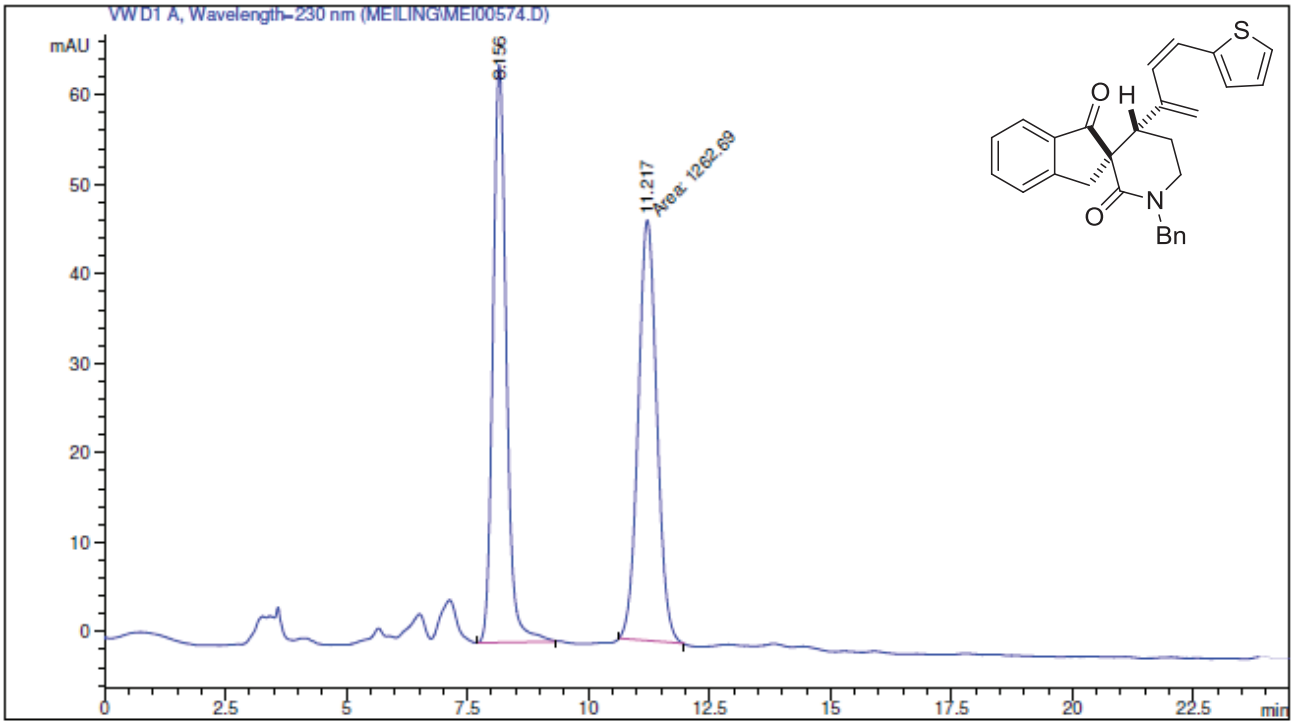


^{13}C NMR spectra of **2q**



2q **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.156	VB	0.2945	1241.73877	64.53635	49.5817
2	11.217	MM	0.4481	1262.68860	46.96820	50.4183

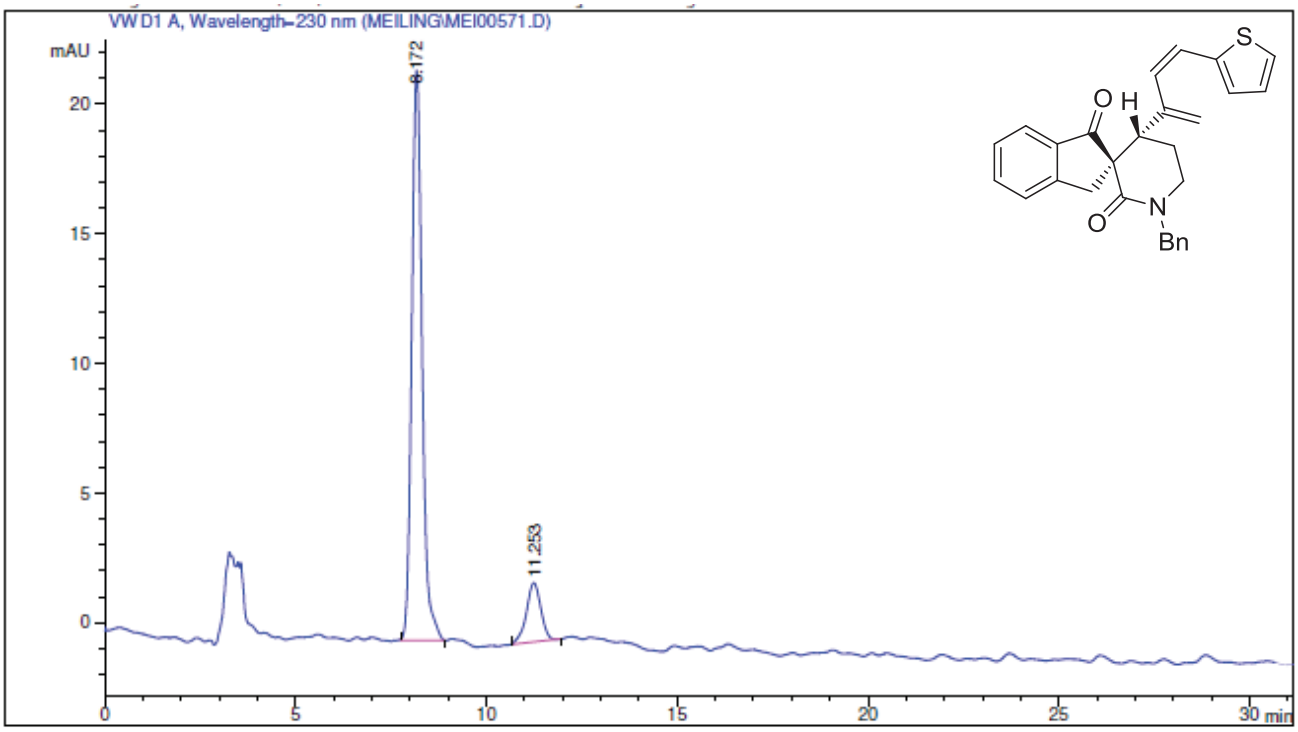
Totals : 2504.42737 111.50455

Results obtained with enhanced integrator!

*** End of Report ***

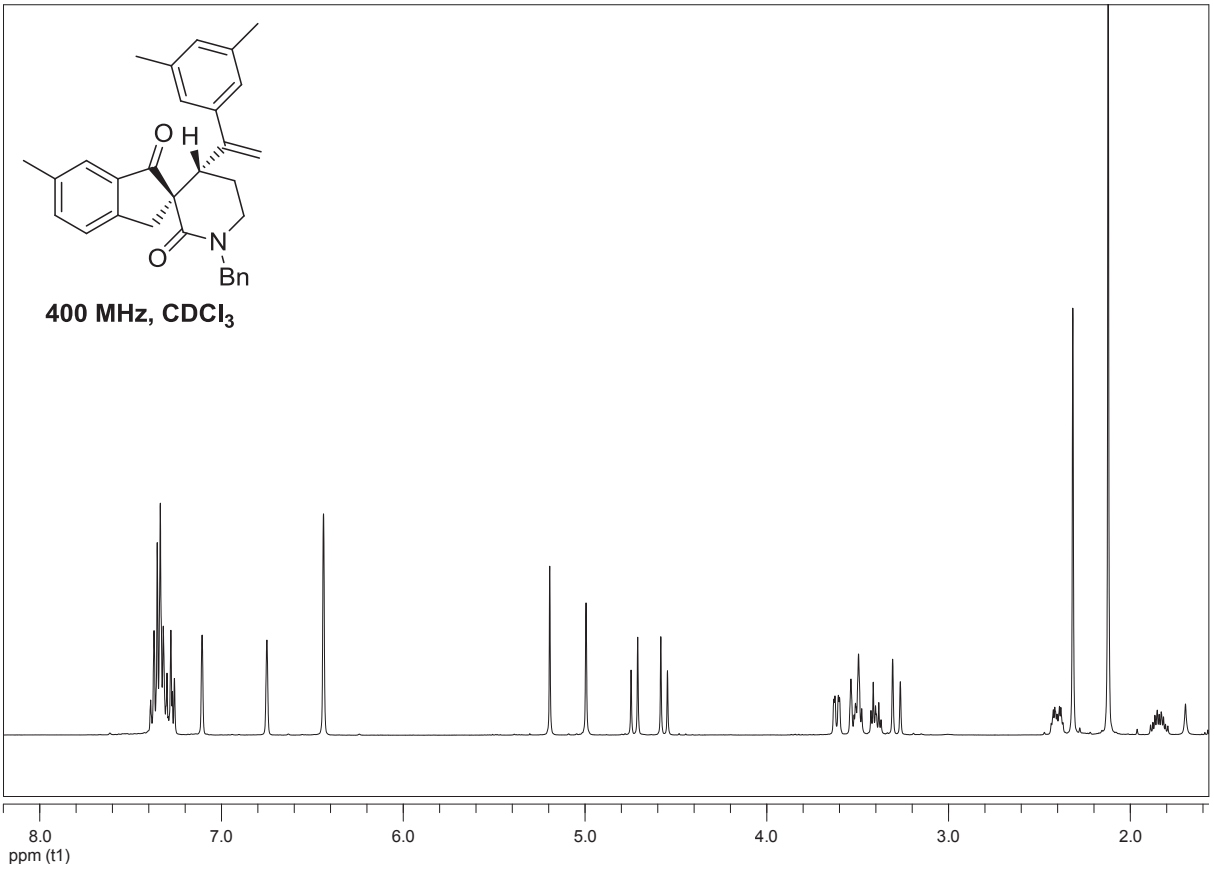
2q **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

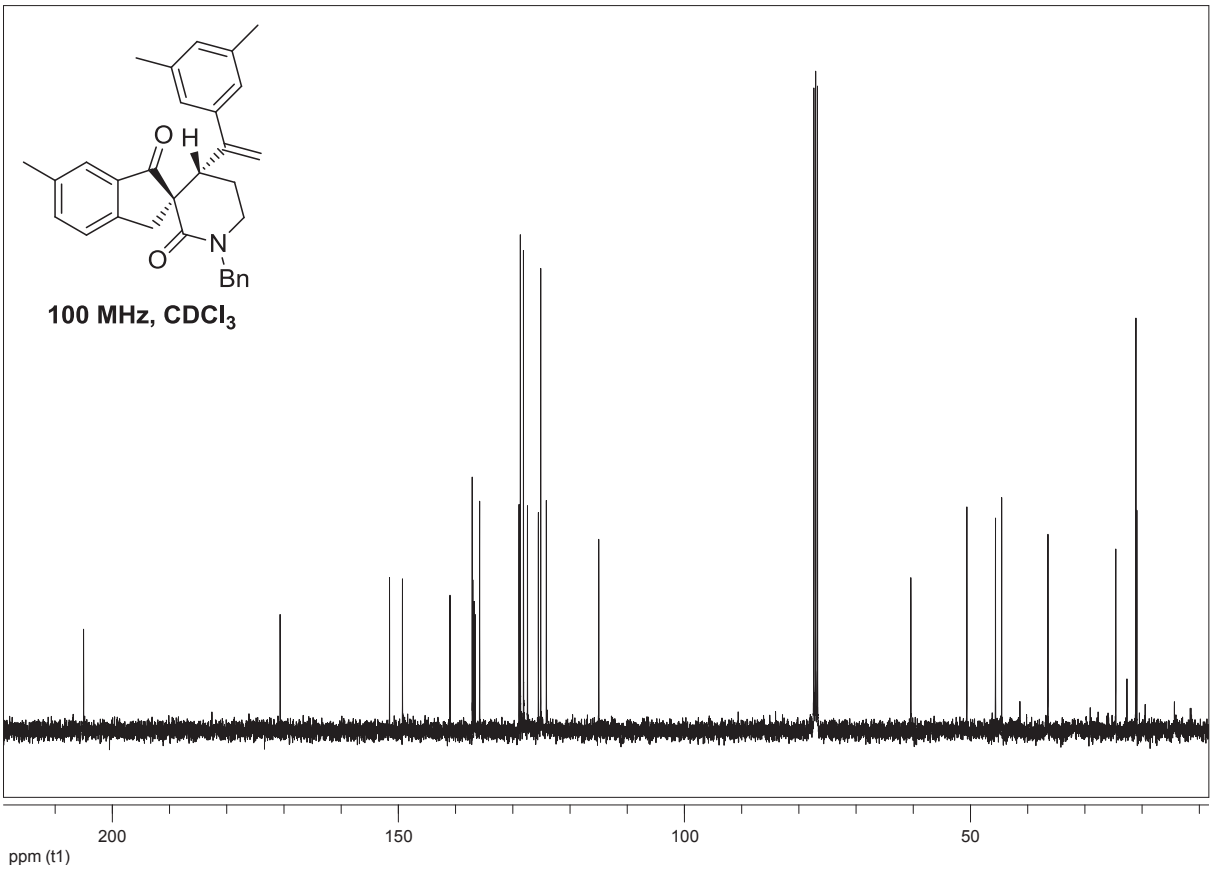



```
------------------------------------------------------------------------
                        Area Percent Report
------------------------------------------------------------------------

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.172 BP    0.2894  415.32596   21.98704  87.3919
   2  11.253 BP    0.3136   59.91946    2.28006  12.6081

Totals :                   475.24541   24.26710

 Results obtained with enhanced integrator!
------------------------------------------------------------------------
                        *** End of Report ***
```

^{1}H NMR spectrum of **4a**

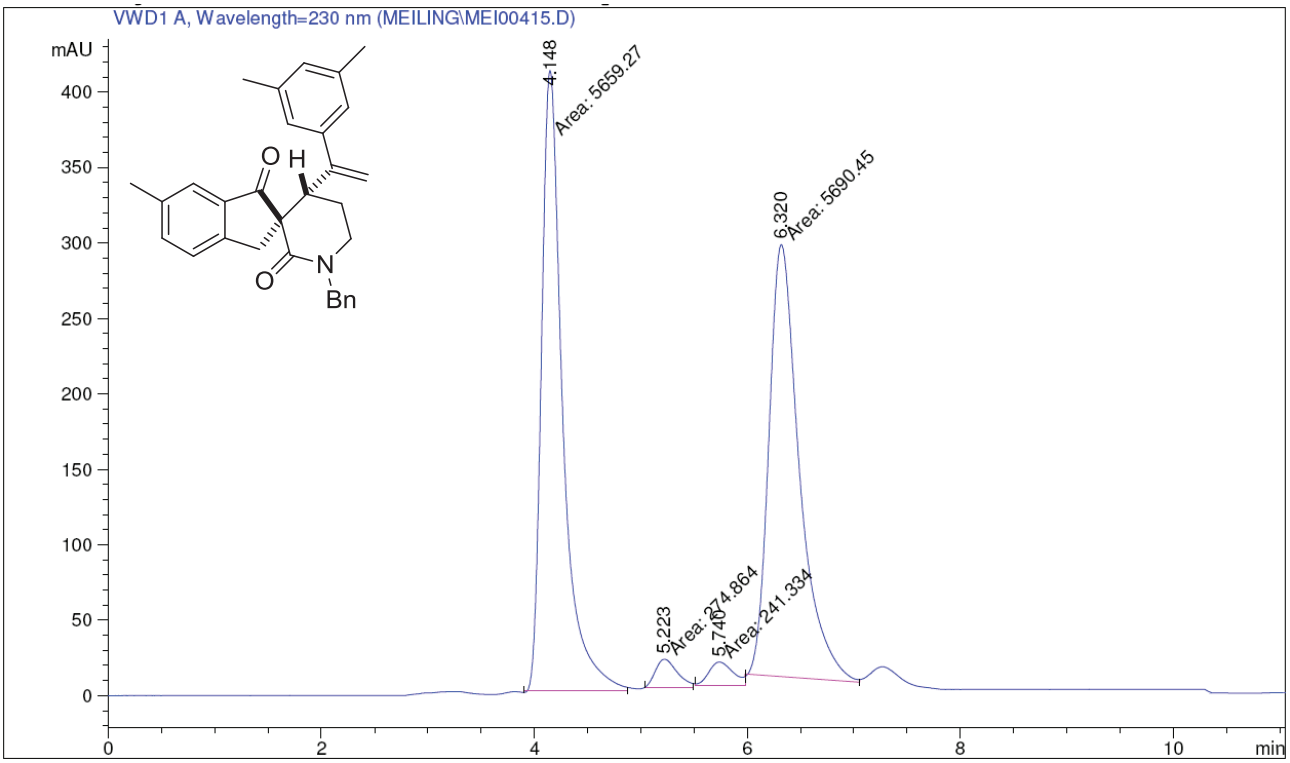


^{13}C NMR spectrum of **4a**



4a **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

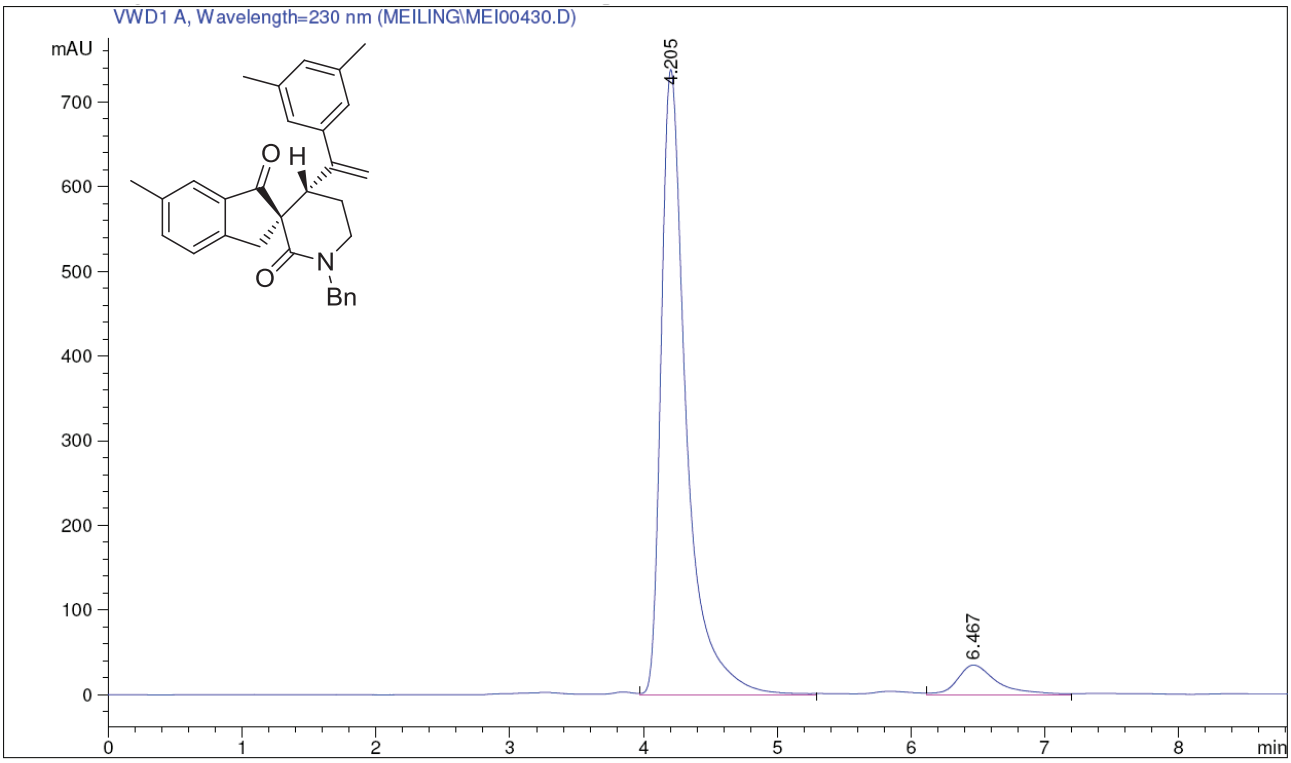
Racemic: Mixture of 2 diastereomers




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.148 MM    0.2295 5659.27100  411.05594  47.6935
   2   5.223 MM    0.2409  274.86374   19.01653   2.3164
   3   5.740 MM    0.2630  241.33392   15.29310   2.0338
   4   6.320 MM    0.3313 5690.45117  286.25748  47.9563

Totals :                  1.18659e4   731.62304

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

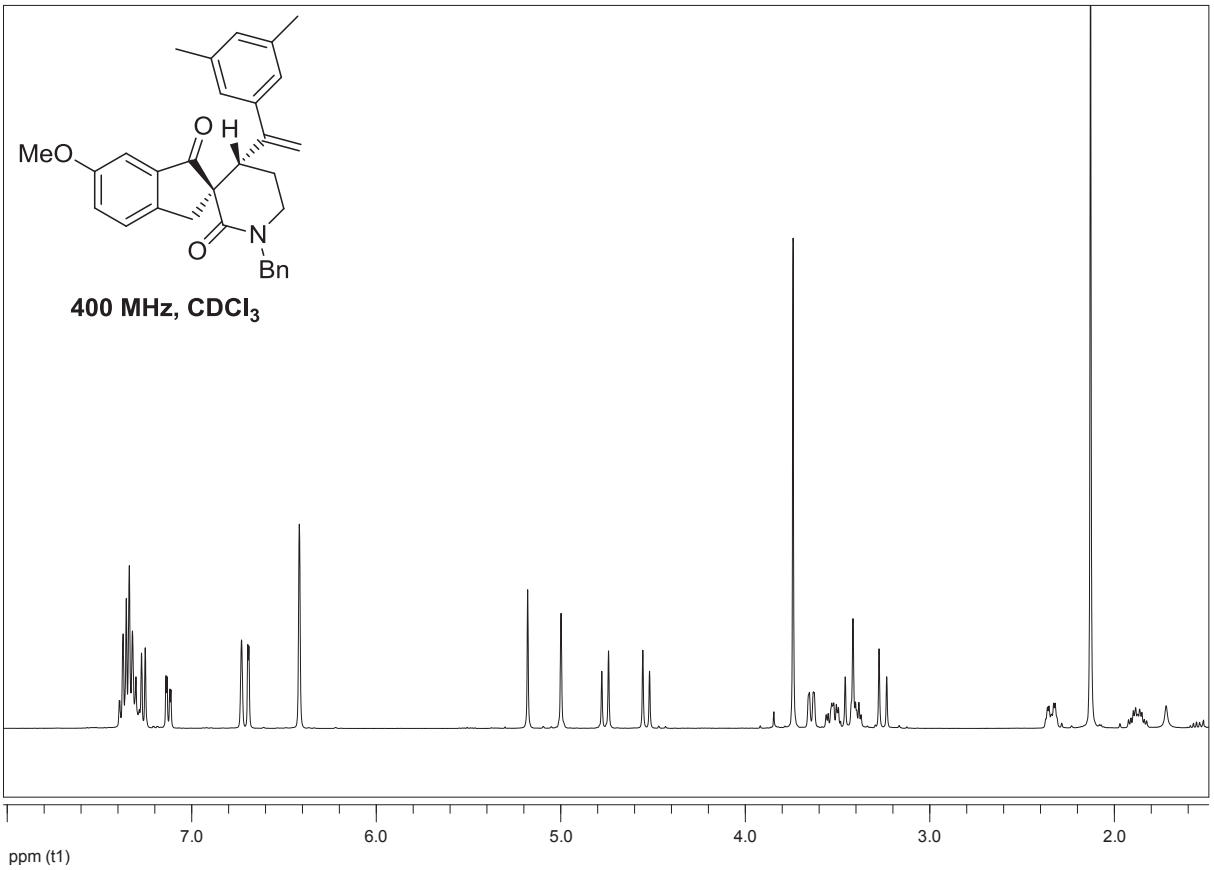
4a **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

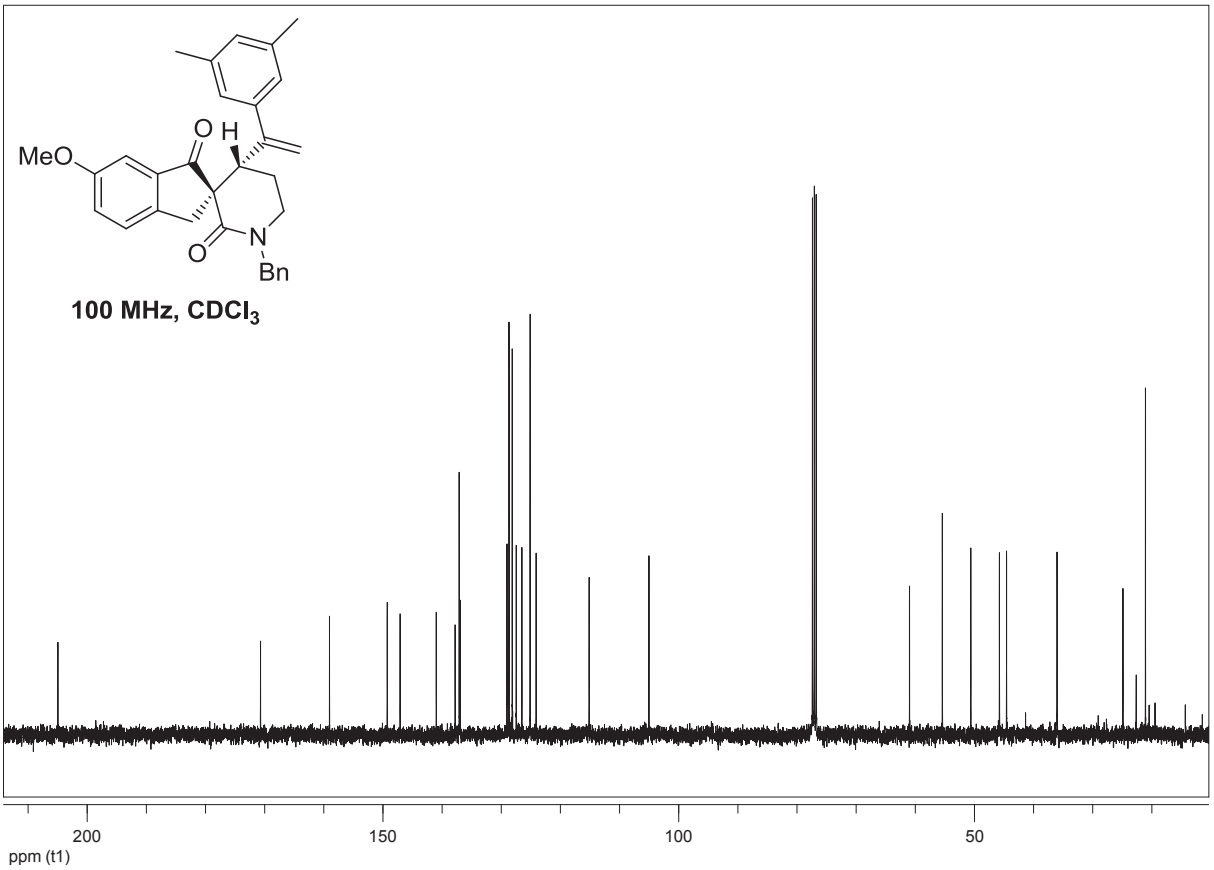



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.205 VB    0.1951 9693.18555  738.70569  92.9223
   2   6.467 VV    0.3086  738.30811   35.22147   7.0777

Totals :                  1.04315e4   773.92715

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

^{1}H NMR spectrum of **4b**

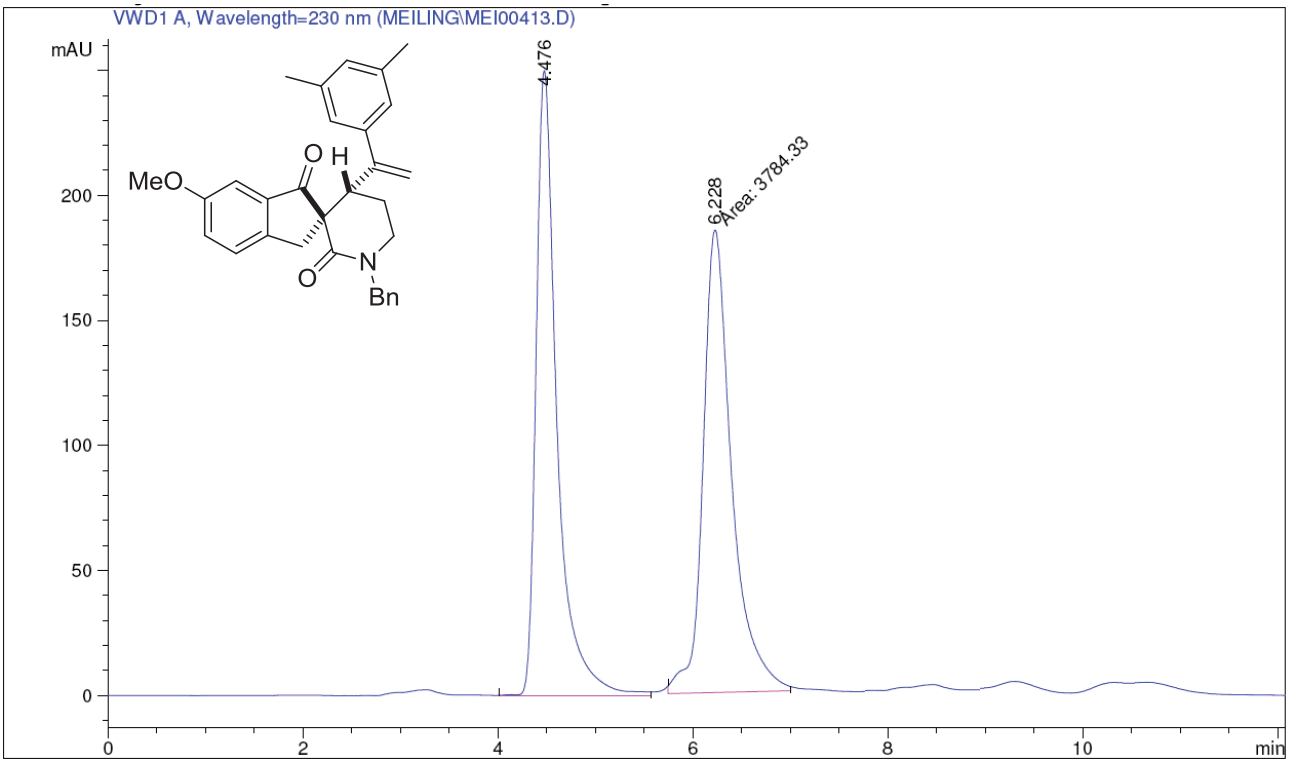


^{13}C NMR spectrum of **4b**



4b **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

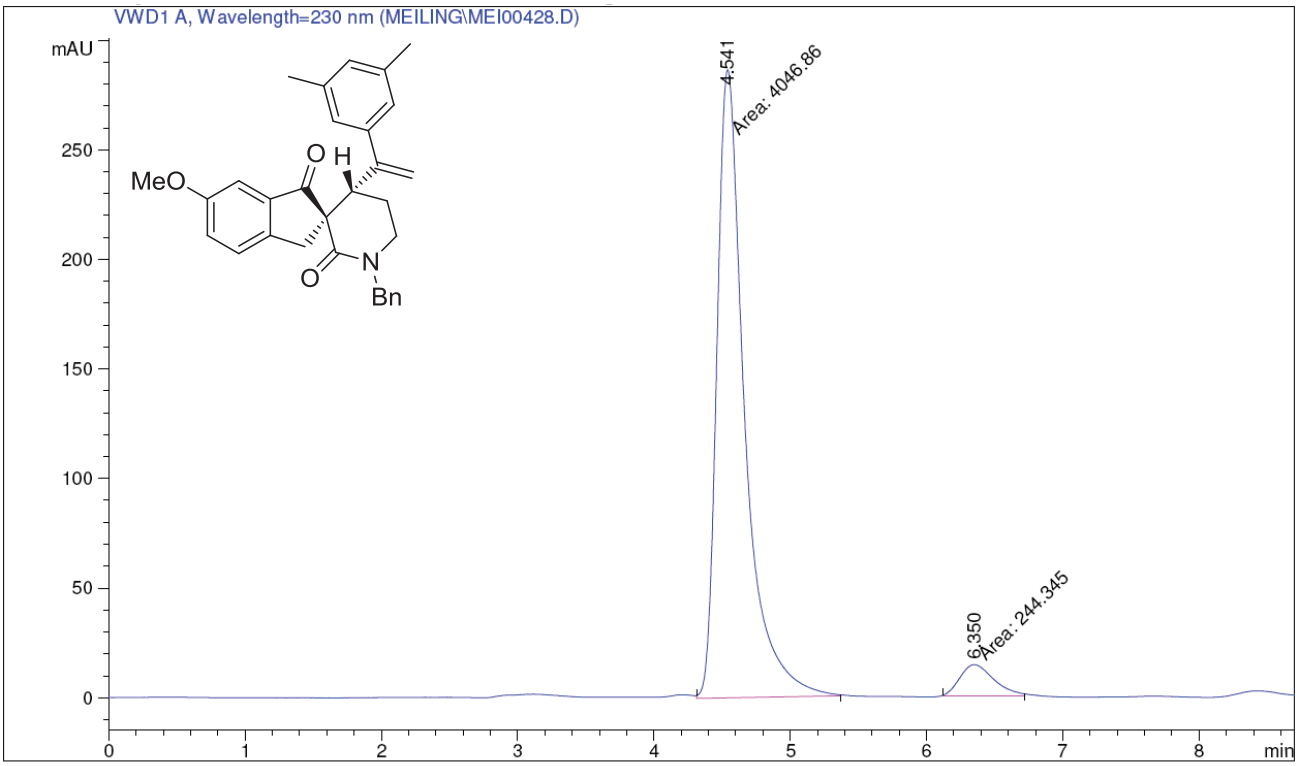
Racemic




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.476 BV    0.2218 3722.85571  249.92801  49.5906
   2   6.228 MM    0.3410 3784.33057  184.98912  50.4094

Totals :                  7507.18628  434.91713

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

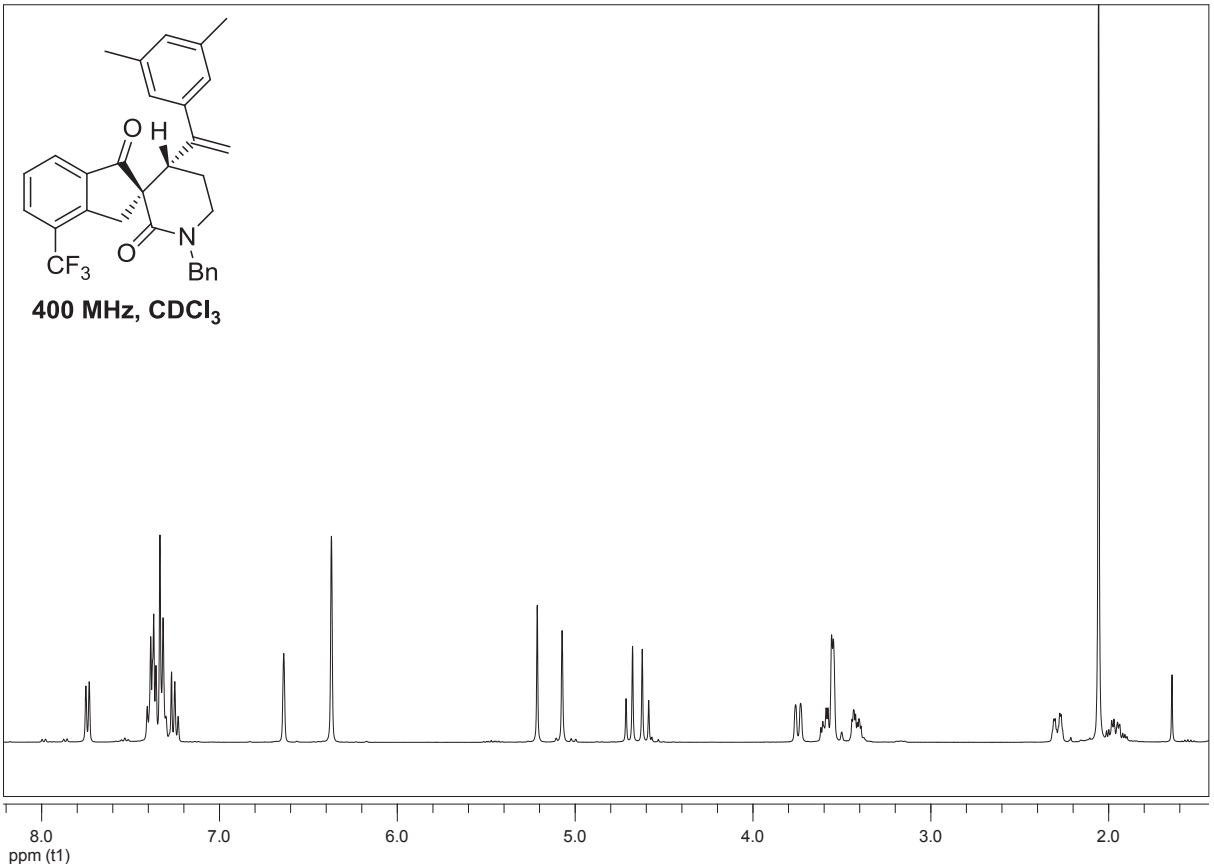
4b **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

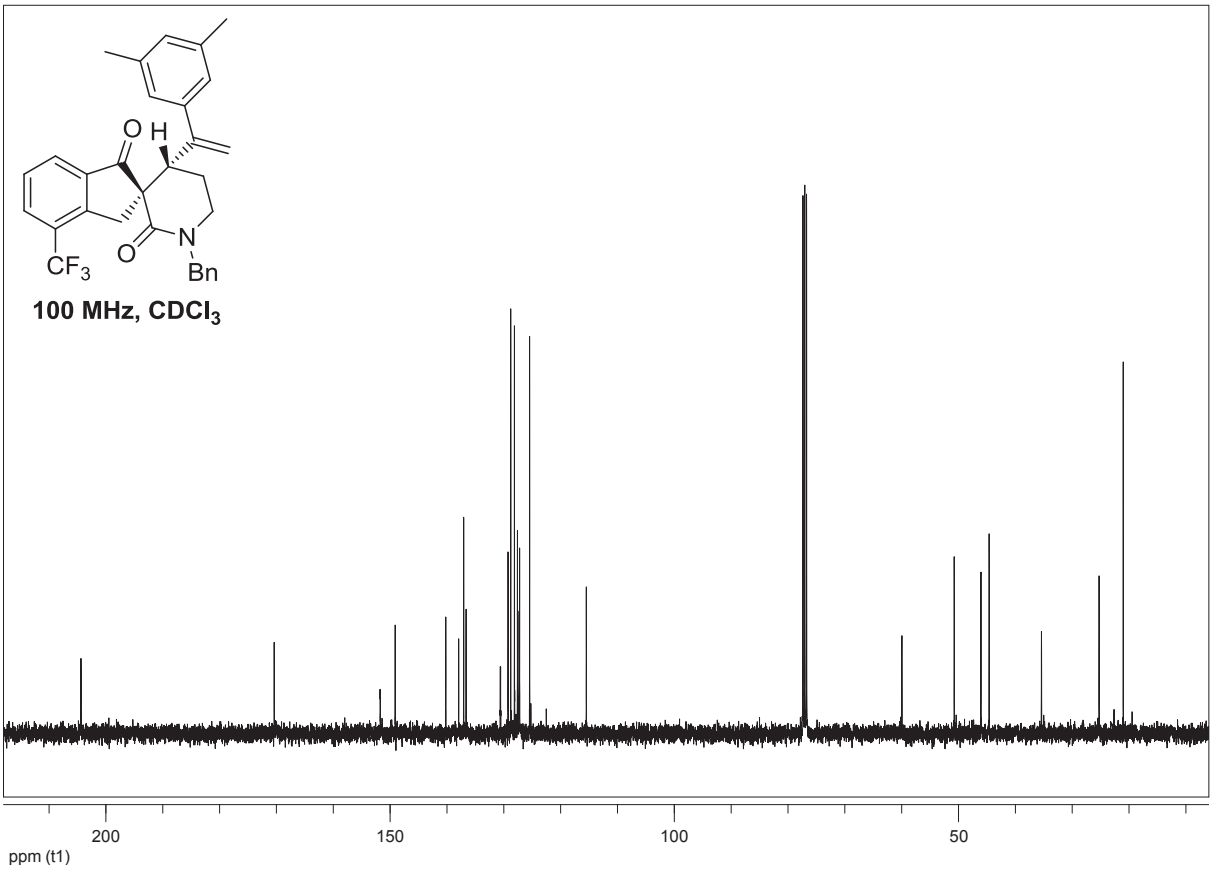



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.541 MM    0.2353 4046.85742  286.67120  94.3059
   2   6.350 MM    0.2870  244.34535   14.19119   5.6941

Totals :                  4291.20277  300.86239

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **4c**

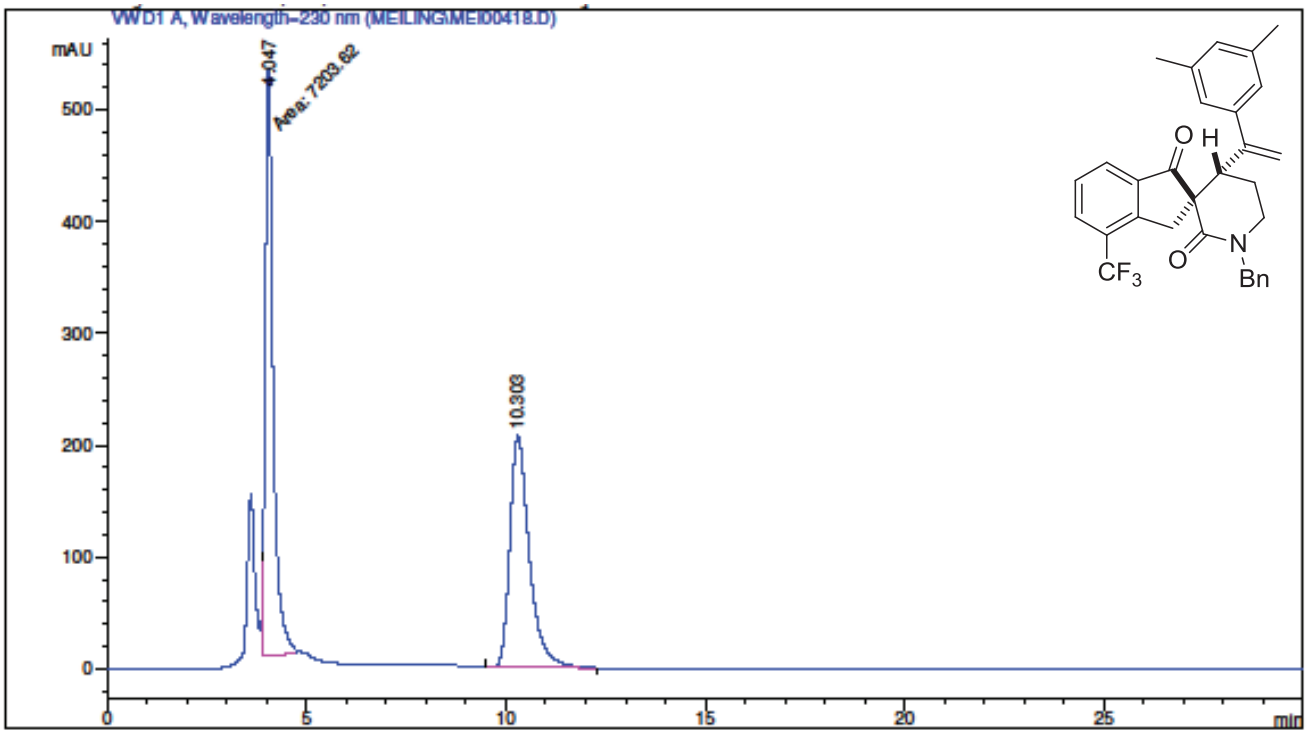


^{13}C NMR spectrum of **4c**



4c **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

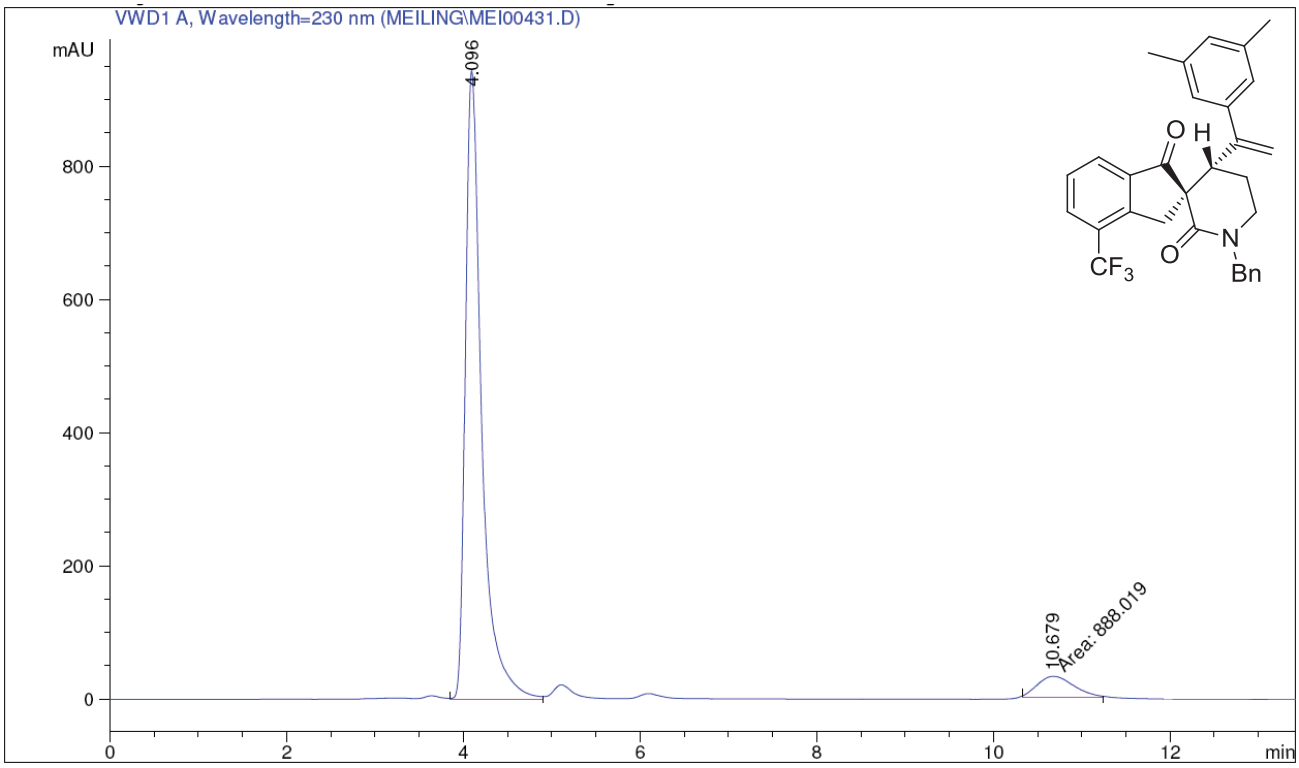
Racemic




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.047 MM    0.2288 7203.61963  524.84137  50.5337
   2  10.303 PB    0.5043 7051.45605  207.08084  49.4663

Totals :                  1.42551e4   731.92221
```

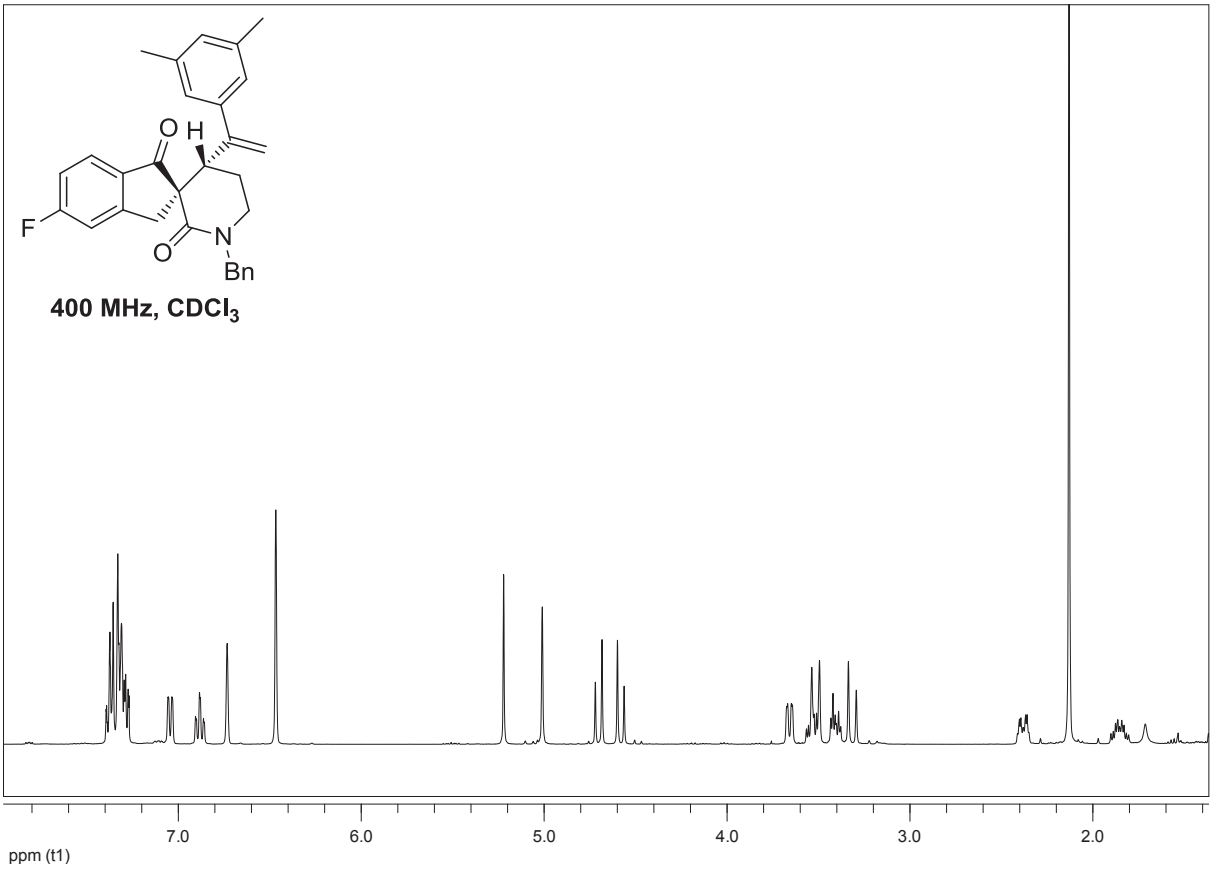
4c **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

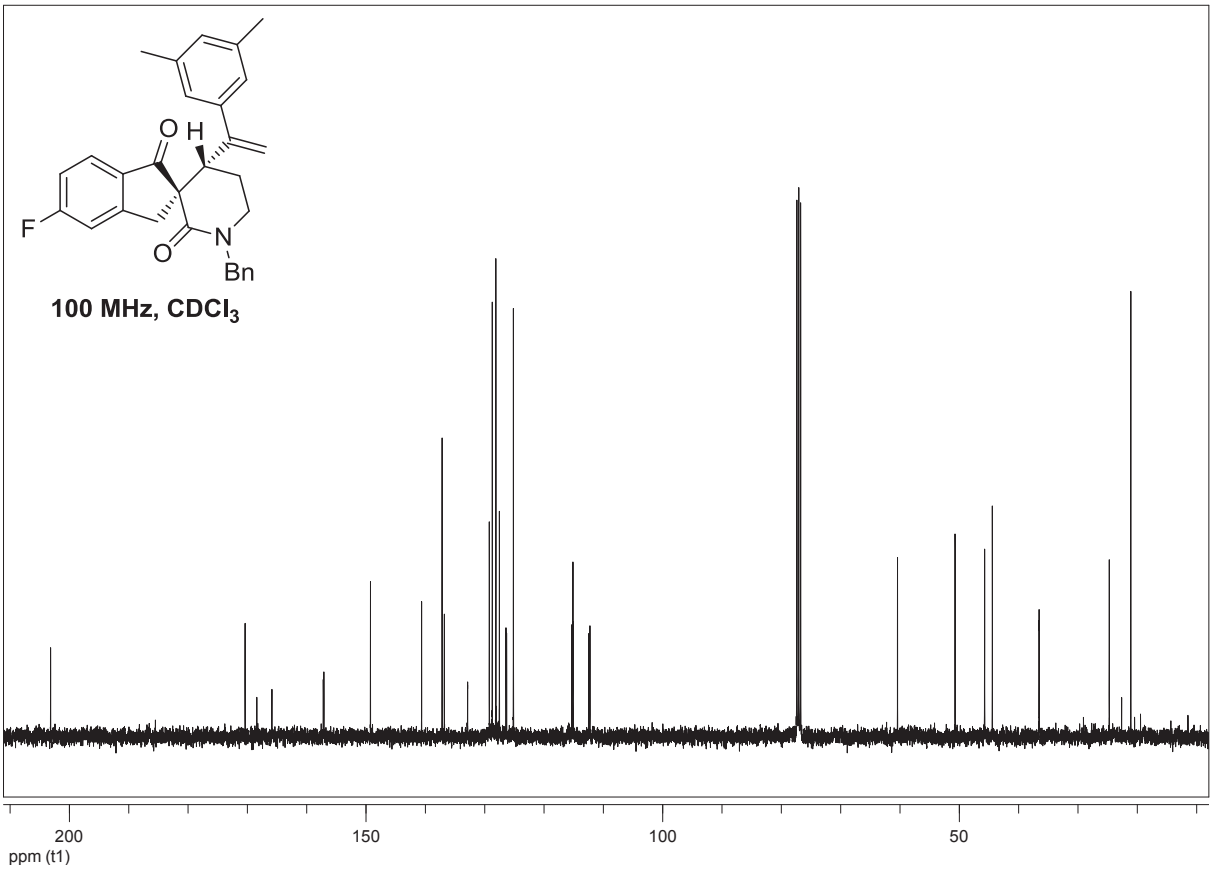



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.096 VV    0.1913 1.20677e4   943.10663  93.1458
   2  10.679 MM    0.4727  888.01855   31.30884   6.8542

Totals :                  1.29558e4   974.41547

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

^{1}H NMR spectrum of **4d**

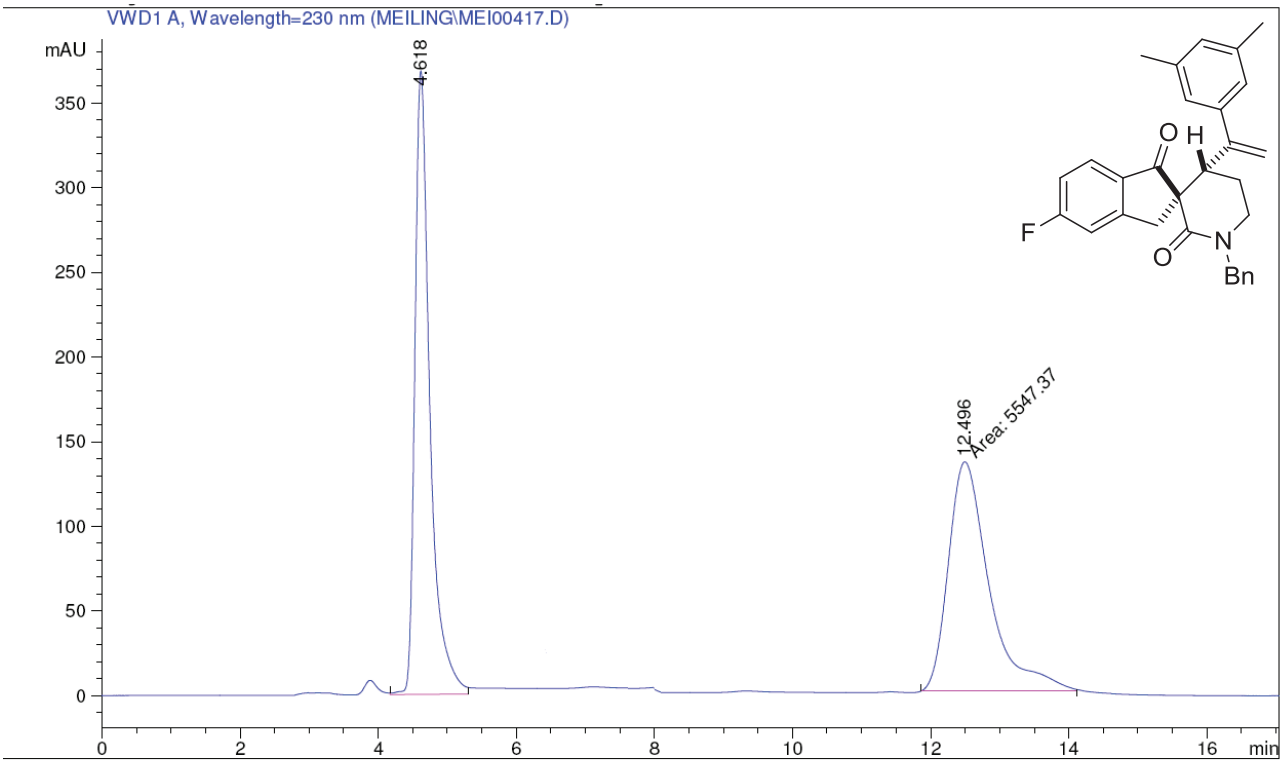


^{13}C NMR spectrum of **4d**



4d **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

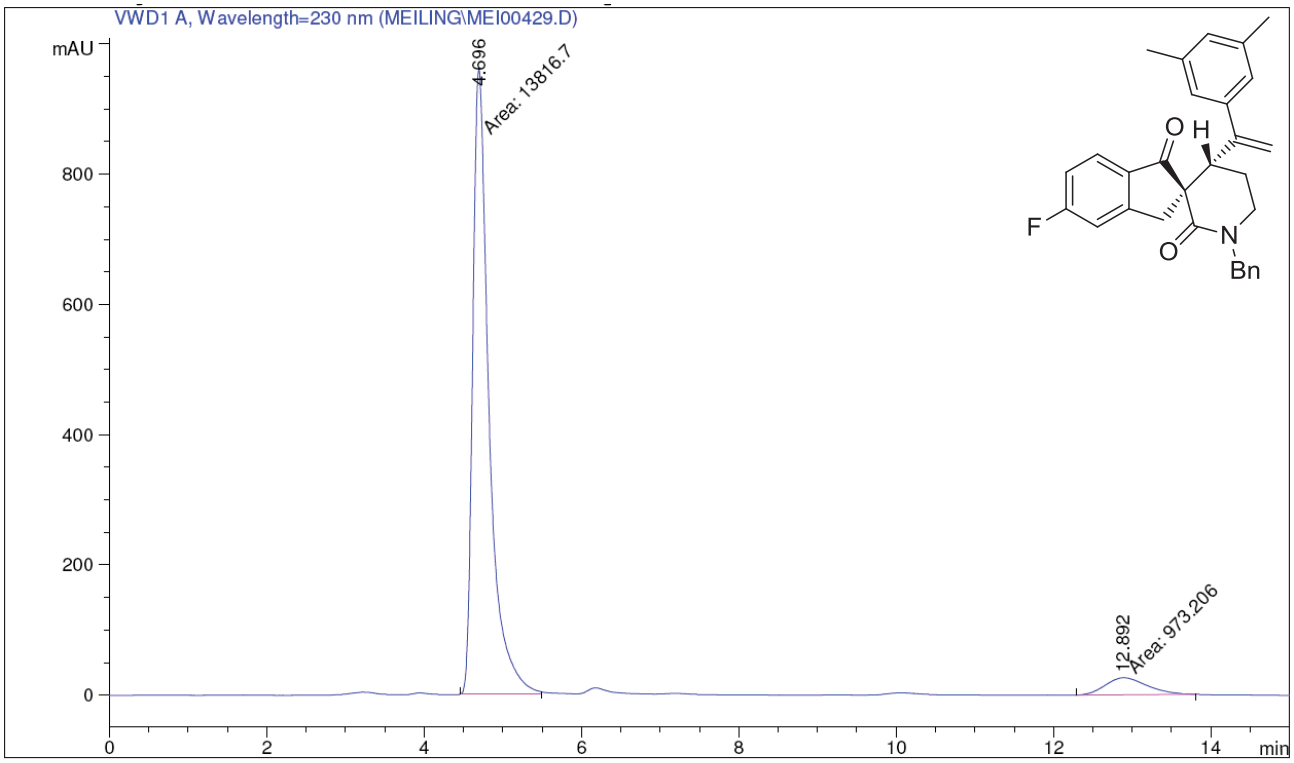
Racemic




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.618 VV    0.2268 5582.42969  368.31384  50.1575
   2  12.496 MM    0.6837 5547.37207  135.22995  49.8425

Totals :                  1.11298e4   503.54379

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

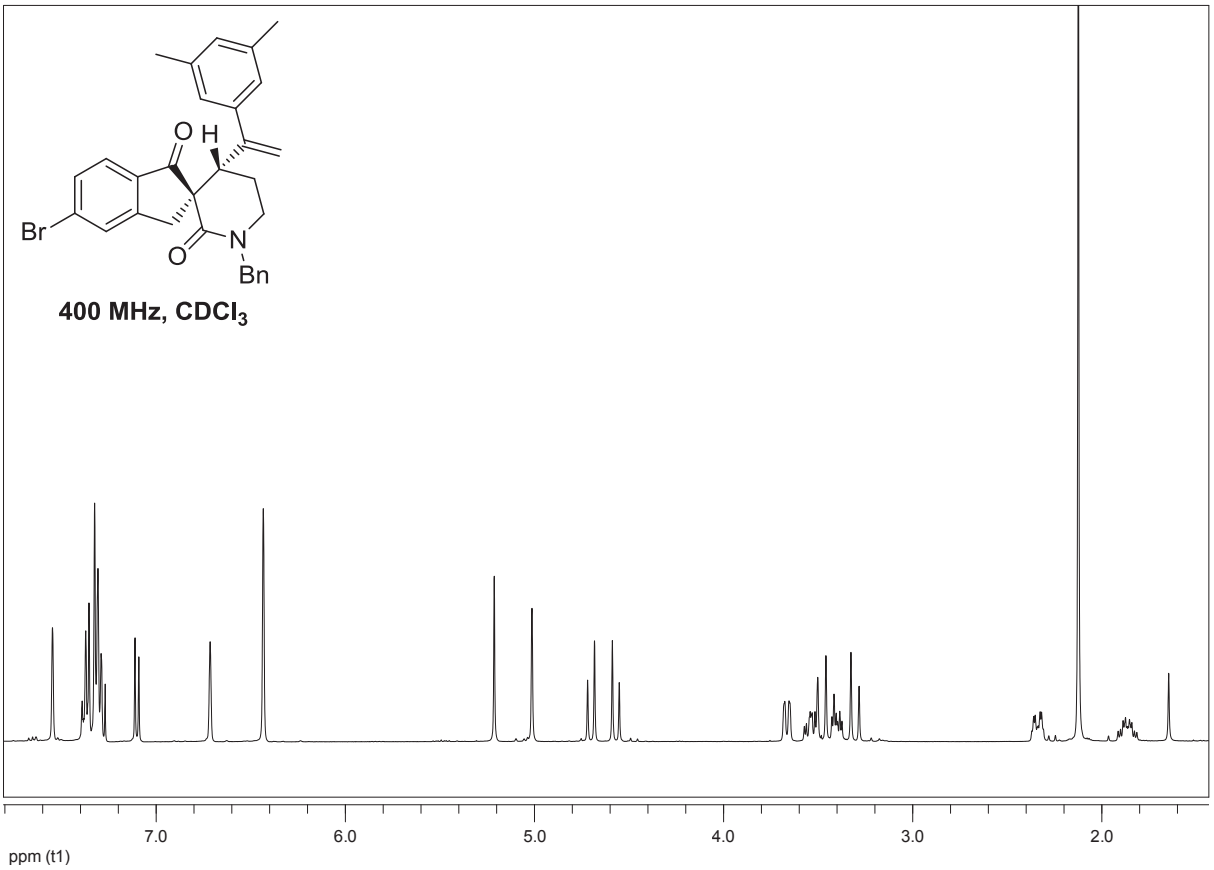
4d **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

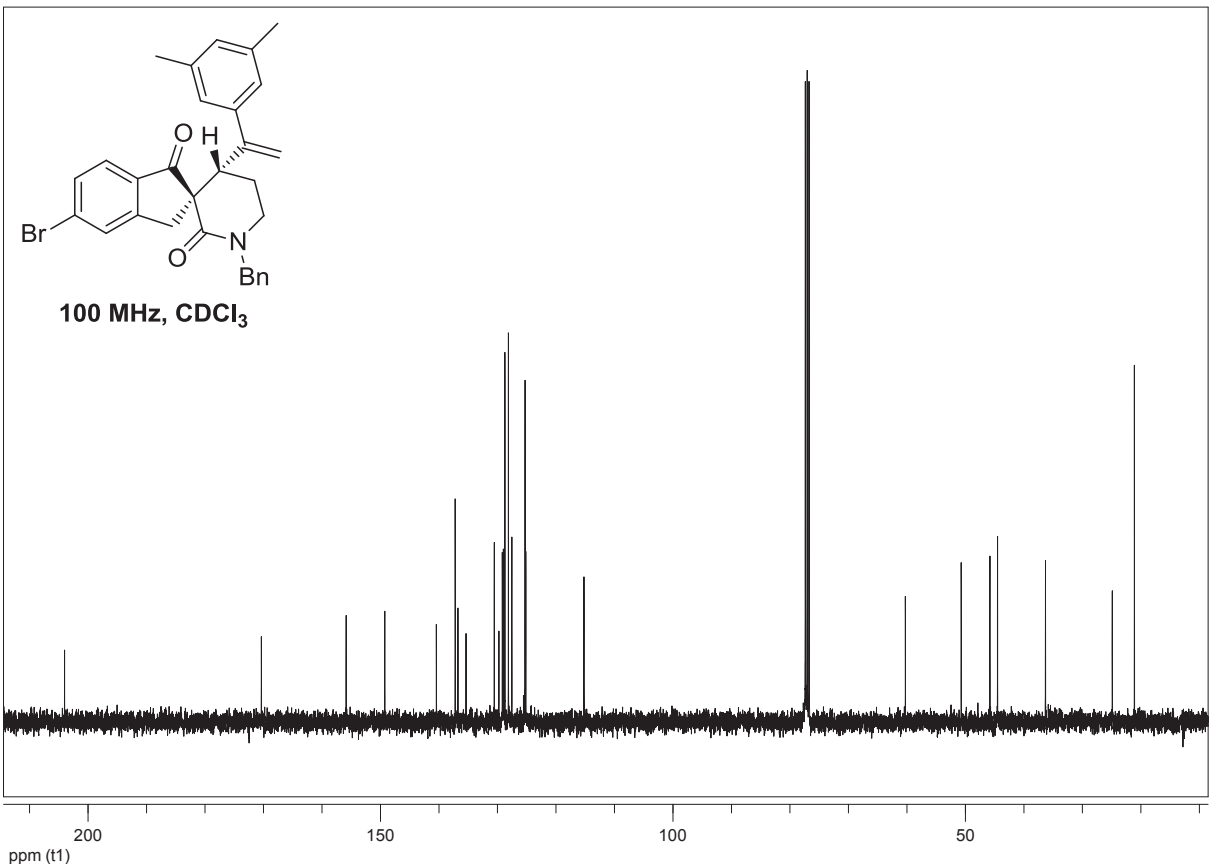



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.696 MM    0.2402 1.38167e4   958.80286  93.4198
   2  12.892 MM    0.6201  973.20599   26.15772   6.5802

Totals :                  1.47899e4   984.96058

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **4e**

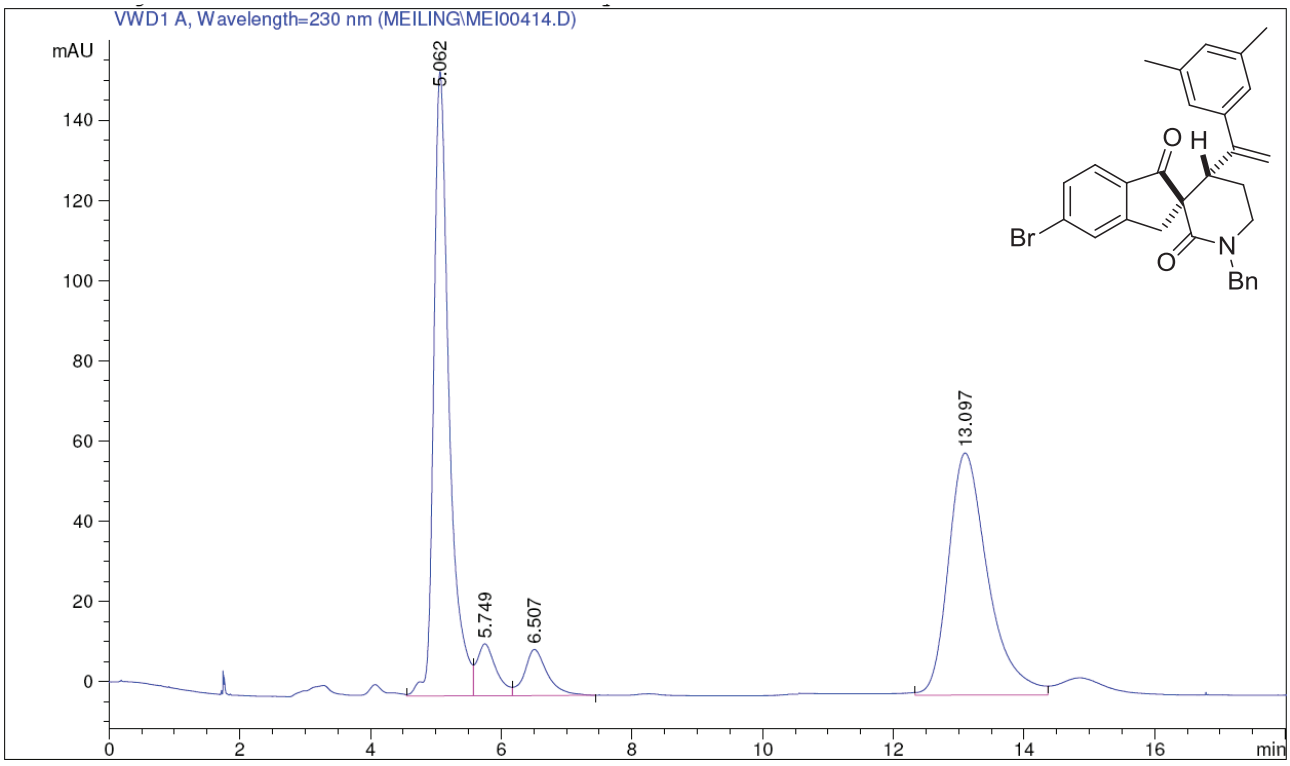


^{13}C NMR spectrum of **4e**



4e **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

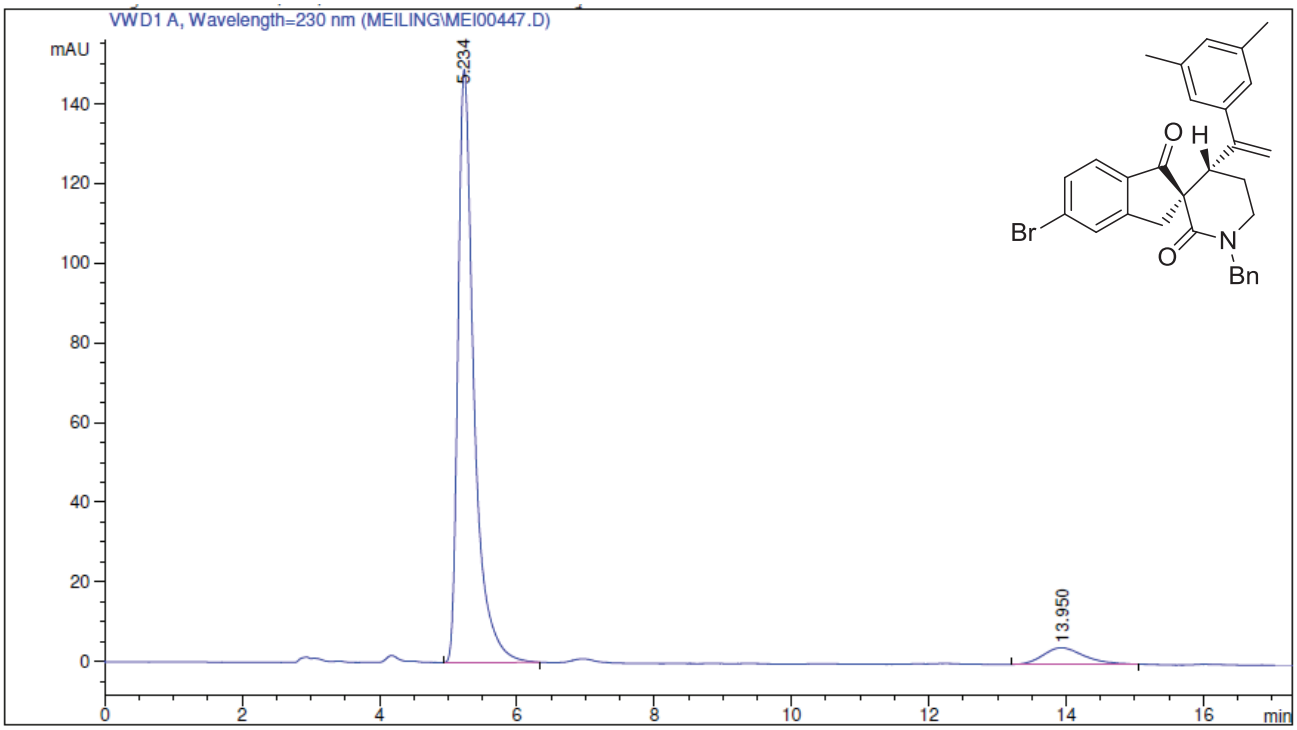
Racemic: Mixture of 2 diastereomers




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.062 VV    0.2464 2566.47437  155.62262  45.4135
   2   5.749 VV    0.2981  266.49860   12.95062   4.7157
   3   6.507 VB    0.3498  279.47913   11.49050   4.9454
   4  13.097 VV    0.6347 2538.89648   60.35764  44.9255

Totals :                  5651.34857  240.42137

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

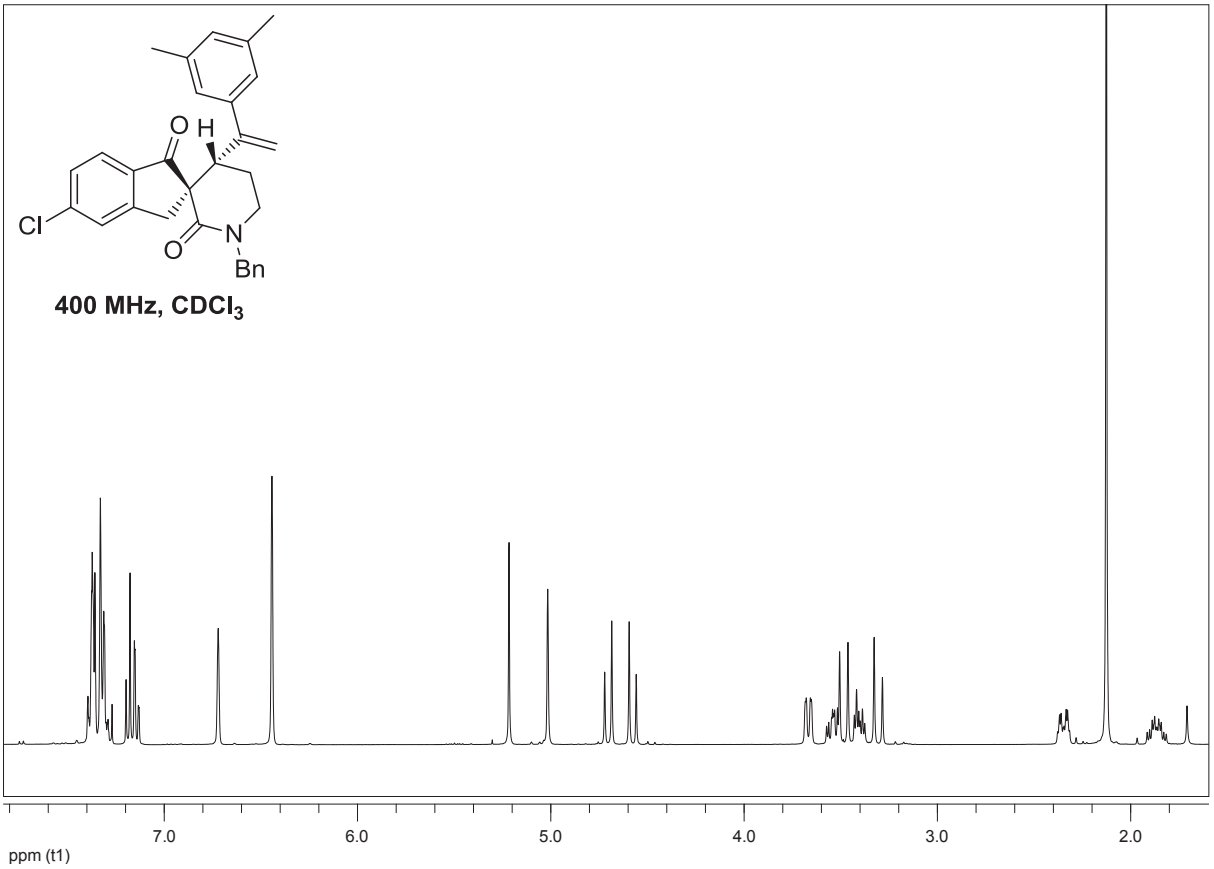
4e **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

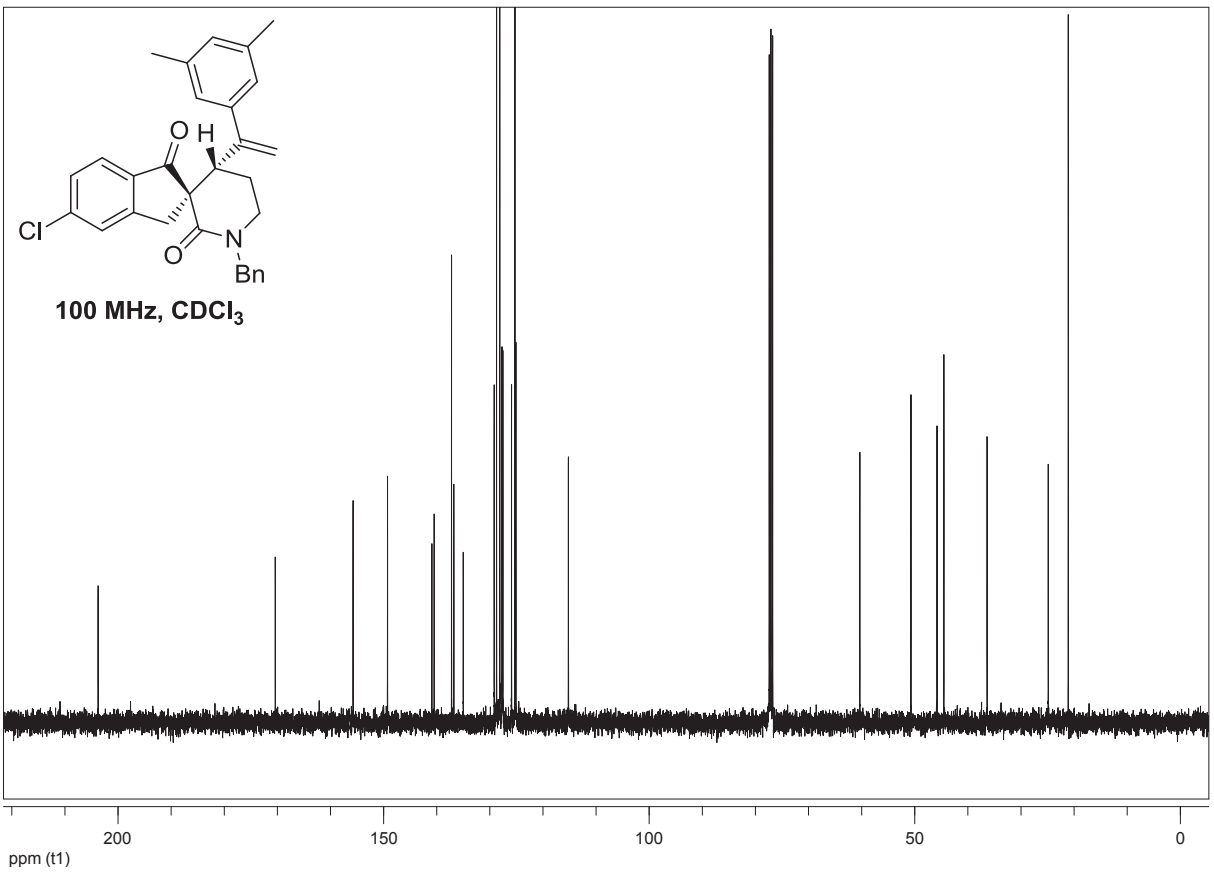



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.234 BB    0.2404 2402.33911  148.78294  93.0042
   2  13.950 PV    0.5057  180.70349    4.21924   6.9958

Totals :                  2583.04260  153.00218
```

^{1}H NMR spectrum of **4f**

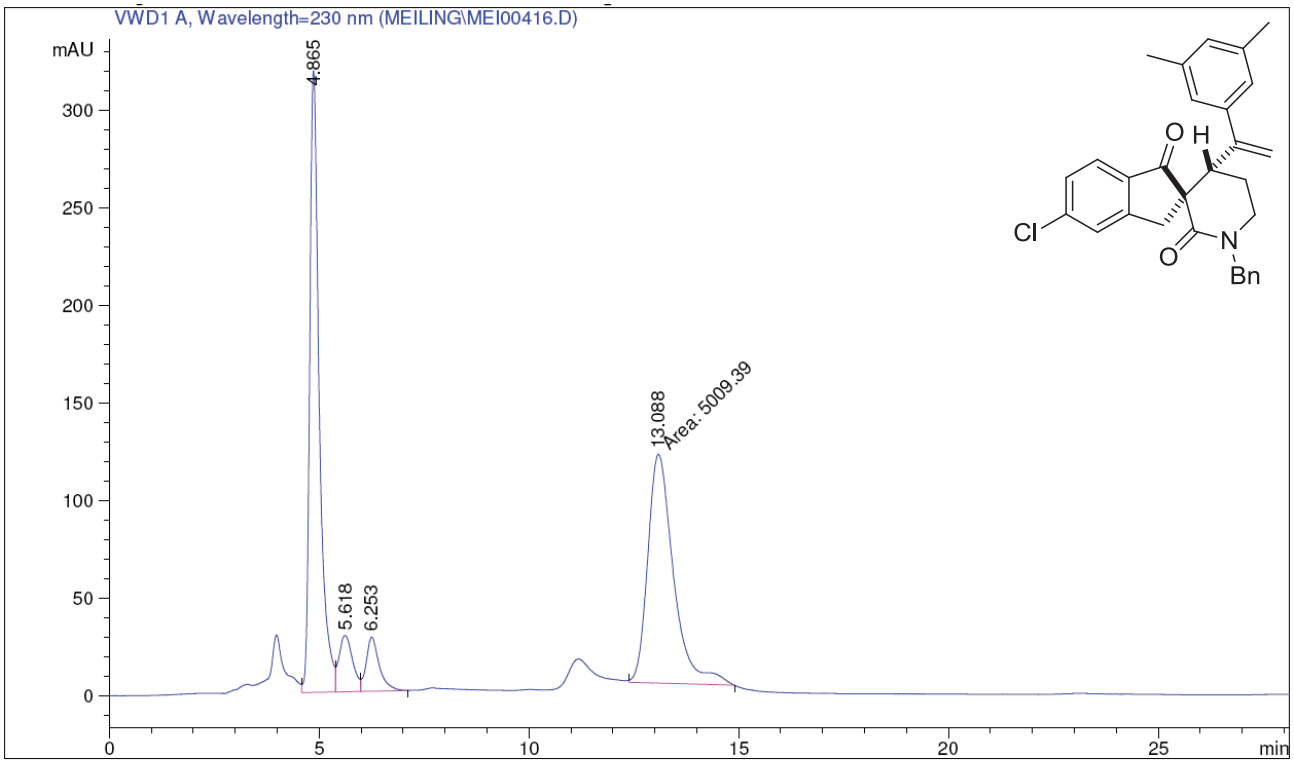


^{13}C NMR spectrum of **4f**



4f **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

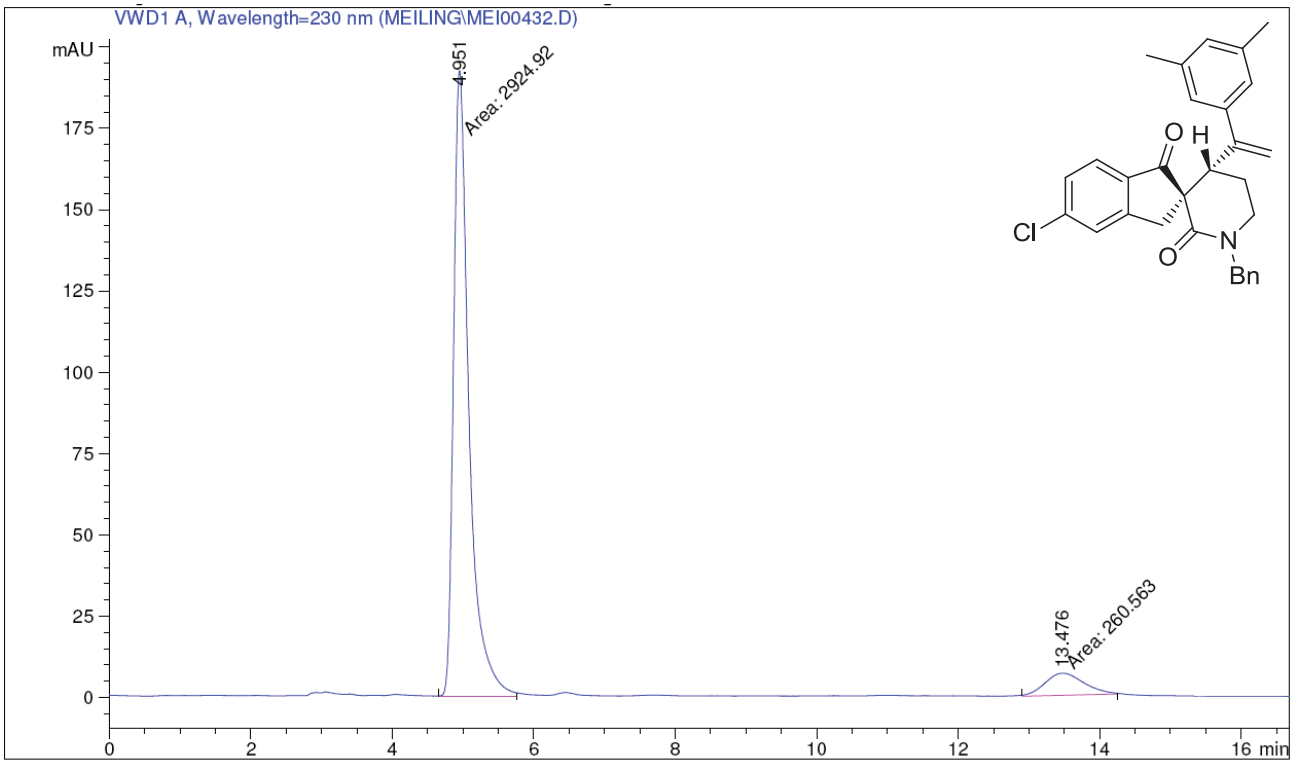
Racemic: Mixture of 2 diastereomers




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.865 VV    0.2370 5050.77832  318.48273  44.5748
   2   5.618 VV    0.3493  662.00482   28.89533   5.8424
   3   6.253 VB    0.3212  608.84778   27.83079   5.3733
   4  13.088 MM    0.7114 5009.39160  117.35179  44.2095

Totals :                  1.13310e4   492.56063

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

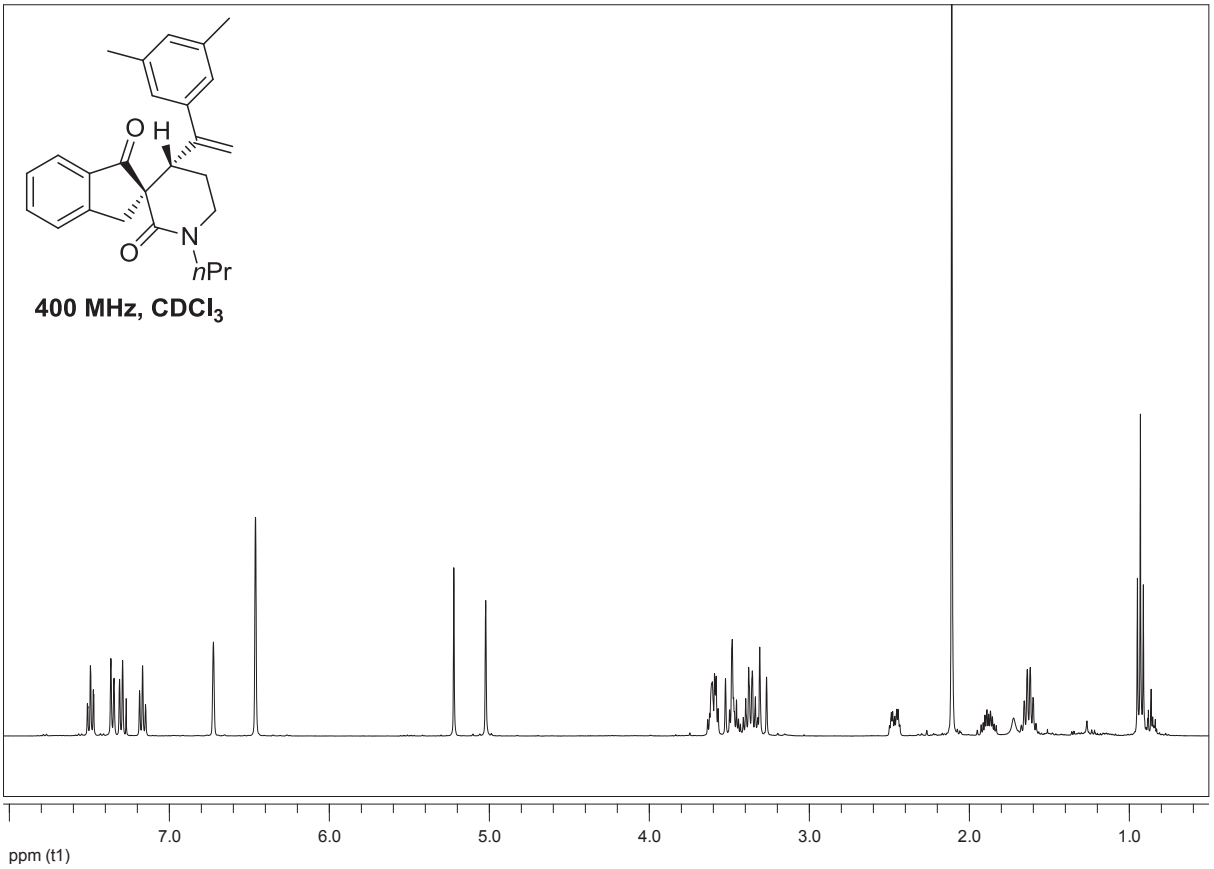
4f **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

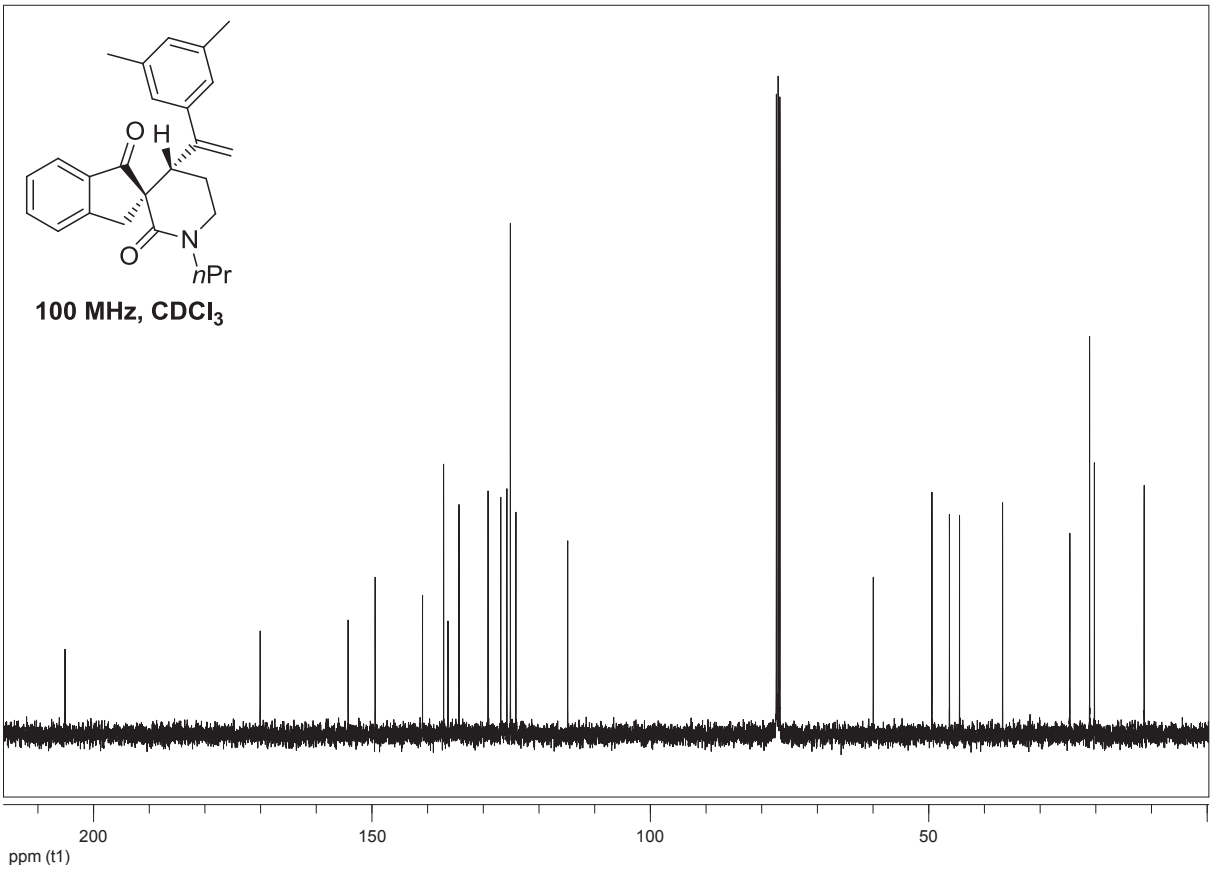



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.951 MM    0.2531 2924.92310  192.59633  91.8203
   2  13.476 MM    0.6384  260.56314    6.80290   8.1797

Totals :                  3185.48624  199.39922

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

^{1}H NMR spectrum of **4g**

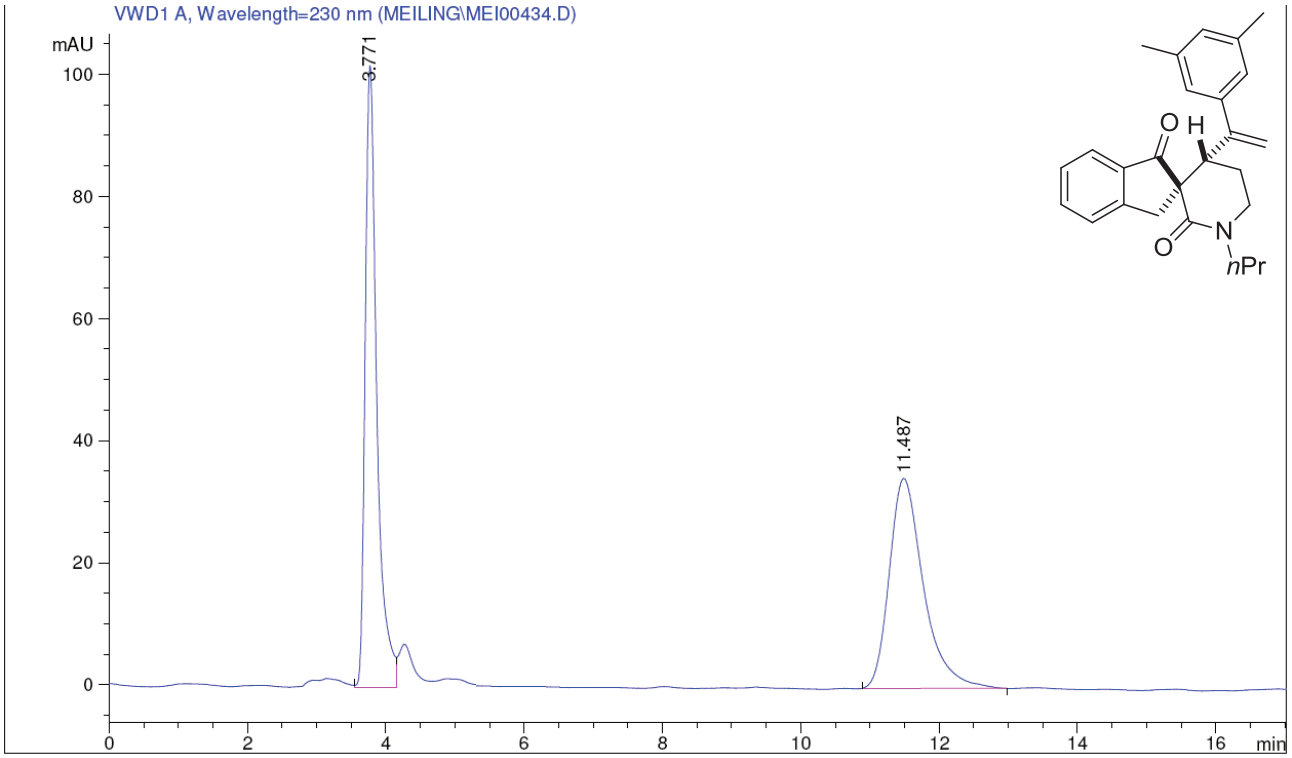


^{13}C NMR spectrum of **4g**



4g **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

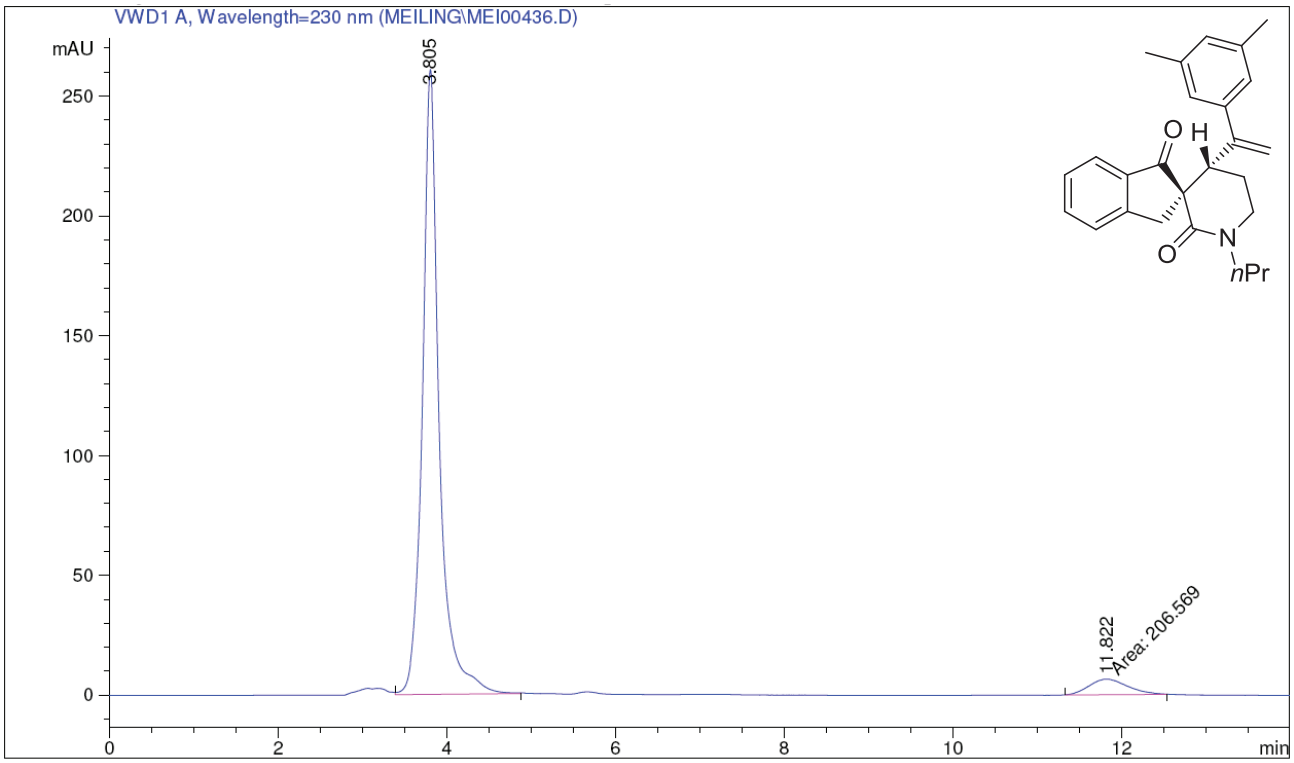
Racemic




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.771 VV    0.1764 1189.15588  101.73064  50.1467
   2  11.487 BP    0.5171 1182.19604   34.38982  49.8533

Totals :                  2371.35193  136.12046

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

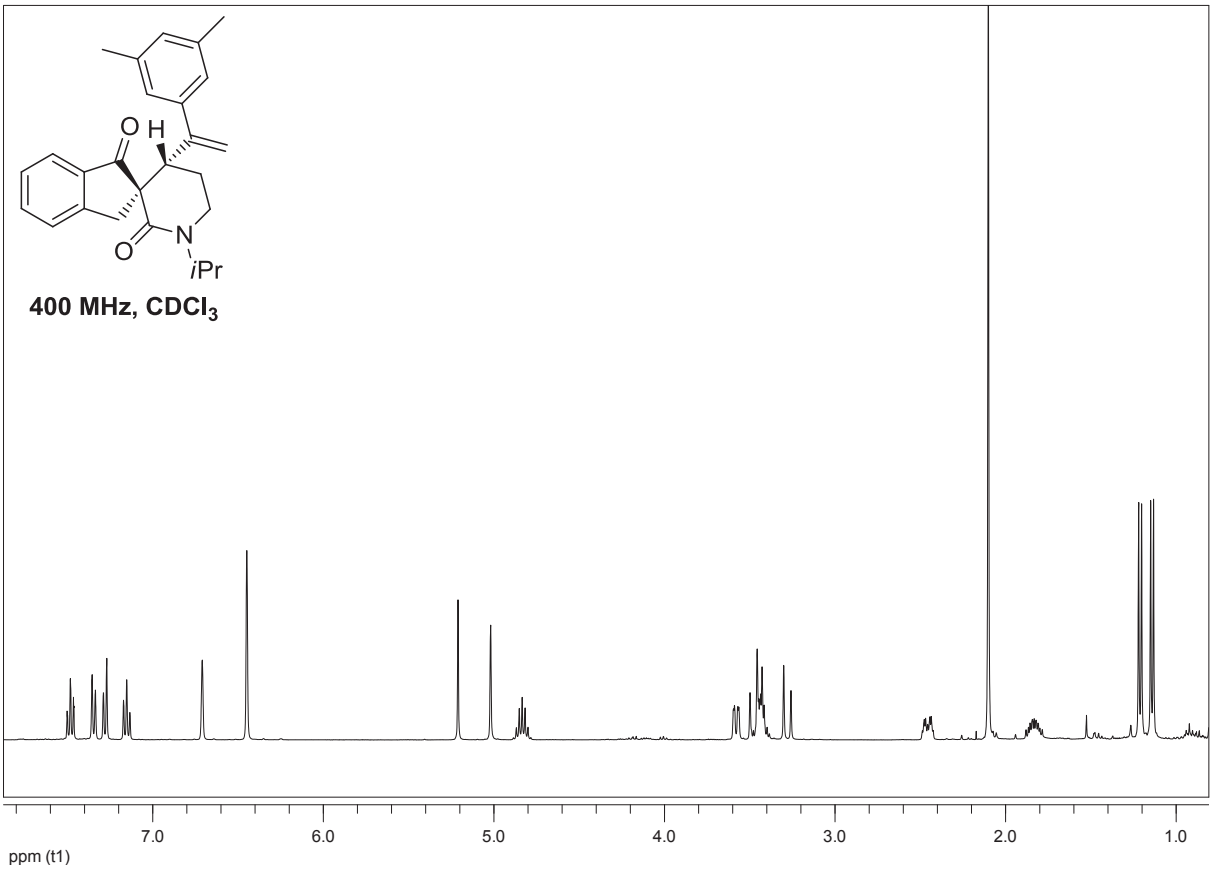
4g **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

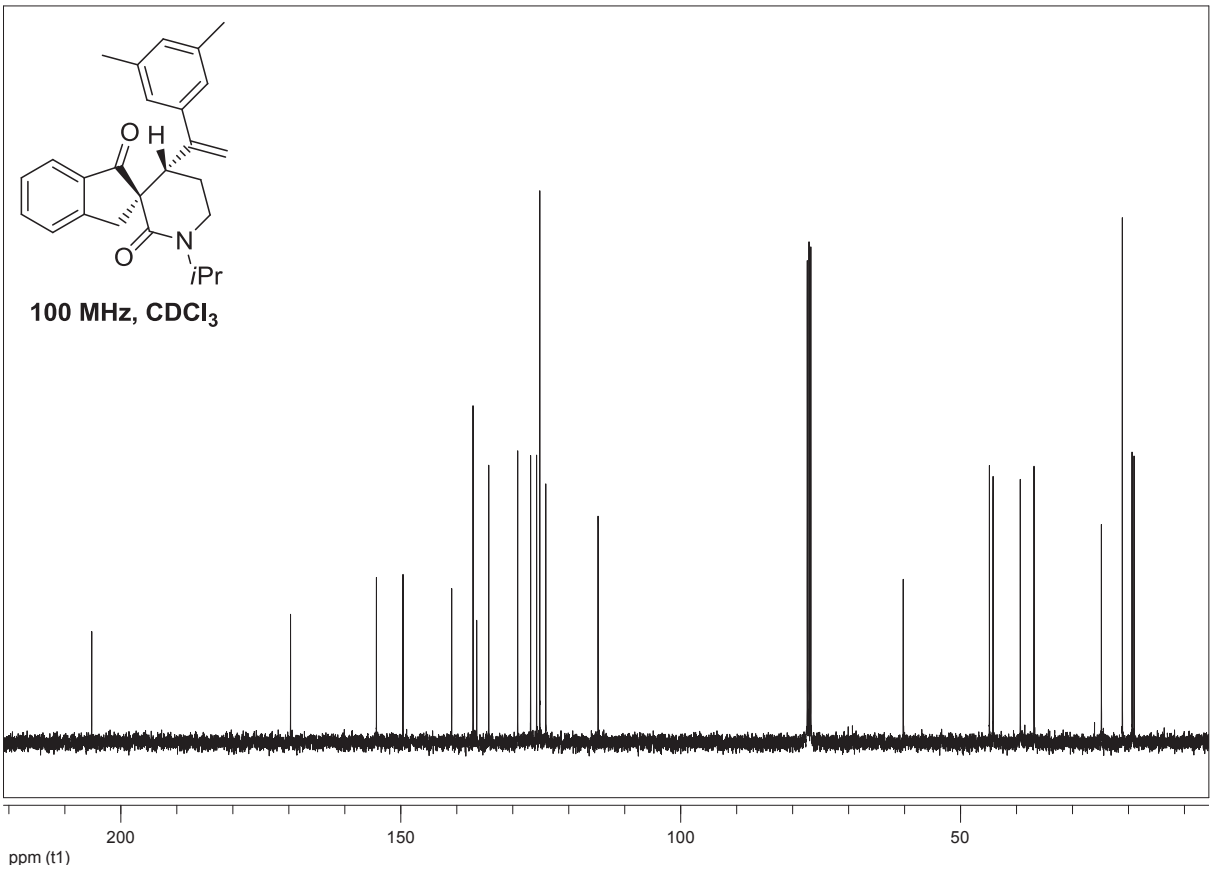



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.805 VB    0.2018 3616.96313  260.76331  94.5974
   2  11.822 MM    0.5320  206.56888    6.47171   5.4026

Totals :                  3823.53201  267.23502

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

^{1}H NMR spectrum of **4h**

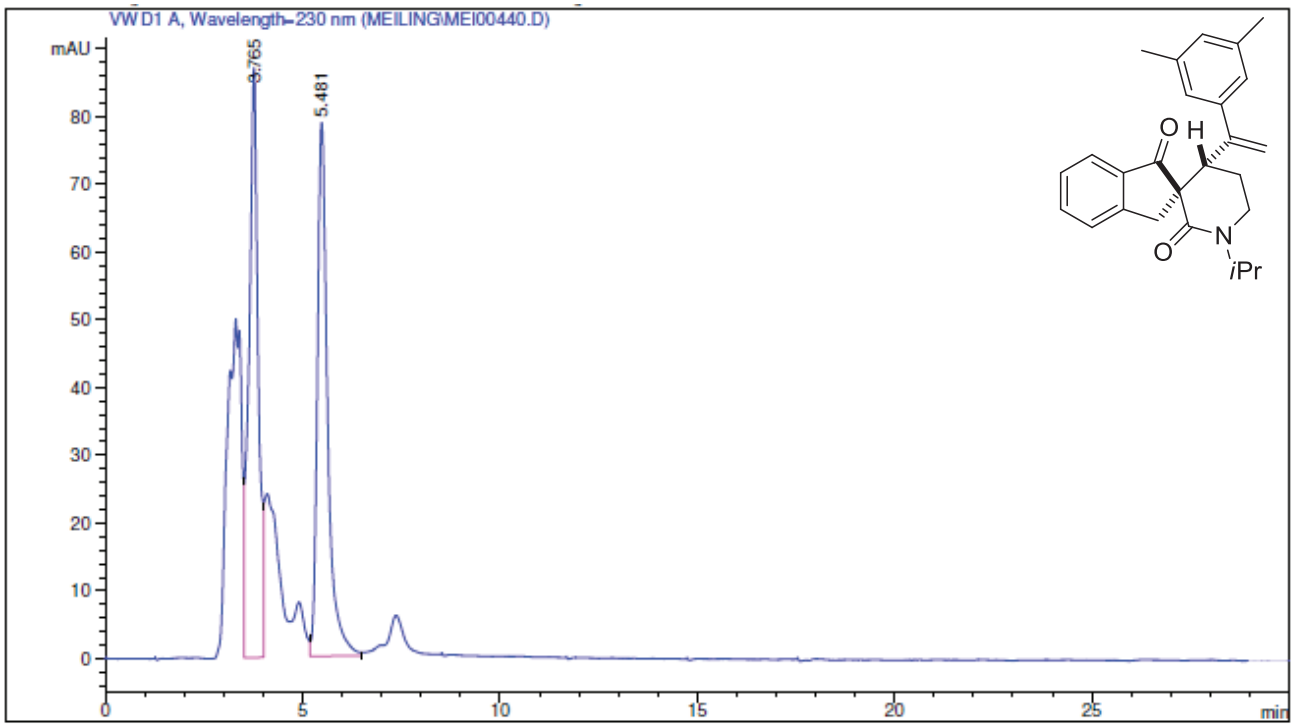


^{13}C NMR spectrum of **4h**



4h **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.765	VV	0.2284	1428.35999	87.07842	49.9523
2	5.481	VB	0.2709	1431.08606	78.79088	50.0477

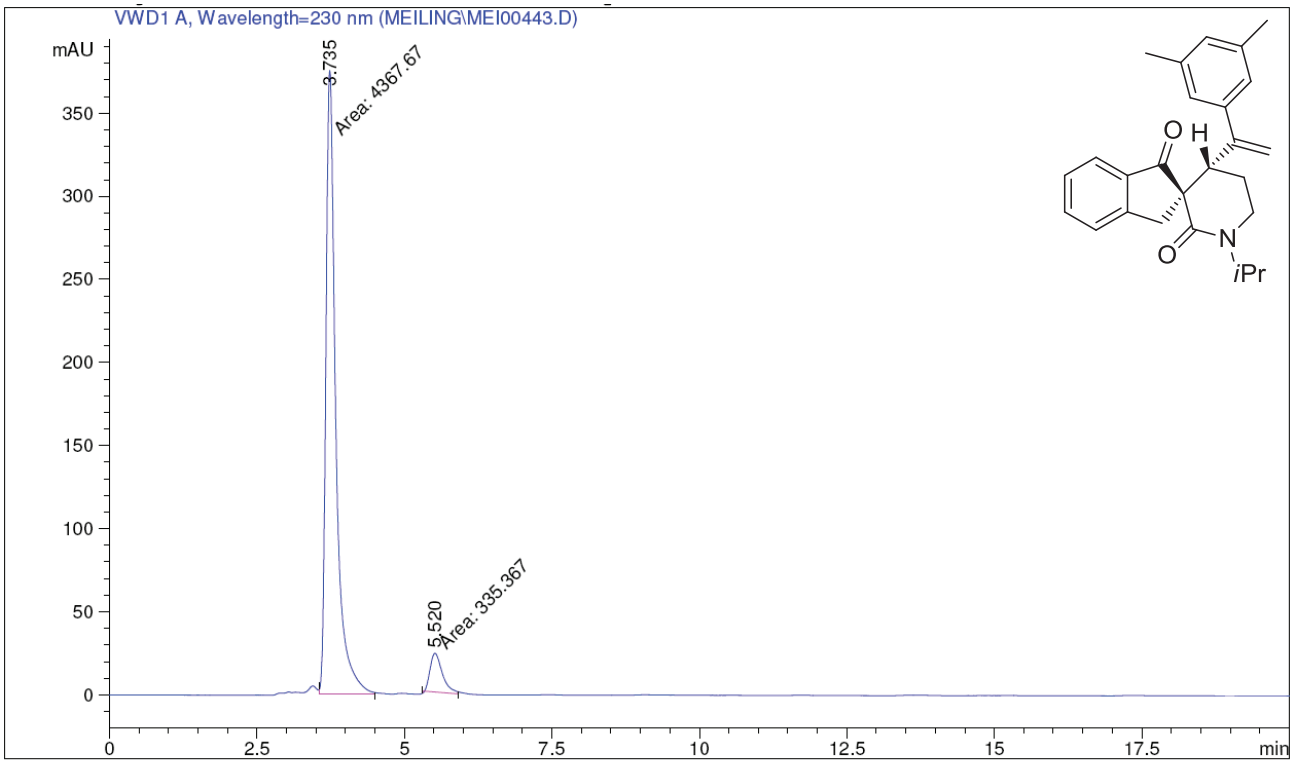
Totals : 2859.44604 165.86930

Results obtained with enhanced integrator!

*** End of Report ***

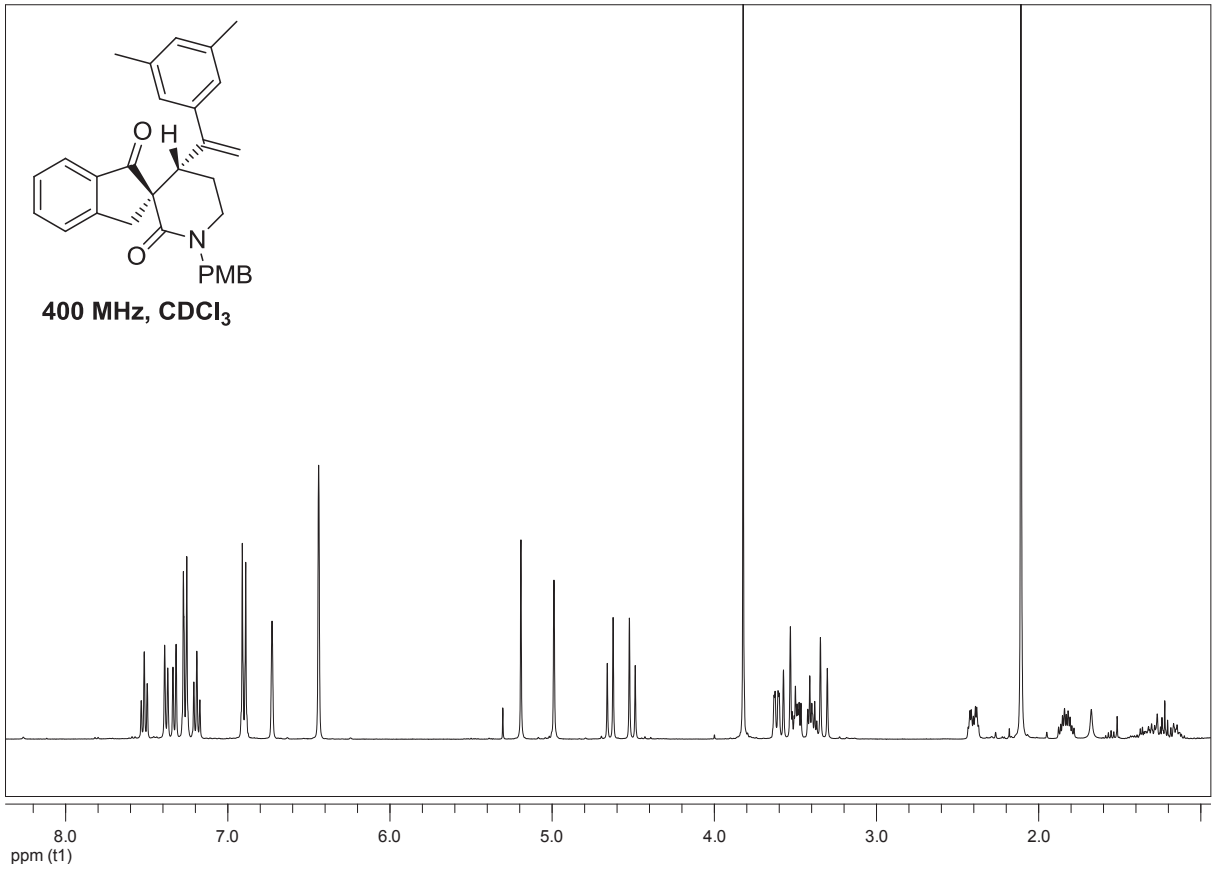
4h **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

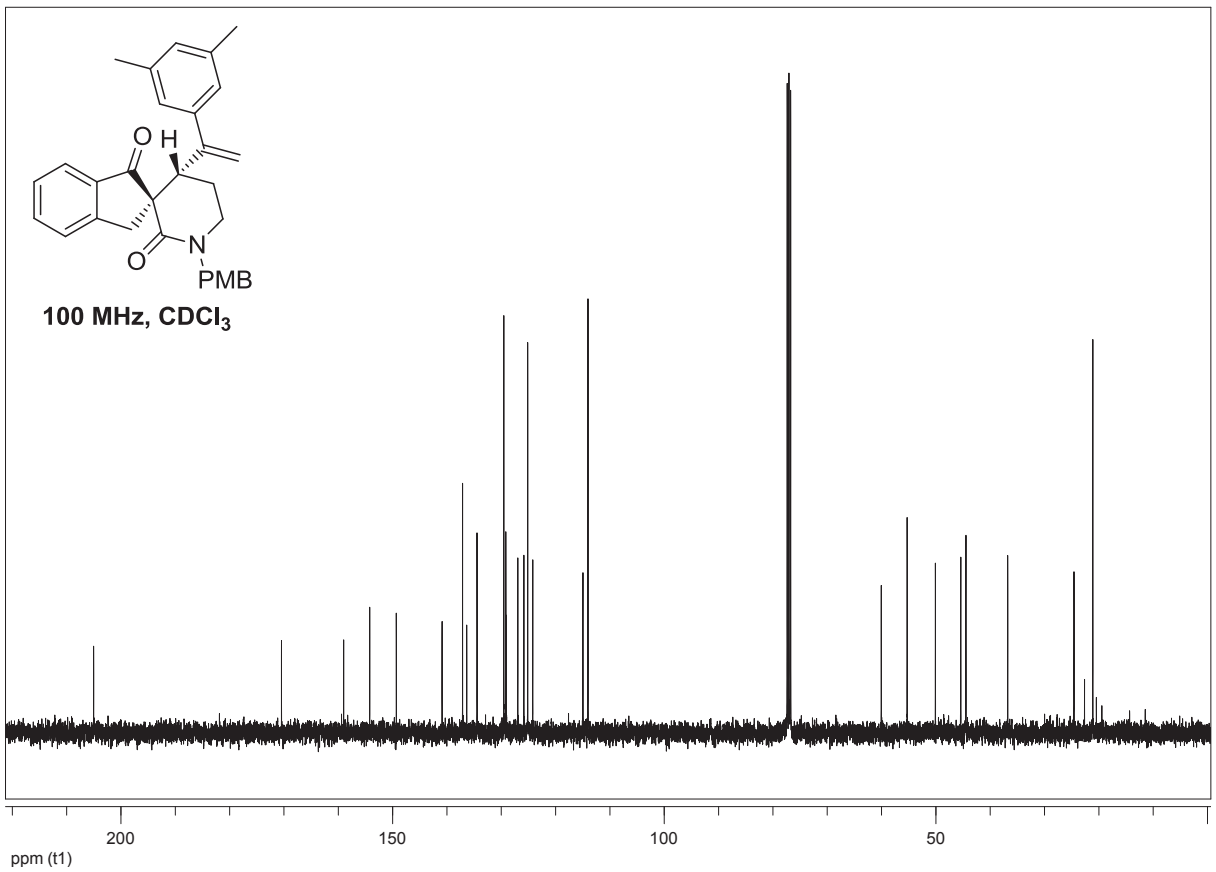



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.735 MM    0.1940 4367.67285  375.19400  92.8691
   2   5.520 MM    0.2403  335.36673   23.25805   7.1309

Totals :                  4703.03958  398.45205

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **4i**

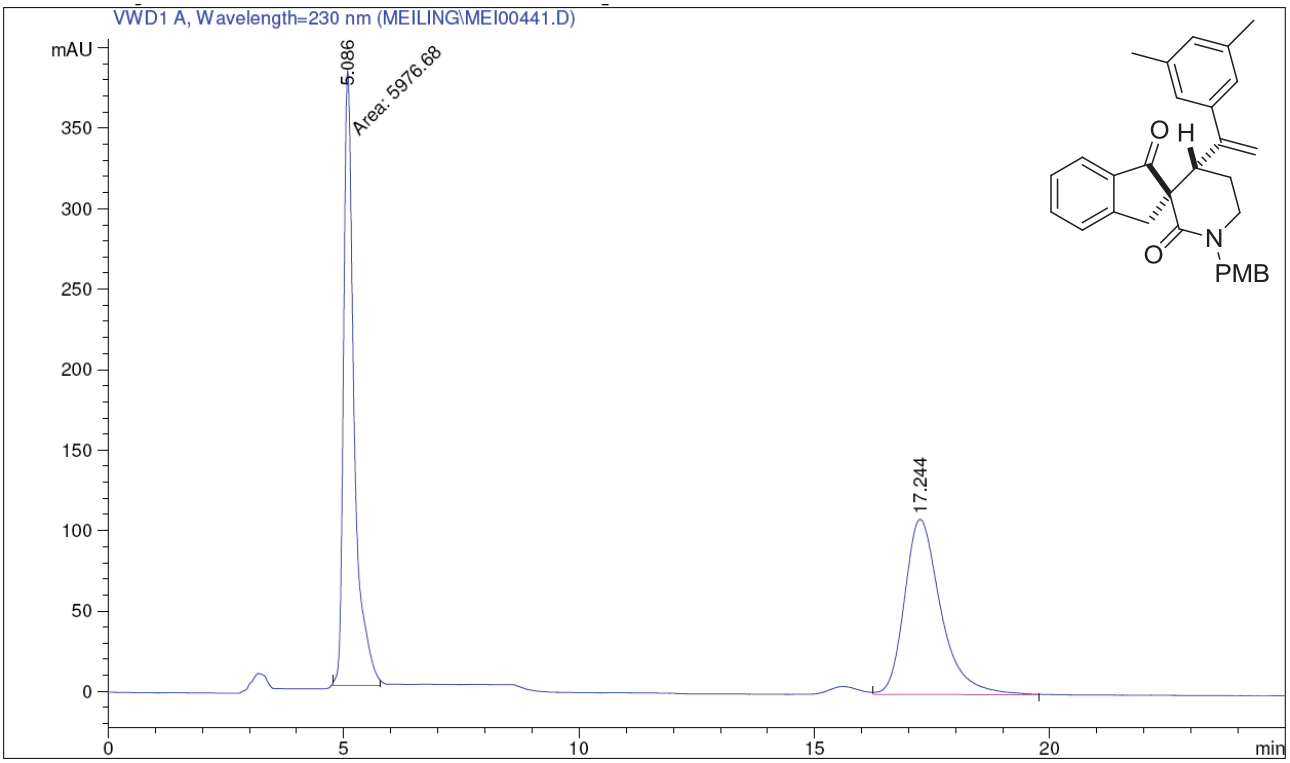


^{13}C NMR spectrum of **4i**



4i **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

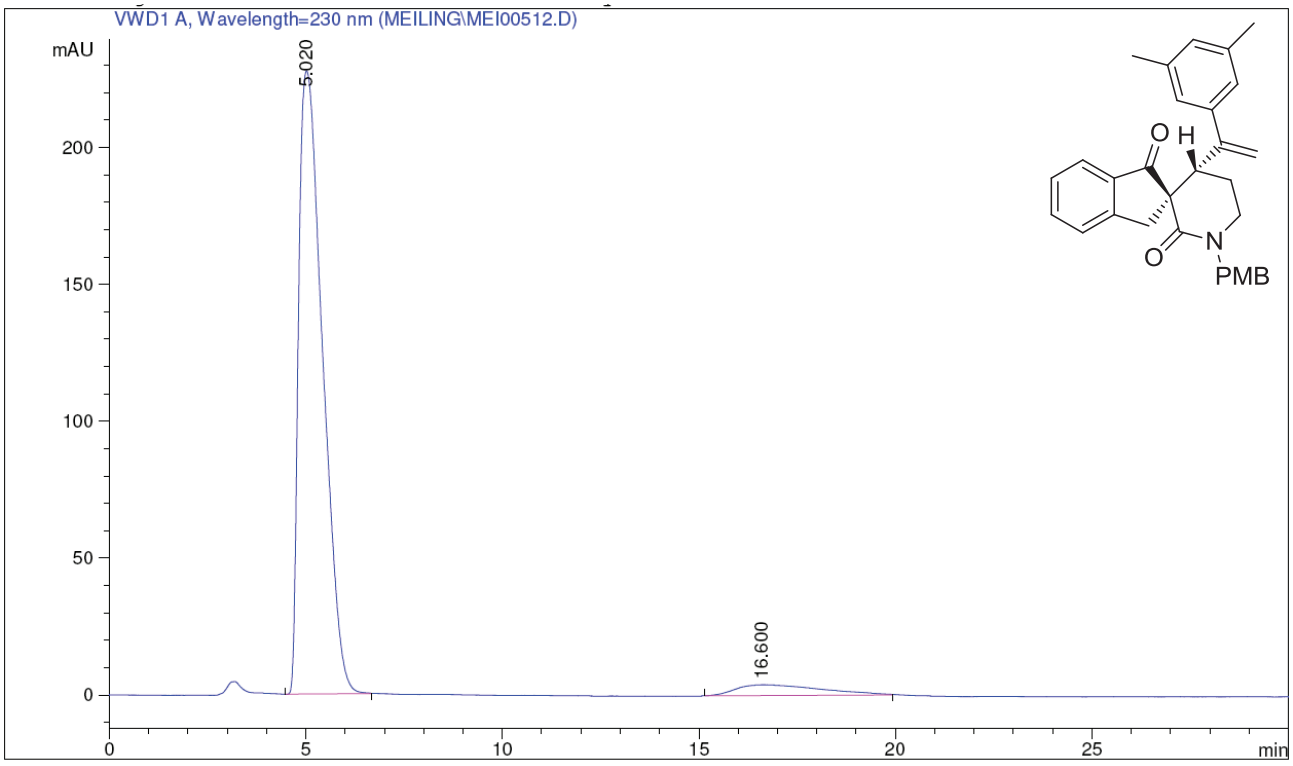
Racemic




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.086 MM    0.2608 5976.67676  381.91660  50.6011
   2  17.244 VB    0.8135 5834.68750  108.81854  49.3989

Totals :                  1.18114e4   490.73514

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

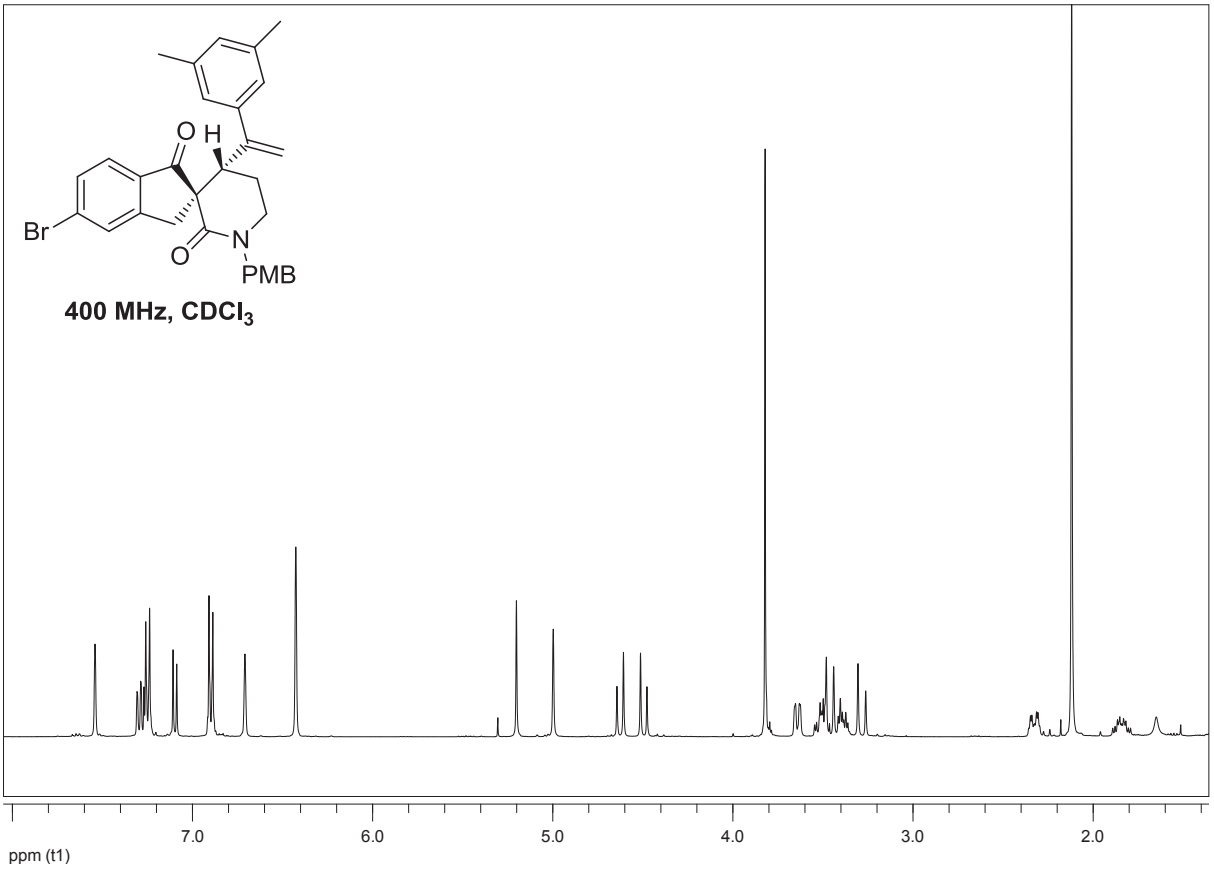
4i **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

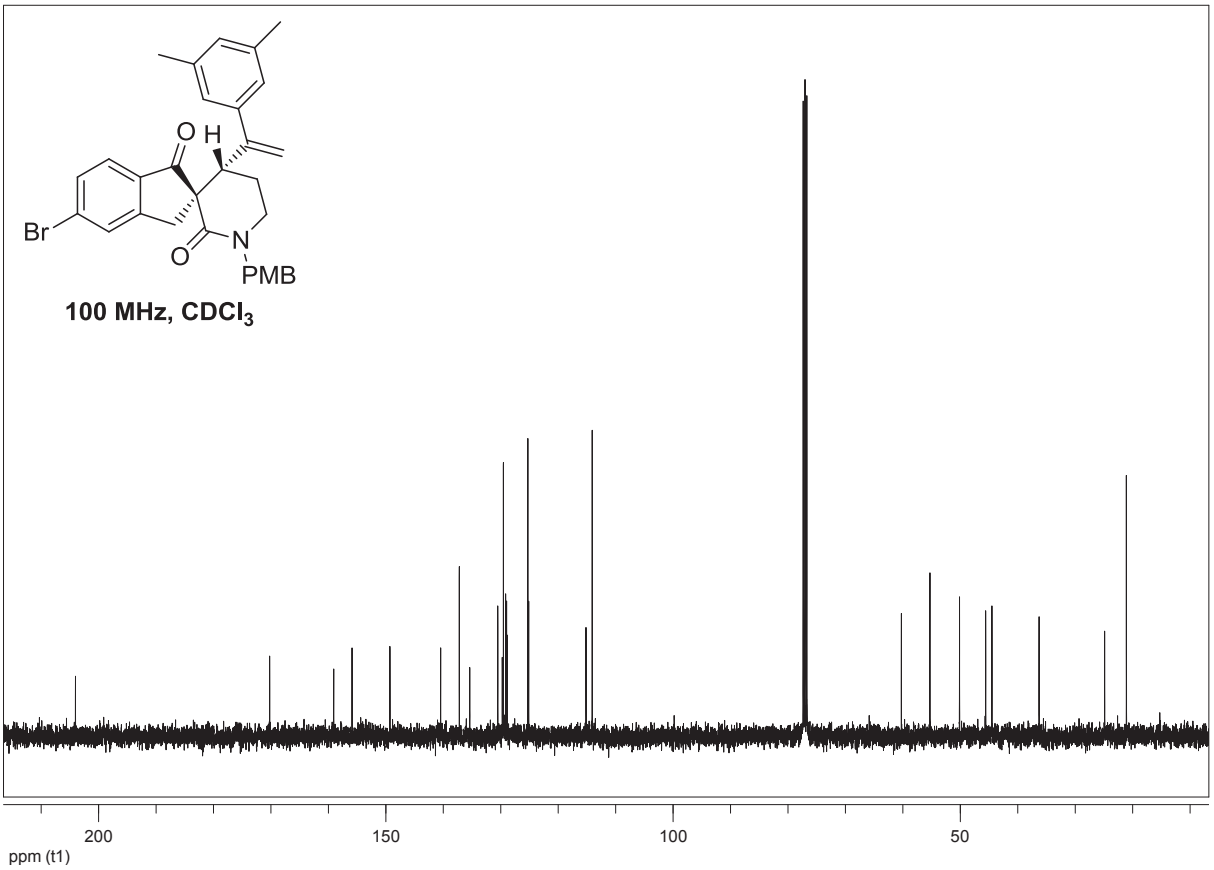



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.020 PB    0.6451 9619.87695  227.61391  94.0664
   2  16.600 BB    1.7918  606.81012    3.96868   5.9336

Totals :                  1.02267e4   231.58259

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

^{1}H NMR spectrum of **4j**

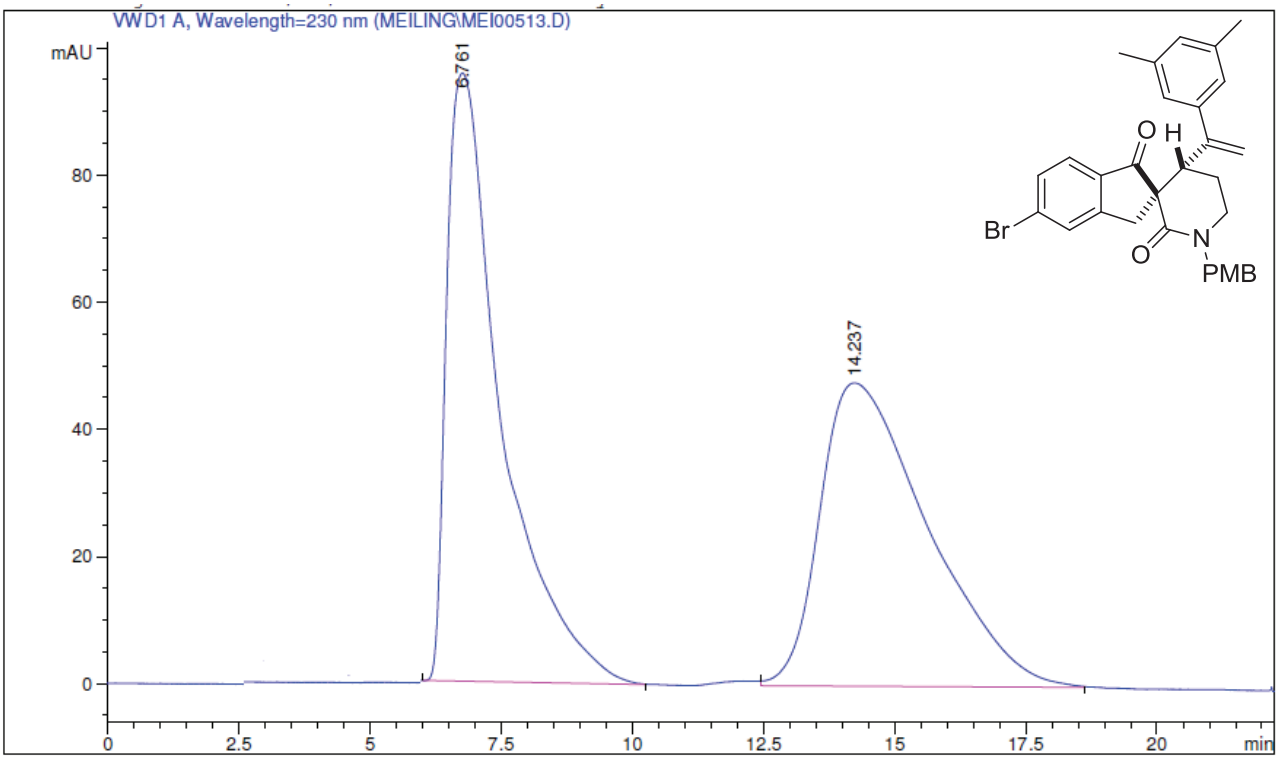


^{13}C NMR spectrum of **4j**



4j **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

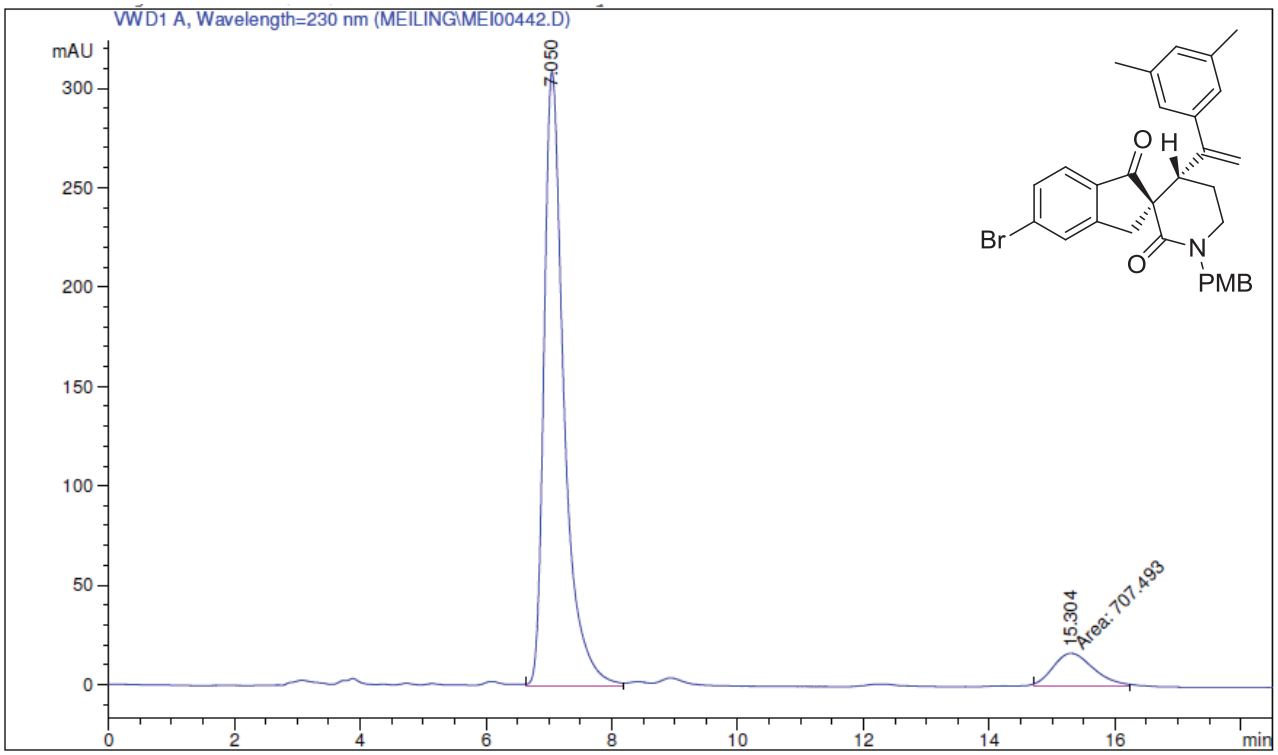
Racemic




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.761 PB    1.0621 6939.38135   95.68015  50.4794
   2  14.237 BB    1.8914 6807.58057   47.68995  49.5206

Totals :                  1.37470e4   143.37010

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```

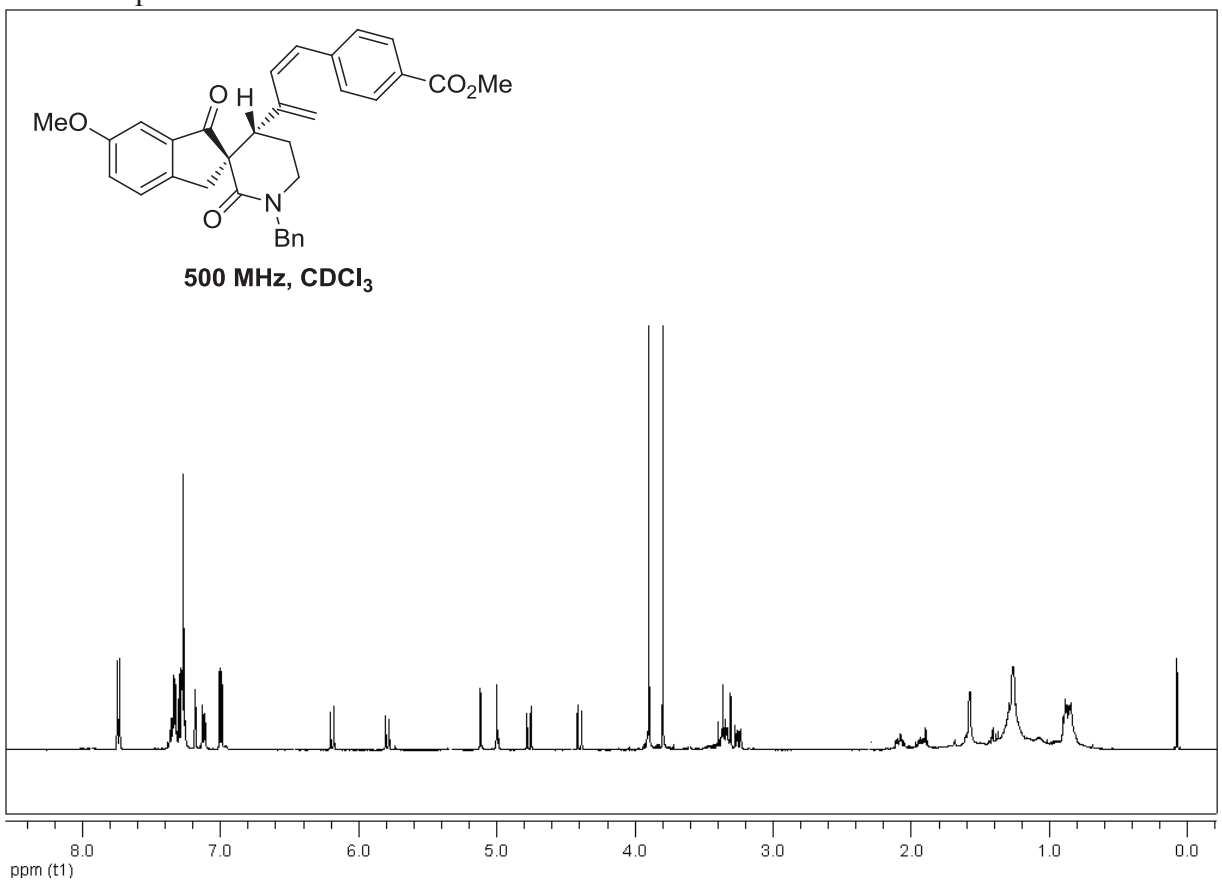
4j **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

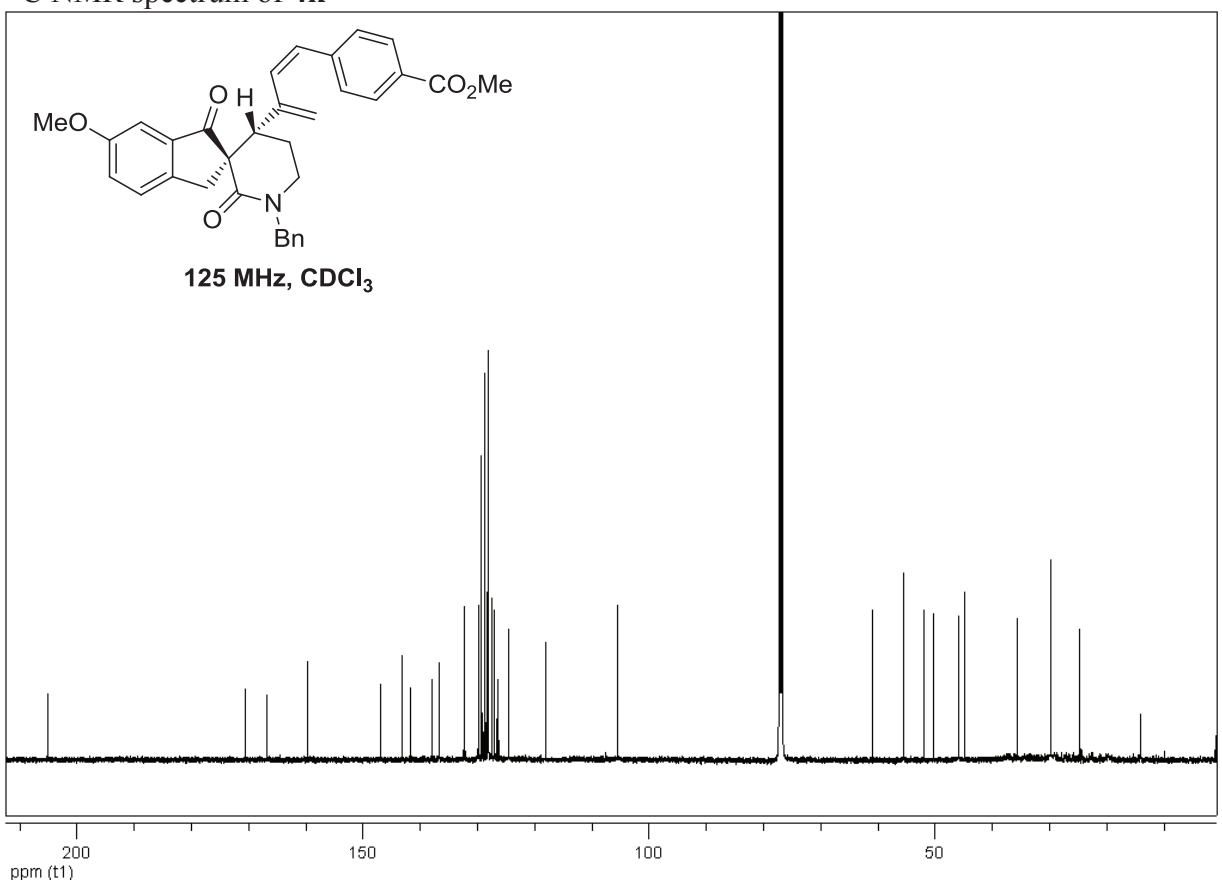



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.050 BV    0.3309 6807.20361  309.08539  90.5852
   2  15.304 MM    0.7316  707.49316   16.11778   9.4148

Totals :                  7514.69678  325.20317

 Results obtained with enhanced integrator!
=====================================================================
                        *** End of Report ***
```

^{1}H NMR spectrum of **4k**

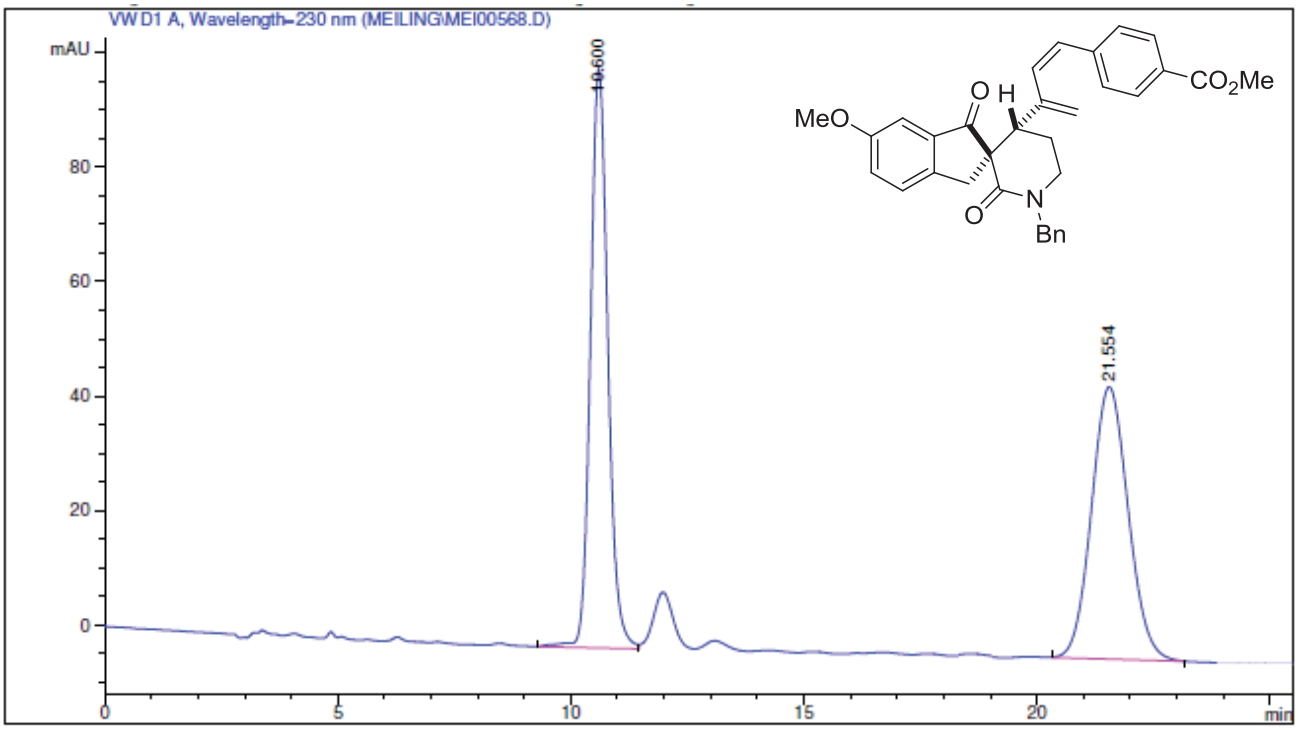


^{13}C NMR spectrum of **4k**



4k **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

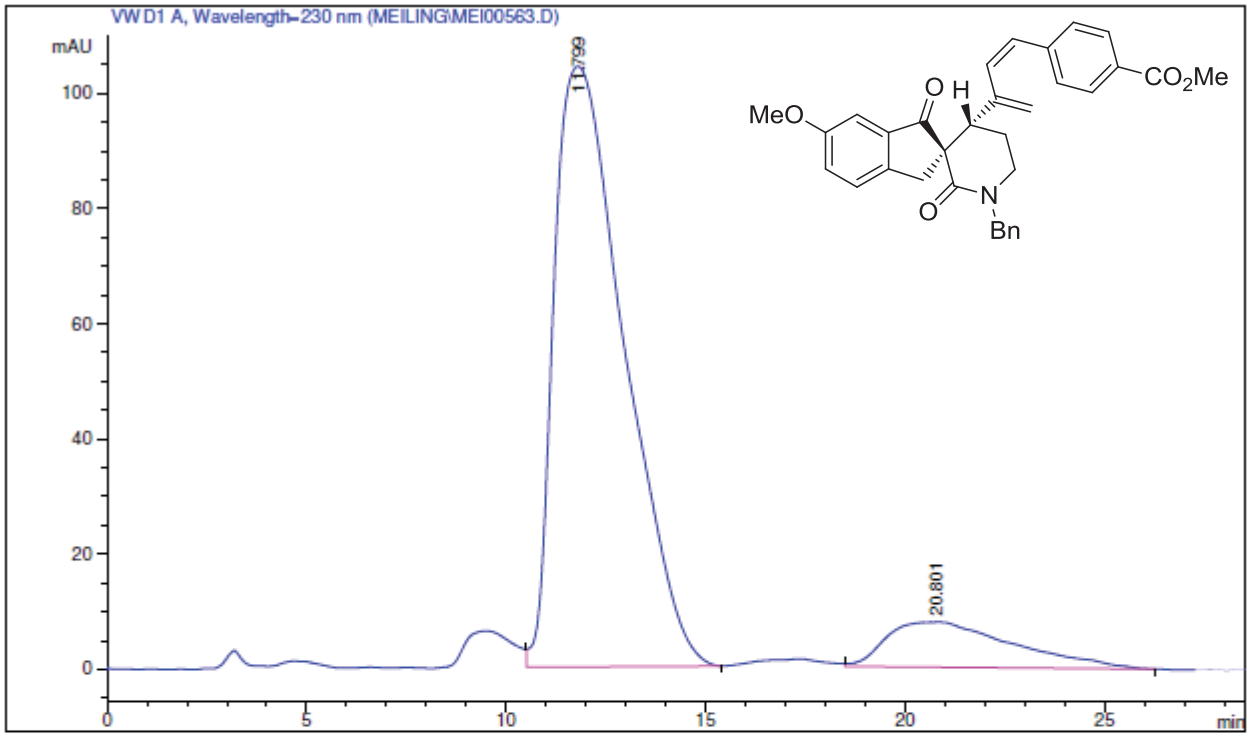
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.600	BB	0.3945	2634.79565	101.28857	50.2120
2	21.554	BB	0.6805	2612.54712	47.58736	49.7880
Totals :				5247.34277	148.87593	

Results obtained with enhanced integrator!

*** End of Report ***

4k **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

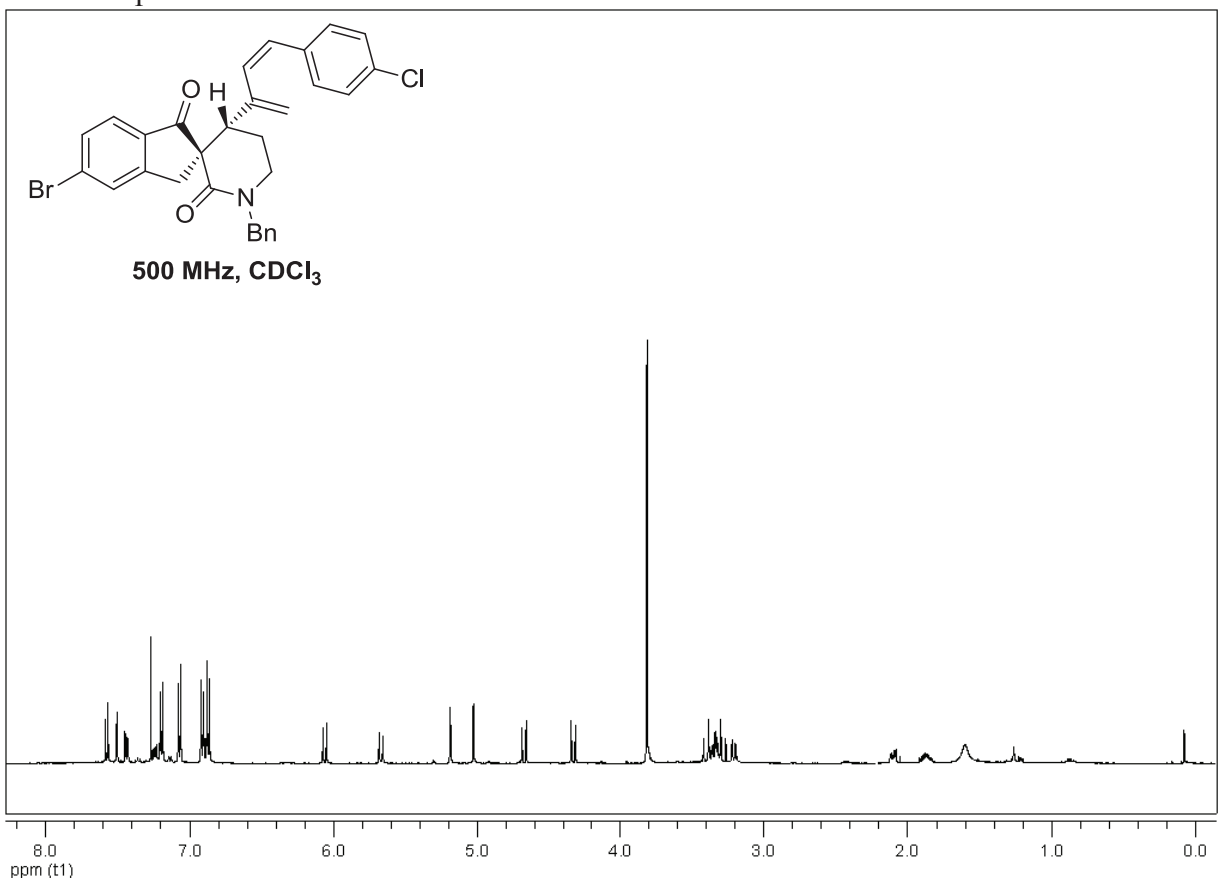
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.799	VP	1.8634	1.27633e4	104.32079	87.9747
2	20.801	VB	2.5974	1744.61340	7.86037	12.0253

Totals : 1.45079e4 112.18116

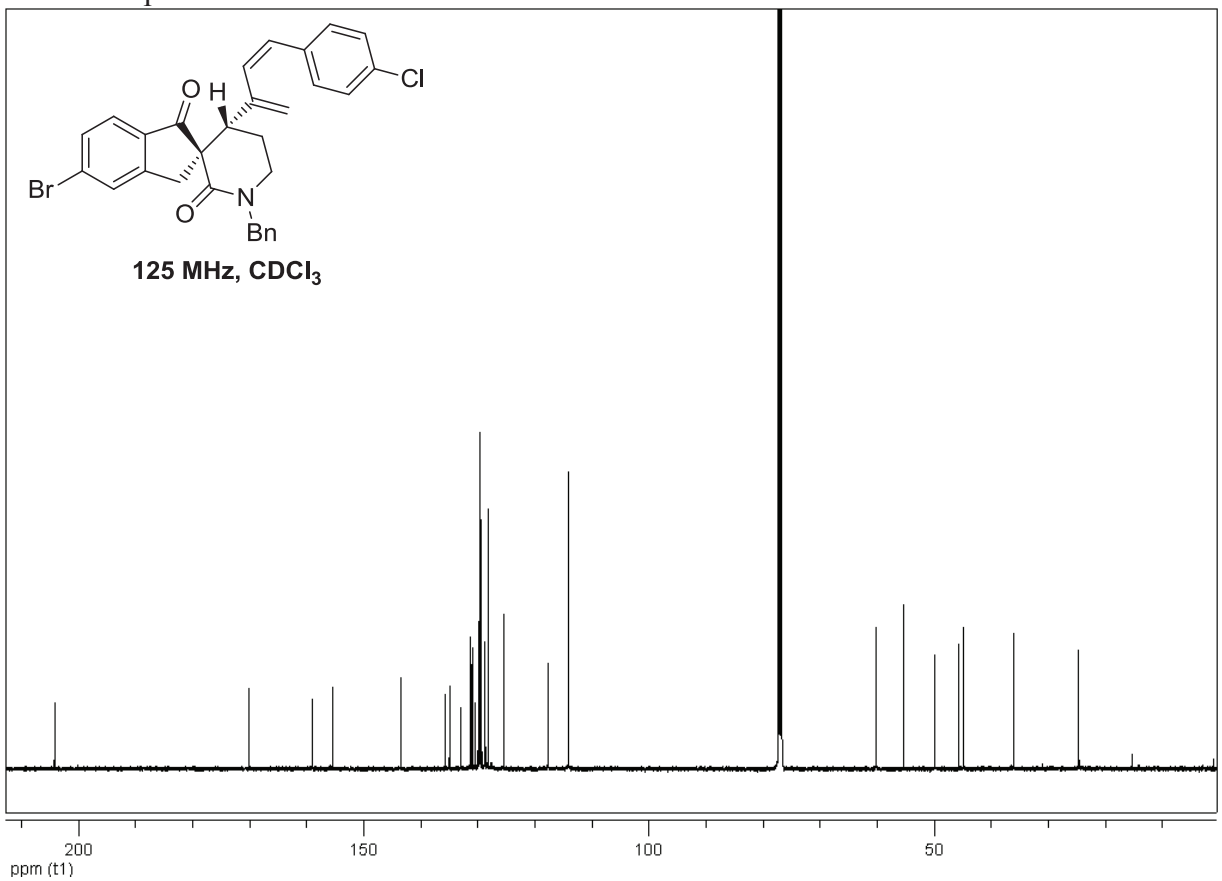
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectrum of **4l**

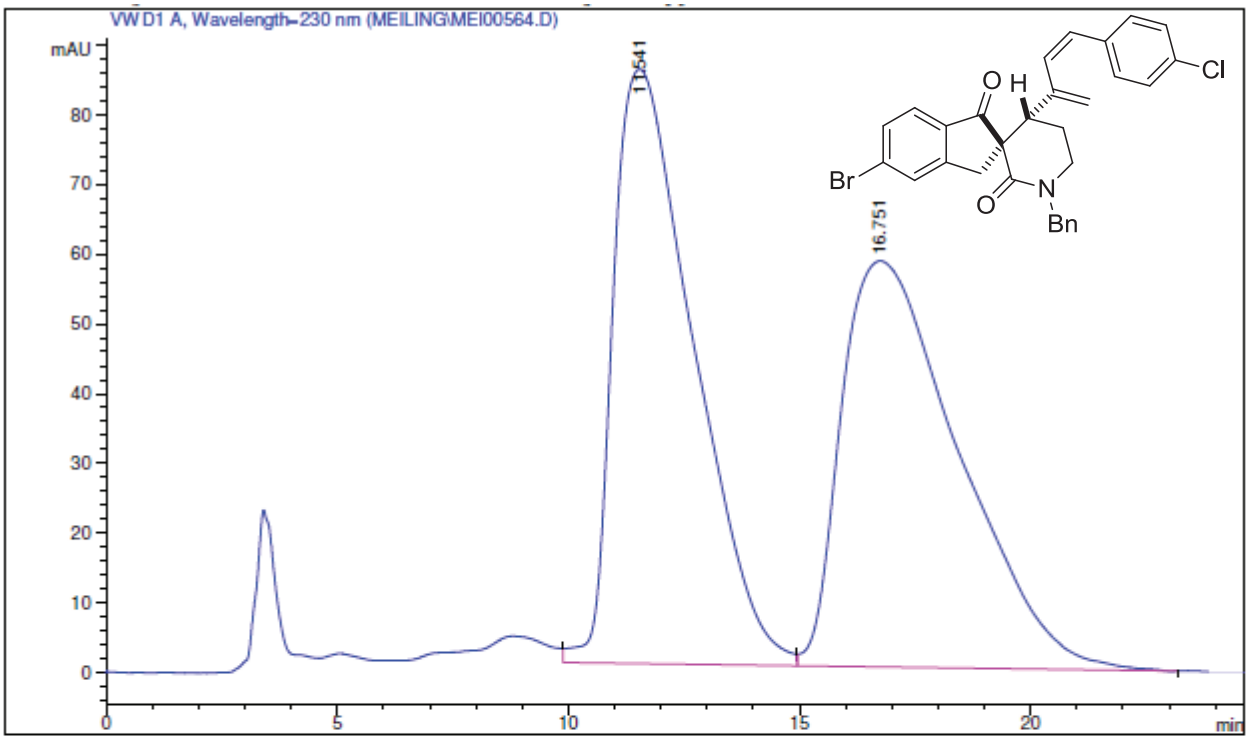


^{13}C NMR spectrum of **4l**



4l **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Racemic



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.541	VV	1.7703	1.03022e4	85.22606	50.0227
2	16.751	VP	2.4068	1.02928e4	58.21448	49.9773

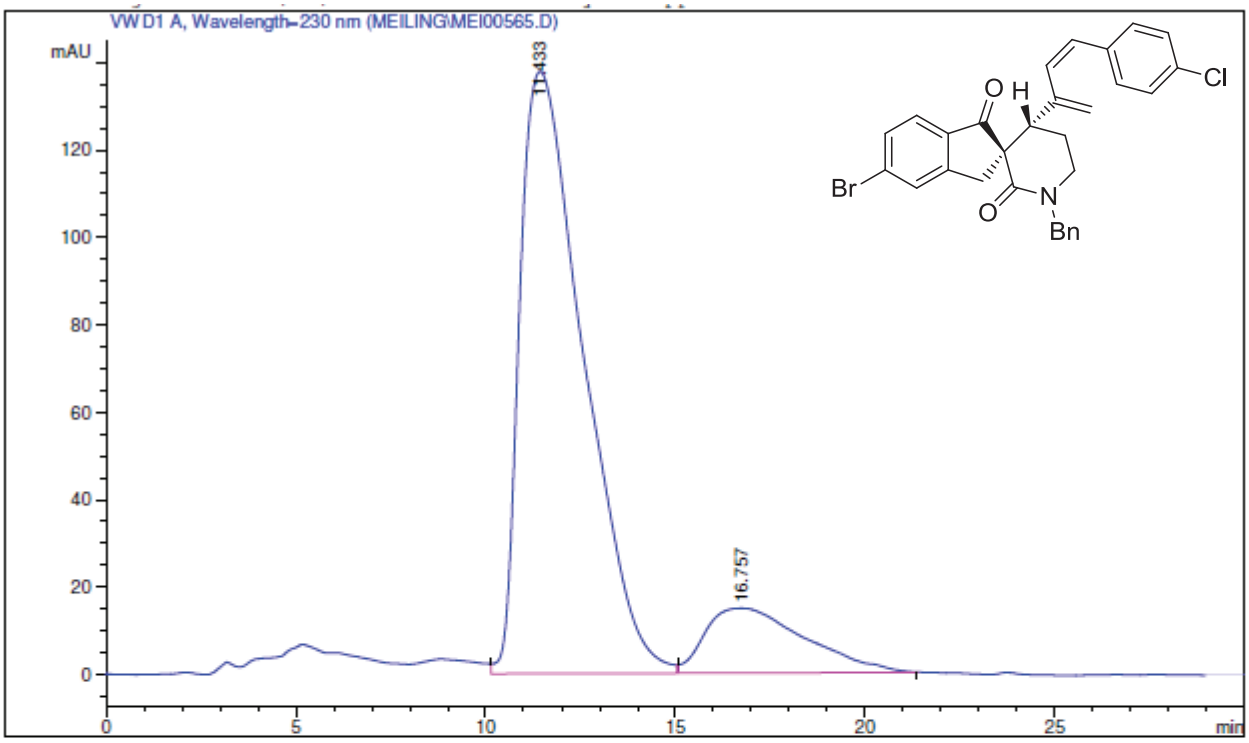
Totals : 2.05950e4 143.44054

Results obtained with enhanced integrator!

*** End of Report ***

4l **HPLC:** Chiralcel AD; hexane/isopropanol 70:30; 1.0 mL/min

Enantioenriched



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

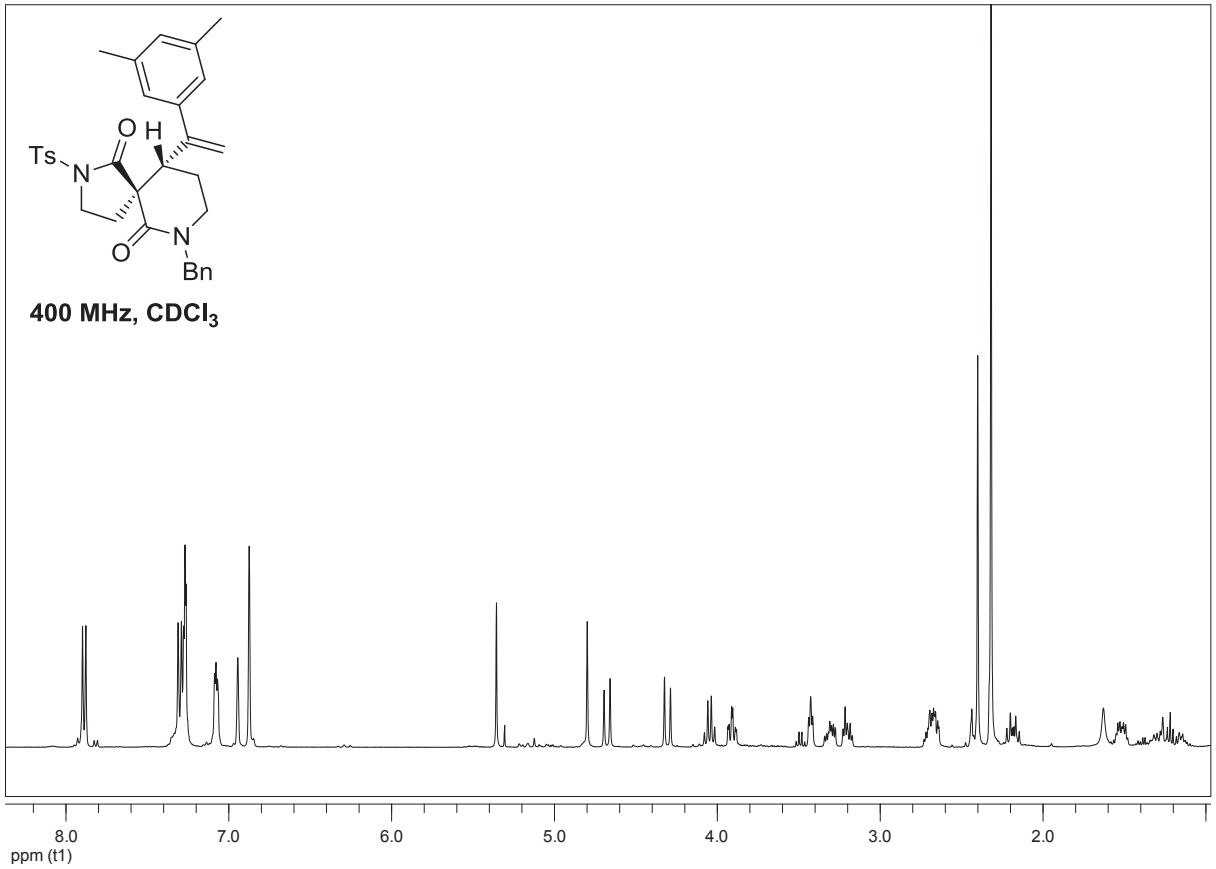
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.433	VB	1.7444	1.60339e4	137.70506	85.5557
2	16.757	BB	2.1423	2706.98291	14.81083	14.4443

Totals : 1.87409e4 152.51589

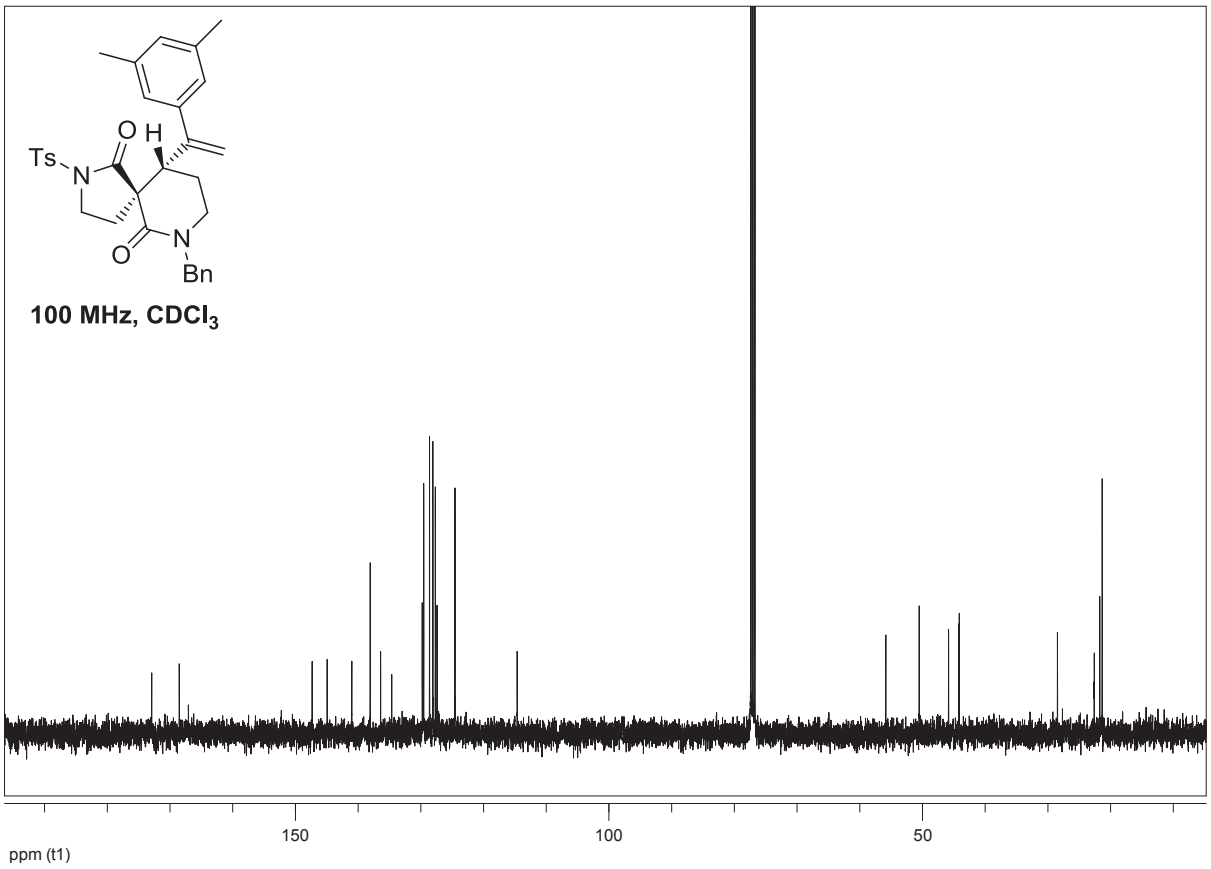
Results obtained with enhanced integrator!

*** End of Report ***

^{1}H NMR spectrum of **4m**

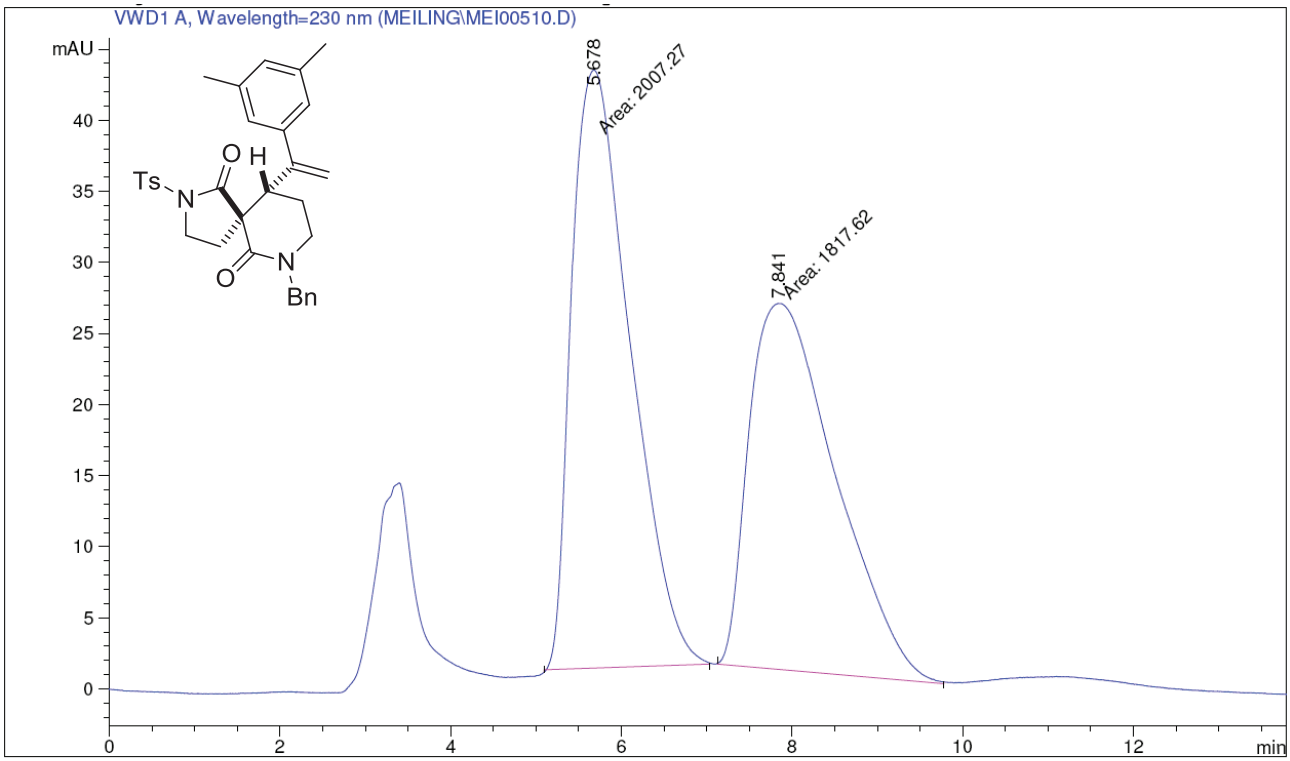


^{13}C NMR spectrum of **4m**



4m **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

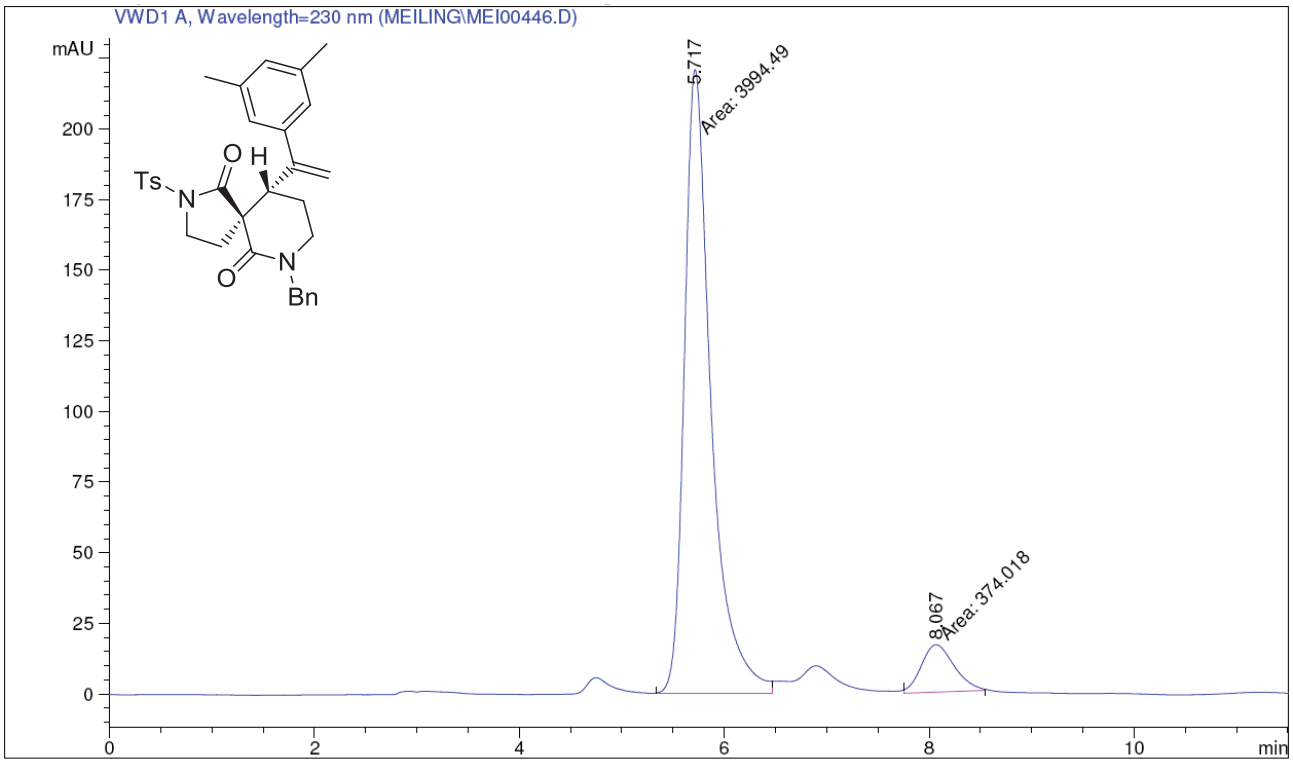
Racemic




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.678 MM    0.7947 2007.27356   42.09686  52.4792
   2   7.841 MM    1.1759 1817.62085   25.76171  47.5208

Totals :                  3824.89441   67.85857

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

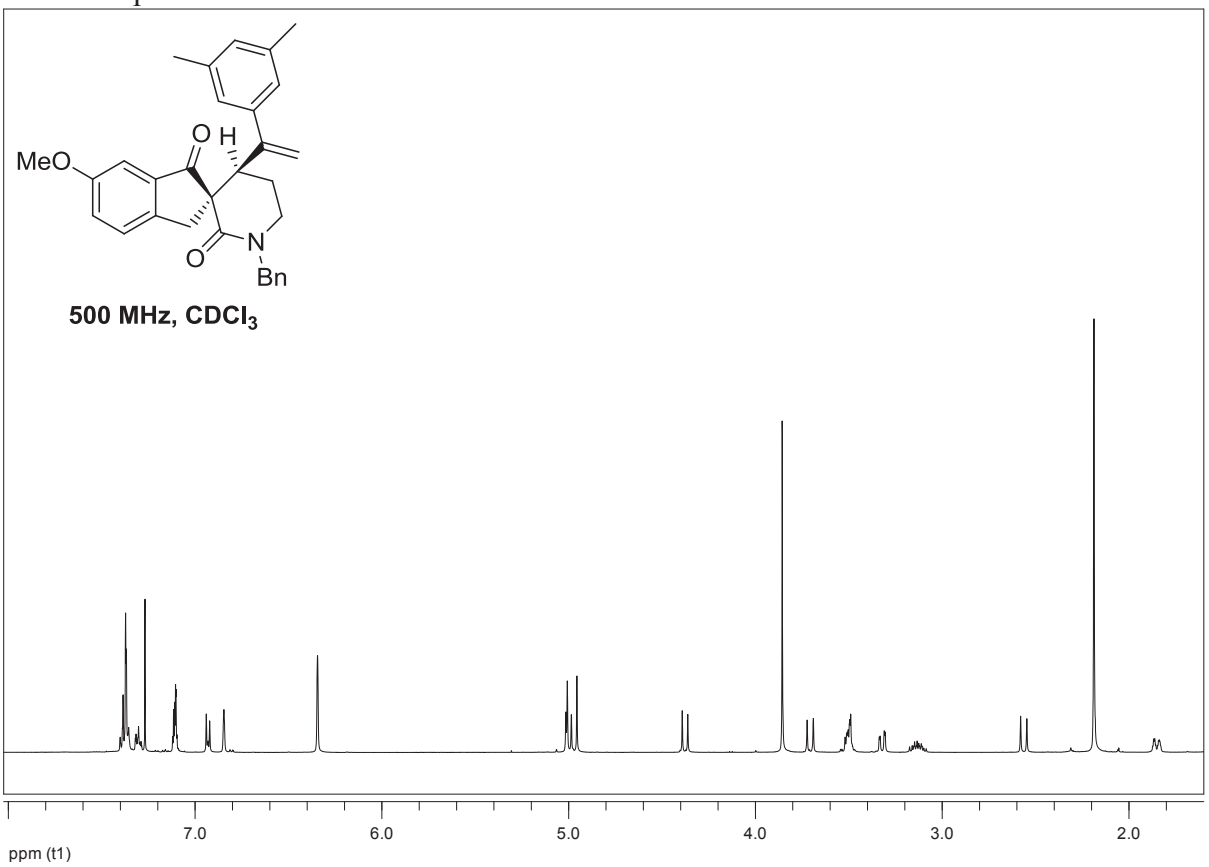
4m **HPLC:** Chiralcel AD; hexane/isopropanol 60:40; 1.0 mL/min

Enantioenriched

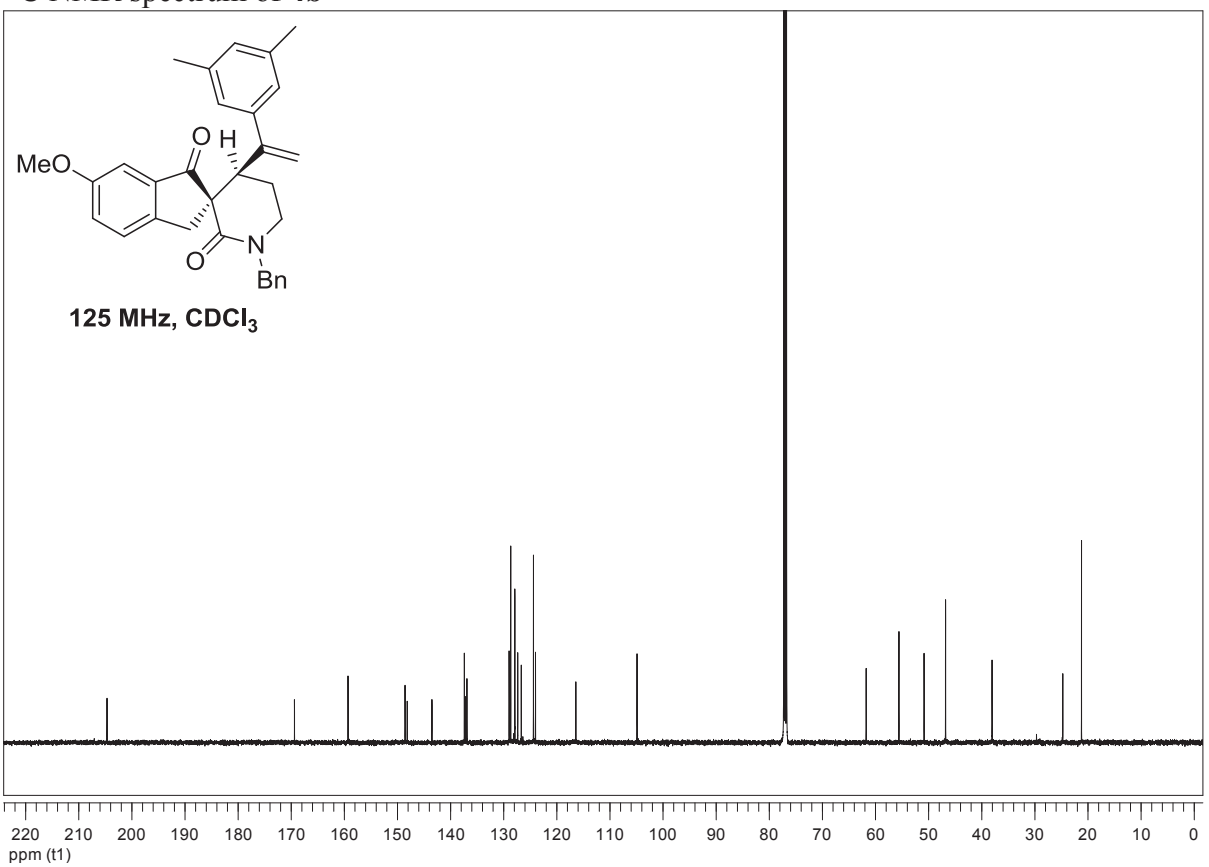



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.717 MM    0.3015 3994.48901  220.79837  91.4383
   2   8.067 MM    0.3722  374.01828   16.74965   8.5617

Totals :                  4368.50729  237.54802

 Results obtained with enhanced integrator!
=====================================================================
                      *** End of Report ***
```

^{1}H NMR spectrum of **4b′**

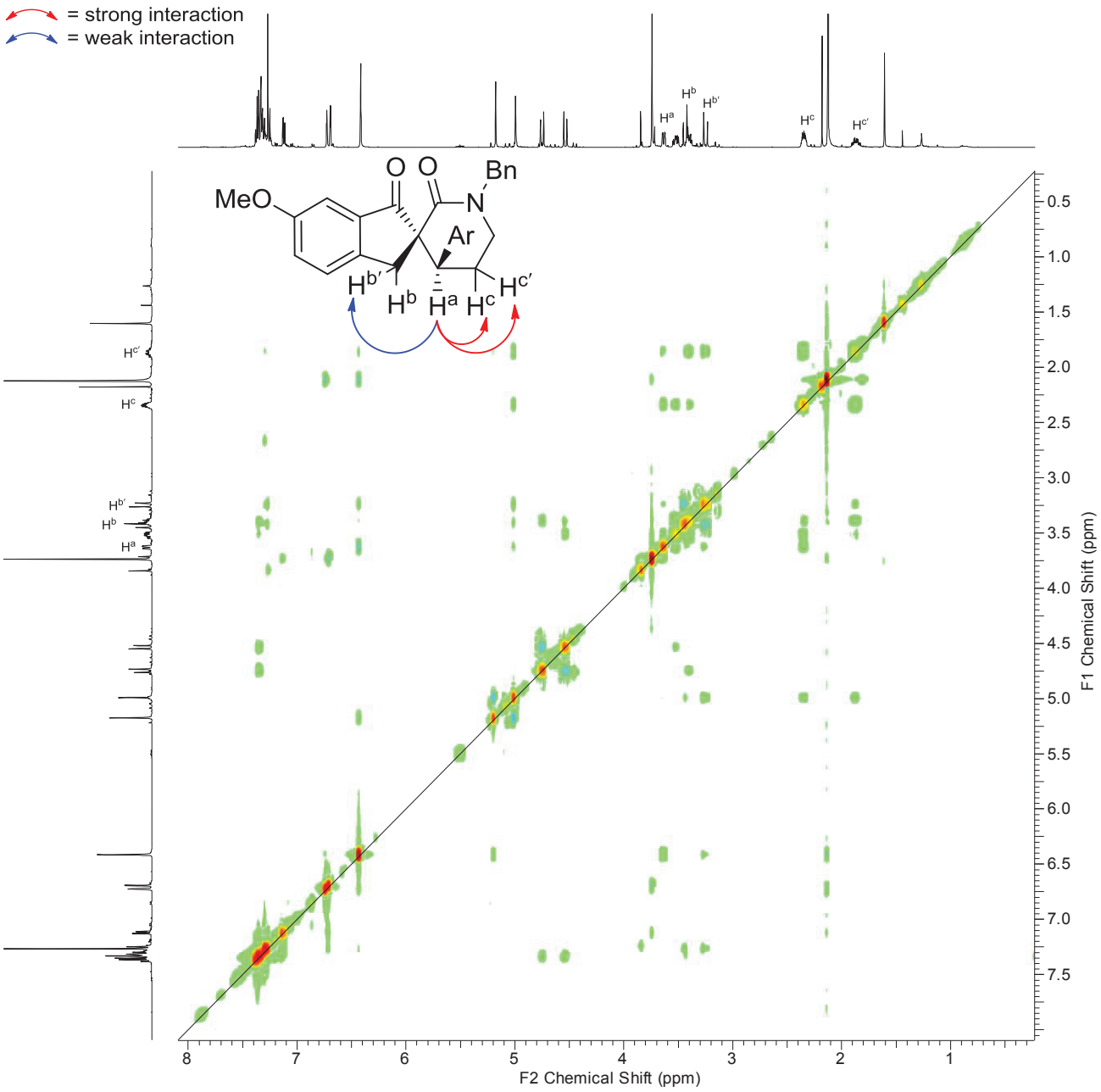


^{13}C NMR spectrum of **4b′**

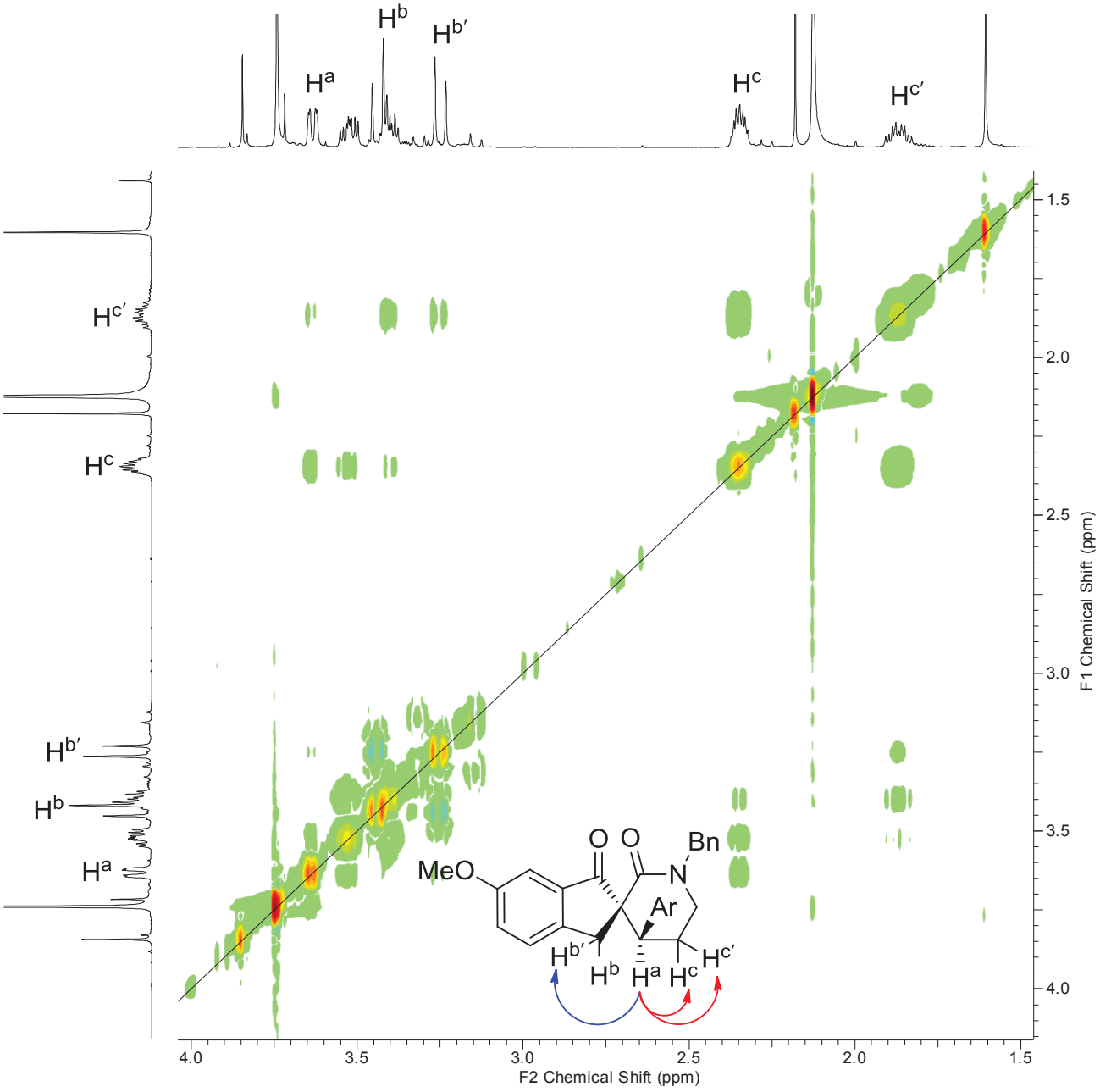


9. Relative stereochemistry assignment of 4b and 4b′ using NOESY analysis

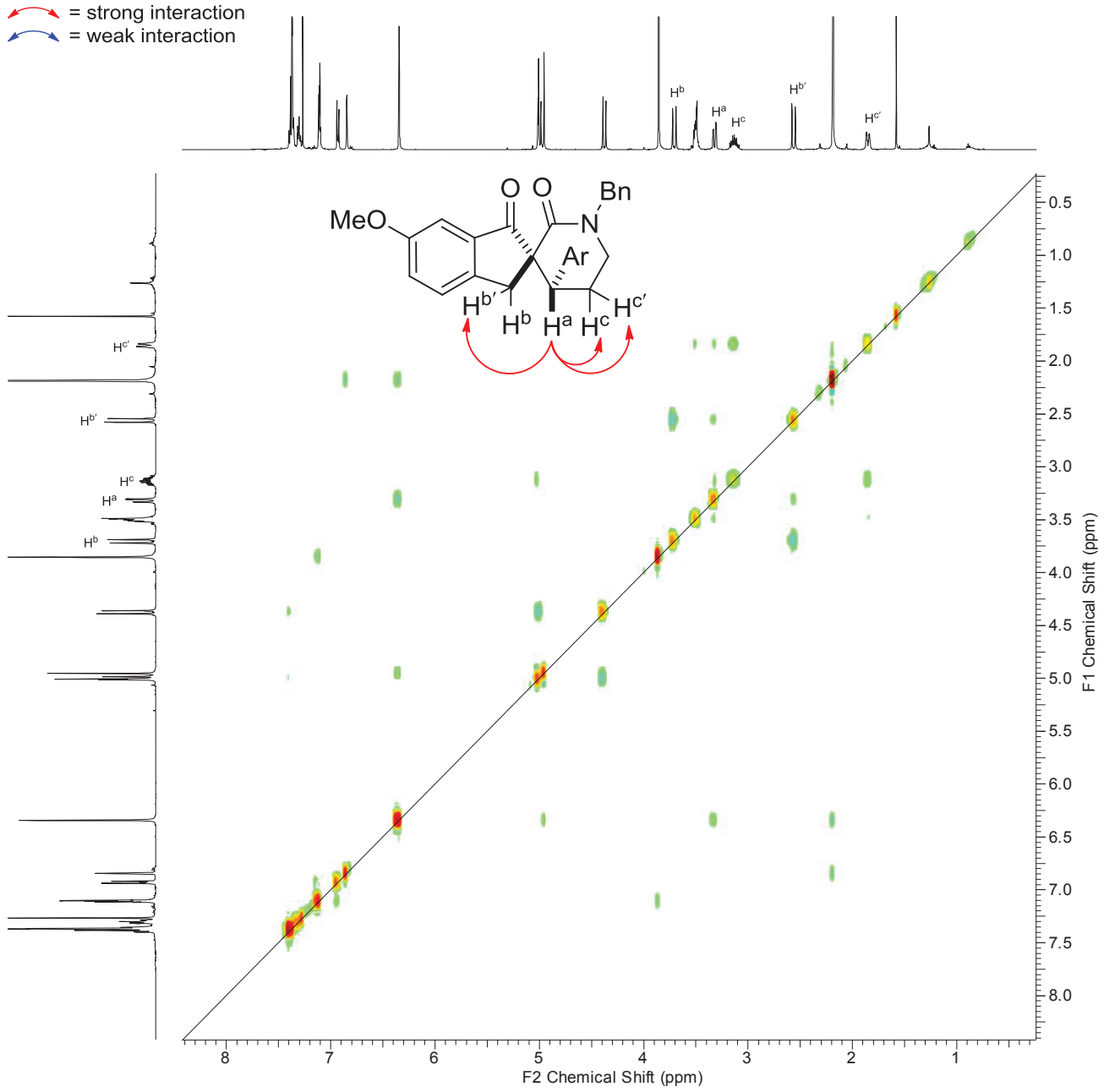
NOSEY of **4b** (500 MHz, $CDCl_3$)



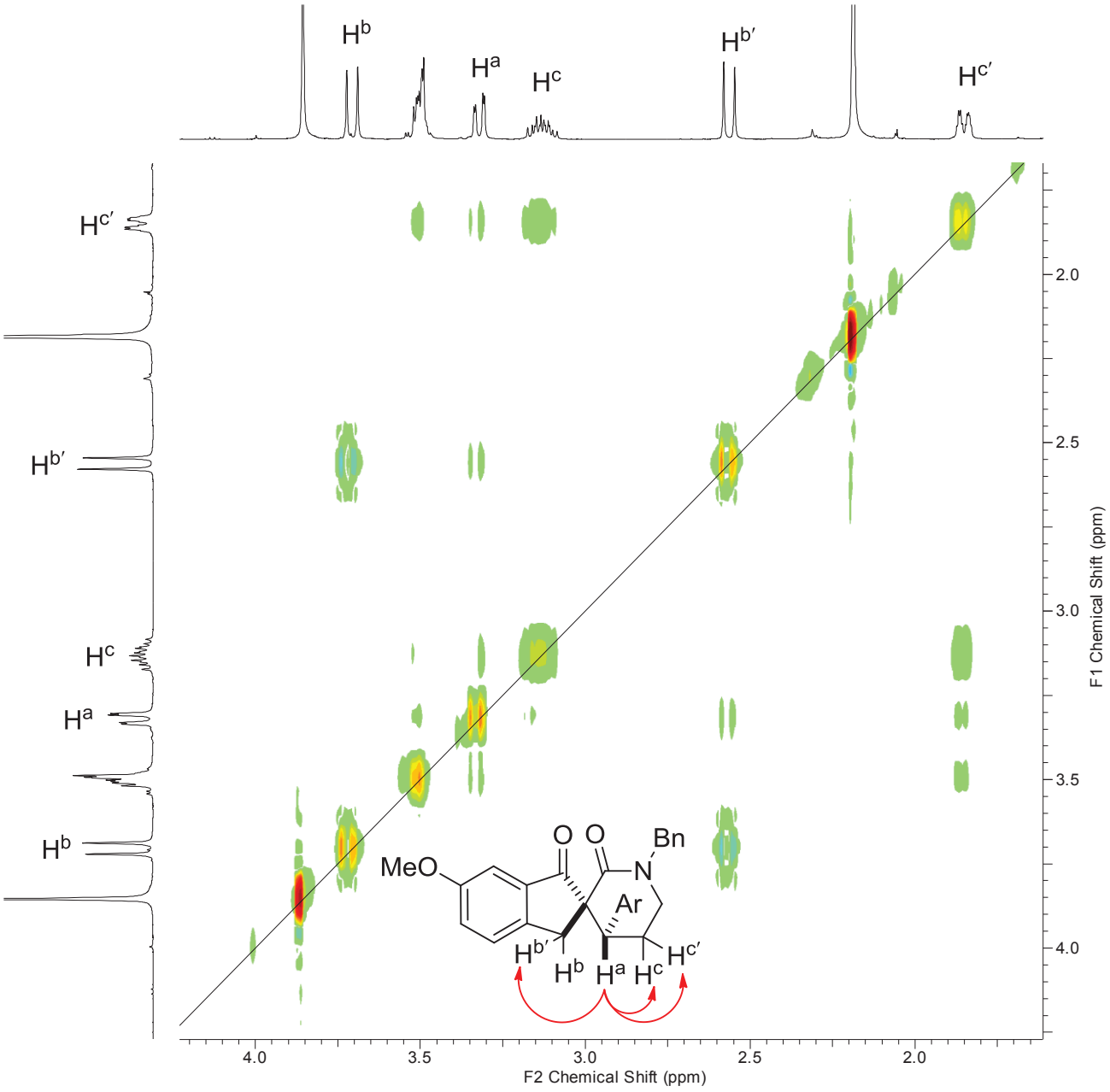
NOESY of **4b** (500 MHz, $CDCl_3$)



NOESY of **4b′** (500 MHz, $CDCl_3$)



NOESY of **4b′** (500 MHz, $CDCl_3$)



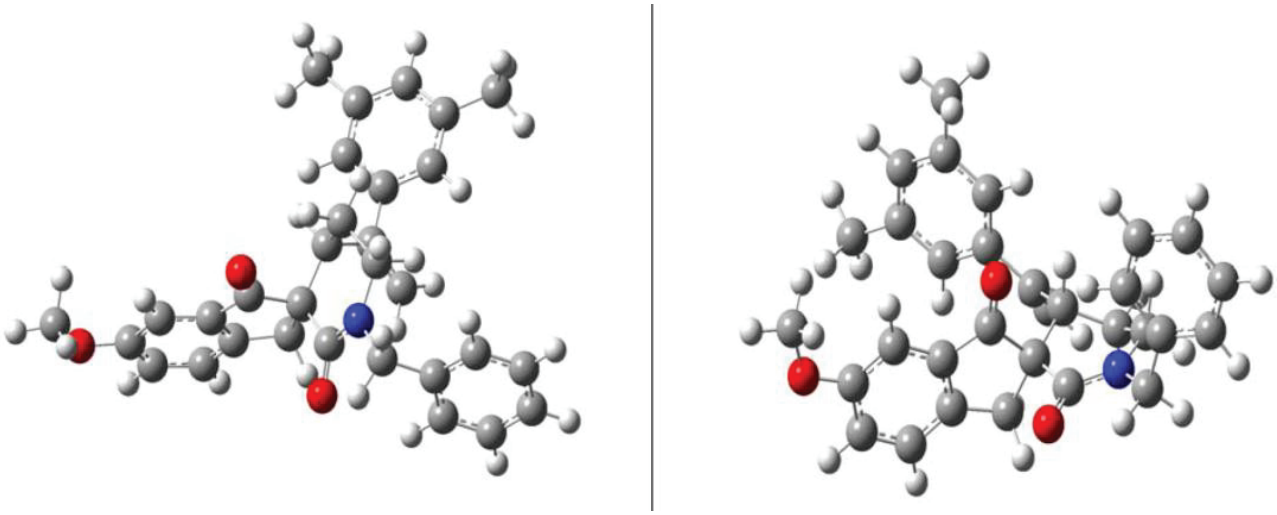
10. Determination of the Absolute Configuration of 4b using Vibrational Circular Dichroism.

Experimental Details

Infrared and VCD spectra of the compound under study was obtained using a BioTools Chiral*IR*-2X dual PEM spectrometer, as installed at the European Centre for Chriality.[1] A 0.16M solution of the sample dissolved in $CDCl_3$ was used in combination with a 100 micron liquid cell equipped with BaF_2 windows. Baseline corrections were obtained by using the spectra of a pure solvent. For the solution and the pure solvent, 60000 scans were recorded at 4 cm^{-1} resolution and averaged.

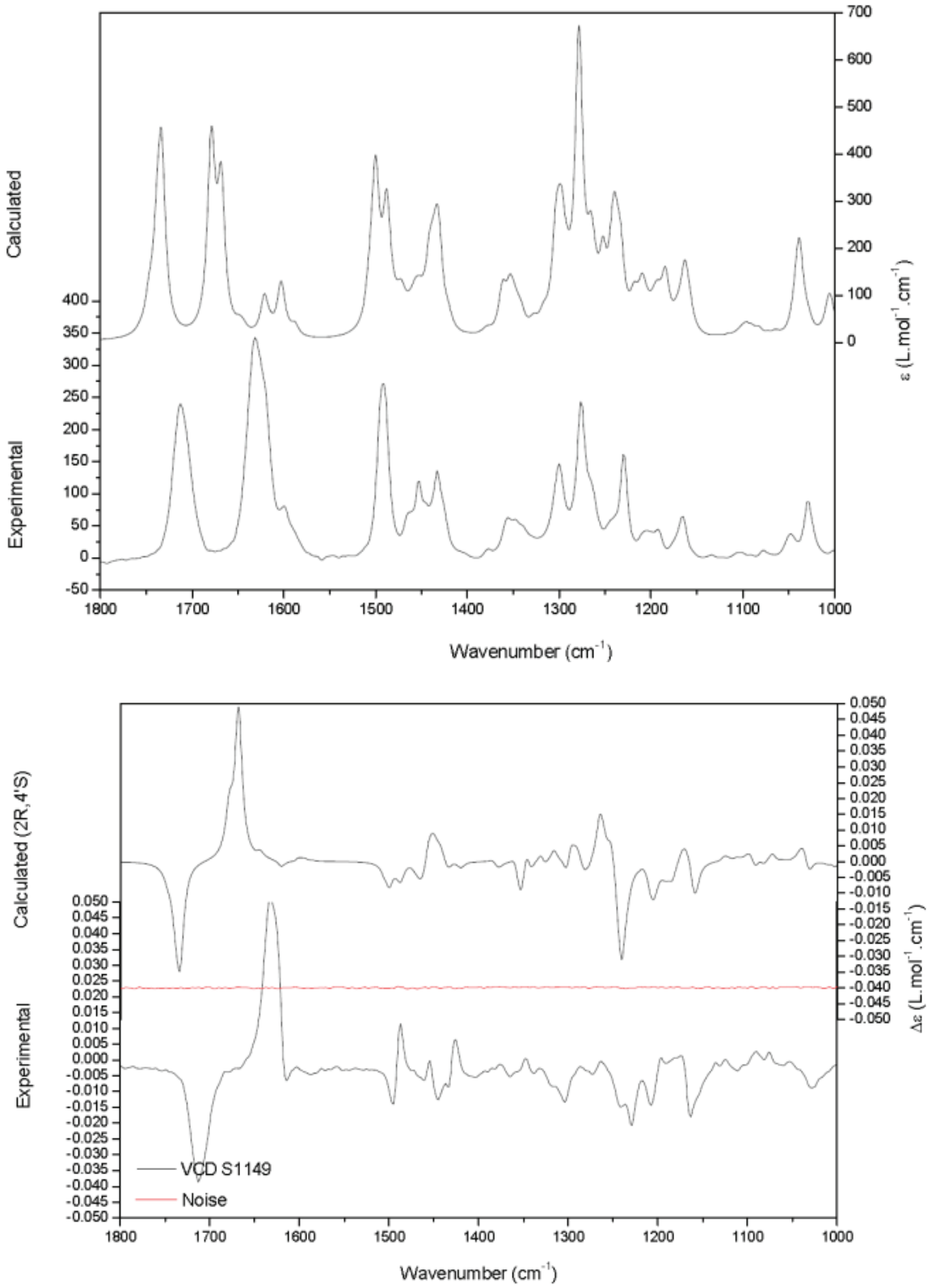
Computational details

The experimental spectra obtained were compared with predicted spectra derived for the (2*R*,4′*S*) stereoisomer. Conformational analyses were performed using the MMFF94S, MMFF and SYBYL force fields. The geometries derived from the molecular mechanics simulations were optimized at the B3LYP/6-31G*, using a SCRF model to account for solvent polarization. Gaussian09[2] was used for all DFT calculations. Boltzmann weighted IR and VCD spectra were obtained by assuming Lorentzian band profiles with a FWHH of 10 cm^{-1}. The Boltzmann populations used were based on the standard enthalpies obtained. The number of unique conformations used to calculate the Boltzmann weighted IR and VCD spectra was 31. The two most abundant conformations, with a predicted relative population of 27.5 and 12.7%, are:



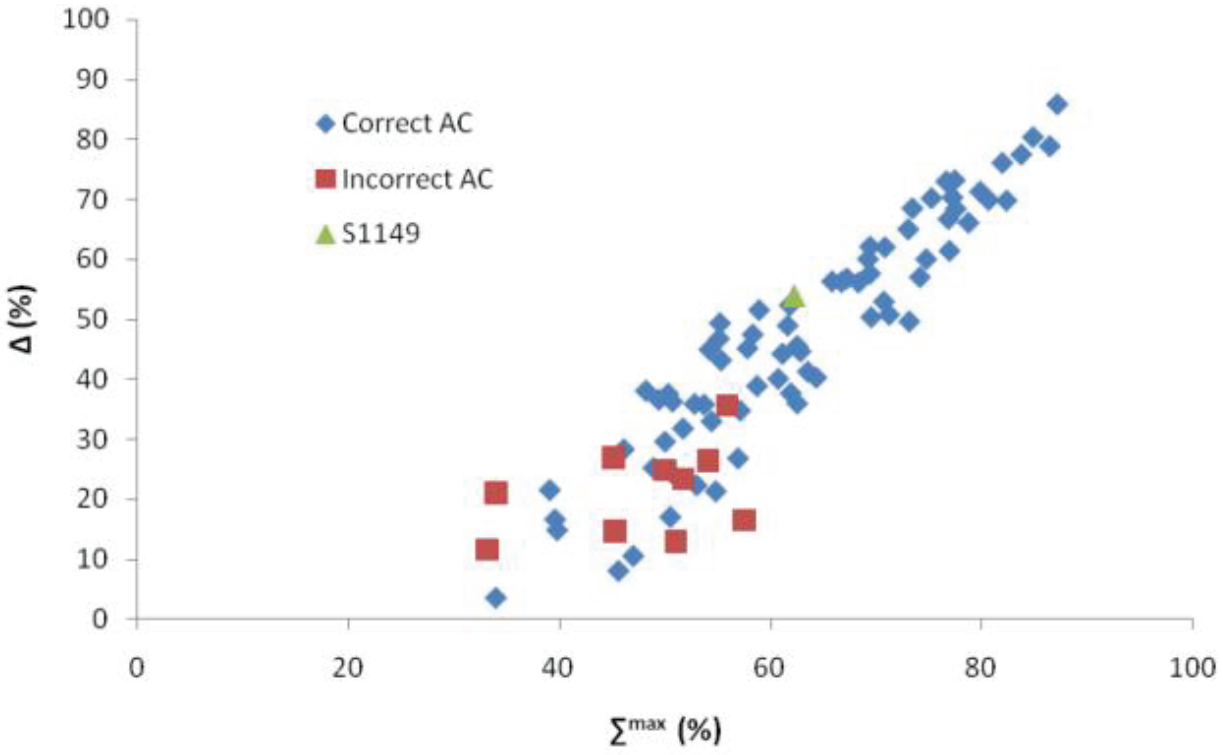
Absolute Configuration

The experimental IR and VCD spectra and the predicted spectra of the (2*R*,4′*S*) stereoisomer obtained for **4b** are shown. The calculated data, based upon a uniform scaling factor of 0.968 for the frequencies, neatly reproduces the characteristic patterns in IR and VCD. The agreement between experiment and theory confirms the proposed (2*R*,4′*S*) stereochemistry.



Numerical data confirming the assignment of the absolute configuration as (2*R*,4′*S*) was obtained using the CompareVOA algorithm as described in ref.[3] The IR similarity index, based upon a scaling factor of the calculated frequencies of 0.968, was determined to be 95.2%. The corresponding values for the VCD spectra obtained for the (2*R*,4′*S*) and (2*S*,4′*R*) diastereoisomers were 62.2% and 8.2%,

respectively, and lead to a enantiomeric similarity index Δ equal to 54%. The localization of the current assignment with respect to the database of correct and incorrect assignments supporting the compareVOA algorithm is shown below. The confidence level for the assignment is 99%.



References:

[1] European Centre for Chirality, www.chiralitycentre.eu

[2] Gaussian 09, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

[3] E. Debie, E. De Gussem, R.K. Dukor, W. Herrebout, L.A. Nafie, P. Bultinck, *ChemPhysChem* **2011**, *12*, 1542.