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

Asymmetric synthesis of *trans*-4,5-disubstituted γ-butyrolactones involving a key allylboration step. First access to (-)-nicotlactone B and (-)-galbacin.

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I. General information

Tetrahydrofuran (THF) was distilled over sodium/benzophenone, dichloromethane (DCM) was distilled over P_2O_5. Amines including triethyamine were distilled over potassium hydroxide and trifluoroacetic anhydride was distilled over P_2O_5. Alcohols were distilled over calcium hydride (CaH_2). All aldehydes were distilled prior to their used.
NMR spectra were recorded on Bruker apparatus at 300, 400 or 500 MHz for ^1H and 75, 101 or 126 MHz for ^{13}C. Chemical shifts of ^1H and ^{13}C NMR were referenced to Me_4Si as internal reference. Data are represented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant J (Hz) and integration. Assignments are made with the aid of DEPT 135, COSY and HMQC experiments.

All high-resolution mass spectra (HRMS) were recorded on a Bruker Micro-Tof-Q II or on a Waters Q-Tof 2 at the CRMPO (Centre Régional de Mesures de Physiques de l'Ouest – Rennes- France) using positive ion electrospray.

Purifications on a silica gel were carried out on Acros silica gel 0.006-0.200 mm, 60 A. Analytical thin layer chromatography was performed on Merck Silica gel 60 F_{254} plates.

X-ray crystallographic data were collected on an APEXII crystal diffractometer.

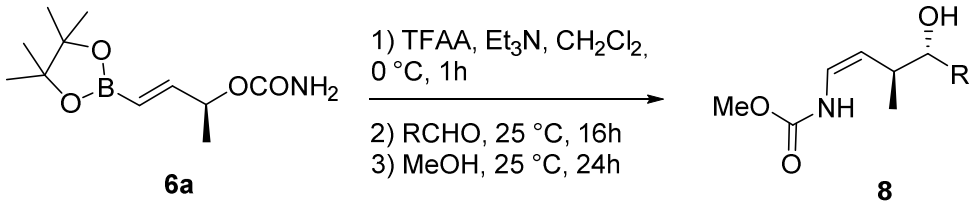
The optical rotations were measured on a Perkin Elmer Model 341 polarimeter (sodium D-line : 589 nm and mercury I-line : 365 nm).

Melting points were measured on a melting point apparatus Stuart SMP10.

All analytical high-performance liquid chromatography (HPLC) were performed on an Agilent Technologies equipped with diode array UV detectors, using Chiralcel OD-H column.

Enantioenriched compounds **6** were prepared according to a literature procedure.[1]

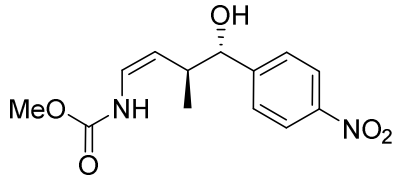
II. General procedure for acyclic enecarbamate synthesis



To a solution of boronate (1eq.) in dry dichloromethane (0.1M), under argon atmosphere, were added trifluoroacetic anhydride (3 eq.) and triethylamine (4.5 eq.). The solution was stirred at 0° C for an hour then aldehyde (1.2 eq.) was added. The resulting solution was stirred at 0 ° C for an hour and then at 25 ° C for 16 hours.

Methanol was added and the solution was stirred at 25 ° C for 24 hours. The reaction medium was concentrated under *vacuo*. The crude product was purified by silica gel chromatography to give the desired compound.

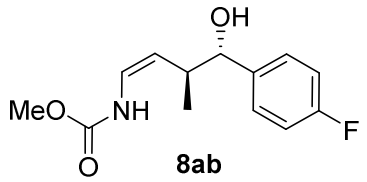
(*Z*)-Methyl ((3*S*,4*S*)-4-hydroxy-3-methyl-4-(4-nitrophenyl)but-1-en-1-yl)carbamate (8aa)



Prepared starting from **6a** (0.42 mmol, 100 mg) using *p*-nitrobenzaldehyde (0.50 mmol, 76 mg). The crude was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 7/3) to give **8aa** (105 mg, 89%) as a yellow oil.

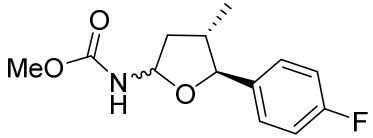
R_f = 0.13 (cyclohexane/AcOEt, 7/3)
$[\alpha]_I^{20}$ = - 34 (c 2.50, CH_2Cl_2)
^{1}H NMR (400 MHz, Acetone-d6, δ ppm) 8.20 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 10.0 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 6.41 (dd, *J* = 10.0 , 10.0 Hz, 1H), 4.77 – 4.72 (m, 1H), 4.62 – 4.52 (dd, *J* = 10.0, 9.0 Hz, 1H), 3.62 (s, 3H), 2.99 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, Acetone-d6, δ ppm) 155.3, 153.0, 147.9, 128.5, 124.5, 123.7, 111.2, 77.7, 52.3, 39.0, 17.9.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}N_2O_5Na$ $[M+Na]^+$ 303.0951; found 303.0951.

(*Z*)-Methyl ((3*S*,4*S*)-4-hydroxy-3-methyl-4-(4-fluorophenyl)but-1-en-1-yl)carbamate (8ab)



8ab

Prepared starting from **6a** (0.42 mmol, 100 mg) using *p*-trifluoromethylbenzaldehyde (0.50 mmol, 76 mg). The crude was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 7/3) to give a mixture of **8ab** and **9ab** as a yellow oil for which the ratio was estimated around to 16/84 (60 mg, 56%) based on ^{1}H NMR spectrum.

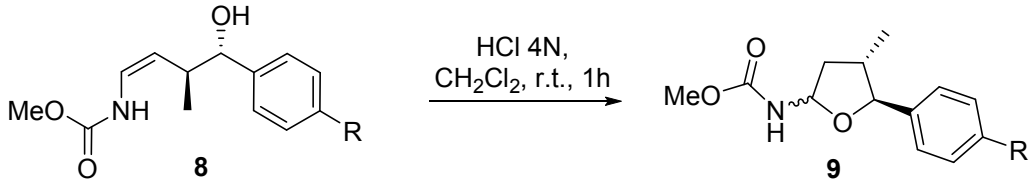


9ab

R_f = 0.25 (cyclohexane/AcOEt, 7/3)

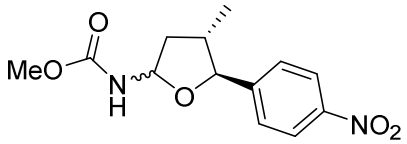
^{1}H NMR (400 MHz, Acetone-d6, δ ppm) 7.99 (d, *J* = 8.3 Hz, 0.16H), 7.48-7.37 (m, 2H), 7.15-7.06 (m, 2.504H), 6.98 (br s, 0.336H), 6.45 (dd, *J* = 10.0, 10.0 Hz, 0.16H), 5.85-5.76 (m, 0.336H), 5.69 - 5.62 (m, 0.504H), 4.56 (dd, J = 9.9, 9.9 Hz, 0.16H), 4.52-4.48 (dd, *J* = 6.8, 3.9 Hz, 0.16 H), 4.44 (d, *J* = 3.9 Hz, 0.16H), 4.43 (d, *J* = 8.9 Hz, 0.336H), 4.33 (d, *J* = 8.9 Hz, 0.504H), 3.65 (s, 0.48H), 3.63 (s, 1.51H), 3.61 (s, 1.01H), 2.99-2.82 (m, 0.16H), 2.61-2.52 (m, 0.336H), 2.32-2.19 (m, 0.504H), 2.15 (ddd, J = 12.8, 7.2, 2.8 Hz, 0.504H), 2.10-1.99 (m, 0.84H), 1.80-1.70 (m, 0.336H), 1.08 (d, *J* = 6.5 Hz, 0.1.51H), 1.01 (d, *J* = 6.5 Hz, 1.01H), 0.86 (d, *J* = 6.8 Hz, 0.48H).

III. General procedure for hemiaminals synthesis



To a solution of pure enecarbamate **8** or a mixture of **8** and **9** (1 eq.) in dry dichloromethane (0.05M), under argon atmosphere, was added HCl 4N in dioxane (0.2 eq.). The mixture was stirred at room temperature for one hour. After completion, the reaction media is evaprated under *vacuo*. The crude product was purified by silica gel chromatography to give the desired compound. **9**.

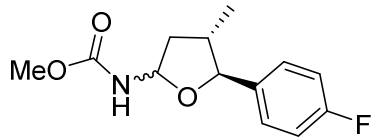
Methyl ((4S,5S)-4-methyl-5-(4-nitrophenyl)tetrahydrofuran-2-yl)carbamate (9aa)



Prepared starting from **8aa** (0.36 mmol, 100 mg). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 6/4) to give **9aa** (94 mg, 93%) as an orange solid (mixture of diastereoisomers, 59/41).

R_f = 0.28 (cyclohexane/AcOEt, 6/4)
m.p. = 96-98 ° C
$[\alpha]_I^{20}$ = - 35 (c 2.70, CH_2Cl_2)
^{1}H NMR (300 MHz, Acetone-d6, δ ppm) 8.21 (d, *J* = 8.8 Hz, 1,18H), 8.20 (d, *J* = 8.8 Hz, 0.82H), 7.67 (d, *J* = 8.8 Hz, 1.18H), 7.66 (d, *J* = 8.6 Hz, 0.82H), 7.10 (br s, 0.41H), 7.04 (br s, 0.59H), 5.92 – 5.77 (m, 0.59H), 5.70 (m, 0.41H), 4.59 (d, *J* = 9.5 Hz, 0.59H), 4.50 (d, *J* = 8.5 Hz, 0.41H), 3.64 (s, 1.77H), 3.61 (s, 1.23H), 2.59 (m, 0.59H), 2.30 (m, 0.41H), 2.22 – 2.12 (m, 0.59H), 2.21 – 2.11 (m, 0.41H), 2.09 – 2.01 (m, 0.41H), 1.79 (m, 0.59H), 1.10 (d, *J* = 6.5 Hz, 1.23H), 1.07 (d, *J* = 6.5 Hz, 1.77H).
^{13}C NMR (75 MHz, Acetone-d6, δ ppm) 157.1, 156.9, 150.8, 150.2, 148.4, 148.3, 128.1, 128.0, 124.2, 124.1, 87.4, 85.7, 83.7, 83.3, 52.0, 44.4, 42.3, 41.0, 40.8, 16.0, 15.1.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}N_2O_5Na$ $[M+Na]^+$ 303.0951; found 303.0951.

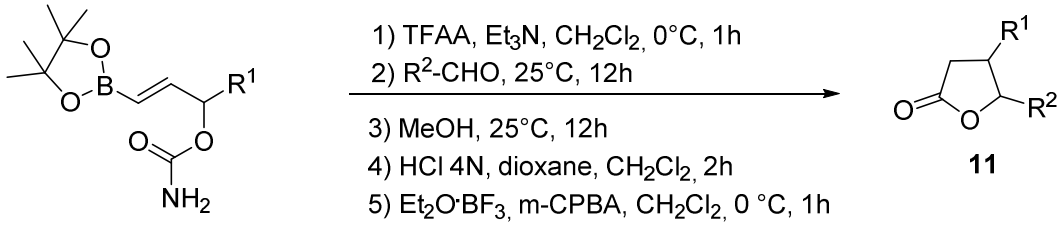
Methyl ((4S,5S)-4-methyl-5-(4-trifluoromethylphenyl)tetrahydrofuran-2-yl)carbamate (9ab)



Prepared starting from a mixture of **8ab and 9ab** (0.40 mmol, 100 mg). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 6/4) to give **9ab** (96 mg, 95%) as a colourless oil (mixture of diastereoisomers, 57/43).

R_f = 0.25 (Cyclohexane/AcOEt 7/3).
$[\alpha]_I^{20}$ = - 79 (c 2.60, CH_2Cl_2).
^{1}H NMR (300 MHz, Acetone-d_6, δ ppm) 7.48 – 7.34 (m, 2H), 7.15 – 7.05 (m, 2.57H), 7.00 (br s, 0.43H), 5.85 – 5.73 (m, 0.57H), 5.69 – 5.60 (m, 0.43H), 4.43 (d, *J* = 9.5 Hz, 0.57H), 4.32 (d, *J* = 8.7 Hz, 0.43H), 3.63 (s, 1.29H), 3.61 (s, 1.71H), 2.61 – 2.50 (m, 0.57H), 2.32 – 2.16 (m, 0.43H), 2.21 – 2.01 (m, 0.43H), 2.05 – 1.99 (m, 1H), 1.80-1.67 (m, 0.57H), 1.03 (d, *J* = 6.6 Hz, 1.29H), 1.00 (d, *J* = 6.6 Hz, 1.71H).
^{13}C NMR (101 MHz, Acetone-d6, δ ppm) 162.2 (d, *J* = 243.2 Hz), 156.3, 156.1, 137.9 (d, *J* = 3.0 Hz), 137.5, 128.3 (d, *J* = 8.1 Hz), 114.8 (d, *J* = 21.4 Hz), 87.1, 85.2, 82.3, 81.9, 51.0, 43.2, 41.1, 40.1, 14.9, 14.2.
^{19}F NMR (376 MHz, Acetone-d6, δ ppm) -117.0
HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}FNO_3Na$ $[M+Na]^+$ 276.1006; found 276.1006.

VI. General procedure for lactones synthesis



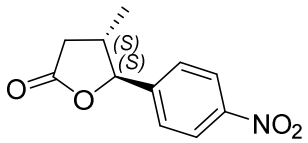
(*S*,*E*)-**6a**, R^1 = Me
(*R*,*E*)-**6a**, R^1 = Me
(*S*,*E*)-**6b**, R^1 = C_5H_{11}

To a solution of boronate **6** (1eq.) in dry dichloromethane (0.1M), under argon atmosphere were added trifluoroacetic anhydride (3 eq.) and triethylamine (4.5 eq.). The solution was stirred at 0 ° C for an hour and then, aldehyde (1.2 eq.) was added. The resulting solution was stirred at room temperature for 12 hours.

Methanol (1 eq.) was added and the solution was stirred at room temperature for 12 hours. To the reaction medium was added methanol (20 eq.) and HCl 4N in dioxane (10 eq.). The solution was stirred at room temperature for additionally 2 hours. The reaction media was diluted with dichloromethane and neutralized with NaOH 2M. The aqueous layer was extracted with dichloromethane. Organic layers were dried over $MgSO_4$, filtered, and concentrated under *vacuo.*

To a solution of the crude in dry dichloromethane (0.15M), cooled at 0 ° C, were added $Et_2O{\cdot}BF_3$ (3 eq.) and a solution of m-CPBA (3 eq.) in dry dichloromethane (0.5M). The mixture was stirred at 0 ° C for 1 hour and quenched with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under *vacuo*. The crude product was purified by silica gel chromatography to give the desired lactones **11**.

(4*S*,5*S*)-4-methyl-5-(4-nitrophenyl)dihydrofuran-2(3H)-one (11aa)

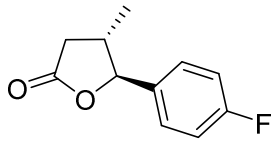


Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using *p*-nitrobenzaldehyde (0.50 mmol, 76 mg).The crude product was purified by chromatography (silica gel, eluent: pentane/Et_2O, 7/3 to 0/10) to give **11aa** (81 mg, 87%) as an orange oil.

R*f* = 0.12 (pentane/Et_2O, 1/1)
$[\alpha]_D^{20}$ = + 13 (c 1.60, CH_2Cl_2)
^{1}H NMR (400 MHz, Acetone-d6, δ ppm) 8.29 (d, *J* = 8.7 Hz, 2H), 7.73 (d, *J* = 8.7 Hz 2H), 5.21 (d, *J* = 8.5 Hz, 1H), 2.78 (dd, *J* = 16.3, 7.2 Hz, 1H), 2.61 – 2.52 (m, 1H), 2.47 (dd, *J* = 16.3, 10.5 Hz, 1H), 1.23 (d, *J* = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, Acetone-d6, δ ppm) 175.8, 148.9, 147.2, 128.1, 124.5, 86.8, 40.7, 37.2, 16.1.
Chiral HPLC : Chiralcel OD-H, hexane/i-PrOH = 90/10, flow rate = 1.0 mL/min, 230 nm, $t_{(S,S)}$ = 59.6 min, , $t_{(R,R)}$ = 64.9 min. (see afterward the chromatogram at page S33) *ee* = 98%.

HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}NO_4Na$ $[M+Na]^+$ 244.0580; found 244.0579.

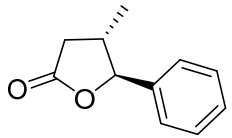
(4*S*,5*S*)-5-(4-fluorophenyl)-4-methyldihydrofuran-2(3H)-one (11ab)



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using *p*-fluorobenzaldehyde (0.50 mmol, 54 µL). The crude product was purified by chromatography (silica gel, eluent: pentane/Et_2O, 9/1 to 7/3) to give **11ab** (47 mg, 58%) as a yellow oil.

R_f = 0.14 (pentane/Et_2O, 7/3)
$[\alpha]_I^{20}$ = + 30 (c 1.05, CH_2Cl_2)
^{1}H NMR (300 MHz, Acetone-d6, δ ppm) 7.56-7.44 (m,, 2H), 7.23-7.14 (m, 2H), 5.02 (d, *J* = 8.6 Hz, 1H), 2.74 (dd, *J* = 16.0, 7.2 Hz, 1H), 2.55-2.53 (m, 1H), 2.41 (dd, *J* = 16.0, 10.7 Hz, 1H), 1.15 (d, *J* = 6.4 Hz, 3H).
^{19}F NMR (282 MHz, Acetone-d6, δ ppm) -115.2.
^{13}C NMR (75 MHz, Acetone-d6, δ ppm) 176.0, 163.6 (d, *J* = 245.0 Hz), 135.8 (d, *J* = 3.1 Hz), 129.4 (d, *J* = 8.5 Hz), 116.2 (d, *J* = 21.8 Hz), 87.7, 40.6, 37.5, 16.0.
HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}FO_2Na$ $[M+Na]^+$ 217.0635; found 217.0636.

(4*S*,5*S*)-4-methyl-5-phenyldihydrofuran-2(3H)-one (11ac)[2]

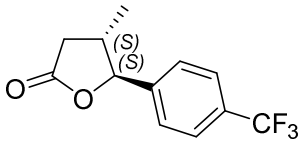


Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using benzaldehyde (0.50 mmol, 52 µL). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 8/2) to give **11ac** (34 mg, 46%) as a colourless oil.

R_f = 0.33 (cyclohexane/AcOEt, 8/2)
$[\alpha]_D^{20}$ = - 9 (c 0.75, $CHCl_3$)
^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 7.45 – 7.34 (m, 5H), 5.01 (d, *J* = 8.5 Hz, 1H), 2.74 (dd, *J* = 16.0, 7.2 Hz, 1H), 2.60 – 2.46 (m, 1H), 2.40 (dd, *J* = 16.0, 10.6 Hz, 1H), 1.16 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (75 MHz, Acetone-d6, δ ppm) 176.1, 139.7, 129.4, 129.3, 127.2, 88.4, 40.6, 37.6, 16.1.

HRMS (ESI) *m/z* calcd. for $C_{11}H_{12}O_2Na$ $[M+Na]^+$ 199.0729; found 199.0729.

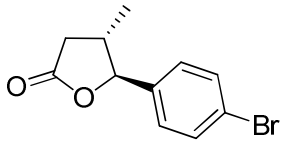
(4*S*,5*S*)-4-methyl-5-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3H)-one (11ad)



Prepared starting from (*S*,*E*)-**6a** (0.21 mmol, 51 mg) using *p*-(trifluoromethyl)benzaldehyde (0.25 mmol, 34 µL).The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 8/2) to give **11ad** (41 mg, 81%) as an orange oil.

R*f* = 0.21 (cyclohexane/AcOEt, 8/2)
$[\alpha]_I^{20}$ = + 15 (c 0.40, CH_2Cl_2)
^{1}H NMR (300 MHz, Acetone-d6, δ ppm) 7.78 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 5.15 (d, *J* = 8.3 Hz, 1H), 2.77 (dd, *J* = 15.9, 7.0 Hz, 1H), 2.64 – 2.50 (m, 1H), 2.45 (dd, *J* = 15.9, 10.4 Hz, 1H), 1.21 (d, *J* = 6.3 Hz, 3H).
^{19}F NMR (282 MHz, Acetone-d6, δ ppm) -63.1.
^{13}C NMR (75 MHz, Acetone-d6, δ ppm) 175.9, 144.5 (q, *J* = 1.3 Hz), 130.9 (q, *J* = 32.2 Hz), 127.8, 126.4 (q, *J* = 3.9 Hz), 125.2 (q, *J* = 271.3 Hz), 123.4, 87.3, 40.7, 37.3, 16.2.
HRMS (ESI) *m/z* calcd. for $C_{12}H_{11}F_3O_2Na$ $[M+Na]^+$ 267.0603; found 267.0604.

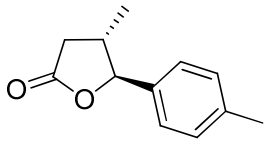
(4*S*,5*S*)-5-(4-bromophenyl)-4-methyldihydrofuran-2(3H)-one (11ae)



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using 4-bromobenzaldehyde (0.50 mmol, 92 mg). The crude product was purified by chromatography (silica gel, eluent: pentane/Et_2O, 10/0 to 8/2) to give **11ae** (69 mg, 64%) as a slight yellow oil.

R*f* = 0.27 (cyclohexane/AcOEt, 8/2)
$[\alpha]_I^{20}$ = + 41 (c 1.45, CH_2Cl_2)
^{1}H NMR (300 MHz, Acetone-d6, δ ppm) 7.60 (d, *J* = 8.5 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 5.02 (d, *J* = 8.4 Hz, 1H), 2.74 (dd, *J* = 15.7, 6.9 Hz, 1H), 2.58 – 2.46 (m, 1H), 2.41 (dd, *J* = 15.7, 10.7 Hz, 1H), 1.16 (d, *J* = 6.3 Hz, 3H).
^{13}C NMR (75 MHz, Acetone-d6, δ ppm) 175.9, 139.1, 132.5, 129.3, 122.8, 87.5, 40.6, 37.4, 16.0.
HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}BrO_2Na$ $[M+Na]^+$ 276.9835; found 276.9837.

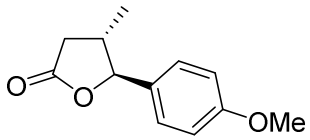
(4*S*,5*S*)-4-methyl-5-(p-tolyl)dihydrofuran-2(3H)-one (11af)



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using 4-methylaldehyde (0.50 mmol, 60 µL). The crude product was purified by chromatography (silica gel, eluent: pentane/Et_2O, 9/1 to 8/2) to give **11af** (32 mg, 40%) as a orange oil.

R_f = 0.27 (pentane/Et_2O, 9/1, 5% Et_3N)
$[\alpha]_I^{20}$ = + 30 (c 0.35, CH_2Cl_2)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.25 – 7.14 (m, 4H), 4.91 (d, *J* = 8.3 Hz, 1H), 2.78 (dd, *J* = 16.9, 7.6 Hz, 1H), 2.56 – 2.39 (m, 1H), 2.36 (s, 3H), 2.33 (dd, *J* = 16.9, 10.5, 1H), 1.18 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 176.3, 138.8, 135.0, 129.5, 126.1, 88.4, 39.9, 37.5, 21.3, 16.6.
HRMS (ESI) *m/z* calcd. for $C_{12}H_{14}O_2Na$ $[M+Na]^+$ 213.0886; found 213.0887.

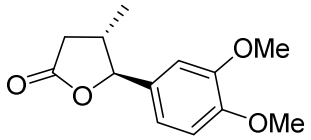
(4*S*,5*S*)-5-(4-methoxyphenyl)-4-methyldihydrofuran-2(3H)-one (11ag)[3]



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using 4-methoxybenzaldehyde (0.50 mmol, 60 µL). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 8/2 to 7/3) to give **11ag** (41 mg, 47%) as an orange oil.

$[\alpha]_D^{20}$ = + 13 (c 0.75, $CHCl_3$); litt : $[\alpha]_D^{25}$ = + 12 (c 1.00, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.26 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.88 (d, *J* = 8.5 Hz, 1H), 3.82 (s, 3H), 2.78 (dd, *J* = 16.9, 7.7 Hz, 1H), 2.54 – 2.43 (m, 1H), 2.33 (dd, *J* = 16.9, 10.7 Hz, 1H), 1.16 (d, *J* = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 176.2, 160.1, 129.8, 127.7, 114.2, 88.3, 55.5, 39.8, 37.6, 16.4.
HRMS (EI) *m/z* calcd for $C_{12}H_{14}O_3Na$ $[M+Na]^+$ 229.0835; found 229.0836.

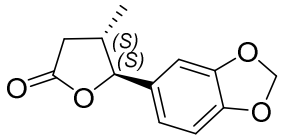
(4*S*,5*S*)-5-(3,4-dimethoxyphenyl)-4-methyldihydrofuran-2(3H)-one (11ah)



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using 3,4-dimethoxybenzaldehyde (0.50 mmol, 84 mg). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 7/3) to give **11ah** (30 mg, 30%) as a green oil.

R_f = 0.20 (cyclohexane/AcOEt, 7/3)
$[\alpha]_I^{20}$ = + 37 (c 0.33, CH_2Cl_2)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 6.90 – 6.81 (m, 3H), 4.88 (d, *J* = 8.6 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.80 (dd, *J* = 16.9, 7.6 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.34 (dd, *J* = 16.9, 10.8 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 176.3, 149.6, 149.5, 130.3, 119.0, 111.1, 109.1, 88.5, 56.2, 56.1, 39.9, 37.6, 16.5.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}O_4Na$ $[M+Na]^+$ 259.0940; found 259.0940.

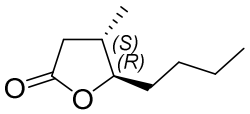
(4*S*,5*S*)-5-(benzo[d][1,3]dioxol-5-yl)-4-methyldihydrofuran-2(3H)-one (11ai)



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using piperonal (0.50 mmol, 76 mg). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 9/1 to 8/2) to give **11ai** (39 mg, 42%) as a colourless oil.

R_f = 0.19 (cyclohexane/AcOEt, 8/2)
$[\alpha]_I^{20}$ = + 94 (c 0.35, CH_2Cl_2)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 6.86 – 6.77 (m, 3H), 5.98 (s, 2H), 4.84 (d, *J* = 8.5 Hz, 1H), 2.78 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.32 (dd, *J* = 16.8, 10.8 Hz, 1H), 1.16 (d, *J* = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 176.0, 148.3, 148.2, 131.7, 120.2, 108.4, 106.5, 101.5, 88.4, 39.9, 37.5, 16.5.
HRMS (ESI) *m/z* calcd. for $C_{12}H_{12}O_4Na$ $[M+Na]^+$ 243.0628; found 243.0628.

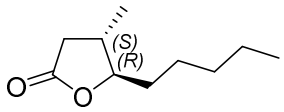
(4*S*,5*R*)-5-butyl-4-methyldihydrofuran-2(3H)-one (11aj)[2]
(+)-trans-whiskey lactone (2)



Prepared starting from (*S*,*E*)-**6a** (0.42 mmol, 100 mg) using pentanal (0.64 mmol, 68 µL). The crude product was purified by chromatography (silica gel, eluent: pentane/Et_2O, 10/0 to 8/2) to give (+)-whiskey lactone **2** (26 mg, 40%) as a colourless liquid.

$[\alpha]_D^{20}$ = + 50 (c 0.6, $CHCl_3$); litt : $[\alpha]_D^{25}$ = + 59.6 (c 0.71, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.00 (ddd, *J* = 8.2, 7.3, 4.1 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.25 – 2.12 (m, 2H), 1.73 – 1.54 (m, 3H), 1.41– 1.31 (m, 3H), 1.13 (d, *J* = 6.4 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 176.7, 87.6, 37.3, 36.2, 33.8, 28.0, 22.6, 17.6, 14.0.
HRMS (ESI) *m/z* calcd. for $C_9H_{16}O_2Na$ $[M+Na]^+$ 179.1042; found 179.1043.

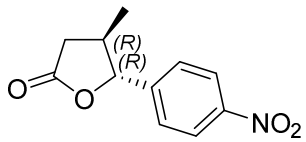
(4*S*,5*R*)-4-methyl-5-pentyldihydrofuran-2(3H)-one (11ak)[4]
(+)-*trans*-cognac lactone (3)



Prepared starting from (*S,E*)-**6a** (0.42 mmol, 100 mg) using hexanal (0.50 mmol, 60 µL). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 8/2) to give (+)-cognac lactone **3** (28.6 mg, 40%) as a colourless oil.

R_f = 0.19 (cyclohexane/AcOEt, 8/2)
$[\alpha]_D^{20}$ = + 70 (c 0.27, $CHCl_3$); litt : $[\alpha]_D^{25}$ = + 72 (c 1.00, $CHCl_3$)
^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 4.03 (td, *J* = 7.6, 4.0 Hz, 1H), 2.75 – 2.61 (m, 1H), 2.31 – 2.13 (m, 2H), 1.73 – 1.60 (m, 4H), 1.38 – 1.28 (m, 4H), 1.15 (d, *J* = 6.4 Hz, 3H), 0.92 (t, *J* = 5.8 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 176.6, 87.5, 37.2, 36.1, 34.0, 31.6, 25.4, 22.5, 17.5, 14.0.
HRMS (ESI) *m/z* calcd. for $C_{10}H_{18}O_2Na$ $[M+Na]^+$ 193.1198; found 193.1199.

(4*R*,5*R*)-4-methyl-5-(4-nitrophenyl)dihydrofuran-2(3H)-one (11ba)

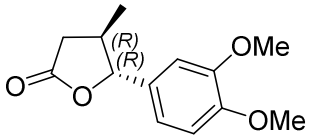


Prepared starting from (*R,E*)-**6a** (0.42 mmol, 100 mg) using *p*-nitrobenzaldehyde (xx mmol, xx mg).The crude product was purified by chromatography (silica gel, eluent: pentane/Et_2O, 7/3 to 0/10) to give **11ba** (68 mg, 73%) as an orange oil.

R*f* = 0.12 (pentane/Et_2O, 1/1)
$[\alpha]_D^{20}$ = -12 (c 1.60, CH_2Cl_2)
^{1}H NMR (400 MHz, Acetone-d6, δ ppm) 8.29 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.8 Hz 2H), 5.21 (d, *J* = 8.5 Hz, 1H), 2.78 (dd, *J* = 16.3, 7.2 Hz, 1H), 2.61 – 2.52 (m, 1H), 2.47 (dd, *J* = 16.3, 10.5 Hz, 1H), 1.23 (d, *J* = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, Acetone-d6, δ ppm) 175.8, 148.9, 147.2, 128.1, 124.5, 86.8, 40.7, 37.2, 16.1.
Chiral HPLC : Chiralcel OD-H, hexane/i-PrOH = 90/10, flow rate = 1.0 mL/min, 230 nm, **6ba** 64.9 min.

HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}NO_4Na$ [M+Na]+ 244.0580; found 244.0581.

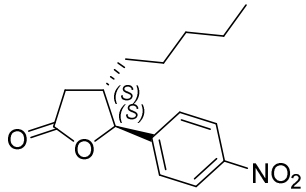
(4*R*,5*R*)-5-(3,4-dimethoxyphenyl)-4-methyldihydrofuran-2(3H)-one (11bh)



Prepared starting from (*R*,*E*)-**6a** (0.42 mmol, 100 mg) using 3,4-dimethoxybenzaldehyde (0.50 mmol, 84 mg). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 7/3) to give **11bh** (32 mg, 32%) as a green oil.

R_f = 0.20 (cyclohexane/AcOEt, 7/3)
$[\alpha]_I^{20}$ = - 35 (c 0.33, CH_2Cl_2)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 6.90 – 6.81 (m, 3H), 4.88 (d, *J* = 8.6 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.80 (dd, *J* = 16.9, 7.6 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.34 (dd, *J* = 16.9, 10.8 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 176.3, 149.6, 149.5, 130.3, 119.0, 111.1, 109.1, 88.5, 56.2, 56.1, 39.9, 37.6, 16.5.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}O_4Na$ $[M+Na]^+$ 259.0940; found 259.0941.

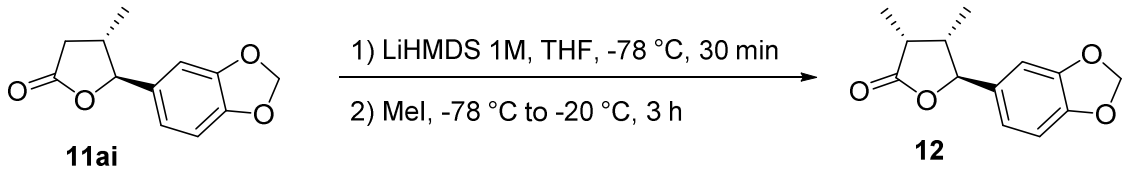
(4*S*,5*S*)-5-(4-nitrophenyl)-4-pentyldihydrofuran-2(3H)-one (11ca)



Prepared starting from (*S*,*E*)-**6b** (0.37 mmol, 110 mg) using 4-nitrobenzaldehyde (0.44 mmol, 67 mg). The crude product was purified by chromatography (silica gel, eluent: cyclohexane/AcOEt, 9/1) to give **11ca** (68 mg, 66%) as an orange oil.

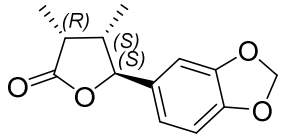
R_f = 0.26 (cyclohexane/AcOEt, 8/2)
$[\alpha]_D^{20}$ = + 15 (c 0.50, CH_2Cl_2)
^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 8.26 (d, *J* = 8.8 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 5.10 (d, *J* = 7.3 Hz, 1H), 2.89 – 2.71 (m, 1H), 2.48 – 2.28 (m, 2H), 1.71 – 1.55 (m, 1H), 1.55 – 1.42 (m, 1H), 1.39 – 1.17 (m, 6H), 0.92 – 0.80 (m, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 175.3, 148.1, 145.7, 126.7, 124.1, 85.2, 53.4, 45.1, 34.9, 32.1, 31.6, 30.9, 22.4, 14.2, 13.9.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{19}NO_4Na$ $[M+Na]^+$ 300.1206; found 300.1207.

V. Synthesis of (-)-galbacin

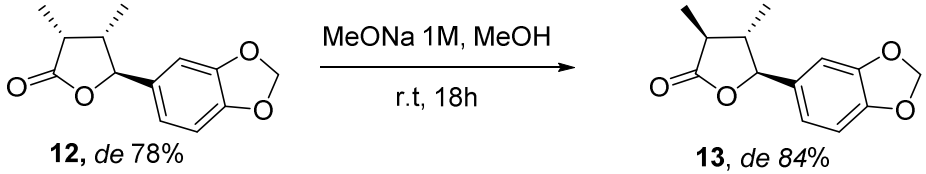


To a solution of lactone **11ai** (0.672 mmol, 148 mg, 1.0eq) in dry tetrahydrofurane (0.19 M), under argon atmosphere and cooled at -78° C, was added a solution of 1M LiHMDS in THF (1.4eq). The solution was stirred at -78° C during 30 minutes. Then, MeI (6 eq.) was added and the solution was left to warm up to -20° C in 3 hours. The mixture was quenched with a saturated solution of ammonium chloride and diluted with AcOEt. Two phases were separated and 3 extractions were realized with AcOEt on the aqueous phase. The organic phases were washed with saturated NaCl solution , combined, dried over $MgSO_4$, filtered and concentrated under *vacuo*. The crude product was purified by chromatography (silica gel, eluent : cyclohexane/AcOEt 9/1 to 8/2) to give **12** (*d.e* 78%) as a yellow oil (92 mg, 72% yield).

(3*R*,4*S*,5S)-5-(benzo[d][1,3]dioxol-5-yl)-3,4-dimethyldihydrofuran-2(3H)-one (12)[5]



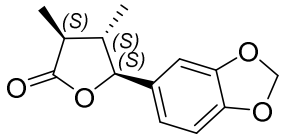
R_f = 0.30 (cyclohexane/AcOEt, 8/2)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 6.85 – 6.73 (m, 3H), 5.96 (s, 2H), 4.94 (d, *J* = 6.8 Hz, 0.89HH), 4.72 (d, *J* = 9.9 Hz, 0.11H), 2.77 (qd, *J* = 7.7 , 7.7 Hz, 0.89H), 2.51-2.47 (m, 0.89H), 2.33 (qd, *J* = 11.9, 7.0 Hz, 0.11H), 2.06 – 1.86 (m, 0.11H), 1.29 (d, *J* = 7.0 Hz, 0.33H), 1.21 (d, *J* = 7.6 Hz, 2.67H), 1.11 (d, *J* = 6.5 Hz, 0.33H). 1.06 (d, *J* = 7.0 Hz, 2.67H), .
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 179.6, 178.5, 148.2, 148.1, 147.9, 132.2, 131.3, 120.5, 119.5, 108.3, 108.2, 106.7, 106.2, 101.4, 86.4, 85.8, 47.9, 43.5, 42.3, 38.5, 14.4, 13.1, 12.5, 10.4.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{14}NaO_4$ $[M+Na]^+$257.0784; found 257.0785.



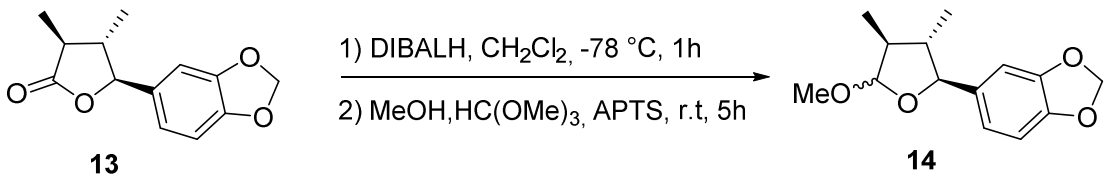
12, *de* 78% **13**, *de 84%*

To a solution of lactone **12** (0.39 mmol, 1 eq.) in MeOH (0.25M) was added dropwise a solution of MeONa 1M (2.5 eq.). The mixture was stirred at room temperature for 18 hours. The reaction media was quenched with saturated NaCl solution. The aqueous phase was extracted with 3x4mL Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under *vacuo*. The crude product was purified by chromatography (silica gel, eluent : cyclohexane/AcOEt 9/1 to 8/2) to give **13** (*d.e* 84%) as a yellow oil (77 mg, 85% yield)

(3*S*,4*S*,5*S*)-5-(benzo[d][1,3]dioxol-5-yl)-3,4-dimethyldihydrofuran-2(3H)-one (13)[6]
(-)-Nicotlactone B



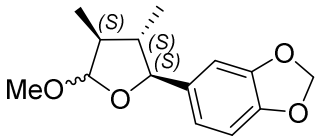
R_f = 0.30 (cyclohexane/AcOEt, 8/2)
$[\alpha]_D^{20}$ = - 27 (c 0.45, MeOH); litt : $[\alpha]_D^{25}$ = - 18 (c 0.03, MeOH)
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 6.85 – 6.73 (m, 3H), 5.96 (s, 2H), 4.94 (d, *J* = 6.8 Hz, 0.08H), 4.72 (d, *J* = 9.9 Hz, 0.92H), 2.77 (qd, *J* = 7.7 , 7.7 Hz, 0.08H), 2.51-2.47 (m, 0.08H), 2.33 (qd, *J* = 11.9, 7.0 Hz, 0.92H), 2.06 – 1.86 (m, 0.92H), 1.29 (d, *J* = 7.0 Hz, 2.76H), 1.21 (d, *J* = 7.6 Hz, 0.24H), 1.11 (d, *J* = 6.5 Hz, 2;76H). 1.06 (d, *J* = 7.0 Hz, 0.24H), .
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 178.5, 148.2, 148.1, 131.3, 120.5, 108.3, 106.7, 101.5, 86.4, 85.8, 47.9, 43.5, 14.5, 13.1.
HRMS (ESI) *m/z* calcd. for $C_{13}H_{14}NaO_4$ $[M+Na]^+$257.0784; found 257.0785.



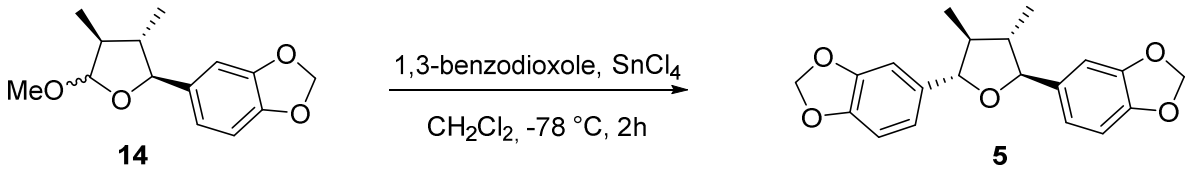
13 **14**

A solution of alkylated lactone **13** (0.30 mmol, 1 eq.) in dichloromethane (0.32M), under argon atmosphere, was cold at -78 ° C. A solution of DIBALH 1M (1.6 eq.) in hexane was added and the mixture was stirred at -78 ° C for one hour. Then, methanol (0.1M), trimethyl orthoformate (3.7 eq.) and APTS.H_2O (3.4 eq.) were added. The mixture was stirred at room temperature for 5 hours. The reaction media was cold at 0 ° C and saturated $NaHCO_3$ was added. The aqueous phase was extracted with 3x2mL AcOEt. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under *vacuo*. The crude product was purified by chromatography (silica gel, eluent : cyclohexane/AcOEt 10/0 to 9/1) to give **14** (50 mg, 67%) as a yellow oil (mixture of diastereoisomers, 1/1).

5-((2*S*,3*S*,4*S*)-5-methoxy-3,4-dimethyltetrahydrofuran-2-yl)benzo[d][1,3]dioxole (14)



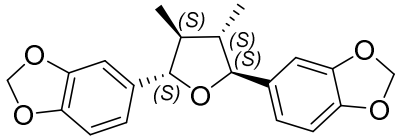
R_f = 0.39 (cyclohexane/AcOEt, 9/1)
^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 6.90-6.87 (m, 1H), 6.81 – 6.73 (m, 2H), 5.94 (s, 2H), 4.83 (d, *J* = 4.3 Hz, 0.5H), 4.76 (d, *J* = 4.1 Hz, 0.5H), 4.45 (d, *J* = 9.6 Hz, 0.5H), 4.36 (d, *J* = 8.9 Hz, 0.5H), 3.47 (s, 1.5H), 3.43 (s, 1.5H), 1.89 – 1.76 (m, 1H), 1.62 – 1.50 (m, 1H), 1.15 (d, *J* = 7.0 Hz, 1.5H), 1.03 (d, *J* = 6.2 Hz, 1.5H), 0.95 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 148.0, 148.0, 147.4, 147.2, 136.5, 134.5, 120.6, 120.5, 111.5, 108.1, 107.9, 107.4, 107.1, 106.6, 101.1, 101.1, 89.6, 86.7, 56.0, 55.3, 50.2, 48.9, 46.8, 46.4, 16.1, 14.1, 14.1, 11.2.
HRMS (ESI) *m/z* calcd. for $C_{14}H_{18}NaO_4$ $[M+Na]^+$ 273.1097; found 273.1098.



14 **5**

A solution of acetal **14** (0.16 mmol, 1 eq.) in dichloromethane (0.06M) was cold at – 78 ° C. Then, 1,3-benzodioxole (6.9 eq.) and $SnCl_4$ (1.5 eq.) were added and the mixture was stirred at – 78 ° C for 2 hours. A saturated NH_4Cl solution was added and the aqueous phase was extracted with 3x2mL CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under *vacuo*. The crude product was purified by chromatography (silica gel, eluent : pentane/ CH_2Cl_2 7/3 to 5/5) to give (-)-galbacin (46 mg, 85%) as a colourless oil.

5,5'-((2*S*,3*S*,4*S*,5*S*)-3,4-dimethyltetrahydrofuran-2,5-diyl)bis(benzo[d][1,3]dioxole) (5)[7]
(-)-galbacin



R_f = 0.12 (pentane/ CH_2Cl_2 5/5)
$[\alpha]_D^{20}$ = - 103 (c 0.88, $CHCl_3$); litt : $[\alpha]_D^{25}$ = - 119 (c 0.02, $CHCl_3$)
^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 6.91 (d, *J* = 1.6 Hz, 2H), 6.83 (dd, *J* = 8.0, 1.6 Hz, 2H), 6.77 (d, *J* = 7.9 Hz, 2H), 5.94 (s, 4H), 4.59 (d, *J* = 9.2 Hz, 2H), 1.83 – 1.67 (m, 2H), 1.02 (d, *J* = 6.1 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$, δ ppm) 147.9, 147.1, 136.5, 119.9, 108.1, 106.7, 101.1, 88.4, 51.2, 13.9
HRMS (ESI) m/z. calcd. for $C_{20}H_{20}NaO_5$ $[M+Na]^+$ 363.1202; found 363.1203.

References

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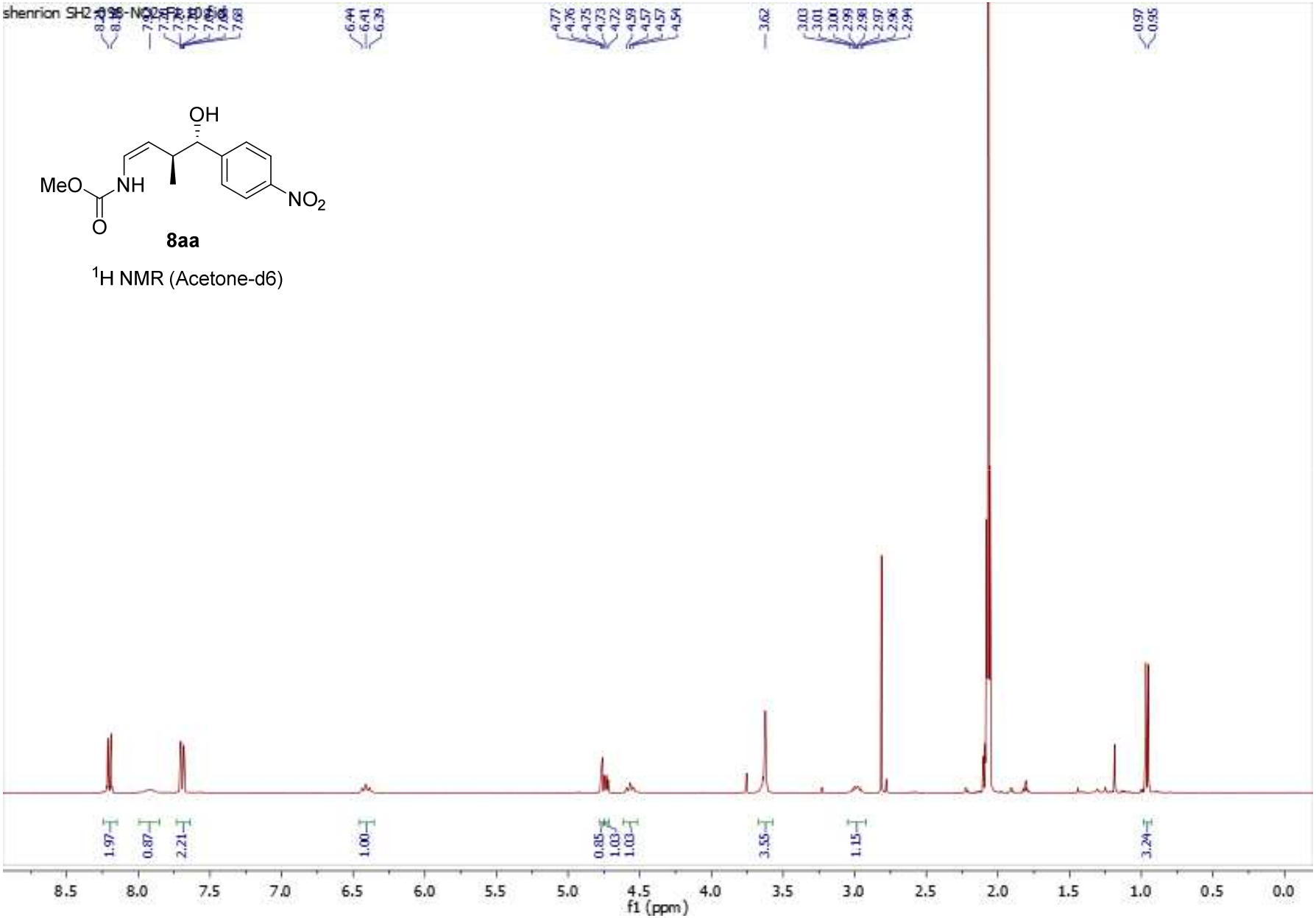
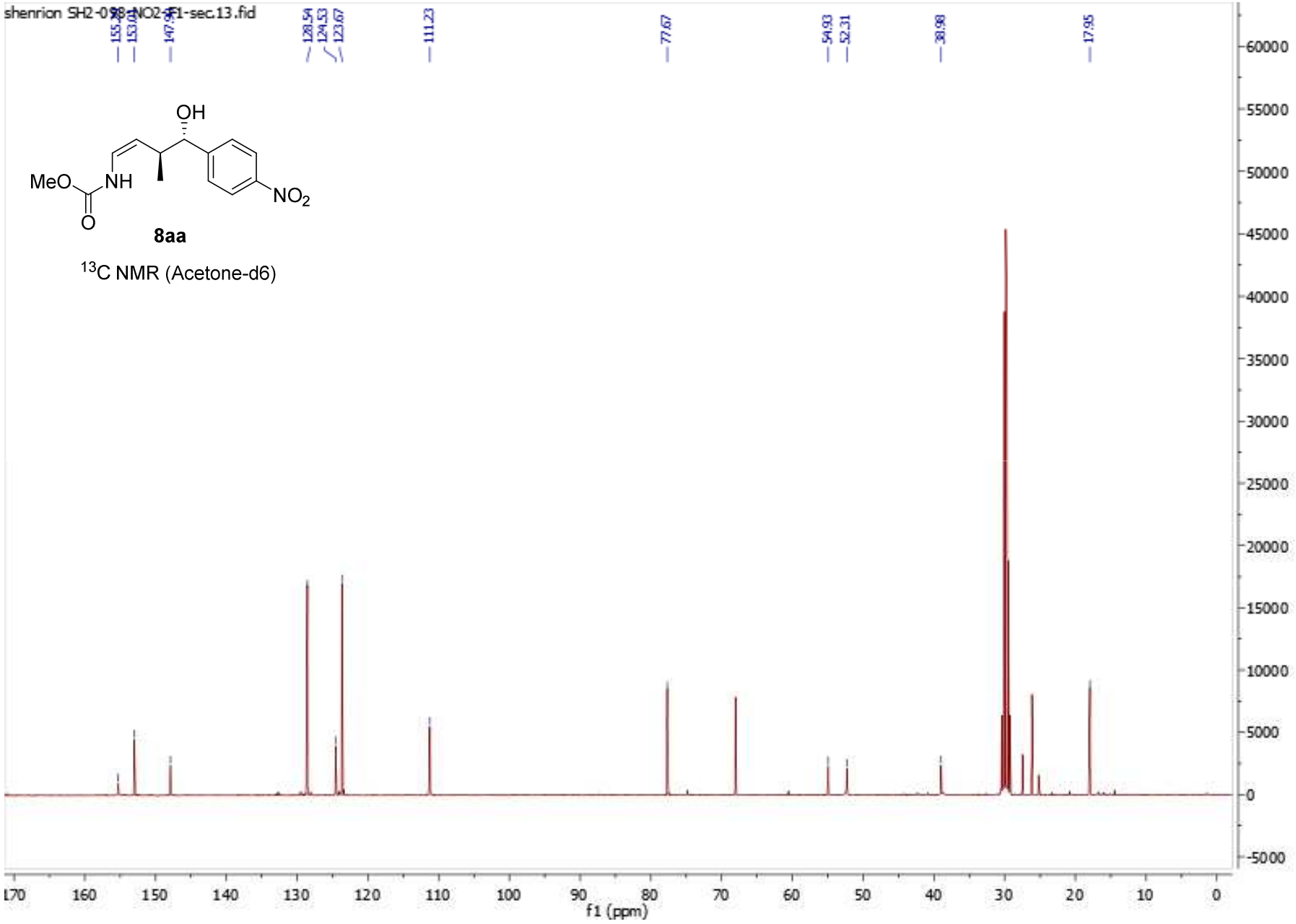
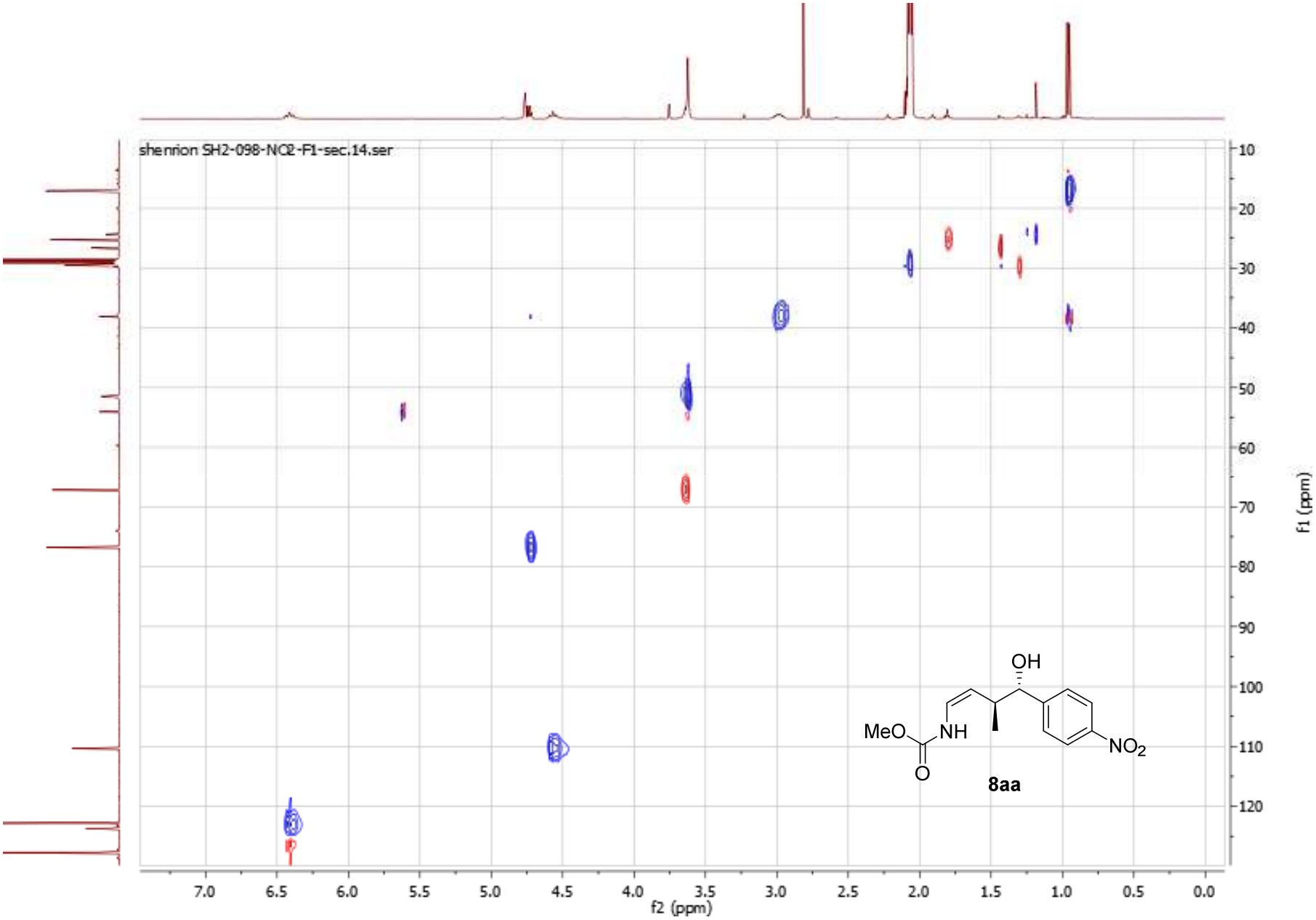

OH
MeO
NH
O
NO2
8aa
1H NMR (Acetone-d6)
f1 (ppm)


shenrion SH2-098-NO2-F1-sec.13.fid
155.78
153.62
147.31
128.54
124.53
123.67
111.23
77.67
54.93
52.31
38.98
17.95
OH
MeO
NH
O
NO2
8aa
13C NMR (Acetone-d6)
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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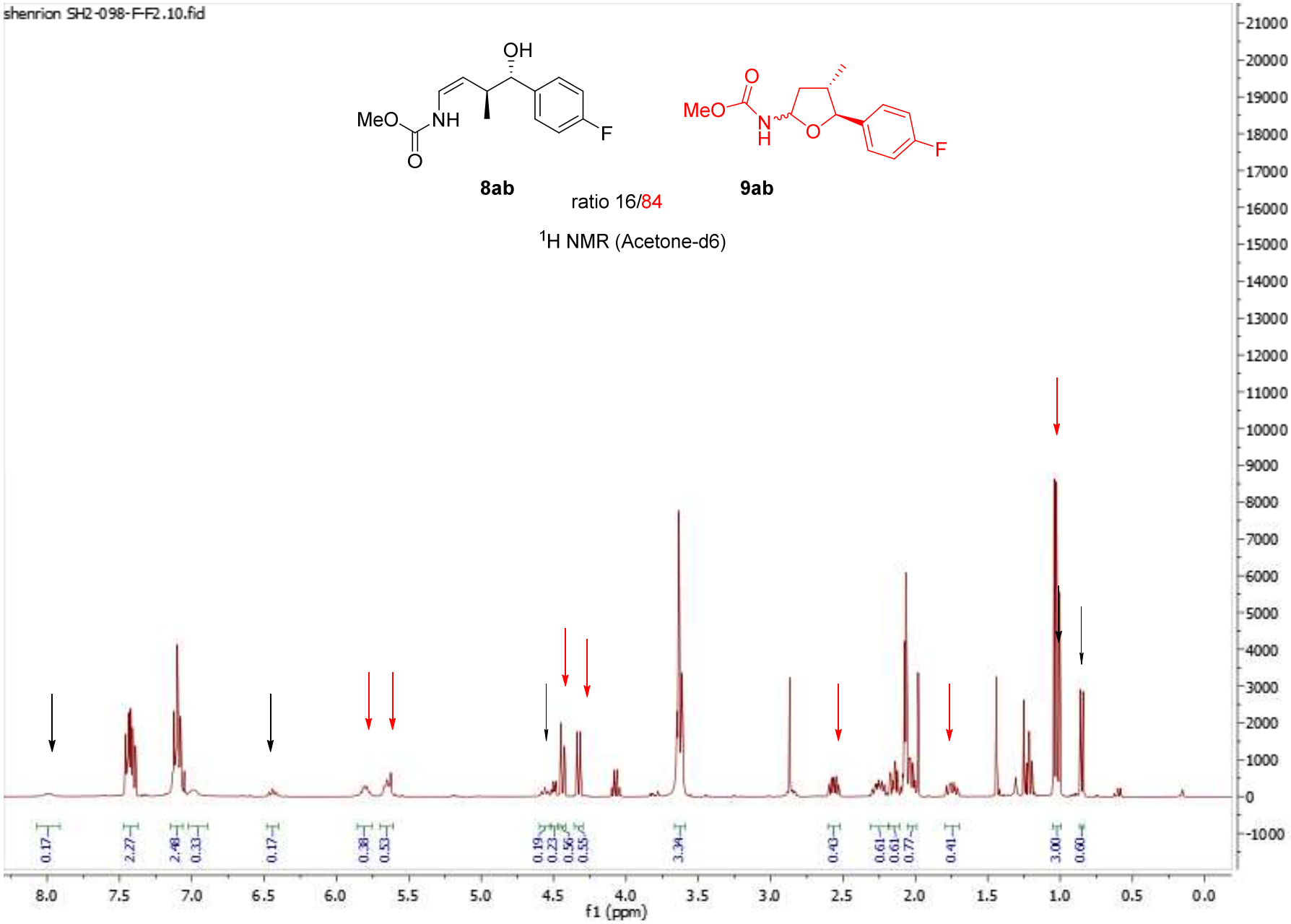
f2 (ppm)
f1 (ppm)
OH
MeO
NH
O
NO2
8aa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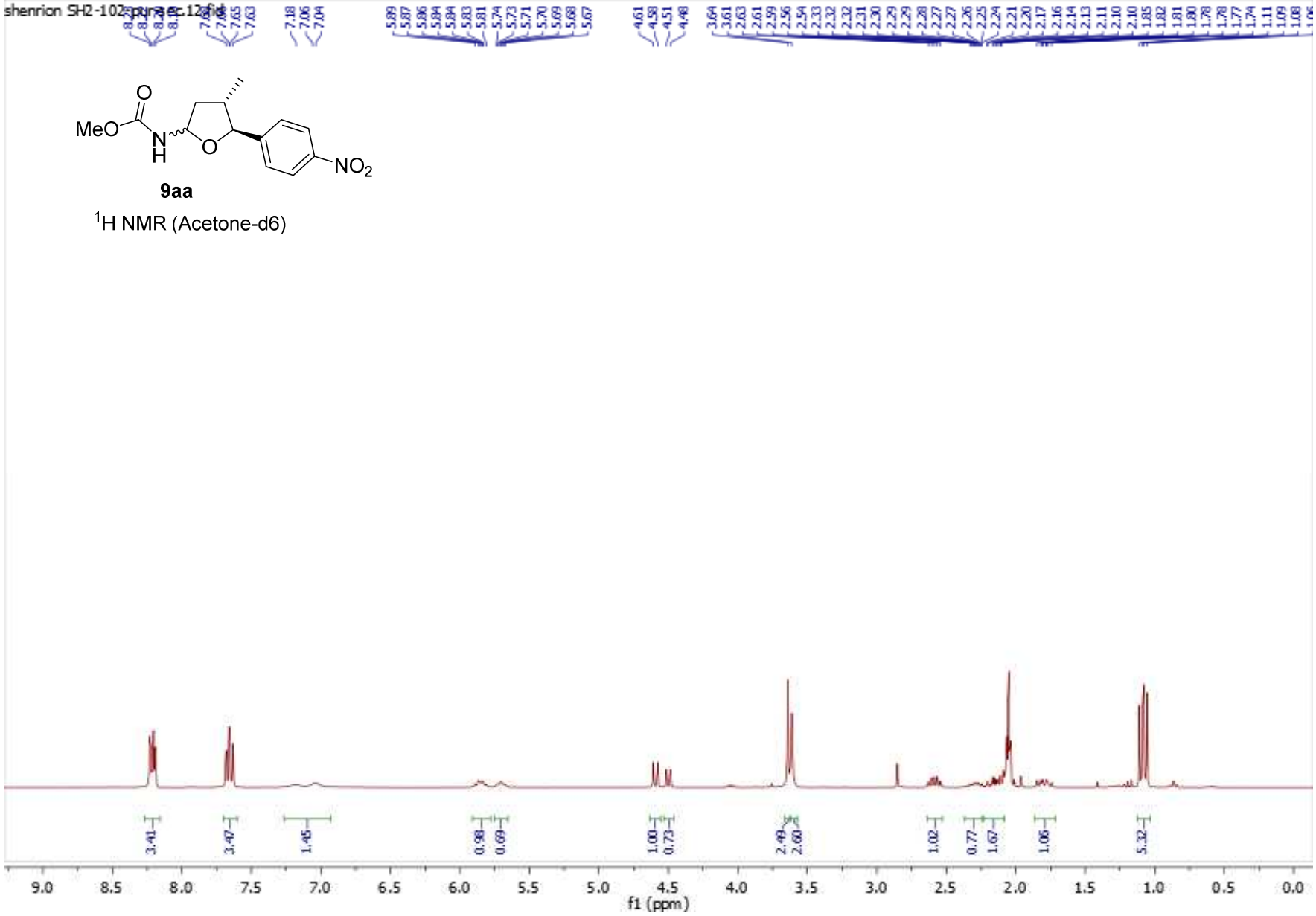
OH
MeO
NH
O
F
8ab
ratio 16/84
MeO
O
N
H
O
F
9ab
^{1}H NMR (Acetone-d6)
f1 (ppm)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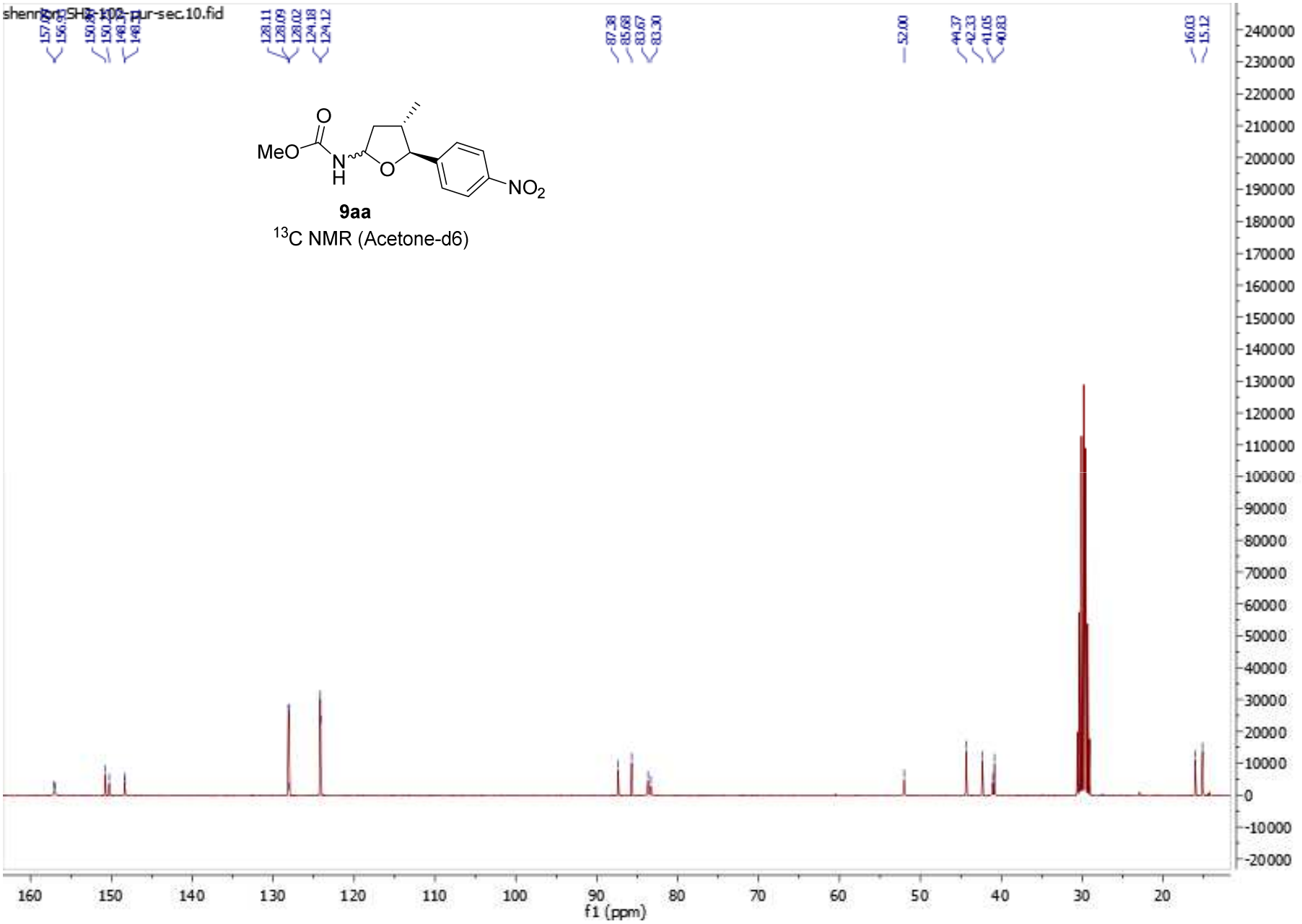
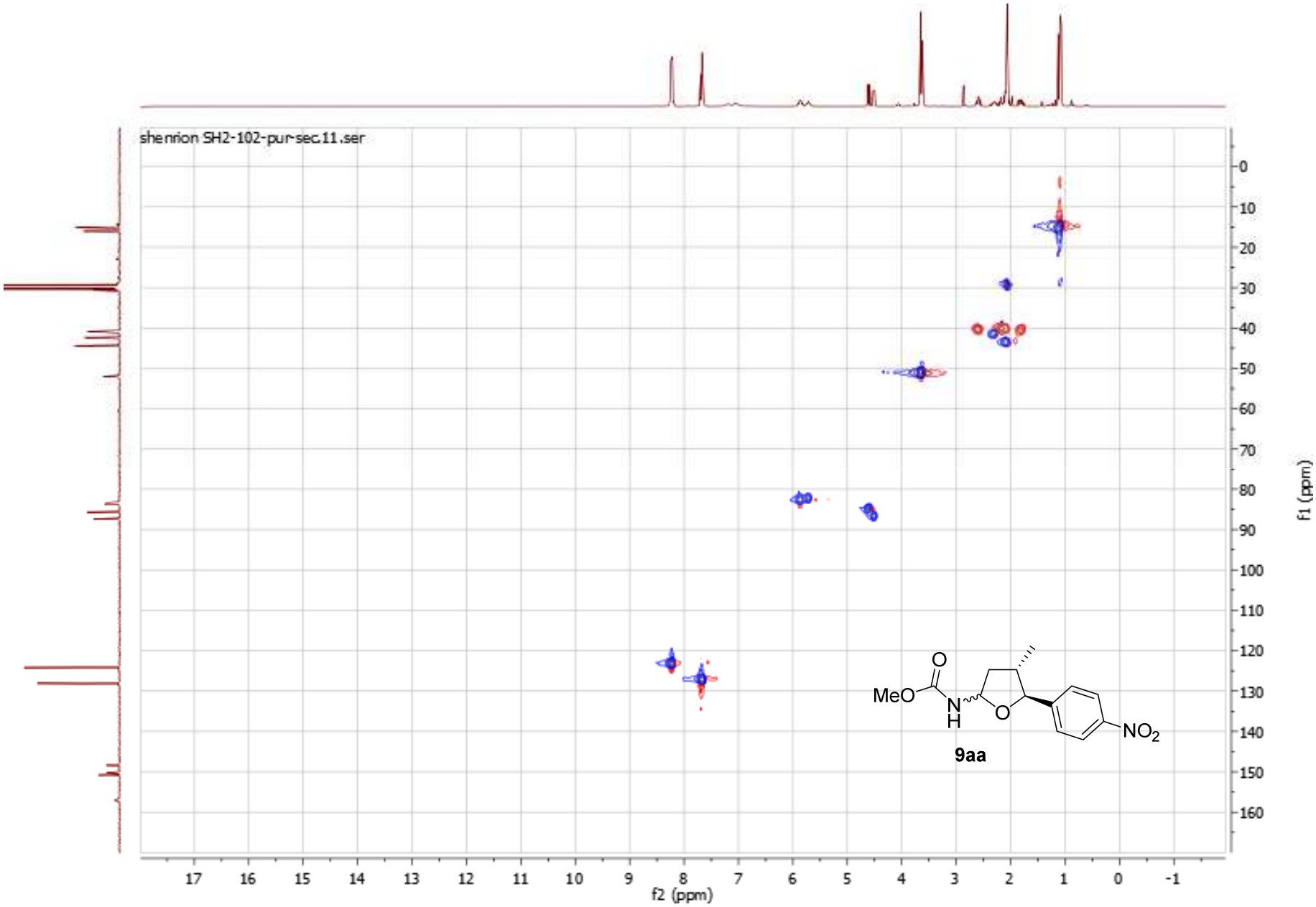
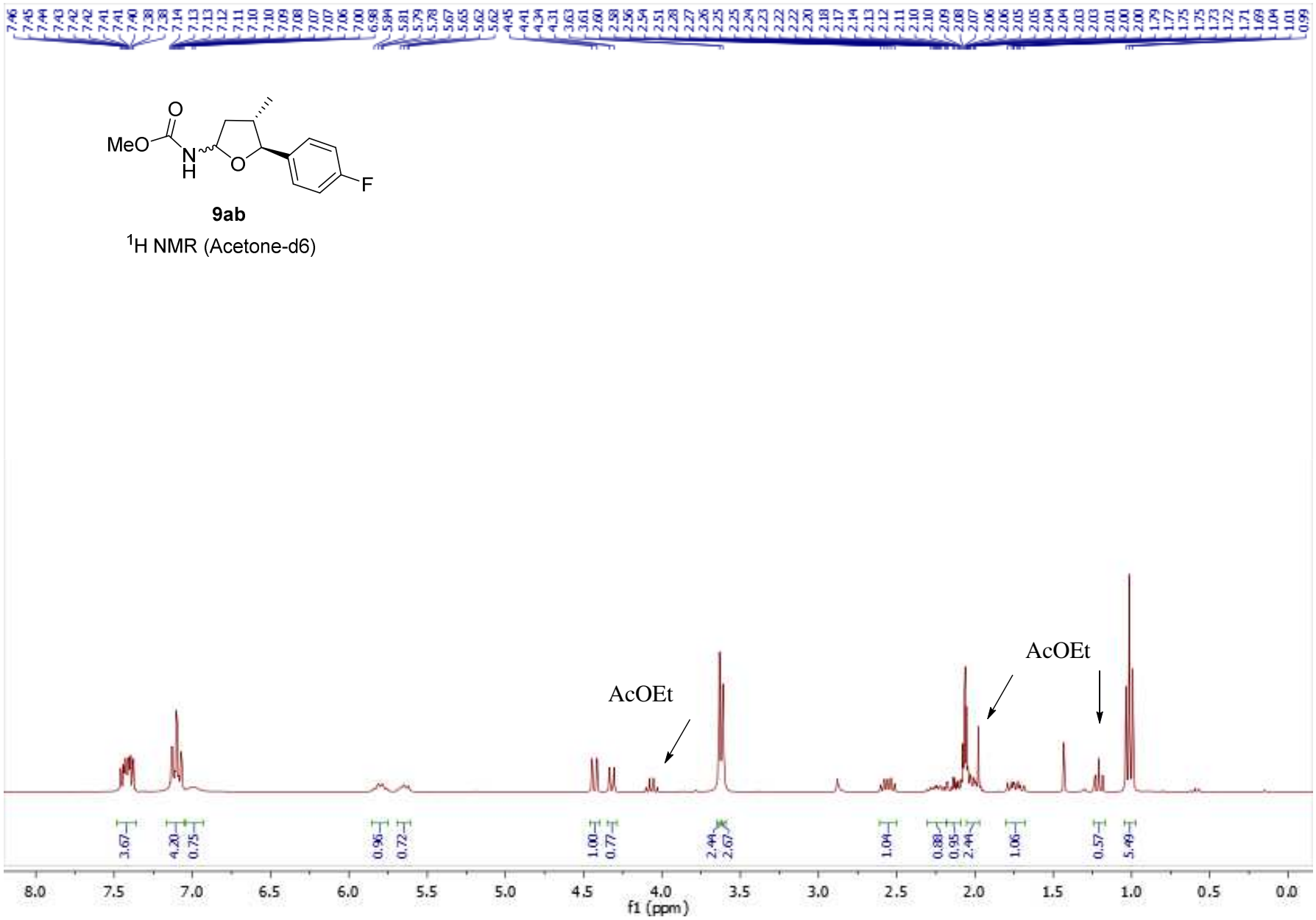
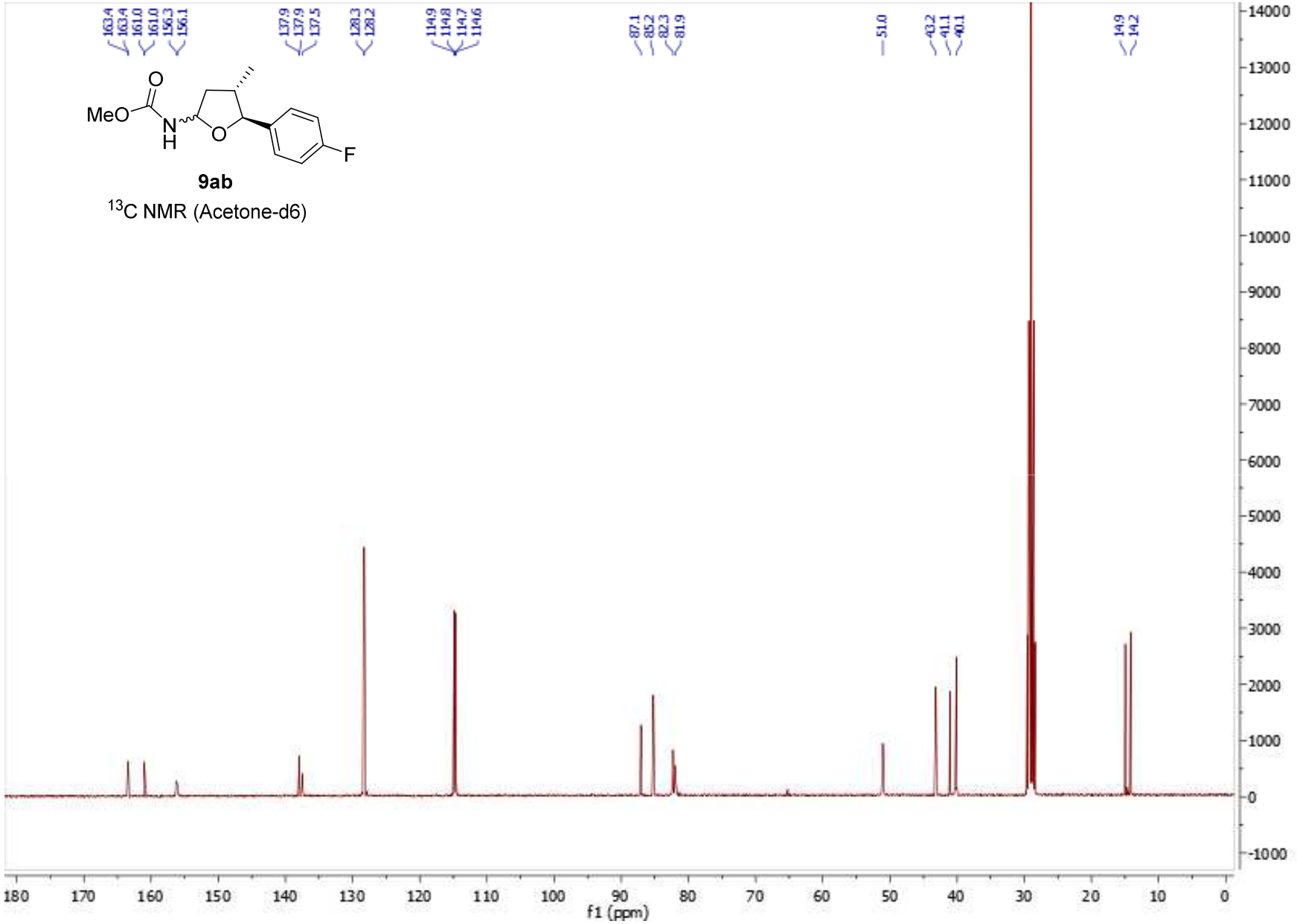
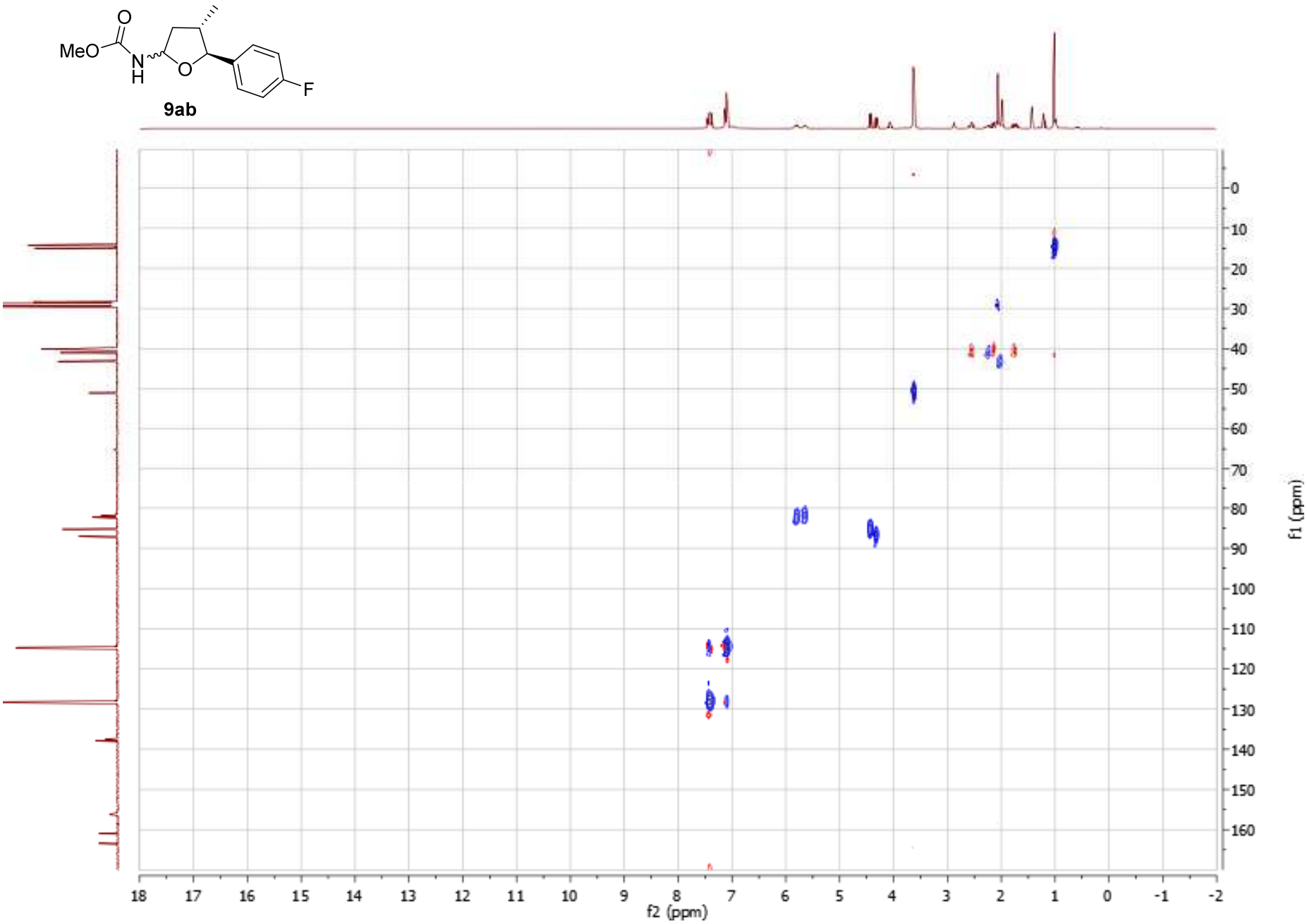
MeO
O
N
H
O
NO2
9aa
1H NMR (Acetone-d6)
3.41
3.47
1.45
0.98
0.69
1.00
0.73
2.49
2.60
1.02
0.77
1.67
1.06
5.32
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

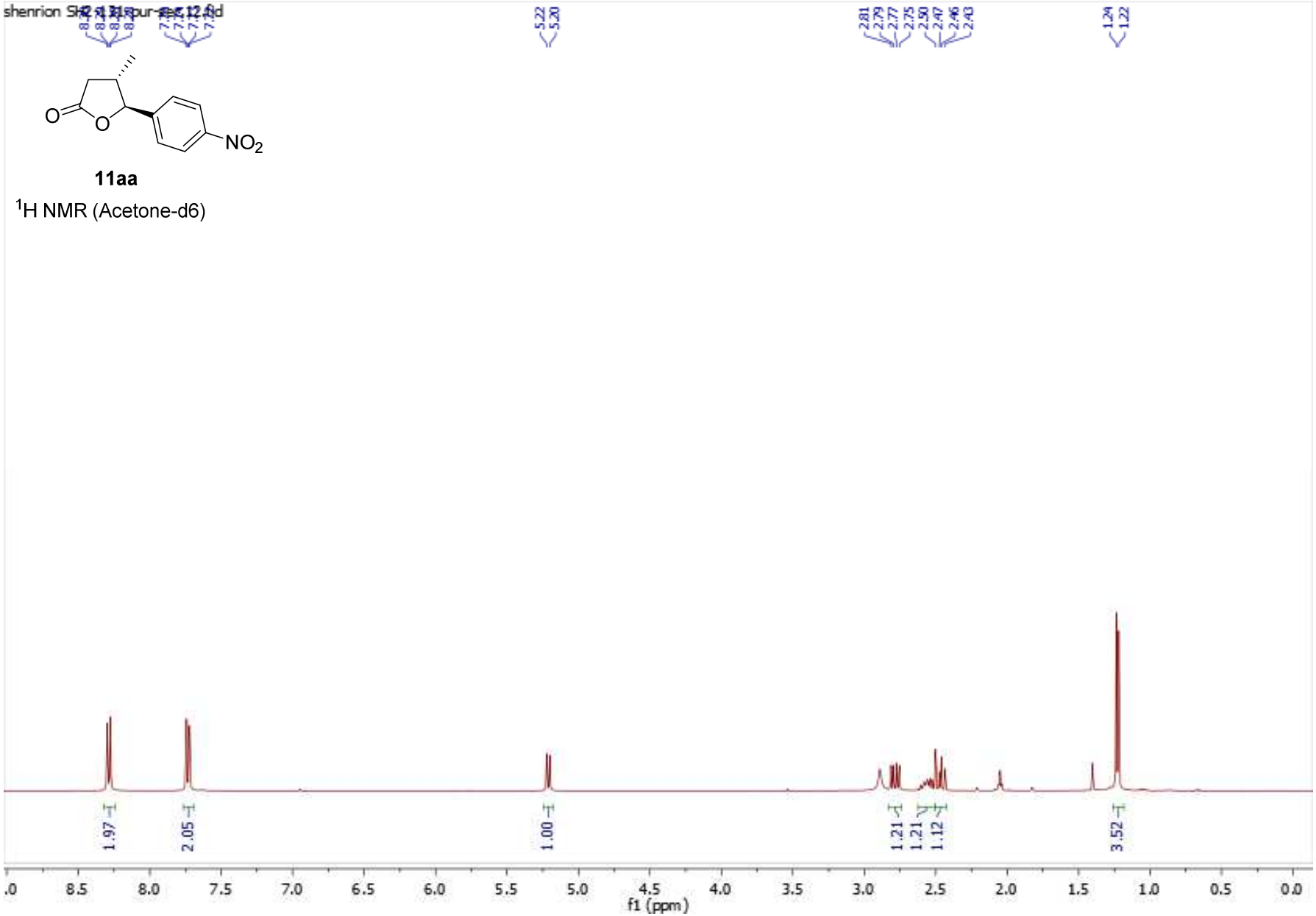

shenrong-SHZ-102-pur-sec.10.fid
157.67
156.53
150.88
150.14
148.31
148.11
128.11
128.09
128.02
124.18
124.12
87.38
85.68
83.67
83.30
52.00
44.37
42.33
41.05
40.83
16.03
15.12
MeO
O
N
H
O
NO2
9aa
13C NMR (Acetone-d6)
240000
230000
220000
210000
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
-20000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

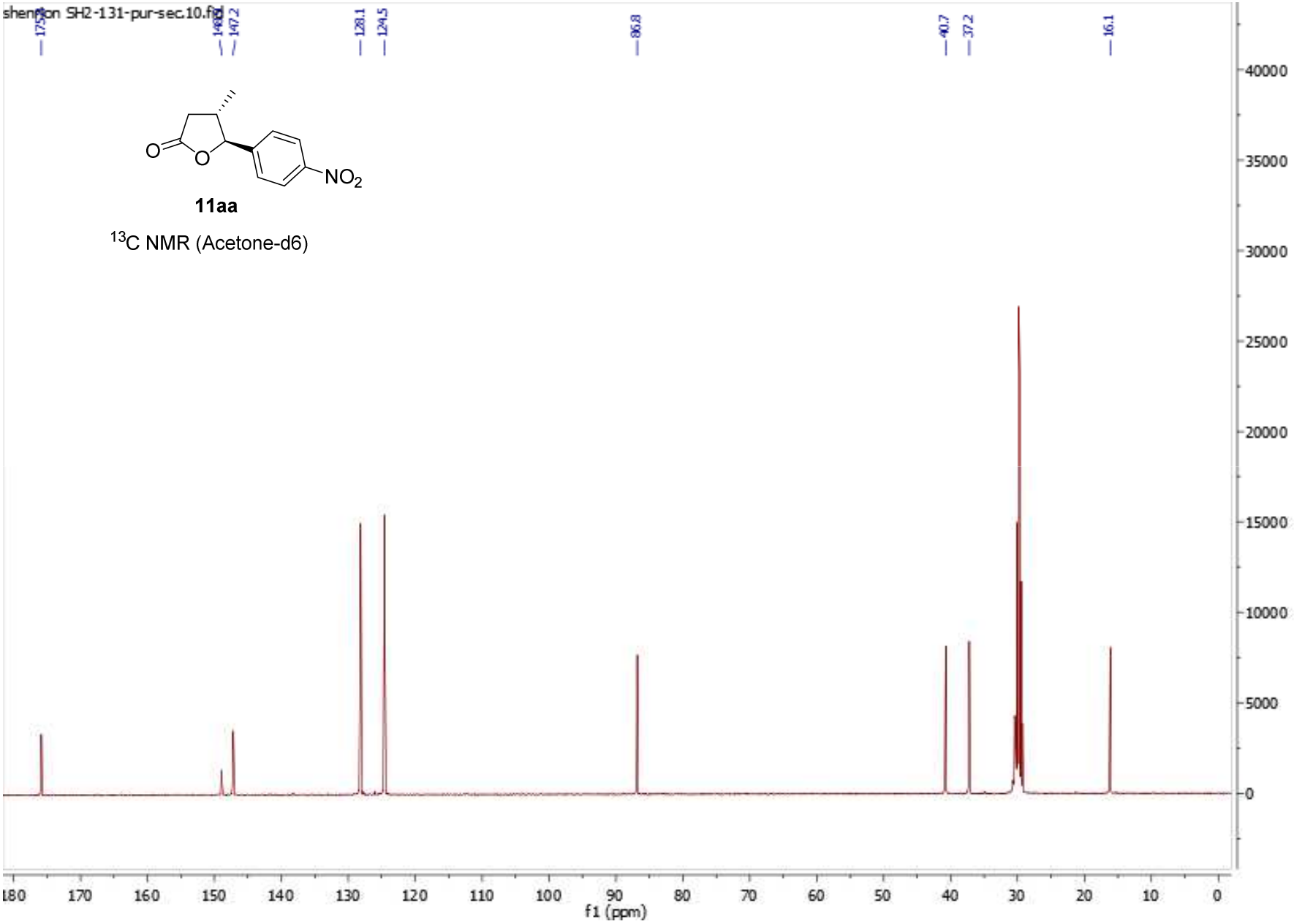

shenrion SH2-102-pur-sec.11.ser
f2 (ppm)
f1 (ppm)
MeO
O
N
H
O
NO2
9aa

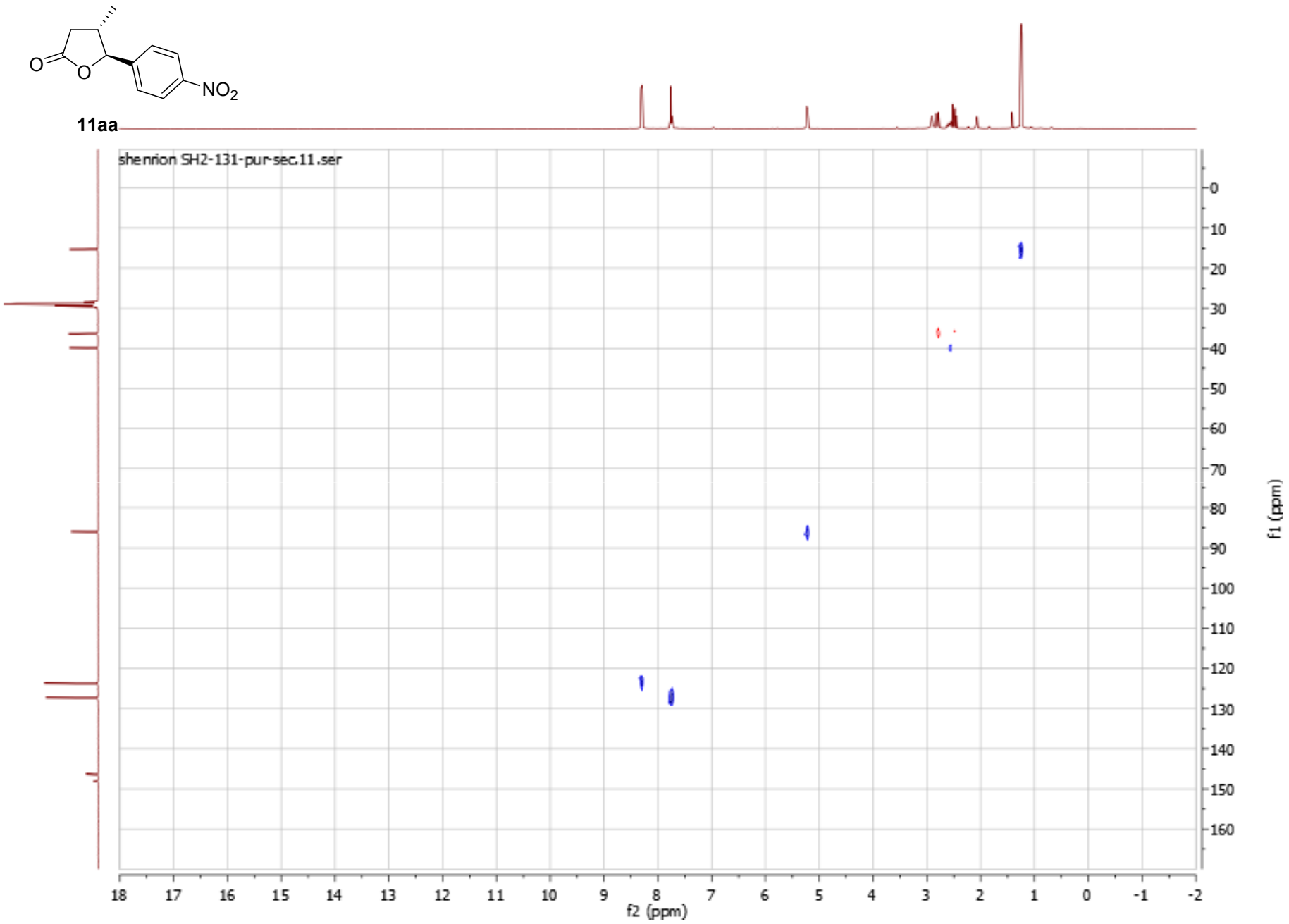

MeO
O
N
H
O
F
9ab
1H NMR (Acetone-d6)
AcOEt
AcOEt
f1 (ppm)

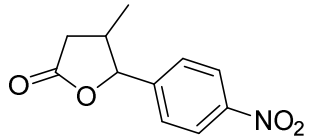

163.4
163.4
161.0
161.0
156.3
156.1
137.9
137.9
137.5
128.3
128.2
114.9
114.8
114.7
114.6
87.1
85.2
82.3
81.9
51.0
43.2
41.1
40.1
14.9
14.2
MeO
O
N
H
O
F
9ab
13C NMR (Acetone-d6)
f1 (ppm)


MeO
O
N
H
O
F
9ab
f2 (ppm)
f1 (ppm)


shenrion SH2-141-pur-eac-12.fid
O
O
NO2
11aa
1H NMR (Acetone-d6)
8.24
8.23
8.22
8.21
7.74
7.73
7.72
7.71
5.22
5.20
2.81
2.79
2.77
2.75
2.50
2.47
2.46
2.43
1.24
1.22
1.97
2.05
1.00
1.21
1.21
1.12
3.52
f1 (ppm)

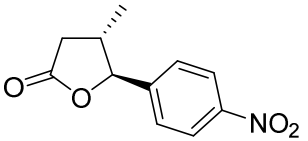

shenton SH2-131-pur-sec.10.fid
175.3
148.0
147.2
128.1
124.5
86.8
40.7
37.2
16.1
O
O
NO2
11aa
13C NMR (Acetone-d6)
40000
35000
30000
25000
20000
15000
10000
5000
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


11aa
shenrion SH2-131-pur-sec.11.ser
f2 (ppm)
f1 (ppm)

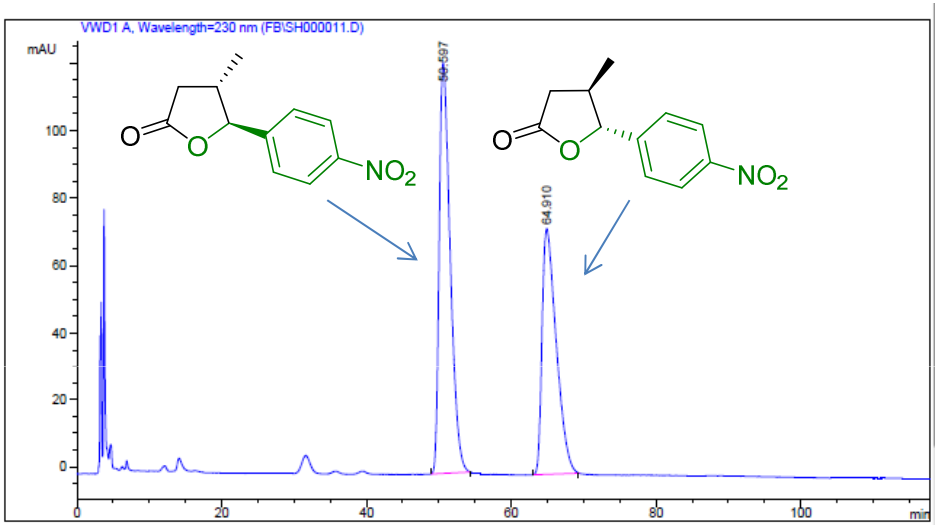


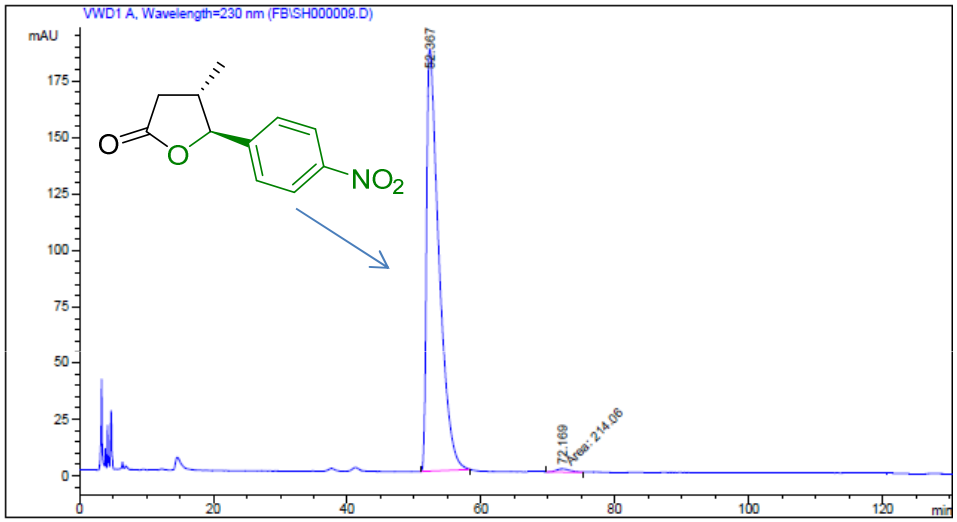
Racemic mixture

HPLC



(4*S*,5*S*)-**11aa**, 98 % *ee*



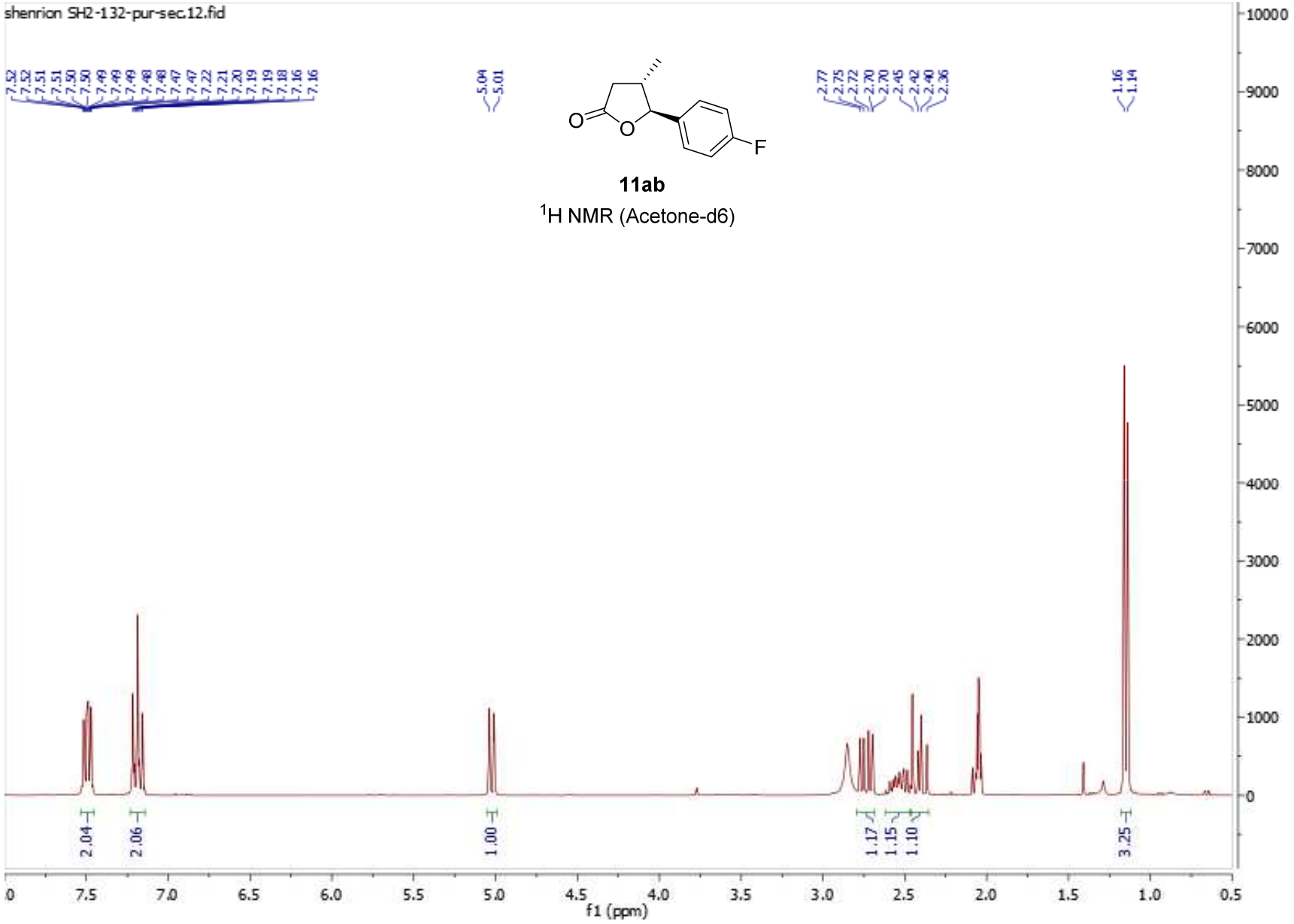


Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	50.597	BB	1.6213	1.28998e4	122.10625	56.4091
2	64.910	BB	1.9201	9968.53223	73.23064	43.5909
Totals :				2.28684e4	195.33690	

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	52.367	BB	1.7738	2.40999e4	187.07767	99.1196
2	72.169	MM	2.3863	214.05952	1.49503	0.8804
Totals :				2.43140e4	188.57270	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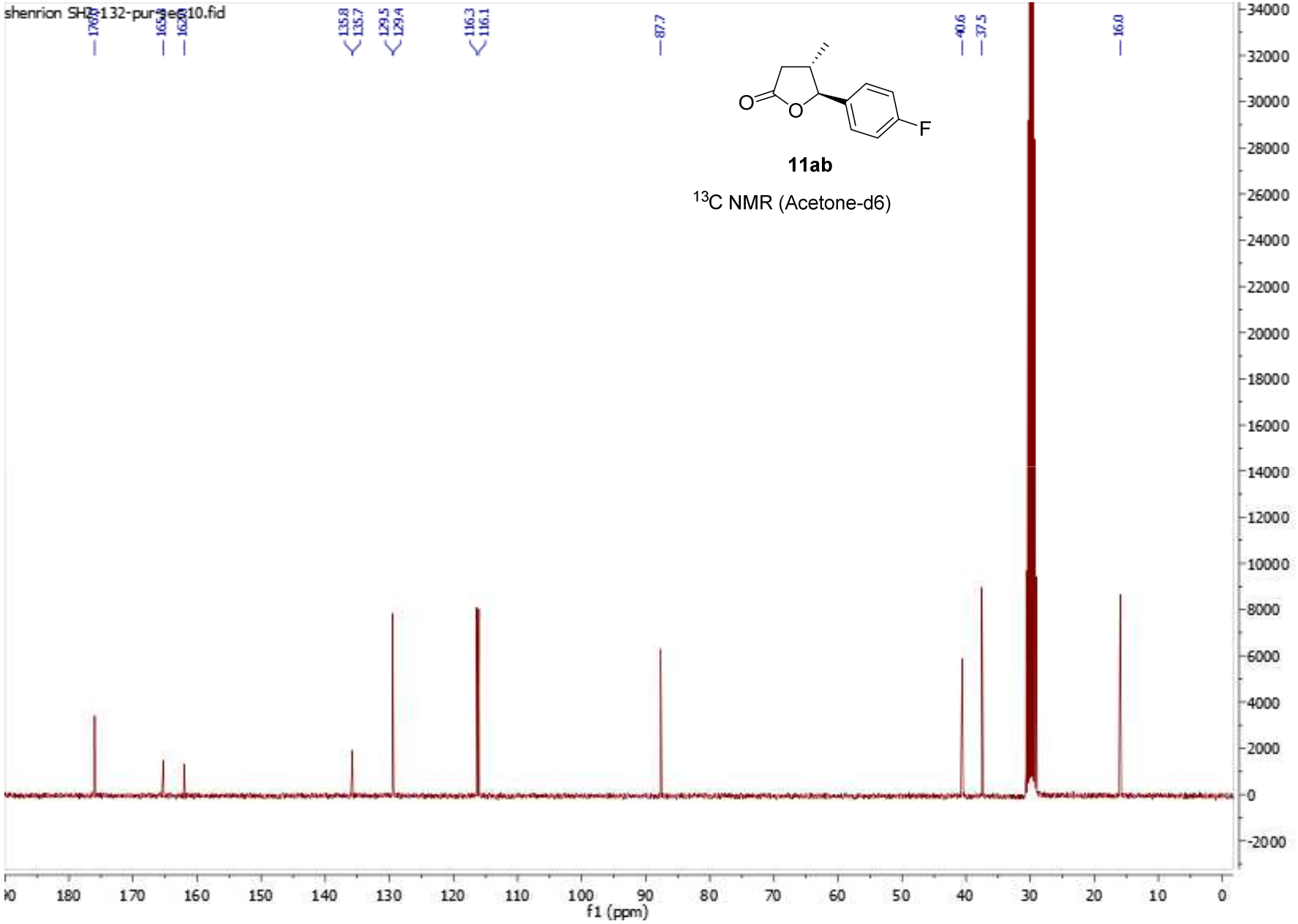
7.52 7.52 7.51 7.51 7.50 7.50 7.49 7.49 7.49 7.48 7.48 7.47 7.47 7.22 7.21 7.20 7.19 7.19 7.18 7.16 7.16
5.04 5.01
2.77 2.75 2.72 2.70 2.70 2.45 2.42 2.40 2.36
1.16 1.14
O
O
F
11ab
1H NMR (Acetone-d6)
2.04 2.06 1.00 1.17 1.15 1.10 3.25
f1 (ppm)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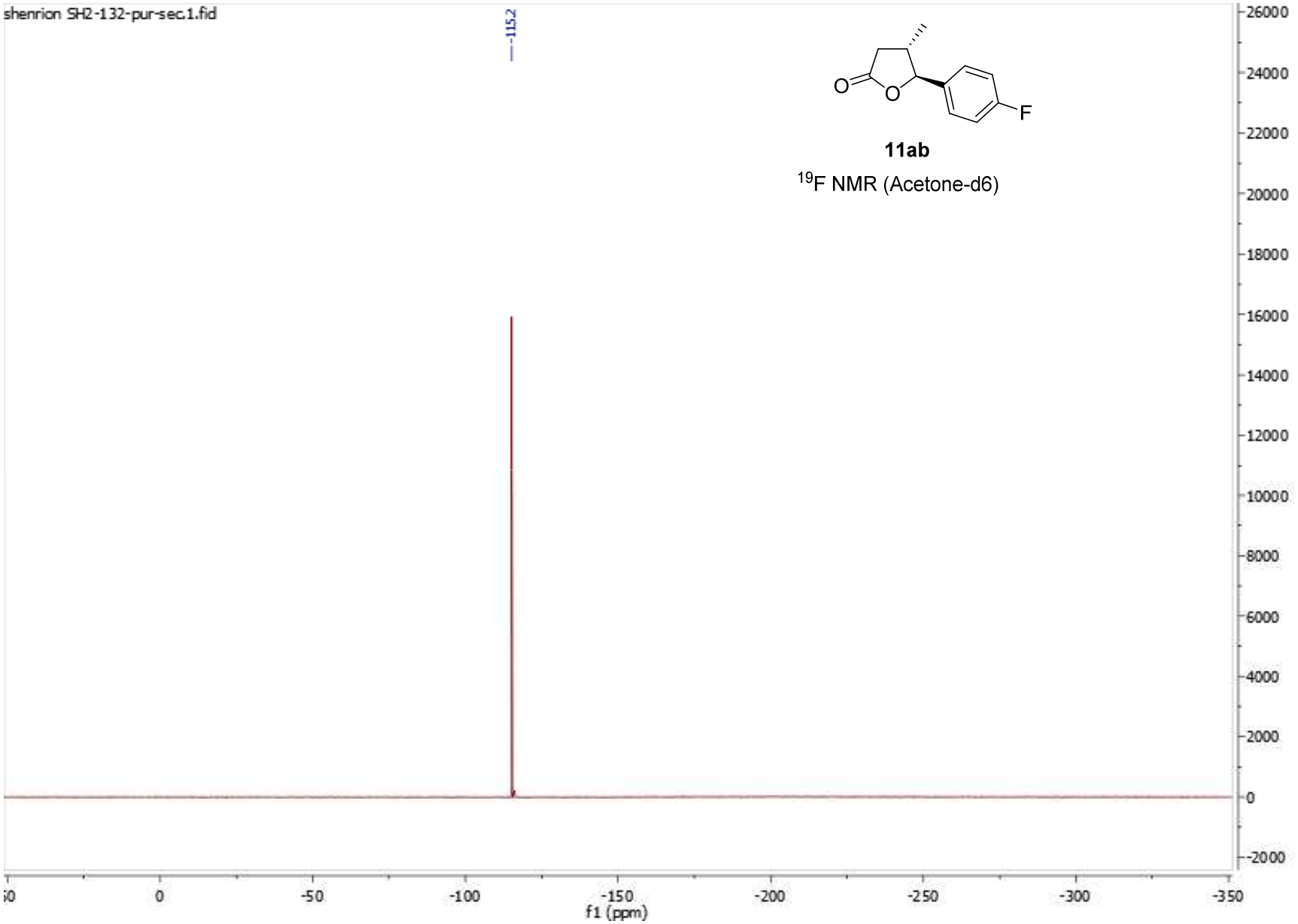
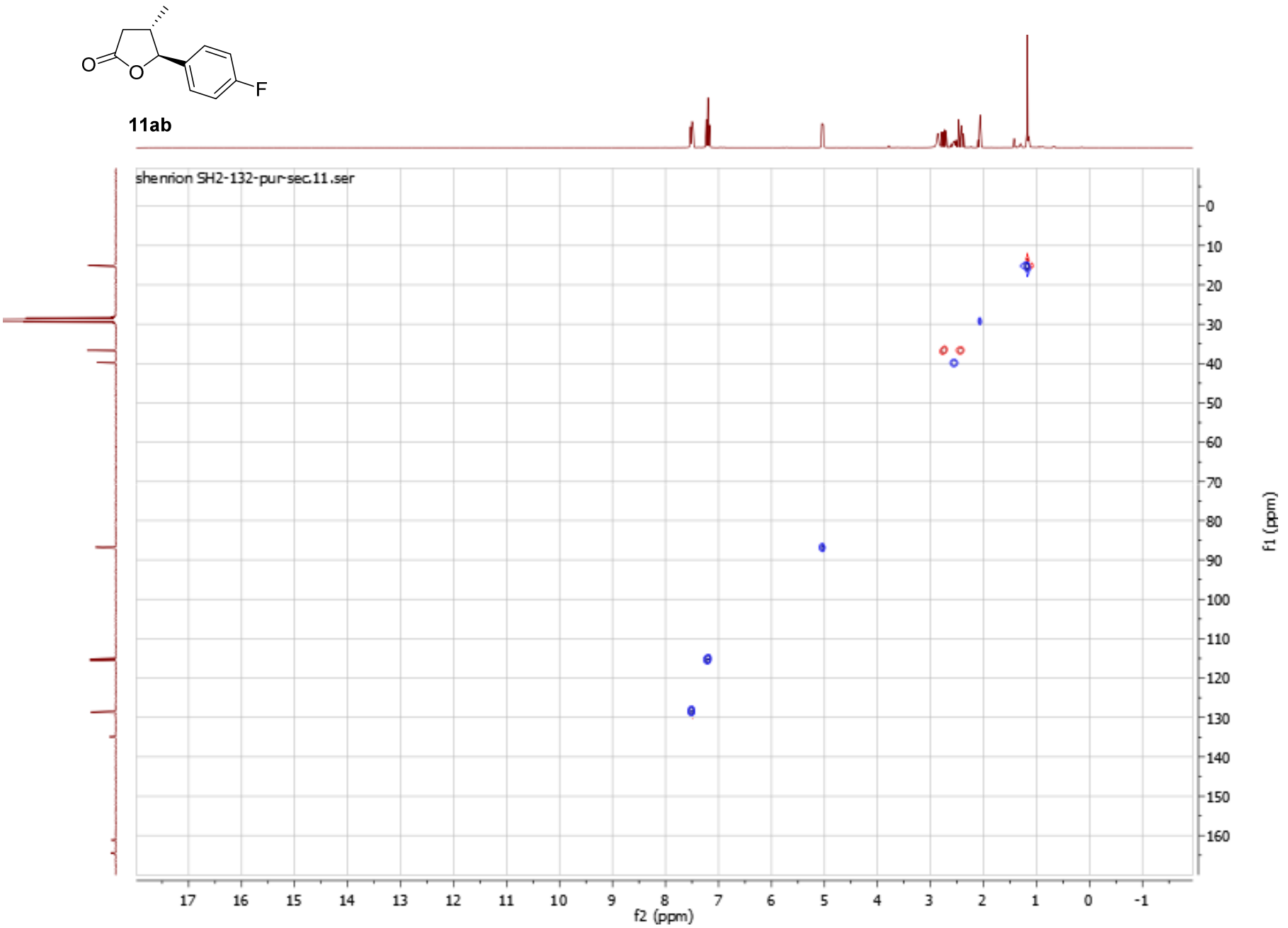
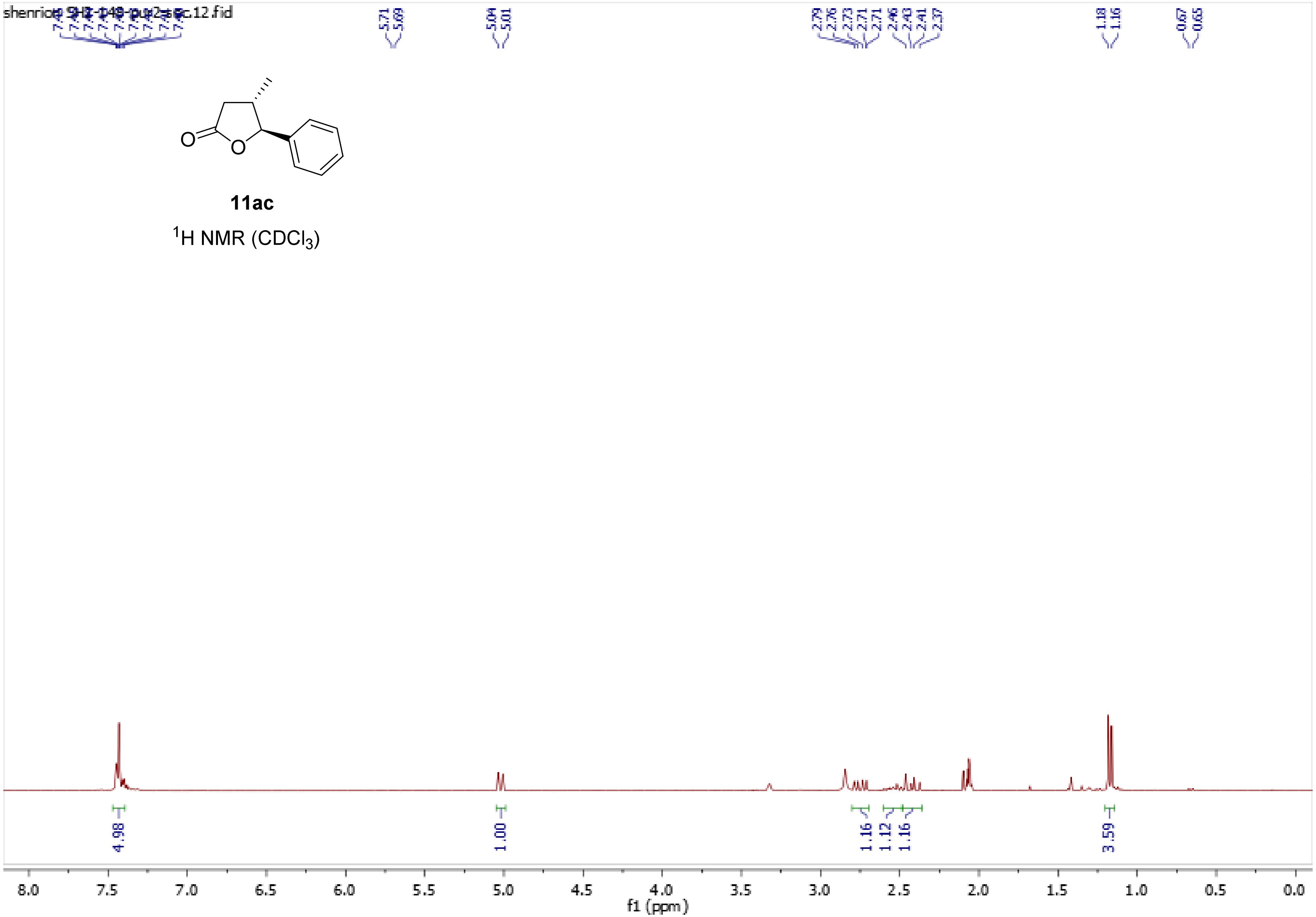
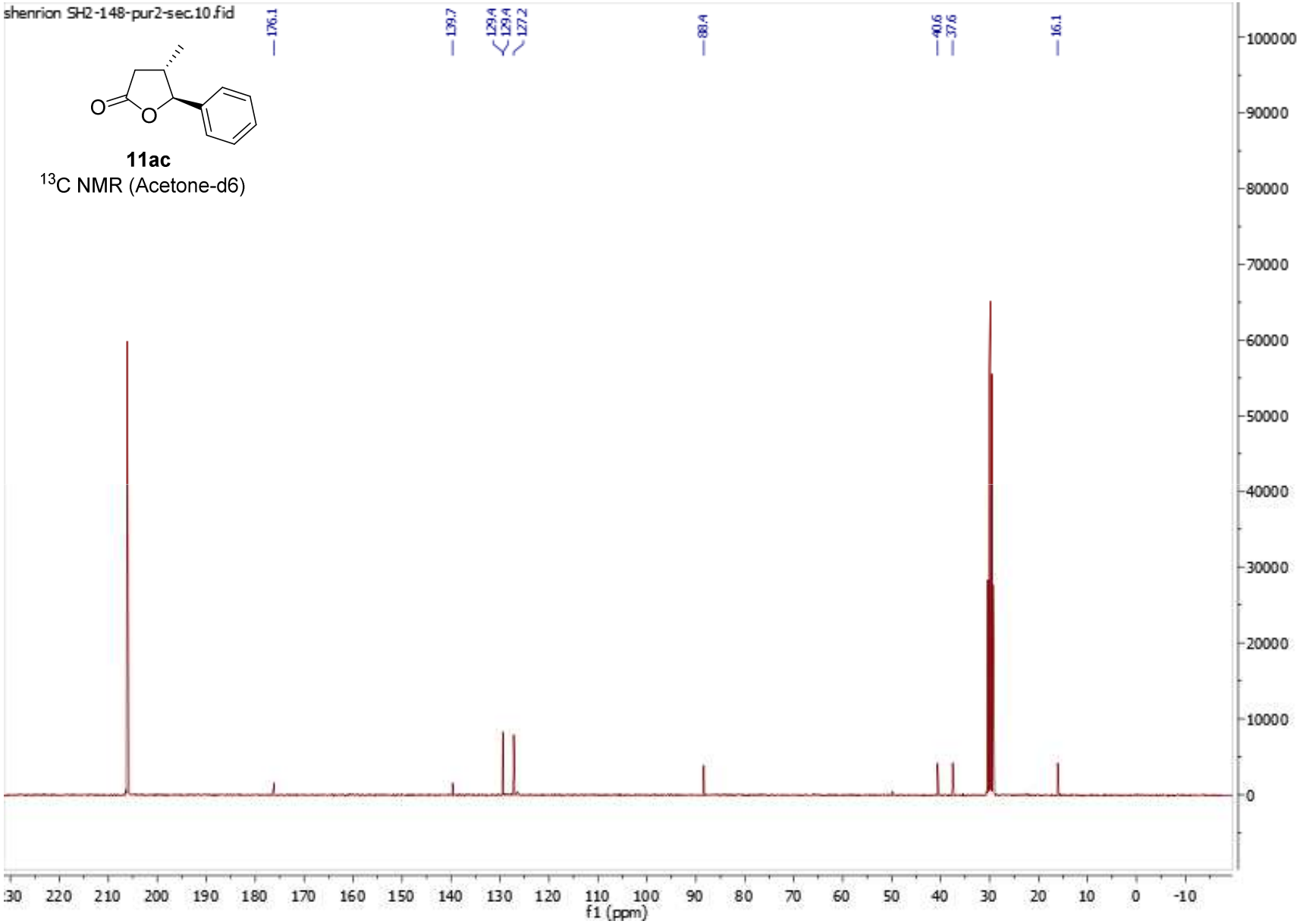
176.7
165.3
162.6
135.8
135.7
129.5
129.4
116.3
116.1
87.7
40.6
37.5
16.0
O
O
F
11ab
13C NMR (Acetone-d6)
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


shenrion SH2-132-pur-sec.1.fid
-115.2
O
O
F
11ab
^{19}F NMR (Acetone-d6)
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)


11ab
O
O
F
shenrion SH2-132-pur-sec.11.ser
f2 (ppm)
f1 (ppm)


11ac
1H NMR (CDCl3)
5.71
5.69
5.04
5.01
2.79
2.76
2.73
2.71
2.71
2.46
2.43
2.41
2.37
1.18
1.16
0.67
0.65
4.98
1.00
1.16
1.12
1.16
3.59
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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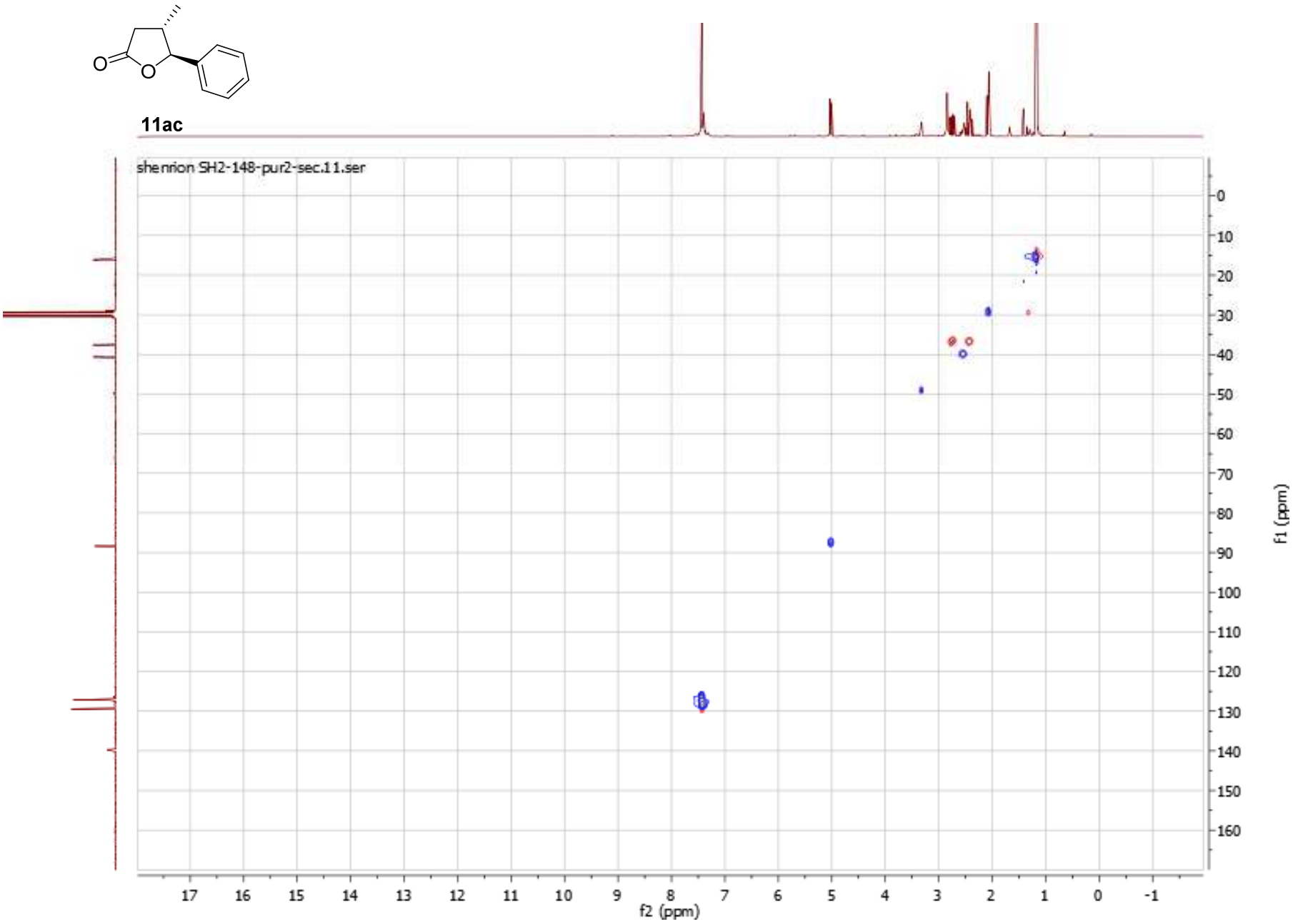
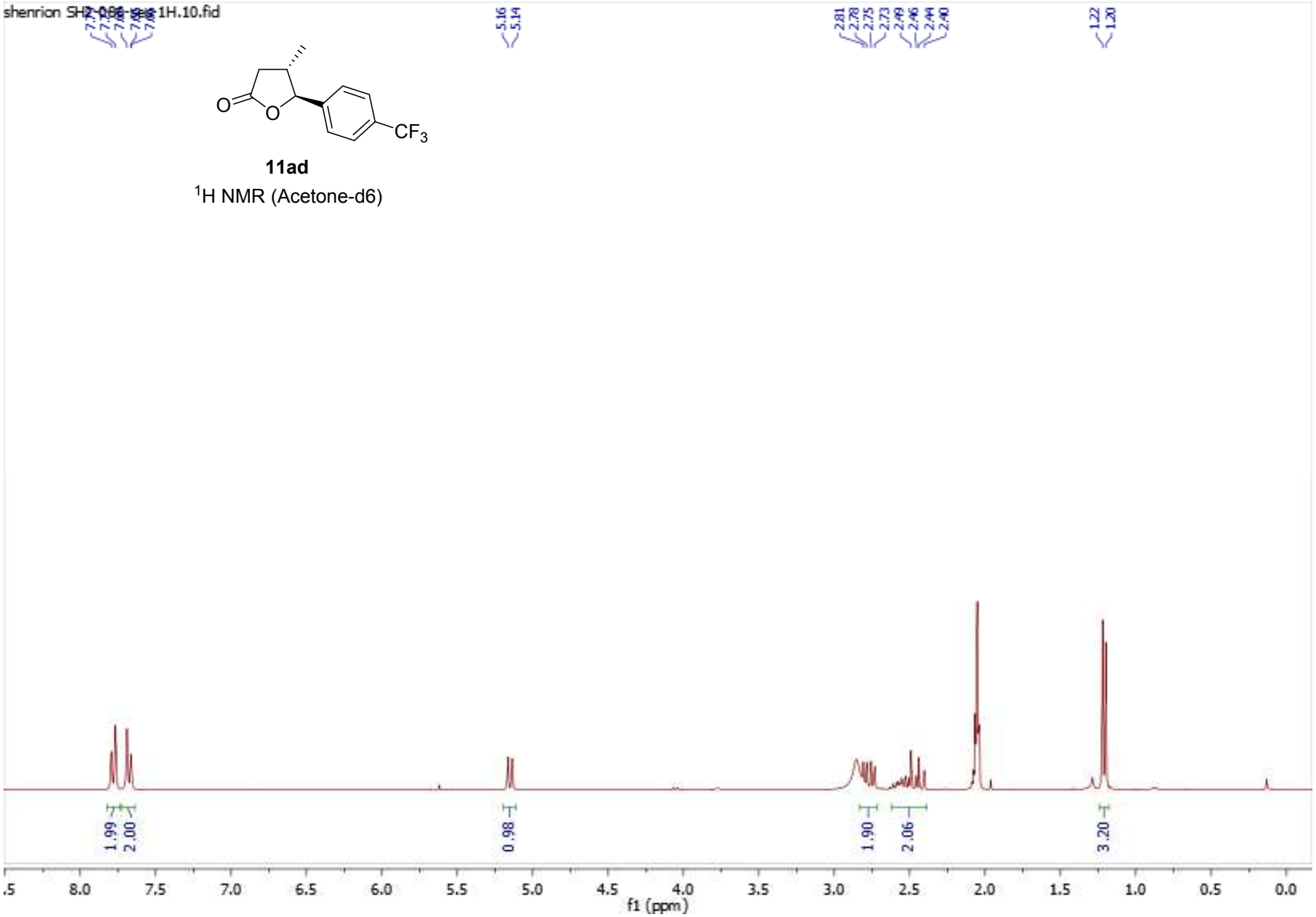
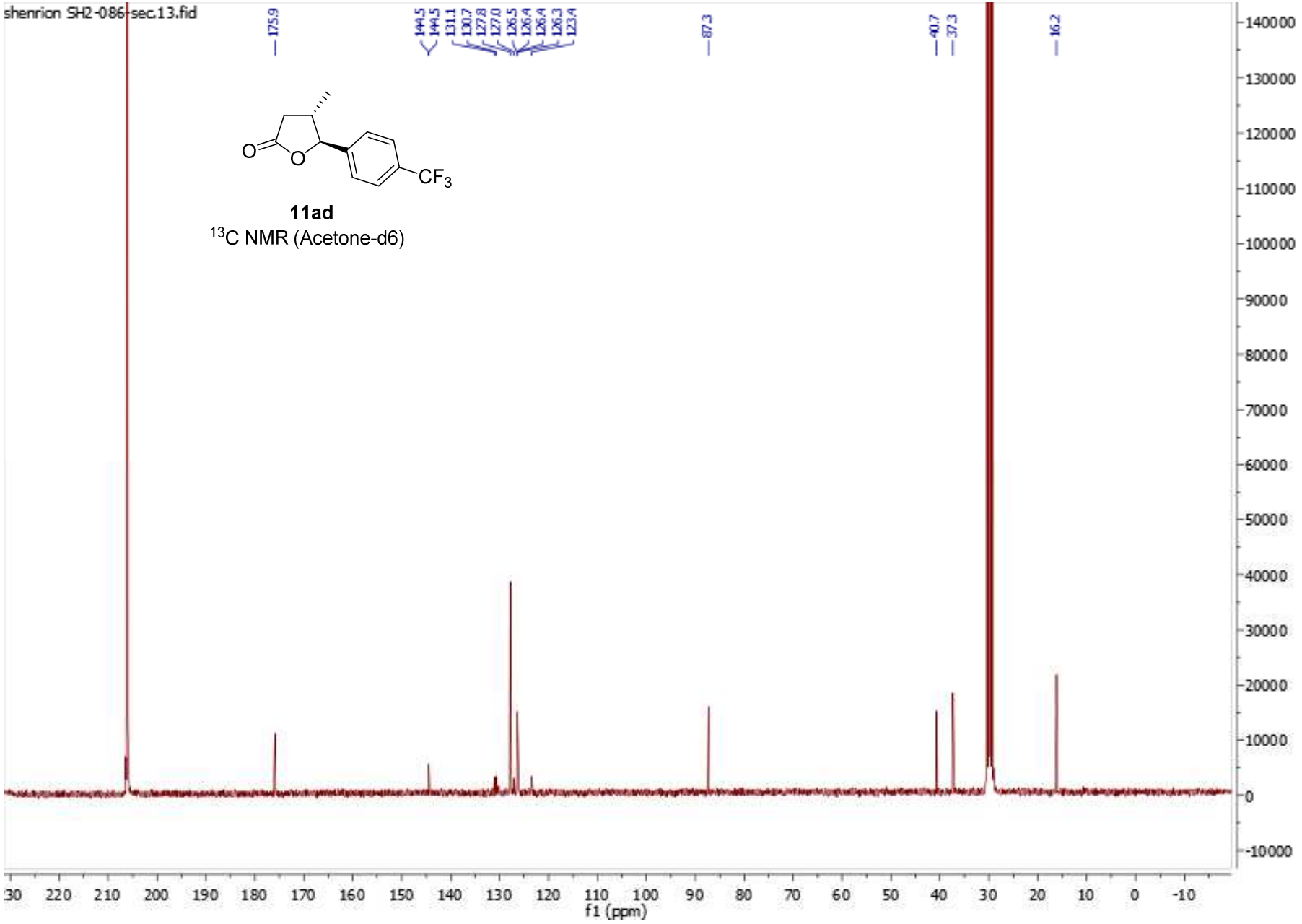
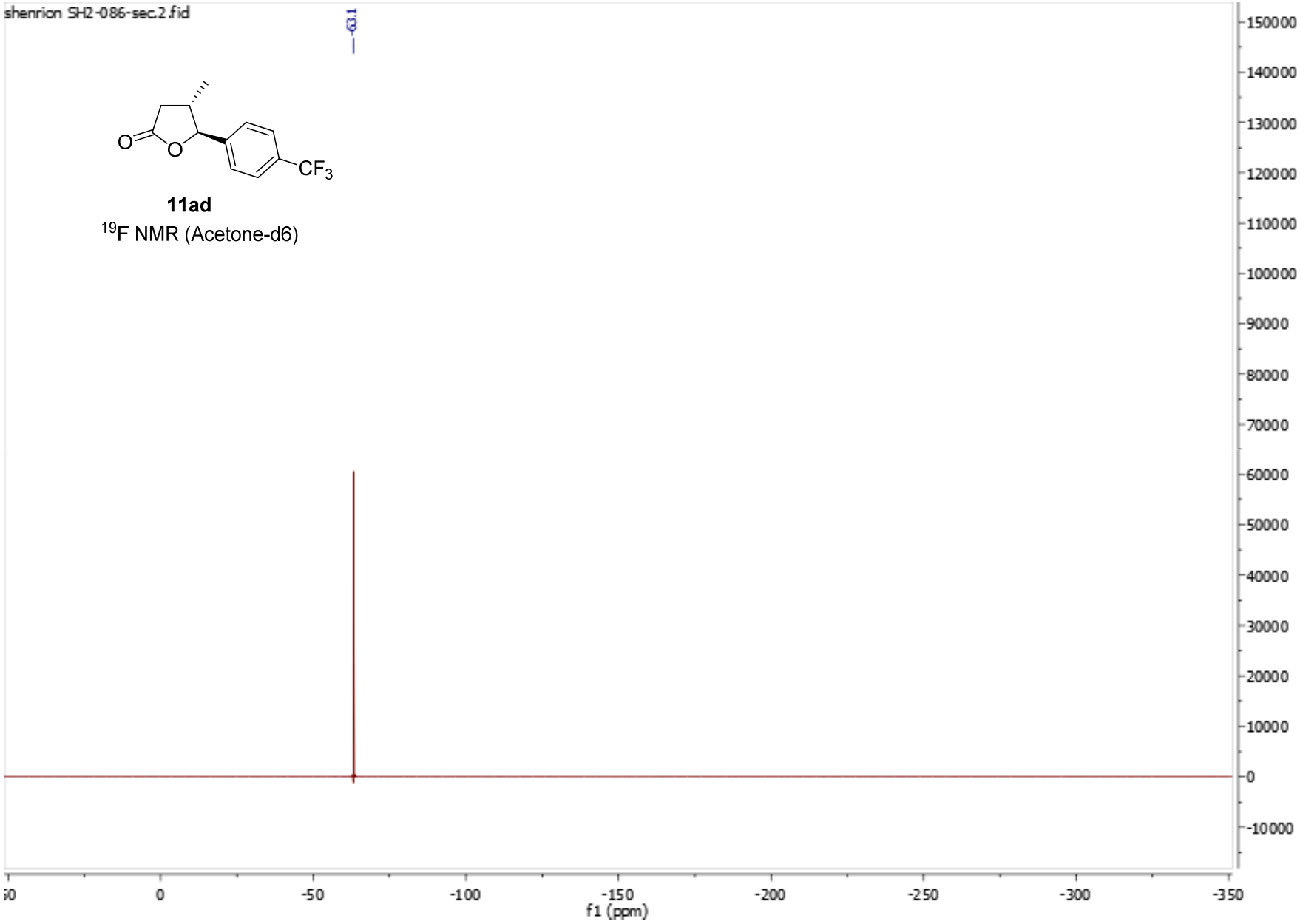
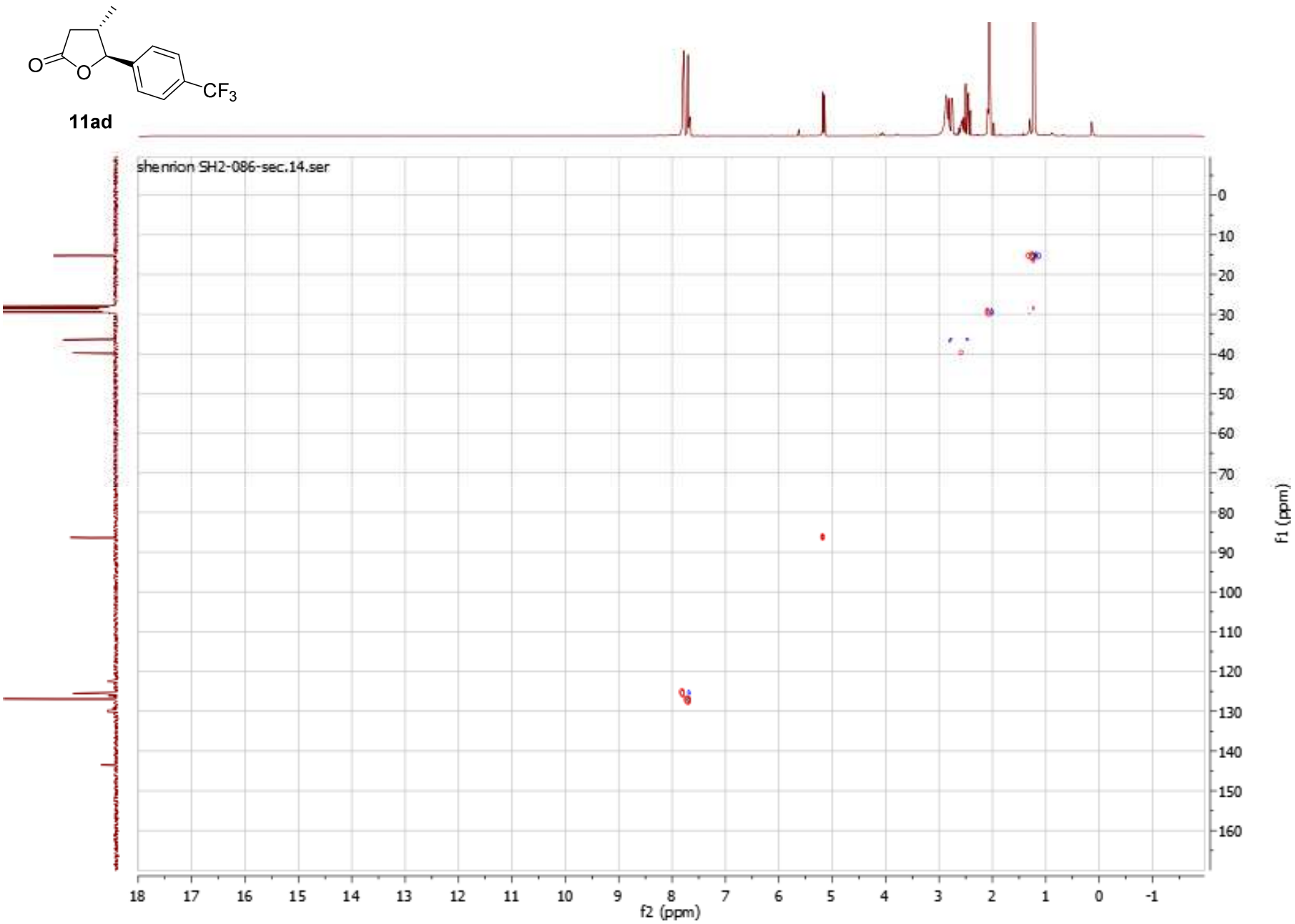
176.1
139.7
129.4
129.4
127.2
88.4
40.6
37.6
16.1
O
O
11ac
13C NMR (Acetone-d6)
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

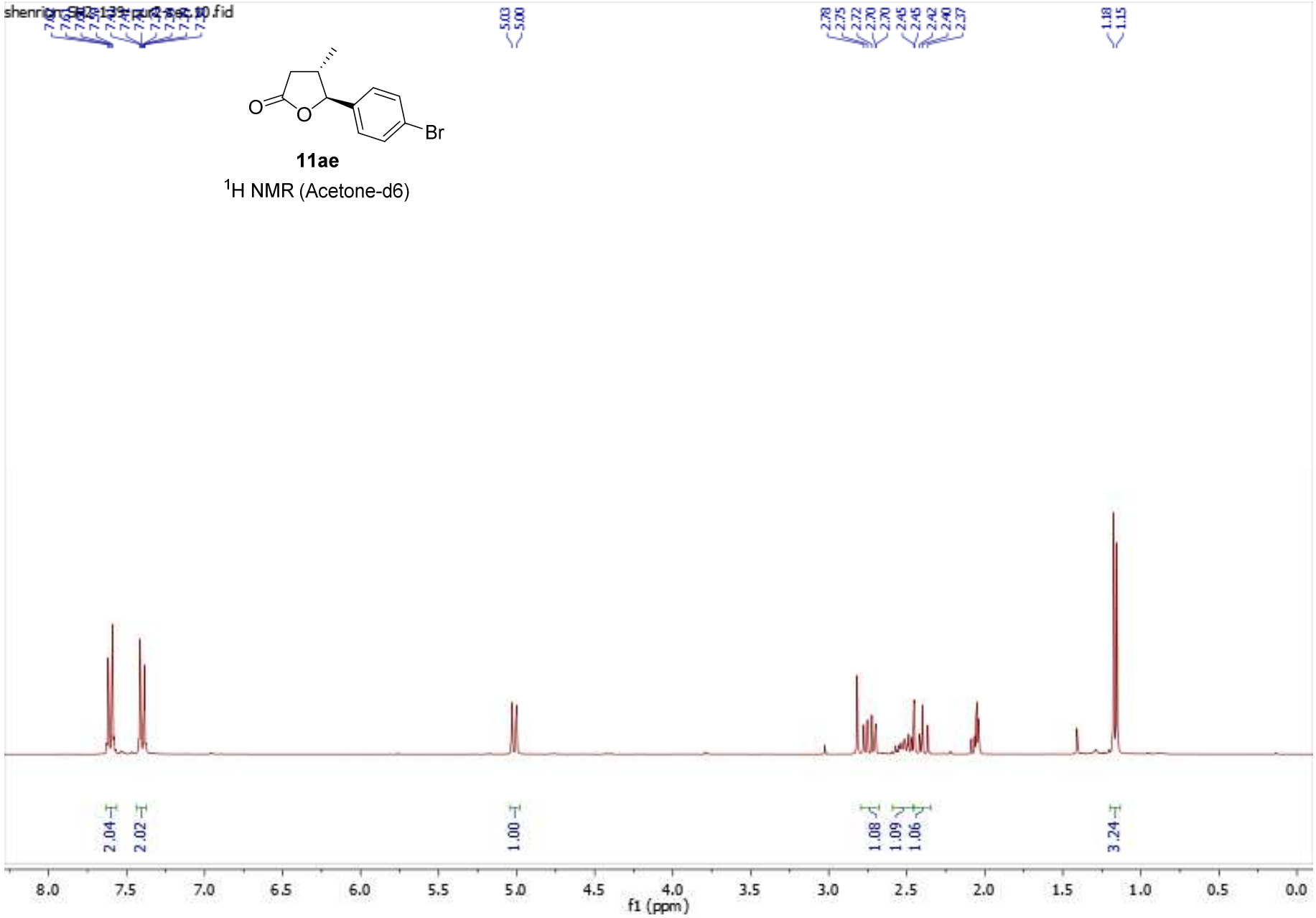

11ac
shenrion SH2-148-pur2-sec.11.ser
f2 (ppm)
f1 (ppm)

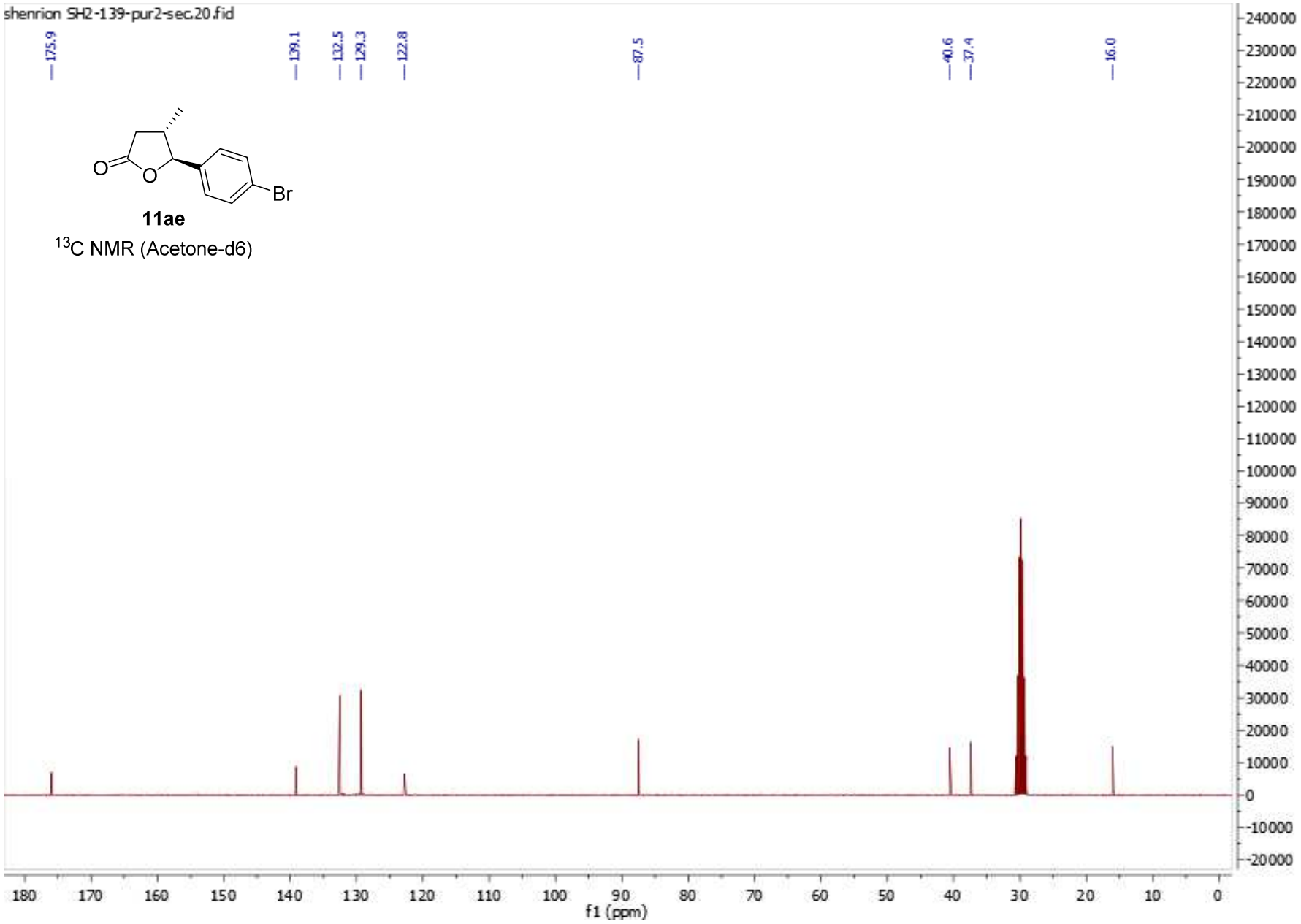

shenrion SH2-098-sec-1H.10.fid
O
O
CF3
11ad
1H NMR (Acetone-d6)
7.77
7.75
7.68
7.66
7.48
7.46
5.16
5.14
2.81
2.78
2.75
2.73
2.49
2.46
2.44
2.40
1.22
1.20
1.99
2.00
0.98
1.90
2.06
3.20
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

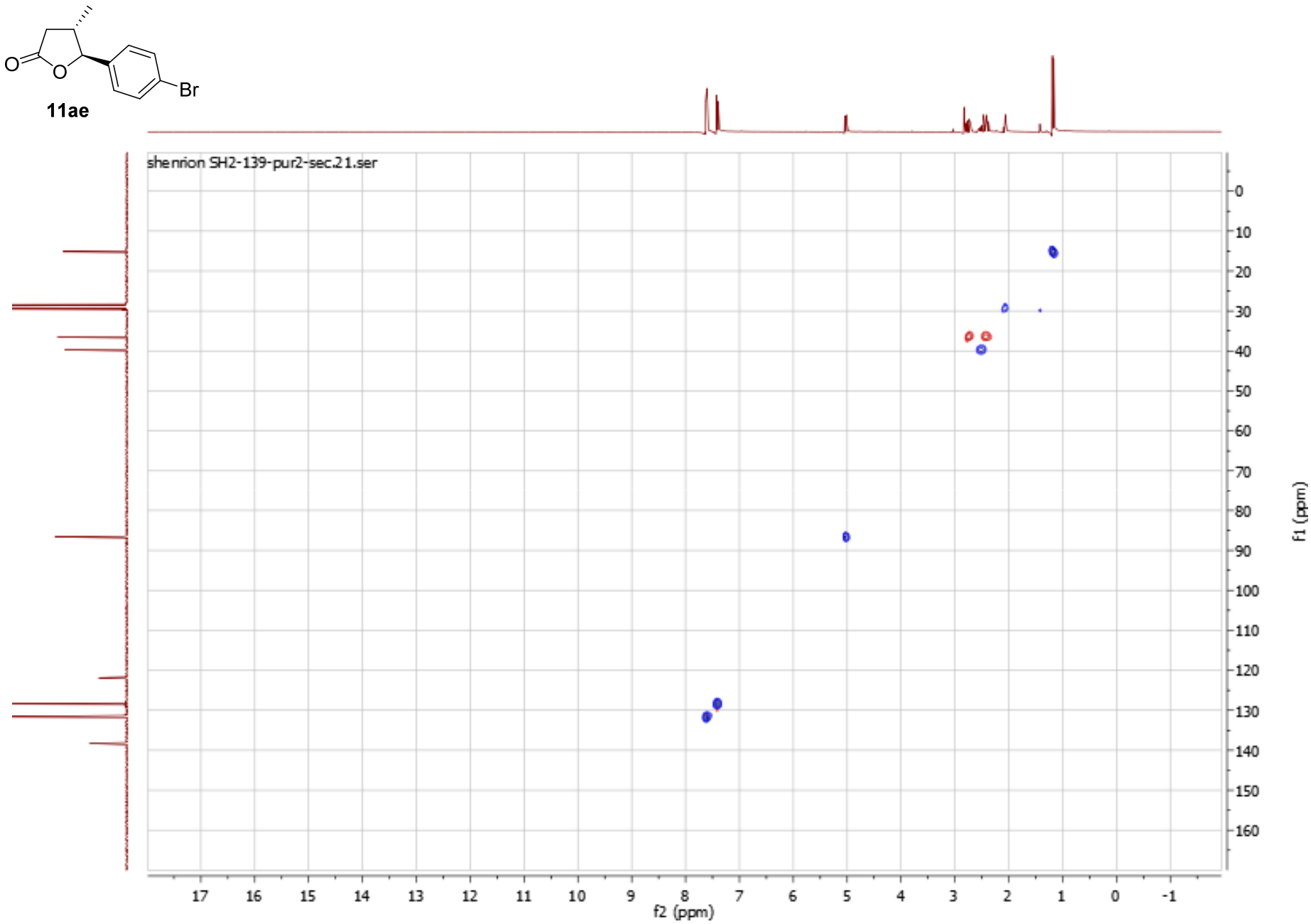

shenrion SH2-086-sec.13.fid
175.9
144.5
144.5
131.1
130.7
127.8
127.0
126.5
126.4
126.4
126.3
123.4
87.3
40.7
37.3
16.2
O
O
CF3
11ad
13C NMR (Acetone-d6)
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

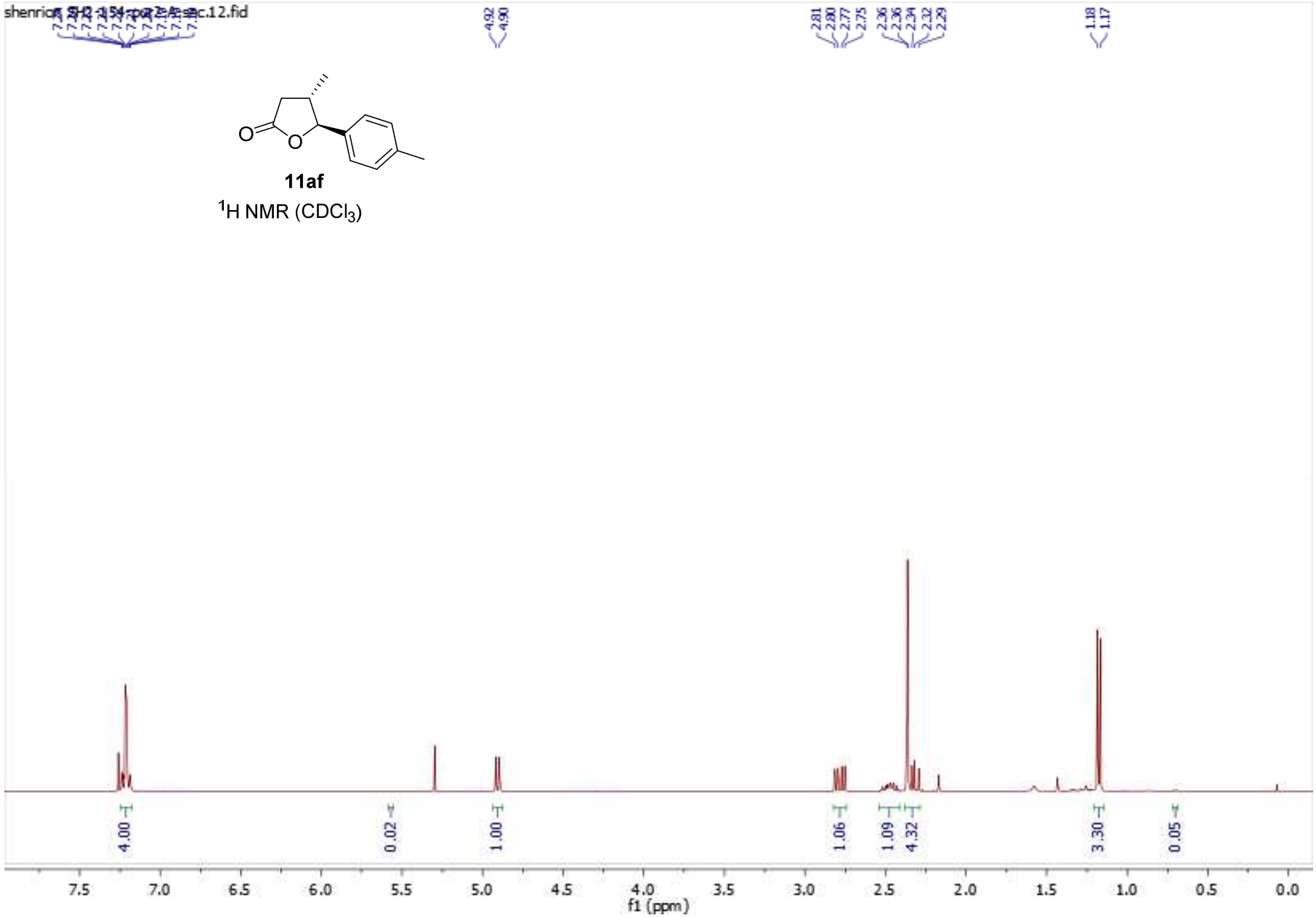

shenrion SH2-086-sec.2.fid
-63.1
O
O
CF3
11ad
19F NMR (Acetone-d6)
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)

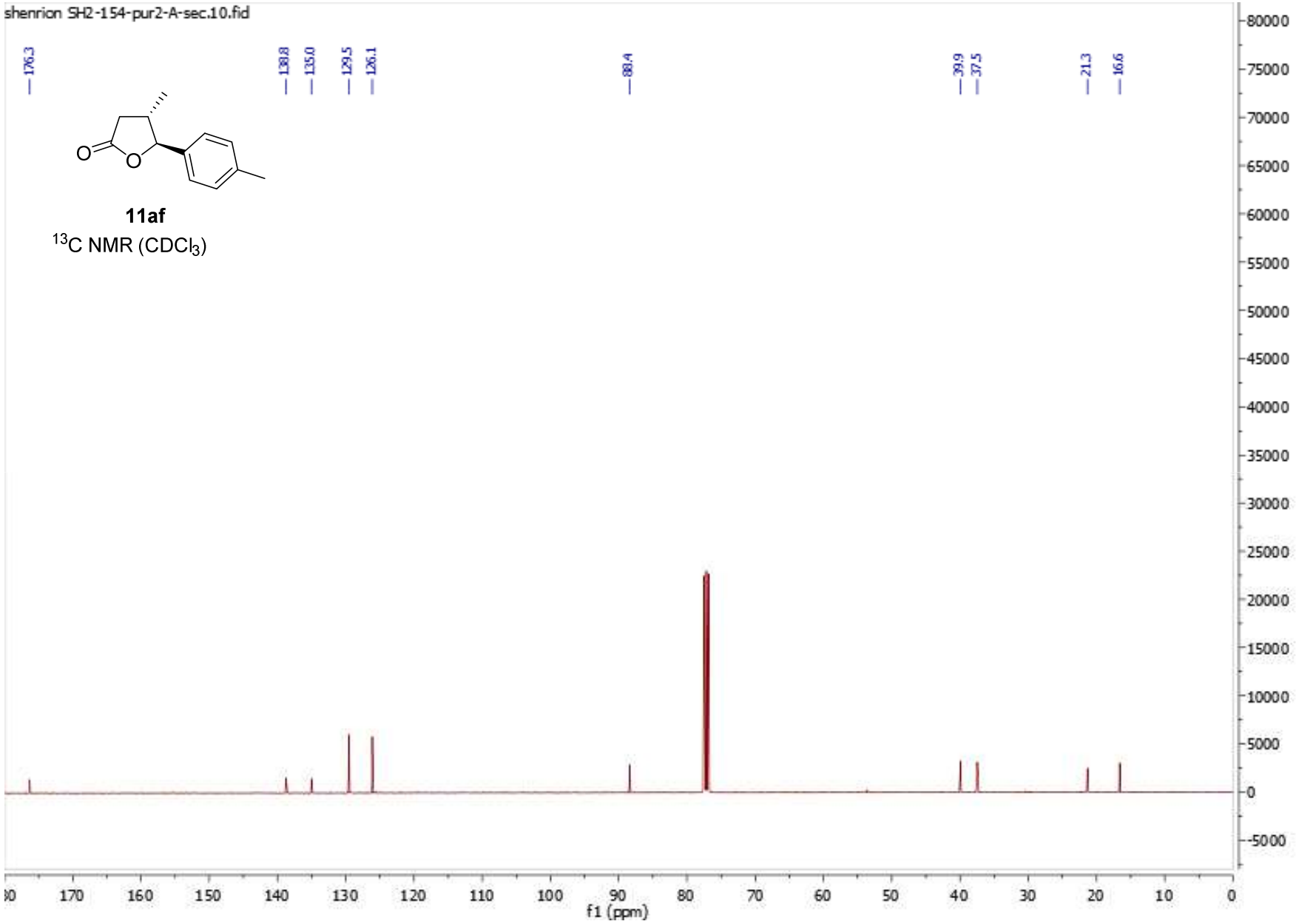

11ad
shenrion SH2-086-sec.14.ser
f2 (ppm)
f1 (ppm)

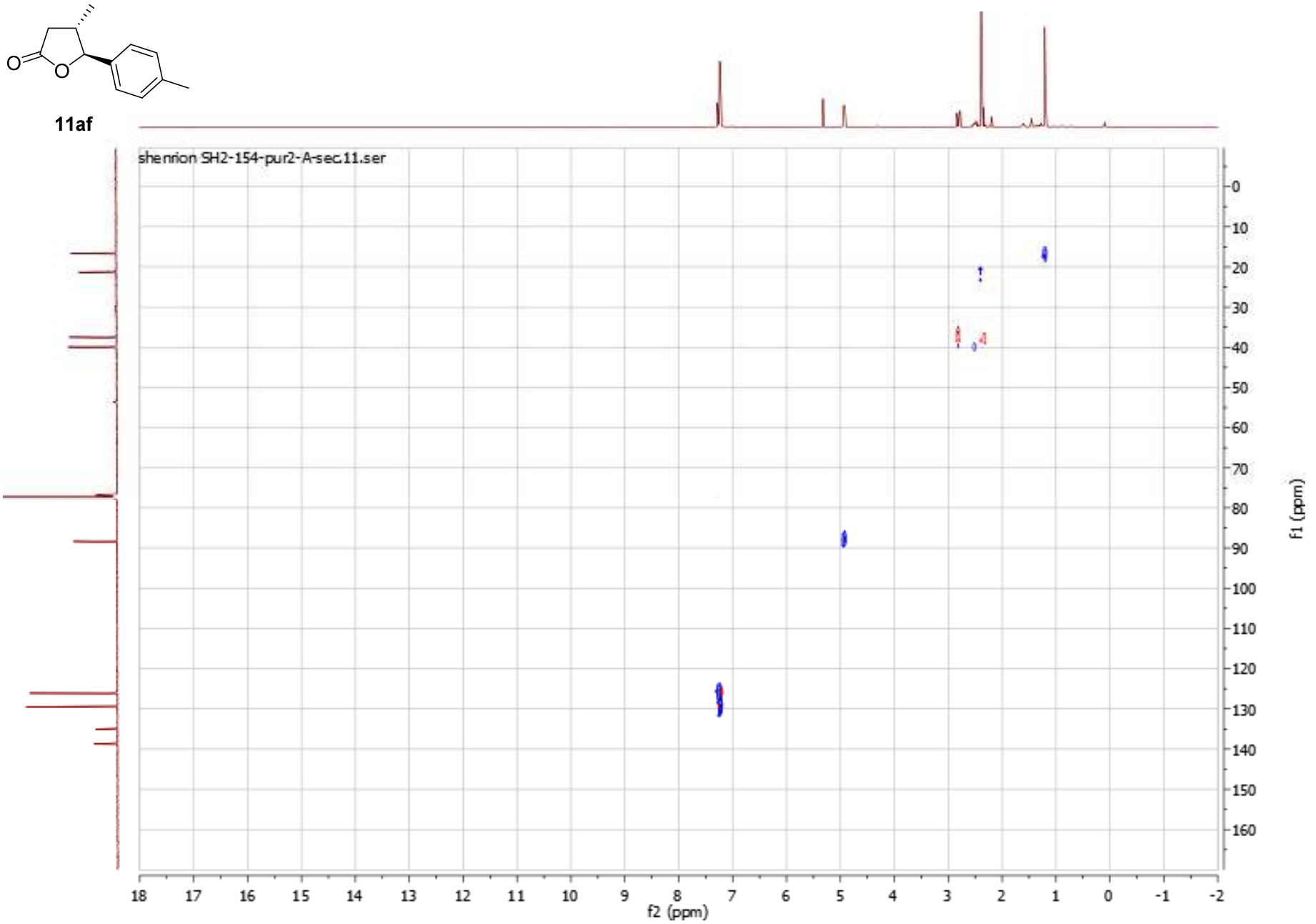

O
O
Br
11ae
1H NMR (Acetone-d6)
f1 (ppm)

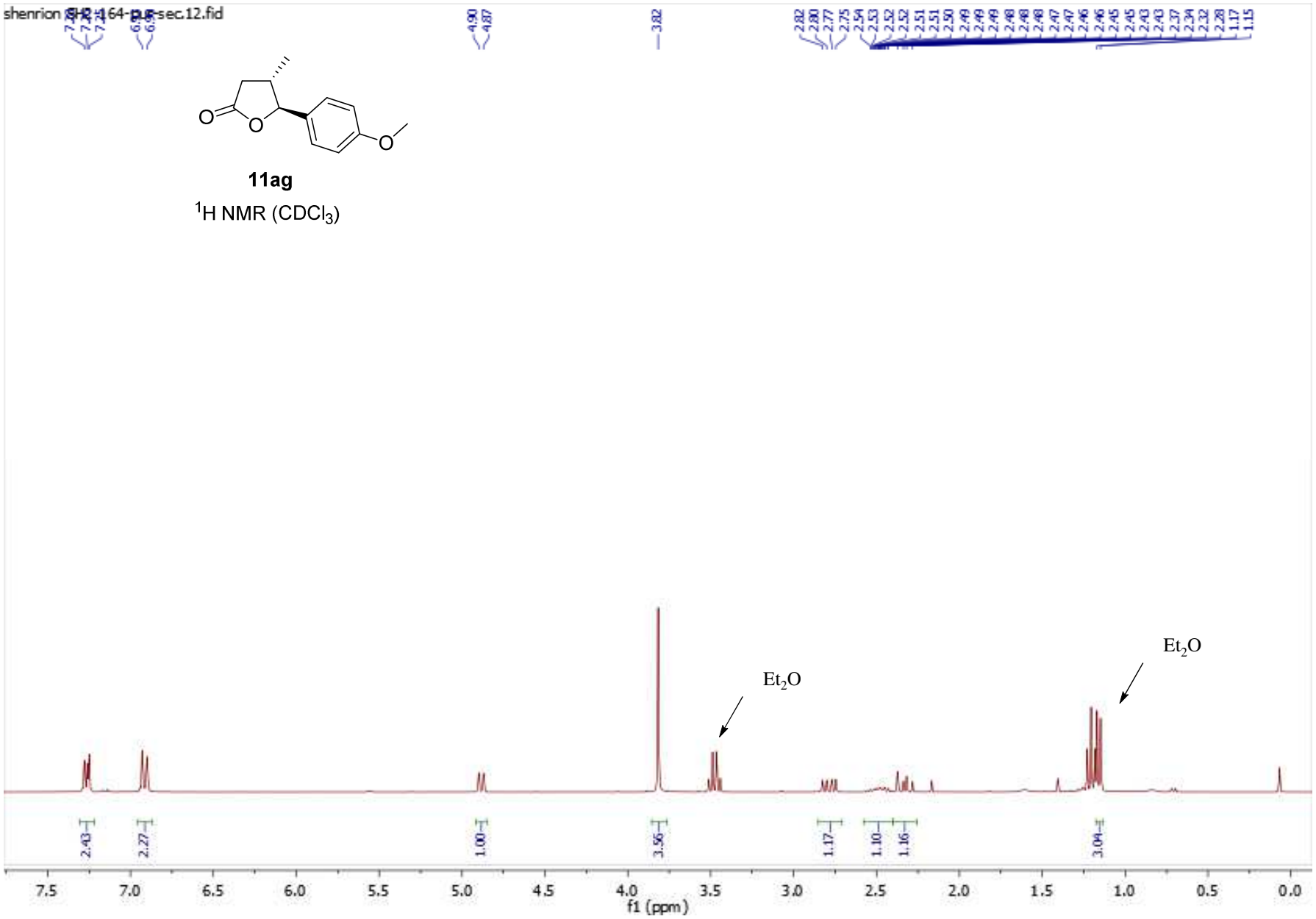

shenrion SH2-139-pur2-sec.20.fid
175.9
139.1
132.5
129.3
122.8
87.5
40.6
37.4
16.0
O
O
Br
11ae
13C NMR (Acetone-d6)
240000
230000
220000
210000
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
-20000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

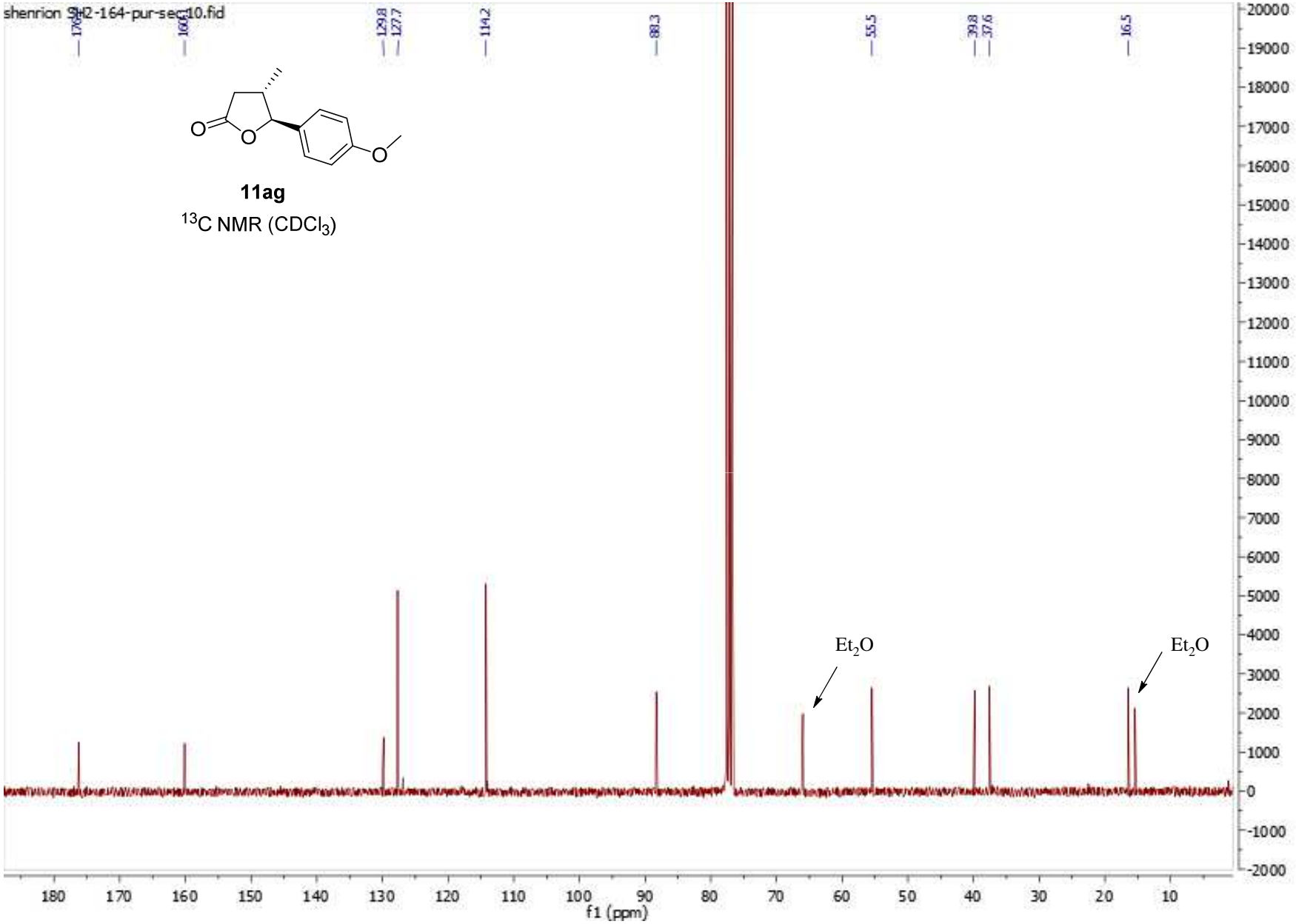

O
O
Br
11ae
shenrion SH2-139-pur2-sec.21.ser
f2 (ppm)
f1 (ppm)

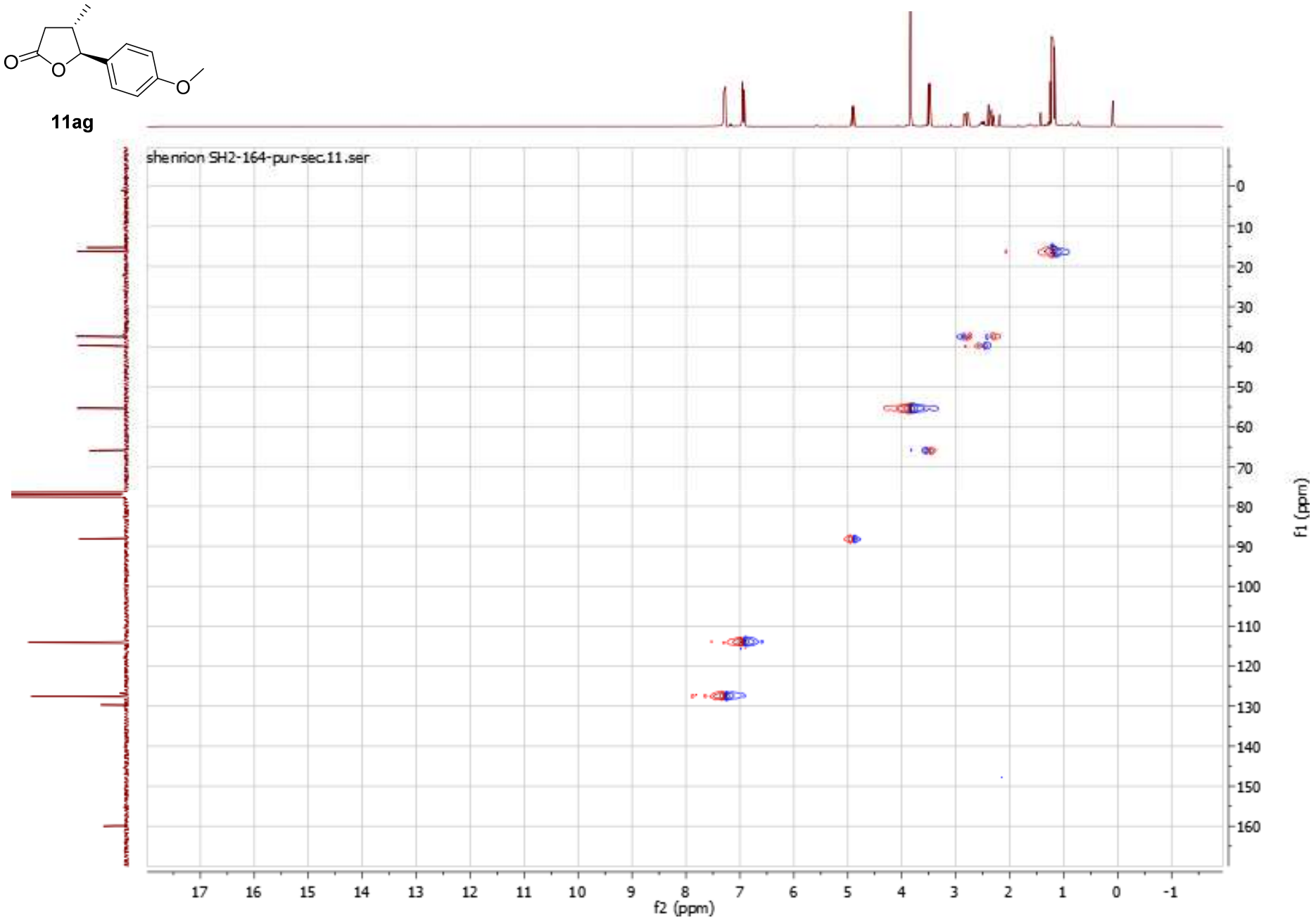

shenrica
4.92
4.90
2.81
2.80
2.77
2.75
2.36
2.36
2.34
2.32
2.29
1.18
1.17
O
O
11af
1H NMR (CDCl3)
4.00
0.02
1.00
1.06
1.09
4.32
3.30
0.05
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

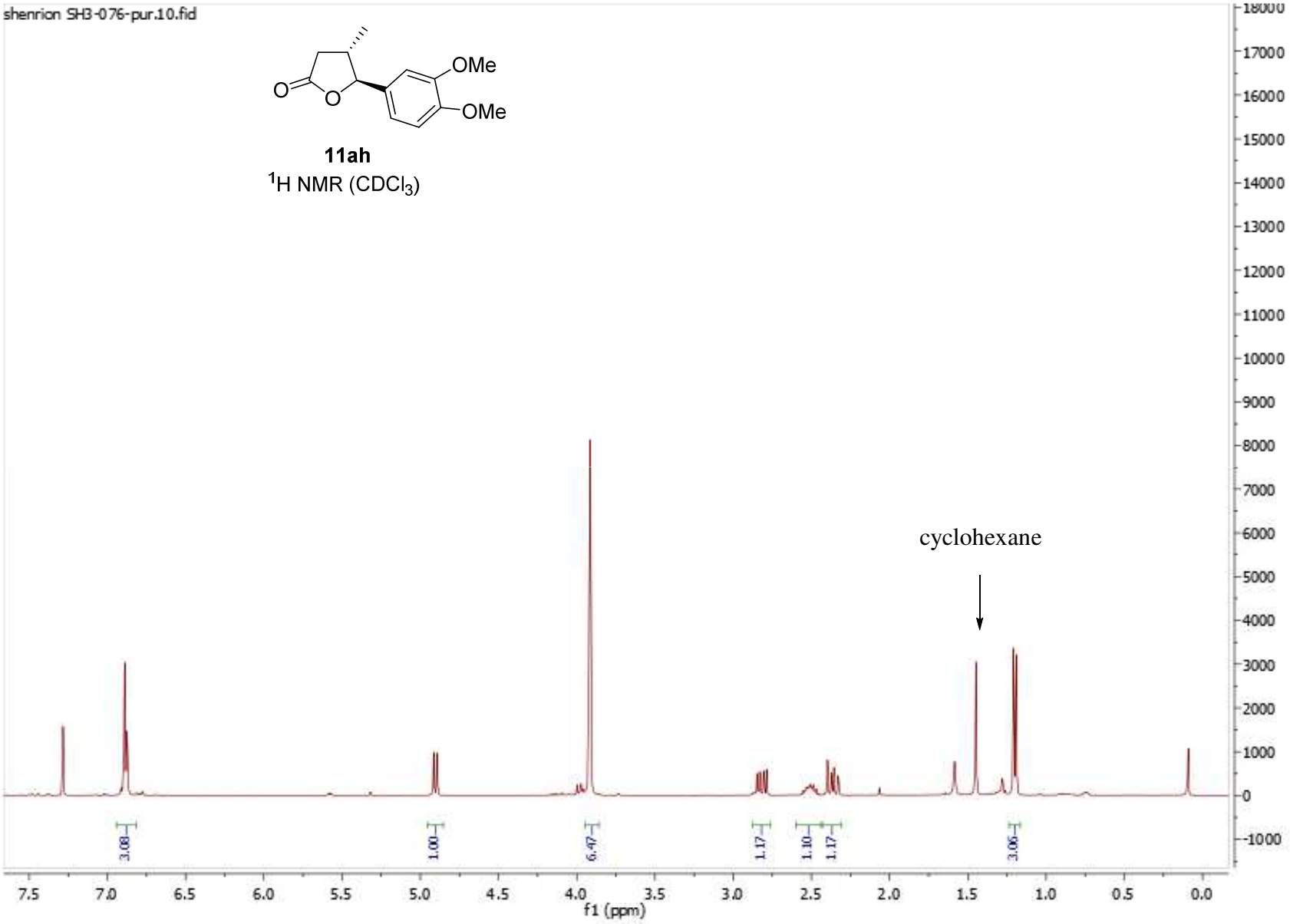

shenrion SH2-154-pur2-A-sec.10.fid
176.3
138.8
135.0
129.5
126.1
88.4
39.9
37.5
21.3
16.6
O
O
11af
^{13}C NMR ($CDCl_3$)
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

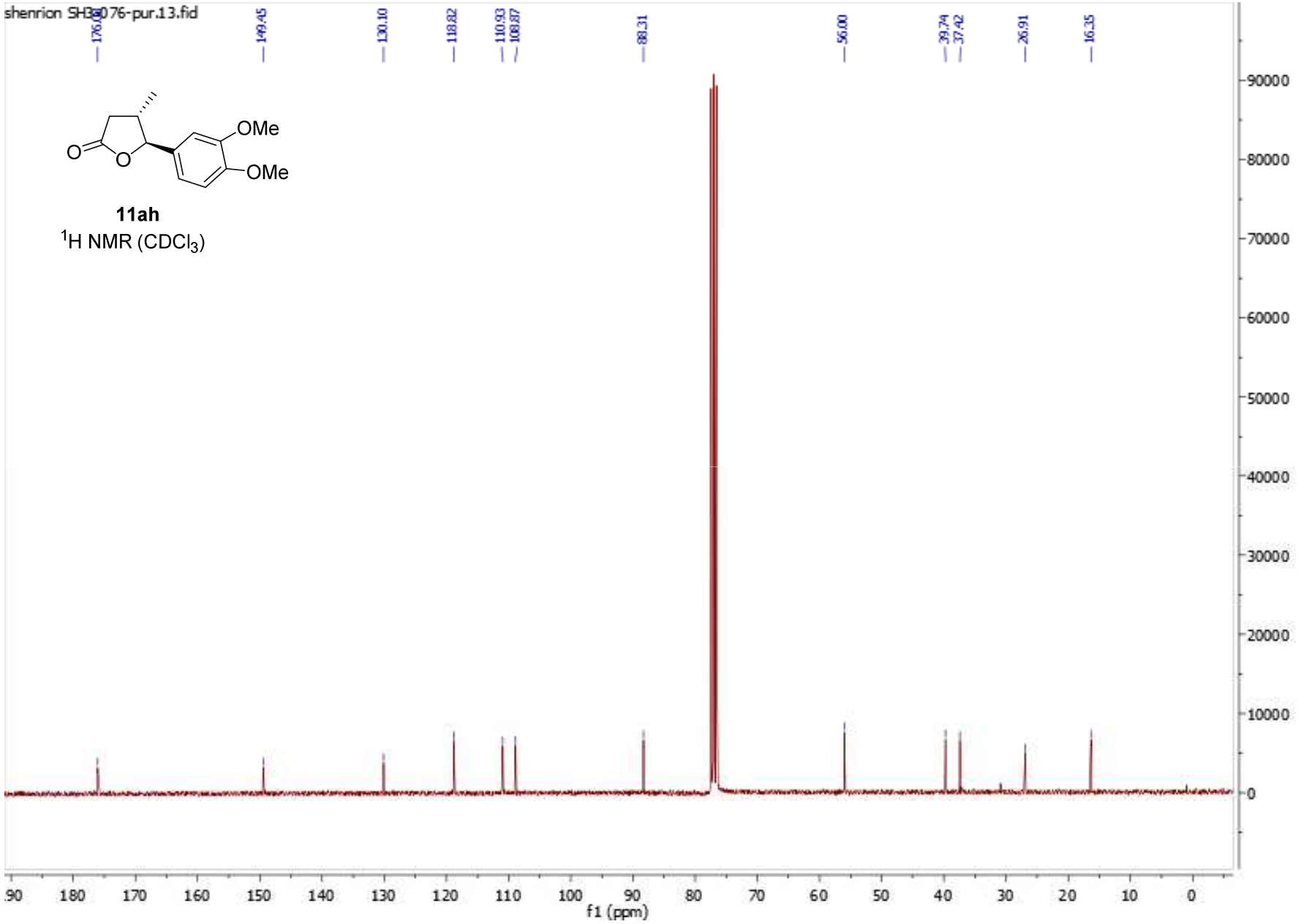

11af
shenrion SH2-154-pur2-A-sec.11.ser
f2 (ppm)
f1 (ppm)

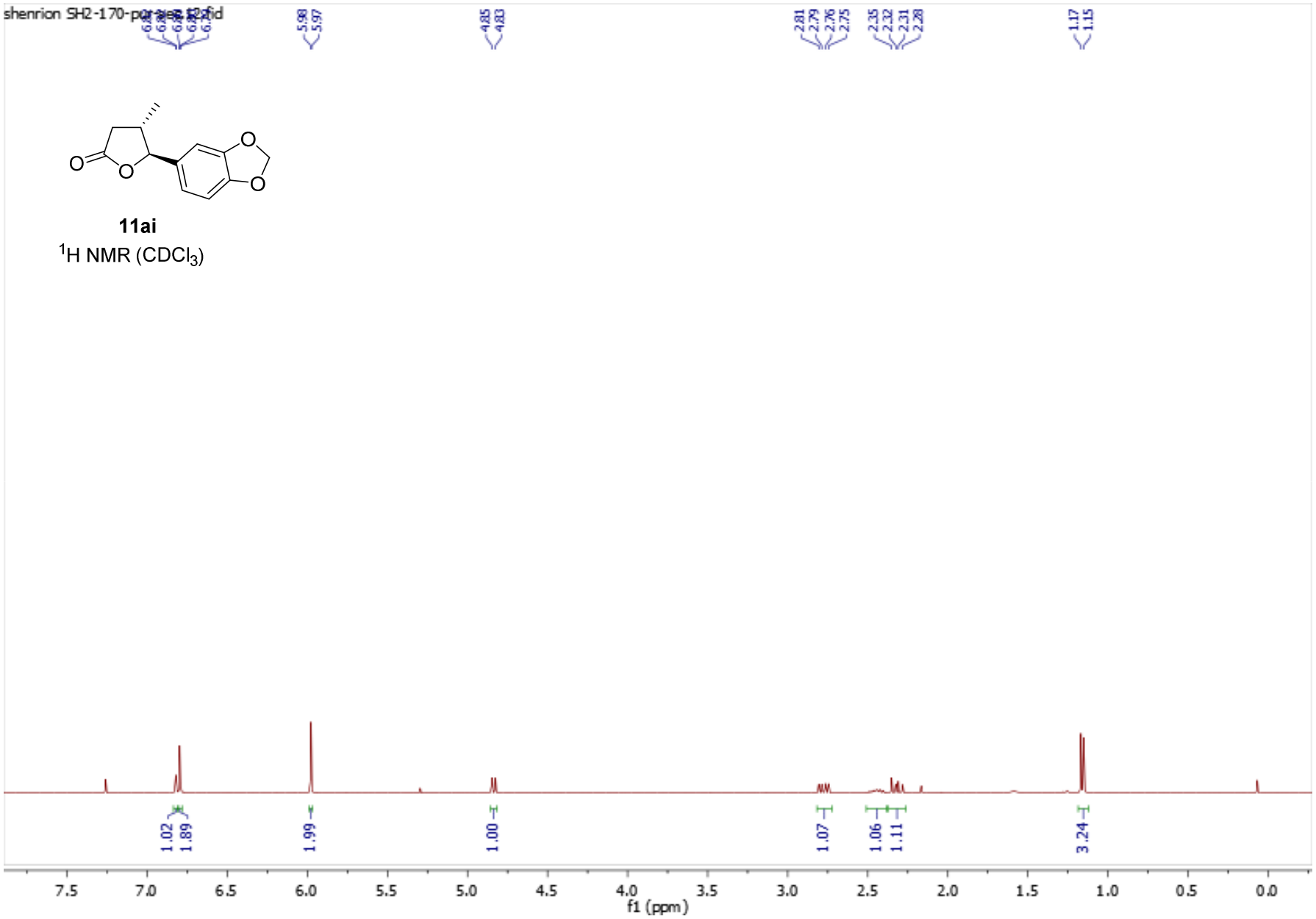

shenrion-SHZ-164-pure-sec.12.fid
11ag
^{1}H NMR ($CDCl_3$)
Et$_2$O
Et$_2$O
f1 (ppm)


shenrion 9/H2-164-pur-sec-10.fid
176.8
160.0
129.8
127.7
114.2
88.3
55.5
39.8
37.6
16.5
O
O
O
11ag
^{13}C NMR ($CDCl_3$)
Et_2O
Et_2O
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


11ag
shenrion SH2-164-pur-sec.11.ser
f2 (ppm)
f1 (ppm)

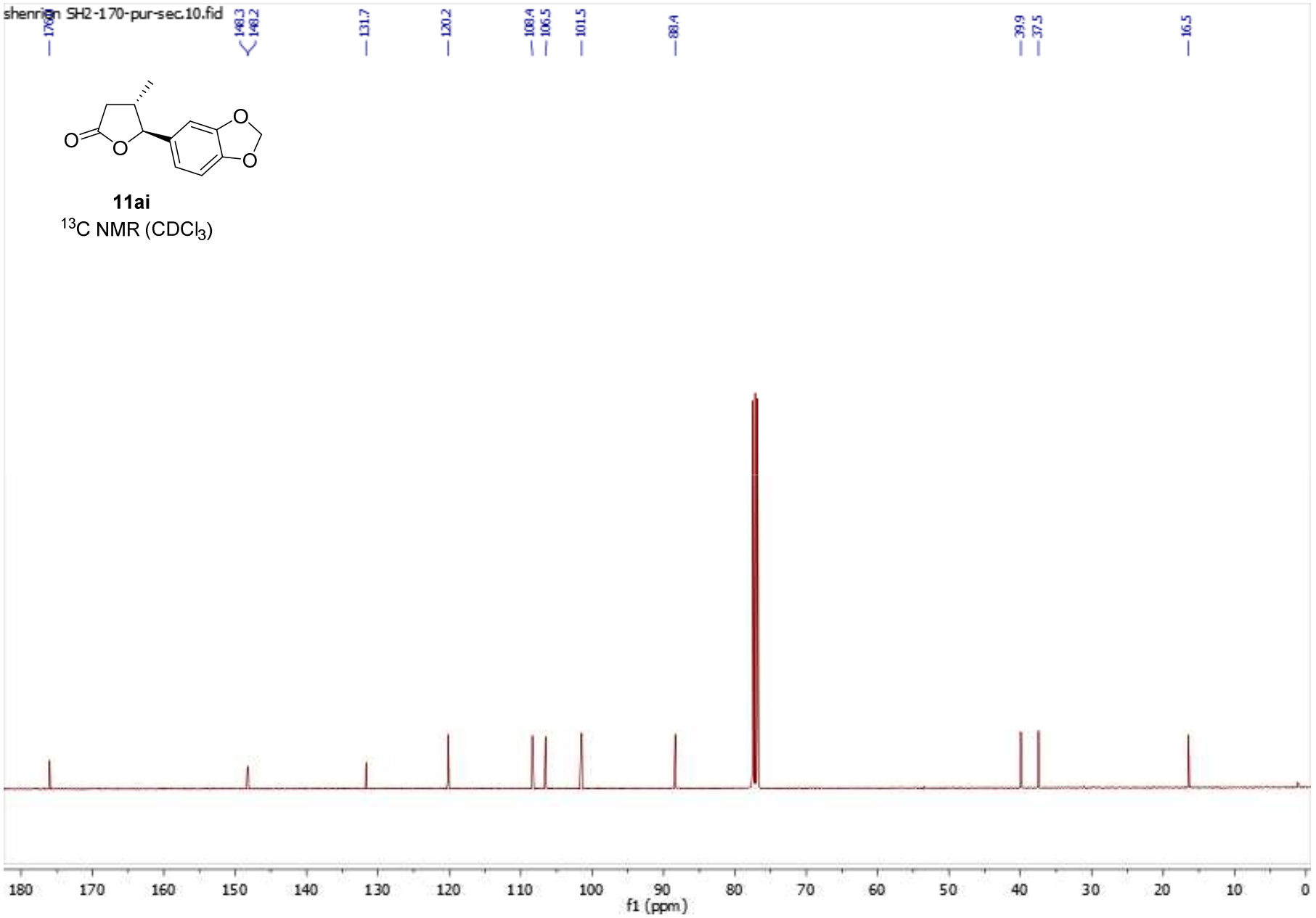

shenrion SH3-076-pur.10.fid
OMe
OMe
O
O
11ah
^{1}H NMR ($CDCl_3$)
cyclohexane
3.08
1.00
6.47
1.17
1.10
1.17
3.06
f1 (ppm)

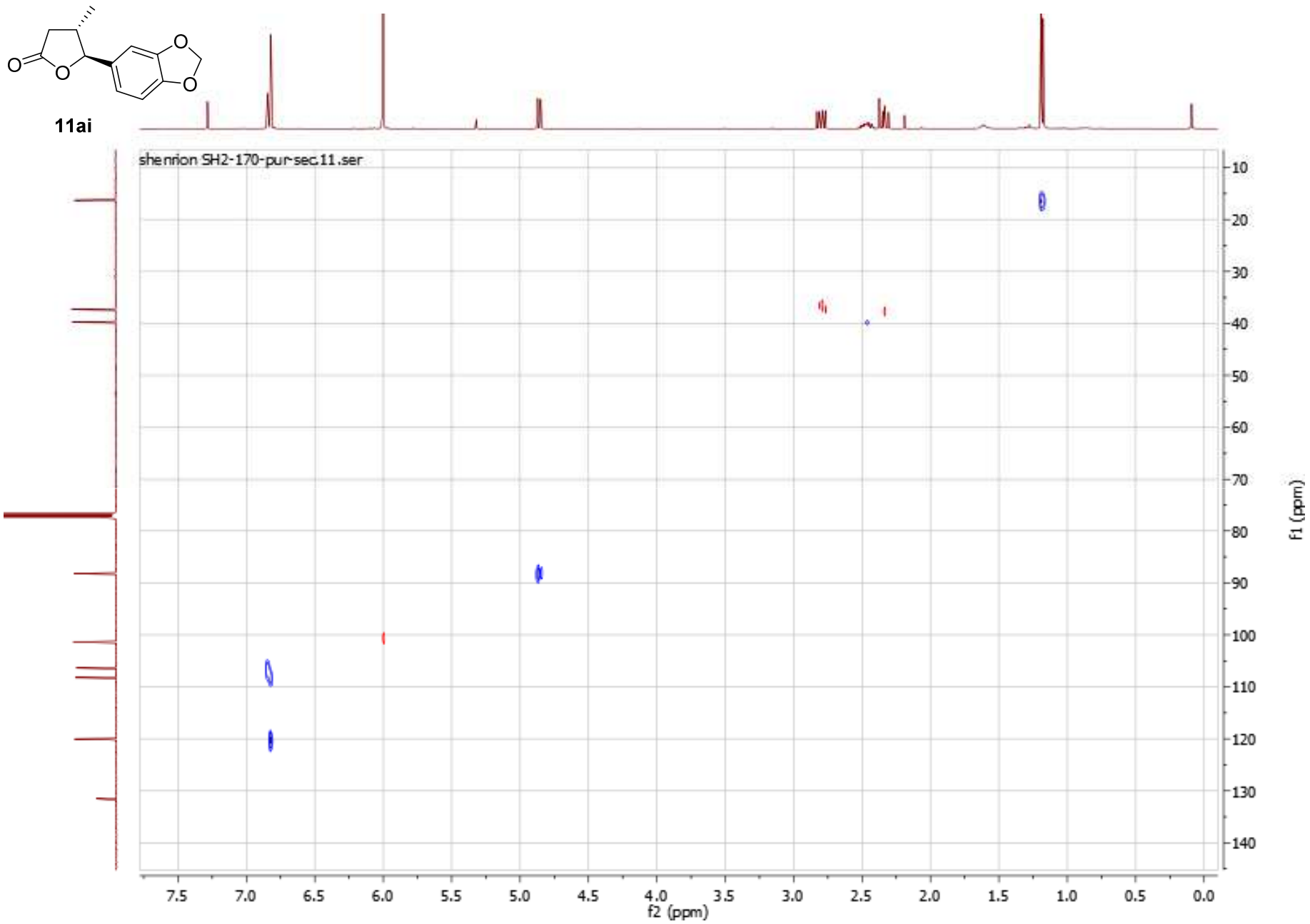

shenrion SH3
076-pur.13.fid
149.45
130.10
118.82
110.93
108.87
88.31
56.00
39.74
37.42
26.91
16.35
OMe
OMe
O
O
11ah
1H NMR (CDCl3)
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

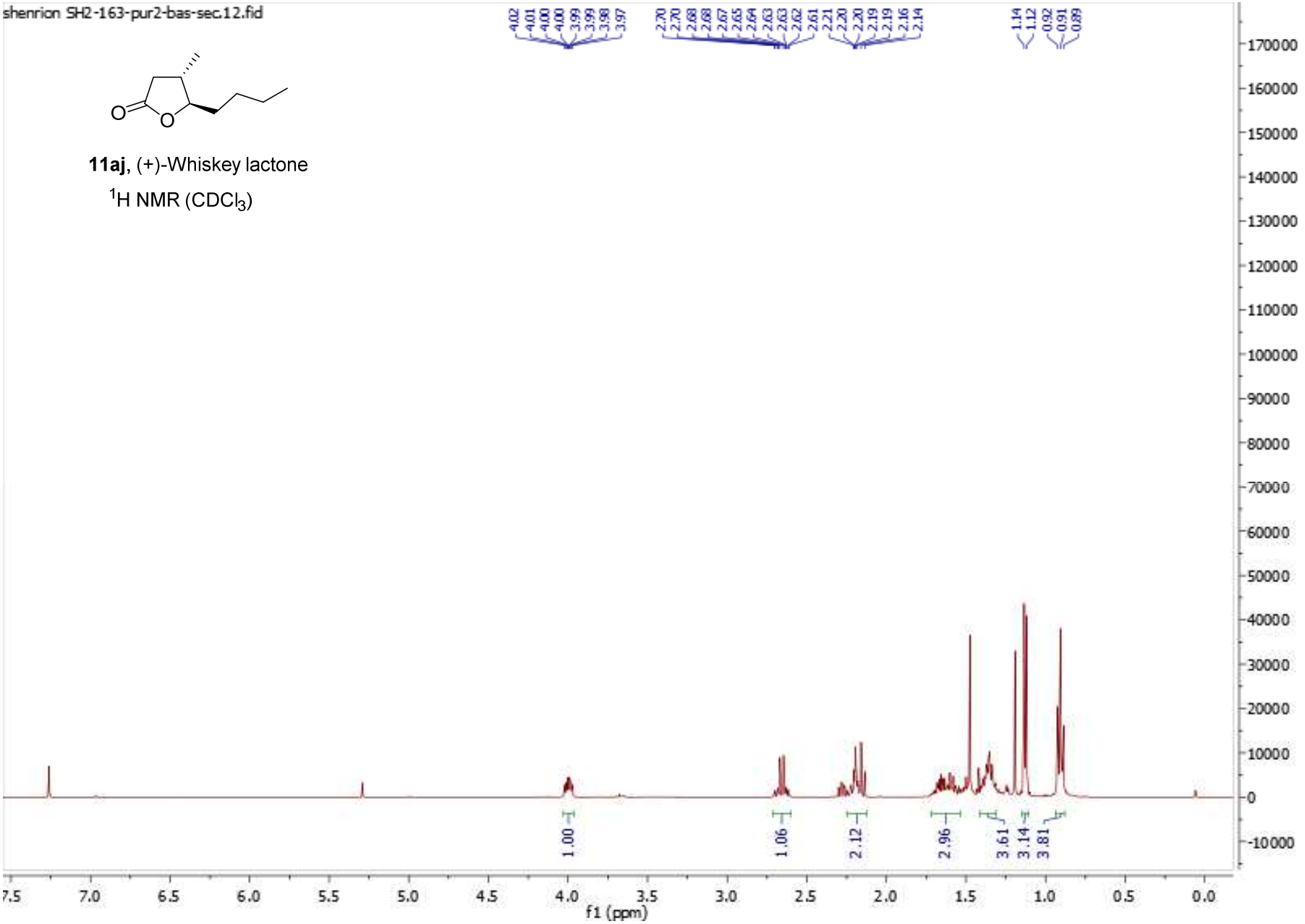


11ai

^{1}H NMR ($CDCl_3$)

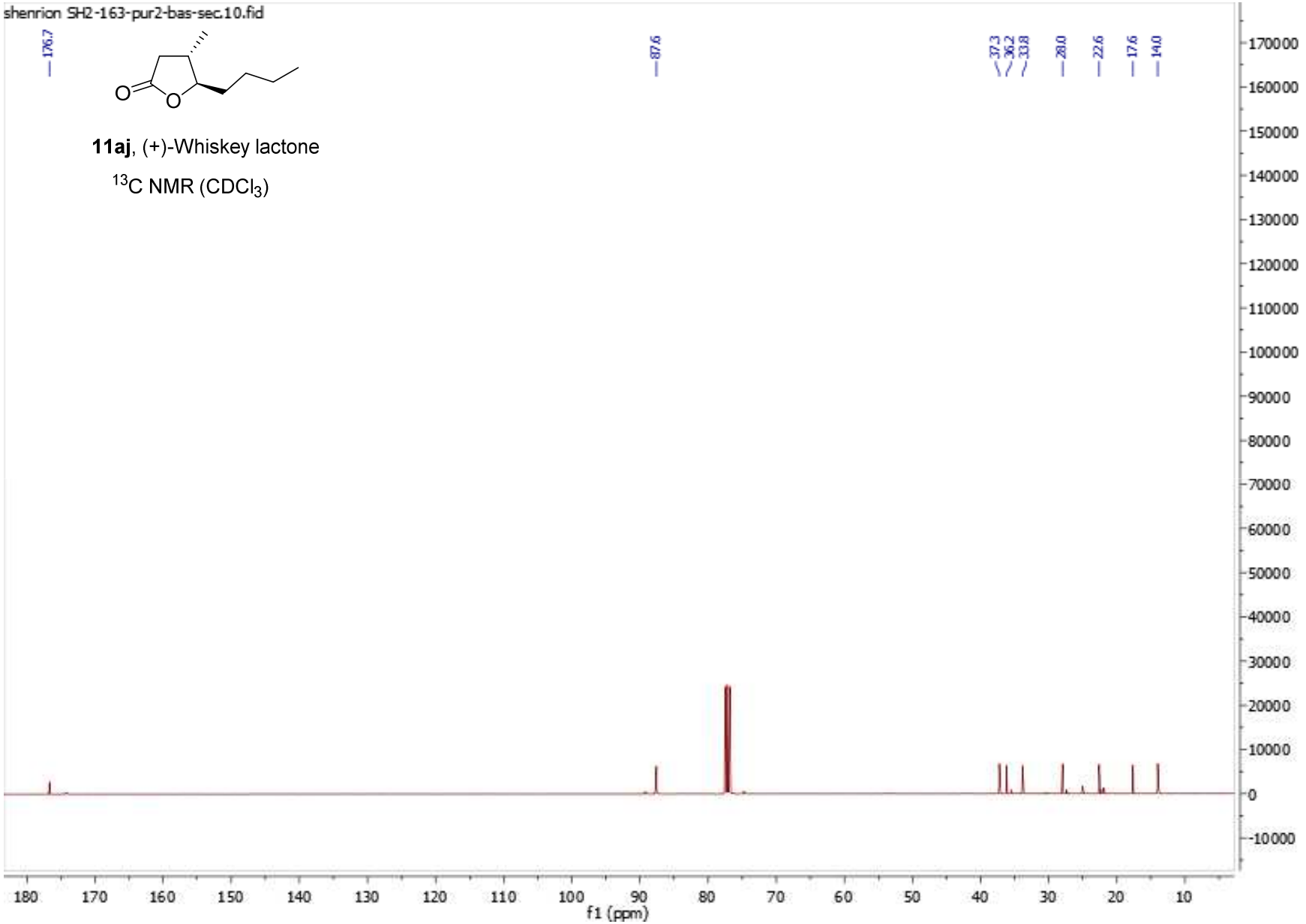

shenrigin SH2-170-pur-sec.10.fid
176.8
148.3
148.2
131.7
120.2
108.4
106.5
101.5
88.4
39.9
37.5
16.5
O
O
O
O
11ai
13C NMR (CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

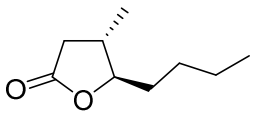

11ai
shenrion SH2-170-pur-sec.11.ser
f2 (ppm)
f1 (ppm)



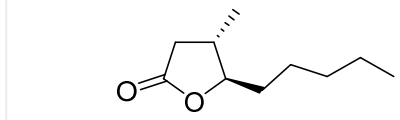
11aj, (+)-Whiskey lactone

^{1}H NMR ($CDCl_3$)


shenrion SH2-163-pur2-bas-sec.10.fid
176.7
87.6
37.3
36.2
33.8
28.0
22.6
17.6
14.0
O
O
11aj, (+)-Whiskey lactone
13C NMR (CDCl3)
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

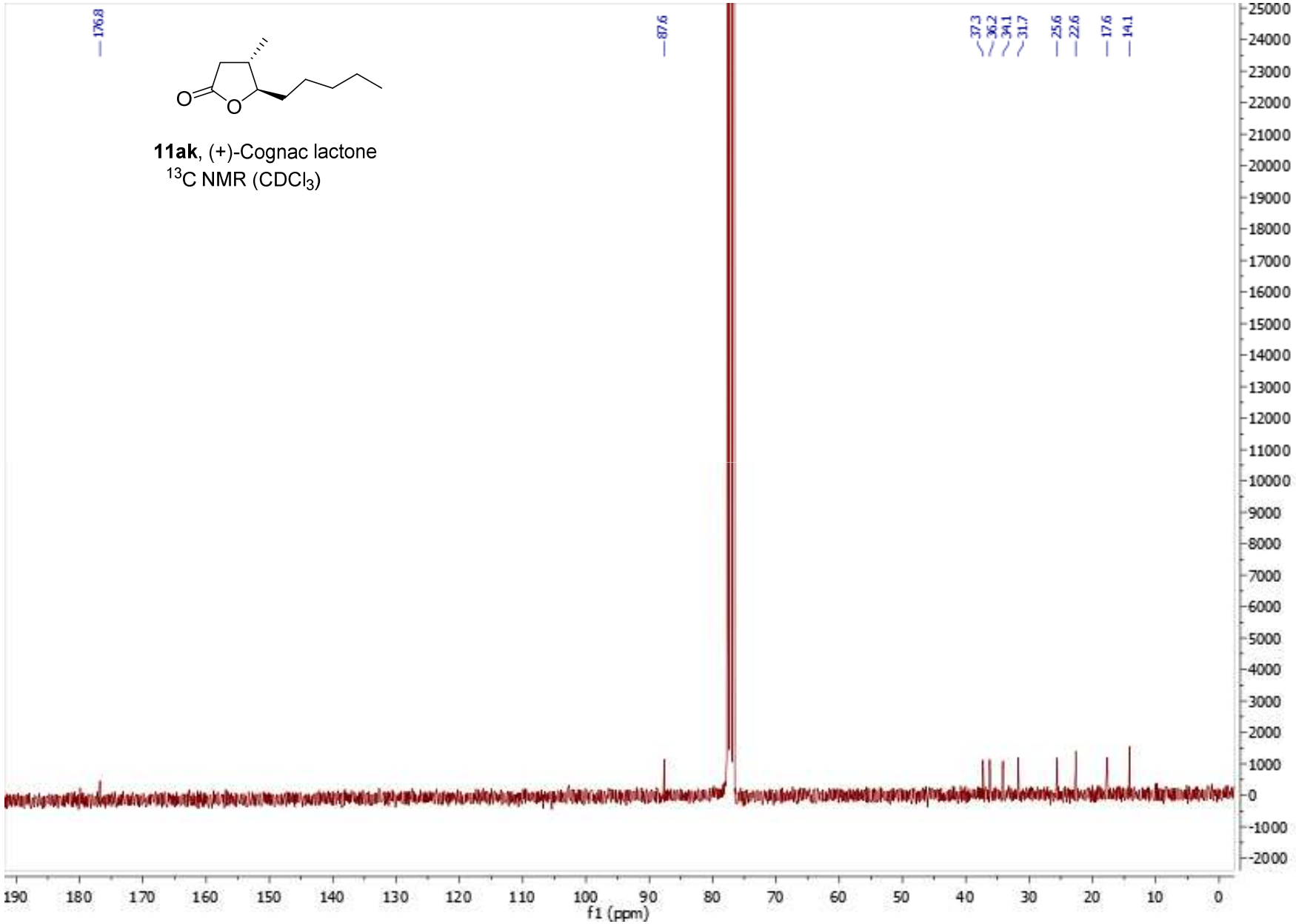


11aj, (+)-Whiskey lactone



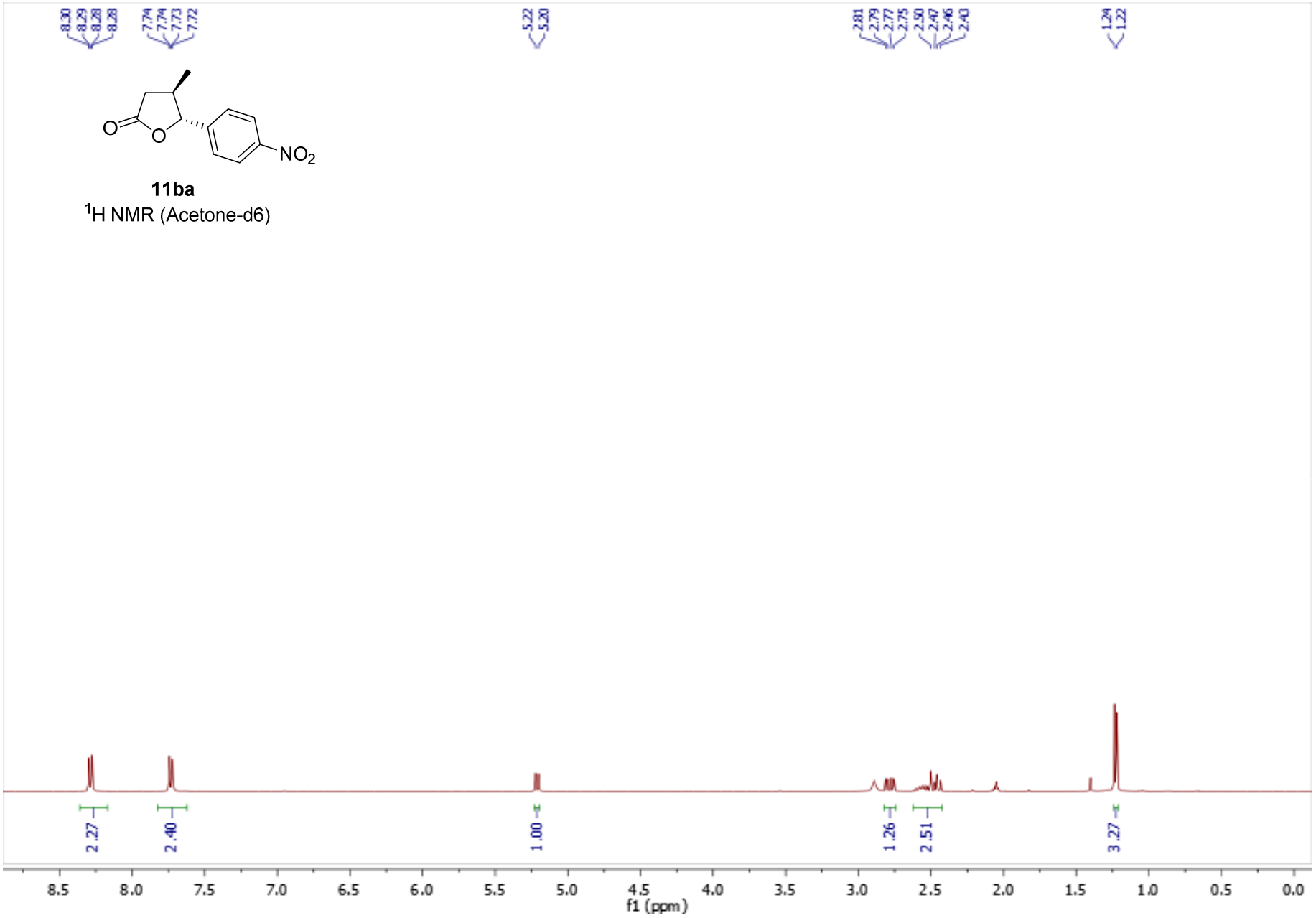
11ak, (+)-Cognac lactone

^{1}H NMR ($CDCl_3$)



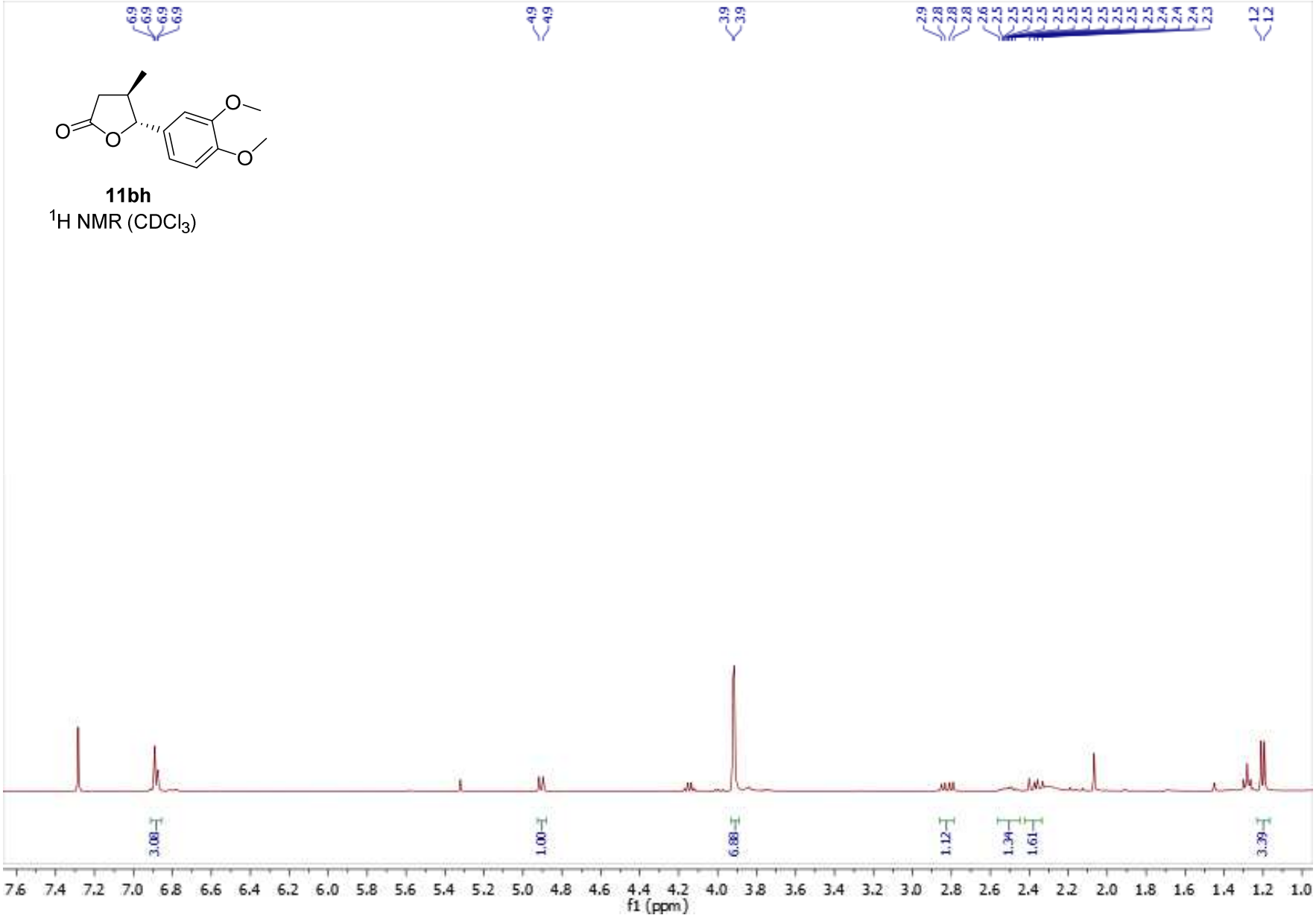
11ak, (+)-Cognac lactone

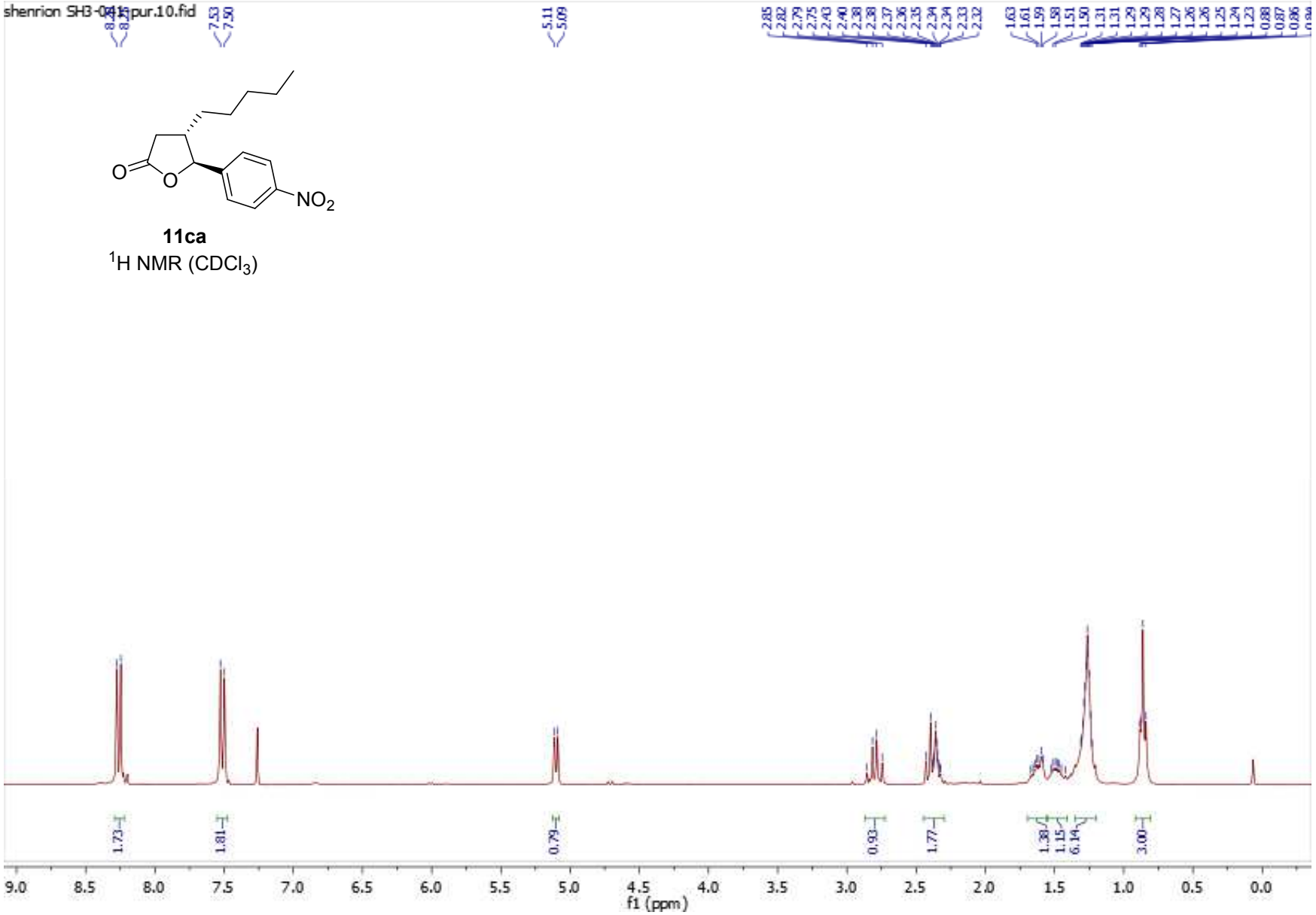
^{13}C NMR ($CDCl_3$)

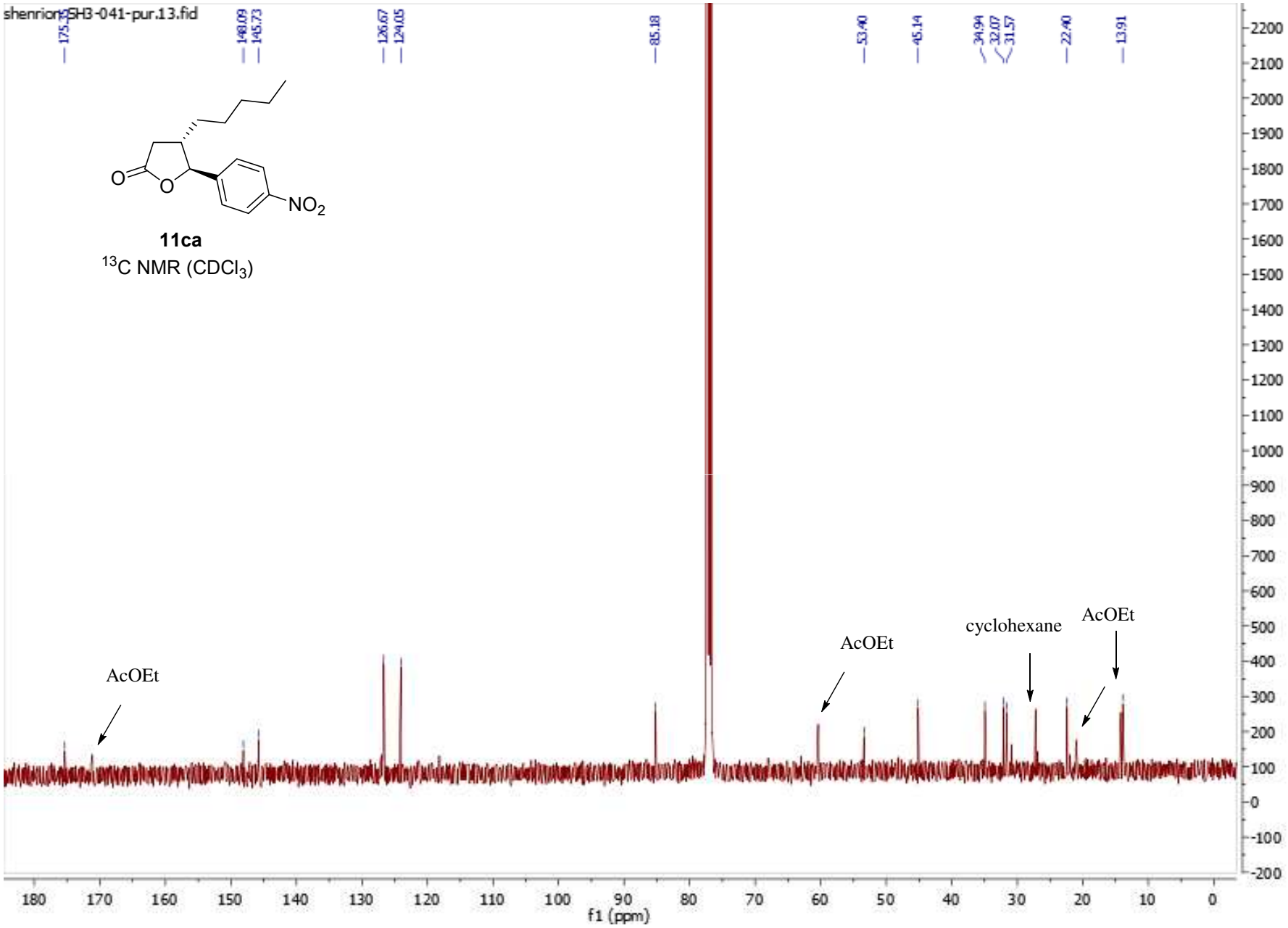


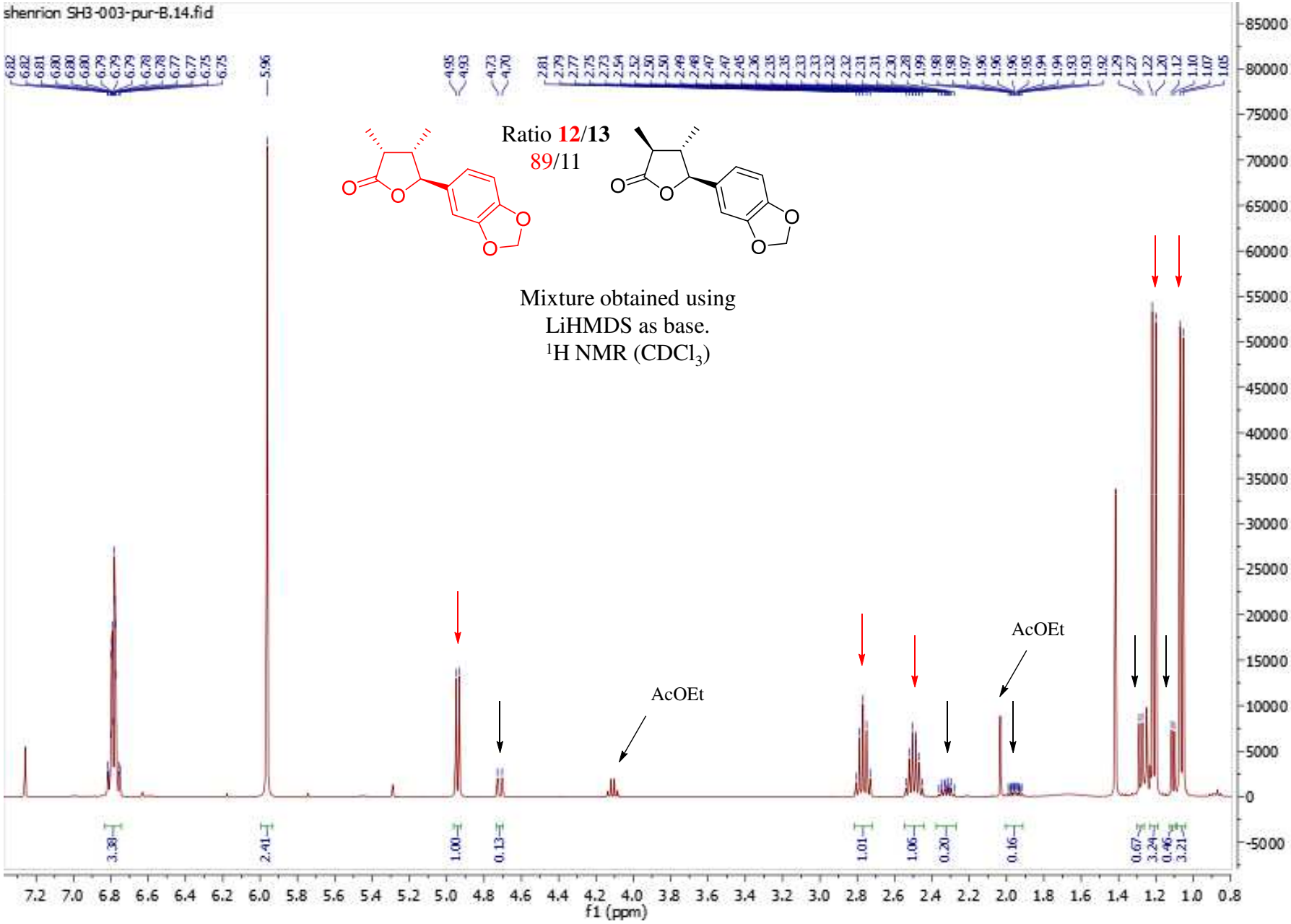
11ba

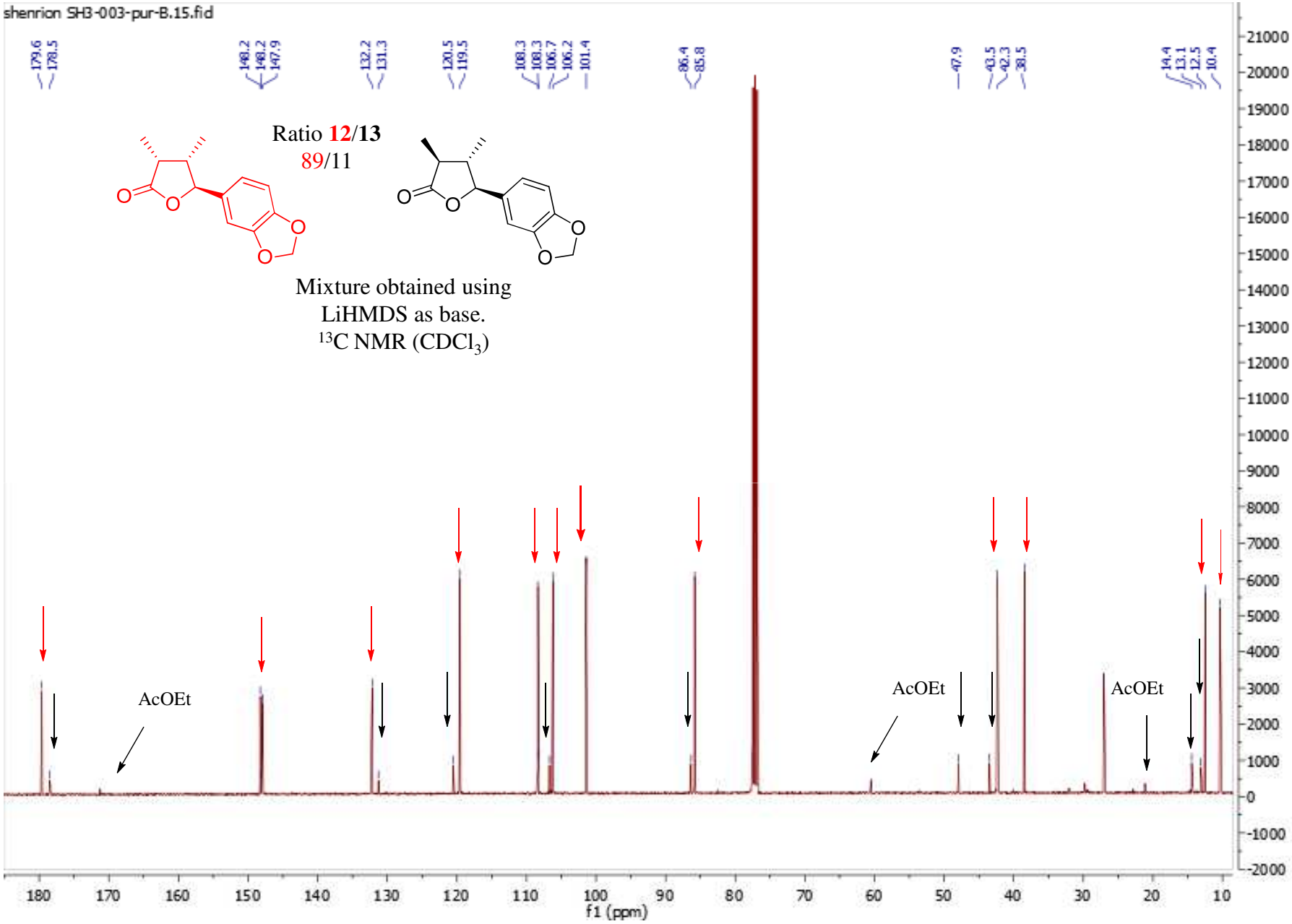
^{1}H NMR (Acetone-d6)

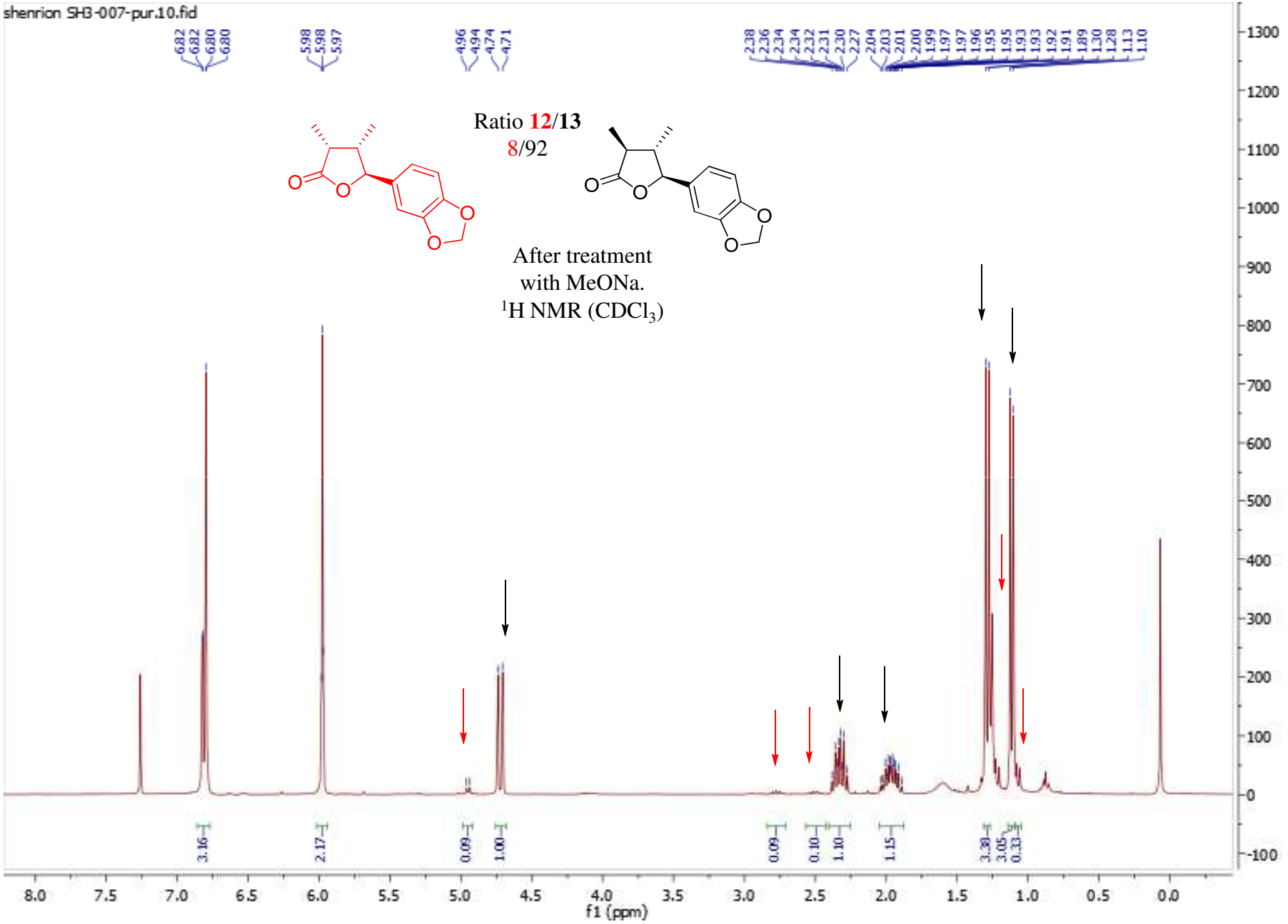

6.9
6.9
6.9
6.9
4.9
4.9
3.9
3.9
2.9
2.8
2.8
2.8
2.6
2.5
2.5
2.5
2.5
2.5
2.5
2.5
2.5
2.5
2.5
2.4
2.4
2.4
2.3
1.2
1.2
O
O
O
O
11bh
1H NMR (CDCl3)
3.00
1.00
6.88
1.12
1.34
1.61
3.39
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)

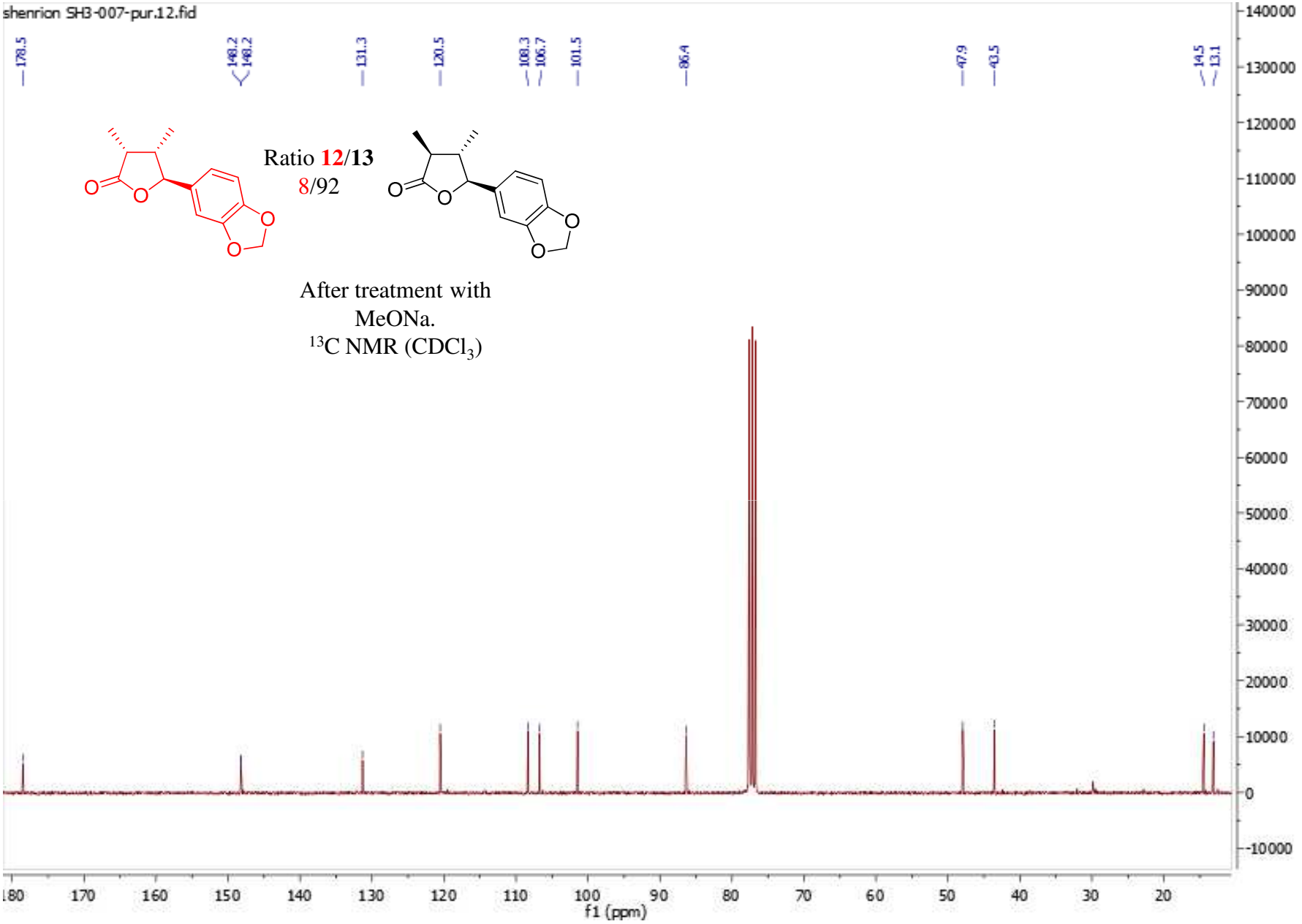

shenrion SH3-041qpur.10.fid
O
O
NO2
11ca
1H NMR (CDCl3)
f1 (ppm)

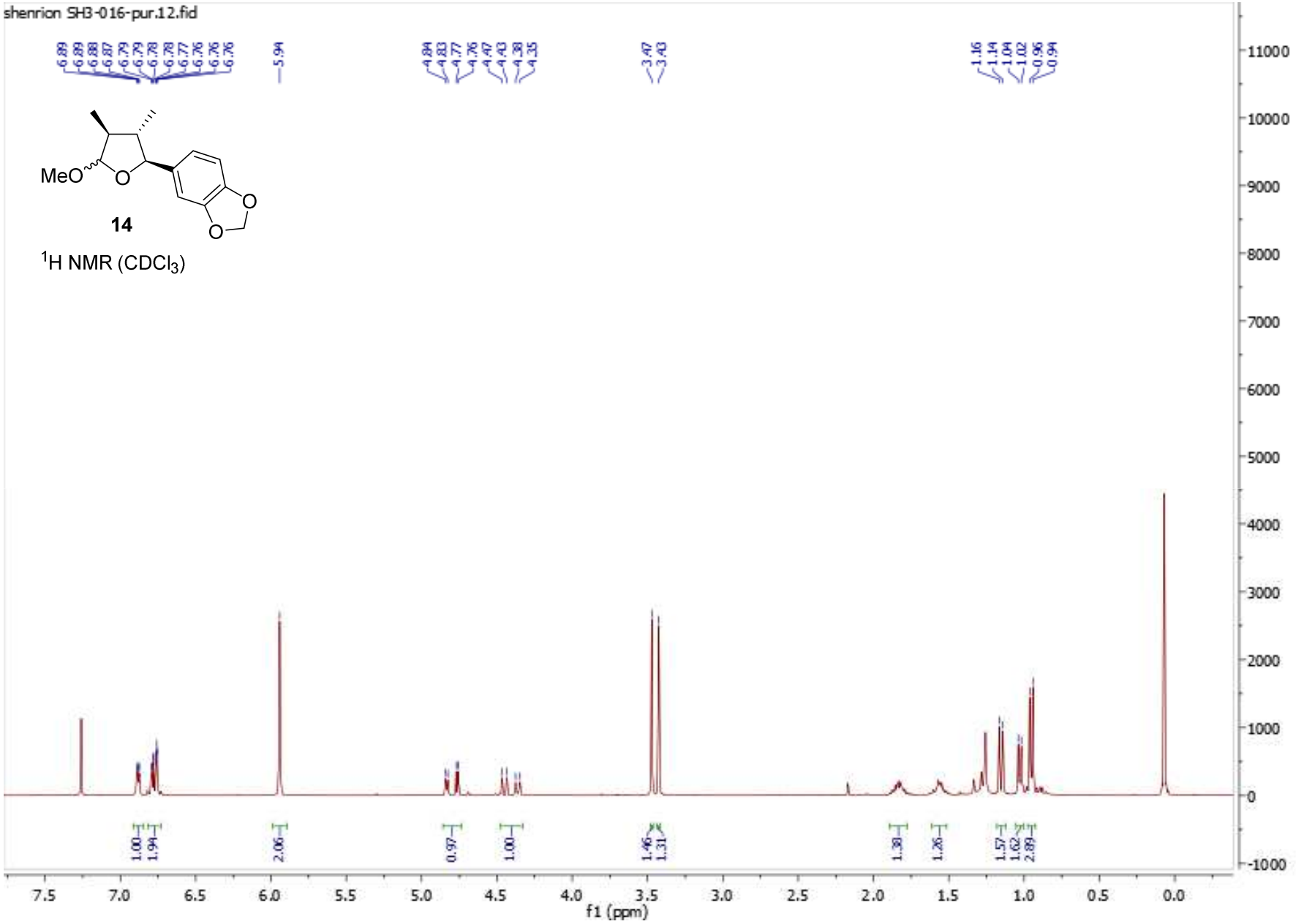

shenrion-SH3-041-pur.13.fid
175.35
148.09
145.73
126.67
124.05
85.18
53.40
45.14
34.94
32.07
31.57
22.40
13.91
O
O
NO2
11ca
13C NMR (CDCl3)
AcOEt
AcOEt
cyclohexane
AcOEt
f1 (ppm)

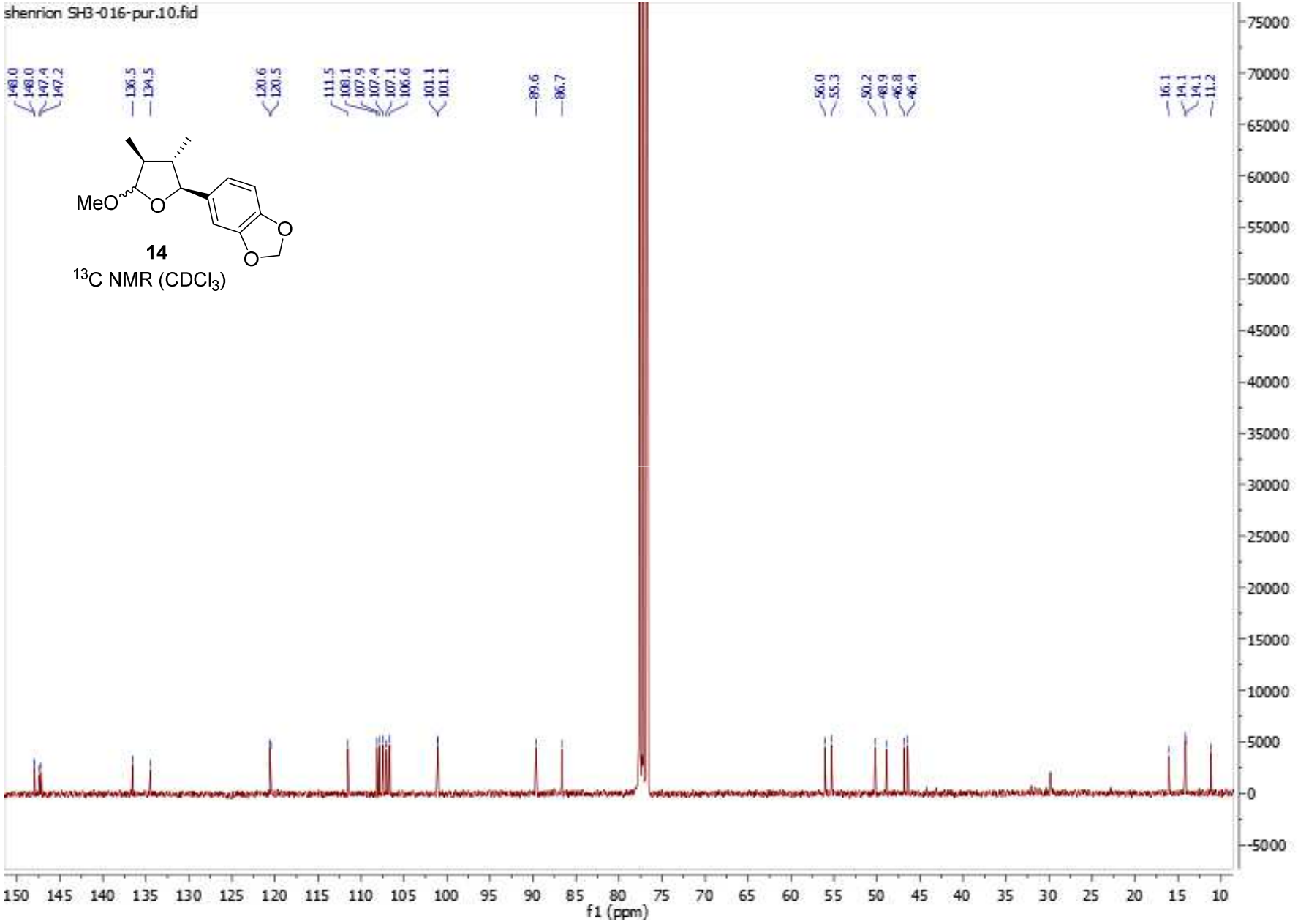

shenrion SH3-003-pur-B.14.fid
Ratio 12/13
89/11
Mixture obtained using
LiHMDS as base.
^{1}H NMR ($CDCl_3$)
AcOEt
AcOEt
f1 (ppm)

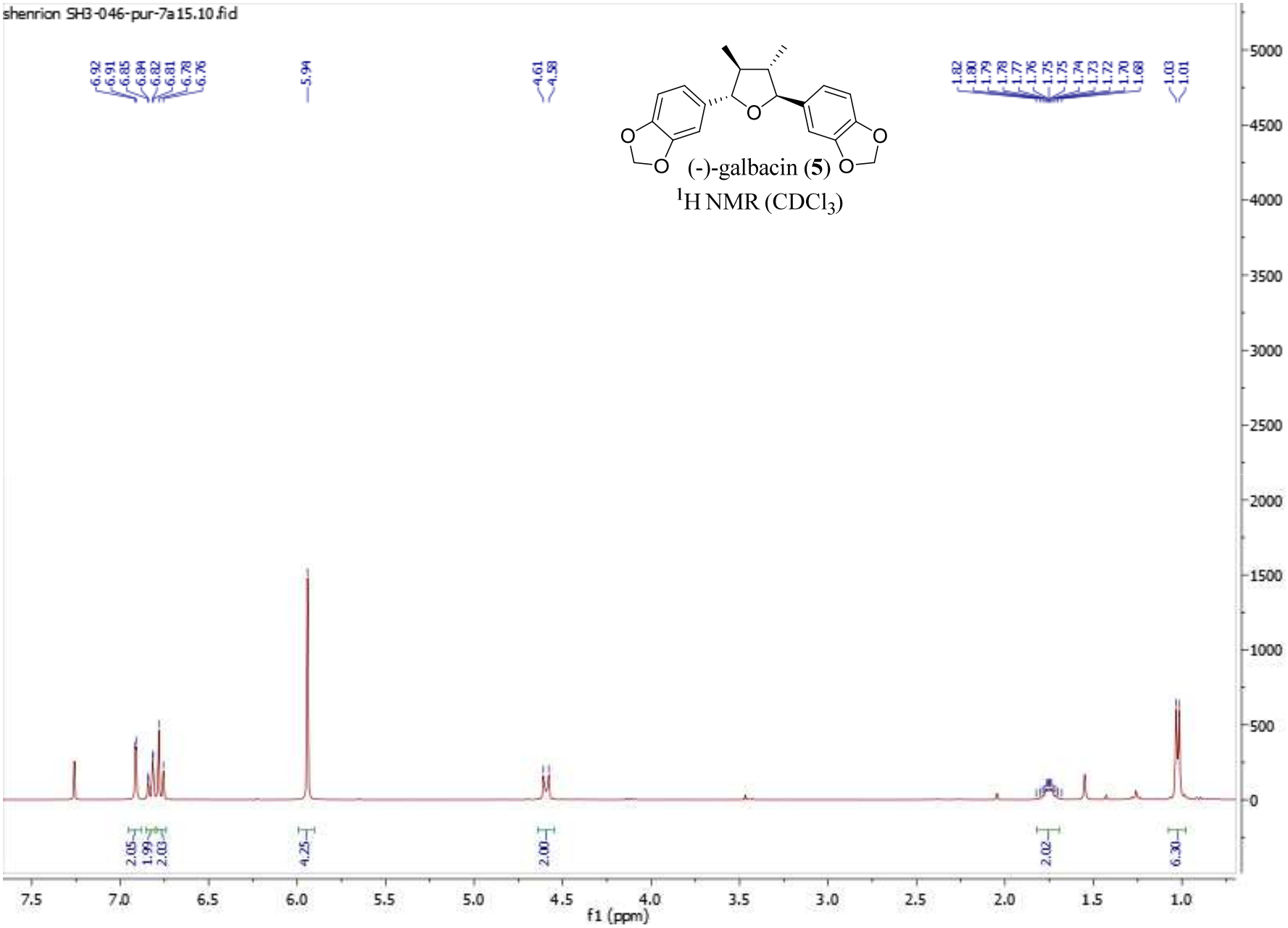

shenrion SH3-003-pur-B.15.fid
Ratio 12/13
89/11
Mixture obtained using
LiHMDS as base.
^{13}C NMR ($CDCl_3$)
AcOEt
AcOEt
AcOEt
f1 (ppm)

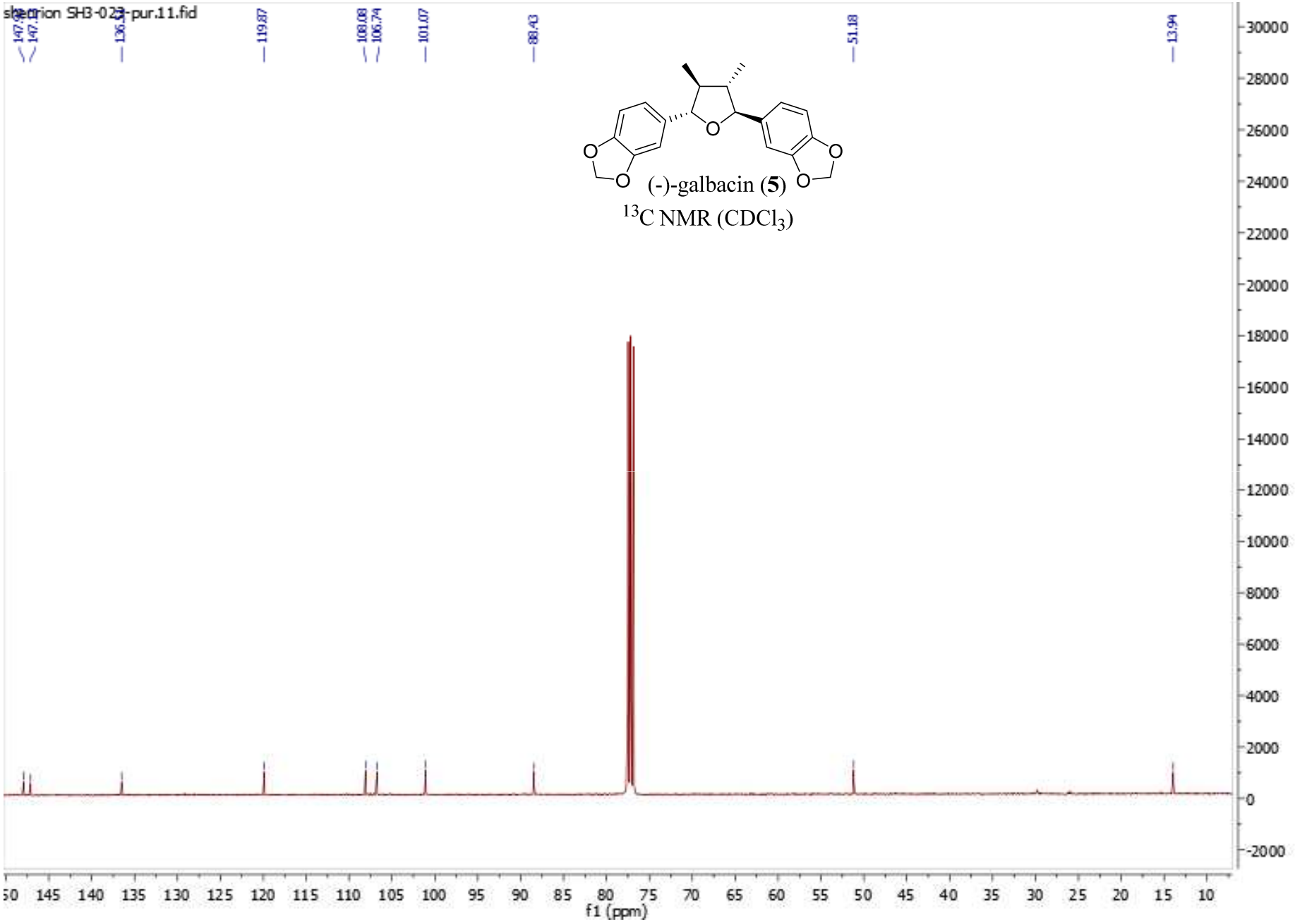

shenrion SH3-007-pur.10.fid
Ratio 12/13
8/92
After treatment
with MeONa.
^{1}H NMR ($CDCl_3$)
f1 (ppm)

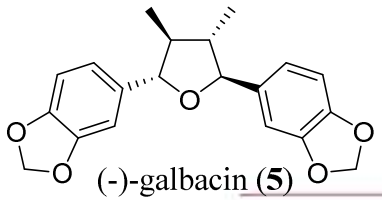

shenrion SH3-007-pur.12.fid
178.5
148.2
148.2
131.3
120.5
108.3
106.7
101.5
86.4
47.9
43.5
14.5
13.1
Ratio 12/13
8/92
After treatment with
MeONa.
13C NMR (CDCl3)
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


shenrion SH3-016-pur.12.fid
6.89
6.89
6.88
6.87
6.79
6.79
6.78
6.78
6.77
6.76
6.76
6.76
5.94
4.84
4.83
4.77
4.76
4.47
4.43
4.38
4.35
3.47
3.43
1.16
1.14
1.04
1.02
0.96
0.94
MeO
O
O
O
14
1H NMR (CDCl3)
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.00
1.94
2.06
0.97
1.00
1.46
1.31
1.30
1.26
1.57
1.62
2.89
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

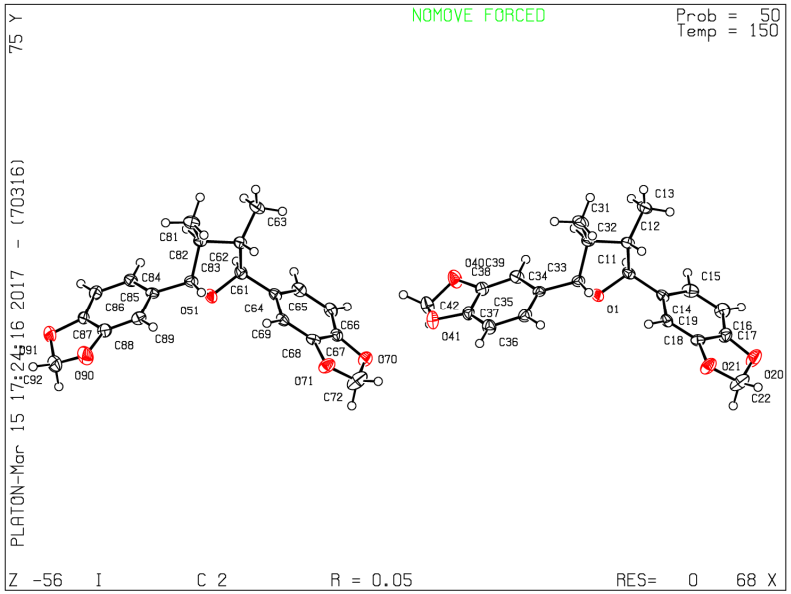

shenrion SH3-016-pur.10.fid
148.0
148.0
147.4
147.2
136.5
134.5
120.6
120.5
111.5
108.1
107.9
107.4
107.1
106.6
101.1
101.1
89.6
86.7
56.0
55.3
50.2
46.9
46.8
46.4
16.1
14.1
14.1
11.2
MeO
O
O
O
14
^{13}C NMR ($CDCl_3$)
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)


shenrion SH3-046-pur-7a15.10.fid
6.92
6.91
6.85
6.84
6.82
6.81
6.78
6.76
5.94
4.61
4.58
1.82
1.80
1.79
1.78
1.77
1.76
1.75
1.75
1.74
1.73
1.72
1.70
1.68
1.03
1.01
(-)-galbacin (5)
1H NMR (CDCl3)
2.05
1.99
2.03
4.25
2.00
2.02
6.30
f1 (ppm)


sheerion SH3-023-pur.11.fid
147.87
147.74
136.23
119.87
108.08
106.74
101.07
88.43
51.18
13.94
(-)-galbacin (5)
13C NMR (CDCl3)
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
50 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)



(-)-galbacin (**5**)



ORTEP plot of the crystal structure of **5** (at 50% probability level)

Crystal structure determination: The data were collected using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). The structure was solved by dual-space algorithm using the *SHELXT* program [1], and then refined with full-matrix least-square methods based on F^2 (*SHELXL*) [2]. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions.

Table xxx. Selected crystal parameters and refinement metrics

Empirical formula	C20 H20 O5
Formula weight	340.36
Temperature	150 K
Wavelength	0.71073 Å
Crystal system, space	groupmonoclinic, C 2
Unit cell dimensions	a = 17.823(2) Å, alpha = 90 °
	b = 6.9975(7) Å, beta = 100.799(5) °
	c = 27.834(4) Å, gamma = 90 °
Volume	3409.9(7) Å3
Z, Calculated density	8, 1.326 (g.cm-3)
Absorption coefficient	0.095 mm-1
F(000)	1440
Crystal size	0.550 x 0.080 x 0.050 mm
Crystal color	colourless

Theta range for data collection	2.980 to 27.485 °
h_min, h_max	-22, 23
k_min, k_max	-8, 9
l_min, l_max	-36, 36
Reflections collected / unique	18156 / 7721 [R(int) = 0.0510]
Reflections [I>2sigma(I)]	5875
Completeness to theta_max	0.997
Absorption correction type	multi-scan
Max. and min. transmission	0.995 , 0.903
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7721 / 1 / 455
Goodness-of-fit	1.024
Final R indices [I>2sigma(I)]	R1= 0.0468, wR2= 0.1010
R indices (all data)	R1= 0.0723, wR2= 0.1107
Largest diff. peak and hole	0.180 and -0.233e.Å-3

VIII. Computational data analysis regarding the methylation step

The alkylation of lithium enolate derived from lactone **11ai** with MeI was studied using density functional theory (DFT). B3LYP1 hybrid DFT functional was used for geometry optimizations. The 6-31+G** basis set was applied to all atoms except for iodine, for which the LANL2DZ2 basis set was used. The combination of the B3LYP with the LANL2DZ basis set has been shown to effectively model the geometries and energies of iodo compounds.3 Frequency calculations were performed to determine the nature of the stationary points. Gibbs free energies were computed at -20 ° C (253.15 K) and 1 atm. Intrinsic reaction coordinates (IRCs) were computed to verify the connectivity between reactants, TSs and products.4 The structures of reactants and products were obtained by the optimization of the last structures on both sides of the IRC calculations. All computations were carried out with the Gaussian 09 suite of programs. The profile reaction for the alkylation of lithium enolate **11aiLi** with MeI is shown in the Figure S1. The reactive-complex **11aiLi+MeI** undergoes *anti* and *syn* attack through the transition structures **TS-*anti*** and **TS-*syn*** yielding the products **P-12+LiI** and **P-13+LiI**, respectively. The formation of the products is exergonic and **P-13+LiI** is more stable than **P-12+LiI** by 1.0 kcal/mol.

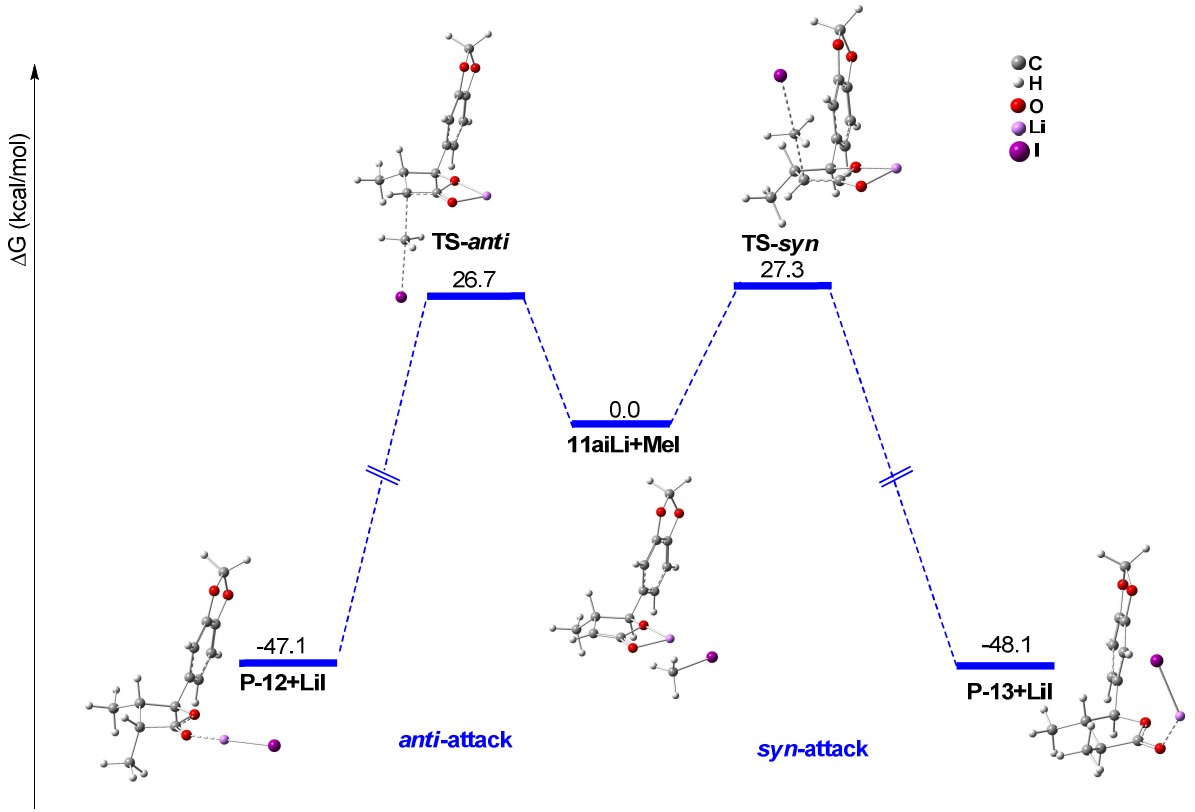


Figure S1. Free energy profile for the reaction of the lithium enolate **11aiLi** with MeI. Optimized geometries of the stationary points are shown.

TS-*anti* is 0.6 kcal/mol more favorable than **TS-*syn*** in Gibbs free energy which correspond to the product ratio *anti*:*syn* = 76:24,6 in good agreement with the experimental result (Figure S2). The Newman projections from the direction along the C3-C4 bond show that **TS-*anti*** has a staggered arrangement, while **TS-*syn*** has a nearly eclipsed arrangement. In **TS-*syn*** there is a small repulsive interaction between H on the incoming methyl group and H on the bulky substituent at C5 which are separated by 2.37 Å, less than the sum of their van der Waals radii (2.4 Å). In **TS-*anti*** there is also a contact between H on methyl iodine and H on the methyl group at C4 that is slightly larger than the sum of the Van der Waal radii.

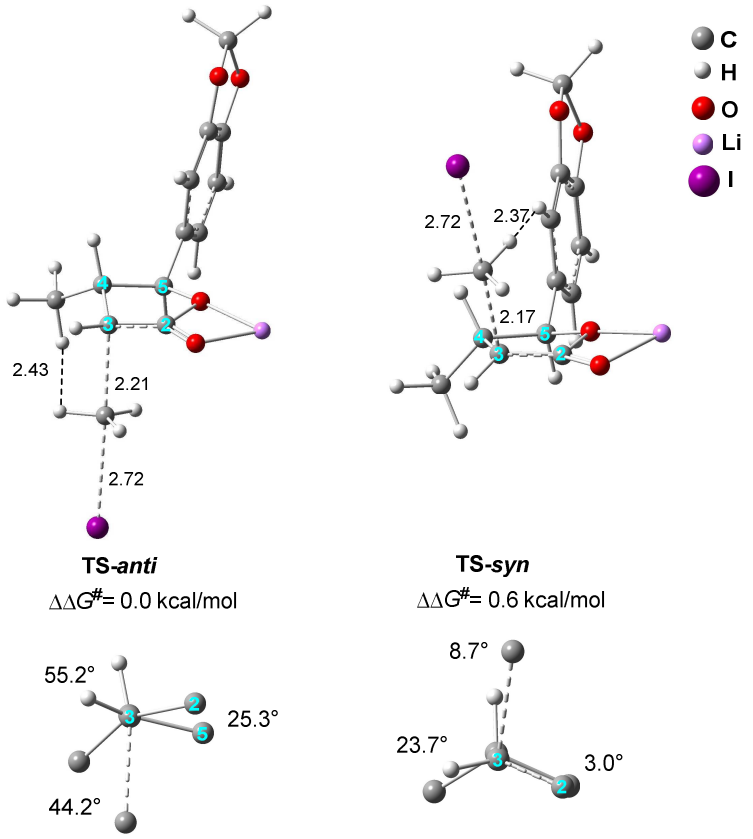


Figure S2. Transition structures for the *anti*- and *syn*-attacks of MeI on the lithium enolate derived from lactone **11ai**. Selected distances are in Å. DD*G*# is the relative Gibbs free energies. Newman projections are viewed from the direction along the C3-C4 bond.

The results reveal that the alkylation of lithium enolate **11aiLi** with MeI is kinetically controlled and that the experimentally observed selectivity is mainly attributed to torsional effects in the transition structures, although the steric effects are also significant which is consistent with previous theoretical studies.

Cartesian coordinates, absolute electronic energies (including zero-point energy -ZPE- corrections) and free energies calculated at 253.15 K and 1atm of the stationary points. Imaginary frequencies of transition structures.

11aiLi+MeI

C	0.087232	3.150848	0.867487
O	-0.007244	1.116116	-0.208376
C	1.278560	1.672615	-0.578948
C	1.492724	2.883124	0.384845
C	-0.741235	2.128116	0.561679
O	-1.954822	1.765064	0.741960
C	2.189123	4.057298	-0.317097
C	2.338409	0.598136	-0.549622
Li	-1.667960	0.229900	-0.217243
C	-4.883810	0.438948	0.927124
I	-4.073010	-1.211380	-0.289089
C	2.534681	-0.164927	0.626089
C	3.538076	-1.110042	0.605258
C	4.339819	-1.321359	-0.517906
C	4.167167	-0.595315	-1.678475
C	3.141551	0.372576	-1.672485
O	5.222515	-2.349051	-0.265535
O	3.895091	-2.001518	1.594729
C	5.125455	-2.584538	1.145987
H	-0.206258	4.003710	1.464280
H	1.180402	2.053997	-1.604705
H	2.147200	2.564817	1.214232
H	3.181696	3.771322	-0.688122
H	1.589043	4.416963	-1.161245
H	2.323442	4.893680	0.377341
H	-4.052461	1.124713	1.084175
H	-5.242627	-0.014194	1.847498
H	-5.689149	0.875641	0.342401
H	1.916101	-0.016026	1.504491
H	4.784350	-0.767626	-2.553377
H	2.974266	0.962581	-2.569216
H	5.108595	-3.659434	1.334420
H	5.967992	-2.094478	1.655421

Sum of electronic and zero-point Energies = -823.439193 au.
Sum of electronic and thermal Free Energies = -823.481921 au.

TS-*anti*

1 imaginary frequency : -454.15 cm^{-1}

C	2.623079	0.577027	0.495114
H	2.155110	-0.070626	-0.224157
H	3.037717	1.519831	0.179002
H	2.799268	0.220263	1.494823
I	4.940612	-0.647098	-0.230177
O	-0.510955	1.292002	-0.793484
C	-0.802527	0.085188	-0.004737
C	-0.318378	0.448162	1.427085
C	0.728643	1.518001	1.143561
C	0.415295	2.108816	-0.074477
O	0.800187	3.104283	-0.742531
C	0.129502	-0.782551	2.223882
C	-2.247848	-0.305017	-0.166718
Li	-0.084470	2.498626	-2.224779
C	-3.275276	0.607971	0.173210
C	-4.575914	0.173382	0.032419
C	-4.886694	-1.110408	-0.422972
C	-3.904269	-2.017169	-0.765660
C	-2.569629	-1.584639	-0.631849
O	-6.251086	-1.252432	-0.497202
O	-5.738547	0.874003	0.253561
C	-6.789712	-0.100272	0.168649
H	-0.165393	-0.708790	-0.410527
H	-1.161748	0.900322	1.972873
H	1.160407	2.118367	1.935409
H	0.490380	-0.486371	3.214178
H	-0.708886	-1.472459	2.370836
H	0.935467	-1.326236	1.721395
H	-3.055276	1.610011	0.525554
H	-4.148281	-3.010232	-1.125956
H	-1.769196	-2.271756	-0.890909
H	-7.614941	0.305774	-0.418608
H	-7.108057	-0.381584	1.181971

Sum of electronic and zero-point Energies = -823.399020 au.
Sum of electronic and thermal Free Energies = -823.439382 au.

TS-*syn*

1 imaginary frequency : -472.54 cm^{-1}

C	-0.940355	2.559427	0.451563
O	0.658242	2.204150	-1.177175
C	1.406150	2.092128	0.085629
C	0.305860	2.096336	1.193846
C	-0.640398	2.725605	-0.895426
O	-1.254419	3.087715	-1.932838
C	0.706777	2.968763	2.390604
C	2.343108	0.914501	0.032889
Li	0.102657	2.463892	-2.993019
C	1.841680	-0.400407	-0.129278
C	2.762526	-1.426200	-0.155189
C	4.135228	-1.199945	-0.020270
C	4.649370	0.070923	0.138057
C	3.720260	1.130541	0.157140
O	4.807969	-2.392418	-0.113065
O	2.537069	-2.767276	-0.342155
C	3.791204	-3.408609	-0.072525
H	-1.698771	3.172253	0.922836
H	1.995630	3.013495	0.162046
H	0.173830	1.069400	1.562399
H	1.635769	2.608392	2.847766
H	0.850641	4.012917	2.089066
H	-0.071274	2.944824	3.160270
H	0.781782	-0.605971	-0.230692
H	5.715081	0.244432	0.236790
H	4.088877	2.145163	0.279331
H	3.992233	-4.153435	-0.844391
H	3.765017	-3.855853	0.930333
C	-2.218671	0.817423	0.244857
H	-2.932504	1.313476	-0.391222
H	-1.444763	0.211107	-0.192414
H	-2.367567	0.788903	1.311593
I	-3.772817	-1.415114	0.096714

Sum of electronic and zero-point Energies = -823.397849 au.
Sum of electronic and thermal Free Energies = -823.438457 au.

P-12+LiI

C	-0.219266	4.268965	-0.086311
I	-5.030157	-1.187934	-0.109319
O	0.161196	0.989876	-0.387963
C	1.537887	1.518576	-0.529696
C	1.646297	2.552619	0.614811
C	0.186131	3.047037	0.765097
C	-0.597763	1.829602	0.312019
O	-1.785253	1.604287	0.514440
C	2.723306	3.611894	0.383089
C	2.522995	0.383319	-0.526892
Li	-3.159222	0.405615	0.225938
C	2.552317	-0.532618	0.551892
C	3.498499	-1.533349	0.499994
C	4.400369	-1.649881	-0.560806
C	4.389378	-0.771024	-1.625023
C	3.421616	0.252122	-1.590350
O	5.199417	-2.746171	-0.367145
O	3.702519	-2.555720	1.391492
C	4.888657	-3.234389	0.948812
H	-0.000248	4.123837	-1.149348
H	-1.291444	4.456696	0.015962
H	0.316699	5.159303	0.252688
H	1.564065	2.019390	-1.503716
H	1.899493	1.998011	1.527349
H	-0.070112	3.252570	1.809227
H	2.758542	4.320246	1.216988
H	3.708634	3.141976	0.304961
H	2.547985	4.179839	-0.536258
H	1.847374	-0.475925	1.374111
H	5.081167	-0.873777	-2.453294
H	3.374409	0.953944	-2.418074
H	4.695783	-4.308282	0.900752
H	5.718068	-2.999603	1.628319

Sum of electronic and zero-point Energies = -823.514719 au.

Sum of electronic and thermal Free Energies = -823.556966 au.

P-13+LiI

C	-1.593863	2.744183	0.283086
O	-0.409995	1.619956	-1.409591
C	0.612820	2.157278	-0.479611
C	-0.181770	2.425446	0.817189
C	-1.632804	1.914827	-0.985341
O	-2.628778	1.520397	-1.591469
C	0.444822	3.501419	1.702220
C	1.772188	1.204977	-0.391541
Li	-3.071273	-0.272829	-1.582515
C	-2.765066	2.474476	1.229288
I	-2.536177	-2.024013	0.133939
C	1.557878	-0.149543	-0.037040
C	2.678395	-0.947068	0.064058
C	3.968292	-0.458689	-0.163530
C	4.197840	0.855765	-0.516842
C	3.064470	1.683973	-0.632387
O	4.877424	-1.476594	-0.024701
O	2.742943	-2.288641	0.347500
C	4.134245	-2.584127	0.514658
H	-1.622279	3.795943	-0.048267
H	0.945598	3.103368	-0.922504
H	-0.239057	1.483467	1.377892
H	1.456431	3.215524	2.007402
H	0.506170	4.462179	1.176500
H	-0.145284	3.650891	2.611633
H	-3.717204	2.705322	0.743604
H	-2.783496	1.423830	1.535739
H	-2.679653	3.098787	2.123766
H	0.564582	-0.560452	0.122802
H	5.198599	1.226861	-0.707038
H	3.203773	2.723153	-0.917124
H	4.383453	-3.491129	-0.039472
H	4.362136	-2.685001	1.584673

Sum of electronic and zero-point Energies = -823.517336 au.

Sum of electronic and thermal Free Energies = -823.568879 au.

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