Isothiourea-Catalysed Enantioselective Radical Conjugate Addition under Batch and Flow Conditions

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1. General methods and commercial starting materials

Starting materials and solvents for the reactions were acquired from commercial sources (Acros Organics, Aldrich Chemical Co., Alfa Aesar, TCI Chemicals, Fluorochem and/or BLDpharm) unless otherwise specified. For thin layer chromatography (TLC), silica gel plates with fluorescence indicator 254 nm were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of potassium permanganate in water followed by heating. Flash column chromatography was performed using Geduran® Silica Gel 60 (0.040-0.063 nm). Cyclohexane and ethyl acetate for flash column chromatography were acquired from commercial sources and were used without previous purification. NMR spectra were acquired on a *Bruker Avance 300 MHz spectrometer*, running at 300 and 75 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$, 7.26 ppm; and CD_3OD, 3.31 ppm for ^{1}H-NMR; 77.2 ppm and 49.0 ppm for ^{13}C-NMR, respectively). ^{13}C-NMR was acquired on a broad band decoupled mode. ^{19}F-NMR spectra were acquired on a *Bruker Avance 500 MHz spectrometer* running at 470 MHz. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), sext (sextet), hept (heptet), m (multiplet), dd (doublet of doublets), dt (double of triplets), qd (quartet of doublets). Electrospray ionization has been used for measuring the exact mass (indicated for each case): HRMS (ESI) (Electrospray ionization mass spectroscopy) was acquired with an *Agilent Technologies 6120 Quadrupole LC/MS*. In this technique, *MassWorks software ver. 4.0.0.0 (Cerno Bioscience*) was used for the formula identification. *MassWorks* is a MS calibration software which calibrates for isotope profile as well as for mass accuracy, allowing highly accurate comparisons between calibrated and theoretical spectra.[1]

1.1. Batch Setup

For the photocatalytic reactions in batch, a 23W CFL was used as light source.

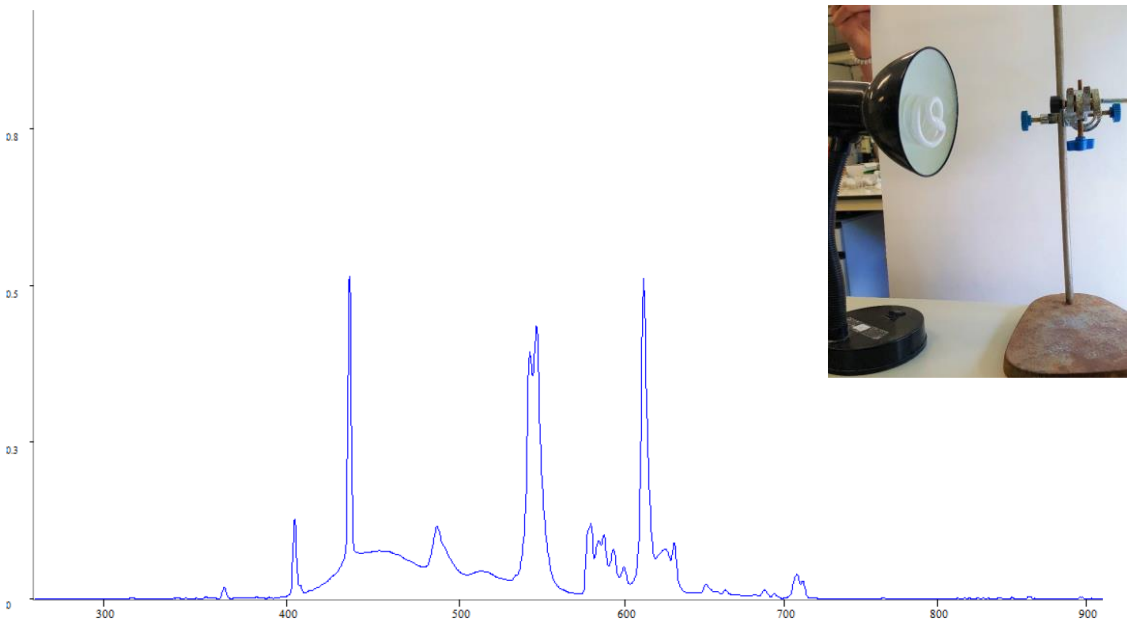


Figure S1. Emission spectrum of 23W CFL (400-700 nm) and imagine of the lamp used.

1.2. Flow Setup

-Homemade Setup

All continuous-flow experiments were carried out using a homemade flow-setup (**Figure S2**) including a 15 mL perfluoroalcoxy (PFA) reactor coil (inner diameter: 1.6 mm, external diameter 3.0 mm) and a lamp white LED (60W). Each reaction mixture was injected under inert atmosphere using Vapourtec E-series injection system.

Figure S2

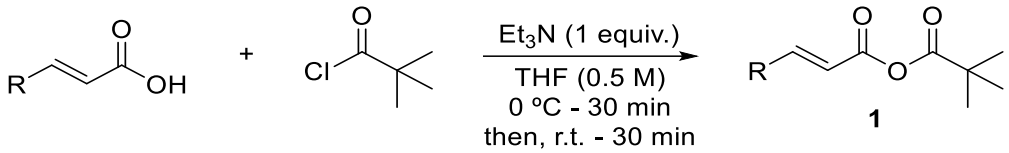
-Vapourtec setup

Some preliminary experiments were carried out using a commercially available Vapourtec E-series device equipped with a UV-150 photoreactor (**Figure S3**) including a 15 mL perfluoroalcoxy (PFA) reactor coil (inner diameter: 1.6 mm, external diameter 3.0 mm) and a lamp LED (60W, 420 nm, 450 nm, or 470 nm).

Figure S3

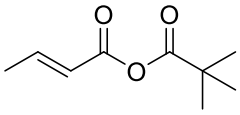
2. General procedure A: Synthesis of starting materials

2.1. General procedure A1: Synthesis of α,β-unsaturated anhydrides



They were prepared following a modified procedure described in the literature:[2] A solution of pivaloyl chloride (1.0 equiv.) in THF (5 mL) was added dropwise over an ice-cooled solution of the corresponding α,β-unsaturated acid (10.0 mmol) and triethylamine (1.0 equiv.) in THF (20 mL). The mixture was stirred 30 minutes at 0°C, then it was warmed to room temperature and stirred for further 30 min. The crude was filtered and rinsed with THF (2 x 5 mL). The filtrated was concentrated under reduced pressure to give pure product **1** as a colourless oil.

(*E*)-But-2-enoic pivalic anhydride (1a)



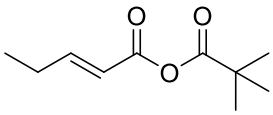
Following the general procedure A1, (*E*)-but-2-enoic acid (860.9 mg, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1a** as a colourless oil (96% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.21 – 6.73 (m, 1H), 5.86 (dd, *J* = 15.5, 1.6 Hz, 1H), 1.93 (d, *J* = 6.9 Hz, 3H), 1.25 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.3, 162.1, 149.4, 122.3, 40.1, 26.7 (3C), 18.5 ppm.

HRMS (ESI$^+$): calculated for $C_9H_{15}O_3$ $[M-H]^+$: 171.1016; found: 171.1027.

(*E*)-Pent-2-enoic pivalic anhydride (1b)



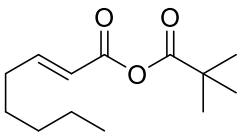
Following the general procedure A1, (*E*)-pent-2-enoic acid (1.00 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1b** as a colourless oil (88% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.13 (dt, *J* = 15.7, 6.3 Hz, 1H), 5.83 (dt, *J* = 15.7, 1.7 Hz, 1H), 2.37 – 2.18 (m, 2H), 1.26 (s, 9H), 1.08 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.3, 162.4, 155.4, 119.9, 40.1, 26.7 (3C), 25.8, 12.0 ppm.

HRMS (ESI$^+$): calculated for $C_{10}H_{17}O_3$ $[M-H]^+$: 185.1172; found: 185.1170.

(*E*)-Oct-2-enoic pivalic anhydride (1c)



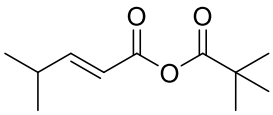
Following the general procedure A1, (*E*)-oct-2-enoic acid (1.40 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1c** as a colourless oil (95% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.08 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.84 (dt, *J* = 15.5, 1.5 Hz, 1H), 2.24 (qd, *J* = 7.3, 1.6 Hz, 2H), 1.62 – 1.40 (m, 2H), 1.32 – 1.24 (m, 13H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.3, 162.3, 154.4, 120.7, 40.1, 32.6, 31.4, 27.6, 26.7, 26.6 (3C), 22.5, 14.0 ppm.

HRMS (ESI$^+$): calculated for $C_{13}H_{23}O_3$ $[M-H]^+$: 227.1642; found: 227.1647.

(*E*)-4-Methylpent-2-enoic pivalic anhydride (1d)



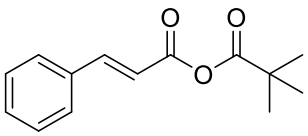
Following the general procedure A1, (*E*)-4-methylpent-2-enoic acid (1.14 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1d** as a colourless oil (91% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.05 (dd, *J* = 15.7, 6.6 Hz, 1H), 5.79 (dd, *J* = 15.7, 1.5 Hz, 1H), 2.61 – 2.40 (m, 1H), 1.28 (s, 9H), 1.08 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.3, 162.7, 160.1, 118.1, 40.1, 31.4, 26.7 (3C), 21.1 ppm.

HRMS (ESI$^+$): calculated for $C_{11}H_{19}O_3$ $[M-H]^+$: 199.1329; found: 199.1311.

(*E*)-Cinnamic pivalic anhydride (1e)



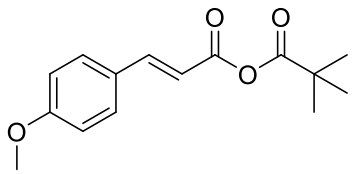
Following the general procedure A1, (*E*)-but-2-enoic acid (1.48 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1e** as a colourless oil (83% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.76 (d, *J* = 16.0 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.48 – 7.36 (m, 3H), 6.44 (dd, *J* = 16.0 Hz, 1H), 1.33 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.2, 162.8, 148.6, 133.8, 131.4, 129.2 (2C), 128.7 (2C), 117.0, 40.2, 26.7 (3C) ppm.

HRMS (ESI$^+$): calculated for $C_{14}H_{17}O_3$ $[M-H]^+$: 233.1172; found: 233.1166.

(*E*)-3-(4-Methoxyphenyl)acrylic pivalic anhydride (1f)



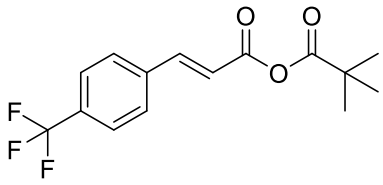
Following the general procedure A1, (*E*)-3-(4-methoxyphenyl)acrylic acid (1.78 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1f** as a colourless oil (92% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (d, *J* = 15.8 Hz, 1H), 7.54 – 7.45 (m, 2H), 7.04 – 6.86 (m, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 3.85 (s, 3H), 1.32 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.4, 163.2, 162.4, 148.4, 130.6 (2C), 126.6, 114.7 (2C), 114.3, 55.6, 40.1, 26.8 (3C) ppm.

HRMS (ESI$^+$): calculated for $C_{15}H_{19}O_4$ $[M-H]^+$: 263.1278; found: 263.1781.

(*E*)-3-(4-(Trifluoromethyl)phenyl)acrylic pivalic anhydride (1g)



Following the general procedure A1, (*E*)-3-(4-(trifluoromethyl)phenyl)acrylic acid (2.19 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1g** as a white solid (80% yield).

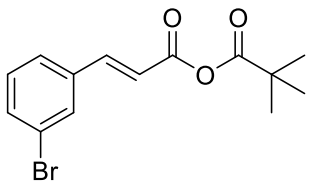
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.78 (d, *J* = 16.0 Hz, 1H), 7.71 – 7.63 (m, 4H), 6.52 (d, *J* = 16.0 Hz, 1H), 1.33 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.0, 162.3, 146.4, 137.2, 132.7 (q, *J* = 32.8 Hz), 128.8 (2C), 126.2 (q, *J* = 3.8 Hz, 2C), 123.9 (q, *J* = 272.3 Hz), 119.7, 40.3, 26.7 (3C) ppm.

^{19}F-NMR (470 MHz, $CDCl_3$): δ -63.0 ppm.

HRMS (ESI$^+$): calculated for $C_{15}H_{16}F_3O_3$ $[M-H]^+$: 301.1046; found: 301.1045.

(*E*)-3-(3-Bromophenyl)acrylic pivalic anhydride (1h)



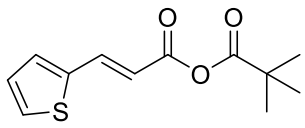
Following the general procedure A1, (*E*)-3-(3-bromophenyl)acrylic acid (2.27 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1h** as a colourless oil (86% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.70 – 7.61 (m, 2H), 7.59 – 7.49 (m, 1H), 7.49 – 7.42 (m, 1H), 7.35 – 7.22 (m, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 1.31 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.0, 162.3, 146.6, 135.8, 134.0, 131.2, 130.7, 127.2, 123.3, 118.5, 40.2, 26.7 (3C) ppm.

HRMS (ESI$^+$): calculated for $C_{14}H_{16}BrO_3$ $[M-H]^+$: 311.0277; found: 311.0289.

Pivalic (*E*)-3-(thiophen-2-yl)acrylic anhydride (1i)



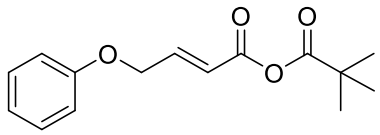
Following the general procedure A1, (*E*)-3-(thiophen-2-yl)acrylic acid (1.54 g, 10 mmol) and pivaloyl chloride (1.2 mL, 10 mmol) gave product **1i** as a pale yellowish solid (79% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 15.6 Hz, 1H), 7.46 (d, *J* = 5.1 Hz, 1H), 7.33 (d, *J* = 3.7 Hz, 1H), 7.09 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.21 (d, *J* = 15.6 Hz, 1H), 1.31 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.2, 162.7, 140.7, 139.0, 132.6, 130.2, 128.6, 115.4, 40.1, 26.7 (3C) ppm.

HRMS (ESI$^+$): calculated for $C_{12}H_{15}O_3S$ $[M-H]^+$: 239.0736; found: 239.0721.

(*E*)-4-phenoxybut-2-enoic pivalic anhydride (1j)



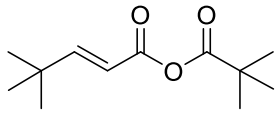
Following the general procedure A1, (*E*)-4-phenoxybut-2-enoic acid (475 mg, 2.67 mmol) and pivaloyl chloride (0.33 mL, 2.67 mmol) gave product **1j** as a yellowish oil (87% yield).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H), 7.20 (dt, *J* = 15.7, 3.8 Hz, 1H), 7.03 – 6.98 (m, 1H), 6.95 – 6.90 (m, 2H), 6.27 (dt, *J* = 15.7, 2.2 Hz, 1H), 4.74 (dd, *J* = 3.8, 2.2 Hz, 2H), 1.30 (s, 9H) ppm.

^{13}C-NMR (101 MHz, $CDCl_3$): δ 173.9, 161.7, 157.9, 146.8, 129.7, 121.7, 120.8, 114.7, 66.3, 40.1, 26.6 ppm.

HRMS (ESI$^+$): calculated for $C_{15}H_{18}O_4Na$ $[M+Na]^+$ requires 285.1103, found 285.1090 (-2.4 ppm).

(*E*)-4,4-dimethylpent-2-enoic pivalic anhydride (1k)



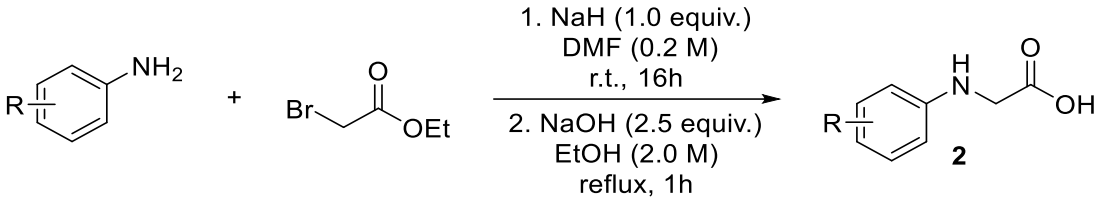
Following general procedure A1, (*E*)-4,4-dimethylpent-2-enoic acid (369 mg, 2.88 mmol) and pivaloyl chloride (0.35 mL, 2.88 mmol) gave product **1k** as a clear, colourless liquid (90% yield).

^{1}H-NMR (500 MHz, $CDCl_3$): 7.08 (d, *J* = 15.8 Hz, 1H), 5.76 (d, *J* = 15.9 Hz, 1H), 1.29 (s, 9H), 1.11 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): 174.3, 163.7, 163.0, 116.2, 40.1, 34.4, 28.6, 26.7.

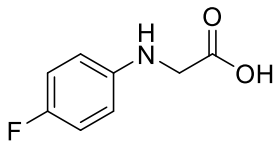
HRMS (ESI$^+$): calculated for $C_{12}H_{20}O_3Na$ $[M+Na]^+$ requires 235.1310, found 235.1300 (-2.1 ppm)

2.2. General procedure A2: Synthesis of α-amino acids



They were prepared following a modified procedure described in the literature:[3] The corresponding aniline (10 mmol) and ethyl 2-bromoacetate (10 mmol) were dissolved in dry DMF (50 mL). NaH (10 mmol) was slowly added and left stirring at room temperature overnight. Solvent was removed under reduced pressure and brine (50 mL) was added to the residue. Then, it was extracted with ethyl acetate (3 x 50 mL) and combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The crude ester was reflux for 1 hour in 5M aqueous solution of NaOH (2.5 equiv.) and ethanol (5 mL). After cooling to room temperature, it was extracted with ethyl acetate (20 mL) and aqueous layer was acidified with concentrated HCl to pH=5, observing a precipitate. The precipitate was filtered, washed with water (5 mL) and dried using a schelnk line to give pure α-amino acid **2**.

(4-Fluorophenyl)glycine (2b)



Following the general procedure A2, 4-fluoroaniline (1.11 g, 10 mmol) and ethyl 2-bromoacetate (1.1 mL, 10 mmol) gave, after hydrolysis, product **2b** as a pale brown solid (56% yield).

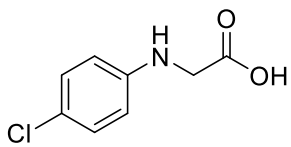
^{1}H-NMR (300 MHz, CD_3OD): δ 6.87 (t, *J* = 8.8 Hz, 2H), 6.60 (dd, *J* = 8.8, 4.4 Hz, 2H), 3.84 (s, 2H) ppm.

^{13}C-NMR (75 MHz, CD_3OD): δ 175.0, 157.4 (d, *J* = 233.6 Hz), 145.9, 116.3 (d, *J* = 22.6 Hz, 2C), 114.9 (d, *J* = 7.5 Hz, 2C), 46.8 ppm.

^{19}F-NMR (470 MHz, CD_3OD): δ -130.3 ppm.

HRMS (ESI$^+$): calculated for $C_8H_9FNO_2$ $[M-H]^+$: 170.0612; found: 170.0615.

(4-Chlorophenyl)glycine (2c)



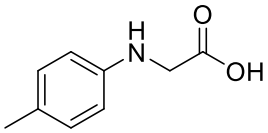
Following the general procedure A2, 4-chloroaniline (1.27 g, 10 mmol) and ethyl 2-bromoacetate (1.1 mL, 10 mmol) gave, after hydrolysis, product **2c** as a pale orange solid (20% yield).

^{1}H-NMR (300 MHz, CD_3OD): δ 7.08 (d, *J* = 8.8 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 3.85 (s, 1H) ppm.

^{13}C-NMR (75 MHz, CD_3OD): δ 174.8, 148.2, 129.8 (2C), 122.9, 115.0 (2C), 46.2 ppm.

HRMS (ESI$^+$): calculated for $C_8H_9ClNO_2$ $[M-H]^+$: 186.0316; found: 186.0326.

***p*-Tolylglycine (2d)**



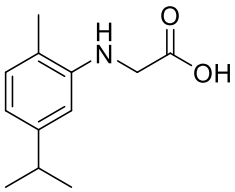
Following the general procedure A2, *p*-toluidine (1.07 g, 10 mmol) and ethyl 2-bromoacetate (1.1 mL, 10 mmol) gave, after hydrolysis, product **2d** as a pale orange solid (69% yield).

^{1}H-NMR (300 MHz, CD_3OD): δ 6.95 (d, *J* = 8.4 Hz, 2H), 6.56 (d, *J* = 8.5 Hz, 2H), 3.83 (s, 2H), 2.20 (s, 3H) ppm.

^{13}C-NMR (75 MHz, CD_3OD): δ 175.2, 146.8, 130.5 (2C), 128.3, 114.5 (2C), 47.0, 20.5 ppm.

HRMS (ESI$^+$): calculated for $C_9H_{12}NO_2$ $[M-H]^+$: 166.0863; found: 166.08760.

(5-Isopropyl-2-methylphenyl)glycine (2e)



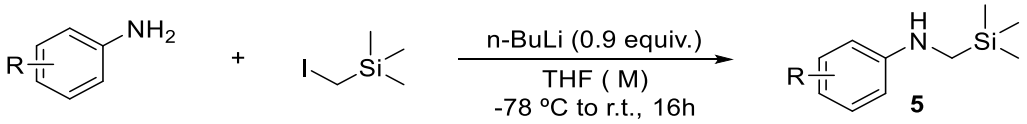
Following the general procedure A2, 5-isopropyl-2-methylaniline (1.49 g, 10 mmol) and ethyl 2-bromoacetate (1.1 mL, 10 mmol) gave, after hydrolysis, product **2e** as a pale brown solid (81% yield).

^{1}H-NMR (300 MHz, CD_3OD): δ 6.92 (d, *J* = 7.6 Hz, 1H), 6.50 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.36 (d, *J* = 1.7 Hz, 1H), 3.92 (s, 2H), 2.78 (hept, *J* = 6.9 Hz, 1H), 2.14 (s, 3H), 1.20 (d, *J* = 6.9 Hz, 6H) ppm.

^{13}C-NMR (75 MHz, CD_3OD): δ 175.2, 148.9, 146.7, 131.0, 121.3, 116.5, 109.5, 46.5, 35.4, 24.6 (2C), 17.1 ppm.

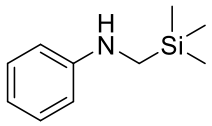
HRMS (ESI$^+$): calculated for $C_{12}H_{18}NO_2$ $[M-H]^+$: 208.1332; found: 208.1341.

2.3. General procedure A3: Synthesis of α-silyl anilines



They were prepared following a procedure described in the literature:[5] *n*-Butyllithium (1.1 equiv, 2.5 M in hexanes) was added dropwise to a solution of the corresponding aniline (1.0 equiv.) in anhydrous THF (0.33 M) under N_2. The resulting mixture was allowed to warm to room temperature and stir for 3 hours. After cooling to 0 °C, (Iodomethyl)trimethylsilane (1.1 equiv.) was added dropwise to the mixture. The resulting mixture was then allowed to warm to room temperature and stir overnight. Sat. NH_4Cl (aq.) was then added slowly, followed by an equal volume of H_2O. The mixture was then extracted with EtOAc (× 3), the organic phases were then combined, washed (brine), dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. The crude product was then purified, as specified, either via column chromatography or distillation under reduced pressure.

***N*-((trimethylsilyl)methyl)aniline (5a)**

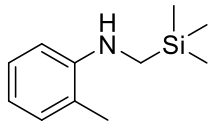


Following the general procedure A3, aniline (0.91 mL, 10.0 mmol) and (iodomethyl)trimethylsilane (1.63 mL, 11.0 mmol) gave product **5a** as a yellow oil (90% yield) after vacuum distillation.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.21-7.15 (m, 2H) 6.72-6.64 (m, 3H), 3.46 (s, 1H), 2.50 (s, 2H), 0.14 (s, 9H) ppm.

^{13}C-NMR (101 MHz, $CDCl_3$): δ 150.7, 129.3, 117.1, 112.5, 33.7, -2.5 ppm.

2-methyl-*N*-((trimethylsilyl)methyl)aniline (5b)

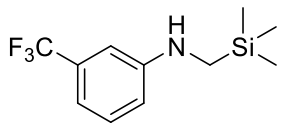


Following the general procedure A3, *o*-toluidine (1.06 mL, 10.0 mmol and (iodomethyl)trimethylsilane (1.63 mL, 11.0 mmol) gave product **5b** as a clear, colourless oil (68% yield) after vacuum distillation.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.20-7.13 (m, 1H), 7.07-7.01 (m, 1H), 6.75-6.70 (m, 1H), 6.68-6.62 (m, 1H), 3.34 (s, 1H), 2.52 (s, 2H), 2.14 (s, 3H), 0.16 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ 148.4, 129.9, 127.3, 121.7, 116.6, 109.5, 33.4, 17.4, -2.5 ppm

3-(trifluoromethyl)-N-((trimethylsilyl)methyl)aniline (5c)



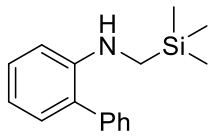
Following the general procedure A3, 3-(trifluoromethyl)aniline (1.61 g, 10.0 mmol) and (iodomethyl)trimethylsilane (1.63 mL, 11.0 mmol) gave product **5c** as a clear oil (52%) after vacuum distillation.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.26-7.22 (m, 1H), 6.93-6.90 (m, 1H), 6.87-6.85 (m, 1H), 6.81-6.76 (m, 1H), 3.67 (s, 1H), 2.51 (m, 2H), 0.15 (s, 9H) ppm.

^{19}F-NMR (471 MHz, $CDCl_3$): δ -62.8 ppm

HRMS (ESI$^+$): calculated for $C_{11}H_{17}F_3NSi$ $[M+H]^+$ requires 248.1082, found 248.1077

N-((trimethylsilyl)methyl)-[1,1'-biphenyl]-2-amine (5d)



Following the general procedure A3, [1,1'-biphenyl]-2-amine (1.69 g, 10.0 mmol) and (iodomethyl)trimethylsilane gave product **5d** (1.63 mL, 11.0 mmol) as a pale yellow oil (57% yield) after column chromatography (1% to 5% EtOAc in petrol).

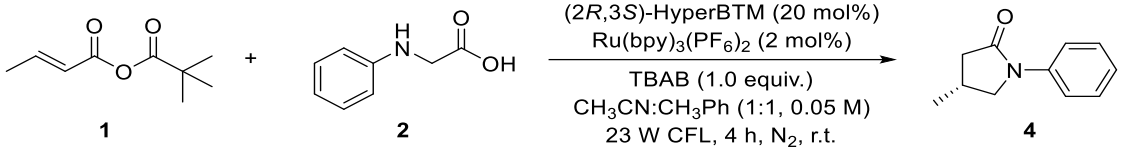
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.45-7.42 (m, 4H), 7.39-7.34 (m, 1H), 7.31-7.26 (m, 1H), 7.13-7.09 (m, 1H), 6.84-6.80 (m, 1H), 6.80-6.75 (m , 1H), 3.384 (s, 1H), 2.49 (s, 2H), 0.02 (s, 9H) ppm.

^{13}C-NMR (101 MHz, $CDCl_3$): 147.3, 139.5, 129.9, 129.5, 128.9 (2C), 127.5, 127.3, 116.6, 110.1, 33.3, -2.6.

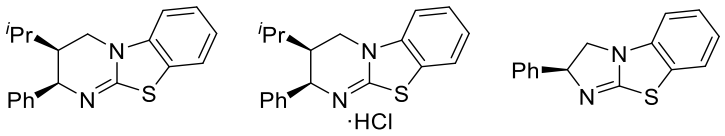
HRMS (ESI$^+$): calculated for $C_{16}H_{22}NSi$ $[M+H]^+$ requires 256.1522, found 256.1522

3. Optimization tables

Table S1. Optimization of addition of α-amino acids in batch conditions.



1 **2** **4**

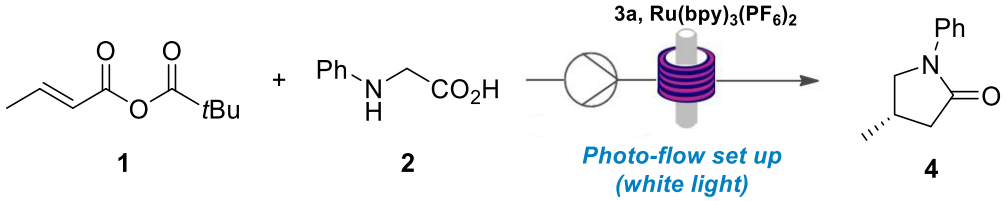


(2*R*,3*S*)-HyperBTM (3a) **(2*R*,3*S*)-HyperBTM·HCl (3b)** **(*S*)-BTM (3c)**

Entry[a]	*Deviation from optimized conditions*	*Yield (%)*[b]	*er (%)*[c]
1	**No deviation**	**65 (59)**	**81:19**
2	(2*R*,3*S*)-HyperBTM·HCl (**3b**) *instead of* **3a**	n.r.	-
3	(*S*)-BTM (**3c**) *instead of* **3a**	24	55:45
4	*fac*-Ir(ppy)$_3$ *instead of* Ru(bpy)$_3$(PF$_6$)$_2$	45	70:30
5	4-CzIPN *instead of* Ru(bpy)$_3$(PF$_6$)$_2$	30	80:20
6	Ru(bpy)$_3$Cl$_2$ *instead of* Ru(bpy)$_3$(PF$_6$)$_2$	n.r.	-
7	CH_3CN *instead of* CH_3CN:CH_3Ph	70	70:30
8	CH_3Ph *instead of* CH_3CN:CH_3Ph	n.r.	-
9	CH_3CN:CF_3Ph *instead of* CH_3CN:CH_3Ph	59	81:19
10	CH_3CN:^{t}BuOMe *instead of* CH_3CN:CH_3Ph	34	81:19
11	DCM:CH_3Ph *instead of* CH_3CN:CH_3Ph	25	83:17
12	TBAB: 0.5 equiv. of *instead of* 1.0 equiv.	76	75:25
13	TBAB: 1.5 equiv. of *instead of* 1.0 equiv.	53	81:19
14	K_2HPO_4 (1 equiv.)	40	81:19
15	K_2HPO_4 *instead of* TBAB	42	75:25
16	TBAC *instead of* TBAB	46	80:20
17	TBAI *instead of* TBAB	30	82:18
18	Blue LED	43	79:21
19	No light	n.r.	-
20	No photocatalyst	n.r.	-

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), TBAB (1 equiv.), Ru(bpy)$_3$(PF$_6$)$_2$ (2 mol%), (2*R*,3*S*)-HyperBTM (**3a**) (20 mol%), MeCN:MePh (1:1, 0.05 M) at r.t, under N_2 was irradiated using a 23W CFL during 4h. [b] ^{1}H-NMR yields using 1,3,5-trimethoxybenzene as internal standard. Isolated yield in brackets. [c] Enantiomeric ratio was measured by Supercritical Fluid Chromatography (SFC) using chiral columns.

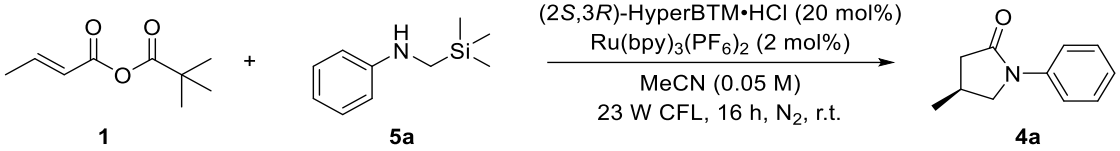
Table S2. Optimization of addition of α-amino acids in flow conditions.



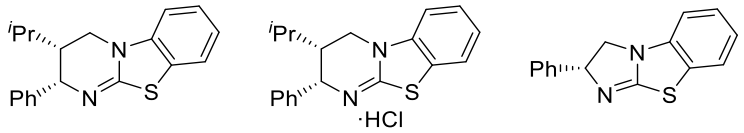
Entry[a]	*Deviation from optimized conditions*	*Yield (%)*[b]	*er (%)*[c]
1	**No deviation**	**81 (73)**	**73:27**
2	0.13 mL/min (120') *instead of* 0.25 mL/min (60')	81	73:27
3	Absence of K_2HPO_4	<5	73:27
4	0.5 mL/min (30') *instead of* 0.25 mL/min (60')	62	73:27
5	Purple LED *instead of* White LED	70	73:27
6	Blue LED (450 nm) *instead of* White LED	57	73:27
7	Blue LED (470 nm) *instead of* White LED	20	73:27

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), TBAB (1 equiv.), K_2HPO_4 (0.5 equiv.), $Ru(bpy)_3(PF_6)_2$ (2 mol%), (2*R*,3*S*)-HyperBTM (**3a**) (20 mol%), MeCN:MePh (1:1, 0.05 M) at r.t, under N_2 was pump by Vapourtec system at 0.25 mL/min (60 min residence time) and irradiated with White LED. [b] ^{1}H-NMR yields using 1,3,5-trimethoxybenzene as internal standard. Isolated yield in brackets. [c] Enantiomeric ratio was measured by Supercritical Fluid Chromatography (SFC) using chiral columns.

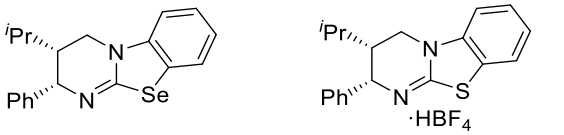
Table S3. Optimization of Brønsted acid using α-silyl amines.



1 **5a** **4a**



(2*S*,3*R*)-HyperBTM (3a') **(2*S*,3*R*)-HyperBTM·HCl (3b')** **(*R*)-BTM (3c')**

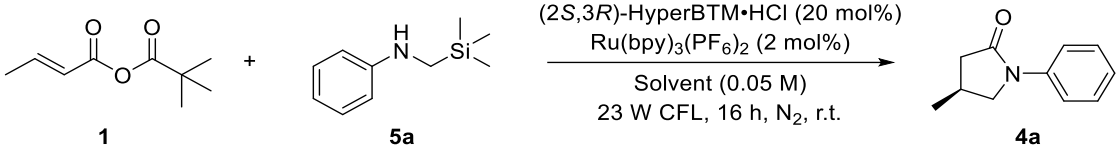


(2*S*,3*R*)-HyperSeBTM (3d') **(2*S*,3*R*)-HyperBTM·HBF_4 (3e')**

Entry[a]	*Deviation from optimized conditions*	*Yield (%)*[b]	*er (%)*[c]
1	**No deviation**	**80**	**79:21**
2	(2*S*,3*R*)-HyperBTM *instead of* (2*S*,3*R*)-HyperBTM•HCl	**37**	**76:24**
3	(*R*)-BTM *instead of* (2*S*,3*R*)-HyperBTM•HCl	**17**	**55:45**
4	(2*S*,3*R*)-HyperSeBTM *instead of* (2*S*,3*R*)-HyperBTM•HCl	**16**	**77:23**
5	Ph_2PO_2H & **3a'** *instead of* (2*S*,3*R*)-HyperBTM•HCl	**81**	**77:23**
6	Benzoic acid & **3a'** *instead of* (2*S*,3*R*)-HyperBTM•HCl	**44**	**77:23**
7	(–)-camphorsulfonic acid & **3a'** *instead of* (2*S*,3*R*)-HyperBTM•HCl	**59**	**54:46**
8	(2*S*,3*R*)-HyperBTM•HBF_4 *instead of* (2*S*,3*R*)-HyperBTM•HCl	**70**	**73:27**
9	No $Ru(bpy)_3(PF_6)_2$	**0**	**N/A**
10	No light	**0**	**N/A**

[a] Reaction conditions: **5a** (0.15 mmol), **1a** (0.18 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mol%), (2*S*,3*R*)-HyperBTM•HCl (**3a**) (20 mol%), MeCN (0.05 M) at r.t, under N_2 and irradiated with 23W CFL. [b] ^{1}H-NMR yields using 1,3,5-trimethoxybenzene as internal standard. Isolated yield in brackets. [c] Enantiomeric ratio was measured by GC analysis on a chiral stationary phase.

Table S4. Optimization of solvent using α-silyl amines.



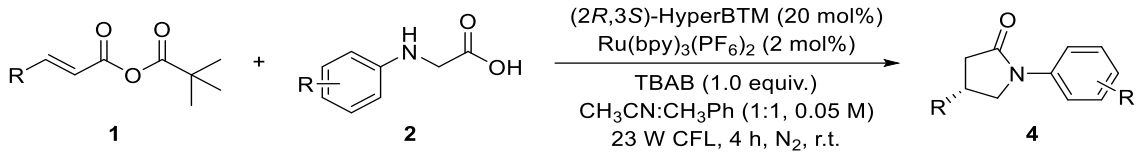
1 **5a** **4a**

Entry[a]	*Solvent*	*Yield (%)*[b]	*er (%)*[c]
1	CH_2Cl_2:PhMe (1:1)	**29**	**96:4**
2	$CHCl_3$:PhMe (1:1)	**9**	**N/A**
3	CH_2Cl_2:PhCl (1:1)	**36**	**95:5**
4	CH_2Cl_2:MeCN (1:1)	**70**	**80:20**
5	CH_2Cl_2:MeCN (2:1)	**68**	**82:18**
6	CH_2Cl_2:Acetone (1:3)	**50**	**87:13**
7	CH_2Cl_2:Acetone (1:1)	**64**	**88:12**
8	CH_2Cl_2:Acetone (3:1)	**54**	**89:11**
9	Acetone:PhMe (1:1)	**7**	**N/A**
10	Acetone:PhMe (1:3)	**7**	**N/A**
11	MeCN	**80**	**79:21**
12	MeCN:MTBE (1:1)	**60**	**88:12**
13	MeCN:$PhCF_3$ (1:1)	**71**	**86:14**
14	MeCN:PhCl (1:1)	**74**	**83:17**
15	MeCN:PhMe (1:1)	**80**	**86:14**
16	*MeCN:PhMe (1:2)*	***62***	***89:11***
17	MeCN:PhMe (1:3)	**52**	**91:9**
18	MeCN:PhCl (1:3)	**55**	**89:11**

[a] Reaction conditions: **5a** (0.15 mmol), **1a** (0.18 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mol%), (2*S*,3*R*)-HyperBTM•HCl (**3a**) (20 mol%), solvent (0.05 M) at r.t, under N_2 and irradiated with 23W CFL. [b] ^{1}H-NMR yields using 1,3,5-trimethoxybenzene as internal standard. Isolated yield in brackets. [c] Enantiomeric ratio was measured by GC analysis on a chiral stationary phase.

4. General procedure B: Enantioselective Radical Conjugate Addition to Anhydrides

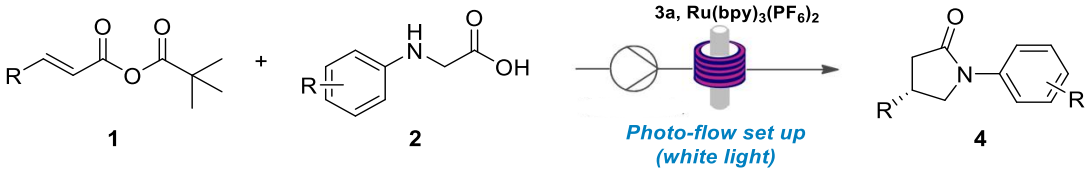
4.1. General procedure B1: Addition of α-Amino acids in batch conditions



1 2 4

Anhydride **1** (0.18 mmol, 1.2 equiv.) was added to a sealed vial followed by $Ru(bpy)_3(PF_6)_2$ (2.6 mg, 0.003 mmol), (2*R*,3*S*)-HyperBTM **3a** (9.3 mg, 0.03 mmol), tetrabutylammonium bromide (48.4 mg, 0.15 mmol) and α-amino acid **2** (0.15 mmol). Toluene (1.5 mL) and acetonitrile (1.5 mL) were added to the vial followed by a magnetic stirrer. The vial was closed with a PTFE/rubber septum and three freeze-pump-thaw cycles were performed. The reaction was irradiated using a white 23W CFL lamp at room temperature for 4 hours. After that, solvents were evaporated under reduced pressure and the crude was checked by ^{1}H-NMR using 1,3,5-trimethoxybencene as internal standard. The crude was purified by flash column chromatography using the eluents indicated in each case to give final product **4**.

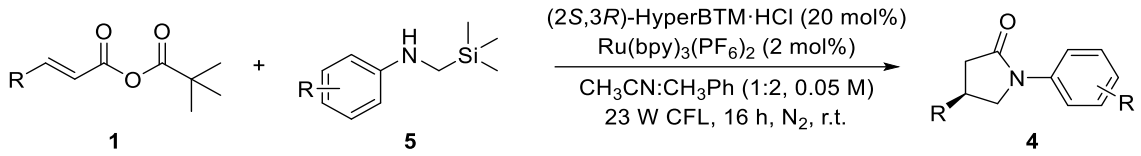
4.2. General procedure B2: Addition of α-Amino acids in flow conditions



1 2 4

Anhydride **1** (0.18 mmol, 1.2 equiv.) was added to a sealed vial followed by $Ru(bpy)_3(PF_6)_2$ (2.6 mg, 0.003 mmol), (2*R*,3*S*)-HyperBTM **3a** (9.3 mg, 0.03 mmol), tetrabutylammonium bromide (48.4 mg, 0.15 mmol), K_2HPO_4 (13.1 mg, 0.075 mmol) and α-amino acid **2** (0.15 mmol). Toluene (1.5 mL) and acetonitrile (1.5 mL) were added. The vial was closed with a PTFE/rubber septum and three freeze-pump-thaw cycles were performed. The reaction was pumped by Vapourtec pump B with a 0.25 mL/min flow rate (60 min residence time) and collected at the end of the reactor. After that, solvents were evaporated under reduced pressure and the crude was purified by flash column chromatography using the eluents indicated in each case to give the final product **4**.

4.3. General procedure B3: Addition of α-Silyl anilines in batch conditions

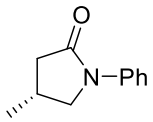


1 **5** **4**

A flame dried vial was charged with anhydride (1.2 equiv.), (2*S*,3*R*)-HyperBTM•HCl (0.20 equiv.) and $[Ru(bpy)_3](PF_6)_2$ (2 mol %). Separately, both MeCN and PhMe were degassed *via* N_2 or Ar sparging for >20 minutes. The α-silyl amine (1.0 equiv.) was then dissolved in MeCN:PhMe (1:2, 0.05 M) and added to the other vial *via* syringe. The resulting mixture was then stirred under 23 W CFL irradiation overnight at room temperature. The mixture was then diluted with EtOAc and washed with sat. $NaHCO_3$. The aqueous phase was then extracted with EtOAc (× 2), the organic phases were then combined, washed (brine), dried ($NaSO_4$) and concentrated under reduced pressure to give the crude residue. The crude product was then purified *via* column chromatography using the conditions specified.

4.4. Experimental Data and Characterization of Products 4

(*R*)-4-Methyl-1-phenylpyrrolidin-2-one (4a)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4a** (B1: 59% yield, 81:19 *er*; B2: 73% yield, 73:27 *er*; B3: 62% yield) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: $[\alpha]^{20}_D$ = +1.56 (*c* 0.64, $CHCl_3$) {Lit.[4] (*ent*) $[\alpha]^{22}_D$ = –3.1 (*c* 1.152, CH_2Cl_2)}

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.67 – 7.56 (m, 2H), 7.47 – 7.31 (m, 2H), 7.21 – 7.07 (m, 1H), 3.95 (dd, *J* = 9.4, 7.2 Hz, 1H), 3.45 (dd, *J* = 9.4, 6.4 Hz, 1H), 2.76 (dd, *J* = 16.6, 8.3 Hz, 1H), 2.68 – 2.48 (m, 1H), 2.26 (dd, *J* = 16.6, 7.2 Hz, 1H), 1.21 (d, *J* = 6.8 Hz, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.0, 139.6, 129.0 (2C), 124.6, 120.1 (2C), 56.1, 41.2, 26.5, 19.7 ppm.

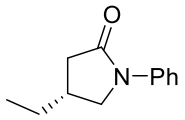
HRMS (ESI$^+$): calculated for $C_{11}H_{14}NO$ $[M-H]^+$: 176.1070; found: 176.1089.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 10.10 min, τ_{major} = 11.06 min (19:81 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 9.89 min, τ_{major} = 11.06 min (27:73 *er*).

B3: The enantiomeric excess was determined by GC analysis using a Restek Rt-βDEXcst (length: 30 m, thickness: 0.25 mm, film thickness: 0.25 µm, carrier gas: He, linear velocity: 28 cmsec^{-1}, temperature: 140 °C, 20 minute hold, ramp to 150 °C (1 °C min^{-1}), 30 minute hold, ramp to 180 °C (1 °C min^{-1}) : τ_{minor} = 61.37 min, τ_{major} = 61.72, 89:1 er.

(*R*)-4-Ethyl-1-phenylpyrrolidin-2-one (4b)



Following the general procedure B, (*E*)-pent-2-enoic pivalic anhydride **1b** (33.2 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4b** (B1: 53% yield, 84:16 *er*; B2: 94% yield, 76:24 *er*, B3: 88%, 89:11 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: **$[\alpha]^{20}_D$** = +9.46 (*c* 0.56, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.66 – 7.53 (m, 2H), 7.42 – 7.31 (m, 2H), 7.21 – 7.09 (m, 1H), 3.93 (dd, *J* = 9.6, 7.6 Hz, 1H), 3.50 (dd, *J* = 9.6, 6.8 Hz, 1H), 2.97 – 2.59 (m, 1H), 2.49 – 2.21 (m, 2H), 1.90 – 1.45 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 173.9, 139.6, 129.0 (2C), 124.6, 120.1 (2C), 54.4, 39.2, 33.3, 27.5, 11.9 ppm.

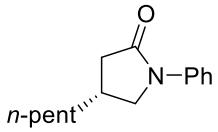
HRMS (ESI$^+$): calculated for $C_{12}H_{16}NO$ $[M-H]^+$: 190.1226; found: 190.1230.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 12.26 min, τ_{major} = 13.48 min (16:87 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 12.52 min, τ_{major} = 13.90 min (24:76 *er*).

B3: The enantiomeric excess was determined by HPLC using a Chiralcel AS-H column [99.5:0.5 Hexane:IPA, 1 mLmin^{-1}, 254 nm, 30 °C] τ_{minor} = 40.98 min, τ_{major} = 43.63 min (89:11 *er*)

(*R*)-4-Pentyl-1-phenylpyrrolidin-2-one (4c)



Following the general procedure B, (*E*)-oct-2-enoic pivalic anhydride **1c** (40.7 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4c** (B1: 77% yield, 84:16 *er*; B2: 95% yield, 76:24 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: **$[\alpha]^{20}_D$** = +3.50 (*c* 1.00, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.60 (d, *J* = 7.6 Hz, 2H), 7.39 – 7.32 (m, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 3.91 (dd, *J* = 9.5, 7.5 Hz, 1H), 3.49 (dd, *J* = 9.5, 6.9 Hz, 1H), 2.72 (dd, *J* = 16.4, 8.1 Hz, 1H), 2.43

(hept, *J* = 7.5 Hz, 1H), 2.29 (dd, *J* = 16.4, 8.1 Hz, 1H), 1.59 – 1.42 (m, 2H), 1.42 – 1.13 (m, 6H), 0.96 – 0.86 (m, 3H) ppm.

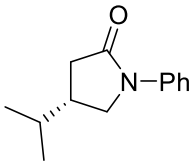
^{13}C-NMR (75 MHz, $CDCl_3$): δ 173.9, 139.6, 129.0 (2C), 124.6, 120.1 (2C), 54.6, 39.6, 34.6, 31.9, 31.8, 27.3, 22.7, 14.2 ppm.

HRMS (ESI$^+$): calculated for $C_{15}H_{22}NO$ $[M-H]^+$: 232.1696; found: 232.1695.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 3.62 min, τ_{major} = 3.81 min (16:84 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 3.47 min, τ_{major} = 3.64 min (24:76 *er*).

(*S*)-4-Isopropyl-1-phenylpyrrolidin-2-one (4d)



Following the general procedure B, (*E*)-4-methylpent-2-enoic pivalic anhydride **1d** (35.7 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4d** (B1: 58% yield, 87:13 *er*, B2: 87% yield, 80.5:19.5 *er*, B3: 74%, 93:7 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: **$[\alpha]^{20}_D$** = +13.63 (*c* 0.80, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.68 – 7.55 (m, 2H), 7.46 – 7.29 (m, 2H), 7.19 – 7.04 (m, 1H), 3.87 (dd, *J* = 9.6, 8.2 Hz, 1H), 3.56 (dd, *J* = 9.6, 8.2 Hz, 1H), 2.68 (dd, *J* = 16.8, 8.2 Hz, 1H), 2.35 (dd, *J* = 16.8, 9.6 Hz, 1H), 2.27 – 1.92 (m, 1H), 1.86 – 1.52 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.0, 139.6, 129.0 (2C), 124.6, 120.1 (2C), 53.2, 38.9, 37.9, 32.7, 20.6, 20.2 ppm.

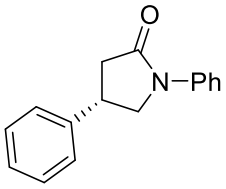
HRMS (ESI$^+$): calculated for $C_{13}H_{18}NO$ $[M-H]^+$: 204.1383; found: 204.1391.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IB-3 column [CO_2/MeOH 95:5 during 20 min, flow rate 1.0 mL/min], τ_{minor} = 9.18 min, τ_{major} = 10.20 min (13:87 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IB-3 column [CO_2/MeOH 95:5 during 20 min, flow rate 1.0 mL/min], τ_{minor} = 9.50 min, τ_{major} = 10.46 min (19.5:80.5 *er*).

B3: The enantiomeric excess was determined by HPLC using a Chiralpak IB column [99.5:0.5 Hexane:IPA, 1 $mLmin^{-1}$, 254 nm, 30 °C] τ_{major} = 35.21 min, τ_{minor} = 41.97 min (93:7 *er*)

(*S*)-1,4-Diphenylpyrrolidin-2-one (4e)



Following the general procedure B, (*E*)-cinnamic pivalic anhydride **1e** (41.8 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4e** (B1: 50% yield, 81:19 *er*, B2: 75% yield, 70:30 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: $[\alpha]^{20}_D$ = -4.33 (*c* 0.60, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.76 – 7.52 (m, 2H), 7.48 – 7.28 (m, 7H), 7.22 – 7.10 (m, 1H), 4.21 (dd, *J* = 9.7, 7.5 Hz, 1H), 3.91 (dd, *J* = 9.7, 7.5 Hz, 1H), 3.79 – 3.63 (m, 1H), 3.04 (dd, *J* = 17.0, 8.8 Hz, 1H), 2.81 (dd, *J* = 17.0, 8.8 Hz, 1H) ppm.

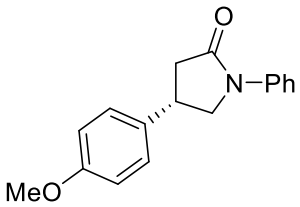
^{13}C-NMR (75 MHz, $CDCl_3$): δ 173.1, 141.8, 139.3, 129.2 (2C), 129.1(2C), 127.5, 127.0 (2C), 124.9, 120.2 (2C), 55.9, 40.5, 37.4 ppm.

HRMS (ESI$^+$): calculated for $C_{16}H_{16}NO$ $[M-H]^+$: 238.1226; found: 238.1232.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 5.31 min, τ_{major} = 5.68 min (81:19 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 5.31 min, τ_{major} = 5.68 min (70:30 *er*).

(*S*)-4-(4-Methoxyphenyl)-1-phenylpyrrolidin-2-one (4f)



Following the general procedure B, (*E*)-3-(4-methoxyphenyl)acrylic pivalic anhydride **1f** (47.2 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4f** (B1: 79% yield, 79:21 *er*; B2: 74% yield, 72:28 *er*, B3: 35% yield, 77:23 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: $[\alpha]^{20}_D$ = -8.71 (*c* 0.85, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.70 – 7.50 (m, 2H), 7.49 – 7.32 (m, 2H), 7.27 – 7.19 (m, 2H), 7.19 – 7.08 (m, 1H), 7.00 – 6.87 (m, 2H), 4.16 (dd, *J* = 9.6, 8.0 Hz, 1H), 3.93 – 3.78 (m, 3H), 3.65 (p, *J* = 8.3 Hz, 1H), 3.00 (dd, *J* = 16.9, 8.7 Hz, 1H), 2.76 (dd, *J* = 16.9, 8.9 Hz, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 173.2, 158.9, 139.3, 133.7, 129.0 (2C), 128.0 (2C), 124.8, 120.1 (2C), 114.5 (2C), 56.1, 55.5, 40.7, 36.7 ppm.

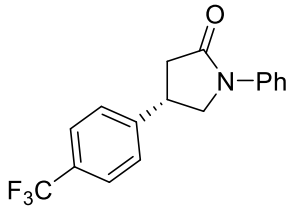
HRMS (ESI$^+$): calculated for $C_{17}H_{18}NO_2$ $[M-H]^+$: 268.1332; found: 268.1322.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 6.23 min, τ_{major} = 6.56 min (21:79 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 6.24 min, τ_{major} = 6.60 min (28:72 *er*).

B3: The enantiomeric excess was determined by HPLC using a Chiralcel AD-H column (90:10 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C), τ_{minor} = 20.96 min, τ_{major} = 28.64 min (23:77 *er*)

(*S*)-1-Phenyl-4-(4-(trifluoromethyl)phenyl)pyrrolidin-2-one (4g)



Following the general procedure B, (*E*)-3-(4-(trifluoromethyl)phenyl)acrylic pivalic anhydride **1g** (54.0 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4g** (B1: 42% yield, 62:38 *er*, B2: 56% yield, 81:19 *er*, B3 22%, 76:24 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 80:20. B1: **[α]$^{20}_D$** = -2.79 (*c* 0.43, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.67 – 7.53 (m, 4H), 7.53 – 7.33 (m, 4H), 7.24 – 7.11 (m, 1H), 4.25 (dd, *J* = 9.7, 8.0 Hz, 1H), 3.90 (dd, *J* = 9.7, 7.0 Hz, 1H), 3.78 (p, *J* = 8.0 Hz, 1H), 3.07 (dd, *J* = 17.0, 8.5 Hz, 1H), 2.79 (dd, *J* = 17.0, 8.5 Hz, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 172.5, 146.0, 139.1, 130.0 (q, *J* = 27.6 Hz), 129.2 (2C), 127.4 (2C), 126.2 (q, *J* = 3.8 Hz, 2C), 125.1, 124.2 (q, *J* = 271.9 Hz), 120.2 (2C), 55.5, 40.2, 37.1 ppm.

^{19}F-NMR (470 MHz, $CDCl_3$): δ -62.6 ppm.

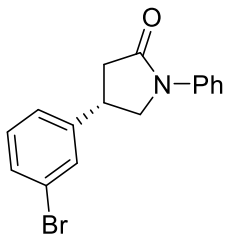
HRMS (ESI$^+$): calculated for $C_{17}H_{15}F_3NO$ $[M-H]^+$: 306.1100; found: 306.1095.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 4.43 min, τ_{major} = 4.85 min (38:62 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 4.52 min, τ_{major} = 4.93 min (19:81 *er*).

B3: The enantiomeric excess was determined by HPLC using a Chiralcel AD-H column [90:10 Hexane:IPA, flowrate 1 mLmin^{-1}, 254 nm, 30 °C], τ_{minor} = 15.19 min, τ_{major} = 17.81 (76:24 *er*).

(*S*)-4-(3-bromophenyl)-1-phenylpyrrolidin-2-one (4h)



Following the general procedure B, (*E*)-3-(3-bromophenyl)acrylic pivalic anhydride **1h** (56.0 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4h** (B1: 47% yield, 79:21 *er*; B2: 61% yield, 79:21 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 80:20. B1: **[α]$^{20}_D$** = -4.26 (*c* 0.54, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.66 – 7.58 (m, 2H), 7.48 – 7.34 (m, 4H), 7.29 – 7.22 (m, 2H), 7.21 – 7.08 (m, 1H), 4.20 (dd, *J* = 9.8, 8.0 Hz, 1H), 3.88 (dd, *J* = 9.8, 7.3 Hz, 1H), 3.78 – 3.58 (m, 1H), 3.03 (dd, *J* = 17.0, 8.8 Hz, 1H), 2.77 (dd, *J* = 17.0, 8.8 Hz, 1H) ppm.

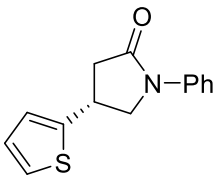
^{13}C-NMR (75 MHz, $CDCl_3$): δ 172.6, 144.1, 139.1, 130.8, 130.7, 130.2, 129.1 (2C), 125.5, 125.0, 123.2, 120.2 (2C), 55.5, 40.2, 37.0 ppm.

HRMS (ESI$^+$): calculated for $C_{16}H_{15}BrNO$ $[M\text{-}H]^+$: 316.0332; found: 316.0349.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 6.02 min, τ_{major} = 6.95 min (79:21 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 6.11 min, τ_{major} = 7.02 min (79:21 *er*).

(*R*)-1-Phenyl-4-(thiophen-2-yl)pyrrolidin-2-one (4i)



Following the general procedure B, pivalic (*E*)-3-(thiophen-2-yl)acrylic anhydride **1i** (42.9 mg, 0.18 mmol) and phenylglycine **2a** (22.7 mg, 0.15 mmol) gave product **4i** (B1: 25% yield, 78:22 *er*; B2: 86% yield, 65:35 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 85:15. B1: **$[\alpha]^{20}_D$** = -1.25 (*c* 0.32, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.65 – 7.55 (m, 2H), 7.47 – 7.34 (m, 2H), 7.23 (dt, *J* = 4.9, 1.0 Hz, 1H), 7.20 – 7.10 (m, 1H), 7.03 – 6.91 (m, 2H), 4.29 – 4.10 (m, 1H), 4.06 – 3.86 (m, 2H), 3.14 – 2.96 (m, 1H), 2.91 – 2.70 (m, 1H) ppm.

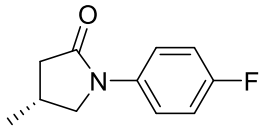
^{13}C-NMR (75 MHz, $CDCl_3$): δ 172.4, 144.9, 139.1, 129.1, 127.3, 125.0, 124.3, 124.2, 120.3, 56.3, 41.4, 33.3 ppm.

HRMS (ESI$^+$): calculated for $C_{14}H_{14}NOS$ $[M\text{-}H]^+$: 244.0791; found: 244.0809.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 5.56 min, τ_{major} = 5.89 min (78:22 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{minor} = 5.69 min, τ_{major} = 6.01 min (65:35 *er*).

(*R*)-1-(4-fluorophenyl)-4-methylpyrrolidin-2-one (4j)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and (4-fluorophenyl)glycine **2b** (25.4 mg, 0.15 mmol) gave product **4j** (B1: 35% yield, 84:16 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 80:20. B1: $[\alpha]^{20}_D$ = -15.00 (*c* 0.12, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.61 – 7.48 (m, 2H), 7.12 – 6.97 (m, 2H), 3.90 (dd, *J* = 9.4, 7.4 Hz, 1H), 3.41 (dd, *J* = 9.4, 6.4 Hz, 1H), 2.74 (dd, *J* = 16.6, 8.3 Hz, 1H), 2.66 – 2.39 (m, 1H), 2.24 (dd, *J* = 16.6, 7.4 Hz, 1H), 1.20 (d, *J* = 6.8 Hz, 3H) ppm.

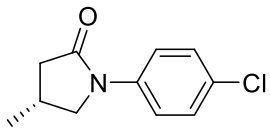
^{13}C-NMR (75 MHz, $CDCl_3$): δ 173.8, 159.6 (d, *J* = 244.1 Hz), 135.7 (d, *J* = 2.8 Hz), 121.8 (d, *J* = 8.0 Hz, 2C), 115.6 (d, *J* = 22.3 Hz, 2C), 56.3, 40.9, 26.5, 19.6 ppm.

^{19}F-NMR (470 MHz, $CDCl_3$): δ -117.9 ppm.

HRMS (ESI$^+$): calculated for $C_{11}H_{13}FNO$ $[M-H]^+$: 194.0976; found: 194.0981.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IC column [CO_2/MeOH 95:5 during 45 min, flow rate 2.0 mL/min], τ_{minor} = 21.89 min, τ_{major} = 23.17 min (84:16 *er*).

(*R*)-1-(4-chlorophenyl)-4-methylpyrrolidin-2-one (4k)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and (4-chlorophenyl)glycine **2c** (27.8 mg, 0.15 mmol) gave product **4k** (B1: 64% yield, 87:13 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 80:20. B1: $[\alpha]^{20}_D$ = -6.67 (*c* 0.45, $CHCl_3$).

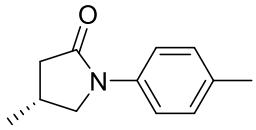
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.59 – 7.50 (m, 1H), 7.35 – 7.28 (m, 1H), 3.91 (dd, *J* = 9.4, 7.6 Hz, 1H), 3.41 (dd, *J* = 9.4, 6.4 Hz, 1H), 2.75 (dd, *J* = 16.7, 8.3 Hz, 1H), 2.66 – 2.44 (m, 1H), 2.25 (dd, *J* = 16.7, 7.4 Hz, 1H), 1.21 (d, *J* = 6.7 Hz, 2H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.0, 138.2, 129.6, 129.0 (2C), 121.1 (2C), 55.9, 41.1, 26.4, 19.6 ppm.

HRMS (ESI$^+$): calculated for $C_{11}H_{13}ClNO$ $[M-H]^+$: 210.0680; found: 210.0685.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 10.23 min, τ_{major} = 10.65 min (13:87 *er*).

(*R*)-4-methyl-1-(*p*-tolyl)pyrrolidin-2-one (4l)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and *p*-tolylglycine **2d** (24.8 mg, 0.15 mmol) gave product **4l** (B1: 75% yield, 78:22 *er*; B2: 80% yield, 72:28 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 80:20. B1: $[\alpha]^{20}_{D}$ = -2.89 (*c* 0.76, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 3.92 (dd, *J* = 9.5, 7.5 Hz, 1H), 3.42 (dd, *J* = 9.5, 6.3 Hz, 1H), 2.74 (dd, *J* = 16.6, 8.3 Hz, 1H), 2.65 – 2.46 (m, 1H), 2.32 (s, 3H), 2.24 (dd, *J* = 16.6, 7.5 Hz, 1H), 1.20 (d, *J* = 6.7 Hz, 3H) ppm.

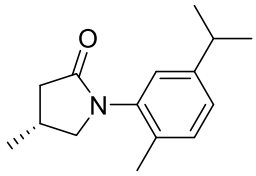
^{13}C-NMR (75 MHz, $CDCl_3$): δ 173.8, 137.1, 134.3, 129.5 (2C), 120.2 (2C), 56.2, 41.1, 26.5, 21.0, 19.7 ppm.

HRMS (ESI$^+$): calculated for $C_{12}H_{16}NO$ $[M-H]^+$: 190.1226; found: 190.1232.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 13.59 min, τ_{major} = 15.06 min (22:78 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 12.41 min, τ_{major} = 13.55 min (28:72 *er*).

(*R*)-1-(5-isopropyl-2-methylphenyl)-4-methylpyrrolidin-2-one (4m)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and (5-isopropyl-2-methylphenyl)glycine **2e** (31.1 mg, 0.15 mmol) gave product **4m** (B1: 79% yield, 68:32 *er*; B2: 95% yield, 63:37 *er*) as a colorless oil which crystallised on standing. Eluent: cyclohexane: ethyl acetate, slow gradient from 95:5 to 75:25. B1: $[\alpha]^{20}_{D}$ = -1.41 (*c* 0.71, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.96 (d, *J* = 2.0 Hz, 1H), 3.82 (dd, *J* = 9.6, 7.4 Hz, 1H), 3.32 (dd, *J* = 9.6, 5.8 Hz, 1H), 2.86 (p, *J* = 6.9 Hz, 1H), 2.79 – 2.54 (m, 2H), 2.35 – 2.23 (m, 1H), 2.20 (s, 3H), 1.28 – 1.18 (m, 9H) ppm.

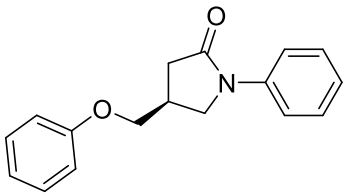
^{13}C-NMR (75 MHz, $CDCl_3$): δ 174.0, 147.8, 137.3, 132.8, 131.2, 126.1, 124.6, 58.2, 39.8, 33.7, 27.6, 24.1 (2C), 20.0, 17.7 ppm.

HRMS (ESI$^+$): calculated for $C_{15}H_{22}NO$ $[M-H]^+$: 232.1696; found: 232.1685.

B1: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 4.85 min, τ_{major} = 5.32 min (68:32 *er*).

B2: The enantiomeric excess was determined by SFC using a Chiralpak IA column [CO_2/MeOH 90:10 during 20 min, flow rate 2.0 mL/min], τ_{minor} = 5.07 min, τ_{major} = 5.64 min (62:38 *er*).

(*S*)-4-(phenoxymethyl)-1-phenylpyrrolidin-2-one (4o)



Following the general procedure B3, (E)-4-phenoxybut-2-enoic pivalic anhydride **1j** (47.2 mg, 0.18 mmol) and *N*-((trimethylsilyl)methyl)aniline **5a** (26.9 mg, 0.15 mmol) gave product **4o** (B3: 49% yield, 85:15 *er*) as a colourless oil. B3: $[\alpha]^{20}_D$ = -5.0 (*c* 0.78, $CHCl_3$).

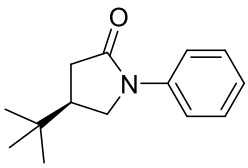
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.60 (m, 2H), 7.42 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.21 – 7.12 (m, 1H), 7.03 – 6.94 (m, 1H), 6.94 – 6.87 (m, 2H), 4.09 – 4.03 (m, 2H), 4.00 (dd, *J* = 9.2, 7.5 Hz, 1H), 3.85 (dd, *J* = 9.9, 5.4 Hz, 1H), 3.05 – 2.91 (m, 1H), 2.84 (dd, *J* = 17.1, 9.0 Hz, 1H), 2.57 (dd, *J* = 17.1, 6.4 Hz, 1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 158.5, 139.2, 129.6, 128.9, 124.7, 121.3, 120.0, 114.5, 69.1, 51.4, 35.6, 31.0.

HRMS (ESI$^+$): calculated for $C_{17}H_{17}O_2NNa$ $[M+Na]^+$ requires 290.1157, found 290.1143.

B3: The enantiomeric excess was determined by HPLC using a Chiralcel AD-H column [95:5 Hexane:IPA, 1 mLmin^{-1}, 254 nm, 30 °C] τ_{minor} = 25.99 min, τ_{major} = 31.09 min (85:15 *er*)

(*R*)-4-(tert-butyl)-1-phenylpyrrolidin-2-one (4n)



Following the general procedure B3, (E)-4,4-dimethylpent-2-enoic pivalic anhydride **1k** (38.2 mg, 0.18 mmol) and *N*-((trimethylsilyl)methyl)aniline **5a** (26.9 mg, 0.15 mmol) gave product **4n** (B3: 33% yield, 95:15 *er*) as a colourless oil. B3: $[\alpha]^{20}_D$ = -8.6 (*c* 0.36, $CHCl_3$).

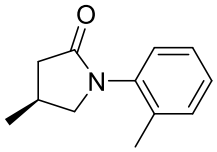
^{1}H-NMR (500 MHz, $CDCl_3$): 7.64 – 7.59 (m, 2H), 7.39 – 7.33 (m, 2H), 7.16 – 7.10 (m, 1H), 3.77 (dd, *J* = 9.7, 8.4 Hz, 1H), 3.65 (dd, *J* = 9.7, 8.2 Hz, 1H), 2.56 (dd, *J* = 17.1, 9.2 Hz, 1H), 2.46 (dd, *J* = 17.1, 9.6 Hz, 1H), 2.39 – 2.28 (m, 1H), 0.96 (s, 9H) ppm.

^{13}C-NMR (126 MHz, $CDCl_3$): δ 173.9, 139.6, 128.9, 124.6, 120.2, 50.4, 42.1, 34.9, 31.8, 27.0 ppm.

HRMS (ESI$^+$): calculated for $C_{14}H_{19}NONa$ $[M+Na]^+$ requires 240.1364, found 240.1353

B3: The enantiomeric excess was determined by HPLC using a Chiralcel AD-H [99:1 Hexane:IPA, 1 mLmin^{-1}, 254 nm, 30 °C] τ_{minor} = 36.71, τ_{major} = 44.24 (95:15 *er*)

(S)-4-methyl-1-(o-tolyl)pyrrolidin-2-one (4p)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and 2-methyl-*N*-((trimethylsilyl)methyl)aniline **5b** (29.0 mg, 0.15 mmol) gave product **4p** (B3: 65% yield, 82:18 *er*) as a colourless oil. B3: $[\alpha]^{20}_{D}$ = +28.8 (*c* 0.24, $CHCl_3$).

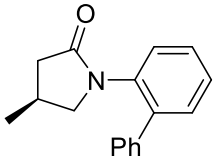
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.28-7.18 (m, 3H), 7.15-7.09 (m, 1H), 3.81 (dd, *J* = 9.7, 7.4 Hz, 1H), 3.30 (dd, *J* = 9.6, 5.7 Hz, 1H), 2.73 (dd, *J* = 16.4, 8.4 Hz, 1H), 2.68-2.56 (m, 1H), 2.23 (s, 3H), 1.23 (d, *J* = 6.7 Hz, 3H) ppm.

^{13}C-NMR (101 MHz, $CDCl_3$): δ 174.0, 137.5, 135.6, 131.2, 127.9, 126.9, 126.6, 58.0, 39.6, 27.5, 19.9, 18.1 ppm.

HRMS (ESI$^+$): calculated for $C_{12}H_{16}NO$ $[M+H]^+$: 190.1232; found: 190.1224 (-1.4 ppm)

B3: The enantiomeric excess was determined by HPLC using a Chiralcel OD-H column [98:2 Hexane:IPA, 1 mLmin^{-1}, 211 nm, 30 °C] τ_{major} = 38.60 min, τ_{minor} = 43.67 min (82:18 *er*)

(S)-1-([1,1'-biphenyl]-2-yl)-4-methylpyrrolidin-2-one (4q)



Following the general procedure B except using PhMe:MeCN (1:2) instead, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and N-((trimethylsilyl)methyl)-[1,1'-biphenyl]-2-amine **5d** (38.3 mg, 0.15 mmol) gave product **4q** (B3: 67% yield, 63:37 *er*) as a colourless oil. B3: $[\alpha]^{20}_{D}$ = +12.9 (*c* 1.19, $CHCl_3$).

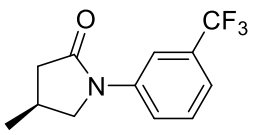
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.44-7.28 (m, 9H), 3.30 (dd, *J* = 9.6, 7.6 Hz, 1H), 2.80 (dd, *J* = 9.5, 5.8 Hz, 1H), 2.59 (dd, *J* = 16.7, 8.4 Hz, 1H), 2.26 (m, 1H), 2.06 (dd, *J* = 16.7, 6.9 Hz, 1H), 0.90 (d, *J* = 6.8 Hz, 3H) ppm.

^{13}C-NMR (126 MHz, $CDCl_3$): δ 175.5, 140.0, 139.2, 136.5, 131.0, 128.7, 128.6, 128.5 (2C), 128.2, 127.7, 57.6, 39.6, 27.1, 19.6 ppm.

HRMS (ESI$^+$): calculated for $C_{17}H_{18}NO$ $[M+H]^+$ requires 252.1388, found 252.1383

B3: The enantiomeric excess was determined by HPLC using a Chiralcel OD-H column [95:5 Hexane:IPA, 1 mLmin^{-1}, 211 nm, 30 °C] τ_{minor} = 17.99 min, τ_{major} = 20.51 min (63:37 *er*)

(S)-4-methyl-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (4r)



Following the general procedure B, (*E*)-but-2-enoic pivalic anhydride **1a** (30.6 mg, 0.18 mmol) and 3-(trifluoromethyl)-N-((trimethylsilyl)methyl)aniline **5c** (37.1 mg, 0.15 mmol) gave product **4r** (B3: 61%, 81:19 *er*) as a colourless oil. B3: $[\alpha]^{20}_{D}$ = -2.2 (*c* 1.32, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.94-7.88 (m, 1H), 7.81 (s, 1H), 7.51-7.45 (m, 1H), 7.41-7.36 (m, 1H), 3.97 (dd, *J* = 9.3, 7.6 Hz, 1H), 3.48 (dd, *J* = 9.3, 6.5 Hz, 1H), 2.79 (dd, *J* = 16.9, 8.4 Hz, 1H), 2.65 – 2.53 (m, 1H), 2.29 (dd, *J* = 16.9, 7.6 Hz, 1H), 1.24 (d, *J* = 6.8 Hz, 3H) ppm.

^{13}C-NMR (126 MHz, $CDCl_3$): δ 174.2, 140.1, 129.5, 123.0, 120.9 (q, *J* = 3.7 Hz) 116.2 (q, *J* = 4.3 Hz), 55.8, 41.1, 26.4, 19.6 ppm.

^{19}F-NMR (471 MHz, $CDCl_3$): δ -62.6 ppm

HRMS (ESI^{+}): calculated for $C_{12}H_{13}F_3NO$ $[M+H]^+$ requires 244.0944, found 244.0948

B3: The enantiomeric excess was determined by HPLC using a Chiralcel IC column [97:3 Hexane:IPA, 2 mLmin^{-1}, 211 nm, 30 °C] τ_{minor} = 10.45 min, τ_{major} = 12.12 min (81:19 *er*).

5. Stern-Volmer Luminescence quenching studies

Emission spectra were recorded on a JASCO Spectrofluorometer FP-8600 equipped with a TC-815 Peltier thermostated single cell holder (water-cooled) controlled by Spectra Manager Version 2.10.01.

For all luminescence quenching experiments, the excitation wavelength was fixed at 420 nm, while the emission spectra were acquired from 500 nm to 700 nm, observing the maximum emission peak for $Ru(bpy)_3(PF_6)_2$ at 597 nm. MeCN was used as solvent.

The emission spectrum of the 0.03 mM solution of $Ru(bpy)_3(PF_6)_2$ is reported in **Figure S4**.

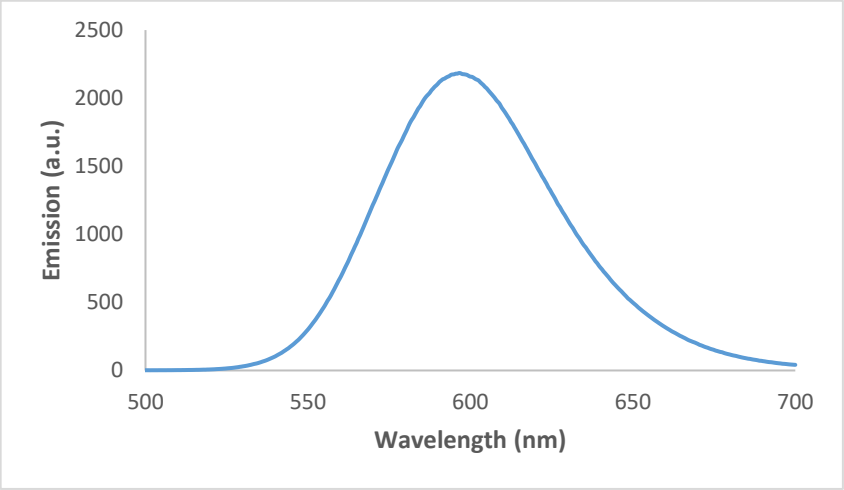


Figure S4 Emission spectrum of $Ru(bpy)_3(PF_6)_2$ (excitation wavelength 420 nm)

In a typical Stern-Volmer luminescence quenching experiment, the appropriate amount of quencher (Q) is added to the MeCN solution of $Ru(bpy)_3(PF_6)_2$ (0.03 mM) in a Teflon-top 10x10 mm precision cell (2.4 mL) made of Quartz SUPRASIL®. After degassing for 30 sec under an argon atmosphere, the emission spectra of the samples were collected.

The Stern-Volmer plots displayed in **Figure S4** show a linear correlation between the concentration of quencher [Q] and I_0/I according to the equation:

$$I_0/I = K_{SV} \times [Q] + 1$$

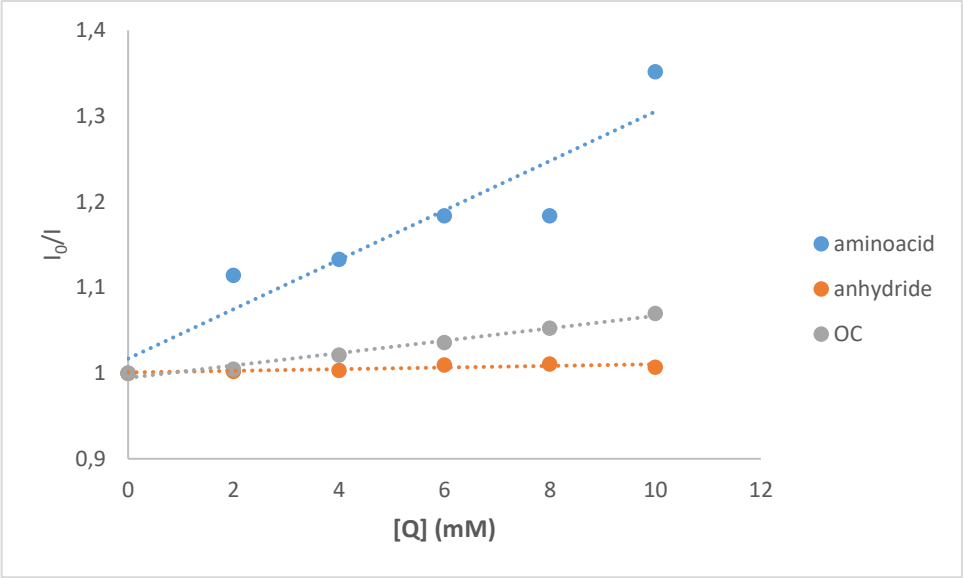


Figure S4 Stern-Volmer quenching plot

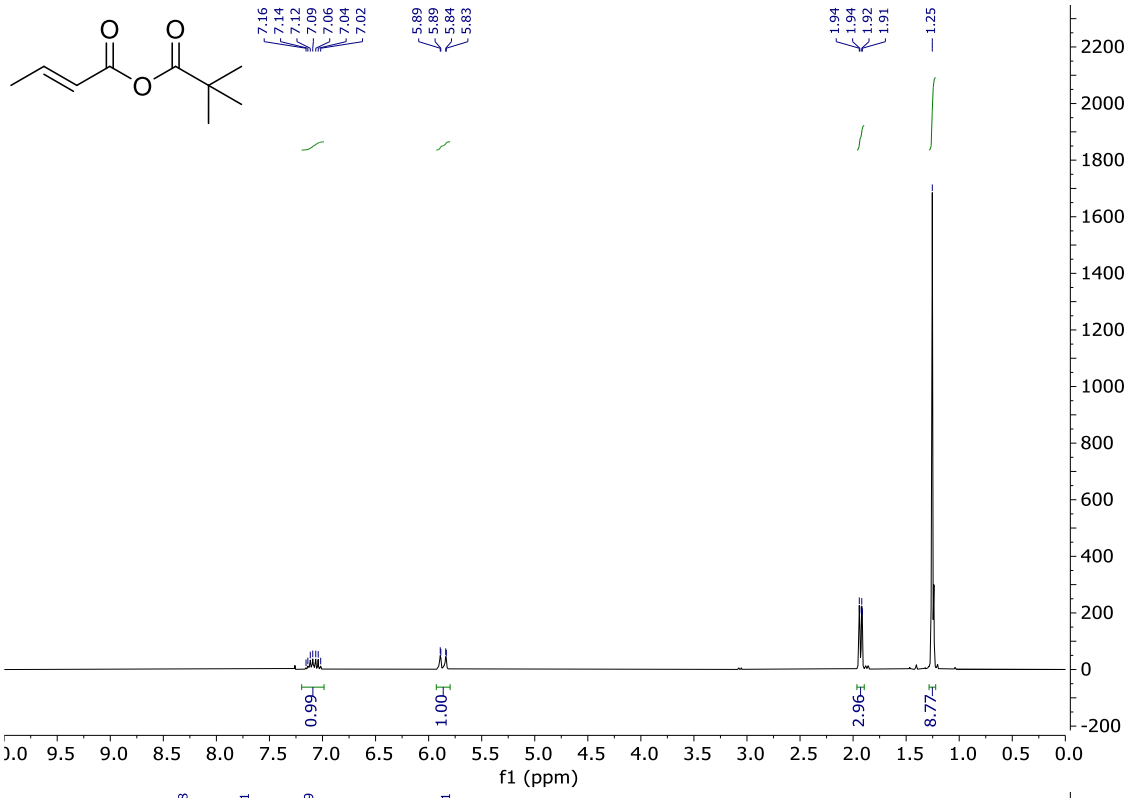
The data plotted in the chart confirms the lack of interaction between the $Ru(bpy)_3(PF_6)_2$ and the anhydride, as well as with the organocatalyst. Furthermore, it presents the possibility of the amino acid quenching the excited state of $^*Ru(bpy)_3(PF_6)_2$, suggesting that the initial step of the reaction should involve the oxidation of the amino acid by $^*Ru(bpy)_3(PF_6)_2$, as proposed in the plausible mechanism (*See main manuscript*).

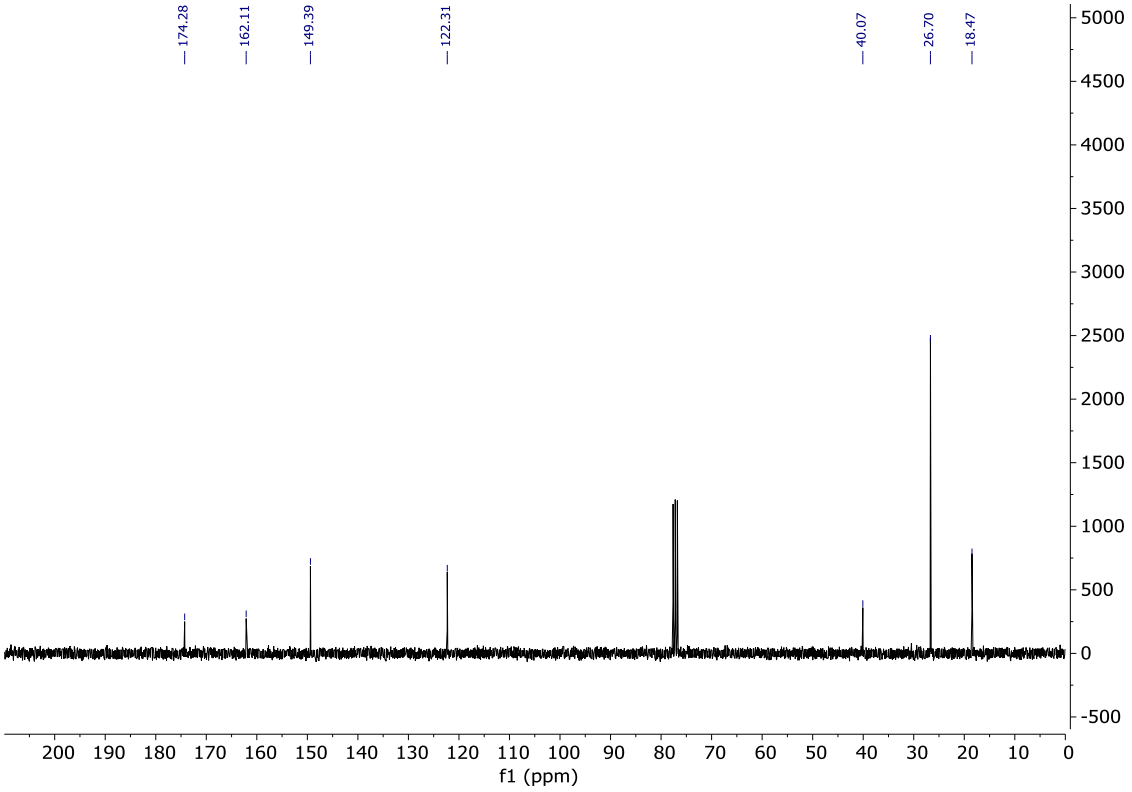
6. References

1. a) Wang, Y.; Gu, M. The Concept of Spectral Accuracy for MS. *Anal. Chem.*, **82**, 7055-7062 (2010); b) Y. Wang, Methods for Operating MS Instrument Systems, United States Patent Nº. 6,983,213, **2006**; c) Ochiaia, N.; Sasamoto, K.; MacNamara, K. Characterization of sulfur compounds in whisky by full evaporation dynamic headspace and selectable one-dimensional/two-dimensional retention time locked gas chromatography–mass spectrometry with simultaneous element-specific detection. *Journal of Chromatography A*, **1270**, 296-304 (2012); d) Ho, H.; Lee, R.; Chen, C.; Wang, S.; Li Z.; Lee, M. Identification of new minor metabolites of penicillin G in human serum by multiple-stage tandem mass spectrometry. *Rapid Commun Mass Spectrom.*, **25**, 25-32 (2011).
2. Hong, Y.-T.; Barchuk, A.; Krische, M. J. Angewandte Chemie, International Edition, **45** (41), 6885-6888 (2006).
3. Staderini, M.; Piquero, M.; Abengózar, M. A.; Nachér-Vázquez, M.; Romanelli, G.; López-Alvarado, P.; Rivas, L.; Bolognesi, M. L.; Menéndez, J. C. Structure-activity relationships and mechanistic studies of novel mitochondria-targeted, leishmanicidal derivatives of the 4-aminostyrylquinoline scaffold, *European Journal of Medicinal Chemistry*, **171**, 38-53 (2019).
4. Espelt, L. R.; McPherson, I. S.; Weinsch, E. M.; Yoon, T. P Enantioselective Conjugate Additions of α-Amino Radicals via Cooperative Photoredox and Lewis Acid Catalysis, *Journal of the American Chemical Society,* **137**, 2452-2455 (2015)
5. Pagire, S. K.; Kumagai, N.; Shibasaki M, Introduction of a 7-aza-6-MeO-indoline auxiliary in Lewis-acid/photoredox cooperative catalysis: highly enantioselective aminomethylation of α,β-unsaturated amides, *Chemical Science*, **11**, 5168-5174 (2020).

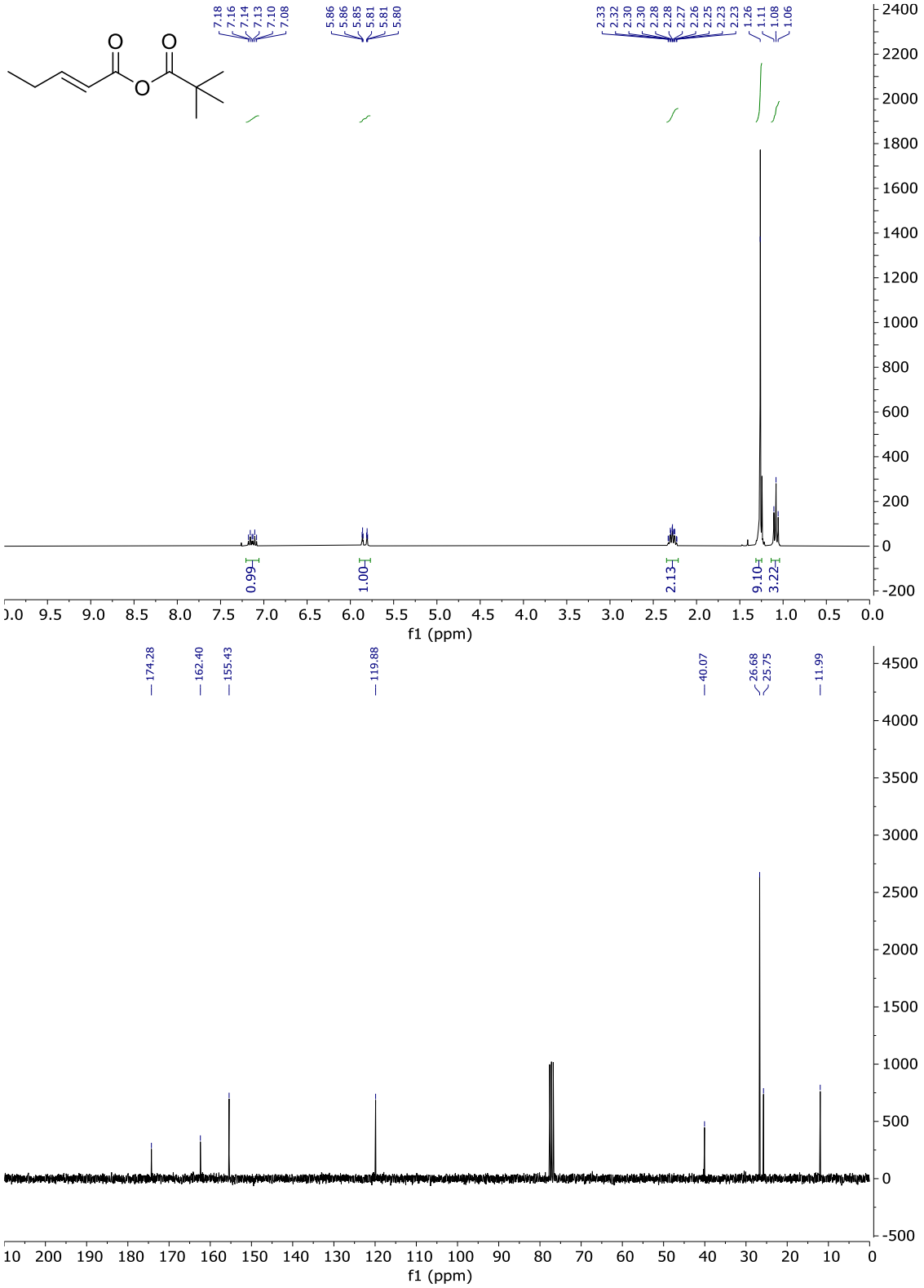
7. Nuclear Magnetic Resonance Spectra

(*E*)-But-2-enoic pivalic anhydride (1a)

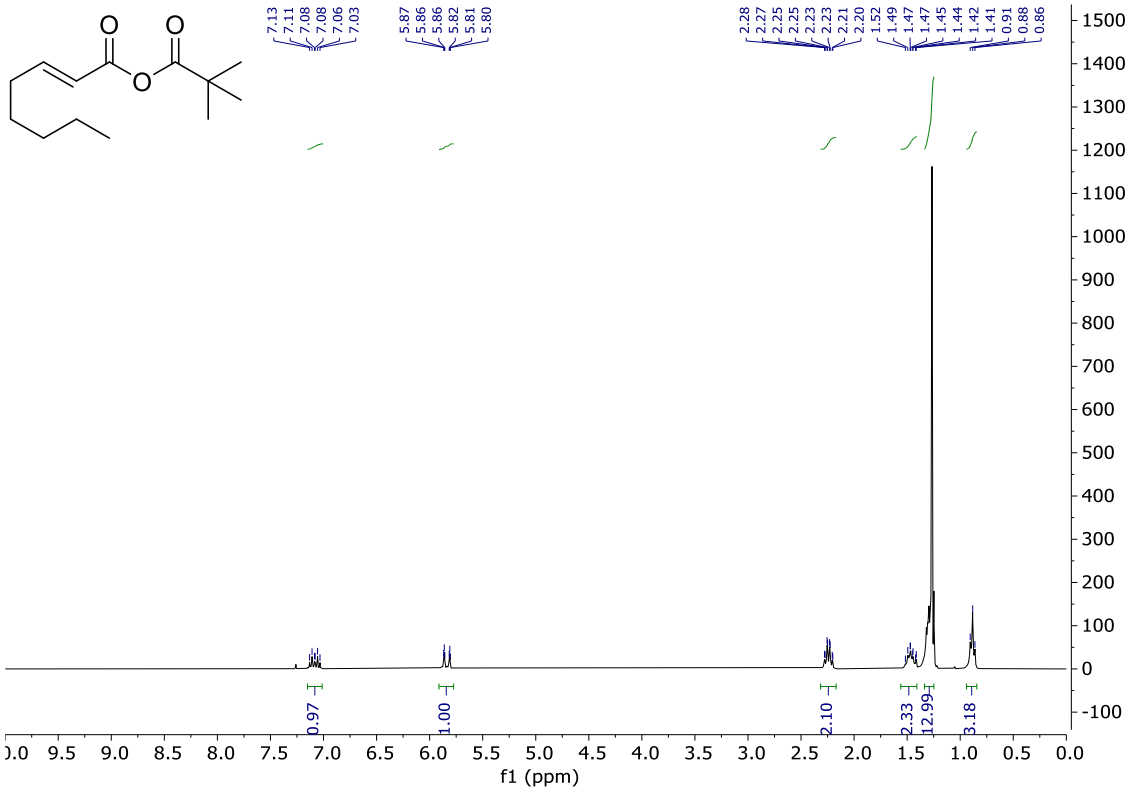


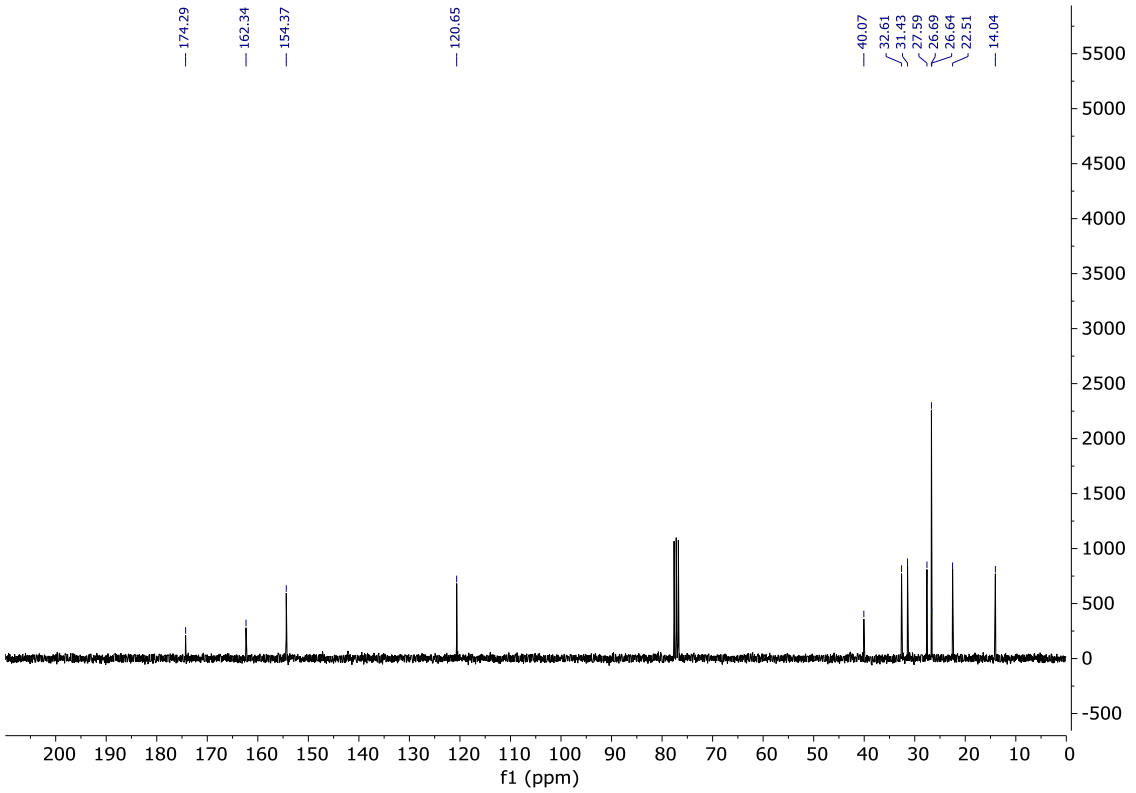


(*E*)-Pent-2-enoic pivalic anhydride (1b)

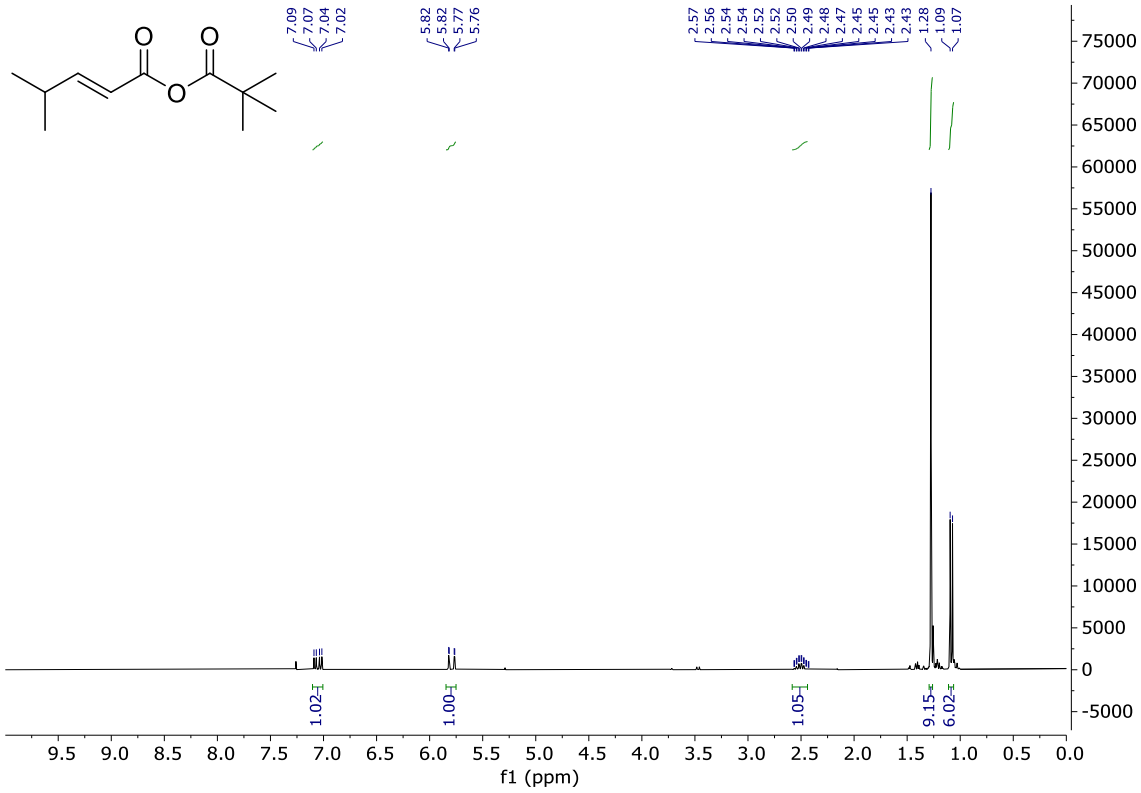


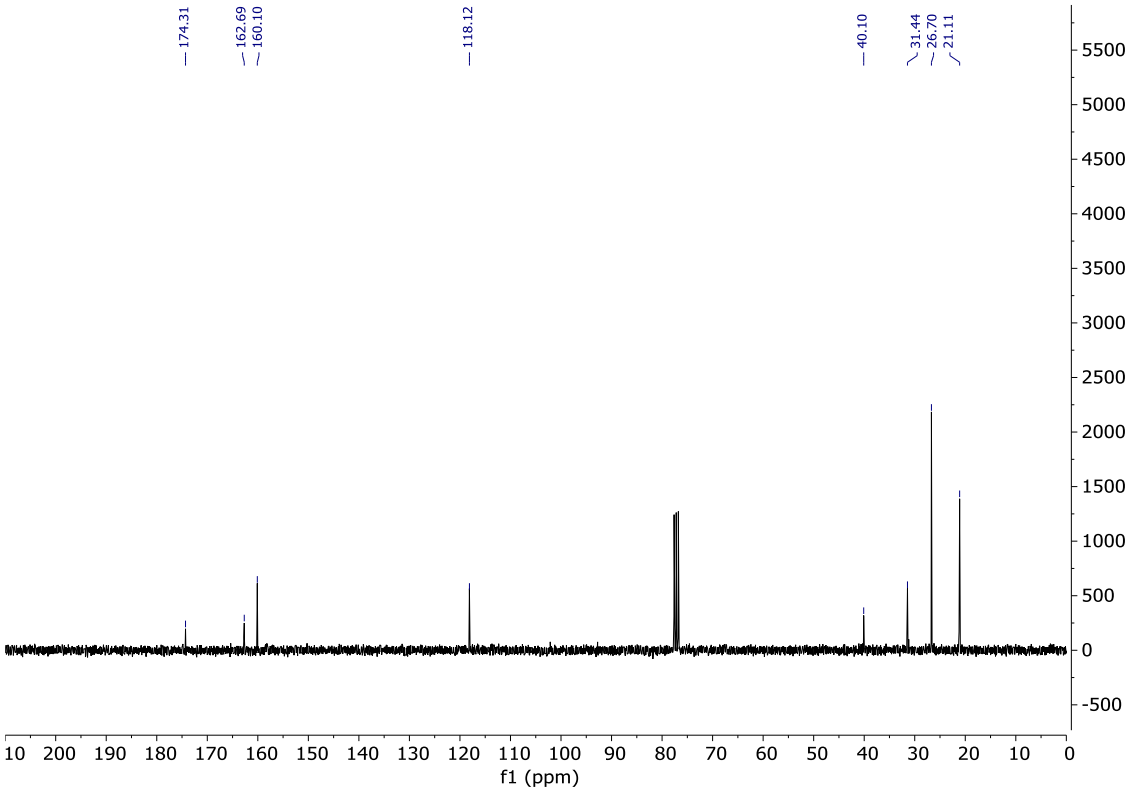
(*E*)-Oct-2-enoic pivalic anhydride (1c)



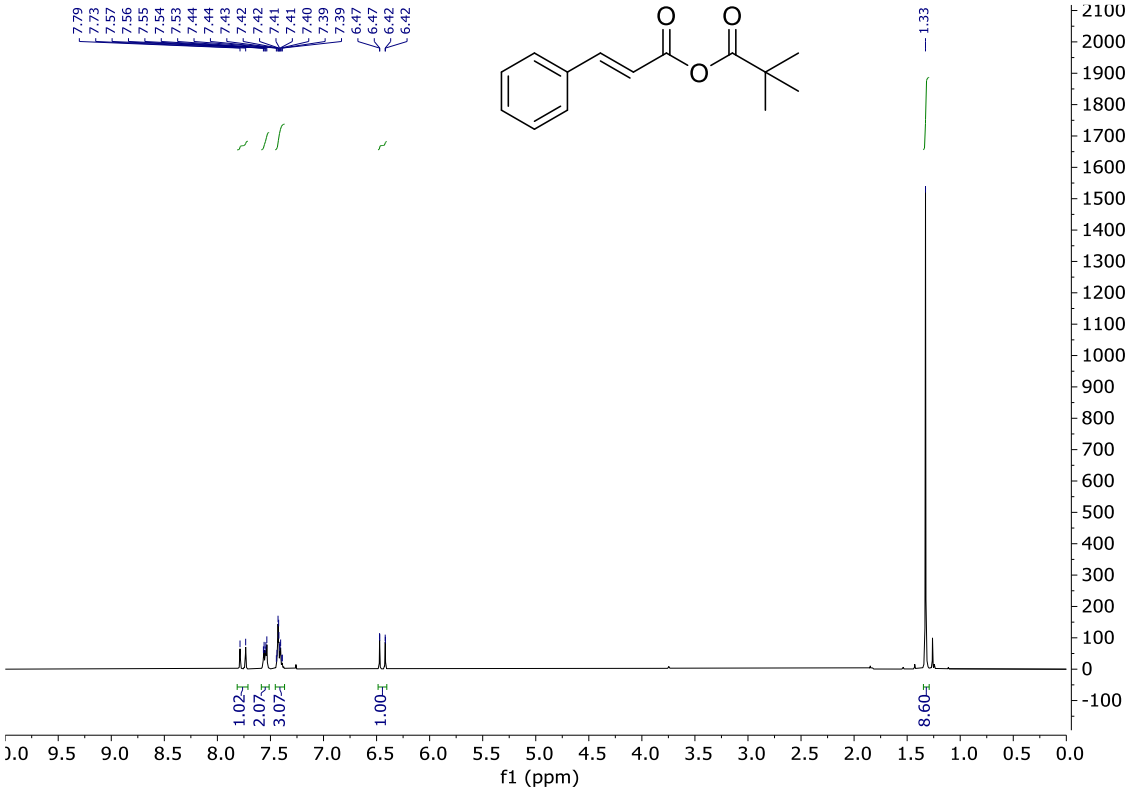


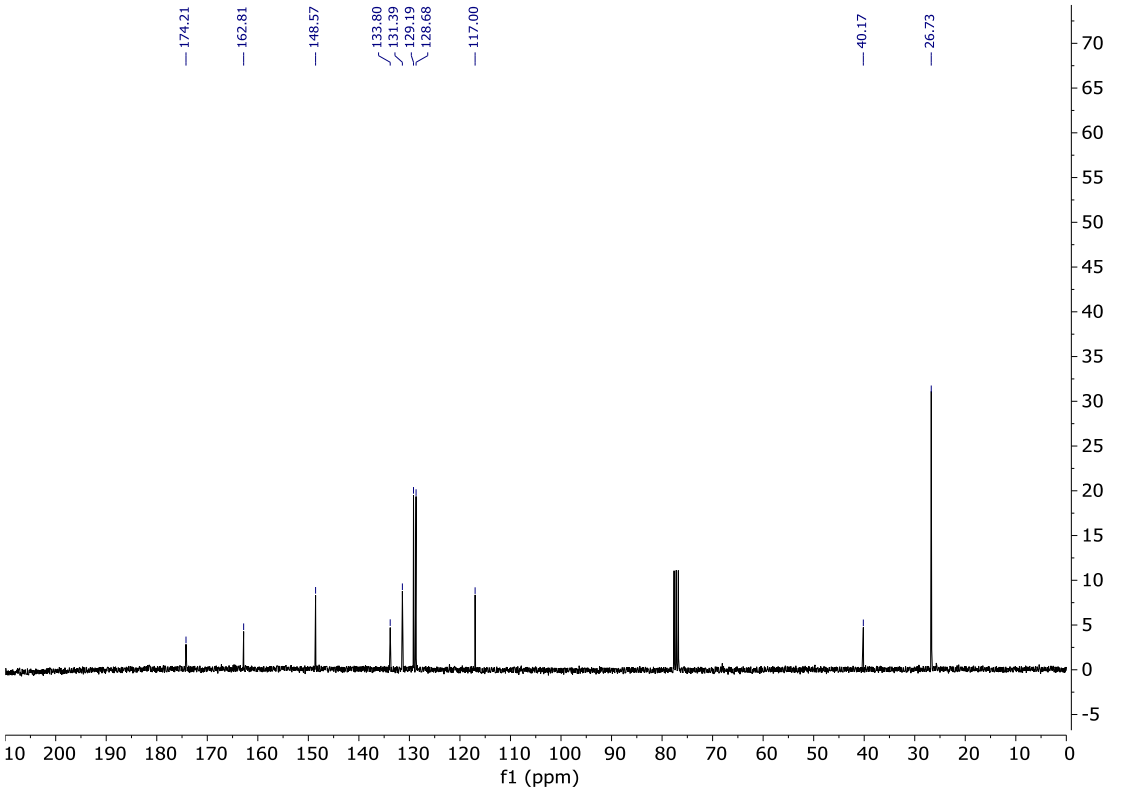
(*E*)-4-Methylpent-2-enoic pivalic anhydride (1d)



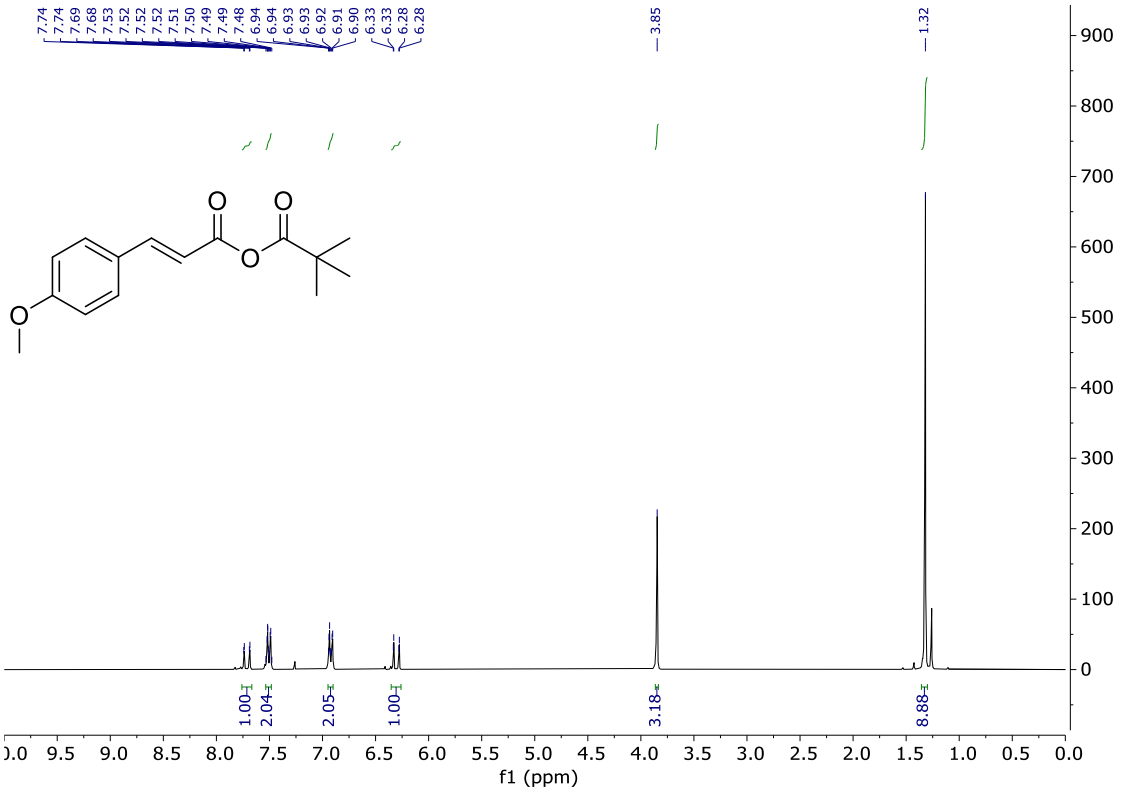


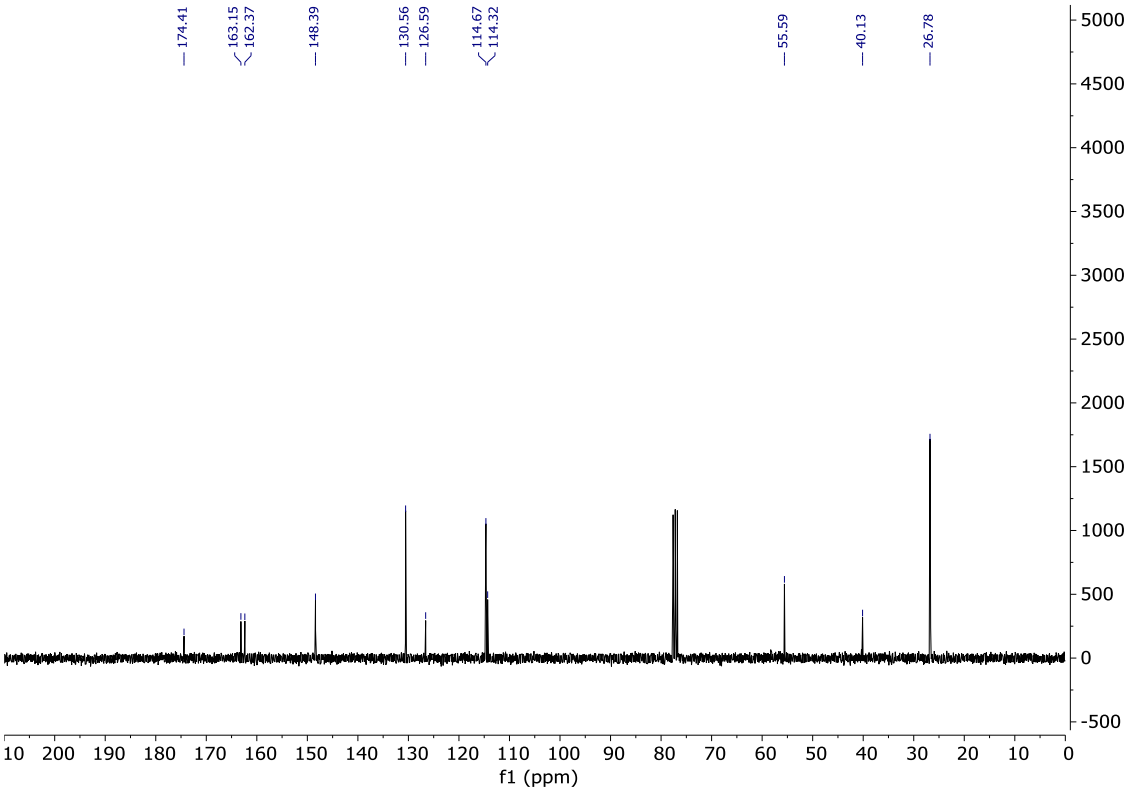
(*E*)-Cinnamic pivalic anhydride (1e)



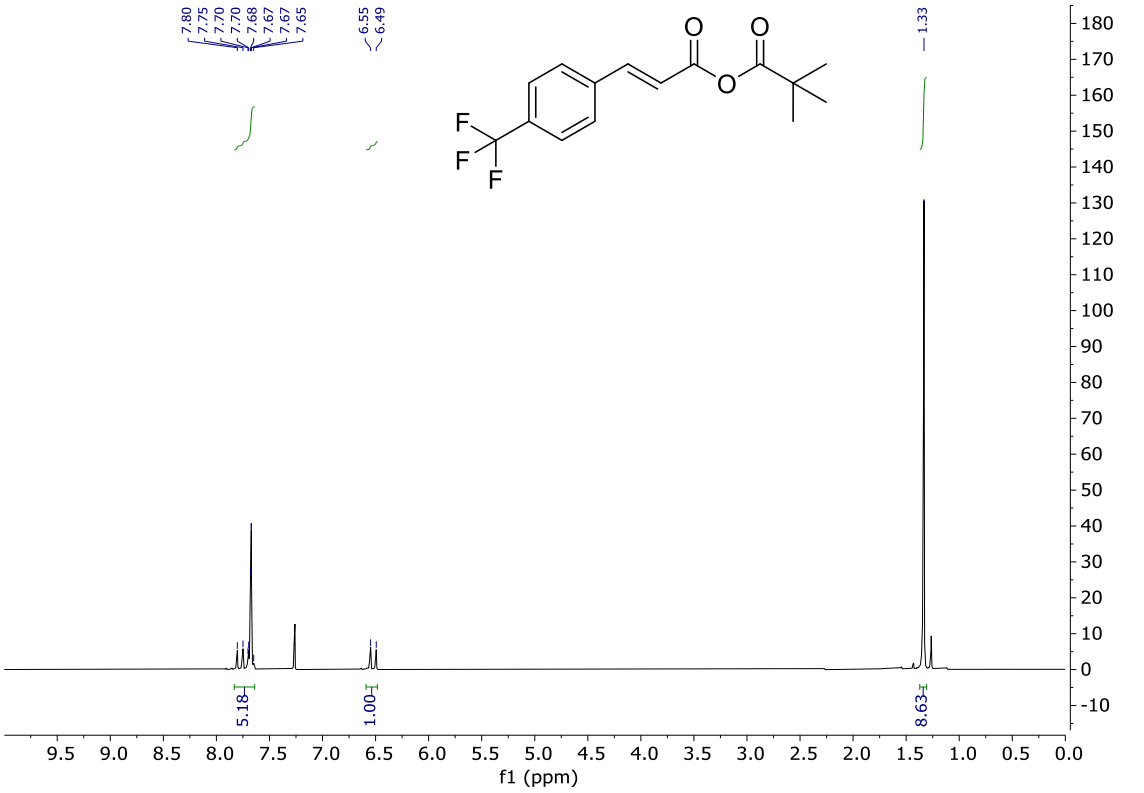


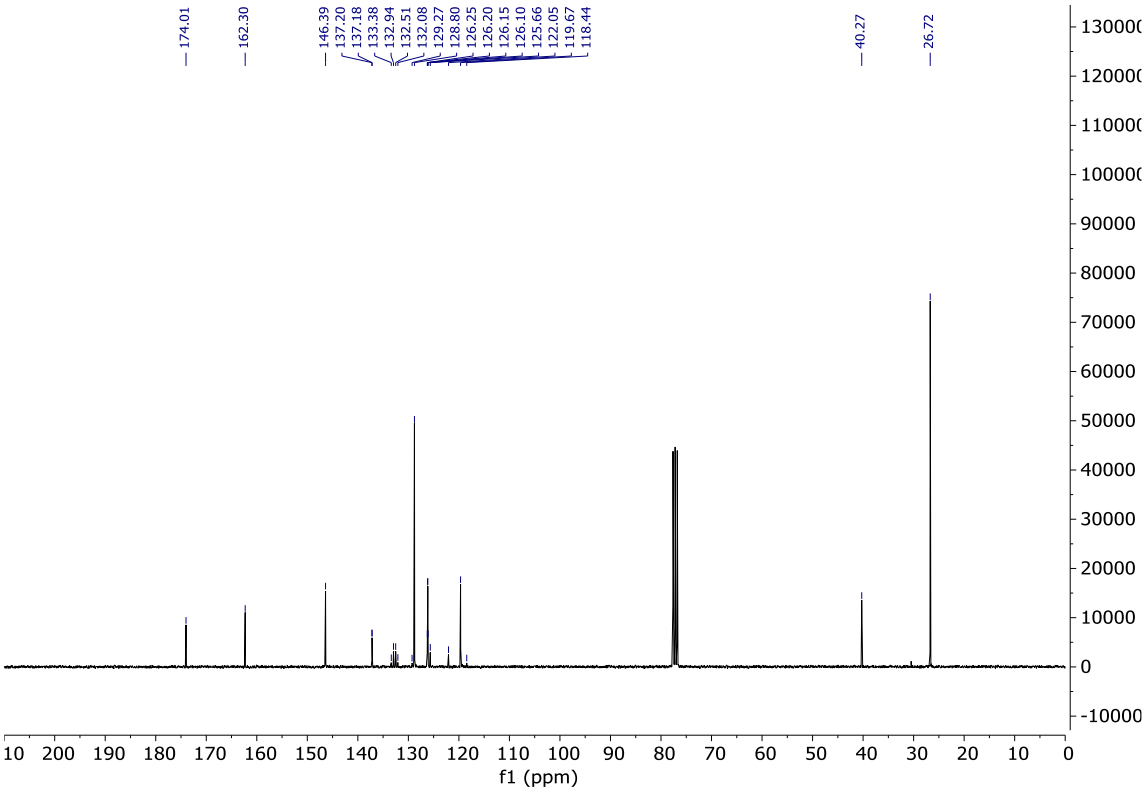
(*E*)-3-(4-Methoxyphenyl)acrylic pivalic anhydride (1f)

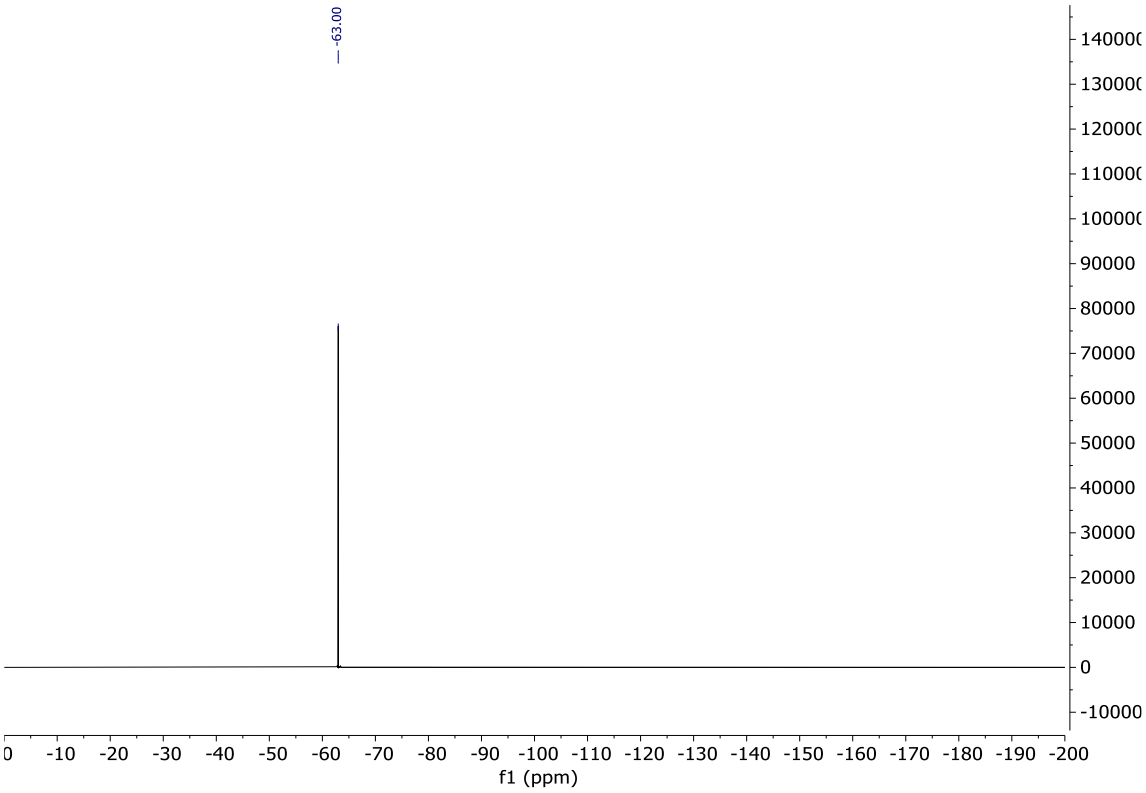




(*E*)-3-(4-(Trifluoromethyl)phenyl)acrylic pivalic anhydride (1g)



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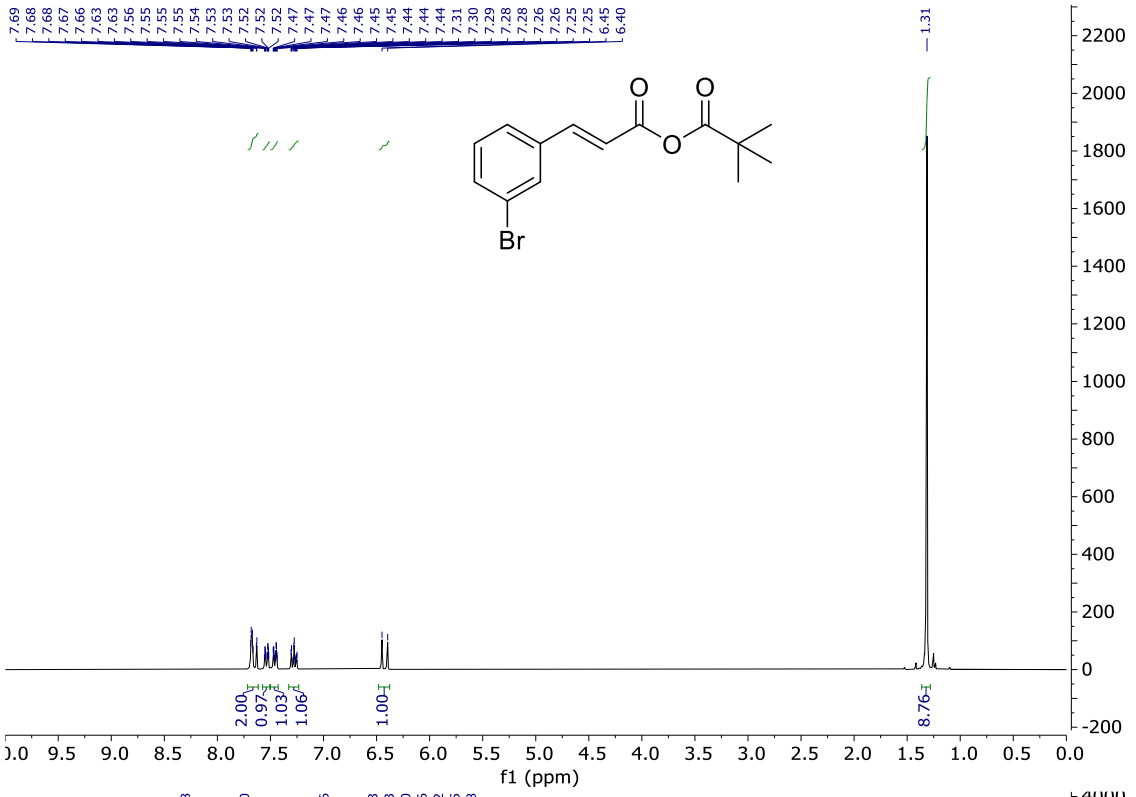
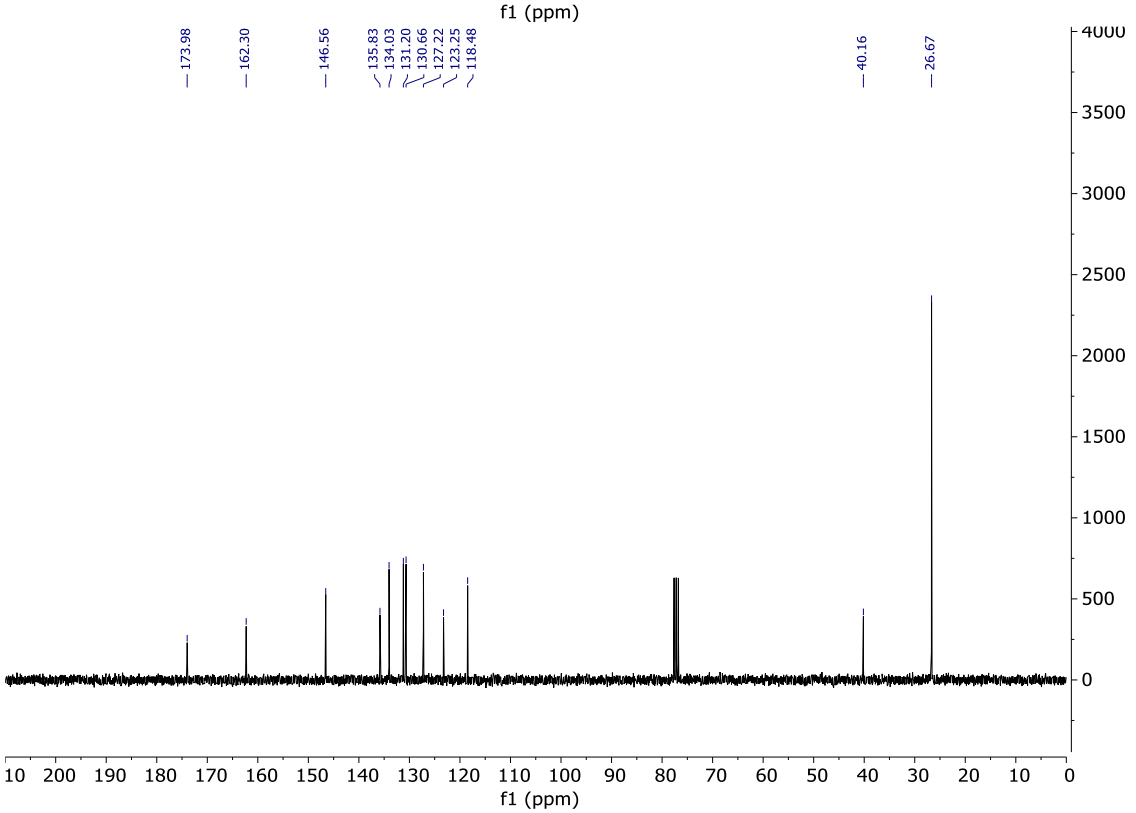
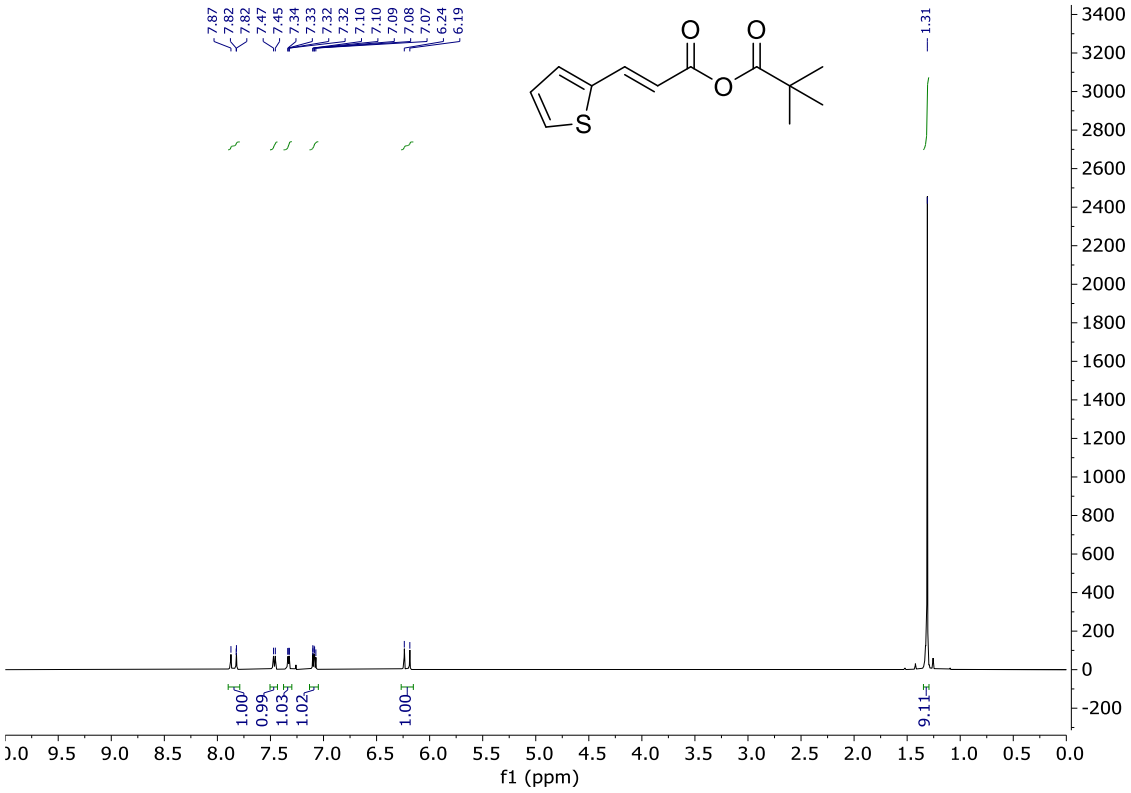
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

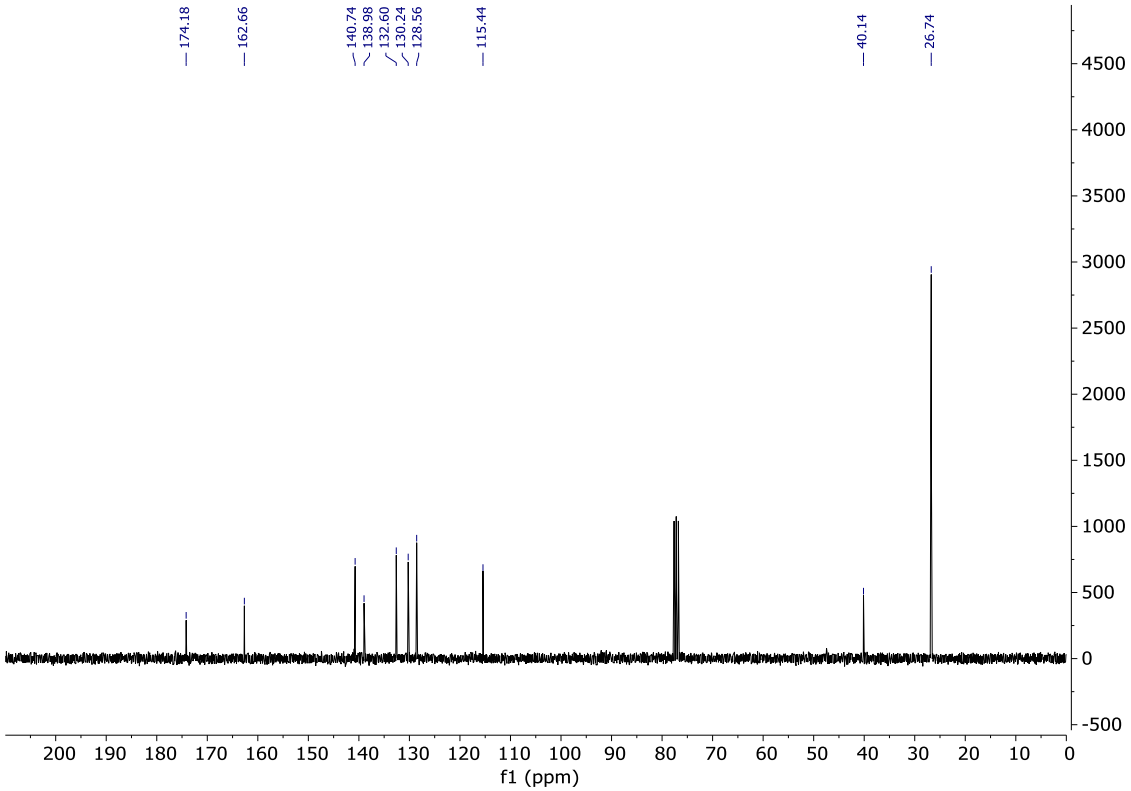
(*E*)-3-(3-Bromophenyl)acrylic pivalic anhydride (1h)



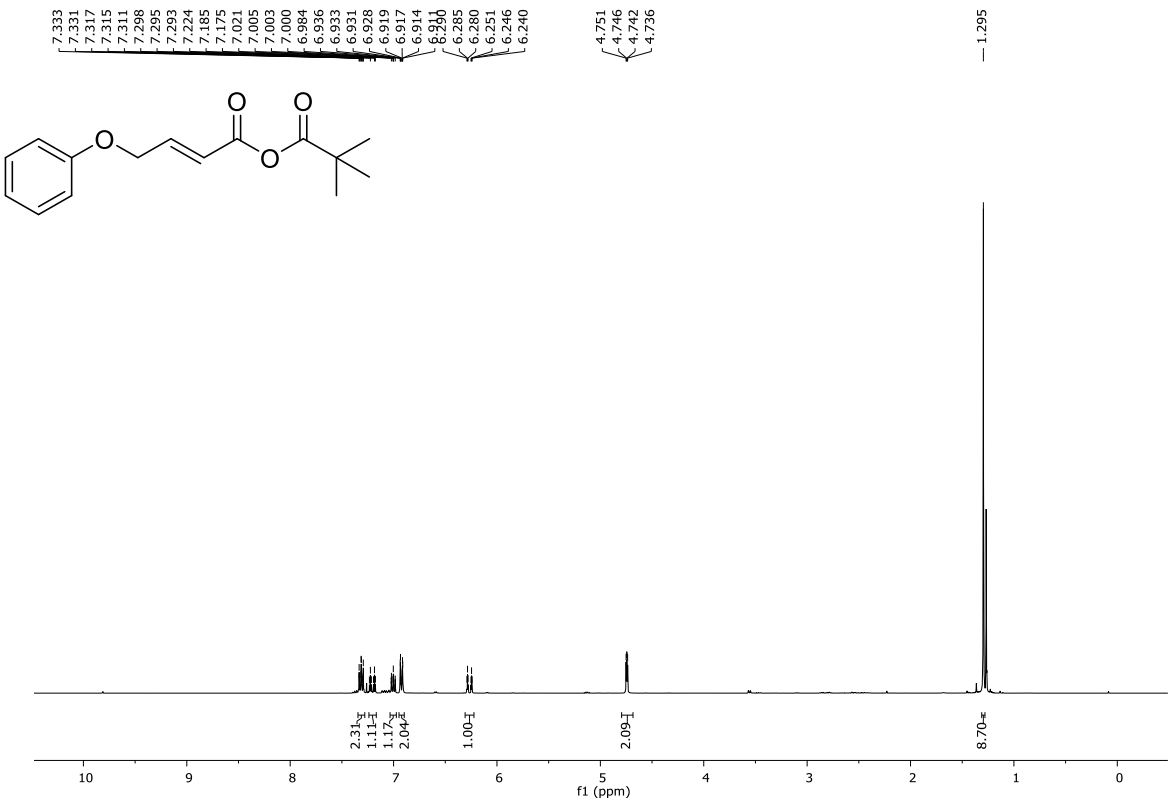


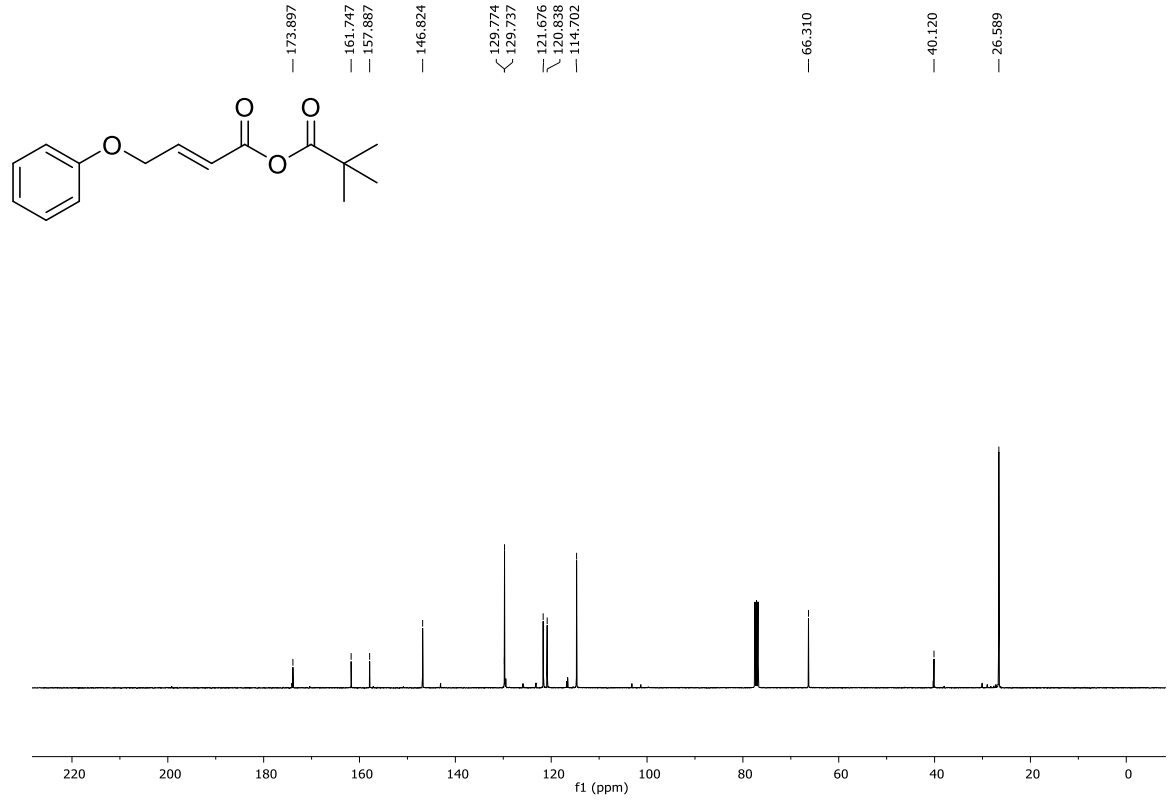
Pivalic (*E*)-3-(thiophen-2-yl)acrylic anhydride (1i)



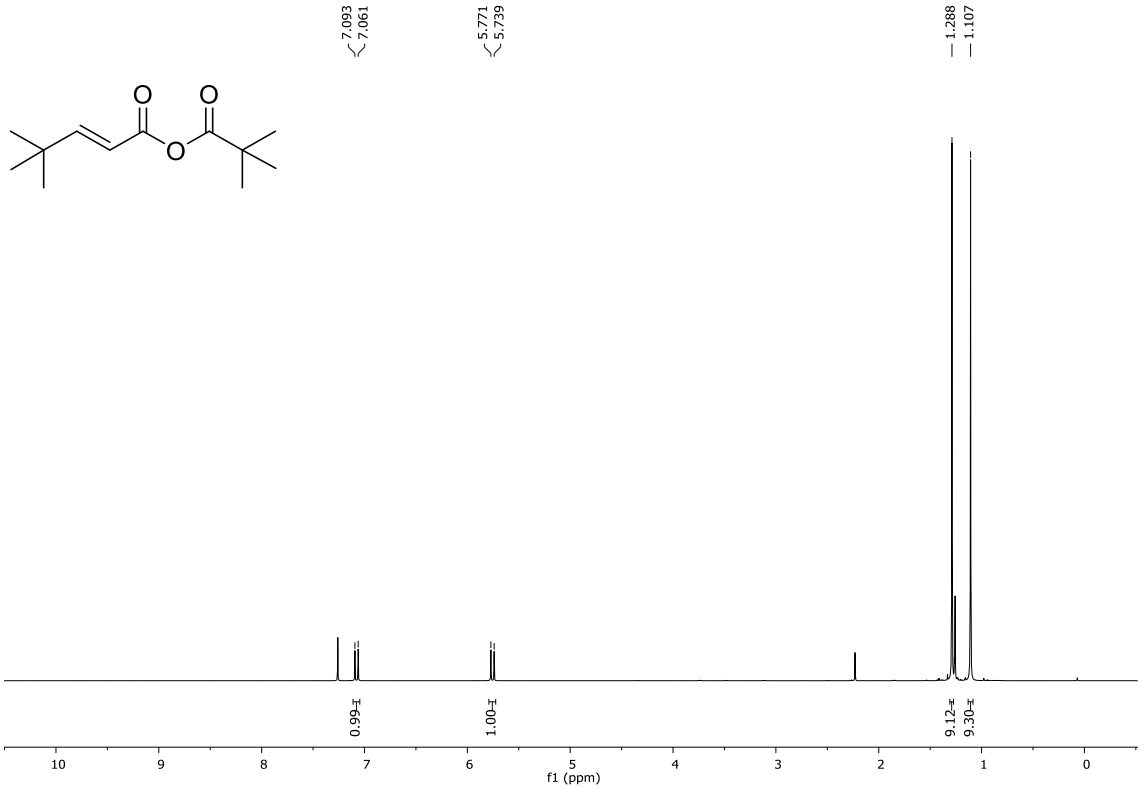


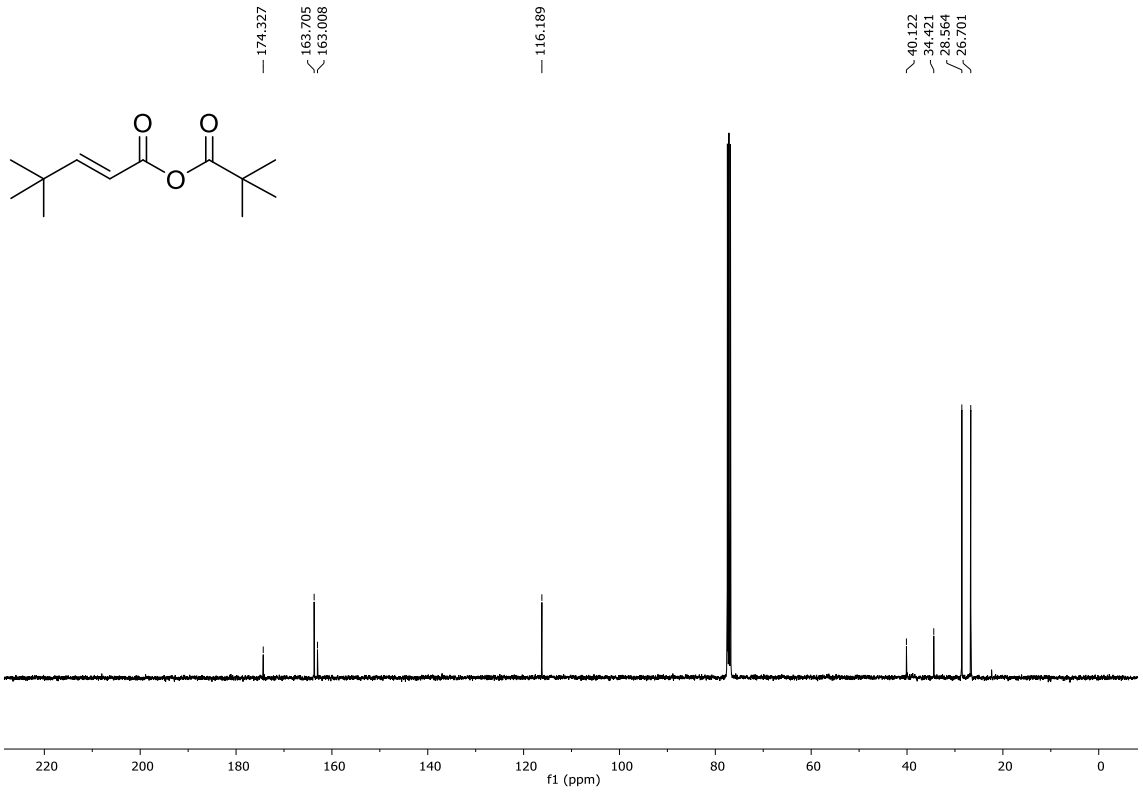
(*E*)-4-phenoxybut-2-enoic pivalic anhydride (1j)



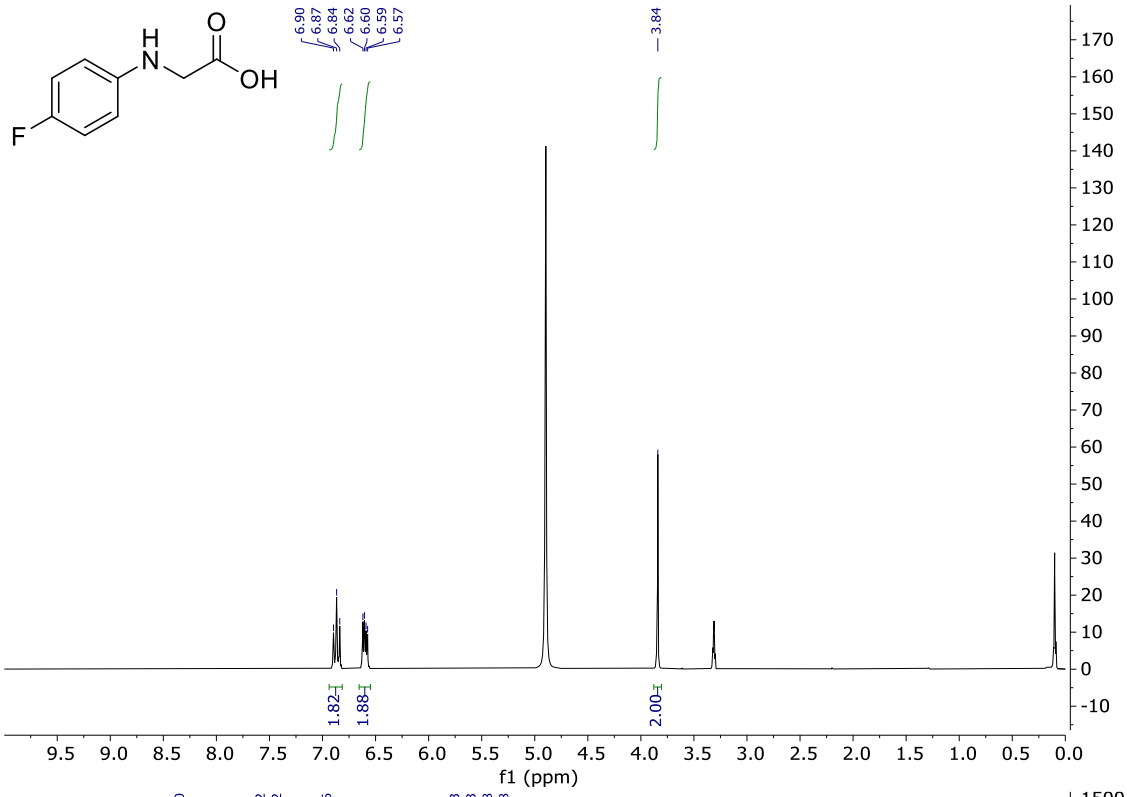


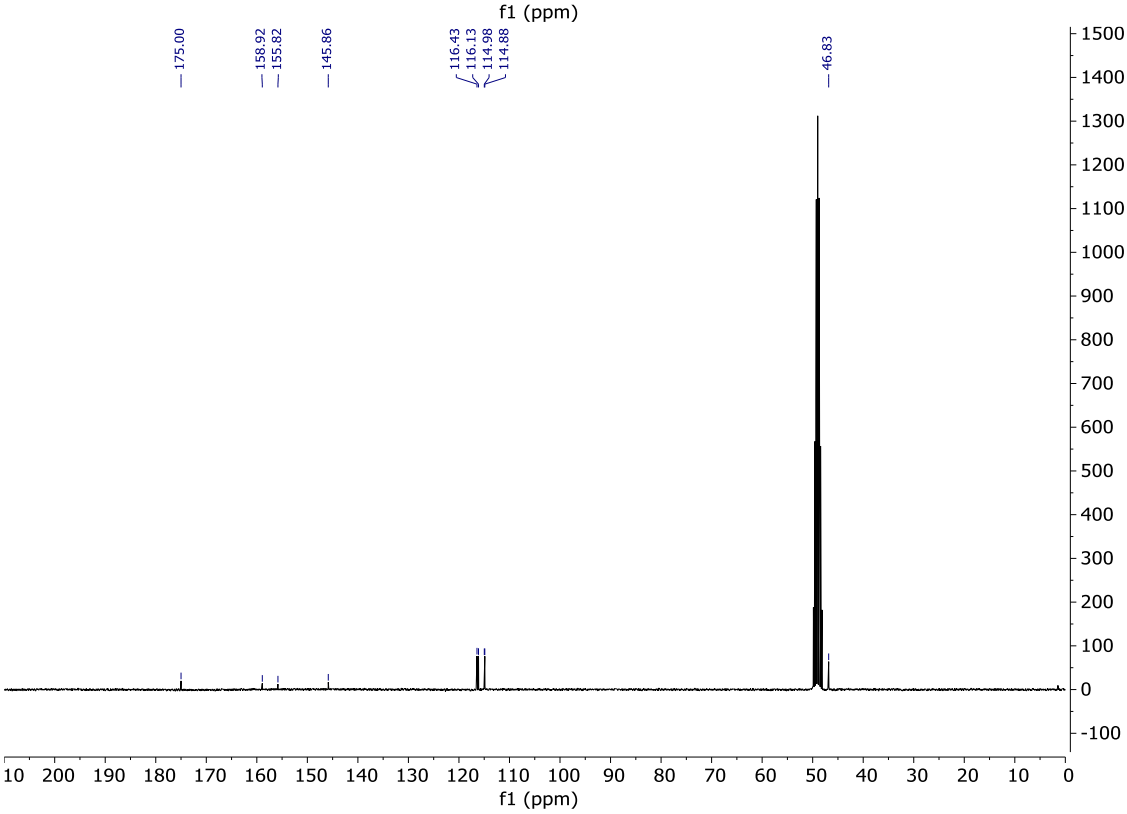
(*E*)-4,4-dimethylpent-2-enoic pivalic anhydride (1k)

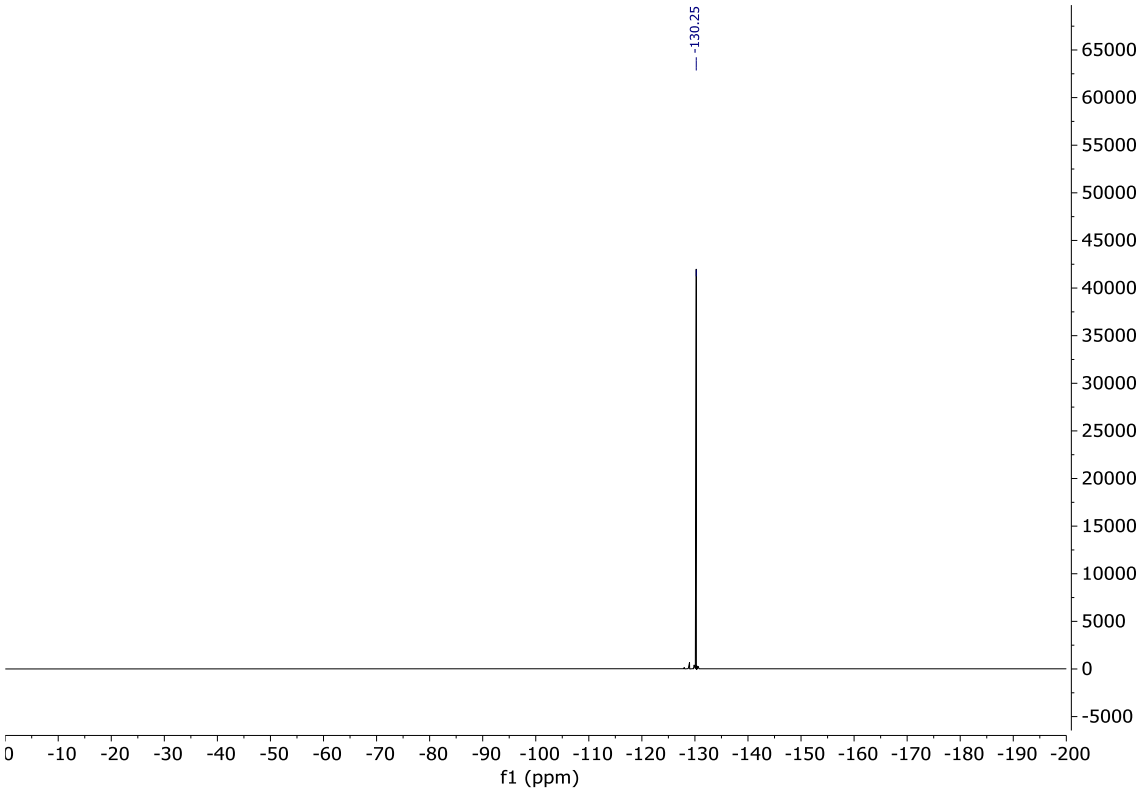




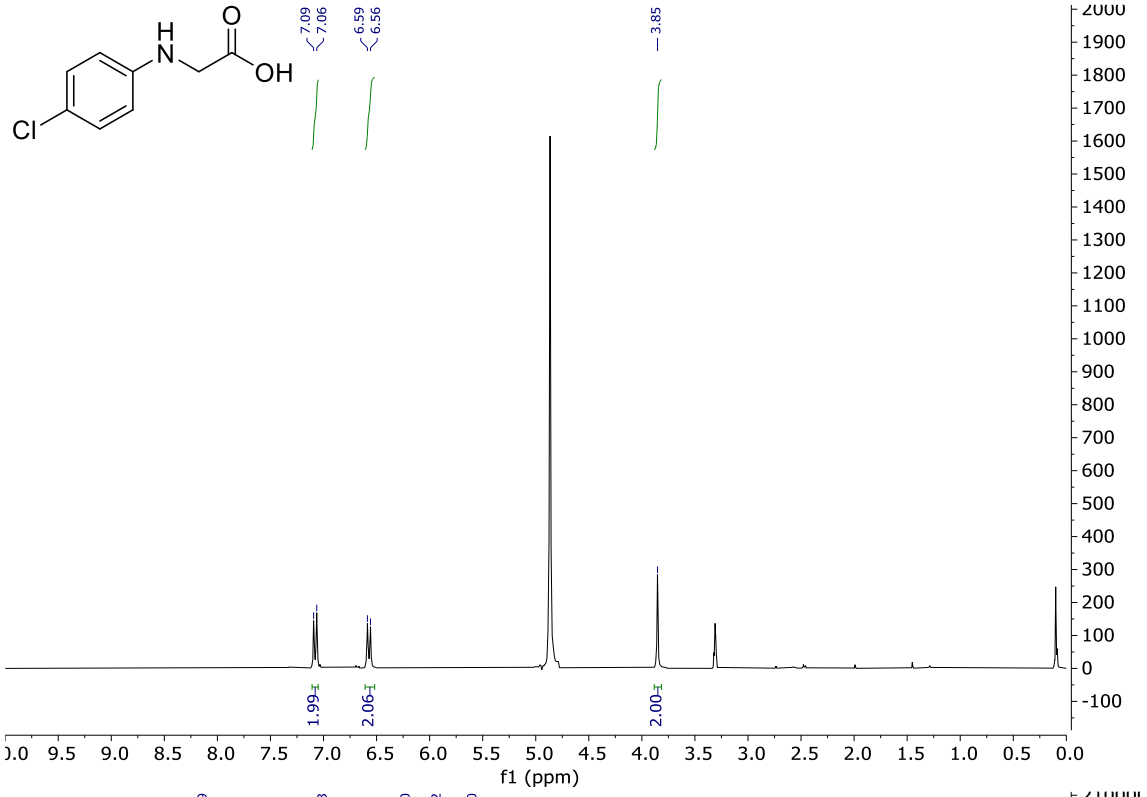
(4-Fluorophenyl)glycine (2b)

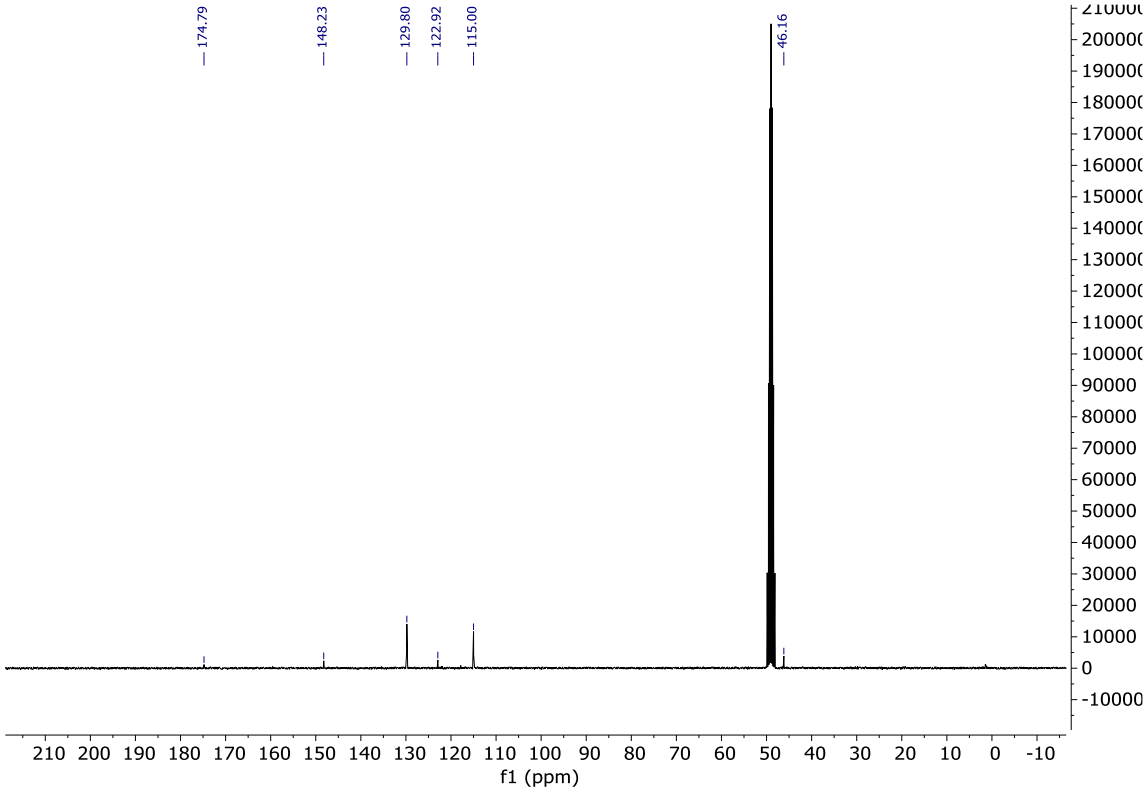




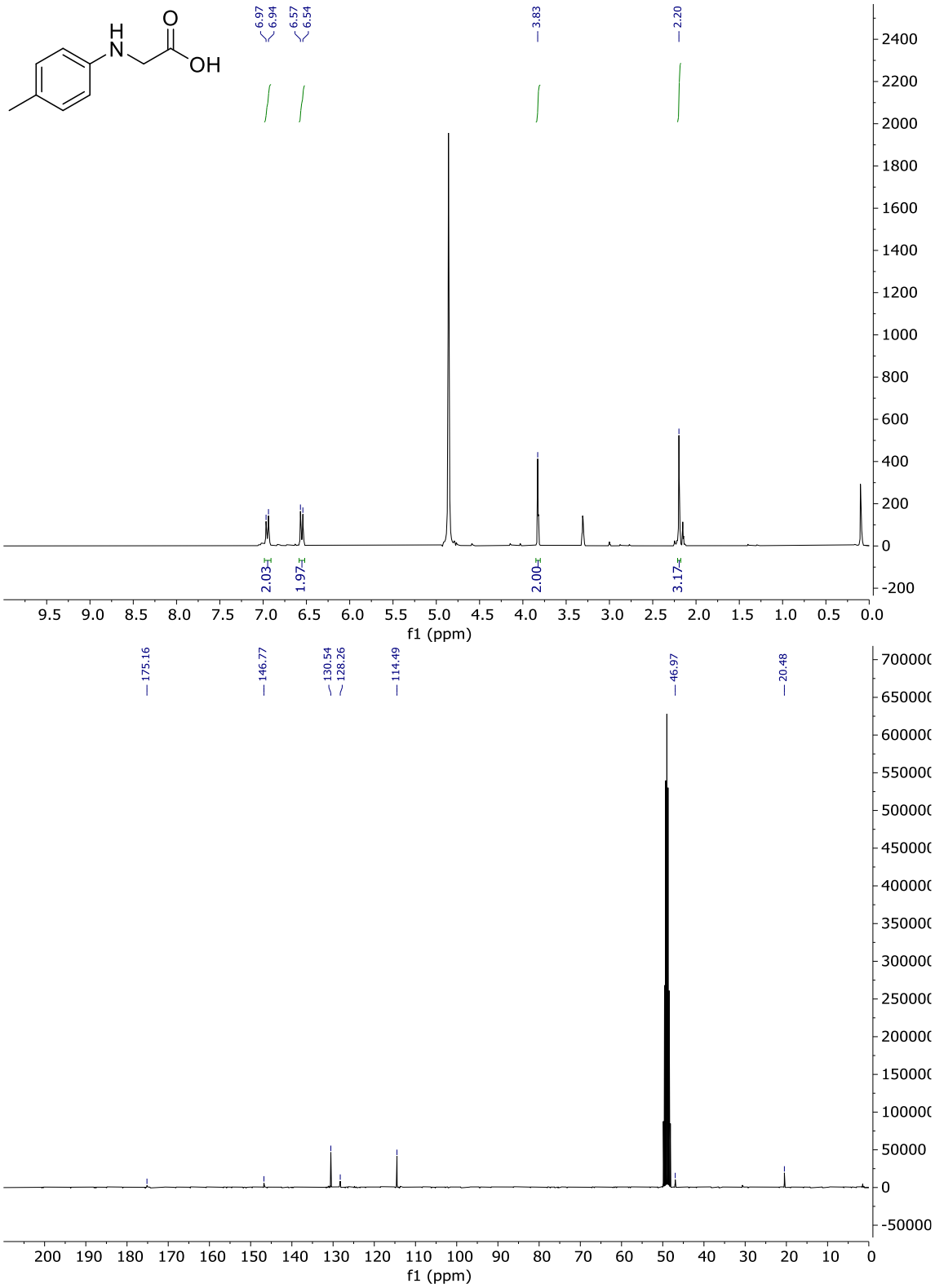

-130.25
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

(4-Chlorophenyl)glycine (2c)

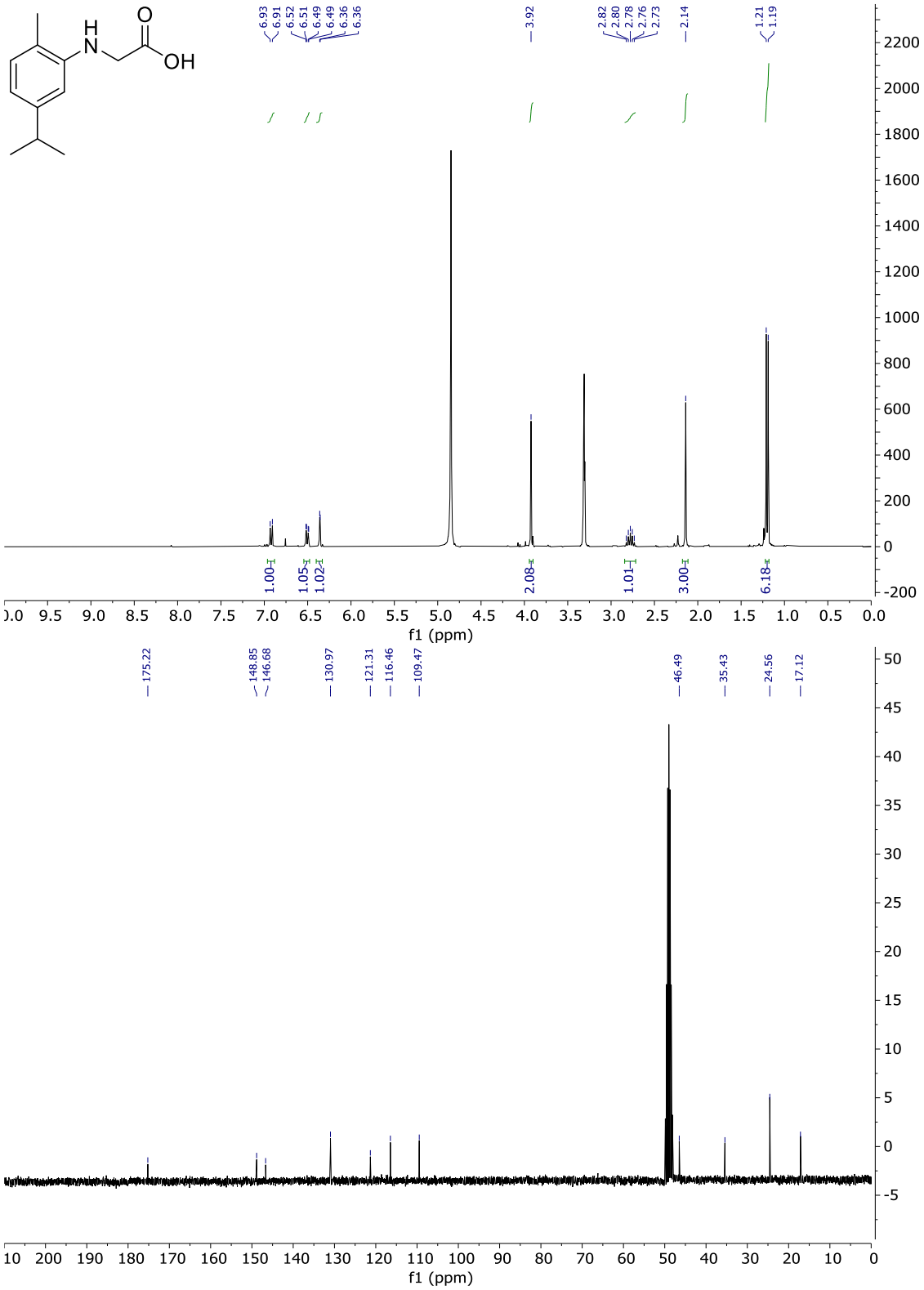




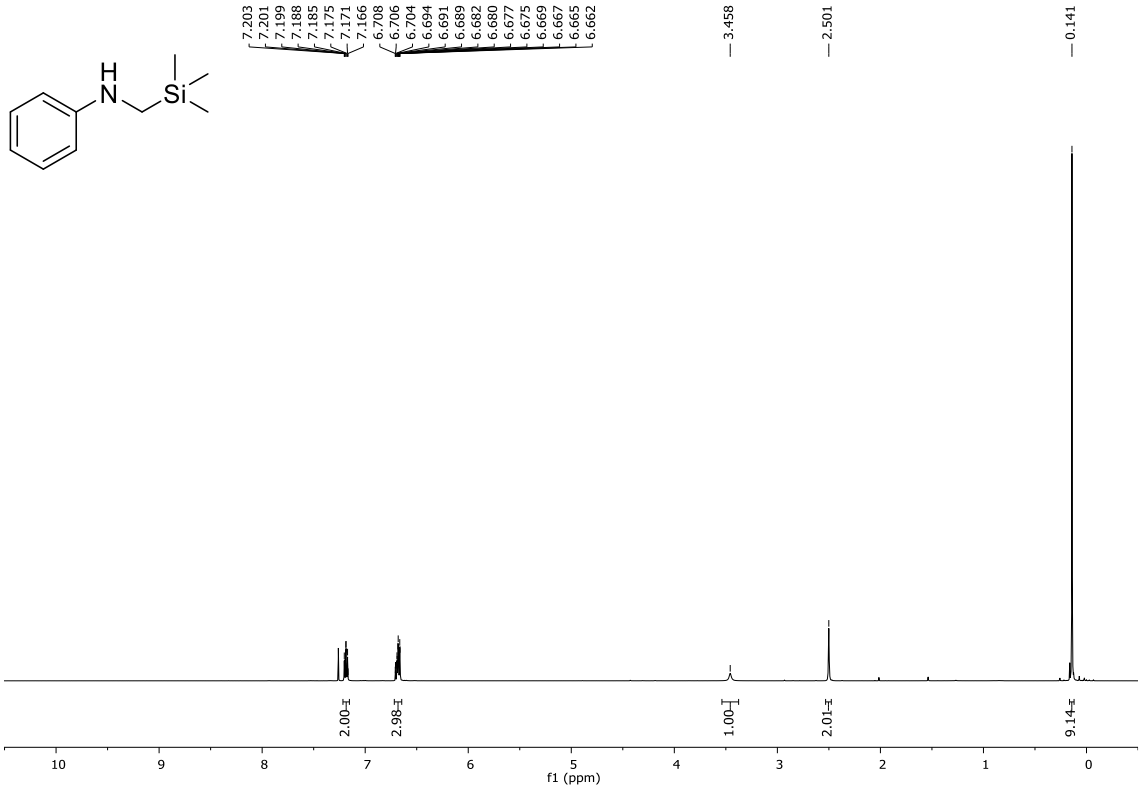
***p*-Tolylglycine (2d)**

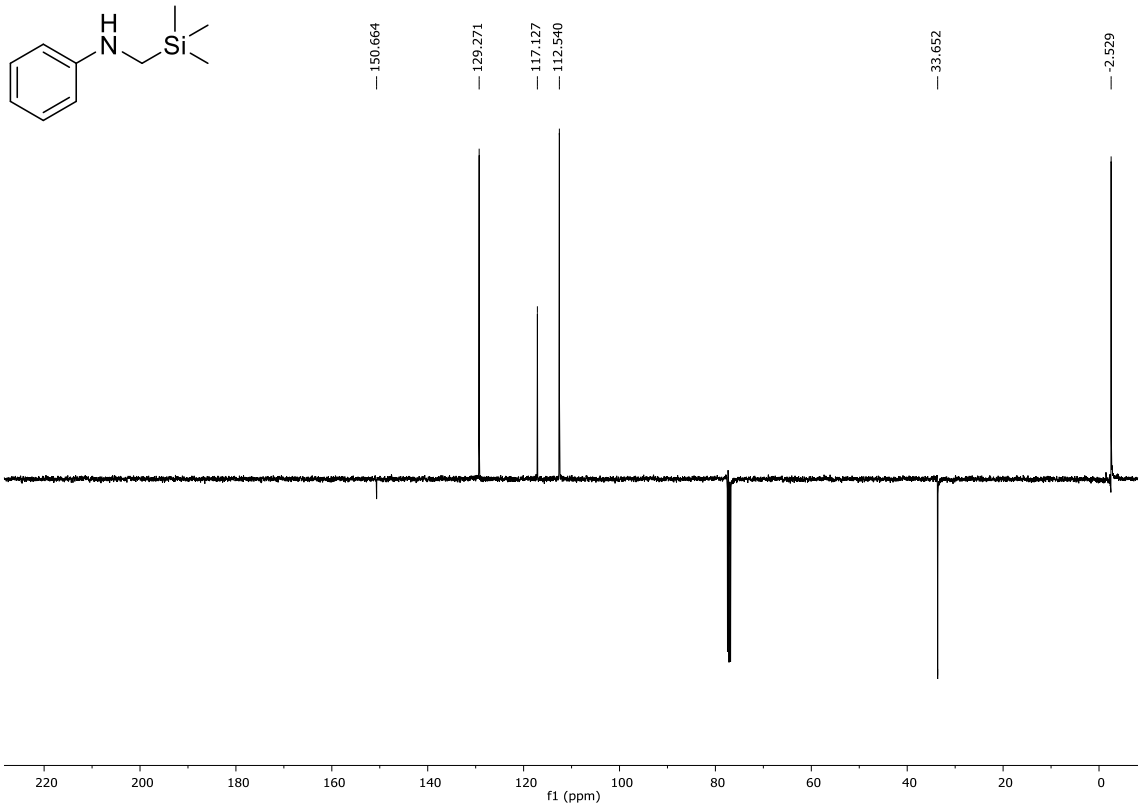


(5-Isopropyl-2-methylphenyl)glycine (2e)

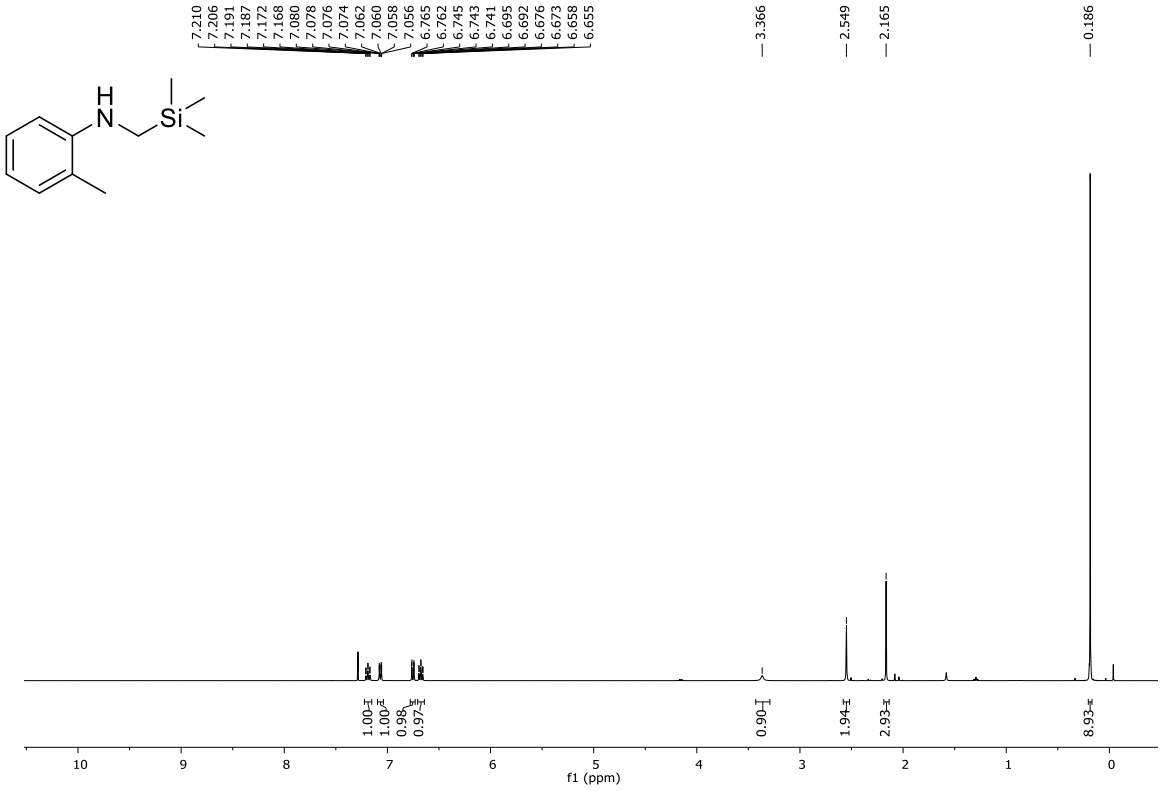


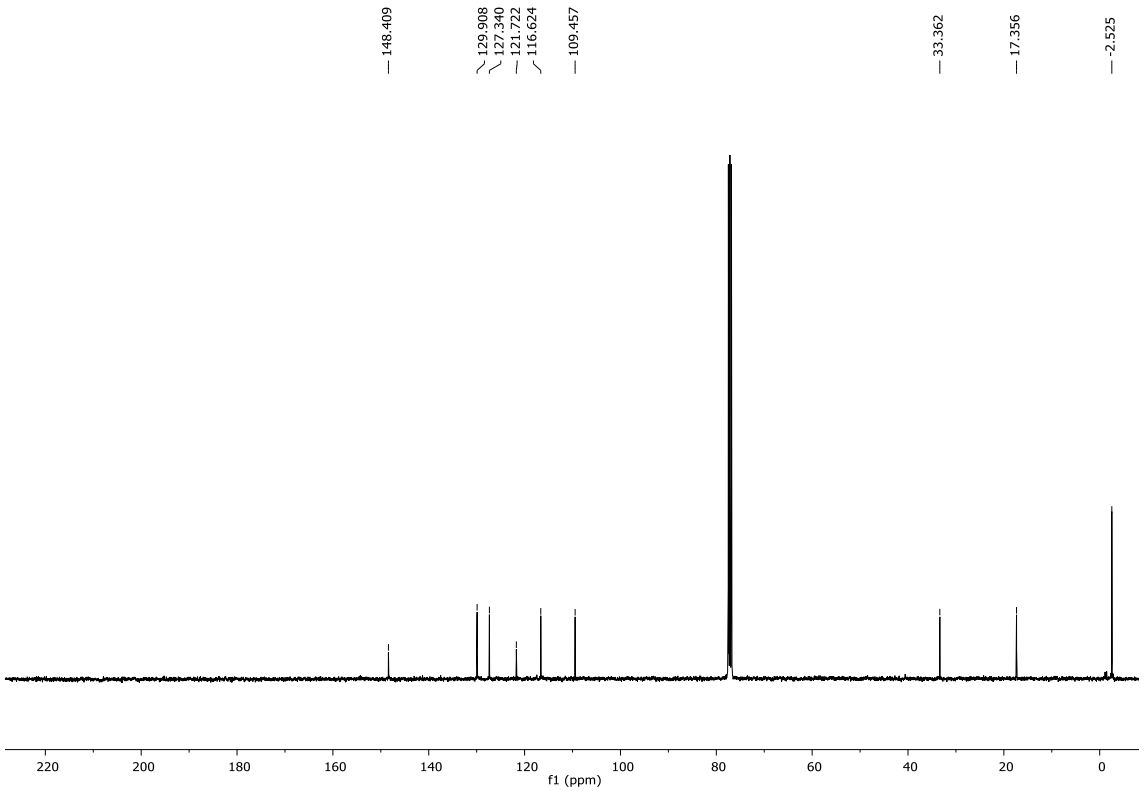
***N*-((trimethylsilyl)methyl)aniline (5a)**



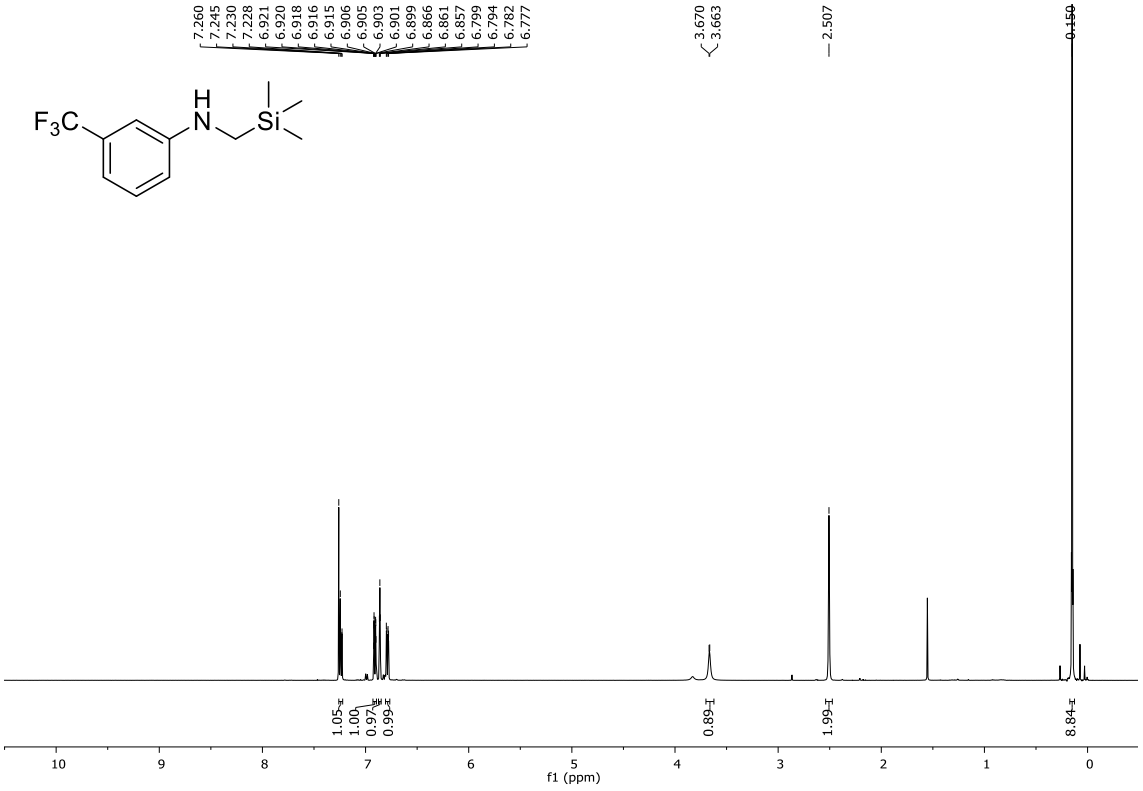


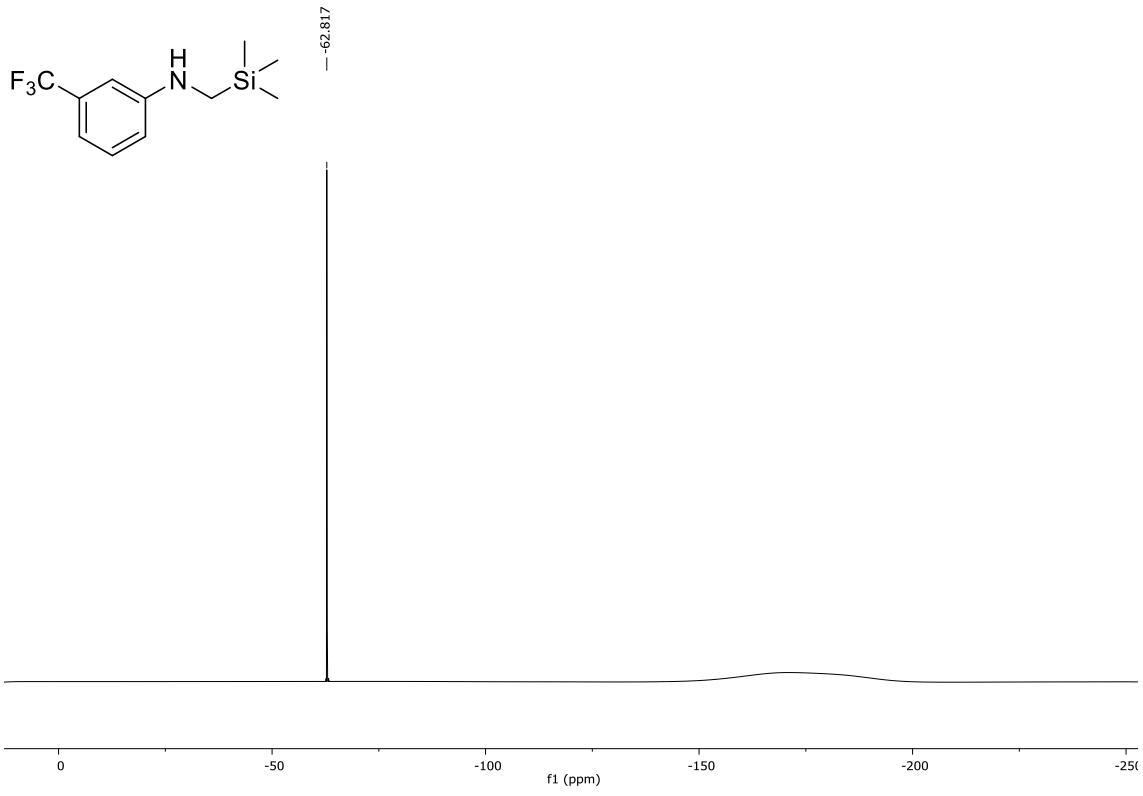
2-methyl-*N*-((trimethylsilyl)methyl)aniline (5b)



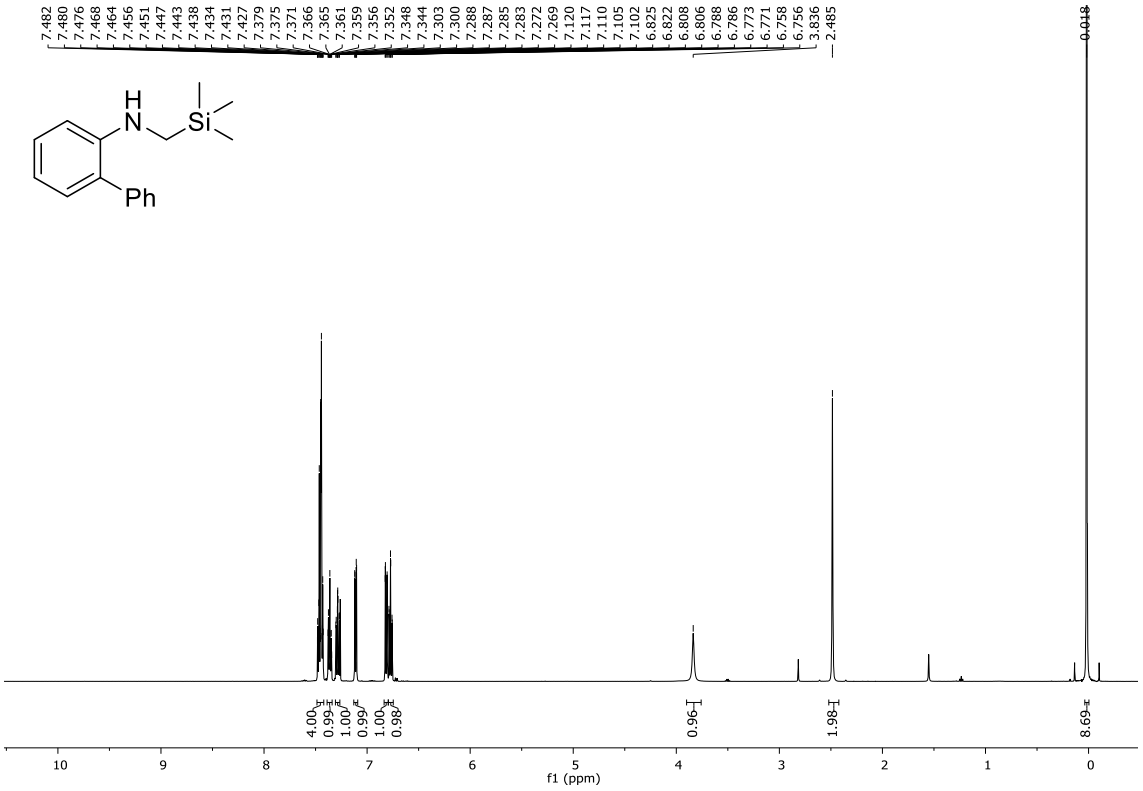


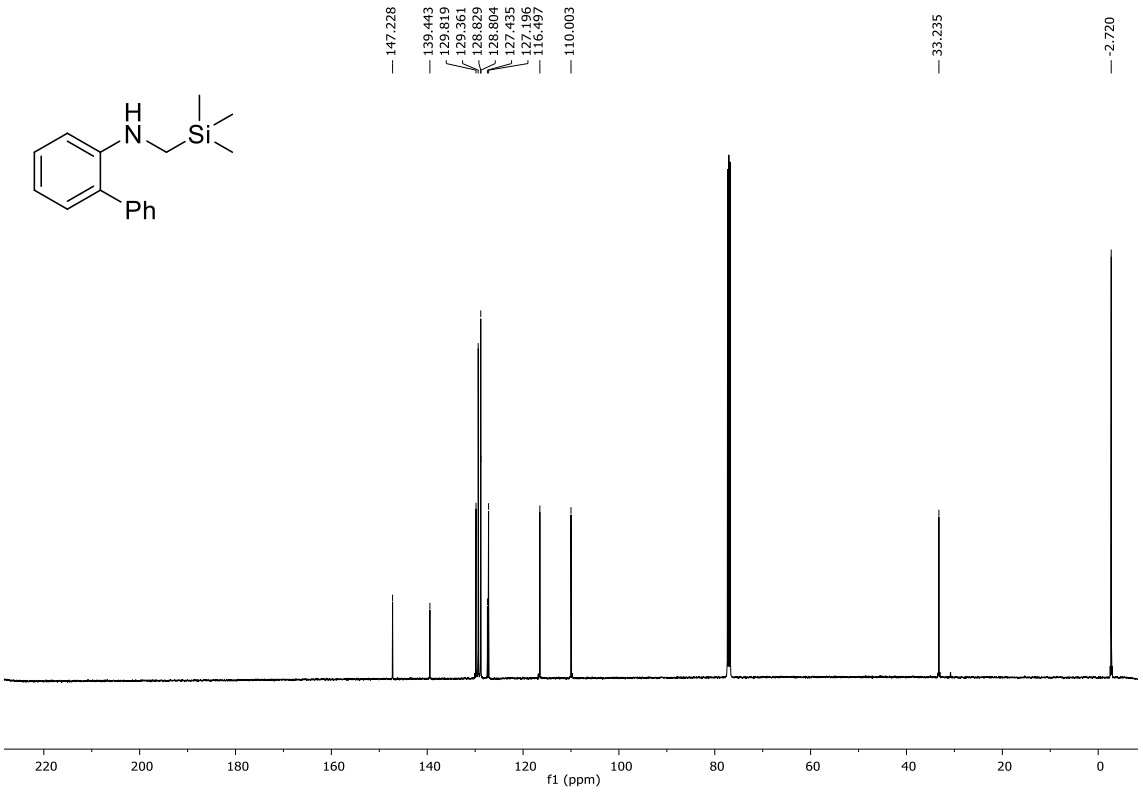
3-(trifluoromethyl)-N-((trimethylsilyl)methyl)aniline (5c)



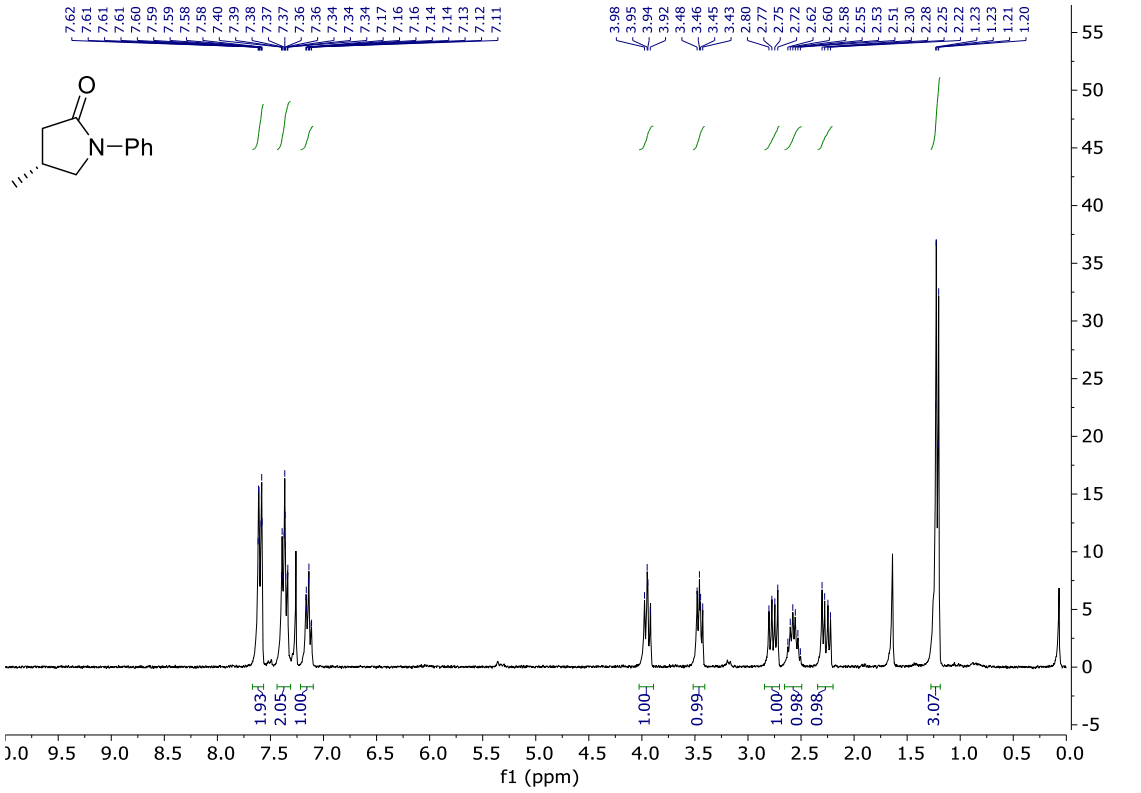


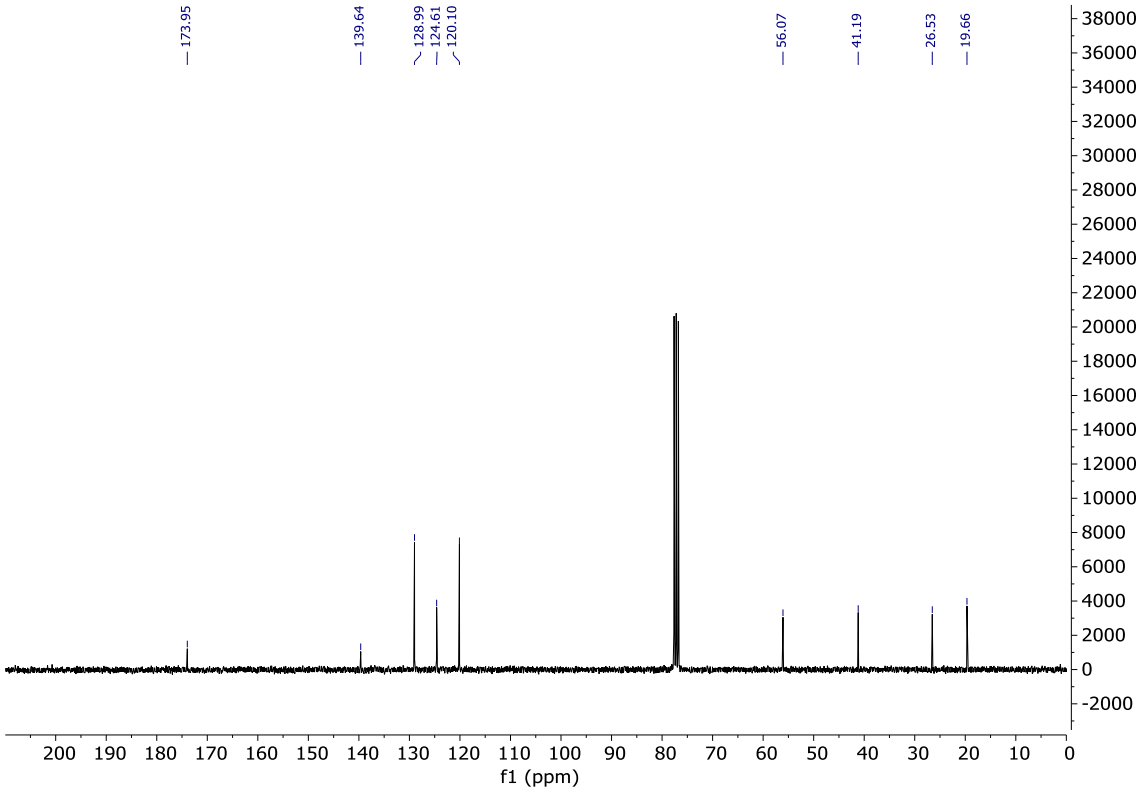
N-((trimethylsilyl)methyl)-[1,1'-biphenyl]-2-amine (5d)



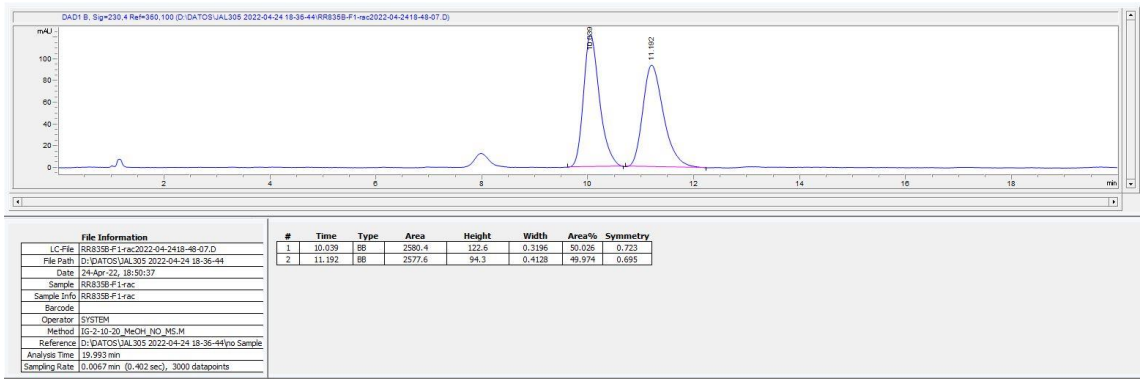


(*R*)-4-Methyl-1-phenylpyrrolidin-2-one (4a)





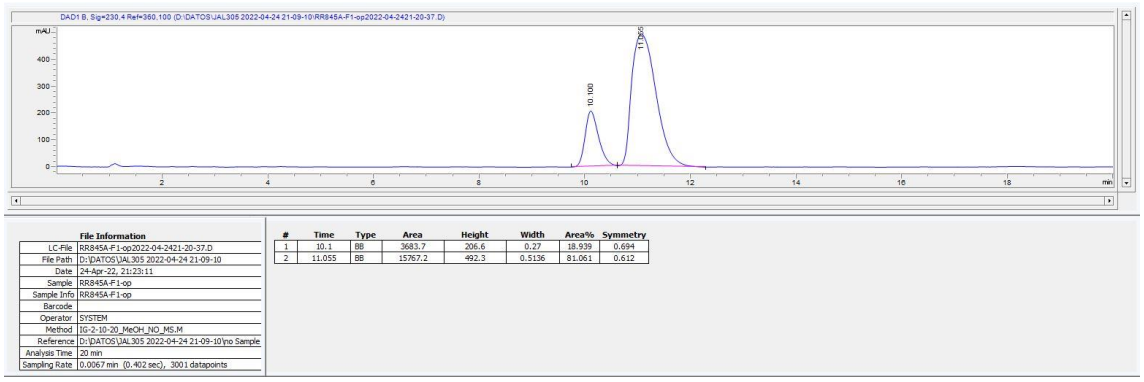
Racemic chromatogram:



File Information	
LC-File	RR835B-F1-rac2022-04-2418-48-07.D
File Path	D:\DATOS\JAL305 2022-04-24 18-36-44
Date	24-Apr-22, 18:50:37
Sample	RR835B-F1-rac
Sample Info	RR835B-F1-rac
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 18-36-44\no Sample
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.039	BB	2580.4	122.6	0.3196	50.026	0.723
2	11.192	BB	2577.6	94.3	0.4128	49.974	0.695

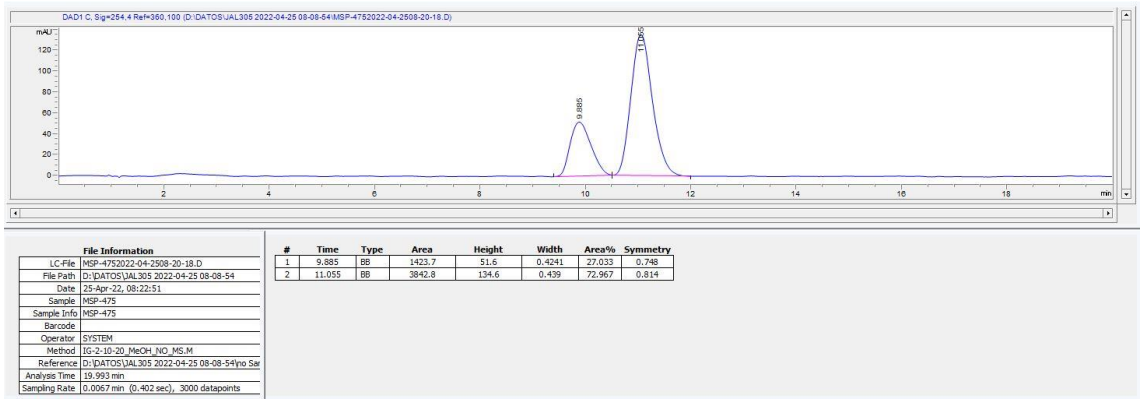
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR845A-F1-op2022-04-2421-20-37.D
File Path	D:\DATOS\JAL305 2022-04-24 21-09-10
Date	24-Apr-22, 21:23:11
Sample	RR845A-F1-op
Sample Info	RR845A-F1-op
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 21-09-10\no Sample
Analysis Time	20 min
Sampling Rate	0.0067 min (0.402 sec), 3001 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.1	BB	3683.7	206.6	0.27	18.939	0.694
2	11.055	BB	15767.2	492.3	0.5136	81.061	0.612

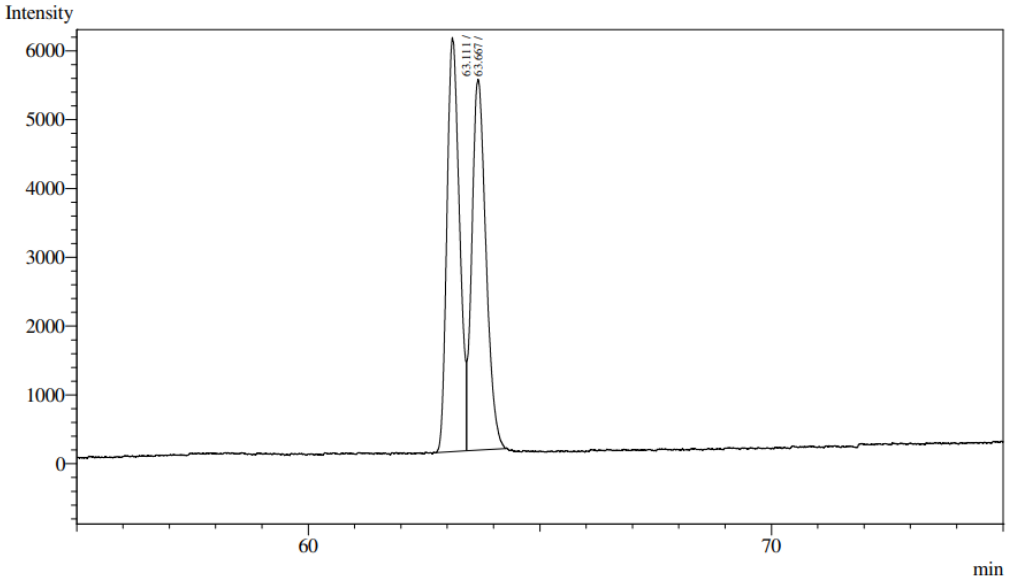
Flow reaction chromatogram (Manuscript, Table 4):



File Information	
LC-File	MSP-4752022-04-2508-20-18.D
File Path	D:\DATOS\JAL305 2022-04-25 08-08-54
Date	25-Apr-22, 08:22:51
Sample	MSP-475
Sample Info	MSP-475
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 08-08-54\no Sa
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

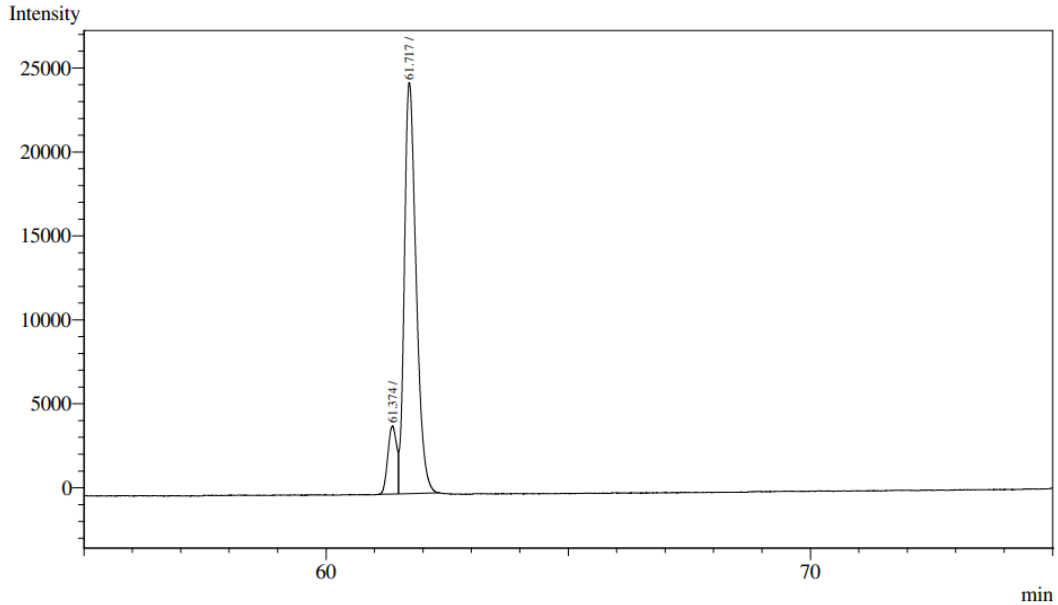
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.885	BB	1423.7	51.6	0.4241	27.033	0.748
2	11.055	BB	3842.8	134.6	0.439	72.967	0.814

Racemic Gas chromatogram



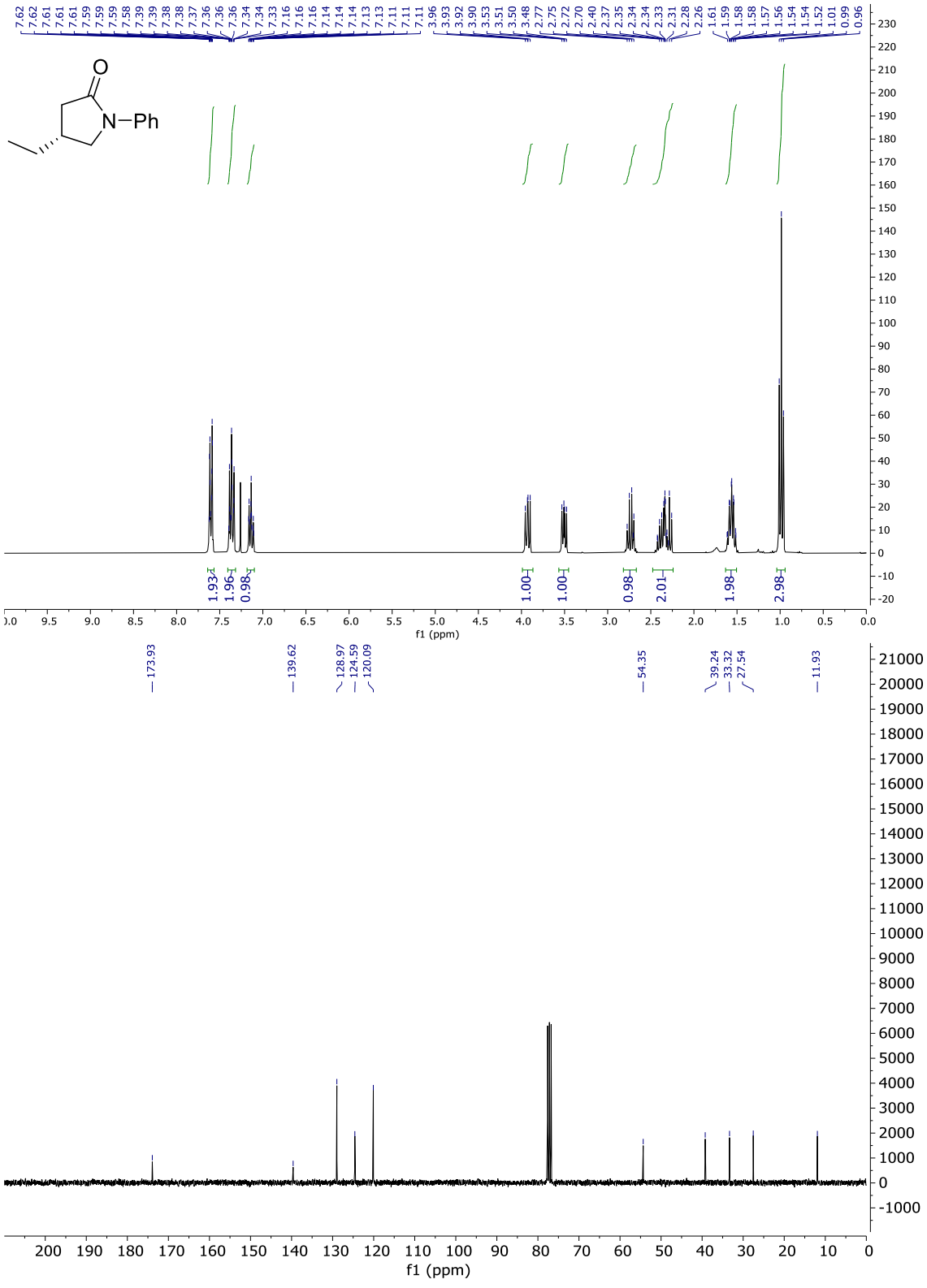
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	63.111	113000	6015	49.589				
2	63.667	114875	5388	50.411		V		
Total		227875	11403					

Batch Reaction Gas chromatogram

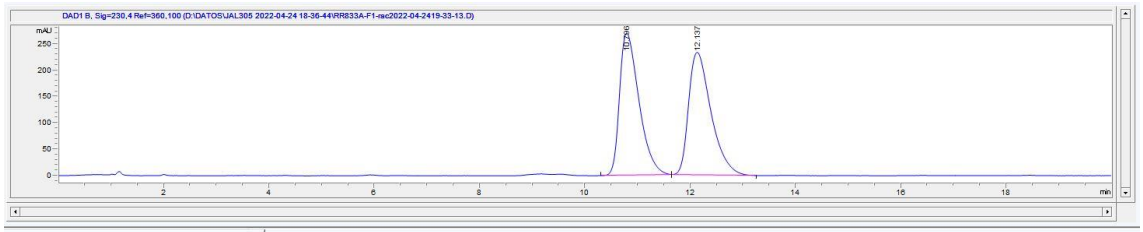


Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	61.374	51095	4060	10.970				
2	61.717	414676	24489	89.030		V		
Total		465771	28549					

(*R*)-4-Ethyl-1-phenylpyrrolidin-2-one (4b)



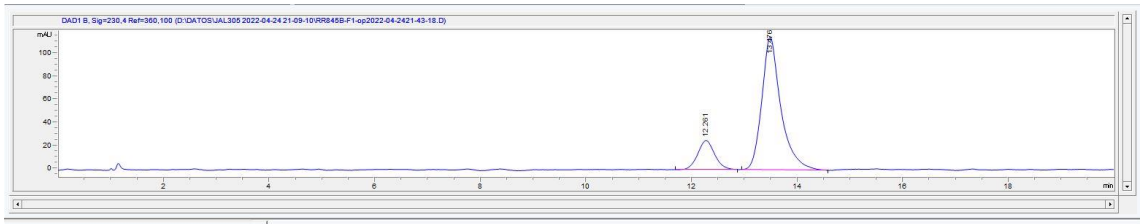
Racemic chromatogram:



File Information	
LC-File	RR833A-F1-rac2022-04-2419-33-13.D
File Path	D:\DATOS\JAL305 2022-04-24 18-36-44
Date	24-Apr-22, 19:35:37
Sample	RR833A-F1-rac
Sample Info	RR833A-F1-rac
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 18-36-44\no Sar
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.796	BB	6866.1	268.5	0.3924	50.063	0.548
2	12.137	BB	6848.9	231.3	0.4475	49.937	0.582

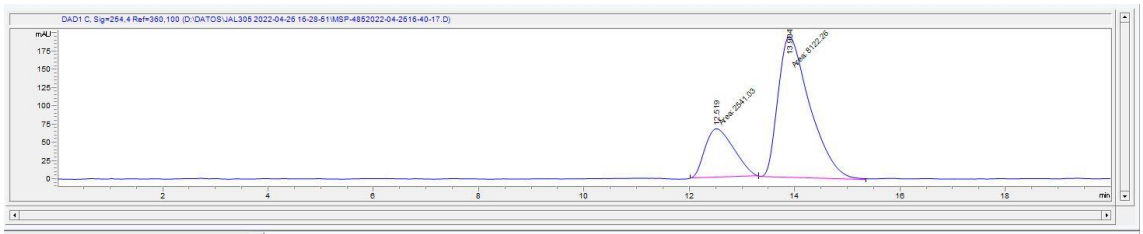
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR845B-F1-op2022-04-2421-43-18.D
File Path	D:\DATOS\JAL305 2022-04-24 21-09-10
Date	24-Apr-22, 21:45:43
Sample	RR845B-F1-op
Sample Info	RR845B-F1-op
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 21-09-10\no Sample
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.261	BB	562.4	25.1	0.3239	16.350	0.912
2	13.476	BB	2877.4	114.7	0.3566	83.650	0.713

Flow reaction chromatogram (Manuscript, Table 4):

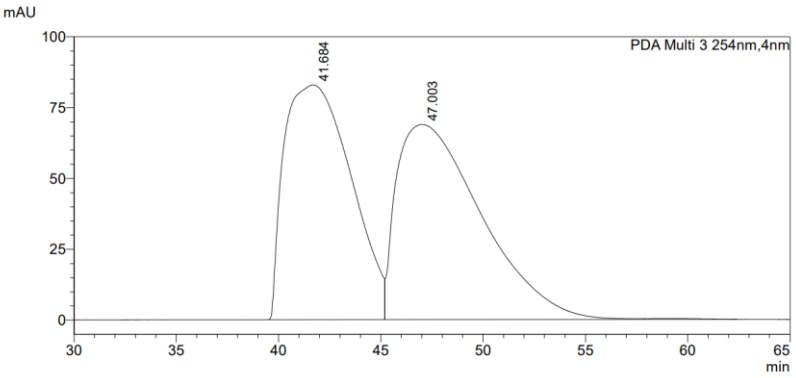


File Information	
LC-File	MSP-485\2022-04-2616-40-17.D
File Path	D:\DATOS\JAL305 2022-04-26 16-28-51
Date	26-Apr-22, 16:42:50
Sample	MSP-485
Sample Info	MSP-485
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-26 16-28-51\no Sar
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.519	MM	2541	66.5	0.6365	23.830	0.661
2	13.904	MM	8122.3	192.6	0.703	76.170	0.536

Batch racemic chromatogram using α-silyl amine

<Chromatogram>



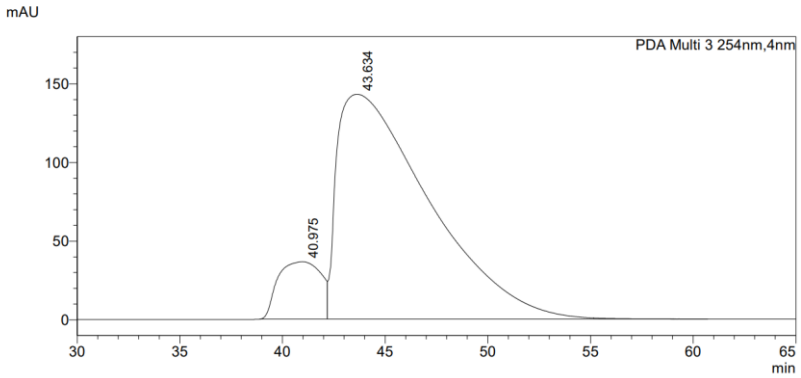
<Peak Table>

PDA Ch3 254nm

Peak#	Ret. Time	Area%
1	41.684	48.577
2	47.003	51.423
Total		100.000

Batch chromatogram using α-silyl amine

<Chromatogram>

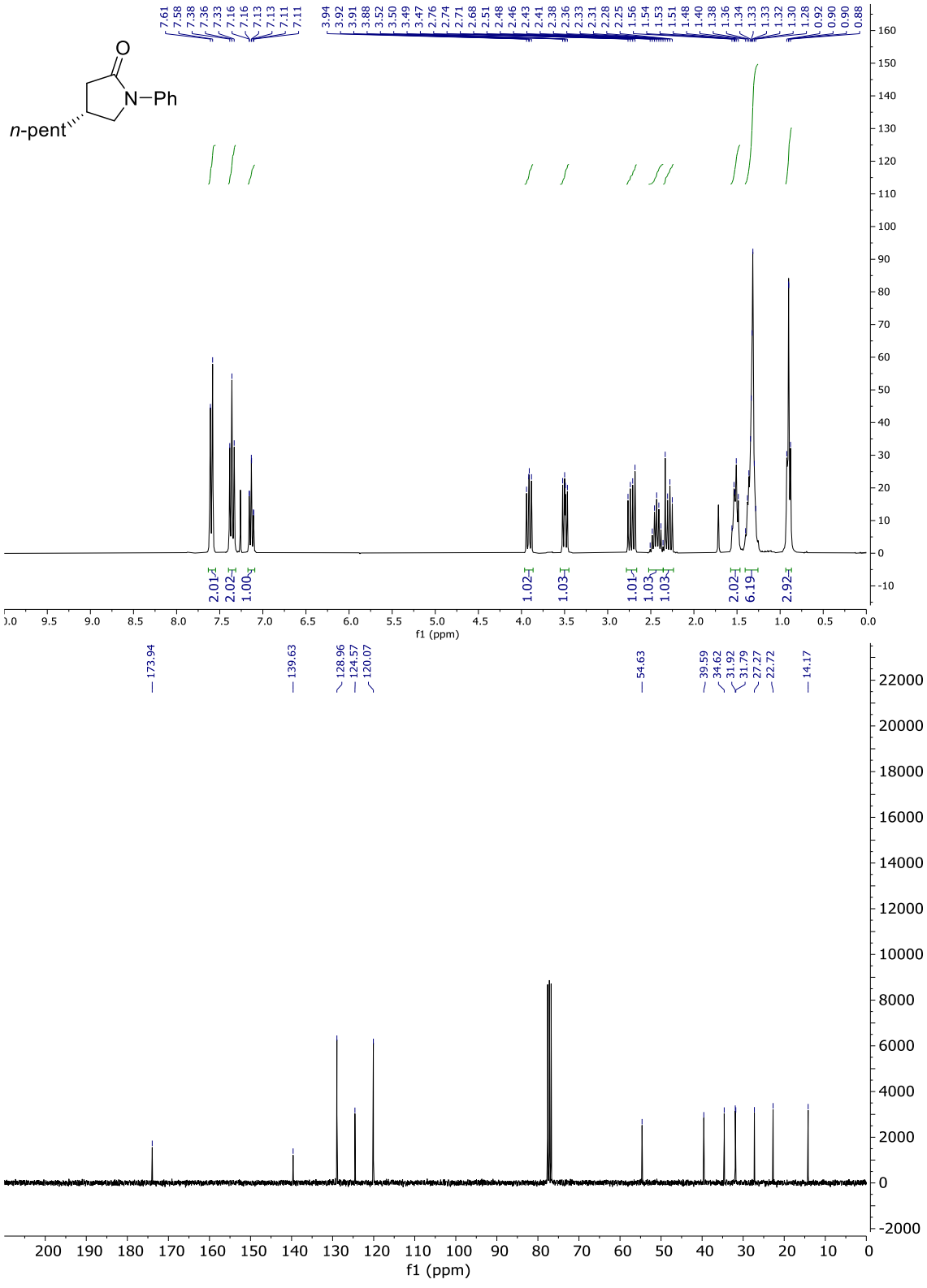


<Peak Table>

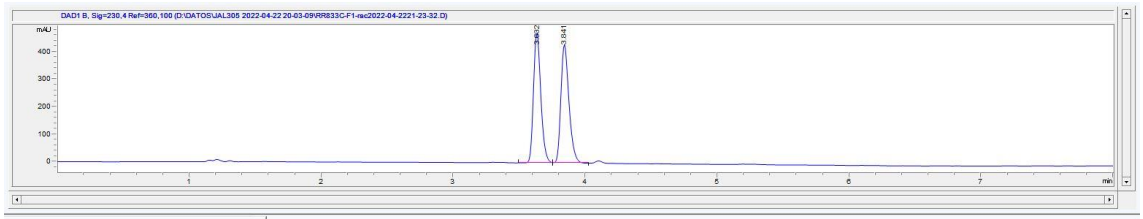
PDA Ch3 254nm

Peak#	Ret. Time	Area%
1	40.975	10.566
2	43.634	89.434
Total		100.000

(*R*)-4-Pentyl-1-phenylpyrrolidin-2-one (4c)



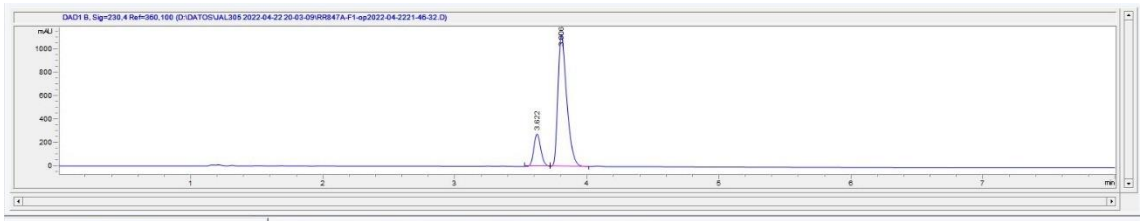
Racemic chromatogram:



File Information	
LC-File	RR833C-F1-rac2022-04-2221-23-32.D
File Path	D:\DATOS\JAL305 2022-04-22 20-03-09
Date	22-Apr-22, 21:26:01
Sample	RR833C-F1-rac
Sample Info	RR833C-F1-rac
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-22 20-03-09\no Sample
Analysis Time	8 min
Sampling Rate	0.0067 min (0.402 sec), 1201 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.632	BB	1820.4	476.2	0.0606	49.945	0.786
2	3.841	BB	1824.4	430.8	0.0654	50.055	0.719

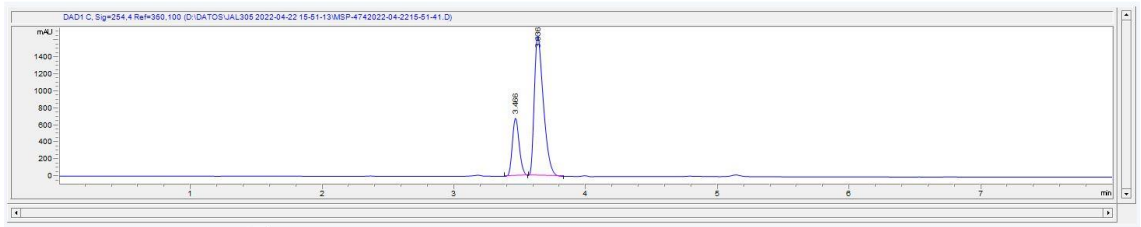
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR847A-F1-op2022-04-2221-46-32.D
File Path	D:\DATOS\JAL305 2022-04-22 20-03-09
Date	22-Apr-22, 21:48:57
Sample	RR847A-F1-op
Sample Info	RR847A-F1-op
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-22 20-03-09\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.622	BB	1015.7	277.1	0.0568	16.294	0.841
2	3.806	BB	5217.5	1135	0.0696	83.706	0.602

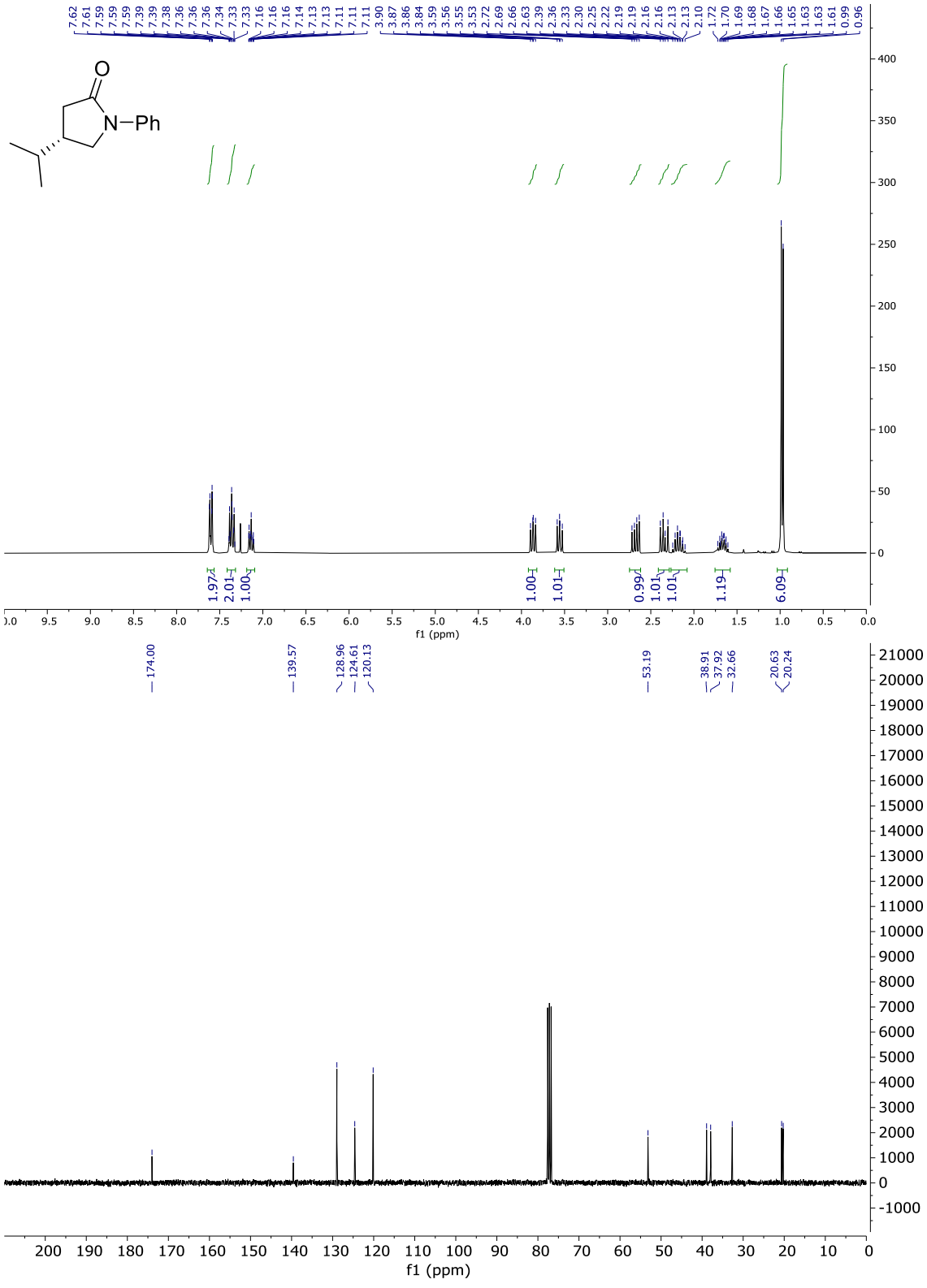
Flow reaction chromatogram (Manuscript, Table 4):



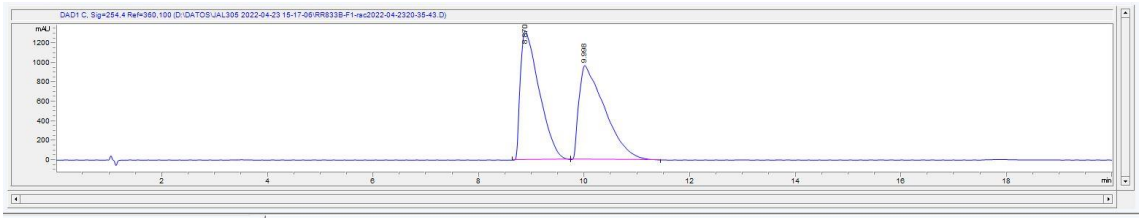
File Information	
LC-File	MSP-4742022-04-2215-51-41.D
File Path	D:\DATOS\JAL305 2022-04-22 15-51-13
Date	22-Apr-22, 15:54:50
Sample	MSP-474
Sample Info	MSP-474
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_MS.M
Reference	
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.466	BB	2472.5	682.7	0.0563	23.856	0.818
2	3.636	BB	7891.8	1658.6	0.0715	76.144	0.575

(*S*)-4-Isopropyl-1-phenylpyrrolidin-2-one (4d)



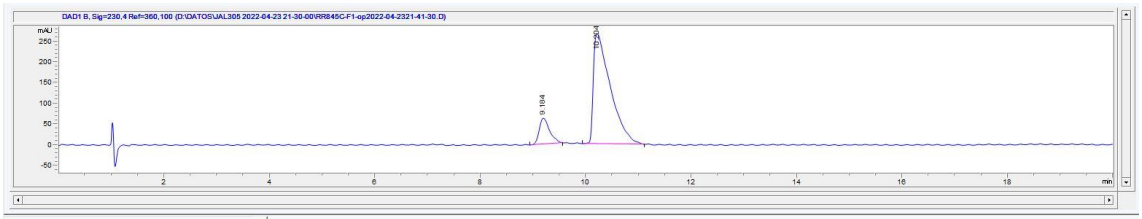
Racemic chromatogram:



File Information	
LC-File	RR833B-F1-rac2022-04-2320-35-43.D
File Path	D:\DATOS\JAL305 2022-04-23 15-17-06
Date	23-Apr-22, 20:38:10
Sample	RR833B-F1-rac
Sample Info	RR833B-F1-rac
Barcode	
Operator	SYSTEM
Method	IB-1-5-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 15-17-06\no Sample
Analysis Time	20 min
Sampling Rate	0.0067 min (0.402 sec), 3001 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.87	BB	32649.9	1317.5	0.3811	49.960	0.328
2	9.998	BB	32701.5	959	0.4658	50.040	0.277

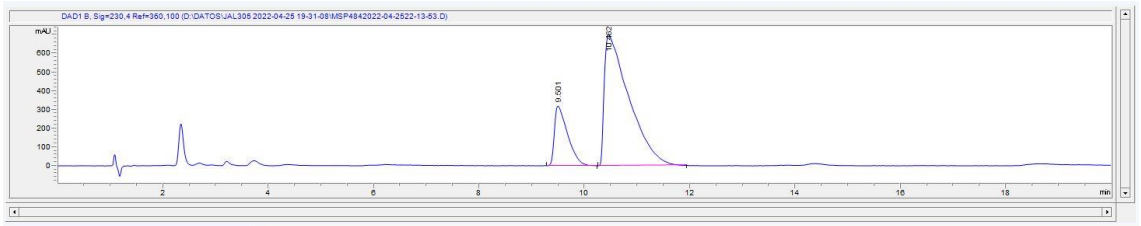
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR845C-F1-op2022-04-2321-41-30.D
File Path	D:\DATOS\JAL305 2022-04-23 21-30-00
Date	23-Apr-22, 21:43:55
Sample	RR845C-F1-op
Sample Info	RR845C-F1-op
Barcode	
Operator	SYSTEM
Method	IB-1-5-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 21-30-00\no Sample
Analysis Time	20 min
Sampling Rate	0.0067 min (0.402 sec), 3001 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.184	BB	870.9	62.9	0.2075	12.723	0.601
2	10.204	BB	5973.9	266.2	0.3158	87.277	0.258

Flow reaction chromatogram (Manuscript, Table 4):

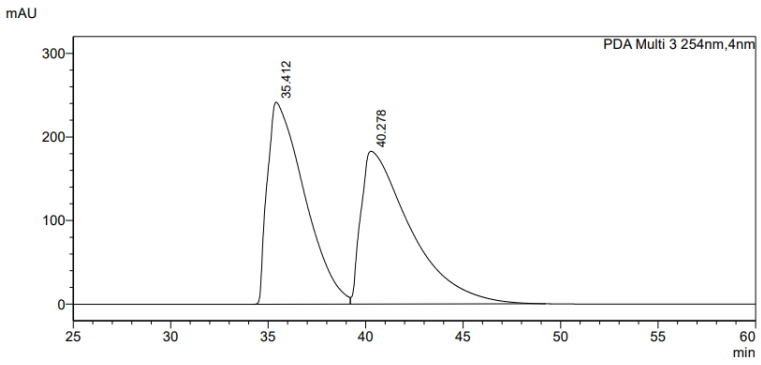


File Information	
LC-File	MSP4842022-04-2522-13-53.D
File Path	D:\DATOS\JAL305 2022-04-25 19-31-08
Date	25-Apr-22, 22:16:19
Sample	MSP484
Sample Info	MSP484
Barcode	
Operator	SYSTEM
Method	IB-1-5-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 19-31-08\no Sar
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.501	BB	5568.1	320.1	0.2449	19.571	0.345
2	10.462	BB	22882.5	703.3	0.4316	80.429	0.194

Racemic chromatogram using α-silyl amine

<Chromatogram>



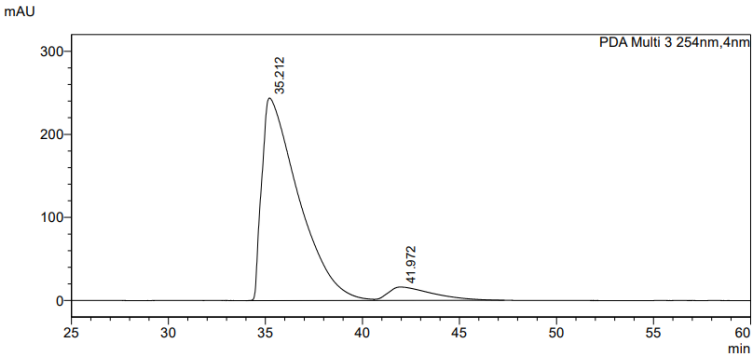
<Peak Table>

PDA Ch3 254nm

Peak#	Ret. Time	Area%
1	35.412	49.729
2	40.278	50.271
Total		100.000

Batch chromatogram using α-silyl amine

<Chromatogram>

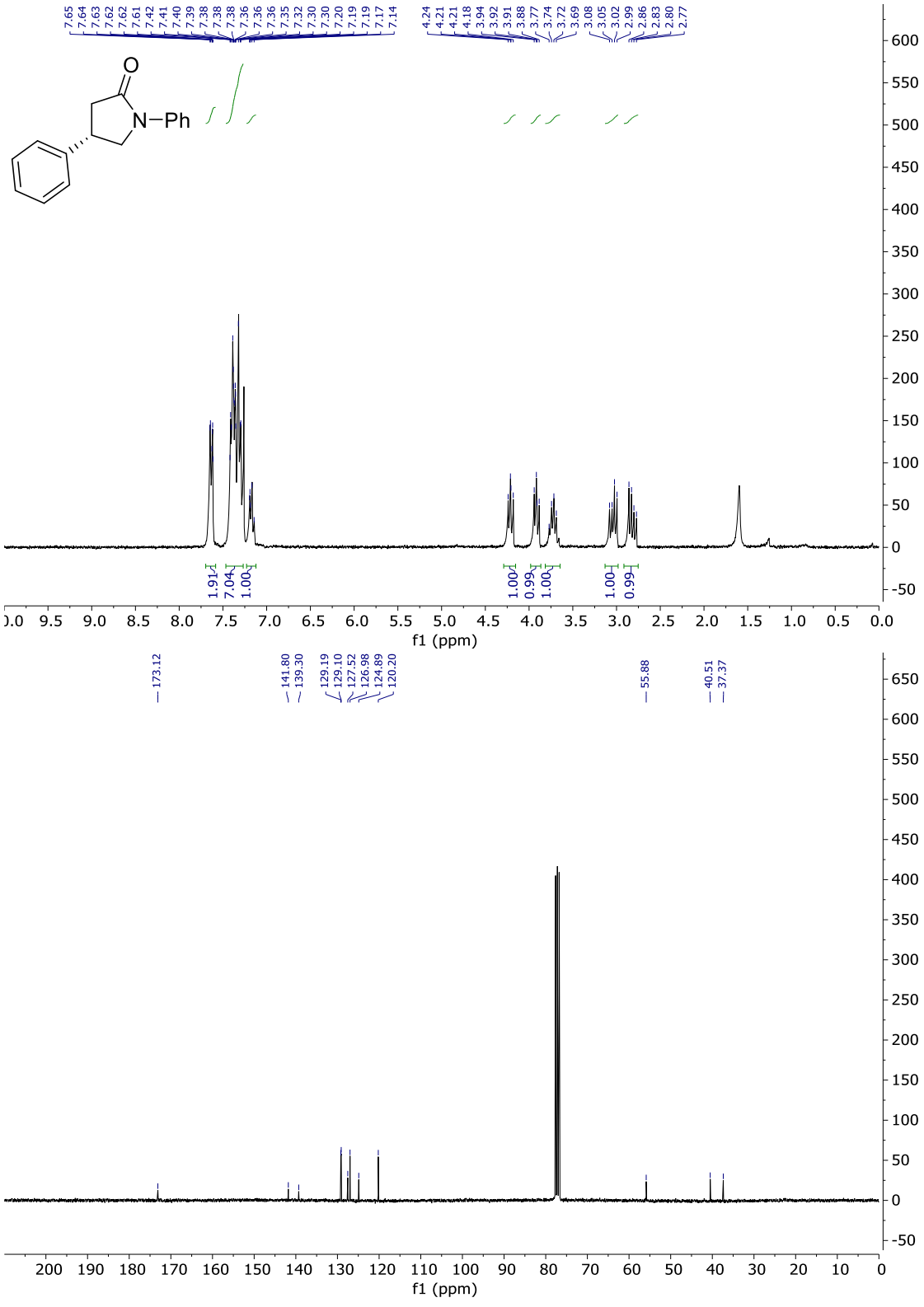


<Peak Table>

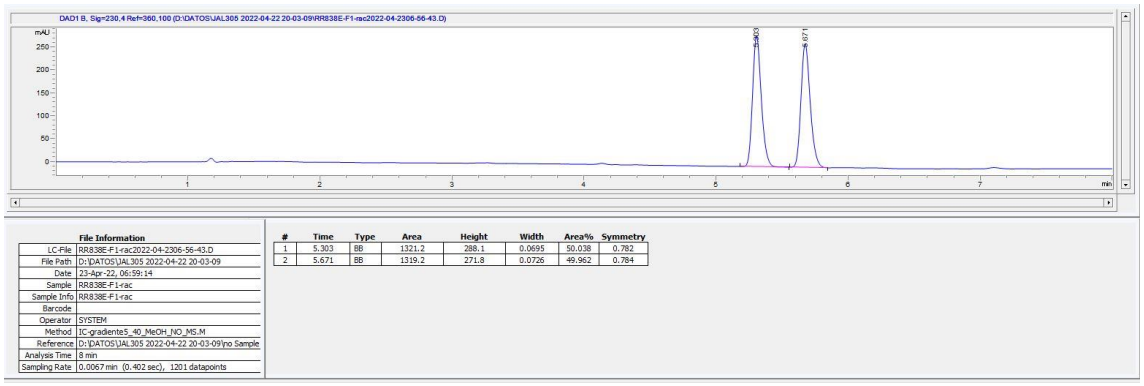
PDA Ch3 254nm

Peak#	Ret. Time	Area%
1	35.212	92.626
2	41.972	7.374
Total		100.000

(*S*)-1,4-Diphenylpyrrolidin-2-one (4e)



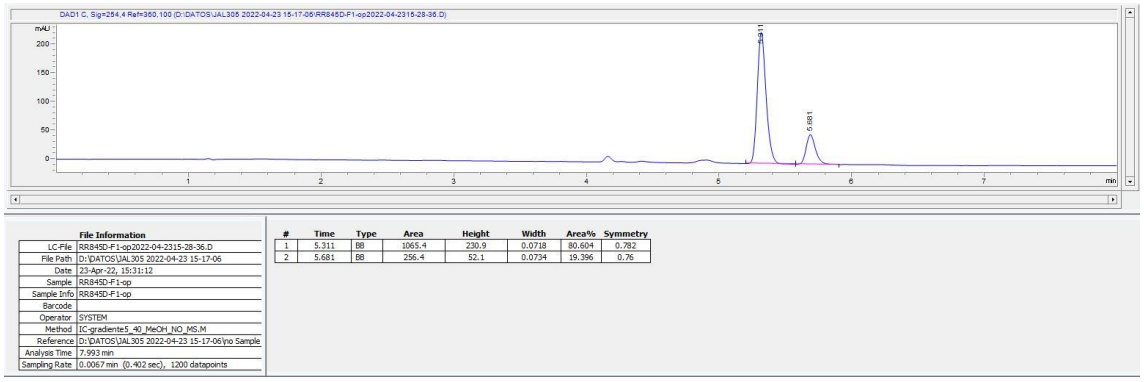
Racemic chromatogram:



File Information	
LC-File	RR838E-F1-rac2022-04-2306-56-43.D
File Path	D:\DATOS\JAL305 2022-04-22 20-03-09
Date	23-Apr-22, 06:59:14
Sample	RR838E-F1-rac
Sample Info	RR838E-F1-rac
Barcode	
Operator	SYSTEM
Method	IC-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-22 20-03-09\no Sample
Analysis Time	8 min
Sampling Rate	0.0067 min (0.402 sec), 1201 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.303	BB	1321.2	288.1	0.0695	50.038	0.782
2	5.671	BB	1319.2	271.8	0.0726	49.962	0.784

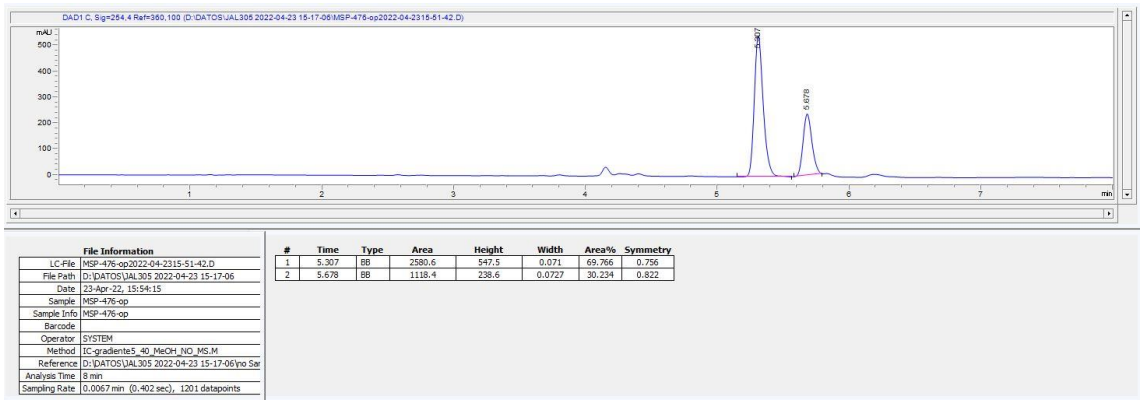
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR845D-F1-op2022-04-2315-28-36.D
File Path	D:\DATOS\JAL305 2022-04-23 15-17-06
Date	23-Apr-22, 15:31:12
Sample	RR845D-F1-op
Sample Info	RR845D-F1-op
Barcode	
Operator	SYSTEM
Method	IC-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 15-17-06\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.311	BB	1065.4	230.9	0.0718	80.604	0.782
2	5.681	BB	256.4	52.1	0.0734	19.396	0.76

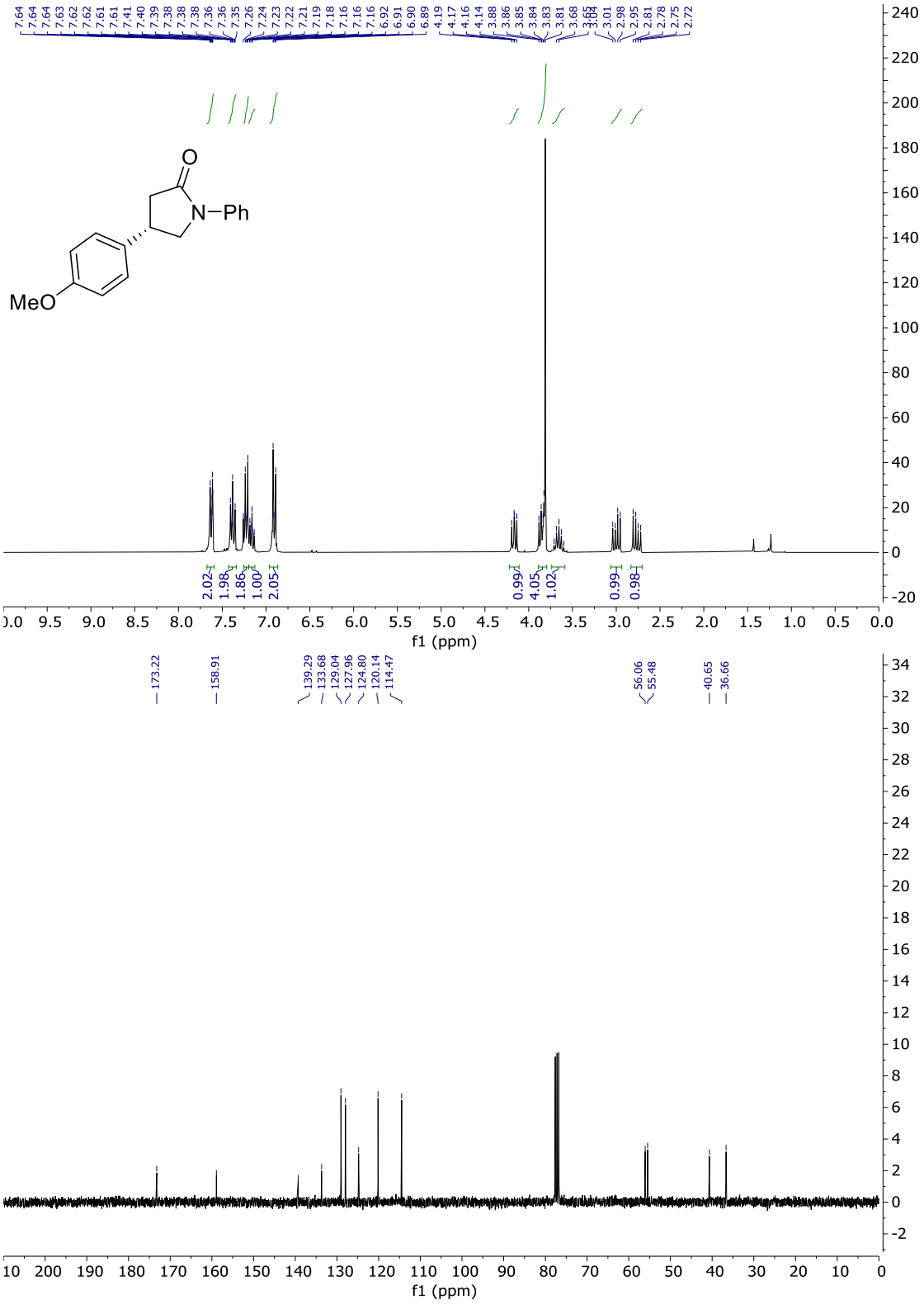
Flow reaction chromatogram (Manuscript, Table 4):



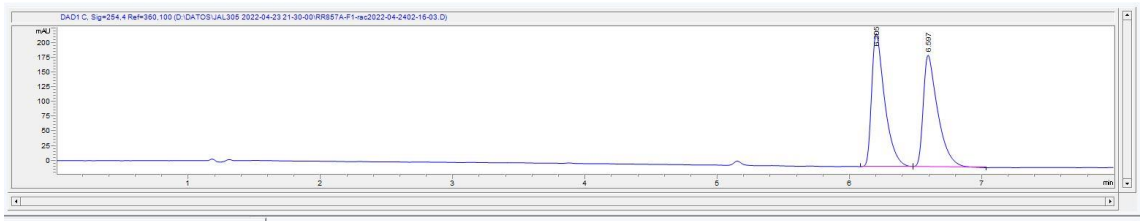
File Information	
LC-File	MSP-476-op2022-04-2315-51-42.D
File Path	D:\DATOS\JAL305 2022-04-23 15-17-06
Date	23-Apr-22, 15:54:15
Sample	MSP-476-op
Sample Info	MSP-476-op
Barcode	
Operator	SYSTEM
Method	IC-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 15-17-06\no Sar
Analysis Time	8 min
Sampling Rate	0.0067 min (0.402 sec), 1201 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.307	BB	2580.6	547.5	0.071	69.766	0.756
2	5.678	BB	1118.4	238.6	0.0727	30.234	0.822

(*S*)-4-(4-Methoxyphenyl)-1-phenylpyrrolidin-2-one (4f)



Racemic chromatogram:



File Information	
LC-File	RR857A-F1-rac2022-04-2402-16-03.D
File Path	D:\DATOS\JAL305 2022-04-23 21-30-00
Date	24-Apr-22, 02:18:34
Sample	RR857A-F1-rac
Sample Info	RR857A-F1-rac
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 21-30-00\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

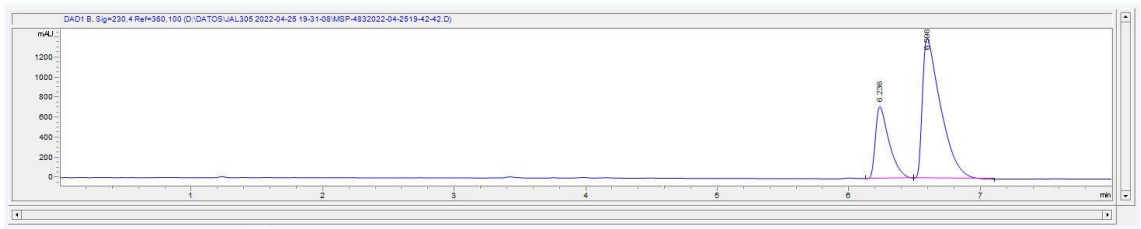
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.205	BB	1541.4	225.2	0.1018	51.676	0.503
2	6.597	BB	1441.4	188.9	0.111	48.324	0.457

Batch reaction chromatogram (Manuscript, Table 2):

File Information	
LC-File	RR857A-F1-op2022-04-2411-11-19.D
File Path	D:\DATOS\JAL305 2022-04-24 10-59-55
Date	24-Apr-22, 11:13:46
Sample	RR857A-F1-op
Sample Info	RR857A-F1-op
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 10-59-55\no Sample
Analysis Time	8 min
Sampling Rate	0.0067 min (0.402 sec), 1201 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.235	BB	1777.1	269.4	0.099	21.202	0.528
2	6.559	BB	6604.7	765.9	0.1286	78.798	0.365

Flow reaction chromatogram (Manuscript, Table 4):

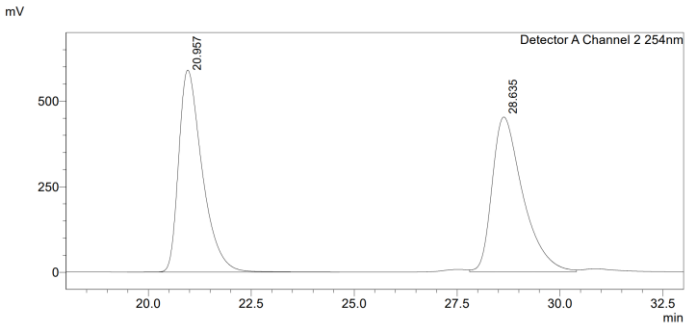


File Information	
LC-File	MSP-4832022-04-2519-42-42.D
File Path	D:\DATOS\JAL305 2022-04-25 19-31-08
Date	25-Apr-22, 19:45:09
Sample	MSP-483
Sample Info	MSP-483
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 19-31-08\no Sar
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.236	BB	5222.8	724.6	0.1061	27.725	0.448
2	6.596	BB	13615.3	1410.1	0.1407	72.275	0.324

Racemic reaction chromatogram (from the α-silyl amine)

<Chromatogram>



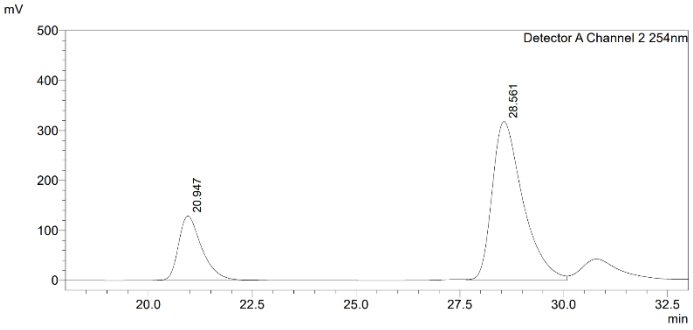
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	20.957	49.931
2	28.635	50.069
Total		100.000

Batch reaction chromatogram (from the α-silyl amine)

<Chromatogram>

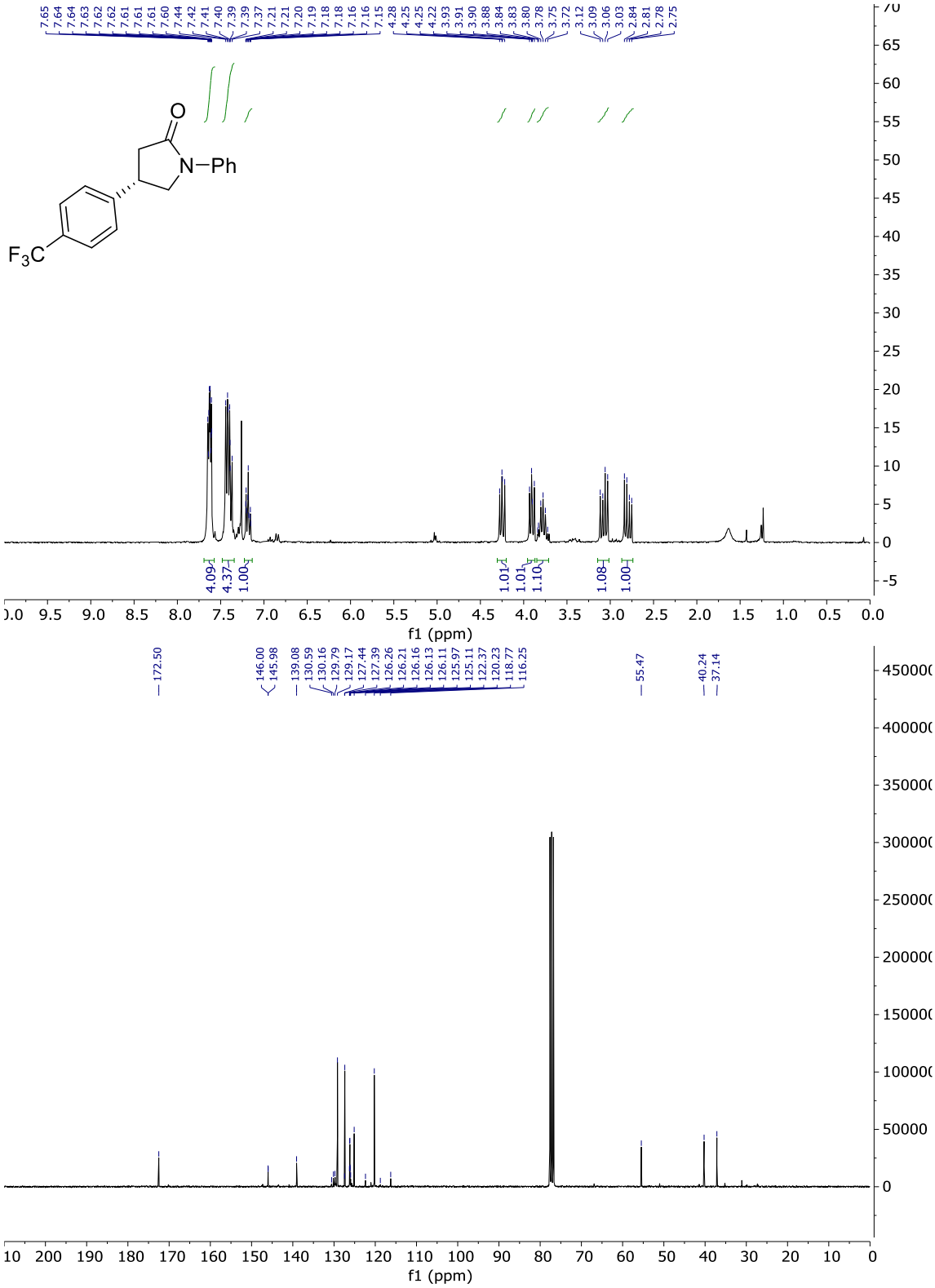


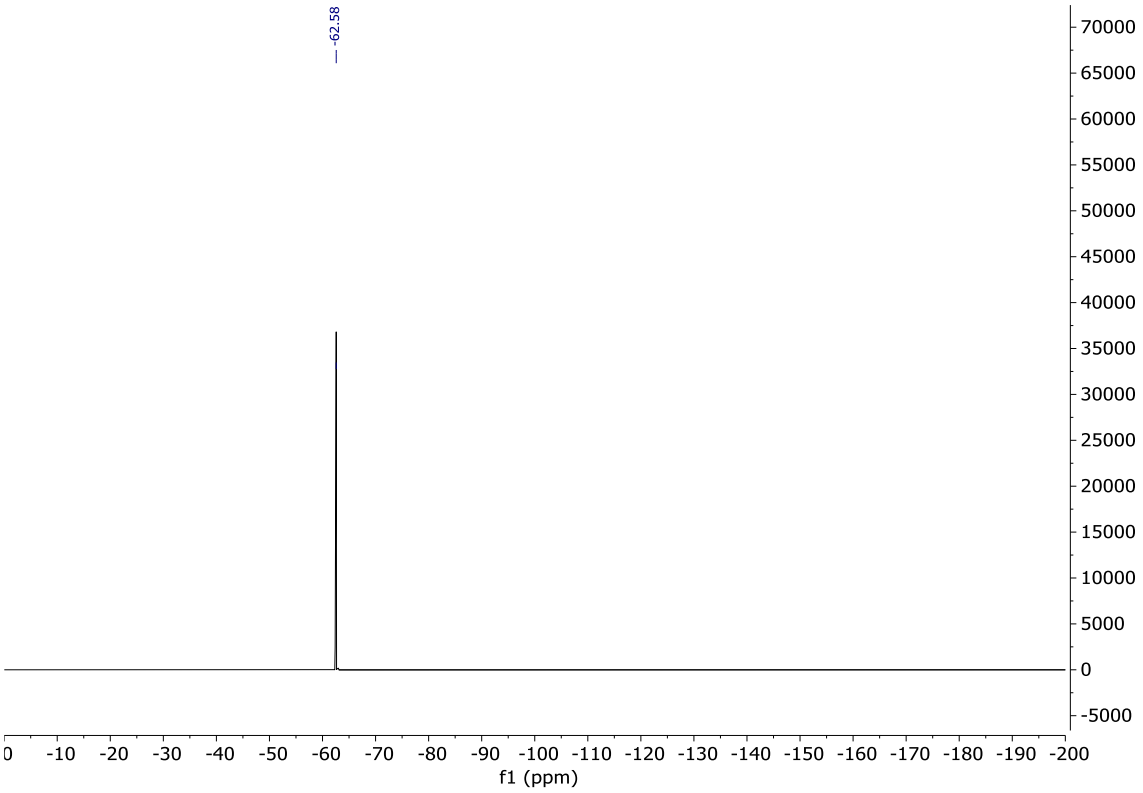
<Peak Table>

Detector A Channel 2 254nm

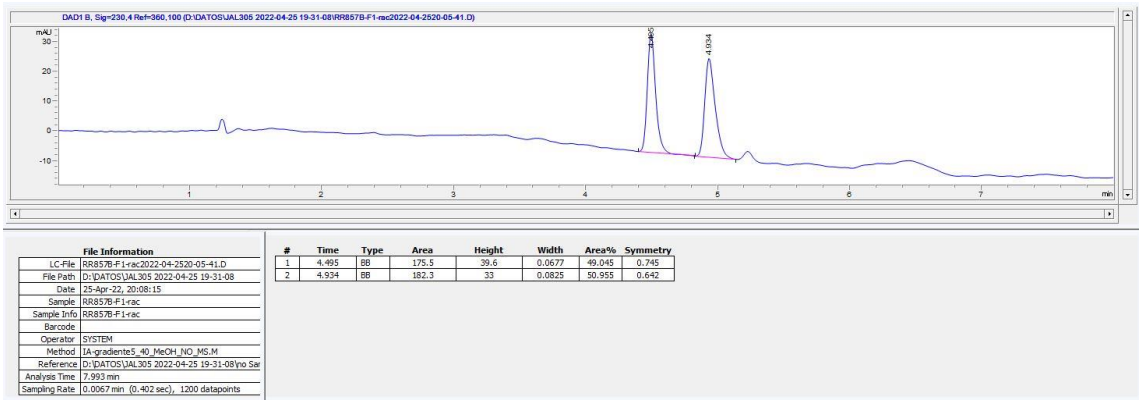
Peak#	Ret. Time	Area%
1	20.947	23.285
2	28.561	76.715
Total		100.000

(*S*)-1-Phenyl-4-(4-(trifluoromethyl)phenyl)pyrrolidin-2-one (4g)





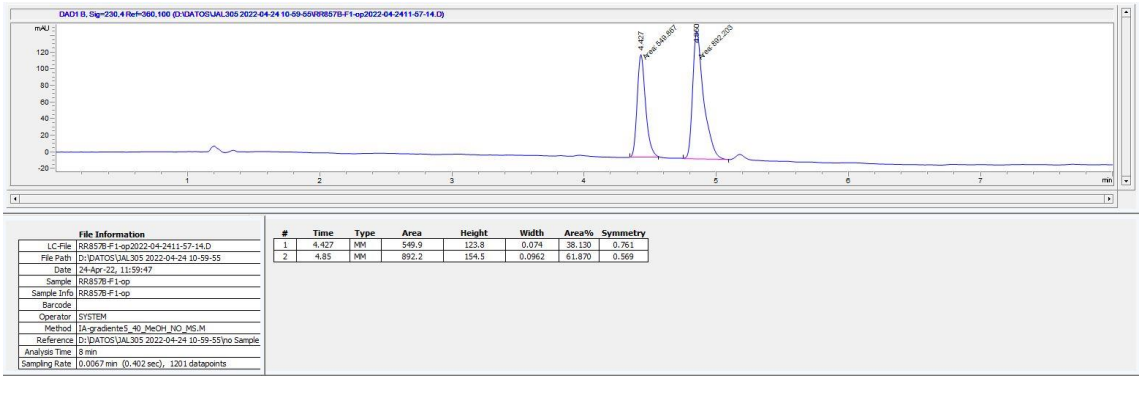
Racemic chromatogram:



File Information	
LC-File	RR857B-F1-rac2022-04-2520-05-41.D
File Path	D:\DATOS\JAL305 2022-04-25 19-31-08
Date	25-Apr-22, 20:08:15
Sample	RR857B-F1-rac
Sample Info	RR857B-F1-rac
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 19-31-08\no Sar
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.495	BB	175.5	39.6	0.0677	49.045	0.745
2	4.934	BB	182.3	33	0.0825	50.955	0.642

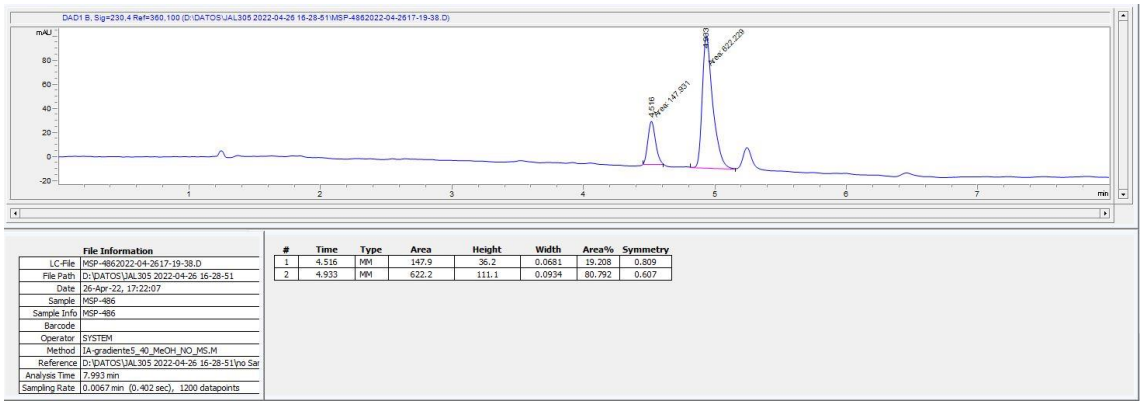
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR857B-F1-op2022-04-2411-57-14.D
File Path	D:\DATOS\JAL305 2022-04-24 10-59-55
Date	24-Apr-22, 11:59:47
Sample	RR857B-F1-op
Sample Info	RR857B-F1-op
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 10-59-55\no Sample
Analysis Time	8 min
Sampling Rate	0.0067 min (0.402 sec), 1201 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.427	MM	549.9	123.8	0.074	38.130	0.761
2	4.85	MM	892.2	154.5	0.0962	61.870	0.569

Flow reaction chromatogram (Manuscript, Table 4):

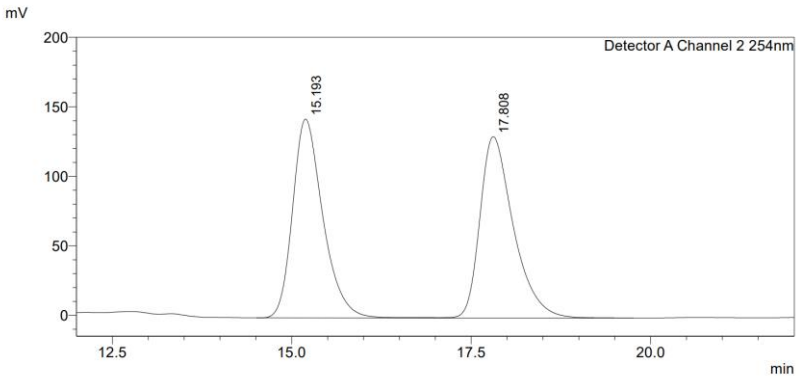


File Information	
LC-File	MSP-4862022-04-2617-19-38.D
File Path	D:\DATOS\JAL305 2022-04-26 16-28-51
Date	26-Apr-22, 17:22:07
Sample	MSP-486
Sample Info	MSP-486
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-26 16-28-51\no Sar
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.516	MM	147.9	36.2	0.0681	19.208	0.809
2	4.933	MM	622.2	111.1	0.0934	80.792	0.607

Racemic reaction chromatogram (from the α-silyl amine)

<Chromatogram>



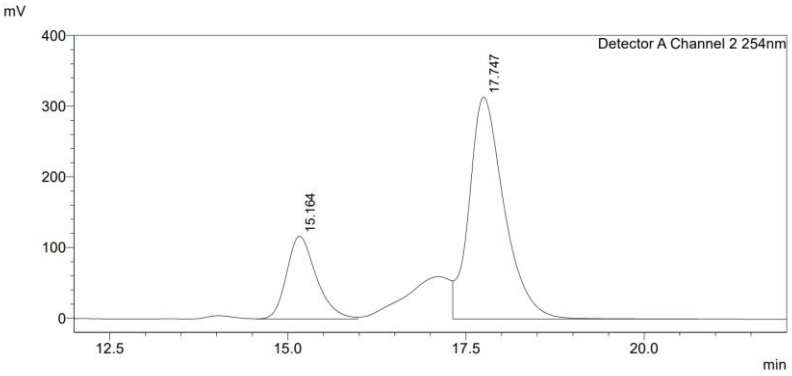
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	15.193	49.847
2	17.808	50.153
Total		100.000

Batch reaction chromatogram (from the α-silyl amine)

<Chromatogram>

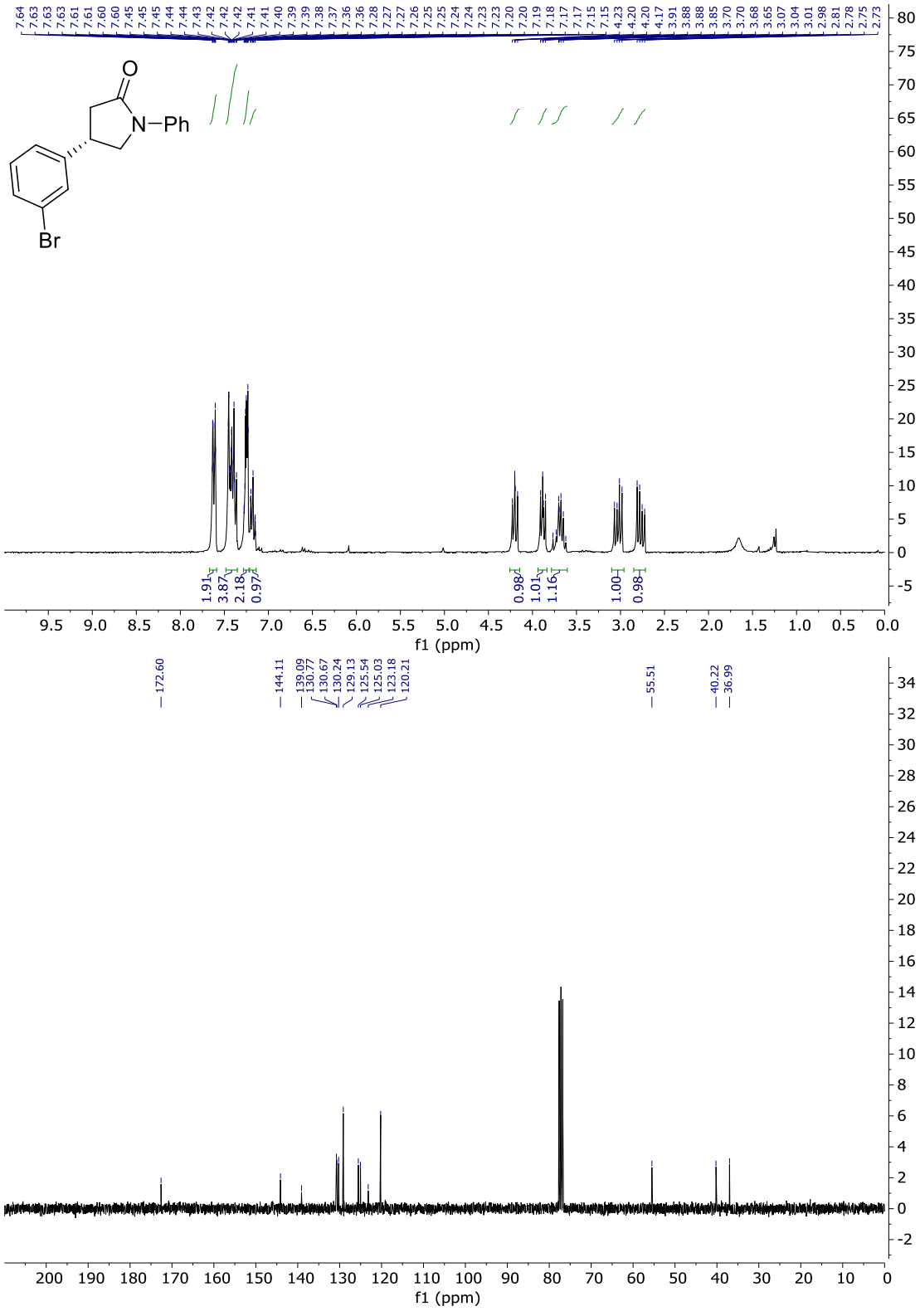


<Peak Table>

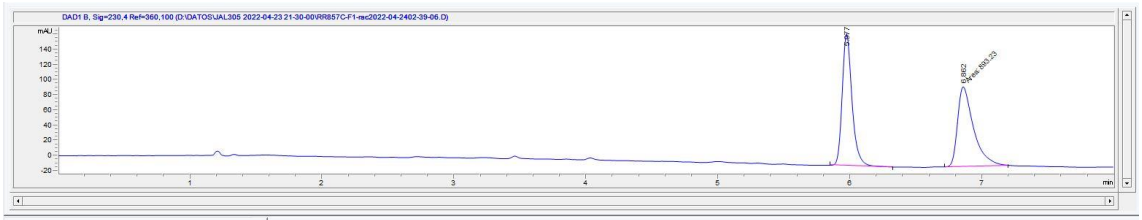
Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	15.164	24.003
2	17.747	75.997
Total		100.000

(*S*)-4-(3-bromophenyl)-1-phenylpyrrolidin-2-one (4h)



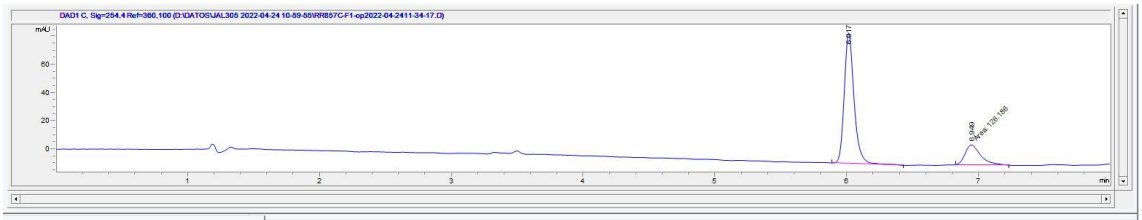
Racemic chromatogram:



File Information	
LC-File	RR857C-F1-rac2022-04-2402-39-06.D
File Path	D:\DATOS\JAL305 2022-04-23 21-30-00
Date	24-Apr-22, 02:41:37
Sample	RR857C-F1-rac
Sample Info	RR857C-F1-rac
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 21-30-00\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.977	BB	899.1	173.7	0.0784	50.165	0.738
2	6.862	MM	893.2	105	0.1417	49.835	0.519

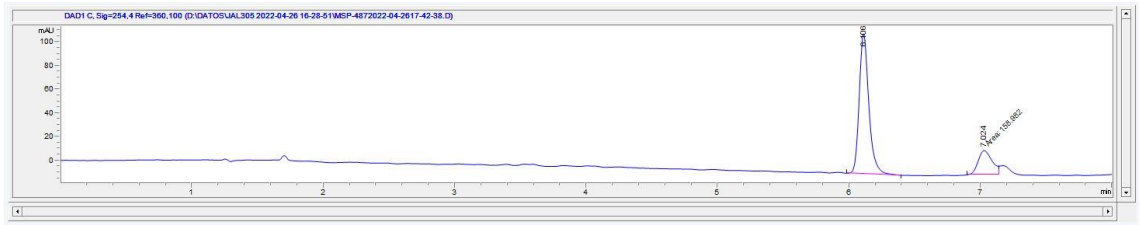
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR857C-F1-op2022-04-2411-34-17.D
File Path	D:\DATOS\JAL305 2022-04-24 10-59-55
Date	24-Apr-22, 11:36:44
Sample	RR857C-F1-op
Sample Info	RR857C-F1-op
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 10-59-55\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.017	BB	483.6	93.2	0.0785	79.307	0.755
2	6.949	MF	126.2	14.6	0.1436	20.693	0.639

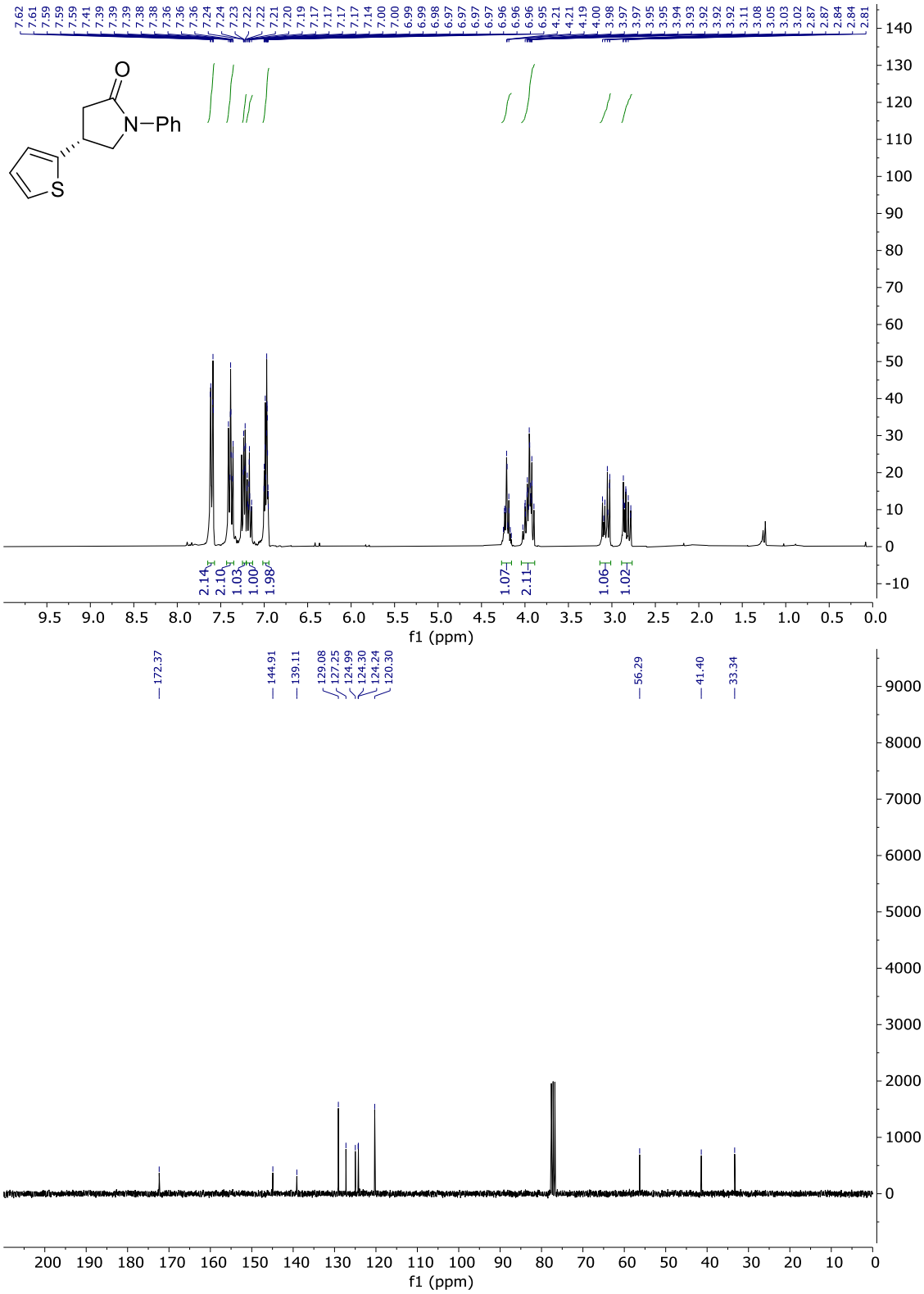
Flow reaction chromatogram (Manuscript, Table 4):



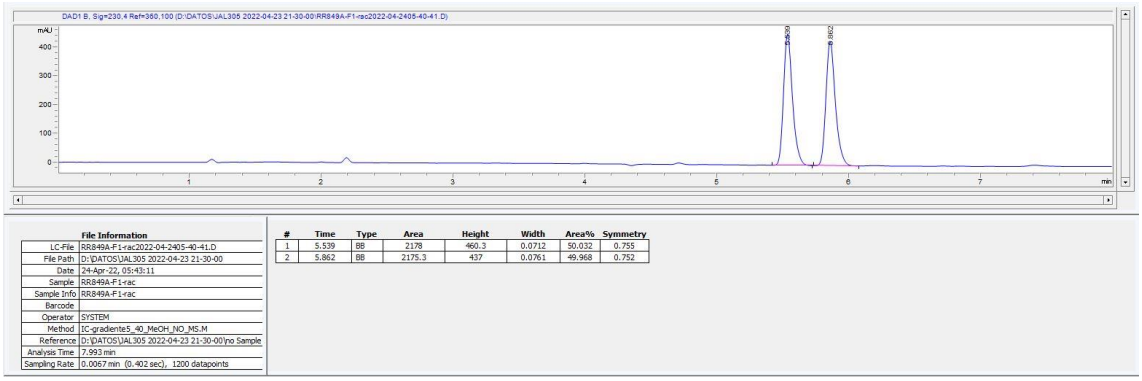
File Information	
LC-File	MSP-4872022-04-2617-42-38.D
File Path	D:\DATOS\JAL305 2022-04-26 16-28-51
Date	26-Apr-22, 17:45:13
Sample	MSP-487
Sample Info	MSP-487
Barcode	
Operator	SYSTEM
Method	IA-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-26 16-28-51\no Sar
Analysis Time	8 min
Sampling Rate	0.0067 min (0.402 sec), 1201 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.106	BB	605.9	118.8	0.0775	79.214	0.747
2	7.024	MF	159	20.7	0.128	20.786	0.717

(*R*)-1-Phenyl-4-(thiophen-2-yl)pyrrolidin-2-one (4i)



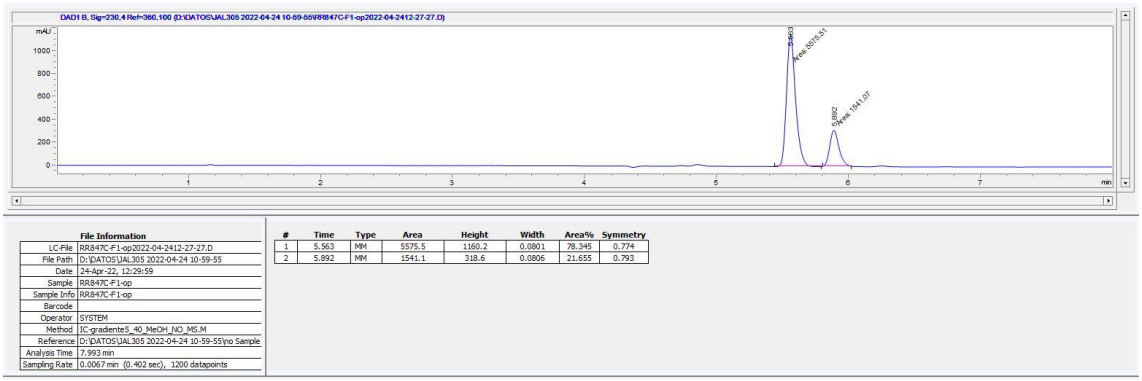
Racemic chromatogram:



File Information	
LC-File	RR849A-F1-rac2022-04-2405-40-41.D
File Path	D:\DATOS\JAL305 2022-04-23 21-30-00
Date	24-Apr-22, 05:43:11
Sample	RR849A-F1-rac
Sample Info	RR849A-F1-rac
Barcode	
Operator	SYSTEM
Method	IC-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 21-30-00\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.539	BB	2178	460.3	0.0712	50.032	0.755
2	5.862	BB	2175.3	437	0.0761	49.968	0.752

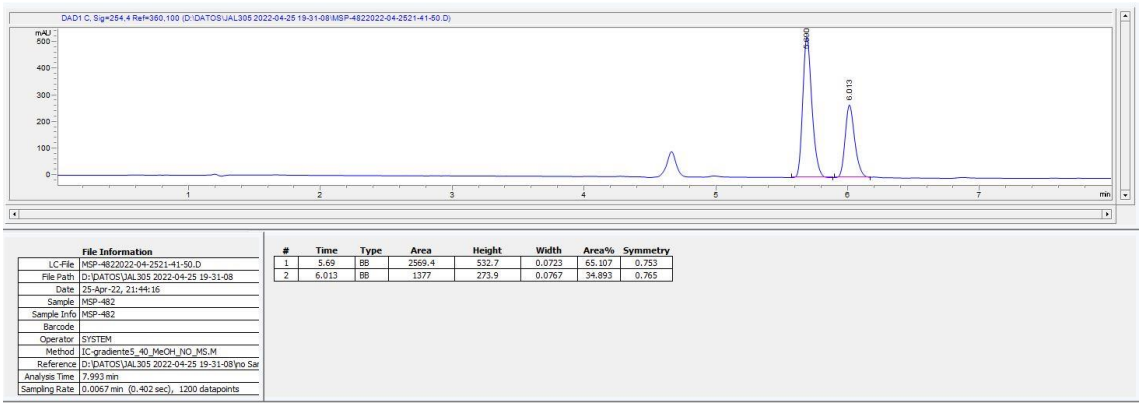
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR847C-F1-op2022-04-2412-27-27.D
File Path	D:\DATOS\JAL305 2022-04-24 10-59-55
Date	24-Apr-22, 12:29:59
Sample	RR847C-F1-op
Sample Info	RR847C-F1-op
Barcode	
Operator	SYSTEM
Method	IC-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 10-59-55\no Sample
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.563	MM	5575.5	1160.2	0.0801	78.345	0.774
2	5.892	MM	1541.1	318.6	0.0806	21.655	0.793

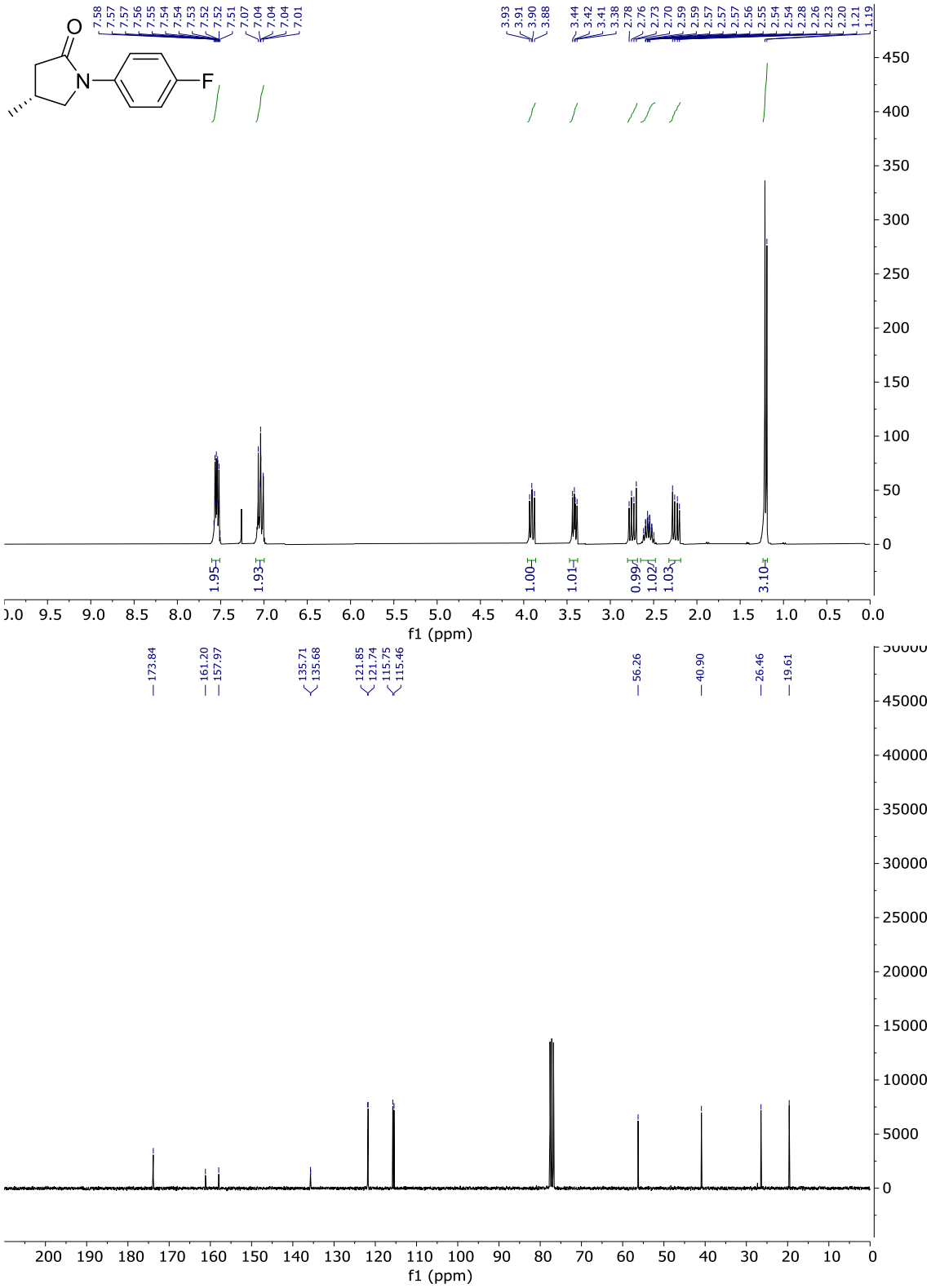
Flow reaction chromatogram (Manuscript, Table 4):

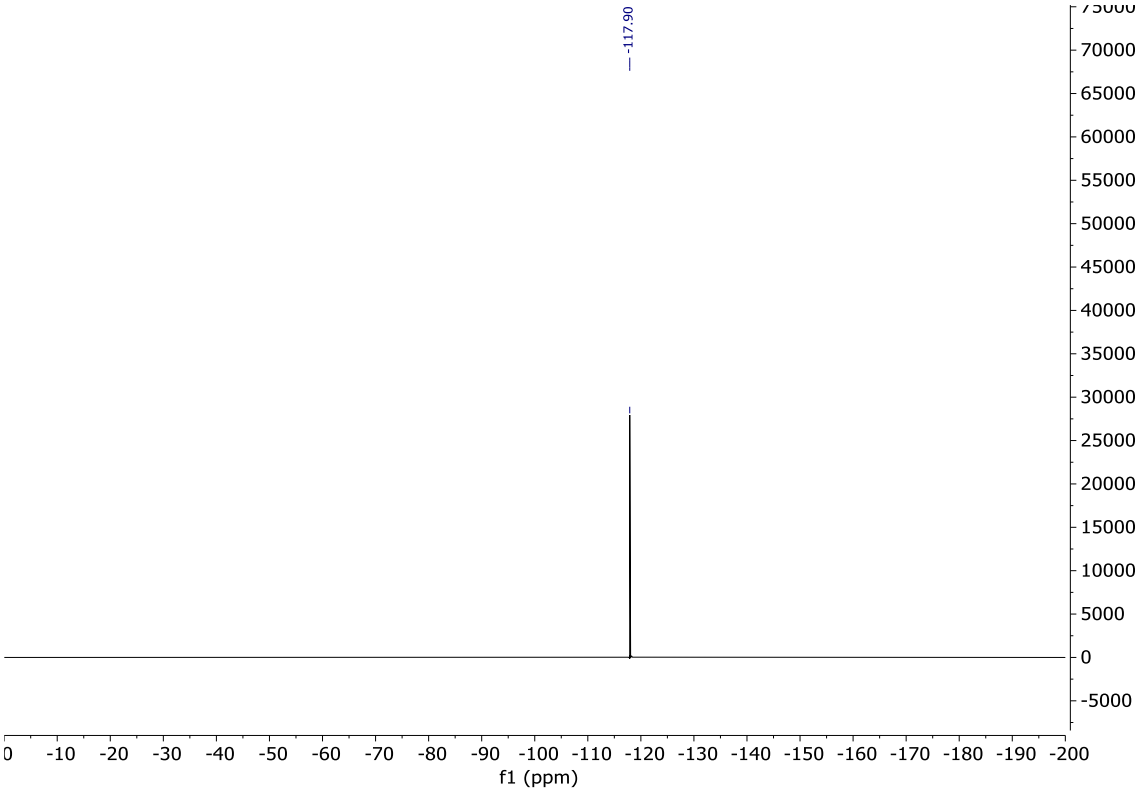


File Information	
LC-File	MSP-4822022-04-2521-41-50.D
File Path	D:\DATOS\JAL305 2022-04-25 19-31-08
Date	25-Apr-22, 21:44:16
Sample	MSP-482
Sample Info	MSP-482
Barcode	
Operator	SYSTEM
Method	IC-gradiente5_40_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 19-31-08\no Sar
Analysis Time	7.993 min
Sampling Rate	0.0067 min (0.402 sec), 1200 datapoints

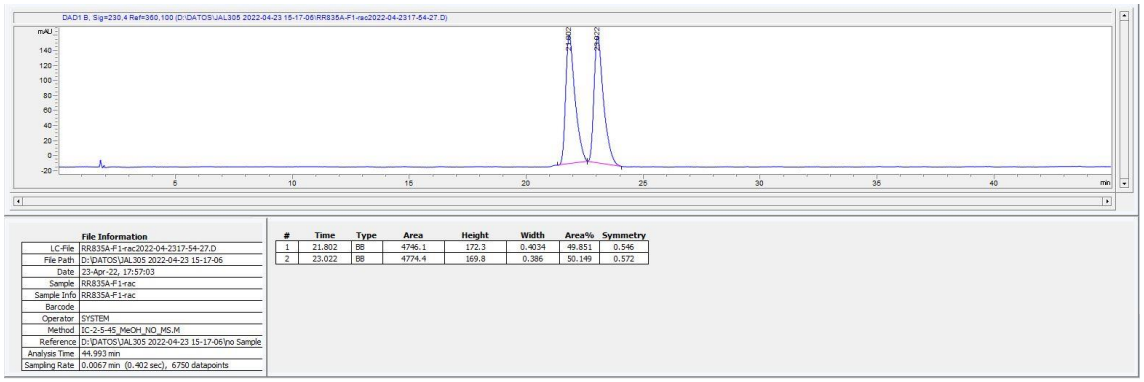
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.69	BB	2569.4	532.7	0.0723	65.107	0.753
2	6.013	BB	1377	273.9	0.0767	34.893	0.765

(*R*)-1-(4-fluorophenyl)-4-methylpyrrolidin-2-one (4j)





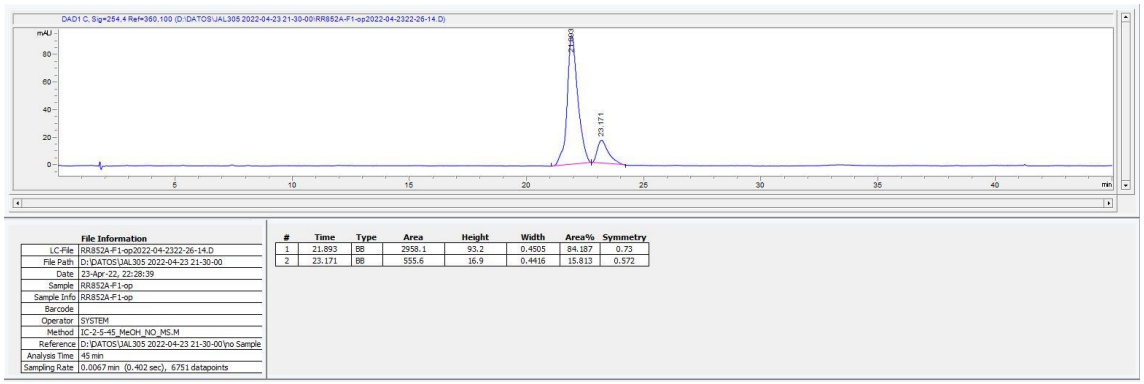
Racemic chromatogram:



File Information	
LC-File	RR835A-F1-rac2022-04-2317-54-27.D
File Path	D:\DATOS\JAL305 2022-04-23 15-17-06
Date	23-Apr-22, 17:57:03
Sample	RR835A-F1-rac
Sample Info	RR835A-F1-rac
Barcode	
Operator	SYSTEM
Method	IC-2-5-45_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 15-17-06\no Sample
Analysis Time	44.993 min
Sampling Rate	0.0067 min (0.402 sec), 6750 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	21.802	BB	4746.1	172.3	0.4034	49.851	0.546
2	23.022	BB	4774.4	169.8	0.386	50.149	0.572

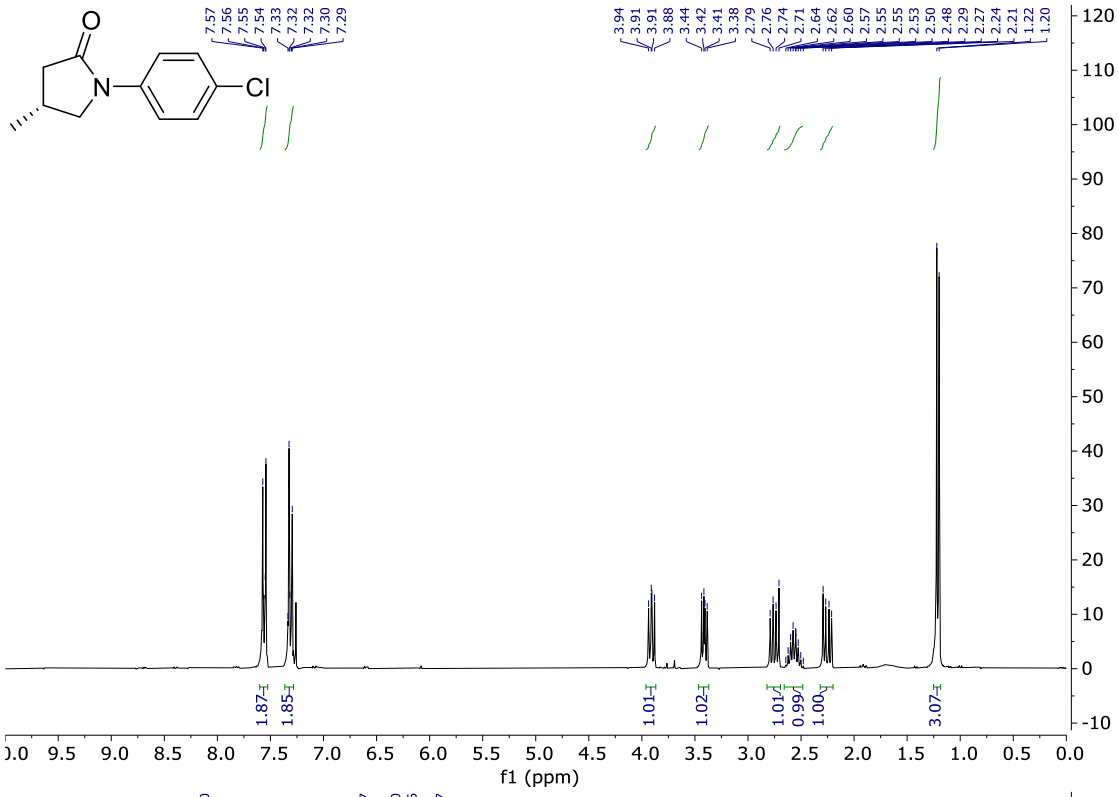
Batch reaction chromatogram (Manuscript, Table 2):

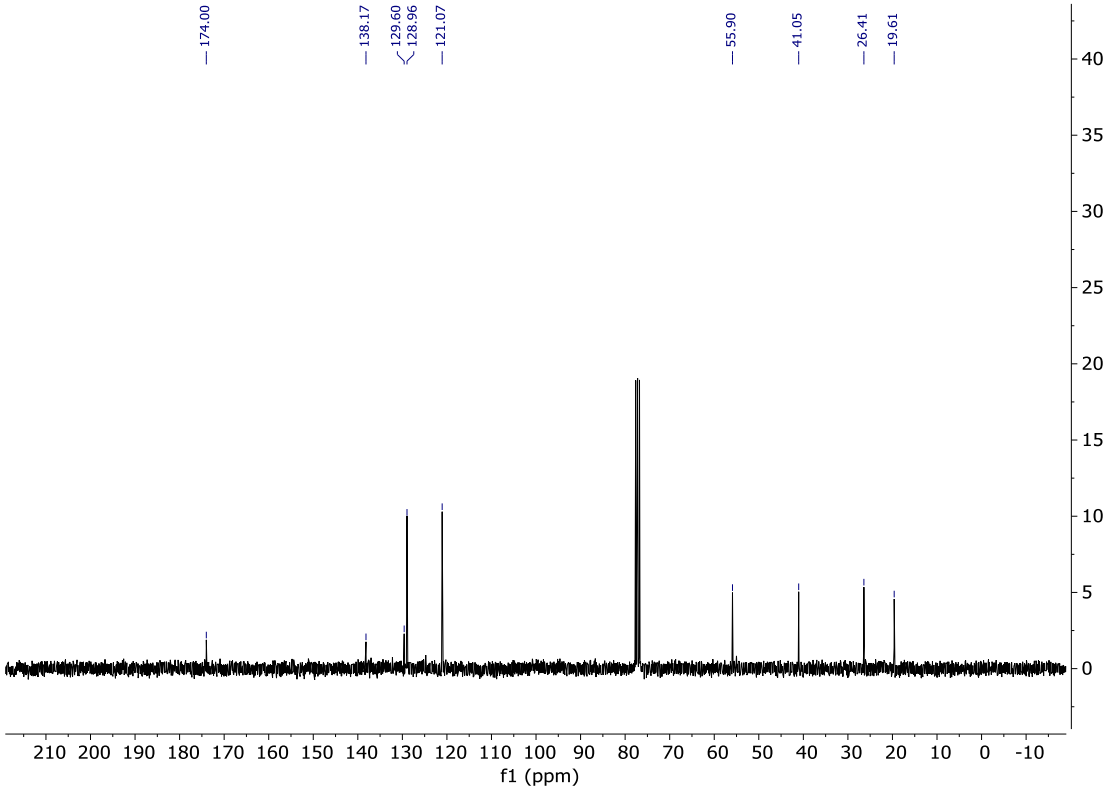


File Information	
LC-File	RR852A-F1-op2022-04-2322-26-14.D
File Path	D:\DATOS\JAL305 2022-04-23 21-30-00
Date	23-Apr-22, 22:28:39
Sample	RR852A-F1-op
Sample Info	RR852A-F1-op
Barcode	
Operator	SYSTEM
Method	IC-2-5-45_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-23 21-30-00\no Sample
Analysis Time	45 min
Sampling Rate	0.0067 min (0.402 sec), 6751 datapoints

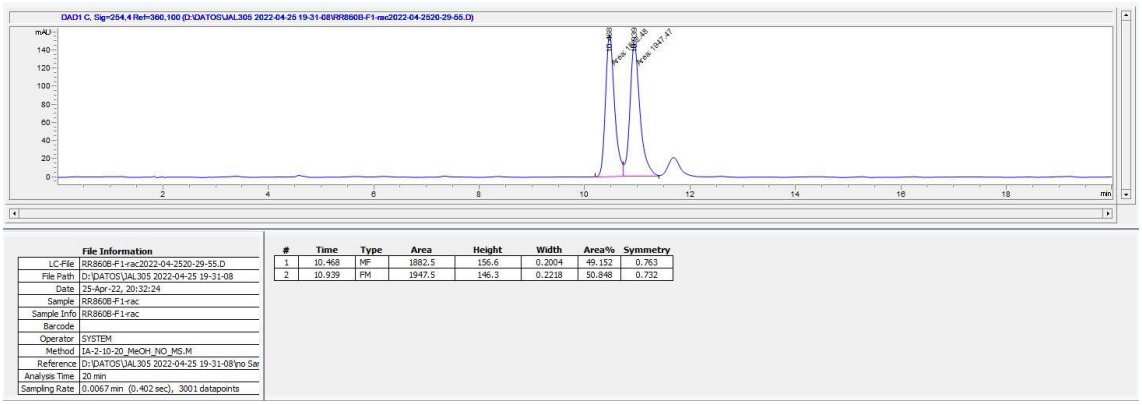
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	21.893	BB	2958.1	93.2	0.4505	84.187	0.73
2	23.171	BB	555.6	16.9	0.4416	15.813	0.572

(*R*)-1-(4-chlorophenyl)-4-methylpyrrolidin-2-one (4k)





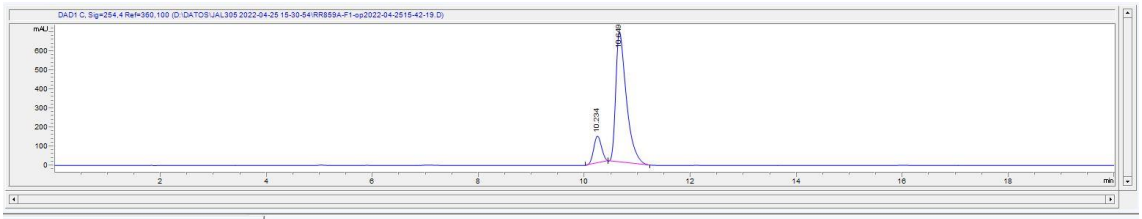
Racemic chromatogram:



File Information	
LC-File	RR860B-F1-rac2022-04-2520-29-55.D
File Path	D:\DATOS\JAL305 2022-04-25 19-31-08
Date	25-Apr-22, 20:32:24
Sample	RR860B-F1-rac
Sample Info	RR860B-F1-rac
Barcode	
Operator	SYSTEM
Method	IA-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 19-31-08\no Sar
Analysis Time	20 min
Sampling Rate	0.0067 min (0.402 sec), 3001 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.468	MF	1882.5	156.6	0.2004	49.152	0.763
2	10.939	FM	1947.5	146.3	0.2218	50.848	0.732

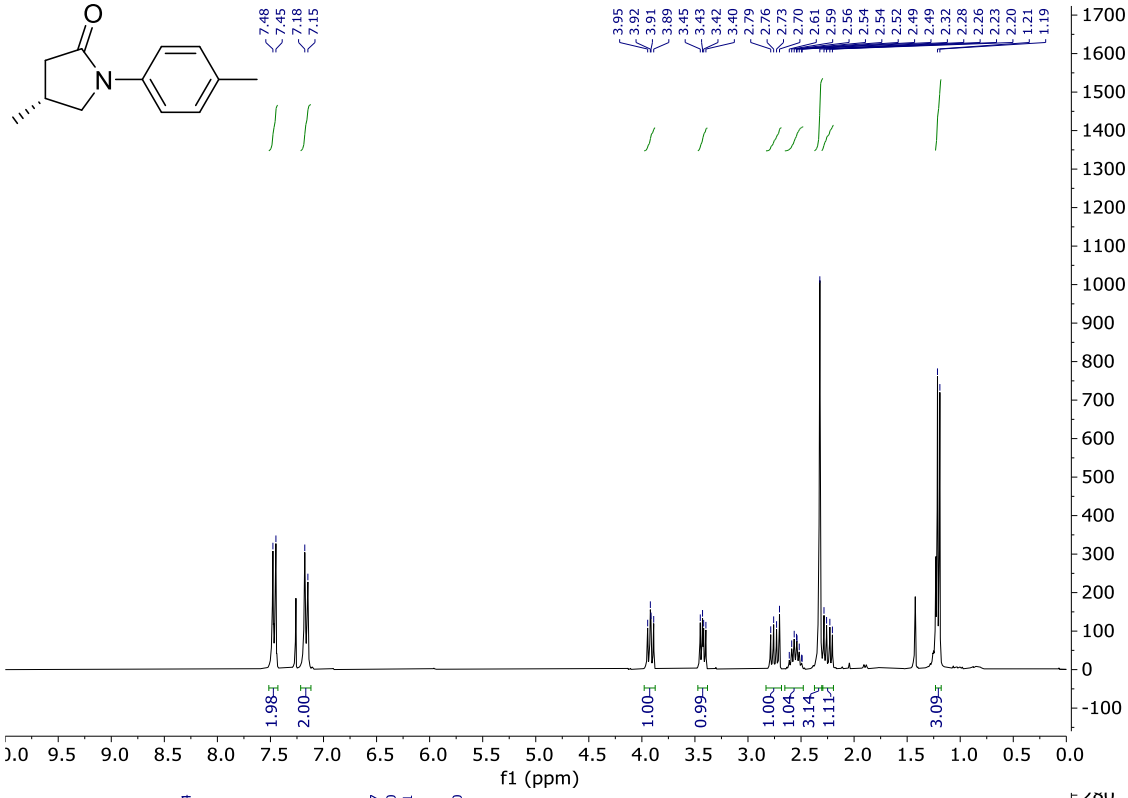
Batch reaction chromatogram (Manuscript, Table 2):

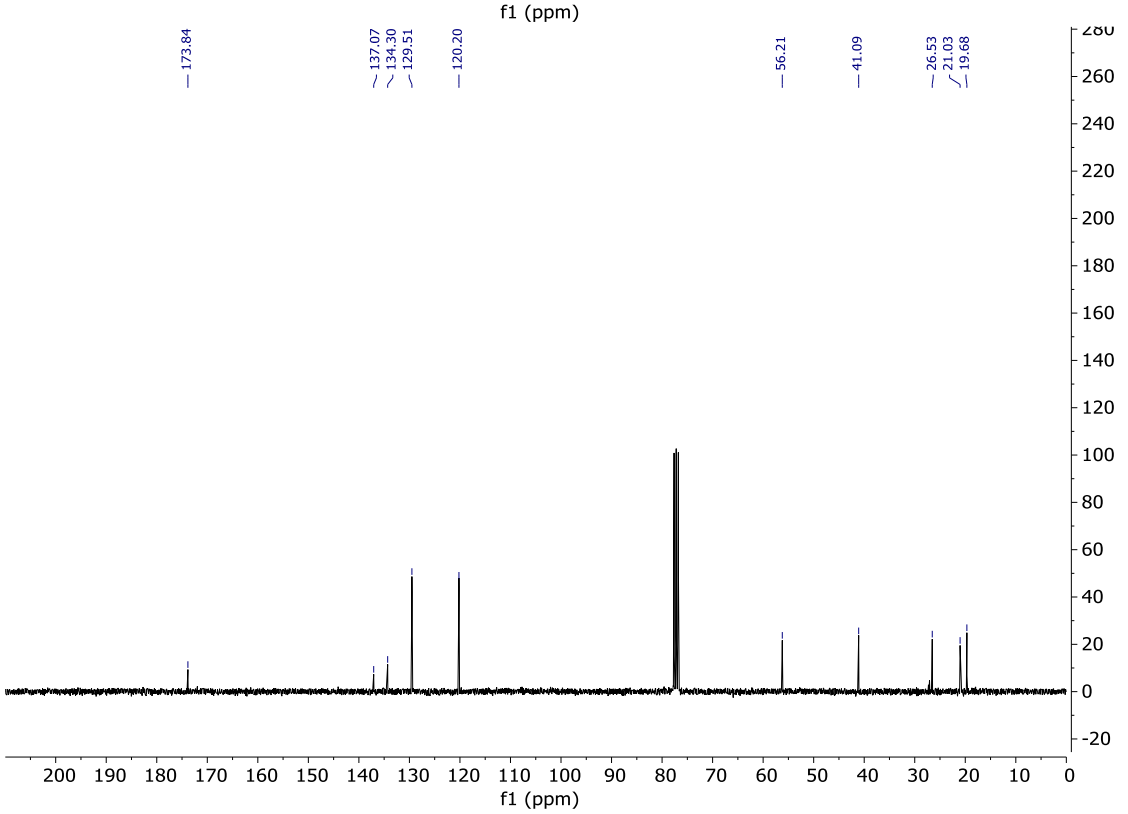


File Information	
LC-File	RR859A-F1-op2022-04-2515-42-19.D
File Path	D:\DATOS\JAL305 2022-04-25 15-30-54
Date	25-Apr-22, 15:44:45
Sample	RR859A-F1-op
Sample Info	RR859A-F1-op
Barcode	
Operator	SYSTEM
Method	IA-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 15-30-54\no Sample
Analysis Time	20 min
Sampling Rate	0.0067 min (0.402 sec), 3001 datapoints

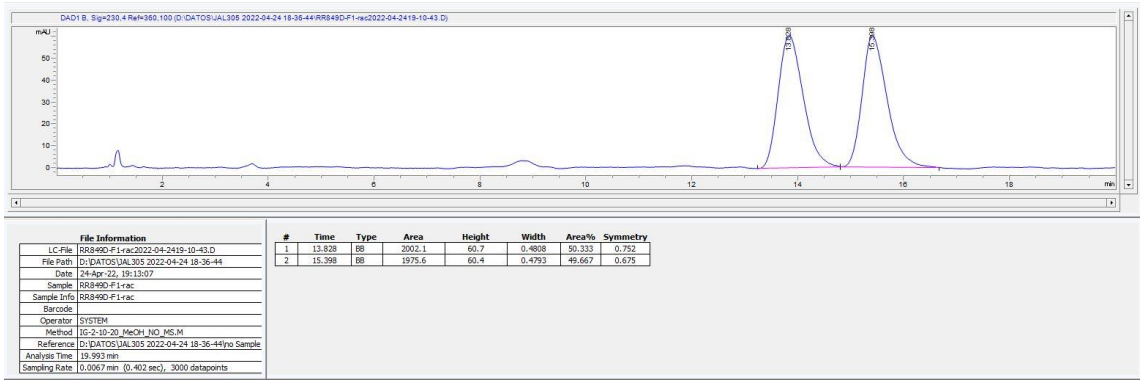
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.234	BB	1474.3	142.8	0.1625	13.435	0.909
2	10.649	BB	9499.8	684.6	0.2079	86.565	0.505

(*R*)-4-methyl-1-(*p*-tolyl)pyrrolidin-2-one (4l)





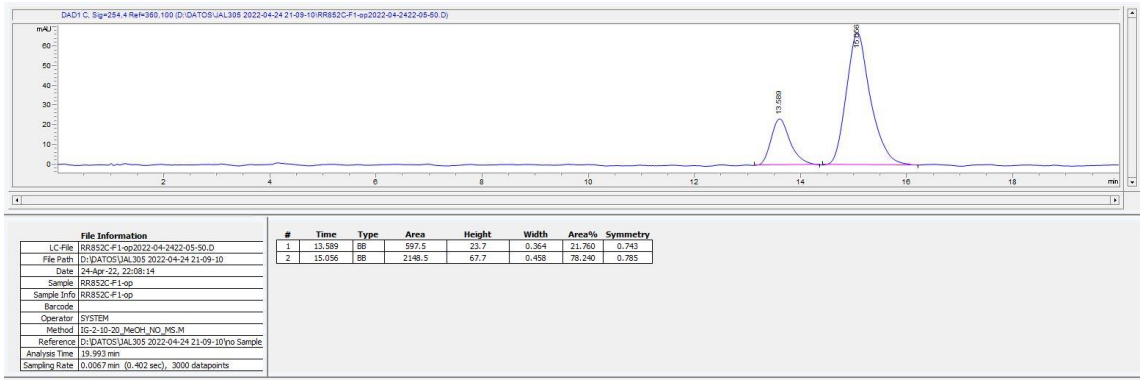
Racemic chromatogram:



File Information	
LC-File	RR849D-F1-rac2022-04-2419-10-43.D
File Path	D:\DATOS\JAL305 2022-04-24 18-36-44
Date	24-Apr-22, 19:13:07
Sample	RR849D-F1-rac
Sample Info	RR849D-F1-rac
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 18-36-44\no Sample
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.828	BB	2002.1	60.7	0.4808	50.333	0.752
2	15.398	BB	1975.6	60.4	0.4793	49.667	0.675

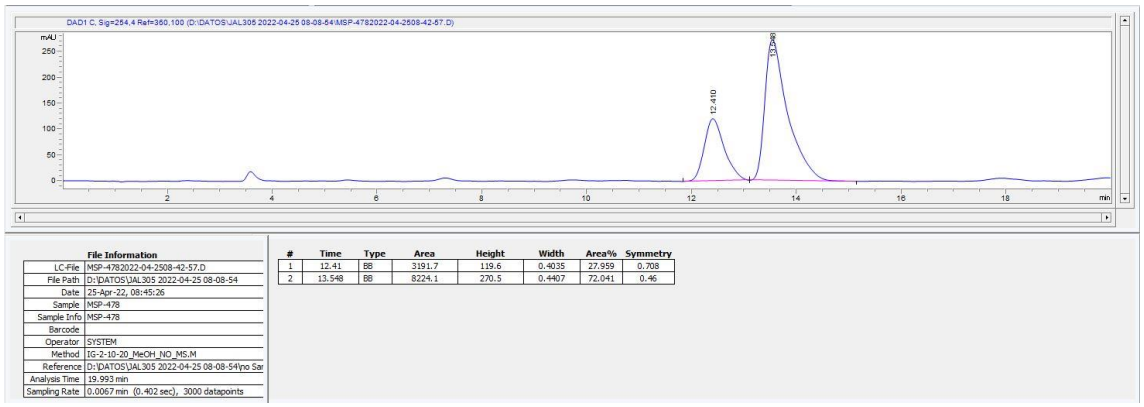
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR852C-F1-op2022-04-2422-05-50.D
File Path	D:\DATOS\JAL305 2022-04-24 21-09-10
Date	24-Apr-22, 22:08:14
Sample	RR852C-F1-op
Sample Info	RR852C-F1-op
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-24 21-09-10\no Sample
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.589	BB	597.5	23.7	0.364	21.760	0.743
2	15.056	BB	2148.5	67.7	0.458	78.240	0.785

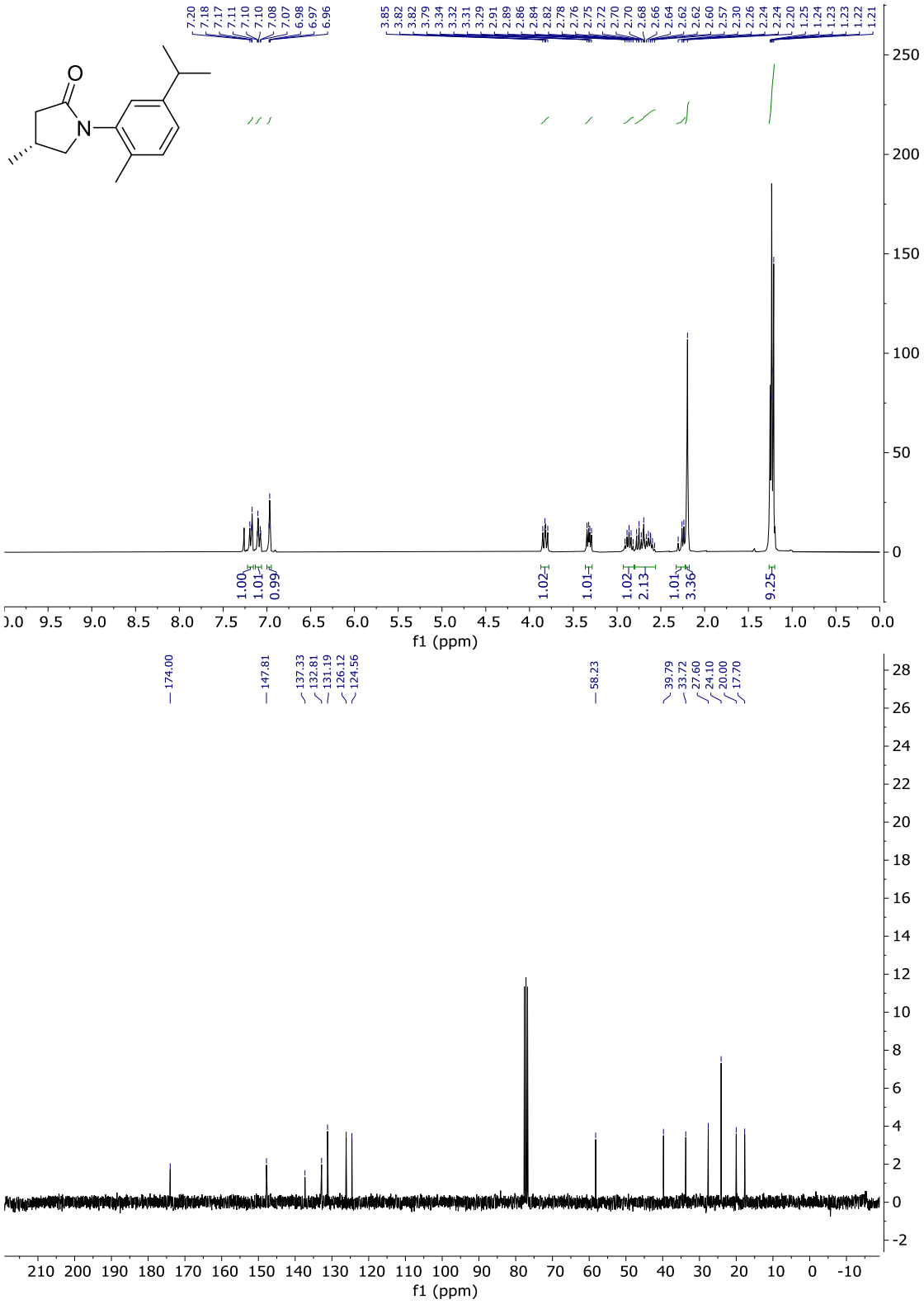
Flow reaction chromatogram (Manuscript, Table 4):



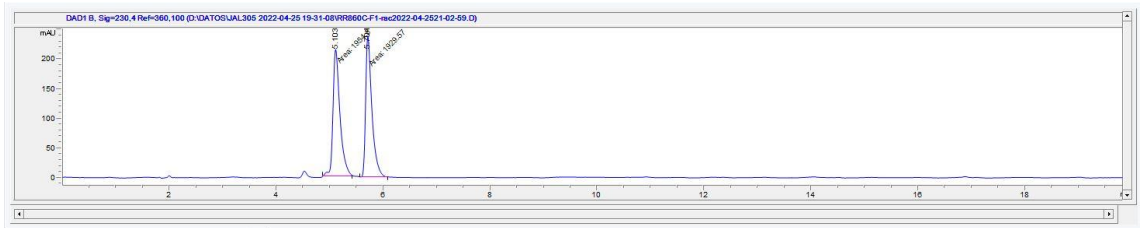
File Information	
LC-File	MSP-4782022-04-2508-42-57.D
File Path	D:\DATOS\JAL305 2022-04-25 08-08-54
Date	25-Apr-22, 08:45:26
Sample	MSP-478
Sample Info	MSP-478
Barcode	
Operator	SYSTEM
Method	IG-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 08-08-54\no Sar
Analysis Time	19.993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.41	BB	3191.7	119.6	0.4035	27.959	0.708
2	13.548	BB	8224.1	270.5	0.4407	72.041	0.46

(*R*)-1-(5-isopropyl-2-methylphenyl)-4-methylpyrrolidin-2-one (4m)



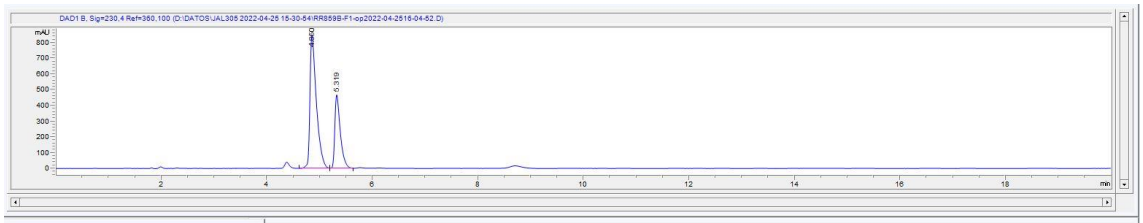
Racemic chromatogram:



File Information	
LC-File	RR860C-F1-rac2022-04-2521-02-59.D
File Path	D:\DATOS\JAL305 2022-04-25 19-31-08
Date	25-Apr-22, 21:05:29
Sample	RR860C-F1-rac
Sample Info	RR860C-F1-rac
Barcode	
Operator	SYSTEM
Method	IA-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 19-31-08\no Sar
Analysis Time	19,993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.103	MM	1954.8	214.6	0.1518	50.325	0.607
2	5.704	MM	1929.6	238.1	0.1351	49.675	0.522

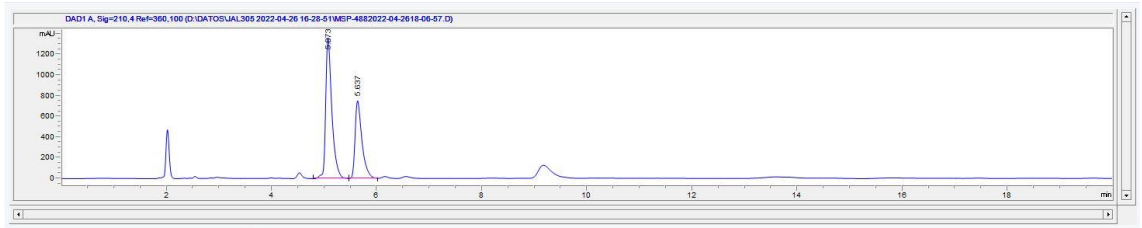
Batch reaction chromatogram (Manuscript, Table 2):



File Information	
LC-File	RR859B-F1-op2022-04-2516-04-52.D
File Path	D:\DATOS\JAL305 2022-04-25 15-30-54
Date	25-Apr-22, 16:07:12
Sample	RR859B-F1-op
Sample Info	RR859B-F1-op
Barcode	
Operator	SYSTEM
Method	IA-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-25 15-30-54\no Sample
Analysis Time	19,993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.85	BB	7139	847.8	0.1242	68.021	0.44
2	5.319	BB	3356.3	465.2	0.1062	31.979	0.492

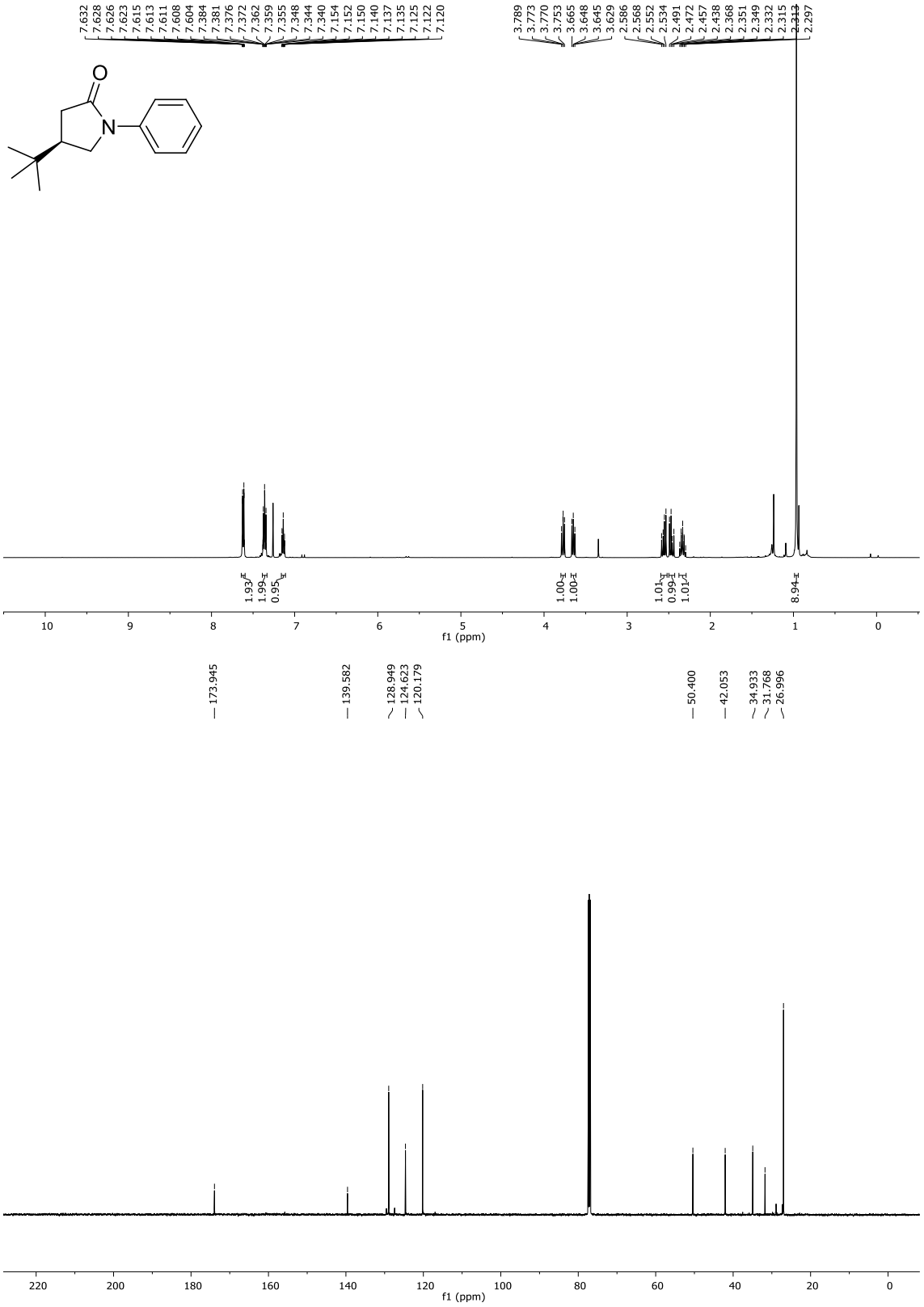
Flow reaction chromatogram (Manuscript, Table 4):



File Information	
LC-File	MSP-4882022-04-2618-06-57.D
File Path	D:\DATOS\JAL305 2022-04-26 16-28-51
Date	26-Apr-22, 18:09:28
Sample	MSP-488
Sample Info	MSP-488
Barcode	
Operator	SYSTEM
Method	IA-2-10-20_MeOH_NO_MS.M
Reference	D:\DATOS\JAL305 2022-04-26 16-28-51\no Sar
Analysis Time	19,993 min
Sampling Rate	0.0067 min (0.402 sec), 3000 datapoints

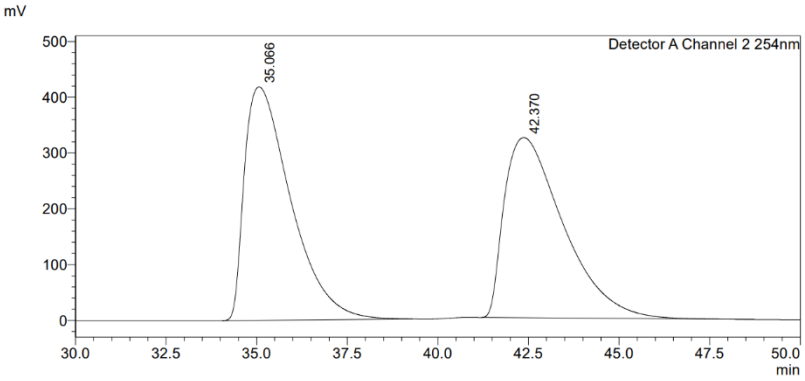
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.073	BB	11216.7	1372.9	0.1213	62.054	0.566
2	5.637	BB	6859.1	757	0.1357	37.946	0.529

(*R*)-4-(tert-butyl)-1-phenylpyrrolidin-2-one (4n)



Racemic chromatogram

<Chromatogram>



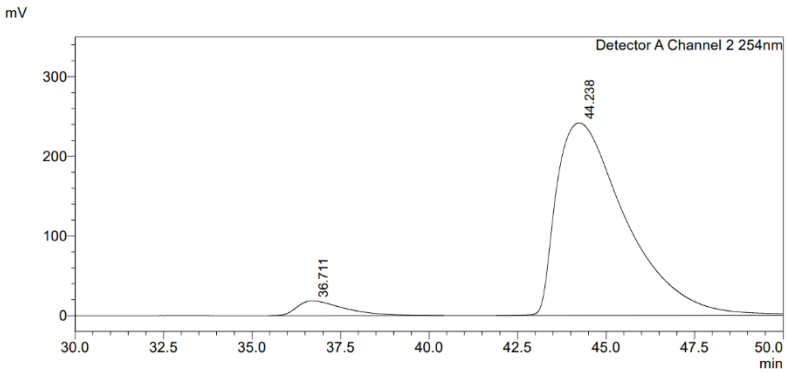
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	35.066	50.384
2	42.370	49.616
Total		100.000

Batch reaction chromatogram

<Chromatogram>

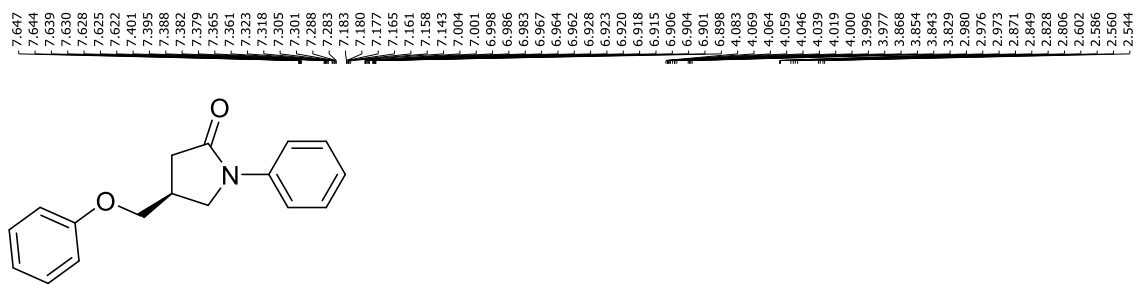


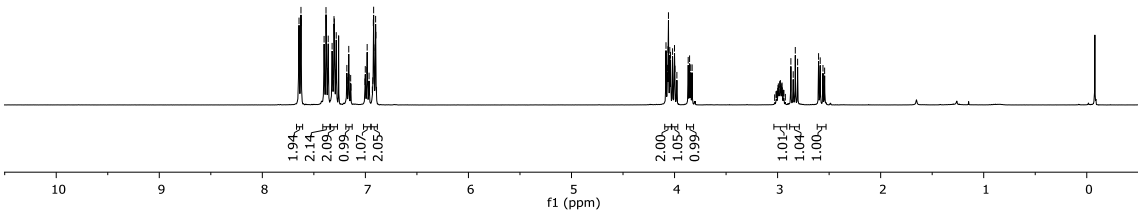
<Peak Table>

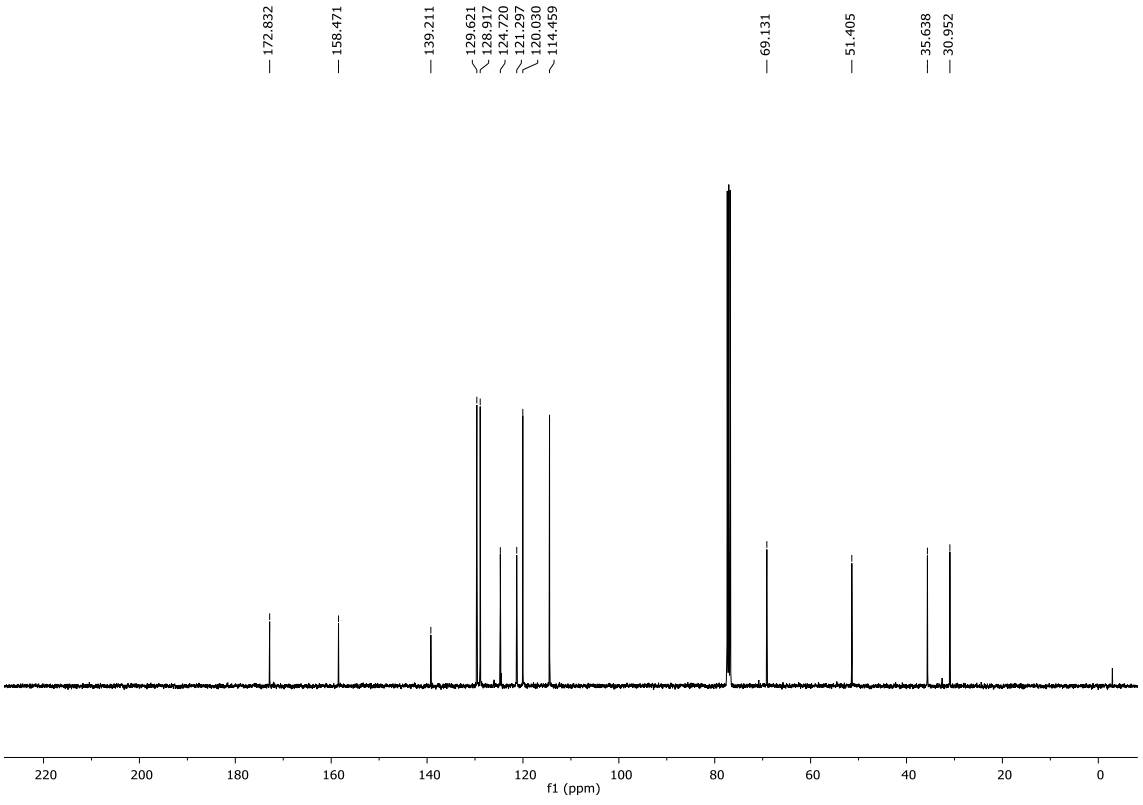
Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	36.711	4.822
2	44.238	95.178
Total		100.000

(*S*)-4-(phenoxymethyl)-1-phenylpyrrolidin-2-one (4o)

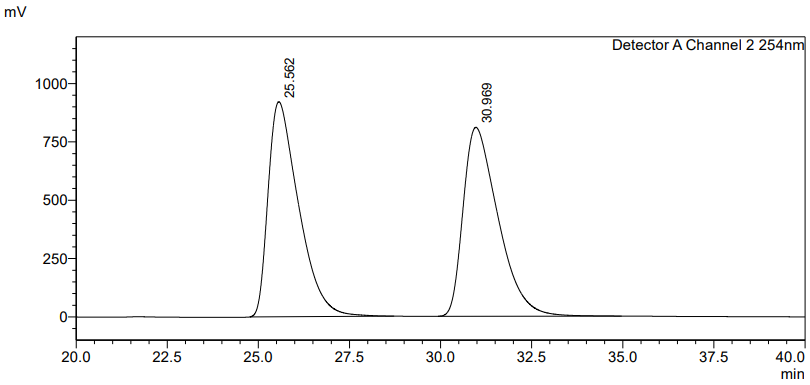






Racemic chromatogram

<Chromatogram>



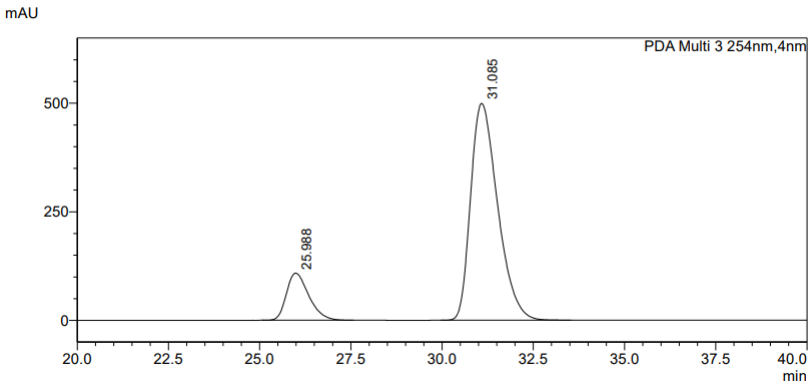
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	25.562	49.817
2	30.969	50.183
Total		100.000

Batch reaction chromatogram

<Chromatogram>

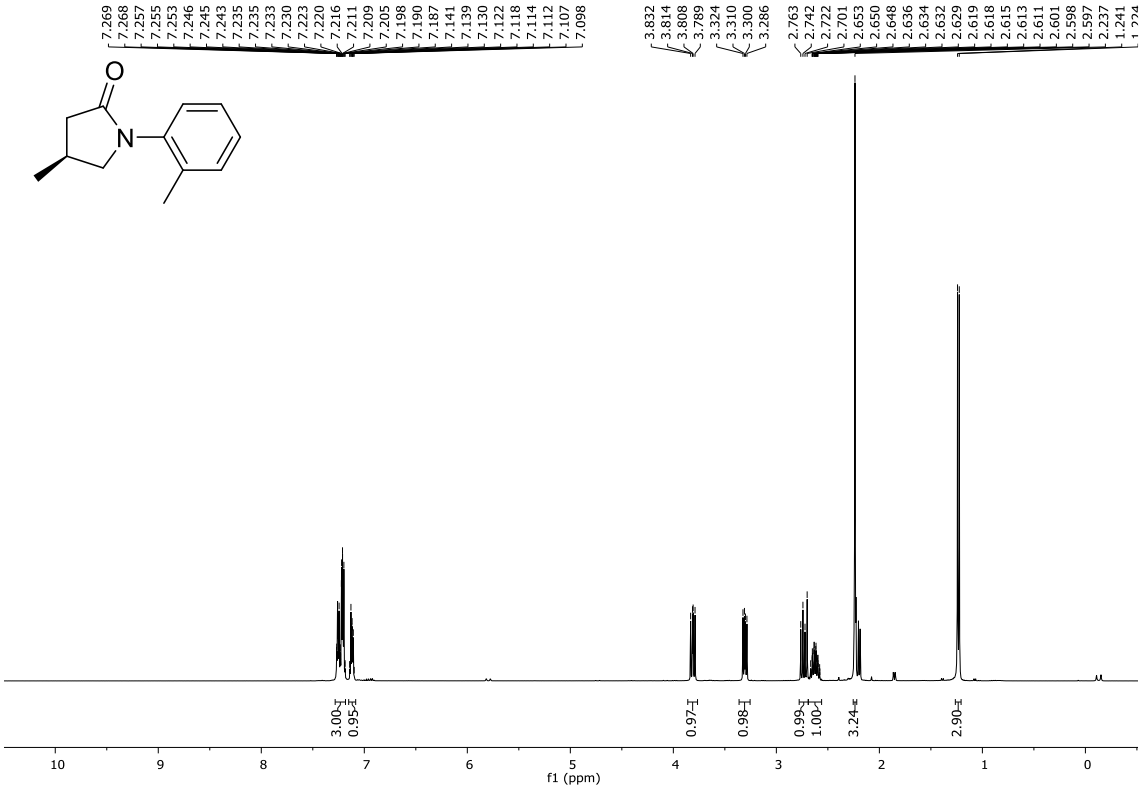


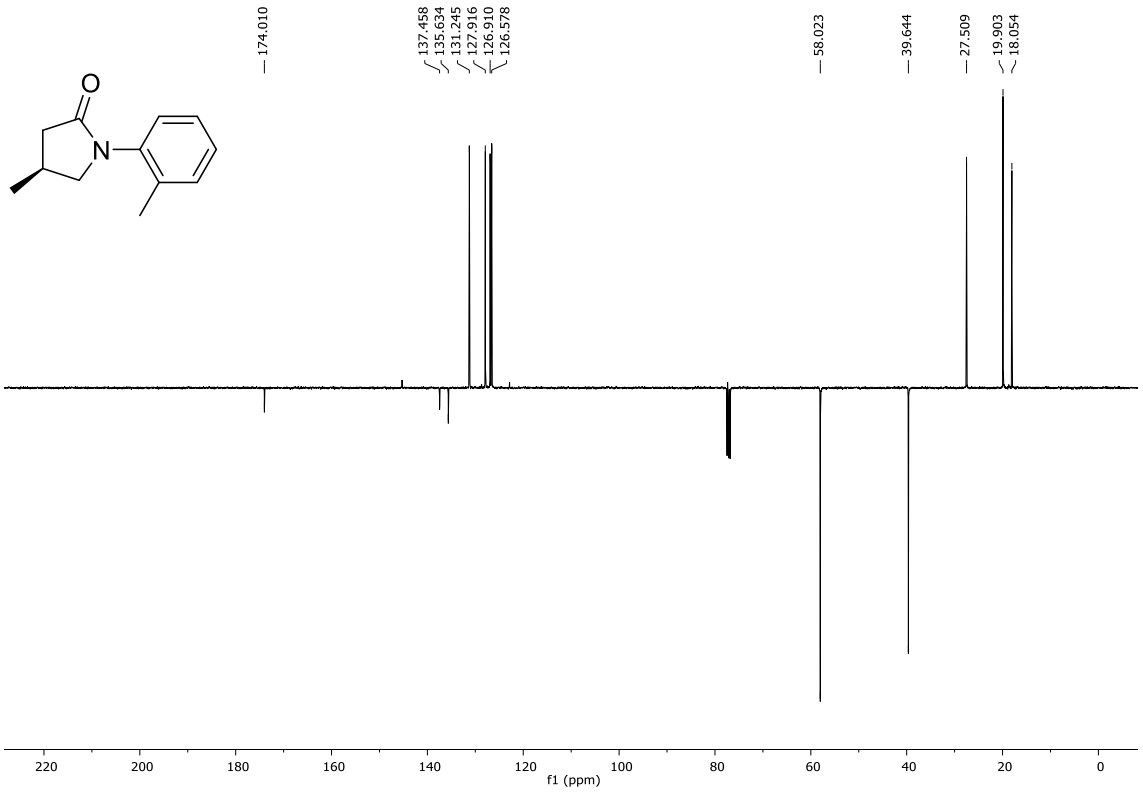
<Peak Table>

PDA Ch3 254nm

Peak#	Ret. Time	Area%
1	25.988	15.201
2	31.085	84.799
Total		100.000

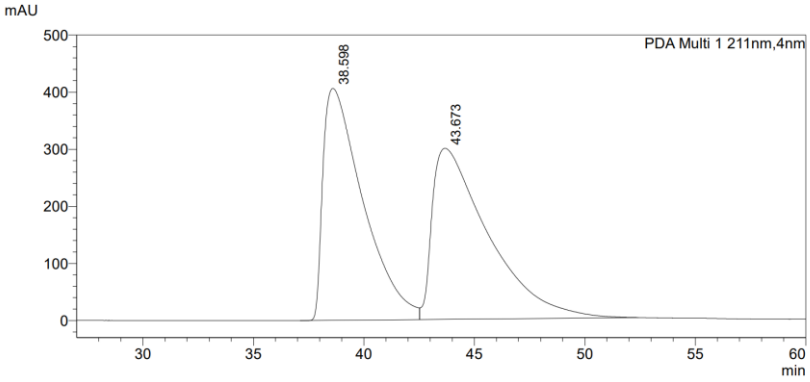
(S)-4-methyl-1-(o-tolyl)pyrrolidin-2-one (4p)





Racemic reaction chromatogram

<Chromatogram>



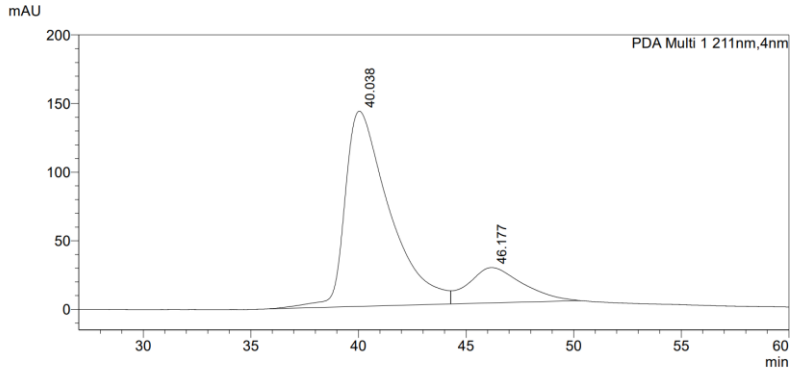
<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	38.598	49.168
2	43.673	50.832
Total		100.000

Batch reaction chromatogram

<Chromatogram>

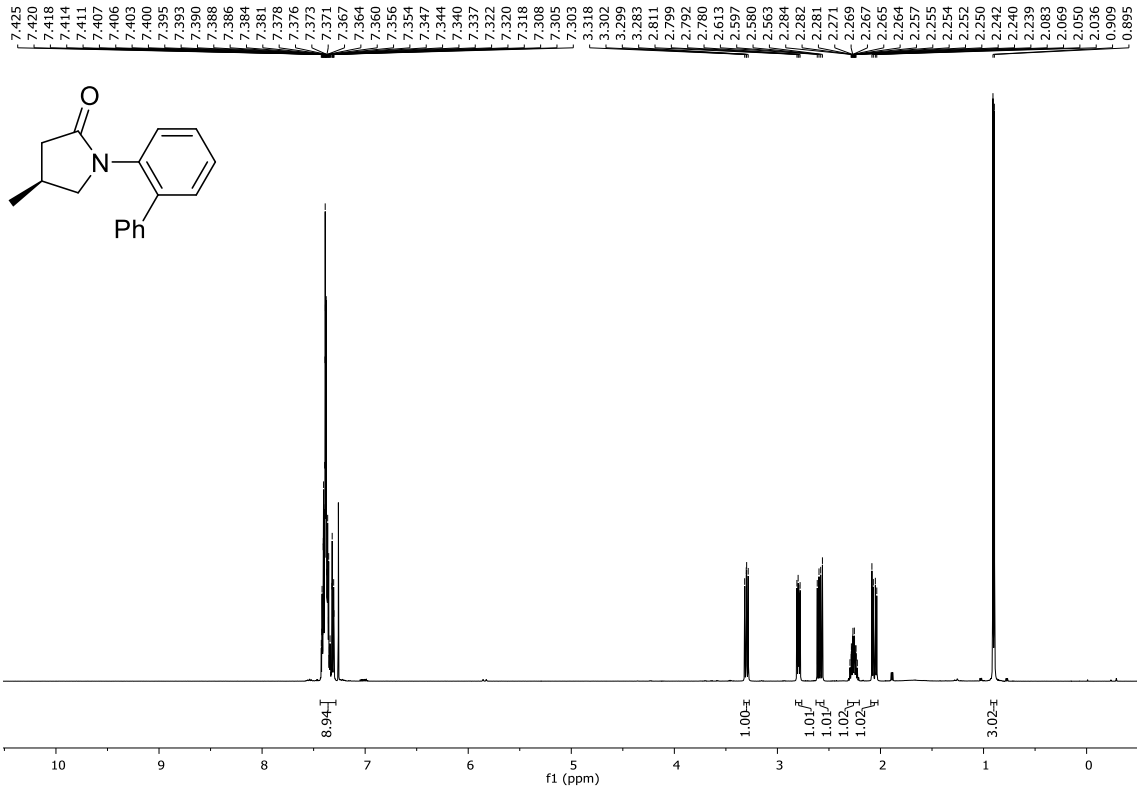


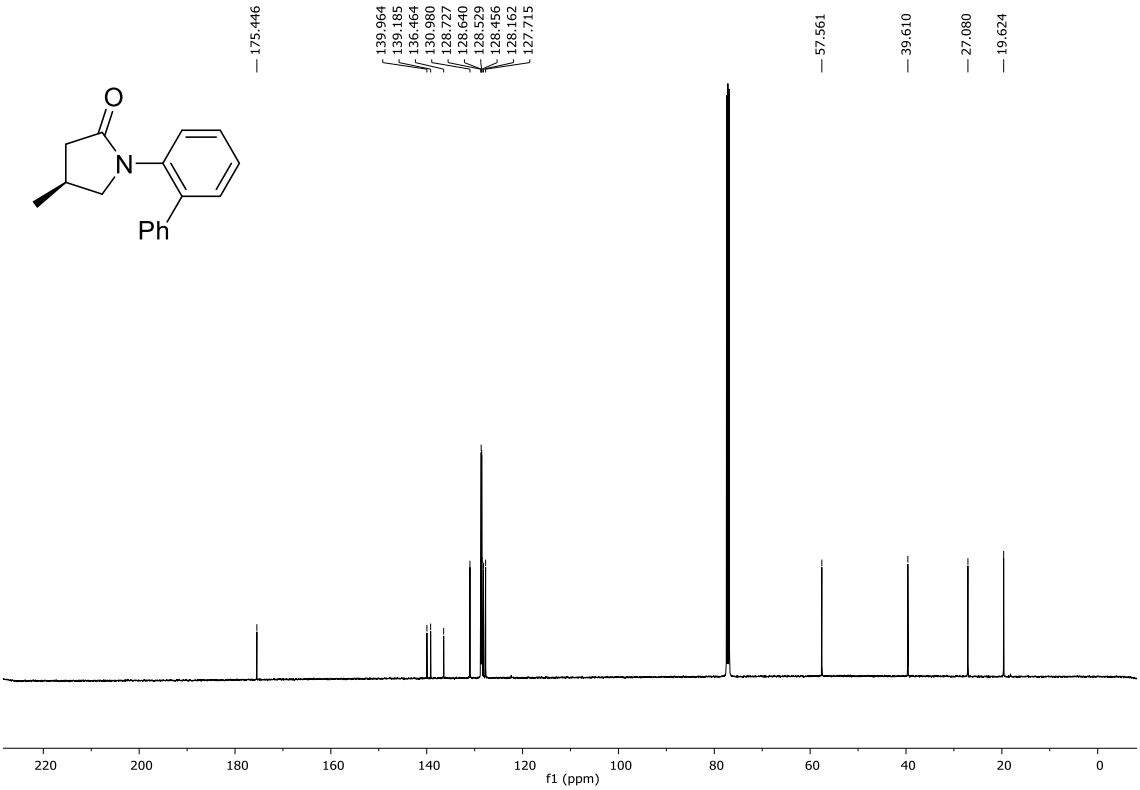
<Peak Table>

PDA Ch1 211nm

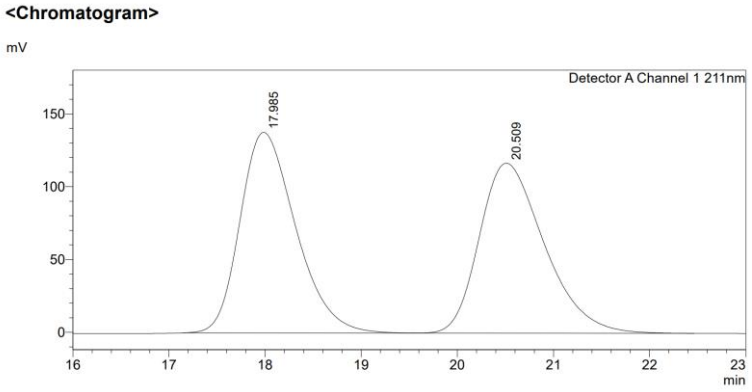
Peak#	Ret. Time	Area%
1	40.038	81.865
2	46.177	18.135
Total		100.000

(S)-1-([1,1'-biphenyl]-2-yl)-4-methylpyrrolidin-2-one (4q)





Racemic Reaction chromatogram

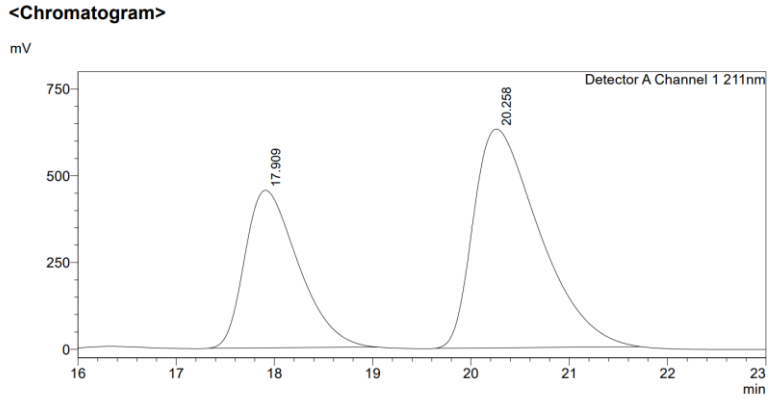


<Peak Table>

Detector A Channel 1 211nm

Peak#	Ret. Time	Area%
1	17.985	50.299
2	20.509	49.701
Total		100.000

Batch Reaction chromatogram

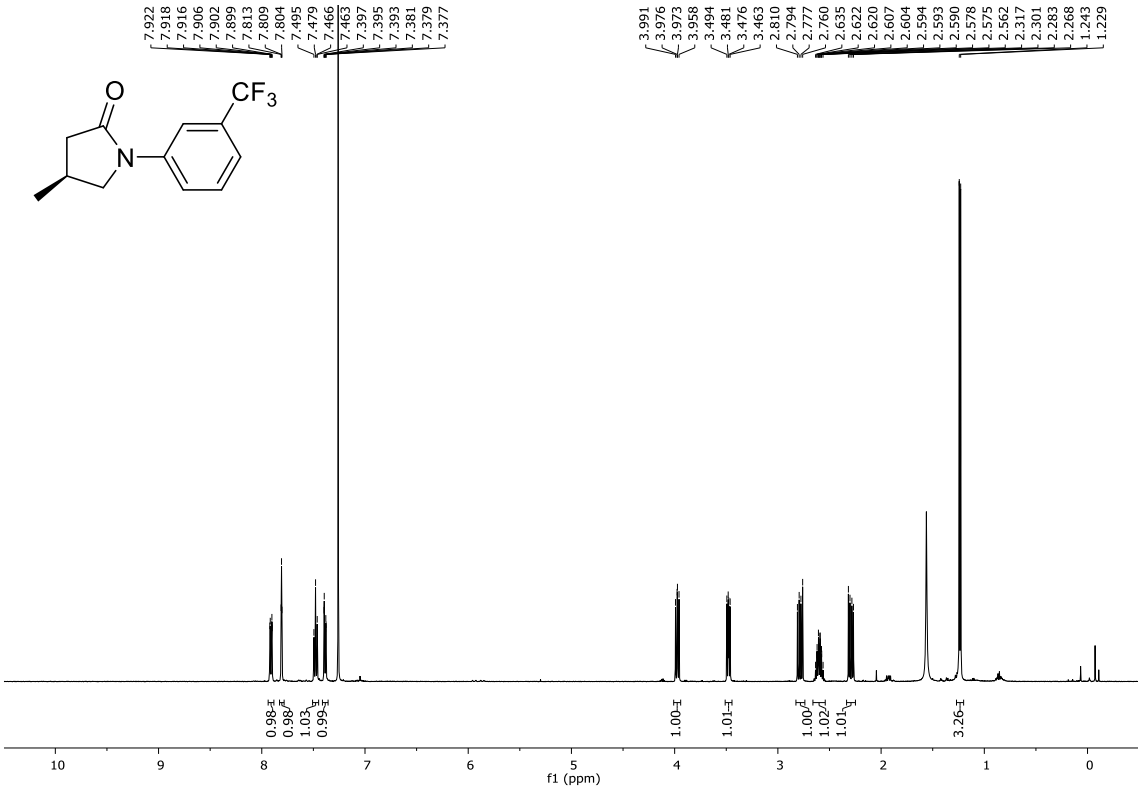


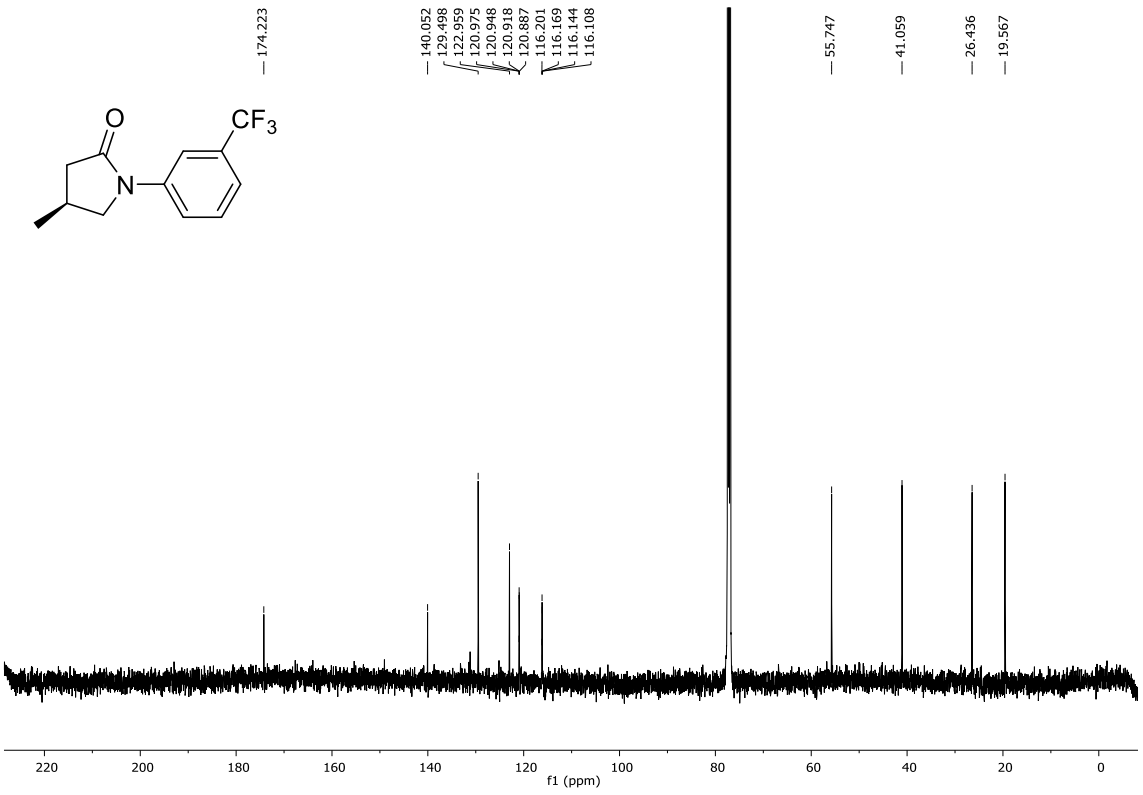
<Peak Table>

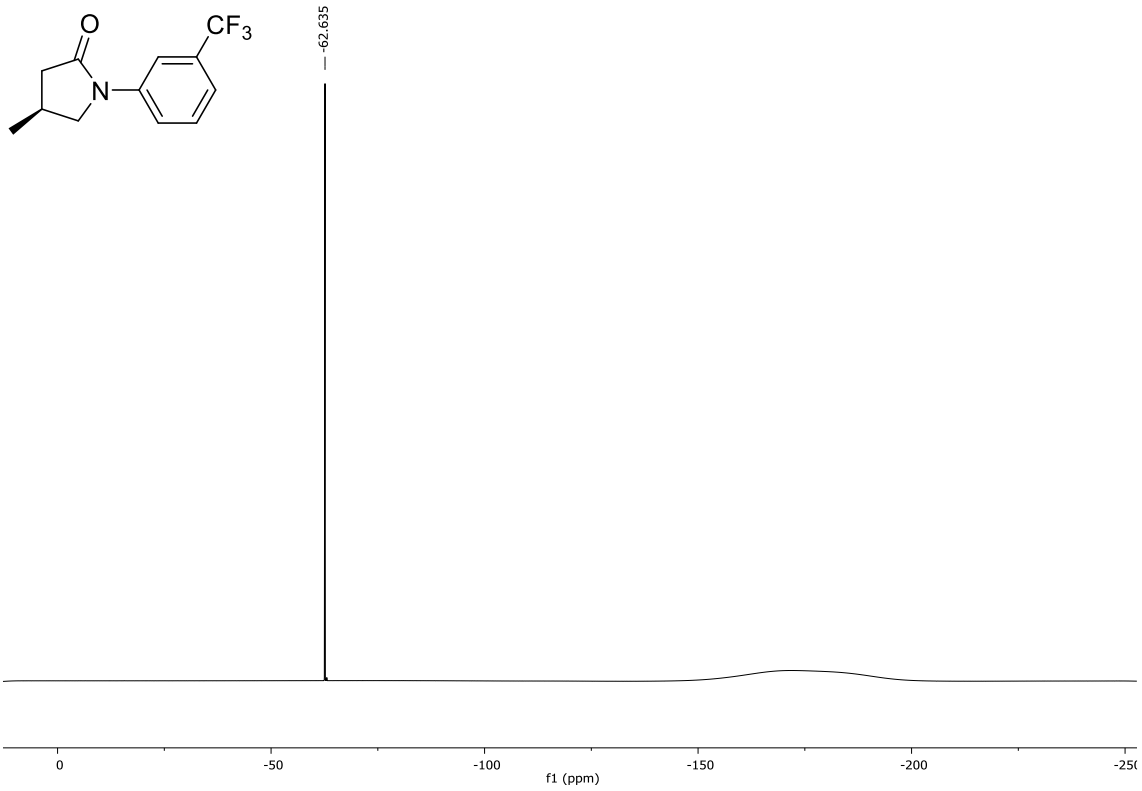
Detector A Channel 1 211nm

Peak#	Ret. Time	Area%
1	17.909	36.707
2	20.258	63.293
Total		100.000

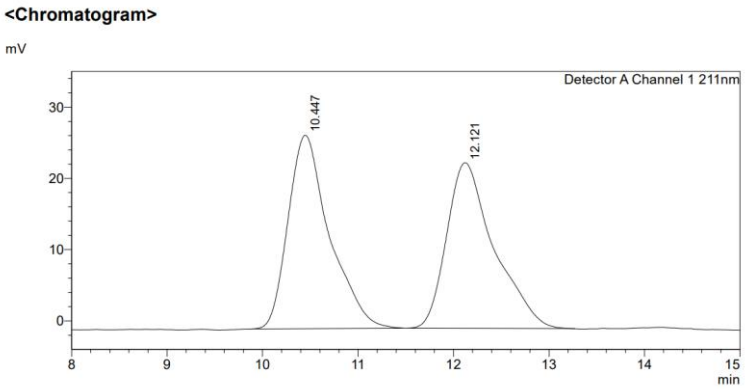
(S)-4-methyl-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (4r)







Racemic Reaction chromatogram

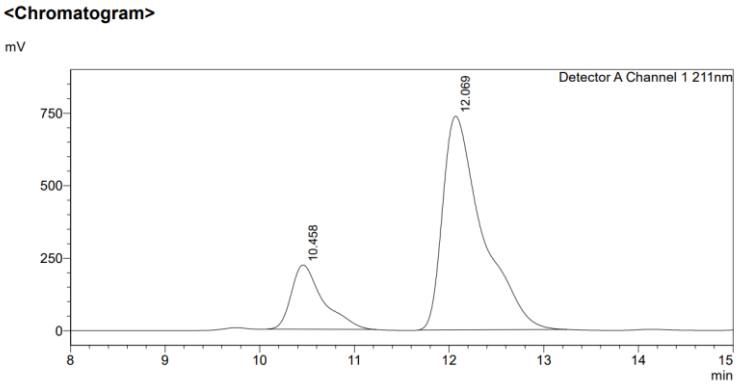


<Peak Table>

Detector A Channel 1 211nm

Peak#	Ret. Time	Area%
1	10.447	50.456
2	12.121	49.544
Total		100.000

Batch Reaction Chromatogram

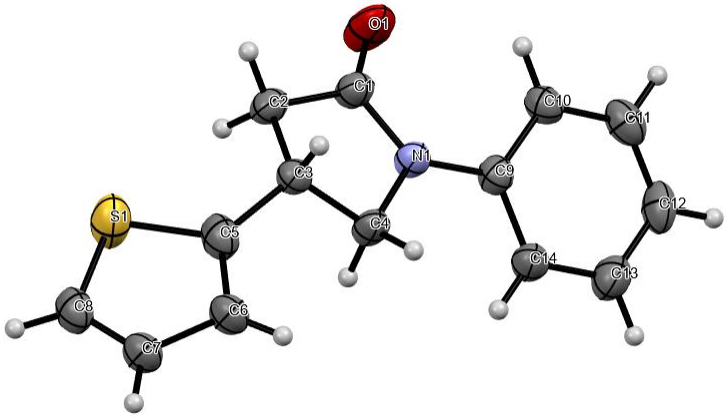


<Peak Table>

Detector A Channel 1 211nm

Peak#	Ret. Time	Area%
1	10.458	19.368
2	12.069	80.632
Total		100.000

8. Single Crystal X-Ray Structure of γ-lactam 4i



CCDC 2168909

A clear colourless, prism-like specimen of $C_{14}H_{13}NOS$, approximate dimensions 0.100 mm x 0.200 mm x 0.200 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å).

The total exposure time was 7.91 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 18463 reflections to a maximum θ angle of 25.33° (0.83 Å resolution), of which 2173 were independent (average redundancy 8.497, completeness = 99.6%, R_{int} = 3.27%, R_{sig} = 1.71%) and 2035 (93.65%) were greater than $2\sigma(F^2)$. The final cell constants of a = 7.3283(4) Å, b = 12.3775(6) Å, c = 13.1594(6) Å, volume = 1193.64(10) $Å^3$, are based upon the refinement of the XYZ-centroids of 7833 reflections above 20 σ(I) with 6.365° < 2θ < 52.12°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.891. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9510 and 0.9750.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21 21 21, with Z = 4 for the formula unit, $C_{14}H_{13}NOS$. The final anisotropic full-matrix least-squares refinement on F^2 with 142 variables converged at R1 = 5.71%, for the observed data and wR2 = 16.69% for all data. The goodness-of-fit was 1.085. The largest peak in the final difference electron density synthesis was 0.864 $e^-/Å^3$ and the largest hole was -0.425 $e^-/Å^3$ with an RMS deviation of 0.076 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.354 g/cm^3 and F(000), 512 e^-.

Table 1. Sample and crystal data.

Identification code	03567	
Chemical formula	$C_{14}H_{13}NOS$	
Formula weight	243.31 g/mol	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.200 x 0.200 mm	
Crystal habit	clear colourless prism	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.3283(4) Å	α = 90°
	b = 12.3775(6) Å	β = 90°
	c = 13.1594(6) Å	γ = 90°
Volume	1193.64(10) $Å^3$	
Z	4	
Density (calculated)	1.354 g/cm^3	
Absorption coefficient	0.252 mm^{-1}	
F(000)	512	

Table 2. Data collection and structure refinement.

Theta range for data collection	3.51 to 25.33°
Index ranges	-8<=h<=8, -14<=k<=14, -13<=l<=15
Reflections collected	18463
Independent reflections	2173 [R(int) = 0.0327]
Coverage of independent reflections	99.6%
Absorption correction	Multi-Scan
Max. and min. transmission	0.9750 and 0.9510
Structure solution technique	direct methods
Structure solution program	XT, VERSION 2018/2
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2019/1 (Sheldrick, 2019)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	2173 / 3 / 142
Goodness-of-fit on F^2	1.085
Final R indices	2035 data; I>2σ(I) R1 = 0.0571, wR2 = 0.1606
	all data R1 = 0.0615, wR2 = 0.1669
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0969P)^2+0.9851P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.06(3)
Largest diff. peak and hole	0.864 and -0.425 $eÅ^{-3}$
R.M.S. deviation from mean	0.076 $eÅ^{-3}$

Table 3. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2).

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C2	0.4203(7)	0.8063(3)	0.3593(4)	0.0355(10)
C1	0.4307(7)	0.7792(4)	0.4703(3)	0.0372(10)
C3	0.3649(6)	0.7002(3)	0.3081(3)	0.0308(9)
C4	0.4443(7)	0.6151(3)	0.3808(3)	0.0364(10)
C5	0.4258(7)	0.6850(4)	0.2001(4)	0.0433(8)
C6	0.4100(7)	0.5878(4)	0.1405(3)	0.0403(8)
C7	0.4835(7)	0.6072(4)	0.0419(3)	0.0403(8)
C8	0.5510(7)	0.7074(4)	0.0272(3)	0.0433(8)
C9	0.4698(6)	0.6110(4)	0.5714(3)	0.0324(9)
C10	0.4262(6)	0.6554(4)	0.6657(3)	0.0355(10)
C11	0.4612(7)	0.5971(4)	0.7540(3)	0.0447(12)
C12	0.5368(8)	0.4963(5)	0.7501(3)	0.0469(13)
C13	0.5803(8)	0.4510(4)	0.6563(4)	0.0466(12)
C14	0.5482(7)	0.5076(4)	0.5675(3)	0.0381(10)
N1	0.4384(6)	0.6687(3)	0.4800(3)	0.0323(8)
O1	0.4367(8)	0.8433(3)	0.5401(3)	0.0680(14)
S1	0.5281(2)	0.78485(12)	0.13172(10)	0.0565(5)

Table 4. Bond lengths (Å).

C2-C1	1.502(7)	C2-C3	1.531(6)
C1-O1	1.215(6)	C1-N1	1.374(5)
C3-C5	1.501(7)	C3-C4	1.538(6)
C4-N1	1.464(5)	C5-C6	1.441(7)
C5-S1	1.703(5)	C6-C7	1.425(6)
C7-C8	1.349(7)	C8-S1	1.686(5)
C9-C10	1.394(6)	C9-C14	1.404(7)
C9-N1	1.418(5)	C10-C11	1.392(6)
C11-C12	1.367(8)	C12-C13	1.392(7)
C13-C14	1.383(6)		

Table 5. Bond angles (°).

C1-C2-C3	104.5(3)	O1-C1-N1	125.4(4)
O1-C1-C2	126.3(4)	N1-C1-C2	108.3(4)
C5-C3-C2	116.4(4)	C5-C3-C4	113.0(4)
C2-C3-C4	102.3(3)	N1-C4-C3	103.5(3)
C6-C5-C3	126.5(4)	C6-C5-S1	110.7(3)
C3-C5-S1	122.8(4)	C7-C6-C5	108.9(4)
C8-C7-C6	115.1(4)	C7-C8-S1	111.7(4)
C10-C9-C14	119.1(4)	C10-C9-N1	121.3(4)
C14-C9-N1	119.6(4)	C11-C10-C9	119.8(4)
C12-C11-C10	121.1(4)	C11-C12-C13	119.6(4)
C14-C13-C12	120.4(5)	C13-C14-C9	120.0(4)
C1-N1-C9	125.8(4)	C1-N1-C4	111.7(4)
C9-N1-C4	121.5(3)	C8-S1-C5	93.6(2)

Table 6. Torsion angles (°).

C3-C2-C1-O1	-165.3(6)	C3-C2-C1-N1	16.7(5)
C1-C2-C3-C5	-152.2(4)	C1-C2-C3-C4	-28.5(4)
C5-C3-C4-N1	156.0(4)	C2-C3-C4-N1	30.0(5)
C2-C3-C5-C6	171.9(5)	C4-C3-C5-C6	53.9(6)
C2-C3-C5-S1	-7.3(6)	C4-C3-C5-S1	-125.4(4)
C3-C5-C6-C7	179.8(5)	S1-C5-C6-C7	-0.8(5)
C5-C6-C7-C8	0.8(6)	C6-C7-C8-S1	-0.4(6)
C14-C9-C10-C11	0.2(7)	N1-C9-C10-C11	-179.1(4)
C9-C10-C11-C12	-0.5(7)	C10-C11-C12-C13	0.3(8)
C11-C12-C13-C14	0.2(8)	C12-C13-C14-C9	-0.5(8)
C10-C9-C14-C13	0.3(7)	N1-C9-C14-C13	179.6(5)
O1-C1-N1-C9	-5.6(9)	C2-C1-N1-C9	172.5(4)
O1-C1-N1-C4	-174.9(6)	C2-C1-N1-C4	3.1(6)
C10-C9-N1-C1	25.7(7)	C14-C9-N1-C1	-153.6(5)
C10-C9-N1-C4	-166.0(5)	C14-C9-N1-C4	14.8(6)
C3-C4-N1-C1	-21.5(5)	C3-C4-N1-C9	168.7(4)
C7-C8-S1-C5	-0.1(4)	C6-C5-S1-C8	0.5(4)
C3-C5-S1-C8	179.9(4)		

Table 7. Anisotropic atomic displacement parameters (Å^2).

The anisotropic atomic displacement factor exponent takes the form:

$-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C2	0.044(2)	0.026(2)	0.037(2)	0.0005(18)	-0.002(2)	0.0027(17)
C1	0.052(2)	0.028(2)	0.032(2)	-0.0022(18)	-0.002(2)	0.005(2)
C3	0.036(2)	0.029(2)	0.027(2)	-0.0013(18)	-0.0023(17)	-0.0004(18)
C4	0.059(3)	0.0242(19)	0.026(2)	-0.0037(16)	-0.002(2)	0.000(2)
C5	0.0489(19)	0.052(2)	0.0291(17)	0.0060(15)	-0.0001(15)	0.0015(17)
C6	0.052(2)	0.0422(18)	0.0266(15)	-0.0042(13)	0.0003(15)	0.0011(15)
C7	0.052(2)	0.0422(18)	0.0266(15)	-0.0042(13)	0.0003(15)	0.0011(15)
C8	0.0489(19)	0.052(2)	0.0291(17)	0.0060(15)	-0.0001(15)	0.0015(17)
C9	0.037(2)	0.033(2)	0.027(2)	0.0008(17)	-0.0044(18)	-0.0010(19)
C10	0.039(2)	0.040(2)	0.027(2)	-0.0038(18)	-0.0010(18)	0.0007(19)
C11	0.046(3)	0.060(3)	0.028(2)	-0.003(2)	0.001(2)	-0.003(3)
C12	0.051(3)	0.057(3)	0.033(2)	0.017(2)	-0.003(2)	-0.002(3)
C13	0.058(3)	0.039(3)	0.044(3)	0.009(2)	-0.002(2)	0.002(2)
C14	0.052(3)	0.031(2)	0.031(2)	-0.0014(18)	0.002(2)	0.000(2)
N1	0.048(2)	0.0255(17)	0.0232(17)	-0.0028(13)	-0.0042(16)	-0.0003(16)
O1	0.136(4)	0.0312(18)	0.0374(19)	-0.0112(15)	-0.008(3)	0.005(2)
S1	0.0829(10)	0.0474(8)	0.0392(7)	0.0036(6)	0.0017(7)	-0.0153(8)

Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2).

	x/a	y/b	z/c	U(eq)
H2A	0.5377	0.8310	0.3342	0.043000
H2B	0.3300	0.8621	0.3470	0.043000
H3	0.2315	0.6946	0.3100	0.037000
H4A	0.3706	0.5499	0.3809	0.044000
H4B	0.5685	0.5966	0.3622	0.044000
H6	0.3599	0.5230	0.1628	0.048000
H7	0.4850	0.5546	-0.0085	0.048000
H8	0.6035	0.7308	-0.0333	0.052000
H10	0.3739	0.7238	0.6696	0.043000
H11	0.4327	0.6273	0.8168	0.054000
H12	0.5589	0.4581	0.8097	0.056000
H13	0.6314	0.3823	0.6534	0.056000
H14	0.5786	0.4772	0.5052	0.046000

Table 9. Hydrogen bond distances (Å) and angles (°).

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
C10-H10···O1	0.93	2.30	2.854(6)	117.5