

SUPPORTING INFORMATION

Expedient Synthesis of Cyclopropane α -Amino Acids by the Catalytic Asymmetric Cyclopropanation of Alkenes using Iodonium Ylides Derived From Methyl Nitroacetate.

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General experimental procedures. Characterization data and ^1H and ^{13}C NMR spectra for new compounds. SFC and GC traces for enantioenriched compounds.

General: All non-aqueous reactions were run under an inert atmosphere (argon) with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.¹ All glassware was stored in the oven and/or was flamedried prior to use under an inert atmosphere of gas. Anhydrous solvents were obtained either by filtration through drying columns (THF, ether, CH₂Cl₂, benzene, DMF, CH₃CN, toluene, hexane, methanol) on a GlassContour system (Irvine, CA) or by distillation over sodium (chlorobenzene, *o*-xylene). Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel (Merck 60 F₂₅₄). Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, ethanolic phosphomolybdic acid, iodine, or aqueous potassium permanganate. Flash column chromatography was performed using 230-400 mesh silica (EM Science or Silicycle) of the indicated solvent system according to standard technique.² Melting points were obtained on a Buchi melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin Elmer Spectrum One FTIR and are reported in reciprocal centimeters (cm⁻¹). Nuclear magnetic resonance spectra (¹H, ¹³C, DEPT 135, COSY, HMQC, NOESY) were recorded either on a Bruker AV 300, AMX 300, AV 400, ARX 400, or DMX 600 spectrometer. Chemical shifts for ¹H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, $\delta = 7.27$ ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, integration, and assignment. Chemical shifts for ¹³C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuteriochloroform (δ 77.00 ppm) as the internal standard. All spectra were obtained with complete proton decoupling. When ambiguous, proton and carbon assignments were established using COSY, HMQC and DEPT experiments. Optical rotations were determined with a Perkin-Elmer 341 polarimeter at 589 or 546 nm. Data are reported as follows: $[\alpha]_{\text{temp}}$, concentration (c in g/100 mL), and solvent. High resolution mass spectra were performed by the Centre régional de spectroscopie de masse de l'Université de Montréal. Combustion analyses were performed by the Laboratoire d'analyse élémentaire de l'Université de Montréal.

The enantioselectivities of asymmetric cyclopropanation were determined using super-critical fluid chromatography (SFC) on a Berger SFC Analytical instrument equipped with a diode array UV detector. Data are reported as follows: (column type, eluent, flow rate, rate and retention time (tr)). Unless otherwise stated, oven temperature was 40 °C. For certain substrates, the enantioselectivities of asymmetric cyclopropanation were determined using analytical gas chromatography on a Hewlett-Packard 5880A gas chromatograph equipped with a splitless mode capillary injector and a flame ionization detector. Unless otherwise noted, the injector and detector temperatures were set to 250 °C and hydrogen was used as the carrier gas (63 psi).

Reagents: Unless otherwise stated, commercial reagents were used without purification. Methyl nitroacetate (**1a**), isopropylidene bis(4-phenyl-2-oxazoline) (**5**), PhI(OAc)₂, AgSbF₆, alkenes **3a-j**, are commercially available from Aldrich Chemical Company. Iodosobenzene was prepared according to known literature procedure.¹ Molecular sieves were dried in oven under reduced pressure at 120 °C for 16 hours and stored in dessicator. Copper(I) reagents, bis(oxazoline) (**5**) and AgSbF₆ were handled under argon and weighed in a glove box. Compounds **4a**, **4b**, **4e**, **4i**, **6a**, **6h** and **7a** were previously reported.^{2,3,4}

¹ Moriarty, R. M.; Bailey, B. R. III; Prakash, O.; Prakash, I. *J. Am. Chem. Soc.* **1985**, *107*, 1375-1378.

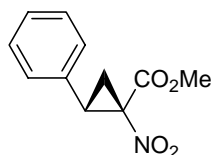
² Charette, A. B.; Wurz, R. P. *J. Mol. Cat. A* **2003**, *196*, 83-91.

³ Wurz, R. P.; Charette, A. B. *Org. Lett.* **2003**, *5*, 2327-2329.

⁴ Wurz, R. P.; Charette, A. B. *J. Org. Chem.* **2004**, *69*, 1262-1269.

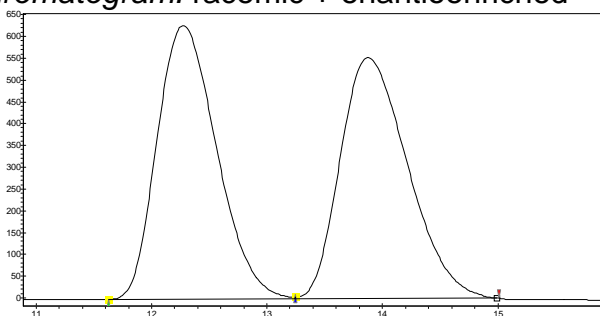
The racemic samples for SFC or GC comparison were prepared by a known literature procedure.³ The absolute stereochemistry of nitrocyclopropanecarboxylate **4a** was determined by derivatization to the known corresponding 1-amino-2-phenylcyclopropane (**7a**) and comparison with reported optical activity.⁵

General procedure for asymmetric Cu(I)-catalyzed cyclopropanation of styrene derivatives with in situ generated ylide. CuCl (1 mg, 0.01 mmol, 2 mol%), AgSbF₆ (4.1 mg, 0.012 mmol, 2.4 mol%) and bis(oxazoline) **5** (4.0 mg, 0.012 mmol, 2.4 mol%) were weighed in the glove box and charged together in a flask. After removal from glove box, the vial was covered with aluminum foil and benzene (5 mL) added. Solution was stirred for 1 hour, after which styrene **3** (2.5 mmol, 5 equiv) was added to catalyst solution. In the meanwhile, PhI=O (121 mg, 0.55 mmol, 1.1 equiv), Na₂CO₃ (122 mg, 1.15 mmol, 2.3 equiv) and molecular sieves (approx. 100 mg) were charged in a vial and purged under argon for 10 mins. Solids were quickly transferred onto catalyst solution, followed shortly by methyl nitroacetate (**1a**). Solution was stirred at room temperature for 3 hours. The reaction was quenched with water (5 mL) and extracted with ethyl acetate (2 x 10 mL). The combined organic layers was dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude oil residue was chromatographed to give the pure 1-nitrocyclopropyl carboxylate **4**, which was then submitted to SFC or GC analysis for enantioselectivity determination.

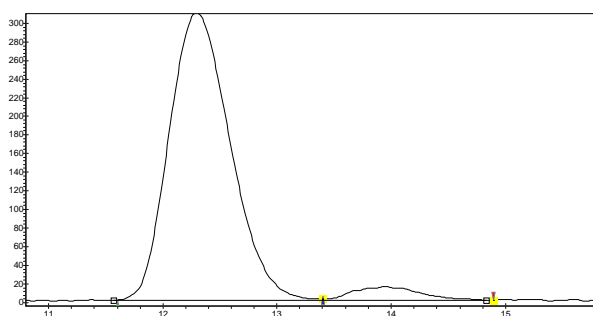


Methyl (1R, 2S)-1-nitro-2-phenylcyclopropanecarboxylate (4a). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the known pure desired cyclopropane derivative **4a** as a white solid (87 mg, 79%, 93:7 *dr*, 91.4% *ee*) mp 33-34 °C, [α]_D²⁰ -67° (c 1, CH₂Cl₂) R_f 0.30 (10% ethyl acetate in hexane) SFC (OJ Chiracel, 0.8% MeOH, 1mL/min, 200 bar) t_r 12.3 min (major enantiomer), t_r 13.9 min (minor enantiomer).

SFC chromatogram: racemic + enantioenriched

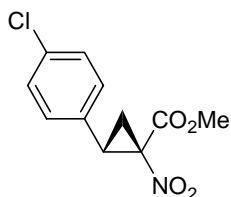


#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enantio 1	11.63	12.27	13.24	50.12	627.5	376.3	50.124
2	enantio 2	13.24	13.87	15.01	49.88	552.6	374.4	49.876
Total					100	1180	750.7	100



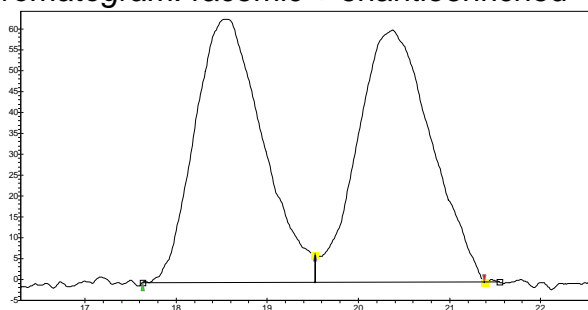
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enantio 1	11.6	12.29	13.3	95.69	307.7	189.9	95.687
2	enantio 2	13.4	13.95	14.9	4.31	13.7	8.6	4.313
Total					100	321.4	198.5	100

⁵ Csuk, R.; Schabel, M. J.; von Scholz, Y *Tetrahedron Asymmetry* **1996**, 7, 3505-3512..

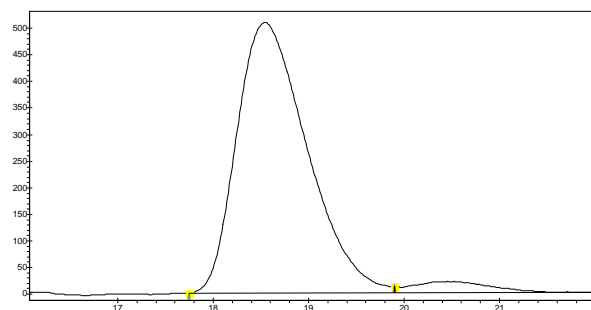


Methyl (1R, 2S)-1-nitro-2-(4-chlorophenyl)-cyclopropanecarboxylate (4b). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the known pure desired cyclopropane derivative **4b** as a clear colorless oil (58 mg, 47%, 92:8 *dr*, 91.4% *ee*) $[\alpha]_D^{20} -59^\circ$ (c 1, CH₂Cl₂) SFC (OJ Chiracel, 0.8% MeOH, 1mL/min, 130 bar) *t*_r 18.5 min (major enantiomer), *t*_r 20.5 min (minor enantiomer).

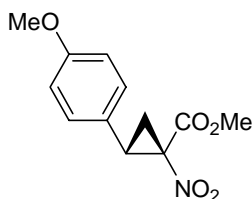
SFC chromatogram: racemic + enantioenriched



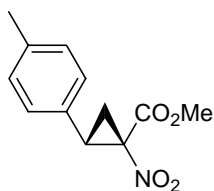
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enanto 1	17.71	18.56	19.57	49.97	66.1	60.7	49.966
2	enanto 2	19.57	20.37	21.4	50.03	62.8	60.8	50.034
Total					100	128.9	121.4	100



#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enanto 1	17.75	18.53	19.9	95.75	508.1	432.2	95.754
2	enanto 2	19.9	20.53	21.99	4.25	20.5	19.2	4.246
Total					100	528.7	451.4	100



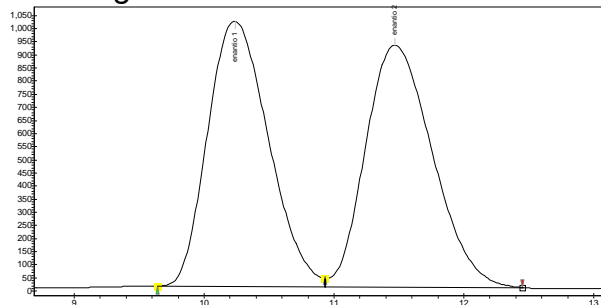
Methyl (1R, 2S)-1-nitro-2-(4-methoxyphenyl)-cyclopropanecarboxylate (4c). The general procedure for the asymmetric cyclopropanation was followed. Yield and diastereoselectivity determined on crude ¹H NMR using trichloroethylene as internal standard. Product could not be purified on silica gel (decomposition) and was submitted directly to decarboxylation conditions to afford nitrocyclopropane derivative **8c**.



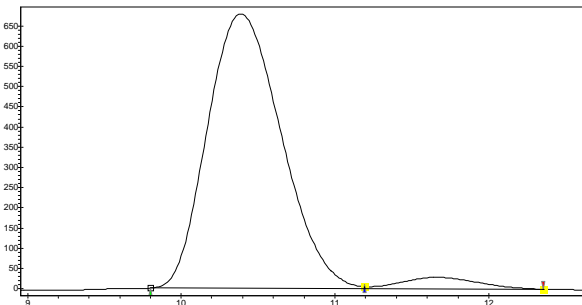
Methyl (1R, 2S)-1-nitro-2-(4-methylphenyl)-cyclopropanecarboxylate (4d). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure desired cyclopropane derivative **4d** as a clear colorless oil (92 mg, 78%, 93:7 *dr*, 91.6% *ee*) *R*_f 0.30 (10% ethyl acetate in hexane) $[\alpha]_D^{20} -34^\circ$ (c 1, CH₂Cl₂). ¹H NMR: (400 MHz, CDCl₃) δ 7.13-7.07 (m, 4H) 3.75-3.71 (dd, *J* = 10.8, 9.2 Hz, 1H) 3.53 (s, 3H) 2.45-2.41 (dd, *J* = 9.2, 6.5 Hz, 1H) δ 2.32 (s, 3H) 2.23-2.18 (dd, *J* = 10.8, 6.5 Hz, 1H) ¹³C NMR: (100 MHz, CDCl₃) δ 162.4, 138.0, 129.1 (2C), 128.8, 128.0 (2C), 71.6, 53.0, 34.0, 21.0, 20.9 IR (neat) 1747 (C=O), 1543, 1438, 1347 (NO₂), 1218, 1146 cm⁻¹. LRMS (APCI, Pos) calcd for

$C_{12}H_{13}O_4N_1$ $[M+H]^+$: 236.2 m/z , found 236.2 m/z SFC (OJ Chiracel, 0.8% MeOH, 1 mL/min, 200 bar) t_r 10.4 min (major enantiomer), t_r 11.6 min (minor enantiomer).

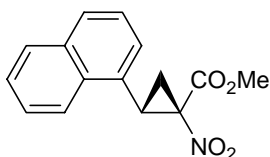
SFC chromatogram: racemic + enantioenriched



#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	enantiomer 1	9.64	10.24	10.93	49.93	1010.8	549.3	49.934
2	enantiomer 2	10.93	11.47	12.45	50.07	921.7	550.8	50.066
Total					100	1932.5	1100.1	100

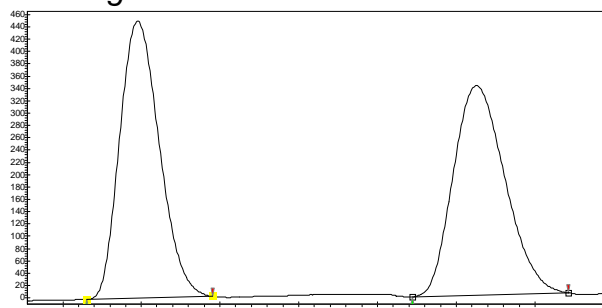


#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	enantiomer 1	9.8	10.39	11.19	95.8	678.5	378.6	95.801
2	enantiomer 2	11.19	11.65	12.36	4.2	28.9	16.6	4.199
Total					100	707.4	395.2	100

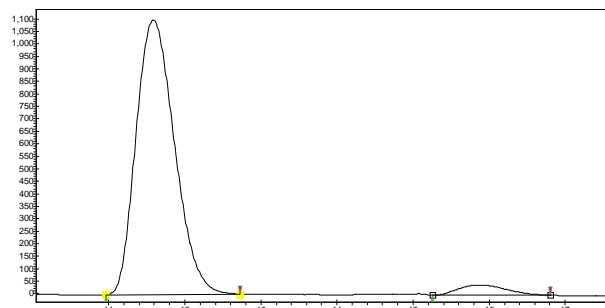


Methyl (1R, 2S)-2-(1-naphthyl)-1-nitrocyclopropanecarboxylate (4e). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the known^x pure desired cyclopropane derivative **4e** as a white crystalline solid (72 mg, 53%, 93:7 *dr*, 91.4% *ee*) $[\alpha]_D^{20} +126^\circ$ (c 1, CH_2Cl_2) SFC (OJ Chiracel, 1.5% MeOH, 1.5 mL/min, 200 bar) t_r 11.6 min (major enantiomer), t_r 15.9 min (minor enantiomer).

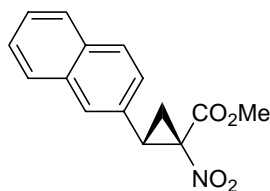
SFC chromatogram: racemic + enantioenriched



#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	enantiomer 1	11.31	11.95	12.91	50.3	449.9	263.1	50.3
2	enantiomer 2	15.44	16.25	17.43	49.7	340.5	260	49.7
Total					100	790.4	523.1	100



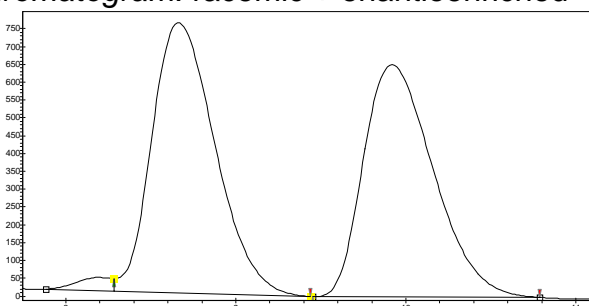
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	enantiomer 1	10.96	11.59	12.73	95.72	1099.1	642.5	95.715
2	enantiomer 2	15.26	15.89	16.8	4.28	39.8	28.8	4.285
Total					100	1138.8	671.2	100



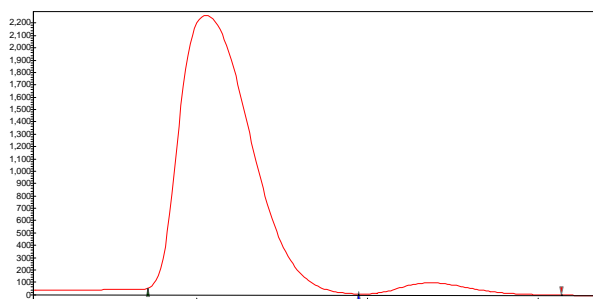
Methyl (1R, 2S)-1-nitro-2-(2-naphthyl)-cyclopropanecarboxylate (4f). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure desired cyclopropane derivative **4f** as a white crystalline solid (100 mg, 74%, 91:9 *dr*, 91% *ee*) R_f 0.33 (10% ethyl acetate in hexane) $[\alpha]_D^{20} -132^\circ$ (c 1.25,

CH₂Cl₂) ¹H NMR: (400 MHz, CDCl₃) δ 7.84-7.79 (m, 3H) 7.65 (s, 1H) 7.51-7.49 (m, 2H) 7.35-7.32 (dd, *J* = 8.5, 1.9 Hz, 1H) 3.95-3.91 (dd, *J* = 10.7, 9.2 Hz, 1H) 3.46 (s, 3H) 2.62-2.58 (dd, *J* = 9.2, 6.6 Hz, 1H) 2.34-2.30 (dd, *J* = 10.7, 6.6 Hz, 1H) ¹³C NMR: (100 MHz, CDCl₃) δ 162.1, 132.6, 129.1, 128.0, 127.5, 127.3, 127.0, 126.2, 126.1, 125.7, 71.4, 52.9, 34.1, 20.7 IR (neat) 1740 (C=O), 1545, 1439, 1349 (NO₂), 1212, 1144 cm⁻¹. LRMS (APCI, Pos) calcd for C₁₅H₁₃O₄N₁ [M+H]⁺: 272.2 *m/z*, found 272.2 *m/z* SFC (OJ Chiracel, 3% MeOH, 2 mL/min, 200 bar) *t*_r 8.1 min (major enantiomer), *t*_r 9.4 min (minor enantiomer). Also, SFC (OJ Chiracel, 2% MeOH, 2 mL/min, 200 bar) *t*_r 11.8 min (major enantiomer), *t*_r 13.9 min (minor enantiomer).

SFC chromatogram: racemic + enantioenriched

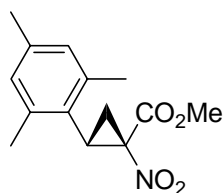
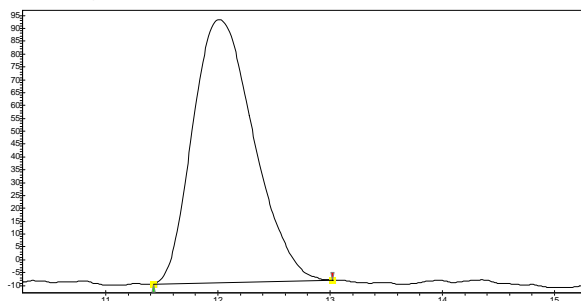


#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enanti 1	8.28	8.67	9.44	51.3	757.5	327.3	51.299
2	enanti 2	9.45	9.92	10.79	48.7	650.6	310.7	48.701
Total					100	1408.1	638	100



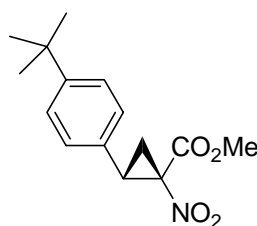
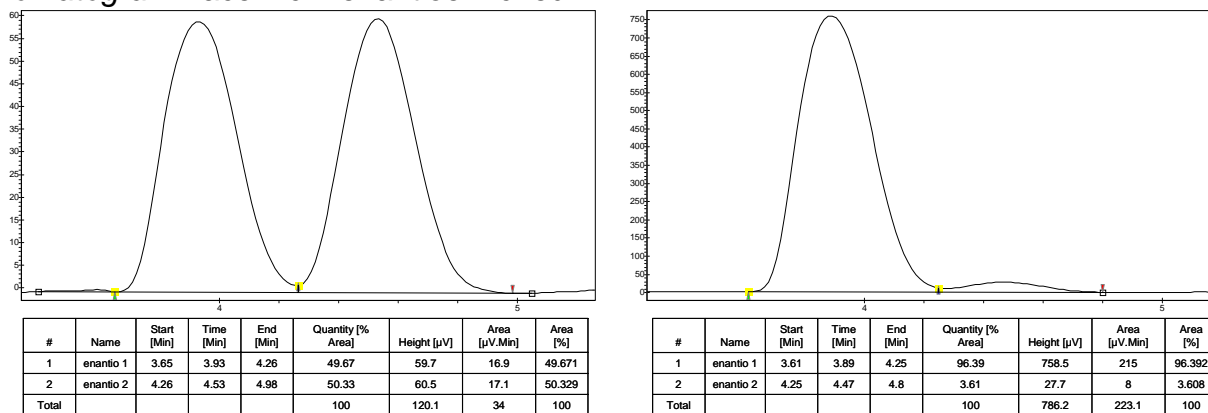
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enanti 1	7.71	8.05	8.95	95.6	2267.3	1097.8	95.598
2	enanti 2	8.95	9.37	10.13	4.4	99.6	50.5	4.402
Total					100	2366.9	1148.4	100

SFC chromatogram: recrystallized



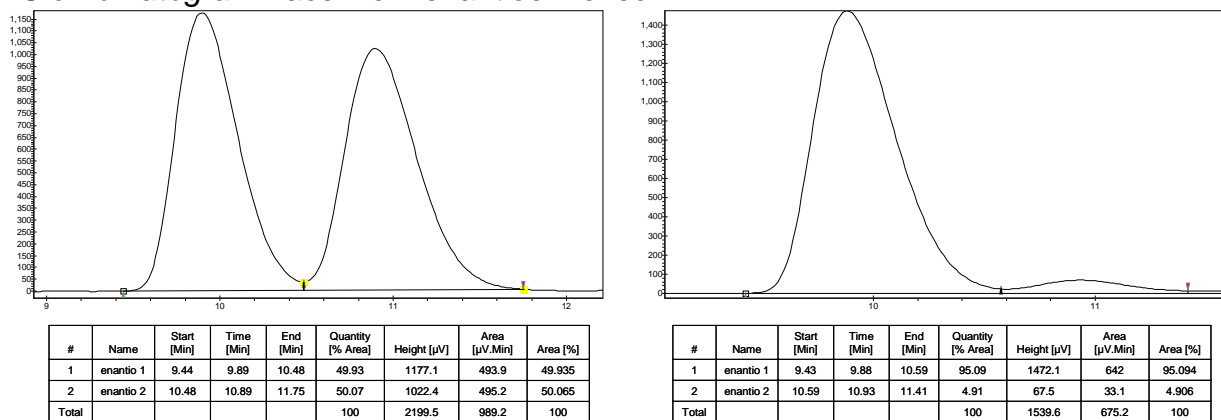
Methyl (1*R*, 2*S*)-1-nitro-2-mesitylcyclopropanecarboxylate (4g). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure desired cyclopropane derivative **4g** as a colorless oil (72 mg, 54%, >95:5 *dr*, 92.8% *ee*) *R*_f 0.33 (10% ethyl acetate in hexane) [α]_D²⁰ -109.5° (c 1, CH₂Cl₂) ¹H NMR: (400 MHz, CDCl₃) δ 6.81 (s, 2H) 3.55-3.52 (m, 4H) 2.58-2.53 (dd, *J* = 9.9, 6.4 Hz, 1H) 2.44-2.39 (dd, *J* = 11.1, 6.4 Hz, 1H) 2.31 (s, 6H) 2.24 (s, 3H) ¹³C NMR: (100 MHz, CDCl₃) δ 163.6, 137.2, 129.2 (2C), 125.8, 71.1, 53.0, 33.0, 25.1 (2C), 20.7, 20.3 IR (neat) 1744 (C=O), 1542, 1437, 1343 (NO₂), 1226, 1144 cm⁻¹. LRMS (APCI, Pos) calcd for C₁₄H₁₆O₄N₁ [M+H]⁺: 264.3 *m/z*, found 264.2 *m/z* SFC (OJ Chiracel, 1.5% MeOH, 1.5 mL/min, 200 bar) *t*_r 3.9 min (major enantiomer), *t*_r 4.5 min (minor enantiomer).

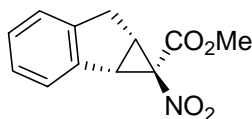
SFC chromatogram: racemic + enantioenriched



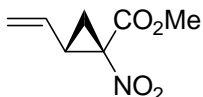
Methyl (1R, 2S)-1-nitro-2-(4-*tert*-butylphenyl)-cyclopropanecarboxylate (4h). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure desired cyclopropane derivative **4h** as a colorless oil (111 mg, 80%, 93:7 *dr*, 90% *ee*) R_f 0.33 (10% ethyl acetate in hexane) $[\alpha]_D^{20}$ -65.5° (c 1, CH_2Cl_2) ^1H NMR: (400 MHz, CDCl_3) δ 7.34-7.31 (d, $J = 8.2$ Hz, 2H), 7.13-7.11 (d, $J = 8.2$ Hz, 2H), 3.76-3.72 (dd, $J = 10.7, 9.2$ Hz, 1H), 3.50 (s, 3H), 2.46-2.42 (dd, $J = 9.2, 6.5$ Hz, 1H), 2.24-2.19 (dd, $J = 10.7, 6.5$ Hz, 1H), 1.29 (s, 9H) ^{13}C NMR: (100 MHz, CDCl_3) δ 162.2, 151.0, 128.6, 127.7 (2C), 125.1 (2C), 71.3, 52.7, 34.2, 33.7, 30.9 (3C), 20.7 IR (neat) 1745 (C=O), 1543, 1438, 1345 (NO_2), 1217 1146 cm^{-1} . LRMS (APCI, Pos) calcd for $\text{C}_{15}\text{H}_{19}\text{O}_4\text{N}_1$ $[\text{M}+\text{H}]^+$: 278.2 m/z , found 278.2 m/z SFC (OJ Chiracel, 0.8% MeOH, 1 mL/min, 200 bar) t_r 9.9 min (major enantiomer), t_r 10.9 min (minor enantiomer).

SFC chromatogram: racemic + enantioenriched



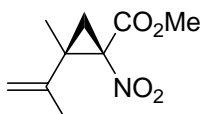
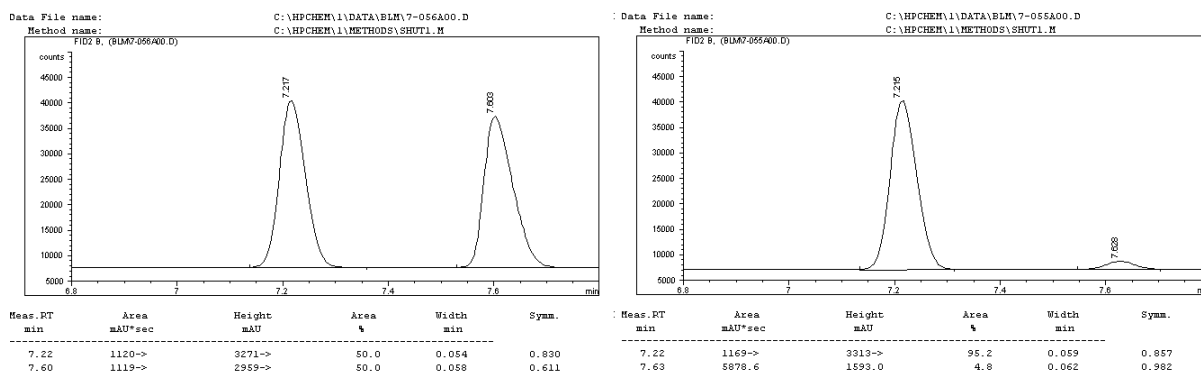


Methyl (1R, 1aS, 6aS)-1-nitro-1, 1a, 6, 6a-tetrahydrocyclopropana[a]indene-1-carboxylate (4i). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure known desired cyclopropane derivative **4i** as a white crystalline solid (84 mg, 72%, >95:5 *dr*) $[\alpha]_D^{20}$ -198° (c 1, CH₂Cl₂). Enantiomeric excess (97.5% *ee*) were determined from the aminocyclopropanecarboxylate derivative **6i**.



Methyl (1R, 2S)-1-nitro-2-vinylcyclopropanecarboxylate (4j). The general procedure for the asymmetric cyclopropanation was followed, except 1,3-butadiene(**3j**) was condensed in a flask at 0 °C and then dissolved in benzene prior to addition onto catalyst. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure desired cyclopropane derivative **4j** as a colorless oil (72 mg, 84%, 82:18 *dr*, 90% *ee*) R_f 0.36 (10% ethyl acetate in hexane) $[\alpha]_D^{20}$ $+12^\circ$ (c 1, CH₂Cl₂) ¹H NMR: (400 MHz, CDCl₃) δ 5.55-5.45 (ddd, $J = 17.2, 10, 7.6$ Hz, 1H), 5.39-5.34 (ddd, $J = 17.2, 1.3, 0.6$ Hz, 1H), 5.28-5.25 (ddd, $J = 10, 1.3, 0.7$ Hz, 1H), 3.85 (s, 3H), 3.12-3.05 (dddd, $J = 10.4, 8.9, 7.6, 0.7, 0.7$ Hz, 1H) 2.08-2.04 (dd, $J = 10.4, 6.5$ Hz), 2.01-1.98 (dd, $J = 8.9, 6.5$ Hz, 1H) ¹³C NMR: (100 MHz, CDCl₃) δ 162.9, 129.7, 120.4, 70.6, 53.2, 32.5, 21.7 IR (neat) 1744 (C=O), 1543, 1439, 1349 (NO₂), 1214, 1146 cm⁻¹. HRMS (EI) calcd for C₇H₉O₄N₁Na₁ [M+Na]⁺: 194.04237 *m/z*, found 194.0426 *m/z* GC (gamma dex 120-125 °C, 0.5 °C/min) t_r 7.21 min (major enantiomer), t_r 7.63 min (minor enantiomer).

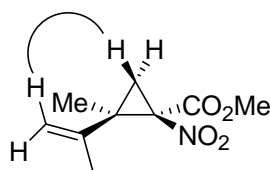
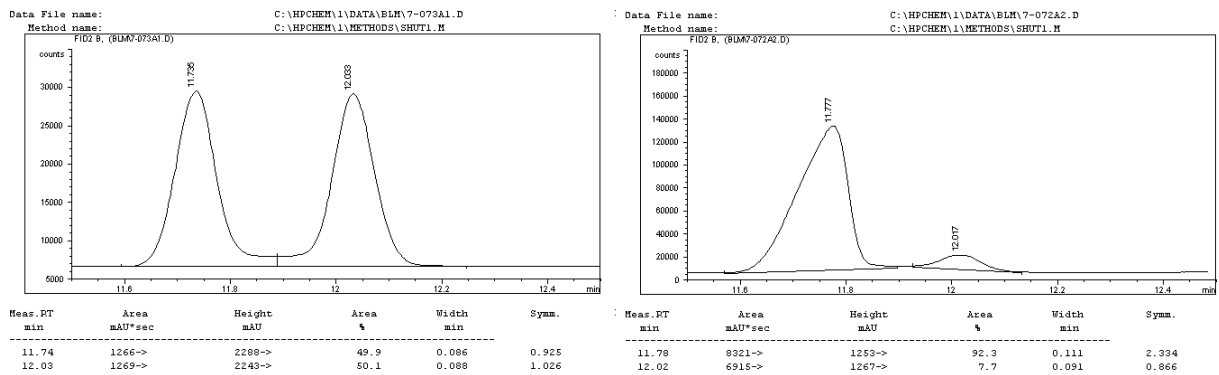
GC chromatogram: racemic + enantioenriched



Methyl (1R, 2R)-2-isopropenyl-2-methyl-1-nitrocyclopropanecarboxylate (4k). The general procedure for the asymmetric cyclopropanation was followed. The crude mixture was purified on silica gel (10% AcOEt/hexane) to afford the pure desired cyclopropane derivative **4k** as a colorless oil (54 mg, 54%, >95:5 *dr*, 85% *ee*) R_f 0.33 (10% ethyl acetate in hexane) $[\alpha]_D^{20}$ -99.5° (c 1, CH₂Cl₂) ¹H NMR: (400 MHz, CDCl₃) δ 4.98 (s, 1H), 4.74 (s, 1H), 3.76 (s, 3H), 2.14-2.12 (d, $J = 6.7$ Hz, 1H), 1.99-1.96 (d, $J = 6.7$ Hz, 1H), 1.76 (s, 3H), 1.33 (s, 3H) ¹³C NMR: (100 MHz, CDCl₃)

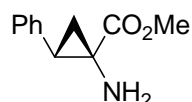
δ 164.8, 142.5, 115.1, 75.9, 53.8, 40.9, 27.8, 21.8, 20.4 IR (neat) 1744 (C=O), 1545, 1438, 1360 (NO₂), 1312, 1241, 1124 cm⁻¹. LRMS (APCI, Pos) calcd for C₉H₁₃O₄N₁ [M+H]⁺: 200.2 *m/z*, found 200.2 *m/z* GC (gamma dex, 120-130 °C, 0.5 °C/min) *t_r* 11.43 (major enantiomer), *t_r* 11.73 (minor enantiomer).

GC chromatogram: racemic + enantioenriched

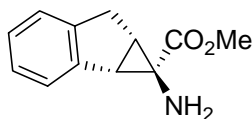


nOe experiment

General procedure for Zn-mediated reduction of nitro into amine. To 1-nitrocyclopropane **4** or **8** (1 mmol) in iPrOH (20 mL) was added 1N aqueous HCl (10 mL, 10 mmol), followed by Zn dust (1.31 g, 20 mmoles). Solution was stirred at room temperature for two hours. Reaction was quenched by addition of NaHCO₃ (sat. sln). Solution was stirred vigorously for 20 mins and then filtered on celite. Organic layer was extracted with CH₂Cl₂ (3X), combined layers were dried on Na₂SO₄, filtered and evaporated. Oil residue was chromatographed with 20% ethyl acetate in hexanes to afford respectively the pure amine **6** or **7**, which was then submitted to SFC analysis for enantioselectivity determination.



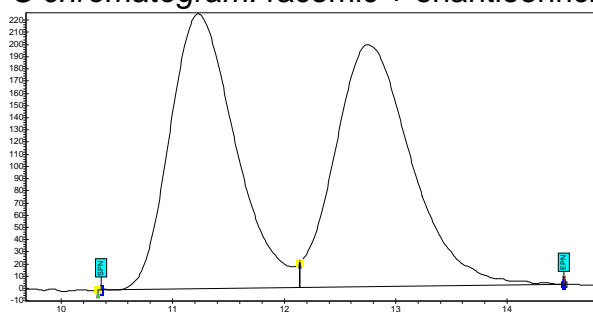
Methyl (1*R*, 2*S*)-1-amino-2-phenylcyclopropanecarboxylate (6a). The general procedure for the Zn-mediated reduction of nitro into amine was followed. Starting with **4a** (110 mg, 0.5 mmol), the crude mixture was purified on silica gel (20% AcOEt/hexane) to afford the known pure desired cyclopropane derivative **6a** as a white solid (85 mg, 89%) [α]_D²⁰ -73° (c 1.5, CH₂Cl₂).



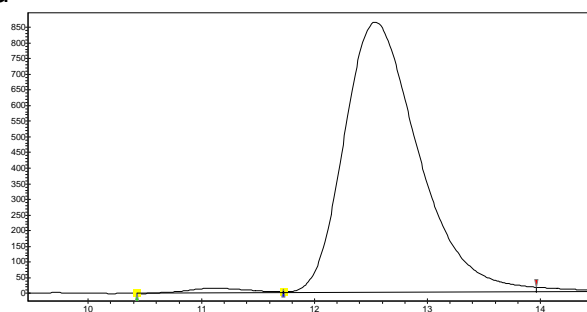
Methyl (1*R*, 1*aS*, 6*aS*)-1-amino-1, 1*a*, 6, 6*a*-tetrahydrocyclopropana[*a*]indene-1-carboxylate (6i). (66 mg, 76%, 97.5% ee). The general procedure for the Zn-mediated reduction of nitro into amine was followed. Oil residue was chromatographed with 20% ethyl acetate in hexanes to afford the pure product as an yellowish oil. *R_f* 0.20 (20% ethyl acetate in hexane) [α]_D²⁰ -242° (c 1,

CH₂Cl₂) ¹H NMR: (400 MHz, CDCl₃) δ 7.29-7.27 (dd, J = 4.3, 1.7 Hz, 1H), 7.12-7.11 (m, 3H), 3.35 (s, 3H), 3.34-3.30 (dd, J = 17.3, 0.9 Hz, 1H), 3.25-3.19 (dd, J = 17.3, 6.9 Hz, 1H), 2.90-2.88 (d, J = 6.8 Hz, 1H), 2.30-2.26 (ddd, J = 6.9, 6.8, 0.9 Hz, 1H), 2.20-1.85 (b, 2H) ¹³C NMR: (100 MHz, CDCl₃) δ 171.4, 144.8, 139.4, 126.1, 125.7, 124.3, 123.5, 51.1, 44.1, 41.6, 33.0, 32.8 IR (neat) 3375 (N-H) 1725 (C=O), 1305, 1130 cm⁻¹. LRMS (APCI, Pos) calcd for C₁₂H₁₃O₂N₁ [M+H]⁺: 204.2 *m/z*, found 204.2 *m/z* SFC (OJ Chiracel, 4% MeOH, 0.8 mL/min, 150 bar) *t*_r 12.6 min (major enantiomer), *t*_r 11.2 min (minor enantiomer).

SFC chromatogram: racemic + enantioenriched

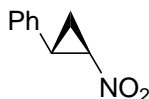


#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enantio 1	10.33	11.23	12.14	49.31	225.6	153.3	49.314
2	enantio 2	12.14	12.75	14.51	50.69	198.6	157.5	50.686
Total					100	424.2	310.8	100



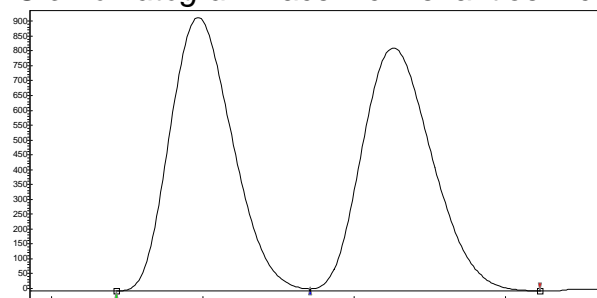
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	enantio 1	10.58	11.16	11.73	1.26	14.8	8.2	1.26
2	enantio 2	11.82	12.57	14.25	98.74	850.4	645.7	98.74
Total					100	865.1	653.9	100

General procedure for decarboxylation of nitro esters 4. 1-nitrocyclopropane carboxylate **4** (1 mmol) was treated with DMSO (5 mL) and NaOH (40 mg, 1 mmol, 1 equiv) dissolved in water (1.6 mL) and stirred at 80 °C for 2 hours. Reaction was quenched with NH₄Cl and aqueous phase was extracted with Et₂O, washed with H₂O, brine and dried over Na₂SO₄. Filtration and solvent removal afforded the crude compound which was chromatographed in 5% AcOEt/hexane to afford the pure 1-nitrocyclopropane **8**, which was then submitted to SFC analysis for enantioselectivity determination.

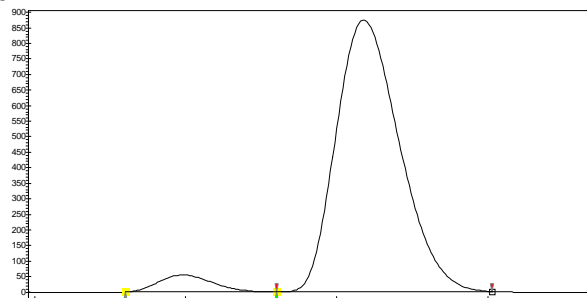


[(1S, 2R)-2-nitrocyclopropyl]benzene (8a). The general procedure for the decarboxylation of nitro esters **4** was followed. Starting from (1*R*,2*S*)-Methyl *E*-1-nitro-2-phenylcyclopropane carboxylate **4a** (90% *ee*). The crude mixture was purified on silica gel (5% AcOEt/hexane) to afford the pure desired cyclopropane derivative **8a** as a colorless oil (129 mg, 79%, 94:6 *dr*, 90% *ee*) *R*_f 0.37 (5% ethyl acetate in hexane) [α]_D²⁰, -312° (*c* 1, CH₂Cl₂) ¹H NMR: (300 MHz, CDCl₃) δ 7.36-7.27 (m, 3H), 7.14-7.12 (m, 2H), 4.44-4.40 (ddd, *J* = 7.2, 3.9, 3.1 Hz, 1H), 3.17-3.11 (ddd, *J* = 10.6, 7.9, 3.1 Hz, 1H), 2.28-2.22 (ddd, *J* = 10.6, 6.3, 3.9 Hz, 1H), 1.71-1.66 (ddd, *J* = 7.9, 7.2, 6.3 Hz, 1H) ¹³C NMR: (75 MHz, CDCl₃) δ 136.8, 129.3(2C), 128.2, 127.1(2C), 62.1, 29.9, 19.2 IR (neat) 1540, 1499, 1362 (NO₂) cm⁻¹. HRMS (EI) calcd for C₉H₁₀O₂N₁ [M+H]⁺: 164.07060 *m/z*, found 164.06997 *m/z* SFC (OJ Chiracel, 1% MeOH, 1 mL/min, 200 bar) *t*_r 11.17 min (major enantiomer), *t*_r 10.0 min (minor enantiomer).

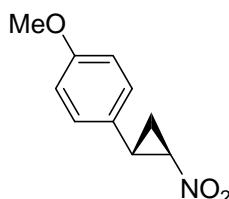
SFC chromatogram: racemic + enantioenriched



#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	enantio 1	9.43	9.97	10.71	50	920.7	441.2	50
2	enantio 2	10.71	11.25	12.23	50	818.5	441.2	50
Total					100	1739.2	882.4	100

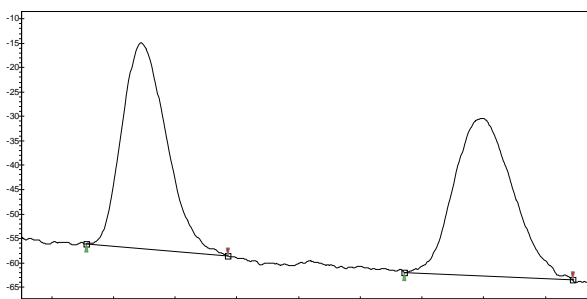


#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	enantio 1	9.6	9.99	10.6	5.08	54.7	22.8	5.076
2	enantio 2	10.6	11.17	12.03	94.92	874.6	426.1	94.924
Total					100	929.3	448.9	100

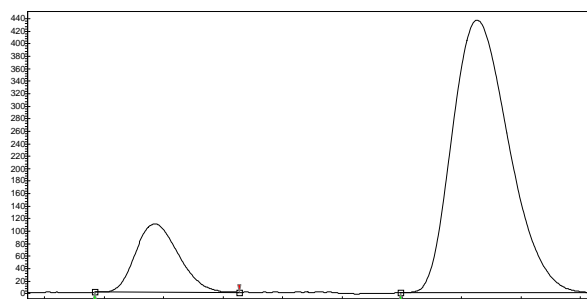


1-methoxy-4-[(1S, 2R)-2-nitrocyclopropyl]benzene (8c). The crude mixture of **4c** (71% yield by internal standard, 92:8 *dr*) was submitted to the general decarboxylation of nitro esters **4** procedure. The crude mixture was then chromatographed (5% AcOEt/hexane) to afford the pure desired cyclopropane derivative **7c** as a colorless oil (44 mg, 76%, >95:5 *dr*, 68% *ee*) R_f 0.37 (5% ethyl acetate in hexane) $[\alpha]_D^{20}$, -146° (c 0.85, CH_2Cl_2) ^1H NMR: (400 MHz, CDCl_3) δ 7.08-7.04 (d, J = 8.6 Hz, 2H), 6.88-6.84 (d, J = 8.6 Hz, 2H), 4.36-4.33 (ddd, J = 7.2, 3.9, 2.9 Hz, 1H), 3.80 (s, 3H), 3.13-3.07 (ddd, J = 10.6, 7.9, 2.9 Hz, 1H), 2.24-2.19 (ddd, J = 10.6, 6.3, 3.9 Hz, 1H), 1.67-1.61 (ddd, J = 7.9, 7.2, 6.3 Hz, 1H) ^{13}C NMR: (100 MHz, CDCl_3) δ 159.0, 128.1, 127.8 (2C), 114.1 (2C), 61.5, 55.2, 28.9, 18.5 IR (neat) 1539, 1516, 1363 (NO_2), 1249, 1179 cm^{-1} . HRMS (EI) calcd for $\text{C}_9\text{H}_{10}\text{O}_2\text{N}_1$ $[\text{M}+\text{H}]^+$: 194.08116 m/z , found 194.08127 m/z SFC (OJ Chiracel, 1% MeOH, 1 mL/min, 200 bar) t_r 24.2 min (major enantiomer), t_r 18.9 min (minor enantiomer).

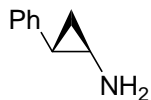
SFC chromatogram: racemic + enantioenriched



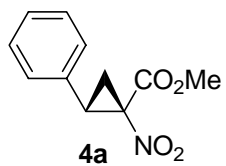
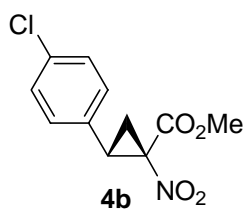
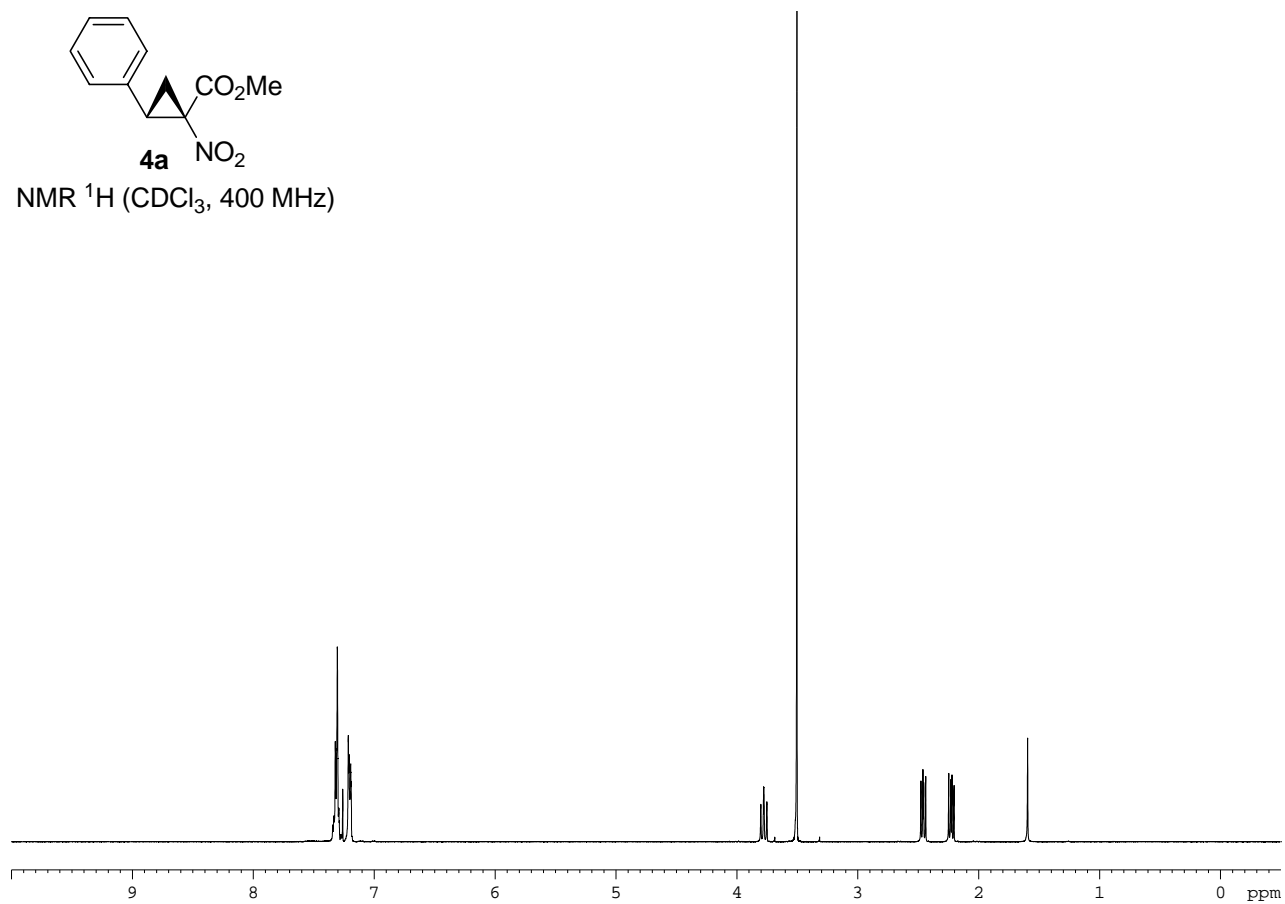
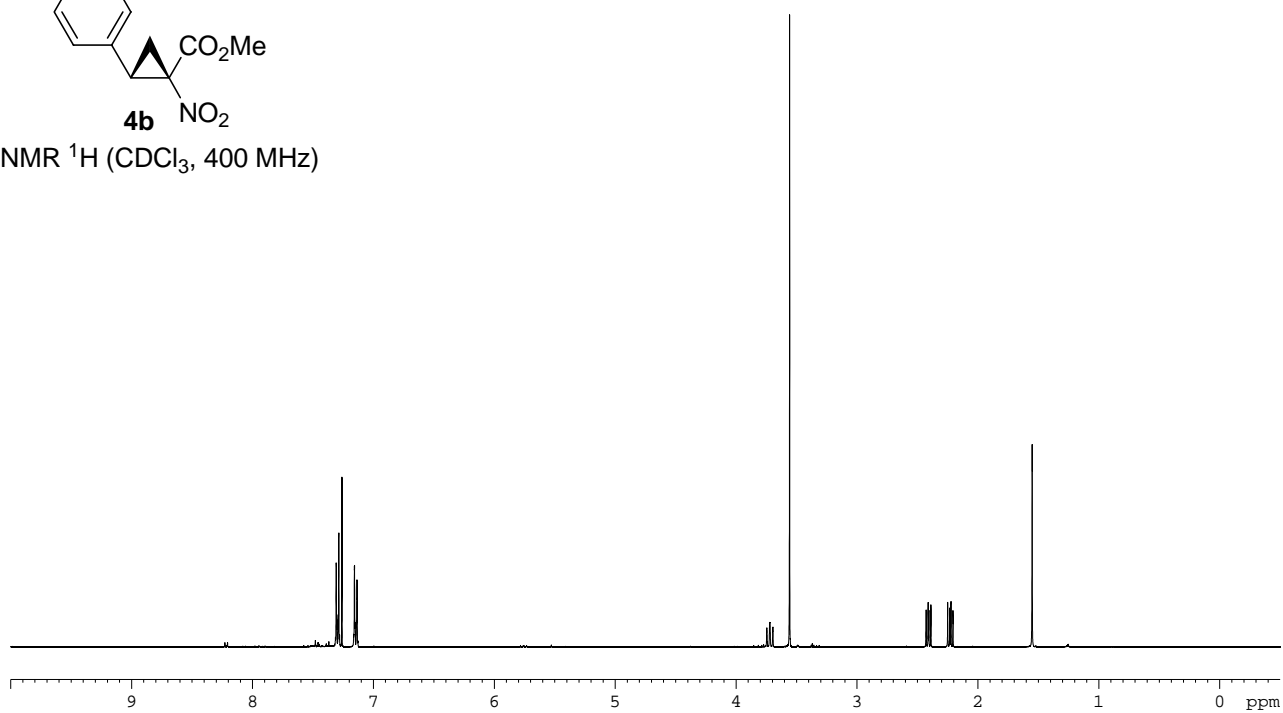
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	enantio 1	17.57	18.45	19.85	49.61	42.1	35.3	49.606
2	enantio 2	22.72	23.99	25.44	50.39	32.4	35.9	50.394
Total					100	74.5	71.2	100

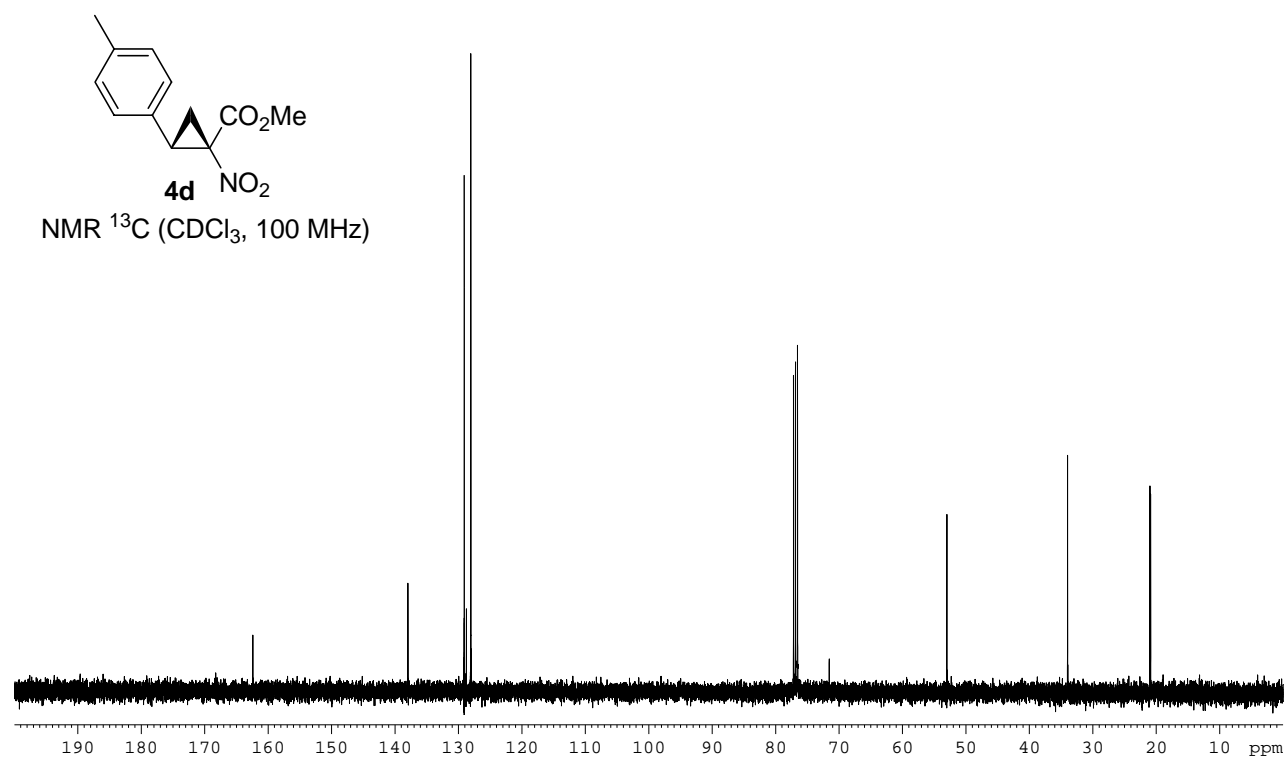
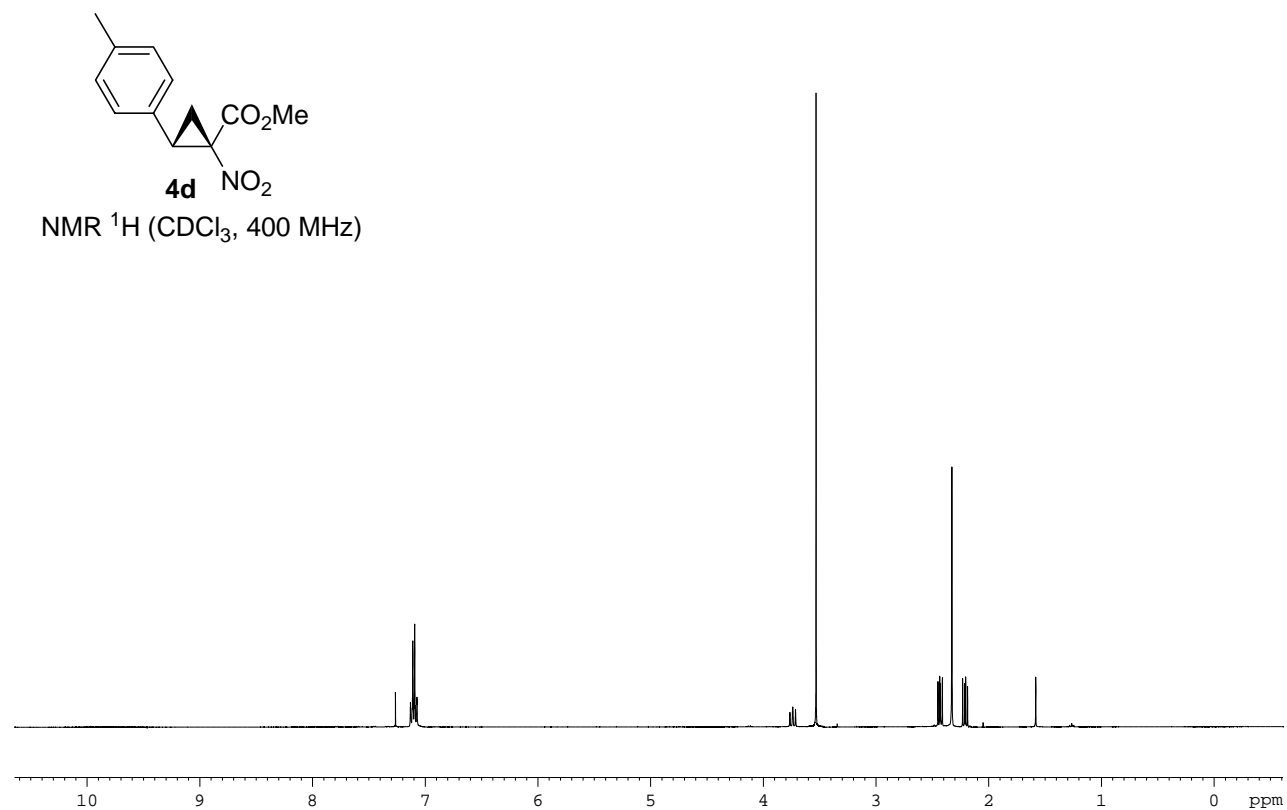


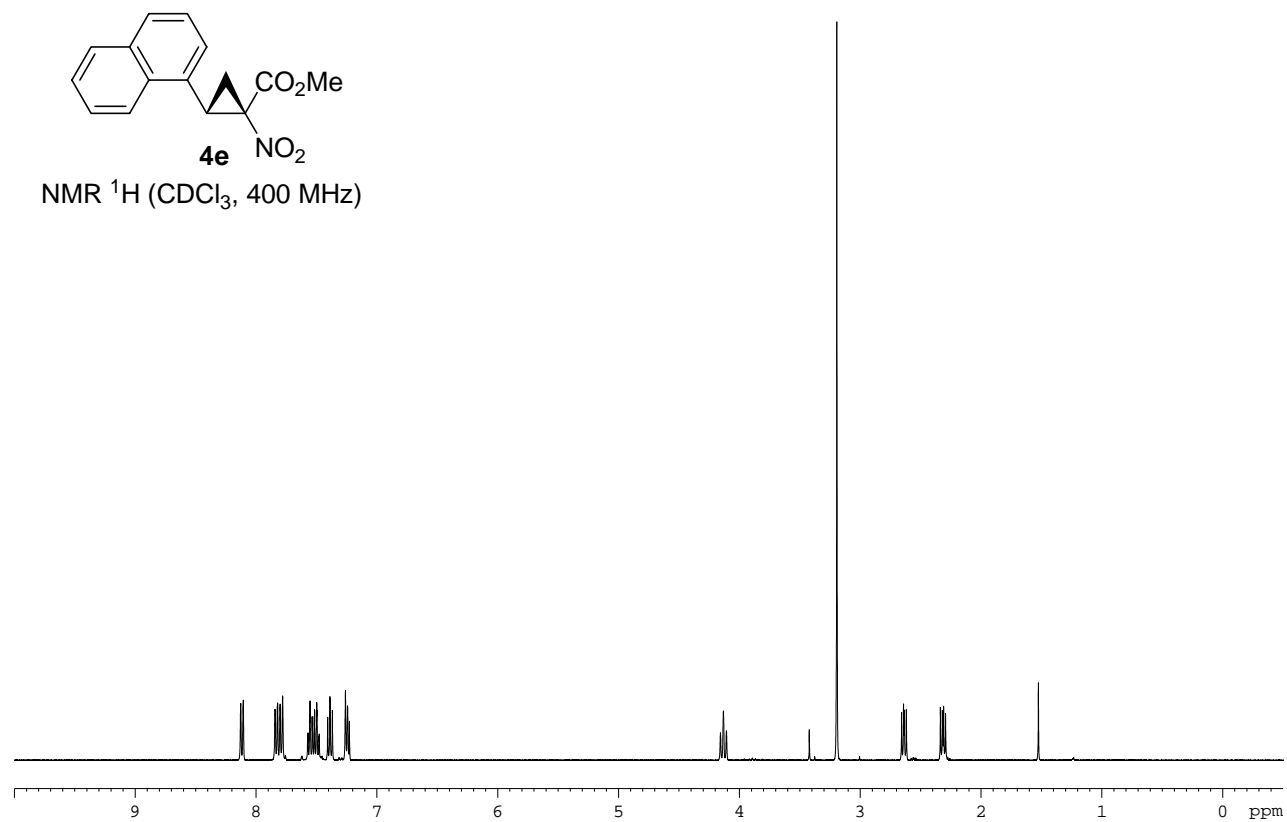
#	Name	Start [Min]	Time [Min]	End [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	enantio 1	17.85	18.87	20.26	16.13	109.6	92.1	16.128
2	enantio 2	22.98	24.25	26.26	83.87	436.4	478.8	83.872
Total					100	546	570.9	100

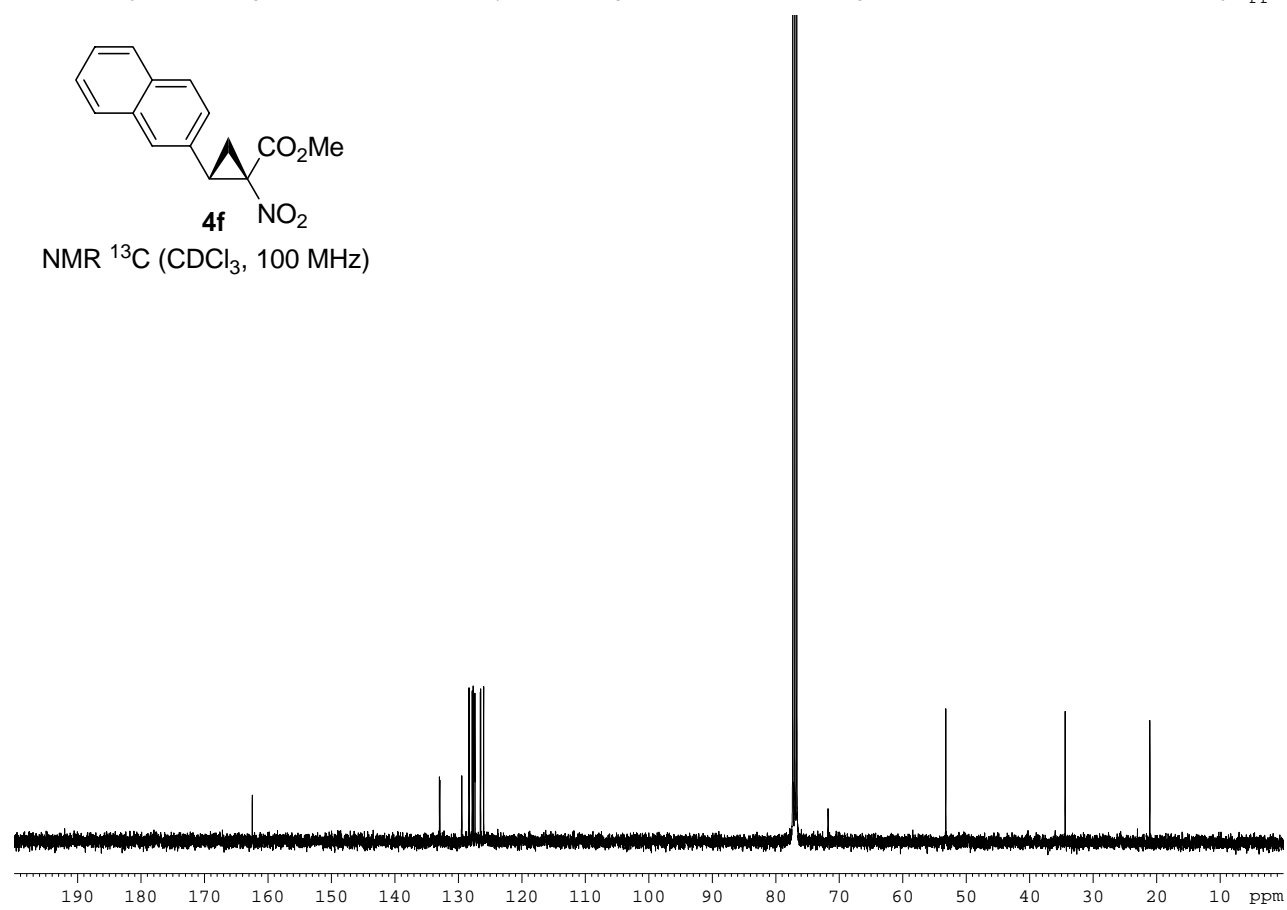
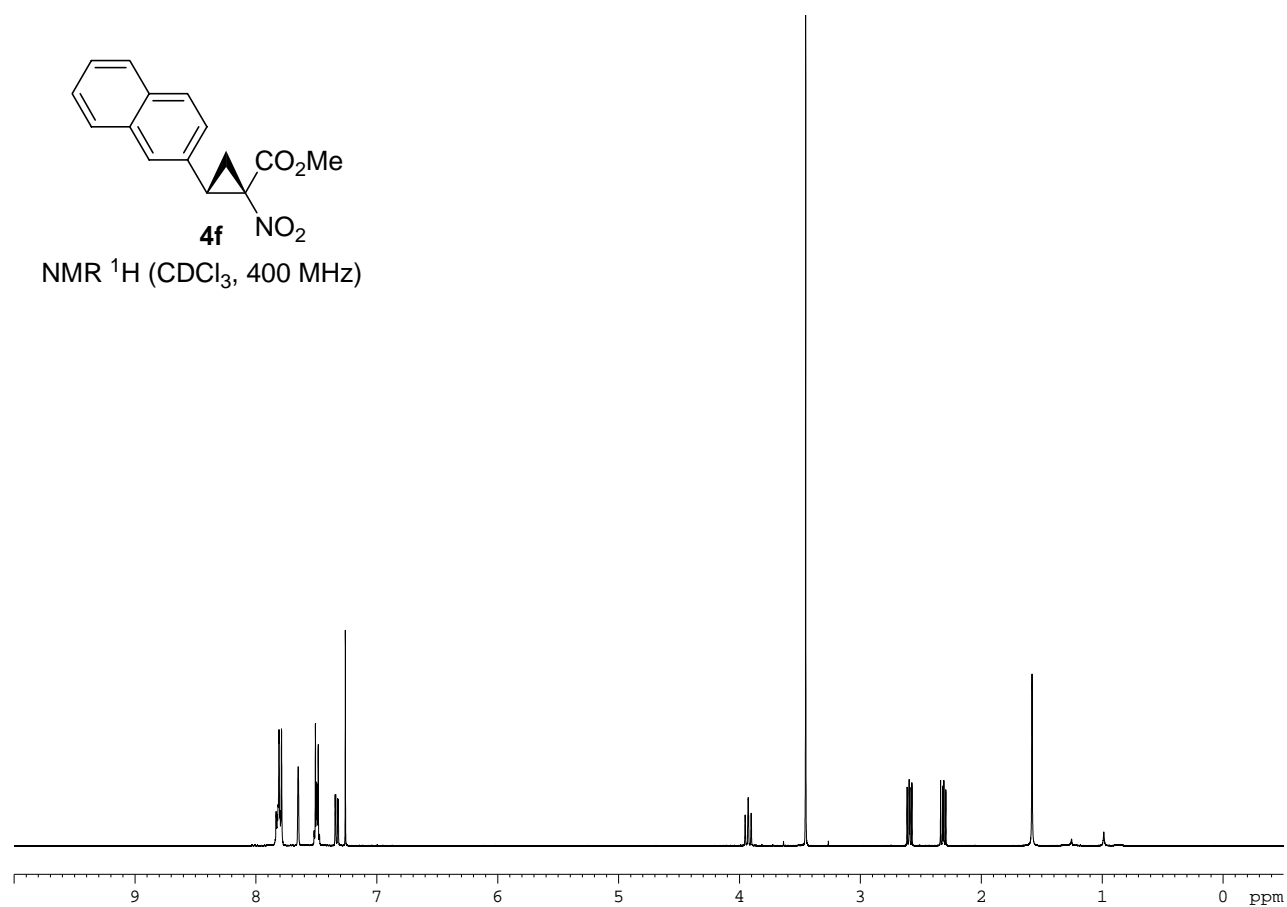


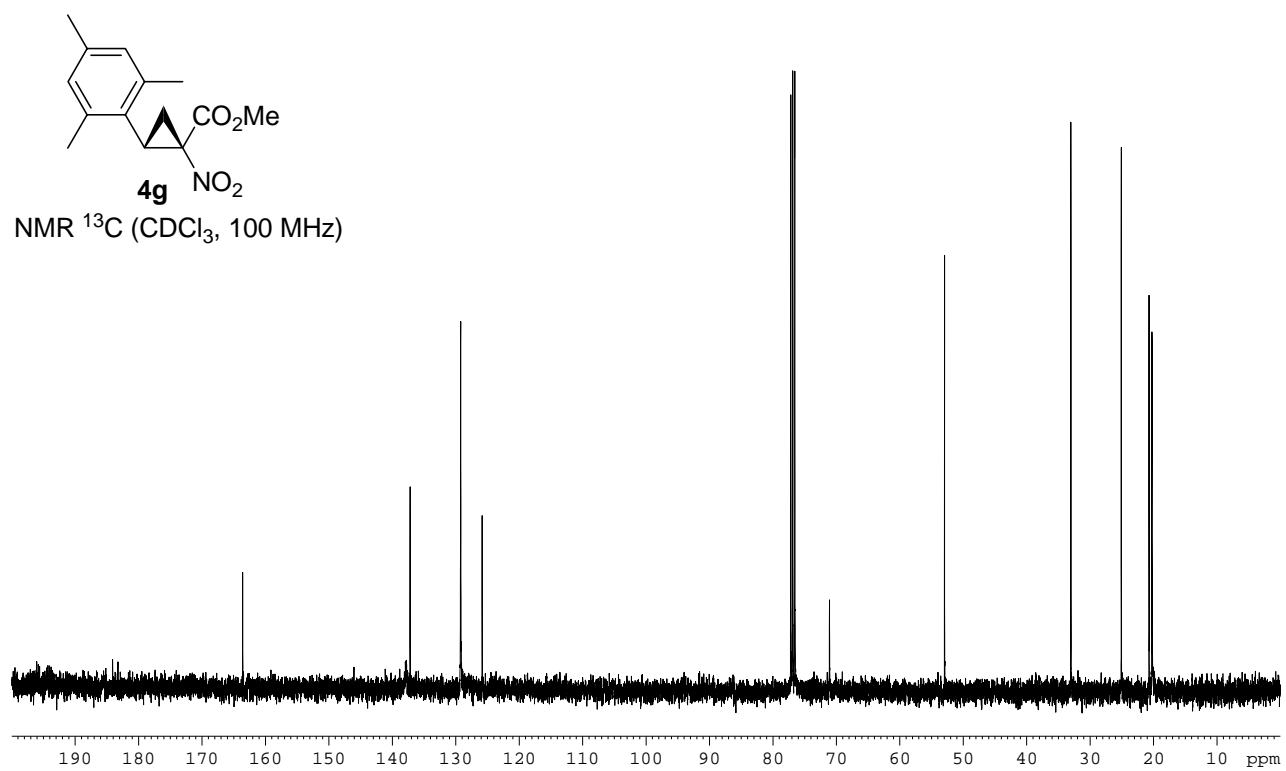
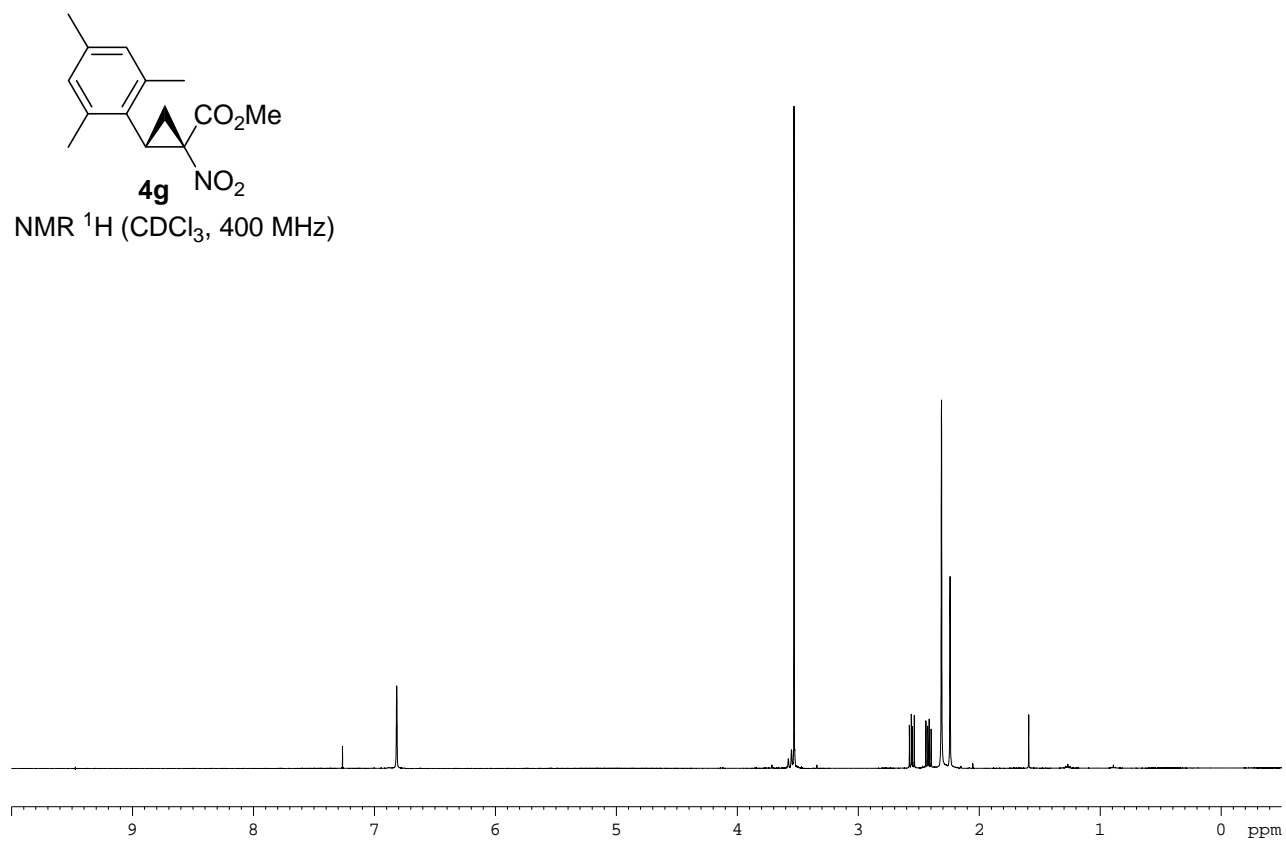
(1R, 2S)-1-amino-2-phenylcyclopropane (7a) Starting with **8a** (129 mg, 90% ee), the general procedure for the Zn-mediated reduction of nitro into amine was followed. Oil residue was chromatographed with 20% ethyl acetate in hexanes to afford the pure known compound as a colorless oil (87 mg, 83%, >95:5 *dr*) R_f 0.27 (5% methanol in dichloromethane) $[\alpha]_D^{20}$, -124 (c 1, CH_2Cl_2). Litt $[\alpha]_D^{20}$, -135.4 (c 0,81, CHCl_3).

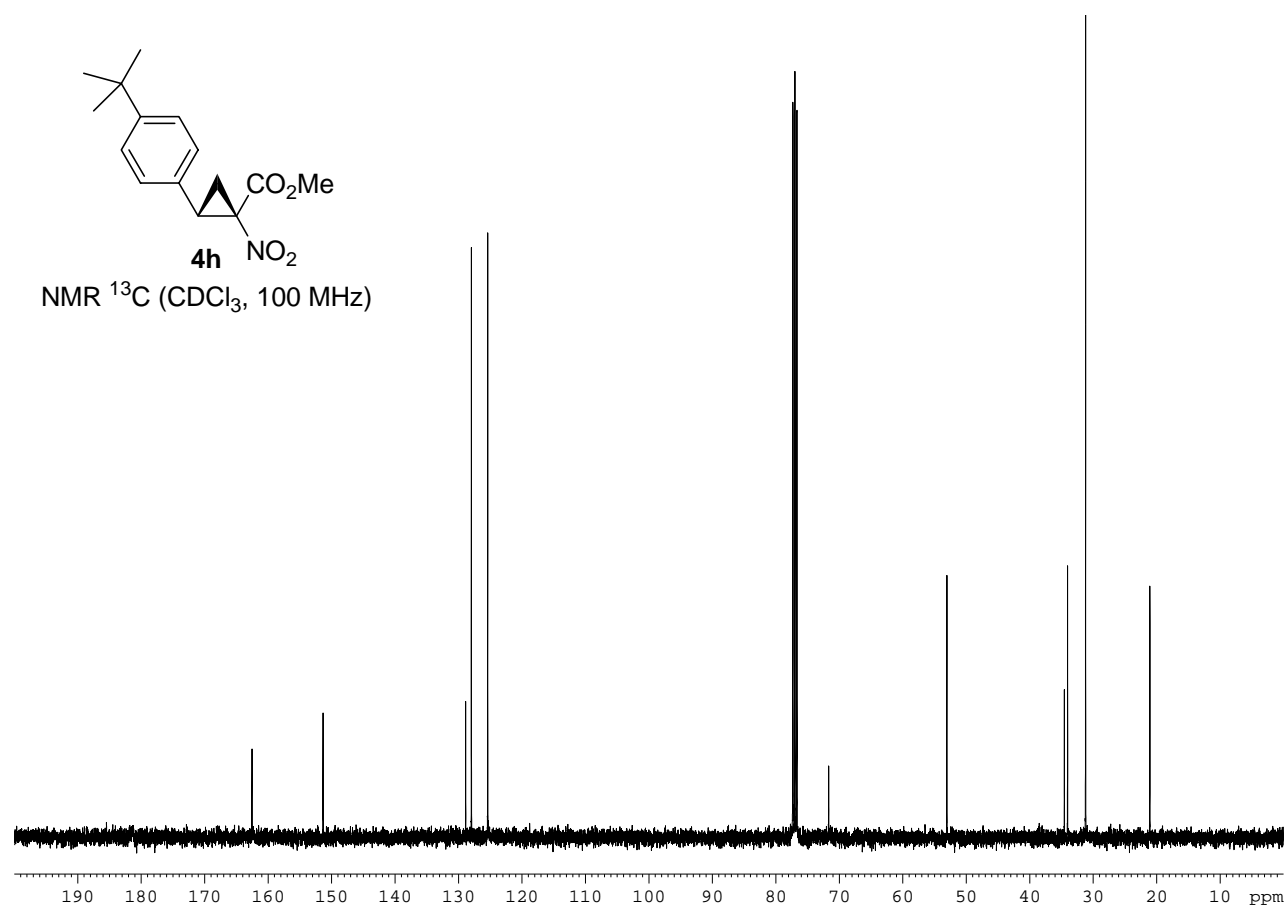
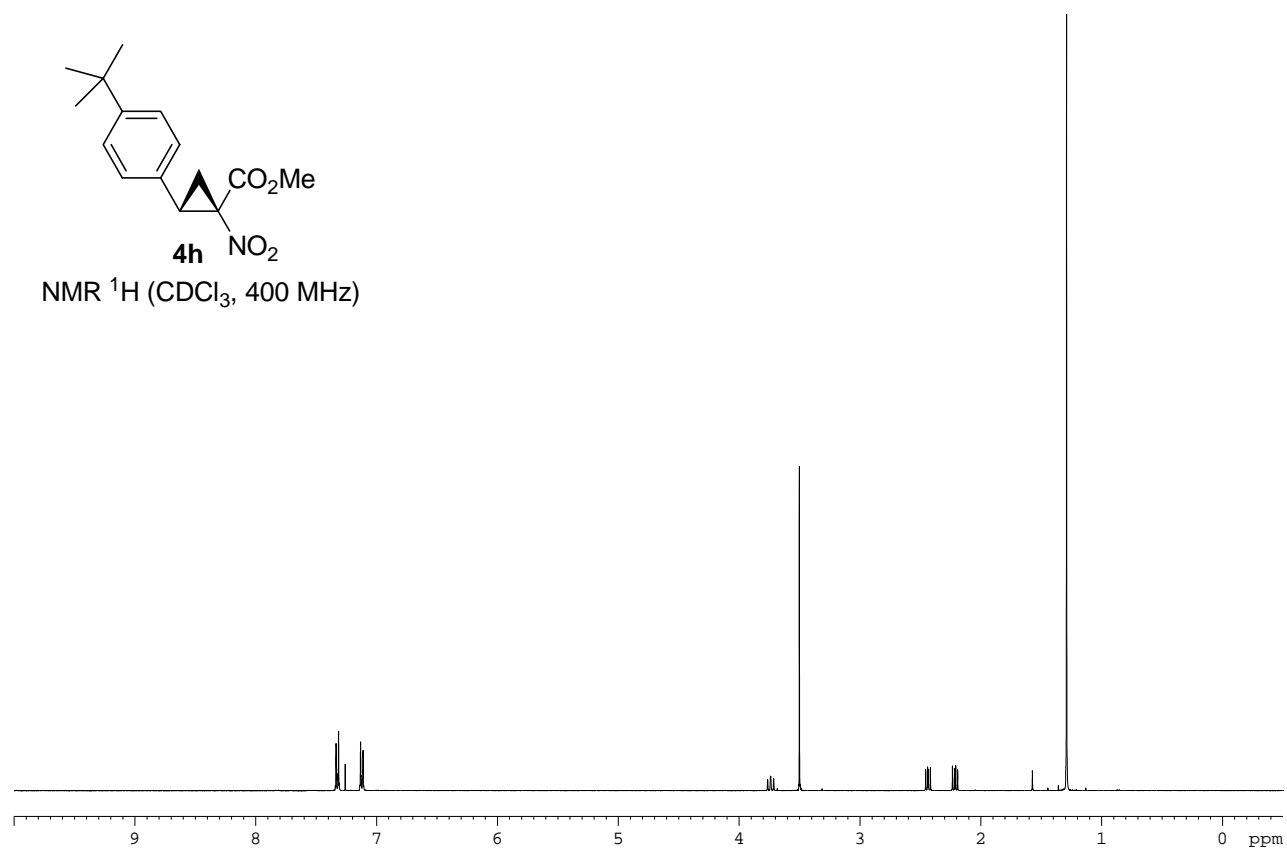
NMR ^1H (CDCl_3 , 400 MHz)NMR ^1H (CDCl_3 , 400 MHz)

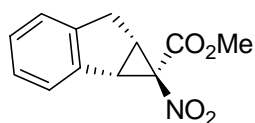
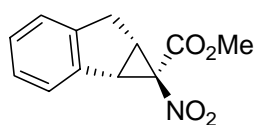
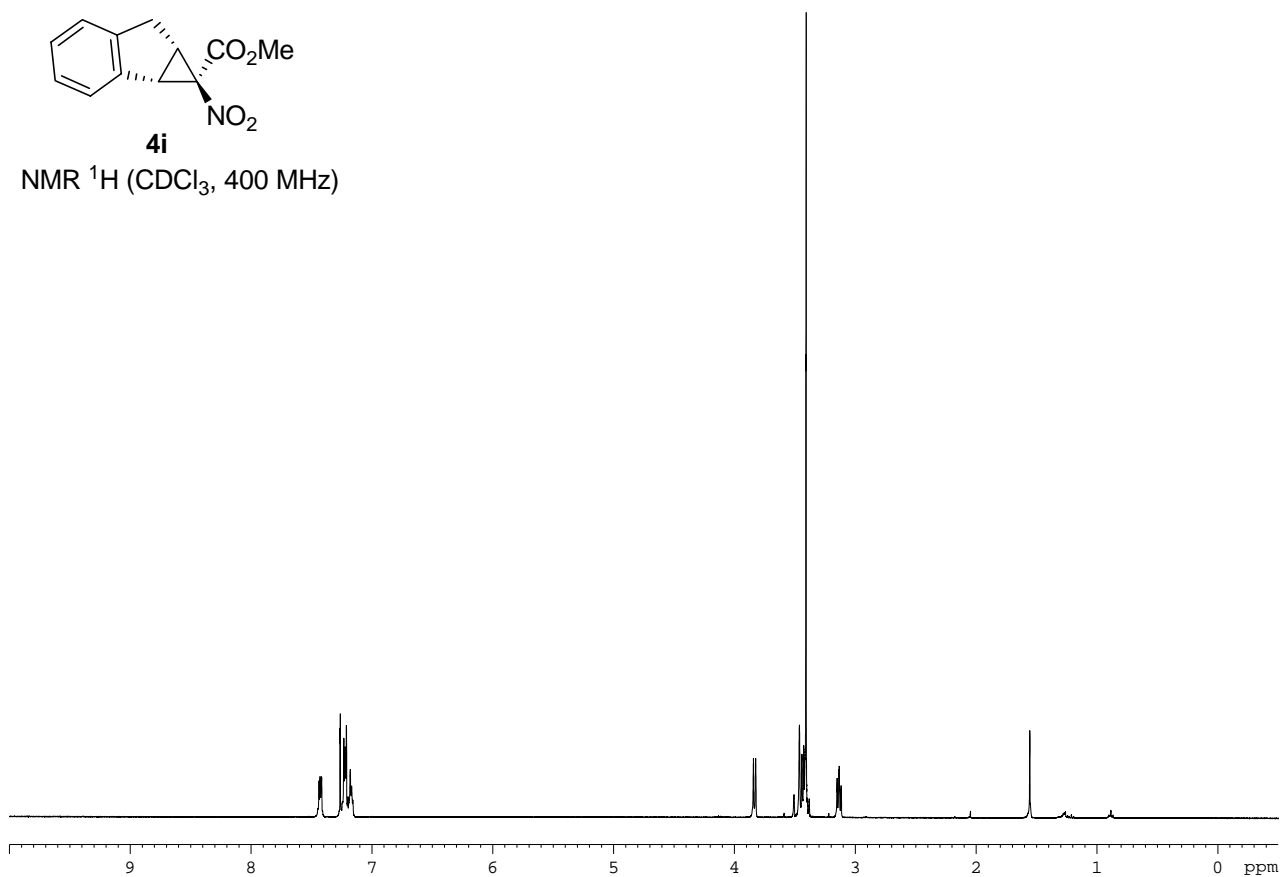
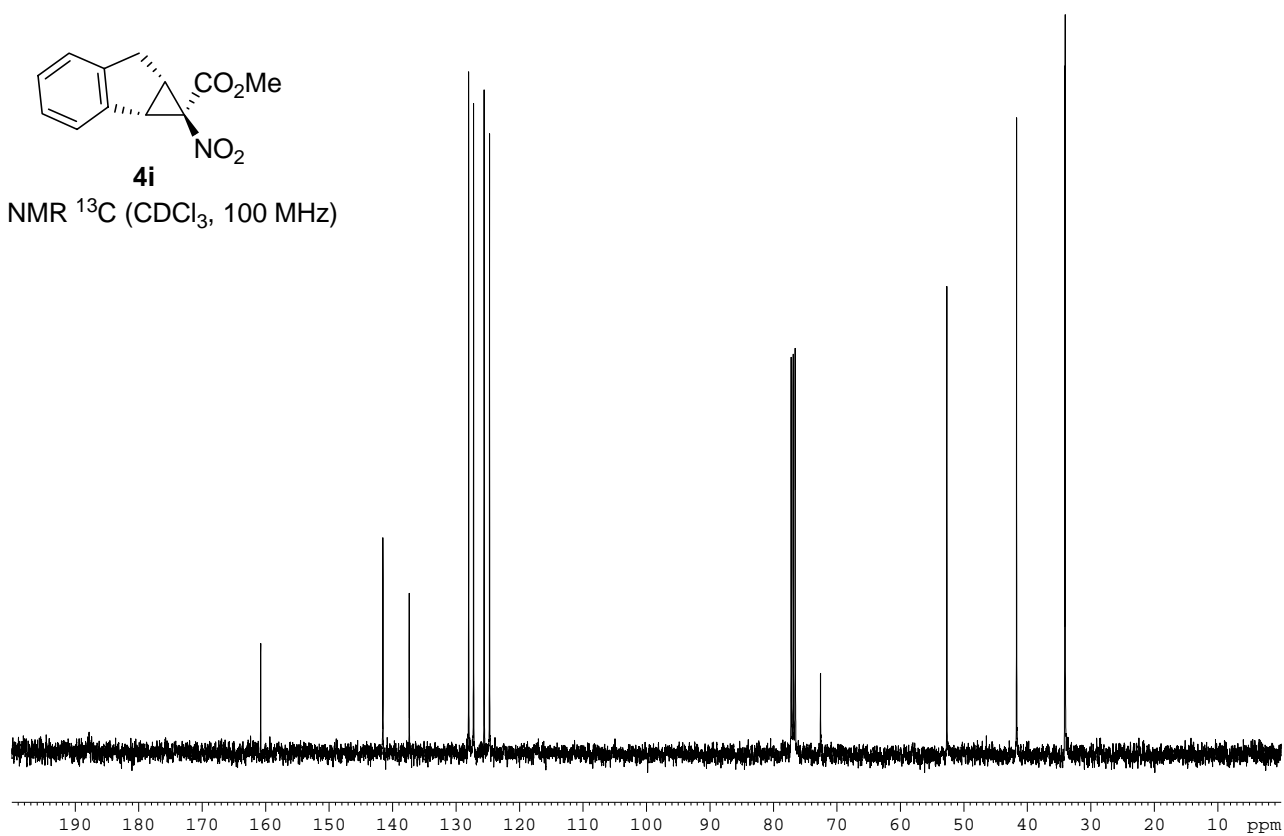


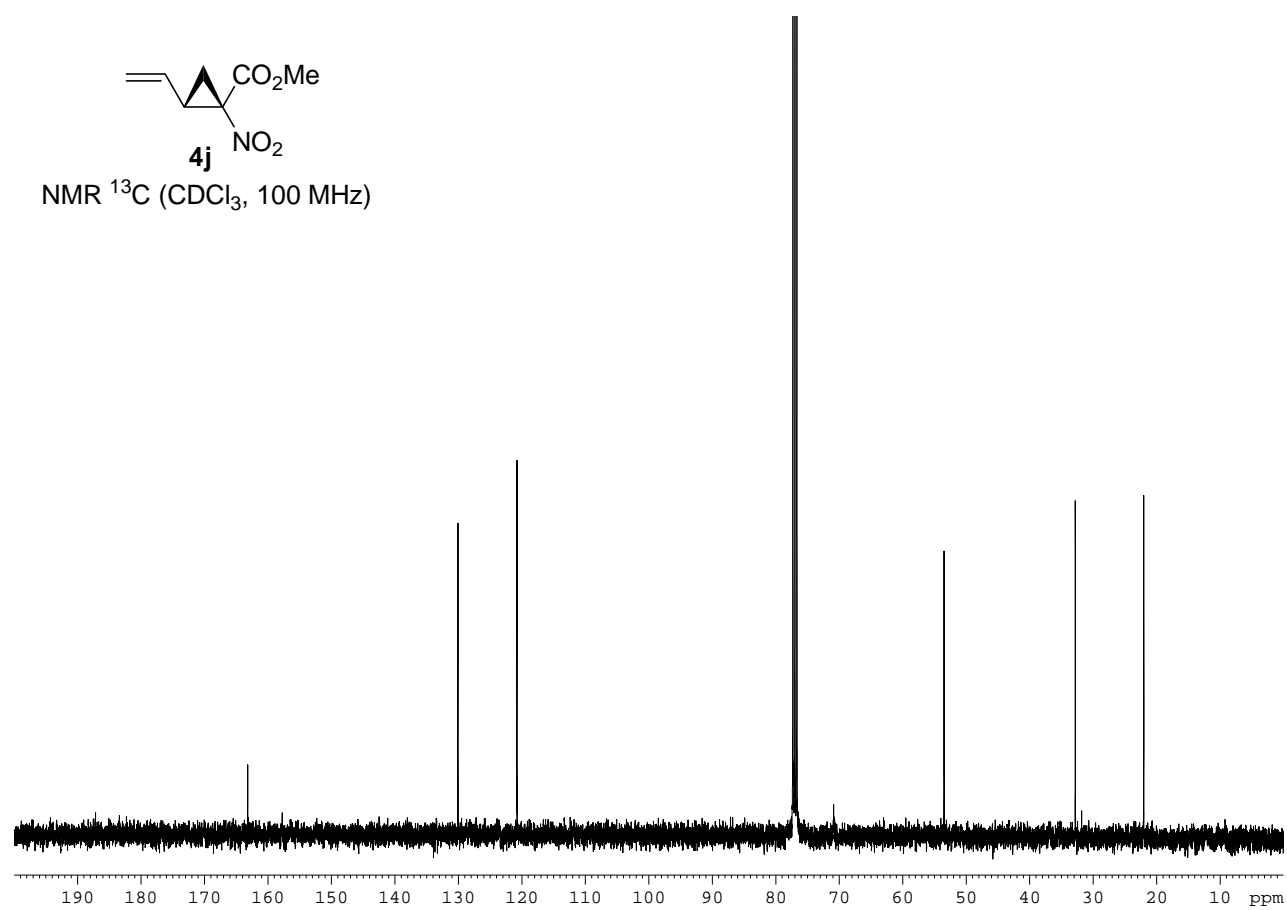
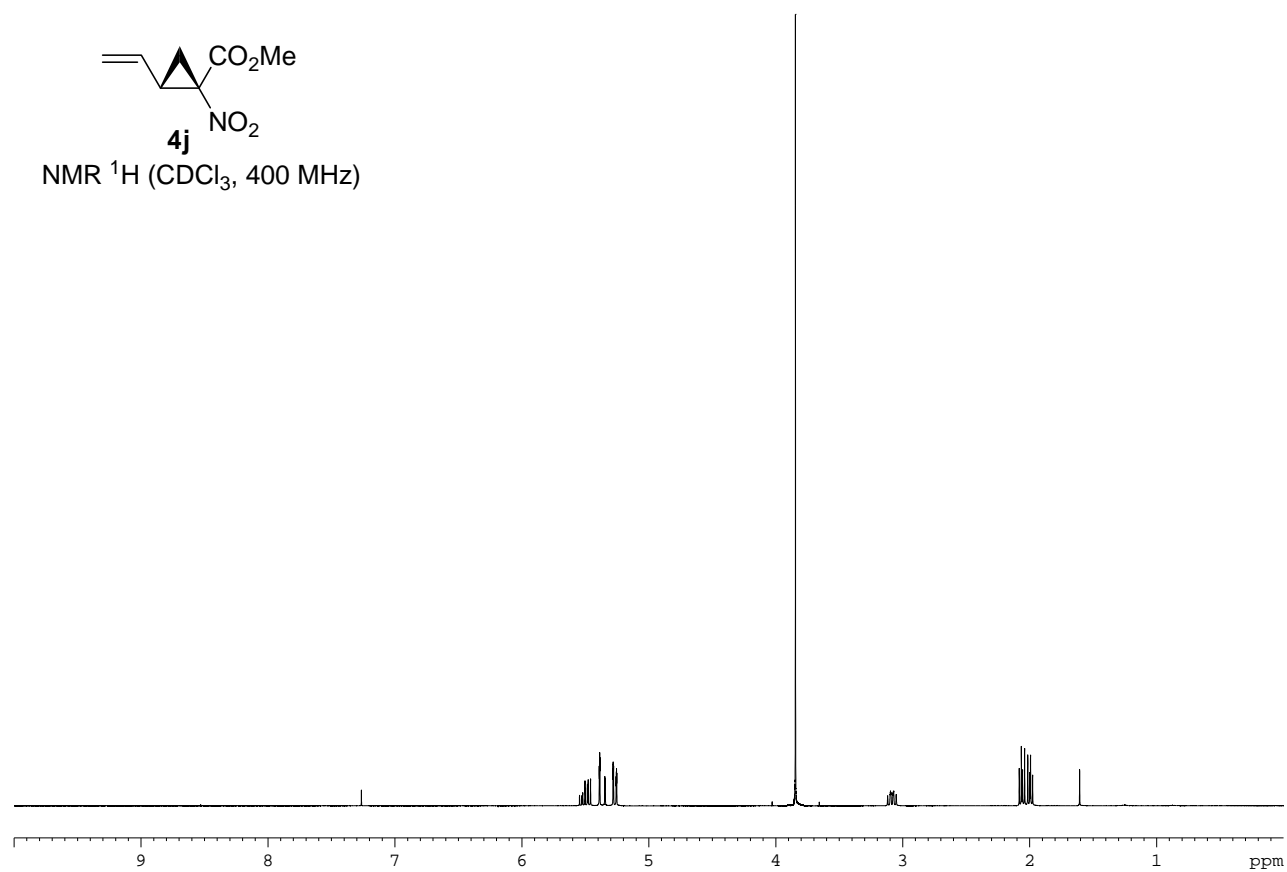


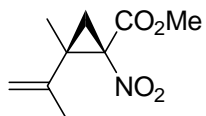
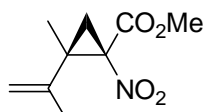
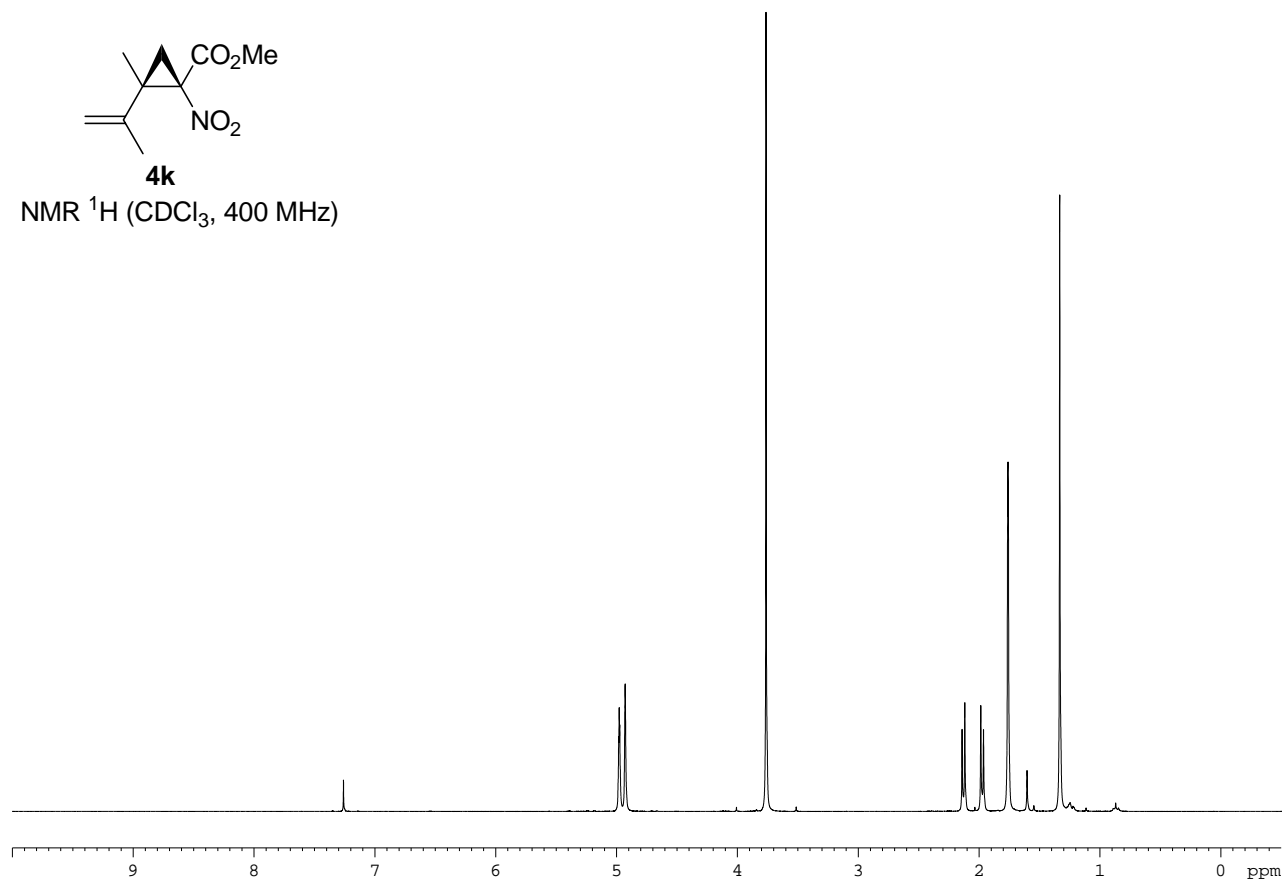
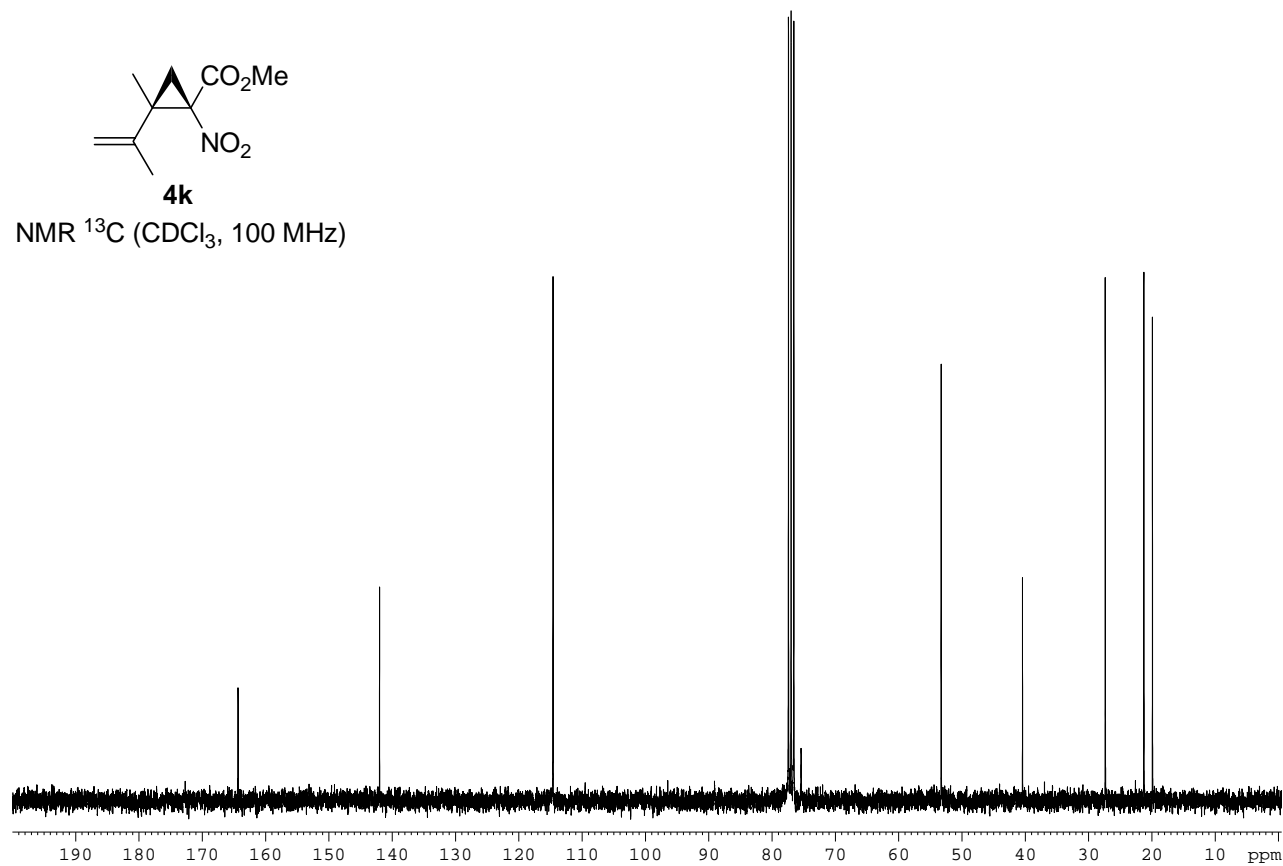


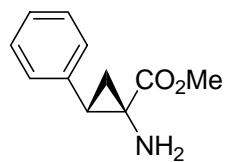




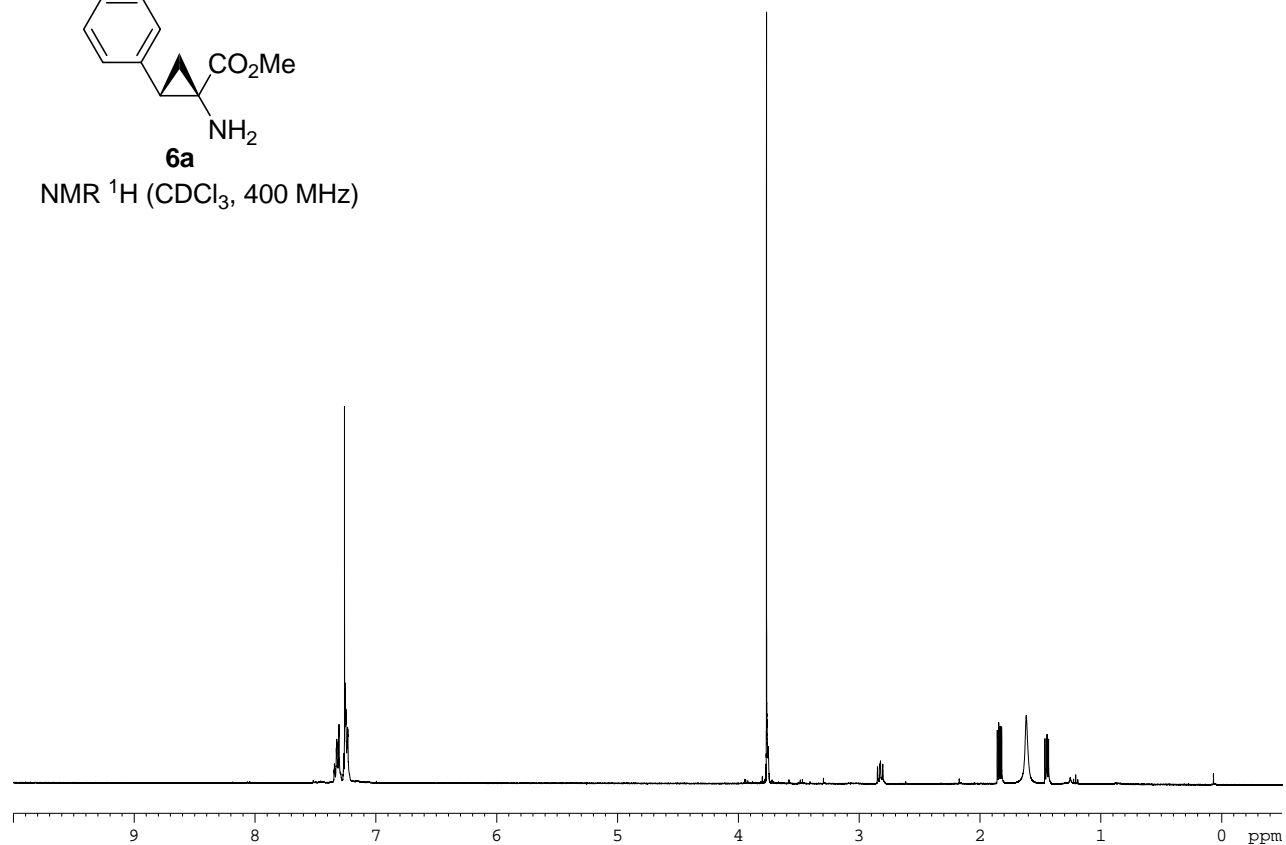
**4i**NMR ¹H (CDCl₃, 400 MHz)**4i**NMR ¹³C (CDCl₃, 100 MHz)

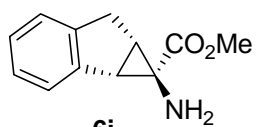
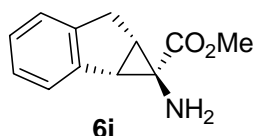
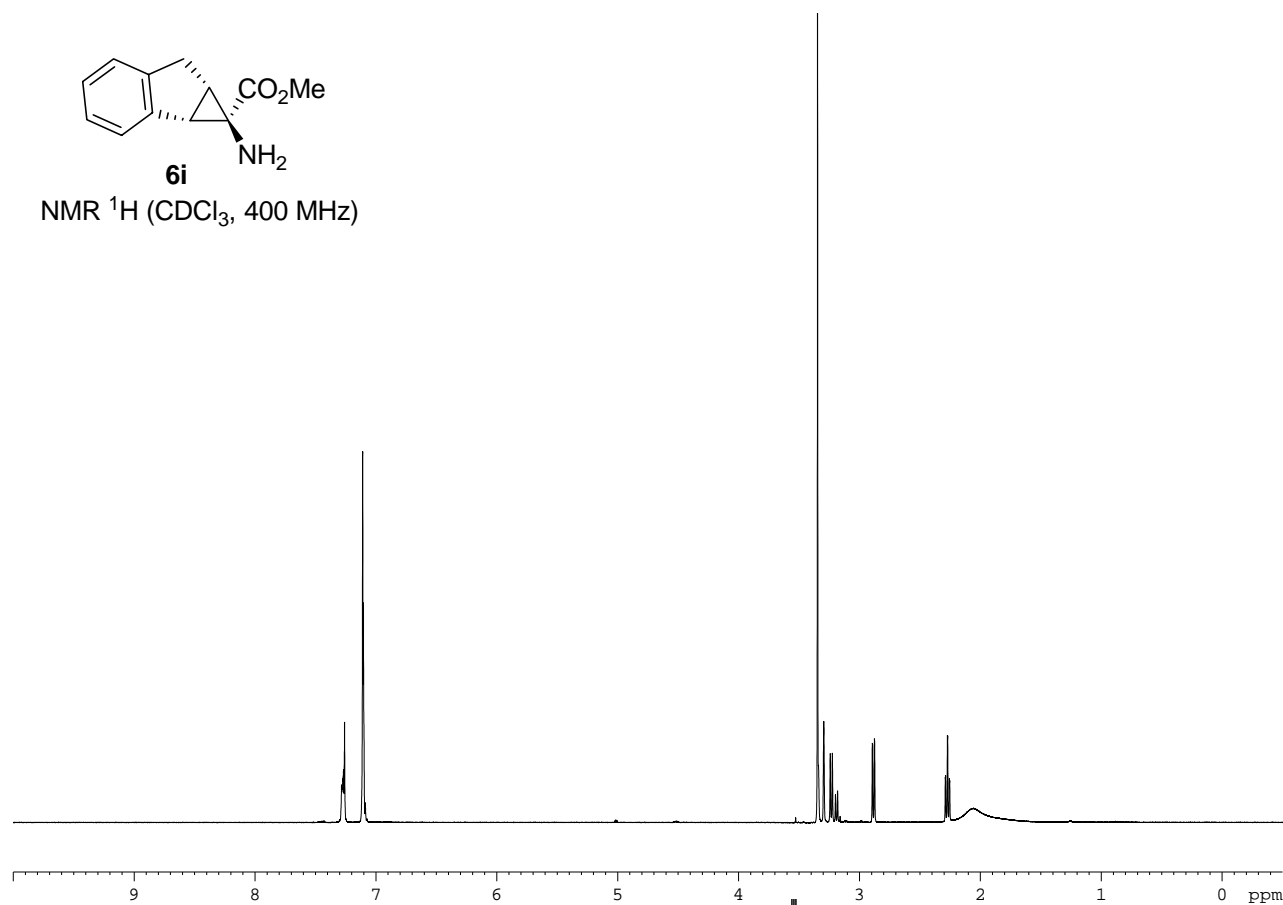


**4k**NMR ^1H (CDCl_3 , 400 MHz)**4k**NMR ^{13}C (CDCl_3 , 100 MHz)



6a
NMR ¹H (CDCl₃, 400 MHz)



NMR ^1H (CDCl_3 , 400 MHz)NMR ^{13}C (CDCl_3 , 100 MHz)