

Supplementary Information for

Dynamic Kinetic Resolution of Dehydrocoronamic Acid

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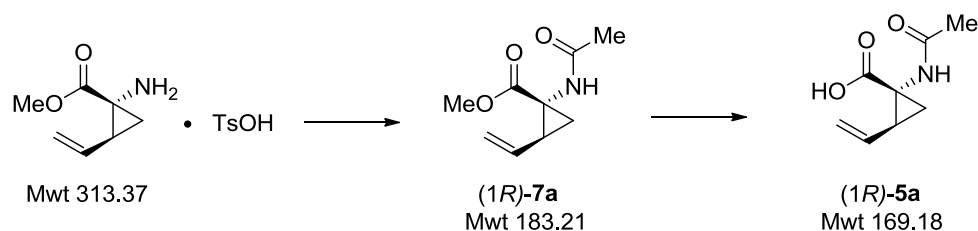
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General.

GC methods were run using a Perkin Elmer Autosystem XL gas chromatograph or an Agilent 6890N GC system. Melting points were obtained a Perkin Elmer DSC6 digital scanning calorimeter and are uncorrected. IR spectra were taken on a Perkin-Elmer Spectrum RX 1 FT-IR System. Proton and ¹³C NMR spectra were recorded on a Bruker AV400 spectrometer using Me₄Si or residual CHCl₃ as an internal reference. Low resolution mass spectra were recorded using a Waters LCT spectrometer using APCI or a Waters Acquity uPLC system coupled to a Waters ZSpray mass spectrometer. GC/MS data was collected on a Thermo Trace 1300 Gas Chromatograph coupled to a Thermo ISQLT mass Specrometer. Optical rotations were determined using a Perkin Elmer 341 polarimeter in units of 10⁻¹ °cm² g⁻¹ (c in g/100 mL). High resolution mass spectra were determined using a Waters Synapt G2 q-TOF spectrometer or a Waters LCT spectrometer with MassWorks software using PEG600 as a standard. Elemental analyses were determined by MEDAC Ltd.

Preparation of (1*R*, 2*S*)-2-Vinyl-1-acetamidocyclopropanecarboxylic Acid (1*R*)-(5a).



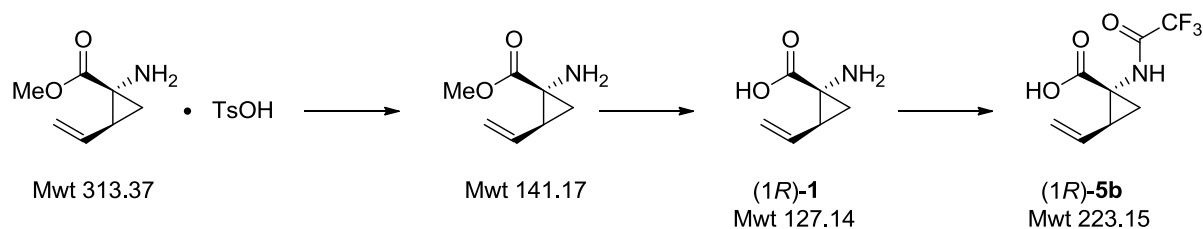
(1*R*, 2*S*)-Methyl 2-vinyl-1-aminocyclopropanecarboxylate tosylate salt¹ (3.22 g, 10.5 mmol) was placed in a flask and sodium acetate (1.69 g, 20.6 mmol), ethyl acetate (15 mL) and acetic anhydride (1.07 mL, 11.3 mmol) were added. The suspension was stirred at room temperature for 16 h, and 20% sodium carbonate solution (15 mL) was added. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 5 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent was evaporated to give (1*R*, 2*S*)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate (1*R*)-(7a) (97.6% ee) as a viscous, yellow oil (1.92 g, 100%). δ_{H} (400 MHz; CDCl₃, Me₄Si): 6.60 and 6.16 (1 H, 2 br s, 1:5.3 ratio), 5.77 (ddd, $J = 17.0, 10.2, 8.8$ Hz) and 5.73 (ddd, $J = 17.0, 10.2, 8.8$ Hz) (1:5.3 ratio, 1 H), 5.34 (dd, $J = 17.2, 1.2$ Hz) and 5.29 (dd, $J = 17.2, 1.2$ Hz) (1:5.3 ratio, 1 H), 5.19 (1 H, dd, $J = 10.4, 1.2$ Hz) and 5.13 (dd, $J = 10.4, 1.2$ Hz) (1:5.3 ratio, 1 H), 3.76 and 3.71 (2s, 1:5.3 ratio, 3 H), 2.24 (q, $J = 8.8$ Hz) and 2.12 (q, $J = 8.8$ Hz) (1:5.3 ratio, 1 H), 2.05 and 2.00 (2s, 1:5.3 ratio, 3 H), 1.90 (1 H, dd, $J = 8.0, 5.6$ Hz) and 1.53 (1 H, dd, $J = 9.6, 5.2$ Hz); δ_{C} (100 MHz; CDCl₃, Me₄Si): 176.6 (s), 175.0 (s), 171.4 (s), 170.8 (s), 133.5 (d), 132.7 (d), 118.8 (t), 118.0 (t), 53.4 (q), 52.8 (q), 41.8 (s), 40.2 (s), 36.8 (d), 33.8 (d), 24.2 (t), 23.2 (t), 23.0 (q) and 20.9 (q).

(1*R*, 2*S*)-Methyl 2-vinyl-1-acetamidocyclopropanecarboxylate (1*R*)-(7a) (1.77 g, 9.66) was placed in a flask and a solution of sodium hydroxide prepared from sodium hydroxide (508 mg, 12.7 mmol) and water (25 mL) was added. The solution was stirred at room temperature for 4 h, then at 20-30 °C for 2 h. The solution was extracted with dichloromethane (3 × 5 mL), then acidified with 1M orthophosphoric acid (15 mL) and extracted with ethyl acetate (5 × 20 mL). The combined ethyl acetate were dried (Na₂SO₄), filtered and the solvent was evaporated to give (1*R*, 2*S*)-2-vinyl-1-acetamidocyclopropanecarboxylic acid (1*R*)-(5a) as a pale yellow solid (1.15 g, 91%). Mp 149-153 °C; ν_{max} (KBr) 3359, 2940 (br), 1734, 1720, 1619, 1543, 1423, 1319, 1286, 1178, 999, 913, 658, 640, 591 and 553 cm⁻¹; δ_{H} (400 MHz; DMSO): 12.4 (1 H, br s), 8.6 (1 H, br s), 5.67 (1 H, dt, $J = 17.3, 9.7$ Hz), 5.26 (1 H, dd, $J =$

aminocyclopropanecarboxylic acid rac-(**1**)³ as a pale yellow solid (8.76 g, 83%). δ_{H} (400 MHz; D₂O): 5.64 (1 H, ddd, $J = 17.9, 9.7, 8.4$ Hz), 5.19 (1 H, dq, $J = 17.2, 0.9$ Hz), 5.03 (1 H, dd, $J = 10.3, 1.7$ Hz), 2.06 (1 H, q, $J = 8.8$ Hz), 1.46 (1 H, dd, $J = 7.8, 6.6$ Hz) and 1.38 (1 H, dd, $J = 10.2, 6.6$ Hz); δ_{C} (400 MHz; D₂O): 172.8 (s), 133.3 (t), 117.9 (d), 41.5 (s), 28.0 (d) and 17.3 (t).

(1*R**, 2*S**)-2-Vinyl-1-aminocyclopropanecarboxylic acid rac-(**1**) (8.65 g, 68.0 mmol), methanol (87 mL), triethylamine (14.2 mL, 102 mmol) and ethyl trifluoroacetate (9.72 mL, 81.6 mmol) were placed in a flask, and the solution was stirred for 18 h at room temperature. Most of the solvent was evaporated under reduced pressure and ethyl acetate (85 mL) was added. 1M Orthophosphoric acid (85 mL) was added, the mixture was shaken and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 20 mL), the combined organic layers were passed through a silica plug, eluting with ethyl acetate, and the solvent was evaporated to give a pale yellow solid (16.4 g). This was taken up in MTBE (15 mL) and heptanes (45 mL) was added. The solution was stirred for 5 h, then filtered and the solid was washed with heptanes-MTBE (3:1, 2 × 20 mL) and dried to give (1*R**, 2*S**)-2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic acid rac-(**5b**) as a pale buff granular solid (11.1 g, 72%). The liquors were concentrated, allowed to stand over 64 h, then filtered to give additional give (1*R**, 2*S**)-2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic acid rac-(**5b**) as a white solid (625 mg, 4%, total 11.6 g, 76%). Mp 135-138 °C; ν_{max} (KBr) 3313, 3075, 1710, 1552, 1435, 1342, 1314, 1251, 1199, 1161, 994, 921, 860, 731 and 620 cm⁻¹; m/z (CI) 224 (100%, M+H) and 206 (60); δ_{H} (400 MHz; CD₃CN): 8.2 (1 H, br s), 8.0 (1 H, br s), 5.79 (1 H, ddd, $J = 17.2, 10.4, 8.8$ Hz), 5.37 (1 H, dd, $J = 17.6, 2.0$ Hz), 5.20 (1 H, dd, $J = 10.2, 1.8$ Hz), 2.32 (1 H, q, $J = 8.9$ Hz), 1.78 (1 H, dd, $J = 8.5, 5.4$ Hz), and 1.54 (1 H, dd, $J = 10.0, 5.6$ Hz); δ_{C} (100 MHz; CD₃CN) 169.5 (s), 157.2 (s, q $J_{\text{C-F}} = 37$ Hz), 133.1 (d), 117.5 (t), 115.5 (s, $J_{\text{C-F}} = 286$ Hz), 38.5 (s), 32.7 (d) and 21.6 (t); δ_{F} (376 MHz, CD₃CN) -76.013; m/z (ES⁻) 222 (100%, M-H); Found: (M+H) 224.0536. C₈H₈F₃NO₃ requires 224.0535; Found: C 42.8%, H 3.8%, N 6.2%. C₈H₈F₃NO₃ requires C 43.1%, H 3.6%, N 6.3%.

Preparation of (1*R*, 2*S*)-2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic Acid (1*R*)-(5b).



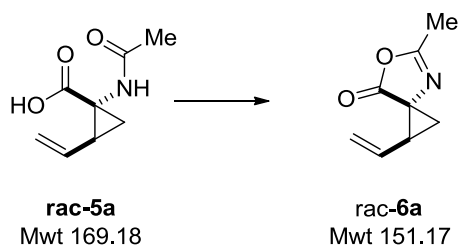
20% sodium carbonate solution (15 mL) was added slowly to (1*R*, 2*S*)-methyl 2-vinyl-1-aminocyclopropanecarboxylate tosylate salt¹ (2.00 g, 6.38 mmol). The solution was extracted with 2-methyltetrahydrofuran (10 × 5 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent was evaporated to give (1*R*, 2*S*)-methyl 2-vinyl-1-aminocyclopropanecarboxylate^{4,5} as a pale yellow, mobile oil (852 mg, 95%). δ_{H} (400 MHz; CDCl₃, Me₄Si): 5.70 (1 H, ddd, $J = 17.2, 10.2, 9.3$ Hz), 5.22 (1 H, ddd, $J = 17.2, 1.8, 0.4$ Hz), 5.04 (dd, $J = 10.4, 1.7$ Hz, 1H), 3.73 (s, 3H), 2.02 (q, $J = 8.7$ Hz, 1H), 2.0 (br s, 2H), 1.56 (dd, $J = 7.5, 4.8$ Hz, 1H) and 1.34 (dd, $J = 9.3, 4.8$ Hz, 1H). δ_{H} (400 MHz; C₆D₆): 6.00 (1 H, ddd, $J = 17.2, 10.2, 9.6$ Hz), 5.26 (1 H, ddd, $J = 17.2, 1.9, 0.5$ Hz), 5.11 (1 H, dd, $J = 10.4, 1.7$ Hz), 3.86 (3 H, s), 2.10 (1 H, q, $J = 8.7$ Hz), 1.61 (1 H, dd, $J = 7.3, 4.4$ Hz), 1.6 (2 H, br s) and 1.21 (1 H, dd, $J = 9.2, 4.5$ Hz).

A solution of sodium hydroxide (249 mg, 6.0 mmol) in water (5 mL) was added to (1*R*, 2*S*)-methyl 2-vinyl-1-aminocyclopropanecarboxylate (852 mg, 6.03 mmol). The solution was stirred for 2 h at room temperature. Freshly washed Amberlite-IRC-50 resin (6.0 g) was added, after which the pH decreased from 14 to 6.7. The suspension was filtered and the solvent was evaporated to give (1*R*, 2*S*)-2-vinyl-1-aminocyclopropanecarboxylic acid (1*R*)-(1)⁴ as a pale yellow solid (773 mg, 100%). δ_{H} (400 MHz; D₂O): 5.61 (1 H, ddd, $J = 17.3, 10.3, 8.2$ Hz), 5.17 (1 H, dd, $J = 17.6, 0.9$ Hz), 5.00 (1 H, dd, $J = 10.6, 0.9$ Hz), 2.02 (1 H, q, $J = 8.7$ Hz), 1.43 (1 H, dd, $J = 7.8, 6.5$ Hz) and 1.35 (1 H, dd, $J = 10.2, 6.4$ Hz); δ_{C} (400 MHz; D₂O): 173.0 (s), 133.3 (t), 117.9 (d), 41.4 (s), 28.0 (d) and 17.3 (t).

(1*R*, 2*S*)-2-Vinyl-1-aminocyclopropanecarboxylic acid (1*R*)-(1) (500 mg, 3.93 mmol), methanol (5 mL), triethylamine (822 μ L, 5.90 mmol) and ethyl trifluoroacetate (562 μ L, 4.72 mmol) were placed in a flask, and the solution was stirred for 3 h at room temperature. Most of the solvent was evaporated under reduced pressure and ethyl acetate (5 mL) was added.

1M Orthophosphoric acid (5 mL) was added, the mixture was shaken and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 5 mL), the combined organic layers were passed through a silica plug, eluting with ethyl acetate, to give, after evaporation of the solvent, (1*R*, 2*S*)-2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic acid (1*R*)-(5b) (>99% ee) as a yellow foam that solidified slowly on standing (835 mg, 95%). δ_{H} (400 MHz; CDCl₃, Me₄Si): 9.0 (1 H, br s), 7.2 (1 H, br s), 5.79 (1 H, ddd, $J = 17.1, 10.2, 8.7$ Hz), 5.38 (1 H, dd, $J = 17.1, 0.7$ Hz), 5.23 (1 H, dd, $J = 10.3, 0.9$ Hz), 2.34 (1 H, q, $J = 9.0$ Hz), 1.97 (1 H, dd, $J = 8.5, 6.0$ Hz) and 1.70 (1 H, dd, $J = 9.8, 6.0$ Hz). δ_{H} (400 MHz; CD₃CN): 9.3 (1 H, br s), 8.2 (1 H, br s), 5.79 (1 H, ddd, $J = 17.1, 10.2, 8.2$ Hz), 5.39 (1 H, dd, $J = 17.1, 0.7$ Hz), 5.24 (1 H, dd, $J = 10.3, 0.9$ Hz), 2.34 (1 H, q, $J = 9.0$ Hz), 1.78 (1 H, dd, $J = 8.5, 6.0$ Hz), and 1.54 (1 H, dd, $J = 9.8, 6.0$ Hz); δ_{C} (100 MHz; CD₃CN) 169.5 (s), 157.2 (s, q $J_{\text{C-F}} = 37$ Hz), 133.1 (d), 117.5 (t), 115.5 (s, $J_{\text{C-F}} = 287$ Hz), 38.5 (s), 32.7 (d) and 21.6 (t); δ_{F} (376 MHz, CD₃CN) -76.814.

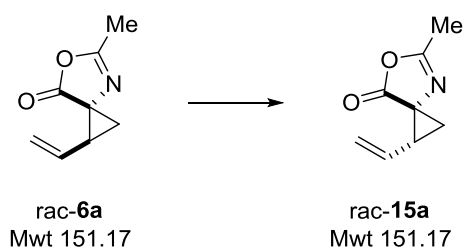
Preparation of (1*R, 3*S**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(6a).**



Dicyclohexylcarbodiimide (2.70 g, 13.0 mmol) was placed in a flask. This was purged with nitrogen and anhydrous acetonitrile (20 mL) was added. (1*R**, 2*S**)-2-Vinyl-1-acetamidocyclopropanecarboxylic acid rac-(5a) (2.01 g, 11.9 mmol) was added in portions while cooling in a water bath over 30 minutes, then the suspension was stirred for 2 h. The suspension was filtered, then the residue was dissolved in MTBE and passed through a silica plug eluting with MTBE, then purified by flash chromatography on silica eluting with heptanes-MTBE (1:1) to give (1*R**, 3*S**)-1-vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(6a) as a colourless, mobile liquid (1.16 g, 90%); ν_{max} (KBr, thin film) 3087, 3016, 2933, 1790, 1673, 1438, 1384, 1305, 1247, 1099, 992, 894, 754 and 681 cm⁻¹; δ_{H} (400 MHz; CDCl₃, Me₄Si): 5.87 (ddd, $J = 17.4, 10.3, 9.3$ Hz, 1H), 5.32 (dd, $J = 17.0, 0.6$ Hz, 1H), 5.20 (dd, $J = 10.4, 0.6$ Hz, 1H), 2.69 (q, $J = 9.1$ Hz, 1H), 2.25 (s, 3H), 2.06 (dd, $J = 9.4, 5.4$

Hz, 1H) and 1.77 (dd, $J = 8.4, 5.2$ Hz, 1H); δ_{H} (400 MHz; CD_3CN): 5.87 (ddd, $J = 17.2, 10.3, 9.8$ Hz, 1H), 5.36 (dd, $J = 17.2, 1.7$ Hz, 1H), 5.20 (dd, $J = 10.4, 1.7$ Hz, 1H), 2.71 (q, $J = 8.9$ Hz, 1H), 2.18 (s, 3H), 2.04 (dd, $J = 9.2, 5.4$ Hz, 1H) and 1.73 (dd, $J = 9.3, 5.4$ Hz, 1H). δ_{C} (100 MHz; CD_3Cl_3 , Me_4Si): 176.1 (s), 162.8 (s), 131.7 (d), 118.5 (t), 52.4 (s), 35.2 (d), 24.4 (t) and 15.4 (q); δ_{C} (100 MHz; CD_3CN): 176.2 (s), 162.2 (s), 131.9 (d), 117.2 (t), 52.0 (s), 34.2 (s), 23.5 (d) and 14.1 (q); GC/MS: 16.62 min (90%, assigned to *trans*-diastereoisomer (**15a**)) m/z (EI) 151 (52%, M^+), 123 (40), 110 (15), 95 (100) and 81 (41) and 16.68 min (10%, assigned to assigned to *cis*-diastereoisomer (**6a**))⁶ m/z (EI) 151 (100%, M^+), 123 (57), 110 (100), 95 (55) and 81 (80). m/z (ES^+) 152 (100%, $(\text{M}+\text{H})^+$) and 110 (42) Found: $(\text{M}+\text{H})$ 152.0712. $\text{C}_8\text{H}_{10}\text{NO}_2$ requires C 152.0710.

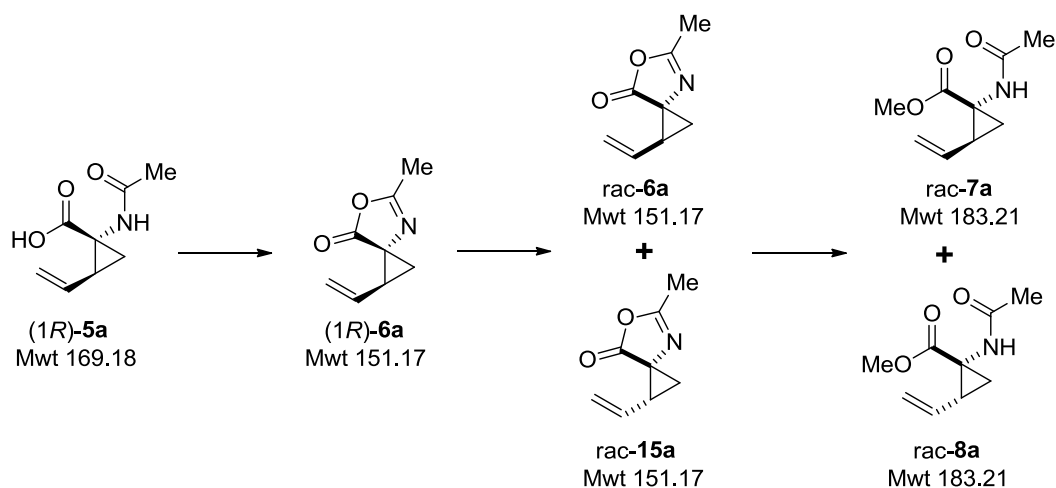
Isomerisation of (1*R, 3*S**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(6a).**



(1*R**, 3*S**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(**6a**) (50 mg \times 2) was dissolved in CDCl_3 (0.5 mL) and CD_3CN (0.5 mL). Samples were heated to 65 °C for 28 h (CDCl_3) and 80 °C and for 28 h (CD_3CN) after which partial conversion to (1*R**, 3*R**)-1-vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(**15a**) occurred. Ratios of **6a**:**15a** were 1:1.4 (CDCl_3) and 1:1.7 (CD_3CN). δ_{H} (400 MHz; CDCl_3 , Me_4Si): 5.69 (1 H ddd, $J = 17.2, 10.2, 9.0$ Hz), 5.32 (1 H, d, $J = 17.2$ Hz), 5.13 (1 H, dd, $J = 10.4, 1.4$ Hz), 2.57 (1 H, q, $J = 8.8$ Hz), 2.27 (s, 3H), 1.95 (1 H, dd, $J = 9.4, 5.4$ Hz) and 2.77 (1 H, dd, $J = 8.4, 5.2$ Hz); δ_{H} (400 MHz; CD_3CN): 5.70 (1 H ddd, $J = 17.2, 10.2, 9.0$ Hz), 5.34 (1 H, dd, $J = 17.2, 1.6$ Hz), 5.18 (1 H, dd, $J = 10.4, 1.2$ Hz), 2.53 (1 H, q, $J = 8.8$ Hz), 2.22 (s, 3H), 1.87 (1 H, dd, $J = 9.2, 5.2$ Hz) and 1.82 (1 H, dd, $J = 7.8, 5.4$ Hz); δ_{C} (100 MHz; CDCl_3): 171.9 (s), 163.1, (s), 133.5 (d), 118.4 (t), 52.2 (s), 35.4 (d), 23.9 (t) and 15.4 (q); δ_{C} (100 MHz; CD_3CN): 177.0 (s), 161.5, (s), 134.0 (d), 117.3 (t), 51.8 (s), 34.5 (d), 22.9 (t) and 14.3 (q). GC/MS: 16.62 min (90%, assigned to *trans*-diastereoisomer (**15a**)) m/z (EI) 151 (52%, M^+),

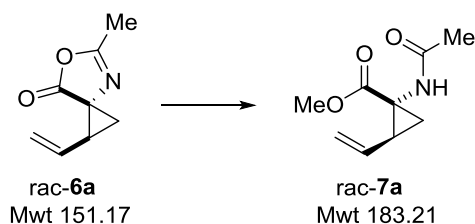
123 (40), 110 (15), 95 (100) and 81 (41) and 16.68 min (10%, assigned to assigned to *cis*-diastereoisomer (**6a**))⁶ (EI) 151 (100%, M⁺), 123 (57), 110 (100), 95 (55) and 81 (80).

Preparation and Isomerisation of (1*S*, 3*R*)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(6a**).**



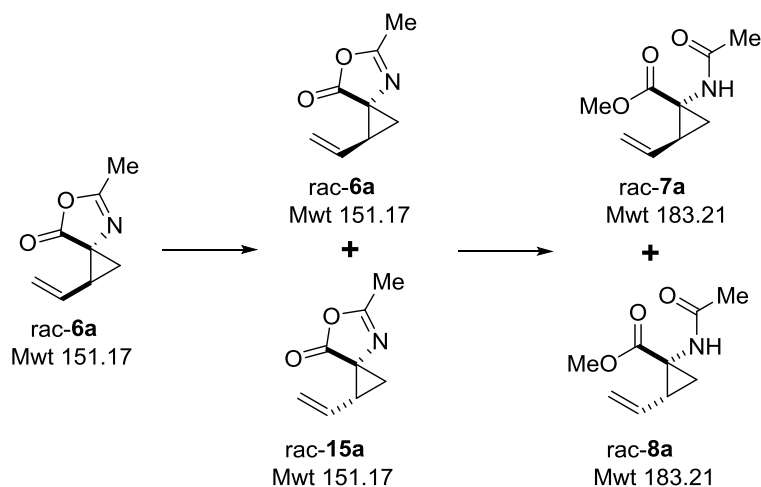
(1*R*, 2*S*)-Vinyl-1-acetamidocyclopropanecarboxylic acid (1*R*)-(**5a**) (97.1% ee, 200 mg, 1.18 mmol) and acetonitrile (1.0 ml) were placed in a Schlenk flask. A solution of dicyclohexylcarbodiimide (293 mg, 1.42 mmol) in acetonitrile (1.0 mL) was added, and the solution was stirred at room temperature for 30 minutes. A solution of potassium carbonate (50 mg, 0.36 mmol) in methanol (10 mL) was prepared. The reaction solution was heated to 80 °C, and samples (3-4 drops) were withdrawn at intervals. Each sample was added to the methanol solution (200 μL), the solution was allowed to stand for 10 minutes, the solvent was evaporated, toluene (100 μL) was added, the sample was filtered, the solvent was evaporated, the residue was dissolved in acetone and the sample was analysed by chiral GC to determine enantiomeric and diastereoisomeric excess. After heating for 4 h, enantiomeric excess was 6.6% and diastereoisomeric excess was 70.9%. The solution was allowed to cool to room temperature and methanol (2 mL) and potassium carbonate (10 mg, 0.046 mmol) were added. The mixture was stirred for 1 h, filtered and the solvent was evaporated to give a mixture of (1*R**, 2*S**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(**7a**) and (1*R**, 2*R**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(**8a**) (6:1) as a colourless, viscous oil (250 mg).

Methanolysis of (1*S, 3*R**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(6a).**



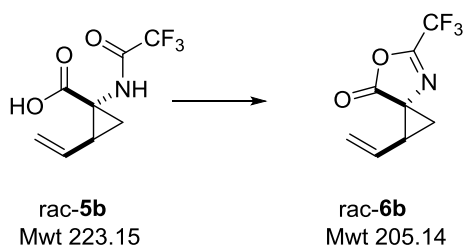
(1*S**, 3*R**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one (400 mg, 2.64 mmol) was dissolved in methanol (4.0 mL). Potassium carbonate (18.2 mg, 0.13 mmol) was added. A rapid exothermic reaction occurred. The solution was stirred at room temperature for 3 h, when citric acid (27 mg) was added. The solvent was evaporated, then MTBE (5 mL) was added. The suspension was filtered and the solvent was evaporated to give crude **7b** as a white solid (480 mg). This was recrystallized by dissolving in MTBE (5 mL), then heptane (5 mL) was added slowly over 2 h to give (1*R**, 2*S**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(**7a**) as a white crystalline solid (424 mg, 87%); Mp 82-84 °C; ν_{\max} (KBr) 3269, 3059, 1731, 1654, 1546, 1436, 1375, 1353, 1322, 1197, 1164, 998, 914, 901, 782, 652 and 612 cm^{-1} ; m/z (LC/MS, CI), retention time 1.17 minutes, 184 (100%, M+H); Found: (M+H) 184.0968. $\text{C}_9\text{H}_{14}\text{NO}_3$ requires 184.0974. Found: C 59.0%, H 7.4%, N 7.6%. $\text{C}_9\text{H}_{13}\text{NO}_3$ requires C 59.0%, H 7.2%, N 7.6%.

Isomerisation and Methanolysis of (1*S, 3*R**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(6a).**



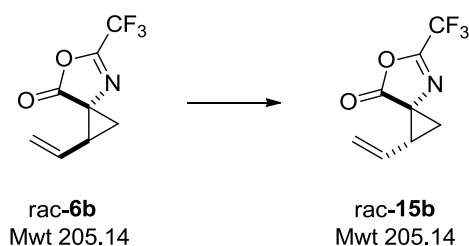
(1*S**, 3*R**)-1-Vinyl-6-methyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one (332 mg, 2.20 mmol) was placed in a Schlenk flask. This was purged with nitrogen, then anhydrous acetonitrile (5 mL) was added. The solution was heated for 8 h, then allowed to cool to room temperature. Methanol (5 mL and potassium carbonate (16 mg, 0.055 mmol) were added, then the solution was stirred for 1h, when citric acid (24 mg, 0.11 mmol) was added. The solvent was evaporated and flash chromatography on silica, eluting with MTBE gave a 2:1 mixture of (1*R**, 2*S**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(7a) and (1*R**, 2*R**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(8a) (inseparable) as a white solid (392 mg, 94%). (1*R**, 2*R**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(8a); δ_{H} (400 MHz; CDCl_3 , Me_4Si): 5.94 (1 H, br s), 5.53 (1 H, ddd, $J = 17.4, 10.3, 7.9$), 5.26 (1 H, d, $J = 17.2$ Hz), 5.20 (1 H, dd, $J = 10.6, 1.0$ Hz), 3.69 (3 H, s), 2.40 (1 H, q, $J = 8.4$ Hz), 2.02 (3 H, s), 1.96 (1H, dd, $J = 12.4, 5.6$ Hz) and 1.27 (1H, dd, $J = 7.2, 5.2$ Hz); δ_{C} (100 MHz; CDCl_3 , Me_4Si): 175.2 (s), 172.1 (s), 171.6 (s), 133.6 (d), 118.4 (t), 52.9 (q), 52.5 (q), 38.7 (s), 30.8 (d), 28.5 (d), 22.9 (q), 22.3 (t) and 20.7 (q); m/z (LC/MS, CI), retention time 1.07 minutes, 184 (100%, M+H); Found: (M+H) 184.0971. $\text{C}_9\text{H}_{14}\text{NO}_3$ requires 184.0974.

Preparation of (1*R, 2*S**)-5-(Trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**6b**).**



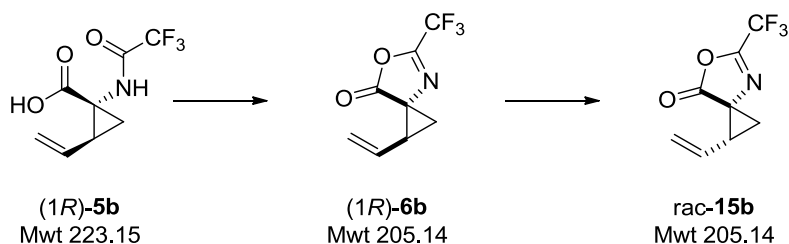
(1*R**, 2*S**)-Methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**5b**) (7.50 g, 33.6 mmol) and dicyclohexylcarbodiimide (6.94 g, 33.6 mmol) were stirred in acetonitrile (157 mL) at ambient temperature for 3 h. The solids were separated by filtration and the solvent was removed. The brown residue was distilled with a Kugelrohr apparatus (b.p. 56 - 60 °C, 3.5×10^{-1} mbar) to give the title compound as colourless oil (6.14 g, 89%). The azlactone rac-(**6b**) is not bench stable, but can be stored for months at -20 °C. ν_{\max} (NaCl plate, thin film): 1835, 1376, 1214, 1165, 1147, 1076, 1037, 977, 917, 881, 772 and 752 cm^{-1} ; δ_{H} (400 MHz; CDCl_3 , Me_4Si): 5.86 (1 H, ddd, $J = 16.8, 10.3, 8.9$ Hz), 5.43 (1 H, d, $J = 16.8$ Hz), 5.33 (1 H, d, $J = 10.4$ Hz), 3.01 (1 H, q, $J = 9.1$ Hz), 2.36 (1 H, dd, $J = 9.2, 5.6$ Hz) and 2.05 (1H, dd, $J = 8.8, 5.6$ Hz); δ_{H} (400 MHz; CD_3CN): 5.86 (1 H, dt, $J = 17.1, 9.7$ Hz), 5.43 (1 H, dd, $J = 17.1, 1.0$ Hz), 5.33 (1 H, d, $J = 10.4$ Hz), 3.01 (1 H, q, $J = 9.1$ Hz), 2.36 (1 H, dd, $J = 9.4, 5.6$ Hz) and 2.05 (1 H, dd, $J = 8.7, 5.7$ Hz); δ_{C} (100 MHz; CDCl_3 , Me_4Si) 172.1, 152.6 (q $J_{\text{C-F}} = 44$ Hz), 129.9, 120.6, 115.3 (q $J_{\text{C-F}} = 272$ Hz), 53.0, 37.8 and 26.3; δ_{C} (100 MHz; CD_3CN): 172.3 (s), 151.4, (s, q $J_{\text{C-F}} = 44$ Hz), 130.4 (d), 119.1 (t), 115.3 (s, $J_{\text{C-F}} = 271$ Hz), 52.9 (s), 37.0 (d) and 25.7 (t); δ_{F} (376 MHz; CDCl_3): -77.210; δ_{F} (376 MHz; CD_3CN): -77.203; m/z (EI) 205 (24%, M^+), 177 (100), 108 (47) and 82 (80). m/z (GC/MS): 14.68 min (5%, assigned to oxepane isomer **16**) (EI) 205 (48%, M^+), 177 (75), 110 (100), 108 (51) and 82 (100), 14.86 min (45%, assigned to 1st cyclopropane diastereoisomer (**6b**)/(**15b**)) m/z (EI) 205 (28%, M^+), 177 (100), 108 (50) and 82 (87) and 14.92 min (50%, assigned to 2nd cyclopropane diastereoisomer (**6b**)/(**15b**))⁶ m/z (EI) 205 (24%, M^+), 177 (100), 108 (47) and 82 (80).⁶

Isomerisation of (1*S, 3*R**)-1-Vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(**6b**).**



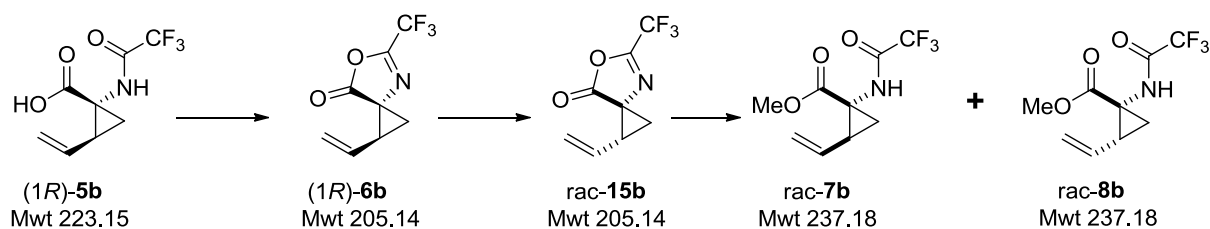
(1*R**, 3*S**)-1-Vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one (1*R*)-(**6b**) (50 mg × 2) was dissolved in CDCl₃ (0.5 mL) and CD₃CN (0.5 mL). Samples were heated to 65 °C for 30 h (CDCl₃) and 80 °C for 24 h (CD₃CN) after which partial conversion to (1*R**, 3*R**)-1-vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(**15b**) occurred. Ratios of **6b**:**15b** were 6.4:1 (CDCl₃) and 3.4:1 (CD₃CN). δ_{H} (400 MHz; CDCl₃, Me₄Si): 5.73 (1 H ddd, $J = 16.9, 10.0, 9.1$ Hz), 5.40 (1 H, d, $J = 16.8$ Hz), 5.29 (1 H, d, $J = 10.4$ Hz), 2.84 (1 H, q, $J = 8.9$ Hz), 2.22 (1 H, dd, $J = 9.0, 5.0$ Hz) and 2.15 (1 H, dd, $J = 8.8, 5.6$ Hz); δ_{H} (400 MHz; CD₃CN): 5.74 (1 H ddd, $J = 17.4, 10.5, 8.9$ Hz), 5.42 (1 H, d, $J = 17.2$ Hz), 5.28 (1 H, d, $J = 10.3$ Hz), 2.87 (1 H, q, $J = 8.9$ Hz), 2.19 (1 H, dd, $J = 8.4, 5.6$ Hz) and 2.17 (1 H, dd, $J = 9.4, 5.8$ Hz); δ_{C} (100 MHz; CDCl₃): 173.9 (s), 152.6, (s, q $J_{\text{C-F}} = 44$ Hz), 132.1 (d), 119.9 (t), 115.3 (s, $J_{\text{C-F}} = 271$ Hz), 52.8 (s), 38.5 (d) and 26.1 (t); δ_{C} (100 MHz; CD₃CN): 173.9 (s), 151.4, (s, q $J_{\text{C-F}} = 44$ Hz), 132.6 (d), 118.5 (t), 115.3 (s, $J_{\text{C-F}} = 271$ Hz), 52.8 (s), 37.7 (d) and 25.5 (t); δ_{F} (100 MHz; CDCl₃): -71.260; δ_{F} (100 MHz; CD₃CN): -72.190; m/z (GC/MS): 14.67 min (5%, assigned to oxepane isomer **16**) (EI) 205 (55%, M⁺), 177 (85), 110 (100), 108 (59) and 82 (100), 14.84 min (45%, assigned to 1st cyclopropane diastereoisomer (**6b**)/(**15b**)) m/z (EI) 205 (30%, M⁺), 177 (100), 108 (52) and 82 (100) and 14.92 min (50%, assigned to 2nd cyclopropane diastereoisomer (**6b**)/(**15b**)) m/z (EI) 205 (24%, M⁺), 177 (100), 108 (49) and 82 (100).⁶

Preparation and Isomerisation of (1*S*, 3*R*)-1-Vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one (1*S*)-(6b).



(1*R*, 2*S*)-2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic acid (1*R*)-(5b) (21 mg, 0.10 mmol) was dissolved in *d*₃-acetonitrile (0.5 mL). Dicyclohexylcarbodiimide (26 mg, 0.13 mmol) was added. A white precipitate formed rapidly. The suspension was filtered, the filtrate was placed in a sample tube. The ¹H NMR spectrum of (1*R*, 3*S*)-1-vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one (1*R*)-(6b) was recorded after standing the sample at room temperature for 2 h. After heating at 80 °C for 5 h, the ratio of (6b) and the diastereoisomer (1*R*^{*}, 3*R*^{*})-1-vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(15b) was 71:29. (1*R*^{*}, 3*R*^{*})-1-Vinyl-6-trifluoromethyl-5-oxa-7-azaspiro[2.4]heptan-5-en-4-one rac-(15b). δ_H (400 MHz; CD₃CN): visible signals 5.73 (1 H ddd, *J* = 17.2, 10.3, 8.8 Hz), 5.43 (1 H, d, *J* = 16.5 Hz), 5.28 (1 H, d, *J* = 10.5 Hz) and 2.86 (1 H, q, *J* = 8.9 Hz).

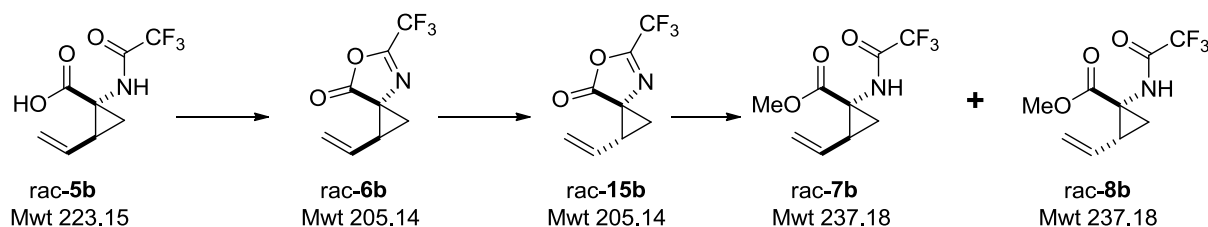
Preparation of (1*R*^{*}, 2*S*^{*})-Methyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(7b) from (1*R*, 2*S*)-Methyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic Acid (1*R*)-(5b).



(1*R*, 2*R*)-Methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate (1*R*)-(5b) (>99% ee, 300 mg, 1.34 mmol) was placed in a Schlenk flask. This was purged with nitrogen and acetonitrile (1 mL) was added. A solution of dicyclohexylcarbodiimide (333 mg, 1.61 mmol) in acetonitrile (2 mL) was added. A solution of potassium carbonate (50 mg, 0.36 mmol) in methanol (10 mL) was prepared. The reaction solution was stirred at room temperature (10 -

15 °C) and samples (3-4 drops) were withdrawn at intervals. Each sample was added to the methanol solution (200 μ L), the solution was allowed to stand for 10 minutes, the solvent was evaporated, toluene (0.5 mL) was added, the sample was filtered, the solvent was evaporated, the residue was dissolved in acetone and the sample was analysed by chiral GC to determine enantiomeric and diastereoisomeric excess. After 23 h, the enantiomeric excess was 13.6% and the diastereoisomeric excess was 98.8%. After 25 h, methanol (3 mL) and potassium carbonate (10 mg, 0.072 mmol) were added. The suspension was stirred for 1 h, filtered, most of the solvent was evaporated and toluene (5 mL) was added. The suspension was filtered, most of the solvent was evaporated and the crude product was purified by flash chromatography on silica eluting with heptane-ethyl acetate (80:20) to give (1*R*, 2*S*)-methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate (1*R*)-(**7b**) (12% ee, *cis/trans* (**7b**)/(**8b**) 189:1, *trans* isomer (**8b**) (racemic) as a colourless, mobile liquid which solidified on standing (224 mg, 70%). δ_{H} (400 MHz; CDCl_3 , Me_4Si): 7.0 (1 H, br s), 5.76 (1 H, ddd, $J = 17.2, 10.3, 8.7$ Hz), 5.36 (1 H, dd, $J = 17.2, 0.8$ Hz), 5.20 (1 H, dd, $J = 10.3, 1.0$ Hz), 3.74 (3 H, s), 1.95 (1 H, dd, $J = 9.8, 5.9$ Hz), 2.25 (1 H, q, $J = 8.9$ Hz), 1.95 (1 H, dd, $J = 8.3, 5.9$ Hz) and 1.64 (1 H, dd, $J = 9.8, 5.9$ Hz). δ_{C} (100 MHz; CDCl_3): 169.2 (s), 158.0 (s, $J_{\text{C-F}} = 37$ Hz), 132.4 (d), 119.1 (t), 115.6 (s, $J_{\text{C-F}} = 287$ Hz), 52.9 (q), 39.7 (s), 33.9 (d) and 22.7 (t). δ_{F} (376 MHz; CDCl_3): -76.040; m/z (ES⁻) 222 (33%, M-CH₃), 112 (10%) and 69 (100); Found: (M-CH₃) 222.0376. C₈H₇F₃NO₃ requires 222.0378.

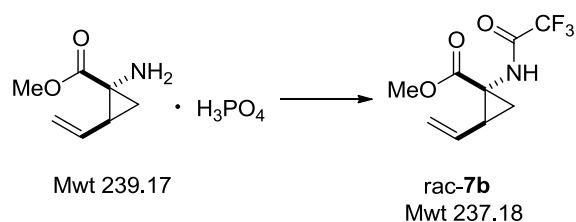
Preparation of (1*R, 2*R**)-Methyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**8b**) from (1*R**, 2*S**)-2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic Acid rac-(**5b**).**



(1*R**, 2*R**)-Methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**5b**) (200 mg, 0.90 mmol) was placed in a Schlenk flask. This was purged with nitrogen, and a solution of dicyclohexylcarbodiimide (221 mg, 1.08 mmol) in anhydrous acetonitrile (1.5 mL) was added. The suspension was heated to reflux for 4 h, cooled to room temperature and methanol (1.5

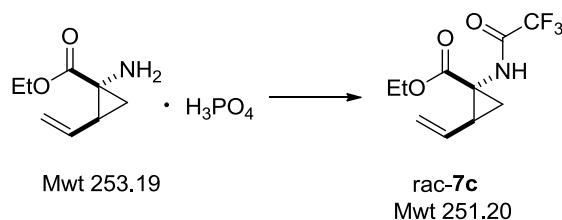
mL) and potassium carbonate (7.5 mg, 0.05 mmol) were added. The suspension was stirred at room temperature for 2 h. Citric acid (10 mg) was added, and the suspension was filtered. The solvent was evaporated and the crude product mixture was purified by flash chromatography on silica, eluting with ethyl acetate-heptane (80:20) to give (1*R**, 2*S**)-methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**7b**) (4:1 **7b**:**8b**) as a yellow, viscous oil (83 mg, 39%) and (1*R**, 2*R**)-methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**8b**) (10:1 **8b**:**7b**) as a pale yellow solid (51 mg, 24%). δ_{H} (400 MHz, CDCl₃, Me₄Si): 6.6 (br s, 1H), 5.52 (ddd, 1H, $J = 17.2, 10.0, 6.7$ Hz, 1H), 5.30 (d, 1H, $J = 17.2$ Hz), 5.29 (1 H, d, $J = 10.2$ Hz), 3.74 (3 H, s), 2.54 (1 H, q, $J = 8.3$ Hz), 2.02 (1 H, dd, $J = 9.4, 5.9$ Hz) and 1.38 (1 H, dd, $J = 7.7, 5.9$ Hz). δ_{C} (100 MHz; CDCl₃, Me₄Si): 170.5 (s), 158.2 (s, $J_{\text{C-F}} = 37$ Hz), 131.6 (d), 120.0 (t), 115.6 (s, $J_{\text{C-F}} = 287$ Hz), 53.0 (q), 38.3 (s), 31.0 (d) and 21.8 (t); δ_{F} (376 MHz, CDCl₃): -75.920. m/z (ES⁻) 222 (10%, M-CH₃), 112 (10%) and 69 (100); Found: (M-CH₃) 222.0368. C₈H₇F₃NO₃ requires 222.0378.

Preparation of (1*R**, 2*S**)-Methyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**7b**).



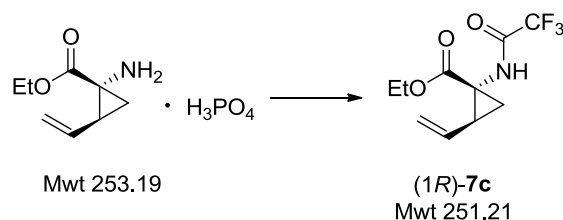
(1*R**, 2*S**)-Methyl 2-vinyl-1-aminocyclopropanecarboxylate phosphate salt² (2.39 g, 10.0 mmol) was dissolved in methanol (20 mL) and triethylamine (3.1 mL, 22 mmol) and ethyl trifluoroacetate (1.31 mL, 11.0 mmol) were added dropwise. After 3 h, additional ethyl trifluoroacetate (1.20 mL, 10.0 mmol) was added. After 4 h, brine (25 mL) was added and the solution was extracted with ethyl acetate (3 × 30 mL), dried (MgSO₄), filtered and the solvent was evaporated to give (1*R**, 2*S**)-methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**7b**) as a mobile, pale yellow oil (1.99 g, 89%). m/z (ES⁻) 222 (33%, M-CH₃) and 69 (10); Found: (M-CH₃) 222.0375. C₈H₇F₃NO₃ requires 222.0378.

Preparation of (1*R, 2*S**)-Ethyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-7c.**



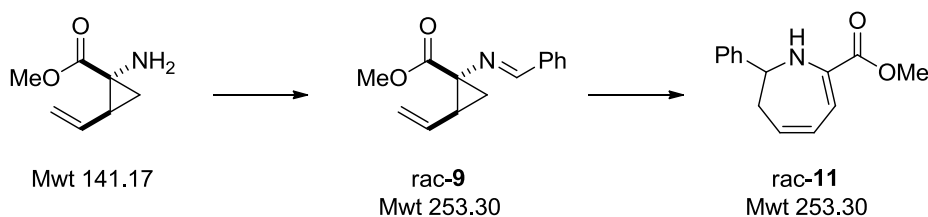
(1*R**, 2*S**)-Ethyl 2-vinyl-1-aminocyclopropanecarboxylate phosphate salt² (2.52 g, 9.95 mmol) was suspended in ethanol (10 mL) and triethylamine (2.08 mL, 14.9 mmol) and ethyl trifluoroacetate (1.42 mL, 11.9 mmol) were added dropwise. After 2 h, additional triethylamine (2.08 mL, 14.9 mmol) was added and the solution was stirred for 16 h. Most of the solvent was evaporated and MTBE (10 mL) and 1M orthophosphoric acid (20 mL) were added. The mixture was shaken and the layers were separated. The aqueous layer was extracted with MTBE (5 mL) and the combined organic layers were washed with saturated sodium bicarbonate solution (20 mL). The aqueous layer was extracted with MTBE (5 mL) and the combined organic layers were passed through a silica plug, eluting with MTBE, to give after evaporation of the solvent, (1*R**, 2*S**)-ethyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**7c**) as a mobile, pale yellow oil (2.27 g, 90%). ν_{\max} (KBr plate, thin film) 3307, 3087, 2988, 1714, 1640, 1539, 1446, 1396, 1374, 1320, 1257, 1180, 1016, 994, 919, 864, 775, 732, 666 and 626 cm^{-1} ; m/z (CI) 252 (100%, M+H); δ_{H} (400 MHz; CDCl_3): 6.9 (1 H, br s), 5.77 (1 H, ddd, $J = 18.1, 10.4, 7.5$ Hz), 5.35 (1 H, d, $J = 17.2$ Hz), 5.19 (1 H, dd, $J = 10.4, 1.6$ Hz), 4.26-4.12 (2H, m), 2.25 (1 H, q, $J = 8.8$ Hz), 1.94 (1 H, dd, $J = 8.4, 6.0$ Hz), 1.64 (1 H, dd, $J = 9.6, 6.0$ Hz) and 1.25 (1 H, dd, $J = 7.2$ Hz); δ_{C} (100 MHz; CDCl_3) 168.6 (s), 157.9 (s, q $J_{\text{C-F}} = 37$ Hz), 132.4 (d), 119.0 (t), 115.6 (s, $J_{\text{C-F}} = 287$ Hz), 62.0 (t), 39.7 (s), 33.7 (d), 22.4 (t) and 14.0 (q); δ_{F} (376 MHz, CDCl_3) -76.124; Found: (ES⁺) (M+H) 252.0839. $\text{C}_8\text{H}_8\text{F}_3\text{NO}_3$ requires 252.0848; Found: C 47.5%, H 4.4%, N 5.6%. $\text{C}_8\text{H}_8\text{F}_3\text{NO}_3$ requires C 47.8%, H 4.8%, N 5.6%.

Preparation of (1*R*, 2*S*)-Ethyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate (1*R*)-(7*c*).



(1*R*, 2*S*)-Ethyl 2-vinyl-1-aminocyclopropanecarboxylate^{2,4} phosphate salt (1.0 g, 3.9 mmol) was dissolved in methanol, then triethylamine (2.7 mL, 8.6 mmol) was added and ethyl trifluoroacetate (2.3 mL, 8.6 mmol) was added dropwise. The solution was stirred overnight, then saturated ammonium chloride solution (20 mL) was added and the mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent was evaporated to give (1*R*, 2*S*)-ethyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate (1*R*)-(7*c*) as a pale yellow, mobile liquid (980 mg, 99%). δ_{H} (400 MHz; CDCl₃, Me₄Si): 6.83 (1 H, br s), 5.77 (1 H, ddd, $J = 17.2, 10.6, 8.6$ Hz), 5.35 (1 H, ddd, $J = 17.1, 1.7, 0.7$ Hz), 5.20 (1 H, dd, $J = 10.5, 1.6$ Hz), 4.26 - 4.13 (2 H, m), 2.25 (1 H, q, $J = 8.9$ Hz), 1.95 (1 H, dd, $J = 8.6, 5.8$ Hz); 1.65 (1 H, dd, $J = 9.8, 6.2$ Hz) and 1.26 (3 H, $J = 7.2$ Hz).

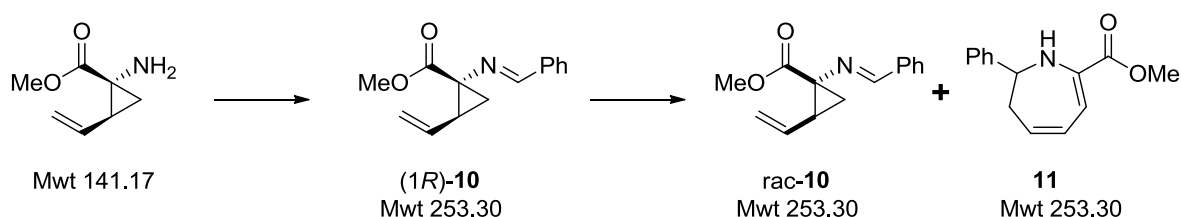
Isomerisation of (1*R**, 2*S**)-Methyl 2-Vinyl-1-(benzylideneamino)cyclopropanecarboxylate¹ (9) to Methyl 7-Phenyl-6,7-dihydro[1*H*]azepine-2-carboxylate¹ rac-(11).



An MTBE solution of (1*R**, 2*S**)-methyl 2-vinyl-1-aminocyclopropanecarboxylate¹ was prepared as described in the preparation of (1*R*)-5*b* from the (1*R*, 2*S*)-tosylate salt using (1*R**, 2*S**)-methyl 2-vinyl-1-aminocyclopropanecarboxylate phosphate salt⁵ (1.00 g, 3.92 mmol) and MTBE (5 × 5 mL). The MTBE solution was evaporated to ~5 mL and benzaldehyde (400 μ L, 3.92 mmol) and magnesium sulfate (0.5 mL) were added. The solution was stirred under nitrogen at room temperature for 64 h. A small sample was evaporated, and the ¹H NMR spectrum in C₆D₆, showing a 9:1 ratio of imine rac-(9) : benzaldehyde was recorded;

δ_{H} (C_6D_6 , 400 MHz) 8.37 (1 H, s), 7.83 (2 H, dd, $J = 10.2, 3.0$ Hz), 7.24-7.19 (3 H, m), 6.05 (1 H, ddd, $J = 17.0, 10.3, 8.9$ Hz), 5.27 (1 H, ddd, $J = 17.1, 1.6, 0.5$ Hz), 5.16 (1 H, dd, $J = 10.2, 1.5$ Hz), 3.48 (3 H, s), 2.33 (1 H, q, $J = 8.2$ Hz), 2.15 (1 H, dd, $J = 8.2, 5.2$ Hz) and 1.61 (1 H, dd, $J = 9.3, 5.2$ Hz). The C_6D_6 solution was heated to 80 °C and the sample was cooled and the ^1H NMR spectrum was recorded at intervals. After 13.5 h, a 7:93 ratio of imine rac-(**9**) and methyl 7-phenyl-6,7-dihydro[1H]azepine-2-carboxylate rac-(**11**) was present. The solvent was evaporated from the sample, CDCl_3 was added and the ^1H NMR spectrum was recorded; δ_{H} (400 MHz; C_6D_6): 7.25-7.05 (4 H, m), 6.34 (1 H, dd, $J = 7.9, 1.7$ Hz), 6.11 (1 H, ddd, $J = 11.0, 8.2, 2.6$ Hz), 5.81 (1 H, ddd, $J = 11.2, 7.4, 4.0$ Hz), 5.6 (1 H, br s), 4.14 (1 H, d, $J = 7.4$ Hz), 3.55 (3 H, s), 2.84-2.75 (1 H, m) and 2.53 (1 H, dd, $J = 17.2, 7.3$ Hz); δ_{H} (400 MHz; CDCl_3 , Me_4Si): 7.37-7.20 (5 H, m), 6.03-5.84 (3 H, m), 5.19 (1 H, br s), 4.14 (1 H, d, $J = 7.4$ Hz), 3.76 (3 H, s), 2.87-2.78 (1 H, m) and 2.67 (1 H, ddt, $J = 17.5, 7.4, 1.5$ Hz).

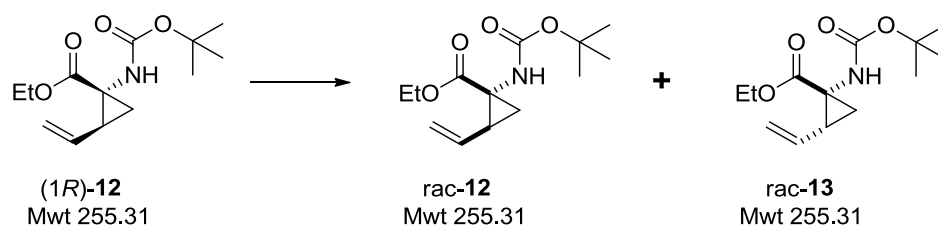
Isomerisation of (1*R*, 2*S*)-Methyl 2-Vinyl-1-(benzylideneamino)cyclopropanecarboxylate (1*R*)-(10).



An MTBE solution of (1*R*, 2*S*)-methyl 2-vinyl-1-aminocyclopropanecarboxylate (>99% ee) was prepared as described from (1*R*, 2*S*)-methyl 2-vinyl-1-aminocyclopropanecarboxylate tosylate salt (1*R*)-(7). TsOH (1.00 g, 3.19 mmol) and MTBE (4×5 mL) instead of 2-methyltetrahydrofuran. The MTBE solution was evaporated to ~5 mL and benzaldehyde (324 μL , 3.19 mmol) and magnesium sulfate (0.5 mL) were added. The solution was stirred under nitrogen at room temperature for 16 h. Toluene (10 mL) was added, the suspension was filtered and the solvent was evaporated to ~10 mL. The solution was heated to 80 °C and samples of ~50 μL were withdrawn at intervals. The enantiomeric excess of the imine (**10**) in the sample was determined by conversion to methyl 2-vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate^{1,7} as follows: to the sample was added 1M hydrochloric acid (1 mL) and toluene (0.5 mL), and the mixture was stirred at room temperature for 2 h. The aqueous phase was basified with 10% sodium carbonate solution (2 mL) and extracted with MTBE (4×1 mL). The combined organic layers were dried

(Na₂SO₄), filtered and di-*tert*-butyl dicarbonate (50 mg, 0.09 mmol) was added. The solvent was evaporated, and THF (5 drops) was added. The solution was stirred for 16 h and the solution was analysed by chiral GC. After 2 h, the enantiomeric excess was 98.1% and the ratio of (1*R*, 2*S*)-methyl 2-vinyl-1-(benzylideneamino)cyclopropanecarboxylate (**10**): methyl 7-phenyl-6,7-dihydro[1*H*]azepine-2-carboxylate (**11**) by ¹H NMR was 1:5.

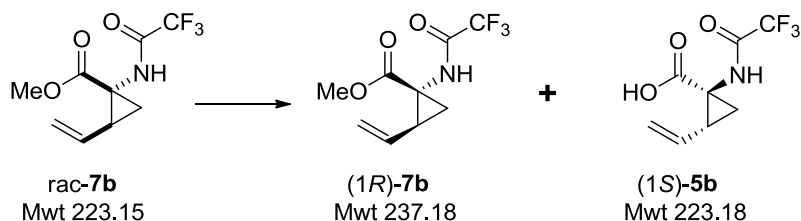
Isomerisation of (1*R*, 2*S*)-Ethyl 2-Vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate¹ (1*R*)-(12) to (1*R, 2*S**)-Ethyl 2-Vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate⁸ rac-(13).**



A solution of (1*R*, 2*S*)-ethyl 2-vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate (1*R*)-(12) (97.9%ee, 130 mg, 0.5 mmol) in *ortho*-dichlorobenzene (1.5 mL) was heated under nitrogen for 16 h, after which the enantiomeric excess of (12) by chiral GC was 91.7% and the diastereoisomeric ratio (12)/(13) was 38.3 : 61.7. The solution was applied to a silica plug packed in dichloromethane-ethyl acetate (95:5). Elution with dichloromethane-ethyl acetate (95:5) followed by heptane-ethyl acetate (70:30) gave a crude mixture of isomers (3:5) as a yellow solid (122 mg). Heptane (0.5 mL) was added, the suspension was stirred for 2 h, filtered, the solid was washed with heptane and dried to give (1*R**, 2*S**)-ethyl 2-vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate rac-(13) as a white solid (20 mg, 15%). (1*R*, 2*S*)-Ethyl 2-vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate (1*R*)-(12). ν_{\max} (KBr plate, thin film) 3360, 2979, 2933, 1727, 1713, 1505, 1392, 1318, 1182, 1250, 1092, 1048, 1029, 996, 907 and 782 cm⁻¹; δ_{H} (400 MHz; CDCl₃, Me₄Si): 5.76 (1 H, ddd, $J = 17.1, 10.3, 8.9$ Hz), 5.6 and 5.2 (1 H, 2 br s), 5.28 (1 H, d, $J = 17.1$ Hz), 5.13 (1 H, dd, $J = 10.3, 1.7$ Hz), 4.24-4.13 (2 H, m), 2.12 (1 H, q, $J = 8.8$ Hz), 1.84-1.70 (1 H, m), 1.46-1.43 (1 H, m), 1.45 (9 H, s) and 1.26 (3 H, t, $J = 6.9$ Hz); δ_{C} (CDCl₃; 100 MHz, Me₄Si): 170.9 (s), 155.8 (s), 133.8 (d), 117.6 (t), 80.0 (s), 61.3 (t), 40.8 (s), 34.1 (d), 28.3 (q), 23.2 (t) and 14.3 (q), $[\alpha]_{\text{D}}^{20} = +37.0^{\circ}$ ($c = 1.02$, CHCl₃). m/z (CI) 256 (5%, M+H), 200 (71) and 156 (100); Found: (M+Na) 278.1366. C₁₃H₂₁NO₄ requires 278.1368. (1*R**, 2*S**)-Ethyl 2-vinyl-1-(*tert*-

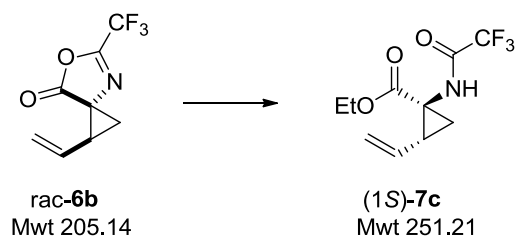
butoxycarbonylamino) cyclopropanecarboxylate rac-(**13**) δ_{H} (400 MHz; CDCl_3 , Me_4Si): 5.39 (1 H, dt, $J = 17.1, 9.0$ Hz), 5.27 (1 H, dd, $J = 17.1, 1.0$ Hz), 5.17 (1 H, dd, $J = 10.3, 1.2$ Hz), 4.9 and 4.7 (2 br s, 1 H), 4.20-4.11 (2 H, m), 2.35 (1 H, q, $J = 8.0$ Hz), 1.95-1.86 (m) and 1.83-1.73 (m) (1 H), 1.45 (9 H, s), 1.25 (3 H, t, $J = 6.9$ Hz) and 1.30-1.22 (m) and 1.15-1.08 (m) (1 H); δ_{C} (100 MHz; CDCl_3 , Me_4Si): 172.3 (s), 156.0 (s), 134.0 (d), 118.2 (t), 80.0 (s), 61.5 (t), 40.0 (s), 39.6 (s), 32.0 (d), 31.2 (d), 28.3 (q), 23.6 (t), 22.9 (t) and 14.2 (q); m/z (CI) 256 (5%, M+H), 200 (71) and 156 (100). Found: (M+Na) 278.1355. $\text{C}_{13}\text{H}_{21}\text{NO}_4$ requires 278.1368.

Resolution of (1*R, 2*S**)-Methyl 2-Vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**7b**) with Subtilisin A.**



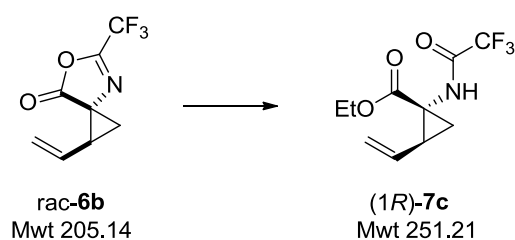
(1*R**, 2*S**)-Methyl 1-(2,2,2-trifluoroacetamido)-2-vinylcyclopropanecarboxylate rac-(**7b**) (1.00 g, 4.20 mmol) was dissolved in DMSO (1.0 mL) and added to potassium phosphate buffer (50 mL, pH 7.0, 0.1M). Subtilisin A (150 mg, 15 wt%) was added and the reaction was stirred at 25 °C for 24 h. The pH was kept at 7.0 by addition of 1 M NaOH. After 24 h GC-control showed full conversion with 99%ee. The reaction mixture was extracted with EtOAc (3 × 30 mL) and the combined organic layers were washed with half concentrated brine (3 × 50 mL), dried over MgSO_4 and concentrated to give enantio-enriched methyl ester (1*S*)-(**7b**) (465 mg, 93%, 99%ee). The aqueous layer was then acidified with 1 M HCl to pH 1 and extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over MgSO_4 to give (1*S*,2*R*)-1-(2,2,2-trifluoroacetamido)-2-vinylcyclopropanecarboxylic acid (1*S*)-(**5b**) (380 mg, 38%, 97.4%ee).

Ethanolysis of (1*R, 2*S**)-5-(Trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(6b) with Novozym 435 to give (1*S*, 2*R*)-Methyl 2-Vinyl-1-(trifluoroacetamido) cyclopropanecarboxylate (1*S*)-(7c).**



(1*R**, 2*S**)-5-(Trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(6b) (1.00 g, 4.88 mmol) was dissolved in MTBE (50 mL) and EtOH (500 μ L). Novozym 435 (Immobilised *Candida antarctica* lipase B, 1.00 g, 100 wt%) was added and the reaction was stirred at 25 $^{\circ}$ C, 250 rpm for 264 h in a 100 mL EasyMax reactor system. 7 min The immobilised enzyme was removed by filtration and washed with MTBE (2 \times 20 mL). The filtrate was concentrated to give the title compound as pale oil (1.16 g, 97%, 95%ee); $[\alpha]_D^{20} = -54.0^{\circ}$ (c = 1.0, MeOH).

Ethanolysis of (1*R, 2*S**)-5-(Trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(6b) with Lipase PS to give (1*R*, 2*S*)-Methyl 2-Vinyl-1-(trifluoroacetamido) cyclopropanecarboxylate (1*R*)-(7c).**



(1*R**, 2*S**)-5-(Trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(6b) (1.00 g, 4.88 mmol) was dissolved in MTBE (50 mL) and EtOH (500 μ L). Amano Lipase PS IM (1.00 g, 100 wt%) was added and the reaction was stirred at 25 $^{\circ}$ C, 250 rpm for 432h in a 100 mL EasyMax reactor system. The immobilised enzyme was removed by filtration and washed with MTBE (2 \times 20 mL). The filtrate was concentrated to give the title compound as pale oil (1.15 g, 96%, 75%ee); $[\alpha]_D^{20} = +35.9^{\circ}$ (c = 1.0, MeOH).

GC Analytical Method for (7a) and (8a).

Instrument: Perkin-Elmer Autostystem Gas Chromatograph.

Column: Chirasil DEX CB (25 m × 0.25 mm, 0.25 μm).

Helium Pressure: 20 psi.

Injector: 220 °C

Detector: 200 °C.

Oven Programme: 135 °C for 20 minutes.

(8a) enantiomer 1: 8.5 minutes.

(8a) enantiomer 2: 8.6 minutes.

(1S)-(7a): 10.7 minutes.

(1R)-(7a): 11.1 minutes.

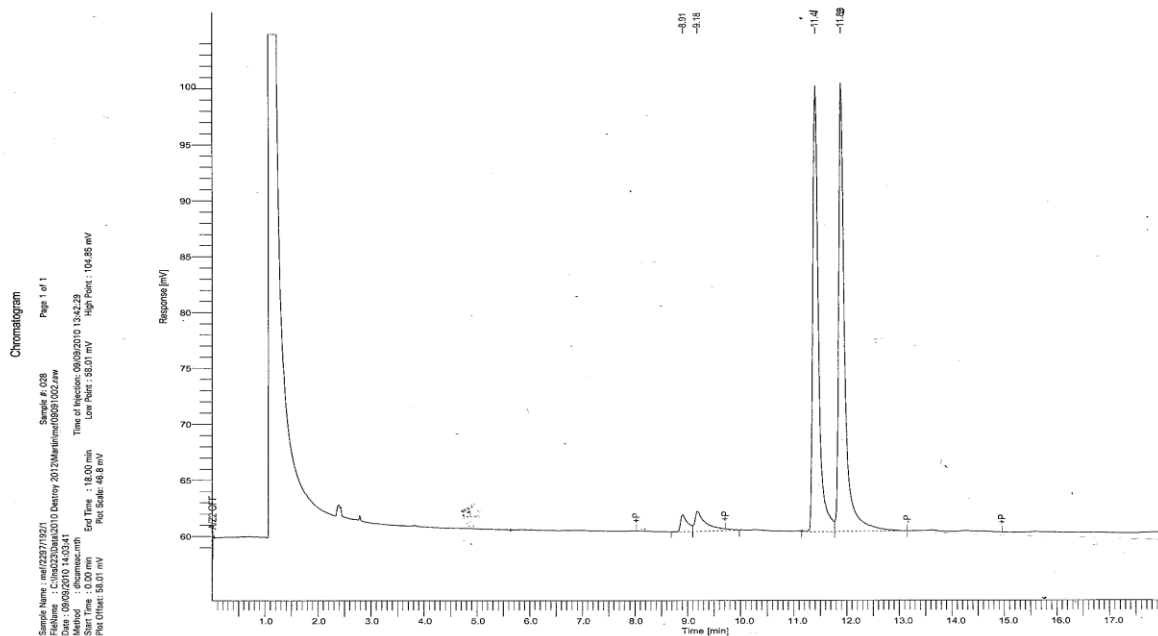


Fig S1 GC Chromatogram of racemic (7a).

GC Analytical Method for (7b) and (8b).

Instrument: Agilent 6890N Gas Chromatograph.

Column: Chirasil DEX CB (25 m × 0.25 mm, 0.25 μm).

Helium Pressure: 20 psi.

Injector: 220 °C

Detector: 200 °C.

Oven Programme: 100 °C for 20 minutes.

Retention Times:

(8b) enantiomer 1: 12.1 minutes

(8b) enantiomer 2: 12.8 minutes

(1S)-(7b): 15.3 minutes.

(1R)-(7b): 15.8 minutes.

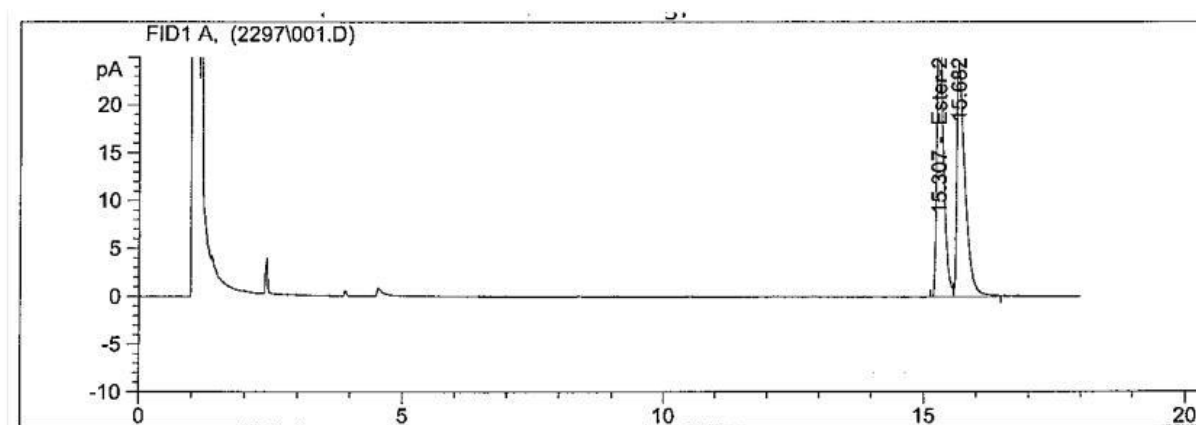


Fig S4 GC Chromatogram of racemic (7b).

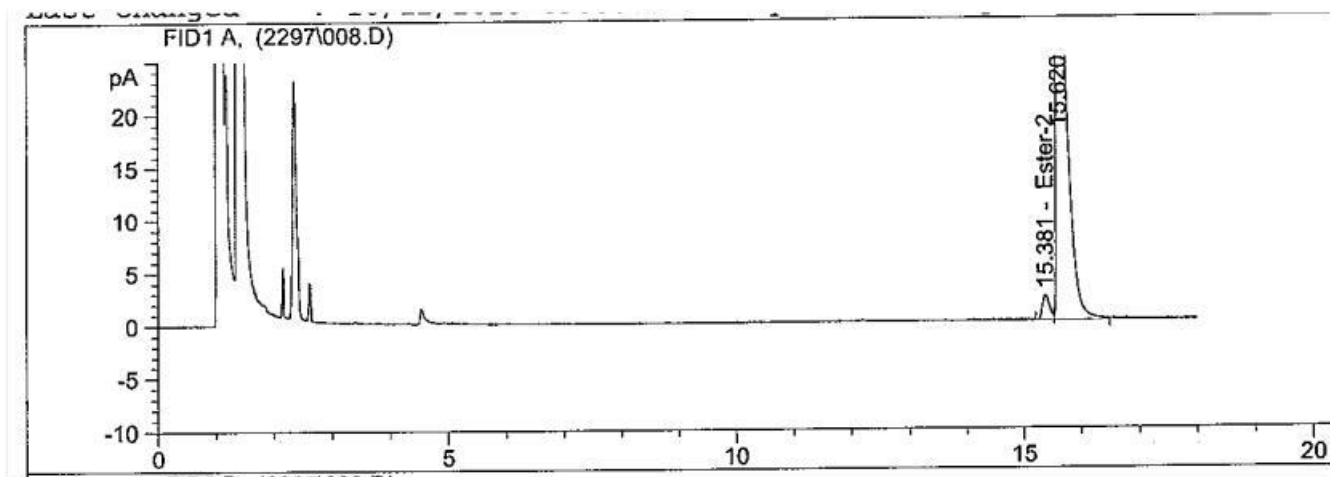


Fig S5 GC Chromatogram of 94%ee (**7b**) from methanolysis of partly isomerised (1*R*)-(**6b**).

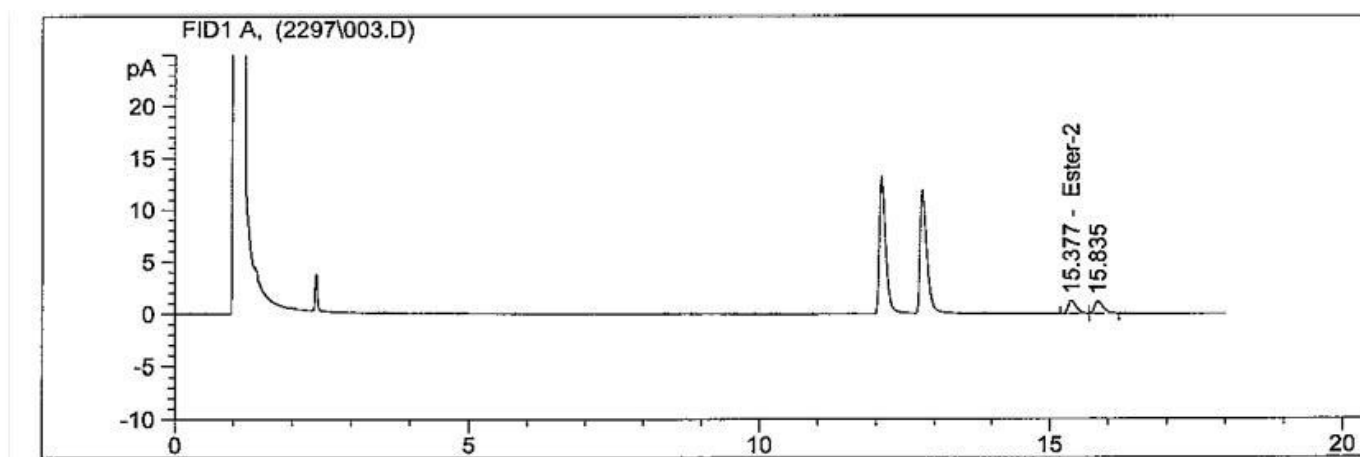


Fig S6 GC Chromatogram of racemic (**7b**)+(**8b**) (1:10).

GC Analytical Method for (7c).

Instrument: Agilent 6890N Gas Chromatograph.

Column: Chirasil DEX CB (25 m × 0.25 mm, 0.25 μm).

Helium Pressure: 20 psi.

Injector: 220 °C

Detector: 200 °C.

Oven Programme: 100 °C for 25 minutes.

Retention times:

(1*S*, 2*R*)-(7c): 22.2 min

(1*R*, 2*S*)-(7c): 23.8 min

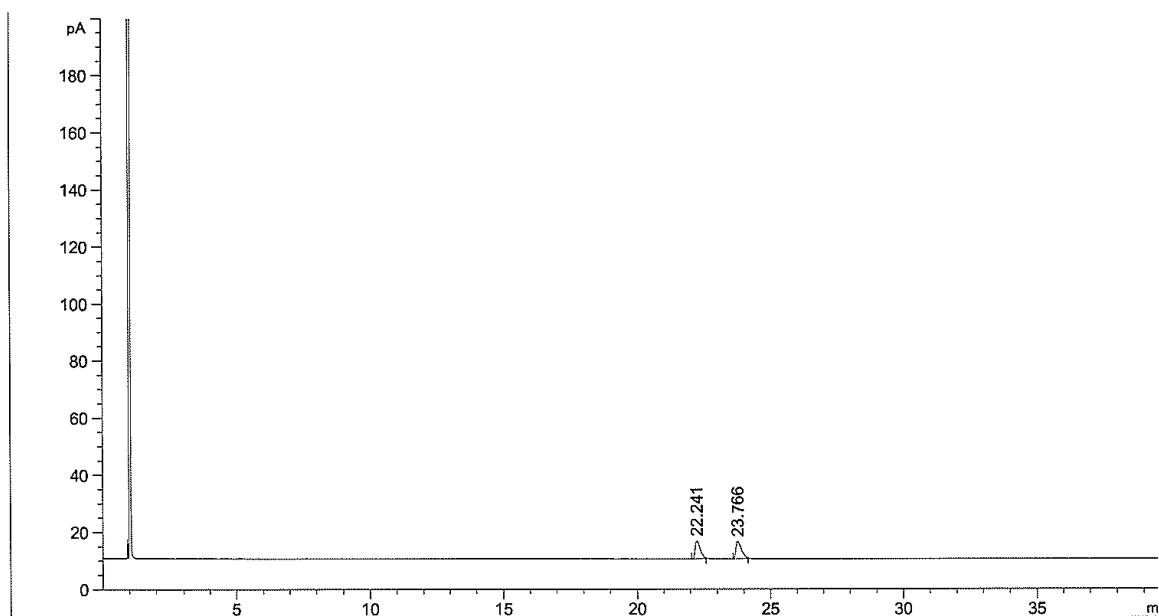


Fig S7 GC Chromatogram of racemic (7c).

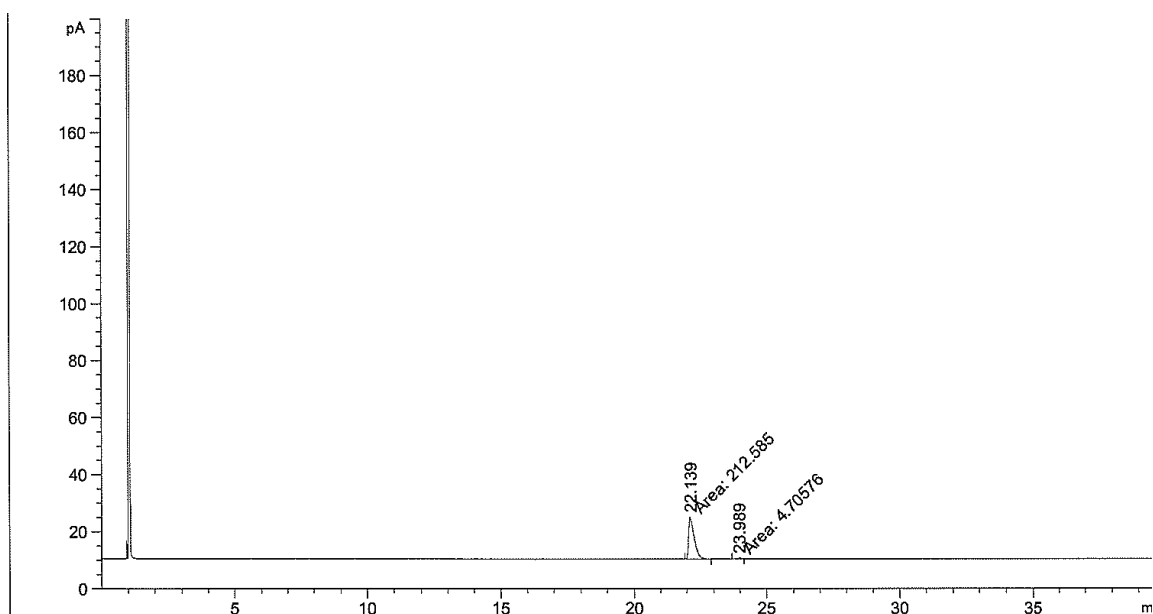


Fig S8 GC Chromatogram of (1*S*)-(7c) (95.6% ee).

GC Analytical Method for (12) and (13).

Instrument: Perkin-Elmer Autostystem Gas Chromatograph.

Column: Chirasil DEX CB (25 m × 0.25 mm, 0.25 μm).

Helium Pressure: 20 psi.

Injector: 220 °C

Detector: 200 °C.

Oven Programme: 145 °C for 20 minutes.

Retention Times:

(13): 8.5 minutes.

(1*S*)-(12): 10.5 minutes.

(1*R*)-(12): 11.5 minutes.

Chromatogram

Sample Name: Racemic_V03163603
 Sample #: 028
 File Name: C:\msdcs\DATA\2010\DATA\20101007_19101007_1.rw
 Date: 19/10/2010 11:38:51
 Method: 100.m
 Start Time: 18.00 min
 End Time: 18.00 min
 Time of Injection: 19/10/2010 11:45:23
 Run Time: 02.00 min
 Low Point: 57.62 mV
 High Point: 86.25 mV
 Plot Offset: 57.62 mV
 Plot Scale: 28.6 mV

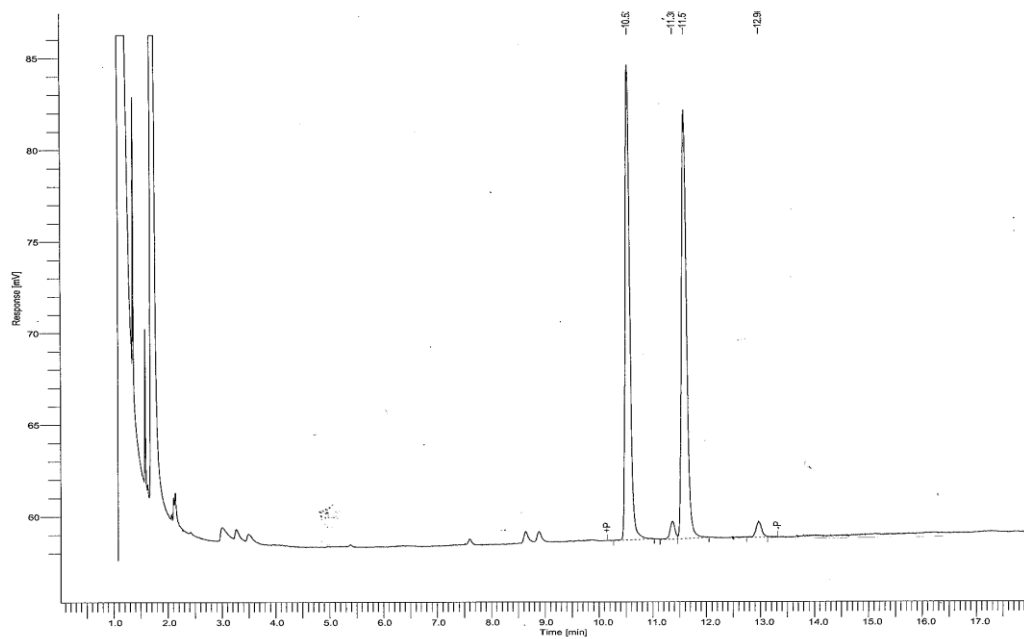


Fig S9 GC Chromatogram of racemic (12).

Chromatogram

Sample Name: _JP72262(2401)
 Sample #: 029
 File Name: C:\msdcs\DATA\2010\DATA\20101007_19101007_1.rw
 Date: 19/10/2010 12:00:09
 Method: 100.m
 Start Time: 18.00 min
 End Time: 18.00 min
 Time of Injection: 19/10/2010 11:38:09
 Run Time: 01.20 min
 Low Point: 55.09 mV
 High Point: 116.25 mV
 Plot Offset: 55.09 mV
 Plot Scale: 61.2 mV

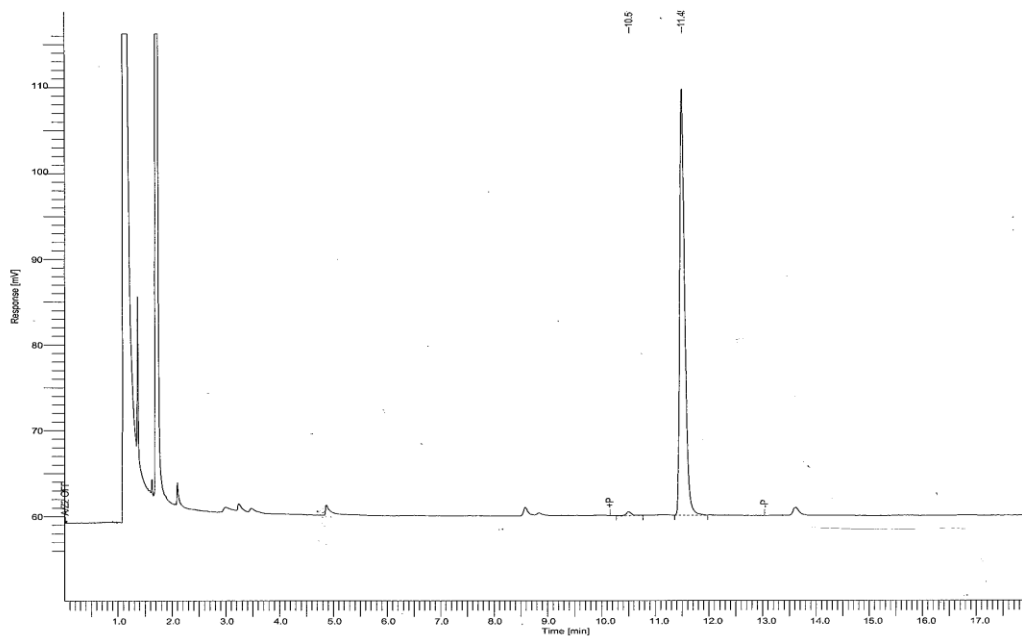


Fig S10 GC Chromatogram of 98% ee (1R)-(12).

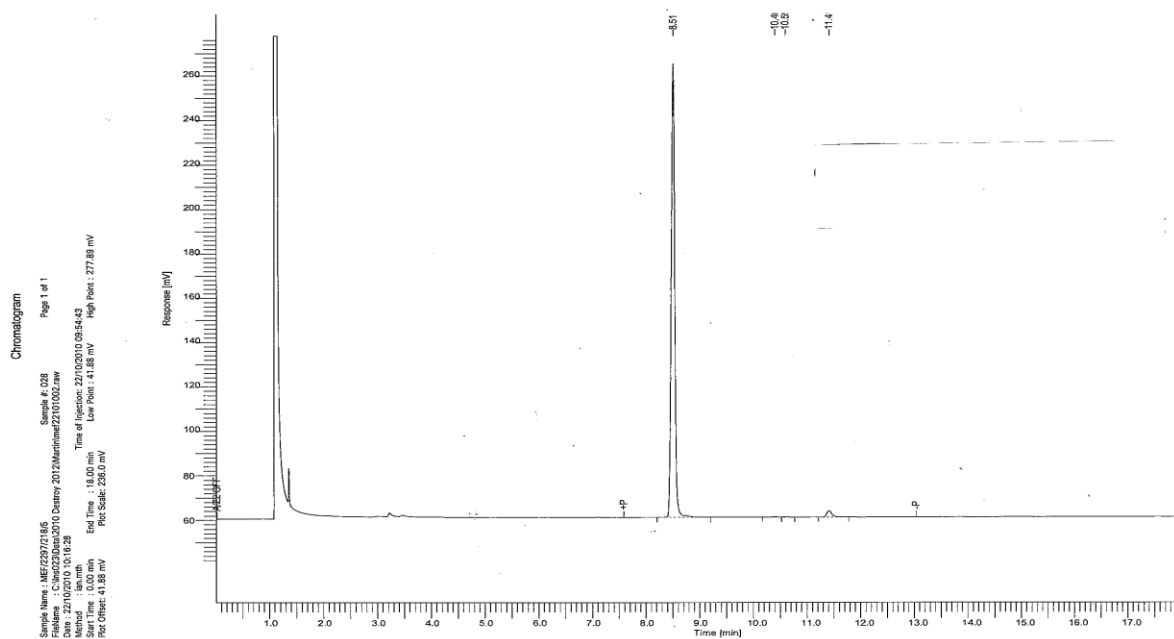


Fig S11 GC Chromatogram of **(13)**.

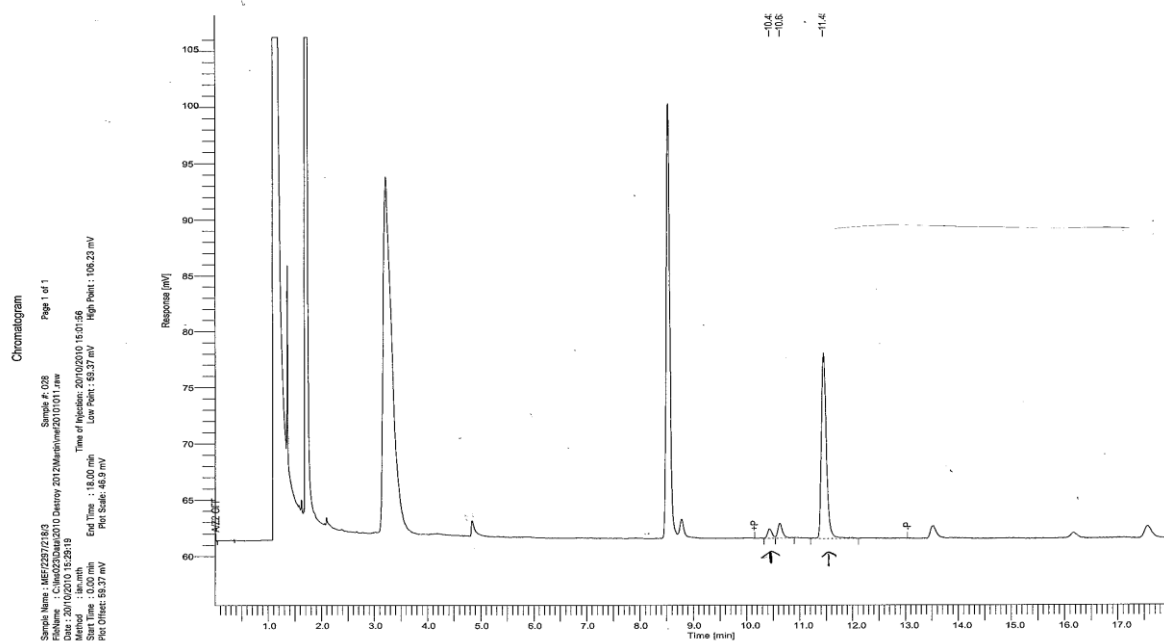


Fig S12 GC Chromatogram of partially isomerised **(1R)**-**(12)** (91% ee), 40:60 ratio of **(12)** to **(13)**.

GC Analytical Methods for **(5a)** and **(5b)**.

The sample was dissolved in methanol, derivatised to the corresponding methyl ester with (trimethylsilyl)diazomethane, diluted with acetone and analysed according to the appropriate method for the methyl esters **(8a)** and **(8b)** described above.

GC/MS Method

Instrument: Thermo Trace 1300 Gas Chromatograph coupled to Thermo ISQLT Mass Spectrometer.

Column: VF Wax (30 m × 0.25 mm, 0.25 µm).

Flow rate: 1.2 mL / min.

Injector: 220 °C

Detector: 180 °C.

Oven Programme: 40 °C for 10 minutes, then ramp at 20 °C / min for 7 minutes.

High Resolution LC/MS Electrospray Ionization Conditions

Instrument: Waters Synapt G2 q-TOF

Capillary Voltage: 2.5kV

Cone Voltage: 30V

Extraction Cone: 4V

Source Temp: 130 °C

Desolvation Gas Flow: 1000Lhr⁻¹

Cone Gas Flow: 100Lhr⁻¹

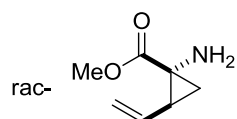
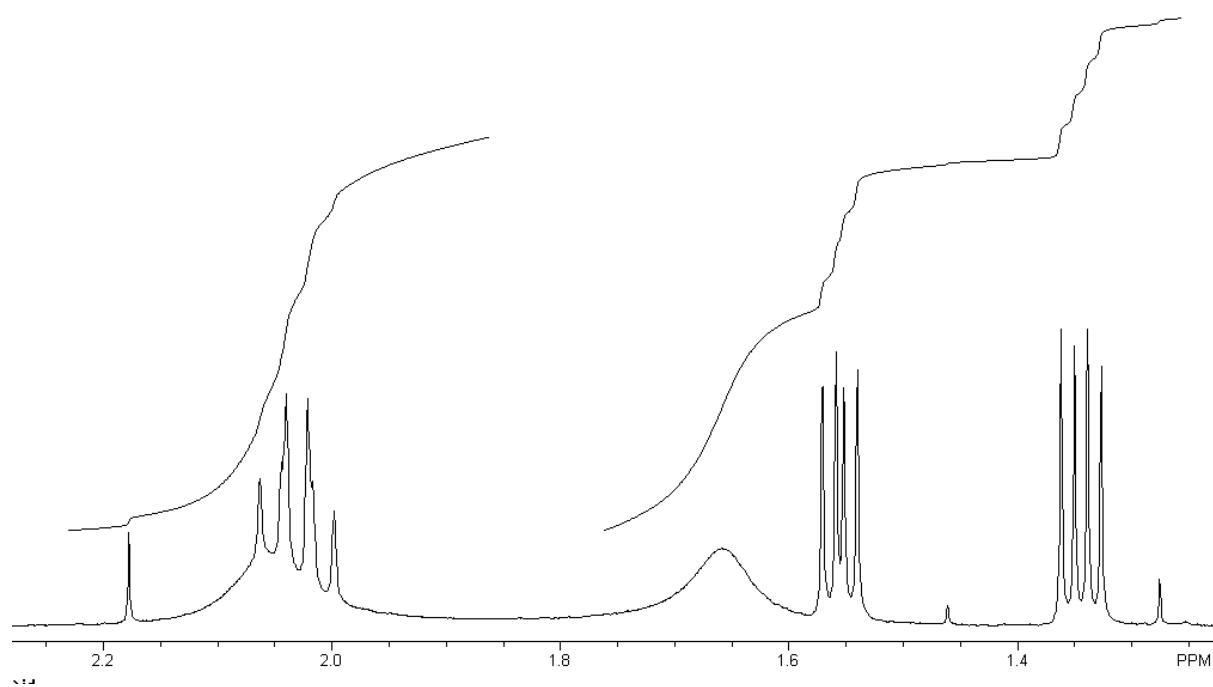
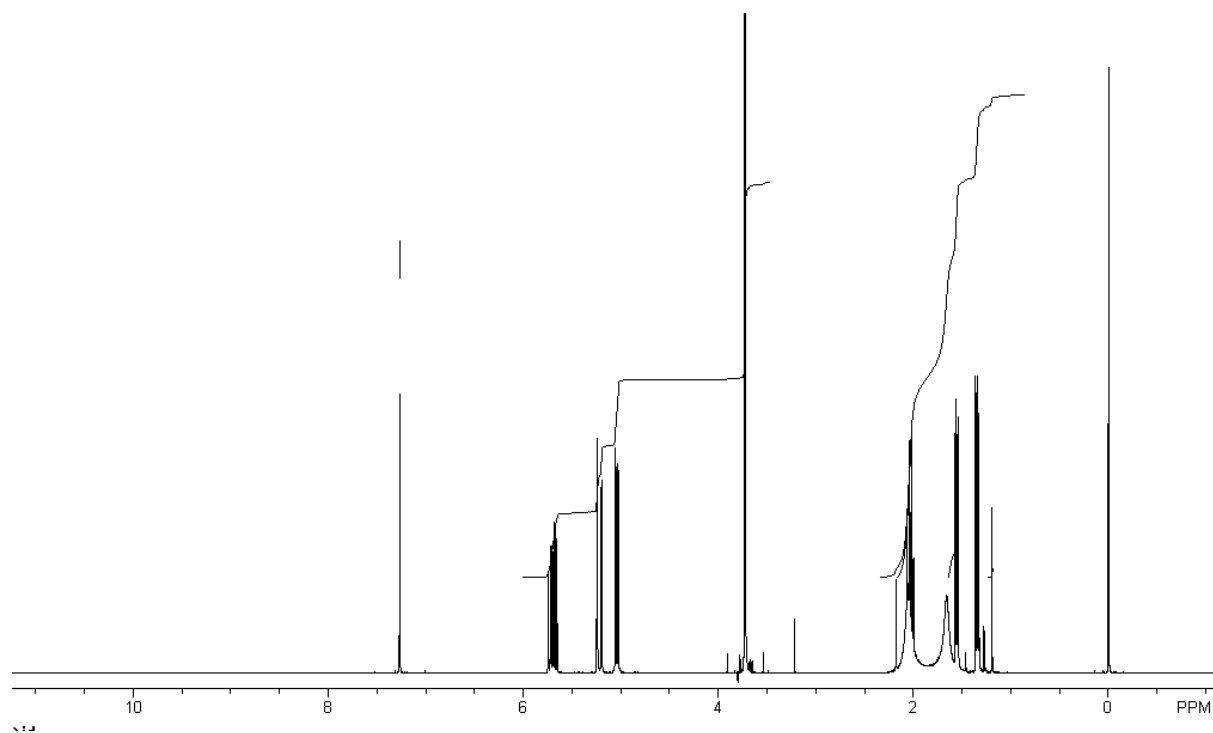
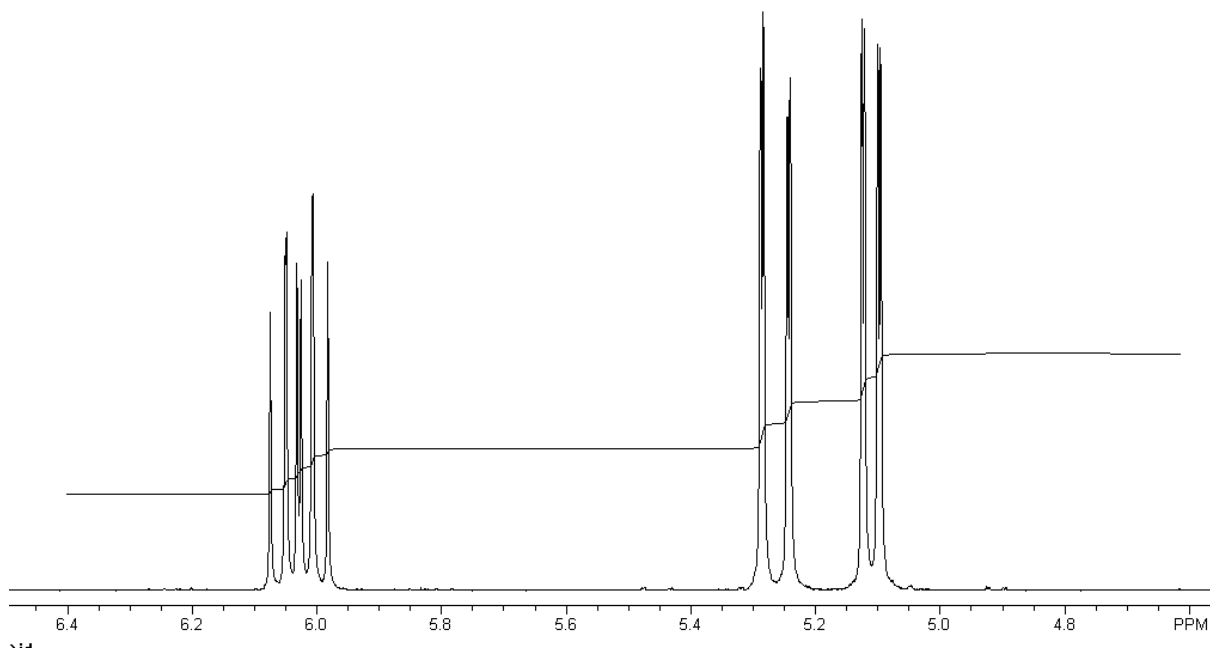
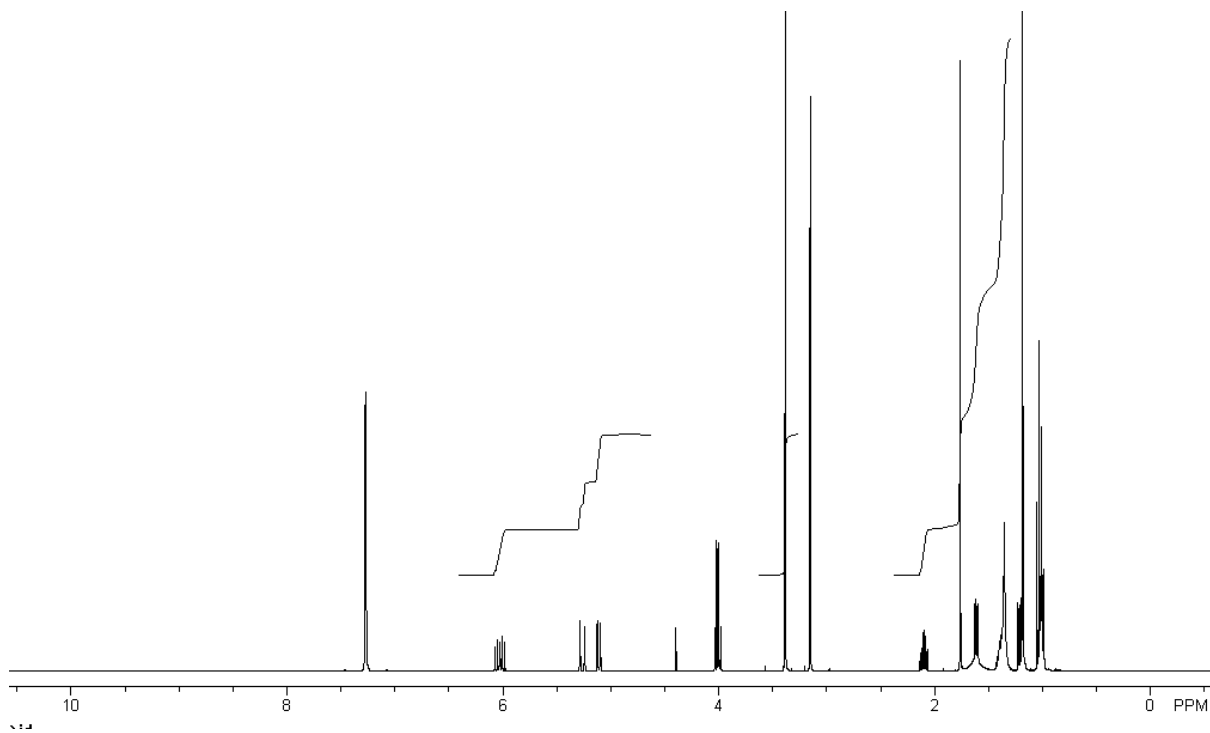


Fig S13 ^1H NMR spectrum and expansions of (1*R**, 2*S**)-methyl 2-vinyl-1-aminocyclopropanecarboxylate (400 MHz; CDCl_3 , Me_4Si).



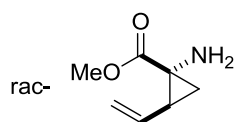
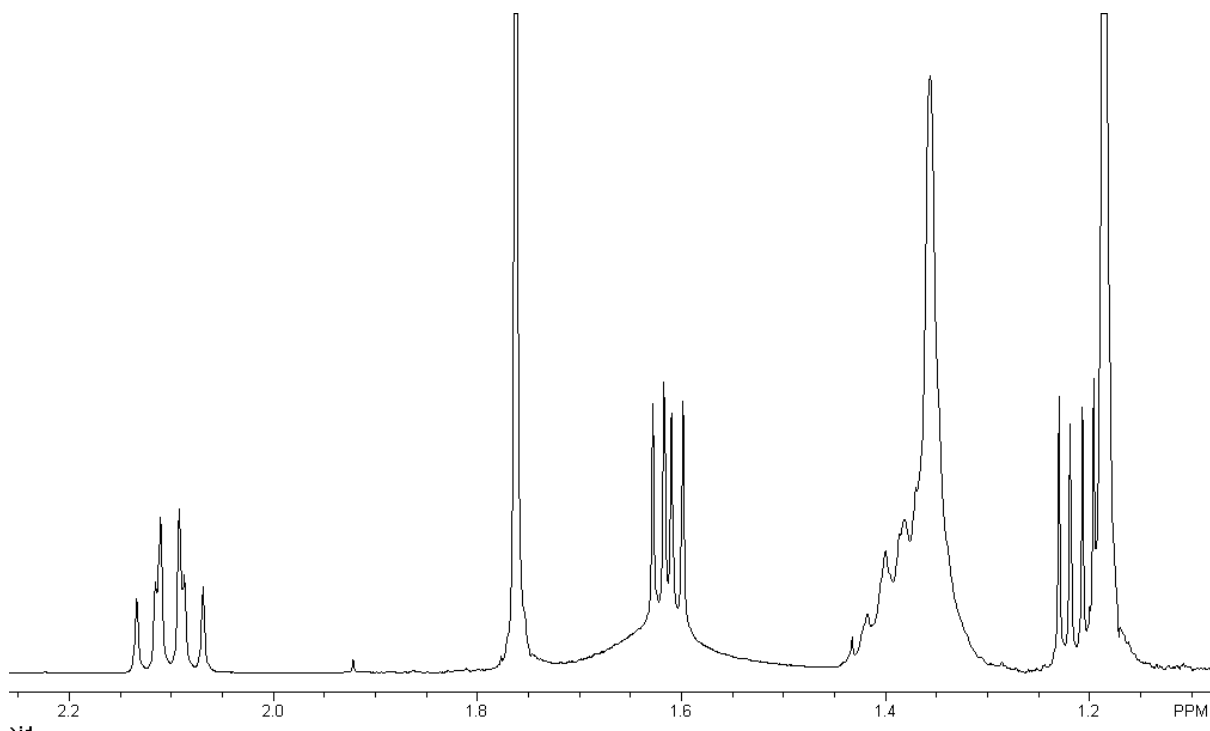
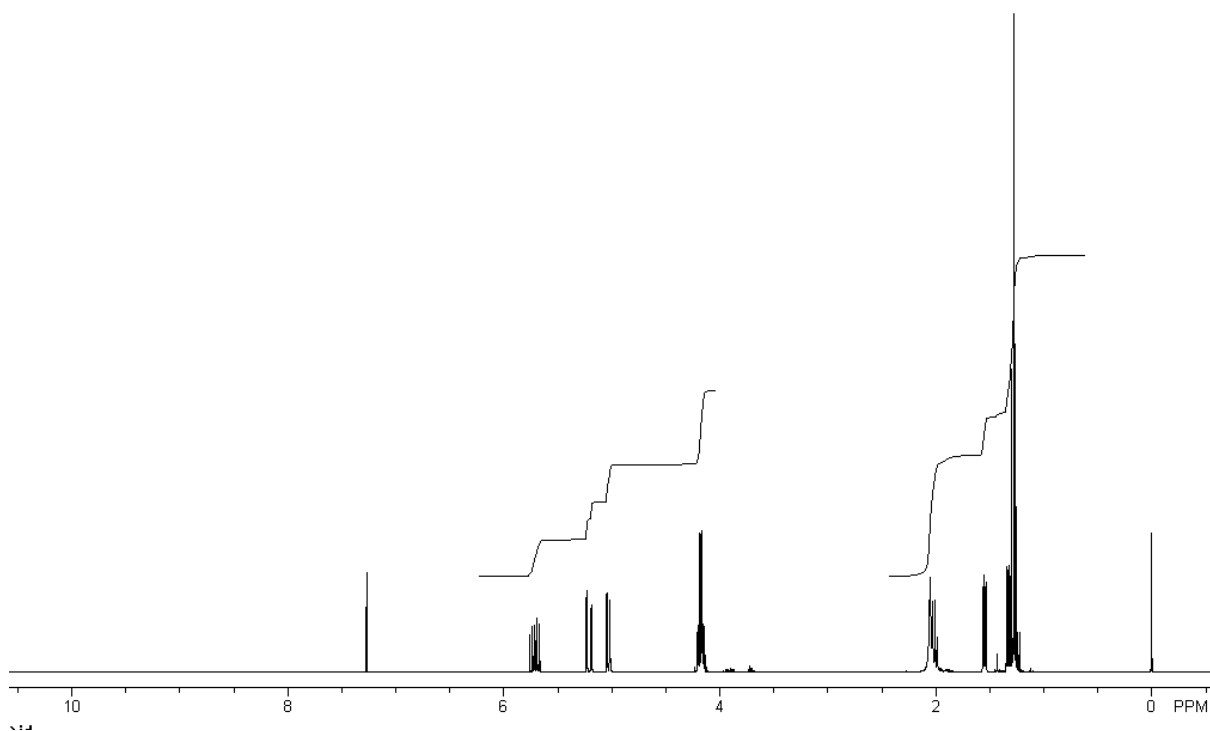


Fig S14 ^1H NMR spectrum and expansions of (1*R**, 2*S**)-methyl 2-vinyl-1-aminocyclopropanecarboxylate (400 MHz; C_6D_6 , also contains some MTBE, heptanes).



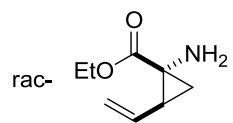
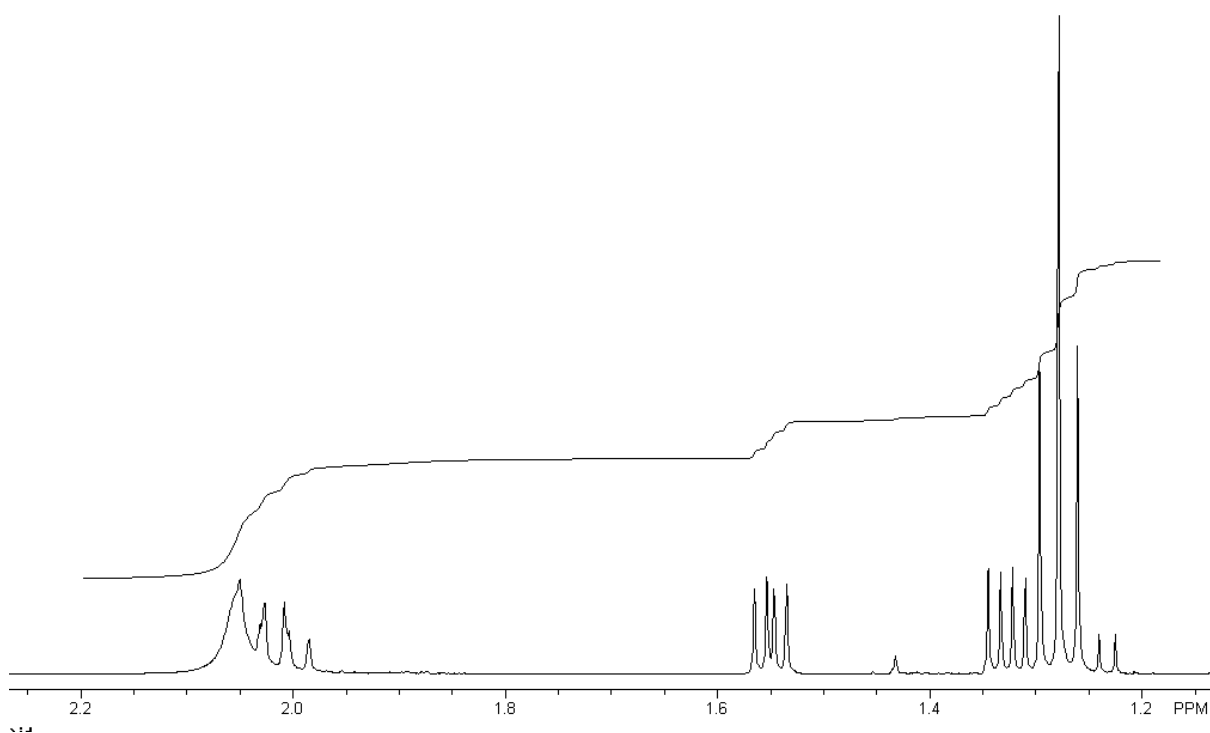
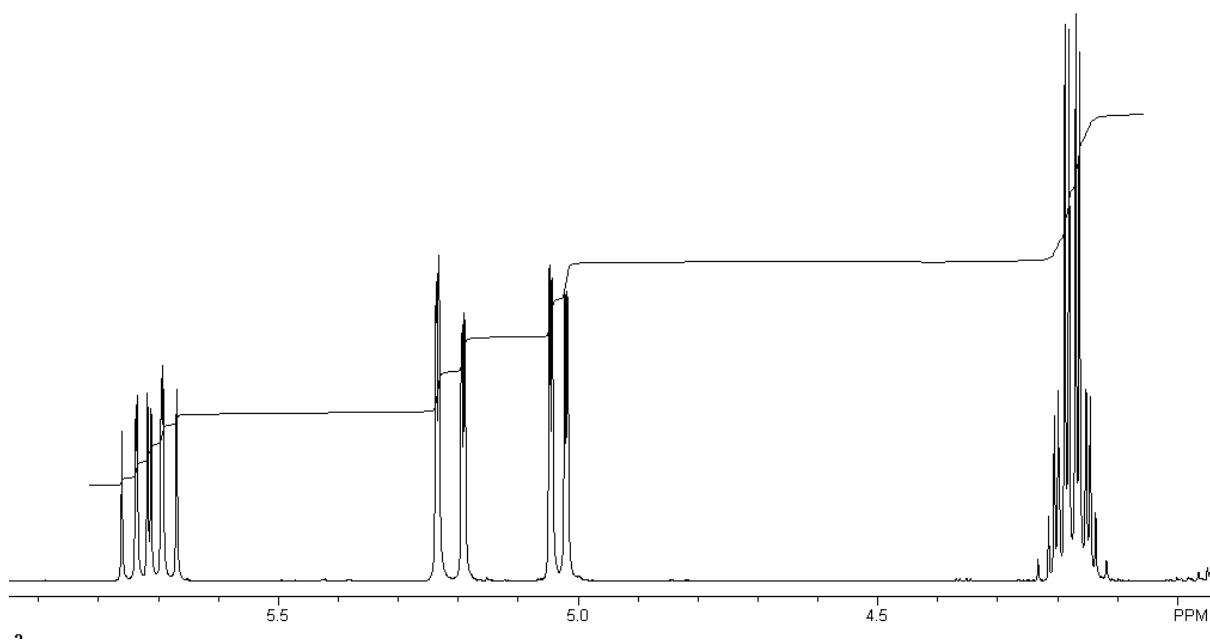
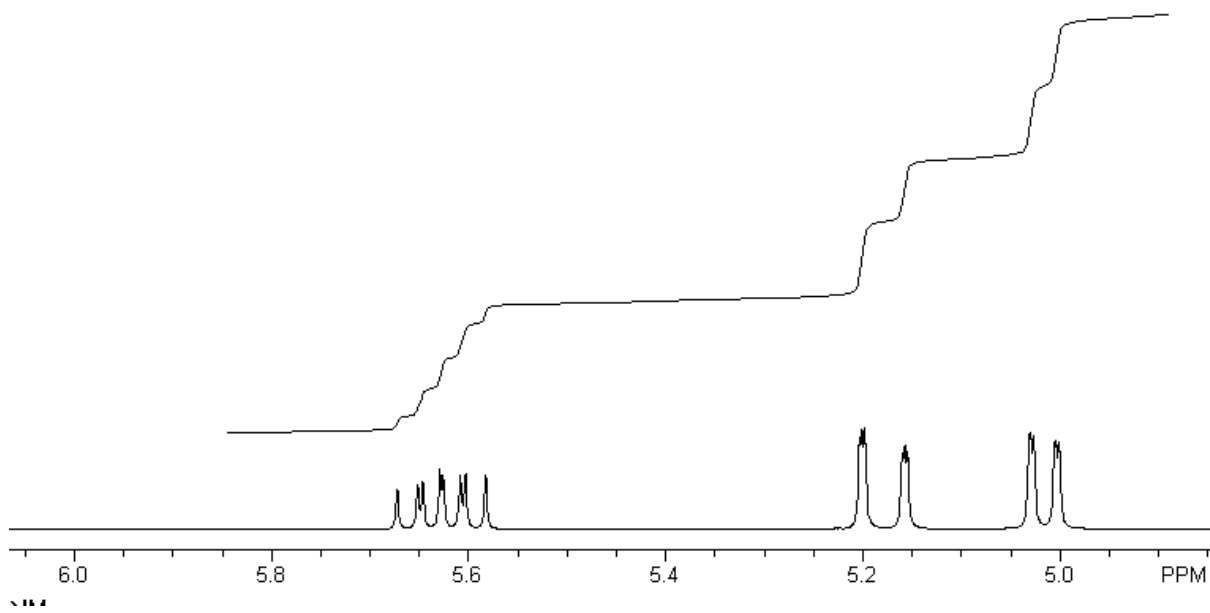
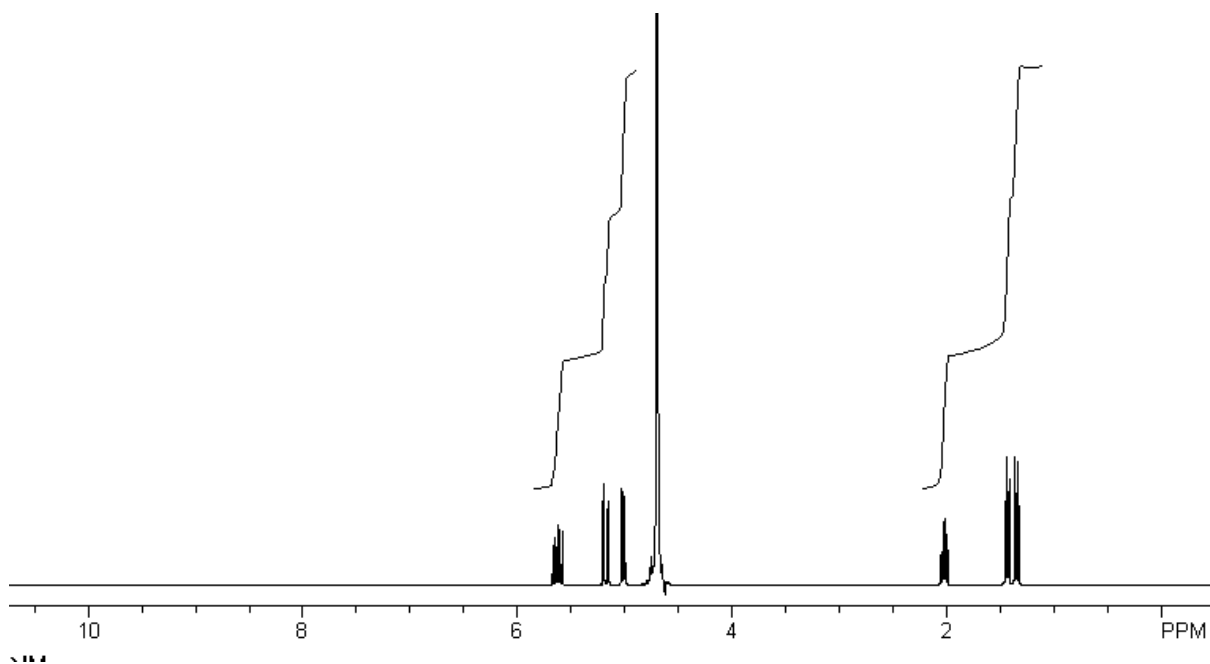


Fig S15 ^1H NMR spectrum and expansions of (1*R**, 2*S**)-ethyl 2-vinyl-1-aminocyclopropanecarboxylate (400 MHz; CDCl_3 , Me_4Si).



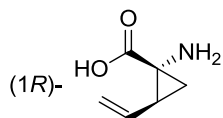
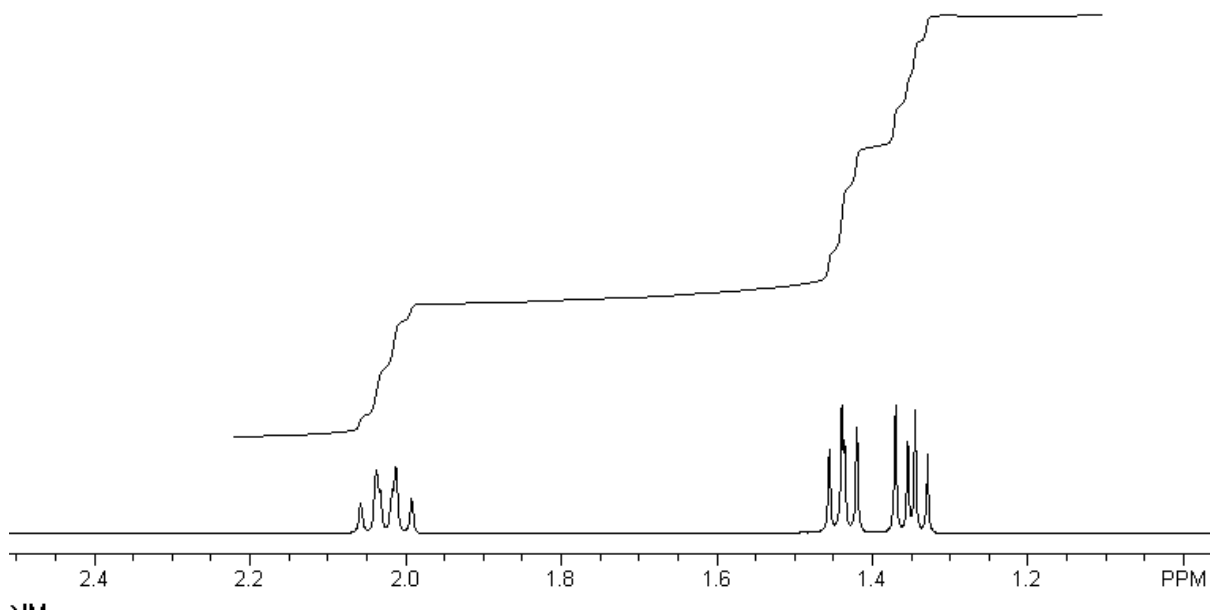
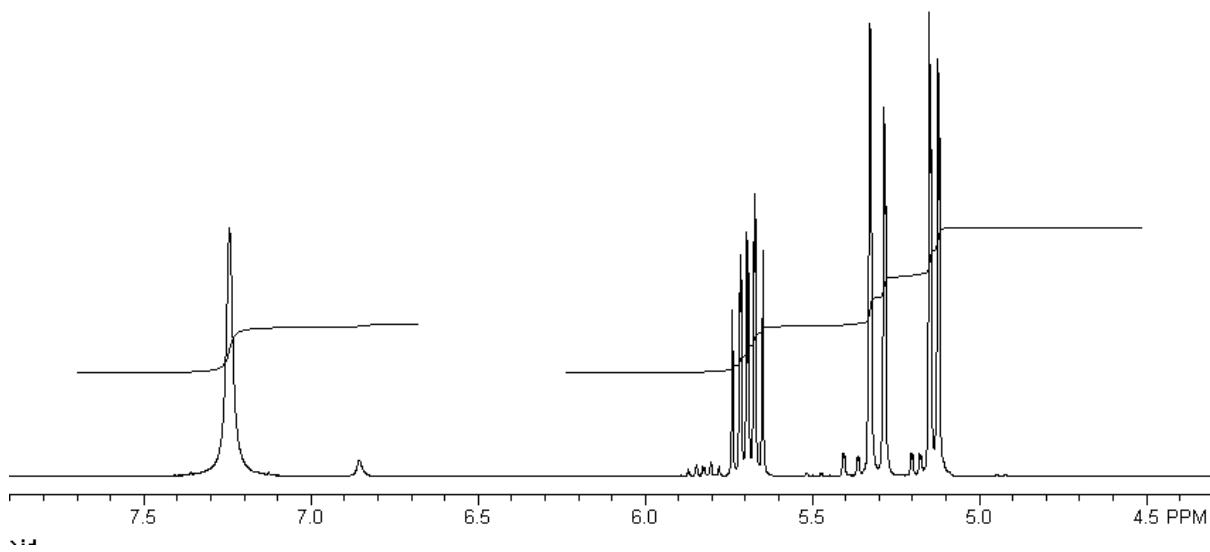
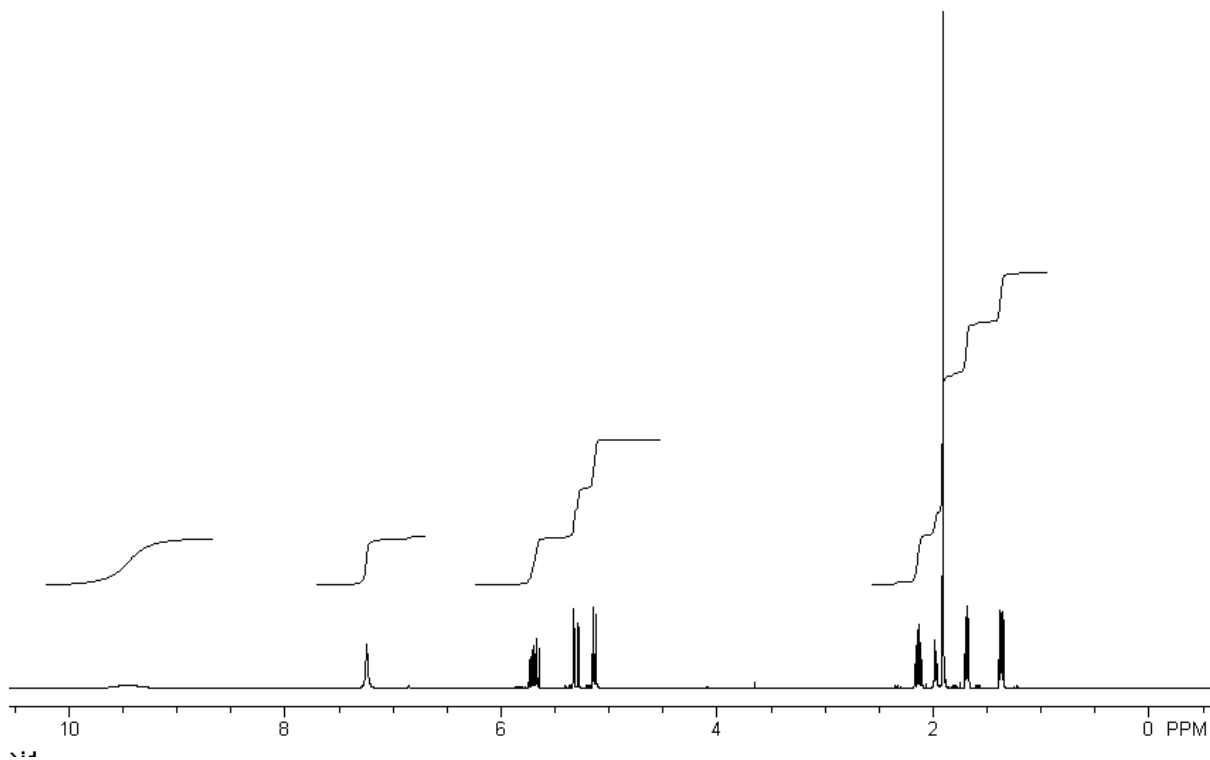


Fig S16 ^1H NMR spectrum and expansions of (1*R*, 2*S*)-2-vinyl-1-aminocyclopropane carboxylic acid (1*R*)-(1) (400 MHz; D_2O).



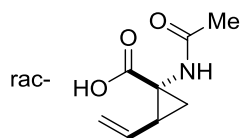
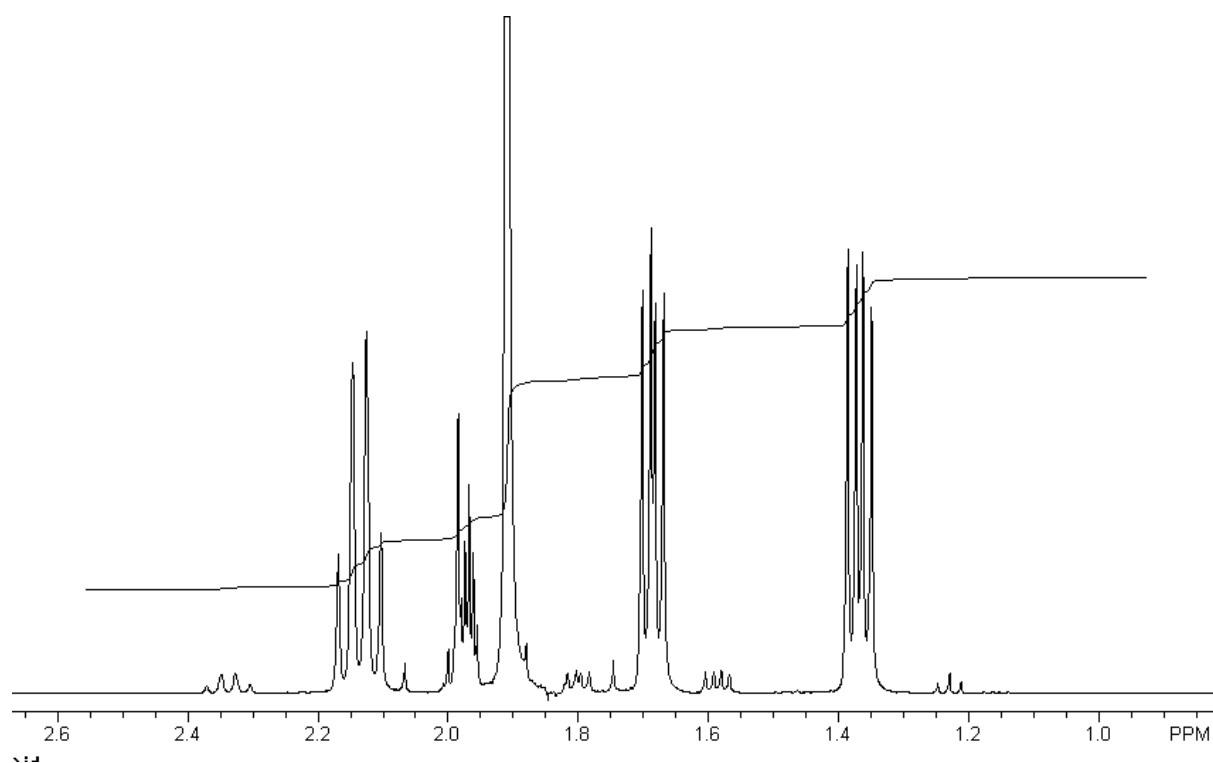
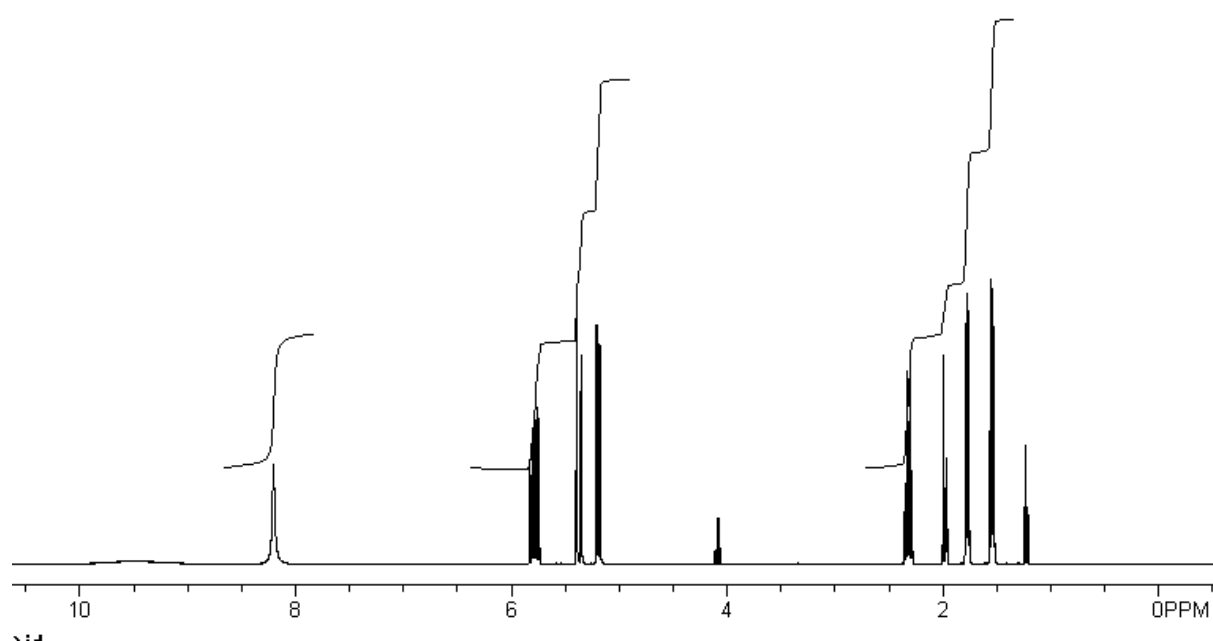


Fig S17 ¹H NMR spectrum and expansions of (1*R**, 2*S**)-2-vinyl-1-acetamidocyclopropanecarboxylic acid rac-(**5a**) (400 MHz; CD₃CN).



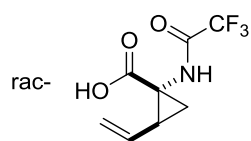
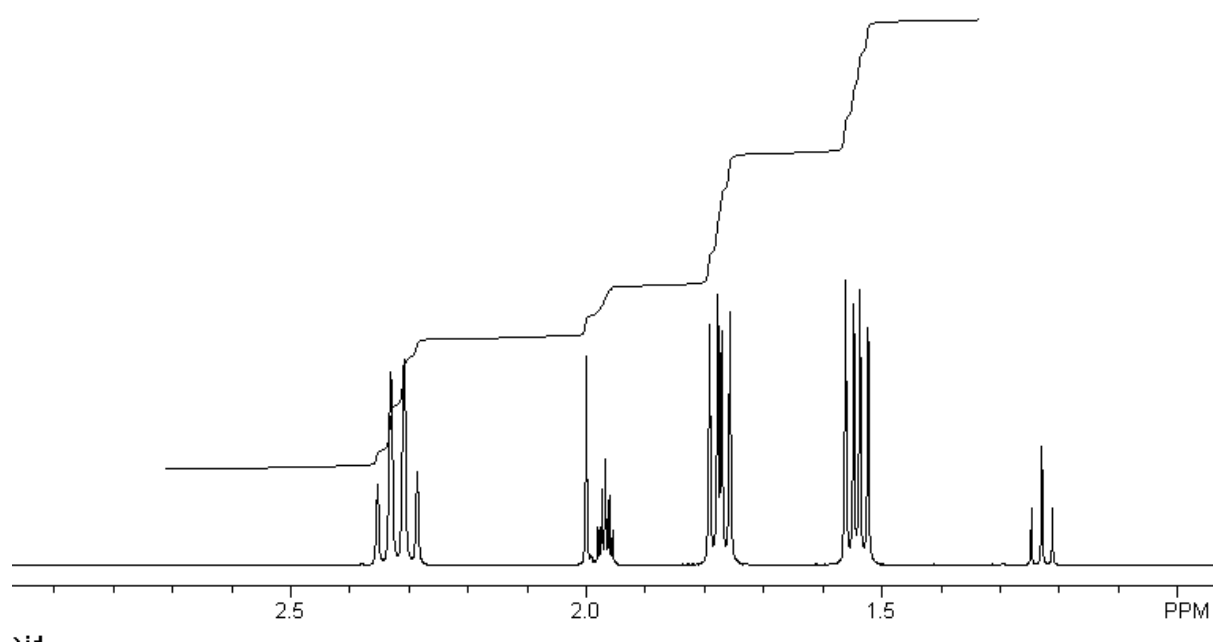
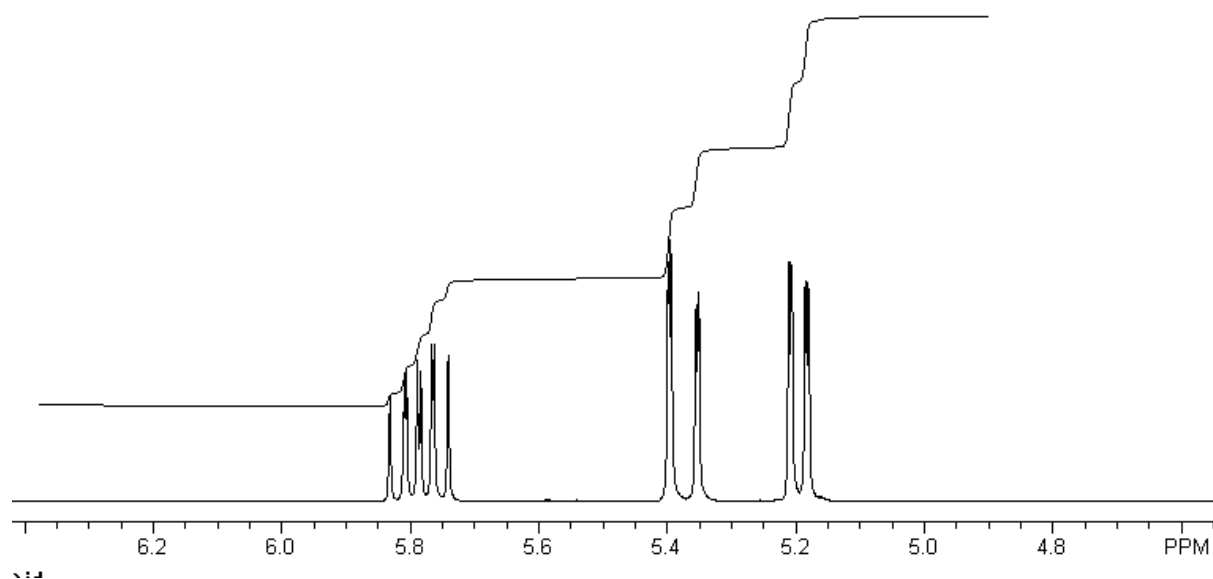
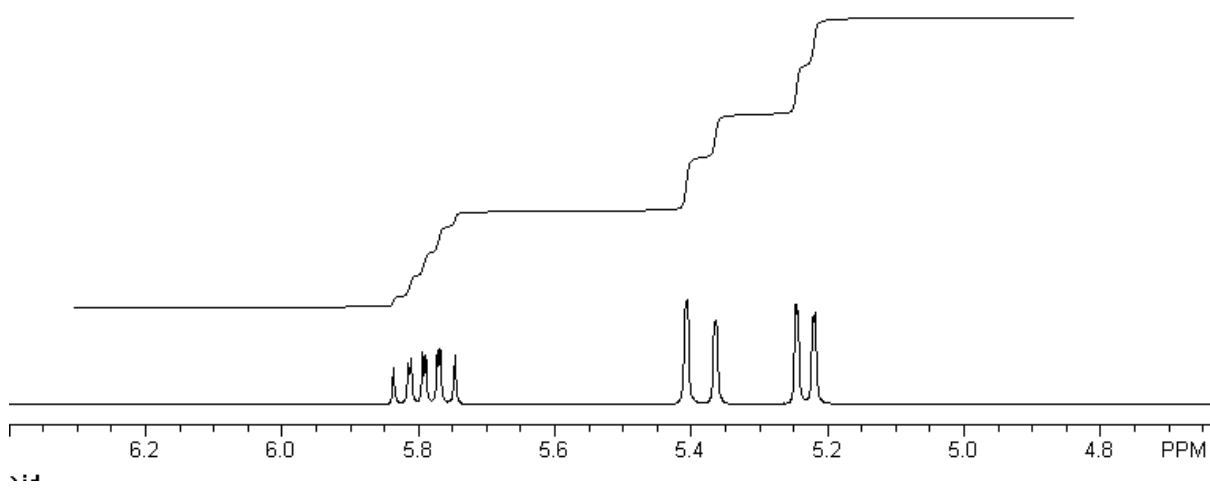
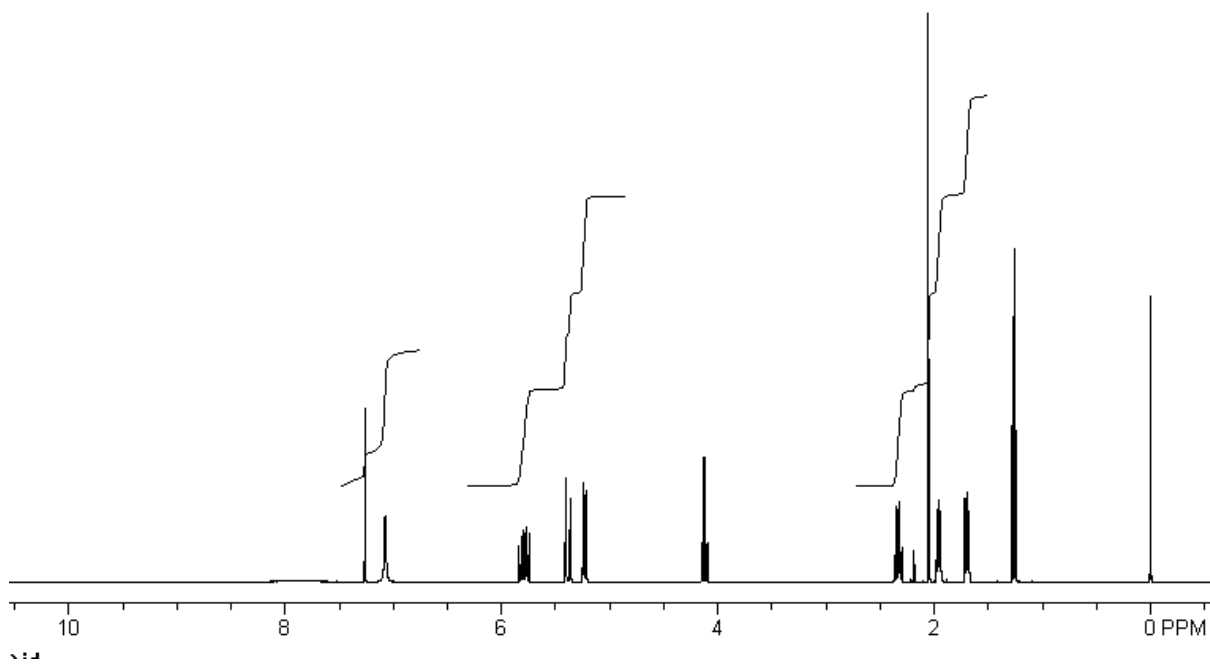


Fig S18 ^1H NMR spectrum and expansions of (1**R*, 2*S**)-2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic acid rac-(**5b**) (400 MHz; CD_3CN) (contains some ethyl acetate).



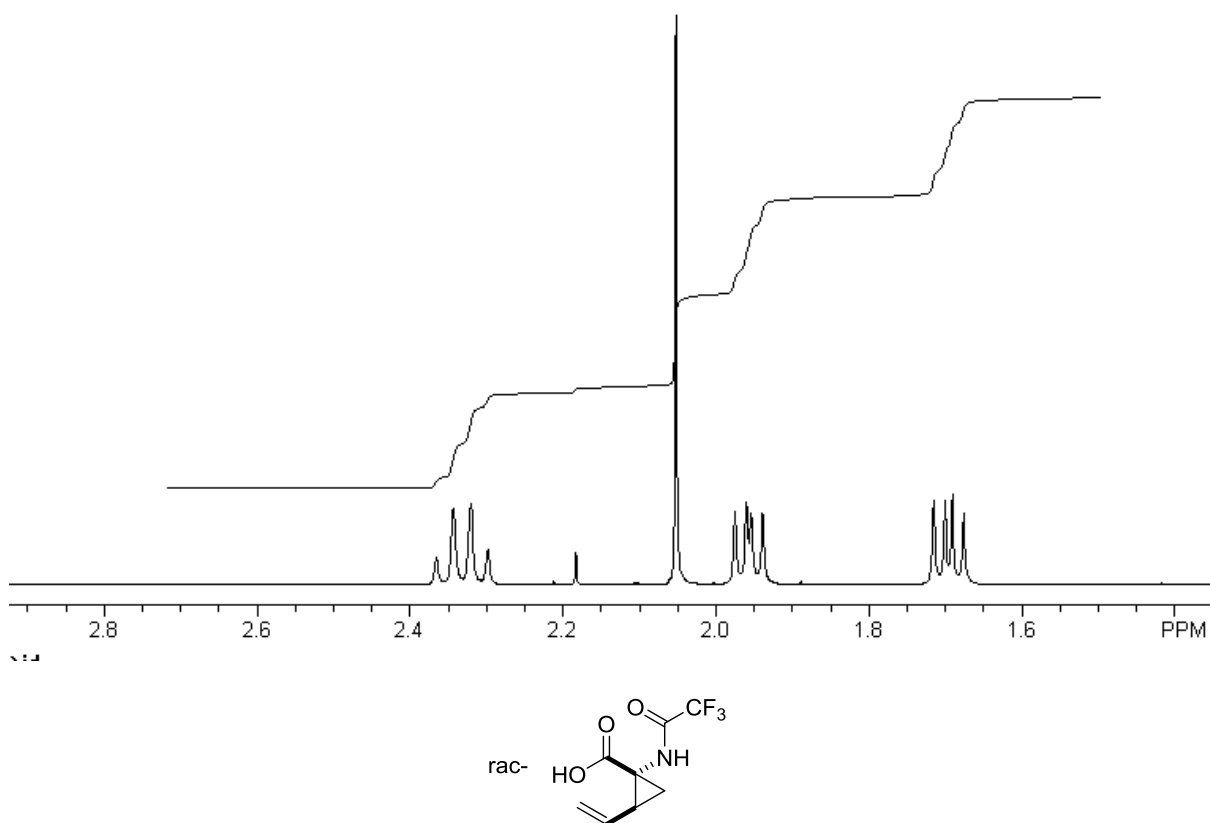
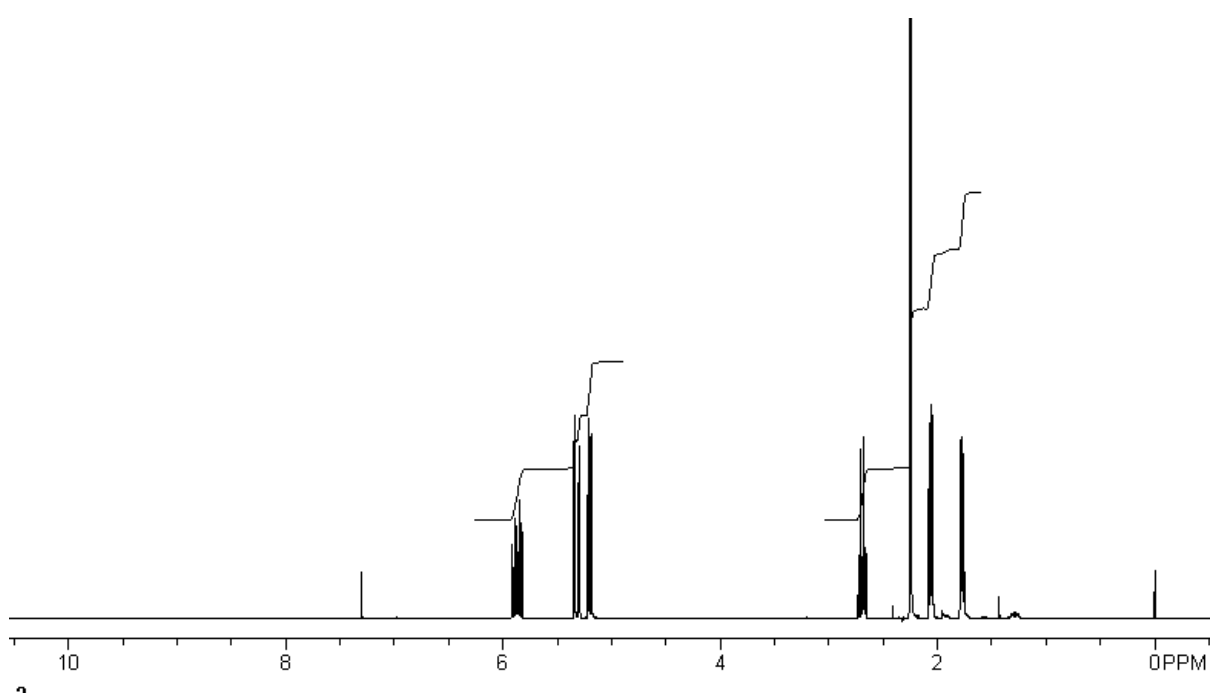


Fig S19 ^1H NMR spectrum and expansions of (1*R**, 2*S**)-2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylic acid rac-(**5b**) (400 MHz; CDCl_3) (contains some ethyl acetate).



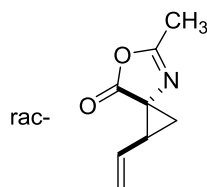
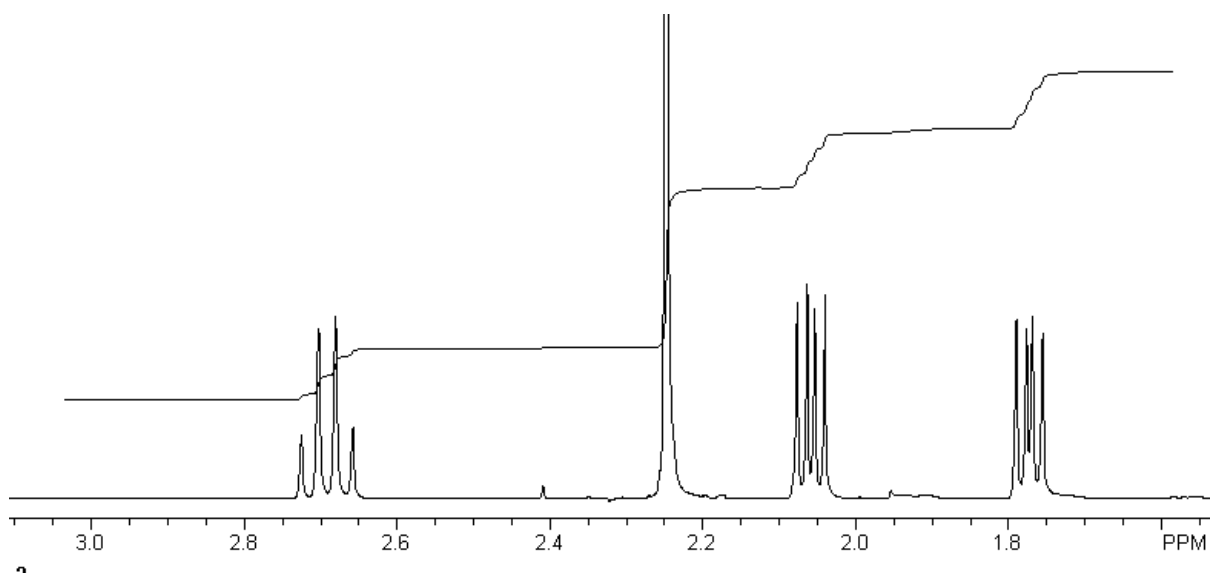
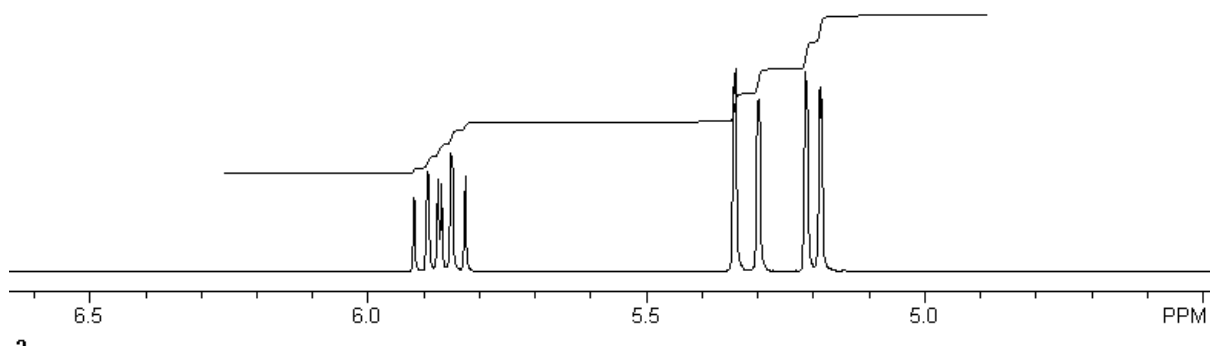
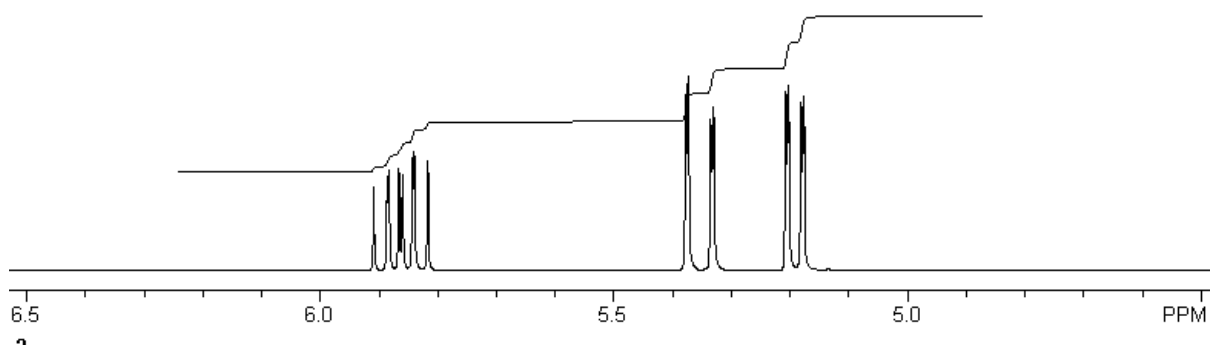
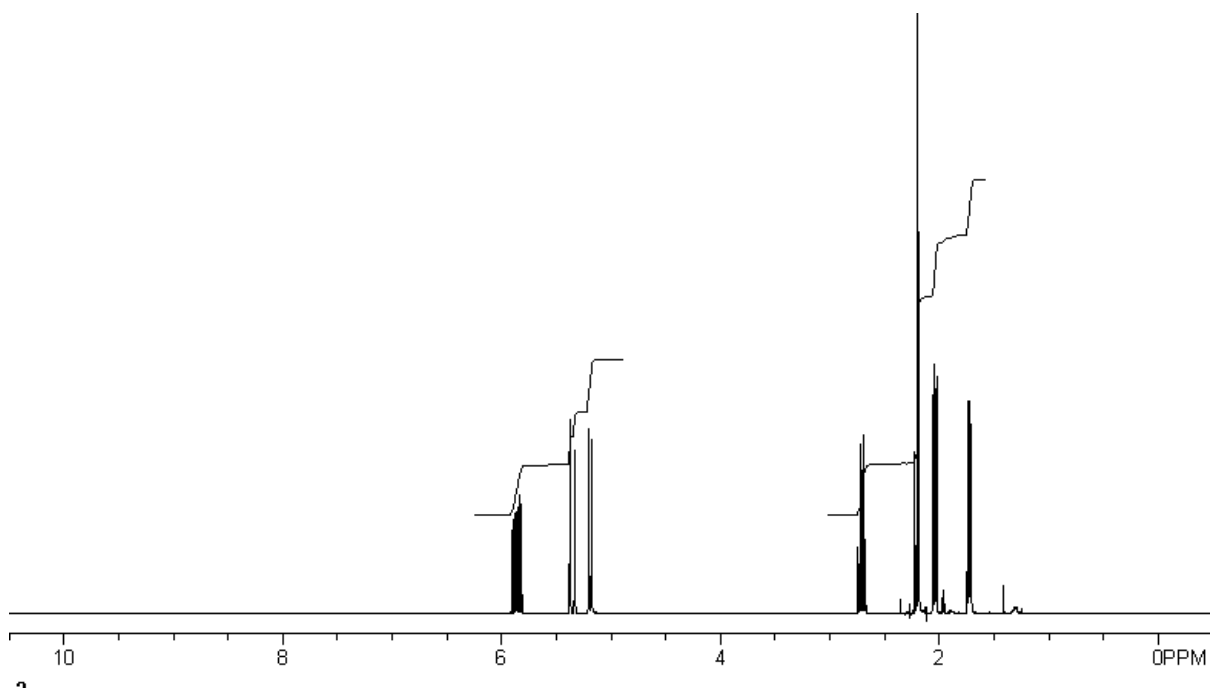


Fig S20 ^1H NMR Spectrum and expansions of (1*R**, 3*S**)-5-methyl-1-vinyl-6-oxa-4-aza spiro[2.4]hept-4-en-7-one rac-(**6a**) (400 MHz; CDCl_3).



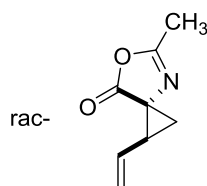
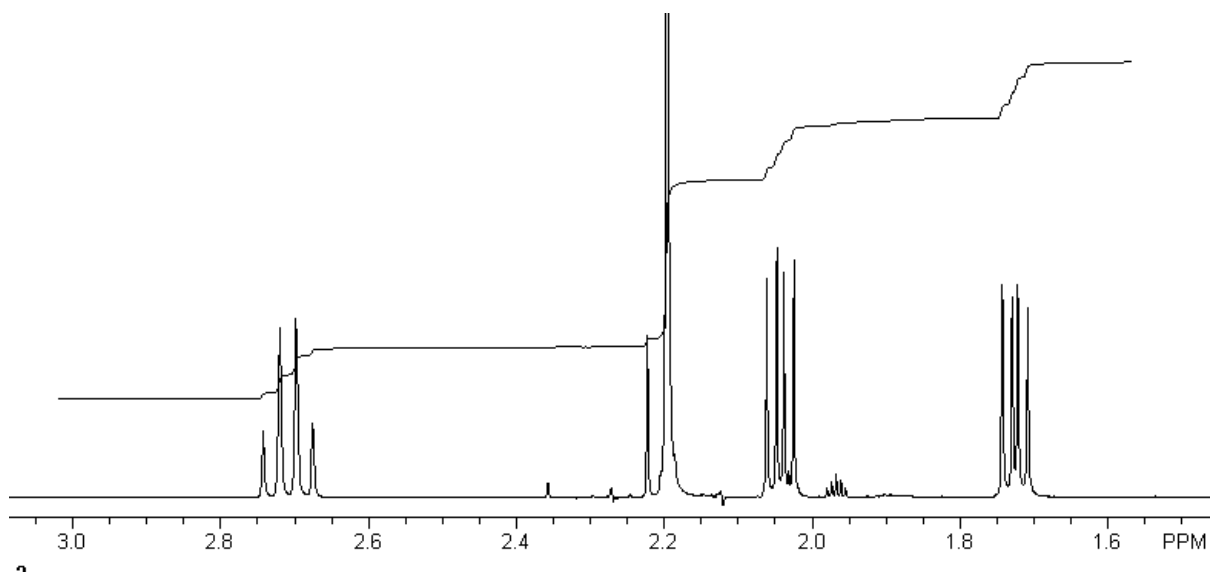
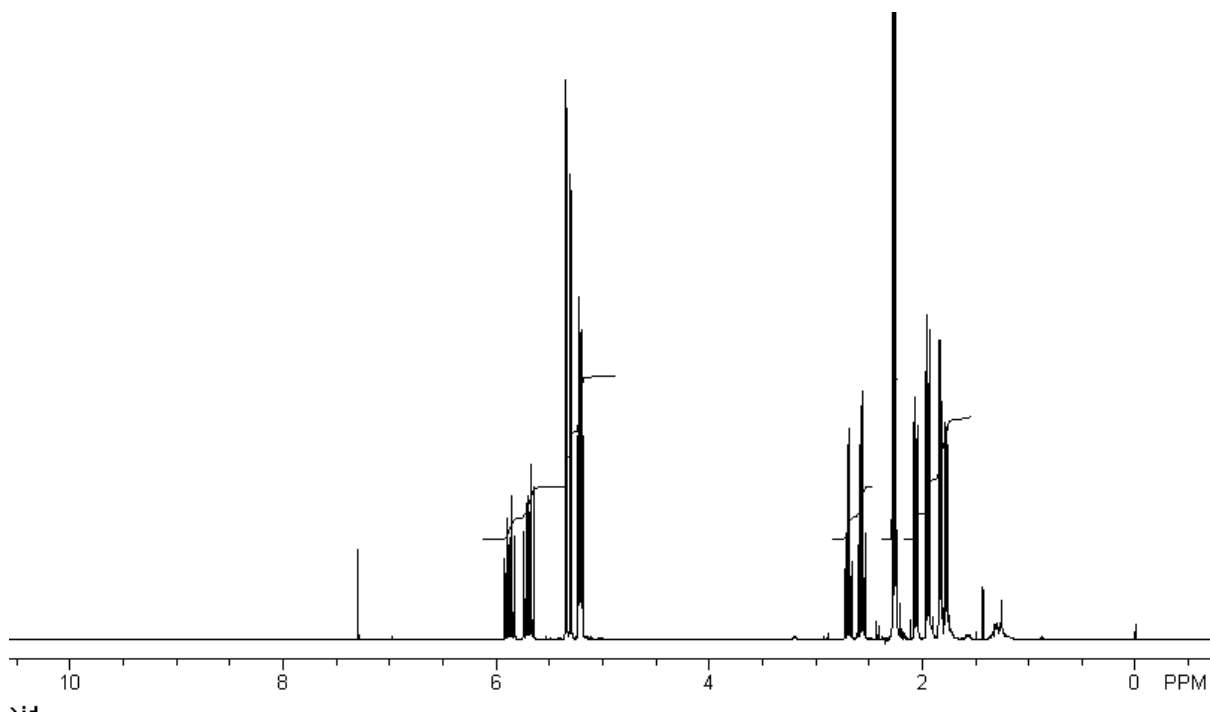


Fig S21 ^1H NMR Spectrum and expansions of (1*R**, 3*S**)-5-methyl-1-vinyl-6-oxa-4-aza spiro[2.4]hept-4-en-7-one rac-(**6a**) (400 MHz; CD_3CN).



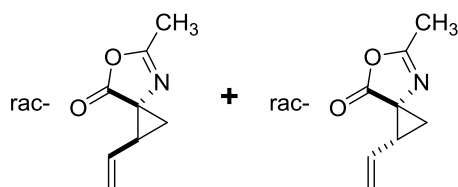
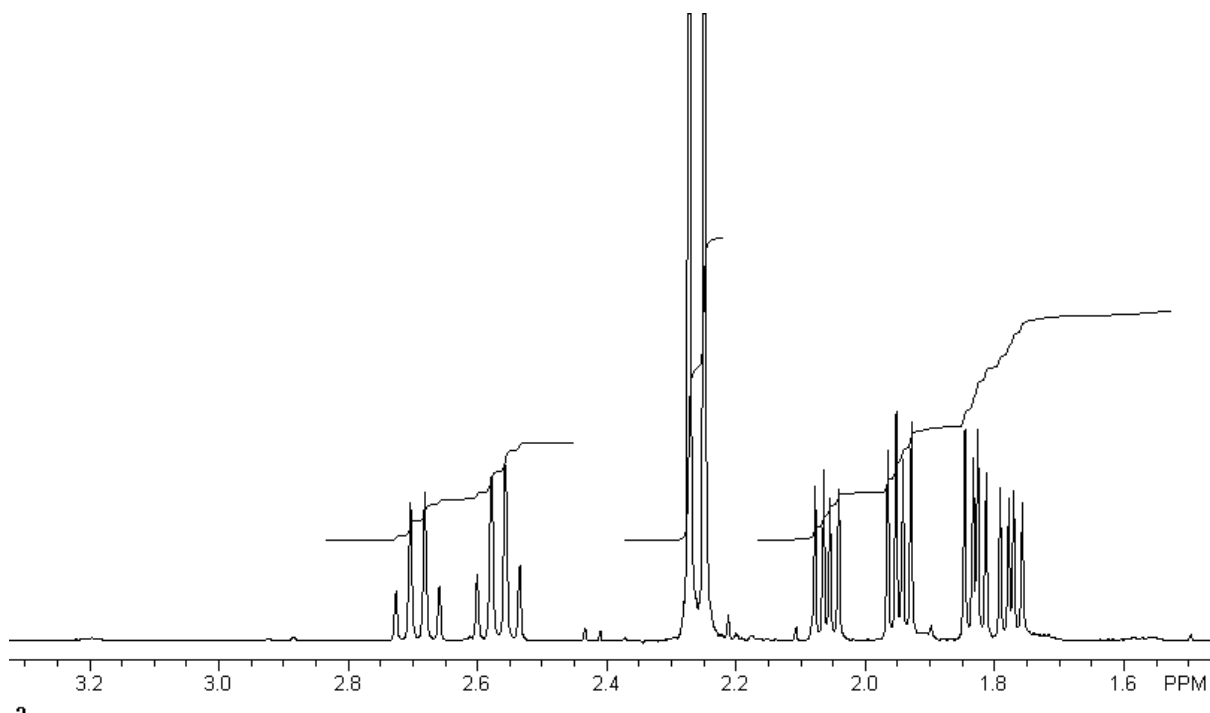
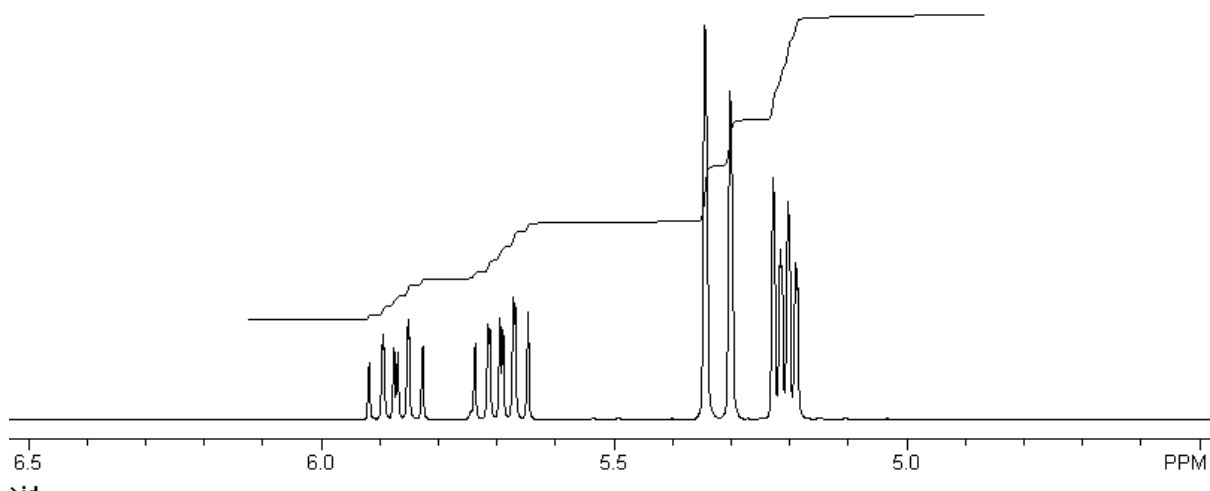
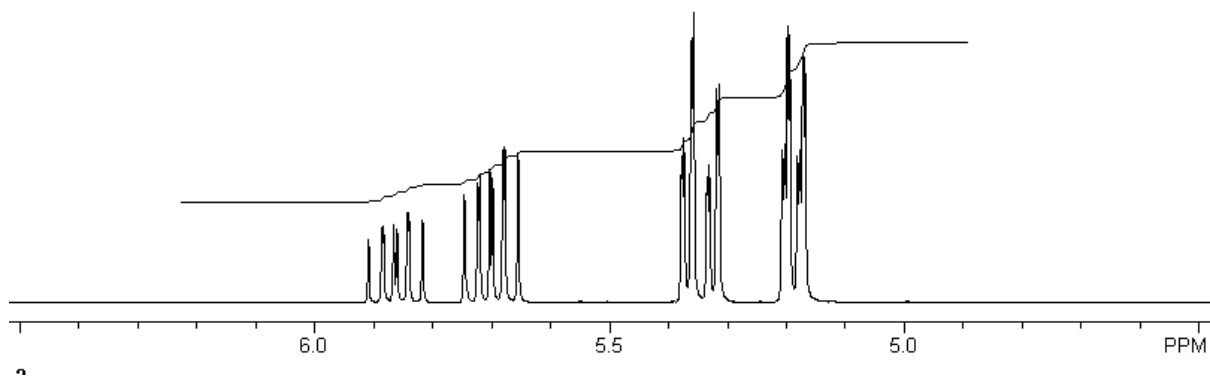
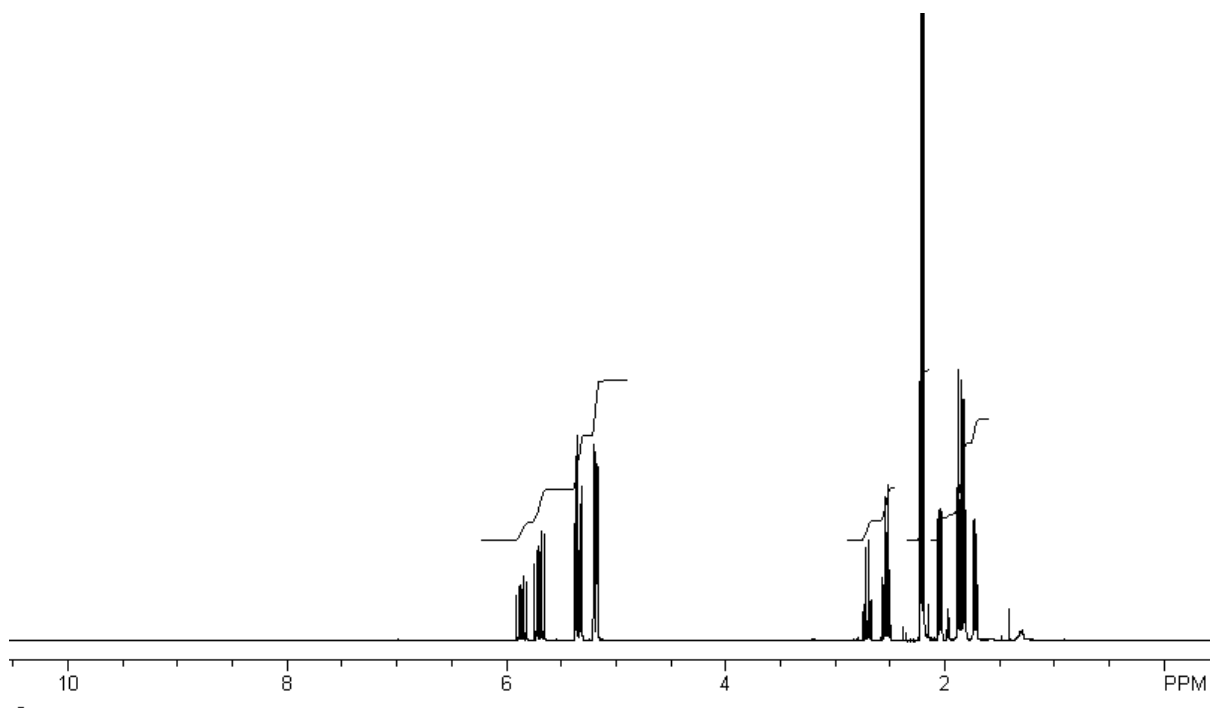


Fig S22 ^1H NMR Spectrum and expansions of isomerised mixture of (1*R**, 3*S**)-5-methyl-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**6a**) and (1*R**, 3*R**)-5-methyl-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**15a**) (400 MHz; CDCl_3).



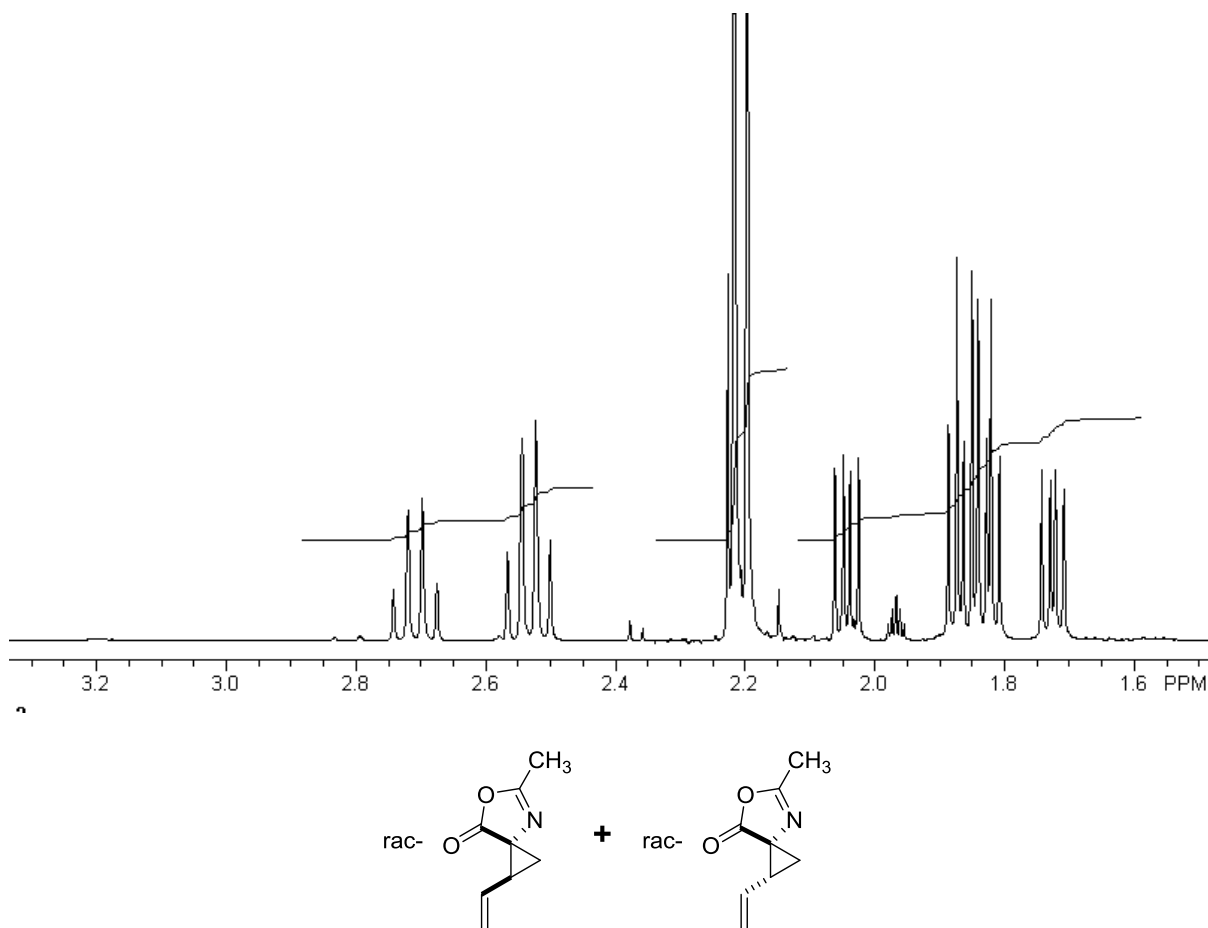
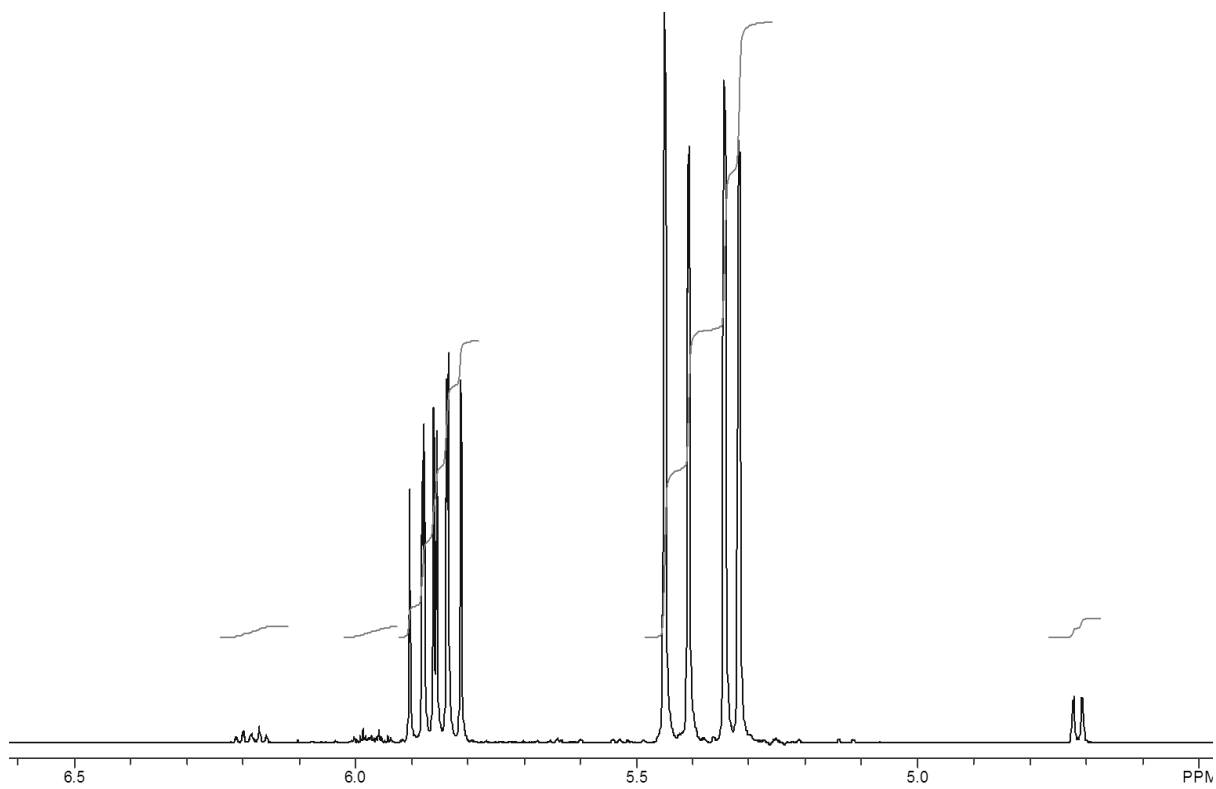
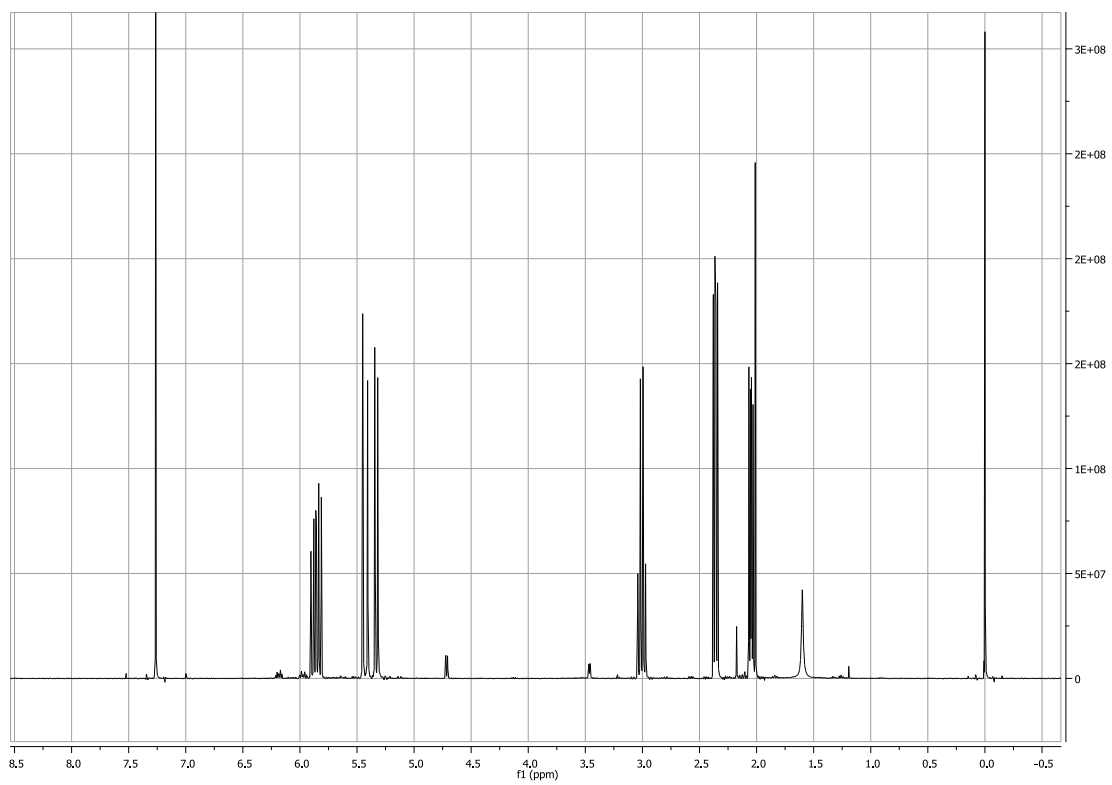


Fig S23 ¹H NMR Spectrum and expansions of isomerised mixture of (1*R**, 3*S**)-5-methyl-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**6a**) and (1*R**, 3*R**)-5-methyl-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**15a**) (400 MHz; CD₃CN).



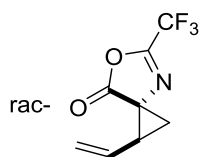
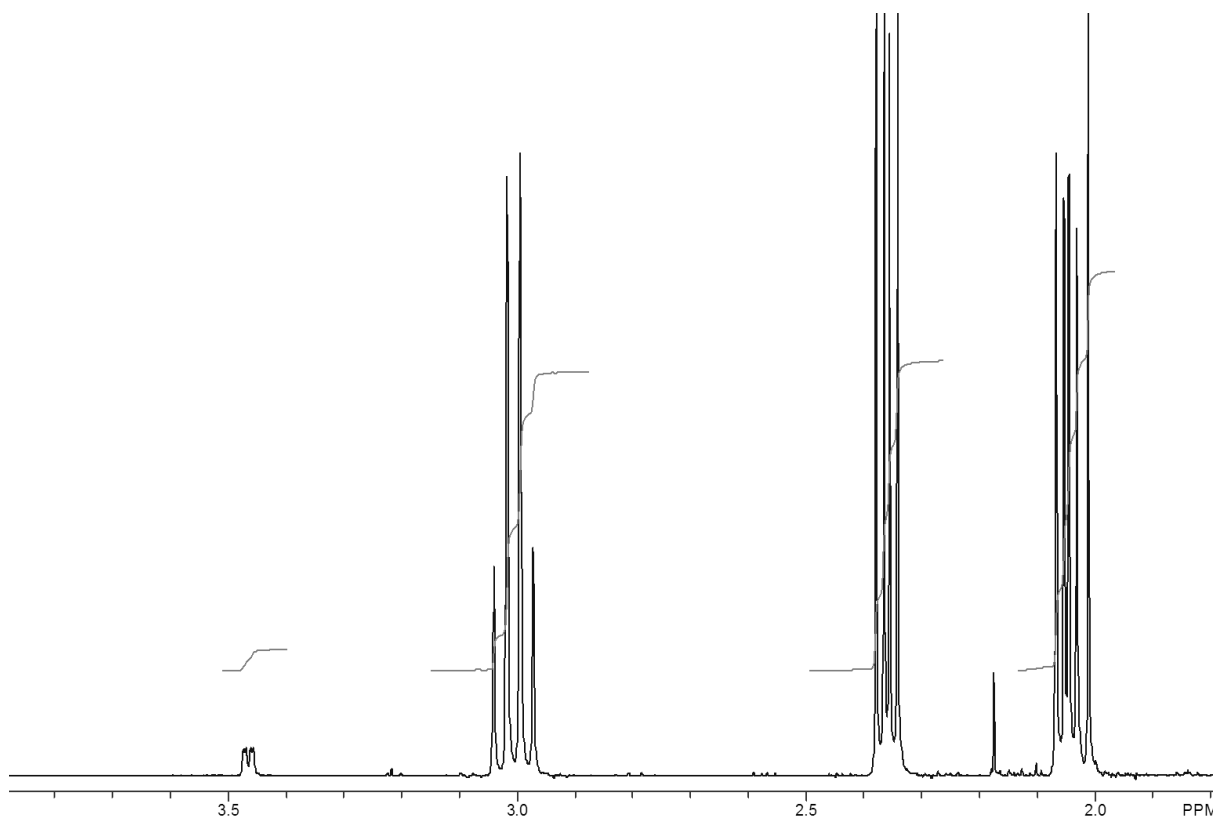
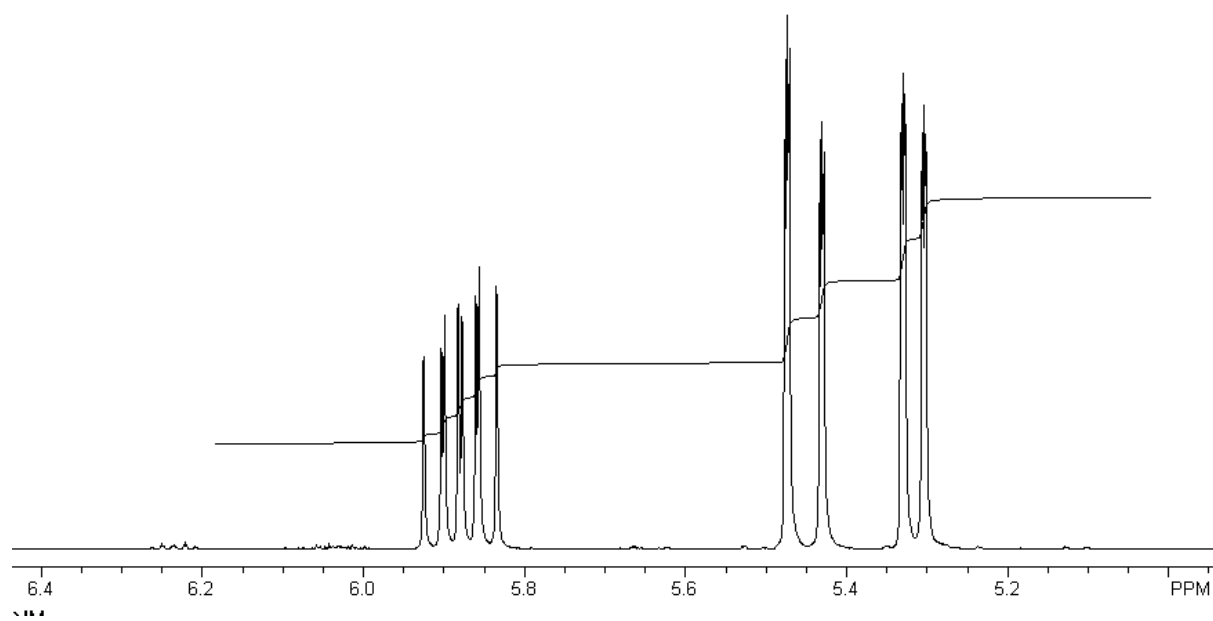
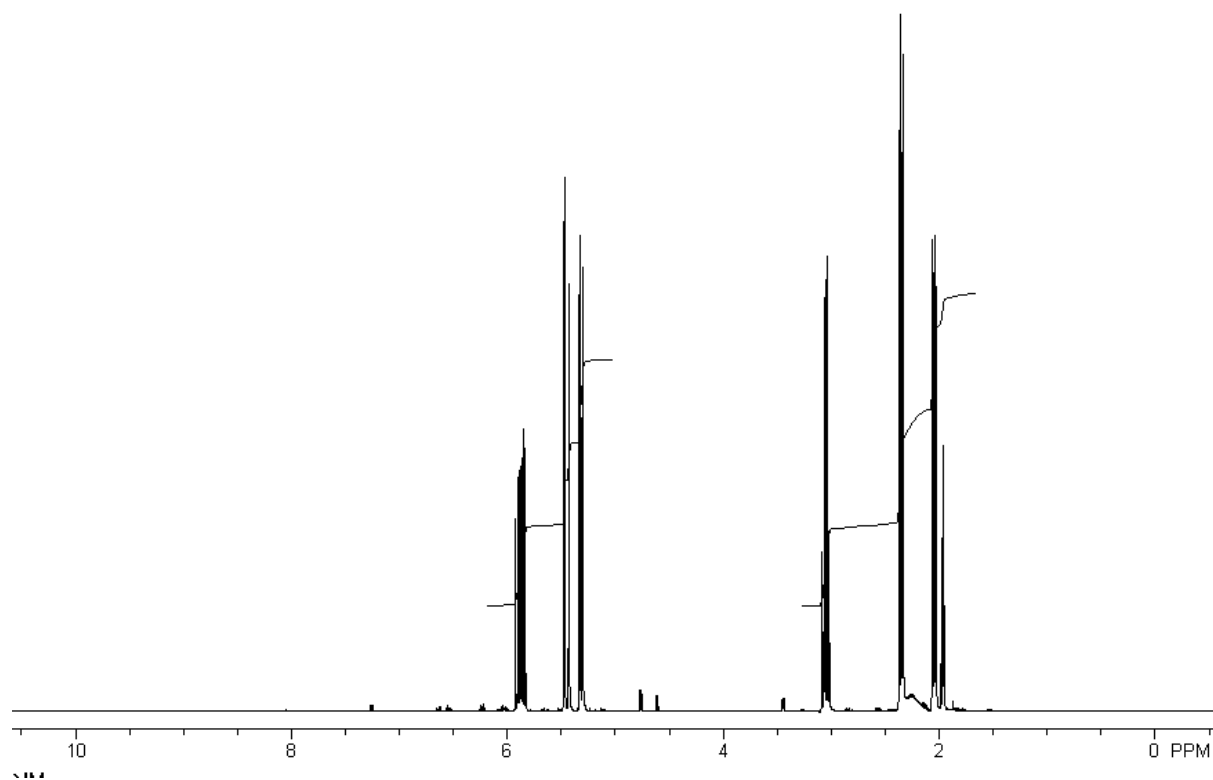


Fig S24 ¹H NMR Spectrum and expansions of (1*R**, 3*S**)-5-(trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**6b**) (400 MHz; CDCl₃).



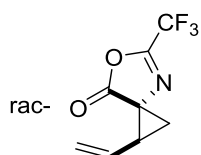
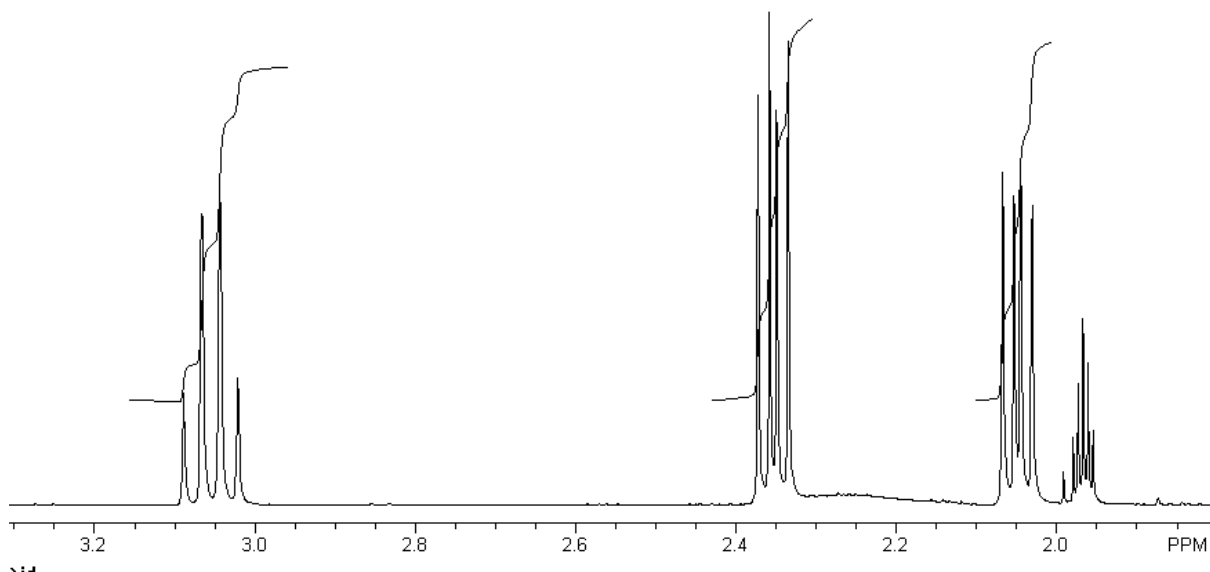
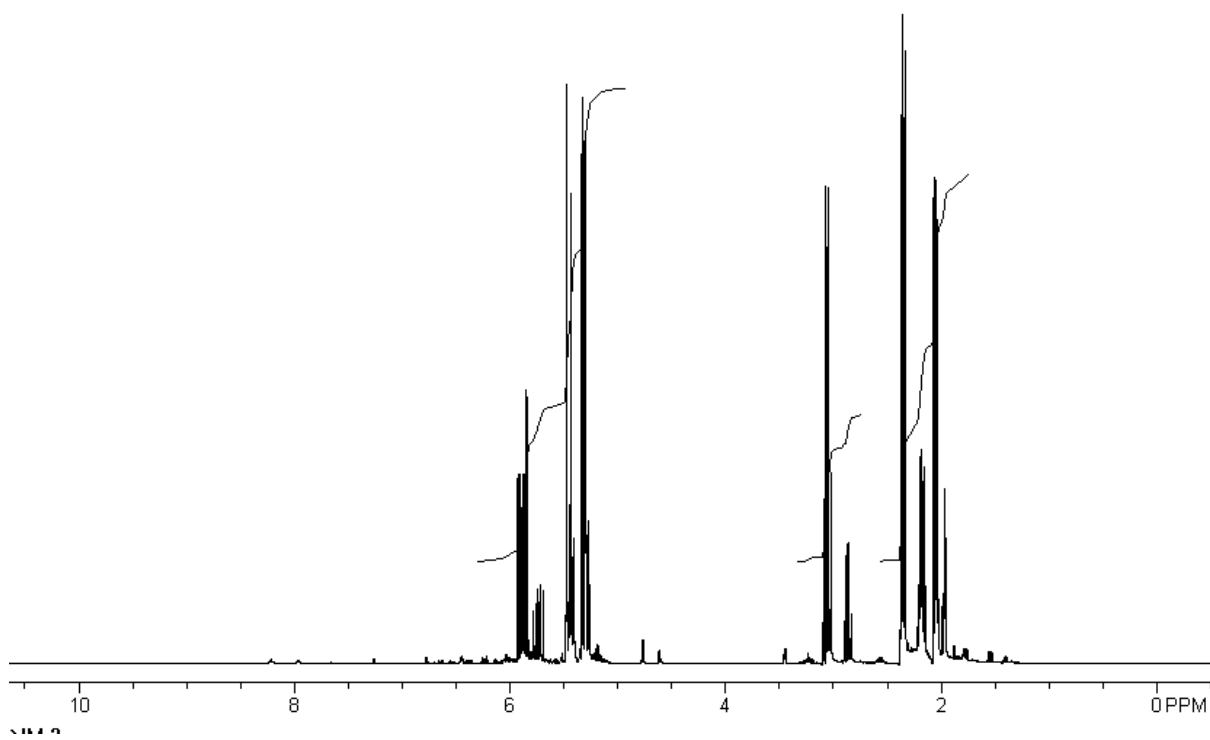


Fig S25 ^1H NMR Spectrum and expansions of (1*R**, 3*S**)-5-(trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**6b**) (400 MHz; CD_3CN).



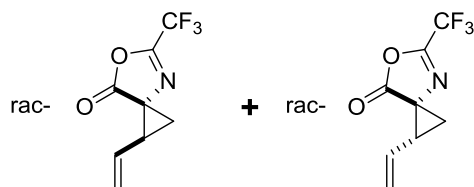
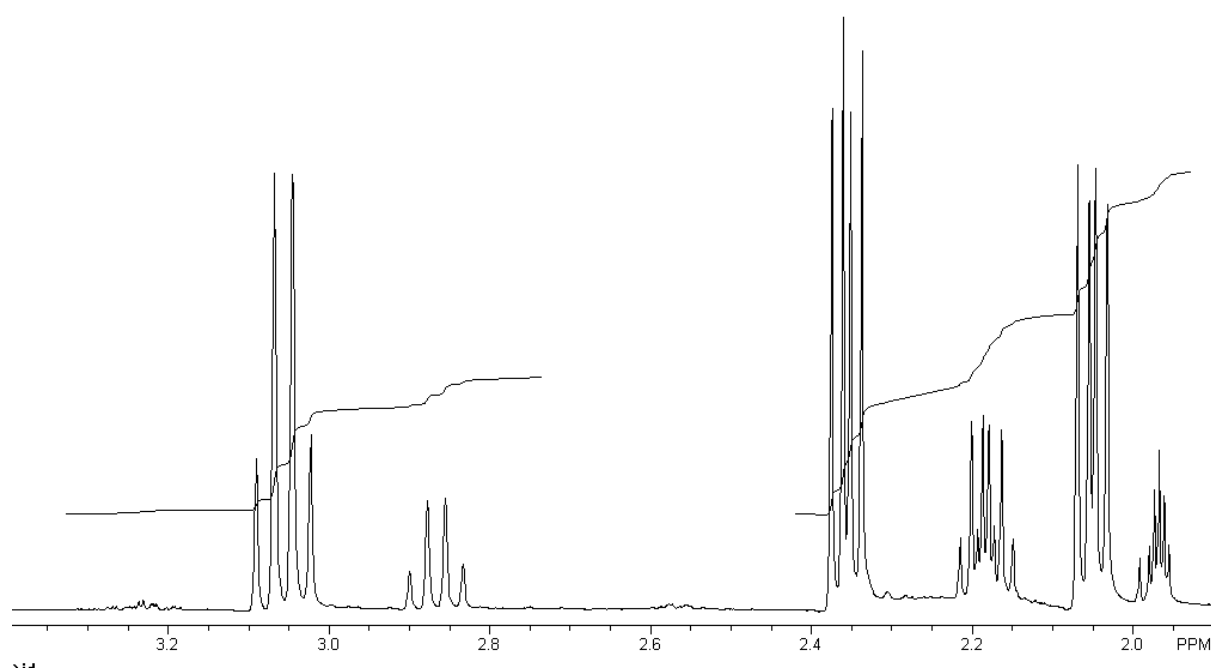
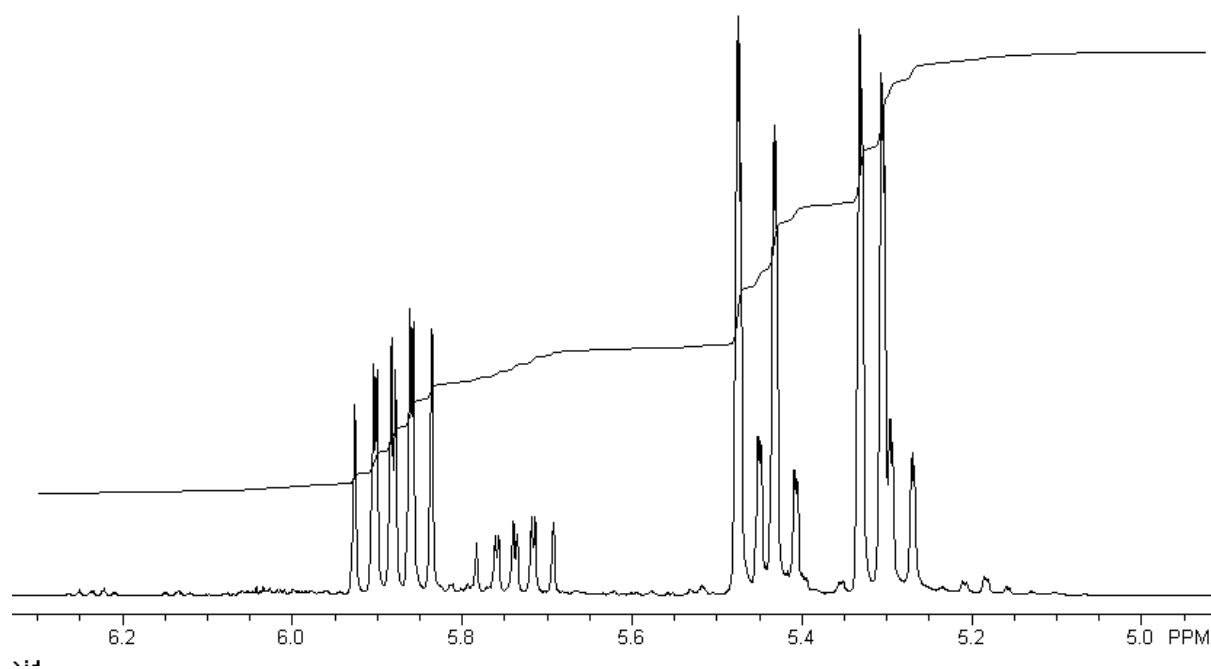
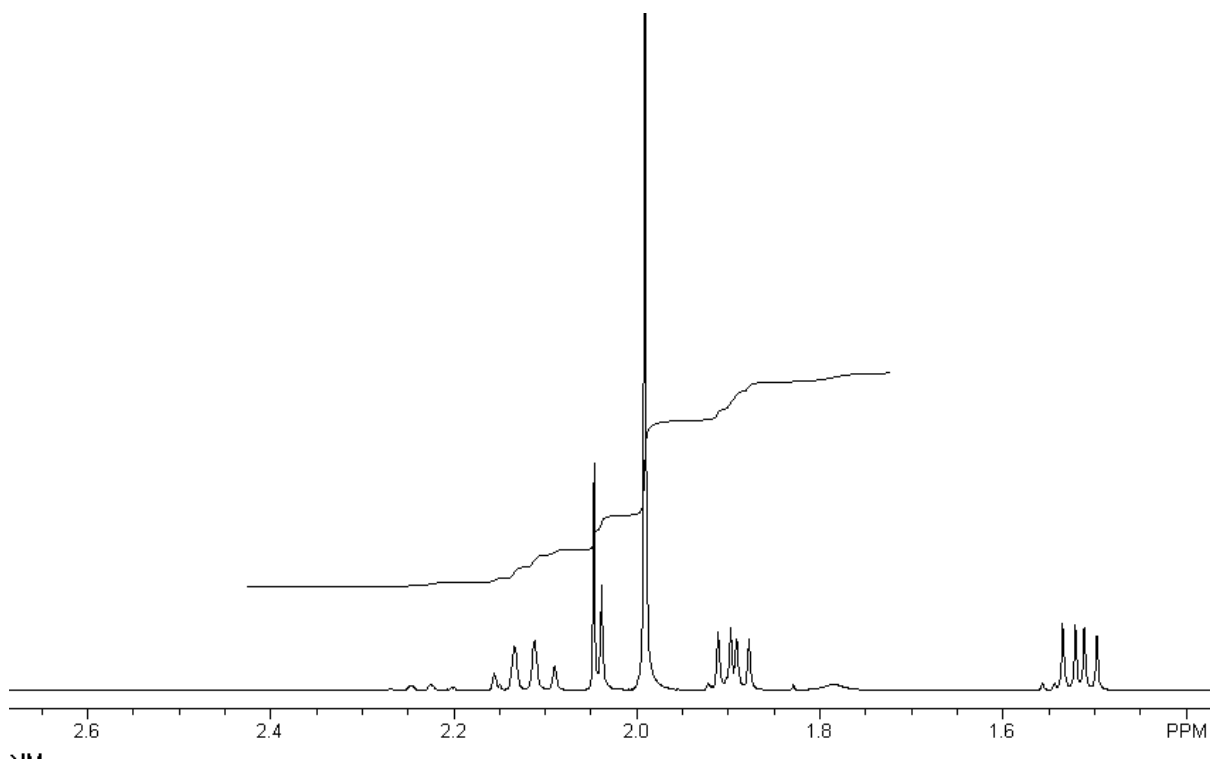
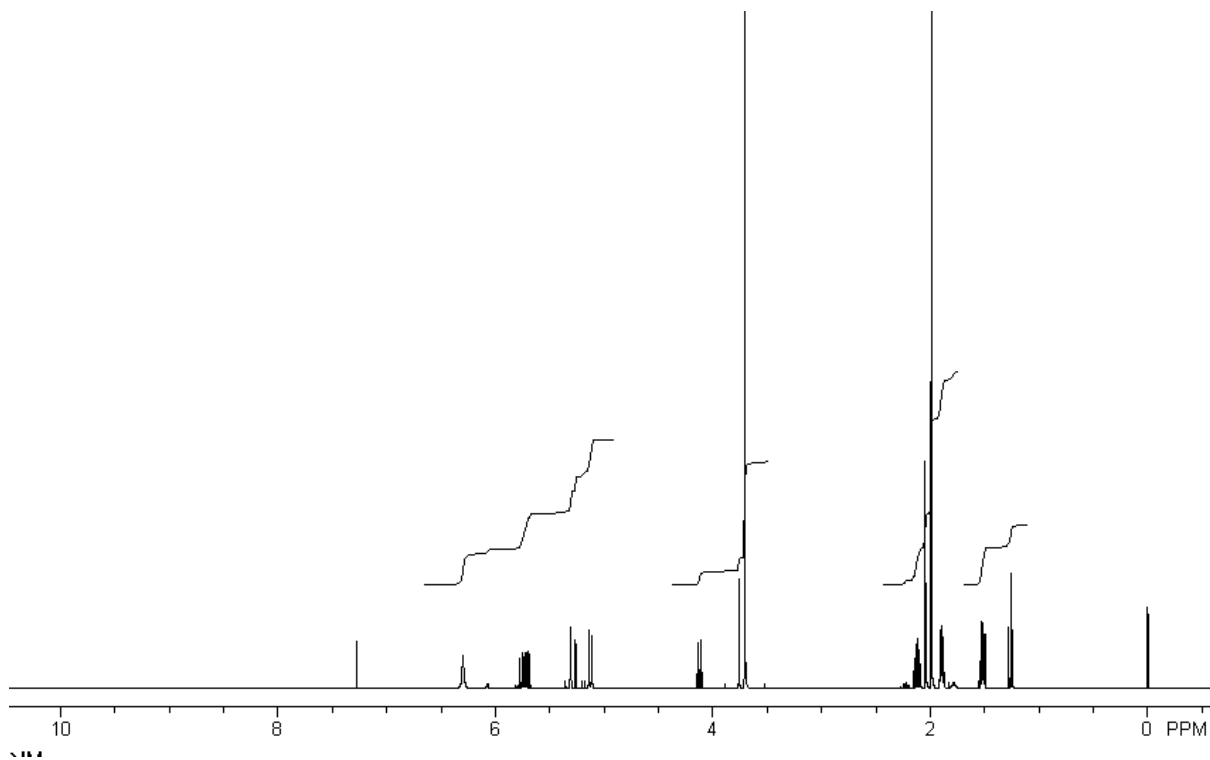


Fig S26 ^1H NMR Spectrum and expansions of crude isomerised mixture of (1*R**, 3*S**)-5-(trifluoromethyl)-1-vinyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one rac-(**6b**) and (1*R**, 3*R**)-5-(trifluoromethyl)-1-vinyl-6-oxa-4-aza spiro[2.4]hept-4-en-7-one rac-(**15b**) (3.4:1) (400 MHz; CD_3CN).



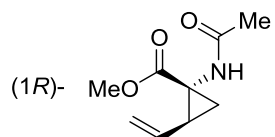
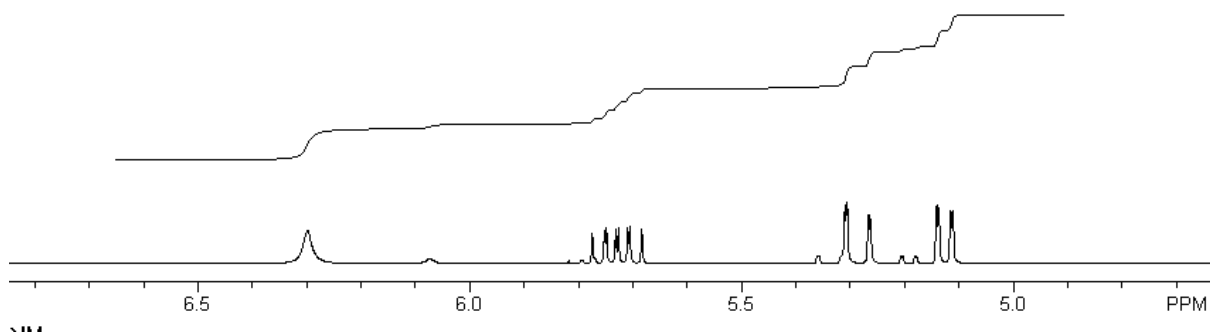
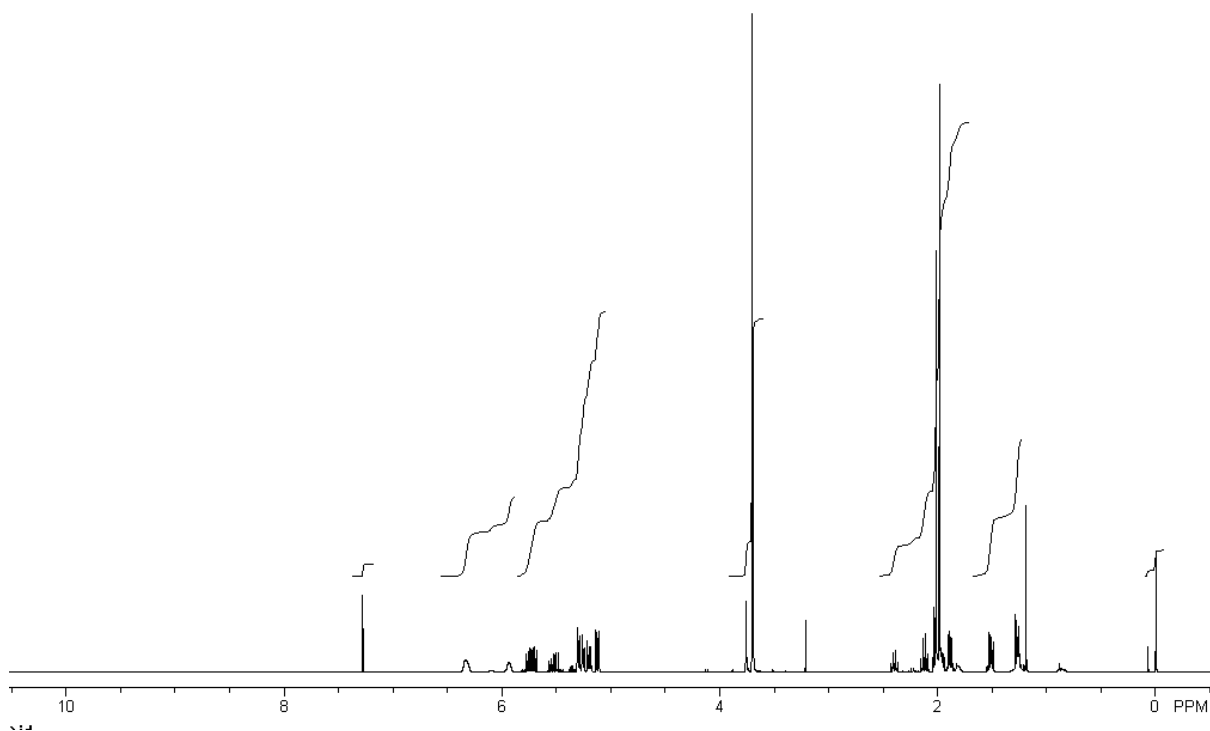


Fig S27 ¹H NMR spectrum and expansions of (1*R*, 2*S*)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate (1*R*)-(7a) (400 MHz; CDCl₃, Me₄Si).



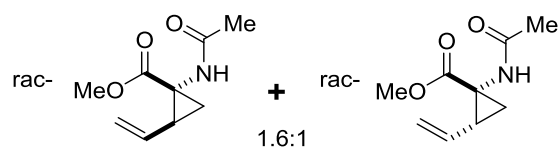
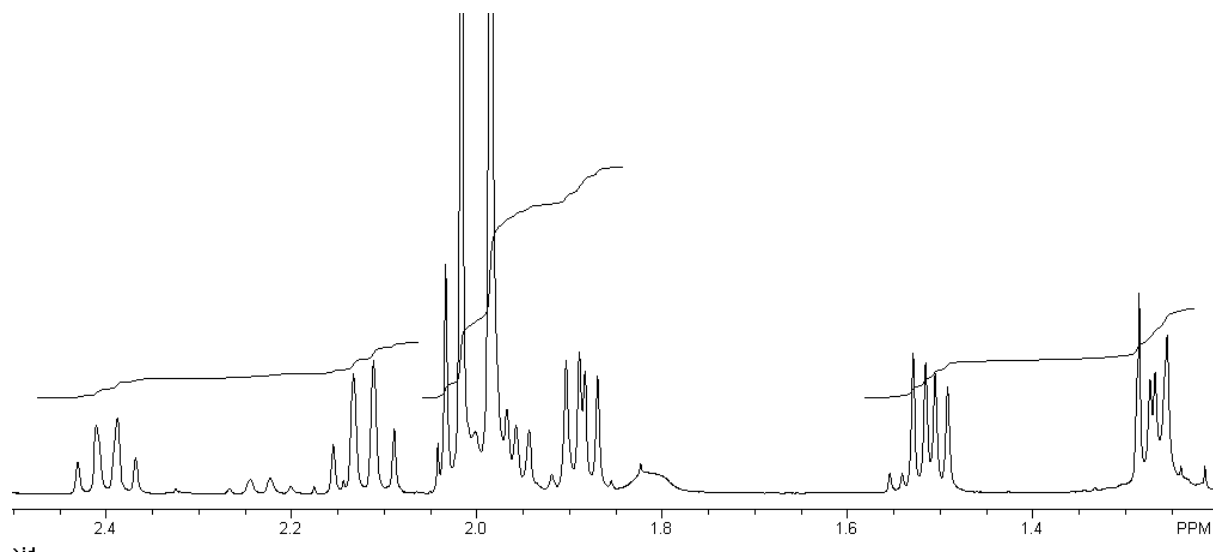
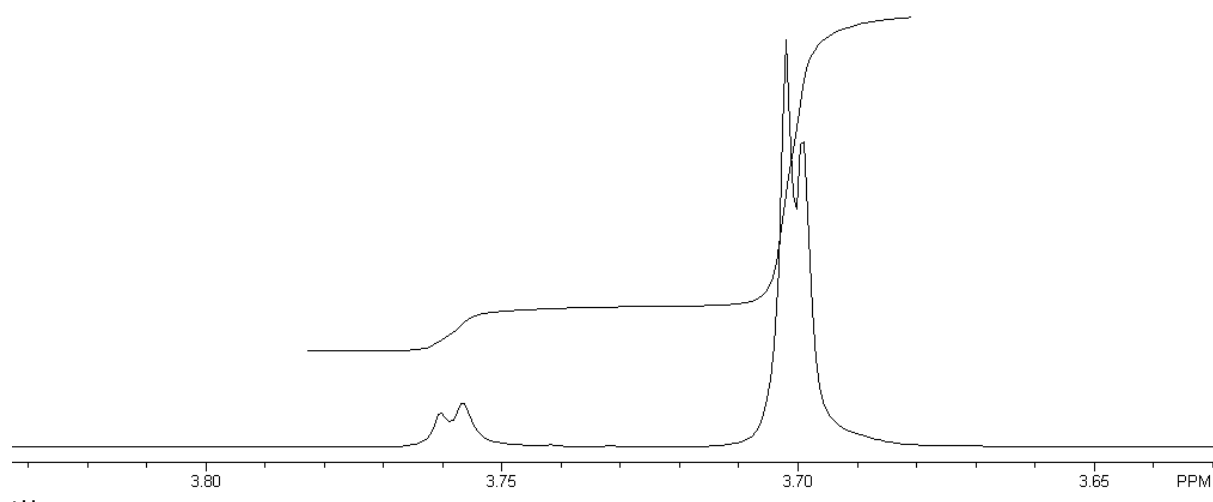
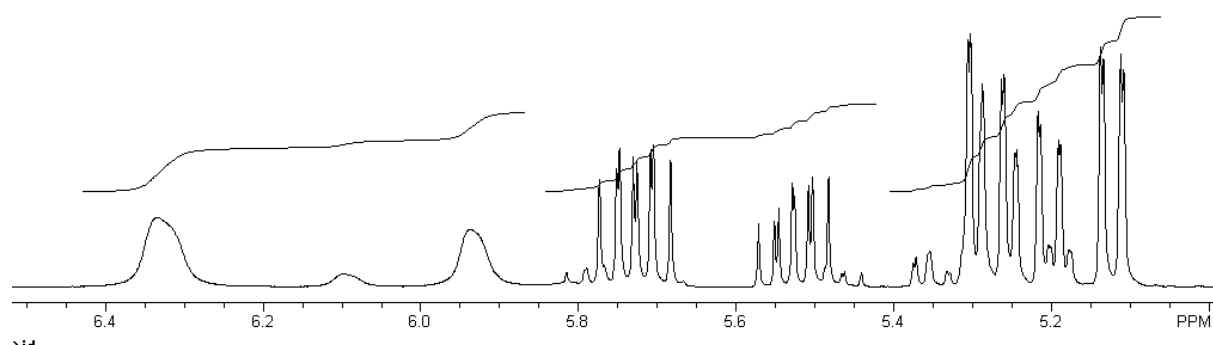
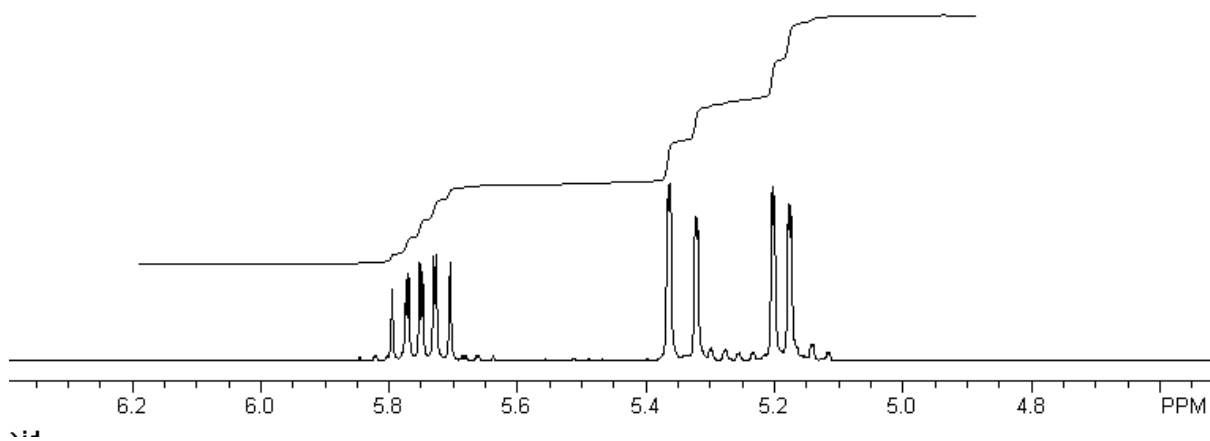
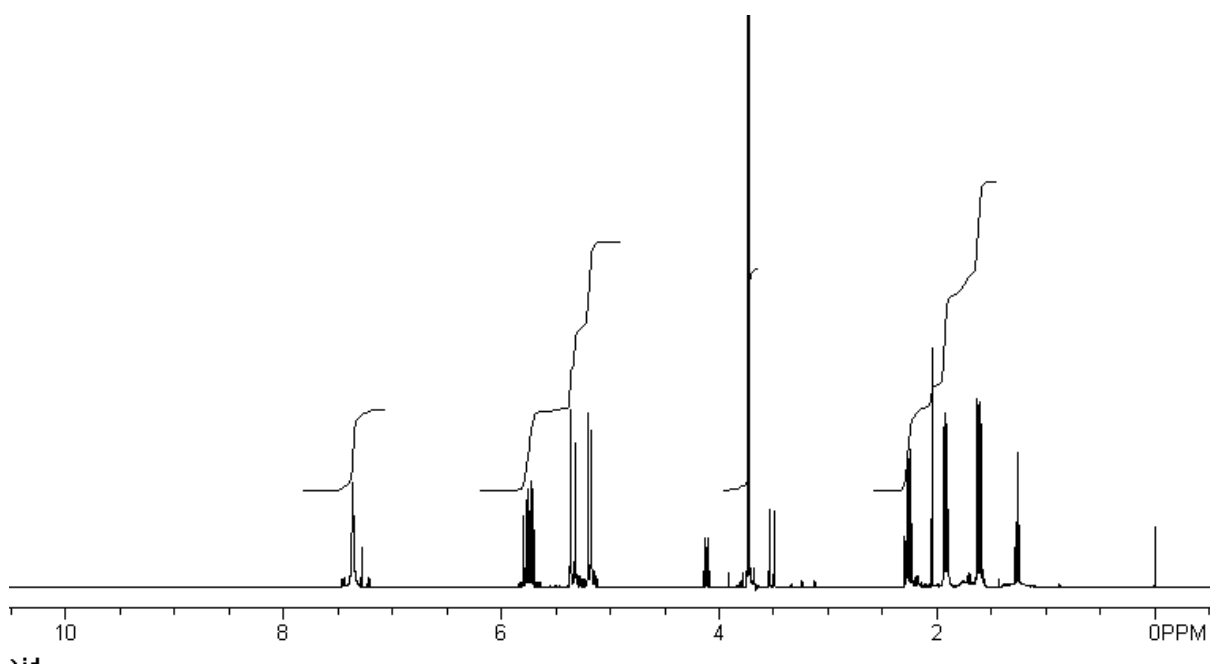


Fig S28 ^1H NMR Spectrum and expansions of mixture of (1*R**, 2*S**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(**7a**) and (1*R**, 2*R**)-methyl 2-vinyl-1-acetamidocyclopropanecarboxylate rac-(**8a**) (1.6:1) (CDCl_3 ; 400 MHz, Me_4Si).



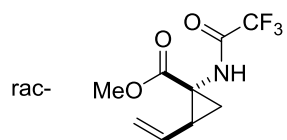
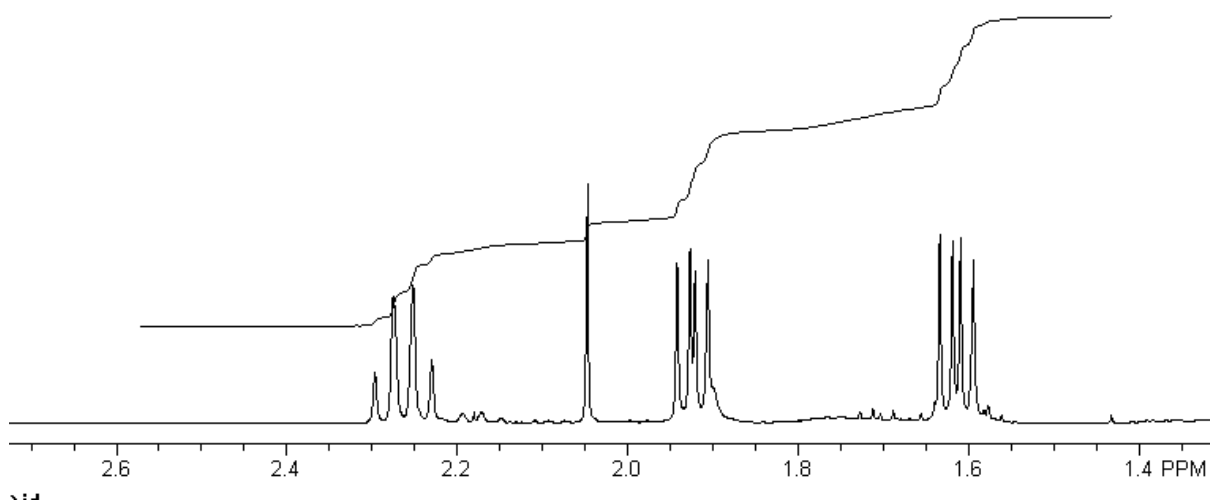
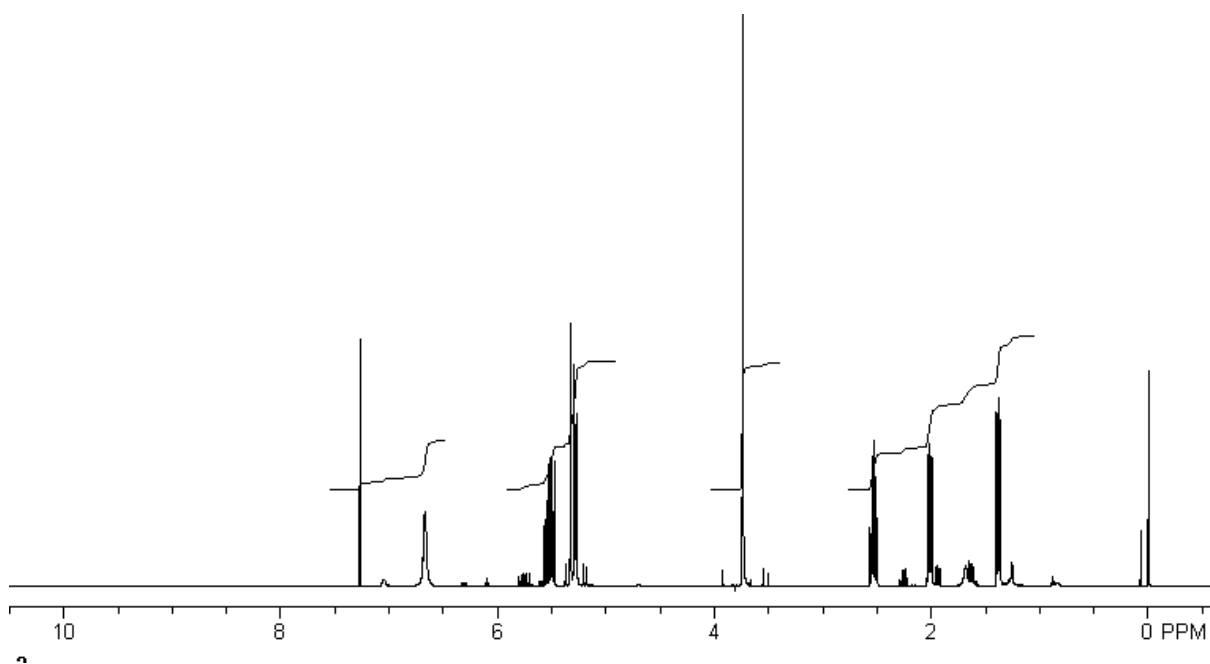


Fig S29 ^1H NMR Spectrum of (1*R**, 2*S**)-methyl 2-vinyl-1-(trifluoroacetamido)cycloprop anecarboxylate rac-(**7b**) (CDCl_3 ; 400 MHz, Me_4Si) (contains some ethyl acetate and DMF).



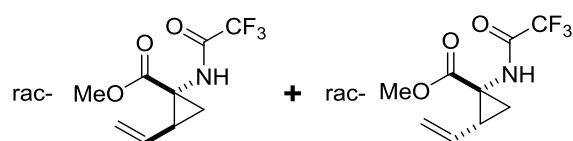
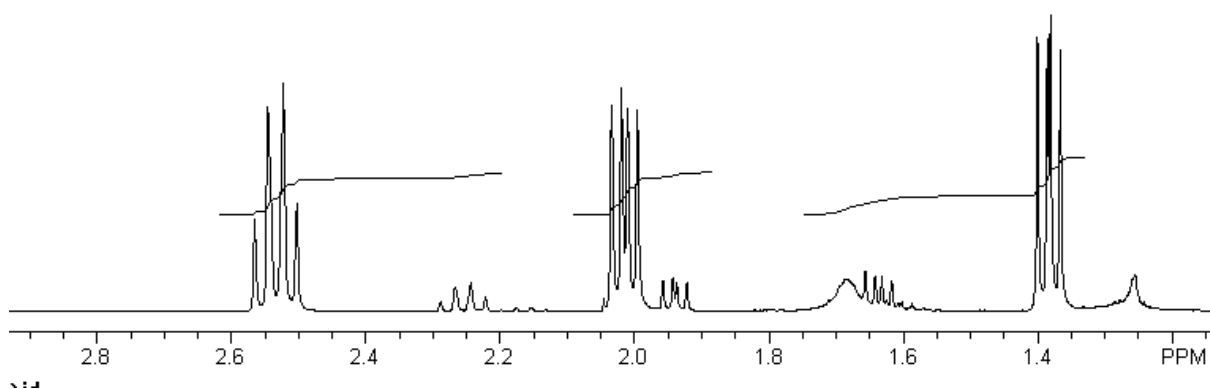
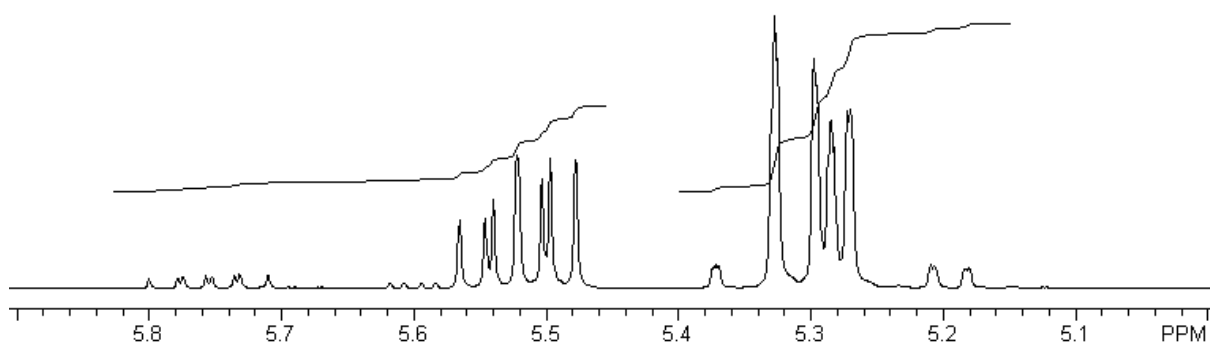
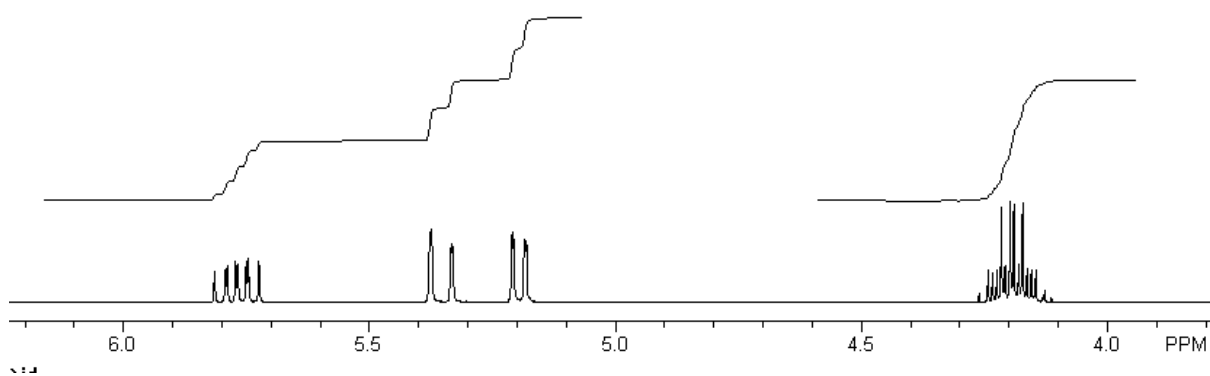
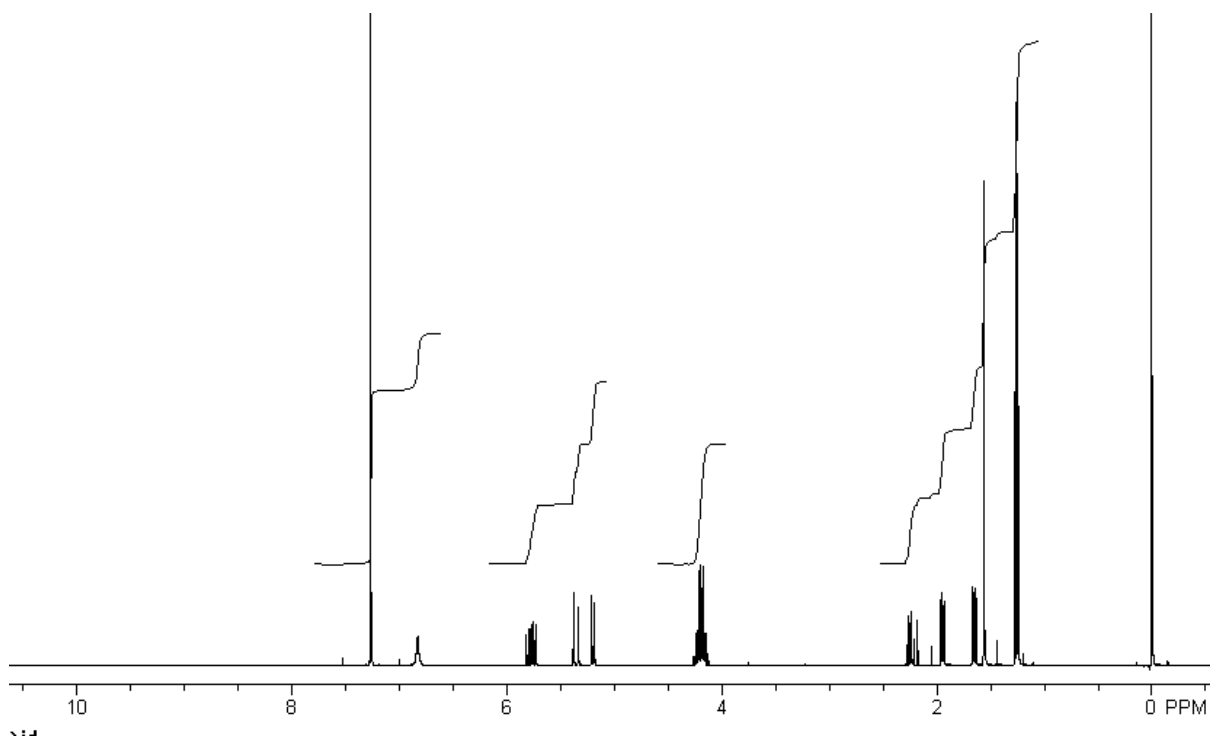


Fig S30 ^1H NMR Spectrum and expansions of mixture of (1*R**, 2*S**)-methyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate rac-(**7b**) and (1*R**, 2*R**)-methyl 2-vinyl(trifluoroacet amido)cyclopropanecarboxylate rac-(**8b**) (1:8) (400 MHz; CDCl_3) (contains some ethyl acetate and DMF).



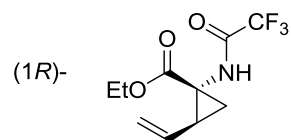
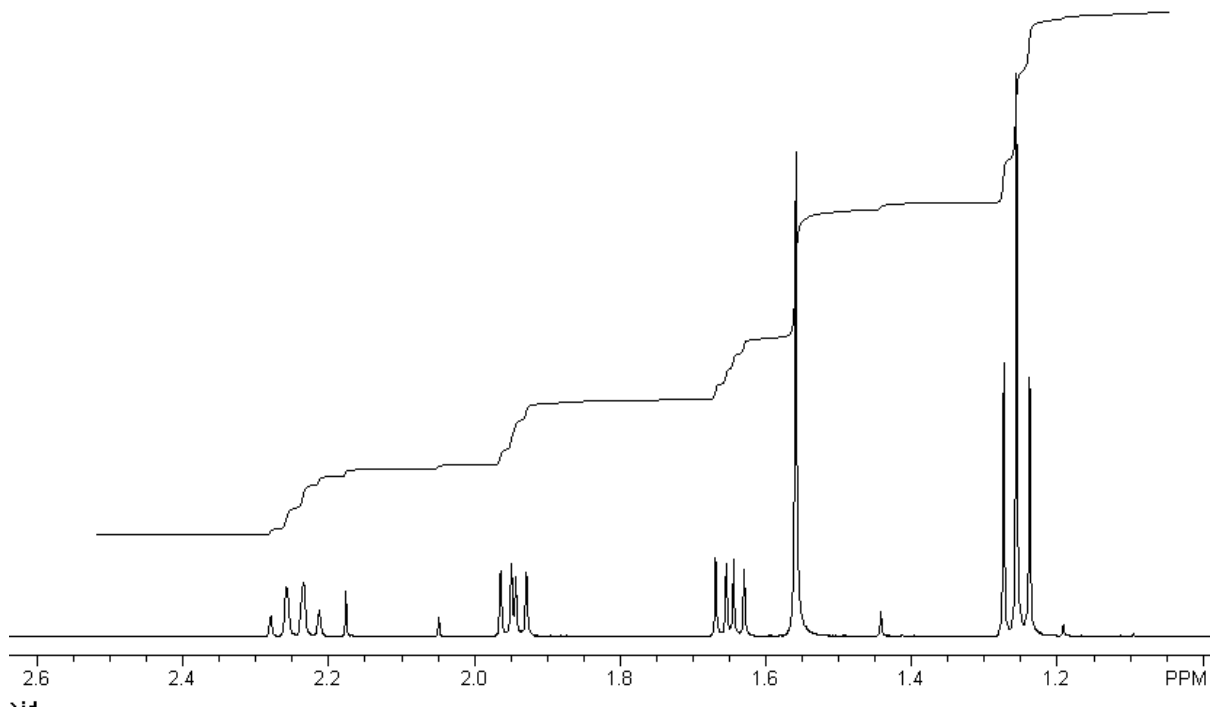
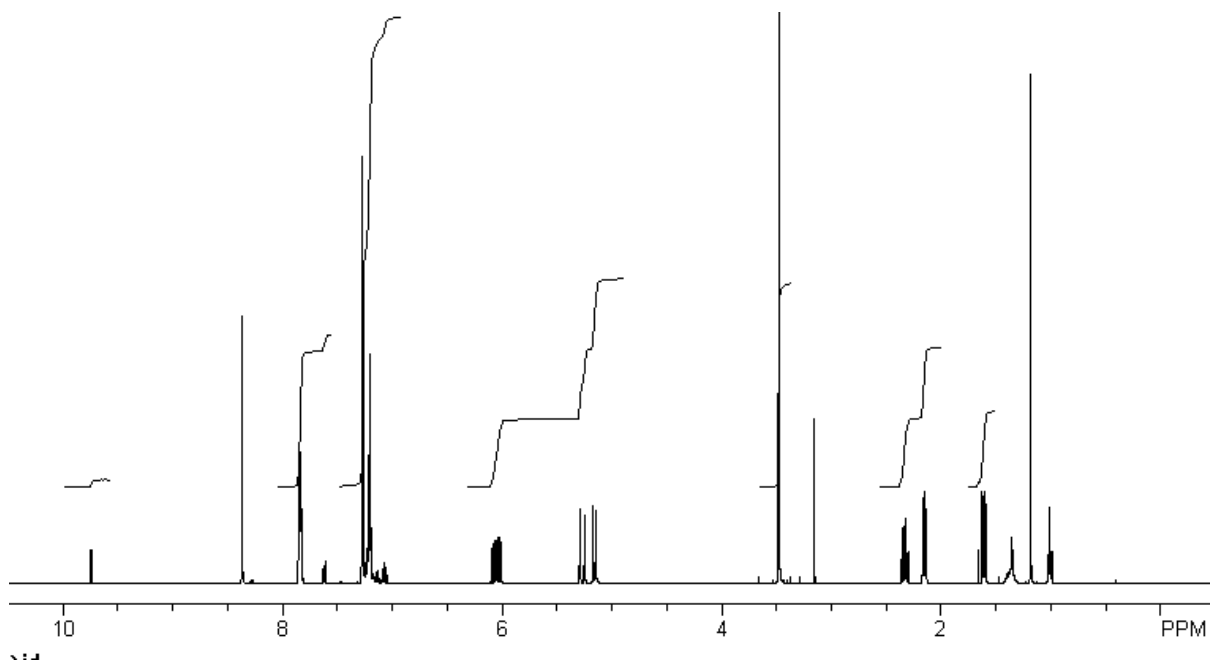


Fig S31 ^1H NMR Spectrum and expansions of (1*R*, 2*S*)-ethyl 2-vinyl-1-(trifluoroacetamido)cyclopropanecarboxylate (1*R*)-(7c) (400 MHz; CDCl_3 , Me_4Si).



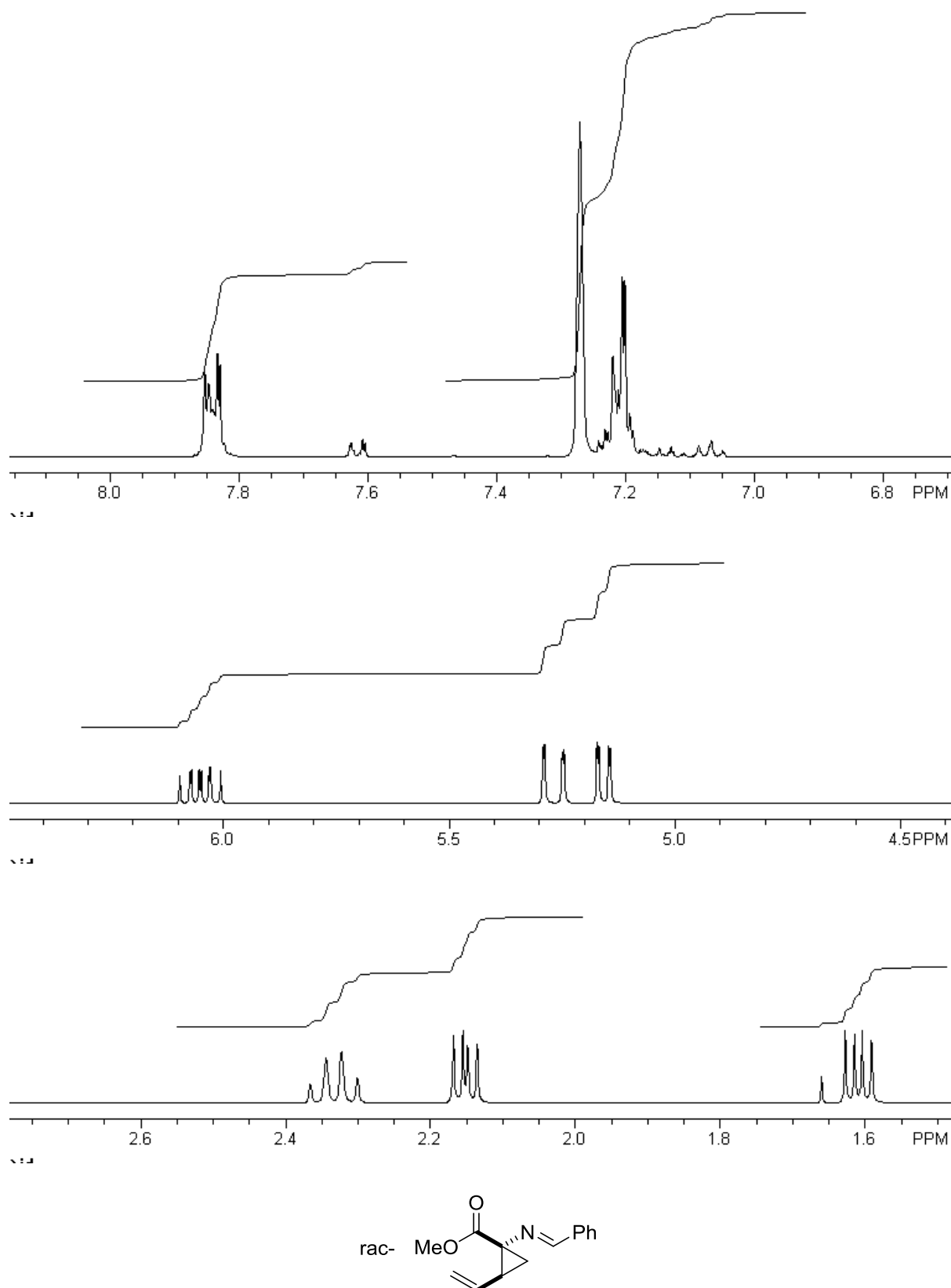
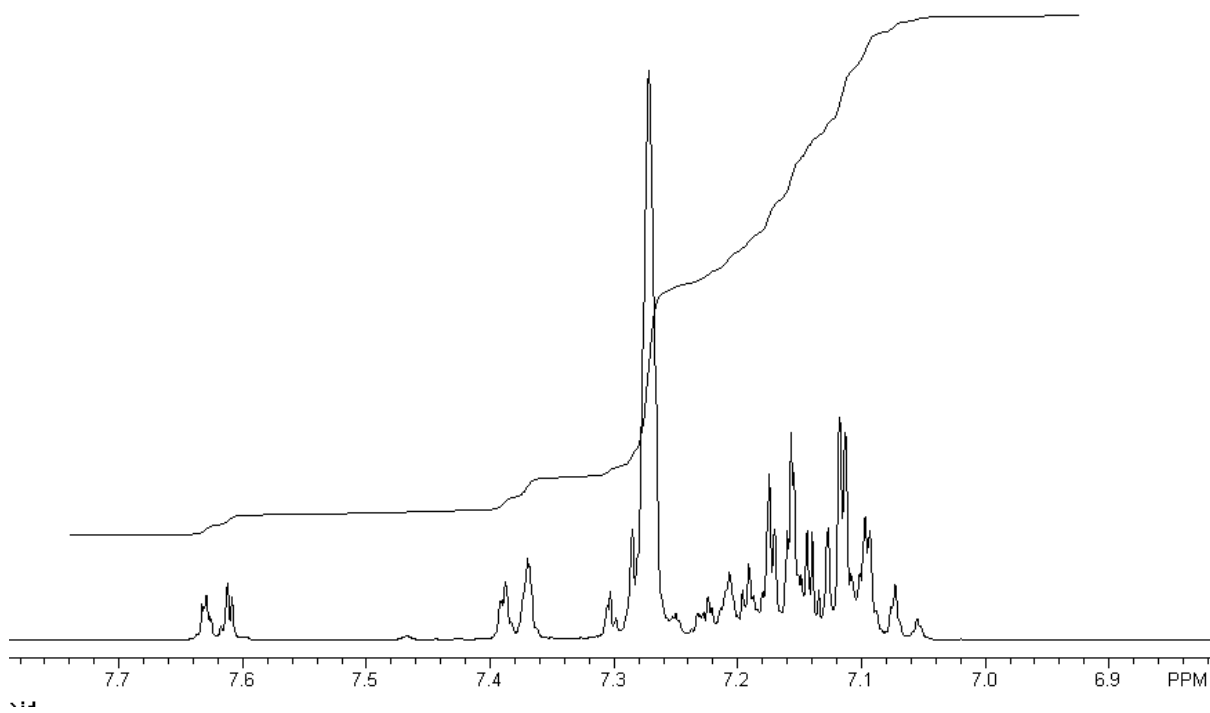
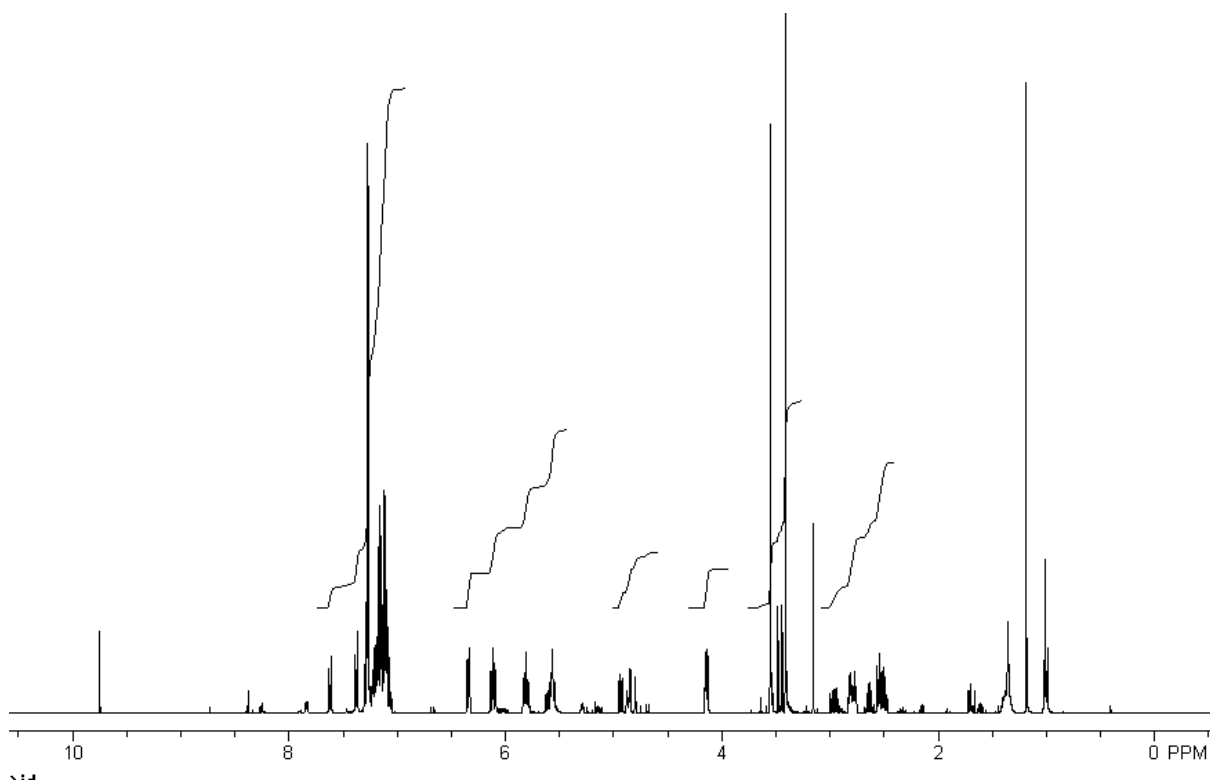
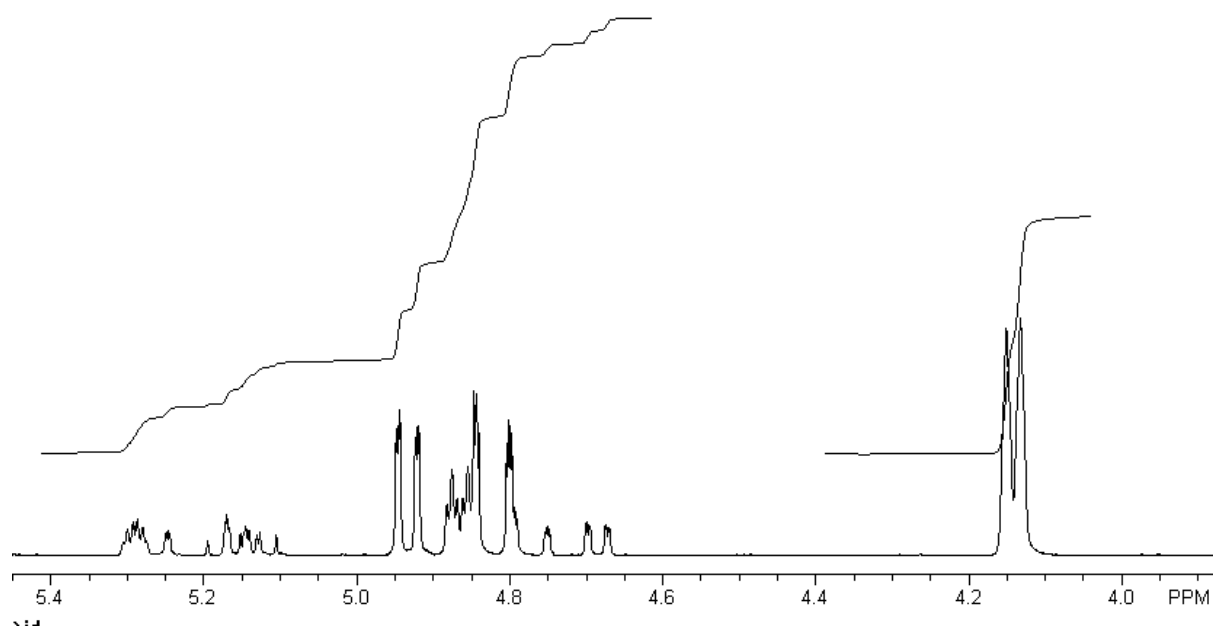
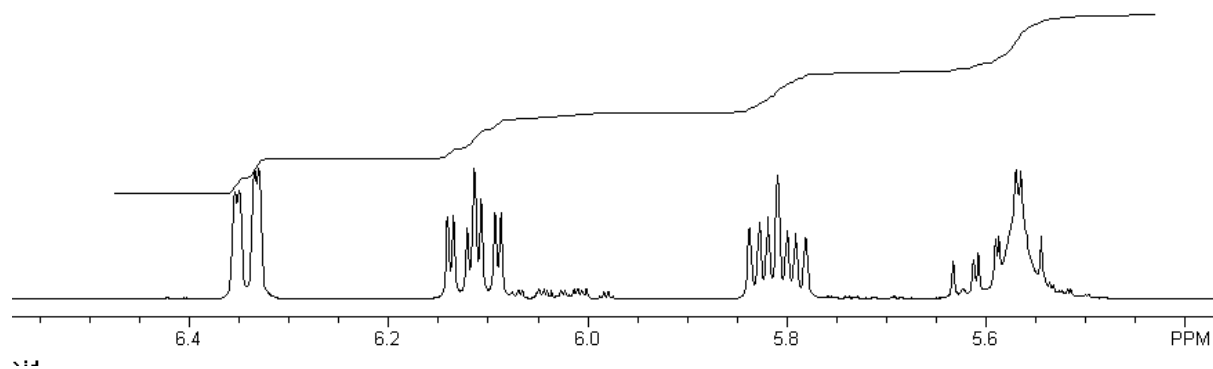


Fig S32 ^1H NMR Spectrum and expansions of (1*R**, 2*S**)-methyl 2-vinyl-1-(benzylideneamino)cyclopropanecarboxylate rac-(**9**) (400 MHz; C_6D_6 , also contains some MTBE, heptanes) (10:1 mixture with benzaldehyde).





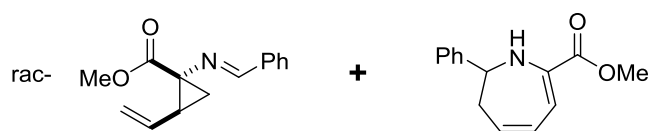
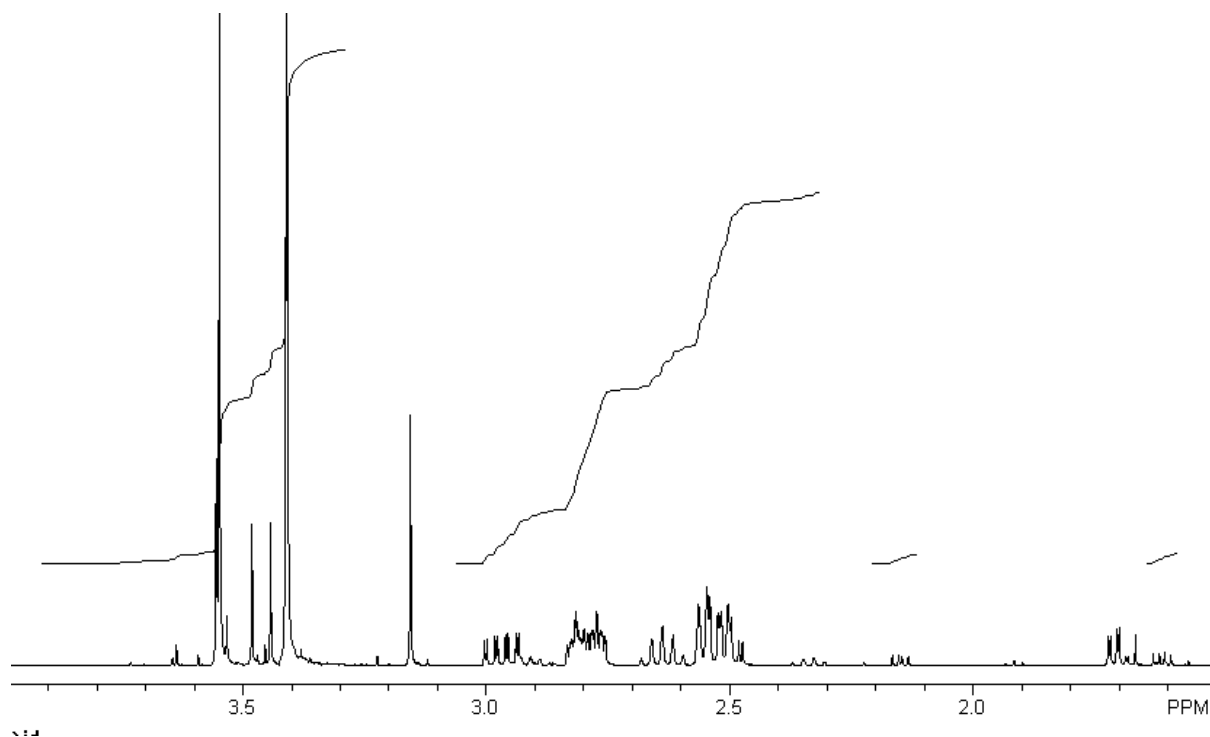
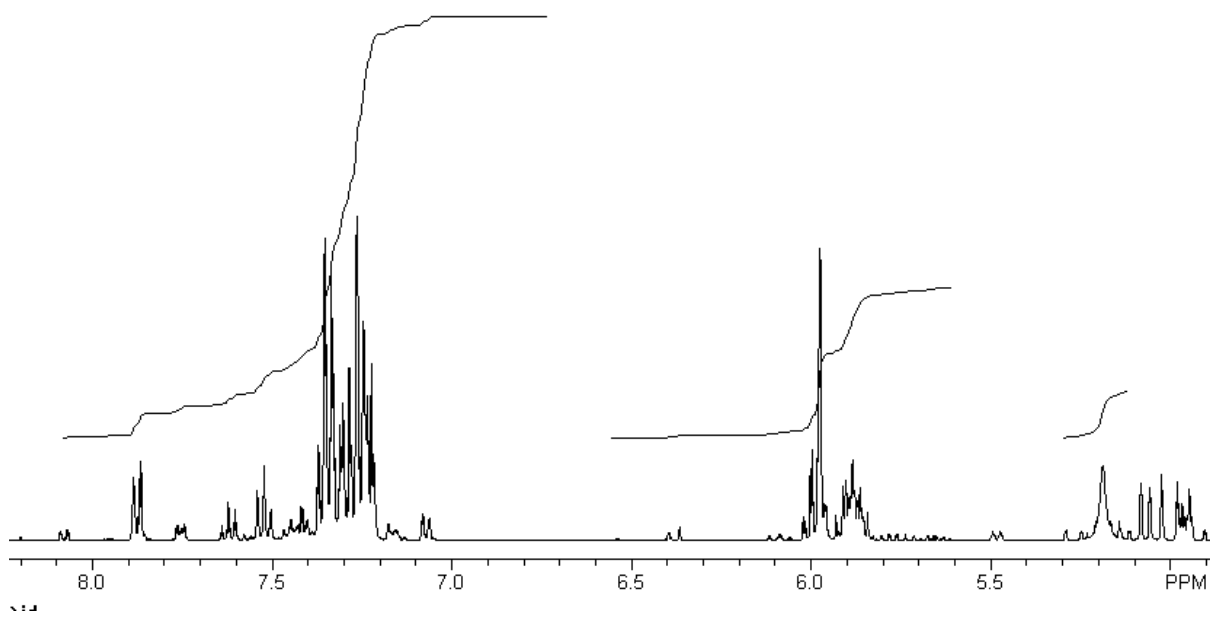
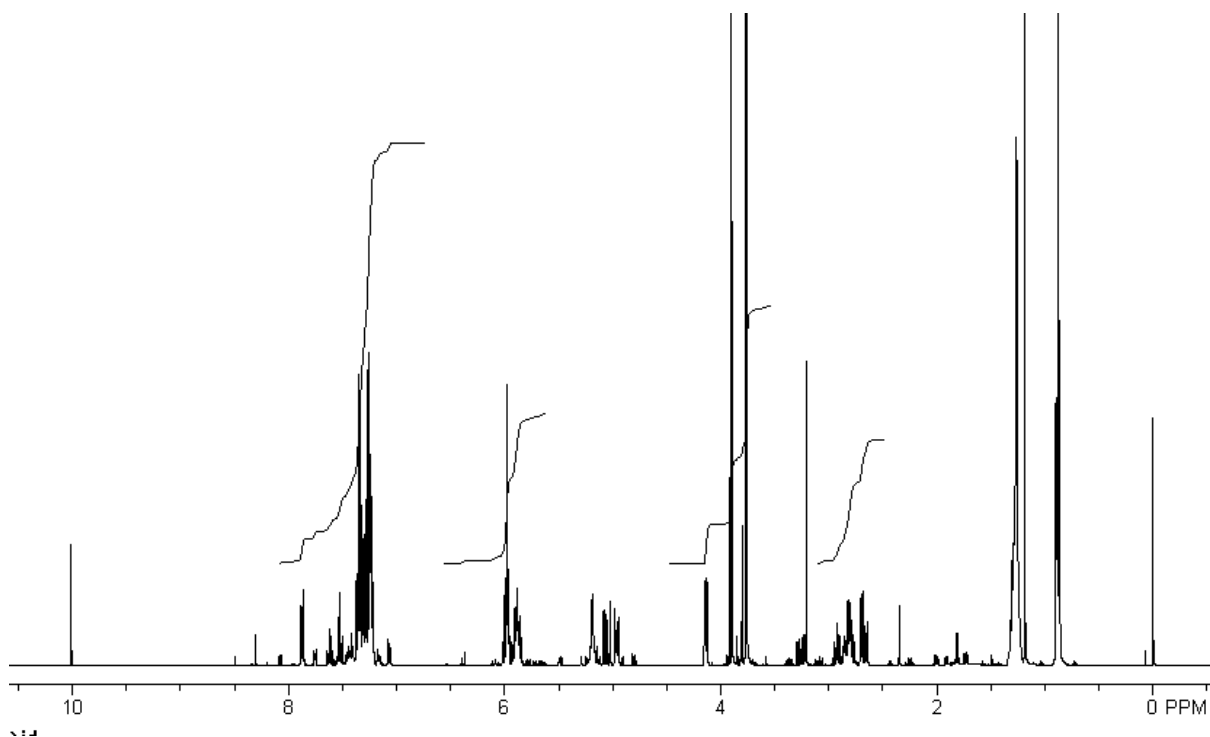


Fig S33 ^1H NMR Spectrum and expansions of crude isomerised mixture of (1*R**, 2*S**)-methyl 2-vinyl-1-(benzylideneamino)cyclopropane carboxylate rac-(**9**) and methyl 7-phenyl-6,7-dihydro[1*H*] azepine-2-carboxylate (**11**) (7:93) (400 MHz; C_6D_6).



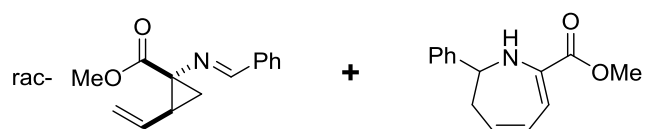
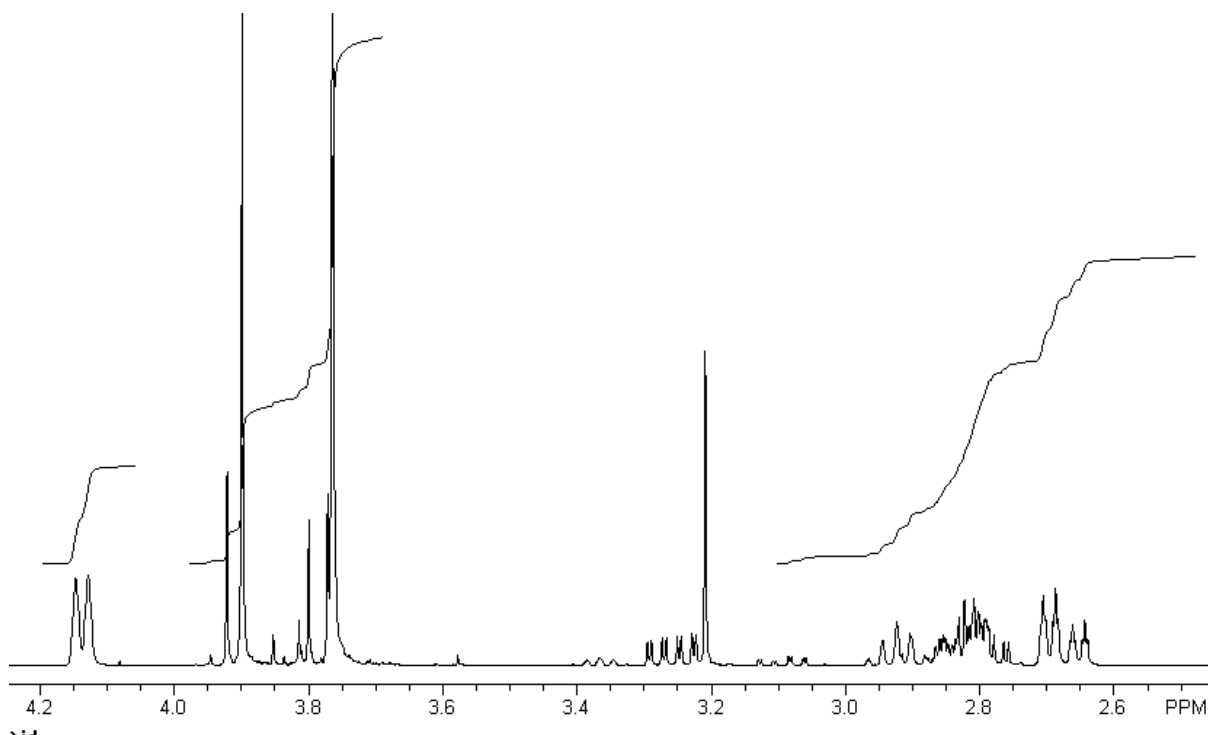
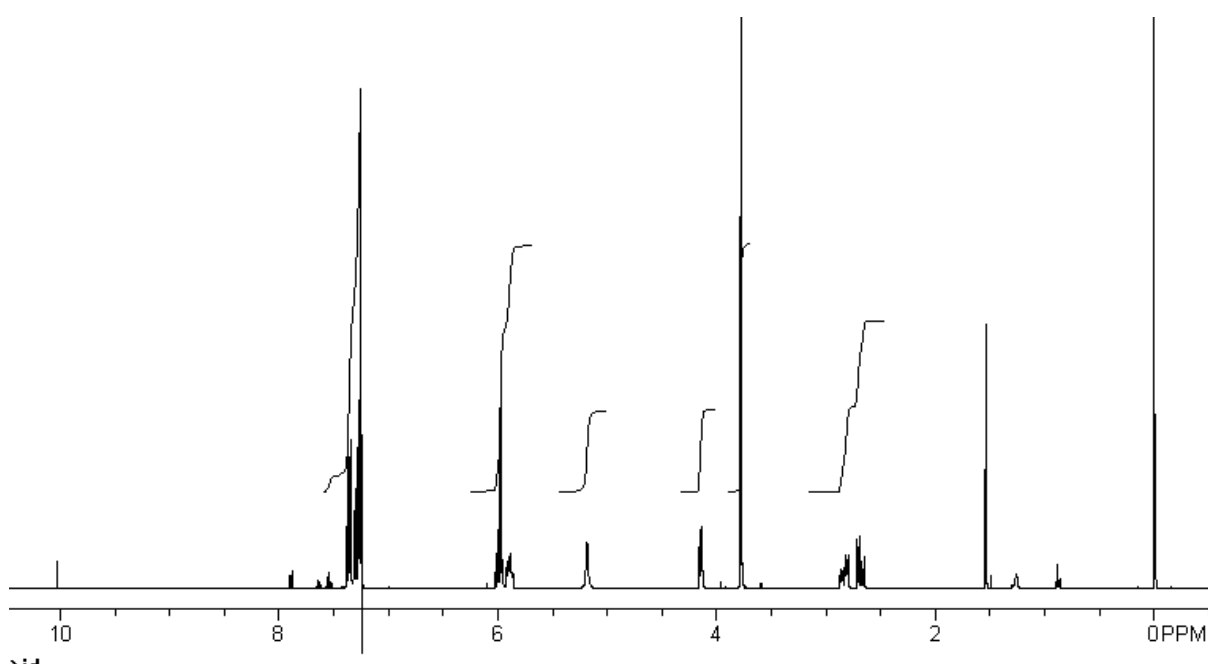


Fig S34 ^1H NMR Spectrum of crude isomerised mixture of (1*R**, 2*S**)-methyl 2-vinyl-1-(benzylidene amino)cyclopropanecarboxylate rac-(**9**) and methyl 7-phenyl-6,7-dihydro [1*H*]azepine-2-carboxylate (**11**) (7:93) (400 MHz; CDCl_3 , Me_4Si).



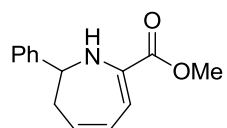
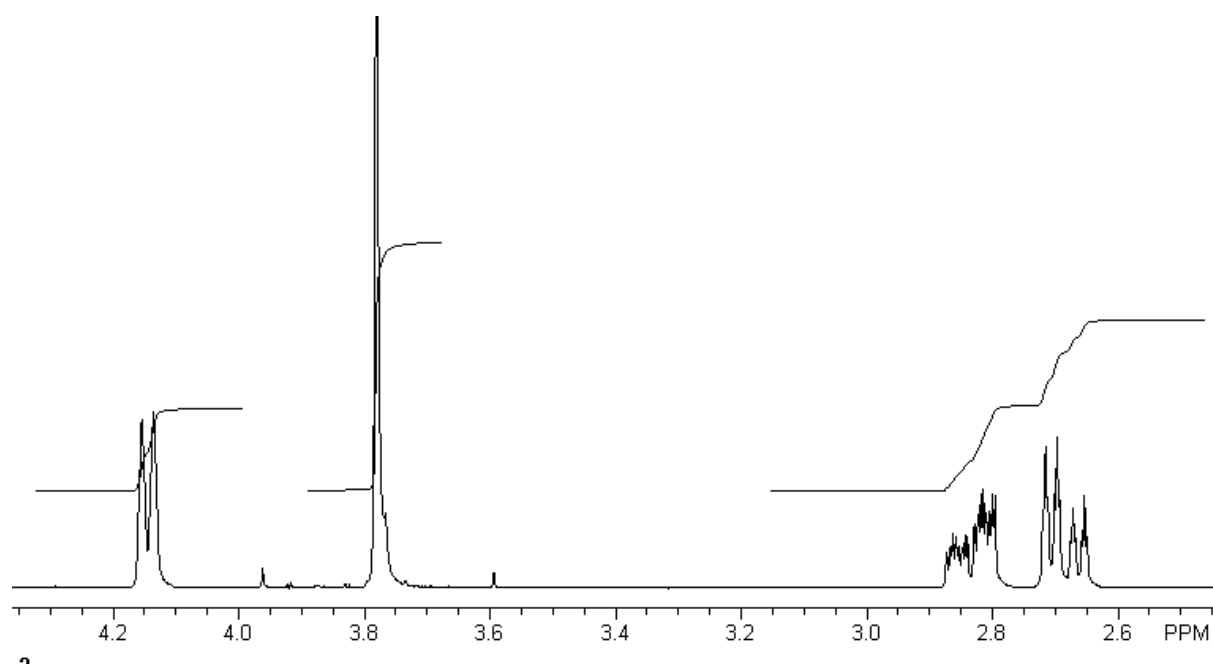
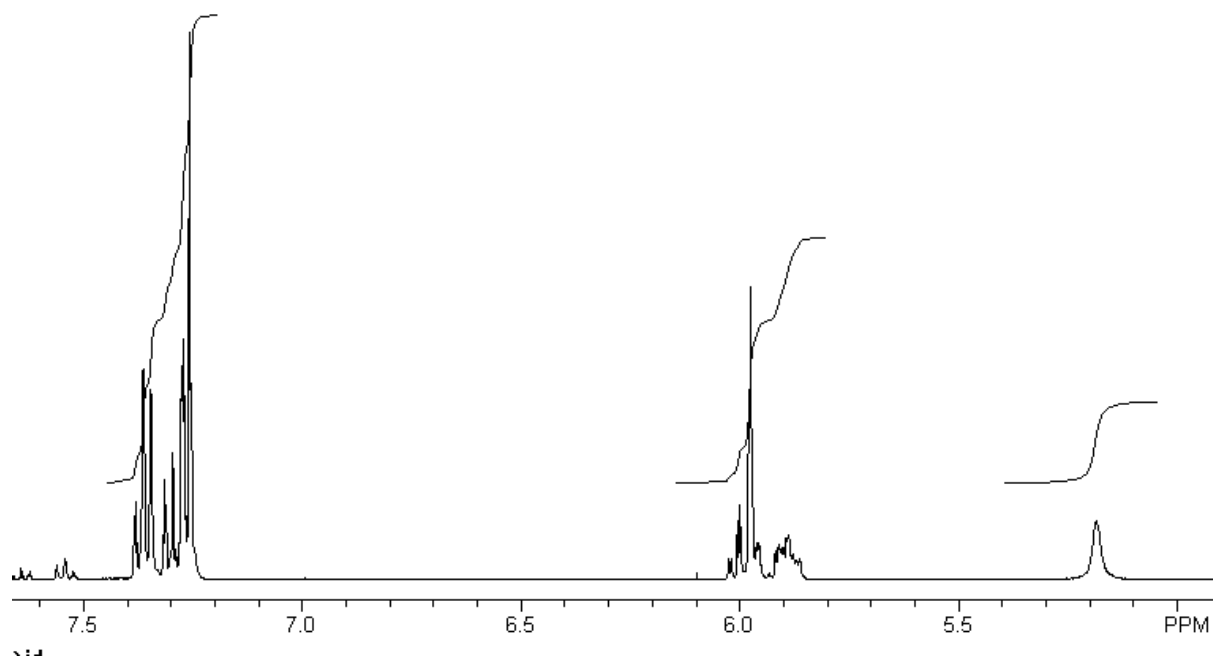
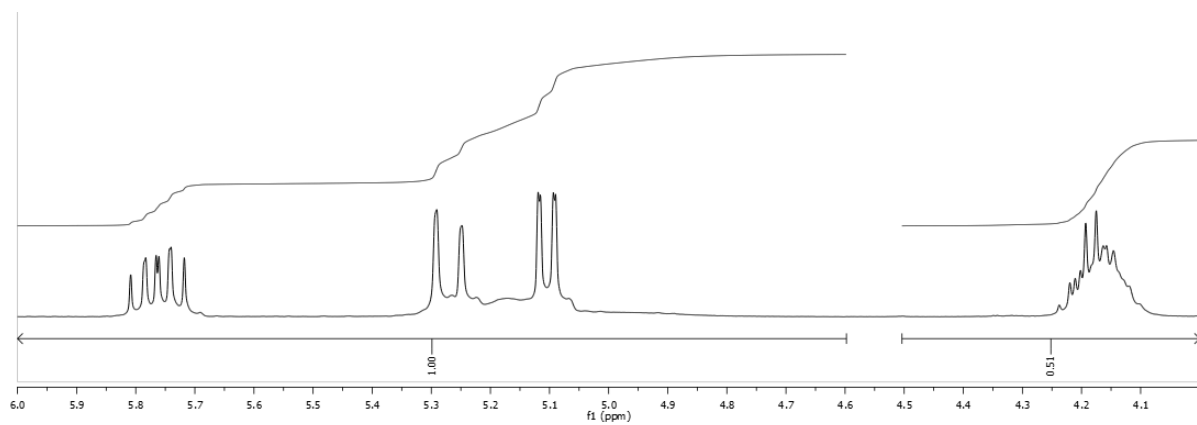
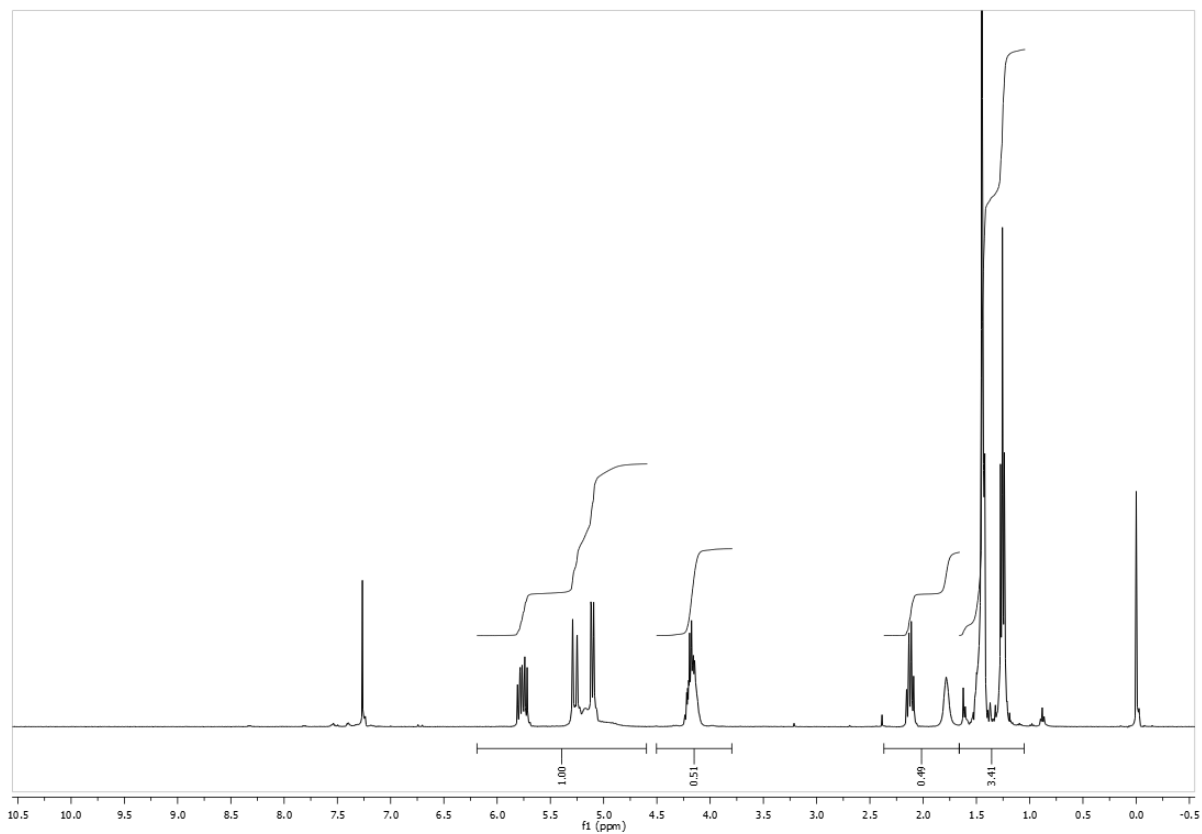


Fig S35 ^1H NMR Spectrum of purified methyl 7-phenyl-6,7-dihydro[1H]azepine-2-carboxylate (**11**) (400 MHz; CDCl_3 , Me_4Si).



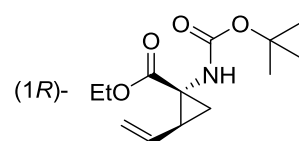
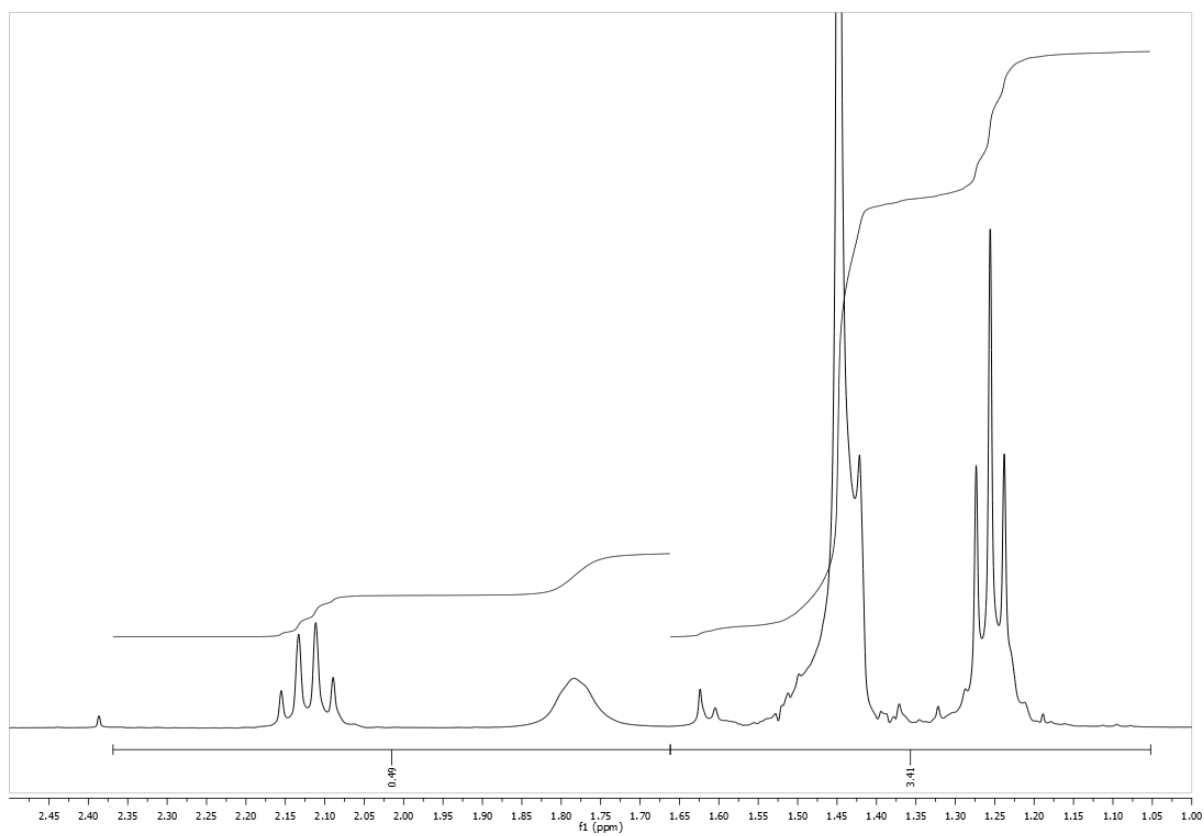
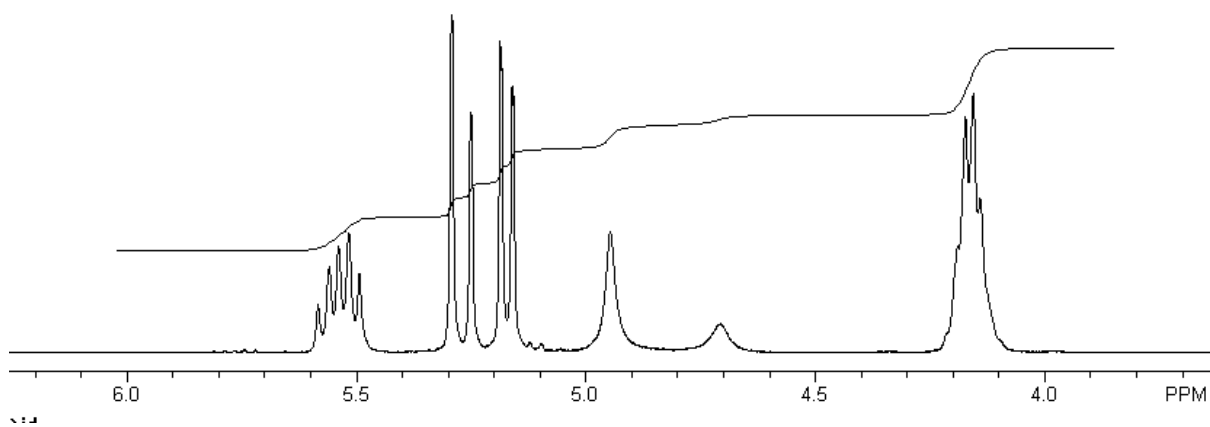
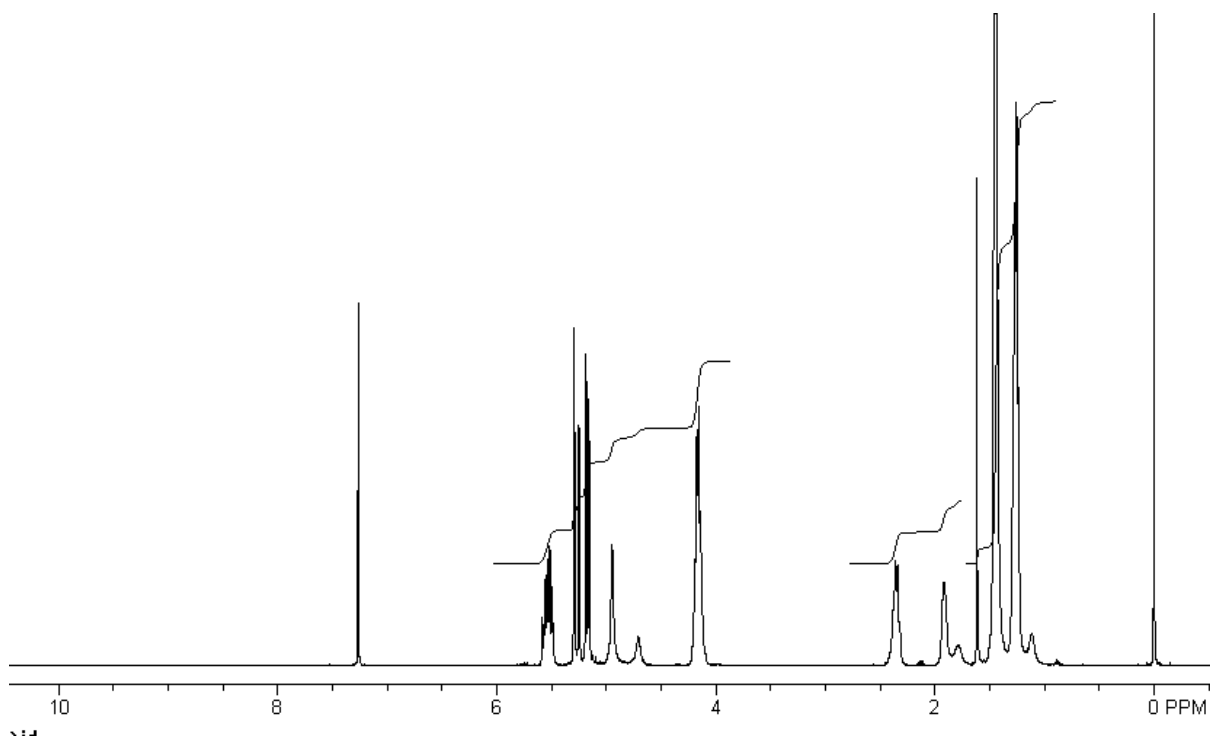


Fig S36 ^1H NMR Spectrum of (1*R*, 2*S*)-ethyl 2-vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate (1*R*)-(12) (400 MHz; CDCl_3 , Me_4Si).



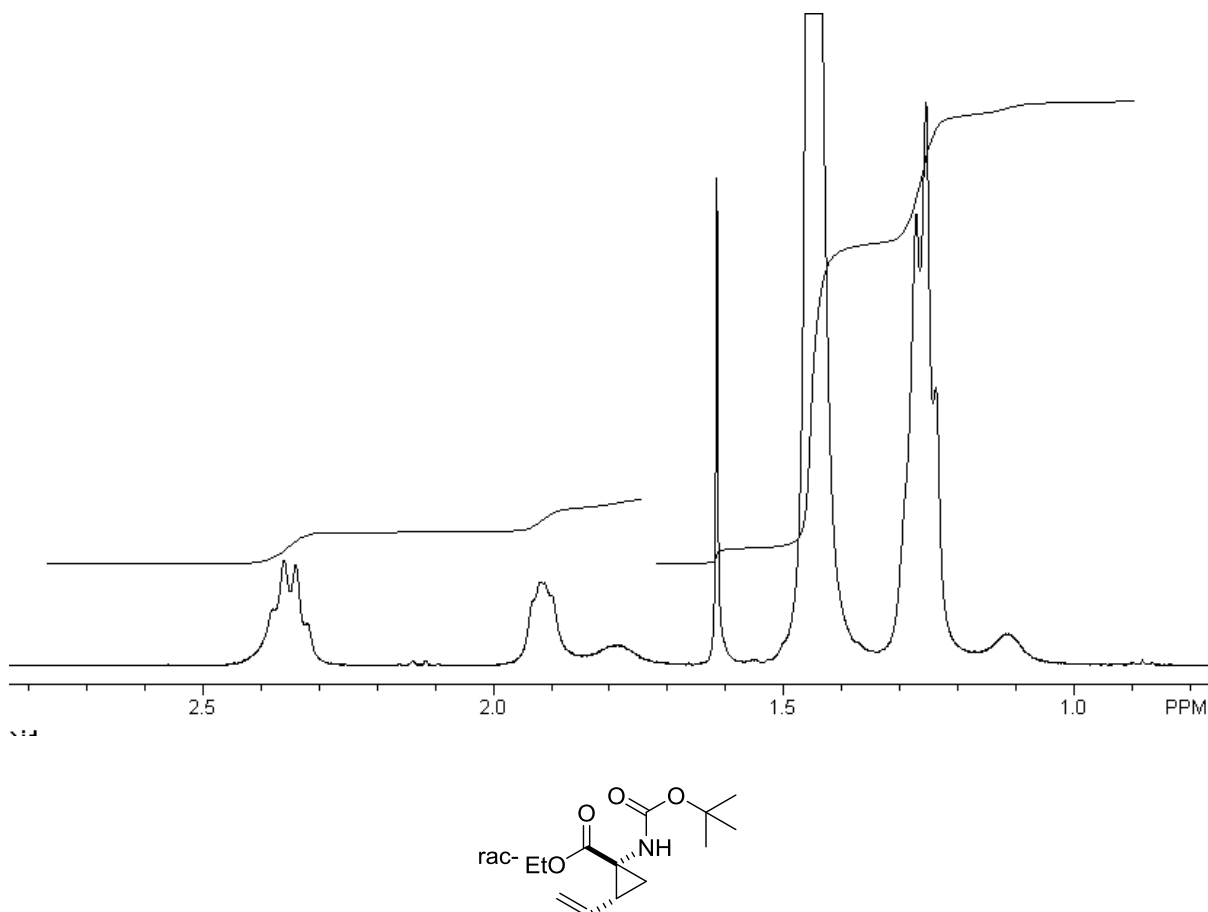


Fig S37 ¹H NMR Spectrum and expansions of (1*R**, 2*R**)-ethyl 2-vinyl-1-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate rac-(**13**) (400 MHz; CDCl₃, Me₄Si).

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