Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

An Expedient Copper-Catalyzed Asymmetric Synthesis of γ-Lactones and γ-Lactams. Application to the Synthesis of Lucidulactone A

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General Information

All solvents and reagents were purchased from commercial suppliers. Diethyl ether and tetrahydrofuran solvents were distilled over sodium benzophenone ketyl.

Nuclear Magnetic Resonance Spectroscopy: ^{1}H NMR spectra were acquired on Bruker DRX500, AVII500 (500 MHz, with cryoprobe) or AVIII400 (400 MHz) spectrometers and were referenced to residual non deuterated solvent peaks in $CDCl_3$ (δ = 7.25), C_5D_5N (δ = 8.74, 7.58, 7.22) or DMSO-d_6 (δ = 2.5). Chemical shifts (δ_H and δ_C) are reported in parts per million (ppm) with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), pentet (pent), and multiplet (m); br = broad, app = apparent. Coupling constants (*J*) are measured to the nearest 0.1 Hz and are presented as observed. ^{13}C NMR spectra were obtained on Bruker AVII500 (126 MHz, with cryoprobe) or AVIII400 (101 MHz) spectrometers and were referenced to solvent peaks in $CDCl_3$ (δ = 77.17), DMSO-d_6 (δ = 39.52) or C_5D_5N (δ = 150.35, 135.91, 123.87).

Mass Spectrometry: Low-resolution mass spectra (m/z) were recorded on a Waters LCT Premier EX mass spectrometer, using electrospray ionization (ESI). High-resolution mass spectra (HRMS) were recorded by the Departmental Mass Spectrometry Service, Swansea University on a Bruker MicroTOF (resolution = 5000 FWHM) using electrospray ionisation (ES^+]. The parent ion $[M]^+$, $[M+H]^+$ or $[M+Na]^+$ is calculated to 4 decimal places from the molecular formula, and all values are within a tolerance of 5 ppm.

Infrared Spectroscopy: IR spectra were recorded using a Perkin Elmer FT-IR spectrometer and were recorded neat. Only strong and selected absorbances are reported. Wavelengths of maximum absorbance (ν_{max}) are quoted in wavenumbers (cm^{-1}). Only selected, characteristic IR absorption data are provided for each compound.

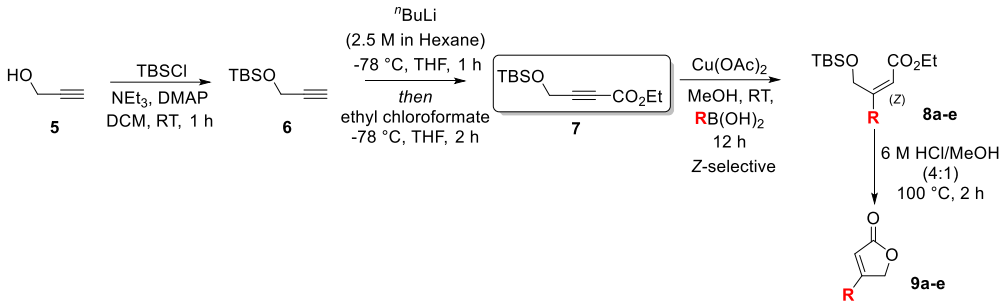
Specific rotations: Optical rotations were recorded on a Perkin Elmer 241 or 341 polarimeter with a path length of 1 dm (using the sodium D line, 589 nm). Specific rotation concentrations are reported in g/100 mL. Temperatures are reported in °C (typically 25 °C).

Chromatography: Column chromatography were carried out using either Merck Geduran® Silicagel 60 (40–63 µm) or Macherey-Nagel Silica 60 M (40 - 63 µm). Thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 F254 plates with visualization by ultraviolet light (254 nm) and/or heating the plate after staining with vanillin or $KMnO_4$.

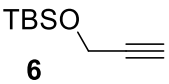
High performance liquid chromatography (HPLC) was performed on an Agilent 1200 Series running in normal phase under UV detection using chiralpak AD-H column (Amylose tris (3,5-dimethylphenylcarbamate) coated on 5µm silica-gel), OD-H column (Cellulose tris (3,5-dimethylphenylcarbamate) coated on 5µm silica-gel), IA-3 column, AS-3 column and OJ-H column (Cellulose tris (4-methylbenzoate) coated on 5µm silica-gel) with hexane and *i*-PrOH used as solvents.

Melting points were measured on BÜCHI melting point B-545 apparatus and are uncorrected.

Four-step synthesis of β-aryl α,β-unsaturated lactones 9a-9e

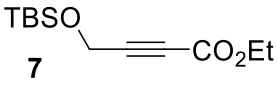


Tert-butyldimethyl(prop-2-yn-1-yloxy)silane (6)



To a stirring clear solution of DMAP (9.58 g, 78.48 mmol, 1.1 eq.) and NEt_3 (19.88 mL, 142.68 mmol, 2.0 eq.) in DCM (300 mL) was added propargyl alcohol **5** (4.0 g, 71.34 mmol, 1.0 eq.) at room temperature. After 5 minutes, TBSCl (12.90 g, 85.60 mmol, 1.2 eq.) was added, all at once, at room temperature. The resulting white suspension was stirred vigorously at room temperature for 1 h. Afterwards, the mixture was poured into a separating funnel and washed with saturated aqueous solution of NH_4Cl (200 mL) and then with de-ionised water (200 mL). The organic layer was further washed with brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude mixture was purified by silica gel chromatography using 2% ethyl acetate in hexane to generate compound **6** as colourless oil (11.8 g, 69.28 mmol, 97% yield). The data obtained agrees with literature data.[1] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.28 (d, *J* = 2.4 Hz, 2H), 2.36 (t, *J* = 2.4 Hz, 1H), 0.89 (s, 9H), 0.10 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 82.5, 72.9, 51.6, 25.9, 18.4, -5.1.

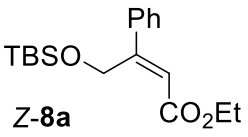
Ethyl 4-((*tert*-butyldimethylsilyl)oxy)but-2-ynoate (7)



In a pre-flame dried round bottom flask and under the inert atmosphere of argon, the solution of compound **6** (3.0 g, 17.61 mmol, 1.0 eq.) in THF (80 mL) was cooled to -78 °C. After 5 minutes, *n*-BuLi (2.5 M in hexanes, 8.45 mL, 21.13 mmol, 1.2 eq.) was added at -78 °C. The resulting clear mixture was stirred at -78 °C for 1 h, followed by the addition of ethyl chloroformate (2.29 g, 21.13 mmol, 1.2 eq.) at -78 °C. The mixture was stirred at -78 °C till completion (approx. 2 h) and then warmed up to room temperature. Afterwards, the mixture was quenched with saturated aqueous solution of NH_4Cl (60 mL) and then extracted with EtOAc (100 mL). The organic layer was further washed with de-ionised water (70 mL). The organic layer was washed with brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude mixture was purified by silica gel chromatography using 5% ethyl acetate in hexane to generate compound **7** as colourless oil (4.07 g, 16.79 mmol, 95% yield). The data obtained agrees with literature data.[2] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.42 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1

Hz, 3H), 0.89 (s, 9H), 0.12 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.5, 85.9, 62.2, 51.6, 25.9, 18.4, 14.2, -5.1.

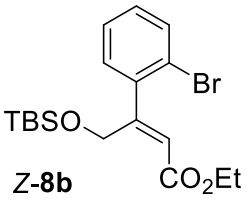
Ethyl (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)-3-phenylbut-2-enoate (**8a**)



Z-**8a**

In a pre-flame dried round bottom flask, phenylboronic acid (1.51 g, 12.38 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (37.5 mg, 0.206 mmol, 0.05 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **7** (1.0 g, 4.12 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at room temperature for 12 h. Afterwards, the mixture was quenched with saturated aqueous solution of NH_4Cl (40 mL) and then extracted with EtOAc (80 mL). The organic layer was further washed with de-ionised water (30 mL). The organic layer was washed with brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude mixture was purified by silica gel chromatography using 3% ethyl acetate in hexane to generate *syn*-hydroarylation[3] product compound *Z*-**8a** as light-yellow oil (1.14 g, 3.55 mmol, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47–7.49 (m, 2H), 7.32–7.34 (m, 3H), 6.04 (s, 1H), 5.20 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H), 0.76 (s, 9H), 0.00 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.1, 158.6, 128.7, 128.4, 128.0, 127.8, 117.7, 60.2, 59.7, 25.7, 18.2, 14.4, -5.2. **HRMS** (ESI): calc. for $C_{18}H_{28}SiO_3$ m/z: 320.1808 found $[M+Na]^+$ 343.1705. **IR (neat)**: 2953, 2855, 1711, 1627, 1463, 1254, 1166, 1090.

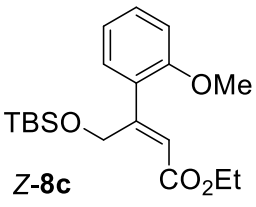
Ethyl (*Z*)-3-(2-bromophenyl)-4-((*tert*-butyldimethylsilyl)oxy)but-2-enoate (**8b**)



Z-**8b**

Same experimental procedure was followed as described for **8a**. 2-Bromophenylboronic acid (2.49 g, 12.38 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (0.226 g, 1.236 mmol, 0.30 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **7** (1.0 g, 4.12 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at room temperature for 12 h. Purification by silica gel chromatography using 3% ethyl acetate in hexane to generate compound *Z*-**8b** as colourless oil (1.51 g, 3.78 mmol, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64–7.66 (m, 1H), 7.49–7.51 (m, 1H), 7.26–7.28 (m, 2H), 5.90 (s, 1H), 5.20 (s, 2H), 4.34 (q, *J* = 8.1 Hz, 2H), 1.44 (t, *J* = 8.1 Hz, 3H), 0.79 (s, 9H), 0.05 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.9, 161.3, 142.1, 141.1, 132.7, 132.2, 127.2, 126.7, 119.3, 61.3, 60.4, 25.6, 18.0, 14.4, -5.5. **HRMS** (ESI): calc. for $C_{18}H_{27}BrO_3Si$ m/z: 398.0913 found $[M+Na]^+$ 421.0810. **IR (neat)**: 2928, 2855, 1711, 1468, 1370, 1252, 1178, 1112, 1026.

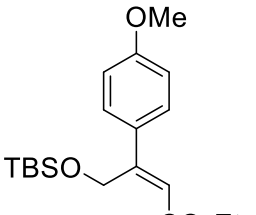
Ethyl (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)-3-(2-methoxyphenyl)but-2-enoate (**8c**)



Z-**8c**

Same experimental procedure was followed as described for **8a**. 2-Methoxyphenylboronic acid (1.88 g, 12.38 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (0.748 g, 4.12 mmol, 1.0 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **7** (1.0 g, 4.12 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at 60℃ for 12 h. Purification by silica gel chromatography using 3% ethyl acetate in hexane furnished compound *Z*-**8c** as colourless oil (1.35 g, 3.85 mmol, 93% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (t, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 5.93 (s, 1H), 5.19 (s, 2H), 4.29 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 0.75 (s, 9H), 0.00 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 161.0, 156.9, 130.0, 129.6, 129.3, 120.3, 118.2, 110.3, 61.3, 60.1, 55.5, 25.6, 18.0, 14.4, -5.4. **HRMS** (ESI): calc. for $C_{19}H_{30}SiO_4$ m/z: 350.1913 found $[M+Na]^+$ 373.1810. **IR (neat)**: 2957, 2855, 1712, 1630, 1461, 1257, 1086, 1010.

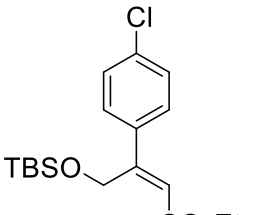
Ethyl (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxyphenyl)but-2-enoate (**8d**)



Z-**8d**

Same experimental procedure was followed as described for **8a**. 4-Methoxyphenylboronic acid (1.88 g, 12.38 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (0.226 g, 1.236 mmol, 0.30 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **7** (1.0 g, 4.12 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at room temperature for 12 h. Purification by silica gel chromatography using 3% ethyl acetate in hexane generated compound *Z*-**8d** as colourless oil (1.25 g, 3.57 mmol, 87% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 8.2 Hz, 2H), 6.02 (s, 1H), 5.18 (s, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.77 (s, 9H), 0.00 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 160.3, 157.8, 131.4, 129.2, 116.1, 113.5, 60.1, 59.5, 55.4, 25.8, 18.2, 14.4, -5.17. **HRMS** (ESI): calc. for $C_{19}H_{30}SiO_4$ m/z: 350.1913 found $[M+Na]^+$ 373.1810. **IR (neat)**: 2953, 2854, 1709, 1603, 1511, 1462, 1251, 1158, 1087.

Ethyl (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)-3-(4-chlorophenyl)but-2-enoate (**8e**)

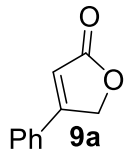


Z-**8e**

Same experimental procedure was followed as described for **8a**. 4-Chlorophenylboronic acid (1.94 g, 12.38 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (0.226 g, 1.236 mmol, 0.30 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **7** (1.0 g, 4.12 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at room temperature for 12 h. Purification by silica gel chromatography using 3% ethyl acetate in hexane generated compound *Z*-**8e** as yellow oil (1.25 g, 3.52 mmol, 85% yield). **^{1}H NMR** (400

MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.00 (s, 1H), 5.15 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.74 (s, 9H), -0.01 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0, 157.4, 137.6, 134.8, 129.2, 128.3, 118.0, 60.4, 59.6, 25.8, 18.2, 14.4, -5.2. **HRMS** (ESI): calc. for $C_{18}H_{27}SiClO_3$ m/z: 354.1418 found $[M+Na]^+$ 377.1315. **IR (neat)**: 2953, 2855, 1712, 1627, 1490, 1253, 1171, 1092, 1012.

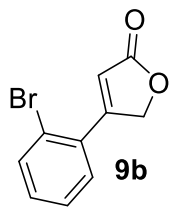
4-Phenylfuran-2(5*H*)-one (**9a**)



9a

A solution of compound *Z*-**8a** (0.50 g, 1.56 mmol) in MeOH (5 mL) was added to 6 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 2 h. The mixture became clear solution after 5 minutes. After the reaction had reached completion (TLC control), it was diluted with EtOAc (50 mL) and transferred into a separating funnel. The aqueous layer was neutralised till pH = 7 using 6 M NaOH (15 mL). The aqueous layer was further extracted with EtOAc. The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced β-substituted, α,β-unsaturated lactone **9a** as white solid (0.23 g, 1.44 mmol, 92% yield). Weaker concentrations (e.g. 2 M or 3 M) of HCl also work perfectly but with longer reaction time. The data obtained agrees with literature data.[4a] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50–7.46 (m, 5H), 6.37 (s, 1H), 5.22 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 164.0, 131.9, 129.8, 129.4, 126.0, 113.2, 71.1.

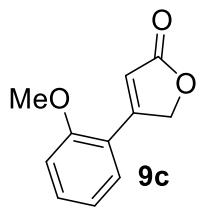
4-(2-Bromophenyl)furan-2(5*H*)-one (**9b**)



9b

Same experimental procedure was followed as described for the synthesis of lactone **9a**. A solution of compound *Z*-**8b** (0.50 g, 1.252 mmol) in MeOH (5 mL) was added to 6 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 2 h. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **9b** as white solid (0.28 g, 1.171 mmol, 94% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.41–7.39 (m, 1H), 7.33–7.31 (m, 2H), 6.56 (s, 1H), 5.23 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 163.5, 134.7, 131.8, 131.5, 129.6, 128.0, 122.2, 119.2, 72.6. **HRMS** (ESI): calc. for $C_{10}H_7BrO_2$ m/z: 237.9629 found $[M+Na]^+$ 260.9526. **IR (neat)**: 3096, 1816, 1729, 1606, 1428, 1311, 1281, 1173, 1045. **MP**: 85–90 °C.

4-(2-Methoxyphenyl)furan-2(5*H*)-one (**9c**)

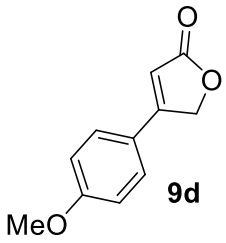


9c

Same experimental procedure was followed as described for the synthesis of lactone **9a**. A solution of compound *Z*-**8c** (0.50 g, 1.426 mmol) in MeOH (5 mL) was added to 6 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 2 h. Purification by silica gel

chromatography using 10-20% ethyl acetate in hexane produced compound **9c** as white solid (0.25 g, 1.314 mmol, 92% yield). The data obtained agrees with literature data.[4b] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44–7.42 (m, 2H), 7.04–7.00 (m, 2H), 6.55 (s, 1H), 5.26 (s, 2H), 3.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.8, 161.0, 158.5, 133.0, 128.5, 121.1, 118.9, 115.1, 111.8, 72.9, 55.6.

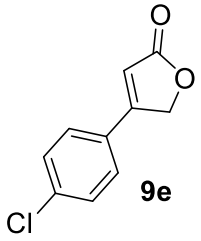
4-(4-Methoxyphenyl)furan-2(5*H*)-one (**9d**)



9d

Same experimental procedure was followed as described for the synthesis of lactone **9a**. A solution of compound *Z*-**8d** (0.50 g, 1.426 mmol) in MeOH (5 mL) was added to 6 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 2 h. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **9d** as white solid (0.21 g, 1.104 mmol, 77% yield). The data obtained agrees with literature data.[4a] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45–7.43 (m, 2H), 6.96–6.94 (m, 2H), 6.22 (s, 1H), 5.17 (s, 2H), 3.85 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.4, 163.6, 162.5, 128.3, 122.4, 114.8, 110.7, 71.0, 55.6.

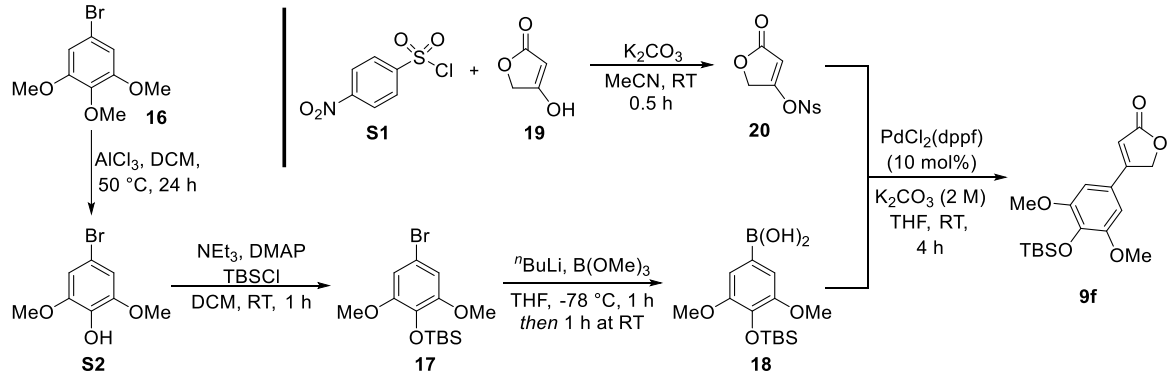
4-(4-Chlorophenyl)furan-2(5*H*)-one (**9e**)



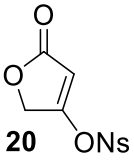
9e

Same experimental procedure was followed as described for the synthesis of lactone **9a**. A solution of compound *Z*-**8e** (0.50 g, 1.409 mmol) in MeOH (5 mL) was added to 6 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 2 h. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **9e** as white solid (0.22 g, 1.130 mmol, 80% yield). The data obtained agrees with literature data.[4a] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (s, 4H), 6.37 (s, 1H), 5.19 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.6, 162.6, 138.1, 129.8, 128.2, 127.8, 113.7, 70.9.

Synthesis of β-aryl α,β-unsaturated lactone 9f

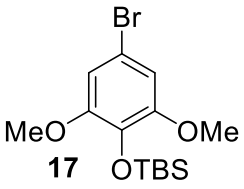


5-Oxo-2,5-dihydrofuran-3-yl 4-nitrobenzenesulfonate (**20**)



Nosyl chloride **S1** (4.87 g, 21.98 mmol, 1.1 eq.) was added, all at once, to a stirring white suspension of commercially available tetronic acid **19** (2.0 g, 19.99 mmol, 1.0 eq.) and potassium carbonate (4.97 g, 35.98 mmol, 1.8 eq.) in acetonitrile (190 mL) at room temperature. The resulting suspension (turned from milky white to light blue) was stirred at room temperature till the reaction had reached completion (approx. 30 minutes, TLC control). Afterwards, the mixture was diluted with EtOAc (150 mL) then washed with saturated aqueous solution of ammonium chloride (100 mL), de-ionised water (80 mL) and brine (90 mL). The organic layer was dried with magnesium sulphate, filtered, and concentrated *in vacuo*. The resulting residue was recrystallised in EtOAc and hexane (1:9). The solid was collected by filtration under vacuo. Compound **20** was obtained as white solid (4.81 g, 16.85 mmol, 84% yield). The data obtained agrees with literature data.[5a] **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.50 (d, *J* = 8.8 Hz, 2H), 8.44 (d, *J* = 8.8 Hz, 2H), 6.10 (s, 1H), 4.93 (s, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 180.9, 154.7, 147.7, 131.0, 127.3, 125.7, 123.8, 100.8, 88.0, 68.2.

(4-Bromo-2,6-dimethoxyphenoxy)(*tert*-butyl)dimethylsilane (**17**)

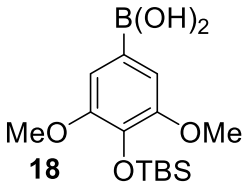


Following literature procedure.[5b] Anhydrous aluminium chloride (8.49 g, 63.74 mmol, 1.5 eq.) was added, all at once, to a stirring solution of commercially available 5-Bromo-1,2,3-trimethoxybenzene **16** (10.5 g, 42.49 mmol, 1.0 eq.) in DCM (200 mL) at room temperature. The resulting mixture was stirred at 50 °C for 24 h under argon. Afterwards (95% completion), the mixture was diluted with DCM (50 mL) and washed with 1 M HCl (2 x 100 mL) twice. The aqueous layer was further extracted with DCM (50 mL). The combined organic layers were washed with brine (200 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*.

Purification by silica gel chromatography using 5-20% EtOAc in hexane furnished the phenol product as white powder **S2**[5b] (8.67 g, 37.52 mmol, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.71 (s, 2H), 5.43 (s, 1H), 3.86 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.7, 134.2, 111.2, 108.6, 56.6.

NEt_3 (10.46 mL, 75.04 mmol, 2.0 eq.) and DMAP (4.58 g, 37.52 mmol, 1.0 eq.) were added to a stirring solution of the phenol **S2** (8.67 g, 37.52 mmol, 1.0 eq.) in DCM (80 mL) at room temperature. After 5 minutes, TBSCl (6.79 g, 45.02 mmol, 1.2 eq.) was added at room temperature. The resulting mixture was left to stir at room temperature till completion (approx. 1 h). Afterwards, the mixture was diluted with DCM (50 mL) then washed with saturated aqueous solution of ammonium chloride (100 mL), water (80 mL) and brine (90 mL). The organic layer was dried with magnesium sulphate, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 1-5% EtOAc in hexane afforded **17**[5c] as colourless oil (11.86 g, 34.14 mmol, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.66 (s, 2H), 3.76 (s, 6H), 0.99 (s, 9H), 0.10 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.4, 133.8, 112.8, 108.9, 56.0, 25.9, 18.8, -4.5.

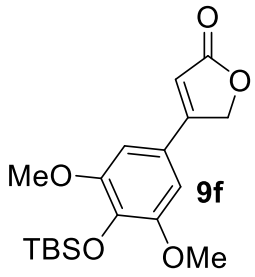
(4-((*Tert*-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)boronic acid (**18**)



18

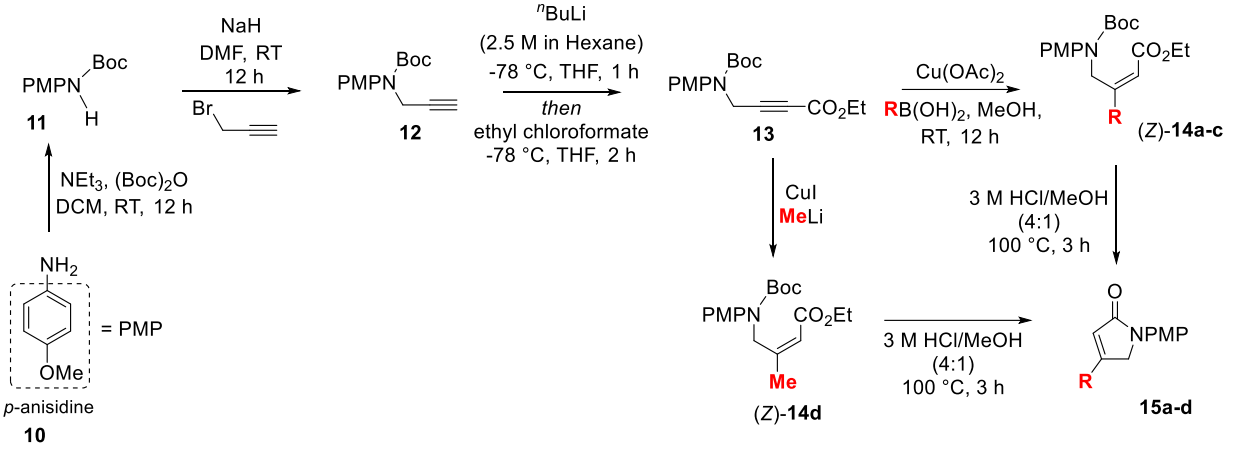
In a pre-flame dried round bottom flask under the inert atmosphere of argon, compound **17** (2.85 g, 8.21 mmol, 1.0 eq.) was dissolved in THF (30 mL) and cooled to -78 °C. After 5 minutes, *n*-BuLi (2.5 M in hexanes, 3.94 mL, 9.85 mmol, 1.2 eq.) was slowly added. The resulting mixture was stirred at -78 °C for 30 minutes, followed by the dropwise addition of $B(OMe)_3$ (1.12 mL, 1.02 g, 9.85 mmol, 1.2 eq.) in THF (9 mL) at -78 °C. The resulting mixture was stirred at -78 °C for 1 h and at room temperature for a further 1 h. The mixture was acidified with 2 M HCl (50 mL) and extracted twice with EtOAc (2x 80 mL). The combined organic layers were washed with brine (40 mL), dried with magnesium sulphate, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 5-10% MeOH in DCM afforded **18** as off-white fluffy solid (1.33 g, 4.27 mmol, 52%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 (s, 2H), 3.91 (s, 6H), 1.03 (s, 9H), 0.17 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.6, 139.3, 112.6, 55.9, 25.9, 18.9, -4.4. **HRMS** (ESI): calc. for $C_{14}H_{25}BO_5Si$ m/z: 312.1564 found $[M+Na]^+$ 335.1461. **IR (neat)**: 2930, 1574, 1413, 1338, 1225, 1123. **MP**: 290–295 °C.

4-(4-((*Tert*-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)furan-2(5H)-one (**9f**)

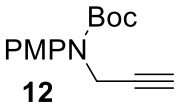


An aqueous solution of potassium carbonate (2 M, 2.52 mL, 5.05 mmol, 2.4 eq.) was added to a stirring solution of boronic acid **18** (0.788 g, 2.524 mmol, 1.2 eq.) in THF (30 mL) at room temperature. After 5 minutes, $PdCl_2$(dppf) (0.154 g, 0.210 mmol, 0.1 eq.) and Nosylate **20** (0.60 g, 2.10 mmol, 1.0 eq.) were added, respectively. The resulting mixture was stirred at room temperature till completion (approx. 4 h; TLC control). The mixture was quenched with saturated aqueous solution of NH_4Cl extracted twice with EtOAc (2x 30 mL). The combined organic layers were washed with de-ionised water (20 mL), brine (20 mL), dried with magnesium sulphate, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 10-30% EtOAc in hexane afforded **9f** as sticky off-white solid. Further recrystallisation in hexane produced **9f** as crystalline white powder (0.55 g, 1.56 mmol, 74%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.66 (s, 2H), 6.23 (s, 1H), 5.18 (s, 2H), 3.83 (s, 6H), 1.00 (s, 9H), 0.14 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 164.3, 152.2, 138.4, 122.3, 111.3, 104.0, 71.1, 56.1, 25.8, 18.9, 4.4. **HRMS** (ESI): calc. for $C_{18}H_{26}O_5Si$ m/z: 350.1550 found $[M+Na]^+$ 373.1447. **IR (neat)**: 2928, 1740, 1618, 1578, 1504, 1461, 1424, 1364, 1338, 1251, 1186, 1157, 1119, 1072. **MP**: 195–200 °C.

Five-step synthesis of β-aryl and β-alkyl α,β-unsaturated lactams 15a-15d



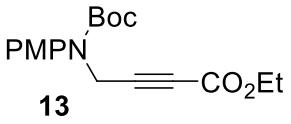
***Tert*-butyl (4-methoxyphenyl)(prop-2-yn-1-yl)carbamate (12)**



Following literature procedure.[6a] $(Boc)_2O$ (17.01 g, 77.95 mmol, 1.2 eq.) was added to a stirring solution of *p*-anisidine **10** (8.0 g, 64.96 mmol, 1.0 eq.) and NEt_3 (18.10 mL, 129.92 mmol, 2.0 eq.) in DCM (200 mL). The resulting mixture was left to stir at room temperature for 12 h. Afterwards, the mixture was washed with de-ionised water (100 mL), saturated aqueous solution of ammonium chloride (100 mL). The organic layer was washed with brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by silica gel chromatography using 10-20% EtOAc in hexane to generate compound **11** (12.33 g, 55.22 mmol, 85%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29–7.27 (m, 2H), 6.87–6.85 (m, 2H), 6.39 (s, 1H, *N*-H), 3.80 (s, 3H), 1.53 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.8, 153.3, 131.5, 120.7, 114.3, 80.3, 55.6, 28.5.

In a pre-flame dried round bottom flask, a solution of compound **11** (2.0 g, 8.96 mmol, 1.0 eq.) in DMF (15 mL) was added slowly to a suspension of NaH (60% wt in mineral oil, 0.43 g, 10.75 mmol, 1.2 eq.) in DMF (30 mL). The resulting clear mixture was stirred at room temperature for 30 minutes, followed by the addition of propargyl bromide (80% wt in toluene, 1.20 mL, 10.75 mmol, 1.2 eq.). The dark-brown mixture was stirred for 12 h at room temperature and quenched with saturated aqueous solution of ammonium chloride (50 mL) and then extracted with EtOAc (40 mL) twice. The combined organic layer was washed with water (50 mL), brine (50 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 5% ethyl acetate in hexane furnished compound **12** as colourless oil (2.6 g, 8.43 mmol, 94%). The data obtained agrees with the literature data.[6b] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20–7.16 (m, 2H), 6.84–6.82 (m, 2H), 4.28 (s, 2H), 3.75 (s, 3H), 2.20 (s, 1H), 1.41 (br s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.9, 154.3, 134.9, 127.8, 113.9, 80.6, 80.0, 71.7, 55.3, 39.9, 28.2.

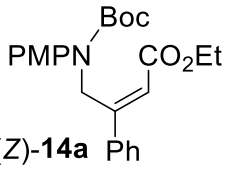
Ethyl 4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)but-2-ynoate (**13**)



13

In a pre-flame dried round bottom flask and under the inert atmosphere of argon, the solution of compound **12** (2.6 g, 9.95 mmol, 1.0 eq.) in THF (30 mL) was cooled to -78 °C. After 5 minutes, *n*-BuLi (2.5 M in Hexanes, 4.78 mL, 11.94 mmol, 1.2 eq.) was added at -78 °C. The resulting clear mixture was stirred at -78 °C for 1 h, followed by the addition of ethyl chloroformate (1.29 g, 11.94 mmol, 1.2 eq.) at -78 °C. The mixture was stirred at -78 °C till completion (approx. 2 h) and then warmed up to room temperature. Afterwards, the mixture was quenched with saturated aqueous solution of NH_4Cl (30 mL) and then extracted with EtOAc (100 mL). The organic layer was further washed with de-ionised water (20 mL). The organic layer was washed with brine (25 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude mixture was purified by silica gel chromatography using 5% ethyl acetate in hexane to generate compound **13** as light-brown oil (1.86 g, 5.58 mmol, 56% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.43 (br s, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 1.41 (br s, 9H), 1.27 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2, 154.3, 153.3, 134.6, 128.0, 114.2, 83.8, 81.2, 75.6, 62.0, 55.4, 28.3, 14.0. **HRMS** (ESI): calc. for $C_{18}H_{23}O_5N$ m/z: 333.1576 found $[M+Na]^+$ 356.1473. **IR (neat)**: 2976, 1700, 1511, 1366, 1242, 1163, 1144.

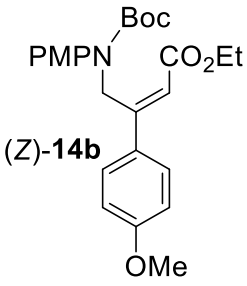
Ethyl (*Z*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-phenylbut-2-enoate (**14a**)



(*Z*)-**14a**

In a pre-flame dried round bottom flask, phenylboronic acid (0.94 g, 7.74 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (23.4 mg, 0.13 mmol, 0.05 eq.) in MeOH (30 mL) at room temperature. After 5 minutes, a solution of compound **13** (0.86 g, 2.58 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting brown mixture was stirred at 60 °C for 24 h. Afterwards, the mixture was quenched with saturated aqueous solution of NH_4Cl (40 mL) and then extracted with EtOAc (100 mL). The organic layer was further washed with de-ionised water (30 mL). The organic layer was washed with brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude mixture was purified by silica gel chromatography using 1% ethyl acetate in hexane. Compound *Z*-**14a** was obtained as light-yellow oil (0.84 g, 2.04 mmol, 79% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20 (br s, 5H), 6.52 (br s, 4H), 5.81 (s, 1H), 5.41 (s, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 3.59 (s, 3H), 1.13–1.11 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.8, 157.4, 156.6, 154.8, 138.8, 129.0, 128.2, 128.1, 127.5, 120.4, 113.2, 79.9, 60.1, 55.2, 28.2, 14.2. **HRMS** (ESI): calc. for $C_{24}H_{29}O_5N$ m/z: 411.2046 found $[M+Na]^+$ 434.1943. **IR (neat)**: 2978, 1702, 1683, 1618, 1511, 1368, 1294, 1246, 1163, 1025.

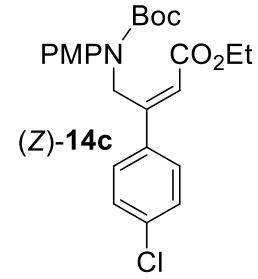
Ethyl (*Z*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-(4-methoxyphenyl)but-2-enoate (**14b**)



(*Z*)-**14b**

Same experimental procedure was followed as described for **14a**. 4-Methoxyphenylboronic acid (1.37 g, 8.99 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (0.163 g, 0.89 mmol, 0.30 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **13** (1.0 g, 2.99 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at room temperature for 12 h. Purification by silica gel chromatography using 5% ethyl acetate in hexane generated compound *Z*-**14b** as colourless oil (1.22 g, 2.76 mmol, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22–7.20 (m, 2H), 6.79–6.77 (m, 2H), 6.64–6.62 (m, 4H), 5.82 (s, 1H), 5.45 (s, 2H), 4.04 (q, *J* = 7.2 Hz, 2H), 3.75 (s, 3H), 3.65 (s, 3H), 1.19–1.17 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.1, 160.5, 157.5, 155.9, 153.3, 150.4, 131.1, 128.9, 128.4, 119.0, 116.0, 114.7, 113.6, 80.0, 60.0, 55.4, 55.3, 28.3, 14.3. **HRMS** (ESI): calc. for $C_{25}H_{31}O_6N$ m/z: 441.2151 found $[M+Na]^+$ 464.2048. **IR (neat)**: 2970, 1683, 1602, 1509, 1365, 1288, 1244, 1164, 1026.

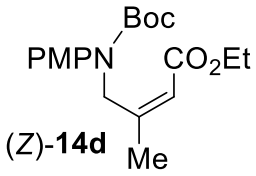
Ethyl (*Z*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-(4-chlorophenyl)but-2-enoate (**14c**)



(*Z*)-**14c**

Same experimental procedure was followed as described for **14a**. 4-Chlorophenylboronic acid (1.41 g, 8.99 mmol, 3.0 eq.) was added to a stirring blue solution of $Cu(OAc)_2$ (0.16 g, 0.89 mmol, 0.30 eq.) in MeOH (20 mL) at room temperature. After 5 minutes, a solution of compound **13** (1.0 g, 2.99 mmol, 1.0 eq.) in MeOH (10 mL) was added at room temperature. The resulting mixture was stirred at room temperature for 12 h. Purification by silica gel chromatography using 10% ethyl acetate in hexane generated compound *Z*-**14c** as white solid (1.18 g, 2.64 mmol, 88% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (br s, 4H), 6.63 (br s, 4H), 5.85 (s, 1H), 5.43 (s, 2H), 4.07 (q, *J* = 7.4 Hz, 2H), 3.68 (s, 3H), 1.20–1.18 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.8, 157.5, 155.3, 135.1, 129.0, 128.4, 128.2, 127.2, 121.1, 120.9, 114.5, 60.3, 55.6, 55.4, 28.3, 14.3. **HRMS** (ESI): calc. for $C_{24}H_{28}NO_5Cl$ m/z: 445.1656 found $[M+Na]^+$ 468.1553. **IR (neat)**: 2971, 1710, 1680, 1629, 1511, 1459, 1367, 1294, 1247, 1176, 1091. **MP:** 120–125 °C

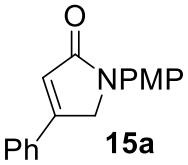
Ethyl (*Z*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-methylbut-2-enoate (14d)



(*Z*)-**14d**

In a pre-flame dried round bottom flask and under the inert atmosphere of argon, MeLi (1.6 M, 3.55 mL, 5.68 mmol, 2.2 eq.) was added to a cooled white suspension of CuI (0.54 g, 2.84 mmol, 1.1 eq.) in THF (35 mL) at 0 °C. The resulting clear solution was stirred at 0 °C for 2 h and then cooled to -78 °C. After 5 minutes, a solution of compound **13** (0.86 g, 2.58 mmol, 1.0 eq.) was added and stirred at -78 °C for additional 1.5 h. The mixture was allowed to warm up to room temperature and quenched with saturated aqueous solution of NH_4Cl (30 mL) and then extracted with EtOAc (60 mL). The organic layer was further washed with de-ionised water (20 mL), brine (25 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude mixture was purified by silica gel chromatography using 10% ethyl acetate in hexane to generate compound *Z*-**14d** as light-brown oil (0.80 g, 2.296 mmol, 89% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.08–7.06 (m, 2H), 6.80–6.78 (m, 2H), 5.66 (s, 1H), 4.93 (s, 2H), 4.03 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 1.92 (s, 3H), 1.40 (br s, 9H), 1.18 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.8, 165.8, 157.4, 155.2, 135.3, 127.8, 127.4, 118.1, 113.8, 60.2, 59.7, 55.4, 28.3, 22.0, 14.2. **HRMS** (ESI): calc. for $C_{19}H_{27}O_5N$ m/z: 349.1889 found $[M+Na]^+$ 372.1786. **IR (neat)**: 2975, 1693, 1511, 1366, 1242, 1141.

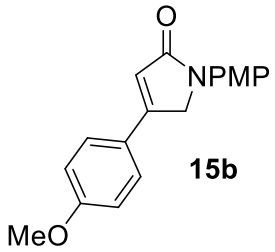
1-(4-Methoxyphenyl)-4-phenyl-1,5-dihydro-2*H*-pyrrol-2-one (**15a**)



15a

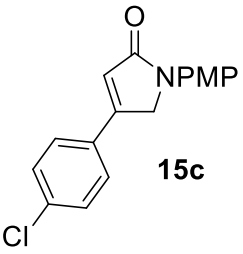
A solution of compound *Z*-**14a** (0.70 g, 1.70 mmol) in MeOH (5 mL) was added to 3 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 3 h. The mixture became clear solution after 5 minutes. After the reaction had reached completion (TLC control), it was diluted with EtOAc (50 mL) and transferred into a separating funnel. The aqueous layer was neutralised till pH = 7 using 3 M NaOH (15 mL). The aqueous layer was further extracted with EtOAc. The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **15a** as white solid (0.37 g, 1.394 mmol, 82% yield). The data obtained agrees with literature data.[7b] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.57–7.55 (m, 2H), 7.46–7.44 (m, 3H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.53 (s, 1H), 4.77 (s, 2H), 3.81 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.3, 156.5, 153.4, 132.6, 131.7, 130.6, 129.2, 126.0, 121.5, 121.1, 114.5, 55.6, 53.8.

1,4-Bis(4-methoxyphenyl)-1,5-dihydro-2*H*-pyrrol-2-one (**15b**)



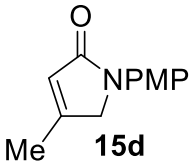
Same experimental procedure was followed as described for the synthesis of lactone **15a**. A solution of compound *Z*-**14b** (0.80 g, 1.81 mmol) in MeOH (5 mL) was added to 3 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 3 h. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **15b** as light-yellow powder (0.38 g, 1.30 mmol, 72% yield). The data obtained agrees with literature data.[7c] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 6.93 (app t, *J* = 8.8 Hz, 4H), 6.38 (s, 1H), 4.71 (s, 2H), 3.85 (s, 3H), 3.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 161.5, 156.4, 153.1, 132.7, 127.5, 124.3, 120.9, 119.3, 114.6, 114.4, 55.6, 55.5, 53.3.

4-(4-Chlorophenyl)-1-(4-methoxyphenyl)-1,5-dihydro-2*H*-pyrrol-2-one (**15c**)



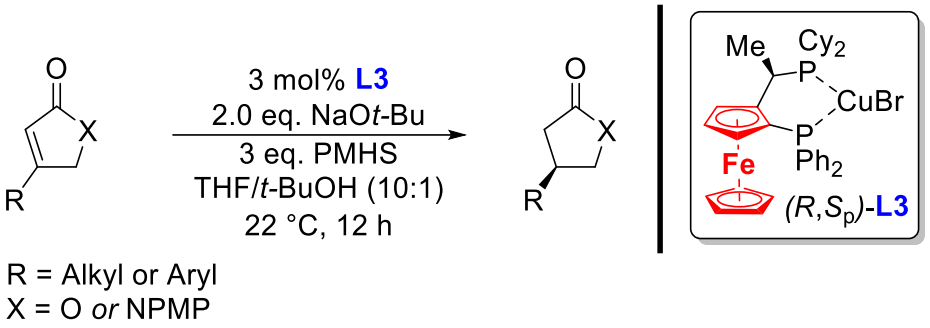
Same experimental procedure was followed as described for the synthesis of lactone **15a**. A solution of compound *Z*-**14c** (0.90 g, 2.02 mmol) in MeOH (5 mL) was added to 3 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 3 h. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **15c** as white solid (0.45 g, 1.51 mmol, 75% yield). The data obtained agrees with literature data.[7c] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.48 (s, 1H), 4.70 (s, 2H), 3.79 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 156.5, 152.0, 136.5, 132.3, 130.1, 129.5, 127.2, 121.9, 121.0, 114.4, 55.6, 53.2.

1-(4-Methoxyphenyl)-4-methyl-1,5-dihydro-2*H*-pyrrol-2-one (**15d**)



Same experimental procedure was followed as described for the synthesis of lactone **15a**. A solution of compound *Z*-**14d** (0.62 g, 1.77 mmol) in MeOH (5 mL) was added to 3 M HCl (20 mL) in a round bottom flask at room temperature. The resulting cloudy white suspension was heated to 100 °C and stirred at this temperature for 3 h. Purification by silica gel chromatography using 10-20% ethyl acetate in hexane produced compound **15d** as light-yellow solid (0.26 g, 1.274 mmol, 72% yield). The data obtained agrees with literature data.[7a] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.3 Hz, 2H), 5.93 (s, 1H), 4.24 (s, 2H), 3.79 (s, 3H), 2.11 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 156.2, 154.4, 132.7, 124.1, 120.8, 114.4, 56.5, 55.6, 15.3.

Asymmetric conjugate reduction catalysed by (R,S_p)-L3



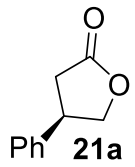
R = Alkyl or Aryl
X = O *or* NPMP

(R,S_p)-L3 was used as a pre-formed complex (bright-red powder). It was synthesised following a literature experimental procedure.[8a]

General experimental procedure for the asymmetric conjugate reduction

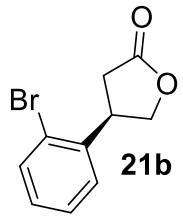
In a pre-flame dried round bottom flask under the inert atmosphere of argon, PMHS (0.30 mL) was added to the stirring red solution of pre-formed complex (R,S_p)-**L3** (6.91 mg, 0.00936 mmol, 0.03 eq.) in THF (5 mL) at room temperature. After 5 minutes, NaO*t*-Bu (60 mg, 0.624 mmol, 2.0 eq.) was added and effervescence occurred. The resulting light-yellow solution was stirred at room temperature for 10 minutes. A solution of β-substituted α,β-unsaturated lactone/lactam (0.312 mmol, 1.0 eq.) in THF (5 mL) was added, followed by the addition of *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control), quenched with saturated aqueous solution of ammonium chloride (30 mL) and extracted with EtOAc (40 mL). The organic layer was washed with de-ionised water (20 mL), brine (35 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 10-20% EtOAc in hexanes furnished chiral γ-lactones and γ-lactams.

(*R*)-4-Phenyldihydrofuran-2(3*H*)-one (**21a**)



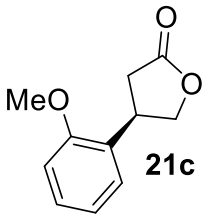
The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (6.91 mg, 0.00936 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (60 mg, 0.624 mmol, 2.0 eq.). A solution of α,β-unsaturated lactone **9a** (50 mg, 0.312 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 10-20% EtOAc in hexanes furnished chiral lactone (*R*)-**21a** (49 mg, 0.302 mmol, 97%) as light-brown oil. The data obtained is in agreement with literature data.[8b,c] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31–7.29 (m, 2H), 7.24–7.22 (m, 1H), 7.18–7.16 (m, 2H), 4.60 (dd, *J* = 9.1, 7.9, Hz, 1H), 4.20 (dd, *J* = 9.0, 7.9, Hz, 1H), 3.72 (pent, *J* = 8.0 Hz, 1H), 2.86 (dd, *J* = 17.4, 8.7, Hz, 1H), 2.61 (dd, *J* = 17.5, 9.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.5, 139.5, 129.3, 127.8, 126.8, 74.1, 41.2, 35.8. **Chiral HPLC**: 99% *ee* using chiral AS-3 column (*i*-PrOH:hexanes = 10:90, 0.8 mL/min, wavelength = 254 nm, 22 °C); t_R = 33.188 min (major), t_R = 37.224 min (minor); $[\alpha]_D^{22}$ = -34.7 (*c* = 0.66, $CHCl_3$). Lit.[8c] $[\alpha]_D^{20}$ = +46.0 (*c* = 0.95, $CHCl_3$) for (*S*)-isomer with 96% *ee*.

(*R*)-4-(2-Bromophenyl)dihydrofuran-2(3*H*)-one (**21b**)



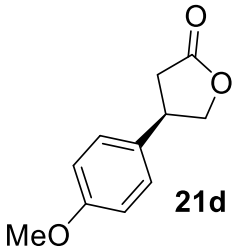
The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (6.91 mg, 0.00936 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (60 mg, 0.624 mmol, 2.0 eq.). A solution of α,β-unsaturated lactone **9b** (74.6 mg, 0.312 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 10-20% EtOAc in hexanes furnished chiral lactone (*R*)-**21b** (54 mg, 0.224 mmol, 71%) as brown oil. The data obtained is in agreement with literature data.[8c,d] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.9 Hz, 1H), 7.25–7.21 (m, 1H), 7.18–7.14 (m, 1H), 7.07–7.03 (m, 1H), 4.59 (dd, *J* = 8.9, 7.3 Hz, 1H), 4.19 (dd, *J* = 9.1, 5.9 Hz, 1H), 4.11 (pent, *J* = 7.4 Hz, 1H), 2.86 (dd, *J* = 17.6, 8.7 Hz, 1H), 2.55 (dd, *J* = 17.5, 6.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.2, 138.9, 133.6, 129.3, 128.4, 126.8, 124.5, 72.9, 40.2, 34.8. **Chiral HPLC**: 98% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 5:95, 0.5 mL/min, wavelength = 254 nm, 22 °C); t_R = 33.692 min (major), t_R = 27.821 min (minor); $[\alpha]_D^{22}$ = -35.6 (*c* = 0.45, $CHCl_3$). Lit.[8c] $[\alpha]_D^{20}$ = +26.6 (*c* = 1, $CHCl_3$) for (*S*)-isomer with 70% *ee*.

(*R*)-4-(2-Methoxyphenyl)dihydrofuran-2(3*H*)-one (**21c**)



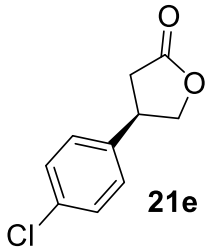
The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.20 mL), pre-formed complex (*R*,S_p)-**L3** (11.3 mg, 0.015 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (98 mg, 1.02 mmol, 2.0 eq.). A solution α,β-unsaturated lactone **9c** (93 mg, 0.51 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 10-20% EtOAc in hexanes furnished chiral lactone (*R*)-**21c** (67 mg, 0.349 mmol, 68%) as brown oil. The data obtained is in agreement with literature data.[8d] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 6.86–6.84 (m, 2H), 4.58 (app t, *J* = 8.5 Hz, 1H), 4.21 (app t, *J* = 8.7 Hz, 1H), 3.88 (pent, *J* = 8.7 Hz, 1H), 3.77 (s, 3H), 2.74–2.72 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.3, 157.3, 128.8, 127.8, 127.7, 120.8, 110.9, 73.0, 55.3, 36.8, 33.9. **Chiral HPLC**: 97% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 4:96, 0.5 mL/min, wavelength = 254 nm, 22 °C); t_R = 25.951 min (major), t_R = 24.881 min (minor); $[\alpha]_D^{22}$ = -39.8 (*c* = 0.96, $CHCl_3$). Lit.[8d] $[\alpha]_D^{20}$ = -48 (*c* = 1.24, $CHCl_3$) for (*R*)-isomer with 91:9 *e.r*.

(*R*)-4-(4-Methoxyphenyl)dihydrofuran-2(3*H*)-one (**21d**)



The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.20 mL), pre-formed complex (*R*,S_p)-**L3** (5.82 mg, 0.00789 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (51 mg, 0.526 mmol, 2.0 eq.). A solution of α,β-unsaturated lactone **9d** (50 mg, 0.263 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 10-20% EtOAc in hexanes furnished chiral lactone (*R*)-**21d** (48 mg, 0.25 mmol, 95%) as white solid. The data obtained is in agreement with literature data.[8d] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 4.62 (app t, *J* = 9.0 Hz, 1H), 4.21 (app t, *J* = 9.0 Hz, 1H), 3.79 (s, 3H), 3.73 (pent, *J* = 8.6 Hz, 1H), 2.88 (dd, *J* = 17.5, 8.6 Hz, 1H), 2.62 (dd, *J* = 17.5, 8.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.6, 159.2, 131.4, 127.8, 114.6, 74.4, 55.4, 40.5, 36.0. **Chiral HPLC**: 98% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 8:92, 0.6 mL/min, wavelength = 254 nm, 22 °C); t_R = 27.743 min (major), t_R = 26.815 min (minor); $[\alpha]_D^{22}$ = -28.0 (*c* = 0.82, $CHCl_3$). Lit.[8d] $[\alpha]_D^{20}$ = -48 (*c* = 0.81, $CHCl_3$) for (*R*)-isomer with 91:9 *e.r*.

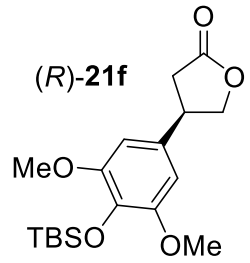
(*R*)-4-(4-Chlorophenyl)dihydrofuran-2(3*H*)-one (**21e**)



21e

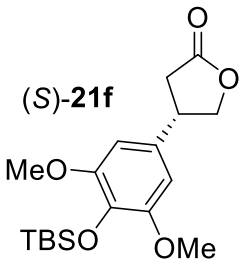
The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (6.91 mg, 0.00936 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (60 mg, 0.624 mmol, 2.0 eq.). A solution of α,β-unsaturated lactone **9e** (61 mg, 0.312 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 10-20% EtOAc in hexanes furnished chiral lactone (*R*)-**21e** (58 mg, 0.295 mmol, 95%) as light-brown oil. The data obtained is in agreement with literature data.[8c,d] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34–7.32 (m, 2H), 7.17–7.15 (m, 2H), 4.64 (app t, *J* = 9.2 Hz, 1H), 4.22 (app t, *J* = 9.2 Hz, 1H), 3.76 (pent, *J* = 8.5 Hz, 1H), 2.92 (dd, *J* = 17.5, 8.8 Hz, 1H), 2.62 (dd, *J* = 17.5, 8.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.0, 138.1, 133.7, 129.4, 128.1, 73.8, 40.6, 35.7. **Chiral HPLC**: 99% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 5:95, 0.5 mL/min, wavelength = 254 nm, 22 °C); t_R = 45.188 min (major), t_R = 43.693 min (minor); $[\alpha]_D^{22}$ = -22.1 (*c* = 0.49, $CHCl_3$). lit.[8d] $[\alpha]_D^{20}$ = -47 (*c* = 1.36, $CHCl_3$) for (*R*)-isomer with 92:8 *e.r*.

(*R*)-4-(4-((*Tert*-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)dihydrofuran-2(3*H*)-one (**21f**)



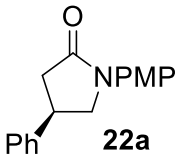
The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (6.32 mg, 0.0086 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (54.8 mg, 0.57 mmol, 2.0 eq.). A solution of α,β-unsaturated lactone **9f** (100 mg, 0.285 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 22 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated chiral lactone (*R*)-**21f** (78.1 mg, 0.222 mmol, 78%) as white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.36 (s, 2H), 4.63 (dd, *J* = 9.1, 7.8 Hz, 1H), 4.25 (dd, *J* = 9.1, 7.7 Hz, 1H), 3.78 (s, 6H), 3.68 (pent, *J* = 7.8 Hz, 1H), 2.89 (dd, *J* = 17.6, 7.8 Hz, 1H), 2.65 (dd, *J* = 17.6, 7.8 Hz, 1H), 0.99 (s, 9H), 0.11 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.6, 152.1, 134.1, 132.0, 103.8, 74.4, 56.0, 41.4, 36.0, 25.9, 18.8, 4.4. **HRMS** (ESI): calc. for $C_{18}H_{28}O_5Si$ m/z: 352.1706 found $[M+Na]^+$ 375.1603. **IR (neat)**: 2931, 1776, 1590, 1515, 1465, 1244, 1177, 1122, 1020. **MP**: 135–140 °C. **Chiral HPLC**: 99% *ee* using chiral OD-H column (*i*-PrOH:hexanes = 7:93, 0.5 mL/min, wavelength = 254 nm, 22 °C); t_R = 31.611 min (major), t_R = 35.965 min (minor); $[\alpha]_D^{22}$ = -21.6 (*c* = 0.23, $CHCl_3$).

(*S*)-4-(4-((*Tert*-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)dihydrofuran-2(3*H*)-one (**21f**)



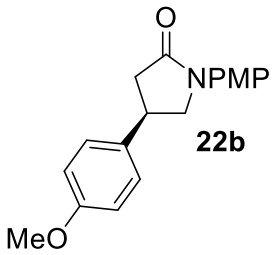
The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.15 mL), pre-formed complex (S,R_p)-**L3** (3.16 mg, 0.0043 mmol, 0.03 eq.) in THF (2.5 mL) and NaO*t*-Bu (27.4 mg, 0.285 mmol, 2.0 eq.). A solution of α,β-unsaturated lactone **9f** (50 mg, 0.143 mmol, 1.0 eq.) in THF (2.5 mL) and *t*-BuOH (0.5 mL). The resulting mixture was stirred at room temperature till completion (approx. 22 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated chiral lactone (*S*)-**21f** (39 mg, 0.111 mmol, 78%) as white solid. **Chiral HPLC**: 99% *ee* using chiral OD-H column (*i*-PrOH:hexanes = 7:93, 0.5 mL/min, wavelength = 254 nm, 22 °C); t_R = 35.047 min (major), t_R = 32.096 min (minor); $[\alpha]_D^{22}$ = +25.5 (*c* = 0.63, $CHCl_3$).

(*R*)-1-(4-Methoxyphenyl)-4-phenylpyrrolidin-2-one (22a)



The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (R,S_p)-**L3** (6.91 mg, 0.00936 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (60 mg, 0.624 mmol, 2.0 eq.). A solution of α,β-unsaturated lactam **15a** (82.78 mg, 0.312 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated chiral lactam (*R*)-**22a** (79 mg, 0.296 mmol, 95%) as white solid. The data obtained is in agreement with literature data.[7b] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.9 Hz, 2H), 7.28 (app t, *J* = 7.4 Hz, 2H), 7.21 (app d, *J* = 7.3 Hz, 3H), 6.83 (d, *J* = 8.8 Hz, 2H), 4.07 (dd, *J* = 9.4, 8.0 Hz, 1H), 3.77 (dd, *J* = 9.4, 7.6 Hz, 1H), 3.71 (s, 3H), 3.61 (pent, *J* = 8.1 Hz, 1H), 2.96 (dd, *J* = 16.9, 8.8 Hz, 1H), 2.69 (dd, *J* = 16.9, 8.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.7, 156.7, 141.9, 132.4, 129.0, 127.3, 126.8, 121.9, 114.2, 56.1, 55.5, 40.2, 37.3. **Chiral HPLC**: 96% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 20:80, 1.0 mL/min, wavelength = 254 nm, 22 °C); t_R = 21.988 min (major), t_R = 15.434 min (minor); $[\alpha]_D^{22}$ = +3.6 (*c* = 0.56, $CHCl_3$). Lit.[9c] $[\alpha]_D^{26}$ = +9.5 (*c* = 1.0, $CHCl_3$) for (*R*)-isomer with 89.2% *ee*.

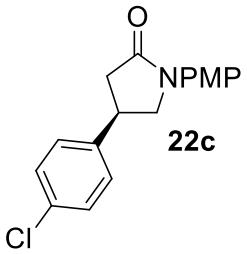
(*R*)-1,4-bis(4-Methoxyphenyl)pyrrolidin-2-one (**22b**)



The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (R,S_p)-**L3** (3.32 mg, 0.00449 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (28.83 mg, 0.300 mmol, 2.0 eq.). A solution of α,β-unsaturated lactam **15b** (44.3 mg, 0.15 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated chiral lactam (*R*)-**22b** (41 mg, 0.137 mmol, 91%) as light yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 6.90–6.88 (m, 4H), 4.11 (dd, *J* = 9.5, 8.0 Hz,

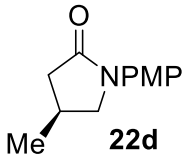
1H), 3.81–3.79 (m, 7H), 3.64 (pent, *J* = 8.2 Hz, 1H), 2.96 (dd, *J* = 16.9, 8.8 Hz, 1H), 2.73 (dd, *J* = 16.9, 8.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.8, 158.8, 156.8, 133.8, 132.5, 127.9, 121.9, 114.4, 114.2, 56.4, 55.6, 55.4, 40.4, 36.7. **HRMS** (ESI): calc. for $C_{18}H_{19}O_3N$ m/z: 297.1365 found $[M+Na]^+$ 320.1262. **IR (neat)**: 2933, 1678, 1507, 1401, 1293, 1227, 1179, 1026. **MP**: 105–110 °C. **Chiral HPLC**: 97% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 20:80, 1.0 mL/min, wavelength = 254 nm, 22 °C); t_R = 35.264 min (major), t_R = 23.822 min (minor); $[\alpha]_D^{22}$ = +9.8 (*c* = 0.61, $CHCl_3$).

(*R*)-4-(4-Chlorophenyl)-1-(4-methoxyphenyl)pyrrolidin-2-one (**22c**)



The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (3.32 mg, 0.00449 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (28.83 mg, 0.300 mmol, 2.0 eq.). A solution of α,β-unsaturated lactam **15c** (45 mg, 0.15 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated chiral lactam (*R*)-**22c** (39 mg, 0.129 mmol, 86%) as white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51–7.49 (m, 2H), 7.37–7.35 (m, 2H), 7.30–7.28 (m, 2H), 6.91–6.89 (m, 2H), 4.15 (dd, *J* = 9.2, 7.9 Hz, 1H), 3.86 (dd, *J* = 9.3, 7.9 Hz, 1H), 3.79 (s, 3H), 3.68 (pent, *J* = 8.1 Hz, 1H), 3.00 (dd, *J* = 17.0, 8.8 Hz, 1H), 2.77 (dd, *J* = 16.9, 8.7 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.7, 156.8, 141.9, 132.4, 129.1, 127.4, 126.9, 122.0, 114.2, 56.2, 55.6, 40.2, 37.3. **HRMS** (ESI): calc. for $C_{17}H_{16}NO_2Cl$ m/z: 301.0870 found $[M+Na]^+$ 324.0767. **IR (neat)**: 2935, 1681, 1507, 1401, 1356, 1294, 1238, 1183, 1030. **MP**: 75–80 °C. **Chiral HPLC**: 95% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 20:80, 1.0 mL/min, wavelength = 254 nm, 22 °C); t_R = 28.875 min (major), t_R = 19.727 min (minor); $[\alpha]_D^{22}$ = +18.4 (*c* = 0.59, $CHCl_3$).

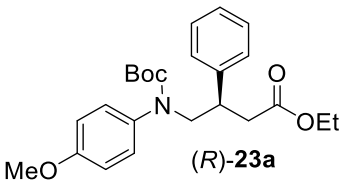
(*S*)-4-Methyl-1-(4-methoxy-phenyl)-pyrrolidin-2-one (**22d**)



The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (6.91 mg, 0.00936 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (60 mg, 0.624 mmol, 2.0 eq.). A solution of α,β-unsaturated lactam **15d** (63.4 mg, 0.312 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated chiral lactam (*S*)-**22d** (60 mg, 0.292 mmol, 94%) as white solid. The data obtained is in agreement with literature data.[7a] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.1 Hz, 2H), 6.87 (d, *J* = 8.2 Hz, 2H), 3.88 (dd, *J* = 9.4, 7.5 Hz, 1H), 3.77 (s, 3H), 3.38 (dd, *J* = 9.4, 6.3 Hz, 1H), 2.71 (dd, *J* = 16.7, 8.4 Hz, 1H), 2.53 (dq, *J* = 13.9, 6.7 Hz, 1H), 2.21 (dd, *J* = 16.6, 7.3 Hz, 1H), 1.18 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 156.6, 132.7, 121.8, 114.1, 56.4, 55.5, 40.8, 26.4, 19.6. **Chiral HPLC**: 98% *ee* using chiral AS-3 column (*i*-PrOH:hexanes =

20:80, 1.0 mL/min, wavelength = 254 nm, 22 °C); t_R = 25.897 min (major), t_R = 23.806 min (minor); $[\alpha]_D^{22}$ = -2.3 (*c* = 0.87 or 8.7 mg/mL, $CHCl_3$).

Ethyl (*R*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-phenylbutanoate (**23a**)

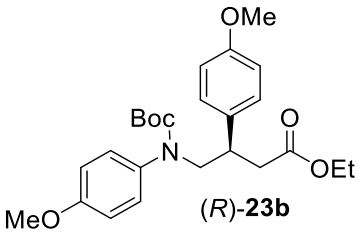


(*R*)-**23a**

The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.20 mL), pre-formed complex (*R*,S_p)-**L3** (5.38 mg, 0.0073 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (46.7 mg, 0.486 mmol, 2.0 eq.). A solution of compound (*Z*)-**14a** (100 mg, 0.243 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated compound (*R*)-**23a** (89 mg, 0.215 mmol, 88%) as colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11–7.09 (m, 2H), 7.07–7.05 (m, 1H), 7.01–6.99 (m, 2H), 6.77–6.75 (m, 2H), 6.67–6.65 (m, 2H), 3.83 (q, *J* = 7.2 Hz, 2H), 3.77–3.75 (m, 1H), 3.65 (br s, 4H), 3.21 (dq, *J* = 15.4, 8.2 Hz, 1H), 2.55 (dd, *J* = 15.4, 9.4 Hz, 1H), 2.43 (dd, *J* = 15.4, 9.3 Hz, 1H), 1.20 (br, 9H), 0.93 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.9, 157.6, 155.0, 141.1, 134.9, 128.38, 128.36, 128.0, 126.8, 113.9, 80.1, 60.3, 55.4, 41.0, 38.6, 28.2, 14.0. **HRMS** (ESI): calc. for $C_{24}H_{31}NO_5$ m/z: 413.2202 found $[M+Na]^+$ 436.2099. **IR (neat)**: 2974, 1731, 1692, 1510, 1245, 1148, 1030. **Chiral HPLC**: 83% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 8:92, 0.8 mL/min, wavelength = 254 nm, 22 °C); t_R = 8.929 min (major), t_R = 8.456 min (minor); $[\alpha]_D^{22}$ = +19.3 (*c* = 1.14, $CHCl_3$).

Large scale (using 1.8 mol% of catalyst): (*Z*)-**14a** (1.71 g, 4.156 mmol, 1.0 eq.), NaO*t*-Bu (0.799 g, 8.311 mmol, 2.0 eq.), complex (*R*,S_p)-**L3** (55 mg, 0.075 mmol, 0.018 eq.), PMHS (4 mL), THF (40 mL) and *t*-BuOH (4 mL). Compound (*R*)-**23a** (1.50 g, 3.627 mmol, 87% yield, 78% *ee*).

Ethyl (*R*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-(4-methoxyphenyl)butanoate (**23b**)

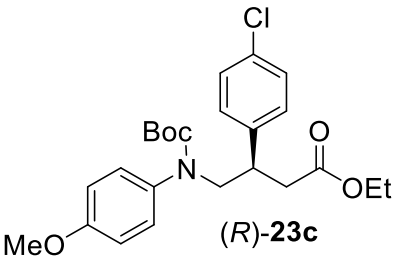


(*R*)-**23b**

The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.30 mL), pre-formed complex (*R*,S_p)-**L3** (5.84 mg, 0.0079 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (50.7 mg, 0.528 mmol, 2.0 eq.). A solution of compound (*Z*)-**14b** (116.5 mg, 0.264 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated compound (*R*)-**23b** (92 mg, 0.21 mmol, 79%) as colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.2 Hz, 2H), 6.89 (br s, 2H), 6.80–6.78 (m, 4H), 3.96 (q, *J* = 7.2 Hz, 2H), 3.86 (br s, 1H), 3.78 (s, 3H), 3.76 (br s, 4H), 3.29 (dq, *J* = 15.4, 7.8 Hz, 1H), 2.66 (dd, *J* = 15.4, 9.4 Hz, 1H), 2.52 (dd, *J* = 15.4, 9.5 Hz, 1H), 1.23 (s, 9H), 0.95 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.1, 158.6, 157.7, 155.2, 135.0, 133.3, 129.1, 128.5, 113.8, 80.2, 60.4, 55.5, 55.3, 40.3, 38.9, 28.3, 14.2. **HRMS** (ESI): calc. for $C_{25}H_{33}NO_6$ m/z: 443.2308 found $[M+Na]^+$

466.2205. **IR (neat)**: 2972, 1731, 1692, 1510, 1390, 1245, 1148, 1031. **Chiral HPLC**: 83% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 8:92, 0.8 mL/min, wavelength = 254 nm, 22 °C); t_R = 13.915 min (major), t_R = 12.718 min (minor); $[\alpha]_D^{22}$ = +21.8 (*c* = 1.71, $CHCl_3$).

Ethyl (*R*)-4-((*tert*-butoxycarbonyl)(4-methoxyphenyl)amino)-3-(4-chlorophenyl)butanoate (23c)



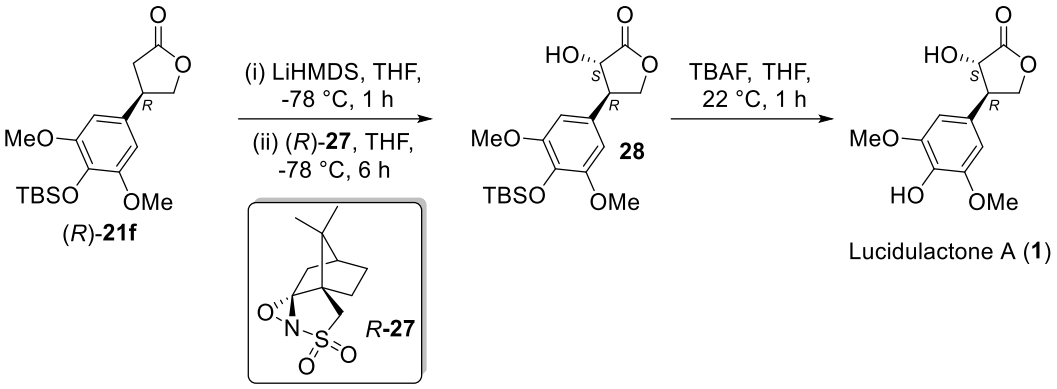
(*R*)-**23c**

The general procedure for the conjugate asymmetric reduction was followed, using PMHS (0.20 mL), pre-formed complex (R,S_p)-**L3** (2.73 mg, 0.0037 mmol, 0.03 eq.) in THF (5 mL) and NaO*t*-Bu (23.6 mg, 0.246 mmol, 2.0 eq.). A solution of compound (*Z*)-**14c** (55 mg, 0.123 mmol, 1.0 eq.) in THF (5 mL) and *t*-BuOH (1 mL). The resulting mixture was stirred at room temperature till completion (approx. 12 h, TLC control). Purification by silica gel chromatography using 20% EtOAc in hexanes generated compound (*R*)-**23c** (52.4 mg, 0.117 mmol, 95%) as light-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11–7.09 (m, 2H), 6.96 (d, *J* = 7.9 Hz, 2H), 6.74 (br s, 2H), 6.67 (d, *J* = 7.8 Hz, 2H), 3.85 (q, *J* = 7.2 Hz, 2H), 3.72–3.70 (m, 2H), 3.66 (s, 3H), 3.21 (dq, *J* = 15.4, 7.9 Hz, 1H), 2.54 (dd, *J* = 15.4, 5.9 Hz, 1H), 2.40 (dd, *J* = 15.4, 5.9 Hz, 1H), 1.21 (br s, 9H), 0.97 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7, 157.8, 155.1, 139.8, 134.8, 132.7, 129.5, 128.5, 128.4, 114.0, 80.3, 60.5, 55.5, 40.6, 38.6, 28.3, 14.2. **HRMS** (ESI): calc. for $C_{24}H_{30}NO_5Cl$ m/z: 447.1813 found $[M+Na]^+$ 470.1710. **IR (neat)**: 2975, 1731, 1691, 1510, 1390, 1290, 1245, 1150, 1031. **Chiral HPLC**: 85% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 8:92, 0.8 mL/min, wavelength = 254 nm, 22 °C); t_R = 10.781 min (major), t_R = 9.905 min (minor); $[\alpha]_D^{22}$ = +27.0 (*c* = 0.77, $CHCl_3$).

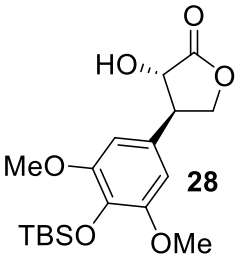
Large scale: (*Z*)-**14c** (1.10 g, 2.46 mmol, 1.0 eq.), NaO*t*-Bu (0.472 g, 4.92 mmol, 2.0 eq.), complex (R,S_p)-**L3** (54.6 mg, 0.074 mmol, 0.03 eq.), PMHS (4 mL), THF (40 mL) and *t*-BuOH (4 mL). Compound (*R*)-**23c** (1.05 g, 2.34 mmol, 95% yield, 85% *ee*).

Conversion of (*R*)-**23c** to (*R*)-**22c**: (*R*)-**23c** (200 mg, 0.446 mmol, 85% *ee*) was dissolved in MeOH (5 mL) and added to a flask containing 6 M HCl (20 mL). The resulting mixture was refluxed for 2 h. (*R*)-**22c** (87.1 mg, 0.289 mmol, 65% yield; 83% *ee*) was obtained as a white solid.

Synthesis of Lucidulactone A (1)

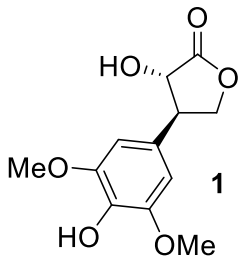


(3*S*,4*R*)-4-(4-((*Tert*-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)-3-hydroxydihydrofuran-2(3*H*)-one (**28**)

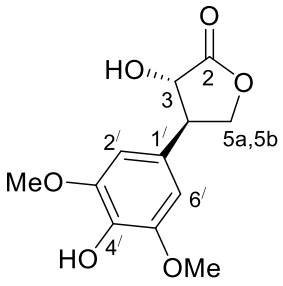


In a pre-flame dried round bottom flask under the atmosphere of argon, chiral lactone (*R*)-**21f** (100 mg, 0.284 mmol, 1.0 eq.) was dissolved in THF (12 mL). The colourless solution was cooled to -78 °C and after 5 minutes, LiHMDS (1.0 M in THF, 0.34 mL, 0.340 mmol, 1.2 eq.) was added at -78 °C. The resulting mixture was left to stir at -78 °C for 1 h followed by the addition of a solution of commercially available (*R*)-**27** (104.1 mg, 0.454 mmol, 1.6 eq.) in THF (6 mL). The reaction was stirred at -78 °C till completion (approx. 6 h; TLC control), then allowed to warm up to room temperature, quenched with saturated aqueous solution of NH_4Cl (30 mL) and extracted with EtOAc (30 mL). The organic layer was washed with de-ionised water (25 mL), brine (25 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture of **28** was used in the next reaction without purification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.45 (s, 2H), 4.63 (t, *J* = 8.7 Hz, 1H), 4.53 (d, *J* = 10.9 Hz, 1H), 4.21 (t, *J* = 10.3 Hz, 1H), 3.79 (s, 6H), 3.60 (q, *J* = 10.3 Hz, 1H), 0.99 (s, 9H), 0.11 (s, 6H). **Chiral HPLC**: 99% *ee* using chiral IA-3 column (*i*-PrOH:hexanes = 7:93, 0.7 mL/min, wavelength = 254 nm, 22 °C); t_R = 25.552 min (major), t_R = 20.179 min (minor).

(3*S*,4*R*)-3-Hydroxy-4-(4-hydroxy-3,5-dimethoxyphenyl)dihydrofuran-2(3*H*)-one (**1**)



In a pre-flame dried round bottom flask under the atmosphere of argon, crude compound **28** (56 mg, 0.152 mmol, 1.0 eq.) was dissolved in THF (12 mL) and TBAF (1.0 M in THF, 0.182 mL, 0.18 mmol, 1.2 eq.) was added at room temperature. The resulting mixture was left to stir till completion (approx. 1 h; TLC control), then diluted with EtOAc (20 mL) and washed with saturated aqueous solution of NH_4Cl (15 mL). The organic layer was washed with de-ionised water (15 mL), brine (15 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography using 40% EtOAc in hexanes. Lucidulactone A **1** (27.4 mg, 0.108 mmol, 71%) was obtained as white solid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.28 (s, 1H), 6.69 (s, 2H), 6.03 (d, *J* = 7.0 Hz, 1H), 4.57 (dd, *J* = 10.9, 7.0 Hz, 1H), 4.46 (t, *J* = 8.4 Hz, 1H), 4.14 (dd, *J* = 10.8, 9.0 Hz, 1H), 3.75 (s, 6H), 3.37–3.43 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 176.6, 148.0, 134.8, 127.2, 105.3, 72.3, 68.9, 56.0, 49.3. **MP**: 105–110 °C **HRMS** (ESI): *m*/*z* calcd for $C_{12}H_{15}O_6$ [M+H] 255.0790, found 255.0789. **IR (neat)**: 3400, 2924, 1771, 1580, 1510, 1459, 1248, 1120. $[\alpha]_D^{22}$ = -80 (*c* = 0.10, MeOH). Lit.[10f] $[\alpha]_D^{23}$ = -82 (*c* = 0.15, MeOH).

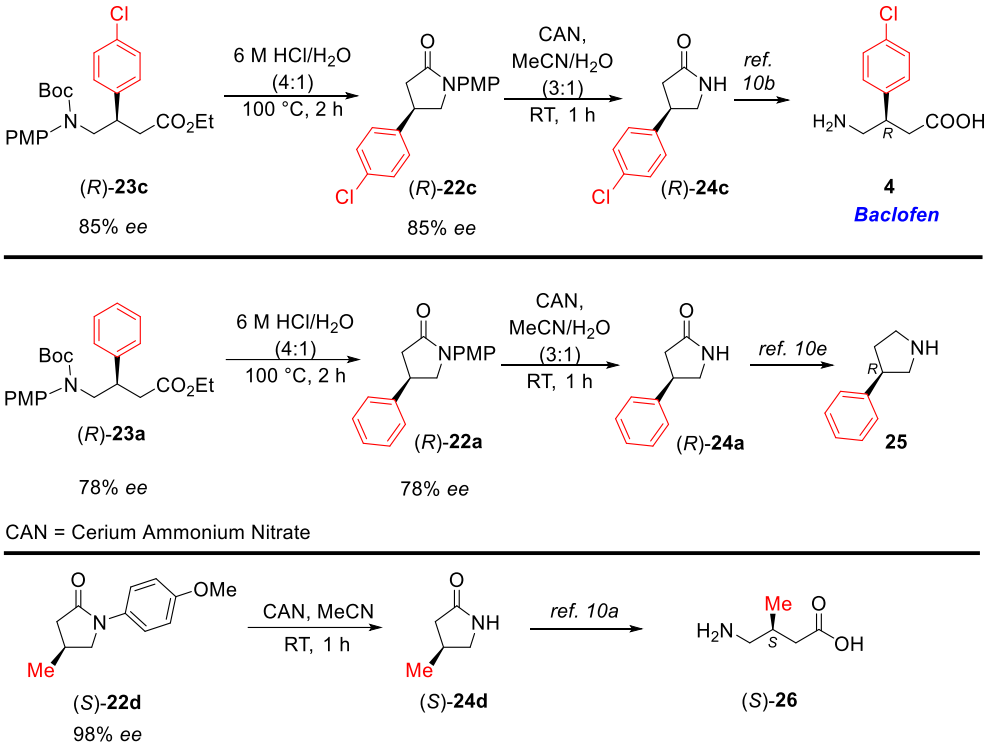


Lucidulactone A (**1**)

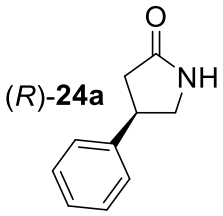
Table 1: Reported and Synthetic ^{1}H and ^{13}C NMR spectra data for compound **1**

	Isolated **1**			Synthetic **1**	
No.	δ_H, *J* (Hz)	δ_C	No.	δ_H, *J* (Hz)	δ_C
2		176.7	2		176.6
3	4.57 dd (11.1, 7.0)	72.4	3	4.57 dd (10.9, 7.0)	72.3
4	3.37-3.40 m	49.3	4	3.37-3.43 m	49.3
5a	4.45-4.47 m	69.0	5a	4.46 t (8.4)	68.9
5b	4.14 dd (11.1, 8.8)		5b	4.14 dd (10.8, 9.0)	
1′		127.2	1′		127.2
2′, 6′	6.69 s	105.3	2′, 6′	6.69 s	105.3
3′, 5′		148.0	3′, 5′		148.0
4′		134.8	4′		134.8
3-OH	6.07 d (7.0)		3-OH	6.03 d (7.0)	
4′-OH	8.32 s		4′-OH	8.28 s	
3′,5′-OCH_3	3.74 s	56.0	3′,5′-OCH_3	3.75 s	56.0

Formal synthesis of β-substituted GABA derivatives and a chiral pyrrolidine

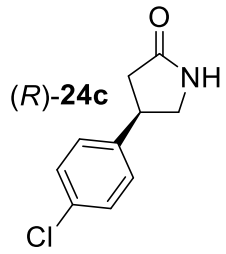


(*R*)-4-Phenylpyrrolidin-2-one (24a)



CAN (0.61 g, 1.12 mmol, 3 eq.) was added portion-wise (1 eq. was added first, then after 15 mins another 2 eq. was added) to a stirring solution of compound (*R*)-**22a** (100 mg, 0.37 mmol, 1.0 eq.) in MeCN (3 mL) and H_2O (1 mL) at room temperature. After the addition of CAN was complete, the resulting light-red solution was stirred till completion (approx. 0.5 hr; TLC control), quenched with saturated aqueous solution of NH_4Cl (10 mL) and extracted with EtOAc (15 mL). The aqueous layer was further extracted with EtOAc twice (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 5-10% MeOH in DCM furnished (*R*)-**24a**[10c,d] (54 mg, 0.335 mmol, 91%) as off-white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.20–7.14 (m, 4H), 3.71 (app t, *J* = 8.7 Hz, 1H), 3.60 (pent, *J* = 8.3 Hz, 1H), 3.35 (dd, *J* = 9.4, 7.4 Hz, 1H), 2.66 (dd, *J* = 16.9, 8.9 Hz, 1H), 2.43 (dd, *J* = 16.9, 8.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.1, 142.2, 128.9, 127.1, 126.8, 49.7, 40.3, 38.1. $[\alpha]_D^{22}$ = -29.3 (*c* = 0.85, $CHCl_3$).

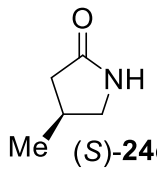
(*R*)-4-(4-Chlorophenyl)pyrrolidin-2-one (24c)



(*R*)-**24c**

CAN (0.27 g, 0.497 mmol, 3 eq.) was added portion-wise (1 eq. was added first, then after 15 mins another 2 eq. was added) to a stirring solution of compound (*R*)-**22c** (50 mg, 0.166 mmol, 1.0 eq.) in MeCN (3 mL) and H_2O (1 mL) at room temperature. After the addition of CAN was complete, the resulting light-red solution was stirred till completion (approx. 0.5 hr; TLC control), quenched with saturated aqueous solution of NH_4Cl (10 mL) and extracted with EtOAc (15 mL). The aqueous layer was further extracted with EtOAc twice (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 5-10% MeOH in DCM furnished (*R*)-**24c**[10b] (30 mg, 0.153 mmol, 92%) as off-white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.84 (br s, 1H), 3.77 (app t, *J* = 8.9 Hz, 1H), 3.66 (pent, *J* = 8.3 Hz, 1H), 3.36 (dd, *J* = 9.3, 7.1 Hz, 1H), 2.72 (dd, *J* = 16.9, 8.9 Hz, 1H), 2.43 (dd, *J* = 16.8, 8.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.7, 140.8, 133.0, 129.1, 128.2, 49.5, 39.7, 38.0. $[\alpha]_D^{22}$ = -23.5 (*c* = 0.51, $CHCl_3$).

(*S*)-4-Methylpyrrolidin-2-one (24d)



(*S*)-**24d**

CAN (0.32 g, 0.584 mmol, 3 eq.) was added portion-wise (1 eq. was added first, then after 15 mins another 2 eq. was added) to a stirring solution of compound (*S*)-**22d** (40 mg, 0.195 mmol, 1.0 eq.) in MeCN (3 mL) and H_2O (1 mL) at room temperature. After the addition of CAN was complete, the resulting light-red solution was stirred till completion (approx. 0.5 hr; TLC control), quenched with saturated aqueous solution of NH_4Cl (10 mL) and extracted with EtOAc (15 mL). The aqueous layer was further extracted with EtOAc twice (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography using 5-10% MeOH in DCM furnished (*S*)-**24d**[10a] (10 mg, 0.100 mmol, 52%) as light brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.68 (br s, 1H), 3.50 (app t, *J* = 8.4 Hz, 1H), 2.96 (dd, *J* = 9.2, 6.1 Hz, 1H), 2.56 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.45 (dd, *J* = 16.5, 8.5 Hz, 1H), 1.94 (dd, *J* = 16.5, 7.2 Hz, 1H), 1.14 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.7, 50.1, 38.5, 29.5, 19.7. $[\alpha]_D^{22}$ = -11.8 (*c* = 0.51, $CHCl_3$). Lit.[11a] $[\alpha]_D^{23}$ = -15 (*c* = 0.20, $CHCl_3$) for the *S*-enantiomer. Lit.[11b] $[\alpha]_D^{23}$ = +30.0 (*c* = 1.08, $CHCl_3$) for the *R*-enantiomer.

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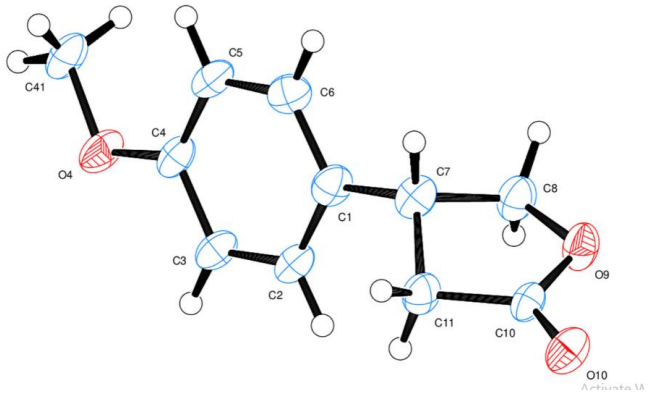
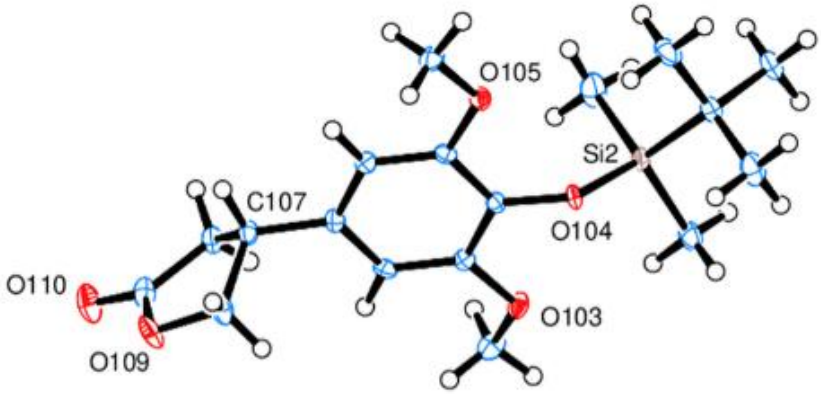
X-ray Crystal Structure Representations

Crystal structure analysis of (*R*)-21d (CCDC 2121166)



Crystal data: $C_{11}H_{12}O_3$, M = 192.21. Monoclinic, space group $P2_1$ (no. 4), a = 7.0003(5), b = 7.5875(3), c = 9.1343(7) Å, β = 106.874(7) °, V = 464.28(5) $Å^3$. Z = 2, Dc = 1.375 g cm^{-3}, F(000) = , T = 100.01(10) K, μ(Cu-Kα) = 8.2 cm^{-1}, λ(Cu-Kα) = 1.54184 Å.

Crystal structure analysis of (*R*)-21f (CCDC 2121167)

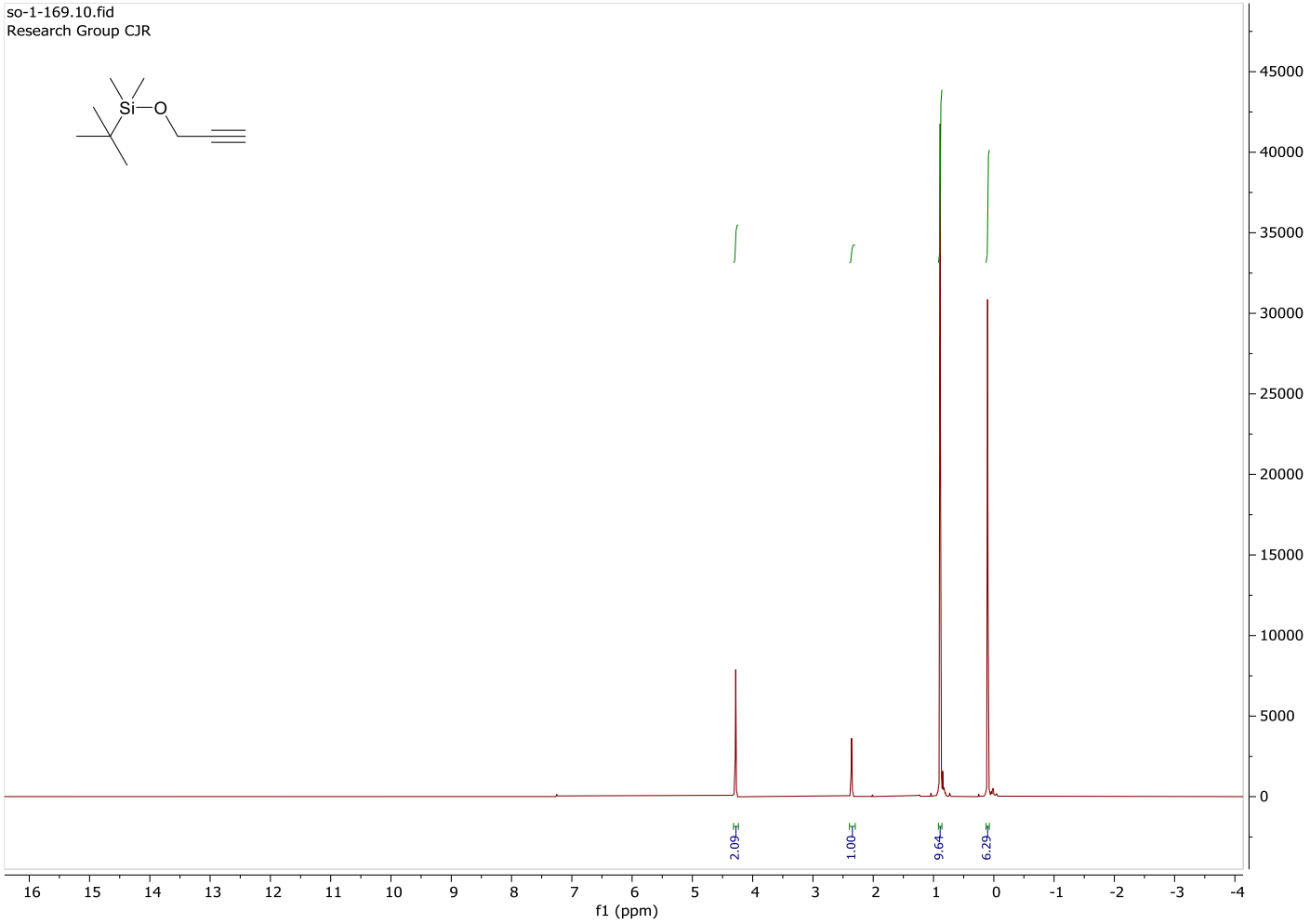


Crystal data: $C_{18}H_{28}O5Si$, M = 352.49. Monoclinic, space group $P2_1$ (no. 4), a = 7.1914(4), b = 10.5484(5), c = 24.6032(13) Å, β = 91.051(4) °, V = 1866.03(17) $Å^3$. Z = 4, Dc = 1.255 g cm^{-3}, F(000) = 760, T = 100.01(10) K, μ(Mo-Kα) = 1.5 cm^{-1}, λ(Mo-Kα) = 0.71073 Å.

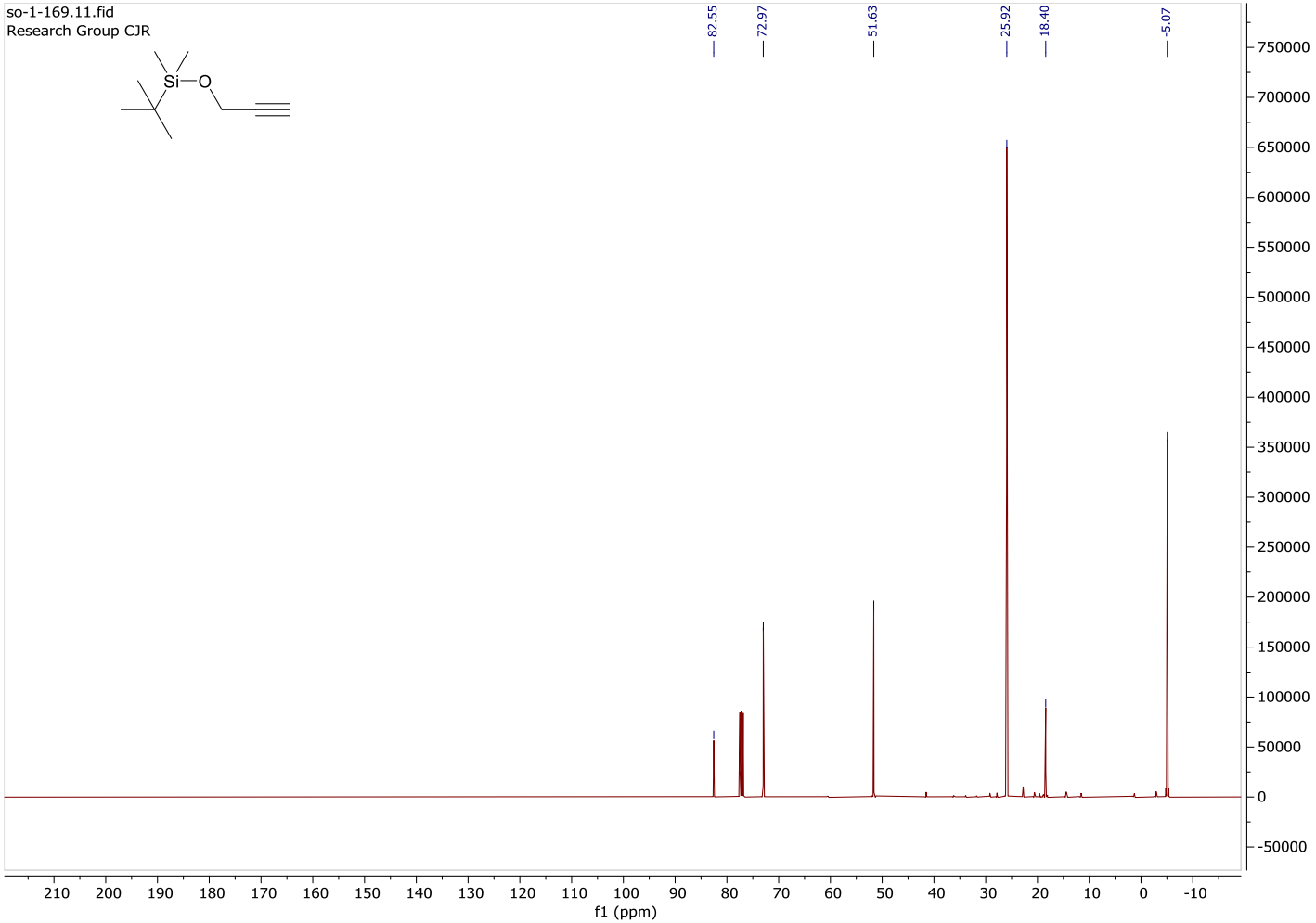
^{1}H and ^{13}C
NMR Spectra

All as: ^{1}H (400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$), unless otherwise stated.

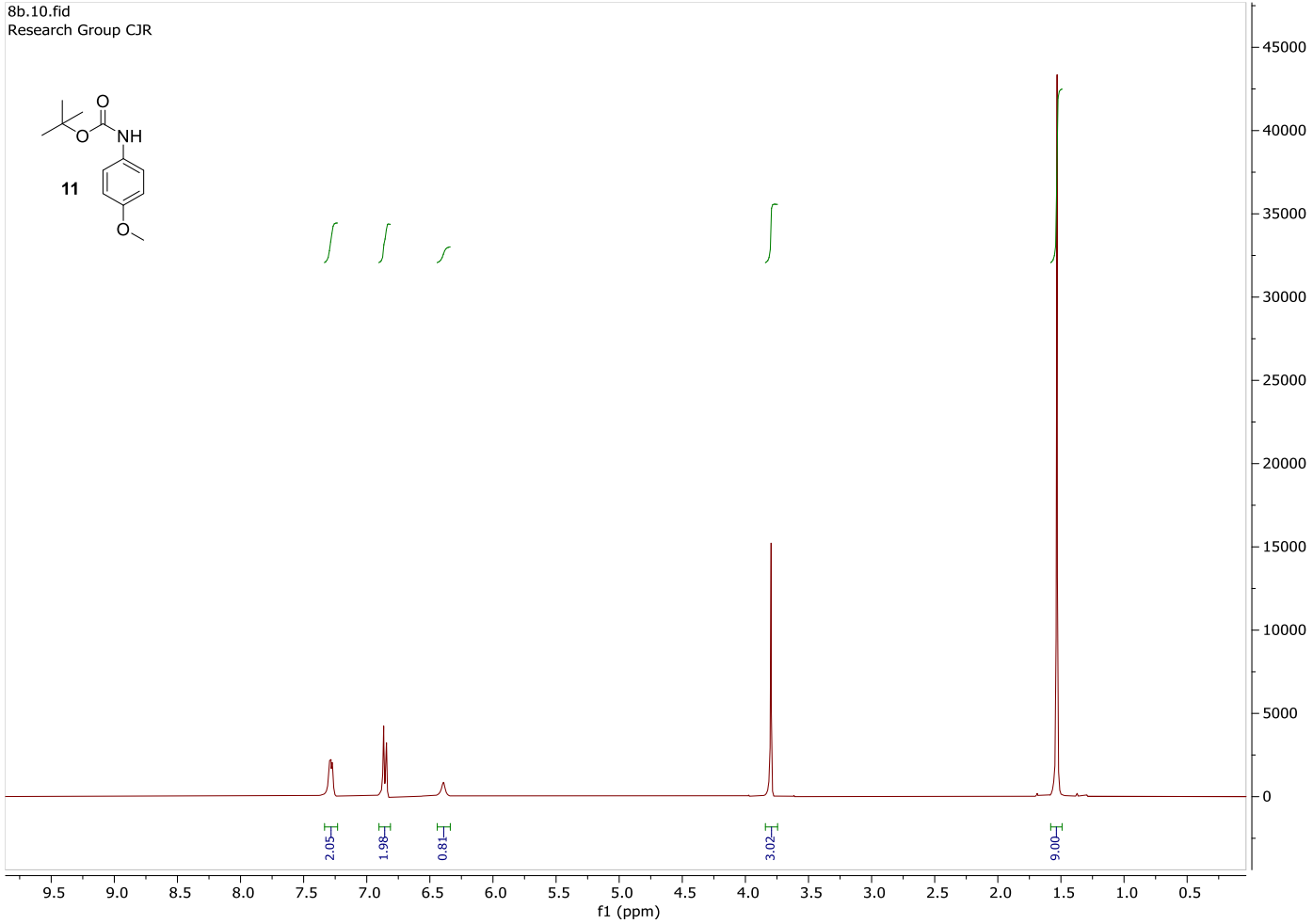
Compound **6** ^{1}H (400 MHz, $CDCl_3$)



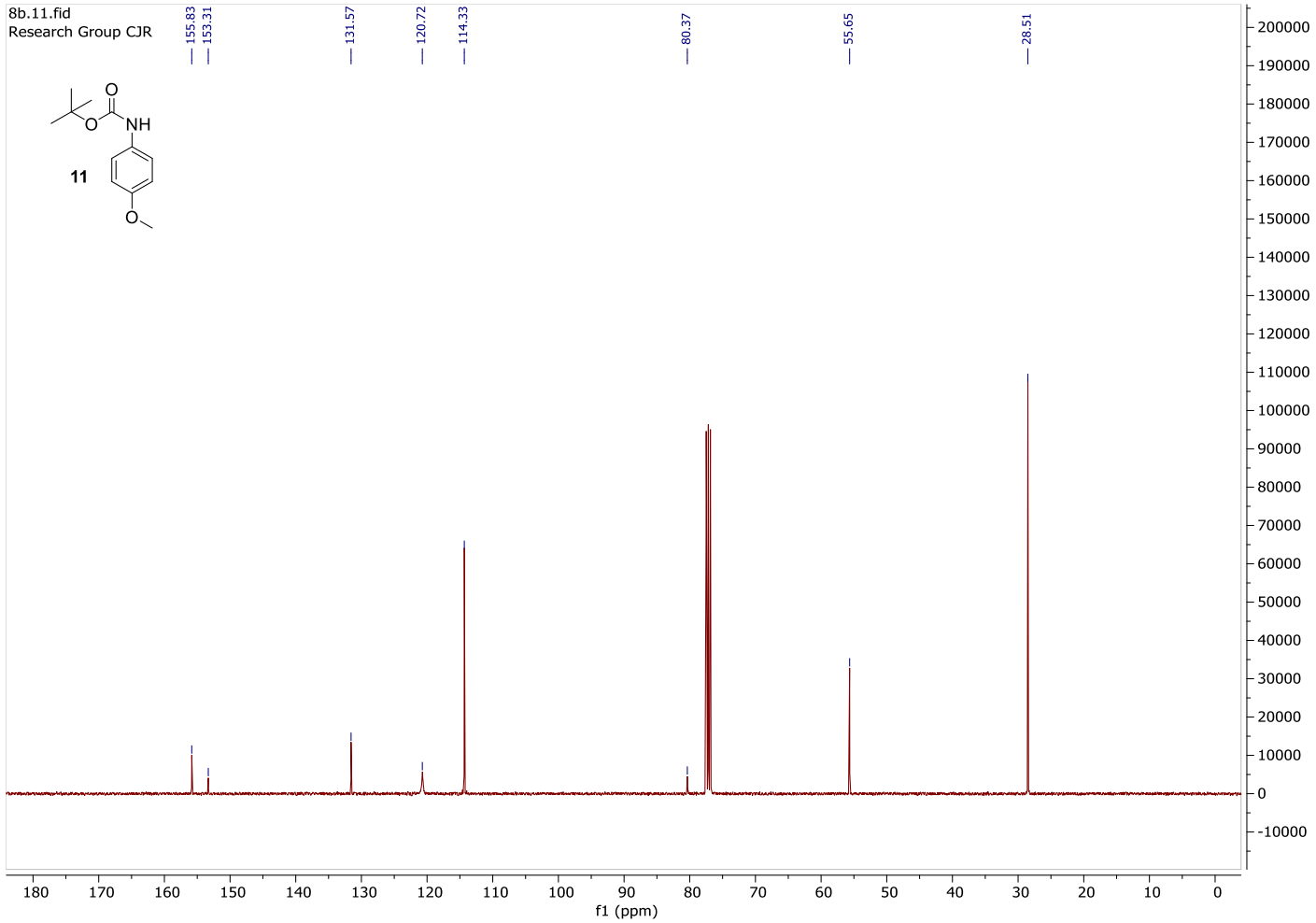
Compound **6** ^{13}C (101 MHz, $CDCl_3$)



Compound **11** ^{1}H (400 MHz, $CDCl_3$)



Compound **11** ^{13}C (101 MHz, $CDCl_3$)



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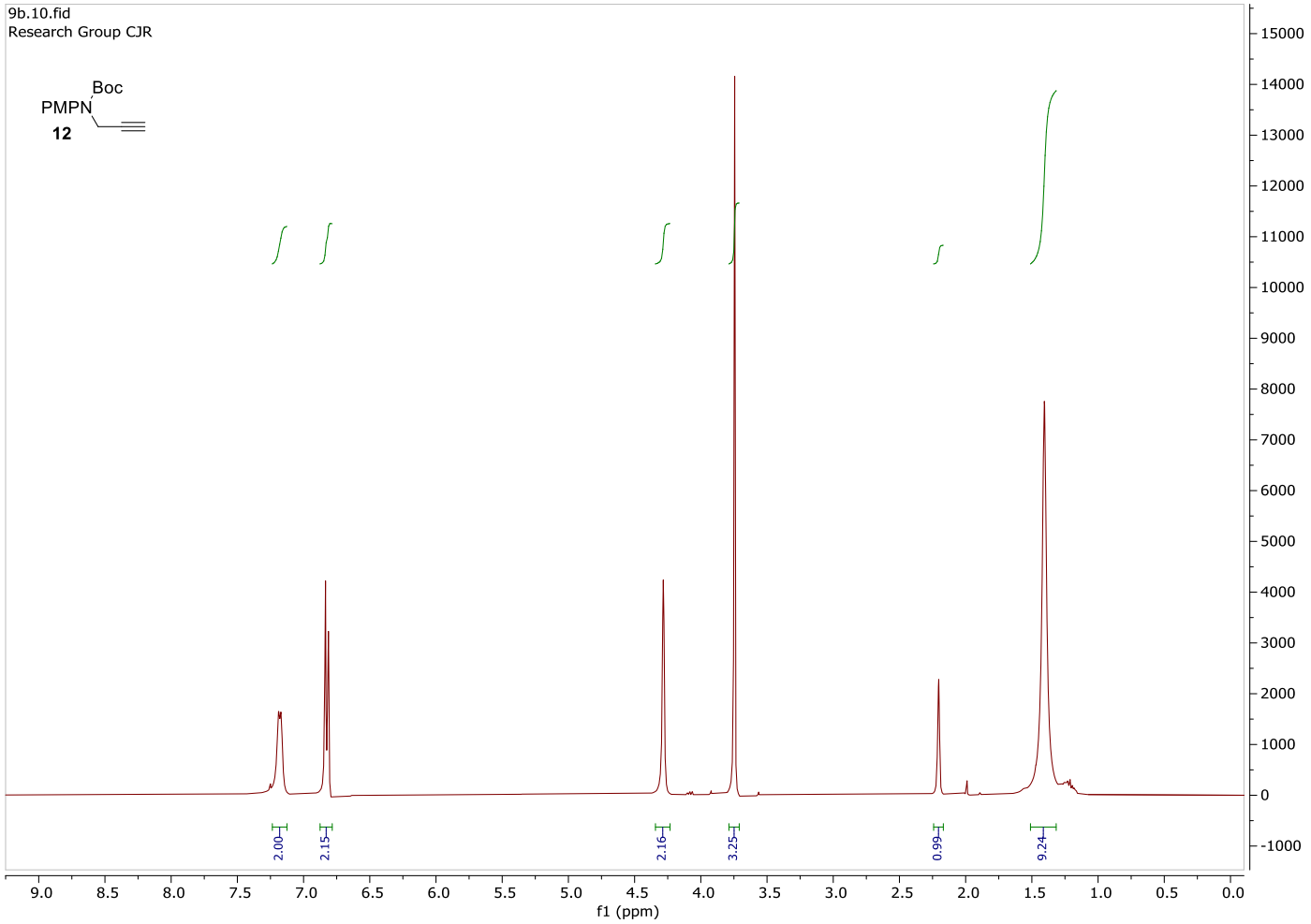

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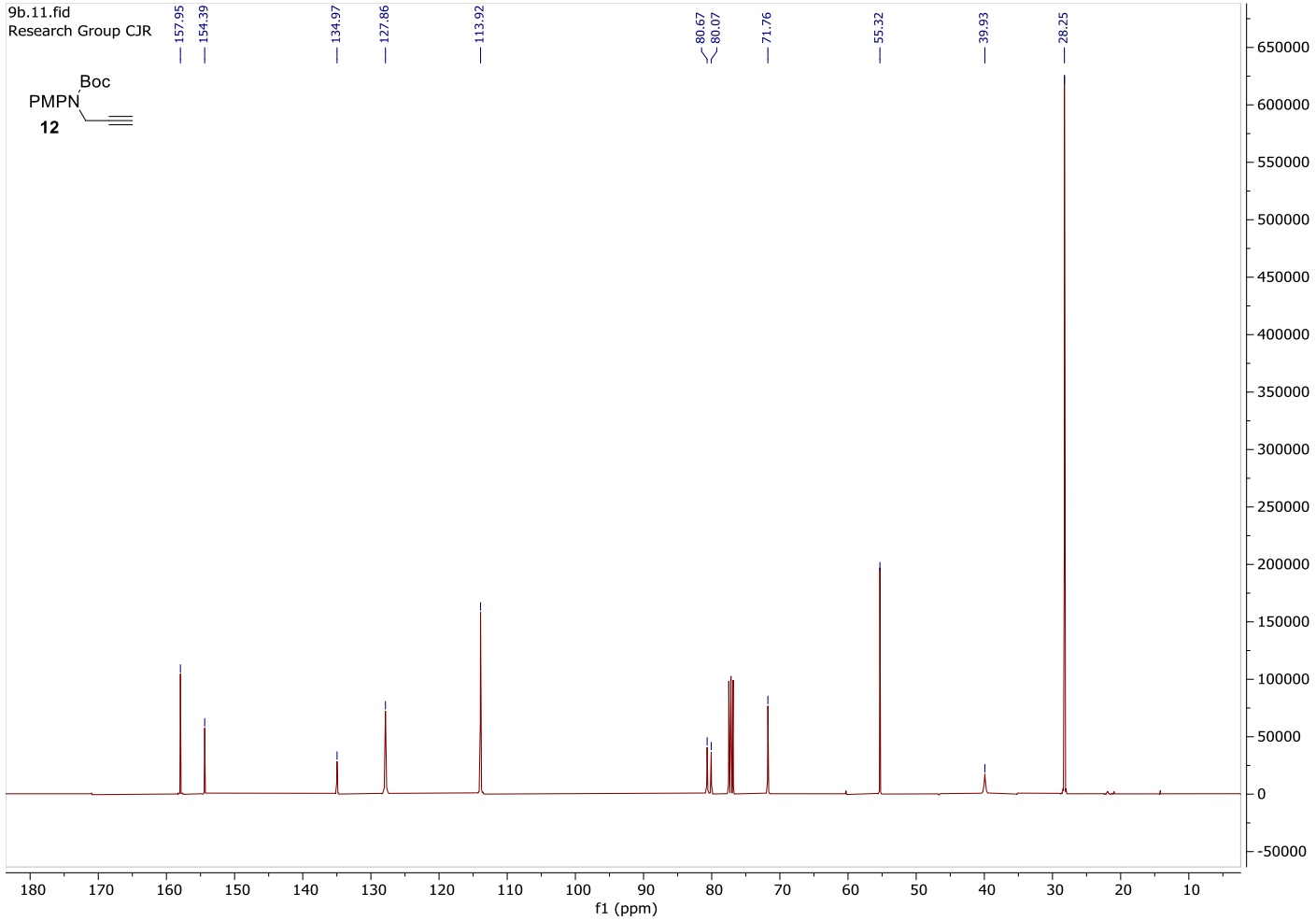
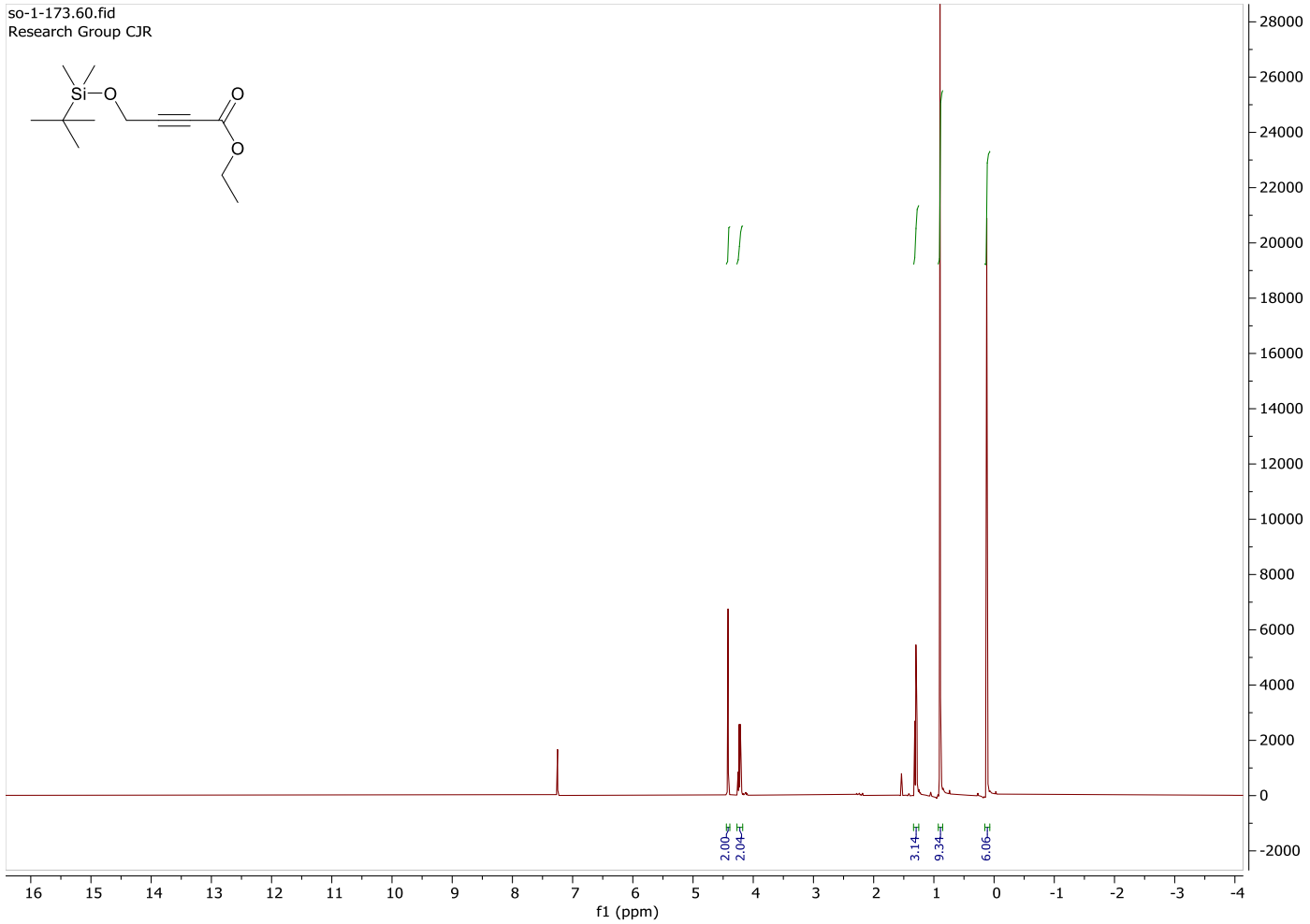
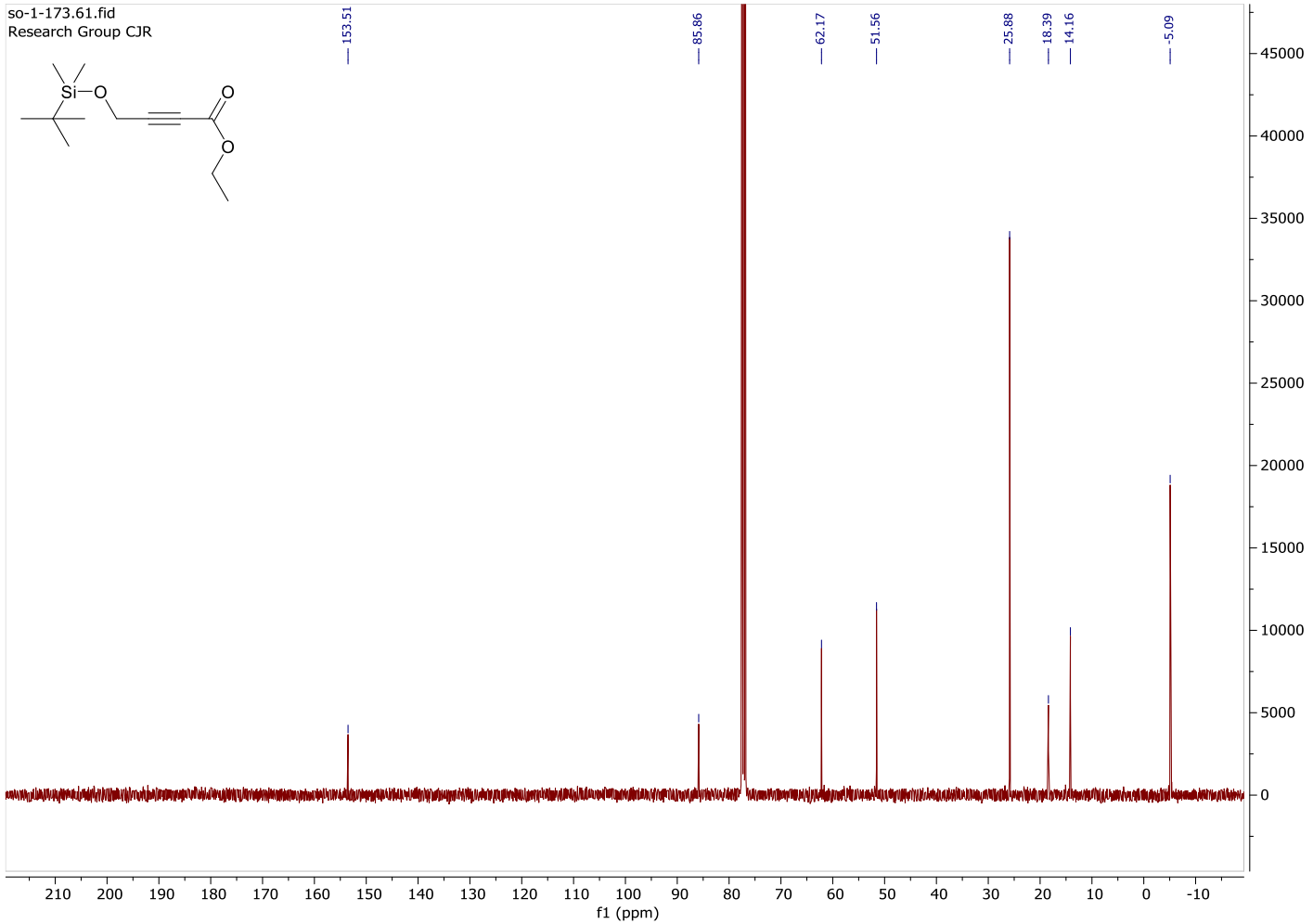


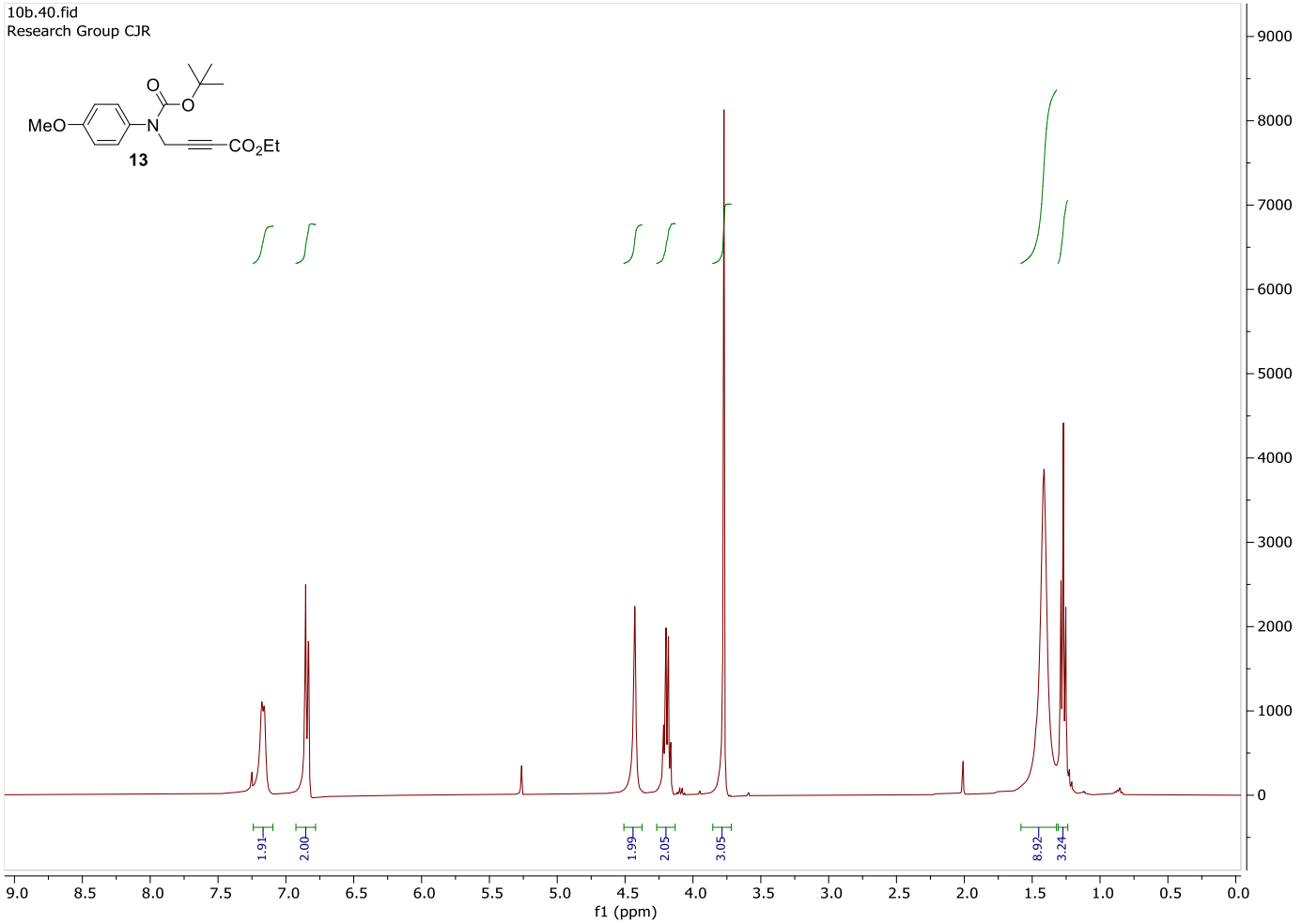
Compound **7** ^{1}H (400 MHz, $CDCl_3$)



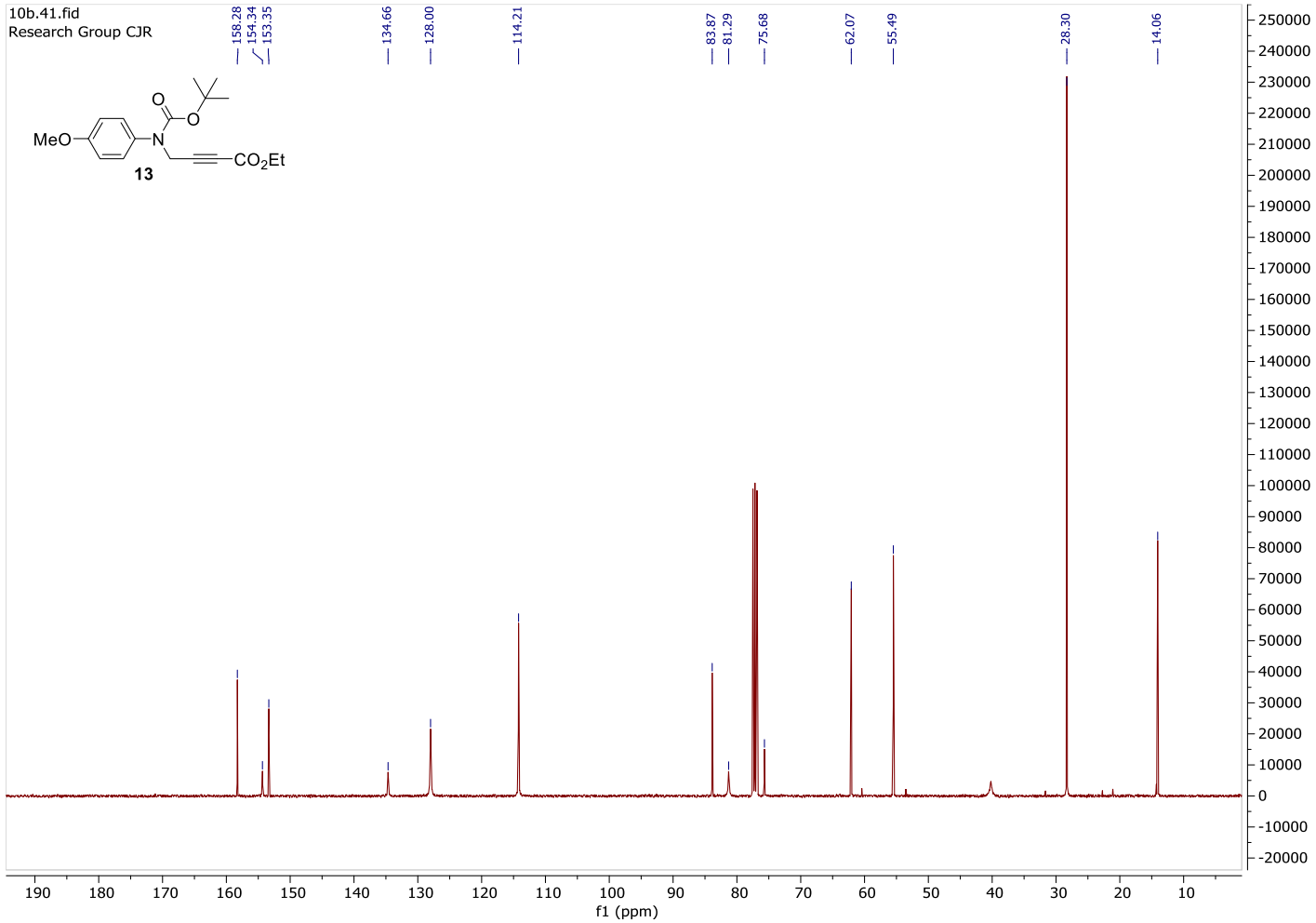
Compound **7** ^{13}C (101 MHz, $CDCl_3$)



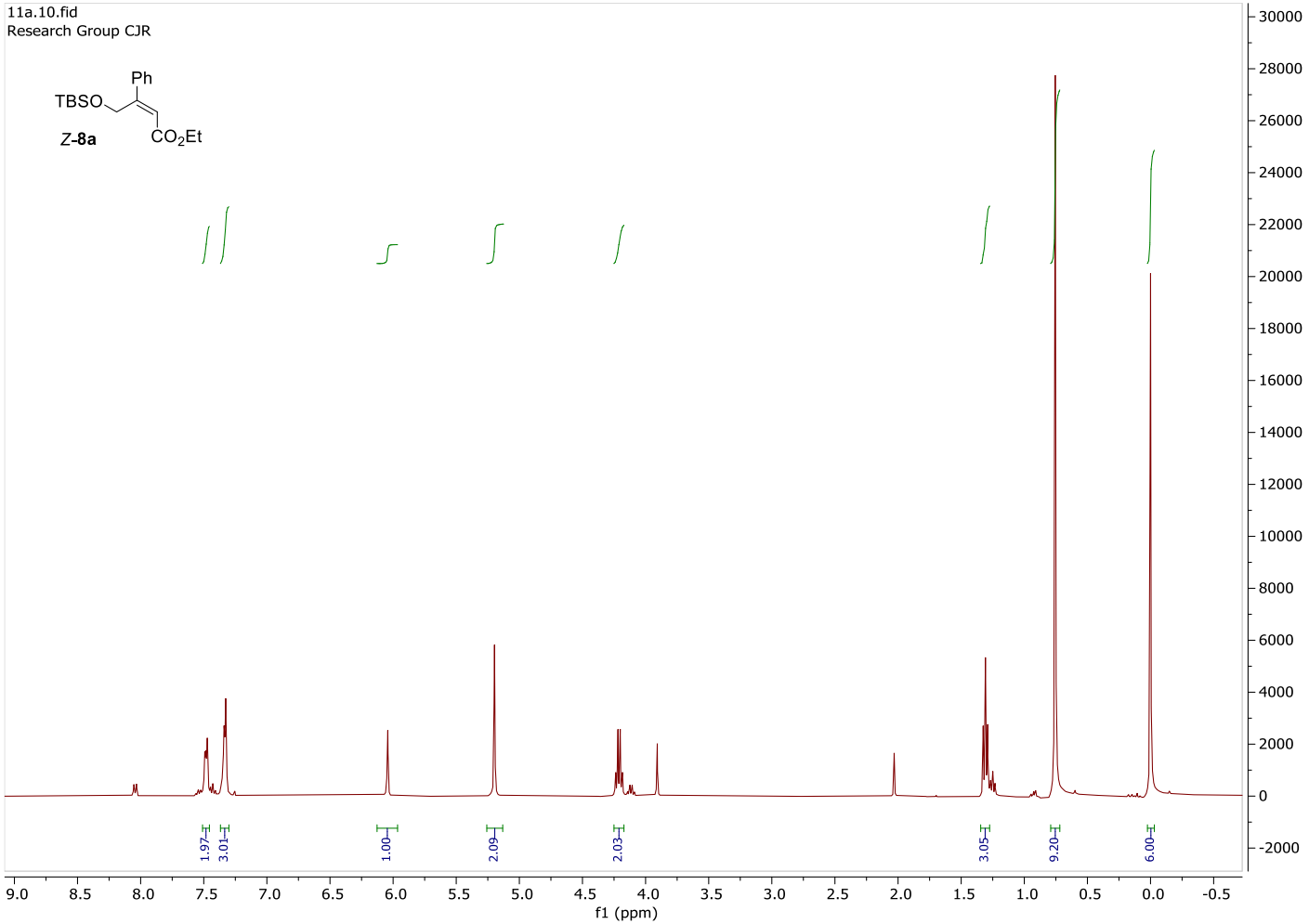
Compound **13** ^{1}H (400 MHz, $CDCl_3$)



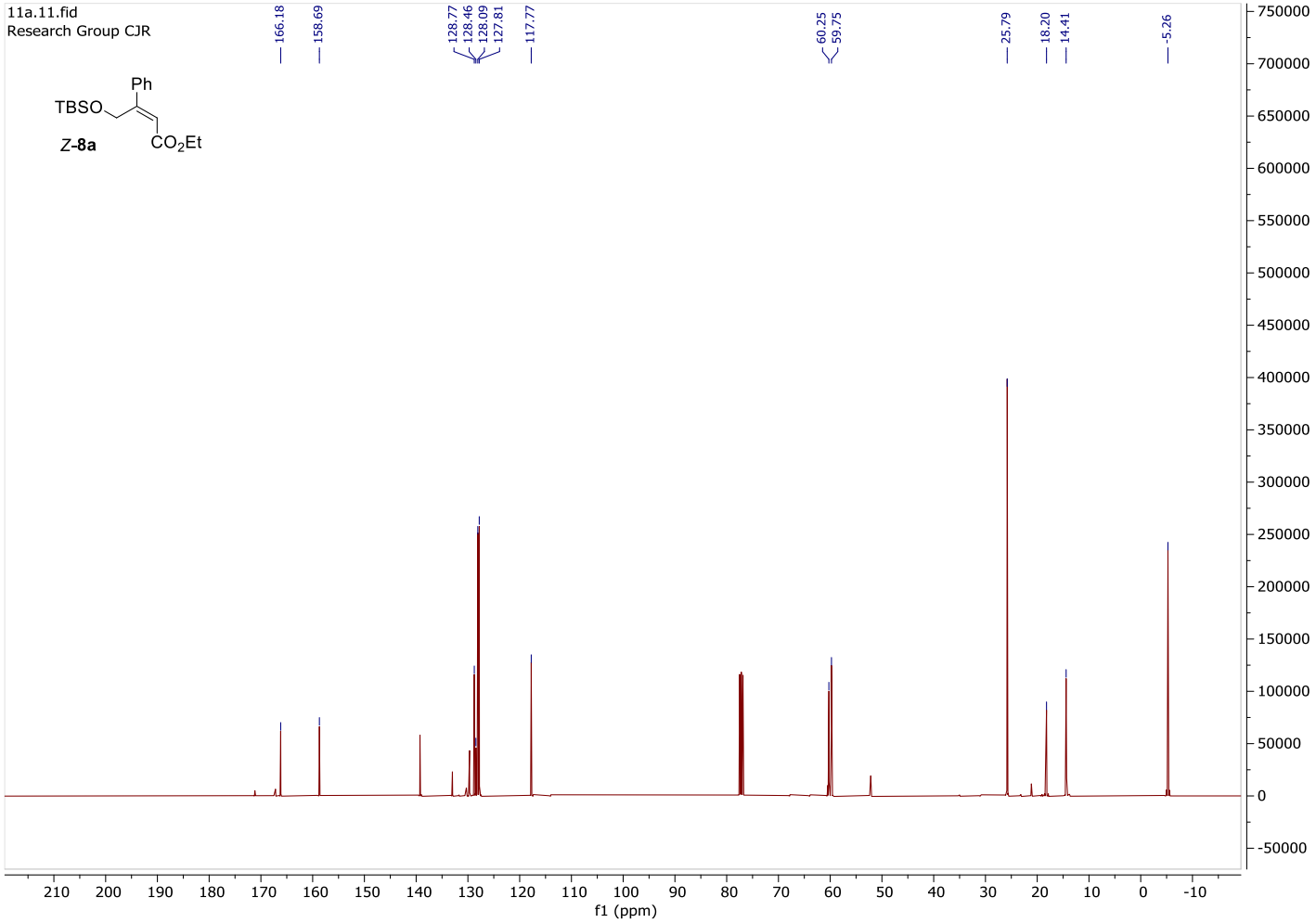
Compound **13** ^{13}C (101 MHz, $CDCl_3$)



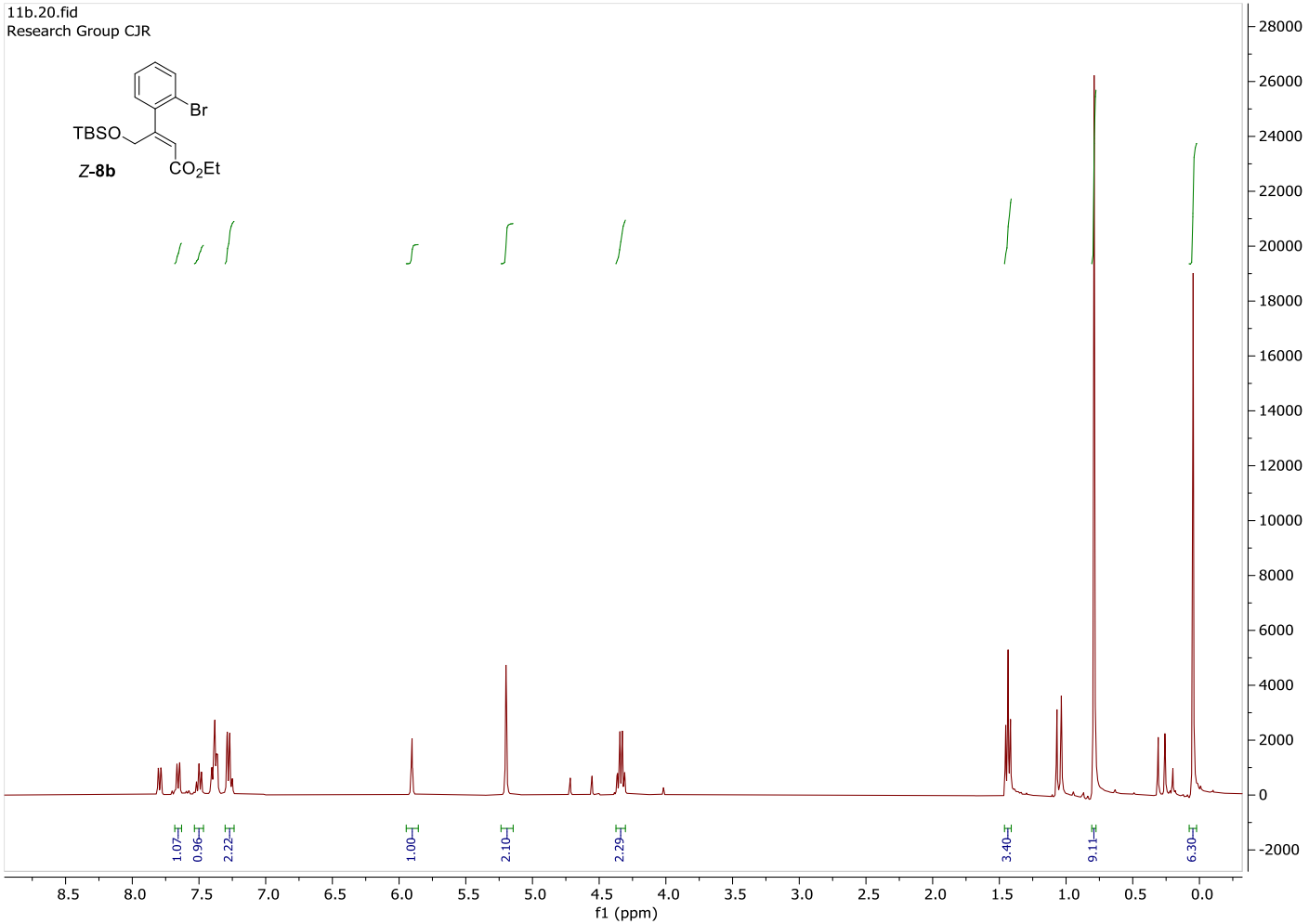
Compound **8a** ^{1}H (400 MHz, $CDCl_3$)



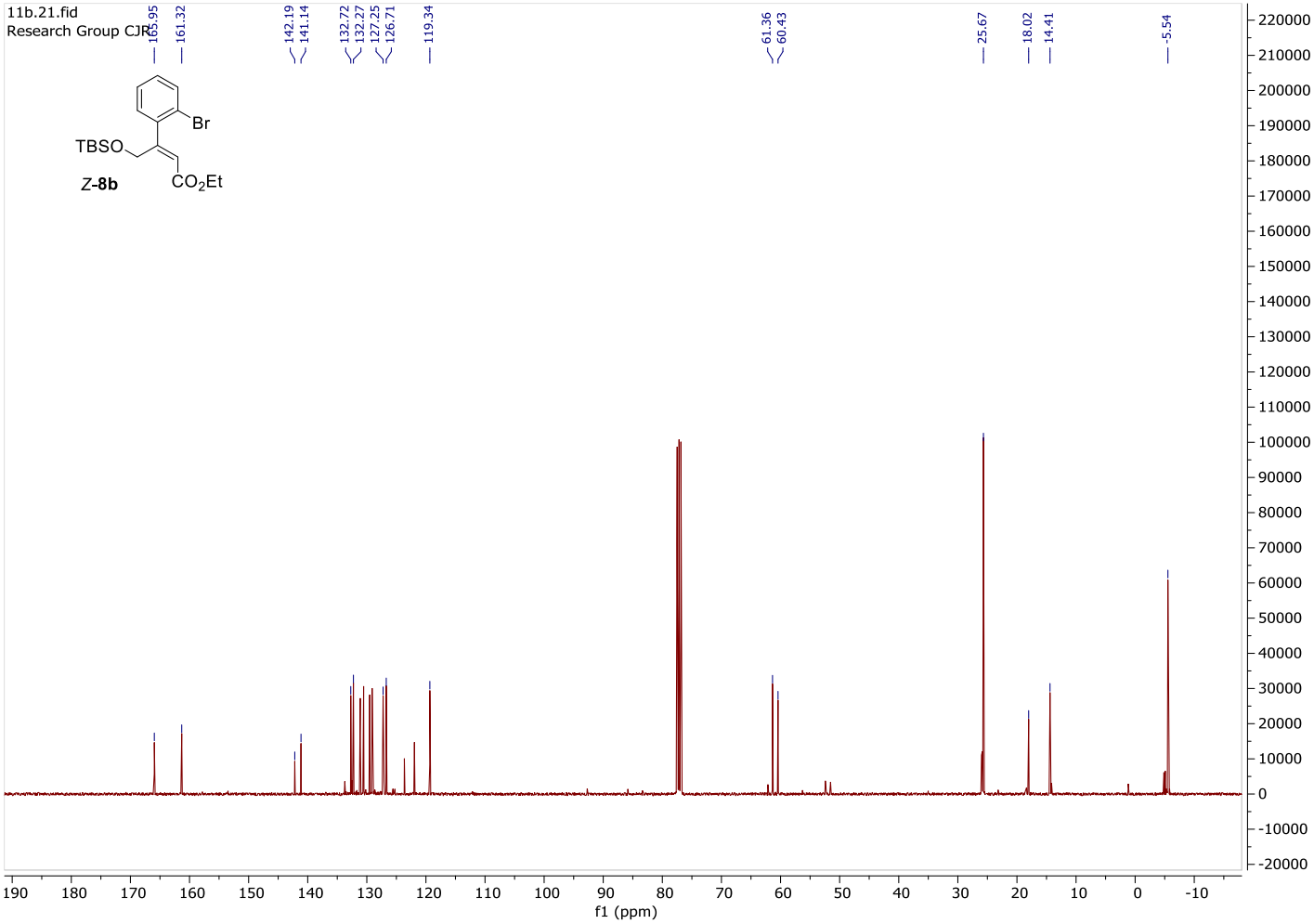
Compound **8a** ^{13}C (101 MHz, $CDCl_3$)



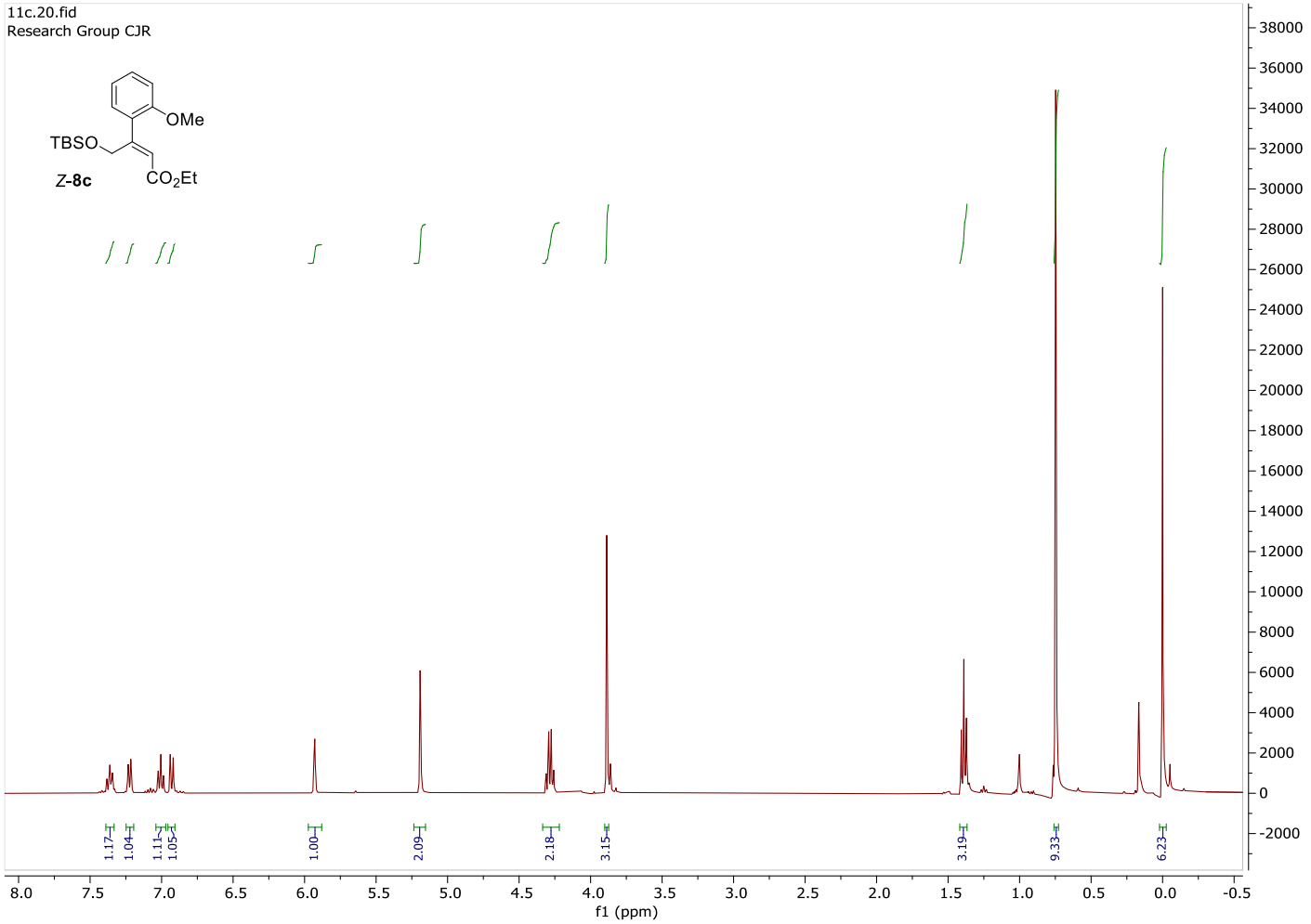
Compound **8b** ^{1}H (400 MHz, $CDCl_3$)



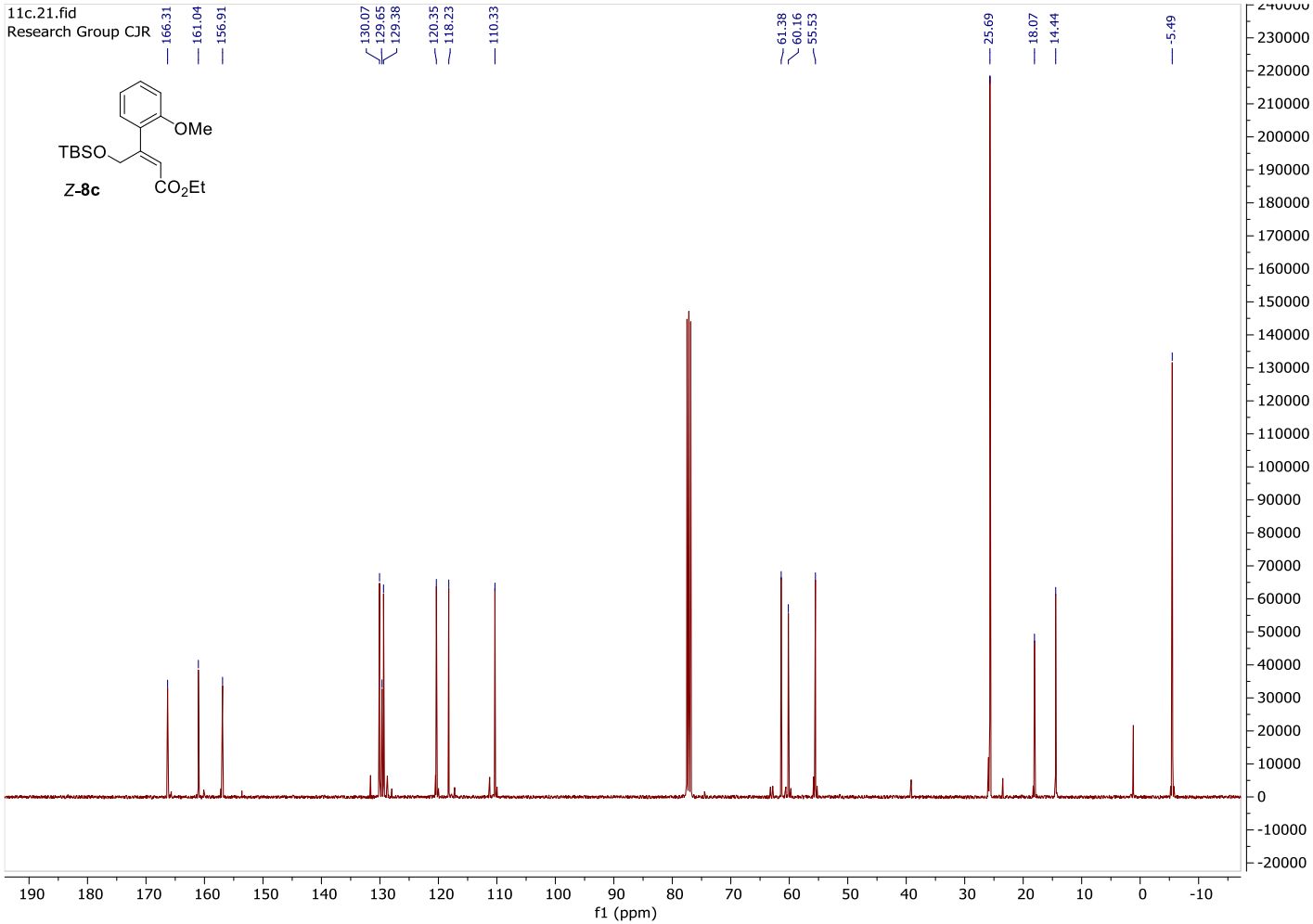
Compound **8b** ^{13}C (101 MHz, $CDCl_3$)



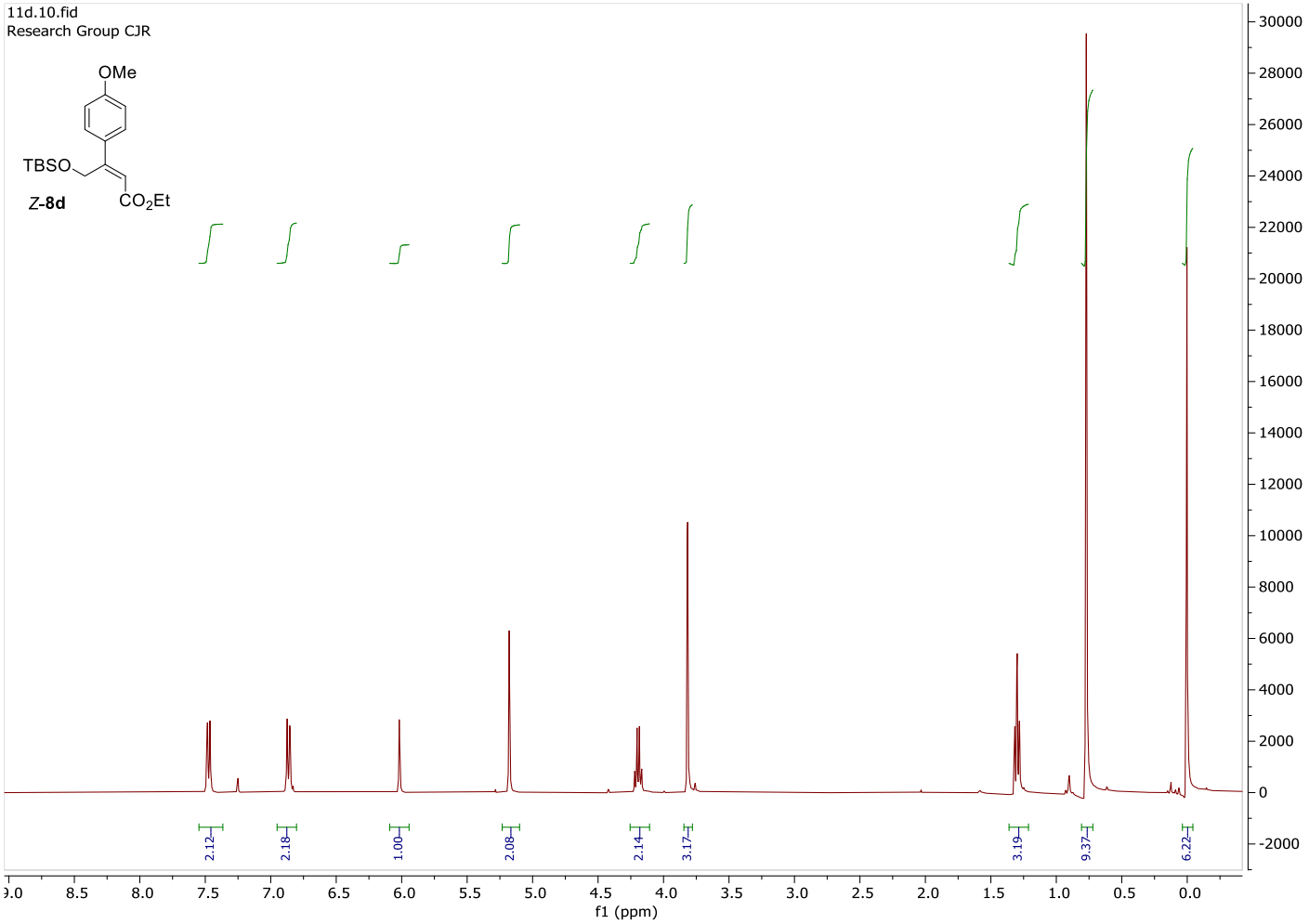
Compound **8c** ^{1}H (400 MHz, $CDCl_3$)



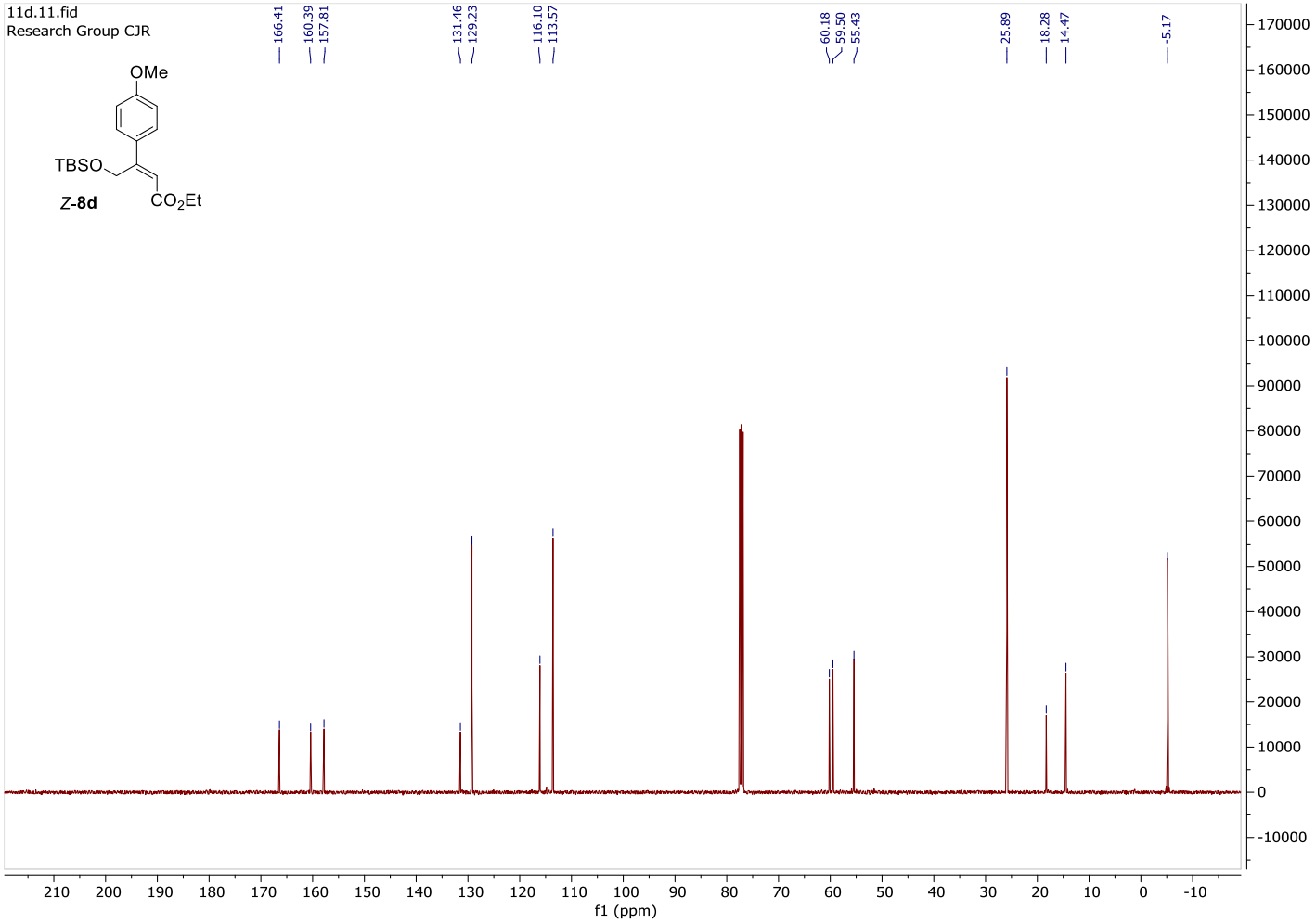
Compound **8c** ^{13}C (101 MHz, $CDCl_3$)



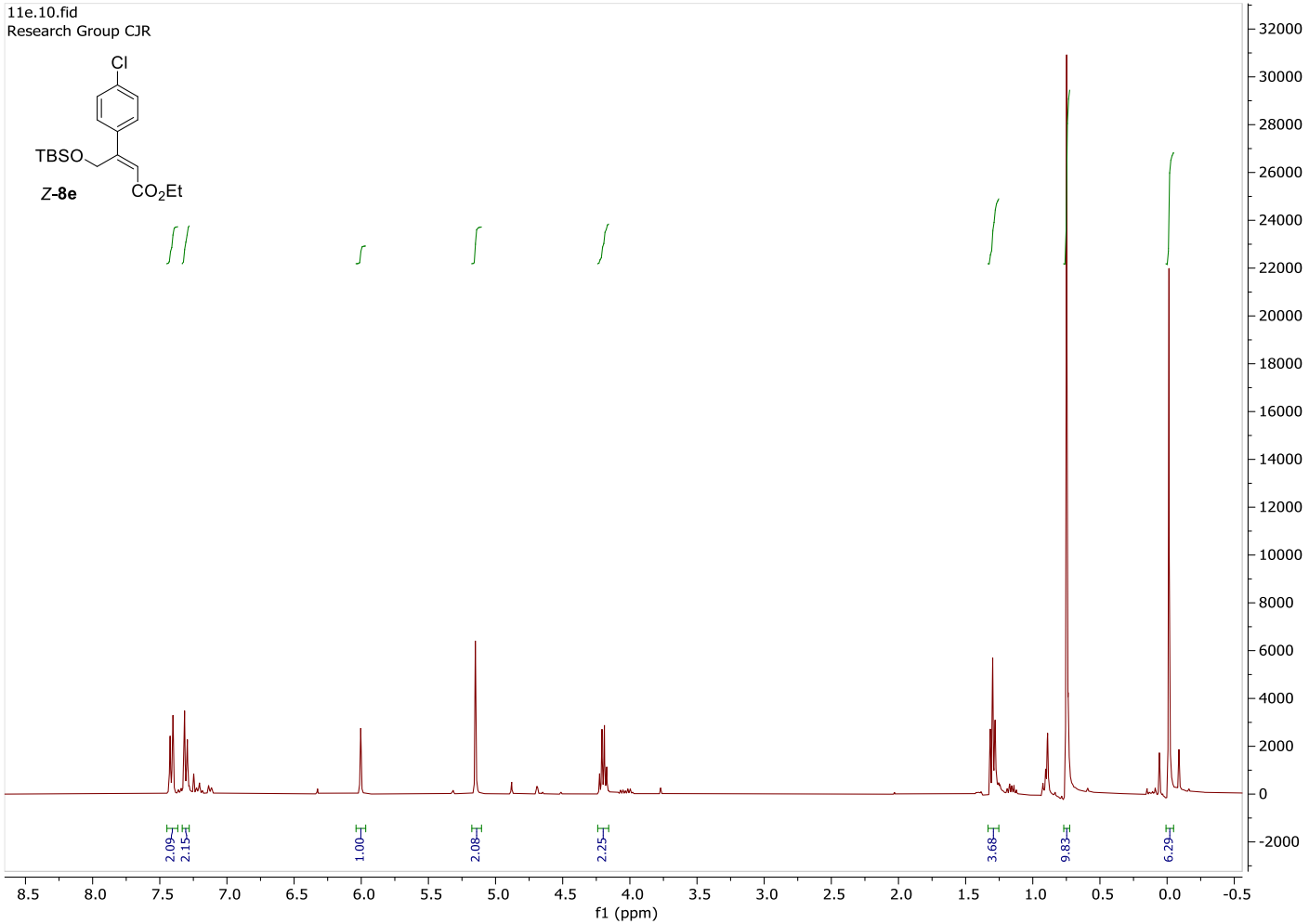
Compound **8d** ^{1}H (400 MHz, $CDCl_3$)



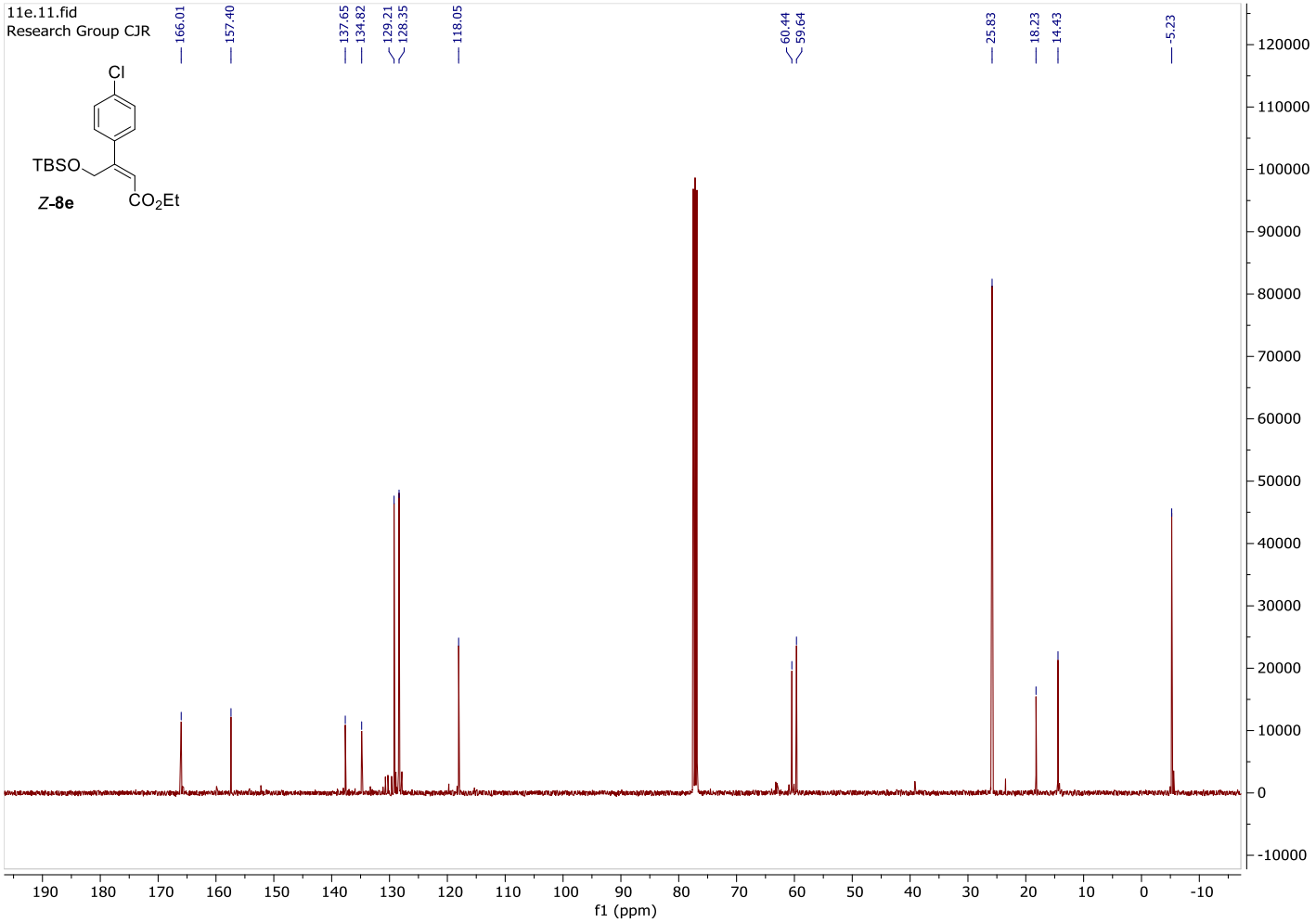
Compound **8d** ^{13}C (101 MHz, $CDCl_3$)



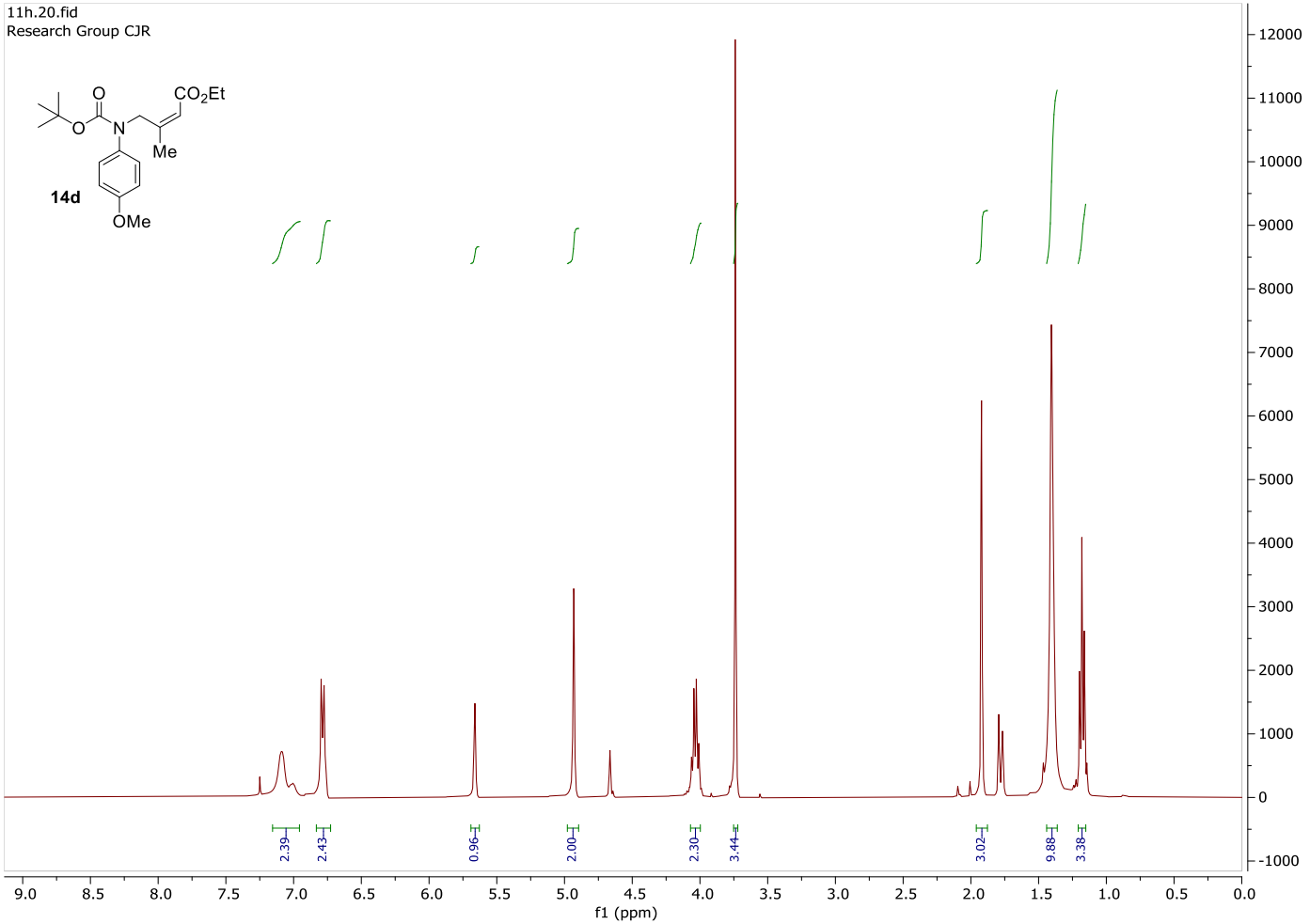
Compound **8e** ^{1}H (400 MHz, $CDCl_3$)



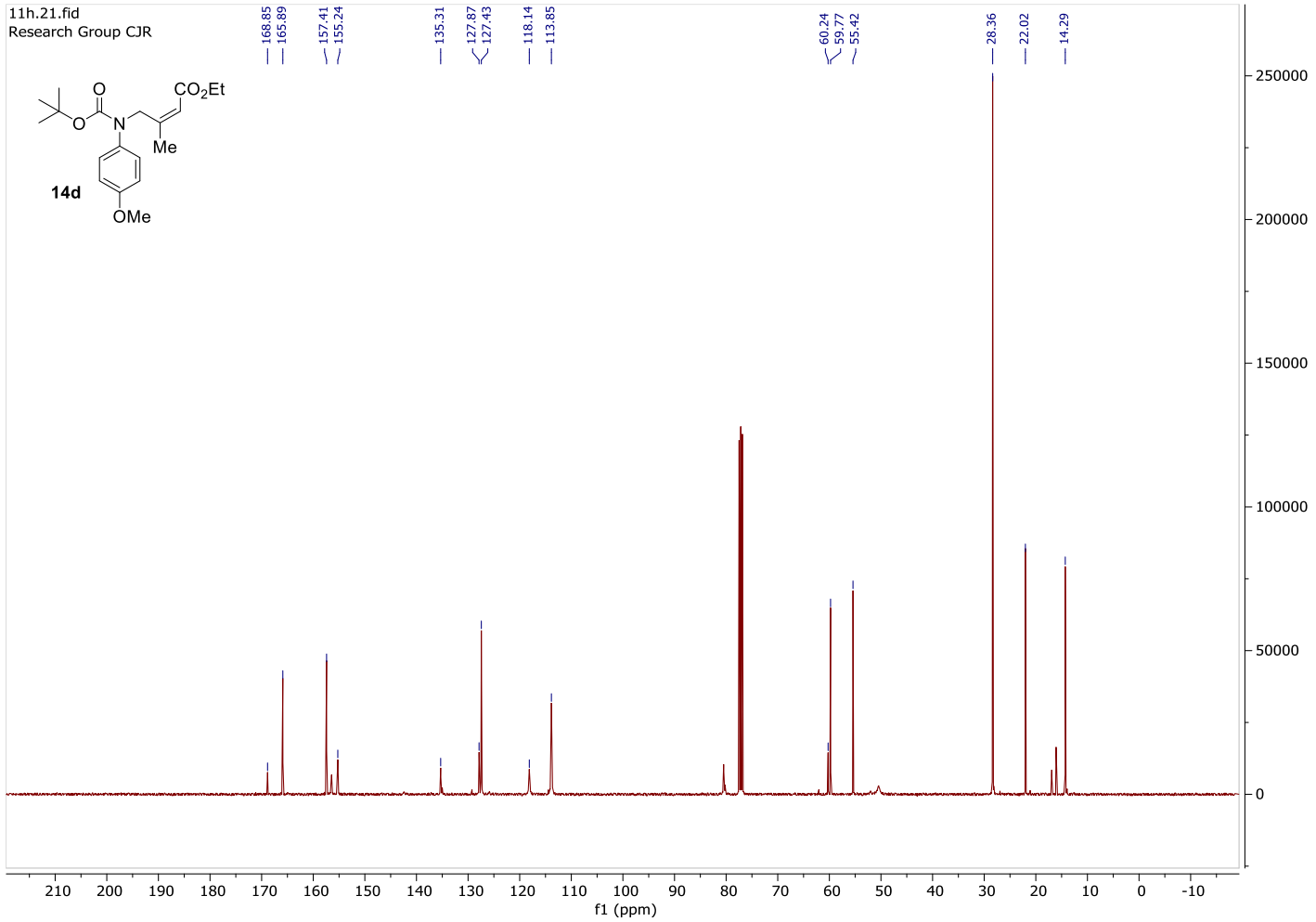
Compound **8e** ^{13}C (101 MHz, $CDCl_3$)



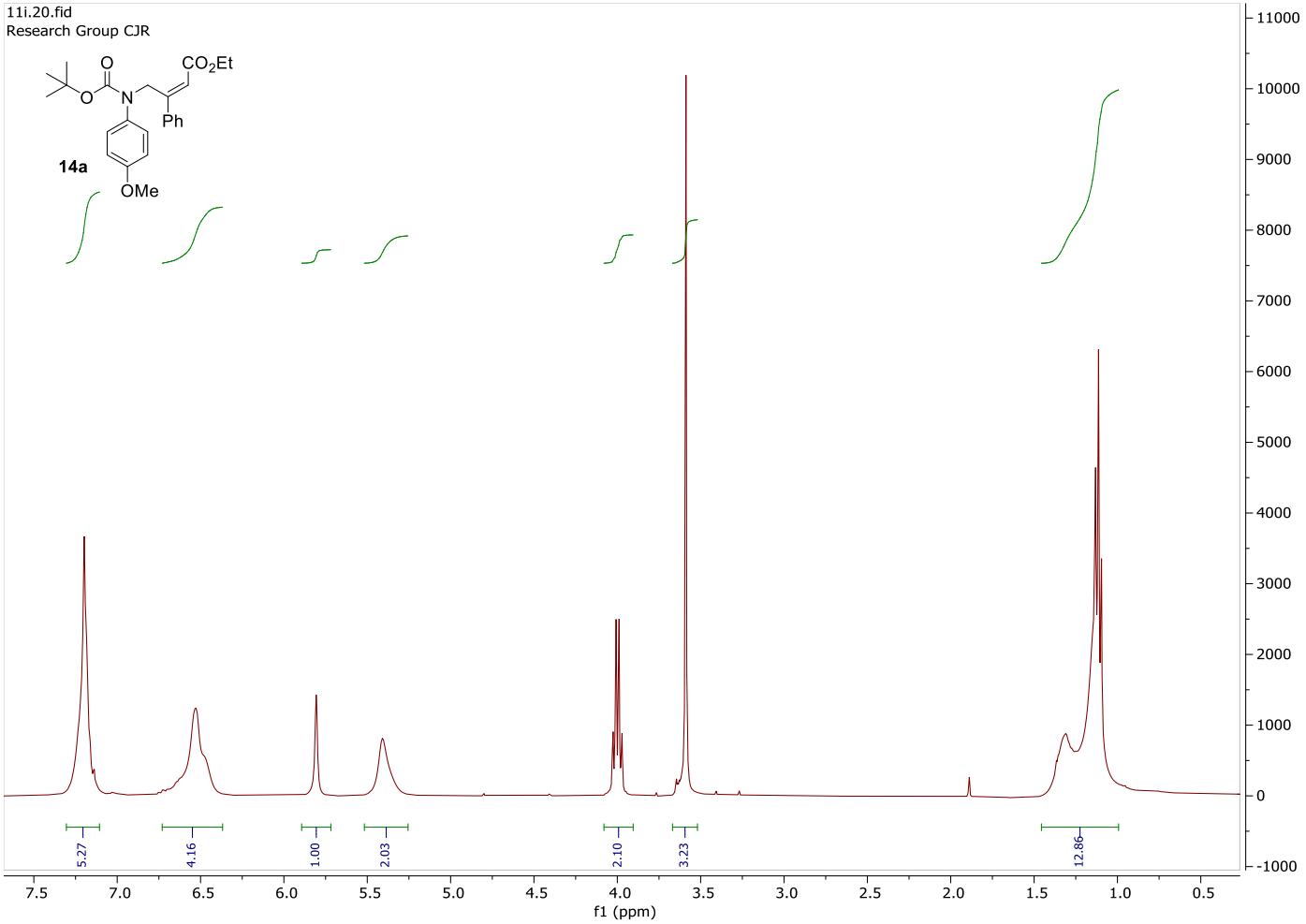
Compound **14d** ^{1}H (400 MHz, $CDCl_3$)



Compound **14d** ^{13}C (101 MHz, $CDCl_3$)



Compound **14a** ^{1}H (400 MHz, $CDCl_3$)



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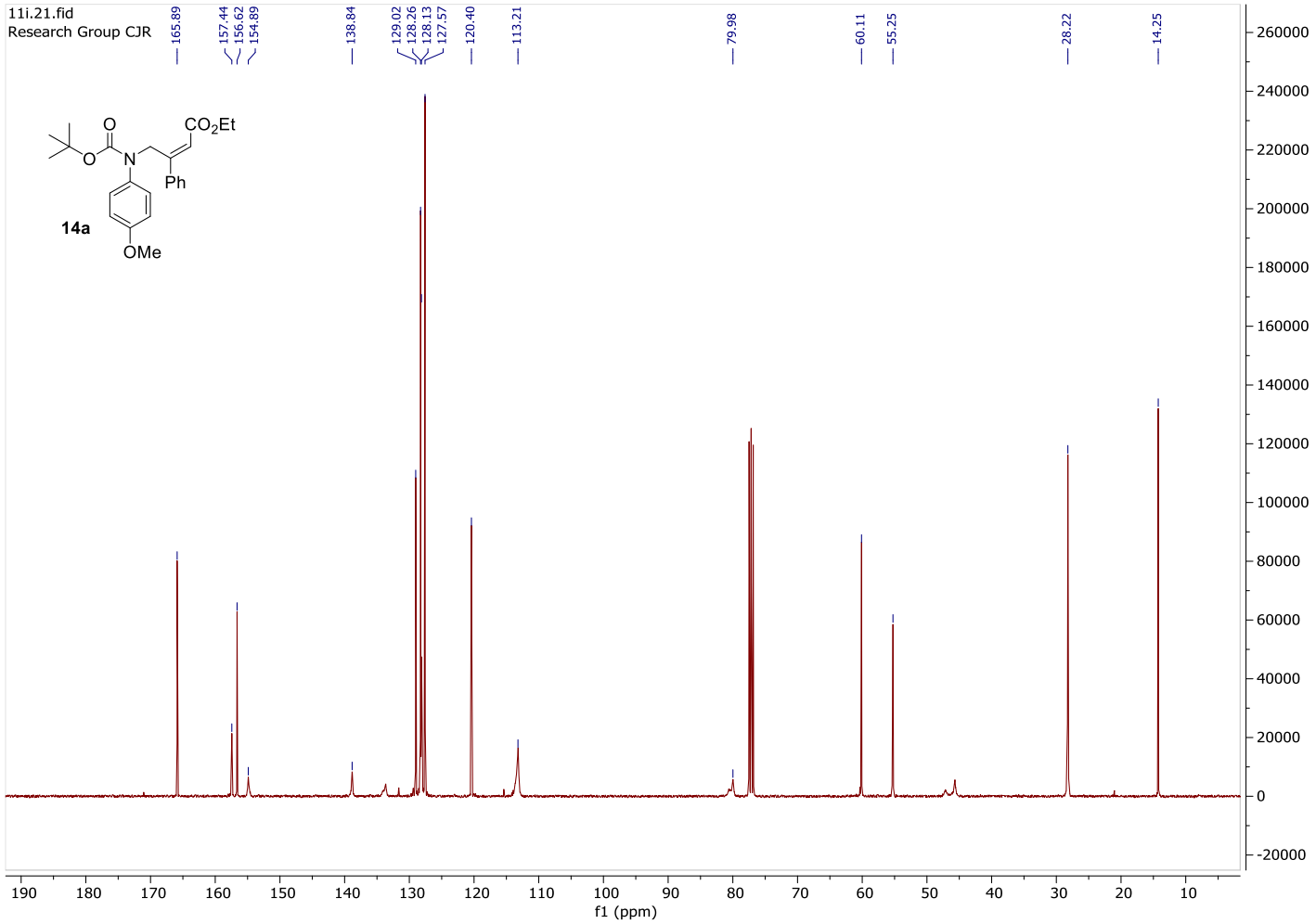
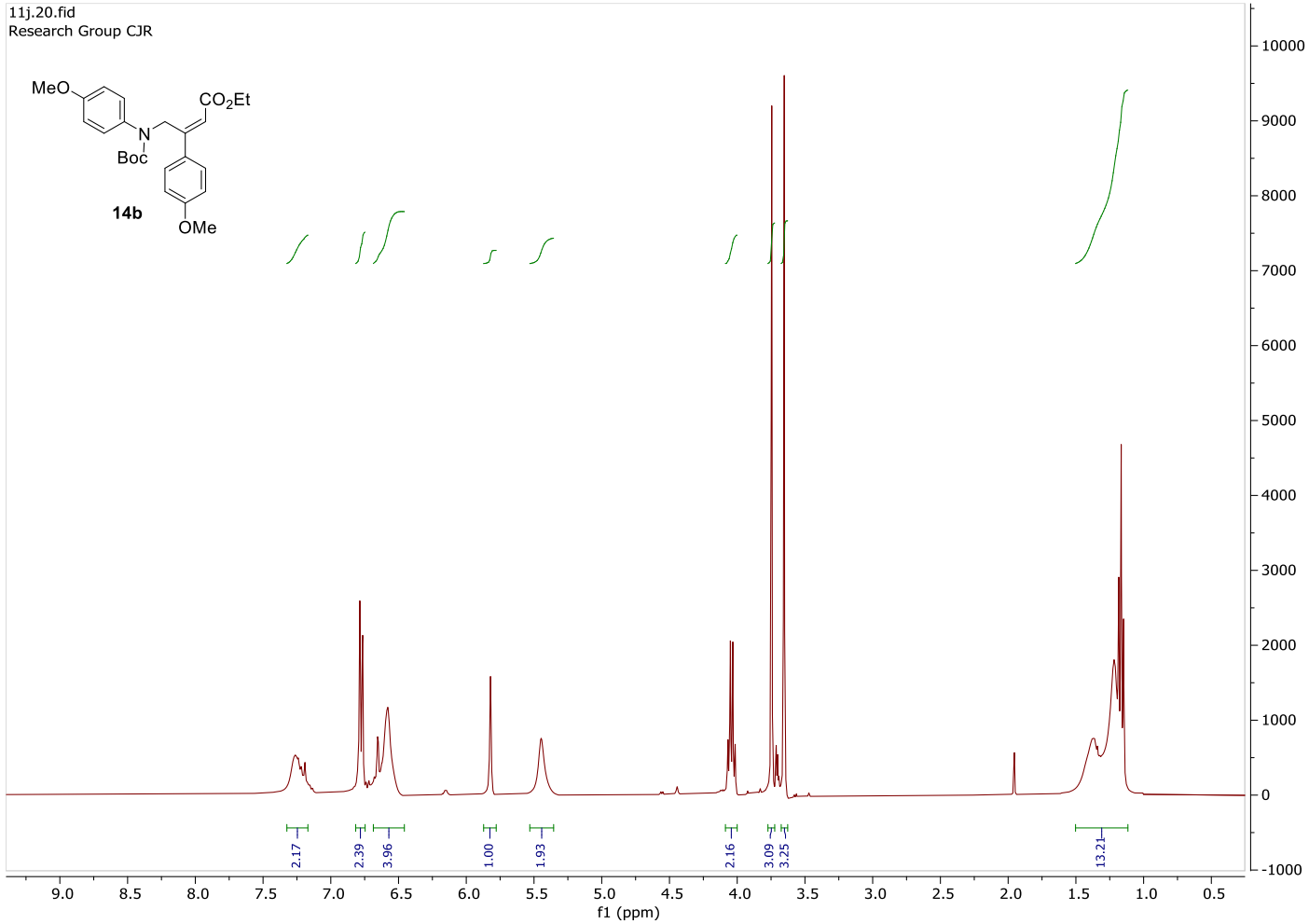
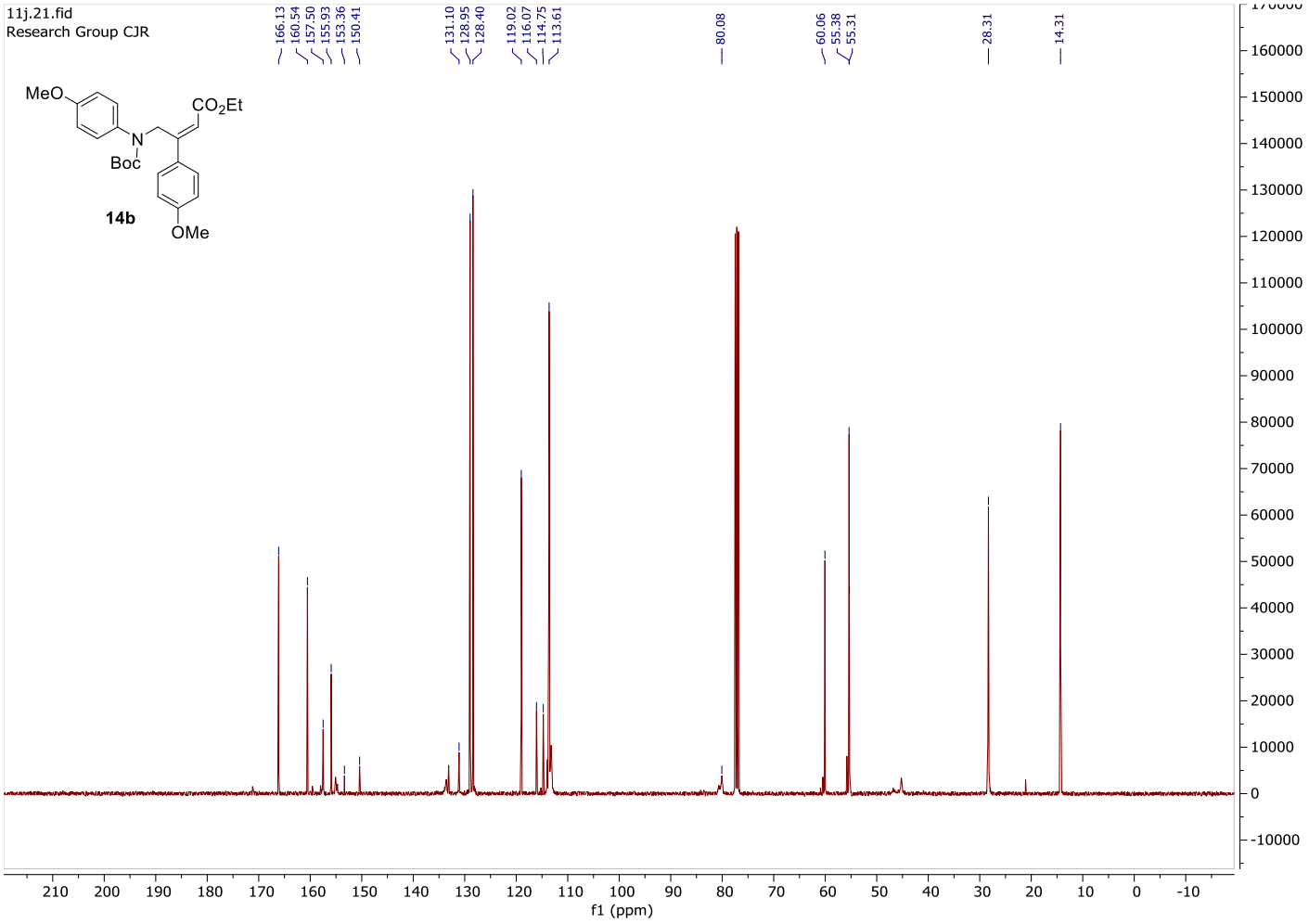


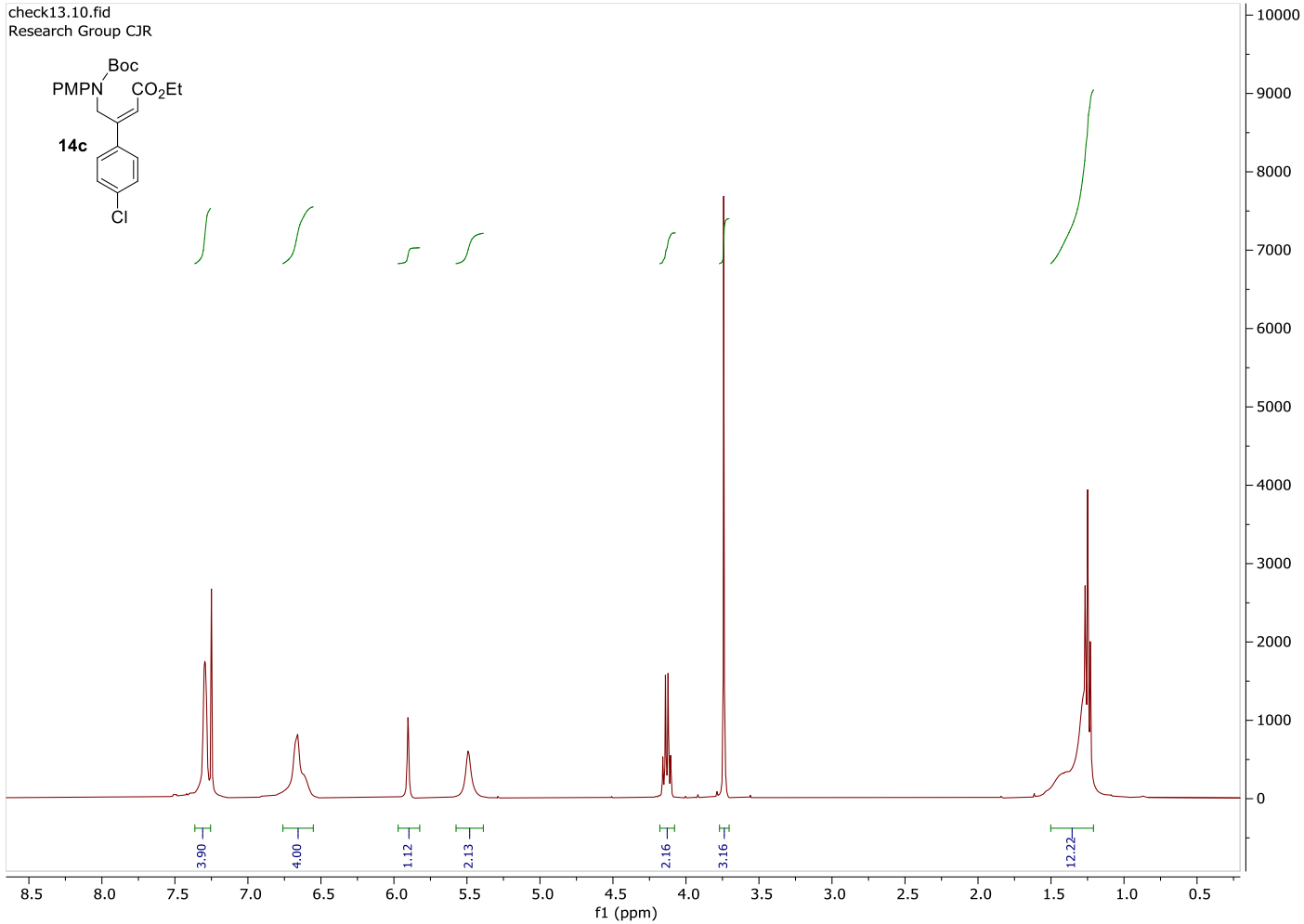
Compound **14b** ^{1}H (400 MHz, $CDCl_3$)



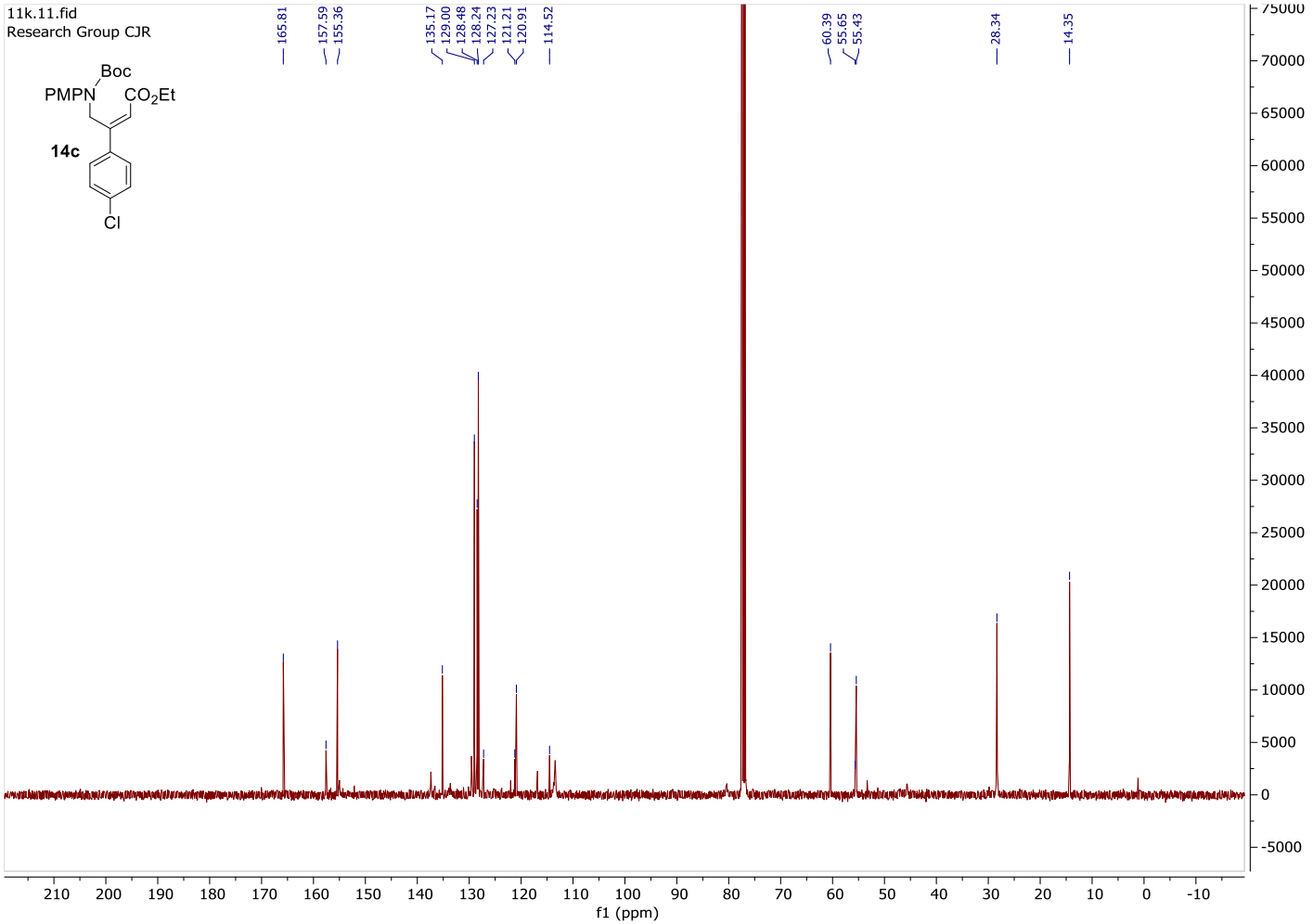
Compound **14b** ^{13}C (101 MHz, $CDCl_3$)



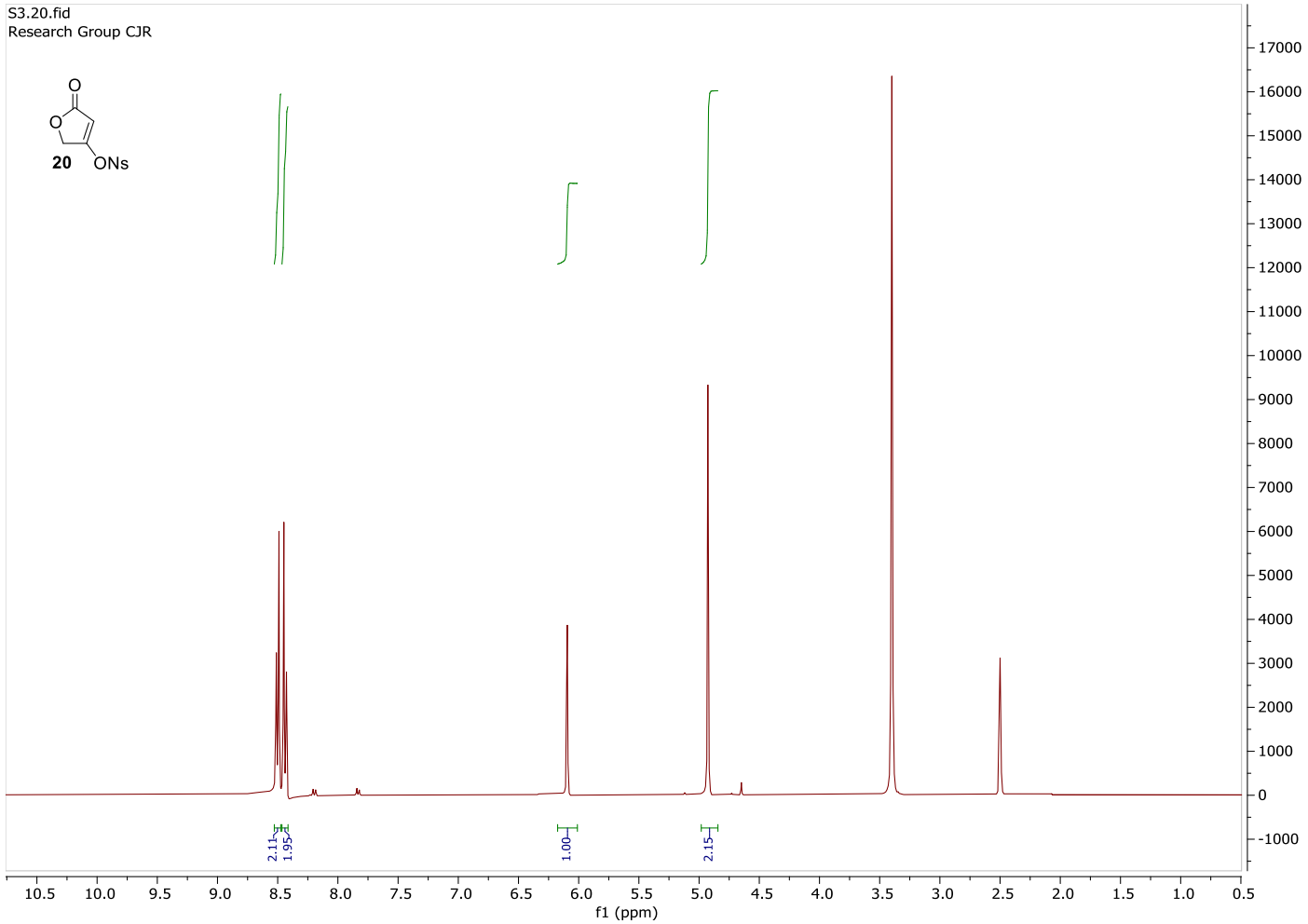
Compound **14c** ^{1}H (400 MHz, $CDCl_3$)



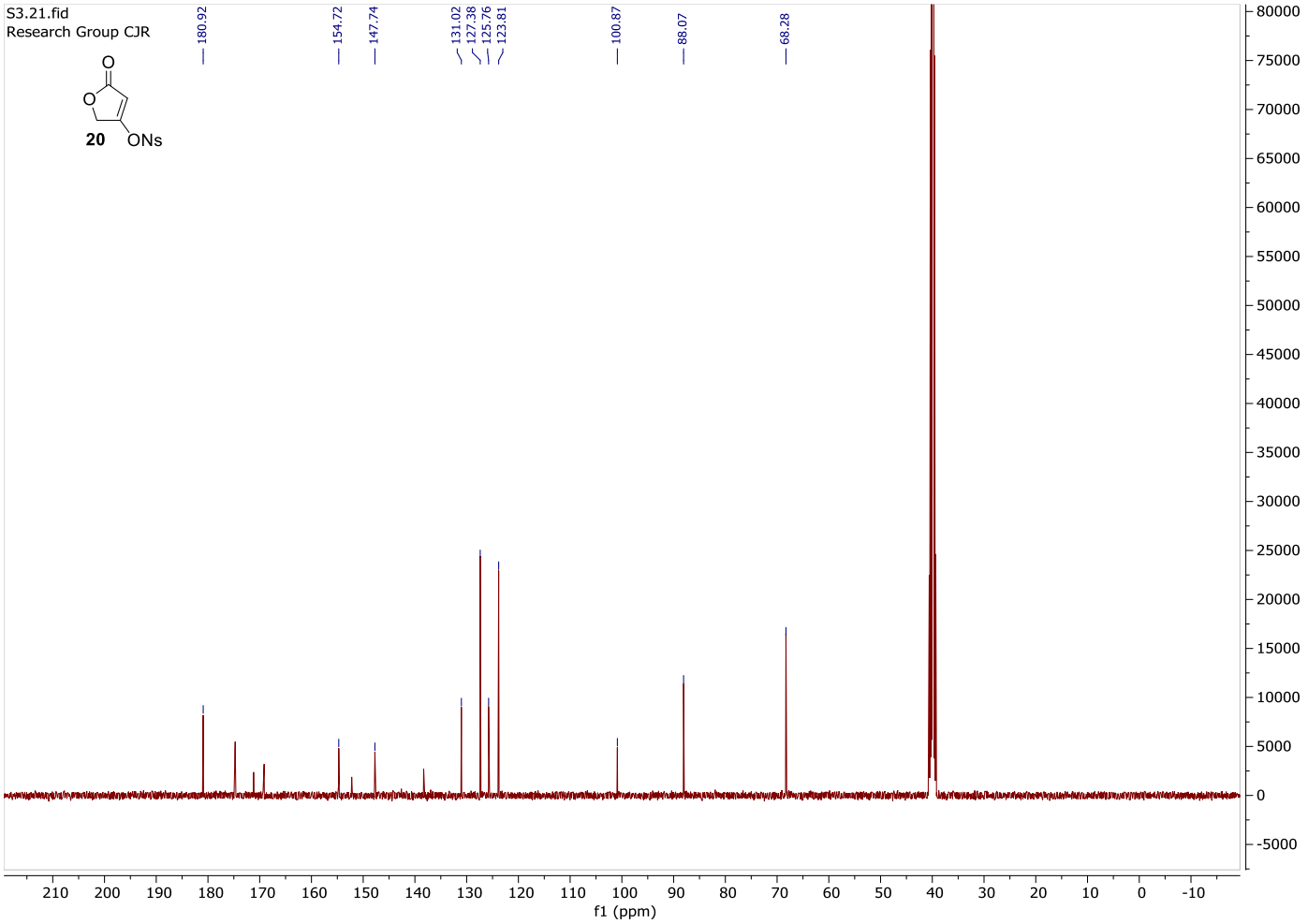
Compound **14c** ^{13}C (101 MHz, $CDCl_3$)



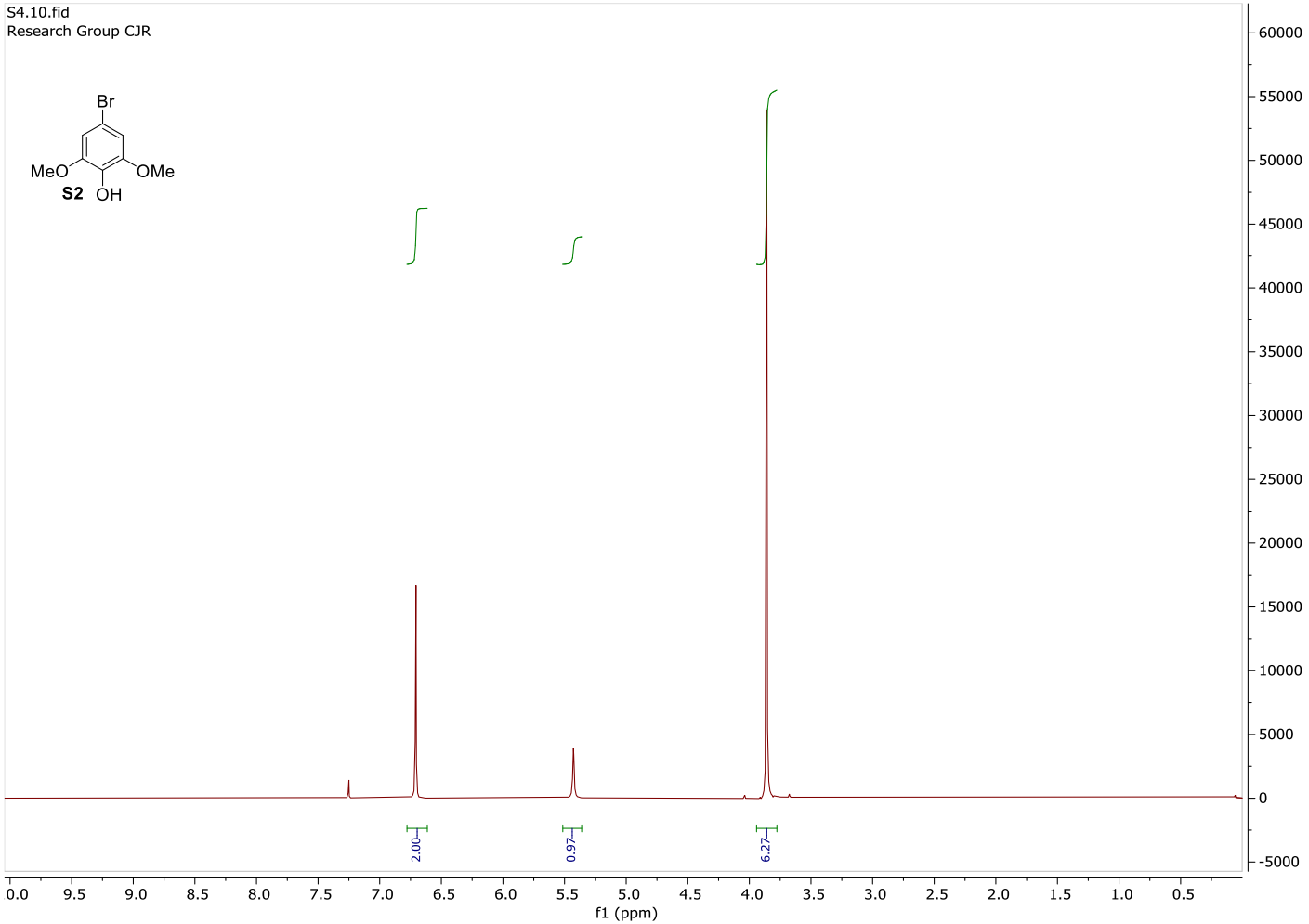
Compound **20** ^{1}H (400 MHz, DMSO-d_6)



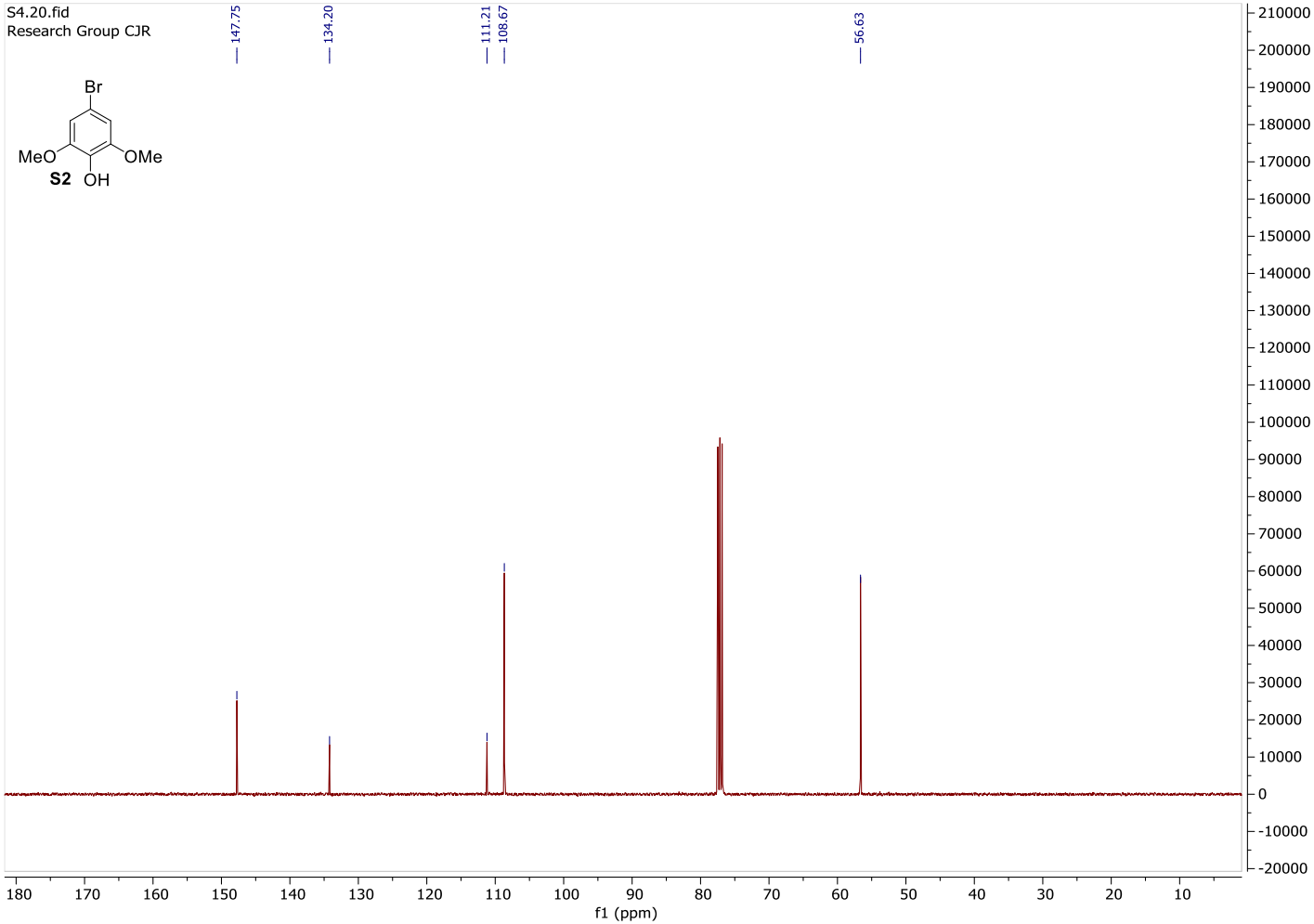
Compound **20** ^{13}C (101 MHz, DMSO-d_6)



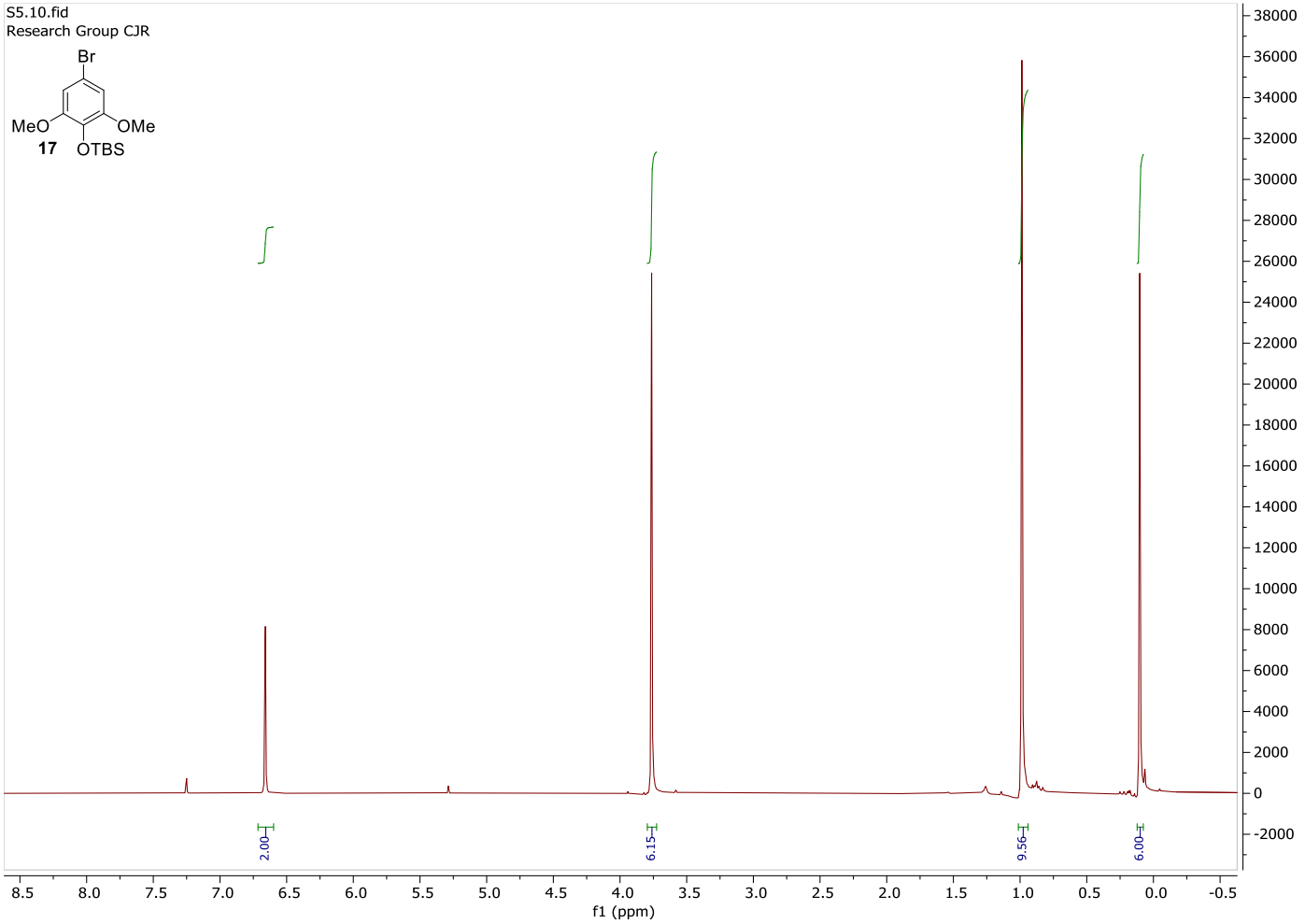
Compound **S2** ^{1}H (400 MHz, $CDCl_3$)



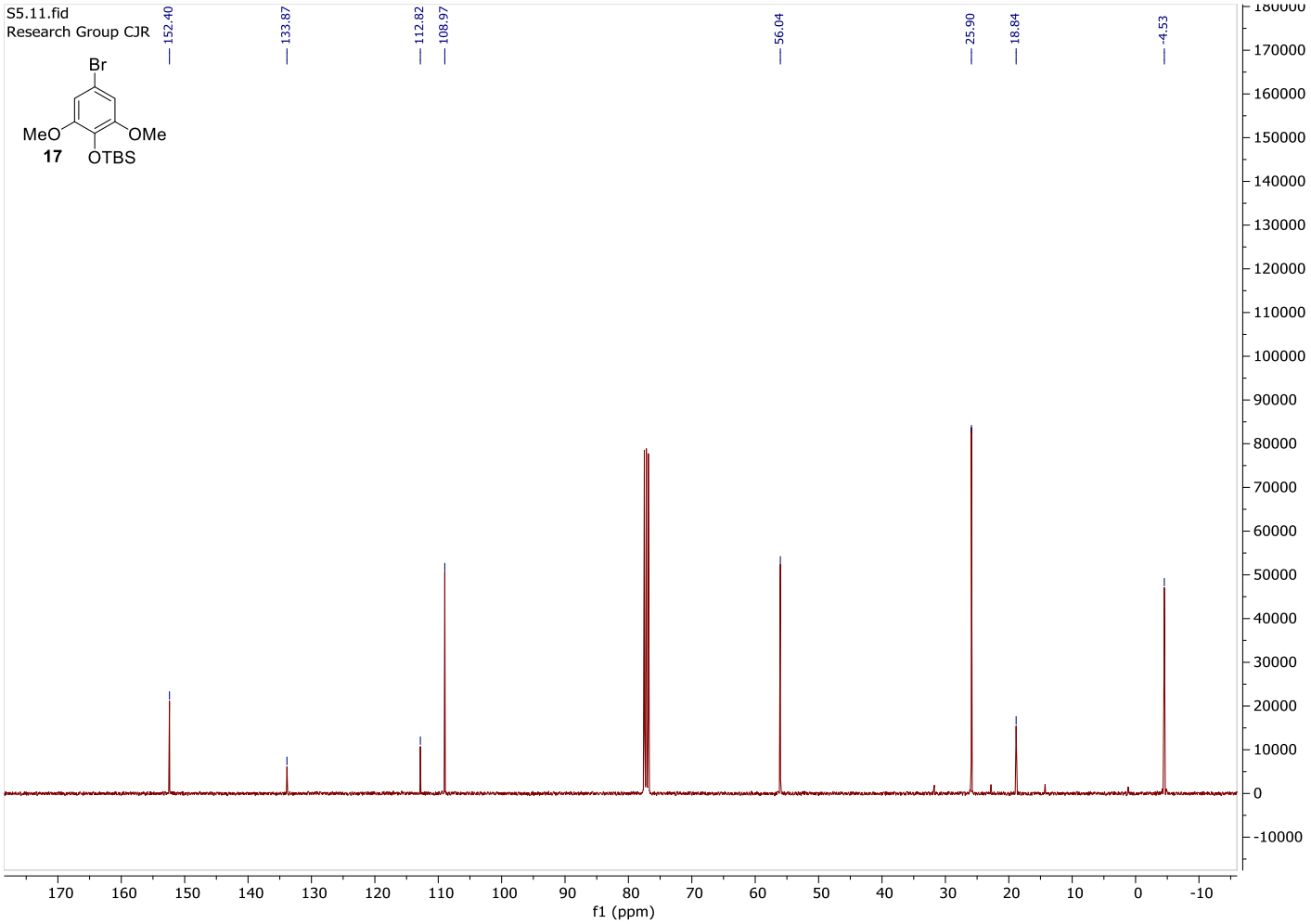
Compound **S2** ^{13}C (101 MHz, $CDCl_3$)



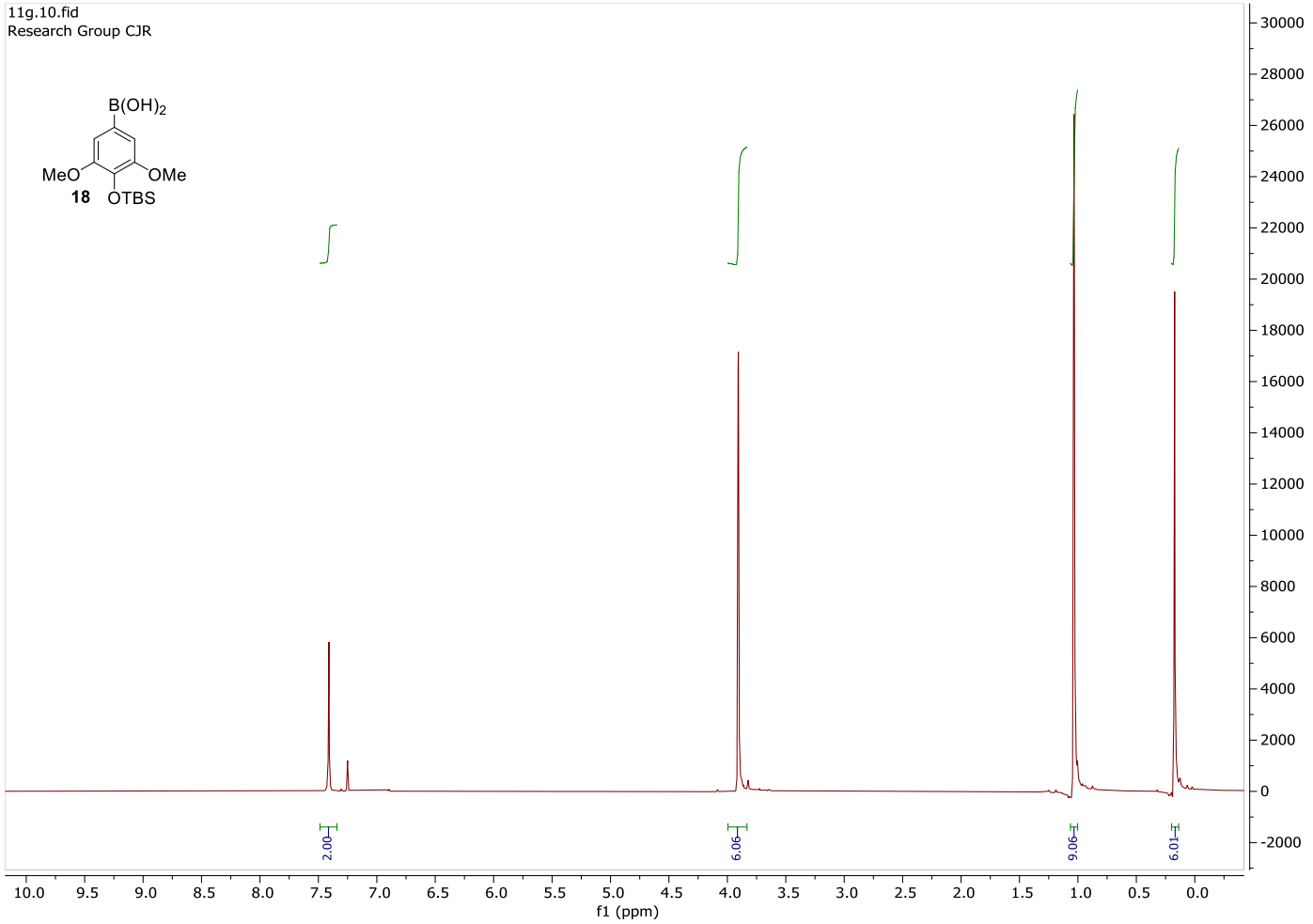
Compound **17** ^{1}H (400 MHz, $CDCl_3$)



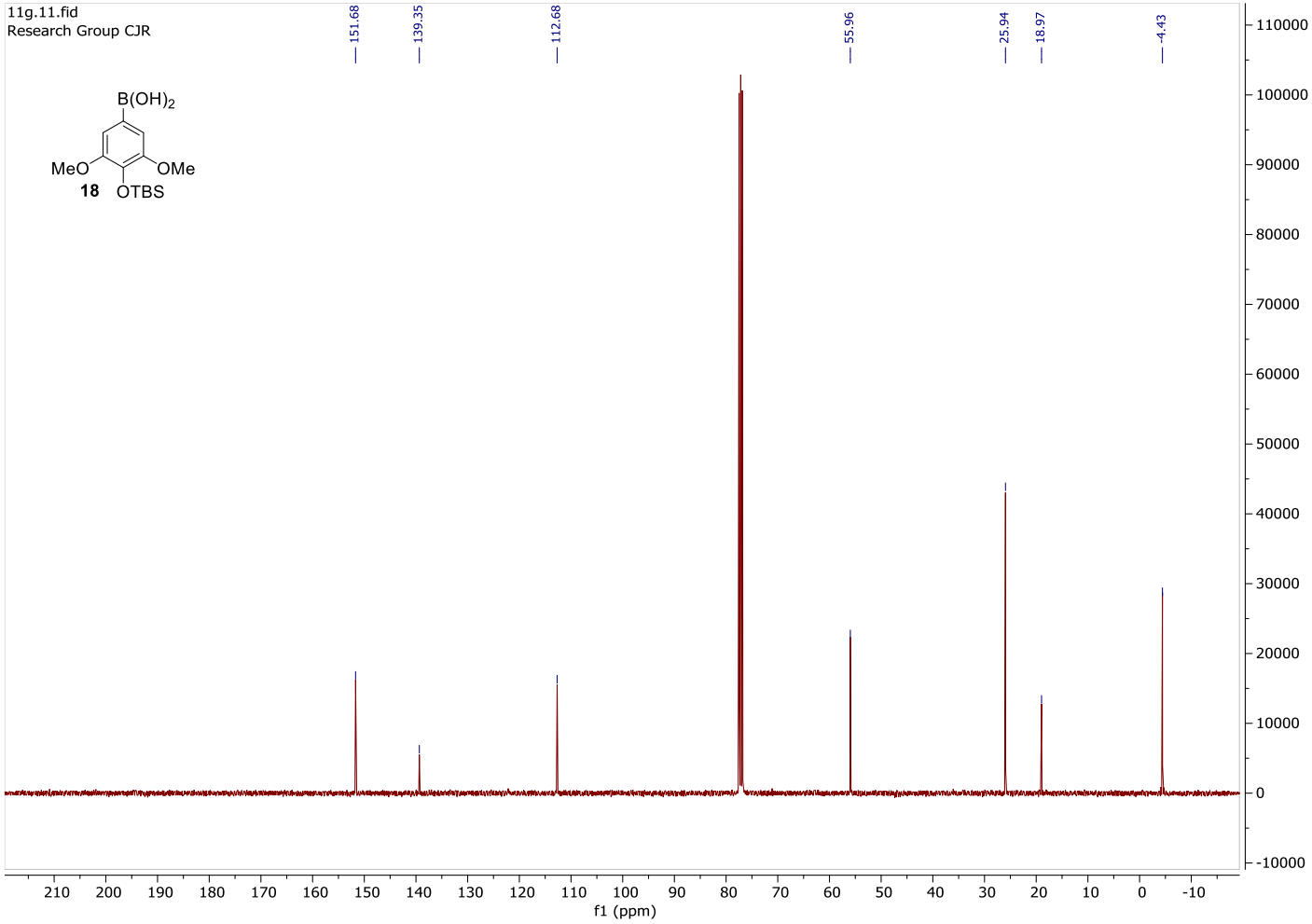
Compound **17** ^{13}C (101 MHz, $CDCl_3$)



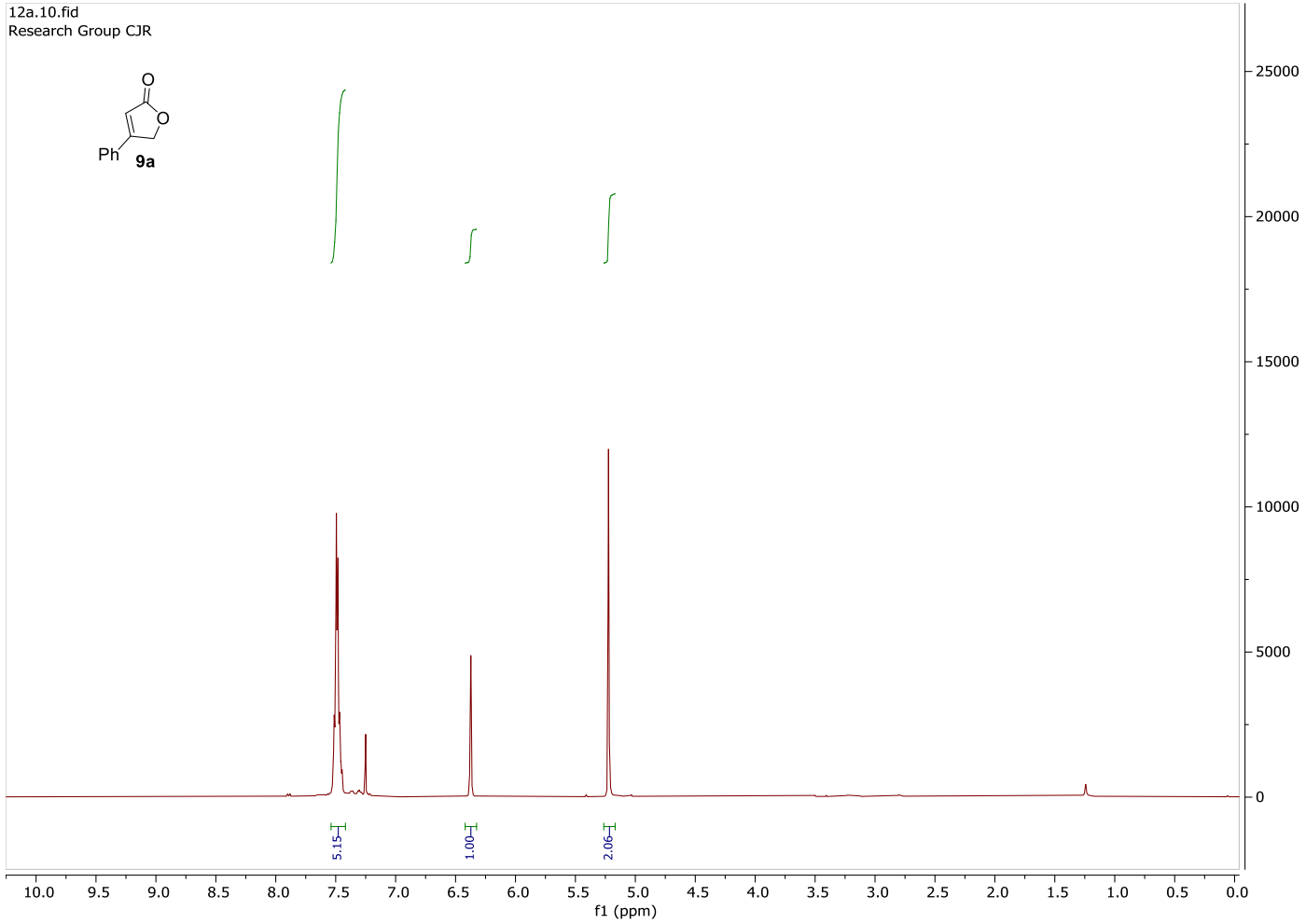
Compound **18** ^{1}H (400 MHz, $CDCl_3$)



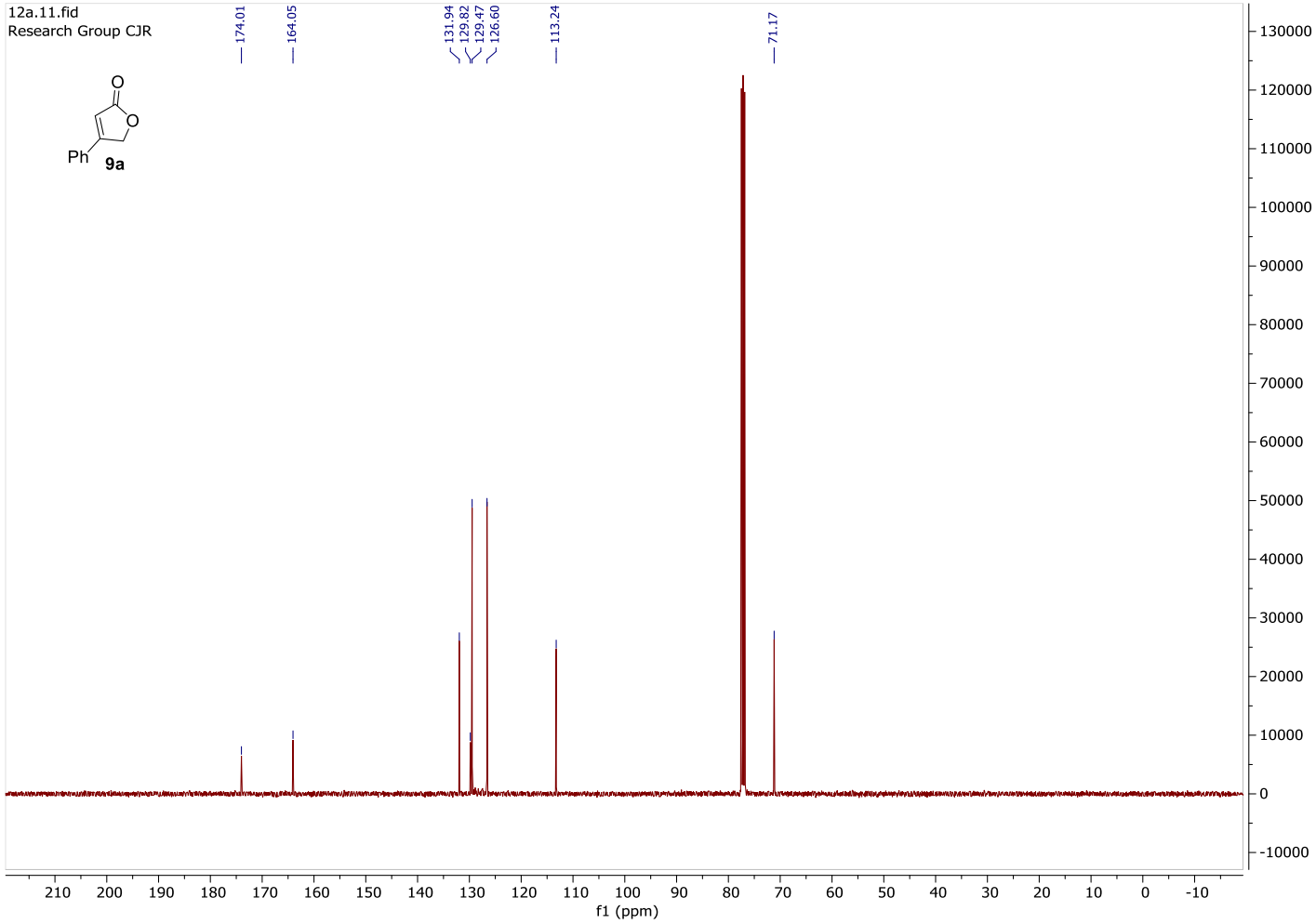
Compound **18** ^{13}C (101 MHz, $CDCl_3$)



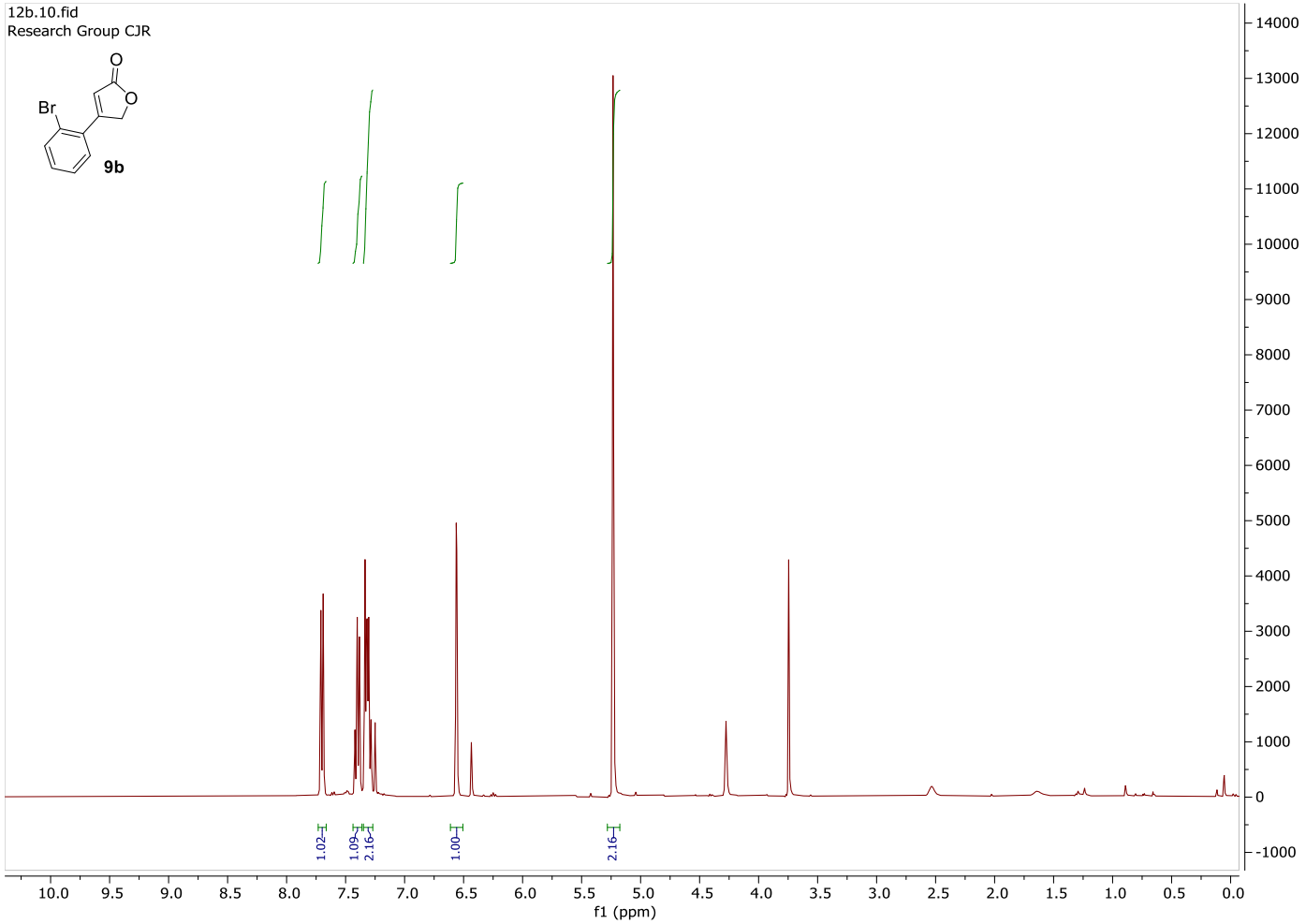
Compound **9a** ^{1}H (400 MHz, $CDCl_3$)



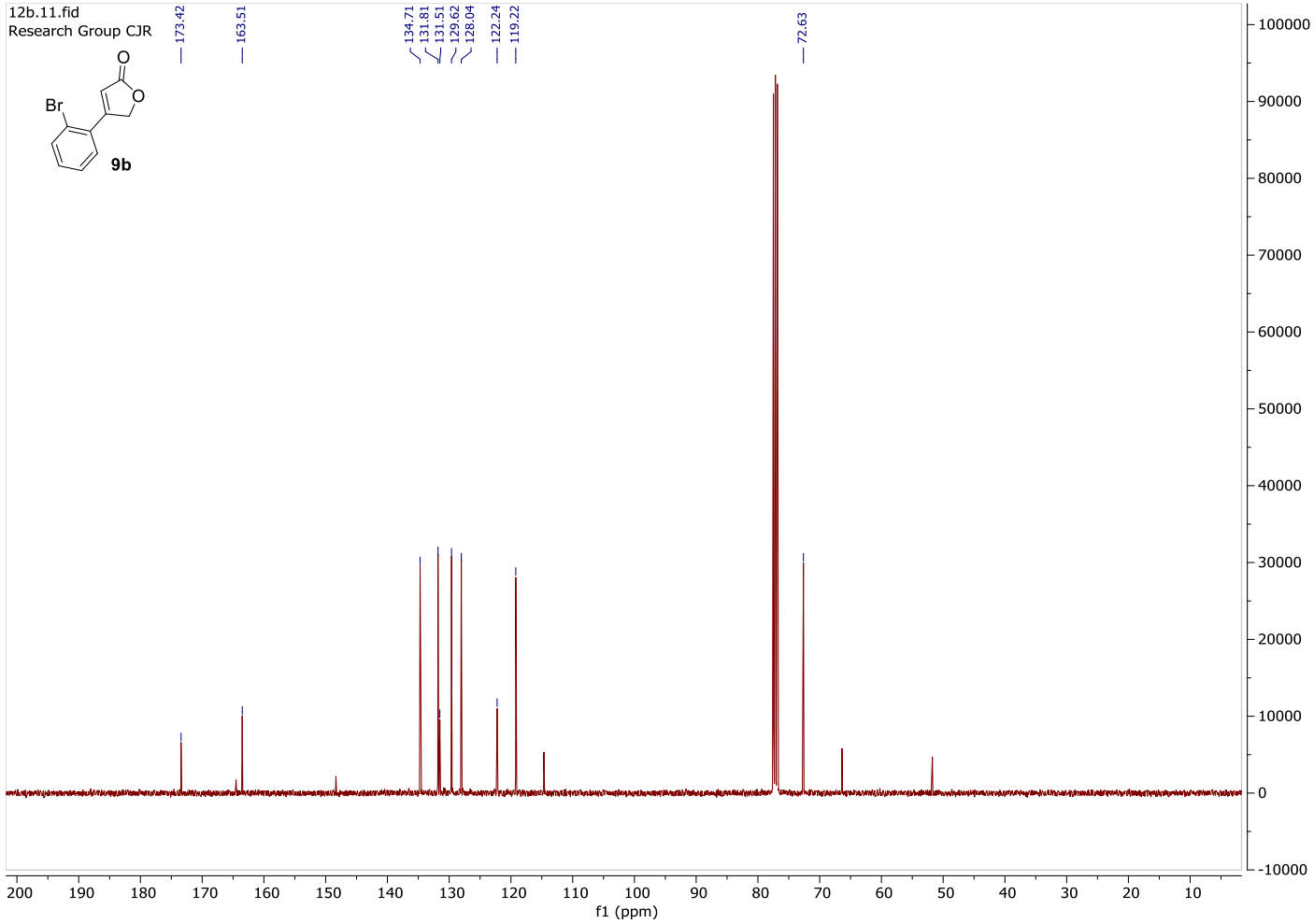
Compound **9a** ^{13}C (101 MHz, $CDCl_3$)



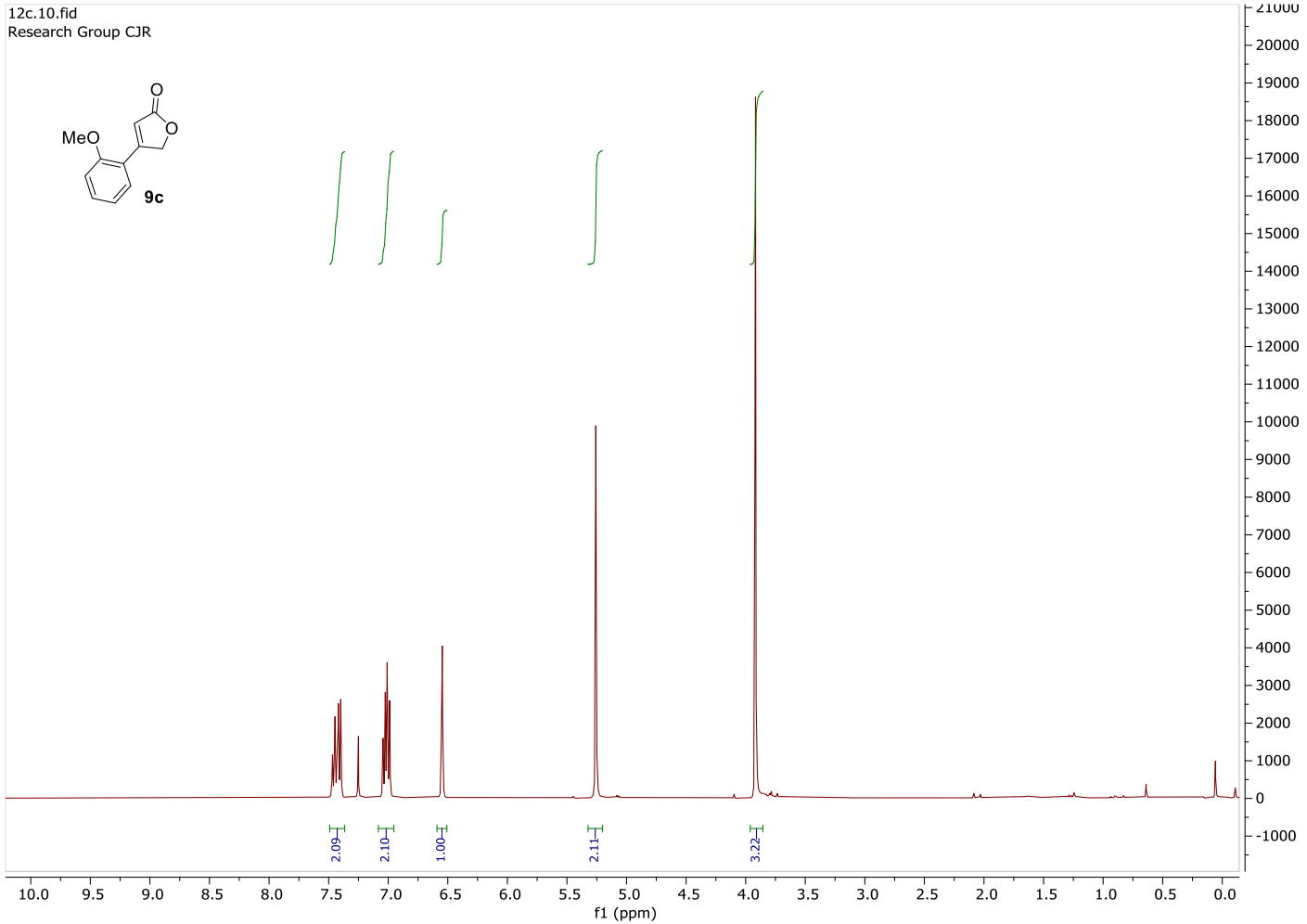
Compound **9b** ^{1}H (400 MHz, $CDCl_3$)



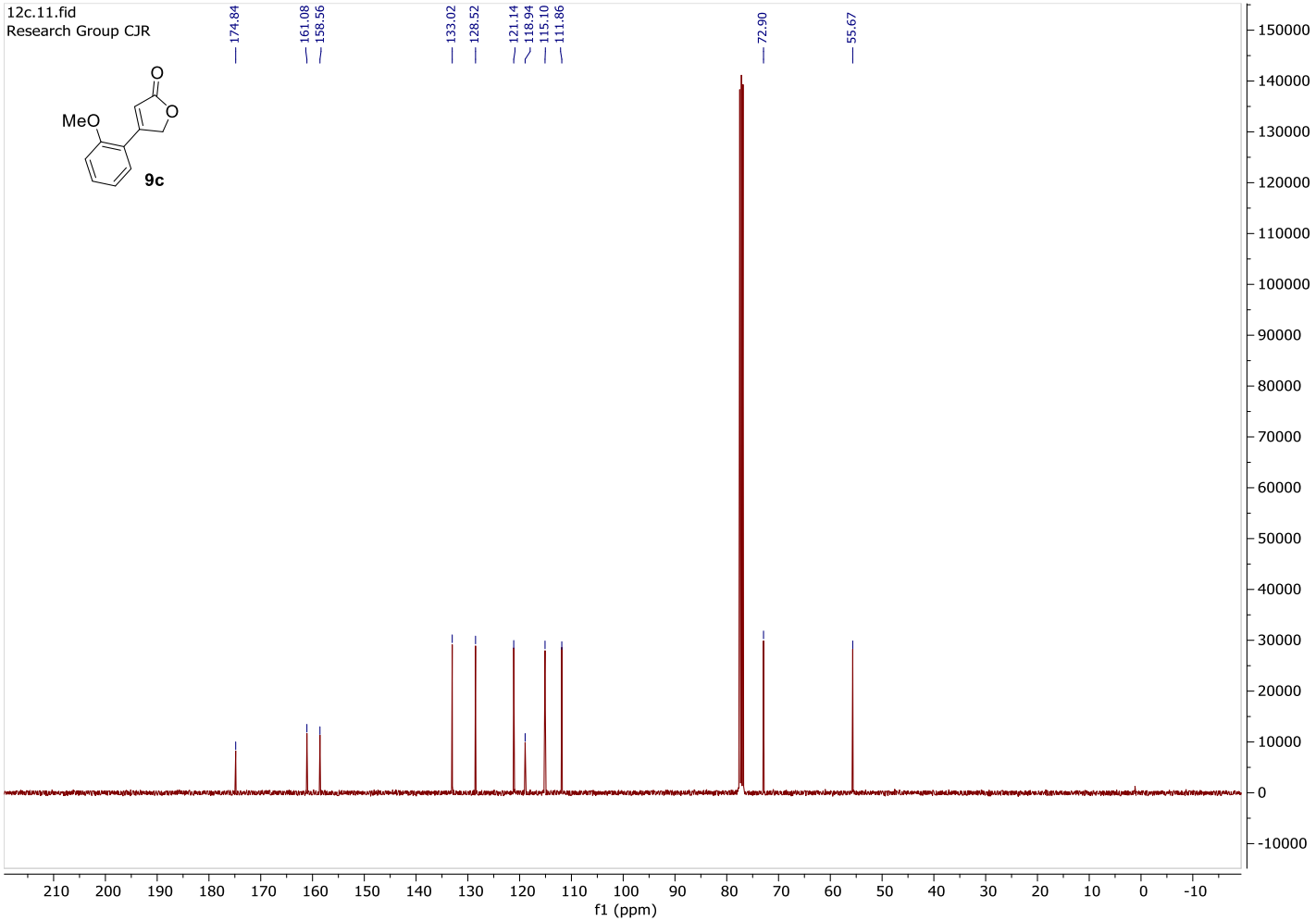
Compound **9b** ^{13}C (101 MHz, $CDCl_3$)



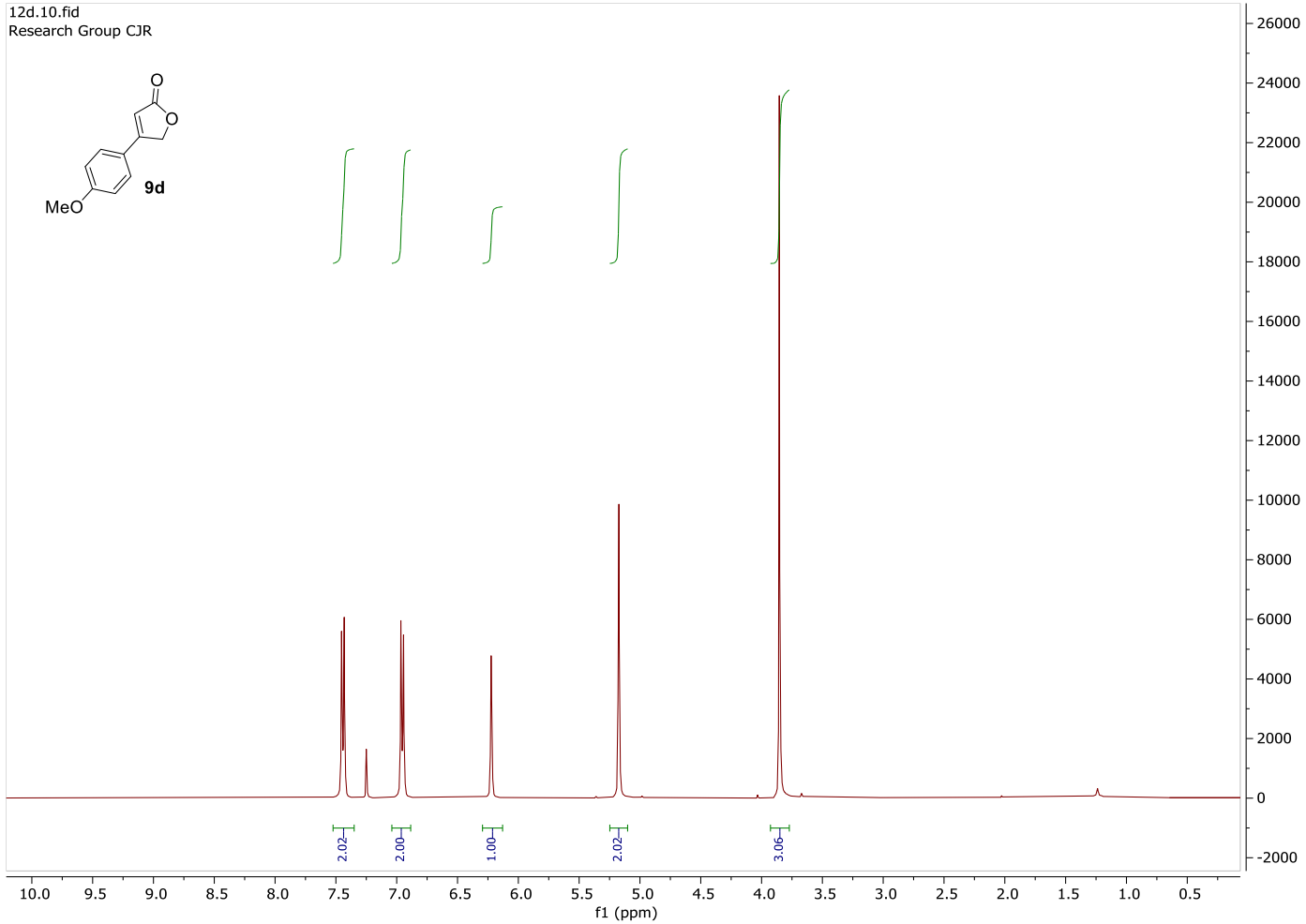
Compound **9c** ^{1}H (400 MHz, $CDCl_3$)



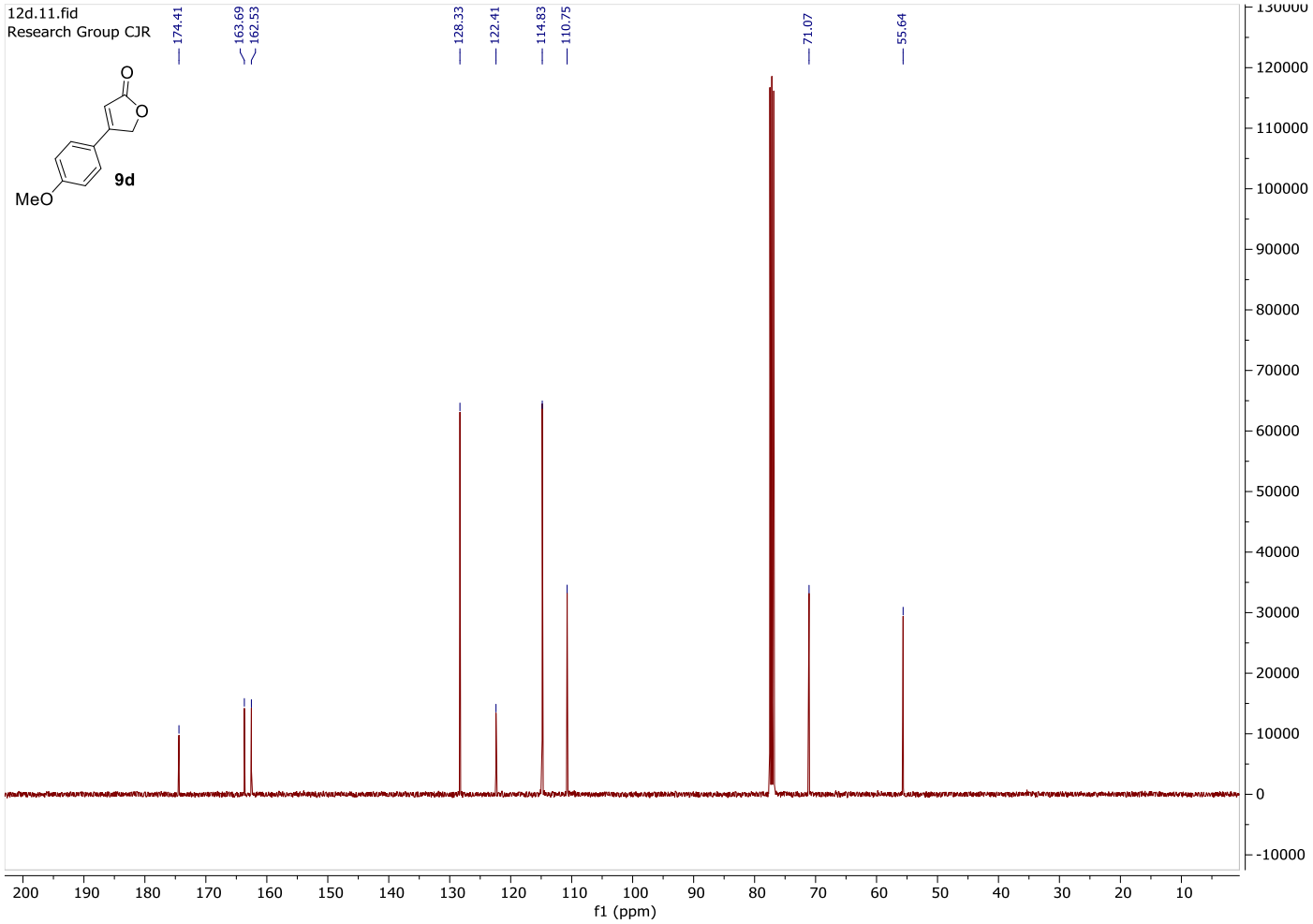
Compound **9c** ^{13}C (101 MHz, $CDCl_3$)



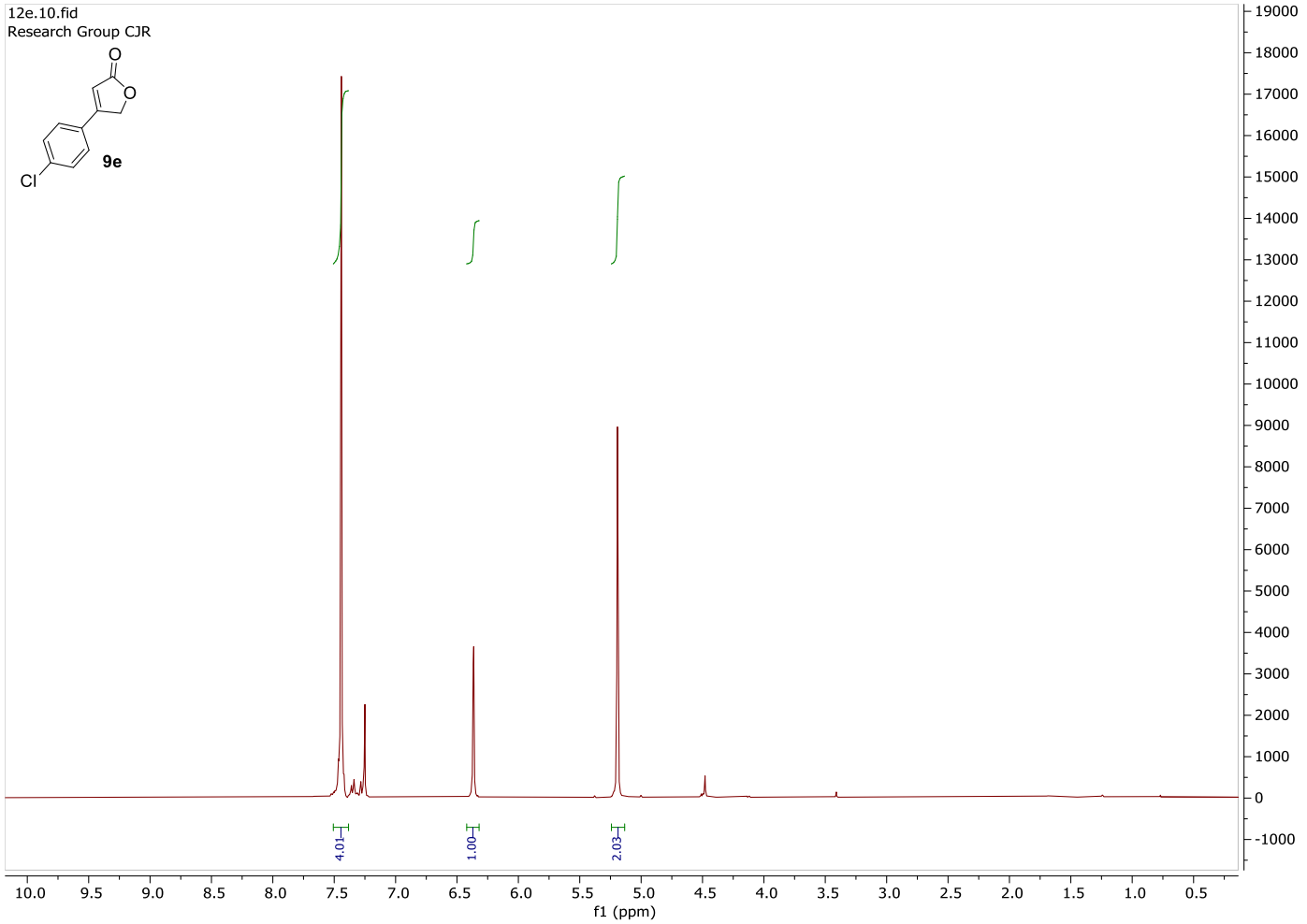
Compound **9d** ^{1}H (400 MHz, $CDCl_3$)



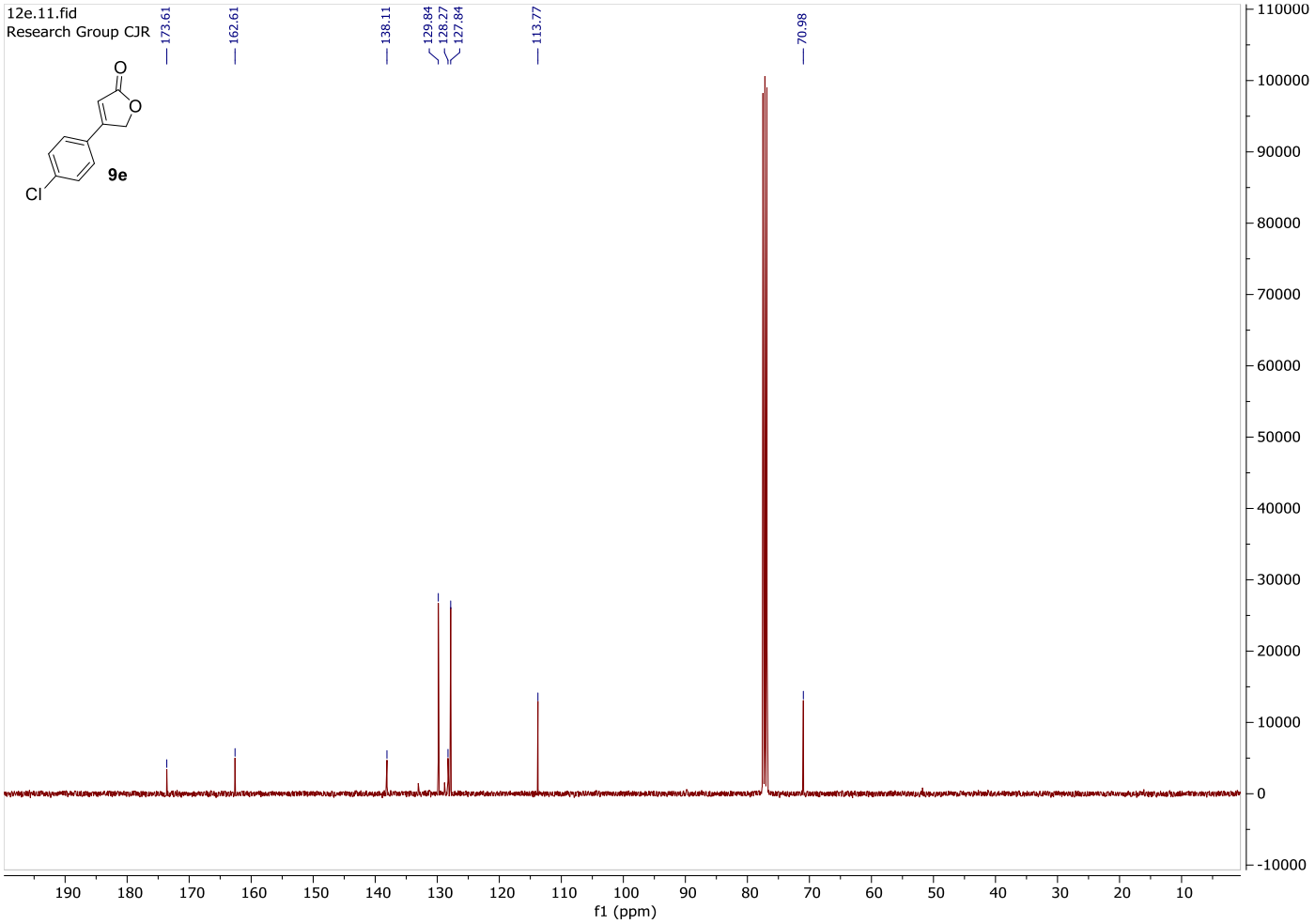
Compound **9d** ^{13}C (101 MHz, $CDCl_3$)



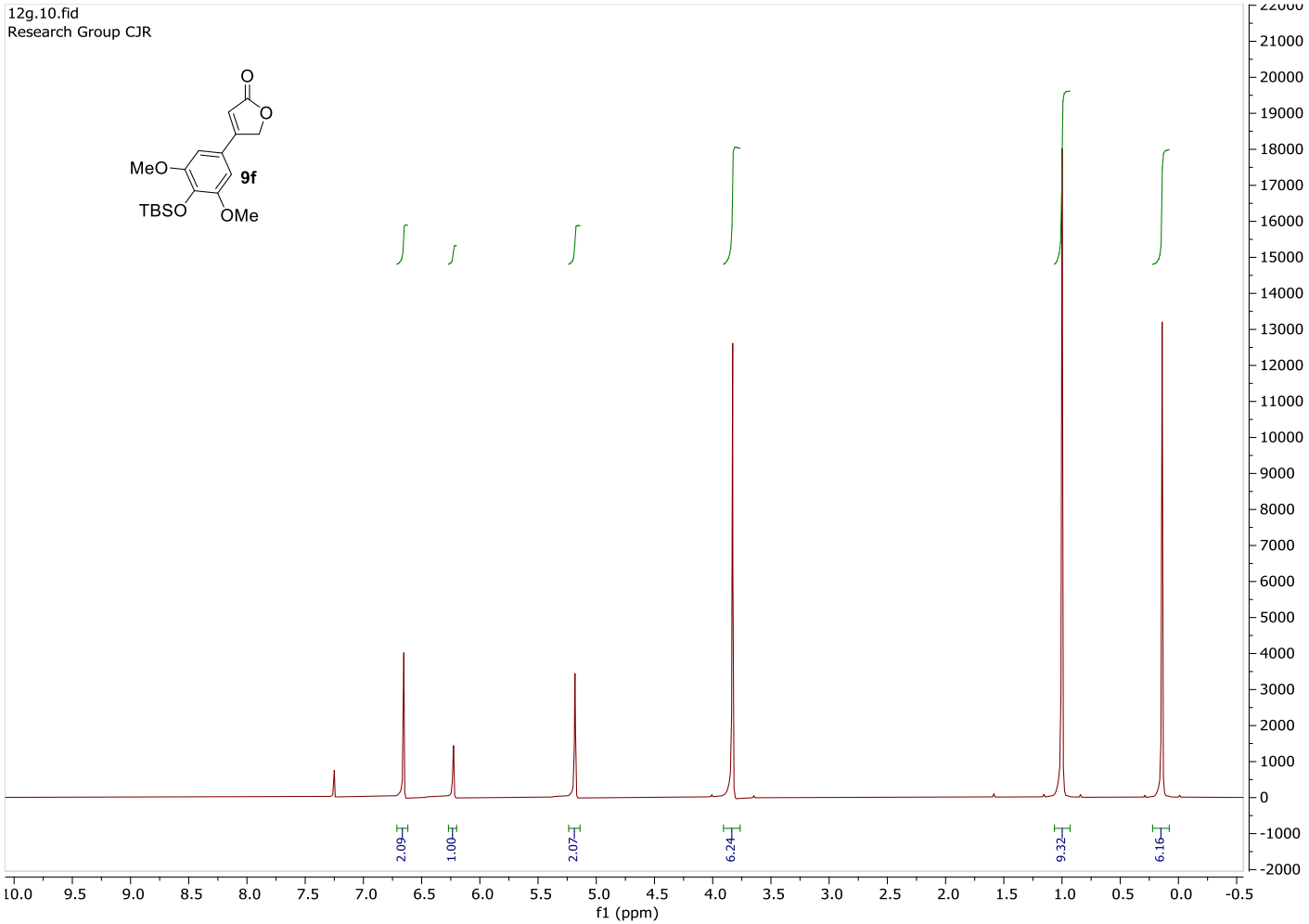
Compound **9e** ^{1}H (400 MHz, $CDCl_3$)



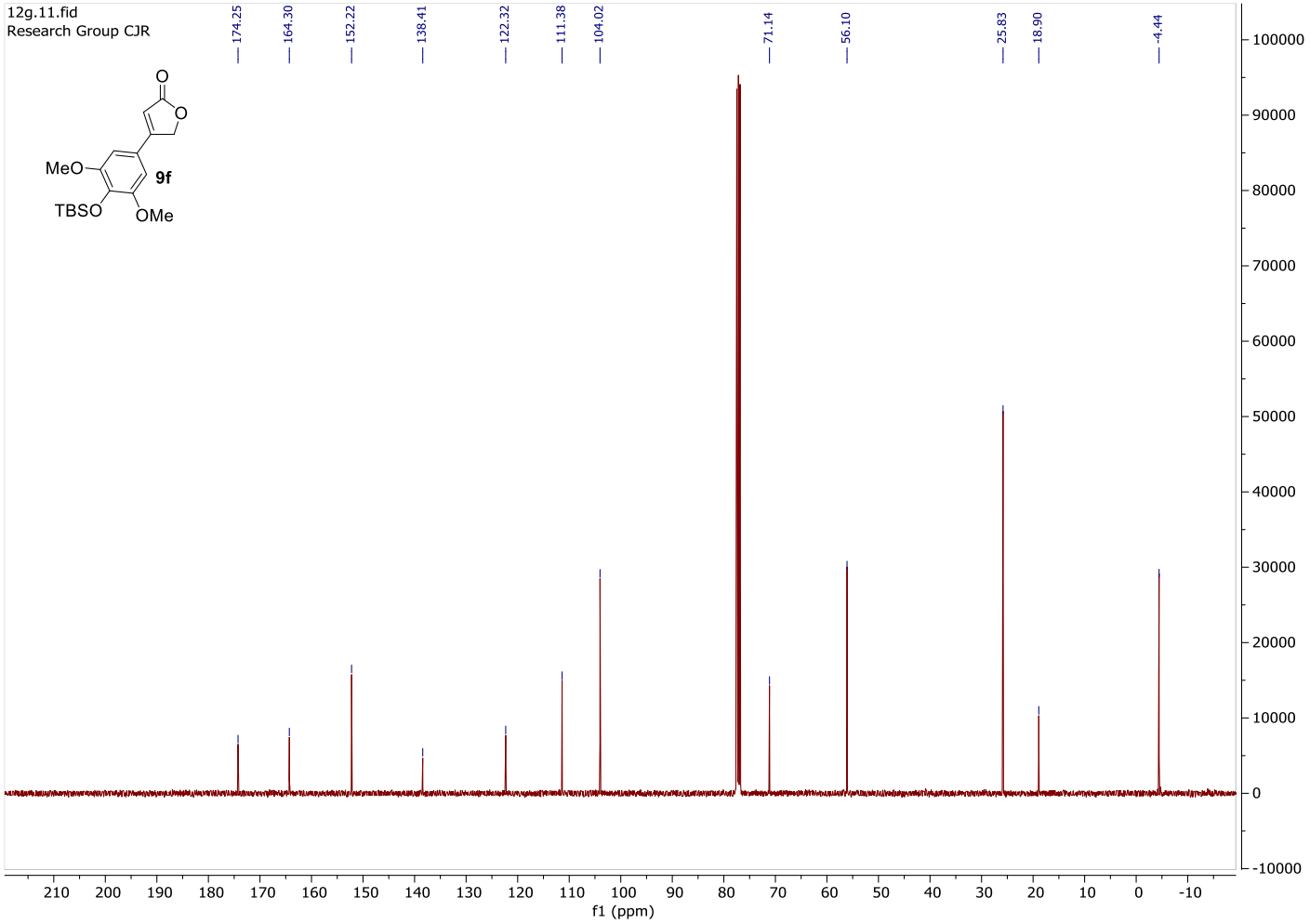
Compound **9e** ^{13}C (101 MHz, $CDCl_3$)



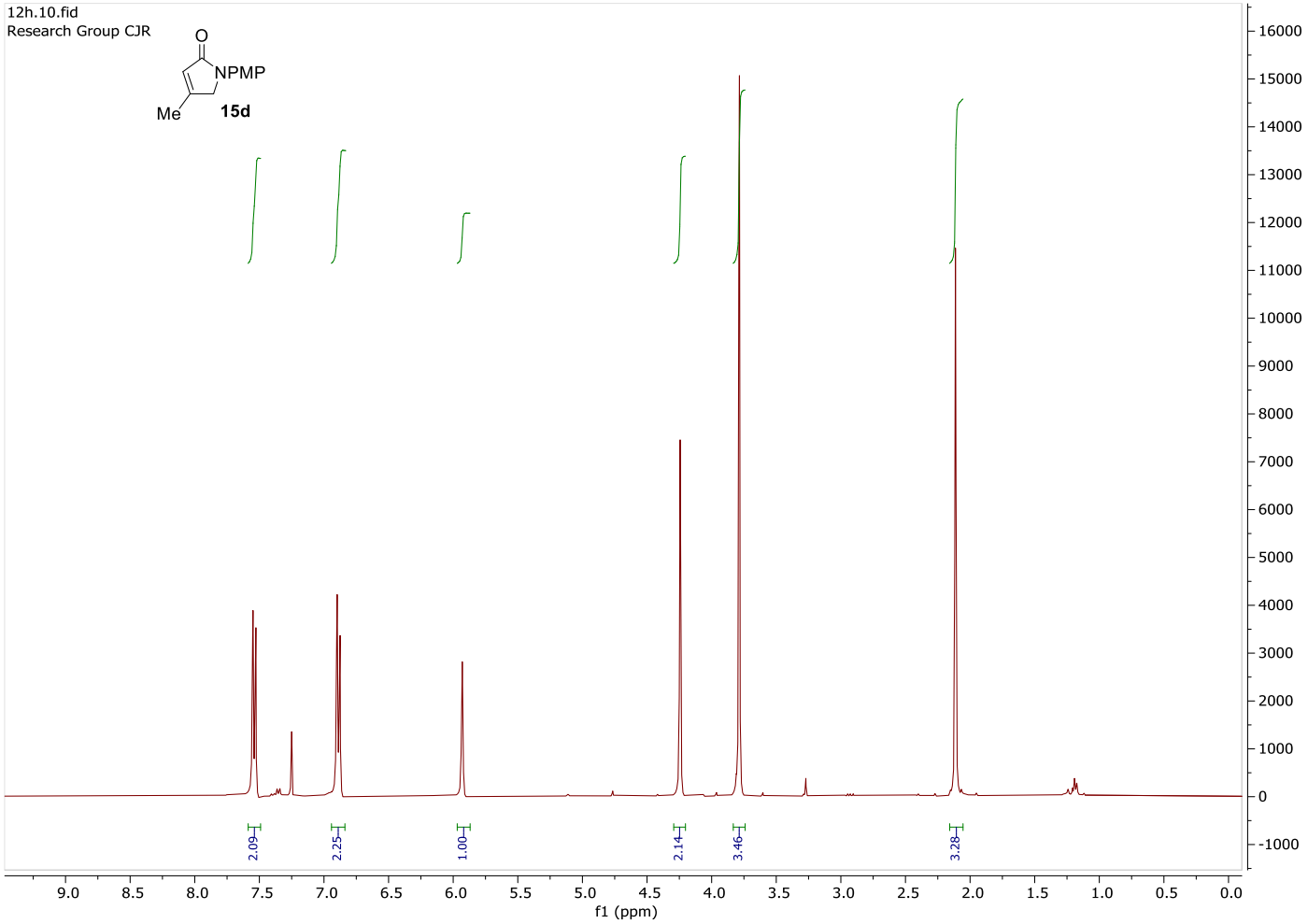
Compound **9f** ^{1}H (400 MHz, $CDCl_3$)



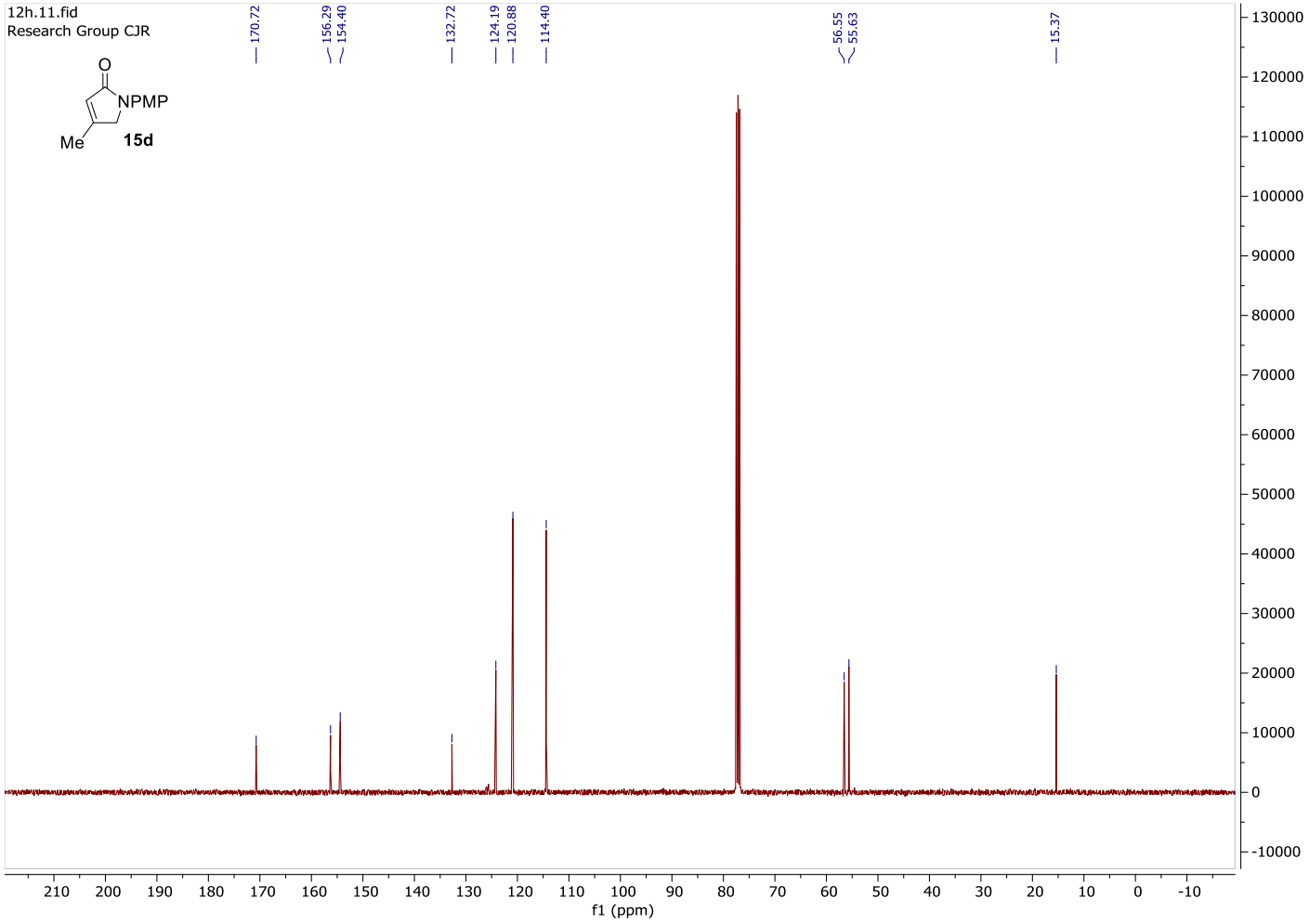
Compound **9f** ^{13}C (101 MHz, $CDCl_3$)



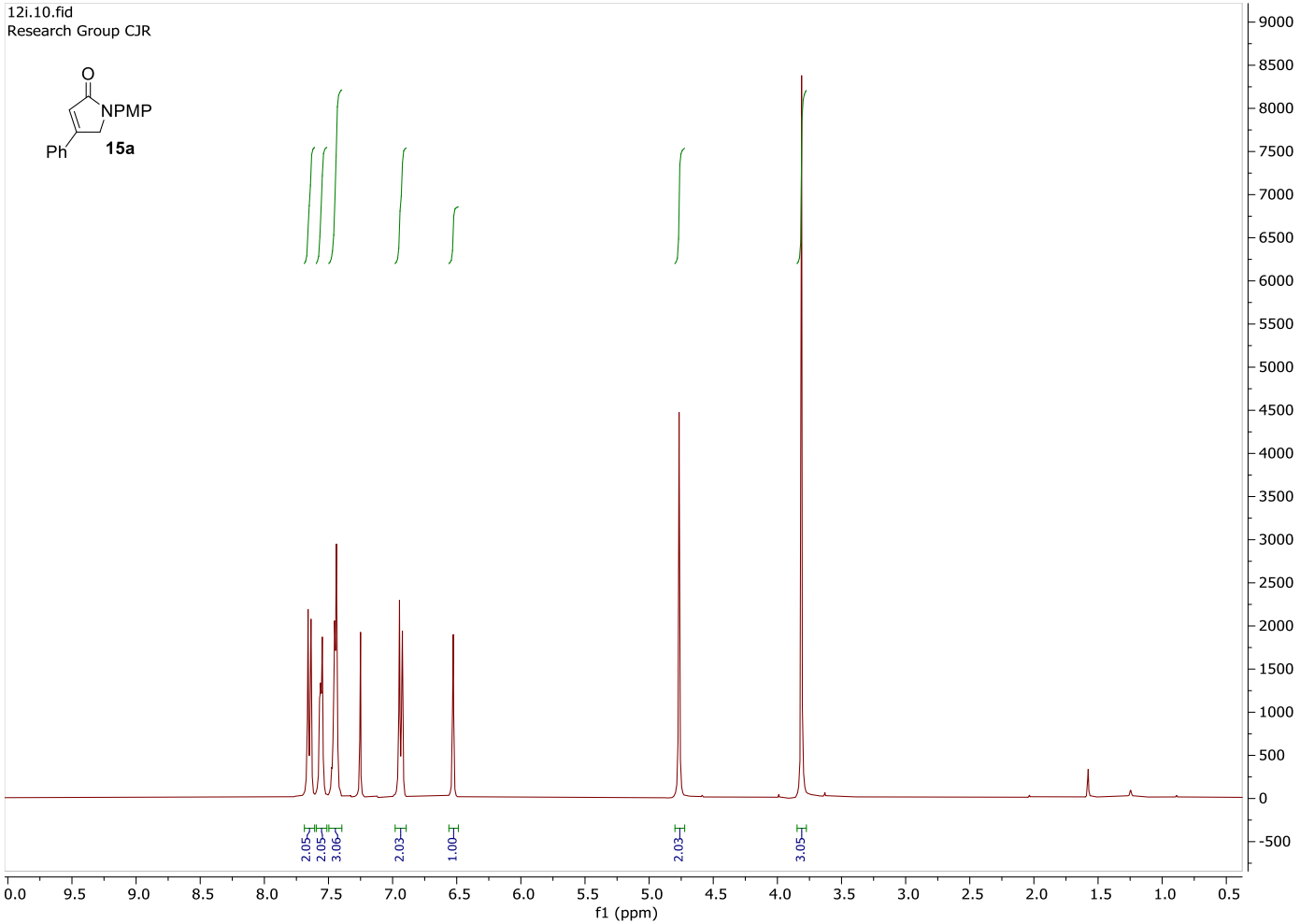
Compound **15d** ^{1}H (400 MHz, $CDCl_3$)



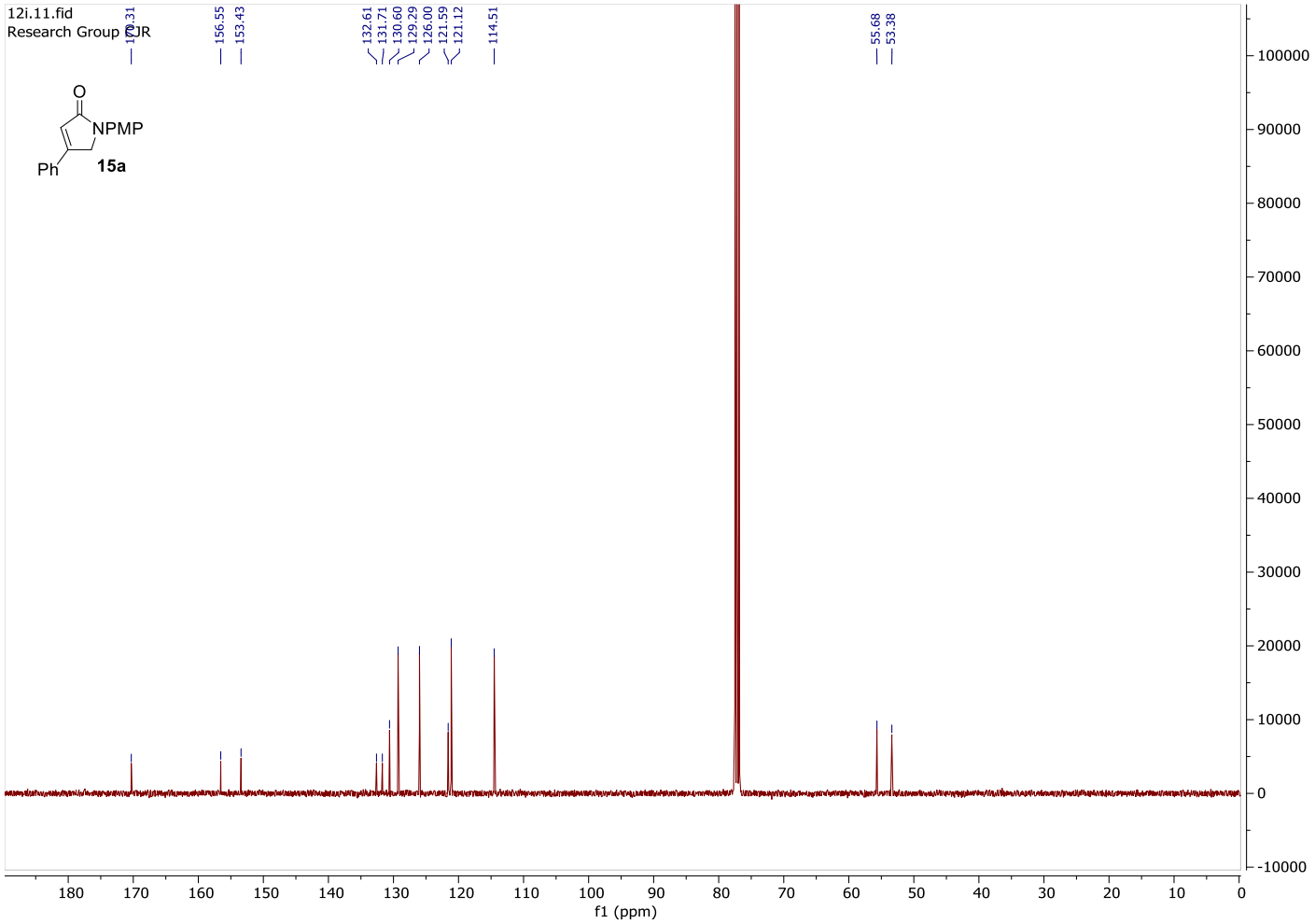
Compound **15d** ^{13}C (101 MHz, $CDCl_3$)



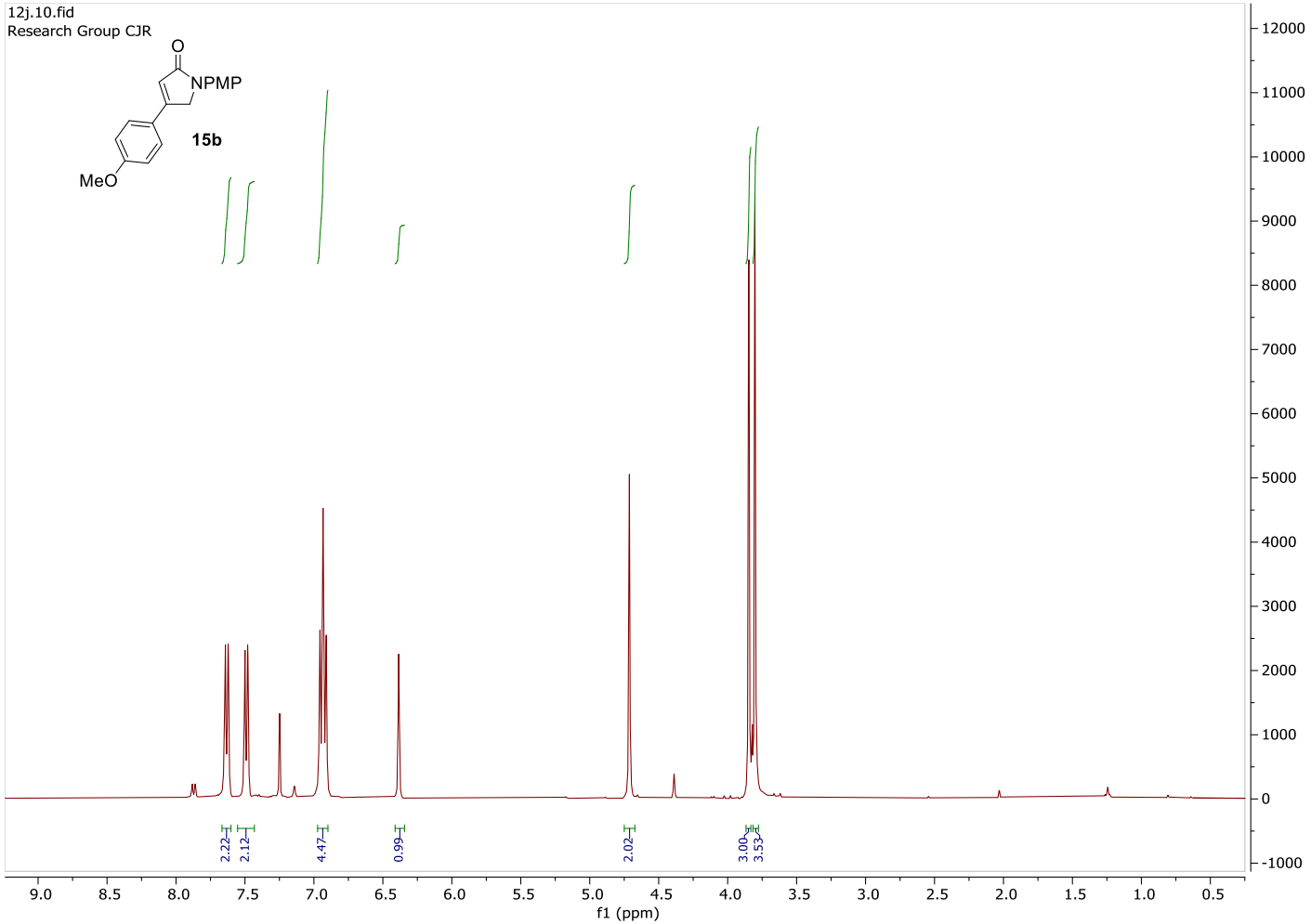
Compound **15a** ^{1}H (400 MHz, $CDCl_3$)



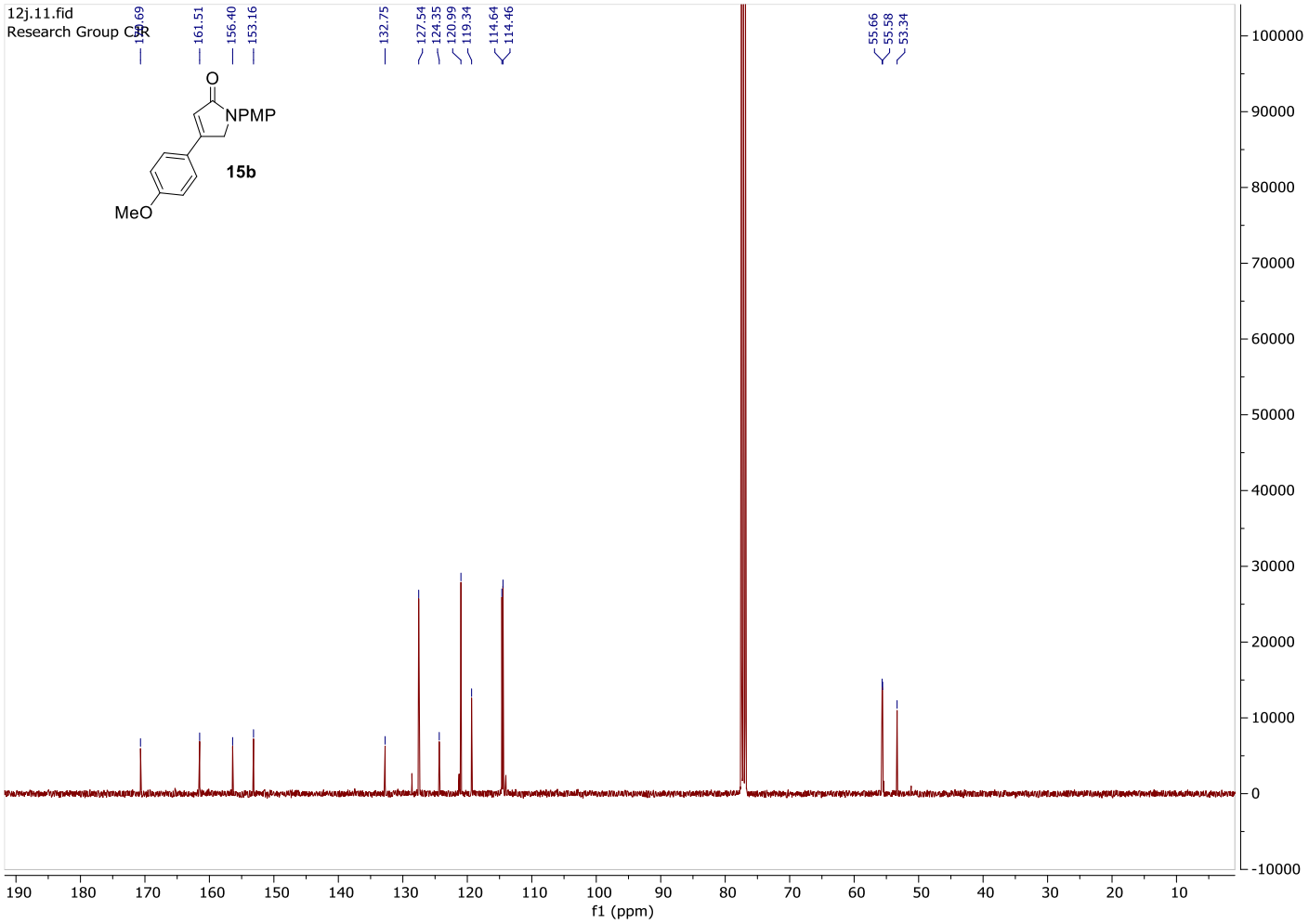
Compound **15a** ^{13}C (101 MHz, $CDCl_3$)



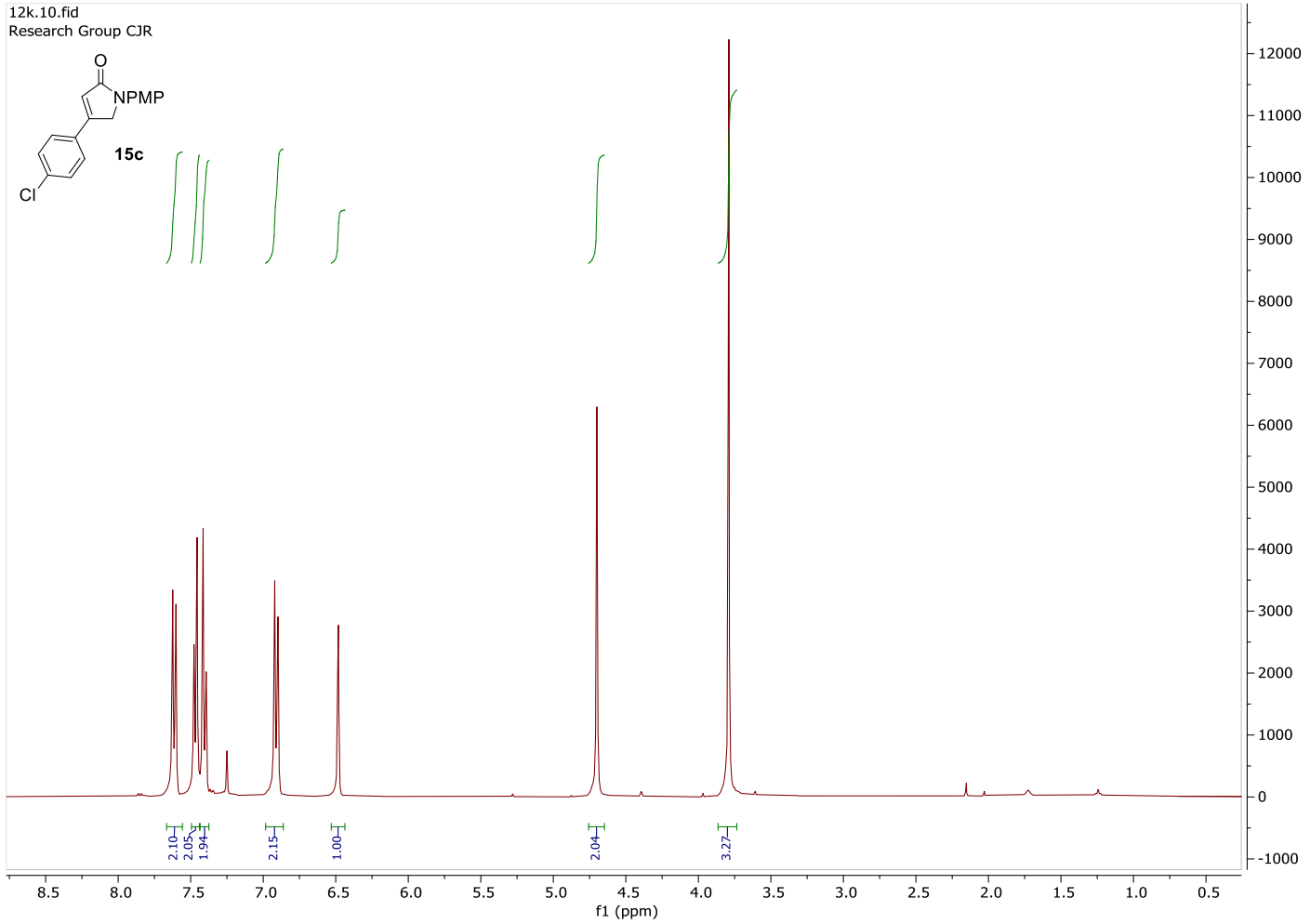
Compound **15b** ^{1}H (400 MHz, $CDCl_3$)



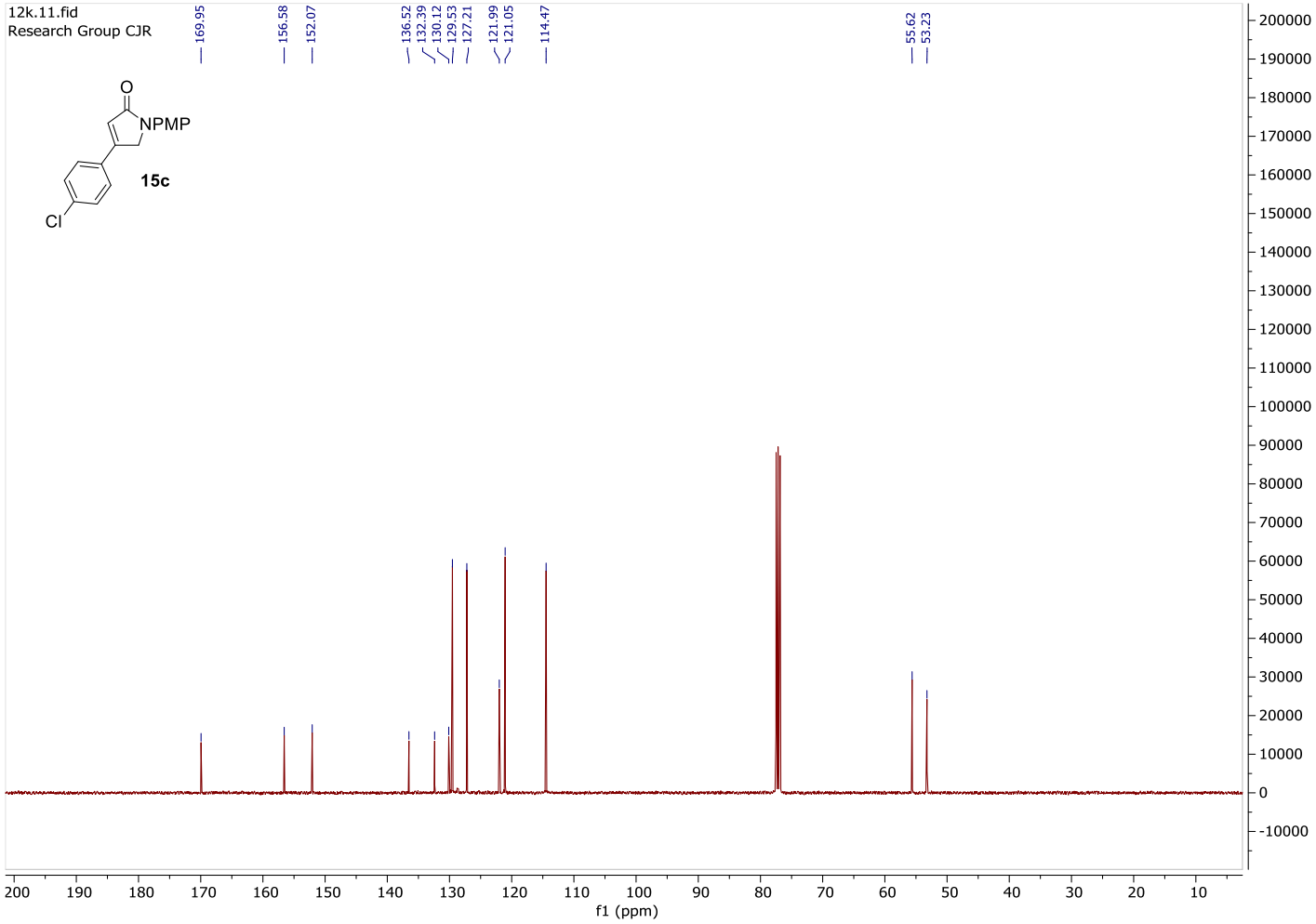
Compound **15b** ^{13}C (101 MHz, $CDCl_3$)



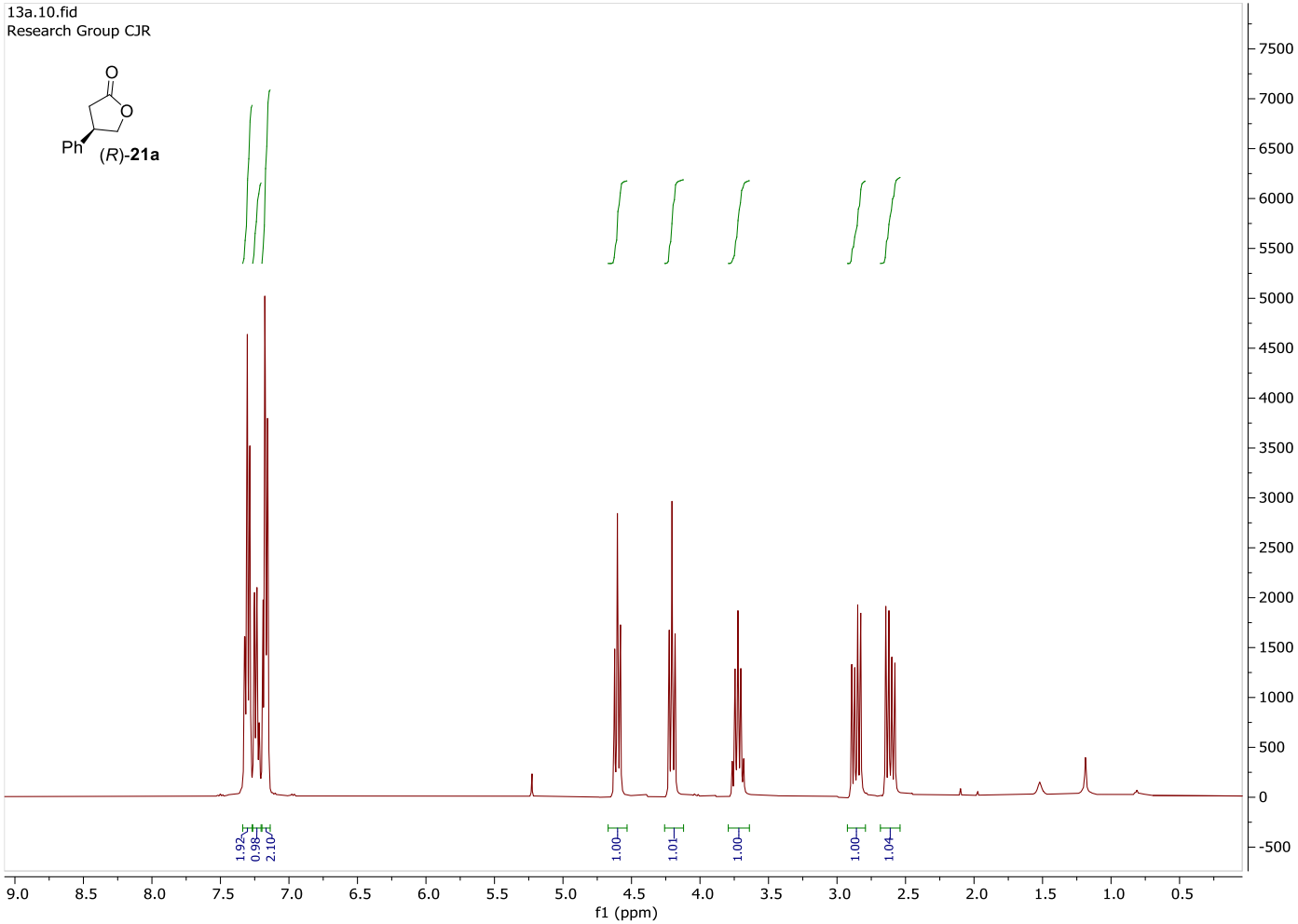
Compound **15c** ^{1}H (400 MHz, $CDCl_3$)



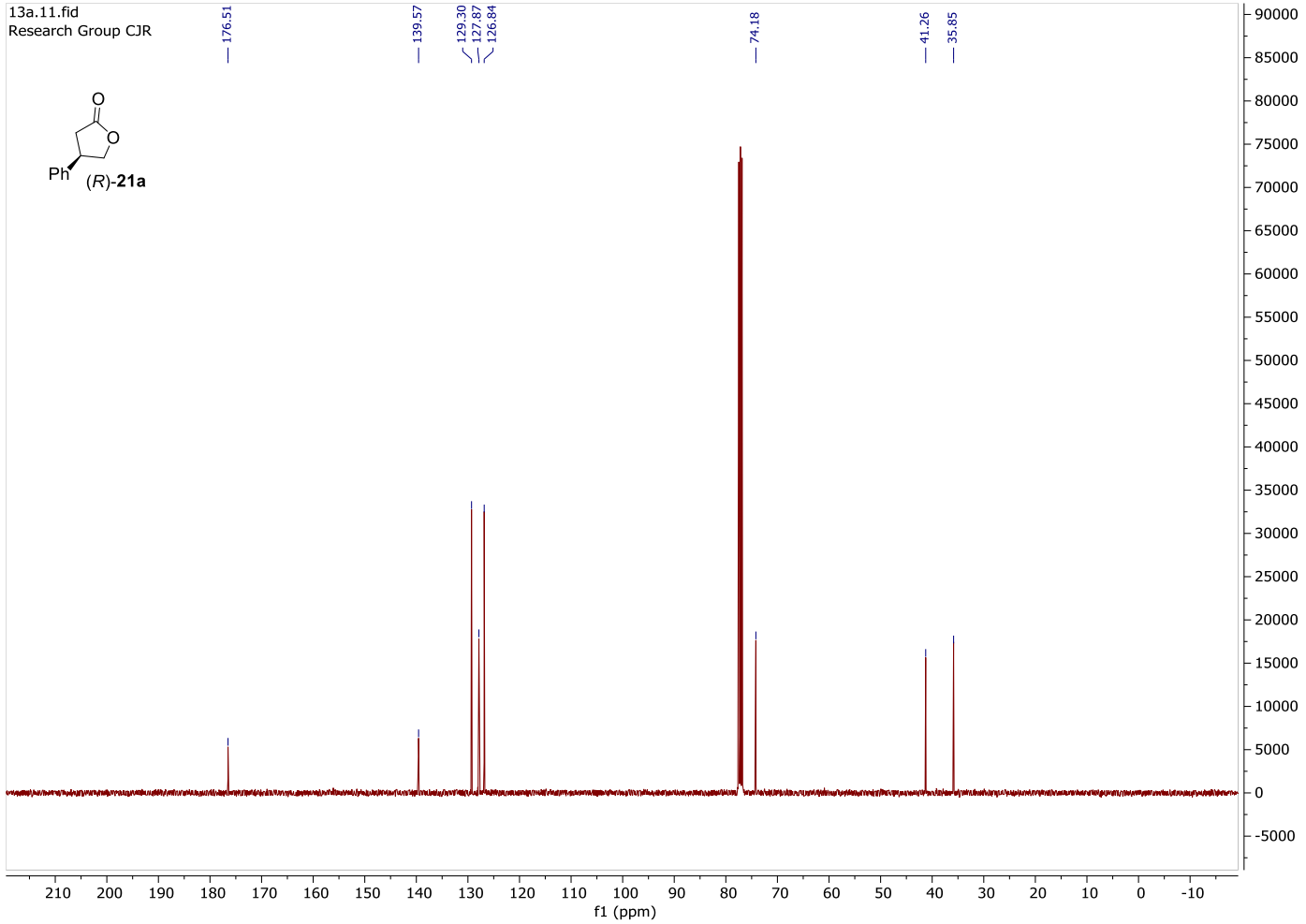
Compound **15c** ^{13}C (101 MHz, $CDCl_3$)



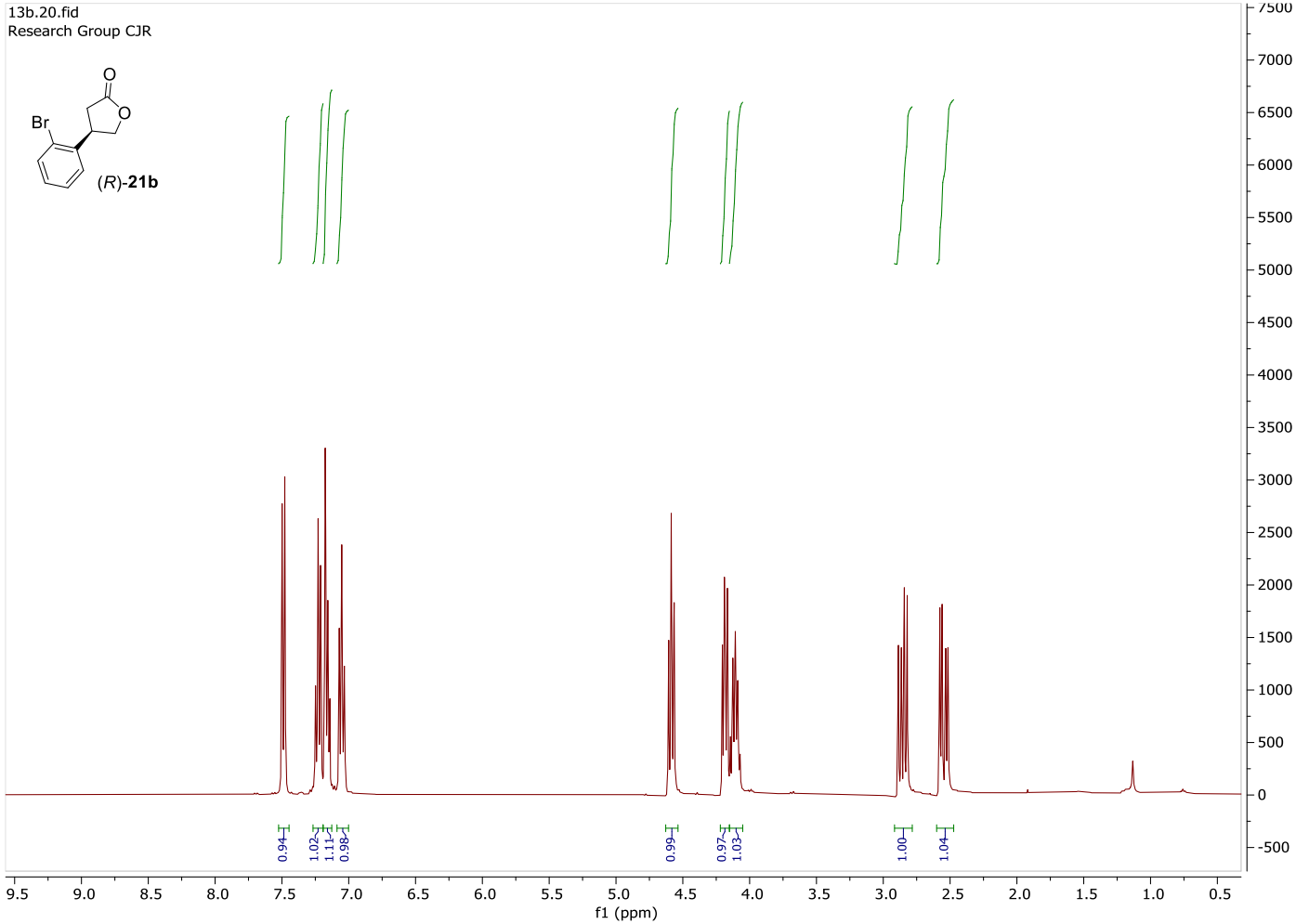
Compound **21a** ^{1}H (400 MHz, $CDCl_3$)



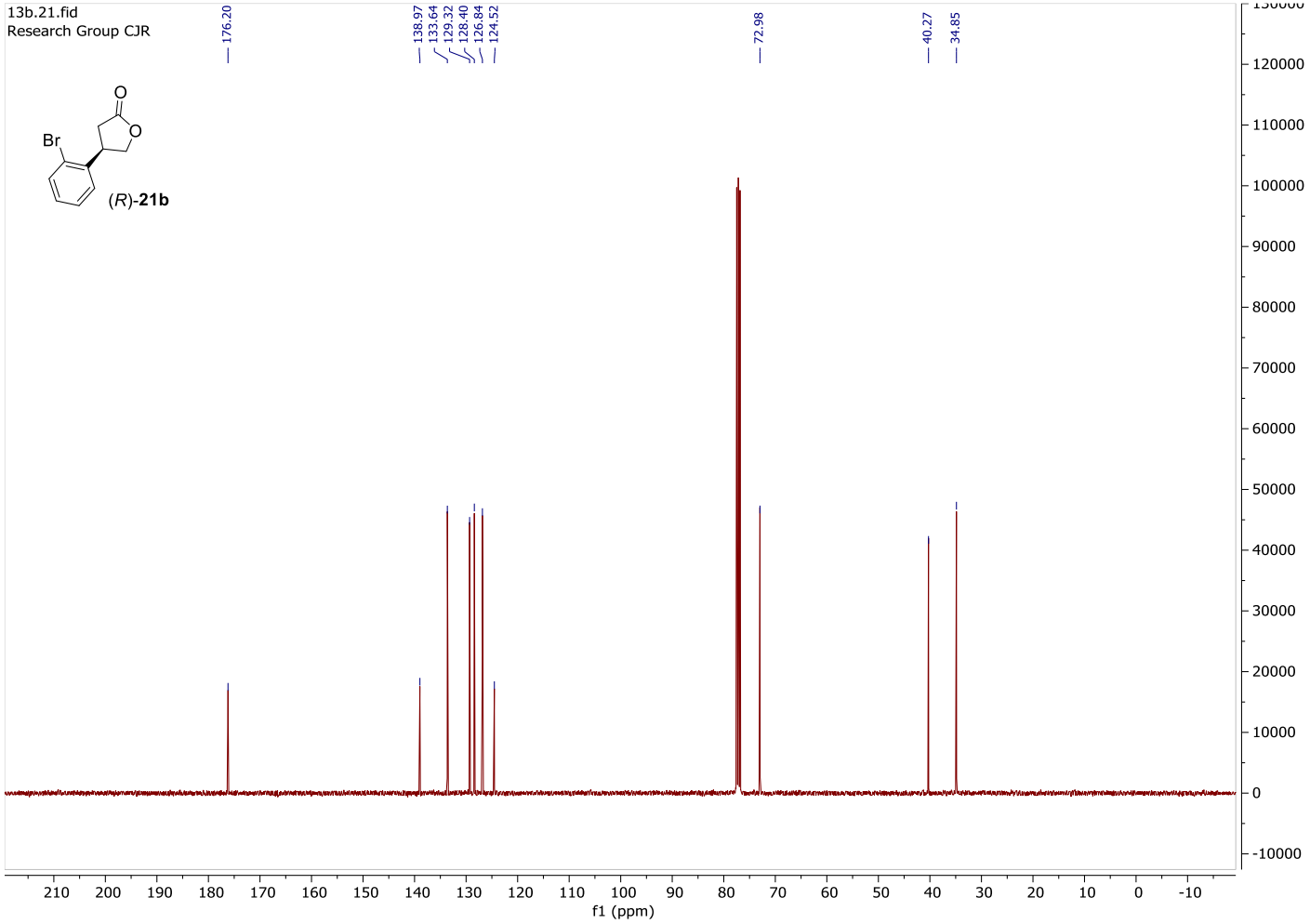
Compound **21a** ^{13}C (101 MHz, $CDCl_3$)



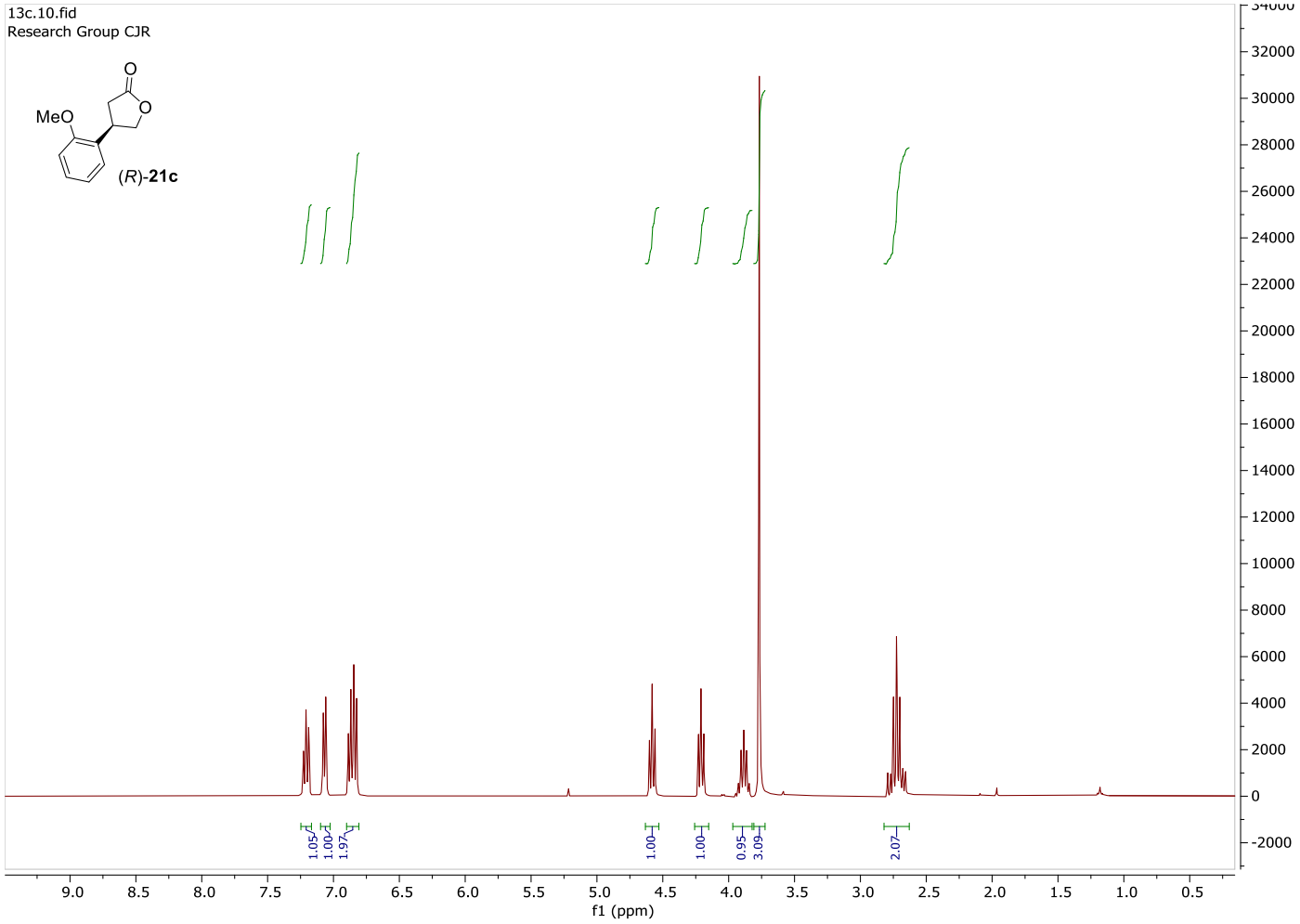
Compound **21b** ^{1}H (400 MHz, $CDCl_3$)



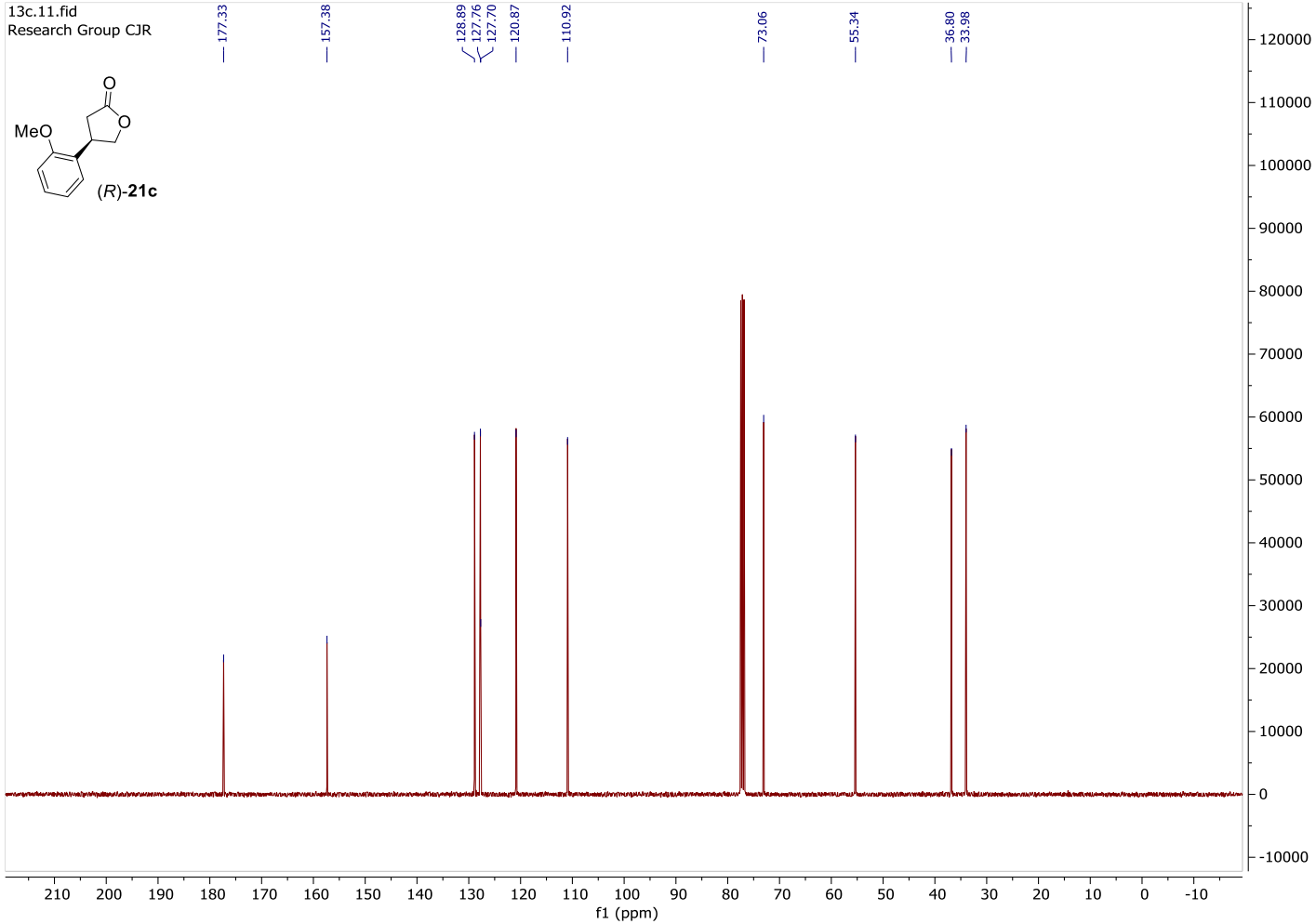
Compound **21b** ^{13}C (101 MHz, $CDCl_3$)



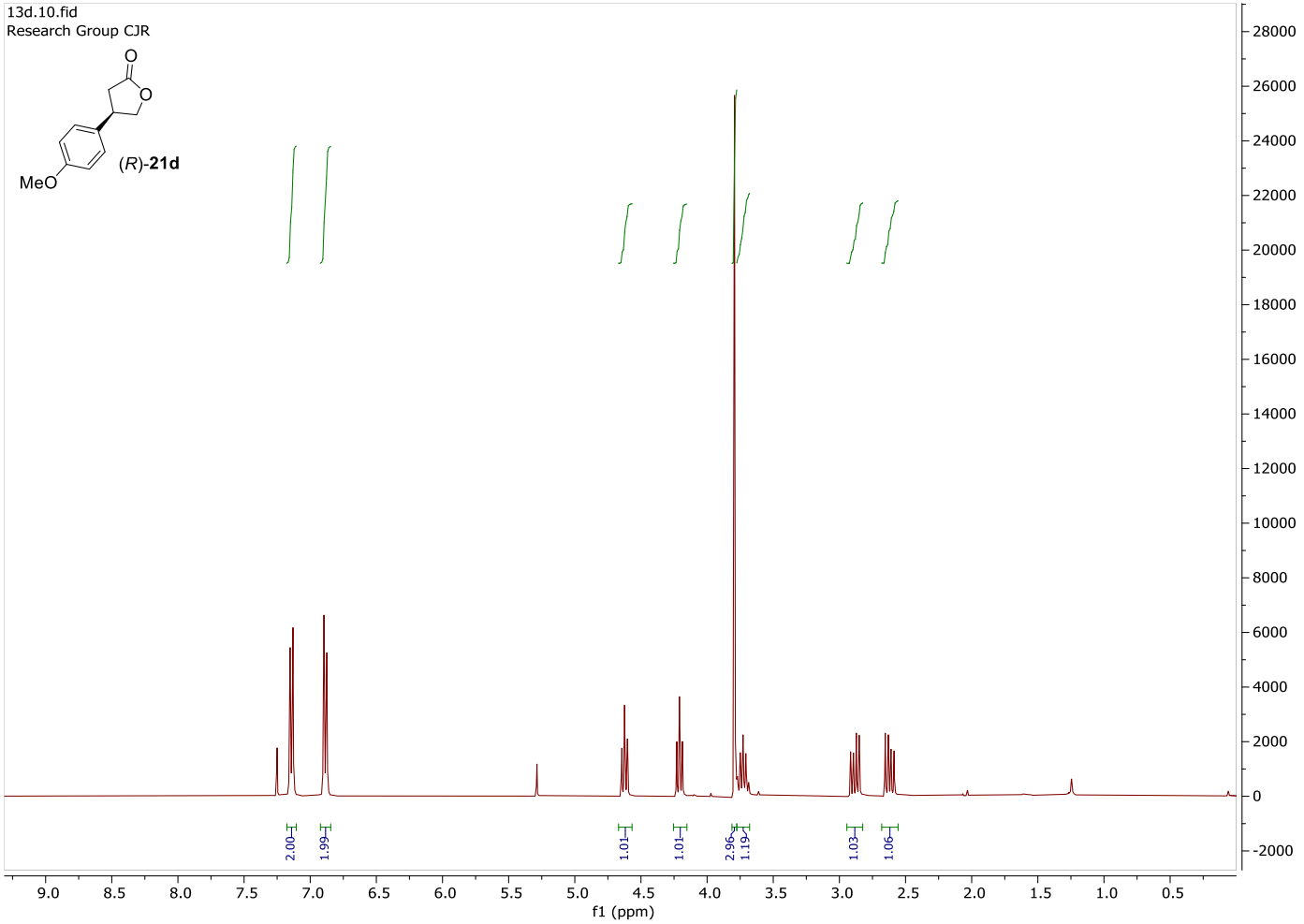
Compound **21c** ^{1}H (400 MHz, $CDCl_3$)



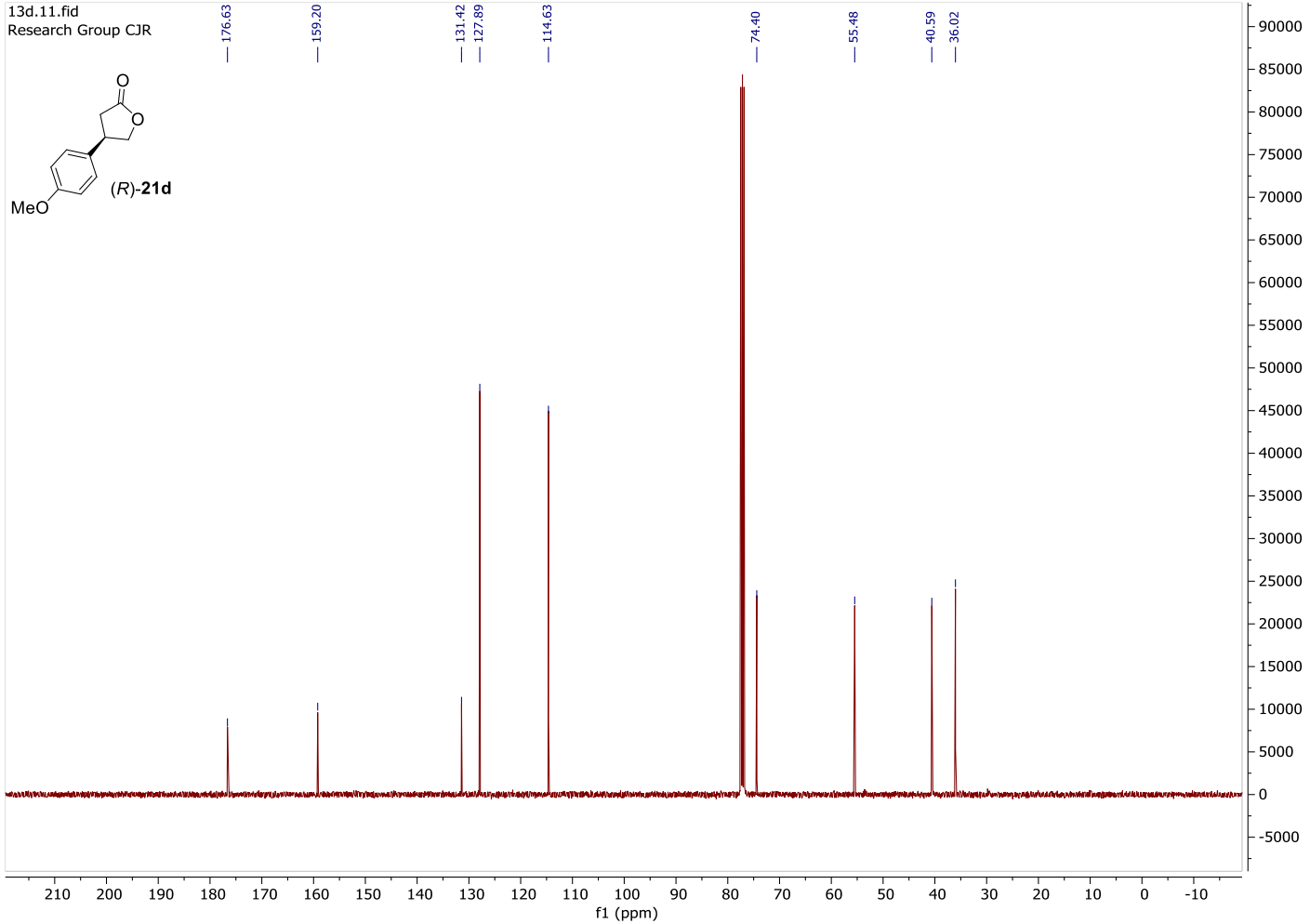
Compound **21c** ^{13}C (101 MHz, $CDCl_3$)



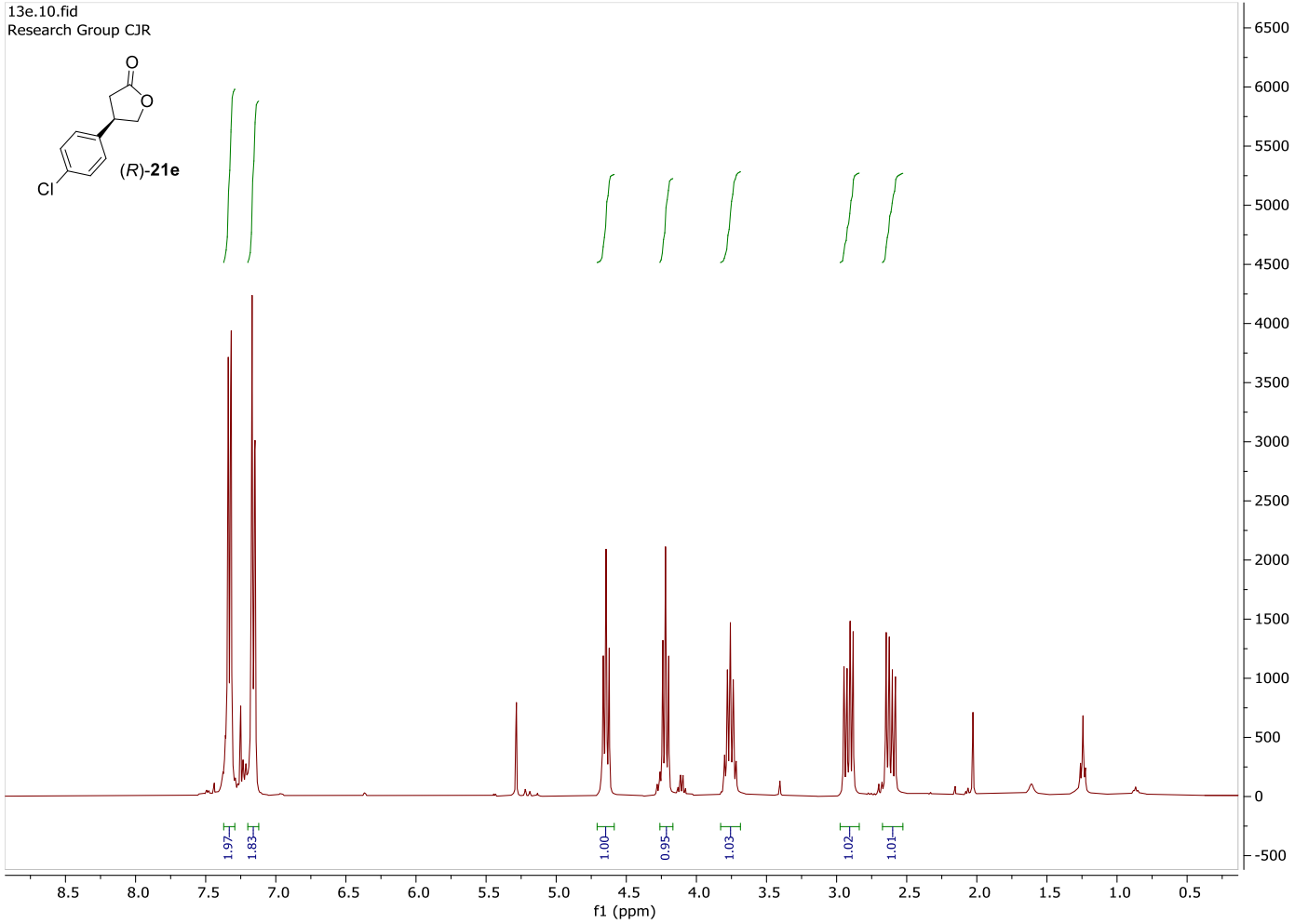
Compound **21d** ^{1}H (400 MHz, $CDCl_3$)



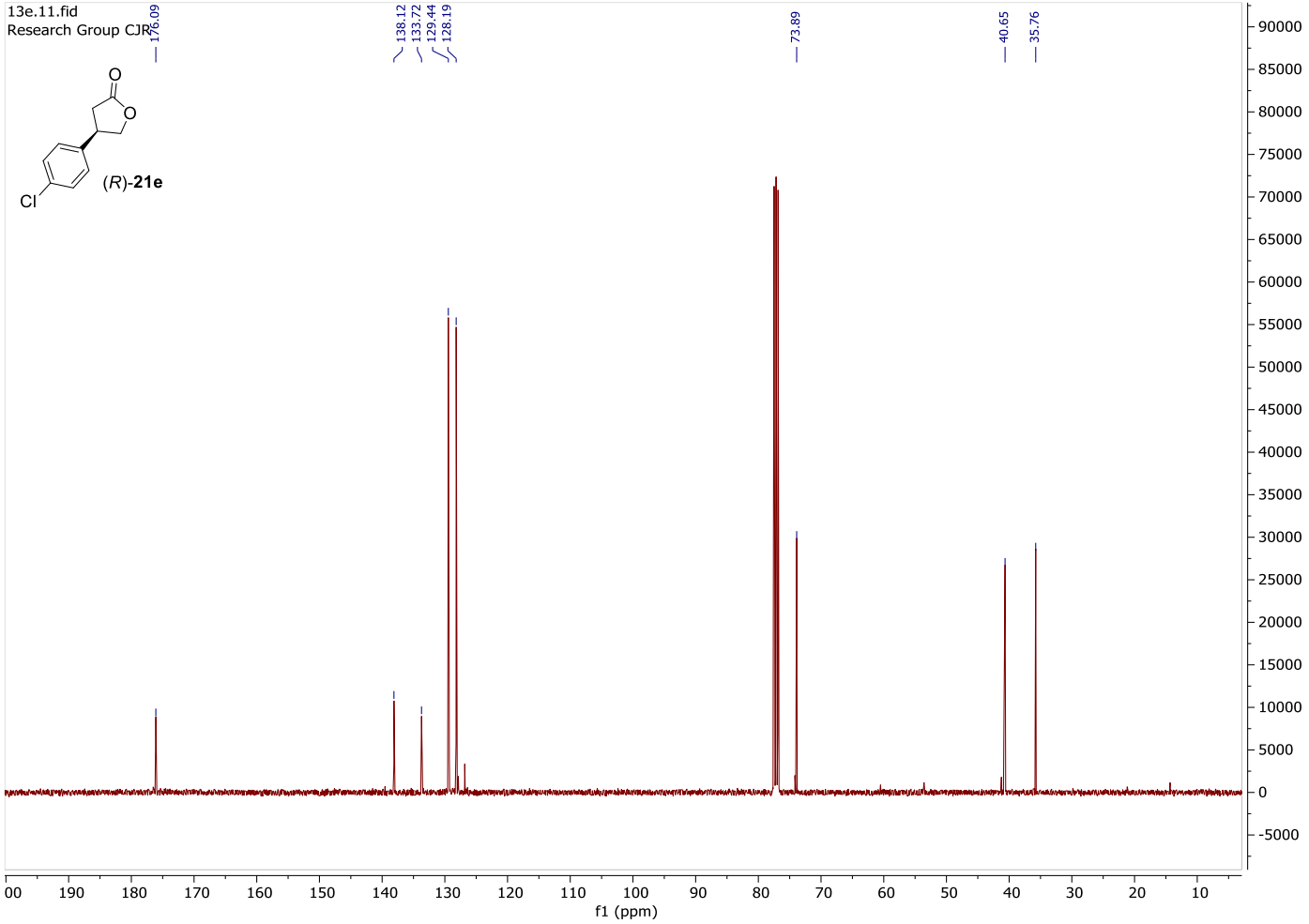
Compound **21d** ^{13}C (101 MHz, $CDCl_3$)



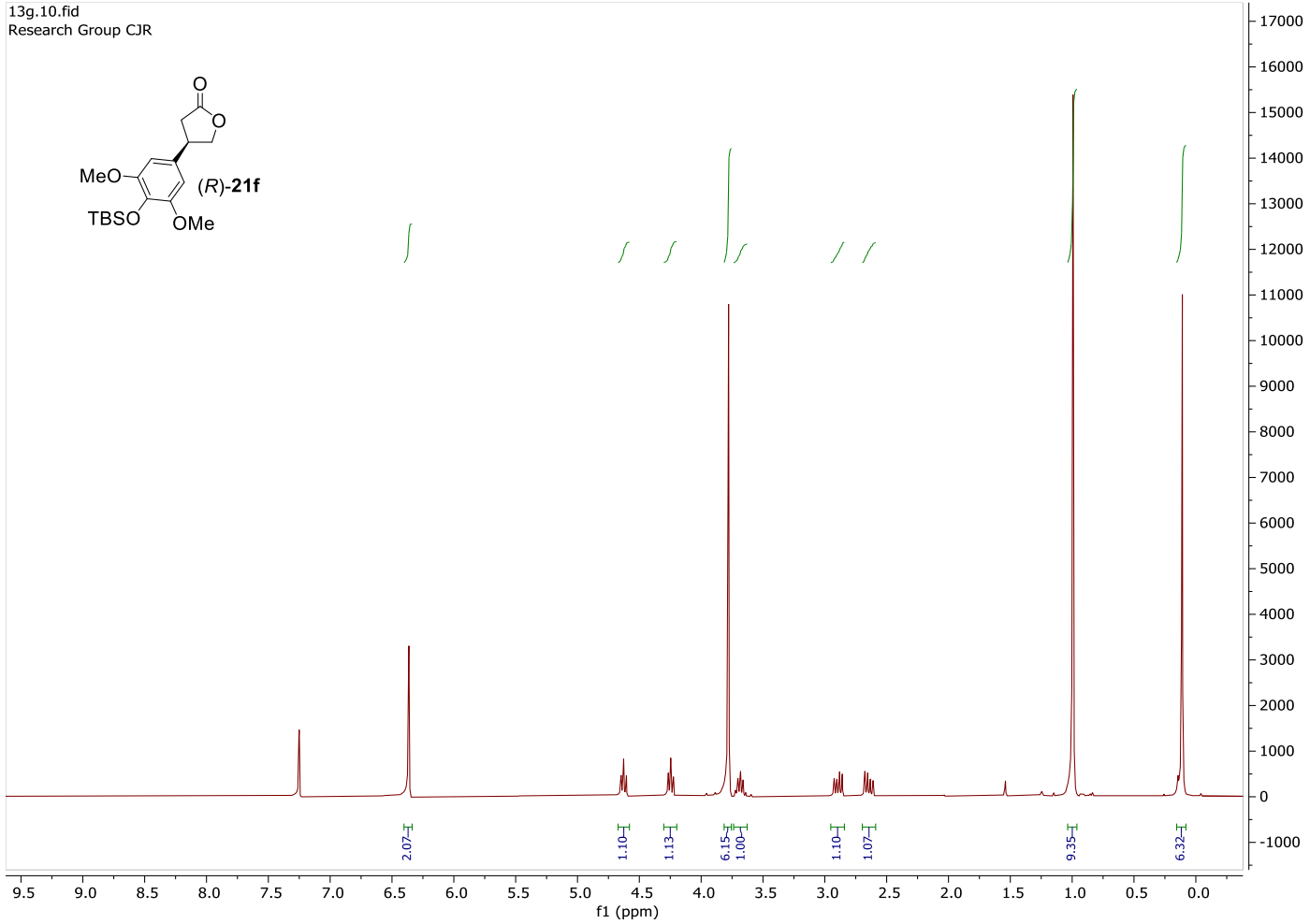
Compound **21e** ^{1}H (400 MHz, $CDCl_3$)



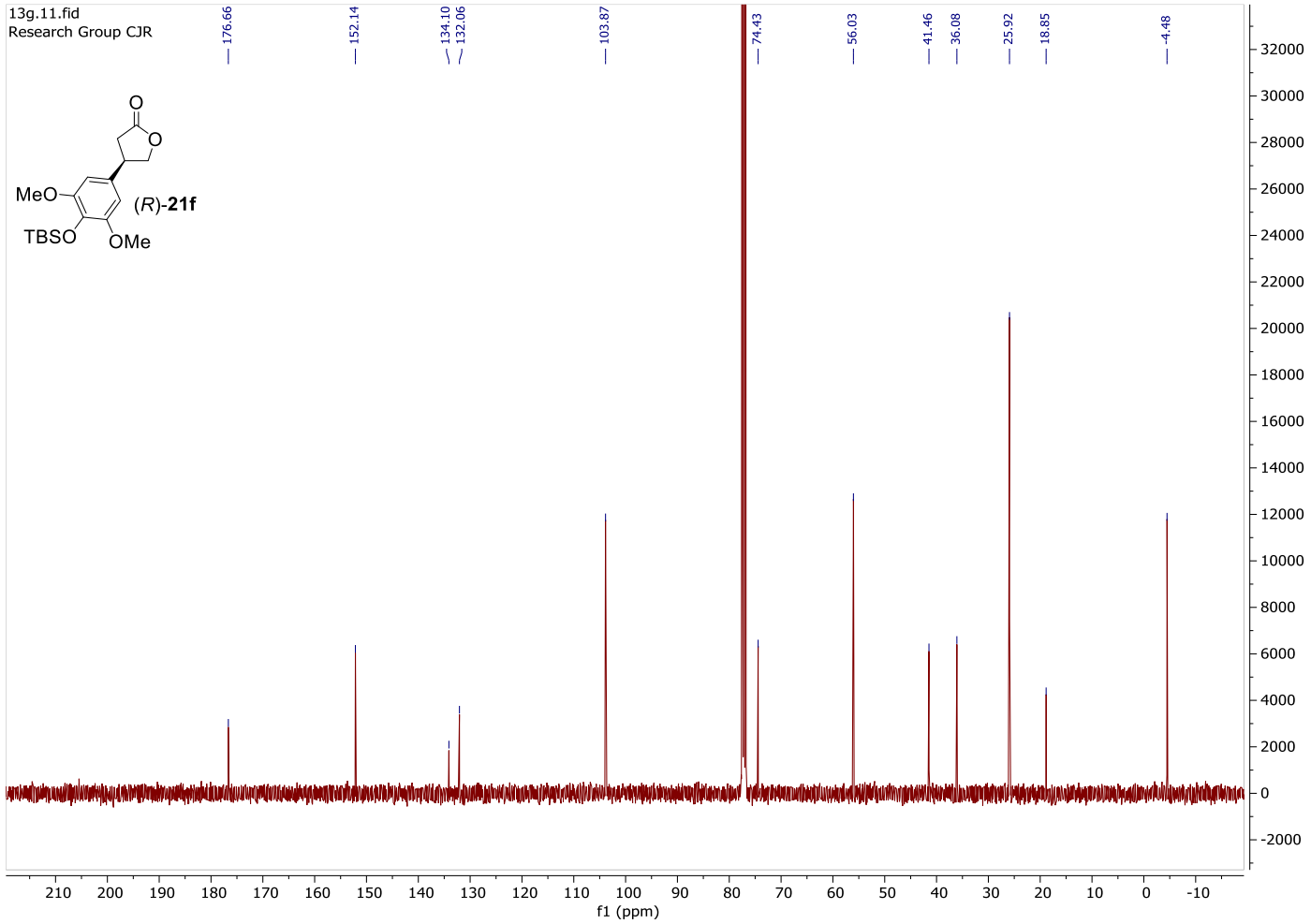
Compound **21e** ^{13}C (101 MHz, $CDCl_3$)



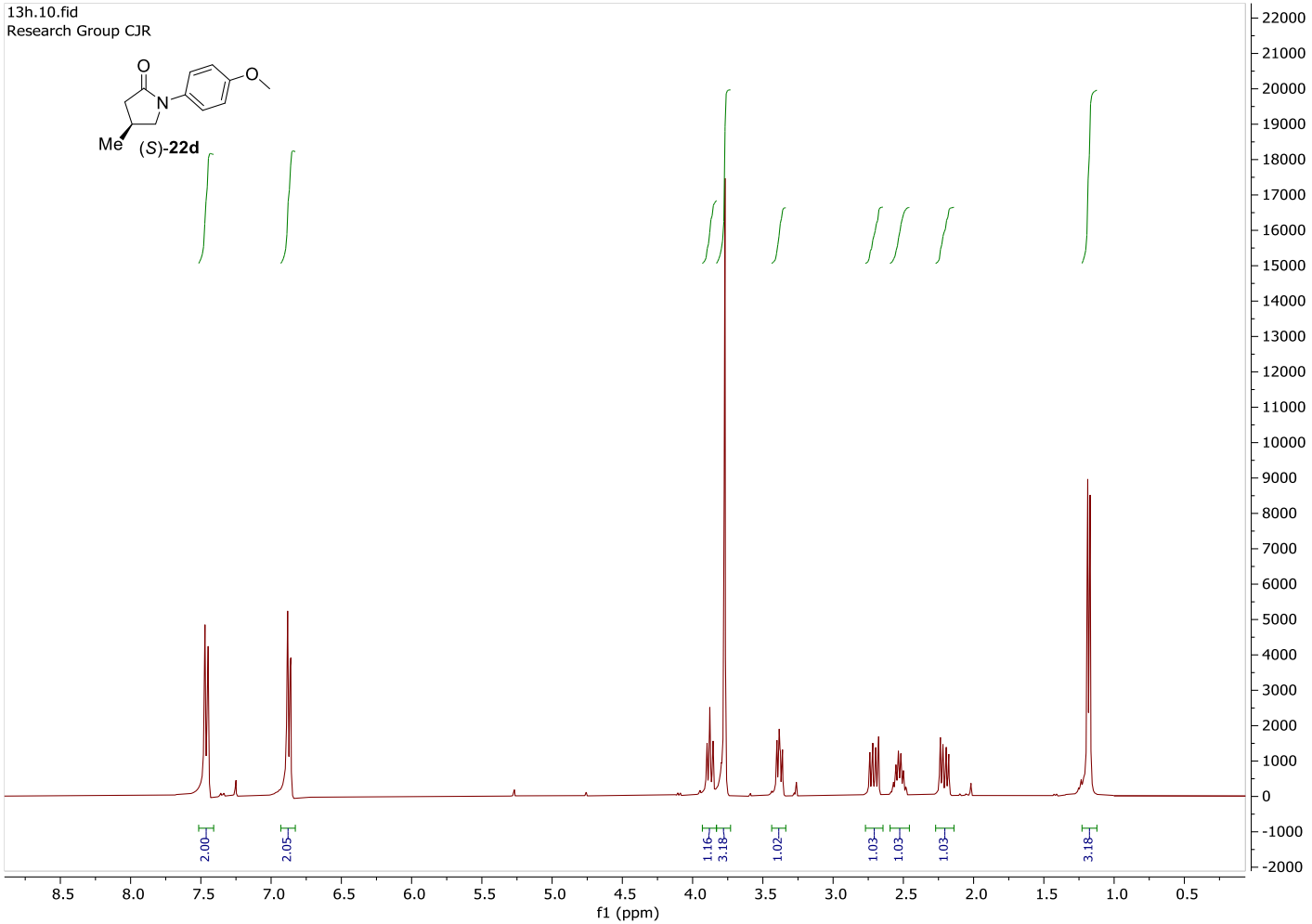
Compound **21f** ^{1}H (400 MHz, $CDCl_3$)



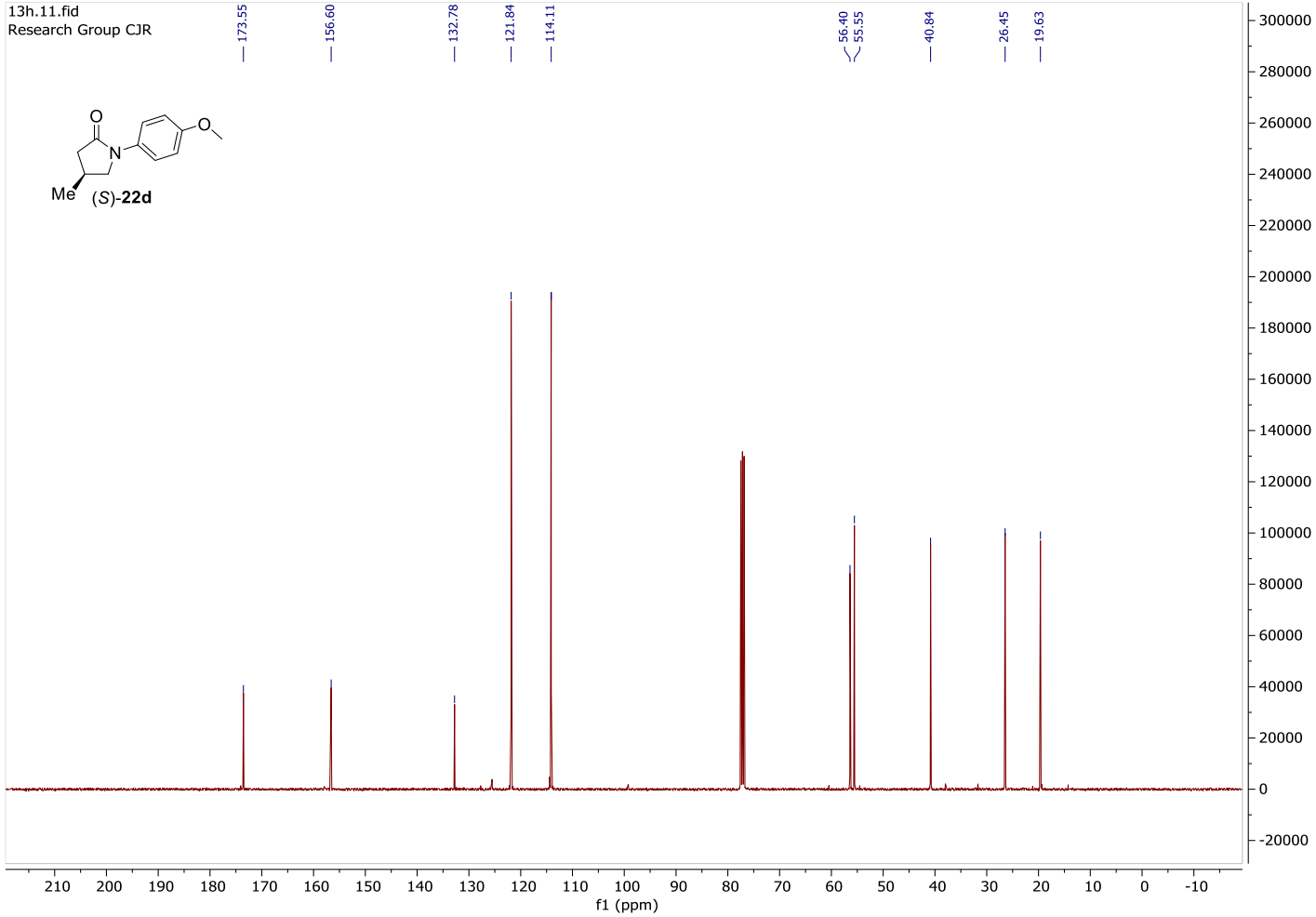
Compound **21f** ^{13}C (101 MHz, $CDCl_3$)



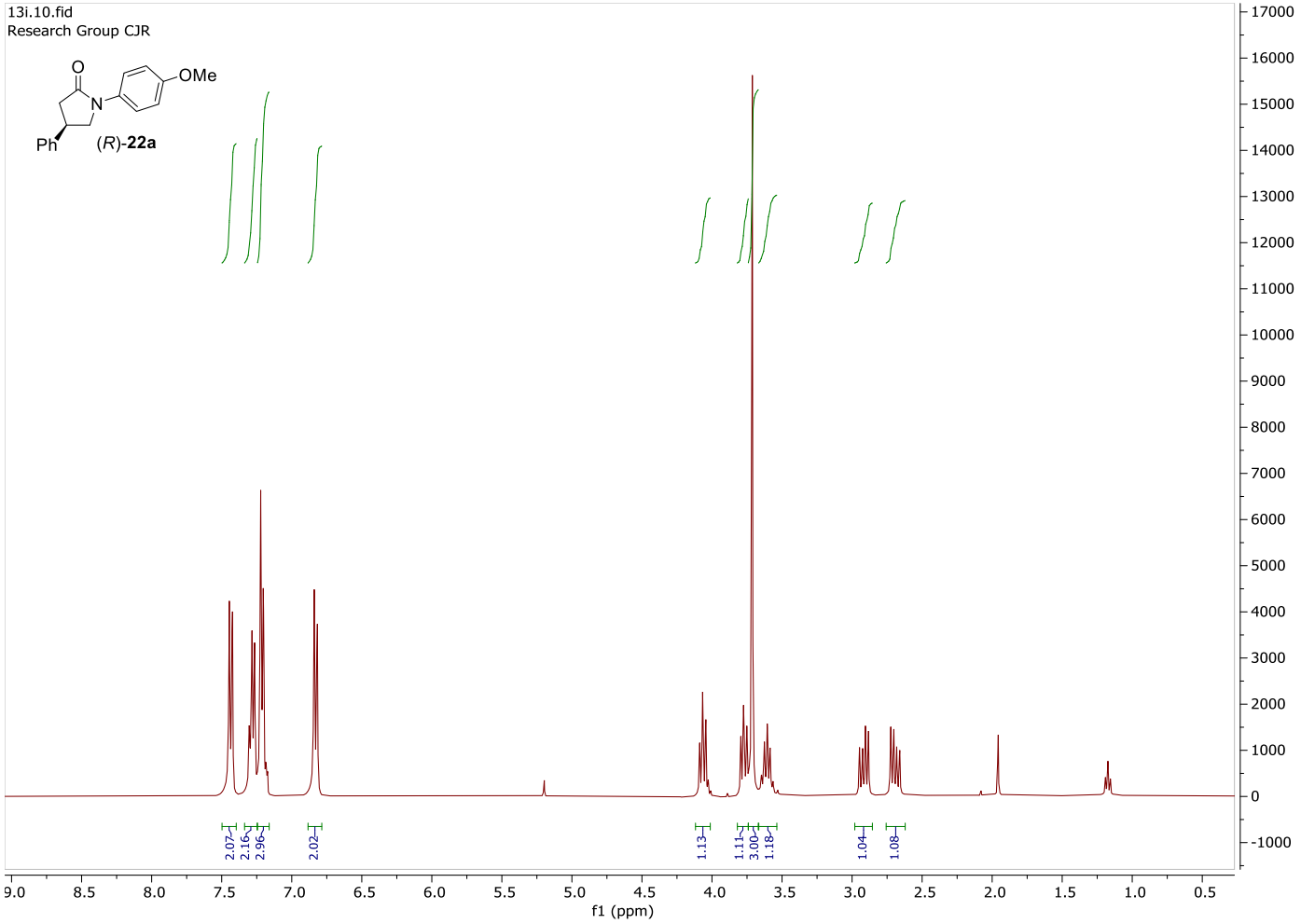
Compound **22d** ^{1}H (400 MHz, $CDCl_3$)



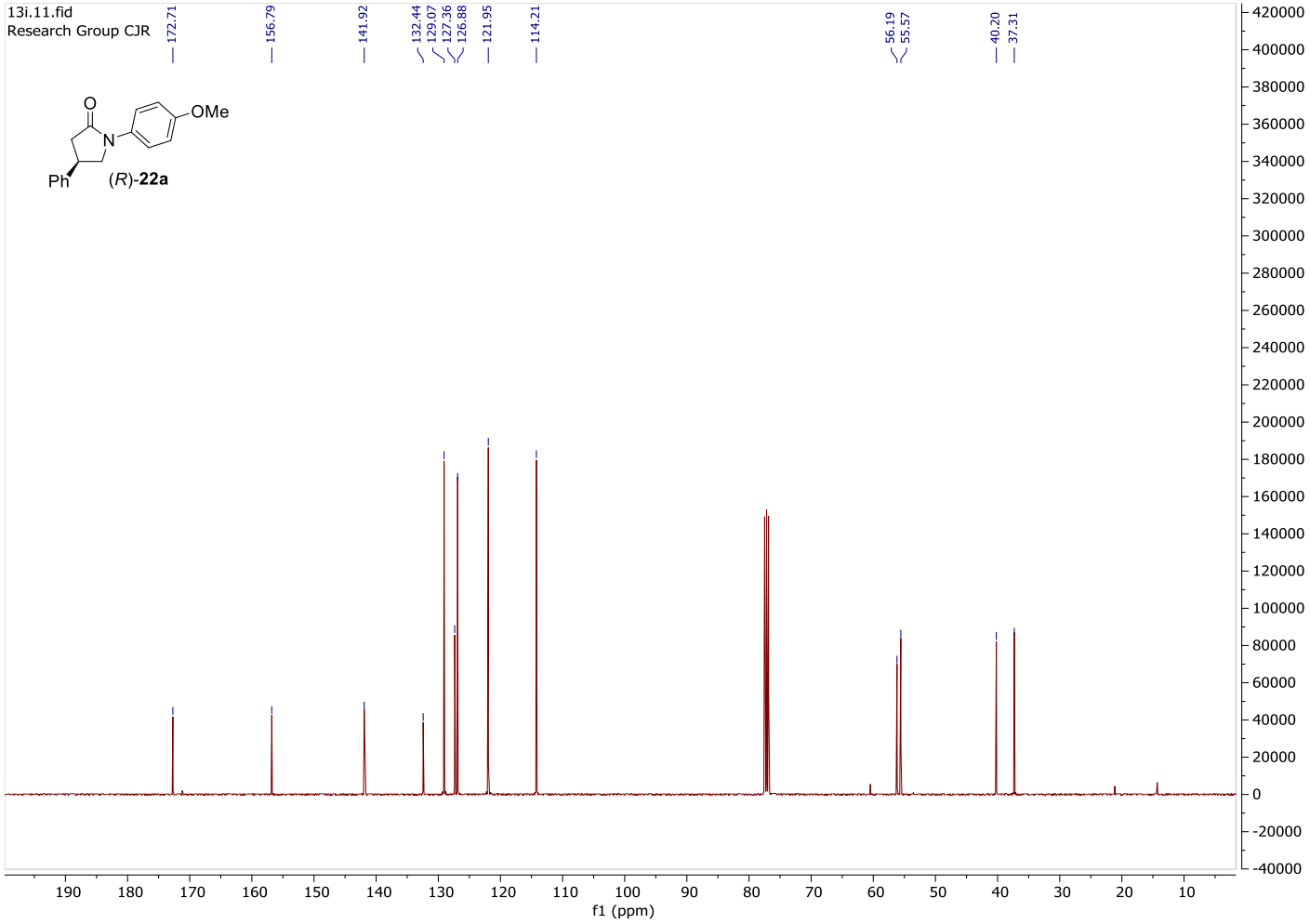
Compound **22d** ^{13}C (101 MHz, $CDCl_3$)



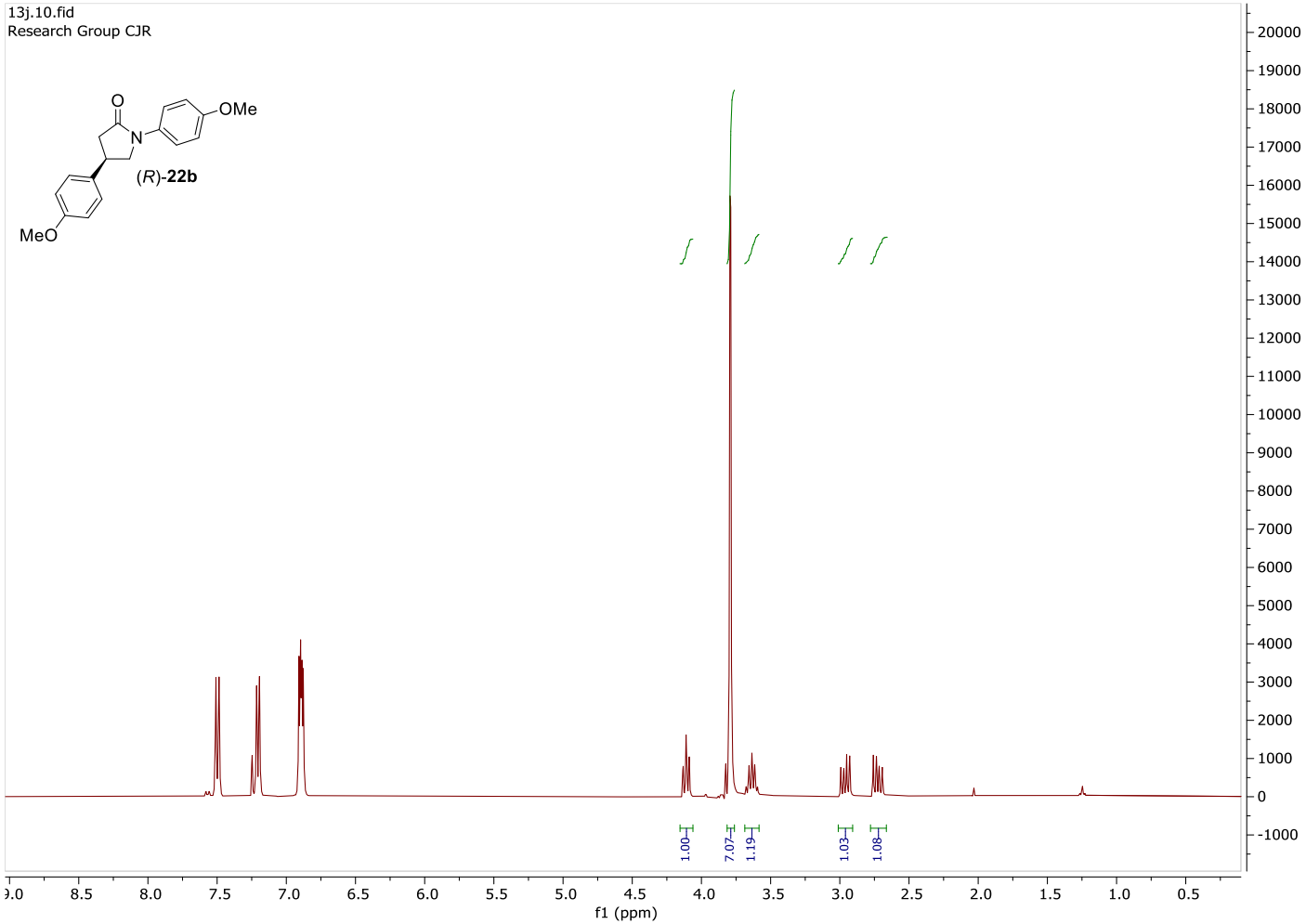
Compound **22a** ^{1}H (400 MHz, $CDCl_3$)



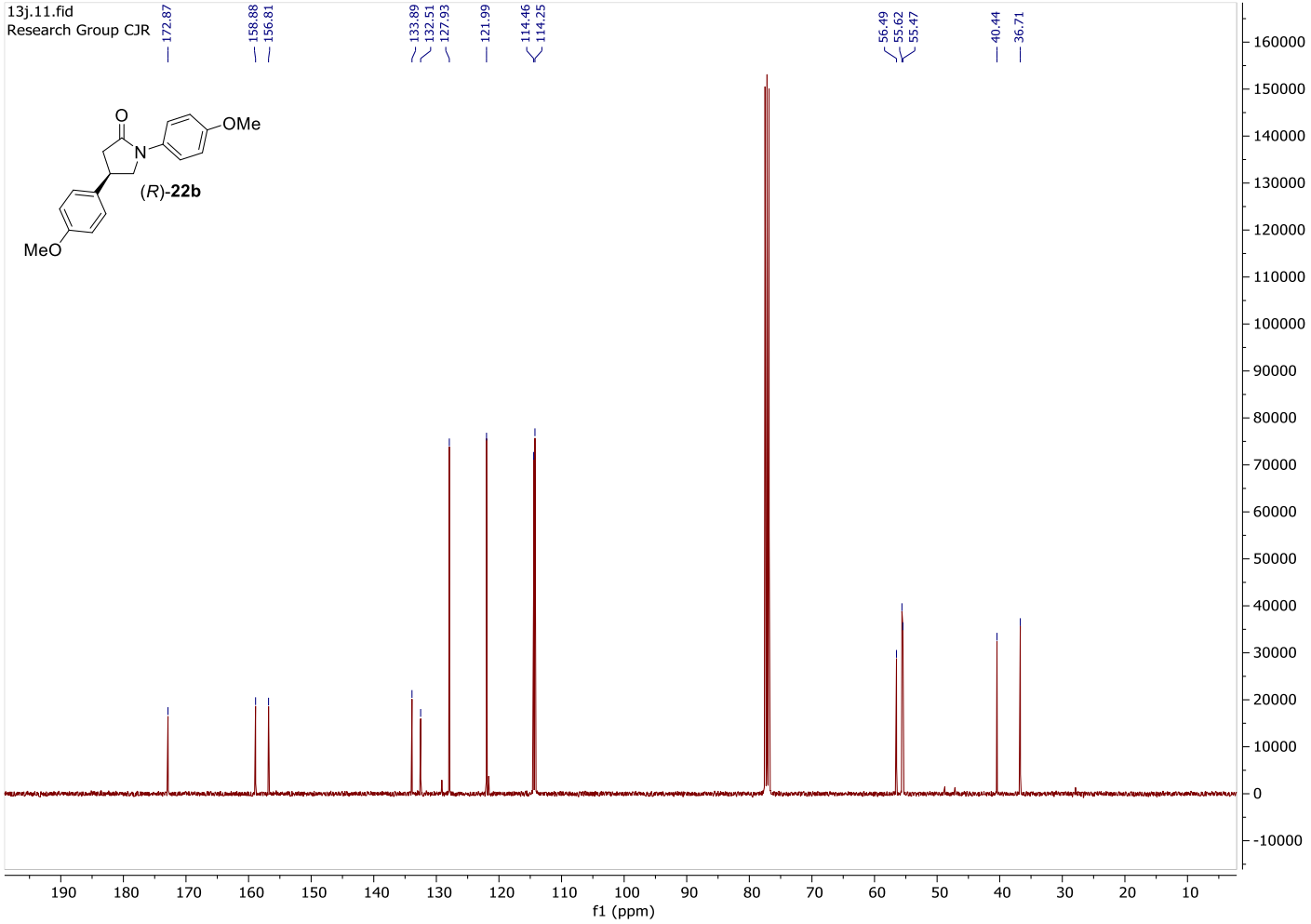
Compound **22a** ^{13}C (101 MHz, $CDCl_3$)



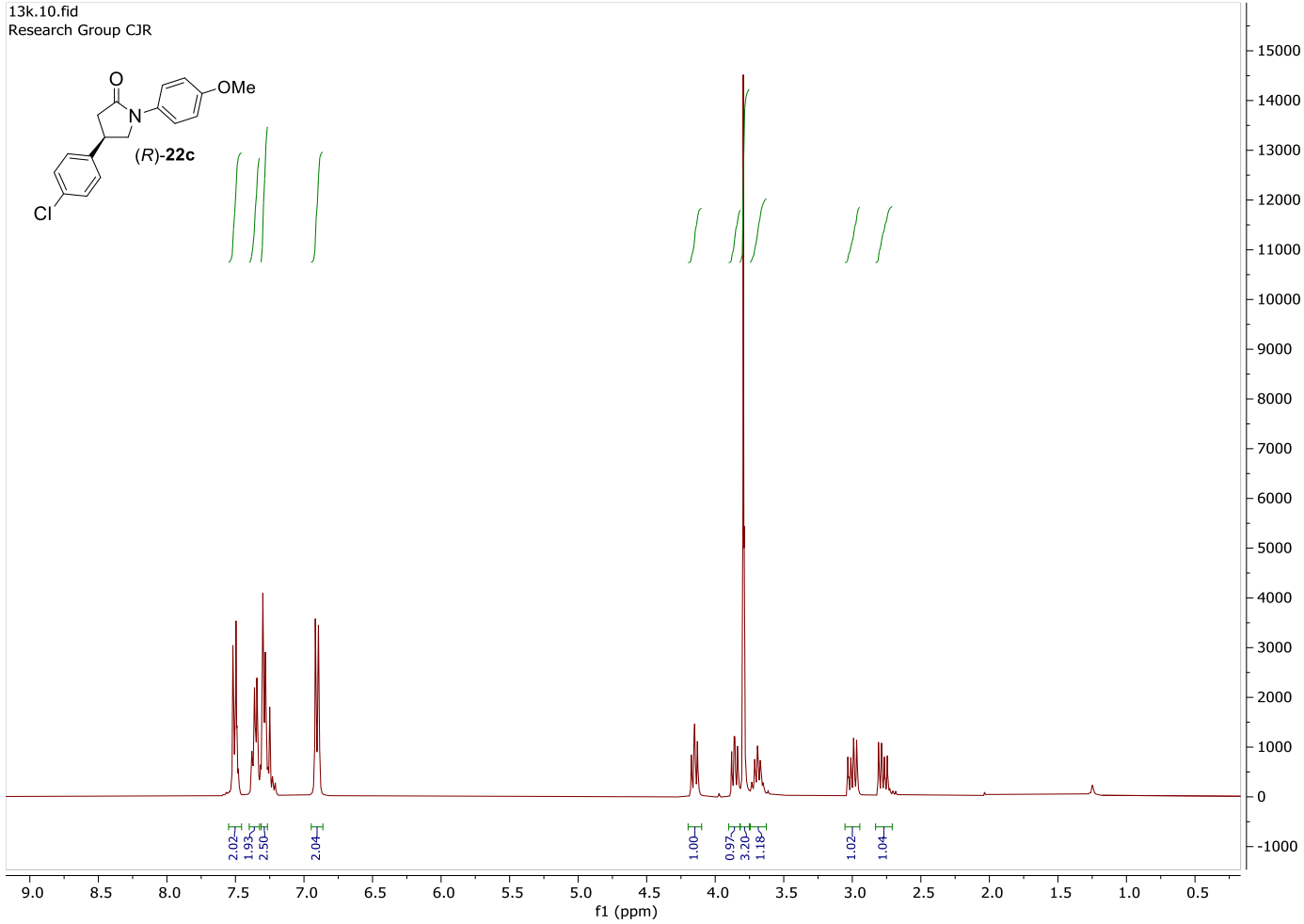
Compound **22b** ^{1}H (400 MHz, $CDCl_3$)



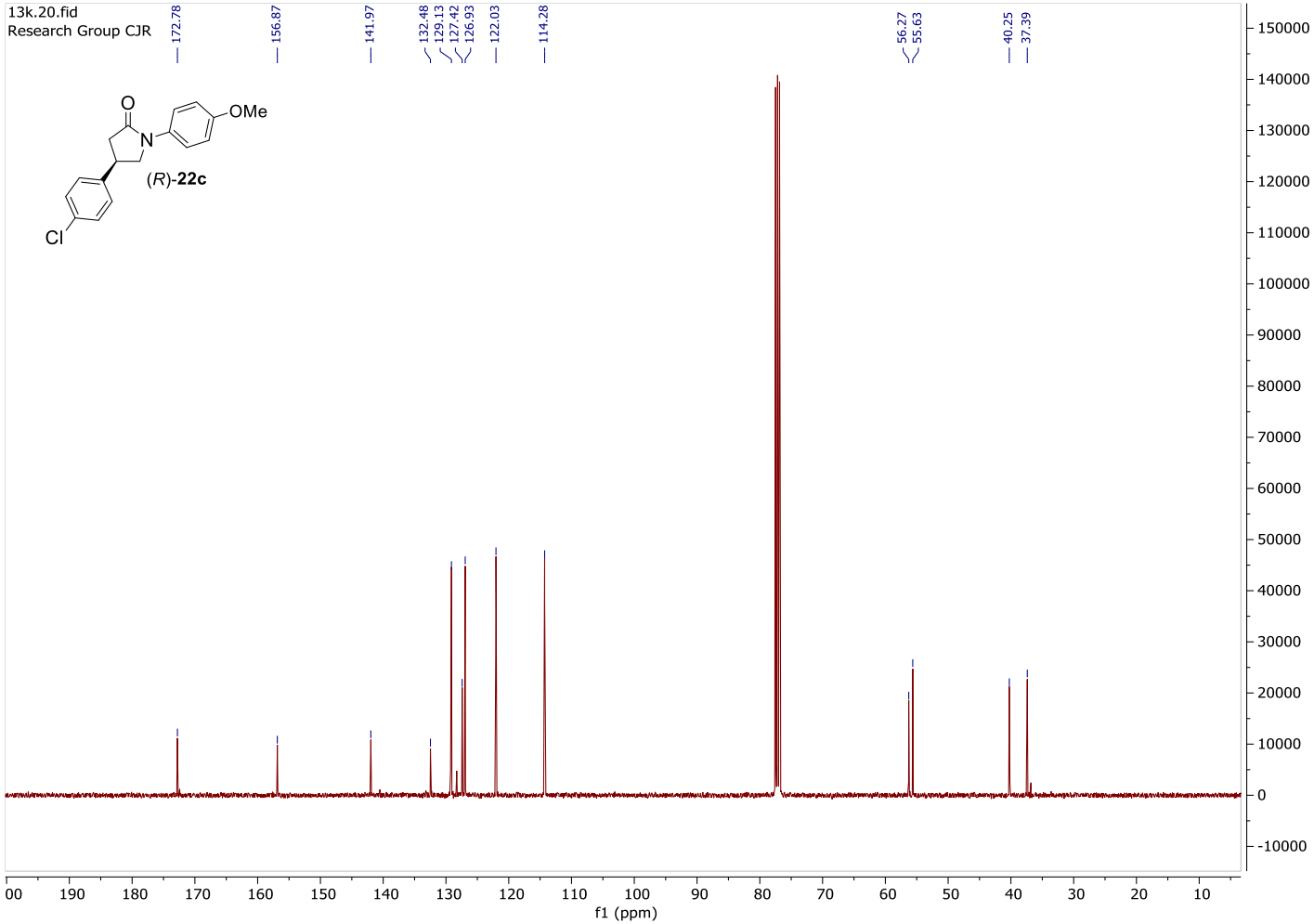
Compound **22b** ^{13}C (101 MHz, $CDCl_3$)



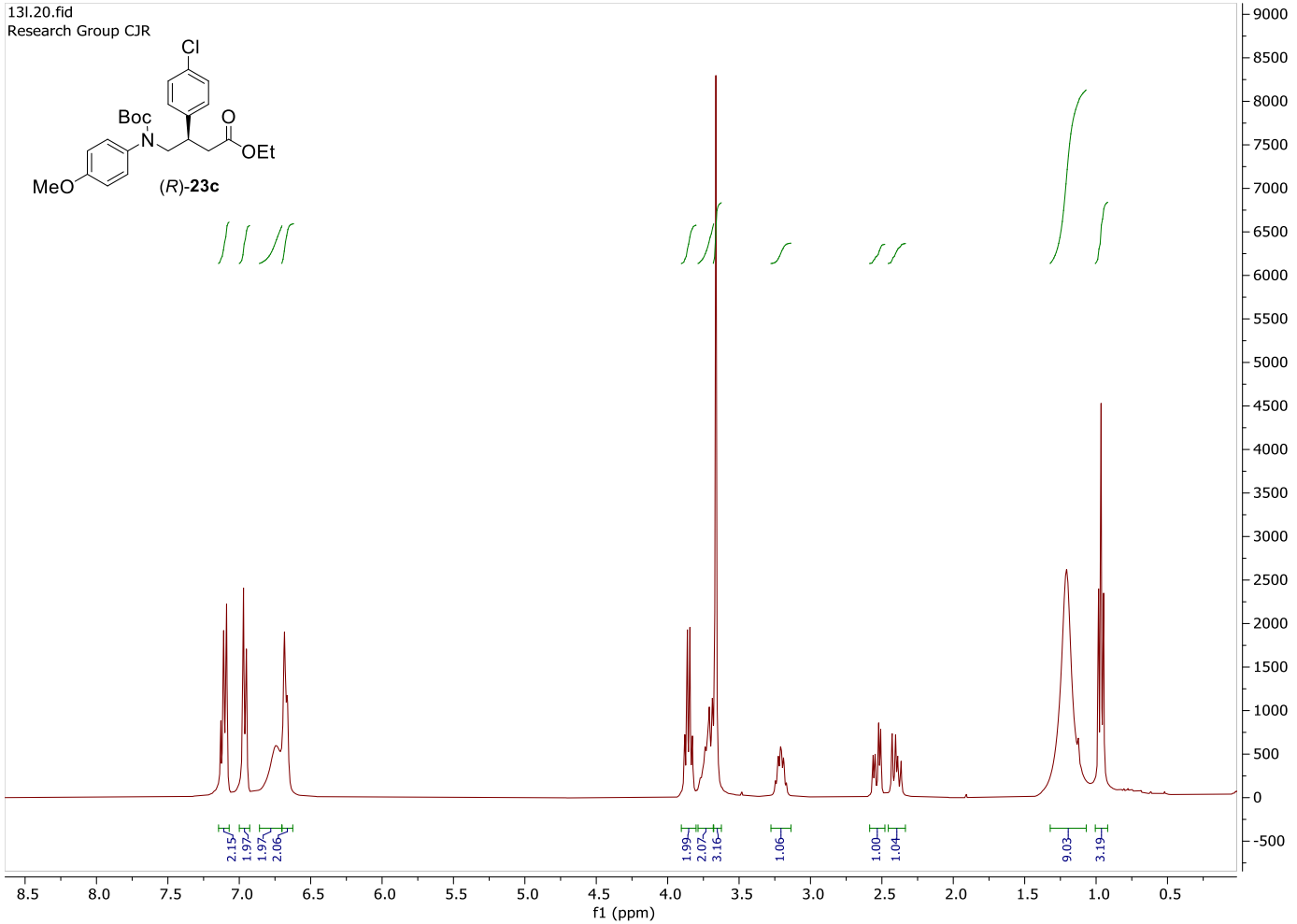
Compound **22c** ^{1}H (400 MHz, $CDCl_3$)



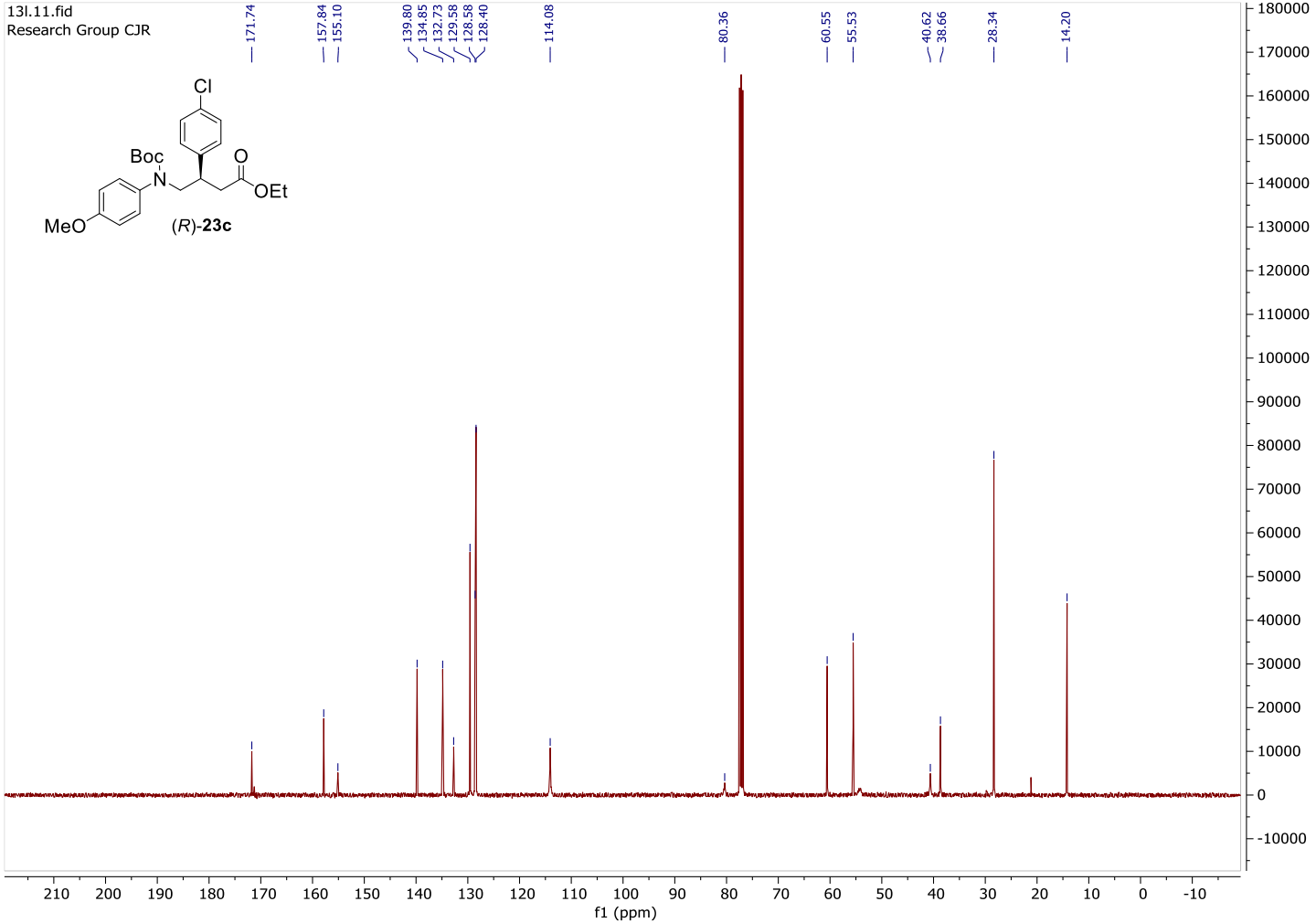
Compound **22c** ^{13}C (101 MHz, $CDCl_3$)



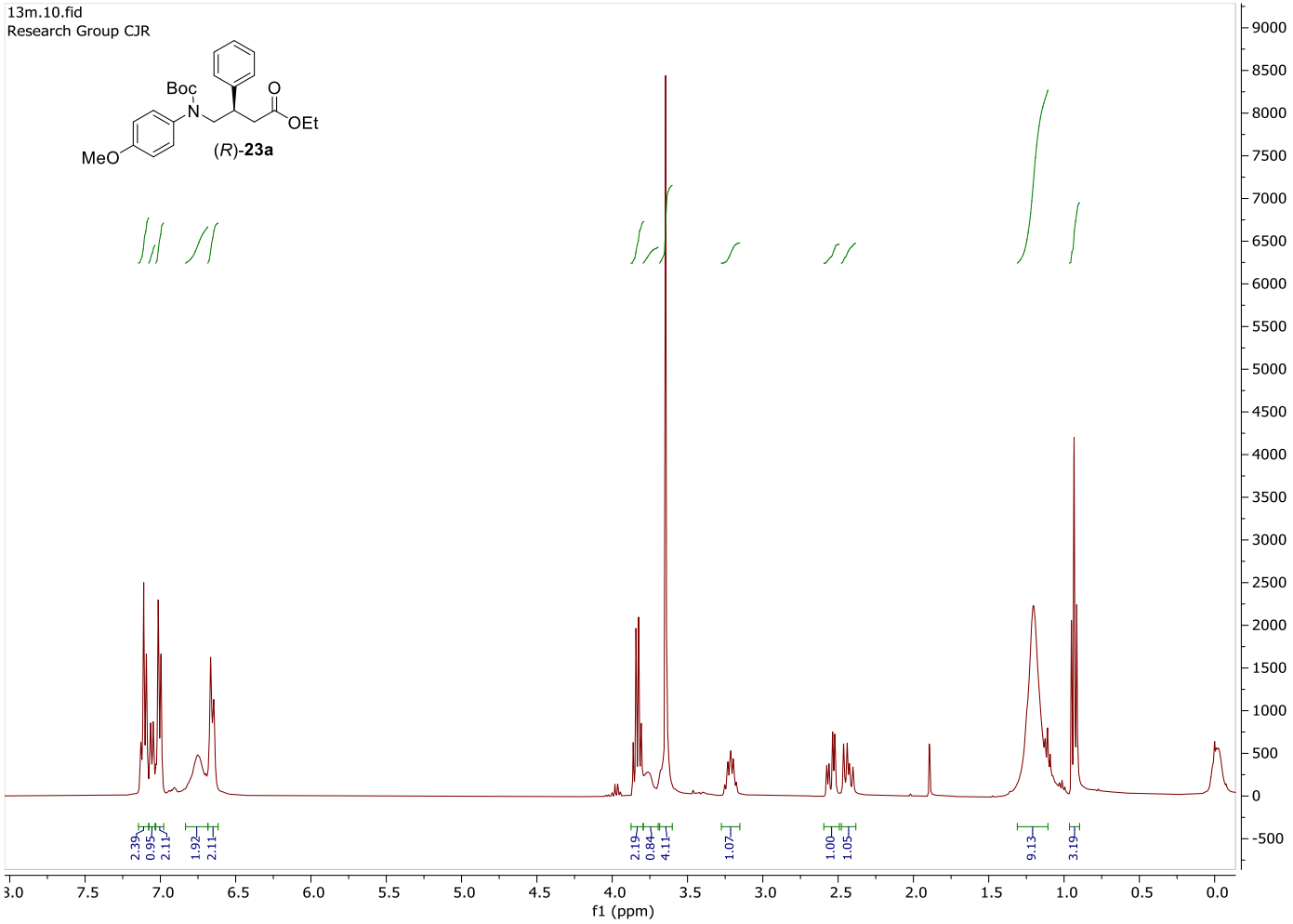
Compound **23c** ^{1}H (400 MHz, $CDCl_3$)



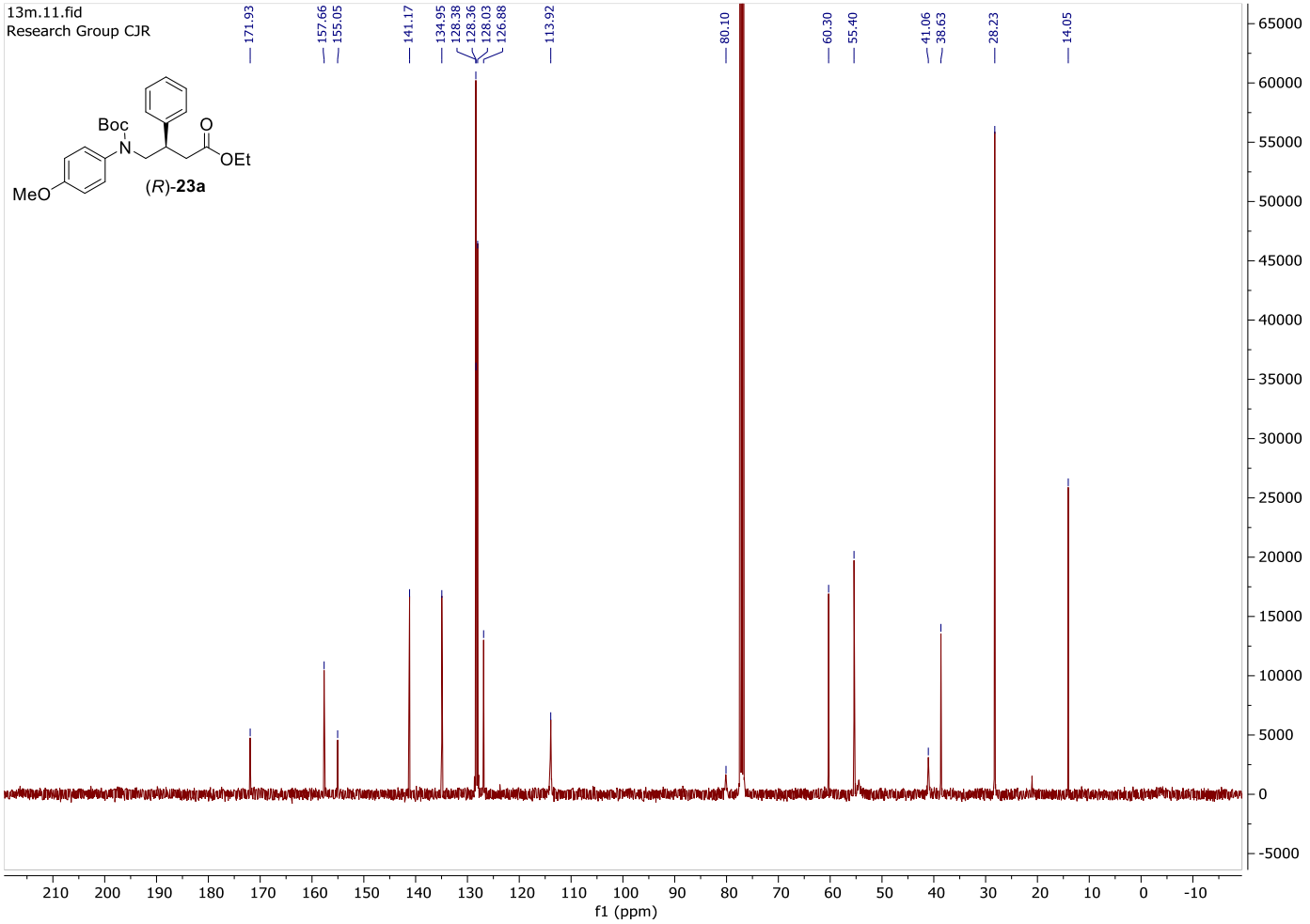
Compound **23c** ^{13}C (101 MHz, $CDCl_3$)



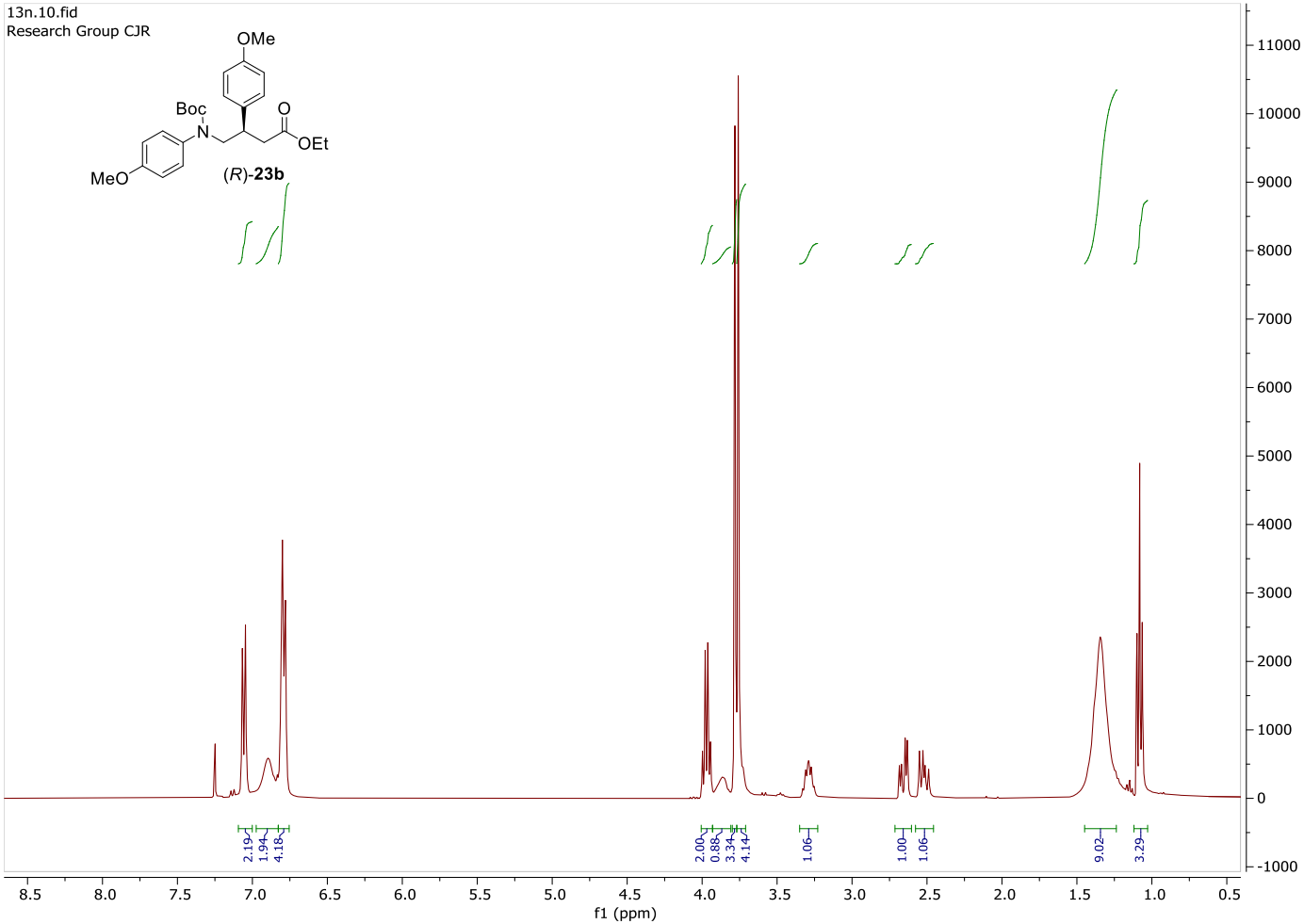
Compound **23a** ^{1}H (400 MHz, $CDCl_3$)



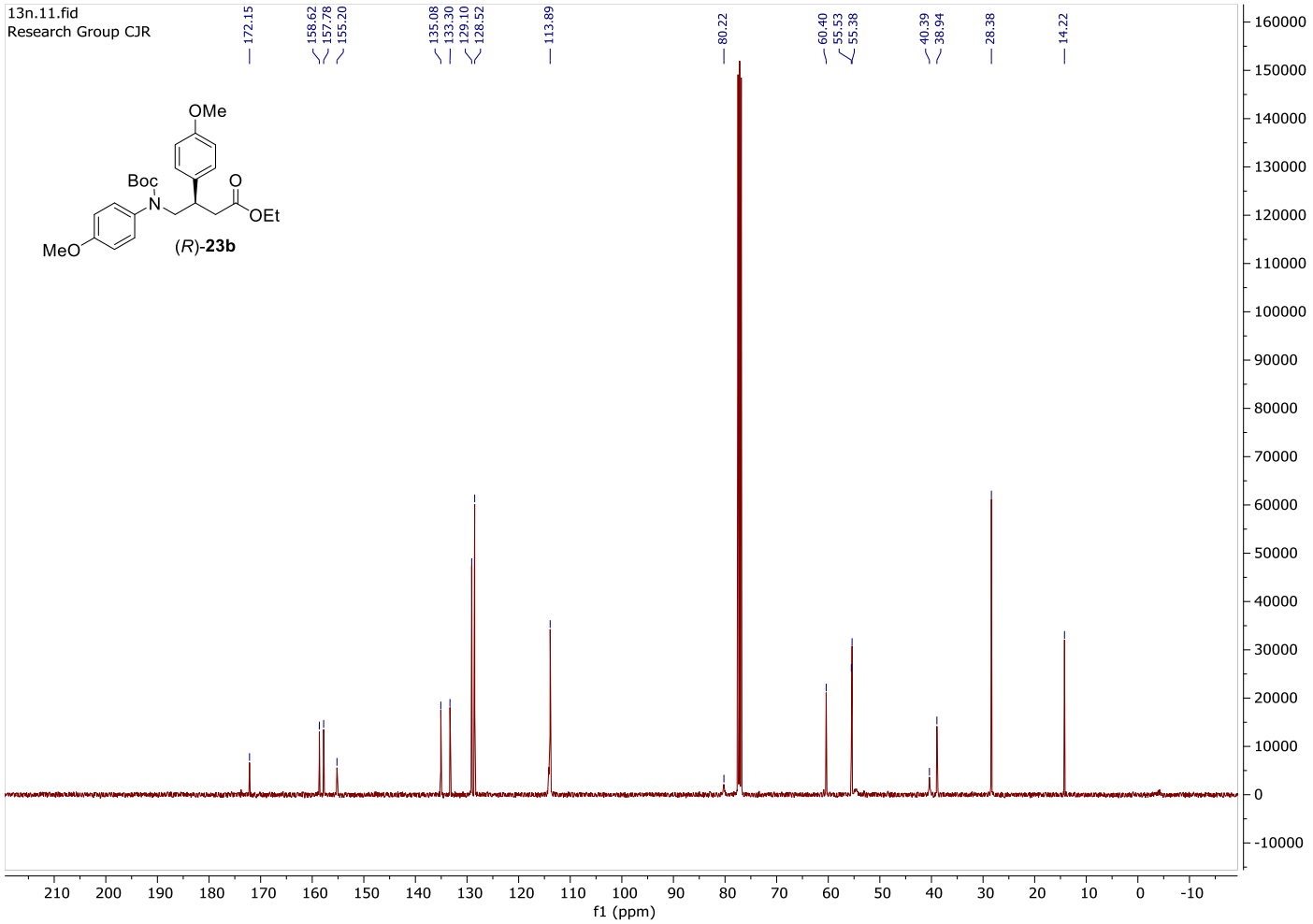
Compound **23a** ^{13}C (101 MHz, $CDCl_3$)



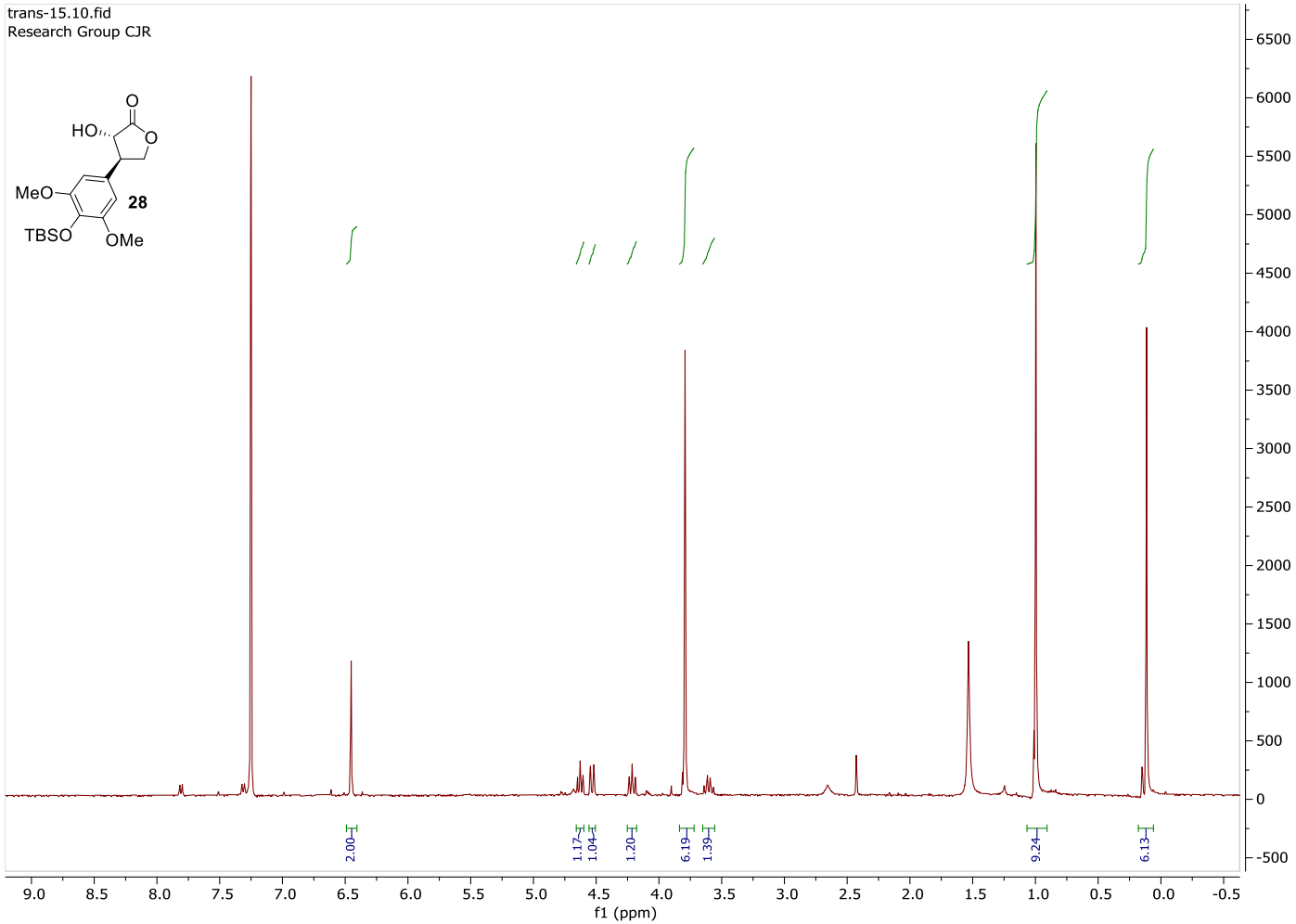
Compound **23b** ^{1}H (400 MHz, $CDCl_3$)



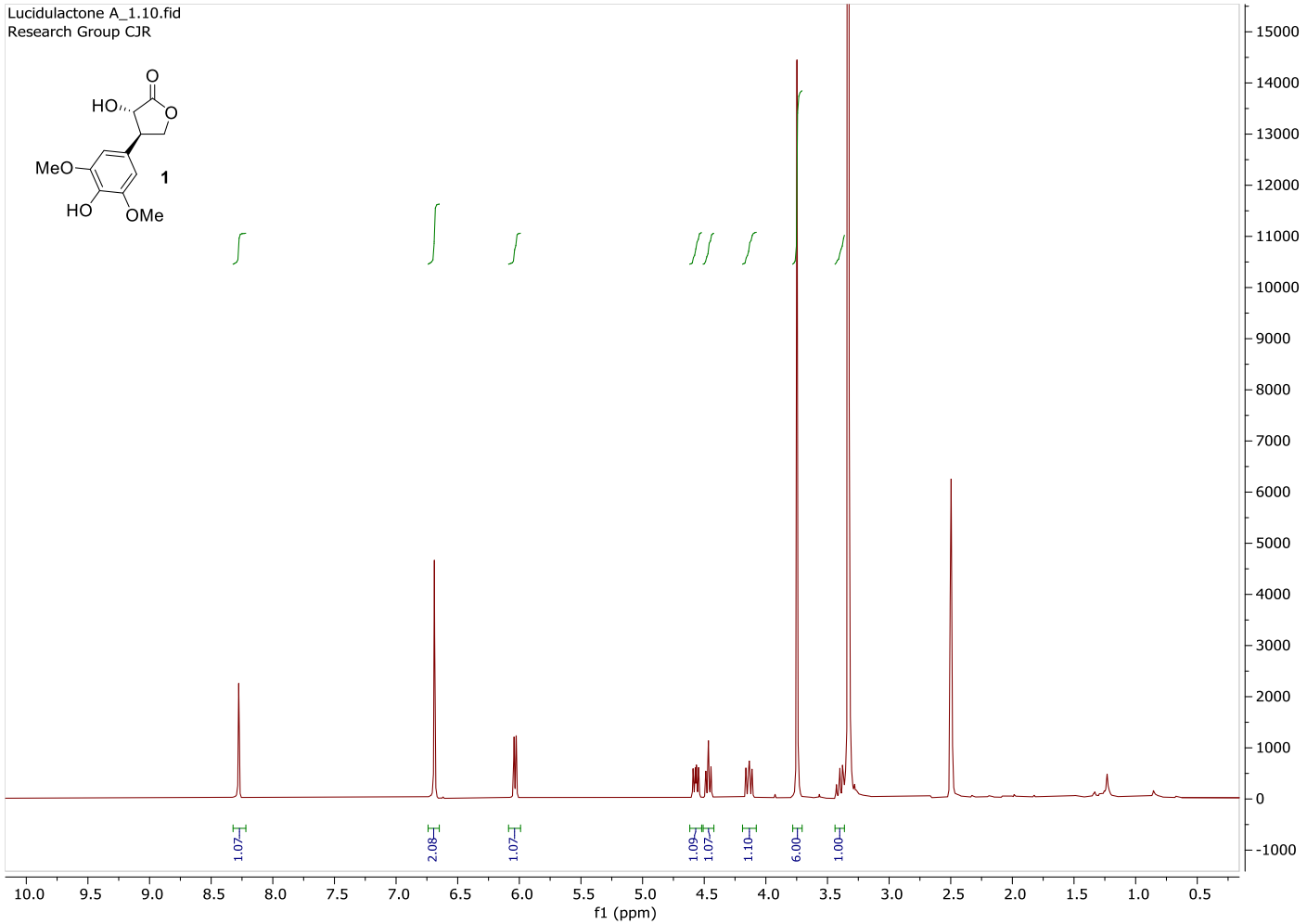
Compound **23b** ^{13}C (101 MHz, $CDCl_3$)



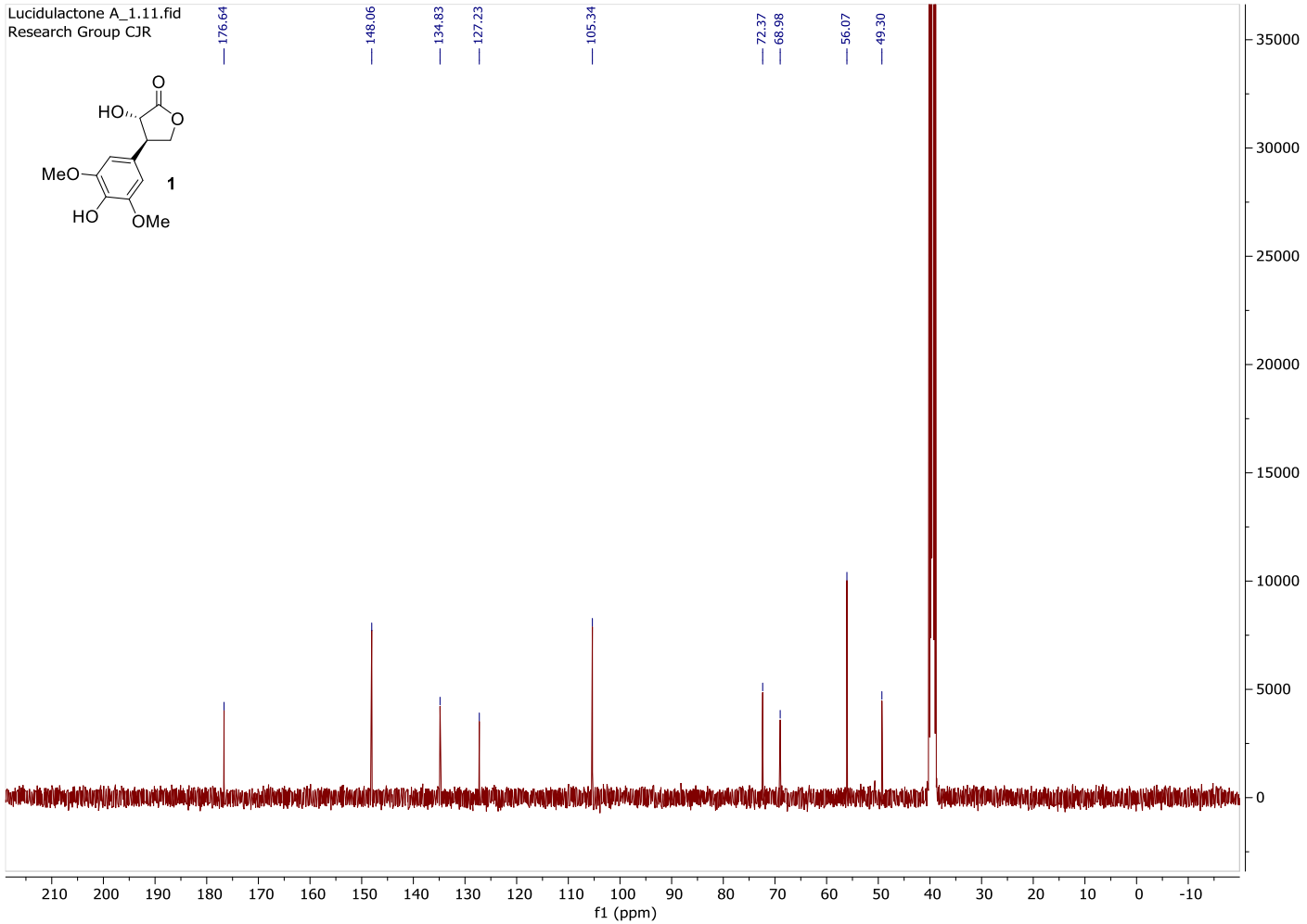
Compound (3*R*,4*S*)-**28** ^{1}H (400 MHz, $CDCl_3$)



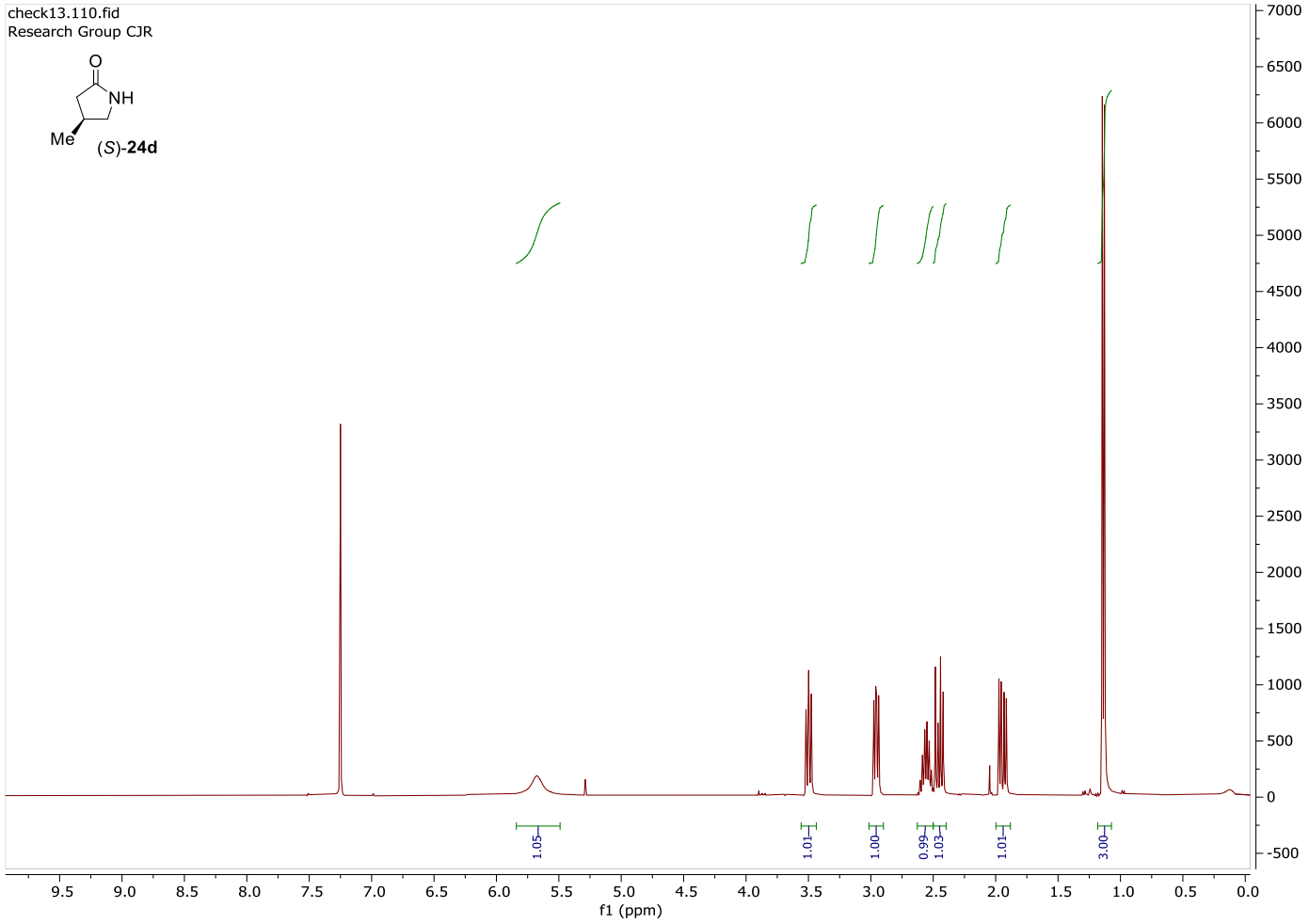
Compound (3*R*,4*S*)-**1** ^{1}H (400 MHz, DMSO-d_6)



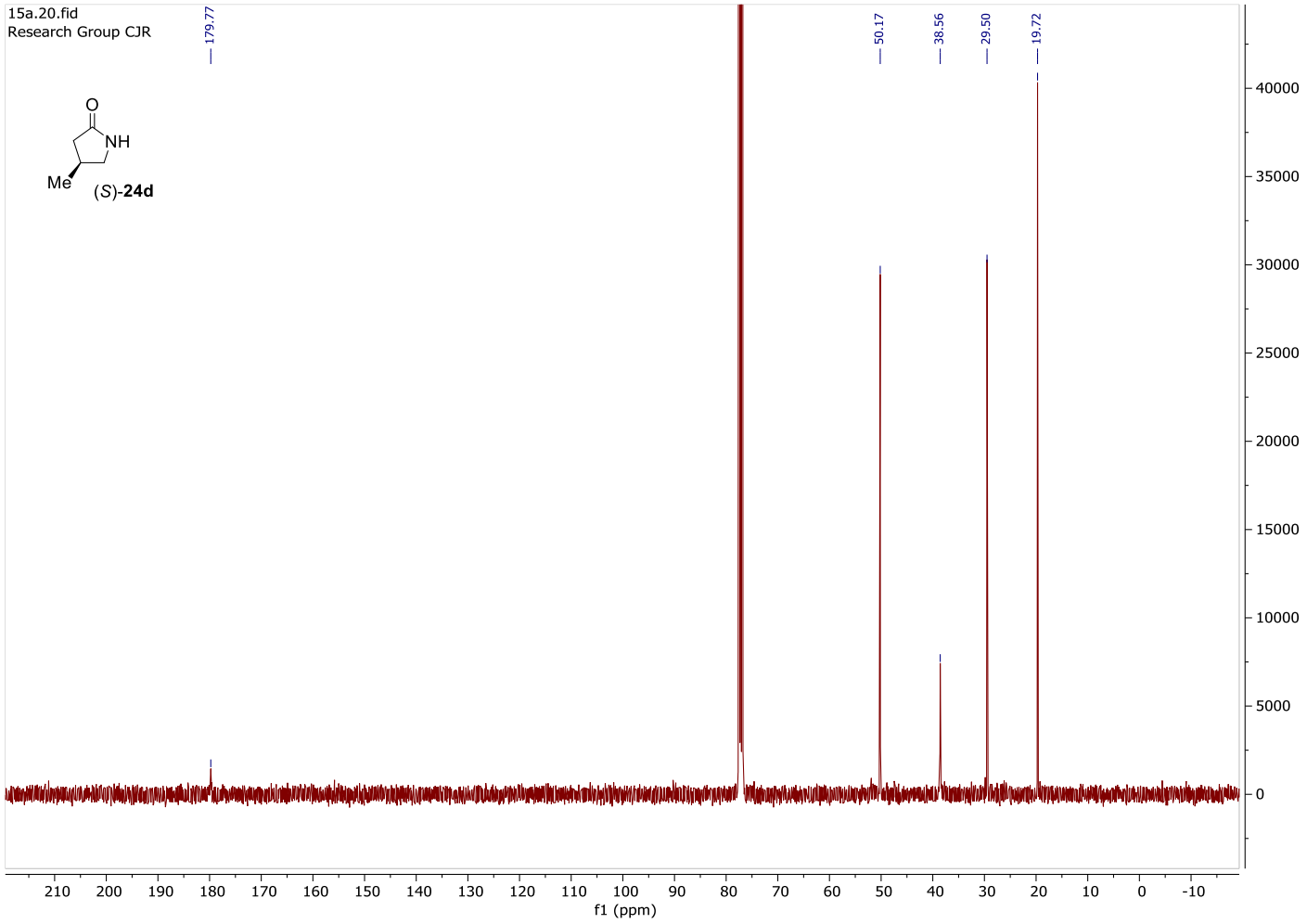
Compound (3*R*,4*S*)-**1** ^{13}C (101 MHz, DMSO-d_6)



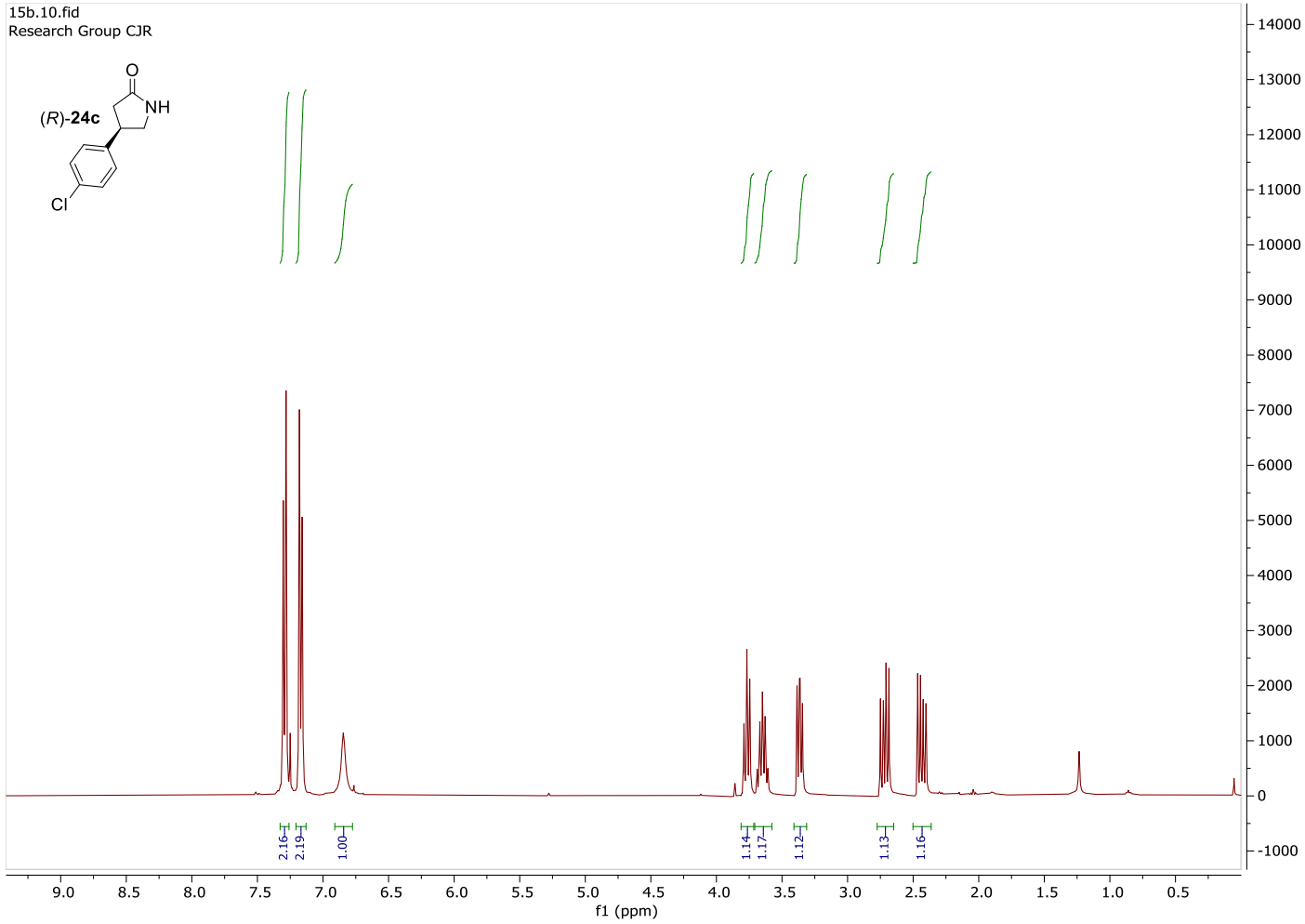
Compound **24d** ^{1}H (400 MHz, $CDCl_3$)



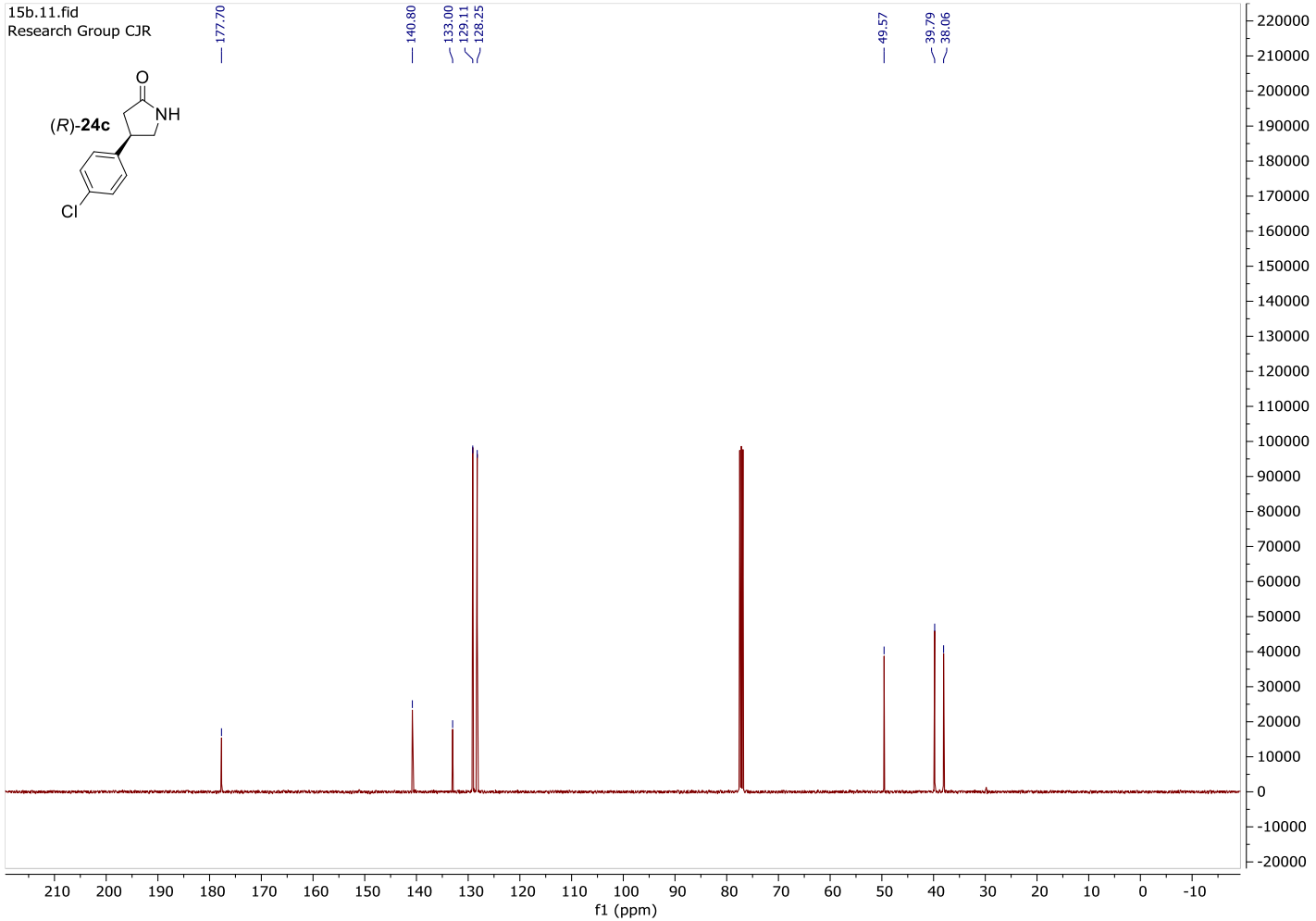
Compound **24d** ^{13}C (101 MHz, $CDCl_3$)



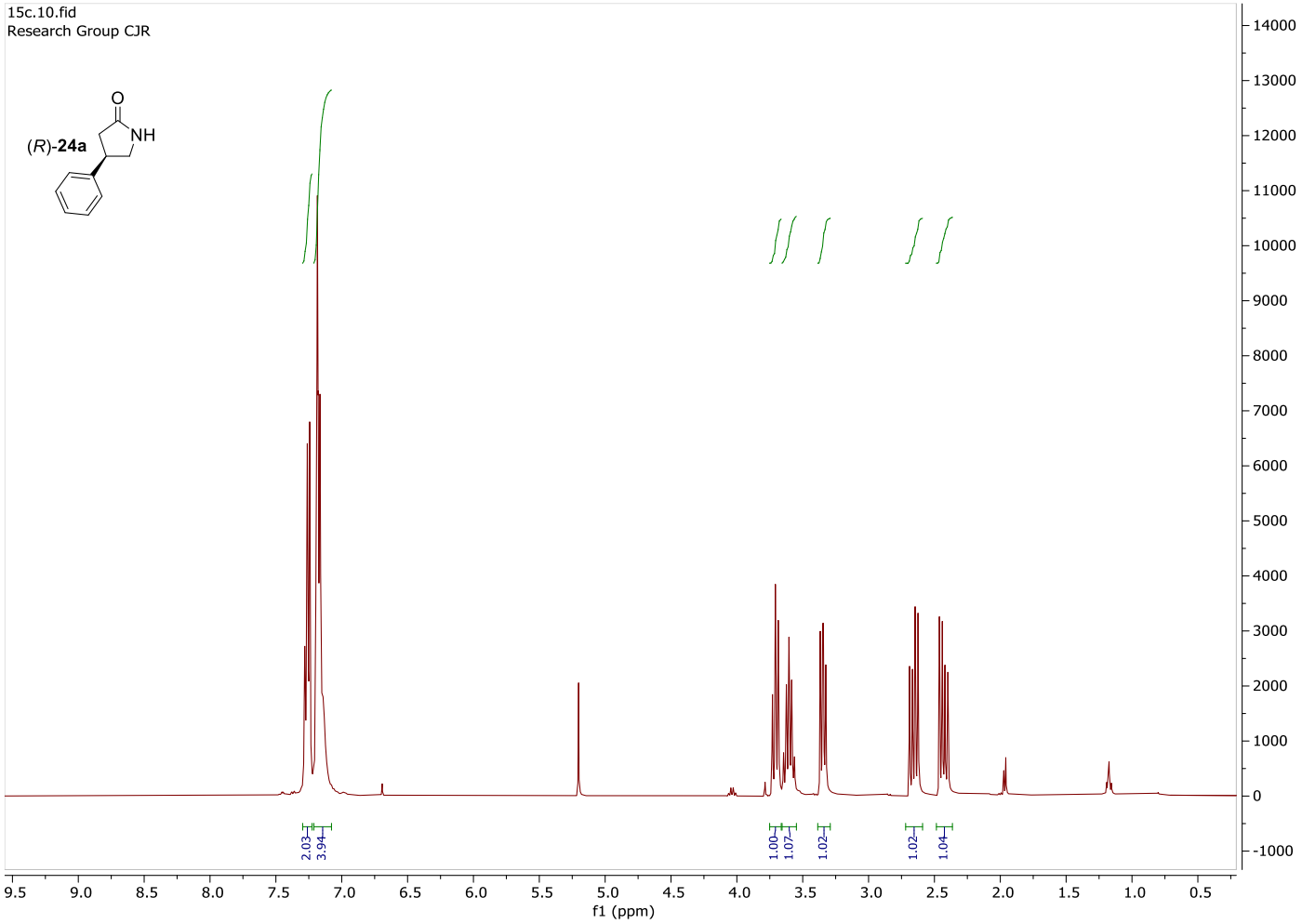
Compound **24c** ^{1}H (400 MHz, $CDCl_3$)



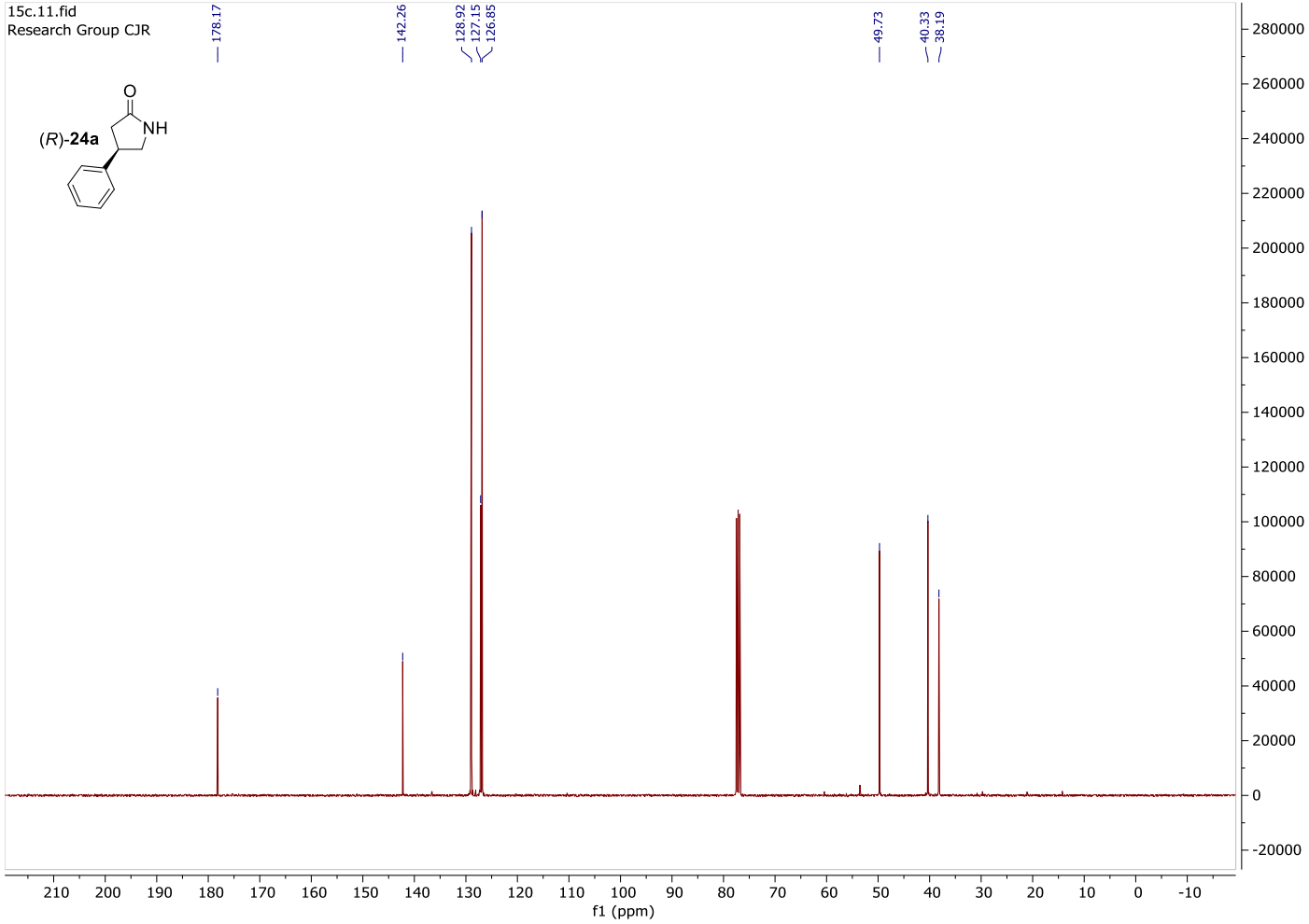
Compound **24c** ^{13}C (101 MHz, $CDCl_3$)



Compound **24a** ^{1}H (400 MHz, $CDCl_3$)

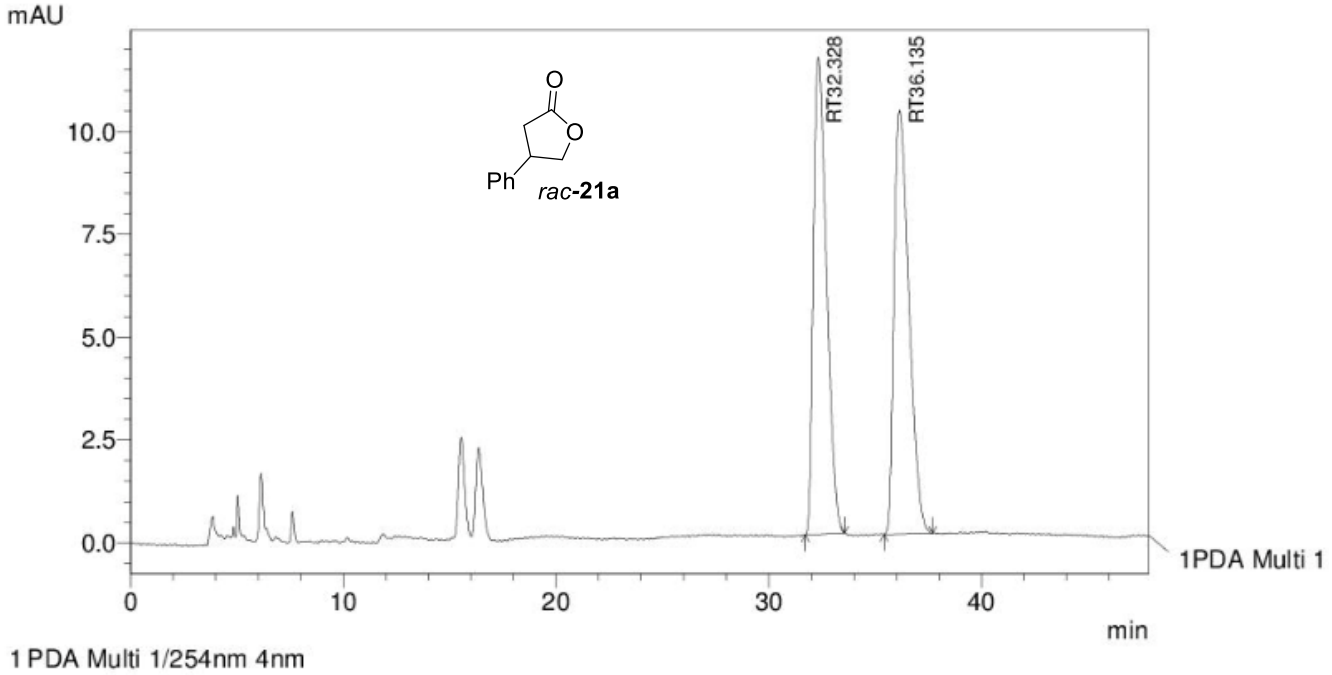


Compound **24a** ^{13}C (101 MHz, $CDCl_3$)



HPLC Data

<Chromatogram>



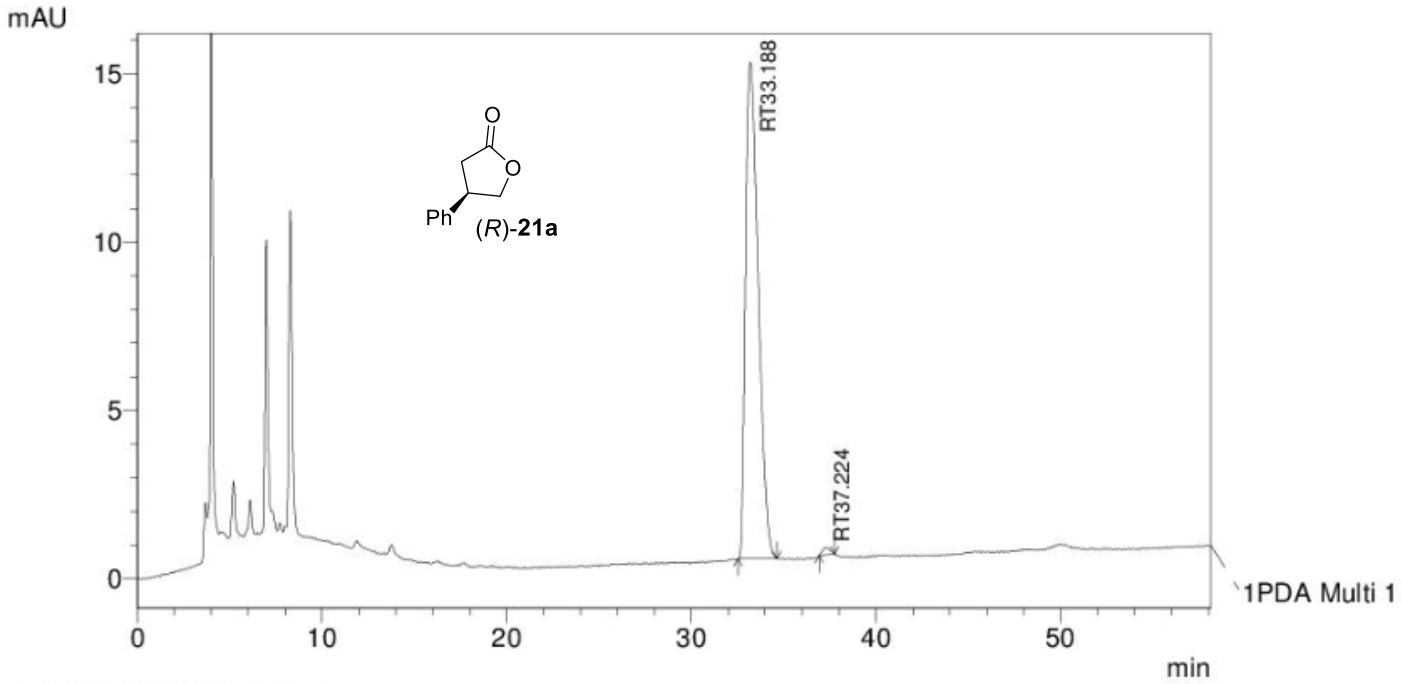
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	linimum Peak Purity Inde	Conc.	Units
1	RT32.328	32.328	497776	Not calculated	0.000	mg/L
2	RT36.135	36.135	503892	Not calculated	0.000	mg/L

<Chromatogram>



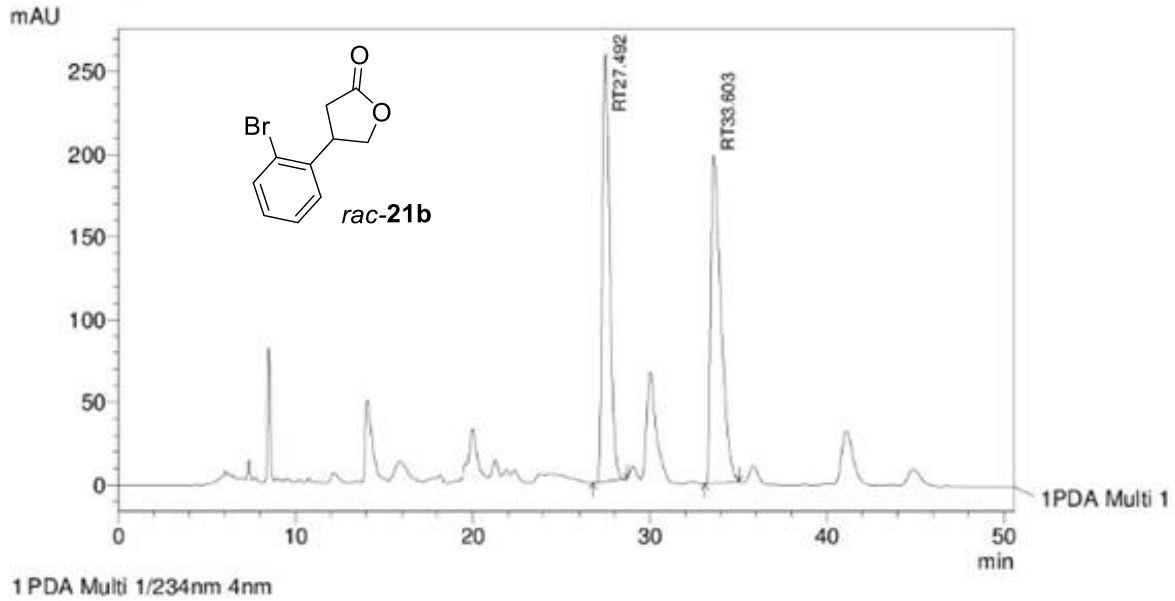
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT33.188	33.188	706102	Not calculated	0.000	mg/L
2	RT37.224	37.224	6064	Not calculated	0.000	mg/L

<Chromatogram>

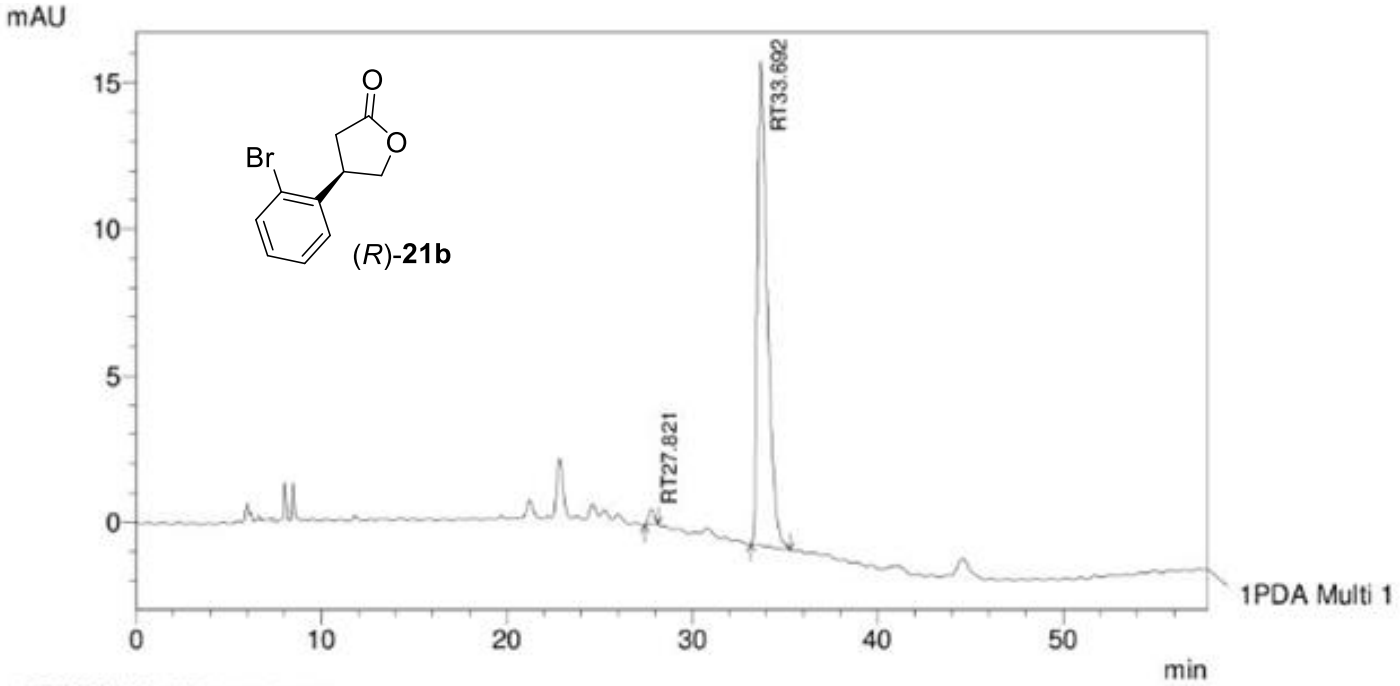


1 PDA Multi 1/234nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT27.492	27.492	7515873	Not calculated	0.000	mg/L
2	RT33.603	33.603	7945243	Not calculated	0.000	mg/L



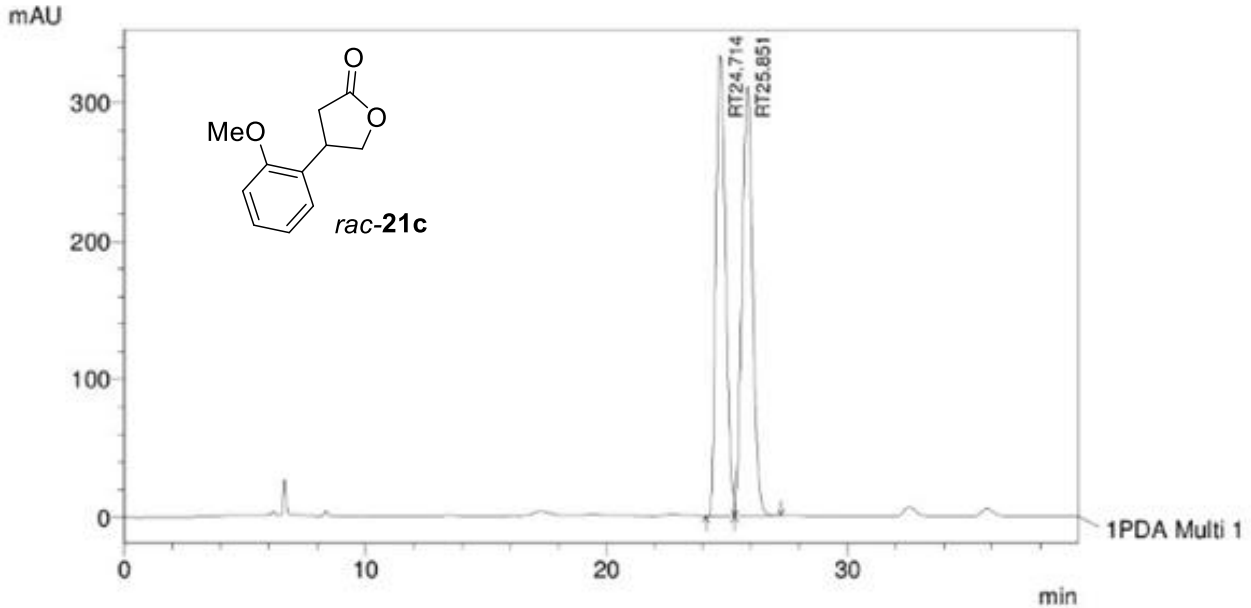
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT27.821	27.821	11500	Not calculated	0.000	mg/L
2	RT33.692	33.692	612820	Not calculated	0.000	mg/L

<Chromatogram>

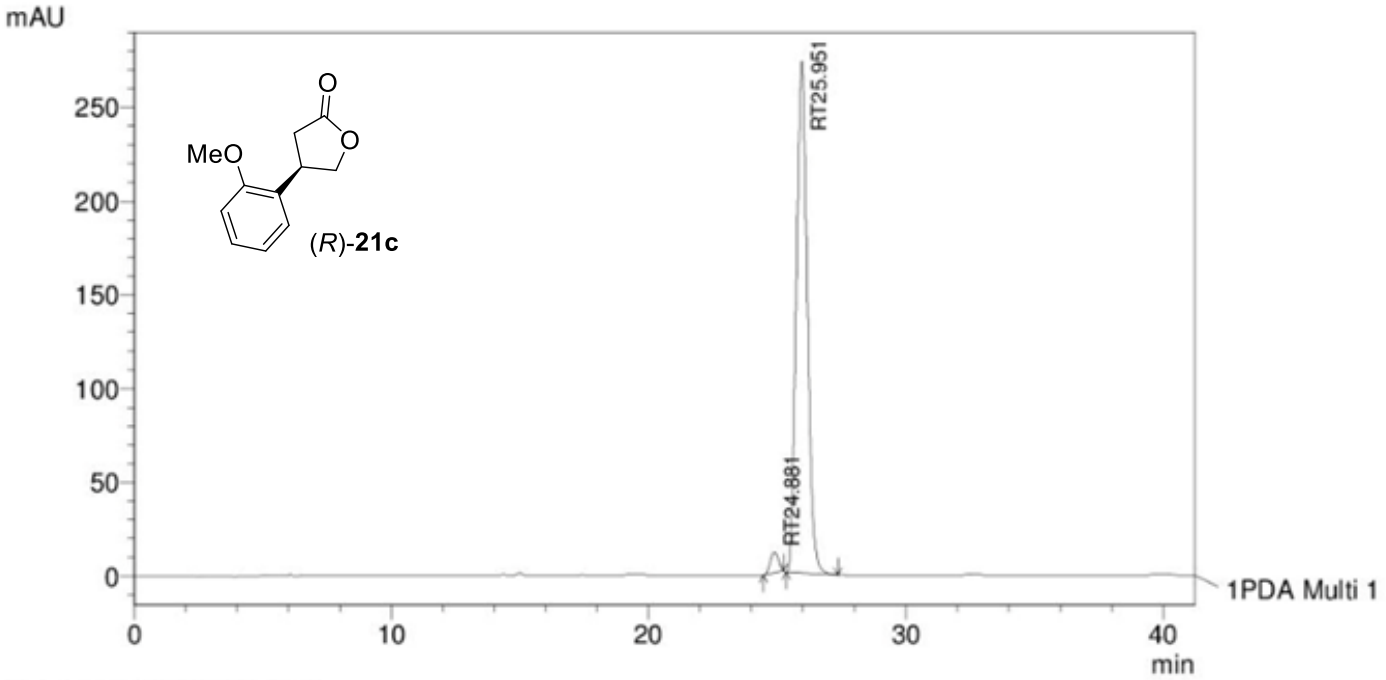


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT24.714	24.714	9387248	Not calculated	0.000	mg/L
2	RT25.851	25.851	9562301	Not calculated	0.000	mg/L

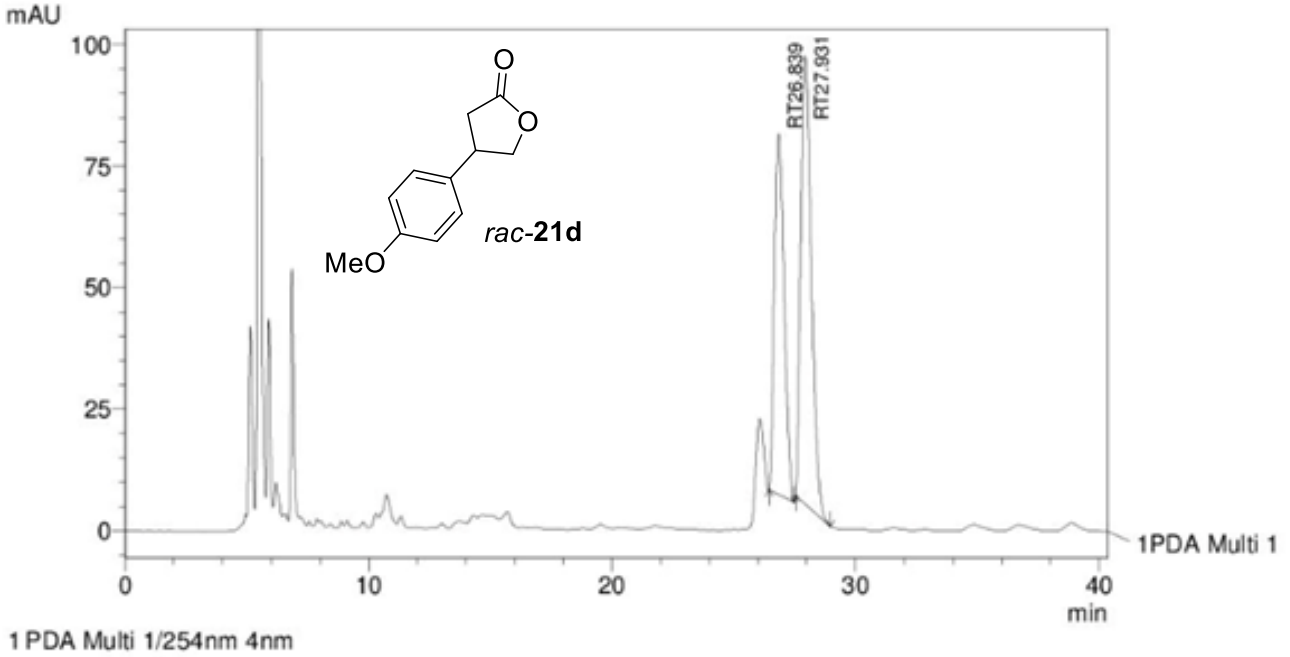


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	linimum Peak Purity Inde	Conc.	Units
1	RT24.881	24.881	244663	Not calculated	0.000	mg/L
2	RT25.951	25.951	8129185	Not calculated	0.000	mg/L



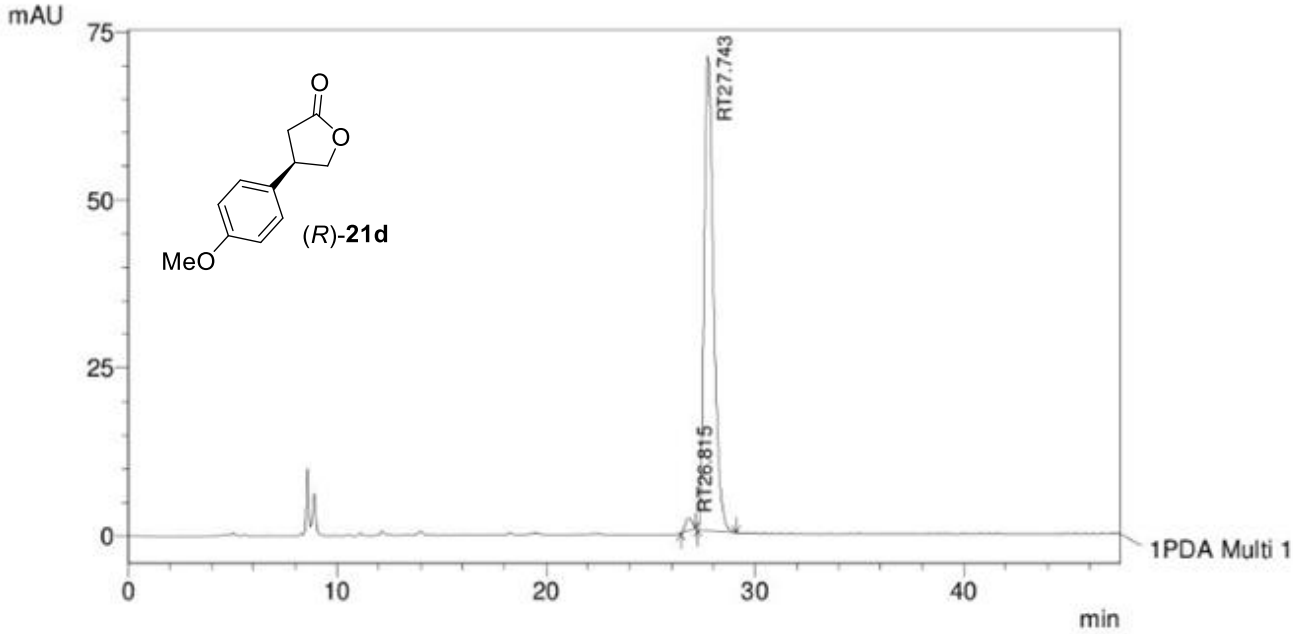
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT26.839	26.839	2063810	Not calculated	0.000	mg/L
2	RT27.931	27.931	2774401	Not calculated	0.000	mg/L

<Chromatogram>

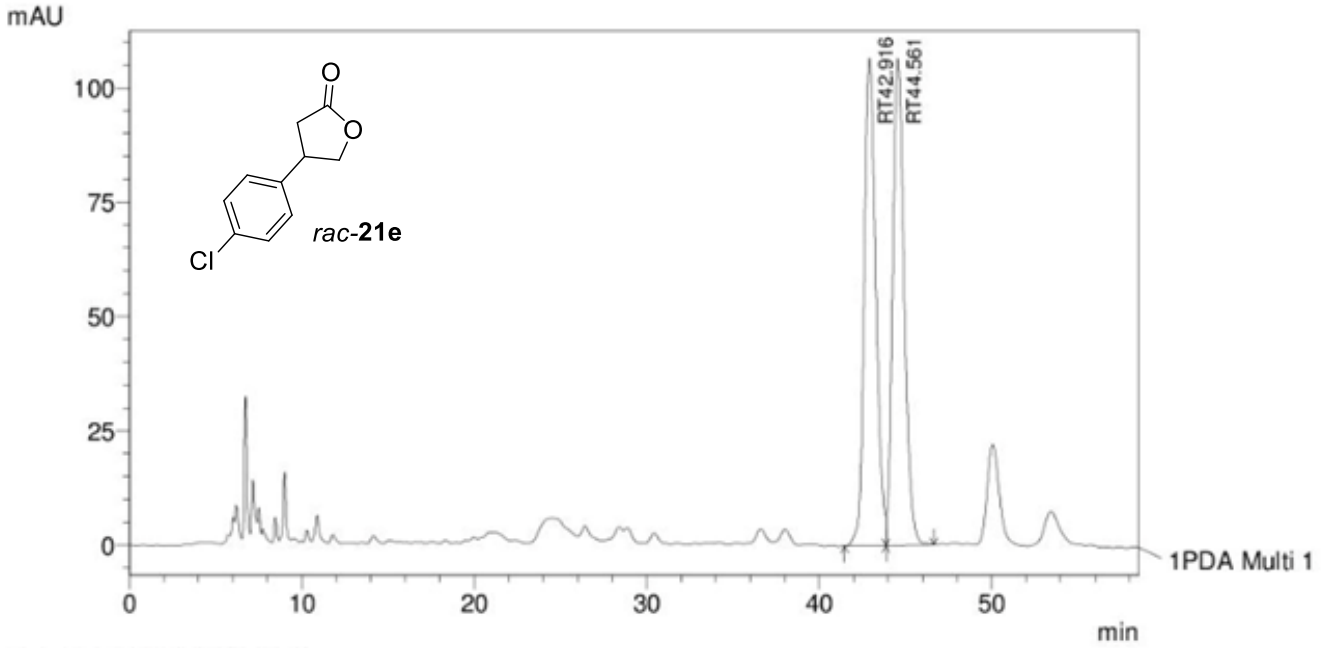


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT26.815	26.815	42713	Not calculated	0.000	mg/L
2	RT27.743	27.743	2212447	Not calculated	0.000	mg/L

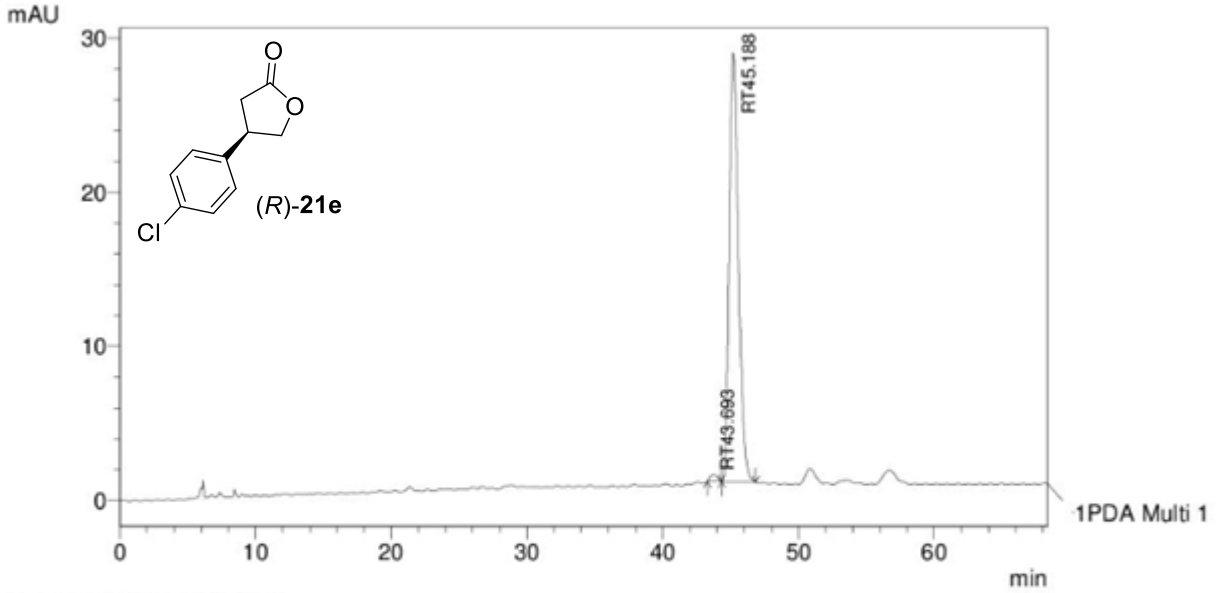


1 PDA Multi 1/234nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT42.916	42.916	5018608	Not calculated	0.000	mg/L
2	RT44.561	44.561	4958197	Not calculated	0.000	mg/L



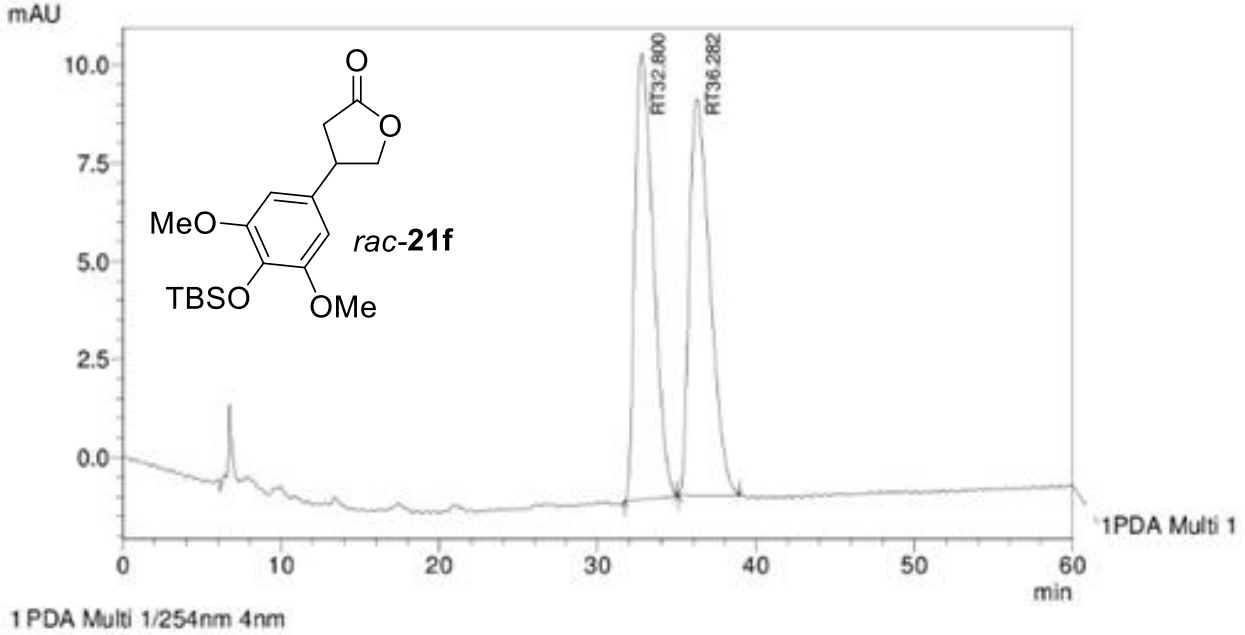
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT43.693	43.693	14959	Not calculated	0.000	mg/L
2	RT45.188	45.188	1317871	Not calculated	0.000	mg/L

<Chromatogram>

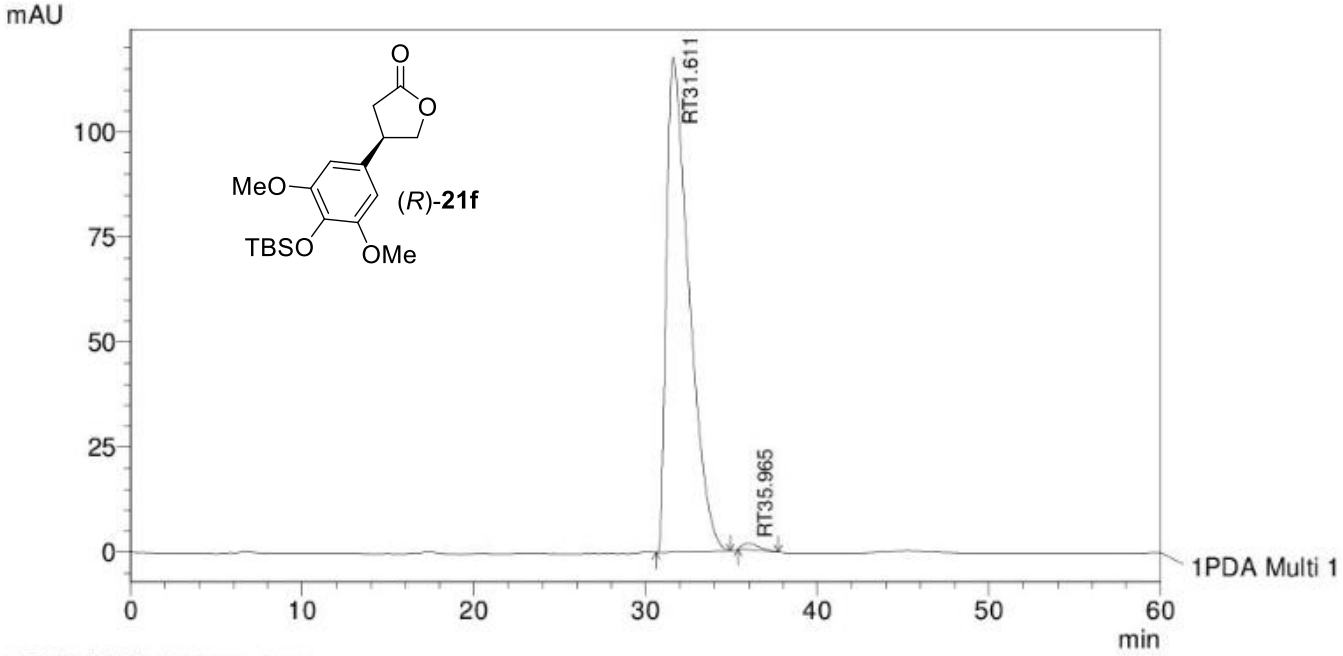


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT32.800	32.800	919337	Not calculated	0.000	mg/L
2	RT36.282	36.282	917766	Not calculated	0.000	mg/L



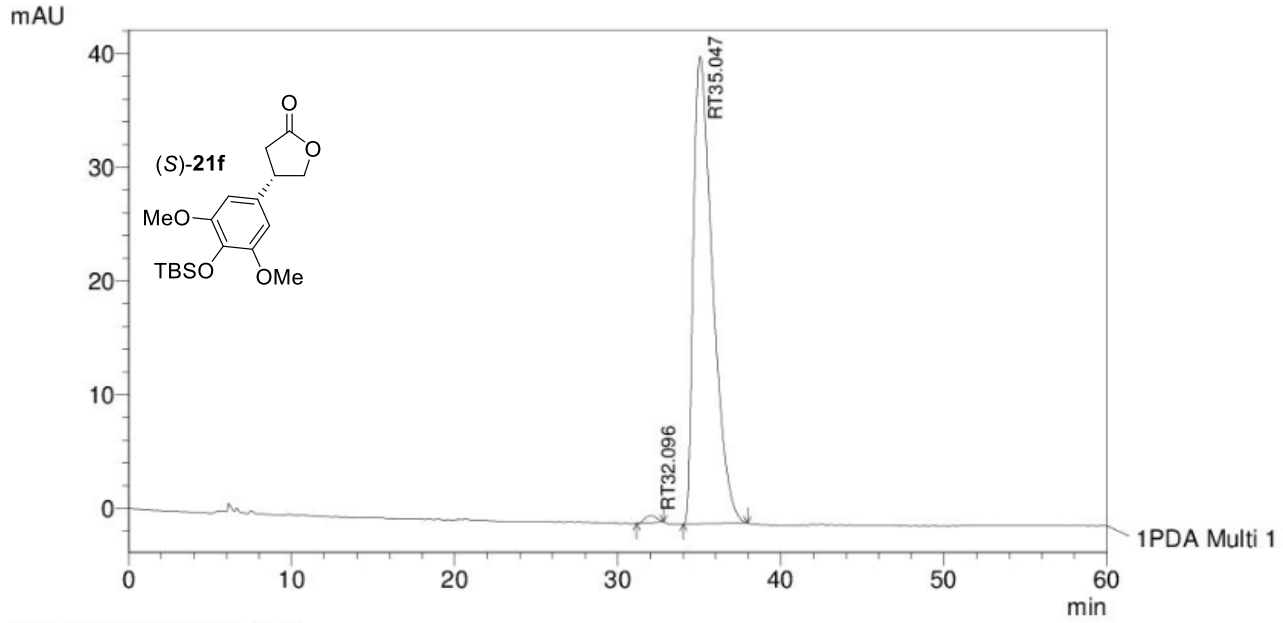
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT31.611	31.611	10773662	Not calculated	0.000	mg/L
2	RT35.965	35.965	106611	Not calculated	0.000	mg/L

<Chromatogram>



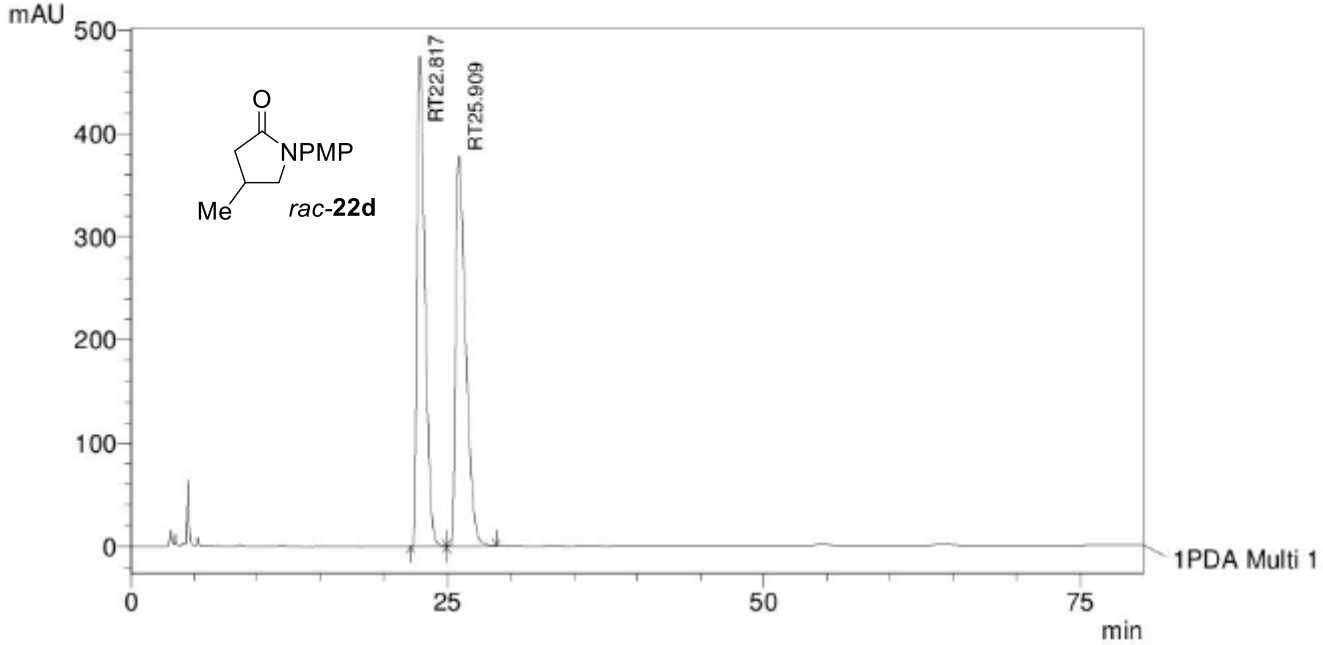
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT32.096	32.096	31147	Not calculated	0.000	mg/L
2	RT35.047	35.047	3372756	Not calculated	0.000	mg/L

<Chromatogram>



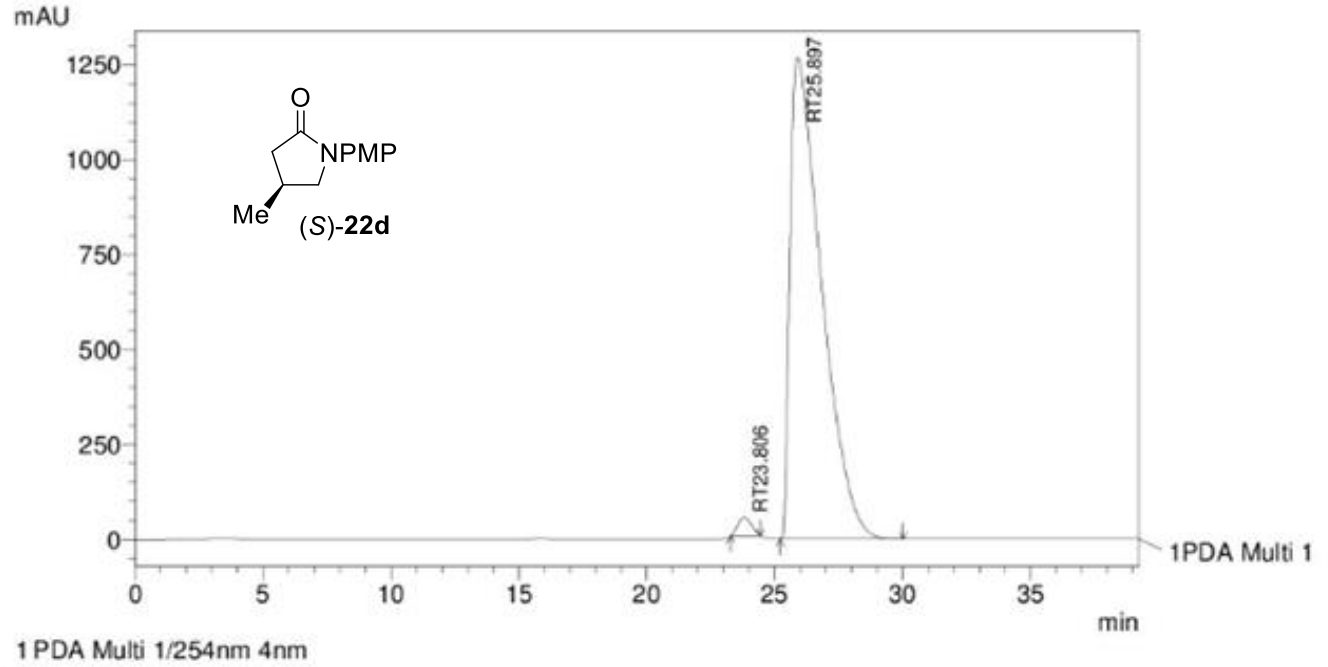
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	linimum Peak Purity Inde	Conc.	Units
1	RT22.817	22.817	20731586	Not calculated	0.000	mg/L
2	RT25.909	25.909	20895543	Not calculated	0.000	mg/L

<Chromatogram>



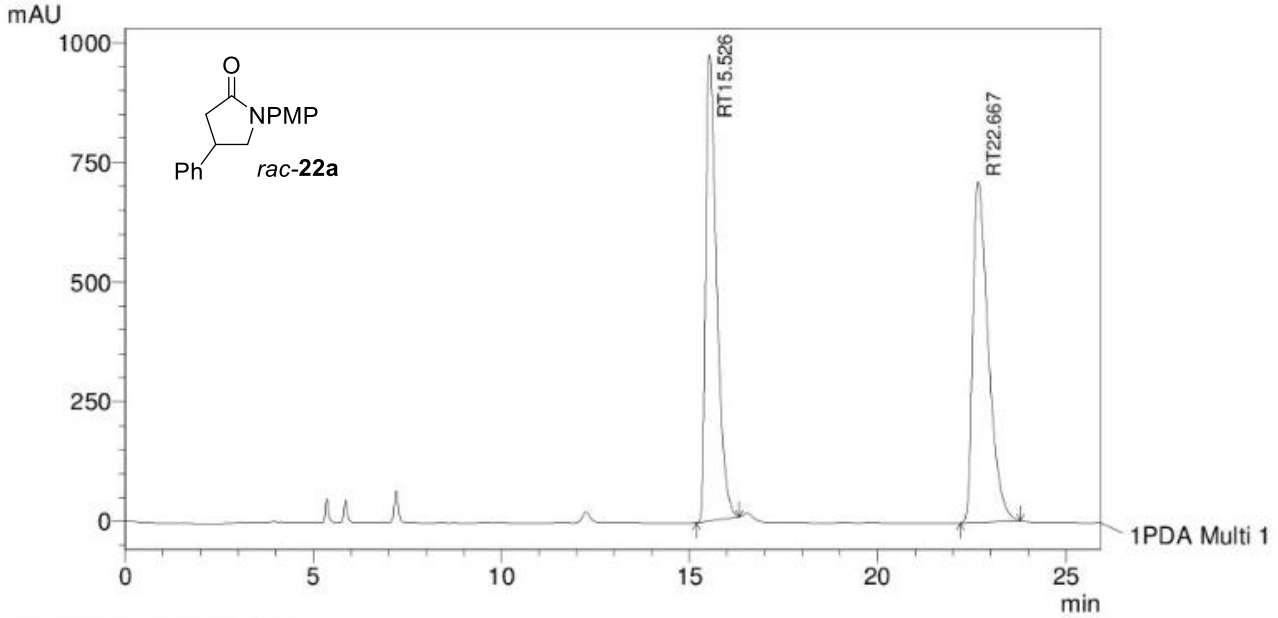
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT23.806	23.806	1791614	Not calculated	0.000	mg/L
2	RT25.897	25.897	108785591	Not calculated	0.000	mg/L

<Chromatogram>



1 PDA Multi 1/254nm 4nm

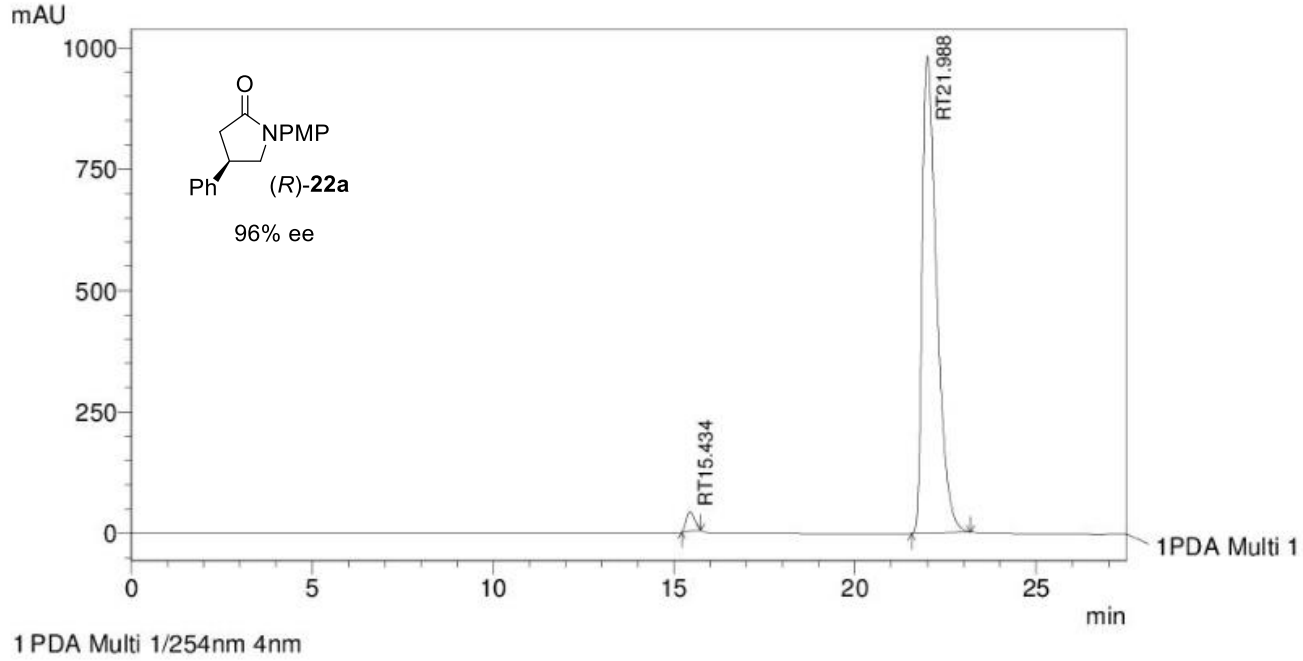
<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT15.526	15.526	19848573	Not calculated	0.000	mg/L
2	RT22.667	22.667	20430496	Not calculated	0.000	mg/L

HPLC of (*R*)-**22a** synthesised from **15a**

<Chromatogram>



1 PDA Multi 1/254nm 4nm

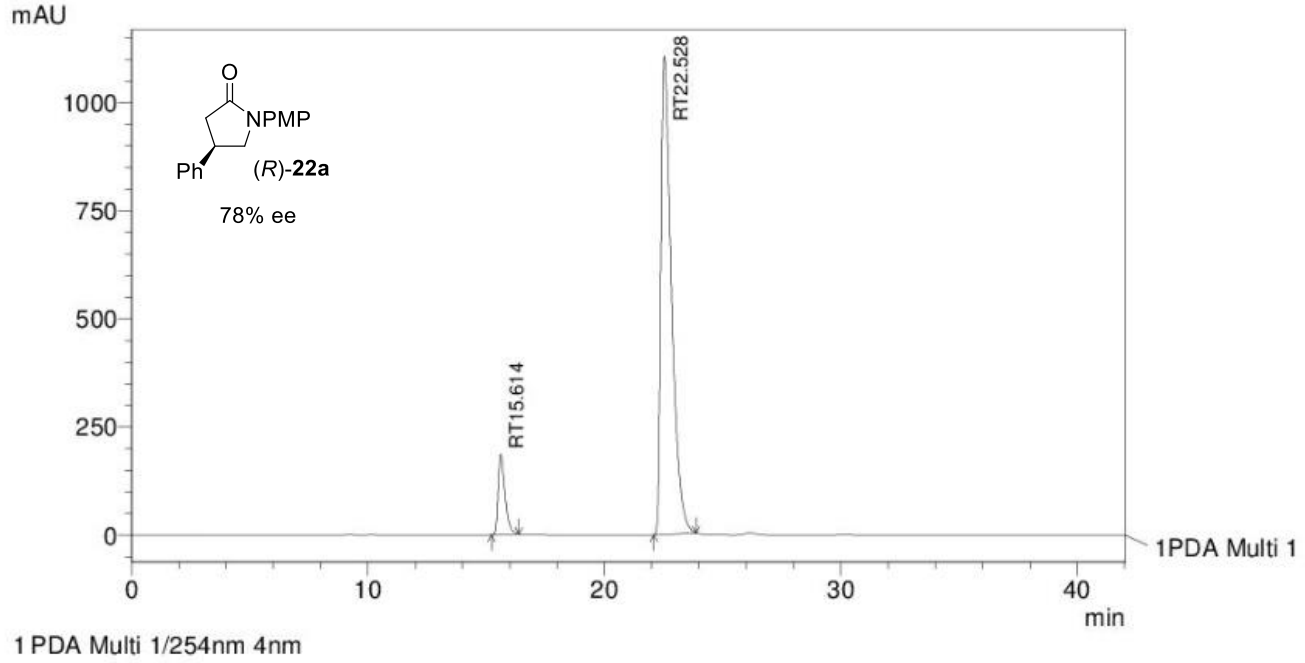
<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT15.434	15.434	645874	Not calculated	0.000	mg/L
2	RT21.988	21.988	27240706	Not calculated	0.000	mg/L

HPLC of (*R*)-**22a** synthesised from (*R*)-**23a** (78% *ee*)

<Chromatogram>

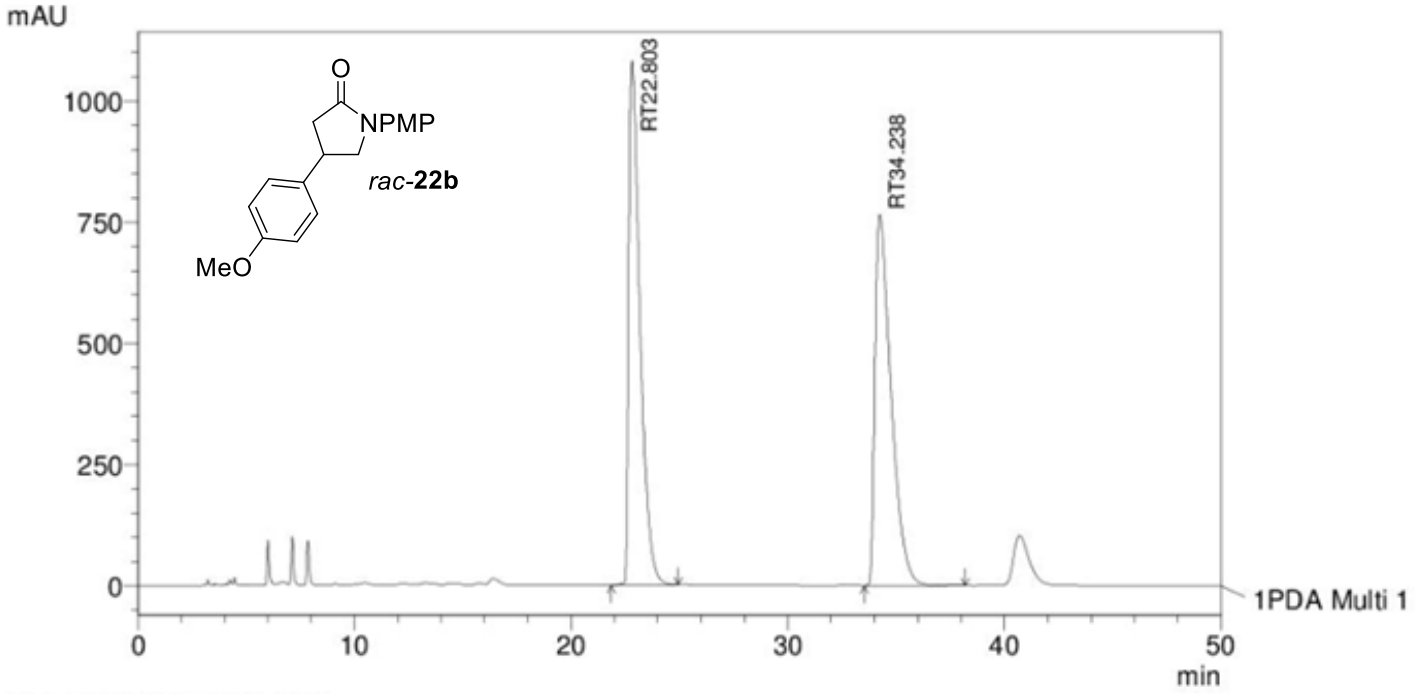


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT15.614	15.614	3754598	Not calculated	0.000	mg/L
2	RT22.528	22.528	34472023	Not calculated	0.000	mg/L

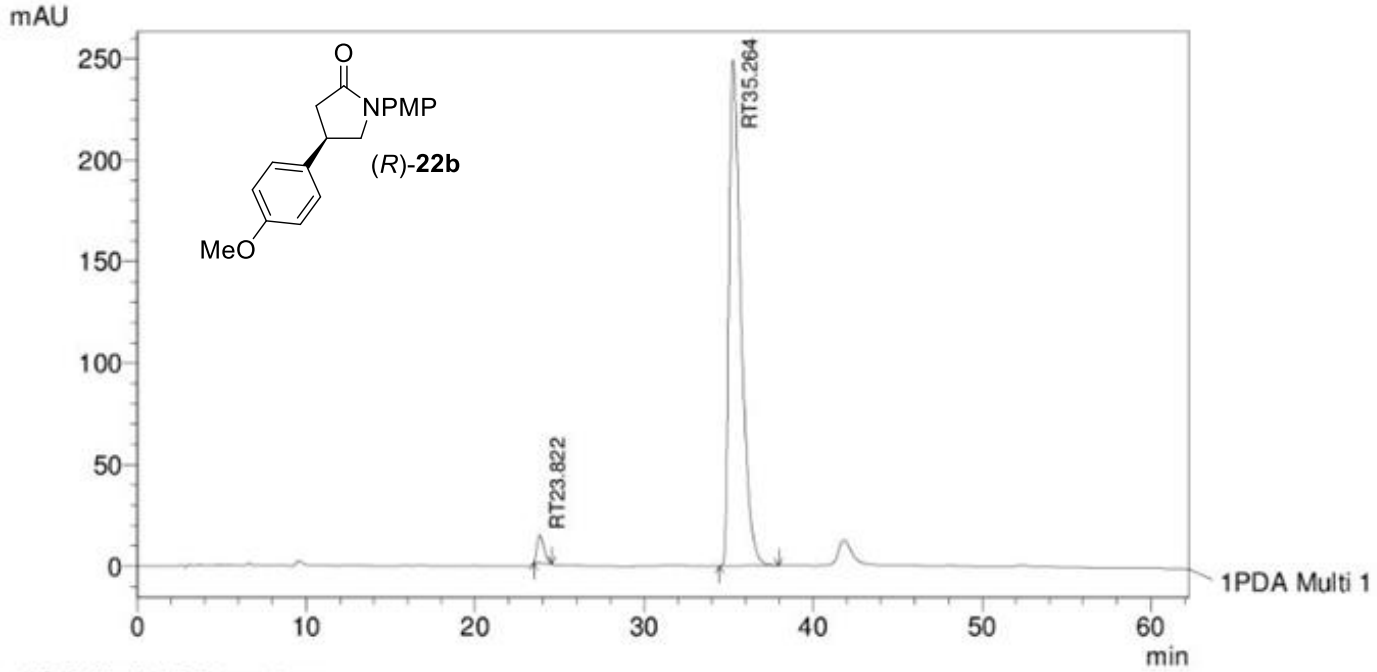


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT22.803	22.803	39006963	Not calculated	0.000	mg/L
2	RT34.238	34.238	39705456	Not calculated	0.000	mg/L



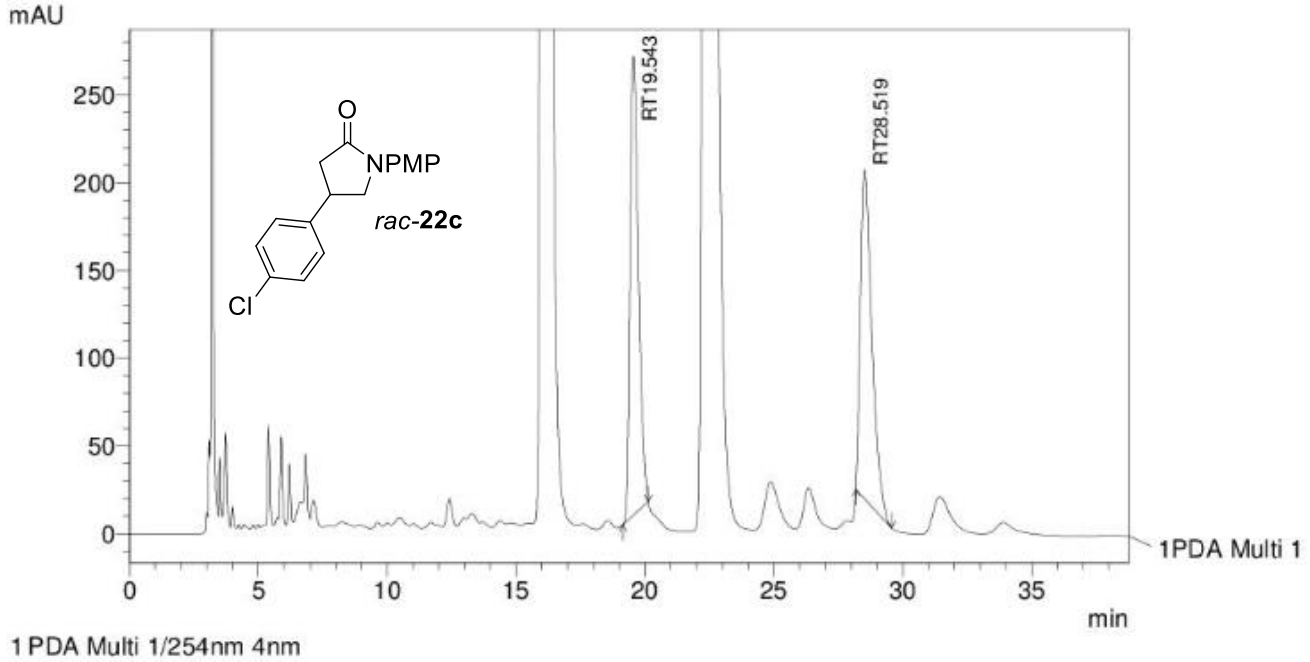
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT23.822	23.822	399928	Not calculated	0.000	mg/L
2	RT35.264	35.264	12313739	Not calculated	0.000	mg/L

<Chromatogram>



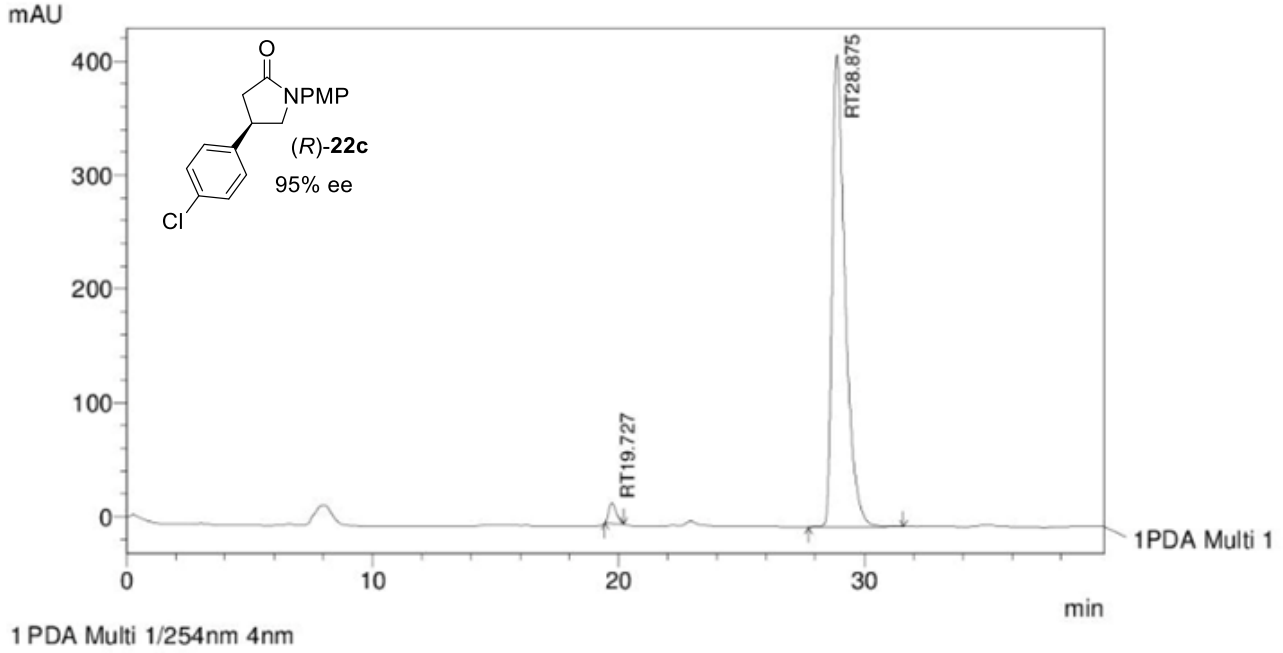
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	linimum Peak Purity Inde	Conc.	Units
1	RT19.543	19.543	5900293	Not calculated	0.000	mg/L
2	RT28.519	28.519	5837371	Not calculated	0.000	mg/L

HPLC of (*R*)-**22c** synthesised from **15c**



1 PDA Multi 1/254nm 4nm

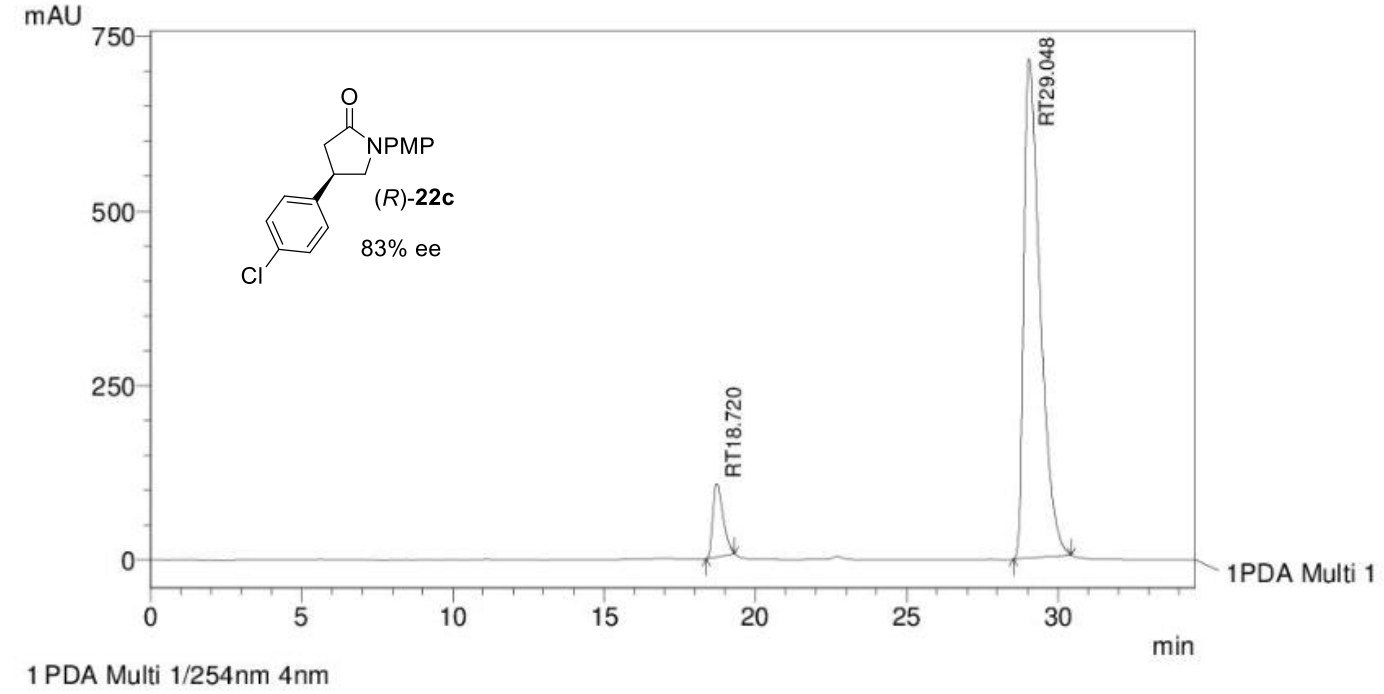
<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT19.727	19.727	385177	Not calculated	0.000	mg/L
2	RT28.875	28.875	15385591	Not calculated	0.000	mg/L

HPLC of (*R*)-**22c** synthesised from (*R*)-**23c** (85% *ee*)

<Chromatogram>



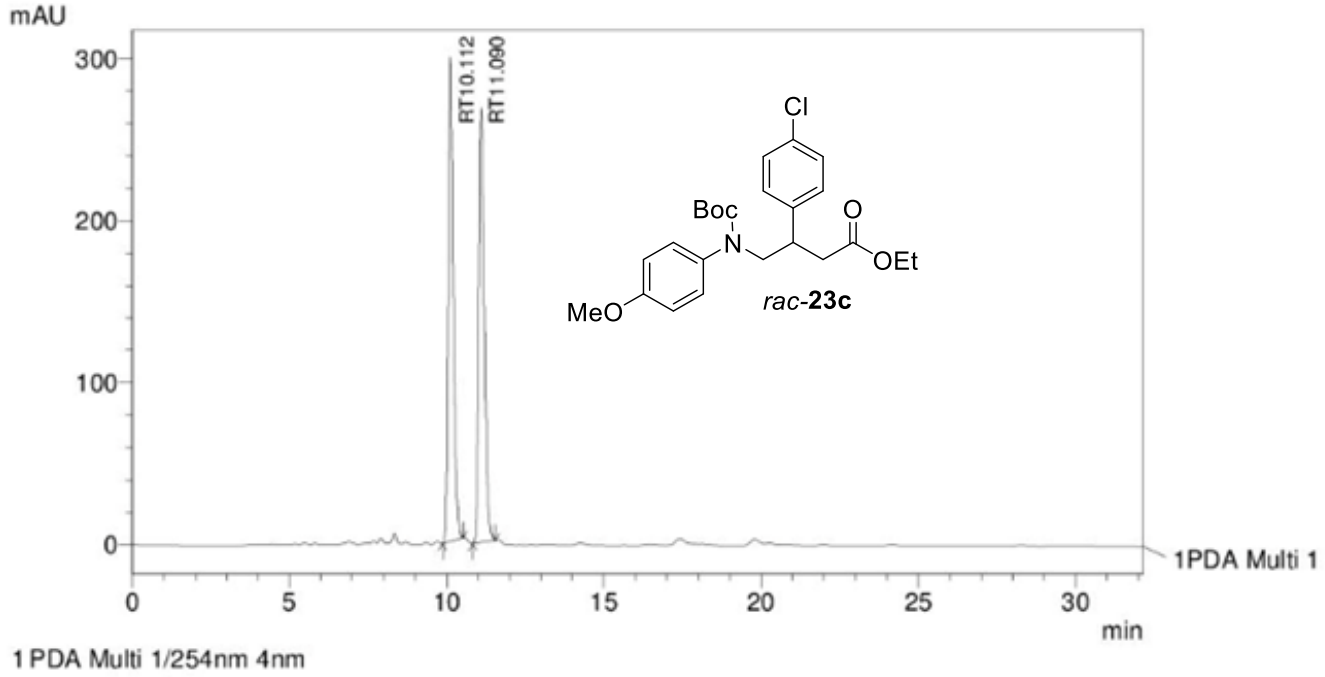
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT18.720	18.720	2475184	Not calculated	0.000	mg/L
2	RT29.048	29.048	26930469	Not calculated	0.000	mg/L

<Chromatogram>



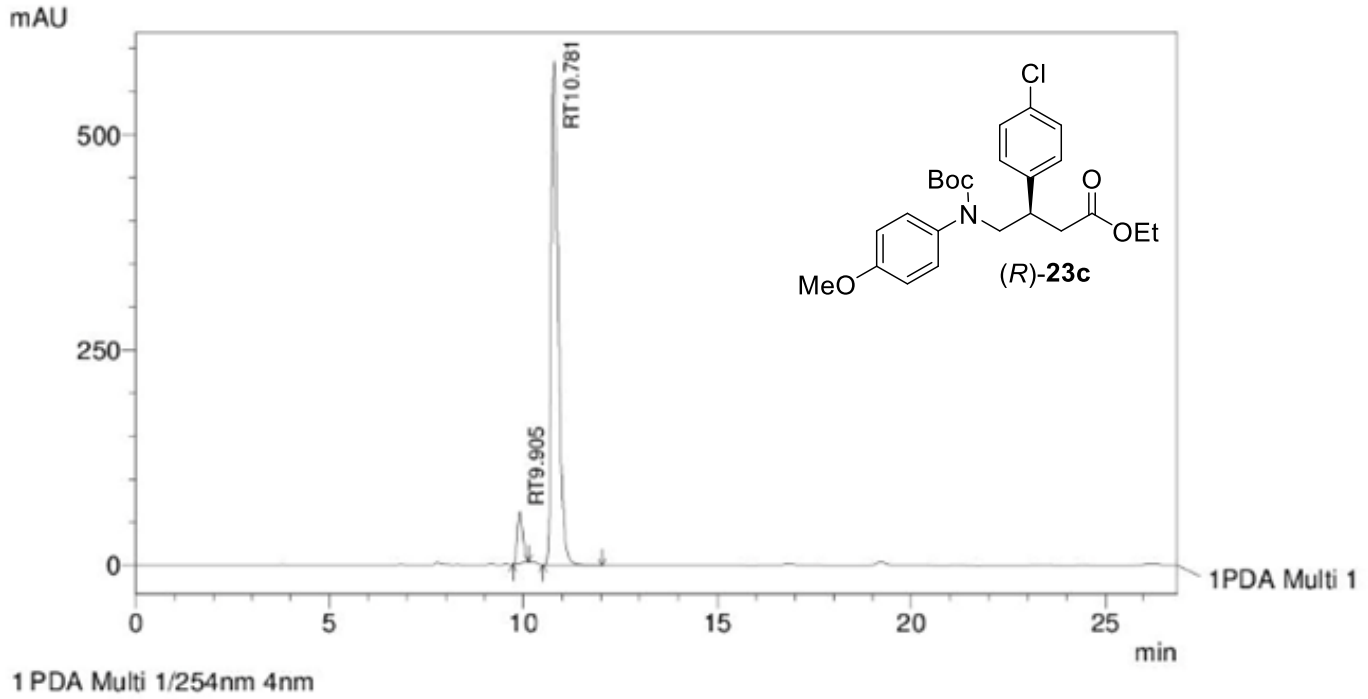
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT10.112	10.112	3340184	Not calculated	0.000	mg/L
2	RT11.090	11.090	3299858	Not calculated	0.000	mg/L

<Chromatogram>



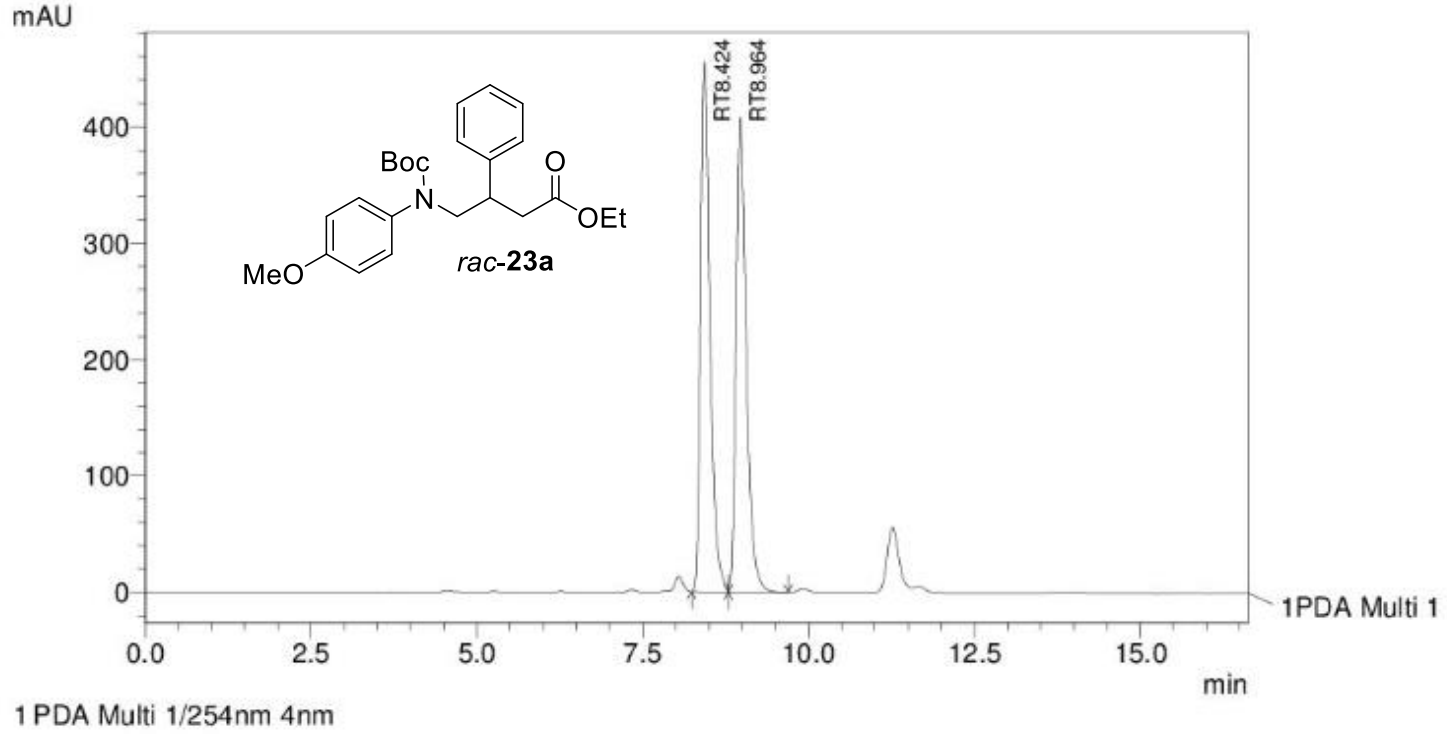
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT9.905	9.905	592115	Not calculated	0.000	mg/L
2	RT10.781	10.781	7369577	Not calculated	0.000	mg/L

<Chromatogram>



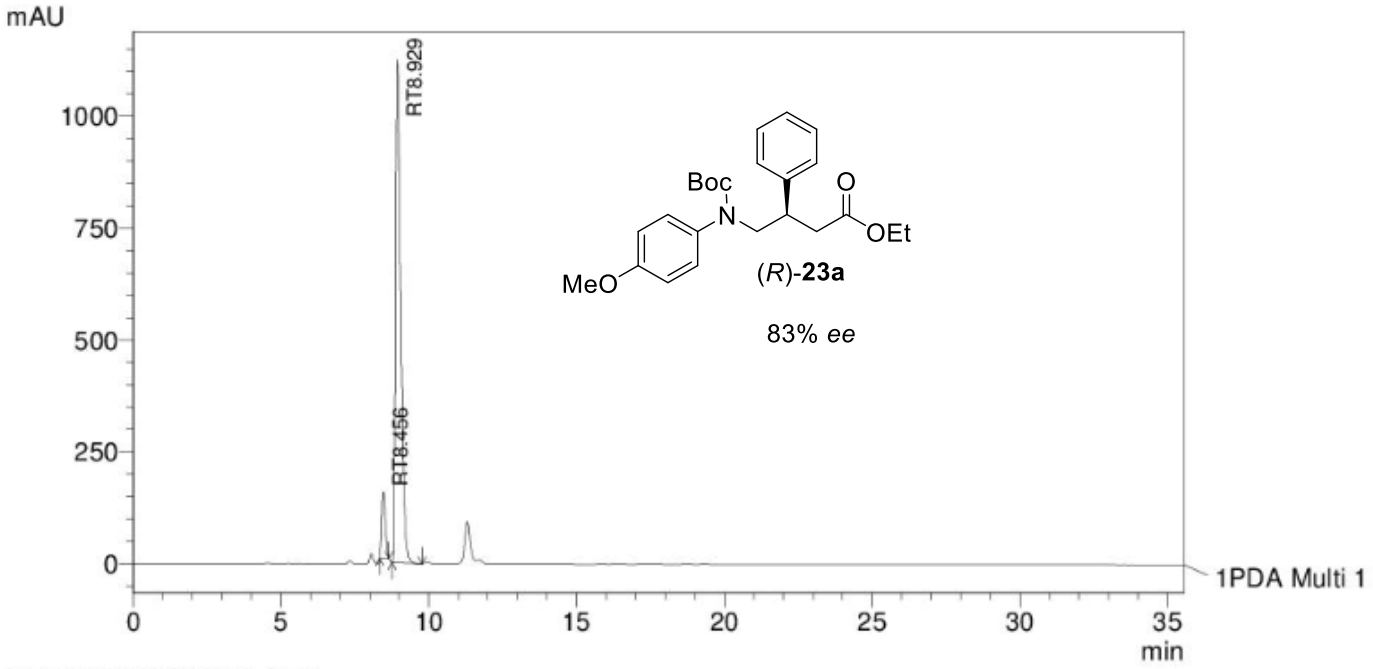
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT8.424	8.424	4518890	Not calculated	0.000	mg/L
2	RT8.964	8.964	4358582	Not calculated	0.000	mg/L

<Chromatogram>



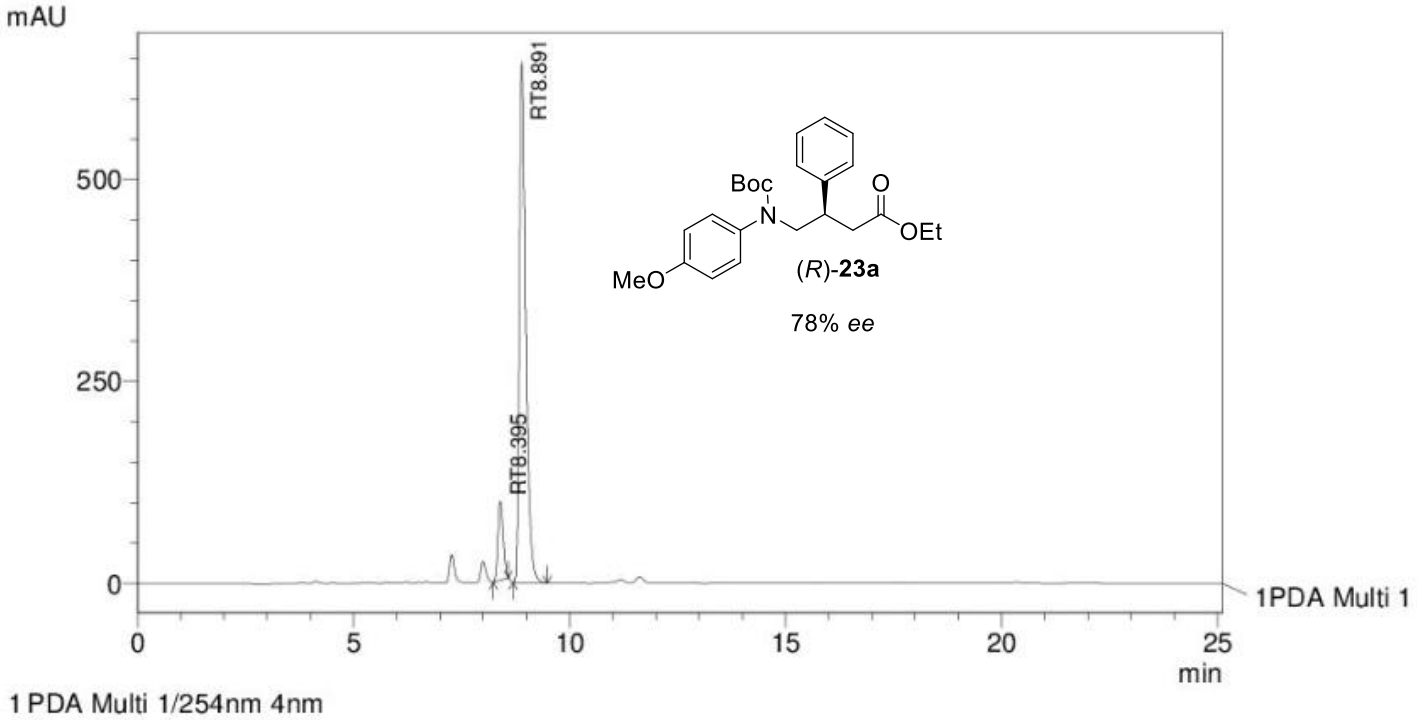
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT8.456	8.456	1281301	Not calculated	0.000	mg/L
2	RT8.929	8.929	13758437	Not calculated	0.000	mg/L

<Chromatogram>



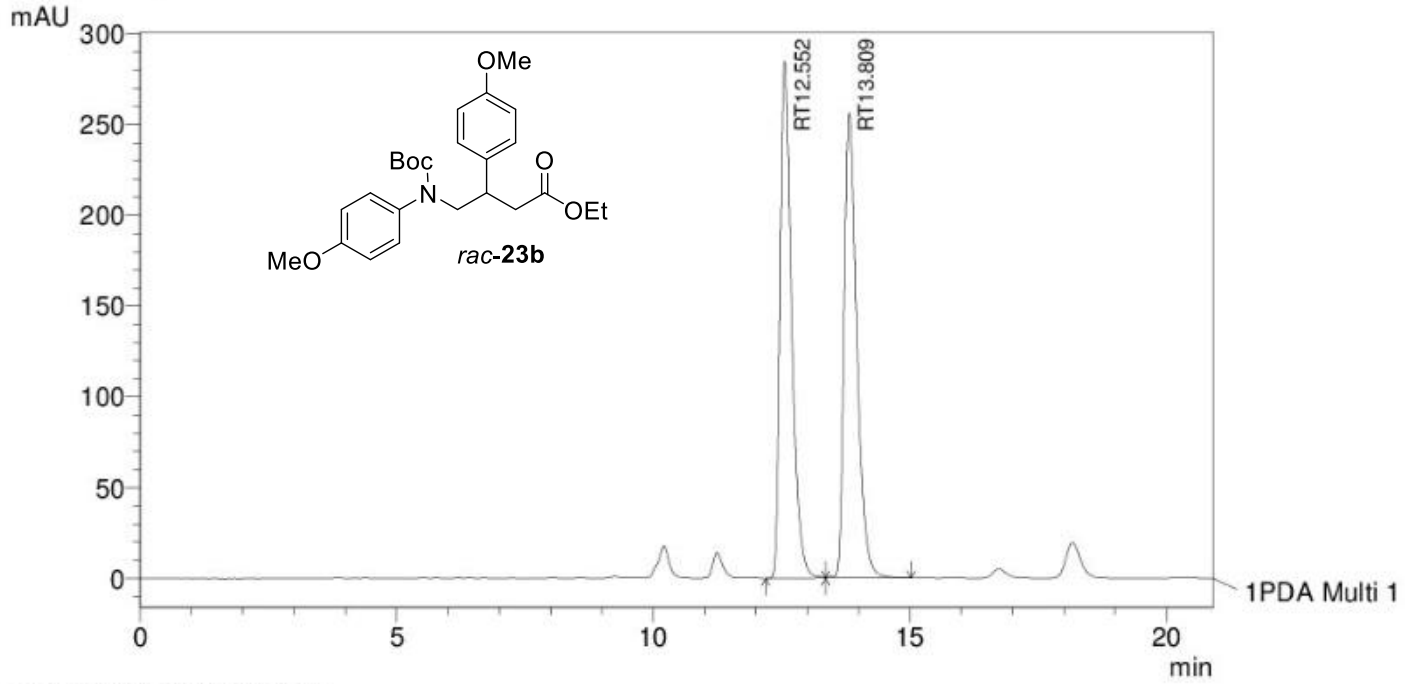
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT8.395	8.395	838561	Not calculated	0.000	mg/L
2	RT8.891	8.891	6713350	Not calculated	0.000	mg/L

<Chromatogram>



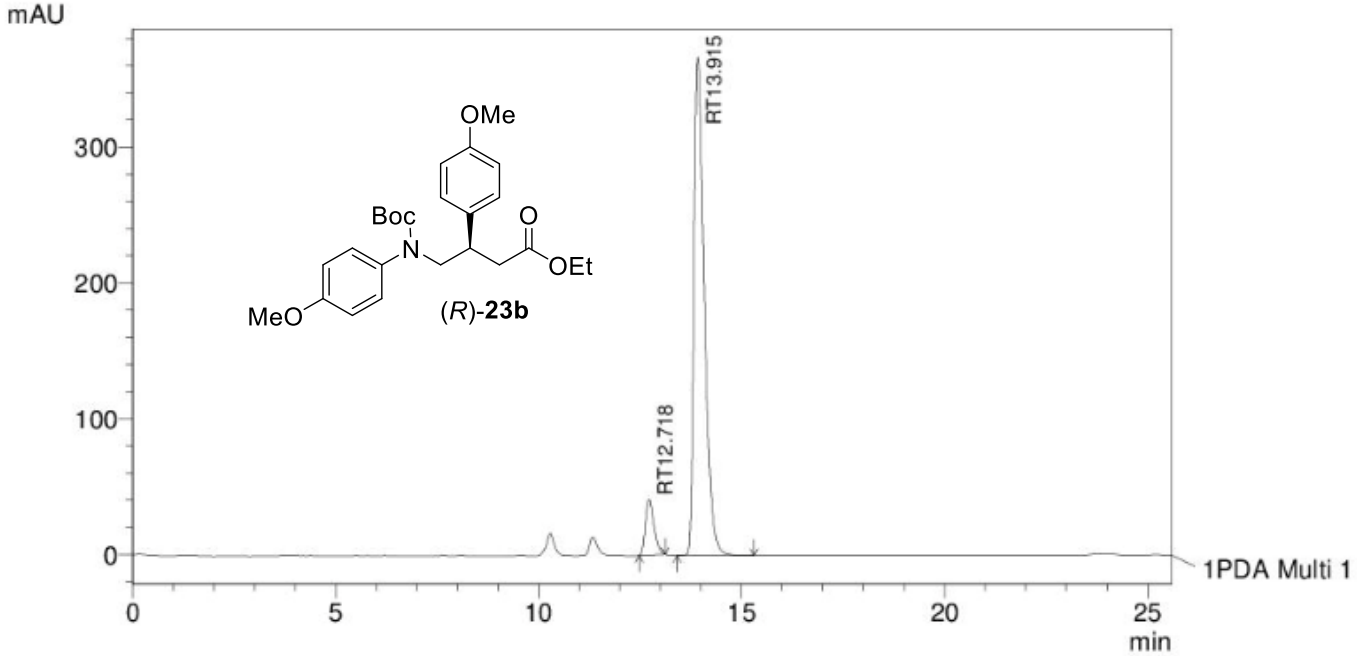
1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT12.552	12.552	4452499	Not calculated	0.000	mg/L
2	RT13.809	13.809	4388815	Not calculated	0.000	mg/L

<Chromatogram>

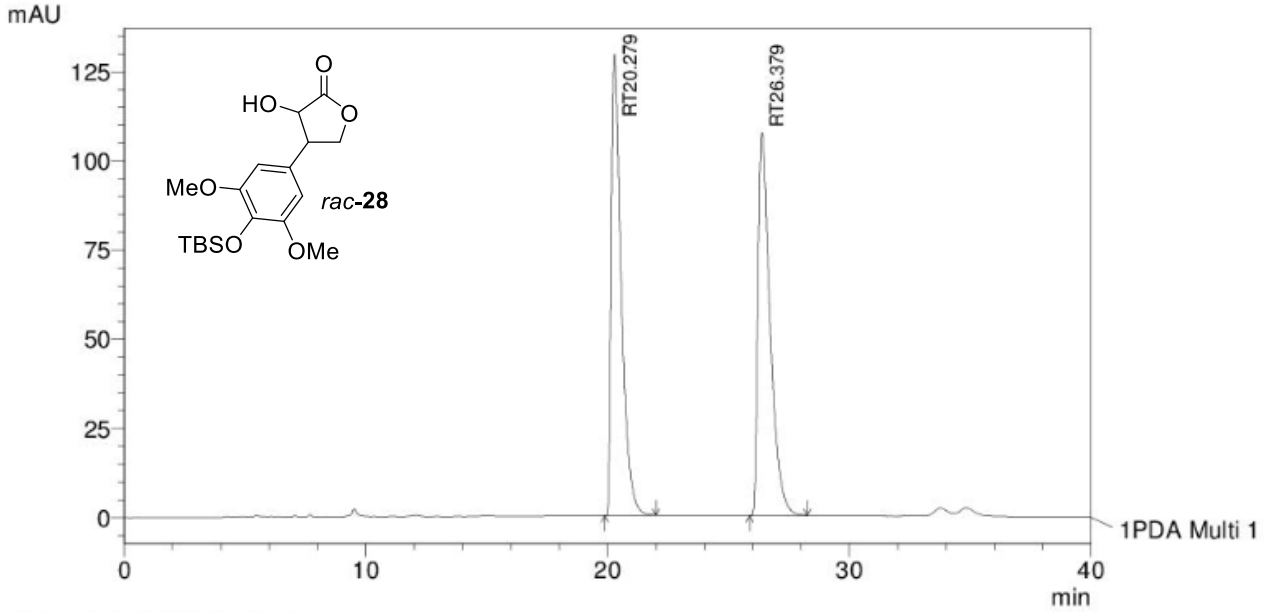


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT12.718	12.718	598850	Not calculated	0.000	mg/L
2	RT13.915	13.915	6502365	Not calculated	0.000	mg/L

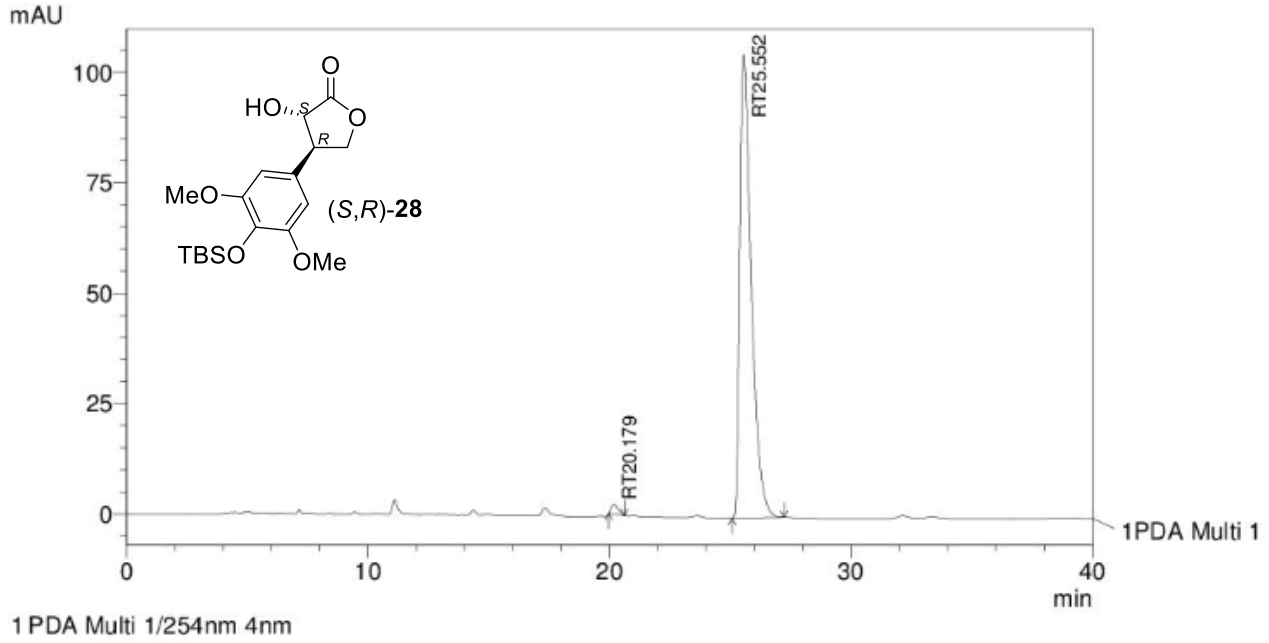


1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	linimum Peak Purity Inde	Conc.	Units
1	RT20.279	20.279	3759693	Not calculated	0.000	mg/L
2	RT26.379	26.379	3766387	Not calculated	0.000	mg/L



1 PDA Multi 1/254nm 4nm

<Results>

PDA

ID#	Name	Ret. Time	Area	Minimum Peak Purity Inde	Conc.	Units
1	RT20.179	20.179	43167	Not calculated	0.000	mg/L
2	RT25.552	25.552	3476928	Not calculated	0.000	mg/L